Solvolysis of 2-Thioxo Bicyclic Bridgehead Derivatives: Evaluation of π-Conjugative Stabilization of α-Thiocarbonyl Carbocations

Kazuhiko Tokunaga, Takafumi Ohtsu, Yasushi Ohga,† and Ken'ichi Takeuchi*

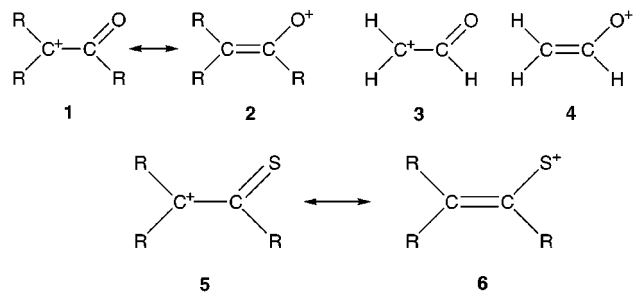
Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-01, Japan

Received October 24, 1997

The ethanolysis rates of 3,3-dimethyl-2-thioxobicyclo[2.2.2]oct-1-yl triflate and 3,3-dimethyl-2-thioxobicyclo[3.2.2]non-1-yl triflate relative to their corresponding parent compounds (3,3-dimethylbicyclo[2.2.2]oct-1-yl triflate and 3,3-dimethylbicyclo[3.2.2]non-1-yl triflate, respectively) at 25.0 °C increase from $10^{-6.2}$ to $10^{-2.5}$. The increase in the rate ratios with the flexibility of the ring system supports the applicability of the authors' methodology to change the conjugative ability of bridgehead carbocations. Formation of 3,3-dimethyl-1,2-epithio-2-ethoxybicyclo[3.2.2]nonane in the ethanolysis of 3,3-dimethyl-2-thioxobicyclo[3.2.2]non-1-yl 2,2,2-trifluoroethanesulfonate indicates cyclization of the intermediate 3,3-dimethyl-2-thioxobicyclo[3.2.2]nonyl cation into an episulfide cation. Computational studies at the HF/6-31G* level indicate that the resonance interaction between the cationic center and the C═S π system is greater in the 3,3-dimethyl-2-thioxobicyclo-[3.2.2]nonyl cation than in the 3,3-dimethyl-2-thioxobicyclo[2.2.2]octyl cation.

Introduction

In the past decade there has been continued interest in the properties of carbocations substituted with electron-withdrawing groups attached directly to the cationic center.[1] Although these cations are considered as highly destabilized owing to the electron-withdrawing inductive effect of the substituents, π-conjugative electron-donating stabilization has been suggested in some carbocations.[1] The α-carbonyl cation is one of the most interesting among such cations and has been extensively studied.[1] Various solvolysis studies have been interpreted to support the notion that the destabilizing inductive effect may be partially offset by a π-conjugative stabilizing effect (**1** ↔ **2**).[1] According to the theoretical study in 1988

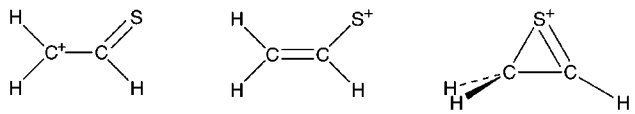


1 **2** **3** **4**

5 **6**

based on HF/6-31G*-optimized geometries of formylmethyl cation **3** and acetaldehyde, it was concluded that the structure **4** is not a significant contributor.[2] Recently, these species have been the subject of calculation at the MP2/6-31G** level, and the optimized MP2/6-31G** structures have been interpreted as indicating a small but significant stabilization of **4** by the conjugating carbonyl group.[3]

The α-thiocarbonyl cation **5** is also of interest since this is intrinsically related to the α-carbonyl cation. Creary and co-workers have carried out solvolysis studies in which α-C(NMe_2)═S cations have been generated and found that the α-C(NMe_2)═S substrates solvolyze with remarkably high reactivity relative to α-H and α-C(NMe_2)═O analogues.[4] This cation-stabilizing effect of the thioamide group was attributed to a conjugative interaction as represented by **6**.[4] Recently, an α-C(NMe_2)═S-substituted cation has been generated by laser excitation, and the relative reactivity of the cation has been examined.[5] It has also been proposed that, in certain instances, neighboring group participation (bridging) is a possible stabilizing contribution in α-thiocarbonyl cations.[4] Several computational studies have shown that structure **8** is an important contributor in



7 **8** **9**

stabilizing the α-thiocarbonyl cation and that cyclized ion **9** is significantly lower in energy than the open ion **7**.[2,3,6]

* Tel: +81 75 753 5689. Fax: +81 75 753 3350. E-mail: ktake@scl.kyoto-u.ac.jp.

† Present address: Faculty of Engineering, Oita University, Oita, 870-11, Japan.

(1) (a) Creary, X. *Chem. Rev.* **1991**, *91*, 1625. (b) Creary, X. *Acc. Chem. Res.* **1985**, *18*, 3. (c) Creary, X.; Hopkinson, A. C.; Lee-Ruff, E. In *Advances in Carbocation Chemistry*, Vol. 1; Creary, X. Ed.; Jai Press Inc.: Greenwich, CT, 1989; pp 45−92.

(2) Lien, M. H.; Hopkinson, A. C. *J. Am. Chem. Soc.* **1988**, *110*, 3788. However, see ref 3.

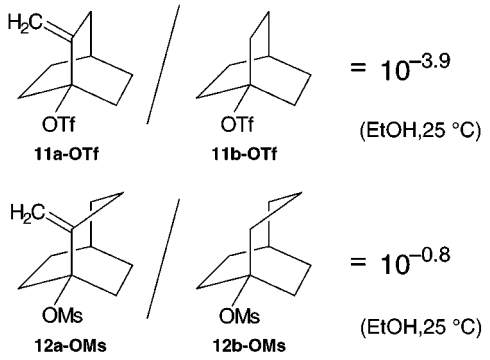
(3) Creary, X.; Wang, Y.-X.; Jiang, Z. *J. Am. Chem. Soc.* **1995**, *117*, 3044.

(4) (a) Creary, X.; Mehrsheikh-Mohammadi, M. E. *J. Org. Chem.* **1986**, *51*, 7. (b) Creary, X.; Aldridge, T. E. *J. Org. Chem.* **1988**, *53*, 3888. (c) Creary, X.; Aldridge, T. E. *J. Org. Chem.* **1991**, *56*, 4280. (d) Creary, X.; Hatoum, H. N.; Barton, A.; Aldridge, T. E. *J. Org. Chem.* **1992**, *57*, 1887.

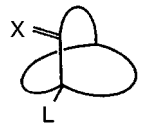
(5) Lew, C. S. Q.; Wong, D. F.; Johnston, L. J.; Bertone, M.; Hopkinson, A. C.; Lee-Ruff, E. *J. Org. Chem.* **1996**, *61*, 6805.

S0022-3263(97)01956-7 CCC: $15.00
Published on Web 03/11/1998

Chart 1



We have been interested in examining the magnitude of π-conjugative stabilization in α-carbonyl cations.[7−9] For this purpose, the solvolysis studies of a series of bridgehead substrates **10** containing the oxo substituent on the



10

X = O, CH_2, S, or H_2

L = leaving group

2-position appeared to be appropriate, since there is no nucleophilic solvent assistance or carbonyl participation from the rear side. In addition, with increase in the ring size, the structure becomes more flexible and more susceptible to π conjugation, with the steric circumstances around the reaction center essentially unchanged.

The feasibility of this methodology has been examined by using the 2-methylene (or allylic) system.[7,8,10] The rate ratio of the 2-methylene bridgehead compound relative to the parent compound increased from $10^{-3.9}$ for **11a-OTf**/**11b-OTf** to $10^{-0.8}$ for **12a-OMs**/**12b-OMs** (Chart 1). The increase in the rate ratio was reasonably attributed to the increase in allylic conjugation. Recently, Creary and Jiang have used a similar approach in the study of α-oximino cations and showed that the rate enhancement parallels that of allyl systems.[11]

On the other hand, the rate ratios of the 2-oxo to the parent compounds are essentially unchanged (**13a-OTf**/**13b-OTf** = $10^{-8.4}$, **14a-OTf**/**12b-OTf** = $10^{-8.3}$) (Chart 2).[7−9] The marked contrast to the case of the 2-methylene system has been interpreted to indicate the unimportance of π-conjugative stabilization of a tertiary α-carbonyl cation.

