71700-73-7; **15**, 71700-74-8; **16**, 71700-75-9; **17**, 71700-76-0; **18**, 71700-77-1; **19**, 71700-78-2; **20**, 71700-79-3; **21**, 71700-80-6; **22**, 71700-81-7; **23**, 71700-82-8; **24**, 71700-83-9; **25**, 71700-84-0; **26**, 71700-85-1; **27**, 71700-86-2; **28**, 71700-87-3; **29**, 71700-87-3; **30**, 71700-88-4; **31**, 71700-89-5; **35**, 71700-90-8; **36**, 71700-91-9; 3-acetoxy-2-cyclohexen-1-one, 57918-73-7; ketene dimethyl acetal, 922-69-0; 1-acetoxy-8,8-dimethoxybicyclo[4.2.0]octan-5-one, 18926-91-5; 5-hydroxy-2-(phenylthio)-1,4-naphthaquinone acetate, 71700-92-0; 5-hydroxy-2-(phenylthio)-1,4-naphthaquinone, 71700-93-1.

Supplementary Material Available: Fractional coordinates (Table III), bond distances (Table IV), and bond angles (Table V) for tetracycle **16** (3 pages). Ordering information is given on any current masthead page.

In Situ Vinylindole Synthesis of Carbazoles[1a,b]

Wayland E. Noland* and Steven R. Wann[1c]

School of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

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The condensation of indole with ketones catalyzed by maleic acid has been utilized as a synthesis of 3-vinylindoles which, acting as dienes, are trapped by in situ Diels–Alder addition to the maleic acid. The resulting tetrahydrocarbazoles undergo double-bond isomerization and selective decarboxylation of the carboxyl group in the indole-2-acetic acid configuration to form 3-R^3- and 4-R^4-substituted-1,2,3,4-tetrahydrocarbazole-2-carboxylic acids which were the products isolated [$R^3 = R^4 = CH_3$; $R^3 = CH_3$, $R^4 = C_2H_5$; $R^3 = H$, $R^4 = CH_2CH(CH_3)_2$; $R^3 + R^4 = (CH_2)_3$; $R^3 = C_6H_5$, $R^4 = CH_3$; $R^3 = H$, $R^4 = CH_2C(CH_3)_3$]. The Diels–Alder reaction is sensitive to steric hindrance in the 3-vinylindole, and the limits have been fairly well defined. Methyl or ethyl esterification converted the acid products to the more soluble esters, which were then dehydrogenated with chloranil in refluxing *o*-xylene or 3–10% palladium-on-carbon in refluxing *o*-dichlorobenzene to the corresponding carbazole-2-carboxylate esters, thus providing an overall synthesis of carbazoles in three laboratory steps from indole. The mass spectral fragmentations of all the compounds described are interpreted in detail.

The Diels–Alder reaction, followed by a dehydrogenation step or other elimination in situ or at a later time, of 3-vinylindole[2] (**1**) or substituted 3-vinylindoles[3] (such as **5**) with dienophiles has been shown to lead, via tetrahydrocarbazoles (such as **3**) from ethylenic dienophiles (such as **2**) or dihydrocarbazoles (such as **7**) from acetylenic dienophiles (such as **6**), to the corresponding carbazoles (such as **4** or **8**). This reaction has been described as the "vinylindole synthesis of carbazoles".[3a]

The acid-catalyzed condensations of 3-unsubstituted indoles with monofunctional methylene or methyl ketones have been postulated to proceed in many cases through intermediate 3-vinylindoles (3-alkenylindoles),[4] and these have been isolated in some cases where the 3-vinylindoles were sufficiently stable under the reaction conditions. Such cases include the reactions of 2-methylindole with desoxybenzoin (1,2-diphenylethanone) to give 2-methyl-3-(1,2-diphenylethenyl)indole[5] and with the cyclohexanone derivative 3,4,4a,9a-tetrahydro-4,4,4a,9-tetramethyl-9*H*-carbazol-2(1*H*)-one to give 3,4,4a,9a-tetrahydro-4,4,4a,9-tetramethyl-2-(2-methylindol-3-yl)-9*H*-carbazole,[4a] the reactions of 1- and 2-methylindole, 1,2-dimethylindole, and 2-phenylindole with 2-indanone to give the corresponding 3-(1*H*-inden-2-yl)indoles in yields of 69, 94, 85, and 85%, respectively,[3b] and the reactions of 2-substituted indoles with methyl ketones to give the corresponding methylvinylindoles (**9**)[4g] and with a variety of six-membered-ring ketones to give the corresponding 3-cycloalkenylindoles.[4h]

We have now combined the synthesis of 3-vinylindoles from ketones with the vinylindole synthesis of tetrahydrocarbazoles in one flask by using indole (1 equiv) and excess ketone precursor **10** as the solvent, usually at reflux, with maleic acid (**11**, 1 equiv) both as the catalyst for 3-vinylindole formation and as the dienophile for the Diels–Alder reaction. These reactions, which constitute an "in situ vinylindole synthesis of tetrahydrocarbazoles", are accompanied by decarboxylation, giving the corresponding substituted tetrahydro-9*H*-carbazole-2-carboxylic acids **12** in 20–57% yield as the sole crystalline products. These acids were converted to their more soluble methyl or ethyl esters **13** to facilitate NMR characterization and solubility in the refluxing *o*-xylene or *o*-dichlorobenzene

(1) Presented in part at (a) the Undergraduate Chemistry Symposium at the Conference on Chemistry: Research and Careers '76—Your Chemical Future, sponsored by the American Chemical Society, Younger Chemists Committee, at North Dakota State University, Fargo, N.D., Nov 6, 1976, and (b) the Second National Student Affiliate Research Symposium, sponsored by the Council Committee on Chemical Education, at the 173rd National Meeting of the American Chemical Society, New Orleans, La., March 22, 1977; Abstract ACSC 45. (c) National Science Foundation Undergraduate Research Participant, summer 1976 (supported by NSF-URP Grant No. SMI-76-02077, to which we are indebted), and senior thesis student, 1976–1977, at the University of Minnesota, Minneapolis, Minn.

(2) Noland, W. E.; Sundberg, R. J. *J. Org. Chem.* **1963**, *28*, 884–5.

(3) (a) Noland, W. E.; Kuryla, W. C.; Lange, R. F. *J. Am. Chem. Soc.* **1959**, *81*, 6010–7. (b) Makky, A.-M. M. M.S. Thesis, University of Minnesota, Minneapolis, Minn., July 1961. (c) Campbell, R. W. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., Aug 1961; *Diss. Abstr.* **1962**, *22*, 3851. (d) Johnson, D. C. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., Nov 1961; *Ibid.* **1962**, *23*, 834. (e) Weinmann (now Mukherjee), J. M. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., Jan 1964; *Ibid.* **1964**, *25*, 1588. (f) Zee, S.-H. M.S. Thesis, University of Minnesota, Minneapolis, Minn., April 1964. (g) Johnson, R. A. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., April 1965; *Ibid.* **1966**, *26*, 5719. (h) Lindberg, S. E. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., April 1969; *Diss. Abstr. Int. B* **1969**, *30*, 2610–1. (i) Sundberg, R. J. "The Chemistry of Indoles"; Academic Press: New York, 1970; pp 125–7. (j) Remers, W. A. In "Indoles, Part 1"; Houlihan, W. J., Ed.; Wiley-Interscience: New York, 1972; Chapter 1, pp 174–5. (k) Hosmane, R. S.; Hiremath, S. P.; Schneller, S. W. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2450–3. (l) Hiremath, S. P.; Purohit, M. G. *Indian J. Chem.* **1974**, *12*, 493–5. (m) Bergamasco, R.; Porter, Q. N.; Yap, C. *Aust. J. Chem.* **1977**, *30*, 1531–44. (n) Bergamasco, R.; Porter, Q. N.; Yap, C. *Ibid.* **1978**, *31*, 1841–4.

(4) (a) Noland, W. E.; Venkiteswaran, M. R.; Richards, C. G. *J. Org. Chem.* **1961**, *26*, 4241–8. (b) Noland, W. E.; Venkiteswaran, M. R.; Lovald, R. A. *Ibid.* **1961**, *26*, 4249–54. (c) Noland, W. E.; Richards, C. G.; Desai, H. S.; Venkiteswaran, M. R. *Ibid.* **1961**, *26*, 4254–62. (d) Noland, W. E.; Venkiteswaran, M. R. *Ibid.* **1961**, *26*, 4263–9. (e) Reference 3i, pp 47–51. (f) Reference 3j, pp 83–5. (g) Simurdak, R. C. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., June 1972; *Diss. Abstr. Int. B* **1974**, *34*, 3175–6. (h) Freter, K. *J. Org. Chem.* **1975**, *40*, 2525–9.

(5) Noland, W. E.; Robinson, D. N. *J. Org. Chem.* **1957**, *22*, 1134–5.

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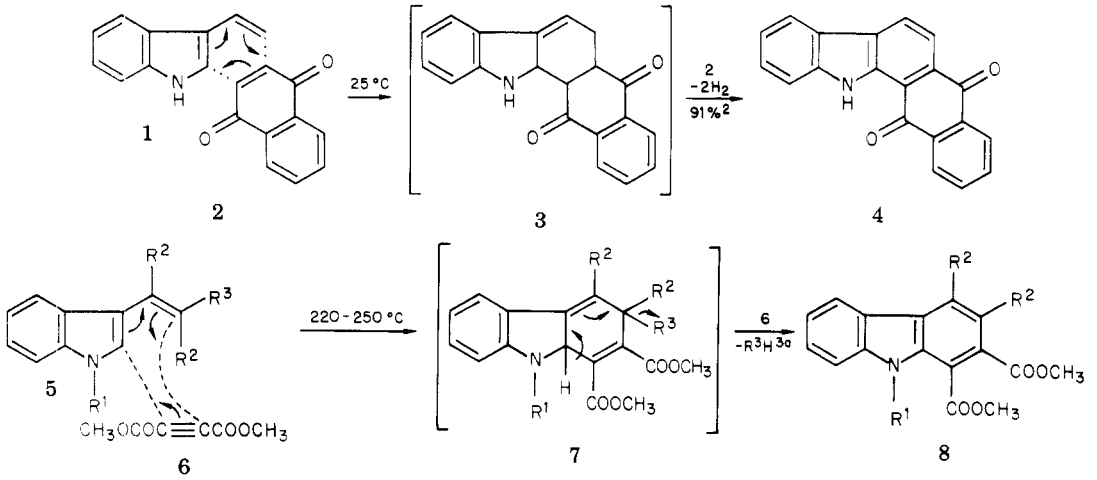
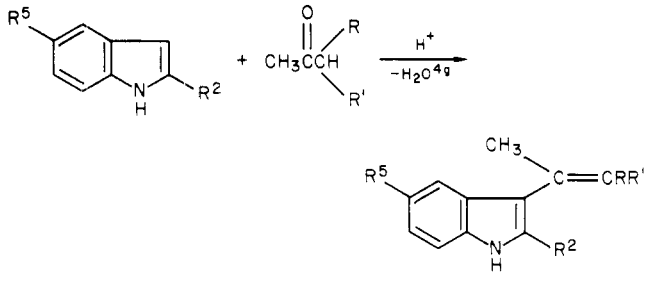
Scheme I



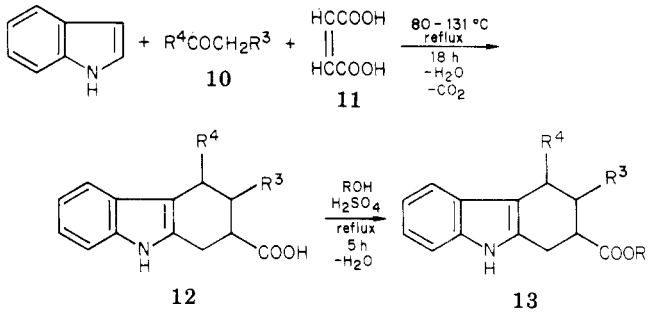
	R^1	R^2	R^3	% yield[3a]
5a, 7a, 8a,	H	$COOCH_3$	H	33-63 (from indole at 25 °C)
5b, 7b, 8b	H	CN	CN	17-30
5c, 7c, 8c	CH_3	CN	CN	44

Scheme II



	R^2	R^5	R	R'	% yield[4g]
9a	CH_3	H	CH_3	CH_3	32
b	CH_3	H	C_2H_5	CH_3	36
c	CH_3	H	$(CH_3)_2CH$	H	11-49
d	C_2H_5	H	$(CH_3)_2CH$	H	15-55
e	CH_3	NO_2	$(CH_3)_2CH$	H	22
f	CH_3	NO_2	C_2H_5	CH_3	not reported

Scheme III



	R^4	R^3	% yield	mp, °C
12a	CH_3	CH_3	24	248-249
b	CH_2CH_3	CH_3	28[a]	236-237
c	$CH_2CH(CH_3)_2$	H	21[b]	215-217
d	$CH_2CH_2CH_2$		57[c]	241-243
e	CH_3	C_6H_5	20[d]	328-329
f	$CH_2C(CH_3)_3$	H	0.1	248-250.5

[a] Refluxed 24 h. Yield includes 21% isolated as the methyl ester. [b] Including 10% isolated as the methyl ester. [c] Including 35% isolated as the methyl ester. [d] Heated at 120 °C instead of the boiling point (216 °C) of 10e.

