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SOLVOLYSES OF 4-METHYLENE-2_{ax}- AND -2_{eq}-ADAMANTYL *p*-TOLUENESULPHONATES: INTERMEDIACY OF CLASSICAL CARBOCATION IN THE AXIAL AND π-BRIDGED CARBOCATION IN THE EQUATORIAL *p*-TOLUENESULPHONATE SOLVOLYSES

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The rates and products of solvolyses of 4-methylene-2_{ax}- and -2_{eq}-adamantyl *p*-toluenesulphonates (tosylates) (4a-OTs and 4e-OTs, respectively) were studied. Compound 4a-OTs solvolysed more slowly than 2-adamantyl tosylate (1) in methanol and 2,2,2-trifluoroethanol (TFE) by factors of 2·3 and 2·5, respectively, at 25°C. However, by taking the inductive decelerating effect of a β-methylene substituent into account, the rates were revealed to be enhanced by σ-participation by a factor of 50. The products of solvolyses of 4a-OTs in methanol, 80% acetone and TFE at 100 °C were 2_{ax}- and 2_{eq}-alkoxy(or hydroxy)-4-methyleneadamantanes (4a-OR and 4e-OR, respectively), *exo*-4-alkoxy(or hydroxy)-5-methyleneprotoadamantane (*exo*-5-OR) and 5-[alkoxy(or hydroxy)methyl]-4-protoadamantene (6-OR) with adamantyl to protoadamantyl product ratios of 39:61 (in methanol), 56:44 (in 80% acetone) and 71:29 (in TFE). Despite the nearly symmetric nature of the intermediate cation, the 4a-OR:4e-OR product ratio was essentially constant with 83:17 (in methanol), 85:15 (in 80% acetone) and 82:18 (in TFE). The formation of considerable amounts of 4e-OR was interpreted as showing the intermediacy of a pair of rapidly equilibrating classical ions. The rates of 4e-OTs were 2300–4300 times faster than those expected from inductive electron-withdrawing effect of a β-methylene substituent. The major product (84·5% in methanolysis and 98·7% in trifluoroethanolysis) was 4e-OR accompanied by small amounts of 2-alkoxy-2,4-methanoadamantane (9-OR) and 2-(alkoxymethyl)-2,4-didehydroadamantane (10-OR), no formation of 4a-OR having been observed. These results suggested that 4e-OTs solvolyses via a π-bridged intermediate cation.

INTRODUCTION

2-Adamantyl tosylate (**1**) has been proposed as a typical secondary compound which undergoes limiting S_N1 (k_c) solvolyses.[1] However, it is still controversial whether the carbocation intermediate is σ-bridged (non-classical) or unbridged (classical).[2,3] In most previous studies, experimental results have been interpreted in terms of the bridged cation. Major retention of configuration of the 2-adamantyl product (**2**) with 64–84% (stereoselectivity estimated from solvolyses of 5-methyl-2-adamantyl or 2_{eq}-adamantyl-4_{eq}-*d* substrates),[4,5] formation of a small amount (0·5%) of 4-protoadamantyl product (**3**)[6,7] and a high *exo*/*endo* reactivity ratio of the order of 10^4 in 4-protoadamantyl solvolyses[7] have been taken as evidence for the formation of a highly unsymmetrical, weakly bridged intermediate cation.

Should the intermediate cation be bridged, the extent of bridging may be increased by introducing an electron-donating substituent such as a methyl group to the 1-position of 2-adamantyl substrates. Studies along this line have been extensively done, and the increased formation of 4-methyl-4-protoadamantanol with a 2-adamantyl to 4-protoadamantyl product ratio of 7:3,[8] the increased rate by a factor of 24–38 on introduction of a methyl group to the 1-position,[8] the methyl-d_3 kinetic isotope effect (1·05) in the solvolysis of 1-(methyl-d_3)-2-adamantyl tosylate[9] and the absence (<3%) of both of inverted 1-methyl-2-adamantanol and 4-methyl-*endo*-4-protoadamantanol in hydrolysis[5] have been interpreted as showing increased bridging in

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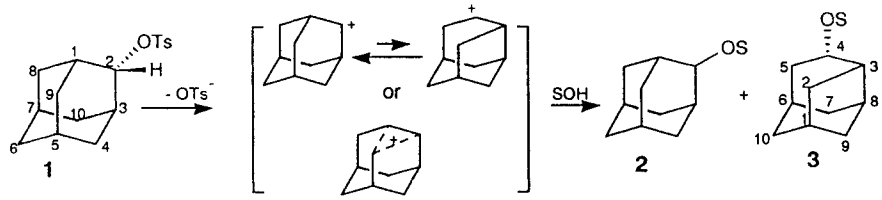
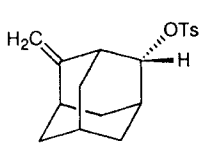


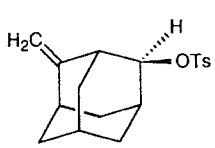
both the transition state and the intermediate. However, the increased rate on introducing the 1-methyl substituent was also explicable on the basis of steric and inductive effects.[10]

On the other hand, recent *ab initio* calculations (6–31G*) indicated a possibility that the 2-adamantyl cation may be neither σ-bridged nor planar, and better described by a rapid equilibrium between two slightly deformed, hyperconjugatively stabilized 2-adamantyl cations which are distinguished by an energy barrier of 2·8 kcal mol^{-1}.[2a] It was suggested that the predominant retention of configuration might be ascribed to the 'memory' of the ground-state configuration in the intermediate cation.[2a] If this is the case, the barrier should be increased by introducing a methyl substituent in the 1-position because of the increased torsional effect between the methyl group and the hydrogen atom at the 2-position. The increased barrier is expected to increase the amount of the retention product, not because of the increased σ-bridging but the extended lifetime of the first-formed cation in solvolysis. However, the significant retention of configuration in the solvolysis of 1-methyl-2-adamantyl tosylate has been ascribed to increased bridging in the intermediate cation.[5]

