186. *Addition Reactions of Heterocyclic Compounds. Part XII.* Pyrroles and Acetylene Derivatives.*

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Acetylenedicarboxylic acid and its dimethyl ester combine with methyl pyrrole-1-carboxylate and 1,2-dimethylpyrrole, respectively, to give the corresponding pyrrolylfumaric acid derivatives; the first reaction also gives a Diels–Alder type adduct.

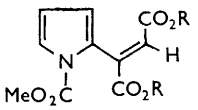
Methyl pyrrole-1-carboxylate and dimethyl acetylenedicarboxylate yield [1] trimethyl pyrrole-1,3,4-tricarboxylate and acetylene, presumably through the intermediacy of a Diels–Alder type adduct (VII). Small yields of isomeric yellow and colourless 1 : 1 molar adducts have now been obtained by using acetylenedicarboxylic acid.

Structure (I), analogous to that of one of the adducts from 1-benzylpyrrole and acetylenedicarboxylic acid,[2] accounts for the properties of the yellow adduct. This adduct gave a strong Ehrlich reaction and with diazomethane afforded a triester (II) which was oxidised to pyrrole-2-carboxylic acid, and alkaline hydrolysis followed by reaction with diazomethane yielded a diester (III) which, unlike compounds (I) and (II), possessed N–H absorption in the infrared region. The ultraviolet absorption spectrum of the diester (III) closely resembles that of the adduct (IV), but as dimethyl 1-benzyl-2-pyrrolylmaleate

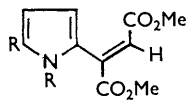
* Part XI, Acheson and Plunkett, *J.*, 1962, 3758.

[1] Acheson and Vernon, *J.*, 1961, 457; Gabel, *J. Org. Chem.*, 1962, **27**, 301.
[2] Mandell and Blanchard, *J. Amer. Chem. Soc.*, 1957, **79**, 6198.

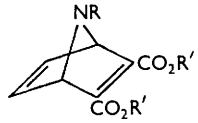
absorbs at somewhat shorter wavelengths [3] compounds (I—IV) are probably all *trans*. Pyrrole and dimethyl acetylenedicarboxylate gave a yellow oil whose analyses corresponded rather poorly to those for a 1 : 1 molar adduct but whose infrared absorption spectrum was very similar to that of the diester (III).



(I ; R = H)
(II ; R = Me)



(III ; R = H)
(IV ; R = Me)



(V ; R = CH_2Ph, R′ = H)
(VI ; R = CO_2Me, R′ = H)
(VII ; R = CO_2Me, R′ = Me)

The colourless adduct (VI) gave a very pale red colour with Ehrlich's reagent and on partial hydrogenation followed by heating with alkali yielded pyrrole-3,4-dicarboxylic acid. The adduct (V) from 1-benzylpyrrole and acetylenedicarboxylic acid behaves analogously [2] and with diazomethane disproportionates to 1-benzylpyrrole and dimethyl acetylenedicarboxylate.[3] The colourless adduct (VI) with an excess of diazomethane gave neither compound (VII) nor its immediate disproportionation products, but yielded dimethyl pyrazole-3,4-dicarboxylate and an *N*-methyl derivative. These pyrazoles were also obtained from dimethyl acetylenedicarboxylate and diazomethane although the formation of only dimethyl pyrazole-3,4-dicarboxylate was detected previously.[4] The *N*-methylation, which probably occurs vicinally to an ester group on analogy with von Auwers's observations,[5] is doubtless facilitated by the ester groups. Partial *N*-demethylation contributes to the high " methoxyl " analysis of the *N*-methylpyrazole.

1,2-Dimethylpyrrole, obtained by Wolff–Kishner reduction of 2-formyl-1-methylpyrrole, is the first *N*-substituted pyrrole which has been observed to yield a 1 : 1 molar adduct with dimethyl acetylenedicarboxylate. The positive Ehrlich reaction and the ultraviolet absorption spectrum of this adduct are incompatible with a bicyclic structure analogous to (V) but are expected of the pyrrolylfumaric ester (IV). 1,2,5-Trimethylpyrrole, obtained from acetonylacetone and methylamine, and 1,2,3,4,5-pentamethylpyrrole gave only dark red tars with dimethyl acetylenedicarboxylate.

