Foiled Conjugation in α-Oximino Carbocations

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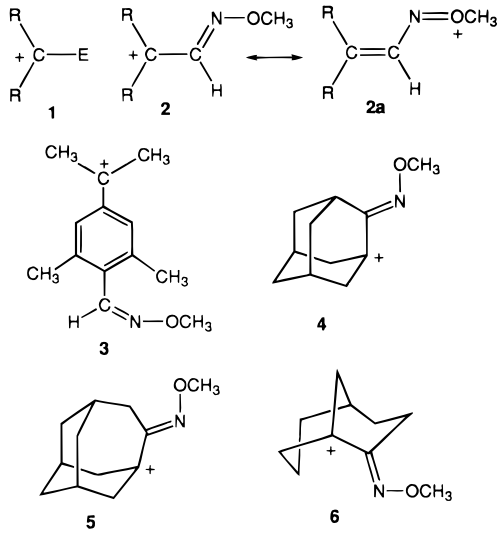
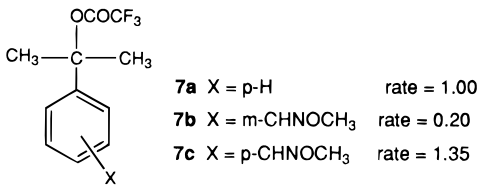
The 4-$CHNOCH_3$ group is a cation-stabilizing group when placed in the para-position of a cumyl cation. The effect of this group on cumyl cations when flanked by adjacent methyl groups has now been determined. Solvolysis rates of 3,5-$(CH_3)_2$-4-$(CHNOCH_3)$cumyl trifluoroacetates are somewhat slower than that of 3,5-dimethylcumyl trifluoroacetate. This is attributed to steric inhibition of the cation-stabilizing resonance effect of the *p*-oximino group. In a 1-adamantyl system, where an α-oximino group has been placed directly adjacent to a developing cationic center, solvolysis rates relative to 1-adamantyl mesylate are slowed by a factor of 10^8. This is attributed a cation-destabilizing inductive effect where geometric constraints prevent stabilizing orbital overlap of the cationic center with the adjacent α-oximino group. This cation-destabilizing effect fades in the homoadamantyl and the bicyclo[3.3.1]nonyl systems, where rate-retarding effects are 1.6×10^4 and 1.5×10^2, respectively. The behavior of geometrically constrained α-oximino cations parallels that of analogously constrained allylic cations. Computational studies at the HF/6-31G* level indicate that twisting the α-oximino group out of planarity with a tertiary cationic center into a perpendicular arrangement decreases stabilization by 21 kcal/mol. These studies suggest that conjugative interactions, and not ground state destabilization, are the most important factors in controlling rates of formation of α-oximino cations from mesylates and trifluoroacetates.

Carbocations **1** substituted with formal electron-withdrawing groups can often be generated with surprising ease.[1] This is illustrated by the α-oximino cations of general structure **2**, which form quite readily under solvolytic conditions.[2,3] Rate comparisons suggest that the α-$CHNOCH_3$ group is substantially more cation stabilizing than α-H and even more stabilizing than α-CH_3. This cation-stabilizing effect by the inductively electron-withdrawing α-$CHNOCH_3$ group was attributed to a conjugative effect as represented by **2a**. This effect was supported by *ab initio* molecular orbital calculations, which reveal extensive charge delocalization in cations such as **2**. In order to better understand the nature of α-oximino stabilization of cations, we have now studied the cations **3**−**6**, where geometric constraints prevent complete overlap of the cationic center with the conjugating C═N bond. Reported here are the results of these studies.



Results and Discussion

One of the classic methods for evaluating the electronic characteristics of a substituent is measurement of the Hammett−Brown σ^+ constant.[4] The *m*-$CHNOCH_3$ group ($\sigma^+ = 0.15$) slows the solvolysis rate of trifluoroacetate **7b** by a factor of 5 relative to the unsubstituted system **7a**.[2] This is indicative of a moderate electron-withdrawing electronic effect which destabilizes the meta-substituted cumyl cation intermediate. By way of contrast, the para-substituted analog **7c** actually solvolyzes 1.35 times *faster* than the unsubstituted cumyl trifluoroacetate **7a**.



We have proposed that a cation-stabilizing resonance interaction offsets the destabilizing inductive effect. To further support this contention, the 3,5-dimethyl-substituted systems **9** and **10** have been prepared and solvolysis rates have been compared to the "unsubstituted" analog **8**. Rates of ethanolysis (Table 1) of these oxime derivatives are depressed relative to **8**. This is attributed to inhibition of the potential cation-stabilizing conjugative

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(1) Creary, X. *Chem. Rev.* **1991**, *91*, 1625.

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

(3) For examples of α-oximino cations under nonsolvolytic conditions, see: (a) Shatzmiller, S.; Lidor, R.; Shalom, E.; Bahar, E.; *J. Chem. Soc., Chem. Commun.* **1984**, 795. (b) Shatzmiller, S.; Shalom, E.; Bahar, E. *J. Chem. Soc., Chem. Commun.* **1984**, 1522. (c) Hansen, J. F.; Strong, S. A. *J. Heterocycl. Chem.* **1977**, *14*, 1289. (d) Hansen, J. F.; Kim, Y. I.; McCrotty, S. E.; Strong, S. A.; Zimmer, D. E. *Ibid.* **1980**, *17*, 475.

(4) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979.

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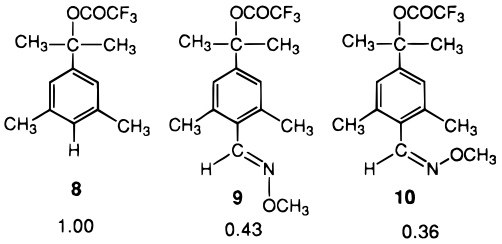
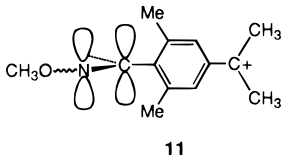
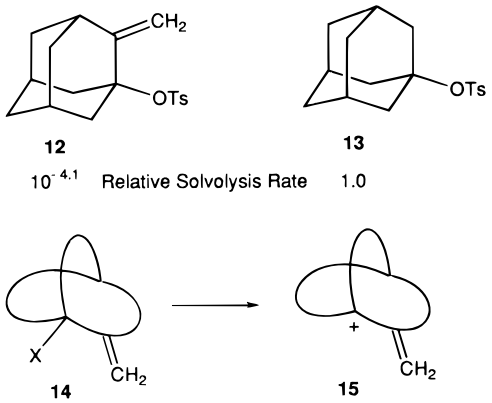
interaction by the *o*-dimethyl substituents; i.e., the cationic intermediate prefers the unconjugated conformation as in **11**.





