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PYRROLE STUDIES—XXIV[1]

THE REACTIONS OF 1-METHYL-2-VINYLPYRROLE AND 1-PHENYL-2-VINYLPYRROLE WITH DIMETHYL ACETYLENEDICARBOXYLATE

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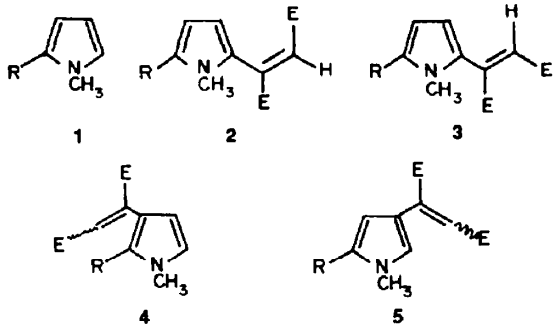
Abstract—The reaction of dimethyl acetylenedicarboxylate with 1-methyl-2-vinylpyrrole is temperature dependent. At 80° the predominant reaction is the $[4\pi + 2\pi]$ cycloaddition to give dimethyl 1-methyl-6, 7-dihydroindole-4, 5-dicarboxylate, whereas at room temperature Michael addition of the acetylenic ester at the 5-position of the pyrrole ring to give fumaric and maleic ester derivatives also occurs. Unequivocal assignment of the configurations of the Michael adducts have been made on the basis of their $^3J_{CO,H}$ coupling constants.

1-Phenyl-2-vinylpyrrole reacts with dimethyl acetylenedicarboxylate to give only the $[4\pi + 2\pi]$ cycloadduct at room temperature and at elevated temperatures.

During the course of our kinetic studies[2,3] on the cycloaddition of 1-methyl-2-vinylpyrrole with dimethyl acetylenedicarboxylate (DMAD) over the temperature range 20–40° we observed that the rate of disappearance of the vinylpyrrole did not correlate with the rate of formation of the expected 6, 7-dihydroindole-4, 5-dicarboxylic ester. This observation contrasts with earlier work,[4] which showed that at 80° the cycloaddition occurs smoothly with formation of only the dihydroindole. When the reaction was monitored at 20° by ^{1}H NMR spectroscopy, it appeared that, although the dihydroindole was being formed directly from the vinylpyrrole, other products which retained the vinyl group were also produced. A preparative scale reaction at 20° resulted in the isolation of two vinylpyrroles in a ratio of *ca* 2:1 and an overall yield of *ca* 30%, in addition to the dihydroindole and polymeric material. Elemental analysis and molecular weight determination established that the vinylic products resulted from a 1:1 addition of DMAD with 1-methyl-2-vinylpyrrole and spectral data indicated that both compounds were Michael-type adducts. Several examples are known of the Michael-type addition of DMAD to α-unsubstituted pyrroles to give products designated as (2-pyrrolyl)fumaric esters.[5] Thus, 1, 2-dimethylpyrrole (**1a**) is reported to give dimethyl (1,5-dimethyl-2-pyrrolyl)fumarate (**2a**).[6] The ^{1}H and ^{13}C NMR data and the electronic spectrum of **2a** were found to be closely similar to those for the major vinylic product obtained from 1-methyl-2-vinylpyrrole and, on this basis, the fumaric ester structure (**2b**) was initially assigned to this product.



1 **2** **3**

4 **5**

a: R = CH_3 **b**: R = $CH{=}CH_2$ **c**: R = CH_2CH_3
E = CO_2CH_3

In our hands, 1, 2-dimethylpyrrole gave a second product with DMAD in low yield, which was isomeric with Acheson's fumarate[7] and had physical properties which were similar to those of the minor product obtained from **1b**, suggesting that, as with the major products, the minor products also had closely related structures. Analysis of the ^{1}H and ^{13}C NMR spectra for the minor products from **1a** and **1b** clearly eliminated the possible structures **4** and **5**. In particular, the positions of the ^{13}C resonances for the ring C atoms and the coupling constants for the ring CH signals identifies the compounds as 2, 5-disubstituted pyrroles.[5] On the basis of Acheson's assignment for the fumaric ester (**2a**), the minor adducts were consequently considered initially to be the maleic esters (**3a** and **3b**). As further confirmation of the relationships between the pairs of adducts from **1a** and **1b**, catalytic hydrogenation of the adducts **2b** and **3b** gave the corresponding 5-ethyl-2-pyrrolyl derivatives (**2c** and **3c**), the spectroscopic properties of which were virtually identical with those of the corresponding 5-methyl compounds (**2a** and **3a**).

