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Solvolyses of 2-Oxo Bridgehead Compounds: A Critical Examination of π-Conjugative Stabilization of α-Carbonyl Carbocations

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The methodology of changing ring flexibility to detect the π-conjugative stabilization of bridgehead carbocations has been applied to eight 2-oxo (X = O) bridgehead carbocations. On the basis of the solvolytic behavior observed in kinetics and product analyses, the eight 2-oxo bridgehead substrates were classified into three categories: three substrates solvolyzing without ion-pair return that leads to primary isomers (class A), three substrates that form primary isomers by ion-pair return during solvolysis (class B), and two substrates that undergo solvent addition to the carbonyl group to form hemiacetals during solvolysis (class C). It was concluded that the substrates of class C could not be used for the present purpose. Essentially constant ethanolysis rate ratios, $k(X = O)/k(X = H_2)$, of $10^{-8.2}$−$10^{-8.7}$ at 25 °C were obtained between four 2-oxo substrates in classes A and B and the corresponding parent unsubstituted ones. The result was interpreted to suggest that the π-conjugative stabilization of tertiary α-carbonyl carbocations is negligibly small, if present. Slightly more negative $k(X = O)/k(X = H_2)$ values of $10^{-9.7}$ and $10^{-9.2}$ for highly flexible bicyclo[4.2.2]dec-1-yl and bicyclo[4.3.1]dec-1-yl systems, respectively, were attributed to complex conformations in the ground and incipient carbocations. PM3 calculations on some 2-methylene and 2-oxo bridgehead carbocations supported the experimental results. Comparison of the solvolysis rates of 1,1,3,3-tetramethyl-2-oxobutyl mesylate with those of 1,1,3,3-tetramethylbutyl mesylate estimated from the rates of the corresponding chloride also failed to support the π-conjugative stabilization of α-carbonyl carbocations.

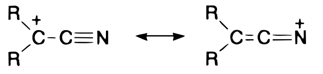
Introduction

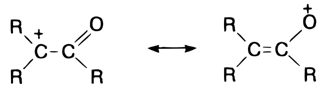
The chemistry of carbocations containing a strongly electron-withdrawing substituent such as a trifluoromethyl, a cyano, or a carbonyl group has been an actively studied area in physical organic chemistry in the past decade.[1]

The electronic effects of the cyano and carbonyl groups are generally interpreted to include the mesomeric effect (−M) as well as the inductive/field effect (−I), both being electron withdrawing, as formulated by the resonance structures **1a** ↔ **1b** and **2a** ↔ **2b**. The −M effect of the cyano group is reflected in its more positive value of σ_p (0.67) than σ_m (0.62).[2] This is also true when the cyano group is conjugated with a carbocationic center through a benzene ring: the σ_p^+ value (0.659) is more positive than σ_m^+ (0.562).[3]

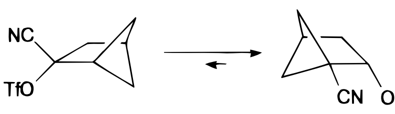

1a **1b** **2a** **2b**

On the contrary, during the past decade a number of solvolysis rate data relevant to α-cyano and α-carbonyl substrates have been interpreted as supporting the notion that the α-cyano and α-carbonyl carbocations are stabilized by electron-donating π conjugation (+M) to an extent as to partly offset their destabilizing inductive effect.[1] In resonance formulations, the positive charge is designated to distribute on the electronegative nitrogen or oxygen atom as shown by **3a** ↔ **3b** and **4a** ↔ **4b**.


3a **3b**


4a **4b**

Recently, the effect of geminal group interaction that destabilizes the ground state and enhances the solvolysis rates has been pointed out by several groups.[4] A typical example is the marked destabilization of **5** in comparison with **6** by 9−10 kcal mol^{-1}.[4a,b]


5 **6**

⊗ Abstract published in *Advance ACS Abstracts,* August 1, 1997.

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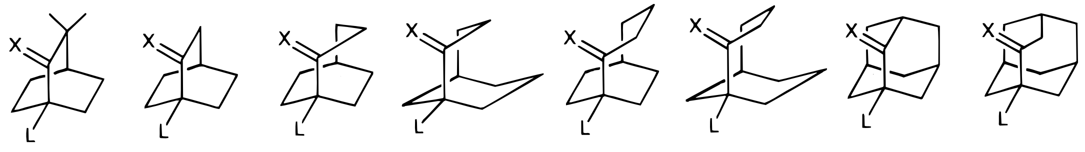
Chart 1

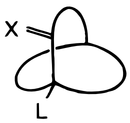


X = O	**8a-L**	**9a-L**	**10a-L**	**11a-L**	**12a-L**	**13a-L**	**14a-L**	**15a-L**
X = CH$_2$	**8b-L**	**9b-L**	**10b-L**	**11b-L**	**12b-L**	**13b-L**	**14b-L**	**15b-L**
X = H$_2$	**8c-L**	**9c-L**	**10c-L**	**11c-L**	**12c-L**	**13c-L**	**14c-L**	**15c-L**

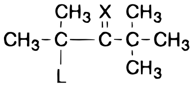
L: OH or leaving group

The carbonyl π conjugation in carbocations was originally postulated by McDonald[5] in the 1960s and examined by Creary and co-workers[1c−e] in the 1980s by using solvolysis. It was found that tertiary α-carbonyl substrates ($R_1R_2CX(C{=}O)R_3$) solvolyze at rates 10^4-10^5 greater than those predicted on substituting a carbonyl group for the methine hydrogen of the corresponding secondary substrates (R_1R_2CXH).[6] The unexpectedly fast rates of solvolysis of the α-carbonyl substrates were explained by postulating π-conjugative stabilization of an incipient carbocation as depicted by **4a** ↔ **4b**.[6] Although these tertiary α-carbonyl substrates were fully proved to react by S_N1 mechanisms,[6] it seemed to us that the comparisons of reactivity between the tertiary α-carbonyl and the secondary substrates were too extreme from the steric viewpoint.

More than 20 years ago, Martin[7a] and Schleyer[7b] independently showed that 2-methylene-1-adamantyl tosylate solvolyzes 10^4 times slower than 1-adamantyl tosylate. We extended the study to flexible cage-shaped bridgehead compounds and showed that the rates of solvolysis of 2-methylene bridgehead compounds **7b** relative to the corresponding saturated parent compounds **7c** markedly accelerate with the increase in ring flexibility because of increased allylic conjugation in the transition state.[7c] Application of this methodology to 2-oxo bridgehead compounds **7a** was expected to permit the evaluation of π-conjugative stabilization of incipient α-carbonyl cations in solvolysis.[7d] This paper describes the details of previous communications[8] and some new data on the solvolyses of various 2-oxo bridgehead compounds, **8a-L**−**15a-L** (Chart 1). The conclusion based on the solvolysis of the cage compounds was also compared with that based on the open-chain compound **16a**.[6]



7a: X = O
7b: X = CH$_2$
7c: X = H$_2$
L = leaving group



$$CH_3-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle L}{|}}{C}}-\overset{\overset{\displaystyle X}{\|}}{C}-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}-CH_3$$

16a: X = O
16c: X = H$_2$
L = leaving group

Results and Discussion

Syntheses. The ketols (**7a-OH**) were prepared by oxidizing the corresponding secondary and tertiary diols which were synthesized by acylative ring expansion of bridgehead aldehydes.[9] All the ketols except for 3,3-dimethyl-1-hydroxybicyclo[2.2.2]octan-2-one (**8a-OH**) were described previously.[9] In this work the dimethyldioxirane oxidation[10] was applied to 3,3-dimethylbicyclo[2.2.2]octane-1,2-diol to give **8a-OH** quantitatively.

A very unfavorable reaction in the solvolyses of α-carbonyl compounds is the addition of a solvent molecule to the carbonyl group to form a hemiacetal prior to solvolysis. With a view to averting this reaction as much as possible, we selected good leaving groups, trifluoromethanesulfonate (triflate, TfO$^-$), and 2,2,2-trifluoroethanesulfonate (tresylate, TrO$^-$). For **8a**−**11a**, **14a**, and **15a**, the triflates were isolated in pure form, but for **12a** and **13a** the triflates were too unstable; therefore, tresylates were used. The parent reference substrates **8c-L**−**15c-L** were described previously.[7c,8]

Solvolysis Rate Studies. The triflates and tresylates of the 2-methylene and parent systems except for the systems **8** and **9** were expected to solvolyze too fast to be followed. Therefore, mesylates, trifluoroacetates, heptafluorobutyrates, chlorides, or bromides were used, and when necessary, 80% ethanol was used instead of ethanol as a solvolysis solvent. In order to estimate the rates of the parent substrates (**7c-L**) having the same leaving group as the 2-oxo substrates (**7a-L**), we used appropriate conversion factors that had been obtained by the solvolysis of 1-adamantyl derivatives (see below).

The solvolytic behavior of the eight 2-oxo substrates (**8a-L**−**15a-L**) was found to be categorized into three classes. The substrates of class A are 3,3-dimethyl-2-oxobicyclo[2.2.2]oct-1-yl triflate (**8a-OTf**), 2-oxobicyclo[3.3.1]non-1-yl triflate (**11a-OTf**), and 4-oxo-3-homoadamantyl triflate (**15a-OTf**) which showed linear first-order kinetics over 80−90% reactions and good Grunwald−

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Table 1. Rate Data for the Solvolyses of Class A Substrates 8a-OTf, 11a-OTf, and 15a-OTf

compd[a]	solvent[b]	temp (°C)	k^c (s^{-1})	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (eu)
8a-OTf	MeOH	125	$1.05 \times 10^{-4\,d}$		
		100	$7.09 \times 10^{-6\,d}$		
		75	$3.03 \times 10^{-7\,d}$		
		25	$(1.2 \pm 0.1) \times 10^{-10\,e}$	31.6 ± 0.2	2.2 ± 0.6
	EtOH	125	$2.81 \times 10^{-5\,d}$		
		100	$1.90 \times 10^{-6\,d}$		
		25	$(3.9 \pm 0.6) \times 10^{-11\,e}$	31.2 ± 0.5	-1.4 ± 1.2
	80% EtOH	100	$1.79 \times 10^{-5\,d}$		
		75	$8.73 \times 10^{-7\,d}$		
		25	$(4.5 \pm 0.4) \times 10^{-10\,e}$	30.6 ± 0.4	1.3 ± 1.1
	60% EtOH	100	$6.94 \times 10^{-5\,d}$		
		75	$3.80 \times 10^{-6\,d}$		
		25	$(2.7 \pm 0.3) \times 10^{-9\,e}$	29.4 ± 0.5	0.8 ± 1.1
	50% EtOH	100	$1.39 \times 10^{-4\,d}$		
		75	$7.38 \times 10^{-6\,d}$		
		25	$(4.8 \pm 0.5) \times 10^{-9\,e}$	29.7 ± 0.4	3.1 ± 0.9
	TFE	100	$3.97 \times 10^{-5\,d}$		
		75	$2.20 \times 10^{-6\,d}$		
		25	$(1.6 \pm 0.1) \times 10^{-9\,e}$	29.3 ± 0.2	-0.6 ± 0.5
	AcOH	125	$5.36 \times 10^{-5\,d}$		
		100	$3.04 \times 10^{-6\,d}$		
		25	$(3.1 \pm 0.3) \times 10^{-11\,e}$	33.3 ± 0.2	5.0 ± 0.6
	HCO_2H	100	$2.87 \times 10^{-4\,d}$		
		75	$1.72 \times 10^{-5\,d}$		
		25	$(1.5 \pm 0.1) \times 10^{-8\,e}$	28.5 ± 0.2	1.2 ± 0.6
11a-OTf	MeOH	50	$4.01 \times 10^{-4\,d}$		
		25	$1.53 \times 10^{-5\,d}$	24.4 ± 0.3	1.3 ± 0.9
	EtOH	50	$8.45 \times 10^{-5\,d}$		
		25	$2.88 \times 10^{-6\,d}$	25.3 ± 0.3	0.9 ± 1.0
	80% EtOH	25	$6.73 \times 10^{-5\,d}$		
	60% EtOH	25	$3.02 \times 10^{-4\,d}$		
	TFE	25	$1.3 \times 10^{-4\,d,f}$		
15a-OTf	MeOH	40	$4.89 \times 10^{-3\,g}$		
		25	$7.30 \times 10^{-4\,g}$	22.9 ± 0.5	4.0 ± 1.6
	EtOH	40	$7.31 \times 10^{-4\,g}$		
		25	$1.04 \times 10^{-4\,d}$	23.5 ± 0.5	2.1 ± 1.6
	80% EtOH	40	$1.96 \times 10^{-2\,g}$		
		25	$(3.11 \pm 0.01) \times 10^{-3\,g}$	22.2 ± 0.3	4.4 ± 0.9
	60% EtOH	25	$(1.94 \pm 0.02) \times 10^{-2\,g}$		
	50% EtOH	25	$(4.79 \pm 0.03) \times 10^{-2\,g}$		
	40% EtOH	25	$(1.33 \pm 0.01) \times 10^{-1\,g}$		
	TFE	25	$5.84 \times 10^{-3\,g}$		
	97% HFIP	25	$4.05 \times 10^{-2\,g}$	19.7 ± 0.2	1.2 ± 0.5
		15	$1.23 \times 10^{-2\,g}$		
		0.3	$1.83 \times 10^{-3\,g}$		
	AcOH	40	$7.48 \times 10^{-4\,d}$		
		25	$9.94 \times 10^{-5\,d}$	24.4 ± 0.5	4.9 ± 1.6

[a] The concentration of the substrate was generally 0.020 mol L^{-1} for titrimetric runs and (1-2) × 10^{-4} mol L^{-1} for conductimetric runs. [b] Percentages ethanol denote % (v/v) of ethanol in ethanol-water at 25 °C, and 97% HFIP means 97% HFIP−3% H_2O by weight. Methanol, ethanol, aqueous ethanols, and TFE contained 0.025 mol L^{-1} 2,6-lutidine. Acetic acid and formic acid contained 0.025 mol L^{-1} sodium acetate or sodium formate, respectively. The runs in 97% HFIP were conducted in the absence of an added base. [c] Determined by a single run with correlation coefficients greater than 0.9999. The data for **15a-OTf** in ethanol and aqueous ethanols at 25 °C are average values of duplicate runs. [d] Determined titrimetrically within an experimental error ± 2%. [e] Extrapolated from data at other temperatures. [f] Initial rate estimated from a curved first-order plot. [g] Determined conductimetrically within an experimental error ± 1%.

