965. *A Molecular Rearrangement during the Reduction of Thionaphthenopyrazole Dioxides.*

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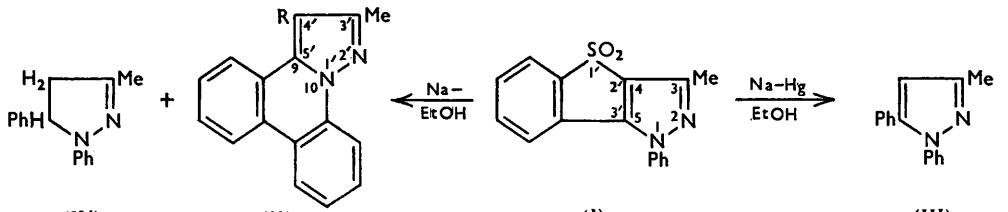
Reduction of 3-methyl-1-phenylthionaphtheno(2′ : 3′-4 : 5)pyrazole 1′ : 1′-dioxide (I) with sodium in ethanol causes an intramolecular rearrangement with the formation of 3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine (II; R = H). The structure of this compound has been ascertained through synthesis.

3-Methyl-1-phenylthionaphtheno(2′ : 3′-4 : 5)pyrazole 1′ : 1′-dioxide (I) (previously referred to as 3-methyl-1-phenyl-4 : 5-thionaphthenopyrazole-1′ : 1′-dioxide [1]), when treated with sodium amalgam in ethanol, undergoes simple fission to 3-methyl-1 : 5-diphenylpyrazole [2] (III). When, however, metallic sodium in boiling ethanol is the reagent, the main product is 3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine-4′-sulphinic acid (II; R = SO_2H) which separates from the reaction mixture as the sodium salt; a small amount of 3-methyl-1 : 5-diphenyl-Δ^2-pyrazoline (IV) is also formed.[2]

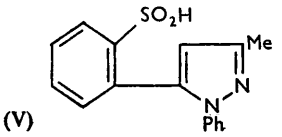


(IV) (II) (I) (III)

The free sulphinic acid (II; R = SO_2H) is very unstable in aqueous solution, especially in the presence of hydrochloric acid, sulphur dioxide being evolved with the formation of 3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine (II; R = H) (previously [2] referred to as compound A). Sulphinic acids which undergo loss of sulphur dioxide usually require a higher temperature for the reaction.[3] Although the sodium salt is stable in alkaline solution, it does not react with benzyl chloride to give a sulphone, but is recovered unchanged after long heating with this reagent. These properties show that this sulphinic acid is different from 3-methyl-1-phenyl-5-pyrazolylbenzene-*o*-sulphinic acid (V) which is readily benzylated and is only slowly decomposed by cold hydrochloric acid.[4] To account for this one might assume that fission of the C–S bond in the original thionaphthenopyrazole dioxide (I) occurs on the side adjacent to the benzene ring, to form 3-methyl-1 : 5-diphenylpyrazole-4-sulphinic acid (VI); the latter was therefore synthesised as follows. Di-(3-methyl-1 : 5-diphenyl-4-pyrazolyl) disulphide, prepared by a modification of Vaillant's method,[5] was reduced to the thiol with sodium dithionite, then benzylated, and the benzyl sulphide was oxidised with hydrogen peroxide in acetic acid to 3-methyl-1 : 5-diphenyl-4-toluene-ω-sulphonylpyrazole (VI; $Ph{\cdot}CH_2{\cdot}SO_2$ instead of SO_2H). This sulphone, on reductive fission with sodium amalgam [6] and subsequent acidification, gave the sulphinic acid (VI). This compound was characterised by its reactions and by benzylation to regenerate the sulphone. Like its isomer (V), it slowly lost sulphur dioxide in the presence of hydrochloric acid to give 3-methyl-1 : 5-diphenylpyrazole (III).[4] Further reduction of the sulphinic acid (VI) with metallic sodium in ethanol gave the thiol (VI; SH instead of SO_2H) and a small quantity of an oil which appeared to be 3-methyl-1 : 5-diphenylpyrazoline (IV).

[1] Barry, Thesis, London, 1933.
[2] Barry and McClelland, *J.*, 1935, 471.
[3] Gessner, *Ber.*, 1876, **9**, 1500.
[4] Barry and Finar, *J.*, 1954, 138.
[5] Vaillant, *Compt. rend.*, 1894, **119**, 647.
[6] Dabby, Kenyon, and Mason, *J.*, 1952, 4881.

