An unstrained homoallylic secondary adamantyl toluene-*p*-sulfonate solvolyses with σ-bond migration to give a protoadamantyl substituted allylic carbenium ion

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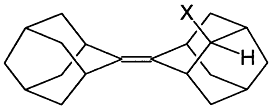
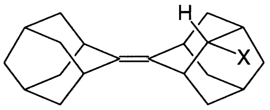
The aqueous ethanolysis of 4-adamantylidene-2$_{ax}$-adamantyl toluene-*p*-sulfonate (tosylate) (1a–OTs) shows a sensitivity (*m* value) of 0.86 ± 0.05 to the ionizing power of the solvent. 1a–OTs reacts approximately 4.7-fold faster than 2-adamantyl tosylate in 80 : 20 v/v ethanol–water at 25 °C. The solvolysis reactions of 1a–OTs result in complete (>95%) rearrangement of the substituted adamantyl ring into a protoadamantyl ring *via* a solvent-equilibrated allylic carbenium ion intermediate. The extrapolated α-secondary deuterium kinetic isotope effect for solvolysis of 1a–OTs in 60 : 40 v/v ethanol–water at 25 °C is 1.16 ± 0.02, while comparable values for solvolysis of the epimeric 2$_{eq}$ tosylate 1e–OTs measured in several ethanol–water mixtures at 25 °C fall in the range 1.14–1.17. These results are consistent with a 1a–OTs solvolysis reaction transition state that involves concerted σ-bond participation and departure of the tosylate leaving group.

Introduction

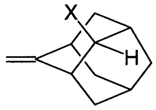
Recent results have shown that the homoallylic adamantylideneadamantyl tosylate (**1e–OTs**) solvolyses between 2 × 10^5 and 4 × 10^6 faster than 2-adamantyl tosylate in reactions run at 25 °C in various aqueous solvent mixtures of methanol, ethanol, propan-2-ol or acetone.[1] A reduction of approximately 7.7 kcal mol^{-1} (1 cal = 4.184 J) in the activation enthalpy ($\Delta H^{\ddagger}$) for the solvolysis in 80% ethanol–water accounts for the observed rate acceleration that occurs upon addition of the homoallylic adamantylidene group.[1] In a similar study by Takeuchi *et al.*, solvolysis of the methylidene-substituted adamantyl tosylate **2e–OTs** in both methanol and trifluoroethanol gave the much smaller rate accelerations of 16 and 30, respectively.[2] Aqueous ethanolysis of **1e–OTs** yields **1e–OH** and **1e–OEt**, two products that are formed with complete retention of stereochemistry.[1] Based on this stereochemical result, the solvolysis of **1e–OTs** was proposed to proceed through the homoallylic carbenium ion **3–Ad**. Similarly, the three products **2e–OCH$_3$**, **6–OCH$_3$** and **7–OCH$_3$** formed in the methanolysis of **2e–OTs** are consistent with this reaction proceeding *via* the homoallylic carbenium ion **3–CH$_2$** (Scheme 1).[2]



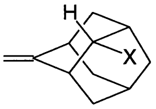
1a
X = OTs
X = OH
X = OEt



1e
X = OTs
X = OH
X = OEt
X = Br

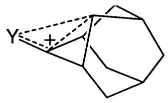


2a
X = OTs



2e
X = OTs

In contrast, solvolysis reactions involving the epimeric methylidene-substituted adamantyl tosylate **2a–OTs** are slower than the corresponding reactions of 2-adamantyl tosylate.[2] The four isolated products from **2a–OTs** methanolysis are consistent with the formation of two equilibrating carbenium ions, **4–CH$_2$** and **5–CH$_2$**, and the partial conversion of **4–CH$_2$** to the bicyclobutenium ion **3–CH$_2$** (Scheme 2).[2]



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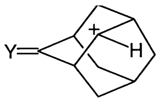

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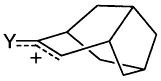
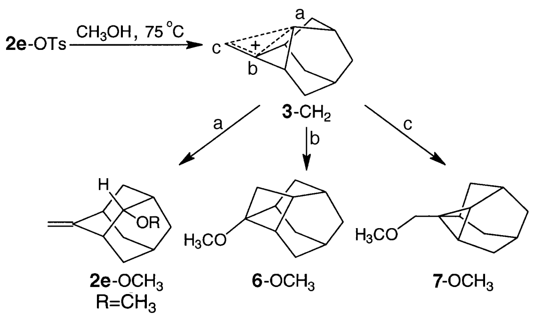


5

Y = CH$_2$
Y = Ad (adamantylidene)



Scheme 1

The following report is an investigation of solvolysis reactions involving the 'pseudo-axial' adamantylideneadamantyl tosylate **1a–OTs**, with particular focus on the nature of the carbenium ion intermediates formed during these reactions.

Experimental

Materials and methods

Ethanol was dried by distillation from magnesium ethoxide. A 'Milli-Q ultra pure water' system was utilized as an additional purification treatment for de-ionized water. NMR spectra were run on either a Bruker AMX-400 or a Bruker AMX-600 spectrometer, using $CDCl_3$ as the solvent and as the internal reference (*J* values are given in Hz). Mass spectra were acquired on a Hewlett Packard 5985 mass spectrometer using

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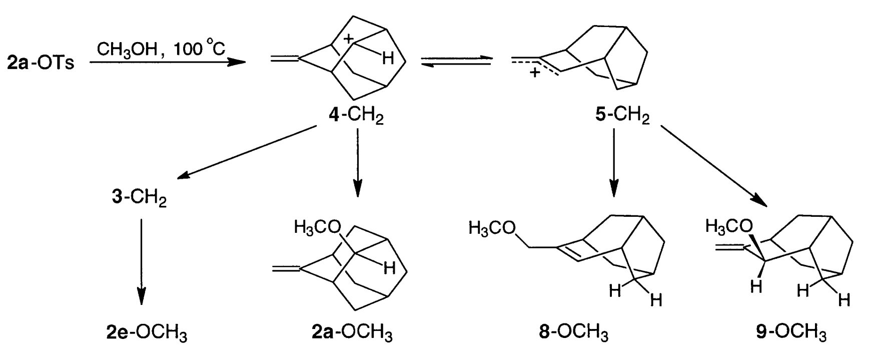


Scheme 2

electron impact ionization (70 eV). All melting points are uncorrected.

