732. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part XIV.*[1] *Rates and Products of Chlorination of Methyl-substituted Biphenyls in Acetic Acid.*

By P. B. D. de la Mare, D. Muriel Hall, Margaret M. Harris,
M. Hassan, E. A. Johnson, and N. V. Klassen.

The rates of chlorination, and the ratio of chlorine consumed to hydrogen chloride liberated, have been examined for a number of methyl-substituted biphenyls. For most of these, the isomeric proportions of products of monosubstitution have been determined by vapour-phase chromatography. The reactivities are compared with predictions based on the additivity of substituent effects. The results bear on the transmission of substituent effects through the biaryl system, and on the extent to which substituents in the 2-position in the biphenyl nucleus can sterically inhibit conjugation.

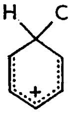
Aromatic chlorination in acetic acid has a simple kinetic form, $-\mathrm{d}[\mathrm{Cl_2}]/\mathrm{d}t = k_2[\mathrm{ArH}][\mathrm{Cl_2}]$, as has been established for many systems of widely different structures and reactivities.[2-4] It is a heterolytic process, being faster in polar solvents and in the presence of added electrolytes.[3] The effects of added electrolytes establish [5,6] that the electrophile is molecular chlorine.

It has generally been accepted that these reactions are processes of substitution in the aromatic nucleus, and that (in the absence of certain recognisable structural complications [7,8]) the effects of substituents on the rate are independent and additive. This has been the basis of discussions of the rates of these reactions made by a number of groups of workers; [2,4,8] they include theoretical discussions [9-11] of the degree to which the transition states for these reactions approximate to the form indicated in the annexed formula (I).

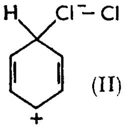
---

[1] Part XIII, de la Mare and Hilton, *J.*, 1962, 997.
[2] Orton and Bradfield, *J.*, 1927, 986; Bradfield and Jones, *Trans. Faraday Soc.*, 1941, **37**, 726.
[3] de la Mare and Robertson, *J.*, 1943, 279.
[4] H. C. Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 5175; 1959, **81**, 5615, 5621.
[5] Robertson, Dixon, Goodwin, McDonald, and Scaife, *J.*, 1949, 294.
[6] Robertson, *J.*, 1954, 1267.
[7] de la Mare and Hassan, *J.*, 1958, 1579.
[8] de la Mare and Ridd, "Aromatic Substitution—Nitration and Halogenation," Butterworths Scientific Publns., London, 1959.
[9] Dewar and Mole, *J.*, 1957, 342.
[10] R. D. Brown, *J.*, 1959, 2224, 2232.
[11] Mason, *J.*, 1959, 1233.

With recognised limitations [7,8] it appears to be possible to treat the effects of alkyl, alkoxyl, and acetamido-groups on these lines to a reasonable approximation. Interest arises, therefore, particularly for the theoretical reasons mentioned in Part X,[12] in applying the same principles to substitution in biphenyl and its derivatives. Our studies of the products of some of the reactions, reported in previous papers in this series,[1,12] have revealed complications, in that the reaction path does not always lead entirely to simple products of substitution, and probably [13] involves an intermediate (*e.g.*, II) of more complicated structure than (I). This reduces the usefulness of detailed discussion of the rates of formation of minor products of substitution in these compounds, since one cannot determine whether the diversion to other side-reactions occurs at the expense equally of the intermediates leading to substitution at each of the available positions. However, survey of the relative reactivities, and of the major products of substitution where these are known, has revealed trends which we regard as theoretically and practically significant. The following discussion, which in general accords with our preliminary accounts,[14,15] supersedes these in detail.



(I)



(II)

EXPERIMENTAL

Some of the materials and experimental methods have been described elsewhere.[1,7,12] The following methylbiphenyls were prepared by Gomberg's method: 2-methylbiphenyl (Found: C, 92·7; H, 7·8. Calc. for $C_{13}H_{12}$: C, 92·9; H, 7·1%); 3-methylbiphenyl, n_D^{25} 1·6007; 4-methylbiphenyl, m. p. 46·8°. They were purified by chromatography on silica gel or alumina, and characterised by their infrared spectra. Vapour-phase chromatography showed that our specimen of 2-methylbiphenyl contained a small amount (*ca.* 2%) of biphenyl, so a purer sample was also investigated; the results were almost identical. The following compounds were prepared by Ullmann's method: 2,2′-dimethylbiphenyl, m. p. 19·5°, b. p. 258°/760 mm.; 4,4′-dimethylbiphenyl, m. p. 121°; 3,4,3′,4′-tetramethylbiphenyl, m. p. 76° (for this compound we are indebted to Professor E. E. Turner, F.R.S.). 3,3′-Dimethylbiphenyl, m. p. 9°, b. p. 286°/760 mm., was prepared by deaminating 4,4′-diamino-3,3′-dimethylbiphenyl, itself prepared from *o*-nitrotoluene by reduction to the hydrazo-compound followed by rearrangement. 2,6-Dimethylbiphenyl, prepared as described elsewhere,[16] had m. p. −5°, n_D^{20} 1·5752, and was uniform on vapour-phase chromatography.

3-Chloro-2,2′-dimethylbiphenyl was prepared from *o*-iodotoluene and 2-chloro-6-iodotoluene (itself obtained from 3-chloro-*o*-toluidine) by the Ullmann procedure. It was isolated by vapour-phase chromatography. The 4- and 5-chloro-2,2′-dimethylbiphenyls were prepared similarly from *o*-iodotoluene and the appropriate chloro-2-iodotoluene; they were identified and characterised similarly.

Mixed Ullmann procedures were used to prepare 3-, 4-, 5-, and 4′-chloro-2-methylbiphenyl. Appropriate fractions were isolated by vapour-phase chromatography. Their identities were confirmed by the fact that their ultraviolet spectra were almost the same as those of the corresponding dimethylbiphenyls. Their infrared spectra are recorded in Table 1.

