CLXIV.—*Reciprocal Induced Polarity Effects in Cresols and their Derivatives. Properties of the Isomeric Methoxybenzyl Bromides.*

By ARTHUR LAPWORTH and JOHN BALDWIN SHOESMITH.

THE total influence which one atom or group exerts on the properties of another elsewhere in the same molecule is doubtless highly complex and probably the resultant of several simultaneous effects. There appear to be, for example, (*a*) general polar effects, certain atoms tending to raise or lower the affinity of the molecule as a whole for an electric charge (Flürscheim, T., 1909, **49**, 1627 ;

compare also *Mem. Manchester Phil. Soc.*, 1920, **64**, ii, 1 *et seq.*, and Kermack and Robinson, this vol., p. 428 *et seq.*, (b) induced polar effects, and (c) steric effects. It is as yet scarcely possible to define precisely the proportion attributable to each of these in any single instance, but there is some reason to suppose that the range and periodicity peculiar to each type of effect may furnish a means of doing so. Thus a property which is found to rise and fall alternately in proceeding from one atom to another in order may be suspected to be one influenced by induced polarity effects. Steric effects are likely to recur at longer intervals, probably of five or six atoms in saturated, open-chain compounds; whilst general polar effects are likely to be periodic only when associated with steric effects, with which, therefore, they would probably agree in periodicity.

Systematic measurements, therefore, may ultimately make it possible to foretell the total result of the combined general and induced polar effects produced on replacement of one atom or group in a molecule by another, but at present the data are insufficient, and comparisons of properties are best restricted to those of position isomerides or to those of different atoms in one and the same compound. Even as it is, general polar and steric influences cannot wholly be eliminated in studying the operations of induced alternate polarities, but some assistance may be derived from the circumstance that steric influence appears to be very effective only when the atoms concerned occupy certain relative positions—for example, ortho-positions in benzene di-derivatives, and α -positions in open-chain carbonyl compounds.

Attention was recently directed by one of us to the properties of the isomeric cresols (*Mem. Manchester Phil. Soc.*, 1920, **64**, ii, 10). Using the generalised diagram

and assuming that the hydrogen atoms of a methyl group attached to an aromatic nucleus can act as "positive key atoms"—an assumption conveyed by the dots attached to their polar signs, the induced polarities to be expected are indicated. In the case of the *m*-hydroxyl group, the natural relative polarities of the atoms (with which the capacity for ionisation is associated) are, as the above diagram shows, enhanced by the induced ones, whilst in the *o*- and

p-hydroxyl groups the induced polarities are in the opposite sense to the natural polarities; this is in agreement with the measurements of Dawson and Mountford (T., 1918, **113**, 937), who found that *m*-cresol has a higher ionisation constant than either *o*- or *p*-cresol. It was further suggested that, as the *o*-hydroxyl group is separated from the methyl group by fewer intervening atoms than the *p*-hydroxyl group, the lower ionisation of *o*-cresol as compared with *p*-cresol is explained; the authors now think, however, that much value must not be attached to this point, since in other cases, including those dealt with in the present paper, the order which di-derivatives of benzene showing induced polar effects usually take is para-ortho-meta, whilst an induced polar effect alone would be expected to give rise to the order, ortho-para-meta. The frequent displacement of the ortho-compounds from what would appear to be their natural positions may be due, either to the special force of steric effects in the ortho-positions or to a tendency of activated forms to assume *p*-quinonoid rather than *o*-quinonoid configurations.

The agreement between the requirements of the principle of induced alternate polarities and the observed properties of the three cresols being so striking, the authors decided to direct their attention to the possibility of demonstrating that such effects may be reciprocal and that the elements of the hydroxyl group—more particularly the oxygen atom—may in turn affect the properties of the methyl groups in similar alternating manner. Thus the hydrogen atoms of the methyl group in *m*-cresol should exhibit an enhanced positive polar character in virtue of the position of the strongly negatively polar oxygen. Definite polar character in hydrogen directly attached to carbon is, however, not easy to detect except in association with certain complexes, and it appeared likely that the point could be demonstrated more readily by studying the properties of halogen in a similar position. Great practical difficulties connected with the properties of hydroxybenzyl haloids also made it necessary to use their methyl ethers, the methoxybenzyl bromides.

In these three compounds the oxygen atoms, acting as negative key atoms, were expected to give rise to the induced polarities indicated in the formulæ. The *o*- and *p*-isomerides thus contain

halogen with their natural negative polarity enhanced, whilst in the *m*-isomeride the opposite is the case.

