for 16 h at reflux under an atmosphere of nitrogen (Dean–Stark apparatus). The solution was cooled and vigorously stirred over anhydrous potassium carbonate for 5 min and then the mixture was filtered and the solvent evaporated to give a pale yellow solid (1.16 g, ca. 100%). Recrystallization from dichloromethane/petroleum ether provided a solid which was identical in all respects with the ether adduct **4f** obtained by method 1.

11,11-Dimethyl-10,12-dioxahexacyclo[7.6.1.1^{6,13}.0^{2,7}.0^{5,15}.0^{9,13}]-3-heptadecene (12). A solution of the ketal **4g** (198 mg, 0.5 mmol, tri-*n*-butylstannane (320 mg, 1.1 mmol), and azobis(isobutyronitrile) (2 mg) in toluene (1 mL) was heated for 23 h at reflux under an atmosphere of nitrogen. Carbon tetrachloride (1 mL) was added and refluxing was continued for 2 h. The solution was cooled to ambient temperature and diluted with ether/dichloromethane (2:1, 15 mL). The mixture was treated with a solution of potassium fluoride (2 g) in water (10 mL) and was vigorously stirred for 0.25 h. The suspension of tri-*n*-butylstannyl fluoride was filtered and the aqueous layer was separated and extracted with ether/dichloromethane (2:1, 10 mL). The organic extracts were washed with 10% aqueous sodium bicarbonate (15 mL), dried ($MgSO_4$), and concentrated. The residue was dissolved in 95% ethanol (5 mL) heated at reflux and sodium metal (805 mg, 35.0 mmol) was added in portions over 1.5 h. More 95% ethanol (2 mL) was added to the thick mixture and refluxing was continued for 2.5 h. The solution was cooled to ambient temperature and poured into ice water (15 mL). The organic material was extracted into petroleum ether (3 × 10 mL), washed with water (10 mL) and saturated sodium chloride solution (10 mL), dried ($MgSO_4$), and evaporated to give a yellow oil (180 mg). Chromatography on neutral alumina (Woelm, activity 1) with dichloromethane/petroleum ether (1:1) as the eluent afforded the ketal **12**: mp 84–86 °C; IR (CCl_4) 3050, 1365, 1375 cm^{-1}; ^{1}H NMR (CCl_4) δ 6.03 (dd, J = 5 and 2 Hz, 2 H), 1.96 (br s, 2 H), 1.87 and 1.39 (ABq, J = 9 Hz, 8 H), 1.30 (s, 6 H); MS, m/e 258 (M^+), 243 ($M^+ - CH_3$), $M^+ - CH_3$ calcd for $C_{17}H_{22}O_2$ 243.138496, found 243.138077.

11-Oxa-2,5-dichlorohexacyclo[7.6.1.1^6,13.0^2,7.0^{5,15}.0^{9,13}]heptadecane (13). To a solution of the ether **4f** (1.464 g, 4.0 mmol) in ethyl acetate (40 mL) was added 5% palladium on carbon catalyst (75 mg) and triethylamine (1.01 g, 10 mmol). The mixture was stirred for 3 h at ambient temperature and pressure under a hydrogen atmosphere. The catalyst and triethylamine hydrochloride were removed by filtration through Celite and the filtrate was evaporated to give the dichloro ether **13** (0.957 g, 80%). An analytical sample, mp 98–99 °C, was prepared by sublimation at 90 °C (0.5 mm) ^{1}H NMR ($CDCl_3$) δ 3.52 (s, 4 H), 2.41 (br s, 4 H), 2.29 (s, 4 H), 1.80 (center of a merging ABq, J = 14 Hz, 8 H); MS, m/e 298, 300, 302 (M^+). Anal. Calcd for $C_{16}H_{20}Cl_2O$: C, 64.22; H, 6.74. Found: C, 64.47; H, 6.99.

16-Oxapentacyclo[8.4.3.0^{1,10}.0^{4,13}.0^{7,12}]heptadeca-3,7-diene (14) and 11-Oxahexacyclo[7.6.1.1^{6,13}.0^{2,7}.0^{5,15}.0^{9,13}]heptadecane (16). To a suspension of sodium–potassium alloy (0.4 mL, 346 mg, ~9.6 mmol) in ether (25 mL) was added the dichloro ether **13** (530 mg, 1.77 mmol) in one portion. The mixture turned dark blue and was stirred for 16 h at room temperature under a nitrogen atmosphere. Excess alloy was destroyed by the cautious addition of ethanol (2 mL). Water (50 mL) was added, the aqueous layer was extracted with ether (2 × 50 mL), and the organic layer was dried ($MgSO_4$) and evaporated to give a solid (380 mg, 94%) which consisted of a mixture of the diene **14** and the ether **16**, (ca. 3:1). The two components were separated (Merck Lobar RP8 column, 7.5% aqueous methanol). The diene **14** eluted first: mp 91–94 °C; IR ($CDCl_3$) 3040, 1650, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.11 (t, J = 4 Hz, 2 H), 3.68 and 3.30 (ABq, J = 10 Hz, 4 H), 2.51 (br s, 2 H), 1.5–2.4 (complex, 10 H), 1.18 (d of ABq, J = 12 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 142.1 (s), 120.5 (d), 79.5 (t), 41.6 (s), 38.0 (d), 34.0 (t), 29.6 (t), 28.9 (t) ppm; MS, m/e 228 (M^+), M^+ calcd for $C_{16}H_{20}O$ 228.151406, found 228.151629.

The ether **16** eluted second: mp 51–53 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.44 (s, 4 H), 1.95 (br s, 4 H), 1.75 (d, J = 12 Hz, 1.48 (br s, 4 H), 0.99 (br s, 2 H), 0.92 (d, J = 12 Hz, 4 H); ^{13}C NMR ($CDCl_3$) 81.2 (t), 41.9 (s), 35.2 (d), 34.6 (d), 33.7 (t), 26.1 (t) ppm; MS, m/e 230 (M^+), M^+ calcd for $C_{16}H_{22}O$ 230.167055, found 230.167785.

3,13-Dimethylene-8-oxapentacyclo[8.3.1.1^{2,6}.0^{4,12}.0^{6,10}]pentadecane (15). The diene **14** (120 mg, 0.53 mmol) was vaporized at 120 °C (0.4 mm) and passed through a hollow quartz tube (40 × 3 cm) heated at 500 °C. The pyrolysate condensed on a cold finger at 15 °C (100 mg, 83%). Flash chromatography of the condensate on silica gel, with 50% dichloromethane/petroleum ether as the eluent, afforded the diene **15** as a white solid: mp 93–96 °C; IR ($CDCl_3$) 3080, 1650, 1050, 880 cm^{-1}; ^{1}H NMR ($CDCl_3$) 4.46 (s, 4 H), 3.47 (s, 4 H), 2.75 (br s, 4 H), 1.91 and 1.22 (ABq, J = 12 Hz, 8 H); ^{13}C NMR ($CDCl_3$) 153.9, 104.2, 80.5, 42.7, 41.0, 36.2 ppm; MS, m/e 228 (M^+), M^+ calcd for $C_{16}H_{20}O$ 228.151406, found 228.151629.

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Registry No. 3a, 85710-40-3; **3b**, 85760-84-5; **4a**, 85710-41-4; **4b**, 82491-28-9; **4c**, 82491-31-4; **4d**, 85710-42-5; **4e**, 85710-43-6; **4f**, 85710-44-7; **4g**, 85710-45-8; **4h**, 85710-46-9; **5**, 85710-47-0; **6**, 493-04-9; **7**, 85710-48-1; **8a**, 16573-72-1; **8b**, 39623-22-8; **8c**, 4578-96-5; **8d**, 30483-18-2; **8e**, 3642-06-6; **8f**, 15405-67-1; **8g**, 69998-91-0; **9a**, 85760-85-6; **9b**, 82491-29-0; **9c**, 82491-30-3; **10**, 85710-49-2; **11**, 85710-50-5; **12**, 85710-51-6; **13**, 85710-52-7; **14**, 85710-53-8; **15**, 85710-54-9; **16**, 85710-55-0; tetrachlorothiophene 1,1-dioxide, 72448-17-0; 11-aza-11-chlorosulfonyl-12-oxotricyclo[4.4.2.0^{1,6}]dodeca-3,8-diene, 85710-56-1; acetylene dicarboxylic acid, 142-45-0; butadiene, 106-99-0; 1,4,4a,5,8,8a-hexahydronaphthalene-*cis*-4a,8a-dicarboxylic acid, 3642-04-4; *cis*-4a,8a-dihydroxy-1,4,4a,5,8,8a-hexahydronaphthalene, 69998-88-5.

Indole-2,3-quinodimethanes: A New Strategy for the Synthesis of Tetracyclic Systems of Indole Alkaloids

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Abstract: The imine **7**, derived from *N*-[(4-methoxyphenyl)sulfonyl]-2-methylindole-3-carboxaldehyde (**6**) and 4-pentenylamine, on treatment with a range of chloroformates gave *cis*-octahydropyridocarbazoles **8**, in yields ranging from 43 to 92%. Similarly the series of imines **18–24** derived from **6** and the corresponding amine gave, on treatment with the mixed carbonic anhyride from ethyl chloroformate and 4-pentenoic acid **25**, the tetracyclic amides **26–31**. The equivalent series of transformations with a 4a-ethyl group present leads directly to cis-fused tetracyclic precursors **40–42** and **45**. The structure and relative stereochemistry of the tetracyclic carbamate **43** is confirmed by single-crystal X-ray crystallography. Some general examples of indole-2,3-quinodimethane cyclizations that give fused pentacyclic and spirocyclic compounds **49**, **50**, and **51** directly are described.

Historically speaking, the area of indole alkaloids has fascinated organic chemists for the last 100 years.[1] It is only relatively recently that modern methods of spectroscopy, and X-ray crystallography, have removed the onerous burden of structural elu-

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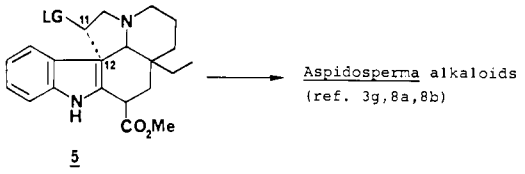
Scheme 1



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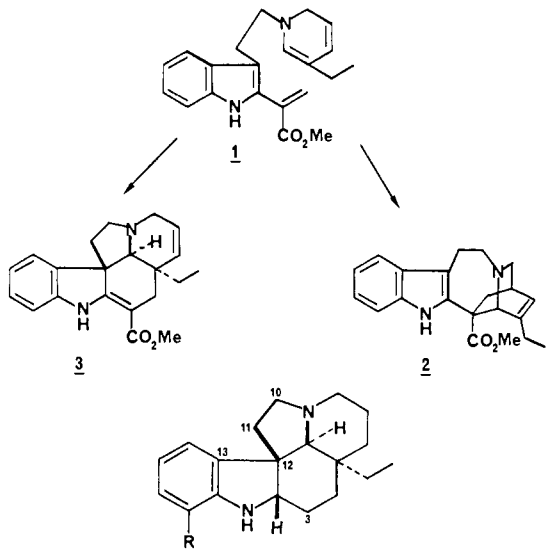
cidation and left the organic chemist unfettered to pursue the synthesis of these molecules. The Aspidosperma alkaloids have attracted a great deal of attention because of their central place in the biosynthesis of monoterpenoid-derived indole alkaloids.[2] The tryptamine-derived biosynthetic intermediate dehydrosecodine (**1**) and its postulated conversion into catharanthine (**2**) (Iboga) and tabersonine (**3**) (Aspidosperma) have inspired many fascinating synthetic ventures to emulate these biosynthetic proposals.[3]



A large number of other interesting strategies have been used to construct the Aspidosperma skeleton, from the first synthesis of aspidospermine (**4**, R = OMe) utilizing the classical Fischer-indole synthesis[4] to the most recent photoisomerization of 1-acylindoles to 3-acylindoles[5] and the aza-Cope rearrangement approach.[6] With so many valuable and diverse synthetic approaches to these alkaloids,[7] it might be expected that it would be difficult to locate any unifying feature within these strategies. Fortunately the simplifying ideas of biosynthesis enable us to state that all but two of these approaches either have the two-carbon tryptamine intact from the outset or create the C_{12}–C_{13} bond from the Fischer-indole synthesis. All of the approaches based upon the biosynthetic proposal **1**–**3** have the tryptamine two-carbon bridge intact from the beginning.[3] Only the Ziegler[3g] and the Wenkert–Potier[8] approaches (and more recently Natsume)[8b] attempt to make the C_{11}–C_{12} bond (Scheme I). It should be noted that in the conversion of the elaborated gramine derivative **5** into the pentacyclic Aspidosperma system[3g,8] the yield is very low, presumably reflecting, to some degree, the difficulty in making a quaternary carbon at C_{12}.

The strategy described here is based upon gramine chemistry[10] and as such is a pronounced departure from previous methods. Recently we observed that indole-2,3-quinodimethane intermediates **12a** can be generated and trapped in an intramolecular manner to provide cis-fused tetracyclic products.[9] *N*-[(4-Methoxyphenyl)sulfonyl]-2-methylindole-3-carboxaldehyde (**6**) was converted into the imine **7**, which on treatment with various alkyl chloroformates gave the octahydropyridocarbazoles **8**.

For a range of chloroformates E–C_1 where E = CO_2CH_2Ph, CO_2Et, CO_2Ph, and CO_2Me, the yields of tetracyclic adducts **8** were 0%, 43%, 68%, and 88%, respectively. Only in the case of the adduct **8** (E = CO_2Me) were we able to remove the carbamate group, to give the secondary amine **10**, and then only when the (*p*-methoxyphenyl)sulfonyl group had first been removed from

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(9) A detailed description of the experiments that led to the discovery of this reaction, along with some initial results, has already been published (Gallagher, T.; Magnus, P. *Tetrahedron* **1981**, *37*, 3889). Its extension to the total synthesis of *dl*-aspidospermidine: Gallagher, T.; Magnus, P. *J. Am. Chem. Soc.* **1982**, *104*, 1140; **1983**, *105*, accompanying paper.

