466. 1 : 8-*Dihydroxynaphthalene.*

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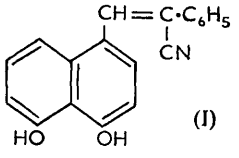
Methylation of 1 : 8-dihydroxynaphthalene gave, at variance with the literature, both a mono- and a di-ether. Formylation and acetylation of the latter occurred at position 4. The 4-ethyl and 4-methyl derivatives were prepared; the dimethyl ether of the latter underwent formylation at position 5. Some other derivatives of 1 : 8-dihydroxynaphthalene have been synthesised.

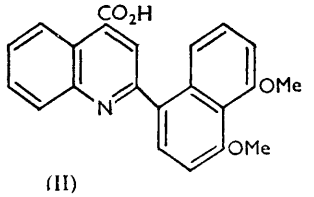
Notwithstanding the ready accessibility of 1 : 8-dihydroxynaphthalene, little is known concerning its reactions, and even the structure of its methylation products has not yet been elucidated. Heller and Kretzschmann [1] treated 1 : 8-dihydroxynaphthalene with dimethyl sulphate in aqueous alkali and obtained a compound, m. p. 50°, stated to be the dimethyl ether, but Staudinger, Schlenker, and Goldstein [2] obtained, in the same way, only the monomethyl ether, m. p. 55—56°, which Böeseken and Smitt [3] also isolated as the sole product on use of diazomethane. It has now been found that methylation of 1 : 8-dihydroxynaphthalene with dimethyl sulphate in aqueous alkali affords the monomethyl ether and smaller amounts of the true dimethyl ether, m. p. 157°; the yield of the latter is increased by using ethanol as solvent. The previous failure to prepare the dimethyl ether was due to the cryptophenolic nature of 8-methoxy-1-naphthol, on account of which it is only sparingly soluble in aqueous alkalis and evades further methylation.

Formylation of 1 : 8-dimethoxynaphthalene with dimethylformamide and phosphorus oxychloride [4] gave 4 : 5-dimethoxy-1-naphthaldehyde, whose constitution followed from the fact that the acrylonitrile resulting from its alkali-catalysed condensation with benzyl cyanide was demethylated by pyridine hydrochloride to β-(4 : 5-dihydroxynaphthyl)-α-phenylacrylonitrile (I); had the formyl group entered the position *ortho* to a methoxy-radical, this reaction sequence would have led to a coumarin.[5] Friedel–Crafts acetylation of 1 : 8-dimethoxynaphthalene afforded a single ketone, which was 1-acetyl-4 : 5-dimethoxynaphthalene, as its Pfitzinger reaction with isatin yielded a cinchoninic acid (II) identical with the acid resulting from a Doebner reaction of 4 : 5-dimethoxy-1-naphthaldehyde with aniline and pyruvic acid.

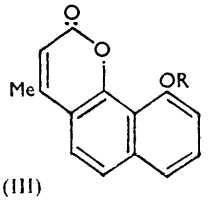


(I)

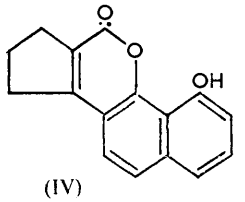
Homologues of 1 : 8-dihydroxynaphthalene were prepared by Wolff–Kishner reduction of 4 : 5-dimethoxy-1-naphthaldehyde and 1-acetyl-4 : 5-dimethoxynaphthalene, and their demethylation led to 4 : 5-dihydroxy-1-methyl- and 1-ethyl-4 : 5-dihydroxy-naphthalene. Formylation of 4 : 5-dimethoxy-1-methylnaphthalene gave an aldehyde which was



(II)



(III)



(IV)

probably 4 : 5-dimethoxy-8-methyl-1-naphthaldehyde as its formyl group was sterically hindered and it failed to give an acrylonitrile with benzyl cyanide in the usual conditions. Wolff–Kishner reduction was successful, but the demethylation product of 1 : 8-dimethoxy-4 : 5-dimethylnaphthalene was highly autoxidisable and could not be obtained

[1] Heller and Kretzschmann, *Ber.*, 1921, **54**, 1098, 3330.
[2] Staudinger, Schlenker, and Goldstein, *Helv. Chim. Acta*, 1921, **4**, 334, 339.
[3] Böeseken and Smitt, *Rec. Trav. chim.*, 1939, **58**, 125.
[4] Cf. Buu-Hoï and Lavit, *J.*, 1955, 2776.
[5] Buu-Hoï *et al.*, *J.*, 1951, 2307; *J. Org. Chem.*, 1954, **19**, 1391, 1548.

pure. Unlike the dimethyl ethers of all the other dihydroxynaphthalenes, whose picrates are orange-yellow to orange-red, 1 : 8-dimethoxynaphthalene and its homologues give brown-red to brown-violet picrates.

