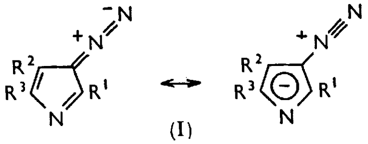
655. 3-*Diazopyrroles.*

By J. M. TEDDER and B. WEBSTER.

Three different methods have been used to synthesise 3-diazopyrroles: (*a*) normal diazotisation of the 3-aminopyrrole,[1] (*b*) direct introduction of the diazo-group with nitrous acid,[2] and (*c*) a two-stage process analogous to (*b*) in which the intermediate nitroso-pyrrole is isolated and then treated with nitric oxide. The last two reactions were only successful with pyrroles in which the α-positions were blocked and attempts to make 2-diazopyrroles have so far failed. The diazopyrroles are converted into diazonium salts by mineral acids, but these fail to couple even with resorcinol in acidic media. However, azo-dyes can be prepared either by adding the diazopyrrole to fused β-naphthol or by refluxing a neutral solution of β-naphthol with the diazo-compound.

IN 1953 Doering and De Puy reported the synthesis of diazocyclopentadiene.[3] However, two heterocyclic analogues of this compound, 3-diazo-2,5-diphenylpyrrole (I; $R^1 = R^3 =$ Ph, $R^2 =$ H) and 3-diazo-2,4,5-triphenylpyrrole (I; $R^1 = R^2 = R^3 =$ Ph) were known nearly sixty years before.[1] Angelico originally prepared 3-diazo-2,4,5-triphenylpyrrole by treating 3-amino-2,4,5-triphenylpyrrole with nitrous acid.[1] We have repeated Angelico's preparation and have also obtained this compound directly from the parent pyrrole by treatment with excess of buffered nitrous acid in conditions originally developed for the preparation of diazonium salts from phenols.[2] When this method was employed with 2,5-diphenylpyrrole two diazo-compounds were formed. The major product proved to be 3-diazo-4-nitro-2,5-diphenylpyrrole (I; $R^1 = R^3 =$ Ph, $R^2 = NO_2$), together with a small amount of the expected 3-diazo-2,5-diphenylpyrrole. The direct diazotization procedure is invariably accompanied by the formation of nitrate, so that the concurrent nitration observed in this case is readily explained.[4] 3-Diazo-2,5-diphenylpyrrole was



(I)

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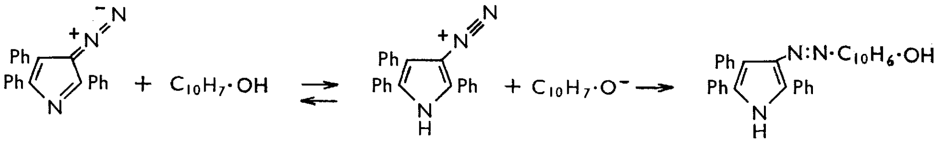
[1] Angelico, *Atti R. Accad. Lincei*, 1905, **14**, II, 167.
[2] Tedder and Theaker, *J.*, 1958, 2573.
[3] Doering and De Puy, *J. Amer. Chem. Soc.*, 1953, **75**, 5955.
[4] Tedder and Theaker, *Tetrahedron*, 1959, **5**, 288.

