Intramolecular Hydrogen Bonds in Aromatic Sulphoxides: ^{1}H Nuclear Magnetic Resonance and Acidity Constant Measurements

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Comparative examination of the ^{1}H n.m.r. chemical shifts and acidity constants of *o*-methylsulphinylphenol and *o*-hydroxyacetophenone shows that intramolecular hydrogen bonding is stronger for the carbonyl compound. The effect of bulky groups *ortho* to the $SOCH_3$ and $COCH_3$ groups indicates that these have different intramolecular hydrogen bonding patterns and different stereochemical requirements for molecular stabilization, when attached to an unsaturated system. Parallel behaviour is also found for the corresponding amino-derivatives. Possible electronic interactions between the sulphinyl group and the unsaturated ring in aromatic sulphoxides are discussed.

It is known that sulphoxides give a strong intermolecular hydrogen bond with acidic protons.[1-3] This kind of effect is stronger than those for the corresponding sulphones [1,4] and ketones.[5] Several measurements have been performed with the aid of i.r. spectroscopy [2,4-7] employing phenols, alcohols, or chloroform as the source of acidic protons. ^{1}H N.m.r. spectroscopy has also proved a powerful tool in the study of hydrogen bonding of sulphoxides with protic molecules.[7-9] The ability of sulphoxides to form a strong hydrogen bond is most probably related to their high polarity leading to high electron density on the oxygen atom, as shown by the

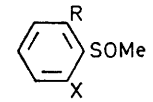
[1] D. Barnard, J. Fabian, and M. P. Koch, *J. Chem. Soc.*, 1949, 2442.
[2] P. Biscarini, G. Galloni, and S. Ghersetti, *Boll. sci. Fac. Chim. ind. Bologna*, 1963, **21**, 154.
[3] H. H. Szmant, 'Organic Sulphur Compounds,' ed. N. Kharasch, Pergamon Press, Oxford, 1961, vol. 1.
[4] E. D. Amstutz, I. M. Hunsberger, and J. J. Chessick, *J. Amer. Chem. Soc.*, 1951, **73**, 1220.
[5] M. Tamres and S. Searles, jun., *J. Amer. Chem. Soc.*, 1959, **81**, 2100.
[6] S. Ghersetti, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 17.
[7] L. Lunazzi and F. Taddei, *Spectrochim. Acta*, 1968, **24A**, 1479.
[8] A. L. McClellan, S. W. Nicksic, and J. C. Guffy, *J. Mol. Spectroscopy*, 1963, **11**, 340.
[9] D. P. Eyman and R. S. Drago, *J. Amer. Chem. Soc.*, 1966, **88**, 1617.

high bond moment of the S=O group.[10,11] It has been demonstrated that,[12] at least for oxygen as a proton acceptor, the hydrogen bond is stronger when the X–H axis of the acidic proton is collinear with the lone pair on the oxygen atom of the acceptor. Also the trigonal lone-pair situation is more favourable than the tetrahedral one for hydrogen bond formation.[12] In 2′-hydroxyacetophenone and 2-hydroxybenzaldehyde, where there are O–H and C=O groups in the same molecule, strong intramolecular hydrogen bonding has been revealed by ^{1}H n.m.r., i.r.,[13] and dissociation constant measurements.[14] In these molecules the geometrical requirements for hydrogen bonding are completely fulfilled when the O–H and C=O bonds are coplanar, a condition which also represents the best situation for electronic stabilization of the molecule through π conjugation between the C=O group and the benzene ring. In the case of *o*-hydroxyphenyl sulphoxides the situation could, in principle, be a little different: it is known that π conjugation between the S=O bond and the benzene ring is not relevant.[1,11,15] Some interaction in the excited states between the lone pair of sulphur and the π electron system of the benzene ring has been invoked[15,16] to interpret the electronic spectra of aromatic sulphoxides. Even if some π conjugation takes place[17,18] between the S=O group and unsaturated systems, this seems better represented by a $(p–d)\pi$ mechanism, which does not require[19] a specific orientation of the planes of the S=O bond and phenyl ring. In view of the pyramidal arrangement of this group,[20] if the electronic stabilization of an aromatic sulphoxide does not require the coplanarity of the phenyl ring with the S=O group, one would expect sulphinyl compounds to exhibit less stable intramolecular hydrogen bonding and opposite sensitivity to *ortho*-groups than carbonyl compounds where coplanarity is required.

