Structural Factors for the Formation of Propellane-Type Products in the Solvolysis of Bicyclic Bridgehead Compounds

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Methanolyses of 2-oxobicyclo[3.3.1]non-1-yl triflate, 3,3-dimethyl-2-oxobicyclo[3.3.1]non-1-yl triflate, and 2-oxobicyclo[4.3.1]dec-1-yl mesylate gave the corresponding propellanone in 12%, 20%, or 3.2% yield, respectively, beside substitution or rearranged products under typical conditions. No propellane-type product was obtained in the solvolyses of 1-bromobicyclo[3.3.1]nonane, 2-methylidenebicyclo[3.3.1]non-1-yl heptafluorobutyrate, and 3,3-dimethyl-2-thioxobicyclo[3.3.1]non-1-yl tosylate. The factors that permit the formation of the propellane-type product from the intermediate bridgehead cations are examined with the aid of theoretical calculations at PM3 and B3LYP/6-31G*.

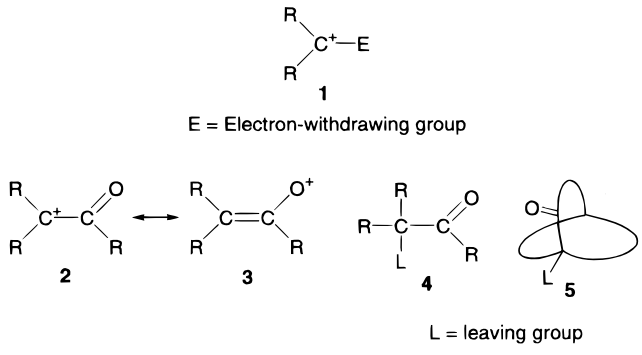
Introduction

Carbocations **1** (Chart 1) substituted with an electron-withdrawing group directly attached to the cationic center are commonly referred to as "destabilized" owing to the inductive (−I) effect of the substituents.[1−5] The α-carbonyl cation **2** is one of the most interesting among such cations, and numerous α-carbonyl cations have been generated as intermediates in solvolysis reactions or under stable ion conditions.[5]

α-Carbonyl cations can be formed as intermediates of solvolyses via k_C processes from many tertiary systems **4** containing an α-carbonyl group.[3−5] These cations can undergo solvent capture to give substitution products, or sometimes rearrangement or 1,2- or 1,3- proton detachment can occur to form various products. If the carbonyl group is activated by a strongly electron-withdrawing leaving group (L), carbonyl addition of solvent can also compete with the direct solvent displacement. To preclude this, an appropriate buffer is sometimes added to solvolysis solvents.

In the course of our study on α-carbonyl cations,[6−9] we were interested in examining the magnitude of resonance contribution[1−5] as represented by **2** ↔ **3**. For this purpose, the solvolysis studies on the bridgehead substrates **5** containing an oxo substituent at a vicinal position appeared to be appropriate, since they are free from nucleophilic solvent assistance and carbonyl participation from the rear side of the bridgehead carbon. Solvolyses of various 2-oxo compounds were studied, and the solvolytic behavior observed in kinetics and product analyses has been categorized.[8b]

Chart 1



Previously, we reported that the methanolysis of 2-oxobicyclo[3.3.1]non-1-yl triflate (**6-OTf**) gave [3.3.1]-propellanone **12** as a minor product.[8b,10] While a variety of methods have been developed to prepare small-ring propellanes,[11] this finding provides the first example of the σ-bond formation between a bridgehead cationic carbon and another bridgehead carbon in solvolysis. To reveal the factors involved in the formation of the propellanone in the solvolyses of **6-OTf**, the work has been extended to other ring systems. This paper describes the solvolyses of 2-oxobicyclo[3.3.1]non-1-yl triflate (**6-OTf**), 2-oxobicyclo[4.3.1]dec-1-yl mesylate (**7-OMs**), 3,3-dimethyl-2-oxobicyclo[3.3.1]non-1-yl triflate (**8-OTf**), 2-methylidenebicyclo[3.3.1]non-1-yl heptafluorobutyrate

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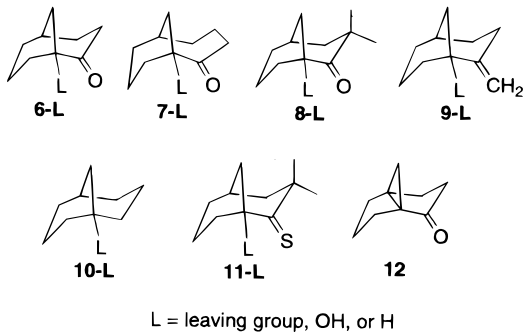
Chart 2



(n-$C_3F_7CO_2$−) (**9-OHFB**), 1-bromobicyclo[3.3.1]nonane (**10-Br**), and 3,3-dimethyl-2-thioxobicyclo[3.3.1]non-1-yl tosylate (**11-OTs**) (Chart 2). To illuminate the effect of the substituent and the ring size on the stability and reactivity of the bridgehead cations, we carried out PM3 and ab initio calculations for carbocations and related species.

Results and Discussion

Syntheses of Solvolysis Substrates. Precursor alcohols, 1-hydroxybicyclo[3.3.1]nonan-2-one (**6-OH**),[8b] 2-methylidenebicyclo[3.3.1]nonan-1-ol (**9-OH**),[12] and 1-hydroxybicyclo[4.3.1]decan-2-one (**7-OH**),[8b] were prepared by previously reported methods and converted to the corresponding triflate, heptafluorobutyrate, and methanesulfonate (mesylate), respectively.[13] 1-Bromobicyclo-[3.3.1]nonane (**10-Br**) was prepared following the previously reported method.[14] 1-Hydroxy-3,3-dimethylbicyclo-[3.3.1]nonan-2-one (**8-OH**) was prepared from **8-OMe** by the cleavage of the methyl ether by using chlorotrimethylsilane/NaI.[15] Compound **8-OMe** was obtained by the methylation[16] of **6-OH** using $NaNH_2$ and CH_3I. The thioxo alcohol **11-OH** was derived from the ketol **8-OH** via thionation[17] of the 2-hydrazono alcohol. The two methyl groups on the C(3) position of **11-OH** and its homologues preclude thioenolization of the thiocarbonyl group.

Solvolysis Rates. To estimate 10 half-lives for product studies, the solvolysis rates were required. The rates of **6-OTf**[8b] and **9-OHFB**[12] in MeOH and EtOH were reported previously. The rates of **7-OMs**, **8-OTf**, **10-Br**, and **11-OTs** were determined in MeOH and/or EtOH. **6-OTf** and **10-Br** were also subjected to solvolysis in DMSO. The rate data determined in this study are summarized in Table 1.

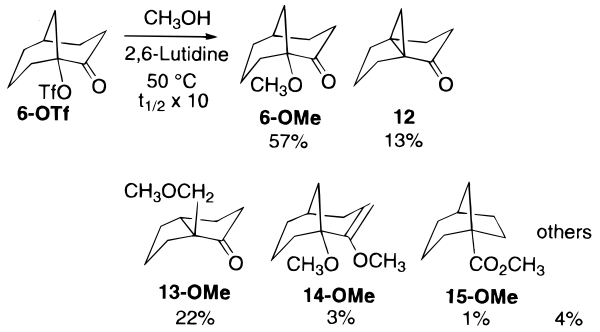
Products of Solvolyses of 2-Oxobicyclo[3.3.1]non-1-yl Triflate (6-OTf). Four products were previously reported for the methanolysis of **6-OTf** in the presence of 2,6-lutidine at 25 °C, i.e., **6-OMe** (38%), 2,3,5,6-tetrahydro-3a,6a-methano-1*H*,4*H*-pentalen-1-one (**12**) (15%), 1-(methoxymethyl)bicyclo[3.3.0]octan-2-one (**13-OMe**) (30%), methyl bicyclo[3.2.1]octane-1-carboxylate

Table 1. Rate Constants of Solvolysis of Various Bridgehead Substrates[a]

compd	solvent	T/°C	k_1/s^{-1}	$\Delta H^{\ddagger}$[b]/ kcal mol^{-1}	$\Delta S^{\ddagger}$[b]/ cal mol^{-1}K^{-1}
6-OTf	DMSO	25.0	3.05×10^{-4} [c]		
7-OMs	MeOH	25.0	1.94×10^{-9} [d]	29.8	1.5
		75.0	3.12×10^{-6} [e]		
		100.0	5.9×10^{-5} [c]		
8-OTf	MeOH	0.0	2.69×10^{-6} [c]		
		25.0	1.08×10^{-4} [c]	23.0	0.3
		50.0	2.22×10^{-3} [c]		
10-Br	MeOH	25.0	3.95×10^{-7} [d]	26.0	1.9
		50.0	1.26×10^{-5} [e]		
		75.0	2.46×10^{-4} [e]		
	DMSO	25.0	1.51×10^{-8} [d]	22.2	−19.9
		75.0	3.77×10^{-6} [c]		
		100.0	3.41×10^{-5} [c]		
11-OTs	MeOH	25.0	1.54×10^{-5} [e]	20.9	−10.5
		50.0	2.54×10^{-4} [e]		
	EtOH	25.0	1.76×10^{-6} [e]	20.4	−16.5
		50.0	2.72×10^{-5} [e]		

[a] The rates were titrimetrically determined by a single run for 0.02 or 0.01 M substrates in the presence of 0.025 M 2,6-lutidine. [b] At 25.0 °C. [c] Initial rate. [d] Extrapolated from data at other temperatures. [e] The correlation coefficient for the first-order plot was greater than 0.998.