Winstein $mY_{2-\mathrm{AdOTf}}$ correlations.[11] The class B substrates are 2-oxobicyclo[3.2.2]non-1-yl triflate (**10a-OTf**), 2-oxobicyclo[4.2.2]dec-1-yl tresylate (**12a-OTr**), and 2-oxobicyclo[4.3.1]dec-1-yl tresylate (**13a-OTr**), which showed curved first-order kinetics, whereas their mY_x relations by using initial rates were linear. It was found that these substrates undergo rearrangement to an isomeric triflate or tresylate and that the rearranged product further solvolyzes. The class C substrates, 2-oxobicyclo[2.2.2]oct-1-yl triflate (**9a-OTf**) and 2-oxo-1-adamantyl triflate (**14a-OTf**), showed curved first-order kinetics. Their initial rates could be determined, but they gave curved Arrhenius plots and random mY_x relations. These results suggested that the class A and class B substrates were usable, but the class C ones were unsuitable for kinetic studies. The solvolytic behaviors of all the α-carbonyl substrates used in this work are described below in detail.

Solvolyses of Class A Substrates 8a-OTf, 11a-OTf, and 15a-OTf. These three substrates followed good first-order kinetics over 80−90% reactions in all the solvents tested. The rate constants are summarized in Table 1. In the case of **8a-OTf**, the rates in methanol were determined at three temperatures (75, 100, 125 °C) to give a nicely linear Arrhenius plot (r = 0.999 98). Most of the entropies of activation are small positive values in agreement with previous observations by Kevill[12a] and Bentley.[12b] The three triflates showed nicely linear $mY_{2-\mathrm{AdOTf}}$ relations for the solvents AcOH, HCO_2H, ethanol, methanol, and aqueous ethanol (Figure 1). The

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(11) For a leading review and compilation of $Y_{2-\mathrm{AdOTf}}$ values, see: Bentley, T. W.; Llewellyn, G. *Progr. Phys. Org. Chem.* **1990**, *17*, 121.

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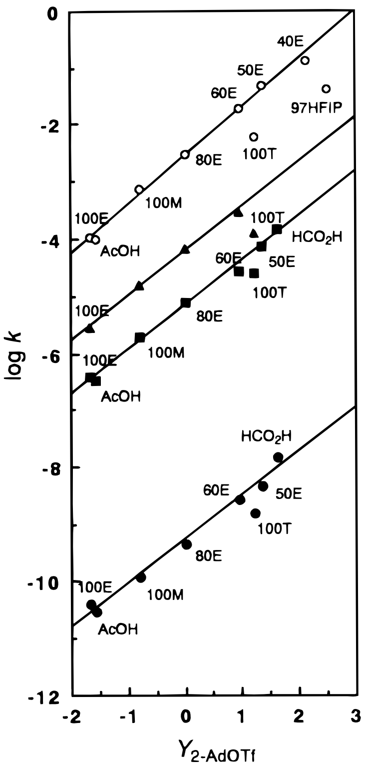
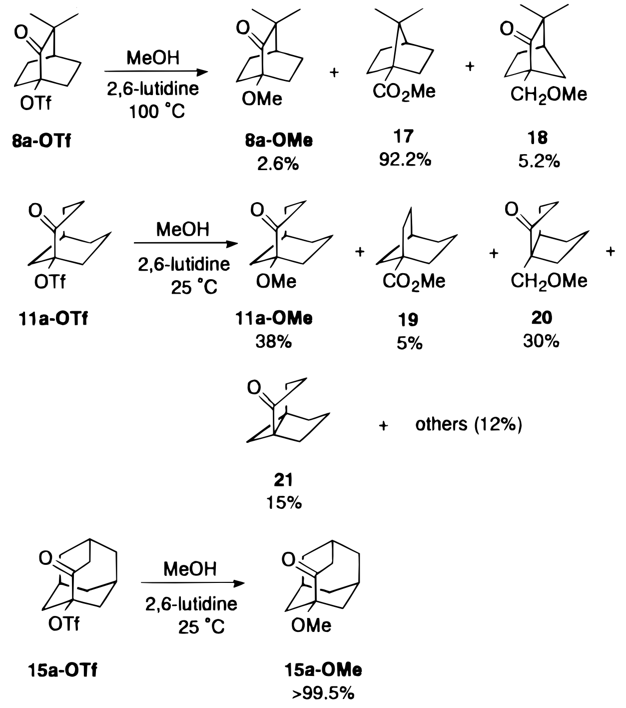


Figure 1. The mY_{OTf} relations for the solvolyses at 25 °C of **8a-OTf** (solid circle, $m = 0.77 \pm 0.03$, $r = 0.995$), **10a-OTf** (solid square, $m = 0.78 \pm 0.03$, $r = 0.997$), **11a-OTf** (solid triangle, $m = 0.78 \pm 0.02$, $r = 0.999$), and **15a-OTf** (open circle, $m = 0.85 \pm 0.03$, $r = 0.997$). The points for 100T and 97HFIP are excluded in the least-squares calculations. E and M stand for ethanol and methanol, respectively, and the attached numbers mean their vol % in aqueous solutions. 100T and 97HFIP mean 2,2,2-trifluoroethanol and 97% (w/w) 1,1,1,3,3,3-hexafluoro-2-propanol, respectively.

points for TFE and 97% HFIP that somewhat deviate downward have not been included in the least-squares calculations. Since such deviations have also been observed in the solvolyses of 3-oxobicyclo[2.2.2]oct-1-yl triflate[13a] and 4-oxo-2-adamantyl triflates,[13b] the present deviations would also be ascribed to the same reason that is characteristic of the oxo compounds. Presumably, the acidic TFE and HFIP strongly solvate at the oxo group and make the oxo group more electron withdrawing than in neutral solvents. The ordinary behavior of acetic and formic acids in the $mY_{2\text{-AdOTf}}$ relations (Figure 1) would be ascribed to the unavailability of a hydroxylic proton owing to dimer formation. The m values are 0.77 ± 0.03 ($r = 0.995$) (**8a-OTf**), 0.78 ± 0.02 ($r = 0.999$) (**11a-OTf**), and 0.85 ± 0.03 ($r = 0.997$) (**15a-OTf**).[14]

The product studies were conducted for methanolysis at appropriate temperatures in the presence of 2,6-lutidine: the product distributions are shown in Scheme 1. Except for the case of **15a-OTf** that exclusively afforded the corresponding methyl ether, **8a-OTf** and **11a-OTf** gave complex product mixtures. GLC analyses of the methanolysis product from **8a-OTf** showed the formation of **8a-OMe** (2.6%) and two Wagner–Meerwein rearrangement products, i.e., methyl 7,7-dimethylbicyclo[2.2.1]heptane-1-carboxylate (**17**) (92.2%) and 1-(methoxymethyl)-3,3-dimethylbicyclo[2.2.1]heptan-2-one (**18**) (5.2%). The products **8a-OMe** and **17** were identified by comparing their spectra and GLC retention times with those of authentic samples. **18** was identified on the basis of the ^{1}H NMR coupling of the methylene attached to the chiral bridgehead position and nonequivalence of the two geminal methyl groups in ^{13}C NMR (δ 21.5, 23.1).

Scheme 1



The methanolysis of **11a-OTf** at 25 °C was found by GLC to afford four major products, i.e., **11a-OMe** (38%), methyl bicyclo[3.2.1]octane-1-carboxylate (**19**) (5%), 1-(methoxymethyl)bicyclo[3.3.0]octan-2-one (**20**) (30%), 2,3,5,6-tetrahydro-3a,6a-methano-1*H*,4*H*-pentalen-1-one[15a] (**21**) (15%), and several unidentified compounds amounting to 12%. **11a-OMe** and **19** were identified by the comparison of NMR spectra with those of related compounds. **20** was characterized by spectral data and the Wolff–Kishner reduction to (methoxymethyl)bicyclo[3.3.0]octane, whose spectral data agreed with those of an authentic sample. **21** was identified on the basis of perfect agreement of the spectral data with those reported.[15b]

Solvolyses of Class B Substrates 10a-OTf, 12a-OTr, and 13a-OTr. These three substrates showed curved first-order correlations when $\ln(a/a - x)$ was plotted against reaction time. The mode of curvature of **10a-OTf** was different from that of **12a-OTr** and **13a-OTr**; in the solvolysis of **10a-OTf** a slight upward drift was detected, whereas for the latter two compounds a marked downward drift was observed. In Table 2 are given the initial first-order rate constants. Since these rate constants are somewhat rough values, the activation parameters may not be wholly reliable, although the Arrhenius plot for the solvolysis of **10a-OTf** in 80% ethanol at 0, 25, and 50 °C was nicely linear ($r = 1.000$). Despite the use of initial rates, the mY plots were linear, giving m values of 0.78 ± 0.03 ($r = 0.995$), 1.03 ± 0.05 (r

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(14) The errors are given as standard errors.

(15) (a) The formation of **21** was reported in a separate communication: Takeuchi, K.; Ohga, Y.; Tokunaga, K.; Tsugeno, A. *Tetrahedron Lett.* **1996**, *37*, 8185. The details will be reported elsewhere. (b) Mash, E. A.; Nelson, K. T. *Tetrahedron* **1987**, *43*, 679.

Table 2. Initial First-Order Rate Constants for the Solvolyses of Class B Substrates 10a-OTf, 12a-OTr, and 13a-OTr

compd[a]	solvent[b]	temp (°C)	k^c (s^{-1})	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (eu)
10a-OTf	MeOH	25	1.91×10^{-6}		
	EtOH	50	8.82×10^{-6}		
		25	3.74×10^{-7}	23.6 ± 0.8	−8.7 ± 2.5
	80% EtOH	50	1.66×10^{-4}		
		25	7.88×10^{-6}	22.7 ± 0.3	−5.8 ± 1.2
		0	2.18×10^{-7}		
	60% EtOH	25	2.75×10^{-5}		
	50% EtOH	25	7.30×10^{-5}		
	TFE	25	2.44×10^{-5}		
	AcOH	25	3.14×10^{-7}		
	HCO_2H	25	1.49×10^{-4}		
12a-OTr	MeOH	75	2.77×10^{-4}		
		50	2.10×10^{-5}		
		25	$(1.0 \pm 0.2) \times 10^{-6\,d}$	22.5 ± 1.2	−11 ± 3
	EtOH	75	4.58×10^{-5}		
		50	3.09×10^{-6}		
		25	$(1.3 \pm 0.2) \times 10^{-7\,d}$	23.5 ± 0.9	−11 ± 3
	80% EtOH	50	1.38×10^{-4}		
		25	9.40×10^{-6}	20.0 ± 0.7	−15 ± 3
	60% EtOH	25	5.78×10^{-5}		
13a-OTf	MeOH	50	1.55×10^{-5}		
		25	3.01×10^{-7}	29.6 ± 0.7	11 ± 3
	EtOH	75	8.71×10^{-5}		
		50	3.20×10^{-6}		
		25	$(6.7 \pm 1.0) \times 10^{-8\,d}$	28.9 ± 0.9	5.8 ± 2.6
	80% EtOH	25	3.24×10^{-6}		
	60% EtOH	25	1.52×10^{-5}		

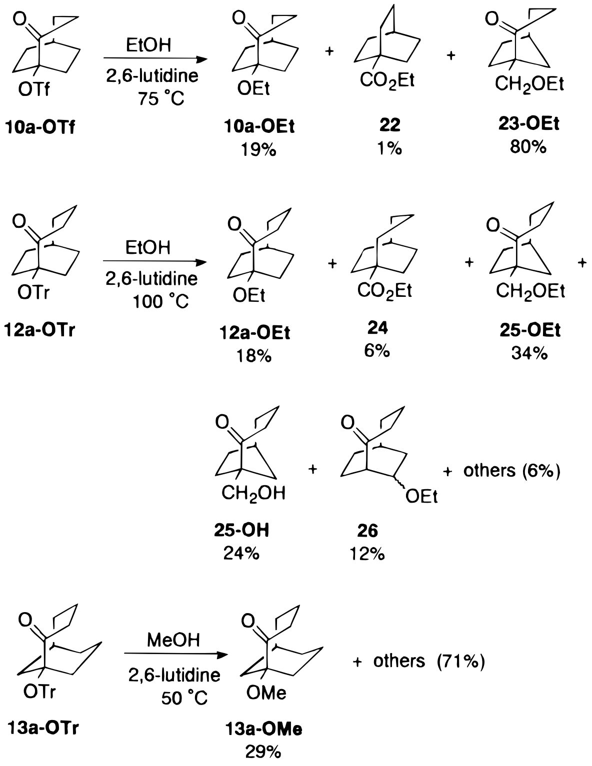
[a] The concentration of the substrate was generally 0.020 mol L^{-1}. [b] Methanol, ethanol, aqueous ethanols, and TFE contained 0.025 mol L^{-1} 2,6-lutidine. Acetic acid and formic acid contained 0.025 mol L^{-1} sodium acetate or soldium formate, respectively. Percentages ethanol denote % (v/v) of ethanol in ethanol−water at 25 °C. [c] Initial rate determined titrimetrically by a single run within an experimental error ± 5%. [d] Extrapolated from data at other temperatures.