The chloro-3-methylbiphenyls and chloro-3,3′-dimethylbiphenyls were all obtained by mixed Ullmann procedures, from a chloro-3-iodotoluene and either iodobenzene or *m*-iodotoluene. The mixed iodo-compounds (0·5—1 g.) were heated under a vacuum at 250—270°

---

[12] Beaven, de la Mare, Hassan, Johnson, and Klassen, *J.*, 1961, 2749.

[13] de la Mare and Klassen, *Chem. and Ind.*, 1960, 498; de la Mare, Klassen, and Koenigsberger, *J.*, 1961, 5285.

[14] de la Mare, Hall, Harris, and Hassan, *Chem. and Ind.*, 1958, 1086.

[15] de la Mare, "Theoretical Organic Chemistry," Kekulé Symposium, Butterworths Scientific Publns., London, 1959, p. 219.

[16] Johnson, *J.*, 1957, 4155.

TABLE 1.

Infrared absorption bands (cm.$^{-1}$; range, 640—1610 cm.$^{-1}$) of some chloro-2-methylbiphenyls.

3-Chloro-		4-Chloro-		5-Chloro-		4′-Chloro-	
648m	1147w	668vw	1124m	649m		667w	1124w
				668w			1160w
701s		701s	1176sh	701s	1172w	694w	1176w
714m	1195w	717w	1193m	714w		727s	
759s	1258w	764s		731m	1250w	742s	1279w
782sh					1285w	758s	
788m	1379w	770s	1377w		1389m		1385m
		821s	1393w	812s		807w	1395m
845w	1425s			835s		833s	
	1449s	871s	1443s	884m	1443m	866w	1453m
916w	1493w	915w	1477vs	917w	1481s	942w	1479s
989m	1538w	994m		990w			1493sh
1001m	1558m	1009s		1000w	1558w	1009s	
	1592w		1587w	1018m		1020m	
1027m		1029w	1595m	1041w	1592m	1033w	1598w
1050s			1608m			1052w	
1073w		1073m		1074w			
		1099s		1096s		1091s	

with copper bronze (2 g.). The products were complex, but the principal peak in the vapour-phase chromatogram was in each case readily identified and a quantity of the corresponding material sufficient for determination of the necessary spectra was collected. The necessary iodo-compounds were obtained as follows. *m*-Iodotoluene was prepared from *m*-toluidine which had been purified through its acetyl derivative. 2-Chloro-3-iodotoluene was obtained from 2-chloro-3-nitrotoluene as described by Cohen and Dakin.[17] 2-Chloro-5-iodotoluene was obtained through *N*-acetyl-3-chloro-*p*-toluidine, *N*-acetyl-5-chloro-2-nitro-*p*-toluidine, and 2-chloro-5-nitrotoluene. 4-Chloro-3-iodotoluene was derived through the sequence *N*-acetyl-5-chloro-*o*-toluidine, *N*-acetyl-5-chloro-4-nitro-*o*-toluidine, and 4-chloro-3-nitrotoluene. Most of the products were liquids at room temperature; but 4-chloro-3-methylbiphenyl had m. p. 37°, and 4,4′-dichloro-3,3′-dimethylbiphenyl, which was obtained as a by-product from the Ullmann reactions involving 5-iodo-2-chlorotoluene, had m. p. 58°; similarly were obtained 3,3′-dichloro-2,2′-, m. p. 75°, and 2,2′-dichloro-3,3′-dimethylbiphenyl, m. p. 113°.

2′-Chloro-3-methylbiphenyl * was obtained from *m*-toluidine and chlorobenzene by the modified Gomberg procedure described by Hwang.[18] The 3′- and the 4′-chloro-isomer were removed easily by vapour-phase chromatography, but although their retention volumes were slightly different they could not be obtained pure by using the columns available to us. The retention volumes of the various fractions are recorded in later Tables. Infrared absorption spectra of some of these derivatives of 3-methylbiphenyl and of 3,3′-dimethylbiphenyl are given in Tables 2 and 3.

3-Chloro-4-methylbiphenyl, m. p. 33°, was prepared from 3-chloro-*p*-toluidine and benzene by the modified Gomberg procedure described by Hwang.[18] 2′-Chloro-4-methylbiphenyl was prepared similarly from *p*-toluidine and chlorobenzene, the reaction mixture being heated at 100° on a steam-bath; the isomers were removed by vapour-phase chromatography. 4′-Chloro-4-methylbiphenyl, m. p. 125° (lit.,[19] 122°) was obtained by the mixed Ullmann procedure, followed by vapour-phase chromatography, the appropriate fraction being isolated. 3′-Chloro-4-methylbiphenyl was obtained only as a mixture with 4′-chloro-4-methylbiphenyl from the modified Gomberg reaction used to prepare 2′-chloro-4-methylbiphenyl; vapour-phase chromatography under the conditions that we were able to adopt for isolation of the fractions only partly resolves the 3′- from the 4′-chloro-isomer. 2-Chloro-4-methylbiphenyl was also only obtained as a mixture with the 2′-chloro-compound, since the appropriate fraction from vapour-phase

---

* For convenience of discussion we retain unprimed numerals for positional locants of the methyl group in monomethylbiphenyls throughout this paper, in spite of any requirements of systematic nomenclature to the contrary.

[17] Cohen and Dakin, *J.*, 1901, 1127.

[18] Hwang, *Acta Chim. Sinica*, 1959, **33**, 171.

[19] Gomberg and Pernert, *J. Amer. Chem. Soc.*, 1926, **48**, 1379.

chromatography of the product of chlorination of 4-methylbiphenyl contains both isomers. The infrared spectra of these materials are recorded in Table 4. Those of 3-chloro-, 2′-chloro-,

TABLE 2.

Infrared absorption bands (cm.$^{-1}$; range, 630—1660 cm.$^{-1}$) of some chloro-3,3′-dimethylbiphenyls.