The effect of rotating a conjugating group out of conjugation with a cationic center was first investigated in the classic study of Martin[5] and Schleyer.[6] In the tosylate **12**, the inductive effect of the double bond results in a retardation of solvolytic rate relative to the model substrate **13**. This approach has been greatly extended by Takeuchi, who carried out solvolytic studies on a series of substrates of general structure **14**.[7] Depending on ring size, interaction of the developing cationic center of **15** with the double bond led to varying degrees of rate enhancement or rate retardation.

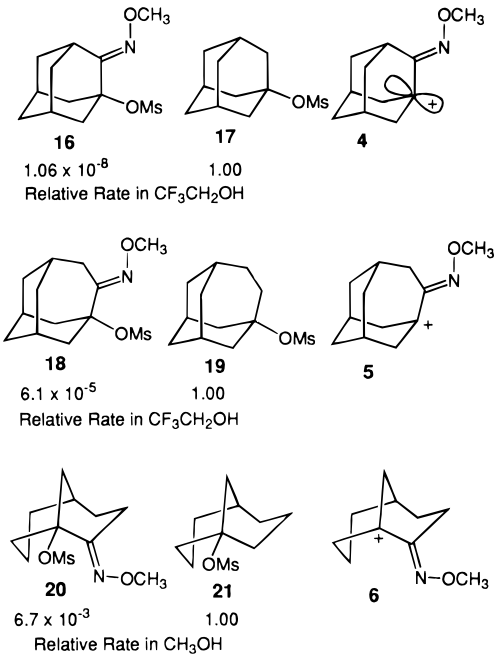


We have used a similar approach in the study of α-oximino cations. The mesylates **16**, **18**, and **20** were prepared and solvolyzed in various solvents. In all cases the simple substitution products were the only products formed. Rate data are given in Table 1, along with data for the model systems **17**, **19**, and **21** lacking the oxime group. Comparison of the rate of **16** with that of 1-adamantyl mesylate, **17**, shows that the oxime group slows the rate by a factor of 10^8. This enormous rate retardation is attributed to an inductive effect of the oximine group which is directly attached to the developing cationic center of **4** but cannot interact in a conjugative fashion with that orthogonal cationic center. By way of contrast, our previous study[2] has shown that the

Table 1. Solvolysis Rates of Substrates in Various Solvents at 25 °C

substrate	solvent	k^a (s^{-1})
8	EtOH	9.82×10^{-4}
9	EtOH	4.25×10^{-4}
10	EtOH	3.56×10^{-4}
16	CF_3CH_2OH	3.16×10^{-9} [b]
		2.92×10^{-6} (80.0 °C)
		2.14×10^{-5} (100.0 °C)
17	CF_3CH_2OH	2.99×10^{-1}
18	CF_3CH_2OH	3.46×10^{-3}
19	CF_3CH_2OH	5.66×10^{1} [c]
20	CH_3OH	1.82×10^{-5}
21	CH_3OH	2.71×10^{-3}
25	CF_3CH_2OH	5.58×10^{-5} [d]
26	CF_3CH_2OH	7.91×10^{-6} [d]
32	CF_3CH_2OH	3.74×10^{-3}

[a] Maximum standard deviations in duplicate runs were ±1.5% for rates determined by the ^{1}H NMR method of ref 23. See the Experimental Section for the kinetic method. [b] Extrapolated from data at higher temperature. [c] Estimated from the rate of the corresponding trifluoroacetate (2.01×10^{-4} s^{-1}) and a mesylate/trifluoroacetate rate ratio of 2.81×10^5. See ref 8. [d] Reference 23.

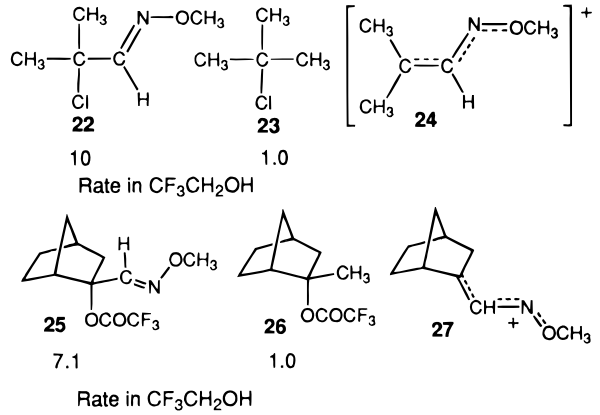


oxime group, when allowed to interact with a cationic center in a conjugative fashion, is even more cation stabilizing than an α-CH_3 group. Hence, studies on **22** and **25** show that cations **24** and **27** form under solvolytic conditions even faster than the *tert*-butyl and 2-methylnorbornyl cations, respectively. Cations **24** and **27** are highly delocalized intermediates, with charge dispersed onto nitrogen and oxygen atoms. The cation-destabilizing effect of the electron-withdrawing oxime group is completely offset in these two α-oximino carbocations.

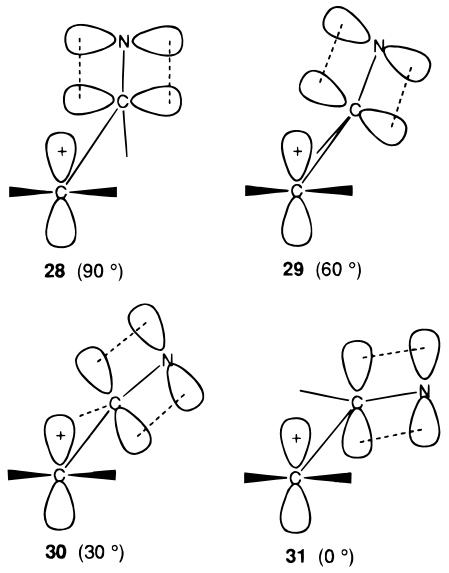
The effect of the oxime group on the solvolysis of mesylate **18** is also to retard the rate relative to that of the model substrate **19**.[8] However, the rate-retarding effect of $10^{-4.2}$ is not as large as in mesylate **16**. These data suggest that the cationic center of **5** is beginning to exhibit a small amount of conjugation with the C=N

(5) Ree, B. R.; Martin, J. C. *J. Am. Chem. Soc.* **1970**, *92*, 1660.
(6) Buss, V.; Gleiter, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 3927.
(7) Takeuchi, K.; Kitagawa, T.; Ohga, Y.; Toshida, M.; Akiyama, F.; Tsugeno, A. *J. Org. Chem.* **1992**, *57*, 280.