Scheme 1



(**15-OMe**) (5%), and several unidentified compounds amounting to 12% (Scheme 1).[8b,10] In the present study, the reaction was conducted at 50 °C to give the result shown in Scheme 1. By careful separation of the mixture of the unidentified compounds by HPLC, 1,2-dimethoxybicyclo[3.3.1]non-2-ene (**14-OMe**) (3%) was isolated.[18] The yield of **12** was similar between the two experiments at 25 and 50 °C, but the yields of **6-OMe** and **13-OMe** considerably changed, perhaps because the rearrangement to **13-OTf** via ion pair return was facilitated at higher temperature.

Effects of Solvent and Added Base on the Yield of [3.3.1]Propellanone. The yield of propellanone **12** in the methanolysis of **6-OTf** changed when the added base was varied (Table 2). When 2,6-lutidine (pK_a 6.72) is added to methanolysis, the yield of the propellanone is the highest at 13%. The use of a stronger base, triethylamine (pK_a 10.72),[19,20] decreases the yield of propellanone **12** to 2%. This implies that the added base does not play a role in abstracting the proton attached to the C(5) position. Rather, triethylamine appears to catalyze the carbonyl addition of the solvent that leads to Favorskii rearrangement-type product **15-OMe** (Scheme 2). The formation of **15-OMe** is markedly facilitated by sodium methoxide, most probably owing to the direct addition of the methoxide ion to the carbonyl group. The

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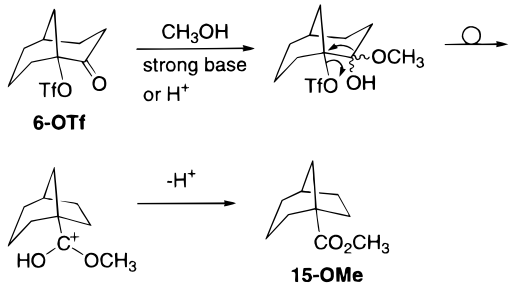
(18) The identification of **14** was based on the elemental analysis and the spectral data shown in Experimental Section.

Table 2. Product Distributions in the Methanolysis of 2-Oxobicyclo[3.3.1]non-1-yl Triflate (6-OTf)[a]

					product yield[d]/%				
entry	base[b]	pK_a	T/°C	time[c]	**6-OMe**	**12**	**13-OMe**	**14-OMe**	**15-OMe**
1	no bufffer		25	$t_{1/2} \times 6$	17	0	0	13	69
2	2,6-di-*tert*-butylpyridine	3.58[e]	50	$t_{1/2} \times 10$	14	5	9	31	35
3	pyridine	5.22[f]	50	$t_{1/2} \times 10$	21	8	14	35	21
4	2,6-lutidine	6.72[f]	50	$t_{1/2} \times 10$	57	13	22	3	1
5	triethylamine	10.72[g]	50	$t_{1/2} \times 10$	60	2	3	0	32
6	$NaOCH_3$		50	$t_{1/2} \times 10$	12	0	0	0	86

[a] Concentration of the triflate was 0.020 M. [b] 0.025 M. [c] The $t_{1/2}$ denotes the half-life of entry 4. [d] Determined by GLC. For the structures, see Scheme 1. [e] In 50% aqueous ethanol at 50 °C; ref 19. [f] In water at 25 °C. *Encyclopedia of Chemical Technology*, 3rd ed.; John Wiley and Sons: New York, 1984; Vol. 19, p 455. [g] In water at 25 °C; ref 20.

Scheme 2



increased formation of **15-OMe** in the absence of a base (entry 1, Table 2), or when 2,6-di-*tert*-butylpyridine (pK_a 3.58; entry 2, Table 2) and pyridine (pK_a 5.22; entry 3, Table 2), weaker bases than 2,6-lutidine, are used in place of 2,6-lutidine is most probably ascribed to acid-catalyzed carbonyl addition of methanol (Scheme 2).

The propellanone formation is highly dependent on solvent (Table 3). The solvolysis in TFE or AcOH buffered with 2,6-lutidine or NaOAc, respectively, gave a bridgehead substitution product in 83% or 90% yield, respectively, and **12** was not found to the limit of detection (1%) by ^{13}C NMR and GLC.[21] On the other hand, the use of DMSO and DMF as solvent (with added 2,6-lutidine) increased the yield of **12** to 48 and 25%, respectively. The greater yields of **12** in DMSO and DMF than those in MeOH and EtOH can be explained by the greater ability of the former solvents to abstract a proton; the donor numbers (DN)[22] of DMSO (29.8) and DMF (26.6) are significantly greater than those of MeOH (19) and EtOH (20). The fact that **12** was not detected in the solvolysis in TFE and AcOH is consistent with the very low estimated[23] DN of 10.

Products of Solvolysis of 2-Oxobicyclo[4.3.1]dec-1-yl Mesylate (7-OMs). [4.3.1]Propellanone **16** was detected in 3% yield by GLC in the solvolysis product of 2-oxobicyclo[4.3.1]dec-1-yl mesylate (**7-OMs**). Identification of **16** rests upon exact mass (calcd. 150.1045 and found 150.1044) and perfect agreement of the ^{13}C NMR data with the authentic[24,25] sample. Compounds **17**−**19** were also obtained (Scheme 3).[26,27] Scheme 3 shows the product distribution determined by GLC analysis. The ^1H and ^{13}C NMR suggested that the trans isomer of **17** was also formed in 4% yield, but further characterization will be required (see the Supporting Information).

The structure of **17** was estimated from the resemblance of its ^1H and ^{13}C NMR spectra to those[28] of 6-hydroxy-1-methyl-*cis*-bicyclo[4.3.0]nonan-2-one (**20**). The ^1H NMR spectrum of **17** showed a singlet at δ 1.14 (s, 3H), which is in accord with a singlet at δ 1.18 (s, 3H) for **20**. The ^{13}C NMR spectrum of **17** showed signals at δ 87.9 (C) and 60.3 (C), which are close to the respective signals at δ 93.0 (C) and 59.46 (C) in the data for **20**. The positions of other signals for methyl and methylene carbons of **17** are also close to those reported for **20** (Chart 3).[28]

Two processes seemed probable for the formation of **17** (Scheme 4). The bridgehead cation $\mathbf{7}^+$ might rearrange into **22** via a two-step process through a primary cation **21** (or by a concerted mechanism) to give **17** [process (a)]. On the other hand, the cyclopropane moiety of the [4.3.1]-propellanone **16** might be protonated[29] and cleaved [process (b)] to give **22**. To distinguish between the two possibilities, the solvolysis in methanol-*d* was carried out. If the opening of protonated cyclopropane ring occurred [process (b)], a deuterium would have been incorporated into the methyl group on the C(1)-position of **17** as in **23**.

The relative intensities of the signals corresponding to ether **17** in the ^1H NMR spectrum of the crude product from the solvolysis in methanol-*d* were similar to those corresponding to **17** from the methanolysis of **7-OMs**. In the ^{13}C NMR spectrum of **17** from the reaction in methanol-*d*, the signal of the methyl group attaching at the C(1)-position was a singlet. These observations show that the methyl group is not CH_2D but CH_3. Consequently, it is concluded that **17** forms via process (a). Since the migrating hydride is located close to the CH_2^+ moiety, direct 1,3-hydride shift would proceed in **21** to give **22**.

