Directive Effects in Benzylic Hydrogen Atom Abstraction. Part VI.[1] Halogenation of Arethyl Fluorides

By Kheng H. Lee,* S. E. Loke, and G. H. Yeoh, Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia

The relative rates of halogenation of $XC_6H_4CH_2CH_2F$ with N-bromosuccinimide in CCl_4 at 80° and with sulphuryl chloride in benzene at 40° are correlated by the Hammett equation to give ρ^+ −1·43 (r 0·996) and ρ −0·96 (r 0·985), respectively. The different nature of the transition states of atomic bromine and the benzene-complexed chlorine atom with the substrates $XC_6H_4CH_2Y$ previously noted has been consistently observed. Deuterium isotope effects in the N-bromosuccinimide bromination of PhCHDY and $PhCD_2Y$ have been measured for Y = Ph, CH_2Cl, CH_2F, and Cl and these values are related to the relative reactivity of the undeuteriated compounds.

RECENT studies [1-4] on the halogenation of the series $XC_6H_4CH_2Y$, where Y = Cl, H, CH_2Cl, and Me with N-bromosuccinimide (NBS) in carbon tetrachloride and with sulphuryl chloride in benzene show that nuclear substituent effects as measured by the relative rate constants k/k_0 obey the $\rho\sigma^+$ relationship for bromination whereas the $\rho\sigma$ relationship prevails for chlorination in benzene solution. These results have demonstrated that either σ or σ^+ constants can be adequately used in correlating data in benzylic hydrogen atom abstraction by the radicals in these halogenation reactions. It was shown [1] that Y = CH_2F has a strong deactivating effect on the reactivity of the phenethyl fluoride compared with toluene towards benzylic halogenation by

these two reagents. We now report on the investigation of the polar effects in the halogenation of the series $XC_6H_4CH_2CH_2F$ which should be an excellent system to test the significance in the choice of σ and σ^+ constants in the Hammett equation. The deuterium isotope effects in the NBS bromination of PhCHDY and $PhCD_2Y$ where Y = Cl, CH_2Cl, CH_2F, and Ph were measured, and these results and other available data correlated with the relative reactivity values in $PhCH_2Y$.

EXPERIMENTAL

Materials.—Substituted phenethyl alcohols [2] were converted into the tosylates which were in turn transformed [2] to the fluorides $XC_6H_4CH_2CH_2F$ in 42—55% yield after

[1] Part V, K. H. Lee and T. O. Teo, *J.C.S. Perkin II*, 1973, 1617.

[2] K. H. Lee, *J.C.S. Perkin II*, 1973, 693.

[3] K. H. Lee and T. O. Teo, *J.C.S. Perkin II*, 1973, 689.

[4] T. P. Low and K. H. Lee, *J. Chem. Soc. (B)*, 1970, 535.

removal of olefinic material by concentrated H_2SO_4 extraction. The pure (g.l.c.) fluorides have the following constants: X, b.p. at 35 mmHg, and n_D^{25}: H, 72·5—73°, 1·4900 (lit.,[5] b.p. 55—56° at 12 mmHg); p-Bu^t, 124—125°, 1·4892 (lit.,[6] b.p. 83—85° at 4 mmHg, 1·4897); p-Me, 89—90°, 1·4885 (Found: C, 78·5; H, 7·7; F, 13·7. $C_9H_{21}F$ requires C, 78·3; H, 7·9; F, 13·8%); p-Cl, 107—108°, 1·5110 (lit.,[5] b.p. 79—80° at 9 mmHg); m-Cl, 106—107°, 1·5116 (Found: C, 60·7; H, 5·0; F, 11·8. C_8H_8ClF requires C, 60·6; H, 5·1; F, 12·0%); p-F, 79—80°, 1·4668 (Found: C, 67·9; H, 5·4; F, 26·7. $C_8H_8F_2$ requires C, 67·6; H, 5·7; F, 26·7%); m-F, 79—80°, 1·4688 (Found: C, 67·9; H, 5·75; F, 27·1. $C_8H_8F_2$ requires C, 67·1; H, 5·7; F, 26·7%); p-Br, 67—68·5° at 1 mmHg, 1·5370 (Found: C, 47·4; H, 4·0; Br, 39·4; F, 9·5. C_8H_8BrF requires C, 47·3; H, 3·9; Br, 39·4; F, 9·4%). The n.m.r. spectra (CCl$_4$) of all these fluorides show the four sets of triplets found in $PhCH_2CH_2F$ which has δ 2·62—2·85(t), 3·00—3·20(t), 4·00—4·22(t), 4·78—5·00(t), and 7·12(s).