With such a background, we wished to design a system which would permit nearly symmetric σ-bridging in the intermediate cation (if it were non-classical) *without any substituent on the bridgehead carbon adjacent to the cationic centre.* As a candidate we examined the solvolyses of 4-methylene-2_{ax}- and -2_{eq}-adamantyl tosylates (**4a-OTs** and **4e-OTs**, respectively). The experimental results with respect to **4a-OTs** have been most reasonably interpreted in terms of a pair of rapidly equilibrating classical cations.[11] On the other hand, **4e-OTs** solvolysed by a completely different mechanism, and its solvolytic behaviour was explained on the basis of the formation of a π-bridged cation.



4a-OTs



4e-OTs

RESULTS

Syntheses

4-Methylene-2-adamantanols (**4a-OH** and **4e-OH**) were conveniently prepared in a manner different from a reported method.[12] The Wittig methylenation of the *tert*-butyldimethylsilyl ethers of 4-oxo-2_{ax}- and -2_{eq}-adamantanols[13] followed by desilylation of the produced 4-methylene products afforded the corresponding 4-methylene-2-adamantanols (**4a-OH** and **4e-OH**). The alcohols were converted into the tosylates in the usual manner.

Solvolysis rates

The rates of solvolyses were determined titrimetrically in methanol and 2,2,2-trifluoroethnol (TFE) in the presence of 2,6-lutidine: the results are given in Table 1. All the rate runs followed satisfactory first-order kinetics ($r > 0{\cdot}999$).

Solvolysis products from 4-methylene-2_{ax}-adamantyl tosylate (4a-OTs)

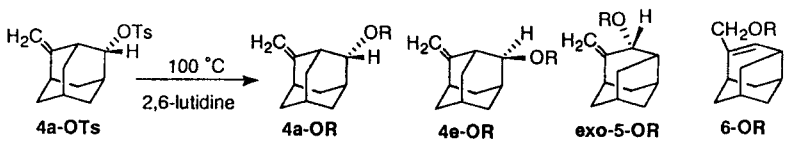
The solvolyses of **4a-OTs** (0·04 M) were conducted in MeOH, 80% acetone and TFE at 100 °C in the presence of excess 2,6-lutidine (0·05 M). In order to minimize possible isomerization and further reactions of kinetic control products, the solvolysis was interrupted at 3·5 half-lives in hydrolysis in 80% acetone and at 5 half-lives in methanolysis and trifluoroethanolysis. In all the solvents, four products, 2_{ax}- and 2_{eq}-alkoxy(or hydroxy)-4-methyleneadamantanes (**4a-OR** and **4e-OR**, respectively), *exo*-4-alkoxy (or hydroxy)-5-methylene-protoadamantane (***exo*-5-OR**) and 5-(alkoxy(or hydroxy) methyl)-4-protoadamantene (**6-OR**), were formed as kinetic control products (Figure 1). The product distributions were determined by GLC and ^{13}C NMR of crude products.

Each component in the crude products was separated or concentrated by medium-pressure liquid chromatography on silica gel and identified by ^{13}C and ^{1}H NMR spectroscopy. Compounds **4a-OMe** and **4e-OMe** were also prepared by methylation of corresponding alcohols **4a-OH** and **4e-OH** and used for identification of methanolysis products. The stereochemistry of

Table 1. Titrimetric rates of solvolyses of 1-adamantyl tosylate (**1**) and 4-methylene-2_{ax}- and -2_{eq}-adamantyl tosylates (**4a-OTs** and **4e-OTs**, respectively)

Compound	Solvent	Temperature (°C)	k_1 (s^{-1})[a]	Relative rates at 25 °C: MeOH	Relative rates at 25 °C: TFE	$\Delta H‡$ (kcal mol^{-1})	$\Delta S‡$ (e.u.)
1	MeOH	25	$2{\cdot}90 \times 10^{-9}$ [b]	1·0			
	TFE	25	$1{\cdot}51 \times 10^{-6}$ [b]		1·0		
4a-OTs	MeOH[c]	25	$1{\cdot}27 \times 10^{-9}$ [d]	0·44		29·5	−0·4
		75	$1{\cdot}86 \times 10^{-6}$				
		100	$3{\cdot}42 \times 10^{-5}$				
	TFE[c]	25	$6{\cdot}13 \times 10^{-7}$		0·41	21·1	−16·0
		35	$2{\cdot}28 \times 10^{-6}$				
		50	$1{\cdot}06 \times 10^{-5}$				
4e-OTs	MeOH[c]	25	$4{\cdot}64 \times 10^{-8}$ [d]	16		27·7	0·9
		50	$1{\cdot}88 \times 10^{-6}$				
		75	$4{\cdot}46 \times 10^{-5}$				
	TFE[c]	25	$4{\cdot}59 \times 10^{-5}$		30	20·4	−10·0
		40	$2{\cdot}50 \times 10^{-4}$				

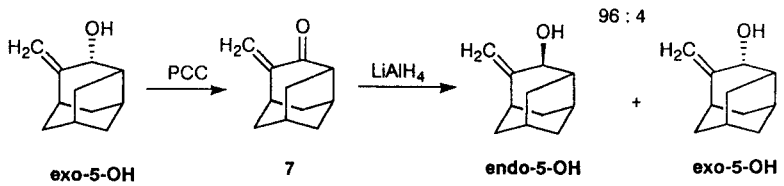
[a] Determined in a single run. In all cases the correlation coefficient for the first-order plot was greater than 0·999 within an experimental error of ±2%.
[b] See Ref. 1b.
[c] The concentrations of substrate and 2,6-lutidine were $2{\cdot}5 \times 10^{-3}$ and 5×10^{-3} M, respectively.
[d] Extrapolated from data at higher temperatures.



