博士論文

縮環インドール骨格を構築する
不斉分子内 5 員環形成反応と分子間 7 員環形成反応の開発

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略語表

1,2-DCE: 1,2-dichloroethane
Ac: acetyl
aq.: aqueous
Ar: Aryl
ATR: attenuated total reflection
BARF: tetrakis[3,5-bis(trifluoromethyl) phenyl]borate
BHT: 2,4-di-*tert*-butyl-4-methylphenol
BINOL: 1,1'-bi-2-naphthol
Bn: benzyl
BOX: bisoxazoline
br: broad
calcd: calculated
CAN: ammonium cerium nitrate
CMHP: cumene hydroperoxide
CPME: cyclopentyl methyl ether
℃: degrees Celsius
d: day(s)
d: doublet (spectral)
DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene
DMA: *N,N*-dimethylacetamide
DMDO: dimethyldioxirane
DMF: *N,N*-dimethylformamide
dr: diastereomeric ratio
E: entgegen
EDG: electron-donating group
ee: enantiomeric excess
e.g.: exempli gratia
equiv.: equivalent
ESI: electrospray ionization
Et: ethyl
EWG: electron withdrawing group
g: gram(s)
h: hour(s)
HPLC: high performance liquid chromatography
HRMS: high resolution mass spectrometry
Hz: hertz
ImQ: bis-imino bis-quinoline
*i*Pr: isopropyl
IR: infrared
L: liter(s)
L.A.: Lewis acid
LG: leaving group
LHMDS: lithium hexamethyldisilazide
m: milli
m: multiplet (spectral)
m-: meta
μ: micro
M: molar (moles per liter)
*m*CPBA: 3-chloroperoxybenzoic acid
Me: methyl
min: minute(s)
MOM: methoxymethyl
MS: molecular sieves
MS: mass spectrometry
MVK: methyl vinyl ketone
m/*z*: mass-to-charge ratio
N: normality
NBS: *N*-bromosuccinimide
*n*Bu: normal butyl
nm: nanometer
NMR: nuclear magnetic resonance
NOE: nuclear Overhauser effect
NOESY: nuclear Overhauser effect spectroscopy
N.R.; no reaction
o-: ortho

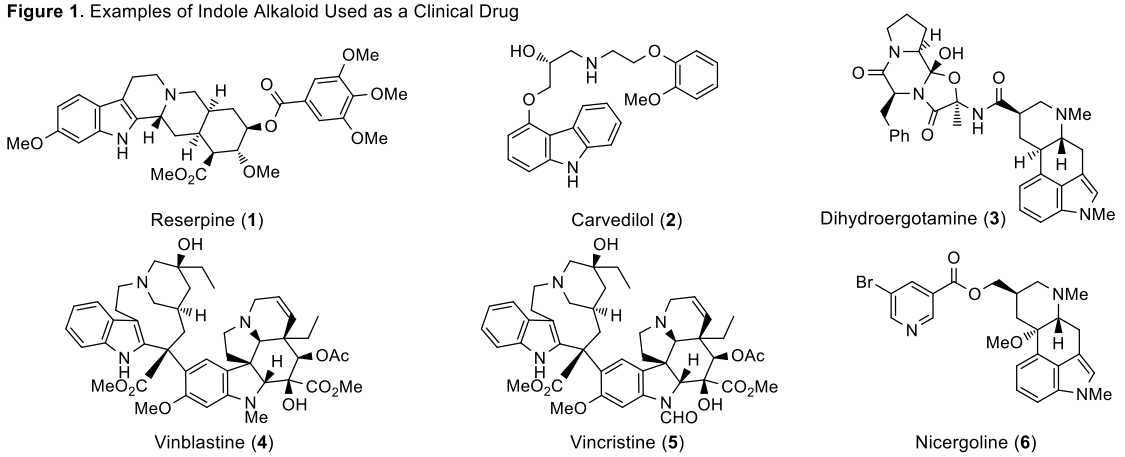
p-: para
PG: protective group
Ph: phenyl
PIDA: iodobenzene diacetate
PMP: *p*-methoxyphenyl
ppm: pert(s) per million
PTSA: *p*-toluenesulfonic acid
q: quartet (spectral)
quant.: quantitative yield
R: rectus
recov.: recovery of starting material
rt: room temperature
S (*Si*): sinister
s: singlet (spectral)
sat.: saturated
solv.: solvent
t: triplet (spectral)
*t*Bu: tertiary butyl
temp.: temperature
Tf: trifluoromethanesulfonyl
THF: tetrahydrofuran
TIPS: triisopropylsilyl
TLC: thin layer chromatography
TMP: 2,4,6-trimethoxyphenyl
tR: retention time
Ts: *p*-toluenesulfonyl
Z: zusammen

第一章；インドールアルカロイド

第一節；インドールアルカロイドとその有用性

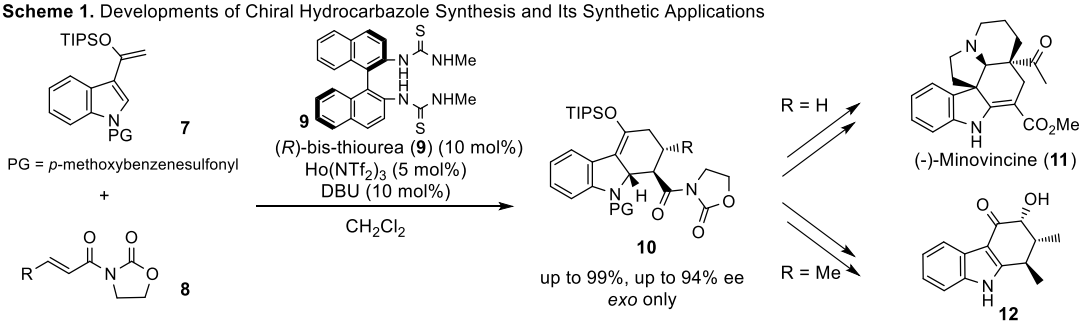
インドールアルカロイドはトリプトファンから生合成されるアルカロイドの総称であり、これらインドールアルカロイドの多くは多様な縮環インドール骨格を持っている。縮環インドールアルカロイドは様々な生物活性を示す化合物群であることが知られており、降圧薬であるレセルピン(**1**)や抗癌剤であるビンブラスチン(**4**)のように、医薬品としても利用されている(Figure 1)。[1] これら医薬品は天然インドールアルカロイドを利用しているもののみならず、ジヒドロエルゴタミン(**3**)のように天然物の誘導体を利用しているものもある。そのため、創薬研究においては天然インドールアルカロイドおよびその誘導体を利用した構造活性相関研究が盛んに行われている。

Figure 1. Examples of Indole Alkaloid Used as a Clinical Drug



天然インドールアルカロイドや上記の医薬品の構造を見ると、多くの縮環インドールアルカロイドがカルバゾール骨格を持っていることが分かる。そのため、様々な研究グループによりカルバゾール骨格の合成法が報告されてきた。[2] 著者の所属研究室でも独自に開発した不斉触媒を利用した光学活性ヒドロカルバゾール合成を達成しており、また、合成したヒドロカルバゾールを用いた天然物合成も行ってきた(Scheme 1)。[3] このことからも、縮環インドール合成法の開発はインドールアルカロイドの合成、ひいては創薬研究の加速につながることが期待できる。

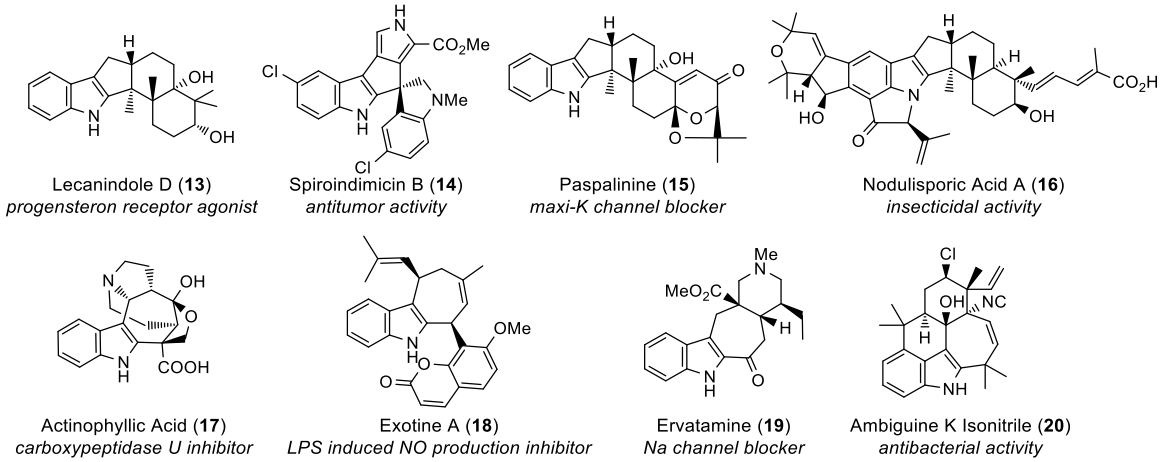
Scheme 1. Developments of Chiral Hydrocarbazole Synthesis and Its Synthetic Applications



第二節；シクロペンタ・シクロヘプタ[*b*]インドール骨格

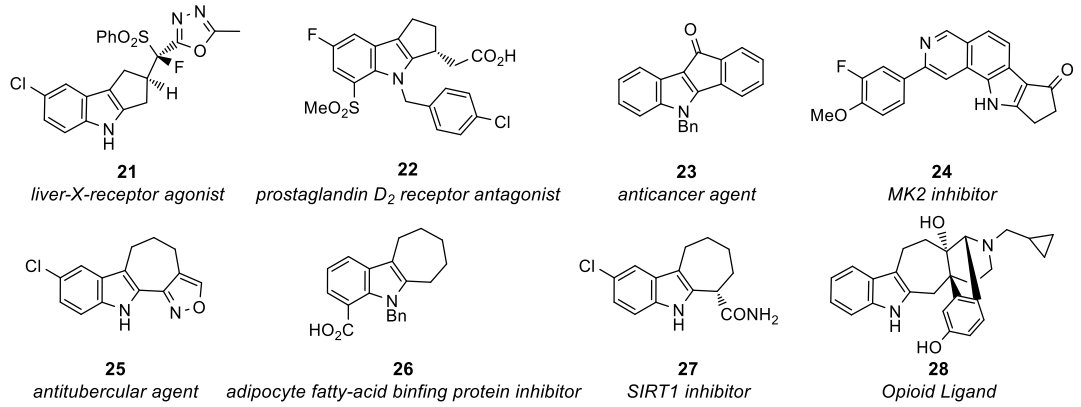
インドールアルカロイドにはカルバゾール骨格以外にも多様な縮環構造を含む化合物が報告されており、5 および 7 員環縮環インドール骨格を含む化合物も多く知られている。こうした化合物の中には有用な生物活性を示すものが多く存在する(Figure 2)。[4]

Figure 2. Examples of Natural Products Containing 5- or 7-Membered Ring Fused Indole Motif



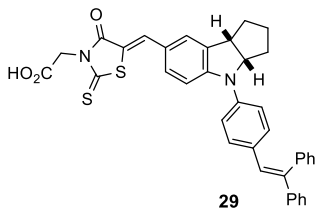
また、天然物のみならず、5 および 7 員環縮環インドール骨格を持つ非天然化合物の中にも魅力的な生物活性を示す化合物が多数報告されてきた(Figure 3)。[5] こうした非天然化合物の中には極めて単純な構造の化合物も含まれており、5 および 7 員環縮環インドール骨格そのものが創薬研究において有用な骨格構造であると考えられる。

Figure 3. Unnatural Biologically Active Compounds



縮環インドールおよびその誘導体の利用は医薬分野のみにとどまらない。例えば **29** のような 5 員環縮環インドリン誘導体は、色素増感太陽電池材料として研究されている(Figure 4)。[6] こうした背景の下、5 および 7 員環縮環インドール骨格の効率的合成法の開発が強く求められている。

Figure 4. Dye-Sensitized Solar Cell

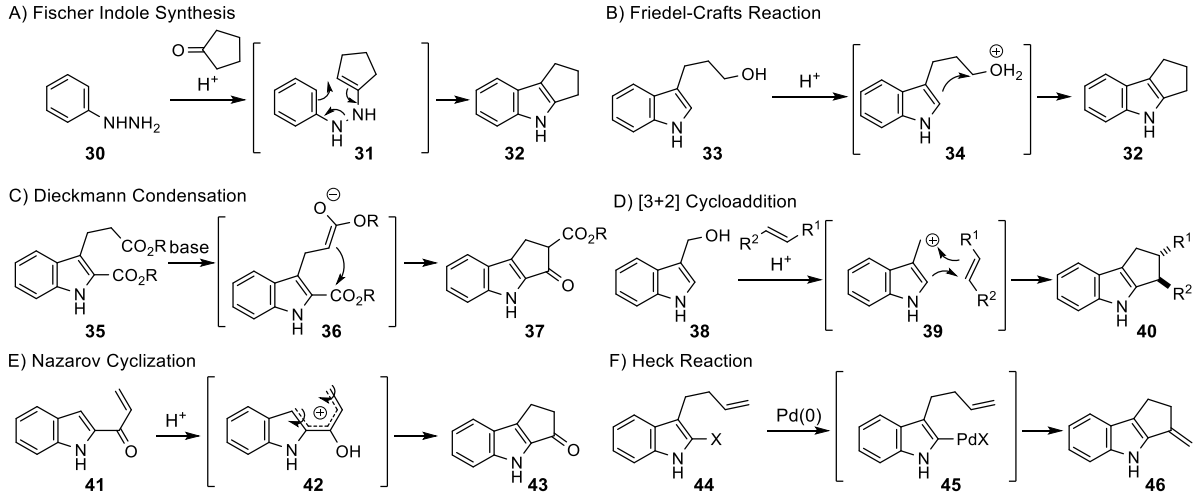


第二章；5 および 7 員環縮環インドールの合成

第一節；5 員環縮環インドール合成

5 員環縮環インドールは Fischer インドール合成法や Friedel-Crafts 反応を利用した合成法を始めとし、様々な手法が報告されてきた(Scheme 2)。[1b,7] 中でも Nazarov 環化を利用した手法は様々な官能基を導入した基質を利用でき、また生成物の構造変換も容易である。そのため、多様な官能基が導入された環構造を有するインドールアルカロイド類の合成に有用な手法であると考えられる。さらに近年、不斉 Nazarov 環化の開発も複数報告されるようになっている。そのため、インドール誘導体を利用したエナンチオ選択的 Nazarov 環化の開発は、光学活性 5 員環縮環インドールアルカロイド類の合成につながり、創薬研究にも活かされることが期待できる。

Scheme 2. Examples of Cyclopenta[*b*]indole Skeleton Synthesis



第二節；Nazarov 環化

Nazarov 環化はジビニルケトン **47** から多置換 5 員環生成物 **50** を与える 4π電子環状反応である(Scheme 3)。[8] また、反応はペンタジエニルカチオン **48** を中間体としており、それ故ペンタジエニルカチオンを生じる様々な前駆体を Nazarov 基質として利用することが可能である(Figure 5)。[9]

Scheme 3. Reaction Mechanism of Nazarov Cyclization

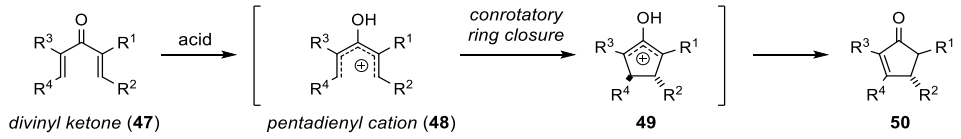
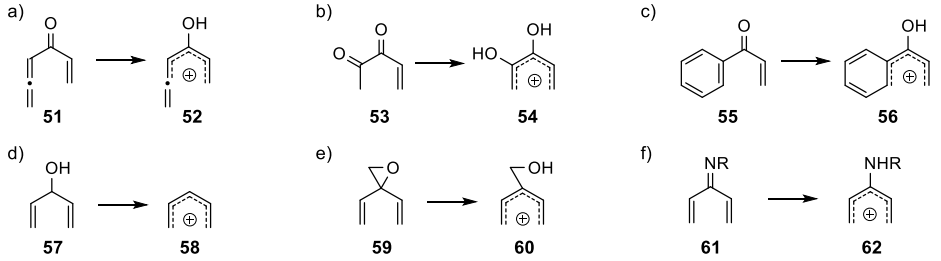
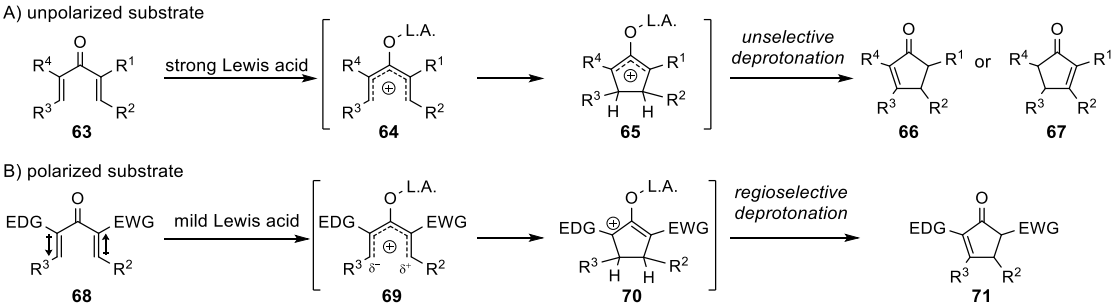


Figure 5. Generation of Pentadienyl Cation from Various Substrates



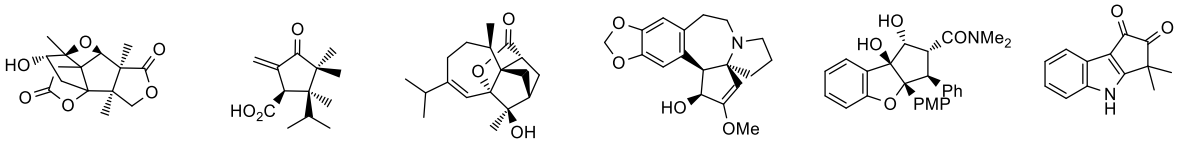
しかしながら一般に、Nazarov 環化の促進には強い Lewis 酸(e.g. BF_3, $SnCl_4$, $AlCl_3$)が必要であり、また、脱プロトン化における位置選択性の制御が困難であった(Scheme 4, A)。これ対し Frontier らは、分極した基質 **68** を用いることで基質の反応性と生成物の選択性が改善できることを報告した(Scheme 4, B)。[10] その結果、様々な Lewis 酸が反応に用いられるようになり、Cu(II)をはじめ Ir(III)、Pd(II)、V(IV)、Ca(II)などの多様な金属塩を使用した Nazarov 環化が報告されてきた。[11]

Scheme 4. Polarized Nazarov Cyclization



Nazarov 環化により得られる生成物に対しては種々の変換反応が可能である。こうしたことから、Nazarov 生成物を合成中間体として利用した様々な化合物の合成がこれまでに報告されてきた(Figure 6)。[12]

Figure 6. Selected Examples of Natural Products Synthesized by Using Nazarov Cyclization

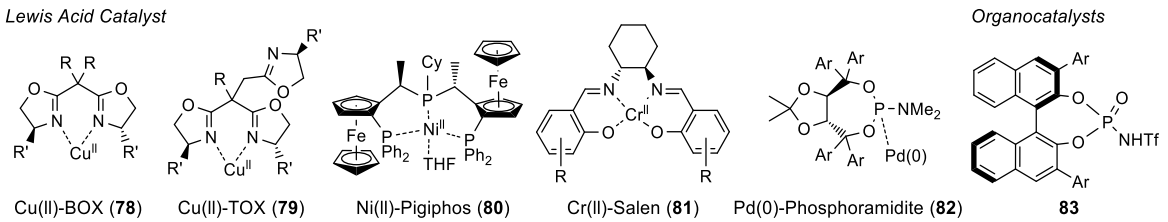


Merrilactone A (**72**) Xanthocidine (**73**) Nanolobatolide (**74**) Cephalotaxine (**75**) Rocaglamide (**76**) Bruceoline E (**77**)

第三節；エナンチオ選択的 Nazarov 環化

エナンチオ選択的に Nazarov 環化を進行させるためには、結合形成時の回転選択性をいかに制御するかが課題とされてきた。こうした中、ジビニルケトンを基質としたエナンチオ選択的 Nazarov 環化は 2003 年の Trauner らの報告を皮切りに、現在までに複数種のキラル金属錯体お

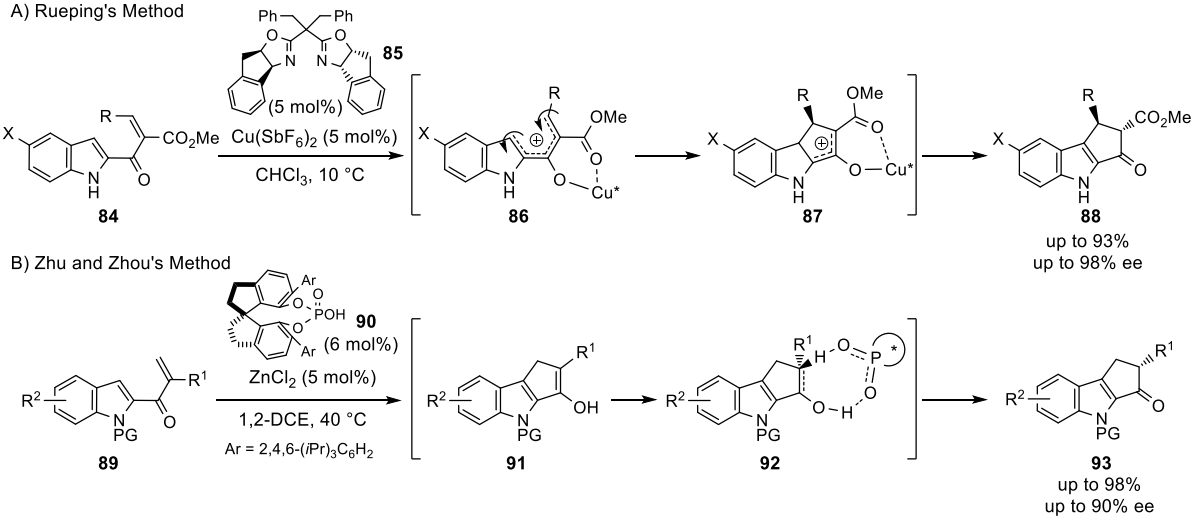
Figure 7. Examples of Chiral Catalyst for the Enantioselective Nazarov Cyclization



よび有機分子触媒を用いた手法が報告されてきた(Figure 7)。[13] しかし、アリールビニルケトン(Figure 5, c)は反応性が低いため不斉反応への展開が困難であり、成功例は限られている。[14,15]

Rueping らおよび Zhu、Zhou らはビニルアシル側鎖を持つインドール誘導体を基質としたエナンチオ選択的 Nazarov 環化を報告しているが、基質適用範囲は限定的であった(Scheme 5)。[14b,c]

Scheme 5. Enantioselective Nazarov Cyclization Using Indole Derivatives

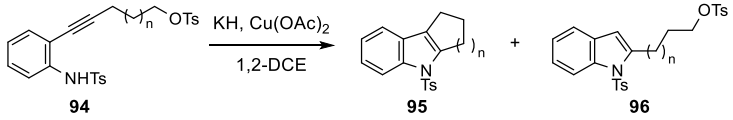


多様な置換基パターンを有するインドールアルカロイドおよびその誘導体を合成するためには、広範な基質が利用可能な不斉 Nazarov 環化条件の開発が求められる。そこで著者は、従来にない新たな不斉触媒を Nazarov 環化に適用させることで、基質適用範囲の拡大が図れると考えた。

第四節；7 員環縮環インドール合成

7 員環縮環インドール合成においては、Fischer インドール合成法が用いられてきた。しかしながら Fischer インドール合成法は、適切な官能基が導入されたヒドラジンおよびシクロヘプタノンの調製や非対称ケトンを用いた際の位置選択性の制御といった点が課題であった。また、7 員環構築は一般に、5 および 6 員環構築に比べて困難であるとされている。そのため、5 および 6

Table 1. Synthesis of Cycloalka[*b*]indole



entry	n	**95** (%)	**96** (%)
1	1	67	0
2	2	64	13
3	3	0	59

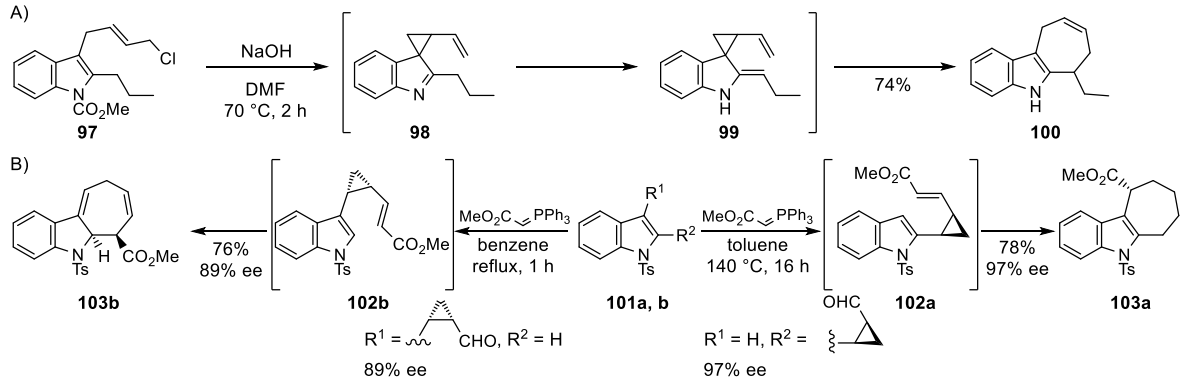
員環構築と同様の手法を用いることで 7 員環構築が可能であるとは限らない(Table 1)。[16]

こうした中で新たな骨格構築法の開発が盛んに行われ、種々の 7 員環縮環インドール合成法が報告されてきた。[17] 以下に代表的な例を示す。

1. シグマトロピー転位

Shinha らは **97** を NaOH で処理することにより、メトキシカルボニル基の脱離を伴いながらジビニルシクロプロパン **99** を発生させ、続く[3.3]-シグマトロピー転移によりシクロヘプタ[*b*]インドールが合成されることを報告した(Scheme 6, A)。[17a] また、Gaich らは光学活性なシクロプロパン **101** を用いた 7 員環合成を検討した。シグマトロピー転移において、シクロプロパンの立体化学が生成物に反映されることで、光学純度を損なうことなく **103** を得た(Scheme 6, B)。[17b]

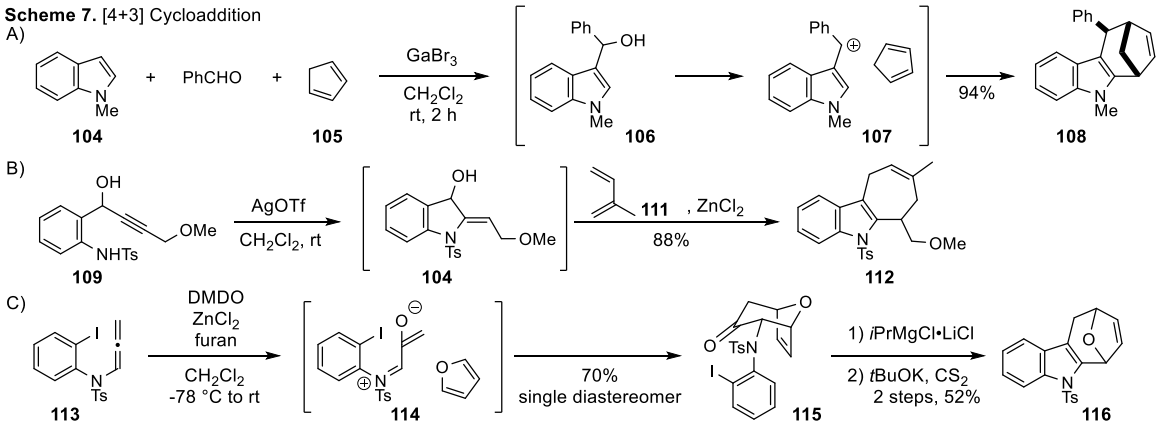
Scheme 6. [3.3] Sigmatropic Rearrangement of Divinylcyclopropane



2. [4+3]環化付加

Wu らはインドールとアルデヒドまたはケトンとの反応により得らえるインドリルアルコール **106** が、Lewis 酸触媒条件下[4+3]環化付加を進行させることを報告した。反応はジエンを 4 炭素ユニットとして利用しており、**106** からカチオン種 **107** が生じることにより進行するとされている(Scheme 7, A)。[17c] これ以降、ジエンを用いた[4+3]環化付加による 7 員環縮環インドール合成法が複数報告されてきた。

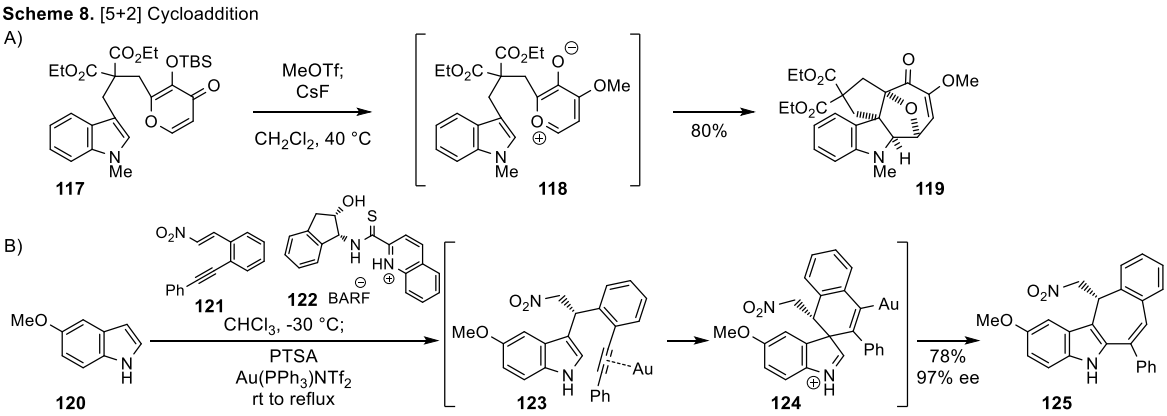
Xue および Li らは AgOTf によるヒドロアミノ化と、続く[4+3]環化付加により 7 員環縮環インドール **112** を合成した。反応はワンポットで進行し、窒素の保護基を Boc 基や Bn 基にした際には反応が進行しなかったことから、Ts 保護が重要であるとされている(Scheme 7, B)。[17d] また、Hsung らはアレナミド **113** の酸化により生じた **114** とフランとの[4+3]環化付加により 7 員環生成物 **115** を単一ジアステレオマーとして得た。その後、**115** の Grignard 反応と脱水を行うこと



によりシクロヘプタ[*b*]インドール **116** を 3 工程で合成した(Scheme 7, C)。[17e]

3. [5+2]環化付加

Li らは **117** の MeOTf によるメチル化と、CsF による脱シリル化により双性イオン **118** を生じさせてインドールの C2-C3 を二炭素ユニットとして利用した[5+2]環化付加を行い、7 員環を構築した。反応は分子内のみならず分子間反応にも適用可能であり、ジアステレオ選択的に化合物を得た(Scheme 8, A)。[17f]また、Enders らはキラルチオアミド **122** を触媒としたエナンチオ選択的 Friedel-Crafts 反応と、Au 触媒を用いた *6-endo-dig* 環化/環拡大を組み合わせることで、光学活性シクロヘプタ[*b*]インドール **125** を合成した(Scheme 8, B)。[17g]



このように 7 員環縮環インドール合成法の開発が行われてきたが、これらの手法は未だ天然物等複雑な環構造を有する化合物の合成には適用されていない。そのため、複雑な環構造を有するインドールアルカロイドおよびその誘導体合成を可能とする新規 7 員環縮環インドール合成法の開発が求められている。一方、7 員環縮環インドールは多様な生物活性を示すことが報告されているため、従来とは異なる置換様式を持つ化合物の合成は新たな創薬シードの創出につながることが期待できる。そのため、構造活性相関研究を容易にする 7 員環縮環インドール合成法の開発も併せて求められている。

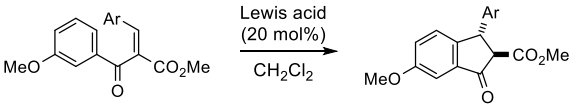
第一章；触媒的不斉 Nazarov 環化反応の開発

第一節；不斉リガンドの探索

アリールビニルケトンを利用した不斉 Nazarov 環化においては、基質の反応性の低さが課題の一つとされている。そこで、高い Lewis 酸性を有する金属トリフリックイミド(NTf_2)塩を触媒として利用することとした。[18] その結果、金属 NTf_2 塩を利用することで反応性が改善されることを確認した(Table 2)。

新規不斉触媒を探索するにあたり、まず従来の不斉 Nazarov 環化において利用例の多い Cu-BOX 錯体を用いた反応を検討したところ、中程度のエナンチオ選択性で生成物が得られ

Table 2. Comparison of Metal OTf and NTf_2 Salt



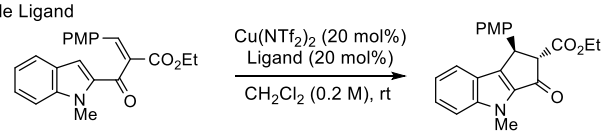
126
Ar = *o*-methoxyphenyl

127 (dr = 20/1)

entry	Lewis acid	temp. (°C)	time (h)	**127** (%)	recov. (%)
1[a]	$Yb(OTf)_3$	60	38	87	0
2	$Yb(NTf_2)_3$	rt	4.5	97	0
3	$Cu(OTf)_2$	rt	24	66	33
4	$Cu(NTf_2)_2$	rt	9	95	0
5	$Ni(OTf)_2$	rt	24	0	98
6	$Ni(NTf_2)_2$	rt	24	25	74

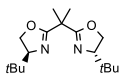
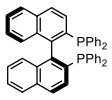
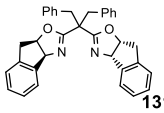
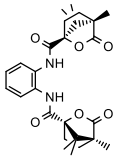
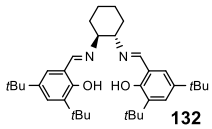
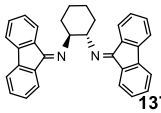
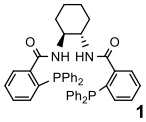
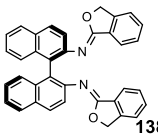
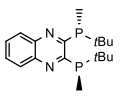
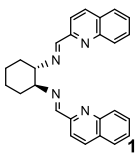
[a]Reaction was carried out using 1,2-DCE as a solvent.

Table 3. Survey of Suitable Ligand



128a

129a (dr = 10/1)

entry	Ligand	time (min)	yield (%)	% ee	entry	Ligand	time (min)	yield (%)	% ee
1[a]	 **130**	15	97	28	6	 **135**	10	98	0
2[a]	 **131**	20	91	65	7	 **136**	10	99	1
3	 **132**	10	98	0	8	 **137**	60	99	0
4	 **133**	10	99	4	9	 **138**	10	99	-1
5	 **134**	10	99	0	10	 **139**	330	92	-11

[a]Reaction was carried out using 10 mol% of catalyst and ligand.

た(Table 3, entries 1, 2)。続けて $Cu(NTf_2)_2$ 触媒条件下、より高いエナンチオ過剰率で生成物を与える不斉リガンドを探索したが、検討した不斉リガンドは BOX リガンドを上回る結果を与えなかった(entries 3~10)。しかしながら、四座配位 Schiff 塩基リガンド ImQ (**139**)を利用した際に 11% ee で **129a** が得られた。ImQ およびその類縁体が不斉反応へと利用された例は少なく、Nazarov 環化への適用は報告されていなかった。[19] そのため、ImQ およびその類縁体を不斉 Nazarov 環化へと適用させることができれば、基質適用範囲の拡大が実現できると期待された。そこで、ImQ を不斉リガンドとした反応条件を検討した。

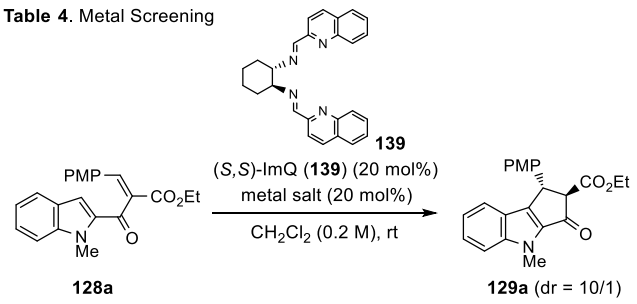
第二節；反応条件の最適化検討

1. 金属塩

各種金属塩を検討したところ、遷移金属塩を用いた際に良好な収率で環化体が得られた(Table 4, entries 1~6)。中でも $Ni(NTf_2)_2$ は高い触媒活性を示し、反応は 30 分で完結した。先の検討において $Ni(NTf_2)_2$ より $Cu(NTf_2)_2$ は高い触媒活性を有することが示された(Table 2)。そのため、本結果は金属塩単体による触媒活性とは異なっており、このことから、金属種によって ImQ と形成する錯体の構造が異なることが推察された。また、エナンチオ選択性に関しても $Ni(NTf_2)_2$ を用いた際が最も高く、53% ee で環化体が得られた。

$Yb(NTf_2)_3$ は触媒活性が高く、高収率で生成物を与えた。しかしながら、エナンチオ選択性は発現しなかったため ImQ と錯体を形成しなかったと考えられる。同様に、$Al(NTf_2)_3$ を利用した際にもエナンチオ選択性は発現しなかった(entries 7, 8)。本結果より、$Ni(NTf_2)_2$/ImQ 錯体がインドール誘導体の不斉 Nazarov 環化に有効な不斉環境を構築することが判明したため、$Ni(NTf_2)_2$ を金属触媒として以降の検討に用いることとした。

Table 4. Metal Screening



128a **129a** (dr = 10/1)

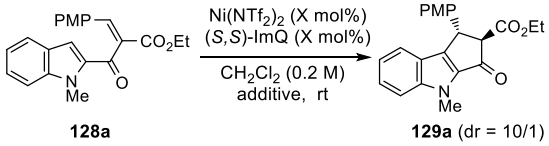
entry	metal salt	time (h)	yield (%)	% ee
1	$Mn(NTf_2)_2$	4	84	3
2	$Fe(NTf_2)_2$	2	99	35
3	$Co(NTf_2)_2$	24	87	26
4	$Ni(NTf_2)_2$	0.5	98	53
5	$Cu(NTf_2)_2$	5	93	16
6	$Zn(NTf_2)_2$	1.5	94	12
7	$Yb(NTf_2)_3$	0.2	97	-3
8	$Al(NTf_2)_3$	24	13	-6

2. 触媒量と添加剤

ImQ は Schiff 塩基リガンドであるため、系中に存在する水による加水分解が懸念された。実際に、水が存在する条件においては反応性・選択性ともに低下した。そこで、MS4Å を乾燥剤として添加したところエナンチオ選択性が向上した(Table 5, entries 1~3)。

乾燥剤を添加した条件で触媒量を 10 mol%に減じたところ、エナンチオ選択性が向上した(entry 4)。これは MS4Å の触媒に対する重量比が上昇したことに起因しており、触媒を 20 mol%用いた場合にも MS4Å の量を増加させることで同等のエナンチオ過剰率で環化体が得られた。し

Table 5. Effect of Additive



128a **129a** (dr = 10/1)

[a]500 mg/mmol of additive was used unless otherwise noted.
[b]CH_2Cl_2 and water were mixed and water layer was removed by separating funnel before use.

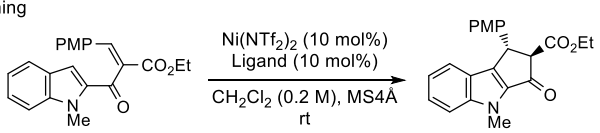
entry	catalyst (mol%)	additive[a]	time (h)	yield (%)	% ee
1	20	-	0.5	98	53
2	20	water[b]	1.5	91	19
3	20	MS4Å	0.1	93	66
4	10	MS4Å	0.3	97	74
5	5	MS4Å	5.5	98	68
6	10	MS3Å	24	67	57
7	10	MS5Å	0.3	93	64
8	10	Na_2SO_4	1.5	97	9
9	10	DRIERITE	24	73	24

かしながら、5 mol%まで触媒量を減じた際には反応時間が大幅に延長したため、触媒量は 10 mol%が適量であると判断した(entry 5)。なお、各種乾燥剤を検討した結果、本反応においては MS4Å が最も適していることが判明した(entries 6~9)。

3. 不斉 Schiff 塩基リガンド

ImQ およびその類縁体はアルデヒドとキラルジアミンから容易に合成可能な化合物群である。そこで種々の四座配位 Schiff 塩基リガンドを合成し、リガンド構造の最適化を行った(Table 6)。まず、アルデヒドユニットを種々変更したリガンドを検討したところ、ピリジン環 5 位に置換基を導入することにより選択性が向上した(entries 1~4)。この際、同様の分子半径を有するメチル基およびブロモ基を導入したリガンドは、それぞれ同じ選択性で生成物を与えた一方で反応性に

Table 6. Ligand Screening



128a **129a** (dr = 10/1)

entry	Ligand	time (h)	yield (%)	% ee
1	R = H (**140**)	0.4	93	27
2	5-Me (**141**)	5	93	49
3	5-Br (**142**)	2.5	96	49
4	5-Ph (**143**)	1	92	37
5	6-Ph (**144**)	2	98	1
6	**145**	24	94	32
7	X = N (**139**)	0.3	97	74
8	CH (**146**)	3	95	3
9	Y, Z = O, CH (**147**)	0.2	97	0
10	S, CH (**148**)	1	99	2
11	S, N (**149**)	0.3	88	67
12	**150**	24	86	-60
13	**151**	0.2	98	66
14	**152**	0.3	96	45
15	**153**	0.2	93	-58

差が生じた。そのため、エナンチオ選択性にはリガンドの立体的要素が強く影響しており、電子的影響は錯体の Lewis 酸性に影響するものの選択性への影響は小さいことが示された。一方、6 位に置換基を導入した際には反応性および選択性が低下した(entry 5)。これは Ni 錯体における基質配位場が阻害されたことに起因すると考えられる。同様の理由から、側鎖がキノリル基である ImQ に比べて側鎖にベンゾ[*h*]キノリル基を有する **145** では反応性および選択性が低下したと考えられる(entries 6, 7)。

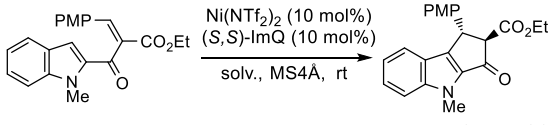
ここで、リガンド側鎖芳香環上に存在する窒素原子の必要性について検討した。ナフチル基を側鎖に有するリガンド **146** を用いた場合にはラセミ体が得られたため、イミン窒素のみでなく芳香族窒素も錯体形成に関与していることが示された(entry 8)。次に、窒素以外のヘテロ原子として酸素および硫黄による配位を狙ったリガンド **147** および **148** を用いたが選択性は発現せず、同様の骨格でベンゾチアゾリル基を導入した **149** では 67% ee で環化体が得られた(entries 9~10)。そのため、窒素 4 原子による配位が不斉 Nazarov 環化に対して有効な不斉環境を持つ錯体形成に必須であることが判明した。

続いて、各種キラルジアミン由来のリガンドも検討したが、ImQ が最も高いエナンチオ選択性を発現した(entries 12~15)。興味深いことに、類似の骨格構造を有する ImQ (**139**)とシクロヘキセンジアミン由来の **150** では生成物の立体選択性が逆転した。**150** を用いた際に反応性が大幅に低下したことからも、両リガンドを用いた際に形成される錯体構造が異なることが考えられた。

4. 反応溶媒と濃度

ハロゲン系溶媒を用いた際には CCl_4 を除き比較的良好な反応性と選択性を示した(Table 7, entries, 1~6)。一方、極性溶媒である THF、MeCN、DMA を用いた際には反応性・エナンチオ選択性ともに低下した。これは溶媒和による Ni 塩の Lewis 酸性の減弱、および錯体形成の阻害に起因していると考えられた(entries 7~9)。$MeNO_2$ を溶媒として用いた場合、ハロゲン系溶媒と同程度の反応性・選択性を示した(entry 10)。しかしながら、$MeNO_2$ を溶媒として用いた際には触媒量の低減に伴い反応性・選択性ともに低下したため、溶媒として不適当であると判断した。

Table 7. Solvent Screening



128a **129a** (dr = 10/1)

entry	solvent	conc. (M)	time (h)	**129a** (%)	% ee	recov. (%)
1	CH_2Cl_2	0.2	0.1	93	66	0
2	$CHCl_3$	0.2	0.3	94	62	0
3	CCl_4	0.2	24	88	-2	0
4	1,2-DCE	0.2	0.3	95	63	0
5	PhF	0.2	0.1	89	66	0
6	PhCl	0.2	0.5	92	59	0
7	THF	0.2	24	28	4	60
8	MeCN	0.2	24	39	21	59
9	DMA	0.2	24	trace	54	96
10	$MeNO_2$	0.2	0.1	89	62	0
11	CH_2Cl_2	0.1	0.3	98	80	0
12	CH_2Cl_2	0.05	0.3	97	80	0

ここで、溶媒濃度を 0.1 M へと希釈したところ選択性が 80% ee まで向上した。更なる濃度希釈による選択性の改善は起こらなかったため、溶媒濃度 0.1 M を最適条件として設定した(entries 11, 12)。なお、希釈に伴う選択性向上の理由については現在のところ明らかとなっていない。

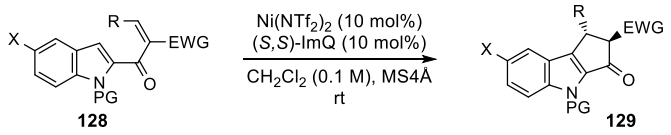
第三節；基質一般性の検討

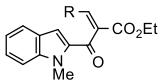
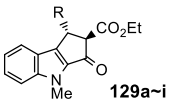
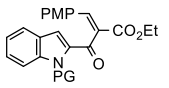
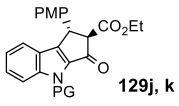
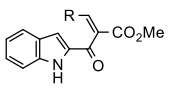
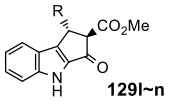
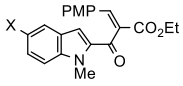
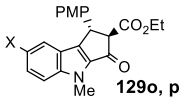
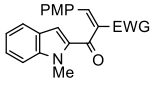
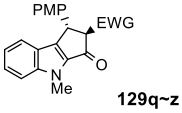
これまでの検討により得られた最適条件を用いて、基質検討を行った。検討にはケトンβ位の置換基(R)、インドール窒素の保護基(PG)、インドール環上の置換基(X)、および電子求引性基(EWG)をそれぞれ変更した基質を用いた。

1. オレフィン上の置換基 (R)

種々の芳香環・ヘテロ芳香環・シンナミル基を導入した基質が、良好なエナンチオ選択性で生成物を与えた。一方、**128c** は反応性が高く室温では選択性が発現しなかったため、－20 ℃で反応を行ったが 37% ee にとどまった(Table 8, entries 1~6)。アルキニルおよびアルキル置換の化合物に関しては良好な収率で生成物を与えるもののエナンチオ選択性が低く、$Ni(NTf_2)_2$/ImQ 触媒条件には適していないと考えられる(entries 7~9)。

Table 8. Substrate Scope and Limitations



entry	substrate		product	time (h)	yield (%)	% ee	dr
1		PMP (**128a**)	 **129a~i**	0.3	98	80	10/1
2		*o*-methoxyphenyl (**128b**)		0.3	91	66	14/1
3[a,d]		TMP (**128c**)		44	96	37	-[e]
4		Ph (**128d**)		0.3	86	69	>201
5	R =	2-furyl (**128e**)		0.5	94	73	14/1
6		cinnamyl (**128f**)		48	83	66	8/1
7		phenylethynyl (**128g**)		72	87	40	-[e]
8		methyl (**128h**)		48	82	33	20/1
9[b]		cyclohexyl (**128i**)		6	95	14	-[e]
10		Bn (**128j**)	 **129j, k**	1	95	66	10/1
11[b,c]	PG =	Ts (**128k**)		48	82	53	13/1
12		PMP (**128l**)	 **129l~n**	13	93	80	20/1
13	R =	Ph (**128m**)		37	93	84	-[e]
14		*p*-chlorophenyl (**128n**)		67	84	82	>20/1
15		F (**128o**)	 **129o, p**	0.3	95	80	13/1
16	X =	OMe (**128p**)		0.3	95	77	12/1
17		CO_2tBu (**128q**)		0.3	99	72	8/1
18[b]		$CONMe_2$ (**128r**)		14	96	91	-[e]
19[b]		$CONBn_2$ (**128s**)		36	94	80	3/1
20[b]		CO(4-morpholinyl) (**128t**)		24	99	75	>20/1
21		COMe (**128u**)	 **129q~z**	0.2	89	80	>20/1
22	EWG =	CO*t*Bu (**128v**)		48	83	30	>20/1
23		CO(cyclopropyl) (**128w**)		0.2	92	32	-[e]
24		COPh (**128x**)		0.5	83	26	>20/1
25		CO(1-pyrrolyl) (**128y**)		17	90	34	>20/1
26		$PO(OEt)_2$ (**128z**)		24	quant.	73	>20/1

[a]Reaction was carried out at -20 °C. [b]Reaction was carried out at 40 °C. [c]Reaction was carried out using 20 mol% of $Ni(NTf_2)_2$ and (*S,S*)-ImQ. [d]Concentration of reaction media was 0.2 M. [e]Minor diastereomer was not detected.

2. インドール環上の官能基 (PG, X)

インドール窒素の保護基として Me 基よりも嵩高い Bn 基や Ts 基を導入したところ、エナンチオ選択性が低下した(entries 10, 11)。保護基が嵩高くなることで錯体との相互作用が大きくなり、エナンチオ選択性の低下につながったと考えられる。しかしながら、無保護の基質において良好な選択性で生成物が得られたため、本触媒条件においては窒素原子の保護は必須ではないことが判明した(entries 12~14)。また、インドール 5 位に導入した置換基は反応性・選択性のいずれにも影響を及ぼさなかった(entries 15, 16)。

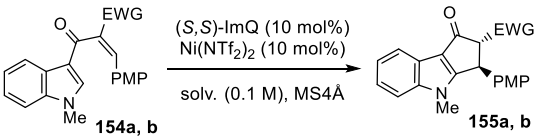
3. 電子求引性基 (EWG)

種々の電子求引性基を導入した基質を反応に付したところ、エステル・アミド・リン酸エステルを導入した基質において良好な選択性で生成物が得られた(entries 17~20, 26)。この際、ケトアミド構造を持つ基質は反応性が低く、反応の進行に加熱が必要であったものの **129r** を 91% ee で与えた。一方、アセチル基を導入した **128u** は反応性が高く、**129u** を 80% ee で与えた(entry 21)。しかしながら、その他のジケトン型基質に関しては 30% ee 程度で生成物を与える結果となった(entries 22~24)。**128v** においては反応性が低下していることから、嵩高い *t*Bu 基の影響により触媒への配位が阻害されたことが考えられる。また、**128y** においても選択性が低下した(entry 25)。ImQ はキノリン構造を有しているため、**128x** や **128y** は電子求引性基中の芳香環が ImQ 中のキノリン環と相互作用したことが選択性の低下につながったと考えられる。また、シクロプロパン中の炭素は sp2 様の軌道となっているため、**128w** に関しても同様の理由で選択性が低下したと考えられる。

4. 3 位置換インドール誘導体

154a は反応性が低く、本反応条件において反応が進行しなかった。そこで、より反応性の高いジケトン誘導体 **154b** を不斉反応条件へと付した。しかしながら、80 ℃まで昇温したものの収率 32%にとどまり、不斉収率も 14% ee であった。高温条件下でも反応が十分に進行しなかった理由として、$Ni(NTf_2)_2$/ImQ 錯体が分解し、触媒活性が低下したことが考えられた(Table 9)。

Table 9. Reaction Using 3-Substituted Indole Derivatives



154a, b **155a, b**

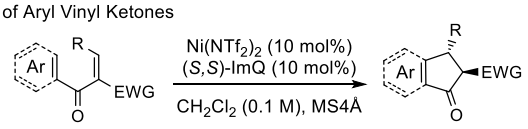
entry	EWG	solv.	temp. (°C)	time (h)	yield (%)	% ee	recov. (%)
1	CO_2Me	CH_2Cl_2	40	24	0	-	85
2	COMe	1,2-DCE	80	168	32	14	64

5. インドール以外のアリールビニルケトン

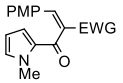
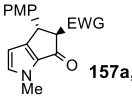
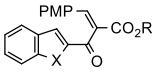
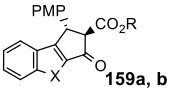
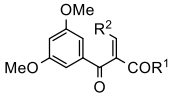
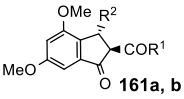
$Ni(NTf_2)_2$/ImQ 触媒条件の基質適用範囲拡大をはかるべく、インドール以外の Nazarov 基質も検討した(Table 10)。ピロール誘導体はインドール誘導体に比べて反応性が劣るものの良好な収率・エナンチオ選択性で生成物を与えた(entries 1, 2)。一方、ベンゾフラン **158a** やベンゾチオフェン **158b** は高温条件下でも反応が進行しなかった(entries 3, 4)。ベンゼン誘導体についても検討したものの、生成物の選択性は 30% ee 程度にとどまった(entries 5, 6)。

以上の結果から、$Ni(NTf_2)_2$/ImQ 触媒は広い官能基許容性を有する触媒として不斉 Nazarov 環化を進行させ、特に含窒素芳香族化合物を基質とした反応に適していることが明らかとなった。

Table 10. Asymmetric Reaction of Aryl Vinyl Ketones



156, 158, 160 **157, 159, 161**

entry	substrate		product	temp. (°C)	time (h)	yield (%)	% ee	dr
1[a]		EWG = CO_2Et (**156a**)	 **157a, b**	40	24	69	77	17/1
2[a]		COMe (**156b**)		rt	17	80	72	>20/1
3[a,b]		X = O, R = Et (**158a**)	 **159a, b**	80	72	0	-	-
4[a,b]		X = S, R = Me (**158b**)		80	48	0	-	-
5		R^1 = PMP, R^2 = Me (**160a**)	 **161a, b**	40	96	38	34	>20/1
6		R^1 = TMP, R^2 = OMe (**160b**)		rt	1	95	27	-[c]

[a]Reaction was carried out using 20 mol% of $Ni(NTf_2)_2$ and (*S,S*)-ImQ. [b]Reaction was carried out in 1,2-DCE (0.2 M). [c]Minor diastereomer was not detected.