	R^4	R^3	R	% yield	mp, °C
13a	CH_3	CH_3	C_2H_5	76	128-128.5
b	CH_2CH_3	CH_3	CH_3	66	169-171
c	$CH_2CH(CH_3)_2$	H	CH_3	87	167-169
d	$CH_2CH_2CH_2$		CH_3	91	145-146
d'	$CH_2CH_2CH_2$		C_2H_5	86	115-115.5
e	CH_3	C_6H_5	CH_3	73	183-185

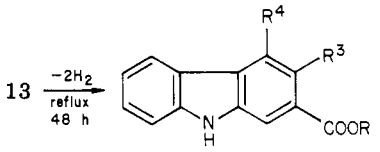
used as solvents for the dehydrogenation. Chloranil/*o*-xylene or 3–10% palladium-on-carbon/*o*-dichlorobenzene was used to convert **13** to the fully aromatic carbazole-2-carboxylate esters **14**. The latter step completes the in situ vinylindole synthesis of carbazoles.

The ultraviolet spectra of the tetrahydro-9*H*-carbazole-2-carboxylic acids **12** and their esters **13** contain an intact indole chromophore. This indicates that the double bond from the Diels–Alder reaction of the 3-vinylindole **15** with maleic acid, which would be expected to be initially in the 4,4a-position of the adduct **16**, has isomerized to the indole position shown in **17**. Once the indole configuration has been restored (**17**), decarboxylation of the 1-carboxyl group, which is in the indole-2-acetic acid configuration, can account for the regioselective loss of a single carboxyl group to give **12**, since decarboxylation of indole-2-acetic acids is known to be a facile reaction,[6] especially from work in the Iboga alkaloid series.

The NMR spectra, and the mass spectra which are discussed in a subsequent section and in the supplementary material, are consistent with the structures assigned to **12–14**. The melting points of **12** and **13**, and the NMR data reported in the Experimental Section, suggest that the compounds isolated are single *dl* pairs rather than mixtures of the possible diastereoisomers which could result from the chirality at the carbons bearing the carboxylate, R^3, and R^4 groups. Since the isolated yields are not quantitative, however, it cannot rigorously be claimed that these are the only stereoisomers present in the crude reaction mixtures. An unexpected finding was the 4-(2-

(6) (a) King, F. E.; L'Ecuyer, P. *J. Chem. Soc.* **1934**, 1901–5. (b) Hahn, G.; Bärwald, L.; Schales, O.; Werner, H. *Justus Liebigs Ann. Chem.* **1935**, *520*, 107–23. (c) Janot, M.-M.; Goutarel, R. *C. R. Hebd. Seances Acad. Sci.* **1955**, *241*, 986–7. (d) Bartlett, M. F.; Dickel, D. F.; Taylor, W. I. *J. Am. Chem. Soc.* **1958**, *80*, 126–36. (e) Schindler, W. *Helv. Chim. Acta* **1958**, *41*, 1441–3. (f) Renner, U.; Prins, D. A.; Stoll, W. G. *Ibid.* **1959**, *42*, 1572–81. (g) Gorman, M.; Neuss, N.; Cone, N. J.; Deyrup, J. A. *J. Am. Chem. Soc.* **1960**, *82*, 1142–5. (h) *Ibid.* **1965**, *87*, 93–9.

Scheme IV

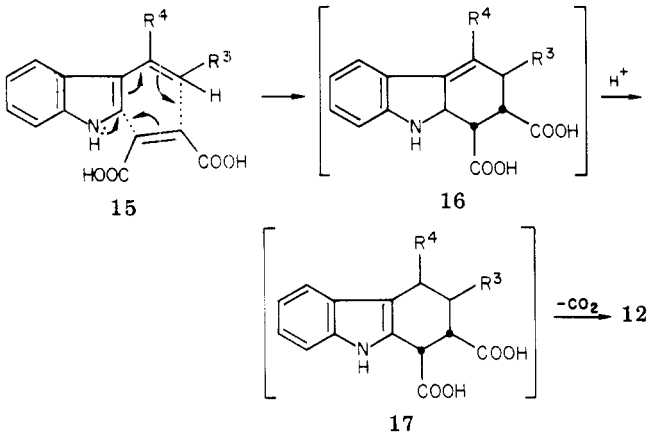


14

	R^4	R^3	R	method[a]	% yield	mp, °C
14a	CH_3	CH_3	C_2H_5	A	25	130-131
				B[b]	12	
b	CH_2CH_3	CH_3	CH_3	B	12	124-126
c	$CH_2CH(CH_3)_2$	H	CH_3	A	85	181-182.5
d	$CH_2CH_2CH_2$		CH_3	B[c]	1	252-253
e	CH_3	C_6H_5	CH_3	B[d]	2	320 (chars)

[a] Method: A, chloranil, o-xylene; B, 3-10% Pd-C, o-dichlorobenzene. [b] o-Xylene was used as the solvent. [c] Refluxed 35 h. [d] Refluxed 20 h.

Scheme V



methylpropyl) substitutent in **12c** (and correspondingly in **13c** and **14c**). By analogy with the formation of the 3,4-dimethyl derivative in **12a** (and **13a** and **14a**) and the 4-methyl-3-phenyl derivative in **12e** (and **13e** and **14e**), a 4-methyl-3-(methylethyl) adduct (**12**, $R^3 = CH(CH_3)_2$, $R^4 = CH_3$) would have been expected from the thermodynamically more stable 3-vinylindole isomer (**15**, $R^3 = CH(CH_3)_2$, $R^4 = CH_3$). This seemed especially likely since the thermodynamically more stable 3-vinylindoles (**9c–e**) are the ones which have been isolated[4g] from the corresponding reactions of the same ketone (**10c**) with 2-methylindole, 2-ethylindole, and 2-methyl-5-nitroindole. The formation of **12c** must indicate that the steric limits of the Diels–Alder reaction have been exceeded in the transition state for formation of the alternative so that maleic acid selects out the less sterically hindered and less thermodynamically stable 3-vinylindole isomer (**15**, $R^3 = H$, $R^4 = CH_2CH(CH_3)_2$). Then the question arises: Is a sufficient amount of this 3-vinylindole formed by kinetic control to account for the 21% yield of **12c** formed, or is the reacting 3-vinylindole formed by equilibration of the more stable to the less stable isomer under the acidic conditions of the reaction? The equilibration hypothesis could be consistent with the Curtin–Hammett principle in this particular case. If this were generally true, however, one would also expect to see the Diels–Alder adducts from the lowest energy (least sterically hindered) transition states in other cases, but this was not true with **12a** and **12e**. Furthermore, when the reaction was attempted with 3-methyl-2-butanone (**10**, $R^3 = H$, $R^4 = CH(CH_3)_2$), no crystalline product, such as an analogue of **12**, was isolated. This could mean either that the ketone was too sterically hindered to react at all or that the 3-vinylindole which did form as the kinetically controlled product was almost exclusively the tetrasubstituted, trimethyl derivative (**9**, $R = R' = CH_3$, $R^2 = R^5 = H$), which was too sterically hindered to undergo subsequent Diels–Alder reaction. Support for the latter alternative is provided by the fact that a reaction attempted under comparable conditions with a sterically hindered ketone, 4,4-dimethyl-2-pentanone (**10**, $R^3 = H$, $R^4 = CH_2C(CH_3)_3$), gave a very small yield (0.1% pure, isolated by chromatography) of **12f**, the structure and method of formation of which appear quite analogous to that of **12c**, but the major crystalline product (isolated in 15–22% yield) was the interesting intramolecular Diels–Alder product **21**[7] (predominantly the cis isomer). This product is derived exclusively from a reaction of indole with itself (to form triindole) and then with maleic acid and does not involve the ketone at all. Since no such product was isolated with 3-methyl-2-butanone, this suggests that the indole was consumed in reaction with that ketone (presumably to form a 3-vinylindole) and was not left for the slower dimerization and trimerization reaction with itself. Taking all of the foregoing facts into account, we are inclined to believe that the Diels–Alder reaction proceeds with the 3-vinylindoles which are formed by kinetic control until its steric limits are exceeded.

The mechanism proposed for formation of **21**[7] (via maleyltriindole (**18**) and the 3-vinylindole **19**) is an earlier example of the in situ vinylindole synthesis of carbazoles, being an intramolecular Diels–Alder version of the same (giving the intermediate adduct **20**) and having a completely analogous decarboxylation step (**20** → **21**).

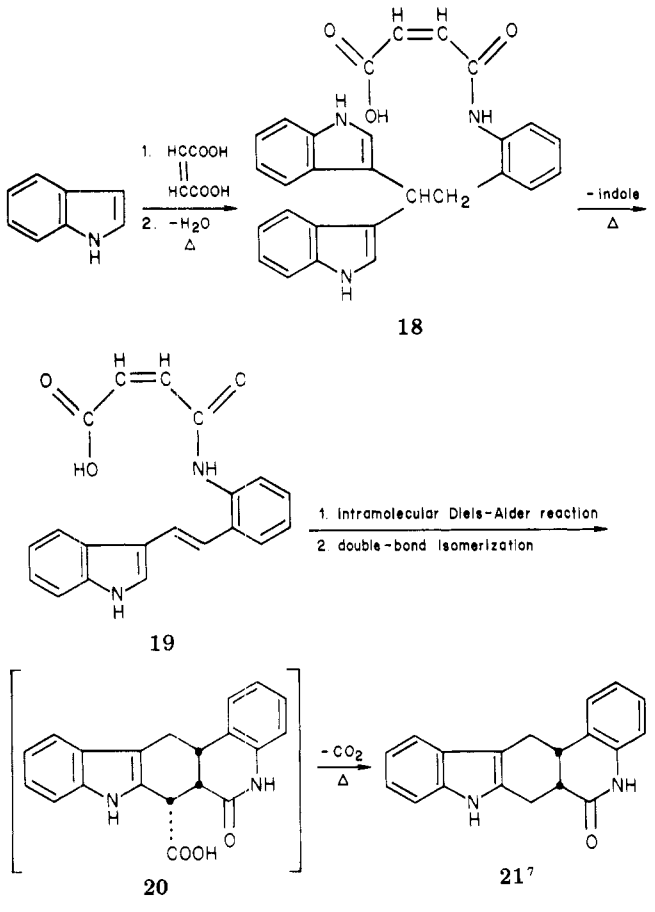
Mass Spectra

In the mass spectra of the tetrahydrocarbazole acids **12** and their esters **13**, the most characteristic peak in the 3-substituted derivatives is M − $R^3CH{=}CHCOOR$, attributed to the retrodiene **22** from a retro-Diels-Alder reaction[8a] involving loss of the elements of a 3-substituted acrylic acid derivative. This is the base peak with the acid **12a** and its ethyl ester **13a**, where $R^3 = CH_3$, and **12e** and its methyl ester **13e**, where $R^3 = C_6H_5$. The retro-Diels–Alder reaction also provides the retrodiene base peak (**22**) with the intramolecular Diels–Alder product **21**, which is consistent with its similar structure. The retrodiene peak (**22**) is still significant with the acid **12b** (31% relative intensity) and its methyl ester **13b** (41–55), where also R^3

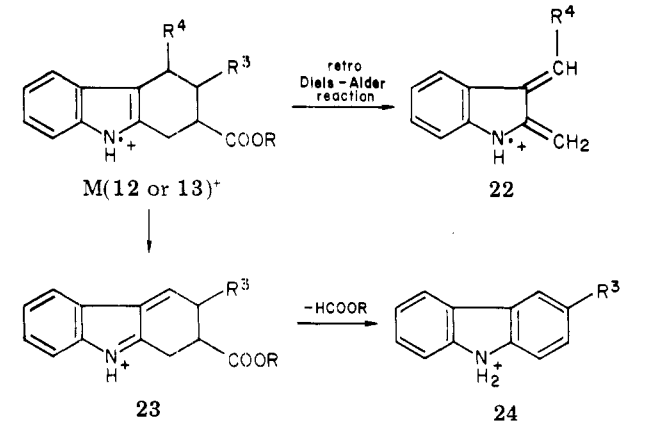
(7) Sellstedt, J. H. Ph.D. Thesis, University of Minnesota, Minneapolis, Minn., Nov 1965; *Diss. Abstr. B* **1967**, *27*, 2300.

