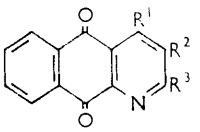
1134. *Some Derivatives of 1-Aza-anthracene-9,10-quinone*

By K. Schofield and D. E. Wright

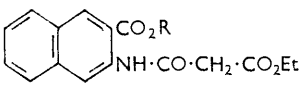
Syntheses of 2,4-dihydroxy-1-aza-anthracene and 2,4-dihydroxy-1-aza-anthracene-9,10-quinone are described.

In connection with work on the fungal pigment phomazarin [1] we needed some derivatives of 1-aza-anthracene-9,10-quinone of the type (I). Quinones of this series are best prepared by oxidation of the corresponding 1-aza-anthracenes.



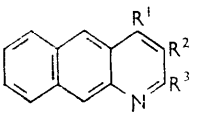
(I)

(a) $R_1 = R_3 = OH$, $R_2 = CO_2H$
(b) $R_1 = R_3 = OH$, $R_2 = H$
(c) $R_1 = R_3 = Cl$, $R_2 = H$



(II)

(a) R = Et
(b) R = Me



(III)

(a) $R_1 = R_3 = OH$, $R_2 = CO_2H$
(b) $R_1 = R_3 = OH$, $R_2 = H$
(c) $R_1 = R_3 = Cl$, $R_2 = H$

To obtain the latter we adopted a method used in the quinoline series by Lutz and his co-workers.[2] Reaction of ethyl 2-amino-3-naphthoate with diethyl malonate gave the malonamide (IIa) in good yield. Cyclisation of this compound with sodium ethoxide gave a mixture of (IIIa) and its ethyl ester. A similar mixture was obtained by ring-closure of the methyl ester (IIb) with sodium methoxide in pyridine. With sodium hydrogen carbonate in methanol or with caustic soda these mixtures gave by hydrolysis and partial decarboxylation mixtures of (IIIa) and (IIIb). Further heating of the latter mixtures with sodium hydroxide gave (IIIb). This could not be obtained by cyclisation of ethyl or methyl 2-acetamido-3-naphthoate with sodium in toluene.[3] With phosphoryl chloride (IIIb) gave (IIIc).

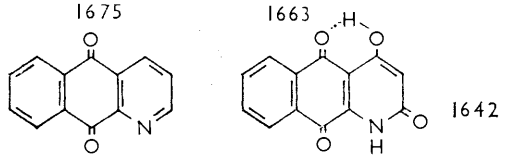
Catalytic hydrogenation of (IIIc) with palladised charcoal in the presence of magnesium oxide [4] gave a mixture of unchanged (IIIc) and 1,2,3,4-tetrahydro-1-aza-anthracene. We failed to dehydrogenate the tetrahydro-compound.[5] Reaction of (IIIc) with hydrazine and palladised charcoal [6] gave deeply coloured, high-melting products, and reaction with toluene-*p*-sulphonylhydrazine [5] gave mainly a mono-toluene-*p*-sulphonylhydrazine derivative, from which, by decomposition with alkali, a low yield of a chloro-1-aza-anthracene was obtained.

When (IIIb) was oxidised with chromic acid extensive decomposition occurred, but oxidation of the mono-acetate formed by prior acetylation of (IIIb) gave 2,4-dihydroxy-1-aza-anthracene-9,10-quinone (Ib) in good yield.

With methyl iodide and silver oxide (Ib) gave 2,4-dimethoxy-1-aza-anthracene-9,10-quinone which with methanolic sodium hydroxide gave what was evidently a mixture of hydroxy-methoxy-1-aza-anthracene-9,10-quinones (cf. the behaviour of phomazarin [1]). With phosphoryl chloride (Ib) gave 2,4-dichloro-1-aza-anthracene-9,10-quinone (Ic), and thence, by catalytic hydrogenation, 1-aza-anthracenequinone. Again, an attempt to use toluene-*p*-sulphonylhydrazine for this purpose gave only deeply coloured, high-melting substances.

[1] K. Schofield and D. E. Wright, unpublished work.
[2] R. E. Lutz, G. Ashburn, J. A. Freek, R. H. Jordan, N. H. Leake, T. A. Martin, R. J. Rowlett, and J. W. Wilson, *J. Amer. Chem. Soc.*, 1946, **68**, 1285.
[3] J. N. Ashley, W. H. Perkin, and R. Robinson, *J.*, 1930, 382.
[4] N. Whittaker, *J.*, 1951, 1565.
[5] A. Albert, D. J. Brown, and H. Duewell, *J.*, 1948, 1284.
[6] W. L. Mosby, *Chem. and Ind.*, 1959, 1348.