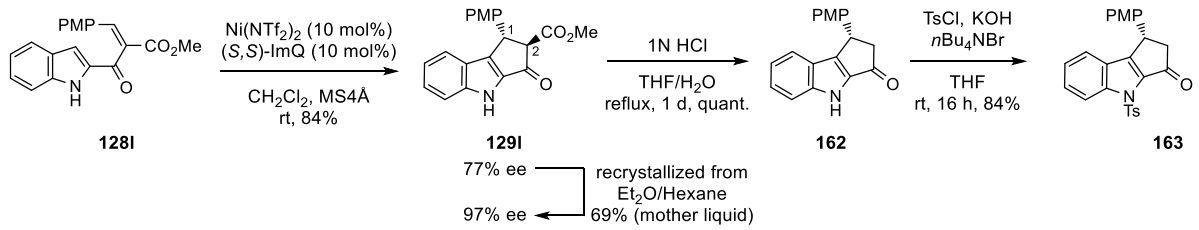
これにより、従来報告が無かった種々の官能基を有するシクロヘプタ[*b*]インドールをエナンチオ選択的に合成することが可能となった。

第四節；Nazarov 環化体の変換反応と絶対立体化学の決定

Nazarov 環化により得られる生成物は種々の変換反応へと適用可能であり、複雑な化合物の合成中間体として利用されてきた。[12] そこで、著者の合成した化合物に対しても種々の変換反応を検討するとともに、環化体の絶対立体化学を決定することとした。

環化体 **129l** は既知化合物であり、X 線結晶構造解析により C1 および C2 の置換基が *trans* 配置であることが確認されている。[11f] また ^{1}H NMR のカップリング定数より、他の環化体においても主生成物は C1 および C2 の置換基が *trans* 配置の環化体であると決定した。生成物のジアステレオ選択性は環化後に生じるエノールのプロトン化により決定される。生成物にはケト-エノール平衡が成り立つため、本反応条件においては熱力学的に有利な *trans* 体が主として得られたと考えられる。

Scheme 9. Transformation for Determination of Absolute Configuration

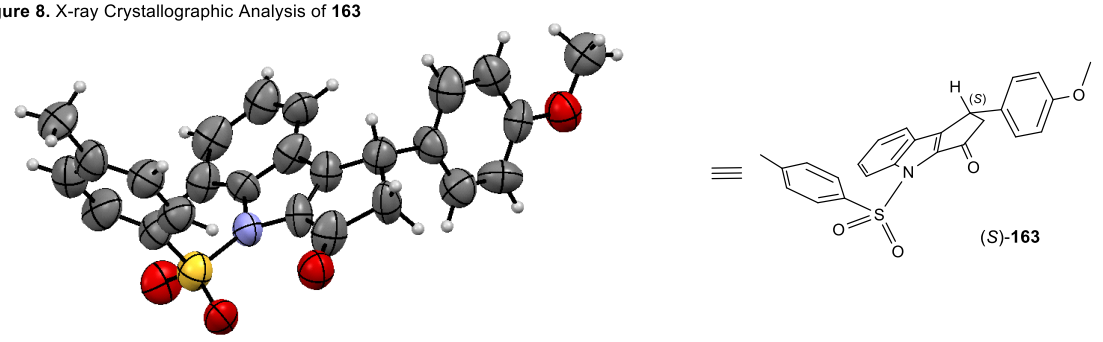


128l **129l** **162** **163**

77% ee → 97% ee (recrystallized from Et_2O/Hexane 69% (mother liquid))

不斉 Nazarov 環化により得られた環化体 **129l** の再結晶により、母液から 97% ee で **129l** を得た後、脱炭酸とインドール窒素の Ts 保護を行い、**163** を得た(Scheme 9)。得られた **163** の X 線結晶構造解析を行い、$Ni(NTf_2)_2$/(*S,S*)-ImQ 錯体を用いた不斉 Nazarov 環化において得られた環化体 **129l** の絶対立体化学を(1*S*,2*R*)体であると決定した(Figure 8)。

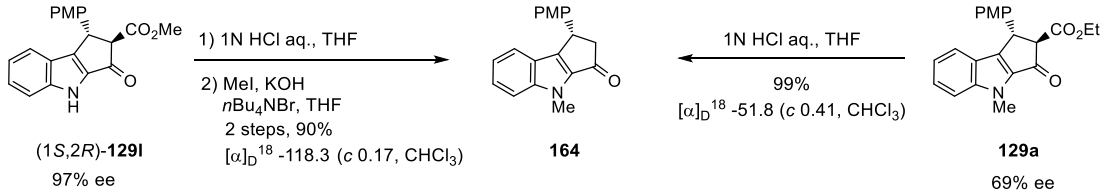
Figure 8. X-ray Crystallographic Analysis of **163**



F value: 0.06(10)

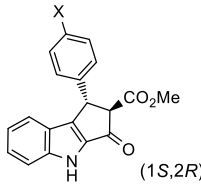
また (1*S*,2*R*)-**129l** より調製した **164** の旋光度と、不斉反応により得られた **129a** より調製した **164** の旋光度の符号が一致したことから、両者は同じ絶対立体化学であると判明した(Scheme 10)。

Scheme 10. Determination of Absolute Configuration of Other Compound



加えて、環化体 **129m** および **129n** は既知化合物であるため、報告された(1*R*,2*S*)体との旋光度を比較した。その結果、旋光度が逆の符号を示したことから今回著者の用いた不斉反応条件により得られた環化体 **129m** および **129n** は(1*S*,2*R*)体であることを確認した。そのため、全ての環化体が同一の絶対立体化学を有すると判断した。これらの結果より、各環化体の絶対立体化学を決定した。なお、(1*R*,2*S*)-**129n** の絶対立体化学は X 線結晶構造解析により決定されている(Table 11)。[14b]

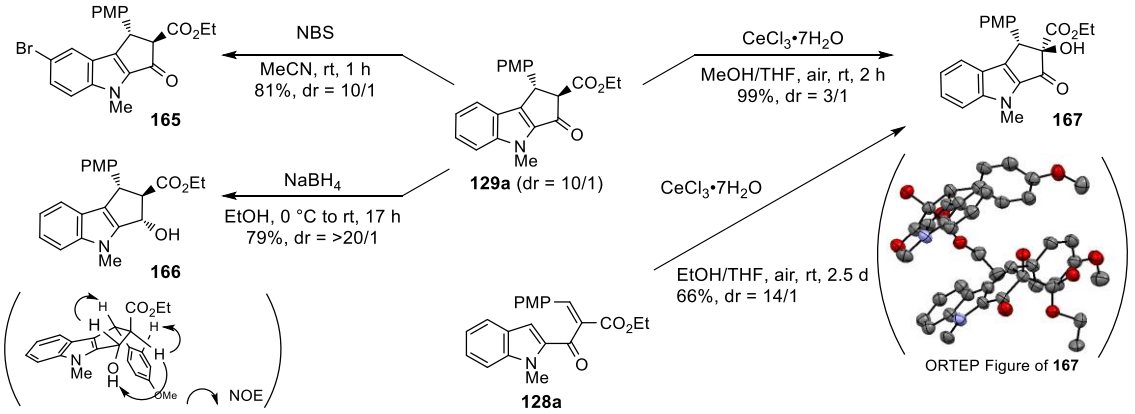
Table 11. Comparison of Optical Rotation



entry	X	$[\alpha]_D^{rt}$ (CH_2Cl_2) synthesized	reported (1*R*,2*S*)
1	H (**129m**)	+78.1 (*c* 1.00, 84% ee)	-99.3 (*c* 6.6)
2	Cl (**129n**)	+53.9 (*c* 1.00, 82% ee)	-71.5 (*c* 3.3)

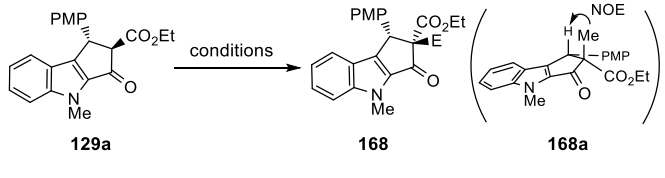
上記の検討の過程で脱炭酸が酸性条件下、高収率で進行することが明らかとなったため、更なる変換反応を検討した(Scheme 11)。NBS を添加することでインドール環 5 位のブロモ化が速やかに進行した。また、ケトンカルボニルの還元は PMP 基を避ける方向から還元剤が接近することにより、立体選択的に **166** を与えた。得られた生成物 **166** の立体化学は NOE 相関により決定した。続いて、カルボニルα位の酸化を試みた。しかしながら、種々の酸化剤(CMHP, PIDA, *m*CPBA, CAN)との反応では望みの環化体は得られなかった。ここで、空気雰囲気下 $CeCl_3$ を作用させたところ望みの環化体が 99%で得られた。[20]**167** の立体化学は X 線結晶構造解析により決定した。$CeCl_3$ は Lewis 酸としての性質も有しており、**128a** に空気雰囲気下 $CeCl_3$ を作用させたところ、Nazarov 環化に続くカルボニルα位の酸化反応がワンポットで進行して、**167** が得られた。

Scheme 11. Transformations



さらに、環化体 **129a** は種々の求電子剤と温和な条件下反応し、アルキル化体 **168** を高収率・高ジアステレオ選択的に与えた(Table 12)。なお、得られたアルキル化体 **168** の立体化学は NOE 相関により決定した。ここで、MVK を用いた Michael 付加に関して $Ni(NTf_2)_2$ 触媒条件下で反応を行ったところ、168d が高収率で得られた(entry 5)。そこで、ワンポットでの不斉 Nazarov 環化－Michael 付加による不斉 4 級炭素構築を試みた。

Table 12. Alkylation

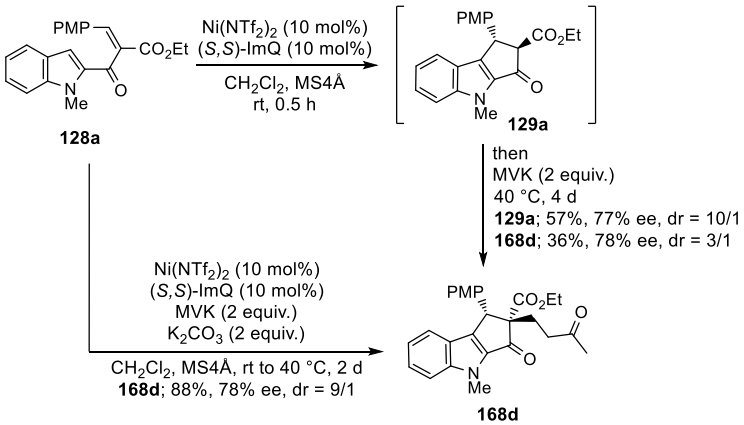


entry	electrophile	conditions	time (h)	yield (%)	dr
1	MeI	A	13	75	6/1
2	allyl bromide	A	24	97	14/1
3	methyl acrylate	A	20	99	>20/1
4	MVK	A	13	quant.	14/1
5	MVK	B	36	98	>20/1

conditions A; electrophile, K_2CO_3, nBu$_4$NBr , THF, rt
B; electrophile, $Ni(NTf_2)_2$, CH_2Cl_2, 40 °C

まず不斉 Nazarov 環化の条件下 **128a** を反応させて、TLC 上で **128a** の消失および **129a** の生成を確認した後に MVK を添加した。しかしながら、本条件では Michael 付加体の収率は 36%にとどまった。反応が十分に進行しなかった理由として、錯体を形成したことにより Ni の Lewis 酸性が低下していたことが考えられたため、塩基を添加して反応の促進を図った。併せて、反応系中に混入する水の影響を低減するために、全ての試薬を反応開始時に加えることとした。その結果、**168d** は 88%で得られた。また、エナンチオ選択性は 78% ee であり、不斉 Nazarov 環化により得られた **129a** と同等の選択性であったため、MVK および K_2CO_3 は不斉反応を阻害しないことが判明した(Scheme 12)。

Scheme 12. Construction of Quaternary Carbon Center in One-Pot



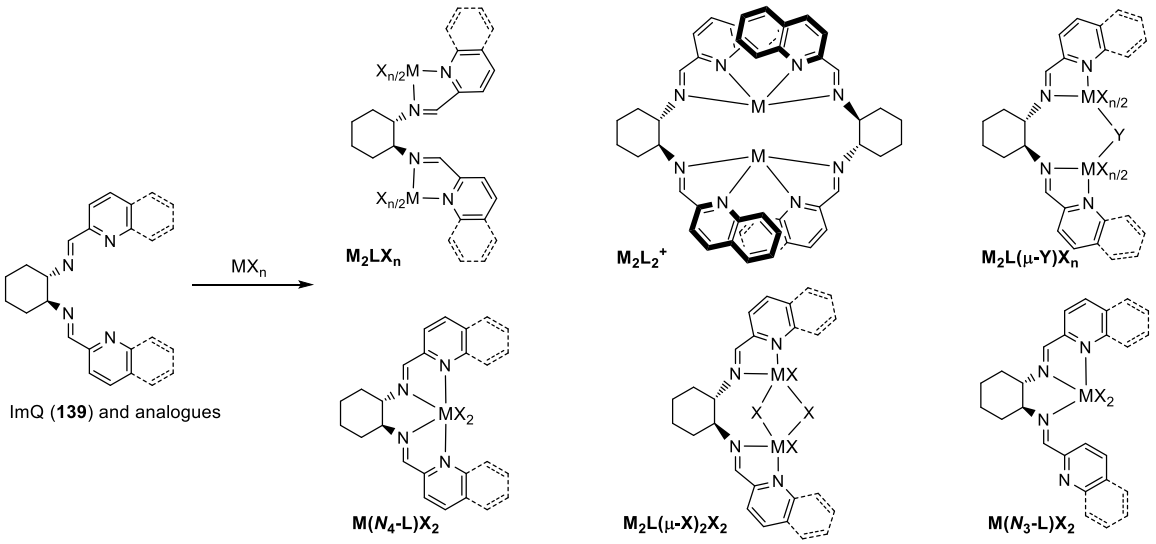
第二章；錯体構造とエナンチオ選択性発現機序の解明

第一節；Ni(NTf$_2$)$_2$/ImQ 錯体構造の解明

四座配位 Schiff 塩基リガンドである ImQ およびその類縁体は下記のような様々な構造の金属錯体を形成すること報告されており、その構造はリガンド構造、金属種、カウンターアニオン等により変化する(Figure 9)。[21] 例えば Cu(OTf)$_2$ は M(N_4-L)X$_2$ や M$_2$L$_2^{+}$の錯体を形成することが報告されている。また、NiI$_2$ はトルエン-エタノール混合溶媒中 M(N_3-L)X$_2$ および M$_2$L(μ-Y)X$_n$ 錯体を形成すると報告されている。このように、同一金属種を用いた際にも錯体構造が変化するため、反応に寄与する錯体の構造を推測することは困難であった。そこで、不斉 Nazrov 環化を進行させる Ni(NTf$_2$)$_2$/ImQ 錯体の構造解明に着手した。

ところで、こうした ImQ およびその類縁体を利用した錯体は NMR や MS などによる解析も行われているが、構造の決定には X 線結晶構造解析が用いられてきた。そこで、著者も X 線結晶構造解析による Ni(NTf$_2$)$_2$/ImQ 錯体の構造解明を試みた。

Figure 9. Coordination Modes for 1,2-Diaminocyclohexyl Bis(iminopyridyl/quinolyl) Ligands

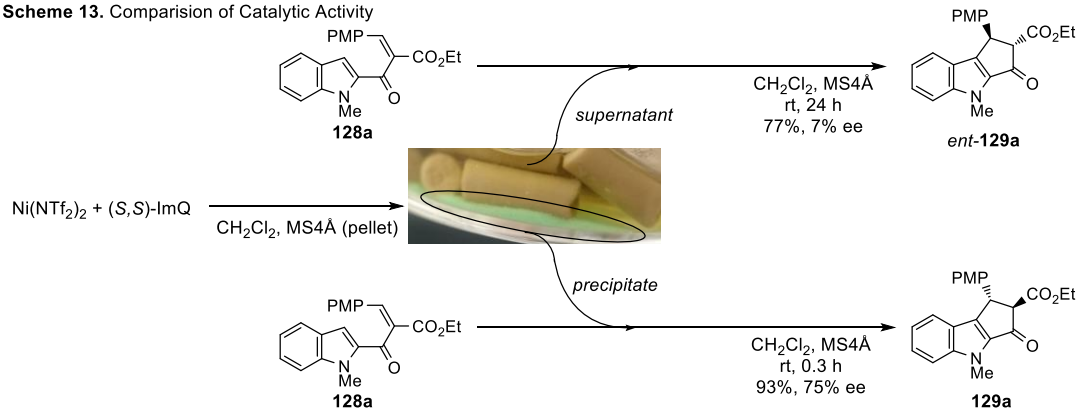


1. X 線結晶構造解析

Ni(NTf$_2$)$_2$/ImQ 錯体調製時には沈澱物が析出していた。そこで、沈澱物と可溶性成分を分離してそれぞれ不斉 Nazarov 反応に用いることで、不斉反応を進行させる活性錯体種の局在を調べた。その結果、沈澱成分が活性錯体種であることが明らかとなった(Scheme 13)。沈澱成分は結晶性を有していたが、空気中で容易に分解したため X 線結晶構造解析への適用が困難であった。そのため、より安定な結晶性錯体の調製が必要となった。

錯体の中心金属の配位場を埋めることにより錯体の安定性が向上すると考え、種々の外部配位子を検討することとした。まず金属 NO$_3$ 塩の錯体において、カウンターアニオンである NO$_3$ が二座配位子として錯体を形成した例が報告されていたため、Ni(NO$_3$)$_2$ を用いた錯体の結晶化を試

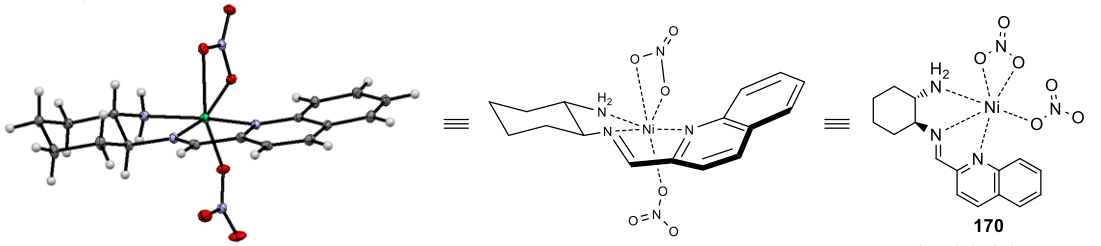
Scheme 13. Comparision of Catalytic Activity



みた。[22] 種々錯体調製条件を検討したものの、得られた錯体は ImQ が一部加水分解した配位子 **169** から形成される錯体種であった(Figure 10)。その結果、Lewis 酸存在下 ImQ は容易に加水分解されることが示唆された。このことは $Ni(NTf_2)_2$/ImQ 錯体である沈澱成分の不安定性、および不斉反応における乾燥剤(MS4Å)の必要性とも一致する。

Figure 10. Complex of $Ni(NO_3)_2$ and ImQ

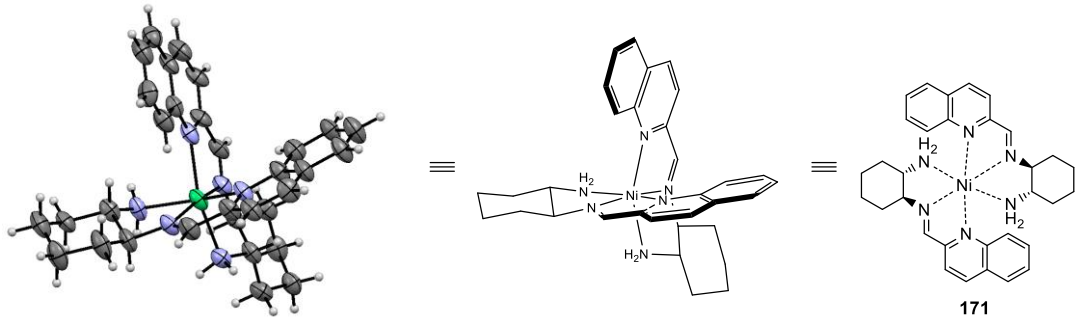
A) $Ni(NO_3)_2 \cdot 6H_2O$ + (*S*,*S*)-ImQ in $MeCN/Et_2O$



170

[Ni/**169**/2(NO_3) complex]

B) $Ni(NO_3)_2 \cdot 6H_2O$ + (*S*,*S*)-ImQ + NH_4PF_6 in $MeOH/Et_2O$



PF_6 anions and Et_2O has been omitted for clarity.

171

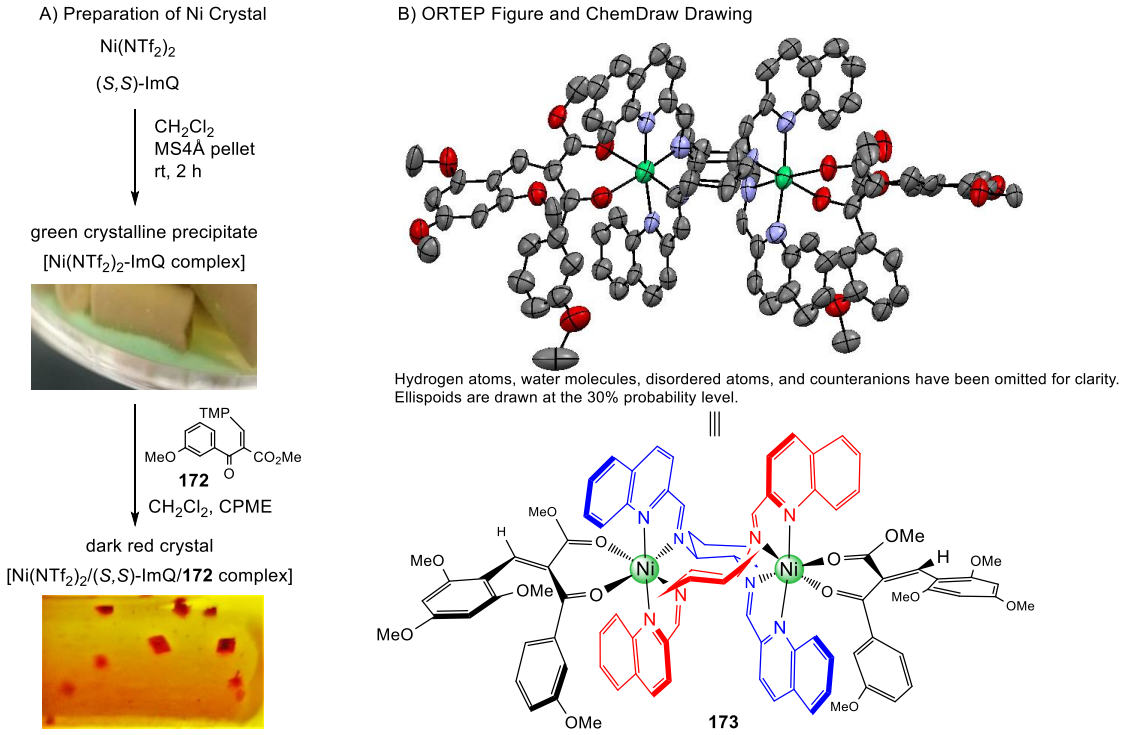
[Ni/2(**169**) complex]

続いて、調製した $Ni(NTf_2)_2$/ImQ 錯体にジカルボニル化合物を配位させることで、錯体の安定性向上を図った。この際、より反応遷移状態に近い錯体構造を視覚化するため、ジカルボニル化合物として Nazarov 基質を添加することとした。その結果、$Ni(NTf_2)_2$/ImQ 錯体に反応性の低い基質 **172** を添加した後に貧溶媒として CPME を加えたところ、比較的安定な赤色結晶が析出した。本結晶を用いて X 線結晶構造解析を行った結果、得られた結晶は M_2L_2型の Ni 二核錯体であることが判明した(Figure 11)。

錯体は 2 分子の Ni に対して 2 分子の ImQ が互い違いに配位することにより、二重らせん様の構造を形成していることが明らかとなった。また、カウンターアニオン(NTf_2)は全て解離してお

り、Nazarov 基質は錯体の両末端から Ni に二座配位していた。この際、錯体に配位した基質は分子構造がねじれてプラスのヘリシティーを有していることが確認できた。

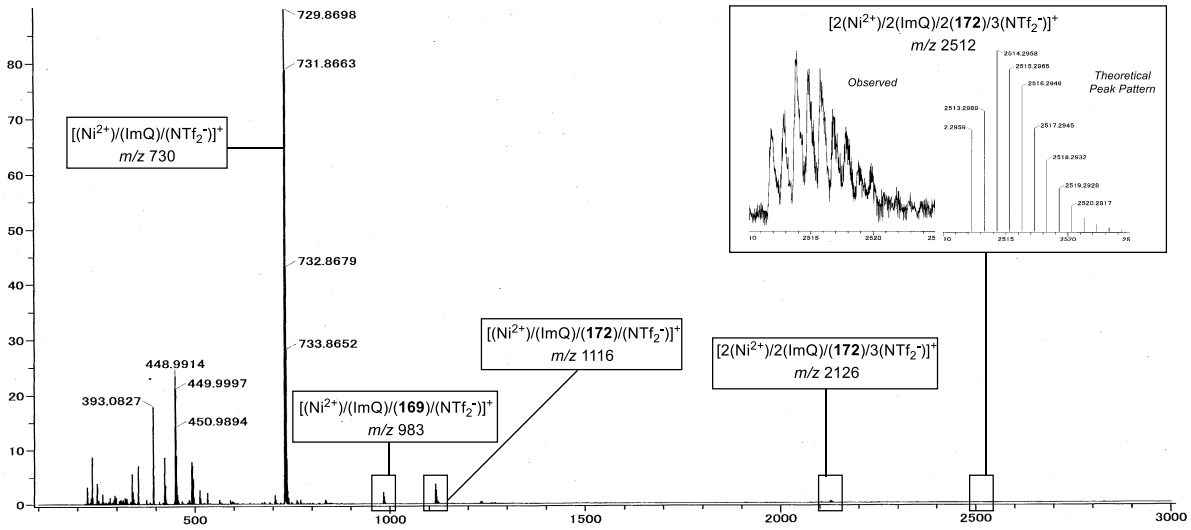
Figure 11. X-ray Crystallographic Analysis of Ni Complex **173**



2. ESI-MS 解析

X 線結晶構造解析により $Ni(NTf_2)_2$/ImQ 錯体は Ni 二核錯体であることが判明した。そこで、反応溶液中における二核錯体の存在を確認した。ESI-MS 解析の結果、*m/z* 2512 において二核錯体に相当するイオンピークが観測され、同位体推定の結果とも良い一致を示した。これにより、二核錯体が溶液中にも存在することが示唆された(Figure 12)。

Figure 12. ESI-MS Analysis of $Ni(NTf_2)_2$/ImQ/**172** Complex.

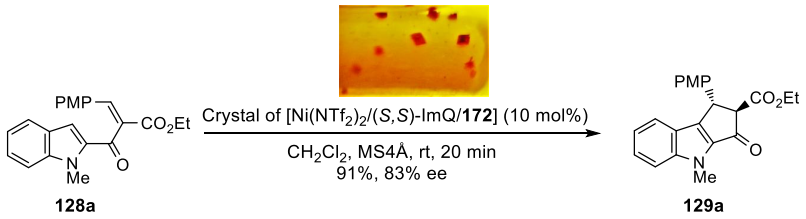


ESI-MS 解析においては二核錯体に相当するイオンピークのみならず、複数種のイオンピークが観測された。これらのイオンピークは Ni/ImQ の単核錯体や、加水分解された **169** との錯体に相当する *m/z* 値であった。先述したように、ImQ やその類縁体を用いた錯体形成においては同一溶液中においても複数種の錯体が形成されることが報告されていたため、本系においても複数種の錯体が形成されていたものと考えられる。このことは先の実験において、Ni 錯体の可溶性成分および沈澱成分が異なる反応性・エナンチオ選択性を示したことからも示唆された。また、$Ni(NTf_2)_2$/ImQ 錯体は容易に分解するため、ESI-MS 測定条件下における分解も考えられる。

3. 活性錯体種の確認

これまでの検討により、Ni 二核錯体が不斉 Nazarov 環化における活性錯体であることが示唆された。そこで、Ni 二核錯体の赤色結晶を単離し、不斉 Nazarov 環化に利用した。その結果、83% ee で環化体が得られた(Scheme 14)。本結果より、X 線結晶構造解析により構造決定した Ni 二核錯体は、反応系中で用時調製した $Ni(NTf_2)_2$/(*S,S*)-ImQ 錯体と同様の選択性および反応性で不斉 Nazarov 環化を進行させることが明らかとなった。そのため、不斉 Nazarov 環化を進行させる活性触媒は Ni 二核錯体であると結論付けた。

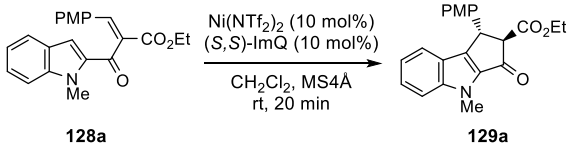
Scheme 14. Asymmetric Reaction Using Crystal of Ni Complex



128a **129a**

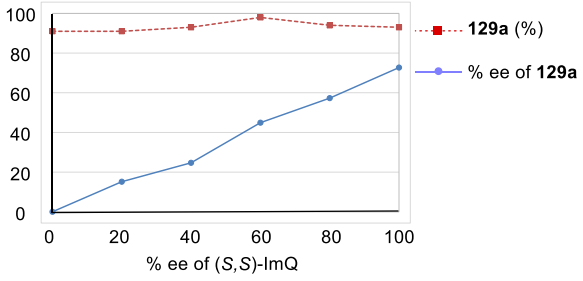
上記の検討結果より不斉反応には Ni 二核錯体が関与していることが判明した。しかしながら、本錯体を利用した不斉 Nazarov 環化において非線形効果は観測されなかった(Figure 13)。そのため、本実験結果より $M_2L_2^+$型の Ni 二核錯体が不斉 Nazarov 環化における活性触媒種であることを示す結果は得られなかった。

Figure 13. Non-linear Effects



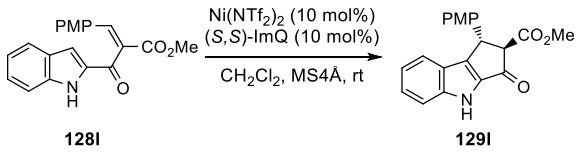
128a **129a**

entry	% ee of (*S,S*)-ImQ	yield (%)	% ee
1	100	94	73
2	80	94	57
3	60	98	45
4	40	93	25
5	20	91	15
6	0	91	0



一方、生成物のエナンチオ過剰率の経時変化を調べたところ、わずかながらエナンチオ過剰率が向上していっていた(Table 13)。本結果は生成した光学活性な環化体 **129l** が不斉反応の進行に関与していることを示唆しており、即ち Ni 錯体に環化体が配位した状態で新たな基質の不斉 Nazarov 環化が進行したと考えられる。M(N_4-L)X_2 型のような錯体では Ni の配位場はリガンドと基質によって埋められてしまうため、このような不斉増幅は観測されないと考えられる。そのため、本結果は二核錯体が不斉反応を進行させていることを示す結果であると考えられる。

Table 13. Chiral Amplification



128l **129l**

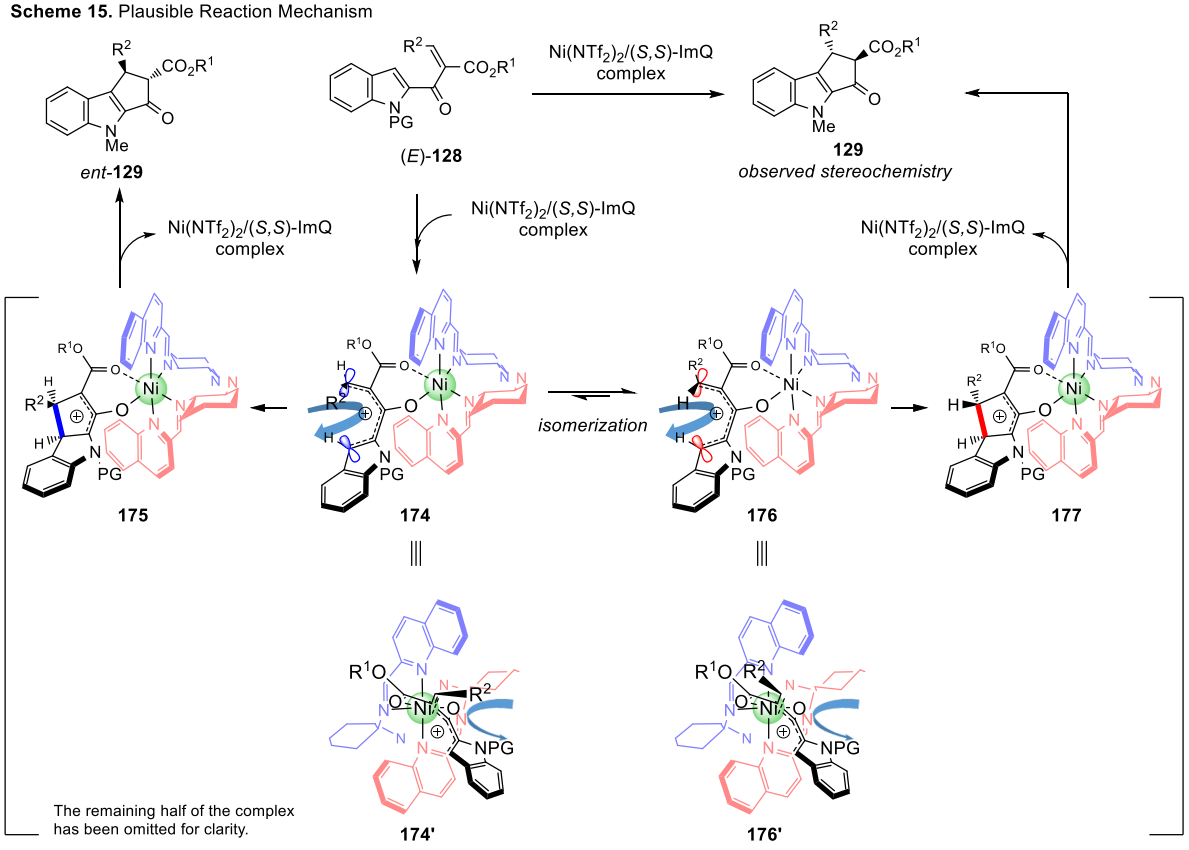
entry	time (min)	conversion (%)	% ee	entry	time (min)	conversion (%)	% ee
1	5	4	75	6	30	29	77
2	10	9	76	7	40	39	78
3	15	15	78	8	50	47	78
4	20	19	77	9	60	55	78
5	25	24	77	10	780	100	79

第二節；立体選択性発現機構の考察

1. エナンチオ選択的 Nazarov 環化

X 線結晶構造解析により明らかとなった Ni(NTf₂)₂/(*S,S*)-ImQ 錯体の構造情報をもとに、エナンチオ選択的 Nazarov 環化の反応メカニズムを考察した(Scheme 15)。前述のように、Ni(NTf₂)₂/(*S,S*)-ImQ 錯体に配位した基質は分子構造がねじれてプラスのヘリシティーを持った

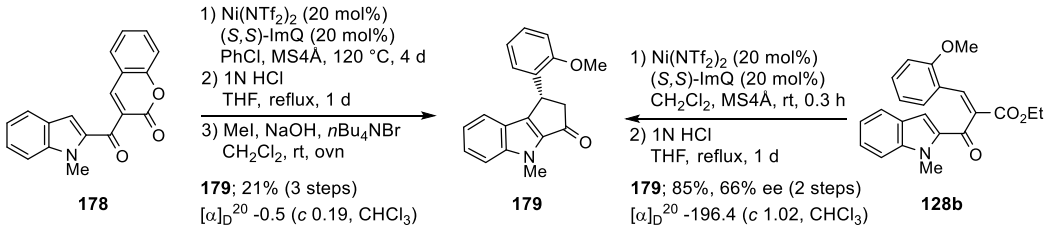
Scheme 15. Plausible Reaction Mechanism



コンフォメーション **174** をとると考えられる。その後、青で示した 2 つのローブが重なるように C-C 結合が形成されると **175** になる。この際、$Ni(NTf_2)_2$/(*S,S*)-ImQ 錯体は基質のねじれの向きを制御することで C-C 結合形成の向きを規定して、エナンチオ選択的に生成物を与えたと考察できる。しかしながら、本メカニズムではエナンチオ選択性が逆転し、*ent*-**129** を与えると推測される。そこで、反応系中において基質二重結合部位の異性化が進行していると考えた。

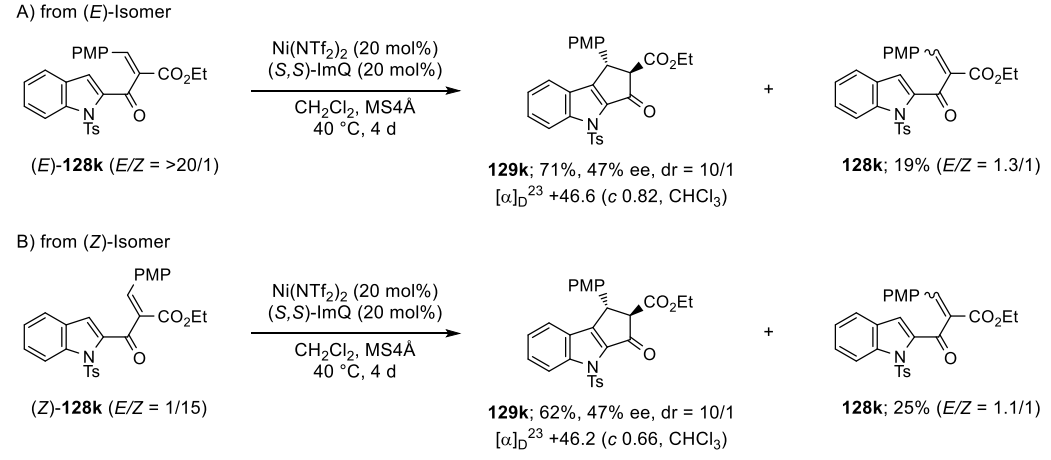
即ち、(*E*)-体のコンフォメーションである **174** からオレフィンの異性化が進行して、置換基 R^2 の向きが逆転した(*Z*)-体のコンフォメーション **176** となる。**176** においても基質はプラスのヘリシティーを持ったコンフォメーションをとると考えられる。その結果赤で示したローブが重なり、立体選択的に C-C 結合を形成することにより **177** となり、観測された生成物 **129** を与えたと考察した。(*Z*)-体のコンフォメーション **176** では、(*E*)-体のコンフォメーション **174** において生じるインドール環と置換基 R^2 との立体反発が解消されるため、C-C 結合形成が容易であると考えられる。

Scheme 16. Asymmetric Reaction Using Cyclic (*Z*)-Isomer



推定したメカニズムを検証するため、反応系中におけるオレフィンの異性化を実験的に確認することとした。(*Z*)-体に固定された環状化合物 **178** を不斉反応に付せば(*E*)-体のコンフォメーションからの結合形成が進行しなくなるため、エナンチオ選択性の向上が期待された。また、得られた生成物の絶対立体化学を(*E*)-体の基質 **128b** から得られた生成物 **179** と比較することで、反応系中におけるオレフィン異性化の有無が確認できると考えた。しかしながら **178** は反応性が低く、反応の進行には高温条件が必要であった。そのため、エナンチオ選択的に生成物を得ることはできなかった(Scheme 16)。

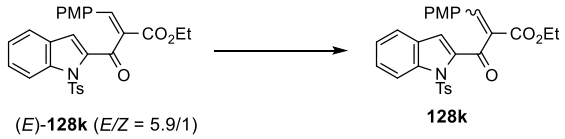
Scheme 17. Asymmetric Reaction from (*E*)- and (*Z*)-Isomer



そこで、(*E*)-および(*Z*)-体の基質 **128k** をそれぞれ不斉 Nazarov 環化の条件に付して、生成物の立体化学を比較することとした(Scheme 17)。その結果、いずれの異性体からも同じ絶対立体化学の環化体 **129k** が得られた。また、原料 **128k** は(*E*)-および(*Z*)-体のいずれを用いた際にも異性体混合物として回収された。このことから、$Ni(NTf_2)_2$/(*S,S*)-ImQ 触媒条件下においてオレフィンの異性化が進行していることが明らかとなった。

また、基質の異性化は Ni 触媒存在下において加速されていることも確認した(Table 14)。

Table 14. Isomerization Experiments Under Thermal and Lewis Acidic Conditions



entry	conditions	recovered **128k** (*E*/*Z*)
1	CH_2Cl_2, rt, 1 h	4.8/1
2	$Ni(NTf_2)_2$/(*S,S*)-ImQ (20 mol%)	1.1/1
	CH_2Cl_2, MS4Å, rt, 1 h	

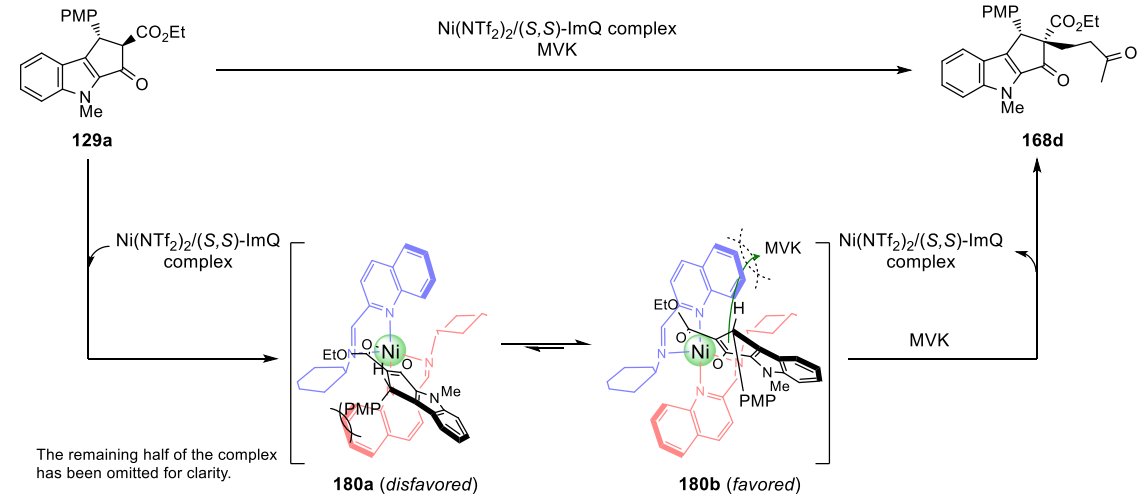
128k was quantitatively recovered in both cases.

2. ジアステレオ選択的 Michael 付加

先の検討において、$Ni(NTf_2)_2$ 触媒条件下に比べて $Ni(NTf_2)_2$/(*S,S*)-ImQ 触媒条件下では Michael 付加体 **168d** のジアステレオ選択性が低下していた(第一章、第四節)。そこで、Ni 二核錯体の構造情報を基に、Michael 付加におけるジアステレオ選択性についても考察した。

$Ni(NTf_2)_2$ 触媒条件下、**129a** の Michael 付加は PMP 基を避けるように求電子剤(MVK)が反応することで、ジアステレオ選択的に生成物が得られたと考えられる。一方、$Ni(NTf_2)_2$/(*S,S*)-ImQ 触媒条件下では **129a** は不斉 Ni 錯体に配位することでエノラートを生じる。この際、PMP 基と錯体中の赤で示したキノリン環との立体反発を避けるように **180b** のように配位していると考えられる。そのため、**180b** 中のエノラート *Si* 面が青で示したキノリン環と接近することで *Si* 面での MVK との反応が抑制され、生成物のジアステレオ選択性が低下したと考えられる(Scheme 18)。

Scheme 18. Plausible Reaction Mechanism



第三節；シクロヘキセン型リガンドが形成する錯体構造の考察

不斉四座配位 Schiff 塩基リガンドを種々検討する過程で、シクロヘキサンジアミン由来の ImQ(**139**)とシクロヘキセンジアミン由来の **150** が異なるエナンチオ選択性を持っていることが判明した(第一章、第二節)。このことから、両リガンドが Ni とそれぞれ異なる形式の錯体を形成していることが考えられた。そこで、$Ni(NTf_2)_2$/**150** 錯体の構造決定も試みることとした。

1. ESI-MS 解析

$Ni(NTf_2)_2$/ImQ 錯体同様、$Ni(NTf_2)_2$/**150** 錯体に関しても質量分析により溶液中に含まれる錯体を検出することとした。なお、$Ni(NTf_2)_2$/**150** 錯体は CH_2Cl_2 溶液中で沈殿物を生じなかったた

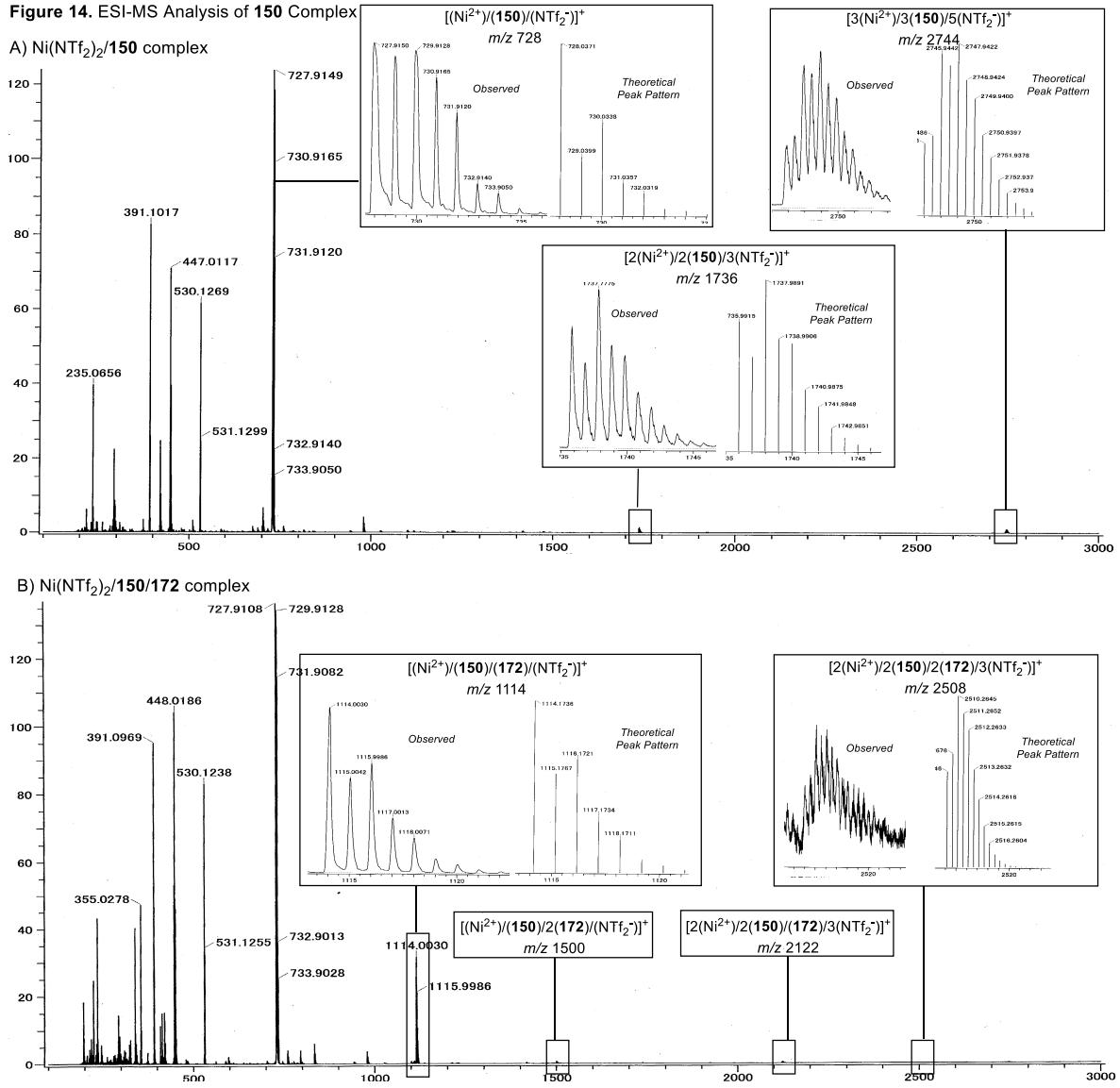


Figure 14. ESI-MS Analysis of **150** Complex

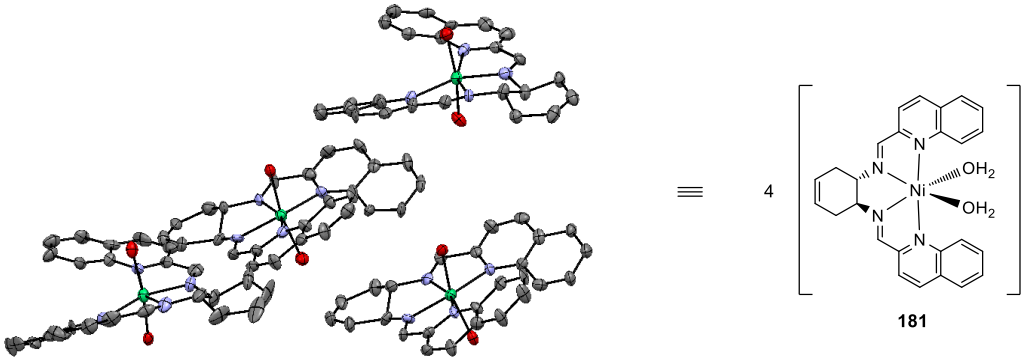
め、基質 **172** 添加前および添加後の両条件において ESI-MS 解析を行った(Figure 14)。

Ni(NTf$_2$)$_2$/**150** 錯体でも Ni(NTf$_2$)$_2$/ImQ 錯体同様、基質 **172** の添加前・添加後いずれの条件においても複数種のイオンピークが観測された。その中で二核錯体のイオンピークも観測されたが、基質添加後 *m/z* 2508 のピーク強度が極めて弱く、Ni(NTf$_2$)$_2$/ImQ 錯体とは異なり二核錯体が主として形成されていない、または二核錯体がより不安定であると推測した。しかしながら、ESI-MS 解析の結果から錯体構造を推測することは困難であったため、Ni(NTf$_2$)$_2$/**150** 錯体についても X 線結晶構造解析によりその構造を解明することとした。

2. X 線結晶構造解析

Ni(NTf$_2$)$_2$/**150** 錯体においてもダミー基質を添加した条件で錯体の結晶化を行うべく、種々の Nazarov 基質やβ-ジカルボニル化合物を添加した条件を検討したものの、X 線結晶構造解析に適した結晶は得られなかった。ここで、調製した Ni(NTf$_2$)$_2$/**150** 錯体の CH_2Cl_2 溶液にトルエンを添加したところ黄色針状結晶が析出した。得られた結晶の X 線結晶構造解析を行ったところ、M(*N*$_4$-L)X$_2$ 型錯体に 2 分子の水が配位した結晶であることが判明した(Figure 15)。錯体調製は乾燥剤を添加した条件で行っていたため、水分子はトルエン添加時に混入したものと考えられる。

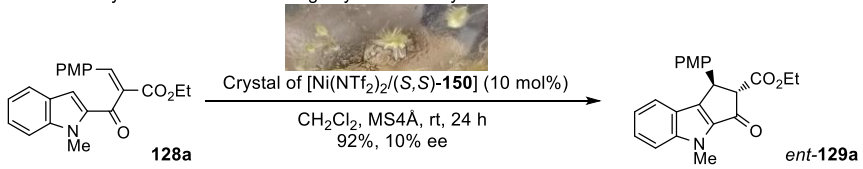
Figure 15. X-ray Crystallographic Analysis of Ni/**150** Complex



Hydrogen atoms and counteranions have been omitted for clarity. Ellispoids are drawn at the 30% probability level.

続いて、得られた結晶を不斉 Nazarov 環化に利用したところ、Ni(NTf$_2$)$_2$/(*S,S*)-**150** 錯体は Ni(NTf$_2$)$_2$/(*S,S*)-ImQ 錯体とは逆のエナンチオ選択性を持っていることが判明した(Scheme 19)。しかしながら、得られた生成物のエナンチオ過剰率はわずか 10% ee であり、反応系中で用時調製した錯体を利用した場合とは異なる結果となった(第一章、第二節)。そのため、本結果より Ni(NTf$_2$)$_2$/**150** 錯体の構造を決定するには至らなかった。

Scheme 19. Asymmetric Reaction Using Crystal of Ni Crystal

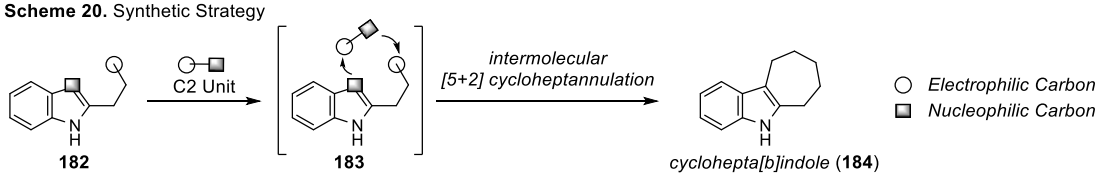


第三章；分子間[5+2]環化付加反応による 7 員環縮環インドールの合成

第一節；基質設計

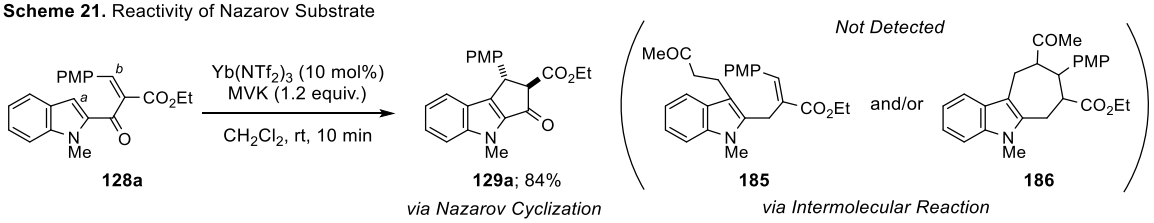
インドールは高い求核性を有する芳香族化合物であり、種々の求電子剤と反応する。そのため、側鎖に求電子炭素を有する **182** のようなインドール誘導体はドナー・アクセプター型の 5 炭素ユニットとして利用可能であり、分子間反応により 7 員環構築が可能であると考えた(Scheme 20)。

Scheme 20. Synthetic Strategy



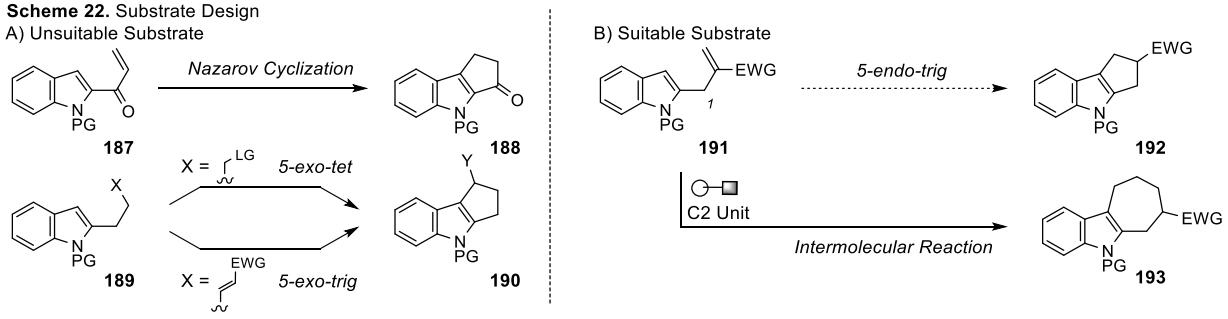
ここで、Nazarov 環化で利用していた基質 **128** に着目すると、分子内にインドールに由来する求核性炭素(C_a)と側鎖に由来する求電子炭素(C_b)が含まれていることが分かる。そのため、Nazarov 基質はドナー・アクセプター型 5 炭素ユニットとして機能すると考えた。しかしながら、Nazarov 基質 **128a** は Lewis 酸触媒条件下において速やかに Nazarov 環化が進行し、分子間反応へ適用することは困難であった(Scheme 21)。そこで、分子内反応の進行を抑制し、7 員環縮環インドール合成へ利用可能な基質の設計を行った。

Scheme 21. Reactivity of Nazarov Substrate



Baldwin 則に従うと、*5-endo-trig* 環化の進行は不利であるとされている。そこで、**191** のような化合物を基質として設計した(Scheme 22, B)。**191** は側鎖 1 位にカルボニル基を持たないため Nazarov 環化は進行せず、同時に Nazarov 基質に比べてインドール 3 位の求核性が向上しているため、種々の求電子剤との反応が可能であると考えられる。

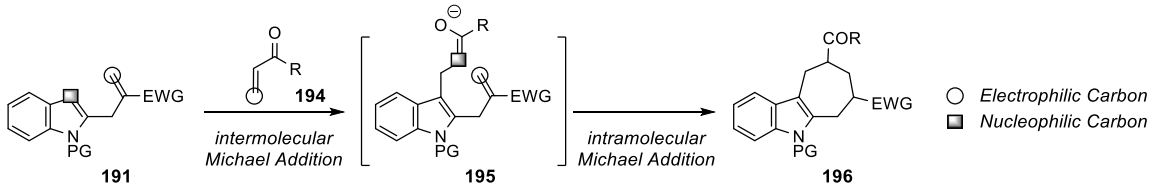
Scheme 22. Substrate Design



第二節；エノンを利用した 7 員環形成反応の検討

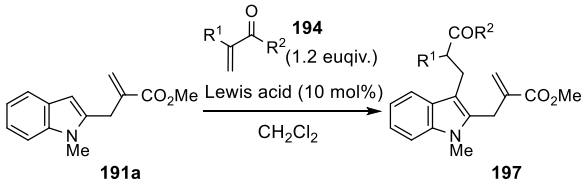
不飽和カルボニル化合物はカルボニルβ位において、種々の求核剤と共役付加反応が進行する。一方、反応により生じた飽和カルボニル化合物はエノラートを経由して種々の求電子剤と反応する。即ち、不飽和カルボニル化合物はドナー・アクセプター型の 2 炭素ユニットとして利用可能であると考えられる。2 炭素ユニットとしてエノンを利用するとインドール基質 **191** との分子間 Michael 付加が進行し、その後生じたエノラート **195** による分子内 Michael 付加により 7 員環構築が可能であると考えた(Scheme 23)。

Scheme 23. 7-Membered Ring Construction Using Enone



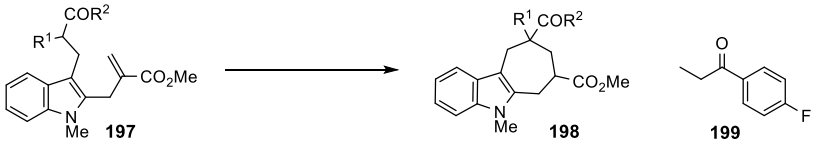
Lewis 酸触媒条件下でのインドール **191a** とエノンとの反応を行ったところ、想定通り **191a** の分子内 5 員環形成反応の進行は確認できなかった。MVK (**194a**)は Ni 触媒条件下容易にインドール **191a** と反応し、Michael 付加体 **197a** を与えた。一方、一置換エノン **194b** は MVK に比べて反応性が低く、反応の進行に加熱を要した(Table 15)。

Table 15. Intermolecular Michael Addition to Enone



entry	enone	Lewis acid	conditions	yield (%)
1	R^1 = H, R^2 = Me (**194a**)	$Ni(NTf_2)_2$	rt, 1 h	99
2	R^1 = Me, R^2 = *p*-F-C_6H_4 (**194b**)	$Yb(NTf_2)_3$	40 °C, 14 h	82

Table 16. Cyclization from Michael Adducts

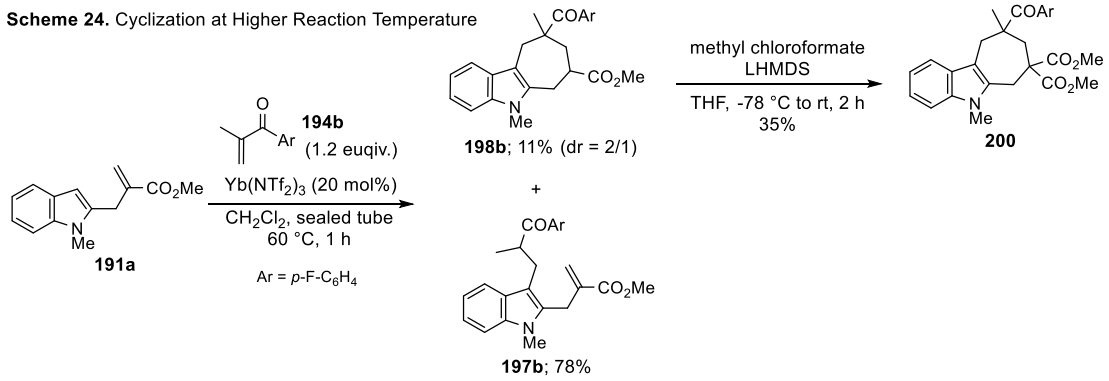


entry	substrate	conditions	results
1	**197a**	*t*BuOK (1 equiv.), THF, rt, 1 h	decomp.
2	**197a**	$Ni(NTf_2)_2$ (10 mol%), K_2CO_3 (1 equiv.), CH_2Cl_2, rt to 60 °C, 2 d	N.R.
3	**197a**	NEt_3, THF, 60 °C, 2 d	N.R.
4	**197b**	*t*BuOK (1 equiv.), THF, rt, 1 h	decomp.
5	**197b**	NEt_3 (1 equiv.), NiCl (50 mol%), CH_2Cl_2, rt to 60 °C, sealed tube, 2.5 d	N.R.
6	**197b**	$Al(O\textit{i}Pr)_3$ (1 equiv.), THF, rt to 60 °C, 15 h	N.R.
7	**197b**	$Yb(NTf_2)_3$ (10 mol%), CH_2Cl_2, 40 to 60 °C, sealed tube, 20 h	**197b**; 90%
8	**197b**	$Yb(NTf_2)_3$ (10 mol%), NEt_3 (20 mol%), CH_2Cl_2, 40 to 60 °C, sealed tube, 21 h	N.R.
9	**197b**	$Yb(NTf_2)_3$ (10 mol%), NaH (50 mol%), CH_2Cl_2, 40 to 60 °C, sealed tube, 19 h	**197b**; 89%
10	**197b**	HCl (3 equiv.), 1,2-DCE, 60 to 100 °C, sealed tube, 37 h	**197b**; 85%
11	**197b**	$Yb(NTf_2)_3$ (10 mol%), HCl (1 equiv.) 1,2-DCE, 60 °C, sealed tube, 14 h	**197b**; trace, **199**; 58%

次に、得られた付加体 **197** から環化体 **198** への変換を検討した。種々の酸性・塩基性条件下にて反応を検討したが、原料回収又は基質の分解が進行するのみで **198** は得られなかった(Table 16)。entry 11 ではケトン **199** が得られたがインドールに由来する化合物は分解しており、単離されなかった。以上の結果より、付加体 **197** から 7 員環形成反応を進行させることは困難であると結論付けた。

ここで、**197b** の合成(Table 15, entry 2)を行う際に 60 ℃まで昇温した条件で反応を行ったところ、**197b** と共に環化体 **198b** が得られた。エノンとの反応により環化体が得られることが判明したため、反応条件の検討を行うこととした。なお、環化体 **198b** は分離困難な異性体混合物として得られたため、ジエステル **200** へと変換した後に構造決定を行った(Scheme 24)。

Scheme 24. Cyclization at Higher Reaction Temperature



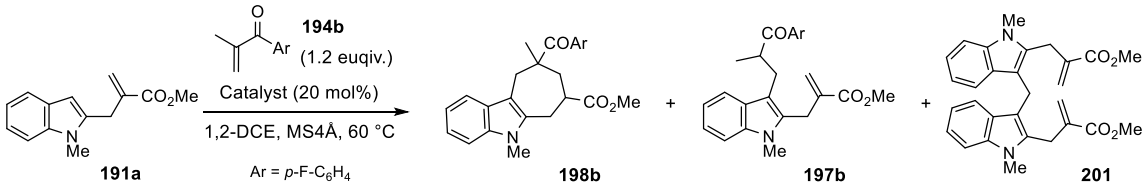
第三節；条件検討

反応条件の検討を行うにあたり水の影響を調べたところ、含水条件では環化体 **198b** が得られずに付加体 **197b** がほぼ定量的に得られた。そこで、乾燥剤(MS4Å)を添加した条件で種々の酸触媒を検討した(Table 17)。

$Yb(NTf_2)_3$ を用いた際には環化体が 26%で得られたのに対し、$Yb(OTf)_3$ を触媒として用いたところ反応が進行しなかったため、本反応には強い Lewis 酸が必要であると考えた(entries 1, 2)。そこで、種々の金属 NTf_2 塩を検討したところ、Mn, Fe, Co 塩を用いた際に 20%前後の収率で **198b** が得られた(entries 3~10)。一方、Lewis 酸性の強い $AlCl_3$, $TiCl_4$, BF_3･OEt_2 では環化体は得られなかった(entries 11~13)。Brønsted 酸についても検討したものの、付加体 **197b** を与えるのみであった(entries 14, 15)。

種々の触媒を検討したものの、いずれの条件においても主生成物として付加体 **197b** が得られる結果となった。ここで、望みの環化体 **198b** を与えた触媒[$Yb(NTf_2)_3$, $Mn(NTf_2)_2$, Fe $(NTf_2)_2$, $Co(NTf_2)_2$]を比べると、Co 塩はジアステレオ選択性が高く、副生成物 **201** の形成量が少なかっ

Table 17. Catalyst Screening

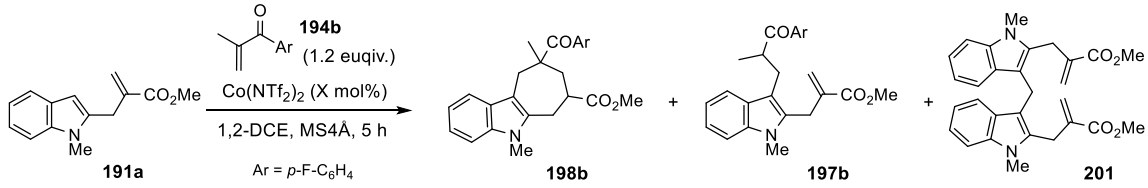


entry	Catalyst	time (h)	**198b** (%)	**197b** (%)	**201** (%)	recov. (%)
1	$Yb(NTf_2)_3$	5	26 (dr = 1.1/1)	36	10	23
2	$Yb(OTf)_3$	24	0	0	0	quant.
3	$Al(NTf_2)_3$	24	2 (dr = 2/1)	28	3	59
4	$In(NTf_2)_2$	5	5 (dr = 2/1)	89	0	6
5	$Mn(NTf_2)_2$	5	18 (dr = 1.7/1)	63	0	6
6	$Fe(NTf_2)_2$	5	17 (dr = 1.4/1)	57	0	0
7	$Co(NTf_2)_2$	5	23 (dr = 2.5/1)	51	3	4
8	$Ni(NTf_2)_2$	5	4 (dr = 1.4/1)	66	trace	11
9	$Cu(NTf_2)_2$	5	0	15	7	59
10	$Zn(NTf_2)_2$	5	4 (dr = 3.3/1)	81	0	0
11	$AlCl_3$	1	trace	90	0	trace
12	$TiCl_4$	1	0	66	0	0
13	BF_3•OEt_2	5	0	21	0	59
14	HCl	24	0	12	0	77
15	TFA	24	0	37	0	50

た。そこで、Co 塩を触媒として用いて更なる条件検討を行った(Table 18)。

反応温度を 80 ℃まで昇温したところ、環化体の収率が 51%まで向上した(entry 2)。そこで、反応を封管中およびマイクロウェーブ照射条件でも検討したが、これらの条件では付加体 **197b** が主生成物として得られた(entries 3, 4)。続いて、ラジカル反応の進行を考慮し、BHT を添加して反応性の変化を調査したが、entry 2 の結果と比較して大きな変化は見られなかった(entry 5)。そのため、本反応ではラジカルは生成していないと判断した。なお、付加体 **197b** の収率が増加した理由としては、BHT が Brønsted 酸として作用したことが考えられる。試薬の当量を検討したところ、触媒は 10 mol%まで減じても 20 mol%用いた際と同等の結果を与えた。一方、エノン **194b** を 2 当量まで増やしても環化体 **198b** の収率向上にはつながらなかった(entries 6, 7)。

