Solvolysis of Secondary Alkyl Azoxytosylates. A New Reaction related to Solvolytic Deamination and Arenesulphonate Solvolysis

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The rates of solvolysis of 2-adamantyl azoxytosylate have been measured in hexafluoropropan-2-ol (HFIP), trifluoroethanol (TFE), aqueous hexafluoropropan-2-ol (97HFIP), aqueous trifluoroethanol (97TFE), aqueous ethanol (50E and 80E), and aqueous methanol (80M) at 3—5 temperatures between *ca.* 23 and 70 °C, and activation parameters have been determined. The O-^{2}H solvent kinetic isotope effect has been measured for HFIP (k^H/k^D $1.02_5 \pm 0.02$ at 50.8 °C) and secondary α-deuterium kinetic isotope effects have been determined in 97HFIP (k^H/k^D 1.090 ± 0.005; 40.2 °C), 50E (1.091 ∓ 0.006; 51.0 °C), and 80E (1.133 ∓ 0.009; 60.9 °C). Neither methanesulphonic acid in 80M nor pyridine in TFE gives rise to a significant rate enhancement, and there is hardly any salt effect due to low concentrations of tetrabutylammonium perchlorate in 97TFE. 2-Adamantyl tosylate is formed in parallel with solvolysis product in ethanol and weakly aqueous ethanol, and is the sole organic product from reactions in chloroform and toluene. No relatively long lived intermediate such as 2-adamantyl tosylate is involved in the reaction in 97TFE, 80M, and 90M. The kinetics and product results are satisfactorily accommodated by a mechanism involving initial unimolecular rate-determining synchronous fragmentation of the substrate to give nitrous oxide and an ion-pair. This ion-pair is then either captured by solvent to give solvolysis product or, in the less polar media, undergoes ion-pair combination to yield covalent 2-adamantyl tosylate. Bicyclo[2.2.2]octan-2-yl azoxytosylate has also been prepared, and rates and activation parameters have been determined in 97HFIP and 80M. There is no evidence from this limited study of a mechanism different from that of the 2-adamantyl analogue. Rates and activation parameters for the solvolysis of cyclohexyl azoxytosylate have also been determined in an even more limited study using only 97HFIP. Rates are slower than those for the other two compounds, but the mechanism appears to be the same.

Solvolytic deamination of alkyl primary amines by nitrous acid is a complex reaction proceeding through several steps and involving unstable diazo-intermediates (Scheme 1, left).[1] The nature of the alkyl group, among other factors, affects whether diazonium or, as shown, carbonium ions intervene as the main product-determining intermediates.[2,3] Although deaminations have been known and investigated for many years,[4,5] there are still major uncertainties regarding mechanism. The principal difficulty is that the rate laws are complicated and relate to the early nitrosation steps of the reaction.[1] Consequently, all that is known of the more interesting later steps which involve reactive intermediates is based upon product analyses,[6] some including isotopic labelling studies.[7] A second problem is that the instability of products to reaction conditions was not fully appreciated during early investigations; thirdly, analytical methods have often been inadequate for the task.

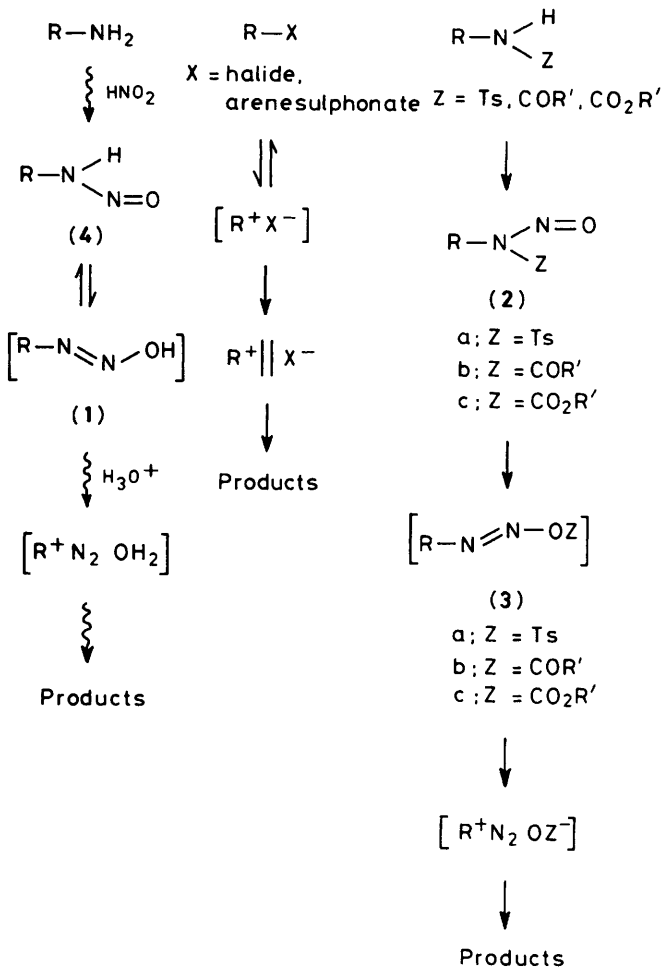
The mechanism involving diazonium ion intermediates which is usually presented for such reactions relies more upon analogy with the corresponding reactions of aromatic primary amines than upon sound and directly relevant experimental evidence.[1] The quality and volume of results from mechanistic studies of deamination are, therefore, in contrast to the output of the research effort devoted over a shorter time to studies of solvolysis of alkyl halides and arenesulphonates, other reactions that may involve carbonium ion intermediates (Scheme 1, centre) but which are usually amenable to interpretable kinetic analysis.

Although deamination and arenesulphonate solvolysis of a secondary alkyl residue may both involve carbonium ion intermediates,[6] the two reaction types show different and often unrelated product distributions.[8,9] In particular, cyclohexyl arenesulphonates mainly give elimination, some unrearranged substitution with predominant inversion of configuration, and appreciable rearrangement *regardless* of whether the leaving group is axial or equatorial in the ground-state conformation.[10] In contrast, an axial amine gives a product distribution similar to that found from the corresponding arenesulphonate whereas its equatorial diastereoisomer gives a completely different analysis, mainly unrearranged substitution with predominant retention of configuration, some elimination, and very little rearrangement.[11]

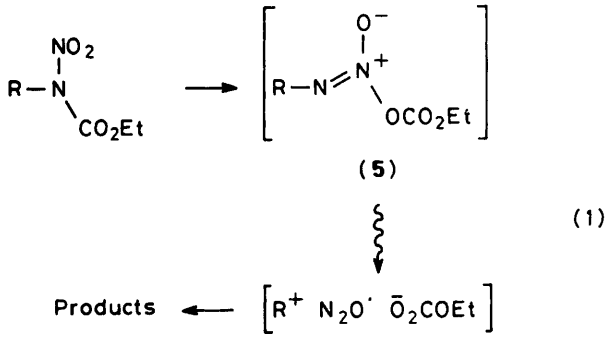
Clearly, a very desirable objective is to prepare stable analogues of the diazo-intermediates (**1**) in Scheme 1 and investigate their reactions by kinetic as well as product analytical techniques. Furthermore, some sort of link between solvolytic deamination and arenesulphonate solvolysis should help to account for the major differences between these reaction types which appear to share other mechanistic features. Solvolysis of nitrososulphonamides (**2a**) (Scheme 1, right) was an obvious approach but its usefulness was restricted by the tendency of the substrates to denitrosate under acidic conditions rather than isomerize to the diazo-tosylate (**3a**).[12]

The development of newer methods of deamination, principally by White and Huisgen and their collaborators, was a major step forward.[5,13,14] Nitroso-amides (**2b**) and nitroso-carbamates (**2c**) shown on the right of Scheme 1 are relatively stable analogues of the unstable nitroso-amines (**4**) shown on the left. These give diazo-intermediates (**3b** and **c**) upon rearrangement prior to heterolytic fragmentation. Triazenes[15] $RNHN_2$-Ar are stable tautomers of diazo-compounds RN_2NHAr, nitrogen analogues of (**3a—c**), and the elusive diazo-intermediate (**1**) in the nitrous deamination of alkyl primary amines.

