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Cyclohepta[*b*]indole Synthesis through [5+2] Cycloaddition: Bifunctional Indium(III)-Catalyzed Stereoselective Construction of 7-Membered Ring Fused Indoles

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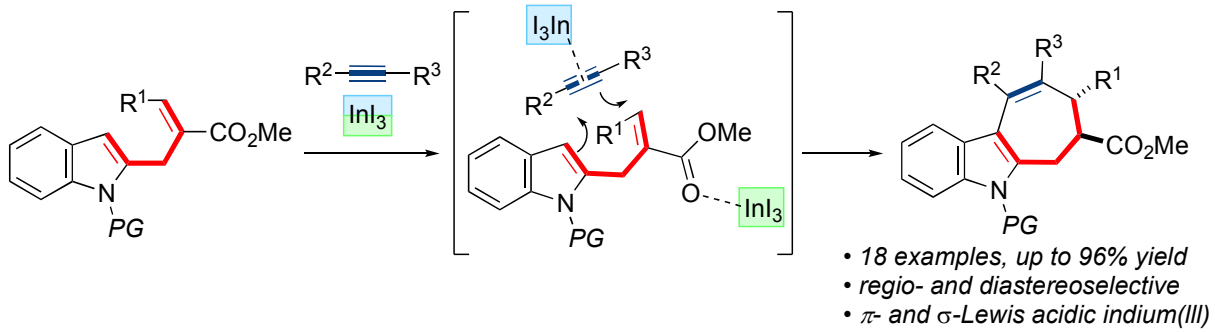


Abstract

A new approach for the synthesis of highly functionalized tetrahydrocyclohepta[*b*]indoles through [5+2] cycloaddition was developed. Two carbon-carbon bonds were formed by the simple addition of an indium catalyst, which acted as both a π-Lewis acid and σ-Lewis acid to activate the alkyne and unsaturated ester, respectively. The reaction could be applied to various substrates and proceeded regio- and diastereoselectively in all cases.

Introduction

The cyclohepta[*b*]indole skeleton has been found in various natural and non-natural compounds that show a wide range of biological activity (Figure 1).[1] For instance, **4** has antitubercular activity (MIC = 3.12 μg/mL),[1d] **5** was reported to be an adipocyte fatty-acid binding protein inhibitor (IC_{50} = 450 nM),[1e] and **6** inhibited one of the histone decarboxylase SIRT1 (IC_{50} = 63 nM).[1f] Thus, the cyclohepta[*b*]indole skeleton is attracting interest in the field of medicinal chemistry as a potential therapeutic compound. This interest, along with the difficulty of constructing its seven-membered ring, has inspired organic chemists to develop methods for synthesizing the cyclohepta[*b*]indole skeleton.[2] A common approach to this skeleton in an intermolecular fashion is through the use of indole derivatives as a donor-acceptor type (D-A) substrate. Scheme 1 shows examples of indoles as a C-3 (**7** or **8**, Scheme 1, A) or C-4 (**11**, Scheme 1, B) D-A substrate in [4+3] cycloaddition.[3]

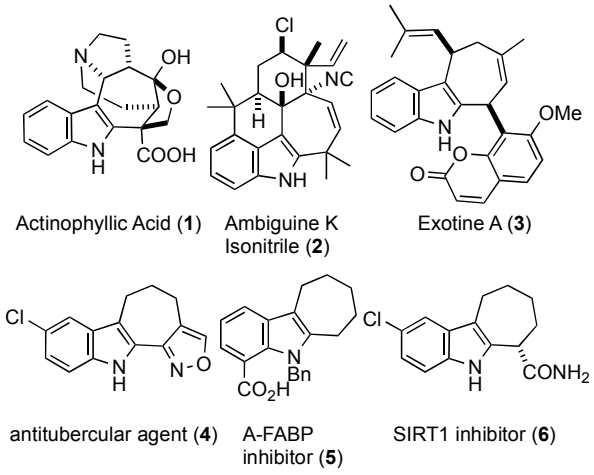
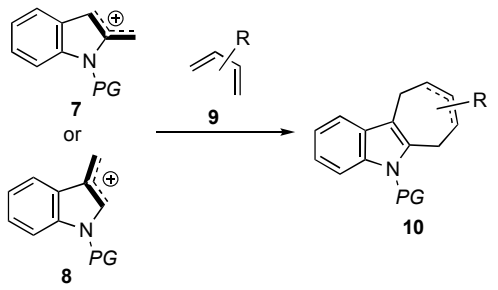


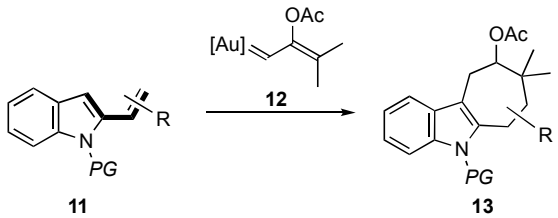
Figure 1. Representative Compounds Containing Cyclohepta[*b*]indole

