

CLXIII.—*The Influence of Substitution in the Nucleus on the Rate of Oxidation of the Side-chain. II. Oxidation of the Halogen Derivatives of Toluene.*

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OUR first paper on this subject contained an account of the action of dilute nitric acid on the mono- and di-chlorotoluenes (Trans., 1904, 85, 174).\*

We have now studied the behaviour of the isomeric chlorobromotoluenes and dibromotoluenes and the 2:6-chloroiodo-, bromoiodo-,

• Our attention has been called to the fact that, in the brief reference which we made to previous investigations on this subject, we omitted—the oversight was quite unintentional—to mention the name of Professor Ira Remsen. The statement contained in Lellmann's *Organische Synthese*, and referred to by us, that “negative atomic groups in the ortho-position protect the alkyl group from the action of acid oxidising agents, whereas alkaline oxidising agents attack this group,” was the outcome of a series of investigations carried out by Remsen and his pupils from 1877 onwards, which appeared in the *American Chemical Journal*. The above statement, in the light of Prof. Remsen's subsequent work, requires modification. He finds that negative atomic groups in the ortho-position protect the alkyl group from the action of oxidising agents, but it is not true that alkaline oxidising agents attack this group, although there are some cases in which this last statement holds good.

and di-iodo-toluenes. The last three lose iodine readily on oxidation with dilute nitric acid, and the same is true of the moniodo-compounds, although to a much smaller extent. In consequence of this decomposition, the study of the dihalogen compounds containing iodine was discontinued.

The following table contains a synopsis of the results with the three series of dihalogen compounds, the substances on the left being least, those on the right most rapidly oxidised. The bracket indicates an approximately equal rate of oxidation.

TABLE I.

Cl : Cl.....	3 : 5	2 : 5	2 : 6	2 : 3	2 : 4	3 : 4
Cl : Br ...	3 : 5	2 : 5	2 : 6	2 : 3	2 : 4	3 : 4
Br : Cl ...		2 : 5		2 : 3	2 : 4	3 : 4
Br : Br ...	3 : 5	2 : 3	2 : 5	2 : 6	2 : 4	3 : 4

The order of oxidation is the same in all three series with the exception of the 2 : 3-dibromotoluene, which follows the 3 : 5- instead of the 2 : 5- and 2 : 6-compounds, as in the other two series. This fact is of some importance and will be referred to again.

The experiments have been carried out in the apparatus previously described (*loc. cit.*) and with about the same quantity of materials. The amounts of unchanged substance and acid have been estimated in each case, but the results are calculated from the amount of acid as yielding on the whole the most trustworthy figures. From the acid, the corresponding amount of toluene derivative has been calculated and given in parts per hundred of substance taken.

The following table gives the figures for the chlorobromotoluenes :

TABLE II.

Cl : Br.	Per cent. oxidised.	Δ	Δ per cent. oxidised.	Cl : Br.	Per cent. oxidised.	Δ	Δ per cent. oxidised.
2 : 3	59.0	3.2	5	2 : 6	46.1	1.1	1.3
3 : 2	62.2			3 : 4	84.4		
2 : 4	74.6			4 : 3	83.5		
4 : 2	71.1	3.5	5	3 : 5	28.4		
2 : 5	45.4						
5 : 2	48.1						

A comparison of the pairs of compounds with reversed positions of the halogens indicates that the compound in which bromine occupies the meta-position is the less oxidised of the two. Thus, 2 : 3-, 2 : 5-,

and 4 : 3-chlorobromotoluenes are less oxidised than the complementary compounds of each pair. The same is true of bromine in the ortho-position, the 4 : 2-compound being less oxidised than the 2 : 4-compound. The influence of the meta-bromine is least in the 3 : 4-compounds. The following is a similar table containing the results of two experiments made with the dibromotoluenes.

TABLE III.

Br : Br.	Per cent. oxidised.		Br : Br. .	Per cent. oxidised.	
	I.	II.		I.	II.
2 : 3	22.7	17.6	2 : 6	26.5	25.7
2 : 4	50.0	53.3	3 : 4	49.8	51.7
2 : 5	23.3	21.7	3 : 5	13.6	14.6

Making allowance for the various sources of experimental error incidental to the process, the results are fairly concordant. These errors may arise from the method of analysis, which does not afford great precision; from a portion of partially oxidised material remaining as aldehyde with the unchanged substance; from differences in the surface of contact exposed to the action of the acid and from the different solubilities in nitric acid of the halogen compounds and their oxidation products. We have tried as far as possible to obviate the source of error due to surface of contact by carefully selecting tubes of the same diameter. In the experiments which we have now to record, where comparative determinations of three series of halogen compounds have been made, we have used in all cases tubes made from the same length of tubing, and therefore as nearly as possible identical in diameter and approximately so in length.