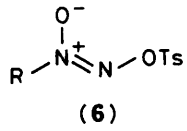
One rational strategy was to destabilize the potential carbonium ion that the diazo-intermediate (**3**) would give in the hope that its rate of decomposition would be rendered slow enough for it to be isolable. Even (**5**), the precursor of the very unstable 1-norbornyl cation in equation (1), has only a fleeting existence at −65 °C.[16,17] So far, therefore, no diazo-intermediates (**1**) or analogues have been produced that are stable at room temperature in protic solvents.



Scheme 1. Some reactions involving secondary alkylcarbonium ion intermediates (R = secondary alkyl)



Our approach was to investigate the solvolysis of alkyl azoxytosylates (**6**), compounds whose very existence was initially regarded as surprising in view of the instability of analogues.[17] They are well suited for both aspects referred to above – substrates to allow kinetic analysis of a reaction apparently related to deamination, and, consequently, to act as a mechanistic link between solvolytic deamination and arenesulphonate solvolysis.[18] Several alkyl azoxytosylates were known and, indeed, mechanisms of some of their reactions had already been investigated. Stevens[19] had noted that such compounds are ambident electrophiles, but, in general, results



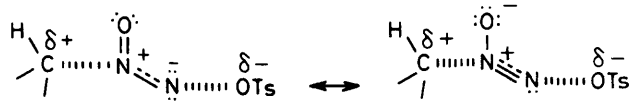
(**6**)

a; R = 2-adamantyl
b; R = cyclohexyl
c; R = bicyclo[2.2.2]octan-2-yl

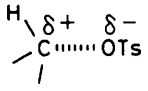
R—OTs

(**7**)

a; R = 2-adamantyl
b; R = cyclohexyl



(**8**)



(**9**)

from solvolytic studies were disappointing. Freeman and Lillwitz[20] reported that only the tertiary alkyl compounds (which were not isolated) underwent solvolysis, and very strongly basic conditions were required for the decomposition of primary and secondary analogues at normal temperatures to give carbonyl compounds. These studies, however, were carried out before highly ionizing non-nucleophilic solvents such as hexafluoropropan-2-ol (HFIP) and trifluoroethanol (TFE) came into common use.[21,22] These newer solvents invariably lead to solvolytic rate constants far higher than are found for solvents such as aqueous ethanol or methanol, or carboxylic acids, for substrates that react by ionization.

We presently report our results for the solvolysis of 2-adamantyl, cyclohexyl, and bicyclo[2.2.2]octan-2-yl azoxytosylates (**6a, b,** and **c**). The first of these was chosen because of the central importance of the adamantyl system in modern solvolytic studies, due principally to the pioneering work of Schleyer and his associates.[23] The cyclohexyl analogue (**6b**), a known compound,[20,24] is a simple secondary system which, like (**6a**), has no complicating stereochemical features. Unlike the 2-adamantyl compound, however, (**6b**) lacks β-carbon branching and is susceptible to rear-side nucleophilic attack at C-1. The bicyclo-octyl analogue (**6c**) shares some features with (**6a** and **b**) but in addition has the potential for reacting through a well characterized non-classical carbonium ion intermediate.[25]

Methods and Procedures.—Preparations of all substrates were based upon literature methods. Our data for known compounds were in agreement with earlier reports; new compounds had appropriate spectroscopic properties and gave acceptable combustion analytical results. The structural data for (**6a**) have already been reported[18] and include no exceptional features. In common with other oxydiazo compounds,[17,24] it has the *Z*-configuration. Our current usual kinetics method involves microcomputer-controlled automatic monitoring of the u.v. absorbance and temperature of the

substrate solution against time in the thermostatted cell block of a spectrophotometer, and has already been described.[26]

Solvolysis of alkyl tosylates gives substitution and elimination products that may react further in very non-basic solvents such as TFE or HFIP with the toluene-*p*-sulphonic acid that is also generated in the reaction, if the solution is not buffered with, at least, a low concentration of water. The products of these secondary reactions often have u.v. absorbances comparable with, or even higher than, that of the initial tosylate with the consequence that clean first-order kinetics are not observed by u.v. spectroscopy under these circumstances. In contrast, the u.v. molar absorbtivity of an alkyl azoxytosylate is so much higher at the monitoring wavelength than that of any conceivable product that clean first-order rate laws are always obtained by u.v. spectrophotometric monitoring of reactant even in anhydrous TFE and HFIP without any additional buffer or co-solvent.

Some rate constants were measured by conductivity using methods and procedures established by others.[21,27,28] In view of the earlier findings of Shiner[21] using *p*-bromobenzenesulphonic acid, we assumed that the conductivity of 97TFE solutions of toluene-*p*-sulphonic acid at less than 10^{-3} mol dm^{-3} would be directly proportional to concentration and, indeed, we obtained excellent first-order rate constants by this technique. In subsequent control experiments, we did, however, observe evidence of ion-pairing in 97TFE, *i.e.* curvature in plots of conductance *versus* molar concentration of standard solutions of toluene-*p*-sulphonic acid but this became pronounced only outside the concentration range of our kinetics experiments ($> 10^{-3}$ mol dm^{-3}). In a few experiments, we monitored the decrease in u.v. absorbance and the increase in electrical conductivity simultaneously (but in separate cells). This corresponds to following the rate of disappearance of reactant (**6a**) and the concurrent rate of formation of a reaction product, toluene-*p*-sulphonic acid.

The approximate rate of thermolysis of (**6a**) in deuteriochloroform at 60 °C was measured by n.m.r. spectroscopy by monitoring the decrease in intensity of the 2-H singlet of the azoxytosylate at τ 5.7 and the concomitant increase in the singlet at τ 5.3 due to the 2-H of the corresponding tosylate (**7a**). After 16 h, the two were of approximately equal intensity (*k ca.* 1×10^{-5} s^{-1}) and, at completion, the whole spectrum was indistinguishable from that of pure authentic 2-adamantyl tosylate. Computer-assisted monitoring of the relative intensities of these two signals using perdeuteriotoluene as solvent and thermostatting of the n.m.r. probe allowed more accurate rate constants to be determined at each of five temperatures from 62 to 103 °C. The precision on these rate constants and on the temperatures at which they were determined is poorer than that on solvolytic rate constants and temperature measurements in kinetics runs by u.v. spectroscopy or conductivity. Consequently, the results by n.m.r. spectroscopy are quoted in Table 1 to fewer significant figures. Their subsequent fit to the Eyring equation, however, is still very satisfactory (correlation coefficient > 0.998). The result at 62 °C is the same as the approximate value obtained at about this temperature using deuteriochloroform as solvent.

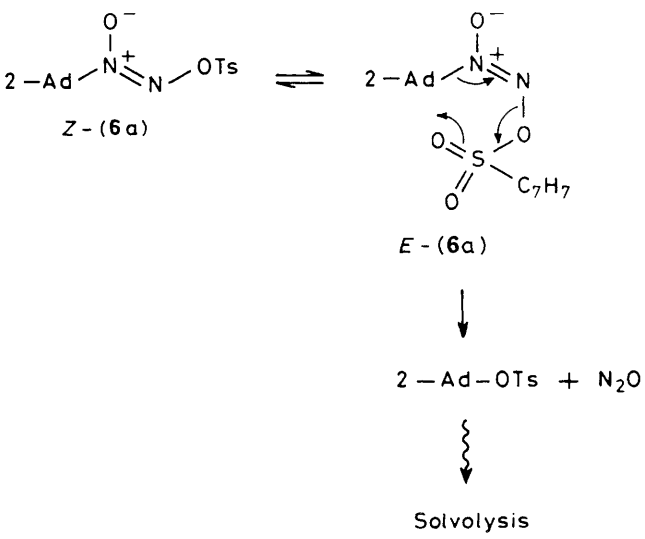
The thermal decomposition of cyclohexyl azoxytosylate (**6b**) in deuteriotoluene was less clean and no acceptable rate constants were obtained by the n.m.r. technique although at 70 °C the rate of reaction appeared to be similar to (but somewhat slower than) that of the 2-adamantyl analogue.

