750. *Sulphonation of Arylpyrazoles. Part I. Monosulphonation Products of 3-Methyl-1,5-diphenylpyrazole.*

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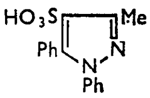
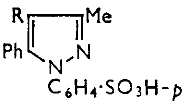
3-Methyl-1,5-diphenylpyrazole is monosulphonated by oleum at 30—35°, partly in the 4-position of the pyrazole ring, and partly in the *para*-position of the 5-phenyl nucleus. No substitution occurs in the *N*-phenyl nucleus at this temperature. The products have been identified by synthesis, one of the requisite diketones, *p*-(1,3-dioxobutyl)benzenesulphonic acid, being made from the pentane-2,4-dione copper complex.

THE author's failure to obtain the chloride of 3-methyl-1,5-diphenylpyrazole-4-sulphonic acid (I) by wet chlorination of the corresponding disulphide [1] led to the following investigation. Sulphonation of the parent pyrazole with oleum (SO_3 20%) at 30—35° gave an ~1 : 1 mixture of the 4-sulphonic acid (I), and the 3-methyl-1-phenyl-5-pyrazolylbenzene-*p*-sulphonic acid (III; R = H). The non-reactivity of the *N*-phenyl nucleus under these conditions is remarkable, considering the ready entry of groups into it during halogenation and nitration.[1,2] The compound, which would have resulted from such a reaction, and of which no trace was found in the sulphonation mixture, was first prepared by Claisen and Roosen,[3] and assumed by them to be 3-methyl-5-phenyl-1-*p*-sulphophenylpyrazole (II; R = H). The structures of this acid and of the sulphonation product (III; R = H) have been proved by conversion into the phenols by alkaline fusion,[3] and comparison of these with the hydroxyphenylpyrazoles prepared from the corresponding amino-compounds (II and III; R = H; NH_2 in place of SO_3H). To ensure that the sulpho-group of the acid (III; R = H) had entered the nucleus in the *para*-position and had not shifted during the fusion, the sulphonic acid was synthesized as follows. Condensation of pentane-2,4-dione copper complex with the dichloride of *p*-sulphobenzoic acid in chloroform gave the triketone (IV; R = Ac), only the COCl group reacting; this product was decomposed by warm water to give the sulphonic acid (IV; R = H; SO_3H in place of SO_2Cl) (cf. Barry [4]).



(I)



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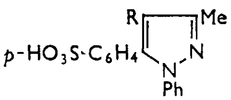
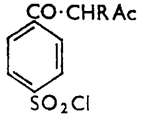


(III)



(IV)

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[1] Barry, *J.*, 1958, 1171.

[2] Finar and Simmonds, unpublished work; Finar and Hurlock, *J.*, 1957, 3024.

[3] Claisen and Roosen, *Annalen*, 1894, **278**, 296.

[4] Barry, *J.*, 1960, 670.

This diketone readily condensed with phenylhydrazine to give the compound (III; R = H).

Both isomers (II and III; R = H) gave the chlorides when heated with phosphorus pentachloride, with simultaneous entry of chlorine into the 4-position of the pyrazole nucleus. The presence of the 4-substituent was demonstrated by failure to brominate the compounds; also by sulphonation of 4-chloro-3-methyl-1,5-diphenylpyrazole (I; Cl, in place of SO_3H) to give the same compound (III; R = Cl; SO_2Cl in place of SO_3H).

The sulphonic acid (I) is interesting because of the rarity of pyrazole-4-sulphonic acids in the literature.[5,6] It is a weak acid and cannot be quantitatively titrated; the sulpho-group is unexpectedly labile, being replaced by bromine on treatment with bromine water and by hydrogen when the compound is heated with 3M-hydrochloric acid or fused with alkali. The last reaction is in keeping with Ackerman's failure [6] to prepare 4-cyano-3,5-dimethylpyrazole from the corresponding sulphonic acid, by fusion with potassium ferrocyanide. A similar lability has been observed with 3'-methylpyrazolo(5',1'-9,10)phenanthridine-4'-sulphonic acid.[7] The structure of the acid (I) has been confirmed by relating it to the corresponding disulphide.[1] Conversion into the chloride and reduction in acid solution gave the thiol, which on oxidation gave di-(3-methyl-1,5-diphenyl-4-pyrazolyl) disulphide. Reduction of the chloride with sodium amalgam gave the sulphinic acid, which on benzylation gave benzyl 3-methyl-1,5-diphenyl-4-pyrazolyl sulphone (I; $Ph\cdot CH_2\cdot SO_2$ in place of SO_3H). The sulphonic acid (I) was also made by chlorination of 4-benzylthio-3-methyl-1,5-diphenylpyrazole (I; $Ph\cdot CH_2S$ in place of SO_3H) in aqueous acetic acid and hydrolysis of the resulting sulphonyl chloride: this chloride is identical with that prepared directly from the acid (I).

