Chemical Reviews

Volume 91, Number 8 December 1991

Electronegatively Substituted Carbocations

XAVIER CREARY

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556

Received April 23, 1991 (Revised Manuscript Received July 8, 1991)

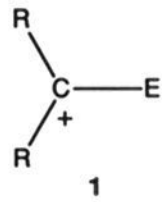
Contents

I.	Introduction	1625
II.	The α-Trifluoromethyl Cation	1626
III.	The α-Cyano Cation	1638
IV.	The α-Carbonyl Cation	1643
V.	The α-Thiocarbonyl Cation	1664
VI.	The α-Imino Cation	1667
VII.	The α-Phosphoryl Cation	1668
VIII.	The α-Thiophosphoryl Cation	1670
IX.	The α-Sulfonyl Cation	1671
X.	The α-Sulfinyl Cation	1672
XI.	The α-Nitro and α-Nitroso Cations	1673
XII.	Recent Developments	1674
XIII.	References	1675

Xavier Creary was born on September 27, 1946 in Montclair, NJ. He received his B.S. from Seton Hall University in 1968 and his Ph.D from The Ohio State University in 1973. After a year as a postdoctoral at the University of California at Santa Cruz, he joined the faculty at the University of Notre Dame in 1974, where he is currently professor of Chemistry. His interests in mechanistic and synthetic organic chemistry were nurtured and greatly influenced by guidance in the laboratories of Professor Daniel P. Weeks as an undergraduate, Professor Paul G. Gassman as a graduate student, and Professor Joseph F. Bunnett as a postdoctoral. His current research interests are in the areas of synthetic and mechanistic organic chemistry, with special interests in the chemistry of carbocations, free radicals, carbenes, electron transfer initiated reactions, acid catalysis, and the chemistry of diazocompounds and diazirines.

I. Introduction

Carbocations are a class of reactive intermediates of fundamental importance in organic chemistry. As such, these intermediates have continued to hold the interest of organic chemists since Hughes and Ingold first formalized the S_N1 concept.[1] An almost countless number of carbocations have been generated and features leading to stability and instability have been the topic of a myriad of studies. A fundamental dogma in the carbocation area holds that since this intermediate is intrinsically electron-deficient, electron-donating groups will stabilize a carbocation. This review article will deal with carbocations **1** that are substituted in the opposite sense, i.e. these cations have a formally electron-withdrawing group directly attached to the carbocation center.



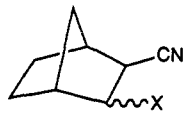
1

Carbocations such as **1**, where the group E represents an electronegative substituent, have also been referred to as "destabilized carbocations" in the past. For long it was generally believed in the organic chemical community that such intermediates were intrinsically unstable and therefore would form only with great reluctance and only under forcing conditions. Over the past decade there has been intense interest in the chemistry of carbocations of general structure **1**. Contrary to earlier views, a number of laboratories have shown that a wide variety of such cations can indeed be generated, studied, and used in synthetic applications. A number of short reviews[2-6] have appeared which deal in part with cations containing a specific electronegative group E. This review will attempt to present a general summary of the chemistry of cations **1** and to show that **1** is indeed a respectable cationic intermediate.

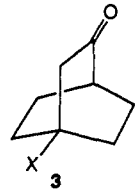
Before proceeding it is necessary to define the scope of this review article, i.e., what is the nature of the group

0009-2665/91/0791-1625$09.50/0

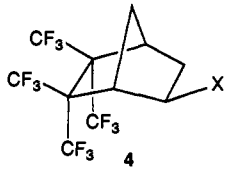
E in the cation 1? This review has been limited to cations where the group E is *directly* attached to the cationic center. Systems such as 2,[7] 3,[8] 4,[9] and 5,[10] where an electron-withdrawing group is further removed from a developing cationic center, give some fascinating chemistry, but will not be explicitly covered by this review. Carbocations substituted directly with



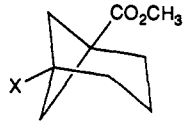
2



3



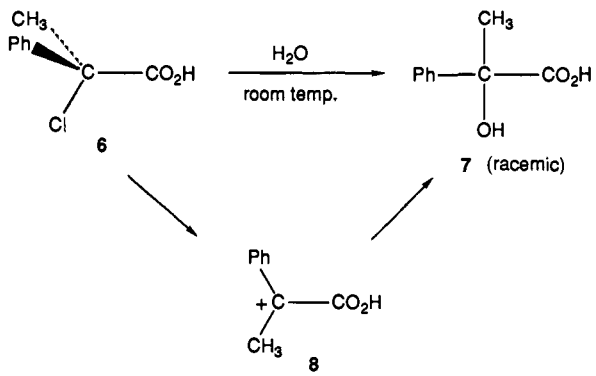
4



5

electronegative elements carrying nonbonding electrons (such as halogen or oxygen) will also not be covered. The group E will be limited to other substituents which are traditionally thought of as being electron withdrawing as measured by positive σ_p and σ^+ values. These groups all increase the acidity of benzoic acids when substituted in the para position. They also slow the solvolysis rate of substituted cumyl chlorides, $ArCMe_2Cl$, (relative to the *p*-H analogue) when placed in the para position of the aromatic ring. These groups have traditionally been thought of as carbocation destabilizing groups. They are also considered carbanion stabilizing groups. Table I summarizes σ^+ values for a variety of groups E, most of which will be dealt with in this review.

A bit of historical perspective is also quite appropriate before proceeding. Even before the concept of carbocationic intermediates was developed, reactions were described in the literature which can now be recognized as proceeding by way of cations substituted with electron-withdrawing groups. For example, McKenzie and Clough[11] reported in 1910 that the optically active α-chloro acid **6** readily hydrolyzed in aqueous solution at room temperature to give the completely racemic α-hydroxy acid **7**. It now seems quite reasonable to suggest that the intermediacy of the carboxy substituted cation **8** accounts for the racemized product. While no attempt has been made to exhaustively survey the early literature for reactions that proceed by way of electronegatively substituted carbocations, undoubtedly many such examples exist.



6 7 (racemic) 8

TABLE I. Substituent Constants for Various Groups

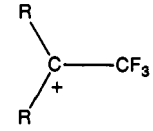
substituent	σ^+ (σ_p)	substituent	σ^+ (σ_p)
p-H	0.000 (0.000)	*p*-$PO(OEt)_2$	0.505 (0.52)
p-CF_3	0.596 (0.54)	*p*-$PS(OEt)_2$	0.431
p-CN	0.659 (0.660)	*p*-$SOCH_3$	0.414
p-COPh	0.406	*p*-SOPh	0.416
p-CO-*t*-Bu	0.293	*p*-SO_2CH_3	0.697 (0.72)
p-CO_2CH_3	0.466	*p*-SO_2Ph	0.670
p-CO_2H	0.399	*p*-NO_2	0.790 (0.778)
p-$CONMe_2$	0.24	*p*-$CSNMe_2$	−0.01

TABLE II. Hammett ρ^+ Values for Hydration of Various Alkenes

substrate	ρ^+	ref
$ArC(CF_3)=CH_2$ (10)	−4.0	12
$ArCH=CH_2$ (13)	−3.6	13
$ArC(CH_3)=CH_2$ (14)	−2.9	14
$ArC(OAc)=CH_2$ (15)	−1.9	15

II. The α-Trifluoromethyl Cation

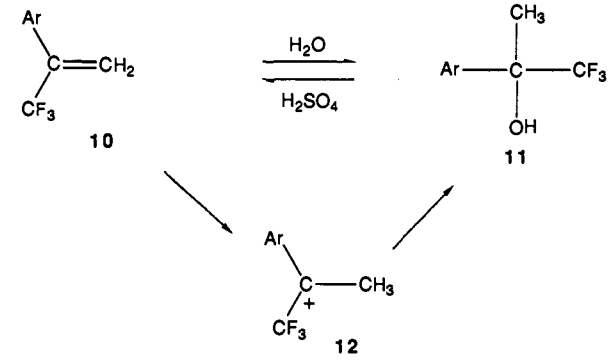
The trifluoromethyl group is one of the most potent electron-withdrawing groups as reflected by Hammett substituent constants. Placing this group directly on a cationic center, as in **9**, would appear to represent a formidable task. Nonetheless numerous studies have now firmly established such cations as viable and fascinating intermediates.



9

A. From Alkene Protonation

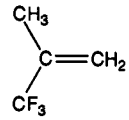
The Tidwell group has carried out extensive studies involving cations of general type **9**. One of the first studies involved protonation of alkenes **10** in sulfuric acid solutions of relatively high acidity.[12] The alkenes **10** underwent acid-catalyzed hydration via rate limiting formation of the cationic intermediates **12**. Rates were dramatically slower than those of the α-methyl styrenes or styrenes. Hammett ρ^+ values for protonation of **10**



10 11 12

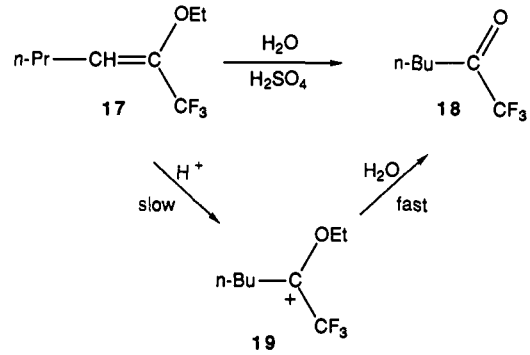
and related substrates are listed in Table II. The ρ^+ value of −4.0 for **10** is larger than those of analogues **13**–**15** and these ρ^+ values show an increased response of the aryl substituent as the intrinsic stability of the cationic intermediate decreases. These ρ^+ values support the suggestion that the cation **12** is destabilized by the α-CF_3 substituent. These ρ^+ values are, however, distinctly smaller than those obtained when the same cations are generated in a solvolytic fashion. The differences in ρ^+ values are also small and it can be con-

cluded that ρ^+ values determined from alkene protonation are not a very sensitive probe for intrinsic carbocation stability. Attempts to observe protonation of the alkene **16** were unsuccessful.[12]



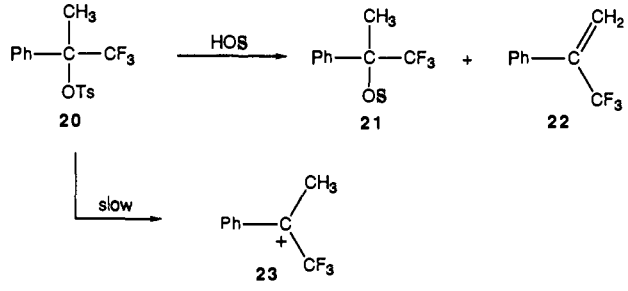
16

Hydration of the alkene **17** has also been studied in aqueous sulfuric acid.[16] This substrate is the least reactive enol ether studied to date with respect to acid-catalyzed hydration. The low reactivity of **17** reflects the electron-withdrawing properties of the α-CF_3 group. If one assumes that the effects of the OEt substituent and the CF_3 group are additive, then a γ^+ value of 4.49 can be calculated for a CF_3 group directly attached to a cationic center.



B. From Solvolysis Reactions

A variety of α-CF_3-substituted cations have been generated by the solvolytic route. The tosylate **20** solvolyzes in a variety of solvents to give mixtures of substitution and elimination products **21** and **22**.[17] Large rate increases are seen with increasing solvent ionizing power. Figure 1 shows a correlation of solvolysis rates of **20** in various solvents with rates of 2-adamantyl tosylate (Y_{OTs} values) in the same solvents. This Winstein–Grunwald plot has an m value of 1.01. Methyl CD_3 isotope effect studies gave an α-CH_3/α-CD_3 isotope effect ranging from 1.26–1.63. Added salts gave modest rate increases as would be expected for a reaction proceeding via a cationic intermediate. These studies all point to rate limiting formation of the α-CF_3 substituted cation **23**.



Substituent effect studies[18] on substituted analogues **24** also pointed to rate-limiting formation of an α-CF_3-substituted cation **25**. The Hammett–Brown ρ^+ value of −7.5 (−6.09 using the Yukawa–Tsuno treatment) suggested a cationic intermediate with high electronic demand on the aryl group substituent. The ρ^+ value for the corresponding bromides was −10.3 and

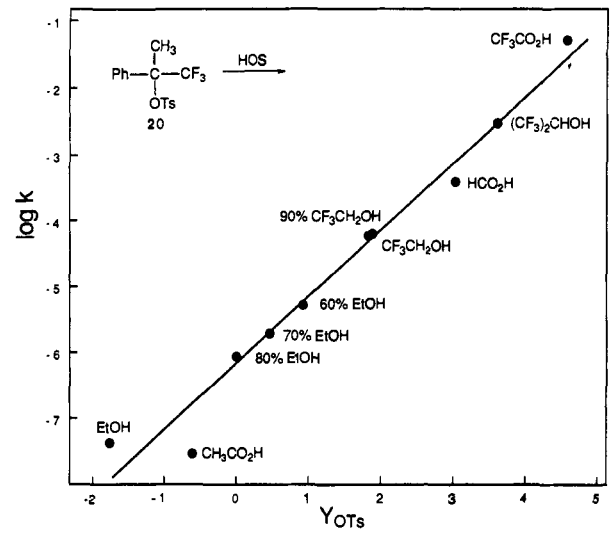
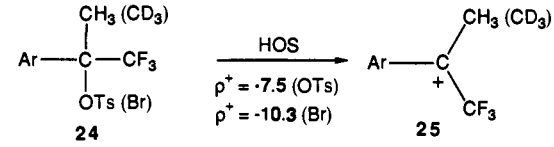


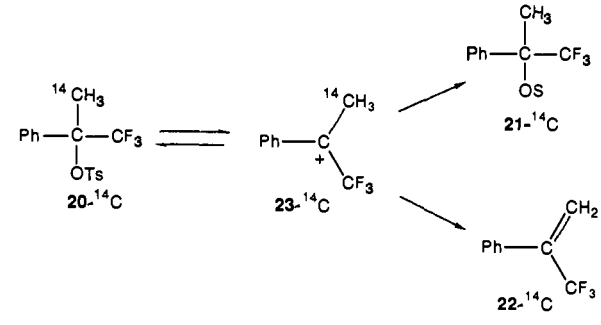
Figure 1. A plot of log k for solvolysis of **20** vs Y_{OTs} values.

also suggests a cationic intermediate with extremely high electron demand.[18c] The α-CH_3/α-CD_3 isotope effect in solvolyses of **24** was shown to be substituent dependent, ranging from 2.13 for the m-Cl derivative to 1.38 for p-H to 1.04 for the p-CH_3 derivative.[19] On the basis of these isotope effects, it was proposed that the contribution of the α-methyl group to stabilization of **25** varies with the aryl substituent. The possibility remains that cation formation may be reversible and elimination becomes rate determining in systems that show larger isotope effects.



24 **25**

A ^{14}C labeling study on **20**-^{14}C provides additional insight into the solvolysis of **20**.[20] The isotope effect, $k(\mathbf{20})/k(\mathbf{20}\text{-}^{14}C)$, was 1.008 ± 0.002. There should be no isotope effect if ionization were completely rate limiting. There should also be no isotope effect in the capture of **23** with solvent. It was found that, on incomplete reaction of **20**-^{14}C, radioactivity in the recovered unreacted tosylate exceeded the original radioactivity in **20**-^{14}C. This was presumably a result of an isotope effect (estimated at 1.05) in the proton-loss step leading to the 15% elimination product. This would increase the radioactivity in the cation **23**-^{14}C. Internal return would result in increased radioactivity in recovered **20**-^{14}C. This provides evidence that formation of **23** is at least partially reversible. If ionization were completely irreversible, then recovered tosylate would retain the same radioactivity as in the starting tosylate **20**-^{14}C.



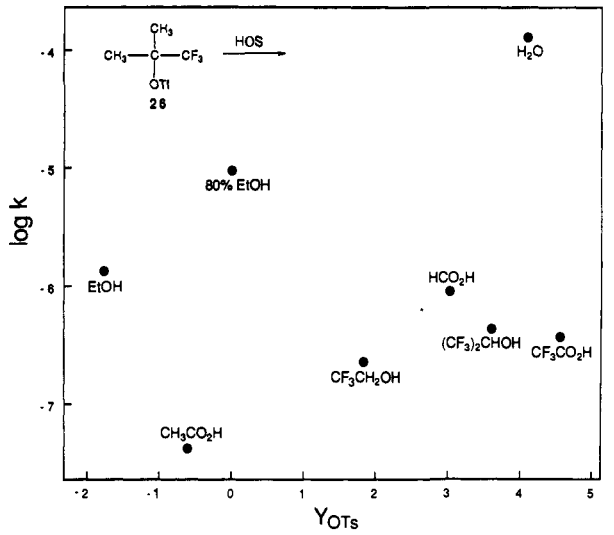
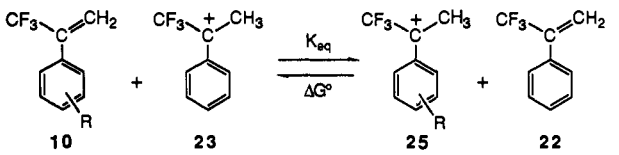


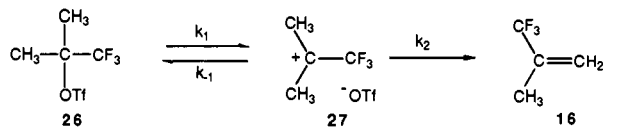
Figure 2. A plot of log k for solvolysis of **26** vs Y_{OTs} values.

Although this section deals with the solvolytic generation of α-CF_3 carbocations, a gas-phase study of Tsuno et al. is pertinent.[21] The relative stabilities of ions **25** in the gas phase (as determined by equilibrium constants and $\Delta G°$ values) were studied using pulsed ion cyclotron resonance mass spectrometry. Attempts to correlate stabilities of **25** with gas-phase σ^+ values led to deviations from linearity. Cations **25** that contained electron-donating groups such as p-CH_3, p-SCH_3, and p-OCH_3 were more stable than predicted on the basis of σ^+ values. This indicated greater stabilization of **25** by the stronger para π-donor substituents than in the analogous cumyl cations ($ArCMe_2^+$). The results were also analyzed in terms of the Yukawa–Tsuno equation, $\log (k/k_0) = \rho(\sigma° + r\Delta\sigma_R^+)$.[22] The value of r for **25** was 1.40, which is considerably larger than the defining value of 1.00 for the cumyl cation. This r value also indicates that there is a greater resonance stabilizing contribution in **25** than in the cumyl cation.



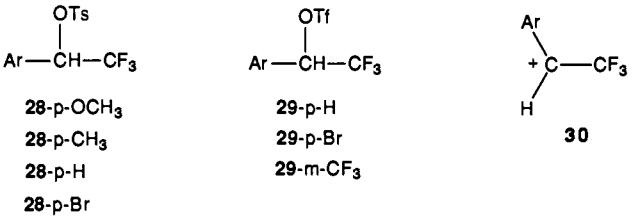
10 **23** **25** **22**

The triflate **26** has been solvolyzed in a variety of solvents and in all cases, gives exclusively the elimination product **16**.[23] Rates are 10^6 to 10^4 slower than those of isopropyl triflate in the same solvents. The solvent effect (Figure 2) is decidedly different from that of **20**. The rate spread is rather small and there is no correlation with 2-adamantyl tosylate solvolysis rates. Both solvent ionizing power and solvent nucleophilicity/basicity are important in determining rate. Significant rate increases are observed when basic salts such as NaOAc or NaN_3 are added while the addition of sodium chloride gives smaller rate increases. Methyl CD_3 isotope effects in various solvents give an average value of $k(\mathbf{26})/k(\mathbf{26}\text{-}d_3) = 1.78$. Deuteration of the second methyl group resulted in an average value of $k(\mathbf{26})/k(\mathbf{26}\text{-}d_6)$ was 3.80 which suggests a primary isotope effect. On the basis of these data, it was concluded that solvolysis of **26** proceeds via a reversibly formed cationic intermediate **27**, which undergoes rate-limiting proton loss induced by solvent or added base.



26 **27** **16**

The secondary benzylic systems **28** and **29** have also been studied under solvolytic conditions, where simple substitution products were produced.[24] Solvolysis rates of the tosylates **28**-p-OMe, **28**-p-CH_3, and **28**-p-H correlated with Y_{OTs} solvent ionizing power parameter with m_{OTs} values of 0.76, 0.94, and 0.79, respectively. The triflate derivative **29**-p-H gave a poor correlation with Y_{OTs} values. However correlation of rates of **29**-p-H with Y_{OTf} values (based on solvent effects on 7-norbornyl triflate solvent effects) gave a much improved correlation and an m_{OTf} value of 0.84. These solvent effects were interpreted in terms of rate-limiting formation of the secondary benzylic α-CF_3-substituted cations **30**. Hammett ρ^+ values were somewhat solvent dependent and ranged from of −6.7 in CF_3CO_2H to −10.1 in HOAc and 80% EtOH. The triflate derivatives **29** gave a ρ^+ value of −7.4 in CF_3CO_2H. These substituent effects indicated a very strong demand for stabilization in the transition state for formation of cation **30**.

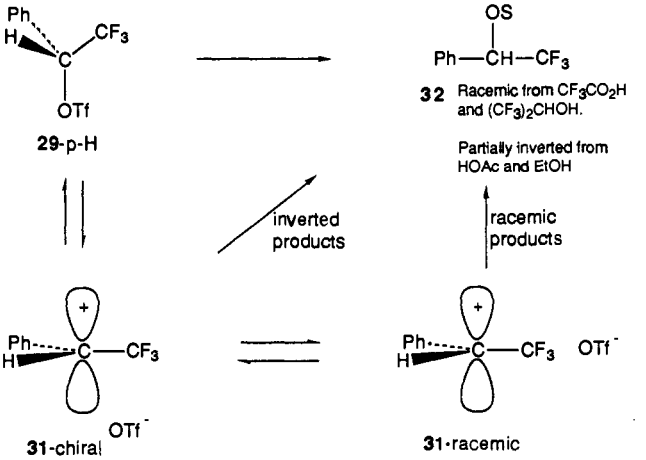


28-p-OCH_3
28-p-CH_3
28-p-H
28-p-Br

29-p-H
29-p-Br
29-m-CF_3

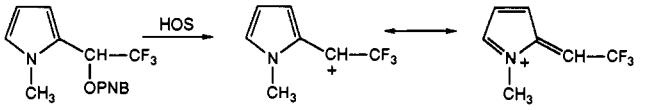
30

The stereochemistry of solvolytic substitution reactions of triflate **29**-p-H was studied in detail.[24] Solvolysis of the optically active triflate gave racemic products in CF_3CO_2H and $(CF_3)_2CHOH$. A substantial amount of inverted product (41%) along with racemized product (59%) were formed in acetolysis of **29**-p-H. Ethanolysis also gave substantial inversion. Racemization rates (k_α) in CF_3CO_2H and $(CF_3)_2CHOH$ exceeded product formation rates as determined by UV spectroscopy (k_{UV}). These observations suggest formation of an ion pair **31** which undergoes racemization, return to the covalent triflate, and formation of racemized product.



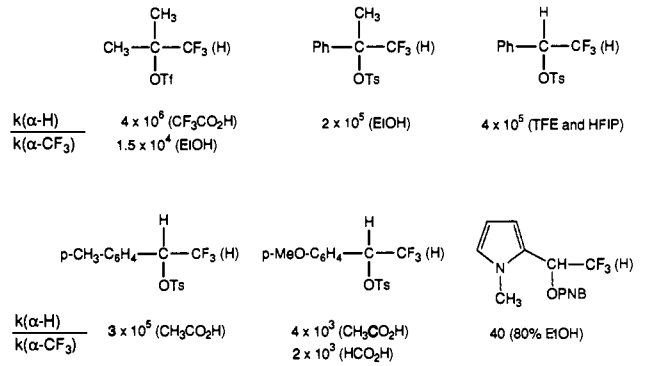
The p-nitrobenzoate derivative **33** has been solvolyzed and rates have been determined in six solvents.[25]

This *p*-nitrobenzoate is only 40 times less reactive than the α-H analogue. This extraordinary reactivity of the α-CF_3 system **33** is indicative of a cationic intermediate with extensive charge delocalization into the pyrrole ring as in **34b**.



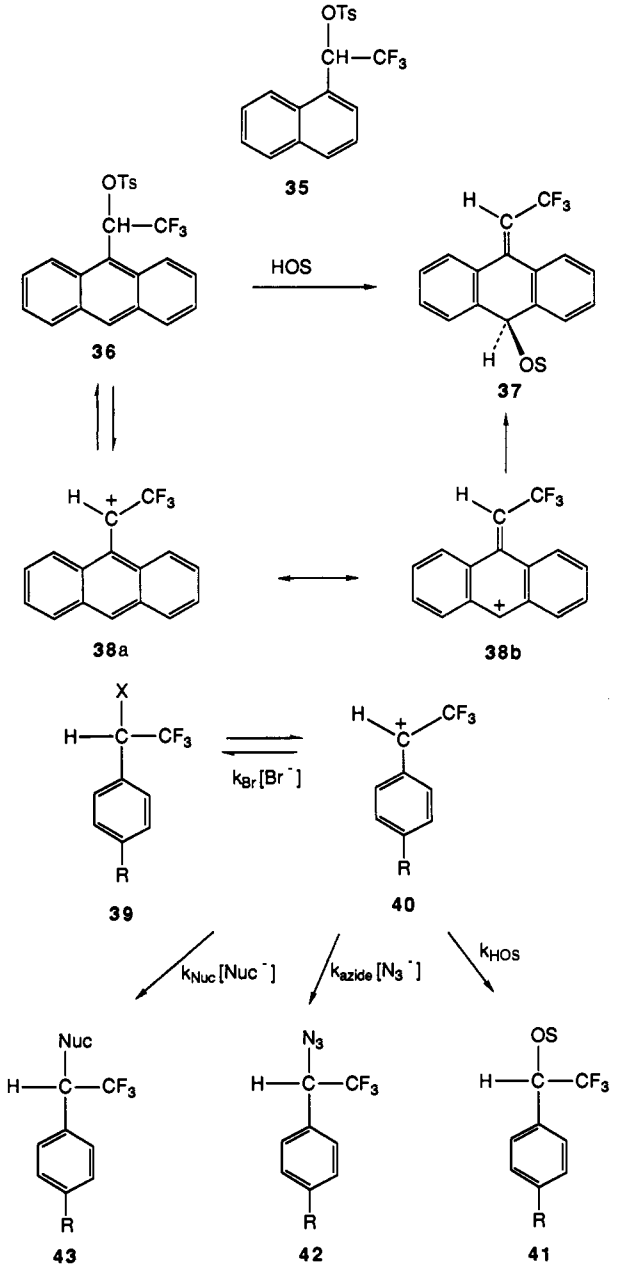
33 **34a** **34b**

Shown below are a summary of the rate effect of α-CF_3 relative to α-H analogues on solvolytic processes proceeding via cationic intermediates. The rate retarding effect of the CF_3 group ranges from 4×10^6 down to 40, depending on the system studied. From these data it is clear that the effect of the α-CF_3 is not constant, but depends on a variety of factors. One of the most important factors appears to be the extent of charge delocalization into adjacent conjugating systems.



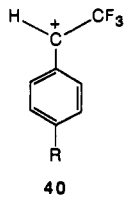
The α-CF_3-substituted 1-naphthyl and 9-anthryl systems **35** and **36** solvolyze with m_{OTs} values of 0.94 and 0.64, respectively.[26] The 1-naphthyl system **35** gave simple substitution products in HOAc and EtOH. The polarimetric rate constant of (*R*)-(−)-**36** in CF_3CH_2OH is 1.3 times greater than the rate of product formation. The system **36** gave ring-substituted products **37** in EtOH, HOAc, and CF_3CH_2OH. These data are interpreted in terms of aryl delocalized α-CF_3-substituted cations which can return to covalent starting sulfonate ester or form products by solvent attack at the cationic center (or a ring carbon in the case of **36**). In the case of **36**, the electron-withdrawing α-CF_3 group induces attack at the ring position with ultimate formation of **37**.

Extensive studies have been carried out by Richard on the series of derivatives of general structure **39** where the leaving group X represents tosylate, mesylate, bromide, and *p*-nitrobenzoate.[27] In the case of X = Br, solvolysis of the *p*-OCH_3 derivative in aqueous trifluoroethanol led to a substantial common ion rate suppression when bromide ion was added to the solvolysis mixture. Addition of other anionic nucleophiles (such as N_3^- and I^-) led to the corresponding azide and iodide substitution products **42** and **43** (Nuc = I). In the case of the electron-donor *p*-NMe_2, *p*-OCH_3, and *p*-SMe substituents, rates were independent of added azide ion or iodide ion. The amount of substitution products **42** and **43** ranged from 30 to 100%. Solvolysis of **39** (R = *p*-NMe_2) led to complete formation of **42** (R = *p*-NMe_2) and no solvolysis product **41** when azide concentration was 0.5 M.

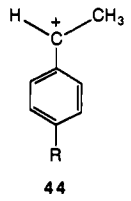


The common ion rate suppression provides convincing evidence for the involvement of a reversibly formed α-CF_3 cation **40** which can react with bromide ion to reform covalent bromide **39**, or with solvent to form the substitution product **41**, or with added nucleophiles to give substitution products **42** and **43**. These studies also give insight into the nature of cations **40**. Ratios of k_{azide}/k_{HOS} can be determined from ratios of **43** to **42**. The cation **40** (R = *p*-NMe_2) is the most selective in its ability to discriminate between azide ion and solvent. Selectivity decreases as the substituent in **40** becomes less cation stabilizing, as revealed by k_{azide}/k_{HOS} ratios. This is expected on the basis of selectivity–reactivity considerations. If one assumes that rates of reaction of cations **40** with azide ion are diffusion controlled ($k_{azide} = 5 \times 10^9\ M^{-1}\ s^{-1}$), then rates of reaction of cations **40** with solvent HOS can be calculated. These values of k_{HOS} in 50% aqueous trifluoroethanol vary from 6×10^9 to 800 s^{-1} as R varies from *p*-CH_3 to *p*-NMe_2.

Selectivities in reactions of the α-CF_3-substituted cations **40** with nucleophiles were very similar to those of the methyl analogue **44**, despite the much lower



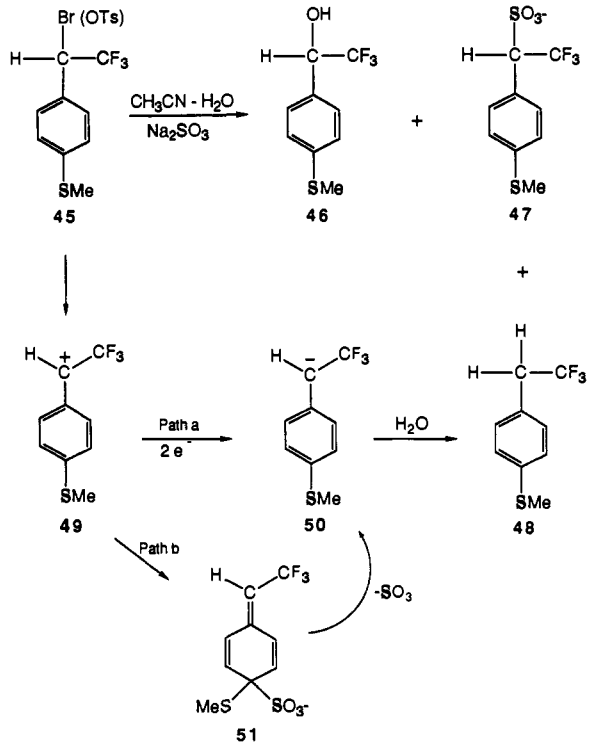
R in 40	k_{azide}/k_{HOS}
p-CH_3	0.80
p-OCH_3	95
p-SCH_3	400
p-NMe_2	6×10^6



40 44

stability of **40**. This is unexpected on the basis of the reactivity–selectivity principle where less-stable cations are expected to be more reactive and less selective. The unexpectedly slow rate of reaction of cations **40** with solvent (determined using the diffusion controlled value of k_{azide} for reaction of **40**) was suggested to result from a large resonance interaction in **40** which delocalizes charge away from the benzylic carbon. This would increase the barrier for solvent capture since much of the resonance stabilization would be lost in the transition state as the nucleophile interacts with **40**. Therefore **40** was not unusually reactive with solvent. Large electrostatic or homoconjugative barriers to capture of **40** with solvent or added nucleophile (analogous to the interactions that cause slow S_N2 reactions of α-CF_3 systems) could also account for the unexpected kinetic stability of **40**.

Solvolysis of bromide or tosylate **45** in aqueous acetonitrile with added sodium sulfite gave the products **46–48** in a process which was zero order in added sulfite.[28] Formation of the cation **49**, followed by capture of water or added sulfite ion accounts for the products **46** and **47**. Two plausible mechanisms were suggested for the formation of the novel reduction product **48**. The first mechanism involved two single electron transfers to the cation **49** to give the anion **50**, followed by protonation. Alternatively, **48** could arise by capture of sulfite ion by **49** at the para position. Extrusion of neutral SO_3 from **51** would also give **50** and subsequently the reduction product **48**.



The cation **49** (as well as the *p*-OCH_3 analogue) has also been captured by various amines to give the

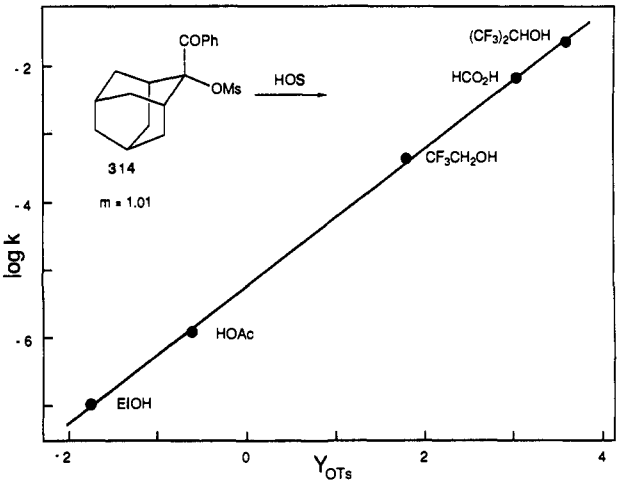
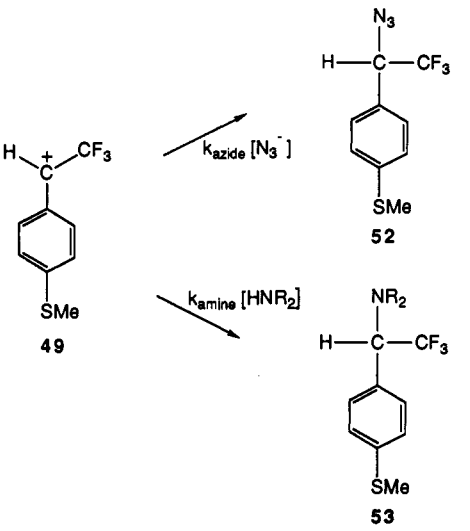
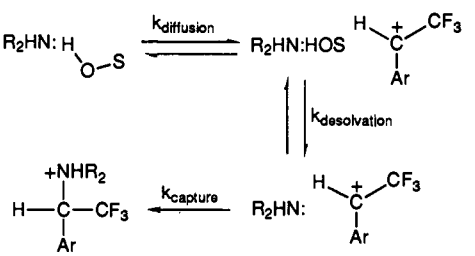


Figure 3. A plot of log k for solvolysis of **314** vs Y_{OTs} values.

products **53** as well as by azide ion to give **52**.[29] Values of k_{azide}/k_{amine} were calculated from **52**:**53** product ratios determined in competition experiments. Values of

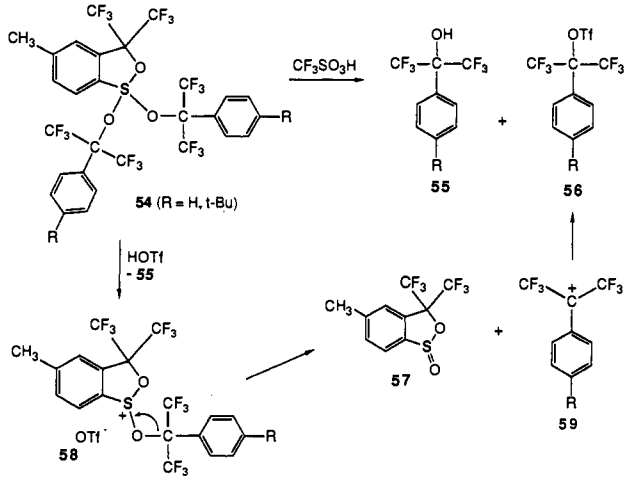


k_{amine} were calculated using the diffusion limited value of 5×10^9 M^{-1} s^{-1} for k_{azide}. Values of k_{amine} for various amines decreased somewhat with increasing amine basicity, i.e. $CF_3CH_2NH_2$ gave more amine product than $CH_3CH_2NH_2$. This unexpected behavior constituted evidence that the rate-limiting step in reaction of cation **49** with amines is not diffusion together of the cation and the solvated amine. Instead it is proposed that desolvation of the amine (freeing up of the electron pair for reaction with cation) is rate limiting. The less basic amines desolvate more readily and hence react faster with **49**.

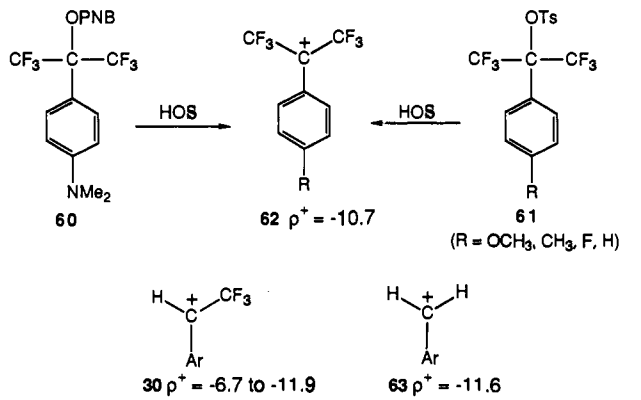


One of the most remarkable discoveries was the finding that cations containing two α-CF_3 groups could be generated. This type of intermediate, first postu-

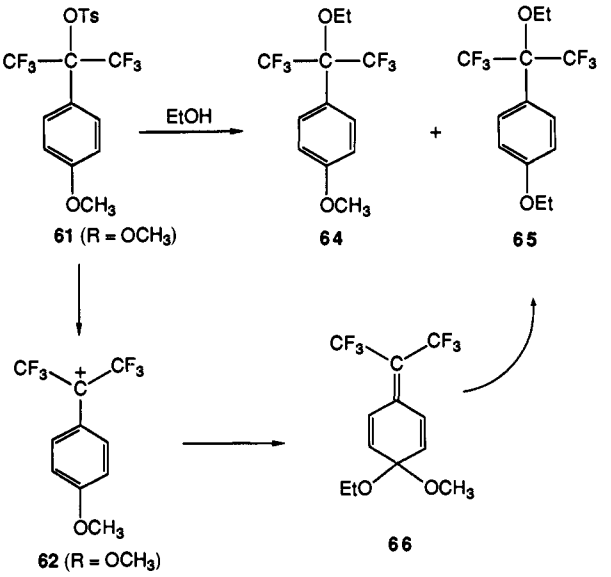
lated by Martin and Astrologes,[30] was formed in the reaction of the trialkoxysulfurane **54** with triflic acid, which led to the products **55–57**. The origin of the triflate product **56** was the cation **59**, which was produced by cleavage of the sulfonium triflate **58**. The triflate **56** was also found to solvolyze when heated in ^{18}O-enriched water to give a ^{18}O-labeled alcohol **55**, presumably via the same cationic intermediate **59**.



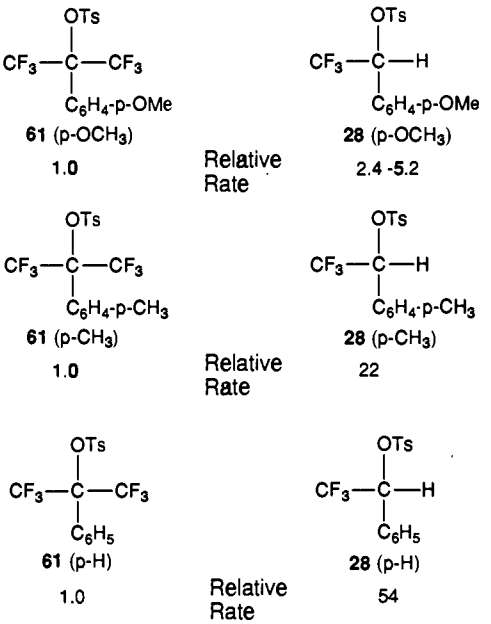
Detailed solvolytic studies have been carried out by the Tidwell group on the *p*-nitrobenzoate **60** and the tosylates **61**, which give simple substitution products when reacted in a variety of solvents.[31] The Hammett ρ^+ value for these systems is −10.7 and covers a reactivity range of 10^{19}. This confirms the intermediacy of intermediates of type **62**, where two potent electron-withdrawing groups are directly attached to a formal cationic center. The ρ^+ value is not substantially larger than for the α-H analogues **28** and **29** where values range from −6.7 to −11.9. The ρ^+ value for $ArCH_2OMs$ in $(CF_3)_2CHOH$ solvent (where **63** is the cationic intermediate) is −11.6.[32] This has led to the suggestion that there is an upper limit to ρ^+ values in solvolytic reactions which is about −10 to −12. In cations such as **30**, there is extensive charge delocalization to the para position. Hence placement of a second electron-withdrawing group at the cationic center as in **62** therefore has little effect on the response of the substituent or on the ρ^+ value.



Further evidence for the extensive charge delocalization in **62** comes from product studies on **61** (R = OCH_3) in ethanol which gave a 50/50 mixture of **64** and **65**. The origin of the product **65** was suggested to be competitive solvent capture of **62** at the para position of the ring. Subsequent nucleophilic attack of solvent on **66** at the carbon bearing the CF_3 groups would lead to the observed product **65**. Studies in CD_3OH lead to the same conclusions.

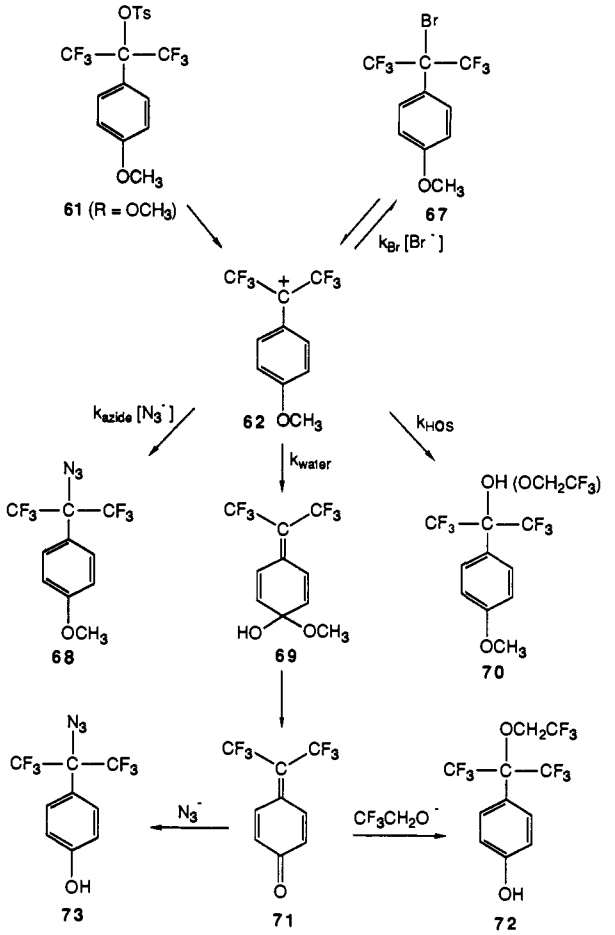


α-H/α-CF_3 rate ratios in solvolyses of **61** are truly remarkable. They are substantially less than commonly observed values in the range of 10^5–10^6. The tosylate **61** (*p*-OCH_3) is only 2.4 to 5.2 times less reactive than the α-H analogue **28** (*p*-OCH_3), i.e. replacement of hydrogen with a second CF_3 group has an almost negligible rate effect. In the toluoyl system **61** (*p*-CH_3) the



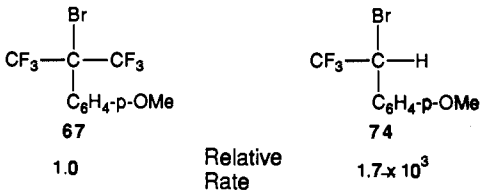
rate-retarding effect of the second CF_3 group is a factor of 22, and in the unsubstituted system **61** (*p*-H) the effect increased further to a factor of 54. These rate data provide further evidence for extensive charge delocalization into the aromatic ring. In the transition state for solvolysis of **28** (*p*-OCH_3) or **61** (*p*-OCH_3), the developing charge is substantially on the aromatic ring and hence the additional CF_3 group has a negligible rate-retarding effect. The rate-retarding effect of the second CF_3 group in **61** (*p*-CH_3) and **61** (*p*-H) increases somewhat as the ability of these aromatic rings to delocalize charge decreases.