To substantiate that this methodology is useful for examining the π-conjugative effect of a heteroatom substituent containing lone-pair electrons, we extended the

Chart 2

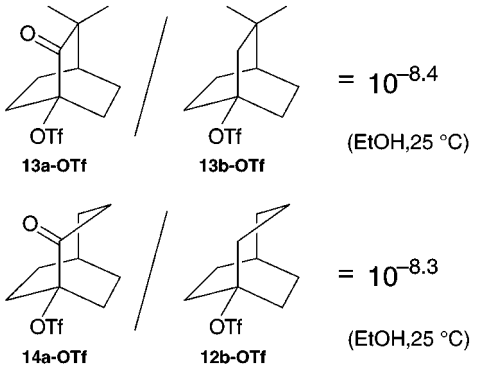
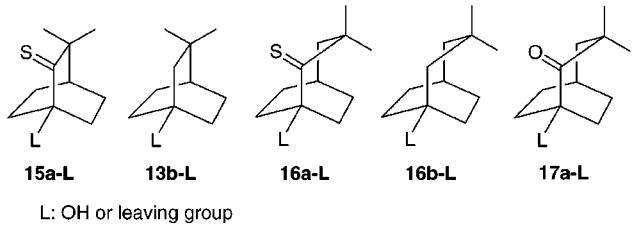


Chart 3



L: OH or leaving group

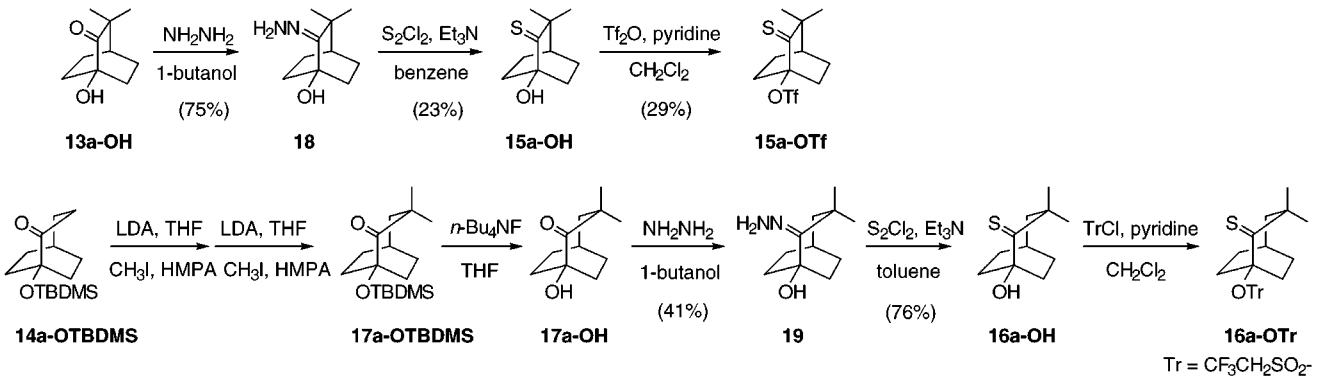
work to α-thiocarbonyl cations.[12] We report here full details on the solvolysis studies of 2-thioxo bicyclic bridgehead compounds and computational studies of the corresponding 2-thioxo bridgehead cations (Chart 3). The π-conjugative effect of the 2-thioxo group (**5** ↔ **6**) on the carbocation stability has been evaluated by comparing the rate ratios **15a-OTf**/**13b-OTf** and **16a-OTf**/**16b-OTf**. We have also presented here the rate of **16b-OTf**, which was not determined in the previous paper[12] because of lengthy pathways in synthesis of precursor alcohol **16b-OH**. Previously, the value of **16a-OTf**/**16b-OTf** had to be replaced by **16a-OTf**/**12b-OTf**, since the effect of introducing two methyl groups to the C(3)-position of **12b-OTf** on the ethanolysis rate was presumed to be negligible.[12] In this paper, the newly determined rate of **16b-OTf** has enabled the more accurate reevaluation of the π-conjugative stabilization in the intermediate 2-thioxo cation by using **16a-OTf**/**16b-OTf**, which is more appropriate for comparison with **15a-OTf**/**13b-OTf**.

Results

Synthesis of Solvolysis Substrates. The starting ketols **13a-OH** and **14a-OH** were prepared by a previously reported method.[10] **14a-OH** was subjected to repeated methylation of the C(3)-position of the *tert*-butyldimethylsilyl (TBDMS) ether of **14a-OH** (**14a-OTBDMS**), and a mixture of monomethylated and dimethylated products was obtained (Scheme 1). The dimethylated product of **17a-OTBDMS** was separated by medium-pressure column chromatography (MPLC), and subjected to cleavage of the TBDMS ether to afford **17a-OH**. The intermediate 2-thioxo alcohols **15a-OH** and **16a-OH** were derived from the corresponding ketols **13a-OH** and **17a-OH** via thionation[13] of the 2-hydrazono alcohols **18** and **19**, respectively. The 2-thioxo alcohol **15a-OH** was converted to the triflate **15a-OTf**. The rate

(6) Bertone, M.; Vuckovic, D. L.; Cunje, A.; Rodriquez, C. F.; Lee-Ruff, E.; Hopkinson, A. C. *Can. J. Chem.* **1995**, *73*, 1468.
(7) Takeuchi, K.; Akiyama, F.; Ikai, K.; Shibata, T.; Kato, M. *Tetrahedron Lett.* **1988**, *29*, 873.
(8) Takeuchi, K.; Yoshida, M.; Ohga, Y.; Tsugeno, A.; Kitagawa, T. *J. Org. Chem.* **1990**, *55*, 6063.
(9) Takeuchi, K.; Ohga, Y.; Yoshida, M.; Ikai, K.; Shibata, T.; Kato, M.; Tsugeno, A. *J. Org. Chem.* **1997**, *62*, 5696.
(10) Takeuchi, K.; Kitagawa, T.; Ohga, Y.; Yoshida, M.; Akiyama, F.; Tsugeno, A. *J. Org. Chem.* **1992**, *57*, 280.
(11) Creary, X.; Jiang, Z. *J. Org. Chem.* **1996**, *61*, 3482.
(12) Tokunaga, K.; Ohga, Y.; Takeuchi, K. *Tetrahedron Lett.* **1996**, *37*, 2241.
(13) Okazaki, R.; Inoue, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3541.

Scheme 1



of the triflate **16a-OTf** was expected to be too fast to be measured; therefore, the alcohol **16a-OH** was converted to the 2,2,2-trifluoroethanesulfonate (tresylate) **16a-OTr**. The parent substrate **13b-OTf** was previously synthesized and the rate was reported.[7−9] The parent bridgehead alcohol **16b-OH** was prepared by bridgehead oxidation of 3,3-dimethylbicyclo[3.2.2]nonane, obtained by the Wolff−Kishner reduction of the 3,3-dimethylbicyclo-[3.2.2]nonan-2-one.[14] The alcohol was converted to the mesylate **16b-OMs**, which was expected to solvolyze at a rate convenient for measurement. New precursor ketol **17a-OH** was converted to the triflate **17a-OTf**.

Solvolysis Rates. The solvolyses were conducted in the presence of 2,6-lutidine, and the rates were determined either titrimetrically or conductometrically. The rates of **16a-OTf** and **16b-OTf** were expected to be too fast to be measured. Therefore, the substrates containing an appropriate leaving group such as tresylate **16a-OTr** and mesylate **16b-OMs** were used for measurement, and the ethanolysis rates of the triflates **16a-OTf** and **16b-OTf** were estimated by using the rate ratio $k_{OTf}/k_{OTr} = 9.75 \times 10^3$ or $k_{OTf}/k_{OMs} = 1.41 \times 10^6$, respectively, which had been determined for the ethanolysis of 1-adamantyl substrates at 25 °C.[15] Since the substrates **16a-OTr** and **16b-OMs** were very unstable to water and column chromatography, crude substrates were used for solvolysis studies without further purification. The tresylate **16a-OTr** was 70−80% pure on the basis of its ^{13}C NMR spectrum; the impurities were the starting alcohol and the products assumed to be formed during workup, which do not influence the solvolysis rate. The purity of **16b-OMs** was ca. 75% on the basis of the ^{13}C NMR spectrum, and the sole impurity was the starting alcohol. The triflates **15a-OTf** and **17a-OTf** were essentially pure (>97%) on the basis of their ^{13}C NMR spectra. The substrates **15a**, **16a-OTr**, and **16b-OMs** followed good first-order kinetics ($r > 0.99$) over 70−80% reactions. The first-order plot for ethanolysis of 2-oxo substrate **17a-OTf** showed a slight upward drift. Similar tendency was observed in the ethanolysis of **14a-OTf**, which was caused by isomerization of **14a-OTf** to (2-oxobicyclo[3.2.1]-oct-1-yl)methyl triflate of higher reactivity.[9] Most probably, similar isomerization might occur in the ethanolysis of **17a-OTf**. Consequently, the initial first-order rate constants are used as the rates of S_N1 solvolysis for **17a-OTf**. The rate data and activation parameters are summarized in Table 1.

