The Preparation and Properties of Some Dipyrazolyls.

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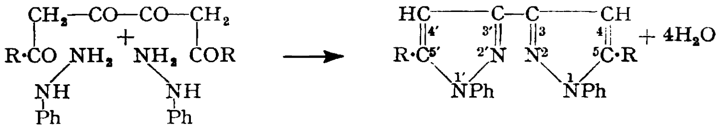
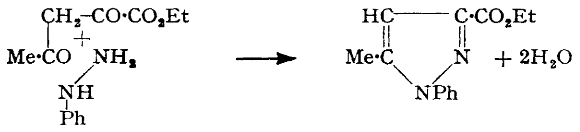
The preparations of 5 : 5′-dimethyl-1 : 1′-diphenyl- and 1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl have been repeated, and the 3 : 5′-isomer of the latter has been isolated. Evidence is given for the orientations of these two isomers, and some 4 : 4′-di-substituted derivatives of all three compounds have been prepared.

ACCORDING to Claisen and Roosen (*Annalen*, 1894, **278**, 294), two mols. of phenylhydrazine condense with one of octane-2 : 4 : 5 : 7-tetraone (I; R = Me) or 1 : 6-diphenylhexane-1 : 3 : 4 : 6-tetraone (I; R = Ph) in glacial acetic acid to form respectively 5 : 5′-dimethyl-1 : 1′-diphenyl- (II; R = Me) and 1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl (II; R = Ph).


(I)

(II)

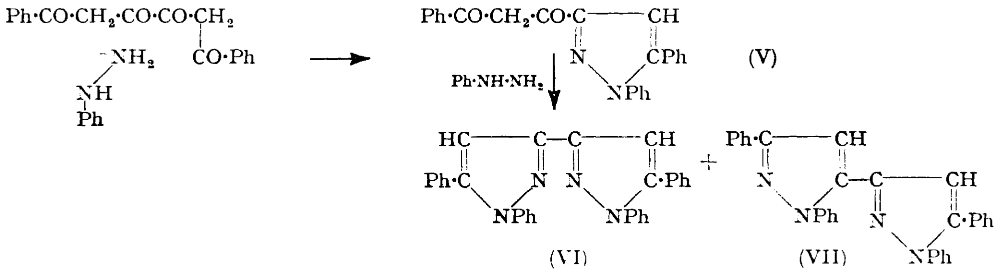
These orientations were assumed by analogy with the condensation of ethyl 2 : 4-dioxopentanoate (III) and phenylhydrazine to form mainly ethyl 5-methyl-1-phenylpyrazole-3-carboxylate (IV) (Claisen, *ibid.*, p. 269). The condensations with the tetraketones have been repeated, and the 3 : 3′-dipyrazolyls isolated, but from 1 : 6-diphenylhexane-1 : 3 : 4 : 6-tetraone, 1 : 1′ : 3′ : 5-tetraphenyl-3 : 5′-dipyrazolyl (VII) was also isolated. The orientations of the isomers have been established as follows. From the reaction between phenylhydrazine (one mol.) and 1 : 6-diphenylhexane-1 : 3 : 4 : 6-tetraone (one mol.) in acetic acid were obtained unchanged tetraketone, the 3 : 3′-dipyrazolyl (II; R = Ph), and 3-α-benzoylacetyl-1 : 5-diphenylpyrazole (V). The ketone (V), on treatment with phenylhydrazine (one mol.) in acetic acid, gave two dipyrazolyls, one of which must be the 3 : 3′- (VI), and the other the 3 : 5′-isomer (VII). Infra-red absorption spectra measurements showed that Claisen and Roosen's dipyrazolyl is more symmetrical than the new compound; therefore the former is (VI) and the latter is (VII).


(III)

(IV)

The isolation of the two isomers suggests that the reaction proceeds via (V) even when two mols. of phenylhydrazine are used, and is not as Claisen and Roosen (*loc. cit.*) suggested, a termolecular reaction.

In 1-phenylpyrazole standard reactions lead to 4-substituted derivatives (cf. Finar and Godfrey, *J.*, 1954, 2293), and so it has been assumed that the dipyrazolyls produce the corresponding 4 : 4′-disubstituted compounds. All three dipyrazolyls are readily converted into the corresponding 4 : 4′-dibromo-compounds, but when chloromethylated in acetic and (cf. Cambron, *Canad. J. Res.*, 1939, **17**, *B*, 10), only 1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl formed a 4 : 4′-bischloromethyl compound which could be isolated.



