174. *Heterocyclic Nitrogen Compounds. Part I. Derivatives of* 7 : 16-*Diazanaphthacene.*

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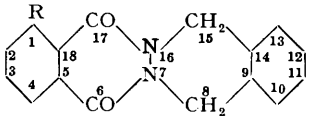
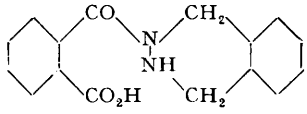
The synthesis of 6 : 17-*diketo*-6 : 8 : 15 : 17-*tetrahydro*-7 : 16-*diazanaphthacene* (I, R = H) has been achieved by condensation of (1) *o*-xylylene dibromide with phthalaz-1 : 4-dione and (2) phthaloyl chloride with 1 : 2 : 3 : 4-tetrahydrophthalazine hydrochloride. The second method has been used to obtain the 1-*nitro*- and the 1-*amino*-derivative.

The study of compounds derived from 7 : 16-diazanaphthacene was commenced because they belong to a class of compound which offered a new method of approach for the resolution of compounds owing their asymmetry to the disposal of valencies around tervalent nitrogen atoms. In these compounds two ring systems are fused together through vicinal nitrogen atoms and the non-planar disposal of the nitrogen valencies would require that the portions of the molecule on either side of the 7 : 16 nitrogen–nitrogen bond lie in different planes. Suitable substitution at a carbon atom of a benzenoid nucleus would then give an asymmetric molecule. For racemisation to occur, it would be necessary for both nitrogen atoms to pass through the planar condition, which might be expected to require a higher energy of activation than for a like change with a single tervalent nitrogen atom linked to three independent radicals. One of the probable causes of the failure to resolve tervalent nitrogen compounds should thus be either reduced or eliminated (compare Maitland, *Ann. Reports*, 1939, 241). The present work describes the preparation of some diketo-compounds of this class. It is proposed later to investigate the stereochemical properties of compounds of this class and especially of the reduced tetrahydrodiazanaphthacenes suitably substituted in one of the benzene nuclei.

(I.) 

 (II.)

6 : 8 : 15 : 17-Tetraketo-6 : 8 : 15 : 17-tetrahydro-7 : 16-diazanaphthacene was described by Drew and Hatt (J., 1937, 16). The preparation of substituted compounds of that type was found by them to be difficult and for this reason we have investigated direct syntheses of more reduced compounds rather than attempting the reduction of their tetraketo-compounds.

The *diketo*-compound (I, R = H) was obtained in 65% yield by heating together *o*-xylylene dibromide and phthalaz-1 : 4-dione; from the considerable amount of tarry matter also formed, only *N*-phthalimidophthalimide could be isolated. 5-Nitrophthalaz-1 : 4-dione and 6-chlorophthalaz-1 : 4-dione reacted with xylylene dibromide, but gave intractable resins, showing that this method of synthesis is of limited application.

That a phthalazine ring was formed in this reaction with *o*-xylylene dibromide was shown by ring cleavage with alcoholic sodium ethoxide to 2-*o*-carboxybenzoyltetrahydrophthalazine (II), which was subsequently oxidised to phthalic acid and phthalazine.

The second method of preparation of (I, R = H) by condensation of phthaloyl chloride and tetrahydrophthalazine hydrochloride proceeded smoothly and appears to be a general method.

Experimental

All m. p.'s are corrected.

