

Superacid promoted reactions of *N*-acyliminium salts and evidence for the involvement of superelectrophiles†‡

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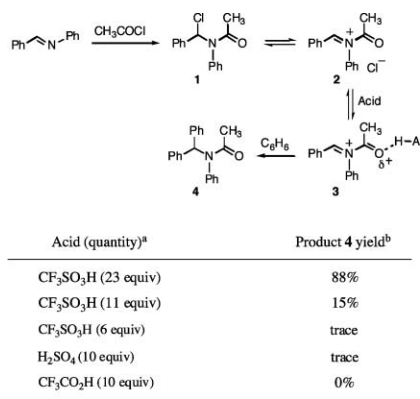
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Experimental and theoretical studies suggest the involvement of dicationic, superelectrophilic *N*-acyliminium ions in conversions catalyzed by superacids.

Over the years, it has been observed that a variety of cationic electrophiles exhibit significantly enhanced reactivities in superacids. This led to a proposal by Olah and coworkers that electrophiles like the nitronium cation (NO_2^+) possessing non-bonded electron pairs are capable of interacting with strongly acidic media, producing in the limiting case dicationic species (*i.e.*, HNO_2^{2+}).¹ Due to their ability to react with very weak nucleophiles, Olah referred to these species as superelectrophiles. Superelectrophiles have since been proposed in many synthetically useful reactions, they have been directly observed in NMR and mass spectral studies, and one example has even been proposed in a biochemical transformation.²

The acid-catalyzed reactions of *N*-acyliminium salts are well known and have great value in synthetic methodologies.³ Many of these transformations involve generating the cationic *N*-acyliminium ions in excess strong acid. Although these are the types of conditions that could suggest the involvement of superelectrophiles, there has been almost no work done to explore the possibility that superelectrophiles may be involved in this class of reactions. Perhaps the most closely related work was our recent study of the aza-Nazarov reaction and Olah's α -imido-methylation of deactivated arenes by *N*-hydroxymethylphthalimide in superacid.⁴ In the following manuscript, we present experimental evidence for the involvement of protosolvated *N*-acyliminium ions in superacid-catalyzed reactions. We also report results from spectroscopic and computational studies related to these super-electrophilic species.

In order to evaluate the effects of acidity on a conversion involving *N*-acyliminium salts, the reaction of acetylated benzilidene aniline with benzene was studied (Scheme 1).⁵ Two notable observations were seen: the yield of product **4** increases markedly with the acidity and quantity of the acid catalyst. These results are consistent with protosolvation of the *N*-acyliminium ion to give an electrophile with increasing dipositive character (*i.e.* **3**). Since the *N*-acyliminium ion itself is a weak base, increasing acid strength should favor

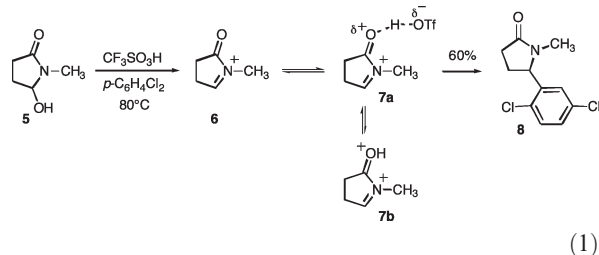


^aReaction conditions: **2** (1.0 mmol), CH₂Cl₂ (5 mL), then C₆H₆ (1 mL), and acid, RT, 2 hrs. ^bGC-FID yields.

Scheme 1 Results from the reactions of **2** with varied acids.

generation of the protosolvated species. Similarly, increasing quantities of superacid tends to increase the bulk acidity of the reaction media.⁶

One characteristic of superelectrophiles is their ability to react with weak nucleophiles, such as deactivated arenes and saturated hydrocarbons.² Only a few types of *N*-acyliminium ions have been shown to react with deactivated arenes like *o*-, *m*- or *p*-dichlorobenzene and these reactions have likewise required excess acid to effect the transformations.⁷ As part of our studies, the acid-catalyzed reactions of the pyrrolidinone derivative (**5**) were examined (eqn (1)).§