Scheme 1. Cyclohepta[*b*]indole Synthesis Using Indole Derivative as a Donor-Acceptor Type Substrate

A) C-3 D-A Indole Substrate **7** or **8**



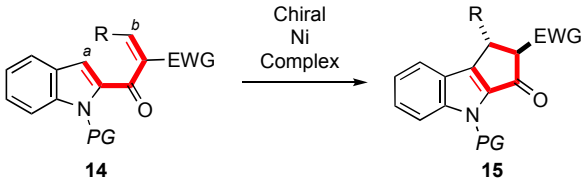
B) C-4 D-A Indole Substrate **11**



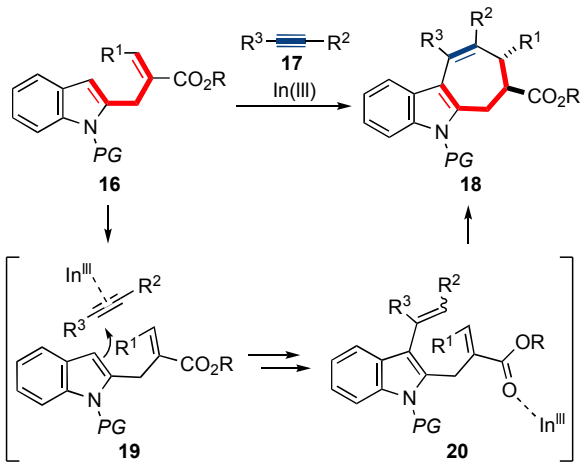
Recently, we achieved the synthesis of cyclopenta[*b*]indoles **15** from indole derivative **14** via enantioselective Nazarov cyclization (Scheme 2, A).[4] This indole derivative **14** contains both nucleophilic carbon (C_a) and electrophilic carbon (C_b), and therefore compound **14** and its derivatives would act as C-5 donor-acceptor type (D-A) substrates in an intermolecular reaction. Thus, we designed suitable C-5 D-A indole substrate **16** for intermolecular cycloaddition by removal of the carbonyl group adjacent to the indole ring in **14** to improve the nucleophilicity of the indole as well as to suppress Nazarov cyclization. Cycloheptannulation would be achieved by using an appropriate C-2 D-A type substrate, and we found that alkynes were suitable for this purpose.[5] Alkynes introduce an olefin moiety in the resulting seven-membered ring, which is amenable to various functionalizations. Herein, we report a novel [5+2] cycloaddition between indole **16** and alkyne using indium(III) as a sole catalyst that acts as both a π- and σ-Lewis acid to construct a cyclohepta[*b*]indole skeleton in one-step (Scheme 2, B).

Scheme 2. Cyclization of C-5 Donor-Acceptor Type Indole Derivatives

A) Previous Work: Enantioselective Nazarov Cyclization



B) This Work: Intermolecular [5+2] Cyclization

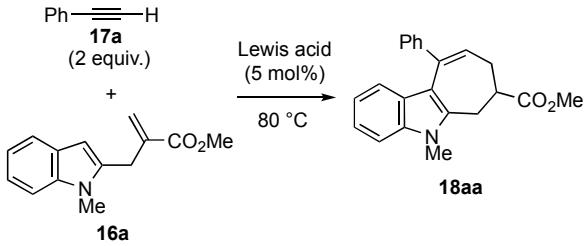


Results and Discussion

The [5+2] cycloaddition of indole **16** and alkyne requires the activation of both an alkyne and unsaturated ester depicted as **19** and **20**. Therefore a catalyst that can act as both a π- and σ-Lewis acid is required for the reaction to proceed. Indium(III) salts have been used as a Lewis acidic catalyst in various transformations,[6] in which they were used to activate functional groups such as carbonyl groups, epoxides, aziridines, halides, alkenes and alkynes. These results indicated that indium(III) salts could act as both π- and σ-Lewis acids. As an initial trial, the reaction of indole **16a** and phenylacetylene (**17a**) was carried out under $InBr_3$ catalysis at 80 ºC, and we obtained the cyclized product **18aa** in 85% yield (Table 1, entry 1). To optimize the reaction conditions, we surveyed suitable solvents and catalysts. The reaction proceeded smoothly to give **18aa** in good yield in aromatic solvents (entries 1 and 2). On the contrary, the reactivity was much lower when the reaction was carried out in

1,2-DCE, $MeNO_2$ or MeCN (entries 3-5). InI_3 also gave **18aa** in 89% yield in 5 hours in toluene (entry 6), while we still recovered **16a** in 4%. With the use of 10 mol% of InI_3 and 4 equivalents of **17a**, **16a** was consumed to give **18aa** in 92% (entry 7). $In(OTf)_3$ catalyzed the cycloaddition, however, the catalytic activity was much lower than that of indium halides (entry 8). GaI_3 had lower reactivity than indium(III) halides (entry 9). Although Friedel-Crafts alkenylation using $GaCl_3$ at a lower reaction temperature has been reported,[7] $GaCl_3$ could not catalyze the reaction and gave **18aa** in moderate yield even with a stoichiometric amount of reagent (entries 10 and 11). When gold(I) catalyst, which has been used as an activator of alkynes in various reactions,[8] was examined, it gave **18aa** in 64% yield after 24 hours (entry 12). Although other Lewis acids that have been used in Friedel-Crafts alkenylation[9] were examined, those trials resulted in lower catalytic activity than in the case of indium(III) halides.

