min, the mixture was cooled and extracted with benzene–hexane (1:1). The extracts were washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water and dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was distilled to give **3d**, 95 mg (90%), as white crystals: mp 55–57 °C; IR (Nujol) 2932, 2850, 1602, 1516, 1462, 1378, 1352, 1270, 1252, 1168, 778 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.85 (q, J = 10.6 Hz, 2 H), 7.44–8.03 (m, 7 H). Anal. Calcd for $C_{12}H_9F_3$: C, 68.57; H, 4.32. Found: C, 68.38; H, 4.45.

***N*-[2,2,2-Trifluoro-1-(phenylthio)ethyl]acetamide (18a).** To a solution of **7b** (113 mg, 0.5 mmol) in acetonitrile (1 mL) was added $SnCl_4$ (0.09 mL, 0.75 mmol), and the mixture was stirred at room temperature for 3 days. The reaction mixture was neutralized with aqueous sodium hydrogen carbonate and extracted with AcOEt several times. The extracts were washed with water and brine, dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was chromatographed on silica gel to provide **18a**, 85 mg (70%), as colorless crystals: mp 128 °C; IR (Nujol) 3284, 2952, 2924, 1670, 1532, 1254, 1168, 1112, 812, 748, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.99 (s, 3 H), 5.82 (dq, J_{H-F} = 7.5 Hz, J_{H-H} = 3.0 Hz, 1 H), 5.89 (br d, 1 H), 7.35–7.56 (br, 5 H). Anal. Calcd for $C_{10}H_{10}F_3NOS$: C, 48.19; H, 4.04; N, 5.62. Found: C, 48.32; H, 3.95; N, 5.87.

***N*-[2,2,2-Trifluoro-1-(phenylthio)ethyl]benzamide (18b).** To a solution of **7b** (113 mg, 0.5 mmol) and benzonitrile (0.5 mL, 5.0 mmol) in dichloroethane (1.5 mL) was added boron trifluoride etherate (0.12 mL, 1.0 mmol), and the mixture was heated at reflux for 3 days. After cooling, the reaction mixture was neutralized with aqueous sodium hydrogen carbonate and extracted with AcOEt several times. The usual workup provided **18b**, 116 mg (71%), as colorless crystals: mp 135 °C; IR (Nujol) 3264, 3064, 2924, 2856, 1650, 1516, 1258, 1110, 862, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.99 (dq, J_{H-F} = 7.3 Hz, J_{H-H} = 2.8 Hz, 1 H), 6.35–6.45 (br d, 1 H), 7.25–7.70 (m, 10 H). Anal. Calcd for $C_{15}H_{12}F_3NOS$: C, 57.87; H, 3.89; N, 4.50. Found: C, 57.70; H, 3.97; N, 4.72.

***N*-[2,2,2-Trifluoro-1-(phenylthio)ethyl]-3-butenamide (18d):** colorless crystals; mp 116 °C; IR (Nujol) 3264, 2924, 2856, 1964, 1660, 1106, 924, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.98 (d, J = 7.7 Hz, 2 H), 5.19 (dd, J = 17.0 Hz, J = 1.5 Hz, 1 H), 5.24 (dd, J = 10.0 Hz, J = 1.5 Hz, 1 H), 5.78 (ddq, J = 10.0 Hz, J = 17.0 Hz, J = 7.0 Hz, 1 H), 5.81 (dq, J = 7.0 Hz, J = 10.0 Hz, 1 H), 5.85–5.95 (br d, 1 H), 7.25–7.60 (br, 5 H). Anal. Calcd for $C_{12}H_{12}F_3NOS$: C, 52.36; H, 4.39, N, 5.09. Found: C, 52.45; H, 4.34; N, 5.42.

***N*-[2,2,2-Trifluoro-1-(phenylthio)ethyl]-2-propenamide (18e):** colorless crystals; mp 118 °C; IR (Nujol) 3288, 2924, 1664, 1532, 1412, 1308, 1202, 1070, 972, 808, 694 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.76 (dd, J = 10.3 Hz, J = 1.0 Hz, 1 H), 5.85 (dq, J = 6.6 Hz, J = 2.2 Hz, 1 H), 5.80–6.00 (br, 1 H), 6.06 (dd, J = 10.3 Hz, J = 16.9 Hz, 1 H), 6.32 (dd, J = 16.9 Hz, J = 1.0 Hz, 1 H), 7.30–7.60 (br, 5 H). Anal. Calcd for $C_{11}H_{10}F_3NOS$: C, 50.57; H, 3.86; N, 5.36. Found: C, 50.33; H, 4.10; N, 5.20.

***N*-[2,2,2-Trifluoro-1-(phenylthio)ethyl]-2-phenylethanamide (18c):** colorless crystals; mp 143 °C; IR (Nujol) 3268, 2924, 1668, 1522, 1454, 1268, 1236, 1114, 976, 862, 816, 696 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.56 (s, 2 H), 5.67 (br, 1 H), 5.80 (dq, J_{H-F} = 7.2 Hz, J_{H-H} = 10.1 Hz, 1 H), 7.10–7.40 (m, 10 H). Anal. Calcd for $C_{16}H_{14}F_3NOS$: C, 59.07; H, 4.34; N, 4.31. Found: C, 59.02; H, 4.60; N, 4.19.

1-(Trifluoromethyl)isothiochroman (16): viscous oil; bp 105–110 °C (5 mmHg); IR (neat) 3032, 2932, 1498, 1312, 1248, 1160, 1104, 610, 880, 768, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.71 (dt, J = 12.0 Hz, J = 6.0 Hz, 1 H), 3.10 (dd, J = 6.0 Hz, J = 6.0 Hz, 2 H), 3.17 (dd, J = 12.0 Hz, J = 6.0 Hz, 1 H), 4.34 (q, J = 9.3 Hz, 1 H), 7.15–7.35 (m, 4 H). Anal. Calcd for $C_{10}H_9F_3S$: C, 55.04; H, 4.16. Found: C, 54.80; H, 3.98.

1-(Trifluoromethyl)-3-butenyl phenyl sulfide (17): viscous oil; bp 85–90 °C (5 mmHg); IR (neat) 3084, 2988, 2920, 1740, 1646, 1252, 1168, 1102, 924, 704, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (m, 1 H), 2.65 (m, 1 H), 3.38 (ddq, J_{H-F} = 8.3 Hz, J = 4.3 Hz, J = 10.0 Hz, 1 H), 5.22 (dd, J = 6.9 Hz, J = 1.4 Hz, 1 H), 5.23 (dd, J = 16.7 Hz, J = 1.4 Hz, 1 H), 5.95 (dddd, J_1 = 16.7 Hz, J_2 = 10.4 Hz, J_3 = 7.0 Hz, J_4 = 7.0 Hz, 1 H), 7.25–7.55 (m, 6 H). Anal. Calcd for $C_{11}H_{11}F_3S$: C, 56.88; H, 4.77. Found: C, 56.87; H, 4.63.

Reactions of 2-Vinylindoles with Carbodienophiles: Synthetic and Mechanistic Aspects

Manfred Eitel and Ulf Pindur*

Department of Chemistry and Pharmacy, University of Mainz, Saarstrasse 21, D-6500 Mainz 1, Federal Republic of Germany

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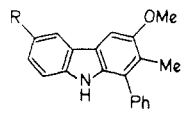
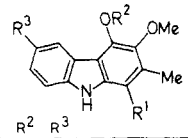
Reactions of selectively functionalized 2-vinylindoles with acyclic and cyclic carbodienophiles proceed with high regio- and/or stereoselectivities to furnish Diels–Alder adducts, Diels–Alder ene products, and Michael adducts. This methodology provides a convenient route to functionalized indoles, carbazoles, and [c]pyrrolo-annelated carbazoles with substitution patterns that are not easily obtained by the usual routes. Some mechanistic aspects of the chemistry of 2-vinylindoles are discussed.