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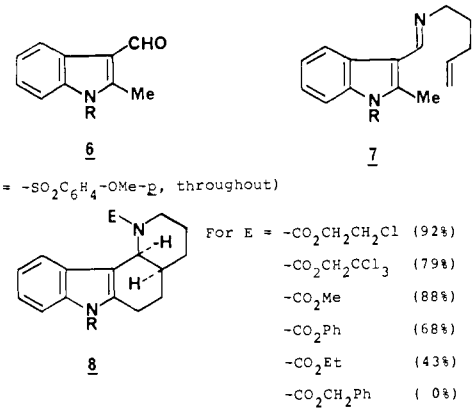
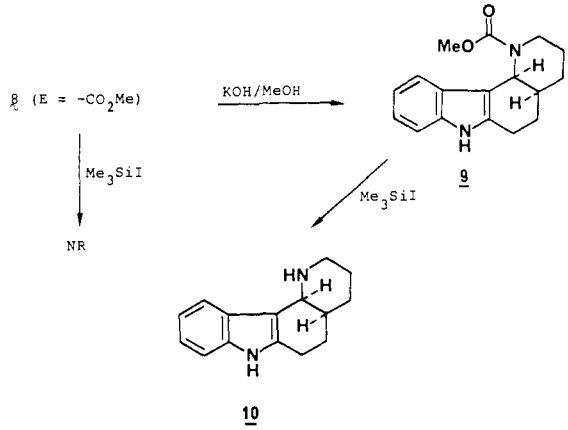
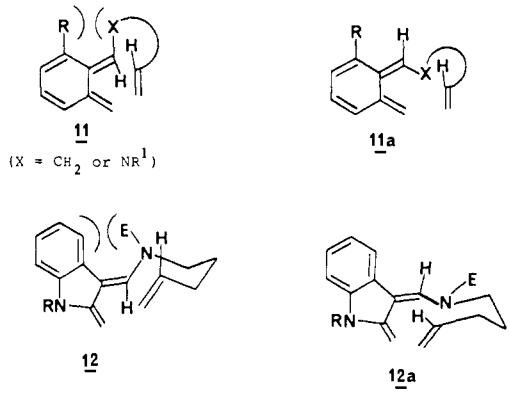


the indolic nitrogen atom to give **9**.



Results

Before proceeding directly to the above two problems, it is useful to mention some important points concerning the key cyclization reaction itself, **7** to **8**. The intramolecular trapping of a monobenzenoid-derived *o*-quinodimethane has been generally assumed to have the geometry indicated in **11**.[11] At first sight this seems reasonable since the products formed, in particular those that have subsequently been converted into estrone, have the newly formed ring junction (B/C for steroids) predominantly trans fused.[12] The steric interaction between the exocyclic methylene group and the X group (usually CH_2 or NR) is assumed to destabilize the configuration **11a**, in favor of **11**. On the other hand the steric interaction between the X group and R, in **11**, could be rendered particularly unfavorable, especially if R is large and therefore destabilizes this configuration. For the indole-2,3-quinodimethane system **12**, the steric repulsion between the substituent at the 3-position and the benzenoid ring (also C_4 hydrogen atom) makes this configuration less likely. We favor the transition state **12a**, designated as *exo*-E, since without exception, we have only observed cis-fused tetracyclic compounds.[13] No trans-fused isomers



have been detected. It was suggested[9] that the cis-fused stereochemical outcome of the intramolecular [2 + 4] reaction could be the result of the potential ability of the tetracyclic products to take advantage of typical gramine chemistry and undergo reversible elimination, thus enabling any kinetically formed trans-tetracyclic product that might be present to be converted into the cis-fused product (Scheme II).

Recently,[14] we have found that the acetylenic system **13** readily cyclizes at 130 °C in the presence of methyl chloroformate and diisopropylethylamine to give the 1,4-dihydrocarbazole **14** without irreversible elimination to the aromatized carbazole **15**, under these conditions. This result would appear to discount the possibility of Scheme II and strongly support the transition state **12a**, where the geometrical configuration of the dienamine system, in an exo array, determines the stereochemistry of the product.[15]

Deethyl Exocyclic Carbamate Series. For convenience, and since there is such a marked difference in the two series, we have separated the two types of cyclization reactions by the designation exocyclic and endocyclic (Scheme III). (The terms exo and endo refer to the position of the carbonyl group.)

To examine the formation of pentacyclic Aspidosperma systems, we required a tetracyclic amine, namely, **16**, where the indole nitrogen atom is protected by the (*p*-methoxyphenyl)sulfonyl group. As already alluded to,[9] we had been unable to deprotect the piperidine nitrogen atom (removal of the carbamate group) without first removing the (*p*-methoxyphenyl)sulfonyl group protection from the indole nitrogen atom. Consequently we examined other specific chloroformates that could be removed under reductive conditions. Treatment of the imine **7** with 2-chloroethyl chloroformate[16] in chlorobenzene, in the presence of diisopropylethylamine at 0 °C, followed by rapid heating to 135 °C gave the tetracyclic carbamate **8** (E = $CO_2CH_2CH_2Cl$) in 92% yield. This is the most rapid and highest yielding cyclization we have encountered to date. No evidence for the formation of trans ring fusion could be found.

The 2-chlorocarbamate **8** (E = $CO_2CH_2CH_2Cl$) was exposed to a number of reductive conditions, compatible with the other functionality, in attempts to produce the required amine **16**. Treatment of **8** (E = $CO_2CH_2CH_2Cl$) with Zn/AcOH or $CrCl_2$/HCl gave no reaction. Tri-*n*-butyltin hydride in xylene initiated by AIBN did not convert **8** (E = $CO_2CH_2CH_2Cl$) into **16**. Turning to more powerful reducing agents, and the elegant

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(12) Funk, R. L.; Vollhardt, K. P. C. *Chem. Soc. Rev.* **1980**, 41. Oppolzer, W.; Bättig, K.; Petrzilka, M. *Helv. Chim. Acta* **1978**, *61*, 1945. Djuric, S.; Sarkar, T.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 6885. Kametani, T.; Nemoto, H.; Ishikawa, H.; Shiroyama, K.; Fukumoto, K. *Ibid.* **1976**, *98*, 3378.

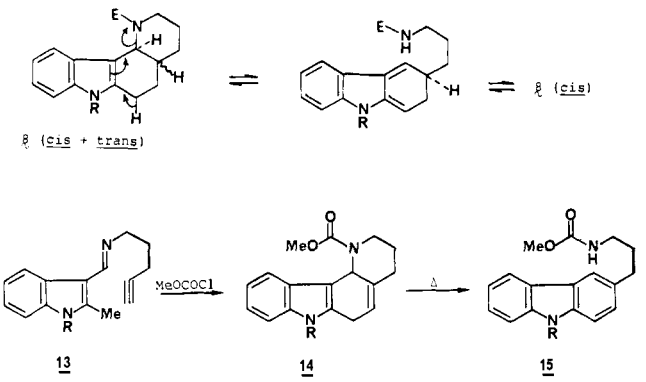
(13) Dr. Peter Gund (merck) using the Merck Molecular Modeling System demonstrated that there is virtually no energy difference between **12** and **12a** and that steric interactions twist the nitrogen atom of the dienamine out of conjugation with the diene system for both isomers. Interestingly, when applied to **11**/**11a** for R = Me and X = NMe_2, the structure **11a** is favored by 0.6 kcal. Again in both **11** and **11a** the nitrogen lone pair is orthogonal to the diene π-system. As a note of caution, these particular calculations do not really apply to transition states and also have no Coulombic energy form in the ground-state classical mechanical energy calculations. Since this applies to both sets of compounds, the differences (or lack of) might be useful but should be regarded as tentative. Dr. Peter Gund is gratefully thanked for his time and interest in this matter.

(14) Gallagher, T.; Magnus, P., unpublished results. See also: Exon, C.; Gallagher, T.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1982**, 613.

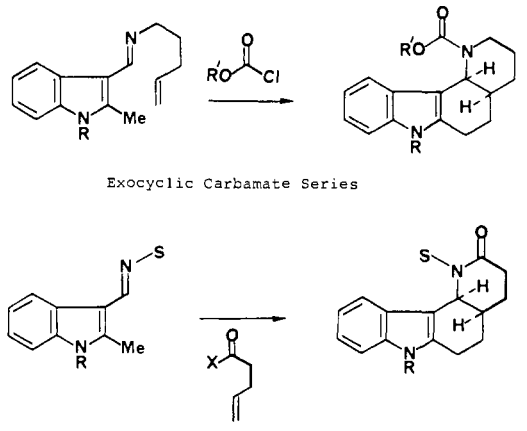
(15) Boeckman, R. K., Jr.; Alessi, T. R. *J. Am. Chem. Soc.* **1982**, *104*, 3216. Roush, W. R.; Gillis, H. R.; Ko, A. I. *Ibid.* **1982**, *104*, 2269.

(16) Gross, H.; Rieche, A.; Moft, E. *Chem. Ber.* **1961**, *94*, 544.

Scheme II



Scheme III



Exocyclic Carbamate Series

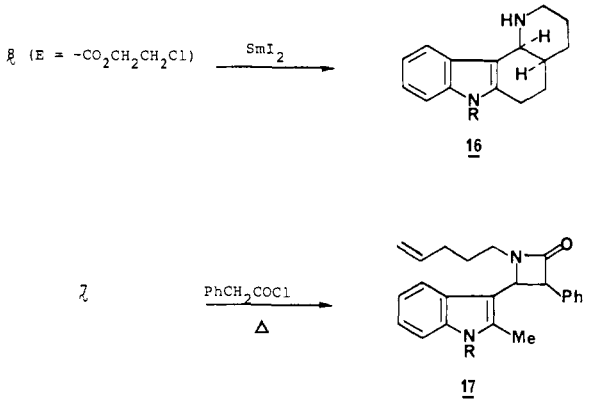
Endocyclic Amide Series

work of Ugi[17] and Scheffold,[18] we treated **8** (E = $CO_2CH_2CH_2Cl$) with $Zn/H_2O/THF/EtOH$/vitamin B_{12}(aquo) at 70 °C under degassed conditions for several days. The major product was the 2-hydroxyethyl carbamate **8** (E = $CO_2CH_2CH_2OH$).

It was evident from the above difficulties that an extremely powerful reducing agent that is soluble in aprotic solvents was required. In particular samarium diiodide[19] (Sm^{II}/Sm^{III} = −1.55 V in H_2O) appeared suitable, since it can be readily made in anhydrous THF. Exposure of **8** (E = $CO_2CH_2CH_2Cl$) to freshly prepared samarium diiodide ($Sm/ICH_2CH_2I/THF$) at 70 °C for 7 h cleanly gave **16** in 70% yield. The overall yield from the imine **7** to **16** is 64%.

An alternative sequence to the amine **16** is treatment of **7** with 2,2,2-trichloroethyl chloroformate/N-*i*-Pr_2Et in chlorobenzene at 0 °C, followed by heating at 135 °C for 1.25 h to give **8** (E = $CO_2CH_2CCl_3$) (79%), followed by reductive elimination[20] with $Zn/AcOH/H_2O$ to give **16** (86%) in an overall yield of 69%. This latter procedure is more convenient. Treatment of **8** (E = $CO_2CH_2CH_2Cl$) with KO-*t*-Bu/THF at −15 °C gave **8** (E = $CO_2CH{=}CH_2$) (>95%) that could not be converted into **16** under a variety of electrophilic conditions.[21]

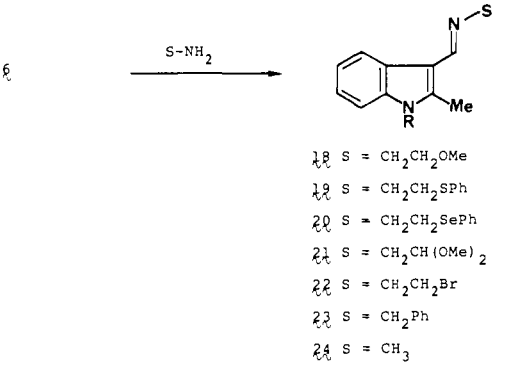
It should be noted that with **16** now available, its conversion into pentacyclic Aspidosperma systems was examined by attaching various functionalized acyl derivatives at the piperidine nitrogen atom, for example, **8** (E = $COCH_2SPh$).[9] Obviously a more direct route to such an acyl derivative would be to treat the imine **7** with the appropriate functionalized acylating agent, such as $PhSCH_2COCl$ or a mixed anhydride, directly. Unfortunately no useful results were obtained from this more direct approach. The reason for this failure appears to be the intervention of ketene chemistry to give β-lactams. This can be attributed to the ease with which these particular activated esters form ketenes,[22] especially in the presence of tertiary amines. Indeed, treatment of the imine **7** with $PhCH_2COCl$ under the usual conditions for tetracycle formation gave the β-lactam **17** (83%) as the only characterizable product.



Quite generally, the indole-2,3-quinodimethane cyclization does not work well if ketene pathways [2 + 2] can intervene in the initial acylation step.