Products of Solvolysis of 3,3-Dimethyl-2-oxobicyclo[3.3.1]non-1-yl Triflate (8-OTf). Propellanone **24** was obtained in the solvolysis of **8-OTf** in 20% yield

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(20) Riddick, J. A.; Bunger, W. B. In *Organic Solvents*, 3rd ed.; Wiley-Interscience: New York, 1970; p 440.
(21) The identification of the products for solvolysis in EtOH, trifluoroethanol (TFE), AcOH, DMF, and DMSO rests on the resemblance of the ^{13}C NMR spectra to those of the corresponding methanol adducts or the authentic samples.
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(25) Private communication from Professor M. G. Banwell, The Australian National University, Canberra, is gratefully acknowledged.
(26) Previously, it was reported that the methanolysis of 2-oxobicyclo-[4.3.1]dec-1-yl 2,2,2-trifluoroethanesulfonate yielded the bridgehead substitution product **7-OMe** (29%) and a mixture of unidentified products (71%).[8b]
(27) **18** was identified on the basis of the symmetric structure shown by ^{13}C NMR.
(28) Caine, D.; McCloskey, C. J.; Derveer, D. V. *J. Org. Chem.* **1985**, *50*, 175.
(29) Protonated cyclopropane ring can open in some cases; see: March, J. *Advanced Organic Chemistry: Reactions, Mechanism and Structure*, 4th ed.; John Wiley & Sons: New York; 1992; pp 755−758 and pp 1056−1063.

Table 3. Product Distribution in the Solvolysis of 2-Oxobicyclo[3.3.1]non-1-yl Triflate (6-OTf) under Various Reaction Conditions[a]

					product and yield[c]/%				
entry	solvent	base[b]	*T*/°C	time	**6-OR**	**12**	**13-OR**	**14-OR**	**15-OR**
1	MeOH	2,6-lutidine	50	$t_{1/2} \times 10$	57[d]	13	22[d]	3[d]	1[d]
2	EtOH	2,6-lutidine	50	$t_{1/2} \times 10$	48[e]	14	31[e]	2[e]	2[e]
3	TFE[f]	2,6-lutidine	50	$t_{1/2} \times 10$	83[g]	0	2[g]	0	13[g]
4	AcOH	NaOAc	25	$t_{1/2} \times 10$	90[h]	0	3[h]	0	0
5	DMF[i]	2,6-lutidine	75	$t_{1/2} \times 10$	22[j]	25	45[j]	<3[j]	0
6	DMSO	2,6-lutidine	25	$t_{1/2} \times 10$	14[k]	48	7[k,l]	0	0

[a] [**6-OTf**]$_0$ = 0.02 M. [b] 0.025 M. [c] The product distributions were determined by GLC except for entries 3 and 4, where ^{13}C NMR was used. For the structures of the products, see Scheme 1 for R = Me as an example. [d] R = CH_3. [e] R = C_2H_5. [f] 2,2,2-Trifluoroethanol. [g] R = CF_3CH_2. [h] R = CH_3CO. [i] Containing 0.006 M H_2O. [j] R = CHO. [k] R = H. [l] Containing 2-oxobicyclo[3.3.0]oct-1-yl carbaldehyde (26%).

Scheme 3

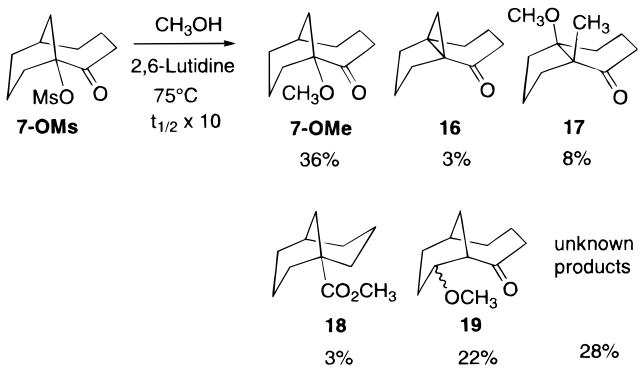
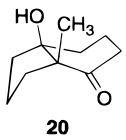
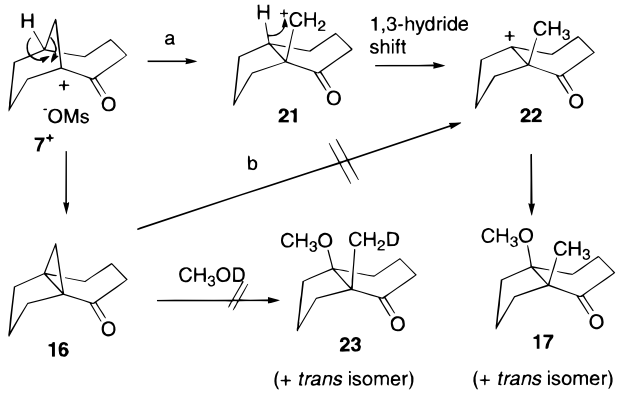


Chart 3



Scheme 4



Scheme 5

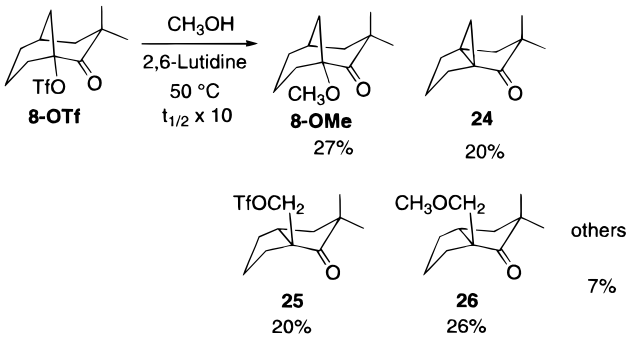
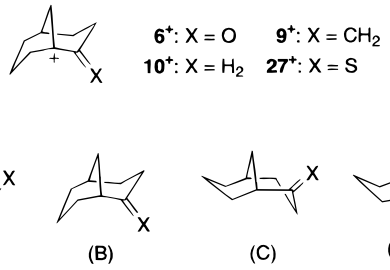


Chart 4



(Scheme 5). Identification of **24** rests upon exact mass (calcd. 164.1201, found 164.1198) and close resemblance of its ^{13}C NMR spectrum to that of [3.3.1]propellanone **12**. Primary triflate **25**, whose formation is ascribable to ion pair return, and corresponding methyl ether **26** were also obtained. Spectral evidence for **24**−**26** is given in the Experimental Section.

Products of Solvolyses of 2-Methylidene, 2-Thioxo, and Parent Substrates. No propellane-type product was obtained in the solvolyses of 2-methylidenebicyclo-[3.3.1]non-1-yl heptafluorobutyrate (**9-OHFB**), 1-bromobicyclo[3.3.1]nonane (**10-Br**), and 3,3-dimethyl-2-thioxobicyclo[3.3.1]non-1-yl tosylate (**11-OTs**).[30] The solvolyses of 2-methylidene derivative **9-OHFB** were conducted in MeOH and TFE in the presence of excess 2,6-lutidine for 51 h at 75 °C and for 1.3 h at 50 °C, respectively. The products were identified as the bridgehead ethers, **9-OMe** and **9-OTFE**, respectively, on the basis of the ^{13}C NMR spectra.[30] The product in the methanolysis of **10-Br** for 10 half-lives at 75 °C was solely the bridgehead substitution product: even when DMSO was used as solvent (for 10 half-lives at 100 °C), the propellane was not detected by GLC and ^{13}C NMR analyses. The methanolysis of 3,3-dimethyl-2-thioxobicyclo[3.3.1]non-1-yl tosylate (**11-OTs**) for 10 half-lives at 50 °C gave unrearranged **11-OMe** in 100% yield, on the basis of the GLC and ^{13}C NMR analyses.[31]

Theoretical Calculations on Bridgehead Carbocations and Propellanes. Computational studies were carried out for a series of bicyclo[3.3.1]non-1-yl cations **6**$^+$, **9**$^+$, **10**$^+$, and **27**$^+$ (Chart 4) to shed light on the structure and reactivity of intermediate bridgehead cations. Since these species can exist in different conformations, e.g., chair-chair, chair-boat, boat-chair, and

(30) These observations are in accord with the previous report[12] that the solvolysis of crude **9-OMs** in 80% ethanol gave only bridgehead substitution products **9-OH** and **9-OEt**. The product of solvolysis of **10-Br** in 80% ethanol buffered with Na_2CO_3 (5 molar amount of **10-Br**) for 2 h reflux was also studied following a previously reported procedure.[14] GLC and ^{13}C NMR analyses showed that the bridgehead substitution is the sole reaction.