Because of the importance of the results to our own work, we have also repeated earlier kinetic investigations[29] of the solvolysis of 2-adamantyl tosylate in 97TFE and 97HFIP but including measurements at four rather than just two temperatures. Our results merely refine the earlier ones and are shown in Table 2.

Results and Discussion

Thermolysis of 2-adamantyl azoxytosylate in non-nucleophilic solvents was shown by n.m.r. spectroscopy to give the corresponding tosylate cleanly, a result which was corroborated by actual isolation of (**7a**) in high yield and its characterization by m.p. and i.r. 2-Adamantyl tosylate was also characterized after isolation in low yield from the faster reaction of (**6a**) in anhydrous ethanol, a strongly nucleophilic medium but still only weakly ionizing. As water was added to the ethanol to increase the ionizing power, the rate of reaction became faster but the yield of (**7a**) decreased and was at about the limit of detection by t.l.c. in 80E.

Many azoxy compounds are known to react by complex mechanisms that involve free radical intermediates.[1,30] White *et al.*[17] have presented evidence, however, that free radicals are not involved in the reaction of isobutyl azoxytosylate in non-polar solvents. We were unable to detect adamantane, a likely product of a radical mechanism, in the solvolysis of (**6a**) in polar media and conclude that no such mechanism is involved here either. We were also unable to detect adamantanone and so exclude base-induced mechanisms of the type which were established by Freeman and Lillwitz[20] in the decomposition of (**6b**) and simpler analogues under strongly basic conditions. A mechanism which also had to be considered involved *Z*–*E* isomerization of (**6a**) followed by a concerted cyclic reaction with the extrusion of nitrous oxide to give (**7a**) (Scheme 2). The second step of this mechanism is analogous to one proposed[14] for the reaction of nitrosamides but subsequently shown by isotopic labelling studies to be inoperative.[31] According to the reaction conditions, 2-adamantyl tosylate would then be either stable (toluene, chloroform) or undergo further solvolytic decomposition (HFIP, TFE, and aqueous alcohols). The cyclic mechanism *via* the tosylate should lead to a quantitative conversion of (**6b**) into cyclohexyl tosylate in deuteriotoluene. In fact (**6b**) gives not only (**7b**) but also cyclohexene and, presumably, toluene-*p*-sulphonic acid, and the ratio of cyclohexyl tosylate–cyclohexene remains constant as the reaction proceeds. Clearly, therefore, cyclohexyl tosylate and cyclohexene plus toluene-*p*-sulphonic acid are kinetically controlled products formed by parallel routes rather than an initial product and its subsequent decomposition product. (This reaction is analogous to the reported formation of isobutene plus toluene-*p*-sulphonic acid from isobutyl azoxytosylate in chloroform.[17]) The rate of the reaction of (**6b**) is comparable with or slower than the rate of reaction of (**6a**)



Scheme 2.

Table 1. Rate data for 2-adamantyl azoxytosylate[a]

Solvent	T/°C	10^5k/s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
HFIP	50.09	224	89[b]	−21[b]
	42.31	94.9		
	32.53	32.2		
	23.30	10.2		
	25.00	12.7[c]		
97HFIP	62.17	629	90[d]	−20[d]
	49.65	176		
	40.75	73.3		
	32.08	23.1		
	25.00	10.3[c]		
TFE	61.21	164	101[e]	3[e]
	50.84	54.3		
	41 61	17.2		
	33.35	5.58		
	25.00	1.85[c]		
97TFE	69.34	276	89[f]	−35[f]
	54.47	67.0		
	47.05	30.7[g]		
	46.14	25.9		
	36.82	9.20		
	26.76	2.94		
	25.00	2.31[c]		
98.4: 1.6 TFE–pyridine[h]	66.66	224	108[d]	23[d]
	53.35	48.5		
	45.61	19.5		
	36.95	4.99		
	25.00	0.969[c]		
50E	60.97	103	108[e]	20[e]
	50.62	27.4		
	41.95	8.20		
	32.81	2.68		
	25.00	0.808[c]		
80E	61.86	39.7	110[e]	17[e]
	48.76	8.60		
	34.21	1.06		
	25.00	0.282[c]		
80M	61.30	56.6[i]	105[b]	7[b]
	49.85	14.7		
	42.30	5.49		
	33.99	1.80		
	25.00	0.506[c]		
[$^2H_8$]Toluene[j]	103	78	107[d]	−22[d]
	93	27		
	82	11		
	72	3.4		
	62	1.0		
	25	0.008[c]		

[a] All rate constants are mean values from several determinations;[26] estimated maximum errors in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, ± 3 kJ mol^{-1} and ± 7 J K^{-1} mol^{-1} except where otherwise indicated. [b] $r > 0.999$. [c] Calculated from results at other temperatures. [d] $r > 0.998$. [e] $r > 0.999$. [f] $r > 0.9998$. [g] Mean of duplicate measurements by conductivity not used in determination of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$; result of k 29.5 × 10^{-5} s^{-1} calculated at this temperature from the results at other temperatures by u.v. spectroscopy. Furthermore, the rate of solvolysis of (**6a**) was monitored at 41.7 °C by simultaneous monitoring of the decrease in u.v. absorbance and the increase in electrical conductance. Mean rate constants by the two methods are 15.9 × 10^{-5} and 15.7 × 10^{-5} s^{-1}. The result calculated for this temperature from the u.v. results at other temperatures is 16.4 × 10^{-5} s^{-1}. [h] By conductance. [i] In addition, simultaneous rate measurements by u.v. and conductivity were made with the following results; 61.45 °C: 55.9 × 10^{-5} and 54.7 × 10^{-5} s^{-1}; 61.59 °C: 55.9 × 10^{-5} and 55.4 × 10^{-5} s^{-1}. In analogous simultaneous u.v. and conductivity runs in 90M at 61.6 °C, rate constants of 33.3 × 10^{-5} and 35.3 × 10^{-5} s^{-1} were obtained. [j] Determined by n.m.r.; estimated maximum errors on $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, ± 6 kJ mol^{-1} and ± 16 J K^{-1} mol^{-1}.

whereas it should be appreciably faster by the above mechanism since intramolecular formation of the cyclic transition state from *E*-(**6b**) introduces much less strain than does the corresponding process from *E*-(**6a**).

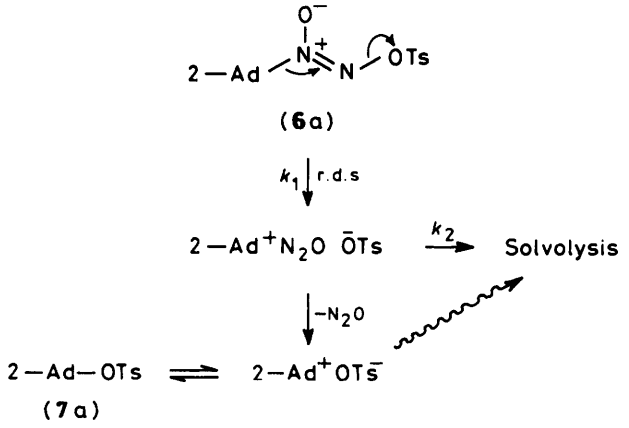
It may still be possible to conceive of alternative routes from (**6a**) with (**7a**) as an essential intermediate in the formation of solvolysis products [equation (2)]. Good estimates of rate constants k_2 for the solvolysis of (**7a**) in the media which we have used are available.[29,32,33] Consequently, by a kinetic analysis of the stepwise reaction of equation (2) we can establish that (**7a**) should increase up to and remain at readily detectable concentrations for a very considerable proportion of the overall reaction time. And, according to this mechanism, the concentration of a final product, *e.g.* toluene-*p*-sulphonic acid, should not increase as a simple exponential function but by the familiar sigmoid curve characteristic of stepwise first-order processes. We monitored simultaneously the decrease in

$$(\mathbf{6a}) \xrightarrow{k_1} (\mathbf{7a}) \xrightarrow{k_2} \text{Products} \qquad (2)$$