The test on which the authors relied for comparing the negative polarity of the bromine atoms was based on the double decomposition of the halogen compounds with alkalis

In accordance with this polar reaction, the compounds with more "negative" halogen, namely, the *o*- and *p*-compounds were expected to react most readily with alkalis, and the experiment confirmed this expectation in full, for the *m*-compound reacted very much more slowly than did the other two, which, except as emulsions (in which case relative solubilities are confusing factors), lost their bromine as bromidion so rapidly that the velocity of reaction could not be measured. There was evidence that the *o*-compound was slightly less reactive than the *p*-compound either when emulsified or when in solution.

Halogen, as one of us has previously shown, may exhibit reactions in which it appears to behave as with a positive polar character (*Mem. Manchester Phil. Soc.*, 1920, **64**, ii, 8). Thus, when situated in the α -position in ketones, and even more markedly in that position in 1 : 3-diketones, 1 : 3-ketonic esters, and malonic esters, it is known to be very readily replaced by hydrogen. This sometimes happens when hydrogen bromide is present, as in the case of α -bromo-acetoacetic ester,

and more frequently with hydrogen iodide, in which case the preceding equation may, of course, be modified thus :

More recently Nicolet (*Amer. Chem. J.*, 1921, **43**, 2081) has interpreted replacement of iodine by hydrogen in certain aromatic compounds as due to "positive halogen" on similar grounds.

The induced positive polar character of the bromine atom in *m*-methoxybenzyl bromide suggested that the "reactivity" of the three isomerides when tested as to their ease of reduction by hydrogen iodide should be the inverse of that observed when tested by the ease of hydrolysis. Experiment entirely confirmed this surmise. Whilst the contrast between the *m*-compound and the other two isomerides was not so very great as before, it was still very decided; and this fact provides, in combination with the other data given in this paper, a striking example of the applicability

of the principle of induced alternate polarities when sources of confusion can be to a considerable extent eliminated.

In the following figure are shown in continuous lines curves which correspond with one series of measurements made on the hydrolysis of the three isomerides under comparable conditions, and three others, in interrupted lines, corresponding with a series of measurements on their reduction by hydrogen iodide. The inversion

of the order of reactivity in passing from one reaction to the other, the clear separation of the *m*-derivative from its isomerides, which do not greatly differ from one another in both reactions, is clearly seen.

EXPERIMENTAL.

Preparation of the Methoxybenzyl Bromides.

A long series of experiments which were made by one of us with the object of preparing the three isomeric methoxybenzyl alcohols

and the corresponding bromides in quantity from the cresols will be dealt with in another communication. In the present paper will be described only the more important observations made in connexion with the conversion of the isomeric hydroxybenzaldehydes into the corresponding methoxybenzyl bromides, and the properties of the latter.

o-Hydroxybenzyl alcohol was obtained in the most satisfactory yield (70 per cent.) by the reduction of salicylaldehyde (12 grams), emulsified in 100 c.c. of water, with carefully washed, 1.5 per cent. sodium amalgam (300 grams) in presence of sodium hydrogen carbonate (about 25 grams). Addition of the amalgam and bicarbonate was made gradually, with constant shaking and cooling. The subsequent isolation of the alcohol by acidification, extraction with ether, and removal of unchanged aldehyde by means of sodium hydrogen sulphite solution need not be described in detail, but it is desirable to note that great care must be exercised to remove all traces of acids before attempting to proceed with purification of the alcohol, otherwise resinification may take place with serious loss (compare Manasse, *Ber.*, 1894, **27**, 2411; Lederer, *J. pr. Chem.*, 1894, [ii], **50**, 225).

o-Methoxybenzyl alcohol was best obtained by alkylation of the hydroxy-alcohol in the mode recommended by Pschorr, Wolfe, and Buckow (*Ber.*, 1900, **33**, 165). Attempts to prepare it from *o*-methoxybenzaldehyde by reduction or by the Cannizzaro reaction gave poor yields or impure products. The product used for conversion into the bromide boiled at 246—247° at atmospheric pressure.

o-Methoxybenzyl bromide was made by passing gaseous hydrogen bromide into a solution of *o*-methoxybenzyl alcohol in twice its volume of cold dry benzene. The solution gradually became turbid and green, and after two hours was separated from the watery deposit, dried over calcium chloride, filtered through glass-wool, and fractionated under reduced pressure. The bulk of the bromide boiled at 118°/18 mm., and analysis for ionisable bromine showed it to be pure.

m-Hydroxybenzyl alcohol was readily obtained in 80 per cent. yield by reduction of the corresponding aldehyde with sodium amalgam, as described in the case of the corresponding ortho-derivative.