(8) The rate of mesylate **19** was estimated from that of the corresponding trifluoroacetate derivative. A mesylate/trifluoroacetate rate ratio of 2.81×10^5 was measured for the 1-adamantyl system **17**, and this value was used to calculate the rate of **19**.



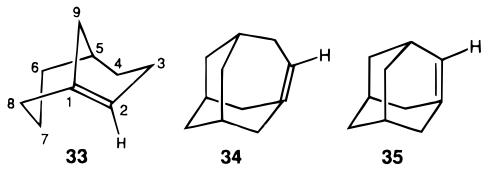
bond. In the cation **4**, the C═N bond is held rigidly orthogonal to the cationic center, as depicted in **28**. However, the additional methylene group in **5** renders this cation less rigid, and hence, the double bond in **5** can achieve partial overlap with the cationic center, as depicted in **29**.



The solvolytic rate data for the bicyclic mesylate **20** indicate that the importance of conjugation has again increased, but not to the extent that the inductive effect of the oxime group is entirely negated. The rate-retarding effect of the oxime group is now only a factor of 149 and suggests that there is significant overlap of the cationic center of **6** with the C═N bond as depicted in **30**. However, the overlap in cation **6** is still not equivalent to that in the unconstrained cations **24** and **27**, where conjugative stabilization is maximal (as depicted in **31**).

The kinetic behavior of mesylates **16**, **18**, and **20** and trifluoroacetate **25** can be compared to that of the allylic derivatives **12**, **14a**, and **14b** (studied by Martin,[5] Schleyer,[6] and Takeuchi[7]) and the allylic trifluoroacetate **32**. As in the case of α-oximino cations, the rate-retarding effect of a perpendicular allylic double bond is maximal and decreases as the double bond is brought into conjugation. Thus, a plot (Figure 1) of solvolytic rate data for the oxime derivatives **16**, **18**, **20**, and **25** vs analogous data for the allylic systems **12**, **14a**, **14b**, and **32** is linear. This linear free energy relationship supports the idea that geometric inhibition of resonance stabilization operates in a parallel fashion in both allylic and α-oximino constrained carbocations.

The rate data on mesylate **16** imply a substantial interaction of the C═N bond with the adjacent developing cationic center in **6**. The bridgehead alkene **33** can be considered as a model for the interaction of adjacent sp^2-hybridized centers in the bicyclo[3.3.1]nonyl system. This strained alkene **33** can be isolated and is thermally stable at room temperature.[9] The interaction of the sp^2-hybridized centers in **33** is therefore quite good despite the bridgehead nature of this alkene. This is in contrast to the alkene **34** which readily dimerizes at room temperature[10] and the alkene **35** which dimerizes when warmed above 70 K.[11] It is therefore reasonable to expect a substantial interaction of the cationic center of **6** with the adjacent unsaturated center.



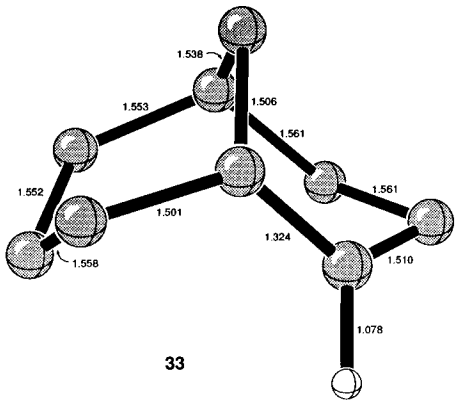
Computational Studies. In order to gain further insights into the nature of cations **4**−**6** and the ability of the oxime group to interact with cationic centers, *ab initio* molecular orbital computational studies[12] were carried out on these cations, as well as on the hydrocarbons **33**−**35**. These alkenes present a useful model for the interaction of a bridgehead sp^2-hybridized carbons with an adjacent sp^2-hybridized carbon. The HF/6-31G*-optimized geometries of **33**−**35** are shown with all but the olefinic hydrogens removed for clarity. These geometries all indicate a significant interaction between the two sp^2-hybridized centers. In the case of alkene **33**, the C_1C_3H plane is only rotated 15° with respect to the $C_2C_8C_9$ plane (as shown in the Newman projection **33a**). In other words, the p-bond in this alkene is distorted by a relatively small amount. This computational result is in line with the observed kinetic stability of this alkene.[10] The alkene **34** is more twisted than **33**, with the analogous interplanar angle being 30° in **34**. Finally, the alkene **35** is the most twisted of the three, with a 49° interplanar angle. However, the fact that the angle is not 90°, and the C═C bond length (1.339 Å) is significantly shorter than a normal C−C bond, suggests that

(9) (a) Wiseman, J. R.; Pletcher, W. A. *J. Am. Chem. Soc.* **1970**, *92*, 956. (b) Marshall, J. A.; Faubl, H. *J. Am. Chem. Soc.* **1970**, *92*, 948.

(10) Martella, D. J.; Jones, M., Jr.; Schleyer, P. v. R.; Maier, W. F. *J. Am. Chem. Soc.* **1979**, *101*, 7634.

(11) (a) Conlin, R. T.; Miller, R. D.; Michl, J. *J. Am. Chem. Soc.* **1979**, *101*, 7637. (b) Michl, J.; Radziszewski, G. J.; Downing, J. W. *Pure Appl. Chem.* **1983**, *55*, 315.

(12) 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.; 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 B.3, Gaussian, Inc., Pittsburgh, PA, 1995.