Table 2. Rate data for 2-adamantyl tosylate[a]

Solvent	T/°C	$10^5\,k$/s^{-1}	$\Delta H^{\neq}$/kJ mol^{-1}	$\Delta S^{\neq}$/J K^{-1} mol^{-1}
97HFIP	49.65	70.7	68[b] (75)	−96[b] (−71)
	41.95	33.5		
	35.60	23.3		
	26.40	8.81		
	25.00	7.97[c] (9.75)[d]		
97TFE	71.80	37.7	105[e] (97)	−6[e] (−30)
	61.93	12.3		
	52.06	3.98		
	44.84	1.51		
	25.00	0.102[c] (0.164)		

[a] Estimated maximum errors in $\Delta H^{\neq}$ and $\Delta S^{\neq}$, ± 3 kJ mol^{-1} and ± 8 J K^{-1} mol^{-1}. Results from ref. 29 given in parentheses. [b] $r > 0.995$. [c] Calculated from results at other temperatures. [e] $r > 0.999$. [d] Other results of 8.68, 8.84, and 7.17 have been reported.[33]



Scheme 3.

Table 3. Solute effects upon solvolysis rates

Substrate	Solvent	T/°C	Solute[a]	Solute concentration (mol dm^{-3})	$10^5 k$/s^{-1}
2-Adamantyl azoxy-tosylate	97TFE	42.73	A	0	16.9
				0.010	17.3
				0.020	18.4
				0.030	18.6
				0.040	18.4
2-Adamantyl azoxy-tosylate	80M	61.6	B	0	54.0
				0.067	55.8
				0.177	53.2
				0.297	58.3
2-Adamantyl tosylate	97TFE	62.18	A	0	12.7
				0.010	12.1
				0.020	12.3
				0.10	12.7

[a] A = Tetrabutylammonium perchlorate; B = methanesulphonic acid.

concentration of (**6a**) by u.v. spectrophotometry (k_1) and the increase in acid concentration by conductivity in 97TFE, 80M, and 90M. In each of the three solvents, the two methods gave strictly first-order rate laws with identical rate constants. These results rule out not only Scheme 2 but any sequential two-step mechanism of equation (2) *via* (**7a**) or any other relatively long lived intermediate.

Solvent and Solute Effects.—The increasing rate constants with the increasing ionizing power of the solvent and the isolation of 2-adamantyl tosylate in the poorer ionizing media are as expected on the basis of a mechanism involving rate-determining ionization shown in Scheme 3. According to this mechanism, formation of 2-adamantyl tosylate by anion–cation combination in solvents not conducive to ion-pair separation is parallel and in competition with capture of the cation by solvent. If formed, (**7a**) may, perhaps, also undergo subsequent solvolysis according to its own reactivity under the experimental conditions of the reaction. But (**7a**) is not a necessary intermediate in the solvolysis of (**6a**), and it appears to be formed to any appreciable extent only in 80E and solvents less ionizing, and not at all in media such as TFE and HFIP with or without water as cosolvent.

The results in Table 3 show that the solvolysis of (**6a**) in 97TFE has a barely detectable salt effect. This is surprising for an ionic reaction but, as is also shown in Table 3, it appears equally true of the solvolysis, in the same medium, of 2-adamantyl tosylate itself, a compound whose solvolysis rate is much more dependent upon the ionizing nature of the medium (Table 4).

The results in TFE containing pyridine (Table 1) show that there is no appreciable base-catalysed reaction, and methanesulphonic acid (Table 3) gave rise to no catalysis in aqueous methanol.

Deuterium Kinetic Isotope Effects.—(a) *Solvent k.i.e.* The 2-adamantyl structure effectively precludes any major nucleophilic assistance to reaction at the alkyl end,[23] and the absence of catalysis by methanesulphonic acid suggests that added proton electrophiles are uninvolved in the reaction. The possibility remained, however, that the effect of any acidic solute is swamped by some sort of electrophilic facilitation by the solvent itself. To test this possibility, we prepared the O–^{2}H analogue of hexafluoropropan-2-ol and sought a solvent deuterium kinetic isotope effect.[34] As the results in Table 5 show, such an effect is barely detectable. It appears, therefore, that the heterolytic decomposition of (**6a**) is unassisted by any readily identifiable specific catalytic effect.

(b) *α-K.i.e.* The appreciable secondary α-deuterium kinetic isotope effects shown in Table 6 establish that cleavage of the C–N bond is involved in the rate-determining step. The magnitude of the value in the most ionizing medium, 1.09, is low, however, compared with the limiting value of 1.23 for 2-adamantyl arenesulphonates.[35–37] And, in so far as it changes at all, it is actually higher (1.13) in the more nucleophilic but less ionizing medium, 80E. α-Deuterium kinetic isotope effects of secondary alkyl arenesulphonates which are susceptible to S_N2 reactions invariably decrease as the medium becomes more nucleophilic and less ionizing.[35,36] We conclude that there is no intermolecular nucleophilic contribution in aqueous ethanol

Table 4. Comparison of 2-adamantyl azoxytosylate and 2-adamantyl tosylate[a]

	Azoxytosylate			Tosylate		
	10^5k/s^{-1} (25 °C)	$\Delta H^{\circ\ddagger}$/kJ mol^{-1}	$\Delta S^{\circ\ddagger}$/J K^{-1} mol^{-1}	10^5k/s^{-1} (25 °C)	$\Delta H^{\circ\ddagger}$/kJ mol^{-1}	$\Delta S^{\circ\ddagger}$/J K^{-1} mol^{-1}
HFIP	12.7	89	−21	14.7[b]	69[b]	−86[b]
97HFIP	10.3	90	−20	7.97 (9.75)	68 (75)	−96 (−71)
97TFE	2.31	89	−35	0.102 (0.164)	105 (97)	−6 (−30)
TFE	1.85	101	3	0.14[b]	102[b]	−15[b]
50E	0.808	108	20	0.047[c]	112[c]	10[c]
80E	0.282	110	17	0.0024[c]	113[c]	−13[c]

[a] Results in parentheses taken from ref. 29. [b] Ref. 33. [c] Ref. 32.

Table 5. Solvent deuterium kinetic isotope effect upon the solvolysis of 2-adamantyl azoxytosylate in HFIP at 50.8 °C

Solvent Isotope	10^5k/s^{-1} 1	2	3	Mean
^{1}H	190	196	196	194
^{2}H	189	187	192	189
k^H/k^D	1.00_5	1.04_8	1.02_1	1.02_5

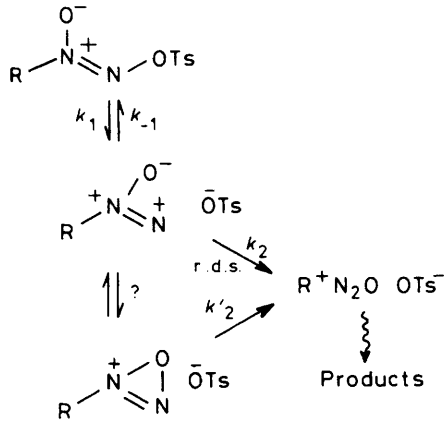
Table 6. α-Deuterium kinetic isotope effects upon the solvolysis of 2-adamantyl azoxytosylate[a]

Solvent	T/°C	10^5k^H/s^{-1}	k^H/k^D
97HFIP	40.2	55.0	1.090 ± 0.005
50E	51.0	28.6	1.091 ± 0.006
80E	60.9	32.8[b]	1.133 ± 0.009[b]

[a] k^H results are means of five consecutive measurements; k^H/k^D results are the means of five k^H/k^D ratios, each k^H and k^D pair obtained from simultaneous runs. [b] Mean of 4 measurements.

and that the rate-determining step is the same in both solvents. We still have to account for the results being as low as 1.09—1.13 however. Our mechanism supplies one reason and the general (qualitative) theory of secondary deuterium kinetic isotope effects (such as there is one) supplies another. We believe both are valid.