Table 1. Optimization of the Reaction Conditions



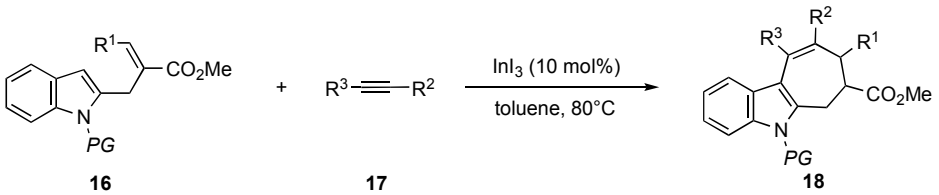
entry	Lewis acid	solvent	time (h)	yield (%)
1	$InBr_3$	toluene	6	85
2	$InBr_3$	PhCl	7	83
3	$InBr_3$	1,2-DCE	24	32
4	$InBr_3$	$MeNO_2$	24	7
5	$InBr_3$	MeCN	24	20
6	InI_3	toluene	5	89
7[a]	InI_3	toluene	5	92
8	$In(OTf)_3$	toluene	6	15
9	GaI_3	toluene	6	64
10[b]	$GaCl_3$	toluene	22	7
11[c]	$GaCl_3$	CH_2Cl_2	1	61
12	$(PPh_3)AuCl/AgSbF_6$	toluene	24	64

[a]The reaction was carried out using 10 mol% of InI_3 and 4 equivalents of **17a**. [b]The reaction was carried out at room temperature. [c]The reaction was carried out at 0 ºC using 100 mol% of $GaCl_3$.

The substrate scope and limitations of InI_3-catalyzed intermolecular [5+2] cycloaddition were performed using 10 mol% of InI_3 and 4 equivalents of alkyne (Table 2). Although **17b** required a higher reaction temperature, *o*-, *m*-, and *p*-tolylacetylenes (**17b, c, d**) gave **18** in excellent yields (entries 2-4). **17e** with an electron-rich aromatic ring gave **18ae** in moderate yield because of the instability of **17e** (entry 5). On the contrary, electron-deficient alkynes **17f** and **17g** gave **18** in excellent yields (entries 6 and 7). Alkynes with a heteroaromatic ring were also reacted with indole **16a** to give **18** in good to excellent yields (entries 8-11). Because aliphatic acetylene **17l** and internal alkyne **17m** showed lower reactivity than aromatic terminal alkynes, a higher reaction temperature was required to promote the reaction. As a result, isomerization of olefin of **16a** occurred preferentially, and desired **18** was obtained in low yield (entries 12 and 13). Notably, the reaction using **17l** gave a complex

mixture of products. Among them, we detected **18al** as a minor cyclized product, and unexpected product **21** was obtained in 38% yield. Next, we examined several types of indole substrates. Not only *N*-benzyl indole **16b**, but also non-protected derivative **16c** could be used in this reaction (entries 14 and 15). The reaction of **16c** proceeded at the indole C3 position selectively and no *N*-alkenylated product was observed at all. Additionally, indole substrates with a β-substituted unsaturated ester moiety (**16d, e, f**) gave **18** in good to excellent yields with excellent diastereoselectivity, although the reaction using these indole derivatives required a longer reaction time (entries 16-18). The stereochemistry of **18da** was determined by X-ray crystallographic analysis.[10]

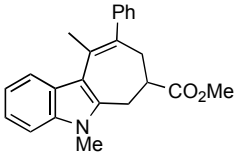
Table 2. Substrate Generality



16 **17** (4 equiv.) **18**

16a: *PG*=Me, R^1=H
16b: *PG*=Bn, R^1=H
16c: *PG*=H, R^1=H
16d: *PG*=Me, R^1=4-MeO-C_6H_4-
16e: *PG*=Me, R^1=2-furyl
16f: *PG*=Me, R^1=*n*-Pr