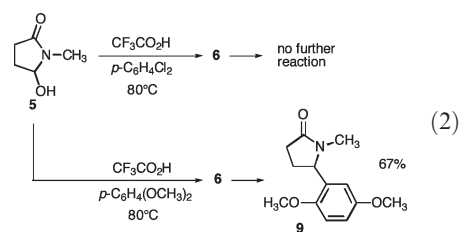
(1)

In the reaction with *p*-dichlorobenzene and CF₃SO₃H, pyrrolidinone **5** is arylated in reasonably good yield (60%) to give product **8**. Similar results are obtained from the superacid-promoted reaction of *o*-dichlorobenzene and compound **5**. It is proposed that the *N*-acyliminium ion (**6**) is formed¶ and protonation of this species leads to the superelectrophile (**7a** or **7b**). When the substantially weaker acid CF₃CO₂H is used in the same transformations, there are no reactions with the deactivated arene nucleophile (eqn (2)).

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‡ Dedicated to Professor George A. Olah on the occasion of his 80th birthday.



However when the activated arene and stronger nucleophile, *p*-dimethoxybenzene, is reacted with compound **5** in $\text{CF}_3\text{CO}_2\text{H}$, the arylated product (**9**) is formed. This indicates that the weaker acid is capable of producing the *N*-acyliminium ion (**6**), but without further protolytic activation, the *N*-acyliminium ion is not sufficiently electrophilic to attack *p*-dichlorobenzene. Reaction in superacid leads to the formation of dication **7a** or **7b** and subsequent chemistry with the deactivated arene. When the pyrrolidinone (**5**) is reacted with benzene and $\text{CF}_3\text{SO}_3\text{H}$, the phenylated product (1-methyl-5-phenylpyrrolidin-2-one) is obtained in 86% yield. An earlier report describes a similar reaction between the *N*-acyliminium ion **6** (formed by decarbonylation of pyroglutamic acids) and benzene in the weaker acid system, $\text{P}_2\text{O}_5\text{-CH}_3\text{SO}_3\text{H}$, however the yield is only 27%.⁸ This suggests a greater degree of *N*-acyliminium ion protosolvation in the superacidic $\text{CF}_3\text{SO}_3\text{H}$.

In order to further explore this chemistry, theoretical calculations were done to estimate the effects of protosolvation on the energetics of the *N*-acyliminium ions (**6** and **7b**) and its reaction with benzene. Calculations were done at the HF/6-311+G(d) and MP2/6-311+G(d) levels of theory (Fig. 1).⁹ Two stereoisomers of

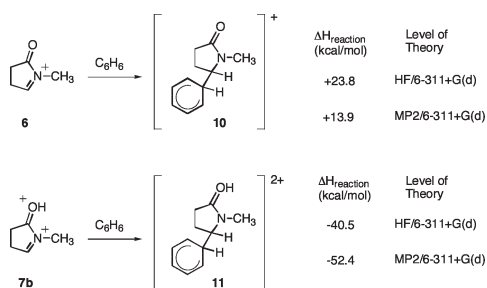


Fig. 1 Calculations related to the phenylation of **6** and **7b** and the estimated $\Delta H_{\text{reactions}}$ for the respective σ -complexes **10** and **11**.

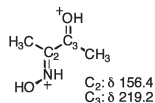
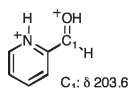
Table 1 ^{13}C and ^1H NMR spectral data for pyrrolidinone **5** in acidic media and the calculated ^{13}C NMR data (MP2/6-311+G(d) level) for **6** and **7b** (*trans* stereoisomer)