= 0.998), and 0.94 ± 0.08 (r = 0.993) for **10a-OTf**, **12a-OTr**, and **13a-OTr**, respectively.[14] The $mY_{2\text{-AdOTf}}$ plot for **10a-OTf** is given in Figure 1.

The products of ethanolysis of **10a-OTf** in the presence of 2,6-lutidine were studied at 75 °C. The major product was 1-(ethoxymethyl)bicyclo[3.2.1]octan-2-one (**23-OEt**) (80%): 1-ethoxybicyclo[3.2.2]nonan-2-one (**10a-OEt**) (19%) and ethyl bicyclo[2.2.2]octane-1-carboxylate (**22**) (1%) were also formed (Scheme 2). The formation of a large amount of **23-OEt** and the upward curvature of the first-order plot indicated the involvement of isomerization of **10a-OTf** to (2-oxobicyclo[3.2.1]oct-1-yl)methyl triflate (**23-OTf**) of higher reactivity as shown in Scheme 3.

With a view to obtaining supporting evidence for this isomerization, the solvolysis of **23-OTf** was conducted. **23-OTf** was prepared from **23-OH** that was formed in the hydrolysis of **10a-OTf** in 80% acetone. The product of solvolysis of **23-OTf** in ethanol was exclusively the corresponding ethyl ether **23-OEt**. The rates of solvolysis in MeOH, EtOH, and aqueous EtOH at 50 °C in the presence of 0.025 mol L^{-1} 2,6-lutidine are summarized in Table 3. The rates are very close to each other with an m value of 0.19 (r = 0.994), showing that **23-OTf** solvolyzes by a k_s route. It is to be noted that the rates of **23-OTf** are greater than those of **10a-OTf**, approximately 30-fold times those in EtOH, and 4-fold times those in 80% EtOH. The faster rates are in accord with the fact that an attempt to directly observe **23-OTf** by NMR during solvolysis failed. The reaction pathway is summarized in Scheme 4.[16]

Scheme 2



The ethanolysis of **12a-OTr** and **13a-OTr** showed downward drifts of first-order plot as exemplified by the behavior of **12a-OTr** at 75 °C (Figure 2). At approximately 2 half-lives the plot approached a straight line with a rate constant ~3 × 10^{-6} s^{-1}, which was about 15 times smaller than the initial rate constant of 4.58 × 10^{-6} s^{-1}. From our experience in the solvolyses of **10a-OTf**, we presumed that the primary tresylates, which would form on rearrangement and ion-pair return, solvolyze slower than the starting tresylates **12a-OTr** and **13a-OTr**. In the present work, the behavior of **12a-OTr** was studied in greater detail than that of **13a-OTr**, since the product from **13a-OTr** was a very complex mixture of

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(16) No effort has been made to differentiate between the intermediates having a protonated cyclopropane ring and a primary cationic carbon in Schemes 4 and 5.

Scheme 3

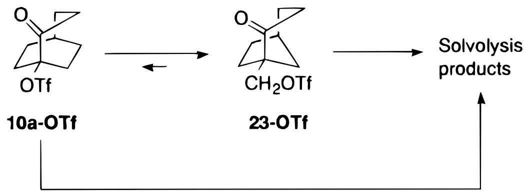
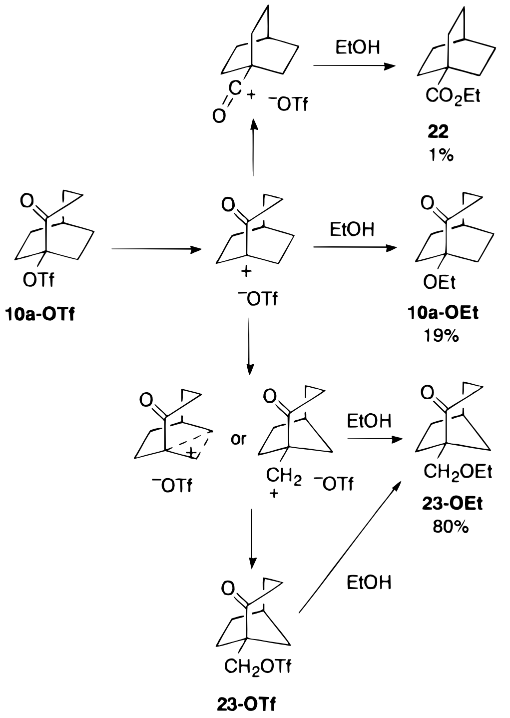


Table 3. First-Order Rate Constants for the Solvolyses of 23-OTf at 50 °C

solvent[a]	k^b (s^{-1})
EtOH	3.06×10^{-4} [c]
80% EtOH	7.12×10^{-4} [d]
60% EtOH	1.04×10^{-3} [d]
MeOH	5.42×10^{-4} [d]

[a] Buffered with 0.025 mol L^{-1} 2,6-lutidine. [b] Determined by a single run with correlation coefficients greater than 0.999. [c] Determined titrimetrically by using 0.005 mol L^{-1} of the substrate. [d] Determined conductimetrically by using 2×10^{-4} mol L^{-1} of the substrate.

Scheme 4



many components. We postulated that **12a-OTr** would rearrange to (2-oxobicyclo[4.2.1]non-1-yl)methyl tresylate (**25-OTr**) that solvolyzes approximately 15 times slower than **12a-OTr**. This was proved in two ways. First, **25-OTr** was synthesized and solvolyzed in ethanol (0.025 mol L^{-1} 2,6-lutidine) at 75 °C. The solvolysis showed good first-order kinetics, and the rate constant (3.07×10^{-6} s^{-1}) agreed well with that obtained from the later linear portion of the first-order plot in Figure 2. Second, direct ^{13}C NMR measurements of a reaction solution in ethanol with initial concentrations of 0.74 mol L^{-1} **12a-OTr** and 0.75 mol L^{-1} 2,6-lutidine clearly showed that **12a-OTr** solvolyzed accompanied by rearrangement to **25-OTr**. At 34 h the signals of **12a-OTr** almost completely disappeared and those of **25-OTr** were observed.

The products of solvolyses are summarized in Scheme 2. The products **12a-OEt** and **24** were identified from the similarity of ^{13}C NMR spectra to those of **12a-OH** and the carboxylic acid corresponding to **24**, respectively.

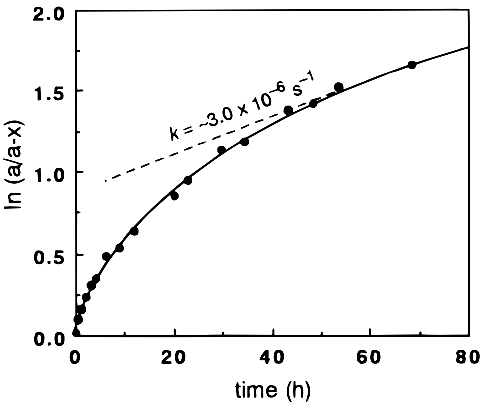


Figure 2. Plot of ln($a/a - x$) against reaction time in the ethanolysis of **12a-OTr** (0.00502 mol L^{-1}) in the presence of 2,6-lutidine (0.025 mol L^{-1}) at 75 °C.

Characterization of **25-OEt** and **25-OH** was based on the presence of an ethoxymethyl or a hydroxymethyl group that is attached to the bridgehead chiral carbon. The formation of 8-ethoxybicyclo[4.2.2]decan-2-one (**26**) indicates the involvement of a hydride shift in the first-formed bridgehead carbocation to give a secondary carbocation as the precursor of **26**. A rather unexpected product was **25-OH** that was suspected to be formed by the sulfur–oxygen cleavage of the primary tresylate Actually, ethanolysis of **25-OTr** at 125 °C in the presence of excess 2,6-lutidine gave the corresponding ethyl ether **25-OEt** and primary alcohol **25-OH** in 26 and 74% yields, respectively.

Complex reactions of tresylates have been a recent topic.[17] The S–O cleavage of **25-OTr** by ethanol would give **25-OH** and ethyl tresylate. The fact that the ethanolyses of **12a-OTr** and **25-OTr** could be titrimetrically followed means that these tresylates must react at rates much slower than the rate of acid formation from ethyl tresylate. Actually, ethyl tresylate solvolyzed much faster than **12a-OTr** and **25-OTr** by factors of 20 and 300, respectively, at 75 °C in the presence of 0.025 mol L^{-1} 2,6-lutidine [k: 5.18×10^{-6} (25 °C); 8.46×10^{-5} (50 °C); 9.25×10^{-4} s^{-1} (extrapolated to 75 °C)]. The solvolysis pathway of **12a-OTr** is illustrated in Scheme 5.[16]

Solvolyses of Class C Substrates 9a-OTf and 14a-OTf. These two triflates exhibited very peculiar kinetic behavior. Even in the presence of added 2,6-lutidine (0.025–0.028 mol L^{-1}) in ethanol, their first-order plots showed an upward drift as the reaction proceeded. We interpret this behavior as the result of hemiacetal formation (Scheme 6). The plot approached linear lines when the initial concentrations of the triflates were decreased from 0.02 mol L^{-1} to 10^{-3}–10^{-4} mol L^{-1}. Obviously, the formed triflic acid catalyzed the reaction even in the presence of an excess amount of 2,6-lutidine, and the catalysis decreased with the decrease in the triflic acid concentration.[18] Because of these ambiguities, the two triflates were excluded as substrates for kinetic studies. It is surprising, however, that all of these peculiar

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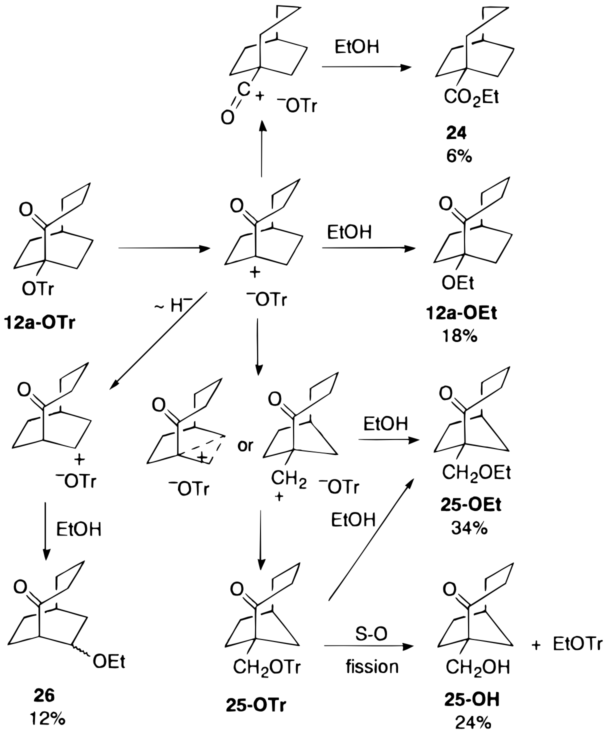
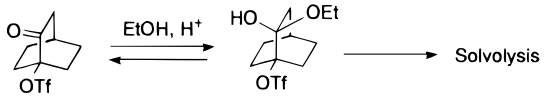
(17) (a) King, J. F.; Gill, M. S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1612. (b) Jennissen, H. P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2495. (c) King, J. F.; Gill, M. S. *J. Org. Chem.* **1996**, *61*, 7250.

