# **872.** *Heterocyclic Diazo-compounds. Part III.*[1] *4-Diazopyrazoles Prepared by the Direct Introduction of the Diazonium Group into the Pyrazole Nucleus.*

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The technique for the direct introduction of the diazonium group has been applied to four pyrazoles, and the resulting diazonium salts have been converted into diazopyrazoles by treatment with alkali. Similar pyrazole nuclei were found to require greatly different conditions, and attempts to prepare a 3-diazopyrazole by this technique were unsuccessful. 4-Diazopyrazoles proved to be stable compounds which couple with β-naphthol in an inert solvent faster than do analogous diazopyrroles.

THE first heterocyclic diazo-compound, 3-diazoindazole, was prepared by Bamberger in 1897, by diazotisation of the amino-compound, followed by treatment of the diazonium salt with alkali.[2] Subsequently pyrazolediazonium salts were prepared by diazotisation of aminopyrazoles,[3] but diazopyrazoles were not described until recently.[4] The preparation of heterocyclic amino-compounds is often tedious and the products are frequently unstable. Success in preparing 3-[5] and 2-diazopyroles[1] by direct introduction of the diazonium group led us to extend the work to other heterocyclic nuclei.

First, an aqueous solution of 3,5-dimethylpyrazole (I; $R = R' = Me$) was treated with " buffered nitrous acid " (10 mol. of hydrochloric acid + 15 mol. of sodium nitrite in dilute aqueous acid[6]). This technique, which had been developed for the preparation of diazonium salts from phenols, gave on neutralisation with sodium hydrogen carbonate

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[1] Part II, Tedder and Webster, *J.*, 1962, 1638.

[2] Bamberger, *Ber.*, 1899, **32**, 1773.

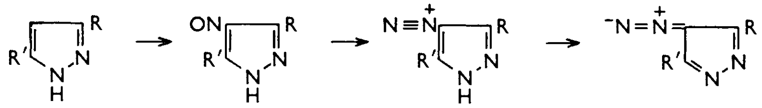
[3] Knorr and Stolz, *Annalen*, 1896, **293**, 68; Morgan and Reilly, *J.*, 1913, **103**, 808; 1914, **105**, 439.

[4] Reimlinger, Overstraeten, and Viehe, *Chem. Ber.*, 1961, **94**, 1036; Farnum and Yates, *J. Amer. Chem. Soc.*, 1962, **84**, 1399.

[5] Tedder and Webster, *J.*, 1960, 3270.

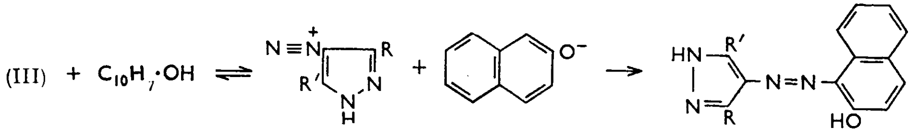
[6] Tedder and Theaker, *J.*, 1958, 2573.

~20% yield of a yellow impure diazonium chloride (II; R = R′ = Me, X = Cl), m. p. 165—168°, $\nu_{max.}$ 2235 cm.$^{-1}$. In more acidic conditions the yield of diazonium salt was improved and conversion into the diazo-compound ensured by use of strong alkali. The



(I) (II) (III)

diazopyrazole (III; R = R′ = Me), obtained in nearly 70% yield, was a stable, pale yellow solid. It coupled rapidly in boiling chloroform with β-naphthol, to give an azo-dye (IV; R = R′ = Me), identical with that obtained by Morgan and Reilly[3] from the pyrazolediazonium chloride and an aqueous alkaline solution of β-naphthol.



(IV)