Introduction

Carbazoles with carbon substituents at the 1- and 2-positions constitute the frameworks of both the hyellazoles **1**, isolated from the blue-green alga *Hyella caespitosa*,[1] and the carbazomycins **2**, produced by the actinomycete *Streptoverticillium ehimence*.[2] The same structural features are also to be found in the pyrido[4,3-*b*]carbazole alkaloids ellipticine (**3a**), 9-methoxyellipticine (**3b**), and olivacine (**4**). The significant antibiotic activity of carbazomycin B (**2b**)[2] as well as the antitumor action of **3**[3,4] and analogues of the series of annelated carbazoles[3,4] have



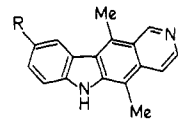
1a R = H hyellazole
b R = Cl chlorohyellazole



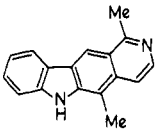
	R^1	R^2	R^3	
2a	Me	H	H	carbazomycin A
b	Me	Me	H	B
c	Me	H	OMe	C
d	Me	Me	OMe	D
e	CHO	H	H	E (=carbazomycinal)
f	CHO	H	OMe	F (=6-methoxycarbazomycinal)

(1) Cardelina, J. H., II; Kirkup, M. P.; Moore, R. E.; Mynderse, J. S.; Seff, K.; Simmons, C. J. *Tetrahedron Lett.* **1979**, 4915.
(2) Naid, T.; Kitahara, T.; Kaneda, M.; Nakamura, S.; *J. Antibiot.* **1987**, *40*, 157 and references cited therein.

0022-3263/90/1955-5368$02.50/0

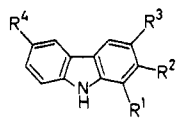


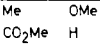
3a R = H ellipticine
b R = OMe 9-methoxyellipticine

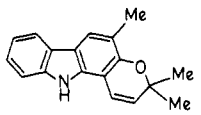


4 olivacine

directed the attention of several research groups to this interesting class of compounds.[5-19] Many other carbazole alkaloids with [*a*] annelation and/or 1,3-, 2,3-, 1,2,3-, 1,2,5-, and 1,3,5-substitution patterns (e.g., compounds **5** and **6**)



	R^1	R^2	R^3	R^4	
5a	H	H	Me	OMe	glycozoline
b	H	OH	CO_2Me	H	mukonidine
c	OMe	H	CO_2Me	H	mukonine
d	OMe		CHO	H	indolizine

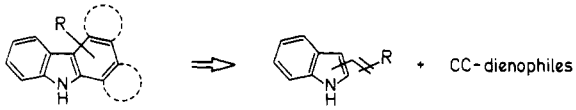


6 girinimbin

are also of interest for the development of pharmacologically active structures.[17] However, syntheses of the polysubstituted and functionalized carbazoles or indoles required as building blocks for the preparation of such alkaloids are rather difficult to achieve by the usual methods. Hence there is a need for the development of novel, highly selective, and effective synthetic strategies.[20]

We have been studying the [4 + 2] cycloaddition reactions of vinylindoles for the key step in the synthesis of carbazoles (Scheme I).[9,21-25] We now report the full details

Scheme I. Retrosynthetic Route to Functionalized and/or Annelated Carbazoles via a Diels–Alder Reaction



functionalized and a- or c-annellated carbazoles

2- or 3-vinylindoles

of our preliminary communication[21] on the [*b*] annelation and functionalization of the indole moiety via the reactions of 2-vinylindoles with carbodienophiles. In addition, we discuss some mechanistic aspects of 2-vinylindole chemistry.

Results and Discussion

I. Synthetic Results and Reactivity Aspects. The qualitative application of the PMO theory (in simplified form, the FMO concept)[26-29] has frequently proved of value for predicting the results of Diels–Alder reactions. Predictions based on theoretical concepts are also useful for synthesis planning in natural product chemistry. The π_Z electron densities and HOMO energies of the 2-vinylindoles **7a–i**[31] as well as those of 2-vinylindole[24] itself were calculated by using the π-VESCF method (Table I).[30]

In Table I are listed the HOMO energy differences of the 2-vinylindoles in relation to 2-vinylindole[24] (for predicting an FMO-controlled reaction[27,28]) and the π_Z electron density differences at the C2′ and C3 positions in relation to those of 2-vinylindole (for predicting a polarity-controlled process[27,29]). Some other coefficients of the atoms C2′ and C3 that may be useful for predicting the regiochemistry in the Diels–Alder step[26-29] are included.

In a $HOMO_{diene}$-controlled Diels–Alder reaction of 2-vinylindoles, the compounds **7a–c** and 2-vinylindole[24] should be the more reactive dienes in this series. The calculated differences in the $HOMO_{diene}$ coefficients at C2′ and C3 suggest that good regioselectivity should be observed in the Diels–Alder reactions of compounds **7a,d–g,i**. The π electron densities at the potential reaction centers C2′ and C3 reflect a high polarization at C2′ in **7b,d–i** and a high polarization at C3 in the enamine functions in **7a–c**. The LUMO energies and the LUMO coefficients of some carbodienophiles are given in Table II; these values were calculated by using the more sophisticated MNDO method.[32]

(3) Kansal, V. K.; Potier, P. *Tetrahedron* **1986**, *42*, 2389.
(4) Archer, S.; Ross, B. S.; Pica-Mattocia, L.; Cioli, D. *J. Med. Chem.* **1987**, *30*, 1204.
(5) Pindur, U. *Chimia*. In press.
(6) Kano, S.; Sugino, E.; Hibino, S. *J. Chem. Soc., Chem. Commun.* **1980**, 1241.
(7) Kano, S.; Sugino, E.; Shibuya, S.; Hibino, S. *J. Org. Chem.* **1981**, *46*, 3856.
(8) Takano, S.; Suzuki, Y.; Ogasawara, K. *Heterocycles* **1981**, *16*, 1479.
(9) Pindur, U.; Pfeuffer, L. *Heterocycles* **1987**, *26*, 325. Pindur, U. *Heterocycles* **1988**, *27*, 1253. Pindur, U.; Pfeuffer, L. *Tetrahedron Lett.* **1987**, *28*, 3079.
(10) Gribble, G. W.; Saulnier, M. G. *Heterocycles* **1985**, *23*, 1277.
(11) Kashima, C.; Hibi, S.; Maruyama, T.; Harada, K.; Omote, Y. *J. Heterocycl. Chem.* **1987**, *24*, 913.
(12) Hewlins, M. J. E.; Jackson, A. H.; Long, A.; Oliveira-Campos, A.; Shannon, P. V. R. *J. Chem. Res. (M)* **1986**, 2645.
(13) Benzies, D. W. M.; Fresneda, P. M.; Jones, R. A., McNab, H. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1651.
(14) Stephanson, G. R. *J. Organomet. Chem.* **1985**, *286*, C41.
(15) Differding, E.; Ghosez, L. *Tetrahedron Lett.* **1985**, *26*, 1647.
(16) Narasimhan, N. S.; Gokhale, S. M. *J. Chem. Soc., Chem. Commun.* **1985**, 86.
(17) For reviews on numerous carbazole alkaloids, see: Bhattacharyya, P.; Chakraborty, D. P. *Prog. Chem. Org. Nat. Prod.* **1987**, *52*, 160. Pindur, U. *Chimia*. In press.
(18) For consecutive Fe-induced CC and CN linkages in the total synthesis of carbazomycins, see: Knölker, H.-J.; Bauermeister, M.; Bläser, D.; Boese, R.; Pannek, J.-B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 225.
(19) For newer strategies to hyellazoles and carbazomycins, see: Moody, C. J.; Sha, P. *J. Chem. Soc., Perkin Trans. 1* **1989**, 376.
(20) For the first review on the indole-2,3-quinodimethane Diels–Alder methodology, see: Pindur, U.; Abdoust-Houshang, E. *Chem. Rev.* **1989**, *89*, 1681.
(21) Eitel, M.; Pindur, U. *Heterocycles* **1988**, *27*, 2353.
(22) Pindur, U.; Pfeuffer, L.; Kim, M.-H. *Helv. Chim. Acta* **1989**, *72*, 65. Pindur, U.; Kim, M.-H. *Tetrahedron* **1989**, *45*, 6427. Pindur, U.; Kim, M.-H.; Eitel, M. *Tetrahedron Lett.* **1990**, *31*, 1551.
(23) Pfeuffer, L.; Pindur, U. *Helv. Chim. Acta* **1988**, *71*, 467.
(24) For synthesis, reactivity, and MNDO calculations of 2-vinylindole, see: Eitel, M.; Pindur, U. *Helv. Chim. Acta* **1988**, *71*, 1060.
(25) Pfeuffer, L.; Pindur, U. *Helv. Chim. Acta* **1987**, *70*, 1419.
(26) Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4092. Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361.
(27) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; John Wiley & Sons: New York, 1976.
(28) Fukui, K. *Acc. Chem. Res.* **1971**, *4*, 57.
(29) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. Sustmann, R.; Lücking, K.; Kopp, G.; Rese, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1713. For a discussion of the mechanistic problems of Diels–Alder reactions and definitions of terms such as "synchron, concerted, two-step, two-stage, biradical, and biradicaloid", see: Dewar, M. J. S.; Olivella, S.; Stewart, J. P. *J. Am. Chem. Soc.* **1986**, *108*, 5771.
(30) (a) The notorious weaknesses of this MO process, especially for systems containing heteroatoms, as compared to the semiempirical MNDO and AM1 methods are well known.[30b] However, the results obtained for the conjugated structures of interest provide useable data for a qualitative explanation of the reactions of compounds **7** with carbodienophiles. (b) pi-VESCF routine, see: Clark, T. *Computational Chemistry*; Wiley-Interscience: New York, 1985. For SCF MO and force field calculations, the full version of the MMX program from Serena Software, Bloomington, IN, was used. MMX version by K. E. Gilbert and J. J. Gajewski based on MM2 (Allinger, QCPE 395) and MMP1 Pi (Allinger, QCPE 318) modified by K. Steliou.
(31) For newer synthetic developments leading to 2-vinylindoles, see: Pindur, U.; Eitel, M. *Synthesis* **1989**, 364.