Acid (acid strength)	Temp./ $^\circ\text{C}$	NMR signals
$\text{CF}_3\text{CO}_2\text{H}$ ($H_0 -2.7$)	25	^{13}C : Complex spectrum (ca. 20 peaks)
$\text{FSO}_3\text{H-SO}_2\text{ClF}$ ($H_0 -15$)	-40	^{13}C , δ : 24.7, 30.7, 33.9, 178.4, 198.6 ^1H , δ : 2.28 (2H), 2.75 (2H), 2.91 (3H), 8.92 (1H)
$\text{FSO}_3\text{H-SbF}_5\text{-SO}_2\text{ClF}$ ($H_0 -25$)	-40	^{13}C , δ : 25.4, 31.5, 34.2, 181.9, 201.3 ^1H , δ : 2.26 (2H), 2.70 (2H), 2.82 (3H), 8.87 (1H) Major product
		^{13}C , δ : 31.3, 35.4, 36.4, 200.6, 214.3 ^1H , δ : 3.01 (2H), 3.10 (3H), 3.19 (2H), 9.42 (1H) Minor product
Calculated NMR signals (6):		^{13}C , δ : 23.0, 29.7, 37.5, 179.2, 207.7
Calculated NMR signals (7b):		^{13}C , δ : 30.7, 37.1, 44.1, 226.5, 244.4

dication **7b** were calculated to be minima on the potential energy surface with the *trans*-protonated structure found to be 3.1 kcal mol⁻¹ more stable than the *cis*-protonated structure (MP2/6-311+G(d) level). For the calculated gas-phase reactions, the conversion of the monocationic electrophile **6** to the σ -complex **10** is found to be somewhat endothermic. At the MP2/6-311+G(d) level, no minimum could be found for the σ -complex and during optimization, complex **10** dissociates to benzene and **6**. If the ring-ring bond is fixed however, the potential energy of the resulting structure can be estimated. Protonation of **6** gives the super-electrophile **7b**, which is found to react with benzene in an initial reaction step that is significantly exothermic. At both levels of theory, structure **11** is found at a minimum on the potential energy surface. In accord with earlier theoretical studies on super-electrophiles,² reactions that disperse the positive charge tend to be energetically favorable. In the case of **7b**, formation of the σ -complex (**11**) leads to wide separation of the two positive charges. Similarly, the protosolvated species (**7a**) is expected to possess favorable energetics in its reaction with benzene.

Using stable ion conditions pioneered by Olah and co-workers, varied onium cations and electrophiles have been directly observed over the years by low temperature NMR spectroscopy.¹⁰ The pyrrolidinone derivative (**5**) was studied by stable ion conditions using low temperature ^{13}C NMR and the results are consistent with the formation of the protosolvated species in superacidic media. With solvation in $\text{CF}_3\text{CO}_2\text{H}$, compound **5** gives a complex NMR spectrum with roughly twenty ^{13}C NMR peaks (Table 1). This complex spectrum is likely the result of an equilibrium mixture containing the starting pyrrolidinone **5**, the *N*-acyliminium ion **6**, and other species. In superacidic FSO_3H , a clean spectrum is generated from the pyrrolidinone **5**, and the data suggests complete conversion to the *N*-acyliminium ion **6**. Based on the calculated spectrum for **6**, the peaks at δ 178.4 and 198.6 are assigned to the carbonyl and iminium carbons, respectively. The observed chemical shift values from FSO_3H are in good agreement with both the calculated spectrum for **6** and the reported ^{13}C NMR spectrum of an *N*-acyliminium ion.¹¹ Analysis of the ^1H NMR also suggests clean formation of the *N*-acyliminium ion **6**, with the iminium proton appearing down-field at δ 8.92. When the pyrrolidinone derivative **5** is reacted with $\text{FSO}_3\text{H-SbF}_5$ at -40°C , two sets of NMR peaks are observed in the ^1H and ^{13}C spectra (formed in roughly a 6 : 1 ratio). The major product gives ^{13}C

resonances at: δ 25.4, 31.5, 34.2, 181.9, 201.3. These peaks are assigned to the *N*-acyliminium ion **6**. The smaller set of peaks appear at: δ 31.3, 35.4, 36.4, 200.6, 214.3, and based on the deshielding of the carbons, these peaks can be assigned to the protosolvated species **7a**. Likewise, all of the ^1H NMR peaks are significantly deshielded (note the iminium proton at δ 9.42), suggesting the protosolvated structure **7a**. The new carboxonium proton of **7a** is not seen in the ^1H NMR, possibly due to rapid exchange or being obscured by the large ^1H signal from the acidic media. The carboxonium carbon of superelectrophile **7a** is observed at δ 200.6 and this is similar to the carboxonium ^{13}C resonances of other dicationic systems. For example, the ^{13}C NMR spectra of diprotonated 2-pyridinecarbaldehyde and 2,3-butanedione monooxime were recently reported and the respective carboxonium carbons are found at δ 203.6 and 219.2.¹²



