PERKIN 2 COMMUNICATION

An unusually large kinetic Br/Cl leaving group effect for the solvolysis of 1-halospiro[adamantane-2,2′-adamantane]

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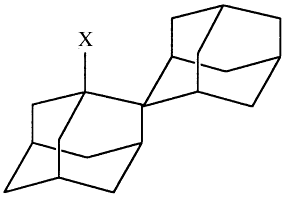
The very large k_{Br}/k_{Cl} leaving group effects of 2300–4500 for solvolysis of 1-halospiro[adamantane-2,2′-adamantane] compounds in slightly ethanolic or aqueous acetone are consistent with the occurrence of F-strain.

Recently, we showed[1] that 1-chlorospiro[adamantane-2,2′-adamantane] **1a** solvolyses rapidly, about 10^8 times faster than 1-chloroadamantane, even in solvents of poor to moderate ionising power (Y_{Cl} range of −3.2 to −0.8). This observation was in accord with indications of considerable F-strain within **1a**, based on calculations using Allinger's MM2(85) force field[2] for a series of substrates, including **1a**, and the MM2 force field with the addition of the UNICAT 4 parameter set[3] for the derived carbocations. In the corresponding acetate the oxygen atom attached to C-1 is less than 2.3 Å from the nearest methylene hydrogens,[4] substantially less than the sum of the van der Waals radii of the oxygen and hydrogen atoms (2.6 Å). The thermal rearrangements of **1a** and of 1-bromospiro[adamantane-2,2′-adamantane] **1b** have been shown to give good yields of the corresponding secondary 4-halo derivative, and a fragmentation–recombination mechanism, favoured by the ease of forming the required intermediate tertiary cation, was proposed.[5] Appreciable F-strain effects had been indicated previously for a 2-substituted 1-adamantyl system by the observation that (*Z*)-2-ethylidene-1-adamantyl derivatives solvolyse about 10^3 times faster than the corresponding (*E*) isomers.[6]



1a X = Cl
b X = Br

For those solvolytic displacement reactions which are influenced by F-strain effects, one would predict that, when two leaving groups are compared kinetically, there will be a steric bulk effect superimposed upon the usual nucleofugality effect, and that this effect will be especially important when the change concerns the atom directly attached to the α-carbon.[7] In particular, one would expect that enhanced k_{Br}/k_{Cl} values will be observed for identical solvolyses of **1a** and **1b**. It has been suggested that the small increases in the Br/Cl rate ratios as one goes from primary to secondary to tertiary halides are due to F-strain effects.[8]

A large effect is already indicated by the semi-quantitative observation that, while **1a** can be manipulated under conditions of reasonably low humidity, the same conditions lead to rapid hydrolysis of **1b**, which has been isolated only with contamination by the corresponding 1-hydroxy compound.[5,9] Microanalysis of a sample of **1b** (stored under vacuum), immediately prior to use in kinetic experiments, gave values of 69.1 and 8.3% for carbon and hydrogen, respectively, consistent with a mixture which is 93% **1b** and 7% the corresponding 1-hydroxy compound. Further quantitative support for a large element effect came from the observation that, while **1a** can be kept with very little loss as a 0 °C solution in carefully purified acetone[10] for several days, **1b** solvolyses in acetone at 0 °C with a half-life of only 32 min. Acetone has been shown to be an effective nucleophile. For example, in the solvolysis of 2-octyl bromobenzenesulfonate in acetone-rich solvents, the acetoxonium ion is formed and, in the presence of either water or methanol, proceeds to octan-2-ol.[11]

Table 1 Specific rates of solvolysis of the 1-halospiro[adamantane-2,2′-adamantane] compounds **1a** (X = Cl) and **1b** (X = Br) at 0.0 °C[a]

Solvent (v/v)	$k_{Br}/10^{-4}$ s^{-1} [b]	$k_{Cl}/10^{-7}$ s^{-1} [b]	k_{Br}/k_{Cl} [c]
Acetone	3.56 ± 0.21	*ca.* 0.5	
Acetone–EtOH (98:2)	7.37 ± 0.19	2.09 ± 0.17	3530
Acetone–EtOH (97:3)	8.81 ± 0.20	3.58 ± 0.29	2460
Acetone–EtOH (96:4)	10.9 ± 0.5	4.80 ± 0.27	2270
Acetone–EtOH (95:5)	24.8 ± 1.4	6.77 ± 0.14	3620
Acetone–H_2O (99:1)	24.7 ± 1.8	5.51 ± 0.14	4480

[a] Kinetics followed by titration of developed acid. [b] With associated standard deviations. [c] k_{1b}/k_{1a}.