(1*R,2*S**)-2-Hydroxy-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[3.3.1.1^{3,7}]$decane (1a–OH).** Lithium aluminium hydride (0.4 g) was added in one portion with stirring to a solution of 2-oxo-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[3.3.1.1^{3,7}]$-decane[3] **10** (1.0 g, 3.5 mmol) in dry diethyl ether (40 cm^3). Stirring was continued for 10 min, at which point the excess lithium aluminium hydride was destroyed by the careful addition of water. The ethereal layer was washed with dilute hydrochloric acid and brine, dried and evaporated to dryness. Flash chromatography of the mixture using silica gel with ethyl acetate–hexane (5% v/v) as the eluent gave the 2*R* isomer **1e–OH** (0.67 g, 66%) and the required 2*S* isomer **1a–OH** (0.35 g, 34%); mp 167–168 °C (recrystallized from aqueous methanol) (Found: C, 84.3; H, 10.0. $C_{20}H_{28}O$ requires C, 84.45; H, 9.9%); δ_H(400 MHz; $CDCl_3$) 1.60–2.02 (23 H, m), 2.85 (1 H, br s), 2.94 (1 H, br s), 2.99 (2 H, br s) and 3.79–3.85 (1 H, m).

(1*R,2*S**)-2-Tosyl-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo-$[3.3.1.1^{3,7}]$decane (1a–OTs).** A solution of the 2*S* alcohol **1a–OH** (0.2 g; 0.7 mmol) and tosyl chloride (1.0 g; 5.2 mmol) in pyridine (10 cm^3) was stirred at room temp. for 3 d. Methanol (40 cm^3) was added and the resulting solution was cooled to −5 °C overnight. The resulting colourless crystals (0.21 g; 68%) were collected by filtration. Mp 179–180 °C (Found: C, 73.8; H, 7.8. $C_{27}H_{34}O_3S$ requires C, 73.9; H, 7.8%); δ_H(400 MHz; $CDCl_3$) 1.55–1.92 (20 H, m), 1.92–2.00 (1 H, m), 2.00–2.05 (1 H, m), 2.44 (3 H, s), 2.68 (1 H, br s), 2.82–2.90 (2 H, m), 2.96 (1 H, br s), 4.68 (1 H, m), 7.30 (2 H, m) and 7.78 (2 H, m); δ_C(100 MHz; $CDCl_3$) 21.6, 26.9, 28.4, 28.45, 30.8, 32.0, 32.3, 33.1 (2 C), 36.2, 36.7, 37.2, 38.4, 38.8, 39.2, 39.4, 39.6, 39.7, 86.8, 126.6, 127.5, 129.6, 135.0, 138.2 and 144.0; *m*/*z* 438 (M^+, 100%), 439 (32.2), 440 (9.2), 441 (2.1).

(1*R,2*S**)-2-Ethoxy-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[3.3.1.1^{3,7}]$decane (1a–OEt).** Sodium hydride (100 mg) and 18-crown-6 (50 mg) were added to a solution of the alcohol **1a–OH** (34 mg) in ethyl bromide (2 cm^3) and the mixture was stirred at room temp. for 18 h. At the end of this time period, ethyl acetate was added to the mixture and the excess sodium hydride was destroyed by the addition of water. The organic layer was washed with water, dried and evaporated to dryness. Flash chromatography using silica gel and the eluent hexane followed by ethyl acetate–hexane (5% v/v) gave **1a–OEt** (14 mg, 38%); mp 86–87 °C (Found: C, 84.6; H, 10.3. $C_{22}H_{32}O$ requires C, 84.6; H, 10.3%); δ_H(400 MHz; $CDCl_3$) 1.16 (3 H, t, *J* 7), 1.53–2.01 (22 H, m), 2.81 (1 H, br s), 2.85 (1 H, br s), 2.90 (1 H, br s), 3.09 (1 H, br s), 3.29–3.39 (1 H, m) and 3.46–3.55 (2 H, m); δ_C(100 MHz; $CDCl_3$) 15.7, 27.9, 28.6, 28.7, 31.4, 32.3 (2 C), 33.0, 33.5, 35.5, 36.6, 37.4, 38.4, 39.2, 39.5, 39.5_5, 39.8, 39.9, 62.4, 82.8, 129.5, 135.8.

(1*R,2*R**)-2-Deuterio-2-hydroxy-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[3.3.1.1^{3,7}]$decane ($[^2H_1]$1e–OH) and (1*R**, 2*S**)-2-deuterio-2-hydroxy-4-tricyclo$[3.3.1.1^{3,7}]$decan-2-ylidenetricyclo$[3.3.1.1^{3,7}]$decane ($[^2H_1]$1a–OH).** The compounds $[^2H_1]$-**1a–OH** and $[^2H_1]$**1e–OH** were synthesized by reduction of ketone **10** using lithium aluminium deuteride in a procedure that is analogous to the reaction with lithium aluminium hydride reported above.

(1*R,2*S**)-2-Deuterio-2-tosyl-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[3.3.1.1^{3,7}]$decane ($[^2H_1]$1a–OTs).** Synthesis of $[^2H_1]$**1a–OTs** employed a procedure that was analogous to that for **1a–OTs** reported above; mp 179–180 °C. The peaks observed in the ^1H NMR (400 MHz; $CDCl_3$) spectrum of $[^2H_1]$-**1a–OTs** corresponded to those seen in the spectrum of **1a–OTs**, except that the peak at δ 4.86 was absent; *m*/*z* 439 (M^+, 100%), 440 (29.5), 441 (10.4), 442 (2.0).