	4a-OR	4e-OR	exo-5-OR	6-OR
In MeOH, R=Me	32.5	6.6	49.8	11.1
In 80% acetone, R=H	47.0	8.6	41.7	2.7
In TFE, R=CF_3CH_2	58.0	13.0	28.3	0.7

Figure 1. Product distributions (%) in the solvolyses of **4a-OTs**

***exo*-5-OH** was verified by ^1H NMR NOE difference experiments (see Experimental). The essential absence (<0·1%) of ***endo*-5-OH** in the solvolysis product was shown by comparing the ^1H NMR spectrum of the product with that of ***endo*-5-OH** that was unambiguously prepared as major product (*endo* : *exo* = 96 : 4) by $LiAlH_4$ reduction of 5-methylene-4-protoadamantanone (**7**) (Scheme 1). ***exo*-5-OMe** and ***exo*-5-OTFE** were identified on the basis of marked similarities of their NMR spectra to that of ***exo*-5-OH**. Assignment of the structure of **6-OMe** rests on ^1H NMR (270 MHz) signals of two nonequivalent methy-



Scheme 1

Table 2. Selected ^{13}C NMR ($CDCl_3$) chemical shift data of adamantyl (**4**), protoadamantyl (**5**) and 2,4-methanoadamantyl (**9**) products

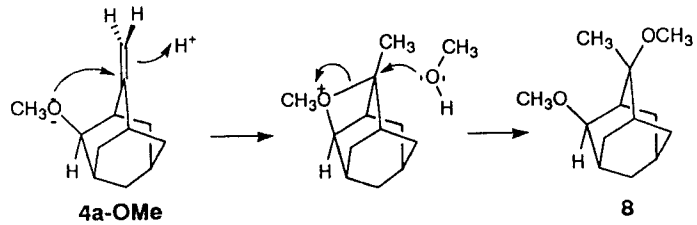
Compound	Olefinic	Methine	Methylene	Others
4a-OH[a,b]	105·5, 153·2	26·6, 34·2, 38·0, 45·8, 74·9	33·4, 35·7, 37·7, 38·6	
4a-OMe[c]	103·6, 154·0	27·3, 33·2, 38·2, 42·5, 84·4	31·0, 36·0, 38·2, 39·3	55·2 (OCH_3)
4e-OH[a,b]	103·0, 155·4	27·3, 34·0, 37·5, 45·3, 74·3	30·4, 32·5, 36·5, 39·0	
4e-OMe[a,c]	103·0, 155·5	27·3, 31·3, 38·0, 42·2, 83·3	30·9, 33·0, 36·5, 39·1	55·4 (OCH_3)
4e-OTFE[c]	103·7, 154·8	27·2, 31·6, 37·8, 42·6, 83·6	30·8, 32·9, 36·4, 39·0	65·7 (q, $J = 34$ Hz), 124·2 (q, $J = 278$ Hz)
***exo*-5-OH**[c]	114·0, 155·9	31·4, 35·3, 37·2, 39·4, 74·5	32·2, 36·0, 40·5, 42·5	
***exo*-5-OMe**[c]	115·2, 149·9	31·4, 35·3, 37·0, 37·9, 83·4	31·8, 35·4, 41·1, 42·3	55·5 (OCH_3)
9-OMe[a,c]		25·6, 28·4, 29·6, 34·7, 42·4	30·7, 31·5, 32·3, 34·5, 34·6	50·5 (OCH_3), 79·0 (quart C)

[a] Agreed well with data in Ref. 12.
[b] Rccorded at 22·5 MHz.
[c] Recorded at 67·8 MHz.

Table 3. Selected ^1H NMR ($CDCl_3$) chemical shift data of adamantyl (**4**, **8**), protoadamantyl (**5**), protoadamantenyl (**6**), 2,4-methanoadamantyl (**9**) and 2,4-didehydroadamantyl (**10**) products