Table 2 The k_{Br}/k_{Cl} ratios for $(CH_3)_3CX$ solvolyses (or decompositions) in various solvents.[a]

Solvent	k_{Br}/k_{Cl}
HOAc	15
MeOH	23
EtOH	52
Nitromethane	479
Acetone	589
DMF	724

[a] Values at 25.0 °C from a compilation by Abraham (ref. 13) of specific rates from the literature.

Since **1b** solvolysed extremely rapidly in the solvents used in the previous study of **1a**,[1] both **1a** and **1b** were studied at 0.0 °C in acetone containing 1% water or 2–5% ethanol (Table 1). Even under conditions considerably more severe (refluxing for 20 h with hydrochloric acid in aqueous DMF)[9] than those employed here, **1b** is converted only to the corresponding 1-hydroxy compound. We assume, therefore, that nucleophilic substitution is the sole reaction under our conditions. The k_{Br}/k_{Cl} ratios of 2300–4500 are considerably higher than values previously reported for other systems. These data can be compared, for example, with the specific rates of solvolysis for benzhydryl halides under more typical conditions, which correspond to k_{Br}/k_{Cl} values of 22 in 80% acetone at 25 °C[12a] and 34 in 90% acetone at 50 °C,[12b] while for *tert*-pentyl halides in 80% ethanol at 25 °C the ratio is 40.[12c]

The maximum values previously observed have been for reactions in non-hydroxylic solvents, and Abraham[13] has compiled (logarithmic) specific rate constants for reactions at 25 °C of *tert*-butyl bromide and chloride in both hydroxylic and non-hydroxylic solvents. Some typical k_{Br}/k_{Cl} values derived from these data are reported in Table 2. The highest ratios are for the non-hydroxylic solvents but they are still appreciably lower than for the solvolyses of **1a** and **1b** in acetone containing fairly small amounts of ethanol or water (Table 1). A measure of the influence of the addition of water to an aprotic solvent can be obtained from studies of the solvolyses of the *tert*-butyl halides in aqueous dioxane.[14] The k_{Br}/k_{Cl} values of 48, 58 and 73 in 70, 80 and 90% dioxane, respectively, rise with increase in the proportion of the aprotic component but, even at 90% dioxane, they are considerably less than in a pure aprotic solvent (Table 2). It follows that the k_{Br}/k_{Cl} rate ratio for reactions of *tert*-butyl halides in a non-hydroxylic solvent must show a marked decrease upon addition of small amounts of a hydroxylic component, which means that the value of 589 in acetone should be considered as very much a maximum value compared to the higher ratios in Table 1.

The MM2 steric energies of typical bridgehead tertiary bromides are about 0.6 kcal mol^{-1} (1 cal = 4.184 J) higher than those of the corresponding chlorides, whereas for **1a** and **1b** the difference is 3.0 kcal mol^{-1}. In a previous correlation[1] of *p*-toluenesulfonate solvolysis rates (data for other leaving groups being normalised) against steric energy differences, $\Delta E_{st}(R^+ - RCl)$, it was found that only 40% of the latter was reflected in log k_{OTs}. This would suggest that if bridgehead bromides followed the same sort of correlation,[15] then the k_{Br}/k_{Cl} ratio for the 1-spiro[adamantane-2,2′-adamantane] system would be enhanced relative to the value for other bridgehead systems by a factor of only *ca.* 10. Data on ‘other bridgehead systems’ include an extrapolated value of about 40 for 1-haloadamantanes in ethanol at 25 °C.[8] Using a tabulation, largely of extrapolated values, by Bingham and Schleyer,[16a] Bentley and Roberts[16b] have reported for five bridgehead halides, including the 1-adamantyl system, k_{Br}/k_{Cl} ratios in the range of 32–47 for solvolyses in 80% ethanol at 70 °C. Incorporation of the factor of 10 (see above) leads to a k_{Br}/k_{Cl} ratio of only 400 for **1**, neglecting, however, the difference in solvents. Moreover, the fact that the tosylate equivalents of **1a** and 1-chloroadamantane lie some 3 and 1.8 log units, respectively, above the log k_{OTs} *vs.* $\Delta E_{st}(R^+ - RCl)$ correlation indicates that their reactivities, particularly that of **1a**, are not well modelled, casting some doubt on the small leaving group steric effect predicted by molecular mechanics.

In conclusion, 1-bromospiro[adamantane-2,2′-adamantane] **1b** is much more reactive than the chloro compound **1a,** with k_{Br}/k_{Cl} ratios for solvolyses in acetone (containing small amounts of water or ethanol) that are substantially higher than values previously obtained for substitution and/or elimination reactions of other *tert*-alkyl halides, even in non-hydroxylic solvents. Relief of F-strain would appear to be largely responsible for this enhancement.

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