Cyclopentannulation of 3-Alkylindoles: A Synthesis of a Tetracyclic Subunit of the Kopsane Alkaloids

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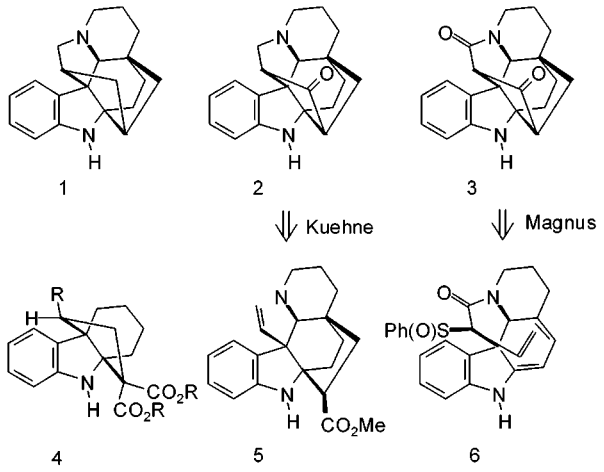
Indoles which bear an alkyl substituent in the 3-position undergo a [3 + 2] annulation reaction when treated with 1,1-cyclopropane diesters in the presence of $Yb(OTf)_3$ resulting in 2,3-cyclopentanoindolines. Typically, the reactions are performed at elevated temperatures or at ultrahigh pressures. In cases where steric crowding is an issue, ultrahigh pressures are required. In reactions involving substituted cyclopropanes, significant regio- and diastereocontrol was observed. When the substituent was aromatic or olefinic, the reactions took place at ambient temperature and pressure. The applicability of this methodology to the preparation of a key tetracyclic subunit of the kopsane alkaloids was demonstrated.

Introduction

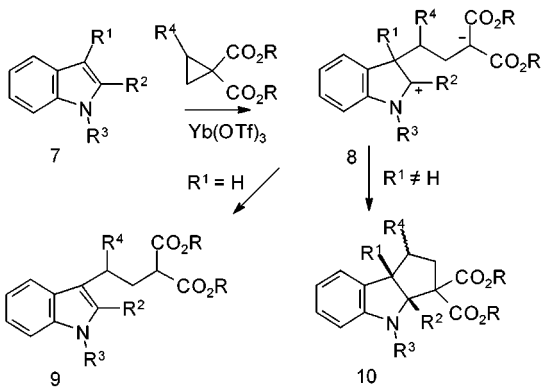
The class of naturally occurring indole alkaloids represented by kopsane **1** has been known for over a century,[1] but it was not until 1965 when several alkaloids were isolated from the stem bark of *Pleiocarpa mutica* that the correct structures were proposed.[2] These compounds have an unusual and architecturally beautiful structure. Kopsine exhibits cholinergic activity and on this basis was included in the strychnos alkaloid series until the structure was elucidated. Despite the synthetic challenge that these compounds pose, surprisingly few groups have engaged in synthetic activities directed toward their preparation. Magnus has prepared racemic 10,22-dioxokopsane **3** and kopsanone **2** using a Diels−Alder cycloaddition of substrates such as **6**[3] while Kuehne[4] uses the unusual tandem addition/cyclization of **5** as the final transformation toward the synthesis of **2**. Herein we report our initial synthetic efforts which have resulted in an efficient formation of substrates of type **4** which possess the tetracyclic core present in kopsane and related alkaloids.



Recently, we disclosed in two preliminary communications the reactions of indoles **7** with 1,1-cyclopropanediesters catalyzed by ytterbium trifluoromethanesulfonate (Scheme 1). In cases where the indole was unsubstituted at the 3-position, the product was one in which alkylation took place to yield the 2-carboalkoxy-4-indolyl butanoate **9**.[5] If, instead, a 3-alkylindole was used, the intermediate **8** could not undergo aromatization and underwent an annulative process via attack of the malonate ion onto the putative immonium ion to produce compounds such as **10**.[6]

It occurred to us that if a tetrahydrocarbazole was used as the indolic partner in the above reaction the product would be a propellane type of annulation product, which constitutes a substructure present in the kopsane alkaloids. We immediately began efforts to probe the feasibility of this approach. Scheme 2 shows a proposed retrosynthesis of kopsane. Diels−Alder substrate **11** would be a key intermediate and would be prepared by oxidative cleavage and derivatization of the styrenyl bond in **12**. The starting materials for the proposed sequence would be the protected tetrahydrocarbazole-4-one **13** and the