5-Ethoxy-3-methylpyrazole (I; R = Me, R′ = OEt) proved more reactive and the original " buffered nitrous acid " method was effective. This diazopyrazole was an oil but it coupled readily with β-naphthol in an inert solvent to give a crystalline red dye (IV; R = Me, R′ = OEt). 3,5-Diphenylpyrazole (I; R = R′ = Ph) was unaffected by " buffered nitrous acid " and surprisingly the more acidic conditions found optimum for 3,5-dimethylpyrazole were also completely without effect. However, treating the pyrazole with sodium nitrite in acetic anhydride gave a little diazopyrazole, together with much *N*-acetylpyrazole, and using an excess of acetic acid as solvent gave a 32% yield of the diazopyrazole. Acetic acid and sodium nitrite, without acetic anhydride, were ineffective. The curious feature of 4-diazo-3,5-diphenylpyrazole (III; R = R′ = Ph) was its very high melting point (224°). The difference in the conditions required to introduce the diazonium group into 3,5-dimethyl- and 3,5-diphenyl-pyrazole was unexpected, but even more surprising was the discovery that neither set of conditions developed for these two compounds was at all effective with 3-phenylpyrazole (I; R = Ph, R′ = H). Eventually a poor yield of crude 4-diazo-3-phenylpyrazole (III; R = Ph, R′ = H) was prepared by a two-stage process in which the pyrazole was mercurated with mercuric acetate and the purified mercury derivative was then treated with nitrosylsulphuric acid. The identity of the crude diazopyrazole was confirmed by coupling it with β-naphthol, to yield the azo-dye (IV; R = Ph, R′ = H), which was characterised. This reaction, involving initial mercuration, was based on previous work in which the diazonium group has been introduced directly into deactivated nuclei.[7] A similar technique was employed in an attempt to prepare 3-diazo-4,5-diphenylpyrazole as an example of a 3-diazopyrazole. Treatment of 3,4-diphenylpyrazole with a solution of sodium nitrite in concentrated sulphuric acid was ineffective, but the addition of mercuric ions as catalyst brought about reaction and when the mixture was poured into water a diazonium salt was detected. However, no diazo-compound could be extracted from an alkaline solution of the diazonium salt. The azo-β-naphthol dye was prepared and from its properties (notably the fact that it did not form a complex with cupric ions) it was concluded that the diazonium group had been introduced into the *para*-position to the 4-phenyl group.

Attempts to introduce the diazonium group directly into indazole failed. It had been

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[7] Tedder and Theaker, *J.*, 1957, 4008.

found previously that the carboxyl groups in *o*- and *p*-hydroxybenzoic acid [8] and in pyrrolecarboxylic acids [1] are readily replaced by the diazonium group. Treatment of indazole-3-carboxylic acid with buffered nitrous acid gave some diazoindazole but attempts to purify the product were unsucessful.

The reactions of various nitrous acid solutions with imidazole was also studied, but none yielded a diazo-compound. 4-Methyl-2-phenylimidazole, when treated with the acetic acid–anhydride mixture used for 3,5-diphenylpyrazole, gave traces of both diazonium salt and diazo-compound but the yields were too small for characterisation.

## EXPERIMENTAL

3,5-*Dimethylpyrazole*-4-*diazonium Chloride*.—3,5-Dimethylpyrazole (4·8 g.) was suspended in a solution of sodium nitrite (34·5 g.) in water (100 c.c.). The suspension was cooled to 10° and 2N-hydrochloric acid (125 c.c.) was added to give a homogeneous yellow-green solution. The reactants were maintained at 5° for 20 hr. and then treated with sulphuric acid to destroy the excess of nitrite. The solution was neutralised with sodium hydrogen carbonate and extracted with chloroform. The extract was dried and concentrated and the diazonium salt precipitated by addition of ether. The diazonium salt (0·5 g.) recrystallised from ethanol–dioxan to give pale yellow crystals, m. p. 165—168° (decomp.) (lit.,[4] 150—160°), $\nu_{max.}$ (KBr disc) 2235 cm.$^{-1}$ (diazo) (Found: C, 38·2; H, 4·5. Calc. for $C_5H_7ClN_4$: C, 37·9; H, 4·4%).

4-*Diazo*-3,5-*dimethylpyrazole*.—3,5-Dimethylpyrazole (3·6 g.) and sodium nitrite were suspended in water (75 c.c.). 2N-Hydrochloric acid (188 c.c.) was added slowly at 5°, to give a homogeneous yellow-green solution which was kept at 5° for a further 24 hr. Additional 2N-hydrochloric acid (95 c.c.) was then added and the whole was kept for a further 24 hr. The excess of nitrous acid was decomposed with sulphamic acid, and the solution was rendered alkaline with 2N-sodium hydroxide. The alkaline solution (total vol. 560 c.c.) was saturated with sodium chloride (200 g.), and the diazo-compound extracted with chloroform. The extract was dried ($Na_2SO_4$) and evaporated under reduced pressure, to yield the 4-diazo-3,5-dimethylpyrazole as pale yellow crystals (3·3 g.). The product contained a trace of chloride which could not be removed by repeated recrystallisation, and the best analysis obtained was 1% low in carbon (Found: C, 48·0; H, 4·9. Calc. for $C_5H_6N_4$: C, 49·2; H, 4·9%); this material had m. p. 62—64°; $\nu_{max.}$ (KBr disc) 2195 cm.$^{-1}$ (diazo). A benzene solution of the diazo-compound and β-naphthol (in molar proportions of 1 : 5) was refluxed, although coupling commenced before the solution was heated. The unchanged β-naphthol was extracted with aqueous sodium hydroxide, and the residual chloroform solution evaporated to yield the crude dye. Recrystallisation from acetone gave orange-red 1-(3,5-dimethylpyrazol-4-ylazo)-2-naphthol, m. p. 251° (lit.,[4] 251—252°), $\lambda_{max.}$ 401 mμ (ε 14,100 in 95% ethanol) (Found: C, 67·4; H, 5·4; N, 21·2. Calc. for $C_{15}H_{14}N_4O$: C, 67·7; H, 5·3; N, 21·0%).