Richard et al. have also carried out solvolytic studies on tosylate 61 (p-OCH_3) and on the bromide analogue 67 which give further insight into the nature of the cationic intermediate.[33] Solvolysis of the tosylate in aqueous trifluoroethanol with added azide gave the alcohol and ether 70 along with the azide 68. Also formed was the quinone methide 71 which could be observed spectroscopically. Subsequent reaction of 71 with trifluoroethanol or azide ion under the reaction conditions led to formation of the phenols 72 and 73. These products are proposed to arise from capture of the cation 62 with azide ion or solvent. Reaction of water at the para position of 62 would lead to 71 which is the source of 72 and 73. Ratios of 68/70 could be used to determine selectivities of the proposed cationic intermediate 62.

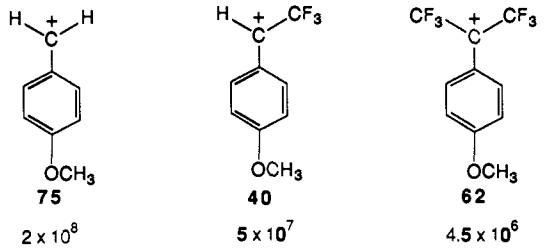


The tosylate/bromide rate ratio, $k(61)/k(67)$ was 9 × 10^4, a value much larger than "normal" values of about 5000. This was considered evidence that reaction of the tosylate 61 (p-OCH_3) is accelerated by relief of ground-state strain. The much larger α-H/α-CF_3 ratio of 1.7 × 10^3 seen for bromides 74 and 67 also suggests that ground-state strain may be important in determining the rate of solvolysis of 61 (p-OCH_3). X-ray crystallographic data for 61 (p-H) also showed distortions from ideal tetrahedral geometries which may be indicative of a strained ground state.[34]

Selectivities (k_{azide}/k_{HOS}) of cations 75, 40, and 62 were also used to calculate rate constants for reaction of these cations with solvent (50% aqueous trifluoroethanol) by assuming diffusion controlled rates (5 × 10^9) of reaction with azide ion. Increasing CF_3 substitution decreases rate of reaction with solvent. It was proposed

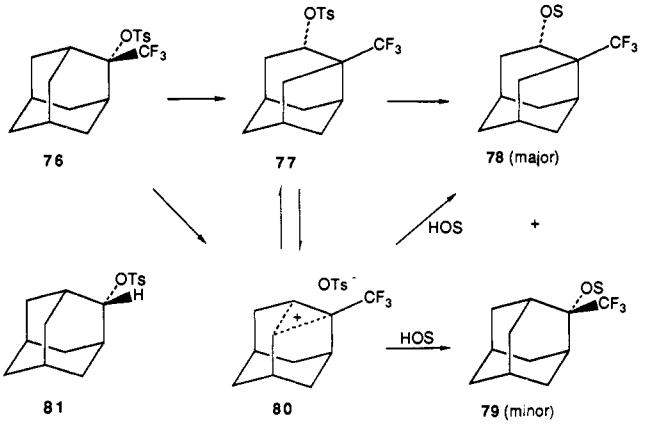


that this effect was partly due to the α-CF_3 groups which sterically hinder the addition of solvent to the cations. Charge delocalization into the aromatic rings of 40 and 62 was another factor contributing to the decreased rates of reaction of these cations with solvent.

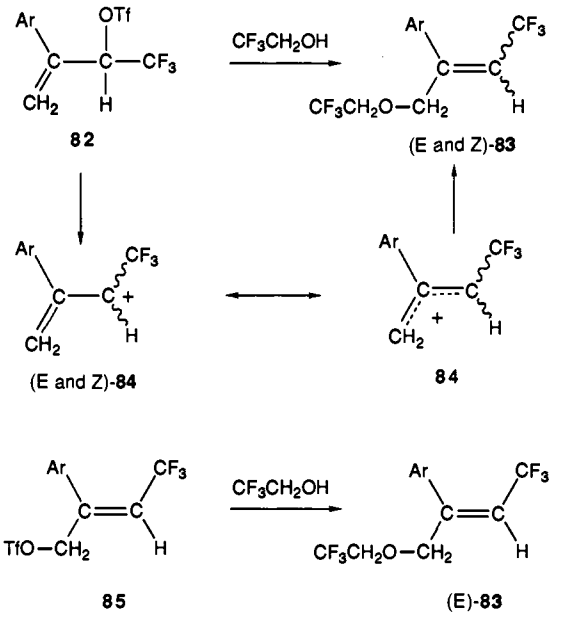


Rate Constants for Solvent Addition in 50% Aqueous CF_3CH_2OH

The 2-adamantyl system 76 solvolyzes to give initially the tosylate 77, a product of internal return.[35] Under the reaction conditions, 77 is subsequently converted to the products 78 and 79. Tosylate 76 has an unexpectedly high reactivity. 2-Adamantyl tosylate (81) is only 1.37 to 2.84 times more reactive, depending on solvent. This is the lowest α-H/α-CF_3 value observed to date. A mechanism involving the ion pair 80 has been proposed. The remarkably high reactivity of 76 is attributed to electron donation from the C_3–C_4 σ-bond (a k_Δ process) and also to relief of ground-state strain in 76. It is estimated that 6.5 kcal/mol of strain is relieved as the congested CF_3 group in 76 moves into a less-crowded environment in the solvolysis transition state.

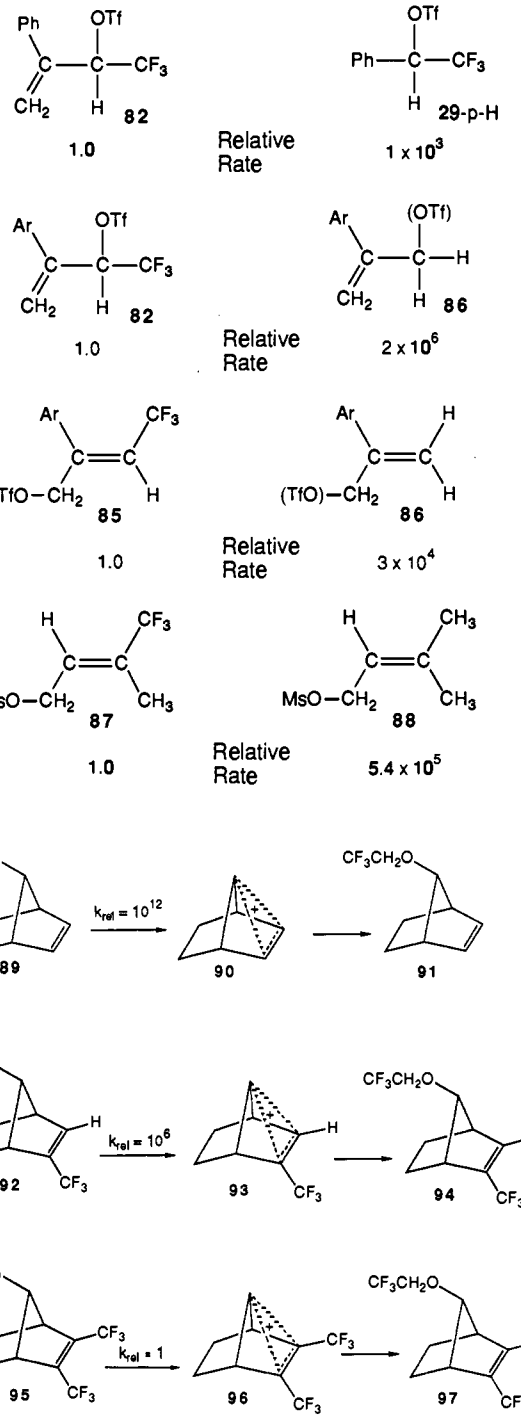


The allylic triflates 82 have been examined by Gassman and Harrington.[36] Trifluoroethanolysis gave only the rearranged products 83. The proposed mechanism involves the allylic α-CF_3-substituted cation 84. Charge distribution in the cation 84 determines the position of solvent capture, which occurs exclusively at the allylic position not bearing the CF_3 group. The allylic triflate 85 also solvolyzes via the same cationic intermediate (E)-84 to give exclusively (E)-83. These allylic cations showed no tendency to undergo electrocyclic ring closure to form aryl-substituted cyclopropyl cations.



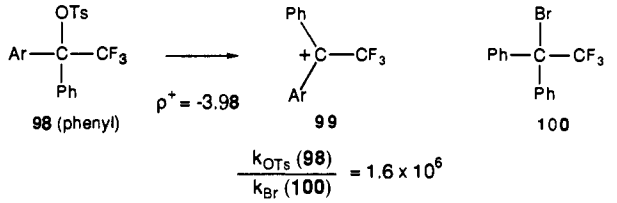
The rate effects of the CF_3 groups have been determined in solvolyses of **82**. The triflate **82** (Ar = Ph) is about 10^3 times less reactive than the closely related system **29**-*p*-H. In view of the fact that vinyl and phenyl often have similar rate effects on reactions proceeding via cationic intermediates, this rate ratio is of interest. Under conditions of increased electron demand, the phenyl group is **29**-*p*-H appears to be more capable of charge delocalization than the vinyl group in **82**. The α-H/α-CF_3 rate ratio for **82** is about 2×10^6 as determined from the rate of **86** (extrapolated from the tosylate rate). This value might be a bit exaggerated since the trifluoroethanolysis rate of **86** is probably enhanced somewhat (by approximately a factor of 10) relative to a true k_c process. The substrates **85** were approximately 50–100 times more reactive than the isomeric triflates **82**. Corresponding α-H/α-CF_3 rate ratios are approximately 3×10^4. This compares to an earlier report by Poulter, Satterwhite, and Rilling,[37] where replacement of CH_3 with CF_3 slowed solvolysis rate of the allylic mesylate **87** by a factor of 5.4×10^5. This contrasted with S_N2 reactions on allylic systems, where substitution of CF_3 for the CH_3 group in the reaction of iodide ion with 1-chloro-2-butene actually led to a rate increase.[38]

The 4-methoxybenzenesulfonate esters **89**, **92**, and **95** have been studied in order to determine the effect of CF_3 substitution on double bond participation.[39] These substrates gave exclusively products of stereochemical retention when solvolyzed in CF_3CH_2OH. The CF_3 group in **92** retards solvolysis rate by a factor of 10^6 relative to **89** and the second CF_3 group in **95** gives a further rate retardation of 10^6. These data argue in favor of a symmetrical double bond interaction during ionization leading to the delocalized homoallylic cations **90**, **93**, and **96**. The cumulative effect of the CF_3 groups suggests that the cationic intermediates are not unsymmetrical rapidly equilibrating classical ions. Even the bis-CF_3-substituted system **95** appears to give the nonclassical ion **96**, as evidenced by the retained product. Despite this participation, **95** is 17 times less reactive than the parent saturated 7-norbornyl system.

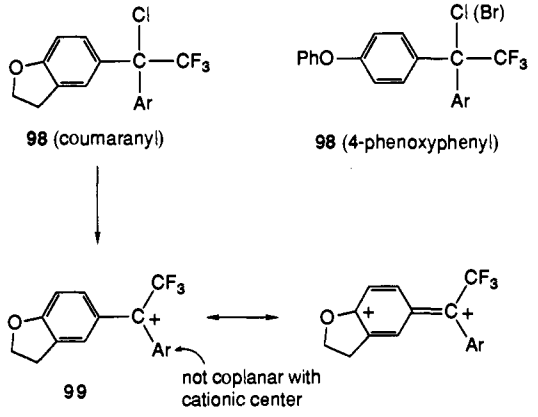


The diaryl-substituted tosylates **98**, where the aryl ring is substituted with electron-withdrawing groups, were solvolyzed.[40] The Hammett ρ^+ value was −3.98 and this value was considered small for an α-CF_3 system. The derivative **98** (Ar = *p*-$CF_3C_6H_4$) was slightly more reactive than **98** (Ar = *m*-$CF_3C_6H_4$), which was also unexpected on the basis of σ^+ values. These data, along with the unusually large tosylate/bromide rate ratio, k(**98**)/k(**100**), of 1.6×10^6, were taken as evidence for an unusually congested, sterically strained ground state in **98**. The low ρ^+ value arose from the inability of the aryl groups to become coplanar with the developing cationic center in **99**.

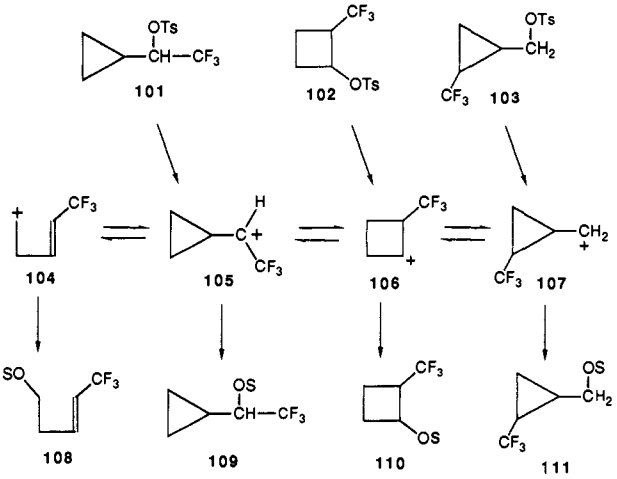
In order to shed further light on the suggestion that the aryl rings in cations such as **99** have difficulty achieving coplanarity, a series of diaryl substituted derivatives **98** (coumaranyl) and **98** (4-phenoxyphenyl)



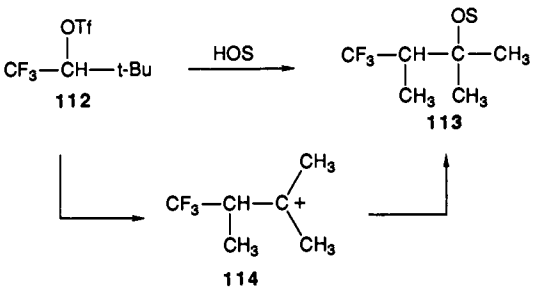
were solvolyzed.[41] The p-CF_3 derivatives were more reactive that the m-CF_3 derivatives. These inverse reactivities were interpreted in terms of cationic intermediates **99**, where charge delocalization involves mainly the strong electron-donating coumaranyl or the 4-phenoxyphenyl rings. A stronger cation destabilizing inductive effect by the m-CF_3 group resulted in lower reactivity in the m-CF_3 derivatives. A caution concerning interpretations using the Yukawa–Tsuno equation was presented.[41]



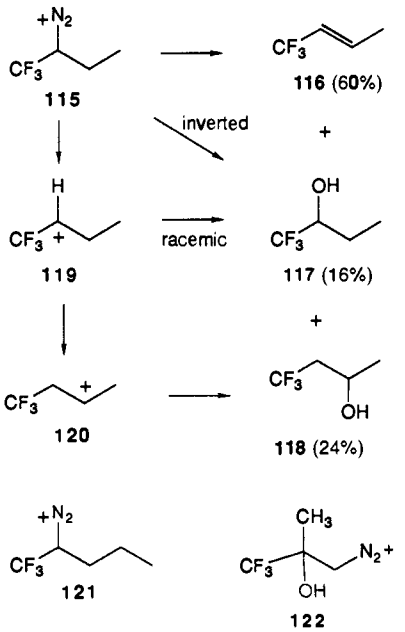
The cyclopropylcarbinyl tosylate **101** solvolyses to give varying amounts of rearranged products **108**, **110**, and **111**, and only traces of the unrearranged product **109**.[42] These products are derived from the α-CF_3-substituted cyclopropylcarbinyl cation **105** (which is undoubtedly stabilized by delocalization involving the adjacent cyclopropyl ring), which can rearrange to the cyclobutyl cation **106**, or the homoallyl cation **104**, or the cyclopropylcarbinyl cation **107**. This cyclopropylcarbinyl–cyclobutyl-homoallylic cation manifold can also be entered starting with the cyclobutyl tosylate **102** or the alternative cyclopropylcarbinyl tosylate **103**.



Solvolysis of the secondary triflate **112** gave exclusively rearranged products **113**.[43] Rates in different solvents correlated with those of 2-adamantyl triflate with an m_{OTf} value of 0.40. This relatively small response to solvent ionizing power and the rearranged products suggest a k_Δ mechanism, bypassing a discrete α-CF_3-substituted cation.



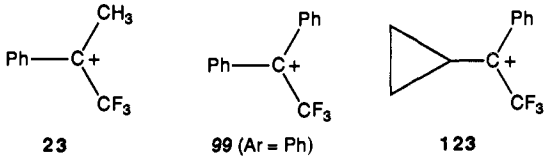
The possibility of generating simple secondary α-CF_3 cations has also been addressed by Kirmse.[44] Aqueous deamination of CF_3-containing amines gave products derived from the diazonium ions **115** and **121**. The diazonium ion **115** led to the elimination product **116** as well as the alcohols **117** and **118**. Studies on an optically active amine showed that the alcohol **117** was 70% inverted and 30% racemized. A study in D_2O also showed that the racemized **117** could not all be accounted for by racemization of **115** by way of a diazo compound. A plausible mechanism for solvolysis of **115** would involve the cation **119** as an intermediate, which could rearrange via a 1,2-hydride shift. The diazonium ion **121** also gave an unrearranged hydrolysis product, as well as products derived from hydride shifts. The substrate **122** gave only 1.4% 1,1,1-trifluoro-2-butanone (derived from a pinacol type rearrangement). These studies attest to the relative reluctance of simple secondary α-CF_3 cations to form and their propensity to rearrange via hydride shifts.



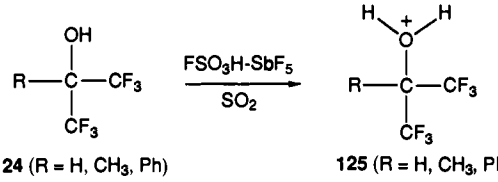
C. α-Trifluoromethyl Cations under Stable Ion and Nonnucleophilic Conditions

Before many of the detailed solvolytic studies were carried out on α-CF_3-substituted cations, the cations **23**, **99**, and **123** were generated by Olah and Pittman.[45] Reaction of the precursor alcohols with FSO_3H–SbF_5 in SO_2 at low temperature gave solutions of these cations under stable ion conditions. These ions are sufficiently stabilized by charge delocalization into the aryl

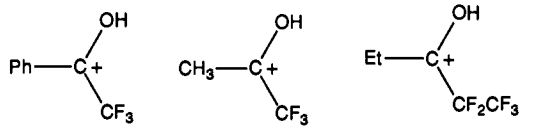
ring or the cyclopropane ring that they can be observed by NMR spectroscopy. ^{19}F spectra show that the CF_3 group in **23** is shifted by 24.8 ppm relative to the alcohol precursor, while in the more delocalized cations **99** and **123**, shifts relative to the precursor alcohols are decreased to 7.6 and 9.1 ppm, respectively. The alcohols **124** having two CF_3 groups are simply protonated under these conditions and do not ionize further to give stable carbocations. The ions **126–128** could also be observed in FSO_3H–SbF_5–SO_2 by protonation of trifluoroacetophenone, trifluoroacetone, and pentafluoroethyl ethyl ketone, respectively, at −60 °C.



23 **99** (Ar = Ph) **123**

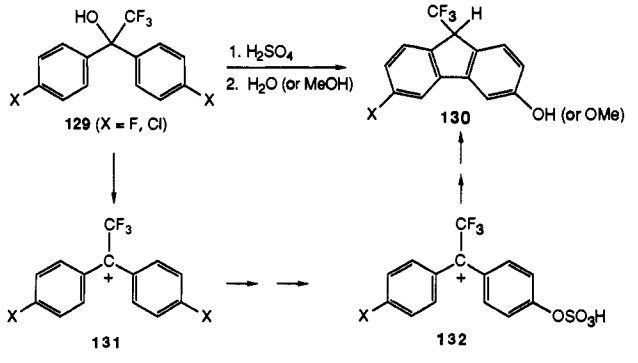


124 (R = H, CH_3, Ph) **125** (R = H, CH_3, Ph)



126 **127** **128**

One of the earliest studies in which an α-CF_3-substituted cation is proposed is the cyclodehydration of the *p*-fluoro- and *p*-chloro-substituted alcohols **129** in H_2SO_4, where which fluorenones **130** are produced.[46] These reactions are proposed to involve the cations **131**. It was proposed that one of the halogens can be replaced by solvent during the process. Cyclization, proton loss, and hydrogen migration gives the fluorene product.



129 (X = F, Cl) **130** OH (or OMe) **131** **132**

It has also been found that the unsubstituted alcohol **133** cyclizes in polyphosphoric acid to give **135**, presumably by an analogous mechanism involving electrocyclization of the ion **99**.[47] The ion **99** could also be generated under nonnucleophilic conditions by protonation of the alcohol **133** with H_2SO_4 in chloroform[48] or CF_3SO_3H in benzene.[49] In chloroform, a modest yield (25%) of the fluorene **135** was formed, while in benzene, **136** is formed (26–43% yield) along with the dimer **137** and trimer **138**. In benzene, the electrocyclization process which leads to **135** is apparently slow relative

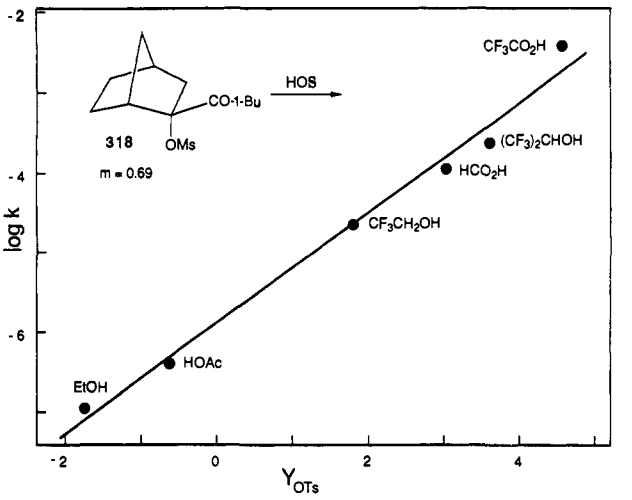
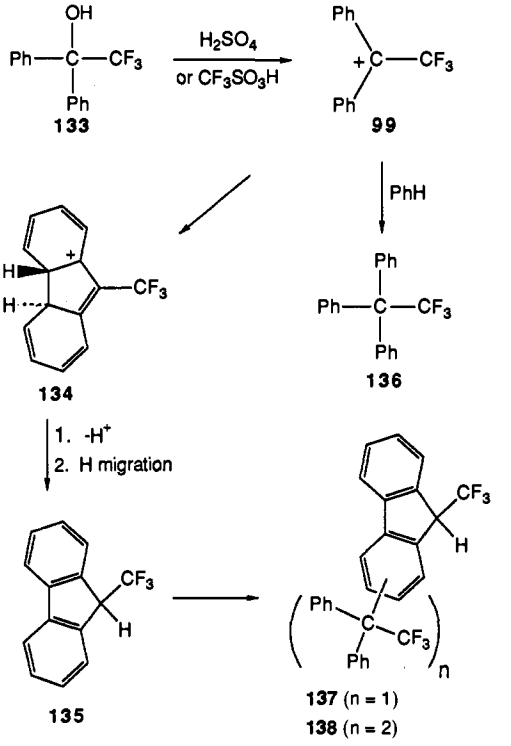


Figure 4. A plot of log k for solvolysis of 318 vs Y_{OTs} values.

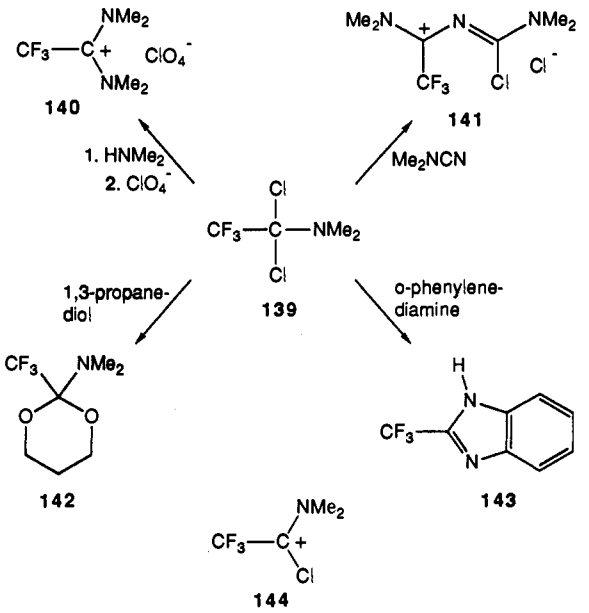
to further alkylation of the fluorene product. This accounts for the formation of **137** and **138**.



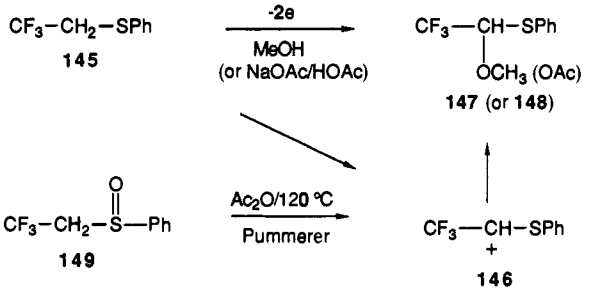
133 **99** **134** **136** **135** **137** (n = 1) **138** (n = 2)

D. α-Trifluoromethyl Cations in Synthetic Applications

A number of syntheses have been carried out which involve α-CF_3-substituted cationic intermediates. Among these are the development of methods for the introduction of functionality adjacent to the CF_3 group. Viehe has prepared a number of CF_3-substituted derivatives starting with (1,1-dichloro-2,2,2-trifluoroethyl)dimethylamine (**139**).[50] This α-chloro amine, which is a distillable liquid, reacted with dimethylamine to give, after ion exchange, the perchlorate derivative **140** as an isolable salt. Reaction with Me_2NCN led to the highly delocalized salt **141**, while reaction with 1,3-propanediol and phenylenediamine gave the acetal **142** and the heterocyclic product **143**, respectively. While the mechanism for these transformations was not explicitly discussed, the CF_3-substituted iminium cation **144** is a likely intermediate.

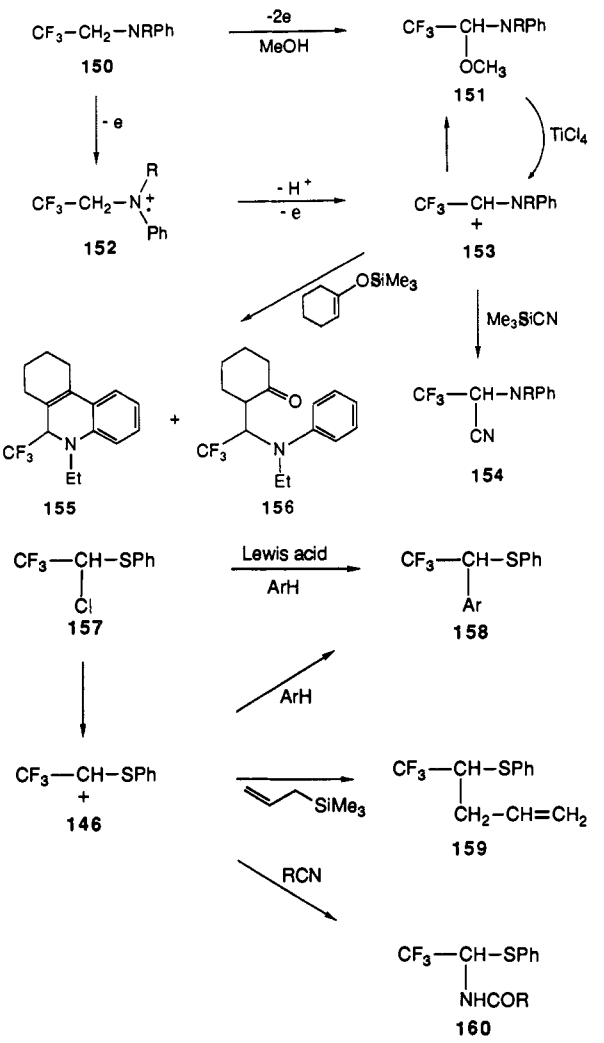


Fuchigama has prepared the methyl ether **147** and the acetate **148** by anodic oxidation of **145**.[51] These oxidations presumably involve the α-CF_3 cation **146**, which is trapped by nucleophile under the oxidation conditions. An alternative method, involving the Pummerer rearrangement of sulfoxide **149**, gave only a 42% yield of the acetate **148**. Unfortunately, Lewis acid promoted nucleophilic substitution reactions of **147** and **148** were not successful.

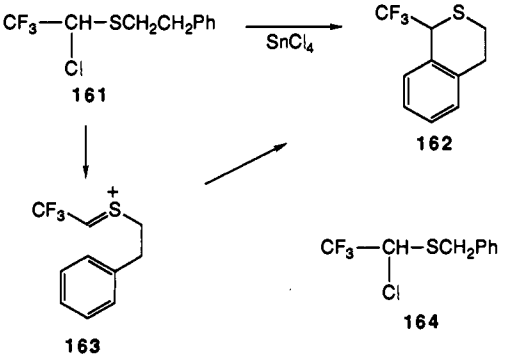


Anodic oxidation of the amines **150** in an alkaline methanol solution gave the α-methoxylated product **151**.[52] The radical cation **152** and the α-CF_3-substituted cation **153** (an iminium cation) are suggested intermediates. In contrast to the thiophenoxy analogue **147**, treatment of the methyl ether **151** with $TiCl_4$ regenerated the cation **153**, which could be trapped by carbon nucleophiles. Reaction with trimethylsilyl cyanide gave the nitrile **154**, while trapping with the silyl enol ether of cyclohexanone provided the heterocyclic compound **155** (43%) along with the amino ketone **156** (27%).

The α-chloro sulfide **157** (prepared by chlorination of **145**) can be used to generate the cation **146** under Lewis acid conditions, where **146** can be trapped by aromatic substrates.[53] Rates of consumption of **157** by arene proceeded in the order anthracene > toluene > benzene > chlorobenzene. This suggests that the arene may participate intermolecularly in the rate-determining step. Reaction of optically active **157** with naphthalene gave a racemic product, as well as racemized **157** when the reaction was interrupted short of completion. This argues in favor of the intermediate **146**. Allylation of **146** (to afford **159**) was accomplished by treatment with allyltrimethylsilane, and reaction with various nitriles resulted in the formation of amides **160**.

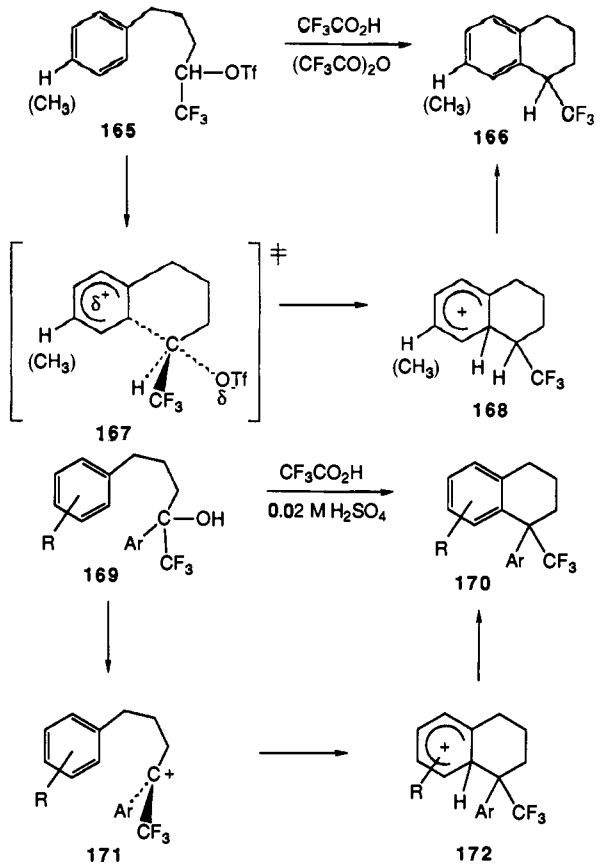


Intramolecular arylation of the sulfur-stabilized α-CF_3 cation **163** derived from **161** was observed.[53] Only intermolecular reactions were seen in the system **164** containing one less methylene group.

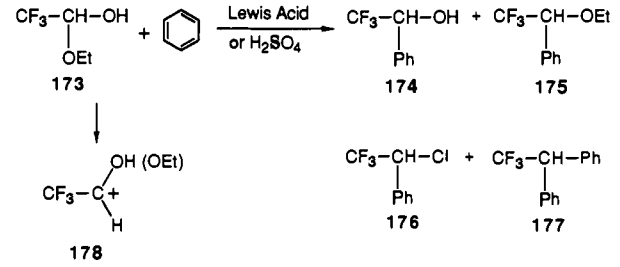


The secondary triflates **165** lead to the CF_3-substituted tetralins **166** under trifluoroacetolysis conditions.[54] These cyclizations are proposed to occur via k_Δ processes involving aryl ring participation since the discrete secondary α-CF_3 cation is presumably quite unstable. 4-Chloro- or 4-methoxy-substituted analogues of **165** did not cyclize under these conditions.

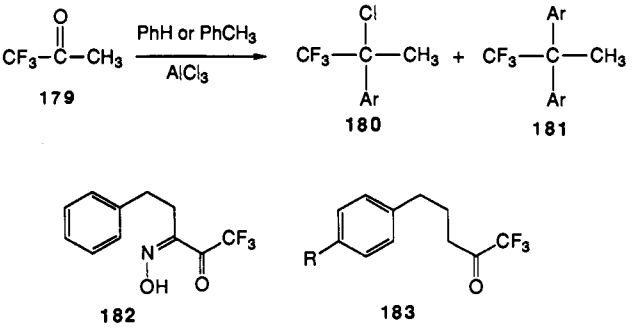
The alcohols **169** also give CF_3-substituted tetralins **170** when heated in CF_3CO_2H containing 0.02 M sulfuric acid.[54] Rates were independent of the substituent R, but quite dependent on the substituent in the Ar group. This reflects the high degree of cationic character in the intermediate leading to cyclization.



Phenylation of the hemiacetal derivative of trifluoroacetaldehyde (173) under Lewis acid or protic acid conditions gave varying amounts of 174–177.[55] The heteroatom-stabilized α-CF_3 cation 178 is a presumed intermediate.



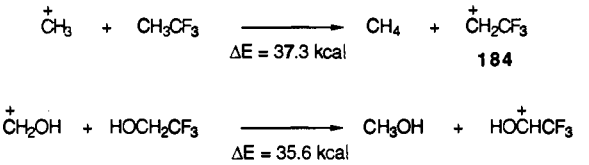
Analogous arylations to give the chloride 180, along with varying amounts of the diarylation product 181, could be observed when 1,1,1-trifluoroacetone (179) was treated with benzene or toluene in the presence of $AlCl_3$.[56] Intramolecular reactions of the trifluoromethyl ketones 182[57] and 183[58] under Lewis or protic acid catalysis led to the formation of tetralin derivatives. Similar methodology gave limited success in formation of CF_3-substituted indane derivatives from trifluoromethyl ketones.[59]



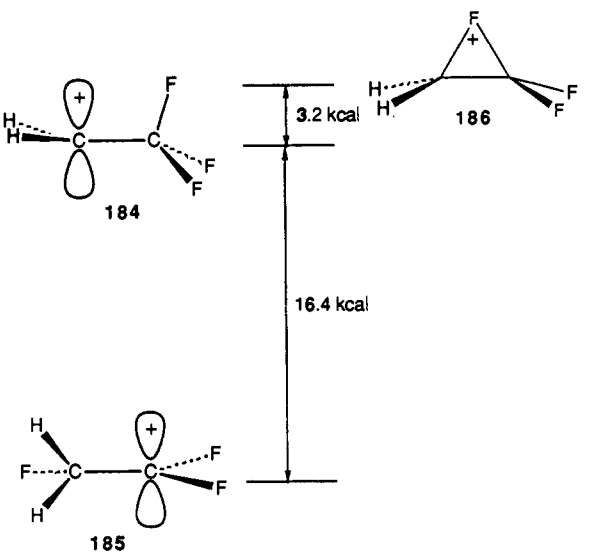
E. Computational Studies on α-Trifluoromethyl Cations

The simplest α-CF_3 cation 184 has not been generated to date. However, a number of ab initio calculations have been carried out on this cation. An early study by Paddon-Row and Houk[60] at the STO-3G level showed that the preferred conformation of 184 has one C–F bond coplanar with the vacant orbital of the cation and tilted slightly toward that vacant orbital. The HCH plane in 184 is tilted slightly toward the coplanar C–F bond. These distortions were the same type as seen in the ethyl cation. However it was concluded that there was no hyperconjugative stabilization by the CF_3 group. A later study[61] on 184 showed that, under conditions of extreme electron demand, substituents that are commonly considered π-acceptors can become π-donors. The order of π-donor ability was $CF_3 < NO_2 < CHO < CN$.

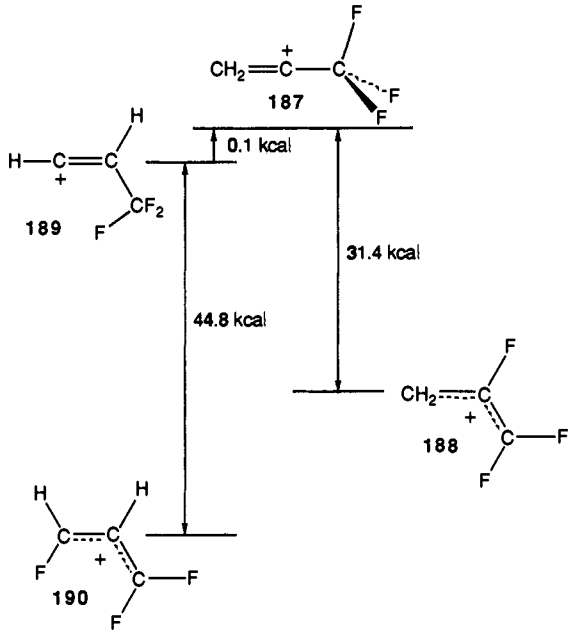
The magnitude of α-CF_3 destabilization has also been determined by applying computational methods to the isodesmic reactions shown.[62] At the 4-31G level, the value for ΔE of +37.3 kcal is indicative of a very large destabilization in cation 184. The hydroxymethyl cation is also destabilized by the CF_3 group by a comparable favor.



A more detailed computational study[63] on 184 at the 6-31G* level confirmed the earlier structural results and also examined the cation 185 derived from 1,2-fluorine migration. Both 184 and 185 correspond to energy minima, with 185 lying 16.4 kcal below the α-CF_3 cation 184. The barrier to fluorine migration in 184 (transition state represented by 186) is only 3.2 kcal. The rearranged cation 185 has the preferred conformation shown and derives stabilization from π-donation from the α-fluorines and also from C–H hyperconjugation. Despite these computational findings on the simplest α-CF_3 cation 184 there is as yet no evidence for fluorine migration in an α-CF_3 cation in solution.



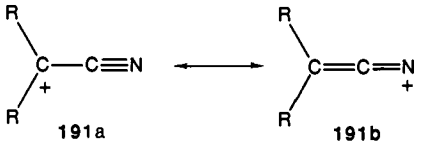
In order to evaluate the potential for fluorine migration in carbocations, computational studies have been carried out on the α-CF_3-substituted vinyl cation 187.[64] Two low-energy pathways are available for rearrangement of 187. One involves 1,2-fluorine migration (6.1 kcal barrier) and leads to the allyl cation 188 which is 31.4 kcal below 187. The other involves a 1,2-hydrogen shift (0.3 kcal barrier) to give the primary vinyl cation 189. 1,3-Fluorine migration in 189 (0.3 kcal barrier) gives the allyl cation 190, which is the global minimum 44.9 kcal below 187. Of interest is the greater stability of the allyl cation 190 relative to the isomeric allyl cation 188. Extensive π-donation from the three fluorine atoms in 190 (as opposed to two fluorines in 188) accounts for these relative energies.



In summary, a large variety of cations containing α-CF_3 groups have been generated. Methods include alkene protonation, solvolytic reactions, alcohol protonation, anodic oxidation, and Lewis acid promoted reactions. These cations appear to exert great demands on adjacent groups for stabilization. Rates of generation depend greatly on the ability of the adjacent group to satisfy these electronic demands. Rates can be retarded by much as 10^6 relative to α-H analogues. On the other hand, rates can in certain cases, approach those of the α-H analogues. Ground-state steric effects can be an important factor in determining these rates of formation of α-CF_3-substituted cations. Lifetimes of these intermediates are also subject to steric and delocalization effects. Effective ways have been developed that utilize α-CF_3 cations for the introduction of the CF_3 group into compounds of synthetic interest. Indeed, many α-CF_3 cations are quite viable in synthetic and mechanistic studies despite the electronic demands of the CF_3 group.

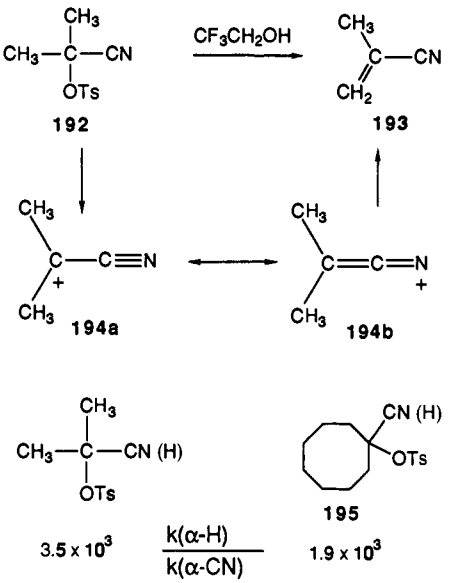
III. The α-Cyano Cation

The cyano group is generally considered by organic chemists to be strongly electron withdrawing. This is borne out by σ_p and σ^+ values (Table I) which indicate that the cyano group is even more electron withdrawing than the CF_3 group. Despite this fact, a number of cations have been generated which have the cyano group directly attached to the cationic center as in 191. Indeed, not only are such cations viable, but substantial evidence has been presented that in some instances they can derive substantial stabilization from a mesomeric interaction as represented by 191b.



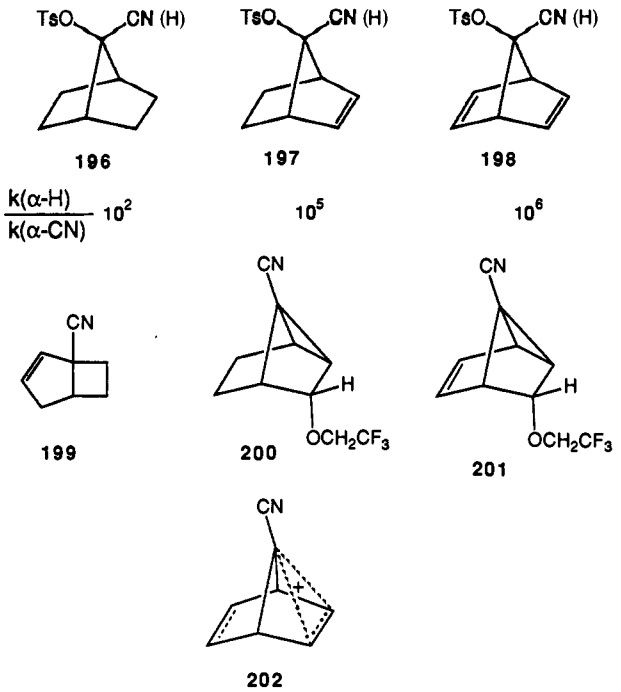
A. From Solvolysis Reactions

The first detailed studies to evaluate the properties of cations of general type 191 were carried out by the Gassman group.[65] Solvolysis of 192 led exclusively to methacrylonitrile 193. The rate-retarding effect of the cyano group (relative to the α-H analogue *i*-PrOTs) was 3.5×10^3 and was considered to be smaller than expected on the basis of the electron-withdrawing properties of the cyano group. Nucleophilic solvent participation in solvolysis of 192 was ruled out by examination of the relatively hindered 195 in the nonnucleophilic solvent CF_3CH_2OH. β-Deuterium isotope effects in 192 argued against a concerted rate-limiting elimination mechanism. The low α-H/α-CN rate ratio was proposed to result from a balancing of the destabilizing inductive effect of the cyano group with a stabilizing mesomeric effect as in 194b.