Deethyl Endocyclic Amide Series. So far, we have only described the systems where the imine contains an olefinic bond appropriately situated for intramolecular trapping by an indole-2,3-quinodimethane (Scheme III). It is, of course, possible to reverse these roles and acylate an imine with a reagent that has an olefinic bond correctly placed for intramolecular trapping (Scheme III). A most attractive feature of this alternative mode is that the imine can, from the outset, contain the two carbon atoms (C_{10} and C_{11}) necessary to form the tryptamine bridge in the basic Aspidosperma skeleton. In this way, it should be possible to assemble all the atoms (C, H, and N) of the Aspidosperma system in a single step and complete the final bond between C_{11} and C_{12} in the subsequent step(s).

Treatment of **6** with a range of primary amines in dichloromethane, in the presence of 4-Å molecular sieves, provided the series of amines **18–24** in virtually quantitative yields. The



formation of these imines is best checked by NMR observing the complete disappearance of the formyl proton and the appearance a singlet (δ 8.40–8.60 depending upon the specific imine). In all but one case a single geometrical isomer was formed, presumably the E isomer. Only in the N–Me imine **24** did the NMR (δ 8.47 and 8.49) show evidence for the other geometrical isomer.

When a solution of the imine **21**, in chlorobenzene at 20 °C, was treated with the mixed carbonic anhydride from ethyl chloroformate and 4-pentenoic acid **25** and the mixture heated to 135 °C for 3.5 h, two products were obtained after chromatography, the ethoxy adduct **32** (19%) and the required tetracyclic amide

(17) Eckert, H.; Schrauzer, G. N.; Ugi, I. *Tetrahedron* **1974**, *31*, 1399. Eckert, H.; Ugi, I. *Liebigs Ann. Chem.* **1979**, 278.

(18) Scheffold, R.; Amble, E. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 629. Professor Scheffold is thanked for experimental details concerning the B_{12} reaction.

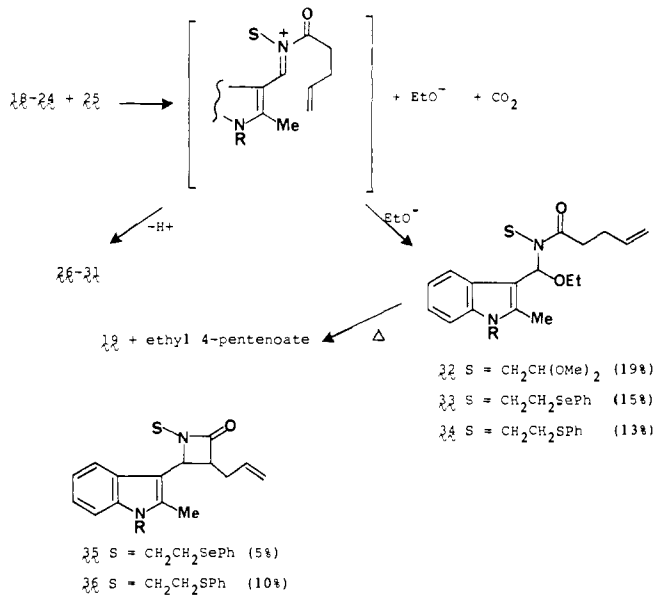
(19) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693. Kagan, H. B.; Namy, J. L.; Girard, P. *Tetrahedron* **1981**, 175. Ananthanarayan, T. P.; Gallagher, T.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1982**, 709.

(20) Just, G.; Grozinger, K. *Synthesis* **1976**, 457.

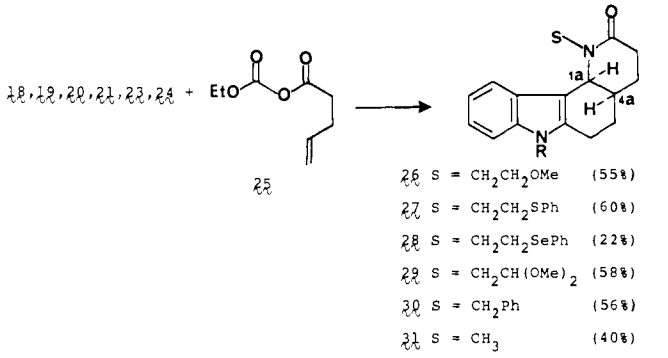
(21) Olofson, R. A.; Yamamoto, Y. S.; Wancowicz, D. J. *Tetrahedron Lett.* **1977**, 1563.

(22) Lacey, R. N. *Adv. Org. Chem.* **1960**, *2*, 213.

Scheme IV



29 (58%). The stereochemistry at the newly formed ring junction was readily assigned as cis since the proton at C_{1a} appears at δ 4.77 as a doublet ($J_{1a,4a}$ = 4 Hz). Similarly for the other imines **18–24** (except **22**) the cyclization to give tetracyclic amides **26–31**



proceeded in yields between 22% and 60%, with the ethoxy adducts **32**, **33**, and **34** being the main byproducts, and small amounts of β-lactams **35** and **36** being formed. In no case were we able to isolate any tetracyclic amides with a trans-fused ring junction.

The conversion of the imine **19** into the tetracyclic amide **27** is a very clean reaction (as judged by TLC). Two byproducts were isolated, the ethoxy adduct **34**, formed by trapping the intermediate acyliminium ion (Scheme IV) with the ethanol liberated from the mixed anhydride, and the β-lactam **36**, a product of a ketene pathway. Scheme IV shows an intermediate iminium ion, which reacts further by an intermolecular process with the ethoxide generated in the acylation step. Circumstantial evidence indicates, however, that the ethoxy adducts are formed in the initial acylation step by a concerted reaction and not in a separate bimolecular process. This manifests itself most acutely in the series with an ethyl group at the new ring fusion, where the ethoxy adducts become problematic. For the thiophenyl ethyl series **19**, into **27** (60%), the unwanted adducts **34** (13%) and **36** (10%) are not too deleterious.

Acid or base (TsOH, Et_3N, N-*i*-Pr_2Et) catalysis of the above cyclization caused, in the case of acid, no cyclization (destruction to intractable material). In the case of base, the ethoxy adduct **34** was no longer present, but the β-lactam **36** became a major (≥30%) byproduct. It might have been reasonably expected that the ethoxy adduct **34** would reversibly eliminate ethanol on heating to give back the intermediate iminium ion (Scheme IV), which can lose a proton to give the tetracyclic amide **27**. Unfortunately this is not so. Prolonged heating of **34** (180 °C) gave the starting imine **19** and ethyl 4-pentenoate.

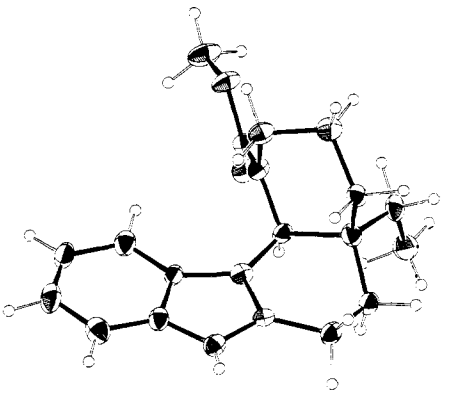
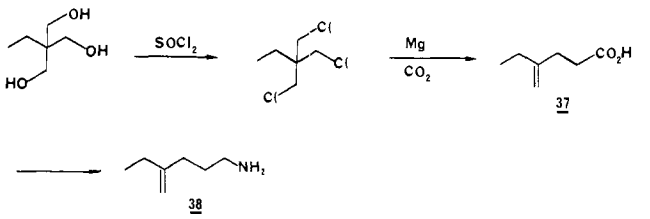


Figure 1.

Scheme V



Efforts to suppress the formation of these byproducts will be described in the *ethyl* series, but it is worth noting that the use of other acyl derivatives of 4-pentenoic acid gave no tetracyclic amides at all. Only the ethyl carbonic–carboxylic anhydrides have proved useful.

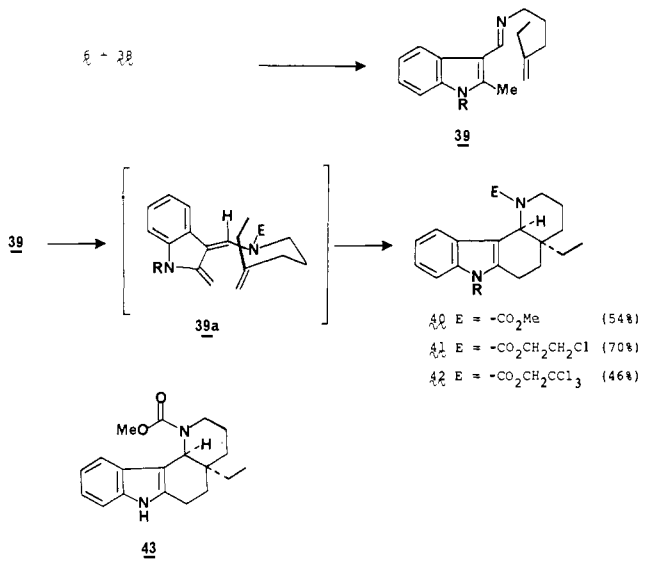
4a-Ethyl Exocyclic Carbamate Series. While the intramolecular trapping of the indole-2,3-quinodimethane, in the exocyclic carbamate series, works in yields as high as 90% when a monosubstituted alkene is employed, it would be expected that a 2,2-dialkyl-substituted alkene could drastically slow down the cyclization. It is important that a 2,2-dialkyl system works in a synthetically viable way; otherwise this strategy will not allow direct access to the naturally occurring Aspidosperma alkaloids.

The required 4-ethyl-4-pentenylamine **38** was prepared from 4-ethyl-4-pentenoic acid, **37**,[23] by the method shown in Scheme V. Treatment of **6**, with **38** in the presence of 4-Å molecular sieves gave the imine **39** (≥95%). When the imine **39** was treated with methyl chloroformate in the presence of diisopropylethylamine, in chlorobenzene at 0 °C, then heated to 135 °C for 3 h the tetracyclic carbamate **40** (54%) was formed. While in the deethyl series the coupling of H-1a/H-4a (J_s = ca. 2–4 Hz) allows the assignment of relative stereochemistry at the newly formed ring fusion (see ref 9 for definitive X-ray crystallographic proof of the stereochemical assignments), it is not a foregone conclusion that the ethyl series has the same cis relative configuration, and of course, the NMR handle is absent. The tetracycle **40** was treated with aqueous potassium hydroxide in methanol to give the free indole **43**, which gave suitable crystals for single-crystal X-ray crystallography (Figure 1).[24]

It is reasonable to postulate that the exclusive formation of this cis-fused C/D ring junction is a result of the exo-E geometry of the indole-2,3-quinodimethane intermediate **39a**. The conformation of the D ring in **43** in the crystal is a chair, which interestingly contrasts with the boat conformation of ring D in

(23) McCaffery, E. L.; Shalaby, S. W. *J. Organomet. Chem.* **1967**, *8*, 17.

(24) Compound **43** crystallizes in the orthorhombic space group $Pna2_1$ with a = 9.622 (4), b = 19.792 (11), and c = 8.669 (4) Å and D_{calcd} = 1.257 gm cm^{-3} for Z = 4 at −161 °C. All data were collected at low temperature. The Picker goniostat, experimental details, and data handling techniques have been described in detail previously (Huffman, J. C.; Lewis, L. N.; Caulton, K. G. *Inorg. Chem.* **1980**, *19*, 2755). The structure was solved by direct methods using the 1124 nonzero data (out of 1169) and refined by full-matrix least squares to final residuals of R(F) = 0.032 and R_w(F) = 0.031. Complete crystallographic details are available from the Chemistry Library, Indiana University, Bloomington, IN, Request Molecular Structure Center Report No. 81059.



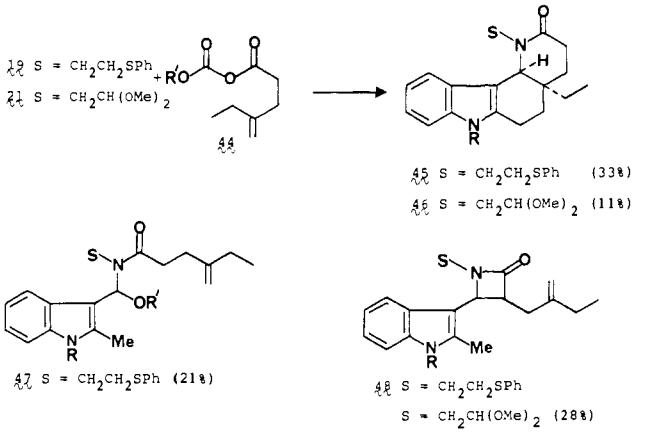
aspidospermine (**4**, R = OMe) itself.[25] Presumably the C_{10}–C_{11} tryptamine bridge exerts sufficient constraint upon the flexibility of the D ring to lock it in a boat conformation. Recently Kunesch and Wenkert have isolated and elucidated the structures of Aspidosperma-type alkaloids that do not possess the C_{10}–C_{11} bridge, of which the compounds described here **40**–**43** are prototypes with the correct relative stereochemistry but lacking a 3,4-epoxy group.[26]

Treatment of the imine **39** with 2-chloroethyl chloroformate, using the conditions described for **40**, gave **41** in 70% yield. Similarly 2,2,2-trichloroethyl chloroformate converted **39** into **42** in 46% yield.

The yields in the 4a-ethyl series are about 20–25% lower than the deethyl series, and the rate of cyclization is approximately the same. This implies that the indole-2,3-quinodimethane intermediate is an extremely electron deficient diene. While the 4-ethyl-4-pentenyl trap is more sterically encumbered, it is also more electron rich than a monosubstituted alkene, and it appears that these two opposing influences closely balance each other.

4a-Ethyl Endocyclic Amide Series. Although the indole-2,3-quinodimethane cyclization in the 4a-ethyl exocyclic carbamate series proved to be very straightforward, the situation in the endocyclic amide series is considerably more complicated.

