Electrophilic Aromatic Substitution. Part XVII.[1] Protiodetritiation of Some Cycloalkyl- and Secondary Alkyl-benzenes. A Linear Free Energy Relationship for *ortho*-Aromatic Substitution

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From the measured rates of protiodetritiation of some cycloalkyl- and secondary alkyl-benzenes (RPh) by trifluoroacetic acid at 70°, partial rate factors for *ortho*- and *para*-substitution have been determined as follows: (R =) cyclobutyl, 455, 1 070; cyclopentyl, 473, 1 195; cyclohexyl, 406, 886; 1-methylethyl, 223, 544; 1-methylpropyl, 244, 690; 1-ethylpropyl, 196, 682; 1-ethylbutyl, 217, 685. With the exception of the last two compounds, each alkylbenzene gives a constant log f_o : log f_p ratio of 0.865 ± 0.025 as do a large number of other aromatic compounds in hydrogen exchange; this ratio is precisely predicted by the charge distribution in the Wheland intermediate. This correlation permits the first assignment of meaningful σ^+_{ortho} substituent constants for application to electrophilic substitutions of these compounds (but not their analogous side-chain reactions). Exchange at the *ortho*-positions of 1-ethylbutyl- and 1-ethylpropyl-benzene may be slightly hindered; exchange in these compounds was also accompanied by an intermolecular surface-catalysed migration of the alkyl group which may be sterically accelerated. Reasons for the greater electron-supplying abilities of the cyclic substituents relative to their open chain analogues and for the greater electron-supplying ability of these and other bulky substituents in hydrogen exchange compared with side-chain solvolyses, are discussed; the greater activation by the cyclopentyl substituent relative to the other cycloalkyl groups (excluding cyclopropyl) may be due to steric enhancement of hyperconjugation, and this phenomenon is proposed to account for the very high reactivity of acenaphthene in electrophilic substitution.

THE electronic effects of cycloalkyl groups in general have received relatively little attention compared with other common substituents. The principal data (which are concerned largely with the cyclopropyl substituent) are summarised in terms of σ values in Table 1; these show a large measure of consistency, particularly with regard to the high polarizability of the cyclopropyl group.

The reactivity of cycloalkylbenzenes have been studied even less in electrophilic substitution, the only data available referring to nitration. These show that the cyclopropyl group is more reactive than the cyclobutyl or isopropyl groups [2] and gives a very high *ortho* : *para* substitution ratio (especially with nitric acid in acetic anhydride) values of 2.5—4.8 at 10—25°,[3,4] 4:0—4.7 at −40 to −50°[5,6] being obtained. (Ketcham *et al.*[6] showed that this high ratio was considerably diminished by using acetyl nitrate prepared at low temperatures.) This high ratio has also been confirmed by Baas and Wepster [7] who found that the *para*-partial rate factors for the cycloalkylbenzenes (PhR) were in the order: (R =) cyclopropyl > cyclopentyl > cyclohexyl > cyclobutyl > (isopropyl).

With the intention of examining this order further and also to evaluate the cause of the high *ortho* : *para*-substitution ratio for cyclopropylbenzenes we initiated our investigation of the rate of hydrogen exchange of some secondary alkyl- and cycloalkyl-benzenes. Unfortunately, because of the instability of cyclopropylbenzene in trifluoroacetic acid this part of our original objective could not be realised. However, during the progress of

[1] Part XVI, R. Taylor, *J.C.S. Perkin II*, 1975, 1287.
[2] Yu. S. Shabarov, N. A. Donskaya, L. D. Sychkova. and R. Ya. Levina, *Vestnik. Moskov. Univ., Ser. II, Khim.*, 1966, **20**(5), 73 (*Chem. Abs.*, 1966, **64**, 4890).
[3] R. C. Hahn, T. F. Corbin, and H. Shechter, *J. Amer. Chem. Soc.*, 1968, **90**, 3404.
[4] L. M. Stock and P. E. Young, *J. Amer. Chem. Soc.*, 1972, **94**, 4247.
[5] Yu. S. Shabarov, V. K. Potapov, and R. Ya. Levina, *J. Gen. Chem.* (*U.S.S.R.*), 1964, **34**, 2865.
[6] R. Ketcham, R. Cavestri, and D. Jambotkar, *J. Org. Chem.*, 1963, **28**, 2139.
[7] J. M. A. Baas and B. M. Wepster, *Rec. Trav. chim.*, 1972, **95**, 285.

this work an important feature of hydrogen exchange came to light relating to a linear free energy correlation between *ortho*- and *para*-substitution,[8] and the present data provide further evidence for this correlation.