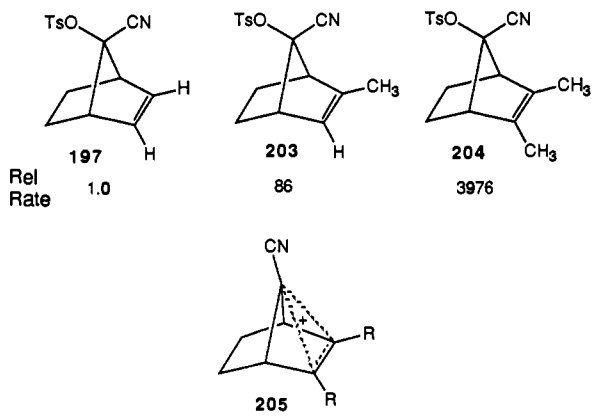


The bicyclic systems 196–198 were examined in order to determine to effect of the cyano group in systems solvolyzing with neighboring group participation (k_Δ).[66] In trifluoroethanol, the cyano derivative 196 gave mostly the alkene 199 derived from neighboring σ-bond participation, along with a small amount of unrearranged solvolysis product. The unsaturated derivative 197 gave 200, while 198 gave a dimeric product derived from 201. Rates were again compared to the α-H analogues. Rate retardation by the α-cyano group in 196 is a relatively small factor of 10^2. However in 197 (and 198), where massive neighboring group participation (giving ions of type 202) is available, the demand for mesomeric stabilization by α-cyano in the intermediate cation is minimal. Therefore rates are slowed

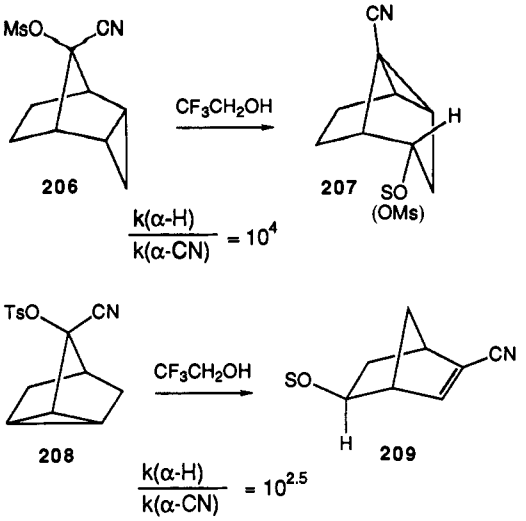
substantially relative to the α-H analogue due to the inductive effect of the cyano group on the delocalized ion **202**.



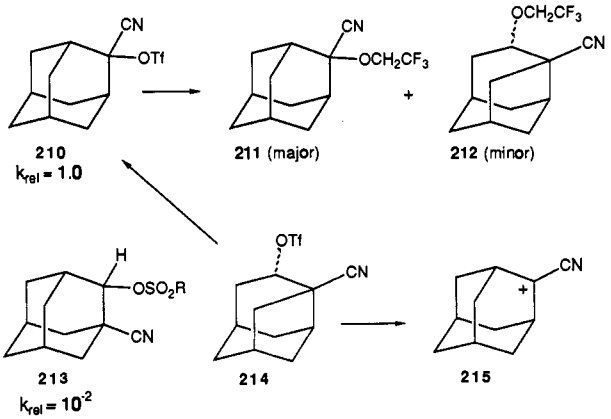
Additional methyl substitution on the double bond has been used to probe the nature of neighboring group participation in solvolyses in **203** and **204**.[67] Rates are enhanced by factors of 86 and 3976, respectively, as methyl groups are placed on the double bond. The effect of the participating double bond on solvolyses of **197**, **203**, and **204** is therefore magnified (relative to the effect in the α-H analogues where relative rates are 1:13:148). As before, the cumulative methyl effect ($k_{204} \approx (k_{203})^2$) argues in favor of symmetrical double bond participation leading to the delocalized ions **196**. As expected, products were derived from solvent capture at the 2, 3, or 7 positions.



The effect of the α-cyano group on neighboring cyclopropyl participation has also been investigated using systems **206** and **208**.[68] The α-H/α-CN rate ratio indicates that there is a delicate balance between inductive destabilization and mesomeric stabilization of the intermediates in solvolyses of these derivatives. As delocalization of charge increases, the mesomeric effect decreases more rapidly than the inductive effect. In the intermediate derived from **208**, charge is so effectively delocalized by the adjacent cyclopropyl group that both mesomeric and inductive effects of the cyano group are relatively small.

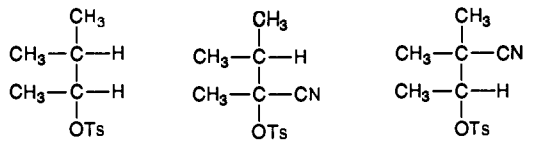


Further evidence for the importance of mesomeric α-cyano stabilization of carbocations comes from a study of the adamantyl systems **210** and **213**.[69] Trifluoroethanolysis of **210** gave the substitution product **211** along with small amounts of the rearranged product **212**. Data on the tosylate derivatives showed that **210** was 1.9×10^3 times less reactive than the α-H analogues, 2-adamantyl tosylate. Comparison of the α-cyano system **210** with the β-cyano system **213** showed that **210** is approximately 10^2 more reactive than **213**. This is despite the closer proximity of the cyano group in **210** to the developing cationic center. The rationale for this was mesomeric cyano stabilization in the cation **215** derived from **210**. Additionally, an attempt to prepare the triflate **214** from the corresponding alcohol led to the isolation of the rearranged triflate **210** (presumably via internal return from a tight ion pair **215**). This also implies a greater stability of an α-cyano cation relative to a β-cyano cation.



Examination of the systems **216–218** also confirms that the rate retarding effect of a β-cyano group exceeds that on an α-cyano group.[70] Mesomeric stabilization of the cationic center by the α-cyano group is the suggested reason for the smaller than expected α-cyano effect.

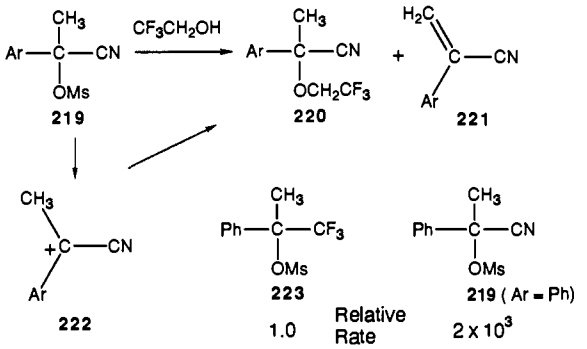
The benzylic mesylates **219** were also solvolyzed in CF_3CH_2OH, where mixtures of substitution and elimination products **220** and **221** were formed.[71] The ρ^+ value of −6.7 suggested a higher demand for aryl group stabilization than in the α-H or α-CH_3 analogues. The



216 217 218

k_{rel} 1.0 1.9×10^{-4} 1.3×10^{-8}

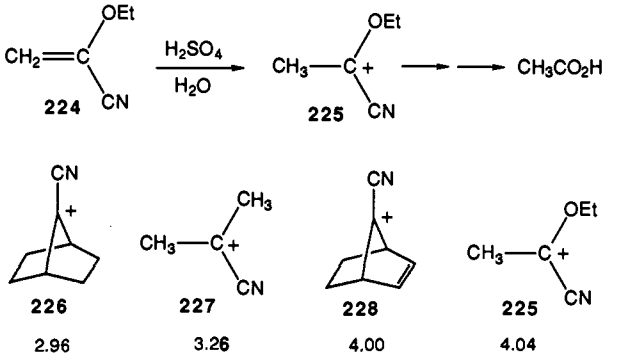
fact that solvolysis of **219** (Ar = Ph) was 2×10^3 faster than the CF_3 analogue **223** (despite the greater electron-withdrawing properties of CN based on σ^+ values) suggested that there is some transition-state charge delocalization onto the cyano group in the cation **222**.



219 **220** **221** **222** **223** **219** (Ar = Ph)

Relative Rate: 1.0 2×10^3

The acid-catalyzed hydration of the enol ether **224**, which proceeds via the ethoxy stabilized α-cyano cation **225**, has also been studied.[16] Rate data has been used to calculate a γ^+ values (group σ^+ values) for the cyano group. This γ^+ value, which measures the ability of the cyano group to stabilize or destabilize a cation, was not constant, but varied with cation structure. In the relatively unstable cation **226**, where there is large demand for mesomeric cyano stabilization, this group is a weaker net electron-withdrawing group (smaller γ^+). In the cation **225**, which is stabilized by the ethoxy group, the cyano group exerts far more of its electron-withdrawing properties (larger γ^+). It is concluded that α-cyano has a variable electronic effect which depends on intrinsic cation stability.



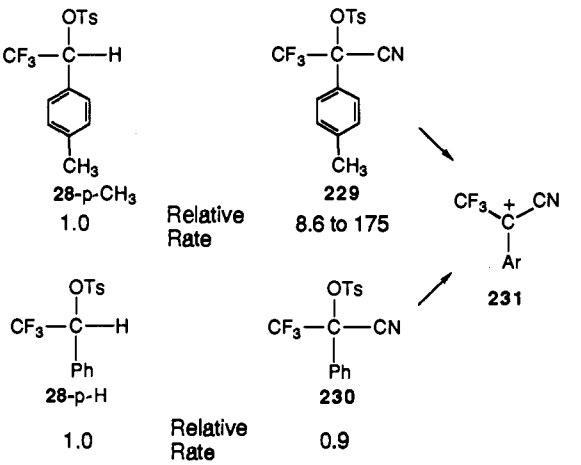
224 **225** CH_3CO_2H

226 **227** **228** **225**

2.96 3.26 4.00 4.04

γ^+ values for the cyano group

One of the most remarkable α-cyano effects is seen in solvolyses of the tosylate **229**, where there is an additional electron-withdrawing α-CF_3 group also attached to the incipient cationic center.[31] Tidwell has shown that **229** and **230** (as well as the bis-CF_3 analogues **61**) solvolyze via the "doubly destabilized" cations **231**. Whereas the rate-retarding effect of the second CF_3 group in solvolysis of **61** was unusually small, the effect of the cyano group in solvolysis of **229** is truly remarkable. The α-cyano system **229** actually solvolyzes *faster* than the α-H analogue **28**-*p*-CH_3 in all solvent systems studied. The unexpectedly rapid rate of solvolyses of **61** was attributed to a possible ground-state steric effect and also to extensive charge delocalization onto the aromatic ring. The CN group is "smaller" than the CF_3 group, and hence steric effects should be less important in solvolysis of **229** and **230**. Mesomeric stabilization by the α-cyano group can account for part of the enhanced rates of **229** and **230**.



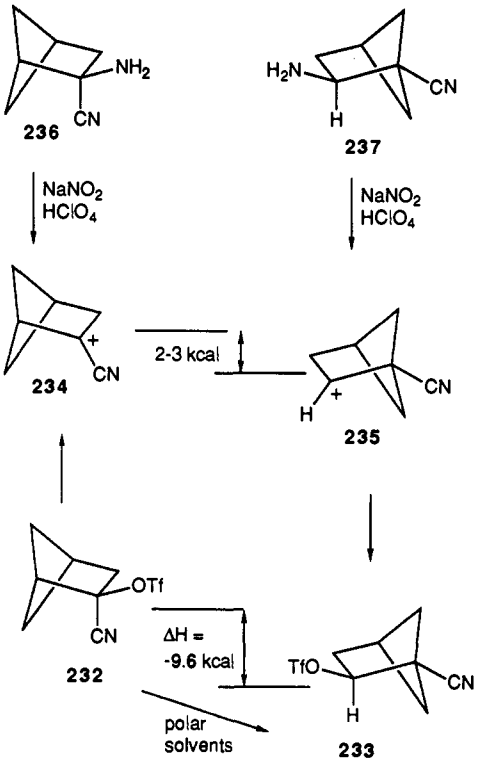
28-*p*-CH_3 **229** **231**

Relative Rate: 1.0 8.6 to 175

28-*p*-H **230**

Relative Rate: 1.0 0.9

The α-cyano triflate **232** (as well as the analogous brosylate) has been studied by Kirmse.[72] This substrate rearranges quantitatively in polar solvents to the unreactive β-cyano triflate **233**. The enthalpy change for this rearrangement has been determined calorimetrically and indicates that **232** is 9.6 kcal less stable than the rearranged triflate **233**. This rearrangement is proposed to occur by initial formation of the α-cyano cation **234** which rearranges to the β-cyano cation **235**. Internal return at the tight ion-pair stage gives **233**.



236 **237** $NaNO_2$ $HClO_4$ **234** 2-3 kcal **235** **232** ΔH = -9.6 kcal polar solvents **233**

The ions **234** and **235** have also been generated by deamination of the amines **236** and **237**.[72] Studies on optically active systems suggest that ions **234** and **235**

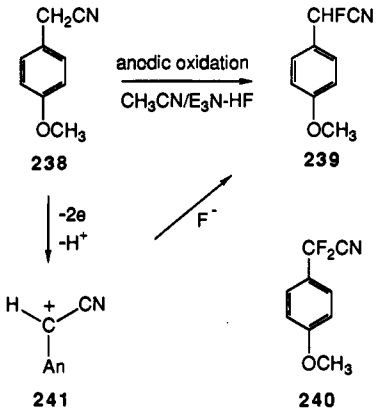
are classical intermediates (with **235** lying 2–3 kcal below **234**) that can interconvert or be captured by solvent. This is contrary to previous studies that suggest that α-cyano cations are more stable than β-cyano cations. The relative ground-state stabilities of **232** and **233** offer a reason for the more rapid solvolysis of **232**, despite the greater stability of the β-cyano cation.

Computational studies offer some insights into the relative energies of **232** and **233**.[73] The cyano and triflate groups in **232** are both electron-withdrawing and attached to the same carbon. Computational studies on $CH_2(CN)OF$ and $CH_2(CN)OBH_2$ (where F and BH_2 are used to model σ-acceptor and π-acceptor properties of Tf) indicate a destabilizing geminal group interaction between CN and OF or OBH_2. An analogous destabilizing geminal group interaction between CN and OTf would account for a major portion of the ground-state energy difference between **232** and **233**. This suggests that destabilizing geminal ground-state interactions should be considered when evaluating solvolytic reactions.

It should be noted that the relative ground-state stabilities of **232** and **233** may not be completely general. In the adamantyl triflates **210** and **214**, ground-state stabilities are in the opposite sense, i.e. the β-cyano triflate **214** rearranges to the α-cyano triflate **210**, implying greater stability of the α-cyano triflate.

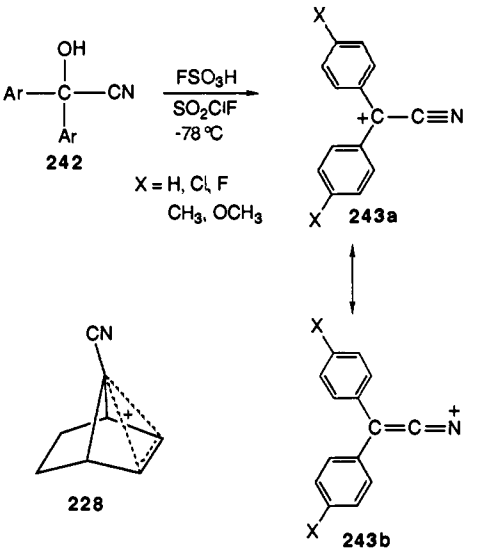
B. α-Cyano Cations from Anodic Oxidation

Electrochemical oxidation of the benzylic nitrile **238** in acetonitrile containing fluoride ion gave the monofluoro or difluoro derivatives **239** and **240**.[74] These oxidations, which presumably involve the α-cyano cation **241**, provide a convenient route to α-fluoro nitriles.



C. α-Cyano Cations under Stable Ion Conditions

The cations **243** were prepared under stable ion conditions by ionization of the corresponding benzophenone cyanohydrins **242** in superacid media.[75] These ions show significant charge delocalization involving the aryl rings, as indicated by ^{13}C NMR spectra. Additionally, examination of the substituent effect on the cationic carbon showed that the shift decreased from δ 168.8 for the unsubstituted analogue (X = H) to δ 147.6 for X = OCH_3. Shifts of the cationic carbon correlated with those of the cationic carbon of 1-aryl-1-cyclopentyl cations, but the slope was only 0.57. This relatively low slope is indicative of an additional charge delocalization mechanism in **243** involving the cyano group as in **243b**.

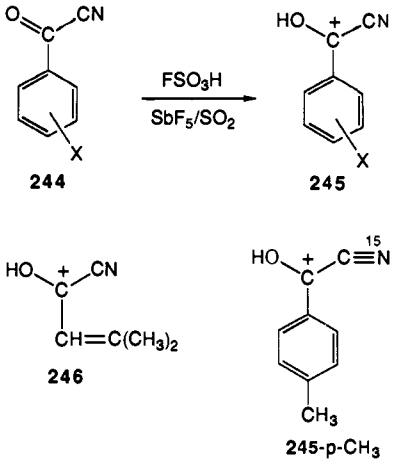


Further evidence for mesomeric charge delocalization comes from ^{15}N NMR spectra. The ^{15}N NMR spectrum of **243** (X = H) shows a signal at δ 283 which is 30 ppm *deshielded* relative to the cyanohydrin precursor. This ^{15}N shift is between that of a nitrile (δ 253) and an imine (δ 318) and indicative of charge delocalization onto nitrogen. Evidence for decreasing mesomeric stabilization as the aryl group becomes more electron donating also comes from ^{15}N spectra. As substituents vary from *p*-H to *p*-OCH_3, ^{15}N shifts decrease from δ 283 to δ 260. This is indicative of decreasing positive charge on nitrogen as demand for mesomeric stabilization decreases.

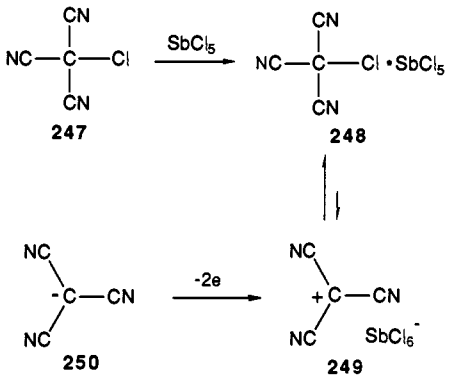
The 7-cyano-2-norbornenyl cation (**228**), previously generated under solvolytic conditions,[66] has also been produced under stable ion conditions.[75] NMR data indicate that this ion is indeed a delocalized bishomoaromatic system. It has also been suggested that there is some charge delocalization into the cyano group of **228**. Attempts to generate other less stabilized α-cyano cations such as **194**, **215**, and **223** under stable ion conditions were not successful.

A series of hydroxy stabilized α-cyano cations **245** (and **246**) have been formed under stable ion conditions by protonation of the corresponding aroyl cyanides **244**.[76] The ^{15}N-labeled cation **245**-*p*-CH_3 has been examined by ^{15}N NMR spectroscopy and shows a signal at δ 271.1. This signal is shifted 15.3 ppm downfield from the ketone precursor. This indicates that conjugative stabilization involving the cyano group of **245**-*p*-CH_3 is still operative despite the extensive charge delocalization due to the hydroxyl group and the aromatic ring.

A intriguing report has appeared concerning the chemistry of chlorotricyanomethane (**247**).[77] This material forms a solid 1:1 adduct, **248**, with antimony pentachloride. Conductance measurements in methylene chloride and ^{13}C NMR studies suggest that this adduct is essentially covalent in nature with perhaps a small amount of the cation **249** existing in solution. At 0.25 M **248**, it is suggested that about 0.1% is dissociated to $SbCl_6^-$ and $C(CN)_3^+$. On the basis of the fact that tricyanomethide ion, **250**, undergoes two electron oxidations in solution, it has also been suggested that the ion **249** is involved as a transient intermediate in

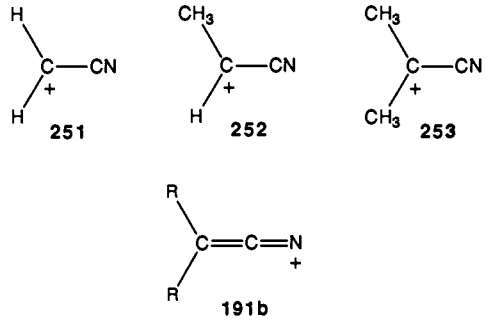


oxidation processes. Further studies are necessary to confirm these mechanistic suggestions.

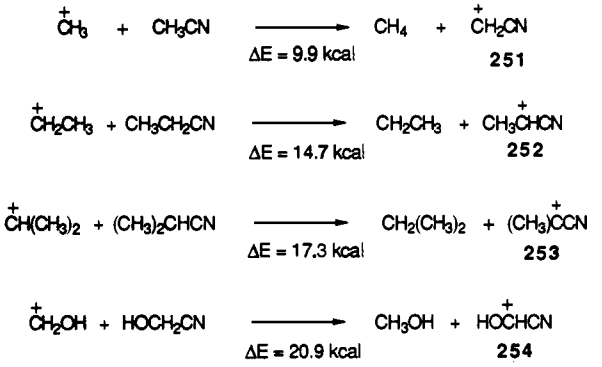


D. Computational Studies on α-Cyano Substituted Cations

The first computational study on α-cyano cations was the PRDDO study of Dixon and Gassman.[78] These studies, as well as a full ab initio study, indicated that cations **251**, **252**, and **253** have C–C bond lengths considerably shorter than that of CH_3CN. The bond orders of the C–C bonds were 1.42, 1.31, and 1.23 respectively. Bond orders of the C–N bonds were 2.52, 2.63, and 2.71, respectively, and bond lengths were also longer than in CH_3CN. These data, as well as other features of the computations support the suggestion of charge delocalization in α-cyano cations as represented by **191a** and **191b**. The importance of mesomeric charge delocalization decreases in the series as methyl substitution increases.



A computational study by Paddon-Row and Houk at the 4-31G//STO-3G level indicated similar C–C bond shortening and C–N bond lengthening in **251** relative to CH_3CN.[79] This is due to the π-donor effect of the cyano group. Additionally, the isodesmic reaction shown indicates that **251** is destabilized relative to the methyl cation (α-H analogue) by 9.9 kcal. This compares to a 37.3 kcal destabilization by an α-CF_3 group.[62] Isodesmic reactions show that destabilization by α-cyano groups increases with successive introduction of methyl groups in **252** and **253**. The π-donor effect of the cyano group appears to be rapidly attenuated as the cations become stabilized by methyl substitution. This is in line with experimental findings.[16,66] Hydroxyl substitution also has an analogous effect.[62] Cyano destabilization of cation **254** amounts to 20.9 kcal since the π-donor effects of the cyano group is substantially attenuated.



The electronic effect of the cyano group on a series of cyano-substituted probe molecules (such as $^-CH_2CN$, p-$NCC_6H_4CH_2^+$, $^+CH_2CN$, etc.) has been calculated at the STO-3G or 4-31G levels.[61,80] These calculations show that under extreme electron demand, substituents such as cyano, which is commonly a π-acceptor, can become a π-donor. The term *amphielectronic* has been used to describe this dual behavior of the cyano group.

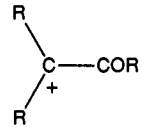
Computational results on **251**, **252**, and **253** using STO-3G, 4-31G, and double ζ plus polarization (DZP) basis sets (as well as the PRDDO method) have been compared.[81] At all levels, C–C bond shortening and C–N bond lengthening is observed relative to the hydrocarbon analogues, CH_3CN, CH_3CH_2CN and $(CH_3)_2CHCN$. The C–C bonds of **251–253** have partial double bond character, while the C–N bonds have lost some triple bond character. These bond changes are progressive as expected for decreasing charge delocalization in the series **251**, **252**, and **253**. At the STO-3G level the $^+CH_2CN/CH_3CN$ pair is 0.1 kcal more stable than the CH_3^+/CH_4 pair. However at the DZP level, the order is reversed with the $^+CH_2CN/CH_3CN$ pair now being 15.8 kcal less stable. It appears that minimal basis sets overestimate the absolute stabilities of α-cyano cations. At all levels, the α-cyano cation **252** is more stable than the isomeric β-cyano cation $^+CH_2CH_2CN$. All of these theoretical studies agree with the conclusion that the α-cyano group destabilizes a cation inductively, but can provide considerable conjugative stabilization by charge delocalization to nitrogen of the cyano group.

In summary, cations containing a directly attached cyano group can be generated. Such cations form, in certain instances, at rates that exceed expectations based on the electron-withdrawing properties of the cyano group. Thus stabilities of α-cyano cations generally exceed those of α-trifluoromethyl cations. A number of rate, NMR, and computational studies point

to mesomeric stabilization of such cations, where charge is further delocalized onto the nitrogen atom of the cyano group. The extent of this mesomeric stabilization depends on the intrinsic demand for stabilization in the specific α-cyano cation.

IV. The α-Carbonyl Cation

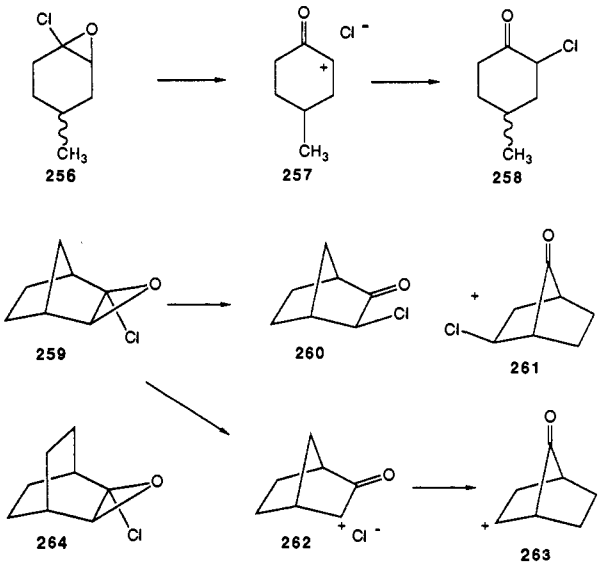
The carbonyl group is one of the most important functional groups in organic chemistry. Its electron-withdrawing conjugative and inductive properties permit facile generation of enolate anions. This feature, as well as the ability of nucleophiles to directly attack the carbonyl group or its protonated form, lead to much of the diverse chemistry of this functional group. Despite the general perception of the carbonyl group as an electron-withdrawing carbanion-stabilizing group, numerous carbocations of type **255** have been generated. The effect of the carbonyl group on such cations will be the focus of this section of the review.



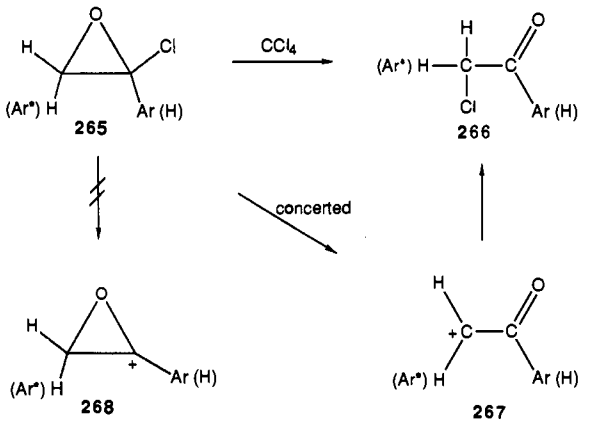
255

A. From α-Halo Epoxides

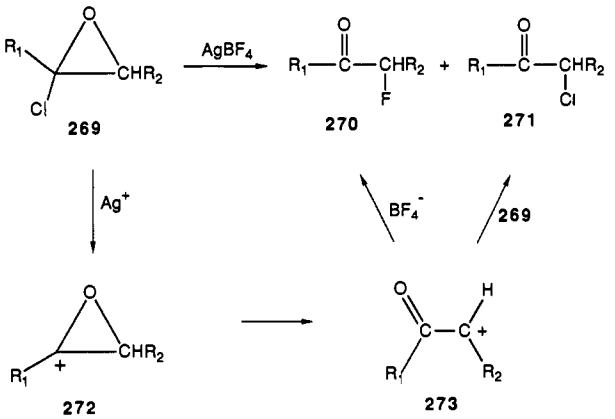
McDonald and co-workers have carried out pioneering studies in which α-carbonyl cations are intermediates.[82,83] They have found that α-chloro epoxide **256** thermally rearranges to the α-chloro ketones **258**, while the bicyclic analogue **259** rearranges to give a mixture of **260** and **261**. The α-carbonyl cations **257** and **262** (as tight ion pairs) are suggested intermediates in these rearrangements. The chloro epoxide **264** rearranges by an analogous mechanism.[84]



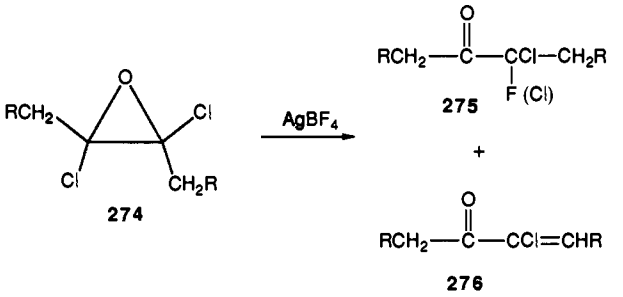
Substituent effect studies have been used to address the intermediacy of the cyclic oxiranyl cation **268** during rearrangement of α-halo epoxides **265**.[85] There is minimal effect on varying the substituent in the group Ar ($\rho^+ = -0.57$). The effect of substituents on Ar* was much larger ($\rho^+ = -3.5$). These substituent effects argue in favor of a concerted C–O bond heterolysis during thermal rearrangement to give the α-carbonyl cation **267** directly. These data suggest that the oxiranyl cation **268** is bypassed on the way to formation of the α-carbonyl cation from chloroepoxides.



The reaction of chloro epoxides **269** with $AgBF_4$ in ether has been studied.[86] The α-fluoro carbonyl products **270** (major) were formed along with minor amounts of the α-chloro carbonyl products **271**. The suggested mechanism involves opening of the oxiranyl cation **272** to give the α-carbonyl cation **273**, followed by fluoride capture or chloride ion abstraction from the starting chloro epoxide. While the oxiranyl cation **272** is shown in the mechanistic scheme, the question of its discrete existence was not addressed.



Under similar conditions, the dichloro epoxides **274** were also treated with $AgBF_4$.[86] Mixtures of the α-fluoro and α-chloro carbonyl compounds **275** were formed, along with the elimination product **276**. These products also arise via α-carbonyl cation intermediates.



Ketones **277** are converted to homologated enones **278** in the presence of benzotrichloride by cathodic reduction.[87] This process presumably involves capture of the anion **279** followed by cyclization to the chloro epoxide **281**. Opening to the α-carbonyl cation **282**, followed by

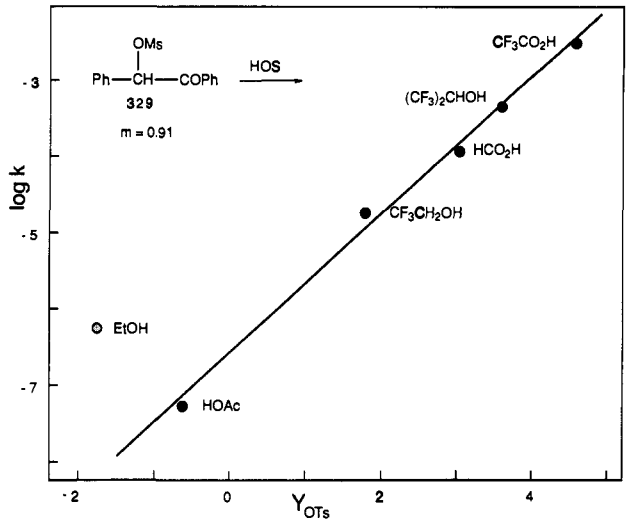
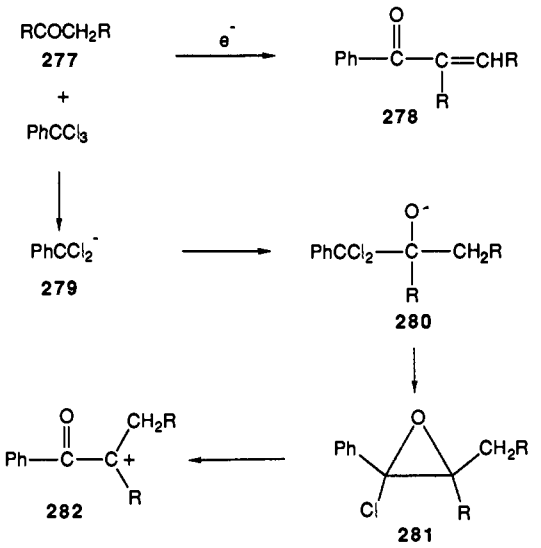


Figure 5. A plot of log k for solvolysis of **329** vs Y_{OTs} values.

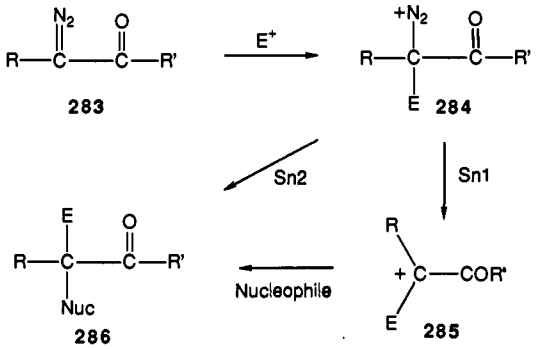
proton loss would give the observed products **278**. This mechanism is supported by addition of **279** to norcamphor, where Wagner–Meerwein rearrangement and hydride shift products indicate cationic intermediates.



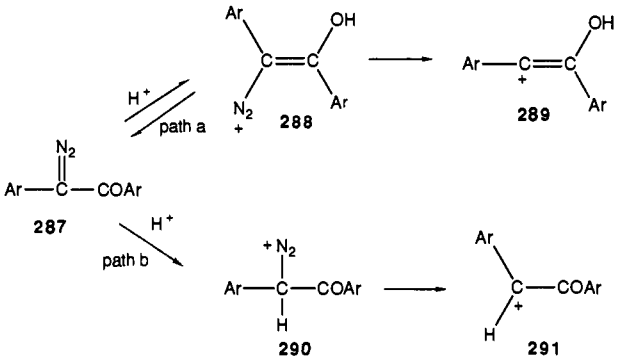
B. From α-Diazo Carbonyl Compounds

α-Diazo carbonyl compounds of general type **283** can react at carbon with electrophiles. While intermediates such as **284** can suffer direct displacement by nucleophiles, if the group E is carbocation stabilizing, then the α-carbonyl cation **285** is a potential intermediate. The protonation of α-diazo compounds **283**, where R = H has been reviewed.[88] In general, such reactions lead to replacement of N_2 from **284** by "assisted" processes which bypass the α-carbonyl cation as a discrete intermediate. In the case of R = alkyl, protonation leads to carbocation derived products.[89] However these products may also be derived from "assisted" (k_Δ) processes and it is not clear that simple secondary α-carbonyl cations can be generated by this method.

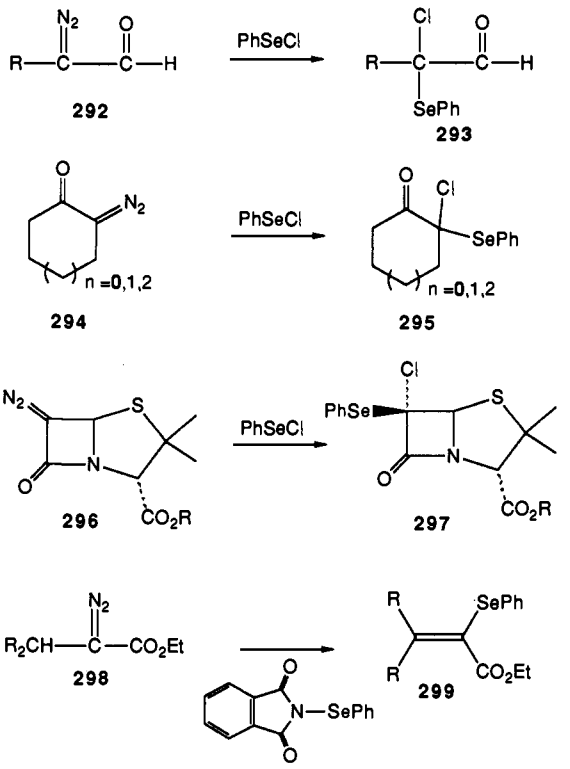
Jugelt and Berseck have carried out detailed protonation studies on α-diazo ketones of type **287**.[90] These substrates undergo substituent-dependent protonation on either oxygen or carbon, leading to two competitive pathways. Protonation on oxygen (reversible), followed by loss of nitrogen, leads to products derived from the



vinyl cation **289**. Protonation on carbon leads to α-hydroxy ketone products, which are derived from capture of the aryl-stabilized α-carbonyl cation **291** by water.

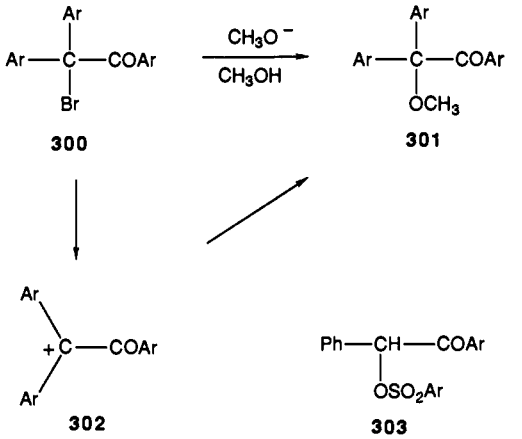


The α-diazo carbonyl compounds **292**,[91] **294**,[91] **296**,[92] and **298**[93] have been reacted with electrophilic selenium-containing reagents with resultant displacement of molecular nitrogen. The precise mechanistic details for formation of **293**, **295**, **297**, and **299** have not been studied in depth. Likely possibilities include bimolecular displacement of N_2 from intermediates analogous to **284** or formation of selenium-stabilized α-carbonyl cations as in **285** (E = SePh).

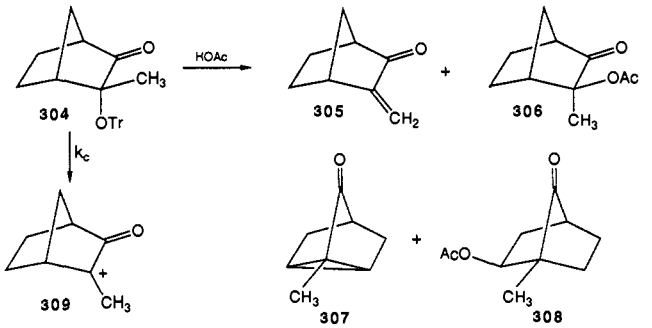


C. From Solvolysis Reactions

The solvolytic route has been used to generate α-carbonyl cation intermediates. Solvolytic rate data has been useful in analyzing carbocation stability and in placing α-carbonyl cations in an overall scheme of cation stabilities. The first studies that suggested the intermediacy of α-carbonyl cations under solvolytic conditions were those of Karavan and Temnikova.[94] The α-halo ketones **300** were found to react with sodium methoxide in methanol to give the methoxy ketones **301**. Kinetic studies implicated the diaryl substituted α-carbonyl cations **302** where charge is undoubtedly substantially delocalized into the aromatic rings. Later studies by Temnikova et al.[95] concluded that formolysis of certain sulfonate derivatives of benzoin (**303**) involved a cation-like transition state.

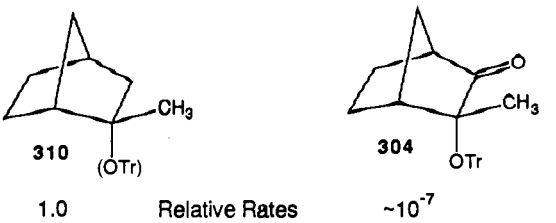


Solvolytic studies have been carried out on the tresylate **304** (OTr = $OSO_2CH_2CF_3$).[96] In acetic acid both rearranged and unrearranged products **305–308** were formed. The leaving group in the endo position pre-

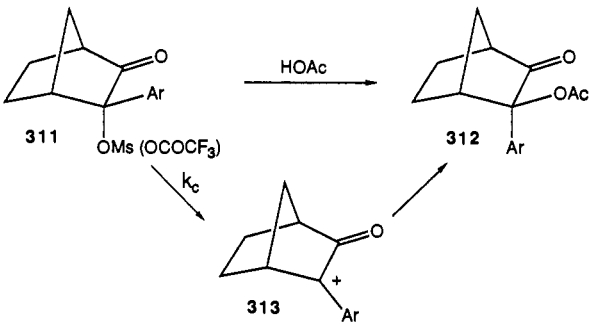


cludes a concerted ionization–Wagner–Meerwein rearrangement process as the origin of the rearranged product. The α-CH_3/CD_3 isotope effect was 1.47. These data all fit a mechanism in which the discrete α-carbonyl cation **309** is the first intermediate (a k_c process). This cation can undergo solvent capture, give 1,2- or 1,3-proton elimination, or Wagner–Meerwein rearrangement to form the observed products. The solvolysis rate of **310** (the α-CH_2 analogue of **304**) was estimated and it was concluded that the carbonyl group retards the acetolysis rate of **304** by a factor of about 10^7 relative to the tertiary analogue **310**.

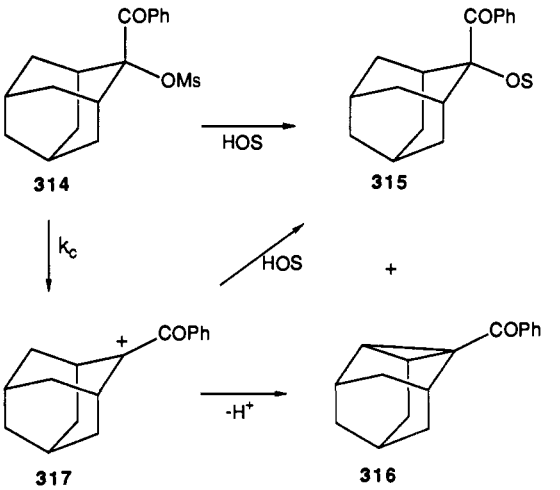
Further evidence for the solvolytic generation of α-carbonyl cations comes from studies on the mesylates and trifluoroacetates **311**, where the aryl group contains electron-donating substituents.[96] In contrast to the methyl analogue **304**, these donor-substituted systems



311 gave only unrearranged acetolysis products **312**, where inversion of configuration has occurred. Electron-withdrawing groups on the aryl ring led to the onset of rearrangement products. Hammett ρ values of −7.1 (HOAc)[96] and −5.7 (EtOH)[97] are in line with a cationic intermediate, **313**, with a high demand for aryl group stabilization relative to the α-CH_2 analogue. The aryl stabilization in the α-carbonyl cation **313** is sufficient to prevent Wagner–Meerwein rearrangement when electron-donating groups are present.



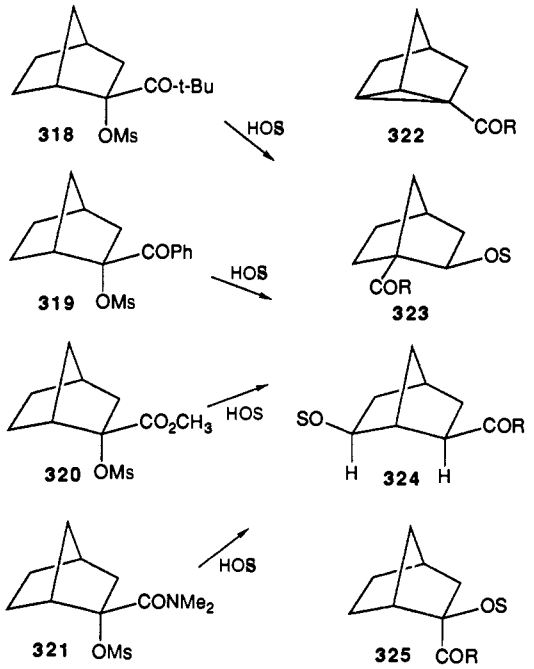
The 2-benzoyl-2-adamantyl mesylate (**314**) has been examined in a variety of solvents, where the substitution product **315** is the major product, and a small amount of the 1,3-elimination product **316** is also formed.[98]



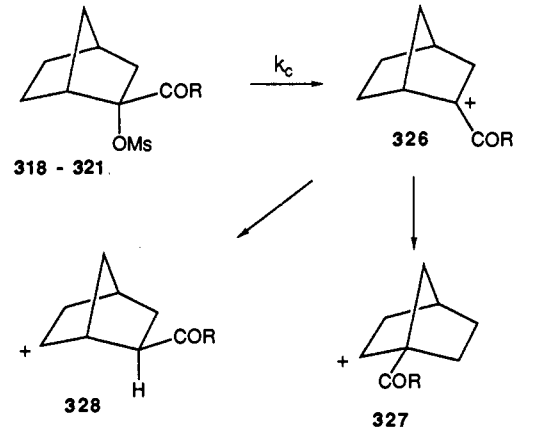
Rate data for **314** in various solvents have been compared to those of 2-adamantyl tosylate,[99] a substrate which undergoes solvolysis by a limiting mechanism (k_c) uncomplicated by nucleophilic solvent involvement. This is shown by the Winstein–Grunwald plot in Figure 3. The correlation is excellent and the m_{OTs} value is 1.01, an expected value for a k_c process. These data are consistent with the α-carbonyl cation **317** which undergoes solvent capture or proton loss to give the observed products **315** and **316**.