(1*R,2*R**)-2-Deuterio-2-tosyl-4-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[3.3.1.1^{3,7}]$decane ($[^2H_1]$1e–OTs).** A solution of hydrogen bromide in dichloromethane (30 cm^3) was generated by the *in situ* reaction of acetyl bromide (1.0 cm^3, 13.5 mmol) and methanol (0.54 cm^3, 13.3 mmol). This solution was cooled to 0 °C and the deuteriated alcohol $[^2H_1]$**1e–OH** (0.16 g, 0.56 mmol) was added in one portion. After stirring the reaction mixture for 60 min, the solvent was removed under reduced pressure. Purification of the residue using flash chromatography on silica gel with hexane as the eluent gave $[^2H_1]$**1e–Br** as a white solid (0.18 g, 90%). All physical properties of the deuteriated material were identical with those of the non-deuteriated compound **1e–Br**.[1] A published procedure was followed for the treatment of $[^2H_1]$**1e–Br** (0.13 g) with silver tosylate (0.30 g) which gave the deuteriated tosylate $[^2H_1]$**1e–OTs** (0.16 g, 58%); mp 155–156 °C (decomp.) [lit., **1e–OTs**,[1] 147–148 °C (decomp.)]. The peaks observed in the ^1H NMR (400 MHz; $CDCl_3$) spectrum of $[^2H_1]$**1e–OTs** corresponded to those seen in the spectrum of **1e–OTs**,[1] except that the peak at δ 4.35 was absent.

(1*R,4*R**)-4-(2-Hydroxyethoxy)-5-tricyclo$[3.3.1.1^{3,7}]$dec-2-ylidenetricyclo$[4.3.1.0^{3,8}]$decane ($11\text{-}OCH_2CH_2OH$).** A mixture of the tosylate **1a–OTs** (2.0 g) and sodium hydrogen carbonate (0.5 g) in ethane-1,2-diol (100 cm^3) was heated at 125 °C for 3 h. Evaporation of the solvent under vacuum (1 mmHg; 100 °C) gave a solid residue which was subsequently dissolved in ethyl acetate (100 cm^3). The solution was washed with both water and a saturated solution of sodium hydrogen carbonate, dried and evaporated to give a crude preparation of **$11\text{-}OCH_2CH_2OH$** (1.58 g). Recrystallization of the crude product (0.5 g) from ethanol–water at ambient temperature gave an analytically pure sample (0.38 g); mp 88–89 °C (Found: C, 80.4; H, 9.8. $C_{22}H_{32}O_2$ requires C, 80.4; H, 9.8%); δ_H(600 MHz; $CDCl_3$) 1.19 (1 H, br d, *J* 12, 2-H_A), 1.33 (1 H, br d, *J* 13, 10-H_A), 1.40 (1 H, dd, *J* 4 and 12, 7-H_A), 1.49 (1 H, br dd, *J* 3 and 8, 9-H_A), 1.63–1.77 (7 H, m), 1.77–1.86 (4 H, m), 1.90–1.96 (4 H, m), 2.03–2.06 (1 H, m, 7-H_B), 2.08 (1 H, t, *J* 6, RO*H*), 2.08–2.11 (1 H, m, 1-H), 2.22 (1 H, br q, *J* 6, 8-H), 2.63–2.68 (1 H, m, 3-H), 2.75 (1 H, br s, 6-H), 2.82 (1 H, br s, 3′-H), 2.91 (1 H, br s, 1′-H), 3.50–3.53 (1 H, m, CH_AH_BOH), 3.58–3.61 (1 H, m, CH_AH_BOH), 3.64–3.72 (2 H, m, $ROCH_2$), 4.31 (1 H, d, *J* 4, 4-H); δ_C(150 MHz; $CDCl_3$) 28.1, 28.4, 31.7 (6-C), 32.4 (8-C), 32.5 (3′-C), 32.7 (7-C), 33.0 (1′-C), 35.6 (1-C), 36.0 (2-C), 37.2 (6′-C), 37.4 (3-C), 38.4, 38.9 (10-C), 39.2, 39.4, 40.0, 42.6

(9-C), 62.4 (CH_2OH), 68.6 ($ROCH_2$), 76.9 (4-C), 127.7 (2′-C) and 146.3 (5-C).

Solvolysis kinetics

Solvolysis kinetics were followed using a Cary-3E UV–VIS spectrophotometer equipped with the Cary six cell Peltier constant temperature accessory. A stock solution of **1a–OTs** in tetrahydrofuran (5 µl; 22.8 mM) was injected into an equilibrated solvent mixture (3 cm^3; 30 min) and the change in absorbance at 232 nm was followed as a function of time. First-order rate constants for the solvolysis reactions were determined by a non-linear least-squares fit to a standard first-order equation. All kinetic runs exhibited clean first-order behaviour for at least four half-lives of reaction.

