

Carbocations in the β -Lactam and β -Thiolactam Series

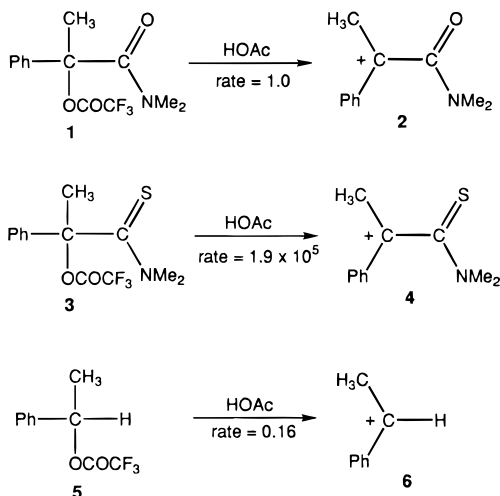
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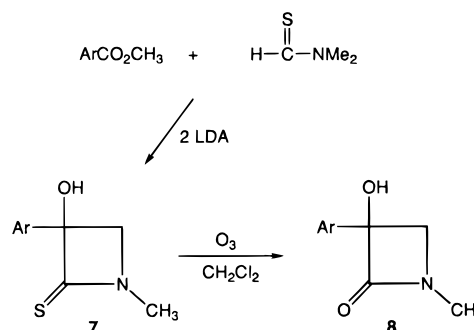
Abstract: Solvolyses of mesylate and trifluoroacetate derivatives of 3-aryl-3-hydroxy-substituted β -thiolactams and β -lactams proceeds to give substitution products in a process which exhibits a large solvent effect as well as large substituent effects. A common ion rate suppression as well as largely racemic products from solvolyses of an optically active substrate all point to the involvement of β -lactam derived carbocationic intermediates. Unlike acyclic analogs, these cations are captured by solvent to give simple substitution products with no competing proton loss. Computational studies suggest that proton loss from these β -lactam derived cationic intermediates is an unfavorable process due to antiaromatic character in the potential elimination product. Computational studies also suggest that C=S and C=O conjugative stabilization of these cations is minimal or non-existent. Substituent effect studies show that the major mode by which these cations derive stabilization is by aryl group charge delocalization. Azide ion in DMSO or DMF reacts with *N*-methyl-3-mesyloxy-3-phenylazetidine-2-thione via a bimolecular substitution mechanism to give the corresponding 3-azido substitution product, which can be converted to *N*-methyl-3-amino-3-phenylazetidine-2-thione.

Solvolytic reactions that proceed via α -carbonyl and α -thiocarbonyl cations have continued to hold our interest.¹ This interest grows out of the high reactivity of substrates such as trifluoroacetates **1** and **3** relative to the α -H analog **5**. Our previous studies² have shown that solvolysis reactions of **1** and **3** in acetic acid give exclusively elimination products. These reactions proceed via the electronegatively substituted cations **2** and **4** at rates that exceed that of the trifluoroacetate **5** despite the electron-withdrawing amide and thioamide groups attached directly to the cationic centers of the intermediates **2** and **4**. Conjugation of the developing cationic center with the C=X bond has been proposed to lead to the relatively high reactivity of substrates such as **1** and **3**.



Recently we have developed a novel and simple synthesis of β -thiolactams **7** and β -lactams **8** substituted in the 3-position with the hydroxyl group.³ We were therefore interested in

developing methods for conversion of the hydroxyl groups of **7** and **8** to other functionality. Incorporation of a leaving group into the 3-position of these substrates should potentially permit the generation of cationic intermediates and hence the introduction of other functionality. These systems should also allow one to compare the behavior α -carbonyl and α -thiocarbonyl cations in β -lactam systems. Reported here are the results of these studies.



Results and Discussion

(a) Solvent Effect Studies. The alcohols **7** and **8** were converted to mesylate derivatives or to other derivatives with appropriate leaving group reactivities. In the case of the *p*-methoxyphenyl derivative, the trifluoroacetate or chloro leaving groups have convenient reactivity, while in the case of the 3,5-bis(trifluoromethyl)phenyl derivative, the triflate leaving group was appropriate. The appropriate derivatives **9** and **10** were reacted in a variety of solvents and the simple substitution products were formed exclusively. Rate data are given in Table 1. Solvent effect studies on **9a** (Ar = Ph) and **10a** (Ar = Ph) reveal large increases in rates with increasing solvent ionizing power. Rates increase by factors of 1.3×10^4 and 4.9×10^3 respectively as solvent is changed from the relatively poorly ionizing solvent ethanol to the highly ionizing hexafluoroisopropyl alcohol solvent.⁴ Winstein–Grunwald *m* values⁵ are 0.89

[®] Abstract published in *Advance ACS Abstracts*, November 15, 1996.

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

(2) (a) Creary, X.; Hatoum, H. N.; Barton, A.; Aldridge, T. E. *J. Org. Chem.* **1992**, 57, 1887. (b) Creary, X.; Aldridge, T. *J. Org. Chem.* **1988**, 53, 3888.

(3) Creary, X.; Zhu, C. *J. Am. Chem. Soc.* **1996**, 117, 5859.

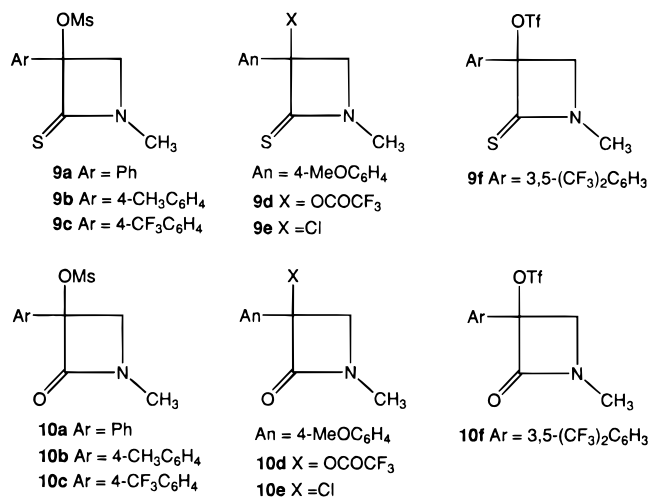
(4) Bentley, T. W.; Bowen, C. T.; Morten, D. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, 103, 5466 and references therein.

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

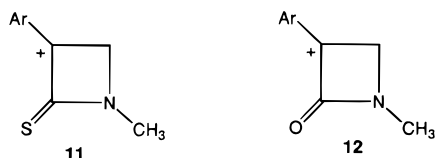
substrate	solvent	k (s ⁻¹) ^a	$k_{\text{C=S}}/k_{\text{C=O}}$
9a (<i>p</i> -H)	CH ₃ CH ₂ OH	1.49×10^{-5}	10.1
	HOAc	2.57×10^{-5}	
	CH ₃ OH	8.55×10^{-5}	
	CF ₃ CH ₂ OH	4.84×10^{-3}	
	HCO ₂ H	3.82×10^{-2}	
	(CF ₃) ₂ CHOH	1.95×10^{-1}	
9b (<i>p</i> -CH ₃)	HOAc	1.88×10^{-3}	6.47
9c (<i>p</i> -CF ₃)	CF ₃ CH ₂ OH	8.17×10^{-7} ^b	26.8
9d (<i>p</i> -OCH ₃)	HOAc	1.18×10^{-4}	3.76
	HOAc ^c	7.37×10^{-5}	
	HOAc ^d	4.48×10^{-5}	
	HOAc ^e	3.91×10^{-5}	
9f (3,5-(CF ₃) ₂)	CH ₃ CH ₂ OH	2.11×10^{-2}	6.94
	HOAc	1.23×10^{-3}	
	CH ₃ OH	8.52×10^{-2}	
	CF ₃ CH ₂ OH	3.36×10^{-2}	
	HCO ₂ H	8.91×10^{-1}	
	CH ₃ CH ₂ OH	2.43×10^{-6}	
10a (<i>p</i> -H)	HOAc	2.55×10^{-6}	
	CH ₃ OH	1.51×10^{-5}	
	CF ₃ CH ₂ OH	2.44×10^{-4}	
	HCO ₂ H	5.86×10^{-3}	
	(CF ₃) ₂ CHOH	1.19×10^{-2}	
	CF ₃ CH ₂ OH	9.68×10^{-2}	
10b (<i>p</i> -CH ₃)	CF ₃ CH ₂ OH	3.04×10^{-8} ^b	
10c (<i>p</i> -CF ₃)	HOAc	3.15×10^{-5}	
10d (<i>p</i> -OCH ₃)	CH ₃ CH ₂ OH	5.23×10^{-3}	
10f (3,5-(CF ₃) ₂)	HOAc	1.77×10^{-4}	
	CH ₃ OH	2.10×10^{-2}	
	CF ₃ CH ₂ OH	1.03×10^{-3}	
	HOAc	3.26×10^{-5}	
1-phenylcyclobutyl trifluoroacetate	HOAc	3.26×10^{-5}	

