2-Addition of Pyrroles to Dimethyl Acetylenedicarboxylate: Michael-Type Adducts and Diels-Alder Products[1]

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Pyrroles 1 having an open 2-position react with dimethyl acetylenedicarboxylate (DMAD) in the presence of a source of active hydrogen, usually provided in the present cases by their own NH groups (if present) or by sufficient acetic acid, to give 1:1 Michael-type adducts at the 2-position (dimethyl 2-pyrrolyl-2-butenedioates), usually as both the *Z* (**3**) and *E* (**4**) isomers. Analogy with the data obtained permits assignment of stereochemistry to several other 1:1 adducts previously reported, including **3g** and **4g** from 2,3-dimethylpyrrole (**1g**) and **3h** from 2,3,4-trimethylpyrrole (**1h**). On the basis of NMR and mass spectral data, the 2:1 adduct of **1f** and DMAD (a coproduct of **3f** and **4f**) is reassigned the structure dimethyl 2,2-bis(3,5-dimethyl-2-pyrrolyl)butanedioate (**9**). Formation of **3** and **4** is usually competitive with Diels-Alder reactions in which the pyrrole acts as a diene. The Diels-Alder reaction tends to be relatively favored in the absence of weak acids such as acetic acid and at higher temperatures than in refluxing ether. The initial 1:1 Diels-Alder adducts (**5**) are unstable and were not isolated. They tend to react by one of four pathways: (1) they revert to **3** and **4**; (2) they react further with DMAD, giving 1:2 adducts of type **6** (tetramethyl 3a,7a-dihydroindole-2,3,3a,4-tetracarboxylates); (3) at higher temperatures (63-160 °C) they undergo retro-Diels-Alder cleavage, giving the corresponding dimethyl N-substituted pyrrole-3,4-dicarboxylates (**7**); (4) they eliminate the bridging nitrogen to give dimethyl 4-substituted phthalates (**14**) or to give (via **5** and **7** and a further Diels-Alder reaction of **7** with DMAD) tetramethyl benzene-1,2,4,5-tetracarboxylate (**24**) from **1p** and **1q**. The 1:2 adducts of type **6** undergo further Diels-Alder reaction at their diene system with DMAD to give as coproducts trimethyl 5-substituted benzene-1,2,3-tricarboxylates (**16**) and trimethyl 1-substituted pyrrole-2,3,4-tricarboxylates (**17**, similar to **7**). In a few instances the 2-vinylpyrroles **3** and/or **4** were observed to act as dienes in a Diels-Alder synthesis of indoles.

Pyrroles **1** sometimes behave as dienes in Diels-Alder reactions ([4 + 2] cycloadditions leading to structures of type **5**) with reactive dienophiles such as dimethyl acetylenedicarboxylate (DMAD) or perfluorobutyne, which, in turn, often lead to further products such as **6** or **7**.[2a] Pyrroles also sometimes behave as nucleophiles in Michael-type additions such as to DMAD or acetylenedicarboxylic acid (ADA).[2] It has been suggested that the cycloaddition is a nonconcerted process in which electrophilic attack by a dienophile occurs first at an α-carbon of the pyrrole, forming a Michael-type adduct as a zwitterion (**2**), which, in the absence of a trapping proton such as from an NH group, cyclizes to a 7-azanorbornadiene system (**5**).[2a] 2-Methylpyrrole (**1c**) with DMAD in benzene and petroleum ether gave two 1:1 Michael-type adducts, which gave the same dihydro derivative on hydrogenation,[3] but it was not determined which was the maleate (**3c**) and which was the fumarate (**4c**) stereoisomer. Similarly, 2,3-dimethylpyrrole (**1g**) with DMAD in benzene-petroleum ether also gave two 1:1 Michael-type adducts (**3g**, **4g**) which gave the same dihydro derivative on hydrogenation.[3b] 2,3,4-Trimethylpyrrole (**1h**), however, is reported to give with DMAD in benzene-petroleum ether only a single 1:1 Michael-type adduct.[3b] 1,2-Dimethylpyrrole (**1d**) with DMAD in ether was also reported to give a single 1:1 adduct for which the fumarate structure **4d** was suggested.[4] Methyl 1-pyrrolecarboxylate (**1t**) gave both maleate (**3t**) and fumarate (**4t**) stereoisomers (and **5t**) in the presence of aluminum chloride; the kinetically favored product **3t** was gradually isomerized to the thermodynamically favored product **4t**.[5] Pyrrole itself (**1a**) gave both stereoisomers **3a** and **4a** (total 67%) and also a little dimethyl (*E*)-1-pyrrolyl-2-butenedioate (6%) when stirred with DMAD at room temperature for 4 days, but when refluxed with DMAD in ether, it slowly gave a modest yield (6-10%) of a 1:2 adduct (**6a**).[6] In contrast, 1-methylpyrrole (**1b**) and 1-benzylpyrrole (**1l**) with DMAD gave as primary products only the 1:2 adducts **6b** (70[7]-80%[6]) and **6l** (36%[7]), the structures of which are derivable from an initially formed [4 + 2] cycloadduct of type **5** and further addition of a second molecule of DMAD.[2a,7]

This paper reports that 1-substituted pyrroles give 1:1 Michael-type adducts with DMAD in the presence of a proton donor such as acetic acid and establishes the structures of the stereoisomeric products **3** and **4**. Analytical data and mass, NMR, UV, and IR spectral data, which establish the structure and stereochemistry of the 29 Michael-type adducts prepared, including 15 *Z* (**3**) and 14 *E* (**4**) stereoisomers, are reported in detail in another paper.[1b]

Refluxing a solution of **1b**, DMAD, and glacial acetic acid in a 1:2:1.4 molar ratio in ether for 48 h gave only the 1:2 adduct **6b** in 57% yield, whereas without acid the yields were as high as 70[7]-83%.[6] When the molar ratio of acetic acid was increased tenfold (to 14.2), no **6b** but only the 1:1 Michael-type adducts **3b** and **4b** were isolated (total 52%) in a 2:1 ratio by NMR. By similar procedures, a series of 23 stereoisomeric Michael-type adducts **3** and **4** were obtained from 1-substituted pyrroles, as shown in Table I. Sterically hindered 1-(2,6-dimethylphenyl)pyrrole (**1q**)

(1) (a) From the Ph.D. thesis of Chang Kiu Lee, University of Minnesota, Aug 1976; *Diss. Abstr. Int. B* **1977**, *38*, 1210-1211. We gratefully acknowledge summer fellowships to C.K.L. from the 3M Co., the Eastman Kodak Co. (1973), the General Mills Foundation (1974), and the Camille and Henry Dreyfus Foundation, Inc. (1975), and partial support of this research, including a summer fellowship to C.K.L. (1973), from Hoffman-LaRoche, Inc. (b) For a companion paper on the Michael-type adducts, containing detailed analytical and spectral data, see: Noland, W. E.; Lee, C. K. *J. Chem. Eng. Data*, in press.

(2) See the review by: (a) Jones, R. A.; Bean, G. P. "The Chemistry of Pyrroles"; Academic Press: New York, 1977; pp 256-264. (b) *Ibid.* pp 146-147.

(3) (a) Diels, O.; Alder, K.; Winter, D. *Justus Liebigs Ann. Chem.* **1931**, *486*, 211-225. (b) Diels, O.; Alder, K.; Winckler, H.; Petersen, E. *Ibid.* **1932**, *498*, 1-15.

(4) Acheson, R. M.; Vernon, J. M. *J. Chem. Soc.* **1963**, 1008-1011.

(5) Bansal, R. C.; McCulloch, A. W.; McInnes, A. G. *Can. J. Chem.* **1969**, *47*, 2391-2394.

(6) Lee, C. K.; Hahn, C. S.; Noland, W. E. *J. Org. Chem.* **1978**, *43*, 3727-3729.

(7) Acheson, R. M.; Vernon, J. M. *J. Chem. Soc.* **1962**, 1148-1157.

0022-3263/80/1945-4573$01.00/0

Table I. 2-Addition of Pyrroles (1) to DMAD. 1:1 Michael-Type Adducts: Dimethyl (*Z*)- and (*E*)-2-Pyrrolyl-2-butenedioates (3 and 4) and Other Reaction Products (If Any) Under Representative Conditions[r]

	substituents		products		
pyrrole	R^1	$R^2 = R^3 = H$ unless specified	neat at ~25 °C (N) or refluxing Et_2O (E)[s]	refluxing Et_2O–AcOH[s]	refluxing toluene (T) or xylene (X)[s]
1a	H	H	3a, 4a (N),[a,b] 6a (E)[b]	ne	14b, 16b, 21,[c] tar (X)
b	Me	H	6b (N)[d,e] (E)[b]	3b, 4b	6b, 16b, 17b (T, X)
c	H	R^2 = Me	3c, 4c,[f,g] 3c, 4c (E)	ne	ne
d	Me	R^2 = Me	3d, 4d (N),[h] 3d, 4d (E)	ne	ne
e	Me	R^3 = Me	3e, 6e, 7b, 14e, 16e, 17b (N)	ne	ne
f	H	$R^2 = R^3$ = Me	3f, 4f, 9,[f,i] 3f, 4f (E)[j]	ne	ne
g	H	$R^2 = R^4$ = Me	3g, 4g[k,l]	ne	ne
h	H	$R^2 = R^3 = R^4$ = Me	3h[k,l]	ne	ne
i	*n*-Bu	H	6i (N, E)	3i, 4i	3i, 4i, 16b, 17i (T)
j	*sec*-Bu	H	NR	3j, 4j	3j, 4j (T)
k	*t*-Bu	H	NR	3k, 4k	3k, 4k, 7k (T), 7k (X)
l	CH_2Ph	H	6l (N[e], E)	3l, 4l	6l (T)
m	Ph	H	NR	3m, 4m	NR (T), 7m (X)
n	4-MeOPh	H	NR	3n, 4n	NR (T), 7n (X)
o	4-BrPh	H	NR	3o, 4o	NR (T), 7o (X)
p	2-MePh	H	NR	3p, 4p, 22p	NR (T), 24 (X)
q	2,6-Me_2Ph	H	NR	3q, 22q	NR (T), 24 (X)
r	4-NO_2Ph	H	NR	NR	NR (T), 7r (X)
s	COMe	H	ne	4s[m]	5s[n,o]
t	COOMe	H	ne	3t, 4t, 5t[m,p]	5t[o,q]

[a] Plus dimethyl (*E*)-1-pyrrolyl-2-butenedioate. [b] Reference 6. [c] At 63 °C, neat. [d] On a tenfold larger scale (0.25 mol of 1b) a violent reaction occurred and gave, besides 6b, a variety of other products: 16b, 17b, tetramethyl benzene-1,2,3,4-tetracarboxylate, and tetramethyl 1-methylindole-2,3,6,7-tetracarboxylate.[7] [e] Reference 7. [f] In benzene at 25 °C. [g] Reference 3 and present work. [h] Reference 4 and present work. [i] Reference 9 and present work. [j] At 25 °C. [k] In benzene–petroleum ether at 25 °C. [l] Reference 3b. [m] Product was obtained with $AlCl_3$ in CH_2Cl_2 at 40 °C and not in Et_2O–AcOH. [n] At 125 °C, neat. [o] Reference 8. [p] Reference 5. [q] At 142 °C, neat. [r] Usually for 2-4 days. [s] NR = no reaction; ne = not examined.

gave only the *Z* (maleate) isomer **3q**, while electronegatively substituted 1-(4-nitrophenyl)pyrrole (**1r**) and 1-acetylpyrrole (**1s**) gave no adducts under these conditions. The dissymmetric NH-containing pyrroles **1c** and **1f** gave 1:1 Michael-type adducts (7% **3c** and 6% **4c**, 20% **3f** and 34% **4f**) without the use of acid. The 1-substituted *sec*- (**1j**) and *tert*- (**1k**) butylpyrroles also gave 1:1 Michael-type adducts without acid at higher temperatures in refluxing toluene (9% **3j** and 2% **4j**, 1% **3k** and 19% **4k**, together with a limited amount of **7k**, 2%, as a Diels–Alder-type coproduct from **1k**). Without acid but in refluxing xylene or occasionally at lower temperature in refluxing toluene (**1s**) most of the 1-arylpyrroles (**1m–r**, except **1p** and **1q**) and 1-acetylpyrrole (**1s**) with DMAD gave no Michael adducts but instead the corresponding dimethyl 1-substituted pyrrole-3,4-dicarboxylates (**7**). The formation of **7** can be rationalized through formation (probably reversibly) of the 1:1 Diels–Alder adduct **5** followed by a retro-Diels–Alder cleavage to give acetylene and **7**.

