356. *A Quantitative Study of Homolytic Methylation of Some Monosubstituted Benzenes.*

By B. R. Cowley, R. O. C. Norman, and William A. Waters.

Di-*tert*.-butyl peroxide has been decomposed in hot solutions of chlorobenzene, bromobenzene, nitrobenzene, anisole, and benzonitrile. The products have been separated by distillation and the resulting mixtures of substituted toluenes analysed by vapour-phase chromatography and infrared spectroscopy.

The isomer ratios for methylation resemble, in general, those published for phenylation, but some consistent differences indicated that methyl are more nucleophilic than phenyl radicals.

Comprehensive researches by Hey and his colleagues and by workers in other countries have yielded quantitative information concerning isomer ratios and partial rate factors for the homolytic phenylation of monosubstituted benzenes.[1] Significant features are (i) the prevalence of a high proportion of *ortho*-substituted product, except when steric hindrance is a deterring factor, and (ii) a tendency for the *meta* : *para* ratio to fall below the statistical figure of two for all substituent groups. However, when substituted phenyl radicals are used in place of phenyl itself, the *meta* : *para* ratios change in a way that consistently indicates that free neutral radicals can exhibit dipolar character.[2]

Substantially the same conclusions concerning the dipolar character of free radicals have been reached from studies of free alkyl radicals produced by oxidations involving one-electron transfer.[3] Methyl should be nucleophilic rather than electrophilic since the tendency for electron loss (E_{-e}) by the transfer $\cdot CH_3 \longrightarrow (CH_3^+) + e$ is greater than that for electron gain (E_{+e}) by the process $e + \cdot CH_3 \longrightarrow (\colon CH_3^-)$.

The greater electronegativity of sp^2- than of sp^3-carbon suggests that the methyl radical might lose an electron somewhat more easily than the phenyl radical does, but the difference in electronegativities is small, and there should only be a slight difference between the dipolar characters of the two radicals. Direct comparison between the actions of free methyl and free phenyl radicals in aromatic substitution is thus theoretically important, but the reactivity of simple benzene derivatives with free methyl is so low that until recently the occurrence of nuclear methylation could only be deduced inferentially from the examination of other reaction products, *e.g.*, methylated diaryls produced from the decomposition of di-*tert*.-butyl peroxide in boiling chlorobenzene,[4] or the gaseous products resulting from decomposition of acetyl peroxide in solution in substituted benzenes.[5] However, new techniques (see below) have given reproducible isomer ratios (Table 1) for direct methylation of chlorobenzene, bromobenzene, nitrobenzene, anisole, and benzonitrile by methyl radicals generated by thermal decomposition of dilute solutions of di-*tert*.-butyl peroxide.

In these experiments the big excess of unchanged starting material was removed by slow fractional distillation, vapour-phase chromatography showing that no product was removed therein. Vapour-phase chromatography was also used for analysis of the products; *o*-, *m*-, and *p*-nitrotoluene were quantitatively resolved, with 2 : 4 : 7-trinitrofluorenone as the stationary phase;[6] in other cases the mixture of methylated isomers was separated from other products by collecting the fraction eluted from the column after the appropriate retention time and subjected to infrared analysis. Confirmatory experiments

---

[1] Augood and Williams, *Chem. Rev.*, 1957, **57**, 123.

[2] Dannley and Sternfeld, *J. Amer. Chem. Soc.*, 1954, **76**, 4543; DeTar and Kazimi, *ibid.*, 1955, **77**, 3842; Cadogan, Hey, and Williams, *J.*, 1955, 1425; Shih, Hey, and Williams, *J.*, 1958, 1885.

[3] Mackinnon and Waters, *J.*, 1953, 323.

[4] Beckwith and Waters, *J.*, 1957, 1665.

[5] Heilman, Rembaum, and Szwarc, *J.*, 1957, 1128.