(18) Base-catalyzed hemiacetal formation that causes difficulties in kinetic work has recently been reported for the solvolysis of 2,2-dimethyl-3-oxobicyclo[2.2.1]hept-1-yl triflate in 60% ethanol in the presence of triethylamine: Martinez, A. G.; Barcina, J. O.; Vilar, E. T. *Tetrahedron* **1996**, *52*, 14041.

Scheme 5



Scheme 6



phenomena vanish by introducing methyl groups as in **8a-OTf** or placing a methylene group between the carbonyl group and bridgehead position as in **15a-OTf**. Apparently, these structural modifications retard the solvent addition to the carbonyl group.

^{18}O Exchange in Solvolysis in the Presence of $H_2{}^{18}O$. In the above section we assumed that the addition of a solvent molecule to the carbonyl group would cause abnormal kinetic behavior in **9a-OTf** and **14a-OTf**. With a view to gaining evidence to substantiate this assumption, we examined ^{18}O exchange at the carbonyl oxygen of these triflates and **8a-OTf** and **15a-OTf** as references.

A possibility of ^{18}O exchange in water workup of **14a-OMe** was first examined. **14a-OMe** containing 10 atom % ^{18}O on the carbonyl oxygen (**14a-^{18}O-OMe**) was mixed with an equimolecular amount of triflic acid and 2,6-lutidine in diethyl ether. The solution was washed with saturated aqueous sodium chloride at 0 °C and dried. Mass spectrometric examination showed that only (20 ± 2)% of the labeled ^{18}O remained. The result shows that the addition of water to the carbonyl group of **14a-OMe** is very facile. It is expected that **14a-OTf**, containing a highly electronegative triflate group, would undergo the ^{18}O exchange more easily. **14a-OMe** that was obtained as a product of solvolysis in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O) with added 2,6-lutidine at 25 °C for 10 half-lives was also found to contain (20 ± 2)% of the theoretical amount after water workup. Therefore, ^{18}O exchange undoubtedly occurred during solvolysis.

On the contrary, aqueous treatment of **15a-OTf** enriched with 10 atom % ^{18}O on the carbonyl oxygen did not change the ^{18}O content. Notably, the product of solvolysis **15a-OMe** under the above-mentioned conditions was not enriched by ^{18}O within an experimental error of ±2%. Therefore, the possibility of the carbonyl addition process in the solvolysis of **15a-OTf** was ruled out. The difference in the solvolytic behavior between **14a-OTf** and **15a-OTf** apparently can be attributed to the difference in the steric hindrance around the carbonyl group.

8a-OTf and **9a-OTf** solvolyzed very slowly in 90% methanol−10% $H_2{}^{18}O$ even at 100 °C with a half-life of 11 h for the former. The first-order plot for the solvolysis in 90% MeOH in the presence of 2,6-lutidine at 100 °C was nicely linear for **8a-OTf** but showed an upward drift for **9a-OTf**. Because of the long exposure of the products to a much higher temperature than in the solvolyses of **14a-OTf** and **15a-OTf**, we anticipated the possibility that prolonged reaction time might cause ^{18}O exchange that is not inherent to the solvolysis process. Accordingly, the ^{18}O content in the unreacted triflates was analyzed at 75% conversion. Aqueous treatment was avoided during workup. Mass spectrometric analyses showed that there was no [(0 ± 4)%] ^{18}O exchange in **8a-OTf**, but in **9a-OTf** an exchange of (30 ± 4)% was observed.

Consequently, it is highly probable that **9a-OTf** and **14a-OTf** solvolyze, at least in part, accompanied by solvent addition to the carbonyl group, whereas **8a-OTf** and **15a-OTf** are free of such a pathway.

Rate Ratios $k(X = O)/k(X = H_2)$ and $k(X = CH_2)/k(X = H_2)$. In the present study we employed the rate ratios of α-carbonyl compounds (**7a**) to parent ones (**7c**) as an index to diagnose the presence or absence of carbonyl π conjugation in the carbocationic transition state. It was expected that an increase in the ring flexibility would increase the π conjugation in the carbocation, if it was so effective as to be detected by solvolysis rate studies. The usefulness of this methodology has been proved for π conjugation in allylic (**7b-L**),[7c] thiocarbonyl,[19] and imino[20] systems. Table 4 shows pertinent rate data and rate ratios, $k(X = O)/k(X = H_2)$ and $k(X = CH_2)/k(X = H_2)$, for solvolyses in ethanol or 80% ethanol at 25 °C. The rate constants for all of the allylic substrates (**7b-L**)[7c] and most of the parent ones (**7c-L**)[7c,8b,c] of Table 4 have been reported previously. In the present work the rates of **12c-OTr** and **13c-OTr** have been estimated from those of respective chlorides by using a tresylate/chloride conversion factor for the 1-adamantyl system in ethanol.[21,22]

Previously, we proposed that olefinic strain energies of bridgehead olefins[25] would be a good measure for the

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[19] Tokunaga, K.; Ohga, Y.; Takeuchi, K. *Tetrahedron Lett.* **1996**, *37*, 2241.

[20] Creary, X.; Jiang, Z. *J. Org. Chem.* **1996**, *61*, 3482.

[21] Takeuchi, K.; Ikai, K.; Shibata, T.; Tsugeno, A. *J. Org. Chem.* **1988**, *53*, 2852.

[22] Generally, the bridgehead reactivity ratio between two skeletal systems is reasonably constant, irrespective of the leaving group. Reported data show that the 1-adamantyl/bicyclo[2.2.2]oct-1-yl rate ratio in ethanol at 25 °C is $10^{4.2}$ for triflate[8b,21] or $10^{3.9}$ for tosylates.[23,24a] Changing ethanol to 80% ethanol had only minimal effect on the rate ratio. On the other hand, uncertainties in the conversion factors for changes in the leaving group are estimated to be in the range $10^{\pm 0.2}$ for bridgehead substrates.[24b] Consequently, an allowance of $10^{\pm 0.2}$–$10^{\pm 0.3}$ should be made for $k(X = O)/k(X = H_2)$ ratios. These uncertainties, however, do not alter the conclusion.

[23] Kevill, D. N.; Kolwyck, K. C.; Weitl, F. L. *J. Am. Chem. Soc.* **1970**, *92*, 7300.

[24] (a) Bentley, T. W.; Bowen, C. T.; Morten, D. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5466. (b) Bentley, T. W.; Roberts, K. *J. Org. Chem.* **1985**, *50*, 5852.

Table 4. Rates and Rate Ratios for the Solvolyses of Various Bridgehead Compounds in Ethanol or 80% Ethanol at 25 °C

	k^a (s^{-1})			rate ratio^a	
system	X = O	X = CH$_2$	X = H$_2$	k(X = O)/k(X = H$_2$)	k(X = CH$_2$)/k(X = H$_2$)
3,3-dimethylbicyclo[2.2.2]oct-1-yl triflate (**8**)	$3.9 \times 10^{-11\,b}$		$8.99 \times 10^{-3\,b}$	$10^{-8.4\,b}$	
bicyclo[2.2.2]oct-1-yl (**9**)		$2.96 \times 10^{-7\,b,c}$	$2.14 \times 10^{-3\,b,c}$		$10^{-3.9\,b}$
bicyclo[3.2.2]non-1-yl (**10**)	$3.74 \times 10^{-7\,b}$	$7.17 \times 10^{-6\,c,d}$	$4.75 \times 10^{-5\,c,d}$ $6.7 \times 10^{\,b,e}$	$10^{-8.3\,b}$	$10^{-0.8\,d}$
bicyclo[3.3.1]non-1-yl (**11**)	$2.88 \times 10^{-6\,b}$	$2.83 \times 10^{-3\,c,d}$	$3.28 \times 10^{-4\,c,d}$ $4.6 \times 10^{2\,b,e}$	$10^{-8.2\,b}$	$10^{0.9\,d}$
bicyclo[4.2.2]dec-1-yl (**12**)	$1.3 \times 10^{-7\,f}$	$3.14 \times 10^{-4\,c,g,h}$	$4.51 \times 10^{-6\,g,i}$ $6.3 \times 10^{2\,f,j}$ $4.52 \times 10^{-4\,c,g,h}$	$10^{-9.7\,f}$	$10^{-0.2\,g,h}$
bicyclo[4.3.1]dec-1-yl (**13**)	$6.7 \times 10^{-8\,f}$	$6.88 \times 10^{-5\,c,h,k}$	$7.28 \times 10^{-7\,g}$ $1.0 \times 10^{2\,f,j}$ $1.46 \times 10^{-5\,c,h,k}$	$10^{-9.2\,f}$	$10^{0.7\,h,k}$
3-homoadamantyl (**15**)	$1.04 \times 10^{-4\,b}$	$1.04 \times 10^{-7\,c,h,l}$	$1.42 \times 10^{-6\,c,h,l}$ $1.39 \times 10^{-6\,m}$ $4.9 \times 10^{4\,b,n}$	$10^{-8,7\,b}$	$10^{-1.1\,h,l}$

[a] In ethanol unless otherwise noted. For k's of 2-oxo substrates, see Tables 1 and 2. [b] Triflate. [c] Reference 7c. [d] Mesylate. [e] Estimated by multiplying k of mesylate by a factor of 1.4×10^6 of OTf/OMs rate ratio in ref 21. [f] Tresylate. [g] Chloride. [h] In 80% ethanol. [i] $k = 1.03 \times 10^{-4}$ s^{-1} at 50 °C; $\Delta H^{\ddagger}$ 23.4 kcal/mol; $\Delta S^{\ddagger}$ −4.6 eu. [j] Estimated by multiplying k of chloride by a factor of 1.4×10^8 for OTr/Cl rate ratio in ref 21. [k] Trifluoroacetate. [l] Heptafluorobutyrate. [m] Bromide. [n] Estimated by multiplying k of bromide by a factor of 3.5×10^{10} for OTf/Br rate ratio in ref 21.

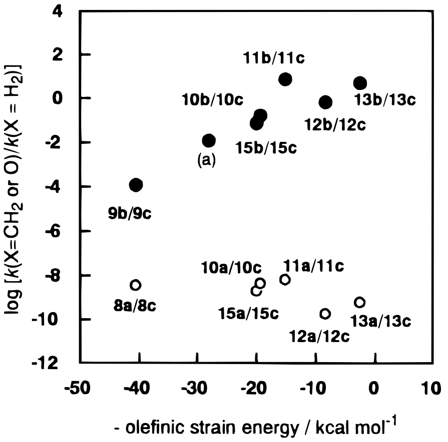

Figure 3. Plots of log[k(X = O)/k(X = H$_2$)] and log[k(X = CH$_2$)/k(X = H$_2$)] against olefinic strain (kcal mol^{-1}) for the solvolysis of various bridgehead compounds in ethanol or 80% ethanol at 25 °C. For the rate data and olefinic strain values, see Table 3 and ref 25, respectively. The point shown by (a) is for the 2-methylenebicyclo[3.2.1]oct-1-yl system, which is described in ref 7c.

conjugative ability of 2-methylene bridgehead carbocations.[7c] It was shown that the more stable the corresponding bridgehead olefin, the easier the allylic conjugation.[7c] A plot of log[k(X = CH$_2$)/k(X = H$_2$)] vs olefinic strain energies for some systems is reproduced in Figure 3. In the same figure, the log[k(X = O)/k(X = H$_2$)] values are also plotted. In contrast with the steep increase in log[k(X = CH$_2$)/k(X = H$_2$)] with decrease in the olefinic strain energy, the log[k(X = O)/k(X = H$_2$)] values are essentially constant. The result suggests that the carbonyl π-conjugative stabilization in the incipient 2-oxo bridgehead carbocations is too small to be detected by using the solvolysis method.[26] The more negative values for **12a/12c** and **13a/13c** than the values for more rigid systems are contrary to the prediction when carbonyl π conjugation is at work in the incipient 2-oxo carbocations. This might be ascribed to highly complex conformations of the systems **12** and **13** in the ground and transition states. The location of the points for **12b/12c** and **13b/13c** that are slightly lower than expected might also be ascribed to similar reasons.

It has been suggested that the preferred formation of rearrangement products **17** (92.2%) and **18** (5.2%) (Scheme 1) might indicate σ-participation leading to a nonclassical ion.[1d,e] On the other hand, we recently reported that the logarithms of the rates of **8a-OTf**, the 2-thioxo derivative of **8a-OTf**, and **9b-OTf** relative to the corresponding parent triflates are linearly correlated with the field/inductive parameter, σ_F,[28] for the group $-C(C_6H_5)=X$ (X = CH$_2$, S, O).[19] The result suggests that the three bridgehead compounds having the bicyclo[2.2.2]octyl structure solvolyze via k_C processes without significant σ-participation. The exclusive bridgehead substitution in the solvolysis of **15a-OTf** suggests that the rearrangement is related to the skeletal structure of the first-formed, classical, bridgehead cation rather than the involvement of a nonclassical ion.