(31) The kinetic study for the solvolysis of 2-thioxo derivative **11-OTs** will be reported elsewhere.

Table 4. Calculated (B3LYP/6-31G*) Electronic Energies of Bridgehead Cations and the Parent Structures[a]

	conformation[c]							
	(A)		(B)		(C)		(D)	
species[b]	energy	ZPE	energy	ZPE	energy	ZPE	energy	ZPE
6$^+$ (X = O)	−425.703038 (0)	127.5	−425.703048 (+0.14)	127.7	−425.698726 (+2.55)	127.4	converged to (C)	
9$^+$ (X=CH_2)	converged to (B)		−389.809211 (0)	143.7	−389.791720 (+9.99)	142.7	−389.802217 (+4.39)	143.7
10$^+$ (X = H_2)	−351.721310 (0)	140.7	−351.719275 (+1.09)	140.5			−351.710451 (+6.25)	140.1
27$^+$ (X = S)	converged to (B)		−748.670731 (0)	126.7	−748.670652 (+0.29)	126.9	converged to (C)	
6-H (X = O)	−426.621074 (0)	136.4	−426.620379 (+0.49)	136.5				
9-H (X=CH_2)	−390.691669	151.6						
10-H (X = H_2)	−352.607983 (0)	148.9	−352.603455 (+2.76)	148.8				
27-H (X = S)	−749.576594 (0)	135.3	−749.575003 (+0.84)	135.1				

[a] Energies in hartree and zero-point energies (ZPE) in kcal mol^{-1}. Relative energies in kcal mol^{-1}, after inclusion of zero-point energies, are given in parentheses. [b] See Figure 1 for the most stable conformations. [c] See Chart 4 for structures of cations and conformations (A), (B), (C), and (D).

Table 5. Calculated (B3LYP/6-31G*) Electronic Energies for Some [3.3.1]Propellane-type Compounds[a]

compd	energy/hartree	ZPE/kcal mol^{-1}
12	−425.379617	120.80
28	−389.448403	135.63
29	−351.363590	132.84
30	−748.337750	119.43

[a] See Figure 2 for the most stable conformations.

boat-boat forms (Chart 4), the most stable conformers were sought by ab initio calculations at HF/3-21G* and B3LYP/6-31G* levels (Table 4).[32] To avoid conformational complexity, 3,3-dimethylated species were not included

For **6**$^+$, **9**$^+$, and **27**$^+$, the most stable conformers were found to be chair-boat (B) form by calculations at B3LYP/6-31G* (Table 4).[39] For bicyclo[3.3.1]non-1-yl cation (**10**$^+$), the chair-chair (A) form is the most stable. For reference systems, **6-H**, **9-H**, **10-H**, and **27-H**, geometry optimizations and energy analyses at B3LYP/6-31G* were also carried out for the chair-chair (A) structures (Table 4).[40] Table 5shows the energies at B3LYP/6-31G* for [3.3.1]-propellanone **12** and related [3.3.1]propellanes **28**−**30**:[45] the optimized geometries for the carbocations and propellanes are shown in Figures 1 and 2, respectively. The calculation results will be used in the following discussions on the mechanism and factors affecting the formation of propellane type products.

Mechanism of Propellanone Formation. A possible mechanism for the formation of [3.3.1]propellanone **12** involves a homohyperconjugative interaction of the bridgehead cationic p orbital with the sp^3 back lobe on the other bridgehead carbon. Della and co-workers attributed the enhanced stability of bicyclo[3.1.1]heptyl cation (**31**) to σ-hyperconjugation as depicted by **31**↔**32** and **33** (Scheme 6).[46−48] Resonance stabilization of **34**↔**35** for the bicyclo-[1.1.1]pent-1-yl cation has also been postulated by the Della group to explain the unexpectedly facile formation of the bicyclo[1.1.1]pent-1-yl cation in solvolysis (Scheme 6).[46,48] On the contrary, the Wiberg group interprets that **34** is a transition state leading to the bicyclo[1.1.0]butyl-1-carbinyl cation (**36**) on the basis of MP2/6-31G* calculations.[49] Promotion of homohyperconjugative interaction by a silyl substituent has been demonstrated in the solvolysis of an open-chain system **37**.[50]

We assume that 2-oxobicyclo[3.3.1]non-1-yl triflate (**6-OTf**) gives an unbridged carbocation as the first intermediate. Concerted processes, in which the σ bond is formed between the bridgehead carbons via simultaneous departure of the nucleofuge (TfO$^-$) and deprotonation, or a bridged ion **38** (Scheme 6) is formed synchronously with ionization, may be less probable. The complex product pattern in the solvolysis of **6-OTf** (Scheme 1) would preclude the possibility of concerted processes. Moreover, the solvolysis of **6-OTf** does not appear to be accelerated by neighboring group participation.[8b] The B3LYP/6-31G*-optimized geometry of cation **6**$^+$ suggests an unbridged carbocation, since the distance between the

(32) Geometries were optimized with Gaussian 94[33] at the Hartree−Fock (HF) level with the 3-21G* basis set[34] and verified to be minima. By using the HF/3-21G*-optimized geometry as starting structure, optimization and energy calculations were carried out with nonlocal hybrid density functional theory (DFT)[35] at the B3LYP level[36, 37] with a larger split-valence d-polarized 6-31G* basis set.[38]

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(39) By inclusion of zero-point energy, the conformer (A) becomes the most stable for **6**$^+$.

(40) For bicyclo[3.3.1]nonanes **6-H**, **9-H**, **10-H**, and **27-H**, the most stable conformers were found to be chair-chair forms on the basis of the heats of formation for some conformers calculated by PM3.[41] For **10-H**, the chair-chair conformation was found to be 2.8 kcal/mol more stable than the chair-boat form; this agrees nicely with recent calculations[42] at BLYP/6-31G* (2.8 kcal/mol), with force-field calculations[43] (2.3 kcal/mol), and with experimental[44] data (2.3 kcal/mol).

(41) MOPAC Ver. 6, Stewart, J. J. P. *QCPE Bull.* **1989**, *9*, 10; Revised as Ver. 6.01 by Hirano, T. University of Tokyo, for UNIX machine *JCPE Newsletter* **1989**, *1*, 10.

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(44) Mastryukov, V. S.; Popik, M. V.; Dorofeeva, O. V.; Golubinskii, A. V.; Vilkov, L. V.; Belikova, N. A.; Allinger, N. L. *J. Am. Chem. Soc.* **1981**, *103*, 1333.

(45) The boat-boat conformer of the [3.3.1]propellanone **12** was found to be the most stable by geometry optimizations and energy calculations at B3LYP/6-31G*. For practical reasons, geometry optimizations and energy calculations for **28**−**30** were carried out only for the boat-boat forms.

(46) (a) Della, E. W.; Schiesser, C. H.: *Strained Bridgehead Cyclobutyl Cations.* In *Advances in Carbocation Chemistry*; Coxon, J. M., Ed.; JAI Press Inc.: CT, 1995; Vol. 2, pp 91−122. (b) Della, E. W.; Pigou, P. E.; Tsanaktsidis, J. *J. Chem. Soc., Chem. Commun.* **1987**, 833. (c) Della, E. W.; Elsey, G. M. *Tetrahedron Lett.* **1988**, *29*, 1299.