m-Methoxybenzaldehyde was made in 86 per cent. yield by the interaction of *m*-hydroxybenzaldehyde, aqueous sodium hydroxide, and methyl sulphate in molecular proportions, the reaction being completed by boiling for several hours.

m-Methoxybenzyl alcohol was obtained by the action of 25 per cent. aqueous potassium hydroxide on the aldehyde, or in better

yield (50 per cent. of the theoretical) by reducing the aldehyde, suspended in water, with sodium amalgam. The methylation of *m*-hydroxybenzyl alcohol (1 mol.) by the action of methyl sulphate ($1\frac{1}{2}$ mols.) and potassium hydroxide dissolved in methyl alcohol also gave yields approximating to 50 per cent. of the theoretical; with a larger proportion of alkylating agent, a product contaminated with much dialkyl derivative is formed.

m-Methoxybenzyl bromide was prepared in much the same way as that above described for the preparation of the ortho-compound. It boiled at $127^{\circ}/16$ mm.*

p-Methoxybenzyl alcohol (anisyl alcohol) was made from anisaldehyde by the Cannizzaro reaction. The product, after one such treatment, was not pure (compare Späth, *Monatsh.*, 1913, **34**, 1995 *et seq.*) and did not yield a satisfactory bromide; it was therefore found necessary to treat it a second time with 25 per cent. alcoholic potassium hydroxide, when the recovered *p*-methoxybenzyl alcohol boiled at $255\text{--}257^{\circ}$ —or decidedly higher and within a narrower range than after the single treatment considered necessary by Späth (*loc. cit.*).

p-Methoxybenzyl bromide, prepared by the same method as was used for the isomerides, had to be distilled under a pressure not exceeding 16 mm., otherwise decomposition took place. It boiled at $128\text{--}129^{\circ}/16$ mm.

(a) *Hydrolysis of the Emulsified Methoxybenzyl Bromides.*

The following data were obtained by merely emulsifying the three bromides with standard sodium hydroxide at constant temperature and determining the diminution in titre against standard acid after various intervals of time. The emulsions were agitated during hydrolysis by a mechanical stirrer of constant efficiency. As the systems were not homogeneous, the results cannot be utilised for calculation of true relative velocity constants, but the numbers illustrate very clearly the great differences in reactivity of the three isomerides and cannot be explained by differences in solubility alone.

In the following tables, the numbers under *t* are the intervals of time in minutes which had elapsed since the initial mixing and the withdrawal of the samples for analysis, whilst those under *x* are the percentage quantities of the compound hydrolysed during those intervals, calculated on the assumption that one molecular proportion of sodium hydroxide is neutralised by the hydrolysis of 1 molecule of the bromide—an assumption justified by the results

* It is worthy of note that of the three methoxybenzyl bromides, the meta-compound has the most marked lachrymatory properties.

1398 LAPWORTH AND SHOESMITH: RECIPROCAL INDUCED

obtained by following the hydrolysis of samples of the three bromides to completion.

(a) *o*-Methoxybenzyl bromide.

		(i)		(ii)	
Temperature		55°		20°	
Wt. of bromide		0.8824 gram		0.6785 gram	
Alkali used		250 c.c. of <i>N</i> /40-NaOH		100 c.c. of <i>N</i> /10-NaOH.	
<i>t.</i>	<i>x.</i>	<i>t.</i>	<i>x.</i>	<i>t.</i>	<i>x.</i>
2.5	37.0	77.5	90.0	15	96.5
7.5	62.0	157.5	99.0	30	100.0
17.5	70.0	237.5	99.0	45	100.0
37.5	78.7	7.5	64.7		

(b) *p*-Methoxybenzyl bromide.

		55°		20°	
Temperature		55°		20°	
Wt. of bromide		0.831 gram		0.7850 gram	
Alkali used		250 c.c. of <i>N</i> /40-NaOH		100 c.c. of <i>N</i> /10-NaOH.	
<i>t.</i>	<i>x.</i>	<i>t.</i>	<i>x.</i>	The substance was almost completely hydrolysed after 2.5 minutes.	
2.5	75.4	37.5	97.9		
7.5	90.8	77.5	99.4		
17.5	94.8				

(c) *m*-Methoxybenzyl bromide.