4-*Diazo*-5-*ethoxy*-3-*methylpyrazole*.—2N-Hydrochloric acid (175 c.c.) was added to a cooled solution (5°) of 5-ethoxy-3-methylpyrazole (4·41 g.) and sodium nitrite (36·2 g.) in aqueous acetone (water 150 c.c., acetone 300 c.c.). After 48 hr. at ~5° the excess of nitrous acid was decomposed by sulphamic acid, and the acetone was evaporated under reduced pressure. The residual solution was rendered alkaline with sodium hydrogen carbonate, and the diazo-compound was extracted with chloroform. The extract was dried ($Na_2SO_4$). Part (90%) of the extract was evaporated under reduced pressure, to leave the crude diazo-compound (1·47 g.) as a yellow oil. Chromatography on activated alumina gave 4-diazo-5-ethoxy-3-methylpyrazole as a golden-yellow oil, $\nu_{max.}$ (liquid film) 2120 cm.$^{-1}$ (diazo). The remainder of the chloroform extract was refluxed for 3 hr. with β-naphthol (0·5 g.), then washed with dilute sodium hydroxide in which the dye was slightly soluble. The chloroform layer was dried and evaporated to yield the crude dye (0·4 g.), m. p. 191°. Chromatography showed it to be a single compound and two recrystallisations from benzene afforded orange 1-(5-*ethoxy*-3-*methylpyrazol*-4-*ylazo*)-2-*naphthol*, m. p. 194°, $\lambda_{max.}$ 402 mμ (ε 14,300 in 95% ethanol) (Found: C, 65·3; H, 5·6; N, 18·4. $C_{16}H_{16}N_4O_2$ requires C, 64·8; H, 5·4; N, 18·9%).

4-*Diazo*-3,5-*diphenylpyrazole*.—Sodium nitrite (8·0 g.) was added to a solution of 3,5-diphenylpyrazole (5·5 g.) in acetic anhydride (200 c.c.). While the mixture was stirred at room temperature, additional portions of sodium nitrite (8·6 g.) were added after 24 hr. and again

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[8] Tedder and Theaker, *J.*, 1959, 257.

after 48 hr. After a total reaction time of 72 hr. the mixture was poured on crushed ice and nitrous acid (sodium nitrite 8·6 g., and 2N-hydrochloric acid 80 c.c.). The aqueous mixture was stirred for an hour, the excess of nitrite destroyed with sulphamic acid, and the solution rendered alkaline with 4N-sodium hydroxide. A pale yellow solid (4·3 g.; m. p. 75—85°) was isolated. Its infrared spectrum showed it to contain both 1-acetyl-3,5-diphenylpyrazole and the desired diazo-compound. The diazo-compound was more soluble and by ether-extraction followed by recrystallisation a total yield of (0·38 g.) of pale yellow 4-*diazo*-3,5-*diphenylpyrazole*, m. p. 224°, $\nu_{max.}$ (KBr disc) 2189 cm.$^{-1}$ (diazo) $\lambda_{max.}$ 354 mμ (ε 7300), was isolated (Found: C, 72·9; H, 4·2; N, 22·4. $C_{15}H_{10}N_4$ requires C, 73·2; H, 4·0; N, 22·8%).

In another experiment 3,5-diphenylpyrazole (3·3 g.) was dissolved in acetic acid (350 c.c.). Acetic anhydride (7·5 c.c.) was added, followed immediately by sodium nitrite (5·2 g.). The mixture was set aside at 10—15°. After 22 and again after 31 hr. similar portions of acetic anhydride and sodium nitrite were added. At the end of 48 hr. the mixture was poured into a stirred solution of sodium nitrite (5·2 g.) and 2N-hydrochloric acid (25 c.c.) in ice-water (400 c.c.). After 0·5 hour's stirring at 0—5° further sodium nitrite (2·6 g.) was added and stirring continued for a total of an hour. The diazo-compound was isolated as before; after recrystallisation a total yield of 1·2 g. of purified 4-diazo-3,5-diphenylpyrazole was obtained.