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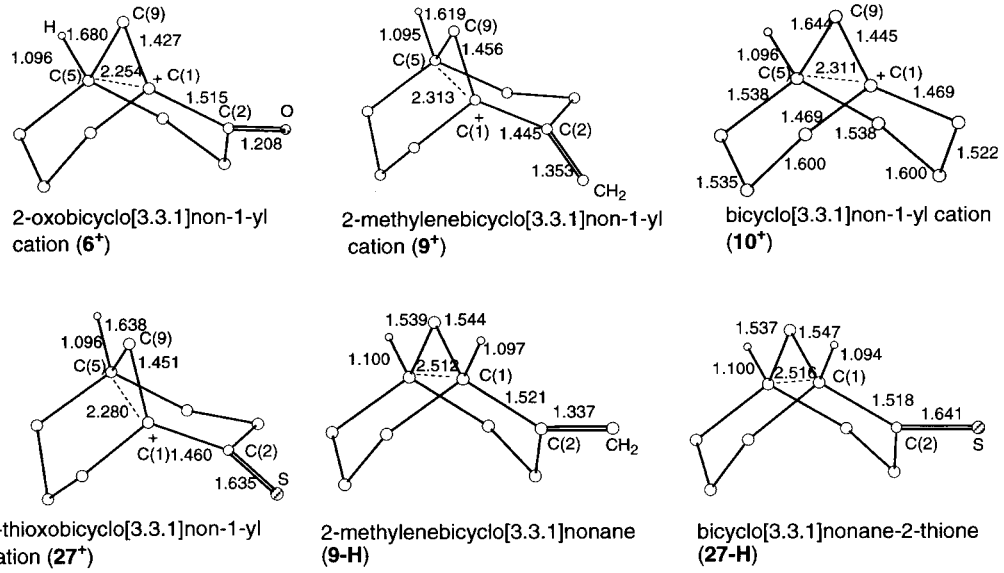


Figure 1. Selected B3LYP/6-31G*-calculated distances (Å) for $\mathbf{6}^+$, $\mathbf{9}^+$, $\mathbf{10}^+$, $\mathbf{27}^+$, **9-H**, and **27-H**.

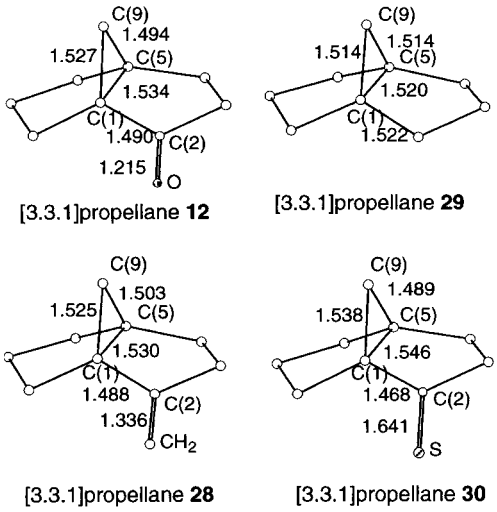
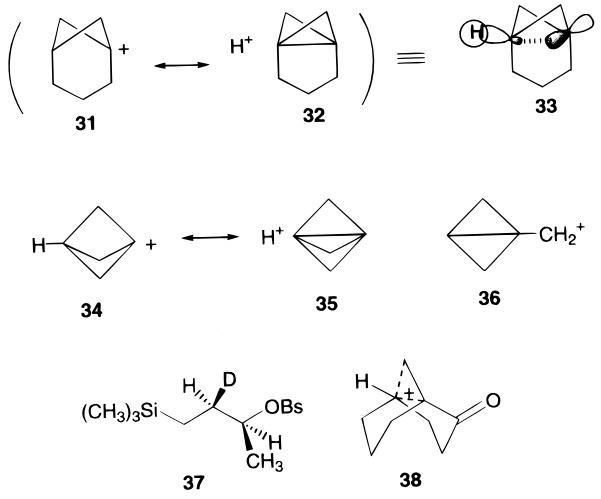


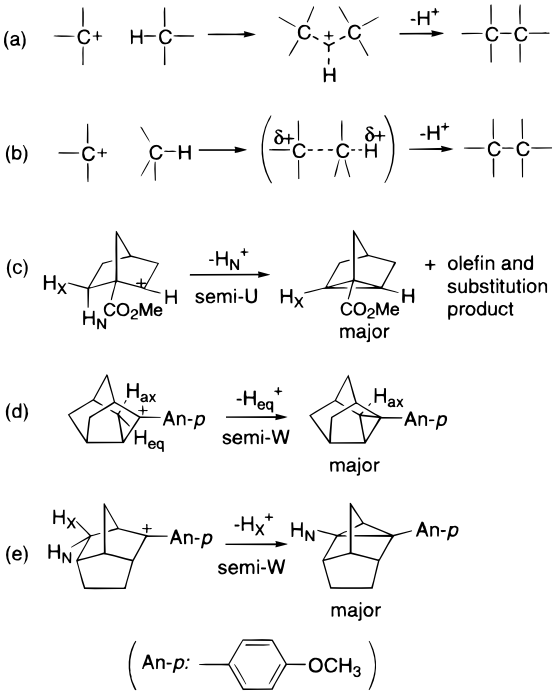
Figure 2. Selected B3LYP/6-31G*-calculated bond distances (Å) for some [3.3.1]propellanes **12**, **28**, **29**, and **30**.

Scheme 6



two bridgehead carbons, C(1) and C(5), of 2.254 Å is too long as compared with the C(5)−C(9) and C(1)−C(9) bond lengths (1.680 and 1.427 Å, respectively) (Figure 1).

Scheme 7



The carbon−carbon bond formation by the attack of a carbocation to a C−H bond is generally interpreted to occur through a nonclassical ion via front-side attack (Scheme 7, (a)).[51] On the other hand, the formation of **12** from $\mathbf{6}^+$ is formally carbon−carbon bond formation by the backside attack of a carbocation to a methine carbon (Scheme 7 (b)). To date numerous examples of 1,3-elimination of carbocations have been reported, but only a few studies have been done on the stereochemical outcomes to our knowledge. Werstiuk reported that the semi-U type deprotonation is preferred (H_{endo}:H_{exo} = 15∼20:1) in the secondary cation (Scheme 7 (c)).[52a] On the other hand, Nickon showed that the semi-W type

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prevails in the *p*-anisyl substituted tertiary cations with deprotonation ratios of H_{eq}:H_{ax} = 7.4:1 (Scheme 7 (d)) and H_{exo}:H_{endo} = 27:1 (Scheme 7 (e)).[52b] Although the detailed mechanism of the electron shift during the deprotonation has not been clarified, it is interesting to point out that the backside attack of a carbocation to a C−H bond (Scheme 7 (b)) is also a common pathway.

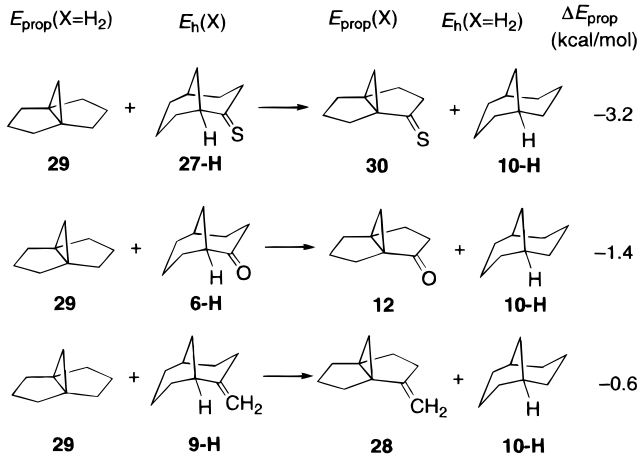
Factors Affecting the Formation of Propellane-Type Product. (a) C(2)-Substituent and Electrophilic Nature of Bridgehead Cationic Carbon. Intuitively, the ease of the C(1)−C(5) bond formation would be controlled by the electron accepting ability of the cationic C(1) carbon, which can be evaluated by LUMO energy levels. Therefore, LUMO energies of 2-substituted bicyclo[3.3.1]non-1-yl cations were calculated by PM3, which decrease in the order $\mathbf{9}^+$ (X = CH_2) (−6.9972 eV), $\mathbf{10}^+$ (unsubstituted) (−7.1000 eV), $\mathbf{27}^+$ (X = S) (−7.3782 eV), and $\mathbf{6}^+$ (X = O) (−7.5826 eV). The lowest LUMO energy of $\mathbf{6}^+$ is consistent with the easiest formation of the corresponding [3.3.1]propellanone **12** through the interaction between the cationic p orbital and the back lobe of the C(5)−H bond. Previously, we reported that some α-carbonyl cations are very strong one-electron oxidizing agents.[53] Although it is not clear if an SET pathway is involved in the C(1)−C(5) bond formation to give **12**, the driving force for the bond formation should be the low LUMO level of $\mathbf{6}^+$.

Another factor for the greatest ability of $\mathbf{6}^+$ to form the C(1)−C(5) bond might be ascribed to the more favorable geometry of $\mathbf{6}^+$ than the other related cations. The B3LYP/6-31G* calculated distance between the two bridgehead carbons C(1) and C(5) in cations decreases in the order $\mathbf{9}^+$ (2.313 Å), $\mathbf{10}^+$ (2.311 Å), $\mathbf{27}^+$ (2.280 Å), and $\mathbf{6}^+$ (2.254 Å). The shortest distance between C(1) and C(5) of $\mathbf{6}^+$ among the four cations also appears to be related to the easiest formation of the C(1)−C(5) bond.