		55°		20°	
Temperature		55°		20°	
Wt. of bromide		0.934 gram		0.8988 gram	
Alkali used		250 c.c. of <i>N</i> /40-NaOH		100 c.c. of <i>N</i> /10-NaOH.	
<i>t.</i>	<i>x.</i>	<i>t.</i>	<i>x.</i>	<i>t.</i>	<i>x.</i>
7.5	1.6	77.5	43.0	45	2.4
17.5	13.3	157.5	66.7	105	4.0
37.5	24.0	15	1.0	185	5.4

(b) *Hydrolysis of Dissolved Methoxybenzyl Bromides.*

Owing to the extremely high speed at which alkalis act on the *o*- and *p*-bromides, it has not been found possible to measure the speed of the reaction in dilute alcohol at 25°.

Using as solvent alcohol, containing about 20 per cent. of water, *p*-methoxybenzyl bromide, initially at concentration about 1 per cent., was almost completely hydrolysed in five minutes after being dissolved, even in absence of alkali; the *o*-isomeride was not completely hydrolysed in the same time, but no satisfactory determinations of the small quantity of unchanged bromide could be practicable. Under the same conditions, *m*-methoxybenzyl bromide (0.1824 gram per 100 c.c. of dilute alcohol) was hydrolysed to the extent of 10, 20, and 33 per cent. in 24, 48, and 72 hours, respectively.

With excess of *N*/50-sodium hydroxide (solvent = alcohol of about 90 per cent.), the results with the *o*- and *p*-isomerides were much as in absence of alkali, hydrolysis being almost complete in

five minutes, but being less rapid with the *o*- than with the *p*-compound. A regular curve of hydrolysis was obtained in this as in the following instance and all previous ones, with the *m*-isomeride, 13, 39, and 59 per cent. being hydrolysed in thirty-five, one hundred and fifty-five, and three hundred and fifteen minutes, respectively.

The same remarks apply to the observations made with *N*/10-sodium hydroxide in 95 per cent. alcohol; but all the changes took place more rapidly; with the *m*-isomeride, 37, 80, and 96 per cent. was hydrolysed in thirty-five, one hundred and fifty-five, and three hundred and fifteen minutes, respectively.

(c) *Reduction of the Methoxybenzyl Bromides by Means of Hydrogen Iodide.*

The tendency of these bromides, especially the para-compound, to resinify in presence of moist hydrogen iodide led to the use of anhydrous acetic acid as solvent. Hydrogen iodide was prepared by a slight modification of the method recommended by Norris and Cottrell (*Amer. Chem. J.*, 1896, **18**, 97), freed from iodine by passing it through a U-tube containing moist red phosphorus distributed on glass-wool, and dried by means of phosphoric oxide. The solution employed in the reductions contained 0.4464 gram of HI per c.c.

The reactions were carried out as follows in a thermostat maintained at 25°.

A quantity of the methoxybenzyl bromide was weighed in a small stoppered vessel, 5 c.c. of the hydrogen iodide solution were added, and reduction was allowed to proceed. Aliquot portions of the solution were removed at intervals, diluted with a large bulk of water, and titrated with *N*/10-sodium thiosulphate.

In the following tables are given, under *t*, the time, in minutes, which had elapsed between the initial mixing and the withdrawal of the sample of solution, and, under *x*, the percentage quantity of bromide reduced, calculated on the assumption that the iodine liberated was produced in accordance with the equation.

(a) *o*-Methoxybenzyl bromide. Weight taken in { (i) 0.772;
gram. { (ii) 0.395.

(i)		(ii)	
<i>t</i> .	<i>x</i> .	<i>t</i> .	<i>x</i> .
5	1.0	5	0
15	2.7	15	3.2
35	10.5	35	7.0
75	16.3	75	10.9
195	26.8	275	23.5

1400 SMYTHE : DECOMPOSITION OF BENZYL DISULPHOXIDE.

(b) *p*-Methoxybenzyl bromide. Weight taken in { (i) 0.902;
gram. { (ii) 0.415.

(i)	
5	0.7
15	1.4
35	2.0
75	3.9
195	5.8

(ii)	
5	1.5
15	2.3
35	1.0
75	3.0
195	3.9

(c) *m*-Methoxybenzyl bromide. Weight taken in { (i) 0.811;
gram. { (ii) 0.50.

(i)	
5	49.8
15	80.6
35	89.7
75	97.4
175	99.8

(ii)	
5	37.0
15	79.5
35	93.3
75	98.5
175	98.0

The authors' thanks are due to the Department of Scientific and Industrial Research for a grant to one of us (J. B. S.) which enabled the work to be done.

CHEMISTRY DEPARTMENT,
UNIVERSITY OF MANCHESTER.

[Received, June 2nd, 1922.]