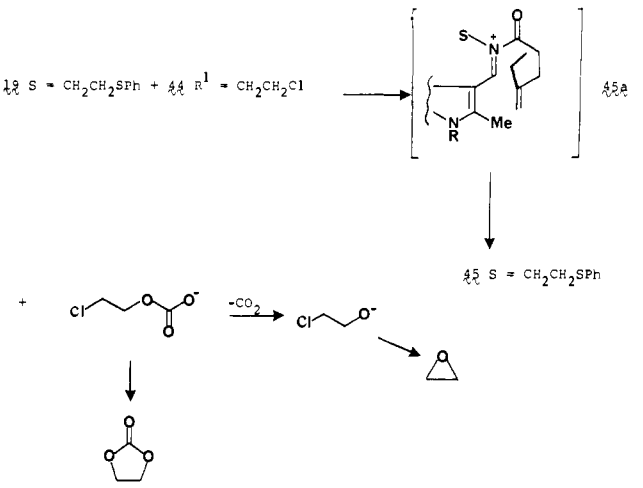
Treatment of the imine **19** with the mixed ethyl carbonic anhydride from 4-ethyl-4-pentenoic acid **44**, at 135 °C in chlorobenzene, gave the ethoxy adduct **47** (21%) and the tetracyclic amide **45** (33%): mp 195–195.5 °C. The structure and relative



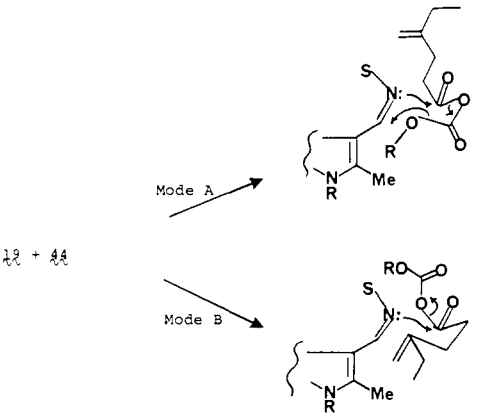
(25) Mills, J. F. D.; Nyburg, S. C. *J. Chem. Soc.* **1960**, 1458. Camerman, A.; Camerman, N.; Trotter, J. *Acta. Crystallogr.* **1965**, *19*, 314. Kennard, O.; Kerr, K. A.; Watson, D. G.; Fawcett, J. K.; Riva di Sanseverino, L. *Chem. Commun.* **1967**, 1286. (−)-Kopsanone methiodide has ring D in a chair (Craven, B. M.; Gilbert, B.; Raes Leme, L. A. *Chem. Commun.* **1968**, 955).

(26) Kunesch, N.; Ardisson, J.; Poisson, J.; Halls, T. D. J.; Wenkert, E. *Tetrahedron Lett.* **1981**, 1981.

Scheme VI



Scheme VII



stereochemistry of **45** was demonstrated by single-crystal X-ray crystallography and will be described in the accompanying paper, since the details are more pertinent to the pentacyclic systems. The yield of **45** represents a 20% reduction compared with the deethyl series.

Treatment of **21** with the mixed carbonic anhydride **44**, in the presence of triethylamine, heated in chlorobenzene at 135 °C, gave the β-lactam **48** (28%) and the tetracyclic amide **46** (11%). It appears that base promotes ketene formation.

Efforts to reduce the amount of ethoxy adduct **47** by using different mixed carbonic anhydrides did not work. For the sequence **44**, R^1 = Me, Et, *n*-Bu, and CH_2CH_2Cl, all of the mixed anhydrides gave approximately the same yield (ca. 20%) of the trapped adduct **47**. We could not use *tert*-butyl or isopropyl mixed carbonic anhydrides since they decomposed at the temperature (135 °C) needed to conduct the cyclization.[27]

The acyliminium ion **45a** would be expected to react with the generated in situ alcohol/alkoxide, either to deacylate **45a** producing the starting imine **19** and the corresponding ester of the pentenoic acid or to add to the iminium ion resulting in the observed adduct **47**. Most remarkably, the 2-chloroethyl carbonate (Scheme VI), which can in effect destroy itself intramolecularly by forming either ethylene oxide[28] and carbon dioxide or ethylene carbonate, which should overwhelmingly compete with any bimolecular trapping to give **47**, did not improve the yield of tetracyclic amide **45** but gave the trapped adduct **47** in the usual 20% yield.

Furthermore, the consistent yields of the alkoxy adducts **47** throughout the series of mixed carbonic anhydrides is unexpected. The most plausible explanation of these observations is that the

(27) Matzner, M.; Kurkjy, R. P.; Cotter, R. J. *Chem. Rev.* **1965**, *65*, 945.

(28) Swain, C. G.; Ketley, A. D.; Bader, R. F. W. *J. Am. Chem. Soc.* **1959**, *81*, 2353.

adducts **47** are formed concertedly with the acylation step via a pseudointramolecular addition of alkoxide to the developing iminium ion (Scheme VII).

The imine **19** can interact with the mixed anhydride in two orientations for the nitrogen lone pair of the imine to have a low-energy trajectory (maximum overlap) with the π-orbital of the ester carbonyl group. Mode A situates the alkoxy group directly over the π-system of the developing acyliminium ion in a six-membered chairlike transition state and leads to the observed adducts **47**. Whereas turning the mixed carbonic acid anhydride around, mode B, allows the acylation step but releases the carbonate group into the surrounding environment. Thus proton loss and cyclization lead to the tetracyclic amide. Consequently the ratio of cyclization to iminium ion trapping is determined by the orientation of the mixed carbonic anhydride with respect to the imine. This interpretation, while speculative, provides a rationalization of our unusual observations.

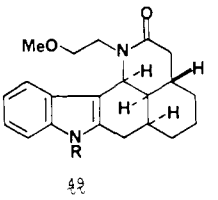
It was hoped that the problems involved with mixed carbonic anhydrides could be circumvented by using different activated esters. Unfortunately this was not so. Treatment of the imine **19** with the acid chloride acylimidazole or acylsulfonate of 4-ethyl-4-pentenoic acid gave no tetracyclic amide **45**, only starting material and decomposition to intractable mixtures. If the cyclication reaction **19** to **45** is carried out at 180 °C, instead of 135 °C, the undesired alkoxy adduct **47** is not formed, but the β-lactam **48** becomes the major byproduct. The tetracyclic amide **45** was formed in the usual 33% yield.

In summary, for the endocyclic amides in the 4a-ethyl series, the indole-2,3-quinodimethane cyclization is a delicately balanced reaction that requires very specific conditions to work. Although the yield of the tetracyclic amide **45** is only 33%, **45** contains all the carbon atoms necessary for aspidospermidine and the correct relative stereochemistry at the C/D ring fusion.

Some General Examples of Indole-2,3-quinodimethane Cyclizations. To illustrate that, apart from enabling a very short and convergent route to tetracyclic precursors of Aspidosperma alkaloids, the indole-2,3-quinodimethane cyclization can be used in a more general sense to construct complicated indole-based polycycles, we carried out a few exemplary experiments.

Treatment of the imine **18** with the mixed ethyl carbonic anhydride made from cyclohex-2-enylacetic acid[29] using the usual conditions (PhCl, 135 °C) gave the pentacyclic amide **49** (31%): mp 190–192 °C. The stereochemistry of **49** is tentatively assigned as cis/cis/trans, on the basis that the product would be formed with the E ring in a chair conformation, whereas the all-cis fusion forces the E ring into a boat conformation. The C/D ring fusion is cis (J = 4 Hz), and the C/E ring is cis enforced. Similarly, cyclopent-2-enylacetic acid[30] ethyl carbonic anhydride on treatment with the imine **18** gave the pentacyclic amide **50** (48%): mp 163–164 °C; assigned the all-cis relative stereochemistry.

A particularly interesting example, from both the structural point of view and the circumstantial evidence it provides in the understanding of the crucial indole-2,3-quinodimethane cyclization process, is the spiro cyclic amide **52**. Treatment of the imine **18** with the mixed ethyl carbonic anhydride derived from (1-allylcyclohexane)carboxylic acid **53**[31] (X = OCO_2Et) using the usual conditions (PhCl, 135 °C) gave no reaction. We have observed in other related extensions of imine acylation reactions that steric hinderance of the acylating agent, or the imine nitrogen atom, retards the reaction. The acid chloride **53** (X = Cl) on treatment with the imine **18** at 135 °C for 4 h gave the spirocyclic amide **52** (38%): mp 193.5–195 °C. Whereas acid chlorides usually give negative results, presumably because of ketene, and subsequent β-lactam formation, obviously **53** cannot, and consequently the cyclization works. Interestingly, the dimeric indole alkaloid isovoafoline **51** has a spiro-linked six-membered ring attached to the 3-position.[32]



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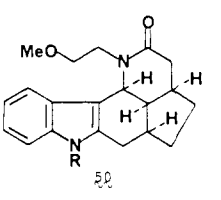

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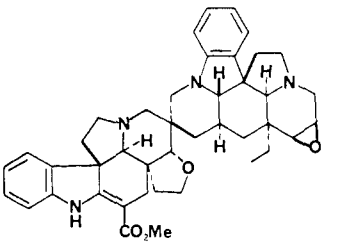
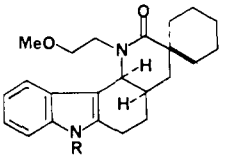
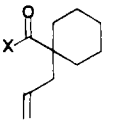


51



52



53 X = OCO_2Et
X = Cl

Summary. The exocyclic carbamate and endocyclic amide routes provide complementary syntheses for making tetracyclic indole alkaloid precursors. In particular they allow for functionalization at C_{11} and C_7, respectively. Both routes readily allow the C_{10}–C_{11} tryptamine two-carbon unit to be introduced in a direct manner. The following paper utilizes the methods and strategy described here for making the C_{11}–C_{12} bond, and subsequently two mutually complementary syntheses of aspidospermidine that illustrate this approach to indole alkaloid synthesis.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer grating spectrometer. ^{1}H NMR spectra were recorded on either a Varian EM-360 spectrometer or Varian HR 220-MHz spectrometer. High-resolution mass spectral data were obtained by Dr. Lubo Baczynskyj and Dick Wnuck of the Upjohn Co. Elemental analyses were carried out by the Midwest Microlab, Indianapolis. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected.

All solvents were dried and purified by standard techniques prior to use. All reactions were run under either nitrogen or argon unless otherwise stated. For experimental procedures of a general nature a complete description is given for a specified example, and subsequent details for other examples include quantities of substrate, yield, and characterization details. Thin layer chromatography (TLC) for monitoring the progress of reactions was conducted with Merck GF_{254} silica gel, aluminum-backed plates. Routine chromatographic purification of compounds was conducted, using Merck silica gel 60-H (catalog No. 7736) with a small hand bellows to develop a pressure gradient. Preparative layer chromatography (PLC) was carried out on Merck precoated plates, silica gel 60-F-254 (0.5 mm thickness). All column chromatography was carried out with petroleum ether (bp 60–80 °C) as the initial eluent; the polarity was progressively increased and the compound eluted with the solvent system given in the text. The products were preadsorbed onto silica gel prior to chromatography. All yields refer to chromatographically pure compounds, but in many cases the products, although pure (TLC, NMR), were foams.

1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-formylindole (6, R = $SO_2C_6H_4OMe$-*p*). To a stirred slurry of sodium hydride (1.89 g, 1.2 equiv 99%) in dry glyme (50 mL) was added 2-methyl-3-formylindole **6** (R = H) (10.5 g) in dry glyme (250 mL). After it was stirred at 20 °C for 1.5 h the mixture was heated at reflux for 15 min and then cooled to −5 °C (ice/salt bath). To this mixture was added (*p*-methoxybenzene)sulfonyl chloride (16.1 g) in dry glyme (50 mL) and imidazole (0.25 g) in dry glyme (2 mL). The mixture was stirred at 20 °C for 15 h and then poured into water (500 mL), and the aqueous solution was

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extracted with chloroform (3 × 500 mL). The combined extracts were washed with 1 N sodium hydroxide solution (500 mL), water (500 mL), and saturated aqueous brine solution (500 mL) and dried ($MgSO_4$). The extracts were concentrated in vacuo to approximately 50 mL and adsorbed onto silica gel. Flash chromatography eluting with chloroform/petroleum ether (4:1) gave **6** (R = $SO_2C_6H_4OMe$-*p*) (7.35 g, recrystallized from $CHCl_3$/petroleum ether). The filtrate from crystallization and mixed fractions from chromatography were combined and rechromatographed to give a further 2.16 g of pure **6** (R = $SO_2C_6H_4OMe$-*p*), resulting in a total yield of 44%: mp 129–130 °C (from $CHCl_3$/hexane). Complete physical characteristic IR, NMR, and MS anal have been reported previously.[9]

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl)]-2-methyl-3-(*N*-4-pentenylformimidoyl)indole (7, R = $SO_2C_6H_4OMe$-*p*). A solution of **6** (R = $SO_2C_6H_4OMe$-*p*) (329 mg, 1 mmol) in benzene (10 mL) was treated with 4-pentenylamine[33] (100 mg, 1.2 mmol). After the solution was stirred for 1 h anhydrous Na_2SO_4 was added, and the mixture was stirred for a further 2 h. The mixture was filtered and allowed to stand over 4-Å molecular sieves for 15 h. Filtration and evaporation gave the imine **7** (>95% crude product, from which the NMR indicated it was pure enough to be used directly in the next step): IR ($CHCl_3$) 1638, 1174 cm^{-1}; NMR ($CDCl_3$) δ 8.58 (1 H, s), 8.44–8.20 (2 H, m), 7.73 (2 H, d, J = 8 Hz), 7.40–7.25 (2 H, m), 6.86 (2 H, d, J = 8 Hz), 5.87 (1 H, m), 5.16–4.83 (2 H, m), 3.76 (3 H, s), 3.56 (2 H, t, J = 6 Hz), 2.71 (3 H, s), 2.19 (2 H, q, J = 6 Hz), 1.81 (2 H, m).