Table 1. Rate Data for the Solvolyses of Various Bridgehead Compounds[a]

substrate	solvent	temp (°C)	k_1 (s^{-1})[b]	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal K^{-1} mol^{-1})
15a-OTf	EtOH	25.0	6.05×10^{-9} [c]	29.7	+3.4
		50.0	3.14×10^{-7} [d]		
		75.0	9.42×10^{-6} [d]		
		100.0	1.74×10^{-4} [d]		
16a-OTf	EtOH	25.0	8.0×10^{-1} [e]		
16a-OTr	EtOH	25.0	8.21×10^{-5} [d]	23.9	+3.0
		0.0	1.86×10^{-6} [d]		
	80% EtOH	25.0	2.01×10^{-3} [f,g]		
	60% EtOH	25.0	1.15×10^{-2} [f,h]		
	MeOH	25.0	3.96×10^{-4} [f,h]		
	TFE	25.0	1.3×10^{-1} [f,g]		
16b-OTf	EtOH	25.0	2.45×10^{2} [i]		
16b-OMs	EtOH	25.0	1.74×10^{-4} [d]	23.0	+1.5
		0.0	4.52×10^{-6} [d]		
17a-OTf	EtOH	25.0	5.73×10^{-7} [d,j]	24.5	−5.1
		50.0	1.51×10^{-5} [d,j]		

[a] Buffered with 0.025 M 2,6-lutidine except in TFE. [b] The correlation coefficient for the first-order plot was greater than 0.99, except for **17a-OTf**. [c] Extrapolated from data at other temperatures. [d] Determined titrimetrically on 0.020 or 0.010 M substrate. [e] Estimated by multiplying k_1 of **16a-OTr** by a factor of 9.75×10^3 for the OTf/OTr rate ratio of the 1-adamantyl system (ref 15). [f] Determined conductometrically on ca. 3×10^{-4} M substrate. [g] Accurate to ±7%. [h] Accurate to ±2%. [i] Estimated by multiplying k_1 of **16b-OMs** by a factor of 1.41×10^6 for the OTf/OMs rate ratio of the 1-adamantyl system (ref 15). [j] Initial rate.

Solvolysis Products. The ethanolyses of **15a-OTf** and **16a-OTr** were carried out in the presence of excess 2,6-lutidine for 10−20 half-lives. The ethanolysis products of **15a-OTf** were isolated by medium-pressure liquid chromatography (MPLC) over silica gel and the product distribution was determined on the basis of the isolated yields of the products. The ethanolysis products of **16a-OTr** were isolated in a similar manner and the product distribution was determined on the basis of the ^{13}C NMR spectrum. The products of the ethanolysis of **15a-OTf** were the corresponding ethyl ether **20** and the Wagner−Meerwein rearrangement products **21** and **22** (Scheme 2). The ethanolysis of **16a-OTr** afforded an episulfide **23** and bridgehead thiols **24** and **25** besides smaller amounts of the normal substitution product **26** and Wagner−Meerwein rearrangement product **27** (Scheme 2).

Identification of **20**−**22** rests on the resemblance of their ^{13}C NMR spectra to those of the corresponding keto analogues. Compounds **23**−**25** were shown not to contain a thiocarbonyl group on the basis of their ^{13}C NMR and IR spectra. ^{13}C and ^{1}H NMR spectra have shown that **23** is not symmetrical but **24** and **25** are. Compound **24**

(14) Muir, D. J.; Stothers, J. B. *Can. J. Chem.* **1993**, *71*, 1099.
(15) Takeuchi, K.; Ikai, K.; Shibata, T.; Tsugeno, A. *J. Org. Chem.* **1988**, *53*, 2852.

Scheme 2

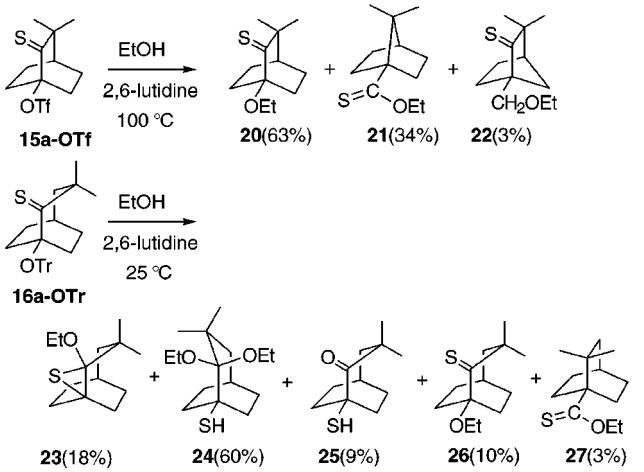
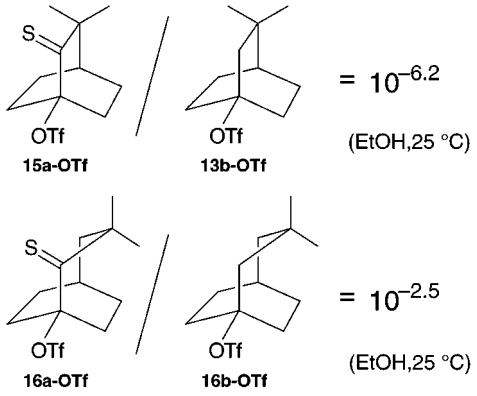


Chart 4



was shown to contain two ethoxyl groups on the basis of its ^{13}C NMR spectrum. In the ^{13}C NMR spectrum of thiol **25**, the signal at 214 ppm has been reasonably assigned to the carbonyl carbon. Absorptions of S−H stretching have been observed in the IR spectra of **24** (2595 cm^{-1}) and **25** (2579 cm^{-1}).

Discussion

Effect of 2-Thiocarbonyl Substituent on Solvolysis Rate. (a) Solvolysis of Bicyclo[2.2.2]octyl System. The 2-thioxobicyclo[2.2.2]octyl derivative **15a-OTf** solvolyzes slower than the parent compound **13b-OTf** by a factor of $10^{6.2}$ (Chart 4). This value is in the middle of the deactivating factor of $10^{8.4}$ for the 2-oxo analogue[7,8] and that of $10^{3.9}$ for the 2-methylene analogue[7,8,10] of bicyclo[2.2.2]octyl system. For the 2-methylene system, the value of $10^{3.9}$ is comparable with that ($10^{4.2}$) determined for the acetolysis of 2-methylene-1-adamantyl and 1-adamantyl tosylates, the former solvolyzing slower than the latter.[7,10,16] Since geometric factors preclude allylic conjugation in the adamantyl system, this deactivating factor of ca. 10^4 has been ascribed to the purely inductive effect (−I) of the methylene group.[7,10,16] To confirm that the deactivating factor for the 2-oxo or 2-thioxo system represents the inductive effect of the 2-oxo or 2-thioxo group, we examined the correlation of the rate ratios of the bicyclo[2.2.2]oct-1-yl system with other inductive parameters. For this purpose, field/inductive parameters, σ_F,[17] appeared to be useful for 2-methylene, oxo, and thioxo substituents C(C_6H_5)=X (X = CH_2, O, or S). The σ_F scale, which has been presented by Taft and coworkers, is based on the ^{19}F NMR shielding effect of the substituent for meta-substituted fluorobenzenes.[17] The log[k(X = CH_2, S, or O)/k(X = H_2)] values of the bicyclo[2.2.2]oct-1-yl system are plotted against the corresponding σ_F values for C(C_6H_5)=X (Figure 1). The log[k(X = CH_2, S, or O)/k(X = H_2)] values linearly decrease with the increase of the σ_F values. Consequently, the increase in the deactivating factors of $10^{3.9}$ for **11a-OTf**/**11b-OTf**, $10^{6.2}$ for **15a-OTf**/**13b-OTf**, and $10^{8.4}$ for **13a-OTf**/**13b-OTf** is associated with the increasing electron-withdrawing effect in the order C=CH_2, C=S, and C=O groups. This linear correlation also supports the notion that the cationic intermediates from the bicyclo[2.2.2]oct-1-yl substrates **11a-OTf**, **15a-OTf**, and **13a-OTf** are free from conjugation because of the perpendicular orientation of the π system relative to the cationic p orbital.

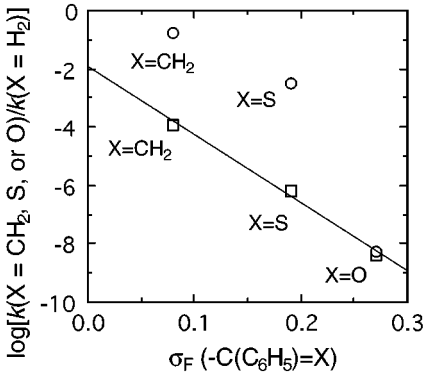


Figure 1. Plot of log[k(X = CH_2, S, or O)/k(X = H_2)] values against σ_F for C(C_6H_5)=X calculated from the substituent ^{19}F NMR shielding effect for meta-substituted fluorobenzenes. Squares and circles are for the bicyclo[2.2.2]oct-1-yl and the bicyclo[3.2.2]non-1-yl system, respectively. For σ_F values, see ref 17.