Compound	Olefinic proton	Other protons
4a-OH[a,b]	4·77 (d, 1H, $J = 2·3$ Hz) 4·67 (d, 1H, $J = 2·3$ Hz)	1·3–2·2 (m, 11H), 2·44 (br s, 2H), 3·88 (br s, 1H)
4a-OMe[c]	4·65 (d, 1H, $J = 2·2$ Hz) 4·58 (d, 1H, $J = 2·2$ Hz)	1·3–2·3 (m, 10H), 2·42 (br s, 1H), 2·62 (br s, 1H), 3·33 (s, 3H), 3·43 (br s, 1H)
4a-OTFE[c,d]	4·67 (d, 1H, $J = 2·2$ Hz) 4·58 (d, 1H, $J = 2·2$ Hz)	3·69 (br s, 1H)
4e-OH[a,b]	4·60 (s, 2H)	1·4–2·7 (m, 13H), 3·84 (br s, 1H)
4e-OMe[c]	4·59 (s, 2H)	1·50 (m, 2H), 1·61 (m, 1H), 1·70–1·86 (m, 3H), 1·90 (m, 1H), 2·03–2·20 (m, 3H), 2·42 (br s, 1H), 2·63 (br s, 1H), 3·28 (br s, 1H), 3·35 (s, 3H)
4e-OTFE[c]	4·61 (s, 2H)	1·48–1·66 (m, 3H), 1·70–1·88 (m, 3H), 1·92 (m, 1H), 2·04–2·25 (m, 3H), 2·43 (br s, 1H), 2·62 (br s, 1H), 3·52 (br s, 1H), 3·84 (q, 2H, $J = 8·8$ Hz)
***exo*-5-OH**[c]	5·03 (s, 1H), 5·00 (s, 1H)	1·18 (m, 1H), 1·40 (m, 1H), 1·46–1·56 (m, 2H), 1·63–1·90 (m, 4H), 2·07–2·19 (m, 2H), 2·31 (br q, 1H, $J = 6·1$ Hz), 2·54 (m, 1H), 2·59 (br s, 1H), 4·33 (d, 1H, $J = 3·6$ Hz)
***exo*-5-OMe**[c,d]	5·10 (br s, 1H) 4·92 (br s, 1H)	1·2–2·8 (m, 12H), 3·28 (s, 3H), 3·72 (d, 1H, $J = 3·8$ Hz)
***exo*-5-OTFE**[c,d]	5·17 (s, 1H), 4·94 (s, 1H)	3·99 (d, 1H, $J = 3·9$ Hz)
6-OH[c,d]	6·08 (d, 1H, $J = 8$ Hz)	4·05 (br s, 2H)
6-OMe[c,d]	6·10 (d, 1H, $J = 6·8$ Hz)	1·2–2·8 (m, 12H), 3·29 (s, 3H), 3·81 (dd, 1H, $J = 12·0$, 1·2 Hz), 3·85 (dd, 1H, $J = 12·0$, 1·2 Hz)
6-OTFE[c,d]	6·17 (d, 1H, $J = 7·2$ Hz)	
8[c]		1·3–2·3 (m, 12H), 1·38 (s, 3H), 3·17 (s, 3H), 3·32 (s, 3H), 3·48 (br s, 1H)
9-OMe[b,c]		1·2–2·3 (m, 15H), 3·15 (s, 3H)
10-OMe[c,d]		3·27 (s, 3H)

[a] Recorded at 89·55 MHz.
[b] Agreed well with data in Ref. 12.
[c] Recorded at 270·05 MHz.
[d] Determined for a product mixture from solvolysis.



Scheme 2

lene protons of the $MeOCH_2$ group at δ 3·81 (dd, $J = 12·0$, 1·2 Hz) and 3·85 (dd, $J = 12·0$, 1·2 Hz) and an olefinic proton at δ 6·10 (d, $J = 6·8$ Hz). Pertinent NMR data are summarized in Tables 2 and 3.

Although the products of solvolysis in 80% acetone and TFE were stable under the reaction conditions, only in methanolysis did the once-formed **4a-OMe** slowly undergo acid-catalysed addition of methanol to the double bond to give a dimethoxy compound, most probably $2_{eq},4_{ax}$-dimethoxy-2-methyladamantane (**8**), even in the presence of 2,6-lutidine, presumably assisted by methoxy participation as shown in Scheme 2. Therefore, the yield of **4a-OMe** given in Figure 1 includes the yield (2·9%) of **8**. In addition, a small amount (0·2%) of 2-methoxy-2,4-methanoadamantane (**9-OMe**) was formed, presumably from once-formed **4e-OMe** (see below).

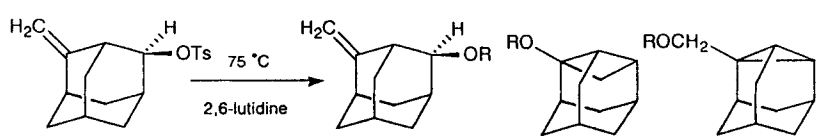
Solvolysis products from 4-methylene-2_{eq}-adamantyl tosylate (4e-OTs)

Solvolyses of **4e-OTs** (0·04 M) were conducted at 75 °C in MeOH and TFE in the presence of excess 2,6-lutidine (0·05 M), and the product distributions were determined by GLC and ^{13}C NMR spectroscopy. The product was composed of only three components, 2_{eq}-alkoxy-4-methyleneadamantane (**4e-OR**), 2-alkoxy-2,4-methanoadamantane (**9-OR**) and 2-(alkoxymethyl)-2,4-didehydroadamantane (**10-OR**). The identification of **9-OR** and **10-OR** rests upon agreement of the NMR data with those for **9-OMe** and **10-OMe** reported by Majerski and Majerski.[12] Pertinent NMR data are summarized in Tables 2 and 3. The formation of 2_{ax}-alkoxy-4-methyleneadamantane (**4a-OR**) was not observed to the limit of detection (0·3%). Although the product distribution in trifluoroethanolysis was essentially constant during solvolysis, that in methanolysis slightly changed in the course of solvolysis: **4e-OMe** slowly isomerized to **9-OMe**. Therefore, the product distribution at $t = 0$ was estimated by extrapolating those at 3·1, 4·8 and 11·2 half-lives. The results are given in Figure 2.

DISCUSSION

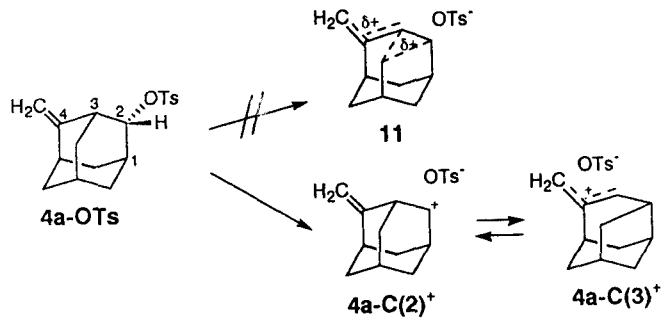
Structure of intermediate cation in the solvolyses of 4a-OTs

The rates of solvolyses of **4a-OTs** were slower than those of 2-adamantyl tosylate (**1**) by factors of 2·3 and 2·5 in methanol and TFE, respectively, at 25 °C. These decelerations would be attributed to the electron-withdrawing effect of the methylene substituent. However, the decelerating effect is small compared with that of the methylene substituent of 3-methylenebicyclo[2.2.2]oct-1-yl triflate: the rate of 3-methylene-