Monitoring the formation of imine **7** by TLC is not feasible because of hydrolysis on the silica gel plate to the starting aldehyde. The conversion was best followed by either IR or NMR.

2-Chloroethyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (8, E = $CO_2CH_2CH_2Cl$). A solution of **7** [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (990 mg, 3 mmol)] in chlorobenzene (30 mL) containing diisopropylethylamine (780 mg, 6 mmol) was cooled to 0 °C, and 2-chloroethyl chloroformate (858 mg, 6 mmol) was added dropwise. The mixture was heated, over a period of 35 min, to 135 °C and maintained at this temperature for 40 min. The above mixture was evaporated in vacuo and the residue dissolved in dichloromethane (30 mL), washed with 2 N HCl (2 × 20 mL), followed by saturated aqueous brine, and dried (Na_2SO_4). Evaporation of the solvent in vacuo and crystallization of the residue from ether/hexane gave **8** (E = $CO_2CH_2CH_2Cl$) 1.29 g (92%): mp 129–131 °C; IR ($CHCl_3$) 1695, 1598, 1260, 1160 cm^{-1}; NMR ($CDCl_3$) δ 8.20 (1 H, d, J = 7 Hz), 7.79–7.66 (2 H, m), 7.36–7.14 (3 H, m), 6.89 (2 H, d, J = 10 Hz), 5.57 (1 H, m), 4.59–4.39 (2 H, m), 4.00 (1 H, m), 3.86–3.68 (2 H, m), 3.79 (3 H, s), 3.09–2.86 (2 H, m), 2.38–1.86 (4 H, m), 1.63–1.36 (4 H, m); MS, m/e calcd for $C_{25}H_{27}{}^{35}ClN_2O_5S$ 502.133, found 502.133. Anal. Calcd for $C_{25}H_{27}ClN_2O_5S$: C, 59.69; H, 5.41; N, 5.83. Found: C, 59.80; H, 5.49; N, 5.83.

2-Hydroxyethyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (8, E = $CO_2CH_2CH_2OH$). A solution of **8** (E = $CO_2CH_2CH_2Cl$) (50 mg, 0.11 mmol) in THF (6 mL) was added to a mixture of vitamin B_{12}(aq) (4 mg), ammonium chloride (120 mg), and freshly activated zinc dust (40 mg) in water (4 mL). Ethanol (3 mL) was added to redissolve precipitated organic material. The solution was heated at reflux under argon for 36 h. The mixture was evaporated in vacuo and the residue dissolved in dichloromethane and dried (Na_2SO_4). Purification by chromatography gave **8** (E = $CO_2CH_2CH_2OH$) (30 mg, 63%) as a colorless foam: IR ($CHCl_3$) 3650–3300, 1675, 1596, 1264 cm^{-1}; NMR ($CDCl_3$) δ 8.20 (1 H, d, J = 7 Hz), 7.82–7.70 (2 H, m), 7.39–7.18 (3 H, m), 6.91 (2 H, d, J = 10 Hz), 5.64 and 5.52 (1 H, br), 4.50–4.32 (2 H, m), 4.14–3.82 (3 H, m), 3.79 (3 H, s), 3.07–2.93 (2 H, m), 2.77 (1 H, OH exchanges with D_2O), 2.41 (1 H, m), 2.09 (1 H, m), 1.97–1.84 (2 H, m), 1.61–1.27 (4 H, m); MS, m/e calcd for $C_{25}H_{28}N_2O_6S$ 484.167, found 484.168.

Vinyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (8, E = $CO_2CH{=}CH_2$). A solution of **8** (E = $CO_2CH_2CH_2Cl$) (94 mg, 0.2 mmol) in THF (5 mL) was added to a stirred slurry of potassium *tert*-butoxide (50 mg, 0.45 mmol) in THF (8 mL) at −15 °C. After 20 min at −15 °C the solution was concentrated in vacuo, ice water (10 mL) added, and the mixture stirred at 0 °C for 20 min. The precipitated solid was filtered off to give **8** (E = $CO_2CH{=}CH_2$) (90%) as a foam that failed to crystallize: IR ($CHCl_3$) 1700, 1645, 1595, 1260, 1145 cm^{-1}; NMR ($CDCl_3$) δ 8.23 (1 H, d, J = 7 Hz), 7.82–7.70 (2 H, m), 7.48–7.18 (3 H, m), 6.91 (2 H, d, J = 10 Hz), 5.61 (1 H, m), 4.93–4.75 (2 H, m), 4.54 (1 H, t, J = 7 Hz), 4.02 (1 H, m), 3.72 (3 H, s), 3.11–2.98 (2 H, m), 2.34 (1 H, m), 2.13 (1 H, m), 2.02–1.84 (2 H, m), 1.68–1.36 (4 H, m); MS, m/e calcd for $C_{25}H_{26}N_2O_5S$ 466.156, found 466.155.

(33) 4-Pentenylamine was prepared by $LiAlH_4$ reduction of 4-pentenenitrile in 74% yield. Braun, J. V. *Justus Liebigs Ann. Chem.* **1911**, *382*, 43.

cis-2,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole (16). Solutions of samarium diiodide in dry THF were prepared as follows. Diiodoethane (141 mg, 0.5 mmol) in dry THF (8 mL) at 20 °C was slowly added, with stirring, to samarium powder (150 mg, 1 mmol) under argon. A deep blue solution was formed. The samarium diiodide solution was stirred at 20 °C for 1 h to ensure complete reaction.

To the above solution was added **8** (E = $CO_2CH_2CH_2Cl$) (235 mg, 0.5 mmol) in dry THF (4 mL). The mixture was heated at reflux for 7 h, during which time the blue solution gradually became pale yellow (Sm^{II}–Sm^{III}). To the above cooled solution was added 1 N HCl (5 mL) and water (60 mL), and the mixture was extracted with EtOAc (4 × 20 mL). The combined extracts were washed with saturated aqueous brine and dried (Na_2SO_4). Evaporation of the extract, in vacuo, gave **16** (140 mg, 71%) as a colorless foam: IR ($CHCl_3$) 3300–2900, 1590, 1260, and 1162 cm^{-1}; NMR ($CDCl_3$) δ 8.18 (1 H, m), 7.75 (2 H, d, J = 10 Hz), 7.58 (1 H, m), 7.23 (2 H, m), 6.82 (2 H, d, J = 10 Hz), 3.98 (1 H, d, J = 2 Hz), 3.75 (3 H, s), 3.25–3.57 (3 H, m), 2.35–1.34 (9 H, m); MS, m/e calcd for $C_{22}H_{24}N_2O_3S$ 396.151, found 396.152.

The aqueous phase was treated with 2 N NaOH solution to precipitate samarium salts and extracted with EtOAc, to give **10** (20 mg).

2,2,2-Trichloroethyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (8, E = $CO_2CH_2CCl_3$). A solution of **7** [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (330 mg, 1 mmol)] in chlorobenzene (10 mL), containing diisopropylethylamine (260 mg), was cooled to 0 °C, and 2,2,2-trichloroethyl chloroformate (424 mg, 2 mmol) was added dropwise. The mixture was heated to 135 °C and held at this temperature for 1.25 h. Evaporation, in vacuo, and purification of the residue by flash chromatography gave **8** (E = $CO_2CH_2CCl_3$) as a colorless foam (450 mg, 79%): IR ($CHCl_3$) 1700, 1598, 1262, 1168, 1147 cm^{-1}; NMR ($CDCl_3$) δ 8.23 (1 H, d, J = 7 Hz), 7.86–7.68 (2 H, m), 7.43–7.14 (3 H, m), 6.95–6.86 (2 H, m), 5.64 (1 H, br s), 5.05–4.77 (2 H, m), 4.09 (1 H, m), 3.79 (3 H, s), 3.09–2.95 (2 H, m), 2.36 (1 H, m), 2.11 (1 H, m), 2.00–1.86 (2 H, m), 1.70–1.36 (4 H, m); MS, m/e calcd for $C_{25}H_{25}{}^{35}Cl_3N_2O_5S$ 570.055, found 570.055.

A solution of **8** (E = $CO_2CH_2CCl_3$) (200 mg, 0.35 mmol) in 9:1 AcOH/H_2O (5 mL) was treated with zinc dust (500 mg) over a 3-h period. After it was stirred for 15 h at 20 °C the solution was filtered and the filtrate concentrated in vacuo to ca. 1 mL. Water (10 mL) and 1 N NaOH (10 mL) were added, with ice-bath cooling, to give a precipitate that was filtered, washed with water, and dried to give **16** (120 mg, 86%). The product was homogeneous by TLC (80% EtOAc/20% MeOH) and identical (IR and NMR) with the material prepared by the samarium diiodide procedure. It was used directly in subsequent reactions without further purification.

β-Lactam Adduct 17. To a solution of the imine **7** (1 mmol) and diisopropylethylamine (0.35 mL, 2 mmol) in chlorobenzene (10 mL) at 0 °C was added freshly distilled phenylacetyl chloride (310 mg, 2 mmol) in chlorobenzene (2 mL). The mixture was heated to reflux for 6 h and cooled to 20 °C, and further portions of diisopropylethylamine (0.35 mL) and phenylacetyl chloride (310 mg) in chlorobenzene (2 mL) were added. Further heating at reflux for 15 h followed by evaporation of the above mixture in vacuo and chromatography of the residue over florisil eluting with EtOAc/petroleum ether (1:3) gave the β-lactam adduct **17** (428 mg, 83%) as an oil: IR ($CHCl_3$) 1737 cm^{-1}; NMR ($CDCl_3$) δ 8.33 (1 H, d, J = 8 Hz), 7.77 (2 H, d, J = 9 Hz), 7.60 (1 H, d, J = 8 Hz), 7.16–7.45 (7 H, m), 6.89 (2 H, d, J = 9 Hz), 5.57–5.78 (1 H m), 4.87–5.00 (2 H, m), 4.75 (1 H, br s), 4.57 (1 H, br s), 3.85 (3 H, s), 3.51 (1 H, 2 t, J_s = 15, 7.5 Hz), 2.61–2.77 (1 H, m), 2.56 (3 H, s), 2.01 (2 H, q, J = 7 Hz), 1.52 (2 H, quintet, J = 7 Hz); MS, m/e calcd for $C_{30}H_{30}N_2O_4S$ 514.192, found 514.191.

General Procedure for Imine Formation (18–24). A solution of **6** (R = $SO_2C_6H_4OMe$-*p*) (330 mg, 1 mmol) in dichloromethane (10 mL) was treated with the appropriate amine (1.05 mmol; see individual examples for details concerning the amine). Freshly activated 4-Å molecular sieves (ca. 5 g) were added, and the mixture was stirred for 15 h. The mixture was filtered, and the filtrate was concentrated in vacuo to give the imine. The imines were all isolated as pale yellow oils and were used without further purification. Both IR and NMR (see individual examples) showed complete conversion of **6** (R = $SO_2C_6H_4OMe$-*p*) into the imine. Yields in the cyclization reactions are based upon **6** (R = $SO_2C_6H_4OMe$-*p*).

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-[*N*-(2-methoxyethyl)formimidoyl]indole (18, S = CH_2CH_2OMe): NMR ($CDCl_3$) δ 8.50 (1 H, s), 8.14–8.46 (2 H, m), 7.67 (2 H, d, J = 9 Hz), 7.18–7.35 (2 H, m), 6.70 (2 H, d, J = 9 Hz), 3.65–3.76 (4 H, m), 3.59 and 3.61 (3 H, 2 s), 3.32 (3 H, s), 2.71 (3 H, s).

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-[*N*-(2-(phenylthio)ethyl)formimidoyl]indole (19, S = CH_2CH_2SPh): IR ($CHCl_3$) 1633 cm^{-1};

NMR ($CDCl_3$) δ 8.50 (1 H, s), 8.30 (2 H, m), 7.74 (2 H, d, J = 10 Hz), 7.52–7.06 (7 H, m), 6.81 (2 H, d, J = 10 Hz), 3.85 (2 H, t, J = 7.5 Hz), 3.75 (3 H, s), 3.30 (2 H, t, J = 7 Hz), 2.70 (3 H, s). Prepared from 2-(phenylthio)ethylamine.

(*E*)-1[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-[*N*-(2-(phenylseleno)-ethyl)formimidoyl]indole (20, S = CH_2CH_2SePh): IR ($CHCl_3$) 1635 cm^{-1}; NMR δ ($CDCl_3$) 8.60 (1 H, s), 8.41–8.15 (2 H, m), 7.75 (2 H, d, J = 10 Hz), 7.61–7.46 (2 H, m), 7.37–7.11 (3 H, m), 6.82 (2 H, d, J = 10 Hz), 3.95 (2 H, t, J = 7 Hz), 3.78 (3 H, s), 3.26 (2 H, t, J = 7 Hz), 2.72 (3 H, s). Prepared from 2-(phenylseleno)ethylamine.

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-[*N*-(2,2-dimethoxy-ethyl)formimidoyl]indole [21, S = $CH_2CH(OMe)_2$]: IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.57 (1 H, s), 8.46–8.13 (2 H, m), 7.75 (2 H, d, J = 10 Hz), 7.43–7.16 (2 H, m), 6.85 (2 H, d, J = 10 Hz), 4.68 (1 H, t, J = 6 Hz), 3.76 (2 H, d, J = 6 Hz), 3.72 (3 H, s), 3.37 (6 H, s), 2.68 (3 H, s). Prepared from 2,2-dimethoxyethylamine.