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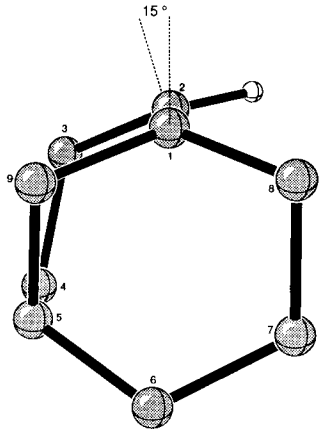
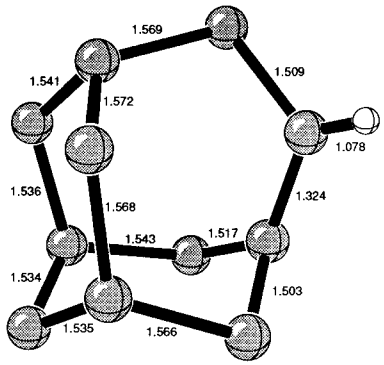


33a

there still remains a significant interaction between the sp^2-hybridized centers of **35**.



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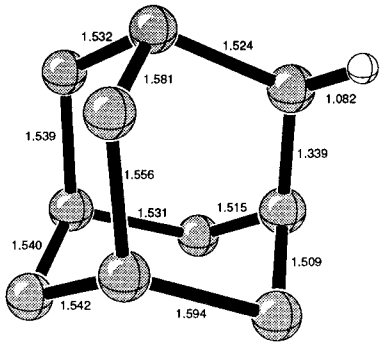
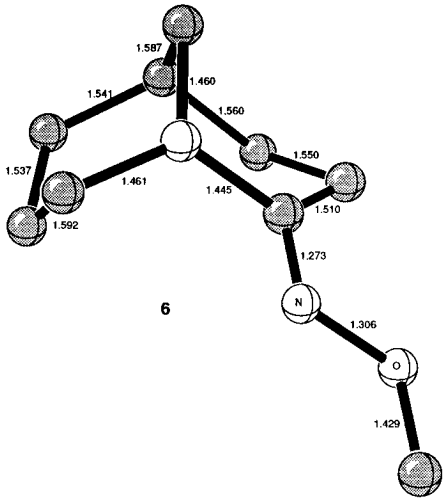


35

The HF/6-31G* geometries of the cations **4**−**6** are also shown, and they parallel those of alkenes **33**−**35**. The C═N bonds of the cations are always twisted out of conjugation with the cationic center, and the amount of twisting is always larger than the analogous alkene twist. In cation **6** the C_1C_3N plane is rotated 31° with respect



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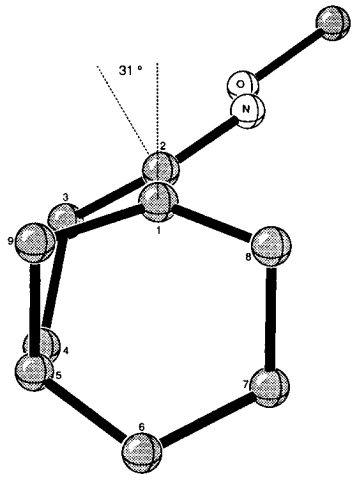
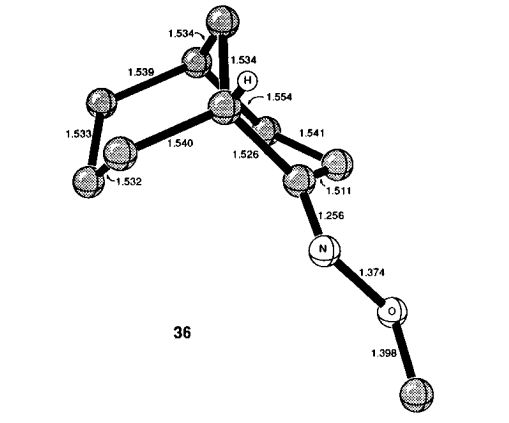
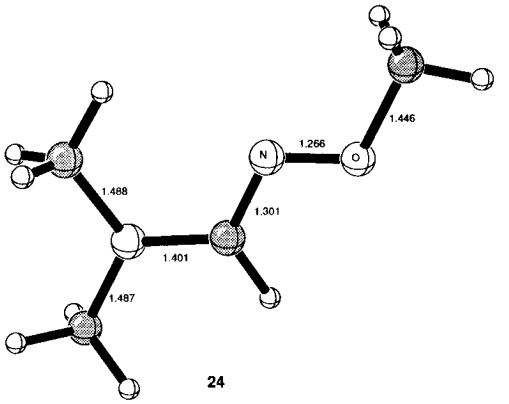


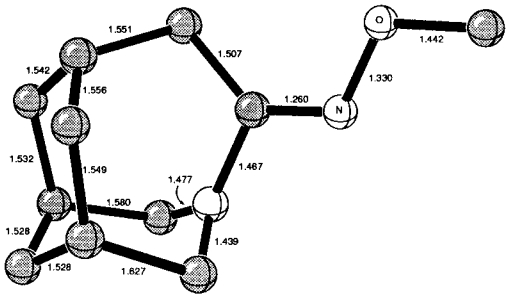
6a

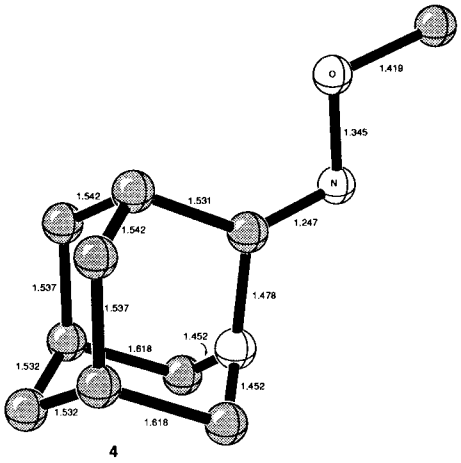
to the $C_2C_8C_9$ plane. This is indicative of a substantial interaction of the cationic center C_1 with the C═N bond, but this interaction is not of the same magnitude as in the alkene **33** (where the interplanar angle is only 15°). A comparison of bond lengths of cation **6** with those of the neutral oxime **36** and the planar cation **24** supports the idea of partial conjugation. The 1.445 Å bond length of the C1C2 bond of cation **6** is between that of the single bond (1.526 Å) of **36** and the conjugated C1C2 bond (1.401 Å) of the planar cation **24**. The CN and NO bonds of cation **6** are also intermediate between those of the oxime **36** and cation **24**. These structural features are all in line with the idea of repressed (but not completely eliminated) C═N conjugation in the cation **6**.

