

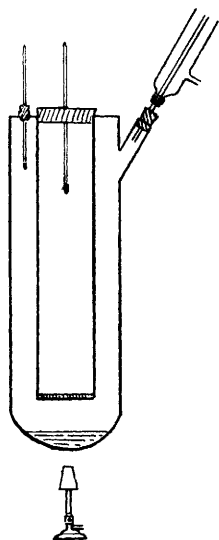
XXI.—*The Influence of Substitution in the Nucleus on the Rate of Oxidation of the Side-chain. I. Oxidation of the Mono- and Di-chlorotoluenes.*

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ISOLATED observations on the effect of different oxidising agents, and on the influence of certain groups in accelerating or retarding oxidation of the side-chain, have been made by different observers, but the subject has never been systematically investigated. Wroblewsky (*Ber.*, 1882, 15, 1021), without giving experimental details, states that "if benzene with hydrocarbon side-chains in which hydrogen is replaced by a halogen or a nitro-group is submitted to oxidation by chromic acid mixture, those side-chains pass into carboxyl which are farthest from the halogen." Lellmann's *Organische Synthese*, p. 196, contains the following statement: "Negative atomic groups in the ortho-position protect the alkyl group from the action of oxidising agents, whereas alkaline oxidising agents attack this group." The exact reference is not given, but the statement is apparently based on that of Wroblewsky and also on certain observations of W. A. Noyes (*Amer. Chem. J.*, 1885, 7, 145; 1886, 8, 185; 1889, 11, 161). The latter investigator found that *o*-bromotoluene is oxidised with difficulty to *o*-bromobenzoic acid by means of potassium ferricyanide; also that *m*-nitrotoluene is less readily oxidised by this reagent than its isomerides. Schöpff (*Ber.*, 1891, 24, 3778) concludes from the results of his attempts to oxidise *o*-bromo-*m*-xylene that "the oxidation of a methyl group in the ortho-position (to bromine) with acid oxidising agents is effected slowly and with difficulty." Rupp (*Ber.*, 1892, 25, 347) experienced the same difficulty with tetrachloro- and tetrabromo-*p*-xylenes, and only succeeded with a mixture of nitric acid and permanganate. It is clear that no satisfactory generalisation can be drawn from these isolated facts. Certain points which were noticed in the course

of the researches in which one of us has been engaged in collaboration with H. D. Dakin (Trans., 1901, 79, 1111) and with S. H. C. Briggs (Trans., 1903, 83, 1213) on the oxidation of the halogen derivatives of toluene suggested the present inquiry.

The method which we have adopted is to heat about a gram of the substance with dilute nitric acid in a sealed tube for a length of time insufficient for complete oxidation, and to estimate the proportion of acidic product and unchanged substance. In our first experiments, the substance was weighed in small specimen tubes which were slipped into the tube containing the acid. The sealed tubes were heated in a cylindrical, jacketed, tin-plate air-bath which was fixed horizontally, the required temperature being attained by boiling turpentine contained in the outer jacket. The results of the experiments with this apparatus were not concordant. We attributed this partly to the specimen tubes, which to some extent protected the substance from the action of the acid. These tubes were therefore discarded and the substance introduced directly into the acid. We found, moreover, that the inner compartment of the air-bath was about  $5^{\circ}$  hotter at the bottom than at the top, so that the lower tubes were at a higher temperature than the upper ones. The horizontal air-bath was therefore replaced by a vertical one, jacketed as before, and covered with flannel as shown in the figure.



The liquid in the jacket was coal-tar naphtha boiling at  $140\text{--}150^{\circ}$ . Although there was still a difference of about  $3^{\circ}$  between the temperature of the top and bottom of the inner compartment, yet as the tubes, which were approximately of equal length, were placed vertically, they were consequently exposed to the same conditions of temperature.