Molecular Orbital Calculations. PM3 calculations were conducted on the 2-oxo and 2-methylene bicyclic bridgehead carbocations and the corresponding hydrocarbons (L = H) through the MOPAC system.[29a] In Table 5 are summarized pertinent bond orders.[29b] A plot of log[k(X = CH$_2$ or O)/k(X = H$_2$)] vs ΔBO($C_\alpha-C_\beta$) (Figure 4) shows that the log[k(X = CH$_2$)/k(X = H$_2$)] value increases with the increase in ΔBO($C_\alpha-C_\beta$). This indicates that the allylic conjugation of an incipient carbocation becomes operative in the 2-methylene system with increasing structural flexibility. On the contrary, the

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(25) Maier, W. F.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 1891.

(26) Hyperconjugative stabilization of the parent carbocations by the hydrogens on the β-carbons would increase as the ring system becomes more flexible. Therefore, the essentially constant rate ratios of k(X = O)/k(X = H$_2$) = $10^{-8.2}$−$10^{-8.7}$ might indicate the gain in the π-conjugative electron donation from an α-carbonyl group with the increase in ring flexibility. On the other hand, a nicely linear correlation of solvolytic reactivities of various bridgehead compounds with a difference in strain energies between the ground state and intermediate carbocations[27] suggests essential constancy of the hydrogen hyperconjugative stabilization, irrespective of structural flexibility.

(27) Müller, P.; Mareda, J. Bridgehead Reactivity in Solvolysis Reactions. In *Cage Hydrocarbons*; Olah, G. A., Ed.; Wiley-Interscience: New York, 1990; pp 189−217.

(28) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

(29) (a) MOPAC Version 6, Stewart, J. J. P. *QCPE Bull.* **1989**, *9*, 10. (b) For notations C_α and C_β, see footnote to Table 5. ΔBO($C_\alpha-C_\beta$) means the increment in $C_\alpha-C_\beta$ bond order on ionization of **7a-H** or **7b-H**.

Table 5. PM3 Calculated Bond Orders for Carbocations and the Corresponding Hydrocarbons (L = Hydrogen)[a]

	2-oxo						2-methylene					
	cation		hydrocarbon		ΔBO		cation		hydrocarbon		ΔBO	
system	$C_\alpha-C_\beta$	$C_\beta=O$	$C_\alpha-C_\beta$	$C_\beta=O$	$C_\alpha-C_\beta$	$C_\beta=O$	$C_\alpha-C_\beta$	$C_\beta=CH_2$	$C_\alpha-C_\beta$	$C_\beta=CH_2$	$C_\alpha-C_\beta$	$C_\beta=CH_2$
8,9	0.896	2.046	0.923	1.935	−0.027	0.111	1.033	1.917	0.978	1.945	0.055	−0.028
10	0.893	2.012	0.924	1.924	−0.031	0.088	1.116	1.808	0.975	1.944	0.141	−0.136
11	0.895	2.000	0.925	1.921	−0.030	0.079	1.181	1.726	0.976	1.943	0.205	−0.217
15	0.896	1.999	0.926	1.912	−0.030	0.087	1.047	1.891	0.977	1.942	0.070	−0.051

[a] The arrangement of atom is $C_\alpha-C_\beta=O$ or $C_\alpha-C_\beta=CH_2$ with C_α being the bridgehead cationic center.

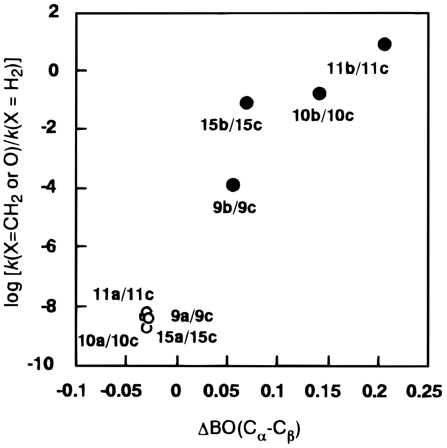
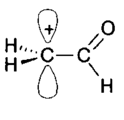


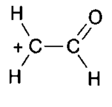
Figure 4. Plots of log[$k(X = O)/k(X = H_2)$] and log[$k(X = CH_2)/k(X = H_2)$] against the bond order difference ($\Delta BO(C_\alpha-C_\beta)$) calculated by PM3 for the solvolysis of various bridgehead compounds in ethanol or 80% ethanol at 25 °C.

$\Delta BO(C_\alpha-C_\beta)$ values for the 2-oxo system are essentially constant at approximately zero irrespective of the ring flexibility. This is in agreement with the above conclusion from experiments that the π conjugation is unimportant in the 2-oxo bridgehead carbocations.

More rigorous ab initio calculations on the 2-oxoethyl cation have been reported independently by the groups of Houk,[30a] Hopkinson,[31] and Creary.[30b] Houk and Creary compared the energies of **27** and **28**: the p−π overlap is inhibited in **27** but permitted in **28**. Houk used a double-ζ plus polarization basis set and concluded that **28** is more stable than **27** by 2.5 kcal mol^{-1}.[30a] Similarly, Creary concluded that **28** is more stable by 1.7 kcal mol^{-1} based on the calculations using MP2/6-31G**.[30b] On the other hand, Hopkinson reported on the basis of calculations using HF/6-31G*-optimized geometries that "there is essentially no double bond character in the C−C bond of the cations, i.e., valence tautomer **29** is not a significant contributor."[31]



27



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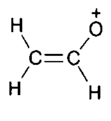
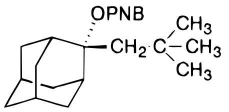


29

In any event, it should be noted that these ab initio calculations have been carried out on a primary cation. It is expected that the π-conjugative stabilization of ca. 2 kcal mol^{-1} (if any) by the contributor **29** would significantly decrease in tertiary α-carbonyl cations.

Origin of Unexpectedly Fast Solvolysis Rates of 1,1,3,3-Tetramethyl-2-oxobutyl Mesylate (16a-OMs). An important fact that led to the proposal of π-conjugative stabilization of α-carbonyl carbocation (**4a** ↔ **4b**) was the faster rate of solvolysis of **16a-OMs** than isopropyl mesylate by a factor of 55 in 97% HFIP at 25 °C.[6] Since **16a-OMs** was predicted to solvolyze 10^3−10^4 times slower than isopropyl mesylate on the basis of inductive effects, the major contribution of π conjugation (**4a** ↔ **4b**) was proposed to explain the net rate acceleration of 10^4−10^5. The steric acceleration of solvolysis of **16a-OMs** by the back strain (B-strain) was evaluated to be unimportant[6a] on the basis that 2-neopentyl-2-adamantyl *p*-nitrobenzoate (**30**) solvolyzes only 10 times faster than 2-methyl-2-adamantyl *p*-nitrobenzoate (**31**).[32] Nevertheless, we wish to point out that the steric acceleration was overly underestimated.



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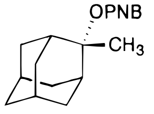
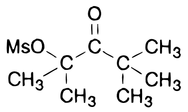
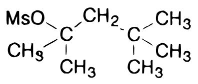


31

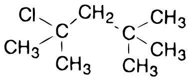
It is appropriate for the rate comparison to be made between **16a-OMs** and 1,1,3,3-tetramethylbutyl mesylate (**16c-OMs**). Because of difficulties in the synthesis of highly unstable **16c-OMs**, we focused on **16c-Cl**.



16a-OMs



16c-OMs



16c-Cl

About five decades ago, Brown and Fletcher found that **16c-Cl** solvolyzed 21 times faster than *tert*-butyl chloride in 80% ethanol at 25 °C and attributed this acceleration to partial relief of the ground state B-strain in the transition state.[33] In the 1980s, the involvement of nucleophilic solvent assistance in *tert*-butyl solvolyses in aqueous ethanol solvents was disclosed.[34] Recently, we found a nicely linear Grunwald−Winstein type relation of **16c-Cl** with the Y_{Cl} parameter[34] that is based on 1-adamantyl chloride.[35] This indicates that **16c-Cl** solvolyzes without significant nucleophilic solvent assistance. Actually, the **16c-Cl**/*t*-BuCl rate ratio in TFE at 25 °C is 275: an extrapolation of the mY_{Cl} plot to TFA

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(30) (a) Dixon, D. A.; Eades, R. A.; Frey, R.; Gassman, P. G.; Hendewerk, M. L.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 3885. (b) Creary, X.; Wang, Y.-X.; Jiang, Z. *J. Am. Chem. Soc.* **1995**, *117*, 3044.

(31) Lien, M. H.; Hopkinson, A. C. *J. Am. Chem. Soc.* **1988**, *110*, 3788.

(32) Fry, J. L.; Engler, E. M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1972**, *94*, 4628.

(33) (a) Brown, H. C.; Fletcher, R. S. *J. Am. Chem. Soc.* **1949**, *71*, 1845. (b) Brown, H. C.; Berneis, H. L. *J. Am. Chem. Soc.* **1953**, *75*, 10.

(34) Bentley, T. W.; Carter, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 5741.

(35) Takeuchi, K.; Ohga, Y.; Ushino, T.; Takasuka, M. *J. Phys. Org. Chem.* **1996**, *9*, 777.

Table 6. ^{13}C NMR Spectral Data (δ, $CDCl_3$) of 8a-OH and the 2-Oxo Bridgehead Triflates or Tresylates

compd	methine	methylene	quart C	C=O	CF_3	other C
8a-OH	38.0	23.2, 30.3	45.7, 74.2	220.7		23.7 (CH_3)
8a-OTf	37.2	23.4, 28.4	48.1, 96.8	209.9	118.2 (q, J = 319 Hz)	23.8 (CH_3)
9a-OTf	26.7	26.2, 28.2, 44.5	96.9	204.4	118.1 (q, J = 319 Hz)	
10a-OTf	26.5	24.7, 28.2, 28.4, 35.8	99.8	205.6	118.0 (q, J = 319 Hz)	
11a-OTf	30.9	21.3, 27.7, 29.9, 34.3, 38.6, 39.2	99.0	204.1	118.0 (q, J = 319 Hz)	
12a-OTr	24.6	21.1, 22.8, 30.7, 34.4, 40.6, 55.0 (q, J = 32.4 Hz)	95.4	212.8	121.0 (q, J = 278 Hz)	
13a-OTr	32.1	21.8, 22.6, 29.2, 35.9 36.6, 38.7, 43.2, 54.8 (q, J = 32.9 Hz)	94.9	211.6	121.0 (q, J = 277 Hz)	
14a-OTf	30.6, 47.5	34.4, 37.5, 44.0	97.9	204.4	118.2 (q, J = 319 Hz)	
15a-OTf	25.4, 27.9	33.7, 35.6, 38.3, 45.6	103.5	204.5	118.2 (q, J = 319 Hz)	

suggests a rate ratio of 950.[36] Thus, the rear-side shielding effect and the B-strain effect by the neopentyl group are enormous in **16c-Cl**. Consequently, it would be appropriate to attribute more than 50% of the rate-enhancing effect (10^2−10^3 of 10^4−10^5) in **16a-OMs**, which is structurally similar to **16c-Cl**, to the relief of the B-strain in the transition state. The rest of the effect may be ascribed to destabilization of the ground state by geminal interaction. [4a]

An examination of **16a-OMs**/**16c-OMs** rate ratios also supports the unimportance of π conjugation shown by **4a** ↔ **4b**. Assuming that the OMs/Cl rate ratios for the 1-adamantyl system[37,38] are applicable to **16c-L**, we obtain the **16a-OMs**/**16c-OMs** rate ratios of $10^{-7.9}$ in ethanol and $10^{-8.4}$ in acetic acid at 25 °C. These values are very close to the representative **7a/7c** rate ratios of $10^{-8.2}$−$10^{-8.7}$ that were obtained in this work.[39] Consequently, so long as we used the rate ratios $k(X = O)/k(X = H_2)$ as an index to diagnose the π-conjugative stabilization of α-carbonyl carbocations, we were unable to obtain supporting evidence not only for our bicyclic systems but also for the open-chain system **16a-OMs**.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 60, 90, or 270 MHz. ^{13}C NMR spectra were recorded at 22.5, 25, or 68 MHz. Gas chromatographic analyses were conducted on a PEG 20M column (3 mm × 2 m). Mass spectra were recorded on a GC-MS spectrometer. Elemental analyses were performed by the Microanalytical Center, Kyoto University, Kyoto. Ketols **9a-OH**,[7c,10] **10a-OH**,[7c] **11a-OH**−**13a-OH**,[9b] **14a-OH**,[7c,10] **15a-OH**,[7a,b,10] and ethyl tresylate[40] were reported previously. Solvolysis solvents were purified by previously described methods.[21] Anhydrous solvents used for synthesis were purified by the standard procedures. 2,6-Lutidine was distilled over CaH_2. Other commercially available reagents were of a reagent-grade quality and used as received. Medium-pressure liquid chromatography (MPLC) and conventional liquid chromatography were conducted on Merck silica gel 60 (230−400 mesh) and Nacalai Tesque silica gel No. I (60−200 mesh), respectively.