(8) Budzikiewicz, H.; Djerassi, C.; Williams, D. H. "Mass Spectrometry of Organic Compounds"; Holden-Day: San Francisco, 1967: (a) pp 21–2, 632–3; (b) pp 394–7; (c) pp 81–3.

Scheme VI



Scheme VII



= CH_3. It is overshadowed, however, by the loss of the 4-ethyl substituent, which becomes the base peak in the methyl ester and, with concomitant loss of the carboxyl group, also in the acid. The retro-Diels–Alder reaction does not occur with the acid **12c** and its methyl ester **13c** or with the acid **12f**, which have only hydrogen as a substituent in the 3-position (R^3 = H), since loss of the 4-(2-methylpropyl) or 4-(2,2-dimethylpropyl) group dominates.

With all the tetrahydrocarbazole acids **12** and esters **13** the molecular ion, M, is at least a minor and often a significant peak, with the following percent relative intensities: **12a**, 10–33; **13a**, 23–25; **12b**, 35; **13b**, 44–45; **12c**, 17–21; **13c**, 16; **12e**, 10–11; **13e**, 10; **12f**, 18–30; also for **21**, 37–70. The molecular ion is the base peak only with **12d**, nearly so with its methyl ester **13d** (97–100), and still a strong peak with its ethyl ester **13d′** (59–73). These latter strong peaks are probably also due, at least in part, to a retro-Diels–Alder reaction. In this case the retrodiene and retrodienophile remain connected through the original cyclopentane ring, so there is no loss of elements from the molecular ion.

The loss of the 4-alkyl group, M – R^4, which would give a resonance-stabilized indol-3-yl methyl cation (**23**), often in conjunction with loss of a formate group (**24**), is another major feature in the fragmentation of the tetrahydrocarbazole acids and esters. This cleavage of the 4-alkyl group is analogous to the β cleavage of enamines,[8b] in which the 1-, 2-, and 3-positions of the indole nucleus function as the enamine. Loss of the 4-alkyl group gives the base peak with the acids **12c** and **12f** and nearly so with the methyl ester **13c** (96), in both of which the retro-Diels–Alder reaction does not occur. Loss of the 4-methyl or 4-ethyl group is a significant fragmentation pathway with the acids **12a** (22–31) and **12b** (63). With the corresponding esters, loss of the 4-methyl group alone is a minor factor with **13a** (10–12), but loss of the 4-ethyl group becomes the base peak with **13b**. Concomitant loss of the 4-alkyl group and formic acid or ester, M – R^4 – HCOOR, giving an aromatic carbazolium cation **24**, is also a major pathway. It gives the base peaks with the acid **12b** and the ester **13c**, significant peaks with **12a** (12–24), **13a** (24–27), **12b** (24), **13b** (75–90), **12c** (45–49), and **12f** (47–49), and a minor peak with **12e** (2–18).

The stability of the carbazole-2-carboxylate esters is shown by the fact that the molecular ion, M, is the base peak in all cases but one, **14c**, where it is the second most important peak (45). In this case, cleavage at the benzyl carbon,[8c] involving loss of methylethyl from the 2-methylpropyl group, becomes the base peak, of mass 238, and is probably the 2-(methoxycarbonyl)indolo[2,3]tropylium ion. The mass spectra of the products **12–14** are discussed much more fully in the supplementary material.

Experimental Section

Ultraviolet spectra (UV) were determined on a Cary Model 11 or 15 or a Beckman DK-2 recording spectrophotometer. Infrared spectra (IR) were determined on a Perkin-Elmer 257 or 727B or a Beckman Acculab 1 recording spectrophotometer. Nuclear magnetic resonance spectra (NMR) were determined on a Varian Associates T-60 60-MHz spectrometer. Electron-impact mass spectra (MS) were determined on an AEI MS-30 spectrometer at 70 eV, except at 20 eV where stated, by Dr. Roger A. Upham (to whom we are indebted for helpful discussions) and Edmund A. Larka.

Preparation of 1,2,3,4-Tetrahydro-9*H*-carbazole-2-carboxylic Acids (12). General Method. A solution of indole (7.0 g, 60 mmol) and maleic acid (7.0 g, 60 mmol) in the ketone (50 mL, 354–563 mmol) was refluxed for 18 h. Then most of the ketone was removed at aspirator pressure, usually in a rotating evaporator, leaving a dark red to dark brown tar which was worked up as individually described, with any variations in procedure noted.

1,2,3,4-Tetrahydro-3,4-dimethyl-9*H*-carbazole-2-carboxylic Acid (12a). Diethyl ether was added to the brown, viscous tar prepared by the general method, causing precipitation of a white solid, which was crystallized from 95% ethanol, giving **12a** as a white powder (3.49 g, 24%): mp 248–249 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 228 (4.57), 275 (sh) (3.84), 283 (3.88), 290 nm (3.83); IR (Nujol) 3400 (s) (NH), ~3180–2380 (br m) (OH), 1675 (s) (C=O), 1615 (mw) (C=C) cm^{-1}; NMR [$(CD_3)_2SO$)] δ 0.72 (d, J = 7 Hz, 3 H, 3-CH_3), 1.39 (d, J = 7 Hz, 3 H, 4-CH_3), ~2.68–4.0 (complex multiplet with a sharp peak at δ 2.83, 6 H, 1,1,2,3,4-H, OH, H_2O), ~6.61–7.68 (cm, 4 H, aromatic H), 10.65 (br d, J ~4 Hz, 1 H, NH); MS (20 eV) (relative intensity >5) m/e 244 (10, M + 1), 243 (61, M), 228 (31, M – CH_3), 182 (12, M – CH_3 – HCOOH), 158 (12), 157 (100, M – CH_3CH=CHCOOH, retro-Diels–Alder diene); high-resolution MS (relative intensity ≥6; calcd) m/e 244.1290 (6; $^{12}C_{14}{}^{13}CH_{17}NO_2$, 244.1292), 243.1256 (33; $C_{15}H_{17}NO_2$, 243.1259, M), 228.1033 (22; $C_{14}H_{14}NO_2$, 228.1025),

182.0964 (24; $C_{13}H_{12}N$, 182.0969), 180.0806 (9; $C_{13}H_{10}N$, 180.0813, M - CH_3 - HCOOH - H_2, indolo[*b*]tropylium cation), 168.0801 (9; $C_{12}H_{10}N$, 168.0813, carbazolium cation), 167.0733 (13; $C_{12}H_9N$, 167.0735, M - $2CH_3$ - HCOOH, carbazole radical cation), 158.0929 (13; $^{12}C_{10}{}^{13}CH_{11}N$, 158.0925), 157.0902 (100; $C_{11}H_{11}N$, 157.0891), 156.0820 (12; $C_{11}H_{10}N$, 156.0813, M - $CH_3CH{=}CHCOOH$ - H), 130.0667 (6; C_9H_8N, 130.0657, quinolinium cation).

Anal. Calcd for $C_{15}H_{17}NO_2$ (243.29): C, 74.05; H, 7.04; N, 5.76. Found: C, 74.05; H, 7.12; N, 5.73.

4-Ethyl-1,2,3,4-tetrahydro-3-methyl-9*H*-carbazole-2-carboxylic Acid (12b). Enough 95% ethanol was added to the dark red, viscous tar prepared by the general method (except that the reaction was refluxed for 24 h) to dissolve the tar without heating. The solution was kept at -20 °C for 3 days, causing precipitation of a yellowish solid (1.07 g, 7%; see the methyl esterification, part B, for isolation of an additional 21% from the mother liquor as the methyl ester), which was crystallized from 95% ethanol, giving **12b** as a white powder: mp 236–237 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 228 (4.49), 276 (sh) (3.77), 283 (3.81), 290 nm (3.85); IR (Nujol) 3400 (s) (NH), ~3700–2500 (br m) (OH), 1675 (s) (C=O), 1615 (mw) (C=C) cm^{-1}; NMR [$(CD_3)_2SO$] δ 0.72 (d, J = 6 Hz, 3 H, 3-CH_3), 1.08 (t, J = 6 Hz, superimposed on a multiplet from δ ~0.88 to 1.93, 5 H, CH_2CH_3), ~1.93–5.20 (complex multiplet with a sharp peak at δ 2.83, 1,1,2,3,4-H, OH, H_2O), ~6.63–7.73 (cm, 4 H, aromatic H), 10.71 (s, 0.7 H, NH); high-resolution MS (relative intensity ≥11; calcd) m/e 257.1417 (35; $C_{16}H_{19}NO_2$, 257.1415, M), 229.1031 (12; $^{12}C_{13}{}^{13}CH_{14}NO_2$, 229.1058), 228.1005 (63; $C_{14}H_{14}NO_2$, 228.1025, M - C_2H_5), 211.1342 (19; $C_{15}H_{17}N$, 211.1361, M - HCOOH), 210.1242 (11; $C_{15}H_{16}N$, 210.1282, M - HCOOH - H), 209.1186 (37; $C_{15}H_{15}N$, 209.1204, M - HCOOH - H_2, 4-ethyl-3-methyl-9*H*-carbazole radical cation), 194.0971 (47; $C_{14}H_{12}N$, 194.0969, M - CH_3 - HCOOH - H_2, 3-methylindolo[*b*]tropylium cation), 183.0970 (20; $^{12}C_{12}{}^{13}CH_{12}N$, 183.1003), 182.0960 (100; $C_{13}H_{12}N$, 182.0969, M - C_2H_5 - HCOOH), 181.0877 (24; $C_{13}H_{11}N$, 181.0891, M - C_2H_5 - HCOOH - H, 3-methylcarbazole radical cation), 180.0795 (31; $C_{13}H_{10}N$, 180.0813, M - C_2H_5 - HCOOH - H_2, indolo[*b*]tropylium ion), 171.1047 (31; $C_{12}H_{13}N$, 171.1048, M - $CH_3CH{=}CHCOOH$, retro-Diels–Alder diene), 168.0803 (25; $C_{12}H_{10}N$, 168.0813, carbazolium cation), 167.0745 (49; $C_{12}H_9N$, 167.0735, M - C_2H_5 - HCOOH - CH_3, carbazole radical cation).

Anal. Calcd for $C_{16}H_{19}NO_2$ (257.32): C, 74.68; H, 7.44; N, 5.44. Found: C, 74.83; H, 7.53; N, 5.36.