Because of the situation in the infrared spectra of phomazarin and its derivatives [1] we examined the infrared spectra of 1-aza-anthracene-9,10-quinone and 2,4-dihydroxy-1-aza-anthracene-9,10-quinone. The former showed carbonyl peaks at 1693 and 1675 cm.$^{-1}$,



(IV) 1693 1691 (V)

assigned as in (IV), whilst the latter showed peaks at 1691, 1663, and 1642 cm.$^{-1}$, assigned as in (V). Chelation stabilises the 4-hydroxy-2-quinolone form.

Experimental

Ethyl 2-(3-Ethoxycarbonylnaphthylamido)malonate (IIa).—Ethyl 2-amino-3-naphthoate (24 g.) and diethyl malonate (100 ml.) were heated rapidly to 165° (oil-bath temperature) and then slowly from 165 to 195° during 1·5 hr. The bath temperature was then raised to 210° for 1 hr., and after the mixture had been kept at room temperature overnight the excess of malonic ester was removed *in vacuo*. The residue was triturated with ether, whereupon a solid (diamide?) separated. The ether solution gave on evaporation an oil which crystallised. Recrystallisation from light petroleum gave yellow prisms (21 g.) of the *amide*, m. p. 74° (Found: C, 66·1; H, 6·0; N, 4·2; C_2H_5O, 26·7. $C_{18}H_{19}O_5N$ requires C, 65·8; H, 5·8; N, 4·25; C_2H_5O, 27·4%).

The corresponding *methyl ester amide* was prepared in the same way from methyl 2-amino-3-naphthoate [itself obtained by methanol–sulphuric acid esterification of the acid and forming from light petroleum pale yellow prisms, m. p. 102° (lit.,[7] m. p. 104—105°)], and crystallised from light petroleum as pale yellow prisms, m. p. 109—111° (Found: C, 64·8; H, 5·5; N, 4·6. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4; N, 4·45%).

Methyl 2-Acetamido-3-naphthoate.—The ester (1·4 g.) and acetic anhydride (7 ml.) were heated at 100° for 10 min. Working up in the usual way and crystallisation from light petroleum gave the *amide* (1·3 g.) as felted needles, m. p. 128—129° (Found: C, 69·4; H, 5·3; N, 5·7. $C_{14}H_{13}O_3N$ requires C, 69·2; H, 5·35; N, 5·8%).

2,4-Dihydroxy-1-aza-anthracene.—(*a*) To a boiling, stirred solution of the ethyl ester amide (IIa, 21 g.) in anhydrous ether (500 ml.) was added dropwise a solution of sodium (1·72 g.) in anhydrous ethanol (100 ml.) over 1·5 hr. A yellow solid separated and after being kept overnight the mixture was evaporated to dryness. The residue, 2N-sodium hydroxide (100 ml.) and water (200 ml.) were heated and stirred at 100° for 5 hr. Acidification precipitated a yellow solid (13 g.) which was washed with water and ethanol and dried (m. p. >350°). Its insolubility made recrystallisation difficult, and for the purpose of analysis a sample of *2,4-dihydroxyaza-anthracene* (Found: C, 74·6; H, 4·6; N, 6·85. $C_{13}H_9NO_2$ requires C, 74·0; H, 4·3; N, 6·65%) was obtained by dissolution in 2N-sodium hydroxide and precipitation with acetic acid.

(*b*) To a stirred suspension of sodium methoxide (0·2 g.) in anhydrous pyridine (5 ml.) was added with stirring, during 15 min., a solution of the methyl ester amide (IIb, 1 g.) in pyridine (4 ml.). The mixture was stirred at room temperature for 2 hr., then at 110° for 3 hr., and added to water (50 ml.). Acidification gave a yellow solid (0·75 g.) which was washed with water and heated at 100° for 6 hr. with 2N-sodium hydroxide (10 ml.). Addition of water and acidification gave a yellow solid, identical with that described above.

The dihydroxy-compound (5 g.), acetic anhydride (100 ml.), and sulphuric acid (0·5 ml.) were warmed together gently until a solution was formed. The solution was boiled for 5 min. and poured on ice. The yellow precipitate (6 g., m. p. 272—276°) gave yellow matted needles (2·05 g.) of the *monoacetate*, m. p. 284—286° (decomp.) (Found: C, 70·7; H, 4·6; N, 5·6. $C_{15}H_{11}NO_3$ requires C, 71·2; H, 4·4; N, 5·5%) on crystallisation from cellosolve.

2,4-Dichloro-1-aza-anthracene.—The dihydroxy-compound (4 g.) and phosphoryl chloride

[7] U.S.P. 1,903,880/1933 (*Chem. Abs.*, 1923, **27**, 3343).

(50 ml.) were boiled together for 1 hr. Phosphoryl chloride was removed *in vacuo* and the residue was added to ice. Basification with ammonia, collection, washing with water and drying *in vacuo* gave the product (5·2 g., m. p. 144—146°). Recrystallisation from light petroleum gave yellow prisms of 2,4-*dichloro*-1-*aza-anthracene*, m. p. 155° (Found: N, 5·8; Cl, 28·3. $C_{13}H_7Cl_2N$ requires N, 5·65; Cl, 28·4%).