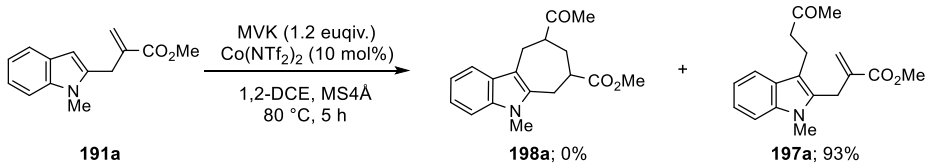
Table 18. Conditions Screening under Co Catalysis



entry	Co cat. (X mol%)	conditions	**198b** (%)	**197b** (%)	**201** (%)	recov. (%)
1	20	60 °C	23 (dr = 2.5/1)	51	3	4
2	20	80 °C	51 (dr = 2.5/1)	26	5	4
3	20	80 °C, sealed tube	8 (dr = 1.7/1)	70	4	2
4	20	80 °C, microwave	14 (dr = 2.5/1)	58	4	3
5	20	80 °C, BHT (20 mol%)	41 (dr = 2.5/1)	45	6	8
6	10	80 °C	49 (dr = 2.5/1)	27	trace	16
7	10	80 °C, using 2 equiv. of **194b**	51 (dr = 2.5/1)	25	0	trace

本手法は 4 級炭素を含む 7 員環構築を可能とする手法であるが、4 級炭素構築が困難であるために環化体の収率が中程度にとどまっていることが懸念された。そこで、エノンとして MVK を用いることで環形成時の立体障害が緩和されて環化体の収率が向上すると考えた。しかしながら、MVK を用いたところ環化体は得られず、付加体 **197a** が 93%で得られるのみだった(Scheme 25)。

Scheme 25. Examination of Cyclization Using MVK

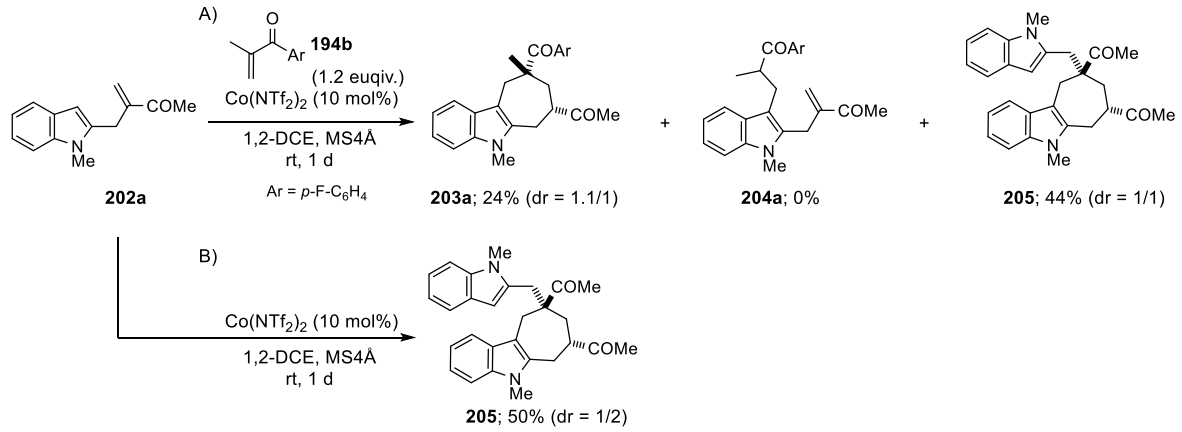


191a **198a**; 0% **197a**; 93%

第四節；ケトン側鎖を持つインドール誘導体を用いた検討

これまでの検討では付加体 **197** が形成されたため、環化体 **198** の収率は中程度にとどまっていた。付加体 **197** からの環形成は進行しなかったものの、高温条件下において環化体が得られたことから、インドール側鎖の不飽和エステルに対する Michael 付加の進行に高い活性化エネルギーを要していると推定した。そのため、インドール側鎖オレフィンの求電子性が向上すれば、7 員環形成が効率的に進行すると考えた。そこで、側鎖の不飽和エステル部位をエノンへと変更することで反応性の改善を図った。

Scheme 26. Cyclization of Enone Type Indole Substrate



202a **203a**; 24% (dr = 1.1/1) **204a**; 0% **205**; 44% (dr = 1/1)

205; 50% (dr = 1/2)

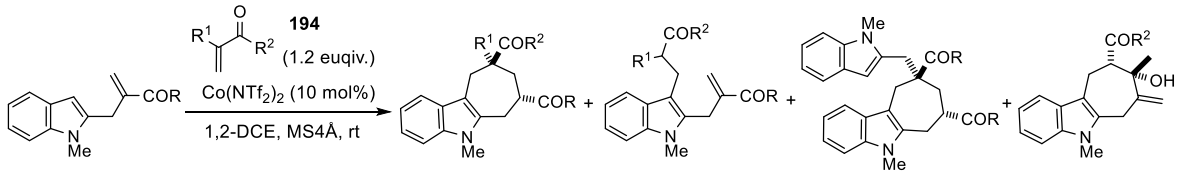
エノン側鎖を持つインドール誘導体 **202a** を反応に付したところ、室温で環化反応が進行し、**203a** が 24%で得られた。さらにこの際、付加体 **204a** は得られなかった(Scheme 26, A)。本結果より、環形成の促進にはインドール側鎖の求電子性を向上させることが有効であることが判明した。しかしながら、**202a** を用いた際には望みの環化体 **203a** に加えて二量化した環化体 **205** が同時に得られた。これは、エノン **194b** のみでなくインドール **202a** の側鎖構造が 2 炭素ユニット

として作用したことで、**203a** および **205** の両環化体が得られたと考えられる。そこで、エノン **194** を添加せずに二量体形成を行ったところ、**205** が 50%で得られた(Scheme 26, B)。

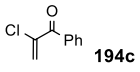
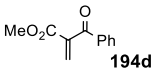
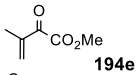
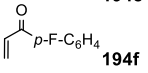
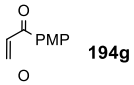
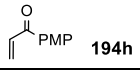
次に、より Michael 受容体としての活性が高い 2 炭素ユニットを利用することで二量体形成の抑制を図った。電子求引性基としてハロゲンを導入した **194c** を用いた際には環形成が進行せず、付加体 **204b** のみが得られた(Table 19, entry 1)。また、β-ケトエステル **194d** は触媒金属に二座配位し、選択的に活性化されることで反応が選択的に進行すると期待したが、付加体 **204c** が得られるのみで望みの環化反応は進行しなかった(entry 2)。α-ケトエステルも同様に触媒金属への二座配位が期待できるが、二量化体 **205** のみを与えた。**194e** は不安定であり、反応系中で速やかに分解したことが考えられた(entry 3)。

無置換エノンを用いたところ、付加体 **204** がわずかに得られたものの二量化が抑制され、**203** が中程度の収率で得られた。しかしながら、望みの 1,4-付加体である **203** とともに 1,2-付加体 **206** が得られたため、選択的に **203** を得ることができなかった(entry 4, 5)。そこで、1,2-付加体の形成を抑制するために、インドール側鎖のケトン部位を嵩高くした **202b** を反応に利用した。その結果、想定通り 1,2-付加体の形成は抑制されたものの、**203g** の収率は 29%にとどまった(entry 6)。

Table 19. Suppression of Dimerization



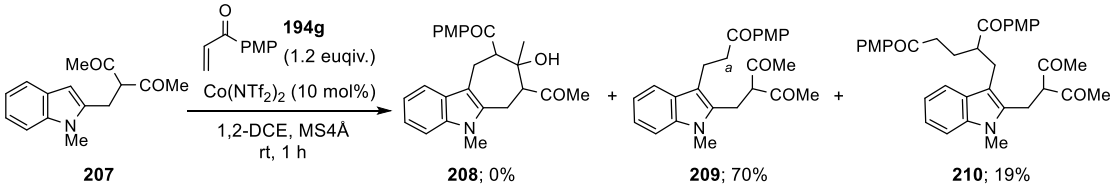
202 **203** **204** **205**; 0% **206**

entry	R	enone **194**	time (h)	**203** (%)	**204** (%)	**205** (%)	**206** (%)	recov. (%)
1	Me (**202a**)	 **194c**	2	0	37	0	0	5
2	Me (**202a**)	 **194d**	1	0	41	0	0	0
3	Me (**202a**)	 **194e**	24	0	0	28 (dr = 3/1)	0	0
4	Me (**202a**)	 **194f**	2	42 (dr = 3.3/1)	4	0	24	3
5	Me (**2021**)	 **194g**	2	49 (dr = >20/1)	7	0	15	13
6	Ph (**202b**)	 **194h**	2	29 (dr = 15/1)	13	0	0	24

一方、1,2-付加体を選択的に得る目的で、ジケトン **207** を反応に付したが、環化反応は進行しなかった(Scheme 27)。2 分子のエノンが反応した **210** が得られたことから **209** の C_a からの求核反応が進行したことが確認できた。しかしながら環化体は得られなかったため、インドール側鎖

にオレフィンが導入されることにより、環形成が進行しやすくなっていると考えられる。

Scheme 27. Reaction of β-Dicarbonyl Compound

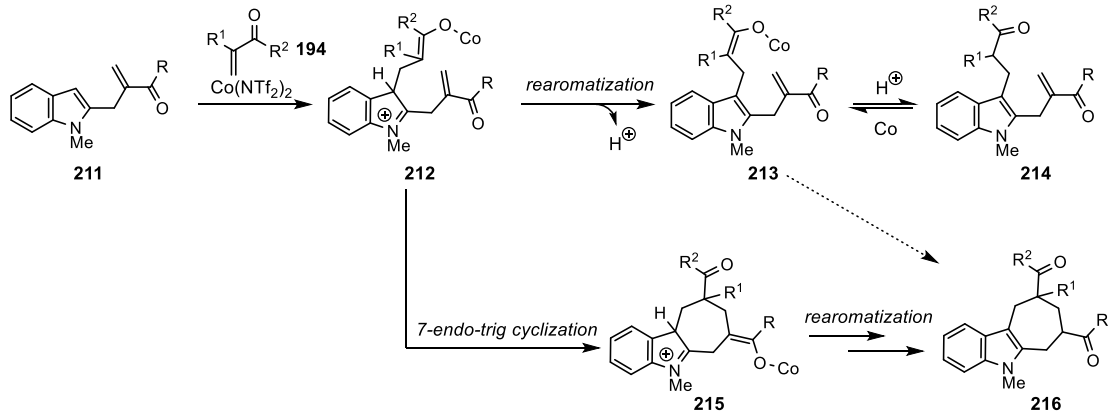


第五節；エノンを利用した 7 員環形成反応における反応メカニズムの考察

1. 1,4-環化体 **198**, **203**, **205**

これまでの検討の結果、付加体からの環形成が進行しないことが判明した。そのため、1,4-環化体は付加体を経由せずに形成されたと考えられる。インドール **211** とエノンとの Michael 付加により得られるインドレニン **212** は、再芳香化することでエノラート **213** となる。しかし、**214** から **216** への反応が進行しなかったことから、環形成はインドレニン **212** から進行したと考察した。インドレニン **212** の *7-endo-trig* 環化により **215** が形成された後、再芳香化することで 1,4-環化体 **216** が得られたと考えられる(Scheme 28)。

Scheme 28. Plausible Reaction Pathway



なお、得られた環化体の相対立体化学は X 線結晶構造解析および NOE 相関により決定した(Figure 16, 17)。

Figure 16. Determination of Stereochemistry

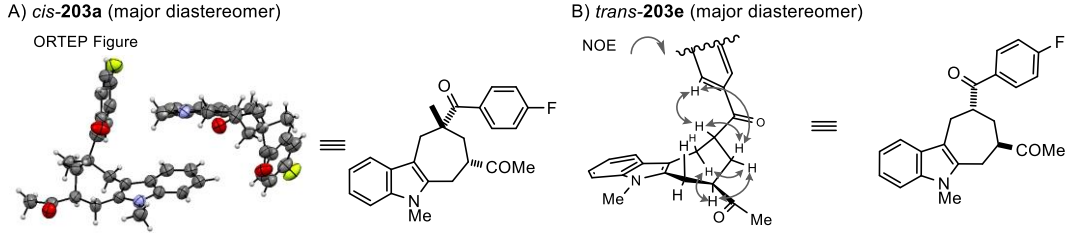
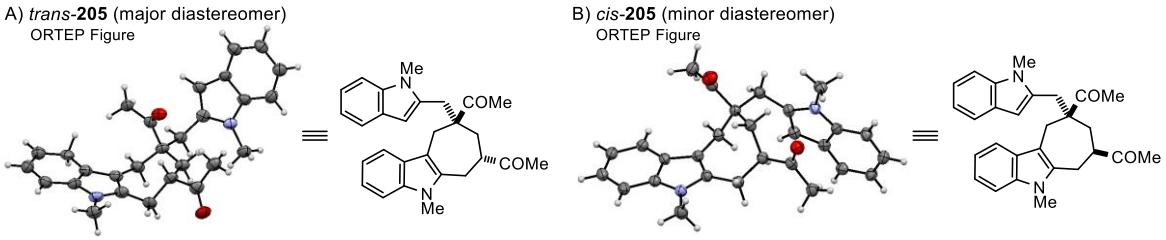


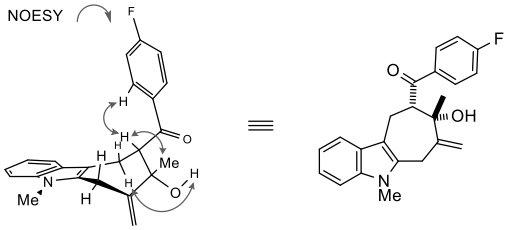
Figure 17. Determination of Stereochemistry



2. 1,2-環化体 **206**

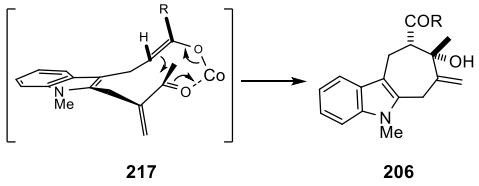
1,2-環化体 **206** の立体化学は NOESY により決定した(Figure 18)。ここで **206** の配座に着目すると、カルボニル酸素が分子内の水酸基と水素結合を形成する配座をとっていると考えられた。このことから、2 つのカルボニル酸素が Co に配位した環状遷移状態 **217** を経由して C-C 結合が形成されたため、1,2-環化体 **206** が単一ジアステレオマーとして得られたと推定した(Figure 19)。

Figure 18. Determination of Stereochemistry



206a' **206a**

Figure 19. Plausible Transition State

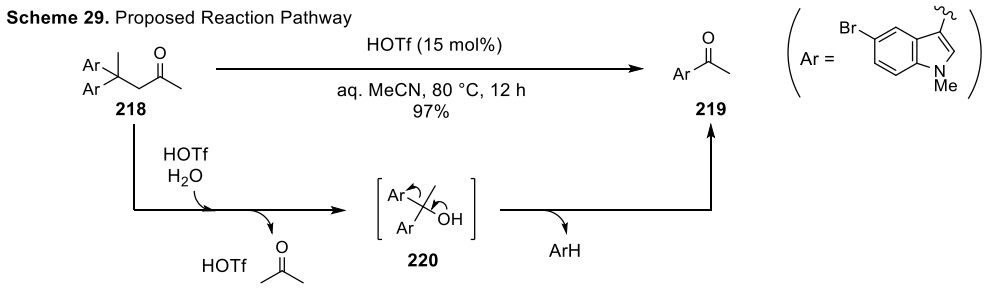


217 **206**

3. ビスインドリルメタン **201**

これまでに、1,3-ジカルボニルユニットを脱離基としたビスおよびトリスアリールメタン誘導体の合成は複数報告されてきた。[23] また、Li らは HOTf 触媒条件下、ケトンの脱離に伴うアシルインドールの合成を報告している(Scheme 29)。[24] そのため、著者の反応系で得られたビスインドリルメタン **201** も同様の機構で形成されたと考えられる。

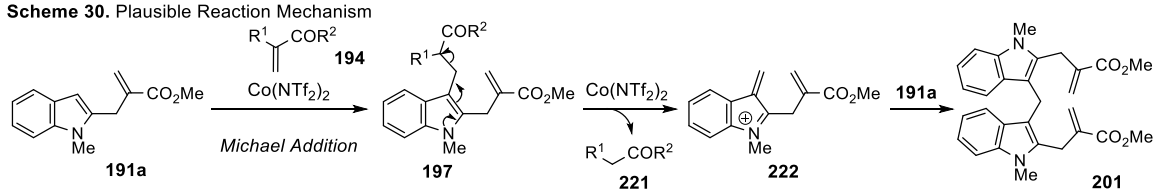
Scheme 29. Proposed Reaction Pathway



即ち、**191a** とエノン **194** との Michael 付加により **197** となった後、Lewis 酸によりケトンが活性化されることでケトン **221** の脱離を伴い中間体 **222** を生じる。その後、もう一分子の **191a**

が中間体 **222** と反応することでビスインドリルメタン **201** を形成したと考えられる(Scheme 30)。

Scheme 30. Plausible Reaction Mechanism



第六節；アルキンを用いる 7 員環形成反応の検討

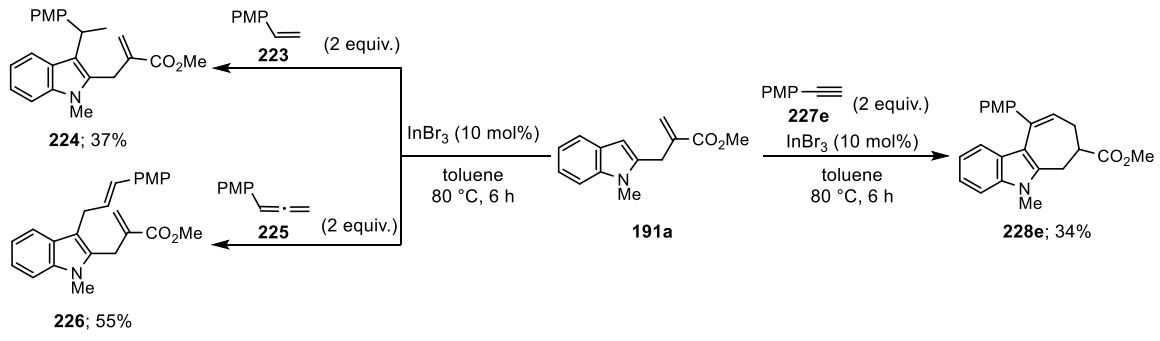
エノンを利用した 7 員環形成反応は反応の選択性の制御が困難であり、望みの環化体は中程度の収率で得られるにとどまった。そこで、新たな 2 炭素ユニットを検討することとした。

炭素-炭素多重結合は 2 炭素ユニットとして様々な環化反応に利用されており、著者の所属研究室でも多重結合を利用した環化反応を報告してきた。[25] そこで、炭素-炭素多重結合を 2 炭素ユニットとして利用した分子間[5+2]環化付加反応による 7 員環縮環インドール合成を試みることとした。

インドール **191a** を利用した 7 員環形成反応においては先のエノンを利用した検討と同様に、まずインドール **191a** と 2 炭素ユニットとの Friedel-Crafts 反応が進行すると考えられる。著者はここで、In(III)に着目した。In(III)は多様な官能基を活性化する Lewis 酸触媒として、Friedel-Crafts 反応によるアルキル化、アシル化、アルケニル化等を進行させることが報告されてきた。また、毒性が低く、安定性や水への許容性が高いことから Friedel-Crafts 反応のみならず様々な反応に利用されてきた触媒である。[26,27] そこで、$InBr_3$ 触媒条件下、代表的な炭素-炭素多重結合であるアルケン、アルキンおよびアレンと **191a** との反応を検討した(Scheme 31)。

アルケンおよびアレンを用いた際には Friedel-Crafts 付加体がそれぞれ 37%、55%で得られた。一方アルキンを用いたところ、環化反応が進行して **228e** が 34%で得られた。そこで、アルキンを 2 炭素ユニットとして利用した 7 員環構築反応の検討を行うこととした。

Scheme 31. Indium Catalyzed Reaction of C-C Multiple Bonds



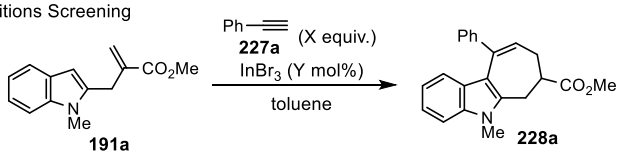
第七節；反応条件の最適化検討

反応条件の検討を行うにあたり、入手容易なフェニルアセチレン(**227a**)を 2 炭素ユニットとして利用することとした。

1. 反応温度と試薬の当量

反応温度を検討したところ、80 ℃では良好な反応性および収率で環化体が得られた。しかし、60 ℃まで反応温度を低下させると反応性が大幅に低下し、収率も 78%に低下した(Table 20, entries 1~3)。続いて、試薬の当量に関して調査を行った。触媒は 5 mol%まで減じても反応性や生成物の収率に大きな変化は見られなかった(entries 4~6)。一方、アルキンを 1.2 当量まで減じると原料残存量が増加した(entries 6, 7)。アルキンは反応条件において重合等の副反応が進行すると考えられ、過剰量の添加が必要であると判断した。

Table 20. Conditions Screening

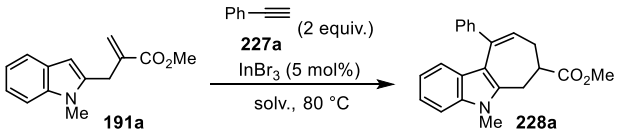


entry	**227a** (X equiv.)	$InBr_3$ (Y mol%)	temp. (°C)	time (h)	yield (%)	recov. (%)
1	4	20	110	1	85	0
2	4	20	80	3	90	trace
3	4	20	60	24	78	3
4	4	10	80	6	86	5
5	4	5	80	6	87	6
6	2	5	80	6	85	7
7	1.2	5	80	6	63	26

2. 反応溶媒

PhCl を溶媒とした際にはトルエンと同等の結果を与えた(Table 21, entries 1, 2)。一方、1,2-DCE や極性溶媒を用いた際には環化体の収率が大幅に低下した(entries 3~6)。そのため、本反応には芳香族系溶媒が適していると判断した。

Table 21. Solvent Screening



entry	solvent	time (h)	yield (%)	recov. (%)
1	toluene	6	85	7
2	PhCl	7	83	7
3	1,2-DCE	24	32	28
4	$MeNO_2$	24	7	74
5	MeCN	24	20	68
6	EtOH	24	0	83

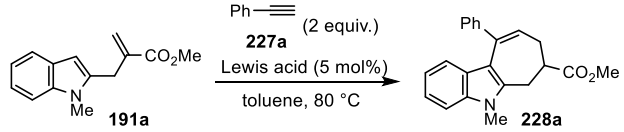
3. Lewis 酸触媒

InI_3 は $InBr_3$ よりも触媒活性が高く、反応時間が短縮されるとともに環化体の収率も 89%に向

上した。一方、$In(OTf)_3$では反応性・収率共に低下した(Table 22, entries 1~3)。次に In と同族元素である Ga 塩を検討したところ、GaI_3を用いた際にも環化体が得られたが InX_3 よりも触媒活性が低かった(entry 4)。$GaCl_3$は低温条件下、Friedel-Crafts アルケニル化を進行させることが報告されていた。[28]そこで、$GaCl_3$を用いて室温で反応を行った。しかしながら、$GaCl_3$は触媒として作用せずに反応が途中で停止してしまい、環化体の収率は 7%であった(entry 5)。そこで、$GaCl_3$の Friedel-Crafts アルケニル化で用いられていた CH_2Cl_2 溶媒中、1 当量の $GaCl_3$ を用いて反応を行ったところ、0 ℃でも反応は円滑に進行して **228a** が 64%で得られた(entry 6)。温和な条件下での反応が可能であったものの、$GaCl_3$は環化体を中程度の収率で与えるにとどまったため、これ以上の検討は行っていない。

アルキンの活性化剤として Au を利用した反応は数多く知られている。[29]そこで Au を触媒とした条件を検討したところ、$AgSbF_6$ と組み合わせて用いることで環化反応が進行することが判明した(entries 7, 8)。しかし、24 時間経過後でも反応が完結しなかったことから、InI_3の方が本反応に適していると判断した。その他にも Friedel-Crafts アルケニル化に利用される Lewis 酸を検討したが、環化体は得られなかった(entries 9~11)。

Table 22. Screening of Lewis Acid



entry	Lewis acid	time (h)	yield (%)	recov. (%)
1	$InBr_3$	6	85	7
2	InI_3	5	89	4
3	$In(OTf)_3$	6	15	69
4	GaI_3	6	64	24
5[a]	$GaCl_3$	22	7	93
6[b]	$GaCl_3$	1	61	9
7	$(PPh_3)AuCl$	6	0	95
8	$(PPh_3)AuCl/AgSbF_6$	24	64	17
9	$FeCl_3$	6	0	85
10	$FeCl_3$/3AgOTf	6	0	78
11	$Pd(OAc)_2$	6	0	93

[a]Reaction was carried out at room temperature.
[b]Reaction was carried out at 0 °C using 100 mol% of Lewis acid in CH_2Cl_2.

種々検討の結果、InI_3が触媒として最も適していると判断した。なお、上記の検討において反応終了後にも原料が残存していたため、基質検討を行うにあたりアルキンを 4 当量、InI_3 を 10 mol%用いることとした。

第八節；基質一般性の検討

基質一般性を検討するにあたり、まず種々のアルキンとの反応を行った(Table 23)。

1. 芳香環置換末端アルキン

反応点近傍に立体障害を持つ o-トリルアセチレン(**227b**)を用いた際には反応を完結させるために昇温する必要があった。そのため、基質オレフィンの異性化が進行した **229** が得られたが、ベ

ンゼン環上の置換基の位置に関わらず芳香環置換アルキンは高収率で環化体を与えた(entries 1~4)。次に置換基の電子的効果を検討したところ、電子求引性基を持つアルキンは高収率で環化体を与えたものの、電子供与性基が導入された **227e** を用いた際に収率が低下した(entries 5~7)。これはアルキンの反応性が高かったために、アルキンの分解等が進行した結果であると考えられる。ヘテロ芳香環置換アルキンも本反応に適用可能であり、環化体がいずれも良好な収率で得られた(entries 8~11)。

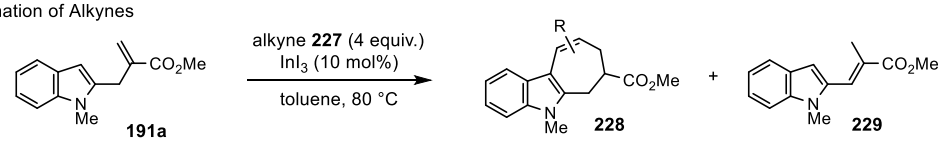
2. アルキル基およびヘテロ原子置換末端アルキン

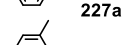
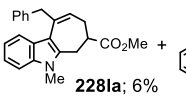
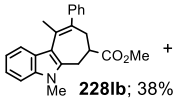
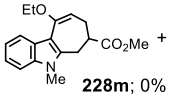
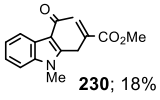
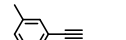
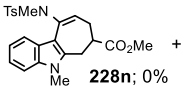
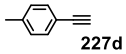
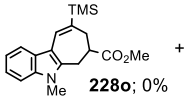
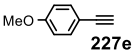
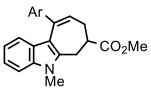
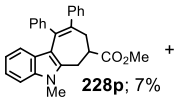
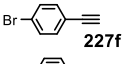
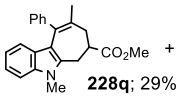
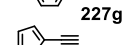
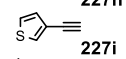
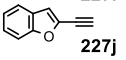
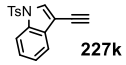
アルキル基が置換したアルキンは芳香環置換アルキンに比べて反応性が低かったため 100 ℃まで昇温する必要があったが、アルキル基置換アルキンを用いた際にも環化体が得られた。しかしながら、想定した環化体 **228la** の収率はわずか 6%であり、4 置換オレフィン構造を持つ **228lb** が主生成物として得られた(entry 12)。ヘテロ原子が置換したアルキンも検討したが、いずれの場合にも環化体は得られなかった(entries 13~15)。

3. 内部アルキン

内部アルキンは末端アルキンに比べて反応性が低く、反応の進行にはより高い反応温度を要した。それゆえインドール基質 **191a** のオレフィン異性化が優先的に進行し、**229** が主生成物として得られた。その結果、環化体は低収率で得られる結果となった(entries 16, 17)。

Table 23. Examination of Alkynes



entry	alkyne	time (h)	products		entry	alkyne	time (h)	products	
1	 **227a**	5		92%	12[a]	 **227l**	24	 **228la**; 6% +  **228lb**; 38%	+ **229**; trace
2[a]	**227b**	24		86% + **229**; 6%	13[c]	**227m**	24	 **228m**; 0% +  **230**; 18%	
3	 **227c**	6		96%	14	**227n**	21	 **228n**; 0%	+ **229**; 31%
4	 **227d**	6		82%	15[a]	**227o**	72	 **228o**; 0%	+ **229**; 67%
5	 **227e**	10	 **228a~k**	51%	16[a]	**227p**	72	 **228p**; 7%	+ **229**; 61%
6	 **227f**	4		95%	17[a]	**227q**	72	 **228q**; 29%	+ **229**; 56%
7	 **227g**	4		89%					
8	 **227h**	10		74%					
9	 **227i**	10		72%					
10	 **227j**	4		66%					
11[b]	**227k**	5		72%					

[a]Reaction was carried out at 80 to 100 °C. [b]Reaction was carried out using 2 equiv. of alkyne. [c]Reaction was carried out at room temperature.

次に種々のインドール誘導体を用いた 7 員環形成反応を検討した(Table 24)。

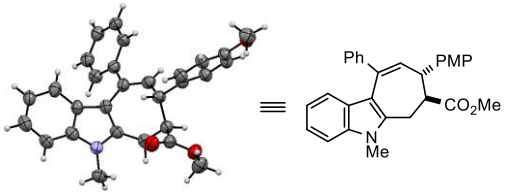
1. インドール窒素の保護基

インドール窒素の保護基として電子供与性の Bn を用いたところ、**228r** が高収率で得られた。また、無保護の基質に関しても反応性に大きな変化はなく、**228s** が 80%で得られた(entries 2, 3)。一方、電子求引性の保護基(Ts)を導入した基質では反応が全く進行せず、原料 **191d** が定量的に回収された(entry 4)。

2. 側鎖オレフィン上の置換基

側鎖に置換基(R)を導入した基質も良好な収率で環化体を与えた。しかしながら、エステルβ位での C-C 結合形成が阻害されたため反応時間が延長した。特にアルキル基を導入した基質 **191g** は反応性が低く、72 時間経過後でも中間体であるアルケニルインドール **231w** が残存していた(entries 5~7)。なお、環化体は高ジアステレオ選択的に得られ、その立体化学は X 線結晶構造解析の結果から *trans* 体であると判明した(Figure 20)。

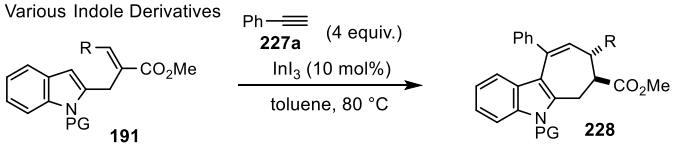
Figure 20. X-Ray Crystallographic Analysis of **228u**

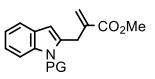
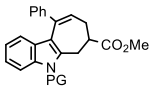
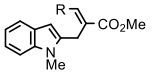
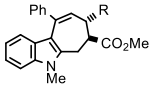
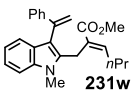
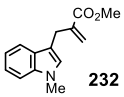
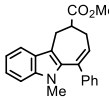
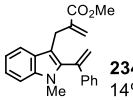
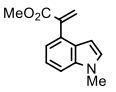
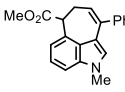
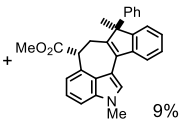


3. 3 位および 4 位置換インドール誘導体

続いて、3 位置換インドール誘導体 **232** を反応に用いた。しかしながら、環化体 **233** は得られ

Table 24. Cyclization Using Various Indole Derivatives

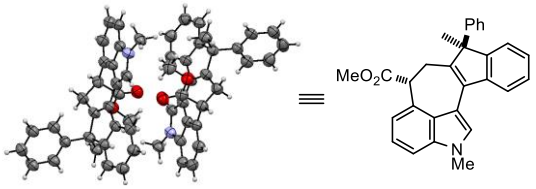


entry	substrate		time (h)	products	
1		Me (**191a**)	5	 **228a, r~t**	92%
2		Bn (**191b**)	2		89%
3	PG =	H (**191c**)	6		80%
4[a]		Ts (**191d**)	72		0%
5		PMP (**191e**)	22		80% (dr = >20/1)
6		2-furyl (**191f**)	24	 **228u~w**	56% (dr = >20/1)
7	R =	*n*Pr (**191g**)	72		60% (dr = >20/1) +  **231w** 11%
8	 **232**		22	 **233** 0% +  **234** 14%	
9	 **235**		6	 **236** 84% +  **237** 9% (dr = 6/1)	

[a]Reaction was carried out at 80 to 100°C.

ず、アルケニルインドール **234** が低収率で得られる結果となった(entry 8)。一方、4 位置換インドール誘導体 **235** は望みの環化体 **236** を 84%で与えた。この際、過剰のフェニルアセチレンが反応することで、インデンが縮環した **237** が併せて得られた(entry 9)。**237** の構造および立体化学は X 線結晶構造解析により決定した(Figure 21)。

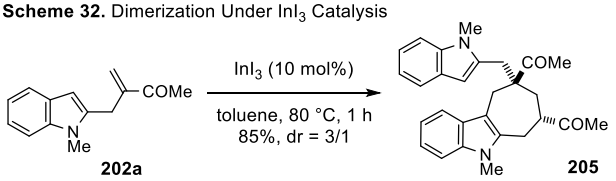
Figure 21. X-Ray Crystallographic Analysis of **237**



4. ケトン側鎖を持つインドール誘導体

エノンを用いた 7 員環形成反応の検討において、インドール側鎖の電子求引性基をエステルからケトンへと変換することで反応性が向上することが判明した。しかしながらアルキンを用いた検討では、インドールとアルキンとの Friedel-Crafts 反応よりもインドール誘導体 **202a** の二量化の進行が速く、望みの反応は進行しなかった。そこで InI_3 触媒条件下、インドール **202a** の二量化を行ったところ、高収率で環化二量化体 **205** が得られた(Scheme 32)。

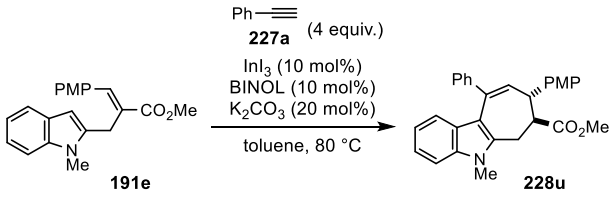
Scheme 32. Dimerization Under InI_3 Catalysis

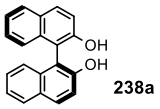
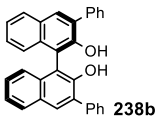


上記の検討の結果、開発した分子間[5+2]環化付加反応は多様な置換基を環上に導入可能な 7 員環縮環インドール合成法であることが示された。形成された 7 員環上にはアルキンや電子求引性基があるため、これらを足掛かりとした有用分子への変換に利用されることが期待できる。

最後に、本反応の不斉化を検討した。InX_3 を触媒とした反応では BINOL を利用した不斉反応が報告されている。[30] そこで、著者の系でも不斉リガンドとして BINOL を利用した不斉反応を試みた。しかしながら、InI_3/BINOL 調製により生じる HI のトラップとして K_2CO_3 を添加した条件で反応を行ったが、エナンチオ選択性は発現しなかった(Table 25)。

Table 25. Asymmetric Reaction



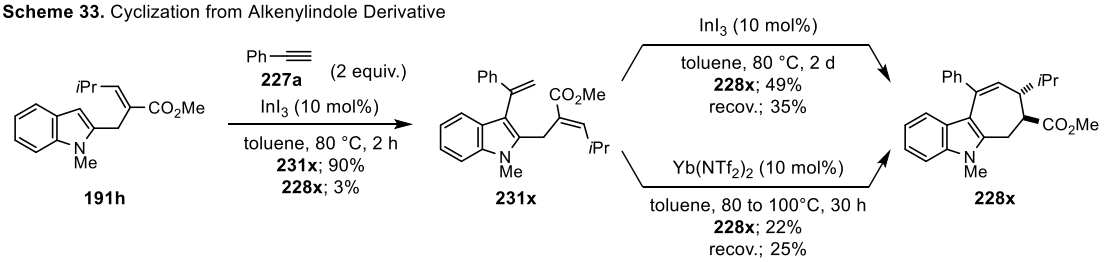
entry	BINOL	time (h)	yield (%)	% ee
1	 **238a**	2	51	0
2	 **238b**	1	13	0

第九節；アルキンを利用した 7 員環形成反応における反応メカニズムの考察

基質検討の過程で、エステルβ位に置換基が導入された基質は Friedel-Crafts アルケニル化が進行したアルケニルインドールを与えることが判明した。アルケニルインドール **231** は本反応に

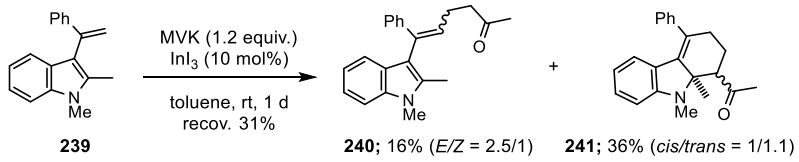
おける中間体と考えられる。そこで、単離した **231x** を環化反応と同じ反応条件に付したところ、環化体が得られた(Scheme 33)。本結果より、開発した分子間[5+2]環化付加反応はアルケニルインドールを中間体とした段階的な C-C 結合形成により環化体を与えることが示された。また、中間体 **231x** からの環化反応は $Yb(NTf_2)_3$ を触媒として用いた際にも進行したことから、不飽和エステル部位が Lewis 酸により活性化されることで *7-endo-trig* 環化が進行したと考えられる。

Scheme 33. Cyclization from Alkenylindole Derivative



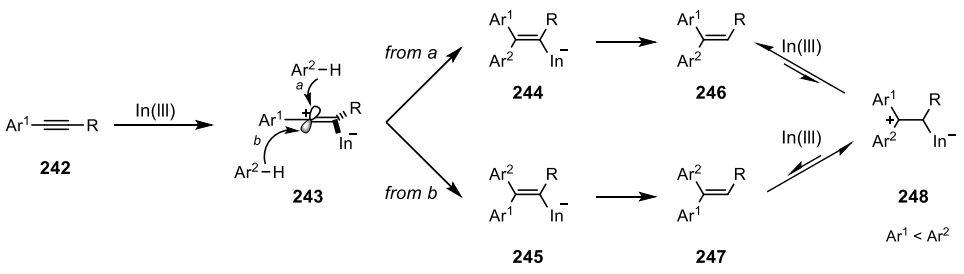
ビニルインドールは不飽和カルボニル化合物と反応し、オレフィンが反応した Michael 付加体を与えることが報告されている。[31] そこで、InI_3 触媒条件下でビニルインドールの Michael 付加が進行するかを確認した(Scheme 34)。MVK を Michael アクセプターとして利用したところ、Michael 付加体 **240** および[4+2]環化付加体 **241** が得られた。InI_3 触媒条件下でもビニルインドールの Michael 付加が進行したため、中間体 **231** は分子内 Michael 付加により環化体 **228** へと変換されたと考えられる。

Scheme 34. Michael Addition of 3-Vinylindole



Friedel-Crafts アルケニル化は In(III)触媒条件下、双性イオン中間体 **243** を経て進行するとされている。そのため、アルケニル化体は異性体混合物として得られるが、**248** を経由して異性化することで熱力学的に安定な生成物へと収束する(Scheme 35)。[26g] 双性イオン中間体 **243** が生じる際にはアルキン上のカチオンがより安定な位置に生じるよう In と反応するため、アルキンとの反応は位置選択的に進行すると考えられる。

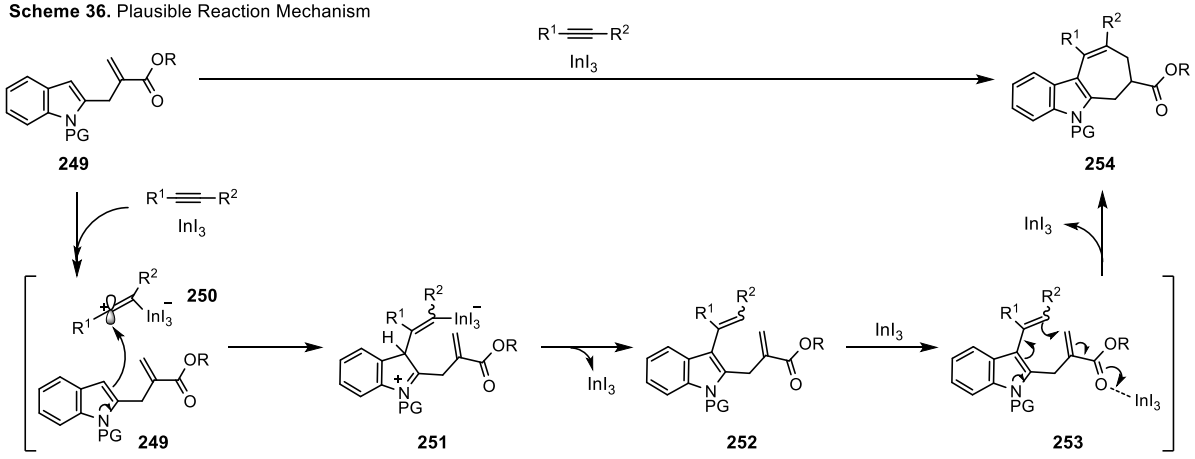
Scheme 35. Proposed Reaction Mechanism of Friedel-Crafts Alkenylation



以上より、アルキンを用いた 7 員環形成反応のメカニズムを次のように推定した(Scheme 36)。

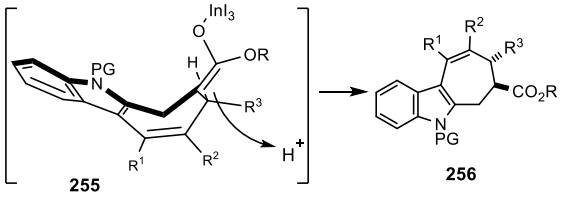
アルキンおよび InI_3 より生じた双性イオン中間体 **250** とインドール **249** との Friedel-Crafts 反応により、アルケニルインドール **252** が生じる。続いて、InI_3 が不飽和エステル部位を活性化することで分子内 Michael 付加が進行し、7 員環縮環インドール **254** を与える。

Scheme 36. Plausible Reaction Mechanism



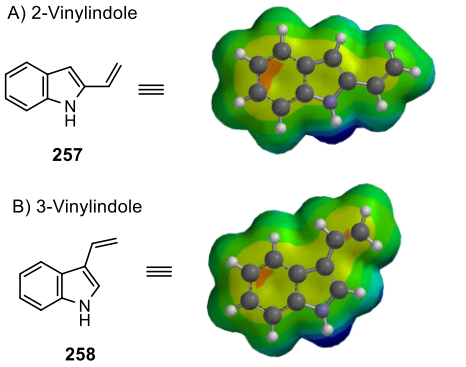
エステルβ位に置換基を持つ基質は分子内 Michael 付加により生じるエステルエノラート **255** が *convex* 面よりプロトン化さたため、ジアステレオ選択的に生成物を与えたと考えられる(Figure 22)。

Figure 22. Stereoselective Protonation of Enolate



3 位置換インドール **232** を基質とした際に環化体が得られなかった理由は、中間体であるアルケニルインドールの求核性が低いためであると考えられる。2-および 3-ビニルインドールの静電ポテンシャルマップを比較すると、ビニル基の電子密度に差があることが分かる(Figure 23)。このことからも、2-ビニルインドールは 3-ビニルインドールに比べて求核性が低いことが示された。

Figure 23. Electrostatic Potential Map

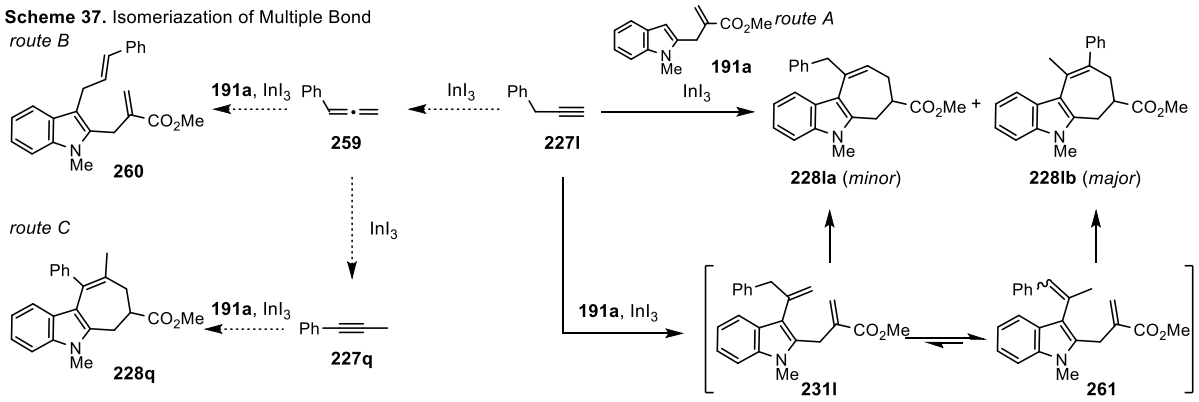


Calculation were performed using
Spartan '14V1.1.2 program package at the B3LYP/6-31G* level.

アルキル基が置換したアルキンを用いた際には **228la** ではなく **228lb** が主生成物として得られた。これは、InI_3 触媒条件下で多重結合が異性化したためであると考えられた。しなしながら、2 炭素ユニットとして用いたアルキンが異性化してアレン **259** や内部アルキン **227q** になっていれば、Scheme 31 および Table 23 の結果から、**260** や **228q** を与えたと考えられる(Scheme 37, route B and C)。そのため、インドールはアルキン **227l** と反応しており、生じる末端アルケン

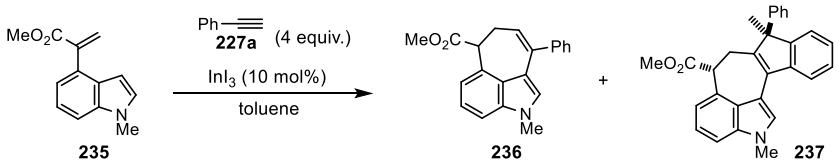
231l がより安定な内部アルケン **261** に異性化したと推定した。**231l** からの環化よりも異性化の進行が速いため **261** となり、環形成が **261** から進行したことで **228lb** が主生成物として得られたと考えられる(route A)。

Scheme 37. Isomeriazation of Multiple Bond



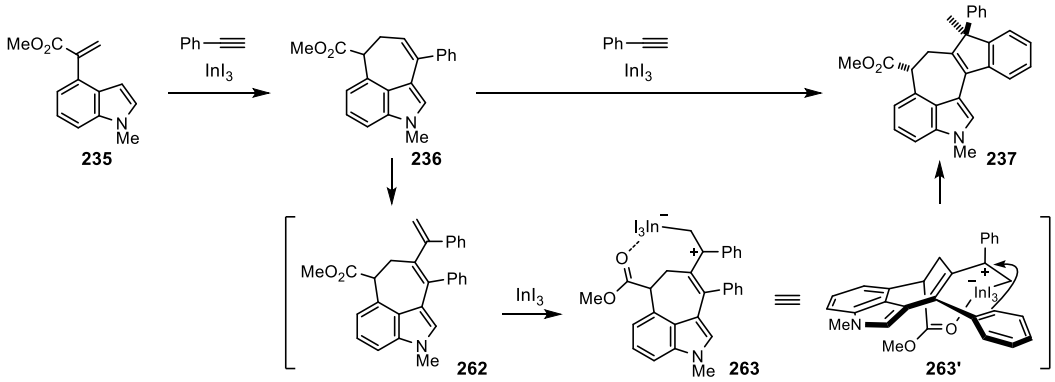
4 位置換インドール **235** を用いた際には、副生成物としてインデンが縮環した **237** が得られてきた。**235** を用いた反応を 100 ℃まで昇温して長時間行ったところ、インデン縮環体 **237** が主生成物として得られた(Table 26)。そのため、**237** は環化体 **236** を中間体として過剰に存在するフェニルアセチレンと反応することで得られたと考えられる(Scheme 38)。この際、5 員環形成時に InI_3 にエステルが配位した **263'**のような遷移状態をとることにより、ジアステレオ選択的に反応が進行したと考えられる。

Table 26. 7-Membered Ring Construction of 4-Substituted Indole Derivative



entry	conditions	**236** (%)	**237** (%)
1	80 °C, 6 h	84	9 (dr = 6/1)
2	80 to 100 °C, 44 h	28	55 (dr = 6/1)

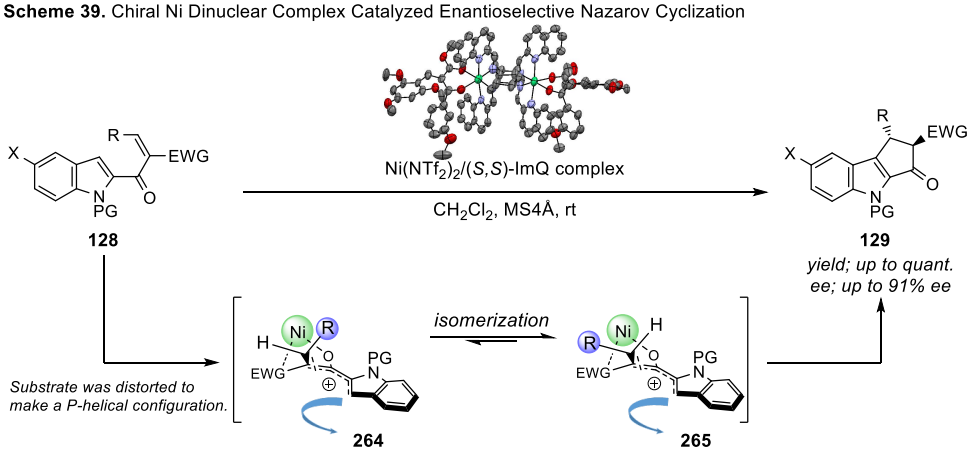
Scheme 38. Plausible Reaction Mechanism



総括

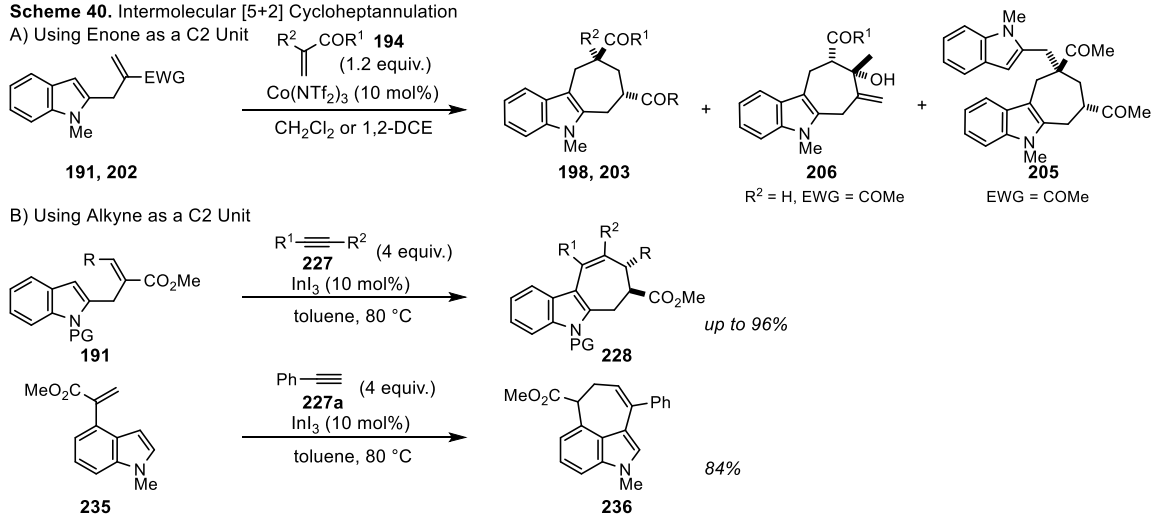
1. $Ni(NTf_2)_2$/ImQ 触媒を利用したインドール誘導体のエナンチオ選択的 Nazarov 環化を開発し、従来報告がなかった多様な官能基を有する光学活性シクロペンタ[*b*]インドールの合成を可能とした。
2. $Ni(NTf_2)_2$/(*S,S*)-ImQ 錯体の構造を X 線結晶構造解析により明らかとし、その構造情報を基にエナンチオ選択性発現メカニズムを解明した。この際、従来の不斉 Nazarov 環化のメカニズムとして提唱されていた回転選択性とは異なり、基質のねじれ方向の選択性がエナンチオ選択性に寄与していることを提唱した。

Scheme 39. Chiral Ni Dinuclear Complex Catalyzed Enantioselective Nazarov Cyclization



3. エノンを利用した 7 員環縮環インドール合成を行い、中程度の収率ながら環化体の合成に成功した。この際、1,4-環化体、1,2-環化体および環化二量体といった複数種の環化体が形成可能であることを見出した。
4. アルキンを利用した分子間[5+2]環化付加反応により、高収率・高ジアステレオ選択的なシクロヘプタ[*b*]インドール合成法を開発した。さらに、同一の反応手法を用いることでシクロヘプタ[*cd*]インドールの合成も達成した。

Scheme 40. Intermolecular [5+2] Cycloheptannulation



実験の部

General Information

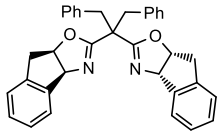
NMR spectra were recorded at 400 or 600 MHz for ^{1}H NMR, and at 100 or 150 MHz for ^{13}C NMR using JEOL JNM-ECP400, -ECS400, -ECZ400, -ECA600 and -ECZ600. Chemical shifts for ^{1}H NMR are reported in parts per million downfield from tetramethylsilane, and are referenced to residual protium in the NMR solvent (for $CDCl_3$ δ: 7.26 ppm, for CD_3OD δ: 3.31 ppm, for acetone-*d*6 δ: 2.05 ppm). For ^{13}C NMR, chemical shifts were reported in the scale relative to the NMR solvent (for $CDCl_3$ δ: 77.0 ppm, for CD_3OD δ: 49.0 ppm, for acetone-*d*6 δ: 206.2 ppm) as an internal reference. Infrared spectra were recorded on an ATR using JASCO FT/IR-230 and FT/IR-4700 spectrometer. Mass spectra were recorded using ESI mode with JEOL JMS-T100LP. The enantiomeric excess was determined by HPLC analysis using JASCO HPLC LC-2000Plus series (PU-2089, CO-2065, UV-2075). All samples were analyzed at 30 °C, measured at 254 nm and flow ratio was 1.0 mL/min. Optical rotations were measured using JASCO P-1020 and P-2200 Polarimeter. X-ray crystal data were collected with Rigaku VariMax with RAPID diffractometer at –180±1 °C using filtered Cu-Kα radiation. Ratio of isomers were determined by ^{1}H NMR spectroscopy unless otherwise noted.

Reactions were carried out in dry solvents under argon atmosphere, unless otherwise noted. Dry CH_2Cl_2, THF and toluene were purchased from Kanto Chemical Co., Inc. $Ni(NTf_2)_2$ was purchased from Aldrich as a hydrate, and it was dried at 120 °C under 0.05 mmHg for 4 h before use. Flash column chromatography was performed with Wakogel® 60N from Wako Pure Chemical Industries, Ltd. TLC was performed on Merck TLC Silica gel 60 F_{254}. Celite® was used with Celite® 545. MS 4 Å was purchased from Aldrich (powder, -325 mesh particle size) and Wako Pure Chemical Industries, Ltd. (pellet). Other solvents and reagents were purified by usual methods.

第一章に関する実験

Chiral Ligand Synthesis

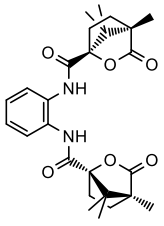
(3a*S*,3a'*S*,8a*R*,8a'*R*)-2,2'-(1,3-diphenylpropane-2,2-diyl)bis(3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazole)[32] (**131**)



The solution of (3a*S*,3a'*S*,8a*R*,8a'*R*)-2,2'-methylenebis[3a,8a-dihydro-8*H*-indeno[1.2-*d*]oxazole] (120 mg, 0.36 mmol) in THF (1.8 mL) was added LHMDS (1.0 M in THF, 0.8 mL) at -78 °C. The mixture was stirred for 1 h. BnBr (95 μL, 0.8 mmol) was added to the solution and the reaction mixture was stirred at 0 °C for 6 h. The reaction was quenched with *sat.* NH_4Cl *aq.*, the layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **131** as a colorless solid (169 mg, 92% yield). Further purification was achieved by crystallization from CH_2Cl_2/Hexane (152 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.05 (d, *J* = 16.9 Hz, 2H), 3.05 (d, *J* = 14.7 Hz, 2H), 3.24 (d, *J* = 14.2 Hz, 2H), 3.34 (dd, *J* = 6.4, 17.9 Hz, 2H), 5.30 (ddd, *J* = 1.4, 6.9, 7.8 Hz, 2H), 5.60 (d, *J* = 7.8 Hz, 2H), 6.74 (d, *J* = 7.3 Hz, 4H), 6.81 (dd, *J* = 7.3, 7.3 Hz, 4H), 6.99 (t, *J* = 7.3 Hz, 2H), 7.27-7.36 (m, 6H), 7.46 (d, *J* = 7.8 Hz, 2H).

(1*S*,1'*S*,4*R*,4'*R*)-*N*,*N*'-(1,2-phenylene)bis(4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxamide) (**136**)



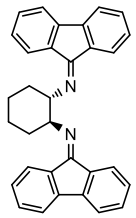
$(COCl)_2$ (222 μL, 2.6 mmol) was added to the solution of (-)-camphanic acid (208 mg, 1 mmol) and DMF (8 μL, 0.1 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The solution was stirred for 2 h at room temperature and excess $(COC)_2$ was removed under reduced pressure to afford acyl chloride as a colorless solid.

The solution of prepared acyl chloride in CH_2Cl_2 (1 mL) was added to the solution of *o*-phenylenediamine (54 mg, 0.5 mmol) and pyridine (121 μL, 1.5 mmol) in CH_2Cl_2 (2 mL) at 0 °C. The reaction mixture was stirred for 30 min at the same temperature and quenched with H_2O. The layers were separated and water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **136** as a colorless solid (206 mg, 88% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (s, 6H), 1.13 (s, 6H), 1.19 (s, 6H), 1.73 (ddd, *J* = 4.0, 10.4, 14.4 Hz, 2H), 1.96-2.08 (m, 4H), 2.65 (ddd, *J* = 3.2, 11.6, 14.4 Hz, 2H), 7.26 (dd, *J* = 3.6, 5.6 Hz, 2H), 7.61 (dd, *J* = 3.6, 5.6 Hz, 2H), 8.62 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.5, 16.5, 16.7, 29.0, 30.7, 54.2, 55.4, 92.4, 124.9, 126.7, 129.1, 166.3, 17.6; IR (neat) ν: 2968, 1786, 1674 cm^{-1}; HRMS (ESI) *m/z* calcd for

$C_{26}H_{32}N_2NaO_6$ $[M+Na]^+$ 491.2158, found 491.2155; $[\alpha]_D^{24}$ -15.1 (*c* 1.00, $CHCl_3$).

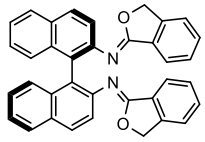
***N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(9*H*-fluoren-9-imine)** (**137**)



The mixture of (1*S*,2*S*)-(+)-cyclohexanediamine (57 mg, 0.5 mmol), 9-fluorenone (180 mg, 1 mmol) and $MgSO_4$ (60 mg) in toluene (4.7 mL) was stirred at reflux temperature for 14 h. The resulting mixture was added 1*N* KOH aq. and layers were separated. The waste layer was extracted with CH_2Cl_2 three times and conbined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was recrystallized from CH_2Cl_2/Hexane to afford **137** as a colorless solid (68 mg, 31% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.62-1.74 (m, 2H), 1.87-2.01 (m, 4H), 2.15 (d, *J* = 14.0 Hz, 2H), 4.85-4.91 (m, 2H), 7.06 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.25 (ddd, *J* = 1.2, 7.6, 7.6 Hz, 2H), 7.34 (ddd, *J* = 1.2, 7.6, 7.6 Hz, 2H), 7.41 (dd, *J* = 8.0, 8.0 Hz, 4H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.60 (d, *J* = 7.2 Hz, 2H), 8.18 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.6, 31.9, 65.8, 118.8, 120.0, 122.7, 127.7, 127.9, 128.1, 130.2, 130.7, 132.2, 138.9, 140.6, 143.7, 161.2; IR (neat) ν: 1638, 1604 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{32}H_{27}N_2$ $[M+H]^+$ 439.2174, found 439.2189; $[\alpha]_D^{21}$ -148.2 (*c* 1.00, $CHCl_3$).

(*R*)-(1*Z*,1'*Z*)-*N*,*N*'-([1,1'-binaphthalene]-2,2'-diyl)bis(isobenzofuran-1(3*H*)-imine) (**138**)



$NaBH_4$ (114 mg, 3 mmol) was added to the mixture of 2-cyanobenzaldehyde (393 mg, 3 mmol) in EtOH (23 mL) at -78 °C and the mixture was warmed to 0 °C over 30 min. The Reaction mixture was poured into H_2O and extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and dry HCl (2.0 M in Et_2O, 3.7 mL) was added at 0 °C. The resulting suspension was filtrated and the colorless crystals were washed with Et_2O to afford 1,3-dihydro-iminoisobenzofuran hydrochloride[33] (**S1**) as a colorless solid (419 mg, 82% yield).