[6] Norman, *Proc. Chem. Soc.*, 1958, 151.

showed that the mixture of isomers could be collected without preferential loss. Our results are in Table 1, with the data of Eliel *et al.*[7] for the methylation of toluene.

TABLE 1. *Percentages of* ortho-, meta-, *and* para-*isomers obtained by free-radical methylation.*

	Methyl derivative					Methyl derivative			
Compound	*ortho*	*meta*	*para*	Temp.	Compound	*ortho*	*meta*	*para*	Temp.
PhCl	64	25	11	130°	$PhNO_2$	65·5	6	28·5	143°
PhBr	67·5	23	9·5	145	PhCN	48	9	43	133
PhOMe	74	15	11	140	PhMe	56·5	26·5	17	110

Whilst all the methylations produced involatile polymeric material, *e.g.*, aryl coupling products, dimethylation was insignificant with the dilute solutions of di-*tert.*-butyl peroxide used. Anisole, however, yielded a small quantity of free phenol (Kharasch and Huang[8] have shown that many phenol ethers, though not anisole itself, can be dealkylated by free radicals at a much lower temperature than that of our experiments).

Benzonitrile has an unexpectedly high methyl affinity,[5] which is consistent with the occurrence of the addition of methyl radicals to the C≡N group; and phenyl-radical attack on the carbon atom of the cyano-group is known; but although products from the addition of methyl radicals to the cyano-group were searched for, none could be detected. With nitrobenzene, side reactions involving the nitro-group probably occur, since the reaction mixture rapidly darkens; this is not the case with the aryl halides.

Although total rate factors for methylation of benzene derivatives are available from work by Heilman *et al.*,[5] it is impossible to obtain accurate partial rate factors by combining these total rate factors with our isomer ratios, since the two sets of experiments were conducted at different temperatures and it is known that isomer ratios can change considerably over a 100° temperature range.[10] An attempt was made to establish a new scale of total rate factors by comparing the overall extent of methylation of chlorobenzene with that of benzene, but because of the low reactivity of benzene the molar ratio benzene : chlorobenzene had to be high to give sufficient reaction for quantitative measurement; this caused the reflux temperature to be too low for sufficient methylation to occur.

Differences between phenylation and methylation can be discussed in terms of isomer ratios. Table 2*A* lists percentages of *ortho*-substitution for both groups, and Table 2*B* lists *meta* : *para* ratios.

TABLE 2.

Compound	PhMe	PhCl	PhBr	PhOMe	$PhNO_2$	PhCN *
		(*A*) *Ortho* (%)				
Phenylation	71	62	49	67	62·5	60
Temp.	80°	80°	80°		80°	
Methylation	56·5	64	67·5	74	65·5	48
Temp.	110°	130°	145°	140°	143°	133°
		(*B*) *Meta* : *para* ratio				
Phenylation	1·32	1·71	1·91	1·20	0·36	0·33
Methylation	1·56	2·27	2·42	1·36	0·21	0·21

* Approximate values.

Substitution by both phenyl and methyl occurs predominantly in the *ortho*-position; the somewhat higher figures for methylation, especially with bromobenzene, possibly indicate slightly less steric hindrance to methylation than to phenylation. If so, however, the figures[7] for methylation of toluene at 110° are anomalous, for a higher *ortho* : *para* ratio would be expected.

A slight, but clear, polar difference between phenyl and methyl radicals is evident here.

---

[7] Eliel, Rabindran, and Wilen, *J. Org. Chem.*, 1957, **22**, 859.
[8] Kharasch and Huang, *ibid.*, 1952, **17**, 669.
[9] Hanby and Waters, *J.*, 1939, 1792.
[10] Cf. Kent and Norman, *J.*, 1959, 1724.

