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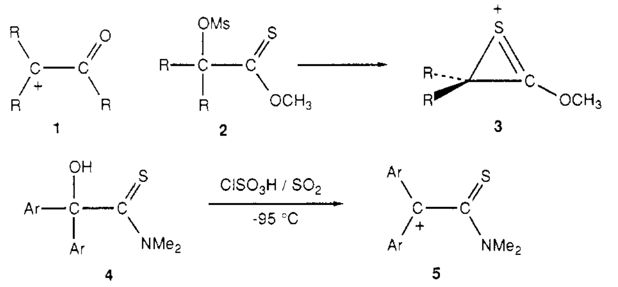
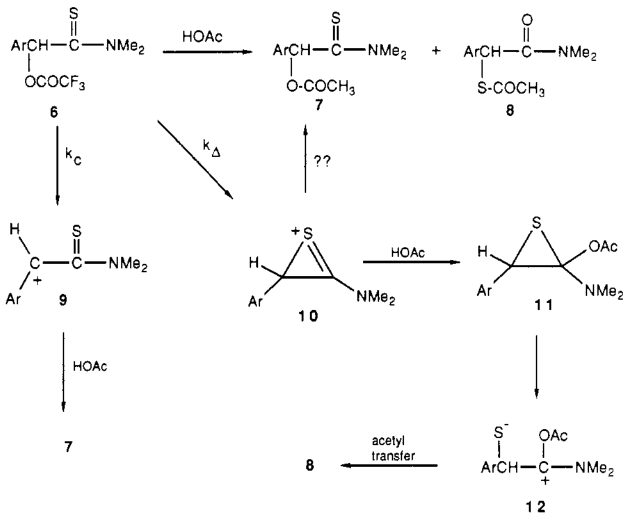
Carbocation Stabilization by the Thioamide Group

Summary: The thioamide group, CSNMe$_2$, when attached to a developing carbocationic center, can be a very effective carbocation stabilizing group. Stabilization occurs by either sulfur participation leading to the formation of cyclized ions or by extensive conjugative charge delocalization onto sulfur.

Sir: We have been interested in the mechanisms by which carbocations substituted with formally electron-withdrawing groups derive stabilization.[1] This interest is an outgrowth of the observation that many cations of type **1**, substituted with the carbonyl group can be generated with surprising ease.[2] A fundamental question concerns the nature of such cations. Are they open or closed ions? A previous study[3] led us to conclude that, unlike their carbonyl counterparts, thiocarbonyl esters of the type **2** react by way of the closed cations **3**. Recently it has been found that related thioamide substituted cations **5** can be formed under stable ion conditions.[4] We now report our findings on the behavior of certain thioamide substituted carbocations under solvolytic conditions.



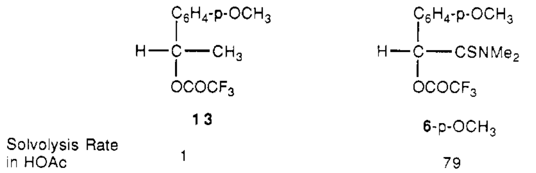
A series of trifluoroacetates **6** were prepared and reacted in acetic acid at room temperature where they were converted to products at convenient rates. Rate data are given in Table I. These substrates are considerably more reactive than the C=O analogues where mesylate derivatives are necessary to achieve convenient reactivity.[5] The products derived from acetolysis of **6** are the simple substitution product **7** and the rearranged product **8**. The ratio of these two products (Table II) is substituent dependent. The rearranged product **8** is suggested to arise via the k_Δ process which leads to the cyclized ion **10**.



Solvent capture at the carbon carrying the dimethylamino group followed by ring opening and acetyl group transfer would give the rearranged product **8**. This process is analogous to that suggested for the ester **2** where R = CH$_3$.[3] The simple substitution product **7** could be derived in principle from nucleophilic solvent opening at the benzylic position of the cyclized ion. Alternatively a competing k_c process, giving the open ion **9**, followed by solvent capture, would give this unrearranged product **7**.

