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THE CHLORINATION OF *O*-CRESOL IN ORGANIC SOLVENTS

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Abstract—A study has been made of the effect of solvent on the mechanism of chlorination of *o*-cresol. The ratio of 4 chloro-*o*-cresol:6 chloro-*o*-cresol produced has been correlated with steric hindrance of the 6-position by hydrogen bonded solvent molecules. Anomalous high yields of 4–6 dichloro-*o*-cresol in polar solvents at low temperatures have been explained in terms of hydrogen bonding involving the aromatic π-electrons of *o*-cresols as indicated by the temperature dependence of the IR frequency of ring deformation near 1600 cm^{-1}.

INTRODUCTION

It has been pointed out[1] in a general discussion of aromatic chlorination that observed *ortho:para* ratios may be accounted for in terms of electron distribution in the substrate molecule. When reactants are of high reactivity the transition state during chlorination involves only minor deformation of the aromatic system, so that relative reactivities of the *ortho-* and *para-* positions are determined by their relative electron densities in the ground state. It is known that the ratio of isomers produced may be affected by the influence of the solvent on the chlorinating agent. For example the non-catalysed chlorination of toluene in acetonitrile and acetic acid shows significant differences in the isomer ratio,[2] and an extension of this work[3] shows that reaction of chlorine with toluene in a variety of solvents gives monochlorotoluene with a varying *ortho:para* ratio, nitromethane giving the greatest amount of *para*-isomer and aqueous hydrochloric acid the least. The change in selectivity is explained by proposing that the effective reagent is a complex between molecular chlorine and the solvent which is more selective than chlorine alone because its increased bulk increases its own steric requirements and because it has a greater response to the steric requirements of the substituent groups in the molecule being chlorinated.

The *ortho:para* ratio characteristic of a molecule in a particular reaction is, therefore, a function of its electron distribution and it has been shown that the ratio may be affected by interaction between the solvent and the reagent. Relatively little work, has, however, been done on systems in which the *ortho:para* ratio is affected by interaction between solvent and substrate molecule, but the chlorination of *o*-cresol in organic solvents described below is believed to be a reaction of this type.

DISCUSSION

Table 1 shows the effect on *ortho:para* ratio of chlorinating *o*-cresol (25% w/w) in various organic solvents with an equimolar amount of chlorine, and Table 2 lists

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[1] R. O. C. Norman and G. K. Radda, *J. Chem. Soc.* 3610 (1961).
[2] L. J. Andrews and R. M. Reefer, *J. Amer. Chem. Soc.* **81**, 1063 (1959).
[3] L. M. Stock and A. Himoe, *Tetrahedron Letters* 9 (1960).

the results of corresponding chlorinations with sulphuryl chloride. The solvent is seen to have a marked effect on the ratio of 4-chlorocresol to 6-chlorocresol. In other experiments solvents such as nitrobenzene which give enhanced formation of 4-chlorocresol were mixed with a 10-molar excess of solvent such as benzene which does not give the effect. The mixed solvent has little effect on *ortho:para* ratio.

To examine the possibility of these results arising from deformation of the aromatic system of the *o*-cresol, some corresponding chlorinations of phenol with sulphuryl chloride were carried out in various solvents, which have a negligible effect on the *ortho:para* ratio (Table 3). Since deformation of the aromatic system would be roughly the same for phenol as for *o*-cresol it may be assumed that the results shown in Tables 1 and 2 do not arise from this cause. In the same way solvation of the chlorinating agent does not offer an adequate explanation of the results, since if this is the determining factor the solvent would affect the *ortho:para* ratio of chlorophenol as much as that of chlorocresol.

Solvent-phenol bonding may however be appreciable and the effect of eighteen solvents on the degree of solvent-phenol bonding has been measured.[4] Least association of solvent and phenol is found with carbon tetrachloride and association progressively increases in the order benzene < nitromethane < nitrobenzene < diethyl ether. Benzene is found to be oriented in two positions relative to the phenol ring with its molecular plane parallel with or vertical to the —OH group, depending on whether association is via OH groups or the π-electrons of the benzene. The reason for the varying isomer ratios given in Tables 1 and 2 is believed to be the hydrogen bonding of the —OH of the cresol with solvent (Table 4).