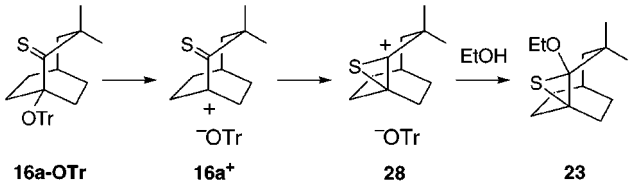
The almost linear plot in Figure 1 implies that the solvolysis mechanisms for the bicyclo[2.2.2]oct-1-yl substrates are similar. In the case of the 2-methylene derivative **11a-OTf**, it solvolyzes via a k_C process to give solely a bridgehead substitution product. Consequently, it is reasonable to conclude that the solvolyses of **11a-OTf**, **15a-OTf**, and **13a-OTf** proceed via k_C processes. The present result is not consistent with the notion that **13a-OTf** may well be a k_Δ substrate and that its rate might be accelerated to some extent by σ-participation.[1a,c]

(b) Solvolysis of the Bicyclo[3.2.2]nonyl System. The rate ratio of 2-thioxobicyclo[3.2.2]nonyl derivative **16a-OTf** relative to the parent compound **16b-OTf** is $10^{-2.5}$, which is much larger than that ($10^{-6.2}$) of **15a-OTf**/**13b-OTf** for the bicyclo[2.2.2]octyl system. The gain of $10^{3.7}$ (=$10^{-2.5}/10^{-6.2}$), which corresponds to ca. 5 kcal mol^{-1}, is reasonably attributed to the increase in π conjugation in the incipient carbocation from **16a-OTf**. To what extent is conjugation attained in the solvolysis of **16a-OTf**? It has recently been reported by the Creary group that, when α-thiocarbonyl conjugative stabilization is minimal or nonexistent in the intermediate cation, the solvolysis rate of cyclic α-thioamide compound relative

(16) (a) Ree, B. R.; Martin, J. C. *J. Am. Chem. Soc.* **1970**, *92*, 1660. (b) Buss, V.; Gleiter, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 3927. (c) Takeuchi, K.; Ohga, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 833.

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

Scheme 3



to the unsubstituted compound is $10^{-3.1}$.[18] The related acyclic α-thioamide compound solvolyzes faster than the unsubstituted methyl analogue by a factor of ca. 10^2, and this was attributed to a significant conjugative stabilization in the intermediate cation.[4,18] If this ratio of 10^2 is chosen for the fully conjugated system, the increase in rate ratio from null to full conjugation can be assumed to be ca. 10^5 ($=10^2/10^{-3}$). By use of this assumption, the rate ratio of **16a-OTf**/**16b-OTf** can be interpreted to indicate realization of ∼70% thiocarbonyl conjugation in the solvolysis of **16a-OTf**.

The development of the thiocarbonyl π conjugation is represented in Figure 1 as the upward shift of the point of the log[k(X = S)/k(X = H_2)] value of the bicyclo[3.2.2]-non-1-yl system from the line of the bicyclo[2.2.2]oct-1-yl system. This upward shift is comparable to the case of log[k(X = CH_2)/k(X = H_2)] for the 2-methylene system.

Contrary to the 2-thioxo or 2-methylene analogues, the values of log[k(X = O)/k(X = H_2)] remain constant at approximately −8 (Figure 1). A reasonable interpretation of the marked contrast is that the conjugative stabilization of α-carbonyl cations, if present, is too small to be detected by the present methodology.

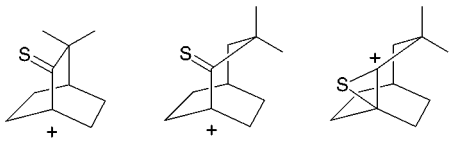
What makes the difference in conjugative ability between the thiocarbonyl and carbonyl groups? One explanation could be the different polarizability of the C=S bond from that of the C=O bond. According to calculations on H_2C=S (B3LYP/6-311+G**) by Schleyer, the C=S σ bond is polarized by 11% toward carbon and the π bond toward sulfur to an equal extent.[19] On the contrary, both the C=O σ and π bonds are polarized by 31% toward oxygen on the basis of calculations on H_2C=O (B3LYP/6-311+G**).[19]

Solvolysis Mechanism. The most notable feature is that episulfide **23** and bridgehead thiols **24** and **25** formed in the reaction of **16a-OTr**. The formation of **23**−**25** indicates the involvement of episulfide cation **28** in the solvolysis (Scheme 3). It has been proposed that, in certain instances, the thiocarbonyl group can interact with a cationic center to form cyclized ions.[4] Large rate enhancements have been observed in such cases.[4] In the case of **16a-OTr**, this type of assistance, which involves the direct formation of **28**, means "frontside S_N2" mechanism. We assume that this would be highly improbable. To obtain some supporting evidence for the S_N1 nature, we examined the mY relationship for **16a-OTr**.

Figure 2 shows the mY relations of **16a-OTr** in ethanol, methanol, 2,2,2-trifluoroethanol, and aqueous ethanol solvents (80 and 60%) at 25 °C by the use of $Y_{2\text{-AdOTr}}$.[20] The nicely linear mY relation (m = 0.88, r = 0.979) provides the S_N1 nature of the solvolysis of **16a-OTr**. It has been proposed that substrates reacting by neighboring group participation (k_Δ process) give m values significantly smaller than 1.00, probably because of delocalization of the positive charge.[21] However, it is also notable that the bridgehead substitution product **26** was formed in 10% yield. This indicates that the bridgehead cation intermediate is first formed before being captured by the solvent. If the thiocarbonyl group concertedly accelerates the release of the leaving group in ionization of **16a-OTr**, the solvolysis would give exclusively an episulfide **23** and related thiols **24** and **25**. Therefore, the m value of 0.88 may well be regarded as close to 1.00, and the solvolysis of **16a-OTr** may be classified as a k_C process. This idea is also supported by the m value for the solvolysis of **14a-OTf** (m = 0.78 ± 0.03, r = 0.997),[9] in which there would be no neighboring group participation.

Contrary to the solvolysis of **16a-OTr**, products supposed to be formed via cyclization were not obtained in the solvolysis of **15a-OTf**. This contrasting result clearly shows that the flexible framework of the cation **16a**$^+$ from **16a-OTr** enables the cyclization of **16a**$^+$ into episulfide cation **28** (Scheme 3).

Computational Studies on Cationic Intermediates. To better understand the nature of the 2-thioxo bridgehead cations, ab initio molecular orbital studies[22] were carried out on these cations. The target species are 3,3-dimethyl-2-thioxobicyclo[2.2.2]oct-1-yl cation (**15a**$^+$),



3,3-dimethyl-2-thioxobicyclo[3.2.2]non-1-yl cation (**16a**$^+$), and 3,3-dimethyl-1,2-epithiobicyclo[3.2.2]non-1-yl cation (**28**). These cations were optimized at the HF/6-31G* level,[23] and the optimized geometries are shown in Figures 3, 4, and 5 with all hydrogens removed for clarity. Both **16a**$^+$ and **28** are at minima, and **28** is the preferred structure to **16a**$^+$ on the basis of their calculated electronic and zero-point energies shown in the captions to the figures.

The C1−C2 bond length (1.445 Å) of **16a**$^+$ is shorter than that (1.467 Å) of **15a**$^+$, while the C2−S bond length (1.608 Å) of **16a**$^+$ is longer than that (1.596 Å) of **15a**$^+$.

(18) Creary, X.; Zhu, C.; Jiang, Z. *J. Am. Chem. Soc.* **1996**, *118*, 12331.

(19) The calculations on H_2C=S (B3LYP/6-311+G**) were previously reported briefly by Huisgen et al.: see Huisgen, R.; Fisera, L.; Giera, H.; Sustmann, R. *J. Am. Chem. Soc.* **1995**, *117*, 9671. Prof. Rolf Huisgen, Universität München, informed us the results of the calculations by Prof. Paul v. R. Schleyer, University of Erlangen. We are grateful to Prof. Huisgen for disclosure of the results prior to publication. We are also grateful to Prof. Schleyer for providing us with the results of the calculations.

(20) The $Y_{2\text{-AdOTr}}$ values for EtOH, 80% EtOH, 60% EtOH, MeOH, and 2,2,2-trifluoroethanol are −1.798, 0, 0.951, −1.044, and 1.628, respectively, see ref 15. The $Y_{2\text{-AdOTr}}$ values were also reported by Kevill and Hawkinson: see Kevill, D. N.; Hawkinson, D. C. *J. Org. Chem.* **1989**, *54*, 154.

(21) Bentley, T. W.; Llewellyn, G. In *Progress in Physical Organic Chemistry*; Taft, R. W., Ed.; John Wiley & Sons: New York, 1990; Vol. 17, pp 121−158 and references therein.

(22) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94, Revision D.3*; Gaussian, Inc.: Pittsburgh, PA, 1995.

(23) A reviewer pointed out that HF/6-31G* is generally not reliable for carbocations and that for such large systems B3LYP/6-31G* should be used instead.[24] The further calculation will be reported elsewhere.