2-Chloro-		4-Chloro-		6-Chloro-	
645m	1046s	685m	1066m	629m	1083s
701s	1095w	706w	1095vw	637m	1095m
724m	1117w		1139vw	700s	1138m
731m	1168w		1167vw	720w	1164w
774s	1385sh	781s	1379m	784s	1208w
786sh	1401m	806w	1449sh	809s	1250w
812m	1439sh	822m	1456sh		1379m
883w	1449s	840m	1466s	880m	1464s
901w	1460s	903vw		909vw	1475sh
968vw	1587s	998vw	1575w	1000vw	
1013vw	1605m	1043s	1608m	1031s	1597m

TABLE 3.

Infrared absorption bands (cm.$^{-1}$; range, 630—1660 cm.$^{-1}$) of some chloro-3-methylbiphenyls.

2-Chloro-		4-Chloro- *		6-Chloro-		2′-Chloro-		3′- + 4′-Chloro-	
617w	1119m						1124w	617w	
640m				637w				662sh	1136w
	1155w		1147vw		1140m			668sh	
	1172w					674w	1163vw	678sh	1167w
696s		694m		696s	1190vw	699s		690s	1190w
725m	1245w	715w				721w	1247w	709w	
					1255vw	735m		738w	1258w
756s		760s		763s		752s		753s	1290w
785s	1379m		1379nj			787s	1374vw	775vs	1375sh
		820m		811s	1389m			830s	1397s
861w	1404s					856vw	1418sh	859m	
897vw	1441s	883m		884w		883vw	1431m	877s	1439sh
914w			1460nj	914vw		905vw	1466s	905sh	1460sh
966vw	1493w				1471s	943vw		971w	1471s
					1475sh	1000vw		1000m	
1002w				1020m				1013ms	1504sh
1029m		1046m		1034m		1034s	1563w	1038m	1550sh
1045s		1064m					1587w	1056m	1570s
1073m	1582m	1075sh, w †		1075sh	1595w	1075m		1081s	1587s
1081w				1085s		1093vw	1608w	1095s	

* Mulls in Nujol. † See text (p. 3790).

TABLE 4.

Infrared absorption bands (cm.$^{-1}$; range, 650—1600 cm.$^{-1}$) of the chloro-4-methylbiphenyls.

2-Chloro- *		3-Chloro- †		2′-Chloro-		3′-Chloro- *	4′-Chloro- †	
684m	*ca.* 1072m	687sh	1073w	662m		687m		1086m
698s		694s						1094m
707sh					1109w			1101vw
717w		720m		729s	1122m		720m	
			1151w	733sh	1155vw		735m	1163w
		758s		752vs	1181w	760m		
	1208w		1258w		1206vw	777s		
	1253w	821m	1294w	817vs	1244w	815ms	805s	1307w
		841m	1372nj		1403m		840m	
863m		877m	1449nj	862w	1429m	880m		1374nj
910w			1471m	939w	1466s			1449nj
ca. 995m		995w		1003m	1511w		1000m	
		1020w	1538m	1033s	1563w	1035m	1012w	
		1052s	1600m	1070m	1587w		1036w	

* Principal bands, derived from spectra of mixtures; see text. † Mulls in Nujol.

and 4′-chloro-4-methylbiphenyl are complete spectra of specimens that we believe to be essentially pure. Those of 2-chloro- and of 3′-chloro-4-methylbiphenyl are the principal bands which we consider can be unambiguously identified in the spectrum of the appropriate mixture by comparison of the spectrum of this with the spectrum of the other component. The intensities assigned to these bands may in some cases have been under-estimated.

m-Xylene was prepared by deamination of 2,6-dimethylaniline, which itself had been purified through its acetyl derivative. It was carefully dried and fractionated; it had b. p. 138·5°/760 mm., n_D^{20} 1·4971. Its rate of chlorination (k_2 = 16·3 l. mole^{-1} min.$^{-1}$) agrees satisfactorily with the value given by Brown and Stock[4] (k_2 = 17·1 l. mole^{-1} min.$^{-1}$). The rates of chlorination were determined by conventional methods, described in earlier papers.[3,7] Correction was made, where necessary, for loss of chlorine by volatility. For a number of the compounds, the ratio of hydrogen chloride produced to chlorine consumed was also estimated in separate experiments, as described elsewhere.[12,13] The values, given in Table 5, refer to concentrations of chlorine (*ca.* 0·015M) similar to those used in the rate measurements, and generally to concentrations of aromatic compound five times greater than that of chlorine; no significant difference was observed with change in the ratio of concentrations of reactants over quite a wide range.

TABLE 5.

Rates of chlorination, percentage of hydrogen chloride liberated, and oxygen-content of product, in acetic acid at 25°.

Compound (ArH)	$\frac{[HCl] \text{ produced}}{[Cl_2] \text{ consumed}}$ (%)	k_2 (l. mole^{-1} min.$^{-1}$) (mean)	$k_{re.}$ (PhH = 1)	O : 2Cl (atoms in crude product) *
Biphenyl	82·5	0·0383	426	0·04
2-Methylbiphenyl	85	0·019	224	0·15
3-Methylbiphenyl	96	5·0	55,600	0·17
4-Methylbiphenyl	82	0·18	2000	0·06
2,2′-Dimethylbiphenyl	87	0·0263	292	0·10
3,3′-Dimethylbiphenyl	97	15·8	176,000	0·14
4,4′-Dimethylbiphenyl	72	0·42	4670	0·04
2,6-Dimethylbiphenyl	102	6·8	75,600	N.D.‡
3,4,3′,4′-Tetramethylbiphenyl	N.D.	116	1,290,000	N.D.
m-Xylene (cf. ref. 4)	N.D.	16·3	180,000	N.D.
Toluene (cf. refs. 4,7)	94	0·0324	360	N.D.
Benzene (cf. refs. 4,7)	N.D.	0·000090 †	1	N.D.
Anisole	100	~750	~8,300,000	N.D.