The bound solvent molecules will have a shielding effect on the *ortho*-position but will leave the *para*-position open to attack and thus enhance the yield of the 4-chloro isomer. The absence of the effect in phenol chlorination shows that the methyl group in *o*-cresol plays an important part by forcing the solvent molecule over to shield the other *o*-position and when this group is absent the solvation of the —OH is not sufficient by itself to hinder appreciably the approach of the chlorinating agent to either *ortho* position. The solvating group may of course, be another molecule of *o*-cresol which probably contributes to the excess of *para* substitution when *o*-cresol is chlorinated in the absence of solvent. When solvents such as carbon tetrachloride which do not bond at all with *o*-cresol, are used at a high enough concentration to diminish considerably cresol-cresol bonding, chlorination gives almost equal amounts of *ortho*- and *para* isomers. The failure of 10% nitrobenzene in carbon tetrachloride to give enhanced *para*-substitution probably arises from similar diminution of solvent-cresol bonding.

The above explanation of the effect of solvent on *ortho:para* ratio in chlorination may be supplemented by the solvation of the chlorinating agent which has been already demonstrated for the chlorination of toluene in solvents.[2,3] The sensitivity of the *ortho:para* ratio to the degree of solvent-cresol bonding will be increased as the bulk of the chlorinating agent increases by solvation. A similar reason probably contributes to the larger amounts of 4-chlorocresol produced by chlorination with the relatively bulky sulphuryl chloride compared with molecular chlorine.

An unexpected result is the sharp increase in the proportion of dichloro-*o*-cresol

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[4] R. Mecke, *Disc. Farad. Soc.* **9**, 161 (1950).

TABLE 1. CHLORINATION WITH CHLORINE

Solvent	Temp °C	Molar comp. of products				Ratio $\frac{4\text{ COC}}{6\text{ COC}}$	Ratio $\frac{\text{OC}+\text{DCOC}}{4\text{ COC}+6\text{ COC}}$
		4 COC %	6 COC %	OC %	DCOC %		
No solvents	+50	52·2	22·6	16·4	8·8	2·3	·34
Nitromethane	−33	65·8	10·0	12·8	11·4	6·6	·32
Nitromethane	+50	75·8	11·9	10·0	2·3	6·4	·14
Nitrobenzene	+3	76·0	15·0	4·5	4·5	5·1	·10
Nitrobenzene	+50	76·8	14·4	4·4	4·4	5·3	·10
Lactonitrile	−40	35·9	7·0	19·7	37·4	5·1	1·33
Laconitrile	+50	52·9	13·2	23·0	10·9	4·0	·51
Diethyl ether	−10	72·2	14·9	3·3	9·6	4·9	·15
Diethyl ether	+34	71·3	20·1	0	8·6	3·5	·09
Di-isopropyl ether	−15	68·5	12·3	8·6	10·6	5·6	·24
Di-isopropyl ether	+50	74·4	17·5	2·9	5·2	4·3	·09
Ethylene glycol	−45	41·4	9·9	23·7	25·0	4·2	·95
monomethyl ether	+50	62·6	16·6	12·6	8·2	3·8	·26
Dioxan	−20	38·4	22·4	20·0	19·2	1·7	·64
Dioxan	+50	54·4	33·4	8·2	4·0	1·7	·14
Tetrahydrofuran	−50	25·7	11·3	33·9	29·1	2·3	1·70
Tetrahydrofuran	+50	64·5	25·7	6·4	3·4	2·6	·11
Diphenyl oxide	+50	37·3	27·6	31·5	3·6	1·4	·54
Polyethylene glycol	+50	49·1	11·9	22·9	16·1	4·1	·64
Ethyl alcohol	−25	41·7	13·8	18·3	26·2	3·0	·80
Ethyl alcohol	+50	54·8	16·6	20·9	7·7	3·3	·40
Ethyl acetate	−40	34·9	12·5	38·7	13·9	2·8	1·11
Ethyl acetate	+50	69·3	18·4	8·8	3·5	3·8	·16
Acetic acid	+5	44·7	16·4	31·7	7·2	2·7	·64
Acetic acid	+50	54·0	26·2	10·8	9·0	2·1	·28
Acetonitrile	−40	52·3	10·9	14·0	22·8	4·7	·58
Acetonitrile	+50	70·2	14·6	7·8	7·4	4·8	·18
Methylene chloride	−20	58·6	22·4	5·5	13·5	2·6	·23
Methylene chloride	+40	59·6	27·9	0·6	11·9	2·1	·14
Chloroform	−10	51·6	35·3	3·5	9·6	1·5	·15
Chloroform	+50	39·1	41·2	4·8	14·9	0·9	·25
Carbon	−10	43·1	36·8	13·7	6·4	1·2	·25
tetrachloride	+50	43·6	47·8	2·3	6·3	0·9	·09
Benzene	+3	42·2	37·6	16·0	4·2	1·1	·25
Benzene	+50	37·1	38·5	21·8	2·6	1·0	·32
Benzotrifluoride	+12	50·3	33·0	7·6	9·1	1·5	·20
Benzotrifluoride	+50	52·3	31·2	11·2	5·3	1·7	·20
Pyridine	−25	36·5	17·2	31·5	14·8	2·1	·86
Pyridine	+50	40·0	19·9	27·6	12·5	2·0	·67
Chloral	−25	45·8	16·3	7·4	30·5	2·8	·61
Chloral	+50	51·5	22·2	17·6	8·7	2·3	·36
Liquid SO_2	−20 to −30	55·0	8·8	31·5	4·7	6·3	·57