EXPERIMENTAL

Sulphonic Acids.—*3-Methyl-1-phenyl-5-pyrazolylbenzene*-p-*sulphonic acid.* (1) 3-Methyl-1,5-diphenylpyrazole (10 g.) was dissolved in concentrated sulphuric acid (20 c.c.) and cooled to 10°. Oleum (40 c.c.; SO_3 20%) was added portionwise at 30—35°. After 1 hr. at this temperature, a test portion gave no turbidity on being made alkaline and the whole was then mixed with ice (100 g.). The white precipitate of the *sulphonic acid* (5·8 g., 43%) was filtered off (Found: equiv., 312 $C_{16}H_{13}N_2\cdot SO_3H$ requires equiv., 314). It was converted into the chloride (for identification see below).

(2) The copper complex of pentane-2,4-dione (1 mol.) was condensed with the acid chloride (2 mol.) in the usual manner, except that no water was used during the working-up. Evaporation of the chloroform solvent gave p-*(2-acetyl-1,3-dioxobutyl)benzenesulphonyl chloride* (60%), m. p. 97—99° (from ligroin) (Found: Cl, 11·86. $C_{12}H_{11}ClO_5S$ requires Cl, 11·75%). Boiling this triketone (4 g.) with water (100 g.) containing charcoal for 2 hr. gave a nearly colourless solution of *p*-(1,3-dioxobutyl)benzenesulphonic acid which was heated for 2 hr. with phenylhydrazine (1·1 mol.) and then cooled, giving the pyrazolesulphonic acid, identical with the above product (proved by conversion into the chloride, mixed m. p., and infrared spectra).

3-Methyl-1,5-diphenylpyrazole-4-sulphonic acid. (*a*) The filtrate from the above sulphonation (1) was neutralized with barium carbonate, filtered, and evaporated to dryness under reduced pressure to give a barium salt (9 g., 55%), identified by conversion into the chloride.

(*b*) 4-Chlorosulphonyl-3-methyl-1,5-diphenylpyrazole (see below) was heated with an excess of ethanolic 20% potassium hydroxide for ½ hr. Evaporation to dryness gave the potassium salt, acidification of which produced the sulphonic acid [chloride proved identical with that from method (*a*) by mixed m. p. and infrared spectra].

Sulphonyl Chlorides.—(1) By heating the potassium or barium salts or the free sulphonic acids (1 mol.) with phosphorus pentachloride (2 mol.) the corresponding chlorides were produced, *viz.*, p-*(4-chloro-3-methyl-5-phenylpyrazol-1-* (93%), m. p. 154—156° (from ligroin) (Found: Cl, 19·1; S, 8·7. $C_{16}H_{12}Cl_2N_2O_2S$ requires Cl, 19·3; S, 8·7%), and *-5-yl)-benzenesulphonyl*

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[5] Knorr, *Annalen*, 1894, **279**, 188; Ioffe and Khavin, *J. Gen. Chem.* (*U.S.S.R.*), 1944, **14**, 822.
[6] Morgan and Ackerman, *J.*, 1923, 1308.
[7] Barry, Finar, and Simmonds, *J.*, 1956, 4974.

chloride (98%), m. p. 167—167·5° (from acetone) (Found: Cl, 19·6; N, 7·3; S, 8·8%. $C_{16}H_{12}Cl_2N_2O_2S$ requires Cl, 19·3; N, 7·6; S, 8·7%), and 3-methyl-1,5-diphenylpyrazole-4-sulphonyl chloride (60%), m. p. 127—128° (from acetone) (Found: Cl, 10·9; S, 9·4. Calc. for $C_{16}H_{13}ClN_2O_2S$: Cl, 10·7; S, 9·6%).