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-[*N*-(2-bromoethyl)-formimidoyl]indole (22, S = CH_2CH_2Br): IR ($CHCl_3$) 1635 cm^{-1}; NMR δ ($CDCl_3$) 8.47 (1 H, s), 8.29 (2 H, m), 7.27 (2 H, d, J = 9 Hz), 7.28 (2 H, m), 6.80 (2 H, d, J = 9 Hz), 3.95 (2 H, t, J = 6 Hz), 3.70 (3 H, s), 3.59 (2 H, t, J = 6 Hz), 2.71 (3 H, s). Prepared from 2-bromoethylamine, which was liberated in situ from the hydrobromide salt by treatment with triethylamine.

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-(*N*-benzylformimidoyl)indole (23, S = CH_2Ph): IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.64 (1 H, s), 8.42–8.60 (1 H, m), 8.20–8.40 (1 H, m), 7.75 (2 H, d, J = 9 Hz), 7.70–7.50 (7 H, m), 6.77 (2 H, d, J = 9 Hz), 4.84 (2 H, s), 3.66 (3 H, s), 2.77 (3 H, s).

(*E*)/(*Z*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-(*N*-methylformimidoyl)indole (24, S = Me): NMR ($CDCl_3$) δ 8.47 and 8.49 (1 H, two s for E and Z isomers), 8.15–8.40 (2 H, m), 7.71 (2 H, d, J = 9 Hz), 7.20–7.40 (2 H, m), 6.77 (2 H, d, J = 7 Hz), 3.63 (3 H, s), 3.48 (3 H, br s), 2.72 (3 H, s).

2-(Phenylseleno)ethylamine.[34] Diphenyl diselenide (6.0 g, 0.2 mol) in absolute EtOH (100 mL) was treated with sodium borohydride (1.54 g, 0.04 mol) over a 20-min period. To the resulting solution was added 2-bromoethylamine hydrobromide (8.2 g, 0.04 mol) in absolute EtOH (60 mL). The mixture was heated at reflux for 3.5 h, cooled to 20 °C, and filtered. The filtrate was acidified with concentrated HCl and the solution concentrated in vacuo to approximately 80 mL. To this concentrate was added 50% aqueous NaOH solution and the mixture extracted with ether (3 × 40 mL). The combined extracts were washed with water, followed by saturated brine, and dried (Na_2SO_4). Evaporation of the solvent and distillation of the resulting oil gave 2-(phenylseleno)ethylamine (6.1 g, 76%): bp 74–78 °C (0.15 mmHg); IR (neat) 3360, 1575 cm^{-1}; NMR ($CDCl_3$) δ 7.61–7.40 (2 H, m), 7.34–7.16 (3 H, m), 2.92 (4 H, br s), 1.26 (2 H, s, NH_2, exchanged with D_2O). Anal. Calcd for $C_8H_{11}NSe$: C, 48.00; H, 5.54; N, 7.00. Found: C, 47.87; H, 5.55; N, 6.88.

Mixed Carboxylic–Carbonic Anhydrides. Ethyl 4-Pentenoyl Carbonate (25). A solution of 4-pentenoic acid[35] (600 mg, 6 mmol) and dry triethylamine (606 mg, 6 mmol) in dichloromethane (20 mL) at 0 °C was treated with ethyl chloroformate (654 mg, 6 mmol). After 0.5 h at 0 °C the solution was concentrated in vacuo, and chlorobenzene (20 mL) was added to the residue. The mixture was filtered to remove triethylamine hydrochloride, and the filtrate containing the mixed anhydride was used directly in the subsequent cyclization reactions. The same procedure was used to prepare ethyl 4-ethyl-4-pentenoyl carbonate (**44**).

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-(2-methoxyethyl)-2*H*-pyrido[3,2-*c*]carbazol-2-one (26, S = CH_2CH_2OMe).** To a solution of the imine **18** (2.5 mmol) in chlorobenzene (25 mL) heated at reflux was added a solution of the ethyl carbonic anhydride **25** (5 mmol) in chlorobenzene (5 mL). The mixture was heated at reflux for 5 h, cooled to 20 °C and evaporated in vacuo, and the residue was flash chromatographed to give **26** (S = CH_2CH_2OMe) (645 mg, 55%): mp 178 °C (from $CHCl_3$/petroleum ether); IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.23 (1 H, dd, J = 6, 8 Hz), 7.73 (2 H, d, J = 9 Hz), 7.53 (1 H, br d, J = 7 Hz), 7.23–7.39 (2 H, m), 6.88 (2 H, d, J = 9 Hz), 4.73 (1 H, d, J = 4 Hz), 3.77 (3 H, s), 3.10 (3 H, s), 2.90–3.68 (6 H, m), 1.77–2.48 (6 H, m), 1.52–1.68 (1 H, m). Anal. Calcd for $C_{25}H_{28}N_2O_5S$: C, 64.09; H, 6.02; N, 5.98. Found: C, 63.84; H, 6.17; N, 5.83.

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-[2-(phenylthio)ethyl]-2*H*-pyrido[3,2-*c*]carbazol-2-one (27, S = CH_2CH_2SPh).** To a solution of the imine **19** (S = CH_2CH_2SPh) [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (330 mg, 1 mmol)] in chlorobenzene (12 mL) was added a solution of the mixed carbonic anhydride **25** (prepared as described from 4-pentenoic acid and ethyl chloroformate) (2 mmol) in chlorobenzene (4 mL), and the mixture was heated at 135 °C for 3 h. Evaporation of the mixture in vacuo and chromatography of the residue on elution with $CHCl_3$/petroleum ether (1:4) gave the *ethoxy adduct* **34** (S = CH_2CH_2SPh) (203 mg, 34%) as a pale yellow oil: IR ($CHCl_3$) 1640, 1592, 1168 cm^{-1}; NMR ($CDCl_3$) δ 8.26 (1 H, d, J = 7 Hz), 7.86–7.58 (3 H, m), 7.40–6.90 (8 H, m), 6.74 (2 H, d, J = 10 Hz), 5.76 (1 H, m), 5.16–4.82 (2 H, m), 3.71 (3 H, s), 3.77–3.10 (5 H, m), 2.60 (3 H, s), 2.80–2.08 (5 H, m), 1.23 (3 H, t, J = 7 Hz).

Continued elution with $CHCl_3$/petroleum ether (3:2) gave the *tetracycle* **27** (S = CH_2CH_2SPh) (240 mg, 44%): mp 164–166 °C (from methanol); IR ($CHCl_3$) 1630, 1595 cm^{-1}; NMR ($CDCl_3$) δ 8.29 (1 H, d, J = 7 Hz), 7.75 (2 H, d, J = 10 Hz), 7.50–7.41 (3 H, m), 7.13–7.05 (3 H, m), 6.97–6.88 (2 H, m), 6.82 (2 H, d, J = 10 Hz, 4.73 (1 H, d, J = 3.5 Hz), 3.70 (3 H, s), 3.45–3.25 (2 H, m), 3.14–2.79 (2 H, m), 2.45–2.25 (3 H, m), 2.20–1.77 (5 H, m), 1.64 (1 H, m). Anal. Calcd for $C_{30}H_{30}N_2O_4S_2$: C, 65.91; H, 5.53; N, 5.12. Found: C, 65.97; H, 5.41; N, 4.95.

In another experiment conducted in a modified way (see below) we were able to isolate the β-lactam adduct **36** (S = CH_2CH_2SPh).

A solution of the mixed anhydride **25** (12 mmol) in chlorobenzene (28 mL) was added by motorized syringe over a 3-h period to a hot (135 °C) solution of the imine **19** (S = CH_2CH_2SPh) [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (1.65 g, 5 mmol)] in chlorobenzene (60 mL). When the addition was complete (3 h) the mixture was evaporated in vacuo and the residue taken up in methanol heated at reflux (ca. 30 mL). The tetracyclic adduct **27** (S = CH_2CH_2SPh) (1.65 g, 60%) crystallized from the mixture immediately. Concentration of the filtrate and subsequent chromatography gave the ethoxy adduct **34** (S = CH_2CH_2SPh) (386 mg, 13%) and the β-lactam adduct **36** (S = CH_2CH_2SPh) (275 mg, 10%): IR ($CHCl_3$) 1745, 1592, 1168 cm^{-1}; NMR ($CDCl_3$) δ 8.27 (1 H, m), 7.70 (2 H, d, J = 10 Hz), 7.49–7.06 (8 H, m), 6.80 (2 H, d, J = 10 Hz), 5.77 (1 H, m), 5.06–4.80 (2 H, m), 4.55 (1 H, d, J = 2.5 Hz), 3.72 (3 H, s), 3.61–3.34 (2 H, m), 3.04–2.83 (3 H, m), 2.55 (3 H, s), 2.62–2.30 (2 H, m).

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-[2-(phenylseleno)ethyl]-2*H*-pyrido[3,2-*c*]carbazol-2-one (28, S = CH_2CH_2SePh).** To a solution of the imine **20**, prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (330 mg, 1 mmol), in chlorobenzene (10 mL) at 20 °C was added the ethyl carbonic anhydride prepared from 4-pentenoic acid (200 mg, 2 mmol) in chlorobenzene (5 mL). The mixture was heated to 135 °C for 3.5 h. Evaporation of the solvent in vacuo, followed by flash chromatography, gave on elution with $CHCl_3$/petroleum ether (7:3) the tetracycle **28** (132 mg, 22%): mp 143–144 °C (from MeOH); IR ($CHCl_3$) 1640, 1596, 1171 cm^{-1}; NMR ($CDCl_3$) δ 8.29 (1 H, d, J = 7 Hz), 7.73 (2 H, d, J = 10 Hz), 7.48–7.23 (4 H, m), 7.04 (4 H, br s), 6.77 (2 H, d, J = 10 Hz), 4.66 (1 H, br s), 3.73 (1 H, m), 3.64 (3 H, s), 3.50–3.20 (2 H, m), 3.00 (1 H, m), 2.79 (1 H, m), 2.45–1.75 (7 H, m), 1.61 (1 H, m); MS, m/e calcd for $C_{30}H_{30}N_2O_4S^{80}Se$ 594.109, found 594.111. Anal. Calcd for $C_{30}H_{30}N_2O_4SSe$: C, 60.70; H, 5.09; N, 4.72. Found: C, 60.58; H, 5.16; N, 4.82.

In addition to the desired tetracyclic adduct **28**, two other products were obtained. **33** (R = CH_2CH_2SePh) (15%): IR (thin film) 1650, 1595, 1174 cm^{-1}; NMR ($CDCl_3$) δ 8.27 (1 H, d, J = 7 Hz), 7.77–7.64 (3 H, m), 7.39–7.05 (8 H, m), 6.86 (2 H, d, J = 10 Hz), 5.68 (1 H, m), 5.04–4.89 (2 H, m), 3.75 (3 H, s), 3.59–3.32 (5 H, m), 3.23 (1 H, m), 2.66 (1 H, m), 2.52 (3 H, s), 2.39–2.00 (2 H, m), 1.25 (3 H, t, J = 7 Hz). **35** (R = CH_2CH_2SePh) (5%): NMR ($CDCl_3$) δ 8.22 (1 H, m), 7.65 (2 H, d, J = 10 Hz), 7.40–7.00 (8 H, m), 6.80 (2 H, d, J = 10 Hz), 5.73 (1 H, m), 5.16–4.80 (2 H, m), 4.50 (1 H, d, J = 2 Hz), 3.71 (3 H, s), 3.58–2.11 (9 H, m), 2.50 (3 H, s); IR ($CHCl_3$) 1735, 1592, and 1165 cm^{-1}.

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-[2,2-dimethoxyethyl]-2*H*-pyrido[3,2-*c*]carbazol-2-one [29, S = $CH_2CH(OMe)_2$].** To a solution of the imine **21**, prepared from the aldehyde 6 (R = $SO_2C_6H_4OMe$-*p*) (2.30 g, 7 mmol), in chlorobenzene (120 mL) at 20 °C was added the ethyl carbonic anhydride prepared from 4-pentenoic acid (1.50 g, 15 mmol) in chlorobenzene (40 mL). The mixture was heated to 135 °C for 3.5 h. Evaporation of the solvent in vacuo, followed by flash chromatography, gave on elution with $CHCl_3$/petroleum ether (3:7) the ethoxy adduct **32** [R = $CH_2CH(OMe)_2$] (670 mg, 19%) as a pale yellow oil. IR ($CHCl_3$) 1638, 1595, 1160, 1065 cm^{-1}; NMR ($CDCl_3$) δ 8.27 (1 H, d, J = 7 Hz), 7.80–7.68 (3 H, m), 7.34–7.18 (3 H, m), 6.89 (2 H, d, J = 10 Hz), 5.84 (1 H, m), 5.11–4.93 (2 H, m), 3.79 (3 H, s), 3.75 (1 H, m), 3.66–3.48 (2 H, m), 3.38 (1 H, m), 3.16 (1 H, m), 3.09 (3 H, s), 3.02 (3 H, s), 2.68–2.60 (2 H, m), 2.59 (3 H, s), 2.41 (2 H, q, J = 7 Hz), 1.29 (3 H, t, J = 7 Hz). Continued elution with

(34) 2-(Selenophenyl)ethylamine has been reported but with no experimental details (Heck, J. V.; Christensen, B. G. *Tetrahedron Lett.* **1981**, 5027).
(35) Linstead, R. P.; Rydon, H. N. *J. Chem. Soc.* **1933**, 580.