These results exclude the possibility that 3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine (II; R = H) is formed by rearrangement after the loss of sulphur dioxide from the sulphinic acid (V) or (VI). The sulphinic acid (II; R = SO_2H) must be formed by a rearrangement during the initial reduction of the thionaphthenopyrazole dioxide. In view of the structure of the sulphinic acid (II; R = SO_2H), it must be formed by rupture of the C–S bond on the side adjacent to the benzene ring, followed by a rotation of this ring



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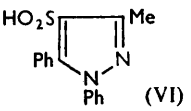
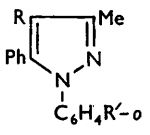


(VI)

about the remaining bond, and the formation of a new bond with the *ortho*-position of the *N*-phenyl nucleus. It is not clear at present whether the mechanism involves free-radical formation, induced by the metallic sodium, or whether the reducing conditions and the presence of hydrogen are necessary. The sodium ethoxide may also play a part.

Attempts to degrade the phenanthridine (II; R = H) have proved fruitless so far, the compound being resistant to all reducing or oxidising agents except acid dichromate or acid permanganate which destroy it.[2,7] It was thought, however, that the pyrazole nucleus might be weakened towards oxidising agents by the introduction of a hydroxyl group as follows. The sodium sulphinate (II; R = SO_2Na) gave, with sodium hypochlorite, a sulphonyl chloride (II; R = SO_2Cl). At this stage came the first direct evidence that the sulphinic acid group is in the reactive (4′) position of the pyrazole nucleus, since the sulphonyl chloride did not react with bromine in organic solvents. 3′-Methylpyrazolo(5′ : 1′-9 : 10)phenanthridine itself is very reactive towards electrophilic reagents, which preferentially attack the 4′-carbon atom in all cases.[7] Fusion of the corresponding sulphonic acid (II; R = SO_3H) with alkali gave, instead of the expected hydroxy-compound, the original 3′-methylpyrazolophenanthridine (II; R = H) by removal of the sulphonic acid group. The sulphonic acid was also hydrolysed in aqueous solution, slowly in the cold, rapidly on warming. Oxidation experiments with the sulphonic acid gave either unchanged material or unworkable tars.



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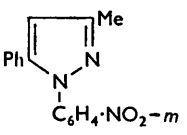

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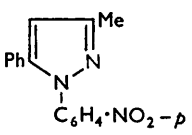

(IX)

With the failure to obtain analytical evidence for the structure of the nucleus (II), attention was turned to synthesis. 1-*o*-Aminophenyl-3-methyl-5-phenylpyrazole (VII; R = H, R′ = NH_2) was prepared by condensation of benzoylacetone with *o*-nitrophenylhydrazine, and reduction of the product with zinc and hydrochloric acid. The diazotised amine lost nitrogen on treatment with hypophosphorous acid, giving 3′-methylpyrazolo-(5′ : 1′-9 : 10)phenanthridine (II; R = H), whereas a simple deamination would have given methyldiphenylpyrazole.

Next, the nitro-compound (VII; R = H, R′ = NO_2) was brominated, to give the 4-bromo-derivative (VII; R = Br, R′ = NO_2), then reduced to the amine, and the diazotised amine was treated with hypophosphorous acid, giving 4′-bromo-3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine (II; R = Br). Reduction and deamination of the isomeric nitro-compounds (VIII and IX) gave only 3-methyl-1 : 5-diphenylpyrazole.

Experimental

3-Methyl-1-phenylthionaphtheno(2′ : 3′-4 : 5)pyrazole 1′ : 1′-Dioxide.—Condensing dithiosalicylic acid with acetylacetone in concentrated sulphuric acid at 45—50°, leaving the mixture

[7] Smith, Thesis, London, 1939.

overnight, and running it slowly into ice-cold water with stirring gave an almost quantitative yield of nearly pure 2-acetyl-3-hydroxythionaphthen.[8] The crude pyrazole, obtained by condensation with phenylhydrazine hydrochloride, was oxidised to the dioxide, which has now been observed to crystallise in two modifications, m. p. 180° and m. p. 187°, with a transition temperature at about 180°. Recrystallisation of the higher-melting modification regenerates that of m. p. 180°, while keeping this for several months causes the m. p. to rise.