Bromination of phenethyl fluoride with NBS yielded 92% $PhCHBrCH_2F$, b.p. 78—80° at 1 mmHg, n_D^{25} 1·5484 (Found: C, 47·4; H, 3·9; F, 9·2; Br, 39·0. C_8H_8BrF requires C, 47·3; H, 3·9; F, 9·3; Br, 39·4%), δ 4·22—4·35 (1H, t), 4·80—5·08 (2H, m), and 7·30 (5H, s). Reduction of PhCHO and PhCO$_2$Me with lithium tetradeuterioaluminate (Merck; deuterium content >99%) gave PhCHDOH and PhCD$_2$OH, respectively, which were treated with SOCl$_2$ to give PhCHDCl, b.p. 87—89° at 35 mmHg, n_D^{25} 1·5354 (lit.,[7] b.p. 68—70° at 16 mmHg, n_D^{20} 1·5385), and PhCD$_2$Cl, b.p. 84—86° at 35 mmHg, n_D^{25} 1·5350 (lit.,[7] b.p. 75—77° at 22 mmHg, n_D^{20} 1·5377). [α,α-^{2}H$_2$]Diphenylmethane,[3] n_D^{25} 1·5732, was prepared as previously described. Redistilled Bu$^n_3$SnCl (15·6 g) in ether was added dropwise to LiAlD$_4$ (2 g) in ether followed by pure PhCHBrCH$_2$Cl (19·7 g) in ca. 0·25 h, and the mixture refluxed a further 1 h. The product was isolated in the usual manner by distillation. Redistillation gave 53% PhCHDCH$_2$Cl, b.p. 99—101° at 35 mmHg, n_D^{25} 1·5272, δ 2·94 (m, CHD), 3·57 (d, CH$_2$), and 7·16(s). [α-^{2}H]-β-Fluoroethylbenzene, b.p. 74—76° at 35 mmHg, n_D^{25} 1·4898, δ 257—3·30(m), 4·03—4·33(m), 4·83—5·05(m), and 7·17(s), was similarly prepared from the bromofluoride.

Treatment of [α,α-^{2}H$_2$]benzylmagnesium chloride with solid CO$_2$ in ether gave 76% PhCD$_2$CO$_2$H which on reduction with LiAlH$_4$ yielded 76% PhCD$_2$CH$_2$OH, b.p. 122—123° at 35 mmHg, n_D^{25} 1·5206. This alcohol (6·8 g) was converted into the tosylate in the usual manner. The crude tosylate was treated [5] with KF in ethylene glycol to give PhCD$_2$CH$_2$F (1·71 g), b.p. 74—75° at 35 mmHg, n_D^{25} 1·4902, δ (CCl$_4$) 4·09(d), 4·87(d), and 7·14(s). All the deuteriated compounds gave single peaks on g.l.c. and from their n.m.r. spectra appeared not to contain undeuteriated isomers. All competing substrates and g.l.c. and n.m.r. standards used were >99% pure by g.l.c. analysis. Other materials were purified in the usual manner.[1-4]

Competitive Reactions.—These were carried out as previously described.[1-4] In the NBS brominations at 80° the competing substrates were 0·2M each in CCl$_4$ with NBS (40 mol %). For chlorination at 40° with SO$_2$Cl$_2$

[5] C. H. Depuy and C. A. Bishop, *J. Amer. Chem. Soc.*, 1960, **82**, 2535.

all reactants were 0·4M in benzene and irradiation times were 0·4—1·2 h to allow 25—40% consumption of the competing substrates. A 300 W sunlamp was used as light source for all reactions. All g.l.c. estimations[1-3] of the unconsumed substrates were subject to errors of ≤ ±2%, and n.m.r. determinations[1-3] were reproducible to ≤ ±4%. In the bromination reactions the total substrates consumed were usually 96—102% of the NBS used. The results, calculated by the relative rate equation,[8] are given in detail in Supplementary Publication No. SUP 21162 (7 pp.) * and summarised in Table 1.

Measurements of Deuterium Isotope Effects.—Intramolecular deuterium isotope effects in NBS brominations of PhCHDCH$_2$Cl and PhCHDCl were estimated by a combination of g.l.c. and n.m.r. methods. The k_H/k_D value in PhCHDCH$_2$F could not be measured by these methods as neither PhCDBrCH$_2$F nor PhCHBrCH$_2$F could be estimated cleanly by n.m.r. without other interfering chemical shifts. The k_H/k_D values in NBS bromination of PhCD$_2$CH$_2$F, Ph$_2$CD$_2$, and PhCD$_2$Cl relative to the undeuteriated isomers were measured by the usual competitive technique using suitable standard substrates with which the deuteriated and undeuteriated materials were compared. The results are summarised in Table 2.

