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Supplementary Material Available: Detailed X-ray crystal data for compound **38** (12 pages). Ordering information is given on any current masthead page.

Intramolecular Diels–Alder Reactions of Indole-3-acrylates

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Indole-3-carboxaldehyde was alkylated to give the N-alkylated indole-3-carboxaldehydes **1a–d** and **4**. These were extended by two carbon atoms with methyl (triphenylphosphoranylidene)acetate to the methyl indole-3-acrylates **2a–d** and **5**. When these indoles were heated to 300 °C the (tetrahydro)carbazoles **3a–d** and **6a** were obtained. Compound **3c** represents a novel ring system. Indole-3-carboxaldehyde was also acylated to give the N-acylated indole-3-carboxaldehydes **1e,f**. These were carbon extended to the N-acylated indole-3-acrylates **2e,f** which upon heating to 300 °C gave the (tetrahydro)carbazoles **3e,f** and **6b**.

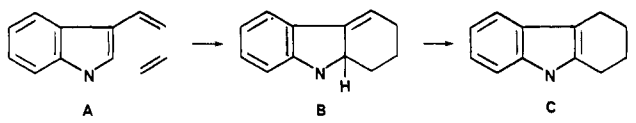
The Diels–Alder reaction as a tool for the simultaneous construction of two carbon–carbon bonds has received much attention both from synthetic[1] and theoretical[2] chemists. We have studied the intramolecular (4 + 2) cycloaddition with indole-3-acrylates substituted on the indole nitrogen with an appropriately unsaturated chain.

The classical Diels–Alder reaction with 3-vinylindoles (A) would lead to compounds of the general structure B, which then might undergo a hydrogen shift to form indoles of the general structure C (Scheme I). A direct reaction from A → C, with B serving as an intermediate, would disguise the Diels–Alder reaction and make this type of ring construction a priori less obvious. The reaction A → B has been described for the intermolecular addition of 3-vinylindoles[3] to 1,4-quinones and other dienophiles.

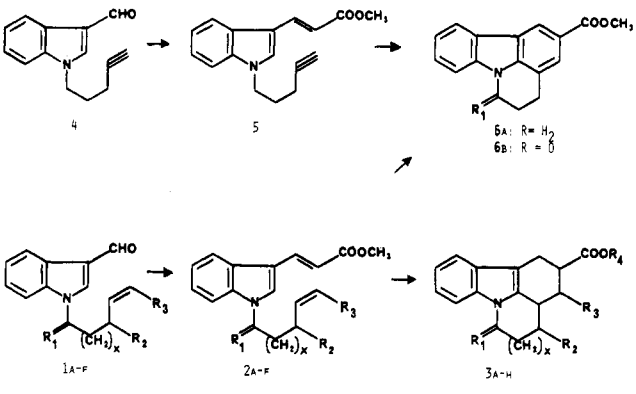
The first step in the preparation of the precursor for an intramolecular Diels–Alder reaction was the alkylation of the sodium salt of indole-3-carboxaldehyde with 5-bromopentene[4] to the aldehyde **1a** in 87% yields. From this compound the N-substituted indole-3-acrylic acid methyl ester (**2a**) was obtained via a Wittig reaction with methyl (triphenylphosphoranylidene)acetate[5] in refluxing toluene in 80% yield (Scheme II). Cyclization of **2a** was accomplished by heating the compound to 300 °C for 2 h with exclusion of air under an atmosphere of nitrogen at normal pressure. Crystallization of the cold glassy product from ether allowed the isolation of 43% of a pure isomer of mp 119–121 °C. The second isomer was secured in 13% yield from the mother liquors of the cyclization and had a melting point of 99–101 °C.

The assignment of the stereochemistry to the two isomers was based on the 500-MHz NMR spectra of the two compounds. Two-dimensional carbon–hydrogen correlated spectra on $\mathbf{3a}_2$ readily allowed the assignment of all carbon and proton resonances except for those associated with C5-H and C3a-H (see Figure 3). The key protons for the assessment of the stereochemisty of $\mathbf{3a}_1$ and $\mathbf{3a}_2$ are on carbons 4 and 5. The spectra of those protons are shown in Figures 1 and 2, respectively. In the case of the higher melting anti isomer $\mathbf{3a}_1$, the resonance at δ 1.57 can be assigned to the axial proton on C4. The coupling pattern observed is due to a combination of one geminal and one

Scheme I



Scheme II



	x	R_1	R_2	R_3	R_4
a	1	H_2	H	H	CH_3
b	2	H_2	H	H	CH_3
c	1	H_2	$(CH_2)_2$		CH_3
d	1	H_2	$(CH_2)_3$		CH_3
e	1	O	H	H	CH_3
f	1	O	$(CH_2)_3$		CH_3
g	1	H_2	H	H	H
h	1	H_2	$(CH_2)_3$		H

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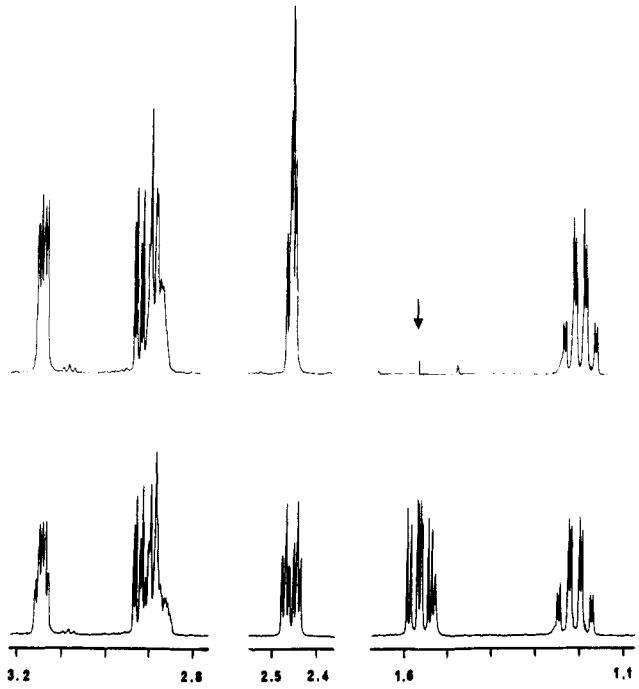

Figure 1. Partial 500-MHz NMR spectrum of $3a_1$. Lower trace represents the normal spectrum; upper trace represents the decoupled spectrum with frequency of irradiation indicated by the arrow.