Scheme 1



(1) Greshoff, M. *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 3537−3550.
(2) Achenbach, H.; Biemann, K. *J. Am. Chem. Soc.* **1965**, *87*, 4944−4950.
(3) (a) Magnus, P.; Gallagher, T.; Brown, P.; Huffman, C. *J. Am. Chem. Soc.* **1984**, *106*, 2105−2114. (b) Gallagher, T.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2086−2087.
(4) Kuehne, M. E.; Seaton, P. J. *J. Org. Chem.* **1985**, *50*, 4790−4796.
(5) Harrington, P.; Kerr, M. A. *Tetrahedron Lett.* **1997**, 5949−5952
(6) Kerr, M. A.; Keddy, R. G. *Tetrahedron Lett.* **1999**, 5671−5675.

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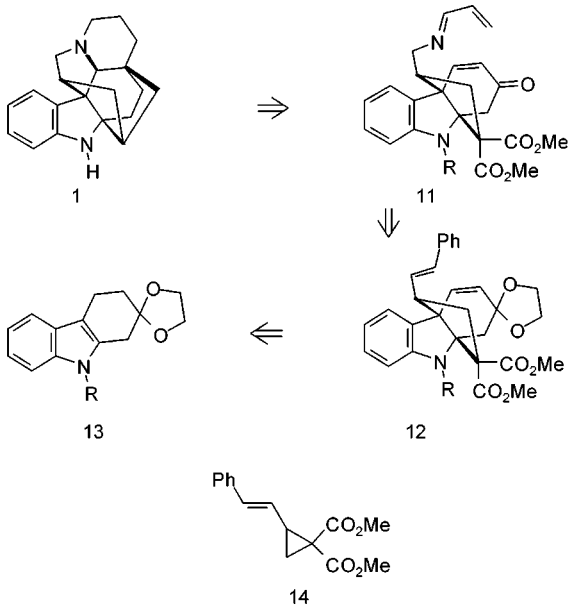
Scheme 2



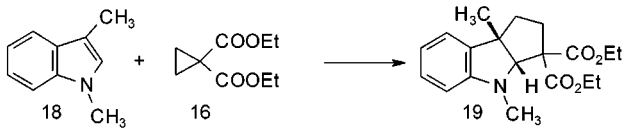
styrenyl-substituted cyclopropane **14**. Herein, we present a detailed discussion of the annulation reaction, its scope and limitations, substrate tolerance, and the application to the chemical synthesis of the architecturally complex kopsane alkaloids.

Results and Discussion

Initially a study was undertaken to probe the optimal conditions for the annulation reaction. Skatole **15** appeared to be the ideal substrate based on its availability and structural suitability; however, complications arose in which the only product observed, in the reaction with cyclopropane **16**, was one in which the nitrogen atom (now removed from participation in aromaticity) attacked a second equivalent of the cyclopropane giving **17** in 75% yield. To focus our attention on the annulation reaction and avoid *N*-alkylation, 1,3-dimethylindole was then chosen for the optimization study along with the commercially available diethyl 1,1-cyclopropanedicarboxylate.

Table 1 illustrates the results of a study in which the conditions of the annulation reaction were varied. Several items from this table are worthy of note. The first and most starkly obvious observation from the table is that the yields appear to be mediocre at best. This belies the fact that the reactions are extremely free of byproducts and leads one to question the reason for the low yields. The only other isolable material from the reaction is the indole starting material. No cyclopropane was present upon workup. It is suspected that the cyclopropane underwent decomposition that was competitive with the desired reaction to form byproducts which were never isolated and did not interfere with the purification of the desired cycloadducts. Although a comprehensive screening of solvents was not carried out, acetonitrile appeared to be the solvent of choice. Polar solvents such as ethanol, DMF, and THF were detrimental to the course of the reaction, presumably due to coordination to the Lewis acid catalyst. Our previous experience suggested that we employ ytterbium triflate[7] as a Lewis acid although we surveyed several others such as $BF_3{\cdot}Et_2O$, $ZnCl_2$, and $Sc(OTf)_3$ with little success. Typically, 5 mol % of $Yb(OTf)_3$ was employed; increased quantities afforded no advantage. Finally, it was noted that for the simple system, high pressures[8] and thermal conditions were equally effective in promoting the cycloaddition.