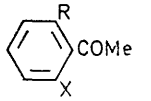
We have studied dissociation constants and ^{1}H n.m.r. spectra of phenols with *ortho*-sulphinyl and -carbonyl groups with a view to clarifying the stereochemical requirements of the S=O group for intramolecular hydrogen bonding in aromatic systems, thereby shedding light on the electronic interactions involved between this group and a π electron system and, in consequence, on its electronic structure.

RESULTS AND DISCUSSION

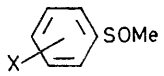
The derivatives (1) and (2) were examined both by determining dissociation constants and by measuring the chemical shifts of the O–H proton at infinite dilution in [^{2}H]chloroform and acetone. The corresponding derivatives where R = H and the O–H group is *meta* or *para* to the acetyl (4) and methylsulphinyl (3) groups were also analysed to check the electronic effects of carbonyl and sulphinyl groups in conditions



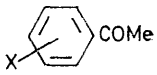
(1) X = OH (5) X = NH_2
a; R = H
b; R = Me
c; R = Bu^t



(2) X = OH (6) X = NH_2
a; R = H
b; R = Me



(3) X = OH (7) X = NH_2
a; *meta*
b; *para*



(4) X = OH (8) X = NH_2
a; *meta*
b; *para*

where *ortho* effects are not present. The latter compounds have been extensively analysed,[14,17] but we remeasured their properties to obtain homogeneous experimental results. The amino-derivatives (5)—(8) were also studied for the same purpose. The experimental results are collected in Tables 1 and 2. The

TABLE 1

Acidity constants and δ_{OH} values, measured in [^{2}H]chloroform and acetone for phenols substituted with methylsulphinyl and acetyl groups. Chemical shifts [δ (p.p.m.)] from tetramethylsilane were extrapolated to infinite dilution; pK_a values, measured in aqueous solution, were extrapolated to zero ionic strength

Compound	pK_a	$\delta_{OH}(CDCl_3)$	δ_{OH}(Acetone)
(1a)	7·60	10·22	9·90
(1b)	8·78	10·75	11·13
(1c)	9·50	10·96	11·31
(2a)	10·22; 10·07 [a]	12·05	12·17
(2b)	9·14	12·28	9·92
(3a)	8·79; 8·75 [b]	5·12	8·66
(3b)	8·43; 8·28 [b]	5·21	8·92
(4a)	9·19; 9·19 [c]	4·97	8·57
(4b)	8·05; 7·87; [a] 8·05 [c]	5·21	9·12

[a] Ref. 14. [b] Ref. 17. [c] Ref. 25.

[10] L. E. Sutton, 'Determination of organic structures by physical methods,' eds. E. A. Braude and F. C. Nachod, Academic Press, New York, 1965, p. 395.
[11] For the electronic characteristics of the S=O bond see (*a*) C. C. Price and S. Oae, 'Sulphur Bonding,' Ronald Press, New York, 1962; (*b*) Y. A. Kolesnik and V. V. Kozlov, *Russian Chem. Rev.*, 1965, **87**, 519.
[12] W. G. Schneider, *J. Chem. Phys.*, 1955, **23**, 26.
[13] S. Forsen and B. Akermark, *Acta Chem. Scand.*, 1963, **17**, 1907.
[14] L. B. Magnusson, C. Postmus, jun., and C. A. Craig, *J. Amer. Chem. Soc.*, 1963, **85**, 1711.
[15] G. Leandri, A. Mangini, and R. Passerini, *J. Chem. Soc.*, 1957, 1386.
[16] K. Mislow, M. M. Green, P. Laur, H. T. Melillo, T. Simmons, and A. L. Ternay, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 1958.
[17] F. G. Bordwell and P. J. Boutan, *J. Amer. Chem. Soc.*, 1957, **79**, 717.
[18] F. G. Bordwell and G. D. Cooper, *J. Amer. Chem. Soc.*, 1952, **74**, 1058.
[19] A. M. Moriarty, *Tetrahedron Letters*, 1964, 509.
[20] A. Kucsman, *Acta Chim. Acad. Sci. Hung.*, 1953, **47**, 3.