A Hammett plot of the rate data (Figure 1) is not linear and indicative of a mechanistic changeover. Also of interest is the relatively small rate spread of only 1.1×10^3 despite substituents ranging from *p*-methoxy to 3,5-bis(trifluoromethyl). We have arbitrarily drawn a line connecting the *p*-CF$_3$ and the 3,5-(CF$_3$)$_2$ systems (ρ^+ value of −1.2). This region represents the area where the k_Δ process leading to cyclized ions **10** is dominant. The other line is arbitrarily drawn between the *p*-OCH$_3$ and the *p*-CH$_3$ substrates (slope of −2.4)[6] and represents the region where the k_c process leading to open ions of type **9** is dominant. This plot suggests that **6**-*p*-OCH$_3$ reacts mostly by the k_c process.

The most striking feature of the reaction of **6**-*p*-OCH$_3$ in acetic acid is the rate. The acetolysis rate of **6**-*p*-OCH$_3$ is 79 times faster than that of the α-methyl analogue, *p*-CH$_3$OC$_6$H$_4$CH(CH$_3$)OCOCF$_3$ (**13**). The CSNME$_2$ group, which is a potent carbanion stabilizing group,[7] therefore exceeds the methyl group in its ability to stabilize carbocations.



The *p*-nitrobenzoate **14**, on solvolysis in 80% aqueous acetone, gave exclusively the elimination product **15** presumably via the intermediacy of the corresponding thioamide substituted cation. Proton loss from this intermediate leads to the product **15**. The norbornyl system **16**

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[1] For review and leading references on cations substituted with electron-withdrawing groups, see: (a) Bégué, J.-P.; Charpentier-Morize, M. *Acc. Chem. Res.* **1980**, *13*, 207–212. (b) Gassman, P. G.; Tidwell, T. T. *Acc. Chem. Res.* **1983**, *16*, 279–285. (c) Creary, X. *Acc. Chem. Res.* **1985**, *18*, 3–8. (d) Tidwell, T. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 20–32.

[2] (a) Creary, X. *J. Am. Chem. Soc.* **1984**, 106, 5568–5577. (b) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, 104, 4151–4162.

[3] Creary, X.; Mehrsheikh-Mohammadi, M. E. *J. Org. Chem.* **1986**, *51*, 7–15.

[4] Ablenas, F. J.; George, B. E.; Maleki, M.; Jain, R.; Hopkinson, A. C.; Lee-Ruff, E. *Can. J. Chem.* **1987**, *65*, 1800–1803.

[5] Creary, X.; McDonald, S. R.; Eggers, M. E. *Tetrahedron Lett.* **1985**, *26*, 811.

[6] This does not imply that the ρ^+ value for the k_c process is −2.4. The rate of **6**-*p*-CH$_3$ may well have a significant k_Δ component since it appears to fall in the region of the mechanistic change.

[7] α-Thioamide anions are readily formed. For representative examples, see: (a) Schuijl, P. J.; Bos, H. J. T.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 123. (b) Tamura, Y.; Furukawa, Y.; Mizutani, M.; Kitao, O.; Yoshida, Z. *J. Org. Chem.* **1983**, *48*, 3631. (c) Tamura, Y.; Harada, T.; Iwamoto, H.; Yoshida, Z. *J. Am. Chem. Soc.* **1978**, *100*, 5221.