(b) Effect of C(2)-Substituent on the Stability of Propellane-Type Products. It is well-known that a π accepting group attached to a cyclopropane ring stabilizes the system by HOMO−LUMO interaction.[54,55] This concept has successfully been applied to the explanation of the effect of a C(7)-substituent on the equilibrium between 1,3,5-cycloheptatriene and norcaradiene,[56] and barriers to internal rotation of cyclopropylmethanal and related compounds.[57] The HOMO−LUMO interaction in the 1-substituted cyclopropanes has been interpreted as shortening (strengthening) the C(2)−C(3) bond and lengthening the C(1)−C(2) and C(1)−C(3) bonds.[54−56]

The C(5)−C(9) bond length in the B3LYP/6-31G*-optimized geometries of [3.3.1]propellanes decreases in the order **29** (1.514 Å), **28** (1.503 Å), **12** (1.494 Å), and **30** (1.489 Å) (Figure 2). Conversely, the sequence of the respective C(1)−C(5) bond lengths is just opposite, i.e., 1.520, 1.530, 1.534, and 1.546 Å. The geometries indicate that the thioxo propellane **30** is electronically most stabilized among the four propellane-type compounds. Energetics from the B3LYP/6-31G* calculations lead to the same conclusion. Scheme 8 shows the ΔE_{prop} values {= $[E_{prop}(X) + E_h(X = H_2)] - [E_{prop}(X = H_2) + E_h(X)]$} for three isodesmic reactions for propellane formation calculated from the energies of relevant species at B3LYP/6-31G* (Tables 4 and 5).

Scheme 8



The ΔE_{prop} values (kcal mol^{-1}) of −3.2, −1.4, −0.6, and 0 (by definition) for **30**, **12**, **28**, and **29**, respectively, suggest that the thermodynamic stability decreases in this order, and that the thiocarbonyl group is a stronger π acceptor than carbonyl and vinyl groups. Despite the greater π acceptor ability of the thiocarbonyl group, no propellane-type product has been detected in the solvolysis of 2-thioxo compound **11-OTs**. The formation of the propellane-type product only from 2-oxo compounds suggests that the relatively low LUMO energy levels of the intermediate 2-oxo carbocations facilitate the formation of the 2-propellanones.

Conclusions

Methanolyses of 2-oxobicyclo[3.3.1]non-1-yl triflate (**6-OTf**), 3,3-dimethyl-2-oxobicyclo[3.3.1]non-1-yl triflate (**8-OTf**), and 2-oxobicyclo[4.3.1]dec-1-yl mesylate (**7-OMs**) gave the corresponding propellanones in 12%, 20%, and 3.2% yield, respectively, under typical solvolysis conditions. The use of DMF and DMSO as solvent markedly increases the yield of [3.3.1]propellanone **12** from **6-OTf**. The solvent basicity (donor number) is an important factor. Acidic or strongly basic conditions inhibit the formation of **12** by changing the reaction from S_N1 to solvent addition to the carbonyl group. No propellane-type product was obtained in the solvolysis of 1-bromobicyclo[3.3.1]-nonane (**10-Br**), 2-methylidenebicyclo[3.3.1]non-1-yl heptafluorobutyrate (**9-OHFB**), and 3,3-dimethyl-2-thioxobicyclo[3.3.1]non-1-yl tosylate (**11-OTs**). The results of experimental and computational studies show that three-carbon and one-carbon bridges in the substrate (such as bicyclo[3.3.1]nonyl and bicyclo[4.3.1]decyl systems) and the highly destabilized, electrophilic nature of bridgehead cations such as 2-oxo cations are necessary for the formation of propellane-type products in solvolysis.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 90, 270, or 400 MHz. ^{13}C NMR spectra were recorded at 22.5, 68, or 100 MHz. GLC 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. Starting ketols **6-OH** and **7-OH** were reported

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(54) Hoffmann, R. *Tetrahedron Lett.* **1970**, 2907.
(55) Günther, H. *Tetrahedron Lett.* **1970**, 5173.
(56) Review: Balci, M. *Turkish J. Chem.* **1992**, *16*, 8.
(57) Pawar, D. M.; Noe, E. A. *J. Org. Chem.* **1998**, *63*, 2850.

previously.[58] Solvolysis solvents were purified by previously described methods.[59] 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 reagent-grade quality and used as received. Medium-pressure liquid chromatography (MPLC) was conducted on Merck silica gel 60 (230−400 mesh).

Product of Methanolysis of 6-OTf. A reported procedure was followed.[8b] A solution of **6-OTf** in excess 2,6-lutidine (or another base such as pyridine, 2,6-di-*tert*-butylpyridine, or triethylamine) in methanol was kept in a constant-temperature bath (25.0 or 50.0 °C) for 10 or 100 half-lives. GLC analyses of the diethyl ether solutions showed the product distribution given in Scheme 1 and Table 2. Separation and identification of the products **6-OMe**, **12**, **13-OMe**, and **15-OMe** were previously reported.[8b,10] The newly identified product **14-OMe** was isolated as an oil by MPLC (SiO_2, hexane-diethyl ether) followed by HPLC (μ-polarsil 9 mm × 30 cm, hexane-diethyl ether). **14-OMe**: IR (neat) 3054, 1657 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 4.80 (dd, 1H, J = 4.6, 2.6 Hz), 3,54 (s, 3H), 3.24 (s, 3H), 2.51−2.39 (m, 1H), 2.28−2.15 (m, 2H), 1.9−1.3 (m, 8H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.5 (CH_2), 29.5 (CH), 30.4 (CH_2), 32.9 (CH_2), 34.3 (CH_2), 34.8 (CH_2), 50.2 (CH_3), 54.3 (CH_3), 75.6 (C), 97.7 (CH), 153.9 (C). Anal. Calcd for $C_{11}H_{18}O_2$: H, 9.95; C, 72.49. Found: H, 10.12; C, 72.34.

2-Oxobicyclo[4.3.1]dec-1-yl Mesylate (7-OMs). The literature[60] procedure was followed. To a solution of **7-OH**[8b] (0.302 g, 1.80 mmol) and triethylamine (0.38 mL, 2.7 mmol) in CH_2Cl_2 (9 mL) was added methanesulfonyl chloride (0.15 mL, 2.0 mmol) at −20 °C, and then the mixture was stirred for 1 h. The reaction mixture was worked up in a usual manner to give a yellow liquid (0.45 g), which on MPLC (SiO_2, hexane-diethyl ether 4:1) gave **7-OMs** (0.28 g, 63%) as colorless crystals: mp 68.5−69.5 °C (from hexane); IR (CCl_4) 2933, 1712, 1357, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 2.96 (s, 3H), 2.83 (d, 1H, J = 13.5 Hz), 2.62 (dd, 1H, J = 13.5, 6.2 Hz), 2.46 (1H, br), 2.17−2.28 (m, 2H), 1.20−1.92 (m, 10H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.9 (CH_2), 22.8 (CH_2), 29.4 (CH_2), 32.0 (CH), 36.1 (CH_2), 36.8 (CH_2), 38.4 (CH_2), 40.3 (CH_3), 43.1 (CH_2), 91.6 (C), 211.9 (C). Anal. Calcd for $C_{11}H_{18}O_4S$: H, 7.37; C, 53.64. Found: H, 7.33; C, 53.60.