OC = *o*-cresol
4 COC = 4chloro-*o*-cresol
6 COC = 6chloro-*o*-cresol
DCOC = 4 6-dichloro-*o*-cresol

which is formed as the temperature is reduced, the effect being particularly marked with tetrahydrofuran and lactonitrile. In most of the experiments in Table 1 there was slight over- or under- chlorination which affected the amount of dichloro-*o*-cresol formed, but a molar ratio which corrects for this experimental error is:

$$\frac{\text{mols } o\text{-cresol} + \text{dichloro-}o\text{-cresol}}{\text{mols 4-chloro-}o\text{-cresol} + \text{6-chloro-}o\text{-cresol}}$$

and the variation of this molar ratio with temperature is shown in Table 1.

Investigation by IR examination of the effect of temperature on a range of *o*-cresol solutions shows that when a high degree of hydrogen bonding of solvent to *o*-cresol (or 4-chloro-*o*-cresol) occurs this is marginally increased by lowering the temperature from +20° to −50°. This agrees with the results in Tables 1 and 2 which show that reduction in chlorination temperature from +50° to the lowest temperature above −50° at which the solvent does not deposit crystals, has little effect on the ratio of 4-chloro-*o*-cresol to 6-chloro-*o*-cresol formed. Thus the increase in the amount of dichloro-*o*-cresol produced on lowering the temperature does not arise from a diminution in strength of the cresol-solvent hydrogen bond.

TABLE 2. CHLORINATION WITH SULPHURYL CHLORIDE

Solvent	Temp °C	Molar comp. of products 4 COC %	6 COC %	OC %	DCOC %	Ratio $\frac{4\ \text{COC}}{6\ \text{COC}}$
No Solvent	+50	67·2	17·1	14·9	0·8	3·9
Nitromethane	−33	82·1	11·1	5·8	1·0	7·4
Nitromethane	+50	79·6	14·6	4·1	1·7	5·5
Nitrobenzene	0	84·1	13·8	2·1	n.d.	6·1
Nitrobenzene	+50	62·3	12·4	25·3	n.d.	5·0
Diethyl ether	−40	83·0	12·7	n.d.	4·3	6·6
Diethyl ether	+30	79·9	19·3	n.d.	0·8	4·1
Carbon tetrachloride	0	64·9	25·9	7·7	1·5	2·5
Carbon tetrachloride	+50	63·4	30·4	4·5	1·7	2·1
Benzene	0	71·9	21·7	6·4	n.d.	3·3
Benzene	+50	48·7	43·6	6·4	1·3	1·1

TABLE 3. CHLORINATION OF PHENOL WITH SULPHURYL CHLORIDE

Solvent	Temp °C	Molar comp. of products Phenol %	2-Chloro-phenol %	4-Chloro-phenol %	4,6-Dichloro-penol %	Ratio $\frac{\text{4 Chlorophenol}}{\text{2 Chlorophenol}}$
No Solvent	+30	12·9	24·1	61·3	1·7	2·5
Nitrobenzene	+30	24·1	25·9	70·7	1·3	2·7
Nitromethane	+30	24·0	23·7	48·2	4·1	2·0
Diethyl Ether	+30	11·3	27·7	59·6	1·4	2·2