TABLE 1

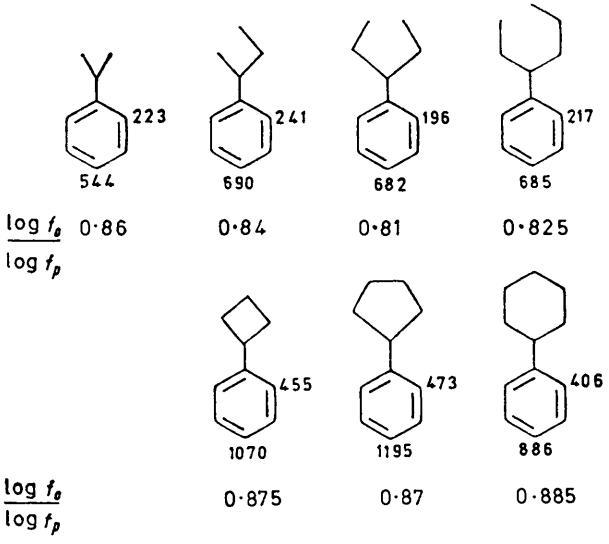
σ Values for *p*-cycloalkyl substituents

Substituent	σ_I	σ_R	σ_p	σ_p^+
Cyclopropyl	−0.08 [a]	−0.13 [a]	−0.21 [a]	−0.41 [b]
	−0.06 [c]	−0.153 [c]	−0.213 [c]	−0.44 [d]
	+0.01 [e]		−0.19,	−0.48 [g]
			−0.24 [f]	
			−0.21 [h]	−0.54 [i]
			−0.217 [j]	−0.462 [j]
Cyclobutyl			−0.188 [j]	−0.290 [j]
Cyclopentyl			−0.196 [j]	−0.303 [j]
Cyclohexyl	−0.067 [k]		−0.196 [j]	−0.285 [j]

[a] R. G. Pews, *J. Amer. Chem. Soc.*, 1967, **89**, 5605. [b] L. B. Jones and V. K. Jones, *Tetrahedron Letters*, 1966, 1493. [c] O. A. Yuzhakova, V. F. Bystrov, and R. G. Kostyanovskii, *Bull. Acad. Sci., U.S.S.R.*, 1966, 218. [d] L. B. Jones and V. K. Jones, *Tetrahedron Letters*, 1968, 1431. [e] B. R. Ree and R. C. Martin, *J. Amer. Chem. Soc.*, 1970, **92**, 1660; [f] R. Levina, P. A. Ghimbitskii, L. P. Guseva, and P. K. Agasya, *J. Gen. Chem. (U.S.S.R.)*, 1964, **34**, 144. [g] H. C. Brown and J. D. Cleveland, *J. Amer. Chem. Soc.*, 1966, **88**, 2051. [h] J. Smejkal, J. Jones, and J. Farkas, *Coll. Czech. Chem. Comm.*, 1964, **29**, 2950, [i] R. S. Brown and T. G. Traylor, *J. Amer. Chem. Soc.*, 1973, **95**, 8025. [j] Ref. 3. [k] L. S. Levitt and B. W. Levitt, *Tetrahedron*, 1973, **29**, 941.

RESULTS AND DISCUSSION

Rate coefficients for the exchange are given in Table 2, and the derived partial rate factors together with $\log f_o$: $\log f_p$ values displayed in Scheme 1.



SCHEME 1 Partial rate factors for protiodetritiation in CF_3CO_2H at 70°

A number of features emerge from these results. (i) The cycloalkyl groups activate in the order cyclopentyl > cyclobutyl > cyclohexyl, and σ_p^+ values of −0.346, −0.352, and −0.338 respectively, may be derived. This activation order is exactly the same as observed in the solvolysis (Table 1), though an important difference is that in the solvolysis these groups are *less* activating than *p*-methyl (*i.e.* in the ' hyperconjugative ' order) whereas in hydrogen exchange they are more activating than *p*-methyl (*i.e.* in the inductive order). This result parallels the relative reactivity orders for *p*-methyl and *p*-t-butyl groups in solvolysis [9] and in hydrogen exchange in trifluoroacetic acid.[10] It is becoming increasingly clear that the solvolysis reaction produces diminished σ values (*i.e.* more positive values) for bulky groups *e.g.* tertiary alkyl and cycloalkyl, as described here, and also for the $SiMe_3$ group.[11] Since the bulky groups produce their biggest activating effect under poorly solvating conditions *i.e.* hydrogen exchange in trifluoroacetic acid, or in gas-phase eliminations, there can now be little doubt that the ' hyperconjugative ' order observed in the solvolysis is not due to hyperconjugation at all, but rather to steric hindrance to solvation [12] which is sufficiently severe in the solvolysis for even the *m*-alkyl groups to activate in this ' hyperconjugative ' order.[9]

TABLE 2

Rate coefficients for detritiation of $[^3H]C_6H_4R$ in trifluoroacetic acid at 70°

R	$10^7k/s^{-1}$	R	$10^7k/s^{-1}$
o-1-Ethylbutyl	20.6	*o*-Cyclohexyl	38.5
p-1-Ethylbutyl	65.2	*p*-Cyclohexyl	84.1
o-1-Ethylpropyl	18.6	*o*-Cyclopentyl	45.0
p-1-Ethylpropyl	64.7	*p*-Cyclopentyl	113.5
o-1-Methylpropyl	22.9	*o*-Cyclobutyl	43.2
p-1-Methylpropyl	65.6	*p*-Cyclobutyl	101.4
o-1-Methylethyl	21.2		
p-1-Methylethyl	51.7		

The above observations clearly have wide implications with regard to the concept of hyperconjugation and which we hope to discuss at a later time along with even more conclusive results which we have obtained in the gas phase. Our view is that evidence for hyperconjugation as a mode of electron release is now sufficiently widespread and unambiguous for the concept not to be in doubt. (One need for example look no further than the large differences in σ and σ^+ for the *p*-methyl substituent). Ironically however, it now appears very probable that the reversal of the inductive order of electron release by alkyl groups which led Baker and Nathan to propose the concept of hyperconjugation [13] was due to this electronic effect at all but to a solvent effect. The assumption over many years, that the concept of hyperconjugation and the most acceptable alternative which would lead to the same observable, namely steric hindrance to solvation, were mutually exclusive can now be recognized as being both unnecessary and a decisive factor in causing the arguments relating to hyperconjugation to have been so protracted.

