273. *Derivatives of* o-*Hydroxybenzylsulphonic Acid.*

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For further study of the alkali derivatives of di-2-hydroxynaphthyl-1-methane we required the unsymmetrical derivatives of the latter, and the experiments now described were undertaken with the object of synthesising these. A suitable process has been found in the reaction between 2-naphthol and its 1-methanesulphonate which is shown to be reversible. Sodium 2-hydroxybenzylsulphonate and its nuclear homologues may be obtained (1) from the relevant phenol with formaldehyde and sodium sulphite, (2) from the 2-hydroxybenzyl alcohol and sodium bisulphite, but the reactivities of these products with 2-naphthol are in general less than that of 2-hydroxynaphthyl-1-methanesulphonate. An interpretation of the notably high activity of R in $C_{10}H_6OH{\cdot}CH_2R$ is offered and this has led to the observation that 2-hydroxynaphthyl-1-thiolsulphonate is readily formed from sodium sulphite and di-2-hydroxynaphthyl 1-sulphide.

Further study of the covalent alkali derivatives of di-2-hydroxynaphthyl-1-methane and di-2-hydroxynaphthyl 1-sulphide required unsymmetrical derivatives of these types; methods of synthesising these from the chloro-thiols are available in the sulphide series (J., 1930, 1741) but not in the methane series. The experiments now recorded were undertaken in order to render the unsymmetrical derivatives of the latter group available. There is no doubt that reaction of 2-naphthol or its derivatives with 2-hydroxynaphthyl-1-methanol would lead to the desired result, but the latter substance is not easily available (Betti and Mundici, *Gazzetta*, 1906, **36**, 660; Shoesmith and Rubli, J., 1927, 3101) whilst the 1-chloromethyl derivative is unknown. According to patent literature (D.R.P. 87,335) sodium 2-naphthol-1-methanesulphonate is formed by heating an aqueous solution of formaldehyde and sodium sulphite with 2-naphthol. Very little is known of the sequence of reactions taking place in this process, but it may be noted that Cohen and Clutterbuck (J., 1923, **123**, 2510), having isolated 2-hydroxynaphthyl-1-methanol as a subsidiary product, were inclined to regard the formation of sulphonate as taking place as follows:

$$C_{10}H_7OH \longrightarrow C_{10}H_6(OH){\cdot}CH_2{\cdot}OH \xrightarrow{Na_2SO_3} C_{10}H_6(OH){\cdot}CH_2{\cdot}SO_3Na + NaOH$$

In the present experiments, however, the occurrence of this alcohol among the products has not been confirmed. Instead, di-2-hydroxynaphthyl-1-methane has always been met with;

in fact, a relatively large amount of this substance, evidently arising from the condensation of 2-naphthol with formaldehyde (Manasse, *Ber.*, 1894, **27**, 2412), is liberated at an early stage but this diminishes as the reaction proceeds. Further experiment has established the fact that di-2-hydroxynaphthyl-1-methane is resolved by hot aqueous sodium sulphite into sodium 2-naphthoxide and sodium 2-naphthol-1-methanesulphonate (I, *a*); moreover, the process is reversible, the methane derivative being readily formed from the sulphonate with excess of naphthoxide (I, *b*).

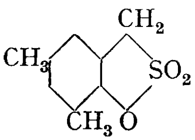
$$\text{(I.)} \quad (C_{10}H_6{\cdot}OH)_2CH_2 + Na_2SO_3 \underset{b}{\overset{a}{\rightleftarrows}} C_{10}H_6(OH){\cdot}CH_2{\cdot}SO_3Na + C_{10}H_7{\cdot}ONa$$

Not all derivatives of di-2-hydroxynaphthyl-1-methane are so easily resolved by sulphite as the parent substance; for example, the 6 : 6′-dibromo-derivative remains almost unattacked under the same conditions, and the unsubstituted monomethyl ether behaves similarly. Nevertheless, when 6-bromo-2-naphthol is used instead of 2-naphthol in the reaction with sulphite and formaldehyde, satisfactory yields of 6-bromo-2-naphthol-1-methanesulphonate are obtained together with *bis*-(*6-bromo-2-hydroxynaphthyl*)-1-*methane*. For these reasons it is concluded that in the original process the source of 2-naphthol-1-methanesulphonate is at least twofold : fission of the methane (I, *a*) and condensation of sodium 2-naphthoxide with formaldehydebisulphite (II).