The calculated geometry of cation **5** is in line with a further decrease in the importance of conjugation of the cationic center with the oxime functionality relative to the less constrained cation **6**. The cationic center of **5** is rotated 60° with respect to the oxime group. The substituted 1-adamantyl cation **4** is now completely unconjugated with the oxime group as revealed by the calculated geometry (90° rotation of the cationic center relative to the C═N bond). The β-C−C bonds of the ring are significantly lengthened (1.618 Å), which suggests









that cation **4** receives stabilization mainly by the type of interaction represented in **4a** (or **4b**). The unimportance of C=N conjugation is manifested by the $^{+}$C−C, C=N, and N−O bond lengths which retain alternating single, double, and single bond character, respectively.

The effect of twisting the cationic center out of conjugation with the C=N bond was also examined using the isodesmic reactions 1 and 2 (Scheme 1).[13] Results of these calculations at the HF/6-31G* level are shown in Table 2. While formation of the planar conjugated cation **24** is favored by 7.3 kcal/mol, the reaction becomes increasingly unfavorable as the oxime group is twisted out of conjugation with the cationic center. In the case of the perpendicular α-oximino cation **4**, the destabilization relative to the 1-adamantyl cation amounts to 14.4 kcal/mol. The overall effect of rotating the oxime group from the completely aligned arrangement in **24** to the perpendicular arrangement in **4** is therefore a 21.7 kcal/mol decrease in stabilization.

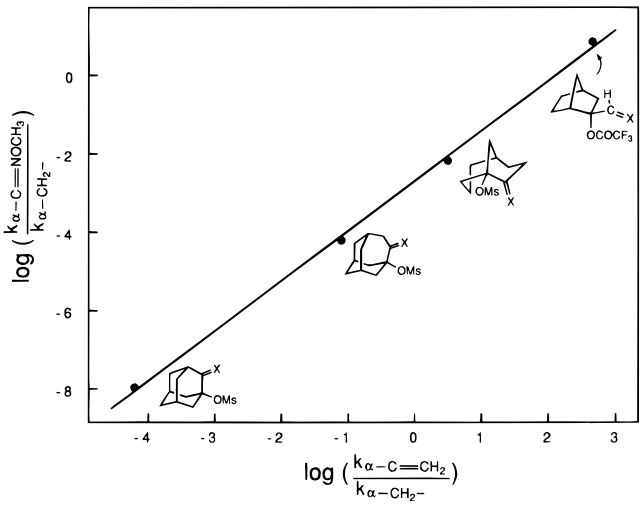
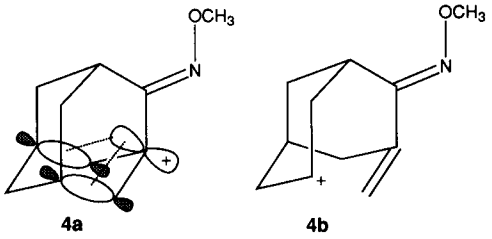


Figure 1. Plot of log k_{rel} for solvolysis of α-$CNOCH_3$ systems vs log k_{rel} for solvolysis of α-$C{=}CH_2$ systems.



Finally, the effect of twisting the stabilizing oxime group out of conjugation with the cationic center can be evaluated theoretically in the cation **24**. Energies of geometrically constrained cations were calculated as a function of the NCCC dihedral angle. Energies of these cations were calculated by rotating the oximino group out of conjugation with the cationic center by 10° increments. These rotated cations were further constrained to prevent closure to cyclized cations by fixing the NCC angle at 116.9° (the same as the optimized angle in the planar cation **24**). The results of these calculations are displayed in Figure 2. The effect of this rotation is to destabilize the cation by 20.9 kcal/mol as the dihedral angle is increased to 90°. This value of 20.9 kcal/mol is consistent with the net destabilization (21.7 kcal/mol) calculated from the isodesmic reactions in Table 2.

Conclusions. The cation-stabilizing effect of a 4-$CHNOCH_3$ group on a cumyl cation can be negated by placement of methyl groups in the 3- and 5-positions on the phenyl ring. This is attributed to steric inhibition of

(13) An alternative approach to evaluating this effect is the calculation of hydride affinities. Relative hydride affinities of cations **4**, **5**, **6**, and **24** are 0, 1.8, 6.6, and 15.2 kcal/mol, respectively, at the HF/6-31G* level.

Scheme 1

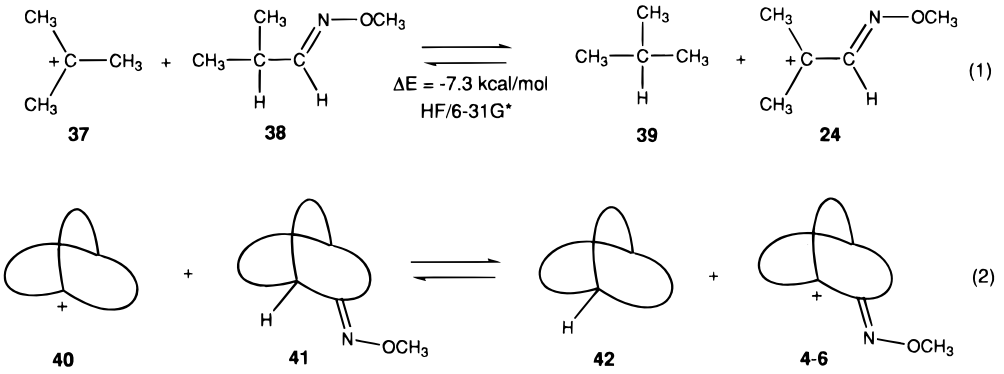


Table 2. Calculated Values (HF/6-31G*) of Δ*E* (kcal/mol) for the Isodesmic Reactions 1 and 2

system	α-oximino cation	Δ*E* (kcal/mol)
adamantyl	**4**	14.4
homoadamantyl	**5**	11.9
bicyclo[3.3.1]nonyl	**6**	4.3
tert-butyl	**24**	−7.3

the cation-stabilizing resonance effect of the oximino group. The oximino group now becomes a weak cation-destabilizing group. The α-oximino group can also become a relatively strong cation-destabilizing group when geometric constraints prevent interaction with an adjacent cationic center. Hence, placement of an oximino group adjacent to the cationic center in a 1-adamantyl system slows the rate of cation formation by a factor of 10^8. This cation-destabilizing effect fades as geometric constraints are lessened in the homoadamantyl and the bicyclo[3.3.1]nonyl systems. The behavior of these geometrically constrained α-oximino cations parallels that of analogously constrained allylic cations. Computational studies at the HF/6-31G* level indicate that twisting the α-oximino group out of planarity with a tertiary cationic center into a perpendicular arrangement decreases stabilization by 21 kcal/mol.