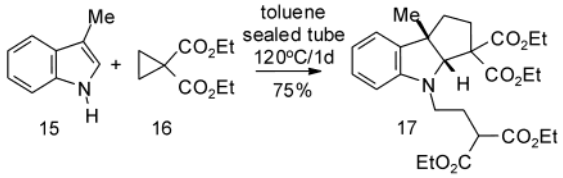
Table 1. Optimization of Annulation Conditions



entry	Lewis acid	solvent	conditions	time	yield (%)
1	$Yb(OTf)_3$[a]	CH_3CN	reflux	2 d	37
2	$Yb(OTf)_3$	CH_3CN	120 °C	21 h	41
3	$Yb(OTf)_3$	CH_3CN	13 kbar/rt	1 d	11
4	$Yb(OTf)_3$	CH_3CN	13 kbar/rt	3 d	24
5	$Yb(OTf)_3$	CH_3CN	13 kbar/rt	5 d	34
6	$Yb(OTf)_3$	CH_3CN	13 kbar/rt	7 d	39
7	$Sc(OTf)_3$	CH_3CN	13 kbar/rt	7 d	35
8	$Yb(OTf)_3$	CH_2Cl_2	13 kbar/rt	7 d	13
9	$Yb(OTf)_3$	$PhCH_3$	165 °C	1 d	33
10	$Yb(OTf)_3$	THF	96 °C	1 d	13
11	$Yb(OTf)_3$	EtOH	120 °C	1 d	8
12	BF_3Et_2O	CH_2Cl_2	rt	4 d	5
13	$ZnCl_2$	THF	95 °C	1 d	4
14	$ZnCl_2$	CH_3CN	120 °C	1 d	2
15	$Yb(OTf)_3$	DMF	reflux	1 d	1

[a] Used as the hydrate.

Scheme 3



In most of the reactions performed at elevated temperatures during the course of the optimization study, a byproduct **22** was formed in very small amounts, where the cyclopropane **16** had alkylated the indole **18** at the 2-position (Scheme 4). It has been shown in related systems[9] that this is likely a migration (from **20** to **21**) followed by proton loss, rather than a direct attack at the 2-position.

The reaction outlined in Table 1 was applied to a variety of substrates[10] (Chart 1), and the results are shown in Table 2. Several items are worthy of note. The

(7) The mild, noncorrosive, yet reactive nature makes this catalyst an excellent choice for work in our high pressure chemical reactor. Accidental contact of a corrosive catalyst with the highly machined surfaces of the reactor bore could lead to destruction of the instrument. For the use of ytterbium triflate in synthesis, see: (a) Marshman, R. W. *Aldrichimica Acta* **1995**, *28*, 77, and (b) Kobayashi, S. In *Lanthanides: Chemistry and Use in Organic Synthesis*; Kobayashi, S., Ed.; Springer: New York, 1999; pp 63−118.

(8) For general references on hyperbaric conditions in organic synthesis, see: (a) Klarner, F.-G.; Diedrich, M. K.; Wigger, A. E. In *Chemistry Under Extreme or Non-Classical Conditions*; van Eldik, R.; Hubbard, C. D., Eds.; Wiley: New York, 1997; Chapter 3. (b) Jurczak J.; Gryko, D. T. In *Chemistry Under Extreme or Non-Classical Conditions*; van Eldik, R.; Hubbard, C. D., Eds.; Wiley: New York, 1997; Chapter 4. (c) Isaacs, N. S. In *High-Pressure Techniques in Chemistry and Physics*; Holzapfel, W. B.; Isaacs, N. S., Eds.; Oxford: New York, 1997; Chapter 7.

(9) Jackson, A. H.; Naidoo, B,; Smith, P. *Tetrahedron* **1968**, *24*, 6119−6129.

(10) The cyclopropanes were prepared according to literature procedures. For the preparation of **27**, **28**, and **29**, see: Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353−1364. For the preparation of **26**, see: Kierstead, R. W.; Linstead, R. P.; Weedon, B. C. L. *J. Chem. Soc.* **1952**, 3610−3616.