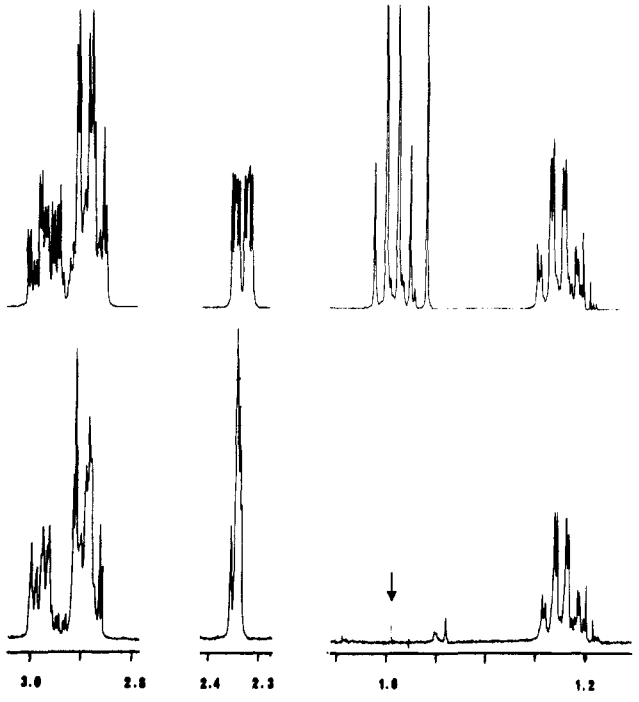

Figure 2. Partial 500-MHz NMR spectrum of $3a_2$. Upper trace represents the normal spectrum; lower trace represents the decoupled spectrum with frequency of irradiation indicated by the arrow.

trans coupling of similar magnitude with one small cis coupling, while in the case of the lower melting syn isomer

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Table I. ^{13}C NMR Data, Including DEPT of $3a_1$ and $3a_2$

$3a_1$	DEPT	$3a_2$	assignt
22.4	CH_2	23.5	C2
23.4	CH_2	24.3	C6
27.8	CH_2	27.8	C3
31.3	CH_2	32.8	C4
30.1	CH	33.7	C3a
38.3	CH	41.0	C5
42.4	CH_2	42.4	C1
51.7	CH_3	51.6	OCH_3
105.0	C	105.5	C6a
109.2	CH	109.0	C10
118.0	CH	117.8	C9
119.3	CH	119.4	C8
120.7	CH	120.7	C7
128.1	C	127.7	C6b
137.0	C	136.9	C10a
137.7	C	137.7	C3b
175.6		175.8	C=O

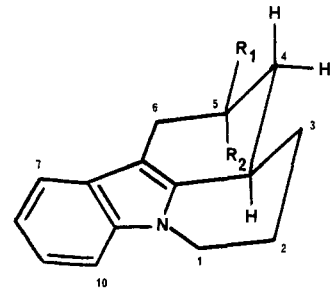

Figure 3. $3a_1$: R_1 = H; R_2 = COOMe. $3a_2$: R_1 = COOMe; R_2 = H.

$3a_2$, the same axial proton gave rise to a quartet due to a combination of one geminal and two trans couplings of similar magnitude. The proton assigned to C5 (δ 3.15) for compound $3a_1$ is clearly seen to be in equatorial disposition while the same proton (δ 2.98) in compound $3a_2$ seems to be axially oriented (see Figures 1 and 2). For a definitive assignment we had to distinguish between the two axially oriented protons on C3a and C5, respectively. Homo decoupling at the chemical shift δ 1.25 which was assigned to the axial proton on C3 caused a change of the spectrum of the signal at δ 2.90 and no change at the signal at δ 2.98, confirming the identity of the axial proton on C5, thus allowing the unequivocal assignment of all carbon and proton resonances.

The assignment of the stereochemistry is also consistent with the observed ^{13}C NMR spectra of the isomers $3a_1$ and $3a_2$ (see Table I). Upfield shifts for the aliphatic carbons C2, C3a, C4, C5, and C6 for the isomer $3a_1$ relative to the shifts observed for the isomer $3a_2$ indicate the ester in $3a_1$ is axially disposed.[6] These data would be incompatible with one of the ester containing rings existing in a boatlike conformation. The coupling patterns for the two AB protons adjacent to the indole nitrogen are virtually identical for $3a_1$ and $3a_2$, suggesting this ring conformation is the same for the two systems.

In order to test the hypothesis that compound $3a_1$ is the kinetic product of cyclization and rearranged to $3a_2$ under the reaction conditions, a sample of $3a_1$ was heated to 300 °C for 1 h under an atmosphere of argon. The crude product was analyzed by HPLC and was found to consist, besides other components which were not identified, of a mixture of $3a_1$ and $3a_2$. The ratio of the two components of interest was estimated to be 43:18, which is in close agreement with the 43:13 ratio found for the isolated products from the initial Diels–Alder cyclization. The

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same observation was made when the axial ester $3a_1$ was heated to 300 °C for 2 h. However, when compound $3a_2$ was subjected to these conditions no appreciable amount of $3a_1$ was formed. Equilibration of $3a_1$ in refluxing methanol for 1 h in the presence of sodium methoxide gave a mixture containing 44% of $3a_1$ and 56% of $3a_2$ (Figure 3).