In the presence of hydrogen chloride, 1 : 8-dihydroxynaphthalene and one mol. of ethyl acetoacetate give 4'-hydroxy-4-methyl-7 : 8-benzocoumarin (III; R = H), behaviour reminiscent of that of 1 : 5-dihydroxynaphthalene;[6] 8-methoxy-1-naphthol yielded in the same conditions 4'-methoxy-4-methyl-7 : 8-benzocoumarin (III; R = Me), which was converted by pyridine hydrochloride into the phenol (III; R = H). 4'-Hydroxy-3 : 4-*cyclo*penteno-7 : 8-benzocoumarin (IV), was similarly obtained by condensation with ethyl *cyclo*pentanone-2-carboxylate, and the *cyclo*hexene analogue analogously.

Experimental

Methylation of 1 : 8-*Dihydroxynaphthalene*.—To a freshly prepared solution of 1 : 8-dihydroxynaphthalene (20 g.; m. p. 145—146°) in 10% aqueous potassium hydroxide (155 c.c.), dimethyl sulphate (36 g.) was added in small portions with stirring, and the mixture then refluxed for 10 min. Further potassium hydroxide (10 g.) was stirred in, then more dimethyl sulphate added until the solution was acid, at which point the process was repeated once more. The products were then taken up in benzene, the benzene solution washed with dilute aqueous sodium hydroxide, then with water, and dried (Na_2SO_4), the solvent removed, and the residue distilled *in vacuo*. The distillate (b. p. 167—168°/12 mm.) gave on crystallisation from ethanol : (*a*) less soluble 1 : 8-*dimethoxynaphthalene*, leaflets (7 g.), m. p. 157° (Found : C, 76·9; H, 6·5; O, 17·1. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4; O, 17·0%), whose *picrate* formed brown-red needles, m. p. 172°, from ethanol (Found : N, 9·8. $C_{18}H_{15}O_9N_3$ requires N, 10·1%); and (*b*) more soluble 8-methoxy-1-naphthol (8 g.), m. p. 55—56°, which was insoluble in dilute aqueous alkali.

When the methylation was performed in ethanol (150 c.c.), the yields of 1 : 8-dimethoxynaphthalene and 8-methoxy-1-naphthol were 15·5 g. and 3 g. respectively.

4 : 5-*Dimethoxy*-1-*naphthaldehyde*.—1 : 8-Dimethoxynaphthalene (20 g.), dimethylformamide (10 g.), phosphorus oxychloride (18·5 g.), and dry toluene (20 c.c.) were refluxed for 3 hr. on a water-bath, and the greenish crystalline mass formed was treated with hot concentrated aqueous sodium acetate for 30 min. The aldehyde was taken up in benzene, the benzene solution washed with dilute hydrochloric acid then with water, and dried ($CaCl_2$), the solvent removed, and the residue fractionated *in vacuo*. 4 : 5-*Dimethoxy*-1-*naphthaldehyde* (19 g.), b. p. 221°/12 mm., formed colourless needles, m. p. 95°, from ethanol, and gave a red colour in sulphuric acid (Found : C, 72·1; H, 5·6. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%). The *thiosemicarbazone* crystallised as pale yellow needles, m. p. 259° (darkens from 240°), from acetic acid (Found : C, 57·8; H, 5·0. $C_{14}H_{15}O_2N_3S$ requires C, 58·1; H, 5·2%).

β-(4 : 5-*Dimethoxynaphthyl*)-α-*phenylacrylonitrile*.—A warm solution of the foregoing aldehyde (2 g.) and benzyl cyanide (1·3 g.) in ethanol (40 c.c.) was shaken with 20% aqueous sodium hydroxide (5 c.c.), and then left at room temperature for 30 min. The yellow precipitate of *acrylonitrile* formed on dilution with water was collected, washed with water, and recrystallised from ethanol–benzene, giving lemon-yellow needles (1·5 g.), m. p. 176°; this compound is thermochromic, becoming orange when heated and reverting to pale yellow on cooling (Found : C, 79·8; H, 5·5. $C_{21}H_{17}O_2N$ requires C, 80·0; H, 5·4%).

β-(4 : 5-*Dihydroxynaphthyl*)-α-*phenylacrylonitrile* (I).—The foregoing acrylonitrile (1 g.) and pyridine hydrochloride (6 g.) were refluxed for 10 min. and, after cooling, water was added. The orange *product* precipitated was collected, washed with water, and recrystallised from acetic acid, giving yellow needles (0·6 g.), m. p. 212° (darkens from 190°), dissolving in aqueous sodium hydroxide to an orange-yellow solution (Found : C, 77·2; H, 4·7; O, 13·1; N, 4·6. $C_{19}H_{13}O_2N,0{\cdot}5H_2O$ requires C, 77·0; H, 4·7; O, 13·5; N, 4·7%).