Scheme II

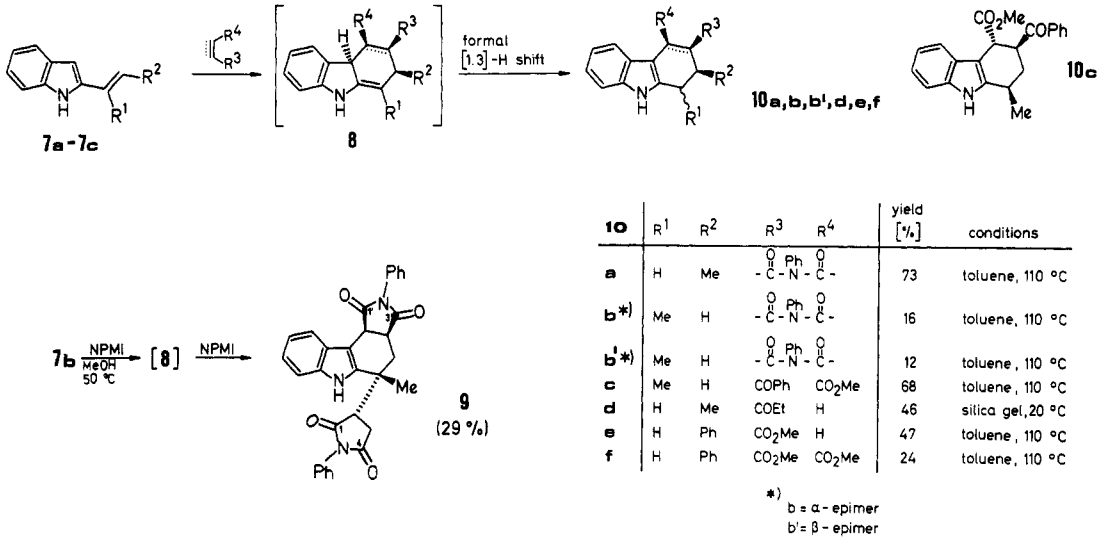
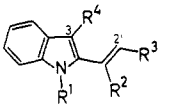


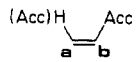
Table I. π-VESCF Calculations of the 2-Vinylindoles 7



7	R^1	R^2	R^3	R^4	ΔE_{HOMO}[a] [eV]	π_Z electron density[a] C2′	π_Z electron density[a] C3	HOMO coefficient C2′	HOMO coefficient C3
a	H	H	Me	H	0.203	−0.077	0.011	−0.3792	0.4782
b	H	Me	H	H	0.038	0.061	0.003	−0.4158	0.4656
c	H	H	Ph	H	−0.005	0.053	−0.008	−0.3687	0.4376
d	H	H	CO_2Me	H	−0.523	0.061	−0.025	−0.3199	0.4649
e	Me	H	CO_2Me	H	−0.513	0.063	−0.026	−0.3227	0.4593
f	H	H	CHO	H	−0.546	0.061	−0.026	−0.3213	0.4562
g	H	H	COMe	H	−0.624	0.074	−0.026	−0.3214	0.4536
h	Me	H	NO_2	H	−0.829	0.100	−0.032	−0.4061	0.4146
i	Me	H	CO_2Me	Me	−0.353	0.066	−0.011	−0.3452	0.4426
j	H	Me	Me	H	0.124	−0.134	0.015		

[a] A geometry-optimized coplanar *s-cis* conformation was calculated throughout; the difference values are referred to 2-vinylindole[24] (R^1, R^2, R^3, R^4 = H; E_{HOMO} = −10.3570 eV; HOMO coefficients C2′ = −0.4158, C3 = 0.4656; π_Z electron density C2′ = 0.9972, C3 = 1.0337).

Table II. LUMO Energies of Some Carbodienophiles from MNDO Calculations[32]



dienophile	E_{LUMO} [eV]	LUMO coefficient *a*	LUMO coefficient *b*
N-phenylmaleimide	−1.16	0.549	−0.549
acrolein	−0.03	0.643	−0.456
1-penten-3-one	0.05	0.621	−0.437
methyl acrylate	−0.11	0.689	−0.521
methyl propynoate	0.267	0.550	−0.430

From the large number of possible combinations of compounds **7** with the tested carbodienophiles, only reactions that gave products with an analytically interpretable spectrum are considered in the following discussion. The pronounced $HOMO_{diene}$ reactivity of 2-vinylindole[24] prompted us to investigate the reactions of **7a–c** with the carbodienophiles *N*-phenylmaleimide (NPMI), methyl (*E*)-3-benzoylacrylate, 1-penten-3-one, methyl acrylate, and dimethyl acetylenedicarboxylate (Scheme II). All reactions proceeded through a Diels–Alder step to furnish the primary cycloadducts **8**, which were stabilized, in contrast to the Diels–Alder products of 3-vinylindoles,[23,25] by a spontaneous, formal [1,3]-hydrogen shift to produce the carbazoles **10a–f** (Scheme II). The unsymmetrical dienophiles reacted regioselectively in accord with the predictions of the FMO concept, although the regiochemistry of the reaction with methyl (*E*)-3-benzoylacrylate to form **10c** should be controlled by steric effects in the transition state. In the reaction of **7b** with NPMI, the hydrogen shift did not take place stereospecifically in boiling toluene and we isolated two epimeric products, **10b** and **10b′**. When the reaction was performed in methanol at 50 °C, the initial cycloadduct **8** was additionally captured by a stereospecific, orbital symmetry-allowed ene reaction to yield **9**. In Diels–Alder reaction of **7b** with methyl (*E*)-3-benzoylacrylate, the hydrogen shift occurred stereospecifically to yield **10c** as the sole product. In none of these reactions was it possible to detect either a betaine intermediate originating from a stepwise process or a Michael-type adduct. Furthermore, no isomerization of **7a** or **7c** took place in the reaction medium. The stereochemistry of the cycloadducts **10** was not changed when the reactions were carried out in the polar solvent methanol. Thus we consider that the first step of the sequence yielding **8** is a concerted $HOMO_{diene}$–$LUMO_{dienophile}$-controlled Diels–Alder process.