^{1}H NMR (400 MHz, CD_3OD) δ: 5.96 (s, 2H), 7.77 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.98 (dd, *J* = 7.6, 7.6 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H).

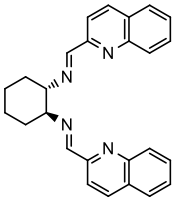
NEt_3 (326 μL, 2.6 mmol) was added to the mixture of (*R*)-1,1'-binaphthyl-2,2'-diamine (114 mg, 0.4 mmol) and **S1** (204 mg, 1.2 mmol) in MeOH (6 mL) at 0 °C. The mixture was heated to reflux temperature and stirred for 5 days. The reaction mixture was filtrated through Celite® and concentrated under reduced pressure. The residue was recrystallized from CH_2Cl_2/Hexane to afford **134** as a pale brown solid (22 mg, 11% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.05 (d, *J* =14.4, 2H), 4.83 (d, *J* = 14.8, Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.18 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.28-7.34 (m, 6H), 7.42 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 7.4 Hz, 2H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.85 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 71.8, 120.7, 122.9, 123.9, 124.5, 125.5, 126.4, 127.5, 127.6, 128.3, 130.4, 130.7, 131.3, 133.7, 143.1, 144.2, 158.3; IR (neat) ν: 3052, 1681, 1615, 1591 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{36}H_{24}N_2NaO_2$ $[M+Na]^+$ 539.1736, found 539.1732; $[\alpha]_D^{21}$ +639.9 (*c* 0.33, $CHCl_3$).

General Procedure for Tetradentate Schiff Base Ligand

The solution of chiral diamine (0.5 mmol) and 2-quinolinecarboxaldehyde (157 mg, 1 mmol) in EtOH (2.5 mL) was stirred at room temperature for 14 h. The solvent was removed under reduced pressure and the residue was purified by recrystallization.

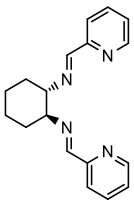
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(quinolin-2-yl)methanimine) (**139**)



The reaction was carried out as described in the general procedure. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **139** as a colorless solid (118 mg, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.57-1.60 (m, 2H), 1.89-1.92 (m, 6H), 3.64-3.66 (m, 2H), 7.49 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.66 (ddd, *J* = 1.2, 6.8, 6.8 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 2H), 8.07 (s, 4H), 8.51 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.4, 32.7, 73.8, 118.5, 127.1, 127.6, 128.7, 129.4, 129.5, 136.3, 147.6, 154.9, 161.8; IR (neat) ν: 2920, 2858, 1642 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{24}N_4Na$ $[M+Na]^+$ 415.1899, found 415.1906; $[\alpha]_D^{20}$ -82.2 (*c* 1.01, $CHCl_3$).

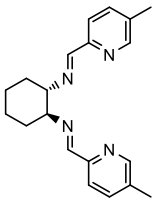
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(pyridin-2-yl)methanimine) (**140**)



The reaction was carried out on a 1 mmol scale in MeOH. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **140** as a colorless solid (206 mg, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.49-1.57 (m, 2H), 1.80-1.90 (m, 6H), 3.50-3.57 (m, 2H), 7.23 (dddd, *J* = 1.2, 1.2, 4.8, 4.8 Hz, 2H), 7.64 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.88 (dd, *J* = 1.2, 7.8 Hz, 2H), 8.31 (s, 2H), 8.55 (dd, *J* = 1.2, 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.3, 32.7, 73.5, 121.3, 124.4, 136.4, 149.2, 154.6, 161.4; IR (neat) ν: 3386, 2933, 2860, 1645 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{20}N_4Na$ $[M+Na]^+$ 315.1586, found 315.1580; $[\alpha]_D^{20}$ +174.1 (*c* 1.01, $CHCl_3$).

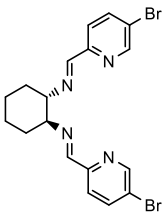
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(5-methylpyridin-2-yl)methanimine) (**141**)



The reaction was carried out on a 0.3 mmol scale following the general procedure. The residue was purified by recrystallization from Et_2O/Hexane to afford **141** as a colorless solid (76 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.48-1.53 (m, 2H), 1.83-1.88 (m, 6H), 2.30 (s, 6H), 3.45-3.53 (m, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 8.28 (s, 2H), 8.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.4, 24.4, 32.7, 73.5, 120.9, 134.3, 137.0, 149.6, 152.2, 161.3; IR (neat) ν: 2927, 2857, 1645 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{24}N_4Na$ $[M+Na]^+$ 343.1899, found 343.1901; $[\alpha]_D^{25}$ +227.5 (*c* 1.00, $CHCl_3$).

(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(5-bromopyridin-2-yl)methanimine) (**142**)

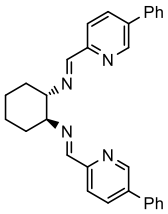


The reaction was carried out on a 0.3 mmol scale following the general procedure. The reside was purified by recrystallization from Et_2O/Hexane to afford **142** as a colorless solid (80 mg, 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.48-1.53 (m, 2H), 1.78-1.89 (m, 6H), 3.47-3.53 (m, 2H), 7.78 (d, *J* = 1.2 Hz, 4H), 8.23 (s, 2H), 8.60 (dd, *J* = 1.2, 1.2 Hz, 2H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ: 24.2, 32.6, 73.5, 122.0, 122.3, 139.1, 150.3, 152.9, 160.4; IR (neat) ν: 2934, 2846, 1650 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{18}Br_2N_4Na$ $[M+Na]^+$ 470.9796, found 470.9803; $[\alpha]_D^{25}$ +239.4 (*c* 1.01, $CHCl_3$).

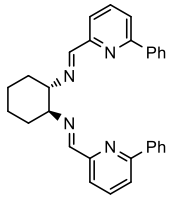
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(5-phenylpyridin-2-yl)methanimine) (**143**)



The reaction was carried out on 0.18 mmol scale following the general procedure. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **143** as a colorless solid (55 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.52-1.56 (m, 2H), 1.84-1.91 (m, 6H), 3.55-3.61 (m, 2H), 7.34 (tt, *J* = 2.4, 7.2 Hz, 2H), 7.44 (dd, *J* = 7.6, 7.6 Hz, 4H), 7.55 (dd, *J* = 1.6, 7.2 Hz, 4H), 7.85 (dd, *J* = 2.0, 8.0 Hz, 2H), 7.97 (d, *J* = 7.6 Hz, 2H), 8.38 (s, 2H), 8.79 (d, *J* = 0.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.4, 32.8, 73.7, 121.3, 127.1, 128.3, 129.1, 134.8, 137.30, 137.34, 147.7, 153.4, 161.1; IR (neat) ν: 2932, 2854, 1645 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{28}N_4Na$ $[M+Na]^+$ 467.2212, found 467.2194; $[\alpha]_D^{27}$ +343.5 (*c* 1.05, $CHCl_3$).

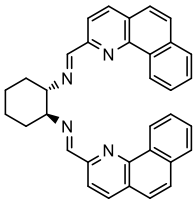
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(6-phenylpyridin-2-yl)methanimine) (**144**)



The reaction was carried out on a 0.3 mmol scale following the general procedure. The residue was purified by recrystallization from Et_2O/Hexane to afford **144** as a colorless solid (77 mg, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.51-1.54 (m, 2H), 1.82-1.91 (m, 6H), 3.58 (dd, *J* = 4.0, 4.8 Hz, 2H), 7.37-7.47 (m, 6H), 7.64 (dd, *J* = 1.2, 8.0 Hz, 2H), 7.70 (dd, *J* = 8.4 Hz, 2H), 7.89 (dd, *J* = 1.2, 8.0 Hz, 2H), 7.94 (ddd, *J* = 1.6, 1.6, 6.8 Hz, 4H), 8.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.4, 32.7, 73.6, 119.3, 121.2, 126.9, 128.7, 128.9, 137.1, 139.1, 154.7, 156.8, 162.2; IR (neat) ν: 2928, 2856, 1648 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{28}N_4Na$ $[M+Na]^+$ 467.2212, found 467.2206; $[\alpha]_D^{23}$ -176.2 (*c* 1.0, $CHCl_3$).

(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(benzo[h]quinolin-2-yl)methanimine) (**145**)

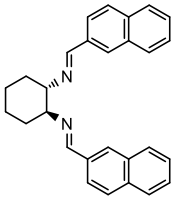


The reaction was carried out on a 0.25 mmol scale and stirred at refluxing temperature. The residue was purified by recrystallization from CH_2Cl_2 to afford **145** as a colorless solid (115 mg, 93% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.58-1.63 (m, 2H), 1.90-1.99 (m, 6H), 3.68-3.74 (m, 2H), 7.56 (d, *J* = 8.8 Hz, 2H), 7.62-7.72 (m, 6H), 7.82 (d, *J* = 7.6 Hz, 2H), 8.06 (d, *J* = 8.4 Hz, 2H), 8.20 (d, *J* = 8.0 Hz, 2H), 8.67 (s, 2H), 9.24 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.5, 32.8, 73.9, 119.0, 124.2, 125.1, 126.8, 126.9, 127.7, 128.0, 128.2, 131.4, 133.5, 136.0, 145.7, 153.5, 162.7; IR (neat) ν: 2928, 2856, 1643 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{34}H_{29}N_4$ $[M+H]^+$ 493.2392, found 493.2407; $[\alpha]_D^{20}$ -682.2 (*c* 1.01, $CHCl_3$).

(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(naphthalen-2-yl)methanimine)[34] (**146**)

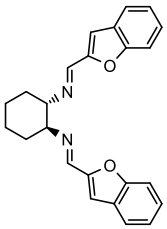
The reaction was carried out on a 1 mmol scale and stirred at refluxing temperature for 4.5 h in MeOH. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **146** as a colorless solid (272 mg,



70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.52-1.58 (m, 2H), 1.87-1.95 (m, 6H), 3.47-3.54 (m, 2H), 7.40 (ddd, *J* = 1.6, 6.0, 6.0 Hz, 2H), 7.43 (ddd, *J* = 1.6, 5.6, 5.6 Hz, 2H), 7.72-7.76 (m, 6H), 7.84-7.86 (m, 4H), 8.36 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.5, 33.0, 74.0, 123.9, 126.2, 126.8, 127.7, 128.2, 128.5, 129.4, 133.0, 134.5, 161.2; IR (neat) ν: 2918, 2855, 1638 cm^{-1}; $[\alpha]_D^{23}$ +149.5 (*c* 1.0, $CHCl_3$).

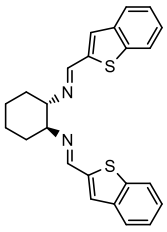
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(benzofuran-2-yl)methanimine) (**147**)



The reaction was carried out on a 0.3 mmol scale following the general procedure. The residue was purified by recrystallization from Et_2O/Hexane to afford **147** as a colorless solid (89 mg, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.47-1.52 (m, 2H), 1.89-1.94 (m, 6H), 3.50-3.57 (m, 2H), 6.89 (s, 2H), 7.18 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.31 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 2H), 8.19 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.3, 32.8, 74.3, 111.5, 112.1, 121.8, 123.1, 126.3, 127.7, 150.5, 152.3, 155.4; IR (neat) ν: 2928, 2857, 1640 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{22}N_2NaO_2$ $[M+Na]^+$ 393.1579, found 393.1581; $[\alpha]_D^{25}$ +544.1 (*c* 1.00, $CHCl_3$).

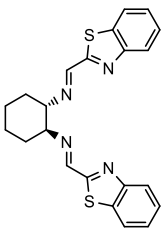
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(benzo[b]thiophen-2-yl)methanimine) (**148**)



The reaction was carried out on a 0.3 mmol scale following the general procedure. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **148** as a colorless solid (75 mg, 62% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.46-1.51 (m, 2H), 1.81-1.92 (m, 6H), 3.38-3.45 (m, 2H), 7.24-7.32 (m, 4H), 7.35 (s, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.75 (d, *J* = 7.6 Hz, 2H), 8.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.3, 32.6, 73.4, 122.5, 124.3, 124.4, 125.7, 127.4, 139.3, 140.3, 142.6, 155.1; IR (neat) ν: 2928, 2855, 1628 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{23}N_2S_2$ $[M+H]^+$ 403.1303, found 403.1297; $[\alpha]_D^{25}$ +482.9 (*c* 1.00, $CHCl_3$).

(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohexane-1,2-diyl)bis(1-(benzo[d]thiazol-2-yl)methanimine) (**149**)

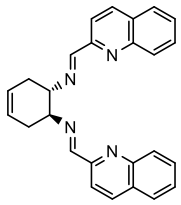


The reaction was carried out on a 0.3 mmol scale following the general procedure. The residue was purified by recrystallization from CH_2Cl_2/Et_2O/Hexane to afford **149** as a colorless solid (93 mg, 77% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.51-1.55 (m, 2H), 1.84-1.92 (m, 6H), 3.58-3.65 (m, 2H), 7.38 (ddd, *J* = 1.2, 7.6, 7.6 Hz, 2H), 7.43 (ddd, *J* = 1.6, 7.2, 7.2 Hz, 2H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.98 (d, *J* = 7.6 Hz, 2H), 8.49 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.1, 32.2, 73.3, 121.9, 123.9, 126.2, 126.4, 135.0, 153.5, 155.5, 167.2; IR (neat) ν: 2929, 2858, 1635 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{20}N_4NaS_2$ $[M+Na]^+$ 427.1027, found 427.1025; $[\alpha]_D^{24}$ +474.2 (*c* 1.00, $CHCl_3$).

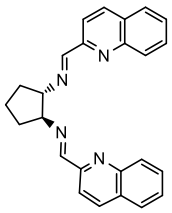
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclohex-4-ene-1,2-diyl)bis(1-(quinolin-2-yl)methanimine) (**150**)

The reaction was carried out on a 0.3 mmol scale following the general procedure. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **150** as a pale brown solid (108 mg, 92% yield).



^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.38 (d, *J* = 17.2 Hz, 2H), 2.58 (ddd, *J* = 4.0, 4.0, 15.6 Hz, 2H), 3.95 (dd, *J* = 4.4, 4.4 Hz, 2H), 5.81 (d, *J* = 2.4 Hz, 2H), 7.49 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.66 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.73 (d, *J* = 7.6 Hz, 2H), 8.04-8.09 (m, 6H), 8.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.2, 70.0, 118.5, 124.8, 127.2, 127.6, 128.7, 129.4, 129.6, 136.4, 147.6, 154.8, 162.2; IR (neat) ν: 3023, 2843, 1641, 1596, 1558, 1502 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{22}N_4Na$ $[M+Na]^+$ 413.1742, found 413.1740; $[\alpha]_D^{24}$ -107.2 (*c* 1.00, $CHCl_3$).

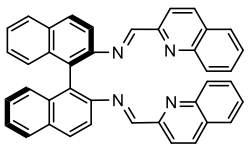
(1*E*,1'*E*)-*N*,*N*'-((1*S*,2*S*)-cyclopentane-1,2-diyl)bis(1-(quinolin-2-yl)methanimine) (151)



The suspension of (1*S*,2*S*)-*trans*-1,2-cyclopentanediamine dihydrochloride (51.9 mg, 0.3 mmol) and 2-quinolinecarboxaldehyde (94 mg, 0.6 mmol) in EtOH (3 mL) was added triethylamine (232 μL, 0.6 mmol). The reaction mixture was stirred for 14 h at room temperature and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed with 0.5 N KOH *aq*. Organic layer was concentrated under reduced pressure and purified by recrystallization from CH_2Cl_2/Hexane to afford **151** as a colorless solid (74 mg, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72 (dt, *J* = 8.8, 8.8 Hz, 1H), 2.03-2.14 (m, 3H), 2.20-2.28 (m, 2H), 4.02-4.08 (m, 2H), 7.53 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.68 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 8.14-8.19 (m, 4H), 8.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.5, 33.0, 77.4, 118.6, 127.2, 127.6, 128.7, 129.5, 129.6, 136.4, 147.7, 154.8, 162.1; IR (neat) ν: 2965, 2868, 1641, 1593, 1503 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{22}N_4Na$ $[M+Na]^+$ 401.1742, found 401.1753; $[\alpha]_D^{24}$ -2.1 (*c* 1.00, $CHCl_3$).

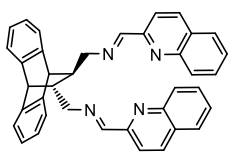
(*R*)-(1*E*,1'*E*)-*N*,*N*'-([1,1'-binaphthalene]-2,2'-diyl)bis(1-(quinolin-2-yl)methanimine)[19d] **(152)**



The reaction was carried out on a 0.2 mmol scale and stirred at refluxing temperature for 6 h. The mixture was filtrated and precipitate was washed with EtOH to afford **152** as a yellow solid (60 mg, 54% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 (dd, *J* = 0.8, 6.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.43 (ddd, *J* = 1.6, 6.8, 6.8 Hz, 2H), 7.51 (ddd, *J* = 1.2, 6.8, 6.8 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.64 (ddd, *J* = 1.6, 6.8, 6.8 Hz, 2H), 7.74 (d, *J* = 7.2 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.95 (d, *J* = 8.4 Hz, 4H), 8.04 (d, *J* = 8.4 Hz, 2H), 8.63 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 117.9, 118.4, 125.3, 126.6, 127.0, 127.4, 127.6, 127.9, 128.0, 128.6, 128.7, 129.4, 129.6, 132.2, 133.4, 136.4, 147.1, 147.6, 154.9, 160.6; IR (neat) ν: 1593 cm^{-1}; $[\alpha]_D^{21}$ +24.3 (*c* 0.53, $CHCl_3$).

(1*E*,1'*E*)-*N*,*N*'-((11*R*,12*R*)-(9,10-dihydro-9,10-ethanoanthracene-11,12-diyl)bis(methylene))-bis(1-(quinolin-2-yl)methanimine) (153)



The reaction was carried out on a 0.21 mmol scale and stirred at refluxing temperature. The residue was purified by recrystallization from CH_2Cl_2/Hexane to afford **153** as a colorless solid (82 mg, 73% yield).

^{1}H NMR (400 MHz, C_6D_6) δ: 3.94 (s, 2H), 4.15 (s, 2H), 7.03 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.07-7.22 (m, 10H), 7.28 (d, *J* = 7.6, Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 8.13

(d, *J* = 8.4 Hz, 2H), 8.67 (s, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ: 52.3, 77.6, 118.9, 124.4, 126.4, 126.5, 127.2, 127.9, 129.0, 129.5, 130.3, 136.1, 141.6, 142.3, 148.5, 155.3, 163.0; IR (neat) ν: 2867, 1635 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{36}H_{27}N_4$ $[M+H]^+$ 515.2236, found 515.2240; $[\alpha]_D^{23}$ -156.4 (*c* 1.00, $CHCl_3$).

Synthesis of $M(NTf_2)_n$

$Al(NTf_2)_3$[35]

Al powder (31 mg, 1.2 mmol) was added to the solution of trifluoromethanesulfonimide (844 mg, 3 mmol) in H_2O (5 mL). The mixture was stirred for 5 h at refluxing temperature and filtrated through filter paper to remove excess Al. H_2O was remove under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 6 h to afford white solid (268 mg, 31%). ^{19}F NMR (376 Hz, acetone-d6) δ: -79.81.

$Mn(NTf_2)_2$[35]

Manganese(II) carbonate (184 mg, 1.6 mmol) was added to the solution of trifluoromethanesulfonimide (844 mg, 3 mmol) in H_2O (5 mL). The mixture was stirred for 30 min at refluxing temperature and filtrated through filter paper to remove excess $MnCO_3$. H_2O was removed under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 6 h to afford white solide (869 mg, 93%).

$Fe(NTf_2)_2$[35]

Fe (420 mg, 7.5 mmol) was added to the solution of trifluoromethanesulfonimide (844 mg, 3 mmol) in H_2O (4.2 mL). The mixture was stirred for 1 h at refluxing temperature and filtrated through filter paper to remove excess Fe. H_2O was removed under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 4 h to afford pale red solid (880 mg, 95%).

$Co(NTf_2)_2$[35]

Cobalt(II) carbonate (190 mg, 1.6 mmol) was added to the solution of trifluoromethanesulfonimide (844 mg, 3 mmol) in H_2O (5 mL). The mixture was stirred for 1 h at room temperature and filtrated through filter paper to remove excess $CoCO_3$. H_2O was removed under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 6 h to afford red solid (873 mg, 94%). ^{19}F NMR (376 Hz, acetone-d6) δ: -79.44.

$Ni(NTf_2)_2$[35]

Nickel(II) hydroxide (148 mg, 1.6 mmol) was added to the solution of trifluoromethanesulfonimide (844 mg, 3 mmol) in H_2O (5 mL). The mixture was stirred for 1 h at refluxing temperature and filtrated through filter paper to remove excess $Ni(OH)_2$. H_2O was removed under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 6 h to afford pale yellow solid (854 mg, 92%). ^{19}F NMR (376 Hz, acetone-d6) δ: -79.65.

$Cu(NTf_2)_2$[36]

Trifluoromethanesulfonimide (714 mg, 2.5 mmol) in H_2O (14 mL) was added dropwise to the mixture of CuO (100 mg, 1.3 mmol) in H_2O (14 mL) at room temperature. Resulting mixture was heated to 70 °C and stirred for 2 h at the same temperature. The solution was filtrated through filter paper. H_2O was removed

under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 10 h to afford greenish solid (607 mg, 77%). ^{19}F NMR (376 Hz, acetone-d6) δ: -79.74.

$Zn(NTf_2)_2$[35]

Zn powder (131 mg, 2 mmol) was added to the solution of trifluoromethanesulfonimide (844 mg, 3 mmol) in H_2O (5 mL). The mixture was stirred for 10 h at room temperature and filtrated through filter paper to remove excess Zn. H_2O was remove under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 6 h to afford white solid (859 mg, 92%). ^{19}F NMR (376 Hz, acetone-d6) δ: -79.90.

$Yb(NTf_2)_3$[35]

The mixture of Yb_2O_3 (200 mg, 0.5 mmol) and trifluoromethanesulfonimide (875 mg, 3 mmol) in H_2O (1.7 mL) was stirred for 1 h at refluxing temperature. H_2O was removed under reduced pressure and residue was dried at under 0.04 mmHg at 120 °C for 10 h to afford white solid (997 mg, 97%). ^{19}F NMR (376 Hz, acetone-d6) δ: -79.90.

Substrate Synthesis for Nazarov Cyclization

Synthesis of β-Dicarbonyl Compound

General Procedure A

$(COCl)_2$ (508 μL, 6 mmol) was added dropwise to the mixture of carboxylic acid (5 mmol) and DMF (40 μL, 0.5 mmol) in CH_2Cl_2 (10 mL) at 0 °C. Resulting solution was warmed to room temperature. After stirred for 2 h, excess $(COCl)_2$ was removed under reduced pressure to afford acyl chloride.

LHMDS (1.0 M in THF, 10 mL, 10 mmol) was added dropwise to the solution of ethyl acetate (488 μL, 5 mmol) in THF (25 mL) at –78 °C and stirred for 2 h at the same temperature. CH_2Cl_2 (5 mL) solution of prepared acyl chloride was added to the solution and stirred at –78 °C. After the reaction was completed, *sat.* NH_4Cl *aq.* was added. The layers were separated, and the water layer was extracted with Et_2O three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography.

General Procedure B

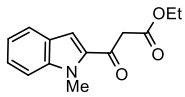
The mixture of methyl ester (4 mmol) and NaH (320 mg, 8 mmol) in THF (10 mL) was heated to 60 °C. To this mixture, solution of ketone (4 mmol) in THF (3 mL) was added dropwise. The resulting mixture was stirred for 2 h at 60 °C. The mixture was cooled to 0 °C, quenched with H_2O, and neutralized by AcOH. The layers were separated and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography.

General Procedure C

The solution of ketone (4 mmol) in toluene (2 mL) was added to toluene (6 mL) mixture of NaH (60% dispersion, 448 mg, 11.2 mmol) and dimethyl carbonate (674 μL, 8 mmol) at reflux temperature. The

resulting mixture was stirred for 2 h. The mixture was cooled to 0 °C, neutralized by AcOH and diluted with water. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography.

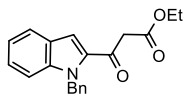
ethyl 3-(1-methyl-1*H*-indol-2-yl)-3-oxopropanoate (**S2a**)



The reaction was carried out as described in the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **S2a** as a brown liquid (1031 mg, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 7.2 Hz, 3H), 3.99 (s, 2H), 4.09 (s, 3H), 4.23 (q, *J* = 7.2 Hz, 2H), 7.17 (ddd, *J* = 2.4, 5.6, 7.6 Hz, 1H), 7.31 (s, 1H), 7.38-7.43 (m, 2H), 7.70 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.2, 47.2, 61.5, 110.4, 112.8, 121.0, 123.1, 125.7, 126.5, 133.9, 140.5, 167.6, 185.5; IR (neat) ν: 1734, 1657, 1614, 1512 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{15}NNaO_3$ $[M+Na]^+$ 268.0950, found 268.0957.

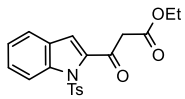
ethyl 3-(1-benzyl-1*H*-indol-2-yl)-3-oxopropanoate (**S2b**)



The reaction was carried out on a 2 mmol scale of carboxylic acid following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **S2b** as a pale yellow solid (530 mg, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.2 Hz, 3H), 3.97 (s, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 5.86 (s, 2H), 7.05 (d, *J* =7.2 Hz, 2H), 7.16-7.23 (m, 3H), 7.35-7.40 (m, 3H), 7.72 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 47.3, 48.2, 61.5, 111.0, 113.8, 121.3, 123.2, 126.0, 126.5, 126.8, 127.1, 128.5, 133.4, 138.0, 140.4, 167.5, 185.1; IR (neat) ν: 1734, 1658, 1613, 1513 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{19}NNaO_3$ $[M+Na]^+$ 344.1263, found 344.1255.

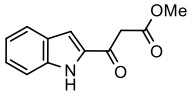
ethyl 3-oxo-3-(1-tosyl-1*H*-indol-2-yl)propanoate (**S2c**)



The reaction was carried out on a 3 mmol scale of carboxylic acid following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **S2c** as a brown liquid (844 mg, 73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.24 (t, *J* = 7.2 Hz, 3H), 2.34 (s, 3H), 4.19 (q, *J* = 7.2 Hz, 2H), 7.19 (s, 1H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.28 (dd, *J* = 6.8, 6.8 Hz, 1H), 7.46 (ddd, *J* = 1.6, 7.2, 8.8 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 8.13 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 21.6, 48.6, 61.5, 115.8, 118.9, 123.0, 124.6, 127.2, 127.4, 128.0, 128.5, 129.5, 134.4, 138.9, 145.1, 166.9, 186.4; IR (neat) ν: 1736, 1686, 1597, 1530 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NO_5S$ $[M+H]^+$ 386.1062, found 386.1069.

methyl 3-(1*H*-indol-2-yl)-3-oxopropanoate (**S2d**)

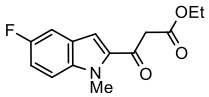


The solution of 1-(1*H*-indol-2-yl)ethan-1-one (478 mg, 3 mmol) and dimethyl carbonate (886 μL, 10.5 mmol) in THF (10 mL) was added to THF (50 mL) mixture of NaH (60% dispersion, 312 mg, 7.8 mmol) at 0 °C. The resulting mixture was heated to 40 °C and

stirred for 30 h at the same temperature. The mixture was cooled to room temperature and added *sat.* NH_4Cl *aq.* The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **S2d** as a brownish solid (495 mg, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.77 (s, 3H), 3.98 (s, 2H), 7.17 (ddd, *J* = 1.2, 6.8, 8.0 Hz, 1H), 7.38 (ddd, *J* = 1.2, 6.4, 8.4 Hz, 1H), 7.43 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 9.07 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 45.2, 52.6, 111.1, 112.3, 121.2, 123.2, 127.0, 127.4, 134.2, 137.9, 167.7, 184.4; IR (neat) ν: 3321, 1735, 1644, 1574, 1522 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{11}CsNO_3$ $[M+Cs]^+$ 349.9793, found 349.9800.

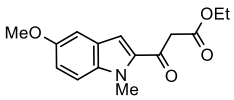
ethyl 3-(5-fluoro-1-methyl-1*H*-indol-2-yl)-3-oxopropanoate (**S2e**)



The reaction was carried out on a 3 mmol scale of carboxylic acid following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **S2e** as a yellow viscous liquid (618 mg, 78% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 6.8 Hz, 3H), 3.97 (s, 2H), 4.07 (s, 3H), 4.23 (q, *J* = 6.8 Hz, 2H), 7.17 (ddd, *J* = 2.4, 9.2, 9.2 Hz, 1H), 7.26 (s, 1H), 7.31-7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.4, 47.2, 61.6, 107.0 (d, *J* = 22.9 Hz), 111.5 (d, *J* = 9.5 Hz), 112.2 (d, *J* = 4.8 Hz), 115.8 (d, *J* = 26.7 Hz), 125.6 (d, *J* = 9.5 Hz), 136.0 (d, *J* = 215.5 Hz), 157.0, 159.3, 167.5, 185.5; IR (neat) ν: 1740, 1669, 1520, 1196 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}FNNaO_3$ $[M+Na]^+$ 286.0855, found 286.0854.

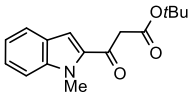
ethyl 3-(5-methoxy-1-methyl-1*H*-indol-2-yl)-3-oxopropanoate (**S2f**)



The reaction was carried out on a 3.9 mmol scale of carboxylic acid following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **S2f** as a pale yellow solid (904 mg, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 7.6 Hz, 3H), 3.85 (s, 3H), 3.97 (s, 3H), 4.05 (s, 3H), 4.22 (q, *J* = 7.2 Hz, 2H), 7.05 (d, *J* = 2.4 Hz, 1H), 7.08 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.21 (s, 1H), 7.29 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.3, 47.2, 55.6, 61.5, 102.3, 111.4, 112.0, 118.6, 125.9, 134.0, 136.1, 154.8, 167.7, 185.2; IR (neat) ν: 1739, 1662, 1520, 1217 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{17}NNaO_4$ $[M+Na]^+$ 298.1055, found 298.1057.

***tert*-butyl 3-(1-methyl-1*H*-indol-2-yl)-3-oxopropanoate**[37] (**S2g**)

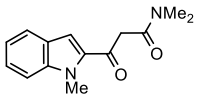


The mixture of **S2a** (245 mg, 1 mmol) and dibutyltin oxide (25 mg, 0.1 mmol) in *t*BuOH (5 mL) and toluene (5 mL) was heated to 110 °C. The mixture was stirred for 2.5 d and filtrated through Celite®. Solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **S2g** as a pale yellow solid (176 mg, 64% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.46 (s, 9H), 3.89 (s, 2H), 4.08 (s, 3H), 7.16 (ddd, *J* = 2.8, 4.8, 7.6 Hz, 1H), 7.29 (s, 1H), 7.37-7.42 (m, 2H), 7.69 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.0, 32.2, 48.5,

81.9, 110.4, 112.5, 120.8, 123.1, 125.7, 126.3, 134.1, 140.3, 166.8, 186.0; IR (neat) ν: 1727, 1659, 1513 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{19}NNaO_3$ $[M+Na]^+$ 296.1263, found 296.1265.

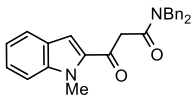
***N*,*N*-dimethyl-3-(1-methyl-1*H*-indol-2-yl)-3-oxopropanamide** (**S2h**)



The reaction was carried out on a 3 mmol scale following the general procedure A and stirred at –78 °C to room temperature. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **S2h** as a brown solid (410 mg, 56% yield).

^1H NMR (400 MHz, $CDCl_3$) δ: 3.00 (s, 3H), 3.09 (s, 3H), 4.06 (s, 3H), 4.10 (s, 2H), 7.15 (ddd, *J* = 2.0, 6.0, 8.0 Hz, 1H), 7.35-7.41 (m, 2H), 7.43 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.1, 35.6, 38.0, 47.0, 110.3, 113.0, 120.8, 123.2, 125.7, 126.4, 134.0, 140.4, 167.0, 187.0; IR (neat) ν: 1637, 1512 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}CsN_2O_2$ $[M+Cs]^+$ 377.0266, found 377.0274.

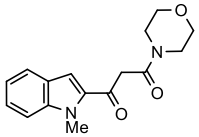
***N*,*N*-dibenzyl-3-(1-methyl-1*H*-indol-2-yl)-3-oxopropanamide** (**S2i**)



The reaction was carried out on a 4 mmol scale following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **S2i** as a pale yellow solid (1191 mg, 75% yield).

^1H NMR (400 MHz, $CDCl_3$) δ: 4.05 (s, 3H), 4.17 (s, 2H), 4.56 (s, 2H), 4.67 (s, 2H), 7.14-7.18 (m, 3H), 7.29-7.40 (m, 11H), 7.68 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.1, 46.9, 48.4, 50.6, 110.3, 112.9, 120.8, 123.1, 125.7, 126.4, 127.4, 127.7, 128.1, 128.6, 129.0, 134.0, 136.1, 136.7, 140.4, 167.9, 186.9; IR (neat) ν: 1667, 1646, 1514, 1464, 1452, 1426, 752, 738 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{24}N_2NaO_2$ $[M+Na]^+$ 419.1736, found 419.1735.

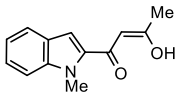
1-(1-methyl-1*H*-indol-2-yl)-3-morpholinopropane-1,3-dione (**S2j**)



The reaction was carried out on a 4 mmol scale following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **S2j** as a pale yellow solid (904 mg, 79% yield).

^1H NMR (400 MHz, $CDCl_3$) δ: 3.56-3.58 (m, 2H), 3.68-3.72 (m, 6H), 4.06 (s, 3H), 4.11 (s, 2H), 7.16 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.36-7.42 (m, 2H), 7.47 (s, 1H), 7.70 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.2, 42.3, 46.7, 46.9, 66.6, 66.7, 110.3, 113.4, 120.9, 123.2, 125.7, 126.6, 133.8, 140.5, 165.5, 186.6; IR (neat) ν: 1637, 1464, 1273, 1115, 755, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}N_2NaO_3$ $[M+Na]^+$ 309.1215, found 309.1216.

(*Z*)-3-hydroxy-1-(1-methyl-1*H*-indol-2-yl)but-2-en-1-one (**S2k**)

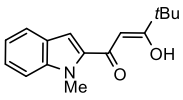


The reaction was carried out following the general procedure B. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **S2k** as a yellow solid (635 mg, 74% yield).

^1H NMR (400 MHz, $CDCl_3$) δ: 2.13 (s, 3H), 4.10 (s, 3H), 6.16 (s, 1H), 7.15 (ddd, *J* = 1.6, 6.0, 8.0 Hz, 1H), 7.17 (s, 1H), 7.34-7.40 (m, 2H), 7.66 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.1, 32.3, 98.3, 109.2, 110.2, 120.6, 122.4, 125.3, 126.2, 134.3, 140.3, 183.3, 184.8; IR (neat) ν: 1615, 1516, 1457, 1387 cm^{-}

[1]; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}NNaO_2$ $[M+Na]^+$ 238.0844, found 238.0850.

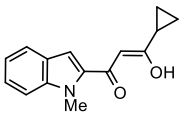
(*Z*)-3-hydroxy-4,4-dimethyl-1-(1-methyl-1H-indol-2-yl)pent-2-en-1-one (**S2l**)



The reaction was carried out following the general procedure B and stirred for 8 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **S2l** as a brown liquid (783 mg, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (s, 9H), 4.10 (s, 3H), 6.24 (s, 1H), 7.15 (ddd, *J* = 1.2, 6.4, 7.6 Hz, 1H), 7.19 (s, 1H), 7.33-7.40 (m, 2H), 7.67 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.5, 32.3, 37.9, 93.8, 108.9, 110.2, 120.6, 122.4, 125.2, 126.2, 134.9, 140.2, 185.4, 193.8; IR (neat) ν: 2965, 1603 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{19}NNaO_2$ $[M+Na]^+$ 280.1314, found 280.1313.

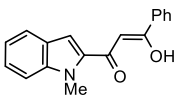
(*Z*)-3-cyclopropyl-3-hydroxy-1-(1-methyl-1H-indol-2-yl)prop-2-en-1-one (**S2m**)



The reaction was carried out following the general procedure B and stirred for 3 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **S2m** as a yellow solid (807 mg, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92-0.99 (m, 3H), 1.12 (ddd, *J* = 4.0, 4.0, 8.0 Hz, 1H), 1.20 (ddd, *J* = 4.0, 4.0, 7.2 Hz, 2H), 1.68 (tt, *J* = 4.0, 8.0 Hz, 1H), 2.16 (tt, *J* = 4.0, 8.0 Hz, 0.5H), 4.07 (s, 3H), 4.08 (s, 1.5H), 4.17 (s, 1H), 6.28 (s, 1H), 7.12-7.18 (m, 2.5H), 7.31-7.40 (m, 3.5H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.65, 11.9, 17.4, 20.8, 32.2, 32.3, 56.4, 97.3, 108.1, 110.1, 110.4, 113.4, 120.5, 120.9, 122.1, 123.2, 124.9, 125.7, 126.4, 126.5, 134.1, 134.4, 140.1, 140.5, 180.5, 186.7, 191.7, 204.3; IR (neat) ν: 1557 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}NNaO_2$ $[M+Na]^+$ 264.1001, found 264.1002.

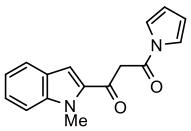
(*Z*)-3-hydroxy-1-(1-methyl-1H-indol-2-yl)-3-phenylprop-2-en-1-one (**S2n**)



The reaction was carried out on the 3 mmol scale of **S3** following the general procedure B using acetophenone and stirred for 2.5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **S2n** as a yellow solid (631 mg, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.14 (s, 3H), 6.82 (s, 1H), 7.16 (ddd, *J* = 1.6, 6.4, 8.0 Hz, 1H), 7.31 (s, 1H), 7.37 (dd, *J* = 8.8, 8.8 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.45-7.55 (m, 3H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.94 (dd, *J* = 1.6, 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.4, 95.3, 109.5, 110.3, 120.7, 122.5, 125.5, 126.2, 126.6, 128.6, 131.9, 134.3, 134.9, 140.4, 177.6, 185.6; IR (neat) ν: 1615, 1570, 1513, 1457, 1381, 1202, 770 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}NO_2$ $[M+H]^+$ 278.1181, found 278.1183.

1-(1-methyl-1H-indol-2-yl)-3-(1H-pyrrol-1-yl)propane-1,3-dione (**S2o**)

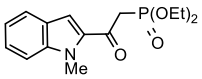


The reaction was carried out on a 4 mmol scale of **S1** following the general procedure A using 1-(1*H*-pyrrol-1-yl)ethan-1-one. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **S2o** as a pale brown solid (693 mg, 65% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.06 (s, 3H), 4.47 (s, 2H), 6.32 (dd, *J* = 2.0, 2.0 Hz, 2H), 7.17 (ddd, *J* = 1.6,

6.4, 8.0 Hz, 1H), 7.37-7.44 (m, 4H), 7.46 (s, 1H), 7.71 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.2, 48.0, 110.5, 113.6, 113.8, 119.6, 121.1, 123.3, 125.7, 126.9, 133.5, 140.7, 164.5, 184.6; IR (neat) ν: 1715, 1653, 1473, 1349, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{14}N_2NaO_2$ $[M+Na]^+$ 289.0953, found 289.0955.

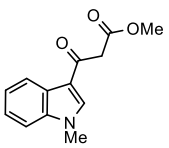
diethyl (2-(1-methyl-1*H*-indol-2-yl)-2-oxoethyl)phosphonate (**S2p**)



LHMDS (1.0 M in THF, 6.7 mL, 6.7 mmol) was added dropwise to the solution of methyl 1-methyl-1*H*-indole-2-carboxylate (610 mg, 3.2 mmol) and diethyl methylphosphonate (566 μL, 3.9 mmol) in THF (10.7 mL) at –20 °C. The resulting solution was warmed to 0 °C and stirred for 3 h. The reaction was quenched with *sat.* NH_4Cl *aq.* and layers were separated. The water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **S2p** as a pale gray solid (894 mg, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.31 (t, *J* = 7.2 Hz, 3H), 3.61 (d, *J* = 22.0 Hz, 2H), 4.07 (s, 3H), 4.67 (dq, *J* = 7.2, 7.2 Hz, 2H), 7.14-7.18 (m, 1H), 7.37-7.42 (m, 3H), 7.71 (dd, *J* = 1.2, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.2 (d, *J* = 6.7 Hz), 32.2, 39.8 (d, *J* = 130.7 Hz), 62.5 (d, *J* = 6.7 Hz), 110.3, 113.8, 120.8, 123.2, 125.6, 126.4, 134.4 (d, *J* = 3.8 Hz), 140.5, 184.4 (d, *J* = 5.7 Hz); IR (neat) ν: 1660, 1257, 1056, 1027 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{21}NO_4P$ $[M+H]^+$ 310.1208, found 310.1207.

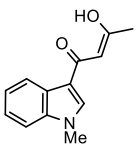
(*Z*)-3-hydroxy-1-(1-methyl-1H-indol-3-yl)but-2-en-1-one (**S2q**)



The reaction was carried out following the general procedure C. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **S2q** as an off-white solid (891 mg, 96% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.74 (s, 3H), 3.85 (d, *J* = 1.4 Hz, 3H), 3.87 (s, 2H), 7.31-7.35 (m, 3H), 7.77 (s, 1H), 8.35-8.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.7, 47.2, 52.4, 109.7, 115.8, 122.5, 123.0, 123.7, 126.2, 136.5, 137.4, 168.6, 185.9; IR (neat) ν: 1735, 1637, 1527 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}NNaO_3$ $[M+Na]^+$ 254.0793, found 254.0792.

(*Z*)-3-hydroxy-1-(1-methyl-1H-indol-3-yl)but-2-en-1-one (**S2r**)

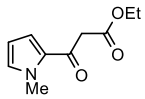


The solution of 1-(1-methyl-1*H*-indol-3-yl)ethan-1-one (693 mg, 4 mmol) and ethyl acetate (430 μL, 4.4 mmol) in THF was added *t*BuOK at 0 °C. Resulting mixture was gradually warmed to room temperature and stirred for overnight. The reaction was quenched with *sat.* NH_4Cl *aq.* and layers were separated. The water layer was extracted with AcOEt. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **S2r** as a pale brown solid (678 mg, 79% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.12 (s, 3H), 3.82 (s, 3H), 5.97 (s, 1H), 7.27-7.36 (m, 3H), 7.69 (s, 1H), 8.24-8.26 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.2, 33.5, 96.7, 109.9, 113.3, 122.0, 123.1, 125.9, 133.6, 137.6, 184.4, 186.3; IR (neat) ν: 1613, 1532, 1470, 1362, 1230, 1095 cm^{-1}; HRMS (ESI) *m/z* calcd for

$C_{13}H_{13}NNaO_2$ $[M+Na]^+$ 238.0844, found 238.0844.

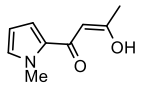
ethyl 3-(1-methyl-1*H*-pyrrol-2-yl)-3-oxopropanoate (**S2s**)



The reaction was carried out on 3.7 mmol scale of carboxylic acid following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **S2s** as a pale brown liquid (377 mg, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 7.2 Hz, 3H), 3.80 (s, 2H), 3.94 (s, 3H), 4.21 (q, *J* = 7.2 Hz, 2H), 6.15 (dd, *J* = 2.4, 4.0 Hz, 1H), 6.85 (s, 1H), 6.96 (dd, *J* = 2.0, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 37.6, 46.4, 61.3, 108.4, 120.4, 129.9, 132.0, 167.9, 182.3; IR (neat) ν: 1732, 1646, 1526 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{10}H_{13}CsNO_3$ $[M+Cs]^+$ 327.9950, found 327.99950.

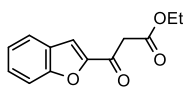
(*Z*)-3-hydroxy-1-(1-methyl-1*H*-pyrrol-2-yl)but-2-en-1-one (**S2t**)



*t*BuOK (911 mg, 8.1 mmol) was added to the solution of 2-acetyl-1-methylpyrrole (500 mg, 4 mmol) and AcOEt (793 μL, 8.1 mmol) in THF (13.5 mL) at 0 °C. The mixture was stirred for 13 h at room temperature and quenched with *sat.* NH_4Cl *aq.* The layers were separated, and the water layer was extracted with Et_2O three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **S2t** as a red liquid (502 mg, 76% yield).

^{1}H NMR (400 MHz, $CDCl_3$, keto/enol = 0.9/1) δ: 2.05 (s, 3H), 2.28 (s, 2.7H), 3.88 (s, 1.8H), 3.94 (s, 2.7H), 3.97 (s, 3H), 5.90 (s, 1H), 6.13-6.15 (m, 1.9 H), 6.81 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.86 (d, *J* = 1.6 Hz, 1H), 6.87 (d, *J* = 1.6 Hz, 0.9H), 6.95 (dd, *J* = 1.6, 4.0 Hz, 0.9H); ^{13}C NMR (100 MHz, $CDCl_3$, keto/enol mixture) δ: 22.6, 30.3, 37.6, 37.7, 55.5, 96.7, 108.4, 108.6, 117.4, 121.0, 129.2, 130.2, 130.9, 132.2, 180.6, 183.2, 183.6, 202.7; IR (neat) ν: 1645, 1624, 1405, 1379 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_9H_{11}NNaO_2$ $[M+Na]^+$ 188.0688, found 188.0686.

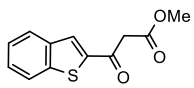
ethyl 3-(benzofuran-2-yl)-3-oxopropanoate (**S2u**)



The reaction was carried out on 3 mmol scale of carboxylic acid following the general procedure A. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **S2u** as a colorless liquid (568 mg, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 7.2 Hz, 3H), 3.80 (s, 2H), 3.94 (s, 3H), 4.21 (q, *J* = 7.2 Hz, 2H), 6.15 (dd, *J* = 2.4, 4.0 Hz, 1H), 6.85 (s, 1H), 6.96 (dd, *J* = 2.0, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 37.6, 46.4, 61.3, 108.4, 120.4, 129.9, 132.0, 167.9, 182.3; IR (neat) ν: 1732, 1646, 1526 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{10}H_{13}CsNO_3$ $[M+Cs]^+$ 327.9950, found 327.99950.

methyl 3-(benzo[*b*]thiophen-2-yl)-3-oxopropanoate (**S2v**)

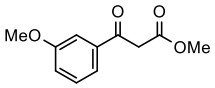


The reaction was carried out following the general procedure C and stirred for 1 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **S2v** as ared liquid (878 mg, 94% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.77 (s, 3H), 4.05 (s, 2H), 7.43 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.49 (dd, *J* = 8.4,

8.4 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 8.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 46.1, 52.7, 123.0, 125.2, 126.2, 127.9, 130.7, 138.9, 142.5, 142.9, 167.3, 186.3; IR (neat) ν: 1660, 1594, 1513 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{10}CsO_3S$ $[M+Cs]^+$ 366.9405, found 366.9407.

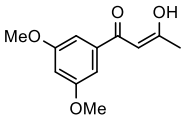
methyl 3-(3-methoxyphenyl)-3-oxopropanoate (**S2w**)



The reaction was carried out following the general procedure C. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **S2w** as a yellow liquid (833 mg, quantitative yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 3.86 (s, 3H), 4.01 (s, 2H), 7.15 (dd, *J* = 2.4, 8.0 Hz, 1H), 7.40 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.49 (d, *J* = 2.4 Hz, 1H), 7.51 (dd, *J* = 1.6, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 45.8, 52.5, 55.4, 112.5, 120.4, 121.2, 129.8, 137.2, 159.9, 167.9, 192.2; IR (neat) ν: 1739, 1684, 1597, 1581 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{11}H_{12}NaO_4$ $[M+Na]^+$ 231.0633, found 231.0629.

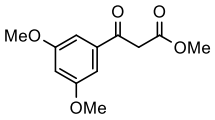
(*Z*)-1-(3,5-dimethoxyphenyl)-3-hydroxybut-2-en-1-onee (**S2x**)



*t*BuOK (673 mg, 6 mmol) was added to the solution of 1-(3,5-dimethoxyphenyl)ethan-1-one (541 mg, 3 mmol) and AcOEt (322 μL, 3.3 mmol) in THF (10 mL) at 0 °C. The mixture was stirred for 17 h at room temperature and quenched with *sat.* NH_4Cl *aq.* The layers were separated, and the water layer was extracted with Et_2O three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **S2x** as a colorless solid (461 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 3.84 (s, 6H), 3.98 (s, 2H), 6.68 (t, *J* = 2.4 Hz, 1H), 7.07 (d, *J* = 2.4 Hz, 2H),; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 45.8, 52.5, 55.6, 106.0, 106.3, 137.7, 160.9, 167.9, 192.1; IR (neat) ν: 1741, 1685, 1590 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{14}NaO_5$ $[M+Na]^+$ 261.0739, found 261.0738.

methyl 3-(3-methoxyphenyl)-3-oxopropanoate (**S2y**)



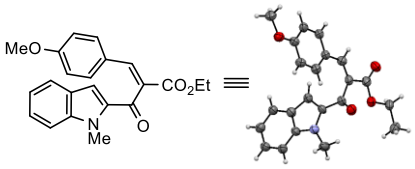
The reaction was carried out on a 9.6 mmol scale of ketone following the general procedure C. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **S2y** as a yellow liquid (2.2 g, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 3.84 (s, 6H), 3.98 (s, 2H), 6.68 (t, *J* = 2.4 Hz, 1H), 7.07 (d, *J* = 2.4 Hz, 2H),; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 45.8, 52.5, 55.6, 106.0, 106.3, 137.7, 160.9, 167.9, 192.1; IR (neat) ν: 1741, 1685, 1590 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{14}NaO_5$ $[M+Na]^+$ 261.0739, found 261.0738.

General Procedure of Knoevenagel Condensation

The solution of **S2** (2 mmol), aldehyde (2 mmol), piperidine (20 μL, 0.2 mmol) and AcOH (52 μL, 1 mmol) in benzene (10 mL) was heated to refluxing temperature and stirred for 4 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography.

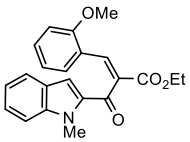
ethyl (*E*)-3-(4-methoxyphenyl)-2-(1-methyl-1*H*-indole-2-carbonyl)acrylate[38] (**128a**)



The reaction was carried out as described in the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128a** as a yellow viscous liquid (640 mg, 88% yield, *E*/*Z* = 17/1). Further purification was achieved by crystallization from Et_2O to afford a colorless solid. The regiochemistry was determined by X-ray crystallographic analysis. Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the Et_2O solution of product and stilled at room temperature for overnight.

Melting Point: 108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.6 Hz, 3H), 3.75 (s, 3H), 4.21 (s, 3H), 4.23 (q, *J* = 7.6 Hz, 2H), 6.76 (d, *J* = 8.8 Hz, 2H), 7.09-7.13 (m, 2H), 7.37-7.43 (m, 4H), 7.59 (dd, *J* = 0.8, 8.4 Hz, 1H), 7.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.1, 55.3, 61.4, 110.4, 114.3, 114.6, 120.7, 123.4, 125.7, 126.0, 129.6, 132.2, 135.0, 140.8, 141.7, 161.2, 165.6, 188.3; IR (neat) ν: 1600, 1638, 1707 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_4$ $[M+Na]^+$ 386.1368, found 386.1382.

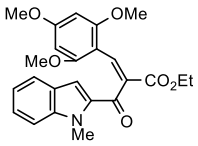
ethyl (*E*)-3-(2-methoxyphenyl)-2-(1-methyl-1*H*-indole-2-carbonyl)acrylate (**128b**)



The reaction was carried out on a 3 mmol scale of **S2a** following the general procedure and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128b** as a yellow viscous liquid (1111 mg, quantitative yield, *E*/*Z* = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, *J* = 6.8 Hz, 3H), 3.84 (s, 3H), 4.14 (s, 3H), 4.25 (q, *J* = 6.8 Hz, 2H), 6.73 (dd, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.10 (ddd, *J* = 3.2, 4.8, 8.0 Hz, 1H), 7.11 (s, 1H), 7.22 (ddd, *J* = 2.0, 8.0, 8.0 Hz, 1H), 7.35-7.37 (m, 3H), 7.59 (d, *J* = 8.0 Hz, 1H), 8.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.0, 55.4, 61.4, 110.3, 110.7, 114.5, 120.4, 120.6, 122.5, 123.3, 125.9, 126.2, 130.0, 131.7, 131.8, 135.1, 137.7, 140.7, 158.0, 165.5, 187.9; IR (neat) ν: 1711, 1639, 1613, 1597, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_4$ $[M+H]^+$ 364.1549, found 364.1546.

ethyl (*E*)-2-(1-methyl-1*H*-indole-2-carbonyl)-3-(2,4,6-trimethoxyphenyl)acrylate (**128c**)

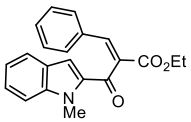


The reaction was carried out following the general procedure and stirred for 1.5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **128c** as a yellow solid (849 mg, 97% yield, *E*/*Z* = 2.9/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ:1.18 (t, *J* = 6.8 Hz, 3H), 3.57 (s, 6H), 3.75 (s, 3H), 4.14 (s, 3H), 4.21 (q, *J* = 6.8 Hz, 2H), 5.96 (s, 2H), 7.03 (s, 1H), 7.10 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.32-7.39 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 8.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 31.9, 54.9, 55.3, 61.0, 90.2, 105.3, 110.1, 112.4, 120.2, 123.0, 125.2, 126.0, 129.8, 135.0, 135.9, 139.9, 159.6, 163.3, 167.0, 186.9; IR (neat) ν: 1705, 1648, 1599, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_6$ $[M+Na]^+$ 446.1580, found 446.1562.

ethyl (*E*)-2-(1-methyl-1*H*-indole-2-carbonyl)-3-phenylacrylate (**128d**)

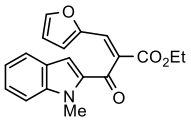
The reaction was carried out following the general procedure and stirred for 4 h. The residue was purified



by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **128d** as a yellow viscous liquid (753 mg, 90% yield, *E*/*Z* = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, *J* = 7.2 Hz, 3H), 4.20 (s, 3H), 4.25 (q, *J* = 7.2 Hz, 2H), 7.09-7.13 (m, 2H), 7.23-7.27 (m, 2H), 7.39-7.45 (m, 5H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.1, 61.6, 110.4, 114.7, 120.8, 123.4, 125.9, 126.5, 128.7, 130.1, 130.2, 132.1, 133.1, 134.8, 140.8, 141.9, 165.3, 187.6; IR (neat) ν: 1716, 1646, 1254, 1200 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_3$ $[M+Na]^+$ 356.1263, found 356.1261.

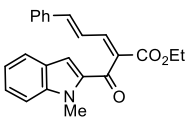
ethyl (*E*)-3-(furan-2-yl)-2-(1-methyl-1*H*-indole-2-carbonyl)acrylate (**128e**)



The reaction was carried out as described in the general procedure and stirred for 1 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **128e** as a brown viscous liquid (601 mg, 93% yield, *E*/*Z* = 12.5/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.23 (t, *J* = 7.2 Hz, 3H), 4.22 (s, 3H), 4.24 (q, *J* = 7.2 Hz, 2H), 6.36 (dd, *J* = 2.0, 4.0 Hz, 1H), 6.67 (d, *J* = 4.0 Hz, 1H), 7.09 (s, 1H), 7.12 (ddd, *J* = 1.2, 6.4, 8.0 Hz, 1H), 7.32 (s, 1H), 7.37-7.44 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.0, 61.5, 110.4, 112.3, 114.1, 117.7, 120.7, 123.2, 126.0, 126.2, 127.6, 128.0, 135.2, 140.7, 146.1, 149.4, 165.2, 186.7; IR (neat) ν: 1714, 1653, 1251, 1211 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{17}NNaO_4$ $[M+Na]^+$ 346.1055, found 346.1054.

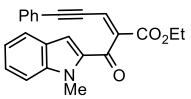
ethyl (2*E*,4*E*)-2-(1-methyl-1*H*-indole-2-carbonyl)-5-phenylpenta-2,4-dienoate (**128f**)



The reaction was carried out as described in the general procedure and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128f** as a dark yellow viscous liquid (579 mg, 81% yield, *E*/*Z* = 4/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.2 Hz, 3H), 4.21 (s, 3H), 4.22 (q, *J* = 7.2 Hz, 2H), 6.86 (dd, *J* = 12.0, 15.6 Hz, 1H), 7.04 (d, *J* = 15.6 Hz, 1H), 7.11 (s, 1H), 7.14 (ddd, *J* = 2.4, 6.4, 8.8 Hz, 1H), 7.26-7.30 (m, 3H), 7.37-7.45 (m, 4H), 7.64 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.65 (d, *J* = 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.1, 61.2, 110.4, 115.1, 120.8, 123.1, 123.4, 126.0, 126.5, 127.6, 128.7, 129.5, 132.1, 135.6, 140.8, 142.7, 143.2, 165.3, 186.5; IR (neat) ν: 1702, 1638, 1613, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{21}NNaO_3$ $[M+Na]^+$ 382.1419, found 382.1420.

ethyl (*E*)-2-(1-methyl-1*H*-indole-2-carbonyl)-5-phenylpent-2-en-4-ynoate[39] (**128g**)

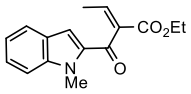


The mixture of **S2a** (491 mg, 2 mmol), phenylpropargyl akdehyde (294 μL, 2.4 mmol), piperidine (20 μL, 0.2 mmol), AcOH (70 μL, 1.2 mmol) and $MgSO_4$ (48 mg) in toluene (10 mL) was stirred at room temperature for 1 day. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128g** as a brown solid (586 mg, 82%, *E*/*Z* =5/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.25 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.6 Hz, 0.6H), 4.04 (s, 0.6H), 4.18 (s, 3H), 4.26 (q, *J* = 7.2 Hz, 2H), 4.34 (q, *J* = 7.6 Hz, 0.4H), 6.86 (s, 0.2H), 7.09-7.39 (m, 11.8H), 7.54 (dd, *J* = 2.0, 7.6 Hz, 0.2H), 7.67 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 14.1, 31.8, 31.9, 61.4,

61.6, 84.7, 85.3, 104.1, 105.2, 110.3, 114.1, 115.2, 120.7, 120.9, 121.5, 122.0, 123.0, 123.1, 123.3, 123.9, 125.7, 126.0, 126.4, 126.5, 128.2, 128.4, 129.4, 129.7, 131.8, 132.1, 134.2, 134.3, 140.6, 140.7, 141.5, 141.9, 164.0, 164.4, 183.6, 184.8; IR (neat) ν: 2196, 1715, 1652, 1246 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{19}NNaO_3$ $[M+Na]^+$ 380.1263, found 380.1265.

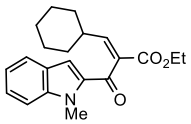
ethyl (*E*)-2-(1-methyl-1*H*-indole-2-carbonyl)but-2-enoate[40] (**128h**)



The solution of **S2a** (491 mg, 2 mmol) and piperidine (20 μL, 0.2 mmol) in EtOH (2 mL) was added acetaldehyde (119 μL, 2 mmol) at 0 °C. The reaction mixture was gradually warmed to room temperature and stirred for 4 h then water was added to reaction mixture. The layers were separated and water layer was extracted with Et_2O three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128h** as an orange viscous liquid (164 mg, 37% yield, *E/Z* = 5/1).

^1H NMR (400 MHz, $CDCl_3$) δ: 1.98 (t, *J* = 7.6 Hz, 3H), 1.85 (d, *J* = 7.6 Hz, 3H), 4.16 (s, 3H), 4.19 (q, *J* = 7.6 Hz, 2H), 7.10 (s, 1H), 7.16 (ddd, *J* = 3.2, 4.8, 8.0 Hz, 1H), 7.39-7.42 (m, 2H), 7.66 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 15.5, 32.0, 61.1, 110.4, 114.6, 120.8, 123.2, 125.9, 126.5, 135.0, 135.6, 140.7, 142.4, 164.6, 186.8; IR (neat) ν: 1714, 1642, 1613, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{17}NNaO_3$ $[M+Na]^+$ 294.1106, found 294.1105.

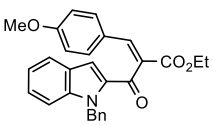
ethyl (*E*)-3-cyclohexyl-2-(1-methyl-1*H*-indole-2-carbonyl)acrylate (**128i**)



The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128i** as a yellow viscous liquid (660 mg, 97% yield, *E/Z* = 8.3/1).

^1H NMR (400 MHz, $CDCl_3$) δ: 1.14-1.26 (m, 9H), 1.65-1.71 (m, 4H), 2.18-2.29 (m, 1H), 4.16 (s, 3H), 4.17 (q, *J* = 6.8 Hz, 2H), 6.93 (d, *J* = 7.2 Hz, 1H), 7.10 (s, 1H), 7.17 (ddd, *J* = 2.8, 4.4, 7.2 Hz, 1H), 7.38-7.42 (m, 2H), 7.67 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 24.9, 25.5, 31.7, 32.0, 38.6, 61.1, 110.4, 114.5, 120.7, 123.3, 125.8, 126.3, 132.5, 135.2, 140.7, 151.8, 165.1, 186.9; IR (neat) ν: 2925, 2850, 1716, 1644, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{25}NNaO_3$ $[M+Na]^+$ 362.1732, found 362.1735.

ethyl (*E*)-2-(1-benzyl-1*H*-indole-2-carbonyl)-3-(4-methoxyphenyl)acrylate (**128j**)

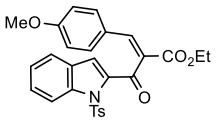


The reaction was carried out on a 1 mmol scale of **S2b** following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128j** as a yellow solid (348 mg, 83% yield, *E/Z* = >20/1). Further purification was achieved by recrystallization from Et_2O/Hexane to afford a pale yellow solid.

