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ON CARBONYL PARTICIPATION IN SOLVOLYSES OF α-KETO MESYLATES

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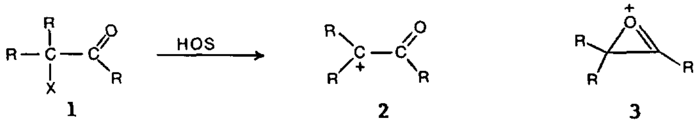
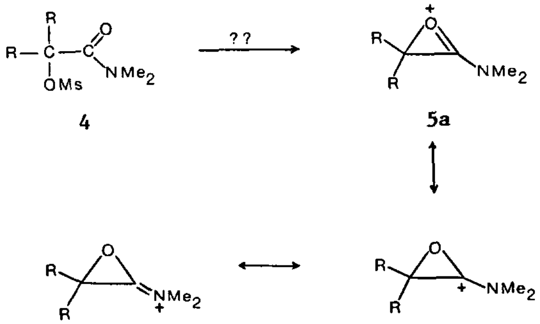
Abstract: α-Amido mesylates generally solvolyze giving α-keto cations, bypassing cyclic ions derived from carbonyl (k_Δ) participation. A possible exception is the N,N-dimethylamido mesylate derived from (S)- mandelic acid in trifluoroacetic acid which gives a small amount (9%) of retained product.

We have been interested in the solvolytic reactivity of α-keto mesylates and triflates,**1**.[1] Many of these systems **1** solvolyze via cationic intermediates, **2**. However one possible intermediate potentially derived from solvolytic reaction of **1** is the oxiranyl ion **3**, which would result from interaction of the carbonyl non-bonding electrons with the developing vacant orbital of the incipient cationic center in **1**.[2] Indeed, theoretical calculations[3] suggest that such an intermediate **3** (R=H) is lower in energy than the open α-keto cation,**2**. We have now carried out studies on amido mesylates of type **4**[4] which were designed to evaluate the propensity for carbonyl participation in solvolysis. It was felt that such systems, due to the increased carbonyl nucleophilicity induced by the nitrogen nonbonding electron pair, offered the "best chance" for the observation of k_Δ derived ions such as **5**.



1 **2** **3**



4 **5a** **5b** **5c**

Mesylate **6**[5] was solvolyzed in a variety of solvents. Rates[6] were largely dependent on solvent ionizing power, indicative of the intervention of a cationic intermediate. The m value (Figure 1) was 0.60. Both unrearranged and rearranged substitution and elimination products were formed.[7] These products, **7-11**, are consistent with the intermediacy of the open cation **12** and not the oxiranyl cation **14**. Such a cation **14** should not undergo Wagner-Meerwein

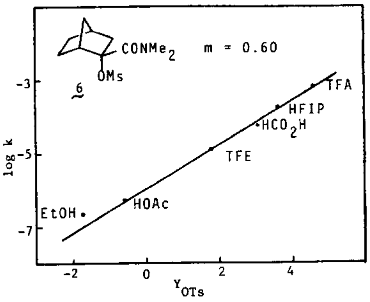


Figure 1. A plot of log k for solvolysis of **6** vs. Y_{OTs}.

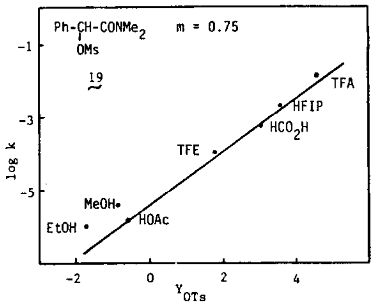
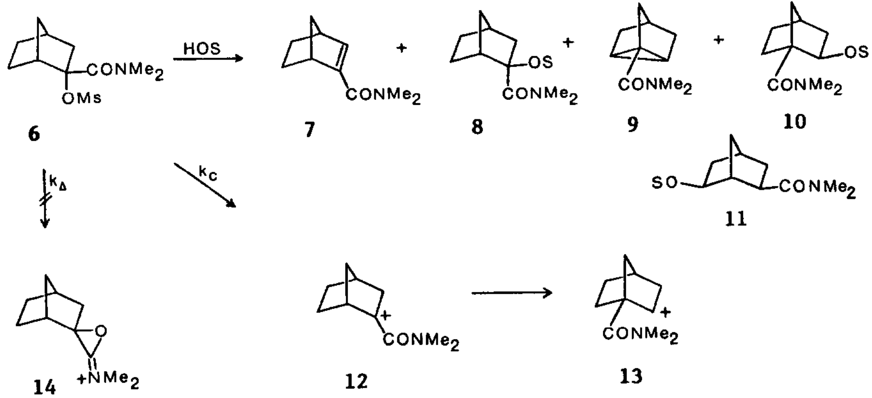