Dehalogenation Experiments.—(*a*) The dichloro-compound (1·6 g.), ethanol (20 ml.), water (10 ml.), magnesium oxide (1·6 g.), and palladised charcoal (0·5 g., 5%) were shaken with hydrogen. The theoretical uptake (289 ml.) was achieved in 3·5 hr. though hydrogen was still being absorbed and some starting material was still present in suspension. The mixture was filtered and the filtrate was added to water. A yellow solid (0·5 g.) was precipitated which from light petroleum gave yellow prisms (0·3 g.), m. p. 149—150° (Found: C, 85·1; H, 6·9; N, 7·8. Calc. for $C_{13}H_{13}N$: C, 85·3; H, 7·1; N, 7·65%) (m. p.[8] of 1,2,3,4-tetrahydro-1-aza-anthracene, 149°).

(*b*) The dichloro-compound (250 mg.), toluene-*p*-sulphonylhydrazine (0·4 g.), and chloroform (6·5 ml.) were kept for four days at room temperature and the yellow precipitate (180 mg., m. p. 200—203°) was collected. It was heated with cellosolve (4 ml.) and N-sodium hydroxide (4 ml.) at 100° until nitrogen evolution ceased. By addition of water and extraction with ether a solid was isolated which was extracted with boiling light petroleum (b. p. 40—60°). Evaporation of the extract gave the product (10 mg., m. p. 112—120°) which was treated with picric acid in ethanol. The *picrate* separated from cellosolve as small yellow crystals, m. p. 247° (decomp.) (Found: C, 52·3; H, 2·8; N, 12·4. $C_{13}H_8ClN,C_6H_3N_3O_7$ requires C, 51·5; H, 2·5; N, 12·6%).

2,4-*Dihydroxy*-1-*aza-anthracene*-9,10-*quinone*.—To a solution of 2,4-dihydroxy-1-aza-anthracene monoacetate (2 g.) in acetic acid (60 ml.) was added, with stirring at 100° during 30 min., a solution of chromium trioxide (4 g.) in water (3 ml.) and acetic acid (12 ml.). After a further 15 min. at 100° the mixture was diluted with water (250 ml.) and the precipitate was collected. It (1·1 g.) was heated at 100° with N-sodium hydroxide (40 ml.) for 40 min. The solution was acidified and the precipitate (0·6 g.) was collected. Crystallisation from cellosolve gave yellow needles of the *quinone*, m. p. 325—330° (decomp.) (Found: C, 64·8; H, 3·2; N, 5·6. $C_{13}H_7NO_4$ requires C, 64·8; H, 2·9; N, 5·8%).

2,4-*Dimethoxy*-1-*aza-anthracene*-9,10-*quinone*.—The dihydroxy-compound (200 mg.), dry chloroform (10 ml.), silver oxide (1·4 g.), and methyl iodide (5 ml.) were heated together under reflux for 3 hr. Filtration and evaporation gave a solid (250 mg.) which on crystallisation from benzene gave yellow needles (180 mg.) of 2,4-*dimethoxy*-1-*aza-anthracene*-9,10-*quinone*, m. p. 217—218° (Found: C, 67·1; H, 4·3; N, 5·5; CH_3O, 23·6. $C_{15}H_{11}NO_4$ requires C, 66·91; H, 4·12; N, 5·2; CH_3O, 23·1%).

2,4-*Dichloro*-1-*aza-anthracenequinone*.—The dihydroxy-compound (0·7 g.) and phosphoryl chloride (14 ml.) were heated under reflux for 3 hr. Working up in the usual way gave the crude product (0·75 g., m. p. 205—210°) which was purified by passage over alumina in benzene, and elution with benzene–ethyl acetate (4 : 1). The single yellow band so isolated arose from 2,4-*dichloro*-1-*aza-anthracene*-9,10-*quinone* which crystallised from ethyl acetate as yellow needles (0·45 g.), m. p. 224—225° (Found: N, 5·2; Cl, 25·6. $C_{13}H_5Cl_2NO_2$ requires N, 5·1; Cl, 25·5%).

Dechlorination of 2,4-*Dichloro*-1-*aza-anthracene*-9,10-*quinone*.—The dichloro-compound (145 mg.), ethanol (10 ml.), water (5 ml.), magnesium oxide (145 mg.), and palladised charcoal (10%, 70 mg.) were shaken with hydrogen until uptake ceased (31 ml. were absorbed). The mixture was filtered and the brownish-red filtrate was aerated for 20 min. When the solution was added to water (50 ml.), red needles (50 mg., m. p. 260—265° with sublimation) separated. Crystallisation from benzene gave pale red needles, m. p. 278—280° (with sublimation), alone and mixed with authentic 1-aza-anthraquinone.

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[8] J. von Braun and H. Gruber, *Ber.*, 1922, **55**, 1710.