Prinzbach and co-workers[8] isolated 1:1 Diels–Alder adducts of type **5** from 1-aryl (**1m,n,o,r**) and 1-acyl (**1s,t**) pyrroles by heating with DMAD at 40–90 °C for 6–24 h. With these substituents, the 1:1 Diels–Alder adducts **5** apparently did not react further with DMAD to give 1:2 adducts (of type **6**) under any conditions tried. Among the pyrroles which have been examined, only pyrrole itself (**1a**[6]) and the primary 1-alkylpyrroles **1b**,[6,7] **1i**, and **1l**[7] gave 1:2 adducts of type **6**, and in these cases no intermediates of type **5** were isolated.

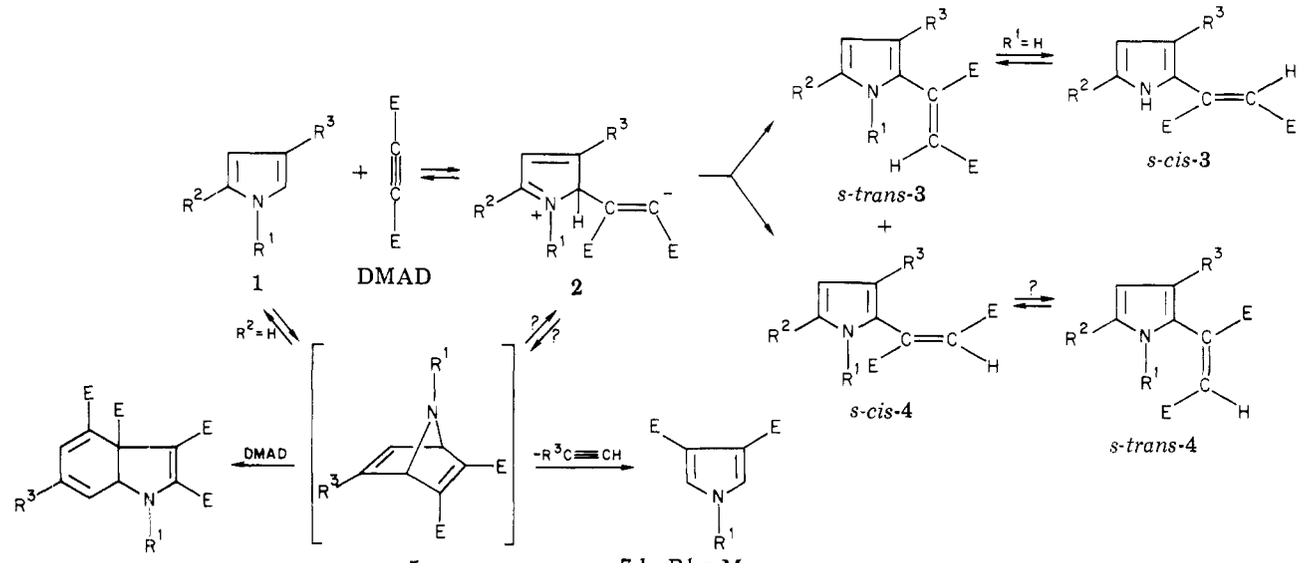
The products formed from pyrroles **1** and DMAD under various typical reaction conditions are summarized in Table I. Formation of the various products can be rationalized (Scheme I) through reversible formation of the 1:1 Diels–Alder adduct **5** as the primary pathway, with 1:1 Michael-type addition to give **3** and **4** through a zwitterionic intermediate (**2**, which may also be an intermediate to **5**) as a secondary pathway. The adduct **5** can then react with a second molecule of DMAD to give **6** when the N substituent is electron-releasing and not too sterically hindering, as with primary alkyl groups such as methyl (**1b**), *n*-butyl (**1i**), and benzyl (**1l**). The steric limits of the reaction are reached, however, with the secondary (**1j**) and tertiary (**1k**) alkyl groups, which do not form **6**. Electron-withdrawing N substituents such as acetyl (**1s**), methoxycarbonyl (**1t**), and aryl (**1m,o,r**) decrease the nucleophilicity of the nitrogen of **5** and, thus, prevent the formation of **6**. Protonation of the nitrogen of **5** in acidic medium should have a similar effect and, in addition, protons would tend to capture the zwitterionic form (**2**), resulting in the formation of the 1:1 Michael adducts (**3** and **4**), as is observed in increasing concentrations of acetic acid. The fact that aluminum chloride also catalyzes and causes irreversible formation of the 1:1 Diels–Alder adduct **5t** (where R^1 = COOMe; along with formation of **3t** and **4t**)[5] may be attributed to the facts that adducts **5** do not require a proton transfer in their formation, and in adduct **5t** the urethane group should be immediately capable of forming a strong, stabilizing complex with aluminum chloride.

Structural Assignments to Previously Reported Michael-Type Adducts

The structural assignments which have been made to the members of the *Z* and *E* series[1b] now make it possible to assign definitive stereochemistry to the 1:1 adducts of 2-methylpyrrole (**1c**) and DMAD first reported by Diels, Alder, and co-workers.[3] Thus, the adduct of melting point 111 °C is the *Z* isomer (**3c**) and that of melting point 52 °C is the *E* isomer (**4c**). The crystalline 1:1 adduct of melting point 92 °C from the reaction of 1,2-dimethylpyrrole (**1d**) with DMAD is the Z isomer (**3d**) rather than the *E* isomer as had been suggested,[4] and the *E* isomer (**4d**) is an oil, thus probably accounting for the fact that it was

(8) Kitzing, R.; Fuchs, R.; Joyeux, M.; Prinzbach, H. *Helv. Chim. Acta* **1968**, *51*, 888–895.

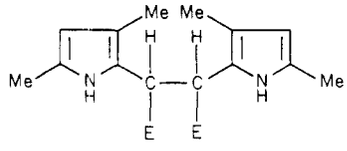
Scheme I[a]



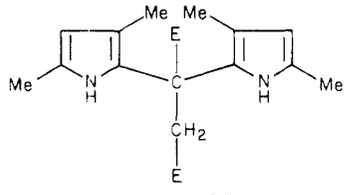
[a] E = COOME.

not isolated previously. If the analogy holds[1b] that the *Z* isomers always melt higher than the *E* isomers, then the two isomers reported from 2,3-dimethylpyrrole (**1g**)[3b] can be assigned accordingly; thus, the adduct of melting point 132 °C would be the *Z* isomer (**3g**) and that of melting point 98 °C would be the *E* isomer (**4g**). For the same reason, because of its high melting point (137–138 °C) and expected lower steric hindrance, the single adduct[3b] from 2,3,4-trimethylpyrrole (**1h**) is assumed to be the *Z* isomer (**3h**).

The reaction of 2,4-dimethylpyrrole (**1f**) with DMAD gave besides the 1:1 adducts **3f** and **4f** also a 2:1 adduct [mp 156.5–157 °C (lit.[9] mp 165 °C)] in 6% yield, for which the symmetrical structure 8 had been proposed.[9] Structure



8, E = COOMe



9, E = COOMe

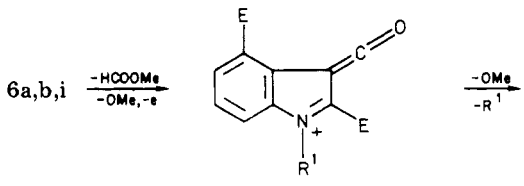
8 would be expected to be derived from further Michael addition to an intermediate 1:1 adduct such as **3f** or **4f**. These adducts, however, should have polarity toward Michael addition opposite to that which would give structure 8 but which should give the unsymmetrical structure **9**. Structure 8 could exist in either a meso or a *dl* form or in a mixture of the two, as it has the tartaric acid type of configuration. Structure **9** would be achiral. The NMR spectrum (in $CDCl_3$) of the 2:1 adduct suggests that the two pyrrole nuclei are equivalent, as singlets are observed for the 3- (δ 1.80) and 5- (δ 2.15) methyl groups, although the 4-proton (δ 5.60) appears as an unresolved multiplet. The two ester methyl groups are nonequivalent, however, and appear as two singlets at δ 3.55 and 3.73. The two side-chain protons appear as a singlet at δ 3.47. The mass spectrum of the 2:1 adduct has as its base peak the fragment M – $COOCH_3$, which could be consistent with either structure 8 or **9**, but it also contains significant peaks at M – CH_2COOCH_3 (relative intensity 22%) and M – $COOCH_3$ – CH_3COOCH_3 (12%). These are more easily rationalized in terms of structure **9** than structure 8 since the mass spectral data[1b] for **3** and **4** show that methyl groups are not at all easily lost from the pyrrole nucleus. For these reasons, the 2:1 adduct of melting point 156.5–157 °C is reassigned structure **9**.

Diels–Alder Adducts. Further Discussion

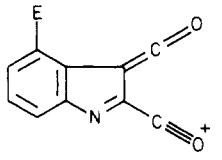
The two new 1:2 adducts from 1,3-dimethylpyrrole (**6e**; 3%, mp 117–120 °C), 1-butylpyrrole (**6i**; 54%, mp 119–121 °C) and DMAD are believed to be similar in structure to those previously reported from pyrrole (**6a**; 6–10%, mp 162–165 °C[6]), 1-methylpyrrole (**6b**; 70[7]–80%[6], mp 145–147 °C[7]), and 1-benzylpyrrole (**6l**; 36%, mp 135 °C[7]). All, except **6e**, have the following similar UV spectral characteristics [CH_3OH; λ_{max} nm (log ϵ)]: **6a**, 272 (4.10), 300 (diffuse sh, 3.76)[6]; **6b**, 275 (4.20), 300 (sh, 3.85)[7]; **6e**, 251 (4.11), 290 (3.05), 311 (sh, 2.56); **6i**, 277 (4.26), 300 (sh, 3.94); **6l**, 277 (4.26), 300 (sh, 3.95).[7] The mass spectra of **6a,b,i,l** are also similar, since all four have their base peak at the fragment M – $HCOOCH_3$ – OCH_3. This probably corresponds to loss of the angular elements of methyl formate (permitting aromatization of the indole nucleus) and a methoxyl group from the conjugated 3-ester group, giving the ion **10** (Scheme II). With **6a** and **6i** the second most important fragment, at *m/e* 228, corresponding to M – $HCOOCH_3$ – $2OCH_3$ – R^1, appears to be a derivative in-

(9) Diels, O.; Alder, K.; Winckler, H. *Justus Liebigs Ann. Chem.* **1931**, *490*, 267–276.