β-(4 : 5-*Dimethoxynaphthyl*)-α-p-*chlorophenylacrylonitrile*.—Prepared from 4 : 5-dimethoxy-1-naphthaldehyde (1 g.) and 4-chlorobenzyl cyanide (0·8 g.), this *nitrile* formed pale yellow needles, m. p. 195°, from ethanol–benzene (Found : C, 71·8; H, 4·5. $C_{21}H_{16}O_2NCl$ requires C, 72·1; H, 4·6%), giving a brown-red halochromy in sulphuric acid.

α-p-*Bromophenyl*-β-(4 : 5-*dimethoxynaphthyl*)*acrylonitrile*, similarly obtained from 4-bromobenzyl cyanide (1 g.), formed yellow needles, m. p. 193°, from ethanol–benzene (Found : C,

[6] Robinson and Weygand, *J.*, 1941, 386.

63·7; H, 4·0. $C_{21}H_{16}O_2NBr$ requires C, 64·0; H, 4·1%). These two nitriles also gave alkali-soluble demethylation products on treatment with pyridine hydrochloride.

4 : 5-*Dimethoxy*-1-*methylnaphthalene*.—A solution of 4 : 5-dimethoxy-1-naphthaldehyde (17 g.) and 95% hydrazine hydrate (7 g.) in diethylene glycol (100 c.c.) was heated for a few minutes for formation of the hydrazone; potassium hydroxide (7 g.) was then added, and the mixture refluxed for 30 min. with removal of water. After cooling, water was added, the product taken up in benzene, the benzene solution washed with dilute hydrochloric acid, then with water, and dried ($CaCl_2$), the solvent removed, and the residue fractionated *in vacuo*. 4 : 5-*Dimethoxy*-1-*methylnaphthalene* (10 g.), b. p. 172—173°/12 mm., formed leaflets, m. p. 65°, from ethanol (Found : C, 77·2; H, 7·1. $C_{13}H_{14}O_2$ requires C, 77·2; H, 6·9%), and gave a *picrate*, brown-red needles, m. p. 169° (darkens from 156°), from ethanol (Found : N, 9·9. $C_{19}H_{17}O_9N_3$ requires N, 9·7%).

4 : 5-*Dihydroxy*-1-*methylnaphthalene*.—The foregoing methyl ether (1·5 g.) was refluxed with pyridine hydrochloride (9 g.) for 15 min.; after cooling, water was added, the product taken up in ether, washed with water, and dried (Na_2SO_4), the solvent removed, and the residue recrystallised twice from benzene. 4 : 5-*Dihydroxy*-1-*methylnaphthalene* (0·8 g.) formed needles, m. p. 134° (Found : C, 75·6; H, 5·4. $C_{11}H_{10}O_2$ requires C, 75·9; H, 5·7%).

1-*Acetyl*-4 : 5-*dimethoxynaphthalene*.—To an ice-cooled suspension of 1 : 8-dimethoxynaphthalene (9 g.) in dry nitrobenzene (100 c.c.) containing acetyl chloride (4·2 g.), aluminium chloride (7·2 g.) was added in small portions with stirring, and the mixture kept overnight at room temperature. After addition of water, the nitrobenzene was steam-distilled, the reaction product taken up in benzene, washed first with dilute aqueous sodium hydroxide, then with water, and dried ($CaCl_2$), the solvent removed, and the residue fractionated *in vacuo*. The *ketone* (8 g.), b. p. 232—233°/15 mm., formed yellowish needles, m. p. 129°, from ethanol and gave a red colour in sulphuric acid (Found : C, 72·9; H, 6·0. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%).

1-*Ethyl*-4 : 5-*dimethoxynaphthalene*.—Prepared by Wolff–Kishner reduction of the foregoing ketone (4·5 g.), this *ether*, b. p. 187—188°/12 mm., formed needles (1·5 g.), m. p. 76°, from ethanol (Found : C, 77·5; H, 7·6. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%); its *picrate* crystallised in brown-violet needles, m. p. 147°, from ethanol (Found : N, 9·2. $C_{20}H_{19}O_9N_3$ requires N, 9·4%). Demethylation of this ether (1·3 g.) with pyridine hydrochloride (8 g.), as above, gave a poor yield of 1-*ethyl*-4 : 5-*dihydroxynaphthalene*, crystallising as prisms, m. p. 84°, from *cyclo*hexane (Found : C, 76·3; H, 6·1. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%).

