

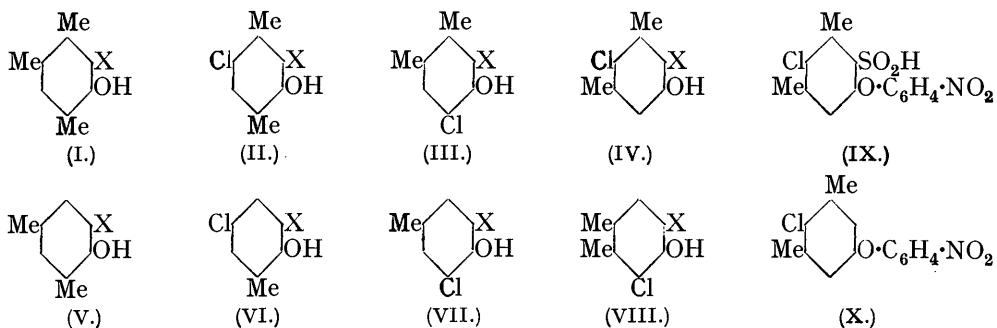
214. *The Rearrangement of ortho-Hydroxy-sulphones. Part VI.*

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DURING a study of the sulphide (J., 1936, 327) derived from 2-nitrophenylchlorothiol and 2-chloro-*m*-5-xyleneol it was observed that the corresponding sulphone (IV, X = SO₂·C₆H₄·NO₂) was very readily converted by alkali into the sulphinic acid (IX). Since in previous experiments the presence of chlorine in this position in similar 2-hydroxy-sulphones

had been found (J., 1934, 422) strongly to retard their rearrangement, it was concluded that this activity might be due to the presence of the 6-methyl group. Further investigation has confirmed this conclusion.

The material examined comprised the sulphones (I) to (VIII) [$X = SO_2 \cdot C_6H_4 \cdot NO_2(o)$] which were obtained by oxidation of sulphides ($X = S \cdot C_6H_4 \cdot NO_2$) generated in most cases by the interaction of 2-nitrophenylchlorothiols and the relevant phenols or chlorophenols. In the case of the sulphide (VII) very poor yields of an impure product were obtained by this method and it was found expedient to chlorinate the product (VII, H instead of Cl) formed from the chlorothiols and *p*-cresol. The structures of the sulphones indicated follow from their mode of formation and from their rearrangement by alkali hydroxide, which demonstrates the ortho-situation of hydroxyl and sulphonyl. Further comment is necessary on the sulphide related to VIII ($X = S \cdot C_6H_4 \cdot NO_2$). Since 3-chloro-*o*-4-xyleneol was not available in sufficient quantity for the direct synthesis of the substance, the product from the chlorothiols and *o*-4-xyleneol was chlorinated. The given



structure is assigned to the chloro-sulphide, since (a) it is different from the sulphide (III) furnished by the interaction of the chlorothiols and 5-chloro-*o*-4-xyleneol and (b) the corresponding sulphone undergoes rearrangement and therefore contains hydroxyl ortho to sulphonyl. The rearrangement of these sulphones (I—VIII) by alkali hydroxide has been demonstrated by the isolation of the sulphinic acids (*e.g.*, IX), which in some cases were characterised as methyl sulphones or disulphides and in all cases were desulphinated. The ethers (*e.g.*, X) then formed were isolated and identified by comparison with materials synthesised from 2-chloronitrobenzene and the relevant phenols. The formation of thioxin dioxides by elimination of sodium nitrite was not observed with the sulphones which underwent rapid rearrangement.

The relative activities of these sulphones were measured under the same conditions as those previously adopted (J., 1934, 423); since the colorimetric process then used was not easily applicable to the more active sulphones, the rearrangement was quantitatively followed in each case by titration of the excess of alkali hydroxide at intervals. For the present purpose it is unnecessary completely to reproduce the data obtained showing the course of rearrangement of each sulphone; the following table shows the approximate time in minutes required for the completion of the process at 50° under the adopted (*loc. cit.*) conditions of molecular dilution and concentration of alkali hydroxide.

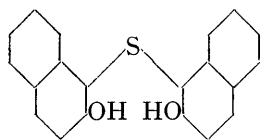
Derivatives of 2'-Nitro-2-hydroxydiphenylsulphone.