Supposing the bromine in the ortho- and meta-positions to retard oxidation more than the chlorine in those positions, the effect should become apparent when the isotopic\* dichloro-, chlorobromo-, and dibromo-toluenes are oxidised together.

The following table contains the results of such a series of determinations. The weights of the substances taken for a given quantity of acid were approximately in the proportion of their molecular weights. The results as a whole are not strictly comparable, as each horizontal series represents a separate experiment. On the other hand, as the temperature and time of heating were nearly the same (with the exception of the 2 : 6 series, where for some unexplained reason the temperature inside the air-bath rose 5° higher than that in the

\* We propose, in future, to employ the word "*isotopic*" (*ἴσος*, equal; *τόπος*, place) in place of the rather awkward expression "similarly substituted."

jacket), the vertical columns should, and do, in fact, correspond closely with the previous tables.

TABLE IV.

	Per cent. oxidised.			
	Cl : Cl.	Cl : Br.	Br : Cl.	Br : Br.
2 : 3	33.2	34.4	35.7	22.8
2 : 4	45.8	42.2*	40.1	42.6
2 : 5	23.5	18.0	19.1*	18.3
2 : 6	38.3	28.5	—	33.7
3 : 4	52.0	54.2	53.9	37.5
3 : 5	11.0	10.3	—	7.6

To render the figures in the horizontal series strictly comparable, the differences should be estimated on the percentage of substance oxidised. The relation of the dichloro- to the dibromo-compounds will then appear as follows :

TABLE V.

	Per cent. oxidised.		$\Delta$	$\Delta$ per cent. oxidised.
	Cl : Cl.	Br : Br.		
2 : 3	33.2	22.8	9.4	28
2 : 4	45.8	42.6	3.2	7
2 : 5	23.5	18.3	5.2	22
2 : 6	38.3	33.7	4.6	12
3 : 4	52.0	37.5	14.5	28
3 : 5	11.0	7.6	3.4	31

It is clear from the table that the dibromotoluenes are in all cases less oxidised than the dichloro-compounds. This result naturally follows from the effect already noted in the case of the chlorobromotoluenes, where bromine in the meta- and ortho-positions was found to retard oxidation more than chlorine. It will be seen, moreover, that where bromine occupies the meta-position, the retarding action is much more pronounced than in the other cases. The 2 : 3-, 2 : 5-, 3 : 4-, and 3 : 5-compounds all contain meta-bromine. It is also evident that the bromine in the para-position has little effect on the rate of oxidation. For if we assume that the lowering of the rate of oxidation in the 2 : 6-dibromo-compound (12 per cent.) is approximately divided between the two bromine atoms, the result will be almost equivalent to the decrease in the 2 : 4-compound (7 per cent.), leaving only 1 per cent. due to the influence of the para-bromine.

\* Owing to insufficient material, this number is not determined directly from experiment, but is calculated from Table II, p. 1623.

These interesting and apparently simple relations which determine the rate of oxidation in the case of the dichloro- and dibromo-compounds seem to vanish when the chlorobromo-derivatives are considered. From analogy with the dichloro- and dibromo-toluenes, the chlorobromotoluenes should occupy a position midway between these two series. The anomalous behaviour of the latter and the complexity of the whole problem involved can only be understood by reference to the rate of oxidation of the monohalogen compounds. The following two typical results are selected from a number of determinations:

TABLE VI.

Name.	I.	II.
	30 mins. 140—148°.	60 mins. 130—135°.
<i>o</i> -Chlorotoluene .....	7.5	8.6
<i>m</i> -Chlorotoluene .....	5.2	7.4
<i>p</i> -Chlorotoluene .....	16.2	13.7
<i>o</i> -Bromotoluene .....	24.7	23.5
<i>m</i> -Bromotoluene .....	17.4	19.0
<i>p</i> -Bromotoluene .....	48.7	43.6
<i>o</i> -Iodotoluene .....	5.2	5.9
<i>m</i> -Iodotoluene .....	7.2	8.6
<i>p</i> -Iodotoluene .....	7.0	7.5

It is evident from these figures that the presence of a bromine atom in the nucleus produces more rapid oxidation of the side-chain than that of a chlorine or an iodine atom. Why is it, then, that two bromine atoms should have the very reverse effect as compared with two chlorine atoms? It is evident that two similar atoms in the nucleus affect one another in a very marked degree. If proof of this were wanting, we have only to consider the effect of two bromine atoms in juxtaposition, namely, in the 2:3- and 3:4-compounds in Table IV. The drop in the rate of oxidation as compared with the isotopic dihalogen compounds is very clearly indicated in this table. Now it is precisely in these two cases that the rate of oxidation of the chlorobromo-compounds is more rapid than in that of the dichloro-compounds. Only one conclusion seems admissible, namely, that dissimilar atoms interfere less with each other's action than similar atoms, and that in consequence this factor must be considered, along with the position of the atoms in the nucleus, in determining the rate of oxidation. These two factors might very well explain the apparent anomalies in the relative rates of oxidation of the isotopic dihalogen compounds. It is impossible, however, with the present data, so to distribute the effect as to be able to predict the precise result in any given case.