Scheme II[a]



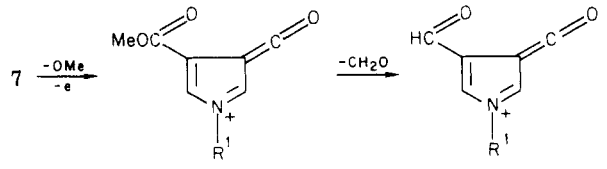
10a, R^1 = H; *m/e* 260
b, R^1 = Me; *m/e* 274
i, R^1 = *n*-Bu; *m/e* 316



11, *m/e* 228

[a] E = COOMe.

Scheme III



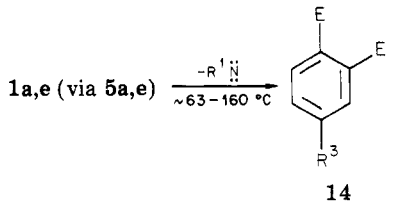
12 13

volving loss from the base peak of a second methoxyl group and of the *N*-R^1 group, for which structure **11** seems to be a reasonable interpretation (R^1 = H, **6a** → **10a** → **11**, 44%[6]; R^1 = *n*-Bu, **6i** → **10a** → **11**, 16%). With **6b**, where loss of the *N*-methyl group would be difficult, this fragmentation was not observed, and the second most important peak, at *m/e* 216 (17%), corresponds to M − $2COOCH_3$ − OCH_3. With **6l**, facile loss of the benzyl group as the tropylium ion (C_7H_7, *m/e* 91) gave a second base peak of equal intensity to the first ($C_{20}H_{16}NO_5$, *m/e* 350) which far overshadowed all other fragmentations, leaving the molecular ion (8%, *m/e* 441) as the third most important peak.

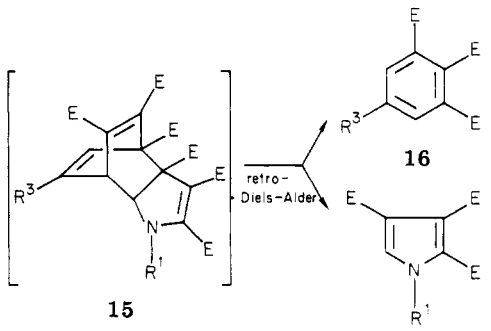
Adduct **6e** appears to be somewhat anomalous, since its major UV band (at 251 nm) occurs 24 nm lower in wavelength than the average of the other adducts and since its mass spectrum is quite different. In **6e** the base peak at *m/e* 166 corresponds to the fragment $C_9H_{12}NO_2$ [CH_3OC-$OC_5H_3(CH_3)N(CH_3)$], involving a more deep-seated fragmentation. The second most important peak, at *m/e* 136 (43%), appears to be a derivative of the base peak, involving further loss of CH_2O, which would correspond to $C_8H_{10}NO[OCHC_5H_3(CH_3)NCH_3]$. The third most important peak, at *m/e* 197 (42%), corresponds to M − $2HCOOCH_3$ − $2OCH_3$. The fragmentation may take a different pathway at least in part because the *N*-methyl group is much more difficult to lose (to give **11**) than the *N*-H proton of **6a** or the *N*-butyl group of **6i**. The IR and NMR spectra of **6e** and **6i**, which are summarized in the experimental section, appear consistent with the structures assigned.

In their mass spectra, all of the compounds **7** (Scheme III) have base peaks at M − OCH_3 (**12**) except that there was a concomitant facile loss with the *N*-*tert*-butyl derivative (**7k**, M − OCH_3 − C_4H_8) of isobutylene and with the *N*-acetyl derivative (**7s**, M − OCH_3 − CH_2CO) of ketene. Similarly, with the 1-(4-nitrophenyl) derivative **7r**, concomitant loss of the nitro group gave the second most important peak, M − OCH_3 − NO_2. Other important peaks with **7**, usually competing for second or third place in importance, with exceptions of the type noted above, are

Scheme IV[a]

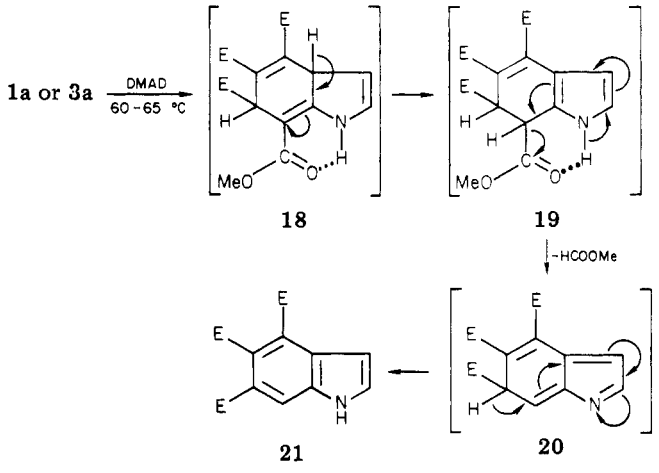


14



15 16

17a, R^1 = H (not isolated)
b, R^1 = Me
i, R^1 = *n*-Bu



18 19 20 21

[a] For **14b**-**16b**, R^3 = H; for **14e**-**16e**, R = Me.

the molecular ion (M) and M − OCH_3 − CH_2O (**13**).

The vigorously exothermic (temperature rose to 160 °C) neat reaction of 1,3-dimethylpyrrole (**1e**) with DMAD in a 1:2 molar ratio gave products similar in variety to those from 1-methylpyrrole (**1b**)[7], including **3e** (10%), **6e** (3%), and **7b** (3%). The other products isolated and characterized (see Scheme IV) were dimethyl 4-methylphthalate (**14e**, 22%), trimethyl 5-methylbenzene-1,2,3-tricarboxylate (**16e**, 25%), and trimethyl 1-methylpyrrole-2,3,4-tricarboxylate (**17b**, 12%). Ester **14e** could be formed by loss of methylnitrene (CH_3N) from intermediate **5e**, a reaction which appears to be competitive with the retro-Diels–Alder cleavage of **5e** to form **7b** and propyne. It is interesting that neither **7b** nor its anticipated competitive product **14b** has been isolated from the corresponding reaction of 1-methylpyrrole (**1b**) with DMAD under any conditions tried.[7] This may relate to the greater steric repulsion of the 5- and 7-methyl groups in **5e** relative to **5b** and to the greater stability of the assumed leaving group, propyne (from **5e**) relative to acetylene (from **5b**). The esters **16e** and **17b** can be formulated as being derived by a Diels–Alder reaction of DMAD across the diene system of **6e** to give intermediate adduct **15**, followed by a retro-Diels–Alder cleavage which produces **16e** as the diene component

(now aromatic) and **17b** as the retro dienophile. The corresponding products **16b** (0.5%) and **17b** (5%) have been isolated from the analogous exothermic reaction of 1-methylpyrrole (**1b**) with DMAD.[7] Similarly, in refluxing toluene another 1-alkylpyrrole, 1-butylpyrrole (**1i**), and DMAD also gave the two analogous Diels–Alder-type coproducts **16b** (4%) and **17i** (1%), besides **3i** (10%) and **4i** (12%). Reaction of pyrrole (**1a**) with DMAD at 63 °C gave, besides the N-alkylated Michael-type adduct, dimethyl (*E*)-1-pyrrolyl-2-butenedioate[6] (5%), a nitrene elimination product (**14b**, 4%), a retro-Diels–Alder product (**16b**, 3%; although the expected coproduct **17a** was not isolated), and trimethyl indole-4,5,6-tricarboxylate (**21**, 1%). The latter appears to be derived from a Diels–Alder reaction of the intermediate 2-vinylpyrrole [**3a**[6] (or **4a**[6])] with DMAD, followed by selective elimination of the 7-methoxycarbonyl group as methyl formate (possibly via intermediates **18** → **19** → **20**, Scheme V). Permissive evidence for the intermediacy of **3a** is provided by the fact that the reaction of **3a** with DMAD at 60–65 °C gave the same indole (**21**, 16%).

Unlike the other N-substituted pyrroles, the 1-(2-methylphenyl)- (**1p**) and 1-(2,6-dimethylphenyl)- (**1q**) pyrroles gave with acetic acid in refluxing ether (besides **3p**, **4p**, and **3q**) 1:2 adducts (**22p**, 8%, mp 143–144 °C, a preparation which has proved difficult to repeat;[10] **22q**, 7%, mp 155–157 °C) which appear to be different from type **6**. The spectral evidence in support of structures **22p** and **22q**, together with a modification of the procedure which has substantially increased the yield of **22q**, will be reported elsewhere.[10] Formation of compounds of type **22** provides an example of the Diels–Alder vinylpyrrole synthesis of dihydroindoles originally proposed (**22**, where the N substituent is Me) by Diels, Alder, and Winckler[9] for what is now known[7] to be **6b**, which was not realized in the case they suggested but has now been realized in others.[1a] At higher temperature in refluxing xylene with DMAD, **1p** and **1q**, unlike the other *N*-arylpyrroles, did not stop at products of type **7**, which were not isolated. Instead, the intermediates of type **7**, probably because of the destabilizing effect of steric inhibition of their pyrrole resonance, apparently underwent further Diels–Alder addition of DMAD to give intermediate adducts of type **23** which then eliminated the sterically hindering nitrogen bridge group as a nitrene to give the tetramethyl benzene-1,2,4,5-tetracarboxylate product (**24**; 4% from **1p**, 37% from **1q**). This process of nitrene elimination would be analogous to the formation of the products **14**.

Experimental Section

Melting points were determined on a calibrated Thomas-Hoover capillary melting point apparatus. Electron-impact mass spectra were determined on an AEI MS-30 spectrometer at 70 eV and 200 °C by Dr. Roger A. Upham (to whom we are indebted for helpful discussions), Edmund A. Larka, and Philip Price, except for **7s**, which was determined on a Finnigan Model 3300 mass spectrometer. Nuclear magnetic resonance (NMR) spectra were determined on a Varian Associates T-60 or A-60 60-MHz spectrometer. Ultraviolet (UV) spectra were determined on a Cary Model 11 recording spectrometer. Infrared (IR) spectra were determined on a Beckman IR-18A or on a Perkin-Elmer Model 257 recording spectrophotometer. Elemental microanalyses were performed by M-H-W Laboratories, except for the microanalyses of **7s** which were performed by the Institute of Physical and Chemical Research, Wako-shi, Saitama-ken, Japan. Column chromatography was conducted by taking the solution or material to be chromatographed, mixing it with the adsorbent to be used, allowing any volatile solvents present, such as diethyl ether or benzene, to evaporate at room temperature in a stream of nitrogen, and then drying it gently, as needed, on a hot plate at <60 °C to produce a powder. The powder was poured onto the top of a column of specified size packed with silica gel (or alumina; Woelm, Eschwege, Germany) for dry column chromatography and eluted with the solvents specified. The eluates were evaporated by using a rotating evaporator under aspirator vacuum. Thin-layer chromatography (TLC) was conducted on 20 × 20 cm plates with 1-mm layers of Brinkman EM silica gel PF-254.