Care was taken to prevent direct contact between the tubes and the metal of the bath by fixing a cork pad at the bottom and covering the tubes with flannel. Under these modified conditions, concordant results were obtained. The substances employed were the three monochlorotoluenes and the six dichlorotoluenes, all of which were carefully purified by fractional distillation, and in the case of 3:5-dichlorotoluene by crystallisation. The monochlorotoluenes were obtained quite colourless by distillation under diminished pressure, but this treatment was not found necessary in the case of the dichlorotoluenes.

The following are the boiling points of the substances employed :

Monochlorotoluenes.			Dichlorotoluenes.		
	b. p.	mm.		b. p.	b. p.
Ortho-	100°	129	2 : 3-	200—202°	2 : 6- 192—194°
Meta-	102	130	2 : 4-	194·5—195·5	3 : 4- 203—204
Para-	85	61	2 : 5-	195—197	3 : 5- m. p. 26—27

A weighed quantity of the substance (about 1 gram) was introduced into the tube, and about six times this amount of dilute acid (1 vol. nitric acid of sp. gr. 1·4 to 2 vols. water) was added and the tube sealed.

In order to ascertain the effect of the length of the tube on the rate of oxidation, equal quantities of 3 : 5-dichlorotoluene were heated in two tubes, one of which was about half the length of the other. It was found that the acid formed in the shorter tube was less pure and rather larger in amount, but the difference was insignificant and would be inappreciable in tubes so nearly of the same length as those which we employed.

The air-bath was closed loosely by a cork holding a thermometer and heated until the temperature was constant. The tubes were then introduced, and when the temperature of the inner compartment reached 138—140° the tubes were left for 1½ hours, during which the temperature of the interior did not exceed 145°. The bath was then allowed to cool and the tubes removed and opened. The method of analysis was as follows: the contents of each tube were in turn rinsed into a separating funnel with ether, the contents being then vigorously shaken, whereby the ether dissolved out the whole of the organic compounds. The acid layer was then drawn off and sodium carbonate solution added in excess to the ether and well shaken to extract the organic acid. The alkaline layer was removed and the ethereal extract washed with a small quantity of water, the washings being added to the alkaline liquid. The ethereal solution, which contained the unaltered substance (possibly also a little aldehyde), was dehydrated over calcium chloride, decanted into a tared flask, the ether removed, and the residue weighed. The alkaline liquid was acidified with hydrochloric acid, extracted with ether, the ethereal solution dehydrated over calcium chloride and treated as described above. The purity of the acid was in each case ascertained from the melting point. This and the total quantity of products obtained when compared with the substance taken was a satisfactory check on the result, although, of course, the method lacks the precision of an exact analytical process.

In the following experiments, all the tubes were heated together under precisely the same conditions.

*1st Series.*

Chloro-toluene.	Actual amount taken.	Calculated to 1 gram.			m. p. of acid.	Correct m. p. of acid.
		Chloro-benzoic acid.	Unchanged substance.	Total.		
Ortho-	1·005	1·011	0·040	1·051	135—136°	137°
Meta-	0·989	1·092	0·029	1·121	145—148	153
Para-	0·964	1·058	0·019	1·077	233—234	236
2:3-	1·332	0·942	0·135	1·077	159—162	163
2:4-	1·035	1·073	0·051	1·124	160—161	160
2:5-	1·065	0·864	0·157	1·021	139—142	153
2:6-	1·036	0·825	0·236	1·061	123—132	139—140
3:4-	1·024	1·060	0·047	1·107	200—201	200—201
3:5-	1·046	0·726	0·297	1·023	183—184	182—183
3:5- (short tube)	0·988	0·759	0·228	0·987	184—205	

It will be seen from the above table that the monohalogen compounds are more rapidly attacked than the majority of the dihalogen derivatives, for the former are almost completely converted into acid, whilst only two of the latter are completely oxidised. The dihalogen compounds show well-marked differences; the 3:5-compound is least attacked. The next in order being the 2:5- and 2:6-isomerides, which are oxidised to approximately the same extent, although the 2:6-compound yields a very impure acid. The 2:3-compound comes next, and finally the 2:4- and 3:4-derivatives, which may be bracketed together as being almost completely oxidised.