^a Maximum standard deviations in duplicate runs were $\pm 1.5\%$. See the Experimental Section for the kinetic method. ^b Extrapolated from data at higher temperature. ^c 0.025 M CF₃CO₂Na added. ^d 0.050 M CF₃CO₂Na added. ^e 0.075 M CF₃CO₂Na added.

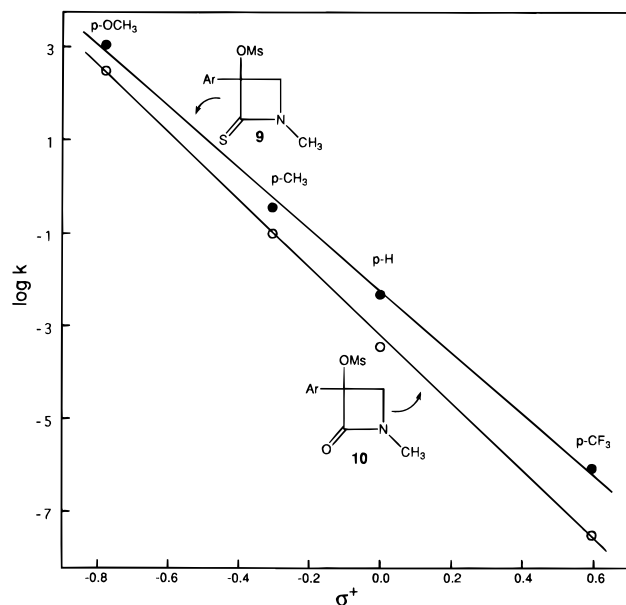
and 0.83 respectively for **9a** (Ar = Ph) and **10a** (Ar = Ph).



These data are consistent with the involvement of cationic intermediates **11** and **12** under solvolytic conditions.



(5) ρ values based on *t*-BuCl were used in this correlation. See: (a) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846. (b) Winstein, S.; Grunwald, E.; Jones, H. W. *J. Am. Chem. Soc.* **1951**, *73*, 2700.

**Figure 1.** A plot of $\log k$ for solvolyses of mesylates **9** and triflates **10** in trifluoroethanol at 25.0 °C vs σ^+ .

The effect of solvent on the rate behavior of triflates **9f** and **10f** contrasts with that of mesylates **9a** and **10a**. While solvolyses of these triflates gives simple substitution products in all solvents, rate data are not in line with a limiting k_{C} process in all solvents. Solvolysis rates are actually faster in methanol than in trifluoroethanol despite the fact that trifluoroethanol is much more highly ionizing. This points to the importance of solvent nucleophilicity in solvolyses of **9f** and **10f**. At the same time, solvent ionizing power is also of importance as evidenced by the HCO₂H/CH₃CO₂H rate ratio. The rate of **9f** is 726 times faster in the more highly ionizing solvent formic acid than in acetic acid, despite the fact that these solvents have comparable nucleophilicities. This behavior is reminiscent of the behavior of 2-propyl tosylate, where both solvent nucleophilicity and solvent ionizing power are important in determining rate.⁶ The behavior of **9f** and **10f** can therefore best be characterized as “borderline”,⁷ i.e., there is evidence for significant solvent involvement in a transition state with developing positive charge at the benzylic carbon atom.

(b) Substituent Effect Studies. A substituent effect study on **9** and **10** shows large increases in rate as the aromatic ring is substituted with increasing electron-donating groups. Mesylate derivatives containing the *p*-anisyl group were too reactive to allow preparation. Therefore rates of the *p*-methoxy substituted mesylates were estimated from those of the corresponding trifluoroacetates **9d** and **10d**. The Hammett–Brown ρ^+ values⁸ in trifluoroethanol (Figure 1) for **9** and **10** are -6.6 and -7.3 , respectively. These ρ^+ values are consistent with cationic intermediates **11** and **12** that have a large demand for stabilization by the aryl substituent. The slightly larger ρ^+ value for β -lactams **10** is indicative of a slightly larger demand for aryl group stabilization in the developing cationic intermediates **12**.

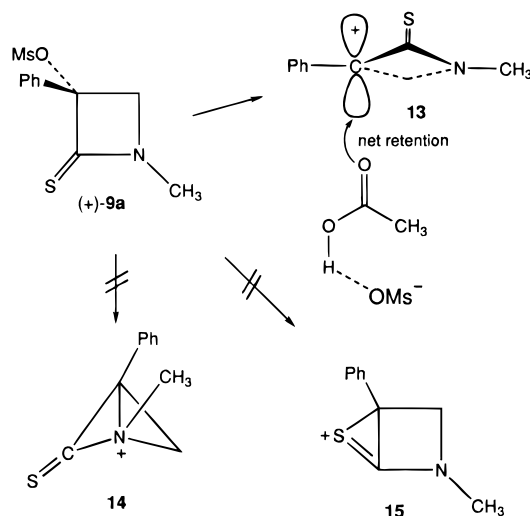
(6) (a) Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7658. (b) Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667.

(7) The detailed mechanism for reaction of so called “borderline” substrates has been a controversial area. See: (a) Allen, A. D.; Kanagasabapathy, V. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1985**, *107*, 4513. (b) Bentley, T. W.; Schleyer, P. v. R. *Adv. Phys. Org. Chem.* **1977**, *14*, 1. (c) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1383. (d) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161. (e) Snee, R. A. *Acc. Chem. Res.* **1973**, *6*, 46.

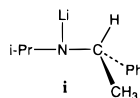
(8) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979.

The relatively large ρ^+ value for the cyclic system **9** contrasts with the behavior of the acyclic system **3** (and substituted phenyl analogs). These acyclic thioamide systems give a nonlinear Hammett plot as well as relatively small substituent effects. For example the rate of the *p*-methoxy analog of **3** is only 118 times faster than that of the unsubstituted system. By way of contrast, the estimated rate increase due to *p*-methoxy substitution in **9** is a factor of 2.34×10^5 . The reasons for small aryl group substituent effects in the acyclic systems have been discussed and are due in part to extensive transition state charge delocalization utilizing the thiocarbonyl group. This decreases the demand for aryl group stabilization of the acyclic carbocationic intermediates.