[8] H. V. Ansell, J. Le Guen, and R. Taylor, *Tetrahedron Letters*, 1973, 13.

[9] H. C. Brown, J. D. Brady, M. Grayson, and W. H. Bonner, *J. Amer. Chem. Soc.*, 1957, **79**, 1899.

[10] R. O. C. Norman and R. Taylor, ' Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965, pp. 208—209.

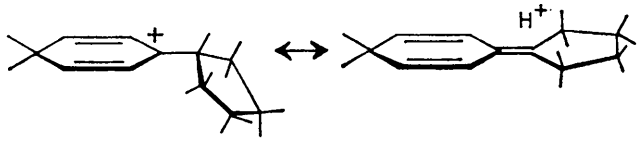
[11] E. Glyde and R. Taylor, *J.C.S. Perkin II*, 1973, 1632.

[12] W. A. Sweeney and W. M. Schubert, *J. Amer. Chem. Soc.*, 1954, **76**, 4625.

[13] J. W. Baker and W. S. Nathan, *J. Chem. Soc.*, 1935, 1844.

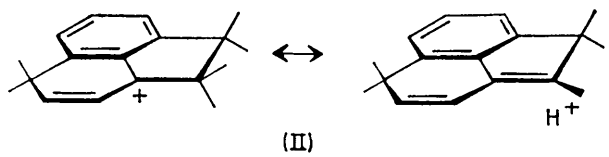
(ii) The greater activation by the cyclopentyl group is also confirmed in nitration, though the order for the cyclohexyl and cyclobutyl group is reversed. This latter is however not outside the experimental error for nitration [7] which is necessarily larger than in hydrogen exchange.

A possible explanation for the greater activation by the cyclopentyl group lies in the eclipsed conformation of the C–H bonds. (This is true also in the cyclobutyl substituent but because of the strain in the ring the eclipsed hydrogens are further apart so the strain due to eclipsing should be less severe). Interaction between the adjacent hydrogens could cause elongation of the C–H bonds and consequent inductive delocalization. In addition (and probably more significantly) the hydrogen attached to C–1 in the cycloalkyl ring will be encouraged to form the hyperconjugative structure (I). One of us



(I)

recently proposed the concept of ' steric enhancement of hyperconjugation ' to account for the apparently high electron release when C–H bonds are forced to lie in a favourable conformation relative to the aromatic ring.[14] The present example is therefore a second manifestation of the phenomenon in which relief of strain in the substituent encourages hyperconjugation, and we believe that this latter may be a very significant factor contributing to the very high reactivity of the *ortho*- and *para*-positions (*i.e.* substituent conjugated positions) in acenaphthene. (For an account of this high reactivity see ref. 14.) In acenaphthene not only are there *two* eclipsed C–H bonds adjacent to *each* ring, but removal of one hydrogen to form the hyperconjugative structure (II)

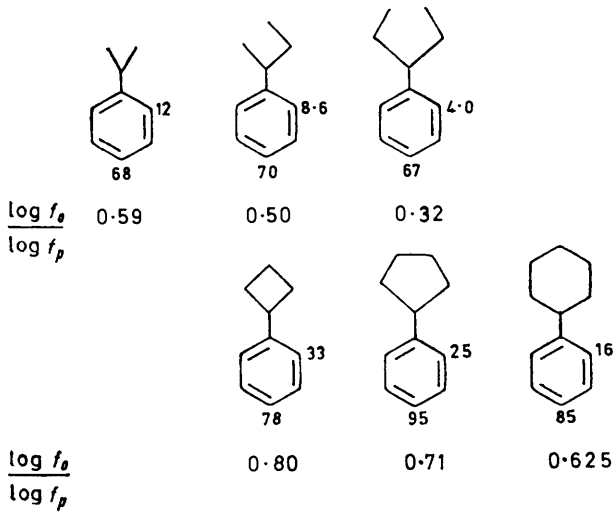


(II)

also disposes of the eclipsing of the other hydrogen bound to the same carbon.