17a: R^2=H, R^3=Ph
17b: R^2=H, R^3=2-Me-C_6H_4-
17c: R^2=H, R^3=3-Me-C_6H_4-
17d: R^2=H, R^3=4-Me-C_6H_4-
17e: R^2=H, R^3=4-MeO-C_6H_4-
17f: R^2=H, R^3=4-Br-C_6H_4-
17g: R^2=H, R^3=4-CF_3-C_6H_4-
17h: R^2=H, R^3=2-thiophenyl
17i: R^2=H, R^3=3-thiophenyl
17j: R^2=H, R^3=2-benzofuranyl
17k: R^2=H, R^3=*N*-Ts-indol-3-yl
17l: R^2=H, R^3=benzyl
17m: R^2=Me, R^3=Ph



21

entry	indole **16**	alkyne **17**	time (h)	product **18**	yield (%)	dr (*trans*/*cis*)
1	**16a**	**17a**	5	**18aa**	92	–
2[a]	**16a**	**17b**	24	**18ab**	86	–
3	**16a**	**17c**	6	**18ac**	96	–
4	**16a**	**17d**	6	**18ad**	82	–
5	**16a**	**17e**	10	**18ae**	51	–
6	**16a**	**17f**	4	**18af**	95	–
7	**16a**	**17g**	4	**18ag**	89	–
8	**16a**	**17h**	10	**18ah**	74	–
9	**16a**	**17i**	10	**18ai**	72	–
10	**16a**	**17j**	4	**18aj**	66	–
11[b]	**16a**	**17k**	5	**18ak**	72	–

12[a]	**16a**	**17l**	24	**18al**[c]	<6	–
				21	38	–
13[a]	**16a**	**17m**	72	**18am**	29	–
14	**16b**	**17a**	2	**18ba**	89	–
15	**16c**	**17a**	6	**18ca**	80	–
16	**16d**	**17a**	22	**18da**	80	>20/1
17	**16e**	**17a**	24	**18ea**	56	>20/1
18	**16f**	**17a**	72	**18fa**	60	>20/1

[a] The reaction was carried out at 80 to 100 °C. [b] The reaction was carried out using 2 equivalents of **17k**. [c] Including inseparable byproducts.

A plausible reaction mechanism is shown in Scheme 3. Indium(III) salt-catalyzed Friedel-Crafts alkenylation has been reported to form zwitterionic intermediate **23**.[11] Carbon-indium bond-formation would occur to form a more stable cationic carbon center, hence Friedel-Crafts alkenylation would proceed regioselectively and subsequent rearomatization/protonation gave alkenylated indole **24**. InI_3 also activated the unsaturated ester moiety as a σ-Lewis acid and 7-membered ring construction proceeded from **25** through intramolecular Michael addition.[12] This step would be slow among these sequential reactions, because substrates with a β-substituted unsaturated ester moiety (**16d, e, f**) required a longer reaction time. A possible 5-*endo* cyclization mode (path *b*) should be much slower than observed 7-*endo* cyclization (path *a*). The resulting indium enolate **26** was protonated from the less hindered convex face, and **18** was diastereoselectively obtained as a *trans*-isomer. When the reaction was performed using aliphatic alkyne **17l**, the alkenylated indole **24al** could be isomerized to internal alkene **24al'** and would give cyclized product **21** (Figure 2).

