431. *Addition Reactions of Heterocyclic Compounds. Part V.* Some Pyrazoles and Methyl Acetylenedicarboxylate.*

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Pyrazole and its 3,5-dimethyl and 3,4,5-trimethyl derivatives reacted with 2 mols. of methyl acetylenedicarboxylate to give methyl αβ-di-1-pyrazolylsuccinates. From the trimethylpyrazole and 1 mol. of the ester the methyl 1-pyrazolylfumarate was obtained. None of these adducts showed an infrared absorption maximum at 3·20μ which is characteristic of the N–H bond in pyrazoles unsubstituted at position 1.

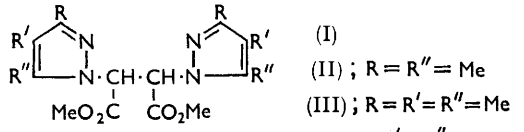
Methyl acetylenedicarboxylate is reported [1] to combine with 2 mols. of pyrazole to give two isomeric adducts, and with 3,5-dimethylpyrazole giving both 1 : 1 and 1 : 2

* Part IV, *J.*, 1960, 1691.

[1] Diels, Alder, Winckler, and Petersen, *Annalen*, 1932, **489**, 1.

adducts; no structures were suggested for these adducts. It is also known [2] that a Michael addition takes place between 3,5-dimethylpyrazole and crotonic acid, as the product is the same as that obtained from 3-hydrazinobutyric acid and acetylacetone. It appeared therefore that the adducts obtained from the acetylenic ester might also be formed through similar Michael additions, and this proved to be the case with several pyrazoles not substituted on the nitrogen atom at position 1.

Pyrazole and its 3,5-dimethyl and 3,4,5-trimethyl derivatives combined with 2 mols. of methyl acetylenedicarboxylate giving products of similar ultraviolet spectra to the parent pyrazoles. As the parent pyrazoles with a hydrogen atom at position 1 possess strong broad absorption bands at *ca.* 3·20 μ, which is in the correct region for a bonded N–H, while this band is absent in the adducts from 3,5-dimethyl- and 3,4,5-trimethyl-pyrazole,

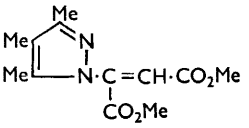


(I)

(II); R = R″ = Me

(III); R = R′ = R″ = Me

otherwise R = R′ = R″ = H



(IV)

it appeared that a double Michael addition had occurred and that the products were (II) and (III). In the case of the adduct from pyrazole (I) a small residual absorption, probably due to impurity, was still observed at 3·20 μ in spite of repeated crystallisation. In confirmation of structure (I) this adduct was recovered unchanged from acetic anhydride, under conditions which were simultaneously shown to acetylate pyrazole itself, and gave no pyrazolecarboxylic acid with potassium permanganate, which converts [3] 4-methylpyrazole into the corresponding carboxylic acid.

The structure of the adduct from 3,5-dimethylpyrazole has been confirmed by synthesis from this pyrazole and methyl αβ-dibromosuccinate; pyrazoles alkylate quite readily with alkyl halides.[4] An objection to this proof, that the ester might be dehydrobrominated to the acetylenic ester, cannot be sustained as 3,5-dimethylpyrazole is very weakly basic and very strong alkali is needed for the dehydrobromination. This adduct (III) does not appear to react with picric or styphnic acids but is dibasic to anhydrous perchloric acid in acetic acid. The 2 : 1 adducts from pyrazole and 3,5-dimethylpyrazole corresponded to two of those reported by Diels and Alder.[1] Unsuccessful attempts were made to isolate an isomeric adduct from pyrazole which was obtained previously on only one occasion.[1]

Diels and Alder describe a 1 : 1 molar adduct from 3,5-dimethylpyrazole and the acetylenic ester. Many unsuccessful attempts were made to prepare this compound, but a presumably similar 1 : 1 adduct was obtained from 3,4,5-trimethylpyrazole. This adduct showed two absorption bands in the carbonyl region of the infrared but no N–H band, and its ultraviolet absorption spectrum indicated more conjugation than that present in 3,4,5-trimethylpyrazole or in ester (III). These results are consistent only with structure (IV), and it is likely that the ester groups are *trans* by analogy with other similar additions.[5] The ultraviolet absorption spectra of all the pyrazoles and their adducts were virtually unchanged by the addition of acid, but on basification the absorption in the region of 2100—2200 Å increased enormously and no maxima could be observed; this change was reversible.

As 1-methylpyrrole with methyl acetylenedicarboxylate gives an adduct, the structure of which is now under investigation, 1-methyl-, 1,3,5-trimethyl-, and 1-phenylpyrazole were prepared. Although these pyrazoles reacted with the acetylenic ester to give deep red products no crystalline materials have so far been isolated.

[2] Alder, K., "Die Methoden der Dien-synthese" (Handbuch der Biologischen Arbeitsmethoden. ed. E. Abderhalden), 1933, p. 3080—3192, Abt. I, Teil 2/II.

[3] Jones, *J. Amer. Chem. Soc.*, 1949, **71**, 3997.