1,2,3,4-Tetrahydro-4-(2-methylpropyl)-9*H*-carbazole-2-carboxylic Acid (12c). Enough 95% ethanol was added to the dark brown, viscous tar prepared by the general method to dissolve the tar without heating. The solution was kept at -20 °C for 1 week, causing precipitation of a yellowish solid (1.75 g, 11%; see the methyl esterification, part B, for isolation of an additional 10% from the mother liquor as the methyl ester), which was crystallized from 95% ethanol, giving **12c** as a white solid: mp 215–217 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 228 (4.56), 275 (sh) (3.82), 282 (3.86), 290 nm (3.81); IR (halocarbon oil) 3400 (s) (NH), ~3190–2500 (br m) (OH), 1685 (s) (C=O), 1615 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 0.94 (d, J = 6 Hz) and 1.05 (d, J = 6 Hz) overlapping to form an apparent triplet [6 H, $CH(CH_3)_2$], ~1.20–3.45 [complex multiplet with a strong peak at δ 2.93, ~9 H, 1,1,2,3,3,4-H, $CH_2CH(CH_3)_2$, OH], ~6.85–7.78 (cm, ~6 H, aromatic H, NH); NMR [$(CD_3)_2SO$] δ 0.91 (d, J = 7 Hz) and 1.02 (d, J = 6 Hz) overlapping to form an apparent triplet [6 H, $CH(CH_3)_2$], ~1.13–5.25 (complex multiplet with a major peak at δ 2.81, 1,1,2,3,3,4-H, OH, H_2O), ~6.71–7.62 (cm, 4 H, aromatic H), 10.61 (s, 0.7 H, NH); NMR (CD_3CN) δ 0.96 (d, J = 7 Hz) and 1.07 (d, J = 6 Hz) overlapping to form an apparent triplet [6 H, $CH(CH_3)_2$], ~1.19–3.46 [complex multiplet with major peaks at δ 2.68 and 2.89, ~9 H, 1,1,2,3,3,4-H, $CH_2CH(CH_3)_2$, OH], ~6.69–7.71 (cm, ~4 H, aromatic H, NH); MS (relative intensity >4) m/e 271 (17, $C_{17}H_{21}NO_2$, M), 215 (13), 214 [100, M - $CH_2CH(CH_3)_2$], 169 [10, M - $CH_2CH(CH_3)_2COOH$ or $^{12}C_{11}{}^{13}CH_{10}N$], 168 [49, M - $CH_2CH(CH_3)_2$ - HCOOH, carbazolium cation], 167 [14, M - $CH_2CH(CH_3)_2$ - HCOOH - H, carbazole radical cation]; high-resolution MS (20 eV) (relative intensity >5; calcd) m/e 271.1576 (21; $C_{17}H_{21}NO_2$, 271.1572, M), 215.0886 (17; $^{12}C_{12}{}^{13}CH_{12}NO_2$, 215.0901), 214.0845 (100; $C_{13}H_{12}NO_2$, 214.0868), 180.0805 (11; $C_{13}H_{10}N$, 180.0813, M - $CH(CH_3)_2$ - HCOOH - H_2, indolo[*b*]tropylium cation), 169.0872 (11; $C_{12}H_{11}N$, 169.0891; or $^{12}C_{11}{}^{13}CH_{10}N$, 169.0847), 168.0800 (45; $C_{12}H_{10}N$, 168.0813), 167.0727 (11; $C_{12}H_9N$, 167.0735).

Anal. Calcd for $C_{17}H_{21}NO_2$ (271.35): C, 75.24; H, 7.80; N, 5.16. Found: C, 75.02; H, 8.01; N, 4.94.

2,3,3a,4,5,10c-Hexahydro-1*H*,6*H*-cyclopenta[*c*]carbazole-4-carboxylic Acid (12d). Ethanol (75 mL) was added to the brick red viscous tar prepared by the general method, causing precipitation of a yellowish solid (3.44 g, 22%; see the methyl esterification, part B, for isolation of an additional 35% from the mother liquor as the methyl ester), which was crystallized twice from ethanol, giving a cream-colored solid: mp 241–243 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 219 (4.57), 275 (sh) (3.84), 282 (3.87), 290 nm (3.81); IR (KBr) 3420 (s) (NH), ~3120–2400 (br m) (OH), 1685 (s) (C=O), 1620 (mw) (C=C) cm^{-1}; IR (Nujol) 3420 (s) (NH), ~3160–2320 (br m) (OH), 1655 (s) (C=O), 1615 (mw) (C=C) cm^{-1}; NMR, too insoluble; high-resolution MS (relative intensity ≥10; calcd) m/e 256.1290 (18; $^{12}C_{15}{}^{13}CH_{17}NO_2$, 256.1292, M + 1), 255.1265 (100; $C_{16}H_{17}NO_2$, 255.1259, M), 226.0909 (17; $C_{14}H_{12}NO_2$, 226.0868, M - C_2H_5), 211.1295 (12; $^{12}C_{14}{}^{13}CH_{16}N$, 211.1316), 210.1292 (71; $C_{15}H_{16}N$, 210.1282, M - COOH), 209.1155 (10; $C_{15}H_{15}N$, 209.1204, M - HCOOH), 208.1136 (20; $C_{15}H_{14}N$, 208.1126, M - HCOOH - H), 207.1038 (12; $C_{15}H_{13}N$, 207.1048, M - HCOOH - H_2, 2,3-dihydro-1*H*,6*H*-cyclopenta[*c*]carbazole radical cation), 206.0953 (11; $C_{15}H_{12}N$, 206.0969, M - HCOOH - 3H), 183.1059 (30; $C_{13}H_{13}N$, 183.1048, M - $CH_2{=}CHCOOH$), 182.0959 (31; $C_{13}H_{12}N$, 182.0969, M - $CH_2{=}CHCOOH$ - H), 181.0857 (17; $C_{13}H_{11}N$, 181.0891, M - $CH_2{=}CHCOOH$ - H_2; or $^{12}C_{12}{}^{13}CH_{10}N$, 181.0846), 180.0813 (48; $C_{13}H_{10}N$, 180.0813, M - $CH_2{=}CHCOOH$ - 3H), 169.0841 (11; $^{12}C_{11}{}^{13}CH_{10}N$, 169.0847), 168.0810 (73; $C_{12}H_{10}N$, 168.0813, M - COOH - C_3H_6, carbazolium cation), 167.0736 (39; $C_{12}H_9N$, 167.0735, M - HCOOH - C_3H_6, carbazole radical cation), 157.0881 (13; $C_{11}H_{11}N$, 157.0891, M - $CH_2{=}CHCOOH$ - HC≡CH), 154.0654 (12; $C_{11}H_8N$, 154.0656, M - $CH_2{=}CHCOOH$ - HC≡CH - 3H), 151.0036 (14), 130.0638 (15; C_9H_8N, 130.0657, quinolinium cation).

Anal. Calcd for $C_{16}H_{17}NO_2$ (255.30): C, 75.27; H, 6.71; N, 5.49. Found: C, 75.41; H, 6.82; N, 5.25.

1,2,3,4-Tetrahydro-4-methyl-3-phenyl-9*H*-carbazole-2-carboxylic Acid (12e). The general method was used except that the solution was heated at 120 °C instead of the boiling point (216 °C) of 1-phenyl-2-propanone. Also, instead of being evaporated first, the ketone solution was cooled and kept at -20 °C for 3 days. The acid **12e** which had precipitated as a white solid (1.0 g, 5%), mp 310–315 °C, was filtered. Then the dark red filtrate was distilled at aspirator pressure to remove most of the ketone. The residual red-brown tar solidified. It was taken up in methanol (~100 mL), which dissolved most of the viscous material, leaving a slightly yellowish precipitate. This was washed with cold methanol (2 mL), leaving additional **12e** as a white solid (2.6 g, 14%; total 3.6 g, 20%), mp 315 °C, which was used without further purification for preparation of the methyl ester. One crystallization from ethanol gave **12e** as a white solid: mp 328–329 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 232 (4.85), 278 (sh) (3.93), 284 (3.98), 291 nm (3.93); IR (Nujol) 3370 (s) (NH), ~3110–2380 (br m) (OH), 1680 (s) (C=O), 1615 (sh, mw) (C=C) cm^{-1}; NMR [$(CD_3)_2SO$] δ 1.34 (d, J = 7 Hz, ~4 H, 4-CH_3), ~2.69–4.69 (complex multiplet with a minor peak at δ 2.91 and major peak at δ 3.63, ~17 H, 5 alicyclic H, OH, H_2O), ~6.56–7.76 (complex multiplet with a major peak at δ 7.06, ~8 H, 9 aromatic H), 10.89 (br s, ~0.5 H, NH); MS (relative intensity ≥5) m/e 306 (2, M + 1), 305 (10, M), 244 (2, M - CH_3 - HCOOH), 168 (1.4, $C_{12}H_{10}N$, carbazolium cation), 167 (2, $C_{12}H_9N$, M - CH_3 - HCOOH - C_6H_5, carbazole radical cation), 158 (11), 157 (100, M - $C_6H_5CH{=}CHCOOH$, retro-Diels–Alder diene), 156 (12, M - $C_6H_5CH{=}CHCOOH$ - H), 130 (5, C_9H_8N, quinolinium cation); high-resolution MS (20 eV) (relative intensity; calcd) m/e 305.1396 (11; $C_{20}H_{19}NO_2$, 305.1415, M), 244.1130 (18; $C_{18}H_{14}N$, 244.1126, M - CH_3 - HCOOH), 168.0784 (6; $C_{12}H_{10}N$, 168.0813), 167.0750 (7; $C_{12}H_9N$, 167.0735), 158.0937 (13; $^{12}C_{10}{}^{13}CH_{12}N$, 158.0925), 157.0888 (100; $C_{11}H_{11}N$, 157.0891), 156.0799 (17; $C_{11}H_{10}N$, 156.0813), 130.0652 (4; C_9H_8N, 130.0657).

Anal. Calcd for $C_{20}H_{19}NO_2$ (305.36): C, 78.66; H, 6.27; N, 4.59. Found: C, 78.87; H, 6.22; N, 4.32.

Attempted Reaction of Indole with 3-Methyl-2-butanone and Maleic Acid. A solution of indole (5.0 g, 42.6 mmol) and maleic acid (5.0 g, 43.0 mmol) in 3-methyl-2-butanone (50 mL,

466 mmol) was refluxed for 18 h. Then most of the 3-methyl-2-butanone was removed in a rotating evaporator, leaving a dark red, viscous tar. The tar was dissolved in ethanol (25 mL) with heating on a steam bath. The solution was kept at −22 °C for 4 days, but no precipitate formed. Addition of a little water (~0.5 mL) gave no precipitate. The ethanol was removed in a rotating evaporator, again leaving a dark red tar. An attempt to methyl esterify any acidic product which might have been present was made by dissolving the tar in methanol (150 mL), adding concentrated sulfuric acid (3 drops), and refluxing the solution for 5 h. The progress of the attempted reaction was followed by TLC on silica gel and elution with 4:1 (v/v) petroleum ether (bp 30–60 °C)–benzene, but periodic spotting with a drop from the reaction mixture showed no movement from the origin indicative of the desired ester.