N.D. = not determined. * Blank determinations made on biphenyl suggest that these figures should all be reduced by *ca.* 0·03. † Corrected for the (solvent) effect of concn. of ArH on rate (cf. refs. 5, 7). ‡ HCl liberated from organic product on alkaline hydrolysis, 26%.

The O : 2Cl ratio in the crude reaction product, isolated as described elsewhere,[12] is also given in Table 5; these values are from analyses by A. Bernhardt.

Vapour-phase Chromatography of Chlorinated Alkylbiphenyls.—The methods have been described elsewhere.[12] Products were isolated in the usual way, care being taken to avoid decomposition during the working-up.

In general, 2- or 6-monochloro-derivatives of any particular hydrocarbon were readily separable from derivatives of the same hydrocarbon substituted elsewhere, with packed columns involving almost any stationary phase. The separation from each other of isomers substituted in the 3-, 4-, and 5-position was not so easy; it was not always possible to achieve resolution adequate for analytical purposes, even with the use of efficient capillary columns, though in some cases (*e.g.*, 3- and 4-chlorobiphenyl[12]) a stationary phase was discovered on which separation could be effected by using a packed column. Some help in identification was gained in certain instances by estimating the electron-capture density of effluent fractions from the capillary column by a suitable detector in series with an argon or photoionisation detector.[20] Although definite (and, in some cases, characteristic) differences in electron affinity exist between position isomers of the monochloro-derivatives of the methyl- and dimethyl-biphenyls, the difference in this respect between the mono- and di-chloro-derivatives of these compounds,

---

[20] Lovelock and Lipsky, *J. Amer. Chem. Soc.*, 1960, **82**, 431; Lovelock, *Nature*, 1961, **189**, 729.

or between the corresponding dichloro- and trichloro-derivatives, appears to be much greater, in fact of a different order (Lovelock, personal communication).

Products from Chlorination.—(*a*) 2,2′-*Dimethylbiphenyl.* Chromatography on a packed column showed that very little of the 6-chloro-derivative was formed in the chlorination. The peak which presumably contained the 3-, 4-, and 5-isomers was not resolved on any stationary phase used. A mixture of the 4- and 5-chloro-compounds prepared as described above proved to be partially separable on a packed Apiezon column, and by running appropriate mixtures it also became clear that there was relatively little of the 4-isomer in the chlorination product.

TABLE 6.

Monochloro-derivatives from chlorination of 2,2′-dimethylbiphenyl.

2,2′-Dimethylbiphenyl	V_R (biphenyl = 1)	Proportion * (%)
3-Chloro-	2·40	56
4-Chloro-	2·55	5
5-Chloro-	2·35	37
6-Chloro-	1·85	2

* Infrared analysis was not used for these mixtures, and the estimated proportions are therefore somewhat less certain than for the other compounds.

The principal products were therefore the 3- and the 5-chloro-derivative. On an efficient capillary column the band was in fact partly resolved into two very closely spaced peaks of fairly similar intensity; in such quantities these could not be other than the 3- and the 5-chloro-derivative, and the electron-capture responses were of the order expected. The vicinal effect, though known to be weak in mixed chloromethylbiphenyls, would probably result in the 3-isomer's being a little less volatile than the 5-, and measurements of retention volumes supported the view that the first of the two peaks was the 5-isomer. The 4-isomer was also resolved sufficiently well on the capillary column to enable an estimate of its amount to be made. Small amounts of the dichloro-derivatives * were detected on the capillary column, but this column also showed that the parent hydrocarbon could not have been quite pure. The observed retention volumes (V_R; biphenyl = 1), and proportions in the product of monochlorination as determined from the ratios obtained by vapour-phase chromatographic analysis, are given in Table 6.

(*b*) 3,3′-*Dimethylbiphenyl.*—The vapour-phase chromatogram obtained by using a packed column showed two major and two minor peaks, and the capillary column did not give any further resolution. The first major peak represented the 2- and the 6-chloro-compounds; the corresponding material was isolated, and had an ultraviolet spectrum ($\lambda_{max.}$ 245 mμ with a relatively shallow minimum at 233 mμ) and an infrared spectrum in agreement with this. Its composition could be estimated by comparison with the spectra of synthetic mixtures, in respect particularly of the shape of the two pairs of peaks at 1046 and 1031 and at 774 and 784 cm.$^{-1}$, respectively. On this basis the chlorination gives only very slightly more 6- than 2-chloro-isomer; we have adopted the ratio 2-Cl : 6-Cl = 48 : 52 for the present discussion.

The second major peak is that of the 4-chloro-isomer; the isolated fraction had an infrared spectrum almost identical with that of synthetic 4-chloro-3,3′-dimethylbiphenyl, with the exception of a very weak band at 1202 and a weak band at 1695 cm.$^{-1}$. Both these were absent from spectra of the synthetic material, and the position of the latter band suggests the possibility that a trace of some oxygen-containing material was present in this fraction. The amount was reduced by heating the product with alkali under reflux before subjecting it to vapour-phase chromatography. It was preceded closely by a very minor component in the position expected for the 5-chloro-derivative, but the ultraviolet spectrum of the isolated fraction ($\lambda_{max.}$ 241 mμ, $\lambda_{min.}$ 225 mμ) rules out this possibility and shows also that this material is not any other chloro-derivative of 3,3′-dimethylbiphenyl which could conceivably have this retention time. The last component observed (*ca.* 5%) agrees in retention time (V_R 7·95) and spectrum ($\lambda_{max.}$ 248 mμ; relatively shallow minimum at 234 mμ) with either 2,4′- or 4,6′-dichloro-3,3′-dimethylbiphenyl. Doubtless a little of the 4,4′-dichloro-derivative is formed, but its quantity must be small. The observed relative retention volumes and ratios of the monochloro-derivatives are given in Table 7.