(c) Chiral Systems. The optically active mesylate (+)-**9a** can be prepared from the corresponding optically active alcohol.⁹ Solvolysis in 80% aqueous acetone leads to an alcohol product **7** (Ar = Ph) which is 98% racemized but also has a 2% ee of the *inverted* alcohol. A control experiment showed that racemization of optically active alcohol does not occur under the solvolysis conditions. This type of solvolysis which proceeds to form a slight excess of the inverted product is often observed.¹⁰ It has been rationalized in terms of a cationic intermediate which has a slight preference for capture of solvent from the rear of the departing leaving group due to a slightly greater shielding of one side of the ion-pair intermediate by the departed mesylate ion. By way of contrast, solvolysis in acetic acid leads to an acetate product which has a 3% ee of the *retained* acetate (which is optically stable under the reaction conditions). This study is also consistent with the involvement of a cationic intermediate. The 3% net retention is believed to be a result of acetate being delivered preferentially to the same side of the cationic intermediate from which the leaving group departed due to hydrogen bonding of acetic acid with the departing mesylate leaving group (as in **13**). Such retentive processes have been observed in the past.¹¹ Cyclized intermediates such as **14** and **15** are probably not involved since they are



(9) This alcohol was prepared by using the chiral base **i** to promote the cyclization of PhCOCSNMe_2 . Full details will be reported elsewhere.



(10) For typical examples for our laboratory, see: (a) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151. (b) Creary, X.; Geiger, C. C.; Hilton, K. *J. Am. Chem. Soc.* **1983**, *105*, 2851. (c) Creary, X.; McDonald, S. R.; Eggers, M. *Tetrahedron Lett.* **1985**, *26*, 811. For earlier examples, see: (d) Doering, W. v. E.; Zeiss, H. H. *J. Am. Chem. Soc.* **1953**, *75*, 4733. (e) Winstein, S.; Morse, B. K. *J. Am. Chem. Soc.* **1952**, *74*, 1133. (f) Steinman, J.; Hammett, L. P. *J. Am. Chem. Soc.* **1937**, *59*, 2536.

Table 2. Azide Products **16** in Solvolyses of Substrates **9** and **10** in 0.2 M NaN_3 in MeOH

substrate	% azide	$k_{\text{azide}}/k_{\text{MeOH}}$ (M^{-1})
9a (<i>p</i> -H)	15	0.86
9b (<i>p</i> -CH ₃)	12	0.69
9c (<i>p</i> -CF ₃)	55 ^a	6.12
9e (<i>p</i> -OCH ₃)	80	20.0
10a (<i>p</i> -H)	32	2.35
10b (<i>p</i> -CH ₃)	39	3.23
10e (<i>p</i> -OCH ₃)	72	12.7

^a After 37% reaction.

too strained to be formed via k_A processes (which could also lead in principle to net retention).

(d) Common Ion Effect. When 0.04 M trifluoroacetate (**9d**, Ar = 4-MeOC₆H₄) is solvolyzed in acetic acid containing 0.05 M sodium acetate, the slope of a first order plot decreases with time. Closer examination shows that **9d** (Ar = 4-MeOC₆H₄) in acetic acid is subject to a common ion rate suppression. As shown in Table 1, addition of external trifluoroacetate ion slows the rate appreciably. The observation of a common ion effect is classic evidence for the involvement of a relatively stable cationic intermediate **11** (Ar = 4-MeOC₆H₄).¹² This cationic intermediate survives past the ion-pair stage to the free ion stage, where it can react with solvent or return to starting trifluoroacetate by reaction with externally added trifluoroacetate ion. A quantitative treatment^{12b} of rate data for **9d** in acetic acid using a kinetic model involving competitive solvent capture and trifluoroacetate ion capture of the cationic intermediate gives $k_{\text{trifluoroacetate}}/(k_{\text{HOAc}}[\text{HOAc}]) = 28 \text{ M}^{-1}$.

(e) Azide Ion Studies. Azide ion is recognized as an effective carbocation trap. Low concentrations of azide ion can often compete with solvent (HOS) to form the corresponding azido derivatives in solvolysis reactions. Since the rate of reaction of azide ion with cations is extremely rapid (close to diffusion controlled),¹³ values of $k_{\text{azide}}/k_{\text{HOS}}$ also allow an estimation of carbocation lifetimes in solution.¹⁴ Additionally, many β -lactams of therapeutic value have a nitrogen atom in the 3-position.¹⁵ Methanolysis reactions of **9** and **10** in the presence of azide ion¹⁶ were therefore carried out in an attempt to form the 3-azido derivatives **16**. Values of $k_{\text{azide}}/k_{\text{MeOH}}$ were determined from the relative amounts of **16** and the methanol displacement product **17** and are listed in Table 2. Reaction of

(11) (a) Okamoto, K.; Kinoshita, T.; Oshida, T.; Yamamoto, T.; Ito, Y.; Dohi, M. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1617. (b) Kinoshita, T.; Komatsu, K.; Ikai, K.; Kashimura, T.; Tanikawa, S.; Hatanaka, A.; Okamoto, K. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1875. (c) Goering, H. L.; Hopf, H. *J. Am. Chem. Soc.* **1971**, *93*, 1224. (d) Bone, J. A.; Pritt, J. R.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1447. For further leading references see: Okamoto, K. In *Advances in Carbocation Chemistry*; Creary, X., Ed.; JAI Press Inc.: Greenwich, CT 1989; Vol. 1, p 171.

(12) (a) March, J. *Advanced Organic Chemistry*, 3rd ed.; John Wiley and Sons, Inc.: New York, 1985; p 261. (b) Hine, J. *Physical Organic Chemistry*, 2nd ed.; McGraw-Hill Book Co., Inc.: New York, 1962; pp 131–5.

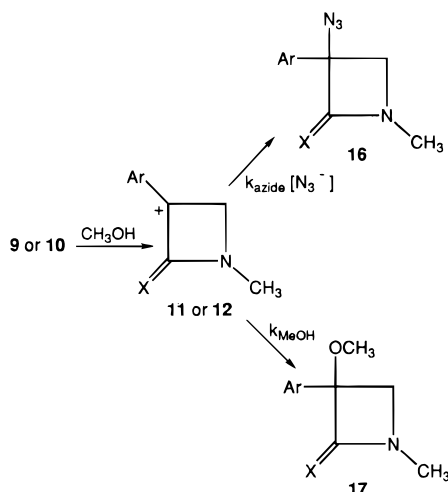
(13) (a) McClelland, R. A.; Banait, N.; Steenken, S. *J. Am. Chem. Soc.* **1986**, *108*, 7023. (b) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1361.

(14) (a) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 4689. (b) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1383. See also: (c) Richard, J. P. In *Advances in Carbocation Chemistry*; Creary, X., Ed.; JAI Press Inc.: Greenwich, CT, 1989; Vol. 1, p 121.

(15) For leading references see: Guzzo, P. R.; Miller, M. J. In *Advances in Nitrogen Heterocycles*; Moody, C. J., Ed.; JAI Press Inc.: Greenwich, CT, 1996; Vol. 2, p 1.

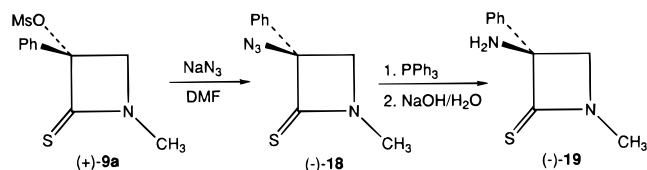
(16) Control experiments show that the rate of methanolysis of **9b** (with ionic strength maintained at 0.1 M with sodium triflate) is independent of the amount of added sodium azide.

the chloride **9e** (Ar = 4-MeOC₆H₄) in methanol containing 0.2 M NaN₃ gave 80% of the azido derivative **16** (Ar = 4-MeOC₆H₄; X = S), along with 20% of the solvent substitution product. This corresponds to a $k_{\text{azide}}/k_{\text{MeOH}}$ ratio of 20 M⁻¹, i.e., azide ion is a relatively effective trap of the cationic intermediate. However, in the case of **9a** (Ar = Ph; X = S) and **9b** (Ar = 4-CH₃C₆H₄; X = S) the azide products are only 15% and 12%, respectively, of the total with the major product being the methanol capture product. The $k_{\text{azide}}/k_{\text{MeOH}}$ ratios of 0.86 and 0.69 M⁻¹ show that azide ion is relatively ineffective at capture of these two cationic intermediates.