Scheme 4

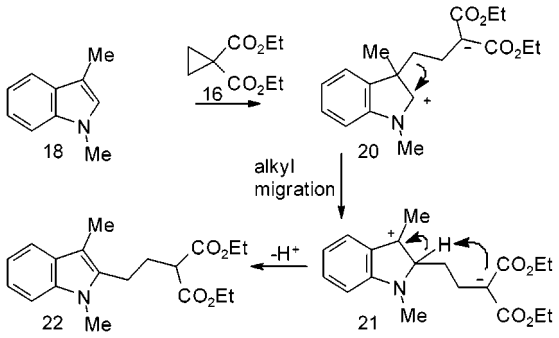
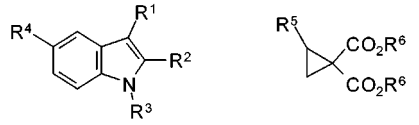


Chart 1. Reaction Substrates for Annulation Study

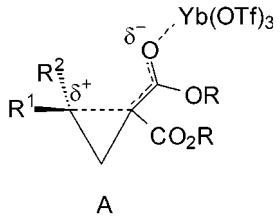


	R^1	R^2	R^3	R^4
18	Me	H	Me	H
23	Me	H	Bn	H
24	Me	Me	Me	H
25	Me	H	Me	OMe

	R^5	R^6
16	H	Et
26	$CH=CH_2$	Me
27	Me	Me
28	Ph	Et
29	CH=CHPh	Me

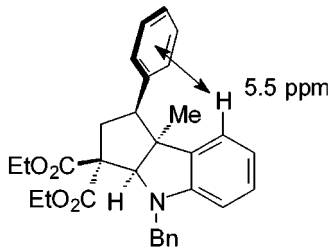
reaction appears to be general in that a variety of substitution motifs are tolerated. In cases where the cyclopropane diester bore additional substituents (**26**, **27**, **28**, and **29**), attack of the nucleophile occurred exclusively at the substituted carbon. This may be rationalized by assuming that the complexation of the Lewis acid to one of the ester carbonyls results in a species such as **A** (Figure 1). Substituents that stabilize the adjacent developing positive charge should facilitate the reaction electronically. Sterically, however, the reactions can be expected to be more difficult. If the substituent is a methyl group (e.g., cyclopropane **27**), steric factors predominate and high pressures are required to overcome the steric barrier (although attack still occurred at the substituted cyclopropyl carbon). In the case of a vinyl, phenyl, or styrenyl moiety (e.g. **26**, **28**, **29**), the electronic effects clearly predominate and the reaction proceeds in generally good yield at 0 °C and one atmosphere, in a shorter period of time. In general, there is little diastereoselectivity observed in the case of the methyl cyclopropane, but the vinyl-, phenyl-, and styrenyl-substituted cyclopropanes reacted with a diastereoselectivity of between 5:1 and 10:1 in favor of the isomer having a trans relationship between the angular methyl group and the substituent on the newly formed cyclopentane ring.[11] It is interesting to note that this substituent is spatially quite close to the hydrogen at the 4-position of the indole (Figure 2). This was further evidenced by the dramatic upfield shift for this proton in the ^{1}H NMR spectrum to about 5.5 ppm. In all cases the major diastereomer could be recrystallized to purity for full characterization. The origin of the selectivity is unclear at present. The

(11) For compounds **35**, **45**, and **51**, the relative stereochemistry was determined by X-ray crystallography. For all other compounds, the relative stereochemistry was determined through observation of the appropriate NOESY correlations.



A

Figure 1. Activation of cyclopropane diesters by $Yb(OTf)_3$.



30

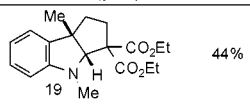
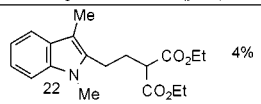
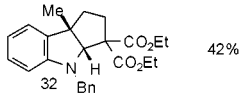
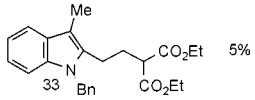
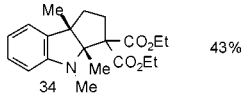
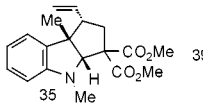
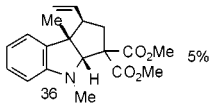
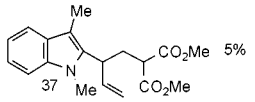
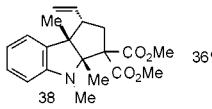
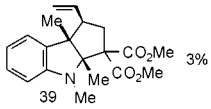
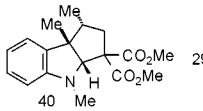
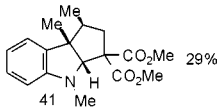
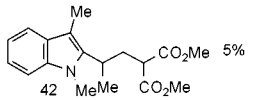
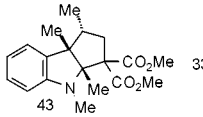
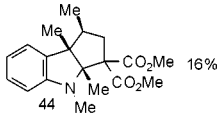
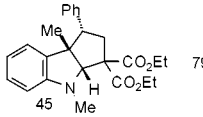
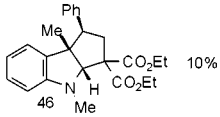
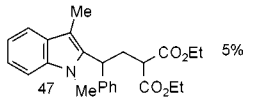
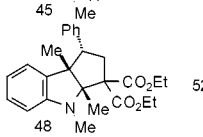
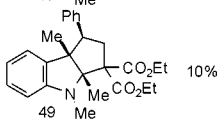
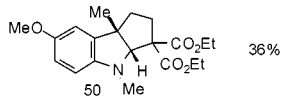
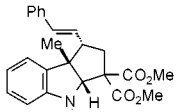
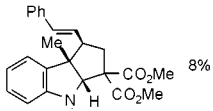
Figure 2. Annulation product **30**.