Alkylation of indole-3-carboxaldehyde with 5-chloropentyne[7] to **4** followed by the Wittig reaction gave the indole-3-acrylate **5**. When this was subjected to 300 °C for 10 min, a dehydrogenation followed the intramolecular Diels–Alder reaction to give the carbazole **6a** in 37% yield.

The azepinocarbazole **3b** was prepared in a similar manner. Indole-3-carboxaldehyde was N-alkylated with 6-bromohexene[8] to **1b** in 87% yield. The subsequent Wittig reaction gave the indoleacrylate **2b** in 71% yield. Heating of **2b** produced the desired cyclized compound **3b** in 10% yield as a (3:5) mixture of diastereoisomers as judged from NMR spectral data of this compound.

The products of the intramolecular cyclizations described above were all tetracyclic indoles and originated from alkylations of indoles with open chain alkenes. If these were substituted by cyclic alkenes, the preparation of pentacyclic indoles should be easily accessible. To explore this possibility indole-3-carboxaldehyde was N-alkylated with 3-(2-chloroethyl)cyclopentene[9] to give **1c** in 39% yield. The transformation to the indoleacrylate **2c** was carried out in 80% yield. Heating of **2c** at 300 °C for 2 h lead to a clean cyclization product of mp 80–81 °C, which was recovered in 46% isolated yield, consisting of a 4:1 mixture of diastereoisomers as indicated by the ^{13}C NMR spectrum of **3c**. To the best of our knowledge this compound is the first representative of a new ring system.

In a similar manner indole-3-carboxaldehyde was alkylated with 3-(2-chloroethyl)cyclohexene[10] to give **1d** in 66% yield. The Wittig reaction produced the indoleacrylate **2d** in 63% yield. When this was subjected to heating at 300 °C for 2 h, the pentacyclic compound **3d** was obtained in 60% yield consisting of a mixture of diastereoisomers. A single isomer of **3d** was obtained in pure form when the above mixture was hydrolyzed under basic conditions to the acid **3h** and reesterified with diazomethane.

So far we have described the intramolecular Diels–Alder reaction of N-alkylated indoleacrylates. We have also studied the cyclization of N-acylated indoleacrylates, and we would like to illustrate this with two examples. Indole-3-carboxaldehyde was acylated with 4-pentenoyl chloride[11] in chloroform in the presence of triethylamine to give the N-acylated product **1e** in 73% yield. From this the *N*-pentenoylindole-3-acrylate **2e** was readily available in 58% yield via the Wittig reaction in refluxing toluene. Upon heating this compound to 300 °C for 5 min under nitrogen at atmospheric pressure, two compounds were obtained following column chromatography on silica gel. The less polar material was assigned structure **6b** on the basis of mass spectral and NMR evidence. Evidently the primary product of cyclization **3e** had lost 2 mol of hydrogen to form the carbazole **6b**. The immediate precursor **3e** of the dehydrogenation product was isolated as the more polar fraction of the cyclization and consisted of a mixture of diastereoisomers. The corresponding acid has been described[12] by Sir Robert Robinson et al. It was obtained as the minor of two products from the Fischer indole reaction of (4-carboxy-1-oxocyclohex-2-yl)-3-propionic acid with phenylhydrazine.

Indole-3-carboxaldehyde was acylated with 2-(2-cyclohexen-1-yl)acetyl chloride[13] as well to give **1f** followed by the Wittig reaction yielding the N-acylated indoleacrylate **2f**. After heating to 300 °C for 10 min, a mixture of diastereoisomers was obtained. A single isomer of **3f** was isolated in pure form following purification by chromatography on silica gel.

Experimental Section

Proton magnetic resonance spectra were obtained on JEOL FX 200 or a Bruker AM-500 spectrometer and are recorded in δ values relative to TMS (tetramethylsilane) as internal standard. Infrared spectra were recorded on an Analect Instrument FX-6200 FTIR and are measured in methylene chloride unless stated otherwise. Thin-layer chromatography (TLC) was carried out on glass plates coated with silica gel HF-254 (E. Merck AG). Mass spectra were measured on a LKB 9000 (low resolution) or on a VG 7070E (high resolution) mass spectrometer. Melting points were taken on a Hoeffler melting point apparatus and are not corrected.

1-(4-Pentenyl)-1*H*-indole-3-carboxaldehyde (1a). In a 1-L flask, 27.8 g (0.66 mol) of 57% NaH was washed 3× with ether and suspended in 50 mL of dry DMF. A solution of 87 g (0.6 mol) of commercial indole-3-carboxaldehyde[14] in 300 mL of DMF was added dropwise. The temperature reached 60 °C. The mixture was sitrred at 70 °C for 30 min. Then 94.5 g (0.63 mol) of commercial 5-bromopentene[4] was added dropwise. After 1 h at room temperature the solvent was evaporated under high vacuum, the residue was extracted 2× with ether, washed with water, and dried (K_2CO_3). After the solvent was removed the product was distilled: yield, 87.5%; bp 160–163 °C (0.3 mmHg); NMR 1.7–2.2 (m, 4, 2 CH_2), 4.05 (t, 2, J = 6 Hz, NCH_2), 4.8–5.2 (m, 2, $=CH_2$), 5.4–6.0 (m, 1, =CH), 7.1–7.4 (m, 3, Ar H), 7.58 (s, 1, NCH=), 8.1–8.4 (m, 1, Ar H), 9.92 (s, 1, CHO); IR 1540, 1665 cm^{-1}.