Considering substituents in groups according to their known directive actions in heterolytic electrophilic substitution, we can see that for *ortho-para*-directing substituents the *meta* : *para* ratio is invariably higher for homolytic methylation than for phenylation; whilst with the two substituents of opposite directive character, nitro and cyano, the *meta* : *para* ratio is lower for methylation than for phenylation. Now, *meta*-substitution of a compound such as toluene, and, still more, *para*-substitution of a compound such as nitrobenzene, is characteristic of nucleophilic substitution, *i.e.*, attack by a group which can donate electrons to the aromatic ring. Thus, in homolytic aromatic substitution the methyl radical shows the same tendency to electron loss that is exhibited by other alkyl radicals, and a greater tendency to such electron loss than is exhibited by the phenyl radical. It is possible, then, for homolytic aromatic substitution, to write an order of increasing electrophilicity, based on this and other work,[2] in which methyl can now be included, as follows: Me < Ph < C_6H_4Cl, $C_6H_4{\cdot}NO_2$.

EXPERIMENTAL

Reaction of Methyl Radicals with Chlorobenzene.—Di-*tert.*-butyl peroxide (13 g.) and purified chlorobenzene (100 ml.) were refluxed together for 72 hr. The temperature was kept near 130° by removing the *tert.*-butyl alcohol and acetone as formed. The remaining low-boiling products and most of the unchanged chlorobenzene (*ca.* 80 ml.) were removed through a fractionating column, and the residue fractionally distilled into fractions, (*a*) b. p. 40—42°/30 mm., (*b*) b. p. 50—70°/30 mm., (*c*) a tarry residue.

Fractions (*a*) and (*b*) were examined by vapour-phase chromatography on a column (450 cm. × 9 mm.) packed with I.C.I. E 301 silicone rubber (20 parts) coated on 30—40 mesh "Sil-o-cel" firebrick (80 parts). The column was operated at 170° at atmospheric pressure with a carrying stream of nitrogen (100 ml./min.), and the material eluted was detected with a conductivity cell. Fraction (*a*) gave one peak only, with a retention time of 19½ min., the same as that of chlorobenzene. Fraction (*b*) gave two peaks: one with a retention time of 19½ min. (chlorobenzene), the other, much weaker, with a retention time of 24 min. A mixture of equal parts of *o*-, *m*-, and *p*-chlorotoluene gave one peak only, with retention time 24 min.; no resolution of the three isomers was observed. Repeated injections of 0·1 ml. samples of fraction (*b*) coupled with collection of the chlorotoluene fraction yielded sufficient material for determination, by infrared spectroscopy, of the proportions of the three isomers present.

Reaction of Methyl Radicals with Bromobenzene.—Di-*tert.*-butyl peroxide (13 g.) and purified bromobenzene (100 ml.) were refluxed together for 32 hr., the temperature being kept at about 145° as above. The low-boiling products and about 75 ml. of unchanged bromobenzene were removed by fractionation, and the fraction of the residue boiling below 90°/13 mm. was examined by vapour-phase chromatography on the column described above, operated at 180° at atmospheric pressure with a carrying stream of nitrogen (30 ml./min.). Injection of a 0·03 ml. sample gave an intense peak with retention time 16 min. and a weaker peak with retention time 24 min., due respectively to bromobenzene and bromotoluenes, the bromotoluene peak not being resolved. A sample of the bromotoluenes was collected and analysed spectroscopically.

Reaction of Methyl Radicals with Anisole.—Di-*tert.*-butyl peroxide (13 g.) and purified anisole (100 ml.) were refluxed together for 40 hr., the temperature being kept at about 140° as above. The low-boiling products and about 75 ml. of the unchanged anisole were removed by fractionation, vapour-phase chromatography of the distillate showing that no methyl tolyl ethers were present. The fraction of the residue boiling below 200° was examined by vapour-phase chromatography on the column described above and in the conditions of the bromobenzene experiment. Injection of a 0·03 ml. sample gave an intense peak with retention time 17½ min. and a small peak with retention time 27 min., these being shown by comparison with authentic materials to be due respectively to anisole and the methyl tolyl ethers, these isomers not being resolved. A sample of the mixed methyl tolyl ethers was collected for analysis.