Scheme 3. Plausible Reaction Mechanism

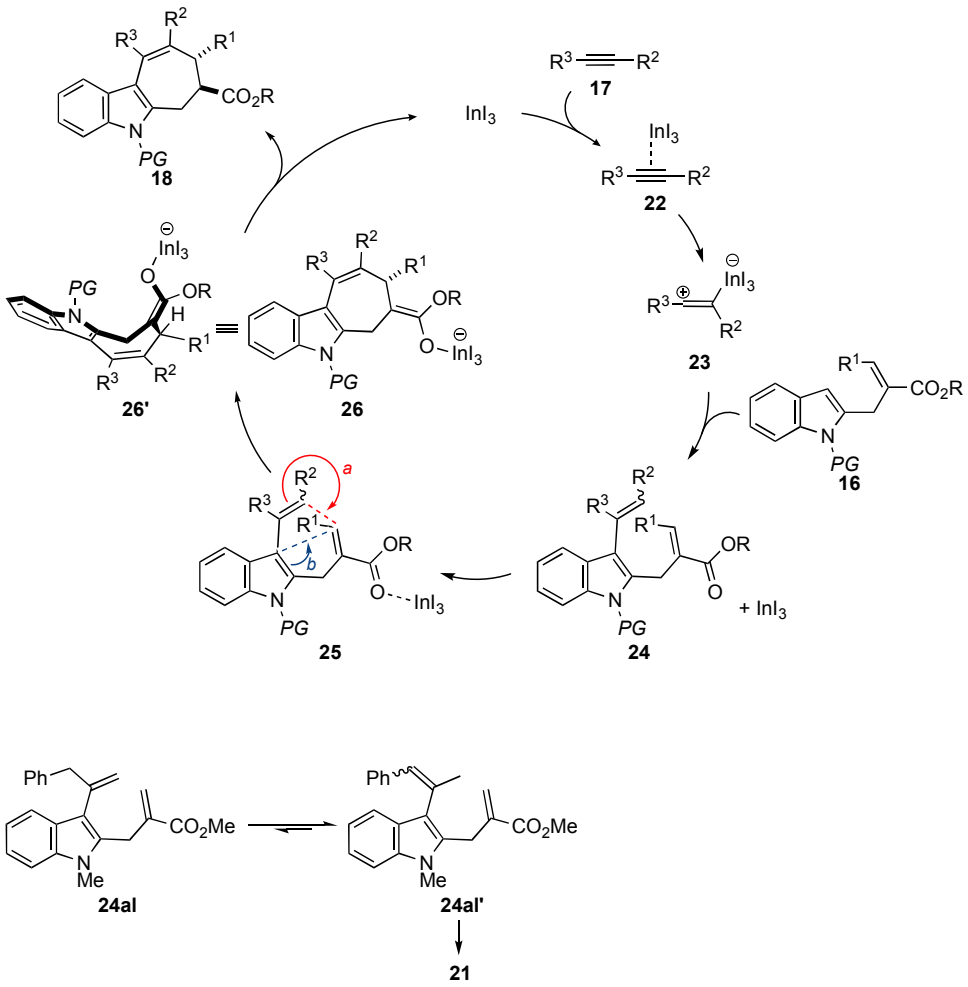
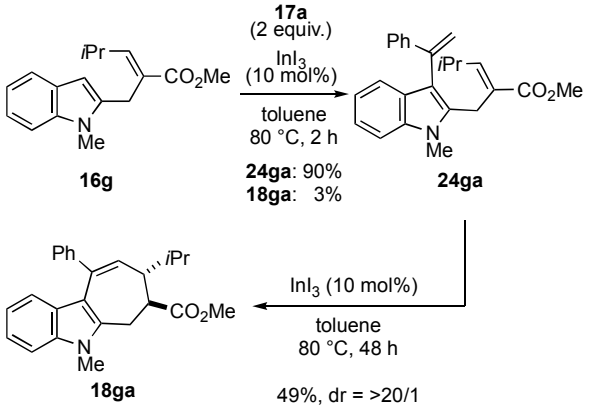


Figure 2. Isomerization of Alkenylindole Intermediate

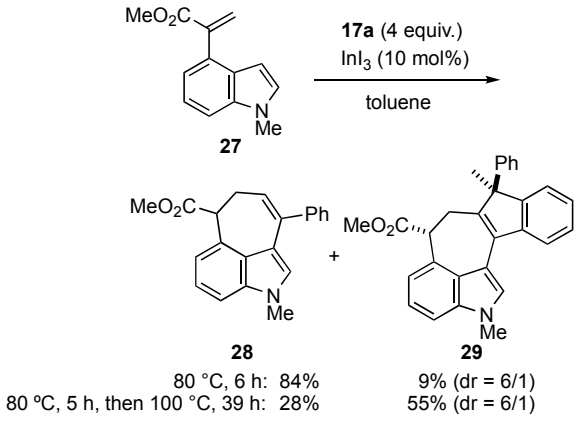
To confirm this mechanism, we examined the cyclization of hypothetical intermediate **24**. Indole **16g** was reacted with phenylacetylene (**17a**) to give **24ga** in 90% yield and cyclized **18ga** was obtained in 3% yield after 2 hours (Scheme 4). Isolated **24ga** was again reacted under InI_3 catalysis and consequently **18ga** was obtained in 49% yield after 48 hours. This result indicated that alkenylated indole **24** was an intermediate for the cyclization, and InI_3 activated both the alkyne and unsaturated ester in the reaction.