The amount of azide product increases again (to 55%) in the case of the more electron-withdrawing p-CF₃-substituted system **10d**. This type of behavior, where selectivity for azide ion decreases, passes through a minimum, and then increases as the substituent becomes more electron-withdrawing, has been observed before.¹⁴ It has been interpreted by Jencks and Richard as being due to a mechanistic change to the so called “enforced S_N2” mechanism.^{7d,14} The transition state for this process has positive charge development on the benzylic carbon, but there is no discrete cationic intermediate with a finite lifetime.

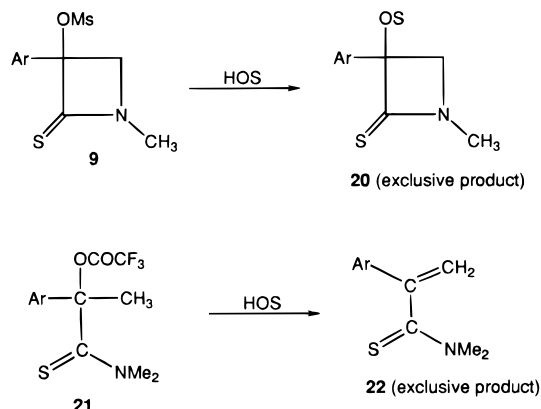
In view of the relatively low yields of azide adducts **16** produced in solvolysis reactions containing added sodium azide, attention was next turned to reaction of mesylates **9** and **10** with azide ion in polar aprotic solvents. The mesylate **9a** reacts with sodium azide in DMF at 70 °C to give a good yield of the azide **18**. This process proceeds with clean inversion, as revealed by examination of the optically active mesylate (+)-**9a**. Subsequent reaction of (–)-**18** with triphenylphosphine and hydrolysis of the intermediate iminophosphorane led to the optically active amine (–)-**19**.



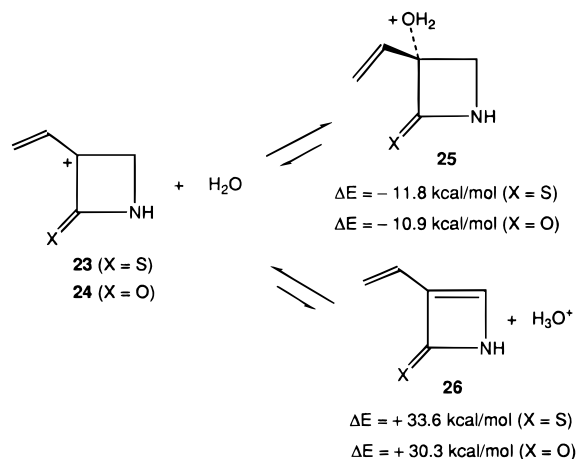
Reaction of the carbonyl analog **10a** with sodium azide in DMSO at 45 °C also proceeds in good yield to give the azido-substituted product in a second order process (first order in azide ion). These processes in DMF and DMSO proceed, in all likelihood, via an S_N2-type mechanism.

(f) Substitution vs Elimination. Computational Studies. The solvolytic behavior of **9** contrasts with that of the acyclic

analog **21** which gave exclusive elimination products **22**.² The formation of elimination product from α-thiocarbonyl cations is the usual fate of such cations which contain β-hydrogen atoms. Although α-carbonyl cations with β-hydrogens can give significant amounts of substitution products, the α-carbonyl cation **2** also gives exclusively the elimination product in acetic acid.¹⁷ We were therefore interested in the contrasting products derived from **9** and **21** (as well as their carbonyl analogs).



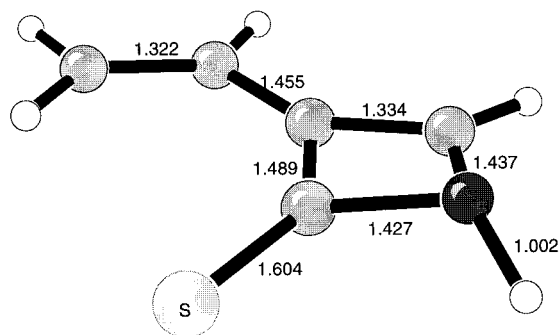
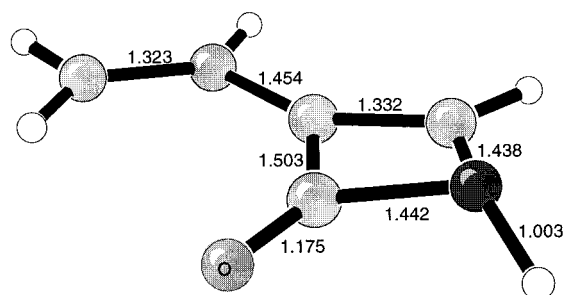
Ab initio computational studies¹⁸ have been used to gain insight into the lack of elimination products from **9** and **10**. The reactions of cations **23** and **24** (where the vinyl group has been used as a phenyl group analog) with water has been analyzed at the HF/6–31G** level. In both cases, reaction with water as a nucleophile to give **25** is an exothermic process with Δ*E* being –11.8 and –10.9 kcal/mol, respectively.



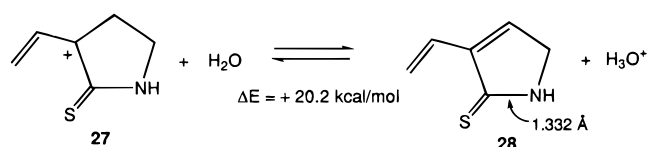
However, reaction with water as a base leading to the elimination product **26** is a highly endothermic process computationally. This study suggests that capture of cations **11** and **12** with nucleophilic solvents should be much more preferable than proton loss to form alkene products.

(17) Creary, X.; Casingsal, V. P.; Leahy, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 1734.

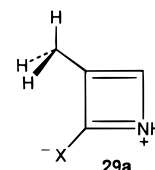
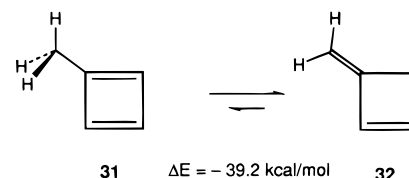
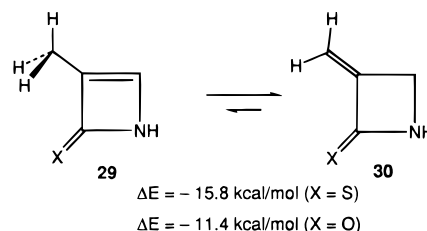
(18) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, 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.

**26** (X = S)**26** (X = O)

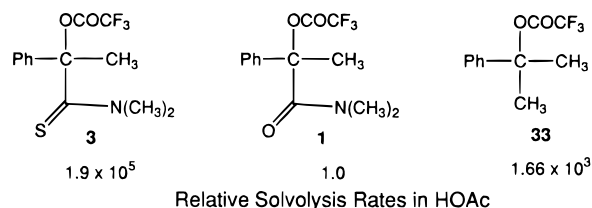
These computational results contrast with those on the next higher homologs **27** and **28**. Proton loss from **27** to water to give the alkene **28** is endothermic (+20.2 kcal/mol), but by a much smaller factor than for formation of **26** (+33.6 kcal/mol). Additionally, the alkene **28** exhibits a shortened C–N bond (1.332 Å) relative to **26**, indicative of a substantial amide resonance interaction in **28**. These results suggest that, relative to **28**, the alkenes **26** are subject to a destabilizing feature.