2-(4 : 5-*Dimethoxy*-1-*naphthyl*)*cinchoninic acid* (II).—(a) *Pfitzinger reaction*. A solution of 1-acetyl-4 : 5-dimethoxynaphthalene (1·5 g.), isatin (1 g.), and potassium hydroxide (1·1 g.) in ethanol (30 c.c.) was refluxed for 48 hr.; water was then added, the neutral impurities were removed in ether, and the filtrate was acidified with acetic acid. The precipitated *acid* crystallised as yellow needles, m. p. 274° (darken from 256°), from ethanol (Found : C, 73·5; H, 4·5. $C_{22}H_{17}O_4N$ requires C, 73·6; H, 4·7%).

(b) *Doebner reaction*. A solution of 4 : 5-dimethoxy-1-naphthaldehyde (1 g.), aniline (0·5 g.), and pyruvic acid (0·45 g.) in ethanol (25 c.c.) was refluxed for 5 hr. The precipitate obtained on cooling was recrystallised twice from ethanol, giving yellow needles, m. p. 273—274° alone or mixed with a sample prepared by method (a).

4 : 5-*Dimethoxy*-8-*methyl*-1-*naphthaldehyde*.—A mixture of 4 : 5-dimethoxy-1-methylnaphthalene (7·8 g.), dimethylformamide (3·7 g.), phosphorus oxychloride (6·8 g.), and dry toluene (8 c.c.) was heated for 5 hr. on a water bath, and the mixture worked up in the usual way. The *aldehyde*, b. p. 226—227°/12 mm., formed yellowish prisms (7·6 g.), m. p. 137°, from ethanol, giving a brown-red colour in sulphuric acid (Found : C, 73·1; H, 6·1. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%). The *thiosemicarbazone* formed pale yellow prisms, m. p. 257° (darken from *ca.* 226°), from acetic acid (Found : C, 59·1; H, 5·5. $C_{15}H_{17}O_2N_3S$ requires C, 59·4; H, 5·6%). This aldehyde gave no substantial amount of condensation product when treated with benzyl cyanide in the presence of aqueous sodium hydroxide.

1 : 8-*Dimethoxy*-4 : 5-*dimethylnaphthalene*.—Reduction of the foregoing aldehyde (6 g.) with hydrazine hydrate (2·5 g.) and potassium hydroxide (2·5 g.) in diethylene glycol (50 c.c.) in the usual way gave a *product* (3·3 g.), b. p. 188—190°/12 mm., needles, m. p. 78° (from ethanol or light petroleum) (Found : C, 77·9; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%), giving a picrate, brown-violet needles, m. p. 181° (from ethanol).

4′-*Hydroxy*-4-*methyl*-7 : 8-*benzocoumarin* (III; R = H).—A water-cooled solution of 1 : 8-dihydroxynaphthalene (4 g.) and ethyl acetoacetate (10 g.) in ethanol (50 c.c.) was saturated with hydrogen chloride, and the mixture left overnight. The *coumarin* precipitated on dilution

with water was washed with ethanol and recrystallised from benzene, giving yellowish, sublimable needles (3 g.), m. p. 224° (Found : C, 74·2; H, 4·5. $C_{14}H_{10}O_3$ requires C, 74·3; H, 4·4%).

4′-*Methoxy*-4-*methyl*-7 : 8-*benzocoumarin* (III; R = Me), similarly prepared from 8-methoxy-1-naphthol (3 g.) and ethyl acetoacetate (7·5 g.), formed sublimable needles, m. p. 205°, from acetic acid (Found : C, 74·9; H, 5·3. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%); demethylation as above gave 4′-hydroxy-4-methyl-7 : 8-benzocoumarin, m. p. 224°.

4′-*Hydroxy*-3 : 4-cyclo*penteno*-7 : 8-*benzocoumarin* (IV).—A water-cooled solution of 1 : 8-dihydroxynaphthalene (1 g.) and ethyl 2-oxo*cyclo*pentanecarboxylate (1·2 g.) in ethanol (10 c.c.) was saturated with hydrogen chloride, and the mixture left overnight. The precipitate obtained on dilution with ethanol formed needles (1 g.), m. p. 213°, from acetic acid (Found : C, 75·9; H, 5·0. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%). 4′-*Hydroxy*-3 : 4-cyclo*hexeno*-7 : 8-*benzocoumarin*, similarly prepared from ethyl 2-oxo*cyclo*hexanecarboxylate (1·3 g.), formed yellowish prisms, m. p. 193°, from benzene (Found : C, 76·5; H, 5·5. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%).

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