No.	Substituents.	Time.	No.	Substituents.	Time.
1	3 : 5 : 6-Trimethyl	<3	6	3 : 5-Dimethyl	95 (93)
2	5-Chloro-3 : 6-dimethyl	15	7	5-Chloro-3-methyl	>150
3	3-Chloro-5 : 6-dimethyl	12	8	3-Chloro-5-methyl	>150
4	5-Chloro-4 : 6-dimethyl	5	9	3-Chloro-4 : 5-dimethyl	>150
5	5 : 6-Benzo	(5)			

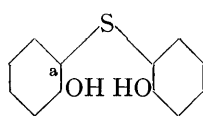
The data in parentheses are those formerly obtained by the colorimetric method. Comparison of Nos. 1, 2, and 3 with 6, 7, and 8 respectively and of 9 with the isomeric 3 clearly shows the remarkable influence of the 6-methyl group; the activity of sulphones containing this substituent is of the same order as that of the 2-naphthol derivative (No. 5).

From previous studies of this intramolecular displacement there is no doubt that the activity of phenolic hydroxyl in these displacements is diminished by electron recession due to the positive *o*-sulphonyl. In seeking an explanation of the present data it is assumed that there are (Bradfield, Jones, and Spencer, J., 1931, 2907) two simultaneous *o*-positions with respect to sulphonyl and it is suggested that the 6-methyl group, by causing electron accession at the sulphonated carbon atom, at least partly overcomes the adverse influence which the sulphonyl exerts on hydroxyl and thus renders the latter more active. This view accords with the behaviour of No. 5, in which electron accession at the α -carbon atom may be inferred from the ability of 2-naphthol to assume the ketonic condition.

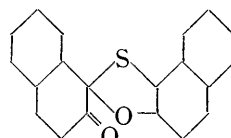
Further evidence showing the influence of 6-methyl substitution on the 2-hydroxyl group has been obtained from a study of di-*o*-hydroxysulphides such as (XI) and (XII). In (XII) the positive sulphonyl of the sulphones is replaced by the thio-group, hence substitution by 6-methyl or by the 5 : 6-benzo-group would by electron accession endow the carbon atom with increased negative character and, according to the views expressed, if this were sufficiently enhanced, the ketonic phase of the phenol might be realised. The smooth conversion of (XI) and its derivatives into the dehydro-compounds (XIII) by alka-



(XI.)



(XII.)



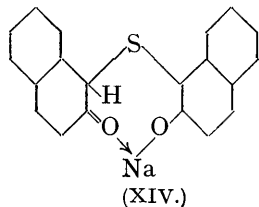
(XIII.)

line oxidation shows that this condition is attained by 5 : 6-benzo-substitution. The formation of dehydro-compounds from derivatives of (XII) has been studied by Lesser and Gad (*Ber.*, 1923, 56, 974). These investigators held erroneous views of the structure of the products concerned, but their results are valuable, since they formulated empirical rules concerning the substitution in (XII) necessary for the formation of a dehydro-derivative. Lesser and Gad concluded that the presence of a tertiary carbon atom in the second *o*-position with respect to sulphur is an essential feature of those sulphides which yield dehydro-derivatives; sulphides without this substituent did not yield them. The experimental results have been repeated, confirmed, and somewhat extended. Inspection of the material examined by Lesser and Gad and by ourselves shows that all those sulphides which furnish dehydro-compounds are either derivatives of 2-naphthol 1-sulphide or, if derived from 2 : 2'-dihydroxydiphenyl sulphide (XII), contain the 6-methyl group. Those of the latter type which do not contain 6-methyl do not yield the simple dehydro-compounds. Altogether nine sulphides have been examined: those in group (1) gave dehydro-derivatives, those in group (2) did not.

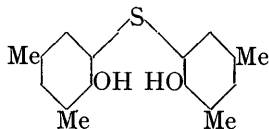
(1) 2-Naphthol 1-sulphide and its derivatives and the sulphides derived from the nuclei of (I), (II), and (IV) ($X = \cdot S$).

(2) 4-Chloro-1-naphthol 2-sulphide, the sulphide derived from (V), *p*-cresol sulphide, *p*-chlorophenol sulphide, 5-chloro-*o*-cresol 3-sulphide, 6-chloro-*m*-cresol 4-sulphide.

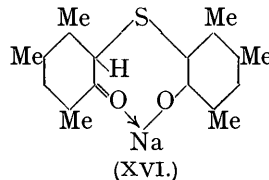
From these results the influence of the 6-methyl group on the character of di-*o*-hydroxy-



(XIV.)