---

* 4,4′-Dichloro-2,2′-dimethylbiphenyl, V_R = 6·35; 5,5′-dichloro-2,2′-dimethylbiphenyl, V_R = 5·50; 1—2% of the product of chlorination.

TABLE 7.

Monochloro-derivatives from chlorination of 3,3′-dimethylbiphenyl.

3,3′-Dimethylbiphenyl	$V_{\rm R}$ (biphenyl = 1)	Proportion (%)
2-Chloro-	3·45	18
4-Chloro-	5·80	62
6-Chloro-	3·50	20

(*c*) 4,4′-*Dimethylbiphenyl.* This gave two monochloro-derivatives as expected, with no evidence of any complications; the results are in Table 8.

TABLE 8.

Monochloro-derivatives from chlorination of 4,4′-dimethylbiphenyl.

4,4′-Dimethylbiphenyl	$V_{\rm R}$ (biphenyl = 1)	Proportion (%)
2-Chloro-	4·05	78
3-Chloro-	6·2	22

(*d*) 2-*Methylbiphenyl.* This gave ~6% of the 6- and 4% of the 2′-chloro-derivative, identified through their relatively low retention times. The main peak was clearly multiple, so the appropriate fraction was isolated, and its infrared spectrum was compared with those of 3-, 4-, 5-, and 4′-chloro-2-methylbiphenyl, and of appropriate mixtures of these substances. The isolated fraction contained no peaks which could not be found in the spectra of one or other of the isomers. The 3-, 4-, and 4′-isomers had characteristic absorption bands, respectively, at 1050, 821, and 742 cm.$^{-1}$, by which the presence of these compounds could be recognised individually. The relative intensities of these and other absorption bands were used to estimate the relative proportions of isomers present, and the estimates were checked by determining the spectra of mixtures of known composition. The results are given in Table 9.

TABLE 9.

Monochloro-derivatives from chlorination of 2-methylbiphenyl.

2-Methylbiphenyl	$V_{\rm R}$ (biphenyl = 1)	Proportion (%)
3-Chloro-	2·30	26
4-Chloro-	2·40	18
5-Chloro-	2·35	30
6-Chloro-	1·75	6
2′-Chloro-	1·65	4
4′-Chloro-	2·35	16

(*e*) 3-*Methylbiphenyl.* Gas-chromatography of the product of chlorination of this compound showed two peaks. The isolated material, which from its retention volume (2·35) should have contained only 2- and 6-chloro-3-methylbiphenyl, had an infrared absorption spectrum consistent with this; and by comparison of this spectrum with those of synthetic mixtures of the components, it is concluded that the product of chlorination contained 2- and 6-chloro-3-methylbiphenyl in the proportion 45 : 55.

The other fraction isolated by gas-chromatography from the product of chlorination of 3-methylbiphenyl was crystalline, but had a low m. p. (*ca.* 25°). It had a retention volume (3·7) which accorded with the view that it contained no substituent in the 2- or 2′-position. Its spectrum was identical with that of synthetic 4-chloro-3-methylbiphenyl, m. p. 37°. It is interesting that for this material a very weak peak at 1075 cm.$^{-1}$ (little more than an inflexion for a Nujol mull) became a peak of medium intensity when the spectrum was determined as a crystalline film from a melt between rock-salt plates.

We did not formally prove that 5- and 3′-chloro-3-methylbiphenyl were absent from the products of these chlorinations; but it is unlikely that any substitution occurred in these positions, each of which is *meta* to an aryl group. We found that 3′- and 4′-chloro-3-methylbiphenyl were only partially separable by gas-chromatography, but the synthetic material (which was a mixture of these) was very rich in strong absorption bands, many of which were absent from the spectra of the products of chlorination. The 3′- and the 4′-isomer would, from the retention volume of the mixture, have appeared in the chlorination product along with the 4-chloro-isomer; but this fraction from the chlorination from its spectrum and m. p.

actually contained only the 4-chloro-3-methylbiphenyl; so the 3′- and the 4′-isomer were absent from the product of chlorination. The absence of the 4′-isomer establishes the absence of the 2′-isomer, since it is most unlikely that one would have been formed without the other. This is consistent with the infrared spectra; there was no sign, in the spectrum of the product of chlorination, of the bands at 674, 735, 1124, and 1608 cm.$^{-1}$ characteristic of 2′-chloro-3-methylbiphenyl.

Some 4,*x*-dichloro-3-methylbiphenyl ($x = 2$, 6, or 2′; about 5% of the total product) seemed also to be present. The proportions of monochloro-derivatives are given in Table 10.

TABLE 10.

Monochloro-derivatives from chlorination of 3-methylbiphenyl.

3-Methylbiphenyl	V_R (biphenyl = 1)	Proportion (%)
2-Chloro-	2·35	17
4-Chloro-	3·70	62
6-Chloro-	2·30	21
2′-Chloro-	2·20	Not detected
3′-Chloro-	3·50	Not detected
4′-Chloro-	3·60	Not detected

(*f*) 4-*Methylbiphenyl.* For the product of chlorination of this compound, the vapour-phase chromatogram showed three peaks. One was in the position expected for the 2- and the 2′-chloro-derivative, and its shape indicated that both isomers were present. The infrared spectrum of the isolated material corresponding with this peak showed the presence of both isomers, with no unexpected absorption bands. The 2′-isomer was clearly present in larger amount and we judge that the ratio of 2′- to 2-chloro-4-methylbiphenyl is about 2 : 1. This figure is adopted in the Discussion, but the consequent uncertainty in the derived percentages is probably about ±5 units %.

The material corresponding to the other peaks was collected as a single fraction. Its infrared spectrum was that of a mixture of the 3- and 4′-chloro-4-methylbiphenyl, with the latter isomer in considerable preponderance.* It was estimated from the vapour-phase chromatogram, and was consistent with the infrared spectrum, that the ratio, 4′- to 3-chloro-4-methylbiphenyl, was 10 : 1. On this basis, the product of chlorination has the composition shown in Table 11.