A benzene solution of the diazo-compound (0·25 g.) and β-naphthol (0·22 g.) was refluxed for 3 hr. and the solvent was then boiled off. The residue was dissolved in chloroform and washed with 2N-sodium hydroxide, 5N-hydrochloric acid, and water. The chloroform layer was dried ($Na_2SO_4$) and evaporated, to yield an orange residue (0·38 g.) which was recrystallised twice from acetone. 1-(3,5-*Diphenylpyrazol*-4-*ylazo*)-2-*naphthol* had m. p. 234°, $\lambda_{max.}$ 422 mμ (ε 11,900 in 95% ethanol) (Found: C, 76·8; H, 4·7; N, 13·9. $C_{25}H_{18}N_4O$ requires C, 76·0; H, 4·6; N, 14·3%). The dye gave an intense red colour in concentrated sulphuric acid.

4-*Diazo*-3-*phenylpyrazole*.—A solution of 3-phenylpyrazole (5·0 g.) and mercuric acetate (11·2 g.) in ethyl acetate was refluxed for 2 hr. On cooling, 4-acetoxymercuri-5-phenylpyrazole was isolated by filtration (yield of purified product 10·3 g.). This (6·8 g.) was added to a cold solution of sodium nitrite (6·1 g.) in concentrated sulphuric acid (60 c.c.). The mixture was stirred for 5 hr. at 3—5°, then added to ice-cold aqueous sodium nitrite. After 0·5 hour's stirring, the aqueous mixture was filtered, treated with sulphamic acid, rendered alkaline with sodium carbonate, and extracted with chloroform. The extract was dried and evaporated, to leave impure 4-diazo-3-phenylpyrazole (0·22 g.), $\nu_{max.}$ (liquid film) 2175 cm.$^{-1}$ (diazo). This viscous diazo-compound was characterised by refluxing it with β-naphthol (0·28 g.) in benzene for 5 hr., the solvent then being boiled off. The residue was dissolved in chloroform and washed with dilute aqueous sodium hydroxide, in which the dye was partly soluble, and then with water. The chloroform solution was dried and evaporated, to leave an orange residue (0·15 g.), m. p. 230°, which was twice recrystallised from benzene. This gave orange 1-(3-*phenylpyrazol*-4-*ylazo*)-2-*naphthol*, m. p. 235—236°, $\lambda_{max.}$ 431 mμ (ε 12,200 in 95% ethanol) (C, 72·7; H, 4·7; N, 17·5. $C_{19}H_{14}N_4O$ requires C, 72·6; H, 4·5; N, 17·8%).

p-(3-*Phenylpyrazol*-4-*yl*)*benzenediazonium Salt*.—Sodium nitrite (1·72 g.) was added to a suspension of mercuric oxide (0·05 g.) in concentrated sulphuric acid (25 c.c.). The mixture was heated to 70° the yellow mercuric oxide being converted into white mercuric sulphate. The mixture was then cooled and 3,4-diphenylpyrazole (1·1 g.) was added. The brown mixture was stirred at 5—8° for 4 hr., then poured into aqueous sodium nitrite (3·45 g.) to which ice had been added, stirred for 0·5 hr., and treated with sulphamic acid. A portion of the solution was saturated with sodium chloride and rendered alkaline with sodium carbonate. No diazo-compound could be extracted with chloroform. The remainder of the solution was treated with β-naphthol, rendered just alkaline with sodium acetate, stirred for ½ hr., and made strongly alkaline with 5N-sodium hydroxide. The red dye was extracted with chloroform; the extract was washed successively with dilute aqueous sodium hydroxide and water and dried. Evaporation left a red residue (0·29 g.) which was recrystallised three times from aqueous alcohol to give 1-[p-(3-*phenylpyrazol*-4-*yl*)*phenylazo*]-2-*naphthol*, m. p. 198° (Found: C, 76·0; H, 5·14; N, 13·6. $C_{25}H_{18}N_4O$ requires C, 76·9; H, 4·6; N, 14·3%), $\lambda_{max.}$ 488 mμ (ε 17,800 in 95% ethanol). The dye formed no complex with copper(II) ions.

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