Table I. Solvolysis Rates[a] in Various Solvents at 25 °C

substrate	solvent	k,[a] s^{-1}
6-p-OCH_3	EtOH	8.66×10^{-2}
	HOAC	2.48×10^{-1}[b]
6-p-CH_3	EtOH	6.40×10^{-3}
	HOAC	1.83×10^{-2}
6-p-H	HOAC	5.31×10^{-3}
6-p-CF_3	HOAC	7.44×10^{-4}
6-3,5-$(CF_3)_2$	HOAC	2.12×10^{-4}
13	HOAC	1.09×10^{-3}
14	80% acetone	3.19×10^{-5} (50 °C)
		4.29×10^{-6} (35 °C)
		9.81×10^{-7} (25 °C)
16	HOAc	3.00×10^{-4} (70 °C)
		2.27×10^{-5} (50 °C)
		5.55×10^{-7} (25 °C)[c]

[a] Determined spectrophotometrically except in the case of **14**, where rates were determined titrimetrically. Rate constants given represent an average of at least two runs with a maximum standard deviation of ±2%. [b] Estimated from the rate in EtOH using the value of 2.86 (determined for 6-p-CH_3) as the HOAc/EtOH rate ratio. The HOAc/EtOH rate ratio is 2.64 for cumyl trifluoroacetate at 25 °C. [c] Extrapolated from data at higher temperatures.

Table II. Products of Solvolysis of 6 in HOAc

aryl group	%7	%8
p-$CH_3OC_6H_4$	100	0
p-$CH_3C_6H_4$	84	16
C_6H_5	73	27
p-$CF_3C_6H_4$	23	77
3,5-$(CF_3)_2C_6H_3$	14	86

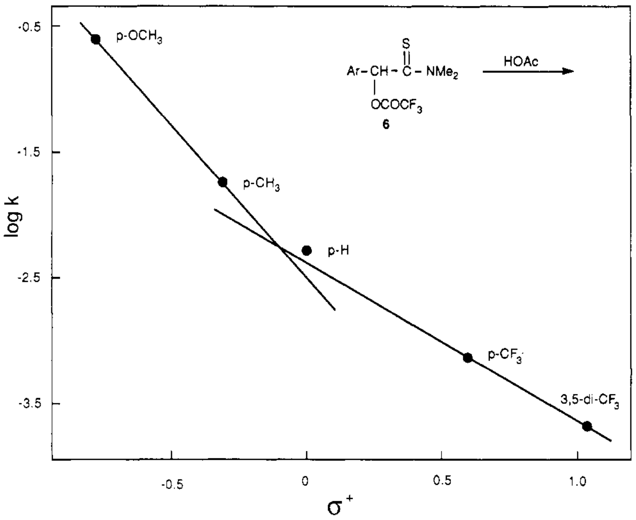
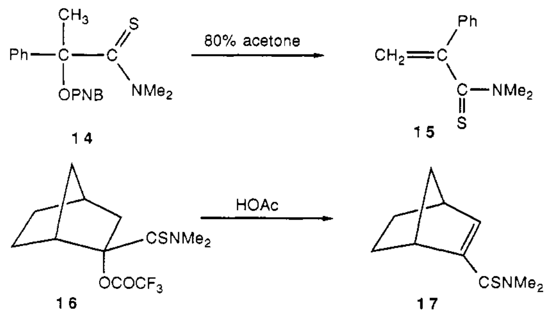
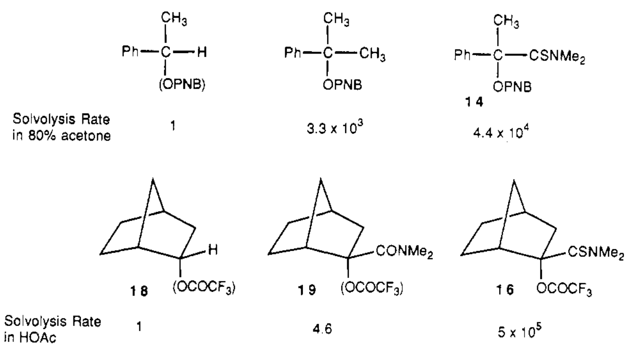


Figure 1. A plot of log k for acetolysis of **6** vs σ^+.