TABLE 11.

Monochloro-derivatives from chlorination of 4-methylbiphenyl.

4-Methylbiphenyl	V_R (biphenyl = 1)	Proportion (%)
2-Chloro-	2·50	15
2′-Chloro-	2·55	30
3-Chloro-	3·85	5
4′-Chloro-	4·0	50

(*g*) 2,6-*Dimethylbiphenyl.* The product of chlorination of 2,6-dimethylbiphenyl gave a single peak ($V_R = 2{\cdot}70$; biphenyl, 1·00; 2,6-dimethylbiphenyl, 1·09) in the gas-chromatogram. The recovered material, which is presumed (see Discussion) to be 3-chloro-2,6-dimethylbiphenyl, had an infrared spectrum with absorption bands at 637m, 700vs, 763s, 806s, 927w, 988m, 1000m, 1021m, 1052s, 1068m, 1144m, 1202w, 1235w, 1374m, 1435s, 1449sh, 1458sh, 1582w cm.$^{-1}$.

DISCUSSION

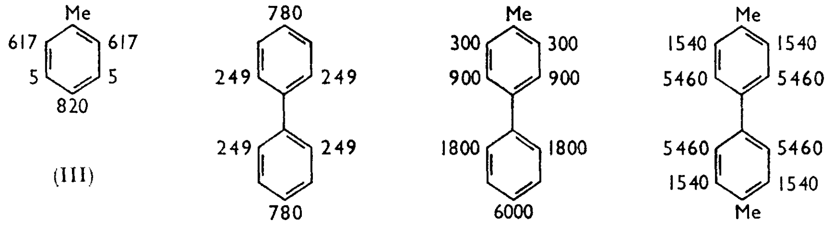
The relative reactivities, and the orientations insofar as they have been determined, for the chlorination of the alkylbiphenyls that have been examined, can be interpreted qualitatively in a fairly simple fashion. In the following discussion it will, in the first instance, be assumed that the side-reactions of addition can be neglected, and that the estimated proportions of monochloro-derivatives represent the proportions of attack on the corresponding positions by molecular chlorine. Since for biphenyl itself these side-reactions account for some 10% of the biphenyl used up,[12] this assumption is not one that

---

* No indication of the presence of the 3′-isomer was detected; for example, the characteristic strong absorption band at 777 cm.$^{-1}$ was absent from all the fractions collected from the chromatogram of the chlorination product.

can be justified rigorously, but it enables us to survey the reactions and look for generalisations and anomalies, and to apply in a semiquantitative way the additivity principle,[8] the best theory currently available for analysing the cumulative effects of substituents on the rate of aromatic chlorination.

(*a*) 4-*Methylbiphenyl and* 4,4′-*Dimethylbiphenyl.*—The following are relative rates, and partial rate factors (*f*) calculated on the basis of the assumptions discussed above, for toluene (III),[4] for biphenyl (IV),[7] and for the 4-methyl-substituted biphenyls (V) and (VI).



Compound:	(III)	(IV)	(V)	(VI)
Relative rate: (PhH = 1)	360	426	2000	4670

As would be expected, the 4-methyl group in 4-methylbiphenyl activates the positions within its own ring. By comparison of the value for the 3-position ($f = 300$) with that for the 2-position in toluene ($f = 617$), it can be estimated that the phenyl group reduces the reactivity of positions *meta* to it by a factor of 0·5. A value of 0·7 was deduced similarly from the relative rates and orientation of chlorination of acetanilide and 4-acetamidobiphenyl.[7]

The influence of the methyl group on the 2-position ($f = 900$), when compared with the partial rate factor for 2-chlorination of biphenyl (249) gives a further measure of the activating power of a *meta*-methyl group, *viz.*, $f = 3·6$. The direct value for this quantity [4] is 5·0. There is some uncertainty, as has already been noted, in the isomer ratios for 4-methylbiphenyl, but it seems that to a fair approximation the additivity principle [8] is applicable to these compounds.

Activation of the nuclear positions by the methyl group extends beyond its own ring; in 4-methylbiphenyl the 2′- and 6′-positions are further activated by factors of more than 6. The rate-enhancing effect of a methyl group in the *ortho*- or *para*-position in toluene is in the range 600—800; so the effect of interposing an aryl group seems to be to reduce considerably the transmission of the effect of the substituent (*i.e.*, by a factor of $\log_{10} 600/\log_{10} 6 = 2·8/0·8 =$ *ca.* 3, when calculated as a ratio of free energies of activation). This result accords qualitatively with what is known concerning the diminution in effectiveness of other substituents in such circumstances. Thus, for chlorination it has been estimated that a nitro-group deactivates *ortho*- and *para*-positions by a factor of more than 10^4, whereas *p*-nitrobiphenyl reacts with chlorine some 2×10^2 less rapidly than does biphenyl.[8,21] Similarly, on the scale for which the reaction constant, ρ, for the effects of substituents on the logarithm of the dissociation-constant ratio for substituted benzoic acids is 1, that for biphenyl-4-carboxylic acids [22] is 0·35, a result which indicates a reduction in transmission by a factor of 2·7 in free-energy terms.

Substitution in 4,4′-dimethylbiphenyl is also more rapid than in biphenyl. It will be noted, however, that the extra activation is not confined to the position conjugated with the methyl group through the Ar–Ar bond; the 2-position in 4,4′-dimethylbiphenyl ($f = 5460$) is more reactive than that in 4-methylbiphenyl ($f = 900$), but the same is true

[21] Hartman and Robertson, *J.*, 1945, 891.

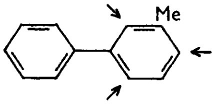
[22] Berliner and Blommers, *J. Amer. Chem. Soc.*, 1951, **73**, 2479; Berliner, Newman, and Riaboff, *ibid.*, 1955, **77**, 478.

for the corresponding 3-positions ($f = 1540$ and 300, respectively). This suggests that the extra activation involves a general increase in polarisability of the system, rather than a specific activation of a hyperconjugative nature.