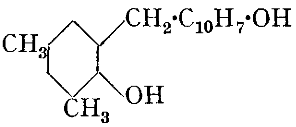
$$\text{(II.)} \quad C_{10}H_7{\cdot}ONa + CH_2(OH)(SO_3Na) \longrightarrow H_2O + C_{10}H_6(ONa)(CH_2{\cdot}SO_3Na)$$

Support for the process indicated by Cohen and Clutterbuck has not been found by isolation of the methanol, but since the conversion of this into the sulphonate by sodium sulphite is without doubt attainable, their suggested process may be regarded as a third possible source of the product.

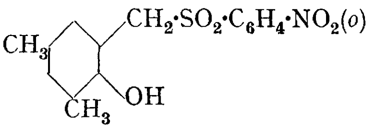
The process I, *b* may conveniently be used for the synthesis of unsymmetrically substituted di-2-hydroxynaphthyl-1-methanes; the method is illustrated by the cases of the 3-*bromo*- and 6-*bromo*-derivatives. With the object of widening the application of this process, other means of obtaining *o*-hydroxymethanesulphonates were sought. It is now shown that these may be obtained by the interaction of sodium bisulphite and 2-hydroxybenzyl alcohol or its nuclear homologues, as well as by the reaction of formaldehyde and sodium sulphite with suitable phenols. The products were characterised by conversion into the " benzylsultones " (Marckwald and Fahne, *Ber.*, 1898, **31**, 1868), *e.g.*, (III). Except in the case of the dimethyl derivative (compare III) the yields of the sulphonates under the usual conditions were relatively small and it is noteworthy that benzyl alcohol does not exhibit this behaviour. Moreover, the reactivities of these sulphonates with sodium 2-naphthoxide was poor compared with that of 2-naphthol-1-methanesulphonate, (IV), for example, being obtained only in small yield. This *substance*, however, may be obtained in good yield by the interaction of 2-naphthol and 5-chloromethyl-*m*-4-xylenol.



(III.)



(IV.)



(V.)

Sulphones such as (V), generated by reaction of a sulphinate with the 2-hydroxybenzyl chloride, have also been examined. Under mildly alkaline conditions these substances suffer fission at the $-CH_2{\cdot}SO_2-$ group, the sulphinate being regenerated; in fact, the sulphone (V) did not undergo the intramolecular displacement characteristic of the homologous 2′-nitro-2-hydroxydiphenylsulphones (J., 1934, 422).

On reviewing the facts now recorded, together with others such as the fission of di-2-hydroxynaphthyl-1-methane by alkaline reduction (Fries and Hubner, *Ber.*, 1906, **39**, 435), it is evident that the group R in $HO{\cdot}C_{10}H_6{\cdot}CH_2R$ possesses exceptionally high mobility. This circumstance is adequately explained by the work of Baddeley and Bennett (J., 1933, 263), who have shown that the hydrolysis of substituted benzyl chlorides is favoured by electron accession at the methane carbon atom. In the present case this electron accession is evidently due to the *o*-phenolic ion and is further increased by attachment of the methane carbon atom to the 1-position in the 2-naphthol nucleus. Finally, it may be observed that according to these views a similar behaviour must be expected of di-2-hydroxynaphthyl 1-sulphide. Facts fulfilling this requirement are forthcoming; *e.g.*, the sulphide in alkaline media may assume the keto-hydroxy-condition (J., 1930, 959), it is converted by alkaline reduction into 2-naphthol and 2-hydroxy-1-thiolnaphthalene, whilst it is now shown that like the methane derivative (I, *a*) it is resolved by sodium sulphite into 2-naphthol and the *thiolsulphonate* $C_{10}H_6(OH)(S{\cdot}SO_3Na)$.

EXPERIMENTAL.

Di-2-hydroxynaphthyl-1-methane.—Formaldehyde (19 g.; 40%) was added to a solution of sodium sulphite (63 g.) in water (250 c.c.) containing 2-naphthol (36 g.) in suspension. This was heated (10 mins., 100°) and the crystalline material (15 g.) which had separated was identified as di-2-hydroxynaphthyl-1-methane by its m. p. (199°) and by conversion into the acetyl derivative, m. p. 214° (Manasse, *loc. cit.*, gives m. p. 214°). In a duplicate experiment the di-2-hydroxynaphthol-1-methane almost entirely dissolved after continued heating (3 hrs.).

An aqueous solution of sodium hydroxide (50 c.c., 4%) containing 2-naphthol (3·6 g.) and sodium 2-hydroxynaphthyl-1-methanesulphonate (6·5 g.) was boiled (6 hrs.). The insoluble material obtained by acidifying the cooled mixture with acetic acid yielded di-2-hydroxynaphthyl-1-methane (3·6 g.).