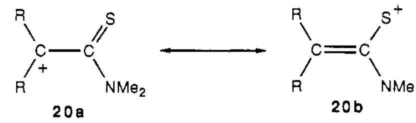
gave an analogous elimination product **17** when solvolyzed in acetic acid.



As before, analysis of the rate data is quite revealing. The α-thioamide system **14** solvolyzes via a cationic intermediate far more readily than the α-H analogue and even more readily than the α-CH_3 analogue.[8] The trifluoroacetate **16** is substantially more reactive than the α-H analogue **18** or the amide analogue **19**.[9]



The cation stabilizing ability of $CSNMe_2$ therefore appears to exceed that of methyl and can approach that of the phenyl group. This remarkable cation stabilizing ability is attributed to extensive charge delocalization as represented by **20b**. This type of charge delocalization



is analogous to that suggested for α-carbonyl cations,[2] which leads to greater than expected stability in these intermediates. The much greater stabilizing ability of the thiocarbonyl group reflects the greater importance of **20b** relative to the oxygen analogue. Rate data suggest that **20b** is a *major* contributor. This is a result of the lower electronegativity of sulfur relative to oxygen which renders sulfur more capable of supporting positive charge. This suggestion is in line with recent theoretical calculations of Lien and Hopkinson,[11] which imply charge delocalization in **20** (where R = H) can be significant.

In summary, the $CSNMe_2$ group, which is a potent carbanion stabilizing group, is also a very effective carbocation stabilizing group. This is attributed to a significant conjugative interaction of the cationic center with the thiocarbonyl group. Such cations form even more readily than the α-methyl analogues. Substrates containing the thioamide group, under conditions of appropriate electron demand, can also solvolyze via cyclized ions involving thiocarbonyl participation. This k_Δ mode of stabilization can also lead to enormous rate enhancements in solvolytic processes.

Acknowledgment is made to the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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(8) The rate ratio of α-phenethyl p-nitrobenzoate to cumyl p-nitrobenzoate is estimated from the rate ratio of the corresponding chlorides. See Shiner et al. [(a) Shiner, V. J., Shiner, Dowd, W.; Fisher, R. D.; Hartshorn, R. S.; Kessick, M. A.; Nilakofsky, L.; Rapp, M. W. *J. Am. Chem. Soc.* **1969**, *97*, 4838] for data on α-phenethyl chloride in 50–80% EtOH. See Okamoto et al. [(b) Okamoto, Y.; Inukai, T.; Brown, H. C. *J. Am. Chem. Soc.* **1958**, *80*, 4972–4976] for data on cumyl chloride. See Brown and Peters [(c) Brown, H. C.; Peters, E. N. *J. Am. Chem. Soc.* **1973**, *95*, 2400] for data on cumyl p-nitrobenzoate.

(9) The rates of **18** and **19** are estimated from the rates of the corresponding mesylates[2b,5] assuming a mesylate/trifluoroacetate ratio of 10^5.[10]

(10) See Creary [Creary, X. *J. Org. Chem.* **1979**, *44*, 3938] for determination of this mesylate/trifluoroacetate rate ratio.

(11) Lien, M. H.; Hopkinson, A. C. *J. Am. Chem. Soc.*, in press. We thank Professors Lien and Hopkinson for providing us with a copy of their manuscript prior to publication.

(12) **Note added in proof**: Recent studies show that acetolysis of optically active 6-p-OCH_3 gives a substantial amount of net retention. This indicates a significant k_Δ component in acetolysis of 6-p-OCH_3.

Registry No. 6-*p*-OCH_3, 115245-15-3; 6-*p*-CH_3, 115245-16-4; 6-*p*-H, 115269-71-1; 6-*p*-CF_3, 115245-17-5; 6-3,5-$(CF_3)_2$, 115245-18-6; 13, 82638-98-0; 14, 115245-19-7; 16, 115245-20-0.