Product of Methanolysis of 7-OMs. A solution of **7-OMs** (0.674 g, 2.74 mmol) in 0.050 M 2,6-lutidine in methanol (68 mL) was divided into two portions, and the one portion (14 mL) was heated at 75 °C for 61.7 h (1 half-life) and the other (54 mL) at 75 °C for 24 days (10 half-lives). After most of the methanol had been evaporated, the residue was dissolved in diethyl ether and worked up in a usual manner to give a yellow liquid (0.130 and 0.382 g, respectively). GLC analyses of the diethyl ether solutions showed the product distribution given in Scheme 3. Separation of the latter portion by MPLC (SiO_2, hexane−diethyl ether) gave methyl ester **18** (51 mg), a mixture (29 mg) of 6-methoxy-1-methylbicyclo[4.3.0]nonan-2-one (**17**) and **7-OMe** (7:3 in mol, by ^{13}C NMR), **7-OMe** (40 mg), a mixture (81 mg) of **7-OMe**, **19**, and unknown compounds, and a mixture of [4.3.1]propellanone **16** and an unknown compound (15 mg), all as a liquid, in this sequence. **7-OMe**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.11−2.00 (m, 10H), 2.25−2.54 (m, 4H), 2.72−2.85 (m, 1H), 3.21 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.3 (CH_2), 22.5 (CH_2), 29.7 (CH_2), 31.8 (CH), 32.6 (CH_2), 34.4 (CH_2), 36.3 (CH_2), 42.1 (CH_2), 50.4 (CH_3), 79.8 (C), 213.7 (C). **16**: ^1H NMR ($CDCl_3$, 270 MHz) δ 2.17 (d, 2H, J = 1.3 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.3 (CH_2), 20.1 (CH_2), 20.4 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 33.4 (CH_2), 35.9 (CH_2), 37.7 (C), 42.0 (C), 210.7 (C); HRMS (EI+) calcd for $C_{10}H_{14}O$ 150.1045, found 150.1044. **17**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.14 (s, 3H), 3.19 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 17.9 (CH_3), 18.9 (CH_2), 20.6 (CH_2), 26.9 (CH_2), 30.0 (CH_2), 32.6 (CH_2), 37.1 (CH_2), 49.8 (CH_3), 60.3 (C), 87.9 (C), 214.0 (C). **18**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.27 (br s, 4H), 1.39−2.19 (m, 9H), 2.26 (dt, 2H, J = 3.0, 7.4 Hz), 3.64 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 21.9 (CH_2), 27.9 (CH), 30.3 (CH_2), 33.3 (CH_2), 36.1 (CH_2), 41.1 (C), 51.6 (CH_3), 179.3 (C). **19**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.20−2.55 (m, 13H), 2.68 (br s, 1H), 3.34 (s, 3H), 3.79 (d, 1H, J = 2.9 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.3 (CH_2), 24.5 (CH_2), 24.7 (CH_2), 25.6 (CH_2), 29.6 (CH), 36.6 (CH_2), 44.2 (CH_2), 48.8 (CH), 55.8 (CH_3), 77.4 (CH), 216.2 (C).

Product of Solvolysis of 7-OMs in Methanol-*d*. A solution of **7-OMs** (0.247 g, 1.00 mmol) in 0.050 M 2,6-lutidine in methanol-*d* (25.0 mL) was kept at 75 °C for 25 days. After most of the methanol-*d* had been evaporated, the residue was worked up in a usual manner to give a yellow liquid and the product distribution was determined by GLC and NMR.

1-Methoxy-3,3-Dimethylbicyclo[3.3.1]nonan-2-one (8-OMe). The literature[16] procedure was followed. To a stirred suspension of freshly powdered $NaNH_2$ (318 mmol) in THF (53 mL) was added a solution of **6-OH** (8.17 g, 53.0 mmol) in THF (53 mL) and the mixture heated under reflux for 2 h with stirring. The mixture was cooled and CH_3I (318 mmol) was added slowly before the mixture was refluxed for 17 h, at which time a second addition of CH_3I (106 mmol) was made. After a reflux period of 4 h, the mixture was cooled to 0 °C and the excess $NaNH_2$ decomposed with cold water. The mixture was extracted with ether and the ether extract was washed with water and 10% NaCl and dried ($MgSO_4$). Evaporation of the solvent followed by MPLC (SiO_2, hexane−diethyl ether) afforded **8-OMe** (8.63 g, 83%) as a pale yellow liquid. Adding hexane to the liquid and cooling at −20 °C afforded white crystals: mp 49.0−50.0 °C; IR (CCl_4) 2828, 1711, 1464 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.16 (s, 3H), 1.24 (s, 1H), 1.37−1.73 (m, 6H), 1.88−1.98 (m, 1H), 2.09 (dd, 4H, J = 15, 10 Hz), 2.43−2.53 (m, 1H), 2.59−2.68 (m, 1H), 3.20 (s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.6 (CH_2), 26.9 (CH_3), 27.6 (CH), 31.5 (CH_3), 32.1 (CH_2), 34.2 (CH_2), 38.3 (CH_2), 40.6 (CH_2), 44.1 (C), 51.0 (CH_3), 79.3 (C), 219.2 (C). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.14; H, 10.45.

1-Hydroxy-3,3-dimethylbicyclo[3.3.1]nonan-2-one (8-OH). The literature[15] procedure was followed. To a solution of **8-OMe** (8.63 g, 44.0 mmol) and NaI (13.2 g, 87.9 mmol) in CH_3CN (124 mL) was added chlorotrimethylsilane (11.2 mL, 87.9 mmol) and the solution was heated at reflux for 17 h. The reaction mixture was quenched with water and extracted with ether. The combined extracts were washed with 10% $Na_2S_2O_3$ and saturated aqueous NaCl and dried ($MgSO_4$). Evaporation of the solvent followed by MPLC (SiO_2, hexane-diethyl ether 8:2) afforded **8-OH** (5.83 g, 73%) as a yellow liquid. Adding hexane to the liquid and cooling at −20 °C afforded pale yellow crystals: mp 57.0−58.0 °C; IR (CCl_4) 3554, 1703, 1464 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.18 (2, 3H), 1.25 (s, 3H), 1.40−1.86 (m, 8H), 2.13 (dd, 1H, J = 15, 10 Hz), 2.30 (br d, 1H, J = 13 Hz), 2.40−2.50 (m, 1H), 3.46 (s, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.9 (CH_2), 26.7 (CH_3), 27.6 (CH), 33.1 (CH_3), 33.6 (CH_2), 35.0 (CH_2), 40.4 (CH_2), 40.7 (CH_2), 42.8 (C), 74.1 (C), 223.1 (C). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.00; H, 9.97

3,3-Dimethyl-2-oxobicyclo[3.3.1]non-1-yl Triflate (8-OTf). To a solution of **8-OH** (0.500 g, 2.74 mmol) and pyridine (0.434 g, 5.49 mmol) in CH_2Cl_2 (9.8 mL) was added a solution of triflic anhydride (0.929 g, 3.29 mmol) in CH_2Cl_2 (9.8 mL) with stirring at 0 °C over 10 min and stirring continued for 1 h. The reaction mixture was worked up at 0 °C in a usual manner to give crude **8-OTf** of approximately 91% purity as assessed by ^{13}C NMR as a yellow liquid (1.07 g), which was used for solvolysis studies without further purification: IR (CCl_4) 1727, 1210 cm^{-1}; ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.7 (CH_2), 27.5 (CH_3), 29.1 (CH), 32.9 (CH_2), 34.1 (CH_3), 35.0 (CH_2), 37.6 (CH_2), 40.0 (CH_2), 45.4 (C), 96.2 (C), 118.0 (CF_3, J = 319 Hz), 212.1 (C).

Product of Methanolysis of 8-OTf. A solution of **8-OTf** (0.750 g, 2.50 mmol) and 0.050 M 2,6-lutidine in methanol (62 mL) was kept at 50 °C for 52 min (10 half-lives). After most of the methanol had been evaporated, the residue was worked up in a usual manner to give a yellow liquid (0.485 g).

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Separation by MPLC (SiO_2, hexane-diethyl ether) gave a mixture (30 mg) of (3,3-dimethyl-2-oxobicyclo[3.3.0]oct-1-yl)-methyl triflate (**25**) and unidentified compounds, a mixture (224 mg) of 3,3-dimethyl-(1-methoxymethyl)bicyclo[3.3.0]octan-2-one (**26**), 3,5,6- trihydro-2,2-dimethyl-3a,6a-methano-1*H*,4*H*-pentalen-1-one (**24**), and unidentified compounds, **24** (15 mg), and **8-OMe** (95 mg), all as a liquid, in this sequence. The molar amounts of products **8-OMe** and **24**−**26** were calculated on the basis of the ^{13}C NMR spectra for these crude products, and the total product ratio is shown in Scheme 5. **24**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2 (CH_2), 24.9 (CH_2), 26.2 (CH_2), 27.3 (CH_3), 28.9 (CH_3), 31.6 (CH_2), 38.9 (C), 43.2 (CH_2), 47.5 (C), 50.7 (C), 217.8 (C); HRMS (EI+) calcd for $C_{11}H_{16}O$ 164.1201, found 164.1198. **25**: ^1H NMR ($CDCl_3$, 270 MHz) δ 4.28 (d, 1H, J = 9.2 Hz), 4.67 (d, 1H, J = 9.6 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.5 (CH_2), 24.5 (CH_3), 25.0 (CH_3), 31.3 (CH_2), 32.7 (CH_2), 40.4 (CH), 41.3 (CH_2), 46.8 (C), 60.6 (C), 77.1 (CH_2), 118.6 (CF_3, J = 320 Hz), 222.2 (C); HRMS (EI+) calcd for $C_{12}H_{17}F_3O_4S$, 314.0800, found 314.0795. **26**: ^1H NMR ($CDCl_3$, 270 MHz) δ 3.13 (d, 1H, J = 8.9 Hz), 3.50 (d, 1H, J = 8.9 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.7 (CH_2), 24.1 (CH_3), 24.9 (CH_3), 31.8 (CH_2), 33.2 (CH_2), 40.2 (CH), 41.7 (CH_2), 46.7 (C), 58.8 (CH_3), 61.7 (C), 75.7 (CH_2), 225.9 (C).