In MeOH, R=Me	(t = 0	84.5	15.0	0.5)[a]
	3.1 half-lives	83.1	16.4	0.5
	4.8 half-lives	82.1	17.3	0.6
	11.2 half-lives	79.4	20.2	0.4
In TFE, R=CF_3CH_2	10 half-lives	98.7	0.8	0.5

Figure 2. Product distributions (%) in the solvolyses of **4e-OTs**. [a]Extrapolated values



Scheme 3

bicyclo[2.2.2]oct-1-yl triflate is 142 times slower than that of parent bicyclo[2.2.2]oct-1-yl triflate in 80% ethanol at 25 °C.[14] Therefore, it would be sound to conclude that the rate of solvolysis of **4a-OTs** is approximately 50 times faster than that predicted on the basis of the electron-withdrawing effect of the methylene substituent. The net acceleration suggests the delocalization of the developing positive charge in the transition state to C-3 and further to the methylene substituent through allylic conjugation. However, the charge delocalization in the transition state does not necessarily indicate the intermediacy of a σ-bridged cation as depicted by **11**. As discussed below, the product study rather suggested the intermediacy of a pair of rapidly equilibrating classical cations **4a-C(2)**$^+$ and **4a-C(3)**$^+$ (Scheme 3).

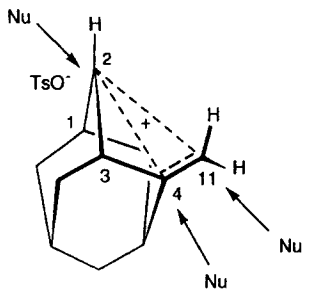
The ratios between the products with adamantyl structure and those with protoadamantyl structure are 39:61 in methanolysis, 56:44 in hydrolysis in 80% acetone and 71:29 in trifluoroethanolysis. Therefore, should the intermediate cation be bridged, the extent of σ-bridging would be nearly symmetric, leading to predominant formation of retention products. In reality, however, considerable amounts of equatorial (rear-side attack) product were formed with essentially constant axial to equatorial ratios in the adamantyl product, i.e. 83:17 (in MeOH), 85:15 (in 80% acetone) and 82:18 (in TFE). The similar axial to equatorial product ratios between methanolysis and trifluoroethanolysis indicate that a k_s process is unimportant. The equatorial stereoselectivity of 15–18% despite the advanced symmetric nature of the intermediate cation would be more reasonably explained in terms of a classical ion **4a-C(2)**$^+$ than assuming a non-classical ion **11**.

It might be argued that the non-classical ion as shown by **11** should not exist since delocalization of positive charge to the methylene substituent permits the existence of an allylic cation **4a-C(3)**$^+$ (Scheme 3). However, such an argument favouring the existence of **4a-C(3)**$^+$ on the one hand results in the support of intermediacy of a classical ion **4a-C(2)**$^+$ on the other. Nevertheless, the present conclusion should not generally be applied to all 2-adamantyl cations. At least, the results obtained in the solvolyses of **4a-OTs** suggest a possibility that a stabilizing substituent on the C-1 bridgehead position allows the 1-substituted 2-adamantyl cation to exist as a classical ion, as pointed out by Fărcaşiu.[10]

Structure of intermediate cation in the solvolyses of 4e-OTs

The solvolytic behaviour of 4-methylene-2$_{eq}$-adamantyl tosylate (**4e-OTs**) was markedly different from that of **4a-OTs** with respect to both the rates and products. The rate of **4e-OTs** was faster than parent 2-adamantyl tosylate (**1**) in both of MeOH and TFE by factors of 16 and 30 respectively, (Table 1). If we employ 1/142 as the inductive decelerating effect of a β-methylene group,[14] the observed rates are evaluated to be enhanced by a factor of 2300 or 4300. In addition to the enhanced rates, **4e-OTs** showed product distributions which were markedly different from those of **4a-OTs**. For example, in methanolysis, **4a-OTs** gave **4a-OMe** (32·5%), **4e-OMe** (6·6%), ***exo*-5-OMe** (49·8%) and **6-OMe** (11·1%), whereas **4e-OTs** afforded **4e-OMe** (84·5%), **9-OMe** (15·0%) and **10-OMe** (0·5%) (see Figures 1 and 2). It is noted that **4e-OTs** gave only the retention product **4e-OMe**, no inversion product **4a-OMe** having been detected. These results from rate and product studies are reasonably explained in terms of π-participation by the methylene group in ionization and the formation of a π-bridged cation as depicted by **12**. The attack of a solvent molecule on the C-2, C-4 or C-11 of **12** can explain the formation of retention product **4e-OR**, a 2,4-methanoadamantane **9-OR** or a 2,4-didehydroadamantane **10-OR**, respectively.

These products have been observed to form in the reaction of 2,4-methano-2,4-didehydroadamantane (**13**) with AcOH, MeOH, and HCl in benzene via the same π-bridged intermediate as proposed in this work (Scheme 4).[12]



12

Compound **4e-OTs** is structurally similar to 3-β-cholesteryl tosylate (**14**), which showed a relative rate with respect to cyclohexyl tosylate of 100 in actolysis at 50 °C and gave a product with complete retention of configuration via a homoallylic cation (**15**) (Scheme 5).[15] However, π bridging in the intermediate cation **12** from **4e-OTs** appears to be more advanced than in **15** for geometric reasons. Advanced π bridging in **15** would cause severe strain of the ring containing $C_\gamma = C_\delta$ because the spatial distance between C_α and C_δ has to be shortened. This notion is supported by the formation of the four-membered ring product **9-OR** from **4e-OTs**, which was not the case in the solvolysis of **14**.