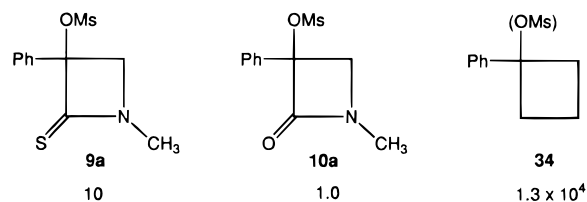
Insight into the highly endothermic reaction which forms **26** can also be gained by an additional computational study (HF/6-31G**). The endocyclic–exocyclic double bond preference in **29** and **30** has been evaluated and the endocyclic double bond in **27** is quite unfavorable ($\Delta E = -15.8$ and -11.4 kcal/mol) relative to the exocyclic double bond of **28**. These values are significant but smaller than that calculated for the methylcyclobutadiene–methylenecyclobutene systems **29** and **30**. The amides **29** (as well as amides **26**) are not planar molecules, i.e., the nitrogen atom is slightly removed from the plane defined by the three ring carbons. Additionally, the nitrogen is highly pyramidalized and the N4–C1 bonds of **29** are unusually long (1.428 and 1.444 Å, respectively) for thioamides and amides. These features all point to a lack of π -interaction of the nitrogen of **29** with the adjacent C=O or C=S bond. In valence bond terms, stabilization of **29** by amide resonance as in **29a** is minimal due to the antiaromatic character in forms represented by **29a**. This accounts for the highly endothermic deprotonation reactions of **23** and **24** with water. In terms of solvolysis reactions of **9** and **10**, cationic intermediates such as **11** and **12** do not undergo proton loss since the potential alkene products have low stability.



(g) Rate Comparisons. An analysis of rates of solvolyses of **9** and **10** is quite informative. Previous studies have shown that α -thiocarbonyl derivatives are much more reactive than α -carbonyl analogs under solvolytic conditions.² For example, the thioamide **3** is 1.9×10^5 times more reactive than the amide **1**. It is even more reactive than the tertiary analog, cumyl trifluoroacetate, **33**. By way of contrast, this present study shows that the β -thiolactam **9a** is *only* 10 times more reactive than the β -lactam **10a**. In fact, the entire series of β -thiolactams **9** are only slightly more reactive than the β -lactams **10** (Table 1). The mesylate **9a** is significantly less reactive than the tertiary analog **34** (estimated from the trifluoroacetate rate). The mesylate **9a** is even 1.7×10^3 times *less reactive* than the acyclic trifluoroacetate **3** in acetic acid. This result is even more striking in view of the fact that mesylates can be up to 10^5 times more reactive than the analogous trifluoroacetate derivative.¹⁹ These data point to cationic intermediates **11** and **12** which are not significantly stabilized by thiocarbonyl or carbonyl conjugation.



Relative Solvolysis Rates in HOAc



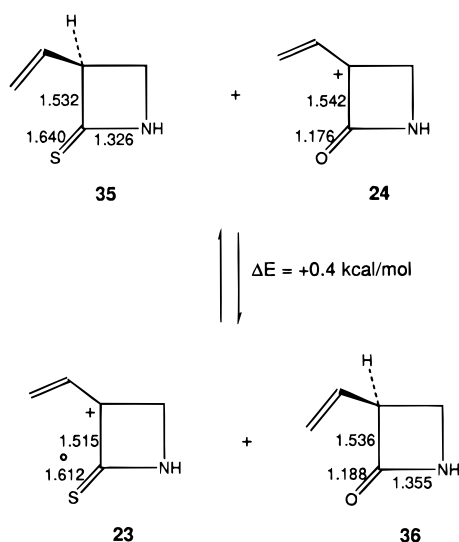
Relative Solvolysis Rates in HOAc

The relatively large ρ^+ value for the cyclic system **9** contrasts with the behavior of the acyclic system **3** (and substituted phenyl

(19) (a) Noyce, D. S.; Virgilio, J. A. *J. Org. Chem.* **1972**, *37*, 2643. For further examples of this large mesylate/trifluoroacetate rate ratio, see also: (b) Creary, X. *J. Org. Chem.* **1979**, *44*, 3938. (c) Creary, X.; Jiang, Z. *J. Org. Chem.* **1996**, *61*, 3482.

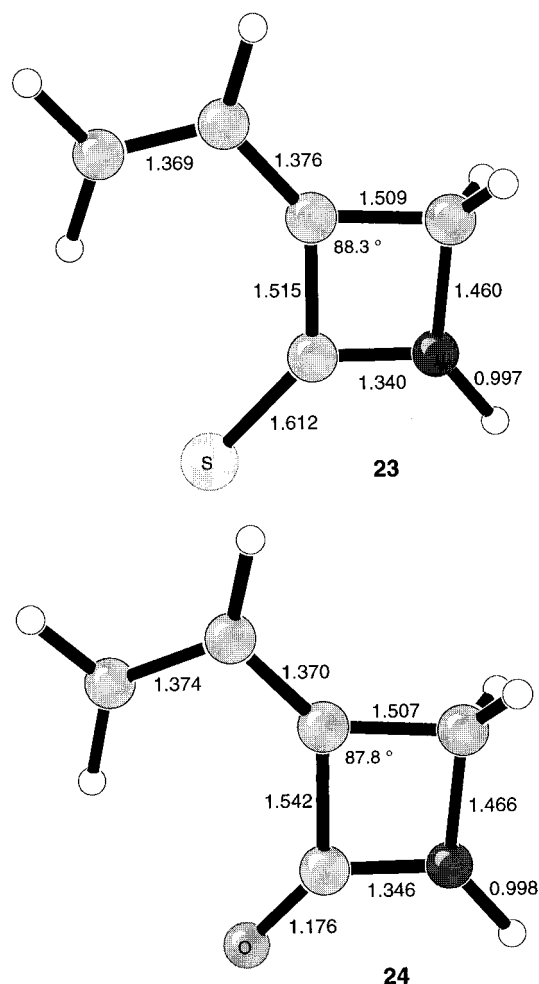
analog). These acyclic thioamide systems give a non-linear Hammett plot as well as relatively small substituent effects.^{2a} For example, the rate of the *p*-methoxy analog of **3** is only 118 times faster than that of the unsubstituted system. By way of contrast, the estimated rate increase due to *p*-methoxy substitution in **9** is a factor of 2.34×10^5 . The reasons for small aryl group substituent effects in the acyclic systems have been discussed^{2a} and are due in part to extensive transition state charge delocalization utilizing the thiocarbonyl group. This decreases the demand for aryl group stabilization of the acyclic carbocationic intermediates. The much larger substituent effects in **9** and **10** are indicative of cationic intermediates **11** and **12** devoid of thiocarbonyl or carbonyl conjugation.

(h) Computational Studies on Cationic Intermediates. In order to shed further light on the cationic intermediates **11** and **12**, the hydride transfer reaction of **24** with **35** has been evaluated computationally. This isodesmic reaction suggests that the α -thiocarbonyl cation **23** and the α -carbonyl cation **24** are comparable in stability. Previous computational studies have all suggested that α -thiocarbonyl cations are substantially stabilized relative to α -carbonyl analogs.²⁰ This has been attributed to extensive charge delocalization onto the sulfur atom of α -thiocarbonyl cations. However, the computational study on **23** and **24** is completely in line with our solvolytic rate study, which suggests that **11** and **12** are also comparable in stability.