Melting Point: 111 °C; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.17 (t, *J* = 6.8 Hz, 3H), 3.72 (s, 3H), 4.20 (q, *J* = 6.8 Hz, 2H), 6.02 (s, 2H), 6.60 (d, *J* = 8.8 Hz, 2H), 7.11-7.17 (m, 3H), 7.22-7.29 (m, 6H), 7.35 (ddd, *J* = 1.2, 8.4, 8.4 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 48.0, 55.2, 61.3, 110.9, 114.1, 115.8, 121.0, 123.5, 125.6, 126.2, 126.8, 126.9, 127.2, 128.5, 129.3, 132.3, 134.2, 138.2, 140.7, 141.8, 161.1, 165.6, 187.8; IR (neat) ν: 2979, 1708, 1638, 1600, 1510 cm^{-1};

HRMS (ESI) *m/z* calcd for $C_{28}H_{26}NO_4$ $[M+H]^+$ 440.1862, found 440.1873.

ethyl 3-(4-methoxyphenyl)-2-(1-tosyl-1*H*-indole-2-carbonyl)acrylate (**128k**)

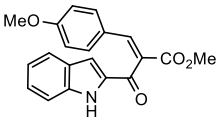


The reaction was carried out as described in the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 3/1) to afford **128k** as a yellow amourphous (766 mg, 76% yield, *E*/*Z* = 1/1). *E* and *Z* isomers cloud be separated, and its configuration was determined by analysis of $^3J_{C,H}$ coupling constants.[41]

(*E*)-**128k**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.20 (t, *J* = 7.2 Hz, 3H), 2.43 (s, 3H), 3.76 (s, 3H), 4.21 (q, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 7.23 (s, 1H), 7.24-7.28 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.50 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.90 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 2H), 8.29 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 21.7, 55.3, 61.5, 114.3, 115.7, 121.4, 123.3, 123.8, 125.2, 127.2, 127.8, 128.4, 128.5, 129.5, 129.6, 132.8, 137.1, 138.1, 140.3, 143.5, 144.6, 161.6, 184.0; IR (neat) ν: 1709, 1664, 1597, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{26}NO_6S$ $[M+H]^+$ 504.1481, found 504.1482.

(*Z*)-**128k**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.29 (t, *J* = 7.6 Hz, 3H), 2.36 (s, 3H), 3.85 (s, 3H), 4.37 (q, *J* = 7.2 Hz, 2H), 6.90 (d, *J* = 9.2 Hz, 2H), 6.99 (s, 1H), 7.26 (d, *J* = 7.2 Hz, 2H), 7.29 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.44 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.56 (s, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 21.6, 55.4, 61.8, 114.3, 114.9, 115.4, 122.5, 124.1, 125.3, 126.8, 127.8, 128.4, 129.6, 132.4, 132.5, 135.1, 136.8, 137.3, 145.1, 145.3, 162.1, 167.3, 184.8; IR (neat) ν: 1726, 1647, 1596, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{25}NNaO_6S$ $[M+Na]^+$ 526.1300, found 526.1300.

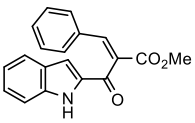
methyl (*E*)-2-(1*H*-indole-2-carbonyl)-3-(4-methoxyphenyl)acrylate[14b] (**128l**)



The reaction was carried out as described in the general procedure, and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128l** as a yellow solid (476 mg, 71% yield, *E*/*Z* = 14/1). Further purification was achieved by recrystallization from CH_2Cl_2/Hexane to afford a yellow solid.

Melting Point: 164-166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.71 (s, 3H), 3.76 (s, 3H), 6.72 (d, *J* = 9.2 Hz, 2H), 7.05 (s, 1H), 7.10 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.34 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.37 (d, *J* = 9.2 Hz, 2H), 7.44 (d, *J* = 8.4, Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.97 (s, 1H), 9.39 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.5, 55.2, 112.3, 112.7, 114.3, 121.1, 123.4, 125.4, 126.9, 127.4, 127.5, 132.3, 135.0, 138.2, 143.3, 161.4, 165.8, 187.3; IR (neat) ν: 3318, 1702, 1598, 1571, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_4$ $[M+H]^+$ 336.1236, found 336.1236.

methyl (*E*)-2-(1*H*-indole-2-carbonyl)-3-phenylacrylate[14b] (**128m**)

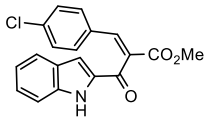


The reaction was carried out as described in the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128m** as a pale yellow solid (526 mg, 86% yield, *E*/*Z* = 14/1). Further

purification was achieved by recrystallization from CH_2Cl_2/Hexane to afford a colorless solid.

Melting Point: 160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.78 (s, 3H), 7.03 (d, *J* = 1.2 Hz. 1H), 7.11 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.20-7.28 (m, 3H), 7.35 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.41-7.45 (m, 3H), 7.60 (d, *J* = 8.4 Hz, 1H), 8.03 (s, 1H), 9.24 (brs, 1H); HRMS (ESI) *m/z* calcd for $C_{19}H_{16}NO_3$ $[M+H]^+$ 306.1130, found 306.1130.

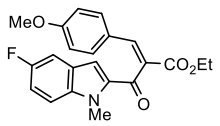
methyl (*E*)-3-(4-chlorophenyl)-2-(1*H*-indole-2-carbonyl)acrylate[14b] (**128n**)



The reaction was carried out as described in the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128n** as a yellow solid (425 mg, 63% yield). Further purification was achieved by recrystallization from AcOEt/Hexane to afford a yellow solid.

Melting Point: 178-181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.79 (s, 3H), 7.01 (dd, *J* = 1.2, 2.4 Hz, 1H), 7.13 (ddd, *J* = 1.2, 6.8, 8.0 Hz, 1H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.37 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.44 (dd, *J* = 1.2, 8.4 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.95 (s, 1H), 9.13 (brs, 1H); HRMS (ESI) *m/z* calcd for $C_{19}H_{15}ClNO_3$ $[M+H]^+$ 340.0741, found 340.0749.

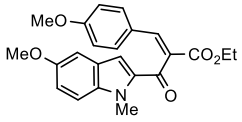
ethyl (*E*)-2-(5-fluoro-1-methyl-1*H*-indole-2-carbonyl)-3-(4-methoxyphenyl)acrylate (**128o**)



The reaction was carried out as described in the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128o** as a yellow solid (801 mg, quantitative yield, *E*/*Z* = 15/1). Further purification was achieved by trituration from Et_2O to afford a colorless solid.

Melting Point: 100-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.2 Hz, 3H), 3.75 (s, 3H), 4.19 (s, 3H), 4.24 (q, *J* = 7.2 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.78 (s, 1H), 7.15 (ddd, *J* = 2.0, 8.8, 8.8 Hz, 1H), 7.20 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.34 (dd, *J* = 4.0, 9.2 Hz, 1H), 7.39 (d, *J* = 9.2 Hz, 2H), 7.85 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.2, 55.2, 61.4, 107.2 (d, *J* = 22.9 Hz), 111.4 (d, *J* = 11.9 Hz), 113.8 (d, *J* = 5.7 Hz), 114.3, 115.5 (d, *J* = 26.7 Hz), 125.6, 125.9 (d, *J* = 9.5 Hz), 129.5, 132.2, 136.1, 137.5, 141.8, 158.0 (d, *J* = 236.4 Hz), 161.3, 165.4, 188.3; IR (neat) ν: 1714, 1651, 1604, 1516, 1258, 1200, 1176 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{20}FNNaO_4$ $[M+Na]^+$ 404.1274, found 404.1275.

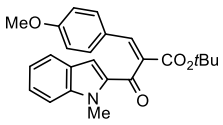
ethyl (*E*)-2-(5-methoxy-1-methyl-1*H*-indole-2-carbonyl)-3-(4-methoxyphenyl)acrylate (**128p**)



The reaction was carried out as described in the general procedure and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **128p** as a dark yellow amorphous (712 mg, 91% yield, *E*/*Z* = 6/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.2 Hz, 3H), 3.75 (s, 3H), 3.79 (s, 3H), 4.18 (s, 3H), 4.23 (q, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 2.0 Hz, 1H), 7.03 (s, 1H), 7.07 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.32 (d, *J* = 9.2 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 32.2, 55.2, 55.7, 61.3, 102.6, 111.4, 113.8, 114.2, 118.5, 125.7, 126.1, 129.7, 132.2, 135.1, 136.5, 141.5, 154.6, 161.2, 165.6, 187.9; IR (neat) ν: 1714, 1645, 1603, 1516, 1257, 1215, 1201, 1176 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{23}NNaO_5$ $[M+Na]^+$ 416.1474, found 416.1476.

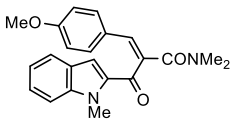
***tert*-butyl (*E*)-3-(4-methoxyphenyl)-2-(1-methyl-1*H*-indole-2-carbonyl)acrylate** (**128q**)



The reaction was carried out on a 1 mmol scale following the general procedure and stirred for 18 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128q** as a yellow viscous liquid (273 mg, 44% yield, *E*/*Z* = 9/1). Further purification was achieved by recrystallization from Et_2O/Hexane to afford a colorless solid.

Melting Point: 95-96 °C; ^{1}H NMR (400 MHz, CD_3OD) δ: 1.40 (s, 9H), 3.72 (s, 3H), 4.15 (s, 3H), 6.81 (d, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.10 (s, 1H), 7.38 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.40 (d, *J* = 9.2 Hz, 2H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.74 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ: 28.2, 32.4, 55.8, 83.0, 111.5, 115.3, 115.5, 122.0, 124.2, 127.0, 127.4, 127.8, 132.4, 133.2, 136.3, 142.1, 142.4, 163.0, 166.1, 190.4; IR (neat) ν: 2976, 1709, 1643, 1601, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{26}NO_4$ $[M+H]^+$ 392.1862, found 392.1870.

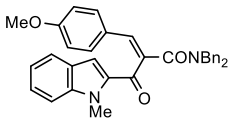
(*E*)-3-(4-methoxyphenyl)-*N*,*N*-dimethyl-2-(1-methyl-1*H*-indole-2-carbonyl)acrylamide (**128r**)



The reaction was carried out on a 1.6 mmol scale following the general procedure and stirred for 18 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **128r** as a yellow amorphous (577 mg, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.94 (s, 3H), 3.13 (s, 3H), 3.85 (s, 3H), 4.02 (s, 3H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.17 (ddd, *J* = 2.4, 6.0, 7.6 Hz, 1H), 7.24 (s, 1H), 7.39-7.43 (m, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.55 (s, 1H), 7.70 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.8, 34.7, 37.6, 55.3, 110.2, 112.9, 114.4, 120.7, 122.9, 125.75, 125.81, 126.0, 131.6, 134.6, 134.7, 140.2, 141.2, 161.4, 168.4, 185.4; IR (neat) ν: 1596, 1508 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{23}N_2O_3$ $[M+H]^+$ 363.1709, found 363.1711.

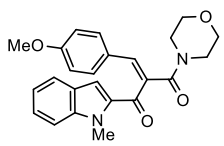
(*E*)-*N*,*N*-dibenzyl-3-(4-methoxyphenyl)-2-(1-methyl-1*H*-indole-2-carbonyl)acrylamide (**128s**)



The reaction was carried out as described in the general procedure and stirred for 18 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/6) to afford **128s** as a yellow amorphous (928 mg, 90% yield, *E*/*Z* = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (s, 3H), 3.94 (s, 3H), 4.37 (brs, 1H), 4.45 (brs, 1H), 4.58 (brs, 1H), 4.70 (brs, 1H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 6.4 Hz, 2H), 7.15-7.40 (m, 12H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.59 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.7, 46.4, 51.2, 55.4, 110.2, 113.0, 114.3, 120.7, 123.0, 125.7, 125.8, 126.0, 127.4, 127.6, 128.1, 128.5, 128.6, 129.3, 132.0, 134.76, 134.79, 135.5, 135.9, 140.2, 142.1, 161.5, 168.5, 185.7; IR (neat) ν: 1634, 1615, 1511, 1261, 1178, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{34}H_{30}N_2NaO_3$ $[M+Na]^+$ 537.2154, found 537.2158.

(*E*)-2-(4-methoxybenzylidene)-1-(1-methyl-1*H*-indol-2-yl)-3-morpholinopropane-1,3-dione (**128t**)

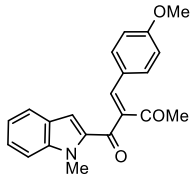


The reaction was carried out as described in the general procedure and stirred for 18 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **128t** as a yellow amorphous (797 mg, 99% yield, *E*/*Z* = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.39 (brs, 4H), 3.72 (brs, 2H), 3.81 (brs, 2H), 3.85 (s, 3H), 4.02 (s, 3H), 6.93 (d, *J* = 8.8 Hz, 2H), 7.17 (ddd, *J* = 2.4, 4.8, 8.0 Hz, 1H), 7.26 (s, 1H), 7.40-7.41 (m,

2H), 7.50 (d, *J* = 8.8 Hz, 2H), 7.53 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.8, 41.8, 46.8, 55.4, 66.4, 66.6, 110.3, 113.5, 114.4, 120.8, 123.0, 125.76, 125.77, 126.0, 131.6, 134.0, 140.4, 141.1, 161.5, 166.8, 185.3; IR (neat) ν: 1634, 1512, 1464, 1260, 1232, 1179 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{24}N_2NaO_4$ $[M+Na]^+$ 427.1634, found 427.1635.

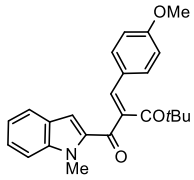
(*E*)-2-(4-methoxybenzylidene)-1-(1-methyl-1*H*-indol-2-yl)butane-1,3-dione (**128u**)



The reaction was carried out on a 1.5 mmol scale of **S2f** following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128u** as a yellow amorphous (419 mg, 69% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.40 (s, 3H), 3.74 (s, 3H), 4.23 (s, 3H), 6.76 (d, *J* = 8.4 Hz, 2H), 7.09 (s, 1H), 7.11 (ddd, *J* = 1.6, 5.6, 7.6 Hz, 1H), 7.37-7.41 (m, 4H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.2, 32.2, 55.3, 110.4, 114.3, 115.0, 120.9, 123.4, 125.6, 125.9, 126.6, 132.4, 134.9, 138.1, 140.6, 140.9, 161.4, 190.6, 195.8; IR (neat) ν: 1662, 1636, 1602, 1513, 1262, 1178 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_3$ $[M+Na]^+$ 356.1263, found 356.1261.

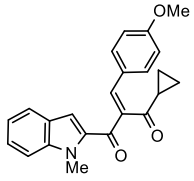
(*E*)-2-(4-methoxybenzylidene)-4,4-dimethyl-1-(1-methyl-1*H*-indol-2-yl)pentane-1,3-dione (**128v**)



The reaction was carried out following the general procedure and stirred for 3 days. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford the 2.8/1 mixture of **128v** and **129v** (609 mg). This mixture was dissolved in CH_2Cl_2 and added methyl acrylate (90 μL, 1mmol), KOH (56 mg, 1mmol) and *n*Bu_4NBr (catalytic amount). The mixture was stirred at room temperature for 3.5 days and added water. The layers were separated and water layer was extracted with CH_2Cl_2. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128v** as a yellow viscous liquid (400 mg, 53% yield in 2 steps, *E/Z* = 3.7/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.16 (s, 9H), 1.27 (s, 2.25H), 3.73 (s, 0.75H), 3.83 (s, 3H), 4.00 (s, 3H), 4.18 (s, 0.75H), 6.74 (d, *J* = 8.8 Hz, 0.5H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.10 (ddd, *J* = 2.4, 5.2, 8.0 Hz, 0.25H), 7.15 (s, 0.25H), 7.19 (ddd, *J* = 2.4, 5.6, 8.0 Hz, 1H), 7.22 (s, 1H), 7.34 (d, *J* = 8.8 Hz, 0.5H), 7.37-7.42 (m, 4.5H), 7.45 (s, 0.25H), 7.54 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 0.25H), 7.72 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.0, 27.7, 31.7, 32.0, 45.3, 45.7, 55.2, 55.3, 110.3, 112.9, 114.1, 114.2, 114.9, 120.8, 120.9, 122.9, 123.4, 125.76, 125.82, 126.26, 126.28, 126.4, 131.7, 131.8, 134.5, 135.4, 139.5, 139.7, 140.3, 140.7, 140.8, 141.7, 160.7, 161.3, 186.2, 189.3, 205.6, 213.1; IR (neat) ν: 1696, 1603, 1511, 1261, 1180 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1732.

(*E*)-1-cyclopropyl-2-(4-methoxybenzylidene)-3-(1-methyl-1*H*-indol-2-yl)propane-1,3-dione (**128w**)

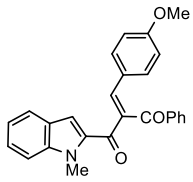


The reaction was carried out following the general procedure and stirred for 7 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **128w** as a yellow amorphous (551 mg, 77% yield, *E/Z* = 15/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.91 (ddd, *J* = 4.0, 4.0, 11.2 Hz, 2H), 1.17 (ddd, *J* = 3.6,

3.6, 7.2 Hz, 2H), 2.25 (tt, *J* = 4.0, 8.0 Hz, 1H), 3.73 (s, 3H), 4.23 (s, 3H), 6.76 (d, *J* = 8.4 Hz, 2H), 7.10 (ddd, *J* = 2.4, 5.6, 8.0 Hz, 1H), 7.15 (s, 1H), 7.38-7.74 (m, 4H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.1, 18.3, 32.1, 55.2, 110.4, 114.2, 115.2, 120.8, 123.4, 125.8, 125.9, 126.6, 132.3, 135.2, 138.3, 139.6, 140.9, 161.2, 190.7, 197.7; IR (neat) ν: 1634, 1602, 1512, 1263, 1174, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$ 360.1600, found 360.1600.

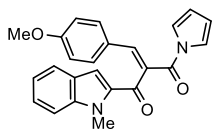
(*E*)-2-(4-methoxybenzylidene)-1-(1-methyl-1*H*-indol-2-yl)-3-phenylpropane-1,3-dione (**128x**)



The reaction was carried out following the general procedure and stirred for 19 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128x** as a yellow amorphous (700 mg, 89% yield, *E*/*Z* = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 3.78 (s, 3H), 3.99 (s, 3H), 4.17 (s, 3H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 7.10 (ddd, *J* = 2.0, 5.2, 7.6 Hz, 1H), 7.16-7.20 (m, 2H), 7.31-7.57 (m, 17H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.86 (d, *J* = 7.2 Hz, 2H), 8.05 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 1.8, 32.1, 55.28, 55.31, 110.3, 110.4, 113.2, 114.3, 114.6, 120.7, 120.8, 123.0, 123.3, 125.7, 125.8, 125.9, 126.0, 126.4, 128.4, 128.8, 128.9, 129.3, 129.4, 132.1, 132.28, 132.31, 133.8, 134.6, 135.3, 136.5, 138.00, 138.82, 138.5, 140.3, 140.8, 143.4, 144.0, 143.4, 144.0, 161.39, 161.42, 186.2, 189.3, 194.9, 197.1; IR (neat) ν: 1652, 1632, 1599, 1512, 1264, 1178 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{22}NO_3$ $[M+H]^+$ 396.1600, found 396.1604.

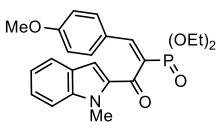
(*E*)-2-(4-methoxybenzylidene)-1-(1-methyl-1*H*-indol-2-yl)-3-(1*H*-pyrrol-1-yl)propane-1,3-dione (**128y**)



The reaction was carried out following the general procedure and stirred for 18 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **128y** as a yellow amorphous (684 mg, 89% yield, *E*/*Z* =9/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 4.01 (s, 3H), 6.27-6.33 (m, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.18 (ddd, *J* = 4.0, 4.0, 8.0 Hz, 1H), 7.24 (s, 1H), 7.36-7.41 (m, 4H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.82 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.9, 55.4, 110.4, 113.0, 114.1, 114.6, 120.8, 120.9, 123.0, 125.1, 125.8, 126.1, 132.0, 132.6, 134.1, 140.4, 144.4, 162.0, 166.1, 184.3; IR (neat) ν: 1705, 1613, 1600, 1512, 1468, 1325, 1291, 1263, 1180, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{21}N_2O_3$ $[M+H]^+$ 385.1552, found 385.1551.

diethyl (*E*)-(1-(4-methoxyphenyl)-3-(1-methyl-1*H*-indol-2-yl)-3-oxoprop-1-en-2-yl)phosphonate (**128z**)

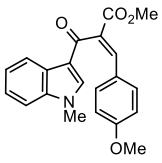


The reaction was carried out as described in the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **128z** as a yellow viscous liquid (826 mg, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 6.8 Hz, 6H), 3.71 (s, 3H), 4.17 (s, 3H), 4.17 (dq, *J* = 7.2, 7.2 Hz, 4H), 6.72 (d, *J* = 8.8 Hz, 2H), 7.09 (ddd, *J* = 2.8, 4.8, 8.0 Hz, 1H), 7.20 (s, 1H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.37-7.38 (m, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 25.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.2

(d, *J* = 6.7 Hz), 32.1, 55.2, 62.6 (d, *J* = 5.7 Hz), 110.3, 114.1, 115.9, 120.6, 123.5, 125.8, 126.43 (d, *J* = 21.0 Hz), 126.45, 128.8 (d, *J* = 173.6 Hz), 131.7, 134.4 (d, *J* = 2.8 Hz), 140.8, 145.9 (d, *J* = 6.7 Hz), 160.9, 187.9 (d, *J* = 9.5 Hz); IR (neat) ν: 1635, 1604, 1513, 1259, 1052, 1029 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{27}NO_5P$ $[M+H]^+$ 428.1627, found 428.1627.

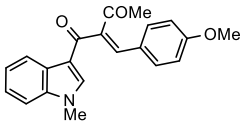
methyl (*E*)-3-(4-methoxyphenyl)-2-(1-methyl-1*H*-indole-3-carbonyl)acrylate (**154a**)



The reaction was carried out on a 1 mmol scale following the general procedure and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **154a** as a pale yellow foam (334 mg, 96% yield, *E*/*Z* = >20/1). Further purification was achieved by recrystallization from CH_2Cl_2/Hexane to afford a colorless solid (292 mg).

^1H NMR (400 MHz, CD_3OD) δ: 3.72 (s, 3H), 3.73(s, 3H), 3.75 (s, 3H), 6.73 (ddd, *J* = 2.4, 2.4, 9.2 Hz, 2H), 7.31-7.39 (m, 3H), 7.46 (ddd, *J* = 2.8, 2,8, 8.8 Hz, 2H), 7.53 (s, 1H), 7.84 (s, 1H), 8.51 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ: 33.6, 52.4, 55.2, 109.8, 114.2, 116.4, 122.7, 123.0, 123.7, 125.8, 126.2, 129.7, 132.4, 137.9, 138.0, 141.0, 161.1, 166.6, 189.2; IR (neat) ν: 2951, 1706, 1601, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_4$ $[M+Na]^+$ 372.1212, found 372.1218.

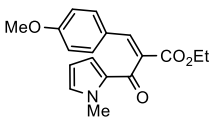
(*E*)-2-(4-methoxybenzylidene)-1-(1-methyl-1*H*-indol-3-yl)butane-1,3-dione (**154b**)



The reaction was carried out following the general procedure and stirred for 10 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **154b** as a pale yellow foam (524 mg, 79% yield).

^1H NMR (400 MHz, CD_3OD) δ: 2.37 (s, 3H), 3.72 (s, 6H), 6.73 (d, *J* = 8.8 Hz, 2H), 7.33-7.38 (m, 3H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.50 (s, 1H), 7.68 (s, 1H), 8.52 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ: 27.5, 33.6, 55.2, 109.8, 114.2, 116.6, 122.6, 123.0, 123.8, 125.7, 126.1, 132.6, 137.9, 138.1, 138.4, 139.0, 161.2, 191.8, 196.1; IR (neat) ν: 1658, 1622, 1614, 1601, 1525, 1513, 1262, 1179 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_3$ $[M+Na]^+$ 356.1263, found 356.1264.

ethyl (*E*)-3-(4-methoxyphenyl)-2-(1-methyl-1*H*-pyrrole-2-carbonyl)acrylate (**156a**)

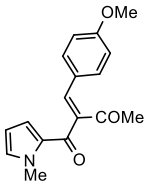


The reaction was carried out on a 1.7 mmol scale following the general procedure and stirred for 23 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/4) to afford **156a** as a yellow viscous liquid (447 mg, 84% yield, *E*/*Z* = 14/1). Further purification was achieved by trituration from Et_2O to afford a colorless solid.

Melting Point: 120-121 °C; ^1H NMR (400 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 3.77 (s, 3H), 4.08 (s, 3H), 6.01 (dd, *J* = 2.0, 4.4 Hz, 1H), 6.69 (d, *J* = 4.4 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.87 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.2, 37.5, 55.3, 108.9, 114.2, 122.6, 125.9, 130.9, 132.4, 132.5, 138.1, 139.8, 161.2, 186.9, 195.9; IR (neat) ν: 1624, 1601, 1512, 1404, 1264, 1178, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1106, found 306.1107.

(*E*)-2-(4-methoxybenzylidene)-1-(1-methyl-1*H*-pyrrol-2-yl)butane-1,3-dione (**156b**)

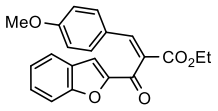
The reaction was carried out on a 1.8 mmol scale following the general procedure and stirred for 6 h. The



residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **156b** as a pale yellow solid (401 mg, 79% yield). Further purification was achieved by trituration from Et_2O to afford a colorless solid.

Melting Point: 120-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 3.77 (s, 3H), 4.08 (s, 3H), 6.01 (dd, *J* = 2.0, 4.4 Hz, 1H), 6.69 (d, *J* = 4.4 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.87 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.2, 37.5, 55.3, 108.9, 114.2, 122.6, 125.9, 130.9, 132.4, 132.5, 138.1, 139.8, 161.2, 186.9, 195.9; IR (neat) ν: 1624, 1601, 1512, 1404, 1264, 1178, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1106, found 306.1107.

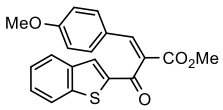
ethyl (*E*)-2-(benzofuran-2-carbonyl)-3-(4-methoxyphenyl)acrylate (**158a**)



The reaction was carried out following the general procedure and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **158a** as a yellow viscous liquid (565 mg, 81% yield, *E*/*Z* = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (s, 3H), 3.94 (s, 3H), 4.37 (brs, 1H), 4.45 (brs, 1H), 4.58 (brs, 1H), 4.70 (brs, 1H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 6.4 Hz, 2H), 7.15-7.40 (m, 12H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.59 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.7, 46.4, 51.2, 55.4, 110.2, 113.0, 114.3, 120.7, 123.0, 125.7, 125.8, 126.0, 127.4, 127.6, 128.1, 128.5, 128.6, 129.3, 132.0, 134.76, 134.79, 135.5, 135.9, 140.2, 142.1, 161.5, 168.5, 185.7; IR (neat) ν: 1634, 1615, 1511, 1261, 1178, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{34}H_{30}N_2NaO_3$ $[M+Na]^+$ 537.2154, found 537.2158.

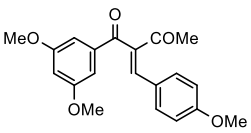
methyl (*E*)-2-(benzo[*b*]thiophene-2-carbonyl)-3-(4-methoxyphenyl)acrylate (**158b**)



The reaction was carried out on a 2.4 mmol scale following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **158b** as a brown amorphous (1003 mg, 84% yield). Further purification was achieved by crystallization from EtO_2 to afford pale brown solid (683 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.74 (s, 3H), 3.78 (s, 3H), 6.77 (d, *J* = 8.8 Hz, 2H), 7.37 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.46 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.83 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.6, 55.3, 114.4, 123.1, 125.05, 125.07, 126.3, 127.3, 132.0, 138.9, 143.1, 143.2, 143.4, 161.6, 165.5, 189.9; IR (neat) ν: 1715, 1646, 1597, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{16}NaO_4S$ $[M+Na]^+$ 375.0667, found 375.0667.

(*E*)-1-(3,5-dimethoxyphenyl)-2-(4-methoxybenzylidene)butane-1,3-dione (**160a**)

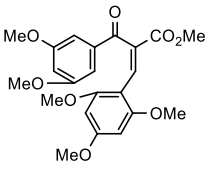


The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **160a** as a yellow viscous liquid (284 mg, 50% yield, *E*/*Z* = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.36 (s, 3H), 3.77 (s, 3H), 3.79 (s, 6H), 6.64 (t, *J* = 2.4 Hz, 1H), 6.77 (ddd, *J* = 1.6, 1.6, 8.4 Hz, 2H), 7.09 (d, *J* = 2.4 Hz, 2H), 7.30 (ddd, *J* = 2.0, 2.0, 8.8 Hz, 2H), 7.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.1, 55.3, 55.6, 106.5, 106.8, 114.4, 125.3, 132.5, 137.1, 138.0, 141.1, 161.1, 161.5, 195.7, 198.3; IR (neat) ν: 1682, 1652, 1602, 1514, 1308, 1298, 1262, 1206, 1180,

1159 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NaO_5$ $[M+Na]^+$ 363.1208, found 363.1209.

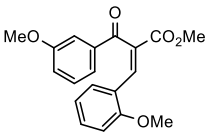
methyl (*E*)-2-(3,5-dimethoxybenzoyl)-3-(2,4,6-trimethoxyphenyl)acrylate (**160b**)



The reaction was carried out on a 3 mmol scale following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **160b** as a pale yellow solid (1205 mg, 97% yield, *E/Z* = 11/1).

^1H NMR (400 MHz, $CDCl_3$) δ: 3.51 (s, 6H), 3.71 (s, 3H), 3.78 (s, 3H), 3.79 (s, 6H), 5.96 (s, 2h), 6.60 (t, *J* = 2.4 Hz, 1H), 7.09 (d, *J* = 2.4 Hz, 2H), 8.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.2, 54.7, 55.3, 55.5, 90.1, 105.0, 105.3, 106.3, 127.9, 135.8, 139.5, 159.6, 160.4, 163.6, 167.2, 193.1; IR (neat) ν: 1711, 1672, 1592 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}NaO_8$ $[M+Na]^+$ 439.1369, found 439.1377.

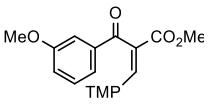
methyl (*E*)-2-(3-methoxybenzoyl)-3-(2-methoxyphenyl)acrylate (**126**)

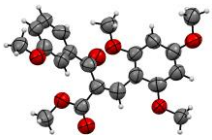


The reaction was carried out on a 1 mmol scale following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/4) to afford **126** as a colorless solid (319 mg, 98% yield, *E/Z* = 17/1).

^1H NMR (400 MHz, $CDCl_3$) δ: 3.750 (s, 3H), 3.754 (s, 3H), 3.82 (s, 3H), 6.74 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.07 (dd, *J* = 2.4, 7.6 Hz, 1H), 7.20-7.24 (m, 2H), 7.28 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 2.0 Hz, 1H), 8.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:52.4, 55.2, 55.4, 110.7, 112.5, 120.47, 120.53, 122.19, 122.24, 129.6, 130.4, 130.5, 131.9, 137.7, 138.8, 157.9, 159.8, 165.8, 195.1; IR (neat) ν: 1717, 1670, 1596, 1580 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NaO_5$ $[M+Na]^+$ 349.1052, found 349.1052.

methyl (*E*)-2-(3-methoxybenzoyl)-3-(2,4,6-trimethoxyphenyl)acrylate (**172**)

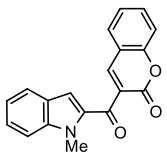




The reaction was carried out on a 1 mmol scale following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **172** as a yellow solid (355 mg, 91% yield, *E/Z* = 10/1). Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of CPME into the CH_2Cl_2 solution of product.

^1H NMR (400 MHz, $CDCl_3$) δ: 3.48 (s, 6H), 3.70 (s, 3H), 3.78 (s, 3H), 3.82 (s, 3H), 5.96 (s, 2H), 7.04 (ddd, *J* = 1.2, 2.8, 8.0 Hz, 1H), 7.30 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.49 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.50 (s, 1H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 52.1, 54.6, 55.33, 55.35, 90.1, 105.0, 112.3, 119.1, 121.8, 128.0, 129.1, 135.9, 138.9, 159.4, 159.6, 163.6, 167.2, 193.3; IR (neat) ν: 1709, 1667, 1598, 1578 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{23}O_7$ $[M+H]^+$ 387.1444, found 387.1438.

3-(1-methyl-1*H*-indole-2-carbonyl)-2*H*-chromen-2-one (**178**)



The reaction was carried out on a 3 mmol scale following the general procedure using salicylaldehyde and stirred for 24 h. The residue was diluted with hexane and resulting precipitates were filtrated. The residual precipitates were recrystallized from CH_2Cl_2/Hexane to afford **178** as a yellow solid (833 mg, 92% yield).

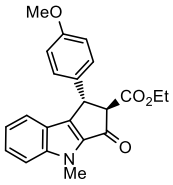
^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.17 (s, 3H), 7.14-7.18 (m, 2H), 7.35 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.40-7.43 (m, 3H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.62-7.66 (m, 2H), 8.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.2, 110.5, 115.6, 116.9, 118.0, 121.1, 123.3, 124.9, 125.7, 126.9, 127.6, 129.0, 133.3, 133.9, 141.0, 143.6, 154.4, 158.4, 182.9; IR (neat) ν: 1720, 1634, 1606, 1567, 1509 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{14}NO_3$ $[M+H]^+$ 304.0974, found 304.0973.

Nazarov Cyclization

General Procedure for Chiral Ni Complex Catalyzed Nazarov Cyclization

The mixture of $Ni(NTf_2)_2$ (12.4 mg, 0.02 mmol), (*S*,*S*)-ImQ (**139**) (7.9 mg, 0.02 mmol) and activated MS 4 Å (100 mg) in CH_2Cl_2 (0.4 mL) was stirred for 2 h at room temperature. The prepared catalyst mixture was diluted with CH_2Cl_2 (1 mL) and **128** (0.2 mmol) in CH_2Cl_2 (0.6 mL) was added. Reaction mixture was stirred at room temperature. The reaction was monitored by TLC and quenched with H_2O after consumption of **128**. The resulting mixture was filtrated through Celite® and extracted with CH_2Cl_2 three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography.

ethyl (1*S*,2*R*)-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129a**)

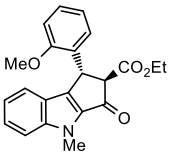


The reaction was stirred for 0.3 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129a** as a pale yellow viscous liquid (71 mg, 98% yield, 80% ee, dr = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, *J* = 7.6 Hz, 3H), 3.79 (s, 3H), 3.81 (d, *J* = 2.8 Hz, 1H), 3.97 (s, 3H), 4.29 (dq, *J* = 2.8, 7.2 Hz, 2H), 4.96 (d, *J* = 2.4 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 7.09 (ddd, *J* = 1.6, 8.0, 8.0 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 30.3, 42.9, 55.3, 61.7, 68.5, 111.1, 114.2, 120.7, 122.4, 122.5, 127.4, 128.4, 133.1, 137.2, 145.5, 145.7, 158.8, 169.2, 187.0; IR (neat) ν: 1732, 1685, 1612, 1546, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_4$ $[M+Na]^+$ 386.1368, found 386.1384; $[\alpha]_D^{18}$ +66.2 (*c* 0.87, $CHCl_3$, 80% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 9.9, 16.8 min.

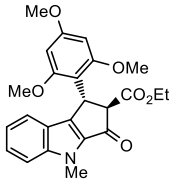
ethyl (1*R*,2*R*)-1-(2-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129b**)

The reaction was stirred for 0.3 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129b** as a yellow viscous liquid (66 mg, 91% yield, 66% ee, dr = 14/1).



^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.35 (t, *J* = 6.8 Hz, 3H), 3.71 (d, *J* = 2.8 Hz, 1H), 3.84 (s, 3H), 3.97 (s, 3H), 4.27-4.37 (m, 2H), 5.23 (d, *J* = 2.8 Hz, 1H), 6.82 (ddd, *J* = 0.8, 8.0, 8.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 7.01 (dd, *J* = 1.2, 7.2 Hz, 1H), 7.14 (ddd, *J* = 1.6, 6.8, 8.0 Hz, 1H), 7.24-7.28 (m, 1H), 7.41-7.45 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.4, 30.2, 38.4, 55.1, 61.4, 67.5, 110.2, 111.1, 120.4, 120.6, 122.8, 123.0, 127.3, 127.4, 128.3, 129.2, 137.6, 145.0, 145.4, 157.2, 169.7, 187.6; IR (neat) ν: 1737, 1683 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_4$ $[M+H]^+$ 364.1549, found 364.1547; $[\alpha]_D^{21}$ –72.3 (*c* 1.02, $CHCl_3$, 66% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 9.7, 10.9 min.

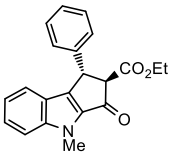
ethyl (1*R*,2*R*)-4-methyl-3-oxo-1-(2,4,6-trimethoxyphenyl)-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129c**)



The reaction was stirred at -20 °C for 44 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **129c** as a colorless solid (81 mg, 96% yield, 37% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.29 (t, *J* = 7.2 Hz, 3H), 3.40 (brs, 3H), 3.79 (s, 3H), 3.93 (s, 6H), 4.17-4,30 (m, 2H), 4.25 (d, *J* = 2.0 Hz, 1H), 5.52 (d, *J* = 2.4 Hz, 1H), 5.98 (brs, 1H), 6.23 (brs, 1H), 7.00 (ddd, *J* = 2.0, 6.8, 8.0 Hz, 1H), 7.28-7.36 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.2, 33.0, 55.2, 55.3, 56.1, 61.2, 64.6, 90.6, 91.1, 108.1, 110.7, 119.8, 122.0, 122.4, 126.7, 136.7, 145.1, 148.2, 158.6, 159.9, 160.3, 170.3, 188.5; IR (neat) ν: 1731, 1682, 1591, 1549 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_6$ $[M+Na]^+$ 446.1580, found 446.1579; $[\alpha]_D^{21}$ -154.7 (*c* 1.03, $CHCl_3$, 37% ee); HPLC conditions: Chiralcel IC, Hexane/*i*PrOH = 80/20, t_R: 29.9, 35.6 min.

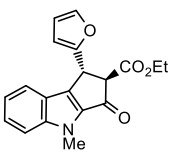
ethyl (1*S*,2*R*)-4-methyl-3-oxo-1-phenyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129d**)



The reaction was stirred for 0.3 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129d** as a colorless solid (57 mg, 86% yield, 69% ee, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.34 (t, *J* = 7.2 Hz, 3H), 3.85 (d, *J* = 2.4 Hz, 1H), 3.97 (s, 3H), 4.26-4.34 (m, 2H), 5.01 (d, *J* = 2.8 Hz, 1H), 7.08 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.23-7.44 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.2, 43.5, 61.7, 68.2, 111.1, 120.7, 122.37, 122.44, 127.3, 127.4, 128.9, 137.2, 141.0, 145.41, 145.43, 169.0, 186.8; IR (neat) ν: 1733, 1696 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_3$ $[M+Na]^+$ 356.1263, found 356.1262; $[\alpha]_D^{29}$ +74.0 (*c* 1.00, $CHCl_3$, 69% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 7.6, 11.3 min.

ethyl (1*R*,2*R*)-1-(furan-2-yl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129e**)

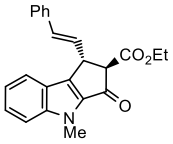


The reaction was stirred for 0.5 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129e** as a yellow viscous liquid (61 mg, 94% yield, 73% ee, dr = 14/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.35 (t, *J* = 7.6 Hz, 3H), 3.94 (s, 3H), 4.06 (d, *J* = 2.8 Hz,

1H), 4.24-4.44 (m, 2H), 5.10 (d, *J* = 2.4 Hz, 1H), 6.17 (d, *J* = 3.2 Hz, 1H), 6.31 (dd, *J* = 1.6, 3.2 Hz, 1H), 7.16 (ddd, *J* = 1.2, 5.6, 8.0 Hz, 1H), 7.37-7.39 (m, 2H), 7.44 (ddd, *J* = 0.8, 6.8, 8.4 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.2, 37.0, 61.9, 64.6, 106.2, 110.3, 111.1, 120.9, 122.3, 122.5, 127.5, 136.7, 142.3, 142.9, 145.4, 153.4, 168.7, 185.9; IR (neat) ν: 1734, 1697 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{17}NNaO_4$ $[M+Na]^+$ 346.1055, found 346.1059; $[\alpha]_D^{27}$ +54.5 (*c* 1.01, $CHCl_3$, 74% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 8.0, 10.4 min.

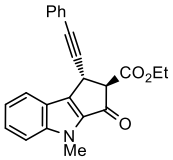
ethyl (1*R*,2*R*)-4-methyl-3-oxo-1-((*E*)-styryl)-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129f**)



The reaction was stirred for 48 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129f** as a yellow viscous liquid (60 mg, 83% yield, 66% ee, dr = 8/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.34 (t, *J* = 7.6 Hz, 3H), 3.80 (d, *J* = 2.8 Hz, 1H), 3.95 (s, 3H), 4.25-4.33 (m, 2H), 4.58 (dd, *J* = 2.8, 8.0 Hz, 1H), 6.37 (dd, *J* = 8.0, 15.6 Hz, 1H), 6.72 (d, *J* = 15.6 Hz, 1H), 7.16 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.23-7.47 (m, 7H), 7.68 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.1, 41.4, 61.6, 65.5, 111.0, 120.7, 122.2, 122.8, 126.3, 127.4, 127.7, 128.5, 128.7, 131.6, 136.4, 136.7, 144.8, 145.3, 169.0, 186.3; IR (neat) ν: 1730, 1685 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{21}NNaO_3$ $[M+Na]^+$ 382.1419, found 382.1418; $[\alpha]_D^{21}$ +63.2 (*c* 0.99, $CHCl_3$, 60% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 8.6, 11.5 min.

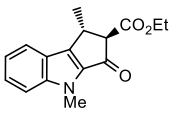
ethyl (1*S*,2*R*)-4-methyl-3-oxo-1-(phenylethynyl)-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129g**)



The reaction was stirred for 72 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **129g** as a yellow viscous liquid (62 mg, 87% yield, 40% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.37 (t, *J* = 7.2 Hz, 3H), 3.91 (s, 3H), 4.16 (d, *J* = 3.2 Hz, 1H), 4.28-4.36 (m, 2H), 4.91 (d, *J* = 3.2 Hz, 1H), 7.23-7.30 (m, 4H), 7.39-7.42 (m, 3H), 7.48 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 29.1, 30.2, 62.0, 65.9, 82.4, 87.1, 111.1, 121.0, 122.0, 122.1, 122.7, 127.7, 128.22, 128.25, 131.7, 135.8, 142.6, 145.4, 168.3, 185.1; IR (neat) ν: 1733, 1697, 756 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{19}NNaO_3$ $[M+Na]^+$ 380.1263, found 380.1262; $[\alpha]_D^{28}$ +40.8 (*c* 1.00, $CHCl_3$, 40% ee); HPLC conditions: Chiralcel AS-H, Hexane/*i*PrOH = 90/10, t_R: 8.1, 10.7 min.

ethyl (1*R*,2*R*)-1,4-dimethyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129h**)

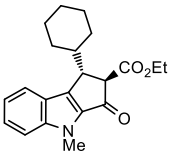


The reaction was stirred for 48 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **129h** as a colorless liquid (32 mg, 82% yield, 33% ee, dr = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, *J* = 7.6 Hz, 3H), 1.57 (d, *J* = 6.8 Hz, 3H), 3.54 (d, *J* = 2.8 Hz, 1H), 3.83 (dq, *J* = 2.8, 7.2 Hz, 1H), 3.90 (s, 3H), 4.22-4.30 (m, 2H), 7.19 (dd, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.8

Hz, 1H), 7.43 (dd, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 20.2, 30.1, 33.4, 61.5, 66.9, 111.1, 120.5, 122.0, 122.3, 127.2, 136.6, 145.3, 148.5, 169.6, 187.2; IR (neat) ν: 1731, 1623 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{17}NNaO_3$ $[M+Na]^+$ 294.1106, found 294.1113; $[\alpha]_D^{23}$ +41.3 (*c* 0.52, $CHCl_3$, 33% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 95/5, t_R: 8.1, 9.0 min.

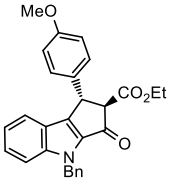
ethyl (1*R*,2*R*)-1-cyclohexyl-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (129i)



The reaction was stirred for 6 h at 40°C and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **129i** as a colorless solid (64 mg, 95% yield, 14% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.03-1.27 (m, 5H), 1.30 (t, *J* = 7.6 Hz, 3H), 1.53 (d, *J* = 11.6 Hz, 1H), 1.66-1.72 (m, 2H), 1.77-1.86 (m, 2H), 1.90-1.99 (m, 1H), 3.73 (dd, *J* = 2.4, 5.2 Hz, 1H), 3.75 (d, *J* = 2.4 Hz, 1H), 3.90 (s, 3H), 4.23 (q, *J* = 7.2 Hz, 2H), 7.18 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.43 (dd, *J* = 8.8, 8.8 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 26.22, 26.25, 26.4, 29.2, 30.1, 31.4, 41.7, 44.9, 61.5, 61.9, 111.1, 120.4, 122.8, 123.0, 127.2, 137.3, 145.3, 146.5, 170.1, 187.7; IR (neat) ν: 2924, 2850, 1732, 1684 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{26}NO_3$ $[M+H]^+$ 340.1913, found 340.1912; $[\alpha]_D^{21}$ +18.0 (*c* 0.95, $CHCl_3$, 14% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 7.2, 10.1 min.

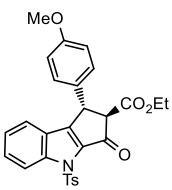
ethyl (1*S*,2*R*)-4-benzyl-1-(4-methoxyphenyl)-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (129j)



The reaction was stirred for 1 h, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129j** as a yellow viscous liquid (83 mg, 95% yield, 66% ee, dr = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, *J* = 7.6 Hz, 3H), 3.79 (s, 3H), 3.84 (d, *J* = 3.2 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 4.99 (d, *J* = 2.8 Hz, 1H), 5.57 (s, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 7.06 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.16 (d, *J* = 8.8 Hz, 2H), 7.25-7.39 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 42.9, 47.6, 55.3, 61.7, 68.5, 111.9, 114.2, 120.9, 122.5, 122.8, 127.3, 127.5, 127.7, 128.4, 128.7, 132.9, 136.9, 137.0, 144.8, 146.3, 158.8, 169.0, 186.8; IR (neat) ν: 1732, 1686, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{26}NO_4$ $[M+H]^+$ 440.1862, found 440.1866; $[\alpha]_D^{20}$ +50.0 (*c* 1.01, $CHCl_3$, 66% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 12.1, 16.9 min.

ethyl (1*S*,2*R*)-1-(4-methoxyphenyl)-3-oxo-4-tosyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (129k)

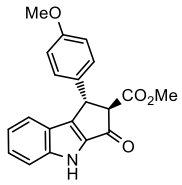


The reaction was stirred for 48 h at 40 °C using 20 mol % of Ni catalyst, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129k** as a yellow solid (82 mg, 82% yield, 53% ee, dr = 13/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, *J* = 7.2 Hz, 3H), 2.39 (s, 3H), 3.78 (s, 3H), 3.85 (d, *J* = 3.2 Hz, 1H), 4.23-4.31 (m, 2H), 4.86 (d, *J* = 3.2 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 2H), 7.05

(d, *J* = 8.8 Hz, 2H), 7.20-7.21 (m, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.53 (ddd, *J* = 4.0, 8.4, 8.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 2H), 8.34 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 21.7, 42.1, 55.3, 61.9, 68.1, 114.4, 115.6, 122.4, 124.0, 124.1, 127.6, 128.4, 129.8, 129.9, 131.2, 135.4, 136.0, 143.8, 145.4, 154.6, 159.1, 168.3, 183.1; IR (neat) ν: 1735, 1706, 1512 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{26}NO_6S$ $[M+H]^+$ 504.1481, found 504.1478; $[\alpha]_D^{22}$ +44.1 (*c* 0.47, $CHCl_3$, 47% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 16.9, 27.3 min.

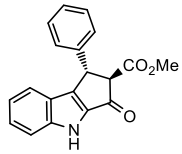
methyl (1*S*,2*R*)-1-(4-methoxyphenyl)-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate[11f,14b] (**129l**)



The reaction was stirred for 13 h, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **129l** as a colorless solid (62 mg, 93% yield, 80% ee, dr = 20/1).

Melting Point: 75 °C (99% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.80 (s, 3H), 3.85 (s, 3H), 3.88 (d, *J* = 2.8 Hz, 1H), 5.02 (d, *J* = 2.8 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.40 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 9.36 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 43.4, 52.8, 55.3, 67.9, 113.7, 114.3, 121.2, 122.2, 122.8, 128.1, 128.4, 132.7, 136.9, 144.4, 148.2, 158.9, 169.5, 186.9; IR (neat) ν: 3253, 1734, 1673, 1611, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_4$ $[M+H]^+$ 336.1236, found 336.1237; $[\alpha]_D^{23}$ +88.1 (*c* 1.00, $CHCl_3$, 99% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 80/20, t_R: 8.4, 13.3 min.

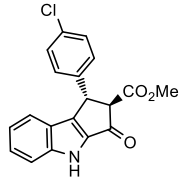
methyl (1*S*,2*R*)-3-oxo-1-phenyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate[14b] (**129m**)



The reaction was stirred for 37 h, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **129m** as a colorless solid (57 mg, 93% yield, 84% ee, dr = 20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.85 (s, 3H), 3.91 (d, *J* = 3.2 Hz, 1H), 5.08 (d, *J* = 2.4 Hz, 1H), 7.10 (ddd, *J* = 0.8, 6.8, 8.0 Hz, 1H), 7.23-7.36 (m, 6H), 7.41 (ddd, *J* = 0.8, 6.8, 8.4 Hz, 1H), 7.49 (ddd, *J* = 0.8, 0.8, 8.4 Hz, 1H), 8.77 (brs, 1H); HRMS (ESI) *m/z* calcd for $C_{19}H_{15}NNaO_3$ $[M+Na]^+$ 328.0950, found 328.0948; $[\alpha]_D^{21}$ +78.1 (*c* 1.00, CH_2Cl_2, 84% ee); HPLC conditions: Chiralcel AD-H, Hexane/*i*PrOH = 90/10, t_R: 13.7, 20.1 min.

methyl (1*S*,2*R*)-1-(4-chlorophenyl)-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate[14b] (**129n**)

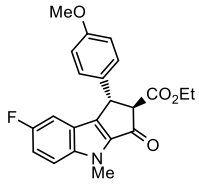


The reaction was stirred for 67 h, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **129n** as a yellow solid (57 mg, 84% yield, 82% ee, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (d, *J* = 3.2 Hz, 1H), 3.85 (s, 3H), 5.06 (d, *J* = 2.8 Hz, 1H), 7.12 (ddd, *J* = 1.2, 7.2, 8.0 Hz, 1H), 7.18 (ddd, *J* = 2.0, 2.0, 8.4 Hz, 2H), 7.30 (ddd, *J* = 2.0, 2.0, 8.4 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 1H), 7.43 (ddd, *J* = 1.2, 7.2, 8.4 Hz, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 8.67 (brs, 1H); HRMS (ESI) *m/z* calcd for $C_{19}H_{14}ClNNaO_3$ $[M+Na]^+$ 362.0560, found 362.0561; $[\alpha]_D^{21}$

+53.9 (*c* 1.00, CH_2Cl_2, 82% ee); HPLC conditions: Chiralcel AD-H, Hexane/*i*PrOH = 90/10, t_R: 14.7, 23.4 min.

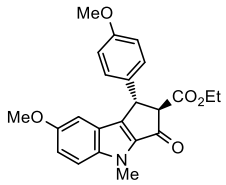
ethyl (1*S*,2*R*)-7-fluoro-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129o**)



The reaction was stirred for 0.3 h, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129o** as a colorless viscous liquid (73 mg, 95% yield, 80% ee, dr = 13/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, *J* = 7.6 Hz, 3H), 3.80 (s, 3H), 3.80 (d, *J* = 2.8 Hz, 1H), 3.96 (s, 3H), 4.24-4.35 (m, 2H), 4.92 (d, *J* = 2.8 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.97 (dd, *J* = 2.8, 9.2 Hz, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 7.17 (ddd, *J* = 2.8, 9.2, 9.2 Hz, 1H), 7.33 (dd, *J* = 4.0, 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.4, 42.7, 55.2, 61.7, 68.4, 106.7 (d, *J* = 22.9 Hz), 112.1 (d, *J* = 9.5 Hz), 114.3, 116.4 (d, *J* = 26.7 Hz), 122.3 (d, *J* = 9.6 Hz), 128.3, 132.7, 138.3, 142.0, 144.8 (d, *J* = 5.7 Hz), 157.8 (d, *J* = 237.4 Hz), 158.9, 168.9, 187.1; IR (neat) ν: 1733, 1697, 1514, 1250, 1161 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{20}FNNaO_4$ $[M+Na]^+$ 404.1274, found 404.1276; $[\alpha]_D^{26}$ +63.1 (*c* 1.01, $CHCl_3$, 80% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 9.9, 15.5 min.

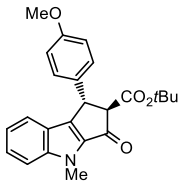
ethyl (1*S*,2*R*)-7-methoxy-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**129p**)



The reaction was stirred for 0.3 h, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129p** as a brown viscous liquid (80 mg, 95% yield, 77% ee, dr = 12/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.34 (t, *J* = 7.2 Hz, 3H), 3.71 (s, 3H), 3.77 (d, *J* = 2.4 Hz, 1H), 3.79 (s, 3H), 3.94 (s, 3H), 4.23-4.33 (m, 2H), 4.93 (d, *J* = 2.8 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.09 (dd, *J* = 2.4, 9.2 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.3, 42.7, 55.2, 55.7, 61.6, 68.5, 102.2, 112.0, 114.2, 118.9, 122.6, 128.3, 133.1, 137.4, 141.0, 144.3, 154.4, 158.7, 169.2, 186.7; IR (neat) ν: 1733, 1694, 1512, 1246, 1175 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{23}NNaO_5$ $[M+Na]^+$ 416.1474, found 416.1486; $[\alpha]_D^{29}$ +0.8 (*c* 1.00, $CHCl_3$, 77% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 13.1, 17.6 min.

***tert*-butyl (1*S*,2*R*)-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]-indole-2-carboxylate** (**129q**)

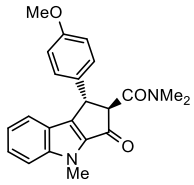


The reaction was stirred for 0.3 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **129q** as a yellow viscous liquid (78 mg, 99% yield, 72% ee, dr = 8/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.53 (s, 9H), 3.71 (d, *J* = 3.2 Hz, 1H), 3.79 (s, 3H), 3.96 (s, 3H), 4.89 (d, *J* = 3.2 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.08 (ddd, *J* = 2.0, 6.0, 8.0 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.37-7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.1, 30.2, 42.9, 55.2, 69.5, 82.0, 111.0, 114.2, 120.6, 122.4, 122.5, 127.2, 128.4, 133.4, 137.4, 145.4, 145.5,

158.7, 168.4, 187.5; IR (neat) ν: 1726, 1686, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_4$ $[M+Na]^+$ 414.1681, found 414.1683; $[\alpha]_D^{21}$ +43.7 (*c* 0.99, $CHCl_3$, 71% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R; 6.8, 14.8 min.

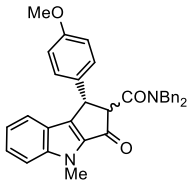
(1*S*,2*R*)-1-(4-methoxyphenyl)-*N*,*N*,4-trimethyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxamide (**129r**)



The reaction was stirred for 14 h at 40 °C and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **129r** as a yellow viscous liquid (69 mg, 96% yield, 91% ee, dr = >20/1).

^1H NMR (400 MHz, $CDCl_3$) δ: 3.06 (s, 3H), 3.13 (s, 3H), 3.79 (s, 3H), 3.92 (s, 3H), 4.19 (d, *J* = 2.8 Hz, 1H), 5.16 (s, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 7.05 (dd, *J* = 6.4, 8.4 Hz, 1H), 7.17 (d, *J* = 8.8 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.35-7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.1, 36.1, 38.1, 42.9, 55.2, 66.1, 110.9, 114.1, 120.4, 122.4, 122.6, 127.2, 128.4, 133.8, 137.1, 145.4, 146.8, 158.6, 168.3, 189.2; IR (neat) ν: 1686, 1640, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}N_2NaO_3$ $[M+Na]^+$ 385.1528, found 385.1529; $[\alpha]_D^{23}$ +142.2 (*c* 1.00, $CHCl_3$, 88% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 60/40, t_R: 6.8, 14.1 min.

(1*S*)-*N*,*N*-dibenzyl-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxamide (*cis*-**129s** and *trans*-**129s**)



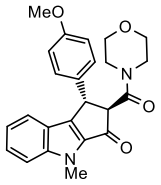
The reaction was stirred for 36 h at 40 °C, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford *trans*-**129s** as a pale yellow amorphous (66 mg, 71% yield, 80% ee) and *cis*-**129s** as a colorless solid (30 mg, 23% yield, 83% ee).

trans-**129s**; ^1H NMR (400 MHz, acetone-*d*6) δ: 3.79 (s, 3H), 3.99 (s, 3H), 4.18 (d, *J* = 15.2 Hz, 1H), 4.85 (d, *J* = 17.6 Hz, 1H), 4.43 (d, *J* = 3.2 Hz, 1H), 5.05 (d, *J* = 17.6 Hz, 1H), 5.16 (d, *J* = 15.2 Hz, 1H), 5.23 (d, *J* = 3.2 Hz, 1H), 6.86 (ddd, *J* = 2.0, 2.0, 8.8 Hz, 2H), 7.03-7.06 (m, 2H), 7.09 (ddd, *J* = 0.8, 6.8, 7.6 Hz, 1H), 7.16-7.19 (m, 4H), 7.27-7.32 (m, 2H), 7.37-7.38 (m, 4H), 7.44 (ddd, *J* = 0.8, 6.8, 8.0 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, acetone-*d*6) δ: 44.2, 49.1, 51.0, 55.5, 67.2, 112.4, 115.0, 121.3, 122.8, 123.4, 127.4, 127.86, 127.91, 128.1, 128.5, 129.3, 129.4, 134.3, 137.7, 138.1, 138.5, 146.2, 146.6, 159.8, 169.8, 189.7, 206.2; IR (neat) ν: 1688, 1645, 1512, 1247, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{34}H_{30}N_2NaO_3[M+Na]^+$ 537.2154, found 537.2153; $[\alpha]_D^{25}$ +97.3 (*c* 1.00, $CHCl_3$, 80% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 60/40, t_R: 9.1, 13.8 min.

cis-**129s**; ^1H NMR (400 MHz, $CDCl_3$) δ: 3.44 (d, *J* = 14.8 Hz, 1H), 3.83 (s, 3H), 3.94 (d, *J* = 17.2 Hz, 1H), 3.98 (s, 3H), 4.48 (dd, *J* = 2.0, 6.8 Hz, 1H), 4.69 (d, *J* = 18.0 Hz, 1H), 4.73 (dd, *J* = 3.2, 6.8 Hz, 1H), 5.27 (d, *J* = 14.8 Hz, 1H), 6.37 (d, *J* = 7.2 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.02 (ddd, *J* = 2.4, 5.6, 8.4 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 2H), 7.13-7.19 (m, 4H), 7.32-7.26 (m, 5H), 7.41-7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.3, 42.5, 47.2, 49.3, 55.0, 61.6, 111.0, 113.8, 120.4, 122.2, 122.3, 126.6, 127.0, 127.9, 128.0, 128.1, 129.0, 129.7, 130.5, 135.5, 136.4, 139.2, 145.3, 146.0, 159.0, 169.2, 190.0; IR (neat) ν: 1697, 1644,

1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{34}H_{31}N_2O_3$ $[M+H]^+$ 515.2335, found 515.2336; $[\alpha]_D^{26}$ +88.5 (*c* 0.76, $CHCl_3$, 84% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 60/40, t_R: 6.9, 8.8 min.