(32) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899, 4907. The program packet MOPAC 4.00 (QCPE 455) was used: Stewart, J. J. P. *QCPE Bull.* **1983**, *3*, 455.

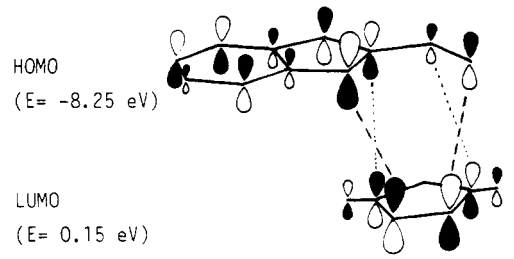
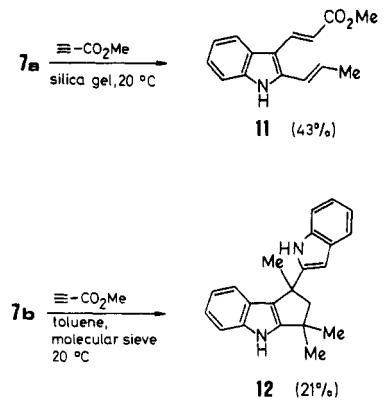


Figure 1. HOMO/LUMO interactions of 2-vinylindole with maleic anhydride according to MNDO calculations:[32] (---) primary orbital interaction, (···) secondary orbital interaction controlling stereochemistry.

Scheme III

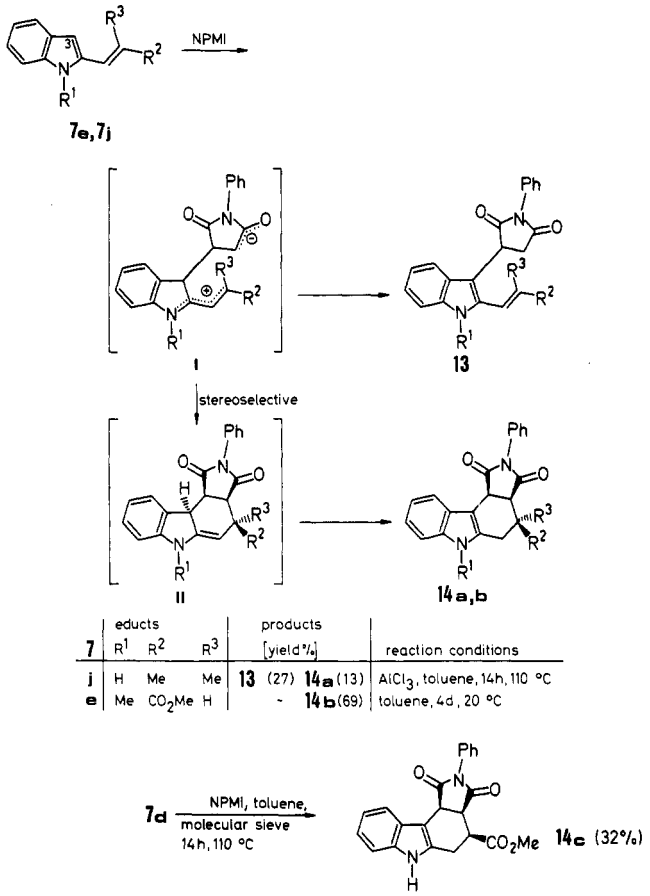


From the unambiguous stereochemistry for **10a,d–f**, it can be deduced that the "endo" products **8** should be formed more rapidly than the "exo" isomers. Apparently the energetically more favorable secondary frontier orbital interaction controls the stereochemistry in the "endo" Diels–Alder transition state[33] before the formal [1,3]-hydrogen shift to form **10** can take place. This hypothesis is only valid when the subsequent hydrogen shift is not the rate-limiting step in both potential routes to the "endo" and "exo" epimers **8**. The secondary frontier orbital interaction in the formation of **8** is shown schematically in Figure 1.

In contrast to the above results, the reactions of **7a,b** with the less dienophilic methyl propynoate (high LUMO energy, Table II) do not give Diels–Alder products. Instead the reaction of **7a** with the alkyne proceeds with regio- and *E* stereoselectivity in a polarity-controlled Michael-type addition (Scheme III) to yield exclusively the 2,3-divinylindole **11**, a starting material for 1,6-electrocyclization to carbazoles.[17] The reactive compound **7b** dimerizes to form **12** at such a rapid rate that reaction with the dienophile cannot take place.

The 2-vinylindoles **7e** and **7j**, which exhibit a higher π-charge density at C3 compared to C2′ (Table I) should serve as polar dienes and undergo nonconcerted (formal) Diels–Alder reactions[29] (Scheme IV). Compound **7j** reacted with NPMI under aluminum trichloride catalysis to produce the Michael-type adduct **13** as well as the cycloadduct **14a**. The 2-vinylindole **7e** reacted smoothly under milder conditions without a Lewis acid catalyst to furnish the cycloadduct **14b** exclusively. The 2-vinylindole **7d**, which is less polarized at C3 (loss of the *N*-methyl group as a positive inductive activating substituent), also gives rise to the carbazole derivative **14c** but under less mild conditions (Scheme IV). In the former two reactions we

Scheme IV



7	educts R¹	R²	R³	products [yield %]		reaction conditions
j	H	Me	Me	**13** (27)	**14a** (13)	$AlCl_3$, toluene, 14h, 110 °C
e	Me	CO_2Me	H	-	**14b** (69)	toluene, 4d, 20 °C

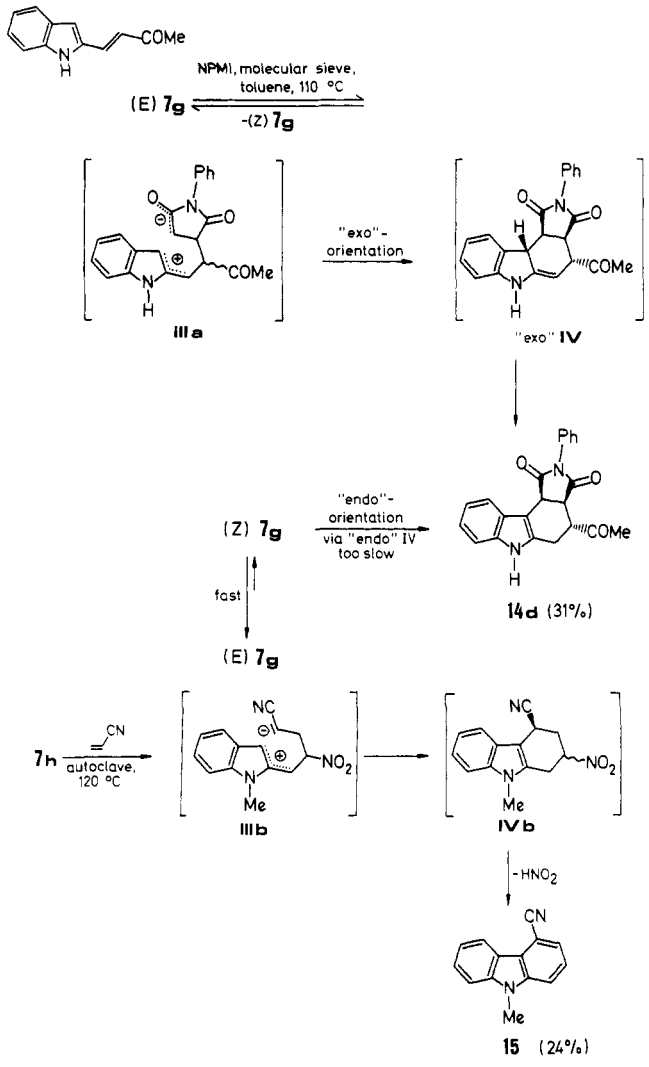
assume that the formation of carbazoles **14a** and **14b** involves a nonconcerted process and the dipolar intermediate I. We favor a zwitterionic intermediate rather than a diradicaloid species.[29] The end groups in the zwitterionic structure stabilize both the positive and the negative charges very well.[23,25] The formation of compound **13** indicates a stepwise mechanism, and the compound itself can be envisioned as a hydrogen-shift-stabilized form of I. MMX force field calculations[30] performed for the intermediates I (with R^1 = H, R^2 = Me, R^3 = Me and R^1 = Me, R^2 = CO_2Me, R^3 = H) reveal considerable double-bond character for the conjugated side chain at the indole C2 position (bond length of the conjugated side chain C–C unit $\approx$ 1.40 Å). Thus rotation of this moiety in I should be slowed down so that stereoselective ring closure to cycloadduct II can take place. II in turn is stabilized by a hydrogen shift to yield **14a** or **14b**.