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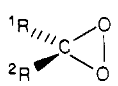
On the Isolation and Characterization of Methyl(trifluoromethyl)dioxirane

Summary: The title dioxirane **1f**, generated by the reaction of CF_3COCH_3 with potassium peroxomonosulfate, has been isolated and fully characterized spectroscopically; it displays a remarkable reactivity in oxygen transfer reactions.

Sir: Isolable[1] dioxirane species (the smallest ring peroxides containing carbon)[2] are known. As an alternative to steric stabilization effected by alkyl groups,[1-4] we wished to try "electronic stabilization", often exhibited by the trifluoromethyl group on highly strained compounds.[5] Dioxiranes **1** and their isomeric counterparts "carbonyl oxides" **2** have been shown to be involved as key intermediates in a number of oxidation processes.[6-8] Only recently, however, did it become possible to provide spectral data and reactivity tests that allow one to differentiate between these elusive entities.[1-4,9-11]



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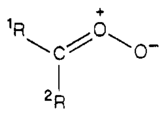

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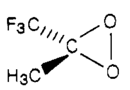

1f

a, $^1R = {}^2R = H$; **b**, $^1R = {}^2R = CH_3$; **c**, $^1R = {}^2R = Ph$; **d**, $^1R = {}^2R = CF_3$; **e**, $^1R = Ph$, $^2R = CF_3$

The trifluoromethyl group can be expected to influence the stability of the small ring in several ways. For one, by drawing electron density from the negative oxygen pole toward the α-carbon, it would discourage formation of dipolar isomers **2**; then, any reaction that is initiated via carbon–oxygen bond rupture in **1**, e.g., dimerization to 1,2,4,5-tetraoxane ("ketone diperoxide"),[1] would be unfavored.

The title compound **1f** was synthesized by the known ketone/caroate method,[1-4] starting with trifluoroacetone (**3**).[12] In order to isolate the dioxirane, we followed a published procedure,[1,4] which was only slightly modified to suit the case at hand.[13] Thus, we were able to collect yellow solutions of **1f** in the parent ketone having concentrations ranging from 0.65 to 0.82 M.[14] This is over 6 times higher than the concentrations of dimethyldioxirane (**1b**) solutions usually attainable by using the same general procedure.[1-4]

The novel dioxirane has a UV absorption with λ_{max} 347 nm ($\epsilon \sim 9$, at 0 °C) that, characteristically,[1-4,10] tails into the visible to over 440 nm (hence its yellow color); it might be ascribed to $n-\pi^*$ excitation.[2,15] Dioxiranes should not exhibit strong infrared bands;[11,15] however, in the difference IR spectrum (vapor phase) of **1f**, significant absorption could be located at 1259, 1189, 971 (w), 839 (w), 731 (w), and 669 (w) cm^{-1}.[16] By way of comparison, the difference IR spectrum of dioxirane **1e** (generated from $Ph\ddot{C}CF_3$ via carbonyl oxide **2e** in oxygen-doped argon matrix) presents bands at 1213, 944, 720, 684, and 643 cm^{-1}.[11b] The salient NMR spectral data of **1f** are summarized in Table I; a comparison with those already reported for **1b** (and for **1d**) corroborates the dioxirane structure. Interestingly, **1d** (UV absorption with λ_{max} 306 nm, extending into the visible)[17] appears to have been generated by the reaction of fluorine gas with the dilithium or the monolithium salt of hexafluoroacetone hydrate, $(CF_3)_2C(OH)_2$.[17]

The yellow solutions of **1f** could be stored at −20 °C with only minor loss of dioxirane content (~6%, 48 h); the decrease in peroxide titer was ca. 30% during 120 h at 0 °C, while a half-life of ~20 h was estimated at 15 °C.[18] Thus, the stability of **1f** appears to be at least comparable to that of **1b**.[1,4] However, in contrast to the dimethyldioxirane case,[1] the loss of **1f** in solution does not lead to the formation of the corresponding ketone diperoxide dimer in any significant extent; rather, NMR analyses showed that the (exothermic) decomposition of **1f** yields mainly methyl trifluoroacetate (CF_3COOCH_3) and trifluoroacetic acid (the hydrolysis product of the latter).[19,20]

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[1] (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847–2853. (b) Murray, R. W.; Jeyaraman, R.; Pillay, M. K. *Ibid.* **1987**, *52*, 746–748 and references.