Product studies

A solution of the tosylate **1a–OTs** (100 mg) in 60% aqueous ethanol (200 cm^3) was heated to 75 °C and allowed to react for 12 h, a reaction time that represented >20 half-lives for hydrolysis. The solvent volume was reduced and the products were extracted with ethyl acetate. A saturated solution of sodium hydrogen carbonate was used to wash the extract layer which was then dried and evaporated to dryness under reduced pressure. Flash chromatography using silica gel with ethyl acetate–hexane (5–20% v/v) as the eluent gave two separate products. One of the two products was identified as the rearranged ethyl ether **11–OEt** (58 mg, 81.4%), mp 69–70 °C (Found: C, 84.5; H, 10.5. $C_{22}H_{32}O$ requires C, 84.6; H, 10.3%); δ_H(400 MHz; $CDCl_3$) 1.18 (3 H, t, *J* 7), 1.20 (1 H, dd), 1.30–1.40 (2 H, m), 1.48 (1 H, dd), 1.60–1.98 (15 H, m), 2.05–2.16 (2 H, m), 2.24 (1 H, br q, *J* 6), 2.58–2.64 (1 H, m), 2.75 (1 H, br s), 2.81 (1 H, br s), 2.94 (1 H, br s), 3.49 (2 H, m) and 4.28 (1 H, d, *J* 4); δ_C(100 MHz; $CDCl_3$) 16.0, 28.1, 28.4, 31.8, 32.4, 32.5 (2 C), 32.7, 35.6, 36.0, 37.2, 37.7, 38.3, 38.9, 39.0, 39.2, 40.0, 42.6, 62.5, 76.0, 127.8, 145.7; *m/z* 312 (M^+, 53.6), 313 (14.4). The other product was identified as the rearranged alcohol **11–OH** (10 mg, 15.4%), white solid, mp 96–98 °C (Found: C, 84.2; H, 9.8. $C_{20}H_{28}O$ requires C, 84.45; H, 9.9%); δ_H(400 MHz; $CDCl_3$) 1.14–1.20 (1 H, m), 1.26–1.33 (2 H, m), 1.47–1.53 (2 H, m), 1.65–1.77 (7 H, m), 1.77–1.88 (4 H, m), 1.89–2.02 (4 H, m), 2.04–2.11 (2 H, m), 2.31 (1 H, br q, *J* 6), 2.50–2.58 (1 H, m), 2.77 (1 H, br s), 2.81 (1 H, br s), 2.98 (1 H, br s) and 4.63 (1 H, d, *J* 4); δ_C(100 MHz; $CDCl_3$) 28.2, 28.4, 31.2, 31.8, 32.3, 32.9, 33.0, 35.3, 36.6, 37.1, 38.4, 38.7, 39.0, 39.9, 40.0, 40.2, 42.7, 69.8, 131.1, 145.7; *m/z* 284 (M^+, 27.7), 285 ($M^+ + 1$, 6.0), 267 ($M^+ - 17$, 5.7), 175 (100).

In a separate experiment, a solution of the tosylate **1a–OTs** (100 mg) in anhydrous ethanol (10 cm^3) was heated in a Carius tube at 100 °C for 30 h. The volume of the solvent was then reduced and the products were extracted with ethyl acetate. The organic extract was washed with a saturated solution of sodium hydrogen carbonate, dried and evaporated to dryness under reduced pressure. Flash chromatography on silica gel with hexane as the eluent gave two separate products. The first product to elute from the column was identified as the rearranged alkene, **11–H** (21 mg, 34%); mp 131–132 °C (Found: C, 89.4; H, 10.5. $C_{20}H_{28}$ requires C, 89.5; H, 10.5%); δ_H(400 MHz; $CDCl_3$) 1.29–1.36 (2 H, m), 1.38–1.45 (2 H, m), 1.57–1.95 (16 H, m), 2.01–2.07 (2 H, m, 4_A-H), 2.17 (1 H, br q, *J* 7), 2.30 (1 H, dd, *J* 4 and 15, 4_B-H), 2.37–2.45 (1 H, m, 3-H), 2.72 (1 H, br s) and 2.78 (2 H, br s); *m/z* 268 (M^+, 100%), 269 (24.1), 270 (2.9). Comparison of the physical properties of the second eluting product with those of an authentic sample of **1a–OEt** (*vide supra*) indicated that the product was **1a–OEt** (48 mg, 67%). When an analogous solvolysis experiment was performed with [$^2H_1$]**1a–OTs**, the mono-deuteriated isotopomer of **11–H** was formed. The deuterated product showed the following differences from the non-deuteriated material in the ^{1}H NMR spectrum: disappearance of the multiplet at 2.37–2.45; replacement of the broad quartet at 2.17 with a broad triplet; collapse of the double doublet at δ 2.30 to a doublet (*J* 15); and simplification of the multiplet at 2.01–2.07 to a doublet (*J* 15).

Product ratios

The relative proportions of the products generated from the solvolysis of **1a–OTs** were determined by adding **1a–OTs** (*ca.* 8 mg) to the appropriate aqueous ethanol solution (30 cm^3), reacting the mixture for a minimum of 10 half-lives and extracting the resulting products from the aqueous solvent with dichloromethane (2 × 10 cm^3). This organic layer was then washed with water, dried, evaporated to dryness under reduced pressure and the residue dissolved in $CDCl_3$ (0.6 cm^3) and the solution filtered through a glass wool plug into a 5 mm NMR tube. The ^{1}H NMR (400 MHz) spectrum was acquired using a standard pulse sequence and the ratio of the alcohol (**11–OH**) to the ether (**11–OEt**) product was determined by integration of the two peaks at δ 4.63 and 4.28.

Stereochemical assignments

The C−C connectivity of the rearranged adamantyl ring system of the final product was assigned using a standard 2D INADEQUATE experiment which was performed on the product obtained from solvolysis of **1a–OTs** in ethane-1,2-diol. The alcohol **11–OCH$_2$CH$_2$OH** (120 mg) was dissolved in $CDCl_3$ (1.5 cm^3) and this solution was filtered through a glass wool plug into a 10 mm NMR tube. The 2D INADEQUATE spectrum was acquired on a Bruker AMX-600 NMR spectrometer using a 10 mm broad-band probe. Acquisition parameters were set so that crosspeaks were observed between alkyl and allylic carbon atoms, but were not observed between alkene and allylic carbon atoms.

Conversion of 11–OCH$_2$CH$_2$OH to 11–OEt

The alcohol **11–OCH$_2$CH$_2$OH** (0.2 g) was added to a solution of tosyl chloride (0.4 g) in pyridine (5 cm^3) and stirred at room temp. for 24 h. Following the addition of ethyl acetate, the organic layer was extracted with dilute hydrochloric acid, water and saturated sodium hydrogen carbonate. The organic layer was dried and evaporated to dryness, the residue was purified using flash chromatography on silica gel with ethyl acetate–hexane (5% v/v) as the eluent to give the tosylate **11–OCH$_2$CH$_2$OTs** as an oil (0.13 g); δ_H(400 MHz; $CDCl_3$) 1.15 (1 H, dt, *J* 2 and 12), 1.21–1.34 (2 H, m), 1.46 (1 H, dd, *J* 2.5 and 11), 1.58–2.16 (18 H, m), 2.43 (3 H, s), 2.50–2.57 (1 H, m), 2.70 (1 H, br s), 2.80 (1 H, br s), 2.86 (1 H, br s), 3.61 (2 H, dt, *J* 5 and 1.5), 4.12 (2 H, t, *J* 5), 4.26 (1 H, d, *J* 4), 7.34 (2 H, m) and 7.80 (2 H, m). Addition of the tosylate **11–OCH$_2$CH$_2$OTs** (0.05 g), with stirring, to a solution of sodium borohydride (0.1 g) in dimethyl sulfoxide (4 cm^3), was followed by heating at 100 °C for 16 h. Ethyl acetate was then added and the organic layer was extracted with water, dried and evaporated to dryness. Flash chromatography of the residue on silica gel with ethyl acetate–hexane (2% v/v) as the eluent gave a colourless solid **11–OEt** (0.023 g) which had identical properties to the product **11–OEt** that was isolated from the solvolysis experiment.