chemical shifts were measured starting from 0·5M solutions and extrapolated to infinite dilution. Acidity constant measurements were carried out in aqueous solution and extrapolated to zero ionic strength. Where

TABLE 2

Acidity constants and δ_{NH_2} values in [^{2}H]chloroform and acetone for anilines substituted with methylsulphinyl and acetyl groups. Chemical shifts [δ (p.p.m.)] from tetramethylsilane were extrapolated to infinite dilution; pK_a values measured in aqueous solution, were extrapolated to zero ionic strength

Compound	pK_a	δ_{NH_2}(CDCl$_3$)	δ_{NH_2}(Acetone)
(5a)	2·53	5·10	5·67
(5b)	2·59	5·45	6·07
(5c)	2·56	5·52	6·11
(6a)	2·70; 2·22 [a]	6·35	6·80
(6b)	2·99	4·55	5·16
(7a)	3·16	3·95	5·07
(7b)	2·81	4·03	5·22
(8a)	3·60; 3·56 [a]	3·76	4·86
(8b)	2·64; 2·19 [a]	4·15	5·48

[a] D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' International Union of Pure and Applied Chemistry, Butterworths, London, 1965.

comparison is possible, it is seen that the data agree with measurements previously reported for similar experimental conditions.

A preliminary check of the electronic effects acting on δ_{OH} of phenols was carried out employing Hammett σ constants. A satisfactory linear plot is obtained both for the measurements in [^{2}H]chloroform and for those in acetone solution. Figure 1 represent the plot for

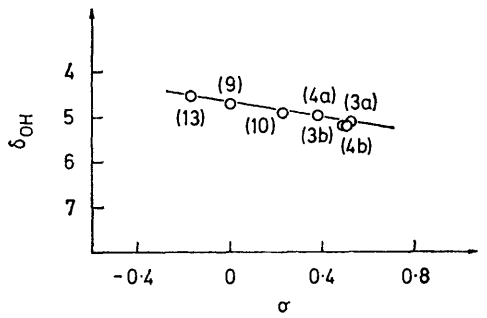


FIGURE 1 Plot of δ_{OH} of phenols, meausred in [^{2}H]chloroform, against Hammett σ constants

the measurements in [^{2}H]chloroform and includes other experimental results relative to the reference compounds collected in Table 3.

The chemical shift of the O–H proton, measured in [^{2}H]chloroform solution, in *o*-methylsulphinylphenol (1a) is at higher field than in the corresponding carbonyl compounds (2a) and this indicates that the S=O group exhibits weaker intramolecular hydrogen bonding than the C=O group. Furthermore, for compound (2a) the δ_{OH} values in acetone, where intermolecular association with the solvent is possible, are not appreciably different from those measured in [^{2}H]chloroform, while in the case of the corresponding sulphoxide (1a) a small high field shift is observed in acetone. This seems to indicate that in acetone intramolecular hydrogen bonding for compound (1a) is partly broken, thereby showing itself to be weaker than in acetophenone. This conclusion is also supported by the pK_a values: the SOMe substituent makes phenol most acidic when in the *ortho*-position, while for carbonyl

TABLE 3

Acidity constants and chemical shifts δ_{OH} and δ_{NH_2} for reference compounds. Chemical shifts [δ (p.p.m.)] from tetramethylsilane were extrapolated to infinite dilution; pK_a values, measured in aqueous solution, were extrapolated to zero ionic strength