(iii) The cycloalkyl groups are all more electron-supplying than the analogous open-chain substituents. We have previously drawn attention to some indications that this might prove to be the case [15] (from data relating to the reactivity of indane, tetralin, and their open-chain analogues).*

The greater activation by the cycloalkyl groups confirms similar indications from some recent work on nitration, the partial ratio factors for which are shown in Scheme 2. Since the cyclohexyl substituent (where steric enhancement of hyperconjugation does not apply) is still *ca.* 30% more reactive towards exchange at the *para*-position than its open-chain analogue, some additional factors must operate. No obvious explanation for this comes to mind save that in the cycloalkyl compounds the most remote C–H bonds have two paths for transmission of the inductive effect to the aromatic ring. The log f_o : log f_p values are, with the exception of 1-ethylpropyl- and 1-ethylbutyl-benzene, a constant value of 0.865 ± 0.025. This extends the range of substituents



SCHEME 2 Partial rate factors for nitration of some alkylbenzenes [7]

which give this value in detritiation in anhydrous trifluoroacetic acid to more than twenty and the available data are given in Table 3. The data cover more than three orders of magnitude in reactivity and a range of substituent types. It seems very relevant therefore that this ratio is predicted from analysis of the charge distribution in the Wheland intermediate, and we have previously argued that it should be given by any substituent which has inductive and conjugative effects acting in concert, or a dominant conjugative effect; [8] values close to that predicted were obtained for the OMe, Me, NO_2, SO_3^-, and CO_2H substituents in a number of reactions believed to have fairly minimal steric requirements.[8]

On the basis of this correlation it appears feasible to propose a realistic set of σ^+_{ortho} values (= 0.87 σ^+_{para}) which are assembled in Table 3. We stress that these values will only be relevant for those reactions in which steric hindrance is minimal, and for electrophilic substitution only; values derived from side-chain reactions do not apply to electrophilic substitution and *vice versa*.[16]

* This may be an additional factor which produces the greater ability of tetrahydrofuran (relative to diethyl ether) to solvate organometallic reagents.

[14] H. V. Ansell and R. Taylor, *Tetrahedron Letters*, 1971, 4515.
[15] R. Taylor, *J. Chem. Soc.* (*B*), 1968, 1559.
[16] R. Taylor, *J. Chem. Soc.* (*B*), 1971, 1450.

Our values do mean that one can calculate the maximum theoretical *ortho*-yield in any given substitution.

It seems probable that exchange in 1-ethylpropyl- and 1-ethylbutyl-benzene is slightly hindered (though one can not be absolutely certain because of the larger error in the rate coefficients for these compounds). It is therefore relevant that the alkyl side chain in these compounds can more closely approach the *ortho*-position than can the substituent in t-butylbenzene (which is not hindered in exchange at the *ortho*-position, this being the only electrophilic substitution in which this is true). By contrast, in the corresponding cycloalkyl compounds this approach is prevented and no steric hindrance is evident from the increasing initial concentration of the aromatic compound.

These results suggested to us that a surface-catalysed side reaction is taking place since the more aromatic compound used the greater the proportion of reaction which can take place independent of the sites on the glass, and the less the importance of the differing numbers of sites available in different samples. Further experiments indicated that less scatter was obtained if the ampoules (soda glass) were washed with distilled water prior to use rather than if they were washed with either chromic acid or alcoholic potash followed by washing with distilled water.

TABLE 3

Values of $\log f_o/\log f_p$ and σ^+_{ortho} for substitution in ArR

R	$\log f_o/\log f_p$	σ^+_{ortho}	R	$\log f_o/\log f_p$	σ^+_{ortho}
Me [a]	0.88	−0.27	1,3-Me_2 [f]	0.885	
Bu^t [a]	0.875	−0.28 [b]	1,2,4-Me_3 [f]	0.895	
CH_2Ph [c]	0.81	−0.19	Ph	0.88 [g]	−0.155 [h]
$(CH_2)_2Ph$	0.87 [d]	−0.23	(Fluorenyl) [i]	0.885	−0.43
OMe [c]	0.92	−0.67	(9,10-DHP) [j]	0.88 [k]	−0.23
SMe [c]	0.88	−0.515	Pr^i	0.86	−0.27
OPh [c]	0.885	−0.455	1-Methylpropyl	0.84	−0.275
SPh [c]	0.88	−0.405	Cyclobutyl	0.875	−0.305
CH_2SiMe_3 [c]	0.81	−0.45	Cyclopentyl	0.87	−0.305
$[CH_2]_2SiMe_3$ [c]	0.91	−0.30	Cyclohexyl	0.885	−0.30
$[CH_2]_3SiMe_3$ [c]	0.88	−0.28			
$[CH_2]_4SiMe_3$ [c]	0.86	−0.28			

[a] Ref. 10. [b] For reaction giving the Baker–Nathan order a value of −0.225 is more appropriate. [c] F. P. Bailey and R. Taylor, *J. Chem. Soc.* (*B*), 1971, 1446. [d] Given as −0.83 in ref. 8 owing to a typographical error. [e] C. Eaborn, T. A. Emokpae, V. I. Sidorov, and R. Taylor, *J.C.S. Perkin II*, 1974, 1454. [f] R. Taylor, 'Specialist Periodical Report, Aromatic and Heteroaromatic Chemistry,' The Chemical Society, 1974, vol. 2, p. 226. [g] This supercedes an earlier less accurate value of −0.90 given in ref. 8 (Y. F. El-Din Shafig, unpublished result). [h] Assuming the standard *para*-value of −0.179 applies; in some reactions of high demand for resonance where a higher *para*-value is needed (*e.g.* −0.24 in hydrogen exchange, R. Baker, C. Eaborn, and R. Taylor. *J.C.S. Perkin II*, 1972, 97) a higher *ortho*-value would be appropriate *e.g.* −0.225 in hydrogen exchange. [i] At the 2- and 4-position (K. C. C. Bancroft, R. W. Bott, and C. Eaborn, *J. Chem. Soc.*, 1964, 4806). [j] Unpublished result for 9,10-dihydrophenanthrene by H. V. Ansell. [k] At the 1- and 3-positions.