Results

Preparation of the desired ‘pseudo-axial’ adamantylideneadamantyl tosylate (**1a–OTs**) from adamantylideneadamantyl ketone[3] (**10**) followed the synthetic route outlined in Scheme 3.

Table 1 presents the observed rate constants for the solvolysis of the ‘pseudo-axial’ tosylate (**1a–OTs**) in ethanol–water mixtures.

Rate constants for the solvolysis of **1a–OTs** at 25 °C (Table 2) were estimated by extrapolation of the observed data using the Eyring equation [$\ln(k_{obs}/T) = \ln(k_B/h) - \Delta H^{\ddagger}/RT + \Delta S^{\ddagger}/R$]. The calculated activation parameters for the solvolysis of **1a–OTs** in 80% aqueous ethanol are $\Delta H^{\ddagger} = 26.3 \pm 0.3$ kcal mol^{-1} and $\Delta S^{\ddagger} = -2.1 \pm 0.9$ cal K^{-1} mol^{-1} (1 cal = 4.184 J).

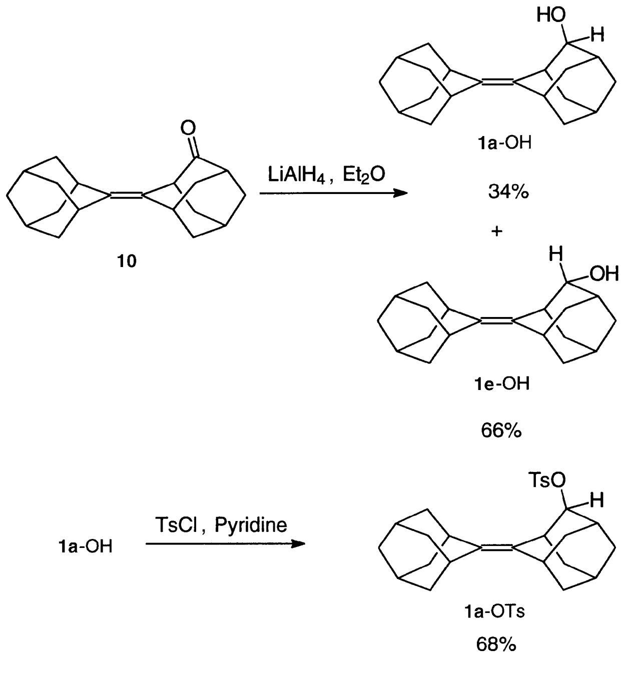
Table 1 Observed first-order rate constants (k_{obs}) for the solvolysis of **1a–OTs** in aqueous ethanol solvent mixtures at various temperatures[a]

Solvent (% ethanol)	$k_{obs}/10^{-5}$ s^{-1} at 60 °C	$k_{obs}/10^{-5}$ s^{-1} at 70 °C	$k_{obs}/10^{-5}$ s^{-1} at 80 °C
80	1.35 ± 0.03	4.3 ± 0.3	13.6 ± 0.2
70	3.48 ± 0.07	10.7 ± 0.3	31 ± 1
60	7.1 ± 0.4	21.7 ± 0.1	62 ± 2
50	15.6 ± 0.1	46.4 ± 0.6	126 ± 2
40	42.8 ± 0.8	121 ± 1	310 ± 10

[a] The quoted values are the mean and the standard deviation from at least three independent kinetic runs.

Table 2 Calculated first-order rate constants (k_{calc}) for the solvolysis of **1a–OTs** in aqueous ethanol solvent mixtures at 25 °C

Solvent (% ethanol)	$k_{calc}/10^{-7}$ s^{-1}
80	1.13
70	3.83
60	8.06
50	20.7
40	71.5



Scheme 3

When the data from Table 2 is fitted to the standard Grunwald–Winstein eqn. (1) using solvolysis data from

$$\log(k/k_{80\%EtOH}) = mY_{OTs} \quad (1)$$

2-adamantyl tosylate[4] to generate Y_{OTs} values, m (the sensitivity parameter for the ionizing power of the solvent) is calculated to be 0.86 ± 0.05. A graph of the data and the computed linear fit is shown in Fig. 1.

Table 3 presents the calculated rate accelerations for the solvolysis of both **1a–OTs** and **1e–OTs**[1] in ethanol–water mixtures with respect to the solvolysis rate for 2-adamantyl tosylate.

Table 3 Calculated rate accelerations for the reactions of **1a–OTs** and **1e–OTs** compared to the solvolysis of 2-adamantyl tosylate in aqueous ethanol solvent mixtures at 25 °C

Solvent (% ethanol)	**1a–OTs**	**1e–OTs**
80	4.7	4.0×10^5
50	4.4	1.5×10^5

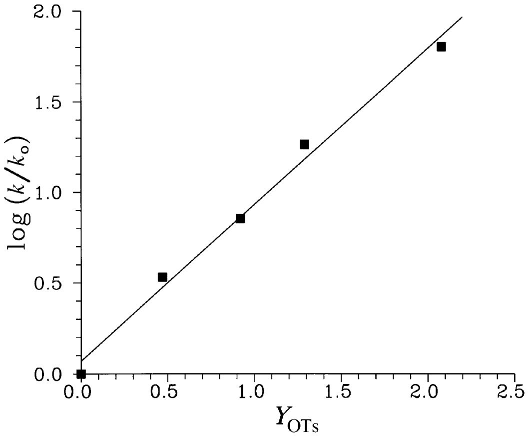
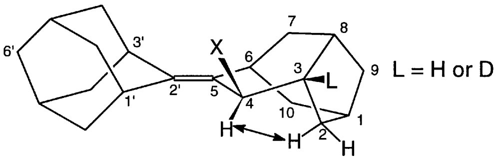


Fig. 1 Correlation of logarithms of solvolysis rates for **1a–OTs** with Y_{OTs}. The displayed line is the calculated fit to the standard Grunwald–Winstein equation.