(XV.)



(XVI.)

sulphides is clear. Further evidence of this influence has been obtained from the behaviour of these sulphides in presence of aqueous sodium hydroxide. It has been shown (this vol., p. 727) that even in presence of excess of this reagent 2-naphthol 1-sulphide yields an insoluble monosodium derivative to which the chelate structure (XIV) has been assigned. This characteristic behaviour is found also among derivatives of (XII) and it permits a sharp

division of these into two groups. Those which, under conditions described in the experimental part, do not yield sodium derivatives of this type are devoid of the 6-methyl group, whereas all those found to exhibit this property contain the 6-methyl substituent. For example, *m*-4-xylenol sulphide (XV), readily soluble in aqueous sodium hydroxide, is typical of the former class; ψ -cumenol sulphide, derived from (XV) by 6-methyl substitution, yields the insoluble covalent monosodium derivative and is typical of the latter.

The following sulphides in group (1) yielded covalent monosodium derivatives; those in group (2) did not.

(1) 2-Naphthol 1-sulphide and its derivatives, the sulphides derived from the nuclei of (I), (II), and (IV).

(2) (XV), *p*-cresol sulphide, *p*-chlorophenol sulphide, and the sulphide derived from the nucleus of (VI).

All di-*o*-hydroxy-sulphides hitherto examined which yield covalent monoalkali derivatives also yielded dehydro-compounds, whereas those incapable of giving these covalent alkali derivatives do not yield dehydro-compounds. In fact the formation of both these classes of derivative evidently depends on the ability of the hydroxy-sulphide to assume the hydroxy-ketonic structure. A similar relation exists among the derivatives of *oo'*-dihydroxydiphenylmethane; these are at present under examination.

EXPERIMENTAL.

The chlorocresols and chloroxylenols required for the synthesis of the 2'-nitro-2-hydroxy-sulphides were obtained by the interaction of the cresol or xylenol and sulphuryl chloride in chloroform. 2-Chloro-*m*-5-xylenol and 5-chloro-*p*-2-xylenol were prepared by the method of Lesser and Gad (*loc. cit.*), and 5-chloro-*o*-cresol and 3-chloro-*p*-cresol by the process recorded by Peratoner (*Gazzetta*, 1898, **28**, 211). In preparing the last-named it was found an advantage to remove any remaining *p*-cresol by sulphonation according to the method of Zincke (*Annalen*, 1903, **328**, 277). The yields of 5-chloro-*o*-4-xylenol obtained by the usual procedure were small and the following conditions were found more satisfactory. A solution of sulphuryl chloride (22.5 g.) in chloroform was gradually added to a cooled (15°) and shaken solution of *o*-4-xylenol (20 g.) in the same solvent. The reaction was completed by warming (30—40°), then dry air was led through the cooled mixture before the solvent was evaporated. When the residue was treated with steam, the desired material volatilised (7 g.). After purification it had m. p. 71° and was identical with an authentic specimen (Hinkel, Collins, and Ayling, J., 1923, **123**, 2973).

Sulphides derived from 2'-Nitro-2-hydroxydiphenyl Sulphide.—These were in most cases prepared by heating molecular proportions of 2-nitrophenylchlorothiol and the relevant phenol at 100—130° until hydrogen chloride ceased to be liberated. The cooled mass was triturated with ether and, if tarry matter was present, the residue was treated with charcoal in acetic acid. When the product was contaminated with bis-2-nitrophenyl disulphide, it was treated with warm 2*N*-sodium hydroxide, in which the latter is insoluble.

The sulphides of this type derived from (I), (IV), and (V) have been previously described (J., 1934, 425, 428; 1936, 328).

5-Chloro-2'-nitro-2-hydroxy-3 : 6-dimethyldiphenyl sulphide (II) formed yellow prisms from acetic acid, m. p. 191° (Found : C, 54.3; H, 4.2; N, 4.4; S, 10.3. C₁₄H₁₂O₃NCIS requires C, 54.3; H, 3.9; N, 4.5; S, 10.3%).

5-Chloro-2'-nitro-2-hydroxy-3-methyldiphenyl sulphide (VI) formed yellow needles from acetic acid, m. p. 139° (Found : C, 53.0; H, 3.5; N, 4.7. C₁₃H₁₀O₃NCIS requires C, 52.8; H, 3.4; N, 4.7%).