Experimental

Methyl Pyrrole-1-carboxylate and Acetylenedicarboxylic Acid.—Methyl pyrrole-1-carboxylate (7·0 g.) was added to acetylenedicarboxylic acid (6·4 g.) in hot benzene (50 ml.), and the mixture was refluxed for 10 hr. The hot solution was decanted from some dark tar and evaporated. Washing the residue with ether (10 ml.) gave back some methyl pyrrole-1-carboxylate (3 g.). The insoluble material was extracted with boiling water (charcoal) and, on cooling, the filtrate deposited a mixture of yellow prisms and small colourless crystals. Some of the yellow crystals were hand-picked and recrystallised from water or acetonitrile, to give *1-methoxycarbonylpyrrol-2-ylfumaric acid* (I) (0·2 g.) as yellow prisms, darkening above 200°, m. p. 215° (decomp.) (Found: C, 50·3; H, 3·9; N, 5·9. $C_{10}H_9NO_6$ requires C, 50·2; H, 3·8; N, 5·9%). *Dimethyl 1-methoxycarbonylpyrrol-2-ylfumarate* (II), obtained with diazomethane, had b. p. 140—150°/0·05 mm. and separated from methanol as yellow needles, m. p. 63° (Found: C, 54·2; H, 4·8; N, 5·8; OMe, 35·0. $C_{12}H_{13}NO_6$ requires C, 53·9; H, 4·9; N, 5·1; 3OMe, 34·8%). It gave a red Ehrlich colour on heating.

The colourless product was partially separated by shaking the lightly crushed mixed crystals with water and decanting the suspension. Recrystallisation from water afforded colourless adduct (VI) (*7-methoxycarbonyl-7-azabicyclo*[2,2,1]*hepta-2,5-diene-2,3-dicarboxylic acid*) (0·4 g.) as a powder, m. p. 197° (decomp.) (Found: C, 50·1; H, 3·8; N, 6·3; OMe, 12·8. $C_{10}H_9NO_6$ requires C, 50·2; H, 3·8; N, 5·9; OMe, 13·0%).

[3] Acheson and Vernon, *J.*, 1962, 1148.
[4] Diels and Thiele, *Ber.*, 1938, **71**, 1173.
[5] von Auwers and Ungemach, *Ber.*, 1933, **66**, 1690; von Auwers and Breyhan, *J. prakt. Chem.*, 1935, **143**, 259.

The remaining unresolved mixture of yellow and white adducts was combined (total 1 g.) with residues obtained on evaporation of aqueous crystallisation mother-liquors and chromatographed on a column of silica gel (100 g.) prepared in benzene. Fractions (600 ml.) were eluted successively with benzene, benzene–chloroform (1 : 1 v/v), chloroform, and chloroform–methanol (9 : 1 v/v), and separately evaporated to sticky residues. That extracted by benzene–chloroform crystallised from water (charcoal), giving some yellow adduct (I) (30 mg.), while the chloroform–methanol extract similarly gave the adduct (VI) (60 mg.). Total yields of the adducts calculated on the pyrrole-1-ester consumed were (I) 3% and (VI) 6%.

Degradation of the Adduct (VI).—(i) The colourless adduct (VI) (150 mg.) in 10% aqueous sodium carbonate (10 g.) was hydrogenated at atmospheric pressure over 5% palladium–charcoal (50 mg.). Hydrogen (1·0 mol.) was absorbed in 15 min., then the rate of absorption decreased and after filtration the solution was refluxed with sodium hydroxide (0·1 g.) for 12 hr. After cooling and acidification by hydrochloric acid, a white precipitate (30 mg.) was formed very slowly and it was collected next morning; it gave a red colour after several minutes' heating with Ehrlich's reagent. Esterification with diazomethane and crystallisation of the product from methanol afforded colourless needles, m. p. 243—244° (18 mg., 7%). This ester gave a purple Ehrlich colour on boiling and was identical in respect of mixed m. p. and infrared absorption spectrum (including $\nu_{max.}$ at 3·05 μ for N–H) with an authentic sample of dimethyl pyrrole-3,4-dicarboxylate [1] of m. p. 245°.

(ii) The colourless adduct (VI) (0·2 g.) in methanol was treated with an excess of diazomethane in ether. Evaporation after 15 min. gave an oil which on distillation gave two fractions of b. p. 100—150°/0·1 mm. (0·15 g.) and 150—200°/0·1 mm. (0·03 g.), severally, which crystallised. The first fraction, on redistillation at 120°/(bath)/0·09 mm., gave a product, m. p. 50—51° alone or mixed with dimethyl 1-methylpyrazole-3,4- or -4,5-dicarboxylate. The second, less volatile product crystallised from benzene–light petroleum (b. p. 60—80°) as needles (Found: N, 15·0. Calc. for $C_7H_8N_2O_4$: N, 15·2%), m. p. 140° alone or mixed with dimethyl pyrazole-3,4-dicarboxylate.

Diazomethane and Dimethyl Acetylenedicarboxylate.—An excess of diazomethane in ether was added gradually to dimethyl acetylenedicarboxylate (2 g.) in methanol (10 ml.), causing effervescence and precipitation of a colourless solid. A portion of the solid was collected immediately and crystallisation from benzene–light petroleum (b. p. 60—80°) gave needles of dimethyl pyrazole-3,4-dicarboxylate, m. p. 140° (lit.,[4] 141°).