Starting Materials. Commercial pyrroles (**1a–c,f,m**) and DMAD were distilled prior to use. Several of the other pyrroles were prepared from reactions of 2,5-dimethoxytetrahydrofuran with the appropriate amines[11] or as otherwise referenced. Dimethyl (*Z*)- and (*E*)-2-pyrrolyl-2-butenedioates (**3a** and **4a**) were prepared as previously reported.[6]

Dimethyl (*Z*)- and (*E*)-1-Methyl-2-pyrrolyl-2-butenedioates (3b and 4b). A yellow solution of **1b**[12] (Aldrich Chemical Co.; 1.00 g, 12.3 mmol), DMAD (3.50 g, 24.6 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 48 h. The ether and acetic acid were distilled off under aspirator vacuum, and the residual black viscous liquid was distilled at 0.25 mm, giving (1) DMAD (1.21 g, 35% recovery, bp 55–76 °C, as shown by NMR in $CDCl_3$) and (2) a 2:1 mixture of **3b** and **4b** (as shown by NMR in $CDCl_3$). Distillate 2 was chromatographed on a column of silica gel (2.5 × 40 cm) and eluted with chloroform to give the following fractions: (1) 20 mL, giving **4b** as a yellow oil (0.32 g, 12%); (2) 20 mL, giving a 1:1 mixture of **3b** and **4b** (0.40 g, 15%), as shown by NMR in $CDCl_3$; (3) 40 mL, giving **3b** as pale yellow prisms (0.48 g, 17%; mp 67–68 °C).

Dimethyl (*Z*)- and (*E*)-5-Methyl-2-pyrrolyl-2-butenedioates (3c and 4c). The procedure, except for the workup, is essentially the same as that previously reported.[3] A solution of **1c**[11,13] (0.90 g, 11.0 mmol) in benzene (3 mL) was cooled to 10 °C in an ice bath, and a solution of DMAD (1.40 g, 9.8 mmol) in benzene (3 mL) was added dropwise with cooling so that the temperature was maintained at 10 °C. The ice bath was removed, and the yellowish brown solution was stirred at room temperature for 20 h. The benzene was removed by vacuum distillation and the yellow residue was crystallized from methanol, giving a mixture of **3c** and **4c** (1.35 g, 62%; 1:1 by NMR; mp 50–100 °C). A portion (0.30 g) was chromatographed on a preparative TLC plate (20 × 20 × 0.1 cm, silica gel) and eluted with benzene, giving two yellow bands: (1) R_f 0.16, (2) R_f 0.56. Each was extracted with chloroform in a Soxhlet extractor. Band 1 gave **3c** as yellow prisms: 0.16 g (7%); mp 110–111.5 °C (lit.[3] mp 111 °C). Band 2 gave **4c** as yellow prisms: 0.13 g (6%); mp 50–51.5 °C (lit.[3b] mp 52 °C).

Dimethyl (*Z*)- and (*E*)-1,5-Dimethyl-2-pyrrolyl-2-butenedioates (3d and 4d). The procedure, except for the workup, which led to isolation of the additional product **4d**, is essentially the same as that of Acheson and Vernon.[4] A yellow solution of **1d**[4] (0.40 g, 4.20 mmol) and DMAD (0.60 g, 4.20 mmol) in diethyl ether (10 mL) was stirred at room temperature for 24 h. The resulting brown solution was evaporated and chromatographed on a column of silica gel (2.5 × 40 cm) by elution with petroleum ether (bp 30–60 °C)–benzene in the following ratios: (1) 1:1, 1.00 L; (2) 1:1, 1.00 L; (3) 1:2, 0.75 L; (4) 1:2, 0.25 L; (5) 1:4, 1.50 L. Fraction 1 gave no organic material. Fractions 2 and 3 gave **4d** as a yellowish brown oil (0.59 g, 59%). Fraction 4 gave a trace amount of a mixture of **3d** and **4d**. Fraction 5 gave **3d** as yellow needles: 0.19 g (20%); mp 90–91.5 °C (lit.[4] 40%, mp 92 °C).

Dimethyl (*Z*)-1,3-Dimethyl-2-pyrrolyl-2-butenedioate (3e), Tetramethyl 3a,7a-Dihydro-1,6-dimethylindole-2,3,3a,4-tetracarboxylate (6e), Dimethyl 1-Methylpyrrole-3,4-dicarboxylate (7b), Dimethyl 4-Methylphthalate (14e), Trimethyl 5-Methylbenzene-1,2,3-tricarboxylate (16e), and Trimethyl 1-Methylpyrrole-2,3,4-tricarboxylate (17b). 1,3-Dimethylpyrrole[14] (**1e**, 0.95 g, 10.0 mmol) and DMAD (2.84 g, 20.0

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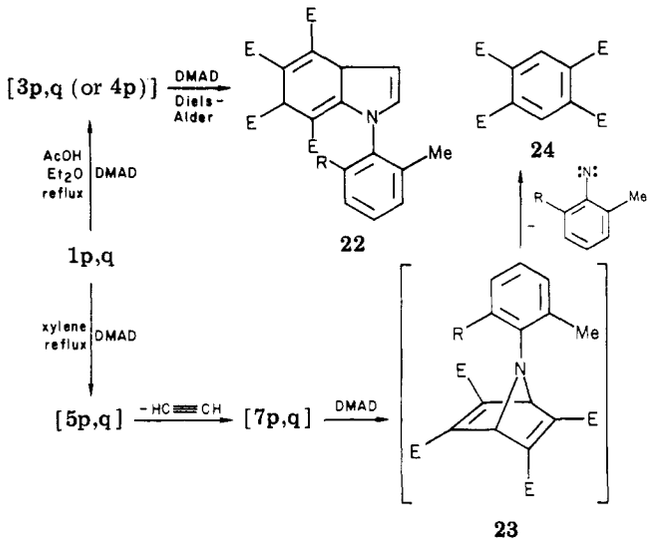
Scheme V[a]



[a] E = COOMe. For **22p** and **23p**, R = H; for **22q** and **23q**, R = Me.

mmol) were mixed at room temperature. A very vigorous reaction occurred within 1 min, and the temperature rose to 160 °C with gas evolution. After being kept at room temperature for 15 h, the dark tarry mixture was chromatographed on a column of silica gel (1.5 × 50 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene [(1) 1:4, 1.25 L; (2) 1:2, 0.50 L; (3) 1:2, 0.15 L; (4) 1:1, 0.15 L], benzene [(5) 0.40 L, (6) 0.75 L, (7) 0.50 L, (8) 1.00 L, (9) 0.75 L], benzene–chloroform [(10) 1:1, 0.50 L], and chloroform [(11) 1.50 L]. Fraction 1 gave no organic material. Fraction 2 gave **14e** as a colorless oil (0.45 g, 22%) having an NMR spectrum in $CDCl_3$ identical with that reported.[15] Fraction 3 gave a trace of a mixture of **14e** and **3e** as shown by the NMR spectrum in $CDCl_3$. Fraction 4 gave **3e** as a pale yellow oil (0.23 g, 10%). Fraction 5 gave a trace of a mixture of **3e** and **16e** as shown by the NMR spectrum in $CDCl_3$. Fraction 6 gave **16e** as a white powder, which was crystallized from benzene–petroleum ether (bp 30–60 °C), giving white crystals: 0.45 g (25%); mp 144–145 °C; UV (CH_3OH) λ_{max} 287 nm (log ϵ 2.96), 295 (2.89); IR (KBr) 1739 (s), 1722 (s, C=O), 1604 (m), 1570 (m, aromatic C=C), 1438 (ms, CH_3), 1275 (s), 1255 (s), 1215 (ms), 1132 (m), 1078 (m), 1004 (m, CO) cm^{-1}; NMR ($CDCl_3$) δ 2.43 (s, 3 H, CH_3), 3.90 (s, 6 H, $2COOCH_3$), 3.97 (s, 3 H, $COOCH_3$), 8.00 (s, 2 H, 4- and 6-H); mass spectrum, *m/e* (relative intensity > 5, M* indicates ^{13}C isotopic peak) 279 (3), 266 (3, M), 236 (13, M* – OCH_3), 235 (100, M – OCH_3).

Anal. Calcd for $C_{13}H_{14}NO_6$ (mol wt 266.25): C, 58.64; H, 5.30. Found: C, 58.59; H, 5.39.

Fraction 7 gave a mixture of **16e** and **17b** (0.11 g, 6%; mp 120–130 °C) which could not be separated by fractional crystallization. Fraction 8 gave **17b** as white prisms, which were recrystallized from methanol, giving white prisms: 0.20 g (12%); mp 163 °C (lit.[7] mp 163 °C). There was no depression in the mixture melting point (163 °C), and the IR (KBr) and NMR ($CDCl_3$) spectra were identical with those of a sample prepared by the reaction of **1b** with DMAD.[7]

Fraction 9 gave **6e** as a yellow powder, which was crystallized from methanol, giving pale yellow prisms: 0.12 g (3%); mp 117–120 °C; UV (CH_3OH) λ_{max} 251 nm (log ϵ 4.11), 290 (3.05), 311 (sh, 2.56); IR (KBr) 1738 (vs), 1707 (s), 1681 (s, C=O), 1646 (w), 1585 (m), 1576 (s, C=C), 1436 (ms, CH_3), 1290 (s), 1269 (s), 1234 (s), 1202 (ms), 1111 (ms), 1098 (m, CO) cm^{-1}; NMR ($CDCl_3$) δ 1.87 (d, $J_{CH_3,7\text{-H}}$ = 1 Hz, 3 H, 6-CH_3), 2.63 (s, 3 H, N-CH_3), 3.70 s, 3 H, $COOCH_3$), 3.80 (s, 3 H, $COOCH_3$), 3.85 (s, 3 H, $COOCH_3$), 3.90 (s, 3 H, $COOCH_3$), 4.70 (d, $J_{7a,7}$ = 10 Hz, 1 H, 7a-H), 5.90 (dd, $J_{7,7a}$ = 10 Hz, $J_{7\text{-H},CH_3}$ = 1 Hz, 1 H, 7-H), 7.27 (s, 1 H, 5-H); mass spectrum, *m/e* (relative intensity > 9) 379 (0.1, M), 197 (42, M – 2 $HCOOCH_3$ – 2 OCH_3), 166 (100, $CH_3OCOC_5H_3(CH_3)NCH_3$), 136 (43, $OCHC_5H_3(CH_3)NCH_3$).

Anal. Calcd for $C_{18}H_{21}NO_8$ (mol wt 397.37): C, 56.99; H, 5.58; N, 3.69. Found: C, 57.07; H, 5.61; N, 3.77.

Fraction 10 gave no organic material. Fraction 11 gave **7b** as colorless prisms: 0.06 g (3%); mp 108–110 °C; UV (CH_3OH) λ_{max} 252 nm (log ϵ 3.98); IR (KBr) 1736 (sh, ms), 1724 (s), 1707 (ms, C=O), 1543 (m, aromatic C=C), 1278 (s), 1183 (m), 1067 (ms, CO) cm^{-1}; NMR ($CDCl_3$) δ 3.63 (s, 3 H, NCH_3), 3.80 (s, 6 H, 2 $COOCH_3$), 7.12 (s, 2 H, 2- and 5-H); mass spectrum, *m/e* (relative intensity > 10) 197 (40, M), 166 (100, M – OCH_3), 136 (51, M – OCH_3 – CH_2O).

Anal. Calcd for $C_9H_{11}NO_4$ (mol wt 197.17): C, 54.82; H, 5.62; N, 7.10. Found: C, 54.58; H, 5.60; N, 6.89.