6 : 17-*Diketo*-6 : 8 : 15 : 17-*tetrahydro*-7 : 16-*diazanaphthacene* (I, R = H).—(1) A mixture of dry phthalaz-1 : 4-dione (16·2 g.) and *o*-xylylene dibromide (27·5 g.) was heated under reflux at 215—220° with exclusion of moisture and occasional shaking. After ¾ hour the product was allowed to cool and ground with alcohol. The crystalline powder was collected, washed with alcohol to remove tar-like impurities, and refluxed with glacial acetic acid (50 ml.) and hydrazine hydrate (1·3 ml.) for 2 hours to destroy the *N*-phthalimidophthalimide present. The product was poured into water, and the solid collected, washed, ground with 2N-ammonia, left overnight, and washed with water (acidification of the filtrates precipitated phthalaz-1 : 4-dione). The dry crude product (17—18 g.) crystallised from alcohol (charcoal) in faintly yellowish leaflets, m.p. 196·5—197·5°, easily soluble in chloroform or acetic acid and soluble in about 12 parts of boiling benzene or 30 parts of hot alcohol [Found : C, 72·4; H, 4·5; N, 10·7; *M* (in camphor), 266. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·5; N, 10·6%; *M*, 264].

Attempts to carry out the condensation in nitrobenzene, tetralin or quinoline were unsuccessful.

(2) 1 : 2 : 3 : 4-Tetrahydrophthalazine hydrochloride (0·09 g.), phthaloyl chloride (0·15 ml.), and a few ml. of dry pyridine were refluxed for 3 hours with exclusion of moisture. After standing, water was added, the mixture evaporated to dryness on a water-bath, the brown crystalline residue made alkaline with N-sodium hydroxide, and the crystalline material collected and washed. Yield 0·12 g., m. p. 191—193° and, after one crystallisation from alcohol, 195—197°, not depressed by the material prepared by method (1).

The *diketo*-compound (I, R = H) gave a colourless solution in sulphuric acid, from which it was recovered unchanged by addition of water. The colourless solution slowly developed a permanent bright green colour at 170—190°. Dilute aqueous acids, hydriodic–acetic acid mixtures (1 : 1), and alcoholic hydrazine were without action on (I, R = H). Hot dilute aqueous alkali slowly dissolved it.

2-o-*Carboxybenzoyl*-1 : 2 : 3 : 4-*tetrahydrophthalazine* (II).—The diketo-compound (I, R = H) (0·5 g.) and 4N-alcoholic sodium ethoxide (16 ml.) were warmed on a water-bath, and the precipitated *sodium* salt of (II) collected, washed with absolute alcohol and ether, and dried under reduced pressure (yield, 0·52 g.) (Found : Na, 7·5. $C_{16}H_{13}O_3N_2Na$ requires Na, 7·55%). This salt was unchanged by prolonged refluxing with alcoholic sodium ethoxide.

The *acid* was precipitated on mixing an ice-cold solution of the sodium salt in 30 parts of water with a little more than the theoretical quantity of 0·5N-hydrochloric acid; it contained water of crystallisation. Cyclisation of the acid to (I, R = H) proceeded slowly at room temperature and rapidly at 70° (Found: equiv., 321; loss by cyclisation at 80° under reduced pressure, 18·9, 19·2, 19·0. $C_{16}H_{14}O_3N_2,2\frac{1}{2}H_2O$ requires equiv., 325; loss, 19·3%).

Oxidation of the Sodium Salt.—The salt (0·166 g.) in 0·2N-sodium hydroxide (30 ml.) was cooled to 2°, and 1% potassium permanganate solution (115 ml.) stirred in during 1 hour. After 6 hours the manganese dioxide was removed and washed and the combined liquids were made strongly alkaline and repeatedly extracted with chloroform. The extracts yielded 0·64 g. of phthalazine, m. p. 90—91° after crystallisation from chloroform and ether; it was identified by mixed m. p. and by conversion into the methiodide. Acidification and ether extraction of the alkaline liquor yielded 0·5 g. of phthalic acid containing traces of a nitrogen-containing acid from which it could be freed by sublimation.