These studies also address the possibility of ground state destabilization of the substrate as the origin of the rapid rates of solvolyses of α-oximino systems. Kirmse and Houk[14] have pointed out that there can be a destabilizing geminal interaction between an electron-withdrawing α-substituent and a leaving group such as triflate or mesylate. This can raise the ground state energy of the substrate, thereby leading to greater than expected solvolysis rates. Our present findings (that rates are so highly dependent on geometry of the incipient cation in a fashion that parallels allyl systems) suggest that ground state destabilization is not the most important factor in the formation of α-oximino cations. The major rate-controlling factor is α-oximino conjugation.

Experimental Section

Preparation of Trifluoroacetate 8. This trifluoroacetate was prepared by reaction of 3,5-dimethylcumyl alcohol in ether with trifluoroacetic anhydride and 2,6-lutidine using the previously described procedure.[15] This trifluoroacetate was stored in ether solution since removal of the ether solvent led to rapid decomposition. NMR spectra were recorded in ether solution after concentration of the solvent used in the work-up: ^{1}H NMR of trifluoroacetate **8** (Et_2O) δ 6.96 (br s, 2 H), 6.89 (br s, 1 H), 2.27, (s, 6 H), 1.82 (s, 6 H); ^{13}C NMR of trifluoroacetate **8** (Et_2O) δ 143.67, 138.13, 129.57, 122.28, 87.53, 27.97, 21.02.

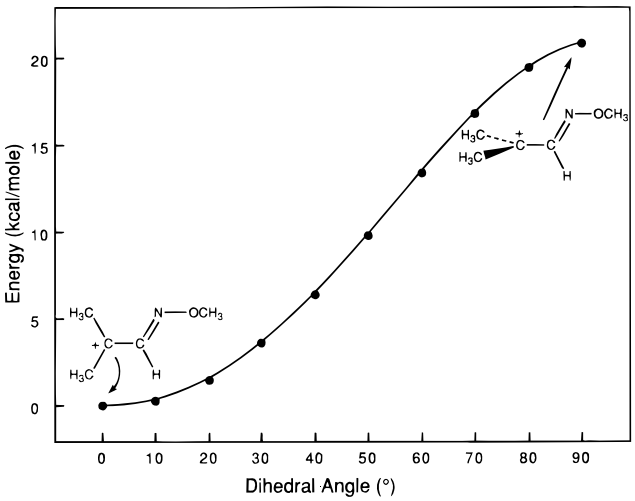
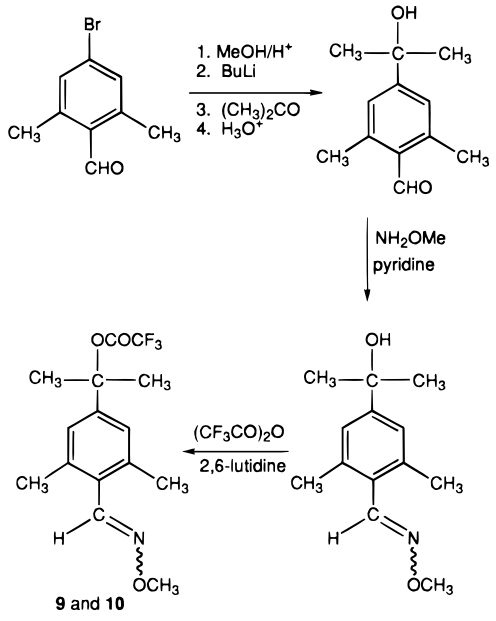


Figure 2. Calculated energies (HF/6-31G*) as the cationic center is rotated out of conjugation with α-$CHNOCH_3$.

Preparation of Trifluoroacetates 9 and 10. These trifluoroacetates were prepared by the sequence shown below. A solution of 6.14 g of 2,6-dimethyl-4-bromobenzaldehyde[16] and



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4.59 g of trimethylorthoformate in 60 mL of methanol was stirred, and 270 mg of *p*-toluenesulfonic acid was added. The mixture was stirred at room temperature for 20 h and 93 mg of sodium methoxide was then added. The excess methanol was removed using a rotary evaporator and the residue taken up into ether and washed with a small amount of water. The ether extract was then washed with saturated NaCl solution and dried over $MgSO_4$. The solvent was removed using a rotary evaporator, and the residue was distilled to give 7.19 g (96% yield) of 2,6-dimethyl-4-bromobenzaldehyde dimethyl acetal: bp 98−100 °C (3 mm); ^{1}H NMR ($CDCl_3$) δ 7.146 (s, 2 H), 5.430 (s, 1 H), 3.390 (s, 6 H), 2.414 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 139.23, 133.30, 131.63, 121.86, 104.33, 55.27, 20.13.

Conversion of 2,6-dimethyl-4-bromobenzaldehyde dimethyl acetal to 2,6-dimethyl-4-(2-hydroxy-2-propyl)benzaldehyde was completely analogous to the previously described procedure:[17] ^{1}H NMR ($CDCl_3$) δ 10.565 (s, 1 H), 7.204 (s, 2 H), 2.614 (s, 6 H), 2.20 (br s, 1 H), 1.577 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 193.12, 154.21, 141.41, 130.85, 125.83, 72.33, 31.54, 20.78.