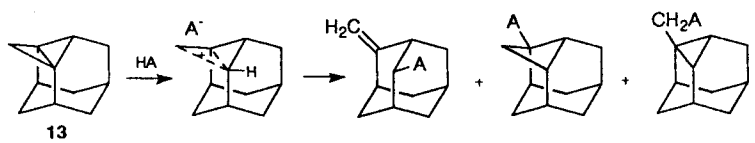
Absence of interconversion between 4a-OTs and 4e-OTs and between their ion-pair intermediates

The rate ratio **4e-OTs**/**4a-OTs** was 37 (in MeOH) or 75 (in TFE) at 25 °C. Moreover, both **4a-OTs** and **4e-OTs** showed good first-order kinetics. If there had been interconversion between the two isomeric tosylates, a curved first-order plot would have been obtained.[16] In addition, the pattern of the product distribution was characteristic of the substrate: **4a-OR**, **5-OR** and **6-OR** were solely formed from **4a-OTs**, and **9-OR** was only formed from **4e-OTs**. These results suggest that the equilibrating pair of ion-pair intermediates [**4a-C(2)** $^+ \rightleftharpoons$ **4a-C(3)**$^+$] OTs^- (Scheme 3) is not transformed into the π-bridged ion **12**, and vice versa. The absence of interconversion at the intermediate stage also suggests that the ionization does not proceed to free-ion stage even in TFE.

EXPERIMENTAL

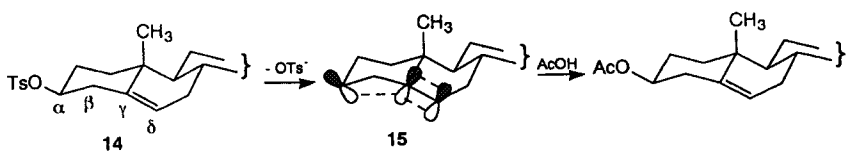
Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 1640 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-FX90A (89·55 MHz) or a JEOL GSX-270 (270·05 MHz) spectrometer with TMS as internal standard. GLC analyses were conducted on a Hitachi 163 gas chromatograph equipped with a flame ionization detector and a Hitachi D-2500 integrator. Medium-pressure liquid chromatography (MPLC) was carried out on Merck silica gel (230–400 mesh). TFE was stored over 5 Å molecular sieves and distilled. Methanol was distilled from sodium methoxide. The other solvents used for syntheses were dried by standard methods. Elemental analyses were performed by the Microanalytical Centre, Kyoto University.

4-Methylene-2$_{ax}$-adamantanol (***4a-OH***). To a mixture of 4_{ax}-hydroxy-2-adamantanone[13] (2·95 g, 17·7 mmol) and 2,6-lutidine (4·2 ml, 36 mmol) in anhydrous CH_2Cl_2 (18 ml) was added *tert*-butyldimethylsilyl triflate (5·1 ml, 22 mmol) at room temperature. After stirring for 90 min, the reaction mixture was washed at 0 °C with H_2O, 10% HCl, saturated $NaHCO_3$ and 10% NaCl solutions and dried ($MgSO_4$). Evaporation of the solvent gave the *tert*-butyldimethylsilyl ether as yellow crystals (4·62 g, 93%), which was shown by ^{13}C NMR to be contaminated by 8% of the equatorial isomer.



13

Scheme 4. HA = HOAc, HCl or HOMe



14 15

Scheme 5

The silyl ether mixture (4·60 g, 16·4 mmol) was treated at 70 °C for 35 min with Ph_3PCH_2 generated from Ph_3PCH_3Br (17·8 g, 49·8 mmol) and NaH in DMSO.[17] The reaction mixture was poured into ice–water and extracted with diethyl ether. The ether extract was washed with saturated NaCl and dried ($MgSO_4$). Evaporation of the ether followed by MPLC (SiO_2) gave the *tert*-butyldimethylsilyl ether of **4a-OH** (**4a-OTBMS**) contaminated by 8% of **4e-OTBMS**; 3·77 g, yield 83%. The silyl ether mixture (3·77 g, 13·5 mmol) was heated in 1 M Bu_4NF solution in THF (27 ml) at 50 °C for 21 h. The reaction mixture was mixed with 5% NH_4Cl (80 ml) with vigorous stirring, extracted with diethyl ether and the ether extract was washed with H_2O, 20% NH_4Cl, 10% NaCl and dried ($MgSO_4$). The ether was evaporated and the crude product was purified by MPLC [SiO_2–7% $AgNO_3$, hexane–diethyl ether (7 : 3)] to give **4a-OH** (1·46 g, 66%), m.p. 189·5–190·0 °C (from hexane) (lit.[12] 162–165 °C). All the spectral data agreed with reported data.[12]

4-Methylene-2$_{eq}$-adamantanol (***4e-OH***). 4_{eq}-Hydroxyl-2-adamantanone[13c] was converted into **4e-OH** similarly to the preparation of **4a-OH** in an overall yield of 64%, m.p. 174·0–174·5 °C (from hexane) (lit.[12] 168–171 °C). All the spectra data agreed with reported data.[12]