Reaction with sodium sulphite. An aqueous solution of sodium hydroxide (40 c.c., 2%) containing sodium sulphite (5 g.) and di-2-hydroxynaphthyl-1-methane (6 g.) was boiled (3 hrs.). Acidification of the cooled mixture yielded the methane (2·2 g.) and 2-naphthol (1·6 g.), the sulphonate remaining in the aqueous liquor.

Sodium 6-bromo-2-hydroxynaphthyl-1-methanesulphonate. Formaldehyde (2·3 c.c., 40%) was added to a suspension of 6-bromo-2-naphthol (6·7 g.) in an aqueous solution of sodium sulphite (30 g.). The crystalline precipitate had not dissolved after the mixture had been heated for 6 hrs.; purified from amyl alcohol, it had m. p. 240° and was identical with a sample of *bis-(6-bromo-2-hydroxynaphthyl-1)-methane* which had been obtained by the method of Fries (*Ber.*, 1906, **39**, 439) from formaldehyde and 6-bromo-2-naphthol in presence of sodium acetate (Found: C, 54·9; H, 3·3. $C_{21}H_{14}O_2Br_2$ requires C, 55·0; H, 3·1%). The aqueous portion of the reacting mixture on acidification with dilute sulphuric acid yielded the desired sodium sulphonate (5 g.), which separated from hot water in plates. The *lead* salt of the *O*-methyl derivative was sparingly soluble in water [Found: C, 31·9; H, 2·7. $(C_{12}H_{10}O_4BrS)_2Pb,2H_2O$ requires C, 31·8; H, 2·6%].

6-Bromodi-2-hydroxynaphthyl-1-methane.—(*a*) An aqueous solution of *N*-sodium hydroxide (40 c.c.) containing 2-naphthol (3 g.) and sodium 6-bromo-2-hydroxynaphthyl-1-methanesulphonate from the foregoing preparation was boiled (6 hrs.), the crystalline material which separated being collected at intervals (1·5 g.). This separated from aqueous alcohol in prisms, m. p. 210° (decomp.) (Found: C, 66·5; H, 4·0. $C_{21}H_{15}O_2Br$ requires C, 66·6; H, 4·0%). (*b*) It was also obtained by boiling the aqueous alkaline solution (*N*/3-NaOH) of 6-bromo-2-naphthol and sodium 2-hydroxynaphthyl-1-methanesulphonate, the product which separated being collected at intervals.

3-Bromodi-2-hydroxynaphthyl-1-methane separated from the boiling solution of 3-bromo-2-naphthol and 2-hydroxynaphthyl-1-methanesulphonate in aqueous *N*/3-sodium hydroxide and was removed from time to time during the course of the reaction (5 hrs.). Purified from alcohol, it had m. p. 200° (decomp.) (Found: C, 66·3; H, 4·1. $C_{21}H_{15}O_2Br$ requires C, 66·6; H, 4·0%).

Sodium 2-Hydroxyphenylmethanesulphonate.—An aqueous solution (150 c.c.) of saligenin (8·2 g.) and sodium bisulphite (7 g.) was boiled (3 hrs.). The cold neutralised solution was evaporated, the residue being extracted with hot alcohol. Further purification of the soluble product yielded the required *sulphonate* in the crystalline state (4·5 g.) (Found: Na, 10·9. $C_7H_7O_4SNa$ requires Na, 10·7%). Further identification was effected by reaction with excess of phosphorus pentachloride, first at 20° and finally at 100° (1 hr.). After admixture with ice, an ethereal extract was obtained, which was kept in presence of sodium bicarbonate and then dried. The crude material remaining after evaporation of the solvent was sublimed in a vacuum. Benzylsultone (*loc. cit.*) was thus obtained, m. p. 86° (Found: C, 49·4; H, 3·5. Calc.: C, 49·6; H, 3·5%).

Sodium *p*-cresol-3-methanesulphonate was obtained (*a*) by reaction of aqueous sodium bisulphite with *p*-cresol-3-methanol (Manasse, *Ber.*, 1894, **27**, 2409) as described in the case of saligenin, or (*b*) by boiling (3 hrs.) an aqueous solution (100 c.c.) containing *p*-cresol (10·8 g.), sodium sulphite (37 g.), and formaldehyde (7·5 g., 40%). The neutralised solution was evaporated, the residue being treated with hot alcohol, which removed the required sulphonate (7 g.). The products from both sources were identified by conversion into the " sultone " by the usual process. 5-*Methylbenzylsultone* formed long needles, m. p. 91·5° (Found : C, 52·0; H, 4·4. $C_8H_8O_3S$ requires C, 52·2; H, 4·3%).