also prepared by a two-stage method in which the pyrrole was first nitrosated by pentyl nitrite and sodium methoxide and the nitroso-compound was then converted into the diazo-compound with nitric oxide. 3-Diazo-5-methyl-2-phenylpyrrole (I; R^1 = Ph, R^2 = H, R^3 = Me) was prepared by the direct method but better yields were obtained by using the two-stage procedure and purifying the nitroso-compound before treating it with nitric oxide. Although 2,5-dimethyl-3-nitrosopyrrole was synthesised we have been unable to isolate 3-diazo-2,5-dimethylpyrrole by this method, by the direct method, or by an adaptation of Doering and De Puy's method (*i.e.*, reaction of toluene-*p*-sulphonyl azide with the lithium derivative of the pyrrole [3]). There was evidence that the last method did yield some diazopyrrole but it could not be isolated. Attempts to prepare diazo-compounds from 2,4-diphenylpyrrole or from pyrrole itself have so far been unsuccessful. 5-Nitroso-2,4-diphenylpyrrole [5] was readily prepared either with nitrous acid or with sodium methoxide and pentyl nitrite, but subsequent treatment with nitric oxide did not convert it into the diazo-compound. Lithium 2,4-diphenylpyrrole reacted sluggishly with toluene-*p*-sulphonyl azide, to yield a blue dye of unknown constitution, with much unchanged starting material. Lithium pyrrole reacted readily with toluene-*p*-sulphonyl azide but only dark decomposition products could be isolated. *N*-Benzylpyrrole was treated with nitrous acid, but neither diazo-compound nor diazonium salt was formed and the reaction apparently has caused ring opening.

As stated by Angelico, 3-diazo-2,4,5-triphenylpyrrole is very stable. The other diazopyrroles, although less stable than the triphenyl derivative, can be handled without special precautions. However, all these compounds are decomposed slowly by light. The diazopyrroles were soluble in moderately strong mineral acid (~5N), and the resultant diazonium salts can be isolated and are fairly stable (cf. Angelico [1]). These diazonium salts failed to couple even with resorcinol in acidic media, while in neutral or alkaline solution the diazopyrroles are precipitated. Although coupling with phenols under normal conditions seems impossible, it has been found possible to prepare the azo-dyes by adding the diazopyrroles to fused β-naphthol or by refluxing the diazopyrrole with β-naphthol in a neutral organic solvent. Presumably the mixture ionises to a small extent into the pyrrolediazonium and β-naphthoxide ions which then couple rapidly.



The properties of the diazopyrroles described so far form a very consistent picture. However, there is a report by H. Fischer that ethyl 4-amino-3,5-dimethylpyrrole-2-carboxylate can be diazotized and that the resultant diazonium salt couples with β-naphthol.[6] This appeared so contrary to our experience that we repeated Fischer's work. Instead of the three-stage process *via* the amino-compound we introduced the diazonium group directly into ethyl 3,5-dimethylpyrrole-2-carboxylate and on treatment with alkali obtained the expected 4-diazo-ester (I; $R^1 = R^2$ = Me, $R^3 = CO_2Et$). The diazonium salt, re-formed in acid solution, failed to couple with alkaline β-naphthol, the diazo-compound being precipitated. However, Fischer observed coupling, not in ordinary alkaline β-naphthol solution, but in sodium hydrogen carbonate solution; we found that under these conditions the brown diazo-compound was again precipitated, but that traces of true azo-dye were also formed. The dye was obtained in good yield by refluxing a chloroform solution of the diazo-compound and β-naphthol, and proved identical with that reported by Fischer.

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[5] Rogers, *J.*, 1945, 590.

[6] Fischer and Stern, *Annalen*, 1926, **446**, 240; Fischer and Zeile, *Annalen*, 1930, **483**, 257.

All the diazopyrroles had a strong sharp infrared band at 2080—2150 cm.$^{-1}$. They are all yellow or yellow-brown and crystalline and absorb between 320 and 400 mμ in the visible and ultraviolet region.

EXPERIMENTAL

2,3,5-*Triphenylpyrrole*.—Phenacyldeoxybenzoin [7] was refluxed with ammonium acetate and acetic acid; the pyrrole, m. p. 142°, separated on cooling.[8]

3-*Nitroso*-2,4,5-*triphenylpyrrole*.—Triphenylpyrrole (5 g.) was dissolved in an ice-cold solution of sodium ethoxide [sodium (0·4 g.) dissolved in ethanol (100 c.c.)], and pentyl nitrite (2 g.) was added. After 2 days the dark brown solution was poured into water (500 c.c.), and the unchanged pyrrole removed. The filtrate was acidified with carbon dioxide, the nitroso-compound separating as an orange-brown precipitate. It recrystallised from alcohol as dark brown needles (2·2 g.), m. p. 195—196° [8] (Found: C, 81·3; H, 5·5; N, 8·1. Calc. for $C_{22}H_{16}N_2O$: C, 81·5; H, 4·9; N, 8·6%).