The α-carbonyl-substituted norbornyl mesylates **318–321** were all examined under various solvolytic conditions.[100] All of these systems gave mixtures of **322–324**. The ester **320** and the amide **321** also gave small amounts of unrearranged substitution product

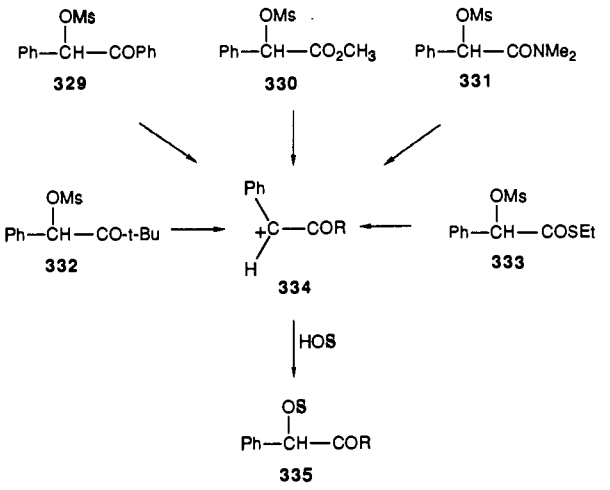
325 when solvolyzed in methanol. In general, large rate increases were seen with increasing solvent ionizing power, but Winstein–Grunwald m values were somewhat less than 1.0. A typical plot is shown in Figure 4.



These rearranged products and the rate increases with solvent ionizing power support the discrete intermediacy of α-carbonyl cations of type **326**. Products **322–325** are derived from Wagner–Meerwein rearrangement (**327**) or from a 1,3-hydride shift (**328**). As implied previously, the endo stereochemistry of the mesylate leaving group insures that ionization and rearrangement cannot be concerted.

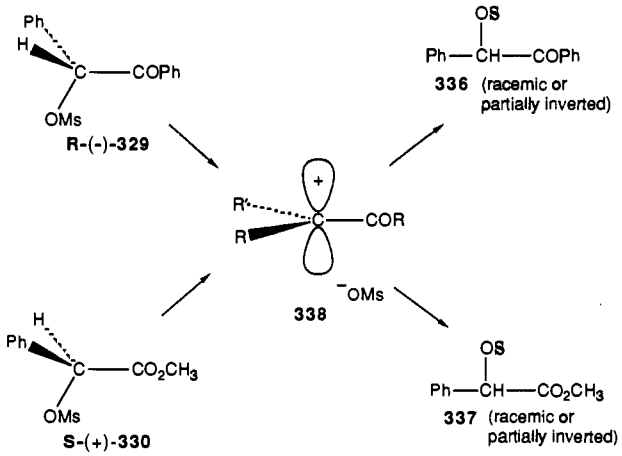


The benzylic mesylates **329–333** have been solvolyzed in a variety of solvents, where all produce the simple substitution products **335**.[100] There are, in general, large rate increases with solvent ionizing power as illustrated for the mesylate **329** in Figure 5. The m_{OTs} value is 0.91 (excluding the ethanol rate data) and suggests that this substrate reacts by a k_c process. The deviation from the line in ethanol suggests that, in this relatively nucleophilic solvent, nucleophilic solvent participation has increased importance and therefore contributes to the rate. The m_{OTs} value for **330** is 0.87 based on actual rates of product formation (k_t). If one considers racemization rates of optically active **330** (k_α) to be a truer measure of ionization rates, then the m_{OTs} value for **330**



is 1.0. These m_{OTs} values are consistent with rate-limiting ionization of **330** to form an α-carbomethoxy cation. The m_{OTs} value for **331** is 0.75 and data for methanol and ethanol deviate slightly in this Winstein–Grunwald plot.

The question of the intermediacy of cyclized ions in solvolyses of **329** and **330** has been addressed by stereochemical studies.[100] Neighboring carbonyl participation, where the oxygen of the carbonyl group becomes attached to the developing cationic center (a k_Δ process), has certain stereochemical consequences. Therefore the optically active mesylates (*R*)-(−)-**329** and (*S*)-(+)-**330** were prepared and studied in various solvents. In CF_3CO_2H mesylate (*R*)-(−)-**329** gave a completely racemized trifluoroacetate product.[6b] Acetolysis gave the corresponding acetate in which a small excess of the *inverted* acetate was formed. Ethanolysis also gave a small excess of the inverted stereoisomer. Results for the mandelate derivative (*S*)-(+)-**330** were similar. Solvolysis in CF_3CO_2H or $(CF_3)_2CHOH$ gave completely racemic products. Acetolysis gave an 11% enantiomeric excess of the inverted acetate. A control experiment showed that independently prepared optically active products were optically stable under the reaction conditions. Additionally, there was no deuterium incorporation in the product when (*S*)-(+)-**330** was solvolyzed in CF_3CO_2D or CH_3CO_2D. Loss of optical activity therefore does not originate from an enolization mechanism.



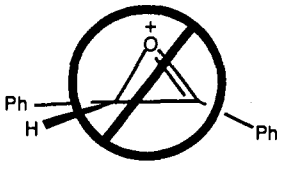
These studies argue in favor of the intermediacy of the open α-carbonyl cation **338** in solvolyses of **329** and **330**. Internal return at an ion-pair stage results in

TABLE III. Stereochemistry of Solvolysis of (*S*)-(+)-331

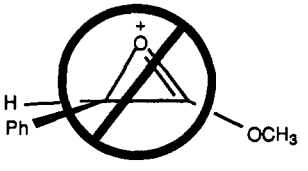
solvent	stereochemistry of reaction
CH_3OH	33% net inversion
HOAc	11% net inversion
CF_3CH_2OH	racemization
$(CF_3)_2CHOH$	racemization
CF_3CO_2H	9% net retention

racemization of (*S*)-(+)-**330** occurring at a faster rate than product formation in CF_3CO_2H and $(CF_3)_2CHOH$. The excess of inverted products from (*R*)-(−)-**329** and (*S*)-(+)-**330** in the more nucleophilic solvents suggests that the α-carbonyl cation intermediates have a shorter lifetime in these solvents. Solvent capture probably occurs at an earlier ion-pair stage and is slightly more probable from the side opposite the mesylate anion in the ion pair **338**.

These stereochemical studies rule out neighboring carbonyl participation leading to cyclized ions in solvolyses of **329** and **330**. If cyclized ions were involved, the opening by solvent at the benzylic carbon would have resulted in products of net retained configuration. The observed *racemization or partial inversion* is completely consistent with open α-carbonyl cations only. Structures **339** and **340** emphasize the fact that these cyclized ions are inconsistent with stereochemical studies.

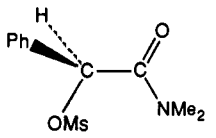


339

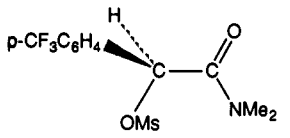


340

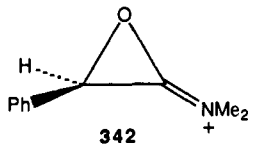
The amide carbonyl group is more nucleophilic than that of ketones or esters. The amide (*S*)-(+)-**331** was therefore solvolyzed in a variety of solvents since this substrate should have a greater propensity to give cyclized ions.[100b] The stereochemical outcome of these solvolyses as determined by product analyses are summarized in Table III. The racemized products seen in CF_3CH_2OH and $(CF_3)_2CHOH$ are again consistent with the intermediacy of an open α-carbonyl cation (as are the partially inverted products in methanol and acetic acid). In trifluoroacetic acid a small enantiomeric excess (9%) of the product has the retained configuration. A potential source of the retained product is a cyclized ion **342** which could have been formed in a k_Δ process from (*S*)-(+)-**331**. However, a study[6b] on (*S*)-(+)-**341**



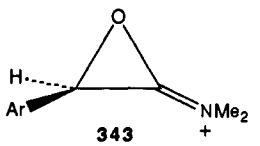
S-(+)-331



S-(+)-341



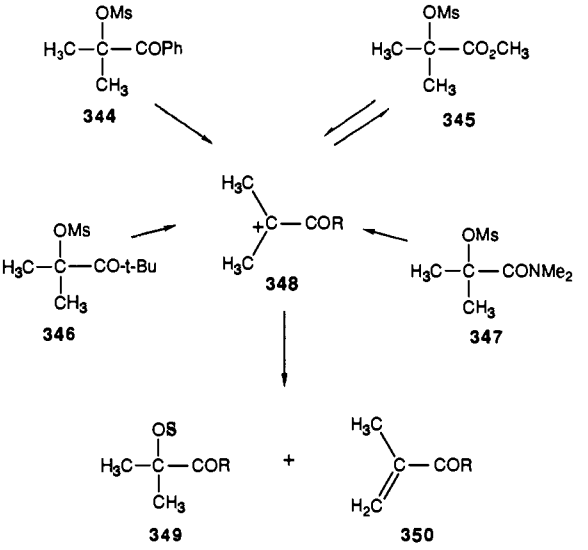
342



343

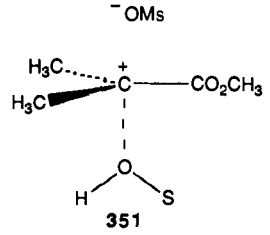
in CF_3CO_2H showed 4% net inverted product despite increased electron demand for carbonyl participation. This implies that (*S*)-(+)-**331** does not react by a partial k_Δ process in CF_3CO_2H despite the observation of 9% net retention. Increasing electron demand predicts that the k_Δ process will be more important in **341** than in **331**. Cyclized ions **342** and **343** therefore do not appear to be involved despite the greater nucleophilic character of the amide carbonyl group. While the origin of net retention in (*S*)-(+)-**331** was uncertain it was noted that such retentive solvolyses not involving k_Δ processes have precedent.[101] Preferential delivery of solvent coordinated to the counterion to the cationic intermediate from the same side that the leaving group departed provides a possible rationale for the partial retention in trifluoroacetolysis of (*S*)-(+)-**331**.

Under solvolytic conditions, the mesylates **344**–**347** all react to give mixtures of substitution and elimination products **349** and **350**.[98] α-Carbonyl cations **348**, which capture solvent or suffer proton elimination, are presumed intermediates. Solvent effect studies give a Winstein–Grunwald m_{OTs} value of 0.63 for **344** and 0.66 for **346**. These solvent effects, although supportive of a transition state with substantial charge development, suggests that nucleophilic solvent involvement may play some role in these solvolyses.



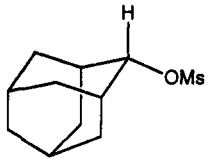
An attempt to correlate the solvolysis rate of the ester **345** with Y_{OTs} values gave a scattered plot. The rate behavior was similar to that of the α-CF_3-substituted triflate **26**, which solvolyzes by a mechanism involving rate-limiting proton loss from a reversibly formed α-CF_3-substituted ion pair **27**. In an analogous fashion, formation of the α-carbonyl cation **348** (R = OCH_3) from **345** may not be truly rate limiting. Solvent capture or proton elimination may be kinetically important. An alternative mechanism that would also account for the kinetic behavior of **345** is the S_N2 (intermediate) mechanism of Bentley and Schleyer.[102] This mechanism would involve formation of the nucleophilically solvated ion pair **351** in which formation of this intermediate is accelerated by more nucleophilic solvents.

The effect of the benzoyl group on the solvolysis rate of **314** has been analyzed[100] by comparison to the rate of the α-H analogue, 2-adamantyl mesylate (**352**). This substrate (**352**) is a model for secondary substrates undergoing solvolysis uncomplicated by nucleophilic solvent involvement. The rate of **314** is 300 times faster



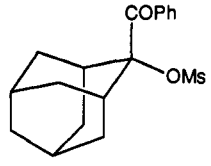
351

than that of **352**, despite the electron-withdrawing benzoyl group. This rate-enhancing effect of the



352

1.0



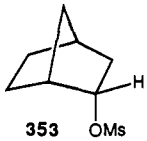
314

Relative Solvolysis Rates

~300

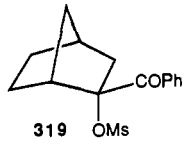
benzoyl group (relative to H) was considered remarkable in view of the fact that *p*-COPh slows the solvolysis rate of cumyl chloride by a factor of 79 ($\sigma^+ = 0.406$). Part of the effect of the benzoyl group could be attributed to ground-state strain that is relieved as the leaving group departs from the relatively hindered ionization center in **314**. Later studies by Tidwell[35] also implicate of ground-state strain as an important factor in solvolyses of the α-CF_3 containing adamantyl system **76**.

The rate behavior of the norbornyl systems **318–321** were also compared to that of the α-H analogue, *endo*-2-norbornyl mesylate (**353**).[100] Rate data for the



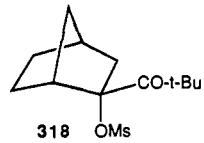
353

1.0



319

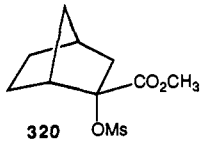
0.12



318

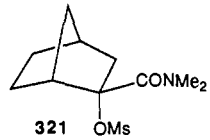
3.7

Relative Solvolysis Rates in HOAc



320

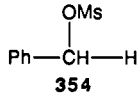
0.013



321

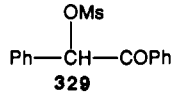
4.6

benzylic mesylates **329–331** were compared to those of the α-H analogue, benzyl mesylate, in the highly ionizing, nonnucleophilic solvent $(CF_3)_2CHOH$ where these solvolyses should be close to limiting (k_c).[98,100]



354

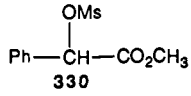
1.0



329

0.05

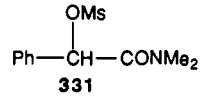
Relative Solvolysis Rates in $(CF_3)_2CHOH$



330

0.02 (k_α)

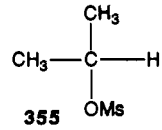
0.005 (k_t)



331

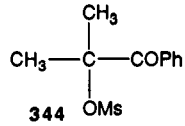
0.28

In a similar fashion, the mesylates **344–346** were also compared to those of the α-H analogue, isopropyl mesylate (**355**).



355

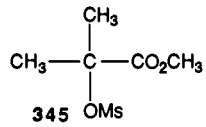
1.0



344

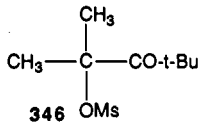
1.5

Relative Solvolysis Rates in $(CF_3)_2CHOH$



345

0.024

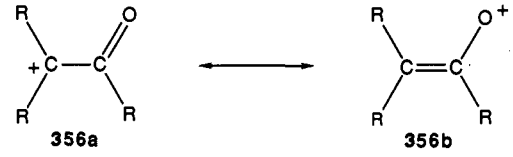


346

55

All of these data show that the rate effect of substitution of carbonyl-containing groups for hydrogen is relatively small (considering the electron-withdrawing properties of *p*-COPh, *p*-CO-*t*-Bu, *p*-CO_2CH_3, and *p*-$CONMe_2$ based on σ^+ values in Table I). The rate retardations are, in all cases, less than in the corresponding para-substituted cumyl cations. It was suggested that some factor at least partially offsets an expected large rate-retarding effect of the carbonyl group on solvolyses of all of these substrates that proceed via α-carbonyl cations. Neighboring carbonyl group participation with resultant anchimeric assistance was ruled out by stereochemical studies. While relief of ground-state strain was believed to be important in the solvolysis of the adamantyl system **352**, some other factor must also operate in less congested systems such as **329–331**.

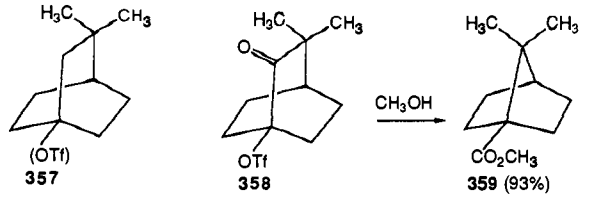
The factor believed to account for the relative ease of formation of α-carbonyl cations was a stabilizing conjugative interaction depicted in **356b**. This type of back-donation of the π-electrons of the carbonyl group, originally postulated by McDonald,[82,83] would partially offset the electron-withdrawing inductive effect of the carbonyl group. This is the same type of conjugative interaction suggested for α-cyano cations of type **182**. Inductive and conjugative effects of the carbonyl group on cationic intermediates were proposed to operate in opposite directions with the net effect being that α-carbonyl cations can be formed at rates comparable to the α-H analogues.

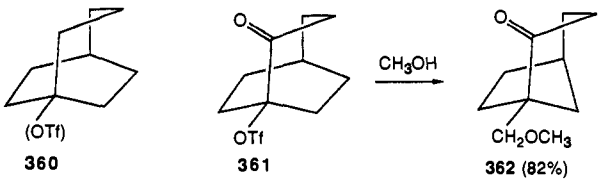


356a 356b

A study by Takeuchi et al.[103] has questioned the importance of carbonyl π-conjugation as in **356b**. The bridgehead triflate **358** was found to solvolyze $10^{8.4}$ times less readily than the α-methylene analogue **357**. The rate of the triflate **357** was estimated from the corresponding mesylate rate. The less-strained triflate **361** reacted $10^{8.3}$ times less readily than the analogue **360** (also estimated from the mesylate rate). On the basis of the expectation that carbonyl conjugation should be more important in solvolysis of **361** than in **358**, it was concluded that carbonyl conjugation in the

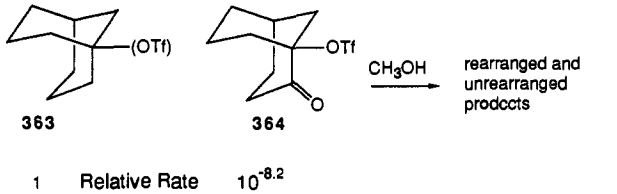
ion derived from 361 was unimportant.

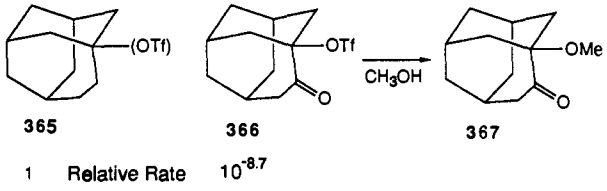




While these rate studies argue for the unimportance of carbonyl conjugation, it was pointed out that product analysis data lead to different conclusions.[6b] Product analyses showed that the solvolysis of both 358 and 361 gave mostly rearranged products. This suggests that 358 and 361 may well be k_Δ substrates, solvolyzing with anchimeric assistance. If 358 is a k_Δ substrate, then the unassisted relative rate of solvolysis of this substrate (k_c) would be less than $10^{-8.4}$ (assuming that 357 is a k_c substrate). One could therefore conclude that 361 is enhanced by carbonyl conjugation. Since it is uncertain to what extent σ-participation (or σ-conjugation) enhances the rate of solvolyses of 358 (or 361), the triflate 358 may not be a good model for the unassisted rate of formation of a perpendicular α-carbonyl cation. Conclusions concerning the generality of carbonyl conjugation using these rate data are therefore suspect.

A subsequent study on 364 and 366 also suggested that carbonyl conjugation was unimportant.[104] The α-keto triflates 364 and 366 were substantially less reactive than α-CH_2 analogues 363 and 365 (extrapolated rates). Increased flexibility in 364 and 366 therefore did not lead to increased α-C=O/α-CH_2 ratios. It was concluded that carbonyl conjugation does not increase relative to the more rigid "parent" systems 358 and 361.



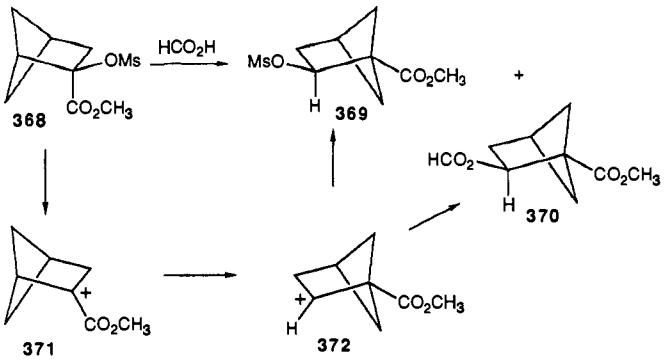


At this point in the review, I would like to briefly digress from presentation of literature studies. Some further comments concerning our proposed carbonyl conjugation, as represented by 356b, are warranted since there now appears to be some controversy. The studies of Takeuchi[103,104] suggest that this effect does not operate. However the studies on 364 and 366 are subject to the same criticism as the study on 358 and 361. As before, the extent of anchimeric assistance in 358, 361, and 364 remains uncertain. Therefore, there is no way to evaluate the *unassisted rate of formation* of a perpendicular α-carbonyl cation. The rate-retarding effects of $10^{-8.2}$ and $10^{-8.7}$ must be compared to values determined on substrates where the unassisted rate of formation of a perpendicular α-carbonyl cation is known. Furthermore, since the conjugative ability of a C=O bond in an α-carbonyl cation is intrinsically less than that of a C=C bond in an allylic cation, there is no reason to expect that a constrained α-carbonyl cation will distort in a similar fashion as the C=C bond in a geometrically constrained allylic cation. Even if one assumes that triflates 358, 361, 364, and 366 are all k_c substrates, then the most that one can conclude is that carbonyl conjugation is unimportant in solvolyses of these geometrically constrained systems. *However this conclusion should not be used to obscure the fact that these constrained systems are far less reactive than unconstrained systems 314, 318–321, 329–333, and 344–347, where triflate derivatives are too reactive to be isolated.*

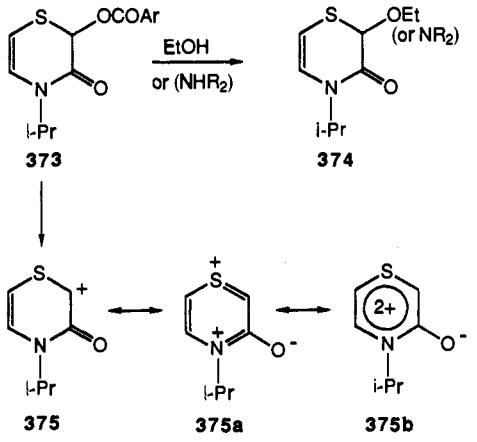
Finally, I would like to emphasize that the importance of forms such as 356b should not be overestimated. Our original comment in 1982[100a] that "...one might expect the carbonyl group in mesylates to slow solvolysis rates by large factors, perhaps as large as 10^5, relative to model mesylates" was just a crude estimate. As with all forms of conjugation and participation, the magnitude of carbonyl conjugation should not be a constant. It should be a delicate function of the demand for conjugation and the ability of the group to supply electron density. Our statement does not attempt to assign a magnitude to rate enhancement due to carbonyl conjugation (which should be variable). It simply implies that the α-keto mesylates studied in this paper reacted qualitatively faster than expected.

Solvolysis of the bicyclic mesylate 368 in formic acid gave the rearranged mesylate 369 as the primary product, along with a smaller amount of the formate 370.[105] The mesylate 368 was 3.2×10^2 times more reactive than the β-carbomethoxy isomer 369 and only 3.6 times less reactive than the α-H analogue, bicyclo[2.2.1]hexy-2-yl mesylate. The rearranged products are derived from internal return or solvent capture of the rearranged ion 372. The unexpectedly rapid rate of solvolysis of 368 was attributed to relief ground-state strain in 368 as the leaving group departs, possible anchimeric assistance by C_1–C_5 bond during ionization, and possibly to carbonyl conjugation in a developing cationic intermediate. It is not possible to determine whether solvolysis of 368 is a k_Δ process with the available data. The behavior of the α-cyano triflate 224 (which is proposed to react by a stepwise mechanism) is very similar to that of 368. Similar ground-state destabilization factors may contribute to the rapid solvolysis rate of 368.

The *m*-chlorobenzoate 373 solvolyzes in alcohol solvents and in the presence of amines to give substitution products.[106] The Winstein–Grunwald *m* value in alcohol solvents is unusually large (1.53) and is indicative of a very polar transition state. The proposed inter-

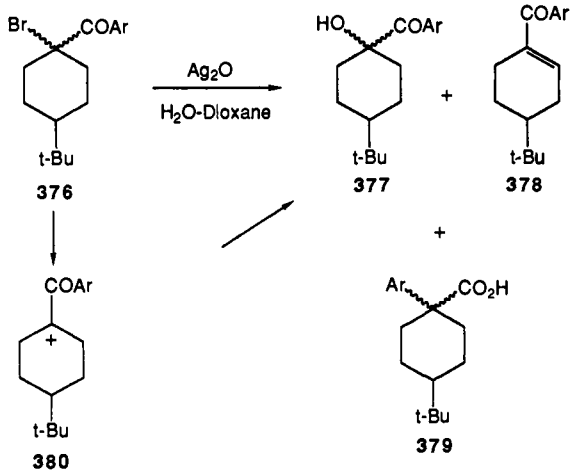


mediate in these transformations is the unusual α-carbonyl cation 375. It was suggested that this cation is actually an aromatic cation as represented by form 375b.



D. From Silver Ion Assisted Reactions

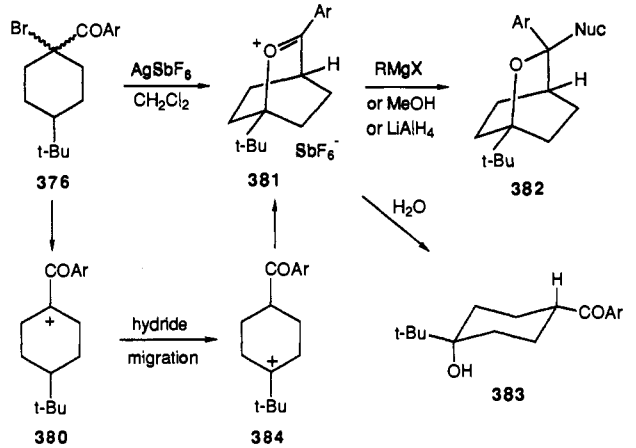
The Charpentier-Morize group has carried out numerous studies in which α-carbonyl cations have been generated by reaction of silver salts with α-halo ketones. One of the earliest examples involves the reaction of the α-bromo ketones 376 with Ag_2O in aqueous dioxane.[107] Depending on the nature of the aryl group, varying mixtures of 377–379 were formed. The carboxylic acids 379 were derived from a semi-benzylic acid type mechanism. The α-carbonyl cations 380 were suggested as intermediates in the formation of 377 and 378.



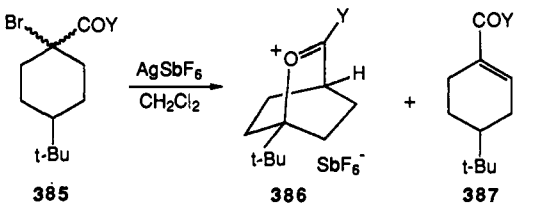
Subsequent studies showed that both isomers of 376 (Ar = phenyl, anisyl) reacted with $AgSbF_6$ to give the stable crystalline salt 381.[108] This salt could be reacted with nucleophiles to give products 382. Reaction with water led to the cis alcohol 383. These products are suggested to arise via the same α-carbonyl cation 380 which lives long enough under these conditions to undergo hydride migration (either stepwise or transannular). Subsequent cyclization via the carbonyl oxygen leads to the isolable salt 381. This methodology for functionalization of the 4-position of a 1-bromo-1-ketocyclohexanes has been used in the synthesis of some monoterpenes via α-carbonyl cations and rearranged oxonium ions.[109]

TABLE IV. ^{13}C NMR Chemical Shifts of Cations 438, α-CF_3, and α-CN Analogues

cation	C+	C=O	C=O of 437
Ph_2C^+COPh	202.8	195.6	200.6
Ph_2C^+COMe	201.7	209.2	208.9
$Ph_2C^+COCF_3$	193.3	184.2	191.4
$Ph_2C^+CO_2H$	193.4	166.9	179.9
$Ph_2C^+CO_2Me$	191.2	168.8	175.0
$Ph_2C^+CONMe_2$	181.8	166.0	172.1
$Ph_2C^+CCF_3$	189.6		
Ph_2C^+CCN	168.8		
Ph_2C^+CH	199.8		



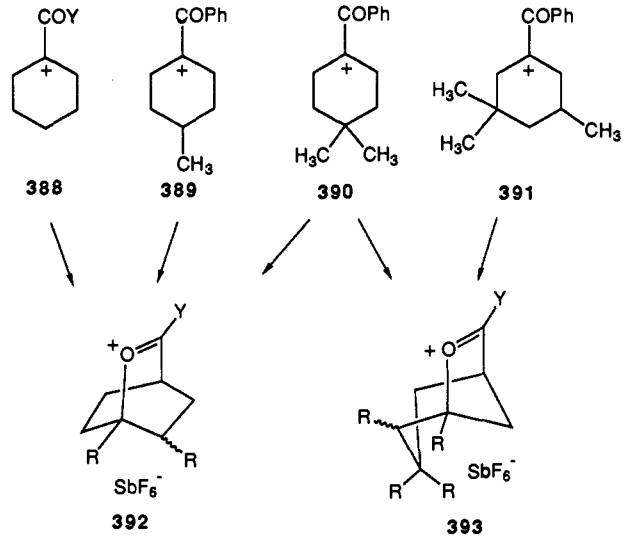
This type of reaction sequence has generality. A number of cyclized ions 386 could also be formed from α-bromo ketones, esters and amides.[110] Also produced in these dehalogenation reactions were small amounts of the elimination products 387. These reactions involve α-carbonyl cations that can rearrange via hydride migration. A study on the 2,2,6,6-tetradeutero analogue of 385 (Y = Ph) showed that hydride migration leading to 386 was a stepwise process and not a concerted transannular process.[112]



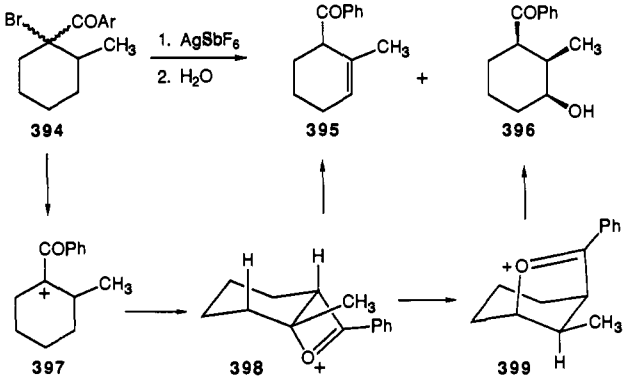
Y = Ar, CH_3, OCH_3, NH_2, NMe_2

Further studies have shown that the α-carbonyl cations 388–391 can be generated as transient intermediates in Ag^+ dehalogenations of the corresponding α-bromo carbonyl compounds.[111] The cations 388 and 389 suffer proton loss to give alkenes, as well as hydride migrations and cyclization to give the bicyclo[2.2.2]-oxonium ions 392. The cation 391 forms the bicyclo-

[3.2.1]oxonium ion **393**, while **390** leads to mixtures of **392** and **393**.

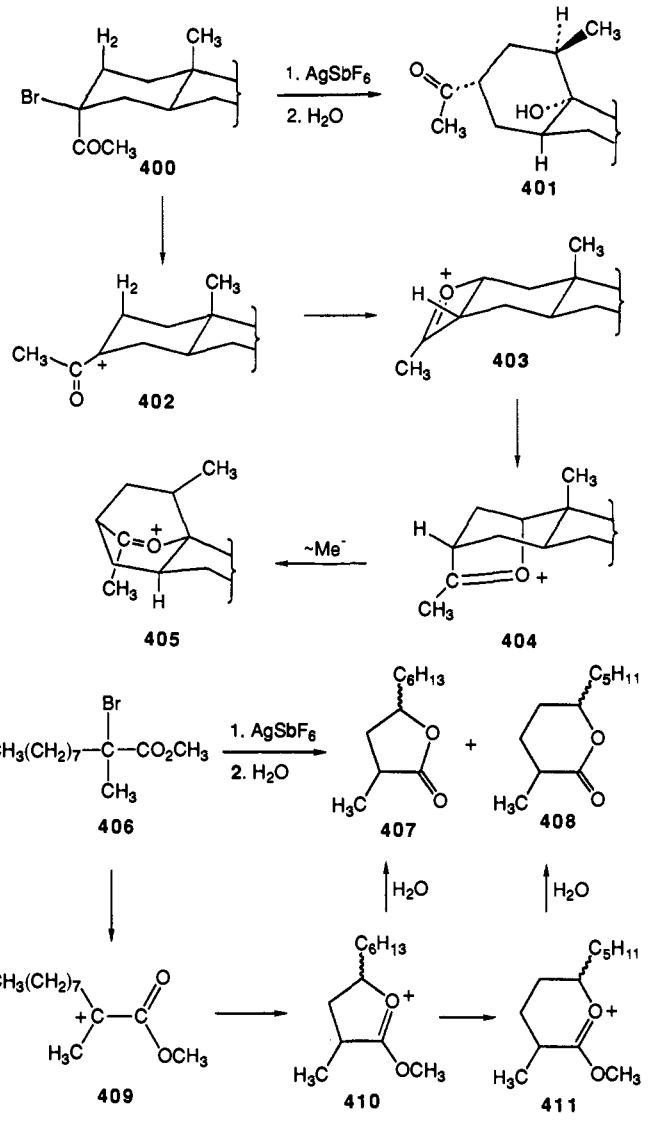


The α-bromo ketone **394** (mixture of isomers) reacts with $AgSbF_6$ at −30 °C to give the oxonium ion **398**, which can be observed spectroscopically.[112] On warming, **398** rearranges to **399**. Addition of water converts these ions to the products **395** and **396**. The α-carbonyl cation **397** is the precursor to these oxonium ions. Deprotonation of **398** (or the open form) is the source of the alkene **395**, while reaction of water at the carbonyl group of **399** would lead to the alcohol **396** with the observed stereochemistry. Dehalogenation of 1-benzoyl-1-bromo-4-*tert*-butyl-2-methylcyclohexanes with $AgSbF_6$ leads to products derived from oxonium ions with bicyclo[4.2.0], -[3.2.1], and -[2.2.2] ring structures.

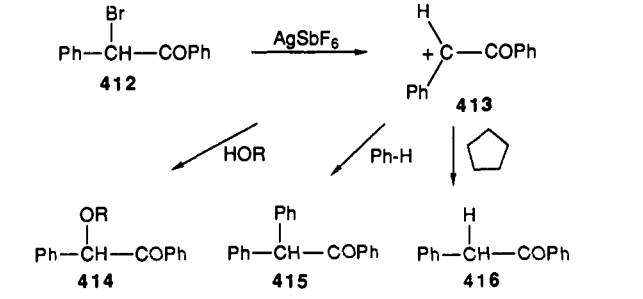


α-Carbonyl cations have been generated in steroidal systems and subsequent rearrangements have resulted in remote functionalization in these systems.[113] As a typical example, treatment to the α-bromo ketone **400** with $AgSbF_6$, followed by water, gave the δ-hydroxy ketone **401**. This transformation is proposed to involve the α-carbonyl cation **402** as well as the oxonium ions **403**–**405** from successive hydride migrations. Cyclic oxirinium ions have been considered as intermediates in these reactions.

This type of remote functionalization via hydride migration can also be observed in the ester **406**.[2,114] Dehalogenation, followed by the addition of water gave mixtures of the lactones **407** and **408**, along with olefinic esters. Hydride migration in the initially formed α-carbonyl cation **409** accounts for these products.

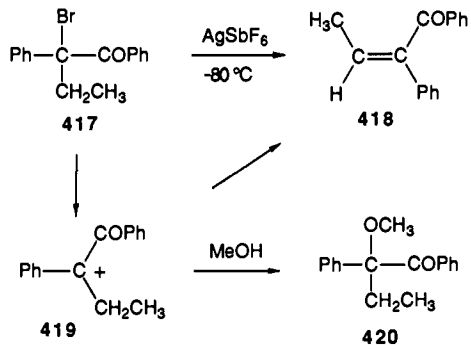


The dehalogenation of the α-bromo ketone **412** with $AgSbF_6$ has also been studied by Charpentier-Morize.[115] When the reaction was carried out at −75 °C in SO_2, spectroscopic evidence indicates the presence of a short-lived α-carbonyl cation **413**. Addition of methanol gave the methyl ether. When the reaction was carried out in benzene at 25 °C, the Friedel–Crafts product **415** was formed. In dichloromethane–cyclopentane, up to 40% desoxybenzoin (**416**) was formed.

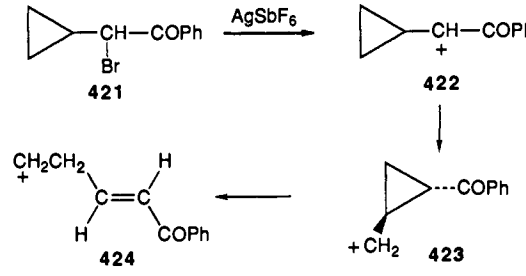


The tertiary α-bromo ketone **417** suffers elimination when treated with $AgSbF_6$ to give exclusively the alkene **418** at −80 °C.[116] When methanol is added, some of the methyl ether substitution product **420** can be isolated, along with elimination products (both isomers).

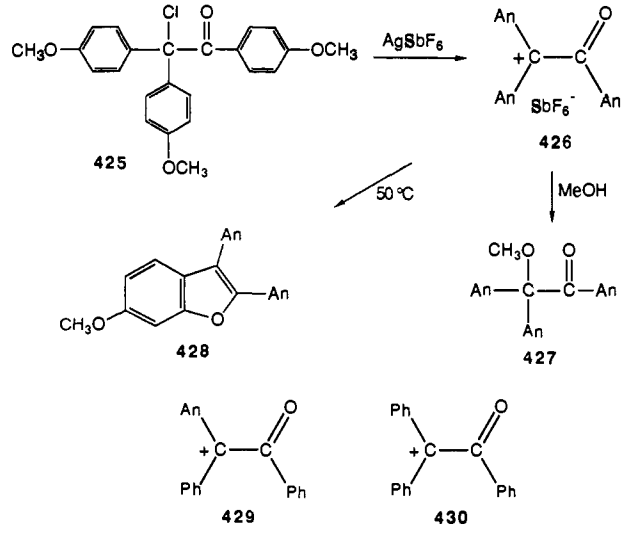
The cyclopropyl-substituted α-carbonyl cation **422** has been generated as a transient intermediate by de-



halogenation of the α-bromo ketone **421**.[117] Chemistry in this system is dominated by rearrangements in the cyclopropylcarbinyl–homoallylic cation manifold. In methanol, products are formally derived from ions **422** and **423**. In benzene, alkylation is observed via cation **423** only, while in *t*-BuOH, products are formally derived from cations **423** and **424**. Products derived from **423** and **424** have exclusively trans stereochemistry.

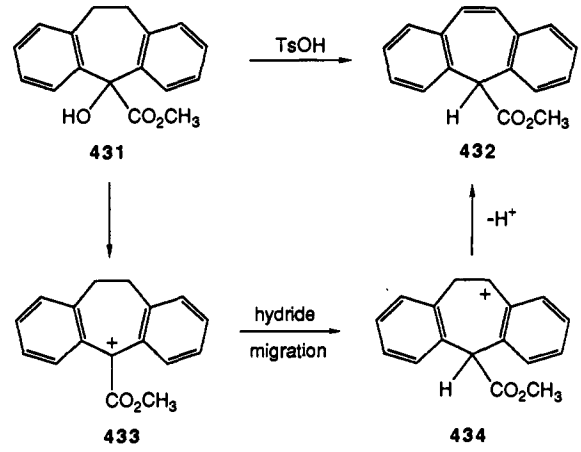


Okamoto has reported the first example of a stable crystalline α-carbonyl cation.[118] Treatment of the chloride **425** with $AgSbF_6$ led to **426** as an isolable salt. Reaction with methanol gave the corresponding methyl ether **427**, while heating in 1,2-dichloroethane gave the benzofuran **428** by an electrocyclization mechanism. The α-carbonyl cations **429** and **430** were also produced (and analyzed by NMR spectroscopy at −78 °C) by the same methodology, but they were too unstable to be isolated at room temperature.

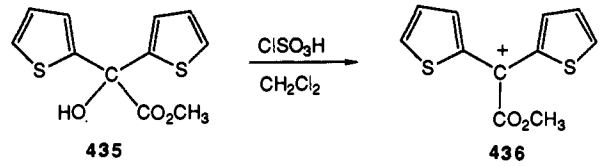


E. α-Carbonyl Cations under Protic and Lewis Acid Conditions

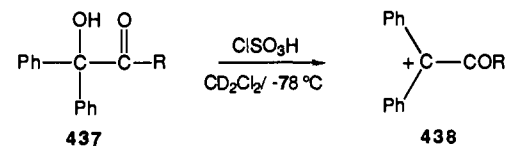
Carbocations are often formed from alcohol or halide precursors under highly acidic conditions. Such methods have been used to generate α-carbonyl cations as well. An early example of such a reaction is the acid-catalyzed dehydration of the α-hydroxy ester **431** which gives the ester **432**.[119] This reaction is proposed to involve formation of the α-carbomethoxy cation **433** which undergoes 1,5-transannular hydride migration. The corresponding α-hydroxy acid gives an analogous transformation.



The α-carbomethoxy cation **436** can be prepared by treatment of the alcohol **435** with $ClSO_3H$ in CH_2Cl_2.[120] NMR and UV spectra are consistent with the cation **436** as a stable entity. Charge is undoubtedly delocalized into the cation stabilizing thiophene rings of **436**. Quenching with alcohols gave the expected ether products.



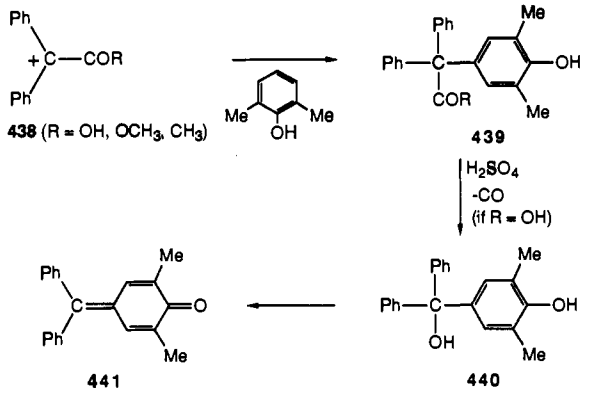
Other aryl-substituted α-carbonyl cations are sufficiently stable for observation in solution under stable ion conditions by NMR spectroscopy.[121] When the α-hydroxy acids, esters, ketones, and amides **437** are mixed with solutions containing $ClSO_3H$ at −78 °C, the resultant solutions of α-carbonyl cations **438** are stable over a period of hours at this temperature. Also produced were analogues of **438**, where one phenyl group is replaced by 1-naphthyl and 5-acenaphthyl groups. ^{13}C NMR chemical shift data for the α-carbonyl cations **438** and related cations are given in Table IV. The cationic carbon atoms of **438** appear in the range of δ 181.8 to 202.8. The corresponding shift of the cationic carbon of the α-H analogue, the diphenylmethyl cation, is δ 199.8 ppm,[122a] while that of the α-CH_3 analogue, $Ph_2C^+CH_3$, is δ 229.3.[122b]



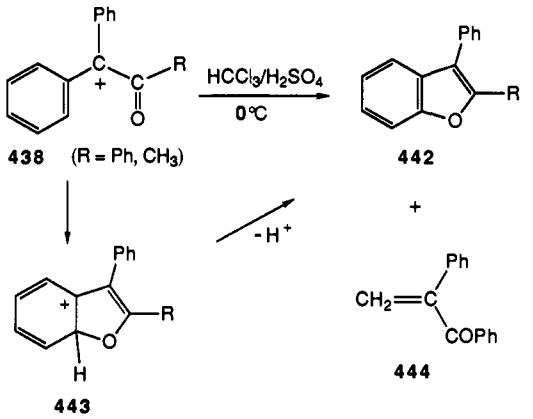
R = Ph, CH_3, CF_3, OH, OCH_3, NMe_2

When cations **438** are generated (from sulfuric acid) in the presence of 2,6-dimethylphenol, the triarylmethane derivatives **439** are formed.[123] For the adducts **439** (R = OH, OCH_3) further decarbonylation was ob-

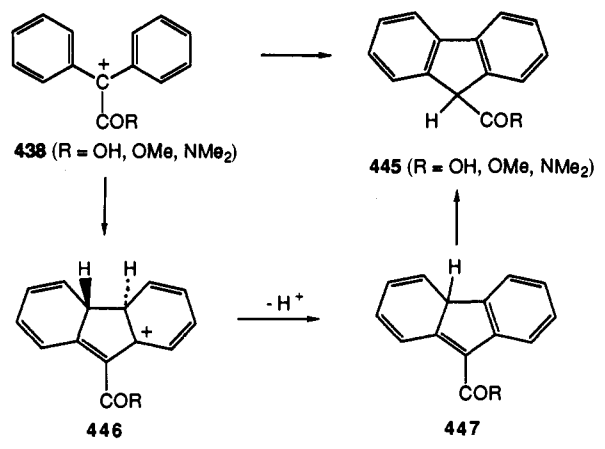
served with subsequent formation of 440 and 3,4-dimethylfuchsone (441).

