

315. Heterocyclic Diazo-compounds. Part II.¹ 2-Diazopyrroles.

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Three examples of the hitherto unknown 2-diazopyrroles have been synthesised by variations of the technique for the direct introduction of the diazonium group. These reactions were much slower than when used for 3-diazopyrroles and there was a much greater tendency to form by-products. 2-Diazopyrroles are more reactive and less stable than 3-diazopyrroles. Pyrrolecarboxylic acids are decarboxylated by nitrous acid in a reaction analogous to that for phenolcarboxylic acids; and 2- and 3-diazopyrrole-carboxylic acid have been converted into diazo-compounds by this process.

ALTHOUGH 3-diazopyrroles have long been known,² 2-diazopyrroles have not previously been reported, undoubtedly because 2-aminopyrroles are very difficult to prepare and show none of the characteristics of primary aromatic amines.³ However, the technique for the direct introduction of the diazonium group developed in these laboratories opened a new route and we have used it for the preparation of 3-diazopyrroles.¹ Pyrroles in which the 2-position is free readily undergo nitrosation and are converted by more nitrous acid or by nitric oxide into the 2-diazopyrroles, though these reactions are very much slower than with 3-nitrosopyrroles.

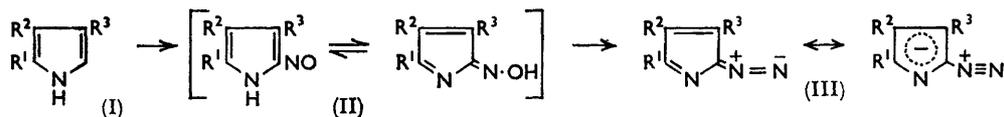
Previously, treatment of 2,5-diphenylpyrrole with buffered nitrous acid yielded 3-diazo-2,5-diphenylpyrrole and 3-diazo-4-nitro-2,5-diphenylpyrrole, the latter predominating.¹ Treatment of 2,4-diphenylpyrrole (I; $R^1 = R^3 = \text{Ph}$, $R^2 = \text{H}$) with buffered nitrous acid for a similar period yielded only the corresponding nitroso-compound (II), but much more

¹ The paper by Tedder and Webster, *J.*, 1960, 3270, is considered to be Part I.

² Angelico, *Atti R. Accad. Lincei*, 1905, **14**, II, 167.

³ Fischer, Guggemos, and Schafer, *Annalen*, 1939, **540**, 45.

prolonged treatment gave a mixture of 2-diazo-3,5-diphenylpyrrole (III; $R^1 = R^3 = \text{Ph}$, $R^2 = \text{H}$) and its 4-nitro-derivative, together with a compound which is believed to be 4-hydroxyimino-2,4-diphenylbut-2-enal, $\text{Ph}\cdot\text{C}(\text{:N}\cdot\text{OH})\cdot\text{CH}=\text{CPh}\cdot\text{CHO}$. The yield of 2-diazo-4-nitro-3,5-diphenylpyrrole was increased at the expense of the un-nitrated diazopyrrole by the addition of one mol. of nitric acid to the reaction mixture half-way through



the reaction. Pure 3-diazo-2,5-diphenylpyrrole had previously been obtained by the action of nitric oxide on a chloroform solution of the corresponding nitroso-compound.¹ 2-Nitroso-3,5-diphenylpyrrole was recovered in good yield after treatment with nitric oxide under the same conditions; very prolonged treatment nevertheless gave crystalline 2-diazo-3,5-diphenylpyrrole, together with 2-nitro-3,5-diphenylpyrrole. The un-nitrated compound is much less stable and the solutions darken fairly rapidly.

3-Acetyl-2-methyl-4-phenylpyrrole was treated with buffered nitrous acid for 72 hr. The expected 4-acetyl-2-diazo-5-methyl-3-phenylpyrrole was isolated in very low yield and proved to be a fairly stable crystalline solid. The alkaline mother-liquor contained another diazo-compound which could not be extracted from the solution until it was rendered acid but was not identified. Two other pyrroles with a free α -position, 3-benzoyl-2-methyl-4-phenylpyrrole and ethyl-2-methyl-4-phenylpyrrole-3-carboxylate also reacted with buffered nitrous acid, giving traces of crystalline diazo-compounds, but the yields were very small and the reactions were not studied in detail.

2-Diazopyrroles are more reactive and less stable than 3-diazopyrroles. They couple more readily with β -naphthol and appear to be more sensitive to light. They have a strong infrared band at 2120—2180 cm^{-1} (see Table), a slightly shorter wavelength than for 3-diazopyrroles. Similarly the ultraviolet absorptions of 2-diazopyrroles, although like those of the 3-diazopyrroles, are shifted to shorter wavelengths. The azo-dyes formed by coupling 2-diazopyrroles with β -naphthol form complexes with the transition metals, especially copper(II), a reaction not shown by dyes derived from 3-diazopyrroles.