Di-(1-benzoylacetonyl) Disulphide (*αα'-Dithiobenzoylacetone*).—Chloroform (180 c.c.) (dried over Na_2SO_4 for 12 hr.), containing copper benzoylacetone (38·5 g.), was dried for a further hour over the same reagent, filtered, and cooled to 0°. Sulphur monochloride (8 c.c.) in chloroform (25 c.c.) was added dropwise to this solution with stirring. After removal of excess of sulphur monochloride with a stream of dry air (2 hr.), evaporation of the chloroform gave a reddish oil (23 g., 60%) which on recrystallisation from ethanol gave the disulphide, m. p. 112—114°. Vaillant [5] obtained only a 30% yield.

Di-(3-methyl-1:5-diphenyl-4-pyrazolyl) Disulphide.—Dithiobenzoylacetone (33 g.; 1 mol.) and phenylhydrazine (16 g., 2 mols.) were heated in glacial acetic acid (200 c.c.) for 1 hr. at 100°. After some hours the solution deposited crystals of the pyrazole (27 g., 58%). Recrystallisation from butan-1-ol gave lemon-yellow crystals m. p. 204° (Vaillant [5] gave m. p. as 162°) (Found: C, 72·5; H, 4·6; N, 10·4; S, 12·1. Calc. for $C_{32}H_{26}N_4S_2$: C, 72·4; H, 4·9; N, 10·6; S, 12·2%).

4-Benzylthio-3-methyl-1:5-diphenylpyrazole.—The preceding disulphide (16 g.) was boiled with ethanol (200 c.c.) and water (400 c.c.) containing sodium dithionite (50 g.) and sodium hydroxide (10 g.). After 1½ hr. the almost clear solution was treated with benzyl chloride (10 c.c.) with shaking, and the mixture heated on the steam-bath for ½ hr. At 0° the *benzyl derivative* separated (14 g., 80%), and formed colourless crystals, m. p. 108°, from ethanol (Found: S, 9·4. $C_{23}H_{20}N_2S$ requires S, 9·0%).

3-Methyl-1:5-diphenyl-4-toluene-ω-sulphonylpyrazole.—The benzyl sulphide (1·5 g.) was dissolved in glacial acetic acid (10 c.c.), and hydrogen peroxide (5 c.c.; 100-vol.) added. After 1 hr. at 100° addition of water precipitated the *sulphone* (1·3 g.) which recrystallised from ethanol as colourless needles, m. p. 162° (Found: C, 70·8; H, 5·2; N, 7·1; S, 8·4. $C_{23}H_{20}O_2N_2S$ requires C, 71·1; H, 5·2; N, 7·2; S, 8·2%).

Reduction of the Sulphone.—The preceding compound (2 g.) was heated in boiling absolute ethanol (50 c.c.) with sodium amalgam (50 g., 5%) for 5—6 hr. After evaporation the yellowish residue (which gave a Smiles sulphinic acid test with anisole and concentrated sulphuric acid) was dissolved in water, and the solution acidified with 3N-hydrochloric acid. The precipitate rapidly became oily and sulphur dioxide was evolved. After being heated for 1 hr. at 100° the residual oil was extracted with chloroform, and the solution dried (Na_2SO_4) and treated with a solution of bromine in chloroform. The precipitated bromo-derivative was recrystallised from ethanol. Its m. p. (72°) was not depressed on admixture with authentic 4-bromo-3-methyl-1:5-diphenylpyrazole (m. p. 73—74°). The reduction with sodium amalgam was repeated with a further quantity of sulphone, the residue after evaporation of the ethanol was dissolved in water (charcoal), and the solution was heated for a few minutes on the steam-bath. Cooling to 0° and careful addition of hydrochloric acid gave a white precipitate of the 3-methyl-1:5-diphenylpyrazole-4-sulphinic acid (Smiles test). A drop of the ethanolic solution from the sodium amalgam reduction gave an intense carmine colour in Knorr's pyrazoline test.

Benzylation of the Sulphinic Acid.—The white precipitate from the last experiment was dissolved in dilute ethanolic potassium carbonate solution, and excess of benzyl chloride added. After 1½ hours' heating at 100° addition of water gave a precipitate of the sulphone which, recrystallised from ethanol had m. p. 162°, not depressed by admixture with 3-methyl-1:5-diphenyl-4-toluene-ω-sulphonylpyrazole.