Dimethyl (*Z*)- and (*E*)-3,5-Dimethyl-2-pyrrolyl-2-butenedioates (3f and 4f) and Dimethyl 2,2-Bis(3,5-dimethyl-2-pyrrolyl)butanedioate (9). The procedure, except for the workup, which led to isolation of the additional products **3f** and **4f**, is essentially the same as that previously reported.[9] A solution of DMAD (1.50 g, 10.5 mmol) in benzene (5 mL) was added very slowly over 1 h to a precooled solution of **1f**[16] (2.00 g, 21.0 mmol) in benzene (5 mL) and kept at 0–5 °C for 1 more h. The solution was then allowed to warm up to room temperature and to stand for 24 h. The resulting black solution was evaporated and chromatographed on a column of silica gel (2 × 50 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene [(1) 4:1, 0.50 L; (2) 4:1, 0.65 L; (3) 3:2, 0.85 L; (4) 1:2, 0.40 L], benzene [(5) 2.25 L], benzene–chloroform [(6) 1:1, 0.50 L], and chloroform [(7) 1.00 L]. Fraction 1 gave unchanged **1f** (0.21 g, 10%) as shown by the NMR spectrum in $CDCl_3$. Fraction 2 gave **3f** as a yellow oil, 0.75 g (20%). Fraction 3 gave a trace of pale yellow oil. Fraction 4 gave **9** as a white powder, which was crystallized from methanol, giving white prisms: 0.20 g (6%); mp 156.5–157 °C (lit.[9] mp 165 °C); UV (CH_3OH, rising end absorption only) λ 220 nm (log ϵ 4.15); IR (KBr) 3430 (ms), 3370 (ms, NH), 1716 (s, C=O), 1592 (sh, w), 1584 (mw, aromatic C=C), 1334 (m), 1195 (ms), 1172 (ms), 1005 (w, CO) cm^{-1}; NMR ($CDCl_3$) δ 1.80 (s, 6 H, 3-CH_3), 2.15 (s, 6 H, 5-CH_3), 3.47 (s, 2 H, aliphatic H), 3.55 (s, 3 H, $COOCH_3$), 3.73 (s, 3 H, $COOCH_3$), 5.60 (m, 2 H, 4-H), 8.37 (br s, 2 H, NH); high-resolution mass spectrum, *m/e* (relative intensity > 9; calcd *m/e*) 332.1738 (37; $C_{18}H_{24}N_2O_4$, 332.1735, M), 274.1622 (20; $^{12}C_{15}{}^{13}CH_{21}N_2O_2$, 274.1637, M* – $COOCH_3$), 273.1600 (100; $C_{16}H_{21}N_2O_2$, 273.1603, M – $COOCH_3$), 259.1457 (22; $C_{15}H_{19}N_2O_2$, 259.1446, M – CH_2 – $COOCH_3$), 199.1266 (12; $C_{13}H_{15}N_2$, 199.1236, M – $COOCH_3$ – CH_3COOCH_3), 122.0609 (18; C_7H_8NO, 122.0606).

Anal. Calcd for $C_{18}H_{24}N_2O_4$ (mol wt 332.40): C, 65.04; H, 7.28; N, 8.43. Found: C, 65.12; H, 7.19; N, 8.25.

Fractions 5 and 6 gave **4f** as a yellowish brown oil, 0.94 g (34%). Fraction 7 gave no organic material.

Dimethyl (*Z*)- and (*E*)-1-Butyl-2-pyrrolyl-2-butenedioates (3i and 4i). A solution of **1i**[11] (1.23 g, 10.0 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 24 h. The ether and acetic acid were evaporated under aspirator vacuum, and the residual solution was chromatographed on a column of silica gel (1.5 × 50 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene: (1) 2:1, 0.20 L; (2) 2:1, 0.15 L; (3) 2:1, 0.15 L; (4) 1:1, 0.50 L. Fraction 1 gave a mixture (0.48 g) of unchanged **1i** and DMAD and a trace of **4i**. Fraction 2 gave **4i** as a yellow oil, 0.23 g (9%). Fraction 3 gave a 3:1 mixture (0.23 g, 9%) of **3i** and **4i** as shown by the NMR spectrum in $CDCl_3$. Fraction 4 gave **3i** as a yellow oil, 0.47 g (19%).

Tetramethyl 1-Butyl-3a,7a-dihydroindole-2,3,3a,4-tetracarboxylate (6i). A solution of freshly distilled **1i**[11] (0.63 g, 5.10 mmol) and DMAD (1.42 g, 10.0 mmol) in diethyl ether (20 mL) was refluxed for 24 h, giving a yellow precipitate. The precipitate was filtered, washed with ether, and recrystallized from methanol, giving **6i** as pale yellow prisms: 1.11 g (54%); mp 119–121 °C; UV (CH_3OH) λ_{max} 277 nm (log ϵ 4.26), 300 (sh, 3.94); IR (KBr) 1760 (s), 1723 (s), 1690 (s, C=O), 1660 (mw), 1581 (ms, C=C), 1485 (m), 1448 (ms), 1362 (ms, CH), 1289 (ms), 1273 (s), 1222 (ms), 1199 (ms), 1142 (ms, CO); NMR ($CDCl_3$) δ 0.70–1.67 (m, 7 H,

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$CH_2CH_2CH_3$), 3.07 (apparent t, 2 H, NCH_2CH_2), 3.60 (s, 3 H, $COOCH_3$), 3.75 (s, 3 H, $COOCH_3$) overlapping 3.78 (s, 3 H, $COOCH_3$), 3.92 (s, 3 H, $COOCH_3$), 5.00 (d, $J_{7a,7}$ = 3 Hz, 1 H, 7a-H), 5.85 (dd, $J_{7,7a}$ = 3 Hz, $J_{7,6}$ = 10 Hz, 1 H, 7-H), 6.25 (dd, $J_{6,7}$ = 10 Hz, $J_{6,5}$ = 6 Hz, 1 H, 6-H), 7.00 (d, $J_{5,6}$ = 6 Hz, 1 H, 5-H); high-resolution mass spectrum, m/e (relative intensity > 4; calcd m/e) 407.1567 (4; $C_{20}H_{25}NO_8$, 407.1580, M), 376.1422 (4; $C_{19}H_{22}NO_7$, 376.1395, M - OCH_3), 317.1212 (19; $^{13}C^{12}C_{16}H_{18}NO_5$, 317.1218, M* - $HCOOCH_3$ - OCH_3), 316.1188 (100; $C_{17}H_{18}NO_5$, 316.1184, M - $HCOOCH_3$ - OCH_3), 260.0570 (6; $C_{13}H_{10}NO_5$, 260.0558, M - $HCOOCH_3$ - OCH_3 - C_4H_8), 246.0758 (8; $C_{13}H_{12}NO_4$, 246.0765, M - $HCOOCH_3$ - $COOCH_3$ - C_3H_6), 228.0314 (16; $C_{12}H_6NO_4$, 228.0296, M - $HCOOCH_3$ - 2 OCH_3 - C_4H_9).

Anal. Calcd for $C_{20}H_{25}NO_8$ (mol wt 407.42): C, 58.96; H, 6.18; N, 3.44. Found: C, 59.20; H, 6.19; N, 3.31.

Dimethyl (*Z*)- and (*E*)-1-Butyl-2-pyrrolyl-2-butenedioates (3i and 4i), Trimethyl 1-Butylpyrrole-2,3,4-tricarboxylate (17i), and Trimethyl Benzene-1,2,3-tricarboxylate (16b). A solution of **1i**[11] (1.23 g, 10.0 mmol) and DMAD (2.84 g, 20.0 mmol) in toluene (25 mL) was refluxed for 45 h. The toluene was distilled off under aspirator vacuum, and the residual black solution was chromatographed on a column of silica gel (1.5 × 50 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene [(1) 2:1, 0.17 L; (2) 2:1, 0.15 L; (3) 2:1, 0.15 L; (4) 1:1, 0.50 L] and benzene [(5) 0.60 L, (6) 1.50 L]. Fraction 1 gave **4i** as a yellow oil (0.23 g, 9%). Fraction 2 gave a 3:1 mixture (0.17 g, 6%) of **3i** and **4i** as shown by the NMR spectrum in $CDCl_3$. Fraction 3 (0.13 g, 5%) was mostly **3i** with a small amount of **16b** as shown by the NMR spectrum in $CDCl_3$. Fraction 3 was rechromatographed on a column of silica gel (2 × 10 cm) and eluted with petroleum ether [(i) 0.41 L], petroleum ether–benzene [(ii) 2:1, 0.50 L; (iii) 1:1, 0.50 L], and benzene [(iv) 0.50 L]. Fractions i and ii gave no organic material. Fraction iii gave **3i** as a yellow oil (68 mg, 2%). Fraction iv gave a mixture of **3i** and **16b** as shown by the NMR spectrum in $CDCl_3$. Fractions 4 and 5 gave a powdery mixture (0.37 g, 20%; mp 70–90 °C) of **16b** and **17i** as shown by the NMR spectrum in $CDCl_3$. This mixture was chromatographed on a preparative TLC plate (20 × 20 × 0.1 cm, silica gel) and eluted with benzene, giving essentially one wide band, which was cut into four bands: (a) R_f 0.53–0.62, (b) R_f 0.44–0.53, (c) R_f 0.32–0.44, (d) R_f 0.15–0.32. The bands were extracted with chloroform in a Soxhlet extractor. Band a gave a white solid, which was recrystallized from methanol, giving colorless prisms together with a white powder. The prisms were picked out by hand and recrystallized from methanol, giving **17i**: 23 mg (1.3%); mp 77–77.5 °C; UV (CH_3OH) λ_{max} 263 nm (log ϵ 4.02), 268 (sh, 4.01); IR (KBr) 1740 (s), 1718 (vs, C=O), 1542 (m), 1522 (m, aromatic C=C), 1265 (vs), 1219 (s), 1200 (s), 1070 (ms, CO); NMR ($CDCl_3$) δ 0.93 (t, 3 H, CH_2CH_3) superimposed on 1.17–2.00 (m, 4 H, $NCH_2CH_2CH_2CH_3$), 3.80 (s, 6 H, 2 $COOCH_3$), 3.92 (s, 3 H, $COOCH_3$), 4.28 (t, 2 H, NCH_2CH_2), 7.29 (s, 1 H, 5-H); high-resolution mass spectrum, m/e (relative intensity > 16; calcd m/e) 297.1192 (23; $C_{14}H_{19}NO_6$, 297.1211, M), 266.1005 (83; $C_{13}H_{16}NO_5$, 266.1027, M - OCH_3), 255.0762 (25; $C_{11}H_{13}NO_6$, 255.0742, M - C_3H_6), 238.1085 (100; $C_{12}H_{16}NO_4$, 238.1079, M - $COOCH_3$), 236.0562 (39; $C_{11}H_{10}NO_5$, 236.0558, M - OCH_3 - C_2H_6), 221.0463 (97; silicone?), 206.0814 (63; $C_{11}H_{12}NO_3$, 206.0816, M - $HCOOCH_3$ - OCH_3), 196.0604 (35; $C_9H_{10}NO_4$, 196.0609, M - $COOCH_3$ - C_3H_6), 178.0146 (93; $C_8H_4NO_4$, 178.0139, M - 2 OCH_3 - C_4H_9).

Anal. Calcd for $C_{14}H_{19}NO_6$ (mol wt 297.31): C, 56.56; H, 6.44; N, 4.71. Found: C, 56.43; H, 6.49; N, 4.45.

Bands b–d gave mixtures of **17i** and **16b**, which were combined and fractionally crystallized from methanol–water, giving **16b** as a white powder: 73 mg (4%); mp 100–101 °C (lit.[7] mp 101 °C). There was no depression in the mixture melting point (100–101 °C) with a sample of **16b** prepared by the reaction of **1b** with DMAD,[7] and the IR (KBr) and NMR ($CDCl_3$) spectra were identical.