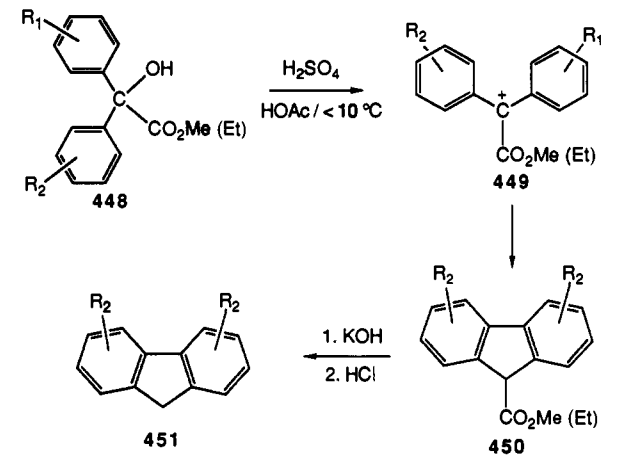


At ambient temperatures ($CHCl_3/H_2SO_4$) the α-carbonyl cations 438 were proposed to undergo cyclization by one of two modes. In the case of the ketone derived cations 438 (R = Ph) and 438 (R = CH_3), cyclization occurs by way of the carbonyl oxygen.[121] Subsequent deprotonation of 443 results in the formation of benzofurans 442 (which can undergo further electrophilic attack to give dimers and trimers under the reaction conditions). The cyclization process is analogous to the benzofuran formation seen from the cation 426.[118] In the case of cation 438 (R = CH_3) up to 20% of the rearranged α,β-unsaturated ketone 444 is seen.[121,124] Potential mechanisms for this transformation have been suggested.



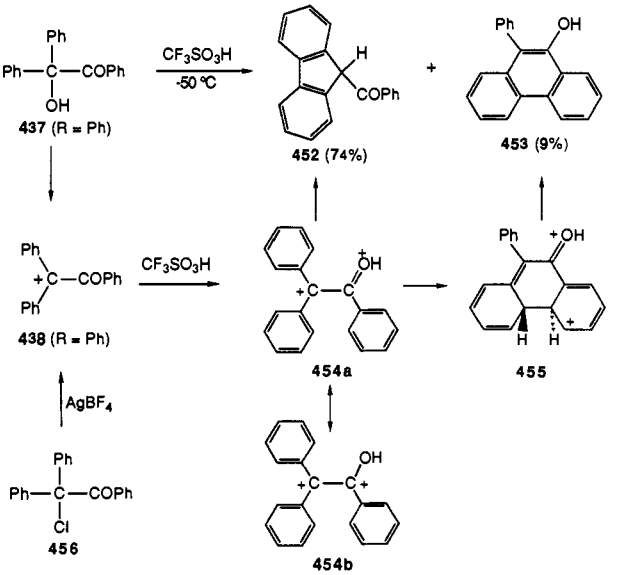
In contrast to the cyclization process seen in ketone analogues of 438, the acid, ester, and amide analogues of 438 ultimately give electrocyclic coupling at the ortho positions of the aromatic rings leading to the fluorene derivatives 445.[121] This electrocyclization has been exploited as a synthetic method for the preparation of benzannelated fluorenes.[125] Thus treatment of a variety of α-hydroxy esters 448 with sulfuric acid in acetic acid gave reasonable yields of the corresponding esters 450. These fluorenyl esters 450 obtained from the acid-catalyzed electrocyclization of the cationic intermediate 449, can be readily saponified and decarboxylated to give the hydrocarbons 451.





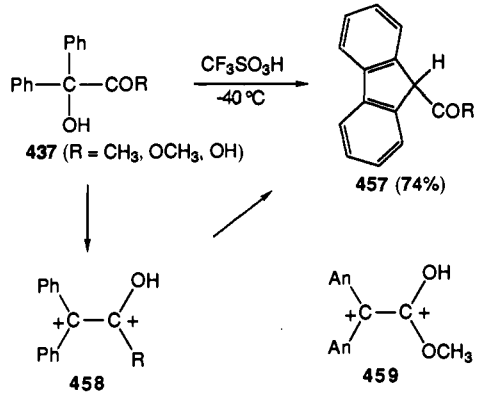
Both proposed modes of cyclization of cations 438 are formal analogues of the 4 π-electrocyclization of the pentadienyl cation. First order rates of disappearance of cations 438 can be easily monitored spectrophotometrically. The ΔG^* values are all ~18 kcal/mol and entropies of activation are all negative, indicative of a more ordered transition state. These activation parameters are similar to those reported[126] for the cyclization of methyl-substituted pentadienyl cations. It was suggested that analogous types of electrocyclization operate in the α-carbonyl cations 438.

In a study aimed at sorting out the features leading to fluorenone formation versus benzofuran formation, it has been suggested that fluorenones do not arise *directly* from α-carbonyl cations. The cations 438 have been generated by Shudo[49] under somewhat different conditions and their behavior is significantly different from that previously described.[121] The α-hydroxy ketone 438 (R = Ph) was reacted in CF_3SO_3H at −50 °C and the fluorene 452 was isolated along with the phenanthrene derivative 453. While benzofuran 442

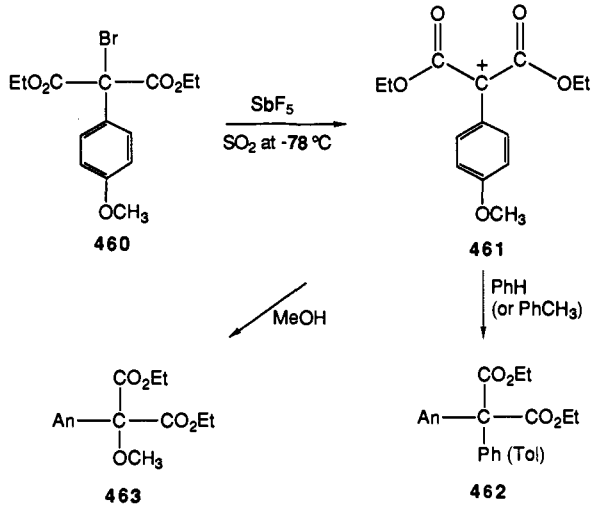


(and alkylated benzofuran) was previously reported in $CHCl_3/H_2SO_4$, no benzofurans were observed in the CF_3SO_3H medium. The cation **438** (R = Ph) could be generated as a stable entity by reaction of the α-chloro ketone **456** with silver salts. However, when the stable cation **438** (R = Ph) was added to CF_3SO_3H at −50 °C, the fluorene **452** and the phenanthrene **453** were then produced. This led to the proposal that the origin of the products **452** and **453** was the dication **454**, which was formed by protonation of the α-carbonyl cation **438** by CF_3SO_3H. It was proposed that increased charge delocalization into the aryl rings of dication **454** facilitates 4π electrocyclization to give fluorene **452**.

The alcohol **437** (R = CH_3) also gave fluorene **457** (R = CH_3) on reaction with CF_3SO_3H at −40 °C, indicating that the benzoyl group is not necessary for fluorene formation. In contrast to the reaction in $HCCl_3/H_2SO_4$, no benzofuran is formed. The chemistry of the α-hydroxy ester **437** (R = OCH_3) and the α-hydroxy acid **437** (R = OCH_3) is also analogous to that of α-hydroxy ketones **437** (R = Ph and CH_3). The dications **458** formed by further protonation of the intermediate α-carbonyl cation are the proposed intermediates leading to fluorene formation. Spectroscopic evidence has also been presented for the existence of the dication **459** in CF_3SO_3H/SbF_5 as a stable entity below 0 °C. This alternative mechanism for fluorene formation helps to clear up previous discrepancies concerning the fate of α-carbonyl cations under stable ion conditions.

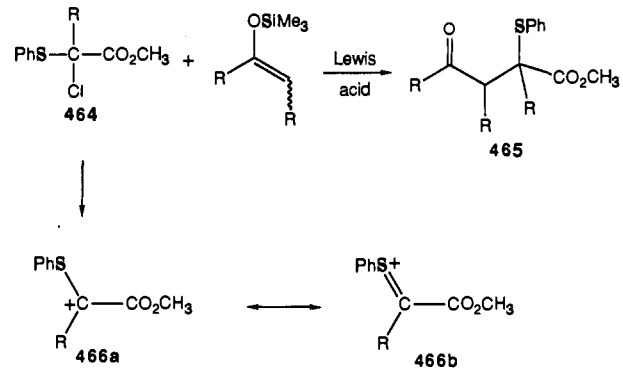


The dicarbonyl-substituted cation **461** can be generated from the bromide **460** by treatment with SbF_5 in SO_2 at −78 °C.[127] This cation can be observed by ^{13}C NMR spectroscopy (C^+ at δ195, C=O at δ 180).

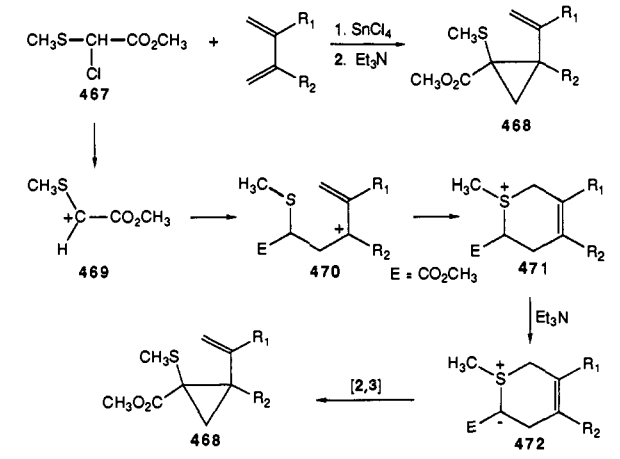


Quenching the cation with benzene or toluene gave the alkylated products **462**. Methanolysis of **460** also occurs at ambient temperature, presumably via cation **461**. Comparable reactions were not observed when the *p*-anisyl group was replaced with phenyl.

Lewis acid catalyzed reactions of the α-chloro sulfides **464** with silyl enol ethers provides a facile synthesis of the γ-keto esters **465**.[128,129] The sulfur-stabilized α-carbomethoxy-substituted cations **466** are likely intermediates. Desulfurization of **465** (via reduction or oxidation to the sulfoxide followed by pyrolysis) led to the saturated or unsaturated γ-keto esters, respectively.

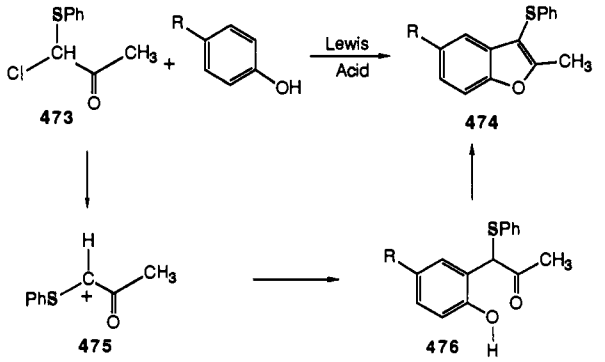


The further synthetic utility of these sulfur-stabilized cations is illustrated in the $SnCl_4$-catalyzed reaction of **467** with conjugated dienes, which leads to the substituted vinylcyclopropanes **468**.[130] These reactions proceed by addition of the sulfur-stabilized α-carbomethoxy cation **469** (or the Lewis acid complex of **467**) to the diene. Further cyclization gives **471**, which is then deprotonated by Et_3N to give the ylide **472**. 2,3-Sigmatropic rearrangement of **472** gives the observed product. This cyclopropanation reaction has generality, with the CH_3SCHCl–$COCH_3$, CH_3SCHCl–COPh, and $CH_3SCHClCN$ reacting with 1,3-cyclohexadiene under these conditions to give the corresponding vinylcyclopropanes.

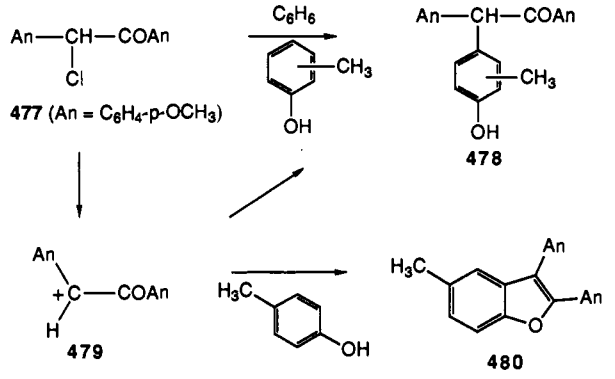


Lewis acid catalyzed reactions of α-chloro-α-thiophenoxy ketones **473** have also been used in the synthesis of benzofurans from phenols.[131] Thus ortho alkylation of phenols by thiophenoxy stabilized α-carbonyl cations **475** leads to the intermediate ketone **476** which cyclized to the benzofurans **474**.

The chloride **477** has been shown to undergo uncatalyzed reaction with a number of phenols in benzene at room temperature.[132] Phenol, o-cresol, and *p*-cresol



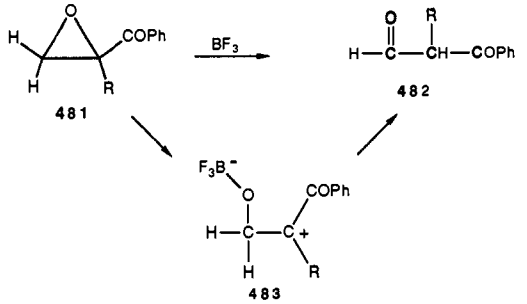
give the alkylated products 478. In the case of *p*-cresol or naphthols, benzofuran formation (analogous to formation of 474) is observed. The α-carbonyl cation 479 is the suggested intermediate. In the case of *p*-cresol or the naphthols, where the para position is blocked, ortho alkylation leads ultimately to the benzofuran 480. These reactions also occur when the anisyl groups are replaced with 3,4-(methylenedioxy)phenyl but no reaction occurs when the anisyl groups are replaced with phenyl.



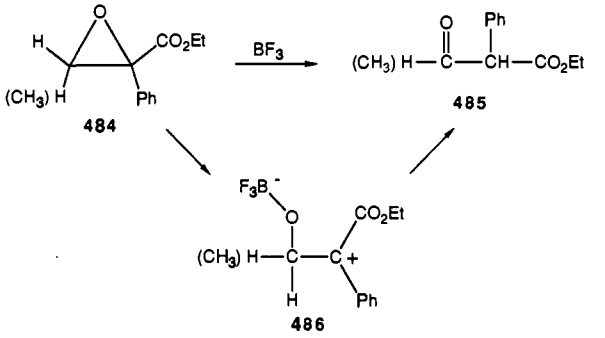
F. Miscellaneous Reactions That Generate α-Carbonyl Cations

Over the years, there have been a number of additional reactions described where α-carbonyl cations may be intermediates. This section deals with some of these transformations where α-carbonyl cations are generated by methods other than from halo epoxides, solvolysis reactions, silver ion promoted reactions, or from alcohols/halides under acidic conditions. In some of these studies, α-carbonyl cations are clearly implicated, while in others the question of their involvement has not been raised. Presented in this section are some selected transformations.

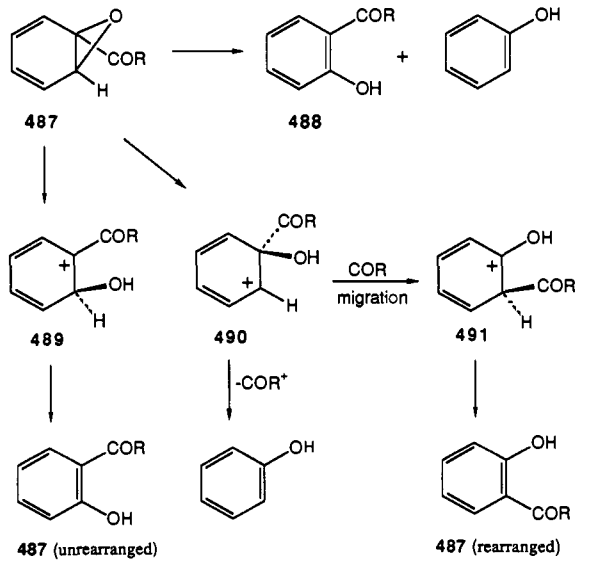
An early study in which α-carbonyl cations are implicated is the BF_3-catalyzed rearrangement of the α,β-epoxy ketones 481 to the carbonyl compounds 482.[133] The α-carbonyl cations 483 are formed in preference to the primary cation that would form on opening of the epoxide in the alternative fashion. It was concluded that α-carbonyl cations were either comparable in stability or more stable than primary cations.



A related study is the BF_3-catalyzed rearrangement of the glycidic esters 484 to the β-keto ester 485.[134] The benzylic α-carbonyl cation intermediate 486 is apparently formed in preference to primary or secondary cations. When both hydrogens in 484 are replaced with methyl groups, then opening of the epoxide leads to the tertiary cation instead of the α-carbonyl cation.

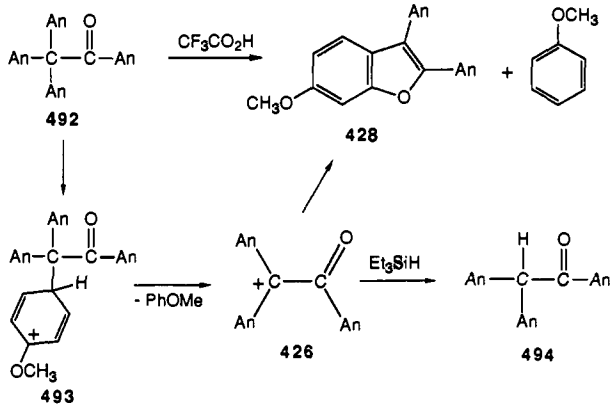


The arene oxides 487 (R = OH, OCH_3, H) aromatize at various pH's to give phenol as well as the substituted phenol 488.[135] In terms of mechanism, the protonated form of 487 can open by competing pathways to give the α-carbonyl cation 489 and the cation 490. Phenol is derived from 490 by loss of H^+ and CO_2 (when R = OH) or loss of H^+ and CO (when R = H). The product 488 can be derived from the α-carbonyl cation 489 or from 490 after the group COR migrates to give cation 491. Deuterium labeling studies have been used to determine the origin of these products. When R = OH, 40% of the products are derived from the cleavage pathway leading to the α-carbonyl cation 489 (at pH = 1). When R = OCH_3, 33% of the product is derived from 489, and when R = H, 11% of products are derived from 489. Thus cleavage of protonated 486 to give the α-carbonyl cation 489 is competitive with cleavage to form the cation 490.

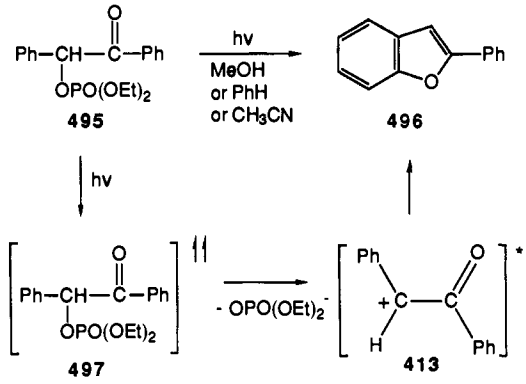


The cation 426 has been generated by Okamoto as the stable hexafluoroantimonate salt.[118] However, prior to this isolation, Okamoto had proposed that this cation is an intermediate in the acid-catalyzed cleavage of

anispinacolone (492).[136] When treated with CF_3CO_2H, the benzofuran 428 was isolated, along with anisole. This transformation is proposed to involve protonation of the pinacolone, loss of anisole, and cyclization of the cation 426. Further evidence for the intermediacy of cation 426 comes from a trapping experiment in which addition of triethylsilane (hydride donor) to the reaction mixture gave 85% of the reduced product 494.

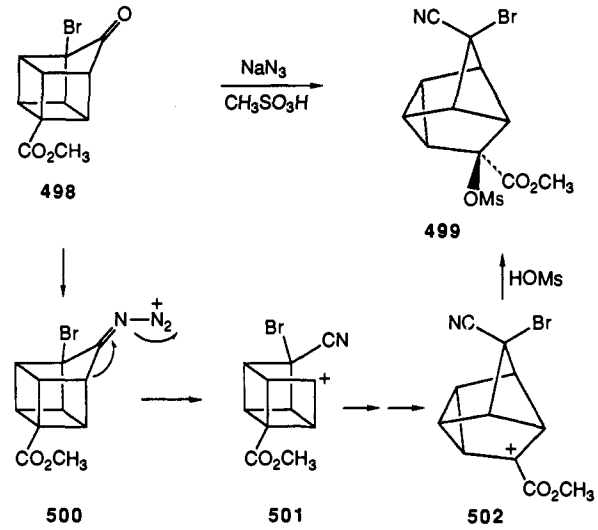


Givens has presented an efficient method for generation of cationic intermediates involving photolysis of phosphate esters.[137] He has observed formation of the benzofuran 496 on photofragmentation of benzoin diethyl phosphate (495). This reaction is thought to occur via the triplet manifold (quenching with piperylene or naphthalene) and gives the intramolecular cyclization product regardless of the reaction medium. The chemistry of the α-carbonyl cation 413* generated by this photochemical method appears to be different from that of 413 generated by other methods.[100a,115]

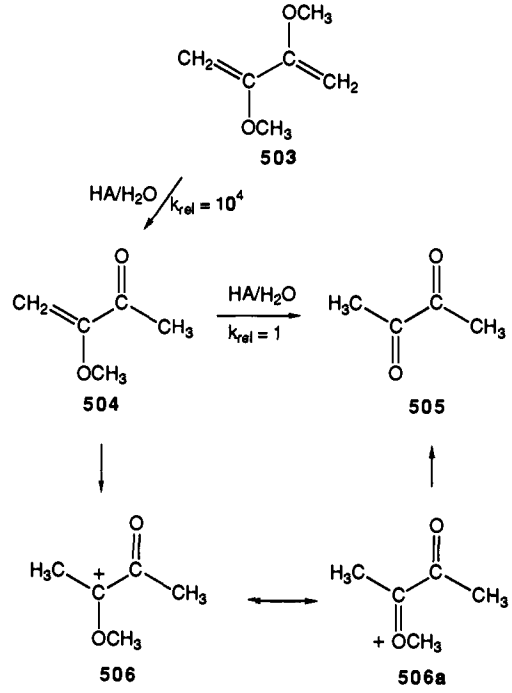


A novel rearrangement of the homocubanone system 498 has been observed under Schmidt conditions where 499 is the major product.[138] Fragmentation of the intermediate 500 gives the cyclobutyl cation 501. A series of cyclobutyl–cyclopropylcarbinyl rearrangements ultimately results in the α-carbomethoxy cation 502, from which the product 499 is derived.

Acid-catalyzed hydrolysis of the 2,3-dimethoxy-1,3-butadiene (503) has been found to occur in two stages.[139] Initially, the enol ether 504 is formed and the second stage of the hydrolysis gives biacetyl (505). Hydrolysis of the acetyl-substituted enol ether 504 is 10^4 times slower than hydrolysis of 503. The mechanism of these hydrolyses involve rate-determining proton transfer from the catalyzing acid. The rate-retarding effect of the acetyl group is due to an electron-withdrawing inductive effect which destabilizes the intermediate α-carbonyl cation 506. The electron-donating resonance



effect of the carbonyl group does not appear to be important. This is consistent with the strong electron supplying resonance effect of the methoxy group (506a) which results in little demand for resonance stabilization by other groups. This is analogous to the effect of the cyano group in acid-catalyzed hydrolysis of the enol ether 216[16] where the resonance stabilizing effect of the α-cyano group was greatly suppressed by the conjugating ethoxy group.



The Pummerer rearrangement has been used to produce a number of sulfur stabilized α-carbonyl cations of type 508. The general method involves treatment of a β-keto sulfoxide under Pummerer conditions (acid, trifluoroacetic anhydride, etc.). The intermediate cations 508 are functionally equivalent to the simple α-carbonyl cation 509 since the thiomethoxy group is easily removed following reaction of cations 508. By using this methodology, treatment of 510 with CF_3CO_2H gave the intramolecular cyclization product 511, presumably via the cation 512.[140a] Carbazoles 513, indoles derived from 514, and benzothiophenes derived from 515 have all been produced by this method.[140b,c]

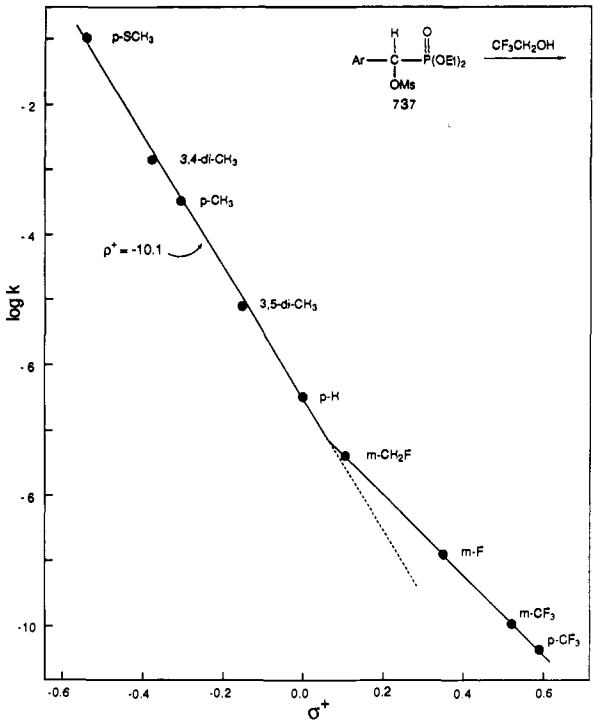
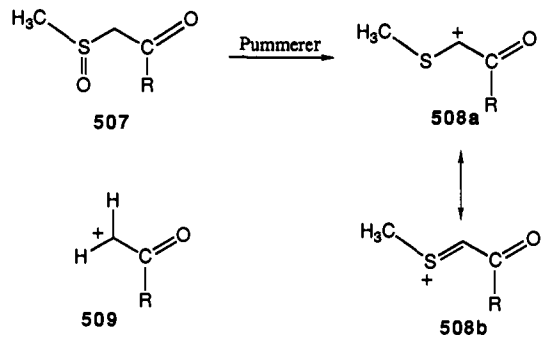
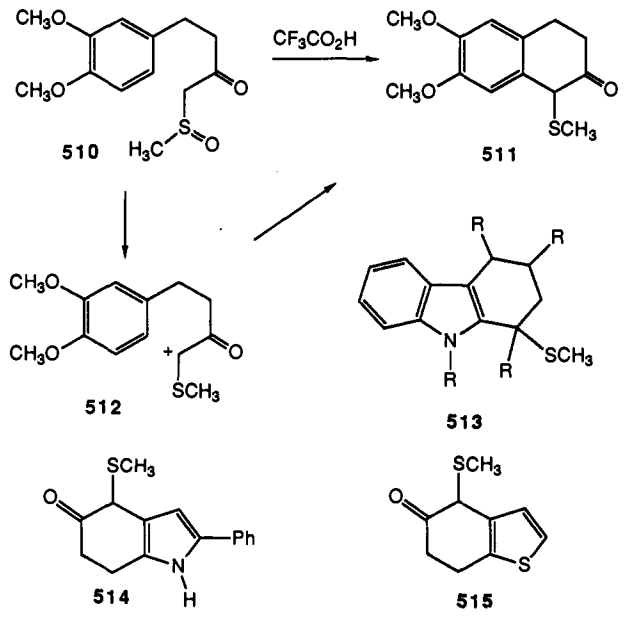


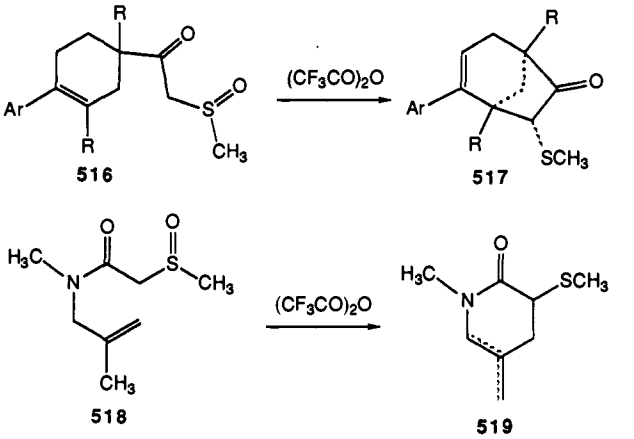
Figure 6. A plot of log k for acetolysis of **737** vs σ^+.



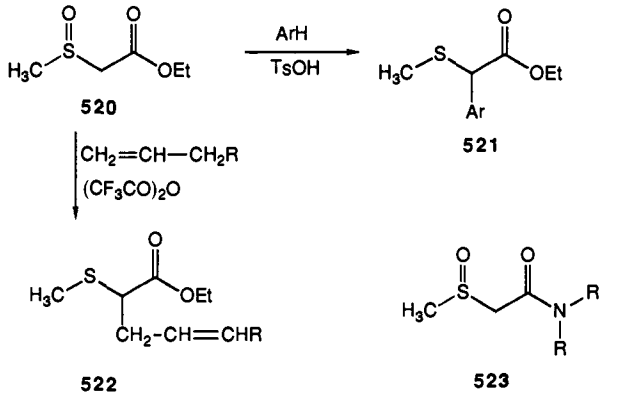
Other analogous examples of intramolecular arylation reactions of cations of type **508** are also known.[141a]



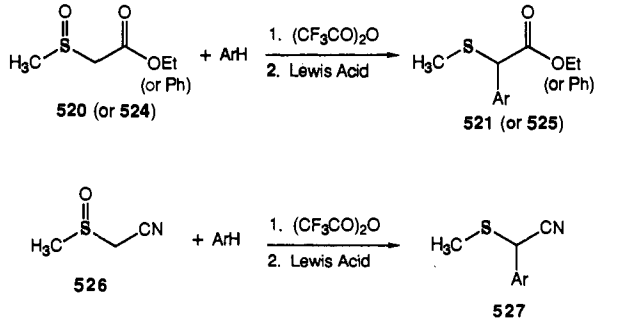
Intramolecular cyclization involving double bonds has also been observed in the Pummerer reaction of β-keto sulfoxides. Thus treatment of **516** with trifluoroacetic anhydride gave the cyclized product **517**.[141b] Similar conditions were used to convert **518** to **519**.[142]



Intermolecular reactions of the cationic intermediate derived from the sulfoxide **520** under Pummerer conditions have also been achieved. Reaction of **520** with aromatic substrates and toluenesulfonic acid (with continuous removal of water) led to **521**,[143] while alkenes reacted to give **522**.[144] In a synthesis of the natural product pellitorine, the amide **523** was reacted with 1-octene under Pummerer conditions to give a key intermediate, the amide analogue of **522**.[145]

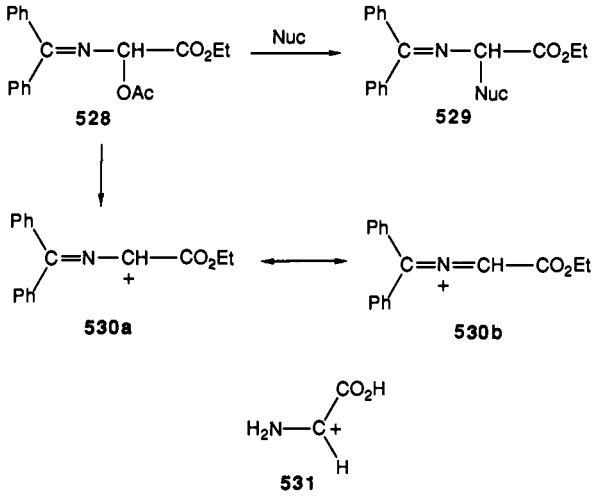


In a related procedure, arylation of **520** (or **524**) could also be accomplished at much lower temperature by subsequent addition of the Lewis acids $SnCl_4$ or $TiCl_4$.[146] The β-cyano sulfoxide **526** could also be arylated under these conditions, presumably via the analogous sulfur-stabilized α-cyano cation.

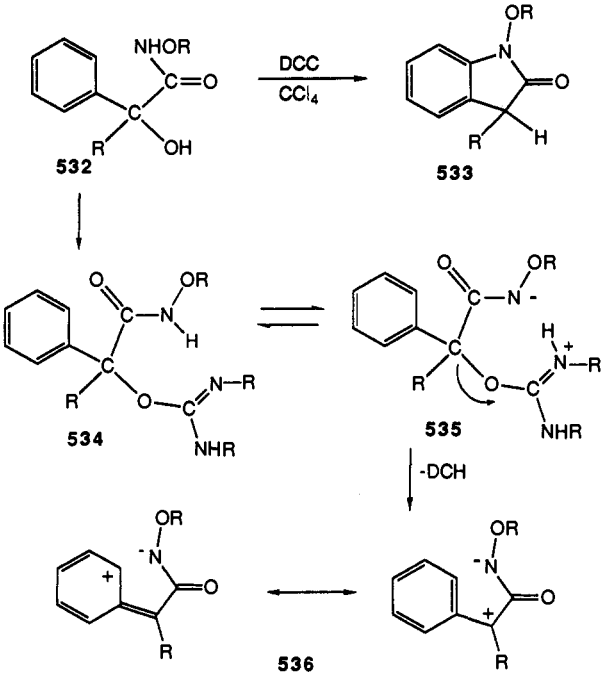


The acetate **528** has been utilized as a synthetic equivalent of the glycine cation (**531**) in reactions with various heterocyclic and carbon nucleophiles.[147] While no evidence was available concerning reaction mechanism, the cation **530** well may be involved under solvolytic conditions (alcohol solvents). Reactions of **528**

with organocopper reagents, which lead to unusual amino acid derivatives, probably bypass such intermediates.



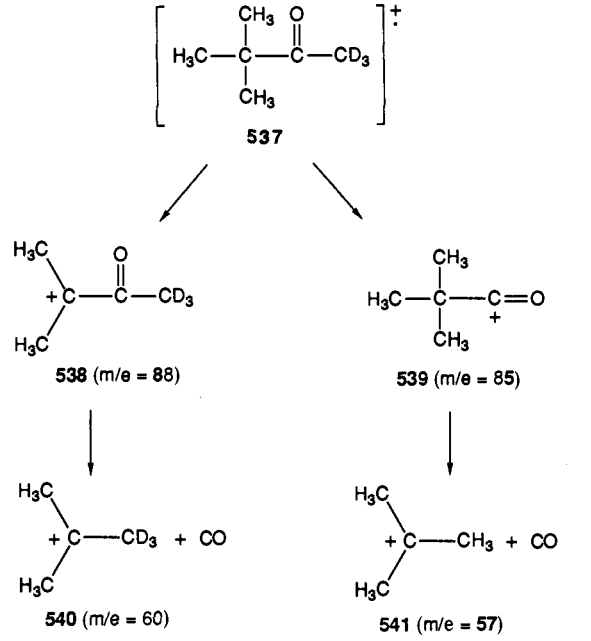
Reaction of the *N*-alkoxy-2-phenylglycolamides **532** with dicyclohexylcarbodiimide led to the cyclized products **533**.[148] These products are proposed to arise via formation of the dipolar intermediate **536**. Ring closure and subsequent rearomatization gives the 1-alkoxyindolin-2-ones **533** in good yield.



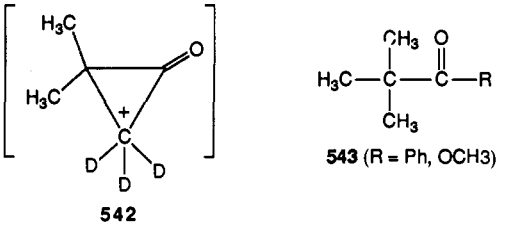
G. α-Carbonyl Cations in the Gas Phase

Certain α-carbonyl cations have been generated and studied using mass spectroscopic techniques. Analysis of metastable ions has provided much information on the fate of these cations in the gas phase. Grützmacher and co-workers have applied these techniques over the years to a systematic study of these ions. The behavior of α-carbonyl cations in the gas phase, where interactions with solvent are precluded, appears to be quite different from solution behavior.

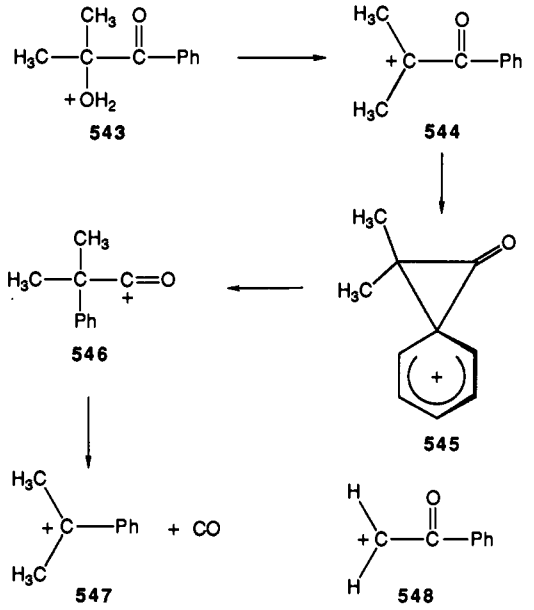
The parent ion derived from pinacolone and the deuterated analogue **537** undergo fragmentation via loss of CH_3 in the mass spectrometer.[149-151] Analysis of the deuterated substrate **537** indicated that the α-carbonyl cation **538** and the acylium ion **539** were formed in a 1:3 ratio and it was concluded that the activation energy for formation of these two ions was similar.[149] The ion **538** rearranges and ultimately forms the labeled *tert*-butyl cation **540** and CO. The shape of the metastable



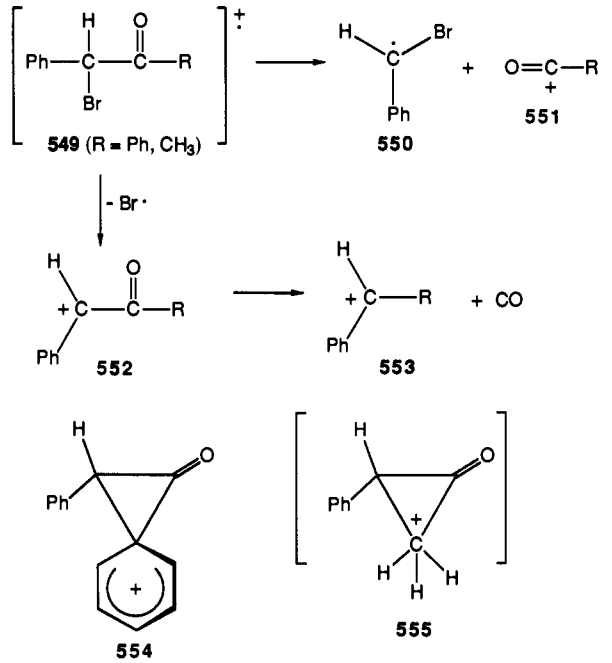
ion derived from the α-carbonyl cation **538** indicates that there is a distinct activation energy for loss of CO.[150] The process is pictured as transition state **542** (a corner-protonated cyclopropane), where CD_3 migration occurs. It is proposed that collapse of **542** occurs directly to the *tert*-butyl cation and CO, bypassing the trimethylacetyl cation **539**. Similar fragmentation processes, involving loss of CH_3 and formation of α-carbonyl cations, are seen in mass spectra of **543** (R = Ph, OCH_3). The activation energy for methyl migration in the α-carbonyl cation **538** is estimated at 13 kcal/mol by MINDO/3 calculations.[151]



Chemical ionization mass spectrometry has been used to generate the tertiary α-carbonyl cation **544** from alcohol and ether precursors.[152] This ion is the base peak in the CI spectrum with isobutane as the reagent gas. MIKE spectra of the metastable ion derived by release of CO from **544** indicate a barrier to rearrangement of this cation. The phenonium ion **545** is the presumed intermediate in this migration. Ultimately the ion **547** is produced from phenyl migration, followed by loss of CO. The primary α-carbonyl cation **548** (also produced by chemical ionization of the corresponding alcohol) undergoes an analogous series of rearrangements. Analysis of the metastable ion produced on loss of CO from the primary ion **548** indicates a smaller kinetic energy release. MNDO calculations are in line with these findings in that rearrangement of **548** to the bridged phenonium ion is exothermic.

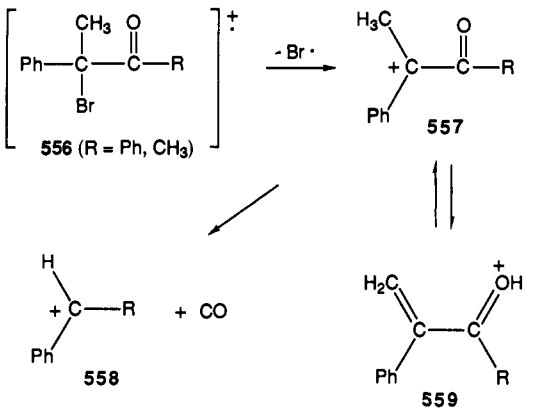


The secondary α-carbonyl cations **552** have been generated by electron-impact ionization of the corresponding bromides **549**.[153] Fragmentation of **549** occurs with formation of the α-carbonyl cation **552** (23–28%) and also with α-cleavage to the acylium ion **551**. As in the case of the ions **538** and **544**, these ions rearrange further by phenyl or methyl migration and loss of CO to give the cations **553**. This is accompanied by a large kinetic energy release. It is suggested that migration proceeds via the phenonium ion **554** or the corner protonated cyclopropane **555**.

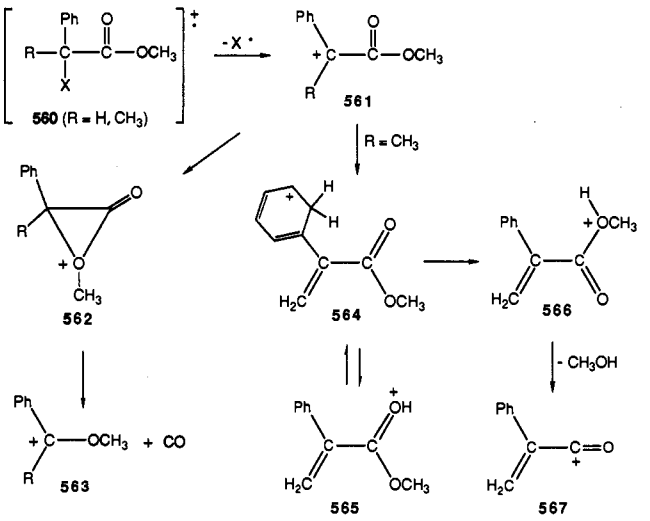


The behavior of the tertiary benzylic substrate **556** (from electron-impact ionization) is analogous to that of secondary systems.[153] The tertiary α-carbonyl cation **557** looses CO to form **558** via migration of Ph or CH_3. Deuterium labeling experiments provide evidence that cation **557** can also rearrange to the O-protonated cation **559**.

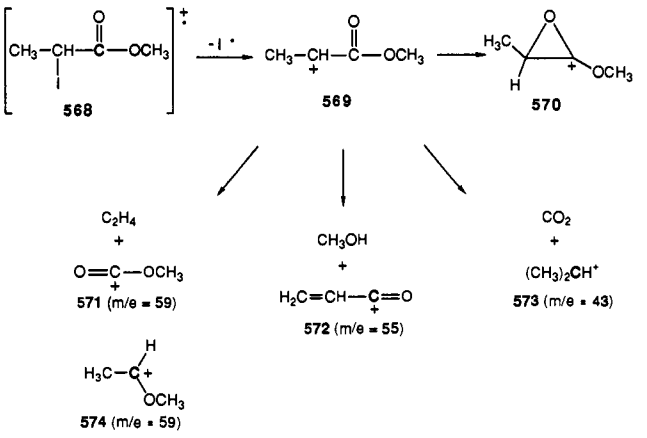
Electron-impact ionization of the benzylic esters **560** gave the secondary and tertiary α-carbomethoxy cations **561**.[154] Rearrangement proceeded with CO loss via the



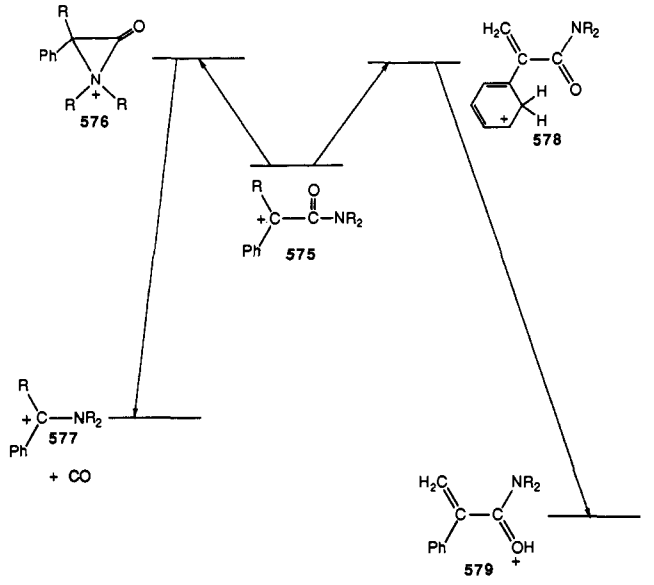
bridged intermediate (or transition state) **562**. The tertiary ion **561** (R = CH_3) underwent a competing rearrangement to give **565**. MIKE and collisional activation spectra, along with deuterium labeling allowed the ion **561** to be distinguished from the more stable isomer **565**. It was concluded that **565** is formed via a mechanism involving the ring protonated form **564**. The fate of **565** was loss of methanol to give the acylium ion **567** at *m/e* 131. The tertiary ion $Me_2C^+CO_2CH_3$ gives an analogous set of rearrangements involving loss of CO and loss of methanol.[155]



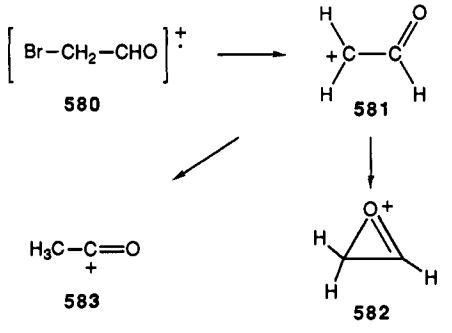
An earlier study on the secondary α-iodo ester **568** under electron-impact ionization led to the observation of the secondary cation **569**.[156] It was pointed out that the isomeric cyclized form **570** could not be ruled out. This cation cleaves further to give fragments at *m/e* 59, 55, and 43. The *m/e* 59 fragment was assigned to the



ion 571 (formed by loss of ethylene). On the basis of the rearrangement processes seen in analogous cations,[154,155] the ion 574 (formed by loss of CO) is a distinct possibility. The acylium ion 572 and the $C_3H_7^+$ cation are proposed fragmentation products.