Figure 2. A plot of log k for solvolysis of 19 vs. Y_{OTs}.

rearrangement leading **13**. Such a cation **14** should not give product **8** with net inversion of configuration. One therefore concludes that the increased nucleophilicity of the amide carbonyl in the 3° system **6** is not sufficient to induce a k_Δ process forming the cyclic ion **14**.



The behavior of mesylate **15** could also be interpreted in terms of an open cation **16** Solvolyses in acetic, formic and trifluoroacetic acids gave only the elimination product **17**. One would expect a cyclic ion such as **18** to lead to substitution products from solvent attack at one (or both) of the ring carbons of **18**.[8] The product **17** is unexpected from the oxiranyl ion **18**, but compatible with the open ion **16**.

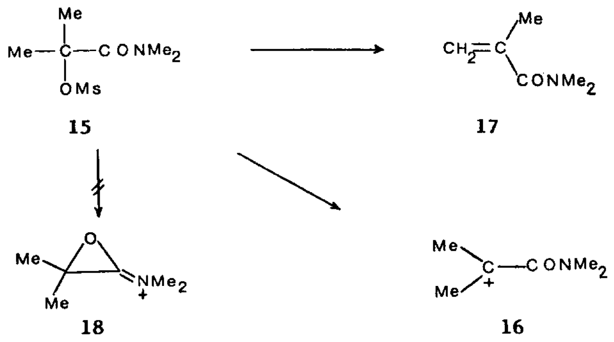
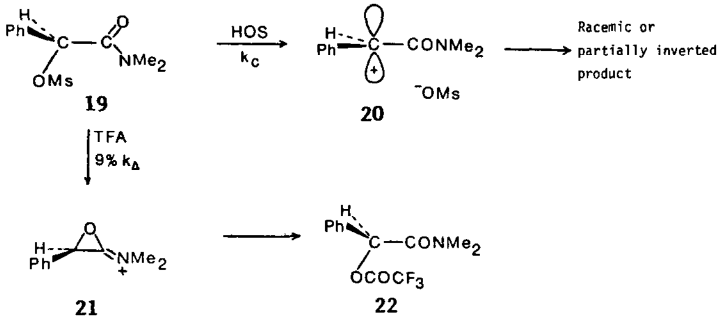


Table 1. Products from Solvolysis of (S)-(+)-**19**

Solvent	Product Rotation[a]	Rotation of (S)-ROS[a]	Stereochemistry of Reaction
MeOH	+5.0	-13.7	33% net inversion
HOAc	-16.5	+154.1	11% net inversion
TFE	-0.4	not determined	racemization
HFIP	-0.0	not determined	racemization
TFA	+12.8	+149.5 in TFA	9% net retention

[a] $[\alpha]_D^{23}$ in acetone except for $ROCOCF_3$

Attention was next turned to the secondary benzylic system **19**, which could be prepared in the optically active form[9]. Rate data[10], presented graphically in Figure 2, suggest a cationic intermediate. Results of solvolysis of (S)-(+)-**19** in various solvents are given in Table 1. The racemized products seen in trifluoroethanol (TFE) and hexafluoroisopropyl alcohol (HFIP) are consistent with the intermediacy of the open cation **20**. The partially inverted products in the more nucleophilic solvents, methanol and acetic acid, suggest preferential solvent capture of an open ion pair from the side opposite the mesylate leaving group.[11]



Data in trifluoroacetic acid (TFA) indicates formation of a small amount (9%) of product of retained configuration. This product may imply that, in this highly ionizing solvent, which is known to support k_Δ processes[12], one is finally beginning to see the intervention of a cyclic ion **21**. Solvent capture of this oxiranyl ion would lead to net retention of configuration and account for the observed products. However the formation of 91% racemized product implies that the major solvolytic process in TFA is formation of the open ion **20**. It should also be noted that there are cases of net retention that do not involve k_Δ processes.[13] Similar processes could also account for the net retention in trifluoroacetolysis of **19**.