With the excess of diazomethane the precipitated pyrazole redissolved in ½ hr., and evaporation gave a partially crystalline residue which had b. p. 110—120° (bath)/0·1 mm., yielding a colourless distillate, m. p. 48—50°. Crystallisation from ether–light petroleum (b. p. 40—60°) gave irregular prisms of *dimethyl 1-methylpyrazole-3,4- or -4,5-dicarboxylate*, m. p. 51—51·5° (Found: C, 48·6; H, 5·3; N, 14·0; OMe, 41·7; OMe and NMe, calc. as Me, 22·6. $C_8H_{10}N_2O_4$ requires C, 48·5; H, 5·1; N, 14·1; 2OMe, 31·3; 3Me, 22·7%).

Oxidation of Dimethyl 1-Methoxycarbonylpyrrol-2-ylfumarate (II).—The triester (5 mg.), 5N-aqueous sodium carbonate (0·05 ml.), and 30% hydrogen peroxide (0·05 ml.) were mixed. After 18 hr. more hydrogen peroxide (0·05 ml.) was added and the mixture was heated at 70° for 1 hr. The residue, obtained on evaporation *in vacuo*, dissolved in water and was acidified by hydrochloric acid and again evaporated. The residue in aqueous ethanol was examined by chromatography (6 hr.) on Whatman No. 1 paper in ascending butan-1-ol (100 ml.)–2N-ammonia (20 ml.). Spraying with Ehrlich's reagent showed a violet spot (R_F 0·93) with a long blue tail and a compound identical in properties with pyrrole-2-carboxylic acid chromatographed alongside [pink (R_F 0·14), becoming violet, then blue; lit.,[6] in this solvent system, R_F 0·12; pyrrole-3-carboxylic acid R_F 0·04].

Dimethyl Pyrrol-2-ylfumarate (III).—The yellow adduct (0·1 g.) and 10% methanolic potassium hydroxide (1 ml.) were heated on the water-bath for 2 hr., cooled, filtered, and evaporated. The residue dissolved in water and acidification to Congo Red gave a yellow precipitate which darkened above 140° but did not melt sharply below 300°. This product in ether with diazomethane gave *dimethyl pyrrol-2-ylfumarate* (III) as a pale yellow oil, b. p. 110°/0·05 mm. (Found: C, 57·8; H, 5·5; N, 7·0; OMe, 28·9, $C_{10}H_{11}NO_4$ requires: C, 57·4; H, 5·3; N, 6·7; 2OMe, 29·6%), $\nu_{max.}$ 3·10 μ (N–H), $\lambda_{max.}$ 3540 Å, that gave a red Ehrlich reaction.

1,2-Dimethylpyrrole.—2-Formyl-1-methylpyrrole (4 g.), 100% hydrazine hydrate (20 ml.), and diethylene glycol (100 ml.) were refluxed for 2 hr. under nitrogen. The condenser was

[6] Nicolaus and Mangoni, *Gazzetta*, 1955, **85**, 1397.

removed and the liquid boiled until the internal temperature reached 220°, to expel the excess of hydrazine. After cooling, potassium hydroxide (10 g.) was added and the mixture gently heated while nitrogen was evolved. The liquid distilling (under nitrogen) up to 200° was then collected (*ca.* 50 ml.) and water (100 ml.) was added. Extraction with light petroleum (b. p. 40—60°) (100 ml.), drying (Na_2SO_4), and distillation gave 1,2-dimethylpyrrole (2·8 g.), b. p. 139—140°/756 mm. (lit.,[7] b. p. 140°).

Reaction of 1,2-*Dimethylpyrrole and Dimethyl Acetylenedicarboxylate.*—1,2-Dimethylpyrrole (0·4 g.) and dimethyl acetylenedicarboxylate (0·6 g.) in ether (10 ml.) were mixed and set aside for 24 hr. at room temperature. Evaporation gave a tar which on crystallisation from methanol afforded *dimethyl* 1,5-*dimethylpyrrol*-2-*ylfumarate* (IV) (0·4 g.), pale yellow crystals, m. p. 92° (Found: C, 60·6; H, 6·1; N, 6·3; OMe, 26·0. $C_{12}H_{15}NO_4$ requires C, 60·8; H, 6·3; N, 5·9; 2OMe, 26·2%).

This adduct (IV) had $\lambda_{max.}$ 3500 Å in methanol; it gave a red Ehrlich colour slowly in the cold, more intensely on heating, and did not react with refluxing methyl iodide.

1,2,5-*Trimethylpyrrole.*—40% Aqueous methylamine (52 g.) was added dropwise in ½ hr. to acetonylacetone (38 g.) and glacial acetic acid (60 g.). After a further ½ hr. the mixture was heated for 1 hr. on the water-bath. The red oil was collected with ether (2 × 100 ml.); the extract was washed with water, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and distilled, yielding 1,2,5-trimethylpyrrole (27 g.), b. p. 166—168°/745 mm. (lit.,[8] b. p. 169°/746 mm.).

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[7] Lukeš and Pliml, *Coll. Czech. Chem. Comm.*, 1956, **21**, 632.
[8] Knorr and Franzen, *Annalen*, 1886, **236**, 304.