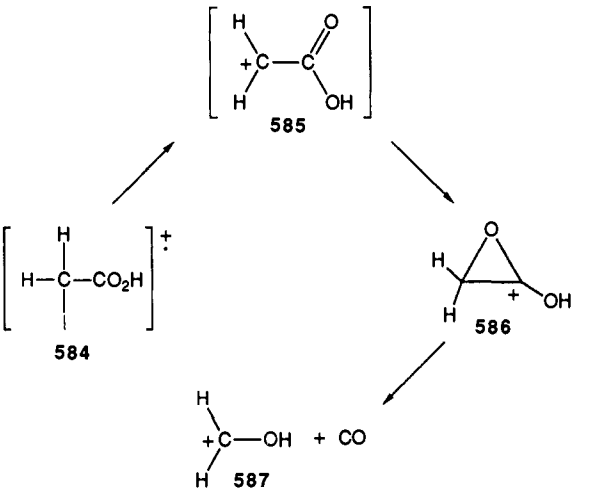
The α-carbamoyl cations 575 have been generated under electron-impact conditions.[157] Rearrangement modes of these cations are similar to that of analogous α-benzoyl and α-carbomethoxy cations. The ion 578 can also transfer a proton to the NR_2 group and lose HNR_2 to generate an acylium ion. MNDO calculations give the energy profile shown. The dimethyl analogues $Me_2C^+CONR_2$ give comparable mass spectral behavior with the exception that $Me_2C^+CONR_2$ and the O-protonated isomer (generated in the CI spectrum of the methacrylamide) interconvert prior to decomposition.[158]



The simplest α-carbonyl cation, the parent system 581, has been generated from bromoacetaldehyde and the $BrCH_2CDO$.[159] Mass spectra from collisionally activated dissociation indicated that 581 partitions between the acylium ion 583 and the cyclized form 582.

The mass spectrum of iodoacetic acid gives a base peak at m/e 59.[160] On the basis of computational studies, which showed that the α-carbonyl cation 585 was not a minimum on the potential energy surface, it was suggested that the cyclic ion 586 was the ion formed when 584 fragments. This cyclic ion further fragments to give the hydroxymethyl cation 587 and CO. Analysis of metastable peaks indicates that this loss of CO has a substantial barrier, which is estimated at 54 kcal.

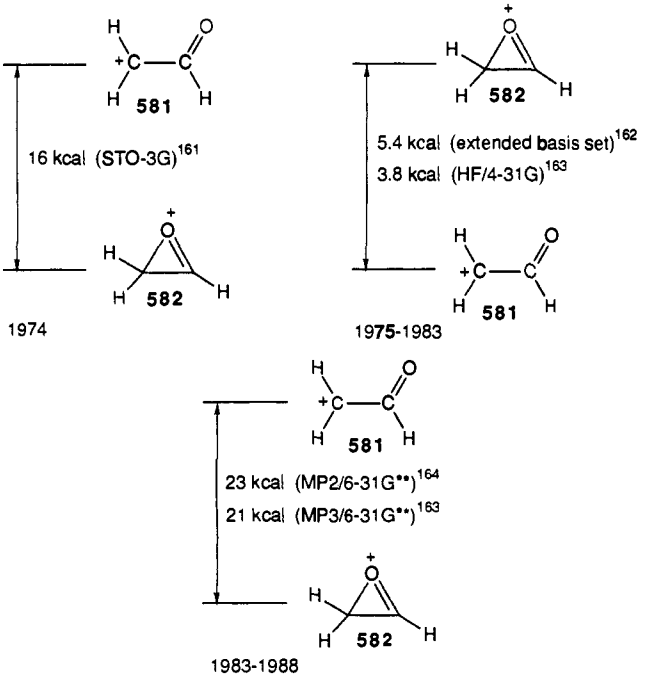
In summary, the behavior of α-carbonyl cations generated in the gas phase in the mass spectrometer differs from solution-phase chemistry. Rearrangement involving loss of CO is a prominent pathway that has not been observed in solution. In solution, collisions with solvent molecules undoubtedly deactivate α-carbonyl cations such that other processes dominate. Gas-phase ions appear to be energetic enough to allow such rearrangements to acylium ions and loss of carbon monoxide.



H. Computational Studies on α-Carbonyl Cations

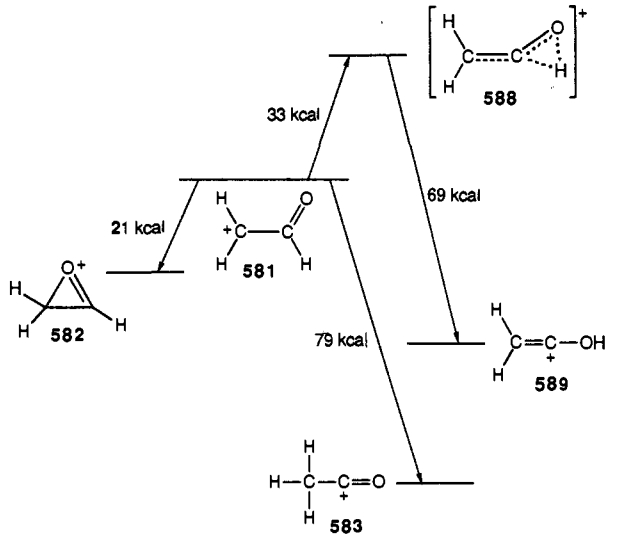
Ab initio molecular orbital calculations have been carried out on the α-carbonyl cation 581 and related ions over the years. These calculations provide insights into features contributing to cation stability in the gas phase. These studies are quite relevant to the mass spectroscopic studies on α-carbonyl cations where the chemistry is significantly different from reactions in solution.

The nature of the α-carbonyl cation (open or closed) has been addressed by computational methods, as has the question of stabilization mechanisms in the open ion. The results of these studies have varied over the years. A calculation from the Charpentier-Morize group in 1974 using a minimal STO-3G basis set placed the

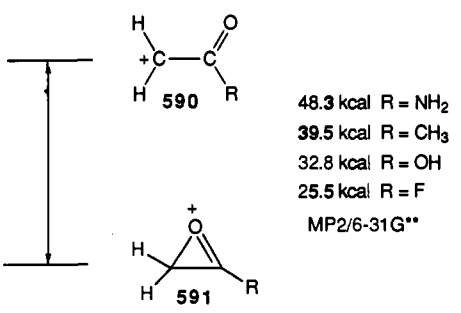


closed ion 16 kcal/mol lower in energy than the open form.[161] However, using a better basis set, in 1975 Schaefer calculated the open α-carbonyl cation **581** to be lower in energy (5.4 kcal/mol) than the oxiranyl cation **582**.[162] In 1983 Radom, using the HF/4-31G basis set, also placed the open form at lower energy (3.8 kcal/mol).[163] However, by using an extended basis set with polarization functions, the latest calculations (Radom in 1983[163] and Lien and Hopkinson in 1988[164]) place the closed form again at lower energy by more than 20 kcal/mol. Additionally, the open form **581** does not represent an energy minimum and cyclizes without barrier to give the closed ion **582**.

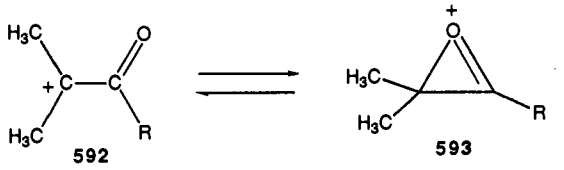
The energy profile for rearrangement of the ion **581** to isomeric $C_2H_3O^+$ cations has also been calculated and is shown.[163] The most stable ion is the acetyl cation **583** which lies 79 kcal below **581**. The open α-carbonyl cation **581** is not at an energy minimum and rearranges without barrier to the acetyl cation **583** (as well as to the closed form **582**). There is an additional barrier of 33 kcal for migration of the formyl hydrogen to oxygen (via transition state **588**) with resultant formation of the hydroxyvinyl cation **589**.



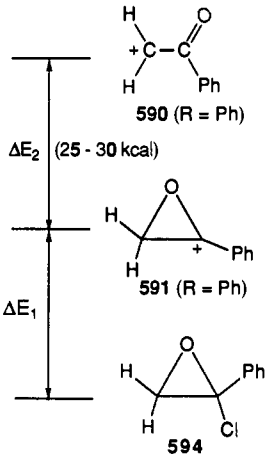
The structures and energies of substituted α-carbonyl cations **590** have also been calculated at the MP2/6-31G** level.[164] These ions all prefer the closed form **591** to a greater degree than does the parent unsubstituted system. The greatest preference for the closed ion is



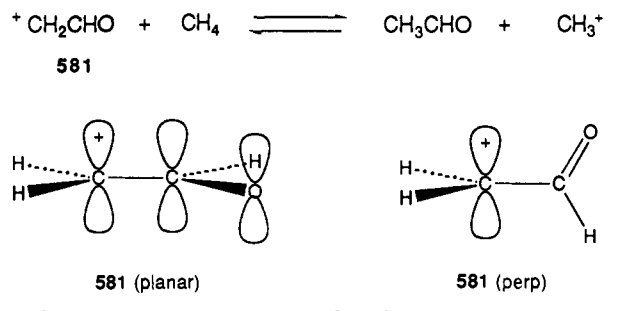
in the case of the NH_2-substituted system which prefers the closed form by 48 kcal/mol. Calculations at a lower level (6-31G*//STO-3G) on the dimethyl-substituted cation **592** gave the opposite effect. The open ion **592** is now favored when R = CH_3 and OH and the closed ion **593** (R = NH_2) is only 7.2 kcal/mol lower than the open ion **592** (R = NH_2). These results are no doubt a result of increased stabilization of the open form by methyl substitution.



A comment pertaining to experimental results in solution is appropriate here. The ion **592** (R = NMe_2) as well as related ions have been generated under solvolytic conditions[100b] and (despite the computational results) there is no evidence for the involvement of the cyclized form. Additionally, on the basis of the calculated energies of ions **590** and **591**, the closed ion **591** (R = Ph) should be approximately 25–30 kcal lower in energy than the open form **590** (R = Ph). Rearrangement of the α-chloro epoxide **594** to the corresponding α-chloro ketone should therefore have a very large activation energy ($\Delta E_1 + \Delta E_2$) if a stepwise mechanism is involved. McDonald's study on the rearrangement of the α-chloroepoxide **594** to α-chloroacetophenone in CCl_4 (where rearrangement occurs readily at 130 °C)[85] is not consistent with these energy considerations. In fact, substituent effect studies suggest that the closed ion **591** is bypassed in favor of the open ion **590**.

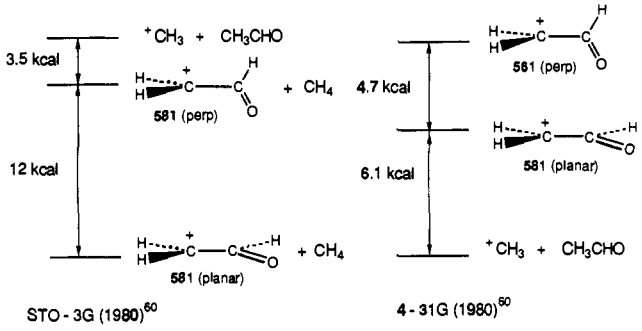


The effect of the formyl group on carbocation stability has been evaluated using the isodesmic reaction of CH_4 with $^+CH_2CHO$. Calculations by Paddon-Row and Houk[80] in 1980 using the STO-3G basis set indicated that the planar α-carbonyl cation **581** (planar) lies 12 kcal/mol lower in energy than the perpendicular cation **581** (perp) where the HCO plane is rotated 90° from the HCH plane. Both the planar and the perpendicular cations are stabilized relative to methyl cation. However, using the 4-31G//STO-3G basis set,

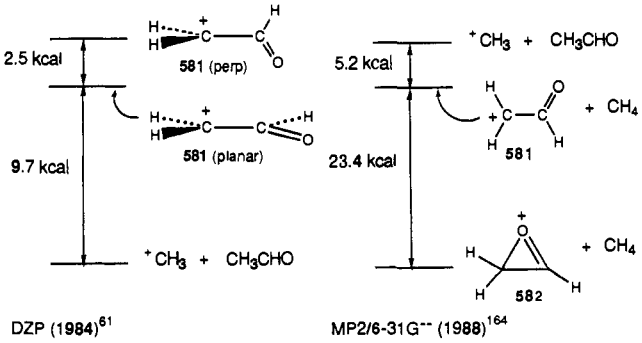


the methyl cation becomes lower in energy. When the carbonyl group is rotated out of conjugation, the destabilization relative to the planar cation is 4.7 kcal/mol. The greater stability of the planar form is attributed to substantial π-donation by the formyl group. It was concluded that inductive destabilization of the methyl cation by substitution of CHO for hydrogen was approximately 19 kcal/mol and π-donation resulted in a stabilization of approximately 13 kcal/mol. However this π-donor ability of the formyl group decreased with methyl substitution and, in the tertiary cation $(CH_3)_2C^+CHO$, it was concluded that π-donation was not a very important factor.

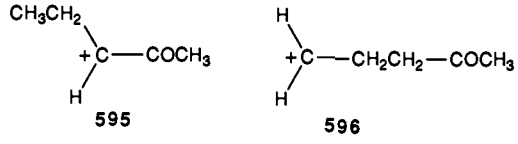
Further calculations in 1984 using a DZP basis set lowered the energy difference between the planar and perpendicular cations to 2.5 kcal/mol.[81] It was also concluded that minimal basis sets tend to overestimate the effect of π-donation. The latest isodesmic calculation[164] using the MP2/6-31G** basis set now places the α-carbonyl cation **581** (which is not at an energy



minimum) 5.2 kcal/mol below the methyl cation and shows only minor deviations in bond lengths from those of CH_3CHO. This latter feature indicates essentially no C–C double bond character in **581**. These calculations call into question the importance of carbonyl conjugation (as in **356b**) as a stabilizing feature in α-carbonyl cations.



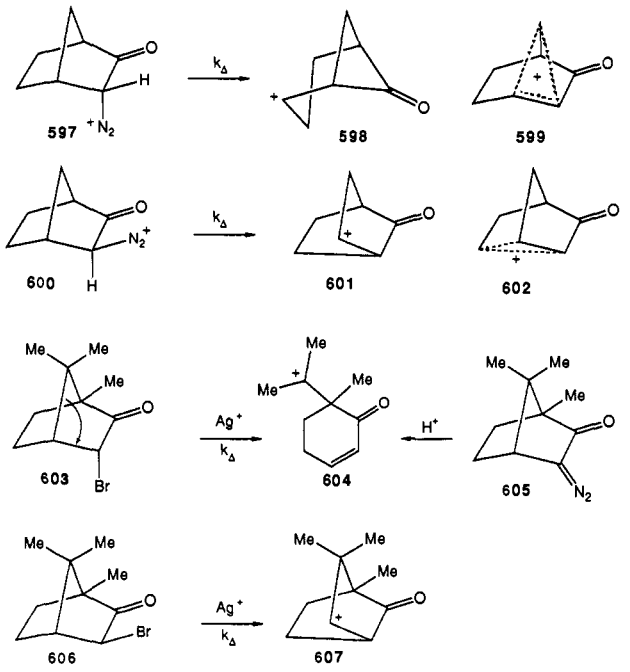
MNDO calculations suggest that the α-carbonyl cation **595** is 4 kcal more stable than the isomeric γ-carbonyl cation **596**.[165] The effect of the $COCH_3$ group is proposed to be a polarization effect. A similar effect is seen in cyano-substituted cations, where the α-cyano cation is more stable than the isomeric γ-cyano cation.



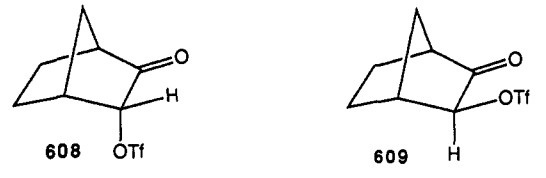
I. Processes Not Involving α-Carbonyl Cations

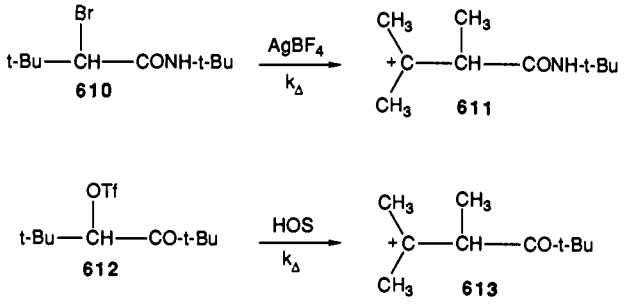
Although the prior sections of this review have shown numerous instances in which α-carbonyl cations have been generated, caution must be exercised before such intermediates are invoked. Other processes can intervene in reactions of systems where a leaving group is placed in the α-position of a carbonyl containing substrate. The k_Δ process, as well as carbonyl addition processes, k_s processes, and mechanisms initiated by enolization can all lead to products that, at first glance, appear to involve discrete α-carbonyl cations. This section will attempt to point out some of these cases where α-carbonyl cations may well be bypassed as discrete intermediates.

Certain secondary carbonyl containing substrates having leaving groups in the α-position can react by the k_Δ route involving concerted Wagner–Meerwein rearrangement processes. The diazonium ions **597** and **600**, formed on protonation of 2-diazonorcamphor[166,167] or deamination of 2-aminonorcamphor,[168] lose nitrogen in k_Δ processes to give products derived from cations **598** and **601** (or possibly delocalized nonclassical ions **599** and **602**). Reaction of the substrates **603** and **606**,[169] with silver salts also leads to rearranged products derived from the k_Δ route. Protonation of the α-diazo ketone **605** also leads to products derived from **604**.[169]



Solvolyses of the related α-keto triflates **608** and **609**[170] undoubtedly proceed by anchimerically assisted k_Δ processes to give structurally rearranged products. Rate data, where the exo isomer **609** is substantially more reactive than the endo isomer **608**, as well as deuterium labeling studies, support the suggested k_Δ route for both substrates.

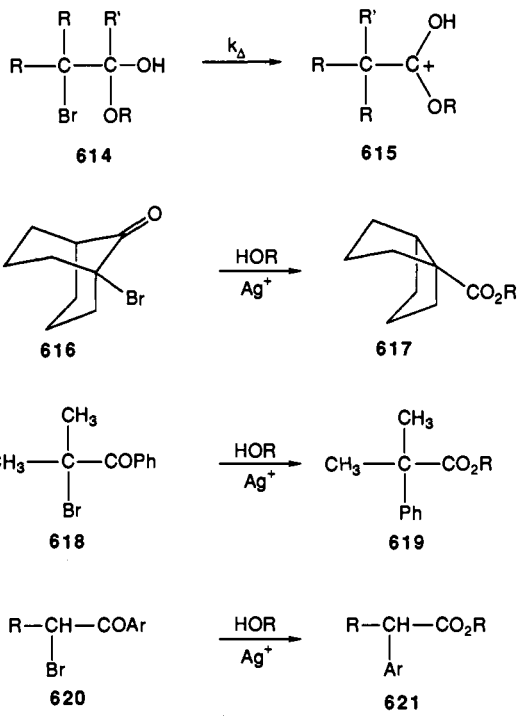




The α-bromo amide **610**[171] and the α-keto triflate **612**[96,170] are two further examples of substrates which react to give rearranged elimination (and substitution) products via the k_Δ route. In all of these secondary substrates, discrete α-keto cations are not the initially formed intermediates. While there is some charge development at the α-position in the transition state for these solvolyses, the initially formed cations are probably Wagner–Meerwein rearranged β-keto cations (or possibly delocalized nonclassical ions). The discrete secondary α-keto cations that would result from the k_c process appear to be too unstable to be solvolytically generated.

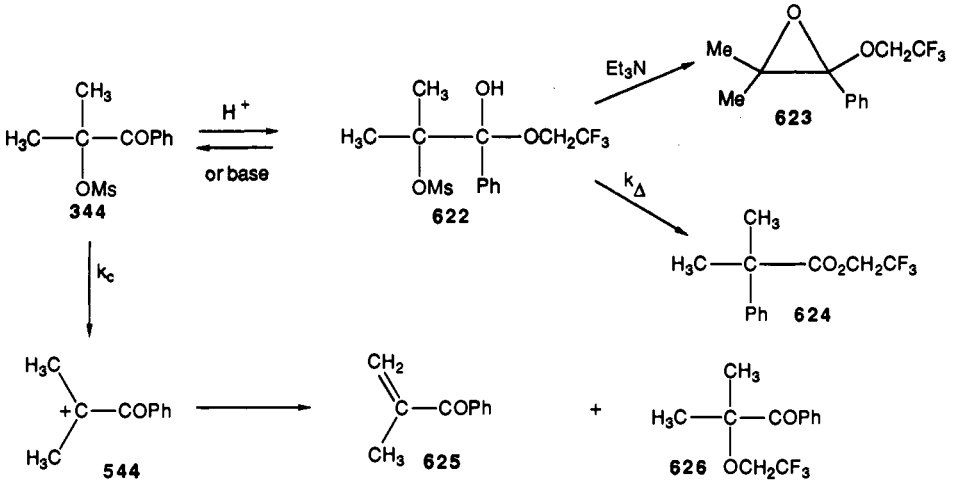
When a leaving group is placed in the α-position relative to a carbonyl group, solvolytic reactions can often occur by prior addition of solvent to the carbonyl as in **614**, followed by subsequent solvolysis of the tetrahedral adduct. α-Carbonyl cations can be bypassed if this mechanism operates. Pertinent examples of this semi-benzylic acid type process include the reactions of the α-bromo ketones **616**,[172] **618**,[172-174] and **620**[175] with silver ion in hydroxylic solvents.

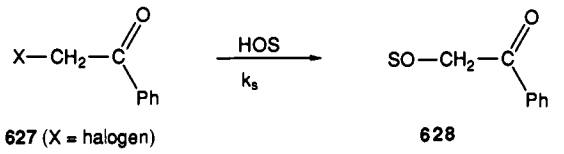
The chemistry of mesylate **344** provides an example of this carbonyl addition process in competition with the k_c process.[98] In carboxylic acid solvents and $(CF_3)_2CHOH$ the products **625** and **626** can easily be interpreted in terms of the intermediate α-carbonyl cation **544**. However, the chemistry in CF_3CH_2OH was much more complex and led to varying mixtures of **623–626**. In this solvent under neutral conditions, the k_c process (leading to **625** and **626**) dominates. However, under acidic or basic conditions, solvent addition to the carbonyl group can lead to the tetrahedral adduct **622**. Solvolysis of **622** by a k_Δ route involving phenyl migration leads to **624**. This is the major competing



process under acidic conditions in CF_3CH_2OH. With added triethylamine, base-catalyzed formation of the hemiketal **622**, followed by base catalyzed mesylate displacement, leads to the alkoxyoxirane **623** as the major product. Under less basic conditions (with 2,6-lutidine as the buffering base) **624** is also produced by an assisted solvolysis of **622**. The bromo ketone **618** also gives substantial amounts of a methoxyoxirane when reacted with Ag_2CO_3 in methanol.[174]

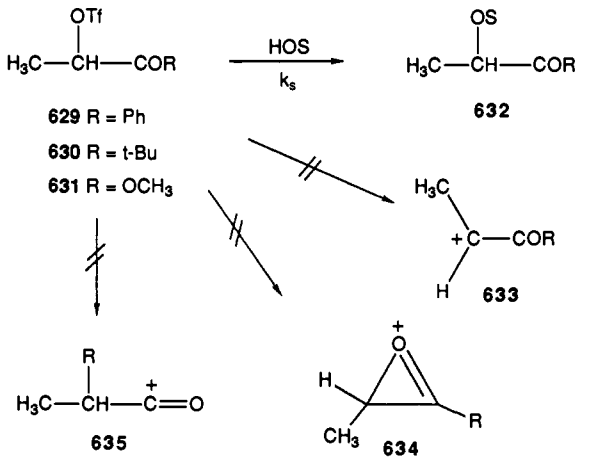
To date, there have been no reports on the successful generation of simple primary or secondary, nonbenzylic α-carbonyl cations under solvolytic or acid-catalyzed conditions. Thus the primary phenacyl halides **627** undergo solvolysis to give only unrearranged substitution products **628**.[176a] Kinetic studies indicate that the mechanism is a highly nucleophilic displacement of halide by the solvent (a k_s process). The silver assisted solvolyses of these substrates also proceed via k_s processes which are electrophilically assisted by the silver ion.[176b] There are no carbocationic intermediates or rearrangement processes.





627 (X = halogen) 628

The secondary α-keto triflates **629–631** readily solvolyzed in a variety of solvents to give simple substitution products.[98] Rates paralleled solvent nucleophilicity rather than solvent ionizing power, being faster in ethanol than in formic acid. Formic acid rates were also faster than rates in CF_3CO_2H. Additionally (*S*)-(−)-**631** gave inverted products when solvolyzed in HCO_2H or CH_3CO_2H. These triflates therefore react by a k_s process involving negligible cationic character in the transition state. Secondary α-carbonyl cations



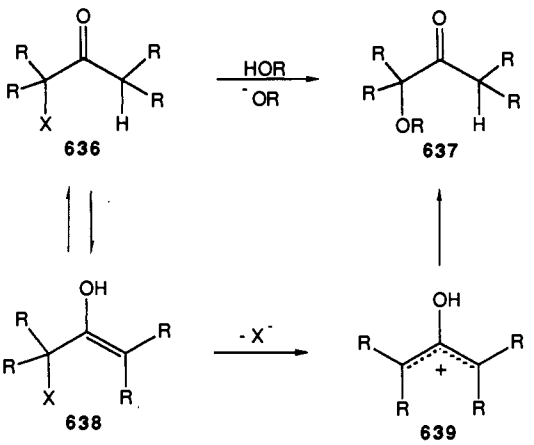
629 R = Ph
630 R = t-Bu
631 R = OCH_3

632 **633** **635** **634**

633 are not involved. Neither are k_Δ processes leading to the cyclized ion **634** or the acylium ion **635**. Even in the highly ionizing nonnucleophilic trifluoroacetic acid solvent there is no evidence for cationic intermediates. Simple secondary α-carbonyl cations therefore appear to be bypassed under solvolytic conditions in favor of direct solvent displacement.

Enolization processes in α-halo ketones (leading to the Favorskii rearrangement) are well documented.[177] Substrates of general structure **636**, containing a leaving group α to a carbonyl group, can also react by an additional cationic mechanism involving solvolysis of an enol allylic derivative, **638**.[178] It has been shown that this process can compete with the Favorski rearrangement in certain cases.[96] The simple substitution products **637** can therefore arise by mechanisms that bypass the α-carbonyl cation. This competing mechanism can be avoided by the incorporation of benzoyl, pivaloyl, carbomethoxy, $CONMe_2$, or a bicyclic framework as the carbonyl component during generation of α-carbonyl cations.

In summary, α-carbonyl cations can be generated by a variety of methods, including rearrangements of α-halo epoxides, α-diazo ketone protonation, silver ion and Lewis acid promoted reactions of α-halo carbonyl compounds, solvolysis reactions, protonation of alcohols, Pummerer rearrangements, and using mass spectroscopic techniques. Under solvolytic conditions, these cations form more easily than can be predicted on the basis of the electron-withdrawing properties (σ values) of carbonyl-containing groups. These cations are formed at rates that approach those of the α-H ana-

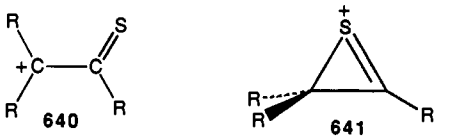


636 **637** **638** **639**

logues. This has led to the suggestion that the carbonyl group can be involved in mesomeric cation stabilization. Computational studies however suggest that this type of conjugative stabilization is of little importance. This cation is now well established as a transient intermediate as well as a long lived species under appropriate conditions. The chemistry of this intermediate has been developed to the point where it has been utilized in the numerous synthetic transformations.

V. The α-Thiocarbonyl Cation

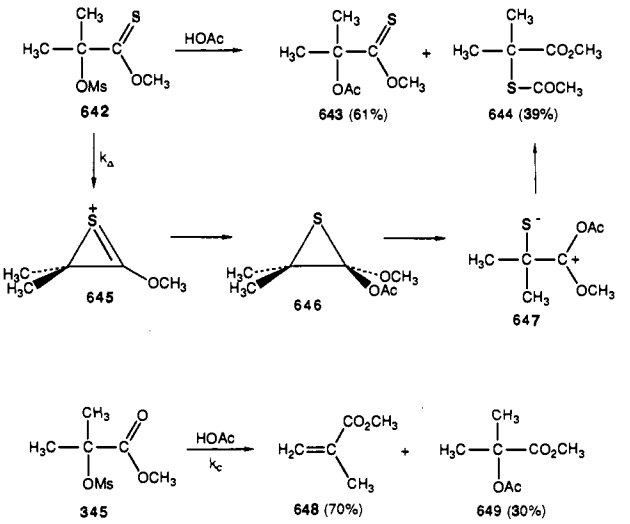
The α-thiocarbonyl cation **640** and the cyclized analogue **641** are intrinsically related to the α-carbonyl cation. Studies have been carried out in which these cations have been generated. Questions concerning the structure of such cations, as well as their stability, have been addressed.



640 **641**

A. The α-Thioester System

The thioester-containing mesylate **642** was solvolyzed in acetic acid and its behavior was compared to the simple ester analogue **345**.[179] The substitution product **643**, along with the rearranged ester **644** were formed. By way of contrast, **345** gave the elimination product **648** (70%) along with the substitution product **649**. In



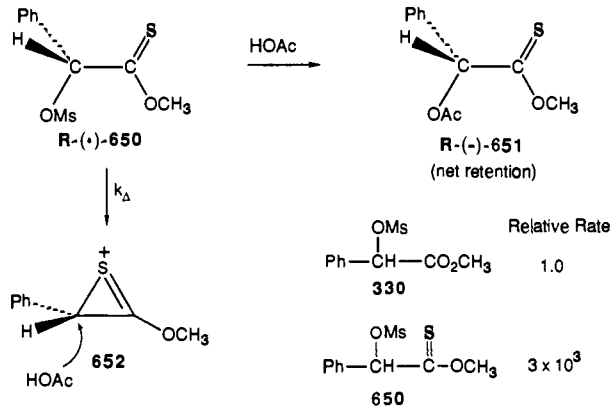
642 **643** (61%) **644** (39%)

645 **646** **647**

345 **648** (70%) **649** (30%)

terms of rate, the thiocarbonyl system **642** is 8×10^3 more reactive than the simple ester **345**. On the basis of the enhanced rate of **642** relative to the simple ester analogue, the formation of the rearranged product **644**, and the lack of elimination product in solvolysis of **642**, it is suggested that the cyclized ion **645** is the intermediate in this solvolysis. Solvent capture at the trigonal carbon, followed by ring opening and acetyl transfer gives the rearranged product **644**. Since no elimination product is seen in solvolysis of **642** (in contrast to the simple ester **345**) it was suggested that the simple substitution product **643** was also derived from the cyclized ion **645**.

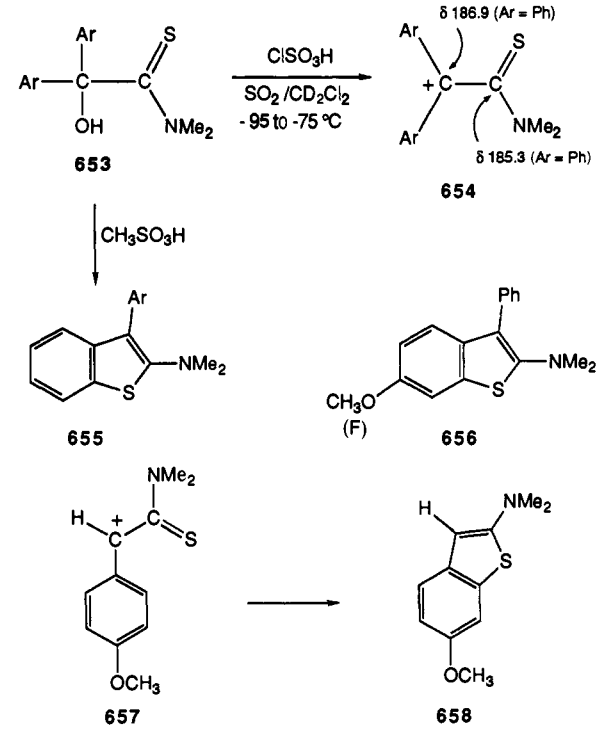
Further evidence for the intermediacy of cyclized ion comes from the acetolysis of mesylate **650**.[179] The acetolysis rate is 3×10^3 times faster than that of the ester analogue **330**, and the optically active mesylate (*R*)-(−)-**650** gave an optically active product with 54% net retention of configuration. The opening of the cyclic ion **652** accounts for the net retention. The origin of the 46% racemized product was uncertain. These studies on **642** and **650** suggest that thiocarbonyl participation leading to cyclized ions can be (unlike carbonyl participation) an important feature in solvolysis reactions.



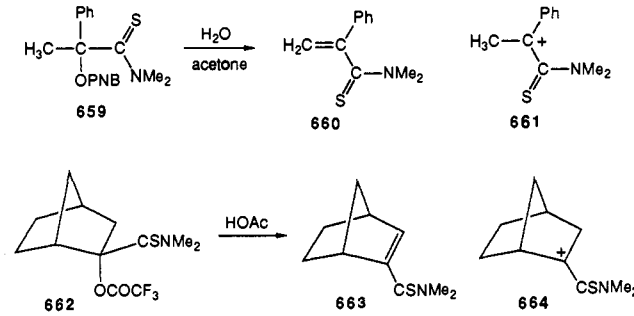
B. The α-Thioamide System

Carbocations substituted with the $CSNMe_2$ group have been generated under stable ion conditions as well as under solvolytic conditions. Thus stable solutions of ions **654** were prepared by protonation of precursor alcohols **653** at low temperature.[180] When treated with methanesulfonic acid at room temperature, good yields of benzothiophenes **655** were formed, presumably by electrocyclization of the cations **654**. Benzothiophenes **655** were also formed on quenching stable solutions of the cations **654** with ice. With unsymmetrical ions **654**, cyclization occurs onto the aryl ring carrying the donor substituent, such that products **656** are formed. These cyclization reactions contrast with reactions of the $CONMe_2$ analogues where fluorene derivatives are formed.[121]

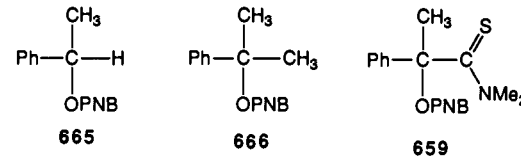
The *p*-methoxy-substituted cation **657** was also generated under stable ion conditions and this ion cyclized to the benzothiophene **658**.[180] NMR spectra of **657** indicate restricted rotation about the C–O bond to the methoxy group. This is indicative of extensive resonance delocalization of charge involving the methoxy group. Attempts to generate the analogous cation with no substituent on the aromatic ring did not give a stable cation.



A number of analogous $CSNMe_2$-substituted cations have been generated under solvolytic conditions.[181] Evidence has been obtained for formation of both cyclized and open ions under solvolytic conditions. The tertiary *p*-nitrobenzoates **659** and **662** gave exclusively the elimination products **660** and **663** and the open cations **661** and **664** are the suggested intermediates.

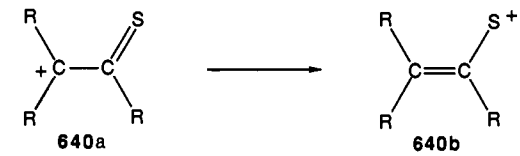


Rate of solvolyses of these two substrates far exceed those of α-H analogues and even surpass those of the α-CH_3 analogues. This was attributed to a major cation



Relative Solvolysis Rates

stabilizing conjugative effect as represented by **640b**. This conjugative interaction, which offsets the electron-withdrawing properties of $CSNMe_2$, was suggested to be much larger than the analogous interaction in α-carbonyl cations.



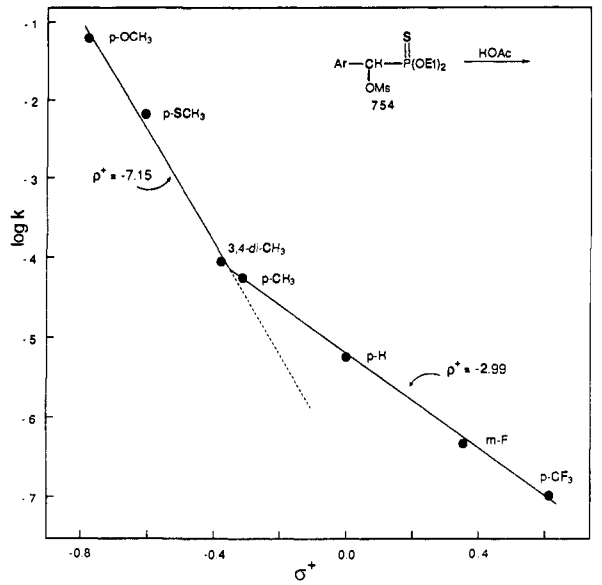
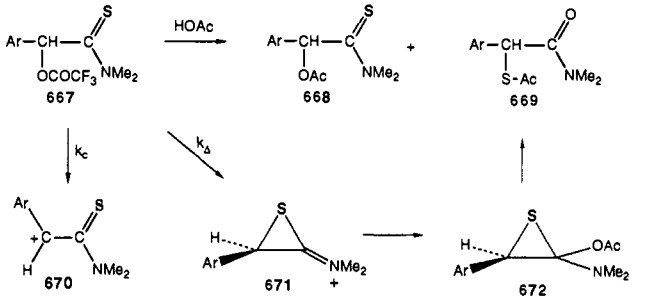
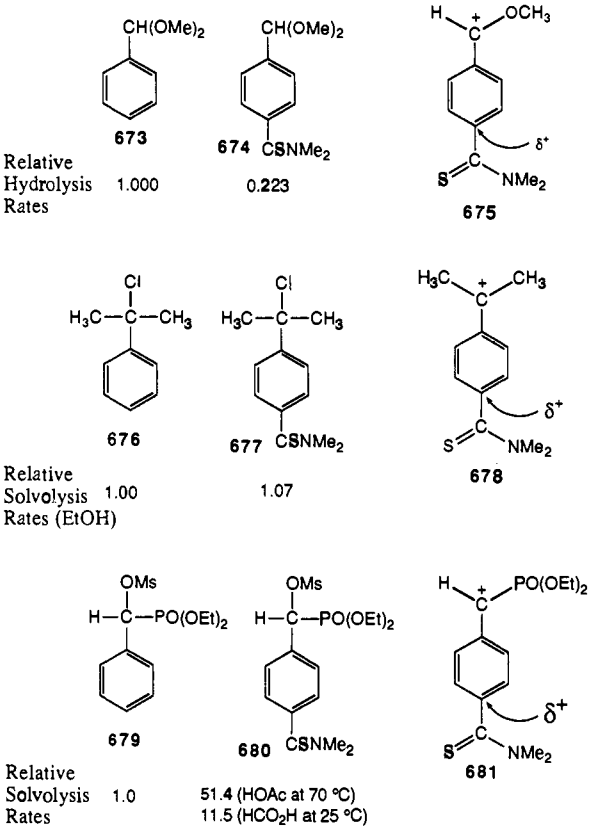


Figure 7. A plot of log k for acetolysis of **754** vs σ^+.

Acetolyses of the trifluoroacetates **667** gave mixtures of the simple substitution product **668** and the rearranged product **669**.[181] Rate data for these reactions did not yield a linear Hammett plot, and this suggested a mechanistic change as substituents on the aryl ring in **667** were varied. Competing k_c and k_Δ processes were proposed, with the k_Δ process leading to the cyclized ion **671**. Solvent capture at the trigonal carbon of **671**, followed by ring opening and acetyl group transfer would give the rearranged product **669**. The unrearranged product **668** could come from either a k_c process or opening of the cyclized ion **671** with solvent at the tetrahedral carbon. The $CSNMe_2$ group therefore appears to be capable of stabilizing cations by a conjugative interaction as well as by a neighboring group participation mechanism leading to cyclized ions.

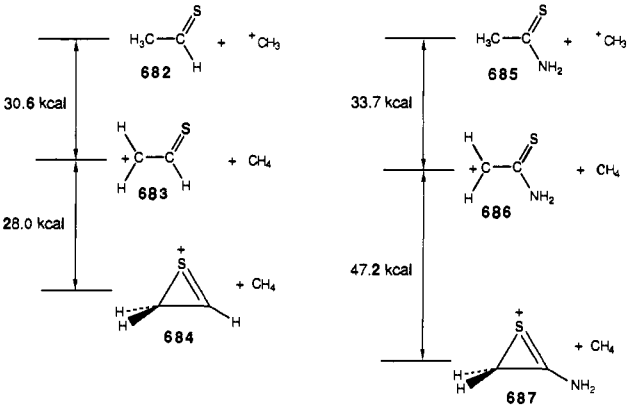


In a related study, the effect of the *p*-$CSNMe_2$ group on the rate of formation of benzylic cations was determined.[182] This group slows the hydrolysis rate of substituted benzaldehyde dimethylacetal **674**. It has a negligible rate effect on the solvolysis rate of the cumyl chloride **677**. However it increases the rate of solvolysis of the phosphonate **680**. These variable rate effects have been interpreted in terms of variable electronic properties of the $CSNMe_2$ group, which can be cation destabilizing, electroneutral, or cation stabilizing, depending on charge demands in specific cations. The extent of charge delocalization onto the *p*-carbon of the intermediate cations **675**, **678**, and **681** determines the extent of conjugative delocalization of charge into the $CSNMe_2$ group. The amphielectronic $CSNMe_2$ group can therefore change from net electron withdrawing in cation **675** to electron donating in **681**.

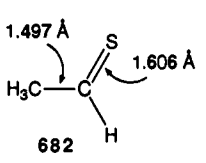


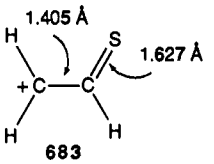
C. Computational Studies on α-Thiocarbonyl Cations

Ab initio molecular orbital calculations at the MP2/6-31G** level have been used to evaluate the α-thiocarbonyl cations **683** and **686** as well as their cyclic isomers **684** and **687**.[164] Relevant energy levels were



determined for the isodesmic reaction with methane. In both cases, the isomeric cyclized ions lie substantially below the open ions. The α-thiocarbonyl cation/CH_4 pair are also significantly lower in energy than the $CH_3^+/CH_3(R)CS$ pair. This suggests significant stabilization of the α-thiocarbonyl cation. Structural changes are also seen when the neutral thiocarbonyl containing molecules **682** and **685** are compared to the open α-thiocarbonyl cations **683** and **686**. The carbon–carbon bond of the cations are shortened relative to the neutrals. A small carbon–sulfur bond increase is also observed. These structural changes are in line with the form **640b** as an important contributor to the structure of the open cation.