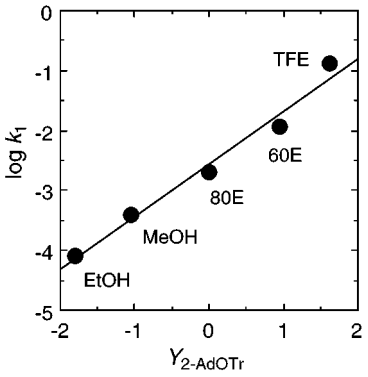


Figure 2. A plot of log k_1 for solvolysis of **16a-OTr** vs $Y_{2-\text{AdOTr}}$ at 25 °C ($m = 0.88$, $r = 0.979$). E stands for ethanol, and the attached numbers mean their vol percentages in aqueous solutions.

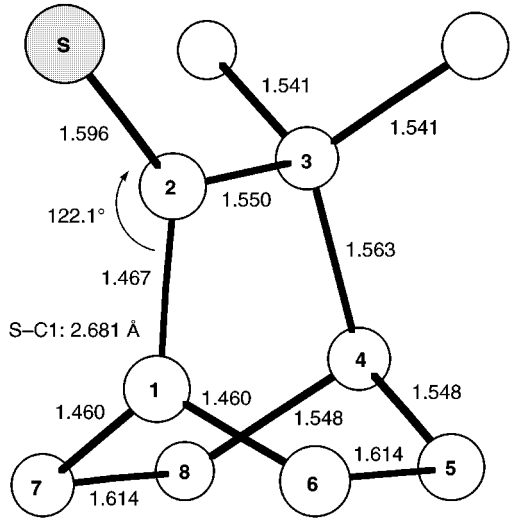


Figure 3. The optimized geometry of 3,3-dimethyl-2-thioxobicyclo[2.2.2]oct-1-yl cation (**15a**$^+$) (HF/6-31G*). The calculated electronic and zero-point energy is −784.37617 hartree.

This is presumably due to the increase in the resonance interaction of the cationic center with the C═S π system in **16a**$^+$ relative to **15a**$^+$.

The bond lengths of the β-C−C bonds of **15a**$^+$ (1.614 Å) are ca. 0.1 Å longer than a normal C−C bond length (for example, 1.53 Å for an ethane). This tendency is the same as that of the previous report by Creary and Jiang that the β-C−C bonds of the α-oximinoadamantyl cation are significantly lengthened.[8] It is suggested that cation **15a**$^+$ is stabilized in a similar manner owing to the interaction between the cationic p orbital and a C−C σ bond.

In the bicyclo[3.2.2]nonyl cation (**16a**$^+$), the C1−C2−S angle of 103.4° is quite smaller than that (122.1°) of the bicyclo[2.2.2]octyl cation (**15a**$^+$). In addition, the distance between C1 and S becomes shorter in **16a**$^+$ (2.400 Å) than that of **15a**$^+$ (2.681 Å). These results indicate that the contribution of the cyclized ion increases in the optimized geometry of **16a**$^+$ relative to **15a**$^+$

The C2−C3 bond (1.513 Å) of the bicyclo[3.2.2]nonyl cation (**16a**$^+$) is ca. 0.04 Å shorter than that (1.550 Å) of the bicyclo[2.2.2]octyl cation (**15a**$^+$). The bond length of one C3−CH_3 (1.552 Å) of **16a**$^+$ is longer than the other C3−CH_3 bond (1.539 Å) and is also longer than the C3−

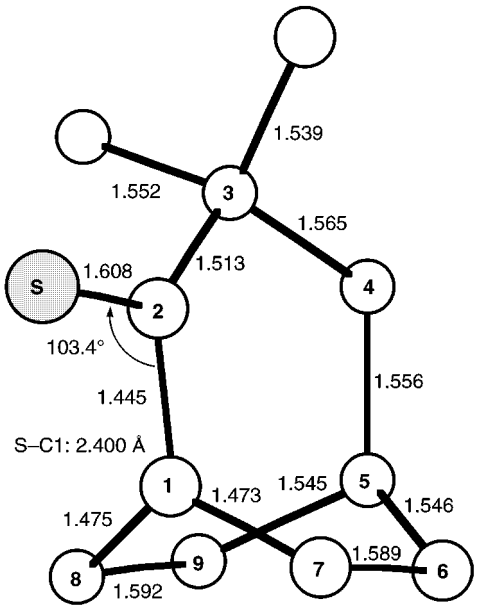


Figure 4. The optimized geometry of 3,3-dimethyl-2-thioxobicyclo[3.2.2]non-1-yl cation (**16a**$^+$) (HF/6-31G*). The calculated electronic and zero-point energy is −823.38731 hartree.

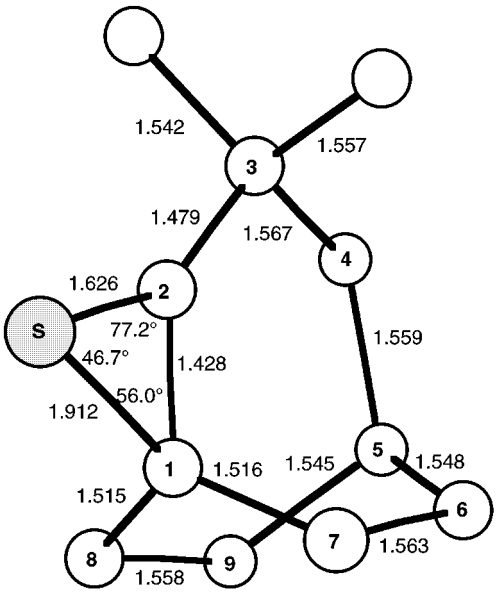


Figure 5. The optimized geometry of 3,3-dimethyl-1,2-epithiobicyclo[3.2.2]non-1-yl cation (**28**) (HF/6-31G*). The calculated electronic and zero-point energy is −823.39206 hartree.

CH_3 bond (1.541 Å) of **15a**$^+$. In cyclized cation **28**, this tendency is represented more significantly; the C2−C3 bond is still shorter (1.479 Å) and one C3−CH_3 bond is still longer (1.557 Å). Consequently, the shortening of the C2−C3 bond and the lengthening of the one-side C3−CH_3 bond (1.552 Å) of **16a**$^+$ might suggest that cation **16a**$^+$ receives stabilization to some extent by the interaction represented in **29** (Chart 5). The π interaction between the C3−CH_3 bond and the C═S π orbital presumably is averted by the more rigid structure of **15a**$^+$.

The magnitude of conjugation in a 2-thioxo cation is related to the angle between the vacant cationic p orbital and the π orbitals of the double bond. In the present work, θ, the angle of twisting of p orbitals, is defined as

Chart 5

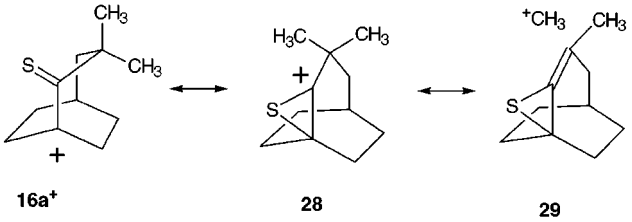
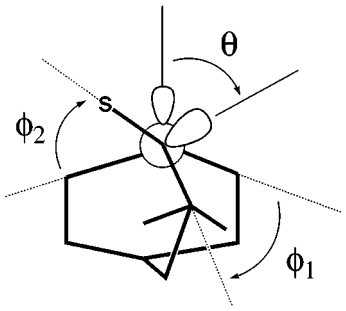


Chart 6



($\phi_1 + \phi_2$)/2 (Chart 6). This is the application of the concept of the distortion at the π bond in a bridgehead olefin.[25] The ϕ_1 and ϕ_2 are distortion angles which are obtained from calculation. When θ is 0°, the p and π orbitals are capable of complete overlap, and when θ is 90°, they are perpendicularly oriented.

In the optimized geometry of the 2-thioxobicyclo[3.2.2]-nonyl cation (**16a**$^+$), the angle of twisting of p orbitals (θ) is 82.5°, and symmetry is lost. On the other hand, the geometry of the 2-thioxobicyclo[2.2.2]octyl cation (**15a**$^+$) remains almost C_s-symmetric, and the angle of twisting of the p orbitals (θ) is 90.0°. This supports the notion that the cationic intermediate **15a**$^+$ is free from conjugation because of the perpendicular orientation of the π system relative to the cationic p orbital. It is also indicated that the more flexible structure of **16a**$^+$ enables an interaction of the π system with the cationic center, whereas in the rigid **15a**$^+$ π-conjugative stabilization cannot occur.

Conclusion

The marked π-conjugative effect of the 2-thioxo group on the carbocation stability has been demonstrated by comparing the rate ratio of **15a-OTf**/**13b-OTf** with **16a-OTf**/**16b-OTf**. The increase in the rate ratios with the flexibility of the ring system supports the applicability of our methodology to detect the enhancement of π conjugation with skeletal flexibility. On the basis of the fact that no appreciable stabilization due to carbonyl conjugation has been detected by our approach, the carbonyl π conjugation in tertiary α-carbonyl cations, if present, is too small to be detected by solvolysis studies. Formation of an episulfide in the solvolysis of **16a-OTr** is explained by ring closure of the 2-thioxo bridgehead cationic intermediate. Computational studies at the HF/6-31G* level indicate that the resonance interaction between the cationic center and the C=S π system is greater in **16a**$^+$ than in **15a**$^+$.