1-(4-Hexenyl)-1*H*-indole-3-carboxaldehyde (1b). Prepared from 84.5 g (0.6 mol) of indole-3-carboxaldehyde, 15.6 g (0.65 mol) of sodium hydride, and 100 g (0.61 mol) of 6-bromohexene[8] in DMF as described above, 114.5 g of the product was obtained: yield 87%; bp 185–190 °C (0.5 mmHg); MS, m/e 227 [M^+]; NMR 1.0–2.4 (m, 6, 3 CH_2), 4.07 (t, 2, J = 7 Hz, NCH_2), 4.7–5.2 (m, 2, $=CH_2$), 5.4–6.1 (m, 1, =CH), 7.1–7.4 (m, 3, Ar H), 7.62 (s, 1, NCH=), 8.1–8.5 (m, 1, Ar H), 9.88 (s, 1, CHO); IR 1530, 1660 cm^{-1}. Anal. Calcd for $C_{15}H_{17}NO$ (227.3): C, 79.3; H, 7.5;, N, 6.2. Found: C, 78.7; H, 7.4; N, 6.1.

1-[2-(2-Cyclopenten-1-yl)ethyl]-1*H*-indole-3-carboxaldehyde (1c). Prepared from 14.5 g (0.1 mol) of indole-3-carboxaldehyde, 2.7 g (0.11 mol) of sodium hydride, and 14 g (0.11 mol) of 3-(2-chloroethyl)cyclopentene[9] in 300 mL of absolute DMF following the procedures described above, 9.5 g of product was obtained after crystallization from toluene/hexane: yield, 39%; bp 172–176 °C (0.13 mmHg); mp 59–60 °C; MS, m/e 239 [M^+]; NMR 1.2–2.8 (m, 7, 3 CH_2 + CH), 4.17 (t, 2, J = 7.5 Hz, NCH_2), 5.4–5.9 (m, 2, CH=CH), 7.1–7.5 (m, 3, Ar H), 7.67 (s, 1, NCH=), 8.1–8.4 (m, 1, Ar H), 10.0 (s, 1, CHO); IR 1540, 1660 cm^{-1}. Anal. Calcd for $C_{16}H_{17}NO$ (239.3): C, 80.3; H, 7.2; N, 5.9. Found: C, 80.1; H, 7.4; N, 6.2.

1-[2-(2-Cyclohexen-1-yl)ethyl]-1*H*-indole-3-carboxaldehyde (1d). From 25 g (0.17 mol) of indole-3-carboxaldehyde, 4.5 g (0.2 mol) of sodium hydride, and 25 g (0.17 mol) of 3-(2-chloroethyl)-cyclohexene[10] in DMF as described above, crude **1d** was obtained. The crude product was crystallized from ether/hexane, and the mother liquors were chromatographed on silica gel with toluene to give a total of 29 g of product: yield, 66%; mp 80–81

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°C; MS, *m/e* 253 [M⁺]; NMR 1.0–2.3 (m, 9, 4 CH_2 + CH), 4.07 (t, 2, *J* = 7 Hz, NCH_2), 5.3–5.9 (m, 2, HC=CH), 7.1–7.4 (m, 3, Ar H), 7.6 (s, 1, NCH=), 8.1–8.4 (m, 1, Ar H), 9.9 (s, 1, CHO); IR 1540, 1665 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO$ (253.3): C, 80.6; H, 7.6; N, 5.5. Found: C, 80.4; H, 7.9; N, 5.3.

1-(4-Pentenoyl)-1*H*-indole-3-carboxaldehyde (1e). To an ice-cold suspension of 5.8 g (0.04 mol) of indole-3-carboxaldehyde in 200 mL of chloroform and 8.1 g (0.08 mol) of triethylamine was added dropwise a solution of 5.3 g (0.05 mol) 4-pentenoyl chloride[11] in 100 mL of chloroform. The mixture was stirred at room temperature overnight, then washed with 2 N HCl solution and 2 N sodium carbonate, dried over sodium sulfate, and chromatographed over silica gel with toluene to give 6.6 g of the desired product: yield, 73%; mp 96–97 °C; MS, *m/e* 227 [M⁺]; NMR 2.4–2.8 (m, 2, CH_2), 2.8–3.2 (m, 2, CH_2), 4.9–5.4 (m, 2, $=CH_2$), 5.6–6.3 (m, 1, =CH), 7.2–7.5 (m, 2, Ar H), 7.97 (s, 1, NCH=), 8.0–8.4 (m, 2, Ar H), 10.0 (s, 1, CHO); IR 1680, 1735 cm^{-1}. Anal. Calcd for $C_{14}H_{13}NO_2$ (227.25): C, 74.0; H, 5.8; N, 6.2. Found: C, 74.0; H, 5.8; N, 6.5.

1-[2-(2-Cyclohexen-1-yl)acetyl]-1*H*-indole-3-carboxaldehyde (1f). A mixture of 34.1 g (0.24 mol) of indole-3-carboxaldehyde and 47.5 g (0.47 mol) of triethylamine in 500 mL of chloroform was treated dropwise with a solution of 40 g (0.25 mol) of 2-(2-cyclohexen-1-yl)acetyl chloride[13] in 100 mL of chloroform. The mixture was stirred at room temperature overnight, washed with 2 N HCl followed by 2 N K_2CO_3, and then dried over Na_2SO_4. The crude product was chromatographed over silica gel with toluene to give 42.4 g of crystalline product: yield, 67%; mp 99–101 °C; MS, *m/e* 267 [M⁺]; NMR 1.2–2.3 (m, 6, 3 CH_2), 2.7–3.1 (m, 3, CH_2 + CH), 5.4–6.0 (m, 2, CH=CH), 7.1–7.5 (m, 2, Ar H), 8.0 (s, 1, NCH=), 8.1–8.5 (m, 2, Ar H), 10.0 (s, 1, CHO); IR 1560, 1680, 1730 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_2$ (267.3): C, 76.4; H, 6.4; N, 5.2. Found: C, 76.0; H, 6.6; N, 5.2.