3,3-Dimethyl-1-hydroxybicyclo[2.2.2]octan-2-one (8a-OH). (a) Chromic Acid Oxidation. To a stirred solution of 3,3-dimethylbicyclo[2.2.2]octane-1,2-diol[9a] (2.50 g, 14.7 mmol) in acetone (52 mL) was added 5.28 mL of Jones reagent containing 3.19 mol L^{-1} H_2CrO_4 over 30 min at 20−25 °C. Excess chromic acid was destroyed by adding 2-propanol until the orange color vanished. The reaction mixture was filtered, the filtrate was stirred with $NaHCO_3$ (1.9 g) for 1.5 h and filtered, and the solvent was evaporated. The residue was dissolved in diethyl ether, and the solution was washed with saturated aqueous NaCl and dried ($MgSO_4$). Evaporation of solvent gave a yellowish solid which contained at least five components (TLC). The solid was again dissolved in diethyl ether and washed with 10% aqueous NaOH and dried ($MgSO_4$). Evaporation of solvent afforded a yellowish semisolid (0.91 g), which was found by TLC to contain at least three components. The semisolid was separated by conventional column chromatography (SiO_2, hexane−diethyl ether 55:45) to give **8a-OH** (0.66 g, 27%) as colorless crystals: mp 116.5−117.0 °C (from pentane); IR (CCl_4) 3520, 1720, 1390 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.14 (s, 6 H), 1.5−2.1 (m, 9 H), 3.2 (s, 1 H). Analytical data were unsatisfactory presumably because of hygroscopicity. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 70.08; H, 9.54. The triflate **8a-OTf** gave satisfactory analytical data (see below). ^{13}C NMR data are given in Table 6.

(b) Dimethyldioxirane Oxidation.[10] To a solution of 3,3-dimethylbicyclo[2.2.2]octane-1,2-diol (0.098 g, 0.58 mmol) in CH_2Cl_2 (15 mL) was added 9.2 mL of 0.0763 mol L^{-1} dimethyldioxirane in acetone at 0 °C, and stirring was continued at 0 °C, while the reaction was followed by TLC. Since the reaction was incomplete even after 9 h, the reaction mixture was stored in a refrigerator for a further 15 h at 3 °C, and then the solvent was rotary evaporated. To the residue was added diethyl ether, and the solution was dried ($MgSO_4$). Evaporation of solvent gave essentially pure **8a-OH** (0.096 g) in 99% yield.

3,3-Dimethyl-2-oxobicyclo[2.2.2]oct-1-yl Triflate (8a-OTf). To a stirred solution of **8a-OH** (0.221 g, 1.31 mmol) and pyridine (0.221 g, 2.79 mmol) in CH_2Cl_2 (2 mL) was added a solution of triflic anhydride (0.468 g, 1.66 mmol) in CH_2Cl_2 (2 mL) under N_2 at 0 °C. The yellowish solution was stored in a refrigerator at 5 °C overnight and then diluted with CH_2Cl_2. The resulting solution was washed at 0 °C with 10% aqueous HCl and water and dried ($MgSO_4$). Evaporation of solvent afforded a colorless solid (0.347 g) which was purified by conventional column chromatography (SiO_2, hexane−diethyl ether 7:3) to give **8a-OTf** (0.338 g, 86%) as colorless crystals: mp 113.0−114.0 °C (from hexane−benzene); IR (CCl_4) 1740, 1410, 1240, 1210, 1140 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.25 (s, 6 H), 1.6−2.6 (m, 9 H). Anal. Calcd for $C_{11}H_{15}F_3O_4S$: C, 44.00; H, 5.03. Found: C, 43.88; H, 4.84. ^{13}C NMR data are given in Table 6.

2-Oxobicyclo[2.2.2]oct-1-yl Triflate (9a-OTf). To a stirred solution of **9a-OH** (0.402 g, 2.87 mmol) and pyridine (0.466 g, 5.89 mmol) in CH_2Cl_2 (4 mL) was added a solution of triflic anhydride (0.972 g, 3.45 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The yellowish solution was stored in a freezer at −15 °C overnight, stirred at 0 °C for 30 min, and then diluted with CH_2Cl_2. The resulting solution was washed at 0 °C with water, 10% aqueous HCl, and water, and dried ($MgSO_4$). Evaporation of solvent afforded yellowish solid (0.68 g) which was recrystallized from hexane−benzene (20:1) to give **9a-OTf** (0.605 g, 77%) as

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[36] The first-order rate constant of **16c-Cl** at 25 °C in TFE is 2.86 × 10^{-2} s^{-1}: the rate constant in TFA is estimated to be 6.1 × 10^{-1} s^{-1} by extrapolation in an mY_{Cl} plot. For the rate constants of *tert*-butyl chloride in TFE and TFA, see, respectively: Shiner, V. J., Jr.; Dowd, W.; Fisher, R. D.; Hartshorn, S. R.; Kessick, M. A.; Milakofsky, L.; Rapp, M. W. *J. Am. Chem. Soc.* **1969**, *91*, 4838. Haake, P.; Ossip, P. S. *J. Am. Chem. Soc.* **1971**, *93*.

[37] The OMs/Cl rate ratios for the 1-adamantyl system at 25 °C are 3.1 × 10^6 in acetic acid and 1 × 10^6 in ethanol; see refs 11, 21, and 34 for rate data. The first-order rate constants at 25 °C of **16c-Cl** in acetic acid and ethanol are 1.61 × 10^{-5} and 3.73 × 10^{-6} s^{-1}, respectively; see refs 33 and 35.

[38] Bentley, T. W.; Carter, G. E. *J. Org. Chem.* **1983**, *48*, 579.

[39] Recently, we suggested that **16a-OMs** may not be a suitable model to attain p−π overlap between the developing cationic p orbital and the carbonyl π orbital, since the leaving mesylate anion most probably leaves along the C=O axis; Takeuchi, K.; Ohga, Y.; Ushino, T. *Chem. Lett.* **1996**, 763.

[40] Ohta, Y.; Kohda, K.; Kimoto, H.; Okano, T.; Kawazoe, Y. *Chem. Pharm. Bull.* **1988**, *36*, 2410.

colorless crystals: mp 81.5−82.5 °C; IR (CCl_4) 1755, 1250, 1210, 1150 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.6−2.6 (m, 11 H). Anal. Calcd for $C_9H_{11}F_3O_4S$: C, 39.71; H, 4.07. Found: C, 39.97; H, 4.00. ^{13}C NMR data are given in Table 6.

2-Oxobicyclo[3.2.2]oct-1-yl Triflate (10a-OTf). To a stirred solution of **10a-OH** (1.39 g, 9.03 mmol) and pyridine (1.53 g, 18.9 mmol) in CH_2Cl_2 (13 mL) was added a solution of triflic anhydride (2.81 g, 10.0 mmol) in CH_2Cl_2 (13 mL) at 0 °C. The resulting pale pink solution was stirred for 3 h at 0 °C and then stored in a freezer at −15 °C overnight. The reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with water, 10% aqueous HCl, water, and saturated aqueous $NaHCO_3$, and dried ($MgSO_4$ + 0.5 g of $NaHCO_3$). Evaporation of solvent afforded a greenish solid, which was recrystallized from hexane (25 mL) under N_2 at −15 °C to give **10a-OTf** (1.66 g, 64%) as colorless crystals: mp 48−50 °C; IR (CCl_4) 1730, 1410, 1210 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.7−2.6 (m, 13 H). Anal. Calcd for $C_{10}H_{13}F_3O_4S$: C, 41.96; H, 4.58. Found: C, 41.54; H, 4.88. ^{13}C NMR data are given in Table 6.

2-Oxobicyclo[3.3.1]non-1-yl Triflate (11a-OTf). To a stirred solution of **11a-OH** (0.200 g, 1.30 mmol) and pyridine (0.21 mL, 2.6 mmol) in CH_2Cl_2 (1.5 mL) was added a solution of triflic anhydride (0.440 g, 1.56 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C. The yellowish solution was further stirred for 30 min at 0 °C and then diluted with CH_2Cl_2. The resulting solution was washed at 0 °C with water, 10% aqueous HCl, 10% aqueous NaCl, and saturated aqueous $NaHCO_3$ and dried ($MgSO_4$ + 0.5 g of $NaHCO_3$). Evaporation of solvent afforded crude **11a-OTf** of approximately 96% purity as assessed by ^{13}C NMR as a yellowish solid (0.305 g): mp 61−64 °C; IR (CCl_4) 1730, 1410, 1210, 1150 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.5−2.7 (m, 13 H). ^{13}C NMR data are given in Table 6. The crystals were unstable in air, and the color changed from white to pale pink on standing at room temperature for a few minutes.

2-Oxobicyclo[4.2.2]dec-1-yl Tresylate (12a-OTr). To a solution of 2,2,2-trifluoroethanesulfonyl chloride (0.769 g, 4.21 mmol) in CH_2Cl_2 (7 mL) was added a solution of **12a-OH** (0.500 g, 2.97 mmol) and pyridine (3.77 g, 47.7 mmol) in CH_2Cl_2 (8 mL) with stirring at 0 °C, and then stirring was continued for 3 h at 0 °C. After subsequent stirring for 12 h at room temperature, the reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with water, 10% aqueous HCl, water, and saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). Evaporation of solvent afforded **12a-OTr** (0.930 g, 99%) as an unstable pale yellow oil, which was used for solvolysis studies without further purification: IR (CCl_4) 1710, 1385, 1325, 1280, 1260, 1185 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.9−3.0 (m, 15 H), 3.83 (q, 2 H, J = 9 Hz). ^{13}C NMR data are given in Table 6.

2-Oxobicyclo[4.3.1]dec-1-yl Tresylate (13a-OTr). To a stirred solution of **13a-OH** (0.551 g, 3.28 mmol) and triethylamine (0.50 g, 4.9 mmol) in CH_2Cl_2 (16 mL) was added 2,2,2-trifluoroethanesulfonyl chloride (0.72 g, 3.9 mmol) at 0 °C, and then stirring was continued for 40 min at −15 °C. The reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with water, 10% aq HCl, water, and saturated aqueous $NaHCO_3$ solution, and dried ($MgSO_4$). Evaporation of solvent afforded a yellowish oil (1.13 g), which was chromatographed with MPLC (SiO_2, hexane, hexane−diethyl ether 4:1) to give 0.74 g colorless crystals. Recrystallization from hexane (16 mL) gave **13a-OTr** (0.670 g, 65%) as colorless crystals: mp 90.0−91.0 °C; IR (CCl_4) 1710, 1380, 1325, 1280, 1260, 1180, 1140, 1100 cm^{-1}; ^{1}H NMR (CCl_4) δ.1.1−3.1 (m, 15 H), 3.80 (q, 2 H, J = 9 Hz). Anal. Calcd for $C_{12}H_{17}F_3O_4S$: C, 45.86; H, 5.45. Found: C, 45.78; H, 5.61. ^{13}C NMR data are given in Table 6.

2-Oxo-1-adamantyl Triflate (14a-OTf). To a stirred solution of **14a-OH** (0.500 g, 3.01 mmol) and pyridine (0.51 g, 6.5 mmol) in CH_2Cl_2 (4 mL) was added a solution of triflic anhydride (0.94 g, 3.3 mmol) in CH_2Cl_2 (4.5 mL) at 0 °C. The resulting solution was further stirred for 2 h at 0 °C and then stored in a refrigerator overnight. The reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with water, 10% aqueous HCl, water, and saturated aqueous $NaHCO_3$, and dried ($MgSO_4$ + 0.5 g of $NaHCO_3$). Evaporation of solvent under N_2 afforded a yellowish solid, which was then dissolved in a mixed solvent of pentane (21 mL) and diethyl ether (21 mL) at reflux under N_2 and recrystallized at −20 °C to give **14a-OTf** (0.680 g, 77%) as highly hygroscopic, unstable, pale yellow crystals: mp 119.0−121.0 °C; IR (CCl_4) 1756, 1415, 1200, 1140 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.9−2.7 (m, 12 H), 2.9 (s, 1 H). Anal. Calcd for $C_{11}H_{13}F_3O_4S$: C, 44.29 H, 4.39. Found: C, 44.53; H, 4.45. ^{13}C NMR data are given in Table 6.

4-Oxo-3-homoadamantyl Triflate (15a-OTf). To a stirred solution of **15a-OH** (0.360 g, 2.00 mmol) and pyridine (0.316 g, 4.00 mmol) in CH_2Cl_2 (3 mL) was added a solution of triflic anhydride (0.677 g, 2.40 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The yellowish solution was stored in a refrigerator overnight and then diluted with CH_2Cl_2. The resulting solution was washed at 0 °C with 10% aqueous HCl and water and dried ($MgSO_4$). Evaporation of solvent afforded a yellowish solid (0.54 g), which was recrystallized from a mixed solvent of pentane (5 mL) and diethyl ether (18 mL) to give **15a-OTf** (0.440 g, 70%) as colorless crystals: mp 88.0−89.0 °C; IR (CCl_4) 1720, 1410, 1210, 1145 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.5−2.6 (m, 13 H), 2.70 (br, 2 H). Anal. Calcd for $C_{12}H_{15}F_3O_4S$: C, 46.15; H, 4.84. Found: C, 46.19; H, 5.06. ^{13}C NMR data are given in Table 6.