Conversion of 2,6-dimethyl-4-(2-hydroxy-2-propyl)benzaldehyde to the *O*-methyl oxime derivative was completely analogous to the previously described procedure.[2] The *O*-methyl oxime consisted of an 88:12 mixture of *anti* and *syn* isomers. These were separated by silica gel chromatography (elution with increasing amounts of ether in hexanes). The *anti*-oxime eluted first followed by the *syn*-oxime. *anti*-Oxime: ^{1}H NMR ($CDCl_3$) δ 8.336 (s, 1 H), 7.154 (s, 2 H), 3.966 (s, 3 H), 2.407 (s, 6 H), 1.92 (br s, 1 H), 1.547 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 149.56, 147.88, 137.49, 127.71, 124.54, 72.26, 61.85, 31.62, 21.44. Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.54; H, 8.66. Found: C, 70.60; H, 8.49.

syn-Oxime: ^{1}H NMR ($CDCl_3$) δ 7.480 (s, 1 H), 7.163 (s, 2 H), 3.895 (s, 3 H), 2.257 (s, 6 H), 1.96 (br s, 1 H), 1.554 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 149.49, 147.17, 135.59, 129.57, 123.38, 72.28, 61.97, 31.64, 20.14; exact mass (FAB) calcd for $C_{13}H_{20}NO_2$ 222.1497, found 222.1472.

Conversion of these oximes to the corresponding trifluoroacetates **9** and **10** was completely analogous to the previously described procedure.[2] These trifluoroacetates were stored in ether solution. Removal of the ether solvent leads to eventual decomposition at room temperature. $CDCl_3$ solutions of **9** and **10** also decompose, and spectra were recorded by concentrating the ether solutions used in the workup of **9** and **10**. Trifluoroacetate **9**: ^{1}H NMR (Et_2O) δ 8.31 (s, 1 H), 7.05 (s, 2 H), 3.90 (s, 3 H), 2.39 (s, 6 H), 1.83 (s, 6 H); ^{13}C NMR (Et_2O) δ 147.08, 143.74, 138.10, 129.52, 124.62, 87.17, 61.40, 27.72, 21.24. Trifluoroacetate **10**: ^{1}H NMR (Et_2O) δ 7.43 (s, 1 H), 7.02 (s, 2 H), 3.80 (s, 3 H), 2.21, (s, 6 H), 1.84 (s, 6 H); ^{13}C NMR (Et_2O) δ 146.17, 136.18, 123.18, 116.45, 87.28, 61.30, 27.86, 19.74.

Preparation of 1-Hydroxy-2-adamantanone *O*-Methyl Oxime. A solution of 158 mg of 1-hydroxy-2-adamantanone[18] in 6 mL of pyridine was stirred as 95 mg of methoxylamine hydrochloride was added. After 20 h at room temperature, the mixture was taken up into ether and the mixture was washed with water. The organic extract was then washed with dilute HCl solution and saturated NaCl solution and then dried over $MgSO_4$. The solvent was then removed using a rotary evaporator leaving 157 mg (85% yield) of 1-hydroxy-2-adamantanone *O*-methyl oxime, mp 47−48 °C, which solidified on standing: ^{1}H NMR ($CDCl_3$) δ 3.851 (s, 3 H), 3.554, (br s, 1 H), 2.187 (br s, 2 H), 2.03 (d, J = 11.7 Hz, 2 H), 1.90−1.65 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 164.47, 70.03, 61.55, 40.98, 36.82, 34.86, 30.41, 29.60. Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78. Found: C, 67.80; H, 8.86.

Preparation of Mesylate 16. Mesylate **16** was prepared by peracid oxidation of the sulfinate ester of 1-hydroxy-2-adamantanone *O*-methyl oxime. A solution of 92 mg of 1-hydroxy-2-adamantanone *O*-methyl oxime and 95 mg of Et_3N in 4 mL of CH_2Cl_2 was cooled to −15 °C, and 70 mg of CH_3SOCl was added. The mixture was then warmed to room temperature for 10 min and then taken up into ether. The mixture was then washed with cold water, dilute HCl solution, and saturated NaCl solution. The organic extract was then dried over $MgSO_4$, and the solvent was removed using a rotary evaporator.

The crude sulfinate ester was dissolved in 6 mL of CH_2Cl_2 and then cooled to 0 °C. *m*-Chloroperbenzoic acid (100 mg of 85%) was then added, and the mixture was then stirred at room temperature for 1.5 h. The mixture was then taken up into ether, and the ether solution was washed with a combined solution of $NaI-Na_2S_2O_3-KOH$. The ether solution was then dried over $MgSO_4$, and the solvents were removed using a rotary evaporator leaving 102 mg (80% yield) of mesylate **16**: mp 57−59 °C; ^{1}H NMR ($CDCl_3$) δ 3.884 (s, 3 H), 3.726 (br s, 1 H), 3.226 (s, 3 H), 2.45 and 2.39 (AB quartet, J = 11.7 Hz, 4 H), 2.28 (m, 2 H), 1.77 (br s, 6 H); ^{13}C NMR ($CDCl_3$) δ 160.08, 87.46, 61.59, 44.92, 40.78, 36.14, 34.69, 31.78, 30.37. Anal. Calcd for $C_{12}H_{19}NO_4S$: C, 52.72; H, 7.01. Found: C, 53.00; H, 7.07.

Preparation of 1-Adamantyl Mesylate, 17. Mesylate **17** was prepared by oxidation of the sulfinate ester of 1-adamantanol using a procedure completely analogous to the preparation of mesylate **16**. Thus, reaction of 370 mg of 1-adamantanol with 359 mg of CH_3SOCl and 492 mg of Et_3N gave 547 mg of the crude sulfinate ester. Oxidation of this ester with 570 mg of 85% *m*-chloroperbenzoic acid gave 549 mg of a mixture consisting of 87% 1-adamantyl mesylate, **17**, and 13% 1-adamantanol. Attempted chromatographic purification on silica gel led to decomposition of **17**. Recrystallization fron hexanes did not improve the purity: ^{1}H NMR of **17** ($CDCl_3$) δ 2.995 (s, 3 H), 2.238 (br s, 9 H), 1.667 (br s, 6 H); ^{13}C NMR ($CDCl_3$) δ 91.85, 42.96, 41.03, 35.61, 31.52. The mixture containing 87% of mesylate **17** was used for kinetic studies.