The orientation in 4,4′-dimethylbiphenyl is similar to that reported for nitration;[23] mainly the 2-isomer is produced. It is interesting that, in terms of the additivity principle, the orientation in this compound can be said to be controlled essentially by the relative *meta*-orientating power (not by the *ortho*, *para*-orientating power) of the groups, for the methyl and phenyl substituents have similar activating powers for the *ortho*-position, but for the *meta*-position the methyl group is activating and the phenyl group is deactivating, so substitution occurs *meta* rather than *ortho* to the methyl group (*i.e.*, *ortho* rather than *meta* to the aryl group). This type of analysis reveals the theoretical and practical difficulties in determining relative directing power of two substituents from orientation obtained by putting two substituents in competition within one and the same molecule.

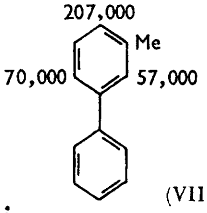
(*b*) 3-*Methylbiphenyl*, 3,3′-*Dimethylbiphenyl*, *and* 3,4,3′,4′-*Tetramethylbiphenyl*.—These compounds, with methyl groups in the 3-positions, are more reactive than the corresponding 4-alkylbiphenyls, for in the former compounds there are positions (cf. formula VII) activated both by *o*(or *p*)-aryl substituents and by *p*(or *o*)-alkyl groups. The vapour-phase chromatograms, supplemented by infrared analysis, confirm that, as would be expected, substitution is predominantly in the 2-, 4-, and 6-position. The results are given as partial rate factors in formulæ (VIII) and (IX).*

If in 3-methylbiphenyl the methyl group ($f_o = 617$) and the phenyl group ($f_p = 780$) were contributing independently and additively to the free energy of activation, the partial rate factor for 4-substitution should be 480,000. The experimental value (206,800) is somewhat less, and indicates that the additivity principle does not hold exactly in this system. The slightly enhanced value for 3,3′-dimethylbiphenyl indicates that the extra methyl group produces a slight increase in polarisability in the adjacent ring.

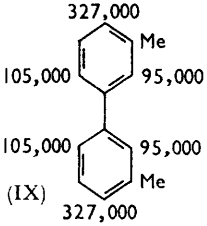


(VII)

Compound:



(VIII)



(IX)

Relative rate: (PhH = 1) 55,600 176,000

3,4,3′,4′-Tetramethylbiphenyl is still more reactive, and would be expected to be substituted in the 2- and the 6-position. The orientation of chlorination has not been determined.

(*c*) 2-*Methylbiphenyl and* 2,2′-*Dimethylbiphenyl*.—Qualitatively, steric effects being neglected, 2-methyl-substituted biphenyls should have reactivities of similar magnitude to those of the corresponding 4-methylbiphenyls. The 2-methyl group must, however, make rotation about the Ar–Ar bond less easy than in biphenyl itself, and must therefore substantially modify the potential conjugation between the aryl groups.

The results indicate that the resulting steric inhibition of conjugation has a remarkable effect both on the rate and on the orientation of chlorination. 2-Methylbiphenyl (X) and 2,2′-dimethylbiphenyl (XI) are both less reactive than biphenyl, whereas the corresponding 4-substituted compounds are considerably more reactive. Further, analogy with the 4-substituted compounds would in the absence of special steric effects lead to the prediction

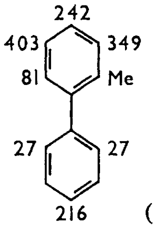
---

* Here, as elsewhere, for positions for which the partial rate factor is not given, these values are considered (see Experimental) to be small relative to values for other positions in the same molecule.

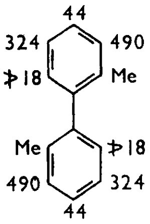
[23] Marler and Turner, *J.*, 1932, 2391.

that chlorination should occur predominantly *ortho* and *para* to the aryl groups. In fact, substitution occurs mainly *ortho* and *para* to the methyl groups.

Compound:



(X)



(XI)

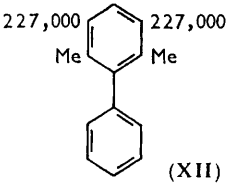
Relative rate: (PhH = 1) 224 292

Partial rate factors calculated from the orientational data with the assumptions already noted are shown in formulæ (X) and (XI). Comparison with toluene (III) shows that the positions *ortho* and *para* to methyl groups (and hence *meta* to an aryl group) are diminished in reactivity only slightly; the effect of the alkyl groups in promoting reactivity is to a large degree maintained in these compounds. The positions *ortho* and *para* to the aryl groups are, however, much diminished in reactivity, whether these positions are in the same ring as the 2-methyl group or not. Clearly the power of the aryl group to promote reactivity is much reduced by the 2-methyl group, and the reduction is greater in 2,2′-dimethylbiphenyl than in 2-methylbiphenyl, as is consistent with the deductions made by Suzuki[24] from ultraviolet spectral data; he concluded that the interplanar angle in 2-methylbiphenyl is 60°, and in 2,2′-dimethylbiphenyl is 70°. We interpret the change in rate of chlorination, and the consequent change in orientation, as resulting from steric inhibition of conjugation; the 2-methyl groups prevent the aryl group from contributing to the reactivity, through their electron-releasing ($+E$) effects, to the extent that similar aryl groups are able to do so in the absence of blocking 2-substituents.