However, in comparison with the chemical shifts of 6.83 and 6.28 ppm, respectively, for the vinylic protons of dimethyl fumarate and dimethyl maleate, the assignment of the (2-pyrrolyl)fumaric ester structures to the compounds having vinylic proton resonances near 5.75 ppm and the maleic ester structures to the compounds showing lower field =CH resonances (Experimental) would appear anomalous. Examination of the long range CH spin coupling of the ^{13}C resonances for the CO groups under high resolution showed a clear distinction between the pairs of compounds, which leads to their unambiguous identification.[8] The lower field ^{13}C=O resonances for the higher m.p. adducts showed a three bond spin coupling of 12 Hz between the carbonyl carbon atom and the vinylic H atom, whereas the higher field ^{13}C=O resonance showed a smaller geminal $^2J_{CO,H}$ coupling of *ca* 1 Hz. In contrast, the lower field ^{13}C=O resonance for the lower m.p. adducts showed a smaller value of only 7 Hz for $^3J_{CO,H}$, whilst the two bond geminal coupling of the higher field ^{13}C=O resonances was 2 Hz. All of the signals were further split by a three bond spin coupling of 4 Hz between the carbonyl C atom and the protons of the respective Me groups. A larger $^3J_{CO,H}$ spin coupling should arise from a *trans*

configuration of the CO group and the vinylic H atom, whilst the *cis* configuration should produce the smaller three bond coupling.[9] This analysis clearly establishes that Acheson's "fumarate"[6] is a maleic ester and, consequently, identifies the major Michael adducts, having the higher m.p.s, from both **1a** and **1b** as dimethyl (2-pyrrolyl)maleates (**3**).

In contrast with the change in the reaction pathway of DMAD with 1-methyl-2-vinylpyrrole with the change in temperature, it was found that 1-phenyl-2-vinylpyrrole gave the $[4\pi + 2\pi]$-cycloadduct exclusively over a temperature range from 20–80°. The rate of the cycloaddition, however, was *ca* 5 times faster than the corresponding rate for 1-methyl-2-vinylpyrrole under similar conditions.[3] This difference in reactivity is probably due to a steric effect of the phenyl substituent, which helps to restrain the diene system in the necessary *cisoid* conformation for the cycloaddition reaction. The failure of the Michael reaction could also be a result of steric hindrance, but may be due partially to an electron withdrawing effect of the phenyl ring.

EXPERIMENTAL

^{1}H NMR spectra were measured for *ca* 0.2 M solns in CCl_4 (unless stated otherwise) using a Varian HA-100 spectrometer. Chemical shifts are reported downfield from the internal standard (Me_4Si). ^{13}C NMR spectra were recorded using a JEOL FX-100 spectrometer operating at 25.05 MHz under conditions which gave a digital resolution equivalent to 0.048 ppm. Samples were prepared as *ca* 0.5 M solns in $CDCl_3$, which also provided the lock signal and chemical shifts are reported relative to Me_4Si. IR spectra were measured as liquid films or as *ca* 0.2 M solns in $CHBr_3$ using a Perkin–Elmer 297 spectrophotometer and electronic spectra were recorded for *ca* 10^{-5} M solns in EtOH using a Unicam SP 8-200 spectrophotometer.

1, 2-*Dimethylpyrrole*[6] had b.p. 140–145° (lit.,[6] b.p. 139–140° at 745 mm). ^{1}H NMR δ 2.06 (s, 3H), 3.29 (s, 3H), 5.60 (m, 1H), 5.72 (t, 1H) and 6.21 ppm (t, 1H). ^{13}C NMR δ 11.8 (C<u>Me</u>), 33.5 (NMe), 106.4 (C3), 106.5 (C4), 120.8 (C5) and 128.7 ppm (C2).