## EXPERIMENTAL.

The chlorobromotoluenes for these experiments were prepared as described by Cohen and Raper (this vol., p. 1262). The dibromotoluenes were obtained in a similar manner, the 2:3-, 2:4-, 2:5-, and 2:6-compounds from the corresponding nitrotoluidines, and the 3:4- and 3:5-isomerides from aceto-*p*-toluidide by bromination. The chloro- and iodo-toluenes and *p*-bromotoluene were obtained from the corresponding toluidines. *o*- and *m*-Bromotoluenes are best prepared from bromo-*m*- and bromo-*p*-acetotoluidides respectively by removing the amino-group. Although, as already stated, the 2:6-chloriodo-, bromiodo-, and di-iodo-toluenes decompose on oxidation with nitric acid liberating iodine, it was thought desirable to record briefly the properties of these new compounds and of such intermediate products as have not been previously described.

2-Chloro-6-iodotoluene was prepared from 2-chloro-6-aminotoluene by the usual method; it is a colourless liquid, boiling at 132—133°/25 mm. and having a sp. gr. 1·844 at 20°/20°.

0.2668 gave 0·4008 AgCl + AgI.

$C_7H_6ICl$  requires 0·3999 AgCl + AgI.

2-Bromo-6-iodotoluene was obtained from 2-bromo-6-aminotoluene. The base forms a benzoyl derivative (m. p. 176—177°) and an acetyl derivative (m. p. 154—155°). Bromiodotoluene is a colourless liquid (b. p. 135—140°/15 mm.; sp. gr. 2·044 at 20°/20°).

0.2106 gave 0.2977 AgBr + AgI.

$C_7H_6IBr$  requires 0.2998 AgBr + AgI.

2:6-Di-iodotoluene.—Nitriodotoluene crystallises in yellow needles (m. p. 34—36°). The 2-iodo-6-aminotoluene is a liquid; its hydrochloride crystallises in plates with a satiny lustre.

The di-iodotoluene crystallises from alcohol in nearly colourless needles (m. p. 40—42°).

0.2058 gave 0.2814 AgI.  $I = 73.87$ .

$C_7H_6I_2$  requires  $I = 73.82$  per cent.

The following tables contain experimental data to which reference has already been made. The strength and quantity of nitric acid used was that employed in the previous experiments with the dichlorotoluenes, namely, 6 c.c. of nitric acid (1 vol. of acid, sp. gr. 1.4, to 2 vols. of water).

*Oxidation of the Chlorobromotoluenes.*

## Series I.

Time, 1½ hours. Temperature, 139—147°.

Cl : Br.	Weight.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
2 : 3	0.994	0.672	0.363	1.035	154—158°	165°
3 : 2	1.019	0.726	0.374	1.100	125—136	143—144
2 : 4	0.998	0.853	0.228	1.081	161—163	166—167
4 : 2	0.993	0.809	0.265	1.074	150—152	154—155
2 : 5	0.989	0.515	0.523	1.038	146—151	155—156
5 : 2	1.029	0.568	0.510	1.078	119—126	148—149
2 : 6	1.000	0.529	0.521	1.050	119—133	143—144
3 : 4	1.003	0.970	0.133	1.103	208—210	218
4 : 3	0.990	0.947	0.132	1.079	208—210	214
3 : 5	0.989	0.322	0.689	1.011	186—187	189—190

*Oxidation of the Dibromotoluenes.*

## Series II.

Time, 1 hour, 40 minutes. Temperature, 130—140°.

Br : Br.	Weight taken.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
2 : 3	0.990	0.252	0.800	1.052	139—144°	149—150°
2 : 4	1.024	0.574	0.519	1.093	156—158	158—159
2 : 5	1.032	0.270	0.819	1.089	140—146	153—154
2 : 6	1.011	0.300	0.777	1.077	93—117	146—147
3 : 4	1.012	0.565	0.514	1.079	225—226	229—230
3 : 5	0.990	0.151	0.838	0.989	210—212	213—214

*Oxidation of the Dibromotoluenes.*

## Series III.

Time, 1 hour, 45 minutes. Temperature, 130—140.5°.