$CHCl_3$/petroleum ether (7:3) gave the tetracyclic adduct **29** (2.02 g, 58%) as a colorless foam: IR ($CHCl_3$ 1640, 1595, 1168 cm^{-1}; NMR ($CDCl_3$) δ 8.18 (1 H, d, J = 7 Hz), 7.75 (2 H, d, J = 10 Hz), 7.57 (1 H, m), 7.36–7.20 (2 H, m), 6.91 (2 H, d, J = 10 Hz), 4.77 (1 H, d, J = 4 Hz), 5.57 (1 H, dd, J_s = 4, 7 Hz), 3.77 (3 H, s), 3.73 (1 H, m), 3.43–2.93 (3 H, m), 3.36 (3 H, s), 3.18 (3 H, s), 2.45–2.00 (5 H, m), 1.91 (1 H, m), 1.66 (1 H, m); MS, m/e calcd for $C_{25}H_{26}N_2O_5S$ (M^+ – MeOH) 446.156, found 446.155.

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-(2-benzyl)-2*H*-pyrido[3,2-*c*]carbazol-2-one (30, S = CH_2Ph).** To a solution of the imine **23** [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (165 mg, 0.5 mmol)] in chlorobenzene (3 mL) heated at reflux was added the mixed carbonic anhydride **34** (1.5 mmol) in chlorobenzene (1.5 mL). After 6 h at reflux, **34** (1.0 mmol) was added and the mixture heated at reflux for 15 h. The mixture was evaporated in vacuo and the residue flash chromatographed, by elution with EtOAc/petroleum ether, to give **30** (S = CH_2Ph) (140 mg, 56%): mp 211.5–212.5 °C (from $CHCl_3$/petrolium ether); IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.23 (1 H, d, J = 9 Hz), 7.72 (2 H, d, J = 9 Hz), 7.02–7.43 (6 H, m), 6.92 (2 H, d, J = 9 Hz), 6.78 (2 H, br d, J = 7 Hz), 4.75 (1 H, d, J = 2.5 Hz), 4.60 (2 H, s), 3.81 (3 H, s), 2.88–2.99 (2 H, m), 2.34–2.64 (2 H, m), 2.03–2.23 (2 H, m), 1.50–1.82 (3 H, m); MS, m/e calcd for $C_{29}H_{28}N_2O_4S$ 500.196, found 500.196.

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-methyl-2*H*-pyrido[3,2-*c*]carbazol-2-one (31, S = Me).** To a solution of the imine **24** (0.5 mmol) in chlorobenzene (3 mL) heated at reflux was added a solution of the mixed anhydride **34** (1.5 mmol) in chlorobenzene (1.5 mL). After 6 h a further quantity of **34** (1.0 mmol) was added and the mixture heated at reflux for 15 h. The solvent was evaporated in vacuo, and the residue was chromatographed over Florisil, followed by flash chromatography eluting with EtOAc/petroleum ether to give **31** (S = Me) (86 mg, 40%): mp 91–92 °C (from $CHCl_3$/petroleum ether); IR ($CHCl_3$) 1640, 1620 cm^{-1}; NMR ($CDCl_3$) δ 8.24 (1 H, br d, J = 6 Hz), 7.73 (2 H, d, J = 9 Hz), 7.28–7.58 (3 H, m), 6.90 (2 H, d, J = 9 Hz), 4.64 (1 H, br s), 3.79 (3 H, s), 3.23–3.38 (1 H, m), 2.87–3.07 (1 H, m), 2.73 (3 H, s), 2.46 (2 H, t, J = 6 Hz), 1.6–2.25 (5 H, m); MS, m/e calcd for $C_{23}H_{24}N_2O_4S$ 424.147, found 424.150. Anal. Calcd for $C_{23}H_{24}N_2O_4S$: C, 52.99; H, 4.63; N, 5.15. Found: C, 52.94; H, 4.56; N, 5.12.

4-Ethyl-4-pentenylamine (38). 4-Ethyl-4-pentenoic acid (9.4 g, 73.4 mmol, prepared by the literature method)[23] in dichloromethane (250 mL) was treated with triethylamine (7.78 g, 73.4 mmol) at 0 °C. After the mixture was stirred for 10 min, a solution of freshly distilled ethyl chloroformate (8.8 g, 80.7 mmol) in dichloromethane (10 mL) was added dropwise. The mixture was stirred for 1 h at 0 °C and then warmed to 20 °C for 0.5 h. The mixture was concentrated in vacuo to approximately 100 mL and cooled to 0 °C, and 0.88 ammonia solution (300 mL) was added. The stirred two-phase mixture was left for 15 h at 20 °C; the organic phase was separated, washed with brine, and dried ($MgSO_4$). Evaporation of the solvent and crystallization of the residue from $CHCl_3$/petroleum ether gave 4-ethyl-4-pentenamide (6.6 g, 70%): mp 79–81 °C; IR ($CHCl_3$) 3530, 3405, 1678, 1645 cm^{-1}; NMR ($CDCl_3$) δ 6.21 (2 H, br), 4.76 (2 H, m), 2.34 (4 H, s), 2.05 (2 H, q, J = 7 Hz), 1.04 (3 H, t, J = 7 Hz). Anal. Calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 66.30; H, 10.28; N, 11.06.

To a stirred slurry of lithium aluminum hydride (1.1 g, 28.9 mmol) in dry ether (30 mL) was added a solution of 4-ethyl-4-pentenamide (3.0 g, 23.6 mmol) in dry ether (60 mL) over a 10-min period. The mixture was stirred for 15 h at 20 °C and cooled to 0 °C, and water (4.5 mL) was cautiously added. The mixture was filtered and washed with ether, and the filtrate was washed with brine and dried (Na_2SO_4). The solvent was carefully evaporated using a 10-cm fractionating column at atmospheric pressure. When the volume was approximately 10 mL the residue was distilled through a short-path apparatus to give **38** (1.3 g, 49%): bp 130–140 °C; IR (thin film) 3700–2300, 1640 cm^{-1}; NMR ($CDCl_3$) δ 4.73 (2 H, br), 2.71 (2 H, t, J = 7 Hz), 2.04 (4 H, q, J = 7 Hz), 1.62 (2 H, q, J = 7 Hz), 1.25 (2 H, br, exchanged by D_2O), 1.02 (3 H, t, J = 7 Hz).

(*E*)-1-[(*p*-Methoxyphenyl)sulfonyl]-2-methyl-3-[*N*-(4-ethyl-4-pentenyl)formimidoyl]indole (39), prepared by the general method described for imine formation: IR ($CHCl_3$) 1638 cm^{-1}; NMR ($CDCl_3$) δ 8.50 (1 H, s), 8.40–8.06 (2 H, m), 7.70 (2 H, d, J = 9 Hz), 7.35–7.14 (2 H, m), 6.80 (2 H, d, J = 9 Hz), 4.74 (2 H, br s), 3.76 (3 H, s), 3.57 (2 H, t, J = 7 Hz), 2.77 (3 H, s), 2.33–1.62 (6 H, m), 1.00 (3 H, t, J = 7 Hz).

Methyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-4a-ethyl-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (40, E = CO_2Me). A solution of the imine **39**, prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (330 mg, 1 mmol), in chlorobenzene (10 mL) containing diisopropylethylamine (260 mg, 2 mmol) was cooled to 0 °C, and freshly distilled methyl chloroformate (285 mg, 3 mmol) was added. The mixture was stirred at 0 °C for 20 min and then heated to 135 °C over 45 min. After 3 h at 135 °C [additional methyl chloroformate (200 mg) was added after 1.5 h] the mixture was evaporated in vacuo, and the residue was purified by flash chromatography. Elution with $CHCl_3$/petroleum ether (1:4) gave **40** (E = CO_2Me) (260 mg, 54%) as a foam: IR ($CHCl_3$) 1683, 1594, 1255, 1160 cm^{-1}; NMR ($CDCl_3$) δ 8.20 (1 H, d, J = 7 Hz), 7.75 (2 H, d, J = 10 Hz), 7.36–7.16 (3 H, m), 6.89 (2 H, d, J = 10 Hz), 5.27 and 5.11 (1 H, 2 br s), 4.07 (1 H, m), 3.86 (3 H, br s), 3.79 (3 H, s), 3.23–2.84 (2 H, m), 2.25 (1 H, m), 2.11–1.18 (9 H, m), 0.86 (3 H, t, J = 7 Hz). MS, m/e calcd for $C_{26}H_{30}N_2O_5S$: 482.187. Found: 482.182.

2-Chloroethyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-4a-ethyl-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (41, E = $CO_2CH_2CH_2Cl$). A solution of the imine **39** [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (330 mg, 1 mmol)] in chlorobenzene (10 mL) containing diisopropylethylamine (260 mg, 2 mmol) was cooled to 0 °C and treated with a solution of 2-chloroethyl chloroformate (286 mg, 2 mmol) in chlorobenzene (1 mL). The above solution was heated to 135 °C over a 0.5-h period and maintained at this temperature for a further 1 h. Evaporation of the solvent in vacuo, followed by flash chromatography of the residue, gave on elution with chloroform/petroleum ether (1:4) **41** (E = $CO_2CH_2CH_2Cl$) (421 mg, 70%) as a colorless glass: IR ($CHCl_3$) 1690, 1592, 1164 cm^{-1}; NMR ($CDCl_3$) δ 8.20 (1 H, d, J = 7 Hz), 7.79–7.68 (2 H, m), 7.34–7.14 (3 H, m), 6.91 (2 H, d, J = 10 Hz), 5.27 and 5.18 (1 H, two br s), 4.61–4.38 (2 H, m), 4.00 (1 H, m), 3.77 (3 H, s), 3.77–3.68 (2 H, m), 3.18–2.84 (2 H, m), 2.25 (1 H, m), 1.82 (1 H, m), 1.75–1.38 (5 H, m), 1.38–1.18 (2 H, m), 0.87 (3 H, t, J = 7 Hz). MS, m/e calcd for $C_{27}H_{31}N_2O_5SCl$: 530.164. Found: 530.165.

2,2,2-Trichloroethyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-4a-ethyl-7-[(*p*-methoxyphenyl)sulfonyl]-1*H*-pyrido[3,2-*c*]carbazole-1-carboxylate (42, E = $CO_2CH_2CCl_3$). A solution of the imine **39** [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (660 mg, 2 mmol)] in chlorobenzene (20 mL) containing diisopropylethylamine (520 mg, 4 mmol) was cooled to 0 °C and treated with 2,2,2-trichloroethyl chloroformate (848 mg, 4 mmol). The mixture was heated to 135 °C and maintained at this temperature for 10 h. During this period additional 2,2,2-trichloroethyl chloroformate (3 × 0.2 mL) was added. After the mixture was cooled to 20 °C, dichloromethane (40 mL) was added, and the solution was washed with 1 N HCl, followed by brine, and dried (Na_2SO_4). Evaporation of the solvent in vacuo, followed by flash chromatography of the residue, gave **42** (E = $CO_2CH_2CCl_3$) (550 mg, 46%): mp 182–184 °C (EtOAc/hexane); IR ($CHCl_3$) 1695, 1590, 1160 cm^{-1}; NMR ($CDCl_3$) δ 8.23 (1 H, d, J = 7 Hz), 7.86–7.68 (2 H, m), 7.36–7.13 (3 H, m), 6.98–6.86 (2 H, m), 5.29 and 5.25 (1 H, 2 br s), 5.05 (d, J = 11 Hz), 4.86 (d, J = 11 Hz), and 4.95 (s) (comprising 2 H, 4.07 (1 H, m), 3.86 (3 H, s), 3.20–2.86 (2 H, m), 2.34 (1 H, m), 1.95–1.20 (8 H, m), 0.93 (3 H, t, J = 7 Hz); MS, m/e calcd for $C_{27}H_{29}Cl_3N_2O_5S$ 598.086, found 598.090. Anal. Calcd for $C_{27}H_{29}Cl_3N_2O_5S$: C, 54.05; H, 4.87; N, 4.67. Found: C, 53.83; H, 4.92; N, 4.76.

Methyl *cis*-2,3,4,4a,5,6,7,11c-Octahydro-4a-ethyl-7*H*-pyrido[3,2-*c*]-carbazole-1-carboxylate (43). A solution of **40** (E = CO_2Me) (260 mg) in methanol (10 mL) and 20% aqueous potassium hydroxide (2 mL) was heated at reflux for 24 h. The cooled mixture was diluted with water (10 mL) and extracted with EtOAc (2 × 10 mL). The combined extracts were dried ($MgSO_4$), evaporated in vacuo, and chromatographed to give **43** (75 mg, 45%): mp 171–172 °C (from benzene/petroleum ether); IR ($CHCl_3$) 3470, 1680 cm^{-1}; NMR ($CDCl_3$) δ 8.15 (1 H, br), 7.30–6.88 (4 H, m), 5.20 (1 H, br s), 3.90 (1 H, br s), 3.82 (3 H, s), 2.55 (2 H, m), 2.87–1.05 (9 H, m), 0.89 (3 H, t, J = 7 Hz). Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 72.80; H, 7.73; N, 8.75.

***cis*-4a-Ethyl-1,3,4,4a,5,6,7,11c-octahydro-7-[(*p*-methoxyphenyl)-sulfonyl]-1-[2-(phenylthio)ethyl]-2*H*-pyrido[3,2-*c*]carbazol-2-one (45, S = CH_2CH_2SPh).** To a solution of the imine **19** (S = CH_2CH_2SPh) [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (990 mg, 3 mmol)] in chlorobenzene (40 mL) at 135 °C was added dropwise the mixed carbonic anhydride **44** [prepared, as described, from 4-ethyl-4-pentenoic acid (756 mg, 6 mmol)] in chlorobenzene (10 mL). After 2.75 h at 135 °C the mixture was evaporated in vacuo, and the residue was purified by flash chromatography to give on elution with $CHCl_3$/petroleum ether (2:3) **47** (S = CH_2CH_2SPh) (338 mg, 21%) as a pale yellow oil: IR ($CHCl_3$) 1645, 1595, 1166 cm^{-1}; NMR ($CDCl_3$) δ 8.27 (1 H, d, J = 7 Hz), 7.79–7.61 (3 H, m), 7.39–7.23 (2 H, m), 7.20–6.91 (5 H, m), 6.75 (2 H, d, J = 10 Hz), 4.70 (1 H, br s), 4.57 (1 H, br s), 3.70 (3 H, s), 3.64–3.11 (5 H, m), 2.84 (1 H, m), 2.66 (3 H, s), 2.54–2.20 (4 H, m), 2.09 (2 H, q, J = 7 Hz), 1.23 (3 H, t, J = 7 Hz), 1.00 (3 H, t, J = 7 Hz).