On the other hand, **14c**, like **10**, should be formed from the less polarized 2-vinylindole **7d** in a process involving a concerted first cyclization step.

2-Vinylindoles **7** that are highly polarized at the 2′-vinyl function (Table I, C2′) should also react with carbodienophiles in a more stepwise process. Their reactions with unsymmetrical dienophiles should then give cycloadducts with the opposite regiochemistry (polarity-controlled orientation of reactants) to those of Scheme II. Thus **7g** reacts with NPMI to form exclusively the carbazole derivative **14d**, which possesses the "exo" configuration in relation to the substrate stereochemistry. On the other hand, **7h**, with a nitro group at C2′, reacts regioselectively with acrylonitrile to form the carbazole **15** (Scheme V). In these two reactions, the high charge density at C2′ should favor an ionic mechanism involving initial attack of the dienophile at C2′ over a concerted step.

(33) Fox, M. A.; Cardona, P.; Kiwiet, N. J. *J. Org. Chem.* **1987**, *52*, 1469. Gleiter, R.; Böhm, M. C. *Pure Appl. Chem.* **1983**, *55*, 237.

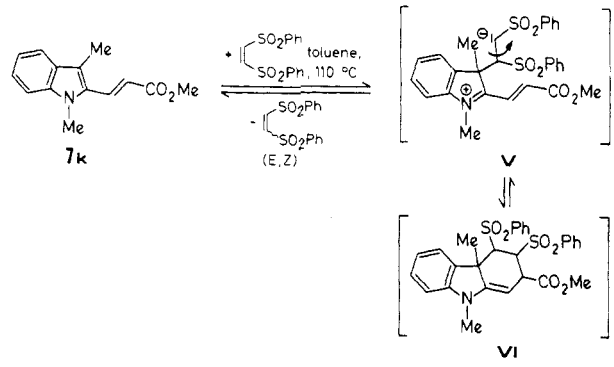
Scheme V



This hypothesis is supported by the fact that (*E*)-**7g** undergoes rapid isomerization in the reaction mixture only in the presence of the carbodienophile. Isomerizations of the diene or dienophile in Diels–Alder reactions have often been suggested as a reason for nonconcerted processes.[29]

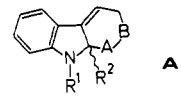
Alternatively, the stereochemistry of **14d** might reflect an exclusive cycloaddition of (*Z*)-**7g** via an "endo" transition state formed from IIIa in a concerted step. However, time-dependent TLC analysis shows that the NPMI-induced isomerization of (*E*)-**7g** to (*Z*)-**7g** is very slow. On the other hand, (*Z*)-**7g** isomerized to the *E* isomer much more rapidly than the formation of **14d** could occur (^{1}H NMR analysis). Thus we can discount the possibility that the stereospecific formation of **14d** involved (*Z*)-**7g**. In addition to slow equilibration with the starting materials, intermediate IIIa should also cyclize, presumably via the sterically less hindered transition state, to "exo" IV. Furthermore, MMX force field calculations[30] have demonstrated that the intermediate "exo" IV is thermodynamically more stable than its "endo" epimer by about 5 kcal/mol (E_{steric}). By analogy, **7h**, with a polarization similar to that of **7g**, should react with acrylonitrile in the same manner. However, the intermediate IVb undergoes rapid stabilization by elimination of HNO_2 to form the more stable 4-cyanocarbazole **15**. The opposite regiochemistry also indicates a polarity-controlled process, and we suggest that a nonconcerted mechanism is responsible for the outcome of this reaction.

Scheme VI



However, the hypothetical mechanism of Scheme V need not imply that only the formulated steps occur. The intermediates IIIa and IIIb could not be detected by ^{1}H NMR spectroscopy. Although this may reflect their short lifetimes, a concerted step to the primarily formed cycloadduct cannot be completely excluded.

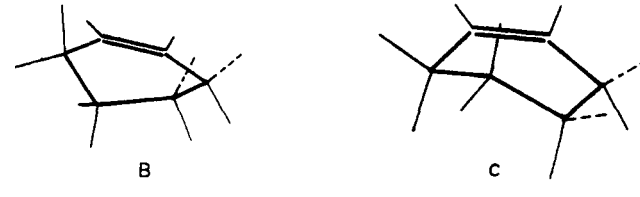
We have previously shown[23,25] that 2-methyl-3-vinylindoles react with a variety of carbodienophiles to form Diels–Alder adducts of the type A. The *o*-aminostyrene chromophore in A is probably responsible for the relatively high stability of this product.

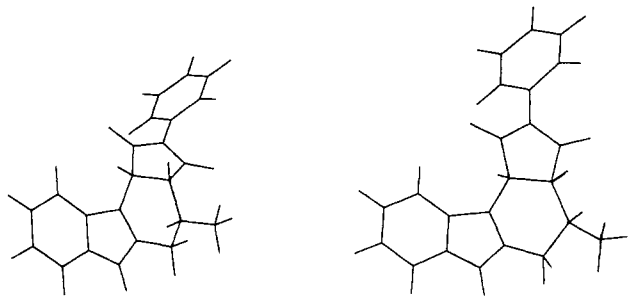


We have now found that 3-methyl-2-vinylindoles do not react under any conditions with dienophiles to produce stable, isolable products. Thus 2-vinylindole **7k** did not react with any of the carbodienophiles and heterodienophiles used in our screening program. The reaction of **7k** with (*Z*)-1,2-bis(phenylsulfonyl)ethene merely isomerized the *Z* dienophile (Scheme VI). We assume an equilibrium between **7k** and V that lies predominantly toward **7k**. Rotation in the carbanionic part of the zwitterion V should result in isomerization of the dienophile before heterolysis takes place. The potential cycloadduct VI no longer possesses a stabilizing *o*-aminostyrene chromophore and cannot be stabilized by a 1,3-hydrogen shift to form an indolic system.

II. Structural Investigations of the [*c*] Annelated Carbazoles. The constitutions and relative configurations of all reaction products were elucidated by high resolution NMR techniques such as selective decoupling experiments and ^{1}H,^{1}H NOE measurements.

As a result of the double annelation of the cyclohexene moiety in the carbazole derivatives **9**, **10a**, **10b**, **10b′**, and **14a–d**, the conformational flexibility of the integrated cyclohexene unit should be restricted, as we have demonstrated previously for analogous cycloadducts of the 3-vinylindole series.[23,25] On the basis of 400-MHz ^{1}H NMR spectra (decoupling experiments, NOE measurements), the cyclohexene rings in the [c] annelated carbazole derivatives described in the present paper should adopt slightly twisted chair or boat conformations B or C, depending on the particular substitution patterns.





17.5 kcal/mol
10a

17.3 kcal/mol
10a'

Figure 2. Minimum energy conformation according to semiempirical AM1 calculations of the "endo" and "exo" epimers **10a** and **10a'**. Energy values are heats of formation (ΔH_f).