Product of Methanolysis of 8a-OTf. A solution of **8a-OTf** (0.600 g, 2.00 mmol) and 2,6-lutidine (0.269 g, 2.51 mmol) in methanol (50.0 mL) was divided into 10 ampules and heated at 100 °C for 240 h (8.8 half-lives). Most of the methanol was distilled off with a Vigreux column, the residue was diluted with diethyl ether, and the solution was washed with saturated aqueous NaCl and dried ($MgSO_4$). A GLC analysis (PEG 20M) showed the product distribution shown in Scheme 1. Most of the solvent was distilled off with a Vigreux column, and the residue was separated by MPLC (SiO_2, hexane−diethyl ether 4:1, 7:3, 1:1) to give **17** (0.295 g, 81%), **18** (21 mg, 5.8%), and **8a-OMe** (9 mg, 2.5%) in this sequence. **17** was identified on the basis of perfect agreement of the GLC retention time with that of an authentic sample prepared from 7,7-dimethylbicyclo[2.2.1]heptane-1-carbonyl chloride and methanol in pyridine. **8a-OMe** was identified on the basis of perfect agreements of the spectral and GLC data with those of an authentic sample (see below). **18**: IR (CCl_4) 2960, 2860, 1730, 1390, 1380, 1190, 1110 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.7−2.3 (m, 7H) partly overlapped with 1.03 (s, 6H), 3.35 (s, 3H), 3.45 (d, 1H, J = 9 Hz), 3.67 (d, 1H, J = 9 Hz); ^{13}C NMR ($CDCl_3$) δ 221.1 (C), 71.0 (CH_2), 59.5 (CH_3), 58.9 (C), 45.2 (CH), 37.6 (CH_2), 27.0 (CH_2), 24.2 (CH_2), 23.1 (CH_3), 21.5 (CH_3).

1-Methoxy-3,3-dimethylbicyclo[2.2.2]octan-2-one (8a-OMe): An Authentic Sample. To a stirred mixture of 1-hydroxy-3,3-dimethylbicyclo[2.2.2]oct-2-yl benzoate[9a] (1.21 g, 4.41 mmol) and CH_3I (2.50 g, 17.6 mmol) in DMSO (10 mL) was added pulverized KOH (0.99 g). The mixture was stirred at room temperature for 40 min, poured into water, and extracted with CH_2Cl_2. The extract was washed with water and dried ($MgSO_4$), and the solvent was evaporated to give crude 1-methoxy-3,3-dimethylbicyclo[2.2.2]oct-2-yl benzoate, which was then saponified in refluxing methanol (20 mL) with KOH (0.9 g) for 3 h. The reaction mixture was diluted with diethyl ether, washed with saturated aqueous NaCl, and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane−diethyl ether 3:2) of the residue gave 1-methoxy-3,3-dimethylbicyclo[2.2.2]octan-2-ol (316 mg) as a colorless liquid in 39% yield based on 1-hydroxy-3,3-dimethylbicyclo[2.2.2]oct-2-yl benzoate: ^{1}H NMR (CCl_4) δ 1.00 (s, 3H), 1.06 (s, 3H), 1.2−2.1 (m, 9H), 2.23 (s, 1H), 3.12 (s, 3H), 3.23 (s, 1H). The 1-methoxy-3,3-dimethylbicyclo[2.2.2]octan-2-ol (315 mg, 1.71 mmol) was oxidized with pyridinium chlorochromate (0.55 g, 2.5 mmol) in CH_2Cl_2 (5 mL) at room temperature for 90 min and worked up in the usual manner to give a yellow liquid (0.298 g), which was purified by MPLC (SiO_2, hexane−diethyl ether 1:1) to give **8a-OMe** (0.187 g): IR (CCl_4) 2950, 1720, 1460, 1380, 1335, 1200, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 6H), 1.5−2.2 (m, 9H), 3.30 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 218.2 (C), 78.8 (C), 51.4 (CH_3), 47.0 (C), 37.5 (CH), 26.9 (CH_2), 23.5 (CH_3), 22.8 (CH_2).

Product of Methanolysis of 11a-OTf. A solution of **11a-OTf** (1.67 g, 5.84 mmol) in 0.050 mol L^{-1} 2,6-lutidine in methanol (146 mL) was kept at 25 °C for 138 h (11 half-lives), and then most of the methanol was evaporated. The residue was diluted with diethyl ether, washed with water, 10%

aqueous HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, and dried ($MgSO_4$). GLC (PEG 20M) analysis of the diethyl ether solution showed the product distribution given in Scheme 1. Separation by MPLC (SiO_2, hexane−diethyl ether 95:5, 85:15) gave methyl bicyclo[3.2.1]octane-1-carboxylate (**19**) contaminated by many components (by ^{13}C NMR) (0.070 g), 1-(methoxymethyl)bicyclo[3.3.0]octan-2-one (**20**) (150 mg), [3.3.1]propellanone **21** (40 mg), and **11a-OMe** (243 mg). **19** was identified on the basis of the agreement of GLC retention time with an authentic sample that was prepared from bicyclo[3.2.1]octane-1-carbonyl chloride and methanol in pyridine. **20**: ^1H NMR ($CDCl_3$) δ 1.3−1.65 (m, 5H), 1.65−1.8 (m, 1H), 1.8−2.0 (m, 1H), 2.0−2.2 (m, 1H), 2.30 (t, 2H, J = 8.2 Hz), 3.16 (d, 1H, J = 8.6 Hz), 3.54 (d, 1H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 223.5 (C), 76.8 (CH_2), 60.7 (C), 59.0 (CH_3), 44.2 (CH), 38.7 (CH_2), 33.6 (CH_2), 33.4 (CH_2), 25.2 (CH_2), 25.0 (CH_2). **20** was derived to 1-(methoxymethyl)-bicyclo[3.3.0]octane by Wolff−Kishner reduction and identified (see below). The spectral data of **21** completely agreed with reported data.[15b]

Wolff−Kishner Reduction of 20. A mixture of **20** (0.150 g, 0.89 mmol), hydrazine hydrate (0.13 mL, 2.7 mmol), KOH (0.18 g), and triethylene glycol (1.2 mL) was heated to 190−200 °C until N_2 evolution stopped. The reaction mixture was poured into water and extracted with pentane. The extract was washed with water and dried ($MgSO_4$), and the solvent was evaporated to give a colorless oil (0.049 g), which was purified by MPLC (SiO_2, hexane−diethyl ether 9:1) to give 1-(methoxymethyl)bicyclo[3.3.0]octane (0.009 g): ^{13}C NMR ($CDCl_3$) δ 81.1 (CH_2), 59.3 (CH_3), 54.5 (C), 46.7 (CH), 37.6 (CH_2), 33.9 (CH_2), 25.7 (CH_2). The ^{13}C NMR data agreed with those of an authentic sample that was prepared by methylation of (1-bicyclo[3.3.0]octyl)methanol with CH_3I in the presence of KOH in DMSO as described above for the methylation of 1-hydroxy-3,3-dimethylbicyclo[2.2.2]oct-2-yl benzoate.

Product of Methanolysis of 15a-OTf. A solution of **15a-OTf** (0.063 g, 0.20 mmol) in 0.0242 mol L^{-1} 2,6-lutidine in methanol (10.0 mL) was kept at 25 °C for 200 min (12.7 half-lives). The reaction mixture was diluted with diethyl ether, washed with saturated aqueous NaCl, 10% aqueous HCl, and saturated $NaHCO_3$, and dried ($MgSO_4$). Evaporation of solvent gave **15a-OMe** (0.035 g) in 89% yield, which was more than 99% pure by GLC: mp 56.0−56.5 °C (from pentane); IR (CCl_4) 2923, 2856, 1710, 1448, 1110, 1082 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4−1.8 (br, 4H), 1.8−2.0 (br, 5H), 2.0−2.3 (br, 4H), 2.5−2.6 (br, 2H), 3.27 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 212.2 (C), 82.8 (C), 50.9 (CH_3), 48.3 (CH_2), 38.1 (CH_2), 36.4 (CH_2), 34.4 (CH_2), 27.6 (CH), 26.0 (CH). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.80; H, 9.36.

Product of Ethanolysis of 10a-OTf. A solution of **10a-OTf** (0.344 g, 1.20 mmol) in 0.050 mol L^{-1} 2,6-lutidine in ethanol (30 mL) was kept at 75.0 °C for 72 h. Analysis of the reaction mixture by GLC exhibited the formation of three products (80%, 19%, and 1%). After most of the ethanol had been evaporated, the residue was dissolved in CH_2Cl_2, washed with 10% aqueous NaCl, 10% aqueous HCl, 10% aqueous NaCl, and saturated $NaHCO_3$, and dried ($MgSO_4$). Evaporation of solvent afforded a liquid, which on MPLC (SiO_2, hexane−diethyl ether (9:1, 4:1)) gave ethyl bicyclo[2.2.2]octane-1-carboxylate (**22**) (0.007 g, 3%), 1-(ethoxymethyl)bicyclo-[3.2.1]octan-2-one (**23-OEt**) (0.159 g, 73%), and 1-ethoxy-bicyclo[3.2.2]nonan-2-one (**10a-OEt**) (0.041 g, 19%) in this sequence. **23-OEt**: IR (liquid film) 1700, 1455, 1375, 1120, 1095 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (t, 3H, J = 7 Hz), 1.4−2.6 (m, 11H), 3.47 (q, 2H, J = 7 Hz), 3.52 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 212.7 (C), 70.1 (CH_2), 66.4 (CH_2), 57.1 (C), 39.9 (CH_2), 35.0 (CH_2), 34.4 (CH), 32.1 (CH_2), 30.3 (CH_2), 28.5 (CH_2), 14.7 (CH_3). **10a-OEt**: IR (liquid film) 1715, 1455, 1395, 1260, 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (t, 3H, J = 7 Hz), 1.4−2.8 (m, 13H), 3.33 (q, 2H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 214.0 (C), 82.3 (C), 58.9 (CH_2), 38.5 (CH_2), 29.4 (CH_2), 28.6 (CH_2), 27.5 (CH), 24.9 (CH_2), 15.9 (CH_3). Ester **22** was identified by comparison of the retention time of GLC with that of an authentic sample.

1-(Hydroxymethyl)bicyclo[3.2.1]octan-2-one (23-OH) by the Hydrolysis of 10a-OTf in 80% Acetone. A solution of **10a-OTf** (0.588 g, 2.05 mmol) in 0.050 mol L^{-1} 2,6-lutidine in 80% acetone (51 mL) was kept at 50 °C for 23 h. After most of the acetone had been rotary evaporated, the residue was extracted with CH_2Cl_2, washed with 10% aqueous NaCl, and dried ($MgSO_4$). Evaporation of solvent afforded a liquid, which on MPLC (SiO_2, hexane−ethyl ether (7 : 3, 3 : 2)) gave **10a-OH** (0.052 g, 16%) as a white powder and **23-OH** (0.188 g, 59%) as a pale yellow liquid, in this sequence. **23-OH**: IR (liquid film) 3450, 1700, 1455, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4−2.7 (m, 11H), 2.87 (s, 1H), 3.70 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 216.3 (C), 66.4 (CH_2), 58.7 (C), 40.8 (CH_2), 35.4 (CH_2), 34.6 (CH), 32.3 (CH_2), 31.5 (CH_2), 28.4 (CH_2).

(2-Oxobicyclo[3.2.1]oct-1-yl)methyl Triflate (23-OTf). Treatment of **23-OH** (0.030 g, 0.195 mmol) with triflic anhydride (0.065 g, 0.23 mmol) and pyridine (0.032 g, 0.405 mmol) in CH_2Cl_2 (4 mL) at 0 °C for 1 h and then at −15 °C overnight followed by usual workup at 0 °C afforded **23-OTf** (0.046 g, 82%) as a pale yellow liquid, which was used for solvoysis studies without further purification: ^{13}C NMR ($CDCl_3$) δ 209.8 (C), 118.6 (q, CF_3, J = 320 Hz), 77.4 (CH_2), 56.3 (C), 40.0 (CH_2), 34.8 (CH_2), 32.0 (CH_2), 30.5 (CH_2), 28.3 (CH_2).