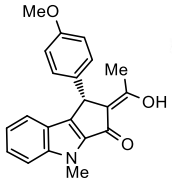
(1*S*,2*R*)-1-(4-methoxyphenyl)-4-methyl-2-(morpholine-4-carbonyl)-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**129t**)

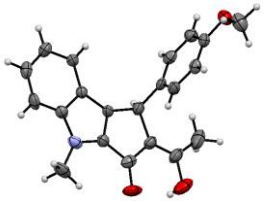


The reaction was stirred for 24 h at 40 °C and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **129t** as a pale yellow amorphous (80 mg, 99% yield, 75% ee, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.36-3.45 (m, 2H), 3.68 (ddd, *J* = 2.8, 8.4, 11.6 Hz, 1H), 3.72-3.87 (m, 7H), 3.94 (s, 3H), 4.04 (ddd, *J* = 3.6, 3.6, 13.6 Hz, 1H), 4.11 (d, *J* = 2.8 Hz, 1H), 5.26 (d, *J* = 2.4 Hz, 1H), 6.84 (ddd, *J* = 2.4, 2.4, 8.8 Hz, 2H), 7.07 (ddd, *J* = 0.8, 6.4, 7.6 Hz, 1H), 7.16 (ddd, *J* = 2.4, 2.4, 8.8 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.41 (ddd, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.1, 42.5, 42.8, 46.9, 55.2, 65.8, 66.8, 67.2, 111.0, 114.2, 120.6, 122.51, 122.54, 127.4, 128.4, 133.7, 136.8, 145.5, 147.0, 158.7, 166.5, 188.6; IR (neat) ν: 1689, 1643, 1512, 1248 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}N_2O_4$ $[M+H]^+$ 405.1814, found 405.1813; $[\alpha]_D^{27}$ +146.7 (*c* 1.01, $CHCl_3$, 75% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 60/40, t_R: 8.1, 53.3 min.

(*S*,*Z*)-2-(1-hydroxyethylidene)-1-(4-methoxyphenyl)-4-methyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one[42] (**129u**)

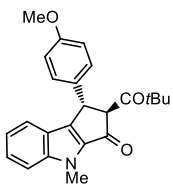




The reaction was stirred for 0.2 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **129u** as a yellow solid (59 mg, 89% yield, 80% ee, keto/enol = 1/7, dr (keto form) = >20/1). Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the CH_2Cl_2 solution of racemic product and stilled at room temperature for overnight.

Melting Point: 144 °C (racemic); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.76 (s, 3H), 3.75 (s, 3H), 3.95 (s, 3H), 4.75 (s, 1H), 6.80 (d, *J* = 8.4 Hz, 2H), 7.02 (ddd, *J* = 4.2, 4.2, 7.8 Hz, 1H), 7.15 (d, *J* = 9.0 Hz, 2H), 7.30-7.31 (m, 2H), 7.36 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 18.9, 30.3, 41.7, 55.1, 110.7, 114.1, 120.0, 120.3, 122.1, 125.9, 128.5, 132.7, 138.4, 140.8, 1444.2, 158.3, 169.4, 187.0; IR (neat) ν: 1652, 1615, 1510, 1217 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_3$ $[M+Na]^+$ 356.1263, found 356.1265; $[\alpha]_D^{29}$ +231.8 (*c* 1.00, $CHCl_3$, 80% ee); HPLC conditions: Chiralcel OJ-H, Hexane/*i*PrOH = 95/5, t_R: 19.4, 40.0 min.

(1*S*,2*S*)-1-(4-methoxyphenyl)-4-methyl-2-pivaloyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**21**)

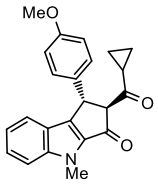


The reaction was stirred for 48 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **21** as a pale yellow solid (63 mg, 83% yield, 30% ee, dr = >20/1).

^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.16 (s, 9H), 3.79 (s, 3H), 3.93 (s, 3H), 4.45 (d, *J* = 2.8 Hz, 1H), 4.67 (d, *J* = 2.4 Hz, 1H), 6.82 (ddd, *J* = 2.0, 2.0, 8.4 Hz, 2H), 7.04 (ddd, *J* = 1.6, 6.4,

8.0 Hz, 1H), 7.08 (ddd, *J* = 2.0, 2.0, 8.8 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.38-7.42 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.5, 30.1, 44.83, 44.85, 55.2, 70.2, 110.0, 114.2, 120.5, 122.3, 122.4, 127.2, 128.4, 133.4, 137.7, 145.3, 147.3, 158.7, 189.8, 212.2; IR (neat) ν: 1707, 1683, 1512, 1249, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{26}NO_3$ $[M+H]^+$ 376.1913, found 376.1914; $[\alpha]_D^{28}$ -59.1 (*c* 1.00, $CHCl_3$, 30% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 7.4, 8.2 min.

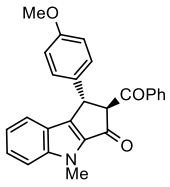
(1*S*,2*S*)-2-(cyclopropanecarbonyl)-1-(4-methoxyphenyl)-4-methyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**128w**)



The reaction was stirred for 10 min and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **128w** as a green foam (66 mg, 92% yield, dr = >20/1, keto/enol = 2.4/1). Enantiomeric excess was determined after conversion to methylated product **S3a**.

^{1}H NMR (400 MHz, $CDCl_3$, keto/enol = 2.4/1) δ: 0.56 (dddd, *J* = 3.6, 8.4, 8.4, 8.4 Hz, 0.4H), 0.81 (dddd, *J* = 3.9, 8.4, 8.4, 8.4 Hz, 0.4H), 0.96-1.05 (m, 2.4H), 1.06-1.20 (m, 2.4H), 1.37 (dddd, *J* = 4.4, 8.0, 8.0, 8.0 Hz, 0.4H), 2.44 (dddd, *J* = 4.4, 8.0, 8.0, 8.0 Hz, 1H), 3.76 (s, 1.2H), 3.77 (s, 3H), 3.95 (s, 3H), 3.99 (s, 1.2H), 4.19 (d, *J* = 2.0 Hz, 1H), 4.98 (s, 0.4H), 5.17 (d, *J* = 2.4 Hz, 1H), 6.81 (d, *J* = 9.2 Hz, 0.8H), 6.82 (d, *J* = 8.8 Hz, 2H), 7.02-7.09 (m, 1.2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 0.8H), 7.28-7.43 (m, 4.2H); ^{13}C NMR (100 MHz, $CDCl_3$, keto/enol mixture) δ: 7.9, 8.0, 11.8, 12.2, 12.7, 20.9, 30.2, 30.4, 40.0, 41.7, 55.1, 55.2, 76.8, 110.7, 111.0, 114.07, 114.14, 119.0, 120.2, 120.6, 121.1, 122.3, 122.45, 122.53, 125.6, 127.3, 128.4, 128.5, 133.1, 133.7, 136.8, 140.3, 144.1, 145.4, 146.1, 158.2, 158.6, 173.8, 186.1, 187.9, 204.6; IR (neat) ν: 1684, 1634, 1510, 1253, 1226, 923, 744 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{21}NNaO_3$ $[M+Na]^+$ 382.1419, found 382.1417; $[\alpha]_D^{27}$ +94.8 (*c* 1.00, $CHCl_3$, 32% ee).

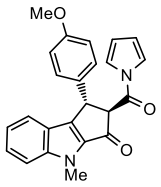
(1*S*,2*S*)-2-benzoyl-1-(4-methoxyphenyl)-4-methyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**128x**)



The reaction was stirred for 0.5 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **128x** as a yellow foam (66 mg, 83% yield, 26% ee, dr = >20/1, keto/enol = 2.6/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.65 (s, 1.2H), 3.77 (s, 3H), 3.93 (s, 3H), 4.03 (s, 1.2H), 4.92 (d, *J* = 2.0 Hz, 1H), 5.22 (s, 0.4H), 5.22 (d, *J* = 2.0 Hz, 1H), 6.59 (ddd, *J* = 2.4, 2.4, 8.8 Hz, 0.8H), 6.82 (ddd, *J* = 2.0, 2.0, 8.4 Hz, 2H), 6.98 (ddd, *J* = 2.4, 2.4, 8.8 Hz, 0.8H), 7.03 (ddd, *J* = 2.0, 6.4, 8.4 Hz, 0.4H), 7.09 (ddd, *J* = 2.0, 7.2, 8.4 Hz, 1H), 7.13 (ddd, *J* = 2.0, 2.0, 8.8 Hz, 2H), 7.28-7.60 (m, 7.8H), 8.03 (dd, *J* = 1.6, 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.1, 30.4, 42.1, 42.5, 55.0, 55.2, 71.7, 110.8, 111.0, 113.7, 114.2, 120.0, 120.4, 120.6, 121.4, 122.1, 122.5, 122.6, 126.3, 127.4, 127.9, 128.26, 128.31, 128.46, 128.49, 128.8, 129.3, 129.4, 129.7, 130.2, 132.3, 132.5, 133.5, 133.6, 133.9, 136.6, 137.0, 138.2, 142.1, 144.5, 145.5, 146.5, 157.9, 158.7, 167.0, 187.9, 188.2, 195.0; IR (neat) ν: 1695, 1672, 1615, 1511, 1250, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{21}NNaO_3$ $[M+Na]^+$ 418.1419, found 418.1420; $[\alpha]_D^{25}$ +110.8 (*c* 1.00, $CHCl_3$, 26% ee); HPLC conditions: Chiralcel OD-H, Hexane/*i*PrOH = 90/10, t_R: 12.6, 17.7 min.

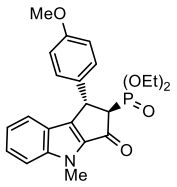
(1*S*,2*R*)-1-(4-methoxyphenyl)-4-methyl-2-(1*H*-pyrrole-1-carbonyl)-1,4-dihydrocyclopenta[*b*]indol-3(2H)-one (**129y**)



The reaction was stirred for 17 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **129y** as a colorless foam (69 mg, 90% yield, 34% ee, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.78 (s, 3H), 3.95 (s, 3H), 4.45 (d, *J* = 2.8 Hz, 1H), 5.26 (d, *J* = 2.4 Hz, 1H), 6.32 (dd, *J* = 2.4, 2.4 Hz, 2H), 6.84 (ddd, *J* = 2.4, 2.4, 8.8 Hz, 2H), 7.09 (ddd, *J* = 1.6, 6.4, 8.0 Hz, 1H), 7.15 (ddd, *J* = 1.6, 1.6, 8.4 Hz, 2H), 7.35-7.46 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.2, 42.7, 55.2, 68.0, 111.1, 113.6, 114.3, 120.2, 120.8, 122.4, 122.5, 127.7, 128.5, 132.8, 136.6, 145.7, 146.3, 158.9, 166.1, 186.0; IR (neat) ν: 1690, 1513, 1351 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{20}N_2NaO_3$ $[M+Na]^+$ 407.1372, found 407.1373; $[\alpha]_D^{24}$ +98.5 (*c* 1.00, $CHCl_3$, 34% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 90/10, t_R: 15.4, 27.7 min.

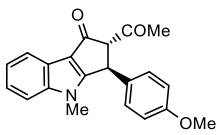
diethyl ((1*S*,2*R*)-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indol-2-yl)phosphonate (**129z**)



The reaction was stirred for 24 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **129z** as a pale yellow solid (86 mg, quantitative yield, 73% ee, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.31 (t, *J* = 6.8 Hz, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 3.42 (dd, *J* = 2.4, 25.2 Hz, 1H), 3.77 (s, 3H), 3.96 (s, 3H), 4.10-4.25 (m, 4H), 4.95 (dd, *J* =2.4, 13.2 Hz, 1H), 6.81 (ddd, *J* = 2.0, 2.0, 8.8 Hz, 2H), 7.07 (ddd, *J* = 2.0, 6.8, 8.4 Hz, 1H), 7.17 (ddd, *J* = 1.6, 1.6, 8.8 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.34-7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.3 (d, *J* = 5.7 Hz), 16.4 (d, *J* = 5.7 Hz), 30.2, 40.8 (d, *J* = 1.9 Hz), 55.2, 60.9, 62.3 (d, *J* = 7.6 Hz), 63.1 (d, *J* = 6.7 Hz), 111.0, 114.0, 120.6, 122.3 (d, *J* = 5.7 Hz), 127.3, 128.4, 133.4 (d, *J* = 2.8 Hz), 138.0 (d, *J* = 5.7 Hz), 145.3, 145.8 (d, *J* = 8.6 Hz), 158.7, 186.9 (d, *J* = 3.8 Hz); IR (neat) ν: 1694, 1513, 1249, 1047, 1031 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{27}NO_5P$ $[M+H]^+$ 428.1627, found 428.1627; $[\alpha]_D^{27}$ +0.7 (*c* 1.01, $CHCl_3$, 73% ee); HPLC conditions: Chiralcel OD-H, Hexane/*i*PrOH = 95/5, t_R: 17.4, 22.3 min.

(2*S*,3*S*)-2-acetyl-3-(4-methoxyphenyl)-4-methyl-3,4-dihydrocyclopenta[*b*]indol-1(2*H*)-one (**155b**)

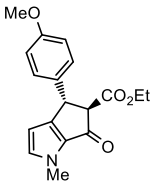


The reaction was stirred for 1 week at 80 °C using 1,2-DCE as a solvent, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **155b** as a colorless wax (21 mg, 32% yield, 14% ee, dr = >20/1, keto/enol = 2/1). Enantiomeric excess was determined after methylation.

^{1}H NMR (400 MHz, $CDCl_3$, keto/enol = 2/1) δ: 1.71 (s, 1.5H), 2.50 (s, 3H), 3.42 (s, 1.5H), 3.45 (s, 3H), 3.79 (s, 4.5H), 4.07 (d, *J* = 2.4 Hz, 1H), 4.75 (s, 0.5H), 5.21 (d, *J* = 2.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.07 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.27-7.26 (m, 4.5H), 7.93 (dd, *J* = 2.0, 8.4 Hz, 1H), 8.00 (dd, *J* = 8.0, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, keto/enol mixture) δ: 18.5, 30.4, 30.5, 30.7, 40.4, 42.5, 55.2, 55.3, 77.6, 110.1, 110.2, 114.4, 114.7, 117.5, 118.5, 121.16, 121.19, 121.2, 121.3,

122.3, 122.8, 123.4, 124.0, 128.5, 129.1, 130.1, 131.2, 142.6, 143.5, 158.8, 159.1, 164.1, 166.6, 168.1, 187.2, 190.1, 202.2; IR (neat) ν: 1684, 837, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_3$ $[M+H]^+$ 334.1443, found 334.1445; HPLC conditions: Chiralcel IB, Hexane/*i*PrOH = 80/20, t_R: 8.8, 11.8 min..

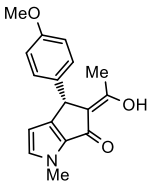
ethyl (4*S*,5*R*)-4-(4-methoxyphenyl)-1-methyl-6-oxo-1,4,5,6-tetrahydrocyclopenta[*b*]pyrrole-5-carboxylate (**157a**)



The reaction was stirred for 24 h at 40 °C using 20 mol % of catalyst, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **157a** as a colorless viscous liquid (43 mg, 69% yield, 77% ee, dr = 17/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, *J* = 7.2 Hz, 3H), 3.69 (d, *J* = 2.8 Hz, 1H), 3.79 (s, 3H), 3.83 (s, 3H), 4.20-4.32 (m, 2H), 4.67 (d, *J* = 3.2 Hz, 1H), 5.99 (d, *J* = 2.8 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 2.4 Hz, 1H), 7.12 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 34.1, 42.8, 55.2, 61.5, 68.5, 105.5, 114.1, 128.3, 132.6, 134.0, 136.5, 153.7, 158.6, 169.5, 183.6; IR (neat) ν: 1728, 1679, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}NNaO_4$ $[M+Na]^+$ 336.1212, found 336.1210; $[\alpha]_D^{20}$ +101.4 (*c* 0.85, $CHCl_3$, 77% ee) ; HPLC conditions: Chiralcel OD-H, Hexane/*i*PrOH = 90/10, t_R: 12.2, 15.3 min.

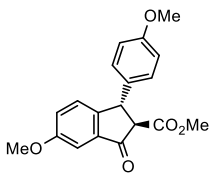
(*S*,*Z*)-5-(1-hydroxyethylidene)-4-(4-methoxyphenyl)-1-methyl-4,5-dihydrocyclopenta[*b*]pyrrol-6(1*H*)-one (**157b**)



The reaction was stirred for 17 h using 20 mol % of catalyst, and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **157b** as a colorless wax (45 mg, 80% yield, 72% ee, dr = >20/1, keto/enol = 0.7/1). Enantiomeric excess was determined after conversion to methylated product **S3b**.

^{1}H NMR (400 MHz, $CDCl_3$, keto/enol = 0.4/1) δ: 1.71 (s, 3H), 2.41 (s, 1.2H), 3.76 (s, 3H), 3.77 (s, 1.2H), 3.81 (s, 1.2H), 3.86 (s, 3H), 3.90 (d, *J* = 2.8 Hz, 0.4H), 4.55 (s, 1H), 4.87 (d, *J* = 2.8 Hz, 0.4H), 5.86 (d, *J* = 2.0 Hz, 1H), 5.97 (d, *J* = 2.0 Hz, 0.4H), 6.08 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 0.8H), 6.85 (d, *J* = 2.4 Hz, 1H), 7.00 (d, *J* = 2.4 Hz, 0.4H), 7.09 (d, *J* = 8.8 Hz, 2.8H); ^{13}C NMR (100 MHz, $CDCl_3$, keto/enol mixture) δ: 18.8, 30.5, 34.0, 34.2, 39.8, 41.6, 55.1, 55.2, 104.1, 105.6, 114.0, 114.1, 119.4, 128.3, 132.0, 133.4, 133.8, 134.1, 134.5, 136.6, 149.8, 154.0, 158.2, 158.5, 167.9, 183.8, 184.9, 202.7; IR (neat) ν: 1682, 1660, 1622, 1511, 1404, 1249, 856, 845 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}NNaO_3$ $[M+Na]^+$ 306.1106, found 306.1105; $[\alpha]_D^{26}$ +185.2 (*c* 1.02, $CHCl_3$, 72% ee).

methyl (1*S*,2*R*)-5-methoxy-1-(4-methoxyphenyl)-3-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**127**)

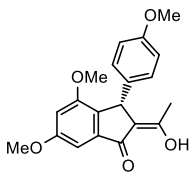


The solution of **126** (33 mg, 0.1 mmol) in CH_2Cl_2 (0.5 mL) was added $Yb(NTf_2)_3$ (20 mg, 0.02 mmol). The reaction mixture was stirred at room temperature for 4.5 h and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **127** as a colorless solid (32 mg, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: .69 (s, 3H), 3.75 (d, *J* = 3.6 Hz, 1H), 3.80 (s, 3H), 3.85 (s, 3H), 5.12 (d, *J* =

3.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.88 (dd, *J* = 6.8, 6.8 Hz, 1H), 7.02 (d, *J* =6.8 Hz, 1H), 7.18-7.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 43.8, 52.6, 55.2, 55.6, 62.0, 105.2, 110.8, 120.6, 124.8, 127.2, 128.5, 128.6, 129.7, 136.5, 149.1, 157.3, 159.7, 169.5, 199.3; IR (neat) ν: 1714, 1648, 1573 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NaO_5$ $[M+Na]^+$ 349.1051, found 349.1056.

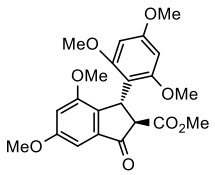
(*S,Z*)-2-(1-hydroxyethylidene)-4,6-dimethoxy-3-(4-methoxyphenyl)-2,3-dihydro-1*H*-inden-1-one (161a)



The reaction was stirred for 96 h at 40 °C and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **161a** as a yellow solid (26 mg, 38% yield, 34% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.80 (s, 3H), 3.62 (s, 3H), 3.76 (s, 3H), 3.85 (s, 3H), 4.76 (s, 1H), 6.53 (d, *J* = 2.0 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 2.4 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.1, 44.6, 55.1, 55.5, 55.7, 96.3, 104.9, 113.5, 117.3, 129.0, 132.6, 134.5, 139.1, 157.1, 158.0, 161.4, 176.2, 193.8; IR (neat) ν: 1653, 1608, 1510, 1304, 1254 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NaO_5$ $[M+Na]^+$ 363.1208, found 363.1206; $[\alpha]_D^{29}$ +58.4 (*c* 1.00, $CHCl_3$, 34% ee); HPLC conditions: Chiralcel OD-H, Hexane/*i*PrOH = 90/10, t_R: 6.3, 9.8 min.

methyl (2*R*,3*R*)-4,6-dimethoxy-1-oxo-3-(2,4,6-trimethoxyphenyl)-2,3-dihydro-1*H*-indene-2-carboxylate (161b)

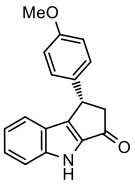


The reaction was stirred for 1 h and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **161b** as a colorless solid (79 mg, 95% yield, 27% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.39 (s, 3H), 3.61 (s, 3H), 3.74 (s, 3H), 3.78 (s, 3H), 3.82 (s, 4H), 3.89 (s, 3H), 5.43 (d, *J* = 1.2 Hz, 1H), 5.97 (s, 1H), 6.17 (s, 1H), 6.54 (s, 1H), 6.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 35.4, 52.5, 55.17, 55.19, 55.6, 55.7, 56.4, 60.6, 91.0, 91.1, 96.2, 106.0, 109.7, 137.4, 139.6, 157.3, 158.8, 159.0, 160.0, 160.8, 170.0, 200.5; IR (neat) ν: 1738, 1708, 1510 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}NaO_8$ $[M+Na]^+$ 439.1369, found 439.1372; $[\alpha]_D^{21}$ -76.1 (*c* 1.01, $CHCl_3$, 27% ee); HPLC conditions: Chiralcel IA, Hexane/*i*PrOH = 80/20, t_R: 7.3, 9.3 min.

Transformations of Nazarov Product

(*S*)-1-(4-methoxyphenyl)-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (162)

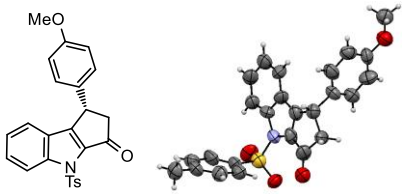


1N HCl *aq.* (5 mL) was added to the solution of **129l** (50 mg, 149 μmol) in THF (2 mL), and it was heated to 100 °C. After stirred for 1 day, the solution was diluted with H_2O and AcOEt. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2,

AcOEt/Hexane = 1/3) to afford **162** as a colorless solid (41 mg, quantitative yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.91 (dd, *J* = 2.0, 18.4 Hz, 1H), 3.56 (dd, *J* = 6.4, 18.0 Hz, 1H), 3.79 (s, 3H), 4.67 (dd, *J* = 2.0, 6.4 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 7.08 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 2H), 7.37-7.40 (m, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 9.82 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 38.8, 51.9, 55.2, 113.7, 114.1, 120.8, 122.0, 123.0, 127.4, 128.2, 134.5, 138.6, 144.2, 149.2, 158.4, 194.2; IR (neat) ν: 3209, 1667, 1509 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{16}NO_2$ $[M+H]^+$ 278.1181, found 278.1180; $[\alpha]_D^{17}$ –136.7 (*c* 0.2, $CHCl_3$, 99% ee).

(*S*)-1-(4-methoxyphenyl)-4-tosyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one[43] (**163**)



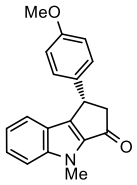
*From **162***; The mixture of **162** (10 mg, 36 μmol, 97% ee), TsCl (8.2 mg, 43 μmol), KOH (3 mg, 54 μmol) and *n*Bu_4NBr (1 piece) in THF (0.2 mL) was stirred for 16 h at room temperature. The mixture was diluted with H_2O, and the layers were separated. The water layer was extracted with $CHCl_3$ three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/4) to afford **163** as a colorless solid (13 mg, 84% yield). Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of Et_2O into the benzene solution of product and stilled at room temperature for overnight.

Melting Point: 161-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.39 (s, 3H), 2.88 (dd, *J* = 2.8, 18.4 Hz, 1H), 3.46 (dd, *J* = 6.8, 18.4 Hz, 1H), 3.77 (s, 3H), 4.47 (dd, *J* = 2.8, 6.8 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 7.20-7.22 (m, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.51 (ddd, *J* = 1.6, 6.8, 8.4 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 2H), 8.34 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.7, 37.9, 51.9, 55.2, 114.3, 115.6, 122.1, 123.9, 124.3, 127.6, 128.1, 129.3, 129.9, 132.9, 135.6, 137.8, 143.5, 145.3, 155.7, 158.7, 189.5; IR (neat) ν: 1703, 1511, 1377, 1177 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{22}NO_4S$ $[M+H]^+$ 432.1270, found 432.1269; $[\alpha]_D^{20}$ –2.9 (*c* 0.18, $CHCl_3$, 99% ee).

*From **129k***; **129k** (32.8 mg, 65 μmmol, 52 % ee) was decarboxylated under the above procedure and stirred for 16 h. The reaction mixture was diluted with H_2O and AcOEt. The layers were separated and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **S5b** as a colorless solid (27 mg, 97% yield). $[\alpha]_D^{25}$ -1.7 (*c* 0.5, $CHCl_3$, 52% ee).

(*S*)-1-(4-methoxyphenyl)-4-methyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**164**)

*From **129l***; Decarboxylation of **129l** was carried out under acidic conditions to afford **162**The mixture of **162** (5 mg, 18 μmol, 97% ee), KOH (2 mg, 36 μmol) and *n*Bu_4NBr (catalytic amount) in THF was added MeI (2.2 μL, 36 μmol). The mixture was stirred for 1 h at room temperature. Water was added to the mixture

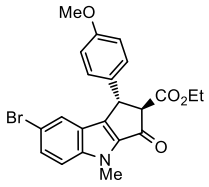


and layers were separated. Water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **164** as a colorless solid (5 mg, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.85 (dd, *J* = 2.8, 18.8 Hz, 1H), 3.50 (dd, *J* = 6.8, 18.4 Hz, 1H), 3.79 (s, 3H), 3.98 (s, 3H), 4.61 (dd, *J* = 2.4, 6.4 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 7.08 (ddd, *J* = 2.8, 4.8, 8.0 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.39-7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.1, 38.2, 52.3, 55.2, 110.9, 114.1, 120.3, 122.2, 122.6, 126.8, 128.1, 134.9, 138.7, 145.0, 146.6, 158.4, 194.0; IR (neat) ν: 1678, 1612, 1509 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NO_2$ $[M+H]^+$ 292.1338, found 292.1338; $[\alpha]_D^{18}$ –118.3 (*c* 0.17, $CHCl_3$, 97% ee).

*From **129a***; 1N HCl *aq.* (3 mL) was added to the solution of **129a** (33 mg, 69% ee) in THF (1 mL), and it was heated to 100 °C. After stirred for 1 day, the solution was diluted with H_2O and AcOEt. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **164** as a pale yellow solid (26 mg, 99% yield). $[\alpha]_D^{18}$ –51.8 (*c* 0.41, $CHCl_3$, 69% ee).

ethyl (1*S*,2*R*)-7-bromo-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**165**)

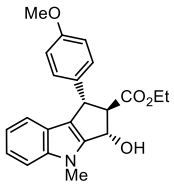


The solution of **129a** (31 mg, 85 μmol) in MeCN (0.5 mL) was added NBS (18 mg, 100 μmol) and stirred for 1 h at room temperature. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **165** as a yellow solid (31 mg, 81% yield, dr = 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, *J* = 7.2 Hz, 3H), 3.79 (d, *J* = 2.8 Hz, 1H), 3.81 (s, 3H), 3.95 (s, 3H), 4.25-4.34 (m, 2H), 4.91 (d, *J* = 2.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz ,1H), 7.47 (d, *J* = 1.2 Hz, 1H), 7.49 (dd, *J* = 1.6, 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 30.4, 42.7, 55.3, 61.8, 68.4, 112.7, 114.0, 114.4, 123.8, 124.6, 128.3, 130.2, 132.6, 137.9, 143.8, 144.4, 158.9, 168.8, 187.0; IR (neat) ν: 1734, 1697, 1249, 1031, 834 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{20}BrNNaO_4$ $[M+Na]^+$ 464.0473, found 464.0472.

ethyl (1*S*,2*R*,3*S*)-3-hydroxy-1-(4-methoxyphenyl)-4-methyl-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**166**)

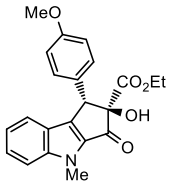
The solution of **129a** (36 mg, 0.1 mmol) in EtOH (1 mL) was added $NaBH_4$ (5.7 mg, 0.15 mmol) at 0 °C.

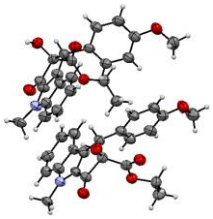


The reaction mixture was gradually warmed to room temperature and stirred for 17 h. Water was added to the solution and extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **166** as a yellow foam (29 mg, 79% yield, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.31 (t, *J* = 7.2 Hz, 3H), 2.16 (brs, 1H), 3.34 (dd, *J* = 4.8, 6.4 Hz, 1H), 3.78 (s, 3H), 3.81 (s, 3H), 4.18-4.30 (m, 2H), 4.52 (d, *J* = 6.0 Hz, 1H), 5.65 (s, 1H), 6.83 (d, *J* = 8.4 Hz, 2H), 6.98 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.19 (ddd, *J* = 1.2, 8.4, 8.4 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 30.3, 45.1, 55.2, 61.0, 72.8, 109.8, 113.8, 119.4, 119.6, 119.7, 121.8, 123.1, 128.7, 135.6, 142.3, 143.4, 158.4, 173.4; IR (neat) ν: 3468, 1728, 1247, 1036, 829, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{23}NNaO_4$ $[M+Na]^+$ 388.1525, found 388.1523.

ethyl (1*S*,2*R*)-2-hydroxy-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**167**)





*From **129a***; The mixture of **129a** (36 mg, 0.1 mmol) and $CeCl_3 \cdot 7H_2O$ (45 mg, 0.12 mmol) in MeOH/THF (5/1, 0.6 mL) was stirred at room temperature for 2 h under air condition. The mixture was diluted with water and AcOEt. Layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **167** as a colorless solid (37 mg, 99%, dr = 3/1).

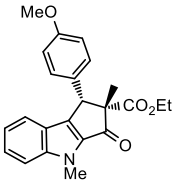
*From **128a***; The mixture of **128a** (10 mg, 28 μmol) and $CeCl_3 \cdot 7H_2O$ (11 mg, 30 μmol) in EtOH/THF (7/1, 0.16 mL) was stirred at room temperature for 2.5 days under air condition. The solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/1) to afford **167** as a colorless solid (7 mg, 66% yield).

Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the Et_2O solution of product

^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.84 (t, *J* = 6.6 Hz, 3H), 4.64 (qd, *J* = 6.6, 10.8 Hz, 1H), 3.78-3.83 (m, 4H), 4.01 (s, 3H), 4.41 (d, *J* = 5.4 Hz, 1H), 4.79 (s, 1H), 6.84 (d, *J* = 7.8 Hz, 2H), 7.14 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.43-7.49 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.6, 30.5, 52.1, 55.2, 62.4, 90.6, 111.2, 113.5, 120.8, 122.9, 123.1, 127.7, 128.1, 129.8, 137.0, 131.9, 145.1, 159.1, 170.7, 188.4; IR

(neat) ν: 3427, 1738, 1698, 1211, 851, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_5$ $[M+Na]^+$ 402.1317, found 402.1317.

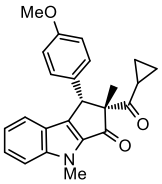
ethyl (1*S*,2*S*)-1-(4-methoxyphenyl)-2,4-dimethyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**168a**)



MeI (7.5 μL, 0.12 mmol) was added to the mixture of **129a** (36 mg, 0.1 mol), K_2CO_3 (17 mg, 0.12 mol) and *n*Bu_4NBr (3.2 mg, 0.01 mmol) in THF (0.5 mL). The reaction mixture was stirred for 13 h at room temperature and then added H_2O. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt.Hexane = 1/5) to afford **168a** as a pale yellow solid (28 mg, 75% yield, dr = 6/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.83 (dd, *J* = 7.6, 7.6 Hz, 3H), 1.74 (s, 3H), 3.47 (qd, *J* = 7.6, 11.2 Hz, 1H), 3.62 (qd, *J* = 7.6, 11.2 Hz, 1H), 3.78 (s, 3H), 4.01 (s, 3H), 4.48 (s, 1H), 6.80 (d, *J* = 9.2 Hz, 2H), 7.08-7.12 (m, 3H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.43-7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 113.5, 21.2, 30.3, 51.8, 55.2, 60.8, 68.3, 111.1, 113.3, 120.5, 122.56, 122.59, 127.1, 129.6, 129.9, 138.3, 142.7, 145.3, 158.9, 170.8, 192.1; IR (neat) ν: 1735, 1693, 850, 746 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{23}NNaO_4$ $[M+Na]^+$ 400.1525, found 400.1526.

(1*S*,2*R*)-2-(cyclopropanecarbonyl)-1-(4-methoxyphenyl)-2,4-dimethyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**S3a**)

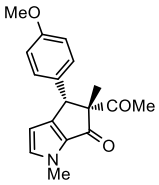


MeI (7 μL, 109 μmol) was added to the mixture of **129w** (26 mg, 72 μmol), KOH (4.9 mg, 87 μmol) and *n*Bu_4NBr (2.3 mg, 7.2 μmol) in THF (0.4 mL). The reaction mixture was stirred for 24 h at room temperature and then added H_2O. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by preparative TLC (SiO_2, AcOEt.Hexane = 1/5) to afford **S3a** as a colorless foam (23 mg, 84% yield, 32% ee).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.17-0.26 (m, 2H), 0.54 (dddd, *J* = 3.2, 7.6, 7.6, 7.6 Hz, 1H), 0.71 (dddd, *J* = 3.6, 7.6, 7.6 ,7.6 Hz, 1H), 1.45 (dddd, *J* = 4.4, 8.0, 8.0, 8.0 Hz, 1H), 1.73 (s, 3H), 3.78 (s, 3H), 4.04 (s, 3H), 4.56 (s, 1H), 6.79 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.13-7.16 (m, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.46-7.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.6, 12.7, 20.7, 21.2, 30.4, 51.4, 55.2, 74.4, 111.2, 113.6, 120.7, 122.8, 122.9, 127.3, 129.5, 129.9, 138.8, 143.2, 145.3, 158.8, 194.0; IR (neat) ν: 1699. 1684. 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{23}NNaO_3$ $[M+Na]^+$ 396.1576, found 396.1577; $[\alpha]_D^{28}$ –89.5 (*c* 0.45, $CHCl_3$, 32% ee); HPLC conditions: Chiralcel OD-H, Hexane/*i*PrOH = 90/10, t_R: 11.3, 21.3 min.

(4*S*,5*R*)-5-acetyl-4-(4-methoxyphenyl)-1,5-dimethyl-4,5-dihydrocyclopenta[*b*]pyrrol-6(1*H*)-one (**S3b**)

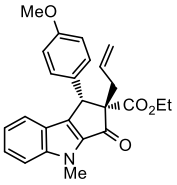
MeI (15 μL, 238 μmol) was added to the mixture of **156b** (45 mg, 159 μmol), KOH (11 mg, 190 μmol) and



*n*Bu$_4$NBr (5 mg, 16 μmol) in THF (0.8 mL). The reaction mixture was stirred for 3 h at room temperature and then added H_2O. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt.Hexane = 1/5) to afford **S3b** as a pale yellow solid (40 mg, 85% yield) and 5-*epi*-**S3b** as a pale brown liquid (6 mg, 13% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.55 (s, 3H), 1.64 (s, 3H), 3.77 (s, 3H), 3.90 (s, 3H), 4.25 (s, 1H), 6.11 (d, *J* = 2.4 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 7.10-7.12 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.2, 28.7, 34.2, 51.3, 55.1, 74.2, 106.0, 113.7, 129.5, 129.7, 133.9, 136.2, 150.8, 158.7, 190.3, 206.5; IR (neat) ν: 1711, 1682, 1514, 1249 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}NNaO_3$ $[M+Na]^+$ 320.1263, found 320.1263; $[\alpha]_D^{25}$ – 61.4 (*c* 1.00, $CHCl_3$, 72% ee); HPLC conditions: Chiralcel AD-H, Hexane/*i*PrOH = 90/10, t_R: 14.8, 15.9 min.

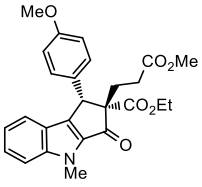
ethyl (1*S*,2*S*)-2-allyl-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**168b**)



Allyl bromide (10.4 μL, 0.12 mmol) was added to the mixture of **129a** (36 mg, 0.1 mol), K_2CO_3 (17 mg, 0.12 mol) and *n*Bu$_4$NBr (3.2 mg, 0.01 mmol) in THF (0.5 mL). The reaction mixture was stirred for 13 h at room temperature and then added H_2O. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt.Hexane = 1/5) to afford **168b** as a pale yellow liquid (46 mg, 97% yield, dr = 14/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.84 (dd, *J* = 7.2, 7.2 Hz, 3H), 2.96 (dd, *J* = 8.4, 14.0 Hz, 1H), 3.03 (dd, *J* = 5.6, 14.0 Hz, 1H), 3.49 (qd, *J* = 7.2, 10.8 Hz, 1H), 3.63 (qd, *J* = 7.2, 10.8 Hz, 1H), 3.67 (s, 3H), 4.01 (s, 3H), 4.68 (s, 1H), 5.12 (d, *J* = 10.8 Hz, 1H), 3.32 (d, *J* = 16.8 Hz, 1H), 5.77 (dddd, *J* = 6.0, 8.4, 9.6, 16.0 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 2H), 7.07-7.12 (m, 3H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.43-7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.5, 30.4, 38.2, 46.6, 55.2, 60.9, 71.3, 111.1, 113.3, 119.9, 120.5, 122.5, 122.7, 127.1, 129.6, 130.1, 132.7, 139.0, 143.4, 145.2, 158.8, 170.4, 191.0; IR (neat) ν: 1734, 1693, 1033, 936, 849, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{25}NNaO_4$ $[M+Na]^+$ 426.1681, found 426.1680.

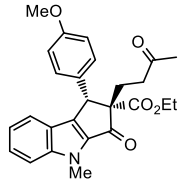
ethyl (1*S*,2*S*)-2-(3-methoxy-3-oxopropyl)-1-(4-methoxyphenyl)-4-methyl-3-oxo-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**168c**)



Methyl acrylate (10.8 μL, 0.12 mmol) was added to the mixture of **129a** (36 mg, 0.1 mol), K_2CO_3 (17 mg, 0.12 mol) and *n*Bu$_4$NBr (3.2 mg, 0.01 mmol) in THF (0.5 mL). The reaction mixture was stirred for 13 h at room temperature and then added H_2O. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt.Hexane = 1/2) to afford **168c** as a colorless liquid (58 mg, 99% yield, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.84 (dd, *J* = 7.2, 7.2 Hz, 3H), 2.42-2.52 (m, 2H), 2.63-2.72 (m, 2H), 3.47 (qd, *J* = 7.2, 11.2 Hz, 1H), 3.60 (qd, *J* = 7.2, 10.8 Hz, 1H), 3.68 (s, 3H), 3.78 (s, 3H), 4.01 (s, 3H), 4.54 (s, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 7.07-7.12 (m, 3H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.44-7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.5, 29.0, 29.7, 30.4, 49.2, 51.7, 55.2, 61.0, 70.8, 111.1, 113.3, 120.7, 122.4, 122.6, 127.3, 129.3, 130.1, 138.6, 143.0, 145.3, 159.0, 170.0, 173.6, 191.0; IR (neat) ν: 1735, 1689, 849, 752 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{27}NNaO_6$ $[M+Na]^+$ 472.1736, found 472.1730.

ethyl (1*S*,2*S*)-1-(4-methoxyphenyl)-4-methyl-3-oxo-2-(3-oxobutyl)-1,2,3,4-tetrahydrocyclopenta[*b*]indole-2-carboxylate (**168d**)



MVK (9.7 μL, 0.12 mmol) was added to the mixture of **129a** (36 mg, 0.1 mol), K_2CO_3 (17 mg, 0.12 mol) and *n*Bu_4NBr (3.2 mg, 0.01 mmol) in THF (0.5 mL). The reaction mixture was stirred for 13 h at room temperature and then added H_2O. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **168d** as a colorless solid (44 mg, quantitative yield, dr = 14/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.85 (dd, *J* = 7.6, 7.6 Hz, 3H), 2.15 (s, 3H), 2.40 (ddd, *J* = 4.4, 8.8, 13.2 Hz, 1H), 2.58-2.67 (m, 2H), 2.80-2.89 (m, 1H), 3.47 (qd, *J* = 7.2, 10.8 Hz, 1H), 3.60 (qd, *J* = 7.2, 10.8 Hz, 1H), 3.78 (s, 3H), 4.01 (s, 3H), 4.50 (s, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 7.06-7.12 (m, 3H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.44-7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.6, 28.7, 30.1, 30.4, 49.9, 55.2, 61.0, 70.8, 111.1, 113.3, 120.7, 122.4, 122.6, 127.3, 129.3, 130.1, 138.5, 143.1, 145.3, 159.0, 170.2, 191.5, 208.0; IR (neat) ν: 1732, 1689, 1251, 850, 750 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{27}NNaO_5$ $[M+Na]^+$ 456.1787, found 456.1784.

Procedure for One-Pot Construction of Quaternary Carbon Center

The mixture of $Ni(NTf_2)_2$ (12.4 mg, 0.02 mmol), (*S,S*)-ImQ (**139**) (7.9 mg, 0.02 mmol), K_2CO_3 (55.3 mg, 0.4 mmol) and activated MS 4 Å (100 mg) in CH_2Cl_2 (0.4 mL) was stirred for 2 h at room temperature. The prepared catalyst mixture was diluted with CH_2Cl_2 (1 mL) and the mixture of **128a** (0.2 mmol) and MVK (32 μL, 0.4 mmol) in CH_2Cl_2 (0.6 mL) was added. Reaction mixture was stirred at room temperature. The reaction was monitored by TLC and after the consumption of **128a**, reaction was warmed to 40 °C. The reaction was quenched with H_2O after 2 days. The resulting mixture was filtrated through Celite® and extracted with CH_2Cl_2 three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford **168d** as a pale yellow viscous liquid (84 mg, 88% yield, 78% ee, dr = 9/1).

$[\alpha]_D^{22}$ –76.9 (*c* 0.38, $CHCl_3$, 83% ee); HPLC conditions: Chiralcel IB - IA, Hexane/*i*PrOH = 70/30, flow: 0.7 mL/min, t_R: 19.6, 22.3 min.

第二章に関する実験

Preparation of Ni Complex for ESI-MS Analysis

The mixture of $Ni(NTf_2)_2$ (3.1 mg, 5 μmol), (*S*,*S*)-ImQ (**139**) (2.0 mg, 5 μmol) and activated MS 4 Å pellet (150 mg) in CH_2Cl_2 (0.2 mL) was stirred for 2 h at room temperature. The solution of **172** (1.9 mg, 5 μmol) in CH_2Cl_2 (0.3 mL) was then added to the mixture. The resulting mixture was stirred for 5 min and diluted by CH_2Cl_2 (5 mL).

The ESI-MS samples of Ni/**150** and Ni/**150**/**172** complexes were prepared following the above procedure.

Reactivity of Soluble Compounds and Insoluble Compounds (Scheme 13)

In reaction vessel A, the mixture of $Ni(NTf_2)_2$ (12.4 mg, 0.02 mmol), (*S*,*S*)-ImQ (**139**) (7.9 mg, 0.02 mmol) and activated MS 4 Å (200 mg) in CH_2Cl_2 (0.3 mL) was stirred for 30 min at room temperature. Activated MS 4 Å was added to reaction vessel B and supernatant in reaction vessel A was removed to reaction vessel B via syringe. Residual precipitate in the reaction vessel A was washed with CH_2Cl_2 (0.2 mL) twice. The solution in reaction vessel A was removed to reaction vessel B. The precipitate in reaction vessel A was diluted with CH_2Cl_2 (0.6 mL). The solution of **128a** (36 mg, 0.1 mmol) in CH_2Cl_2 (0.3 mL) was added to both reaction vessels and stirred at room temperature for appropriate time.

Asymmetric Reaction Using Crystal 173 (Scheme 14)

The mixture of $Ni(NTf_2)_2$ (6.2 mg, 0.01 mmol), (*S*,*S*)-ImQ (**139**) (3.9 mg, 0.01 mmol) and activated MS 4 Å (150 mg) in CH_2Cl_2 (0.3 mL) was stirred for 2 h at room temperature. **172** (3.9 mg, 0.01 mmol) and CPME (1 mL) were added sequentially, and the mixture was stored at room temperature for overnight. Crystals of **173** were generated, and the supernatant was removed via syringe (after this operation, the supernatant was evaporated under reduced pressure to afford the "soluble compounds" (7.7 mg)).

CH_2Cl_2 (0.2 mL) was added to the remaining crystals of **173** (calcd. 6.3 mg, 4.5 μmol) and MS 4 Å. The solution of **128a** (16.4 mg, 45 μmol) in CH_2Cl_2 (0.25 mL) was added to the mixture of **173** and MS 4 Å in CH_2Cl_2. The mixture was stirred for 0.3 h at room temperature. The reaction was quenched with H_2O and extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1.5) to afford (1*S*,2*R*)-**129a** (15 mg, 91% yield, 83% ee, dr = 10/1).

Asymmetric Reaction Using Crystal 181 (Scheme 19)

The mixture of $Ni(NTf_2)_2$ (6.2 mg, 0.01 mmol), **150** (3.9 mg, 0.01 mmol) and activated MS 4 Å (100 mg) in

CH_2Cl_2 (0.3 mL) was stirred for 2 h at room temperature. Toluene (1 mL) was added sequentially, and the mixture was stored at room temperature. Crystals of **181** were generated, and the supernatant was removed via syringe (after this operation, the supernatant was evaporated under reduced pressure to afford the "soluble compounds" (4.1 mg)).

CH_2Cl_2 (0.2 mL) was added to the remaining crystals of **181** (calcd. 6.0 mg, 59 μmol) and MS 4 Å. The solution of **129a** (21.4 mg, 59 μmol) in CH_2Cl_2 (0.1 mL) was added to the mixture of **181** and MS 4 Å in CH_2Cl_2. The mixture was stirred for 24 h at room temperature. The reaction was quenched with H_2O and extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford (1*R*,2*S*)-**129a** (20 mg, 92% yield, 10% ee, dr = 10/1).

Asymmetric Reaction Using Cyclic Substrate 178 (Scheme 16)

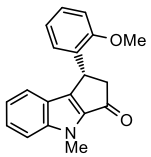
*From **178***; Chiral Ni catalyzed Nazarov cyclization was carried out on a 0.1 mmol scale of **178** in PhCl and stirred for 4 days at 120 °C. The reaction mixture was added brine and $CHCl_3$. The layers were separated and water layer was extracted with $CHCl_3$ three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was added THF (5 mL) and 1N HCl *aq*. (5 mL). The mixture was stirred for 1 day at refluxing temperature. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (0.5 mL) and added NaOH (8 mg, 0.2 mmol), MeI (12 μL, 0.2 mmol) and *n*Bu_4NBr (catalytic amount). Resulting mixture was stirred at room temperature for 13 h and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **179** as a colorless solid (6 mg, 21% in 3 steps). $[\alpha]_D^{20}$ –0.5 (*c* 0.19, $CHCl_3$).

*From **128b***; The reaction was carried out following the general procedure for asymmetric Nazarov cyclization to afford **129b** (94% yield, 66% ee).

1N HCl *aq*. (0.5 mL) was added to the solution of **129b** (38 mg) in THF (0.5 mL), and it was heated to 70 °C. After stirred for 1 day, the solution was diluted with H_2O and AcOEt. The layers were separated, and the water layer was extracted with AcOEt three times. The combined organic layers were dried over Na_2SO_4, filtrated through plug of cotton, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **179** as a colorless solid (27 mg, 90% yield).

(*R*)-1-(2-methoxyphenyl)-4-methyl-1,4-dihydrocyclopenta[*b*]indol-3(2*H*)-one (**179**)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.77 (dd, *J* = 2.4, 18.4 Hz, 1H), 3.56 (dd, *J* = 6.4, 18.4 Hz, 1H), 3.91 (s, 3H),



3.98 (s, 3H), 4.97 (dd, *J* = 2.4, 6.4 Hz, 1H), 6.80 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.98 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.10 (ddd, *J* = 2.8, 4.8, 8.0 Hz, 1H), 2.23 (ddd, *J* = 1.6, 8.0, 8.0 Hz, 1H), 7.40-7.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.1, 32.9, 51.0, 55.4, 110.2, 111.0, 120.3, 120.5, 122.5, 126.6, 127.3, 127.8, 130.9, 139.1, 144.9, 145.6, 157.1, 194.5; IR (neat) ν: 1685, 1057, 753 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NO_2$ $[M+H]^+$ 292.1338, found 292.1339; $[\alpha]_D^{20}$ –196.4 (*c* 1.02, $CHCl_3$, 66% ee).

Asymmetric Nazarov Cyclization Using (*E*)- and (*Z*)-128k (Scheme 17)

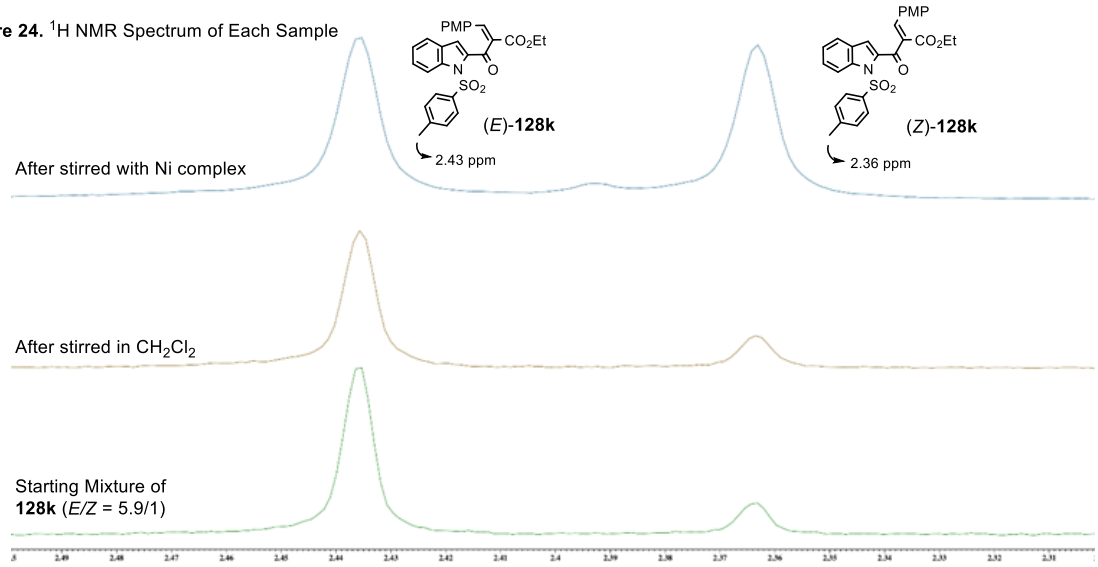
The mixture of $Ni(NTf_2)_2$ (12.4 mg, 0.02 mmol), (*S*,*S*)-ImQ (**139**) (7.9 mg, 0.02 mmol) and activated MS 4 Å (100 mg) in CH_2Cl_2 (0.4 mL) was stirred for 2 h at room temperature. To the catalyst mixture, the solution of (*E*)-**128k** (50.4 mg, 0.1 mmol, *E/Z* = >20/1) or (*Z*)-**128k** (50.4 mg, 0.1 mmol, *E/Z* = 1/15) in CH_2Cl_2 (0.6 mL) was added. The reactions were stirred for 96 h at 40 °C. The reaction was quenched with H_2O. The products were purified according to the general procedure. The results were shown in the main text.

Isomerization Experiments (Table 14)

Thermal Conditions; **128k** (1 mg, 2 μmol) was dissolved in CH_2Cl_2 (0.02 mL) and stirred for 1 h at room temperature. The solution was concentrated under reduced pressure.

Lewis Acidic Conditions; The mixture of $Ni(NTf_2)_2$ (3.7 mg, 6 μmol), (*S*,*S*)-ImQ (**139**) (2.4 mg, 6 μmol) and activated MS 4 Å (100 mg) in CH_2Cl_2 (0.3 mL) was stirred for 2 h at room temperature. **128k** (15 mg, 30 μmol) was added to the mixture and stirred for 1 h at the same temperature. The reaction mixture was purified following the general procedure for Nazarov cyclization to afford **128k** (15 mg, quantitative yield).

Figure 24. ^{1}H NMR Spectrum of Each Sample



第三章に関する実験

Substrate Synthesis

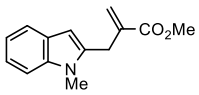
General Procedure for Indole Substrate

The mixture of aldehyde (10 mmol) trimethyl phosphonoacetate (2 g, 11 mmol), AcOH (290 μL, 5mmol) and piperidine (100 μL, 1 mmol) in benzene (20 mL) was stirred at refluxing temperature for 1 day. The resulting mixture was concentrated under reduced pressure and purified by short pad of silica gel to remove unreacted aldehyde. The Knoevenagel product was used without further purification.

$NaBH_4$ (378 mg, 10 mmol) was added to the solution of Knoevenagel product in MeOH (20 mL) at 0 °C. The mixture was gradually warmed to room temperature and stirred for overnight. Solvent was removed under reduced pressure and the residue was diluted with water and AcOEt. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure.

The residue was dissolved in THF (20 mL) and added paraformaldehyde (601 mg, 20 mmol) and K_2CO_3 (2.8 g, 20 mmol). The mixture was stirred at refluxing temperature for 1 day and filtrated through Celite®. The solution was concentrated under reduced pressure. The residue was purified by flash column chromatography.

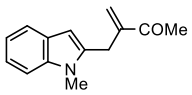
methyl 2-((1-methyl-1*H*-indol-2-yl)methyl)acrylate (**191a**)



The reaction was carried out as described in the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **191a** as a pale yellow viscous liquid (1355 mg, 59% yield in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.61 (s, 3H), 3.79 (s, 5H), 5.36 (s, 1H), 6.29 (s, 1H), 6.31 (s, 1H), 7.08 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.18 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 29.1, 29.5, 52.1, 101.1, 108.9, 119.4, 120.0, 120.9, 126.7, 127.7, 136.7, 137.5, 137.8, 167.1; IR (neat) ν: 1721, 1631, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}NO_2$ $[M+H]^+$ 230.1181, found 230.1182.

3-((1-methyl-1*H*-indol-2-yl)methyl)but-3-en-2-one (**202a**)

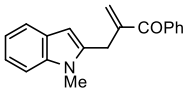


The Knoevenagel condensation was carried out on a 7.2 mmol scale following the general procedure. The residue was dissolved in AcOEt (27 mL) and added 10% Pd/C (140 mg). The reaction mixture was stirred vigorously under H_2 balloon at room temperature for overnight. The mixture was filtrated through Celite®. The filtrate was concentrated under reduced pressure. Horner-Wadsworth-Emmons reaction was carried out following general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **202a** as a colorless solid (762 mg, 59% yield in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.41 (s, 3H), 3.58 (s, 3H), 3.75 (s, 2H), 5.55 (t, *J* = 2.0 Hz, 1H), 6.14 (s, 1H),

6.28 (s, 1H), 7.10 (ddd, *J* = 1.2, 6.8, 8.0 Hz, 1H), 7.17 (ddd, *J* = 1.2, 7.2, 8.4 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.8, 27.5, 29.5, 101.2, 108.9, 119.3, 119.9, 120.9, 127.0, 127.7, 137.4, 137.5, 146.4, 198.9; IR (neat) ν: 1677, 1628, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}NO$ $[M+H]^+$ 214.1232, found 214.1235.

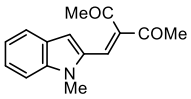
2-((1-methyl-1*H*-indol-2-yl)methyl)-1-phenylprop-2-en-1-one (**202b**)



The Knoevenagel condensation was carried out on a 5 mmol scale following the general procedure. The residue was dissolved in MeOH (25 mL) and added 10% Pd/C (185 mg). The reaction mixture was stirred vigorously under H_2 balloon at room temperature for 8 h. The mixture was filtrated through Celite®. The filtrate was concentrated under reduced pressure. Horner-Wadsworth-Emmons reaction was carried out following general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **202b** as a pale orange solid (190 mg, 14% yield in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.67 (s, 3H), 3.96 (s, 2H), 5.68 (s, 1H), 5.79 (s, 1H), 6.38 (s, 1H), 7.08 (ddd, *J* = 0.8, 6.8, 7.6 Hz, 1H), 7.18 (ddd, *J* = 1.2, 6.8, 8.0 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.45 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.53-7.57 (m, 2H), 7.77-7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 29.1, 29.6, 101.3, 109.0, 119.4, 120.0, 120.9, 127.8, 128.0, 128.3, 129.5, 132.4, 137.1, 137.3, 137.6, 145.2, 197.1; IR (neat) ν: 1653, 746, 700 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NO$ $[M+H]^+$ 276.1388, found 276.1384.

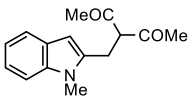
3-((1-methyl-1*H*-indol-2-yl)methylene)pentane-2,4-dione (**S4**)



The mixture of 1-methyl-1*H*-indole-2-carbaldehyde (318 mg, 2 mmol), acetylacetone (215 μL, 2.1 mmol), AcOH (57 μL, 1 mmol), and piperidine (20 μL, 0.2 mmol) in benzene (10 mL) was stirred at refluxing temperature for 6 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **S4** as a yellow solid (329 mg, 68% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 6H), 3.85 (s, 3H), 6.80 (s, 1H), 7.13 (ddd, *J* = 1.6, 6.0, 7.6 Hz, 1H), 7.31-7.35 (m, 2H), 7.60-7.61 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.7, 29.9, 31.0, 107.9, 109.7, 120.8, 121.9, 124.7, 126.6, 127.6, 131.5, 139.0, 141.0, 194.8, 205.8; IR (neat) ν: 1709, 1652, 1615, 1253, 751 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}NNaO_2$ $[M+Na]^+$ 264.1001, found 264.0997.

3-((1-methyl-1H-indol-2-yl)methyl)pentane-2,4-dione (**207**)

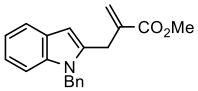


The mixture of **S4** (241 mg, 1 mmol) and 10% Pd/C (24 mg) in MeOH/THF (5/2, 7 mL) was stirred under H_2 balloon at room temperature for 2 h. The mixture was filtrated through Celite® and filtrate was concentrated under reduced pressure. The resiude was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/4) to afford **207** as a yellow solid (235 mg, 97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.11 (s, 6H), 3.66 (s, 2H), 3.75 (s, 3H), 6.11 (s, 1H), 7.08 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.19 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.0, 25.7, 29.5, 99.6, 106.2, 108.7, 119.5, 120.0, 121.1, 127.5, 137.9, 138.7, 191.9;

IR (ATR) ν: 1608, 1469, 1284, 751 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{15}H_{17}NNaO_2$ $[M+Na]^+$ 266.1157, found 266.1163.

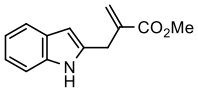
methyl 2-((1-benzyl-1*H*-indol-2-yl)methyl)acrylate (**191b**)



The reaction was carried out on a 2.8 mmol scale following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **191b** as a pale yellow viscous liquid (409 mg, 48% yield in 3 steps.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.71 (s, 2H), 3.72 (s, 3H), 5.27 (s, 2H), 5.43 (s, 1H), 6.25 (s, 1H), 6.36 (s, 1H), 6.95 (d, *J* = 6.9 Hz, 2H), 7.08 (ddd, *J* = 1.4, 6.9, 6.9 Hz, 1H), 7.12 (ddd, *J* = 1.4, 6.9, 6.9 Hz, 1H), 7.18-7.26 (m, 4H), 7.58 (dd, *J* = 2.8, 6.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 29.1, 46.5, 52.0, 101.7, 109.5, 119.6, 120.1, 121.2, 125.9, 126.9, 127.2, 127.9, 128.7, 137.2, 137.3, 137.6, 137.7, 167.0; IR (neat) ν: 1722, 1634, 735 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NO_2$ $[M+H]^+$ 306.1494, found 306.1497.

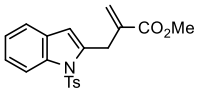
methyl 2-((1*H*-indol-2-yl)methyl)acrylate (**191c**)



The reaction was carried out on a 5 mmol scale following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **191c** as a pale yellow solid (116 mg, 11% yield in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.71 (s, 2H), 3.76 (s, 3H), 5.67 (d, *J* = 0.8 Hz, 1H), 6.23 (s, 1H), 6.26 (d, *J* = 0.8 Hz, 1H), 7.05 (ddd, *J* = 0.8, 8.0, 8.0 Hz, 1H), 7.11 (ddd, *J* = 1.2, 8.0, 8.0 Hz, 1H), 7.26 (dd, *J* = 0.8, 7.6 Hz, 1H), 7.52 (d, *J* = 6.8 Hz, 1H), 8.37 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.3, 52.2, 100.5, 110.6, 119.5, 119.9, 121.2, 127.2, 128.5, 136.0, 136.2, 137.9, 167.8; IR (neat) ν: 3394, 1714, 1631, 746 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{14}NO_2$ $[M+H]^+$ 216.1025, found 216.1019.