Reaction of Indole with 4,4-Dimethyl-2-pentanone and Maleic Acid. 1,2,3,4-Tetrahydro-4-(2,2-dimethylpropyl)-9*H*-carbazole-2-carboxylic Acid (12f) and 6a,7,13,13a-Tetrahydro-8*H*-indolo[2,3-*j*]phenanthridin-6(5*H*)-one (21, Largely the Cis Isomer). A solution of indole (3.5 g, 30 mmol) and maleic acid (3.5 g, 30 mmol) in 4,4-dimethyl-2-pentanone (30 mL, 354 mmol) was refluxed for 18 h. Then most of the ketone was distilled off at aspirator pressure, leaving a dark red tar (15.6 g). The tar was dissolved completely in acetone (100 mL) at room temperature. One portion (30 mL) was adsorbed on silica gel (5 g), the acetone was removed in a rotating evaporator, and the residue was added to a column of silica gel (25 mL, 42.5 g) under petroleum ether (bp 60–70 °C) and chromatographed. Elution with petroleum ether removed first unchanged indole (9 mg, 0.9%). Elution with 9:1 (v/v) petroleum ether–ethyl acetate removed **12f** as a slightly yellowish solid (15 mg, 0.6%), mp 170 °C. Three crystallizations from acetone–petroleum ether gave **12f** as white needles (3.5 mg, 0.1%): mp 248–250.5 °C; IR (KBr) 3400 (s) (NH), ~3240–2300 (br m) (OH), 1690 (s) (C=O) cm^{-1}; NMR [$(CD_3)_2CO$] δ 1.07 [s, $C(CH_3)_3$]; MS (20 eV) (relative intensity >12) *m/e* 285 (30, M), 215 (33, $^{12}C_{12}{}^{13}CH_{12}NO_2$, M − $CH_2C(CH_3)_3$), 214 (100, M − $CH_2C(CH_3)_3$), 169 (20, $^{12}C_{11}{}^{13}CH_{10}N$, M − $CH_2C(CH_3)_3$ − HCOOH), 168 (79, M − $CH_2C(CH_3)_3$ − HCOOH, carbazolium cation), 167 (13, M − $CH_2C(CH_3)_3$ − HCOOH − H, carbazole radical cation), 57 (15, $(CH_3)_3C^+$); high-resolution MS (relative intensity >6 above 69; calcd) *m/e* 285.1722 (18; $C_{18}H_{23}NO_2$, 285.1727, M), 215.0884 (16; $^{12}C_{12}{}^{13}CH_{12}NO_2$, 215.0900), 214.0846 (100; $C_{13}H_{12}NO_2$, 214.0866), 169.0857 (9; $^{12}C_{11}{}^{13}CH_{10}N$, 169.0845), 168.0806 (47; $C_{12}H_{10}N$, 168.0812), 167.0739 (15; $C_{12}H_9N$, 167.0734).

Elution with 4:1 (v/v) petroleum ether–ethyl acetate removed crude **21** as a yellowish white solid (0.28 g, 22%), mp 262–279 °C. Recrystallization from acetone–methanol gave a cream-colored powder, mp 296–299 °C, having an IR spectrum in KBr identical with that of the sample of **21** obtained without chromatography by recrystallization from the other portion of the acetone solution as now described below.

The other portion of the acetone solution (70 mL) was kept for 2 days, during which some evaporation occurred, causing separation of **21** as a slightly yellow solid (0.57 g, 19%; should be included in the yield given above), mp 210–218 °C. Two recrystallizations from acetone–methanol gave a whitish powder: mp 295–303 °C dec. (lit.:[7] for the cis isomer, white needles, mp 337–347 °C with charring at 330 °C; for the trans isomer, white hairlike crystals, mp 318–321 °C); IR (KBr) 3390 (s), 3200 (ms), 3130 (m, sh) (NH), 1675 (s), 1650 (ms, sh) (C=O) cm^{-1} (lit.[7] for the cis isomer (Nujol) 3408 (ms), 3403 (ms), 3320 (w), 3212 (m), 3143 (mw) (NH), 1683 (s), 1660 (m) (C=O) cm^{-1}; the IR spectrum in KBr was essentially identical with those in halocarbon oil and Nujol obtained by Sellstedt[7] for the pure cis isomer); MS (relative intensity ≥8 above 63) *m/e* 289 (14, M + 1), 288 (70, M), 167 (8, M − C_6H_5NCO − H_2, carbazole radical cation), 146 (8, $^{12}C_8{}^{13}CH_7NO$), 145 (20, M − $C_{10}H_9N$, retro-Diels–Alder dienophile), 144 (60, $^{12}C_9{}^{13}CH_9N$ and M − $C_{10}H_{10}N$ or M − C_9H_6NO), 143 (100, M − C_9H_7NO, retro-Diels–Alder diene), 142 (21, M − C_9H_8NO), 130 (49, quinolinium cation), 128 (19), 117 (25, indole radical cation), 116 (15, indole − H), 115 (30, indole − 2H), 102 (15, indole − NH), 90 (17, indole − C_2H_3), 89 (14, C_6H_3N), 77 (15, C_6H_5); high-resolution MS (relative intensity; calcd) *m/e* 289.1299 (11, $^{12}C_{18}{}^{13}CH_{16}N_2O$, 289.1294), 288.1274 (37, $C_{19}H_{16}N_2O$, 288.1261, M), 144.0771 (21, $^{12}C_9{}^{13}CH_9N$, 144.0766), 143.0717 (100, $C_{10}H_9N$, 143.0734), 142.0643 (11, $C_{10}H_8N$, 142.0656).

A sample of **21** obtained from a similar reaction as a white solid, mp 340 °C dec, in 15% yield had a very similar IR spectrum in KBr, but the mass spectra showed it to be slightly less pure: UV (95% C_2H_5OH) λ_{max} (log ϵ) 225 (4.72), 252 (4.26), 274 (sh) (4.08), 276 (sh) (4.07), 281 (sh) (4.04), 288 (sh) nm (3.92) (lit.[7] for the cis isomer, 227 (4.58), 252 (4.18), 274 (sh) (4.01), 282 (sh) (3.97), 290 (sh) nm (3.83)); IR (KBr) 3400 (s), 3210 (ms), 3150 (m, sh) (NH), 1675 (s), 1660 (ms, sh) (C=O) cm^{-1}; NMR [$(CD_3)_2SO$] δ 2.50 [m, $(CD_3)_2SO$] and 3.34 (s, H_2O) overlapping the aliphatic region which appeared to contain peaks at δ 2.72 (0.9), 2.81 (0.8), 3.06 (2.0), 3.61 (0.7), and 3.98 (0.6; total 5.0), 6.70–7.49 (multiplet with major peaks at δ 6.94 and 7.20, 8.0, 8 aromatic H), 10.18 (br s, 0.8, 5-NH), 10.60 (br s, 0.7, 8-NH).

Esterification of the 1,2,3,4-Tetrahydro-9*H*-carbazole-2-carboxylic Acids (13). General Methods. A. Methyl Esters. A solution of the acid (1.0–2.2 g) in methanol (20–50 mL) acidified with concentrated sulfuric acid (3 drops) to pH 1 was refluxed for 5 h, during which all of the acid dissolved. The solution was concentrated in a rotating evaporator until white needles separated. These were filtered and recrystallized from methanol, giving the methyl esters as white needles.

With both methods A and B it is now recommended that the alcohol solution be neutralized by being stirred over solid sodium bicarbonate (~0.5 g). Then, as was done with **13e**, the solution can be concentrated virtually to dryness at the outset to maximize recovery of the ester without damage from sulfuric acid.

B. Ethyl Esters. A solution of the acid (1.5–1.6 g) in absolute ethanol (15 mL) and benzene (15 mL) acidified with concentrated sulfuric acid (3 drops) to pH 1 was refluxed for 5 h under a Dean–Stark distilling receiver to trap the water of reaction. The resulting yellow-to-brick red solution was concentrated in a rotating evaporator until needles formed and was then cooled at −22 °C for 24 h. The resulting tan needles were filtered. The filtrate was diluted with absolute ethanol (30 mL) and stirred over solid sodium bicarbonate (~0.5 g) for 1 h. Then the solution was filtered and concentrated, leaving a red-to-brown semisolid. Crystallization of this and the tan needles from ethanol several times, as needed, gave the ethyl esters as white needles.

Ethyl 1,2,3,4-Tetrahydro-3,4-dimethyl-9*H*-carbazole-2-carboxylate (13a). By method B, **12a** (1.6 g, 6.6 mmol) gave **13a** as white needles (1.35 g, 76%): mp 128–128.5 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 226 (4.43), 276 (sh) (3.71), 283 (3.75), 291 nm (3.68); IR (KBr) 3360 (s) (NH), 1710 (s) (C=O), 1625 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 0.82 (d, J = 7 Hz, 3 H, 3-CH_3), 1.32 (t, J = 7 Hz, OCH_2CH_3) and 1.51 (d, J = 7 Hz, 4-CH_3) overlapping to form an apparent quartet (6 H), ~1.82–3.98 (complex multiplet with a major peak at δ 2.99, 5 H, 1,1,2,3,4-H), 4.22 (q, J = 7 Hz, 2 H, OCH_2CH_3), ~6.48–8.17 (cm, 5 H, aromatic H, NH); MS (relative intensity ≥10) *m/e* 271 (23, M), 256 (10, M − CH_3), 182 (27, M − CH_3 − $HCOOC_2H_5$), 158 (12, $^{12}C_{10}{}^{13}CH_{11}N$), 157 (100, M − $CH_3CH{=}CHCOOC_2H_5$, retro-Diels–Alder diene), 156 (14, M − $CH_3CH{=}CHCOOC_2H_5$ − H); high-resolution MS (relative intensity >7; calcd) *m/e* 271.1567 (25; $C_{17}H_{21}NO_2$, 271.1572, M), 256.1326 (12; $C_{16}H_{18}NO_2$, 256.1337), 182.0918 (24; $C_{13}H_{12}N$, 182.0969), 157.0907 (100; $C_{11}H_{11}N$, 157.0891).

Anal. Calcd for $C_{17}H_{21}NO_2$ (271.35): C, 75.24; H, 7.80; N, 5.16. Found: C, 75.15; H, 8.02; N, 4.92.

Methyl 4-Ethyl-1,2,3,4-tetrahydro-3-methyl-9*H*-carbazole-2-carboxylate (13b). A. From 12b. By method A, **12b** (2.2 g, 8.1 mmol) gave **13b** as white needles (1.8 g, 66%): mp 169–171 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 227 (4.48), 274 (sh) (3.80), 282 (3.84), 290 nm (3.78); IR (KBr) 3340 (s) (NH), 1710 (s) (C=O), 1625 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 0.76 (d, J = 7 Hz, 3 H, 3-CH_3), 1.07 (t, J = 7 Hz, 3 H, CH_2CH_3), ~1.30–3.50 (complex multiplet with a major peak at δ 2.88, ~8 H, 1,1,2,3,4-H, CH_2CH_3), 3.73 (s, ~2 H, OCH_3), ~6.67–8.04 (complex multiplet with a major peak at δ 7.06, 5 H, aromatic H, NH); MS (relative intensity ≥6) *m/e* 272 (9, M + 1), 271 (45, M), 243 (16, $^{12}C_{14}{}^{13}CH_{16}NO_2$ or M − C_2H_4), 242 (100, M − C_2H_5), 212 (7, M − $COOCH_3$), 210 (6, M − $HCOOCH_3$ − H), 183 (17), 182 (90, M − C_2H_5 − $HCOOCH_3$), 181 (6, M − C_2H_5 − $HCOOCH_3$ − H), 180 (9, M − C_2H_5 − $HCOOCH_3$ − H_2), 172 (6), 171 (41, M − $CH_3CH{=}CH$-$COOCH_3$, retro-Diels–Alder diene), 170 (9, M − $CH_3CH{=}CHCO$-OCH_3 − H), 168 (19, carbazolium cation), 167 (26, M − C_2H_5 − $HCOOCH_3$ − CH_3, carbazole radical cation), 156 (10, $C_{11}H_{10}N$); high-resolution MS (relative intensity >5; calcd) *m/e* 272.1699

(4; $C_{17}H_{22}NO_2$, 272.1650, M + 1), 271.1572 (44; $C_{17}H_{21}NO_2$, 271.1572, M), 243.1218 (17; $^{12}C_{14}{}^{13}CH_{16}NO_2$, 243.1214; or $C_{15}H_{17}NO_2$, 243.1259), 242.1193 (100; $C_{15}H_{16}NO_2$, 242.1181), 210.1294 (10; $C_{15}H_{16}N$, 210.1282), 183.0988 (14; $^{12}C_{12}{}^{13}CH_{12}N$, 183.1003), 182.0959 (75; $C_{13}H_{12}N$, 182.0969), 172.1069 (4; $^{12}C_{11}{}^{13}CH_{13}N$, 172.1082), 171.1041 (55; $C_{12}H_{13}N$, 171.1048), 170.0928 (12; $C_{12}H_{12}N$, 170.0969), 168.0807 (18; $C_{12}H_{10}N$, 168.0813), 167.0731 (23; $C_{12}H_9N$, 167.0735), 156.0782 (9; $C_{11}H_{10}N$, 156.0813).