Injection of a larger (0·2 ml.) sample of the distillate gave a further small peak with retention time 22 min.; the material responsible for this peak was collected and was shown by its infrared spectrum to be phenol. The residue from a fractionated sample of the anisole used in these experiments was shown by vapour-phase chromatography not to contain phenol.

Spectroscopic Analysis.—Determinations were carried out with a Perkin-Elmer Recording infrared spectrophotometer (Model 21). Investigations in the 12—14 μ region for solutions of the pure chlorotoluenes, bromotoluenes, and methyl tolyl ethers in carbon disulphide (" AnalaR ") showed that of each of the three groups of compounds each isomer had a characteristic absorption band (see Table 3). The average molecular extinction coefficients were determined from the optical densities of a series of standard solutions. In a 1 mm. cell, solutions with concentrations 1—2 mg./ml. had optical densities suitable for analysis.

In the chlorotoluene mixture collected by vapour-phase chromatography of fraction (*b*) (above), the concentrations of the *ortho*- and *meta*-isomers were calculated by means of the Beer–Lambert law; the *para*-isomer concentration was deduced from a graph of the ratio of *ortho*- to *para*-chlorotoluene in a series of synthetic mixtures against the ratio of the optical densities of the mixtures at 13·41 and 12·45 mμ.

TABLE 3.

	λ (mμ)	Mol. extinction coeff.		λ (mμ)	Mol. extinction coeff.
o-Chlorotoluene	13·41	436 ± 3	*p*-Bromotoluene	12·51	344 ± 14
m-Chlorotoluene	12·98	263 ± 2	Methyl *o*-tolyl ether	13·38	370 ± 4
p-Chlorotoluene	12·45	372 ± 3	Methyl *m*-tolyl ether...	13·08	150 ± 6
o-Bromotoluene	13·45	412 ± 3 ...	Methyl *p*-tolyl ether...	12·26	212 ± 9
m-Bromotoluene	13·02	241 ± 9			

TABLE 4. *Isomer ratios obtained by spectroscopic analysis.*

Expt.	Chlorotoluenes (%)			Bromotoluenes (%)			Methyl tolyl ethers (%)		
no.	*o*-	*m*-	*p*-	*o*-	*m*-	*p*-	*o*-	*m*-	*p*-
1	62·7	26·1	11·2	68·3	21·9	9·8	74·7	14·7	10·6
2	65·0	23·4	11·6	66·8	23·8	9·4	73·3	15·3	11·4
3	63·8	25·6	10·6						
Average	63·8	25·0	11·1	67·55	22·85	9·6	74·0	15·0	11·0

The relative concentrations of isomers in the bromotoluene and methyl tolyl ether mixtures were calculated by means of the Beer–Lambert law. For details see Table 4.

Synthetic mixtures were analysed before and after collection by vapour-phase chromatography. Results (Table 5) confirmed that the collection technique was quantitative within experimental error of the analytical procedure.

TABLE 5. *Isomer ratios of synthetic mixtures before and after vapour-phase chromatography.*

	Chlorotoluenes (%)			Bromotoluenes (%)			Methyl tolyl ethers (%)		
	o-	*m*-	*p*-	*o*-	*m*-	*p*-	*o*-	*m*-	*p*-
Before collection	62·5	22·0	15·5	67·0	21·9	11·1	74·7	14·8	10·5
After collection	63·0	22·5	14·5	69·5	19·2	11·3	75·7	13·5	10·8
Composition of synthetic mixture (by wt.)				67·9	21·7	10·4	74·6	15·2	10·2