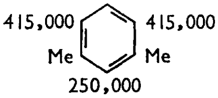
(*d*) 2,6-*Dimethylbiphenyl*.—In 2,6-dimethylbiphenyl (XII), the 3-position is activated by two alkyl groups situated *ortho* and *para* to it; the 4-position is activated by *m*-alkyl groups and only a single *p*-phenyl substituent, itself inhibited sterically from exercising its full activating power; and the 2′- and the 4′-position should be even less activated. So it is to be expected that substitution would occur substantially in the 3-position. Vapour-phase chromatography of the product of chlorination gave only a single peak in the molecular-weight region for a monochloro-derivative, of retention volume (2·70) according with the value expected for a 3-chloro-2,6-dimethylbiphenyl. There was no sign of material of smaller retention volume, as would be expected if 2′-chloro-2,6-dimethylbiphenyl were present. So we attribute the whole of the reactivity of 2,6-dimethylbiphenyl to 3-substitution.

We now have three separate estimates of the reactivity determined by a *m*-phenyl group: (i) from the comparison[7] of 4-acetamidobiphenyl with acetanilide ($f = 0{\cdot}7$);

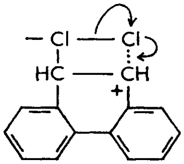
Compound:



(XII)



(XIII)



(XIV)

Relative rate: (PhH = 1) 75,600 180,000

(ii) from comparison of 4-methylbiphenyl with toluene ($f = 0{\cdot}5$, see above); and (iii) from comparison of 2,6-dimethylbiphenyl with *m*-xylene by using our rate measurements and

---

[24] Suzuki, *Bull. Chem. Soc. Japan*, 1959, **32**, 1340, 1350, 1357.

Brown and Stock's orientational data[4] ($f = 0{\cdot}55$; formulæ XII and XIII). It seems from these comparisons that inhibition of conjugation by adjacent methyl groups has little influence on the effect of a phenyl group in influencing substitution at the *meta*-position.

(*e*) *Ratios of Substitution in the* 2- *and the* 4-*Position.*—Substitution *ortho* to an aryl group seems uniformly to be less than the corresponding *para*-substitution. Table 12 shows the ratios for the compounds that we have studied.

TABLE 12.

Ratios of rates of chlorination *ortho* and *para* to aryl groups.

Biphenyl	Positions	Partial rate factors	Rate-ratio
2,2′-Dimethyl-	6 : 4	18 : 44	0·4
2-Methyl-	2′ : 4′	27 : 216	0·12
	6 : 4	81 : 242	0·33
Unsubstd.	2 : 4	249 : 780	0·32
4-Methyl-	2′ : 4′	1800 : 6000	0·30
3-Methyl-	2 : 4	57,000 : 207,000	0·28
	6 : 4	70,000 : 207,000	0·34
3,3′-Dimethyl-	2 : 4	95,000 : 327,000	0·29
	6 : 4	105,000 : 327,000	0·32

There is little indication that the ratio is seriously modified by primary steric effects; for example, in 3-methyl- and 3,3′-dimethyl-biphenyl, chlorine attacks the 2-position, between an aryl and a methyl group, nearly as easily as it attacks the apparently more accessible 6-position. The rather low value for attack on the 2′-position in 2-methylbiphenyl may, however, be an indication that attack of chlorine on such positions is inhibited; the result for 2,2′-dimethylbiphenyl does not bear on this point, since it is only an upper limit for a product formed in very small proportion.

(*f*) *Addition Accompanying Substitution.*—It is difficult to assess to what extent the incursion of addition affects the relative rates of chlorination. At least two quite widely different viewpoints could be taken. The first is to treat additions as reactions which proceed independently of the substitutions and involve different intermediates and transition states. In these circumstances the rate-coefficients for the substitutions can be obtained directly from the product-ratios and measured rates. In the cases we are discussing in this paper, where substitution in all cases predominates over addition, the derived rates of the substitution reactions would be different from those quoted by quite small factors (of less than two). The qualitative discussion would be affected so little that the accompanying addition could essentially be regarded as irrelevant; and the rate coefficients deduced from the product ratios for the formation of minor components of substitution could usefully be interpreted.

If, on the other hand, we take the view which has been derived from detailed examination of addition of chlorine to phenanthrene (cf. ref. 12) and is implicit in the description of the reaction given (1):

$$\mathrm{ArH} + \mathrm{Cl_2} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ArH{,}Cl_2} \xrightarrow{k'} \left\{ \begin{array}{l} \mathrm{ArHCl^+ + Cl^-} \\ \mathrm{ArHCl_2} \\ \text{etc.} \end{array} \right. \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

that addition products are formed by diversion of a common intermediate, ArH,Cl_2, a somewhat different situation arises. The observed rate-coefficient, k_2^{obs}, is then a composite quantity given by the equation, $k_2^{\mathrm{obs}} = k_1k'/k_{-1}$. Structural effects in a general way might well influence the ratio k_1/k_{-1} and k' in similar directions; but k' would also be influenced by any forces within the molecule which assisted partial ionisation of the second chlorine atom (*e.g.*, those indicated in formula XIV).

We have not elucidated the details of the processes leading to addition for the compounds studied in this work. It would appear at first sight (Table 6) that the more reactive compounds (*e.g.*, 3-methyl-, 3,3′-dimethyl-, and 2,6-dimethyl-biphenyl) gave more substitution and less addition, since they all give hydrogen chloride in amount nearly equivalent to the chlorine consumed. This, however, is not the whole story; for all these compounds give appreciable amounts of acetoxychloride adducts, as is shown for the first two by the high ratio of oxygen to chlorine in the crude product of addition, and for the last by the fact that chloride was liberated from the organic product when it was heated with alkali. It seems that addition is a feature of the reactions of all these derivatives of biphenyl, independent of the reactivity.

We are greatly indebted to Mr. S. French for technical assistance, and to Mrs. R. Koenigsberger for determining many infrared spectra.

CHEMISTRY DEPARTMENT, BEDFORD COLLEGE,
REGENT'S PARK, LONDON, N.W.1.
WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE LONDON, GOWER STREET, W.C.1.
MEDICAL RESEARCH COUNCIL, HOLLY HILL, LONDON, N.W.3.

[*Received, March* 19*th*, 1962.]