[2] Curci, R. In *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI: Greenwich, CT; Vol. 2, Chapter 1, in press (a review).

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[4] Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800–2803.

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[7] (a) Jeyaraman, R.; Murray, R. W. *J. Am. Chem. Soc.* **1984**, *106*, 2462–2465. (b) Kumar, S.; Murray, W. *Ibid.* **1984**, *106*, 1040–1045. See also references.

[8] Bailey, P.S. *Ozonization in Organic Chemistry*; Academic: New York, 1978; Vol. 1 and 2 and references quoted therein.

[9] (a) Lovas, F. J.; Suenram, R. D. *Chem. Phys. Lett.* **1977**, *51*, 453–456. (b) Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1978**, *100*, 5117–5122. (c) Martinez, R. I.; Huie, R. E.; Herron, J. T. *Chem. Phys. Lett.* **1977**, *51*, 457–459.

[10] (a) Ganzer, G. A.; Sheridan, R. S.; Liu, M. T. H. *J. Am. Chem. Soc.* **1986**, *108*, 1517–1520. (b) Dunkin, I. R.; Shields, C. J. *J. Chem. Soc., Chem. Commun.* **1986**, 154–156 and references.

[11] (a) Sander, W. W. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 255–257. (b) Sander, W. W. *J. Org. Chem.* **1988**, *53*, 121–126.

[12] Commercial (Aldrich) 1,1,1-trifluoro-2-propanone: bp 22 °C; at −20 °C, pure liquid; ^1H NMR (Me_4Si) δ 2.44 (s); ^{19}F NMR ($CFCl_3$) δ −80.4 (s); $^{13}C(^1H)$ NMR (Me_4Si) δ 23.78 (s, CH_3), 117.1 (q, CF_3, $^1J = 291$ Hz), 190.3 (q, $C{=}O$, $^2J = 36$ Hz); ^{17}O NMR (H_2O, external) δ 577.7; IR (vapor) 1781 ($C{=}O$ stretch), 1434, 1376, 1329, 1225, 1163, 1115, 1024, 968, 724, 614 cm^{-1}.

[13] Batch temperature 5–8 °C, no carrier gas, slight aspiration (water pump, 680–700 mmHg), spiral condenser cooled at −75 °C.

[14] Both iodometry and reaction with PhSMe (^1H NMR analysis) (cf. ref 4) were employed to estimate the dioxirane content of solutions, affording the same results within ±3%. The NMR spectra (Table I) indicated that **1f** was the only peroxide species present in solution.

[15] Gauss, J.; Cremer, D. *Chem. Phys. Lett.* **1987**, *133*, 420–424 and references.

[16] Solutions of **1f** in trifluoroacetone (**3**) and, separately, the pure solvent were vaporized at 22 °C into an 8-cm gas-sampling cell (KBr windows) and FT IR spectra run on a Perkin-Elmer 1710 spectrophotometer; difference spectra were then obtained on a connected P.E. PC7350 data acquisition unit.

[17] Talbott, R. I.; Thompson, P. G. U.S. Patent 3632606, 1972.

[18] In order to obtain reproducible decomposition data, it is important that impurities and trace metals be carefully excluded (cf. ref 6).

[19] We find the following for methyl trifluoroacetate (bp 43 °C): ^1H NMR (CF_3COCH_3, Me_4Si) δ 4.00; ^{19}F NMR (CF_3COCH_3, $CFCl_3$) δ −75.56. Trifluoroacetic acid: ^{19}F NMR (CF_3COCH_3, $CFCl_3$) δ −76.36.