Closer examination of bond lengths gives further insight. The C=S bond length is actually shorter in cation **23** (1.612 Å) than in the neutral molecule **35** (1.640 Å). The C-C bond length in **23** from the cationic center to the adjacent thiocarbonyl carbon atom (1.515 Å) is only slightly shorter than the analogous C-C bond in the neutral **35** (1.532 Å). These features point to only minimal stabilization of **23** due to thiocarbonyl conjugation. As suggested by bond lengths, the major stabilizing feature of cation **23** is allylic conjugation. Analogous bond length data for the α -carbonyl cation **24** and the neutral **36** suggests that cation **24** receives *no* stabilization from carbonyl conjugation. On the other hand, cation **24** is also extensively stabilized by allyl group conjugation and the extent of allyl stabilization is slightly greater than stabilization of the thiocarbonyl cation **23**. The comparable stabilities of **23** and **24** can therefore be attributed to offsetting factors. Thiocarbonyl conjugative stabilization of **23** is quite small and does not approach the magnitude that we have seen

in previous studies on α -thiocarbonyl cations. Carbonyl stabilization of **24** is non-existent. On the other hand, allyl stabilization of carbonyl cation **24** is slightly larger than allyl stabilization of thiocarbonyl cation **23**. In other words, the sum of allyl stabilization and the small amount of thiocarbonyl stabilization in **23** is quite comparable to the allyl stabilization in **24**. Cations **23** and **24** therefore have comparable stabilities.

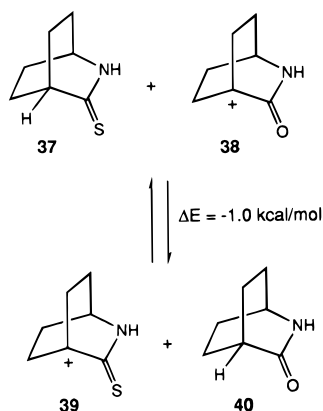


These suggestions on the basis of computational studies are in line with the observed Hammett ρ^+ values. The slightly larger ρ^+ value observed in solvolyses of the β -lactam systems **10** are in line with a slightly larger demand for stabilization of the cationic intermediate by the aryl group. Specifically, the β -thiolactam **9d** is 3.8 times more reactive than the carbonyl analog **10d**. This reactivity difference increases as the substituent becomes more electron-withdrawing and the C=S/C=O rate ratio is 26.8 for the *p*-CF₃ substituted systems **9c** and **10c**. This is a reflection of increased charge delocalization onto the aryl group of the carbonyl cations **12** (relative to the thiocarbonyl cations **11**). The same phenomenon is observed computationally in the allyl analog **24**, where conjugation with the allyl group is slightly greater than in **23**.

Of related interest is a computational study on cations **38** and **39**, where α -carbonyl and α -thiocarbonyl conjugative stabilization is precluded by geometric constraints. As implied by the isodesmic reaction below, these cations also possess comparable stabilities. This study verifies computationally the suggestion that α -carbonyl and α -thiocarbonyl cations will have comparable stabilities in the absence of conjugative effects. Takeuchi has recently verified this suggestion experimentally

(20) (a) Lien, M. H.; Hopkinson, A. C. *J. Am. Chem. Soc.* **1988**, *110*, 3788. (b) Creary, X.; Wang, Y.-X.; Jiang, Z. *J. Am. Chem. Soc.* **1995**, *117*, 3044.

in a study of triflates where conjugation is systematically varied by geometric constraints.²¹



Conclusions. Mesylate and trifluoroacetate derivatives of 3-aryl-3-hydroxy-substituted β -thiolactams and β -lactams (**9** and **10**) can undergo solvolytic reactions via carbocationic intermediates **11** and **12**. Solvent effect studies, substituent effect studies, studies on chiral systems, and the observation of a common ion rate suppression all point to the involvement of carbocationic intermediates. In contrast to open chain analogs, these cationic intermediates do not suffer proton loss, but instead are captured by solvent to give simple substitution products. Computational studies suggest that proton loss from cationic intermediates **11** and **12** will be an unfavorable process due to antiaromatic character in the potential elimination product. In contrast to acyclic analogs, rate studies as well as computational studies suggest that cations such as **11** and **12** have comparable stabilities. C=S and C=O conjugative stabilization of these cations is therefore minimal or non-existent. As revealed by substituent effect studies, the major mode by which cations **11** and **12** derive stabilization is by aryl group charge delocalization. Finally, sodium azide in polar aprotic solvents reacts with mesylates **9** and **10** via a bimolecular substitution mechanism to give the corresponding azido-substitution product.

Experimental Section

Preparation of Mesylates 9 and 10. General Procedure. A solution of the appropriate alcohol (1 equiv) and $\text{CH}_3\text{SO}_2\text{Cl}$ (1.5 equiv) in methylene chloride was cooled to -50°C and Et_3N (1.8 equiv) was added dropwise. The stirred mixture was slowly warmed to 0°C . The mixture was transferred to a separatory funnel with ether, washed rapidly in succession with cold water, cold dilute HCl solution, saturated NaCl solution, and then dried over MgSO_4 . Solvent removal using a rotary evaporator left the corresponding mesylate derivative. The following are representative.

Addition of 488 mg of Et_3N to a solution of 518 mg of **7** ($\text{Ar} = \text{Ph}$) and 461 mg of $\text{CH}_3\text{SO}_2\text{Cl}$ in 8 mL of CH_2Cl_2 gave, after workup, 666 mg (92%) of mesylate **9a**, mp $116\text{--}118^\circ\text{C}$. ^1H NMR (CDCl_3) δ 7.92–7.83 (m, 2 H), 7.52–7.42 (m, 3 H), 4.689 (d, $J = 8.1$ Hz, 1 H), 4.542 (d, $J = 8.1$ Hz, 1 H), 3.199 (s, 3 H), 2.792 (s, 3 H). ^{13}C NMR (CDCl_3) δ 197.14, 132.84, 130.27, 128.76, 128.26, 87.60, 62.38, 41.13, 31.79. Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_3\text{S}_2$: C, 48.69; H, 4.83. Found: C, 48.50; H, 4.87.

The mesylate (+)-**9a** was prepared from (+)-*N*-methyl-3-hydroxy-3-phenylazetidine-2-thione (74% ee)⁹ using an identical procedure.

In similar fashion, mesylate **10a**, mp $95\text{--}97^\circ\text{C}$, was produced from **8** ($\text{Ar} = \text{Ph}$). ^1H NMR (CDCl_3) δ 7.73–7.64 (m, 2 H), 7.50–7.42 (m, 3 H), 4.119 (d, $J = 6.5$ Hz, 1 H), 3.928 (d, $J = 6.5$ Hz, 1 H), 2.948 (s, 3 H), 2.864 (s, 3 H). ^{13}C NMR (CDCl_3) δ 163.96, 132.96, 130.18, 128.93, 127.83, 91.94, 55.73, 40.45, 28.73. Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_4\text{S}$: C, 51.75; H, 5.13. Found: C, 51.81; H, 5.11.