1-*Methyl-2-vinylpyrrole*[4] had b.p. 64° at 14 mm (lit.,[4] b.p. 62–64° at 16 mm). ^{1}H NMR δ 3.43 (s, 3H), 4.91 (dd, J = 1.6 and 11.2 Hz, 1H), 5.33 (dd, J = 1.6 and 17.5 Hz, 1H), 5.90 (m, 1H), 6.17 (dd, 1H), 6.36 (t, 1H) and 6.46 ppm (dd, J = 17.5 and 11.2 Hz, 1H). ^{13}C NMR δ 34.0 (NMe), 106.5 (C4), 107.7 (C3) 110.8 (=CH_2), 123.1 (C5), 125.4 (=CH–) and 132.0 ppm (C2).

1-*Phenyl-2-vinylpyrrole*[4] had b.p. 86–87° at 16 mm (lit.,[4] b.p. 85–86° at 15 mm). ^{1}H NMR δ 4.86 (dd, J = 11 and 1.7 Hz, 1H), 5.34 (dd, J = 17.5 and 1.7 Hz, 1H), 6.12 (dd, 1H), 6.33 (dd, J = 11 and 17.5 Hz, 1H), 6.42 (dd, 1H), 6.62 (dd, 1H) and 7.65 ppm (m, 5H). ^{13}C NMR δ 107.2 (C4), 109.2 (C3), 111.1 (=CH_2), 123.0 (C5), 126.1 (phenyl C2, 6), 126.3 (=CH–), 127.1 (phenyl C4), 129.0 (phenyl C3, 5), 132.2 (C2) and 139.7 ppm (phenyl C1).

Reaction of 1, 2-*dimethylpyrrole with dimethyl acetylenedicarboxylate.* Dimethyl acetylenedicarboxylate (1.8 g, 0.0125 mol) was added to 1, 2-dimethylpyrrole (1.0 g, 0.01 mol) in ether (30 ml) and the mixture was allowed to stand at 20° for 24 hr. Evaporation of the solvent gave an oil, which was purified by tlc on silica with 1:1 petroleum ether (b.p. 40–60°):diethyl ether, to give dimethyl (1, 5-dimethyl-2-pyrrolyl)maleate (0.45 g, 23%)† (R_f 0.40, m.p. 91–92° (lit.,[10] m.p. 92°). ^{1}H NMR $\equiv$ 2.19 (d, J = 0.8 Hz, 3H), 3.53 (s, 3H), 3.67 (s, 3H), 3.79 (s, 3H), 5.73 (s, 1H), 5.81 (dq, J = 0.8 and 4 Hz, 1H) and 6.19 ppm (d, J = 4 Hz, 1H). ^{13}C NMR δ 13.0 (C<u>Me</u>) 32.9 (NMe), 51.6 (OMe), 52.6 (OMe), 108.9 (C4), 109.2 (C3), 115.6 (=C<u>H</u>.CO_2Me), 126.6 (=Ç.CO_2Me), 137.4 (C5), 141.0 (C2, 166.1 (=CH.ÇO_2Me) and 168.2 ppm (=C.ÇO_2Me); ν C=O 1730 and 1710 cm^{-1}; λ_{max} 350 nm (log ϵ 3.37) and *dimethyl* (1, 5-*dimethyl-2-pyrrolyl*) *fumate* (0.1 g, 5%)† (R_f 0.55), m.p. 38–40° (Found: C, 61.0; H, 6.4; N, 5.6. $C_{12}H_{15}NO_4$ requires: C, 60.7; H, 6.4; N, 5.9%). ^{1}H NMR δ 2.14 (d, J = 0.8 Hz, 3H), 3.23 (s, 3H), 3.55 (s, 3H), 3.71 (s, 3H), 5.71 (dq, J = 0.8 and 3.6 Hz, 1H), 5.92 (d, J = 3.6 Hz, 1H) and 6.68 ppm (s, 1H). ^{13}C NMR δ 12.7 (C<u>Me</u>), 31.5 (NMe), 51.8 (OMe), 52.9 (OMe), 107.0 (C4), 111.6 (C3), 124.6 (=Ç.CO_2Me), 128.0 (=ÇH.CO_2Me), 132.1 (C5), 135.7 (C2), 165.7 (=CH.ÇO_2Me) and 167.0 ppm (=C.ÇO_2Me); ν C=O 1720 cm^{-1}; λ_{max} 382 nm (log ϵ 3.49), together with unchanged 1, 2-dimethylpyrrole (0.29 g).