In summary, the studies on mesylates **6**, **15**, and **19** show that carbonyl participation is not an important process in solvolysis of these systems. Only in TFA does mesylate **19** give evidence for partial intervention of an oxiranyl type ion. Since carbonyl participation is not important in the "best case" amide systems, we conclude the carbonyl participation, leading to oxiranyl ions **3**, is highly unlikely in solvolysis of ketone and ester systems **1**.

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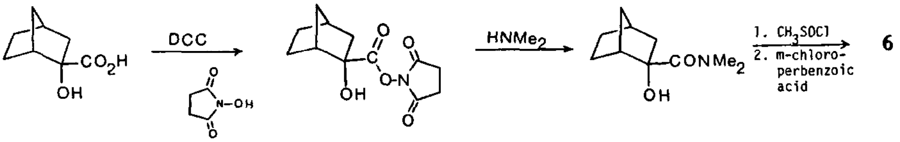
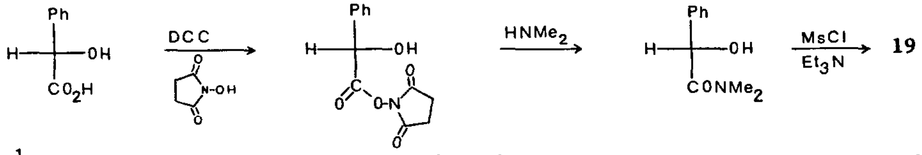
References and notes

1. (a) Creary, X.; Geiger, C. C. J. Am. Chem. Soc. **1982**, 104, 4151-62. (b) Creary, X.; Geiger, C. C. Ibid. **1983**, 105, 7123-9. (c) Creary, X. Ibid. **1984**, 106, 5568-77. (d) Creary, X. Acc. Chem. Res. in press.
2. This type of interaction is distinct from the stabilizing conjugative interaction with the carbonyl π system. For a discussion of this conjugative interaction, see reference 1.
3. Nobes, R. H.; Bouma, W. J.; Radom, L. J. Am. Chem. Soc. **1983**, 105, 309-14.
4. For previous studies involving silver assisted ionization of α-bromoketones, see (a) Sheehan, J. C.; Beeson, J. H. J. Am. Chem. Soc. **1967**, 89, 362-6. (b) Beque, J. P.; Charpentier-Morize, M.; Pardo, C. Tetrahedron Lett. **1971**, 4737.
5. Mesylate **6** was prepared as shown below.



6. $10^7k(s^{-1})$ at 25 C: 2.26 in EtOH; 5.02 in HOAc; 126 in TFE; 531 in HCO_2H; 1790 in 97% HFIP; 6120 in TFA. The line in Fig. 1 omits data in the nucleophilic solvents EtOH and MeOH.
7. In trifluroethanol, **7** ,**8**, **9**, **10** and **11** were formed in a 9:0:59:28:4 ratio. In methanol, the ratio was 28:7:30:35:0.
8. This expectation is based on the fact that analogous cyclic ions such as bromonium ions and episulfonium ions readily capture nucleophiles and give little elimination products.
9. Mesylate (S)-(+)-**19**, was prepared as shown below.



10. $10^6k(s^{-1})$ at 25 C: 1.11 in EtOH; 1.62 in HOAc; 4.21 in MeOH; 119 in TFE; 581 in HCO_2H; 2430 in 97% HFIP; 15300 in TFA. The line in Figure 2 omits data in MeOH.
11. Racemization and partial racemization is not a result of an enolization process. No deuterium is incorporated into the product when **19** was solvolyzed in DOAc or CF_3CO_2D.
12. For representative examples and leading references, see (a) Nordlander, J. E.; Deadman, W. G. J. Am. Chem. Soc. **1968**, 90, 1591-8. (b) Peterson, P. E.; Coffey, F. J. Ibid. **1971**, 5208-11. (c) Nordlander, J. E.; Gruetzmacher, R. R.; Kelly, W. J.; Jindal, S. P. Ibid. **1974**, 96, 181-5.
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