(24) Schreiner, P. R.; Schleyer, P. v. R.; Schaefer, H. F. *J. Org. Chem.* **1997**, *62*, 4216.
(25) Warner, P. M. *Chem. Rev.* **1989**, *89*, 1067 and references therein.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 90, 270, and 400 MHz. ^{13}C NMR spectra were recorded at 22.5, 67.8, and 100 MHz. Gas chromatographic analyses were conducted on a PEG 20M column (3 mm × 2 m). Elemental analyses were performed by the Microanalytical Center, Kyoto University, Kyoto, Japan. Ketols **13a-OH** and **14a-OH** were reported previously.[10] Solvolysis solvents were purified by previously described methods.[15] Anhydrous solvents used for synthesis were purified by the standard procedures. 2,6-Lutidine was distilled over CaH_2. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (triflate) was prepared following a literature procedure.[26] Anhydrous hydrazine was prepared by following a literature procedure.[27] Other commercially available reagents were of a reagent-grade quality and used as received. Medium-pressure liquid chromatography (MPLC) was conducted on Merck silica gel 60 (230−400 mesh).

3,3-Dimethyl-2-hydrazonobicyclo[2.2.2]octan-1-ol (18). To a solution of 3,3-dimethyl-1-hydroxybicyclo[2.2.2]octan-2-one (**13a-OH**)[10] (5.00 g, 29.7 mmol) in 1-butanol (50 mL) was added anhydrous hydrazine (9.4 mL, 297 mmol), and the solution was heated to reflux for 23 h. The reaction mixture was diluted with ether (80 mL) and dried ($MgSO_4$). The solvent was distilled under vacuum, and the pale yellow crystals obtained were subjected to MPLC [SiO_2, hexane−ether (1:4)] to give **18** (4.05 g, 75%) as white crystals: mp 109.0−110.0 °C (from hexane); IR (CCl_4) 3415, 1655, 1614 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.6−2.2 (m, 9H) partly overlapped with 1.4 (s, 6H), 4.4 (br s, 1H), 5.1 (br s, 2H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 22.7 (CH_3), 23.5 (CH_2), 32.1 (CH_2), 38.9 (C), 41.1 (CH), 70.6 (C), 160.2 (C). Anal. Calcd for $C_{10}H_{18}N_2O$: C, 65.90; H, 9.95; N, 15.37. Found: C, 65.91; H, 9.89; N, 15.17.

3,3-Dimethyl-1-hydroxybicyclo[2.2.2]octane-2-thione (15a-OH). The procedure in the literature[13] was followed. To a solution of triethylamine (0.169 mL, 1.21 mmol) in benzene (2.2 mL) at 0 °C were added simultaneously benzene solutions (1.5 mL each) of **18** (0.10 g, 0.549 mmol) and disulfur dichloride (0.074 g, 0.549 mmol) at about the same rate using dropping funnels during 3 min. After stirring for 1 h at room temperature, the reaction mixture was filtered and the filtrate washed with water and dried ($MgSO_4$). Evaporation of solvent followed by MPLC [SiO_2, hexane−ether (9:1)] afforded **15a-OH** (0.023 g, 23%) as yellow crystals. An analytical sample was provided by sublimation at 35−70 °C (2 mmHg): mp 162.0 °C (dec); IR (CCl_4) 3398, 1714, 1126 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.36 (s, 6H), 1.48−1.59 (m, 2H), 1.79−1.87 (m, 3H), 1.98−2.16 (m, 4H), 4.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.5 (CH_2), 30.0 (CH_3), 32.4 (CH_2), 39.1 (CH), 53.7 (C), 83.0 (C), 275.1 (C). Analytical data except for sulfur were satisfactory. Anal. Calcd for $C_{10}H_{16}OS$: C, 65.17; H, 8.75; S, 17.40. Found: C, 65.18; H, 8.92; S, 16.35. HRMS (EI+) calcd for $C_{10}H_{16}OS$ 184.0923, found 184.0935.

3,3-Dimethyl-2-thioxobicyclo[2.2.2]oct-1-yl Triflate (15a-OTf). To a solution of crude **15a-OH** (0.300 g, 1.63 mmol) and pyridine (0.270 g, 3.41 mmol) in CH_2Cl_2 (5 mL) was added a solution of triflic anhydride (0.551 g, 1.95 mmol) in CH_2Cl_2 (5 mL) with stirring at 0 °C over 9 h and then the reaction flask was stoppered and left for 7 days at −1.5 °C. The reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with 10% HCl and water, and dried ($MgSO_4$). Evaporation of solvent followed by MPLC [SiO_2, hexane−ether (9:1)] afforded **15a-OTf** (0.150 g, 29%) as red crystals: mp 50.5−51.5 °C (from hexane); IR (CCl_4) 1416, 1211, 1144 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.38 (s, 6H), 1.85−2.03 (m, 3H), 2.08−2.44 (m, 6H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 23.8 (CH_2), 30.0 (CH_2), 30.2 (CH_3), 37.9 (CH), 56.1 (C), 108.9 (C), 118.2 (q, CF_3, J =

(26) Corey, E. J.; Cho, H.; Rucker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
(27) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. In *Purification of Laboratory Chemicals, 2nd* ed.; Pergamon Press: Oxford, 1980; p 492.

319 Hz), 258.2 (C). Anal. Calcd for $C_{11}H_{15}F_3O_3S_2$: C, 41.76; H, 4.78. Found: C, 41.73; H, 4.83.

1-(*tert*-Butyldimethylsiloxy)-3,3-dimethylbicyclo[3.2.2]nonan-2-one (17a-OTBDMS). The hydroxyl group of **14a-OH**[10] was first protected by *tert*-butyldimethylsilylation. To a solution of **14a-OH** (1.18 g, 7.67 mmol) and 2,6-lutidine (1.8 mL) in CH_2Cl_2 was added *tert*-butyldimethylsilyl triflate[26] at −78 °C over 10 min. After being stirred for 1 h at room temperature, the reaction mixture was diluted with CH_2Cl_2, washed with water, 10% HCl, saturated aqueous $NaHCO_3$, and 10% NaCl, and dried ($MgSO_4$). Evaporation of solvent followed by MPLC [SiO_2, hexane−ether (9:1)] afforded *tert*-butyldimethylsilyl ether **14a-OTBDMS** (1.65 g, 80%) as colorless crystals: ^{13}C NMR ($CDCl_3$, 22.5 MHz) δ −2.6 (CH_3), 18.3 (C), 25.0 (CH_2), 25.9 (CH_3), 27.0 (CH), 28.6 (CH_2), 31.6 (CH_2), 37.0 (CH_2), 79.9 (C), 213.6 (C).

Methylation of the C(3)-position in **14a-OTBDMS** was conducted in a similar manner as that described in the literature.[28] A solution of lithium diisopropylamide (LDA) was prepared from diisopropylamine (2.33 g, 23.0 mmol) and butyllithium (1.6 M in hexane, 14.4 mL, 23.0 mmol) in THF (21.6 mL) at −25 °C for 20 min. To the solution of LDA was added a solution of **14a-OTBDMS** (5.62 g, 20.9 mmol) in THF (12 mL) at −78 °C for 15 min. The solution was stirred at −78 °C for 30 min, and 3.64 mL (20.9 mmol) of HMPA and 1.43 mL (23.0 mmol) of CH_3I were added in this order. The reaction mixture was stirred for additional 25 min at −78 °C and 2.5 h at room temperature and poured into 90 mL of 10% NH_4Cl. The mixture was extracted with ether and the combined ether layers were washed with water and saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and concentrated to dryness; the GLC (PEG 20M) analyses of the resulting oil exhibited that it consisted of 84% of the monomethylated ketone and 16% of the starting ketone. Without purification, this oil was subjected to the same reaction conditions as described above three times. MPLC [SiO_2, hexane−ether (99.5:0.5)] gave **17a-OTBDMS** (3.13 g, 45%) as colorless crystals: mp 65.0−66.0 °C (from hexane); IR (CCl_4) 1707, 1247, 1144 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 0.09 (s, 6H), 0.86 (s, 9H), 1.23 (s, 6H), 1.54−1.92 (m, 10H), 2.10−2.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ −2.6 (CH_3), 18.5 (C), 25.3 (CH_2), 26.2 (CH_3), 28.6 (CH), 31.5 (CH_3), 31.6 (CH_2), 43.6 (C), 44.8 (CH_2), 80.8 (C), 216.4 (C). Anal. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 68.64; H, 11.09.