Preparation of Trifluoroacetates 9d and 10d. A solution of 114 mg of **7** ($\text{Ar} = 4\text{-CH}_3\text{OC}_6\text{H}_4$) (0.511 mmol) and 83 mg of 2,6-lutidine (0.776 mmol) in 1.0 mL of CH_2Cl_2 was cooled to 0°C and 141 mg of trifluoroacetic anhydride (0.671 mmol) in 0.5 mL of CH_2Cl_2 was added dropwise. The stirred mixture was warmed to room temperature and after 10 min 5 mL of ether was added. The mixture was transferred to a separatory funnel, washed rapidly in succession with cold water, cold dilute HCl solution, saturated NaCl solution, and then dried over MgSO_4 . Solvent removal using a rotary evaporator left 160 mg (98% yield) of the trifluoroacetate **9d**, mp $84\text{--}85^\circ\text{C}$. ^1H NMR (CDCl_3) δ 7.690 and 6.945 (AA'BB' quartet, 4 H), 4.620 (d, $J = 8.1$ Hz, 1 H), 4.415 (d, $J = 8.1$ Hz, 1 H), 3.821 (s, 3 H), 3.208 (s, 3 H). ^{13}C NMR (CDCl_3) δ 197.15, 160.84, 156.99 (q, $J = 65$ Hz), 128.84, 124.55, 114.21, 114.08 (q, $J = 284$ Hz), 86.60, 60.73, 55.38, 31.76. Anal. Calcd for $\text{C}_{13}\text{H}_{12}\text{F}_3\text{NO}_3\text{S}$: C, 48.90; H, 3.79. Found: C, 48.79; H, 3.79.

The preparations of trifluoroacetate **10d** and 1-phenylcyclobutyl trifluoroacetate were completely analogous to the above procedure.

Preparation of Triflates 9f and 10f. General Procedure. A solution of alcohol **7** or **8** ($\text{Ar} = 3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3$) (1 equiv) and 2,6-lutidine (2.0 equiv) in CH_2Cl_2 was cooled to -50°C and triflic anhydride (1.5 equiv) was added dropwise. The mixture was warmed to 0°C and ether was added. The mixture was then rapidly washed with cold dilute HCl solution, NaHCO_3 solution, and saturated NaCl solution. The solution was dried over MgSO_4 and the solvent was removed using a rotary evaporator. The residue contained the triflate product as well as a significant amount of the adduct derived from reaction of the triflate with 2,6-lutidine. This byproduct was removed by dissolving the residue in pentane, and washing with dilute HCl solution and saturated NaCl solution, and drying over MgSO_4 . Removal of the pentane solvent using a rotary evaporator left the triflates **9f** or **10f** as unstable oils. These triflates are best stored in the freezer in ether solution. The following is representative.

Reaction of 150 mg of **8** ($\text{Ar} = 3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3$) and 73 mg of 2,6-lutidine in 4 mL of CH_2Cl_2 with 142 mg of triflic anhydride gave, after a workup as described above, 99 mg (66%) of triflate **10f**. ^1H NMR (CDCl_3) δ 8.148 (br s, 2 H), 8.020 (br s, 1 H), 4.174 (d, $J = 7.3$ Hz, 1 H), 4.137 (d, $J = 7.3$ Hz, 1 H), 3.029 (s, 3 H). ^{13}C NMR (CDCl_3) δ 160.54, 134.04, 132.79 (q, $J = 34$ Hz), 128.54 (q, $J = 3$ Hz), 124.89 (heptet, $J = 4$ Hz), 122.68 (q, $J = 273$ Hz), 117.88 (q, $J = 320$ Hz), 93.68, 54.68, 29.23.

Preparation of Chlorides 9e and 10e. A suspension of 130 mg of **7** ($\text{Ar} = 4\text{-MeOC}_6\text{H}_4$) and 330 mg of Na_2CO_3 in 5 mL of ether was stirred at room temperature as 100 mg of SOCl_2 was added. The mixture was stirred for 40 min at room temperature and then the solution was filtered through a small amount of Na_2CO_3 . The ether solvent was removed using a rotary evaporator leaving 138 mg (98%) of chloride **9e** as an oil. ^1H NMR (CDCl_3) δ 7.683 and 6.907 (AA'BB' quartet, 4 H), 4.405 (d, $J = 7.2$ Hz, 1 H), 4.368 (d, $J = 7.2$ Hz, 1 H), 3.811 (s, 3 H), 3.197 (s, 3 H). ^{13}C NMR (CDCl_3) δ 200.30, 160.05, 128.73, 128.39, 113.99, 69.80, 67.23, 55.34, 31.92. Chloride **9e** decomposes on standing at room temperature and is best stored as a solution in ether. The preparation of **10e** from **8** ($\text{Ar} = 4\text{-MeOC}_6\text{H}_4$) was completely analogous.

Solvolyses of Mesylates 9 and 10 in Alcohol Solvents. General Procedure. A solution of the mesylate in the appropriate alcohol solvent containing 1.2 equiv of 2,6-lutidine was kept at room temperature for 10 half-lives. The alcohol solvent was then removed using a rotary evaporator and the residue was taken up into ether. The ether was washed with dilute HCl solution followed by saturated NaCl solution. The ether extract was then dried over MgSO_4 and the solvent was removed using a rotary evaporator leaving the substitution product. The following is representative.

A solution of 147 mg of **9a** in 13 mL of methanol (0.05 M 2,6-lutidine) was kept at room temperature for 40 h. A workup as described above gave 102 mg (91%) of *N*-methyl-3-methoxy-3-phenylazetidine-2-thione, mp $74\text{--}75^\circ\text{C}$. ^1H NMR (CDCl_3) δ 7.69–7.60 (m, 2 H), 7.45–7.31 (m, 3 H), 4.152 (d, $J = 6.9$ Hz, 1 H), 3.970 (d, $J = 6.9$ Hz, 1 H), 3.484 (s, 3 H), 3.183 (s, 3 H). ^{13}C NMR (CDCl_3) δ 202.14, 136.22, 128.71, 128.54, 127.01, 87.14, 62.84, 53.16, 31.44. Anal. Calcd for $\text{C}_{11}\text{H}_{13}\text{NOS}$: C, 63.74; H, 6.32. Found: C, 63.22; H, 6.34.

(21) Tokunaga, K.; Ohga, Y.; Takeuchi, K. *Tetrahedron Lett.* **1996**, 37, 2241.

Solvolysis of Mesylate 9a in Acetic Acid. A solution of 169 mg of mesylate **9a** in 16 mL of acetic acid (0.05 M in NaOAc) was kept at room temperature for 3.5 days. The mixture was then taken up into ether and water and the acetic acid was neutralized by slow addition of solid K₂CO₃. The ether extract was then dried over MgSO₄ and filtered, and the solvent was removed using a rotary evaporator, leaving 141 mg (96%) of *N*-methyl-3-acetoxy-3-phenylazetidine-2-thione, mp 105–106 °C. ¹H NMR (CDCl₃) δ 7.67–7.60 (m, 2 H), 7.44–7.31 (m, 3 H), 4.581 (d, *J* = 8.1 Hz, 1 H), 4.385 (d, *J* = 8.1 Hz, 1 H), 3.201 (s, 3 H), 2.153 (s, 3 H). ¹³C NMR (CDCl₃) δ 200.04, 169.74, 134.68, 128.96, 128.54, 126.44, 84.68, 61.81, 31.69, 21.35. Anal. Calcd for C₁₂H₁₃NO₂S: C, 61.25; H, 5.57. Found: C, 61.27; H, 5.60.

Preparation of (+)-*N*-Methyl-3-acetoxy-3-phenylazetidine-2-thione. A solution of 51 mg of (+)-*N*-methyl-3-hydroxy-3-phenylazetidine-2-thione, [α]_D = +131°, and 68 mg of acetic anhydride in 2 mL of pyridine was stirred as 5 mg of 4-dimethylaminopyridine was added. After 18 h at room temperature, the mixture was taken up into ether and the ether was washed with water, dilute HCl solution, and saturated NaCl solution and dried over MgSO₄. Solvent removal using a rotary evaporator gave 58 mg (94%) of (+)-*N*-methyl-3-acetoxy-3-phenylazetidine-2-thione, [α]_D = +101.6° (acetone).