Methyl 3-[1-(4-Pentenyl)-1*H*-indol-3-yl]-2-propenoate (2a). A mixture of 43 g (0.2 mol) of aldehyde **1a** and 67 g (0.2 mol) of methyl(triphenylphosphoranylidene)acetate[5] in 300 mL of toluene was heated to reflux overnight. The solvent was evaporated and the residue chromatographed on silica gel to give 43.6 g of the product: yield, 80%; mp 94–95 °C; MS, *m/e* 269 [M⁺]; NMR 1.7–2.2 (m, 4, CH_2CH_2), 3.77 (s, 3, OCH_3), 4.05 (t, 2, *J* = 6.5 Hz, NCH_2), 4.8–5.2 (br, 2) and 5.2–6.0 (br, 1, CH_2=CH), 6.4 (d, 1, *J* = 16 Hz, =CH), 7.0–7.4 (m, 4, Ar H), 7.7–8.0 (m, 1, NCH=), 7.9 (d, 1, *J* = 16 Hz, =CH); IR 1540, 1630, 1710 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_2$ (269.2): C, 75.8; H, 7.1; N, 5.2. Found: C, 75.8; H, 7.2; N, 5.1.

Methyl 3-[1-(4-Hexenyl)-1*H*-indol-3-yl]-2-propenoate (2b). Prepared from 68 g (0.3 mol) of aldehyde **1b** and 100 g (0.3 mol) of methyl(triphenylphosphoranylidene)acetate in 400 mL of toluene as described above and after chromatography on silica gel with toluene, 60 g of product was obtained: yield, 71%; mp 65–66 °C; MS, *m/e* 283 [M⁺]; NMR 1.2–2.4 (m, 6, 3 CH_2), 3.77 (s, 3, OCH_3), 4.03 (t, 2, *J* = 7 Hz, NCH_2), 4.8–5.2 (m, 2, $=CH_2$), 5.4–6.2 (br, 1, =CH), 6.33 (d, 1, *J* = 16 Hz, =CH), 7.2–7.5 (m, 4, Ar H), 7.8–8.2 (m, 1, NCH=), 7.83 (d, 1, *J* = 16 Hz, =CH); IR 1530, 1630, 1700 cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO_2$ (283.36): C, 76.3; H, 7.5; N, 4.9. Found: C, 76.2; H, 7.5; N, 4.8.

Methyl 3-[1-[2-(2-Cyclopenten-1-yl)ethyl]-1*H*-indol-3-yl]-2-propenoate (2c). From 7.2 g (0.03 mol) of **1c** and 11.2 g (0.033 mol) of methyl(triphenylphosphoranylidene)acetate in 100 mL of refluxing toluene overnight crude **2c** was obtained. Purification on silica gel with the same solvent gave 7.1 g of product: yield, 80%; mp 76–77 °C; MS, *m/e* 295 [M⁺]; NMR 1.0–2.8 (m, 7, 3 CH_2 + CH), 3.80 (s, 3, OCH_3), 4.02 (t, 2, *J* = 7 Hz, NCH_2), 5.4–5.8 (m, 2, HC=CH), 6.35 (d, 1, *J* = 16 Hz, =CH), 7.0–7.4 (m, 4, Ar H), 7.7–8.0 (m, 1, NCH=), 7.85 (d, 1, *J* = 16 Hz, =CH); IR 1540, 1630, 1700 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_2$ (295.37): C, 77.3; H, 7.2; N, 4.7. Found: C, 77.7; H, 7.6; N, 4.7.

Methyl 3-[1-[2-(2-Cyclohexen-1-yl)ethyl]-1*H*-indol-3-yl]-2-propenoate (2d). From 23.5 g (0.09 mol) of aldehyde **1d** and 31 g (0.09 mol) of methyl (triphenylphosphoranylidene)acetate in 300 mL of toluene as described above crude **2d** was obtained. The crude product was purified on a silica gel column with toluene to give 18.1 g of the product: yield, 63%; mp 94–95 °C; MS, *m/e* 309 [M⁺]; NMR 1.0–2.2 (m, 9, 4 CH_2 + CH), 3.81 (s, 3, OCH_3), 4.15 (t, 2, *J* = 7 Hz, NCH_2), 5.4–5.9 (m, 2, CH=CH), 6.4 (d, 1, *J* = 16 Hz, CH=), 7.1–7.5 (m, 4, Ar H), 7.8–8.0 (m, 1, NCH=), 7.9 (d, 1, *J* = 16 Hz, CH=); IR 1530, 1630, 1700 cm^{-1}. Anal. Calcd for $C_{20}H_{23}NO_2$ (309.4): C, 77.6; H, 7.5; N, 4.5. Found: C, 77.8; H, 7.7; N, 4.3.