2-Diazopyrroles (III)					3-Diazopyrroles			
R^1	R^2	R^3	M. p.	ν_{max} (cm^{-1})	λ_{max} ($\text{m}\mu$)	M. p.	ν_{max} (cm^{-1})	λ_{max} ($\text{m}\mu$)
Ph	H	Ph	104°	2138	345	122°	2095	387
Ph	NO_2	Ph	116.5	2172	—	145	2150	339

Aromatic *o*- and *p*-hydroxy-acids are decarboxylated by nitrous acid and a nitroso- or diazo-group takes the place of the displaced carboxyl group.⁴ A similar reaction has now been found with both α - and β -pyrrolecarboxylic acids: thus 5-ethoxycarbonyl-2,4-dimethylpyrrole-3-carboxylic acid with buffered nitrous acid yielded ethyl 4-diazo-3,5-dimethylpyrrole-2-carboxylate, with an acidic diazo-compound believed to be 4-diazo-3,5-dimethylpyrrole-2-carboxylic acid formed as a result of further hydrolysis. When 4-ethoxycarbonyl-3,5-dimethylpyrrole-2-carboxylic acid was treated with buffered nitrous acid and the reaction was allowed to proceed to completion, only the acidic diazo-compound was detected.

EXPERIMENTAL

Action of Buffered Nitrous Acid on 2,4-Diphenylpyrrole.—2,4-Diphenylpyrrole (2.2 g.) was dissolved in a solution of sodium nitrite (10 g.) in acetone (100 c.c.) and water (50 c.c.). 2N-Hydrochloric acid (25 c.c.) was added; immediately a green colour developed. Further

⁴ Tedder and Theaker, *J.*, 1959, 257.

2N-hydrochloric acid (5 c.c.) was added after the solution had been kept at 0° for 3 days and again after 4 days. After a total time of five days the solution had developed a golden-yellow colour and a pale yellow precipitate had been formed. The precipitate (0.8 g.) was removed and the solution diluted with water (500 c.c.), treated with sulphamic acid, and neutralised with sodium hydrogen carbonate. A flocculent greenish-yellow precipitate was formed and was separated by ether-extraction. The extract contained two diazo-compounds which were separated by chromatography on activated alumina. The first compound eluted, which had a diazo-peak at 2138 cm.⁻¹ in its infrared spectrum, proved rather unstable. The second fraction solidified as red-brown crystals, m. p. 114° (0.002 g.), and had a peak at 2172 cm.⁻¹. The experiment was repeated and β-naphthol was added to the ether extract containing the two diazo-compounds. The ether was evaporated on a steam-bath and coupling took place simultaneously. The dyes were separated by chromatography on activated alumina in benzene. The first dye eluted recrystallised from light petroleum (b. p. 60—80°) to yield 1-(3,5-diphenyl-2-pyrrolylazo)-2-naphthol as dark-red needles (0.05 g.), m. p. 230° (Found: C, 80.8; H, 5.2; N, 10.0. C₂₈H₁₉N₃O requires C, 80.2; H, 4.9; N, 10.8%). The second dye eluted recrystallised from light petroleum (b. p. 60—80°), to yield 1-(3,5-diphenyl-4-nitro-2-pyrrolylazo)-2-naphthol as red-brown needles (0.03 g.), m. p. 241—242° (decomp.) (Found: C, 71.4; H, 4.3; N, 12.6. C₂₈H₁₈N₄O₃ requires C, 71.9; H, 4.1; N, 12.9%). Both dyes gave a blue colour in concentrated sulphuric acid and formed blue chloroform-soluble complexes with copper(II) acetate solution.

The yellow precipitate, removed before the reaction mixture was diluted, recrystallised from aqueous acetone and then had m. p. 190° (decomp.) (Found: C, 76.3; H, 5.3; N, 5.5. C₁₈H₁₂NO₂ requires C, 76.5; H, 5.2; N, 5.6%), ν_{max.} (KBr disc) 1664 cm.⁻¹ (C=O). It decolourised cold permanganate rapidly, gave an intense red-purple colour in concentrated sulphuric acid, and is believed to be 4-hydroxyimino-2,4-diphenylbut-2-enal. The isomeric 4-hydroxyimino-1,3-diphenylbut-2-en-1-one, m. p. 116—117°, was synthesised by the nitrosation of dypnone with pentyl nitrite and sodium ethoxide (Found: C, 76.7; H, 5.3; N, 5.5%) and had ν_{max.} (KBr disc) 1644 cm.⁻¹ (C=O) and very similar properties.

