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Solvolysis of (*Z*)- and (*E*)-2-Ethylidene-1-adamantyl Chlorides and Mesylates. A Unique Example Showing the Greater F-Strain Effect in the Chloride than in the Mesylate

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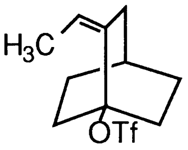
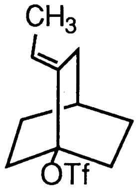
The *Z*/*E* rate ratio in the trifluoroethanolysis at 25 °C of the title chlorides and mesylates are 1023 and 126, respectively, showing the greater front strain (F-strain) effect in the (*Z*)-chloride than in the (*Z*)-mesylate. The results were supported by MM2 and AM1 calculations.

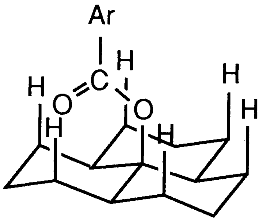
Very recently, we have reported that (*Z*)-2-ethylidenebicyclo[2.2.2]oct-1-yl triflate [(*Z*)-**1-OTf**] solvolyzes 217 times faster than its *E* isomer (*E*)-**1-OTf** in ethanol at 25 °C.[1] The markedly enhanced rate of (*Z*)-**1-OTf** has been attributed to the relief of front strain (F-strain) between the (*Z*)-methyl group and the ether oxygen atom of the leaving group $-O-SO_2CF_3$ on ionization.[1,2] This postulate has been in striking contrast to the interpretation by Brown and Schleyer for the markedly fast rate of solvolysis of *trans*,*trans*,*trans*-perhydro-9b-phenalyl *p*-nitrobenzoate (**2-OPNB**) that the major F-strain is attributed to the repulsion between the carbonyl (and/or the aryl) group, not the ether oxygen atom, and the ring system.[3] Most notably, they found that the chloride **2-Cl** is essentially free from F-strain and exhibits a normal solvolysis rate.[3] These findings have been supported by recent molecular mechanics calculations.[4]



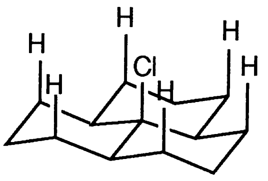
(*Z*)-**1-OTf**



(*E*)-**1-OTf**

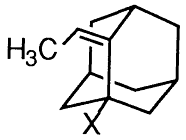


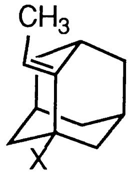
2-OPNB

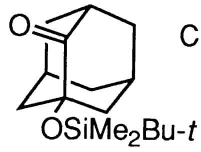


2-Cl

We now wish to report that the *Z*/*E* rate ratio in the solvolysis of (*Z*)- and (*E*)-2-ethylidene-1-adamantyl mesylates [(*Z*)-**3-OMs** and (*E*)-**3-OMs**, respectively] is 126 in 2,2,2-trifluoroethanol (TFE) at 25 °C, whereas the rate ratio is boosted to 1023 for the corresponding chlorides (*Z*)-**3-Cl** and (*E*)-**3-Cl**. Apparently, the (*Z*)-2-ethylidene bridgehead substrates with high structural rigidity are unique in that the F-strain is developed between the atom (in the leaving group) directly attached to the bridgehead carbon and the (*Z*)-methyl group.5)







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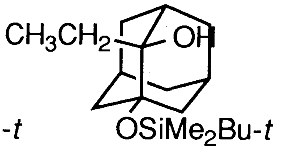

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X = OSO_2CH_3	(*Z*)-**3-OMs**	(*E*)-**3-OMs**
X = Cl	(*Z*)-**3-Cl**	(*E*)-**3-Cl**
X = OH	(*Z*)-**3-OH**	(*E*)-**3-OH**
X = $OSiMe_2Bu$-*t*	(*Z*)-**3-OBDMS**	(*E*)-**3-OBDMS**