Reaction of Methyl Radicals with Nitrobenzene.—Di-*tert.*-butyl peroxide (13 g.), purified nitrobenzene (90 ml.), and benzene (10 ml.) were refluxed together for 30 hr., the temperature being kept at about 143° as above. All material boiling below 120°/12 mm. was removed through a fractionating column; vapour-phase chromatography showed that this fraction contained no nitrotoluenes. The residue was examined by vapour-phase chromatography on a column (760 cm. × 8 mm.) packed with a mixture of 2 : 4 : 7-trinitrofluorenone (20 parts) and 30—50 mesh " Sil-o-cel " firebrick (97½ parts). The column was operated at 200° at slightly reduced pressure with a carrying stream of nitrogen (30 ml./min.). Injection of a sample of the residue into the column gave four peaks, one intense with retention time 40 min. and three smaller peaks with retention times 49½, 60½, and 72 min. These were shown to be due to nitrobenzene and *o*-, *m*-, and *p*-nitrotoluene respectively. The relation between peak area and quantity of material was determined for the nitrotoluenes by injecting standardised mixtures of the isomers under the conditions of temperature, pressure, and flow-rate used for analysis of the product. Two determinations of the isomer ratios in the reaction product were then made, in two different sets of conditions:

Expt. no.	Column temp.	Flow rate (ml./min.)	Inlet pressure (mm.)	Outlet pressure (mm.)
1	190°	37	627	284
2	180°	33	575	250

The isomer ratios, expressed as percentages are:

	Nitrotoluenes		
Expt. no.	*o*-	*m*-	*p*-
1	64·3	6·4	29·2
2	66·5	5·8	27·7
Average	65·4	6·1	28·45

Reaction of Methyl Radicals with Benzonitrile.—Di-*tert.*-butyl peroxide (13 g.), purified benzonitrile (90 ml.), and benzene (10 ml.) were refluxed together for 48 hr., the temperature being kept at about 133° as above. After being heated with dilute hydrochloric acid for 3 min., 1 ml. of the mixture gave a negative test with 2 : 4-dinitrophenylhydrazine. All material boiling below 100° was removed, and the residue was fractionated, unchanged benzonitrile (containing no tolunitriles) distilling at 95°/17 mm. The residue was examined by vapour-phase chromatography in the column described above for the nitrobenzene experiments, operated at 190° at atmospheric pressure with a carrying stream of nitrogen (90 ml./min.). It gave an intense peak with retention time 34 min., a large peak with retention time 41 min., and two small peaks with retention times 53 and 57½ min. These were shown by comparison to be due to benzonitrile and *o*-, *m*-, and *p*-tolunitrile respectively. The peaks due to *m*- and *p*-tolunitrile were not completely resolved; and reduction of the column temperature to 183° gave no marked improvement. The quantity–area relations for the tolunitrile peaks were established as for nitrotoluene, and two determinations of the product composition were made with a column temperature of 183°, flow rate 90 ml./min., inlet pressure 1153 mm., and outlet pressure 756 mm. The isomer ratios found are expressed as percentages:

	Tolunitriles		
Expt. no.	*o*-	*m*-	*p*-
1	48·4	6·0	45·6
2	47·7	11·9	40·4
Average	48	9	43

Because of the unsatisfactory resolution of *m*- and *p*-tolunitrile, their relative concentrations could not be determined with accuracy and the figures given are approximate only.

Reaction of Methyl Radicals with a Mixture of Benzene and Chlorobenzene.—Di-*tert.*-butyl peroxide (13 g.), benzene (50 ml.), and chlorobenzene (50 ml.) were refluxed together for 160 hr., the temperature remaining at 93—97° and no acetone distilling. All material boiling below 100°/25 mm. was collected and examined by vapour-phase chromatography in the column packed with silicone rubber on firebrick described above, operated at 200°. The distillate gave large peaks corresponding to chlorobenzene and benzene, a very small peak due to chlorotoluenes, peaks due to low-boiling materials presumably formed by the decomposition of unchanged peroxide at the high temperature of the column, but no peak corresponding to toluene.

We are indebted to Messrs. A. E. Thompson and F. L. Hastings for assistance in the vapour-phase chromatography.

THE DYSON PERRINS LABORATORY OXFORD. [*Received, October 23rd*, 1958.]