$\log f_o : \log f_p$ ratios. The difference in hindrance between the two sets of compounds is more clearly shown by the data for nitration (a more hindered reaction) given in Scheme 2. If exchange at the *ortho*-positions of 1-ethylpropyl- and 1-ethylbutyl-benzene is hindered it is evidently very slight and these data provide only the third example of hindrance to exchange.[17]

A Surface-catalysed Side Reaction in Detritiation of 1-*Ethylpropyl- and* 1-*Ethylbutyl*-[2-^{3}H]- *and* -[4-^{3}H]-*benzene.* Preliminary kinetic runs to measure the rates of detritiation of these compounds in trifluoroacetic acid at 70° were carried out at the customary low concentration of aromatic compound (*ca.* 5 mg of substrate to 10 ml of acid) but these showed very considerable scatter and moreover the exchange appeared essentially to cease after *ca.* 50% of the initial activity had been lost. Further experiments showed that (a) the amount of scatter decreased if large amounts of aromatic compound were used and (b) the amount of reaction that could be followed before exchange ceased increased with

The effective cessation of exchange which we observed shows that the aromatic compound is being converted to another compound in which exchange is very slow. Two possible side reactions may produce this. (i) Intramolecular rearrangement of s-alkyl[2- or 4-^{3}H] benzene to give a mixture of s-alkyl[2-, 3-, and 4-^{3}H]benzenes, *via* migration of either tritium or the alkyl group. However, this process should go on indefinitely, so the observed detritiation would not effectively cease, in contrast to the experimental observation. (ii) Intermolecular rearrangement of the labelled s-alkylbenzenes to give tritiated benzene and a mixture of *meta*- and *para*-di-s-alkylbenzenes, some of which will be labelled and randomly so. (Formation of the *ortho*-isomers is highly unlikely because of steric hindrance). This is a much more attractive possibility than (i) since here the reverse reaction is not required to take place at the same rate as the initial rearrangement. Furthermore, the rate of exchange of benzene is sufficiently slow under these conditions that during the time that the reaction was followed (*ca.* 300 h) very little exchange in benzene would be expected (<1%), and the mechanism predicts

• A set of σ^+_{ortho} values derived from benzylation have recently been proposed (G. A. Olah, K. Tobayashi, and M. Tashiro, *J. Amer. Chem. Soc.*, 1972, **94**, 7448). Since this reaction is one of the most hindered of all electrophilic substitutions, the values do not appear to be meaningful.

[17] H. V. Ansell, R. B. Clegg, and R. Taylor, *J.C.S. Perkin II*, 1972, 766; H. V. Ansell and R. Taylor, *J.C.S. Chem. Comm.*, 1973, 936.

that half the initial aromatic compound should be converted to benzene so that exchange will effectively cease when the initial activity has dropped by half, exactly as observed.

There are many precedents for intermolecular rearrangement (disproportionation) of alkylbenzenes. The subject has been twice reviewed,[18] and detailed studies [19,20] of the HF–BF_3 and HBr–$AlBr_3$ catalysed disproportionations of alkylbenzenes have established that the ease with which this occurs follows the order $Bu^t > Pr^i > Et > Me$. Furthermore Allen and co-workers showed that the ratio of inter- *versus* intra-molecular rearrangement of alkyltoluenes increases dramatically along the series $Me < Et < Pr^i < Bu^t$ [21] which lends further support to our belief that we are observing an intermolecular disproportionation. Also t-butylbenzene in aqueous perchloric acid–trifluoroacetic acid at 25° has been shown to undergo intermolecular rearrangement to give benzene, and *m*- and *p*-di-t-butylbenzenes. This side reaction is sufficiently minor for it to produce only a small error in the measured rate of detritiation of t-butyl[3-^{3}H]benzene.[22]

The question remains as to why this disproportionation is only observed with any degree of significance with these two secondary alkylbenzenes. Now acid-catalysed cleavages of substituents from aromatic rings are aided by two factors. (i) The first is the stability of the leaving group which in the present case is a secondary carbenium ion. This is less stable than a tertiary carbenium ion (but may rearrange to such an ion during the isomerisation [20]) and this gives rise to the relative ease of disproportionation previously noted.[19,20] (ii) The second is steric acceleration. This is an important factor and is generally provided by bulky *ortho*-substituents. Our rate data show that these secondary alkylbenzenes are more hindered towards exchange at the *ortho*-positions than is t-butylbenzene itself, consequently there is steric crowding between the alkyl group and the *ortho*-hydrogens. We believe this to be the driving force for the disproportionation and it must surely be relevant that the only compounds in the alkylbenzene series for which steric hindrance to exchange has been detected, happen to be the only compounds for which disproportionation is significant.