Anal. Calcd for $C_{17}H_{21}NO_2$ (271.35): C, 75.24; H, 7.80; N, 5.16. Found: C, 75.39; H, 7.95; N, 4.93.

B. From the Mother Liquor of 12b. The ethanolic mother liquor from the filtration of 1.07 g of crude acid **12b** was concentrated in a rotating evaporator on a steam bath. The resulting tar was spread in a thin layer on a large watch glass. After 2 days the large, yellowish white crystals which had formed in the tar were removed by hand and methyl esterified according to general method A. Recrystallization from methanol gave **13b** as white needles (3.39 g, 21%), mp 169–171 °C, indicating that the total yield of the acid **12b** from its preparation was at least 28%.

Methyl 1,2,3,4-Tetrahydro-4-(2-methylpropyl)-9*H*-carbazole-2-carboxylate (13c). A. From 12c. By method A, **12c** (1.8 g, 6.6 mmol) gave **13c** as white needles (1.65 g, 87%), mp 167–169 °C. Two more crystallizations from methanol gave the analytical sample as white needles: mp 167–169 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 227 (4.60), 276 (sh) (3.83), 282 (3.87), 290 nm (3.78); IR (KBr) 3370 (s) (NH), 1710 (s) (C=O), 1625 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 0.95 (d, J = 6 Hz) and 1.08 (d, J = 6 Hz) overlapping to form an apparent triplet [6 H, $CH(CH_3)_2$], ~1.23–3.49 [complex multiplet with a strong peak at δ 2.94, 9 H, 1,1,2,3,3,4-H, $CH_2CH(CH_3)_2$], 3.76 (s, 3 H, $COOCH_3$), ~6.93–8.16 (cm, 5 H, aromatic H, NH); high-resolution MS (relative intensity >6; calcd) m/e 285.1735 (16; $C_{18}H_{23}NO_2$, 285.1728, M), 229.1064 (14; $^{12}C_{13}{}^{13}CH_{14}NO_2$, 229.1058), 228.1030 [96; $C_{14}H_{14}NO_2$, 228.1025, M – $CH_2CH(CH_3)_2$], 169.0821 (14; $^{12}C_{11}{}^{13}CH_{10}N$, 169.0847), 168.0799 [100; $C_{12}H_{10}N$, 168.0813, M – $CH_2CH(CH_3)_2$ – HCOOC-H_3, carbazolium cation], 167.0736 [26; $C_{12}H_9N$, 167.0735, M – $CH_2CH(CH_3)_2$ – $HCOOCH_3$ – H, carbazole radical cation].

Anal. Calcd for $C_{18}H_{23}NO_2$ (285.37): C, 75.75; H, 8.12; N, 4.91. Found: C, 75.82; H, 8.18; N, 4.70.

B. From the Mother Liquor of 12c. The methanolic mother liquor from the filtration of 1.75 g of crude **12c** was diluted carefully with water until it became slightly cloudy. It was warmed on the steam bath until the cloudiness disappeared and was then kept at −20 °C for 24 h. The resulting brown-yellow paste was methyl esterified according to general method A, giving **13c** as white needles (1.63 g, 10%), mp 167–169 °C, indicating that the total yield of the acid **12c** from its preparation was at least 21%.

Methyl 2,3,3a,4,5,10c-Hexahydro-1*H*,6*H*-cyclopenta[*c*]carbazole-4-carboxylate (13d). A. From 12d. By method A, **12d** (1.5 g, 5.9 mmol) gave **13d** as white needles (1.45 g, 91%): mp 145–146 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 228 (4.58), 276 (sh) (3.87), 283 (3.90), 290 nm (3.83); IR (KBr) 3340 (s) (NH), 1710 (s) (C=O), 1625 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.52 (m, 4 H, 2- and 3-CH_2), 2.05 (m, 2 H, 1-CH_2), 2.96 (m, 4 H, 5-CH_2, 3a-CH, 10c-CH), 3.47 (m, 1 H, $CHCOOCH_3$), 3.73 (s, 3 H, OCH_3), 7.14 (cm, 4 H, aromatic 8-, 9-, and 10-H, NH), 7.52 (complex multiplet, 1 H, aromatic 7-H); MS (relative intensity >7) m/e 270 (17, M + 1), 269 (97, M), 211 (17), 210 (100, M – $COOCH_3$), 209 (14, M – $HCOOCH_3$), 208 (28, M – $HCOOCH_3$ – H), 183 (26, M – CH_2=$CHCOOCH_3$), 182 (23, M – CH_2=$CHCOOCH_3$ – H), 181 (17, M – CH_2=$CHCOOCH_3$ – 2H), 180 (38, M – CH_2=$CHCOOCH_3$ – 3H, indolo[2,3]tropylium cation), 169 (11), 168 (68, M – $COOCH_3$ – C_3H_6, carbazolium cation), 167 (37, M – $HCOOCH_3$ – C_3H_6, carbazole radical cation), 130 (13, quinolinium cation); high-resolution MS (relative intensity; calcd) m/e 270.1433 (56; $^{12}C_{16}{}^{13}CH_{19}NO_2$, 270.1449), 269.1433 (100; $C_{17}H_{19}O_2$, 269.1416, M), 210.1233 (86; $C_{15}H_{16}N$, 210.1282), 208.1139 (56; $C_{15}H_{14}N$, 208.1126), 168.0797 (73; $C_{12}H_{10}N$, 168.0813), 167.0753 (37; $C_{12}H_9N$, 167.0735).

Anal. Calcd for $C_{17}H_{19}NO_2$ (269.33): C, 75.81; H, 7.11; N, 5.20. Found: C, 76.09; H, 7.30; N, 5.31.

B. From the Mother Liquor of 12d. The methanolic mother liquor from the filtration of 3.44 g of crude acid **12d** was diluted carefully with water until it became cloudy and then kept for 3 days. The resulting purple paste was methyl esterified according to general method A, giving **13c** as white needles (5.64 g, 35%), mp 145–146 °C, indicating that the total yield of the acid from its preparation was at least 57%.

Ethyl 2,3,3a,4,5,10c-Hexahydro-1*H*,6*H*-cyclopenta[*c*]carbazole-4-carboxylate (13d′). By method B, **12d** (1.5 g, 5.9 mmol) gave **13d′** as white needles (1.44 g, 86%): mp 115–115.5 °C; IR (KBr) 3350 (s) (NH), 1700 (s) (C=O), 1620 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.31 (t, J = 7 Hz, OCH_2CH_3) overlapping 1.53 (m, total 7 H, 2- and 3-CH_2), 2.14 (m, ~3 H, 1-CH_2, 3a-H), 2.95 (m, ~3 H, 5-CH_2, 10c-H), 3.48 (m, 1 H, 4-H), 4.23 (q, J = 7 Hz, 2 H, OCH_2CH_3), 7.20 (cm, 5 H, aromatic 7,8,9,10-H, NH); MS (relative intensity ≥11) m/e 284 (15, M + 1), 283 (73, M), 211 (17), 210 (100, M – $COOC_2H_5$), 209 (16, M – $HCOOC_2H_5$), 208 (23, M – $HCOOC_2H_5$ – H), 183 (23, M – CH_2=$CHCOOC_2H_5$), 182 (19, M – CH_2=$CHCOOC_2H_5$ – H), 181 (14, M – CH_2=$CHCOOC_2H_5$ – 2H), 180 (33, M – CH_2=$CHCOOC_2H_5$ – 3H, indolo[2,3]tropylium cation), 169 (12), 168 (56, M – $COOC_2H_5$ – C_3H_6, carbazolium cation), 167 (28, M – $HCOOC_2H_5$ – C_3H_6, carbazole radical cation), 130 (11, quinolinium cation); high-resolution MS (relative intensity >10; calcd) m/e 284.1624 (15; $^{12}C_{17}{}^{13}CH_{21}NO_2$, 284.1605), 283.1588 (59; $C_{18}H_{21}NO_2$, 283.1572, M), 210.1273 (100; $C_{15}H_{16}N$, 210.1282), 209.1204 (14; $C_{15}H_{15}N$, 209.1204), 208.1125 (22; $C_{15}H_{14}N$, 208.1126), 183.1052 (23; $C_{13}H_{13}N$, 183.1048), 182.0960 (18; $C_{13}H_{12}N$, 182.0969), 181.0895 (23; $C_{13}H_{11}N$, 181.0891), 180.0824 (48; $C_{13}H_{10}N$, 180.0813), 169.0822 (17; $^{12}C_{11}{}^{13}CH_{10}N$, 169.0847), 168.0809 (69; $C_{12}H_{10}N$, 168.0813), 167.0734 (36; $C_{12}H_9N$, 167.0735), 130.0683 (17; C_9H_8N, 130.0657).

Methyl 1,2,3,4-Tetrahydro-4-methyl-3-phenyl-9*H*-carbazole-2-carboxylate (13e). The acid **12e** (1.00 g, 3.27 mmol) was esterified by method A, except that 125 mL of methanol was used, the mixture was refluxed for a total of 9 h (1 h after all of the **12e** had dissolved), and the workup was modified. The resulting green solution was neutralized by being stirred over solid sodium bicarbonate (0.5 g) for 1 h and then evaporated to dryness in a rotating evaporator, leaving yellowish white needles. These were crystallized from 10:1 (v/v) methanol–acetone, giving **13e** as white needles (0.76 g, 73%): mp 183–185 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 228 (4.54), 275 (sh) (3.84), 283 (3.86), 290 nm (3.81); IR (KBr) 3400 (s) (NH), 1730 (s) (C=O), 1630 (mw) (C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.26 (s, 0.5 H, impurity), 1.37 (d, J = 6 Hz, 3 H, 4-CH_3), ~2.78–3.40 (m, ~3 H, 1-CH_2, 4-H), 3.63 (s, OCH_3) superimposed on δ ~3.40–3.98 (m, total 5 H, 2-H, 3-H), ~6.80–8.15 (complex multiplet with a major peak at δ 7.06 and a lesser peak at δ 7.18, 10 H, 9 aromatic H, NH); MS (relative intensity >6) 319 (10, M), 158 (14), 157 (100, M – C_6H_5CH=$CHCOOCH_3$, retro-Diels–Alder diene), 156 (14, M – C_6H_5CH=$CHCOOCH_3$ – H; high-resolution MS (relative intensity >5; calcd) m/e 319.1543 (10; $C_{21}H_{21}NO_2$, 319.1572, M), 158.0933 (11; $^{12}C_{10}{}^{13}CH_{11}N$, 158.0925), 157.0898 (100; $C_{11}H_{11}N$, 157.0891), 156.0817 (10; $C_{11}H_{10}N$, 156.0813).

Anal. Calcd for $C_{21}H_{21}NO_2$ (319.39): C, 78.97; H, 6.63; N, 4.39. Found: C, 78.75; H, 6.70; N, 4.23.

Dehydrogenation of the 1,2,3,4-Tetrahydro Esters to the 9*H*-Carbazole-2-carboxylate Esters. Method A. With Chloranil in Refluxing *o*-Xylene. A solution of the 1,2,3,4-tetrahydro ester (1.0–1.20 g, 3.7–4.20 mmol) and chloranil (tetrachloro-1,4-benzoquinone; 1.81–2.06 g, 2 molar equiv) in *o*-xylene (1,2-dimethylbenzene; 10 mL) was refluxed for 48 h and then allowed to cool. The colored needles which separated were filtered off. The filtrate was diluted with diethyl ether (ethoxyethane; 30 mL) and extracted with aqueous 5% sodium bicarbonate (3 × 75 mL). The ether solution was dried ($CaSO_4$) and concentrated in a rotating evaporator. The green or gray residue was adsorbed on silica gel by dissolving it in acetone, mixing with silica gel (0.5–1.2 g), and evaporating the acetone. The resulting solid was added to a column of silica gel (12 g) under petroleum ether (Skellysolve F, bp 30–60 °C) and chromatographed. Elution with 9:1 (v/v) petroleum ether–benzene removed first any unchanged chloranil as a yellow solid (with **14a**, 15 mg, 8%), followed closely by unchanged 1,2,3,4-tetrahydro ester (**13a**, 0.3 g, 30%; **13c**, 0.15 g, 12%). Further elution, with 4:1 (v/v) petroleum ether–benzene, removed the product.