RESULTS AND DISCUSSION

SO$_2$Cl$_2$ Chlorination.—The relative reactivity of the benzylic hydrogen atoms in XC$_6$H$_4$CH$_2$CH$_2$F toward SO$_2$Cl$_2$ in benzene at 40° was measured against m-chlorotoluene, toluene, and phenethyl chloride as standards. For X = p- and m-chloro it was necessary to use phenethyl chloride as competing substrate as the product PhCHClCH$_2$F interfered in the g.l.c. estimation of ClC$_6$H$_4$CH$_2$CH$_2$F if PhCH$_2$CH$_2$F was used as standard substrate. For X = p-Me m-ClC$_6$H$_4$Me was used as standard since the other product p-ClCH$_2$C$_6$H$_4$CH$_2$CH$_2$F from the β-fluoride has chemical shift at δ ca. 4·10 downfield from the CH$_2$Cl value in m-ClC$_6$H$_4$CH$_2$Cl. The amount of attack at the p-Me group was estimated by the n.m.r. method and used to correct for the relative reactivity value for the p-Me substituent. For X = p-Bu^t toluene was used as standard as a combination of g.l.c. and n.m.r. methods was employed to analyse the substrates and the products such as PhCH$_2$Cl (at δ 4·10) and p-FCH$_2$CH$_2$C$_6$H$_4$CMe$_2$CH$_2$Cl (singlet at δ 3·31 for CH$_2$Cl). The relative reactivity value for p-Bu^t-C$_6$H$_4$CH$_2$CH$_2$F was corrected for attack at the p-Bu^t substituent and is related to the unsubstituted β-fluoride via the value of 0·50 reported[3] for $k(m$-ClC$_6$H$_4$Me/PhMe).

The results of competitive chlorination of XC$_6$H$_4$CH$_2$-CH$_2$F with SO$_2$Cl$_2$ are given in Table 1. Correlation of the data by the Hammett equation using standard statistical methods[9] shows that ρ = −0·96 ± 0·04 (r 0·985) and ρ$^+$ = −0·82 ± 0·08 (r 0·948). The better correlation with the σ constants of McDaniel and

[6] U.S.P. 2,998,460/1961 (*Chem. Abs.*, 1962, **56**, 409f).
[7] S. Meyerson, P. N. Rylander, E. L. Eliel, and J. D. McCollum, *J. Amer. Chem. Soc.*, 1959, **81**, 2606.
[8] K. H. Lee, *Tetrahedron*, 1968, **24**, 4793.
[9] H. H. Jaffe, *Chem. Rev.*, 1953, **53**, 191.

Brown [10] than with the σ^+ constants of Brown and Okamoto [11] is consistent with data previously reported [1-3] for Y = Cl, H, CH_2Cl, Ph, and Me in the

TABLE 1

Substituent effects in the halogenation [a] of $XC_6H_4CH_2CH_2F$

	k/k_0	
X	NBS (80°; CCl_4)	SO_2Cl_2 (40°; C_6H_6)
p-Me	3·14 * ± 0·07	1·52 * ± 0·05
p-Bu^t	2·42 ± 0·02	1·53 * ± 0·02
H	1·00	1·00
p-F	0·90 ± 0·01	0·96 ± 0·04
p-Cl	0·73 ± 0·01	0·75 ± 0·02
p-Br	0·65 ± 0·02	
m-F	0·32 ± 0·01	0·46 ± 0·01
m-Cl	0·28 ± 0·01	0·42 ± 0·01
ρ	−1·64 ± 0·10	−0·96 ± 0·04
r	0·970	0·985
ρ$^+$	−1·43 ± 0·04	−0·82 ± 0·08
r	0·996	0·948

* Corrected for halogenation at substituent.

[a] Based on triplicate experiments given in Supplementary Publication No. SUP 21162.

series $XC_6H_4CH_2Y$ where the benzene-complexed chlorine atom [1-3] is the principal hydrogen abstracting species. The magnitude of the ρ value of −0·96 compared with the values of −0·76 and −0·83 for Y = CH_2Cl and H, respectively, is not unexpected since the reactivity values [1] (per α-hydrogen atom) are 0·54, 0·72, and 1·00 for $PhCH_2CH_2F$, $PhCH_2CH_2Cl$, and PhMe, respectively.