Product of Ethanolysis of 12a-OTr. A solution of **12a-OTr** (0.930 g, 2.96 mmol) in 0.050 mol L^{-1} 2,6-lutidine in ethanol (74 mL) was kept at 100 °C for 140 h. GLC showed the product distribution shown in Scheme 2. Evaporation of the ethanol gave a pale yellow liquid, which on MPLC (SiO_2, hexane−diethyl ether (9:1, 7:3, 1:1)) afforded ethyl bicyclo-[3.2.2]nonane-1-carboxylate (**24**) (0.028 g, 5%), 1-(ethoxy-methyl)bicyclo[4.2.1]nonan-2-one (**25-OEt**) (0.114 g, 20%), 8-ethoxybicyclo[4.2.2]decan-2-one (**26**) (0.048 g, 8%), 1-ethoxy-bicyclo[4.2.2]decan-2-one (**12a-OEt**) (0.064 g, 11%), and 1-(hydroxymethyl)bicyclo[4.2.1]nonan-2-one (**25-OH**) (0.104 g, 21%), all as a liquid, in this sequence. **25-OEt**: ^1H NMR ($CDCl_3$) δ 1.12 (t, 3H, J = 7 Hz), 1.3−2.9 (m, 13H), 3.15 (d, 1H, J = 9 Hz), 3.43 (q, 2H, J = 7 Hz), 3.83 (d, 1H, J = 9 Hz); ^{13}C NMR ($CDCl_3$) δ 217.0 (C), 75.9 (CH_2), 66.5 (CH_2), 59.1 (C), 43.2 (CH_2), 39.6 (CH_2), 38.6 (CH), 35.1 (CH_2), 34.7 (CH_2), 28.3 (CH_2), 21.4 (CH_2). **26**: ^1H NMR ($CDCl_3$) δ 1.15 (t, 3H, J = 7 Hz), 1.3−2.8 (m, 15H), 3.32 (q, 2H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 216.5 (C), 74.3 (CH), 63.5 (CH_2), 51.0 (CH), 41.6 (CH_2), 35.6 (CH_2), 31.6 (CH_2), 25.8 (CH), 22.6 (CH_2), 21.9 (CH_2), 19.2 (CH_2), 15.4 (CH_3). **24**: ^1H NMR ($CDCl_3$) δ 1.22 (t, 3H, J = 7Hz), 0.8−2.0 (m, 15H), 4.08 (q, 2H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 178.9 (C), 60.0 (CH_2), 43.0 (C), 37.4 (CH_2), 35.4 (CH_2), 28.2 (CH_2), 28.1 (CH), 25.4 (CH_2), 21.7 (CH_2), 14.1 (CH_3). **25-OH**: IR (CCl_4) 3500, 1680, 1460, 1400, 1335 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.3−2.9 (m, 14H), 3.50 (d, 1H, J = 11 Hz), 3.73 (d, 1H, J = 11 Hz); ^{13}C NMR ($CDCl_3$) δ 218.4 (C), 69.0 (CH_2), 59.8 (CH_2), 43.1 (CH_2), 39.8 (CH_2), 39.1 (CH_2), 35.3 (CH_2), 33.3 (CH_2), 29.5 (CH_2), 21.2 (CH_2).

(2-Oxobicyclo[4.2.1]non-1-yl)methyl Tresylate (25-OTr). The procedure described for the preparation of **12a-OTr** was followed. Treatment of **25-OH** obtained in the ethanolysis of **12a-OTr** with 2,2,2-trifluoroethanesulfonyl chloride (0.037 g, 0.203 mmol) and pyridine (0.176 g, 2.23 mmol) in CH_2Cl_2 (3.5 mL) at 0 °C for 3 h and then at room temperature overnight followed by usual workup at 0 °C afforded **25-OTr** (0.039 g, 89%) as a pale yellow oil, which was used for solvolysis studies without further purification: ^1H NMR ($CDCl_3$) δ 1.2−3.0 (m, 13H), 3.96 (q, 2H, J = 9 Hz), 4.00 (d, 1H, J = 9 Hz), 4.78 (d, 1H, J = 9 Hz); ^{13}C NMR ($CDCl_3$) δ 213.8 (C), 121.1 (q, CF_3, J = 277 Hz), 76.7 (CH_2), 57.8 (C), 52.0 (q, $CF_3\underline{C}H_2$, J = 33 Hz), 42.8 (CH_2), 39.6 (CH_2), 39.3 (CH), 35.1 (CH_2), 33.8 (CH_2), 29.2 (CH_2), 21.2 (CH_2).

Product of Ethanolysis of 25-OTr. A solution of **25-OTr** (0.039 g, 0.124 mmol) in 0.025 mol L^{-1} 2,6-lutidine in ethanol (24.5 mL) was kept at 125 °C for 90 h. Analysis of the reaction mixture by GLC (PEG 20M) exhibited the formation of **25-OEt** (26%) and **25-OH** (74%), which were identified by comparison with GLC of their authentic samples obtained from ethanolysis of **12a-OTr**.

Monitoring of Solvolysis of 12a-OTr by ^{13}C NMR. A solution of **12a-OTr** (0.117 g, 0.372 mmol) and 2,6-lutidine (0.040 g, 0.373 mmol) in ethanol (0.4 mL) and dichloromethane-d_2 (0.1 mL) was placed in an NMR sample tube. It was immersed in a 75 °C constant temperature bath, and the solvolysis of **12a-OTr** was monitored at intervals by ^{13}C NMR spectrometer.

Product of Methanolysis of 13a-OTr. A solution of **13a-OTr** (0.559 g, 1.78 mmol) in 0.050 mol L^{-1} 2,6-lutidine in methanol (44.5 mL) was heated at 50 °C for 74 h. Most of the methanol was evaporated, and the residue was diluted with diethyl ether, washed with 10% aqueous NaCl, 5% aqueous HCl, 10% aqueous NaCl, and saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). Evaporation of solvent gave a yellow liquid (0.277 g), which showed at least five spots in TLC (SiO_2) analysis. Separation by MPLC (SiO_2) was attempted, but approximately 15 components were present. The major product (0.094 g, 29%) was identified by spectral data as **13a-OMe**: ^{1}H NMR ($CDCl_3$) δ 1.1−2.5 (m, 15H), 3.20 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 213.3 (C), 79.5 (C), 50.2 (CH_3), 41.8 (CH_2), 36.2 (CH_2), 34.2 (CH_2), 32.3 (CH_2), 31.7 (CH), 29.5 (CH_2), 22.5 (CH_2), 21.0 (CH_2).

Solvolysis of 8a-OTf in 90% MeOH−10% $H_2{}^{18}O$. A solution of **8a-OTf** ([M + H]:[M + H] + 2 = 100:(10.0 ± 0.6); 0.120 g, 0.40 mmol) in 0.050 mol L^{-1} 2,6-lutidine in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O) (10 mL) was heated in a constant temperature bath (100.0 °C) for 22 h (75% reaction). After most of the methanol had been removed with an oil pump at 0 °C, the residue was extracted with diethyl ether and the extract was dried ($MgSO_4$). Evaporation of solvent afforded colorless crystals (0.111 g). The isotopic composition of unreacted **8a-OTf** in the solvolysis products was determined by analysis of the mass spectral peaks at [M + H] (301) and [M + H] + 2 (303); the intensity ratio [M + H] : [M + H] + 2 was 100:(10.4 ± 0.5), showing no incorporation of ^{18}O in the carbonyl group.

Solvolysis of 9a-OTf in 90% MeOH−10% $H_2{}^{18}O$. A solution of **9a-OTf** (M:(M + 2) = 100:(9.5 ± 0.9); 0.109 g, 0.40 mmol) in 0.050 mol L^{-1} 2,6-lutidine in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O) (10 mL) was heated in a constant temperature bath (100.0 °C) for 6.3 h (75%). The reaction mixture was worked up as described in the ^{18}O exchange experiment for **8a-OTf**. The isotopic composition of **9a-OTf** in the solvolysis products was determined by analysis of the mass spectral peaks at [M + H] (273) and [M + H] + 2 (275); the intensity ratio [M + H]:[M + H] + 2 was 100:(13.4 ± 0.6).

Solvolysis of 2-Oxo-1-adamantyl Triflate (14a-OTf) in 90% MeOH−10% $H_2{}^{18}O$. (a) Product of Solvolysis of 14a-OTf in Methanol. From **14a-OTf** (0.760 g, 2.55 mmol) in 0.050 mol L^{-1} 2,6-lutidine in methanol (63.7 mL) at 75.0 °C for 40 h was obtained a yellow liquid, which on MPLC (SiO_2, hexane−diethyl ether (9:1, 4:1)) afforded methyl noradamantane-1-carboxylate (0.295 g, 64%) and 1-methoxyadamantan-2-one (**14a-OMe**) (0.075 g, 16%), both as a liquid, in this sequence. **Methyl noradamantane-1-carboxylate:** ^{13}C NMR ($CDCl_3$) δ 177.0 (C), 53.2 (C), 50.9 (CH_3), 46.4 (CH_2), 43.4 (CH), 43.1 (CH_2), 36.9 (CH), 34.2 (CH_2). **14a-OMe**: ^{13}C NMR ($CDCl_3$) δ 213.3 (C), 80.4 (C), 50.7 (CH), 47.9 (CH_3), 43.0 (CH_2), 38.2 (CH_2), 35.0 (CH_2), 29.4 (CH).

(b) Natural Abundance of ^{18}O for 14a-OMe. For the determination of an inherent error of the employed GC-MS instrument, the natural abundance of ^{18}O for **14a-OMe** was measured by analysis of the mass spectral peaks at M (180) and M + 2 (182); the intensity ratio M:(M + 2) was 100:2.2 (expected ratio is 100:1.1).

(c) 1-Methoxyadamantan-2-one Containing ^{18}O at Carbonyl Site (14a-^{18}O-OMe) and Control Experiment. A mixture of **14a-OMe** (0.037 g, 0.205 mmol) in hexane (5.0 mL) and 5% H_2SO_4−95% $H_2{}^{18}O$ (10 atom % ^{18}O) (2.0 g) was heated at reflux for 17 h. The hexane layer was separated, and the aqueous layer was extracted with diethyl ether. To the extract was added a small amount of solid $NaHCO_3$, and the mixture was dried ($MgSO_4$). Evaporation of solvent afforded **14a-^{18}O-OMe** (0.034 g, 92%) as a pale yellow liquid, whose M:(M + 2) intensity ratio was 100:12.9. This labeled methyl ether was dissolved in diethyl ether (50 mL) containing 2,6-lutidine (0.025 g, 0.233 mmol) and triflic acid (0.053 g, 0.188 mmol), and the solution was washed at 0 °C with saturated aqueous NaCl (2 × 20 mL) and dried ($MgSO_4$). Evaporation of solvent followed by GC-MS analysis showed considerable decrease in the M:(M + 2) intensity ratio to 100:4.2.

(d) Product of Solvolysis of 14a-OTf in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O). A solution of **14a-OTf** (0.159 g, 0.533 mmol) in 0.050 mol L^{-1} 2,6-lutidine in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O) (13.32 mL) was kept at 25.0 °C for 158.5 h. After most of the methanol had been removed with a rotary evaporator, the residue was dissolved in diethyl ether (50 mL), and the solution was washed at 0 °C with saturated aqueous NaCl (2 × 20 mL) and dried ($MgSO_4$). The solution was concentrated to 5 mL with a rotary evaporator and subjected to GC-MS. The M:(M + 2) intensity ratio was 100:4.4.

Solvolysis of 4-Oxo-3-homoadamantyl Triflate (15a-OTf) in 90% MeOH−10% $H_2{}^{18}O$. (a) Natural Abundance of ^{18}O for 15a-OMe. The inherent error of the employed GC-MS instrument for the natural abundance of ^{18}O in **15a-OMe** was measured. The intensity ratio M:(M + 2) was 100:2.3 (expected ratio is 100:1.2).

(b) 3-Methoxyhomoadamantan-4-one Containing ^{18}O at Carbonyl Site (15a-^{18}O-OMe) and Control Experiment. The procedure described for the preparation of **14a-^{18}O-OMe** was followed. Treatment of **15a-OMe** (0.067 g, 0.345 mmol) in hexane (5.0 mL) and 5% H_2SO_4−95% $H_2{}^{18}O$ (10 atom % ^{18}O) (2.0 g) at reflux for 19 h followed by workup treatment afforded **15a-^{18}O-OMe** (0.064 g, 97%) as a pale yellow liquid, whose M:(M + 2) intensity ratio was 100:12.8. This labeled methyl ether was dissolved in ethyl ether (50 mL) containing 2,6-lutidine (0.045 g, 0.420 mmol) and triflic acid (0.095 g, 0.337 mmol), and the solution was washed at 0 °C with saturated aqueous NaCl (2 × 20 mL) and dried ($MgSO_4$). Evaporation of solvent followed by GC-MS analysis showed no change in the M:(M + 2) intensity ratio with 100:12.7.

(c) Product of Solvolysis of 15a-OTf in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O). A solution of **15a-OTf** (0.150 g, 0.480 mmol) in 0.050 mol L^{-1} 2,6-lutidine in 90% MeOH−10% $H_2{}^{18}O$ (10 atom % ^{18}O) (12.00 mL) was kept at 25.0 °C for 88 min. The reaction mixture was worked up as described for the experiment on **14a-OTf**. The M:(M + 2) intensity ratio was determined to be 100:2.1.

Kinetic Methods. The preparation of solvents and kinetic studies followed the methods described previously.[21]

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Supporting Information Available: ^{13}C NMR spectra for **18**, **20**, Wolff−Kishner reduction product of **20**, **23-OEt**, **25-OEt**, and **26**, monitoring of solvolysis of **12a-OTr**, first-order plots for the solvolysis of class C substrates, and PM3 net atomic charges for some carbocations (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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