Method B. With 3–10% Palladium-on-Carbon in Refluxing *o*-Dichlorobenzene. Method B gave a purer product than method A because there appeared to be little or no unchanged 1,2,3,4-tetrahydro ester and there was no contamination by unchanged chloranil or its reduction products. A solution of the 1,2,3,4-tetrahydro ester (0.30–1.0 g, 1.1–3.7 mmol) in *o*-dichloro-

benzene (10–20 mL) with 3–10% palladium-on-carbon (Pd–C, containing 7–40 mg of palladium) was refluxed for 48 h. The catalyst was filtered off and the *o*-dichlorobenzene was distilled off at aspirator pressure, bp 75 °C (21 mm). The dark or brown residue was adsorbed on silica gel (1.2–1.4 g, using acetone as described in method A) and chromatographed on a column of silica gel (3.6–12 g) under petroleum ether (bp 30–60 °C). Elution with 4:1 to 1:1 (v/v) petroleum ether–benzene removed first a trace of *o*-dichlorobenzene, if present, and then the product.

Ethyl 3,4-Dimethyl-9*H*-carbazole-2-carboxylate (14a). By Method A. The ester **13a** (1.0 g, 3.7 mmol) and chloranil (1.81 g, 7.4 mmol) in *o*-xylene (7 mL) gave, after filtration of brick red needles of what may be the quinhydrone, workup, and chromatography, first unchanged chloranil (15 mg, 8%) and **13a** (0.3 g, 30%) and then **14a** as cream-colored needles (0.246 g, 25%): mp 130–131 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 227 (sh) (4.16), 251 (4.60), 302 (4.19), 351 nm (3.48); IR (KBr) 3360 (s) (NH), 1695 (s) (C=O), 1635 (m) (aromatic C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.38 (t, J = 7 Hz, 3 H, OCH_2CH_3), 2.55 (s, 3 H, 4-(or 3)-CH_3), 2.70 (s, 3 H, 3-(or 4)-CH_3), 4.39 (q, J = 7 Hz, 2 H, OCH_2CH_3), 7.28 (m, 3 H, 5-, 6-, and 7-H?), 7.55 (apparent s, 1 H, 1-H), ~8.26 (m, 2 H, 8-H, NH?); high-resolution MS (relative intensity >7; calcd) m/e 267.1242 (100; $C_{17}H_{17}NO_2$, 267.1259, M), 239.0909 (15; $^{12}C_{14}{}^{13}CH_{12}NO_2$, 239.0901), 238.0883 (61; $C_{15}H_{12}NO_2$, 238.0867, M – C_2H_5), 222.0925 (31; $C_{15}H_{12}NO$, 222.0919, M – OC_2H_5), 194.0964 (54; $C_{14}H_{12}N$, 194.0969, M – $COOC_2H_5$), 193.0899 (67; $C_{14}H_{11}N$, 193.0891, M – $HCOOC_2H_5$, 3,4-dimethylcarbazol-1-yne radical cation), 192.0781 (15; $C_{14}H_{10}N$, 192.0813, M – $HCOOC_2H_5$ – H), 167.0766 (19; $C_{12}H_9N$, 167.0735, carbazole radical cation).

Anal. Calcd for $C_{17}H_{17}NO_2$ (267.31): C, 76.38; H, 6.41; N, 5.24. Found: C, 76.16; H, 6.30; N, 5.08.

By Method B. The ester **13a** (1.0 g, 3.7 mmol) in *o*-xylene (7 mL) with 5% Pd–C (0.8 g) gave cream-colored needles (0.118 g, 12%), mp 130–131 °C.

Methyl 4-Ethyl-3-methyl-9*H*-carbazole-2-carboxylate (14b). By Method B. The ester **13b** (0.3012 g, 1.11 mmol) in *o*-dichlorobenzene (10 mL) with 3% Pd–C (0.2375 g) gave after workup, chromatography, and elution with 1:1 (v/v) petroleum ether–benzene only **14b**. Two crystallizations from methanol gave **14b** as cream-colored needles (0.0363 g, 12%): mp 124–126 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 229 (sh) (4.33), 252 (4.73), 304 (4.35), 354 nm (3.65); IR (KBr) 3280 (s) (NH), 1690 (s) (C=O), 1625 (m) (aromatic C=C) cm^{-1}; NMR ($CDCl_3$) δ 1.27 (t, J = 7 Hz, 3 H, 4-CH_2CH_3), 2.60 (s, 3 H, 3-CH_3), 3.21 (q, J = 7 Hz, 2 H, 4-CH_2CH_3), 3.85 (s, 3 H, OCH_3), 7.22 (m, 3 H, 5-, 6-, and 7-H?), 7.50 (apparent s, 1 H, 1-H), ~8.10 (m, 1 H, 8-H?), 8.47 (br s, 1 H, NH?); MS (relative intensity ≥10) m/e 268 (19, M + 1), 267 (100, M), 252 (44, M – CH_3), 236 (20, M – OCH_3), 208 (31, M – $COOCH_3$), 207 (42, M – $HCOOCH_3$), 206 (27, M – $HCOOCH_3$ – H), 194 (10, M – $COOCH_3$ + H – CH_3, 3-methylindolo[2,3]tropylium ion), 193 (19, M – $COOCH_3$ – CH_3), 192 (21, M – $HCOOCH_3$ – CH_3), 191 (18, M – $HCOOCH_3$ – CH_3 – H), 180 (11, M – $COOCH_3$ – C_2H_4); high-resolution MS (relative intensity; calcd) m/e 268.1252 (8; $^{12}C_{16}{}^{13}CH_{17}NO_2$, 268.1292), 267.1254 (100; $C_{17}H_{17}NO_2$, 267.1259, M), 252.1055 (22; $C_{16}H_{14}NO_2$, 252.1024), 236.1069 (15; $C_{16}H_{14}NO$, 236.1075), 208.1151 (21; $C_{15}H_{14}N$, 208.1126), 207.1039 (29; $C_{15}H_{13}N$, 207.1048), 193.0912 (15; $C_{14}H_{11}N$, 193.0891), 191.0764 (18; $C_{14}H_9N$, 191.0735), 180.0767 (11; $C_{13}H_{10}N$, 180.0813).

Anal. Calcd for $C_{17}H_{17}NO_2$ (267.31): C, 76.38; H, 6.41; N, 5.24. Found: C, 76.30; H, 6.59; N, 5.03.

Methyl 4-(2-Methylpropyl)-9*H*-carbazole-2-carboxylate (14c). By Method A. The ester **13c** (1.20 g, 4.2 mmol) and chloranil (2.06 g, 8.4 mmol) gave, after filtration of green-black needles, dilution of the filtrate with diethyl ether (50 mL), workup, and chromatography, first unchanged **13c** (0.15 g, 12%) and then **14c** as white needles (1.0 g, 85%): mp 181–182.5 °C; UV (95% C_2H_5OH) λ_{max} (log ϵ) 225 (4.31), 253 (4.81), 307 (4.48), 352 (3.73), 361 nm (3.73); IR (KBr) 3320 (s) (NH), 1700 (s) (C=O), 1625 (m) (aromatic C=C) cm^{-1}; NMR ($CDCl_3$ containing 10% $(CD_3)_2SO$ to enhance solubility) δ 1.03 (d, J = 6.5 Hz, 6 H, $CH(CH_3)_2$), broad multiplet obscured by a H_2O peak at δ 2.60 and $(CD_3)_2SO$ peaks at δ ~2.21 ($CH_2CH(CH_3)_2$), 3.15 (d, J = 7 Hz, 2 H, CH_2CH), 3.99 (s, 3 H, OCH_3), ~6.94–7.59 (broad multiplet with a major absorption centered at δ ~7.47, 3 H, 5-, 6-, and 7-H?), 7.66 (apparent s, 1 H, 1-H), ~7.86–8.37 (multiplet with apparent singlet at 8.08, 2 H, 8-H, 3-H), 10.20 (br s, ~1 H, NH); NMR [$(CD_3)_2CO$] δ 1.03 (d, J = 5.5 Hz, 6 H, $CH(CH_3)_2$), broad multiplet obscured by a H_2O (including NH?) peak at δ 2.97 and $(CD_3)_2CO$ peaks at δ 2.05 ($CH_2CH(CH_3)_2$), 3.22 (d, J = 7 Hz, 2 H, CH_2CH), 4.00 (s, 3 H, OCH_3), ~6.80–8.07 (br m, ~5 H, 5-, 6-, 7-, and 1-H?), ~8.07–8.50 (br m, 2 H, 8-H, and 3-H?); high-resolution MS (relative intensity ≥10; calcd) m/e 282.1457 (10; $^{12}C_{17}{}^{13}CH_{19}NO_2$, 282.1449, M + 1), 281.1425 (45; $C_{18}H_{19}NO_2$, 281.1415, M), 239.0899 (24; $^{12}C_{14}{}^{13}CH_{12}NO_2$, 239.0901; and $C_{15}H_{13}NO_2$, 239.0946, M – $CH_3CH{=}CH_2$, product of a McLafferty rearrangement), 238.0854 (100; $C_{15}H_{12}NO_2$, 238.0867, M – $CH(CH_3)_2$, 2-(methoxycarbonyl)-indolo[2,3]tropylium ion), 180.0806 (15; $C_{13}H_{10}N$, 180.0813, M – $CH_3CH{=}CH_2$ – $COOCH_3$, product of a McLafferty rearrangement), 179.0727 (10; $C_{13}H_9N$, 179.0735, M – $CH(CH_3)_2$ – $COOCH_3$).

Anal. Calcd for $C_{18}H_{19}NO_2$ (281.34): C, 76.84; H, 6.81; N, 4.98. Found: C, 76.67; H, 6.62; N, 4.77.