3-*Nitro*-2,4,5-*triphenylpyrrole*.[9]—A solution of triphenylpyrrole (2 g.) in ether (15 c.c.) was added to a solution of pentyl nitrite (7 g.) in ether (10 c.c.). The combined solution was left for 24 hr., then the ether was evaporated and the crude nitro-compound filtered from excess of pentyl nitrite and alcohol. The crude nitrotriphenylpyrrole recrystallised from aqueous alcohol as yellow needles (1·4 g.), m. p. 188—190° (Found: N, 7·8. Calc. for $C_{22}H_{16}N_2O_2$: N, 8·2%).

3-*Amino*-2,4,5-*triphenylpyrrole*.—3-Nitro-2,4,5-triphenylpyrrole (1 g.) was dissolved in 1 : 1 ethanol–acetic acid. Zinc dust (2·3 g.) was added and the reaction took place very rapidly. Zinc acetate and unchanged zinc were removed and the filtrate was made alkaline, the amine being precipitated. A similar reaction was carried out with 3-nitroso-2,4,5-triphenylpyrrole. The crude amine recrystallised from benzene and light petroleum (b. p. 40—60°) as off-white needles (1·4 g.), m. p. 182—183°.[1]

3-*Diazo*-2,4,5-*triphenylpyrrole*.—(a) *From aminotriphenylpyrrole by diazotisation*.[1] The amine (1 g.) was dissolved in glacial acetic acid (20 c.c.). Sodium nitrite (0·28 g.), dissolved in the minimum volume of water, was added and the solution became orange-brown and warm. On neutralisation with saturated sodium hydrogen carbonate solution the diazo-compound was precipitated. It was filtered off, dried, and recrystallised from benzene–light petroleum (b. p. 40—60°) to yield red-brown needles, m. p. 157—158° (decomp.).

(b) *From triphenylpyrrole by direct introduction of the diazo-group*.[2] Triphenylpyrrole (2·95 g.) was dissolved in a solution of sodium nitrite (15 g.) in acetone (150 c.c.) and water (75 c.c.). 2N-Hydrochloric acid (50 c.c.) was added gradually. The solution was left for 18 hr., then water (1·8 l.) was added and the solution made alkaline. A flocculent orange-brown precipitate of the diazo-compound contaminated with starting material was formed and was collected. The diazo-compound was purified by extracting its solution in ether with 6N-hydrochloric acid. Final traces of ether were removed from the acid extract by suction and the solution was filtered before being rendered alkaline. The nearly pure diazo-compound was isolated by ether-extraction. The extract was dried (Na_2SO_4), and the ether evaporated, to yield 3-diazo-2,4,5-triphenylpyrrole as red-brown needles, m. p. and mixed m. p. 156—157° (Found: C, 82·1; H, 4·7; N, 12·7. Calc. for $C_{22}H_{15}N_3$: C, 82·2; H, 4·7; N, 13·1%), $\lambda_{max.}$ 405 mμ (ε 13,000), $\nu_{max.}$ (KBr disc) 2088 (diazo) cm.$^{-1}$.