Dimethyl (*Z*)- and (*E*)-1-(1-Methylpropyl)-2-pyrrolyl-2-butenedioates (3j and 4j). A yellow solution of **1j**[17] (1.23 g, 10.0 mmol) and DMAD (2.84 g, 20.0 mmol) in toluene (25 mL) was refluxed for 72 h. The resulting black, tarry solution was evaporated and chromatographed on a column of silica gel (2 × 50 cm), by elution with petroleum ether (bp 30–60 °C)–benzene: (1) 3:2, 0.55 L; (2) 3:2, 0.50 L; (3) 1:1, 1.00 L. Fraction 1 gave unchanged DMAD (0.74 g, 26% recovery) as shown by the NMR spectrum in $CDCl_3$. Fraction 2, a mixture, was rechromatographed on a preparative TLC plate (20 × 20 × 0.1 cm, silica gel) by elution with 1:1 petroleum ether–benzene, giving three bands: (1) R_f 0.46–0.85, (2) R_f 0.29–0.46, (3) R_f 0.17–0.29. The bands were cut out and extracted with chloroform in a Soxhlet extractor. Bands 1 and 2 gave **4j** as a yellow oil, 66 mg (2%). Band 3 gave a mixture of **3j** and **4j** as shown by the NMR spectrum in $CDCl_3$. Fraction 3 from the column chromatography gave **3j** as a yellow oil, 0.23 g (9%).

Dimethyl (*Z*)- and (*E*)-1-(Dimethylethyl)-2-pyrrolyl-2-butenedioates (3k and 4k) and Dimethyl 1-(Dimethylethyl)pyrrole-3,4-dicarboxylate (7k). A solution of **1k**[11,12] (1.23 g, 10.0 mmol) and DMAD (2.84 g, 20.0 mmol) in toluene (25 mL) was refluxed for 48 h. The toluene was evaporated under aspirator vacuum without heating, and the residual black solution was chromatographed on a column of silica gel (2 × 50 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene [(1) 2:1, 0.50 L; (2) 1:1, 0.50 L; (3) 1:1, 0.15 L; (4) 1:1, 0.15 L; (5) 1:4, 0.50 L], benzene [(6) 0.50 L], and benzene–chloroform [(7) 4:1, 1.50 L]. Fraction 1 gave no organic material. Fraction 2 gave **4k** as a yellow oil, 0.50 g (19%). Fraction 3 gave a yellow oil (0.28 g, 10%) shown to be a 1:3 mixture of **3k** and **4k** by the NMR spectrum in $CDCl_3$. Fraction 4 gave **3k** as a yellow oil, 0.01 g (1%). Fraction 5 gave a trace amount of **3k** and **7k** as shown by the NMR spectrum in $CDCl_3$. Fraction 6 gave **7k** as a yellow oil: 46 mg (2%); UV (CH_3OH) λ_{max} 250 nm (log ϵ 3.91), 388 (diffuse sh, 3.10); IR (neat) 1725 (s, C=O), 1615 (mw), 1590 (m), 1540 (m, aromatic C=C), 1443 (ms, CH), 1279 (s), 1216 (s), 1175 (s), 1076 (s, CO) cm^{-1}; NMR ($CDCl_3$) δ 1.52 (s, 9 H, CH_3), 3.67 (s, 6 H, $COOCH_3$), 7.40 (s, 2 H,2- and 5-H); high-resolution mass spectrum, m/e (relative intensity ≥ 10; calcd m/e) 239.1140 (24; $C_{12}H_{17}NO_4$, 239.1157, M), 183.0518 (19; $C_8H_9NO_4$, 183.0531, M - C_4H_8), 152.0338 (100; $C_7H_6NO_3$, 152.0347, M - C_4H_8 - OCH_3), 151.0244 (15; $C_7H_5NO_3$, 151.0269, M - C_4H_9 - OCH_3), 122.0240 (10; $C_6H_4NO_2$, 122.0242, M - C_4H_8 - OCH_3 - CH_2O).

Anal. Calcd for $C_{12}H_{17}NO_4$ (mol wt 239.27): C, 60.24; H, 7.16; N, 5.85. Found: C, 59.96; H, 6.93; N, 5.75.

Fraction 7 gave no organic material.

Dimethyl (*Z*)- and (*E*)-1-Benzyl-2-pyrrolyl-2-butenedioates (3l and 4l). A yellow solution of **1l**[12,18] (0.78 g, 5.00 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 48 h. The ether and acetic acid were distilled off under aspirator vacuum. The residual dark brown oil was kept in a refrigerator for 3 days. The crystalline needles which separated were filtered, washed with cold methanol (10 mL), and recrystallized from methanol, giving **3l** as pale yellow needles: 0.55 g (37%); mp 99–101 °C. The filtrate and washings were combined, evaporated, and chromatographed on a column of silica gel (1.5 × 50 cm) by elution with petroleum ether (bp 30–60 °C)–benzene: (1) 1:1, 0.50 L; (2) 2:3, 0.30 L; (3) 2:3, 0.35 L; (4) 1:2, 0.50 L. Fraction 1 gave no organic material. Fraction 2 gave **4l** as a yellow oil, 0.34 g (23%). Fractions 3 and 4 gave additional **3l**, total 0.71 g (47%).

Dimethyl (*Z*)- and (*E*)-1-Phenyl-2-pyrrolyl-2-butenedioates (3m and 4m). A pale yellow solution of **1m**[11,18] (0.72 g, 5.00 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 96 h. The ether and acetic acid were evaporated under aspirator vacuum. The residual brown solution was chromatographed on three preparative TLC plates (20 × 20 × 0.1 cm, silica gel) and eluted with benzene, giving bands at (1) R_f 0.81–0.91, (2) R_f 0.47–0.69, and (3) R_f 0.09–0.34. The bands were cut out and extracted with chloroform in a Soxhlet extractor. Band 1 gave unchanged **1m**: 0.23 g (32% recovery); mp and mmp 61 °C (lit.[11] mp 62 °C). Band 3 gave a yellowish brown gummy material which could not be characterized. Band 2 gave a 1:1 mixture of **3m** and **4m** as a yellow oil (0.38 g, 26%) as shown by the NMR spectrum in $CDCl_3$. The oil was rechromatographed on two preparative TLC plates of silica gel

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by elution with petroleum ether (bp 30–60 °C)–benzene, giving bands at (i) R_f 0.34–0.43, (ii) R_f 0.10–0.34, and (iii) R_f 0.01–0.10. The bands were again cut out and extracted with chloroform in a Soxhlet extractor. Band i gave **4m** as a yellow oil, 0.12 g (9%). Band ii gave a trace amount of **3m** and **4m** as shown by the NMR spectrum in $CDCl_3$. Band iii gave a residue which was triturated with petroleum ether, giving a precipitate. This was crystallized from 1:1 benzene–petroleum ether, giving **3m** as pale yellow prisms: 0.11 g (8%); mp 84–85 °C.

Dimethyl 1-Phenylpyrrole-3,4-dicarboxylate (7m). A solution of **1m**[11,18] (1.43 g, 10.0 mmol) and DMAD (2.84 g, 20.0 mmol) in xylene (25 mL) was refluxed for 4 days. The xylene was distilled off under aspirator vacuum. The residual black tar was chromatographed on a column of silica gel (1 × 50 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene [(1) 1:1, 0.15 L] and benzene [(2) 0.50 L]. Fraction 1 gave **7m** as white prisms, which were recrystallized from methanol, giving white prisms: 1.22 g (48%); mp 117–118 °C (lit.[19] mp 117–118 °C); UV (CH_3OH) λ_{max} 233 nm (log ϵ 4.47), 249 (diffuse sh, 4.33); IR (KBr) 1712 (vs, C=O), 1600 (m), 1540 (ms, aromatic C=C), 1260 (s), 1250 (s), 1075 (s, CO), 760 (s, 5 adjacent aromatic H) cm^{-1}; NMR ($CDCl_3$) δ 3.85 (s, 6 H, 2 $COOCH_3$), 7.40 (m, 5 H, C_6H_5), 7.57 (s, 2 H, 2- and 5-H); high-resolution mass spectrum, m/e (relative intensity > 8; calcd m/e) 259.0842 (49; $C_{14}H_{13}NO_4$, 259.0844, M), 229.0676 (14; $^{13}C^{12}C_{12}H_{10}NO_3$, 229.0694, M* – OCH_3), 228.0629 (100; $C_{13}H_{10}NO_3$, 228.0660, M – OCH_3), 198.0541 (18; $C_{12}H_8NO_2$, 198.0555, M – OCH_3 – CH_2O), 77.0345 (21; C_6H_5, 77.0391).

Anal. Calcd for $C_{14}H_{13}NO_4$ (mol wt 259.26): C, 64.86; H, 5.05; N, 5.40. Found: C, 64.92; H, 4.97; N, 5.41.

Dimethyl (*Z*)- and (*E*)-1-(4-Methoxyphenyl)-2-pyrrolyl-2-butenedioates (3n and 4n). A solution of **1n**[20] (0.14 g, 0.78 mmol), DMAD (0.25 g, 1.76 mmol), and glacial acetic acid (5 mL) in diethyl ether (10 mL) was refluxed for 48 h. The ether and acetic acid were evaporated under aspirator vacuum. The residual brown liquid was chromatographed on a preparative TLC plate (20 × 20 × 0.1 cm, silica gel) by elution with chloroform, giving two bands: (1) R_f 0.49, (2) R_f 0.31. The bands were cut out and extracted with chloroform in a Soxhlet extractor. Band 1 gave **4n** as a yellow oil, 20 mg (9%). Band 2 gave **3n** as pale yellow needles: 78 mg (32%); mp 110–113 °C.

Dimethyl 1-(4-Methoxyphenyl)pyrrole-3,4-dicarboxylate (7n). A solution of **1n**[20] (1.73 g, 10.0 mmol) and DMAD (2.84 g, 20.0 mmol) in xylene (25 mL) was refluxed for 24 h. The xylene was distilled off under aspirator vacuum. The residual dark brown oil was kept in a refrigerator overnight. The resulting white precipitate was filtered and recrystallized from methanol, giving unchanged **1n** as white plates: 0.34 g (20% recovery); mp and mmp 111 °C (lit.[20] mp 112–113 °C). The filtrate (dark brown oil) was chromatographed on a column of silica gel (1 × 50 cm) and eluted with chloroform (6 × 20 mL). Fraction 1 gave additional unchanged **1n**: 0.03 g (total 21% recovery); mp 110–112 °C. Fraction 2 gave a trace amount of a solid mixture of **1n** and **7n**. Fractions 3–5 gave **7n** as a white powder, which was recrystallized from 7:3 benzene–petroleum ether (bp 30–60 °C), giving white crystals: 0.20 g (7%); mp 116–117.5 °C; UV (CH_3OH) λ_{max} 242 nm (log ϵ 4.43); IR (KBr) 1738 (s), 1703 (s, C=O), 1625 (w), 1545 (s, aromatic C=C), 1278 (s), 1265 (s), 1255 (s), 1080 (s, CO) cm^{-1}; NMR ($CDCl_3$) δ 3.72 (s, 6 H, 2 $COOCH_3$) overlapping 3.75 (s, 3 H, $C_6H_4OCH_3$), AB centered at 6.80 and 7.17 (J = 9 Hz, C_6H_4) overlapping 7.30 (s, total 6 H, 2- and 5-H); high-resolution mass spectrum, m/e (relative intensity > 13; calcd m/e) 289.0959 (68; $C_{15}H_{15}NO_5$, 289.0949, M), 259.0819 (15; $^{13}C^{12}C_{13}H_{12}NO_4$, 259.0798, M* – OCH_3), 258.0779 (100; $C_{14}H_{12}NO_4$, 258.0765, M – OCH_3).

Anal. Calcd for $C_{15}H_{15}NO_5$ (mol wt 289.29): C, 62.28; H, 5.23; N, 4.84. Found: C, 62.44; H, 5.23; N, 4.78.

Fraction 6 gave a trace amount of an uncharacterizable tar.

