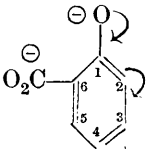
CCXIV.—*The Influence of Substituents on the Reimer–Tiemann Reaction. Part II.*

By Herbert Henry Hodgson and Thomas Alfred Jenkinson.

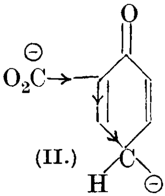
The standardised reaction described by the authors (this vol., p. 469) has been conducted with other phenols and also with bromoform in place of chloroform.

The unusual reactivity of the 2- compared with the 4-position found for 6-chlorophenol ($o/p = 1{\cdot}6$) is shown also, but in diminishing degree, in 6-bromophenol ($o/p = 1{\cdot}25$) and in 6-iodophenol ($o/p = 1{\cdot}07$). This affords additional evidence for the view already put forward (*loc. cit.*, p. 470) that the attraction diminishes with the diminishing positive fields of the halogens, $Cl > Br > I$ (Lapworth and Robinson, *Mem. Manchester Phil. Soc.*, 1928, **72**, 43). An alternative explanation is that the partial deactivation of the anionic oxygen by the positive halogen field reduces the activity of the hydrogen in the 2- and 4-positions to such an extent that the weak kationoid Reimer–Tiemann reagent attacks the more strongly activated 2-hydrogen rather than the weaker though more frequently activated 4-hydrogen [compare Lapworth and Robinson (*loc. cit.*, p. 46) and also the nitration of *o*-halogenoanisoles (Ingold and Smith, J., 1927, 1690)]. Both effects are probably superposed.

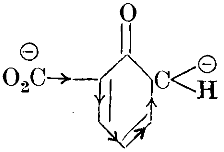
Substitution occurs in salicylic acid almost solely in the 4-position ($o/p = 0{\cdot}06$), probably owing to steric hindrance (compare *o*-cresol, $o/p = 0{\cdot}48$; *loc. cit.*, p. 470). A consideration of the activated phase of the 4-hydrogen (II) shows that the alternating effect of the anionic phenoxide group (I) must be powerfully reinforced by the general (inductive) effect of the anionic carboxyl group (II), whereas in the activated phase of the 2-hydrogen (III) the latter effect is either absent or much reduced, as would be expected, after being transmitted along a chain of six carbon atoms.



(I.)



(II.)



(III.)

That the anionic carboxyl group must reinforce the activity of the 4-hydrogen in the relayed inductive manner above described may be deduced from a consideration, following the analysis of Ingold and Vass (J., 1928, 417), of the combined direct (through space) effects of the two anionic groups on hydrogen in positions 2, 3, 4, and 5. In salicylic acid, both groups contribute activating effects, the results found for deactivating atoms by Ingold and Vass (*loc. cit.*) thus being reversed, the positional order of resultant activation being $(2) > (5) > (3) > (4)$. This direct effect will collaborate with the combined alternating (tautomeric) and inductive (general) effect, but since it favours the 2-position and the experimental result shows almost exclusive activity in the 4-position it must follow that the powerful inductive relayed effect from the anionic carboxyl group, which is really a suppressed alternating effect, greatly exceeds the adverse direct effect [compare Ingold and Vass (*loc. cit.*) who state that even in orientation by –OR the tautomeric (alternating) effect overwhelmingly predominates over the direct effect; and Allan, Oxford, Robinson, and Smith (J., 1926, 401), who examined the direct effects of the ·OR groups in pyrocatechol ethers]. In all the experiments with salicylic acid the absence of resinous products, and therefore of complicating secondary reactions, is noteworthy, and in accordance with the unique reactivity deduced above.

A similar result was found by Traub (D.R.-P. 80195) for the Reimer–Tiemann reaction with guaiacol: 4-hydroxy-3-methoxybenzaldehyde (vanillin) was the main product and only small quantities of 2-hydroxy-3-methoxybenzaldehyde were formed.

Resorcinol monomethyl ether reacted very vigorously and a considerable amount of resinous material was formed. The observation of Tiemann and Parrisius (*Ber.*, 1880, **13**, 2366) was confirmed, *viz.*, that 4-hydroxy-2-methoxybenzaldehyde is produced in much greater yield than 2-hydroxy-4-methoxybenzaldehyde.

The diminished vigour of the reaction in all cases where halogen is present testifies to its deactivating influence. 4-Chloro- and 2 : 6-dichloro-phenol give comparatively very small yields of aldehydes even after prolonged reaction. 3 : 5-Dichloro-4-hydroxybenzaldehyde is volatile in steam, a property doubtless due to co-ordination between the hydroxyl group and the adjacent chlorine atoms (compare Sidgwick and Callow, J., 1924, **125**, 533).

When diethyl-*m*-aminophenol was submitted to the Reimer–Tiemann reaction, dye-formation ensued so rapidly as to prevent quantitative examination of the aldehydes initially produced, although traces were detected by means of *p*-nitrophenylhydrazine.

The Reimer–Tiemann Reaction with Bromoform.—The following results were obtained. Those obtained with chloroform are recorded for comparison.

	Ortho/para ratio.			Ortho/para ratio.	
Initial phenol.	With $CHBr_3$.	With $CHCl_3$.	Initial phenol.	With $CHBr_3$.	With $CHCl_3$.
Phenol	0·44	0·6	Salicylic acid	0·05	0·06
o-Cresol	0·37	0·48	*m*-Cresol	0·85	0·46
o-Chlorophenol	0·71	1·6	*m*-Chlorophenol	0·84	0·71
o-Bromophenol	0·65	1·25	*m*-Bromophenol	0·77	0·72
o-Iodophenol	0·65	1·07	*m*-Iodophenol	0·84	0·78

These results may be explained by assuming that the less energetic kationoid reagent derived from bromoform has a greater specific volume than the reagent derived from chloroform (bromoform has a greater specific volume than chloroform). In phenol and *o*-cresol, hydrogen in the ortho-positions, although strongly activated, is still less favourably situated for reaction than hydrogen in the para-positions owing to increased steric inhibition; therefore the ortho-para ratio diminishes. Steric conditions in the *o*-halogenophenols are more favourable than in phenol and *o*-cresol (compare Hodgson and Jenkinson, *loc. cit.*, p. 470), so the ortho/para ratio increases; but they are less favourable for the bromoform than for the chloroform reagent, and therefore the ratio is smaller in the former case. In the *m*-halogenophenols, powerful halogeno-deactivation of hydrogen in the 4-position causes the attack of the weaker kationoid reagent to be directed more frequently to the more strongly activated hydrogen in the ortho-positions than with the stronger chloroform reagent (compare Lapworth and Robinson, *loc. cit.*, pp. 45, 46). The case of *m*-cresol is anomalous, unless steric conditions are responsible for the increased ortho/para ratio.

When iodoform was used in place of chloroform, the ortho/para ratio for phenol and its *o*-halogeno-derivatives ranged from 0·2 to 0·3, showing the overwhelming effect of steric conditions upon the very feeble kationoid reagent.

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TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, June* 21*st*, 1929.]