2,5-*Diphenylpyrrole*.—This was synthesised by the following reactions. Maleic anhydride + phthaloyl chloride [10] $\longrightarrow$ fumaryl chloride [11] $\longrightarrow$ *trans*-dibenzoylethylene [12] $\longrightarrow$ dibenzoylethane.[13] The last compound was treated with ammonium acetate in acetic acid to yield 2,5-diphenylpyrrole, m. p. 142°.[14]

Action of Buffered Nitrous Acid on 2,5-*Diphenylpyrrole*.—2N-Hydrochloric acid (25 c.c.) was

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[7] Smith, *J.*, 1890, **57**, 643.
[8] Angelico and Calvello, *Gazzetta*, 1901, **31**, II, 4.
[9] Ajello, *Gazzetta*, 1939, **69**, 315.
[10] Kyrides, *J. Amer. Chem. Soc.*, 1937, **59**, 207.
[11] Kyrides, *Org. Synth.*, 1940, **20**, 51.
[12] Lutz, *Org. Synth.*, 1940, **20**, 29.
[13] Conant and Cutler, *J. Amer. Chem. Soc.*, 1922, **44**, 265.
[14] Kapf and Paal, *Ber.*, 1888, **21**, 3061.

added to a solution of diphenylpyrrole (2·2 g.) and sodium nitrite (10 g.) in acetone (150 c.c.) and water (50 c.c.). The reactants were kept at 0° for 18 hr., then filtered. The precipitate (0·46 g.) consisted of brown crystals, m. p. 139—140°, and gave the reactions of a diazopyrrole, but the diazo-peak in its infrared spectrum was split, having maxima at 2095 and 2130 cm.$^{-1}$. More crude diazo-compound was obtained from the filtrate by chloroform-extraction. The chloroform solution was re-extracted with 8N-hydrochloric acid (3 × 100 c.c.); neutralisation of the combined acid solutions yielded the purified diazo-compound, which was finally isolated by ether-extraction. This product (0·40 g.) was very similar to the initial precipitate, having m. p. 139—142° and a split infrared diazo-peak. Fractional recrystallisation from ether–light petroleum gave 3-diazo-4-nitro-2,5-diphenylpyrrole, m. p. 144·5°, as the principal and less soluble component together with 3-diazo-2,5-diphenylpyrrole, m. p. 121—122°.

3-*Diazo*-4-*nitro*-2,5-*diphenylpyrrole*.—2N-Hydrochloric acid (5 c.c.) was added to a solution of 2,5-diphenylpyrrole (2·2 g.) and sodium nitrite (10 g.) in acetone (150 c.c.) and water (50 c.c.). After 24 hr. at 0° a further 5 c.c. of 2N-hydrochloric acid were added and the reactants left for a further 72 hr. The diazo-compound, isolated as before, proved to consist almost entirely of the diazonitropyrrole. Three recrystallisations from ether–light petroleum gave yellow needles of pure 3-*diazo*-4-*nitro*-2,5-*diphenylpyrrole* (0·70 g.), m. p. 144·5—145° (decomp.) (Found: C, 65·9; H, 3·6; N, 19·6. $C_{16}H_{10}N_4O_2$ requires C, 66·2; H, 3·5; N, 19·3%), $\lambda_{max.}$ 339 (ε 8000) and 399 mμ (ε 10,000) in 95% EtOH, $\nu_{max.}$ (KBr disc) (diazo) 2150 cm.$^{-1}$.

3-*Diazo*-2,5-*diphenylpyrrole*.[1]—This was prepared by passing nitric oxide through a chloroform solution of 3-nitroso-2,5-diphenylpyrrole (prepared from the parent pyrrole with pentyl nitrite and sodium ethoxide [8]). The purified diazo-compound had m. p. 122—123° (lit.,[1] 122°) (Found: C, 78·0; H, 4·5; N, 16·9. Calc. for $C_{16}H_{11}N_3$: C, 78·4; H, 4·6; N, 17·1%), $\lambda_{max.}$ 387 mμ (ε 5000) in 95% EtOH, $\nu_{max.}$ (KBr disc) 2095 (diazo) cm.$^{-1}$.