2-Diazo-3,5-diphenylpyrrole.—A fairly rapid stream of nitric oxide was passed through a solution of 2-nitroso-3,5-diphenylpyrrole⁵ (2.48 g.) in dry chloroform (100 c.c.) for 24 hr. The initial green colour of the solution changed to dark orange. The solution was washed with 2N-sodium hydroxide (4 × 50 c.c.), dried, and concentrated. The diazo-compound was purified by chromatography on alumina, and the eluted material recrystallised from ether-light petroleum as rhombs (0.15 g.), m. p. 104—104.5° (decomp.) (Found: C, 78.1; H, 4.9; N, 17.5. C₁₆H₁₁N₃ requires C, 78.4; H, 4.5; N, 17.1%), λ_{max.} 345 mμ (ε 9900) in 95% ethanol, ν_{max.} (KBr disc) 2138 cm.⁻¹ (diazo). It was not very stable and the mother-liquor from the recrystallisation rapidly became red and gradually deposited dark red crystals (0.02 g.), m. p. 250° (Found: N, 11.2%). Acidification of the alkaline washings yielded 2-nitro-3,5-diphenylpyrrole (0.8 g.) which after chromatography, followed by recrystallisation from aqueous alcohol, formed bright yellow needles, m. p. 159° (Found: C, 72.9; H, 4.9; N, 10.5. C₁₆H₁₂N₂O₂ requires C, 72.7; H, 4.6; N, 10.6%).

2-Diazo-3,5-diphenyl-4-nitropyrrole.—2,4-Diphenylpyrrole (2.2 g.) was dissolved in a solution of sodium nitrite (10 g.) in acetone (125 c.c.) and water (50 c.c.). 2N-Hydrochloric acid (25 c.c.) was added, the solution was kept at 0° for 4 days, then filtered, and 2N-nitric acid (5 c.c.) was added. The mixture was left for a further 5 days at 0° during which it developed a golden-yellow colour and a yellow crystalline precipitate had been formed. The precipitate (0.65 g.) was removed and the filtrate was treated as described above. The precipitate formed on neutralisation was extracted in ether and washed with alkali. The residue left after the evaporation of the solvent was chromatographed on activated alumina in chloroform. The first band eluted was blue (cf. ref. 5), and the second band, which was yellow, contained the diazo-compound. The product recrystallised with some difficulty from an ether-light petroleum mixture, yielding 2-diazo-4-nitro-3,5-diphenylpyrrole (0.005 g.), m. p. 116—117°, ν_{max.} (KBr disc) 2172 cm.⁻¹ (diazo). The compound was further characterised by coupling with β-naphthol, yielding a dye, m. p. 241° (see previous experiment), which gave correct analyses.

3-Acetyl-2-methyl-4-phenylpyrrole.—ω-Hydroxyiminoacetophenone, prepared by the action of pentyl nitrite and sodium ethoxide on acetophenone,⁶ was reduced with stannous chloride in

⁵ Rogers, J., 1945, 590.

⁶ Claisen, Ber., 1887, 20, 656.

concentrated hydrochloric acid, to yield ω -aminoacetophenone hydrochloride.⁷ The amino-ketone hydrochloride with acetylacetone in the presence of sodium acetate yielded 3-acetyl-2-methyl-4-phenylpyrrole,⁸ m. p. 150°.

3-Acetyl-5-diazo-2-methyl-4-phenylpyrrole.—3-Acetyl-2-methyl-4-phenylpyrrole (2.0 g.) was dissolved in a solution of sodium nitrite (10 g.) in acetone (70 c.c.) and water (55 c.c.). 2N-Hydrochloric acid (25 c.c.) was added; the solution became green. The reaction was allowed to proceed at 0° for 72 hr. at the end of which the solution was a clear golden-yellow. The excess of nitrous acid was destroyed by sulphamic acid, and the solution was then poured into a solution of sodium hydrogen carbonate (25 g.) in water (1 l.). A yellow-brown precipitate was formed and was extracted with ether. The aqueous solution remained coloured and on treatment with a solution of alkaline β -naphthol gave an unidentified red dye, which recrystallised from chloroform as dark red needles (0.45 g.), m. p. 246—247° (decomp.) (Found: C, 71.4; H, 4.6; N, 9.4%). The main ether fraction was evaporated and the crude diazopyrrole was chromatographed on activated alumina in chloroform and recrystallised from ether-light petroleum (b. p. 40—60°). 3-Acetyl-5-diazo-2-methyl-4-phenylpyrrole was obtained as pale yellow-brown needles (0.05 g.), m. p. 102—103° (Found: C, 69.3; H, 5.0; N, 18.3. $C_{18}H_{11}N_3O$ requires C, 69.3; H, 5.0; N, 18.7%), ν_{\max} (KBr disc) 2146 cm^{-1} (diazo), λ_{\max} 351 $m\mu$ (ϵ 5700) in 95% ethanol.