Preparation of Mesylate 18. 1-Hydroxyhomoadamantan-2-one *O*-methyl oxime was prepared by reaction of 1-hydroxyhomoadamantan-2-one[19] with methoxylamine hydrochloride in pyridine using a procedure completely analogous to the preparation of 1-hydroxy-2-adamantanone *O*-methyl oxime described above. This oxime derivative was converted to mesylate **18**, mp 138−139 °C (90% yield), using a procedure completely analogous to the preparation of mesylate **16** (by initial conversion to the methyl sulfinate ester followed by *m*-chloroperbenzoic acid oxidation to the sulfonate ester): ^{1}H NMR ($CDCl_3$) δ 3.907, (s, 3 H), 3.209 (s, 3 H), 2.649 (d, J = 4.2 Hz, 2 H), 2.40 (d, J = 13.8 Hz, 2 H), 2.33 (m, 2 H), 2.19 (m, 1 H), 2.13 (br s, 2 H), 1.90 (m, 2 H), 1.67 (m, 1 H), 1.58 (m, 1 H), 1.510 (d, J = 13.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 160.64, 92.29, 61.67, 42.99, 40.78, 36.10, 34.31, 32.81, 27.78, 27.52. Anal. Calcd for $C_{13}H_{21}NO_4S$: C, 54.33; H, 7.37. Found: C, 54.32; H, 7.53.

Preparation of 1-Homoadamantyl Trifluoroacetate. A solution of 100 mg of 1-hydroxyhomoadamantane[20] and 110 mg of 2,6-lutidine in 8 mL of ether was cooled to 0 °C, and 177 mg of trifluoroacetic anhydride was added dropwise. The mixture was stirred for 5 min at 0 °C, and water was then added. The ether phase was washed with dilute HCl solution, $NaHCO_3$ solution, and saturated NaCl solution and then dried over $MgSO_4$. Solvent removal using a rotary evaporator left 155 mg of 1-homoadamantyl trifluoroacetate as a clear oil which was used for kinetic studies without further purification: ^{1}H NMR ($CDCl_3$) δ 2.34 (m, 4 H), 2.10 (m, 5 H), 1.88 (m, 2 H), 1.77 (m, 2 H), 1.55 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 155.98 (q, J = 41 Hz), 114.51 (q, J = 287 Hz), 92.76, 43.01, 37.13, 36.21, 35.14, 30.74, 28.96, 27.46; exact mass calcd for $C_{13}H_{17}F_3O_2$ 262.1181, found 262.1135.

Preparation of Mesylate 20. 1-Hydroxybicyclo[3.3.1]-nonan-2-one *O*-methyl oxime was prepared from 1-hydroxybicyclo[3.3.1]nonan-2-one[21] and methoxylamine hydrochloride in pyridine using a procedure completely analogous to the

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preparation of 1-hydroxy-2-adamantanone *O*-methyl oxime described above. Conversion to the mesylate **20**, mp 65−66 °C (80% yield), was completely analogous to the preparations of **16** and **18** (via the sulfinate ester): ^{1}H NMR ($CDCl_3$) δ 3.901 (s, 3 H), 3.099 (s, 3 H), 2.86 (m, 1 H), 2.726 (m, 1 H), 2.58 (m, 1 H), 2.37 (m, 1 H), 2.15 (m, 1 H), 1.98 (m, 2 H), 1.84 (m, 1 H), 1.71 (m, 1 H), 1.50 (m, 3 H), 1.38 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 159.26, 88.27, 61.84, 41.17, 39.82, 37.89, 31.20, 29.16, 24.63, 22.38, 20.24. Anal. Calcd for $C_{11}H_{19}NO_4S$: C, 50.56; H, 7.33. Found: C, 50.57; H, 7.36.

Preparation of Mesylate 21. This mesylate was prepared as previously described.[7]

Preparation of Trifluoroacetate 32. This trifluoroacetate was prepared (90% yield) by reaction of *exo*-2-vinyl-*endo*-2-norborneol in ether with trifluoroacetic anhydride and 2,6-lutidine using the previously described procedure.[15] The neat trifluoroacetate **32** decomposed on prolonged standing at room temperature: ^{1}H NMR ($CDCl_3$) δ 6.064 (d of d, J = 17.4, 10.9 Hz, 1 H), 5.253 (d, J = 17.4 Hz, 1 H), 5.235 (d, J = 10.9 Hz, 1 H), 2.70 (m, 1 H), 2.33 (m, 1 H), 2.13 (d of d of d, J = 14.1, 4.8, 2.7 Hz, 1 H), 1.74−1.42 (m, 5 H), 1.40−1.26 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 156.33 (q, J = 41.4 Hz), 138.95, 115.84, 114.56 (q, J = 286.8 Hz), 92.69, 45.87, 42.67, 37.10, 36.06, 28.55, 22.11l exact mass calcd for $C_{11}H_{13}F_3O_2$ 234.0868, found 234.0883.

Kinetics Procedures. Rates of reaction of the substrates described in this paper were determined by either UV spectroscopy or ^{1}H NMR spectroscopy. Rates of solvolyses of trifluoroacetates **8** (245 nm), **9** (275 nm), and **10** (272 nm) in ethanol were monitored by UV spectroscopy at the wavelengths given using previously described methods.[22] Rates of solvolyses of mesylate **17** (in trifluoroethanol containing 2.5 × 10^{-4} M 2,6-lutidine; 272 nm) and **21** (methanol containing 2.5 × 10^{-4} M 2,6-lutidine; 270 nm) were also monitored by UV spectroscopy. Rates of solvolyses of **16**, **18**, and **32** as well as 1-homoadamantyl trifluoroacetate (in trifluoroethanol containing 0.05 M 2,6-lutidine) and **20** (in methanol containing 0.05 M 2,6-lutidine) were monitored by ^{1}H NMR spectroscopy using the recently described method based on measurement of the chemical shift of the methyl groups of the buffering base 2,6-lutidine.[23]

Computational Studies. *Ab initio* molecular orbital calculations were performed using either the Gaussian 92 or Gaussian 94 series of programs.[12] All structures were characterized as true minima via frequency calculations which showed no negative frequencies.

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Supporting Information Available: A table of HF/6-31G* energies of optimized structures (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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