Determination of the tricyclic ring structure and the stereochemistry of the products involved 2D INADEQUATE, 2D HETEROCOSY and 2D NOESY NMR experiments run on the solvolysis product from the reaction of **1a–OTs** in ethane-1,2-diol. The INADEQUATE spectrum revealed the carbon connectivities for **11–OCH$_2$CH$_2$OH**. The ^{13}C peak assignments are given in the Experimental section and the corresponding designations for the ring carbon atoms are shown as labels on structure **11**. Several of the proton resonances observed in the ^{1}H NMR spectrum (see Experimental section) of **11–OCH$_2$CH$_2$OH** are assigned based on a 2D ^{1}H–^{13}C HETEROCOSY spectrum. An observed cross-peak in the 2D NOESY spectrum, which showed that an NOE correlation exists between the proton on C-4 (δ 4.31) and one of the two protons (δ 1.19) bound to C-2, enabled the absolute stereochemistry of **11–OCH$_2$CH$_2$OH** to be assigned as shown in structure **11** (L = H). When the solvolysis reactions were performed with [^{2}H$_1$]**1a–OTs** the corresponding products that formed were deuteriated on C-3 (structure **11**, L = D).



11 X = H
X = OH
X = OEt
X = OCH$_2$CH$_2$OH
X = OCH$_2$CH$_2$OTs

Reduction of the tosylate (**11–OCH$_2$CH$_2$OTs**) formed from **11–OCH$_2$CH$_2$OH** gave an ethyl ether product which had an identical ^{1}H NMR spectrum to that of the major component isolated from the solvolysis experiments. Accordingly, the major solvolysis product was assigned the structure **11–OEt**. The minor solvolysis product formed in the aqueous ethanolysis of **1a–OTs** was identified as **11–OH** based on a comparison of the ^{1}H NMR spectra obtained from these two compounds. The partition ratio (k_E/k_W) for the formation of **11–OH** and **11–OEt** was calculated according to eqn. (2). A list of the derived ratios is presented in Table 4.

$$\frac{k_E}{k_W} = \frac{[\mathrm{HOH}][\mathrm{ROEt}]}{[\mathrm{EtOH}][\mathrm{ROH}]} \quad (2)$$

Table 4 Comparison of the partition ratios (k_E/k_W) observed in the solvolysis of **1a–OTs** in aqueous ethanol with those for **1e–OTs**, 2-adamantyl tosylate and 2-adamantyl perchlorate

Solvent (% ethanol)	**1a–OTs**[a]	**1e–OTs**[b]	2-Adamantyl tosylate[c]	2-Adamantyl perchlorate[d]
90	—	0.43	0.49	0.64
80	4.6[e]	0.37	0.49	0.52
70	—	0.45	0.53	0.52
60	19.3[f,g]	0.56	0.57[f]	0.55
50	—	0.61	—	0.62

[a] k_E/k_W is a dimensionless ratio of second-order rate constants [see eqn. (2)]. [b] Ref. 1, at 25 °C. [c] Ref. 23, at 100 °C. [d] Ref. 24, at 25 °C. [e] Temperature = 100 °C. [f] Temperature = 75 °C. [g] A value of 11.5 was calculated from the isolated quantities of the two products when the solvolysis reaction was performed on 100 mg of **1a–OTs** at 75 °C (see Experimental section).

Table 5 Observed α-secondary deuterium kinetic isotope effects (k_H/k_D) for the solvolysis of **1a–OTs** in aqueous ethanol solutions at various temperatures[a]

Solvent (% ethanol)	k_H/k_D at 60 °C	k_H/k_D at 70 °C	k_H/k_D at 80 °C
80	1.145 ± 0.021	1.132 ± 0.024	1.167 ± 0.024
60	1.142 ± 0.011	1.130 ± 0.016	1.125 ± 0.019

[a] The quoted values are the mean and the standard deviation from at least three independent kinetic runs.

Table 6 Observed α-secondary deuterium kinetic isotope effects (k_H/k_D) for the solvolysis of **1e–OTs** in aqueous ethanol solutions at 25 °C[a]

Solvent (% ethanol)	k_H/k_D
100	1.155 ± 0.034
90	1.147 ± 0.005
80	1.158 ± 0.012
70	1.167 ± 0.016
60	1.149 ± 0.022
50	1.144 ± 0.006

[a] The quoted values are the mean and the standard deviation from at least three independent kinetic runs.

Ethanolysis of **1a–OTs** under more drastic conditions generated two new products rather than the expected **11–OEt**. These new products are the result of acid-catalysed reactions of **11–OEt**, with the acid component, tosic acid, originating from the initial solvolysis reaction. One of these two new products was shown to be the 'pseudo-axial' ethyl ether **1a–OEt**, while the second product was identified as the reduced, rearranged alkene **11–H**.

Tables 5 and 6 present the α-secondary deuterium kinetic isotope effects (k_H/k_D) observed for, respectively, the solvolysis of **1a–OTs** in aqueous ethanol solvent mixtures at various temperatures and the corresponding reactions performed with **1e–OTs** at 25 °C.