1-*Nitro*-6 : 17-*diketo*-6 : 8 : 15 : 17-*tetrahydro*-7 : 16-*diazanaphthacene* (I, R = NO_2).—Tetrahydrophthalazine hydrochloride (3·1 g.), 3-nitrophthaloyl chloride (6 g.), and dry pyridine (12 ml.) were mixed, and the reddish-brown product heated to refluxing for 3 hours. The excess of pyridine was removed by heating under reduced pressure, and the residue made alkaline with aqueous sodium carbonate. The brown oil which first separated quickly solidified. Considerable losses occurred during purification from tar and a crystalline by-product. The *product*, washed with dilute mineral acid and water and repeatedly crystallised from chloroform–alcohol (charcoal), formed yellow parallelepipeds, m. p. 249—250° (slight decomp.) (Found: C, 62·4; H, 4·0; N, 13·7. $C_{16}H_{11}O_4N_3$ requires C, 62·1; H, 3·6; N, 13·6%). It dissolved readily in chloroform and acetic acid, sparingly in alcohol and acetone, and very sparingly in ether. Its constitution was confirmed by conversion into the red sodium salt of the acid analogue of (II), followed by oxidation with potassium permanganate in a similar manner to that described for (II) to give phthalazine and 3-nitrophthalic acid.

1-*Amino*-6 : 17-*diketo*-6 : 8 : 15 : 17-*tetrahydro*-7 : 16-*diazanaphthacene* (I, R = NH_2).—Stannous chloride (4·5 g.) in concentrated hydrochloric acid (21 ml.) was added to a stirred suspension of the nitro-compound (2·25 g.) in water maintained at 50—70°. After 7—8 hours the mixture was made strongly alkaline with sodium hydroxide and, after standing, filtered, and the *amine* extracted from the precipitate with alcohol. It separated from alcohol in pale yellow rhombs, m. p. 185—187° (decomp.) depending on the rate of heating [Found: C, 68·1; H, 4·7; N, 15·1, 15·2; *M* (in camphor), 268. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%; *M*, 279]. Alcoholic hydrazine hydrate reduced the nitro-compound to an impure amine.

The *benzoyl* derivative of (I, R = NH_2), obtained by the Schotten–Baumann method, crystallised from trichloroethylene and alcohol in fine white needles, m. p. 260—261° (slight decomp.) (Found: N, 10·9. $C_{23}H_{17}O_3N_3$ requires N, 11·0%). The amine can be diazotised by Schoutissen's method (*J. Amer. Chem. Soc.*, 1933, **55**, 4531) and the diazotised solution couples normally with β-naphthol.

1 : 2 : 3 : 4-*Tetrahydrophthalazine Hydrochloride*.—The phthalazine for this preparation was obtained from ωωω'ω'-tetrachloro-*o*-xylene, the method of Gabriel and Pinkus (*Ber.*, 1893, **26**, 2210) being followed except that, in agreement with Paul (*Ber.*, 1899, **32**, 2015), the use of chloroform rather than of benzene was found necessary for complete extraction.

Preparation of tetrahydrophthalazine hydrochloride by the method of Gabriel and Pinkus (*loc. cit.*) gave poor yields due to the method of isolation. Yields, 90% of the theoretical, were obtained as follows: The phthalazine hydrochloride was reduced with a 7% sodium amalgam at 20—25° and, after an unidentified product (yellow crystals, m. p. 229—231°, from alcohol) had been removed, the alkaline filtrate was extracted repeatedly with chloroform. The tetrahydrophthalazine hydrochloride was then precipitated from the dried chloroform solution by saturation with dry hydrogen chloride. The product was sufficiently pure for preparative purposes.

6-*Chlorophthalaz*-1 : 4-*dione*.—4-Chlorophthalimide (Levy and Stephens, J., 1931, 79) (4·54 g.), 100% hydrazine hydrate (6 ml.), and alcohol (50 ml.) were refluxed on a water-bath for 2 hours, and the bulk of the alcohol removed. The residue was dissolved in 5% aqueous sodium hydroxide (charcoal), and the *dione* precipitated from the filtrate with hydrochloric acid. The precipitated material was almost pure, but could be crystallised from acetic acid or sublimed. It formed fine white needles, m. p. 348—350° (in a sealed tube) (Found: C, 49·2; H, 2·6; N, 14·3. $C_8H_5O_2N_2Cl$ requires C, 48·9; H, 2·6; N, 14·3%).

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