(2) 4-Chloro-3-methyl-1,5-diphenylpyrazole was sulphonated at 35—40° as above. Neutralization with potassium carbonate gave the potassium salt (56%). This, dried and refluxed for 3 hr. with thionyl chloride, gave the second (m. p. 167°; mixed m. p. and infrared spectrum) of the above chlorides.

(3) 4-Benzylthio-3-methyl-1,5-diphenylpyrazole (5 g.), prepared from the disulphide by an improved method (zinc dust in boiling ethanolic 6% potassium hydroxide in place of sodium dithionite [7]), was dissolved in warm glacial acetic acid (50 c.c.), and water (1·5 c.c.) was added. Saturation of the solution with chlorine at 0° and gradual dilution gave a white precipitate of the sulphonyl chloride (80%), m. p. 127—128° (from acetone), identical with the chloride prepared from the appropriate barium salt (mixed m. p. and infrared spectrum).

Phenols.—(1) The free sulphonic acid, or the potassium or barium salt, was fused with 1 : 1 sodium and potassium hydroxide at 270—300°. Dilution, and acidification of the mixture with acetic acid, gave 1-*p*-hydroxyphenyl-3-methyl-5-phenylpyrazole, m. p. 208° (cf. Claisen and Roosen,[3] m. p. 206°), and 5-p-*hydroxyphenyl*-3-*methyl*-1-*phenylpyrazole* (90%), m. p. 201° (from aqueous ethanol), softening at 190° and resolidifying (Found: C, 76·5; H, 5·9; N, 11·0. $C_{16}H_{14}N_2O$ requires C, 76·8; H, 5·6; N, 11·0%). 3-Methyl-1,5-diphenylpyrazole-4-sulphonic acid gave an oil (picrate, m. p. 126—127° alone or mixed with 3-methyl-1,5-diphenylpyrazole picrate). Sulphate was found in the aqueous extract from the fusion mixture.

(2) The appropriate amino-compound was diazotized and run into sulphuric acid–sodium sulphate at 140°. The precipitated phenol was filtered off and redissolved in boiling 2N-sodium hydroxide (charcoal). Filtration, acidification, and recrystallization of the precipitate from aqueous ethanol gave the pure phenols, m. p. 208° and 201° respectively, identical (mixed m. p. and infrared spectra) with those produced by fusion of the sulphonic acids.

Reactions of 3-*Methyl*-1,5-*diphenylpyrazole*-4-*sulphonyl Chloride and -sulphonic Acid.*—(*a*) The sulphonyl chloride (0·5 g.) and 5% sodium amalgam (10 g.) were refluxed in ethanol (20 c.c.) during 4 hr. The sodium sulphinate, obtained by evaporation, was redissolved in 10% sodium carbonate solution (25 c.c.), and benzyl chloride (1 c.c.) in ethanol (10 c.c.) was added. After 3 hr. at 100°, addition of water (10 c.c.) gave a precipitate of the sulphone (0·15 g.), m. p. 162° alone or mixed with 3-methyl-1,5-diphenyl-4-toluene-ω-sulphonylpyrazole. Some sulpinic acid (detected by Smiles's test with anisole and sulphuric acid) was recovered by acidification of the filtrate.

(*b*) Granulated zinc (5 g.) was added during 15—20 min. to a boiling solution of the sulphonyl chloride (1 g.) in acetic acid (25 c.c.) containing 5M-hydrochloric acid (10 c.c.). After 1½ hours' further refluxing and filtration, anhydrous ferric chloride (0·5 g.) was added and the solution heated to 100°. Yellow crystals (0·1 g.) of di-(3-methyl-1,5-diphenylpyrazol-4-yl) disulphide, m. p. and mixed m. p. 202°, appeared.

(*c*) A solution of 3-methyl-1,5-diphenylpyrazole-4-sulphonic acid (1·3 g.) in 2·5M-hydrochloric acid (40 c.c.) was heated for 3 hr. at 100°, cooled, and made alkaline with ammonia solution. Extraction with ether gave an oil, which after recrystallization from light petroleum (b. p. 40—60°) melted at 60—62° alone or mixed with 3-methyl-1,5-diphenylpyrazole. The aqueous layer contained sulphate.

(*d*) Addition of bromine water to a solution of the sulphonic acid until a yellow colour persisted gave an oil, which after extraction with ether and washing with aqueous sodium carbonate, gave crystals, m. p. 75° (from ethanol) alone or mixed with 4-bromo-3-methyl-1,5-diphenylpyrazole. The aqueous washings contained sulphate.

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