[4] Auwers and Breyhan, *J. prakt. Chem.*, 1935, **143**, 259, and earlier works; Jones, Mann, and McLaughlin, *J. Org. Chem.*, 1954, **19**, 1428.

[5] Parts I and II, *J.*, 1954, 3240; 1956, 246.

Schönberg and Mostafa [6] claim that anthranil and maleic anhydride combine in toluene to give a 1 : 1 addition compound, for which they proposed two structures; others are possible. All attempts to prepare the adduct under the conditions specified, and in hot xylene irradiated with ultraviolet light, gave back the starting materials; no reaction could be detected between anthranil and methyl acetylenedicarboxylate (at 140°) or hexachlorocyclopentadiene (at 100°).

Experimental

Methyl αβ-*Di*-1-*pyrazolylsuccinate* (I).—Methyl acetylenedicarboxylate (0·9 ml.) and pyrazole [3] (1·0 g.) in ether (20 ml.) were left at room temperature (24 hr.). The precipitate (0·23 g.) was collected and more material (0·32 g.) precipitated slowly during 4 days; evaporation of the filtrate gave more of the same adduct and no trace of an isomer could be detected. Recrystallisation from methanol gave the *succinate* as crystals, m. p. 158° (Found: C, 52·0; H, 5·1; N, 20·2. $C_{12}H_{14}N_4O_4$ requires C, 51·9; H, 5·0; N, 20·2%). In methanol it showed $\lambda_{max.}$ 2175 Å ($\varepsilon_{max.}$ 11,200), and in paraffin paste a single maximum at 5·79 μ in the carbonyl region.

Methyl αβ-*Di*-(3,5-*dimethyl*-1-*pyrazolyl*)*succinate* (II).—(i) This was prepared as above from 3,5-dimethylpyrazole [3·0 g.; $\lambda_{max.}$ 2130 Å ($\varepsilon_{max.}$ 7900) in methanol] and the ester (5·0 g.) in dry ether (87 ml.) and the precipitate collected after 1, 4, and 10 days. The final filtrate on evaporation gave a brown oil, from which no trace of the described 1 : 1-adduct could be obtained. The combined precipitates, all of which melted within a few degrees of the analytical sample, crystallised from ethyl acetate in needles, m. p. 188° (Found: C, 57·3; H, 6·5; N, 16·8. Calc. for $C_{16}H_{22}N_4O_4$: C, 57·2; H, 6·6; N, 16·8%). In methanol the ester showed $\lambda_{max.}$ 2220 Å ($\varepsilon_{max.}$ 14,520) and in paraffin paste one maximum at 5·79 μ in the carbonyl region. Potentiometric titration (84·2 mg.) in acetic acid (10 ml.) by perchloric acid (0·1N) in acetic acid, a glass electrode being used, gave the end point required by a dibasic compound; during the titration the perchlorate was precipitated. The adduct was unchanged after attempted hydrogenation over Raney nickel (5 atm.; 20°).

(ii) 3,5-Dimethylpyrazole (4·0 g.) and methyl αβ-dibromosuccinate (3·18 g.) were refluxed (2·5 hr.) in nitromethane (100 ml.), and most of the solvent was evaporated. The solid was boiled with ethyl acetate, and the mixture filtered hot. The insoluble material was the pyrazole hydrobromide [m. p. 223° (decomp.)], and evaporation of the filtrate gave a solid which after recrystallisation from ethyl acetate yielded a compound identical (infrared absorption spectrum and mixed m. p.) with that obtained by method (i).

Methyl 3,4,5-*Trimethyl*-1-*pyrazolylfumarate* (IV).—3,4,5-Trimethylpyrazole (1·0 g.) and methyl acetylenedicarboxylate (1·3 g.) in ether (45 ml.) were left (1 day), and the mixture evaporated to ⅓ volume. The precipitate, on crystallisation from light petroleum (b. p. 60—80°), gave the *fumarate* as needles, m. p. 96° (Found: C, 56·9; H, 6·2; N, 11·2. $C_{12}H_{16}N_2O_4$ requires C, 57·1; H, 6·3; N, 11·2%). In methanol the ester showed $\lambda_{max.}$ 2950 Å ($\varepsilon_{max.}$ 18,420) and in paraffin paste maxima at 5·72 and 5·86 μ in the carbonyl region.

Methyl αβ-*Di*-(3,4,5-*trimethyl*-1-*pyrazolyl*)*succinate* (III).—This was prepared as described for ester (IV) but by using the pyrazole (1·0 g.), the ester (0·65 g.), and ether (40 ml.) and working up after 4 days. The *succinate* (1·55 g.) crystallised from methanol in needles, m. p. 193° (Found: C, 59·5; H, 6·9; N, 15·2. $C_{18}H_{26}N_4O_4$ requires C, 59·7; H, 7·2; N, 15·5%). In methanol this showed $\lambda_{max.}$ 2320 Å ($\varepsilon_{max.}$ 9750) and in paraffin paste one maximum at 5·79 μ in the carbonyl region.

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[6] Schönberg and Mostapha, *J.*, 1943, 654.