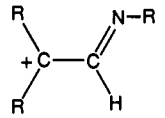




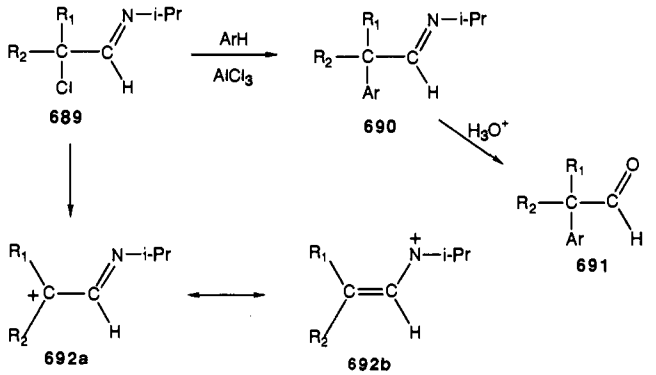
In summary, the chemistry of α-thiocarbonyl cations can be quite different from that of α-carbonyl analogues. They are formed far more easily than carbonyl analogues. Under solvolytic conditions, relatively poor leaving groups can be used to generate such cations. These cations appear to be stabilized by a conjugative interaction with the thiocarbonyl group. Alternatively, these cations can be stabilized by cyclization via sulfur. While no evidence exists for cyclized forms of α-carbonyl cations in solution, the related cyclized sulfur analogues are much more viable. Rates of cation-forming reactions of α-thiocarbonyl substituted systems therefore greatly exceed those of α-H and α-carbonyl analogues.

VI. The α-Imino Cation

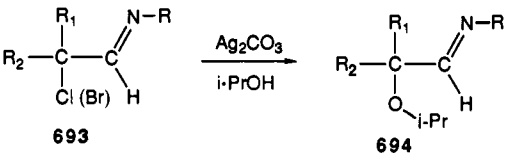
The α-imino cation **688** is also related to the α-carbonyl cation. In principle, charge can be delocalized onto nitrogen. The potential for cyclization via nitrogen also exists in this cation. The α-imino cation is also of interest as a synthetic equivalent of the α-carbonyl cation, since hydrolysis of the imino group would regenerate a carbonyl-containing compound. A number of studies have been carried out in which such cations are proposed as intermediates.



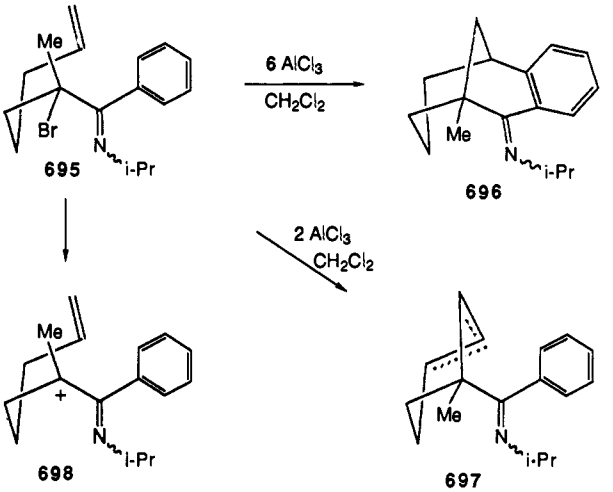
α-Imino cations have been proposed as intermediates in the Friedel–Crafts reaction of aromatics with the α-chloroaldimines.[183] Thus reaction of **689** with aromatics and 2 equiv of $AlCl_3$ gave the arylated aldimines **690** which could serve as precursors to the aldehydes **691**. The possibility exists for charge delocalization onto nitrogen, as in **692b**, as does the possibility of the nitrogen bridging to give a cyclized ion.



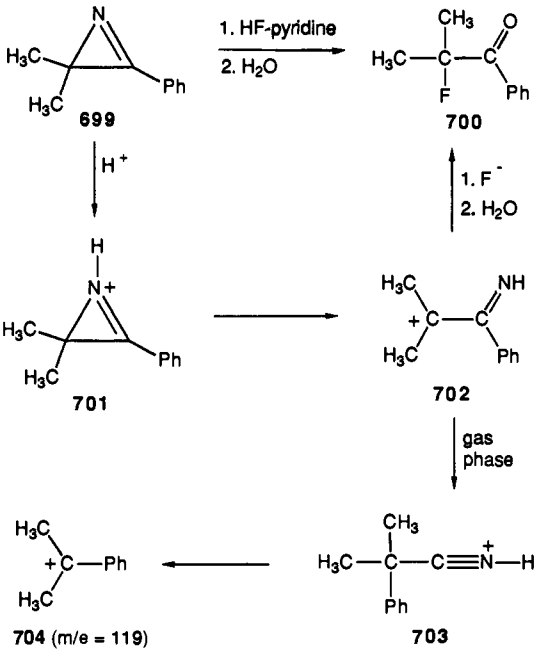
α-Imino cations can also be captured by alcohol solvent as in the silver initiated dehalogenation of chlorides and bromides of general structure **693**.[184] In these reactions, as is the case of arylation reactions of **689**, elimination to generate alkenes is a possible competing reaction when R_1 and R_2 contain hydrogens β to the cationic center.



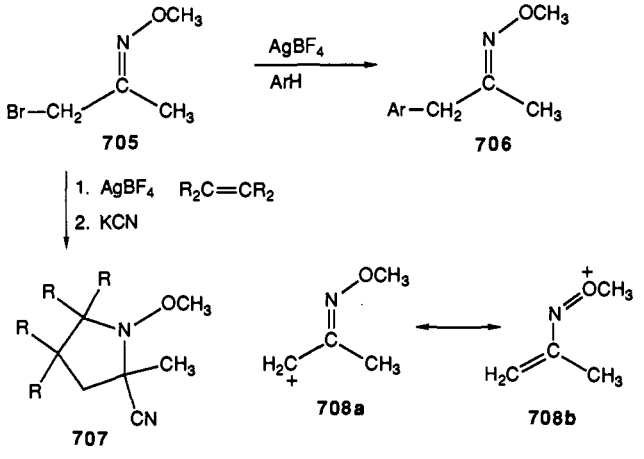
The α-bromo imine **695** gives different cyclized products when treated with varying amounts of $AlCl_3$.[185] Successive cationic cyclizations can lead to **696** and **697**, respectively. Presumably the α-imino cation **698** is involved, but remote participation by the olefinic bond in **695** as the leaving group departs would initiate the same cationic cyclization process. The imines **696** and **697** are readily hydrolyzed to the corresponding ketones.



α-Imino cations can also be generated by protonation of azirines.[186] Reaction of the azirine **699** with HF–pyridine gave, after an aqueous workup, the α-fluoro ketone **700**. Ring opening of the protonated azirine, followed by fluoride capture and hydrolysis is the likely source of the product **700**. The cation **701** can also be generated in the mass spectrometer by chemical ionization (CH_4 or isobutane) of the azirine **699**. Under these conditions, rearrangement occurs by way of the nitrilium ion **703** to give ultimately the cumyl cation **704**.

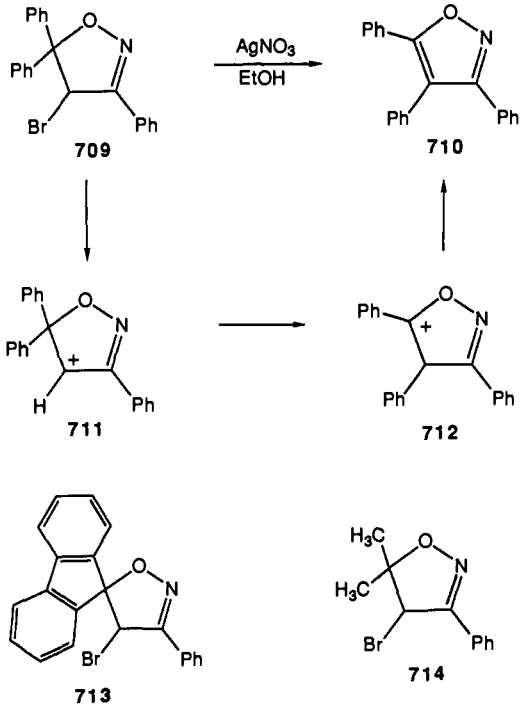


The oxime derivative **705** has also been used as an α-carbonyl cation equivalent via an α-imino cation. Arylation can be achieved by silver-promoted reaction of this bromide with appropriate aromatic substrates.[187] Hydrolysis gave the corresponding arylacetone. The cationic intermediate **708** can also be intercepted with alkenes.[188] After the addition of cyanide ion, the heterocyclic derivatives **707** were produced. The cationic intermediate may be stabilized by the methoxy group as represented by **708b**.



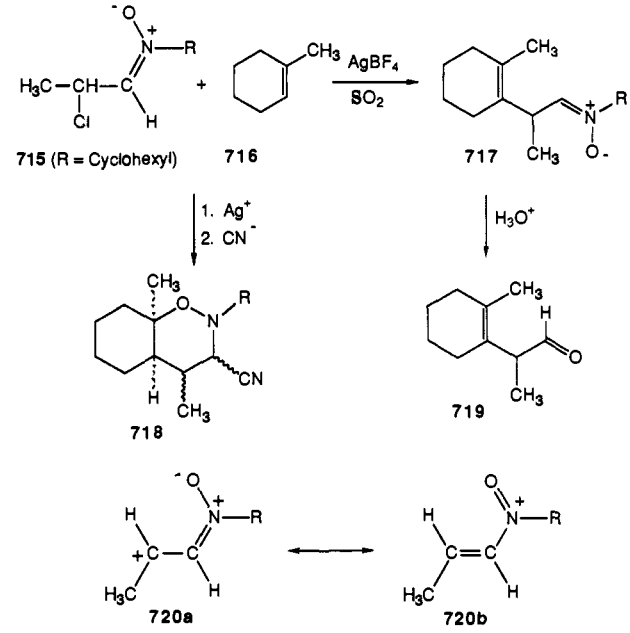
705 706 707 708a 708b

The isoxazole **710** can be prepared by reaction of the bromide **709** with ethanolic $AgNO_3$.[189a] The bromide **713** gives an analogous rearrangement involving ring expansion.[189b] These rearrangements are proposed to occur by way of α-imino cation analogous to **711**. Aryl group migration, followed by proton loss gives the observed products. The bromide **714** gives an unrearranged acetate product when treated with silver acetate in acetic acid. An unrearranged α-imino cation is involved in this process.



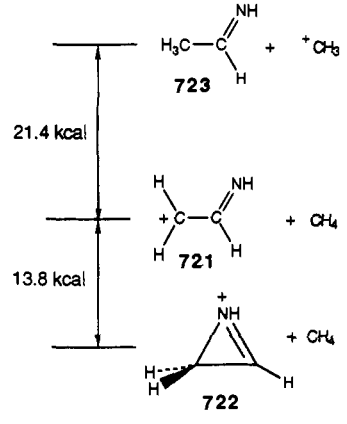
709 710 711 712 713 714

α-Chloronitrones have been reacted with silver salts to give reactions that proceed via analogues of α-imino cations.[190] Eschenmoser has used the α-chloro nitrone **715** as an α-carbonyl cation equivalent. Reaction of **715** with 1-methylcyclohexene and silver ion gives **717** (or workup with cyanide ion gives **718**). Hydrolysis affords the aldehyde **719**. The intermediate **720**, which is a delocalized cation, can also undergo intermolecular arylation. Intramolecular arylations leading to cyclized products can also be observed from aryl-substituted analogues of **720**.



715 (R = Cyclohexyl) 716 717 718 719 720a 720b

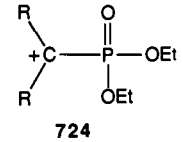
Computational studies on the α-imino cation **721** have been carried out and pertinent energy levels are shown.[191] The cyclized ion **722** lies 13.8 kcal below the open ion **721** at the 4-31G level and 21.9 kcal below at the 6-31G** level. The pertinent isodesmic reaction indicates that the α-imino cation **721** is more stable than the analogous α-carbonyl cation (at the same computational level).



723 721 722

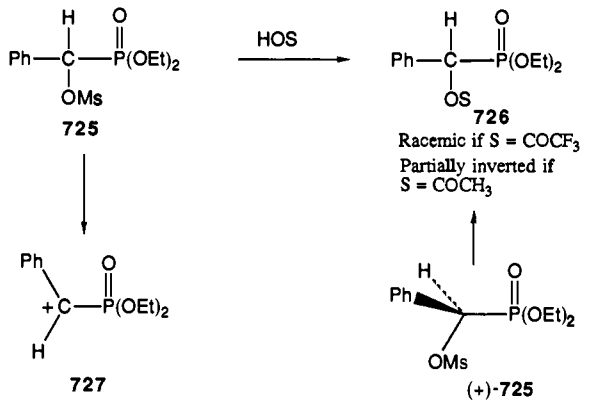
VII. The α-Phosphoryl Cation

The diethyl phosphonate group, $PO(OEt)_2$, is known to stabilize carbanions. This allows facile generation of anions that are used in the Emmons–Wadsworth–Horner modification of the Wittig reaction. In light of the anion-stabilizing ability of this group, the properties of the cationic analogues, **724**, were of interest.

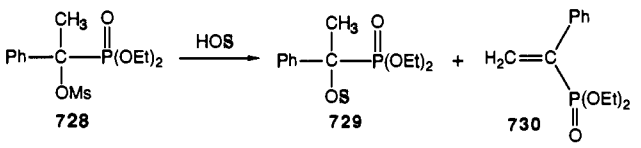


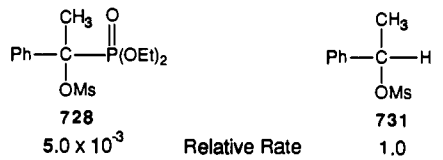
724

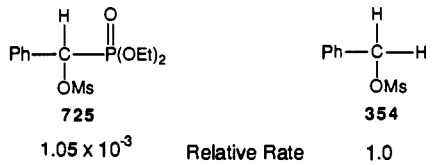
The mesylate derivative **725** underwent solvolysis in a variety of solvents to give substitution products **726**.[192] Large rate increases were seen with solvent ionizing power (m = 0.88). Substitution of α-H for α-D gave an α-deuterium isotope effect in the range of that seen for 2-adamantyl tosylate, a k_c substrate. These data suggest the intermediacy of cation **727** in these substitution reactions. Reaction of the optically active mesylate (+)-**725** in CF_3CO_2H gave a completely racemic product, with racemization rate exceeding solvolysis rate by a factor of 2. In acetic acid, the acetate product was 18% net inverted. These data indicate that a cyclized ion, formed by a k_Δ process, was not involved. Preferential acetic acid capture of an ion pair from the side opposite the departed mesylate leaving group would account for the excess inverted product in HOAc.



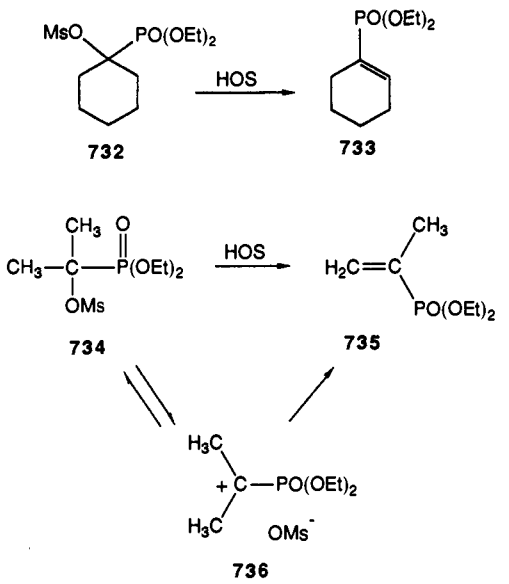
Solvolysis of the mesylate **728** (m = 0.93) gave mixtures of substitution and elimination products **729** and **730**. The mechanism presumably involves an intermediate α-phosphoryl cation. Rates of solvolysis of **728** and **725** are slower than the α-H analogues. However rate retardations were considered smaller than expected based on the electron-withdrawing properties of $PO(OEt)_2$ relative to hydrogen. The possibility of cation stabilization by charge delocalization into the $PO(OEt)_2$ group was considered. The possibility that α-phosphoryl cations could derive some stabilization by a polarization mechanism was also considered.



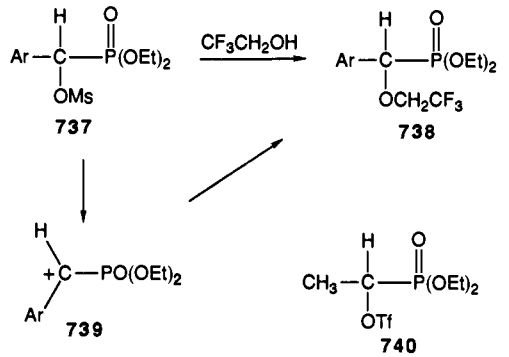




Solvolyses of the mesylates **732** and **734** gave only elimination products. On the basis of a large β-d_6 isotope effect (2.73 to 2.87), it was suggested that the mechanism for **734** involved reversible formation of the cation **736**, which undergoes proton loss at an ion-pair stage.



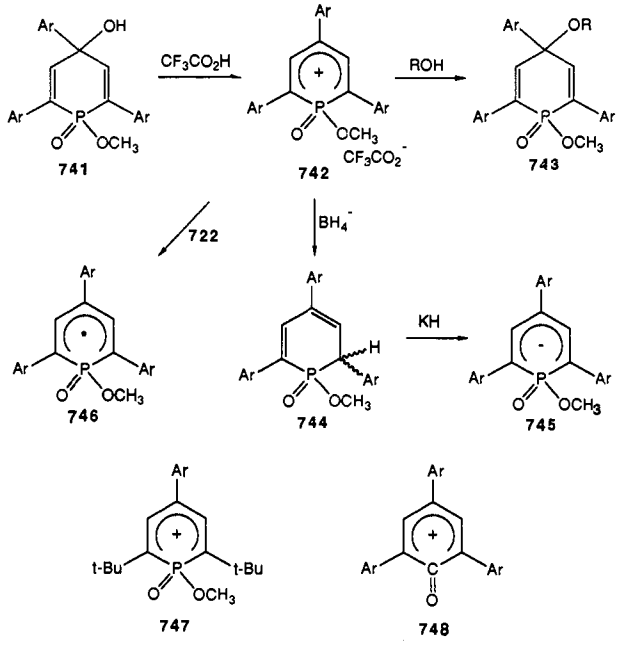
The mesylate derivatives **737** gave simple substitution products in CF_3CH_2OH.[193] The Hammett plot (Figure 6) was nonlinear with a ρ^+ value of −10.1 in the electron-donor substituent region. The substituted α-phosphoryl cation **739** is clearly an intermediate in the electron-donor region. The reason for the nonlinear



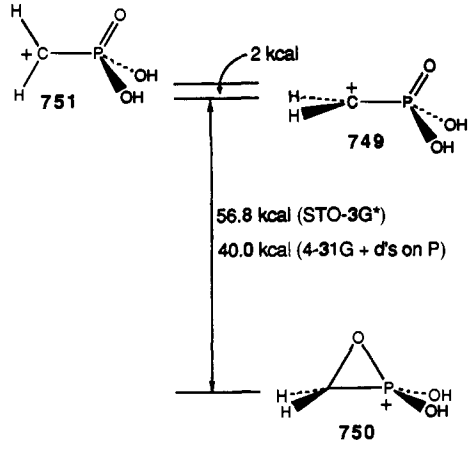
Hammett plot was further investigated by studying the m-F derivative in more detail. Rates of reaction of this substrate in different solvents reflected solvent nucleophilicity as well as ionizing power. The nonlinear Hammett plot was therefore proposed to result from the onset of "borderline" behavior in the electron-withdrawing substituent region. A mechanistic change from k_c to k_Δ in the electron-withdrawing region of the plot was not consistent with the solvent effect study. It was proposed that the mechanistic change that results in the nonlinear Hammett plot was a change from a k_c mechanism to a k_s mechanism. In the k_s region of the plot, there is still substantial cationic character in the transition state, but solvent nucleophilicity is becoming important, i.e., "borderline" behavior is being observed with electron-withdrawing substituents. It was proposed that such subtle mechanistic changes can indeed result in nonlinear Hammett plots. The triflate derivative **740** solvolyzed to give mixtures of substitution and elimination product. Solvent effect and isotope effect studies indicated a transition state with a large amount of nucleophilic solvent involvement (and perhaps some cationic character in HCO_2H and $(CF_3)_2CHOH$). There is no evidence for a k_Δ process

in solvolysis of triflate 740.

A number of vinylogous analogues of α-phosphoryl cations, 742, can be prepared as stable cations in solution by the reaction of alcohols 741 with CF_3CO_2H.[194] These cations add nucleophiles such as water and alcohols to give *E*/*Z* mixtures of 743. Borohydride gives the reduced product 744, which can be deprotonated by potassium hydride. Reaction of the resultant anion 745 with an equimolar amount of the cation 742 gives the delocalized radical 746. The cation 747 where two aryl groups are replaced with *tert*-butyl is also known, as are the carbonyl analogues 748.[195]

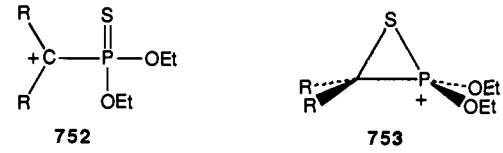


Computational studies have also been carried out on α-phosphoryl cations.[196] As in the case of the α-carbonyl, the α-thiocarbonyl, and the α-imino cation, the energy of the cyclized form 750 lies below that of the open form 749. The form 751, where the cationic center is rotated 90° is slightly higher than 749. The open form does not represent an energy minimum at the STO-3G or STO-3G* levels and this cation closes without barrier to the cyclized form. This energy difference between open and closed forms is basis-set dependent, and calculations at the 4-31G level with incorporation of 3d AO's on phosphorus lowers the energy gap to 40 kcal. Methyl substitution on 749 and 750 also lowers the energy difference between the open and cyclized forms.

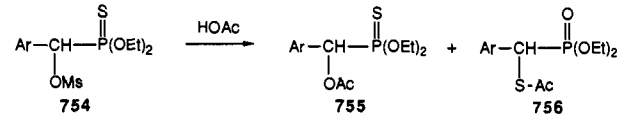


VIII. The α-Thiophosphoryl Cation

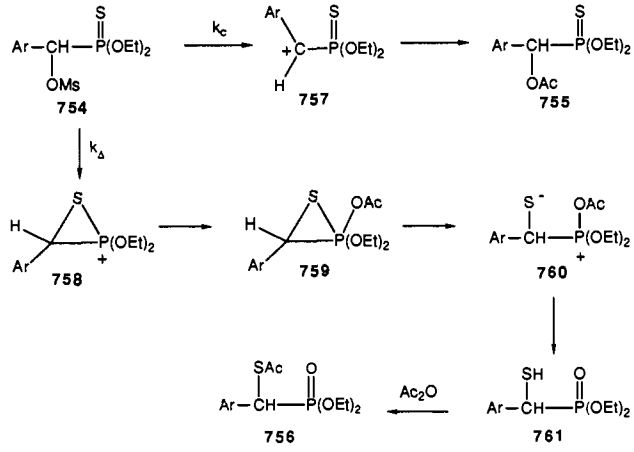
While there is experimental evidence for the formation of α-phosphoryl cations in the open form, there is to date no experimental evidence for the generation of cyclic forms. Sulfur analogues 752 were therefore generated in order to contrast their behavior to that of P=O analogues 724. The question of open ions 752 versus closed ions 753 was addressed.



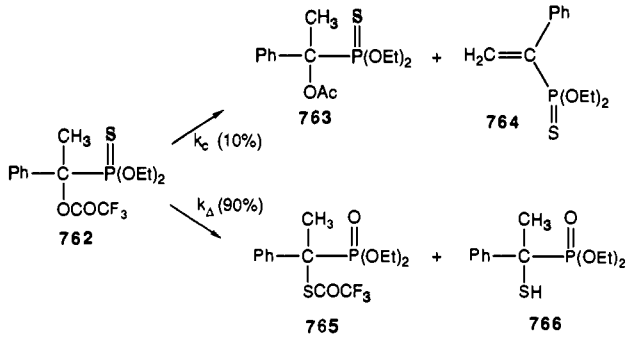
The thiophosphoryl-containing mesylates 754 were solvolyzed in HOAc and the products formed were quite substituent dependent.[179] *p*-OCH_3 and *p*-SCH_3 substitution on the aromatic ring led exclusively to unrearranged products 755, while *p*-H, *m*-F, and *p*-CF_3 substitution led to rearranged products 756 only.



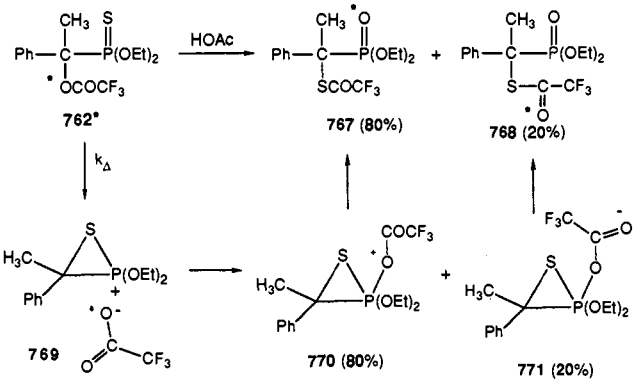
Mixtures of products were seen for *p*-CH_3 or 3,4-dimethyl substituents. A Hammett plot (Figure 7) showed a clear break. These product and rate data suggest two competing mechanisms. A k_c mechanism, involving the open cation 757, was proposed when substituents were strongly electron-donating, while a k_Δ mechanism was suggested for compounds in the region of lower slope. Capture of the cyclized ion 758 with acetic acid followed by ring opening and deacetylation would give 761 which can be detected at early stages of the reaction. Acetylation gives the observed rearranged product 756.



Trifluoroacetate 762 gives acetolysis products derived from competing k_c and k_Δ processes.[179] The substitution product 763 and the alkene 764 are derived from an open α-thiophosphoryl cation, while the rearranged products 765 and 766 are derived from a k_Δ process. The nature of the cyclized ion pair leading to 765 and 766 has been probed using ^{17}O and ^{18}O labeling studies.[197] Thus acetolysis of the labeled substrate 762* gave products in which the label was unequally scram-

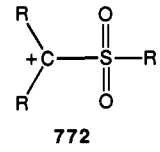


bled between the phosphoryl and the carbonyl group of the product. This suggests that internal return of trifluoroacetate in the ion pair **769** does not result in complete oxygen scrambling. The oxygen that was originally bonded to the incipient cationic center is the one that preferentially returns. The oxygen atoms in the ion pair **769** are therefore functionally nonequivalent. A short lived ion pair that does not reach the solvent separated stage is proposed to account for this incomplete oxygen scrambling.



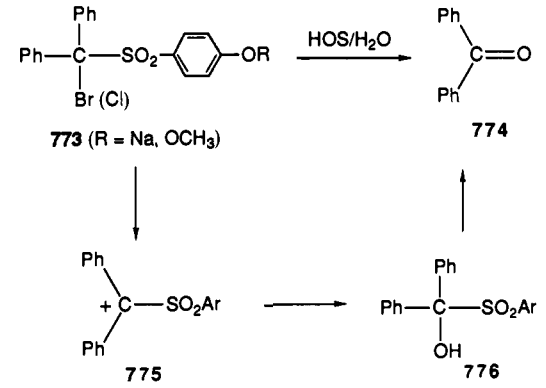
IX. The α-Sulfonyl Cation

The sulfonyl group is another potent carbanion stabilizing group. Hammett σ and σ^+ values (Table I) indicate that this group is even more electron withdrawing than the trifluoromethyl group. Nonetheless, a limited number of α-sulfonyl cations (**772**) have been generated. Quantitative studies allow an evaluation of their stability relative to other electronegatively substituted cations.

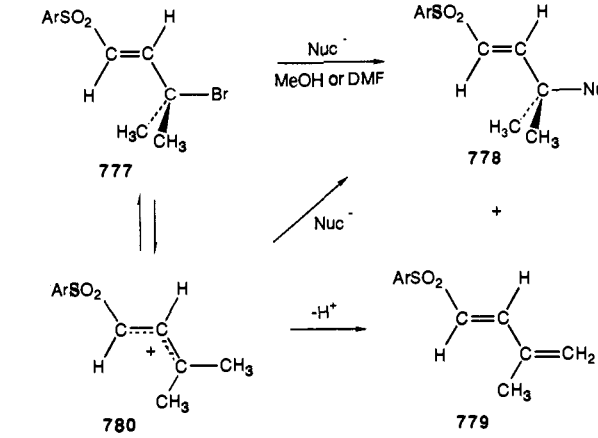


The α-halo sulfones **773** undergo reaction in wet *tert*-butyl alcohol or in wet acetic acid to give benzophenone (**774**).[198] The α-sulfonyl cation **775** is the suggested intermediate. Reaction with water followed by loss of the sulfinic acid from **776** leads to the observed product.

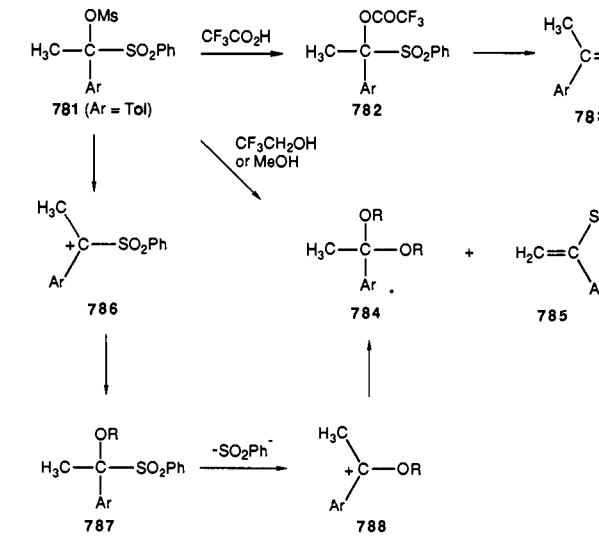
The allylic sulfone **777** undergoes bimolecular nucleophilic substitution reactions to give **778** (along with some elimination product **779**).[199] This unusual bimolecular substitution reaction of a tertiary substrate is proposed to involve the reversibly formed vinylogous α-sulfonyl cation **780**. This intermediate undergoes



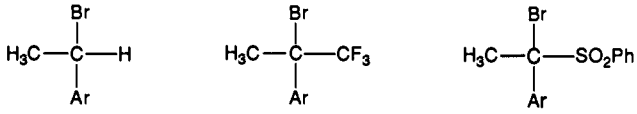
rate-limiting reaction with nucleophiles.



The mesylate **781** reacts in CF_3CO_2H to give the substitution product **782** at short reaction time.[200] Under the reaction conditions, **782** is converted at a slower rate to *p*-methylacetophenone (**783**). In acetic acid, the acetate substitution product is observed, along with the elimination product **785**. In alcohol solvents, acetals **784** are the major products. The response of rate to solvent ionizing power is large (m = 0.85) and a substituent effect study gave a ρ^+ value of −8.0. These data were interpreted in terms of the intermediacy of the α-sulfonyl cation **786** which can capture solvent or eliminate a proton. The initially formed substitution products can undergo subsequent loss of benzenesulfinate ion to give the cation **788**. The leaving group ability of benzenesulfinate therefore accounts for the instability of simple substitution products under the reaction conditions.



The Hammett ρ^+ value of −8.0 indicates a large demand for aryl group stabilization in the cation **786**. Rate data confirm the relative instability of the α-sulfonyl cation. A direct comparison of the solvolysis rate of **791** with that of the α-CF_3 substrate **790** suggests that the α-sulfonyl cation is even less stable than the α-trifluoromethyl cation.

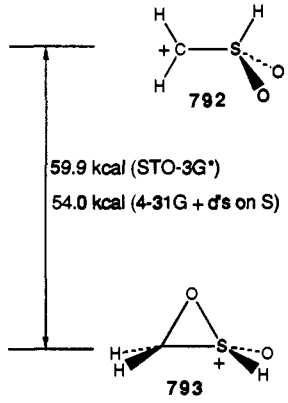


789 **790** **791**

1.0 8.7×10^{-7} 3.8×10^{-9}

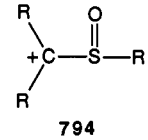
Relative Rates in CF_3CH_2OH (Ar = p-CH_3-C_6H_4)

A computational study on the unsubstituted α-sulfonyl cation **792** shows that it is not an energy minimum and closes without barrier to give the cyclized form **793**.[196] This calculated phenomenon appears to be quite general (if cyclization is possible) for electronegatively substituted cations that carry no further stabilizing groups.



X. The α-Sulfinyl Cation

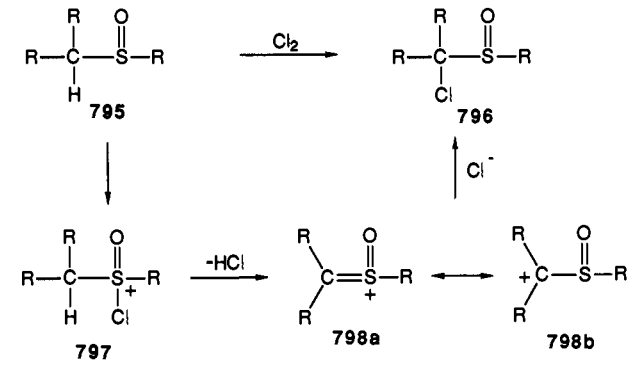
The α-sulfinyl cation (**794**) has been proposed in a number of transformations. Such cations contain a sulfur atom in an oxidation state between that of sulfides and sulfones. Although less electron withdrawing than the sulfonyl group, the sulfinyl group is also a very effective carbanion stabilizing group. The nature of cations directly attached to the sulfinyl group, including the importance of the adjacent nonbonding electrons on sulfur, has been addressed.



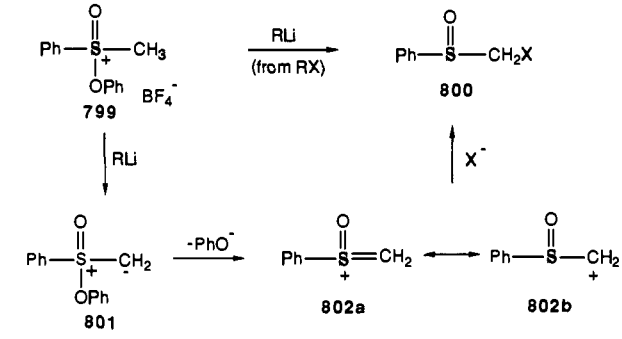
794

Sulfoxides of general structure **795** are readily chlorinated in the α-position by a variety of reagents. The general mechanism of chlorination involves electrophilic halogenation of sulfur to give the chlorosulfoxonium ion **797**.[201,202] Subsequent elimination of HCl gives the ion **798**, which represents an α-sulfinyl cation. Capture of chloride gives the α-chloro sulfoxide **796**.

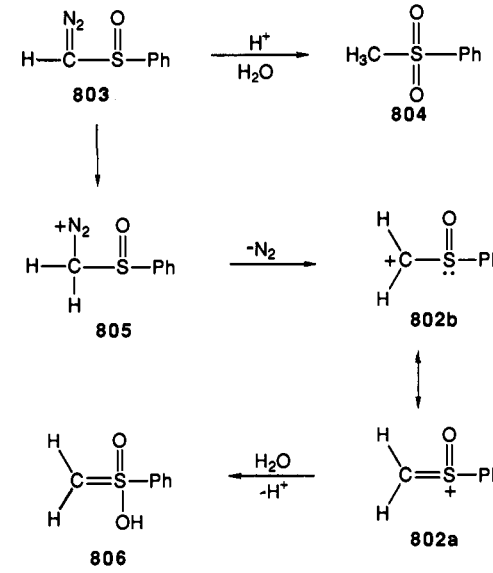
An α-sulfinyl cation has also been suggested in the reaction of the phenylsulfoxonium salt **799** with alkyllithium reagents prepared from the corresponding alkyl halides.[203] Large amounts of the α-halo sulfoxides



800 were formed. A possible mechanism involves deprotonation of **799** with the alkyllithium reagent followed by loss of phenoxide from the ylid **801**. Reaction of the ion **802** with the iodide or bromide present in solution would give the observed α-halo sulfoxides **800**.

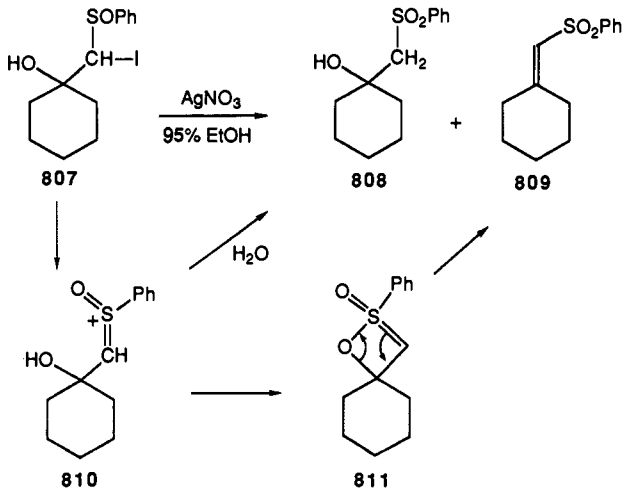


The α-diazo sulfoxide **802** undergoes acid-catalyzed reaction with water to give the sulfone **804**.[204] Protonation of the diazo sulfoxide followed by loss of nitrogen would give the α-sulfinyl cation **802**. Capture of water at sulfur, followed by tautomerization would account for the sulfone product. Reaction of **803** with 48% HI gave phenyl iodomethyl sulfoxide, presumably by capture of **802** by iodide ion.

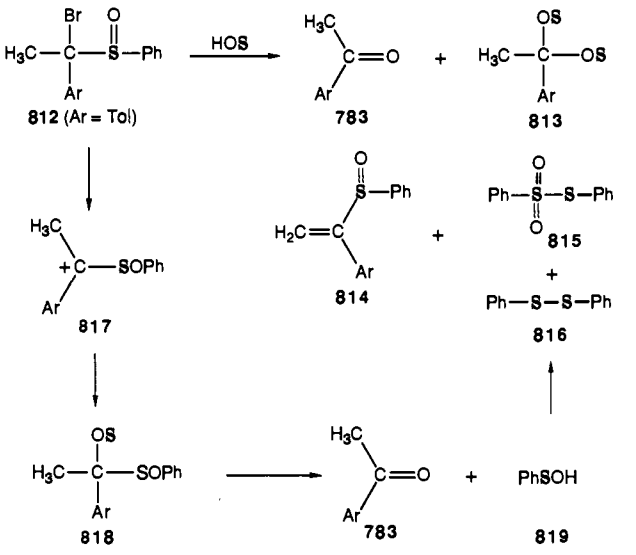


Silver ion assisted solvolysis of the α-iodo sulfoxide **807** gave the β-hydroxy sulfone **808** as well as the vinyl sulfone **809**.[205] The cycloheptane analogue of **807** gave similar behavior. Mechanistically, the α-sulfinyl cation **810** is a proposed intermediate. Reaction with water at sulfur leads to the β-hydroxy sulfone **808** (which is stable under the reaction conditions) while intramo-

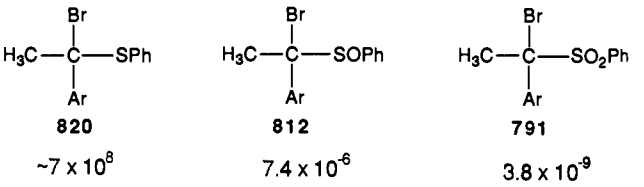
lecular capture of hydroxyl and subsequent collapse of 811 gives the vinyl sulfone 809.



The α-bromo sulfoxide 812 undergoes solvolysis in formic acid, trifluoroethanol, and aqueous acetone to give solvent dependent mixtures of 783 and 813–816.[200] The Hammett ρ^+ value determined on 812 and substituted analogues is −7.2 and suggests that the α-sulfinyl cation 817 is the intermediate. This ρ^+ value also indicates a large demand for aryl group stabilization in such cations. The alkene 814 is formed by proton loss from 817, while the other products are accounted for by solvent capture at the cationic carbon atom. Subsequent loss of PhSOH and disproportionation of this material gives 815 and 816. The chemistry of the α-sulfinyl cation 817 (which captures solvent at carbon) therefore appears to be quite different from that of 802 and 810, where hydroxylic solvents react at sulfur.

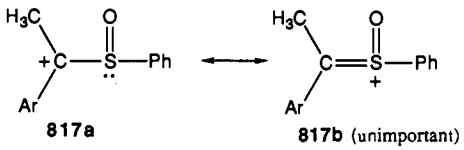


Rate data have been used to evaluate the importance of the nonbonding sulfur electrons as a stabilizing feature in the α-sulfinyl cation 817. The α-sulfinyl system 812 is less reactive than the α-cyano, α-phosphoryl, or α-carbonyl analogues. The solvolysis rate of the α-SPh analogue 820 has been crudely estimated and is about 10^{14} faster than the sulfoxide 812. Hence oxidation of α-SPh to α-SOPh results in a rate reduction of approximately 10^{14}, while further oxidation to α-SO_2Ph results in a further rate reduction of only 1.9×10^3. It is concluded that the first oxidation of sulfide to sulfoxide removes the conjugative ability of the sulfur nonbonding electrons, and further oxidation simply increases the electron withdrawing properties of the substituent. These direct rate comparisons, along with



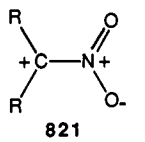
Relative Rates in CF_3CH_2OH (Ar = p-CH_3-C_6H_4)

the Hammett ρ^+ value, imply that the interaction between the sulfur nonbonding electrons with the adjacent cationic center in the α-sulfinyl cation 817 is of minimal importance. These conclusions contrast with previous studies which suggest that forms that delocalize charge onto sulfur are of great importance in cations such as 798, 802, and 810.



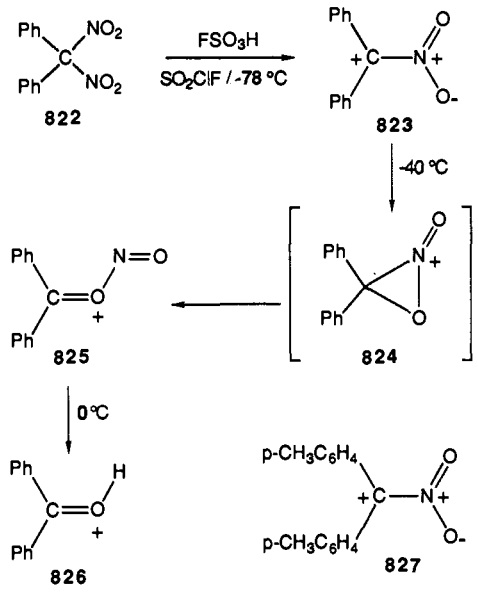
XI. The α-Nitro and α-Nitroso Cations

The nitro group is traditionally considered one of the most electron-withdrawing groups as attested to by its carbanion stabilizing ability and Hammett σ and σ^+ values. There have only been limited attempts to generate α-nitro cations 821.

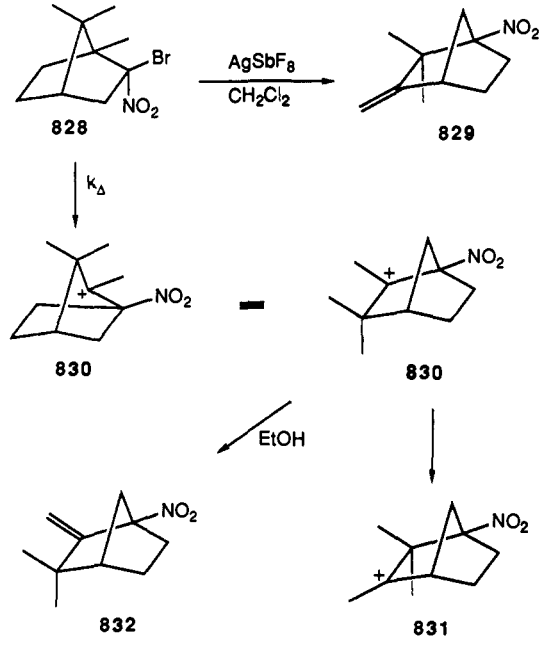


The diphenyl-substituted α-nitro cation 823 has been generated under stable ion conditions at −78 °C by protonation of α,α-dinitrodiphenylmethane (822).[206] This cation rearranges at −40 °C to new species whose spectral data are consistent with the nitrosated benzophenone 825 (or the protonated form of 825). The cyclic form 824 (not observed spectroscopically) is a suggested intermediate in this rearrangement. Further warming to 0 °C leads to loss of NO^+ and formation of protonated benzophenone (826). The p-CH_3 analogue 827 has also been prepared and this cation undergoes a similar set of rearrangements. Attempts to generate the 9-nitro-9-fluorenyl cation from the corresponding dinitrofluorene led only to the observation of protonated fluorenone. The α-nitro cation in this instance is presumably too unstable to be observed spectroscopically.