3-Chloro-2'-nitro-2-hydroxy-5 : 6-dimethyldiphenyl sulphide (III), yellow prisms, had m. p. 189° (Found : C, 54.2; H, 4.1; N, 4.5. C₁₄H₁₂O₃NCIS requires C, 54.3; H, 3.9; N, 4.5%).

3-Chloro-2'-nitro-2-hydroxy-5-methyldiphenyl sulphide (VII) could not be satisfactorily obtained by the usual method. It was readily formed when a solution of sulphuryl chloride (1 mol.) in chloroform was added (18°) to a suspension (1 mol.) of 2-nitrophenyl 4-hydroxy-*m*-tolyl sulphide (J., 1931, 3264) in the same solvent. After removal of the solvent under diminished pressure, the residue was purified as usual; the sulphide had m. p. 142° and was identical with a sample obtained from 3-chloro-*p*-cresol in small yield by the general method described (Found : C, 52.7; H, 3.5; N, 4.8. C₁₃H₁₀O₃NCIS requires C, 52.8; H, 3.4; N, 4.7%).

3-Chloro-2'-nitro-2-hydroxy-4 : 5-dimethyldiphenyl sulphide (VIII). Interaction of *o*-4-xylenol and 2-nitrophenylchlorothiol at 100° readily yielded 2'-nitro-2-hydroxy-4 : 5-dimethyldiphenyl

sulphide (VIII, H instead of Cl), which formed yellow plates, m. p. 157° (Found : C, 61.2; H, 4.9. $C_{14}H_{13}O_3NS$ requires C, 61.1; H, 4.8%). When a suspension of this sulphide (1 mol.) in chloroform was mixed with sulphuryl chloride (1 mol.), chlorination at once began (18°). After 12 hours the solvent was removed under diminished pressure and the residue was purified as usual. The product had m. p. 152° (Found : C, 54.5; H, 4.2; N, 4.3. $C_{14}H_{12}O_3NCIS$ requires C, 54.3; H, 3.9; N, 4.5%).

Sulphones derived from 2'-Nitro-2-hydroxydiphenylsulphone.—These were obtained from the foregoing sulphides by oxidation with hydrogen peroxide in acetic acid. A typical procedure was as follows. Excess (4 mols.) of hydrogen peroxide (30%) was slowly added to a suspension of the sulphide (4 g.) in acetic acid (20—40 c.c.; 100°), the mixture being stirred at intervals. The sulphoxide which at first separated subsequently dissolved and was replaced by the sulphone, the reaction usually being complete in 2—2½ hours. The mixture was then cooled, and the product collected and purified from acetic acid. In the case of the sulphone derived from (I) a large excess of hydrogen peroxide should be avoided, otherwise poor yields result. The products formed colourless or pale yellow, crystalline materials. The following list shows the sulphones obtained, their m. p.'s and analytical data :

Sulphones derived from (I—VIII) (X = $SO_2 \cdot C_6H_4 \cdot NO_2$).								
Derived from	M. p.	Found, %.			Required, %.			
		C.	H.	N.	C.	H.	N.	
I	177°	56.2	4.7	—	56.1	4.7	—	
II	164	48.8	3.8	—	49.1	3.5	—	
III	177	48.9	3.5	4.0	49.1	3.5	4.1	
IV	164	49.3	3.6	—	49.1	3.5	—	
VI	159	47.9	3.3	4.3	47.6	3.1	4.2	
VII	198	47.4	3.3	4.2	47.6	3.1	4.2	
VIII	155	48.8	3.6	4.0	49.1	3.5	4.1	

The sulphone derived from (V) has been previously described (J., 1934, 425).

The rearrangement of these sulphones was effected by 2*N*-sodium hydroxide. In the cases of the sulphones derived from (I), (II), (III), and (IV) the process proceeded (18°) rapidly, the sparingly soluble sulphinate (compare IX) separating. In these cases the sodium salt was collected and converted into characteristic derivatives; it was also submitted to desulphination. In the cases of the sulphones derived from (VI), (VII), and (VIII) the progress of rearrangement was relatively slow and was assisted by a higher temperature (50—60°), which was maintained until the red colour of the solution had faded. After neutralisation the solutions of the sodium sulphinates were submitted to degradation by the following process. An aqueous solution of mercuric chloride (1.5 mols.) was added to the boiling solution of the sulphinate, which was maintained at 100° until sulphur dioxide was no longer liberated. The insoluble mercury derivative was washed and suspended in a boiling mixture of equal parts of alcohol and concentrated hydrochloric acid (1 hour). The cooled solution was diluted and the product which separated was purified from alcohol (charcoal). The ethers (*e.g.*, X) thus obtained were identified by comparison with samples synthesised by the method of Le Fèvre, Saunders, and Turner (J., 1927, 1168) from 2-chloronitrobenzene and the relevant phenol.