Compound	pK_a	δ_{OH} or δ_{NH_2} (CDCl$_3$)	δ_{OH} or δ_{NH_2} (Acetone)
(9) Phenol	9·98 [a]	4·70	8·22
(10) *p*-Chlorophenol	9·42 [a]	4·90	8·52
(11) α-Naphthol	9·30 [a]	5·20	8·95
(12) Vanillin	7·39 [a]	6·15	9·55
(13) *p*-Cresol	10·25 [a]	4·50	7·87
(14) Aniline	4·62; 4·60 [b]	3·45	4·59
(15) *p*-Methoxyaniline	5·31; 5·34 [b]	3·04	4·18
(16) *p*-Chloroaniline	3·98; 3·98 [b]	3·44	4·80
(17) *p*-Anisidine	5·09; 5·07 [b]	3·02	4·27

[a] Ref. 25. [b] D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' International Union of Pure and Applied Chemistry, Butterworths, London, 1965.

derivatives the *ortho*-isomer is the least acidic one. In the case of the carbonyl derivatives (2a), (4a), and (4b) the strongest effect of the COMe group is clearly conjugative in origin, as evidenced by the fact that the *para*-derivative (4b) gives the highest pK_a value: the lowest pK_a value for the *ortho*-isomer is, as commonly accepted,[14] attributed to intramolecular hydrogen bonding. In the case of sulphoxides (1a), (3a), and (3b), the pK_a values are similar for the *meta*- and *para*-isomers, with the *para*-derivative being slightly more acidic, while the highest acidity is found for the *ortho*-derivative. The results show a moderate conjugative effect for the sulphinyl group, as pointed out previously,[17] and from the value relative to the *ortho*-compound it can be deduced that the intramolecular hydrogen bond is easily broken. If the S=O group displays a conjugative effect in addition to its inductive effect, which, as shown by the pK_a values of *meta*-compounds, is higher than that of the C=O group (Hammett constants for *m*-SOMe and *m*-COMe are +0·52 and +0·38 respectively [21]), then the highest pK_a value would occur for the *ortho*-OH group, if intramolecular hydrogen bonding is moderately weak.

The unexpectedly high acidity constant of *o*-methylsulphinylphenol could be explained in terms of anion stabilization if it is assumed that O$^-$ interacts with the positive sulphur atom of the sulphoxide group, as seems

[21] J. Hine, ' Physical Organic Chemistry,' McGraw-Hill, New York, 1962.

to be the case for *o*-hydroxyphenyl phenyl sulphoxide.[22] It is, of course, difficult to assess whether the geometrical requirements for such a situation are fulfilled in the compound considered here. The acidity characteristics of the OH group as deduced by pK_a values may be correlated with the proton chemical shift (Figure 2). The deviations are for *ortho*-derivatives, with a maximum for 2-hydroxyacetophenone (2a). In acetone the OH

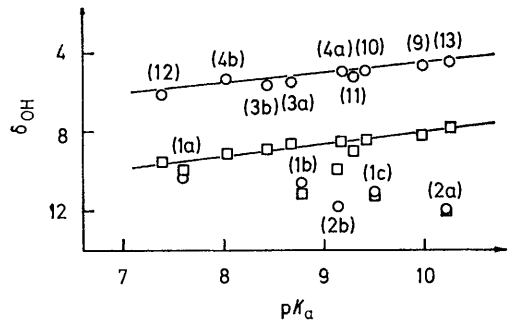


FIGURE 2 Plot of δ_{OH} of phenols measured in [^{2}H]chloroform ○ and acetone □ against the corresponding pK_a values

