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ELECTROPHILIC SUBSTITUTION IN 3,5-XYLENOL

AN EXTREME EXAMPLE OF POSITION SELECTIVITY OF THE REAGENT[1]

Cal Y. Meyers and Giampaolo Picciola
Institute of Industrial Chemistry, University of Bologna, Bologna, Italy

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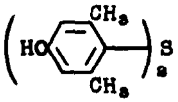
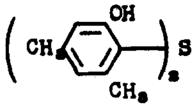
IN studies concerning the effect of thia, sulphinyl and sulphonyl bridges between hydroxyaryl groups, we required both bis-(4-hydroxy-2,6-dimethylphenyl) sulphide (I) and bis-(2-hydroxy-4,6-dimethylphenyl) sulphide (II).

I 

 II

Oae and Zalut[2] recently reported the preparation of I (from 3,5-xylenol and thionyl chloride), evidently as a new compound, m.p. 153°. However, many years ago Dvorkovitz and Smiles[3] reported this same compound (from 3,5-xylenol and sulphur dichloride), but m.p. 265°. These workers also noted a product, m.p. 149°, which they assumed was the isomer, II. The similarity in m.p. of the latter and I (of Oae and Zalut), but the large difference in that of I reported by these different workers, suggested that one of these groups made an erroneous structure assignment. As neither group properly characterized the products and as both of these isomers were vital in our studies, we undertook the necessary characterization. This is

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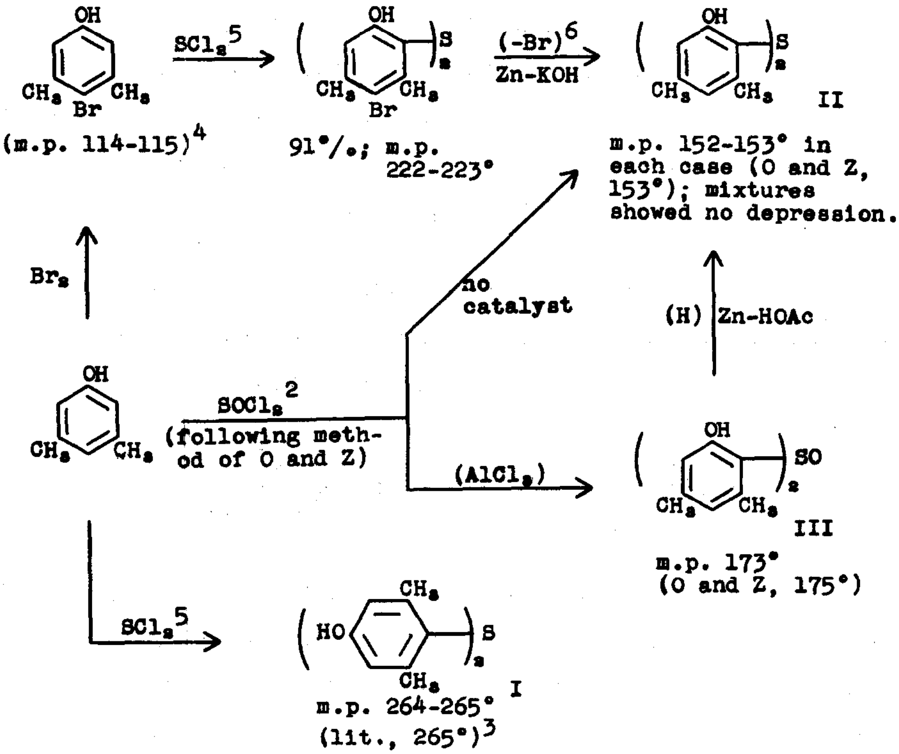
[1] This study is part of a series dealing with the nature of organic sulphur groups, supported by the Petroleum Research Fund; the preceding paper is by C.Y. Meyers, G. Moretti and L. Maioli, J. Org. Chem. 27, 625 (1962).

[2] S. Oae and C. Zalut, J. Amer. Chem. Soc. 82, 5359 (1960).

[3] V. Dvorkovitz and S. Smiles, J. Chem. Soc. 2022 (1938).

summarized by the following reaction series.