presence of a methyl substituent at the 2-position of the starting indole was reasonably well tolerated. Of course, in such cases an analogous rearrangement as in Scheme 4 was not possible and the reactions required more forcing conditions. It is notable that a very congested system involving three contiguous quaternary centers next to a tertiary center can be prepared in reasonable yields; a testament to the efficiency of the reaction.

The 2-alkylated indole resulting from rearrangement were formed in about 5% yield or less. It is interesting to note that if the reaction of 1-benzyl-3-methylindole **23** with **28** was performed at higher temperature, rearrangement was the primary mode of reaction producing **31** in 76% yield (Scheme 5). In addition, it was observed that subjection of the annulation product **30** to thermal conditions produced **31** as well as about 5% of **23**, providing evidence for the reversibility of this process. In a separate experiment, indole **18** was treated with cyclopropane **28** at ambient temperature in the presence of 5 mol % $Yb(OTf)_3$ for 7 days. Daily aliquots analyzed by ^{1}H NMR showed that, other than the initially formed ~5% of compound **47**, no additional rearrangement product was formed. In addition, when the annulation products **45** and **46** were treated under the same conditions, no conversion to **47** was observed. Clearly, elevated temperatures are required to effect significant formation of the thermodynamic product **47**.

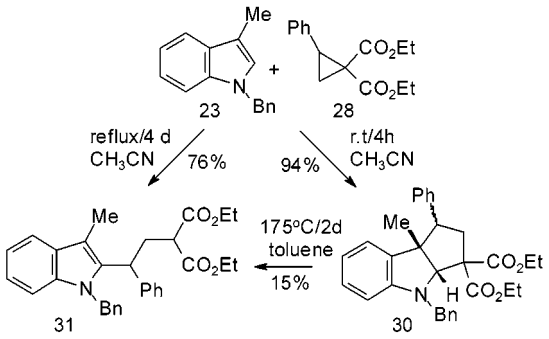
The success of the reactions of 1,2,3-trimethylindole with cyclopropanes held great promise for the extension of this methodology to include tetrahydrocarbazoles as the nucleophiles. Scheme 6 shows the results of an initial survey of several cyclopropane diesters in reaction with *N*-methyltetrahydrocarbazole **53**. The initial reactions using the commercially available unsubstituted cyclopropane diester were unsuccessful, yielding only trace amounts of the desired adduct. The use of the methyl-substituted cyclopropane produced adducts **54a** and **55a** as a 1:1 mixture of diastereomers in 10% yield. As expected, the use of the corresponding vinyl- and phenyl-substituted cyclopropanes resulted in improved yields (21% and 46%, respectively), but again the diastereoselectivity was essentially zero. In the case of the vinyl-cyclopropane, the low yield and lack of diastereoselec-