group should give hydrogen bonding with the solvent; this is clearly observed since δ_{OH} values measured in acetone are at lower field than those measured in [^{2}H]chloroform. Only *o*-hydroxyacetophenone (2a) shows a δ_{OH} which is practically unaffected by intermolecular association, while the *ortho*-sulphoxide (1a) moves slightly upfield (*ca.* 0·3 p.p.m.). The deviation of the sulphinyl derivative (1a) is smaller in acetone. Previous measurements for compounds (1a) and (2a) in dimethyl sulphoxide,[23] where even stronger intermolecular hydrogen bonding than in acetone should be possible, show that the δ_{OH} of *o*-hydroxyacetophenone is almost unaffected (δ 11·97), while for the corresponding sulphinyl derivative (1a) it is found at δ 10·50 and is thus shifted to lower field than in the case of [^{2}H]-chloroform. It is thus reasonable to conclude that in compound (1a) the intramolecular hydrogen bond is largely disrupted in solvents where a strong intermolecular hydrogen bond can be formed, and this should also be so in the case of water, where the pK_a values were measured. These observations seem to indicate clearly that, at least for the compounds examined here, intramolecular hydrogen bonding in sulphoxides is weaker than it is in ketones.

In an attempt to relate this to the electronic structure of aromatic sulphoxides we examined derivatives with methyl or t-butyl substituents *ortho* to the methylsulphinyl group. When these substituents are *ortho* to the acetyl group they should twist it from coplanarity and consequently intramolecular hydrogen bonding should be weakened, since the planar situation is favourable both to electronic stabilization and to strong hydrogen bonding. For sulphinyl derivatives it seems that no special conformational requirements are necessary for weak conjugative interactions between the π cloud of the aromatic ring and the S=O bond. If, however, the lone pair of sulphur (considered as occupying an sp^3 orbital [15]) is kept in a plane also containing the axis of maximum symmetry of the π cloud of the aromatic ring, this should give the best conditions for electronic interaction of the sp^3–p_π type. Such interaction should make the sulphur atom more positive, its *d* orbitals would accordingly be more contracted and stabilized,[24] π bonding with oxygen would be facilitated as a result and the transfer of charge through π–π conjugation from the phenyl ring to the S=O group made easier. If this kind of synergic process is operating, the lone pair of sulphur must be so oriented with respect to the phenyl ring that both the methyl group and the S=O bond of compound (1a) remain out of plane, owing to the pyramidal structure of the sulphinyl group. This would make intramolecular hydrogen bonding weaker than in the case of the corresponding carbonyl compounds. When a bulky group is placed *ortho* to the methylsulphinyl group, steric effects would twist this group in such a way that the S=O bond would be more in the plane of the phenyl ring and the lone pair would be twisted as well with respect to the axis of maximum symmetry of the benzene ring. Furthermore, as a result of this process and of a decreased conjugative effect, we would observe a strengthening of intramolecular hydrogen bonding and the effect should increase the pK_a values of (1b) and (1c) relative to (1a) (Table 1). The pK_a values reported in Table 1 follow the trend expected from this effect while it also seems that δ_{OH} shifts in [^{2}H]chloroform solution agree with increased strength of the intramolecular hydrogen bond. The δ_{OH} values measured in acetone can also be interpreted in this way, since a further low field shift of *ca.* 0·3 p.p.m. with respect to chloroform solution could indicate increased polarity of the S=O group in a solvent with higher dielectric constant. For the carbonyl compounds (2a) and (2b) the expected effect is in the opposite direction owing to the geometry of the carbonyl group, as can be seen from the pK_a values and from the comparison of δ_{OH} in the two solvents employed. Figure 2 shows that the greater the bulk of R, the more compounds (1) deviate from the line correlating compounds in which intramolecular hydrogen bonding is not present, while the opposite holds for compounds (2). An alternative explanation for the pK_a values of compounds (1) based on the electronic effects of the alkyl group does not seem to hold, since *m*-cresol shows an acidity constant which is almost identical with that of phenol itself.[25] Lower stabilization of the anion [22]

[22] C. Y. Meyers, *Gazzetta*, 1963, **93**, 1206.
[23] M. T. Tribble and J. G. Traynham, *J. Amer. Chem. Soc.*, 1969, **91**, 380.
[24] A. J. Banister, L. F. Moore, and J. S. Padley, *Spectrochim. Acta*, 1967, **23A**, 2705.
[25] G. Korthum, W. Vogel, and K. Andrussov, 'Dissociation constants of organic acids in aqueous solution,' International Union of Pure and Applied Chemistry, Butterworths, London, 1961.

could also serve to lower the acidic character of compounds (1b) and (1c), since, according to the electronic mechanism suggested here, the steric effect would decrease the positive character of the sulphur atom, even if the preferred conformational requirements for the anions of these two molecules were those with the S=O group rotated in the opposite direction with respect to the oxygen anion and consequently in the most favourable position for $\overset{\delta+}{S}\cdots O^-$ interactions.