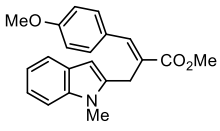
methyl 2-((1-tosyl-1*H*-indol-2-yl)methyl)acrylate (**191d**)

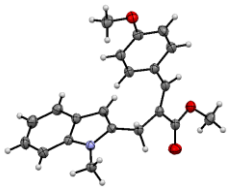


The reaction was carried out on a 2 mmol scale following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **191d** as a colorless liquid (206 mg, 28% yield in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 3.73 (s, 3H), 4.08 (s, 2H), 5.01 (d, *J* = 1.4 Hz, 1H), 6.35 (s, 2H), 7.18-7.21 (m, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.24-7.28 (m, 1H), 7.40 (d, *J* = 7.3 Hz, 1H), 7.70 (d, *J* = 8.7 Hz, 2H), 8.13 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 31.5, 52.0, 110.3, 114.7, 120.3, 123.5, 124.1, 126.5, 127.7, 129.5, 129.8, 135.9, 137.1, 137.3, 138.7, 144.7, 167.0; IR (neat) ν: 1722, 1371, 1174, 814, 750 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{19}NNaO_4S$ $[M+Na]^+$ 392.0933, found 392.0936.

methyl (*E*)-3-(4-methoxyphenyl)-2-((1-methyl-1*H*-indol-2-yl)methyl)acrylate (**191e**)





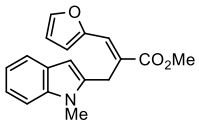
The reaction was carried out on a 4.7 mmol scale following the general procedure. After the reduction with $NaBH_4$, NaH (72 mg, 1.8 mmol, 60% dispersion) was added to the mixture of the residue and *p*-anisaldehyde (183 μL, 1.5 mmol) in toluene (7.5 mL). The mixture and stirred for overnight at 60 °C. The reaction mixture was quenched with *sat*.NH_4Cl *aq*. The layers were separated and water layer was extracted with

AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **191e** as a pale yellow amorphous (354 mg, 26% yield in 3 steps, *E/Z* = 2.2/1). Further purification was achieved by recrystallization from Et_2O to afford (*E*)-isomer as a colorless solid. Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the Et_2O solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.73 (s, 3H), 3.77 (s, 3H), 3.78 (s, 3H), 3.96 (s, 3H), 6.24 (s, 1H), 6.83 (d, *J* = 8.7 Hz, 2H), 7.07 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.19 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 1H), 7.35 (d, *J* = 8.7 Hz, 2H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.1, 29.5, 52.2, 55.3, 99.3, 108.7, 114.1, 119.2, 120.0, 120.8, 126.2, 127.5, 127.8, 131.1, 137.7, 138.2, 141.3, 160.2, 168.6; IR (neat) ν: 1710, 1605, 1512, 1258, 1177, 841, 750 cm^{-1}

HRMS (ESI) *m/z* calcd for $C_{21}H_{22}NO_3$ $[M+H]^+$ 336.1603, found 336.1600.

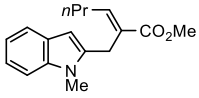
methyl (*E*)-3-(furan-2-yl)-2-((1-methyl-1*H*-indol-2-yl)methyl)acrylate (**191f**)



The reaction was carried out on a 6.3 mmol scale following the general procedure. After the reduction with $NaBH_4$, NaH (380 mg, 9.5 mmol, 60% dispersion) was added to the solution of the residue in THF (13 mL) at 0 °C and stirred for 0.5 h. Furfural (787 μL, 9.5 mmol) was added to the mixture and stirred for another 2 h. The reaction was quenched with *sat*. NH_4Cl *aq*. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **191f** as a red solid (1167 mg, 63% yield in 3 steps, *E/Z* = 3/1). Further purification was achieved by wash the solid with Et_2O to afford pale yellow solid (345 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.76 (s, 3H), 3.78 (s, 3H), 4.20 (s, 2H), 6.11 (s, 1H), 6.43 (dd, *J* = 1.8, 3.2 Hz, 1H), 6.58 (d, *J* = 3.2 Hz, 1H), 7.03 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.15 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.46 (s, 1H), 7.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.8, 29.6, 52.3, 99.0, 108.7, 112.1, 116.1, 119.1, 119.8, 120.5, 124.9, 127.5, 127.8, 137.5, 138.0, 144.7, 150.9, 168.3; IR (neat) ν: 1710, 1636, 1283, 1214, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{18}NNaO_3$ $[M+Na]^+$ 296.1287, found 296.1286.

methyl (*E*)-2-((1-methyl-1*H*-indol-2-yl)methyl)hex-2-enoate (**191g**)



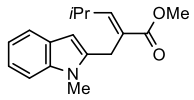
The reaction was carried out on a 2 mmol scale following the general procedure. After the reduction with $NaBH_4$, NaH (80 mg, 2 mmol, 60% dispersion) was added to the solution of the residue in THF (8 mL) at 0°C and stirred for 0.5 h. The solution of butyraldehyde (180 μL, 2 mmol) in THF (2 mL) was added to the mixture and stirred for another 5 h. The reaction mixture was quenched with *sat*.NH_4Cl *aq*. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2,

AcOEt/Hexane = 1/10) to afford (*E*)-**191g** as a yellow viscous liquid (127 mg, 24% yield in 3 steps) and (*Z*)-**191g** as a yellow viscous liquid (48 mg, 15% yield in 3 steps).

(*E*)-**191g**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (t, *J* = 7.3 Hz, 3H), 1.40 (tq, *J* = 7.3, 7.3 Hz, 2H), 2.45 (dt, *J* = 7.3, 7.3 Hz, 2H), 3.62 (s, 3H), 3.73 (s, 5H), 5.79 (t, *J* = 7.3 Hz, 1H), 6.25 (s, 1H), 7.07 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.16 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.26 (d, *J* = 8.2 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 22.5, 29.5, 31.3, 31.5, 51.4, 100.8, 108.8, 119.2, 120.0, 120.8, 127.7, 128.6, 137.5, 137.9, 144.4, 167.9; IR (neat) ν: 1718, 1644, 1217, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}NO_2$ $[M+H]^+$ 272.1651, found 272.1648.

(*Z*)-**191g**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.94 (t, *J* = 7.3 Hz, 3H), 1.51 (tq, *J* = 7.3, 7.3 Hz, 2H), 2.23 (dt, *J* = 7.3, 7.3 Hz, 2H), 3.71 (s, 3H), 3.73 (s, 3H), 3.77 (s, 2H), 6.07 (s, 1H), 7.04 (ddd, *J* = 0.9, 6.9, 7.8 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 1H), 7.14 (ddd, *J* = 1.4, 7.3, 8.2 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 22.0, 24.4, 29.5, 30.9, 51.9, 99.2, 108.7, 119.2, 119.8, 120.6, 127.7, 128.4, 137.5, 138.2, 145.3, 167.9; IR (neat) ν: 1715, 1648, 1211, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}NO_2$ $[M+H]^+$ 272.1651, found 272.1649.

methyl (*E*)-4-methyl-2-((1-methyl-1*H*-indol-2-yl)methyl)pent-2-enoate (**191h**)

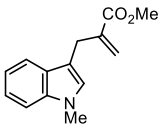


The reaction was carried out on a 2.1 mmol scale following the general procedure. After the reduction with $NaBH_4$, NaH (60 mg, 1.5 mmol, 60% dispersion) was added to the solution of the residue in THF (5 mL) at 0 °C and stirred for 0.5 h. isobutyraldehyde (137 μL, 1.5 mmol) was added to the mixture and stirred for 24 h at room temperature. The reaction was quenched with *sat*. NH_4Cl *aq*. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford (*E*)-**191h** as a pale brown liquid (50 mg, 9% yield in 3 steps) and (*Z*)-**191h** as a pale yellow solid (12 mg, 2% yield in 3 steps).

(*E*)-**191h**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.97 (d, *J* = 6.4 Hz, 6H), 3.20-3.29 (m, 1H), 3.62 (s, 3H), 3.71 (s, 2H), 3.73 (s, 3H), 5.58 (d, *J* = 11.0 Hz, 1H), 6.25 (s, 1H), 7.07 (ddd, *J* = 0.9, 6.9, 7.9 Hz, 1H), 1.17 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.6, 28.6, 29.6, 31.5, 51.6, 100.9, 109.0, 119.4, 120.1, 120.9, 126.4, 127.9, 137.7, 138.0, 150.8, 168.1; IR (neat) ν: 1719, 1646, 1215, 749 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{17}H_{22}NO_2$ $[M+H]^+$ 272.1649, found 272.1651.

(*Z*)-**191h**; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.05 (d, *J* = 6.9 Hz, 6H), 2.67 (sepd, *J* = 6.4, 10.5 Hz, 1H), 3.70 (s, 3H), 3.73 (s, 3H), 3.77 (s, 2H), 6.08 (s, 1H), 6.85 (d, *J* = 10.5 Hz, 1H), 7.04 (dd, *J* = 6.9, 6.9 Hz, 1H), 7.15 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.2, 24.4, 28.3, 29.5, 52.0, 99.1, 108.8, 119.2, 119.8, 120.6, 125.9, 127.7, 137.5, 138.5, 151.6, 168.2; IR (neat) ν: 1716, 1651, 748 cm^{-1}; HRMS (ESI)*m/z* calcd for $C_{17}H_{21}NNaO_2$ $[M+Na]^+$ 294.1471, found 294.1470.

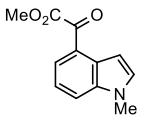
methyl 2-((1-methyl-1*H*-indol-3-yl)methyl)acrylate[44] (**232**)



The mixture of indole-3-carboxaldehyde (726 mg, 5 mmol), MeI (467 μL, 7.5 mmol) and K_2CO_3 (1 g, 7.5 mmol) in DMF (5 mL) was stirred at room temperature for overnight. The mixture was diluted with water and CH_2Cl_2. The layers were separated and water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was used for next step without further purification. The reaction was carried out following the general procedure. After Horner-Wadsworth-Emmons reaction, the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **232** as a pale red liquid (560 mg, 49% yield in 4 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.75 (s, 2H), 3.76 (s, 3H), 5.51 (dt, *J* = 1.4, 1.4 Hz, 1H), 6.18 (d, *J* = 1.4 Hz, 1H), 6.88 (s, 1H), 7.08 (ddd, *J* = 0.9, 6.9, 7.8 Hz, 1H), 7.21 (ddd, *J* = 0.9, 6.9, 8.2 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H).

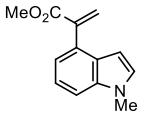
methyl 2-(1-methyl-1*H*-indol-4-yl)-2-oxoacetate (**S5**)



The solution of 4-bromo-1-methyl-1*H*-indole (670 mg, 3.2 mmol) in THF (13 mL) was added *n*BuLi (2.3 mL, 3.8 mmol, 1.55 M in hexane) at -78 °C and stirred for 0.5 h. The solution of dimethyl oxalate (449 mg, 3.8 mmol) in THF (3 mL) was added to the reaction mixture and stirred for another 0.5 h. The reaction was quenched with *sat*. NH_4Cl *aq.* The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **S5** as a yellow viscous liquid (269 mg, 39% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.88 (s, 3H), 4.00 (s, 3H), 7.28-7.32 (m, 3H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.0, 52.5, 102.3, 116.5, 120.4, 123.6, 126.1, 127.2, 132.8, 137.4, 165.2, 187.3; IR (neat) ν: 1739, 1666, 1231, 762 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{12}H_{11}NNaO_3$ $[M+Na]^+$ 240.0637, found 240.0631.

methyl 2-(1-methyl-1*H*-indol-4-yl)acrylate (**235**)

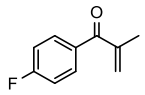


The suspension of methyltriphenylphosphonium bromide (643 mg, 1.8 mmol) in THF (4 mL) was added *t*BuOK (202 mg, 1.8 mmol) at 0 °C. The mixture was stirred for 0.5 h and added the solution of **S5** (269 mg, 1.2 mmol) in THF (2 mL). The reaction mixture was gradually warmed to room temperature and stirred for 4 h. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and water layer was extracted with AcOEt three times. Combined oreganic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **235** as a pale yellow liquid (148 mg, 56% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.78 (s, 6H), 5.97 (s, 1H), 6.37 (d, *J* = 3.2 Hz, 1H), 6.53 (s, 1H), 7.05 (d, *J* = 3.7 Hz, 1H), 7.07 (d, *J* = 7.3 Hz, 1H), 7.22 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 32.9, 52.1, 100.0, 109.3, 119.9, 121.3, 127.1, 127.7, 129.0, 129.5, 136.7, 140.6, 167.8; IR

(neat) ν: 1723, 1618, 1435, 1223, 753 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{13}H_{13}NNaO_2$ $[M+Na]^+$ 238.0844, found 238.0845.

1-(4-fluorophenyl)-2-methylprop-2-en-1-one[45] (**194b**)

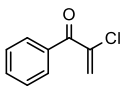


4-fluorobenzaldehyde (536 μL, 5 mmol) was added to the solution of isopropenylmagnesium bromide (12 mL, 6 mmol, 0.5 M in THF) in THF (12 mL) at 0 °C and stirred for 2 h at the same temperature. The reaction was quenched with *sat.* NH_4Cl *aq*. The layers were separated and water layer was extracted with Et_2O three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by short pad of silica-gel (AcOEt/Hexane = 1/10) to afford corresponding alcohol as a colorless liquid.

The solution of synthesized alcohol in CH_2Cl_2 (20 mL) was added MnO_2 (2.2 g, 25 mmol). The suspension was stirred at room temperature to 40 °C for overnight. The reaction mixture was filtrated through Celite® and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **194b** as a colorless liquid (513 mg, 62% yield in 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (s, 3H), 5.58 (s, 1H), 5.90 (s, 1H), 7.12 (dd, *J* = 8.2, 8.2 Hz, 2H), 7.79 (dd, *J* = 5.5, 8.2 Hz, 2H).

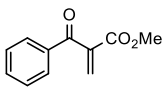
2-chloro-1-phenylprop-2-en-1-one[46] (**194c**)



The mixture of 2-chlroacetophenone (773 mg, 5 mmol), paraformaldehyde (300 mg, 10 mmol), *i*Pr_2NH· TFA (776 mg, 5 mmol) and TFA (40 mL, 0.5 mmol) in THF (15 mL) was stirred at refluxing temperature for 2 h. Additional paraformaldehyde (300 mg, 10 mmol) was added to the mixture and stirred for overnight at the same temperature. The mixture was filtrated through short pad of silica-gel and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **x** as a brown liquid (305 mg, 37% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.10 (d, *J* = 2.3 Hz, 1H), 6.29 (d, *J* = 2.3 Hz, 1H), 7.48 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.60 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.08 (d, *J* = 8.2 Hz, 2H).

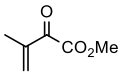
methyl 2-benzoylacrylate[47] (**194d**)



The mixture of methyl 3-oxo-3-phenylpropanoate (891 mg, 5 mmol), paraformaldehyde (300 mg, 10 mmol), *i*Pr_2NH· TFA (776 mg, 5 mmol) and TFA (40 mL, 0.5 mmol) in THF (15 mL) was stirred at refluxing temperature for 2 h. Additional paraformaldehyde (300 mg, 10 mmol) was added to the mixture and stirred for overnight at the same temperature. The mixture was filtrated through short pad of silica-gel and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **x** as a pale yellow liquid (554 mg, 58% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.77 (s, 3H), 6.06 (s, 1H), 6.73 (s 1H), 7.48 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 2H).

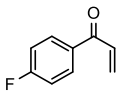
methyl 3-methyl-2-oxobut-3-enoate[48] (**194e**)



The solution of dimethyl oxalate (354 mg, 3 mmol) in THF (15 mL) was added isopropyl magnesium bromide (7.2 mL, 3.6 mmol, 0.5 M in THF) at -78 °C. The mixture was stirred for 2 h at the same temperature and quenched with *sat.* NH_4Cl *aq*. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by Kugelrohr distillation (10 mmHg, 70 °C) and flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **194e** as a pale yellow liquid (34 mg, 9% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.95 (s, 3H), 3.90 (s, 3H), 6.12 (dq, *J* = 0.9, 0.9 Hz, 1H), 6.19 (dq, *J* = 1.4, 1.4 Hz, 1H).

1-(4-fluorophenyl)prop-2-en-1-one[45] (**194f**)

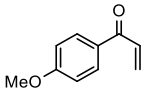


The solution of 4-fluorobenzaldehyde (621 mg, 5 mmol) in THF (20 mL) was added vinyl magnesium bromide (6 mL, 6 mmol) at 0 °C and stirred for 1 h. The reaction was quenched with *sat*. NH_4Cl *aq*. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by short pad of silica-gel.

The product was dissolved in CH_2Cl_2 and MnO_2 (1.9 g, 21 mmol) was added. The suspension was stirred at room temperature for overnight and filtrated through Celite®. The filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **194f** as a pale yellow liquid (146 mg, 19% in 2 steps.)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.95 (dd, *J* = 1.4, 11.0 Hz, 1H), 6.45 (dd, *J* = 1.8, 16.9 Hz, 1H), 7.14 (dd, *J* = 10.5, 17.4 Hz, 1H), 7.16 (dd, *J* = 8.7, 8.7 Hz, 2H), 7.99 (dd, *J* = 5.5, 8.7 Hz, 2H).

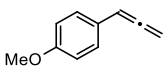
1-(4-methoxyphenyl)prop-2-en-1-one[49] (**194g**)



The mixture of 2-bromo-4'-methoxyacetophenone (2.3 g, 10 mmol) and PPh_3 (2.6 g, 10 mmol) in toluene (10 mL) was stirred at refluxing temperature for 6 h. Resulting suspension was filtrated and precipitate was washed with Et_2O. This precipitate was dissolved in CH_2Cl_2/H_2O (2/3, 25 mL) and added NaOH (480 mg, 12 mmol). The mixture was stirred at room temperature for 4 h. The layers were separated and water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL) and added paraformaldehyde (900 mg, 30 mmol). The mixture was stirred at refluxing temperature for 4 h and filtrated through Celite®. The filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to addord **194g** as a colorless liquid (994 mg, 61% in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.89 (s, 3H), 5.88 (dd, *J* = 1.4, 10.5 Hz, 1H), 6.43 (dd, *J* = 1.8, 17.4 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 7.18 (dd, *J* = 10.5, 16.9 Hz, 1H), 7.97 (d, *J* = 8.7 Hz, 2H).

1-methoxy-4-(propa-1,2-dien-1-yl)benzene[50] (**225**)

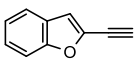


The mixture of 4-vinylanisole (1 g, 7.45 mmol), $HCBr_3$ (1.3 mL, 14.9 mmol), NaOH (1.2 g, 29.8 mmol) and *n*Bu_4NBr (23 mg, 0.07 mmol) in H_2O (3 mL) was stirred at room temperature to 60 °C for 17 h. The mixture was diluted with H_2O and CH_2Cl_2. The layers were separated and water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by short pad of silica-gel (Hexana).

The solution of prepared dibromocyclopropane in THF (20 mL) was added EtMgBr (3 mL, 8.9 mmol, 3 M in Et_2O) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 0.5 h. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and water layer was extracted with Et_2O three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/40) to afford **225** as a pale yellow liquid (921 mg, 80% yield in 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.80 (s, 3H), 5.12 (d, *J* =6.4 Hz, 2H), 6.12 (dd, *J* = 6.9, 6.9 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 2H).

2-ethynylbenzofuran[51] (**227j**)



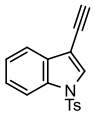
The solution of 2,3-benzofuran (591 mg, 5 mmol) in THF (25 mL) was added *n*BuLi (3.9 mL, 6 mmol, 1.55 M in hexane) at -78 °C. Resulting solution was stirred for 1 h and DMF (580 μL, 7.5 mmol) was added. The reaction mixture was stirred for another 1.5 h and quenched with *sat.* NH_4Cl *aq*. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford 2-benzofurancarboxaldehyde.

The mixture of PPh_3 (2.9 g, 11 mmol) and CBr_4 (1.8 g, 5.5 mmol) in CH_2Cl_2 (20 mL) was stirred at 0 °C for 0.5 h. The solution of synthesized aldehyde in CH_2Cl_2 (5 mL) was added to the mixture. The reaction mixture was gradually warmed to room temperature and stirred for overnight. Then concentrated under reduced pressure. The residue was filtrated through short pad of silica-gel and dissolved in THF (20 mL). *n*BuLi (5.9 mL, 9.1 mmol, 1.55 M in hexane) was added to the solution at -78 °C and stirred for 1.5 h. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **227j** as a pale yellow liquid (264 mg, 41% yield in 3 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.50 (s, 1H), 7.01 (s, 1H), 7.25 (ddd, *J* = 0.9, 7.8, 7.8 Hz, 1H), 7.35 (ddd, *J* = 1.4, 8.2, 8.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H).

3-ethynyl-1-tosyl-1*H*-indole[52] (**227k**)

The mixture of indole-3-carboxaldehyde (726 mg, 5 mmol), TsCl (1049 mg, 5.5 mmol) and NEt_3 (1.4 mL, 10 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 2 h. The reaction was quenched with *sat.*



NH_4Cl *aq.* The layers were separated and water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was used without further purification.

The mixture of PPh_3 (2.9 g, 11 mmol) and CBr_4 (1.8 g, 5.5 mmol) in CH_2Cl_2 (20 mL) was stirred at 0 °C for 0.5 h. The solution of the residue in CH_2Cl_2 (5 mL) was added to the mixture. The reaction mixture was gradually warmed to room temperature and stirred for overnight. Then concentrated under reduced pressure. The residue was filtrated through short pad of silica-gel and dissolved in THF (9 mL). *n*BuLi (2.2 mL, 3.5 mmol, 1.55 M in hexane) was added to the solution at -78 °C and stirred for 18 h at -78 °C to room temperature. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **227k** as a pale purple solid (281 mg, 19% yield in 3 steps).

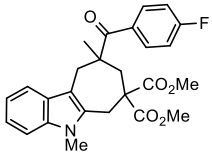
^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.35 (s, 3H), 3.26 (s, 1H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.29 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.37 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J*= 8.7 Hz, 2H), 7.79 (s, 1H), 7.97 (d, *J* = 8.2 Hz, 1H).

7-Membered Ring Construction Using Enone

General Procedure

The mixture of **191** (0.1 mmol), $Co(NTf_2)_3$ (6.2 mg, 0.01 mmol) and activated MS 4 Å (50 mg) in 1,2- DCE (1 mL) was added enone (0.12 mmol). The reaction mixture was stirred for appropriate time. Water was added to the mixture. The mixture was filtrated through Celite® and layers were separate. The water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography.

dimethyl 9-(4-fluorobenzoyl)-5,9-dimethyl-6,8,9,10-tetrahydrocyclohepta[*b*]indole-7,7(5*H*)-dicarboxylate (**200**)

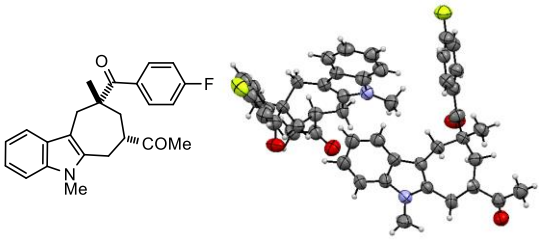


The reaction was carried out following the general procedure and stirred at 80 °C for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **198b** (24 mg, 51% yield, dr = 2.5/1).

The solution of **198b** (24 mg, 0.061 mmol) in THF (0.6 mL) was added LHMDS (92 μL, 0.092 mmol, 1.0 M in THF) at -78 °C and stirred for 1 h at the same temperature. Methyl chloroformate (14 μL, 0.18 mmol) was added to the mixture. The reaction mixture was gradually warmed to room temperature and stirred for overnight. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified

by preparative TLC (SiO_2, AcOEt/Hexane = 1/5) to afford **200** as a yellow viscous liquid (10 mg, 35% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.38 (s, 3H), 2.75 (d, *J* = 14.4 Hz, 1H), 3.05 (d, *J* = 15.0 Hz, 1H), 3.18 (d, *J* = 15.6 Hz, 1H), 3.31 (d, *J* = 16.2 Hz, 1H), 3.35 (d, *J* = 15.6Hz, 1H), 3.50 (d, *J* = 16.8 Hz, 1H), 3.59 (s, 3H), 3.69 (s, 3H), 3.78 (s, 3H), 6.86 (dd, *J* = 8.4, 8.4 Hz, 2H), 6.97 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.11 (dd, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.47 (dd, *J* = 4.8, 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 26.6, 29.4, 29.7, 31.9, 41.6, 51.4, 52.9, 53.1, 55.9, 108.7, 109.2, 114.9 (d, *J* = 21.5 Hz), 117.4, 118.8, 121.0, 127.5, 129.8 (d, *J* = 8.6 Hz), 133.2, 134.7 (d, *J* = 4.4 Hz), 136.4, 163.8 (d, *J* = 249.9 Hz), 171.7, 206.8 (two carbonyl carbon of esters were overlapped); IR (neat) ν: 1737, 1674, 1232, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{26}FNNaO_5$ $[M+Na]^+$ 474.1693, found 474.1695.

1-(9-(4-fluorobenzoyl)-5,9-dimethyl-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indol-7-yl)ethan-1-one (**203a**)



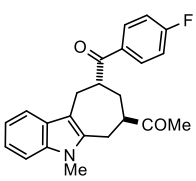
The reaction was carried out following the general procedure and stirred at room temperature for 24 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford *cis*-**203a** as a colorless solid (5 mg, 13% yield) and *trans*-**203a** as pale yellow oil (4 mg, 11% yield). Crystals of *cis*-**203a** suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the Et_2O solution of product.

cis-**203a**; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.47 (s, 3H), 2.13 (d, *J* = 13.8 Hz, 1H), 2.31 (s, 3H), 2.53 (dd, *J* = 11.0, 14.5 Hz, 1H), 2.95 (dd, *J* = 12.4, 15.8 Hz, 1H), 3.09-3.11 (m, 2H), 3.16 (d, *J* = 15.8 Hz, 1H), 3.37 (d, *J* = 15.1 Hz, 1H), 3.63 (s, 3H), 6.92 (dd, *J* = 8.3, 8.3 Hz, 2H), 6.98 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.10 (dd, *J* = 8.3, 8.3 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 7.53 (dd, *J* = 5.5, 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.0, 27.2, 27.9, 29.4, 31.8, 40.1, 46.8, 51.3, 108.4, 108.6, 115.0 (d, *J* = 21.7 Hz), 117.3, 118.9, 120.8, 127.6, 129.9 (d, *J* = 8.7 Hz), 134.6, 135.0, 136.2 164.0 (d, *J* = 250.0 Hz), 206.5, 209.9; IR (neat) ν: 1711, 1672, 1599, 1472, 1233, 846, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{24}FNNaO_2$ $[M+Na]^+$ 400.1689, found 400.1691.

trans-**203a**; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.56 (s, 3H), 2.33 (s, 3H), 2.81 (d, *J* = 13.1 Hz, 1H), 2.92 (d, *J* = 15.1 Hz, 1H), 2.93 (dd, *J* = 12.4, 16.5 Hz, 1H), 3.07-3.10 (m, 2H), 3.54 (d, *J* = 15.1 Hz, 1H), 3.63 (s, 3H), 6.91 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.97 (dd, *J* = 8.3, 8.3 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 1H), 7.07 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 7.56 (dd, *J* = 5.5, 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 27.3, 28.4, 29.5, 33.1, 42.7, 46.7, 50.9, 107.7, 108.6, 115.2 (d, *J* = 21.6 Hz), 117.0, 118.9, 120.6, 127.7, 130.0 (d, *J* = 8.6 Hz), 135.2, 136.0, 136.2, 164.2 (d, *J* = 251.3), 207.0, 211.1; IR (neat) ν: 1710, 1671, 1599, 1472, 1232, 847, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}FNO_2$ $[M+H]^+$ 378.1869, found 378.1866.

1-(9-(4-fluorobenzoyl)-5-methyl-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indol-7-yl)ethan-1-one (**203e**)

The reaction was carried out following the general procedure and stirred at room temperature for 3 h. The

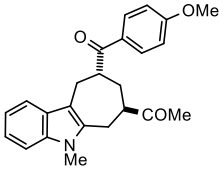


residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford *trans*-**203e** as a yellow oil (12 mg, 32% yield) and *cis*-**203e** as a yellow oil (3 mg, 10% yield).

trans-**203e**; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.20 (ddd, *J* = 5.5, 9.6, 14.4 Hz, 1H), 2.26 (s, 3H), 2.46 (ddd, *J* = 4.1, 9.6, 13.7 Hz, 1H), 3.00 (dd, *J* = 11.0, 15.8 Hz, 1H), 3.16-3.23 (m, 3H), 3.31-3.35 (m, 1H), 3.73 (s 3H), 3.84-3.87 (m, 1H), 7.06 (dd, *J* = 8.3, 8.3 Hz, 1H), 7.13 (dd, *J* = 8.3, 8.3 Hz, 2H), 7.17 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 8.01 (dd, *J* = 5.5, 8.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.8, 26.4, 28.4, 29.5, 33.2, 44.0, 47.7, 108.9, 110.2, 115.9 (d, *J* = 23.0 Hz), 117.3, 119.1, 121.0, 127.2, 131.2 (d, *J* = 8.6 Hz), 132.1 (d, *J* = 3.0 Hz), 135.5, 136.2, 165.8 (d, *J* = 255.6 Hz), 201.0, 209.8; IR (neat) ν: 1709, 1681, 1597, 1472, 1228, 848, 742 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{23}FNO_2$ $[M+H]^+$ 364.1713, found 364.1712.

cis-**203e**; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.09 (ddd, *J* = 11.0, 11.0, 14.4 Hz, 1H), 2.26 (s, 3H), 2.51 (d, *J* = 15.8 Hz, 1H), 2.69 (dd, *J* = 11.0, 11.0 Hz, 1H), 2.84 (dd, *J* = 11.0, 15.1 Hz, 1H), 3.00 (dd, *J* = 11.7, 15.8 Hz, 1H), 3.25 (d, *J* = 15.8 Hz, 1H), 3.36 (d, *J* = 15.1 Hz, 1H), 3.48 (dd, *J* = 11.0, 11.0 Hz, 1H), 3.73 (s, 3H), 7.10 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.16 (dd, *J* = 8.3, 8.3 Hz, 2H), 7.20 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 8.01 (dd, *J* = 5.0, 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 27.2, 27.8, 28.0, 29.6, 35.9, 45.7, 50.8, 109.2, 110.9, 116.0 (d, *J* = 21.6 Hz), 117.3, 119.4, 121.1, 127.1, 131.0 (d, *J* = 8.6 Hz), 131.9, 136.0, 136.3, 165.8 (d, *J* = 254.3 Hz), 200.7, 209.9; IR (neat) ν: 1710, 1682, 1597, 1471, 1227, 847, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}FNNaO_2$ $[M+Na]^+$ 386.1532, found 386.15332.

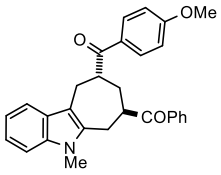
1-(9-(4-methoxybenzoyl)-5-methyl-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indol-7-yl)ethan-1-one (**203f**)



The reaction was carried out following the general procedure and stirred at room temperature for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **203f** as a yellow viscous liquid (18 mg, 49% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.16 (ddd, *J* = 5.6, 9.6, 14.8 Hz, 1H), 2.26 (s, 3H), 2.48 (ddd, *J* = 4.0, 9.6, 13.6 Hz, 1H), 3.00 (dd, *J* = 10.8, 15.6 Hz, 1H), 3.10-3.23 (m, 3H), 3.34 (dddd, *J* = 3.6, 3.6, 9.2, 9.2 Hz, 1H), 3.73 (s, 3H), 3.85-3.89 (m, 1H), 3.87 (s, 3H), 6.93 (d, *J* = 8.8 Hz, 2H), 7.06 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.17 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 7.6 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.7, 26.3, 28.4, 29.5, 33.2, 43.7, 47.7, 55.5, 108.8, 110.3, 113.9, 117.3, 119.0, 120.8, 127.2, 128.5, 130.8, 135.5, 136.1, 163.6, 201.2, 210.1; IR (neat) ν: 1708, 1671, 1601, 1261, 1173, 843, 742 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1734.

(7-benzoyl-5-methyl-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indol-9-yl)(4-methoxyphenyl)methanone (**203g**)

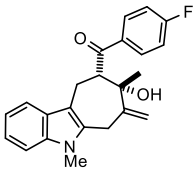
The reaction was carried out following the general procedure and stirred at room temperature for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **203g** as a



yellow viscous liquid (13 mg, 29% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.26 (ddd, *J* = 5.5, 10.3, 15.1 Hz, 1H), 2.47 (ddd, *J* = 4.1, 9.6, 14.4 Hz, 1H), 3.18-3.26 (m, 3H), 3.31 (dd, *J* = 10.3, 15.8 Hz, 1H), 3.59 (s, 3H), 3.85 (s, 3H), 4.00-4.04 (m, 1H), 4.29-4.32 (m, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 7.05 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.16 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.48 (dd, *J* = 8.3, 8.3 Hz, 2H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 8.9 Hz, 2H), 7.99 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.6, 27.3, 29.3, 34.7, 42.2, 43.7, 55.4, 108.8, 110.4, 113.8, 117.4, 119.0, 120.8, 127.3, 128.5, 128.7, 128.8, 130.7, 133.2, 135.6, 135.7, 136.1, 163.4, 201.3, 202.8; IR (neat) ν: 1676, 1600, 1172, 843, 741, 703 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{28}NO_3$ $[M+H]^+$ 438.2069, found 438.2068.

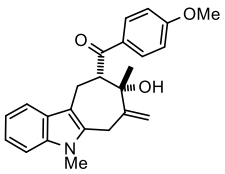
(4-fluorophenyl)(8-hydroxy-5,8-dimethyl-7-methylene-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indol-9-yl)methanone (**206a**)



The reaction was carried out following the general procedure and stirred at room temperature for 3 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **2066a** as a yellow viscous liquid (9 mg, 24% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.51 (s, 3H), 2.90 (d, *J* = 15.6 Hz, 1H), 3.28 (dd, *J* = 10.2, 16.2 Hz, 1H), 3.54 (d, *J* = 15.6 Hz, 1H), 3.75 (s, 3H), 3.84 (d, *J* = 9.0 Hz, 1H), 3.88 (d, *J* = 15.0 Hz, 1H), 5.07 (s, 1H), 5.09 (s, 1H), 5.47 (s, 1H), 7.04 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.09 (dd, *J* = 8.4, 8.4 Hz, 2H), 7.16 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 7.94 (dd, *J* = 5.4, 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 23.3, 28.7, 29.6, 30.7, 53.4, 76.1, 108.9, 110.3, 113.8, 116.0 (d, *J* = 21.6 Hz), 117.2, 119.2, 120.8, 127.1, 131.3 (d, *J* = 8.6 Hz), 132.6 (d, *J* = 2.9 Hz), 136.0, 136.4, 149.5, 166.2 (d, *J* = 255.6 Hz), 203.5; IR (neat) ν: 3452, 1663, 1595, 1227, 855, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}FNNaO_2$ $[M+Na]^+$ 386.1532, found 386.1535.

(8-hydroxy-5,8-dimethyl-7-methylene-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indol-9-yl)(4-methoxyphenyl)methanone (**206b**)

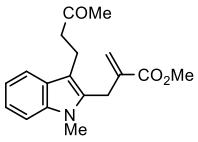


The reaction was carried out following the general procedure and stirred at room temperature for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **206b** as a yellow viscous liquid (6 mg, 15% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.50 (s, 3H), 2.89 (d, *J* = 16.4 Hz, 1H), 3.28 (dd, *J* = 10.0, 16.0 Hz, 1H), 3.54 (d, *J* = 15.6 Hz, 1H), 3.75 (s, 3H), 3.83-3.90 (m, 2H), 3.85 (s, 3H), 5.05 (s, 1H), 5.38 (s, 1H), 5.46 (d, *J* = 0.8 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.03 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.16 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 23.5, 28.8, 20.6, 30.7, 76.1, 108.8, 110.6, 113.6, 114.0, 117.3, 119.0, 120.7, 127.2, 129.1, 131.0, 136.0, 136.5, 149.8, 164.2, 203.8; IR (neat) ν: 3433, 1651, 1600, 1171, 835, 740 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1732.

methyl 2-((1-methyl-3-(3-oxobutyl)-1*H*-indol-2-yl)methyl)acrylate (**197a**)

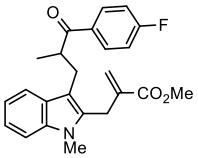
The mixture of **191a** (22.9 mg, 0.1 mmol), MVK (12 μL, 0.15 mmol) and $Ni(NTf_2)_2$ (6.2 mg, 0.01 mmol) in



CH_2Cl_2 (1 mL) was stirred at room temperature for 1 h. The reaction was quenched with water. The layers were separated and water layer was extracted with CH_2Cl_2 three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **197a** as a pale yellow viscous liquid (31 mg, 99% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.10 (s, 3H), 2.72 (t, *J* = 8.0 Hz, 2H), 2.96 (t, *J* = 8.0 Hz,2H), 3.56 (s, 3H), 3.80 (dd, *J* = 2.0, 2.0 Hz, 2H), 3.83 (s, 3H), 5.08 (d, *J* = 0.8 Hz, 1H), 6.22 (d, *J* = 1.6 Hz, 1H), 7.10 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.20 (ddd, *J* = 0.8, 8.0, 8.0 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.4, 26.4, 29.5, 30.1, 44.7, 52.1, 108.9, 111.9, 118.2, 118.9, 121.2, 126.0, 127.1, 132.5, 136.9, 137.9, 167.0, 208.5; IR (neat) ν: 1718, 1632, 1140, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{18}H_{21}NNaO_3$[M+Na]$^+$ 322.1419, found 322.1420.

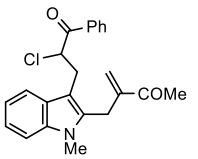
methyl 2-((3-(3-(4-fluorophenyl)-2-methyl-3-oxopropyl)-1-methyl-1*H*-indol-2-yl)methyl)acrylate (197b)



The reaction was carried out following the general procedure and stirred at 80 °C for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **197b** as a yellow viscous liquid (10 mg, 27% yield, Table 18, entry 6).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.20 (d, *J* = 7.6 Hz, 3H), 2.83 (dd, *J* = 8.0, 14.8 Hz, 1H), 3.17 (dd, *J* = 6.4, 14.4 Hz, 1H), 3.52 (s, 3H), 3.70-3.84 (m, 3H), 3.84 (s, 3H), 4.99 (s, 1H), 6.18 (s, 1H), 7.04 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.13 (ddd, *J* = 1.2, 8.0, 8.0 Hz, 1H), 7.20 (ddd, *J* = 0.8, 8.4, 8.4 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz ,1H), 7.86 (dd, *J* = 5.6, 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 17.8, 26.4, 28.3, 29.5, 41.6, 52.0, 108.8, 110.9, 115.4 (d, *J* = 21.0 Hz), 118.3, 119.0, 121.1, 126.0, 127.6, 130.7 (d, *J* = 9.5 Hz), 132.9 (d, *J* = 2.8 Hz), 133.2, 136.9, 137.7, 165.4 (d, *J* = 252.6 Hz), 166.9, 202.8; IR (neat) ν: 1720, 1683, 1231, 1139, 848, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{24}FNNaO_3$ [M+Na]$^+$ 416.1638, found 416.1636.

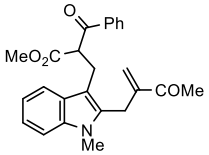
3-((3-(2-chloro-3-oxo-3-phenylpropyl)-1-methyl-1*H*-indol-2-yl)methyl)but-3-en-2-one (204b)



The reaction was carried out following the general procedure and stirred at room temperature for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **204b** as a brown viscous foam (12 mg, 37% yield).

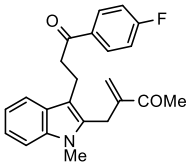
^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 3H), 3.57 (dd, *J* = 6.8, 14.8 Hz, 1H), 3.49 (s, 3H), 3.66 (dd, *J* = 7.2, 15.2 Hz, 1H), 3.82 (dd, *J* = 1.6, 1.6 Hz, 2H), 5.23 (s, 1H), 5.38 (dd, *J* = 6.8, 6.8 Hz, 1H), 6.03 (s, 1H), 7.14 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.21 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.41 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.54 (t, *J* = 6.8 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.1, 25.9, 29.1, 29.6, 55.9, 107.9, 109.1, 118.0, 119.4, 121.3, 126.5, 127.3, 128.7, 128.8, 133.7, 134.6, 135.2, 137.0, 146.0, 193.6, 198.9; IR (neat) ν: 1676, 743, 716, 690 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}ClNNaO_2$ [M+Na]$^+$ 402.1237, found 402.1235.

methyl 2-((1-methyl-2-(2-methylene-3-oxobutyl)-1*H*-indol-3-yl)methyl)-3-oxo-3-phenylpropanoate (204c)



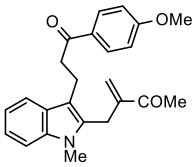
The reaction was carried out following the general procedure and stirred at room temperature for 1 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **204c** as a pale yellow viscous liquid (17 mg, 41% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.41 (s, 3H), 3.42-3.46 (m, 2H), 3.46 (s, 3H), 3.61 (s, 3H), 3.76 (s, 2H), 4.74 (dd, *J* = 7.2, 7.2 Hz, 1H), 5.19 (s, 1H), 6.01 (s, 1H), 7.12 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.18 (dd, *J* = 6.8, 6.8 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.38 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.2, 24.9, 25.9, 29.5, 52.5, 54.7, 108.9, 109.3, 118.1, 119.2, 121.2, 126.4, 127.3, 128.6, 133.4, 134.4, 136.2, 137.0, 146.1, 170.0, 194.9, 198.9; IR (neat) ν: 1739, 1678, 757, 742, 692 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{25}NNaO_4$ $[M+Na]^+$ 426.1681, found 426.1681.

3-((3-(3-(4-fluorophenyl)-3-oxopropyl)-1-methyl-1*H*-indol-2-yl)methyl)but-3-en-2-one (204e)



The reaction was carried out following the general procedure and stirred at room temperature for 3 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **204e** as a pale yellow viscous liquid (2 mg, 4% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 3H), 3.12 (dd, *J* = 5.6, 8.4 Hz, 2H), 3.24 (dd, *J* = 5.2, 7.6 Hz, 2H), 3.53 (s, 3H), 3.77 (s, 2H), 5.32 (t, *J* = 1.6 Hz, 1H), 6.08 (s, 1H), 7.09 (dd, *J* = 8.8, 8.8 Hz, 2H), 7.12 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.21 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.93 (dd, *J* = 4.8, 8.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 18.9, 25.0, 25.9, 29.5, 39.8, 109.0, 112.0, 115.6 (d, *J* = 21.6 Hz), 118.1, 119.0, 121.2, 126.5, 127.2, 130.6 (d, *J* = 10.1 Hz), 133.3 (d, *J* = 3.0 Hz), 137.0, 142.2, 146.2, 165.6 (d, *J* = 252.8 Hz), 198.2, 199.0; IR (neat) ν: 1682, 1597, 1232, 1203, 1156, 840, 742 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}FNNaO_2$ $[M+Na]^+$ 386.1532, found 386.1531.

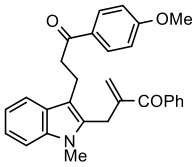
3-((3-(3-(4-methoxyphenyl)-3-oxopropyl)-1-methyl-1*H*-indol-2-yl)methyl)but-3-en-2-one (204f)



The reaction was carried out following the general procedure and stirred at room temperature for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **204f** as a yellow solid (2.5 mg, 7% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.42 (s, 3H), 3.10 (t, *J* = 8.0 Hz, 2H), 3.23 (t, *J* = 7.6 Hz, 2H), 3.53 (s, 3H), 3.77 (s, 2H), 3.86 (s, 3H), 5.32 (s, 1H), 6.08 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 2H), 7.12 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.23 (dd, *J* = 6.8, 6.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 19.2, 25.0, 25.9, 29.5, 39.6, 55.4, 109.0, 112.4, 113.7, 118.2, 119.0, 121.2, 126.5, 127.3, 130.0, 130.3, 133.3, 137.0, 146.3, 163.4, 198.4, 199.0; IR (neat) ν: 1676, 1600, 1260, 835, 743 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1732.

2-((3-(3-(4-methoxyphenyl)-3-oxopropyl)-1-methyl-1*H*-indol-2-yl)methyl)-1-phenylprop-2-en-1-one (204g)

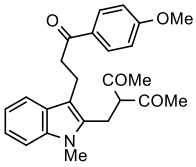
The reaction was carried out following the general procedure and stirred at room temperature for 2 h. The



residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **204g** as a pale yellow viscous liquid (6 mg, 13% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.20 (t, *J* = 7.6 Hz, 2H), 3.27 (t, *J* = 7.6 Hz, 2H), 3.65 (s, 3H), 3.86 (s, 3H), 4.00 (s, 2H), 5.44 (s, 1H), 5.71 (s, 1H), 6.90 (d, *J* = 8.9. Hz, 2H), 7.13 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.22 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.44 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 19.2, 26.6, 29.6, 39.6, 55.4, 109.0, 112.5, 113.6, 118.3, 118.9, 121.2, 127.3, 127.5, 128.3, 129.5, 130.0, 130.3, 132.4, 132.9, 137.0, 137.3, 145.2, 163.3, 197.3, 198.4; IR (neat) ν: 1674, 1654, 1601, 1171, 836, 742, 709 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{27}NNaO_3$ $[M+Na]^+$ 460.1889, found 460.1890.

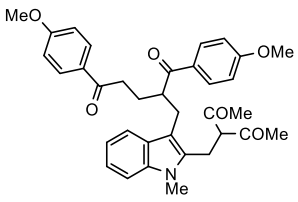
3-((3-(3-(4-methoxyphenyl)-3-oxopropyl)-1-methyl-1*H*-indol-2-yl)methyl)pentane-2,4-dione (**209**)



The reaction was carried out following the general procedure and stirred at room temperature for 1 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **209** as a yellow viscous liquid (28 mg, 70% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.11 (s, 6H), 3.15 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.6 Hz, 2H), 3.35 (d, *J* = 7.2 Hz, 2H), 3.63, (s, 3H), 3.84 (s, 3H), 4.09 (t, *J* = 7.2 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 2H), 7.10 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.19 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.26 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.1, 23.0, 29.8, 30.2, 39.0, 55.4, 67.3, 109.2, 111.8, 113.6, 118.3, 119.1, 121.4, 127.2, 130.0, 130.2, 132.7, 137.2, 163.3, 198.3, 203.1; IR (neat) ν: 1727, 1702, 1674, 1600, 1260, 835, 745 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{27}NNaO_4$ $[M+Na]^+$ 42.1838, found 428.1839.

2-((2-(2-acetyl-3-oxobutyl)-1-methyl-1*H*-indol-3-yl)methyl)-1,5-bis(4-methoxyphenyl)pentane-1,5-dione (**210**)

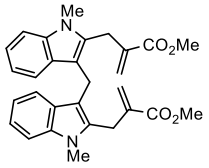


The reaction was carried out following the general procedure and stirred at room temperature for 1 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **210** as a yellow form (11 mg, 19% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.03-2.07 (m, 1H), 2.03 (s, 3H), 2.11 (s, 3H), 2.26 (dddd, *J* = 8.0, 10.8, 10.8, 10.8 Hz, 1H), 2.79 (ddd, *J* = 6.8, 8.0, 15.2 Hz, 1H), 2.94 (dd, *J* = 6.0, 14.4 Hz, 1H), 3.03 (ddd, *J* = 5.2, 8.0, 14.0 Hz, 1H), 3.15 (dd, *J* = 7.2, 15.2 Hz, 1H), 3.20 (dd, *J* = 8.4, 14.0 Hz, 1H), 3.31 (dd, *J* = 7.6, 15.2 Hz, 1H), 3.51 (s, 3H), 3.79 (s, 3H), 3.84 (s, 3H), 4.05 (dd, *J* = 7.2, 7.2 Hz, 1H), 4.02-4.15 (m, 1H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 7.10 (ddd, *J* = 1.2, 5.6, 8.4 Hz, 1H), 7.14-7.18 (m, 2H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.9, 27.6, 27.7, 29.7, 30.1, 30.3, 35.6, 45.4, 55.4, 67.2, 109.2, 110.2, 113.58, 113.63, 118.4, 119.3, 121.3, 127.5, 129.9, 130.3, 130.4, 133.5, 137.2, 163.36, 163.40, 198.3, 202.9, 203.2, 203.5; IR (neat) ν: 1727, 1702, 1671, 1602, 1260, 1173, 843, 743 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{35}H_{37}NNaO_6$

[M+Na]$^+$ 590.2519, found 590.2520.

dimethyl 2,2'-((methylenebis(1-methyl-1*H*-indole-3,2-diyl))bis(methylene))diacrylate (**201**)



The reaction was carried out following the general procedure and stirred at 80 °C for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/2) to afford **201** as a brown viscous liquid (2 mg, 10% yield, Table 17, entry 1).

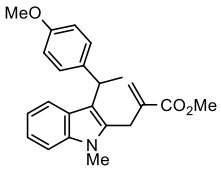
^{1}H NMR (600 MHz, $CDCl_3$) δ: 3.54 (s, 6H), 3.69 (s, 4H), 3.77 (s, 6H), 4.12 (s, 2H), 4.97 (s, 2H), 6.06 (s, 2H), 6.98 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.14 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 19.5, 26.6, 29.4, 52.0, 108.7, 112.0, 118.78, 118.82, 120.9, 125.9, 127.9, 132.6, 136.8, 137.2, 167.0; IR (neat) ν: 1721, 1632, 1140, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{30}N_2NaO_4$ [M+Na]$^+$ 493.2103, found 493.2102.

7-Membered Ring Construction Using Alkyne

Ring Construction Experiments Using Alkene, Alkyne and Allene

The mixture of **191a** (23 mg, 0.1 mmol), $InBr_3$ (3.5 mg, 0.01 mmol) and alkene, alkyne or allene (0.2 mmol) in toluene was stirred at 80 °C for 6 h. The reaction mixture was directly purified by flash column chromatography.

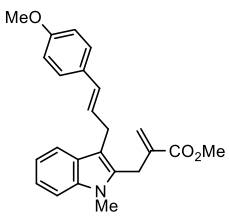
methyl 2-((3-(1-(4-methoxyphenyl)ethyl)-1-methyl-1*H*-indol-2-yl)methyl)acrylate (**224**)



The product was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **224** as a pale yellow viscous liquid (13 mg, 37% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72 (d, *J* = 7.3 Hz, 3H), 3.56 (s, 3H), 3.75 (s, 3H), 3.79 (s, 2H), 3.81 (s, 3H), 4.32 (q, *J* = 7.3 Hz, 1H), 5.09 (s, 1H), 6.20 (s, 1H), 6.77 (d, *J* = 8.7 Hz, 2H), 6.98 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.15 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.2, 26.6, 29.5, 34.8, 52.1, 55.2, 108.9, 113.4, 117.8, 118.7, 120.0, 120.9, 126.3, 126.4, 128.3, 132.0, 137.2, 137.7, 137.9, 157.5, 167.1; IR (neat) ν: 1721, 1511, 1248, 1178, 832, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{25}NNaO_3$ [M+Na]$^+$ 386.1732, found 386.1734.

methyl (*E*)-2-((3-(3-(4-methoxyphenyl)allyl)-1-methyl-1*H*-indol-2-yl)methyl)acrylate (**226**)



Product was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **226** as a yellow viscous liquid (21 mg, 55% yield).

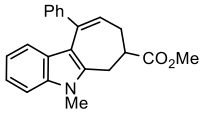
^{1}H NMR (400 MHz, $CDCl_3$) δ:3.59 (s, 3H), 3.59 (d, *J* = 6.4 Hz, 2H), 3.77 (s, 3H), 3.80 (s, 3H), 3.81 (s, 2H), 5.16 (s, 1H), 6.16 (td, *J* = 6.4, 16.0 Hz, 1H), 6.23 (s, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 2H), 7.09 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.19 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.21 (d, *J* = 8.7 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.5, 28.0, 29.6, 52.1, 55.2, 108.8, 111.1, 113.8, 118.7, 118.9, 121.1, 126.3, 127.1, 127.4, 129.1, 130.5, 132.8, 136.9, 137.7, 158.6, 167.2; IR (neat) ν: 1720, 1607, 1511, 1437, 1252,

1197, 836, 741 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_3$ $[M+Na]^+$ 398.1732, found 398.1735.

General Procedure

The mixture of **191** (0.2 mmol), alkyne (0.8 mmol) and InI_3 (9.9 mg, 0.02 mmol) in toluene (2 mL) was stirred at 80 °C for appropriate time. Then, the reaction mixture was directly purified by flash column chromatography.

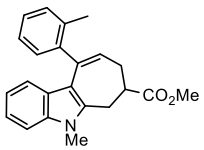
methyl 5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228a**)



The reaction was carried out following the general procedure and stirred for 5 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **228a** as a pale yellow solid (61 mg, 92% yield).

^1H NMR (600 MHz, $CDCl_3$) δ: 2.31 (ddd, *J* = 6.6, 10.2, 12.6 Hz, 1H), 2.50 (ddd, *J* = 5.4, 7.2, 12.6 Hz, 1H), 3.00 (dd, *J* = 7.8, 15.6 Hz, 1H), 3.28 (dd, *J* = 4.8, 15.6 Hz, 1H), 3.43 (dddd, *J* = 5.4, 5.4, 5.4, 7.8 Hz, 1H), 3.70 (s, 3H), 3.86 (s, 3H), 6.29 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.75 (d, *J* = 7.2 Hz, 1H), 6.88 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.14 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.29-7.30 (m, 3H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.37-7.39 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.4, 29.7, 29.8, 51.7, 52.6, 109.1, 111.6, 119.1, 120.2, 120.7, 123.5, 125.9, 127.2, 127.6, 128.0, 136.9, 140.0, 140.6, 140.8, 175.1; IR (neat) ν: 1733, 1610, 1469, 1202, 759, 746, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1651, found 332.1653.

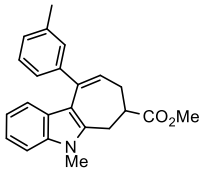
methyl 5-methyl-10-(*o*-tolyl)-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228b**)



The reaction was carried out following the general procedure and stirred at 80 to 100 °C for 19 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228b** as a yellow viscous liquid (59 mg, 86% yield).

^1H NMR (400 MHz, $CDCl_3$) δ: 1.98 (s, 3H), 2.50 (ddd, *J* = 6.4, 9.6, 14.2 Hz, 1H), 2.61 (ddd, *J* = 4.1, 7.8, 14.2 Hz, 1H), 3.11-3.18 (m, 1H), 3.31-3.40 (m, 2H), 3.72 (s, 3H), 3.78 (s, 3H), 5.84 (dd, *J* = 6.0, 7.3 Hz, 1H), 6.34 (d, *J* = 8.2 Hz, 1H), 6.75 (ddd, *J* = 0.9, 6.9, 7.8 Hz, 1H), 7.07 (ddd, *J* = 1.4, 7.3, 8.2 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.19-7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.0, 27.9, 29.7, 30.3, 48.3, 51.9, 108.7, 112.4, 119.3, 119.6, 120.9, 124.2, 125.6, 126.2, 127.1, 129.7, 129.9, 136.4, 136.7, 137.8, 139.8, 142.6, 175.3; IR (neat) ν: 1734, 1610, 1469, 1200, 765, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1807, found 346.1809.

methyl 5-methyl-10-(*m*-tolyl)-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228c**)

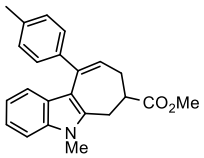


The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228c** as a yellow viscous liquid (66 mg, 96% yield).

^1H NMR (400 MHz, $CDCl_3$) δ: 2.30 (ddd, *J* = 6.9, 10.1, 13.3 Hz, 1H), 2.32 (s, 3H), 2.49 (ddd, *J* = 5.5, 7.3, 13.3 Hz, 1H), 3.00 (dd, *J* = 7.3, 15.1 Hz, 1H), 3.27 (dd, *J* = 5.0, 14.7 Hz, 1H), 3.43 (dddd, *J* = 5.5, 5.5, 7.3, 10.1 Hz, 1H), 3.70 (s, 3H), 3.86 (s, 3H), 6.28 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.88 (ddd, *J* = 0.9, 6.9, 8.2 Hz, 1H), 7.11-7.23 (m, 5H), 7.33 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ: 21.5, 25.5, 29.8, 29.9, 51.9, 52.8, 109.1, 111.8, 119.2, 120.4, 120.7, 123.5, 125.0, 126.0, 127.9, 128.0, 128.3, 137.0, 137.6, 140.1, 140.7, 140.8, 175.3; IR (neat) ν: 1733, 1603, 1469, 1202, 786, 746 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1807, found 346.1805.

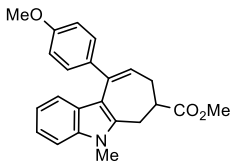
methyl 5-methyl-10-(*p*-tolyl)-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228d**)



The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228d** as a colorless solid (56 mg, 82% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (ddd, *J* = 6.9, 10.5, 13.3 Hz, 1H), 2.37 (s, 3H), 2.47 (ddd, *J* = 5.5, 7.3, 13.3 Hz, 1H), 2.98 (dd, *J* = 7.3, 15.1 Hz, 1H), 3.27 (dd, *J* = 5.0, 15.1 Hz, 1H), 3.42 (dddd, *J* = 5.0, 5.0, 7.3, 10.5 Hz, 1H), 3.70 (s, 3H), 3.86 (s, 3H), 6.27 (dd, *J* = 6.9, 6.9 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 2H), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.28 (d, *J* = 7.8, Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.2, 25.4, 29.8, 29.9, 51.9, 52.9, 109.1, 111.8, 119.2, 120.4, 120.7, 122.8, 126.0, 127.6, 128.8, 136.9, 137.0, 137.9, 140.1, 140.5, 175.3; IR (neat) ν;:1733, 1610, 1469, 1201, 809, 746 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1807, found 346.1806.

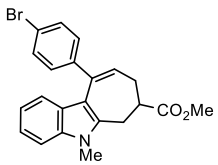
methyl 10-(4-methoxyphenyl)-5-methyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228e**)



The reaction was carried out following the general procedure and stirred for 10 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228e** as a yellow viscous liquid (47 mg, 51% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.28 (ddd, *J* = 6.9, 10.5, 13.3 Hz, 1H), 2.46 (ddd, *J* = 5.5, 7.3, 13.3 Hz, 1H), 2.98 (dd, *J* = 7.3, 15.1 Hz, 1H), 3.26 (dd, *J* = 5.0, 15.1 Hz, 1H), 3.43 (dddd, *J* = 5.0, 5.0, 7.3, 10.1 Hz, 1H), 3.0 (s, 3H), 3.82 (s, 3H), 3.86 (s, 3H), 6.22 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.89 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.14 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.4, 29.80, 29.84, 51.9, 53.1, 55.3, 109.1, 111.9, 113.4, 119.2, 120.4, 120.7, 122.0, 126.0, 128.8, 133.5, 137.0, 140.1, 140.2, 159.0, 175.3; IR (neat) ν: 1733, 1607, 1249, 1034, 809, 745 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_3$ $[M+H]^+$ 362.1756, found 362.1755.

methyl 10-(4-bromophenyl)-5-methyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228f**)

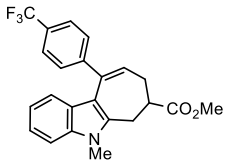


The reaction was carried out following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228f** as a pale yellow foam (78 mg, 95% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.30 (ddd, *J* = 6.9, 10.1, 13.3 Hz, 1H), 2.49 (ddd, *J* = 5.5, 7.3, 13.3 Hz, 1H), 2.98 (dd, *J* = 7.3, 15.1 Hz, 1H), 3.27 (dd, *J* = 5.0, 15.1 Hz, 1H), 3.43 (dddd, *J* = 5.5, 5.5, 7.3, 10.5 Hz, 1H), 3.70 (s, 3H), 3.86 (s, 3H), 6.28 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.15 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.5, 29.8, 29.9, 51.9, 52.6, 109.3, 111.1,

119.4, 120.1, 120.9, 121.2, 124.1, 125.7, 129.3, 131.2, 137.0, 139.65, 139.72, 140.3, 175.1; IR(neat) ν: 1732, 1610, 1470, 1201, 1009, 809, 746 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}BrNO_2$ $[M+H]^+$ 410.0756, found 410.0754.

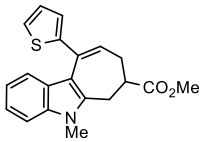
methyl 5-methyl-10-(4-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydrocyclohepta[b]indole-7-carboxylate (228g)



The reaction was carried out following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228g** as a pale yellow foam (71 mg, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.35 (ddd, *J* = 6.9, 10.1, 13.3 Hz, 1H), 2.53 (ddd, *J* = 5.5, 7.3, 13.3 Hz, 1H), 3.00 (dd, *J* = 7.3, 15.1 Hz, 1H), 3.29 (dd, *J* = 5.0, 15.1 Hz, 1H), 3.45 (dddd, *J* = 5.5, 5.5, 7.3, 10.1 Hz, 1H), 3.71 (s, 3H), 3.87 (s, 3H), 6.36 (dd, *J* = 6.9, 6.9 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.16 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.6, 29.8, 29.9, 51.9, 52.5, 109.3, 110.8, 119.5, 120.0, 121.0, 124.4 (q, *J* = 272.2 Hz), 125.0 (q, *J* = 2.9 Hz), 125.6, 127.9, 129.1 (q, *J* = 31.6 Hz), 137.0, 139.6, 140.3, 144.3, 175.1; IR (neat) ν: 1733, 1613, 1326, 1201, 831, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{21}F_3NO_2$ $[M+H]^+$ 400.1524, found 400.1526.