3,3-Dimethyl-1-hydroxybicyclo[3.2.2]nonan-2-one (17a-OH). To a solution of **17a-OTBDMS** (1.03 g, 3.48 mmol) in THF (20 mL) was added a 1.0 M solution of *n*-Bu_4NF in THF (7.0 mL), and the resulting solution refluxed for 18 h under N_2. The reaction mixture was stirred with 4% aqueous NH_4Cl (34 mL) and extracted with ether. The combined extracts were washed with water and 10% NaCl and dried ($MgSO_4$). Evaporation of the ether followed by MPLC [SiO_2, hexane−ether (9:1)] afforded **17a-OH** (0.630 g, 99%) as colorless crystals. An analytical sample was provided by sublimation at 50−70 °C (2 mmHg): mp 99.5−100.5 °C; IR (CCl_4) 3474, 1690, 1108 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.19 (s, 6H), 1.52−1.93 (m, 10H), 2.12 (br s, 1H), 4.26 (s, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 25.5 (CH_2), 28.7 (CH), 29.9 (CH_2), 31.4 (CH_3), 43.2 (C), 44.6 (CH_2), 76.8 (C), 219.2 (C). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.67; H, 10.01.

3,3-Dimethyl-2-hydrazonobicyclo[3.2.2]nonan-1-ol (19). To a solution of **17a-OH** (0.430 g, 2.36 mmol) in 1-butanol (7.4 mL) was added anhydrous hydrazine (3.74 mL, 118 mmol) and the solution was heated to reflux for 46 h. The reaction mixture was poured into ice (40 g) and extracted with ether. The combined extracts were washed with water and 10% NaCl and dried ($MgSO_4$). The solvent was evaporated and the resulting colorless crystals were washed with hexane (3 × 3 mL) to give **19** (0.190 g, 41%) as colorless crystals: mp 148.5−149.5 °C (from hexane); IR ($CHCl_3$) 3585, 3410, 3295, 1621, 1101 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.23 (s, 6H), 1.35−1.52 (m, 3H), 1.55−1.77 (m, 5H), 1.77−2.20 (m, 3H), 2.40−2.55 (m, 2H), 5.10−6.50 (br s, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 25.5 (CH_2), 29.1 (CH), 32.3 (CH_3), 32.4 (CH_2), 38.9 (C), 50.5 (CH_2), 77.7 (C), 158.4 (C). Anal. Calcd for $C_{11}H_{20}N_2O$: C, 67.31; H, 10.27; N, 14.27. Found: C, 67.52; H, 10.55; N, 14.09.

3,3-Dimethyl-1-hydroxybicyclo[3.2.2]nonane-2-thione (16a-OH). The procedure in the literature[13] was followed. To a solution of triethylamine (2.13 mL, 15.3 mmol) in toluene (20 mL) at −78 °C were added simultaneously toluene solutions (180 mL each) of **19** (1.00 g, 5.09 mmol) and disulfur dichloride (0.688 g, 5.09 mmol) at about the same rate using dropping funnels during 40 min. After stirring for 1 h 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 [SiO_2, hexane−ether (9:1)] afforded **16a-OH** (0.77 g, 76%) as yellow crystals. An analytical sample was provided by sublimation at 40−60 °C (2 mmHg): mp 122−124 °C (dec); IR (CCl_4) 3364, 1729, 1089 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.50 (s, 6H), 1.69−2.10 (m, 10H), 2.16−2.26 (m, 1H), 5.20 (s, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 25.8 (CH_2), 28.7 (CH), 33.0 (CH_2), 37.6 (CH_3), 46.9 (CH_2), 51.4 (C), 82.8 (C), 274.7 (C). Anal. Calcd for $C_{11}H_{18}OS$: C, 66.62; H, 9.15; S, 16.17. Found: C, 66.46; H, 9.24; S, 16.08.

3,3-Dimethyl-2-thioxobicyclo[3.2.2]non-1-yl 2,2,2-Trifluoroethanesulfonate (Tresylate) (16a-OTr). To a solution of 2,2,2-trifluoroethanesulfonyl chloride (0.138 mL, 1.21 mmol) in CH_2Cl_2 (2 mL) was added a solution of **16a-OH** (0.200 g, 1.01 mmol) and pyridine (1.30 mL, 16.1 mmol) in CH_2Cl_2 (2.7 mL) with stirring at 0 °C over 5 min, and then stirring continued for 2.5 h. After having been stored in a freezer (4 °C) overnight, the reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with water, 10% HCl, saturated aqueous $NaHCO_3$, and water, and dried ($MgSO_4$). Since a preliminary experiment revealed that **16a-OTr** was too unstable a liquid to isolate at room temperature, the above CH_2Cl_2 solution was stabilized by adding 2,6-lutidine (0.024 mL, 0.242 mmol) and concentrated with a rotary evaporator to give **16a-OTr** (0.476 g) as a red liquid: IR (CCl_4) 1377, 1321, 1260, 1183, 1134 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.48 (s, 6H), 1.56−2.59 (m, 11H), 4.07 (q, 2H, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 24.9 (CH_2), 28.2 (CH), 33.7 (CH_2), 35.7 (CH_3), 48.3 (CH_2), 53.0 (C), 55.9 (CH_2CF_3; q, J = 32.9 Hz), 103.9 (C), 121.1 (CF_3; q, J = 277.2 Hz), 262.3 (C).

3,3-Dimethylbicyclo[3.2.2]nonane. A solution of 3,3-dimethylbicyclo[3.2.2]nonan-2-one[14] (4.77 g, 29.0 mmol), KOH (5.74 g, 87.0 mmol), and hydrazine hydrate (42 mL, 870 mmol) in triethylene glycol (50 mL) was refluxed for 3 h and then heated to 180 °C for 9 h until N_2 evolution stopped. The distillate was added into water (50 mL) and extracted with pentane. The combined extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent afforded a pale orange semisolid (0.966 g). The residue was worked up in a similar manner to give a pale orange semisolid (1.98 g). The crude products were combined and recrystallized from MeOH to give 3,3-dimethylbicyclo[3.2.2]nonane (0.800 g, 18%) as colorless crystals: mp 49.5−50.0 °C; IR (CCl_4) 2900, 1456, 1218 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.05 (s, 6H), 1.54−1.78 (m, 12H), 1.85 (br s, 2H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 26.5 (CH_2), 29.5 (CH), 31.3 (C), 35.4 (CH_3), 49.5 (CH_2).

3,3-Dimethylbicyclo[3.2.2]nonan-1-ol (16b-OH). The literature[29] procedure was followed. To a solution of a mixture of 3,3-dimethylbicyclo[3.2.2]nonane (5.05 g, approximately 23 mmol), acetic acid (63 mL), and acetic anhydride (63 mL) was added chromium trioxide (6.63 g, 66.4 mmol) in small portions over a period of 1.5 h. During addition the reaction mixture was kept below 28 °C by cooling in a water bath. After stirring for 6 h, the reaction mixture was diluted with ice water (210 mL) and extracted with ether. The combined extracts were washed with 10% Na_2CO_3 and water and dried ($MgSO_4$). Evaporation of the solvent afforded a mixture (4.60 g). This mixture was added to a solution of lithium aluminum hydride

(28) Hua, D. H.; Gung, W.-Y.; Ostrander, R. A.; Takusagawa, F. J. *J. Org. Chem.* **1987**, *52*, 2509.

(29) Bingham, R. C.; Schleyer, P. v. R. *J. Org. Chem.* **1971**, *36*, 1198.

(1.9 g, 50 mmol) in ether (40 mL) and stirred for 1 h. Usual workup followed by MPLC [SiO_2, hexane−ether (4:1)] afforded **16b-OH** as a pale yellow semisolid (2.14 g, 80%). The crude **16b-OH** was recrystallized from pentane: mp 85.5−86.5 °C; IR (CCl_4) 3597, 2952, 1458, 1363, 1210, 1035 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.08 (s, 6H), 1.56−1.97 (m, 14H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 25.9 (CH_2), 28.5 (CH), 29.6 (C), 35.1 (CH_2), 35.3 (CH_3), 49.0 (CH_2), 57.4 (CH_2), 71.1 (C); HRMS (EI+) calcd for $C_{11}H_{20}O$ 168.1514, found 168.1515. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.05; H, 12.09.

3,3-Dimethylbicyclo[3.2.2]non-1-yl Mesylate (16b-OMs). The literature[30] procedure was followed. To a solution of **16b-OH** (0.169 g, 1.00 mmol) and triethylamine (0.22 mL, 1.6 mmol) in CH_2Cl_2 (16 mL) was added methanesulfonyl chloride (0.093 mL, 1.2 mmol) at −20 °C over 10 min, and then the mixture stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2, washed at 0 °C with water, 10% HCl, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, and dried ($MgSO_4$). Evaporation of solvent afforded a mixture of **16b-OMs** and the starting alcohol as an unstable liquid (0.267 g), which was used for solvolysis studies without further purification: IR (CCl_4) 1330, 1230, 1167 cm^{-1}; ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 25.7 (CH_2), 27.9 (CH), 30.1 (C), 32.6 (CH_2), 35.1 (CH_3), 41.2 (CH_3), 48.9 (CH_2), 54.1 (CH_2), 96.9 (C).