Scheme 4. Stepwise Ring Construction under InI_3 Catalysis

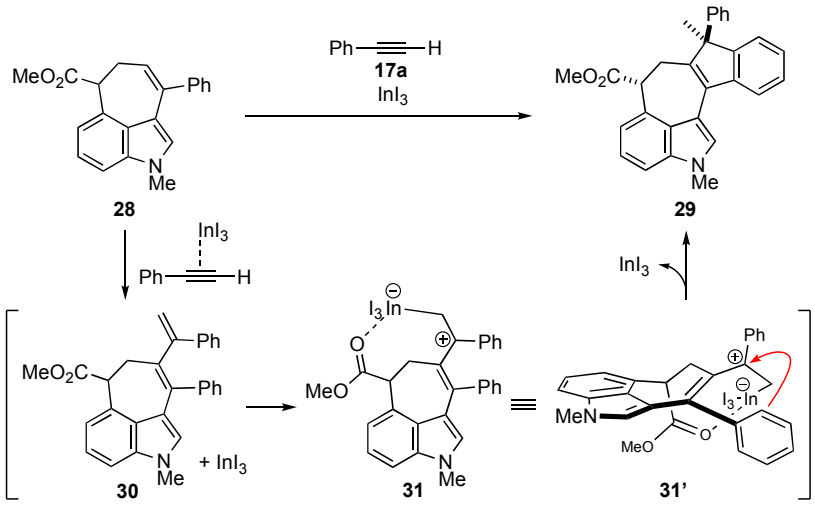


We next examined the synthesis of different types of 7-membered ring fused indole skeleton using this methodology. Indole **27** and **17a** were reacted under optimized conditions and cyclohepta[*c,d*]indole **28** was obtained in 84% yield (Scheme 5). Compounds containing a cyclohepta[*c,d*]indole skeleton have been reported as natural and biologically active compounds.[13] Indole **27** also gave **29** in 9% yield,[10] which was obtained by the reaction with 2 molecules of **17a**, while indole **16** did not give this type of overreacted product. Additionally, **29** was obtained as a major product in 55% yield under an elevated temperature and prolonged reaction time. Therefore, **29** would be generated from **28** with excess alkyne as shown in Scheme 6. An intramolecular interaction of ester moiety and indium to form **31** would contribute to the diastereoselctivity.

Scheme 5. Cyclohepta[*c,d*]indole Synthesis



Scheme 6. Plausible Mechanism for the Generation of 29



Conclusion

In conclusion, we developed a novel method for the synthesis of the cyclohepta[*b*]indole skeleton through an InI_3-catalyzed [5+2] cycloaddition. The reaction proceeded under catalysis by an indium(III) salt as both a π- and σ-Lewis acid, which enabled two types of carbon-carbon bond-formation under a single catalytic system. Additionally, various indole derivatives and alkynes could be used in this reaction to give not only cyclohepta[*b*]indole but also cyclohepta[*c,d*]indole in good to excellent yield. Further studies on synthetic applications and enantioselective reactions are underway.

Experimental Section

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. Chemical shifts for proton are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CDCl_3$ δ: 7.26 ppm). For ^{13}C NMR, chemical shifts are reported relative to the NMR solvent ($CDCl_3$ δ: 77.0 ppm) as an internal reference. Infrared spectra were recorded on an ATR. Mass spectra were recorded using ESI mode with a TOF analyzer. X-ray crystallographic data were collected at −180±1 °C using filtered Cu−Kα radiation. Reactions were carried out in dry solvents under an argon atmosphere, unless otherwise noted. Dry toluene, Lewis acids and alkynes were purchased from a commercial supplier. Other solvents and reagents were purified by usual methods. Flash column chromatography was performed on silica gel (60 μm particles) unless otherwise noted.

General Procedure for the Synthesis of Indole 16. A mixture of 1-methyl-1*H*-indole-2-carbaldehyde (1.6 g, 10 mmol), trimethyl phosphonoacetate (2.0 g, 11 mmol), AcOH (290 μL, 5.0 mmol) and piperidine (100 μL, 1.0 mmol) in benzene (20 mL) was stirred at refluxing temperature for 1 day. The resulting mixture was concentrated under reduced pressure and purified by a 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 the Knoevenagel product in MeOH (20 mL) at 0 °C. The mixture was gradually warmed to room temperature and stirred overnight. The solvent was removed under reduced pressure and the residue was diluted with water and AcOEt. The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure.

The residue was dissolved in THF (20 mL) and paraformaldehyde (601 mg, 20 mmol) and K_2CO_3 (2.8 g, 20 mmol) were added. The mixture was stirred at refluxing temperature for 1 day and filtrated through a pad of Celite®. The solution was concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/15) to afford **16a** as a pale yellow viscous liquid (1355 mg, 59% yield in 3 steps).

Methyl 2-((1-methyl-1*H*-indol-2-yl)methyl)acrylate (**16a**); ^{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.

Methyl 2-((1-benzyl-1*H*-indol-2-yl)methyl)acrylate (**16b**); The reaction was carried out on a 2.8 mmol scale of aldehyde following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **16b** 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 (**16c**); The reaction was carried out on a 5.0 mmol scale of aldehyde following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **16c** as a pale yellow solid (116 mg, 11% yield in 3 steps). Mp: 65-67 ºC. ^{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 (*E*)-3-(4-methoxyphenyl)-2-((1-methyl-1*H*-indol-2-yl)methyl)acrylate (**16d**); The reaction was carried out on a 4.7 mmol scale of aldehyde following the general procedure. After reduction with $NaBH_4$, NaH (72 mg, 1.8 mmol, 60% dispersion) was added to a mixture of the residue and *p*-anisaldehyde (183 μL, 1.5 mmol) in toluene (7.5 mL). The mixture was stirred