Methyl 2,3-Dihydro-1*H*,6*H*-cyclopenta[*c*]carbazole-4-carboxylate (14d). By Method B. The ester **13d** (0.7667 g, 2.84 mmol) in *o*-dichlorobenzene (20 mL) with 3% Pd–C (0.5983 g) was refluxed for 35 h and gave, after workup, chromatography, and elution with 7:3 (v/v) petroleum ether–benzene, somewhat impure **14d** as yellow needles (0.277 g, 37%): mp 240 °C dec; UV (95% C_2H_5OH) λ_{max} (log ϵ) 227 (sh) (4.18), 250 (4.60), 308 (4.34), 361 (3.56), 368 nm (3.59); IR (KBr) 3370 (s) (NH), 1695 (s), 1660 (m) (C=O), 1635 (m) (aromatic C=C) cm^{-1}; MS (relative intensity ≥10) m/e 266 (16, M + 1), 265 (90, M), 264 (12, M – H), 263 (47, M – 2H), 251 (11; $^{12}C_{15}{}^{13}CH_{12}NO_2$, M – CH_3; or $C_{16}H_{13}NO_2$, M – CH_2), 250 (62, M – CH_3), 234 (10, M – OCH_3), 232 (25, M – OCH_3 – 2H), 231 (22, M – OCH_3 – 3H), 207 (12, $^{12}C_{14}{}^{13}CH_{12}N$, M – $COOCH_3$), 206 (68, M – $COOCH_3$), 205 (73, M – $HCOOCH_3$), 204 (100, M – $HCOOCH_3$ – H), 203 (33, M – $HCOOCH_3$ – 2H), 191 (18, M – $COOCH_3$ – CH_3), 176 (11), 149 (13), 116.5 (10), 116 (11), 102.5 (23), 102 (46), 101.5 (14); high-resolution MS (relative intensity >10; calcd) m/e 266.1167 (27; $^{12}C_{16}{}^{13}CH_{15}NO_2$, 266.1136), 265.1102 (100; $C_{17}H_{15}NO_2$, 265.1103, M), 264.0997 (13; $C_{17}H_{14}NO_2$, 264.1024), 263.0919 (30; $C_{17}H_{13}NO_2$, 263.0946), 251.0931 (12; $^{12}C_{15}{}^{13}CH_{12}NO_2$, 251.0901; or $C_{16}H_{13}NO_2$, 251.0946), 250.0868 (71; $C_{16}H_{12}NO_2$, 250.0868), 234.0935 (19; $C_{16}H_{12}NO$, 234.0918), 232.0815 (18; $C_{16}H_{10}NO$, 232.0762), 231.0699 (18; $C_{16}H_9NO$, 231.0684), 207.1008 (15; $^{12}C_{14}{}^{13}CH_{12}N$, 207.1003), 207.0360 (22), 206.0935 (91; $C_{15}H_{12}N$, 206.0969), 205.0862 (86; $C_{15}H_{11}N$, 205.0891), 204.0806 (100; $C_{15}H_{10}N$, 204.0813), 203.0737 (28; $C_{15}H_9N$, 203.0735), 191.0713 (24; $C_{14}H_9N$, 191.0735), 117.0440 (14), 102.5456 (30), 102.0419 (33), 101.5373 (12).

Anal. Calcd for $C_{17}H_{15}NO_2$ (265.30): C, 76.96; H, 5.70; N, 5.28. Found: C, 74.95, 74.67; H, 5.98, 5.81; N, 4.32, 4.12.

A portion of the sample which remained (3 mg) was recrystallized from methanol (10 mL) three times, giving **14d** as white needles (0.1 mg, 1%): mp 252–253 °C; high-resolution MS (relative intensity >7; calcd) m/e 266.1077 (13; $^{12}C_{16}{}^{13}CH_{15}NO_2$, 266.1136, M + 1), 265.1105 (100; $C_{17}H_{15}NO_2$, 265.1103, M), 251.0867 (14; $^{12}C_{15}{}^{13}CH_{12}NO_2$, 251.0901), 250.0839 (60; $C_{16}H_{12}NO_2$, 250.0868, M – CH_3), 232.0757 (15; $C_{16}H_{10}NO$, 232.0762, M – OCH_3 – 2H), 207.1007 (12; $^{12}C_{14}{}^{13}CH_{12}N$, 207.1003; or $C_{15}H_{13}N$, 207.1048, M – $COOCH_3$ + H), 206.0960 (78; $C_{15}H_{12}N$, 206.0969, M – $COOCH_3$), 205.0893 (68; $C_{15}H_{11}N$, 205.0891, M – $HCOOCH_3$), 204.0806 (69; $C_{15}H_{10}N$, 204.0813, M – $HCOOCH_3$ – H), 203.0704 (14; $C_{15}H_9N$, 203.0735, M – $HCOOCH_3$ – 2H), 191.0743 (17; $C_{14}H_9N$, 191.0735, M – $COOCH_3$ – CH_3), 102.0405 (13; $C_{15}H_{10}N/2$, 102.0406, M – $COOCH_3$ – 2H/2).

Methyl 4-Methyl-3-phenyl-9*H*-carbazole-2-carboxylate (14e). By Method B. The ester **13e** (0.45 g, 1.41 mmol) in *o*-dichlorobenzene (20 mL) with 10% Pd–C (92 mg) was refluxed for 20 h. After workup, the orange-brown solid was adsorbed on silica gel (1.4 g) with dichloromethane and chromatographed on a column of silica gel (8 g) under petroleum ether (Skellysolve B, bp 60–70 °C). Elution with 18:1 (v/v) petroleum ether–ethyl acetate removed first a trace of *o*-dichlorobenzene (20 mg) and then an orange solid (0.25 g, 56%), mp ~130 °C. Three crystallizations from acetone with a little methanol gave **14e** as cream-colored needles (7.0 mg, 2%): mp 320 °C, chars; MS (relative intensity ≥10) m/e 316 (24, M + 1), 315 (100, M), 284 (21, M – OCH_3), 269 (12, M – OCH_3 – CH_3), 256 (10, M – $COOCH_3$), 255 (12, M – $HCOOCH_3$), 254 (10, M – $HCOOCH_3$ – H), 113 (12); high-resolution MS (relative intensity; calcd) 316.1296 (11; $^{12}C_{20}{}^{13}CH_{17}NO_2$, 316.1292), 315.1258 (100; $C_{21}H_{17}NO_2$, 315.1259, M), 284.1094 (36; $C_{20}H_{14}NO$, 284.1075), 256.1176 (6;

$C_{19}H_{14}N$, 256.1126), 255.1054 (22; $C_{19}H_{13}N$, 255.1048), 254.1008 (19; $C_{19}H_{12}N$, 254.0970).

Registry No. 10a, 78-93-3; **10b**, 96-22-0; **10c**, 108-10-1; **10d**, 120-92-3; **10e**, 103-79-7; **10f**, 590-50-1; **11**, 110-16-7; **12a**, 71700-53-3; **12b**, 71700-54-4; **12c**, 71700-55-5; **12d**, 71700-56-6; **12e**, 71700-57-7; **12f**, 71700-58-8; **13a**, 71700-59-9; **13b**, 71700-60-2; **13c**, 71700-61-3; **13d**, 71700-62-4; **13d'**, 71700-63-5; **13e**, 71700-64-6; **14a**, 71700-65-7; **14b**, 71700-66-8; **14c**, 71700-67-9; **14d**, 71700-68-0; **14e**, 71700-69-1; **21**, 71700-70-4; indole, 120-72-9; 3-methyl-2-butanone, 563-80-4.

Supplementary Material Available: Detailed mass spectral fragmentations of the compounds (14 pages). Ordering information is given on any current masthead page.

Carbenoid Chemistry. Reaction of Pyrrole Derivatives with Ethyl Diazoacetate[1]

Bruce E. Maryanoff

Chemical Research Department, McNeil Laboratories, Fort Washington, Pennsylvania 19034

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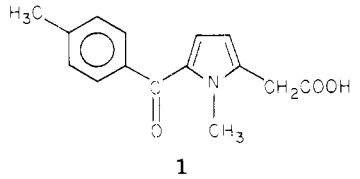
Reaction of *N*-methylpyrrole (NMP) with ethyl diazoacetate (EDA) produced monoacetate adducts **2** and **4**, with a wide range of copper promoting agents. Minor amounts of diacetate adducts (**20a–c**) were also formed (about one-tenth the amount of monoacetates). The relative amounts of **2** and **4** varied according to promoting agent (**2**/**4** ratio ranged from 16/1 to 3/2). The regiochemistry of the reactions served to characterize the relative reactivity of the metal–carbenoid reagents. The least discriminant agents were $Cu(OTf)_2$ and $Cu(BF_4)_2$, and the most discriminant ones (for α substitution) were certain copper(II) 1,3-diketone, salicylaldehyde, and salicylaldimine chelates (**5a**, **5c**, **6c**, **6g**, and **6h**). Certain copper(II) chelates of these classes also furnished optimal yields of **2** (**5g**, **6b**, **6d**, **6e**, **6g–i**, and **8**). Other pyrrolic compounds were also studied with a limited number of promoting agents [generally $Cu(acac)_2$, copper bronze, and/or $Cu(OTf)_2$]. Pyrrole gave 2- and 3-acetates (**13** and **14**), with no N-H insertion product **15**. *N*-Isopropylpyrrole gave 2- and 3-acetates, but *N*-*tert*-butylpyrrole gave only 3-acetate. With a specific promoting agent, the N-substituted pyrroles showed an increasing proportion of β substitution with increasing steric bulk of the N group (*tert*-butyl > isopropyl > methyl > hydrogen). Reaction of 1,2- and 1,3-dimethylpyrroles with EDA afforded mixtures of three isomeric monoacetates; the *C*-methyl substituent exhibited an ortho-directing influence. In the reaction of NMP with EDA, employing certain copper(I) and copper(II) halides, a carbethoxycarbene trimer, triethyl (*E*)-aconitate, was identified; this represents a "propene" trimerization pathway for $:CHCO_2C_2H_5$ as opposed to the more common "cyclopropane" pathway. On the basis of the variation of α/β isomer ratio with promoting agent and the substituent effects, the mechanism of the reaction of *N*-H and *N*-alkyl pyrroles with EDA is depicted as an electrophilic substitution (rather than insertion) process leading directly to acetate adducts (i.e., not involving distinct homopyrrole intermediates).

In connection with a search for new synthetic processes leading efficiently to tolmetin (**1**),[2] an important nonsteroidal antiinflammatory agent for the treatment of arthritis, we initiated a study of the reaction of *N*-methylpyrrole (NMP) with ethyl diazoacetate (EDA). This reaction, with copper metal as a promoting agent,[3] had been reported to afford **2** as the sole monoadduct.[4] However,



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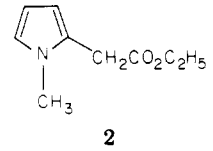

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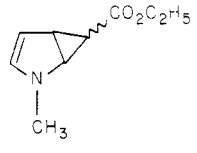

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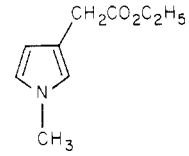

4

a significant amount of another isomer, first suspected to be a product of double-bond insertion (viz., **3**) but later identified as acetic ester **4**, forms as well.[4] This outcome underscores a chemical dichotomy that exists in the reaction of π-excessive heterocycles with carbene entities. For instance, furan and thiophene undergo double-bond insertion to produce cyclopropane species,[5] whereas pyrrole undergoes C–H insertion[4-7] to give products formally derived by electrophilic substitution.

We have examined the reactions of simple pyrrole derivatives with EDA in the presence of transition metal promoting agents. Of particular interest in this work is the effect of metal agent and pyrrole substituents on the regiochemistry of the substitution reactions. In the course of this study, we hoped to find a means of optimizing the **2**/**4** ratio and total yield of **2** in the reaction of NMP and EDA.

Results

***N*-Methylpyrrole.** The reaction of NMP and EDA with the assistance of copper bronze or copper powder, as described by several research groups, produced acetic esters **2** and **4** in ratios (**2**/**4**) ranging from 84/16 to 79/21.[4] Promotion with different transition-metal agents afforded

(1) Presented in part at the 172nd National Meeting of the American Chemical Society, San Francisco, California, Aug 1976.

(2) J. R. Carson, D. N. McKinstry, and S. Wong, *J. Med. Chem.*, 14, 646 (1971). Tolmetin sodium dihydrate is sold by McNeil Laboratories under the registered tradename Tolectin.

(3) The term "promoting agent" is used to mean a material which effectuates or facilitates a chemical reaction even when employed in a much less than stoichiometric amount. The agent functions as a catalyst but may be chemically altered in the course of the reaction, whereas a true catalyst remains unchanged by the reaction that it induces.

(4) B. E. Maryanoff, *J. Heterocycl. Chem.*, 14, 177 (1977); U.S. Patent 4 136 097 (1979).

(5) V. Dave and E. W. Warnhoff, *Org. React.*, 18, 217 (1970).

(6) E. g., A. Gossauer, "Die Chemie der Pyrrole", Springer-Verlag, West Berlin, 1974, pp 126–8.

(7) Double bond insertion was reported for *N*-carbalkoxypyrrole, but this substrate is electronically perturbed, being more like a diene than a pyrrole (see Discussion).[8]

(8) (a) S. R. Tanny, J. Grossman, and F. W. Fowler, *J. Am. Chem. Soc.*, 94, 6495 (1972); (b) J. F. Biellman and M. P. Goeldner, *Tetrahedron*, 27, 2957 (1971).

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