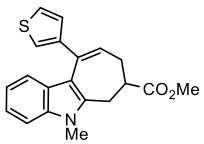
methyl 5-methyl-10-(thiophen-2-yl)-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (228h)



The reaction was carried out following the general procedure and stirred for 10 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228h** as a dark red viscous liquid (50 mg, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.25 (ddd, *J* = 6.9, 10.1, 12.8 Hz, 1H), 2.42 (ddd, *J* = 6.0, 7.3, 13.3 Hz, 1H), 2.96 (dd, *J* = 7.8, 15.1 Hz, 1H), 3.25 (dd, *J* = 4.6, 15.1 Hz, 1H), 3.39-3.46 (m, 1H), 3.69 (s, 3H), 3.86 (s, 3H), 6.41 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.96-6.99 (m, 3H), 7.13-7.20 (m, 3H), 7.34 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.9, 29.5, 29.8, 51.9, 53.4, 109.3, 111.3, 119.4, 120.4, 120.9, 122.8, 124.0, 125.4, 125.7, 127.2, 134.4, 137.0, 140.1, 144.5, 175.1; IR (neat) ν; 1732, 1609, 1469, 1200, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{20}H_{20}NO_2S$ $[M+H]^+$ 338.1215, found 338.1217.

methyl 5-methyl-10-(thiophen-3-yl)-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (228i)

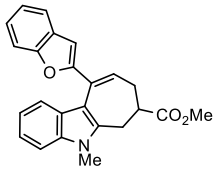


The reaction was carried out following the general procedure and stirred for 10 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228i** as a yellow foam (49 mg, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.27 (ddd, *J* = 6.9, 10.1, 13.3 Hz, 1H), 2.44 (ddd, *J* = 6.0, 7.3, 13.3 Hz, 1H), 2.96 (dd, *J* = 7.3, 14.6 Hz, 1H), 3.24 (dd, *J* = 5.0, 14.6 Hz, 1H), 3.36-3.43 (m, 1H), 3.69 (s, 3H), 3.84 (s, 3H), 6.35 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.95 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.01 (d, *J* = 7.8 Hz, 1H), 7.13-7.17 (m, 3H), 7.25 (dd, *J* = 3.2, 4.6 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.2, 29.5, 29.8, 51.8, 52.8, 109.2, 111.8, 119.3, 120.3, 120.8, 122.0, 122.4, 124.9, 125.9, 127.1, 135.3, 137.0, 139.8, 142.4, 175.2; IR (neat) ν: 1732, 1610, 1469, 1202, 739 cm^{-1}; HRMS (ESI) *m/z* calcd for

$C_{20}H_{20}NO_2S$ $[M+H]^+$ 338.1215, found 338.1215.

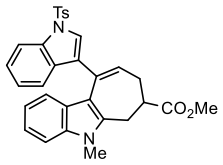
methyl 10-(benzofuran-2-yl)-5-methyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228j**)



The reaction was carried out following the general procedure and stirred for 4 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228j** as a brown solid (49 mg, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32 (ddd, *J* = 7.3, 10.5, 13.3 Hz, 1H), 2.53 (ddd, *J* = 6.0, 7.3, 13.3 Hz, 1H), 2.96 (dd, *J* = 7.8, 15.1 Hz, 1H), 3.27 (dd, *J* = 4.6, 15.1 Hz, 1H), 3.43-3.50 (m, 1H), 3.71 (s, 3H), 3.88 (s, 3H), 6.63 (s, 1H), 6.90 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.05 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.19 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.22 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.28 (dd, *J* = 1.4, 7.3 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.7, 29.2, 29.9, 51.9, 53.2, 104.6, 109.2, 109.5, 110.9, 119.6, 120.3, 120.9, 121.0, 122.6, 124.2, 124.5, 125.6, 129.1, 130.3, 137.0, 140.2, 154.6, 155.4, 175.1; IR (neat) ν: 1732, 1611, 1452, 1200, 750 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{22}NO_3$ $[M+H]^+$ 372.1600, found 372.1597.

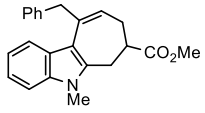
methyl 5-methyl-10-(1-tosyl-1*H*-indol-3-yl)-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228k**)



The reaction was carried out following the general procedure and stirred for 5 h using 0.4 mmol of alkyne. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/4) to afford **228k** as a pale brown foam (76 mg, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.34-2.41 (m, 1H), 2.37 (s, 3H), 2.53 (ddd, *J* = 5.6, 8.0, 13.6 Hz, 1H), 3.04 (dd, *J* = 7.2, 14.8 Hz, 1H), 3.30 (dd, *J* = 5.6, 15.2 Hz, 1H), 3.42 (dddd, *J* = 5.2, .5.2, 7.2, 10.0 Hz, 1H), 3.69 (s, 3H), 3.86 (s, 3H), 6.41 (dd, *J* = 7.2, 7.2 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.68 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.10 (ddd, *J* = 1.2, 8.4, 8.4 Hz, 1H), 7.11 (ddd, *J* = 0.8, 8.0, 8.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.44 (s, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.8 Hz, 2H), 8.04 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.6, 25.7, 29.7, 29.8, 51.9, 52.4, 109.2, 111.4, 113.7, 119.2, 119.9, 120.8, 121.1, 123.3, 123.8, 124.3, 124.56, 124.63, 125.7, 126.9, 129.8, 129.9, 131.7, 135.1, 135.5, 137.0, 139.7, 144.8, 175.1; IR (neat) ν: 1732, 1597, 1469, 1371, 1175, 813, 747 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{31}H_{29}N_2O_4S$ $[M+H]^+$ 525.1848, found 525.1848.

methyl 10-benzyl-5-methyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228la**)

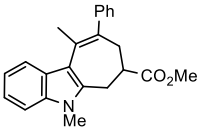


The reaction was carried out following the general procedure and stirred at 80 to 100 °C for 24 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **228la** as a yellow viscous liquid (4 mg, 6% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.15 (ddd, *J* = 6.9, 11.0, 13.8 Hz, 1H), 2.33 (ddd, *J* = 6.9, 6.9, 13.8 Hz, 1H), 2.75 (dd, *J* = 6.9, 14.4 Hz, 1H), 3.12 (dd, *J* = 4.1, 14.4 Hz, 1H), 3.31-3.35 (m, 1H), 3.67 (s, 3H), 3.77 (s, 3H), 3.94 (d, *J* = 15.1 Hz, 1H), 4.03 (d, *J* = 15.1 Hz, 1H), 5.81 (dd, *J* = 6.9, 6.9 Hz, 1H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.11-7.13 (m, 1H), 7.17 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.19-7.20 (m, 4H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.69 (d,

J = 8.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.2, 29.2, 29.7, 42.1, 51.8, 52.8, 109.4, 113.0, 119.4, 119.7, 120.7, 123.3, 125.6, 125.7, 128.1, 128.8, 136.9, 139.1, 140.3, 140.6, 175.4; IR (neat) ν: 1733, 1201, 764, 744, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1807, found 346.1807.

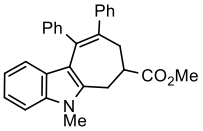
methyl 5,10-dimethyl-9-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228lb**)

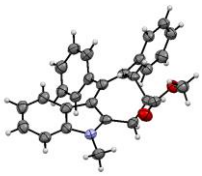


The reaction was carried out following the general procedure and stirred at 80 to 100 °C for 24 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **228lb** as a yellow viscous liquid (25 mg, 38% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.21 (s, 3H), 2.56 (dd, *J* = 12.8, 11.5 Hz, 1H), 2.64 (dd, *J* = 5.5, 12.8 Hz, 1H), 2.92 (dd, *J* = 7.8, 14.7 Hz, 1H), 3.31 (dd, *J* = 3.2, 14.7 Hz, 1H), 3.48 (dddd, *J* = 3.2, 5.5, 7.8, 11.0 Hz, 1H), 3.60 (s, 3H), 3.84 (s, 3H), 7.11 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.20 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.23-7.27 (m, 1H), 7.31-7.39 (m, 5H), 7.69 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.3, 24.6, 29.7, 37.4, 51.7, 53.1, 109.5, 115.4, 119.4, 119.9, 120.7, 125.8, 126.1, 128.1, 128.9, 131.6, 134.3, 137.0, 138.2, 143.8, 175.4; IR (neat) ν: 1732, 1608, 1469, 1203, 763, 745, 703 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1807, found 346.1805.

methyl 5-methyl-9,10-diphenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228p**)

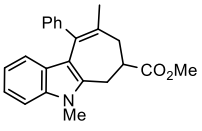




The reaction was carried out following the general procedure and stirred at 80 to 100 °C for 72 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **228p** as a yellow solid (6 mg, 7% yield). Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the CH_2Cl_2 solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.75 (dd, *J* = 11.9, 11.9 Hz, 1H), 2.96 (dd, *J* = 5.5, 12.4 Hz, 1H), 3.07 (dd, *J* = 7.8, 14.7 Hz, 1H), 3.41 (dd, *J* = 3.2, 14.7 Hz, 1H), 3.53 (dddd, *J* = 3.7, 5.0, 8.2, 11.0 Hz, 1H), 3.59 (s, 3H), 3.89 (s, 3H), 6.46 (d, *J* = 7.8 Hz, 1H), 6.80 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.03-7.21 (m, 11H), 7.32 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.7, 29.8, 38.4, 51.8, 53.6, 109.2, 114.8, 120.2, 120.7, 125.9, 126.2, 126.3, 127.5, 127.8, 129.9, 131.0, 135.3, 137.00, 137.02, 140.3, 140.5, 143.1, 175.2; IR (neat) ν: 1732, 1598, 1469, 1202, 765, 740, 702 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{26}NO_2$ $[M+H]^+$ 408.1964, found 408.1962.

methyl 5,9-dimethyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[b]indole-7-carboxylate (**228q**)

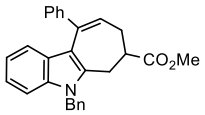


The reaction was carried out following the general procedure and stirred at 80 to 100 °C for 72 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **228q** as a yellow viscous liquid (20 mg, 29% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.04 (s, 3H), 2.44 (d, *J* = 7.8 Hz, 2H), 2.99 (dd, *J* = 7.8, 15.1 Hz, 1H), 3.29 (dd, *J* = 4.6, 14.7 Hz, 1H), 3.49 (ddt, *J* = 5.0, 7.8, 7.8 Hz, 1H), 3.71 (s, 3H), 3.83 (s, 3H), 6.48 (d, *J* = 7.8 Hz, 1H), 6.77 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.06 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.21-7.30 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3, 25.1, 29.7, 37.0, 51.9, 52.0, 108.9, 114.6, 119.1, 119.9, 120.5, 126.2, 126.4, 127.8, 130.1,

131.0, 134.2, 136.8, 138.9, 141.0, 175.5; IR (neat) ν: 1733, 1469, 1202, 772, 744, 704 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}NO_2$ $[M+H]^+$ 346.1807, found 346.1808.

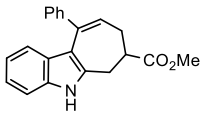
methyl 5-benzyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228r**)



The reaction was carried out following the general procedure and stirred for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228r** as a colorless solid (73 mg, 89% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33-2.48 (m, 2H), 2.96 (dd, *J* = 6.9, 14.6 Hz, 1H), 3.16-3.27 (m, 2H), 3.62 (s, 3H), 5.50 (d, *J* = 16.9 Hz, 1H), 5.60 (d, *J* = 16.9 Hz, 1H), 6.32 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.30 (d, *J* = 6.9 Hz, 2H), 7.08 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.22-7.43 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.7, 29.9, 46.5, 51.8, 52.7, 109.6, 112.5, 119.5, 120.5, 121.2, 124.1, 125.9, 126.2, 127.30, 127.32, 128.1, 128.8, 136.9, 137.9, 140.1, 140.5, 140.8, 175.1; IR (neat) ν: 1732, 1604, 1463, 1200, 762, 736, 700 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{26}NO_2$ $[M+H]^+$ 408.1964, found 408.1965.

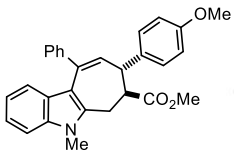
methyl 10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228s**)

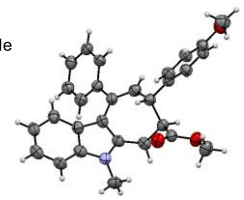


The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **228s** as a yellow viscous liquid (51 mg, 80% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.39 (ddd, *J* = 6.9, 9.6, 13.7 Hz, 1H), 2.53 (ddd, *J* = 5.5, 7.3, 13.3 Hz, 1H), 3.05 (dd, *J* = 7.8, 15.1 Hz, 1H), 3.23 (dd, *J* = 6.0, 15.1 Hz, 1H), 3.38 (dddd, *J* = 6.0, 6.0, 7.8, 9.6 Hz, 1H), 3.70 (s, 3H), 6.25 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 6.86 (ddd, *J* = 0.9, 6.9, 8.2 Hz, 1H), 7.08 (ddd, *J* = 0.9, 7.3, 8.2 Hz, 1H), 7.29-7.30 (m, 4H), 7.37-7.39 (m, 2H), 8.38 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.0, 30.2, 51.3, 52.0, 110.6, 111.9, 119.5, 120.4, 121.2, 123.9, 127.1, 127.3, 127.7, 128.1, 135.5, 138.7, 140.2, 140.9, 175.4; IR (neat) ν: 3377, 1732, 1617, 1205, 738, 702 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$ 318.1494, found 318.1496.

methyl 8-(4-methoxyphenyl)-5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228u**)



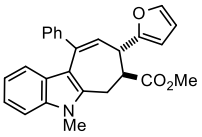


The reaction was carried out following the general procedure and stirred for 22 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **228u** as a pale yellow solid (70 mg, 80% yield). Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the AcOEt solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.16 (dd, *J* = 2.3, 14.7 Hz, 1H), 3.23 (dd, *J* = 7.3, 15.1 Hz, 1H), 3.47 (s, 3H), 3.61 (ddd, *J* = 2.3, 6.9, 12.4 Hz, 1H), 3.79 (s, 3H), 3.80 (s, 3H), 3.81-3.84 (m, 1H), 6.27 (d, *J* = 6.0 Hz, 1H), 6.82 (dd, *J* = 8.2, 8.2 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.92 (ddd, *J* = 0.9, 6.9, 9.2 Hz, 1H), 7.16-7.20 (m, 3H), 7.27-7.29 (m, 3H), 7.36-7.38 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.5, 29.9, 47.9,

51.6, 55.3, 61.8, 109.4, 111.8, 114.0, 119.5, 120.4, 121.0, 126.0, 127.5, 128.0, 128.2, 129.3, 129.6, 135.3, 137.3, 138.9, 140.62, 140.65, 158.3, 174.5; IR (neat) ν: 1733, 1610, 1513, 1469, 1251, 1034, 831, 766, 748, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{28}NO_3$ $[M+H]^+$ 438.2069, found 438.2068.

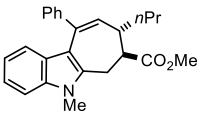
methyl 8-(furan-2-yl)-5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228v**)



The reaction was carried out following the general procedure and stirred for 24 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **228v** as a brown foam (44 mg, 56% yield, di = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.161 (d, *J* = 4.1 Hz, 1H), 3.163 (d, *J* = 5.5 Hz, 1H), 3.57 (s, 3H), 3.75 (ddd, *J* = 4.1, 5.5, 11.9 Hz, 1H), 3.79 (s, 3H), 3.98 (dd, *J* = 6.0, 11.5 Hz, 1H), 6.03 (d, *J* = 3.2 Hz, 1H), 6.27 (dd, *J* = 1.8, 2.8 Hz, 1H), 6.35 (d, *J* = 6.4 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.92 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.17 (ddd, *J* = 0.9, 6.9, 8.2 Hz, 1H), 7.29-7.36 (m, 5H), 7.396 (d, *J* = 7.8 Hz, 1H), 7.404 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.8, 29.7, 41.3, 51.7, 58.8, 105.9, 109.4, 110.1, 111.6, 119.5, 120.2, 121.0, 125.1, 125.7, 127.5, 127.8, 128.1, 137.2, 139.5, 140.0, 140.3, 141.7, 155.3, 174.2; IR (neat) ν: 1734, 1611, 1469, 1213, 1013, 767, 745, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{24}NO_3$ $[M+H]^+$ 398.1756, found 398.1756.

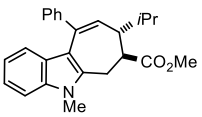
methyl 5-methyl-10-phenyl-8-propyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228w**)



The reaction was carried out following the general procedure and stirred for 72 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **228w** as a yellow solid (45 mg, 60% yield, dr = >20/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (dd, *J* = 7.3, 7.3 Hz, 3H), 1.26-1.53 (m, 4H), 2.56-2.63 (m, 1H), 3.05 (d, *J* = 5.0 Hz, 2H), 3.17 (ddd, *J* = 5.0, 5.0, 11.5 Hz, 1H), 3.70 (s, 3H), 3.75 (s, 3H), 6.04 (d, *J* = 6.0 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 6.89 (ddd, *J* = 0.9, 6.9, 6.9 Hz, 1H), 7.14 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 7.28-7.33 (m, 4H), 7.36-7.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2, 26.4, 29.7, 35.9, 40.5, 51.5, 59.2, 109.2, 112.2, 119.2, 120.3, 120.7, 125.8, 127.3, 127.7, 128.1, 130.0, 137.1, 139.3, 140.5, 140.8, 175.2; IR (neat) ν: 1733, 1611, 1469, 1208, 763, 744, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_2$ $[M+H]^+$ 374.2120, found 374.2120.

methyl 8-isopropyl-5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**228x**)

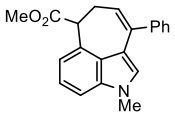


The mixture of **231x** (7.5 mg, 0.02 mmol) and InI_3 (1 mg, 0.002 mmol) in toluene (0.4 mL) was stirred at 80 °C for 2 days. The reaction mixture was purified by flash column chromatography (SiO_2 AcOEt/Hexane = 1/12) to afford **228x** as a pale yellow solid (4 mg, 49% yield, *E/Z* = >20/1) and **231x** (3 mg, 35%).

^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.97 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.73 (dqq, *J* = 41, 6.9, 6.9 Hz, 1H), 2.66 (ddd, *J* = 3.4, 6.2, 11.0 Hz, 1H), 3.01-3.07 (m, 2H), 3.37 (ddd, *J* = 2.8, 6.2, 11.0 Hz, 1H), 3.70 (s, 3H), 3.76 (s, 3H), 6.14 (d, *J* = 6.2 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.30-7.33 (m, 4H), 7.37-7.39 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 17.7, 22.0, 26.4, 29.0,

29.7, 46.2, 51.6, 56.9, 109.2, 112.4, 119.3, 120.3, 120.7, 125.81, 125.84, 127.3, 127.7, 128.1, 137.2, 140.0, 140.5, 141.2, 175.4; IR (neat) ν: 1732, 1611, 1469, 1214, 765, 745, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_2$ $[M+H]^+$ 374.2120, found 374.2119.

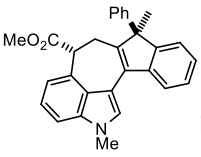
methyl 2-methyl-9-phenyl-6,7-dihydro-2*H*-cyclohepta[*cd*]indole-6-carboxylate (**236**)

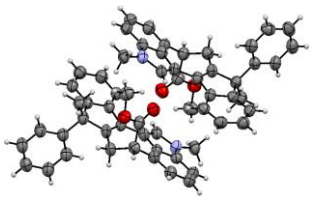


The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **236** as a colorless foam (55 mg, 84% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.76 (ddd, *J* = 1.4, 5.0, 14.7 Hz, 1H), 3.16 (ddd, *J* = 6.9, 7.8, 14.7 Hz, 1H), 3.62 (s, 3H), 3.73 (s, 3H), 4.28 (dd, *J* = 1.8, 6.4 Hz, 1H), 5.72 (dd, *J* = 5.0, 7.8 Hz, 1H), 6.77 (s, 1H), 6.93 (d, *J* = 6.9 Hz, 1H), 7.21-7.28 (m, 3H), 7.31-7.37 (m, 3H), 7.42-7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.4, 32.9, 50.3, 52.0, 108.5, 116.5, 120.0, 121.7, 121.9, 125.3, 127.0, 127.9, 128.9, 129.1, 133.5, 137.5, 139.2, 143.4, 173.6; IR (neat) ν: 1737, 1610, 1460, 1193, 750, 703 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$ 318.1494, found 318.1494.

methyl 6,12-dimethyl-6-phenyl-4,5,6,12-tetrahydrobenzo[2,3]azuleno[4,5,6-*cd*]indole-4-carboxylate (**237**)

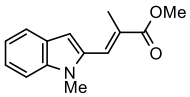




The reaction was carried out following the general procedure and stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **237** as a colorless solid (7 mg, 9% yield, dr = 6/1). Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the toluene solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.70 (s, 3H), 2.72 (dd, *J* = 2.3, 16.0 Hz, 1H), 3.02 (dd, *J* = 6.4, 16.0 Hz, 1H), 3.54 (s, 3H), 3.89 (s, 3H), 4.20 (dd, *J* = 2.3, 6.0 Hz, 1H), 6.86 (d, *J* = 7.3 Hz, 1H), 7.10-7.21 (m, 8H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.33 (ddd, *J* = 1.4, 7.3, 7.3 Hz, 1H), 7.78 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.7, 30.4, 33.1, 49.6, 51.8, 58.0, 108.6, 111.3, 120.2, 120.4, 122.0, 122.8, 125.1, 125.7, 125.9, 126.3, 126.4, 128.3, 131.6, 132.8, 137.1, 142.5, 142.7, 146.6, 154.8, 173.4; IR (neat) ν: 1749, 1618, 1458, 1164, 750, 700 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{26}NO_2$ $[M+H]^+$ 420.1964, found 420.1963.

methyl (*E*)-2-methyl-3-(1-methyl-1*H*-indol-2-yl)acrylate (**229**)

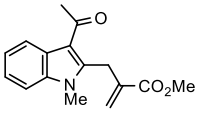


The reaction was carried out following the general procedure and stirred at 80 to 100 °C for 72 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **229** as a pale yellow solid (28 mg, 61% yield, Table 23, entry 16).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.27 (s, 3H), 3.80 (s, 3H), 3.85 (s, 3H), 6.81 (s, 1H), 7.12 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.27 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.8, 29.9, 52.2, 106.0, 109.4, 120.1, 121.2, 123.2, 126.7, 127.7, 128.3, 134.7, 137.8, 168.9; IR (neat) ν: 1709, 1626, 1261, 753 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{14}H_{16}NO_2$ $[M+H]^+$

230.1181, found 230.1182.

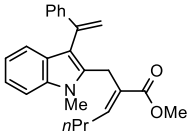
methyl 2-((3-acetyl-1-methyl-1*H*-indol-2-yl)methyl)acrylate (**230**)



The reaction was carried out following the general procedure and stirred at room temperature for 24 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford **230** as a yellow liquid (10 mg, 18% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.68 (s, 3H), 3.67 (s, 3H), 3.83 (s, 3H), 4.30 (dd, *J* = 1.8, 1.8 Hz, 2H), 5.13 (t, *J* = 1.8 Hz, 1H), 6.23 (t, *J* = 1.8 Hz, 1H), 7.29-7.33 (m, 2H), 7.38 (dd, *J* = 3.7, 6.9 Hz, 1H), 8.02 (dd, *J* = 3.2, 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.9, 29.5, 31.5, 52.2, 109.8, 115.1, 120.3, 121.0, 122.1, 122.4, 126.0, 126.1, 136.2, 136.8, 144.2, 166.9, 194.1; IR (neat) ν: 1721, 1644, 1515, 1472, 1214, 743 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{17}NNaO_3$ $[M+Na]^+$ 294.1106, found 294.1106.

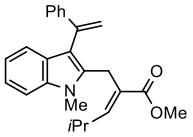
methyl (*E*)-2-((1-methyl-3-(1-phenylvinyl)-1*H*-indol-2-yl)methyl)hex-2-enoate (**231w**)



The reaction was carried out following the general procedure and stirred for 72 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **231w** as a pale yellow viscous liquid (8 mg, 11% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.83 (t, *J* = 7.3 Hz, 3H), 1.31 (tq, *J* = 7.3, 7.3 Hz, 2H), 2.37 (dt, *J* = 7.3, 7.3 Hz, 2H), 3.65 (s, 3H), 3.75 (s, 3H), 3.76 (d, *J* = 1.8 Hz, 2H), 5.25 (d, *J* = 1.8 Hz, 1H), 5.51 (dt, *J* = 1.8, 7.3 Hz, 1H), 5.66 (d, *J* = 1.8 Hz, 1H), 6.97 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.25-7.27 (m, 3H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.35-7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 22.4, 28.6, 29.8, 31.5, 51.5, 108.8, 114.6, 115.7, 119.3, 120.2, 121.3, 127.3, 127.4, 127.5, 128.1, 128.9, 134.9, 136.9, 141.7, 142.5, 143.5, 167.9; IR (neat) ν: 1720, 1645, 1470, 1216, 743 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_2$ $[M+H]^+$ 374.2120, found 374.2119.

methyl (*E*)-4-methyl-2-((1-methyl-3-(1-phenylvinyl)-1*H*-indol-2-yl)methyl)pent-2-enoate (**231x**)

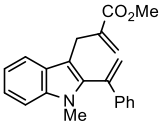


The reaction was carried out on a 0.1 mmol scale following the general procedure and stirred for 2 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **231x** as a pale red solid (34 mg, 90% yield) and **228x** (1 mg, 3% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (d, *J* = 6.4 Hz, 6H), 3.16-3.25 (m, 1H), 3.65 (s, 3H), 3.74 (s, 3H), 3.75 (s, 2H), 5.24 (d, *J* = 1.8 Hz, 1H), 5.28 (d, *J* = 10.1 Hz, 1H), 5.67 (d, *J* = 1.8 Hz, 1H), 6.98 (ddd, *J* = 0.9, 6.9, 7.8 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.19 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 7.24-7.27 (m, 3H), 7.30 (d, *J* = 8.2 Hz, 1H), 7.36-7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.5, 28.5, 29.0, 29.9, 51.6, 108.9, 114.7, 115.9, 119.4, 120.3, 121.4, 126.7, 127.4, 127.5, 127.6, 128.2, 134.9, 137.0, 141.7, 142.6, 149.8, 168.1; IR (neat) ν: 1719, 1469, 1221, 768, 743, 699 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_2$ $[M+H]^+$ 374.2116, found 374.2120.

methyl 2-((1-methyl-2-(1-phenylvinyl)-1*H*-indol-3-yl)methyl)acrylate (**234**)

The reaction was carried out following the general procedure and stirred for 22 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **234** as a brown viscous liquid (9



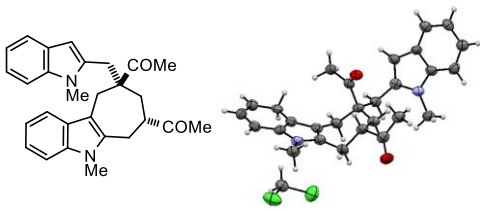
mg, 14% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.38 (s, 3H), 3.75 (s, 3H), 3.77 (s, 2H), 5.33 (s, 1H), 5.38 (s, 1H), 6.00 (s, 1H), 6.18 (s, 1H), 7.11 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.22-7.30 (m, 7H), 7.51 (d, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.9, 30.7, 51.8, 109.2, 110.2, 119.1, 119.2, 119.6, 121.8, 125.5, 126.4, 127.6, 128.1, 128.6, 137.1, 138.5, 139.3, 139.7, 167.9; IR (neat) ν: 1718, 1628, 1613, 1470, 1267, 781, 738, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1651, found 332.1653.

InI_3 Catalyzed Dimerization (Scheme 32)

The mixture of **202a** (42.7 mg, 0.2 mmol) and InI_3 (9.9 mg, 0.02 mmol) in toluene (2 mL) was stirred at 80 °C for 1 h. The reaction mixture was purified by flash column chromatography to afford *trans*-**205** as a colorless solid (27 mg, 64% yield), *cis*-**205** as a colorless solid (9 mg, 21% yield) and trace amount of **202a**.

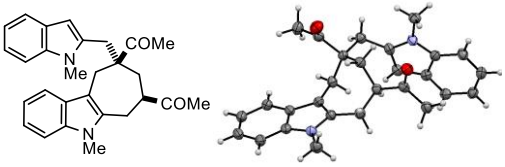
1,1'-(5-methyl-9-((1-methyl-1*H*-indol-2-yl)methyl)-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indole-7,9-diyl)bis(ethan-1-one) (*trans*-**205**)



Colorless solid. Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the CH_2Cl_2 solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.52 (dd, *J* = 10.0, 13.6 Hz, 1H), 1.92 (s, 3H), 2.33 (s, 3H), 2.78-3.13 (m, 7H), 3.60 (s, 3H), 3.65 (s, 3H), 3.65-3.69 (m, 1H), 6.39 (s, 1H), 7.08 (ddd, *J* = 1.2, 6.8, 8.0 Hz, 1H), 7.12 (ddd, *J* = 0.8, 7.2, 8.0 Hz, 1H), 7.16 (ddd, *J* = 0.8, 7.2, 7.2 Hz, 1H), 7.21 (ddd, *J* = 1.2, 8.0, 8.0 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.1, 27.5, 28.4, 29.5, 29.9, 30.8, 37.9, 40.1, 46.6, 54.3, 102.3, 107.3, 109.1, 109.3, 117.1, 119.4, 119.7, 120.2, 120.9, 121.3, 127.62, 127.64, 134.9, 136.2, 136.8, 137.3, 211.0, 212.9; IR (neat) ν: 1705, 1470, 740 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{30}N_2NaO_2$ $[M+Na]^+$ 449.2205, found 449.2205.

1,1'-(5-methyl-9-((1-methyl-1*H*-indol-2-yl)methyl)-5,6,7,8,9,10-hexahydrocyclohepta[*b*]indole-7,9-diyl)bis(ethan-1-one) (*cis*-**205**)

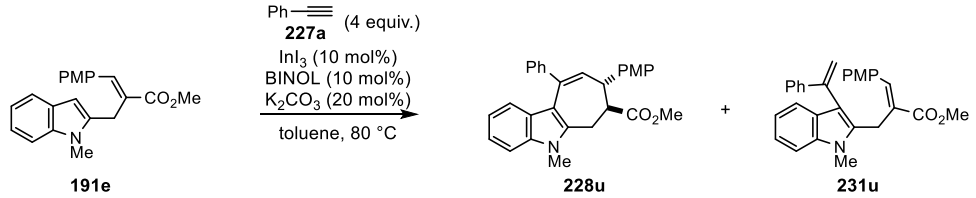


Colorless solid. Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the CH_2Cl_2 solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.93 (s, 3H), 2.13 (s, 3H), 2.26 (dd, *J* = 2.0, 14.4 Hz, 1H), 2.47 (dd, *J* = 11.6, 14.0 Hz, 1H), 2.86 (dd, *J* = 11.6, 16.0 Hz, 1H), 2.99 (dd, *J* = 10.8, 10.8 Hz, 1H), 2.06-3.10 (m, 3H), 3.27 (d, *J* = 15.6 Hz, 1H), 3.35 (d, *J* = 15.2 Hz, 1H), 3.52 (s, 3H), 3.63 (s, 3H), 6.32 (s, 1H), 7.06 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.09 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.11-7.20 (m, 2H), 7.22-7.24 (m, 2H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 25.9, 27.6, 27.8, 29.5, 29.7, 29.9, 34.6, 35.7, 47.0, 55.1, 101.7, 107.5, 108.8, 109.2, 117.3, 119.3, 119.7, 120.1, 121.1, 121.3, 127.70, 127.72, 135.0, 135.3, 136.5, 137.2, 209.7, 211.7; IR (neat) ν: 1699, 1465, 756 cm^{-1};

HRMS (ESI) *m/z* calcd for $C_{28}H_{31}N_2O_2$ $[M+H]^+$ 427.2386, found 427.2387.

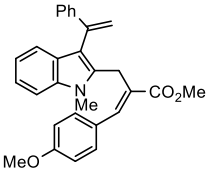
Examination of Asymmetric Reaction (Table 25)



entry	BINOL	time	**228u** (%)	% ee	**231u** (%)	recov. (%)
1	**238a**	2 h	51	0	23	4
2	**238b**	1 h	13	0	63	23

The mixture of InI_3 (9.9 mg, 0.02 mmol), K_2CO_3 (5.5 mg, 0.04 mmol) and BINOL (0.02 mmol) in toluene (1 mL) was stirred for 30 min at room temperature. Resultant mixture was added the solution of **191e** (67 mg, 0.2 mmol) and phenylacetylene (88 μL, 0.8 mmol) in toluene (1 mL) and stirred at 80 °C for appropriate time. Water was added to the mixture and layers were separated. The water layer was extracted with AcOEt three times. The combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography.

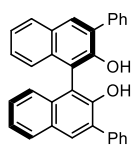
methyl (*E*)-3-(4-methoxyphenyl)-2-((1-methyl-3-(1-phenylvinyl)-1*H*-indol-2-yl)methyl)acrylate (**231u**)



The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **231u** as a pale red viscous liquid (20 mg, 23% yield in entry 2).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.55 (s, 3H), 3.63 (s, 3H), 3.79 (s, 3H), 4.05 (s, 2H), 5.19 (d, *J* = 1.8 Hz, 1H), 5.69 (d, *J* = 1.8 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.98 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.16-7.30 (m, 11H), 7.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.6, 30.1, 51.9, 55.2, 108.6, 113.8, 114.1, 114.4, 115.9, 119.2, 119.5, 121.0, 127.0, 127.2, 127.6, 127.9, 128.1, 131.1, 134.7, 136.6, 139.9, 141.5, 142.0, 159.8, 168.5; IR (neat) ν: 1707, 1604, 1509, 1254, 1175, 835, 779, 741, 698 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{29}H_{28}NO_3$ $[M+H]^+$ 438.2069, found 438.2068.

(*R*)-3,3'-diphenyl-[1,1'-binaphthalene]-2,2'-diol[53] (**238b**)



NaH (27 mg, 0.67 mmol) was added to the solution of (*R*)-3,3'-dibromo1,1'-bi-2-naphthol (133 mg, 0.3 mmol) in THF (1.2 mL) and DMF (0.6 mL) at 0 °C. The mixture was stirred for 30 min at the same temperature and MOMCl (72 μL, 0.95 mmol) was added. The mixture was warmed to room temperature and stirred for 24 h. H_2O was added at 0 °C and layers were separated. The water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford (*R*)-3,3'-dibromo-2,2'-bis(methoxymethoxy)-1,1'-binaphthalene[53] (**S6**) as a brown solid (146 mg, 92 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.57 (s, 6H), 4.81 (d, *J* = 5.2 Hz, 2H), 4.83 (d, *J* = 5.6 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.31 (dd, *J* = 8.4, 8.4 Hz, 2H), 7.44 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 8.27 (s,

2H).

$Pd(PPh_3)_4$ (18 mg, 0.016 mmol) was added to the solution of **S6** (146 mg, 0.28 mmol) in 1,2-DME (1.8 mL). The mixture was stirred for 10 min at room temperature and $PhB(OH)_2$ (110 mg, 0.9 mmol) and 2M Na_2CO_3 aq. (0.3 mL) was added. The mixture was stirred at reflux temperature for 19 h and cooled to room temperature. The reaction mixture was filtrated through short pad of silica gel and solvent was removed under reduced pressure. The residue was dissolved in THF (1.2 mL) and conc. HCl (36 μL) was added. The solution was stirred for 14 h at room temperature and diluted with H_2O. The layers were separated and water layer was extracted with AcOEt three times. Combined organic layer was dried over Na_2SO_4, filtrated through plug of cotton and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford **238b** as a colorless solid (120 mg, 91% yield).

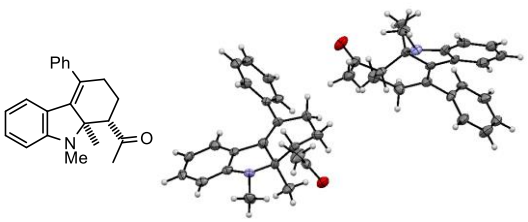
H NMR (400 MHz, $CDCl_3$) δ: 7.23 (d, *J* = 8.4 Hz, 2H), 7.32 (ddd, *J* = 1.2, 8.4, 8.4 Hz, 2H), 7.40 (dd, *J* = 8.4, 8.4 Hz, 2H), 7.42 (d, *J* =7.2 Hz, 2H), 7.50 (dd, *J* = 7.6, 7.6 Hz, 4H), 7.73 (d, *J* = 7.2 Hz, 4H), 7.93 (d, *J* = 8.0 Hz, 2H), 8.03 (s, 2H); HRMS (ESI) *m/z* calcd for $C_{32}H_{21}O_2$ $[M-H]^-$ 437.1542, found 437.1551; $[\alpha]_D^{20}$ +72.3 (*c* 0.70, $CHCl_3$).

Michael Addition of Vinylindole (Scheme 34)

The mixture of 1,2-dimethyl-3-(1-phenylvinyl)-1*H*-indole[a] (124 mg, 0.5 mmol), MVK (61 μL, 0.75 mmol) and InI_3 (25 mg, 0.05 mmol) in toluene (5 mL) was stirred at room temperature for 2 days. The reaction mixture was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford *cis*-**241** as a yellow solid (30 mg, 19% yield), *trans*-**241** as a yellow solid (28 mg, 17% yield) and **240** as a brown liquid (25 mg, 16% yield, *E/Z* = 2.5/1). **240** was obtained as inseparable *E/Z* mixture, so the structure was determined after reduction of olefin.

The solution of **240** (20 mg, 0.063 mmol) in MeOH (3.2 mL) was added 10% Pd/C (2 mg). The reaction mixture was stirred vigorously under H_2 balloon at room temperature for 3 h. The mixture was filtrated through Celite® and filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **S7** as a yellow liquid (18 mg, 87% yield).

1-(9,9a-dimethyl-4-phenyl-2,3,9,9a-tetrahydro-1*H*-carbazol-1-yl)ethan-1-one (*cis*-**241**)

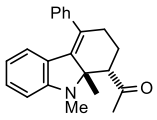


yellow solid. Crystals suitable for X-ray crystallographic analysis were grown by slow diffusion of hexane into the Et_2O solution of product.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.36 (s, 3H), 1.86 (dddd, *J* = 1.4, 4.1, 8.7, 12.8 Hz, 1H), 2.04 (dddd, *J* = 9.2, 9.2, 13.7, 13.7 Hz 1H), 2.38 (s, 3H), 2.40-2.51 (m, 1H), 2.60-2.66 (m, 1H), 2.67 (s, 3H), 3.13 (dd, *J* = 3.7, 13.3 Hz, 1H), 6.28 (d, *J* = 7.3 Hz, 1H), 6.36 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.46 (d, *J* = 7.8 Hz, 1H), 7.01 (ddd, *J* = 1.4, 7.8, 7.8 Hz, 1H), 7.22 (s, 2H), 7.32 (tt, *J* = 1.4, 7.3 Hz, 1H), 7.39 (dd, *J* = 7.8, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 15.9, 22.5, 31.1, 31.6, 33.1, 51.5, 70.3, 107.8, 117.6, 123.3, 125.4, 127.1, 128.1, 128.3, 128.7,

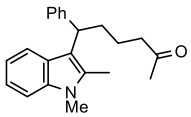
139.1, 142.0, 153.2, 213.4; IR (neat) ν: 1708, 1601, 1473, 766, 749, 702 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}NO$ $[M+H]^+$ 318.1859, found 318.1858.

1-(9,9a-dimethyl-4-phenyl-2,3,9,9a-tetrahydro-1*H*-carbazol-1-yl)ethan-1-one (*trans*-**241**)



^1H NMR (400 MHz, $CDCl_3$) δ: 1.32 (s, 3H), 1.98-2.09 (m, 2H), 2.11 (s, 3H), 2.58-2.63 (m, 2H), 2.76 (s, 3H), 3.38 (dd, *J* = 2.3, 6.4 Hz, 1H), 6.36 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.40 (d, *J* = 6.4 Hz, 1H), 6.44 (d, *J* = 8.2 Hz, 1H), 7.01 (dd, *J* = 6.9, 6.9 Hz, 1H), 7.24-7.28 (m, 2H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.40 (dd, *J* = 7.3, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.6, 22.8, 28.8, 29.5, 29.6, 53.1, 67.8, 107.3, 117.3, 123.5, 125.7, 127.1, 127.9, 128.7, 128.80, 128.82, 135.5, 142.1, 152.3, 210.3; IR (neat) ν: 1697, 1601, 1473, 749, 703 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}NO$ $[M+H]^+$ 318.1855, found 318.1858.

6-(1,2-dimethyl-1*H*-indol-3-yl)-6-phenylhexan-2-one (**S7**)

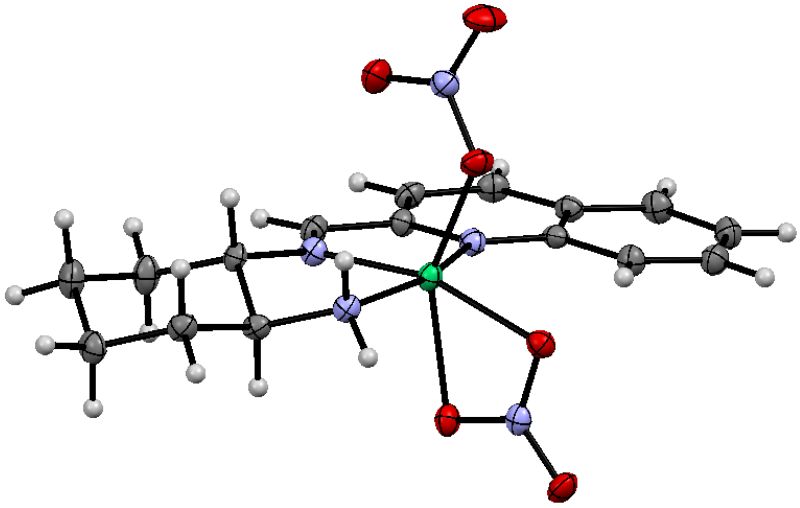


^1H NMR (400 MHz, $CDCl_3$) δ: 1.45-1.65 (m, 2H), 2.04 (s, 3H), 2.21-2.27 (m, 2H), 2.37 (s, 3H), 2.41 (ddd, *J* = 2.3, 7.3, 7.3 Hz, 2H), 3.61 (s, 3H), 4.19 (dd, *J* = 7.3, 8.7 Hz, 1H), 6.98 (dd, *J* = 6.9, 6.9 Hz, 1H), 7.11 (dd, *J* = 6.9, 6.9 Hz, 2H), 7.20-7.24 (m, 3H), 7.33 (d, *J* = 7.3 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.7, 22.8, 29.5, 30.0, 34.0, 42.3, 43.7, 108.6, 113.0, 118.6, 119.3, 120.2, 125.6, 126.7, 127.5, 128.1, 133.3, 136.8, 145.5, 209.1; IR (neat) ν: 1714, 1471, 742, 702 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{25}NNaO$ $[M+Na]^+$ 342.1828, found 342.1834.

Ni 錯体の X 線結晶構造解析データ

Crystal 170 ([Ni^{2+}/**169**/2(NO_3^-)] complex)

The mixture of $Ni(NO_3)_2 \cdot 6H_2O$ (1.5 mg, 5 μmol), (*S*,*S*)-ImQ (**139**) (2.0 mg, 5 μmol) in MeCN (0.5 mL) was stirred for 2 h at room temperature. Et_2O was added to the solution, and it was stored at room temperature for overnight to afford the crystal (**170**) suitable for X-ray crystallographic analysis.



EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{16}H_{19}N_5NiO_6$
Formula Weight	436.06
Crystal Color, Habit	green, block
Crystal Dimensions	0.200 X 0.100 X 0.050 mm
Crystal System	orthorhombic
Lattice Type	Primitive
Lattice Parameters	a = 8.2244(2) Å b = 11.9921(3) Å c = 18.0984(4) Å V = 1785.00(6) $Å^3$
Space Group	$P2_12_12_1$ (#19)
Z value	4
D_{calc}	1.622 g/cm^3
F_{000}	904.00
μ(CuKα)	19.958 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å)
Voltage, Current	40kV, 30mA
Temperature	-180.0°C
Detector Aperture	460 x 256 mm
Data Images	30 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
ω oscillation Range (χ=0.0, ϕ=0.0)	80.0 - 260.0°
Exposure Rate	10.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4°
No. of Reflections Measured	Total: 19007
	Unique: 3268 (R_{int} = 0.0672)
	Friedel pairs: 1381
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.874 - 0.905)

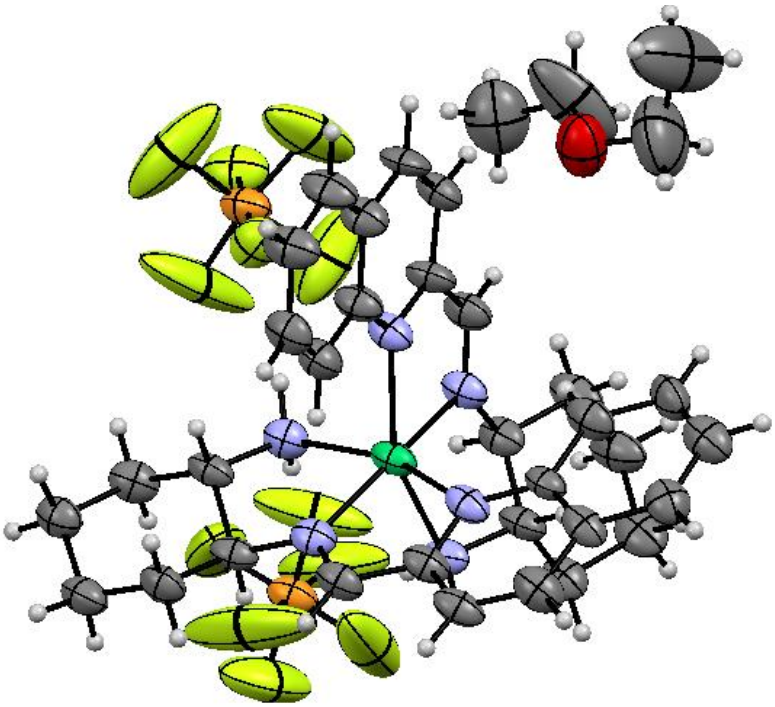
C. Structure Solution and Refinement

Structure Solution	Direct Methods
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\sigma^2(Fo^2) + (0.0432 \cdot P)^2$
	$+ 0.0000 \cdot P]$
	where $P = (Max(Fo^2,0) + 2Fc^2)/3$

$2\theta_{max}$ cutoff	136.4^{o}
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3268
No. Variables	253
Reflection/Parameter Ratio	12.92
Residuals: R1 (I>2.00σ(I))	0.0419
Residuals: R (All reflections)	0.0461
Residuals: wR2 (All reflections)	0.0842
Goodness of Fit Indicator	1.020
Flack Parameter (Friedel pairs = 1381)	0.01(3)
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.51 $e^{-}/Å^{3}$
Minimum peak in Final Diff. Map	-0.30 $e^{-}/Å^{3}$

Crystal 171 ([Ni^{2+}/2(**169**)/2(PF_6^-)] complex)

The mixture of $Ni(NO_3)_2 \cdot 6H_2O$ (1.5 mg, 5 μmol), (*S*,*S*)-ImQ (**139**) (2.0 mg, 5 μmol) in MeOH (0.1 mL) was stirred for 2 h at room temperature. NH_4PF_6 (1.6 mg, 10 μmol) was then added to the mixture. The resulting mixture was stirred for 5 min. Et_2O was added to the solution, and it was stored at room temperature for overnight to afford the crystal (**171**) suitable for X-ray crystallographic analysis.



EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{36}H_{48}F_{12}N_6NiOP_2$
Formula Weight	929.44
Crystal Color, Habit	brown, platelet
Crystal Dimensions	0.300 X 0.200 X 0.020 mm
Crystal System	monoclinic
Lattice Type	Primitive
Lattice Parameters	a = 9.6941(2) Å
	b = 10.6255(2) Å
	c = 20.2666(4) Å
	b = 102.560(1) ^{o}
	V = 2037.60(7) $Å^3$

Space Group	$P2_1$ (#4)
Z value	2
D_{calc}	1.515 g/cm^3
F_{000}	960.00
μ(CuKα)	22.690 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (l = 1.54187 Å)
Voltage, Current	40kV, 30mA
Temperature	-180.0^{o}C
Detector Aperture	460 x 256 mm
Data Images	30 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0^o
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0^o
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0^o
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0^o
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=0.0, ϕ=0.0)	80.0 - 260.0^o
Exposure Rate	10.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4^o
No. of Reflections Measured	Total: 21704
	Unique: 7277 (R_{int} = 0.0722)
	Friedel pairs: 3338
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.722 - 0.956)

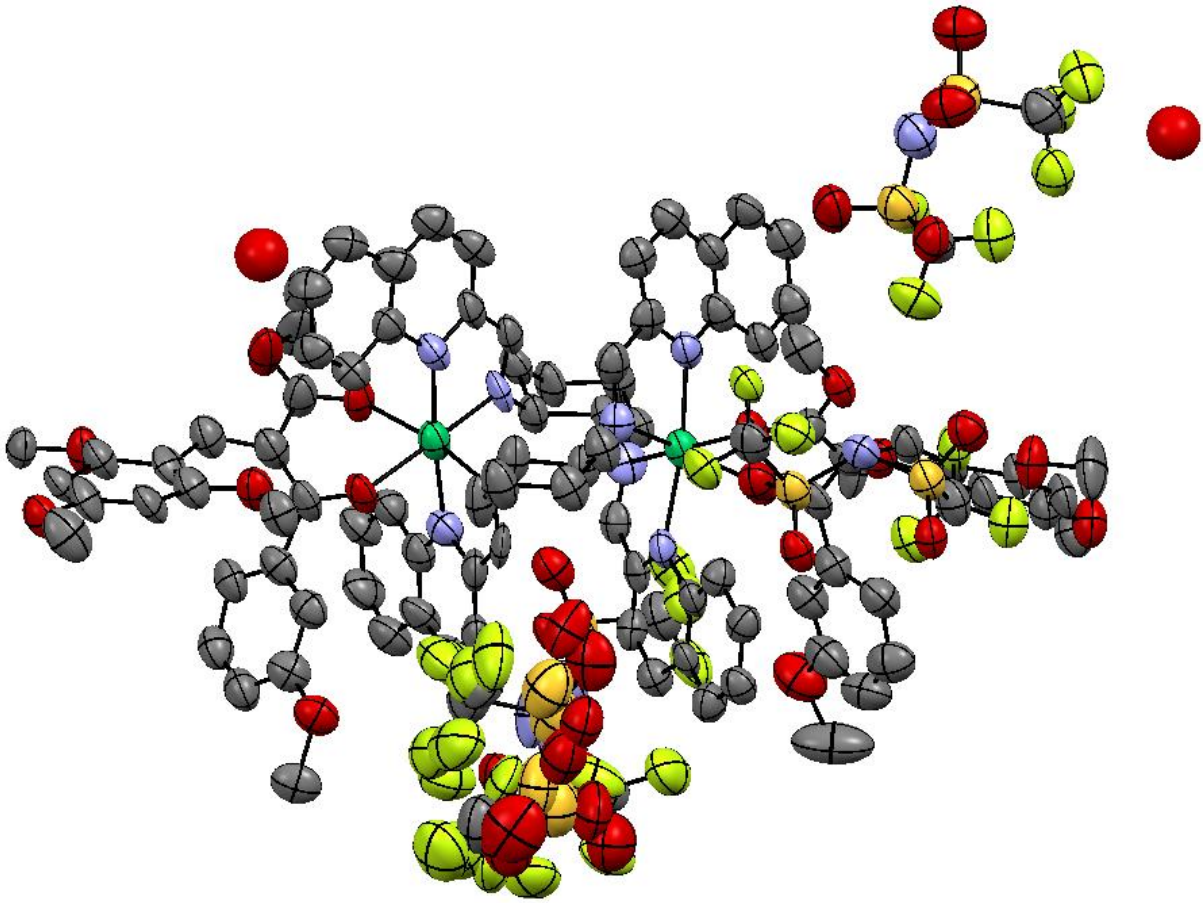
C. Structure Solution and Refinement

Structure Solution	Direct Methods
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w (Fo^2 - Fc^2)^2
Least Squares Weights	w = 1/ [$\sigma^2(Fo^2)$ + (0.1085 · P)^2 + 2.2534 · P] where P = (Max(Fo^2,0) + 2Fc^2)/3
$2\theta_{max}$ cutoff	136.4^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	7277
No. Variables	523
Reflection/Parameter Ratio	13.91
Residuals: R1 (I>2.00σ(I))	0.0807
Residuals: R (All reflections)	0.1067
Residuals: wR2 (All reflections)	0.2270
Goodness of Fit Indicator	1.090
Flack Parameter (Friedel pairs = 3338)	0.00(5)
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	1.15 e^-/Å^3
Minimum peak in Final Diff. Map	-0.76 e^-/Å^3

Crystal 173 ([2(Ni^{2+})/2(**139**)/2(**172**)/4(NTf_2^-)] complex)[54]

The mixture of $Ni(NTf_2)_2$ (6.2 mg, 0.01 mmol), (*S*,*S*)-ImQ (**139**) (3.9 mg, 0.01 mmol) and activated MS 4 Å pellet (200 mg) in CH_2Cl_2 (0.2 mL) was stirred for 2 h at room temperature. **172** (3.9 mg, 0.01 mmol) was then added to the mixture. The resulting mixture was stirred for 5 min. The solution was separated with MS 4 Å, and transferred to another vial. Twice to three times (against the volume of CH_2Cl_2) of cyclopentyl methyl ether was added to the solution, and it was stored at room temperature for overnight to afford the crystal (**173**) suitable for X-ray crystallographic analysis. **173** was isolable under inert gas, whereas it was unstable under ambient air.

Hydrogen atoms are omitted for clarity. Ellipsoids are drawn at the 30% probability level.



EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{51}H_{46}F_{12}N_6NiO_{16}S_4$
Formula Weight	1413.88
Crystal Color, Habit	brown, block

Crystal Dimensions	0.150 X 0.100 X 0.100 mm
Crystal System	monoclinic
Lattice Type	Primitive
Lattice Parameters	a = 13.6455(3) Å
	b = 18.1359(5) Å
	c = 24.9551(6) Å
	b = 104.4654(11) ^{o}
	V = 5980.0(3) Å^{3}
Space Group	$P2_1$ (#4)
Z value	4
D_{calc}	1.570 g/cm^{3}
F_{000}	2888.00
μ(CuKα)	27.523 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å)
Voltage, Current	40kV, 30mA
Temperature	-180.0^{o}C
Detector Aperture	460.0 x 256.0 mm
Data Images	30 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	50.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0^{o}
Exposure Rate	50.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0^{o}
Exposure Rate	50.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0^{o}
Exposure Rate	50.0 sec./^{o}
ω oscillation Range (χ=0.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	50.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4^{o}
No. of Reflections Measured	Total: 64005

	Unique: 21038 (R_{int} = 0.1448)
	Parsons quotients (Flack x parameter): 1405
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.528 - 0.759)

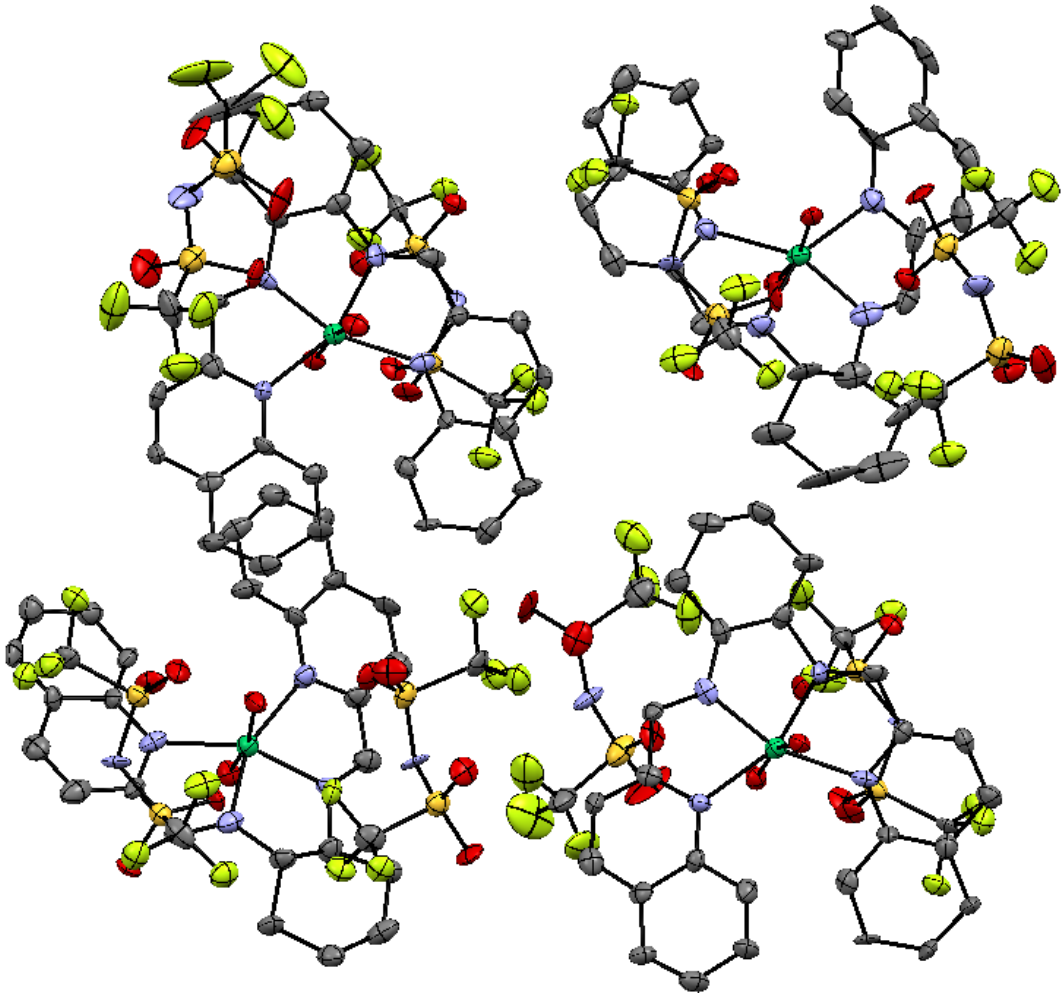
C. Structure Solution and Refinement

Structure Solution	Direct Methods (SHELXT Version 2014/4)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\sigma^2(Fo^2) + (0.2000 \cdot P)^2$
	$+ 0.0000 \cdot P]$
	where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	136.4^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	21038
No. Variables	1678
Reflection/Parameter Ratio	12.54
Residuals: R1 (I>2.00σ(I))	0.1394
Residuals: R (All reflections)	0.3164
Residuals: wR2 (All reflections)	0.4540
Goodness of Fit Indicator	0.961
Flack parameter (Parsons' quotients = 1405)	0.04(4)
Max Shift/Error in Final Cycle	0.004
Maximum peak in Final Diff. Map	0.54 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.70 $e^-/Å^3$

Crystal 181 ([Ni^{2+}/**150**/2(NTf_2^-)/2(H_2O)] complex)

The mixture of $Ni(NTf_2)_2$ (6.2 mg, 0.01 mmol), **150** (3.9 mg, 0.01 mmol) and activated MS 4 Å pellet (200 mg) in CH_2Cl_2 (0.4 mL) was stirred for 2 h at room temperature. The solution was separated with MS 4 Å, and transferred to another vial. Toluene was added to the solution, and it was stored at room temperature for overnight to afford the crystal (**150**) suitable for X-ray crystallographic analysis.

Hydrogen atoms are omitted for clarity. Ellipsoids are drawn at the 30% probability level.



EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{120}H_{88}F_{48}N_{24}Ni_4O_{40}S_{16}$
Formula Weight	4165.84
Crystal Color, Habit	yellow, platelet
Crystal Dimensions	0.500 X 0.350 X 0.020 mm

Crystal System	triclinic
Lattice Type	Primitive
Lattice Parameters	a = 8.8902(2) Å
	b = 20.8960(5) Å
	c = 22.9190(5) Å
	a = 76.397(1) ^{o}
	b = 86.516(2) ^{o}
	g = 83.632(1) ^{o}
	V = 4110.0(2) Å^{3}
Space Group	P1 (#1)
Z value	4
D_{calc}	6.732 g/cm^{3}
F_{000}	8384.00
μ(CuKα)	145.633 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å)
Voltage, Current	40kV, 30mA
Temperature	-180.0^{o}C
Detector Aperture	460 x 256 mm
Data Images	30 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	5.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0^{o}
Exposure Rate	5.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0^{o}
Exposure Rate	5.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0^{o}
Exposure Rate	5.0 sec./^{o}
ω oscillation Range (χ=0.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	5.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4^{o}

No. of Reflections Measured	Total: 43613
	Unique: 24347 (R_{int} = 0.1004)
	Friedel pairs: 9660
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.515 - 0.747)
	Secondary Extinction
	(coefficient: 4.90000e-004)

C. Structure Solution and Refinement

Structure Solution	Charge Flipping (Superflip)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\sigma^2(Fo^2) + (0.1295 \cdot P)^2$
	$+ 0.0000 \cdot P]$
	where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	136.4^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	24347
No. Variables	2271
Reflection/Parameter Ratio	10.72
Residuals: R1 (I>2.00σ(I))	0.1105
Residuals: R (All reflections)	0.2213
Residuals: wR2 (All reflections)	0.3112
Goodness of Fit Indicator	0.997
Flack Parameter (Friedel pairs = 9660)	0.02(4)
Max Shift/Error in Final Cycle	0.005
Maximum peak in Final Diff. Map	1.37 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.72 $e^-/Å^3$

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主論文目録

本学位論文は下記の発表論文による。

1. Catalytic Asymmetric Nazarov Cyclization of Heteroaryl Vinyl Ketones through a Crystallographically Defined Chiral Dinuclear Nickel Complex
   Takuya Takeda, Shinji Harada, Atsushi Nishida *Organic Letters*, **2015**, *17*, 5184-5187.

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1. 「Catalytic Asymmetric Nazarov Cyclization of Heteroaryl Vinyl Ketones through a Crystallographically Defined Chiral Dinuclear Nickel Complex」
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1. 「アリールビニルケトンを基質とした触媒的不斉 Nazarov 環化反応」
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その他

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