The results obtained for the amino-derivatives are parallel to those for the corresponding phenols. For *ortho*-substituted anilines intramolecular hydrogen bonding has been discussed by Krueger.[26,27] The plots of Figure 3 show that the pK_a values and δ_{NH_2} values are linearly correlated in both solvents for compounds where intramolecular hydrogen bonding should not be

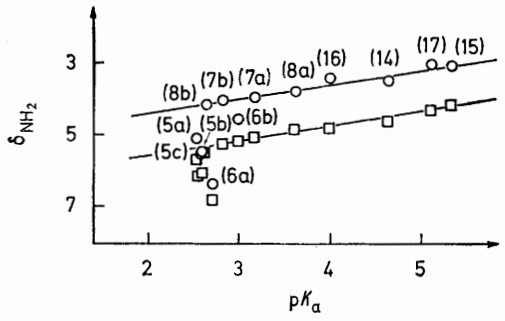


FIGURE 3 Plot of δ_{NH_2} of anilines measured in [^{2}H]chloroform ○ and acetone □ solution against the corresponding pK_a values

present. These plots seem to indicate that for these compounds acidity constants and proton chemical shifts are roughly related to the same kind of phenomenon. Intramolecular hydrogen bonding for the amino-group in the compounds examined here seems, however, very much weaker than in the case of the corresponding phenols, and it is seen in Figure 3 that *o*-methylsulphinylaniline (5a) and the corresponding carbonyl compound (6b), in acetone, fit the correlation line of compounds where intramolecular hydrogen bonding is not present. These results confirm our conclusions regarding the stereochemical requirememts of the carbonyl and sulphinyl group for intramolecular hydrogen bonding.

These data clearly indicate that, in the case of aromatic sulphoxides, a preferred conformation exists for the best conjugative electronic interactions between the S=O group and the phenyl ring (even if these interactions involve *d* orbitals of sulphur which have no special spatial requirements) and that this orientation should depend, even if not to a large extent, on the relative position of the sp^3 lone pair of sulphur and the π aromatic orbitals. Previous failure to observe such an effect is probably due to the choice of compounds examined,[28] since the effect will not be observed if steric factors are introduced in compounds where the conformational situation is of itself unfavourable to this kind of perturbation.

EXPERIMENTAL

Spectra.—^{1}H N.m.r. spectra were recorded on a JEOL JNM-C60-HL spectrometer at a probe temperature of *ca.* 30°. The sample solutions were added with tetramethylsilane as internal standard and, starting with a concentration of *ca.* 0·5M were diluted until it was possible to observe the resonances of the groups of interest (*ca.* 0·01M). The chemical shifts obtained at different concentrations were then extrapolated to infinite dilution. [^{2}H]Chloroform (99·8%) was obtained from CIBA and was not further purified. Acetone was always purified and dried immediately before use.

pK_a *Measurements.*—A recently reported method [29] was employed for obtaining dissociation constants. For the amino-derivatives the corresponding hydrochlorides were employed. For all compounds four different samples in aqueous solution (10^{-2}M) were prepared at different ionic strengths (0·1, 0·05, 0·005, and 0·001M-$NaClO_4$) and titrated with N/10-sodium hydroxide. pH Measurements were obtained from a Beckman Expandomatic pH meter and at least thirty values were gathered for each sample. The pK_a values were obtained by processing [29] the experimental values with the aid of an IBM 1620 computer.

Compounds.—Where not otherwise specified, the derivatives here employed were commercially available or prepared according to known methods.