overnight at 60 °C, and the reaction was quenched with *sat.* NH_4Cl *aq*. The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **16d** as a pale yellow amorphous solid (354 mg, 26% yield in 3 steps, *E/Z* = 2.2/1). Further purification was achieved by recrystallization from Et_2O to afford the (*E*)-isomer as a colorless solid. Crystals suitable for X-ray crystallographic analysis were obtained by slow diffusion of hexane into an Et_2O solution of **16d**.[9] Mp: 123-124 ºC. ^{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 (**16e**); The reaction was carried out on a 6.3 mmol scale of aldehyde following the general procedure. After the reduction with $NaBH_4$, NaH (380 mg, 9.5 mmol, 60% dispersion) was added to 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 additional 2 h. The reaction was quenched with *sat*. NH_4Cl *aq*. The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **16e** as a red solid (1167 mg, 63% yield in 3 steps, *E/Z* = 3/1). Further purification was achieved by washing the solid with Et_2O to afford the (*E*)-isomer as a pale yellow solid (345 mg). Mp: 110-111 ºC. ^{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 $C_{18}H_{18}NO_3$ $[M+H]^+$ 296.1287, found 296.1286.

Methyl (*E*)-2-((1-methyl-1*H*-indol-2-yl)methyl)hex-2-enoate (**16f**); The reaction was carried out on a 2.0 mmol scale of aldehyde following the general procedure. After reduction with $NaBH_4$, NaH (80 mg, 2.0 mmol, 60% dispersion) was added to the residue in THF (8.0 mL) at 0 °C and stirred for 0.5 h. A solution of butyraldehyde (180 μL, 2.0 mmol) in THF (2.0 mL) was added to the mixture and stirred for another 5 h. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford (*E*)-**16f** as a yellow viscous liquid (127 mg, 24% yield in 3 steps) and (*Z*)-**16f** as a yellow viscous liquid (48 mg, 15% yield in 3 steps). (*E*)-**16f**; ^{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.

Methyl (*E*)-4-methyl-2-((1-methyl-1*H*-indol-2-yl)methyl)pent-2-enoate (**16g**); The reaction was carried out on a 2.1 mmol scale of aldehyde following the general procedure. After reduction with $NaBH_4$, NaH (60 mg, 1.5 mmol, 60% dispersion) was added to the residue in THF (5.0 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 the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography

(SiO_2, AcOEt/Hexane = 1/15) to afford (*E*)-**16g** as a pale brown liquid (50 mg, 9% yield in 3 steps) and (*Z*)-**16g** as a pale yellow solid (12 mg, 2% yield in 3 steps). (*E*)-**16g** ; ^{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.

2-Ethynylbenzofuran (**17j**);[14] To a solution of 2,3-benzofuran (591 mg, 5.0 mmol) in THF (25 mL) was added *n*-BuLi (3.9 mL, 6.0 mmol, 1.55 M in hexane) at –78 °C. The resulting solution was stirred for 1 h and DMF (580 μL, 7.5 mmol) was added. The reaction mixture was stirred for additional 1.5 h and quenched with *sat.* NH_4Cl *aq*. The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford 2-benzofurancarboxaldehyde.

A 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. To this solution was added the synthesized aldehyde in CH_2Cl_2 (5.0 mL). The reaction mixture was gradually warmed to room temperature, stirred overnight, and concentrated under reduced pressure. The residue was filtrated through a short pad of silica gel. The solvent was removed under reduced pressure and the residue was 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 the mixture was stirred for 1.5 h. The reaction was quenched with *sat.* NH_4Cl *aq*. The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/20) to afford **17j** 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 (**17k**);[15] A mixture of indole-3-carboxaldehyde (726 mg, 5.0 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 the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was used without further purification.

A 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. To this solution was added the prepared 1-tosyl-1*H*-indole-2-carbaldehyde in CH_2Cl_2 (5.0 mL). The reaction mixture was gradually warmed to room temperature, stirred overnight, and concentrated under reduced pressure. The residue was filtrated through a short pad of silica gel. The solvent was removed under reduced pressure and the residue was dissolved in THF (9.0 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 from –78 °C to room temperature. The reaction was quenched with *sat.* NH_4Cl *aq.* The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **17k** 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).

General Procedure for InI_3-Catalyzed [5+2] Cycloaddition. A mixture of indole **16** (0.2 mmol), alkyne **17** (0.8 mmol) and InI_3 (9.9 mg, 0.02 mmol) in toluene (2.0 mL) was stirred at 80 °C for an appropriate time. The reaction mixture was then directly purified by flash column chromatography.