4-Methylene-2$_{ax}$-adamantyl tosylate (***4a-OTs***). To a solution of **4a-OH** (2·98 g, 18·1 mmol) in pyridine (33 ml) was added *p*-toluenesulphonyl chloride (6·95 g, 36·5 mmol) over 10 min at 0 °C and the mixture was stored for 10 days at 10 °C. The reaction mixture was poured into ice and extracted with diethyl ether. The ether extract was washed with 5% HCl and H_2O and dried ($MgSO_4$). Evaporation of the solvent followed by recrystallization of the residue afforded **4a-OTs** as colourless crystals (4·70g, 81·3%), m.p. 74·0–74 ·5 °C (from hexane). IR (CCl_4): 2924, 2857,1663, 1600, 1496, 1451, 1371, 1178 cm^{-1}. ^1H NMR (89·55 MHz, $CDCl_3$): δ 1·4–2·2 (m, 10 H), 2·42 (s, 3 H, CH_3), 2·49 (br s, 2 H), 4·43 (d, 1 H, J = 2·0 Hz), 4·64 (d, 1 H, J = 2·0 Hz), 4·75 (br s, 1 H), 7·31 (d, 2 H, J = 8·5 Hz), 7·78 (d, 2 H, J = 8·5 Hz). ^{13}C NMR (22·5 MHz, $CDCl_3$): δ 150·7 (C=CH_2); 105·3 (C=CH_2); 21·2, 127·1, 129·3, 134·7, 144·0 ($CH_3C_6H_4$); 26·3, 32·5, 37·3, 42·9, 86·0 (CH); 32·6, 35·7, 37·9, 38·5 (CH_2). Analysis: calculated for $C_{18}H_{22}O_3S$, C 67·89, H 6·96; found, C 67·83, H 7·08%.

4-Methylene-2$_{eq}$-adamantyl tosylate (***4e-OTs***). The method used for the preparation of **4a-OTs** was employed except that the reaction mixture was allowed to stand for 4 weeks at 10 °C. Since **4e-OTs** did not crystallize at room temperature, the crude tosylate was purified by MPLC [SiO_2, hexane–diethyl ether (9 : 1)] to afford a colourless liquid; yield 90%. IR (CCl_4): 2930, 2862, 1657, 1600, 1496, 1450, 1373, 1179 cm^{-1}. ^1H NMR (89·55 MHz, $CDCl_3$): δ 0·8–2·6 (m, 12 H), 2·42 (s, 3 H, CH_3), 4·5–4·7 (3 H, =CH_2 and H-2 overlapped), 7·32 (d, 2 H, J = 8·1 Hz), 7·80 (d, 2 H, J = 8·1 Hz). ^{13}C NMR (22·5 MHz, $CDCl_3$): δ 152·7 (C=CH_2); 104·8 (C=CH_2); 21·2, 127·1, 129·4, 134·4, 144·1 ($CH_3C_6H_4$); 26·5, 32·1, 36·8, 43·1, 84·7 (CH); 30·3, 32·6, 36·0, 38·3 (CH_2). Analysis: calculated for $C_{18}H_{22}O_3S$, C 67·89, H 6·96; found, C 67·96, H 6·93%.

Products of methanolysis; typical procedure. A methanol solution (25·0 ml) containing **4a-OTs** (318 mg, 1·00 mmol) and 2,6-lutidine (0·0500 M) was divided into five 5 ml portions in ampoules and heated at 100 °C. At intervals the solution in an ampoule was transferred into a flask and most of the methanol evaporated. To the residue was added CH_2Cl_2 (24 ml) and the solution was washed at 0 °C with water (10 ml), 10% HCl (2 × 10 ml), 10% NaCl (10 ml) and saturated $NaHCO_3$ solution (10 ml) and dried ($MgSO_4$). The solvent was evaporated and the residual colourless oil was subjected to GLC (PEG 20M, 2 m × 3 mm i.d. column, programmed at 2 °C min^{-1} from 150 to 200 °C) and NMR (^1H 270·05 MHz; ^{13}C 67·8 MHz) analyses. The GLC peaks were assigned by comparing the percentage compositions with ^{13}C NMR signal intensities. The results are summarized in Figures 1 and 2.

2$_{ax}$- and 2$_{eq}$-methoxy-4-methyleneadamantanes (***4a-OMe and 4e-OMe***) *by methylation of 4a-OH and 4e-OH.* A mixture containing **4a-OH** and **4e-OH** in a ratio of 10 : 1 (107 mg, 0·651 mmol) and iodomethane (0·16 ml, 2·6 mmol) were dissolved in DMSO. To this solution was added KOH (0·15 g, 2·7 mmol) and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured into water (30 ml) and extracted with pentane (3 × 10 ml). The combined extract was washed with water (3 × 10 ml) and dried ($MgSO_4$). Evaporation of the solvent afforded a colourless liquid (105 mg), which was found by ^1H NMR to contain **4a-OMe**, **4e-OMe**, **4a-OH** and **4e-OH** in a molar ratio of 61·4 : 8·3 : 29·0 : 1·3. On GLC (PEG 20M) analysis, **4e-OMe** and **4a-OMe** eluted in that sequence.

Identification of 2-methoxy-2,4-methanoadamantane (***9-OMe***) *and 2-(methoxymethyl)-2,4-didehydroadamantane* (***10-OMe***). A product mixture in the methanolysis of **4e-OTs** was chromatographed by MPLC (SiO_2) to afford two fractions, the first fraction containing **4e-OMe** and the second consisting of **4e-OMe** (4·4%), **10-OMe** (12·3%) and **9-OMe** (83·3%). The latter fraction was subjected to ^{13}C NMR (67·8 MHz) and

4e-OMe and **9-OMe** were identified by comparing the ^{13}C NMR δ values with reported data.[12]

Products of hydrolysis; typical procedure. Compound **4a-OTs** (500 mg, 1·57 mmol) was dissolved in 80% acetone (39·3 ml) containing 0·050 M 2,6-lutidine and the resulting solution was heated in ampoules for 28 h (3·5 half-lives) at 100 °C. From the reaction solution was evaporated the acetone and the residue was extracted with CH_2Cl_2. By the usual procedure, the product mixture was obtained as a colourless semi-solid (330 mg), which was subjected to GLC (PEG 20M, 2 m × 3 mm i.d. column, programmed at 2 °C min^{-1} from 150 to 200 °C) and NMR analyses for composition determinations.