Sodium m-4-*Xylenol*-5-*methanesulphonate*.—(*a*) From the interaction of *m*-4-xylenol (12 g.), sodium sulphite (24 g.), and formaldehyde (8 c.c.) in boiling aqueous solution (150 c.c.), the product (14 g.) separated from the concentrated and acidified solution. (*b*) *m*-4-Xylenol-5-methanol, prepared according to Manasse (*loc. cit.*), was conveniently purified by means of the calcium chloride additive compound, which separated when an ethereal solution of the impure material was kept with finely divided fused calcium chloride. Treatment of this additive product with water readily gave the pure methanol, which was converted into the sulphonate by a boiling aqueous solution of sodium bisulphite under the usual conditions. The sulphonate was identified by conversion into 5 : 7-*dimethylbenzylsultone* by the method previously described. This sublimed in long needles, m. p. 92·5° (Found : C, 55·0; H, 5·0; S, 16·2. $C_9H_{10}O_3S$ requires C, 54·6; H, 5·0; S, 16·2%).

Sodium p-2-*Xylenol*-5-*methanesulphonate*.—*p*-2-Xylenol-4-methanol (10 g.) slowly dissolved (5 hrs.) in a boiling solution of sodium bisulphite (28 g.). After the solvent had been removed from the neutralised solution, the residue was treated with hot alcohol, from which the product (10 g.) was isolated. For analysis it was converted into the sparingly soluble *barium* salt, which separated from hot water in needles (Found : Ba, 22·6. $C_{18}H_{22}O_8S_2Ba$ requires Ba, 22·6%).

Sodium 2-*Hydroxynaphthyl*-1-*thiolsulphonate*.—After an aqueous solution (150 c.c.) of sodium sulphite (17 g.) containing di-2-hydroxynaphthyl 1-sulphide (10 g.) in suspension had been boiled (3 hrs.), it was acidified with acetic acid, and the insoluble material was extracted with warm water. The *thiolsulphonate* crystallised from the cooled aqueous extract together with some 2-naphthol, which was removed by solution in ether. Purified from hot water, the product (2·5 g.) formed plates (Found : S, 22·3; Na, 7·9. $C_{10}H_7O_4S_2Na,\frac{1}{2}H_2O$ requires S, 22·3; Na, 8·0%), which were characterised by conversion into di-2-hydroxynaphthyl 1-disulphide with warm aqueous sodium hydroxide and by its reaction with 2-naphthol. A boiling aqueous solution (25 c.c.) containing 2*N*-sodium hydroxide (3 c.c.), the thiolsulphonate (2 g.), and 2-naphthol was cooled and acidified; the insoluble material contained di-2-hydroxynaphthyl 1-sulphide (1 g.) which was identified as usual.

Derivatives of Phenylbenzylsulphone.—The following sulphones were obtained by shaking a suspension of the relevant sodium sulphinate in a benzene solution of 5-chloromethyl-*m*-4-xylenol (Fries and Kann, *Annalen*, 1907, **353**, 359). The required products were isolated from the solution and from the insoluble products of the reaction. *Phenyl*-2-*hydroxy*-3 : 5-*dimethylbenzylsulphone*, purified from acetic acid, had m. p. 87° (Found : C, 65·2; H, 5·9. $C_{15}H_{16}O_3S$ requires C, 65·2; H, 5·8%); p-*tolyl*-2-*hydroxy*-3 : 5-*dimethylbenzylsulphone*, m. p. 103° (Found : C, 66·1; H, 6·1. $C_{16}H_{18}O_3S$ requires C, 66·2; H, 6·2%), and 2′-*nitrophenyl*-2-*hydroxy*-3 : 5-*dimethylbenzylsulphone* (V), pale yellow prisms from alcohol, m. p. 168° (Found : C, 55·8; H, 5·1; S, 9·9. $C_{15}H_{15}O_5NS$ requires C, 56·0; H, 4·7; S, 10·0%). These substances readily suffered fission with aqueous alkali hydroxide, the sulphinate being liberated.

1-(2-*Hydroxy*-3 : 5-*dimethylbenzyl*)-2-*naphthol* (IV) separated (7 g.) when 2-naphthol (6 g.) and 5-chloromethyl-*m*-4-xylenol (5·7 g.) were shaken together with benzene. It was also obtained by boiling a concentrated solution of 2-naphthol and *m*-4-xylenol-5-methanol in acetic acid. It formed needles, m. p. 175° (Found : C, 81·8; H, 6·5. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%), from methyl alcohol. *The diacetyl* derivative, purified from methyl alcohol, had m. p. 99° (Found : C, 76·4; H, 6·2. $C_{23}H_{22}O_4$ requires C, 76·4; H, 6·1%).

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