The magnitude of a secondary α-deuterium kinetic isotope effect depends principally upon the change in the force constants of the vibrations which involve the α-C–H/D bond as the substrate becomes activated complex. The largest effect is anticipated when an sp^3-C–H bending mode becomes an uninhibited out-of-plane bending vibration of an sp^2-C–H.[38] If the transition state of the reaction occurs before this vibrational transformation is complete, *i.e.* if there is still residual bonding between leaving group and the α-carbon in the transition state (**8**), then a reduced effect will be observed. The largest effects (k^H/k^D 1.23 at 25 °C) have been found for limiting solvolyses of 2-adamantyl and other secondary alkyl arenesulphonates and the mechanism ascribed to this reaction initially by Shiner involves reversible ionization followed by rate-determining ion-pair separation.[35,37] Only the changing state of the solvation restricts the out-of-plane bending vibration of the sp^2-C–H/D of the fully developed carbonium ion in the activated complex by this mechanism. Non-limiting but still S_N1 solvolyses of secondary alkyl arenesulphonates[39] in which ionization is rate-determining, activated complex (**9**), lead to a slightly depressed α-k.i.e. (k^H/k^D *ca.* 1.18—1.20).[40] These results indicate that rate-determining ionization of (**6a**) is not, by itself, sufficient to explain the currently observed low values of 1.09—1.13. It is known, however, that the nature of the atom through which the leaving group is bonded has an effect.[35] The α-k.i.e. should be largest when the nucleofuge is bonded to carbon through a hard Lewis base, *e.g.* oxygen, and smallest for a soft leaving group such as iodide. These trends have been established experimentally for alkyl halides.[35,41] The leaving group of an azoxytosylate is bonded to carbon through nitrogen compared with oxygen in a tosylate and this, we believe, contributes to the depressed α-k.i.e.



Scheme 4.

The Rate-determining Step.—The question still remains as to whether the N_2O-separated ion-pair is formed by a synchronous fragmentation of the substrate as shown in Scheme 3 or by a stepwise process. The former would be analogous to the way diazo-intermediates from secondary alkyl primary amines give carbonium ions in the more common deamination-type reactions.[3,11] The secondary α-deuterium kinetic isotope effects given in Table 6 and discussed above require that the rate-determining step includes cleavage of the carbon–nitrogen bond. The only reasonable alternative to a synchronous fragmentation (Scheme 3) involves rate-determining departure of nitrous oxide from a reversibly formed oxydiazonium ion, an electrophilic intermediate which could conceivably ring close to give an oxadiazirenium cation (Scheme 4). The known reluctance of the 2-adamantyl system to be involved in bimolecular reactions[23] requires that the departure of N_2O from whichever hetero-cation is involved in Scheme 4 be another unimolecular heterolysis to give a carbonium ion. And detection of 2-adamantyl tosylate requires that no electrophile in this sequence has a lifetime long enough to allow diffusion away of tosylate anion. Thus, either the fragmentation is synchronous as shown in Scheme 3, or *all* the later steps in Scheme 4 are very fast compared with the diffusional separation of the first-formed ion pair. The synchronous fragmentation seems the mechanism most likely to place the very weakly nucleophilic tosylate anion in a position of such proximity that,

for geometrical reasons, it is able to compete with the much more nucleophilic and more preponderant ethanol or water molecules in capturing the 2-adamantyl cation in aqueous ethanol.

The Nature of the Alkyl Group.—We see in Tables 7 and 8 the results from (**6b** and **c**) and in Table 9 a comparison of the reactions of all three secondary alkyl azoxytosylates. The 2-adamantyl compound is incapable of intermolecular nucleophilic assistance; this is almost certainly true of the bicyclo-[2.2.2]octan-2-yl compound also. The cyclohexyl analogue is, in principle, susceptible to intermolecular nucleophilic attack at the α-carbon but, in contrast to (**6c**), not of intramolecular C–C hyperconjugative assistance. The rate difference between (**6a** and **b**) is in the sense expected of a carbonium ion route, and the similarity between (**6a** and **c**) suggests a very close mechanistic relationship. Either the bicyclo[2.2.2]octan-2-yl compound does not employ its capacity for σ-bridging in the rate-determining step or this sort of facilitation is equally available to the 2-adamantyl analogue.[8,39] Further studies should provide elucidation.

The Mechanism of Solvolysis of 2-Adamantyl Tosylate.—We have already argued that detection of 2-adamantyl tosylate amongst the solvolysis products of (**6a**) is direct evidence for initial ionization of (**7a**) being reversible in its own solvolysis and, hence, not the rate-determining step.[42] Two further aspects of the present investigation constitute independent though less direct supporting evidence. Although there is a trend in the rate constants for solvolysis of (**6a**) with solvent which is qualitatively in the right sense for an ionic mechanism, it is noticeably smaller than the trend in the results for 2-adamantyl tosylate (Table 4). The rate constants for solvolysis of (**6a**) increase by a factor of 45 from 80E to HFIP whereas for (**7a**) the corresponding factor is 6125. According to the mechanism in Scheme 3 for the solvolysis of (**6a**) involving rate-determining fragmentation, the activated complex (**8**) involves partial bonding between C-2 of the adamantyl residue and nitrogen, and between the other nitrogen and the oxygen of the tosylate leaving group. In other words, formation of the activated complex from (**6a**) involves separation of only partial charges. Analogously, if ionization of (**7a**) were rate-determining as is maintained by Schleyer and Bentley,[23,29,32,33,36,43] then only partial charge development would also be involved in the formation of the activated complex (**9**) and a comparable solvent effect would be expected. Progress through the transition state of a reaction whose rate-determining step involves ion-pair separation (the mechanism proposed by Shiner[35,37] and advocated by us[40,42]) requires separation of fully developed charges, and such a mechanism accounts more satisfactorily for the appreciably greater solvent dependence of the rate of solvolysis of (**7a**) compared with (**6a**).

Secondly, bonding through nitrogen in (**6a**) as opposed to oxygen in (**7a**) does not seem sufficient a reason in itself to account for the difference in their solvolytic α-deuterium kinetic isotope effects, 1.09—1.13 and 1.23 respectively, if both compounds react by rate-determining ionization. The difference between these results additionally requires different rate-determining steps, fragmentation for (**6a**) with partial bonding between the α-carbon and leaving group at the transition state, and for (**7a**) ion-pair separation involving a much less congested α-carbon in the activated complex.

Table 7. Rate results for cyclohexyl azoxytosylate in 97HFIP

T/°C	10^5k/s^{-1}	$\Delta H^{\circ\ddagger}$/kJ mol^{-1}	$\Delta S^{\circ\ddagger}$/J K^{-1} mol^{-1}
54.78	14.2	96[a]	−27[a]
48.10	6.39		
33.46	1.14		
25.00	0.378[b]		

[a] $r > 0.999$; estimated maximum errors in $\Delta H^{\circ\ddagger}$ and $\Delta S^{\circ\ddagger}$, ± 3 kJ mol^{-1} and ± 7 J K^{-1} mol^{-1}. [b] Calculated from results obtained at the other temperatures.

Table 8. Rate results for bicyclo[2.2.2]octan-2-yl azoxytosylate

Solvent	T/°C	10^5k/s^{-1}	$\Delta H^{\circ\ddagger}$/kJ mol^{-1}	$\Delta S^{\circ\ddagger}$/J K^{-1} mol^{-1}
97HFIP	52.24	109	92[a]	−21[a]
	42.49	38.1		
	33.40	12.1		
	25.33	4.87		
	25.00	4.53[b]		
80M	62.72	41.8	107[a]	9[a]
	53.38	14.5		
	42.17	3.54		
	31.40	0.731		
	25.00	0.301[b]		

[a] $r > 0.999$, estimated maximum errors in $\Delta H^{\circ\ddagger}$ and $\Delta S^{\circ\ddagger}$, ± 3 kJ mol^{-1} and ± 6 J K^{-1} mol^{-1}. [b] Calculated from results at other temperatures.