The experiment was repeated but β -naphthol was added to the ether extract of the diazo-compound. Evaporation of the ether left the crude azo-dye, which was purified by chromatography on activated alumina and subsequent recrystallisation. Purified 1-(4-acetyl-5-methyl-3-phenyl-2-pyrrolylazo)-2-naphthol (0.15 g.) had m. p. 249—250° (Found: C, 74.7; H, 5.3; N, 11.1. $C_{23}H_{19}N_3O_2$ requires C, 74.8; H, 5.2; N, 11.5%), λ_{\max} 435 $m\mu$ (ϵ 15,000 in 95% ethanol) and gave an intense blue colour in sulphuric acid and formed a blue complex with copper(II) acetate.

5-Ethoxycarbonyl-2,4-dimethylpyrrole-3-carboxylic Acid.⁹—Finely powdered diethyl 3,5-dimethylpyrrole-2,4,-dicarboxylate was added to concentrated sulphuric acid at such a rate that the temperature did not rise above 40°. The mixture was stirred for 0.5 hr., then poured on ice, and the half-ester was isolated in the usual way. It had m. p. 270°.

Action of Buffered Nitrous Acid on 5-Ethoxycarbonyl-2,4-dimethylpyrrole-3-carboxylic Acid.—2N-Hydrochloric acid (25 c.c.) was added to a solution of this acid (2.11 g.) and sodium nitrite (0.77 g.) in acetone (225 c.c.) and water (125 c.c.). After 96 hr. at 0° unchanged starting material (0.77 g.) had been precipitated and was filtered off. Sulphamic acid was added to the filtrate which was then diluted with a solution of sodium hydrogen carbonate (25 g.) in water (3 l.). β -Naphthol (1 g.) in *n*-sodium hydroxide (50 c.c.) was added and the whole left for 5 hr. An acid and a neutral dye were obtained. The latter (0.01 g.) proved to be 1-(5-ethoxycarbonyl-2,4-dimethyl-3-pyrrolylazo)-2-naphthol,¹ m. p. and mixed m. p. 235°. Considerable difficulty was encountered in purifying the acidic dye. Eventually an amorphous red powder (0.006 g.), m. p. 265—267° (decomp.), believed to be 1-(5-carboxy-2,4-dimethyl-3-pyrrolylazo)-2-naphthol (Found: C, 56.0; H, 5.8. $C_{17}H_{15}N_3O_3 \cdot 3H_2O$ requires C, 56.2; H, 5.8%), was obtained. It was soluble in sodium hydrogen carbonate solution and gave a purple colour in concentrated sulphuric acid.

4-Ethoxycarbonyl-3,5-dimethylpyrrole-2-carboxylic Acid.¹⁰—Diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate was refluxed with potassium hydroxide in alcohol until a sample failed to give a precipitate when poured into water. The acid, isolated in the usual way, had m. p. 204°.

Action of Buffered Nitrous Acid on 4-Ethoxycarbonyl-3,5-dimethylpyrrole-2-carboxylic Acid.—The acid (1.5 g.) was dissolved in a solution of sodium nitrite (8 g.) in acetone (250 c.c.) and water (150 c.c.). On the addition of 2N-hydrochloric acid (20 c.c.) gentle effervescence was observed and the solution developed a green colour. After a week at 0° the green colour had been replaced by a yellow-brown one. The excess of nitrite was destroyed with sulphamic acid, and the solution was diluted and neutralised as before. β -Naphthol (1 g.) in *n*-sodium hydroxide (20 c.c.) was added and coupling was allowed to continue for 12 hr. Only an acid dye was formed and this proved difficult to purify. Eventually a red powder (0.05 g.) was obtained from benzene solution on cooling; it had m. p. 222° (decomp.) and is believed

⁷ Rupe, *Ber.*, 1895, **28**, 254.

⁸ Knorr and Lange, *Ber.*, 1902, **35**, 2998.

⁹ Fischer and Walach, *Ber.*, 1925, **58**, 2820.

¹⁰ Knorr, *Annalen*, 1886, **236**, 320.

to be 1-(4-carboxy-3,5-dimethyl-2-pyrrolylazo)-2-naphthol (Found: C, 64.0; H, 5.2; N, 12.2. $C_{17}H_{16}N_2O_3 \cdot \frac{1}{2}H_2O$ requires C, 64.1; H, 5.0; N, 13.1%). It gave a blue colour in concentrated sulphuric acid.

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