2-Hydrazono-3,3-dimethylbicyclo[3.3.1]nonan-1-ol. To a solution of 1-hydroxy-3,3-dimethylbicyclo[3.3.1]nonan-2-one (**8-OH**) (1.09 g, 6.0 mmol) in 1-butanol (15 mL) was added anhydrous hydrazine (19 mL, 600 mmol), and the solution was heated at reflux for 68 h. Most of the solvent and the excess hydrazine was distilled off under vacuum, and the resulting pale red solid was recrystallized from hexane-diethyl ether (1:1) to give 2-hydrazono-3,3-dimethylbicyclo[3.3.1]nonan-1-ol (0.63 g, 53%) as colorless crystals: mp 135.5−136.5 °C; IR (CCl_4) 3586, 3407, 3294, 1627 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.14 (s, 3H), 1.26 (s, 3H), 1.07−1.64 (m, 7H), 1.90 (dd, 1H, J = 10.6, 14.5 Hz), 2.25−2.44 (m, 2H), 2.80 (br d, 1H, J = 10.7 Hz), 2.5−4.1 (br, 1H), 4.1−7.0 (br, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 20.1 (CH_2), 27.8 (CH), 30.3 (CH_3), 33.8 (CH_2), 34.4 (CH_2), 34.9 (CH_3), 37.5 (C), 39.9 (CH_2), 41.3 (CH_2), 73.7 (C), 158.8 (C). Anal. Calcd for $C_{11}H_{20}N_2O$: C, 67.31; H, 10.27; N, 14.27. Found: C, 67.05; H, 10.37; N, 14.31.

1-Hydroxy-3,3-dimethylbicyclo[3.3.1]nonane-2-thione (11-OH). The literature procedure[17] was followed. To a solution of Et_3N (0.71 mL, 5.1 mmol) in toluene (7 mL) chilled at −78 °C was added simultaneously toluene solutions (90 mL each) of 2-hydrazono-3,3-dimethylbicyclo[3.3.1]nonan-1-ol (0.335 g, 1.71 mmol) and disulfur dichloride (0.230 g, 1.71 mmol) at about the same rate using dropping funnels during 40 min. After stirring for 75 min at room temperature, the reaction mixture was filtered and the filtrate washed with water and 10% NaCl and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (hexane-diethyl ether 9:1) afforded **11-OH** (0.178 g, 53%) as a red semisolid. Adding hexane to the semisolid and cooling at −20 °C afforded red crystals: mp 105.5−106.5 °C; IR (CCl_4) 3487, 1116, 1091 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.01−1.29 (m, 1H), 1.36 (s, 3H), 1.44 (s, 3H), 1.30−1.93 (m, 7H), 2.26 (dd, 1H, J = 10.2, 14.9 Hz), 2.34 (br d, 1H, J = 12.9 Hz), 2.46−2.60 (m, 1H), 3.95 (s, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 19.7 (CH_2), 27.2 (CH), 32.5 (CH_3), 33.9 (CH_2), 34.1 (CH_2), 38.6 (CH_3), 40.7 (CH_2), 46.9 (CH_2), 52.1 (C), 79.5 (C), 281.4 (C). Anal. Calcd for $C_{11}H_{18}OS$: C, 66.62; H, 9.15. Found: C, 66.03; H, 9.16. HRMS (EI+) calcd for $C_{11}H_{18}OS$ 198.1078, found 198.1082.

3,3-Dimethyl-2-thioxobicyclo[3.3.1]non-1-yl Tosylate (11-OTs). To a solution of **11-OH** (0.403 g, 2.03 mmol) in THF (8.1 mL) was added a 1.6 M solution of BuLi in hexane (1.3 mL) at −60 °C over 4 min. After the solution had been stirred for 40 min, a solution of *p*-toluenesulfonyl chloride (0.407 g, 2.13 mmol) in THF (8.1 mL) was added at −45 °C over 8 min, and the mixture stirred for 1 h at room temperature. After most of the solvent had been evaporated, the resulting white precipitates were filtered off and the filtrate was concentrated to give a purple liquid. MPLC (hexane-diethyl ether 9:1) gave crude **11-OTs** as a purple liquid (0.443 g). Adding hexane-diethyl ether (95:5) to the liquid and cooling at −20 °C afforded **11-OTs** (0.199 g, 28%) as purple crystals: mp 102.5−103.5 °C; IR (CCl_4) 1600, 1222, 1215, 1174 cm^{-1}; ^1H NMR (270 MHz, CD_2Cl_2) δ 1.10−1.30 (m, 1H), 1.37−1.58 (m, 3H) partly overlapped with 1.40 (s, 3H) and 1.47 (s, 3H), 1.61 (br s, 1H), 1.89 (ddd, 1H, J = 14.2, 11.6, 4.6 Hz), 1.98−2.08 (m, 1H), 2.21 (ddd, 1H, J = 12.6, 3.3, 1.3 Hz), 2.26 (dd, 1H, J = 14.8, 10.6 Hz), 2.43 (s, 3H), 2.51−2.62 (br, 1H), 3.14 (dt, 1H, J = 12.5, 3.6 Hz), 7.32 (d, 2H, J = 8.5 Hz), 7.72 (d, 2H, J = 8.3 Hz); ^{13}C NMR (68 MHz, CD_2Cl_2) δ 18.7 (CH_2), 21.0 (CH_3), 28.0 (CH), 33.1 (CH_2), 33.2 (CH_3), 34.3 (CH_2), 37.3 (CH_3), 39.9 (CH_2), 43.8 (CH_2), 53.7 (C), 94.7 (C), 126.9 (CH), 129.2 (CH), 136.1 (C), 144.1 (C), 266.7 (C). Anal. Calcd for $C_{18}H_{24}O_3S_2$: C, 61.33; H, 6.86. Found: C, 61.27; H, 6.84.

Product of Methanolysis of 11-OTs. A solution of **11-OTs** (0.328 g, 0.929 mmol) in 0.025 M 2,6-lutidine in methanol (46 mL) was kept at 50.0 °C for 7.5 h. After most of the methanol had been removed with a rotary evaporator, the residue was worked up in a usual manner to give 1-methoxy-3,3-dimethylbicyclo[3.3.1]nonane-2-thione (**11-OMe**) (0.198 g, 100%) as a purple liquid. **11-OMe**: ^1H NMR (270 MHz, $CDCl_3$) δ 1.00−1.21 (m, 1H), 1.25 (s, 3H), 1.32 (s, 3H), 1.34−1.63 (m, 6H), 1.90 (br d, 1H, J = 11.8 Hz), 2.14 (dd, 1H, J = 14.8, 10.6 Hz), 2.50 (br d, 1H, J = 10.5 Hz), 2.68 (br dq, 1H, J = 12.5, 3.2 Hz), 3.02 (d, 3H, J = 2.3 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.8 (CH_2), 27.0 (CH), 30.8 (CH_2), 32.9 (CH_3), 34.2 (CH_2), 35.3 (CH_3), 40.0 (CH_2), 44.9 (CH_2), 49.4 (CH_3), 52.7 (C), 85.1 (C), 274.3 (C).

Kinetic Methods. The preparation of solvents and kinetic studies followed the methods described previously.[59]

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Supporting Information Available: Characterization and ^{13}C NMR spectra for **7-OMe**, **14-OMe**, **16**, **17**, trans isomer of **17** (***t*-17**), and **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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