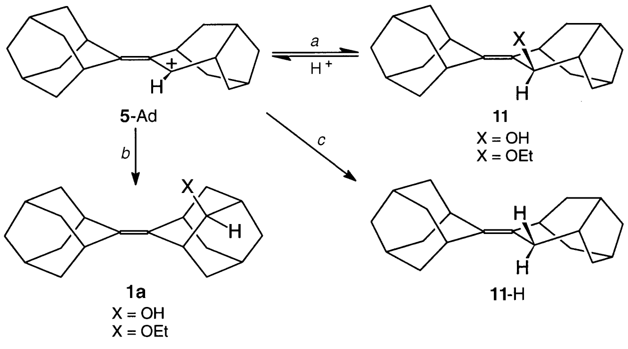
Discussion

Rate data (Table 2) generated from the solvolysis of **1a–OTs** were analysed using the standard Grunwald–Winstein eqn. (1). The standard form of the Grunwald–Winstein equation was utilized in these studies based on the assumption that, during the solvolysis of sterically crowded adamantyl systems, negligible nucleophilic assistance to ionization is provided by the solvent.[5,6] Aqueous ethanolysis of the 'pseudo-axial' tosylate (**1a–OTs**) displayed an *m* value of 0.86 ± 0.05, a value which is greater than the corresponding value of 0.65 ± 0.01 obtained for analogous reactions with **1e–OTs**.[1] Small *m* values (<1) obtained from solvolysis reactions of sterically crowded compounds are consistent with the occurrence of either σ- or π-bond participation during the rate-limiting ionization of the carbon–nucleofuge bond.[7] In a previous study, an *m* value of 0.65 for the solvolysis of **1e–OTs** was interpreted to mean that there is a large degree of π-bond participation at the reaction transition state and that such solvolysis reactions probably proceed through solvent-equilibrated ions.[1] In a related study on the aqueous ethanolysis of **1e–Br**, a common-ion rate depression was observed when bromide ions were added to the reaction medium.[8] This observation is consistent with the formation of solvent-equilibrated ions.[9] When compared to **1e–OTs**, the larger *m* value obtained for the solvolysis reactions of **1a–OTs** indicates that solvation of the developing positive charge at the transition state is more important for reactions involving **1a–OTs** than in the corresponding reactions of **1e–OTs**. Thus, solvolysis of **1a–OTs** must proceed with less charge dispersal at the transition state than does solvolysis of **1e–OTs** and, as a consequence, σ-bond participation during the **1a–OTs** reaction is less effective at stabilizing the developing charge than is the π-bond participation in the solvolysis of **1e–OTs**.

Solvolysis products

The data from Table 3 indicate that the observed solvolysis rates for the adamantylideneadamantyl tosylates **1a–OTs** and **1e–OTs** are governed by the stereochemical orientation of the double bond with respect to the nucleofugic tosylate. Aqueous ethanolysis reactions of **1a–OTs** produce the skeletally rearranged products **11–OH** and **11–OEt** as initial products (>95%), whereas the analogous solvolysis reactions of **1e–OTs** yield products that arise from complete retention of configuration.†,[1] The initial solvolysis products of **1a–OTs** have partition ratios (k_E/k_W) which are much greater than unity (Table 4). In general, values of this magnitude are considered to arise when nucleophilic attack occurs on solvent-equilibrated ions.[11] In this case, the large partition ratios are consistent with the formation of a solvent-equilibrated allylic carbenium ion intermediate (**5–Ad**).‡

When **1a–OTs** is heated in acidic ethanol for an extended period of time, the initial solvolysis product (**11–OEt**) undergoes a further reaction and is replaced by two new products **1a–OEt** and **11–H**. The acid-catalysed reaction of **11–OEt** reforms the carbenium ion **5–Ad**, which can then react in three possible ways. As is shown in Scheme 4, **5–Ad** can: (*a*) undergo solvent capture to yield the allylic protoadamantyl product **11–OEt**; (*b*) undergo rearrangement of the protoadamantyl ring system followed by stereospecific solvent capture to yield **1a–OEt**; or (*c*) abstract a hydride ion, presumably from ethanol, to give the



Scheme 4

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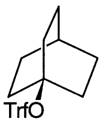
† Similar results were reported by Winstein and co-workers for the acetolysis reactions of *anti*- and *syn*-7-norbornenyl tosylates.[10]

‡ A value of 11.5 for k_E/k_W corresponds to 84.1% of the product being the ethyl ether, while a value of 19.3 corresponds to 89.9% of ether product (see Table 4).

reduced compound **11–H** and acetaldehyde[§] as products. In aqueous ethanol the allylic carbenium ion **5–Ad** partitions predominantly to the protoadamantyl compounds **11–OH** and **11–OEt**, as is shown by the kinetic products of this solvolysis reaction. In contrast, the much slower process of solvent capture to form the thermodynamically more stable adamantyl compounds can only be observed when the reaction conditions are such that formation of the protoadamantyl compounds **11–OH** and **11–OEt** from the carbenium ion **5–Ad** is reversible.[¶]

Nature of the σ-bond interaction

An S_N1 ($D_N + A_N$[12]) solvolysis reaction that involves a substrate modified to contain a non-interacting homoallylic double bond is expected to exhibit a rate decrease of *ca.* 150 when compared to the same reaction carried out with the fully saturated compound.[13] An estimated decrease in rate of this magnitude was calculated from the solvolysis rates obtained for the two bicyclo[2.2.2]octan-1-yl trifluoromethanesulfonate (Trf) **12** and **13**, each of which was reacted at 25 °C in 80% v/v EtOH–H_2O.[13] In an analogous experiment, a 26-fold decrease in rate was observed when solvolysis reactions involving the two homoadamantyl tosylates **14** and **15** were carried out at 75 °C in 70% v/v EtOH–H_2O.[14]



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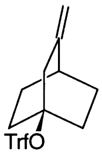

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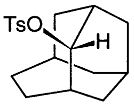

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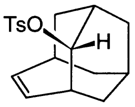

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The observed rate acceleration for the solvolysis reactions of **1a–OTs** relative to those of 2-adamantyl tosylate (Table 3), indicated the occurrence of σ-bond participation during the rate determining step of **1a–OTs** solvolysis. In addition, these reactions yield only rearranged products, indicating that σ-bond participation generates the allylic carbenium ion **5–Ad** as the first-formed intermediate in the solvolysis reactions of **1a–OTs**. If the carbenium ion **4–Ad** were an intermediate in the solvolysis reactions of **1a–OTs**, conversion of this species into the solvent-equilibrated carbenium ion **3–Ad** should occur more rapidly than the corresponding interconversion of **4–CH$_2$** into **3–CH$_2$**, since the stability of bicyclobutenium ions (**3**) increases dramatically upon alkyl substitution. An activation energy of 8.5 kcal mol^{-1} has been calculated for the interconversion of the two, unsubstituted, isoenergetic secondary adamantyl cations.[15] Consequently, the thermodynamically favourable interconversion of **4–Ad** into **3–Ad** should proceed with a lower activation energy.