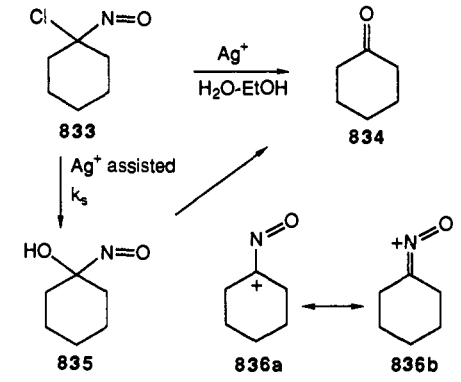
In a related study, the α-nitro-substituted bromide 828 was dehalogenated with silver ion in methylene chloride.[207] The rearranged alkene 829 was formed, presumably via a k_Δ process which generates the β-nitro cation 830 as the first intermediate. Additional rearrangement places the nitro group in 831 further from the cationic center and leads ultimately to the alkene 829. In ethanol, mixtures of 829 and 832 are observed, suggesting that proton loss from 830 can compete with



further rearrangement under more basic conditions. Under the same conditions, 1-bromo-1-nitrocycloxexane was inert, suggesting that a discrete α-nitro cation is bypassed in the reaction of **828** with silver ion.

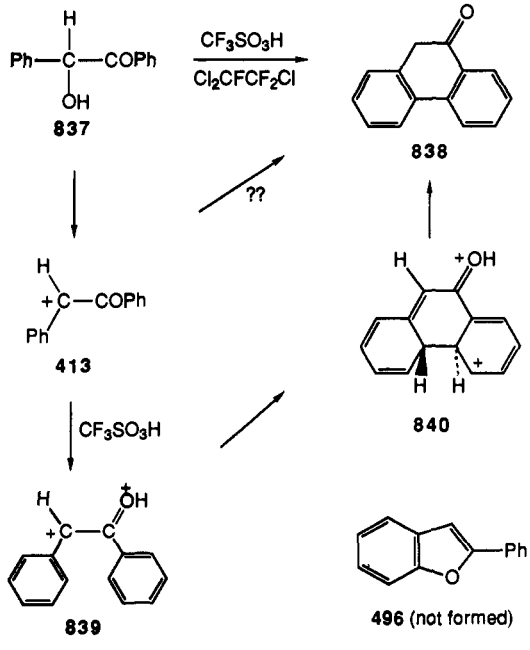


The related nitroso group, N=O, is also considered to be electron withdrawing, and as such, the α-nitroso cation would be of interest. However, this cation has not received much attention. A pertinent reaction is the conversion of 1-chloronitrosocyclohexane (**833**) to cyclohexanone when treated with an aqueous alcohol solution of $AgNO_3$.[208] The nitroso alcohol **835** is a proposed intermediate, which is suggested to arise via a silver ion assisted nucleophilic displacement of chloride by water. Loss of NOH from **835** would give cyclohexanone. This transformation raises questions concerning the α-nitroso cation. Is the cation **836** a plausible intermediate and what is the importance of the nitrogen nonbonding electrons on the stability of this cation? Answers to these questions must await further experimental and theoretical studies.



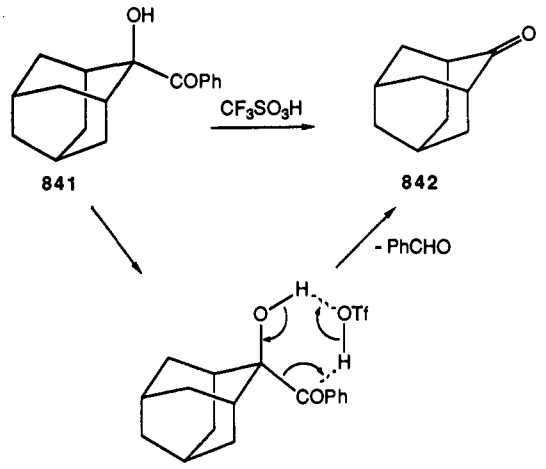
XII. Recent Developments

Since the submission of the original manuscript, additional studies have appeared in the literature which should be included in this review. Olah has carried out a study of reactions of certain α-hydroxy carbonyl compounds with CF_3SO_3H in Freon 113.[209] Reaction of benzoin (**837**) led to the ketone **838**. Of interest is the fact that no fluorenone **496** was produced. The reaction of the α-hydroxy ketone **437** with triflic acid has been repeated in Freon 113 as solvent and the same products are obtained as those previously reported by Shudo[49] using triflic acid as solvent (but in a slightly different ratio). While α-carbonyl cations such as **413** are suggested intermediates in the present paper, no rationale is given for the fact that fluorenone **496** is not formed. Shudo's proposal,[49] which would involve dications **839** and **840**, may well account for the fact that cation **413** leads to fluorenone when generated from the phosphate derivative **495**,[137] but under acidic conditions, the ketone **838** is formed.

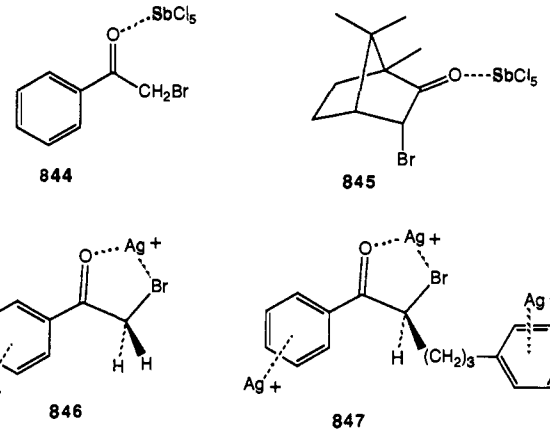


In a related process, reaction of the α-hydroxyketone **841** with CF_3SO_3H in Freon 113 led to adamantanone (**842**). The proposed mechanism does not involve the α-carbonyl cation **317**, but under these conditions, an unusual protonolysis of a carbon–carbon bond of **841** is the proposed mechanism.

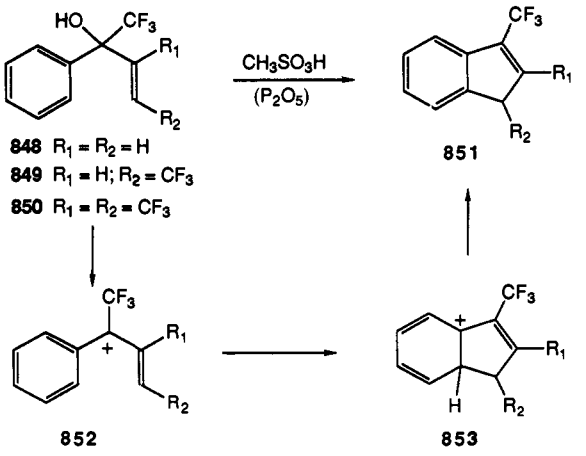
In a study related to the production of α-carbonyl cations using Lewis acids and silver ion, crystal struc-



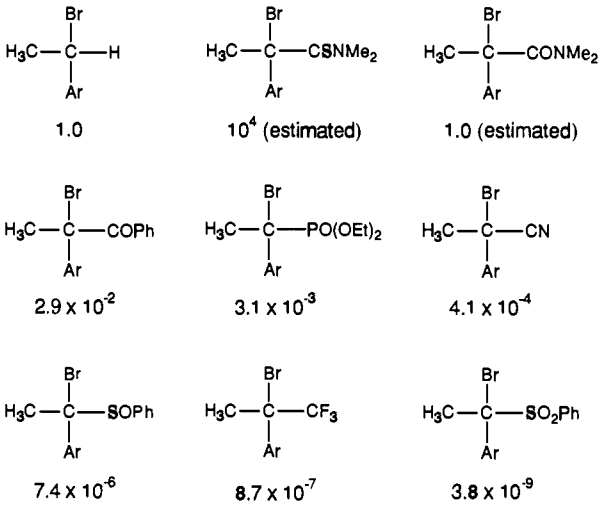
tures have been determined on various complexes of α-bromo ketones with $SbCl_5$ and $AgSbF_6$.[210] The monodentate hard Lewis acid $SbCl_5$ preferentially binds to the carbonyl oxygen atom as in 844 and 845. The soft Lewis acid Ag^+ binds to both the oxygen and the bromine atom as in 846 and 847 (as well as to the π-system of the aromatic rings). Hence $SbCl_5$ activates the carbonyl bond while Ag^+ activates the C–Br bond.



A synthesis of trifluoromethylated indenes has been developed utilizing the allylic alcohols 848–850.[211] Dehydration with methanesulfonic acid (with added P_2O_5 in the case of the bis- and tris-CF_3 substituted system) gave the indenes 851 presumably via the intermediacy of the cations 852 and 853. In a related transformation, dehydration of 1-pentafluoroethyl-1-indanol with CH_3SO_3H gave 1-(pentafluoroethyl)-indene.



In summary, this review has dealt with the chemistry of carbocations that carry an electron-withdrawing group attached directly to the cationic center. In the not-too-distant past, such intermediates were usually suggested with a bit of trepidation. However, this review has illustrated some of the numerous investigations that have occurred over the last two decades. Quantitative studies show that these carbocations are formed at vastly differing rates, indicating greatly differing stabilities. The chart below gives a comparison of solvolytic rates of substrates which generate some of the cations discussed in this review. While rates for formation, and corresponding stabilities can differ greatly, a unifying theme in studies of these intermediates is that such cations do exist. In many instances they can be generated with surprising ease due to cation stabilizing features of formally electron-withdrawing groups. In other instances the inductive effect of the electron-withdrawing group remains a dominating factor. As a result of these studies, cations substituted with electron-withdrawing groups have indeed been elevated to respectability.



Relative Solvolysis Rates in CF_3CH_2OH (Ar = p-CH_3-C_6H_4)

Acknowledgments. The studies from our laboratories cited in this review were supported over the years by the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, and I am grateful for their support. I would also like to acknowledge my co-workers in this area (C. C. Geiger, K. Hilton, T. L. Underiner, S. McDonald, M. Eggers, M. E. Mehrsheikh-Mohammadi, P. A. Inocencio, T. Aldridge, and H. Hatoum) for their extraordinary efforts in carrying out some of these studies.

Note Added in Proof. Two additional studies on α-carbonyl cations have recently appeared,[212,213] as well as a study on α-trifluoromethyl cations.[214]

XIII. References

(1) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Cornell Univ. Press: Ithaca, NY, 1969.
(2) Bégué, J.-P.; Charpentier-Morize, M. *Acc. Chem. Res.* **1980**, *13*, 207.
(3) Gassman, P. G.; Tidwell, T. T. *Acc. Chem. Res.* **1983**, *16*, 279.
(4) Creary, X. *Acc. Chem. Res.* **1985**, *18*, 3.
(5) Tidwell, T. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 20.
(6) (a) Allen, A. D.; Tidwell, T. T. In *Advances in Carbocation Chemistry*; Creary, X., Ed.; JAI Press Inc.: Greenwich, CT,

1989; p 1. (b) Creary, X. *Advances in Carbocation Chemistry*; Creary, X., Ed.; JAI Press Inc.: Greenwich, CT, 1989; p 45. (c) Charpentier-Morize, M.; Bonnet-Delpon, D. In *Advances in Carbocation Chemistry*; Creary, X., Ed.; JAI Press Inc.: Greenwich, CT, 1989; p 219.
(7) (a) Wilcox, C. F. Jr.; Brungardt, B. *Tetrahedron Lett.* **1984**, *25*, 3403. For related systems, see: (b) Wilcox, C. F., Jr.; Tuszynski, W. J. *Tetrahedron Lett.* **1982**, *23*, 3119.
(8) Takeuchi, K.; Yoshida, M. *J. Org. Chem.* **1989**, *54*, 3772.
(9) Kirmse, W.; Mrotzeck, U.; Siegfried, R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 55.
(10) Della, E. W.; Elsey, G. M. *Tetrahedron Lett.* **1988**, *29*, 1299.
(11) McKenzie, A.; Clough, G. W. *J. Chem. Soc.* **1910**, 1016.
(12) Koshy, K. M.; Roy, D.; Tidwell, T. T. *J. Am. Chem. Soc.* **1979**, *101*, 357.
(13) (a) Schubert, W. M.; Keeffe, J. R. *J. Am. Chem. Soc.* **1972**, *94*, 559. (b) Ellis, G. W. L.; Johnson, G. D. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1025.
(14) (a) Deno, N. C.; Kish, F. A.; Peterson, H. J. *J. Am. Chem. Soc.* **1965**, *87*, 2157. (b) Simandoux, J.-C.; Torck, B.; Hellin, M.; Coussemant, F. *Bull. Soc. Chim. Fr.* **1972**, 4402.
(15) Noyce, D. S.; Pollack, R. M. *J. Am. Chem. Soc.* **1969**, *91*, 119.
(16) Allen, A. D.; Shahidi, F.; Tidwell, T. T. *J. Am. Chem. Soc.* **1982**, *104*, 2516.
(17) (a) Allen, A. D.; Jansen, M. P.; Koshy, K. M.; Mangru, N. N.; Tidwell, T. T. *J. Am. Chem. Soc.* **1982**, *104*, 207. (b) Koshy, K. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1980**, *102*, 1216.
(18) (a) Liu, K.-T.; Kuo, M.-Y.; Sheu, C. F. *J. Am. Chem. Soc.* **1982**, *104*, 211–215. (b) Liu, K.-T.; Sheu, C.-F. *Tetrahedron Lett.* **1980**, *21*, 4091. (c) Liu, K.-T.; Wu, Y. W. *J. Chem. Res.* **1984**, 408.
(19) Liu, K.-T.; Wu, Y. W. *Tetrahedron Lett.* **1986**, *27*, 3623.
(20) Guo, Z.; Fry, A. *Tetrahedron Lett.* **1986**, *27*, 5059.
(21) Mishima, M.; Inoue, H.; Fujio, M.; Tsuno, Y. *Tetrahedron Lett.* **1989**, *30*, 2101.
(22) (a) Yukawa, Y.; Tsuno, Y. *Bull. Chim. Soc. Jpn.* **1959**, *32*, 971. (b) Yukawa, Y.; Tsuno, Y.; Sawada, M. *Bull. Chim. Soc. Jpn.* **1966**, *39*, 2274. (c) Yukawa, Y.; Tsuno, Y.; Sawada, M. *Bull. Chim. Soc. Jpn.* **1972**, *45*, 1198. (d) Tsuno, Y.; Kusuyama, Y.; Sawada, M.; Fujii, T. *Bull. Chim. Soc. Jpn.* **1975**, *48*, 3337.
(23) Jansen, M. P.; Koshy, K. M.; Mangru, N. N.; Tidwell, T. T. *J. Am. Chem. Soc.* **1981**, *103*, 3863.
(24) Allen, A. D.; Ambridge, I. C.; Che, C.; Michael, H.; Muir, R. J.; Tidwell, T. T. *J. Am. Chem. Soc.* **1983**, *105*, 2343.
(25) Kwong-Chip, J.; Tidwell, T. T. *Tetrahedron Lett.* **1989**, *30*, 1319.
(26) Allen, A. D.; Girdhir, R.; Jansen, M. P.; Mayo, J. D.; Tidwell, T. T. *J. Org. Chem.* **1986**, *51*, 1324.
(27) (a) Richard, J. P. *J. Am. Chem. Soc.* **1989**, *111*, 1455. (b) Richard, J. P. *J. Am. Chem. Soc.* **1986**, *108*, 6819.
(28) Richard, J. P. *Tetrahedron Lett.* **1989**, *30*, 23.
(29) Richard, J. P. *J. Chem. Soc., Chem. Commun.* **1987**, 1768.
(30) Astrologes, G. W.; Martin, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 4400.
(31) (a) Allen, A. D.; Kanagasabapathy, V. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1986**, *108*, 3470. (b) Allen, A. D.; Kanagasabapathy, V. M.; Tidwell, T. T. *J. Am. Chem. Soc.* **1983**, *105*, 5961.
(32) Creary, X.; Underiner, T. L. *J. Org. Chem.* **1985**, *50*, 2165.
(33) Richard, J. P.; Amyes, T. L.; Bei, L.; Stubblefield, V. *J. Am. Chem. Soc.* **1990**, *112*, 9513.
(34) Kanagasabapathy, V. M.; Sawyer, J. F.; Tidwell, T. T. *J. Org. Chem.* **1985**, *50*, 503.
(35) Allen, A. D.; Krishnamurti, R.; Prakash, G. K. S.; Tidwell, T. T. *J. Am. Chem. Soc.* **1990**, *112*, 1291.
(36) Gassman, P. G.; Harrington, C. K. *J. Org. Chem.* **1984**, *49*, 2258.
(37) Poulter, D. C.; Satterwhite, D. M.; Rilling, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 3376.
(38) McBee, E. T.; Battershell, R. D.; Braendlin, H. P. *J. Am. Chem. Soc.* **1962**, *84*, 3157. (b) Pegolotti, J. A.; Young, W. G. *J. Am. Chem. Soc.* **1961**, *83*, 3258. (c) Hatch, L. F.; Nesbitt, S. S. *J. Am. Chem. Soc.* **1951**, *73*, 358.
(39) Gassman, P. G.; Hall, J. B. *J. Am. Chem. Soc.* **1984**, *106*, 4267.
(40) Liu, K.-T.; Kuo, M.-Y. *Tetrahedron Lett.* **1985**, *26*, 355.
(41) Liu, K.-T.; Chang, S.-M.; Chen, H.-I.; Chiu, P.-F.; Wu, T.-R. *J. Org. Chem.* **1991**, *56*, 1315.
(42) Hanack, M.; Meyer, H. *Justus Liebigs Ann. Chem.* **1968**, *720*, 81.
(43) Roberts, D. D.; Hall, E. W. *J. Org. Chem.* **1988**, *53*, 2573.
(44) Gassen, K. R.; Kirmse, W. *Chem. Ber.* **1986**, *119*, 2233.
(45) (a) Olah, G. A.; Pittman, C. U., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 3310. (b) Olah, G. A.; Prakash, G. K. S.; Arvanaghi, M.; Krishnamurthy, V. V.; Narang, S. C. *J. Am. Chem. Soc.* **1984**, *106*, 2378.
(46) (a) Cohen, S. *J. Am. Chem. Soc.* **1957**, *79*, 1499. (b) Kaluszyner, A.; Cohen, S. *Tetrahedron* **1960**, *11*, 252.
(47) Streitwieser, A., Jr.; Marchand, A. P.; Pudjaatmaka, A. H. *J. Am. Chem. Soc.* **1957**, *89*, 693.
(48) Dao, L. H.; Maleki, M.; Hopkinson, A. C.; Lee-Ruff, E. *J. Am. Chem. Soc.* **1986**, *108*, 5237.
(49) Ohwada, T.; Shudo, K. *J. Am. Chem. Soc.* **1988**, *110*, 1862.
(50) Rover-Kevers, M.; Vertommen, L.; Huys, F.; Merényi, R.; Janousek, Z.; Viehe, H. G. *Angew. Chem., Int. Ed. Engl.* **1981**, *93*, 1023.
(51) (a) Fuchigama, T.; Yamamoto, K.; Nakagawa, Y. *J. Org. Chem.* **1991**, *56*, 137. (b) Fuchigama, T.; Nakagawa, Y.; Nonaka, T. *Tetrahedron Lett.* **1986**, *27*, 3869.
(52) Fuchigama, T.; Nakagawa, Y.; Nonaka, T. *J. Org. Chem.* **1987**, *52*, 5489.
(53) Uneyama, K.; Momota, M.; Hayashida, K.; Itoh, T. *J. Org. Chem.* **1990**, *55*, 5364.
(54) Bonnet-Delpon, D.; Cambillau, C.; Charpentier-Morize, M.; Jacquot, R.; Mesureur, D.; Ourevitch, M. *J. Org. Chem.* **1988**, *53*, 754.
(55) Guy, A.; Lobgeois, A.; Lemaire, M. *J. Fluorine Chem.* **1986**, *32*, 361.
(56) Bonnet-Delpon, D.; Charpentier-Morize, M. *Bull Soc. Chim. Fr.* **1986**, 933.
(57) Fung, S.; Abraham, N. A.; Bellini, F.; Sestanj, K. *Can. J. Chem.* **1983**, *61*, 368.
(58) Bonnet-Delpon, D.; Charpentier-Morize, M.; Jacquot, R. *J. Org. Chem.* **1988**, *53*, 759.
(59) Aubert, C.; Bégué, J.-P.; Bonnet-Delpon, D.; Mesureur, D. *J. Chem. Soc., Perkin Trans. 1* **1989**, 395.
(60) Paddon-Row, M. N.; Santiago, C.; Houk, K. N. *J. Am. Chem. Soc.* **1980**, *102*, 6561.
(61) Reynolds, W. F.; Dais, P.; MacIntyre, D. W.; Topsom, R. D.; Marriot, S.; Nagy-Felsobuki, E.; Taft, R. W. *J. Am. Chem. Soc.* **1983**, *105*, 378.
(62) Paddon-Row, M. N.; Houk, K. N.; Tidwell, T. T. *Tetrahedron Lett.* **1982**, *23*, 383.
(63) Charpentier-Morize, M.; Fossey, J.; Tidwell, T. T.; Wolfe, S. *Can. J. Chem.* **1987**, *65*, 473.
(64) McAllister, M.; Tidwell, T. T.; Peterson, M. R.; Csizmadia, I. G. *J. Org. Chem.* **1991**, *56*, 575.
(65) Gassman, P. G.; Talley, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 1214.
(66) Gassman, P. G.; Talley, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 4138.
(67) Gassman, P. G.; Doherty, M. M. *J. Am. Chem. Soc.* **1982**, *104*, 3742.
(68) Gassman, P. G.; Talley, J. J. *Tetrahedron Lett.* **1981**, *22*, 5253.
(69) Gassman, P. G.; Saito, K.; Talley, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 7615.
(70) Gassman, P. G.; Saito, K. *Tetrahedron Lett.* **1981**, *22*, 1311.
(71) Gassman, P. G.; Guggenheim, T. L. *J. Org. Chem.* **1982**, *47*, 3023.
(72) Kirmse, W.; Goer, B. *J. Am. Chem. Soc.* **1990**, *112*, 4556.
(73) Wu, Y.-D.; Kirmse, W.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 4557.
(74) Laurent, E.; Marquet, B.; Tardivel, R.; Thiebault, H. *Tetrahedron Lett.* **1987**, *28*, 2359.
(75) (a) Olah, G. A.; Arvanaghi, M.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1982**, *104*, 1628. (b) Olah, G. A.; Prakash, G. K. S.; Arvanaghi, M. *J. Am. Chem. Soc.* **1980**, *102*, 6640.
(76) Mertens, A.; Olah, G. A. *Chem. Ber.* **1983**, *116*, 103.
(77) Beaumont, R. C.; Aspin, K. B.; Demas, T. J.; Hoggatt, J. H.; Potter, G. E. *Inorg. Chim. Acta* **1984**, *84*, 141.
(78) Dixon, D. A.; Charlier, P. A.; Gassman, P. G. *J. Am. Chem. Soc.* **1980**, *102*, 3957.
(79) Paddon-Row, M. N.; Santiago, C.; Houk, K. N. *J. Am. Chem. Soc.* **1980**, *102*, 6561.
(80) Reynolds, W. F.; Dais, P.; Taft, R. W.; Topsom, R. D. *Tetrahedron Lett.* **1981**, *22*, 1795.
(81) Dixon, D. A.; Eades, R. A.; Frey, R.; Gassman, P. G.; Hendewerk, M. L.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 3885.
(82) McDonald, R. N.; Tabor, T. E. *J. Am. Chem. Soc.* **1967**, *89*, 6573.
(83) McDonald, R. N.; Steppel, R. N. *J. Am. Chem. Soc.* **1970**, *92*, 5664.
(84) McDonald, R. N.; Steppel, R. N. *J. Org. Chem.* **1970**, *35*, 1250.
(85) McDonald, R. N.; Cousins, R. C. *J. Org. Chem.* **1980**, *45*, 2976.
(86) Griesbaum, K.; Keul, H.; Kibar, R.; Pfeffer, B. *Chem. Ber.* **1981**, *114*, 1858.
(87) Steiniger, M.; Schäfer, H. J. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 125.
(88) Smith, A. B., III; Dieter, R. K. *Tetrahedron* **1981**, 2407.
(89) (a) Dahn, H.; Gold, H.; Ballenegger, M.; Lenoir, J.; Diderich, G.; Malherbe, R. *Helv. Chim. Acta* **1968**, *51*, 2065. (b) Dahn, H.; Ballenegger, M. *Helv. Chim. Acta* **1969**, *52*, 2417.
(90) Jugelt, W.; Berseck, L. *Tetrahedron* **1970**, *26*, 5557.
(91) Buckley, D. J.; Kulkowit, S.; McKervey, A. *J. Chem. Soc., Chem. Commun.* **1980**, 506.

(92) (a) Giddings, P. J.; John, D. I.; Thomas, E. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2757. (b) Giddings, P. J.; John, D. I.; Thomas, E. *Tetrahedron Lett.* **1980**, *21*, 399.
(93) Back, T. G.; Kerr, R. G. *J. Organomet. Chem.* **1985**, *286*, 171.
(94) Karavan, V. S.; Temnikova, T. I. *J. Org. Chem. USSR. (Engl. Transl.)* **1966**, *2*, 1399.
(95) Semenova, S. N.; Dement'eva, L. P.; Morozova, L. M.; Vasil'eva, E. V.; Temnikova, T. I. *J. Org. Chem. USSR. (Engl. Transl.)* **1972**, *8*, 2166.
(96) Creary, X. *J. Org. Chem.* **1979**, *44*, 3938.
(97) Creary, X. *J. Am. Chem. Soc.* **1981**, *103*, 2463.
(98) Creary, X. *J. Am. Chem. Soc.* **1984**, *106*, 5568–5577.
(99) (a) Fry, J. L.; Lancelot, C. J.; Lam, L. K. M.; Harris, J. M.; Bingham, R. C.; Raber, D. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1970**, *92*, 2538. (b) Fry, J. L.; Harris, J. M.; Bingham, R. C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1970**, *92*, 2540. (c) Schleyer, P. v. R.; Fry, J. L.; Lam, L. K. M.; Lancelot, C. J. *J. Am. Chem. Soc.* **1970**, *92*, 2542.
(100) (a) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151–4162. (b) Creary, X.; McDonald, S.; Eggers, M. D. *Tetrahedron Lett.* **1985**, *26*, 811.
(101) (a) Goering, H. L.; Chang, S. *Tetrahedron Lett.* **1965**, 3607. (b) Goering, H. L.; Henning, H. *J. Am. Chem. Soc.* **1971**, *93*, 1224. (c) Okamoto, K.; Kinoshita, T.; Osada, Y. *J. Chem. Soc., Perkin Trans. 2* **1975**, 253. (d) Bone, J. A.; Pritt, J. R.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1447.
(102) (a) Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7658. (b) Raber, D. J.; Neal, W. C., Jr.; Dukes, M. D.; Harris, J. M.; Mount, D. L. *J. Am. Chem. Soc.* **1978**, *100*, 8137. (c) Harris, J. M.; Mount, D. L.; Smith, M. R.; Neal, W. C., Jr.; Dukes, M. D.; Raber, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 8147. (d) Bentley, T. W.; Bowen, T. C.; Morten, D. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5466.
(103) Takeuchi, K.; Akiyama, F.; Ikai, K.; Shibata, T.; Kato, M. *Tetrahedron Lett.* **1988**, *29*, 873.
(104) Takeuchi, K.; Yoshida, M.; Ohga, Y.; Tsugeno, A.; Kitagawa, T. *J. Org. Chem.* **1990**, *55*, 6063.
(105) Della, E. W.; Elsey, G. M.; Skouroumounis, G. *Tetrahedron Lett.* **1986**, *27*, 5993.
(106) Hojo, M.; Masuda, R.; Ichi, T.; Yoshinaga, K.; Yamada, M. *Tetrahedron Lett.* **1982**, *23*, 4963.
(107) Baudry, D.; Bégué, J. P.; Charpentier-Morize, M. *Tetrahedron Lett.* **1970**, 4707.
(108) Bégué, J. P.; Charpentier-Morize, M. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 327.
(109) Bégué, J. P.; Charpentier-Morize, M.; Bonnet-Delpon, D.; Sansoulet, J. *J. Org. Chem.* **1980**, *45*, 3357.
(110) Bégué, J. P.; Charpentier-Morize, M.; Pardo, C. *Tetrahedron* **1975**, *31*, 1919.
(111) Bégué, J. P.; Bonnet, D.; Charpentier-Morize, M.; Pardo, C. *Tetrahedron* **1975**, *31*, 2505.
(112) Bégué, J. P.; Malissard, M. *Tetrahedron* **1978**, *31*, 2095.
(113) Bégué, J. P. *J. Org. Chem.* **1982**, *47*, 4268.
(114) Baudry, D.; Charpentier-Morize, M.; Lefort, D.; Sorba, J. *Tetrahedron Lett.* **1974**, 2499.
(115) (a) Baudry, D.; Charpentier-Morize, M. *Tetrahedron Lett.* **1973**, 3013. (b) Baudry, D.; Charpentier-Morize, M. *Nouv. J. Chim.* **1978**, *2*, 55.
(116) Baudry, D.; Charpentier-Morize, M. *Tetrahedron Lett.* **1972**, 2561.
(117) Pardo, C.; Charpentier-Morize, M. *J. Chem. Soc., Chem. Commun.* **1982**, 1037.
(118) Takeuchi, K.; Kitagawa, T.; Okamoto, K. *J. Chem. Soc., Chem. Commun.* **1983**, 7.
(119) Horning, D. E.; Muchowski, J. M. *Can. J. Chem.* **1968**, *46*, 3665.
(120) Nilles, G. R.; Schuetz, R. D. *Tetrahedron Lett.* **1969**, 4313.
(121) (a) Hopkinson, A. C.; Dao, L. H.; Duperrouzel, P.; Maleki, M.; Lee-Ruff, E. *J. Chem. Soc., Chem. Commun.* **1983**, 727. (b) Dao, L. H.; Maleki, M.; Hopkinson, A. C.; Lee-Ruff, E. *J. Am. Chem. Soc.* **1986**, *108*, 5237.
(122) (a) Kelly, D. P.; Spear, R. J. *Aust. J. Chem.* **1977**, *20*, 1993. (b) Brown, H. C.; Peters, E. N. *J. Am. Chem. Soc.* **1977**, *99*, 1712.
(123) Hopkinson, A. C.; Lee-Ruff, E.; Toone, T. W.; Khazanie, P. G.; Dao, L. H. *J. Chem. Soc. Perkin Trans. 2* **1979**, 1396.
(124) Maleki, M.; Hopkinson, A. C.; Lee-Ruff, E. *Tetrahedron Lett.* **1983**, *24*, 4911.
(125) Hopkinson, A. C.; Lee-Ruff, E.; Maleki, M. *Synthesis* **1986**, 366.
(126) Bladek, R.; Sorenson, T. S. *Can. J. Chem.* **1972**, *50*, 2806.
(127) Fletcher, D.; Ablenas, F. J.; Hopkinson, A. C.; Lee-Ruff, E. *Tetrahedron Lett.* **1986**, *27*, 4853.
(128) Lee, T. V.; Okonkwo, J. O. *Tetrahedron Lett.* **1983**, *24*, 323.
(129) Fleming, I.; Igbal, J. *Tetrahedron Lett.* **1983**, *24*, 327.
(130) Ishibashi, H.; Kitano, Y.; Nakayani, H.; Okada, M.; Ikeda, M. *Tetrahedron Lett.* **1984**, *25*, 4231.
(131) Lee, T. V.; Galan, A. A.; Chapleo, C. B. *Tetrahedron Lett.* **1987**, *28*, 2301.
(132) Kulkarni, G. C.; Karmarkar, S. N.; Kelkar, S. L.; Wadia, M. S. *Tetrahedron* **1988**, *44*, 5189.
(133) House, H. O.; Reif, D. J.; Wasson, R. L. *J. Am. Chem. Soc.* **1957**, *79*, 2490.
(134) Singh, S. P.; Kagan, J. *J. Am. Chem. Soc.* **1969**, *91*, 6198.
(135) Chao, H. S.-I.; Berchtold, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 898.
(136) Okamoto, K.; Nitta, I.; Shingu, H. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 1464.
(137) Givins, R. S.; Matuszewski *J. Am. Chem. Soc.* **1984**, *106*, 6860.
(138) (a) Mehta, G.; Rao, K. S.; Suri, S. C. *J. Chem. Soc., Chem. Commun.* **1980**, 650. (b) Mehta, G.; Rao, K. S.; Suri, S. C. *Tetrahedron Lett.* **1980**, *21*, 3821.
(139) Kresge, A. J.; Yin, Y. *Can. J. Chem.* **1987**, *65*, 1753.
(140) (a) Oikawa, Y.; Yonemitsu, O. *Tetrahedron* **1974**, *30*, 2653. (b) Oikawa, Y.; Yonemitsu, O. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1479. (c) Oikawa, Y.; Yonemitsu, O. *J. Org. Chem.* **1976**, *41*, 1118.
(141) (a) Blair, I. A.; Mander, L. N.; Mundill, P. H. C. *Aust. J. Chem.* **1981**, *34*, 1235. (b) Mander, L. N.; Mundill, P. H. C. *Synthesis* **1981**, 620.
(142) Tamura, Y.; Maeda, H.; Akai, S.; Ishiyama, K.; Ishibashi, H. *Tetrahedron Lett.* **1981**, *22*, 4301.
(143) Tamura, Y.; Choi, H.-D.; Shindo, H.; Uenishi, J.; Ishibashi, H. *Tetrahedron Lett.* **1981**, *22*, 81.
(144) Tamura, Y.; Choi, H.-D.; Maeda, H.; Ishibashi, H. *Tetrahedron Lett.* **1981**, *22*, 1343.
(145) Tamura, Y.; Maeda, H.; Choi, H.-D.; Ishibashi, H. *Synthesis* **1982**, 56.
(146) Stamos, I. K. *Tetrahedron Lett.* **1985**, *26*, 477.
(147) (a) O'Donnell, M. J.; Bennett, W. D.; Polt, R. L. *Tetrahedron Lett.* **1985**, *26*, 695. (b) O'Donnell, M. J.; Falmagne, F.-B. *Tetrahedron Lett.* **1985**, *26*, 699.
(148) Geffken, D.; Strohauer, K. *Z. Naturforsch.* **1985**, *40b*, 398.
(149) Cooks, R. G.; Yeo, A. N. H.; Williams, D. H. *Org. Mass Spectrom.* **1969**, *2*, 985.
(150) Grützmacher, H. F.; Dommröse, A. M.; Neuert, U. *Org. Mass. Spectrom.* **1981**, *16*, 279.
(151) Bouchoux, G.; Hoppilliard, Y.; Jaudon, P. *Tetrahedron Lett.* **1982**, *23*, 3349.
(152) Grützmacher, H. F.; Dommröse, A. M. *Org. Mass Spectrom.* **1983**, *18*, 601.
(153) Dommröse, A. M.; Grützmacher, H. F. *Org. Mass Spectrom.* **1987**, *22*, 437.
(154) Wolf, R.; Dommröse, A. M.; Grützmacher, H. F. *Org. Mass Spectrom.* **1988**, *23*, 26.
(155) Wolf, R.; Grützmacher, H. F. *Org. Mass Spectrom.* **1989**, *24*, 398.
(156) Burgers, P. C.; Holmes, J. L.; Lossing, F. P.; Povel, F. R.; Terlouw, J. K. *Org. Mass Spectrom.* **1983**, *18*, 335.
(157) Grützmacher, H. F.; Wolf, R. *Nouv. J. Chim.* **1988**, *12*, 865.
(158) Wolf, R.; Grützmacher, H. F. *J. Phys. Org. Chem.* **1990**, *3*, 301.
(159) Turecek, F.; McLafferty, F. W. *Org. Mass Spectrom.* **1983**, *18*, 608. For a related discussion, see Burgers, P. C.; Holmes, J. L.; Szulejko, J. E.; Mommers, A. A.; Terlouw, J. K. *Org. Mass. Spectrom.* **1983**, *18*, 254.
(160) Blanchette, M. C.; Holmes, J. L.; Hop, C. E. C. A.; Lossing, F. P.; Postma, R.; Ruttink, P. J. A.; Terlouw, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 7589.
(161) Charpentier-Morize, M.; Lefour, J. M.; Anh, T. N. *Tetrahedron Lett.* **1974**, 1729.
(162) Yarkony, D. R.; Schaefer, H. F. *J. Phys. Chem.* **1975**, *63*, 4317.
(163) Nobes, R. H.; Bouma, W. J.; Radom, L. *J. Am. Chem. Soc.* **1983**, *105*, 309.
(164) (a) Lien, M. H.; Hopkinson, A. C. *J. Am. Chem. Soc.* **1988**, *110*, 3788. (b) Rodriquez, C. F.; Hopkinson, A. C. *Org. Mass Spectrom.* **1985**, *20*, 691.
(165) Aissani, A. M.; Baum, J. C.; Langler, R. F.; Ginsburg, J. L. *Can. J. Chem.* **1986**, *64*, 532.
(166) (a) Yates, P.; Crawford, R. J. *J. Am. Chem. Soc.* **1966**, *88*, 1561. (b) Batattel, R. A.; Yates, P. *Tetrahedron Lett.* **1972**, 1069. For related studies, see: (c) Yates, P.; Kronis, J. D. *Tetrahedron Lett.* **1983**, *24*, 2419.
(167) Siegfried, R. *Chem. Ber.* **1974**, *107*, 1472.
(168) Edwards, O. E.; Dixon, J.; Elder, J. W.; Kolt, R. J.; Lesage, M. *Can. J. Chem.* **1981**, *59*, 2096.
(169) Bégué, J.-P.; Charpentier-Morize, M.; Pardo, C.; Sansoulet *Tetrahedron* **1978**, *34*, 293.
(170) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1983**, *105*, 7123.
(171) Sheehan, J. C.; Beeson, J. H. *J. Am. Chem. Soc.* **1967**, *89*, 362.
(172) Cope, A. C.; Graham, E. S. *J. Am. Chem. Soc.* **1951**, *73*, 4702.
(173) Pasto, D. J.; Sevenair, J. P. *J. Am. Chem. Soc.* **1971**, *93*, 711.
(174) DeKimpe, N.; DeBuyck, L.; Verhé, R.; Schamp, N. *Chem. Ber.* **1983**, *116*, 3631.
(175) Giordano, C.; Castaldi, G.; Casagrange, F.; Abis, L. *Tetrahedron Lett.* **1982**, *23*, 1385.

(176) (a) Pasto, D. J.; Garves, K.; Serve, M. P. *J. Org. Chem.* **1967**, *32*, 774. (b) Pasto, D. J.; Garves, K. *J. Org. Chem.* **1967**, *32*, 778.
(177) (a) Kende, A. S. *Org. React.* **1960**, *11*, 261. (b) Bordwell, F. G. *Acc. Chem. Res.* **1970**, *3*, 281.
(178) Bordwell, F. G.; Carlson, M. W. *J. Am. Chem. Soc.* **1970**, *92*, 3370, 3377.
(179) Creary, X.; Mehrsheikh-Mohammadi, M. E. *J. Org. Chem.* **1986**, *51*, 7.
(180) Ablenas, F. J.; George, B. E.; Maleki, M.; Jain, R.; Hopkinson, A. C.; Lee-Ruff, E. *Can. J. Chem.* **1987**, *65*, 1800.
(181) Creary, X.; Aldridge, T. *J. Org. Chem.* **1988**, *53*, 3888.
(182) Creary, X.; Aldridge, T. *J. Org. Chem.* **1991**, *56*, 4280.
(183) DeKimpe, N.; Verhé, R.; DeBuyck, L.; Schamp, N.; Charpentier-Morize, M. *Tetrahedron Lett.* **1982**, *23*, 2853.
(184) DeKimpe, N.; Verhé, R.; DeBuyck, L.; Schamp, N. *Can. J. Chem.* **1984**, *62*, 1812.
(185) Bégué, J.-P.; Bonnet-Delpon, D.; Charpentier-Morize, M.; Richard, A. *Tetrahedron Lett.* **1985**, *26*, 5681.
(186) (a) Alvernhe, G.; Lacombe, S.; Laurent, A. *Tetrahedron Lett.* **1980**, *21*, 1437. (b) Flammang, R.; Lacombe, S.; Laurent, A.; Maquestiau, A.; Marquet, B.; Novkova, S. *Tetrahedron* **1986**, *42*, 315.
(187) Shatzmiller, S.; Lidor, R.; Shalom, E.; Bahar, E. *J. Chem. Soc., Chem. Commun.* 1984, 795.
(188) Shatzmiller, S.; Shalom, E.; Bahar, E. *J. Chem. Soc., Chem. Commun.* **1984**, 1522.
(189) (a) Hansen, J. F.; Strong, S. A. *J. Heterocycl. Chem.* **1977**, *14*, 1289. (b) Hansen, J. F.; Kim, Y. I.; McCrotty, S. E.; Strong, S. A.; Zimmer, D. E. *J. Heterocycl. Chem.* **1980**, *17*, 475.
(190) Shatzmiller, S.; Gygax, P.; Hall, D.; Eschenmoser, A. *Helv. Chim. Acta* **1973**, *56*, 2961.
(191) Bonnet-Delpon, D.; Charpentier-Morize, M. *Chem. Phys. Lett.* **1985**, *116*, 478.
(192) Creary, X.; Geiger, C. C.; Hilton, K. *J. Am. Chem. Soc.* **1983**, *105*, 2851.
(193) Creary, X.; Underiner, T. L. *J. Org. Chem.* **1985**, *50*, 2165.
(194) (a) Dimroth, K.; Kaletsch, H.; Dave, T. N. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 990. (b) Dimroth, K. *Top. Curr Chem.* **1973**, *38*, 49.
(195) (a) Dimroth, K.; Umbach, W.; Thomas, H. *Chem. Ber.* **1967**, *100*, 132. (b) Dimroth, K.; Laufenberg, J. *Chem. Ber.* **1972**, *105*, 1044.
(196) Pasto, D. J. *J. Org. Chem.* **1985**, *50*, 1014.
(197) Creary, X.; Inocencio, P. A. *J. Am. Chem. Soc.* **1986**, *108*, 5979.
(198) Meyers, C. T.; Hua, H. D. *Phosphorus Sulfur* **1979**, *6*, 197.
(199) (a) Bordwell, F. G.; Mecca, T. G. *J. Am. Chem. Soc.* **1972**, *94*, 2119. (b) Bordwell, F. G.; Pagani, G. A. *J. Am. Chem. Soc.* **1975**, *97*, 118. (c) Bordwell, F. G.; Mecca, T. G. *J. Am. Chem. Soc.* **1975**, *97*, 123. (d) Bordwell, F. G.; Mecca, T. G. *J. Am. Chem. Soc.* **1975**, *97*, 127. (e) Bordwell, F. G.; Wiley, P. F.; Mecca, T. G. *J. Am. Chem. Soc.* **1975**, *97*, 132.
(200) Creary, X.; Mehrsheikh-Mohammadi, M. E.; Eggers, M. D. *J. Am. Chem. Soc.* **1987**, *109*, 2435.
(201) Durst, T.; Tin, K. C.; Marcil, M. J. V. *Can. J. Chem.* **1973**, *51*, 1704.
(202) Klein, J.; Stollar, H. *J. Am. Chem. Soc.* **1973**, *95*, 7437.
(203) Shimagaki, M.; Tsuchiya, H.; Ban, Y.; Oishi, T. *Tetrahedron Lett.* **1978**, 3435.
(204) Venier, C. G.; Wing, F. A., Jr.; Barager, H. J., III. *Tetrahedron Lett.* **1980**, *21*, 3159.
(205) Reutrakul, V.; Panyachotipun, C.; Hahnvajanawong, V.; Sotheeswaran, S. *Tetrahedron Lett.* **1984**, *25*, 1825.
(206) Olah, G. A.; Prakash, G. K. S.; Arvanaghi, M.; Krishnamurthy, V. V.; Naran, S. C. *J. Am. Chem. Soc.* **1984**, *106*, 2378.
(207) Bégué, J.-P.; Pardo, C.; Sansoulet, J. *J. Chem. Res. (S)* **1978**, 52.
(208) Hawthorne, M. F.; Strahm, R. D. *J. Am. Chem. Soc.* **1957**, *79*, 2515.
(209) Olah, G. A.; Wu, A. *J. Org. Chem.* **1991**, *56*, 2531.
(210) Laube, T.; Weidenhaupt, A.; Hunziker, R. *J. Am. Chem. Soc.* **1991**, *113*, 2561.
(211) Gassman, P. G.; Ray, J. A.; Wenthold, P. G.; Mickelson, J. W. *J. Org. Chem.* **1991**, *56*, 5143.
(212) Kitagawa, T.; Nishimura, M.; Takeuchi, K.; Okamoto, K. *Tetrahedron Lett.* **1991**, *32*, 3187.
(213) Richard, J. P.; Amyes, T. L.; Stevens, I. W. *Tetrahedron Lett.* **1991**, *32*, 4255.
(214) Roberts, D. D. *J. Org. Chem.* **1991**, *56*, 5661.