The synthesis of the substrates and rate measurements are as follows. The t-butyldimethylsilyl (BDMS) ether **4** of 1-hydroxy-2-adamantanone6,7) was subjected to a Wittig ethylidenation in THF to give a mixture of (*Z*)-**3-OBDMS** and (*E*)-**3-OBDMS** in an approximate ratio of 10:1.8) After desilylation of the mixture,9) the resulting (*Z*)-**3-OH** and (*E*)-**3-OH** were separated from each other over SiO_2 in yields of 86 and 7%, respectively, based on **4**.10) The *E* alcohol (*E*)-**3-OH** was also synthesized via a different route in a practical yield as follows. The keto silyl ether **4** was treated with ethyllithium in pentane-benzene and then the resulting tertiary alcohol **5** was refluxed with thionyl chloride in benzene in the presence of an excess of pyridine to give (*E*)-**3-OBDMS** and (*Z*)-**3-OBDMS** in an approximate ratio of 95:5.8) Desilylation followed by separation as described above afforded (*E*)-**3-OH** in 74% yield based on **4**. The mesylates11) and chlorides12) were prepared in usual manners. The solvolysis in anhydrous TFE was conducted in the presence of an excess of 2,6-lutidine. All the substrates gave the corresponding gas-chromatographically pure 2,2,2-trifluoroethyl ether as a sole product. The rates were followed conductimetrically or titrimetrically; the results are summarized in Table 1.

The entropies of activation derived from the rate constants at two temperatures are very close between the *Z* and *E* isomers within a difference of as small as 2.7 (±6) J mol^{-1}K^{-1} for both the mesylates and the chlorides. The *Z*/*E* rate ratios of 126 (±3) for the mesylates and 1023 (±160) for the chlorides at 25 °C correspond to $\Delta G^{\ddagger}$ differences of 12.0 (±0.1) and 17.2 (±0.4) kJ mol^{-1}, respectively. The experimentally determined respective $\Delta H^{\ddagger}$ differences are 11.2 (±1) and 16.4 (±2) kJ mol^{-1}, being very close to the corresponding $\Delta G^{\ddagger}$ differences. Therefore, we can safely conclude that the *Z*/*E* rate ratios are controlled essentially by the enthalpy term. We attribute the greater *Z*/*E* rate ratio and the greater difference in $\Delta H^{\ddagger}$ for the chlorides than for the mesylates to greater F-strain in (*Z*)-**3-Cl** than in (*Z*)-**3-OMs**.

Table 1. Rates of Solvolysis of 2-Ethylidene-1-adamantyl Mesylates and Chlorides in 2,2,2-Trifluoroethanol

Substrate	Temp °C	k s^{-1}	$\Delta H_{298}^{\ddagger}$ a) kJ mol^{-1}	$\Delta S_{298}^{\ddagger}$ b) J $mol^{-1}K^{-1}$	k_{rel} at 25 °C
(*Z*)-**3-OMs**	4.1	4.04×10^{-3} c)			
	25.0	4.41×10^{-2} c)	76.1	-15.6	126 ± 3
(*E*)-**3-OMs**	25.0	3.51×10^{-4} c)	87.3	-18.2	1
	40.0	1.99×10^{-3} c)			
(*Z*)-**3-Cl**	25.0	3.95×10^{-6} d,e)	81.6	-74.6	1023 ± 160
	50.0	5.46×10^{-5} f)			
	75.0	5.17×10^{-4} f)			
(*E*)-**3-Cl**	25.0	3.86×10^{-9} d,g)	98.0	-77.3	1
	75.0	1.30×10^{-6} f)			
	100.0	1.33×10^{-5} f)			

a) Accurate to within approximately ±0.6 and ±1 kJ mol^{-1} for mesylates and chlorides, respectively. b) Accurate to within approximately ±3 J $mol^{-1}K^{-1}$. c) Determined conductimetrically within an experimental error of ±1% ($r > 0.999$) by using 2×10^{-4} mol dm^{-3} of the substrate and 1.2×10^{-3} mol dm^{-3} of 2,6-lutidine. d) Extrapolated from data at other temperatures. e) Accurate to within ±5%. f) Determined titrimetrically within an experimental error of ±1.5% ($r > 0.999$) by using 2.0×10^{-2} mol dm^{-3} of the substrate and 2.5×10^{-2} mol dm^{-3} of 2,6-lutidine. g) Accurate to within ±9%.