2-Bromo-3-nitro-t-butylbenzene (18). Sodium metabisulphite (14·4 g) dissolved in water (50 ml) was added to an aqueous solution (1 l) of sodium bromide (15·2 g) and copper sulphate pentahydrate (25 g) warmed at 60—70°. The cuprous bromide formed was decanted, washed with water, and dissolved in aqueous hydrobromic acid (126 ml; 48%) in water (200 ml). The solution was warmed at 50—60° and the diazonium salt of 2-amino-3-nitro-t-butylbenzene [obtained by pouring in crushed ice a solution of amino-derivative [30] (13·4 g) in concentrated sulphuric acid (64 ml) and treating with slightly more than an equimolecular proportion of aqueous sodium nitrite at 15—20°] was added dropwise. The solution obtained was maintained at 60° for 1 h. The compound was then extracted with ether and fractionated in *vacuo*, yield 25 g (96·5%), b.p. 120—121° at 1 mmHg, n_D^{20} 1·5640 (Found: C, 46·65; H, 4·6; N, 5·6. $C_{10}H_{12}BrNO_2$ requires C, 46·55; H, 4·65; N, 5·4%).

Methyl 2-nitro-6-t-butylphenyl sulphide (19). Methanethiol (7·7 g) was slowly bubbled through an aqueous solution (60 ml) of sodium hydroxide (6·4 g) cooled at 5—10°. Compound (18) (20·6 g) dissolved in ethanol (50 ml) was then slowly added to this solution in a nitrogen atmosphere and the mixture was warmed on a steam-bath for 6 h. Most of the methanol was then evaporated off and ground ice added to the concentrated solution giving a solid material which, after crystallization from light petroleum,

[26] P. J. Krueger, *Canad. J. Chem.*, 1962, **40**, 2300.
[27] P. J. Krueger, *Canad. J. Chem.*, 1967, **45**, 2135.
[28] Ref. 11*a*, p. 140.
[29] D. De Filippo and F. Momicchioli, *Tetrahedron*, 1969, **25**, 5733.
[30] H. J. B. Biekart, H. B. Dessens, P. E. Verkade, and B. M. Wepster, *Rec. Trav. chim.*, 1952, **71**, 1245.

yielded 13 g (72%) of *sulphide*, m.p. 52—53° (Found: C, 58·7; H, 6·7; N, 6·5. $C_{11}H_{19}NO_2S$ requires: C, 58·65; H, 6·7; N, 6·25%).

2-*Acetylamino*-6-*t*-*butylphenyl methyl sulphide* (20). Zinc dust (50·7 g) was added in small amounts to a solution of compound (19) (11·2 g) in acetic acid (300 ml) warmed in a steam-bath. When addition was complete the mixture was warmed for 1 h and then filtered to remove unchanged zinc which was washed with a small amount of acetic acid. Acetic anhydride (75 ml) was then added to the filtered acetic acid solution which was subsequently refluxed for 15 min. Most of the acetic acid was then evaporated off and the residue was poured onto ice. The crude compound obtained was crystallized from light petroleum yielding 8 g (67%) of *sulphide* (20), m.p. 72° (Found: C, 65·85; H, 8·0; N, 5·95. $C_{13}H_{19}NOS$ requires C, 65·75; H, 8·05; N, 5·9%).

2-*Acetylamino*-6-*t*-*butylphenyl methyl sulphoxide* (21). Compound (20) was oxidized with peracetic acid (2 equiv.) in acetic acid solution for 48 h at room temperature. Most of the solvent was evaporated off and water and ice were added to the residue which was neutralized with sodium hydrogen carbonate. The compound was extracted several times with chloroform and the residue obtained after evaporation of the solvent was crystallized from ethyl acetate, 82% yield, m.p. 120—123° (Found: C, 61·9; H, 7·5; N, 5·5. $C_{13}H_{19}NO_2S$ requires C, 61·7; H, 7·55; N, 5·55%).