AM1[36] and MMX as well as ALCHEMY II force field[30,33] calculations were performed for both epimers of **10a** to assess thermodynamic stabilities and to predict the energetically most stable conformations (Figure 2). These calculations revealed the existence of energetically minimized conformations with practically equal heats of formation for each epimer. In relation to quantum mechanical calculations, the more simply performed molecular mechanics method[30,33] produced qualitatively identical results. The ^{1}H NMR spectroscopic analysis was in good agreement with both the configuration and the conformation depicted in Figure 2 for **10a**.

Experimental Section

Melting points were determined on a Büchi SMP-20 apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on a Bruker WM-400 (400 MHz) spectrometer with TMS as internal standard. EI-mass spectra (70 eV) were obtained on a Varian MAT 7 spectrometer. Column chromatographic separations were performed on silica gel 60 (Merck, grain size 0.063–0.200 mm) with petroleum ether/ethyl acetate (3:1) as eluent; petroleum ether with the boiling range 40–60 °C was used throughout.

The yields reported refer to isolated, analytically pure products; the yields of the crude products (TLC monitoring) were generally considerably higher. The lower yields are principally attributable to the tendency of 2-vinylindoles to polymerize. For all of the racemic chiral products, the nomenclature for only one enantiomer is used.

General Procedures for the Syntheses of Products 9 to 12 and 14b–d. Procedures Ia/Ib. Vinylindole **7** (1 mmol) and the dienophile (1.1 mmol) were dissolved in toluene (10 mL). After addition of activated molecular sieves (4 Å; 3.0 g), the reaction mixture was stirred at 20 °C (procedure Ia) or under reflux (procedure Ib) for the indicated time. The molecular sieves were then filtered off and washed with ethyl acetate (30–50 mL). The combined filtrates and washings were concentrated and separated by column chromatography over silica gel.

Procedure II. Vinylindole **7** (1.00 mmol) was dissolved in the liquid dienophile (1.5–2.0 mmol) and treated with a 20-fold by weight amount of activated silica gel 60. The mixture was allowed to stand at room temperature for the stated time. The reaction mixture was then extracted with three 20-mL portions of ethyl acetate, and the combined organic extracts were concentrated and separated by column chromatography over silica gel.

***N*-Phenyl-2-(5β-methyl-1,3-dioxo-2-phenyl-1,3,3aα,4,5,-10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazol-5α-yl)-succinimide (9)**: procedure Ia, reaction time 8 h, yield 29%; mp 216 °C (toluene); ^{1}H NMR (CD_3NO_2) δ 1.56 (s, 3 H, CH_3), 2.24 (dd, J = 13.8 Hz, 6.4 Hz, 1 H, C4′β-H), 2 48 (dd, J = 13.8 Hz, 5.6 Hz, 1 H, C4′α-H), 2.83 (dd, J = 18.4 Hz, 5.8 Hz, 1 H, C3 -H), 3.15 (dd, J = 18.4 Hz, 9.3 Hz, 1 H, C3β-H), 3.64 (dd, J = 9.2 Hz, 5.8 Hz, 1 H, C2β-H), 3.72 (mc, 1 H, C3a′α-H), 4.59 (d, J = 8.5 Hz, 1 H, C10c′α-H), 7.09–7.59 (m, 13 H_{Ar}), 7.98 (d, J = 7.9 Hz, 1 H, C10′-H), 9.89 (s, 1 H, NH); EIMS (m/z, rel intensity) 503 ($M^{+\bullet}$, 45), 329 (79), 182 (100), 167 (49). Anal. Calcd for $C_{31}H_{25}N_3O_4$ (503.18): C, 73.93; H, 5.01; N, 8.35. Found: C, 73.29; H, 4.95; N, 8.30.

4β-Methyl-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazole-1,3-dione (10a): procedure Ib, reaction time 40 h, yield 73%; mp 245 °C (petroleum ether/ethyl acetate, 1/1); ^{1}H NMR (acetone-d_6) δ 1.49 (d, J = 7.1 Hz, 3 H, CH_3), 2.40–2.48 (m, 1 H, C4α-H), 2.71 ('dq', J = 16.2 Hz, 10.2 Hz, 1.6 Hz, 1 H, C5β-H), 2.91 (dd, J = 16.0 Hz, 4.7 Hz, 1 H, C5α-H), 3.70 (dd, J = 7.7 Hz, 4.1 Hz, 1 H, C3a-H), 4.43 ('pseudo-sext', J = 7.7 Hz, 1.5 Hz, 1 H, C10c-H), 6.99–7.41 (m, 8 H, phenyl H and C7-H to C9-H), 7.86 (d, J = 7.6 Hz, 1 H, C10-H), 10.15 (s, 1 H, NH); EIMS (m/z, rel intensity) 330 ($M^{+\bullet}$, 100), 183 (58), 168 (97). Anal. Calcd for $C_{21}H_{18}N_2O_2$ (330.14): C, 76.33; H, 5.50; N, 8.48. Found: C, 75.90; H, 5.54; N, 8.42.

5α-Methyl-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazole-1,3-dione (10b): procedure Ib, reaction time 7 h, yield 16%; mp 205 °C (toluene); ^{1}H NMR (CD_2Cl_2) δ 1.39 (d, J = 7.0 Hz, 3 H, CH_3), 1.72 (m, 1 H, C4β-H), 2.64 (mc, 1 H, C4α-H), 3.00 (mc, 1 H, C5α-H), 3.61 (mc, 1 H, C3aα-H), 4.46 (dd, J = 8.3 Hz, 1.7 Hz, 1 H, C10cα-H), 7.12–7.22 (m, 4 H_{Ar}), 7.28–7.50 (m, 4 H_{Ar}), 7.92 (dd, J = 7.5 Hz, 1.5 Hz, 1 H, C10-H), 8.22 (s, 1 H, NH); EIMS (m/z, rel intensity) 330 ($M^{+\bullet}$, 100), 182 (90), 168 (96). Anal. Calcd for $C_{21}H_{18}N_2O_2$ (330.14): C, 76.33; H, 5.50; N, 8.48. Found: C, 76.12; H, 5.48; N, 8.46.

5β-Methyl-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazole-1,3-dione (10b′): procedure Ib, reaction time 7 h, yield 12%; mp 241 °C (toluene); ^{1}H NMR (CD_2Cl_2) δ 1.34 (d, J = 7.0 Hz, 3 H, CH_3), 2.03 (m, 1 H, C4β-H), 2.41 (mc, 1 H, C4α-H), 3.10 (mc, 1 H, C5α-H), 3.44 (mc, 1 H, C3aα-H), 4.40 (dd, J = 8.2 Hz, 1.4 Hz, 1 H, C10cα-H), 7.12–7.20 (m, 4 H_{Ar}), 7.25–7.50 (m, 4 H_{Ar}), 7.98 (dd, J = 7.5 Hz, 1.5 Hz, 1 H, C10-H), 8.22 (br s, 1 H, NH); EIMS (m/z, rel intensity) 330 ($M^{+\bullet}$, 72), 183 (24), 168 (100). Anal. Calcd for $C_{21}H_{18}N_2O_2$ (330.14): C, 76.33; H, 5.50; N, 8.48. Found: C, 76.01; H, 5.46; N, 8.44.