Product of Solvolysis of 15a-OTf in Ethanol. A solution of **15a-OTf** (0.449 g, 1.42 mmol) in 0.050 M 2,6-lutidine in ethanol (35.0 mL) was heated in a constant-temperature bath (100.0 °C) for 13 h (12 half-lives). After most of the ethanol had been removed with a rotary evaporator, the residue was dissolved in ether, and the ether solution was washed with water, cold 5% HCl, water, and saturated aqueous NaCl and dried ($MgSO_4$). Evaporation of the ether afforded a red liquid, which on MPLC [SiO_2, hexane, hexane−ether (97:3)] gave **21** (0.090 g, 0.423 mmol) as a pale yellow liquid, **22** (0.009 g, 0.04 mmol) as a yellow liquid, and **20** (0.166 g, 0.781 mmol) as red crystals, in that order. **20**: mp 62.0−63.0 °C; IR (CCl_4) 1151, 1130, 1048 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.21 (t, 3H, J = 2.2 Hz), 1.30 (s, 6H), 1.76−1.95 (m, 7H), 1.99−2.10 (m, 2H), 3.56 (q, 2H, J = 2.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.6 (CH_3), 23.3 (CH_2), 29.5 (CH_2), 29.8 (CH_3), 38.6 (CH), 54.8 (C), 58.6 (CH_2), 88.9 (C), 272.9 (C). Anal. Calcd for $C_{12}H_{20}OS$: C, 67.87; H, 9.49. Found: C, 67.58; H, 9.23. **21**: IR (CCl_4) 1301, 1251, 1202, 1181, 1032 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.02 (s, 6H), 1.21−1.31 (m, 2H), 1.39 (t, 3H, J = 7.0 Hz), 1.55−1.62 (m, 2H), 1.76 (t, 1H, J = 4.4 Hz), 1.82−1.92 (m, 2H), 2.42−2.51 (m, 2H), 4.50 (q, 2H, J = 4.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.6 (CH_3), 20.3 (CH_3), 28.2 (CH_2), 35.8 (CH_2), 48.2 (CH), 51.2 (C), 63.6 (C), 67.6 (CH_2), 225.7 (C); HRMS (EI+) calcd for $C_{12}H_{20}OS$ 212.1234, found 212.1239. **22**: IR (CCl_4) 1770, 1684, 1278, 1176, 1114 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.03 (s, 1H), 1.15 (s, 3H), 1.18 (t, 3H, J = 6.8 Hz), 1.19 (s, 3H), 1.68−2.01 (m, 5H), 2.34 (m, 1H), 3.53 (qd, 2H, J = 7.2, 2.4 Hz), 3.73 (dd, 2H, J = 15.6, 10.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.1 (CH_3), 24.4 (CH_2), 26.2 (CH_3), 28.3 (CH_3), 30.4 (CH_2), 39.7 (CH_2), 46.8 (CH), 58.3 (C), 67.0 (CH_2), 70.3 (C), 71.2 (CH_2), 277.3 (C); HRMS (EI+) calcd for $C_{12}H_{20}OS$ 212.1234, found 212.1238.

Product of Solvolysis of 16a-OTr in Ethanol. A solution of **16a-OTr** (0.303 g, 0.88 mmol) in 0.050 M 2,6-lutidine in ethanol (22.0 mL) was kept at 25.0 °C for 40.6 h (17 half-lives). After most of the ethanol had been removed with a rotary evaporator, the residue was dissolved in ether and the ether solution washed with water, cold 10% HCl, and saturated aqueous NaCl, and dried ($MgSO_4$). Evaporation of the ether afforded a red liquid, which on MPLC [SiO_2, hexane, hexane−ether (99:1, 97:3)] afforded **23** (0.028 g) as a colorless liquid, a mixture (0.077 g) of **23** and **24** (1:4 in mol ratio, by ^{13}C NMR spectrum) as a pale red liquid, a mixture (0.019 g) of **23**, **24**, **25**, and **27** (2:1:1:1 in mol, by ^{13}C NMR spectrum) as a red liquid, **25** (0.020 g) as a pale yellow liquid, a mixture (0.027 g) of **26** and **16a-OH** (2:1 in mol, by ^{13}C NMR spectrum) as a red liquid, and **26** (0.005 g) as a red semisolid, in this sequence. **16a-OH** obtained here is interpreted to come from the starting **16a-OTr**, which had already contained a few percent of **16a-OH** on the basis of the ^{13}C NMR spectrum. **25** is assumed to have been formed during workup. **23**: IR (CCl_4) 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.11 (t, 3H, J = 6.8 Hz), 1.21 (s, 3H), 1.25 (s, 3H), 1.65−2.40 (m, 11H), 3.62 (1H, d, J = 9.3 Hz, q, J = 6.8 Hz), 3.68 (1H, d, J = 9.3 Hz, q, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.2 (CH_3), 25.7 (CH_2), 27.7 (CH_3), 30.9 (CH_3), 31.7 (CH_2), 31.8 (CH_2), 32.0 (CH), 36.7 (CH_2), 41.1 (C), 50.9 (CH_2), 51.5 (C), 67.6 (CH_2), 91.1 (C); HRMS (EI+) calcd for $C_{13}H_{22}OS$ 226.1391, found 226.1386. **24**: IR (CCl_4) 2595, 2362, 1125, 1080, 1055 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.19 (t, 6H, J = 6.8 Hz), 1.20 (s, 6H), 1.50−2.20 (m, 9H), 2.17 (s, 1H), 2.48 (m, 2H), 3.68 (2H, d, J = 10.0 Hz, q, J = 6.8 Hz), 3.84 (2H, d, J = 9.6 Hz, q, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.3 (CH_3), 27.7 (CH_2), 28.1 (CH), 29.7 (CH_3), 35.0 (CH_2), 43.0 (C), 48.5 (CH_2), 57.5 (C), 59.9 (CH_2), 106.0 (C); HRMS (FAB+) calcd for $C_{15}H_{28}O_2S$ 272.1810, found 272.1815. **25**: IR (CCl_4) 2579, 2358, 1694 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.27 (s, 6H), 1.55−2.29 (m, 11H), 2.71 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.2 (CH_2), 28.4 (CH), 31.3 (CH_3), 33.7 (CH_2), 45.3 (CH_2), 45.5 (C), 57.6 (C), 214.6 (C); HRMS (EI+) calcd for $C_{11}H_{18}OS$ 198.1078, found 198.1070. **26**: ^1H NMR ($CDCl_3$, 400 MHz) δ 1.15 (t, J = 7.1 Hz), 1.41 (s, 6H), 1.42−2.29 (m, 11H), 3.32 (q, 2H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 15.7 (CH_2), 25.0 (CH_2), 29.1 (CH), 32.4 (CH_2), 35.8 (CH_3), 48.4 (CH_2), 52.4 (C), 57.9 (CH_2), 90.5 (C), 270.7 (C); HRMS (EI+) calcd for $C_{13}H_{22}OS$ 226.1391, found 226.1394. **27**: ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 15.3 (CH_3), 24.7 (CH_2), 28.5 (CH), 32.1 (CH_2), 36.5 (CH_3), 47.8 (CH_2), 52.6 (C), 65.8 (CH_2), 96.7 (C), 260.5 (C).

3,3-Dimethyl-2-oxobicyclo[3.2.2]non-1-yl Triflate (17a-OTf). Following the procedure described for the preparation of **15a-OTf**, treatment of **17a-OH** (0.166 g, 0.91 mmol) with triflic anhydride (0.309 g, 1.09 mmol) and pyridine (0.151 g, 1.91 mmol) in CH_2Cl_2 (7.4 mL) at 0 °C for 23 h followed by usual workup at 0 °C afforded 0.208 g of brown crystals. Recrystallization from hexane gave **17a-OTf** (0.083 g, 29%) as pale yellow crystals: mp 94.0−95.0 °C (dec); IR (CCl_4) 1722, 1414, 1208, 1148 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.33 (s, 6H), 1.70−1.89 (m, 4H), 1.90−2.29 (m, 4H), 2.22−2.46 (m, 3H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 24.8 (CH_2), 27.9 (CH), 28.6 (CH_2), 31.0 (CH_3), 43.9 (C), 44.5 (CH_2), 101.8 (C), 118.2 (q, CF_3, J = 319 Hz), 209.1 (C). Anal. Calcd for $C_{12}H_{17}F_3O_4S$: C, 45.85; H, 5.45. Found: C, 45.70; H, 5.60.

Kinetic Methods. The preparation of solvents and kinetic studies followed the methods described previously.[15]

Computational Studies. Ab initio molecular orbital calculations were performed using the Gaussian 94 at the 6-31G* level.[22] Initial STO-3G and 3-21G optimizations were employed to obtain starting structures for the 6-31G* optimization. All structures were characterized as minima by frequency calculation (no imaginary frequencies).

Acknowledgment. Computation time was provided by the Supercomputer Laboratory, Institute for Chemical Research, Kyoto University.

Supporting Information Available: ^{13}C NMR spectra for **15a-OTf**, **16a-OTr**, **20**, **21**, **22**, **23**, **24**, **25**, **26** and 3,3-dimethylbicyclo[3.2.2]nonane (11 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.

JO9719564

(30) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.