Methyl 3-[1-(4-Pentenoyl)-1*H*-indol-3-yl]-2-propenoate (2e). Prepared from 59 g (0.26 mol) of **1e** and 87 g (0.26 mol) of methyl (triphenylphosphoranylidene)acetate in 500 mL of toluene as described above 42.7 g of the product was obtained: yield, 58%; mp 103–105 °C; MS, *m/e* 283 [M⁺]; NMR 2.3–3.1 (m, 4, 2 CH_2) 3.8 (s, 3, OCH_3), 4.9–5.3 (m, 2, $=CH_2$), 5.6–6.2 (m, 1, =CH), 6.4 (d, 1, *J* = 16 Hz, =CH), 7.1–7.8 (m, 3, Ar H), 7.5 (s, 1, NCH=), 7.67 (d, 1, *J* = 16 Hz, =CH), 8.3–8.5 (m, 1, Ar H); IR 1550, 1640, 1720 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_3$ (283.3): C, 72.1; H, 6.1; N, 4.9. Found: C, 72.1; H, 6.3; N, 5.2.

Methyl 3-[1-[2-(2-Cyclohexen-1-yl)acetyl]-1*H*-indol-3-yl]-2-propenoate (2f). A mixture of 40 g (0.15 mol) of **1f** and 49 g (0.15 mol) of methyl (triphenylphosphoranylidene)acetate[5] in 400 mL of toluene was heated to reflux for 12 h and then chromatographed over silica gel to give 38 g of product: yield, 78.5%; mp 109–110 °C; MS, *m/e* 323 [M⁺]; NMR 1.2–2.4 (m, 6, 3 CH_2), 2.7–2.9 (3, CH_2 + CH), 3.8 (s, 3, OCH_3), 5.4–5.9 (m, 2, CH=CH), 6.47 (d, 1, *J* = 16 Hz, =CH), 7.2–7.5 (m, 2, Ar H), 7.63 (s, 1, NCH=), 7.70 (d, 1, *J* = 16 Hz, =CH), 7.6–7.9 (m, 1, Ar H), 8.4–8.6 (m, 1, Ar H); IR 1640, 1715 cm^{-1}. Anal. Calcd for $C_{20}H_{21}NO_3$ (323.4): C, 74.3; H, 6.6; N, 4.3. Found: C, 73.9; H, 6.7; H, 4.1.

2,3,3a,4,5,6-Hexahydro-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylic Acid Methyl Ester (3a). Under an atmosphere of nitrogen, 50 g (0.18 mol) of **2a** was heated to 300 °C for 2 h. The cold residue was crystallized from ether to give 20.8 g of the anti isomer $\mathbf{3a}_1$: yield, 43%; mp 119–121 °C; MS, *m/e* 269 [M⁺]; NMR (500 MHz) 1.2–1.3 (d/q, 1, C3-H_a), 1.5–1.6 (d/t, 1, C4-H_a), 2.0–2.1 (m, 1, C2-H_a), 2.1–2.18 (m, 1, C3-H_e), 2.18–2.25 (m, 1, C2-H_e), 2.4–2.5 (t/d, 1, C4-H_e), 2.8–2.9 (m, 2, C_6-H_a, C3a-H), 3.1–3.2 (m, 1, C5-H_e), 3.3–3.4 (d, 1, C6-H_e), 3.6–3.7 (m, 1, C1-H_a), 3.67 (s, 3, OCH_3), 4.2–4.3 (m, 1, C1-H_e), 7.0–7.5 (m, 4, Ar H); IR 1730 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_2$ (269.33): C, 75.8; H, 7.1; N, 5.2. Found: C, 75.5; H, 7.0; N, 5.0. The same product was obtained when a sample of the acid **3g** was treated with diazomethane followed by recrystallization from ether/hexane. From the mother liquors of the cyclization the syn isomer $\mathbf{3a}_2$ was obtained: yield, 13%; mp 99–101 °C; MS, *m/e* 269 [M⁺]; NMR (500 MHz) 1.2–1.3 (d/q, 1, C3-H_a), 1.5–1.6 (q, 1, C4-H_a), 2.0–2.1 (m, 1, C2-H_a), 2.1–2.2 (m, 1, C3-H_e), 2.2–2.3 (m, 1, C2-H_e), 2.3–2.4 (m, 1, C4-H_e), 2.8–2.85 (m, 1, C6-H_a), 2.85–2.9 (m, 1, C3a-H_a), 2.9–3.0 (m, 1, C5-H_a), 3.1–3.2 (m, 1, C6-H_e), 3.6–3.7 (m, 1, C1-H_a), 3.73 (s, 3, OCH_3), 4.2–4.3 (m, 1, C1-H_e), 7.1–7.5 (m, 4, Ar H); IR 1732 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_2$ (269.33): C, 75.8; H, 7.1. Found: C, 75.6; H, 7.3.

1,2,3,4,4a,5,6,7-Octahydroazepino[3,2,1-*jk*]carbazole-6-carboxylic Acid Methyl Ester (3b). After heating 6.2 g (0.02 mol) of **2b** to 300 °C for 10 h under nitrogen, the crude product was chromatographed on silica gel to give 0.6 g of crystalline product: yield, 10%; mp 78–81 °C; MS, *m/e* 283 [M⁺]; NMR 1.0–3.3 (m, 12, aliphatic H), 4.0–4.8 (m, 2, NCH_2), 3.70 and 3.73 (3:5) (s, 3, OCH_3), 6.8–7.6 (m, 4, Ar H); IR 1731 cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO_2$ (283.36): C, 76.3; H, 7.5; N, 4.9. Found: C, 76.0; H, 7.7; N, 4.8.

2,2a,3,4,4a,4b,5,6-Octahydro-1*H*-cyclopenta[*de*]indolo-[3,2,1-*ij*]quinoline-5-carboxylic Acid Methyl Ester (3c). When 4.8 g (0.016 mol) of **2c** was heated to 300 °C for 2.5 h under nitrogen and the crude was crystallized from ether/hexane, there was obtained 2.2 g of product: yield, 46%; mp 80–81 °C; MS, *m/e* 295 [M⁺]; NMR 1.0–3.1 (m, 12, 4 CH_2 + 4 CH), 3.2–3.4 (m, 1, NCH), 3.71 (s, 3, OCH_3), 3.8–4.2 (m, 1, NCH), 7.0–7.6 (m, 4, Ar H); ^{13}C NMR (ratio of isomers 4:1); IR 1730 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_2$ (295.4): C, 77.3; H, 7.2; N, 4.7. Found: C, 77.3; H, 7.2; N, 4.6.