Dimethyl (*Z*)- and (*E*)-1-(4-Bromophenyl)-2-pyrrolyl-2-butenedioates (3o and 4o). A solution of **1o**[21] (1.11 g, 5.00 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 48 h. The ether and acetic acid were evaporated under aspirator vacuum. The residual yellow oil was kept in a refrigerator overnight. The crystals which separated were filtered and recrystallized from 7:3 benzene–petroleum ether, giving **3o** as pale yellow prisms: 0.22 g (12%); mp 118–120 °C. The filtrate was a 2:1 mixture (0.48 g) of **3o** and **4o** as shown by the NMR spectrum in $CDCl_3$. It was chromatographed on a preparative TLC plate (20 × 20 × 0.1 cm, silica gel) by elution with benzene, giving a wide yellow band. A fraction of R_f 0.65–0.70 was cut out and extracted with chloroform in a Soxhlet extractor, giving **4o** as a viscous yellow oil, 0.11 g (6%).

Dimethyl 1-(4-Bromophenyl)pyrrole-3,4-dicarboxylate (7o). A pale yellow solution of **1o**[21] (1.11 g, 5.00 mmol) and DMAD (1.42 g, 10.0 mmol) in xylene (25 mL) was refluxed for 48 h. The xylene was distilled off under aspirator vacuum. The residual tarry solid was decolorized with charcoal and crystallized from methanol, giving **7o** as a white powder: 0.32 g (19%); mp 153–155 °C; UV (CH_3OH) λ_{max} 241 nm (log ϵ 4.51); IR (KBr) 1745 (s), 1723 (ms, C=O), 1290 (s), 1275 (ms), 1248 (ms), 1088 (s, CO) cm^{-1}; NMR ($(CD_3)_2CO$) δ 3.80 (s, 6 H, 2 $COOCH_3$), 7.67 (s, 4 H, C_6H_4), 7.77 (s, 2 H, 2- and 5-H); high-resolution mass spectrum, m/e (relative intensity > 10; calcd m/e) 338.9957 (49; $C_{14}H_{12}NO_4{}^{81}Br$, 338.9930, M*), 336.9970 (49; $C_{14}H_{12}NO_4{}^{79}Br$, 336.9950, M), 308.9786 (13; $^{13}C^{12}C_{12}H_9NO_3{}^{81}Br$, 308.9779, M** – OCH_3), 307.9748 (95; $C_{13}H_9NO_3{}^{81}Br$, 307.9745, M* – OCH_3), 306.9823 (15; $^{13}C^{12}C_{12}H_9NO_3{}^{79}Br$, 306.9799, M* – OCH_3), 305.9771 (100; $C_{13}H_9NO_3{}^{79}Br$, 305.9765, M – OCH_3), 277.9643 (13; $C_{12}H_7NO_2{}^{81}Br$, 277.9640, M* – OCH_3 – CH_2O), 275.9653 (12; $C_{12}H_7NO_2{}^{79}Br$, 275.9660, M – OCH_3 – CH_2O).

Anal. Calcd for $C_{14}H_{12}NO_4Br$ (mol wt 338.17): C, 49.72; H, 3.58; N, 4.14; Br, 23.63. Found: C, 49.64; H, 3.66; N, 4.04; Br, 23.46.

Dimethyl (*Z*)- and (*E*)-1-(2-Methylphenyl)-2-pyrrolyl-2-butenedioates (3p and 4p) and Tetramethyl 3a,6-Dihydro-1-(2-methylphenyl)indole-4,5,6,7-tetracarboxylate (22p). A solution of **1p**[11] (0.79 g, 5.00 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 48 h. The ether and acetic acid were distilled off under aspirator vacuum. The residual dark brown solution was chromatographed on a column of silica gel (2.5 × 30 cm) and eluted with petroleum ether (bp 30–60 °C)–benzene [(1) 1:1, 1.00 L; (2) 1:2, 1.00 L: (3) 1:2, 0.25 L] and benzene [(4) 1.00 L, (5) 1.00 L]. Fraction 1 gave no organic material. Fraction 2 gave **4p** as a yellow oil, 0.19 g (13%). Fraction 3 gave a trace amount of yellow oil. Fraction 4 gave **3p** as white prisms, which were recrystallized from methanol: 0.27 g (18%); mp 119.5–121 °C. Fraction 5, upon recrystallization from methanol, gave **22p** as white prisms: 0.18 g (8%); mp 143–144 °C.

Anal. Calcd for $C_{23}H_{23}NO_8$ (mol wt 441.44): C, 62.58; H, 5.25; N, 3.17. Found: C, 62.78; H, 5.30; N, 3.13.

Subsequent attempts to repeat the preparation of **22p** have so far been unsuccessful.[10]

Dimethyl (*Z*)-1-(2,6-Dimethylphenyl)-2-pyrrolyl-2-butenedioate (3q) and Tetramethyl 3a,6-Dihydro-1-(2,6-dimethylphenyl)indole-4,5,6,7-tetracarboxylate (22q). A solution of **1q**[11,18] (0.86 g, 5.00 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (10 mL) in diethyl ether (10 mL) was refluxed for 60 h. The ether and acetic acid were distilled off under aspirator vacuum. The residual brown solution was chromatographed on a column of silica gel (2.5 × 15 cm) by elution with petroleum ether (bp 30–60 °C)–benzene [(1) 1:1, 40 mL; (2) 1:1, 200 mL], benzene [(3) 200 mL], and chloroform [(4) 150 mL]. Fraction 1 was a 1:1 mixture (0.45 g) of unchanged **1q** and DMAD as shown by the NMR spectrum in $CDCl_3$. Fraction 2 gave **3q** as pale yellow prisms, which were recrystallized from methanol: 0.13 g (9%); mp 98–99 °C. Fractions 3 and 4 gave **22q** as a white solid, which was recrystallized from methanol, giving white crystals: 0.15 g (7%); mp 155–157 °C.

Anal. Calcd for $C_{24}H_{25}NO_8$ (mol wt 455.47): C, 63.29; H, 5.53; N, 3.07. Found: C, 63.23; H, 5.28; N, 3.08.

Tetramethyl Benzene-1,2,4,5-tetracarboxylate (24). (A) From 1p. A solution of freshly distilled **1p**[11] (1.57 g, 10.0 mmol) and DMAD (2.84 g, 20.0 mmol) in xylene (25 mL) was refluxed for 48 h. The xylene was distilled off under aspirator vacuum. The residual black oil was chromatographed on a column of silica gel (2.5 × 50 cm) by elution with benzene: (1) 100 mL, (2) 50 mL, (3) 300 mL, (4) 100 mL. Fraction 1 gave unchanged **1p** (0.72 g,

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46% recovery) having IR (neat) and NMR ($CDCl_3$) spectra identical with those of the starting material. Fraction 2 gave no organic material. Fraction 3 gave **24** as pale yellowish needles: 0.13 g (4%); mp 140–141.5 °C (lit.[22] mp 141 °C); IR (KBr)[23a,24a] and NMR ($CDCl_3$)[25a] spectra identical with those reported in the literature.

(B) From 1q. A solution of **1q**[11,18] (1.71 g, 10.0 mmol) and DMAD (1.42 g, 10.0 mmol) in xylene (30 mL) was refluxed for 48 h. The xylene was distilled off under aspirator vacuum. The residual black liquid was chromatographed on a column of alumina (1 × 50 cm) by elution with petroleum ether (bp 30–60 °C)–benzene [(1) 4:1, 50 mL; (2) 1:1, 50 mL], benzene [(3) 50 mL, (4) 150 mL, (5) 50 mL], and benzene–chloroform [(6) 1:1, 100 mL]. Fraction 1 gave unchanged **1q** as colorless prisms: 0.88 g (52% recovery); mp 45.5–48 °C; IR (neat melt) and NMR (CS_2) spectra identical with those of the starting material. Fractions 2 and 3 gave a trace of yellow liquid, which was not successfully characterized. Fraction 4 gave **24** as white needles: 0.57 g (37%); mp 139–142 °C (lit.[22] mp 141 °C); IR (KBr)[23a,24a] and NMR ($CDCl_3$)[25a] spectra identical with those reported in the literature.

Dimethyl 1-(4-Nitrophenyl)pyrrole-3,4-dicarboxylate (7r). A solution of **1r**[26] (0.37 g, 2.00 mmol) and DMAD (0.57 g, 4.00 mmol) in xylene (10 mL) was refluxed for 48 h. The tarry solution was kept in a refrigerator overnight. The resulting gray precipitate was filtered and crystallized from methanol, giving **7r** as yellow prisms: 0.07 g (12%); mp 188–191 °C; UV (CH_3OH) λ_{max} 251 nm (log ϵ 4.08), 302 (4.24); IR (KBr) 1750 (ms), 1740 (s), 1725 (s, C=O), 1596 (mw, aromatic C=C), 1532 (s), 1350 (s, NO_2), 1265 (s), 1245 (s), 1074 (ms, CO); NMR ($(CD_3)_2CO$) δ 3.83 (s, 6 H, 2 $COOCH_3$), 8.04 (s, 2- and 5-H) overlapping an AB centered at 8.03 and 8.47 (J = 8.5 Hz, total 6 H, C_6H_4); high-resolution mass spectrum, m/e (relative intensity > 16; calcd m/e) 304.0720 (38; $C_{14}H_{12}N_2O_6$, 304.0694, M), 273.0520 (100; $C_{13}H_9N_2O_5$, 273.0511, M – OCH_3), 227.0592 (51; $C_{13}H_9NO_3$, 227.0581, M – OCH_3 – NO_2), 188.0589 (43; $C_{10}H_8N_2O_2$, 188.0585, M – 2 $COOCH_2$), 142.0647 (23; $C_{10}H_8N$, 142.0656, M – 2 $COOCH_2$ – NO_2; or $^{13}C^{12}C_9H_7N$, 142.0611, M* – $COOCH_3$ – $COOCH_2$ – NO_2), 141.0570 (21; $C_{10}H_7N$, 141.0577, M – $COOCH_3$ – $COOCH_2$ – NO_2), 115.0501 (26), 111.0080 (34).

Anal. Calcd for $C_{14}H_{12}N_2O_6$ (mol wt 304.26): C, 55.27; H, 3.97; N, 9.21. Found: C, 55.01; H, 4.24; N, 8.96.

Dimethyl (*E*)-1-Acetyl-2-pyrrolyl-2-butenedioate (4s). A solution of **1s**[27] (1.10 g, 10.0 mmol), DMAD (1.42 g, 10.0 mmol), and glacial acetic acid (2 mL) in diethyl ether (25 mL) was refluxed for 60 h. The ether and acetic acid were distilled off under aspirator vacuum. The residual yellow liquid was a mixture of unchanged starting materials, as shown by the IR (neat) and NMR ($CDCl_3$) spectra. The liquid was dissolved in methylene chloride (40 mL), and an ice-cold solution of aluminum chloride (2.30 g, 17.2 mmol as $AlCl_3$) in methylene chloride (40 mL) was added. The black solution was refluxed for 1.5 h. Water (75 mL) was added, and the organic layer was separated, washed with water (25 mL), and dried (Na_2SO_4). The dried black solution was evaporated and chromatographed on a column of silica gel (2 × 50 cm) by elution with petroleum ether (bp 30–60 °C) [(1) 0.50 L], petroleum ether–benzene [(2) 2:1, 0.50 L; (3) 1:1, 0.90 L], benzene [(4) 1.25 L], benzene–chloroform [(5) 2:1, 0.50 L; (6) 1:1, 0.50 L], and chloroform [(7) 0.50 L, (8) 1.15 L]. Fractions 1 and 2 gave a 4:9 mixture (0.45 g, 18% recovery) of unchanged **1s** and DMAD as shown by the NMR spectrum in $CDCl_3$. Fractions 3 and 4 gave no organic materials. Fraction 5–7 gave **4s** as pale yellow prisms: 70 mg (3%); mp 45–48 °C.