The sulphone derived from (I) yielded a sulphinic acid (compare IX) which was characterised as 2'-nitro-6-methylsulphonyl-2 : 4 : 5-trimethyldiphenyl ether, m. p. 146° (Found : N, 4.1; S, 9.5. $C_{16}H_{17}O_5NS$ requires N, 4.2; S, 9.5%), and was degraded to 2'-nitro-2 : 4 : 5-trimethyldiphenyl ether, prisms, m.p. 80° (Found : C, 69.7; H, 6.1; N, 5.5. $C_{15}H_{15}O_3N$ requires C, 70.0; H, 5.8; N, 5.5%). This was identical with a synthetic specimen.

The sulphone derived from (II) gave a sulphinic acid which was purified from aqueous acetone. 5-Chloro-2-o-nitrophenoxy-3 : 6-dimethylbenzenesulphinic acid formed prisms, m. p. 125° (Found : C, 48.7; H, 3.9. $C_{14}H_{12}O_5NClS$ requires C, 49.1; H, 3.5%). It yielded a methylsulphone, m. p. 148° (Found : S, 9.2. $C_{15}H_{14}O_5NCIS$ requires S, 9.0%), and was converted by degradation into 4-chloro-2'-nitro-2 : 5-dimethyldiphenyl ether, m. p. 70° (Found : C, 60.8; H, 4.5; N, 4.9. $C_{14}H_{12}O_3NCl$ requires C, 60.5; H, 4.3; N, 5.0%). The latter was also synthesised.

The sulphone derived from (III) was converted into a sulphinic acid which after degradation yielded 2-chloro-2'-nitro-4 : 5-dimethyldiphenyl ether, prisms from alcohol, m. p. 71° (Found : C, 60.9; H, 4.6. $C_{14}H_{12}O_3NCl$ requires C, 60.5; H, 4.3%), and identical with the product of synthesis.

The sulphone derived from (IV) yielded a sulphinic acid which was characterised as 4-chloro-2'-nitro-6-methylsulphonyl-3 : 5-dimethyldiphenyl ether, prisms from alcohol, m. p. 113° (Found : C, 50.5; H, 4.4; N, 4.1; S, 9.4. $C_{15}H_{14}O_5NCIS$ requires C, 50.6; H, 4.0; N, 3.9; S, 9.0%).

The corresponding disulphide had m. p. 142° (Found: C, 54.3; H, 4.1; S, 10.4; *M*, 630. C₂₈H₂₂O₆N₂Cl₂S₂ requires C, 54.4; H, 3.6; S, 10.4%; *M*, 617). Degradation of the sulphonic acid yielded 4-chloro-2'-nitro-3 : 5-dimethyldiphenyl ether (X), m. p. 64° (Found: C, 60.8; H, 4.3; N, 5.0. C₁₄H₁₂O₃NCl requires C, 60.5; H, 4.3; N, 5.0%).

The products obtained by rearrangement of (V) have been previously described (J., 1934, 422).

The sulphone (VI) yielded 4-chloro-2'-nitro-2-methyldiphenyl ether, m. p. 39° (Found: C, 59.0; H, 4.2; N, 5.2. C₁₃H₁₀O₃NCl requires C, 59.2; H, 3.8; N, 5.3%), and 2-chloro-2'-nitro-4-methyldiphenyl ether, m. p. 57° (Found: C, 59.4; H, 4.0; N, 5.5. C₁₃H₁₀O₃NCl requires C, 59.2; H, 3.8; N, 5.3%), was obtained from the sulphone (VII). Both of these ethers were identical with synthetic material.

The sulphone (VIII) gave in the usual manner 2-chloro-2'-nitro-3 : 4-dimethyldiphenyl ether, m. p. 115° (Found: C, 60.3; H, 4.4; N, 4.9. C₁₄H₁₂O₃NCl requires C, 60.5; H, 4.3; N, 5.0%).