Reaction of 1-*methyl-2-vinylpyrrole with dimethyl acetylenedicarboxylate*

(a) *At* 20°. Dimethyl acetylenedicarboxylate (2.64 g, 0.018 mol) was added to 1-methyl-2-vinylpyrrole (1.98 g, 0.018 mol) and hydroquinone (20 mg) in chloroform (20 ml) and the mixture was stirred at 20° for 4 days. Evaporation of the solvent gave an oil, which was separated by preparative tlc on silica with petroleum ether (b.p. 40–60°):diethyl ether (1:1) to give *dimethyl* (5-*vinyl-2-pyrrolyl*) *maleate* (0.93 g, 20%) (R_f 0.40), m.p. 77° (Found: C, 63.1; H, 6.2; N, 5.35. $C_{13}H_{15}NO_4$ requires: C, 62.65; H, 6.0; N, 5.6%). ^{1}H NMR δ 3.57 (s, 3H), 3.64 (s, 3H), 3.76 (s, 3H), 5.16 (dd, J = 11 and 1.5 Hz, 1H), 5.52 (dd, J = 17.5 and 1.5 Hz, 1H), 5.77 (s, 1H), 6.27 (s, 2H) and 6.53 ppm (dd, J = 11 and 17.5 Hz, 1H). ^{13}C NMR δ 33.0 (NMe), 51.8 (OMe), 52.8 (OMe), 107.8 (C4), 111.9 (C3), 115.8 (=ÇH.CO_2Me), 115.8 (=CH_2), 124.9 (=CH–), 128.3 (=Ç.CO_2Me), 139.3 (C5), 140.4 (C2), 165.8 (=CH.ÇO_2Me) and 167.9 ppm (=C.ÇO_2Me); ν C=O 1715 and 1735 cm^{-1}; λ_{max} 277 (log ϵ 3.80) and 366 nm (log ϵ 4.35), *dimethyl* (5-*vinyl-2-pyrrolyl*)*fumarate* (0.41 g, 9%) (R_f 0.55), b.p. 205° at 0.001 mm (Found: C, 63.0; H, 6.3; N, 5.6%). ^{1}H NMR δ 3.35 (s, 3H, 3.58 (s, 3H), 3.74 (s, 3H), 5.04 (dd, J = 11 and 1.5 Hz, 1H), 5.45 (dd, J = 17.5 and 1.5 Hz, 1H), 6.01 (d, J = 4 Hz, 1H), 6.23 (d, J = 4Hz, 1H), 6.53 (dd, J = 11 and 17.5 Hz, 1H) and 6.84 ppm (s, 1H). ^{13}C NMR δ 31.9 (NMe), 51.9 (OMe), 53.0 (OMe), 106.4 (C4), 112.3 (C3), 112.7 (=CH_2), 125.5 (=CH–), 129.1 (=Ç.CO_2Me), 129.3 (=ÇH.CO_2Me), 134.8 (C5), 135.0 (C2), 165.5 (=CH.ÇO_2Me) and 166.6 ppm (=C.ÇO_2Me); ν C=O 1720 cm^{-1}; λ_{max} 282 (log ϵ 3.88) and 378 nm (log ϵ 2.08), together with dimethyl 1-methyl-6, 7-dihydroindole-4, 5-dicarboxylate (0.97 g, 21%) (R_f 0.16), b.p. 159–160° at 0.001 mm (lit.,[4] b.p. 132° at 5×10^{-5} mm) and polymeric material.

(b) *Under reflux conditions.* 1-Methyl-2-vinylpyrrole (1.98 g, 0.018 mol), dimethyl acetylenedicarboxylate (2.64 g, 0.018 mol) and hydroquinone (20 mg) in chloroform (20 ml) were refluxed for 3 hr and the solvent was then removed under vacuum. Analysis of the residual oil by tlc showed the absence of the Michael adducts and the distillation of the oil gave dimethyl 1-methyl-6,7-dihydroindole-4,5-dicarboxylate (3.25 g, 70%) b.p. 155–160° at 0.001 mm.