An examination was made of the temperature dependence of the frequency of the ring deformation vibration near 1600 cm^{-1} for *o*-cresol and 4-chloro-*o*-cresol. The precise frequency of this absorption is dependent on positions of substitution and electronegativity of the substituents.[5] (An increase in electronegativity increases the frequency of absorption). It is found that over the temperature range +45° to −35° the frequency of absorption increases by 3 cm^{-1} for *o*-cresol and 1·5 cm^{-1} for 4-chloro-*o*-cresol in chloral. In tetrahydrofuran the increases are 3·5 cm^{-1} and 1·5 cm^{-1} respectively whereas in carbon tetrachloride both absorption increases by 1·5 cm^{-1}. Thus in both *o*-cresol and 4-chloro-*o*-cresol the electronegativity increases as temperature decreases and therefore the electron density in the aromatic ring decreases. In the solvents chloral and tetrahydrofuran the frequency increases (and hence electron density decreases) are twice as large for *o*-cresol as they are for 4-chloro-*o*-cresol and in carbon tetrachloride the frequency increases are identical. Thus it would be expected that in the polar solvents the rate of chlorination of 4-chloro-*o*-cresol will be decreased by a smaller amount than the rate for *o*-cresol. In carbon tetrachloride both rates would be similarly reduced and although the overall rate of chlorination would be slower there would be no significant increase in the 4,6-dichloro-*o*-cresol yield.

TABLE 4. HYDROXYL STRETCHING FREQUENCIES OF *o*-CRESOL IN VARIOUS SOLVENTS

Solvent	νOH Absorption frequencies		Ratio $\frac{4\,COC}{6\,COC}$
Carbon tetrachloride	3618 cm^{-1}	3470 cm^{-1}	0·9
Nitrobenzene	3530 cm^{-1}		5·0
Nitromethane	3545 cm^{-1}		6·3
Benzene	3565 cm^{-1}	3470 cm^{-1}	1·1

In IR spectrum of *o*-cresol in the CCl_4 two νOH absorptions were evident indicating bonded and non-bonded hydroxyl groups. In nitrobenzene and nitromethane the spectra show a single νOH absorption corresponding to cresol bonded to solvent. In benzene solution a slight shift of the free —OH absorption indicated weak hydrogen-bonding. There was also a broad absorption indicated weak hydrogen-bonding. There was also a broad assumption, weaker than that in CCl_4, which was due to cresol intermolecular hydrogen bonding.

An explanation of these effects is tentatively advanced. In polar solvents at low temperatures hydrogen bonding can occur between the aromatic π-electrons of the cresol and the acidic —OH of another cresol molecule thus reducing electron density in the ring. In 4-chloro-*o*-cresol, although this hydrogen bonding can occur the mesomeric effect of the chlorine will make good any removal of electrons from the aromatic ring. This would explain why the apparent decrease in aromatic electron density in *o*-cresol is greater than for 4-chloro-*o*-cresol. (No evidence has been found for π-hydrogen bonding directly involving the solvent molecules.)

EXPERIMENTAL

B.D.H. laboratory reagents were used throughout except for the *o*-cresol which was Grade 'A' commercial material m.p. 31°.

1. ***Chlorinations with chlorine.*** 1 mole of *o*-cresol (108 g) was dissolved in 3 times its weight of solvent and chlorinated by passing in 1 mole Cl_2 in 1 hr with stirring, at the required temp level. When the solvent was water soluble the products were washed free of HCl and solvent by water

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[5] Bellamy, *The Infra-red Spectra of Complex Molecules* (2nd Edition). P. 71. Methuen (1958).

washing, otherwise the product was washed twice with water then extracted into 10% NaOH aq. and the solvent separated. The alkaline extract was then acidified and the chlorocresol layer separated and dried by distilling off the small amount of water present and returning to the flask the trace of chlorocresol which distilled with the water.

Experiments showed that loss of any of the cresols by preferential extraction into water was negligible. The entire batch of chlorocresol was weighed, sampled and analysed by IR spectroscopy. The total cresol content normally totalled a few percent less than 100 but for ease of comparison all results were adjusted to 100% by simple proportion.

2. *Chlorinations with sulphyryl chloride.* 1 mole of *o*-cresol or phenol (94 gm) was chlorinated by the addition of 1 mole sulphuryl chloride in 15 min with stirring at the required temp. The product was then maintained for a further 45 min at the same temp with stirring, then was worked up by the methods already described, and analysed.

3. *IR absorption measurements.* IR spectra were measured with a Unicam SP 100 spectrometer. The frequency reproducibility is better than $0{\cdot}5\ \mathrm{cm}^{-1}$ at $1600\ \mathrm{cm}^{-1}$, the region where aromatic deformation frequencies were measured.

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