1,2,2a,3,4,5,5a,5b,6,7-Decahydroisoquino[2,1,8-*lma*]carbazole-6-carboxylic Acid Methyl Ester (3d). From 10 g (0.03 mol) of **2d** after heating to 300 °C for 2 h under nitrogen, crude **3d** was obtained. The crude product was crystallized from ether/hexane to give 6 g of a mixture of cyclized diastereoisomers: yield, 60%; mp 128–130 °C; MS, *m/e* 309 [M⁺]; IR 1730 cm^{-1}. Anal. Calcd for $C_{20}H_{23}NO_2$ (309.4): C, 77.6; H, 7.5; N, 4.5. Found: C, 78.0; H, 7.4; N, 4.4. One isomer was obtained in pure form from the acid **3h** after treatment with diazomethane: mp 140–142 °C; NMR 0.6–3.3 (br m, 14, 5 CH_2 + 4 CH), 3.67 (s, 3, OCH_3), 3.4–4.2

(m, 2, NCH_2), 6.9–7.2 (m, 3, Ar H), 7.3–7.6 (m, 1, Ar H); ^{13}C NMR 19.4, 24.7, 25.2, 26.3, 28.2, 32.4, 33.0, 36.4, 38.4, 43.8 (NCH_2), 51.8 (OCH_3), 104.5 (C12b), 109.0 (C9), 117.9, 119.1, 120.3 (C9*, C10*, C11*), 127.9 (C12a), 133.8, 137.3 (C8a*, C12c*), 175.6 (C=O).

2,3,3a,4,5,6-Hexahydro-1-oxo-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylic Acid Methyl Ester (3e) and 2,3-Dihydro-1-oxo-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylic Acid Methyl Ester (6b). The precursor **2e** was heated under nitrogen to 300 °C for 5 min. The crude product was chromatographed on silica gel with toluene. Two products were isolated. The first one to elute was 0.2 g of **6b**. This was recrystallized from ether/hexane to give 0.1 g of pure **6b**: yield, 5%; mp 160–162 °C; MS, *m/e* 279 [M^+]; NMR 3.05 (t, 2, J = 7.7 Hz, CH_2), 3.3 (t, 2, J = 7.5 Hz, CH_2), 3.93 (s, 3, OCH_3), 7.42 (t, 1, J = 7.3 Hz, Ar H), 7.52 (t, 1, J = 7.6 Hz, Ar H), 7.9–8.0 (m, 2, Ar H), 8.4–8.5 (m, 2, Ar H). The second product to elute was 0.7 g of **3e**. This was recrystallized from ether/hexane to give 0.3 g of **3e** as a mixture of diastereoisomers: yield, 15%; mp 138–140 °C; *m/e* 283 [M^+]; NMR 1.5–1.7 (m, 2, CH_2), 2.1–3.3 (m, 8, 3 CH_2 + 2 CH), 3.69 and 3.78 (2 s, 3, OCH_3), 7.2–7.5 (m, 3, Ar H), 8.3–8.4 (m, 1, Ar H); IR 1710, 1735 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_3$ (283.3): C, 72.1; H, 6.1. Found: C, 72.0; H, 5.5.

1,2,2a,3,4,5,5a,5b,6,7-Decahydro-1-oxoisoquino[2,1,8-*lma*]carbazole-6-carboxylic Acid Methyl Ester (3f). After 3.0 g (0.01 mol) of **2f** was heated to 300 °C for 10 min, the crude product was chromatographed on silica gel to give 0.4 g of the crystalline product: yield, 13%; mp 180–182 °C; MS, *m/e* 323; NMR 0.6–3.2 (m, 12, 4 CH_2 + 4 CH), 3.77 (s, 3, OCH_3), 4.0–4.4 (m, 2, O=CCH_2), 6.9–7.4 (m, 3, Ar H), 8.0–8.2 (m, 1, Ar H). Additional fractions (1.0 g; 33% yield) with lower melting points were also collected.

2,3,3a,4,5,6-Hexahydro-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylic Acid (3g). A solution of 2.7 g (0.01 mol) of the ester $\mathbf{3a}_1$ and 1 g (0.02 mol) of KOH in 100 mL of 20% aqueous methanol was heated to reflux for 2 h. After acidification with 2 N HCl extraction with CH_2Cl_2/ethyl acetate gave 1.97 g of the product: yield, 77%; mp 210–212 °C. Anal. Calcd for $C_{16}H_{17}NO_2$ (255.3): C, 75.3; H, 6.7; N, 5.5. Found: C, 75.1; H, 6.7; N, 5.3.

1,2,2a,3,4,5,5a,5b,6,7-Decahydroisoquino[2,1,8-*ml*]carbazole-6-carboxylic Acid (3h). A mixture of 0.5 g (0.002 mol) of ester **3d** and 0.2 g (0.004 mol) of KOH in 10 mL of 80% aqueous methanol was heated to reflux for 2 h, acidified, and extracted with methylene chloride to give 0.27 g of crude acid: mp 210–213 °C [after recrystallization from methylene chloride/hexane the mp was 229–231 °C]; MS, *m/e* 309 [M^+]; IR (Nujol) 1700 cm^{-1}. Anal. Calcd for $C_{19}H_{21}NO_2$ (295.4): C, 77.2; H, 7.2; N, 4.7. Found: C, 76.7; H, 7.5; N, 4.7.