Methyl 3β-benzoyl-1β-methyl-1,2,3,4-tetrahydro-9*H*-carbazole-4-carboxylate (10c): procedure Ib, reaction time 18 h, yield 68%; mp 204–205 °C (toluene); ^{1}H NMR (DMSO-d_6) δ 0.74 (d, J = 6.9 Hz, 3 H, CH_3), 2.58 (d, J = 16.5 Hz, 1 H, C2β-H), 2.64 (m, 1 H, C1α-H), 3.43 (dd, J = 16.0 Hz, 5.4 Hz, 1 H, C2α-H), 3.66 (s, 3 H, CO_2CH_3), 4.26 (d, J = 9.8 Hz, 1 H, C4β-H), 4.31 (dd, J = 9.8 Hz, 2.5 Hz, 1 H, C3α-H), 6.94 (dd, J = 7.7 Hz, 7.7 Hz, 1 H, C6-H or C7-H), 7.01 (dd, J = 7.6 Hz, 7.6 Hz, 1 H, C7-H or C6-H), 7.28 (d, J = 8.0 Hz, 1 H, C8-H), 7.42 (d, J = 7.8 Hz, 1 H, C5-H), 7.56 (dd, J = 7.4 Hz, 7.6 Hz, 2 H, *m*-phenyl H), 7.67 (dd, J = 7.3 Hz, 7.5 Hz, 1 H, *p*-phenyl H), 8.06 (d, J = 7.2 Hz, 2 H, *o*-phenyl H), 10.99 (s, 1 H, NH); EIMS (m/z, rel intensity) 347 ($M^{+\bullet}$, 60), 316 (100), 289 (23), 183 (32), 169 (44). Anal. Calcd for $C_{22}H_{21}NO_3$ (347.15): C, 76.05; H, 6.10; N, 4.03. Found: C, 75.78; H, 6.07; N, 4.01.

2β-Methyl-3β-(1-oxopropan-1-yl)-1,2,3,4-tetrahydro-9*H*-carbazole (10d): procedure II, reaction time 8 h, yield 46%; mp 182–184 °C (ethyl acetate/petroleum ether); ^{1}H NMR (C_6D_6) δ 0.89 (d, J = 6.9 Hz, 3 H, CH_3), 0.98 (t, J = 7.2 Hz, 3 H, CH_2CH_3), 1.96–2.10 (m, 2 H, CH_2CH_3), 2.13 (dd, J = 15.8 Hz, 2.4 Hz, 1 H, C1-H_a), 2.30–2.38 (m, 2 H, C2α-H, C3α-H), 2.51 (dd, J = 16.0 Hz, 5.5 Hz, 1 H, C1-H_b), 2.73 (dd, J = 15.6 Hz, 4.9 Hz, 1 H, C4-H_a), 2.93 (dd, J = 15.0 Hz, 10.0 Hz, 1 H, C4-H_b), 6.40 (s, 1 H, NH), 7.08 (dd, J = 6.1 Hz, 2.8 Hz, 1 H, C8-H), 7.20–7.26 (m, 2 H, C6-H, C7-H), 7.56 (dd, J = 5.9 Hz, 2.8 Hz, 1 H, C5-H); EIMS (m/z, rel intensity) 241 ($M^{+\bullet}$, 75), 185 (63), 158 (100), 144 (88). Anal. Calcd for $C_{16}H_{19}NO$ (241.14): C, 79.62; H, 7.94; N, 5.81. Found: C, 79.11; H, 7.90; N, 5.77.

Methyl 2β-phenyl-1,2,3,4-tetrahydro-9*H*-carbazole-3β-carboxylate (10e): procedure Ib, reaction time 21 days, yield 47%; mp 182 °C (toluene); ^{1}H NMR (DMSO-d_6) δ 2.60 (dd, J = 15.9 Hz, 9.3 Hz, 1 H, C1-H_a), 2.93 (dd, J = 16.4 Hz, 5.3 Hz, 1 H, C1-H_b), 3.05 (dd, J = 16.8 Hz, 3.6 Hz, 1 H, C4-H_a), 3.24 (pseudo-quint, J = 8.8 Hz, 5.0 Hz, 4.5 Hz, 1 H, C2α-H), 3.31 (dd, J = 17.0 Hz, 6.4 Hz, 1 H, C4-H_b), 3.56 (s, 3 H, CH_3), 3.73 (m, J = 5.8

(34) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902. Program AMPAC 1.0: Stewart, J. J. P. *QCPE Bull.* **1986**, *6*, 506.

(35) ALCHEMY II force field program: Tripos Associates, St. Louis, MO. Variation of the COSMIC program: Vinter, J. G.; Davis, A.; Saunders, M. R. *J. Comput.-Aid. Mol. Design* **1987**, *1*, 31.

(36) Narasimhan, N. S.; Kusurkar, R. *Ind. J. Chem.* **1983**, *22b*, 846.

Hz, 5.0 Hz, 3.5 Hz, 1 H, C3α-H), 6.92–7.22 (m, 7 H, phenyl H, C6-H, C7-H), 7.28 (d, J = 8.0 Hz, 1 H, C5-H or C8-H), 7.37 (d, J = 7.7 Hz, 1 H, C8-H or C5-H), 10.82 (s, 1 H, NH); EIMS (m/z, rel intensity) 305 ($M^{+\bullet}$, 50), 220 (17), 144 (100). Anal. Calcd for $C_{20}H_{19}NO_2$ (305.15): C, 78.65; H, 6.27; N, 4.59. Found: C, 77.99; H, 6.18; N, 4.54.

Dimethyl 2-phenyl-1,2-dihydro-9*H*-carbazole-3,4-dicarboxylate (10f): procedure Ib, reaction time 10 h, yield 24%; mp 199 °C (petroleum ether/ethyl acetate); ^{1}H NMR (acetone-d_6) δ 3.17 (dd, J = 17.3 Hz, 1.3 Hz, 1 H, C1-H_a), 3.61 (dd, J = 17.8 Hz, 8.0 Hz, 1 H, C1-H_b), 3.62 (s, 3 H, CH_3), 4.0 (s, 3 H, CH_3), 4.41 (d, J = 8.1 Hz, 1 H, C2-H), 7.06–7.42 (m, 9 H), 10.78 (s, 1 H, NH); EIMS (m/z, rel intensity) 361 ($M^{+\bullet}$, 100), 271 (50), 244 (45). Anal. Calcd for $C_{22}H_{19}NO_4$ (361.13): C, 73.10, H, 5.30; N, 3.88. Found: C, 73.01; H, 5.27; N, 3.85.

Methyl (*E*)-3-[(*E*)-2-(propen-1-yl)-1*H*-indol-3-yl]acrylate (11): procedure II, reaction time 3 days, yield 34%; mp 169 °C (ethyl acetate/petroleum ether); ^{1}H NMR (acetone-d_6) δ 1.98 (dd, J = 6.7 Hz, 1.7 Hz, 3 H, CH_3), 3.73 (s, 3 H, CO_2CH_3), 6.41 (d, J = 15.9 Hz, 1 H, C2-H), 6.50 (dd, J = 15.8 Hz, 6.7 Hz, 1 H, C2″-H), 6.87 (dd, J = 15.9 Hz, 1.7 Hz, 1 H, C1″-H), 7.14–7.24 (m, 2 H, C5′-H, C6′-H), 7.38 (d, J = 7.5 Hz, 1 H, C7′-H), 7.87 (d, J = 7.1 Hz, 1 H, C4′-H), 8.04 (d, J = 15.8 Hz, 1 H, C3-H), 10.87 (s, 1 H, NH); EIMS (m/z, rel intensity) 241 ($M^{+\bullet}$, 71), 183 (100), 168 (63). Anal. Calcd for $C_{15}H_{15}NO_2$ (241.11): C, 74.65; H, 6.27; N, 5.81. Found: C, 74.10; H, 6.21; N, 5.74.

1-(1*H*-Indol-2-yl)-1,3,3-trimethyl-1,2,3,4-tetrahydrocyclopent[*b*]indole (12): procedure Ia, reaction time 2 days, yield 21%; mp 262 °C (petroleum ether/ethyl acetate), attempts at further purification resulted in decomposition; ^{1}H NMR (acetone-d_6) δ 1.36 (s, 3 H, C3-CH_3), 1.44 (s, 3 H, C3-CH_3), 1.86 (s, 3 H, C1-CH_3), 2.54 (d, J = 13.0 Hz, 1 H, C2-H_a), 2.78 (d, J = 13.1 Hz, 1 H, C2-H_b), 6.18 (d, J = 0.5 Hz, 1 H, C3′-H), 6.87–7.03 (m, 4 H, C5-H, C6-H, C5′-H, C6′-H), 7.22 (d, J = 7.9 Hz, 2 H, C7-H, C7′-H), 7.34 (d, J = 8.1 Hz, 1 H, C4-H or C4′-H), 7.40 (d, J = 7.5 Hz, 1 H, C4′-H or C4-H), 9.83 (s, 1 H, N8-H or N1′-H), 10.07 (s, 1 H, N1′-H or N8-H); EIMS (m/z, rel intensity) 314 ($M^{+\bullet}$, 43), 299 (100), 283 (14).