As the monohalogen compounds were too far oxidised for any conclusions to be drawn as to their relative rates of oxidation, a second experiment was made in which the tubes were heated for only half an hour at 140—145°.

Chloro-toluene.	Amount taken.	Calculated to 1 gram.			m. p. of acid.	Correct m. p. of acid.
		Chloro-benzoic acid.	Unchanged substance.	Total		
Ortho-	1·015	0·687	0·307	0·994	135—136°	137°
Meta-	1·011	0·384	0·548	0·932	146—149	153
Para-	1·007	0·998	0·091	1·089	235—236	236

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It is therefore evident that the meta-compound is least affected, then follows the ortho-derivative, and finally the para-isomeride, which is almost entirely converted into the corresponding chlorobenzoic acid.

Two other series of experiments which were made with the dihalogen compounds confirm the results of the first series.

*2nd Series.*

Dichloro- toluene.	Amount taken.	Calculated to 1 gram.			m. p. of acid.	Correct m. p. of acid.
		Dichloro- benzoic acid.	Unchanged substance.	Total.		
2:3	0.993	0.762	0.290	1.052	159—161°	163°
2:4	0.974	0.949	0.119	1.068	159—159.5	160
2:5	0.989	0.614	0.381	0.995	138—142	153
2:6	1.044	0.546	0.451	0.997	115—129	139—140
3:4	0.997	1.025	0.080	1.105	200—201	200—201
3:5	1.000	0.470	0.495	0.965	183—184	182—183

*3rd Series.*

Chloro- toluene.	Amount taken.	Calculated to 1 gram.			m. p. of acid.	Correct m. p. of acid.
		Dichloro- benzoic acid.	Unchanged substance.	Total.		
2:3	1.076	0.773	0.247	1.020	162—163°	163°
2:4	1.030	1.017	0.096	1.113	160—161	160
2:5	1.165	0.631	0.373	1.004	139—142	153
2:6	1.093	0.640	0.342	0.982	114—128	139—140
3:4	1.165	1.060	0.055	1.115	200—201	200—201
3:5	1.000	0.357	0.581	0.938	182—183	182—183

So far as the special conditions of the above experiments are concerned, namely, the use of halogen compounds on the one hand and of nitric acid as oxidising agent on the other, the results are perfectly definite. The meta-compounds retard oxidation, and the para-compounds assist it, whilst the ortho-compounds occupy an intermediate position. Thus, *m*-chlorotoluene and 3:5-dichlorotoluene are least attacked. *p*-Chlorotoluene and the two dichlorotoluenes substituted in the para-position (2:4 and 3:4) are most readily oxidised. It is not clear why the 2:3-dichloro-compound should be more readily

oxidised than the 2:5-derivative, for they are both substituted in the meta- as well as in the ortho-position with respect to the methyl group, nor is it evident why the 2:6- and 2:5-compounds should be oxidised to the same extent. It is interesting to note that Noyes, when working with the nitrotoluenes and potassium ferricyanide, found that the meta-compound is less readily oxidised than the other two isomerides. On the other hand, Wroblewsky's observation (*vide ante*) seems to be only true in part, unless, indeed, chromic acid has a very different action from that of the other two oxidising agents. It is difficult to account for the behaviour of the different isomerides. It is clear that (contrary to the view which we were led to adopt as the result of our preliminary experiments) it is not a question of steric hindrance. The only process which seems to offer any analogy to the present one is that of substitution in the nucleus in which the formation of meta-compounds is sharply differentiated from that of the ortho- and para-compounds, yet it is difficult to see how any process of substitution in the nucleus can be applied to explain the conversion of a side-chain into a carboxyl group. We have accumulated a number of facts in regard to the oxidation of simple and mixed dihalogen derivatives and nitro-halogen compounds of toluene, which we hope shortly to publish.

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