Solvolysis of Mesylate (+)-9a in Acetic Acid. A solution of 60 mg of (+)-**9a** in 6 mL of 0.05 M NaOAc in acetic acid was kept at room temperature for 3 days. A standard workup as described for acetolysis of recemic **9a** gave 51 mg of *N*-methyl-3-acetoxy-3-phenylazetidine-2-thione, [α]_D = +3.1° (acetone).

Solvolysis of Mesylate (+)-9a in Acetone–Water. A solution of 61.5 mg of (+)-**9a** in 5.5 mL of 4:1 acetone/water (by volume) containing 30 mg of 2,6-lutidine was kept at room temperature for 8 days. The acetone was removed using a rotary evaporator and the residue was taken up into ether. The ether extract was washed with dilute HCl, water, and saturated NaCl solution and dried over MgSO₄. Solvent removal using a rotary evaporator left 38 mg of *N*-methyl-3-hydroxy-3-phenylazetidine-2-thione, [α]_D = –2.6° (acetone).

Determination of *k*_{azide}/*k*_{MeOH} Ratios. General Procedure. The appropriate substrate **9** or **10** (approximately 10 mg) was dissolved in 3.5 mL of a 0.20 M solution of NaN₃ in methanol. The mixture was kept at room temperature for approximately 10 half lives and then the methanol was removed using a rotary evaporator. The residue was taken up into ether and water and the ether extract was dried over MgSO₄. After filtration, the solvent was removed using a rotary evaporator and the residue was analyzed for relative amounts of **16** and **17** by ¹H NMR. The following is representative.

Reaction of 10.1 mg of mesylate **9a** in 3.5 mL of 0.20 M NaN₃ in methanol for 18 h at 24 °C gave a mixture of **16** and **17** in a 14.7:85.3 ratio as determined by NMR integration of the doublets at δ 4.054 and 4.156 due to these respective products.

In the case of the relatively unreactive mesylate **9c**, the reaction was worked up after 13 days at room temperature. Most of **9c** remained unreacted and the product ratio reported is based on the 37% of **9c** that had reacted.

Reaction of Mesylate 9a with Sodium Azide. A mixture of 260 mg of NaN₃ and 210 mg of mesylate **9a** in 15 mL of dimethylformamide was heated with stirring at 70 °C for 9 h. The mixture was diluted with 40 mL of water and extracted with two portions of ether. The combined ether extracts were washed with water and saturated NaCl solution and dried over MgSO₄. After solvent removal using a rotary evaporator, the residue was chromatographed on silica gel. Azide **18** (148 mg; 88% yield) eluted with 30% ether in hexanes. IR (CCl₄) 2090, 2120 cm^{–1}. ¹H NMR (CDCl₃) δ 7.71–7.74 (m, 2 H), 7.49–7.36 (m, 3 H), 4.050 (d, *J* = 6.9 Hz, 1 H), 4.012 (d, *J* = 6.9 Hz, 1 H), 3.192 (s, 3 H). ¹³C NMR (CDCl₃) δ 199.55, 134.60, 129.11, 128.79, 126.70, 71.85, 63.62, 31.53. Anal. Calcd for C₁₀H₁₀N₄S: C, 55.03; H, 4.62. Found: C, 55.20; H, 4.54.

In a similar fashion, reaction of 590 mg of (+)-**9a** with 708 mg of NaN₃ in 15 mL of DMF for 8 h at 70 °C gave 360 mg (85%) of (–)-**18**, [α]_D = –221° (CH₃OH).

Preparation of (–)-*N*-Methyl-3-amino-3-phenylazetidine-2-thione, (–)-19. A solution of 335 mg of (–)-**18** and 403 mg of triphenylphosphine in 6 mL of CH₂Cl₂ was stirred at room temperature for 2 days. The solvent was then removed using a rotary evaporator and the crude iminophosphorane was dissolved in 12 mL of tetrahydrofuran. Six milliliters of 5% aqueous NaOH solution was then added and the stirred mixture was heated in an oil bath maintained at 65 °C for 3.5 days. The THF was then removed using a rotary evaporator and the residue was acidified with 10% HCl solution. After extraction with two portions of ether, the aqueous phase was treated with excess Na₂CO₃. The mixture was then extracted with three portions of ether and the combined ether extracts were washed with saturated NaCl and dried over MgSO₄. The solvent was removed using a rotary evaporator and the solid residue was washed with ether. After drying under vacuum, 138 mg (47%) of (–)-*N*-methyl-3-amino-3-phenylazetidine-2-thione, (–)-**19**, remained, mp 110–111 °C; [α]_D = –141° (CH₃OH). This material contained an 80% ee of (–)-**19** as determined by ¹H NMR using the chiral shift reagent tris(3-heptafluoropropyl)hydroxymethylene)((+)-camphorato)europium(III). The ether wash was concentrated using a rotary evaporator and the residue was chromatographed on 6 g of silica gel using ether as an eluent. An additional 71 mg (24%) of amine **19** was obtained which contained a 60% ee of (–)-**19**. ¹H NMR (CDCl₃) δ 7.68–7.60 (m, 2 H), 7.42–7.26 (m, 3 H), 4.065 (d, *J* = 7.0 Hz, 1 H), 3.956 (d, *J* = 7.0 Hz, 1 H), 3.198 (s, 3 H), 2.120 (br s, 2 H). ¹³C NMR (CDCl₃) δ 208.80, 139.69, 128.56, 128.12, 125.99, 69.77, 67.01, 31.68. Anal. Calcd for C₁₀H₁₂N₂S: C, 62.47; H, 6.29. Found: C, 62.37; H, 6.34.

Kinetics Procedures. Rates of reaction of the substrates described in this paper were determined by either ¹H NMR, ¹⁹F NMR spectroscopy or UV spectroscopy. Rates of solvolyses of **9a** and **10a** in methanol and ethanol, as well as **9c** and **10c** in trifluoroethanol, were monitored by ¹H NMR spectroscopy by monitoring the changing of the chemical shift of the methyl groups of the buffering base 2,6-lutidine.²² Rates of solvolyses of trifluoroacetates **9d** and **10d**, triflate **10f**, and 1-phenylcyclobutyl trifluoroacetate in acetic acid (containing 0.05 M sodium acetate) were monitored by ¹⁹F NMR spectroscopy.²³ Solvolyses of **9d** and **10d** in acetic acid (0.05 M sodium acetate), which are subject to a substantial common ion rate suppression, were carried out at low substrate concentrations (0.005 M), where changes in trifluoroacetate ion concentration were minimal over the course of the reaction. Rates of solvolysis of **10a** in acetic acid were monitored by ¹H NMR integration. Rates of solvolyses of **9a** and **10a** in (CF₃)₂CHOH (containing 10^{–3} M Et₃N) were monitored by UV spectroscopy at 264 and 225 nm, respectively, using previously described methods.²⁴ The remainder of the solvolysis rates given in Table 1 were also monitored by UV spectroscopy at wavelengths between 258 and 271 nm. The alcohol solvents all contained 2 × 10^{–4} M 2,6-lutidine, which becomes protonated as the reaction proceeds.

Computational Studies. *Ab initio* molecular orbital calculations were performed using either the Gaussian 92 or Gaussian 94 series of programs.¹⁸ All structures were characterized as true minima via frequency calculations which showed no negative frequencies.

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(22) Creary, X.; Jiang, Z. *J. Org. Chem.* **1994**, *59*, 5106.

(23) Creary, X.; Wang, Y.-X. *J. Org. Chem.* **1992**, *57*, 4761.

(24) Creary, X.; Hatoum, H.; Barton, A.; Aldridge, T. E. *J. Org. Chem.* **1992**, *57*, 1887.