Table 2. The Annulation of Indoles with Cyclopropane Diester

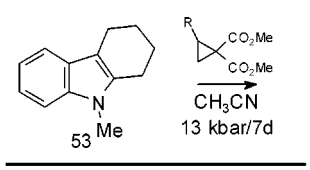
Entry	Indole	Cyclopropane	Conditions[a]	Products (yield)[b,c]	Rearrangement Product (yield)
1	18	16	sealed tube 120°C/1 d	 **19** 44%	 **22** 4%
2	23	16	sealed tube 120°C/1 d	 **32** 42%	 **33** 5%
3	24	16	13 kbar r.t./ 7d	 **34** 43%	
4	18	26	1 atm/0°C 7h	 **35** 39%  **36** 5%	 **37** 5%
5	24	26	1 atm/r.t. 2d	 **38** 36%  **39** 3%	
6	18	27	13 kbar r.t./ 7d	 **40** 29%  **41** 29%	 **42** 5%
7	24	27	13 kbar r.t./ 7d	 **43** 33%  **44** 16%	
8	18	28	1 atm/0°C 6h	 **45** 79%  **46** 10%	 **47** 5%
9	24	28	1 atm/r.t. 1d	 **48** 52%  **49** 10%	
10	25	16	sealed tube 120°C/1 d	 **50** 36%	not isolated
11	18	29	1 atm 0°C/2h	 **51** 67%  **52** 8%	not isolated

[a] All reactions were catalyzed by 5 mol% $Yb(OTf)_3$. [b] Yields refer to isolated materials. [c] The relative stereochemistry was determined by X-ray diffraction of the major isomer or by observation of the appropriate correlations in the NOESY spectra.

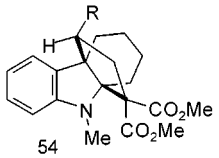
Scheme 5

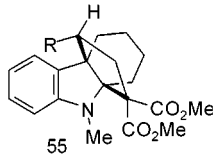


Scheme 6



	R	Yield	54:55
a	Me	10	~1:1
b	CH_2=CH	21	~1:1
c	Ph	46	~1:1
d	PhCH=CH	49	~3:1





tivity was particularly disappointing since oxidative cleavage of the olefin would provide a handle for further elaboration to the kopsane skeleton. To take advantage of the resonance stabilization provided by the phenyl group, the styryl-substituted cyclopropane **29** was employed. This would leave a pendant group which could be oxidatively cleaved for use toward the synthesis of the

kopsane alkaloids. Not surprisingly, the yield of **54d** and **55d** was comparable to that of the phenyl-substituted case but the diastereoselectivity was both unexpected and serendipitous. Compound **54d** was formed in a 3:1 ratio over **55d**. This selectivity is actually opposite to what was observed in the case of the annulation reactions involving 1,2,3-trimethylindole. In most of the cases involving substituted cyclopropanes, the major diastereomer is the one in which the substituent on the newly formed five-membered ring is anti to the angular substituent. In contrast, **54d** has the styryl group syn to the cyclohexane ring (with respect to the newly formed five-membered ring). This relative stereochemistry is the one required for future elaboration to the kopsane-type alkaloids.

In summary, we have disclosed a novel synthetic methodology that allows for the convenient cyclopentannulation of indoles with cyclopropanes. The reaction appears to be general and has been extended to include a tetrahydroarbazole as the indolic nucleophile. Efforts are under way to employ a more functionalized tetrahydrocarbazole in an approach toward the total synthesis of the kopsane alkaloids.

Experimental Section

General Considerations. All reactions were performed in anhydrous acetonitrile either as purchased from VWR (Dri-Solv) or distilled from CaH_2. $Yb(OTf)_3$ was used as the hydrate as purchased from Aldrich. TLC analysis was performed on E Merck glass plates precoated with silica gel 60 F254. Flash column chromatography (FCC) was performed on silica gel purchased from Silicycle. Yields are reported as mixtures of diastereomers with the isomeric ratio determined by integration of the ^{1}H NMR spectrum. In all cases the major isomer was recrystallized to purity for physical characterization. ^{1}H NMR spectra were recorded at 400 MHz or at 600 MHz. ^{13}C NMR spectra were recorded at 100 or 125 MHz. Mass spectra (EI) were recorded using an ionizing voltage of 70 eV.

General Procedure for Annulation of Indoles with Cyclopropanes at Ambient Pressure (Method A). The indole (2 equiv), cyclopropane (1 equiv), and $Yb(OTf)_3$ (5 mol %) were charged into a dry flask equipped with a stirring bar. Acetonitrile was added via syringe, and the mixture was stirred under an atmosphere of argon for the indicated time, at the indicated temperature. Where indicated, high-temperature reactions were performed in a sealed tube. Upon completion of the reaction, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using mixtures of EtOAc and hexanes as the eluent.