This postulate has been supported by MM2(87) calculations on the substrates and AM1 calculations on intermediate carbocations.[13] From lack of the parameters of sulfonates, the MM2 calculations for the mesylates were performed for the corresponding alcohols as surrogates. The MM2 calculations showed that the differences in steric energy between the *Z* and the *E* form are 7.5 kJ mol^{-1} for **3-OH** and 13.4 kJ mol^{-1} for **3-Cl**, the latter value being greater than the former one by 5.9 kJ mol^{-1} in good agreement with the experimentally determined difference in $\Delta\Delta H^{\ddagger}$ of 5.2 [= (98.0 - 81.6) - (87.3 - 76.1)] (±2) kJ mol^{-1}. On the other hand, AM1 calculations showed that the bridgehead cations (*Z*)-$\mathbf{3}^{+}$ and (*E*)-$\mathbf{3}^{+}$ have essentially the same skeletal structure and net atomic charge on the bridgehead carbon, indicating similar stabilities of (*Z*)-$\mathbf{3}^{+}$ and (*E*)-$\mathbf{3}^{+}$.

In conclusion, the markedly greater *Z*/*E* rate ratio for the chlorides than for the mesylates is most probably explicable on the basis of marked F-strain in (*Z*)-**3-Cl**.

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References

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5) The 2-methylene-1-adamantyl cation has been found to be free from allylic conjugation owing to the perpendicular arrangement of the cationic p orbital and the π system.[6)]

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8) The ratio was determined by ^{13}C-NMR.

9) E. W. Collington, H. Finch, and I. J. Smith, Tetrahedron Lett., **26**, 681 (1985).

10) The structures of (Z)-**3-OH** (mp 104.5-105.0 °C) and (E)-**3-OH** (mp 77.0-77.5 °C) were determined by IR, ^{13}C-NMR, and ^{1}H-NMR NOE difference experiments. (Z)-**3-OH**: ^{13}C-NMR ($CDCl_3$) δ 13.4, 30.6, 35.6, 38.6, 43.8, 47.3, 74.8, 113.2, 146.8 ppm. (E)-**3-OH**: ^{13}C-NMR ($CDCl_3$) δ 11.9, 30.5, 32.9, 35.7, 37.7, 47.2, 71.8, 108.0, 148.4 ppm. Details of the NOE difference experiments will be reported in a full paper.

11) Analytically pure (Z)-**3-OMs** (mp 61.0-61.5 °C) and (E)-**3-OMs** (mp 61.5-62.0 °C) were prepared by lithiation of the corresponding alcohols with butyllithium followed by treatment with methanesulfonyl chloride in THF and then purified by medium pressure column chromatography over SiO_2 at -40 °C. (Z)-**3-OMs**: ^{13}C-NMR ($CDCl_3$) δ 13.3, 31.1, 34.8, 37.9, 41.0, 43.8, 44.7, 94.1, 113.6, 142.5 ppm. (E)-**3-OMs**: ^{13}C-NMR ($CDCl_3$) δ 12.0, 31.2, 33.9, 35.2, 37.1, 40.9, 44.5, 92.7, 110.8, 143.0 ppm.

12) Analytically pure (Z)-**3-Cl** (mp 60.0 °C) and (E)-**3-Cl** (mp 43.0-43.5 °C) were prepared by treatment of the corresponding alcohols with thionyl chloride in benzene at reflux in the presence of an excess of pyridine. (Z)-**3-Cl**: ^{13}C-NMR ($CDCl_3$) δ 13.9, 31.5, 35.3, 38.4, 46.1, 50.8, 72.1, 115.5, 143.6 ppm. (E)-**3-Cl**: ^{13}C-NMR ($CDCl_3$) δ 12.2, 29.7, 34.1, 35.3, 37.3, 50.2, 73.6, 113.0, 144.7 ppm.

13) The AM1 and MM2(87) programs were obtained from QCPE.

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