Preparation of Compounds 13 and 14a. *N*-Phenylmaleimide (1.1 mmol) dissolved in toluene (15 mL) was treated portionwise with $AlCl_3$ (1.1 mmol). A solution of 2-vinylindole (1 mmol) in toluene (10 mL) was then added dropwise, and the resultant mixture was heated under reflux for 14 h. Water (50 mL) was added to the cooled mixture, and the organic phase was separated, washed to neutrality with water, dried with Na_2SO_4, and concentrated on a rotary evaporator. Separation of the residue by column chromatography on silica gel gave products **13** (27%) and **14a** (13%).

2-[2-(2-Methylpropen-1-yl)-1*H*-indol-3-yl]-*N*-phenylsuccinimide (13): mp 118 °C (toluene); ^{1}H NMR (acetone-d_6) δ 1.94 (s, 3 H, CH_3), 1.95 (s, 3 H, CH_3), 2.98 (dd, J = 18.2 Hz, 5.5 Hz, 1 H, C3-H_a), 3.51 (dd, J = 18.2 Hz, 9.9 Hz, 1 H, C3-H_b), 4.58 (dd, J = 9.9 Hz, 5.5 Hz, 1 H, C2-H), 6.33 (t, J = 1.3 Hz, 1 H, H_{olefin}), 7.0–7.53 (m, 9 H_{Ar}), 10.10 (s, 1 H, NH); EIMS (m/z, rel intensity) 344 ($M^{+\bullet}$, 66), 197 (23), 182 (100), 170 (88).

4,4-Dimethyl-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazole-1,3-dione (14a): mp 258 °C (toluene); ^{1}H NMR (DMSO-d_6) δ 1.26 (s, 3 H CH_3), 1.33 (s, 3 H, CH_3), 2.74 (d, J = 18.0 Hz, 1 H, C5-H_a), 2.75 (d, J = 18.0 Hz, 1 H, C5-H_b), 3.30 (d, J = 7.7 Hz, 1 H, C3aα-H), 4.45 (dd, J = 7.6 Hz, 1.3 Hz, 1 H, C10cα-H), 6.97 (dd, J = 5.5 Hz, 5.5 Hz, 1 H, C8-H or C9-H), 7.02 (dd, J = 5.5 Hz, 5.5 Hz, C9-H or C8-H), 7.20 (d, J = 7.1 Hz, 2 H, *o*-phenyl H), 7.28 (d, J = 7.2 Hz, 1 H, C7-H), 7.35–7.48 (m, 3 H, *m*- and *p*-phenyl H), 7.74 (d, J = 7.4 Hz, 1 H, C10-H), 11.0 (s, 1 H, NH); EIMS (m/z, rel intensity) 344 ($M^{+\bullet}$, 100), 182 (67), 167 (35). Anal. Calcd for $C_{22}H_{20}N_2O_2$ (344.15): C, 76.88; H, 5.86; N, 8.14. Found: C, 76.78; H, 5.82; N, 8.09.

Methyl 6-methyl-1,3-dioxo-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazole-4β-carboxylate (14b): procedure Ia, reaction time 4 days, yield 69%; mp 241–242 °C (toluene); ^{1}H NMR (DMSO-d_6) δ 2.83 (dd, J = 15.9 Hz, 12.0 Hz, 1 H, C5β-H), 3.15 (dd, J = 16.6 Hz, 4.8 Hz, 1 H, C5α-H), 3.23 (m, 1 H, C4α-H), 3.66 (s, 3 H, CO_2CH_3), 3.73 (s, 3 H, NCH_3), 4.36 (dd, J = 8.3 Hz, 4.9 Hz, 1 H, C3aα-H), 4.52 (d, J = 7.9 Hz, 1 H, C10cα-H), 7.01–7.14 (m, 4 H_{Ar}), 7.31–7.43 (m, 4 H_{Ar}), 7.76 (d, J = 7.8 Hz, 1 H, C10-H); EIMS (m/z, rel intensity) 388 ($M^{+\bullet}$, 100), 329 (42), 241 (8), 183 (77). Anal. Calcd for $C_{23}H_{20}N_2O_4$ (388.14): C, 71.05; H, 5.20; N, 7.21. Found: C, 71.12; H, 5.18; N, 5.20.

Methyl 1,3-dioxo-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*b*]carbazole-4-carboxylate (14c): procedure Ib, reaction time 14 h, yield 32%; mp 226 °C (toluene); ^{1}H NMR (acetone-d_6) δ 3.00 (oct, J = 16.5 Hz, 11.9 Hz, 1.8 Hz, 1 H, C5-H), 3.17 (dd, J = 16.2 Hz, 5.0 Hz, 1 H, C5α-H), 3.25 (m, 1 H, C4α-H), 3.76 (s, 3 H, CH_3), 4.43 (dd, J = 7.8 Hz, 4.4 Hz, 1 H, C3aβ-H), 4.60 (d, J = 7.9 Hz, 1 H, C10cα-H), 7.00–7.10 (m, 2 H, C8-H, C9-H), 7.29–7.39 (m, 4 H, C7-H, *m*- and *p*-phenyl H), 7.86 (d, J = 7.9 Hz, 1 H, C10-H), 10.30 (s, 1 H, NH); EIMS (m/z, rel intensity) 374 ($M^{+\bullet}$, 50), 314 (29), 168 (100). Anal. Calcd for $C_{22}H_{18}N_2O_4$ (374.13): C, 70.56; H, 4.85; N, 7.49. Found: C, 69.88; H, 4.80; N, 7.39.

4α-Acetyl-2-phenyl-1,3,3aα,4,5,10cα-hexahydro-2*H*,6*H*-pyrrolo[3,4-*c*]carbazole-1,3-dione (14d): procedure Ib, reaction time 6 h, yield 31%; mp 278 °C; ^{1}H NMR (CD_3CN) δ 2.86 (dd, J = 15.0 Hz, 7.2 Hz, 1 H, C5α-H), 2.97–3.06 (m, 2 H, C4β-H, C5β-H), 4.33 (dd, J = 6.6 Hz, 1.2 Hz, 1 H, C3aα-H), 4.53 (dd, J = 6.8 Hz, 0.5 Hz, 1 H, C10aα-H), 7.04–7.13 and 7.32–7.42 (2 m, 4 H each, phenyl H, C7-H to C9-H), 7.82 (d, J = 7.1 Hz, 1 H, C10-H), 9.22 (s, 1 H, NH); EIMS (m/z, rel intensity) 358 ($M^{+\bullet}$, 85), 315 (60), 169 (100). Anal. Calcd for $C_{22}H_{18}N_2O_3$ (358.13): C, 73.78; H, 5.07; N, 7.82. Found: C, 73.62; H, 5.05; N, 7.81.

4-Cyano-9-methyl-9*H*-carbazole (15). The preparation was performed as described previously:[36] yield 24%; mp 142 °C (petroleum ether/benzene) (lit.[36] mp 142 °C); ^{1}H NMR (acetone-d_6) δ 4.00 (s, 3 H, CH_3), 7.35 (dd, J = 6.8 Hz, 6.9 Hz, 1 H, C6-H), 7.37–7.67 (m, 4 H_{Ar}), 7.90 (dd, J = 4.5 Hz, 7.4 Hz, 1 H, C1-H), 8.50 (dt, J = 0.9 Hz, 0.9 Hz, 7.1 Hz, 1 H, C5-H). Anal. Calcd for $C_{14}H_{10}N_2$ (206.08): C, 81.52; H, 4.89; N, 13.90. Found: C, 81.45; H, 4.59; N, 13.71.

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Supplementary Material Available: Tables of AM1 calculations for **10a** and **10a′** (12 pages). Ordering information is given on any current masthead page.