Diethyl (3a*R,8b*S**)-4,8b-Dimethyl-1,3a,4,8b-tetrahydrocyclopenta[*b*]indole-3,3(2*H*)-dicarboxylate 19. Method A.** The reaction mixture was prepared using 1,3-dimethylindole (1.452 g, 10 mmol) and diethyl-1,1-cyclopropanedicarboxylate (0.931 g, 5 mmol) and $Yb(OTf)_3$ (0.155 g, 0.25 mmol) in 5 mL of acetonitrile. This mixture was heated at 120 °C in a sealed tube for 2 days and worked up in the usual way to give after purification 0.729 g (44% yield) of **19** as a white solid. mp = 68−69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.07 (t, J = 7.7 Hz, 1H), 6.97 (d, J = 7.3 Hz, 1H), 6.70 (t, J = 7.3 Hz, 1H), 6.43 (d, J = 7.7 Hz, 1H), 4.32−4.07 (m, 5H), 2.83 (s, 3H), 2.23 (ddd, J = 13.0, 13.0, 6.1 Hz, 1H), 2.10−1.99 (m, 2H), 1.64 (ddd, J = 13.0, 13.0, 5.7 Hz, 1H), 1.46 (s, 3H), 1.27 (t, J = 6.9 Hz, 3H), 1.26 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.5, 169.0, 152.9, 137.3, 127.8, 122.3, 118.4, 108.4, 81.9, 67.2, 61.3, 61.0, 54.0, 39.0, 38.7, 32.4, 28.6, 14.1 (2 carbons). IR (thin film) υ = 1731, 1606, 1490 cm^{-1}. EIHRMS for $C_{19}H_{25}NO_4$: found 331.1787, requires 331.1783.; Anal. Calcd for $C_{19}H_{25}NO_4$: C, 68.86; H, 7.60; O, 19.31; N, 4.23. Found: C, 68.62; H, 7.66; O, 19.50; N, 4.15.

Diethyl (1S*,3a*R,8b*S**)-4,8b-Dimethyl-1-phenyl-1,3a,4,8b-tetrahydrocyclopenta[*b*]indole-3,3(2*H*)-dicarboxylate 45. Method A.** The reaction mixture was prepared using 1,3-dimethylindole (0.290 g, 2 mmol) and diethyl 2-phenyl-1,1-cyclopropanedicarboxylate (0.262 g, 1 mmol) and $Yb(OTf)_3$ (0.031 g, 0.05 mmol) in 2 mL of acetonitrile. This mixture was stirred at 0 °C for 6 h and worked up in the usual way to give after purification 0.362 g (89% yield) of **45** and **46** (∼79:10) as a white solid. Physical data for **45**: mp = 80−82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.26−7.25 (m, 3H), 7.03−6.97 (m, 3H), 6.43 (d, J = 8.2 Hz, 1H), 6.30 (t, J = 7.4 Hz, 1H), 5.47 (d, J = 7.4 Hz, 1H), 4.4 (s, 1H), 4.38−4.28 (m, 2H), 4.25−4.14 (m, 2H), 3.04 (dd, J = 14.8, 4.7 Hz, 1H), 2.83 (s, 3H), 2.72 (dd, J = 14.8, 12.8 Hz, 1H), 2.28 (dd, J = 12.8, 4.7, 1H), 1.54 (s, 3H), 1.32 (t, J = 7.0 Hz, 3H), 1.28 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.4, 168.7, 153.9, 138.3, 132.2, 129.0, 127.8, 127.7, 126.9, 125.6, 117.4, 108.4, 82.3, 65.0, 61.5, 61.2, 57.4, 53.3, 39.4, 36.3, 28.6, 14.1, 14.0. IR (thin film) υ = 1730, 1603, 1488 cm^{-1}. EIHRMS for $C_{25}H_{29}NO_4$: found 407. 2101, requires 407.2097. Anal. Calcd for $C_{25}H_{29}NO_4$: C, 73.69; H, 7.17; O, 15.70; N, 3.44. Found: C, 73.95; H, 7.26; O, 15.49; N, 3.40.

General Procedure for Annulation of Indoles with Cyclopropanes at High Pressures (Method B). The reaction mixture as prepared above was transferred to a length of heat-shrinkable Teflon tubing sealed at one end with a brass clamp. The transfer was completed with a small amount of acetonitrile. Excess air was squeezed from the tubing, and it was sealed with a second brass clamp. The vessel was inserted into a LECO Tempres HPC 200 reactor and pressurized at 13 kbar for the indicated period of time. The reaction mixture was worked up as above.