Methyl 5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**18aa**); The reaction was carried out

following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **18aa** as a pale yellow solid (61 mg, 92% yield). Mp: 105-106 ºC. ^{1}H 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 (**18ab**); The reaction was carried out following the general procedure and the mixture was stirred at 80 °C for 5 h and 100 °C for 19 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ab** as a yellow viscous liquid (59 mg, 86% yield). ^{1}H 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 (**18ac**); The reaction was carried out following the general procedure and the mixture was stirred for 6 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ac** as a yellow viscous liquid (66 mg, 96% yield). ^{1}H 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 (**18ad**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ad** as a colorless solid (56 mg, 82% yield). Mp: 153-155 ºC. ^{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 (**18ae**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ae** 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 (**18af**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18af** as a pale yellow foam (78 mg, 95% yield). ^1H 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 (**18ag**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ag** as a pale yellow foam (71 mg, 89% yield). ^1H 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 (**18ah**); The reaction was carried

out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ah** 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 (**18ai**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ai** 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 (**18aj**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18aj** as a brown solid (49 mg, 66% yield). Mp: 138-140 ºC. ^{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 (**18ak**); The reaction was carried out following the general procedure using 0.4 mmol of alkyne. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/4) to afford **18ak** 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 (**18al**) and **methyl 5,10-dimethyl-9-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate** (**21**); The reaction was carried out following the general procedure and the mixture was stirred at 80 ºC for 9 h and 100 °C for 15 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **18al** with inseparable impurities as a yellow viscous liquid (4.0 mg, <6% yield) and **21** as a yellow viscous liquid (25 mg, 38% yield). **18al**; ^{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. **21**; ^{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 5,9-dimethyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[b]indole-7-carboxylate (**18am**); The reaction was carried out following the general procedure and the mixture was stirred at 80 ºC for 9 h and 100 °C for 63 h. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **18am** 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 (**18ba**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ba** as a colorless solid (73 mg, 89% yield). Mp: 158-159 ºC. ^{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 (**18ca**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/8) to afford **18ca** 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 *trans*-8-(4-methoxyphenyl)-5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**18da**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **18da** as a pale yellow solid (70 mg, 80% yield). Crystals suitable for X-ray crystallographic analysis were obtained by slow diffusion of hexane into an AcOEt solution of the product.[9] Mp: 183-185 ºC. ^{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 *trans*-8-(furan-2-yl)-5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**18ea**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **18ea** as a brown foam (44 mg, 56% yield, dr = >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 *trans*-5-methyl-10-phenyl-8-propyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**18fa**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **18fa** as a yellow solid (45 mg, 60% yield, dr = >20/1). Mp: 120-122 ºC. ^{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 *trans*-8-isopropyl-5-methyl-10-phenyl-5,6,7,8-tetrahydrocyclohepta[*b*]indole-7-carboxylate (**18ga**); The reaction was carried out on a 0.1 mmol scale of **16g** following the general procedure using 0.2 mmol of **17a**. After the mixture was stirred for 2 h, the residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/12) to afford **24ga** as a pale

red solid (34 mg, 90% yield) and **18ga** (1.0 mg, 3% yield). **24ga**; Mp: 106-107 ºC. ^{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.

A mixture of **24ga** (7.5 mg, 0.02 mmol) and InI_3 (1.0 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 **18ga** as a pale yellow solid (4 mg, 49% yield, *E/Z* = >20/1) and **24ga** (3 mg, 35%). **18ga**; Mp: 140-141 ºC. ^{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-(1-methyl-1*H*-indol-4-yl)acrylate (**27**); To a 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 the mixture was stirred for 0.5 h. A solution of dimethyl oxalate (449 mg, 3.8 mmol) in THF (3.0 mL) was added, and the reaction mixture was stirred for another 0.5 h. The reaction was quenched with *sat*. NH_4Cl *aq*. The layers were separated and the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/3) to afford methyl

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

To a 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 to a solution of methyl 2-(1-methyl-1*H*-indol-4-yl)-2-oxoacetate (269 mg, 1.2 mmol) in THF (2.0 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 the aqueous layer was extracted three times with AcOEt. The combined organic layers were dried over Na_2SO_4, filtrated through a cotton plug and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/5) to afford **27** 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.

Methyl 2-methyl-9-phenyl-6,7-dihydro-2*H*-cyclohepta[*cd*]indole-6-carboxylate (**28**) and **methyl 6,12-dimethyl-6-phenyl-4,5,6,12-tetrahydrobenzo[2,3]azuleno[4,5,6-*cd*]indole-4-carboxylate** (**29**); The reaction was carried out following the general procedure. The residue was purified by flash column chromatography (SiO_2, AcOEt/Hexane = 1/10) to afford **28** as a colorless foam (55 mg, 84% yield) and **29** as a colorless solid (7.0 mg, 9% yield, dr = 6/1). Crystals of **29** suitable for X-ray crystallographic analysis were obtained by slow diffusion of hexane into a toluene solution of the product.[9]

28; Mp: 173-175 ºC. ^{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. **29**; Mp: 186 ºC (decomp.). ^{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.

Associated Content

Supporting Information

The Supporting Information is available free of charge on the website. NMR spectra for obtained compounds. ORTEP figures of compounds **16d**, **18da**, and **29**.

Acknowledgments

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