1 : 1′ : 5 : 5′-Tetraphenyl- and 5 : 5′-dimethyl-1 : 1′-diphenyl-3 : 3′-dipyrazolyl formed the corresponding 4 : 4′-bisacetoxymercuri-compounds by direct mercuration (cf. Paolini and Silbermann, *Gazzetta*, 1915, **45**, II, 385), and were orientated by conversion into the 4 : 4′-dibromo-compounds.

EXPERIMENTAL

Octane-2 : 4 : 5 : 7-*tetraone* (cf. Claisen and Stylos, *Ber.*, 1888, **21**, 1142; Freri, *Gazzetta*, 1938, **68**, 612).—To sodium methoxide [from methanol (16 g.) and sodium (12·5 g.)] under ether (300 c.c.) at 0° a mixture of dry ethyl oxalate (36·5 g.) and dry acetone (29 g.) was added with stirring during 25 min. The mixture was stirred for 2 days, then a solution of the solid in water (300 ml.) was acidified with acetic acid. After ½ hr. filtration and drying *in vacuo* ($CaCl_2$) gave the pale yellow tetraketone, m. p. 118—120° (21—38%), forming from methanol yellow needles, m. p. 120—121° (Schmidt, *Annalen*, 1950, **569**, 17, gives m. p. 123°).

1 : 6-*Diphenylhexane*-1 : 3 : 4 : 6-*tetraone* (cf. Brömme and Claisen, *Ber.*, 1888, **21**, 1131).—The method was essentially that described above, but all the ethyl oxalate (36·5 g.) and half of the acetophenone (15 g.) were added dropwise, and then 4 hr. later the other half of the acetophenone. The liquid was stirred for 3 days, then worked up. Recrystallisation from chloroform gave bright yellow needles, m. p. 177—179° (62—74%).

5 : 5′-*Dimethyl*-1 : 1′-*diphenyl*-3 : 3′-*dipyrazolyl* (cf. Claisen and Roosen, *Annalen*, 1894, **278**, 294).—Octane-2 : 4 : 5 : 7-tetraone (3·4 g., 0·02 mole) was heated with phenylhydrazine (4·3 g., 0·04 mole) in acetic acid (40 c.c.), on the steam-bath for 1 hr., cooled, and diluted with water, and the precipitate recrystallised from aqueous acetic acid (3·4 g.; 55%) as fine pale buff needles, m. p. 141—142°.

1 : 1′ : 5 : 5′-*Tetraphenyl*-3 : 3′- *and* 1 : 1′ : 3′ : 5-*Tetraphenyl*-3 : 5′-*dipyrazolyl* (*cf.* idem, loc. cit.).—1 : 6-Diphenylhexane-1 : 3 : 4 : 6-tetraone (47·2 g., 0·16 mole) was added to phenylhydrazine (34·6 g., 0·32 mole) in glacial acetic acid (250 c.c.), and the mixture heated on the steam-bath for 3—4 hr. The tetraketone dissolved within a few minutes, and then slowly a precipitate was formed. The mixture was cooled and filtered, and the precipitate washed with acetic acid and then with water, dried at 120°, and recrystallised from benzene (yield, 35·2 g., 49·5%). This was 1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl, m. p. 233° (Claisen and Roosen, *loc. cit.*, give m. p. 232°).

The filtrate was diluted with much water. The precipitated yellow wax was filtered off and dissolved in hot methanol (200 c.c.), and a few drops of water were added. After 3 days a small precipitate was filtered off and the filtrate was evaporated to 170 c.c. and left until a further precipitate was deposited. The filtrate was again reduced in bulk by evaporation, and the process repeated until no further precipitate was deposited. Occasionally a few drops of water had to be added to ensure precipitation; too much water caused an oil to be deposited. All the precipitates were combined, and repeated recrystallisation from methanol (charcoal) and then from light petroleum (b. p. 90—100°) gave 1 : 1′ : 3′ : 5-*tetraphenyl*-3 : 5′-*dipyrazolyl* (12·2 g., 17·3%) as fine white needles, m. p. 135—136° (Found : C, 81·8; H, 5·2; N, 12·7. $C_{30}H_{22}N_4$ requires C, 82·2; H, 5·0; N, 12·8%).