1-(4-Pentynyl)-1*H*-indole-3-carboxaldehyde (4). Prepared from 53 g (0.36 mol) of indole-3-carboxaldehyde, 10 g (0.42 mol) of sodium hydride, and 43 g (0.43 mol) of 5-chloropentyne[6] in DMF as described above, 25.4 g of the product was obtained: yield, 33%; mp 53–54 °C; MS, *m/e* 211 [M^+]; NMR 1.8–2.2 (m, 5, 2 CH_2 + CH), 4.27 (t, 2, J = 6 Hz, NCH_2), 7.1–7.5 (m, 3, Ar H), 7.67 (s, 1, NCH=), 8.1–8.5 (m, 1, Ar H), 9.9 (s, 1, CHO); IR 1540, 1665 cm^{-1}. Anal. Calcd for $C_{14}H_{13}NO$ (211.3): C, 80.0; H, 6.2; N, 6.6. Found: C, 79.7; H, 6.4; N, 6.5.

1-(4-Pentynyl)-1*H*-indole-3-acrylic Acid Methyl Ester (5). Prepared from 21 g (0.1 mol) of **4** and 33.4 g (0.1 mol) methyl (triphenylphosphoranylidene)acetate[5] in 300 mL of toluene as described above to give 19.7 g of the product: yield, 74%; mp 78–79 °C; MS, *m/e* 267 [M^+]; NMR 1.7–2.2 (m, 5, 2 CH_2 + CH), 3.78 (s, 3, OCH_3), 4.2 (t, 2, NCH_2), 6.33 (d, 1, J = 16 Hz, =CH), 7.0–7.4 (m, 4, Ar H), 7.7–8.0 (m, 1, Ar H), 7.83 (d, 1, J = 16 Hz, =CH); IR 1540, 1630, 1705 cm^{-1}. Anal. Calcd for $C_{17}H_{17}NO_2$ (267.3): N, 5.2. Found: N, 5.2.

2,3-Dihydro-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylic Acid Methyl Ester (6a). Under an atmosphere of nitrogen, 11.6 g (0.43 mol) of **5** was heated to 300 °C for 10 min. The residue was chromatographed on silica gel with toluene to give 4.2 g of the product: yield, 36%; mp 108–109 °C; MS, *m/e* 265 [M^+]; NMR 1.8–2.3 (m, 2, CH_2), 2.8 (t, 2, J = 6 Hz, $PhCH_2$), 3.85 (t, 2, NCH_2), 3.9 (s, 3, OCH_3), 7.0–7.5 (m, 3, Ar H), 7.7–7.8 (m, 1, Ar H), 7.9–8.1 (m, 1, Ar H), 8.5–8.6 (m, 1, Ar H); IR 1709 cm^{-1}. Anal. Calcd for $C_{17}H_{15}NO_2$ (265.3): C, 77.0; H, 5.7; N, 5.3. Found: C, 77.2; H, 5.9; N, 5.2.

2,3-Dihydro-1-oxo-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylic Acid (6b). For analytical data see under **3e**.

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Registry No. **1a**, 110206-12-7; **1b**, 110206-13-8; **1c**, 110206-14-9; **1d**, 110206-15-0; **1e**, 110206-16-1; **1f**, 110206-17-2; **2a**, 110206-18-3; **2b**, 110206-19-4; **2c**, 110206-20-7; **2d**, 110206-21-8; **2e**, 110206-22-9; **2f**, 110206-23-0; $\mathbf{3a}_1$, 110206-24-1; $\mathbf{3a}_2$, 110206-25-2; **3b** (isomer 1), 110206-26-3; **3b** (isomer 2), 110206-27-4; **3c**, 110269-33-5; **3d**, 110206-28-5; **3e** (isomer 1), 110206-29-6; **3e** (isomer 2), 110206-30-9; **3f**, 110269-34-6; **3g** (isomer 1), 110206-31-0; **3g** (isomer 2), 110206-32-1; **3h**, 110206-33-2; **4**, 110206-34-3; **5**, 110206-35-4; **6a**, 110222-95-2; **6b**, 110206-36-5; indole-3-carboxaldehyde, 487-89-8; 5-bromopentene, 1119-51-3; 6-bromohexene, 2695-47-8; 3-(2-chloroethyl)cyclopentene, 21298-00-0; 3-(2-chloroethyl)cyclohexene, 19509-51-4; 4-pentenoyl chloride, 39716-58-0; 2-(2-cyclohexen-1-yl)acetyl chloride, 3514-86-1; methyl (triphenylphosphoranylidene)acetate, 2605-67-6; 5-chloropentyne, 14267-92-6.

Total Synthesis of (±)-Lythrancepine II and (±)-Lythrancepine III

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Total syntheses of the Lythraceae alkaloids (±)-lythrancepine II (**2**) and (±)-lythrancepine III (**3**) are described. The syntheses feature a stereoselective *N*-acyliminium ion cyclization (**26** → **27–31**), a mechanistically interesting Eschenmoser sulfide contraction (**16** → **19** and **41** → **42**), and construction of a 13-membered ring by using the Semmelhack–Ullmann procedure.

The Lythraceae alkaloids are a large family of natural products, most of which contain 4-arylquinolizidine substructures.[3,4] Over 10 of these alkaloids are quinolizidine metacyclophanes, exemplified in Figure 1 by lythrancepines I–III (**1–3**) and lythrancine II (**4**). The structure assignments for these natural products are based on several X-ray crystallographic studies, spectral data, and a number of chemical correlations. For example, the structures of **1–3** were assigned on the basis of chemical studies,[5] which

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