NBS Bromination.—Bromination of phenethyl fluoride gave a high yield of $PhCHBrCH_2F$. Except for X = p-Me all competitive brominations with NBS were carried out using $XC_6H_4CH_2CH_2F$ versus $PhCH_2CH_2F$, and analysis for unconsumed substrates (g.l.c.) showed good material balance based on the amount of NBS used. For X = p-Me p-chlorotoluene was used as a standard substrate and the reactivity value in p-MeC$_6$-$H_4CH_2CH_2F$ was corrected for formation of p-BrCH$_2$-$C_6H_4CH_2CH_2F$. The results are in Table 1. Treatment of the data by the Hammett equation shows that ρ$^+$ = −1·43 ± 0·04 (r 0·996) and ρ = −1·64 ± 0·10 (r 0·970). The better correlation with σ$^+$ constants is consistent with previous reports [1-4] in the series XC$_6$-H_4CH_2Y where Y = H, Me, CH_2Cl, Cl, and CH=CH$_2$. The magnitude of the ρ value of −1·43 for XC_6H_4-CH_2CH_2F is the largest found so far compared with the values of −1·35 to −1·38 for $XC_6H_4CH_3$,[1,12] −1·30 for $XC_6H_4CH_2Cl$,[1] and −1·10 for $XC_6H_4CH_2CH_2Cl$.[2]

In order to obtain a clear understanding of the relationship between the ρ values in $XC_6H_4CH_2Y$ and the reactivity values in $PhCH_2Y$ the deuterium isotope effects in the NBS bromination of a number of substrates, PhCHDY and PhCD$_2$Y, have been measured and are summarised in Table 2 together with data

previously reported.[13] For $PhCH_2CH_2F$ and $PhCD_2$-CH_2F m-fluorobenzyl chloride was used as standard substrate in the competitive brominations at 80°. For $PhCD_2CH_2F$ versus m-$FC_6H_4CH_2Cl$ good material balance was achieved by a combination of g.l.c. and n.m.r. analyses. The high value of 5·71 ± 0·12 found for the intermolecular deuterium isotope effect compared with the k_H/k_D values of 4·86 and 5·11 found [13] for $PhCH_2D$ and $PhCHD_2$, respectively, suggests that the energy of activation in the rate-determining step of hydrogen abstraction by atomic bromine is higher in $PhCH_2$-CH_2F than in $PhCH_3$. This is reflected in the reactivity

TABLE 2

Relationship between k_H/k_D values and relative reactivity in benzylic bromination with NBS in CCl_4 at 80°

	k_H/k_D	Reactivity of undeuteriated compounds [a]	ρ$^+$ Values in $XC_6H_4CH_2Y$
PhCHDCH$_3$	2·67 ± 0·04 [b]	23	−0·86 [c]
Ph$_2$CD$_2$	2·93 ± 0·06	18	−0·93 [c] (ρ)
PhCHDCH$_2$Cl	3·86 ± 0·14	1·44	−1·10 [d]
PhCH$_2$D	4·86 ± 0·03 [b]	1·00	−1·38 [e]
PhCHD$_2$	5·11 ± 0·02 [b]	1·00	−1·35 [a]
PhCD$_2$CH$_2$F	5·71 ± 0·12	0·69	−1·43
PhCHDCl	6·14 ± 0·22	0·57	−1·30 [a]
PhCD$_2$Cl	6·13 ± 0·11	0·57	
PhCH$_2$Bu^t		0·68 [f]	−0·75 [f]

[a] From ref. 1. [b] From ref. 13 at 77°. [c] From Table 4 of ref. 4. [d] From ref. 2. [e] From ref. 12. [f] At 70°, from W. D. Totherow and G. J. Gleicher, *J. Amer. Chem. Soc.*, 1969, **91**, 7150.

value of 0·69 : 1·00 and also in the magnitude of the ρ values (see Table 2). Since there is no steric effect to the approach of the bromine atom to the benzylic hydrogen atoms in $PhCH_2CH_2F$ the higher energy of activation is due to deactivation of these hydrogen atoms by purely inductive electron withdrawal by the fluorine atom. The low reactivity of 0·68 in $PhCH_2Bu^t$ can be attributed to steric hindrance to the approach of atomic bromine to the benzylic hydrogen atoms whereas the ρ value of −0·75 for $XC_6H_4CH_2Bu^t$ appears to be in the normal range compared with $XC_6H_4CH_2Me$ (ρ = −0·86) for which the parent compound $PhCH_2Me$ has a relative reactivity of 23.

The intramolecular k_H/k_D value of 6·14 found in PhCHDCl is practically identical to the intermolecular value of 6·13 estimated from the competitive NBS bromination of $PhCH_2Cl$ and $PhCD_2Cl$ with m-FC_6H_4-CH_2Cl as standard substrate. The large deuterium isotope effect is in agreement with the low reactivity value [1] found for $PhCH_2Cl$ towards NBS. Examination of the results in Table 2 shows the qualitative trend in the relationship between k_H/k_D values in $PhCH_2Y$ and the relative reactivity towards atomic bromine, and also with the polar effects as measured by ρ values in $XC_6H_4CH_2Y$.

[10] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.

[11] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.

[12] C. Walling, A. L. Rieger, and D. D. Tanner, *J. Amer. Chem. Soc.*, 1963, **85**, 3129.

[13] K. B. Wiberg and L. H. Slaugh, *J. Amer. Chem. Soc.*, 1958, **80**, 3033.