Reduction of the 3-Methyl-1:5-diphenylpyrazole-4-sulphinic Acid.—The sulphinic acid (0·2 g.) was heated in sodium ethoxide solution (25 c.c.; 5%) for 2 hr. during which sodium (5 g.) was added. The mixture was diluted with water and extracted with ether. Evaporation of the ether gave an oil which gave an intense carmine colour in Knorr's pyrazoline test. The aqueous layer, on acidification with dilute hydrochloric acid and warming to 100°, slowly deposited a white solid, which on recrystallisation from ethanol melted at 200° alone or mixed with di-(3-methyl-1:5-diphenyl-4-pyrazolyl) disulphide.

4'-Chlorosulphonyl-3'-methylpyrazolo(5':1'-9:10)phenanthridine.—Sodium 3'-methylpyrazolo(5':1'-9:10)phenanthridine-4'-sulphinate (sodium sulphinate of compound A) (7 g.), prepared by Barry and McClelland's method,[2] was dissolved in warm 0·5N-sodium hydroxide

(100 c.c.) and filtered. 10% Sodium hypochlorite solution (50 c.c.) was slowly added with shaking. After standing, the precipitate of sulphonyl chloride was cream-coloured and granular (5 g.). Recrystallised from acetone, the *sulphonyl chloride* melted at 165° (Found: C, 57·6; H, 3·3; N, 9·1; S, 9·8; Cl, 11·0. $C_{16}H_{11}O_2N_2ClS$ requires C, 58·0; H, 3·3; N, 8·5; S, 9·7; Cl, 10·7%).

Reduction of the Sulphonyl Chloride.—The sulphonyl chloride (0·5 g.) was heated in ethanol with 5% sodium amalgam (10 g.). The white precipitate which was formed in a few minutes was treated with 3N-hydrochloric acid and, when evolution of sulphur dioxide had ceased, the residual oily solid was recrystallised from dilute ethanol. It then melted at 122° alone or mixed with 3-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine (compound A).

Hydrolysis of the Sulphonyl Chloride.—The sulphonyl chloride (1 g.), suspended in ethanol (100 c.c.), was treated with 50% aqueous potassium hydroxide (20 c.c.) with shaking. The sulphonyl chloride dissolved, and crystals of the potassium sulphonate were deposited.

Alkali Fusion of Potassium 3′-Methylpyrazolo(5′ : 1′-9 : 10)phenanthridine-4′-sulphonate.—Several fusions, in a nickel crucible, of the potassium sulphonate with potassium hydroxide–sodium hydroxide (1 : 1) in air or in nitrogen gave, in all cases, a white sublimate, m. p. 120° [120—124° when mixed with 3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine].

Hydrolysis of 3′-Methylpyrazolo(5′ : 1′-9 : 10)phenanthridine-4′-sulphonic Acid.—Acidification of a solution of the above potassium salt gave a clear solution, which, at room temperature, slowly deposited crystals, m. p. 123° alone or mixed with 3′-methylpyrazolo(5′ : 1′-9 : 10)phenanthridine. The hydrolysis was rapid when the acidified solution was warmed. The filtrate from the deposited crystals gave a test for sulphate (barium chloride).

Conversion of the Salt into the Chloride.—The dry potassium sulphonate (0·5 g.) was warmed with excess of phosphorus pentachloride (1 min.), and the oily residue extracted with acetone. After two recrystallisations from acetone, the chloride had m. p. and mixed m. p. 163°.

3-*Methyl*-1-o-*nitrophenyl*-5-*phenylpyrazole.*—Benzoylacetone (3·1 g.), heated with *o*-nitrophenylhydrazine (2·9 g.) in ethanol (50 c.c.) and concentrated sulphuric acid (6 c.c.) on a steam-bath for 30 min., gave the *pyrazole* (5·1 g., 96%) as pale yellow crystals, m. p. 104° (from ethanol) (Found: C, 68·6; H, 4·8; N, 14·4. $C_{16}H_{13}O_2N_3$ requires C, 68·6; H, 4·8; N, 15·0%).