Dimethyl (5-*ethyl-2-pyrrolyl*)*maleate.* Hydrogenation of dimethyl (5-vinyl-2-pyrrolyl)maleate (0.36 g) in EtOH (5 ml) in the presence of Pd–C (5%, 15 mg) at atmospheric pressure for 18 hr gave *dimethyl* (5-*ethyl-2-pyrrolyl*)*maleate* (0.32 g, 88%), m.p. 85–86°, which was further purified for analysis by preparative tlc on silica using petroleum ether (b.p. 40–60°) as the eluant. (Found: C, 61.8; H, 7.1; N, 5.4. $C_{13}H_{17}NO_4$ requires: C, 62.1; H, 6.8; N, 5.6%). ^{1}H NMR ($CDCl_3$) δ 1.26 (t, 3H), 2.55 (q, 2H), 3.52 (s, 3H), 3.67 (s, 3H), 3.85 (s, 3H), 5.82 (s, 1H), 5.91 (d, 1H) and 6.31 ppm (d, 1H); ^{13}C NMR δ 12.5 (ÇH$_3$CH$_2$), 20.3 (CH$_3$ÇH$_2$), 32.7 (NMe), 51.7 (OMe), 52.8 (OMe), 107.1 (C4), 109.6 (C3), 115.6 (=ÇH.CO_2Me), 126.7 (=Ç.CO_2Me), 141.0 (C2), 143.3 (C5), 166.1 (=CH.ÇO_2Me) and 168.3 ppm (=C.ÇO_2Me); ν C=O 1770 and 1730 cm^{-1}; λ_{max} 244 (infl.) (log ϵ 3.64) and 350 nm (log ϵ 3.99).

Dimethyl (5-*ethyl-2-pyrrolyl*)*fumarate.* Hydrogenation of dimethyl (5-vinyl-2-pyrrolyl)fumarate (0.31 g) under conditions similar to those used for the hydrogenation of the corresponding maleate gave *dimethyl* (5-*ethyl-2-pyrrolyl*)*fumarate* (0.3 g, 96%), m.p. 30–32° (Found: C, 61.7; H, 6.7; N, 5.3%). ^{1}H NMR ($CDCl_3$)δ 1.19 (t, 3H), 2.49 (q, 2H), 3.19 (s, 3H), 3.56 (s, 3H), 3.70 (s, 3H), 5.82 (d, 1H), 6.06 (d, 1H) and 6.78 ppm (s, 1H); ^{13}C NMR δ 12.4 (ÇH$_3$CH$_2$), 20.1 (CH$_3$ÇH$_2$), 31.3 (NMe), 51.9 (OMe), 52.9 (OMe), 105.0 (C4), 111.4 (C3), 124.6 (=Ç.CO_2Me), 127.8 (=ÇH.CO_2Me), 135.5 (C2), 138.2 (C5), 165.7 (=CH.ÇO_2Me), and 167.0 (=C.ÇO_2Me); ν C=O 1725 cm^{-1}; λ_{max} 381 nm (log ϵ 3.29).

†Calculated on unrecovered 1, 2-dimethylpyrrole.

Reaction of 1-phenyl-2-vinylpyrrole with dimethyl acetylenedicarboxylate

(a) *At 20°.* Dimethyl acetylenedicarboxylate (1.44 g, 0.01 mol) was added to 1-phenyl-2-vinylpyrrole (1.69 g, 0.01 mol) and hydroquinone (15 mg) in chloroform (20 ml) and the mixture was stirred at 20° for 4 days. Evaporation of the solvent gave an oil, which was separated by preparative tlc on silica with petroleum ether (b.p. 40–60°):diethyl ether (1:1) to give dimethyl 1-phenyl-6, 7-dihydroindole-4, 5-dicarboxylate (2.0 g, 65%), m.p. 108–109° (lit.,[4] m.p. 109°) and unchanged 1-phenyl-2-vinylpyrrole (0.46 g).

(b) *Under reflux conditions.* 1-phenyl-2-vinylpyrrole (1.69 g, 0.01 mol) and dimethyl acetylenedicarboxylate (1.44 g, 0.01 mol) in chloroform (10 ml) were refluxed for 3 hr. The solvent was removed under vacuum and the dihydroindole diester (2.49 g, 80%) m.p. 109° was recrystallised from benzene.

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[10]This melting point was reported previously for the fumaric ester.[6]