Conversion of the carbenium ion **4–Ad** into the bicyclobutenium ion **3–Ad** which reacts with solvent to give exclusively 'pseudo-equatorial' products would result in solvolysis products having an inverted configuration.[1] Therefore, the reaction of **5–Ad** with ethanol to give **1a–OEt** (or with water to give **1a–OH**) cannot proceed *via* **4–Ad** as a solvent-equilibrated carbenium ion, since this ion would be expected to yield some **1e–OEt** (or **1e–OH**) product. It is more likely that rearrangement of the solvent-equilibrated allylic carbenium ion to reform the adamantyl ring system occurs with solvent participation to give **1a–OEt** or **1a–OH** directly.

The activation parameters for the solvolyses in 80% aqueous ethanol of **1a–OTs**, **1e–OTs**[1] and 2-adamantyl tosylate[||],[16] are, respectively, $\Delta H^‡ = 26.3$, 19.2 and 26.9 kcal mol^{-1} and $\Delta S^‡ = -2.1$, -3.4 and -3.0 cal K^{-1} mol^{-1}. From this information it is clear that the different types of bond participation encountered in the solvolyses of **1a–OTs** and **1e–OTs** cause no significant entropic effects for the three secondary adamantyl tosylates. Rather, the various rates are controlled mainly by the enthalpic component of these $D_N + A_N$ reactions, a contribution which is, to some degree, related to the ability of the different molecular orbitals to provide assistance to ionization.

Comparison of methylidene and adamantylidene derivatives

The 'pseudo-equatorial', substituted adamantyl tosylates **1e–OTs** and **2e–OTs** display a reactivity difference of approximately 1.3×10^5-fold at 25 °C in methanol,[**],[1,2] while the corresponding ratio for the epimeric 'pseudo-axial' tosylates **1a–OTs** and **2a–OTs** measured at 25 °C in, respectively, 80% ethanol–water and in methanol, is 89-fold.[2] These observations indicate that the more electron-rich double bonds of the adamantylidene compounds **1a–OTs** and **1e–OTs** support greater σ- and π-bond participation, respectively, at their individual transition states than do the corresponding methylidene adamantyl tosylates **2a–OTs** and **2e–OTs**. The observed reactivity difference is largest when the more electron-rich homoallylic π-bond interacts directly with the developing p-orbital at the reaction centre. Furthermore, the reactions of **1a–OTs** lead directly to the formation of the carbenium ion **5–Ad**, whereas the data for **2a–OTs** is consistent with the formation of two rapidly equilibrating ions **4–CH$_2$** and **5–CH$_2$** (*vide supra*).

Kinetic isotope effects

Both α- and β-secondary deuterium kinetic isotope effects (SDKIEs) have been used to probe the mechanism of solvolysis reactions.[18] To be useful as a diagnostic tool the maximum possible value of k_H/k_D should be known. For the solvolysis of secondary alkyl sulfonates, the upper limit for an α-SDKIE is approximately 1.22 at 25 °C.[19] An α-SDKIE value of this magnitude has been interpreted to indicate the involvement of rate-determining separation of an intimate ion-pair during the solvolysis of secondary alkyl tosylates.[20] Two independent studies observed that the α-SDKIE for the solvolysis of 2-adamantyl sulfonates is *ca.* 1.22 at 25 °C.[21] Consistent with the interpretation that separation of an intimate ion-pair is rate-determining is the independent observation that extensive oxygen scrambling occurs to ^{18}O-labelled 2-adamantyl tosylate recovered from solvolytic medium.[22] The adamantylidene substituted 2-adamantyl sulfonate **1e–OTs** exhibits an α-SDKIE in the range 1.14–1.17 at 25 °C for aqueous ethanolysis, while the epimeric tosylate **1a–OTs** displays an α-SDKIE of 1.16 ± 0.02[††] for solvolysis in 60/40 v/v EtOH : H_2O at 25 °C. Although these two secondary sulfonates are markedly contrasting in solvolytic reactivity as a result of differing degrees of participation, the measured α-SDKIEs are experimentally indistinguishable. Therefore, for these ionization reactions, the magnitude of an α-SDKIE is not a reliable predictor of the presence or absence of either σ- or π-type participation occurring during the rate-limiting step of the reaction.

Conclusions

A four- to five-fold rate acceleration occurs for the solvolysis reactions of the 'pseudo-axial' adamantylideneadamantyl

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[§] No attempt was made to isolate and quantify the acetaldehyde product.

[¶] A similar set of observations were made in aqueous dioxane: **1a–OTs** gave only **11–OH** when $NaHCO_3$ was added to neutralize the tosic acid formed in the reaction mixture and, in the absence of added $NaHCO_3$, prolonged heating gave **1a–OH**.

[||] Grob *et al.*[17] measured the activation parameters for 2-adamantyl tosylate as $\Delta H^‡ = 27.1$ kcal mol^{-1} and $\Delta S^‡ = -2.4$ cal K^{-1} mol^{-1}.

[**] The difference in solvolytic rate constants is 2.1×10^5 for the reaction of **1e–OTs** in 80% ethanol–water and the reaction of **2e–OTs** in methanol at 25 °C.

[††] Estimated using the relationship $T \ln (k_H/k_D) =$ constant.

tosylate when compared to the solvolysis of 2-adamantyl tosylate. The reactions involve σ-participation of the *antiperiplanar* C–C σ-bond into the nascent *p*-orbital at the developing carbenium ion centre yielding a solvent-equilibrated allylic carbenium ion as the first-formed intermediate.

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