3-*Methyl*-1-m-*nitrophenyl*-5-*phenylpyrazole.*—Benzoylacetone (6·6 g.), heated with *m*-nitrophenylhydrazine hydrochloride (9·5 g.) in acetic acid on a steam-bath for 1 hr., gave on dilution with water the *pyrazole* (9·0 g., 64%) as pale yellow crystals, m. p. 118° (from ethanol) (Found: N, 15·3%).

3-*Methyl*-1-p-*nitrophenyl*-5-*phenylpyrazole.*—Benzoylacetone (2 g.) and *p*-nitrophenylhydrazine (2·1 g.) in ethanol on a steam-bath for 2 hr. gave the pyrazole (2·5 g., 70%), m. p. 100°.[9, 10]

1-*Aminophenyl*-3-*methyl*-5-*phenylpyrazoles.*—The nitro-compound in glacial acetic acid was heated with zinc and concentrated hydrochloric acid until colourless. The amine was extracted with ether from the solution made alkaline with concentrated ammonia solution, and recrystallised from ethanol. The *o*-nitro-compound (2·25 g.) gave 1-(o-*aminophenyl*-3-*methyl*-5-*phenylpyrazole* (1·8 g., 90%), m. p. 134° (Found: C, 76·7; H, 6·0; N, 16·3. $C_{16}H_{15}N_3$ requires C, 77·1; H, 6·0; N, 16·8%). The *m*-nitro-compound (5 g.) gave 1-*m*-nitrophenyl-3-methyl-5-phenylpyrazole (4·15 g., 74%) [*benzoyl derivative*, m. p. 172° (Found: N, 11·5. $C_{23}H_{19}ON_3$ requires N, 11·9%)]. The *p*-nitro-compound (1·4 g.) gave the amine (0·7 g., 56%), m. p. 150° (benzoyl derivative 170°).[10]

4-*Bromo*-3-*methyl*-1-*nitrophenyl*-5-*phenylpyrazoles.*—The pyrazole in glacial acetic acid was treated with bromine at room temperature. Dilution with water gave a yellow precipitate which was dissolved in chloroform and washed with sodium carbonate solution. The chloroform was evaporated and the pale yellow residue recrystallised from ethanol. The *o*-nitro-compound (2 g.) gave the *bromo-derivative* (2·5 g., 98%), m. p. 142° (Found: Br, 22·2. $C_{16}H_{12}O_2N_3Br$ requires Br, 22·3%). The *p*-nitro-compound (2·1 g.) gave the *bromo-derivative* (2·6 g., 100%), m. p. 154° (Found: Br, 21·9%).

1-o-*Aminophenyl*-4-*bromo*-3-*methyl*-5-*phenylpyrazole.*—The nitro-compound (0·55 g.), heated in ethanol with 60% hydrazine hydrate solution and Raney nickel, gave colourless crystals of the *amine* (0·2 g., 40%), m. p. 180° (decomp.) (Found: Br, 24·2. $C_{16}H_{14}N_3Br$ requires Br, 24·4%).

[8] Smiles and McClelland, *J.*, 1921, 1815.
[9] Auwers and Stuhlmann, *Ber.*, 1926, **59**, 1054.
[10] Reilly, Daly, and Drumm, *Proc. Roy. Irish Acad.*, 1931, **40**, *B*, 94.

Hypophosphorous Acid Treatment of the Diazotised Amines.—The amine (0·3 g.) was diazotised in concentrated hydrochloric acid with sodium nitrite solution. After 10 min., the solution was poured into 30% hypophosphorous acid (15 c.c.) and set aside overnight. 1-*o*-Aminophenyl-3-methyl-5-phenylpyrazole gave colourless crystals, m. p. 123—124° (from ethanol) alone or mixed with compound A. 1-*o*-Aminophenyl-4-bromo-3-methyl-5-phenylpyrazole gave colourless crystals, m. p. 139° alone or mixed with "bromo-A." 1-*m*-Aminophenyl- and 1-*p*-aminophenyl-3-methyl-5-phenylpyrazole gave 3-methyl-1 : 5-diphenylpyrazole, characterised by its picrate, m. p. 124°,[11] and its bromo-derivative, m. p. 75°.[12,11]

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[11] Auwers and Mauss, *Ber.*, 1926, **59**, 611.
[12] Knorr and Blank, *Ber.*, 1885, **18**, 316.