Experimental

Commerial deuteriochloroform, [$^2H_8$]toluene, methanesulphonic acid, and spectroscopic-grade absolute ethanol were used without further purification. Methanol and pyridine were fractionally distilled from magnesium methoxide[44] and calcium hydride, respectively. Tetrabutylammonium perchlorate was prepared from commercial aqueous tetrabutylammonium hydroxide and perchloric acid, recrystallized several times from AnalaR grade methanol, then dried under vacuum. Water used to make solvolytic media had been fractionally distilled twice from dilute potassium permanganate using all-glass apparatus. Preliminary n.m.r. reaction rates on (**6a**) and some routine n.m.r. spectral characterizations were carried out using a Perkin-Elmer R32 spectrometer (90 MHz); other routine n.m.r. spectra were recorded on a Perkin-Elmer R24 instrument (60 MHz) also using Me_4Si as internal standard. The more sophisticated reaction rate determinations on (**6a**) by n.m.r. were carried out using a Bruker WP80 spectrometer (80 MHz). All g.l.c. was carried out using a Perkin-Elmer F30 gas chromatograph with nitrogen as carrier. Mass spectra were obtained on a JEOL D-100 double focusing mass spectrometer

Table 9. Comparison of results for 2-adamantyl, bicyclo[2.2.2]octan-2-yl, and cyclohexyl azoxytosylates

Solvent	97HFIP			80M		
Substrate	10^5k/s^{-1} (25 °C)	$\Delta H^{\circ\ddagger}$/kJ mol^{-1}	$\Delta S^{\circ\ddagger}$/J K^{-1} mol^{-1}	10^5k/s^{-1} (25 °C)	$\Delta H^{\circ\ddagger}$/kJ mol^{-1}	$\Delta S^{\circ\ddagger}$/J K^{-1} mol^{-1}
(**6a**)	10.3	90	−20	0.506	105	7
(**6c**)	4.53	92	−21	0.301	107	9
(**6b**)	0.378	96	−27			

and i.r. spectra were recorded on Perkin-Elmer 577 or 197 spectrophotometers. Conductivity cells were made in the department and used in conjunction with a Wayne–Kerr Universal conductivity bridge. Our u.v. kinetics system has already been described.[26]

Adamantanone Oxime.—A solution of adamantanone (4.65 g, 31.0 mmol), hydroxylamine hydrochloride (3.36 g, 48.3 mmol), and sodium acetate (5.28 g, 64.4 mmol) in 1:1 aqueous methanol (80 cm^3) was heated under reflux for 4 h. The mixture was cooled, methanol was evaporated under reduced pressure, then the product was extracted with three portions of dichloromethane. The combined organic phase was washed with brine, dried (Na_2SO_4), and filtered. Evaporation of the solvent left crystals (5.3 g) which were not purified further, m.p. 165—166 °C (lit.,[45] 162.8—163.6 °C); $\bar{\nu}_{max.}$ (KBr) 3 210(s), 3 120(s), 1 675(m), 1 480(m), 1 455(m), 965(s), and 955(sh) cm^{-1}; τ (CCl_4) 1.3 br (1 H, s), 6.4 (1 H, m), 7.4 (1 H, m), and 7.7—8.9 (12 H, m).

N-(2-*Adamantyl*)*hydroxylamine*.—Sodium cyanoborohydride (1.05 g, 16.7 mmol) was added portionwise to a magnetically stirred solution of adamantanone oxime (1.80 g, 10.9 mmol) containing a single very small crystal of Bromocresol Green. A methanolic solution of HCl [prepared from CH_3OH (30 cm^3) and acetyl chloride (5 cm^3)] was added alternately with the cyanoborohydride to maintain the colour of the solution on the yellow side of the yellow–orange borderline.[46] The stirring was continued for a further 4 h, then the methanol was evaporated under reduced pressure at 50 °C. The residue was extracted between dichloromethane and dilute aqueous sodium hydroxide solution, and the aqueous phase was extracted twice more with further portions of dichloromethane. The combined dichloromethane phase was washed with water, dried (Na_2SO_4, K_2CO_3), filtered, and evaporated to give the crude crystalline product (1.92 g). Sublimation of a sample from another preparation (130 °C at 0.1 Torr) gave crystals, m.p. 185—187 °C; $\bar{\nu}_{max.}$ (CCl_4) 3 610(w), 3 280(m), and 1 455 cm^{-1}; τ ($CDCl_3$) 4.25 br (2 H, s), 6.85 (1 H, m), and 7.6—8.9 (14 H, m); *m/z* 167 ($M^{+\bullet}$, 33%), 150 (7), 136 (14), and 135 (100%).

N-*Nitroso*-N-(2-*adamantyl*)*hydroxylamine*.—A solution of sodium nitrite (0.63 g, 9.1 mmol) in water (2 cm^3) was added dropwise over 10 min to a stirred solution of crude *N*-(2-adamantyl)hydroxylamine (0.90 g, 5.4 mmol) in ethanol (6 cm^3) and aqueous hydrochloric acid (2M; 3 cm^3) at 0 °C. After *ca.* 1 h, the reaction mixture was diluted with ice-cold water (200 cm^3) and the thick precipitate was filtered off, washed with ice-cold water, and dried in a vacuum desiccator over KOH at room temperature (0.91 g, 4.6 mmol, 86%); $\bar{\nu}_{max.}$ (KBr) 3 600—3 200, 3 050, 2 920, 2 860, 1 450, 1 080, 1 060, 1 040, 980, 790, 710, 410, and 370 cm^{-1}; τ ($CDCl_3$) 5.35 (1 H, exchangeable by ^2H_2O, m), 7.3 (2 H, m), and 7.9—8.4 (12 H, m). A sample from another preparation, m.p. 137—139 °C (from CCl_4), had no peak at τ 5.35 but another (also exchangeable by ^2H_2O) at τ −1.4 to −3.4 (1 H) (Found: C, 61.4; H, 8.2; N, 14.3. $C_{10}H_{16}N_2O_2$ requires C, 61.2; H, 8.2; N, 14.3%).

2-*Adamantyl Azoxytosylate*.—Toluene-*p*-sulphonyl chloride (recrystallized; 1.20 g, 6.28 mmol) was added to a solution of *N*-nitroso-*N*-(2-adamantyl)hydroxylamine (0.68 g, 3.5 mmol) in dry pyridine (3 cm^3) and the reaction was left at room temperature for 24 h.[47] The reaction was quenched by the addition of ice–water and, after being kept at 0 °C overnight, the mixture was worked up by ether extraction. The aqueous phase was extracted with more ether and the combined ether solution was washed with aqueous $CuSO_4$, water, and aqueous Na_2CO_3. It was dried (Na_2SO_4, K_2CO_3), treated with decolourizing charcoal, filtered, and evaporated under reduced pressure to leave crystals (1.03 g, 2.94 mmol, 85%). Trituration with several portions of pentane gave very pale yellow crystals, m.p. 114—115 °C (0.86 g, 71%). A sample from another preparation was recrystallized from light petroleum (b.p. 40—60 °C) at low temperatures, m.p. 111—113 °C; $\bar{\nu}_{max.}$ (KBr) 2 920(m), 2 860(m), 1 600(m), 1 505(m), 1 455(m), 1 390(s), 1 195(s), 1 180(s), 1 090(m), 920(m), 900(m), 820(m), 805(m), 795(m), 770(m), 725(s), 665(m), 565(m), and 550(s) cm^{-1}; τ ($CDCl_3$) 2.4 (4 H, q), 5.7 (1 H, m) 7.55 (5 H, m), and 7.6—9.0 (12 H, m); $\lambda_{max.}$ (C_2H_5OH) 275 (ε 830) (Found: C, 58.1; H, 6.3; N, 8.2; S, 9.5; $C_{17}H_{22}N_2O_4S$ requires C, 58.3; H, 6.3; N, 8.0; S, 9.15%).