Continued elution with $CHCl_3$/petroleum ether (3:2) gave **45** (S = CH_2CH_2SPh) (570 mg, 33%): mp 195–195.5 °C (from methanol); IR ($CHCl_3$) 1640, 1595, 1265, 1169 cm^{-1}; NMR ($CDCl_3$) δ 8.18 (1 H, d,

J = 7 Hz), 7.72 (2 H, d, J = 9 Hz), 7.50–7.27 (3 H, m), 7.14–7.02 (3 H, m), 6.97–6.86 (2 H, m), 6.79 (2 H, d, J = 9 Hz), 4.34 (1 H, s), 3.68 (3 H, s), 3.72 (1 H, m), 3.34–3.11 (2 H, m), 3.06–2.70 (2 H, m), 2.43 (2 H, t, J = 7 Hz), 2.20 (1 H, m), 2.02 (1 H, m), 1.92–1.52 (3 H, m), 1.20 (2 H, q, J = 8 Hz), 0.85 (3 H, t, J = 8 Hz). Anal. Calcd for $C_{32}H_{34}N_2O_4S_2$: C, 66.86; H, 5.96; N, 4.87. Found: C, 66.89; H, 5.87; N, 4.66.

***cis*-4a-Ethyl-1,3,4,4a,5,6,7,11c-octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-[2,2-dimethoxyethyl]-2*H*-pyrido[3,2-*c*]carbazol-2-one [46, S = $CH_2CH(OMe)_2$].** A solution of the imine **21** [prepared from the aldehyde **6** (R = $SO_2C_6H_4OMe$-*p*) (660 mg, 2 mmol)] in chlorobenzene (15 mL) was treated with the mixed carbonic anhydride **44** [prepared from ethyl chloroformate and 4-ethyl-4-pentenoic acid (4 mmol)], followed by treatment with triethylamine (200 mg, 2 mmol). The mixture was heated to 135 °C for 2 h. Additional mixed carbonic anhydride **44** (1 mmol) was added, and heating was continued for a further 2 h. The mixture was evaporated in vacuo and the residue purified by flash chromatography. Elution with $CHCl_3$/petroleum ether (3:2) gave the β-lactam adduct **48** [S = $CH_2CH(OMe)_2$] (296 mg, 28%): IR ($CHCl_3$) 1746, 1660, 1592, 1168 cm^{-1}; NMR ($CDCl_3$) δ 8.29 (1 H, d, J = 7 Hz), 7.66 (2 H, d, J = 10 Hz), 7.43 (1 H, d, J = 7 Hz), 7.36–7.16 (2 H, m), 6.86 (2 H, d, J = 10 Hz), 4.61 (1 H, s), 4.54 (1 H, d, J = 2 Hz), 4.47 (1 H, s), 4.34 (1 H, dd, J_s = 6, 4 Hz), 3.79 (3 H, s), 3.66–3.48 (2 H, m), 3.18 (3 H, s), 3.15 (3 H, s), 2.73–2.59 (2 H, m), 2.52 (3 H, s), 2.41 (1 H, m), 1.86 (2 H, q, J = 7 Hz), 0.91 (3 H, t, J = 7 Hz); MS, m/e calcd for $C_{28}H_{34}N_2O_6S$ 526.214, found 526.214. Continued elution with $CHCl_3$/petroleum ether (4:1) gave **46** [S = $CH_2CH(OMe)_2$] (117 mg, 11%) as a pale yellow oil: IR ($CHCl_3$) 1645, 1595, 1170 cm^{-1}; NMR ($CDCl_3$) δ 8.20 (1 H, m), 7.75 (2 H, d, J = 10 Hz), 7.61 (1 H, m), 7.36–7.23 (2 H, m), 6.91 (2 H, d, J = 10 Hz), 4.77 (1 H, d, J = 8 Hz), 4.77 (1 H, d), 3.79 (3 H, s), 3.47–3.39 (2 H, m), 3.32 (3 H, s), 3.11 (3 H, s), 3.01 (1 H, m), 2.54–2.34 (3 H, m), 2.09 (1 H, m), 1.93–1.00 (3 H, m), 1.25 (2 H, q, J = 7 Hz), 0.86 (3 H, t, J = 7 Hz). No satisfactory microanalytical or mass spectra data could be obtained due to decomposition.

3,3a,4,5,6,6a,7,8,12c,12d-Decahydro-1-(2-methoxyethyl)-8-[(*p*-methoxyphenyl)sulfonyl]isoquino[8,1-*bc*]carbazol-2(1*H*)-one (49). To a solution of the imine **18** (2.5 mmol) in chlorobenzene (25 mL) heated at reflux was added a solution of the mixed carbonic anhydride prepared from cyclohex-2-enylacetic acid[29] and ethyl chloroformate (5 mmol) in chlorobenzene (5 mL). After 5 h at 135 °C, the mixture was evaporated, and the residue was flash chromatographed to give **49** (396 mg, 31%): mp 190–192 °C (from $CHCl_3$/petroleum ether); IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.25 (1 H, d, J = 8 Hz), 7.68 (2 H, d, J = 9 Hz), 7.18–7.41 (3 H, m), 6.85 (2 H, d, J = 9 Hz), 4.78 (1 H, br d, J = 4 Hz), 4.50–4.64 (1 H, m), 3.77 (3 H, s), 3.50–3.69 (2 H, m), 3.35 (3 H, s), 3.07–3.41 (3 H, m), 2.74–2.93 (1 H, m), 2.45–2.61 (1 H, m), 2.23–2.39 (1 H, m), 1.34–2.18 (9 H, m); MS, m/e calcd for $C_{28}H_{32}N_2O_5S$ 508.203, found 508.208. Anal. Calcd for $C_{28}H_{32}N_2O_5S$: C, 66.12; H, 6.34; N, 5.51. Found: C, 65.22; H, 6.48; N, 5.29.

***cis*-1,3,4,4a,5,6,7,11c-Octahydro-4,5-ethano-7[(*p*-methoxyphenyl)sulfonyl]-1-(2-methoxyethyl)-2*H*-pyrido[3,2-*c*]carbazol-2-one (50).** Following the same procedure as for **49**, except the mixed anhydride was made from cyclopent-2-enylacetic acid,[30] gave **50** (590 mg, 48%): mp 163–164 °C (from $CHCl_3$/petroleum ether); IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 8.28 (1 H, d, J = 8 Hz), 7.73 (2 H, d, J = 9 Hz), 7.17–7.38 (3 H, m), 6.88 (2 H, d, J = 9 Hz), 4.70 (1 H, d, J = 8 Hz), 4.41 (1 H, d t, J = 14 and 4 Hz), 3.78 (3 H, s), 3.49–3.60 (2 H, m), 3.31 (3 H, s), 3.10–3.25 (2 H, m), 2.88–3.08 (2 H, m), 2.40–2.75 (2 H, m), 2.16 (1 H, dd, J = 13 and 5 Hz), 1.63–1.86 (3 H, m), 1.14–1.32 (2 H, m); MS, m/e calcd for $C_{27}H_{30}N_2O_5S$ 494.188, found 494.186.

***cis*-3,3-Pentamethylene-1,3,4,4a,5,6,7,11c-octahydro-7-[(*p*-methoxyphenyl)sulfonyl]-1-(2-methoxyethyl)-2*H*-pyrido[3,2-*c*]carbazol-2-one (52).** To a solution of the imine **18** (1 mmol) in chlorobenzene (10 mL) at 0 °C was added diisopropylethylamine (0.35 mL, 2 mmol), followed by a solution of 1-allylcyclohexane-1-carboxylic acid chloride[35] (343 mg, 2 mmol) in chlorobenzene (2 mL). The above mixture was stirred at 0 °C for 0.5 h then heated at reflux for 3 h. After the solution was cooled to 20 °C, diisopropylethylamine (0.175 mL, 1 mmol) followed by the acid chloride (172 mg, 1 mmol) in chlorobenzene (2 mL) was added, and the mixture was reheated to reflux for 1 h. The mixture was evaporated in vacuo, and the residue was partitioned between $CHCl_3$ (30 mL) and water (20 mL). The organic layer was dried (Na_2SO_4) and evaporated. The residue was flash chromatographed to give **52** (202 mg, 38%): mp 193.5–195 °C (from $CHCl_3$/petroleum ether); IR ($CHCl_3$) 1620 cm^{-1}; NMR ($CDCl_3$) δ 8.25 (1 H, d, J = 8 Hz), 7.70 (2 H, d, J = 9 Hz), 7.51 (1 H, d, J = 7 Hz), 7.18–7.36 (2 H, m), 6.84 (2 H, d, J = 9 Hz), 4.82 (1 H, br s), 4.11–4.25 (1 H, m), 3.76 (3 H, s), 3.48–3.60 (1 H, m), 3.27–3.45 (2 H, m), 3.24 (3 H, s), 3.00–3.14 (2 H, m), 2.23–2.40 (1 H, m), 1.00–2.14 (14 H, m). anal. Calcd for $C_{30}H_{36}N_2O_5S$: C, 67.14; H, 6.76; N, 5.22. Found: C, 67.03; H, 6.92; N, 5.02.

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Registry No. 6 (R = $SO_2C_6H_4OMe$-*p*), 80664-26-2; (*E*)-**7**, 85923-42-8; (±)-**8** (R = $CO_2CH_2CH_2Cl$), 85923-43-9; (±)-**8** (E = $CO_2CH_2CH_2OH$), 85939-39-5; (±)-**8** (E = $CO_2CH{=}CH_2$), 85923-44-0; (±)-**8** (E = $CO_2CH_2CCl_3$), 85923-45-1; (±)-**16**, 85923-46-2; **17**, 85923-47-3; (*E*)-**18** (S = CH_2CH_2OMe), 85923-48-4; (*E*)-**19** (S = CH_2CH_2SPh), 80664-27-3; (*E*)-**20** (S = CH_2CH_2SePh), 85923-49-5; (*E*)-**21** (S = $CH_2CH(OMe)_2$), 85923-50-8; (*E*)-**22** (S = CH_2CH_2Br), 85923-51-9; (*E*)-**23** (S = CH_2Ph), 85923-52-0; (*E*)-**24** (S = Me), 85923-53-1; (*Z*)-**24** (S = Me), 85923-54-2; **25**, 85923-55-3; (±)-**26** (S = CH_2CH_2OMe), 85923-56-4; (±)-**27** (S = CH_2CH_2SPh), 85923-57-5; (±)-**28** (S = CH_2CH_2SePh), 85923-58-6; (±)-**29** (S = $CH_2CH(OMe)_2$), 85923-59-7; (±)-**30** (S = CH_2Ph), 85923-60-0; (±)-**31** (S = Me), 85923-61-1; (±)-**32** (R = $CH_2CH(OMe)_2$), 85923-62-2; (±)-**33** (R = CH_2CH_2SePh), 85923-63-3; (±)-**34** (S = CH_2CH_2SPh), 85923-64-4; **36** (S = CH_2CH_2SPh), 85923-65-5; **38**, 85923-66-6; (*E*)-**39**, 85923-67-7; (±)-**40** (E = CO_2Me), 85923-68-8; (±)-**41** (E = $CO_2CH_2CH_2Cl$), 85923-69-9; (±)-**42** (E = $CO_2CH_2CCl_3$), 85923-70-2; (±)-**43**, 85923-71-3; **44**, 80664-28-4; (±)-**45** (S = CH_2CH_2Ph), 80664-29-5; (±)-**46** (S = $CH_2CH(OMe)_2$), 85923-72-4; (±)-**47** (S = CH_2CH_2SPh), 80664-30-8; **48** (S = $CH_2CH(OMe)_2$), 85923-73-5; (±)-**49**, 85923-74-6; (±)-**50**, 85923-75-7; (±)-**52**, 85923-76-8; $PhSe(CH_2)_2NH_2$, 81418-58-8; $CH_2{=}CH(CH_2)_3NH_2$, 22537-07-1; $H_2NCH_2CH_2OMe$, 109-85-3; $BrCH_2CH_2NH_2$, 107-09-5; $PhCH_2NH_2$, 100-46-9; CH_3NH_2, 74-89-5; 2-methyl-3-formylindole, 5416-80-8; *p*-methoxybenzenesulfonyl chloride, 98-68-0; 2-chloroethyl chloroformate, 627-11-2; 2,2,2-trichloroethyl chloroformate, 17341-93-4; phenylacetyl chloride, 103-80-0; 2-(phenylthio)ethylamine, 2014-75-7; aminoacetaldehyde dimethyl acetal, 22483-09-6; diphenyldiselenide, 1666-13-3; 2-bromoethylamine hydrobromide, 2576-47-8; 4-pentenoic acid, 591-80-0; ethyl chloroformate, 541-41-3; 4-ethyl-4-pentenoic acid, 13722-73-1; cyclohex-2-enylacetic acid ethyl chloroformate carbonic anhydride, 85923-77-9; 1-allylcyclohexane-1-carboxylic acid chloride, 72335-83-2; cyclopent-2-enylacetic acid ethylchloroformate carbonic anhydride, 85976-61-0.