Dimethyl 1-Acetylpyrrole-3,4-dicarboxylate (7s). A solution of **1s**[27] (2.10 g, 18.0 mmol) and DMAD (5.05 g, 35.5 mmol) in xylene (25 mL) was refluxed for 48 h. The resulting tarry solution was vacuum distilled at 2 mm: (1) 3.47 g, bp 68–73 °C; (2) 0.90 g, bp 86–92 °C; (3) 0.64 g, bp 100–155 °C; (4) 0.60 g, bp 160–190 °C. Fraction 1 was unchanged DMAD (69% recovery). Fractions 2 and 3 were 1:1 mixtures of unchanged **1s** and DMAD as shown by NMR. Fraction 4, after being kept at room temperature for 2 days, solidified and was recrystallized from methanol, giving **7s** as a white powder: 0.48 g (12%); mp 83–85 °C; UV (CH_3OH) λ_{max} 249 nm (log ϵ 3.96); IR (KBr) 1758, 1705, 1583 (aromatic C=C), 1250, 1208, 1170 (CO) cm^{-1}; NMR ($CDCl_3$) δ 2.60 (s, 3 H, $COCH_3$), 3.92 (s, 6 H, 2 $COOCH_3$), 7.80 (s, 2 H, 2- and 5-H); mass spectrum, m/e (relative intensity ≥ 12) 225 (3, M), 183 (39, M – CH_2CO), 152 (100, M – CH_2CO – OCH_3), 122 (26, M – CH_2CO – OCH_3 – CH_2O), 120 (12, M – CH_2CO – OCH_3 – CH_3OH).

Anal. Calcd for $C_{10}H_{11}NO_5$ (mol wt 225.20): C, 53.33; H, 4.92; N, 6.22. Found: C, 53.31; H, 5.02; N, 6.46.

Dimethyl (*E*)-1-Pyrrolyl-2-butenedioate,[6] Dimethyl Phthalate (14b), Trimethyl Benzene-1,2,3-tricarboxylate (16b), and Trimethyl Indole-4,5,6-tricarboxylate (21) from 1a. A solution of **1a** (3.35 g, 50.0 mmol) in DMAD (14.21 g, 0.100 mol) was heated at 63 °C under nitrogen for 20 h. The resulting tarry solution was chromatographed on a column of alumina (3 × 35 cm) by elution with petroleum ether (bp 30–60 °C) [(1) 0.30 L], petroleum ether–benzene [(2) 3:2, 1.00 L; (3) 1:1, 0.50 L; (4) 1:1, 1.00 L; (5) 1:2, 1.00 L], and benzene [(6) 1.35 L]. Fractions 1 and 2 gave no organic material. Fractions 3 and 4 gave a 3:2 mixture (0.77 g) of dimethyl (*E*)-1-pyrrolyl-2-butenedioate[6] (5%) and **14b** (3%) as shown by the NMR spectrum in $CDCl_3$. Fraction 5 gave a 1:2:4 mixture (0.35 g) of dimethyl (*E*)-1-pyrrolyl-2-butenedioate[6] (0.4%), **14b** (0.9%), and **16b** (3%) as shown by the NMR spectrum in $CDCl_3$. Fraction 6 gave a yellow oil which crystallized upon being kept in a refrigerator overnight. Recrystallization from methanol gave **21** as pale yellow prisms: 0.12 g (0.8%); mp 113–114 °C; UV (CH_3OH) λ_{max} 250 nm (log ϵ 4.47), 322 (3.91); IR (KBr) 3390 (ms, NH), 1740 (s), 1722 (s), 1690 (s, C=O), 1602 (m, aromatic C=C), 1434 (ms, CH_3), 1317 (s), 1240 (s), 1196 (ms), 1158 (ms, CO) cm^{-1}; NMR ($CDCl_3$) δ 3.93 (s, 3 H, $COOCH_3$), 4.03 (s, 6 H, 2 $COOCH_3$), 6.68 (dd, $J_{3,2}$ = 3.5 Hz, 1 H, 3-H), 7.40 (dd, $J_{2,3}$ = 3.5 Hz, 1 H, 2-H), 8.07 (s, 1 H, 7-H), 10.07 (br s, 1 H, NH); mass spectrum, m/e (relative intensity ≥ 12) 292 (13, M*), 291 (68, M), 261 (17, M* – OCH_3), 260 (100, M – OCH_3), 259 (26, M – CH_3OH), 228 (30, M – OCH_3 – CH_3OH), 201 (27, M – $COOCH_3$ – OCH_3), 142 (17, M – 2 $COOCH_3$ – OCH_3), 114 (12, M – 3 $COOCH_3$).

Anal. Calcd for $C_{14}H_{13}NO_6$ (mol wt 291.26): C, 57.73; H, 4.50; N, 4.81. Found: C, 57.62; H, 4.63; N, 4.75.

Trimethyl Indole-4,5,6-tricarboxylate (21) from 3a and DMAD. A solution of **3a**[6] (0.61 g, 2.90 mmol) in DMAD (0.83 g, 5.80 mmol) was heated at 60–65 °C under nitrogen for 24 h. The resulting black, tarry, gummy material was chromatographed on a column of silica gel (2 × 30 cm) and eluted with petroleum ether (bp 30–60 °C) [(1) 0.50 L], petroleum ether–benzene [(2) 4:1, 0.25 L; (3) 4:1, 0.50 L; (4) 2:1, 0.50 L; (5) 1:1, 0.50 L; (6) 1:2, 0.50 L], benzene [(7) 1.25 L, (8) 1.00 L], and benzene–chloroform [(9) 2:1, 1.00 L]. Fractions 1, 3–5, 7, and 9 gave no organic material. Fraction 2 gave unchanged DMAD (0.23 g, 28% recovery) having IR (neat)[23b,24b] and NMR ($CDCl_3$)[25b] spectra identical with those reported in the literature. Fraction 6 gave a trace of yellow oil which was not successfully characterized. Fraction 8 gave **21** as yellowish white crystals: 0.14 g (16%); mp 110–113 °C; IR (KBr) and NMR ($CDCl_3$) spectra identical with those of the sample prepared from **1a** and DMAD as described above.

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Registry No. 1a, 109-97-7; **1b**, 96-54-8; **1c**, 636-41-9; **1d**, 600-29-3; **1e**, 10524-65-9; **1f**, 625-82-1; **1i**, 589-33-3; **1j**, 20884-13-3; **1k**, 24764-40-7; **1l**, 2051-97-0; **1m**, 635-90-5; **1n**, 5145-71-1; **1o**, 5044-39-3; **1p**, 2437-42-5; **1q**, 15898-23-4; **1r**, 4533-42-0; **1s**, 609-41-6; **3a**, 66653-24-5; **3b**, 74985-91-4; **3c**, 74985-92-5; **3d**, 74985-93-6; **3e**, 74985-94-7; **3f**, 74985-95-8; **3i**, 74985-96-9; **3j**, 74985-97-0; **3k**, 74985-98-1; **3l**, 74985-99-2; **3m**, 74986-00-8; **3n**, 74986-01-9; **3o**, 74986-02-0; **3p**, 74986-03-1;

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Preparation and Bromination of a 3a,6-Dihydroindole[1]

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A 3a,6-dihydroindole was prepared by the Diels–Alder addition of dimethyl acetylenedicarboxylate to dimethyl [*N*-(2,6-dimethylphenyl)pyrrol-2-yl]maleate. Subsequent reaction with bromine gave a 2,3-dibromoindoline which is different from that obtained from the corresponding 3a,7a-dihydroindole.

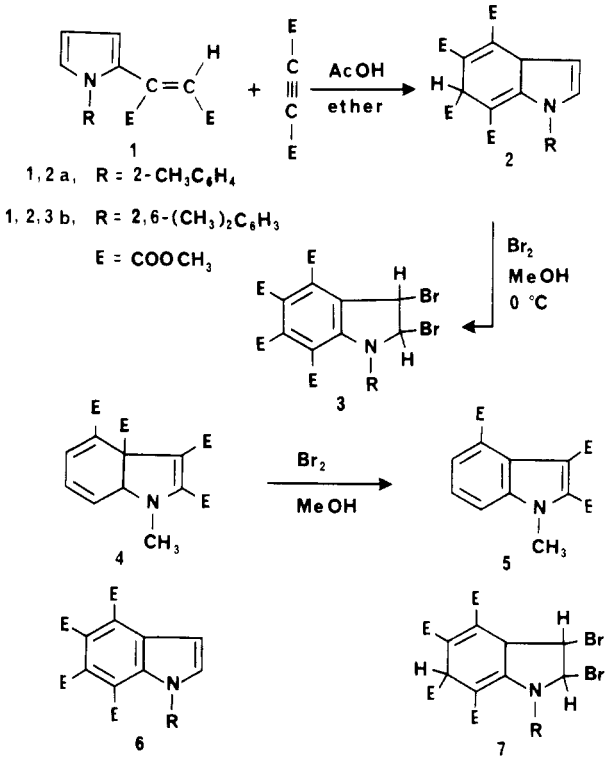
The 3a,6-dihydroindole structure **2** was suggested many years ago for an adduct of 1-methylpyrrole and dimethyl acetylenedicarboxylate (DMAD).[2] The correct structure has subsequently been shown to be **4**.[3] Several reactions have been reported, however, in which indoles are obtained via intermediates of type **2**.[4,5] We now report the isolation of a 3a,6-dihydroindole of this structure.

In an attempt to prepare indole compounds such as **6**, we prepared a series of (pyrrol-2-yl)maleate and -fumarate derivatives.[6] Interestingly, of the many (*N*-alkylpyrrol-2-yl)maleates (e.g., alkyl = CH_3, *n*-C_4H_9, *sec*-C_4H_9, *t*-C_4H_9, $C_6H_5CH_2$) and (*N*-arylpyrrol-2-yl)maleates (e.g., aryl = C_6H_5, *p*-BrC_6H_4, *p*-$(CH_3O)C_6H_4$) or -fumarates, only the bulky *N*-(2,6-dimethylphenyl)pyrrole derivative gave the adduct **2b** (Scheme I). Furthermore, compound **2b** was formed only when **1b** and DMAD were refluxed in ether–glacial acetic acid solution (1:1 by volume). Refluxing in benzene or xylene without the acid gave only tar and mostly recovered starting material. Pyrroles having bulkier N substituents such as a α-naphthyl or triphenylmethyl group did not give maleate or fumarate derivatives at all.

Structure **2b** was deduced by spectroscopic methods. The NMR spectrum ($CDCl_3$, Me_4Si) shows four singlets (δ 3.52, 3.63, 3.77, and 3.93), corresponding to the methyl ester groups, and two singlets at δ 1.92 and 2.03, indicating that the 2′- and 6′-methyl groups are nonequivalent. The cyclohexadiene portion of the 3a,6-dihydroindole moiety seems to have a boat[7] conformation; long-range coupling (1.5 Hz) between the 3a-H and 6-H was observed at δ 4.03 and 4.45 while the coupling between the 3-H and 3a-H was almost negligible. An AB quartet centered at δ 6.32 with J = 3.0 Hz is attributed to the olefinic 2-H and 3-H.

When *N*-(2-methylphenyl)pyrrole was refluxed with DMAD in ether–glacial acetic acid (1:1 by volume) solution, compound **2a** was isolated (8%) together with **1a** (both *E* and *Z* isomers).[6] However, attempts to repeat the isolation of **2a** were unsuccessful. Furthermore, compound **2a** could not be prepared from **1a** (both *E* and *Z* isomers)

Scheme I



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