Bicyclo[2.2.2]*octan-2-one*.—This compound was prepared by oxidation of bicyclo[2.2.2]octan-2-ol[48] using either pyridinium chlorochromate[49] or acidified aqueous sodium dichromate–diethyl ether[50] and used without purification.

Bicyclo[2.2.2]*octan-2-one Oxime*.—This compound was prepared from crude bicyclo[2.2.2]octan-2-one as described above for the adamantane analogue (78%), m.p. (triturated with pentane) 116—119 °C (lit.,[51] 114—118 °C); τ ($CDCl_3$) 0.7 br (1 H, s), 7.6 (3 H, m), and 7.9—8.7 (9 H, m).

N-(*Bicyclo*[2.2.2]*octan-2-yl*)*hydroxylamine*.—This compound was prepared as described above for the adamantyl analogue [79% after sublimation at 95 °C (0.1 Torr)], m.p. (trituration with pentane–ether) 94—95 °C; τ ($CDCl_3$) 3.5 br (2 H, s), 6.6—7.0 (1 H, m), and 7.5—9.2 (12 H, m); $\bar{\nu}_{max.}$ (KBr) 3 600—3 200, 2 940, 2 860, 1 450, 1 360, 925, and 850 cm^{-1}; *m/z* 67 (100%), 79 (49), 81 (58), 109 (100), and 141 ($M^{+\bullet}$, 76) ($C_8H_{15}NO$ requires *M*, 141.1153. Found: $M^{+\bullet}$, 141.1153).

Nitrosation of N-(*Bicyclo*[2.2.2]*octan-2-yl*)*hydroxylamine*.—This reaction was carried out by the method described above for the adamantane analogue. Owing to its apparent instability, the product was tosylated directly without purification.

Bicyclo[2.2.2]*octan-2-yl Azoxytosylate*.—This compound was prepared by the above described Tipson procedure[47] at 0 °C from crude *N*-nitroso-*N*-(bicyclo[2.2.2]octan-2-yl)-hydroxylamine, m.p. (from pentane at low temperature) 82—83 °C; τ ($CDCl_3$) 2.35 (4 H, ABq), 5.4 (1 H, m), 7.50 (3 H, s), and 7.9—8.8 (12 H, m); $\bar{\nu}_{max.}$ (KBr) 2 940, 2 870, 1 530, 1 385, 1 195, 1 175, 750, 560, and 550 cm^{-1}. Analysis by t.l.c. and n.m.r. of a sample in $CDCl_3$ kept at 60 °C for 50 h established complete conversion into bicyclo[2.2.2]octan-2-yl toluene-*p*-sulphonate an authentic sample of which was available.[25]

Cyclohexyl Azoxytosylate.—This known compound was made from *N*-nitroso-*N*-(cyclohexyl)hydroxylamine[24] by the Tipson method[47] at 0 °C, m.p. (pentane) 93—94 °C (lit.,[24] 92—93 °C); τ ($CDCl_3$) 2.35 (4 H, ABq), 5.5—6.0 (1 H, m), 7.53 (3 H, s), and 7.9—9.0 (10 H, m); $\bar{\nu}_{max.}$ (KBr) 2 950, 2 860, 1 600, 1 515, 1 390, 1 195, 1 190, 925, 890, 820, 765, 715, and 555 cm^{-1}. Attempted rate measurements by n.m.r. using solutions in [$^2H_8$]toluene did not lead to rate constants of acceptable precision. The products were seen by n.m.r., however, to be cyclohexene and cyclohexyl toluene-*p*-sulphonate in comparable amounts, and the proportion of these two compounds did not change during the course of the reaction.

Sodium Cyanoborodeuteride.[46]—A freshly prepared solution cautiously made up from acetyl chloride (1.6 cm^3) and deuterium oxide (8 cm^3) was added to a stirred solution of sodium cyanoborohydride (4.0 g, 64 mmol) in deuterium oxide (30 cm^3; 99.8% ^2H) in such quantities and at such a rate as to maintain pH 1.8—2.2 for 30 min. Anhydrous sodium carbonate

was then added until pH > 6. The deuterium oxide was evaporated under reduced pressure, fresh ^2H_2O (30 cm^3) was added, and the process was repeated. The resultant solid product was dried in a vacuum desiccator then stirred for 1 h in THF (50 cm^3). The solution was filtered and evaporation of the solvent left a solid (2.0 g, 50%), the n.m.r. spectrum of which, compared with that of starting material, showed *ca.* 3% residual protium. A portion (1 g) was recycled through the above procedure once more to give powder (0.64 g; 64%) with *ca.* 99% deuterium incorporation by n.m.r.

N-(2-[2-^{2}H]*Adamantyl*)*hydroxylamine*.—A solution made up from acetyl chloride (1 cm^3) and deuterium oxide (1 cm^3) was added dropwise to an initially blue stirred solution of adamantanone oxime (1.1 g, 6.7 mmol), sodium cyanoborodeuteride (0.625 g, 9.49 mmol; 99% ^{2}H), and a small crystal of Bromocresol Green in anhydrous tetrahydrofuran (7 cm^3) to turn and then maintain the solution yellow. After 10 min, no further addition was required and the mixture was stirred overnight. The organic solvent was evaporated, and the residue was made basic with aqueous sodium hydroxide, then extracted three times with ether. The product was isolated in the usual way (0.59 g, 53%); $\bar{\nu}_{max.}$ (CCl_4) 3 600(w), 3 260(m), 2 910(s), 2 850(s), 2 100(w), and 1 450(m) cm^{-1}; τ ($CDCl_3$) 4.05 br (2 H, s) and 7.3—8.7 (14 H, m); resonance at τ 6.85 due to the α-protium compound was not observed.

N-*Nitroso*-N-(2-[2-^{2}H]*adamantyl*)*hydroxylamine*.—This compound was prepared (65%) by the method described above for the protio-analogue: m.p. (CCl_4) 135—136.5 °C; $\bar{\nu}_{max.}$ (KBr) 3 420(m), 3 060(w), 1 450(m), 1 425(m), 1 080(m), 1 050(s), 1 020(m), 960(m), 945(m), 780(m), 710(m), 410(m), and 370(m) cm^{-1}; τ ($CDCl_3$) −2.0 to 0.5 br (1 H, s), 7.35 (2 H, m), and 7.6—8.8 (12 H, m).

2-[2-^{2}H]*Adamantyl Azoxytosylate*.—Aqueous sodium hydroxide (2M; 2 cm^3) was added dropwise over 15 min to a stirred solution of *N*-nitroso-*N*-(2-[2-^{2}H]adamantyl)hydroxylamine (0.39 g, 2.0 mmol) and toluene-*p*-sulphonyl chloride (0.77 g, 4.0 mmol) in acetone (6 cm^3) at 0 °C. Water (4.5 cm^3) was added portionwise over 45 min as the mixture was stirred at 0 °C then a further amount (10 cm^3) was added. The crystalline product was filtered, sucked dry, and recrystallized from ether–dichloromethane at −70 °C (0.61 g, 88%), m.p. 111—112.5 °C; $\bar{\nu}_{max.}$ (KBr) 2 920(s), 2 860(m), 1 600(m), 1 550(m), 1 455(m), 1 390(s), 1 305(m), 1 200(s), 1 190(m), 1 095(m), 910(s), 825(m), 810(sh), 795(m), 765(m), 725(s), 665(m), 565(m), and 550(s) cm^{-1}; τ ($CDCl_3$) 2.4 (4 H, ABq), 7.55 (5 H, m), and 7.7—9.1 (12 H, m); comparison of the integrated signal due to the quartet at τ 2.4 with the vestige of a signal at τ 4.3 showed the deuterium incorporation to be 97.5 ± 0.5%.