*Isolation of 5-methylene-*exo*-4-protoadamantanol (**exo-5-OH**).* From the hydrolysis product of **4a-OTs** was isolated ***exo*-5-OH** by MPLC [SiO_2–7% $AgNO_3$, hexane–diethyl ether (95:5)], m.p. 176·5–177·5 °C (from hexane). ^{13}C and ^1H NMR data are shown in Tables 1 and 2. Analysis: calculated for $C_{11}H_{16}O$, C 80·44, H 9·82; found C 80·48, H 10·11%. 3,5-Dinitrobenzoate, m.p. 149·5–150·5 °C. IR (CCl_4): 3103, 2941, 2870, 1731, 1629, 1549, 1457, 1343, 1273, 1163, 922 cm^{-1}. ^1H NMR (89·55 MHz, $CDCl_3$): δ 1·0–2·9 (m, 12 H), 5·22 (s, 1 H), 5·33 (s, 1 H), 5·83 (d, 1 H, J = 3·7 Hz), 9–9·5 (m, 3 H). ^{13}C NMR (22·5 MHz, $CDCl_3$): δ 161·9 (C=CH_2); 118·3 (=CH_2); 122·0, 129·2, 134·7, 148·5, 149·5 [—$OCOC_6H_3(NO_2)_2$]; 31·7, 35·3, 36·8, 37·6, 78·3 (CH); 32·4, 35·7, 40·3, 42·2 (CH_2). Analysis: calculated for $C_{18}H_{18}N_2O_6$, C 60·33, H 5·06; found, C 60·12, H 5·12%. The *exo* configuration of ***exo*-5-OH** was determined by ^1H NMR NOE difference experiments. When *endo*-2-H was irradiated, the 4-H signal was enhanced by 5·9% and when 4-H was irradiated, the *endo*-2-H signal was enhanced by 6·6%.

*5-Methylene-4-protoadamantanone (**7**).* To a suspension of pyridinium chlorochromate (113 mg, 0·524 mmol) in CH_2Cl_2 (0·6 ml) was added a solution of ***exo*-5-OH** (52 mg, 0·32 mmol) in CH_2Cl_2 (0·6 ml), and the mixture stirred under N_2 at room temperature for 4 h. Diethyl ether (1 ml) was added and the solution was passed through a column of Florisil (1·0 g). The tarry residue was extracted with diethyl ether (4 × 1 ml), and the extracts were worked up similarly. The solvent was evaporated and the residual oil was purified by MPLC [SiO_2, hexane–diethyl ether (9:1)] to give 5-methylene-4-protoadamantanone (**7**) as a colourless oil. IR (liquid film): 2928, 1701, 1629, 1294, 1017 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$): δ 1·58–1·82 (m, 6H), 1·95–2·09 (m, 2H), 2·39 (m, 1H), 2·65 (m, 1H), 2·79–2·91 (m, 2H), 5·14 (d, 1H, J = 1·8 Hz), 5·91 (d, 1H, J = 1·8 Hz). ^{13}C NMR (67·8 MHz, $CDCl_3$): δ 150·3, 204·4 (C), 36·6, 37·2, 38·3, 49·2 (CH), 34·4, 38·6, 38·8, 41·5, 117·5 (CH_2). Analysis: calculated for $C_{11}H_{14}O$, C 81·44, H 8·70; found, C 81·17, H 8·75%.

*Reduction of 5-methylene-4-protoadamantanone (**7**) with $LiAlH_4$.* 5-Methylene-4-protoadamantanone (**7**) (14 mg, 0·088 mmol) was treated with $LiAlH_4$ (5·1 mg, 0·13 mmol) in dry diethyl ether (0·5 ml). The usual work-up of the reaction mixture gave 14 mg of a colourless oil, which was shown by ^1H NMR to consist of two products in a ratio of 96:4, the minor one being ***exo*-5-OH**. The major component was identified as 5-methylene-*endo*-4-protoadamantanol (***endo*-5-OH**) from NMR data. ^1H NMR (270 MHz, $CDCl_3$): δ 1·36–1·75 (m, 8H), 1·83 (m, 1H), 2·16 (br s, 1H), 2·41 (m, 2H), 2·65 (br s, 1H), 4·43 (br d, 1H, J = 4·6 Hz), 4·98 (m, 1H), 5·13 (t, 1H, J = 1·1 Hz). ^{13}C NMR (67·8 MHz, $CDCl_3$): δ 156·0 (C), 34·7, 35·4, 38·5, 40·7, 70·5 (CH), 31·2, 32·7, 41·0, 41·6, 108·5 (CH_2).

Products of trifluoroethanolysis; typical procedure. To a 5·00 ml of a solution of 0·0500 M 2,6-lutidine in TFE which had been heated to 75·0 °C in a constant-temperature bath was added **4e-OTs** (63·7 mg, 0·200 mmol), and the solution kept at 75·0 °C for 20 min (12·9 half-lives). Most of the TFE was rotary evaporated, the residue was dissolved in CH_2Cl_2 and the solution was worked up in the usual manner to give a colourless oil (36·4 mg), which was subjected to GLC (PEG 20M, 2 m × 3 mm i.d. column, programmed at 2 °C min^{-1} from 150 to 200 °C) and NMR analyses.

Kinetic method. The titration method has been described previously.[18] All the rates at 25 °C were determined by the pipetting out method, whereas those of methanolysis at 50, 75 and 100 °C were measured by using ampoules. The ampoule method caused significant titration errors in trifluoroethanolysis, probably because of the formation of HF on sealing the ampoules. Therefore, the reaction was conducted in a 50 ml long-necked flask equipped with a septum cap, and a sample was withdrawn by means of a syringe.

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