In view of these kinetic difficulties, runs on these two secondary alkylbenzenes were carried out at *ca.* 10-fold higher concentration of aromatic compound than is normal. Under these conditions satisfactory first-order kinetic plots were obtained, the quoted rate coefficients being derived over the first 25% of the overall kinetic run (followed to >90% of exchange). Because the kinetics were obviously not as good as usual in hydrogen exchange the rate data for these two compounds are considered to be accurate to only ±10%.

[18] D. V. Nightingale, *Chem. Rev.*, 1939, **25**, 329; G. Baddeley, *Quart. Rev.*, 1954, **8**, 355.
[19] A. P. Lien and D. A. McCaulay, *J. Amer. Chem. Soc.*, 1953, **75**, 2407, 2411.
[20] H. C. Brown and C. R. Smoot, *J. Amer. Chem. Soc.*, 1956, **78**, 2176.

EXPERIMENTAL

In this work *o*- and *p*-alkylbromobenzenes were prepared by bromination of the alkylbenzene with acidified hypobromous acid, and bromine in trifluoroacetic acid respectively as these reagents produce the highest *ortho*- and *para*-yields, respectively.[23] The general method of bromination with hypobromous acid was as follows. Water (100 ml), bromine (24 g, 0.15 mol), and silver sulphate (46.8 g, 0.15 mol) were stirred for 30 min in a 500 ml two-necked flask. Perchloric acid (17 ml of 12M solution, 0.2 mol), dioxan (120 ml), and the aromatic hydrocarbon (0.1 mol) were added, the mixture stirred at 40° during 12 h, cooled, and then worked up in the normal way. For bromination in trifluoroacetic acid, bromine (16 g, 0.1 mol) was dissolved in trifluoroacetic acid (150 ml) and added dropwise during 30 min to a solution of the hydrocarbon (0.1 mol) in trifluoroacetic acid (125 ml). The mixture was heated under reflux during a further 12 h, the acid then mostly removed by distillation (and kept for re-use), and the residue worked up in the normal way.

2-([2-^{3}H]*Phenyl*)*propane*.—2-Phenylpropane (12 g, 0.1 mol) was brominated by the acidified hypobromous acid method. G.l.c. analysis of the crude reaction product indicated the presence of unchanged 2-phenylpropane (40%), 2-(2-bromophenyl)propane (18%), and 2-(4-bromophenyl)-propane (42%); a shoulder on the latter peak indicated the presence also of some *meta*-isomer. Repeated fractional distillation yielded 2-(2-bromophenyl)propane (1.6 g, 8%), b.p. 208—211° at 755 mmHg, n_D^{20} 1.5408 (lit.,[24] 210° at 760 mmHg, n_D^{25} 1.5385). The Grignard reagent prepared from this compound was hydrolysed with tritiated water to give, after work up, 2-([2-^{3}H]*phenyl*)*propane*, b.p. 152° at 760 mmHg, n_D^{20} 1.4908 (lit.,[25] 152° at 760 mmHg, n_D^{20} 1.4911).

2-([4-^{3}H]*Phenyl*)*propane*.—2-Phenylpropane (12 g, 0.1 mol) was brominated by bromine in trifluoroacetic acid. G.l.c. analysis of the crude reaction product indicated the presence of unchanged 2-phenylpropane (50%), 2-(2-bromophenyl)propane (3%), 2-(4-bromophenyl)propane (40%), and dibrominated products (7%). Repeated fractional distillation of this product yielded 2-(4-bromophenyl)-propane (4.0 g, 20%), b.p. 217—219° at 760 mmHg, n_D^{20} 1.5360 (lit., [26] 219° at 760 mmHg, n_D^{25} 1.5337); g.l.c. analysis indicated that this product was 98% pure. The Grignard reagent from this compound was hydrolysed with tritiated water to give, after work up, 2-([4-^{3}H]*phenyl*)*propane*, b.p. 152° at 760 mmHg, n_D^{22} 1.4900.

2-([2-^{3}H]*Phenyl*)*butane*.—*2-Phenylbutan-2-ol*. This was prepared by reacting propiophenone with the Grignard reagent formed from methyl iodide on a 0.5 mol scale. Fractional distillation of the product formed by normal work-up gave 2-phenylbutan-2-ol (80%), b.p. 91° at 4 mmHg, n_D^{20} 1.5182 (lit.,[27] 212° at 760 mmHg, n_D^{22} 1.5158).

[21] R. H. Allen, L. D. Yats, and D. S. Erley, *J. Amer. Chem. Soc.*, 1960, **82**, 4853; R. H. Allen, *ibid.*, 4856.
[22] K. C. C. Bancroft, Ph.D. Thesis, University of Leicester, 1963, p. 171.
[23] Ref. 10, p. 134.
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2-Phenylbutane. 2-Phenylbutan-2-ol (37.5 g, 0.25 mol) dissolved in absolute ethanol (250 ml) was hydrogenated at 45 lb in^{-2} at room temperature using palladized charcoal (3 g) as catalyst. After 1 equiv. of hydrogen had been absorbed the mixture was filtered, and the filtrate distilled to give 2-phenylbutane (32.8 g, 98%), b.p. 174° at 760 mmHg, n_D^{20} 1.4890 (lit.,[28] 173° at 760 mmHg, n_D^{21} 1.4894).