Sulphides derived from (XII).—Those derived from the nuclei of (I), (II), (IV), and (V) were obtained by the method of Lesser and Gad (*loc. cit.*). *p*-Cresol 3-sulphide was not easily obtained in a pure condition by the method of Tassinari (*Gazzetta*, 1887, 17, 93); it was more readily prepared by reducing the corresponding sulphoxide (Gazdar and Smiles, J., 1910, 97, 2248) with zinc wool in boiling acetic acid until the product no longer gave a blue colour in sulphuric acid. 5-Chloro-*o*-cresol 3-sulphide (compare VI) was obtained from the chloro-cresol with sulphur chloride in carbon disulphide at 18–20°. It formed leaflets from aqueous acetic acid, m. p. 145° (Found: C, 53.3; H, 3.9; Cl, 22.6. C₁₄H₁₂O₂Cl₂S requires C, 53.3; H, 3.8; Cl, 22.5%). 4-Chlorophenol 3-sulphide, m. p. 174°, was obtained in a similar manner.

The formation of dehydro-derivatives from sulphides of this type (compare Lesser and Gad, *loc. cit.*) was examined by treating their shaken alkaline solutions with a slight excess of aqueous potassium ferricyanide. The dehydro-derivatives, if formed, separated as orange or red amorphous solids, which were removed by solution in ether. The sulphides which did not form the simple dehydro-derivatives yielded amorphous, pale green material insoluble in ether. The isolation of the dehydro-compounds by this method is not usually easy, since the ethereal extract is apt to contain unchanged sulphide as the covalent sodium compound. They were more readily obtained in a purer condition by warming a benzene solution of the sulphide in presence of excess of lead peroxide. The solid remaining after evaporation of the solvent was purified from aqueous acetic acid; the products formed orange micro-crystalline or amorphous powders. Dehydro-5-chloro-*p*-2-xyleneol 3-sulphide (compare II) had m. p. 165° (Found: C, 56.7; H, 4.4. C₁₆H₁₄O₂Cl₂S requires C, 56.3; H, 4.1%). Dehydro-*ψ*-cumenol sulphide (compare I) had m. p. 97° (Found: C, 71.6; H, 6.6. C₁₈H₂₀O₂S requires C, 72.0; H, 6.7%). Dehydro-2-chloro-*m*-5-xyleneol 6-sulphide (compare IV), an amorphous orange material, was not further investigated, since Lesser and Gad (*loc. cit.*) have already examined its bromine derivative.

The formation of covalent monoalkali derivatives from these sulphides (compare this vol., p. 727) was examined by reaction with aqueous sodium hydroxide (2 mols., 5%). The covalent alkali derivatives, if formed, separated as insoluble crystalline materials, which were removed by solution in ether and isolated by drying in a current of air at 25° after the solvent had been evaporated. Sulphides of this type which did not yield the covalent derivatives completely dissolved in the alkaline medium; ether which had been shaken with these solutions contained only a small amount of the sulphide concerned and no sodium salt. The following covalent monosodium derivatives were all readily soluble in moist ether, forming yellow solutions, and moderately readily soluble in warm chloroform; partial dehydration sometimes took place in the latter solvent.

Monosodium 5-chloro-p-2-xyleneol 3-sulphide, m. p. 255° after some loss of water (Found: Na, 5.1. C₁₆H₁₅O₂Cl₂SNa, 4H₂O requires Na, 5.1%).

Monosodium ψ-cumenol sulphide, m. p. 245° after losing some water at 100° (Found: Na, 5.9. C₁₈H₂₁O₂SNa, 4H₂O requires Na, 5.8%).

Monosodium 2-chloro-m-5-xyleneol 6-sulphide lost water more readily than the derivatives already mentioned; dehydration was completed at 115° in a vacuum (Found: Na, 6.3; H, 4.1. C₁₆H₁₅O₂Cl₂SNa requires Na, 6.3; H, 4.1%). The anhydrous material was insoluble in dry ether and did not melt, having evidently assumed the electrovalent state. In presence of moisture it reverted to the covalent state, being readily soluble in moist ether.

The authors thank Dr. L. Hinkel for an authentic specimen of 5-chloro-*o*-4-xyleneol and are also indebted to the Ministry of Education for Northern Ireland for a grant which enabled one of them to take part in these experiments.