2-*Methyl*-5-*phenylpyrrole*.—1-Phenylpentane-1,4-dione was synthesised by two methods, those of Paal [15] and March.[16] The latter method, involving the condensation of phenacyl bromide (40 g.) with acetylacetone (20 g.) and hydrolysis of the resultant triketone, proved far the more satisfactory. The diketone was converted into the pyrrole by ammonium acetate in refluxing acetic acid as before. 2-Methyl-5-phenylpyrrole recrystallised from aqueous alcohol as off-white crystals, m. p. 96—98° (18 g.), which darkened rapidly in the atmosphere.[8]

2-*Methyl*-4-*nitroso*-5-*phenylpyrrole*.—2-Methyl-5-phenylpyrrole (6 g.) was dissolved in a solution of sodium ethoxide (sodium, 1 g.; ethanol, 25 c.c.), and pentyl nitrite (4·5 g.) was added. After 18 hr. the mixture was diluted to 250 c.c. with water and extracted with ether. Final traces of ether were removed from the aqueous layer by suction, and the solution was then acidified with carbon dioxide. A green precipitate was filtered off. Recrystallised from aqueous methanol the nitroso-compound formed olive-green needles, m. p. 160° (decomp.) (Found: C, 70·9; H, 5·1; N, 15·2. $C_{10}H_{10}N_2O$ requires C, 71·0; H, 5·4; N, 15·1%). The compound is assumed to be 2-*methyl*-4-*nitroso*-5-*phenylpyrrole* because of the ordinary rules of orientation. The properties of the diazo-compound prepared from it (see below) support the view that the nitroso-group is adjacent to the phenyl, and not to the methyl, group.

3-*Diazo*-5-*methyl*-2-*phenylpyrrole*.—Nitric oxide was bubbled through a solution of 2-methyl-4-nitroso-5-phenylpyrrole (0·5 g.) in ethyl acetate (50 c.c.) which changed from green to brown and finally to red. A pale yellow precipitate of the diazonium nitrate was filtered off and then dissolved in water. The diazopyrrole was precipitated from the aqueous solution by the addition of saturated sodium hydrogen carbonate solution. 3-*Diazo*-5-*methyl*-2-*phenylpyrrole* (0·070 g.) was extracted with ether, dried (Na_2SO_4), and recovered. Recrystallisation from benzene–light petroleum (b. p. 40—60°) gave red-brown needles, m. p. 81—82° (decomp.), $\lambda_{max.}$ 360 mμ (ε 10,100) in 95% EtOH, $\nu_{max.}$ (Nujol mull) 2062 (diazo) cm.$^{-1}$ (Found: C, 72·2; H, 4·9; N, 23·2. $C_{10}H_9N_3$ requires C, 72·1; H, 4·9; N, 23·0%).

2,5-*Dimethyl*-3-*nitrosopyrrole*.—2,5-Dimethylpyrrole [17] (b. p. 75°/20 mm.; 4·8 g.) was dissolved in a solution of sodium ethoxide (sodium, 1 g.; ethanol, 25 c.c.), and pentyl nitrite (5 c.c.) was added. The mixture was left for 48 hr. during which it became deep yellow-brown. The sodium salt of 3-hydroxyimino-2,5-dimethylpyrrolenine was precipitated by the addition of a large volume of ether. The free nitroso-compound was liberated as a green precipitate from an aqueous solution of the sodium salt by carbon dioxide in the presence of a small amount

[15] Paal, *Ber.*, 1883, **16**, 2867; 1884, **17**, 914.

[16] March, *Ann. Chim.* (*France*), 1902, **26**, 353.

[17] Young and Allen, *Org. Synth.*, 1936, **16**, 25.

of chloroform (without the chloroform the precipitate was often brown). 2,5-*Dimethyl*-3-*nitrosopyrrole* recrystallised from chloroform as bottle-green needles, m. p. 127° (decomp.) (Found: C, 58·2; H, 7·0; N, 22·8. $C_6H_8N_2O$ requires C, 58·3; H, 6·5; N, 22·5%).

Ethyl 3,5-*Dimethylpyrrole*-2-*carboxylate*.—Diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate [18] was hydrolysed to the half-ester [19] and then decarboxylated by heating it just above its m. p. The ester, recrystallised from aqueous alcohol, had m. p. 122—123°.