2-(2-Bromophenyl)butane. 2-Phenylbutane (13.4 g, 0.1 mol) was brominated with acidified hypobromous acid; g.l.c.-linked mass spectrometric analysis of the crude reaction product indicated the presence of 2-phenylbutane (40%), 2-(2-bromophenyl)butane (20%), and 2-(4-bromophenyl)butane (40%), the latter being contaminated with some *meta*-isomer. Repeated fractional distillation yielded a mixture, b.p. 96° at 8 mmHg, containing 80% of the desired *ortho*-isomer, together with 20% of the *para*-isomer. Further purification by preparative g.l.c. gave 2-(2-bromophenyl)butane (0.1 g), and hydrolysis with tritiated water of the Grignard reagent formed from this compound gave *2-([2-^{3}H]phenyl)butane*, b.p. 174° at 760 mmHg, n_D^{18} 1.4898 (after addition of inactive 2-phenylbutane to facilitate work-up).

2-([4-^{3}H]Phenyl)butane.—*2-(4-Bromophenyl)butane.* 2-Phenylbutane (13.4 g, 0.1 mol) was brominated with bromine in trifluoroacetic acid. Normal work up followed by repeated fractional distillation gave a product, b.p. 96° at 8 mmHg, which was indicated by g.l.c.-linked mass spectrometry to consist of 2-(2-bromophenyl)- (10%) and 2-(4-bromophenyl)-butane (90%). The latter component was separated by preparative g.l.c. and converted to the Grignard reagent which after hydrolysis with tritiated water gave *2-([4-^{3}H]phenyl)butane*, b.p. 174° at 760 mmHg, n_D^{18} 1.4894 (after addition of inactive 2-phenylbutane to facilitate work up).

3-([2-^{3}H]Phenyl)pentane.—*3-Phenylpentan-3-ol.* This was prepared on a 0.5 mol scale by reacting propiophenone with the Grignard reagent formed from ethyl bromide. Normal work up followed by fractional distillation yielded 3-phenylpentan-3-ol (65%), b.p. 223° at 760 mmHg, n_D^{20} 1.5162 (lit.,[29] 109° at 15 mmHg, n_D^{20} 1.5166).

3-Phenylpentane. Hydrogenation of 3-phenylpentan-3-ol (41 g, 0.25 ml) was carried out as for 3-phenylbutan-2-ol to give 3-phenylpentane (35 g, 94%), b.p. 192° at 760 mmHg, n_D^{20} 1.4878 (lit.,[30] 189—191° at 741 mmHg, n_D^{20} 1.4880).

3-(2-Bromophenyl)pentane. This was prepared and purified in exactly the same manner as 2-(2-bromophenyl)butane. Hydrolysis of the Grignard reagent with tritiated water gave *3-([2-^{3}H]phenyl)pentane*, b.p. 193° at 760 mmHg, n_D^{19} 1.4882 (after addition of inactive 3-phenylpentane to facilitate work up).

3-([4-^{3}H]Phenyl)pentane.— *3-(4-Bromophenyl)pentane.* This was prepared and purified in exactly the same manner as 2-(4-bromophenyl)butane. Hydrolysis of the Grignard reagent with tritiated water gave *3-([4-^{3}H]phenyl)pentane*, b.p. 193° at 760 mmHg, n_D^{20} 1.4880 (after addition of inactive 3-phenylpentane to facilitate work up).

3-([2-^{3}H]Phenyl)hexane.—*3-Phenylhexan-3-ol.* This was prepared on a 0.5 mol scale by reacting propiophenone with the Grignard reagent formed from n-propyl bromide. Normal work up followed by fractional distillation yielded 3-phenylhexan-3-ol, b.p. 130° at 23 mmHg, n_D^{20} 1.5108 (lit.,[31] 134° at 27 mmHg, n_D^{20} 1.5100).

3-Phenylhexane. Hydrogenation of 3-phenylhexan-3-ol (44.5 g, 0.25 mol) was carried out as for 2-phenylbutan-2-ol to give 3-phenylhexane (39.7 g, 97%), b.p. 67° at 2 mmHg, n_D^{18} 1.5258 (lit.,[32] 65—66° at 2 mmHg, n_D^{20} 1.5254).

3-(2-Bromophenyl)hexane. This was prepared and purified in the same manner as 2-(2-bromophenyl)butane. Hydrolysis of the Grignard reagent with tritiated water gave *3-([2-^{3}H]phenyl)hexane*, b.p. 70° at 2.5 mmHg, n_D^{20} 1.5250 (after addition of inactive 3-phenylhexane to facilitate work up).

3-([4-^{3}H]Phenyl)hexane.—*3-(4-Bromophenyl)hexane.* This was prepared and purified in the same manner as 2-(4-bromophenyl)butane. Hydrolysis of the Grignard reagent with tritiated water gave *3-([4-^{3}H]phenyl)hexane*, b.p. 67° at 2 mmHg, n_D^{20} 1.5254 (after addition of inactive 3-phenylhexane to facilitate work up).