Br : Br.	Weight taken.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
2 : 3	0.982	0.194	0.845	1.039	148—149°	149—150°
2 : 4	0.993	0.594	0.470	1.064	157—158	158—159
2 : 5	1.003	0.244	0.811	1.055	151—152	153—154
2 : 6	0.984	0.284	0.777	1.061	96—102	146—147
3 : 4	1.007	0.583	0.496	1.079	227—228	229—230
3 : 5	0.988	0.162	0.850	1.012	212—213	213—214

*Oxidation of the Dihalogen Compounds.*

## Series IV.

	Weight taken.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
2 : 3.						
1 h., 30 m. { Cl : Cl	0.845	0.334	0.569	0.903	155—159°	163°
135—140° { Cl : Br	1.029	0.406	0.706	1.112	157—160	165
{ Br : Cl	1.016	0.416	0.676	1.092	125—133	143—144
{ Br : Br	1.475	0.377	1.206	1.583	141—145	149—150

*Oxidation of the Dihalogen Compounds (continued).*

## Series V.

	2 : 4.	Weight taken.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
1 h., 30 m. 135—140°	Cl : Cl	0·810	0·440	0·442	0·882	159—160°	160°
	Br : Cl	0·999	0·459	0·640	1·099	151—153	154—155
	Br : Br	1·408	0·672	0·871	1·543	155—158	158—159

## Series VI.

	2 : 5.						
1 h., 35 m. 135—140°	Cl : Cl	0·806	0·225	0·593	0·818	135—140°	153°
	Cl : Br	1·014	0·209	0·861	1·070	150—152	155—156
	Br : Br	1·426	0·293	1·206	1·499	140—145	153—154

## Series VII.

	2 : 6.						
1 h., 30 m. 135—145°	Cl : Cl	0·795	0·362	0·539	0·901	116—130°	139—140°
	Cl : Br	1·000	0·327	0·768	1·095	103—125	143—144
	Br : Br	1·423	0·538	1·006	1·544	90—118	146—147

## Series VIII.

	3 : 4.						
1 h., 30 m. 135—140°	Cl : Cl	0·796	0·491	0·383	0·874	197—199°	200—201°
	Cl : Br	1·014	0·630	0·487	1·117	201—204	218
	Br : Cl	0·991	0·612	0·480	1·092	203—205	214
	Br : Br	1·416	0·595	0·934	1·529	224—226	229—230

## Series IX.

	3 : 5.						
1 h., 30 m. 135—140°	Cl : Cl	0·811	0·106	0·708	0·814	183—184°	182—183°
	Cl : Br	0·995	0·118	0·891	1·009	191—192	189—190
	Br : Br	1·425	0·122	1·326	1·448	210—211	213—214

*Oxidation of the Monohalogen Compounds.*

## Series X.

Time, 30 minutes. Temperature, 140—148°.

	Weight taken.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
<i>o</i> -Cl	0·994	0·092	not determined		130—131°	137°
<i>m</i> -Cl	0·996	0·064	„	„	144—145	153
<i>p</i> -Cl	0·996	0·200	„	„	234—235	236
<i>o</i> -Br	1·334	0·388	„	„	137—140	148
<i>m</i> -Br	1·336	0·274	„	„	143—145	155
<i>p</i> -Br	1·338	0·766	„	„	242—244	251
<i>o</i> -I	1·718	0·102	„	„	147—148	162—163
<i>m</i> -I	1·728	0·142	„	„	175—177	187—188
<i>p</i> -I	1·738	0·139	„	„	263	265



*Oxidation of the Monohalogen Compounds (continued).*

## Series XI.

Time, 60 minutes. Temperature, 130—135°.

	Weight taken.	Acid.	Unchanged.	Total.	M. p. of acid.	Correct m. p.
<i>o</i> -Cl	1·000	0·107	0·803	0·910	132—134°	137°
<i>m</i> -Cl	0·989	0·091	0·895	0·986	146—148	153
<i>p</i> -Cl	1·003	0·170	0·802	0·972	235—236	236
<i>o</i> -Br	1·359	0·376	0·988	1·364	140—142	148
<i>m</i> -Br	1·358	0·303	1·020	1·323	150—152	155
<i>p</i> -Br	1·349	0·692	0·773	1·465	245—247	251
<i>o</i> -I	1·736	0·117	1·575	1·692	152—157	162—163
<i>m</i> -I	1·740	0·170	1·589	1·759	178—182	187—188
<i>p</i> -I	1·729	0·147	1·597	1·744	263—265	265

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