3-α-*Benzoylacetyl*-1 : 5-*diphenylpyrazole*.—To 1 : 6-diphenylhexane-1 : 3 : 4 : 6-tetraone (58·8 g., 0·2 mole) suspended in acetic acid (750 c.c.) on a steam-bath was added dropwise during 2·75 hr., a solution of phenylhydrazine (21·6 g., 0·2 mole) in acetic acid (250 c.c.). The mixture was heated for a further 1·25 hr., then set aside for 2 days. The precipitate (P) was filtered off. The filtrate was treated with much water and the precipitate (P5) dissolved in hot acetic acid (200 c.c.); cooling gave a precipitate (P6) (2·1 g.). The original precipitate (P) was washed with acetic acid, then with water, dried *in vacuo* ($CaCl_2$), and digested with benzene (2 × 250 c.c.), leaving a residue (R1) (3·1 g.). The benzene extract was evaporated and the residue refluxed with ethyl acetate (400 c.c.) and filtered hot, giving a residue (R2) (3·2 g.). Cooling this filtrate gave a precipitate (P1) (1·2 g.), and evaporation of the mother-liquors therefrom to 300 c.c. gave, after cooling, a precipitate (P2) (1·4 g.). The filtrate from P2, when kept overnight, gave further material (P3) (3·3 g.); removal of this, evaporation to 120 c.c., and cooling gave a solid (P4) (10·1 g.), and a liquor whence no further precipitate was obtained. The material R1 was unchanged tetraketone. Materials R3, P1, and P2 were 1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl. Material P3 and, after recrystallisation from aqueous acetic acid, materials P4 and P6 formed pale yellow needles, m. p. 164—166·5°, and were shown to be 3-α-*benzoylacetyl*-1 : 5-*diphenylpyrazole* (Found: C, 79·1; H, 4·9; N, 8·1. $C_{24}H_{18}O_2N_2$ requires C, 78·7; H, 4·9; N, 7·7%) by formation of a violet colour with ethanolic ferric chloride, a purple colour in Knorr's pyrazoline test, and, on oxidation with alkaline permanganate, 1 : 5-diphenylpyrazole-3-carboxylic acid, m. p. 185—186° (Claisen and Beyer, *Ber.*, 1887, **20**, 2186) alone or mixed with a specimen prepared as below.

Orientation of the Isomeric Tetraphenyldipyrazolyls.—3-α-Benzoylacetyl-1 : 5-diphenylpyrazole (2·9 g., 0·008 mole) and phenylhydrazine (0·97 g., 0·009 mole) in acetic acid (60 c.c.) were heated on the steam-bath for 1 hr., then kept overnight. The precipitate was filtered off and recrystallisation from benzene gave 1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl (2·4 g., 69%), m. p. 232—233°. Dilution of the acetic acid filtrate with water produced a precipitate which, after drying *in vacuo* over calcium chloride and recrystallisation from light petroleum (b. p. 90—100°), gave 1 : 1′ : 3′ : 5-tetraphenyl-3 : 5′-dipyrazolyl (1 g., 23%), m. p. 134·5—135·5°. The infra-red spectra, obtained from Nujol suspensions, were complex and similar, the main difference being that several absorption bands of Claisen and Roosen's dipyrazolyl are split into two bands for the new dipyrazolyl. In general, the lowering of the symmetry in the 3 : 5′-isomer increases the number of bands. In the region of the spectrum most influenced by changes in structure, 1600—650 cm.$^{-1}$, Claisen and Roosen's dipyrazolyl has 19 strong bands, and the new compound has 25.

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1 : 5-*Diphenylpyrazole-3-carboxylic Acid*.—Bischler (*Ber.*, 1892, **25**, 3143) prepared this acid by reaction between benzenediazonium chloride and ethyl phenacylacetoacetate (prepared *in situ* by Paal's method, *Ber.*, 1883, **16**, 2866). By this method we found it very difficult to obtain the acid crystalline. The following modification was more satisfactory (cf. Ossipoff and Korschun, *Chem. Zentr.*, 1903, **7**, II, 1281). To sodium wire (5·4 g., 0·235 g.-atom) under dry ether (400 c.c.) was added ethyl acetoacetate (30 g., 0·23 mole), and the mixture heated under reflux for 6 hr. To this mixture, when cool, was added an ethereal solution of phenacyl bromide (46 g., 0·23 mole) at a rate to maintain gentle reflux. Finally the mixture was refluxed for a further 2 hr. and then set aside overnight. The ethereal solution was washed repeatedly with water, then dried (Na_2SO_4), and the ether removed under reduced pressure. Ethyl phenacylacetoacetate was left as a red oil (56 g.). To this (12·4 g., 0·05 mole) in ethanol (200 c.c.) immersed in ice was added a cold solution of benzenediazonium chloride (4·65 g.), and then sodium acetate (16·4 g., 0·2 mole) in ice-cold water (40 c.c.; cf. Morgan and Reilly, *J.*, 1913, **103**, 808). The mixture was set aside for 24 hr. in ice, then diluted with water, and the oil that separated was heated on the steam-bath for 15 min. with sodium hydroxide (6 g.) in a small amount of water. The liquid, after cooling, was acidified with hydrochloric acid, and the precipitate, after repeated recrystallisation from methanol (charcoal) and then benzene, gave 1 : 5-diphenylpyrazole-3-carboxylic acid (6·7 g., 51%), m. p. 185—186°.