Cyclobutyl[2-^{3}H]benzene.—*[2-^{3}H]Bromobenzene.* This was prepared by hydrolysing with tritiated water the Grignard reagent prepared from 1,2-dibromobenzene (2.36 g, 0.01 mol); inactive bromobenzene was added to facilitate work up.

2-([2-^{3}H]Phenyl)cyclobutanol. The Grignard reagent prepared from [2-^{3}H]bromobenzene (1.2 g, 0.007 mol) was coupled with cyclobutanone (0.5 g, 0.007 mol). Hydrolysis and work up involving chromatography on neutral alumina and recrystallisation from light petroleum gave 1-([2-^{3}H]-phenyl)cyclobutanol, m.p. 39° (lit.,[33] 40—41°). Hydrogenation of this alcohol by the method described above for 2-phenylbutan-2-ol gave a 94% yield of *cyclobutyl[2-^{3}H]-benzene*, b.p. 90° at 30 mmHg, n_D^{18} 1.5274 (lit.,[34] 101—102° at 40 mmHg, n_D^{20} 1.5277).

Cyclobutyl[4-^{3}H]benzene.—This was prepared in exactly the same way as the 2-isomer by using 1,4-dibromobenzene as the starting material.

Cyclopentyl[2-^{3}H]benzene.—*Cyclopentylbenzene.* A Friedel–Crafts reaction between benzene and cyclopentyl bromide on a 0.25 mol scale yielded, after normal work up, cyclopentylbenzene, b.p. 218° at 760 mmHg, n_D^{18} 1.5288 (lit.,[35] 217° at 755 mmHg, n_D^{20} 1.5290).

o-Bromocyclopentylbenzene. Cyclopentylbenzene was brominated by the acidified hypobromous acid method. Work up including repeated fractional distillation yielded a product, b.p. 90° at 1.2 mmHg, indicated by g.l.c.-linked mass spectrometry to consist of 2- and 4-bromocyclohexylbenzene in 70 and 30% respective yields. Further purification by preparative g.l.c. gave *ca.* 0.1 g of *o*-bromocyclopentylbenzene. The Grignard reagent prepared from this compound was hydrolysed with tritiated water to give, after addition of inactive cyclopentylbenzene, *cyclopentyl[2-^{3}H]-benzene*, b.p. 218° at 760 mmHg, n_D^{18} 1.5288.

Cyclopentyl[4-^{3}H]benzene.—Cyclopentylbenzene was brominated with bromine in trifluoroacetic acid. Normal work up and fractional distillation gave *p*-bromocyclopentylbenzene b.p. 93° at 1.3 mmHg, n_D^{18} 1.5644 (lit.,[36] 115—118°

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at 20 mmHg, n_D^{20} 1.5642). Hydrolysis with tritiated water of the Grignard reagent prepared from this compound gave *cyclopentyl*[4-^{3}H]*benzene*, b.p. 218° at 760 mmHg, n_D^{18} 1.5288, after addition of cyclohexylbenzene to facilitate work up.

Cyclohexyl[2-^{3}H]*benzene.*—*Cyclohexylbenzene.* This was obtained in 87% yield by the Friedel–Crafts method previously described,[37] and had b.p. 78° at 0.5 mmHg, n_D^{19} 1.5250 (lit.,[37] 239° at 756 mmHg, n_D^{20} 1.5254)

o-*Bromocyclohexylbenzene.* Bromination of cyclohexylbenzene by the hypobromous acid method yielded after work up involving fractional distillation and preparative g.l.c., *o*-bromocyclohexylbenzene, b.p. 132° at 6 mmHg, n_D^{18} 1.5620 (lit.,[38] 128—130° at 5 mmHg, n_D^{20} 1.5616). Hydrolysis with tritiated water of the Grignard reagent formed from this product, gave, after addition of inactive cyclohexylbenzene to facilitate work up, [2-^{3}H]*cyclohexylbenzene*, b.p. 85° at 0.6 mmHg, n_D^{20} 1.5248.

Cyclohexyl[4-^{3}H]*benzene.*— p-*Bromocyclohexylbenzene.* Bromination of cyclohexylbenzene with bromine in trifluoroacetic acid gave after work-up involving fractional distillation, *p*-bromocyclohexylbenzene, b.p. 119° at 1.6 mmHg, n_D^{18} 1.5610 (lit.,[39] 154—156° at 16 mmHg, n_D^{16} 1.5518). The Grignard prepared from this was hydrolysed with tritiated water to give after addition of inactive cyclohexylbenzene to facilitate work up, *cyclohexyl*[4-^{3}H]*benzene* b.p. 86° at 0.6 mmHg, n_D^{18} 1.5253.

Kinetic studies were carried out as previously described,[40] except for the runs on 1-ethylpropyl- and 1-ethylbutylbenzene where in view of the side reaction described in the Discussion section, *ca.* 50 mg of aromatic compound was used in each run. Runs were duplicated until rates agreeing to within ±2% were obtained. Rates for the 1-ethylpropyl and 1-ethylbutyl compounds were determined from the initial slopes of the kinetic plots and may therefore have only ±10% absolute accuracy.

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