Dimethyl (1*R,3a*R**,8b*S**)-3a,4,8b-Trimethyl-1,3a,4,8b-tetrahydrocyclopenta[*b*]indole-3,3(2*H*)-dicarboxylate 40. Method B.** The reaction mixture was prepared using 1,3-dimethylindole (0.290, 2 mmol), dimethyl 2-methyl-1,1-cyclopropanedicarboxylate (0.172 g, 1 mmol), and $Yb(OTf)_3$ (0.031 g, 0.05 mmol) in 1 mL of acetonitrile. This mixture was held at 13 kbar pressure for 7 days and worked up in the usual way to give after purification 0.184 g (58% yield) of **40** and **41** (∼1:1) as a white solid. Physical data for **40**: mp = 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.09 (t, J = 7.2 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1 H), 6.68 (t, J = 7.6 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1 H), 4.32 (s, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 2.77 (s, 3H), 2.11 (dd, J = 12.4, 4.8 Hz, 1H), 1.94 (dd, J = 14.0, 12.8 Hz, 1H), 1.87−1.79 (m, 1H), 1.43 (s, 3H), 1.01, (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.9, 169.2, 154.0, 132.7, 127.8, 125.0, 117.6, 108.6, 83.3, 65.0, 56.0, 52.6, 52.2, 42.7, 39.8, 39.0, 28.0, 14.9. IR (thin film) υ = 1734, 1605, 1488 cm^{-1}. EIHRMS for $C_{18}H_{23}NO_4$: found 317.1630, requires 317.1627. Anal. Calcd for $C_{18}H_{25}NO_4$: C, 68.12; H, 7.30; O, 20.16; N, 4.41. Found: C, 68.27; H, 7.43; O, 19.90; N, 4.34.

Dimethyl (3S*,4a*R,9a*S**)-9-Methyl-3-[(*E*)-2-pheylethenyl]-1,2,3,4-tetrahydro-9*H*-4a,9a-propanocarbazole-1,1-dicarboxylate 54d. Method B.** The reaction mixture was prepared using *N*-methyl-1,2,3,4 tetrahydrocarbazole (0.370, 2.0 mmol), dimethyl 2-(2-phenylethenyl)-1,1-cyclopropanedicarboxylate (0.573 g, 2.2 mmol), and $Yb(OTf)_3$ (0.061 g, 0.10 mmol) in 1 mL of acetonitrile. This mixture was held at 13 kbar pressure for 7 days and worked up in the usual way to give after purification 0.437 g (49% yield) of **54d** and **55d** (∼3:1) as a solid. Physical data for **54d**: ^{1}H NMR (600 MHz, C_6D_6) δ = 7.31 (d, J = 7.3 Hz, 2H), 7.19 (t, J = 7.7 Hz, 3H), 7.09 (t, J = 7.3 Hz, 1H), 7.04 (d, J = 7.0 Hz, 1 H), 6.73, J = 7.3 Hz, 1H), 6.43 (d, J = 15.8 Hz, 1H), 6.30 (d, J = 7.7 Hz, 1H), 6.28 (dd, J = 15.7, 8.8 Hz, 1H), 3.59 (ddd, J = 14.3, 8.8, 6.2 Hz, 1H), 3.39 (s, 3H), 3.11 (s, 3H), 2.89 (s, 3H), 2.42 (AB of ABX, 2 H), 2.21−2.17 (m, 1 H), 1.47−1.44 (m, 2H), 1.30−1.00 (m, 5H). ^{13}C NMR (125 MHz, C_6D_6) δ = 170.4, 169.8, 151.0, 138.0, 135.3, 132.2, 129.9, 128.8, 128.3, 127.5, 126.7, 121.7, 116.7, 104.3, 80.9, 69.4, 58.3, 51.9, 51.9, 51.8, 38.4, 29.1, 28.0, 24.6, 16.7, 16.3.; IR (thin film) υ = 1732, 1605, 1495 cm^{-1}. EIHRMS for $C_{28}H_{31}NO_4$: found 445.2247, requires 445.2254.

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Supporting Information Available: Complete experimental procedures as well as ^{1}H NMR, ^{13}C NMR, IR, MS, and combustion analysis data for compounds **18**, **32**, **34**, **35**, **38**, **40**, **43**, **45**, **48**, **50**, **51**, **54d**. X-ray crystallographic data for **30**, **35**, and **54d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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