2-*Adamantyl Toluene*-p-*sulphonate*.—This compound was prepared from resublimed adamantan-2-ol (0.982 g) and toluene-*p*-sulphonyl chloride (2.53 g) in anhydrous pyridine by the usual Tipson procedure,[47] m.p. (diethyl ether–pentane) 82.3—83.3 °C (lit.,[52] 82.7—83.7 °C).

Solvolytic Conversion of 2-*Adamantyl Azoxytosylate into* 2-*Adamantyl Tosylate*.—(A) *In deuteriochloroform*. (i) A sample of 2-adamantyl azoxytosylate (25 mg) in $CDCl_3$ (0.5 cm^3) in an n.m.r. tube was kept at 60 (±2) °C in an oil-bath. The decrease in intensity of the signal at τ 5.7 and the corresponding increase of a signal at τ 5.3 were monitored by the periodic recording of spectra. After several days, the spectrum was indistinguishable from that of authentic 2-adamantyl toluene-*p*-sulphonate. The half-life of the conversion (the time at which the two signals referred to had equal intensity) was estimated to be 16 h.

(ii) Another sample of 2-adamantyl azoxytosylate (430 mg, 1.23 mmol) dissolved in $CDCl_3$ (6 cm^3) was kept at 65 °C for 3 days. The mixture was cooled and the solvent evaporated to leave an oil (350 mg, 1.14 mmol, 93%) which, upon crystallization from ether–petroleum spirit, was shown by i.r., m.p., and n.m.r. to be 2-adamantyl toluene-*p*-sulphonate.

(B) *In ethanol*. (i) A solution of 2-adamantyl azoxytosylate (0.16 g, 0.46 mmol) in ethanol (5 cm^3) was stirred in an oil-bath at 60—62 °C for 4 days. The solvent was then evaporated and volatile products were removed under vacuum (0.1 Torr at 40 °C for 24 h) to leave an oil which crystallized. Analysis by t.l.c. (silica; CH_2Cl_2–methanol 9:1) indicated one spot close to the origin (R_F < 0.05) and another with R_F (0.7) identical with that of authentic 2-adamantyl toluene-*p*-sulphonate. Recrystallization of the crude product (ether–petroleum spirit at −70 °C) gave crystals identical by m.p., i.r., n.m.r., and t.l.c. with authentic 2-adamantyl toluene-*p*-sulphonate.

(ii) The progress of a reaction of 2-adamantyl azoxytosylate (3 mg) in ethanol (0.5 cm^3) at 60 °C was monitored by t.l.c. (silica F254; 15% ethyl acetate in petroleum spirit, detection by u.v. or by iodine). As the reaction proceeded, portions were removed and tested. The spot due to the azoxytosylate (R_F 0.45) became less intense as that due to 2-adamantyl tosylate (R_F 0.55, checked with an authentic sample) became more so. This established that the t.l.c. method was capable of detecting low concentrations of 2-adamantyl toluene-*p*-sulphonate under our solvolytic conditions.

(C) *In aqueous ethanol*. (i) 90E. The progress of reaction of 2-adamantyl azoxytosylate (4 mg) in 90E (0.5 cm^3) at 60 °C was monitored by t.l.c. as described above. After 4 h, 2-adamantyl tosylate was the major spot and by 15 h it was the only mobile compound detectable by u.v. irradiation.

(ii) 80E. By the same technique, a reaction of substrate (2 mg) in 80E (0.3 cm^3) at 60 °C was monitored. After 70 min, the main spot by u.v. and I_2 development was starting material with a faint spot at the R_F of 2-adamantyl tosylate. After 135 and 205 min, both compounds were weakly but unambiguously detected by u.v. and I_2.

Product Identification from Solvolysis of (**6a**).—Authentic samples of adamantane, adamantan-2-ol, and adamantanone were available to establish g.l.c. analytical conditions.

(1) 97 TFE. Combined reaction mixtures from several kinetics runs (20 cm^3) were extracted between pentane (3 cm^3) and aqueous sodium carbonate. The pentane solution was washed with water and analysed directly by g.l.c. (2 m Apiezon L; 150 °C). A single major peak (*ca.* 95%) was detected corresponding to 2-adamantyl trifluoroethyl ether [g.l.c.–mass spectrometry, low-resolution mode, *m/z* 79 (37%), 92 (40), 134 (100), 135 (26), and 234 ($M^{+\cdot}$, 10); high-resolution mode, *m/z* 234.1215 ($M^{+\cdot}$); $C_{12}H_{17}F_3O$ requires *M*, 234.1231)] and a minor one (*ca.* 5%) with the same retention time as adamantan-2-ol. Very much smaller peaks were detected which, if adamantane and adamantanone, correspond to yields ≤ 0.6% and ≤ 0.4%, respectively.

(2) 97 HFIP. By the same technique as described above, a single major g.l.c. peak due to 2-adamantyl hexafluoropropan-2-yl ether was detected [g.l.c.–mass spectrometry, low-resolution mode, *m/z* 79 (19%), 92 (19), 134 (43), 135 (18), and 302 ($M^{+\cdot}$, 5%); high resolution mode, *m/z* 302.1097 ($M^{+\cdot}$); $C_{13}H_{16}F_6O$ requires *M*, 302.1105)] and a very much smaller peak corresponding to adamantan-2-ol. Upper limits on the possible formation of adamantane and adamantanone are ≤ 1% and ≤ 0.01%, respectively.

(3) 50E. By the same technique as described above, adamantan-2-ol and 2-adamantyl ethyl ether (g.l.c.–mass spectrometry, high-resolution mode, *m/z* 180.1518 ($M^{+\cdot}$); $C_{12}H_{20}O$ requires *M*, 180.1515) were detected. Upper limits on

the possible formation of both adamantane and admantanone were estimated to be ⩽ 1%.

Hexafluoropropan-2-ol.—Hexafluoropropan-2-ol (Fluorochem; 300 g) was fractionally distilled from barium oxide (2 g), b.p. 59 °C. Only the middle cut of a second fractional distillation was used [specific conductivity < 10^{-9} ohm^{-1} cm^{-1} (lit.,[28] 7 × 10^{-9} ohm^{-1} cm^{-1})].

Trifluoroethanol.—Trifluoroethanol (Aldrich Gold Label; 500 g) was boiled under reflux for 2 h over phosphorus pentaoxide (30 g) then distilled, b.p. 73—74 °C. It was then boiled under reflux over calcium hydride (5 g) for 2 h, distilled, then the middle cut of a final fractional distillation was used [specific conductivity *ca.* 5 × 10^{-9} ohm^{-1} cm^{-1} (lit.,[21] 2 × 10^{-8} ohm^{-1} cm^{-1})].

97HFIP, 97TFE, *and* 98.4:1.6 TFE–*Pyridine.*—These were made by mixing 3 parts by weight of water with 97 parts by weight of purified HFIP or TFE, and 1.6 parts by weight of pyridine with 98.4 parts of TFE.

[O-^{2}H]*Hexafluoropropan-2-ol.*—A mixture of anhydrous hexafluoropropan-2-ol (0.5 mol) and deuterium oxide (1 mol) was fractionally distilled slowly and the fraction of b.p. 56—57 °C was collected. This material was mixed with a fresh portion of ^2H_2O on a 1:2 molar basis and fractionally distilled again. After a total of five such cycles, a fraction was collected which, by n.m.r. analysis, showed no trace of O-^{1}H [< 1% $(CF_3)_2CHO^1H$ in the $(CF_3)_2CHO^2H$)] and complete resolution of the septet of the C-H (split only by the 6 fluorines, *J* 6 Hz) is observed.

50E, 80M, 90M, *and* 80E.—The first three of these solvents were made by mixing 50, 80, or 90 parts by weight of ethanol or methanol with 50, 20, or 10 parts by weight of water; 80E was made by mixing 4 volumes of ethanol with 1 volume of water.

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