These results clearly indicate that the sulphide prepared by Oae and Zalut was not I, but the bis-(2-OH-) isomer, II. Furthermore, the sulphoxide, also assumed to be the bis-(4-OH-) isomer, was really the bis-(2-OH-) isomer, III. In erroneously assigning the bis-4-isomeric structure to these products, respectively, these workers presented structure-property

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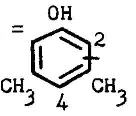
[4] This compound is definitely the 4-Br isomer (see Table 1).

[5] For general procedures for preparing bis-(hydroxyphenyl) sulphides: E.E. Reid, Organic Chemistry of Bivalent Sulfur Vol. II, pp. 223 ff. Chemical Publishing Co., New York (1960).

[6] Following method of W.S. Gump and J.C. Vitucci, J. Amer. Chem. Soc. 67, 238 (1945).

TABLE 1

Reaction Products of 3,5-Xylenol with some Electrophilic Reagents

Reagent	Position attacked	Product, R = 	Yield (%)	M.p. (°C)		
				Found	Lit.	(ref.)
SOCl$_2$ (AlCl$_3$)[a]	2-	(2-R)$_2$SO (III)	85	173	175	2[h]
SOCl$_2$[b]	2-	(2-R)$_2$S (II)	ca. 100	152-153	153 149	2[h,i] 3
SCl$_2$[c]	4-	(4-R)$_2$S (I)	ca. 100	264-265	265	3
HNO$_2$[d]	4-	4-NO-R [g]	95	178-179	173-174	7
Br$_2$[e]	4-	4-Br-R	80	114-115	115-116 112-114	8[j] 9
HNO$_3$[f]	2-	2-NO$_2$-R	30-36	63-64	65-66	10
	and 4-	4-NO$_2$-R	19-25	108-109	108.5	10

[a] In CS$_2$ or CCl$_4$. [b] No catalyst; in CHCl$_3$. [c] No catalyst; in CCl$_4$ or ligroin (CHCl$_3$, ref. 3). [d] NaNO$_2$-conc. HCl. [e] In acetic acid. [f] Conc. HNO$_3$-H$_2$SO$_4$. [g] Our observations (I.R., high acidity and m.p., resistance to normal oxidation and reduction reactions; and the characteristics of the methyl derivative) suggest this compound exists and reacts only as the oxime tautomer. [h] These authors erroneously assumed this to be the 4-isomer. [i] Based on the weight of SOCl$_2$ used their yield was 98.5%. [j] These workers also isolated some 2-isomer, m.p. 54°.

correlations (comparative acidities, U.V. and I.R. spectra) which are not justified.[11]

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[7] H.E. Albert, J. Amer. Chem. Soc. 76, 4985 (1954).

[8] K. von Auwers and E. Borsche, Ber. Dtsch. Chem. Ges. 48, 1715 (1915); K. von Auwers, E. Borsche and R. Weller, Ibid. 54, 1296 and 1310 (1921).

[9] W.B. Reid, U.S. Patent 2,719,851 (1955).

[10] R. Adams and H.W. Stewart, J. Amer. Chem. Soc. 63, 2859 (1941).

[11] The seriousness of these errors and subsequent invalid conclusions becomes evident from recent data illustrating the large differences in acidity between bis-(2-OH-) and bis-(4-OH-) isomers like these: C.Y. Meyers, Ind. Chim. Belg. 27, 538 (1962).

Our structure proof confirms the assignments by Dvorkovitz and Smiles. While the compound m.p. 264-265° was not characterized unequivocally as I, elemental analysis,[3] its formation in ca. 100% yield and comparative I.R. spectra[12] justify this structure.

These observations show that 3,5-xylenol is substituted almost *exclusively* at the 2-position by reaction with thionyl chloride, but at the 4-position (also almost *exclusively*) by reaction with sulphur dichloride. Moreover, in either case the reaction is virtually quantitative. We have found that bromine and also nitrous acid substitute at the 4-position in very high yields, while nitric acid favours the 2-position, although the yield is relatively small. These striking differences in position-selectivity of the reagent in these reactions are summarized in Table 1.

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[12] Bis-(4-hydroxyphenyl) sulphide, OH stretch: 3.02-3.15 μ (Nujol)
2.71 and 2.79 μ (dil. $CHCl_3$)

Compound m.p. 264-265° (I), " " 3.05-3.13 μ (Nujol)
2.70 and 2.78 μ (dil. $CHCl_3$).

Cf. J.L. Binder, J.C. Ambelang and F.J. Webb, *J. Amer. Chem. Soc.* **81**, 3608 (1959).