The calculated gas-phase NMR spectrum of the fully protonated dication (**7b**) shows carboxonium and iminium carbons that are significantly deshielded from the experimentally observed signals in $\text{FSO}_3\text{H-SbF}_5$ solution.¹³ This suggests that the superacid produces the protosolvated species **7a** from the pyrrolidinone **5**, rather than the fully formed dicationic superelectrophile **7b**.

In summary, we have found evidence for the involvement of superelectrophilic intermediates in the superacid-promoted reactions of *N*-acyliminium ions. In the condensed phase, the acid-catalyzed reactions of *N*-acyliminium ions show a significant dependence on acid strength and quantity. Electrophilic strength increases with acidity. The pyrrolidinone **5** is also shown to be capable of reacting with deactivated arenes in superacid. Moreover, both the *N*-acyliminium ion **6** and its protosolvated species (**7a**) can be directly observed by low temperature ^{13}C NMR. Theoretical calculations also show that formation of the superelectrophile **7b** leads to more favorable energetics in the reaction with benzene.

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Notes and references

§ Reaction of pyrrolidinone 5: 1-Methyl-5-hydroxypyrrolidin-2-one¹⁴ (**5**, 0.9 mmol) and *p*-dichlorobenzene (0.5 g, 3.4 mmol) are added to 3 mL of freshly distilled $\text{CF}_3\text{SO}_3\text{H}$ ¹⁵ and the mixture is heated to 80 °C. After stirring for 2 h, the mixture is poured over about 10 g of ice and the resulting solution is extracted with CHCl_3 . The organic phase is washed with water, then brine, and dried with anhydrous Na_2SO_4 . Isolation of the product by column chromatography (hexanes–ether) yields 0.13 g of 5-(2,5-dichlorophenyl)-1-methylpyrrolin-2-one (**8**, 0.54 mmol, 60%) as colorless crystals, mp 59–61 °C (diethyl ether). ^1H NMR (CDCl_3 , 500 MHz): δ 1.73–1.79 (m, 1H), 2.33–2.56 (m, 3H), 2.70 (s, 3H), 4.89–4.93 (m, 1H), 6.98–7.02 (m, 1H), 7.14–7.19 (m, 1H), 7.28 (dd, 1H, $J = 1.0, 8.5$ Hz). ^{13}C NMR

(CDCl_3 , 125 MHz): δ 26.4, 28.6, 29.2, 61.0, 126.4, 129.0, 131.0, 131.4, 133.6, 140.1, 175.7. Low resolution mass spectrum (EI): m/z : 243 (M^+), 188, 115, 98. High resolution mass spectrum for $\text{C}_{11}\text{H}_{11}\text{ONCl}_2$, calc: 243.0218, found: 243.0213. Anal. Calc. for $\text{C}_{11}\text{H}_{11}\text{ONCl}_2$: C, 54.12; H, 4.54; N, 5.74. Found: C, 54.23; H, 4.58; N, 5.72%.

¶ Observation of *N*-acyliminium ion 6: Triple-distilled (Aldrich) FSO_3H (0.5 mL) is added to a dried, Ar-filled test tube (or flask) and cooled to -78 °C. To the FSO_3H is added SO_2ClF ¹⁶ (0.5 mL) and the solution is mixed. 1-Methyl-5-hydroxypyrrolidin-2-one¹² (**5**, 20–30 mg) is then added to the acidic solution. With vigorous stirring, compound **5** dissolves and the resulting solution is transferred to a dried, cold NMR tube (previously cooled to -78 °C). A coaxial insert containing acetone- d_6 is then inserted into the NMR tube and the NMR spectrum is taken with the NMR probe cooled to -40 °C.

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