2-*Amino*-6-*t*-*butylphenyl methyl sulphoxide* (5c). Compound (21) (15·6 g) was dissolved in a water–ethanol (1 : 1) (90 ml) solution of potassium hydroxide (8·4 g) and refluxed on a steam-bath for 8 h. Most of the ethanol was evaporated off and the residue diluted with water. Compound (5c) was extracted with ether and the crude residue obtained after the solvent was removed was crystallized from n-hexane, m.p. 84—85°, yield 92% (Found: C, 62·85; H, 7·75; N, 6·65. $C_{11}H_{17}NOS$ requires C, 62·55; H, 8·1; N, 6·65%). The corresponding hydrochloride had m.p. 122—123°.

2-*Hydroxy*-6-*t*-*butylphenyl methyl sulphoxide* (1c). A solution of compound (5c) (6·3 g) in sulphuric acid (4·8 ml, d^{20} 1·835) in water (30 ml), cooled at 0°, was treated with slightly more than one equiv. of aqueous sodium nitrite. The solution of the diazonium salt was added dropwise to a warm solution of concentrated sulphuric acid (30 ml) and water (250 ml). After extraction with ether the organic solution obtained was extracted with 10% aqueous sodium hydroxide. The alkaline solution was then acidified (Congo Red indicator), extracted with ether, and dried ($MgSO_4$). An oil (5·4 g, 85%) was obtained which was distilled *in vacuo*, b.p. 107° at 0·04 mmHg, n_D^{23} 1·5612 (Found: C, 62·15; H, 7·5; S, 14·7. $C_{11}H_{16}O_2S$ requires C, 62·25; H, 7·6; S, 15·1%).

Methyl 2-*methyl*-6-*nitrophenyl sulphide* (22). With the procedure for compound (19) starting from 2-bromo-3-nitrotoluene [31] an oil was obtained, yield 66%, b.p. 116° at 1·2 mmHg, n_D^{20} 1·3789, m.p. 15—16° (lit.,[32] b.p. 99° at 0·015 mmHg, m.p. 15—16°).

2-*Acetylamino*-6-*methylphenyl methyl sulphide* (23). The procedure for compound (20) yielded a crude compound which was crystallized from n-hexane, yield 58%, m.p. 81° (Found: C, 61·65; H, 6·65; N, 7·15. $C_{10}H_{13}NOS$ requires C, 61·55; H, 6·7; N, 7·2%).

2-*Acetylamino*-6-*methylphenyl methyl sulphoxide* (24). Oxidation of compound (23) was performed as described for compound (21). The crude compound was crystallized from ethyl acetate and had m.p. 118—119° (Found: C, 56·7; H, 6·15; N, 6·75. $C_{10}H_{13}NO_2S$ requires C, 56·85; H, 6·2; N, 6·65%).

2-*Amino*-6-*methylphenyl methyl sulphoxide* (5b). The procedure for compound (5c) was adopted starting from compound (24). The crude compound was crystallized from ethyl acetate and had m.p. 146—147° (Found: C, 56·6; H, 6·5; N, 8·35. $C_8H_{11}NOS$ requires C, 76·8; H, 6·55; N, 8·2%).

2-*Hydroxy*-6-*methylphenyl methyl sulphoxide* (1b). Compound (5b) was treated as described for compound (1c). The crude phenol was crystallized from n-hexane, m.p. 76—77°, yield 76% (Found: C, 56·3; H, 5·8. $C_8H_{10}O_2S$ requires: C, 56·45; H, 5·9%).

2-*Hydroxy*-6′-*methylacetophenone* (2b). The diazonium salt of 2′-amino-6′-methylacetophenone [33] was worked-up following the procedure for compounds (1c) and (1b). The crude oil was purified through sublimation (at room temperature and 0·05 mmHg; collecting surface cooled at −10°). The solid sublimate again became oily, n_D^{20} 1·5612, on reaching room temperature (Found: C, 71·7; H, 6·7. $C_9H_{10}O_2$ requires C, 72·0; H, 6·7%). For this compound m.p. 93—98° had been reported.[34]

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