4 : 4′-*Dibromo-compounds*.—A chloroform solution of the dipyrazolyl was treated with bromine at room temperature, the chloroform evaporated, and the residue recrystallised, giving: 4 : 4′-*dibromo*-5 : 5′-*dimethyl*-1 : 1′-*diphenyl*-3 : 3′-*dipyrazolyl* (from aqueous acetic acid), short cream-coloured rods, m. p. 159—160° (Found: Br, 33·9. $C_{20}H_{16}N_4Br_2$ requires Br, 33·9%); 4 : 4′-*dibromo*-1 : 1′ : 5 : 5′-*tetraphenyl*-3 : 3′-*dipyrazolyl* (from chloroform), pale cream-coloured

plates, m. p. 272—273° (Found : Br, 27·2. $C_{30}H_{20}N_4Br_2$ requires Br, 26·8%) ; 4 : *4′-dibromo-1 : 1′ : 3′ : 5-tetraphenyl-3 : 5′-dipyrazolyl* (from chloroform–ligroin), white rosettes, m. p. 200—201° (Found : Br, 27·1%).

4 : *4′-Bischloromethyl-1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl.*—To a warm solution of the dipyrazolyl (13·2 g., 0·03 mole) in acetic acid (120 c.c.) and concentrated hydrochloric acid (26 c.c.) was added paraformaldehyde (2·4 g., 0·08 mole), and the mixture heated for 2 hr. on the steam-bath, then allowed to cool and filtered. The precipitate was washed with acetic acid and then with water, dried *in vacuo* ($CaCl_2$), and recrystallised from chloroform. This gave the *bischloromethyl compound*, white needles (6·2 g., 39%), m. p. 274—276° (Found : C, 71·3 ; H, 4·5 ; N, 10·4 ; Cl, 13·3. $C_{32}H_{24}N_4Cl_2$ requires C, 71·8; H, 4·5; N, 10·5; Cl, 13·3%).

4 : *4′-Bisacetoxymercuri-5 : 5′-dimethyl-1 : 1′-diphenyl-3 : 3′-dipyrazolyl.*—To the dipyrazolyl (3·14 g., 0·01 mole) in acetic acid (60 c.c.) was added recrystallised mercuric acetate (6·37 g., 0·02 mole), and the mixture heated on the steam-bath for 30 min. To the cool mixture was added water (200 c.c.), and the precipitate was filtered off, washed, and recrystallised from aqueous acetic acid. This gave the 4 : *4′-bisacetoxymercuri-compound* (4·8 g., 58%) as white needles, m. p. 204—204·5° (Found : Hg, 47·9. $C_{24}H_{22}O_4N_4Hg_2$ requires Hg, 48·3%).

4 : *4′-Bisacetoxymercuri-1 : 1′ : 5 : 5′-tetraphenyl-3 : 3′-dipyrazolyl.*—To a suspension of the dipyrazolyl (4·38 g., 0·01 mole) in acetic acid (150 c.c.) was added recrystallised mercuric acetate (6·37 g., 0·02 mole), and the mixture refluxed for 5 hr. The liquid always contained solid; the dipyrazolyl appeared to dissolve and then to be reprecipitated as a white powder. The mixture was allowed to cool, and the solid filtered off and then digested with chloroform (4 × 25 c.c.), and dried. The 4 : *4′-bisacetoxymercuri-compound* (7·6 g., 69%) was a white powder, m. p. 271·5° (Found : Hg, 41·4. $C_{34}H_{26}O_4N_4Hg_2$ requires Hg, 42·0%).

The corresponding 4 : 4′-dibromo-compounds were obtained from the mercuri-compounds by treatment in acetic acid with bromine at room temperature. When boiled with dilute hydrochloric acid, the mercuri-compound of the dimethyldipyrazolyl gave 5 : 5′-dimethyl-1 : 1′-diphenyl-3 : 3′-dipyrazolyl. 1 : 1′ : 5 : 5′-Tetraphenyl-3 : 3′-dipyrazolyl, however, could be obtained from its mercuri-compound only by refluxing the latter for some time with acetic acid containing concentrated hydrochloric acid.

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