Ethyl 4-*Diazo*-3,5-*dimethylpyrrole*-2-*carboxylate*.—The preceding ester (1·8 g.) was dissolved in a solution of sodium nitrite (10 g.) in acetone (75 c.c.) and water (50 c.c.). 2N-Hydrochloric acid (25 c.c.) was added, the solution becoming green. The mixture was left for 48 hr. at 0° at the end of which it was a pale yellow and a brown solid had been precipitated. The solid was removed and the solution diluted to 500 c.c. with water. Excess of nitrite was decomposed by sulphamic acid, and the solution then neutralised with sodium hydrogen carbonate; it became intensely yellow. The diazo-compound was isolated by chloroform-extraction. The extract was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. The residue, a red oil, crystallised at 0° and recrystallised from ether as bright yellow needles of *ethyl* 4-*diazo*-3,5-*dimethylpyrrole*-2-*carboxylate* (0·55 g.), m. p. 79·5—80° (Found: C, 56·3; H, 5·9; N, 21·4. $C_9H_{11}N_3O_2$ requires C, 56·0; H, 5·7; N, 21·7%), $\lambda_{max.}$ 333 mμ (ε 3600), $\nu_{max.}$ (KBr disc) 2155 (diazo) cm.$^{-1}$.

2,4,5-*Triphenyl*-3-*pyrrolylazo*-β-*naphthol*.—β-Naphthol (1 g.) was melted in a test tube and then kept at 130° while 3-diazo-2,4,5-triphenylpyrrole (0·25 g.) was added slowly. The mixture became dark red and heating was continued for an hour. After cooling, the solid mass was dissolved in chloroform and washed with aqueous alkali. Evaporation of the chloroform left the crude dye contaminated with some unchanged diazopyrrole. After three recrystallisations from benzene–light petroleum (b. p. 90—120°) the pure *dye* was obtained as red needles, m. p. 173—174° (Found: C, 82·1; H, 5·5; N, 9·0. $C_{32}H_{23}N_3O$ requires C, 82·6; H, 5·0; N, 9·0%), $\lambda_{max.}$ 460 mμ (ε 18,000) in 95% EtOH.

4-*Nitro*-2,5-*diphenyl*-3-*pyrrolylazo*-β-*naphthol*.—3-Diazo-4-nitro-2,5-diphenylpyrrole (0·2 g.) was added to fused β-naphthol (1 g.) and kept at 130° for an hour. The crude azo-dye was isolated as before and chromatographed on activated alumina. The *dye* which appeared as a black band on the column was developed with benzene and eluted with ether. It then crystallised from aqueous methanol as dark purple plates, m. p. 205° (0·06 g.) (Found: C, 71·1; H, 4·4; N, 12·2. $C_{26}H_{18}N_4O_3$ requires C, 71·9; H, 4·2; N, 12·9%), $\lambda_{max.}$ 485 mμ (ε 17,000) in 95% EtOH. It gave an intense blue colour in concentrated sulphuric acid.

5-*Ethoxycarbonyl*-2,4-*dimethyl*-3-*pyrrolylazo*-β-*naphthol*.—Ethyl 4-diazo-3,5-dimethyl-2-carboxylate (0·23 g.) was added to a solution of β-naphthol (1·0 g.) in chloroform (20 c.c.). The whole was refluxed, a red colour rapidly developing. The chloroform was removed by distillation, the crude residue suspended in aqueous alkali, and the dye re-extracted with chloroform. Evaporation of the solvent left the *dye* which was recrystallised from benzene as orange-red needles (0·19 g.), m. p. 235° (Found: C, 67·7; H, 5·8; N, 12·7. Calc. for $C_{19}H_{19}N_3O_3$: C, 67·7; H, 5·6; N, 12·5%), $\lambda_{max.}$ 452 mμ (ε 20,000) in 95% EtOH.

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[18] Fischer, *Org. Synth.*, 1935, **15**, 17.

[19] Walach, *Ber.*, 1925, **58**, 2820.