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Ester Cleavage in Superacid Media Involving Diprotonated *Gitonic* Carboxonium Dications[1]

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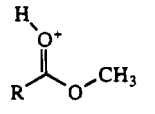
Abstract: The reactivity of protonated and methylated methyl ester in superacidic media was investigated by experiment and theory. Protonated methyl acetate was found to undergo slow acyl oxygen cleavage even at −78 °C in $FSO_3H/SbF_5/SO_2$ solution to give acetyl cation and methyloxonium ion. 1,1-Dimethoxyethyl cation (methylated methyl acetate) was found to undergo slow methyl exchange in CD_3SO_3F/SbF_5 solution. The reaction of 1,1-dimethoxyethyl cation with toluene in the presence of trifluoromethanesulfonic acid at −78 °C gave acylation in 4% yield. Theoretical calculations at the MP4(SDTQ)/6-31G*//MP2/6-31G* level of theory were performed to find stationary points on the potential energy surface of the mono- and diactivated ester system. Based on the available evidence a new mechanism for the acid-catalyzed ester cleavage in superacidic media is proposed.

Introduction

Ester cleavage is among the most extensively studied reactions in organic chemistry. Excellent reviews exist[2] for the four reaction mechanisms that are assumed to be operating under acidic conditions. In the first step of all acid catalyzed mechanisms the ester is protonated. Subsequently, the protonated ester is cleaved in an unimolecular or bimolecular rate determining step. Either the alkyl−oxygen or the acyl−oxygen bond can be broken depending on the nature of the system. According to Ingold terminology the four mechanisms are classified as $A_{ac}1$, $A_{ac}2$, $A_{al}1$, and $A_{al}2$, whereby *e.g.*, $A_{ac}1$ denotes the unimolecular acid catalyzed cleavage of the acyl−oxygen bond.[2c] It is commonly accepted that the first protonation of the ester occurs at the acyl oxygen leading to a stabilized hydroxycarbenium ion.[3] A large number of acyl oxygen protonated esters have been prepared under stable ion conditions. The structure of these intermediates was extensively studied experimentally[4] and theoretically.[5] The *syn*-Z-form **1** was found to be the most stable conformation in solution.[4,6]



syn_H-**Z**

1

The alternative alkyl oxygen protonation to a secondary *O*-acyl oxonium ion was never observed experimentally. Evidence from calculational studies for such species was so far not reported in the literature. Nevertheless, an equilibrium between the alkyl and the acyl oxygen protonation is generally

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(1) Chemistry in Superacids. Part 18. For Part 17 see: Olah, G. A.; Hartz, N.; Rasul, G.; Prakash, G. K. S.; Burkhart, M.; Lammertsma, K.; *J. Am. Chem. Soc.* **1994**, *116*, 3187.

(2) (a) Lowry, T. H., Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, 1987, pp 717−723. (b) Ester Formation and Hydrolysis. In *Comprehensive Chemical Kinetics*; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1972; Vol. 10, Chapter 2 (Kirby, A. J.) and Chapter 3 (Talbot, R. E.). (c) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1969; p 1131.

(3) Birchall, T.; Gillespie, R. J. *Can. J. Chem.* **1965**, *43*, 1045.

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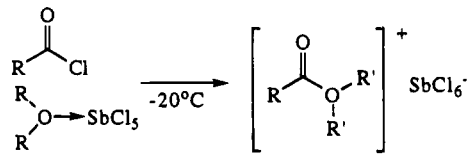
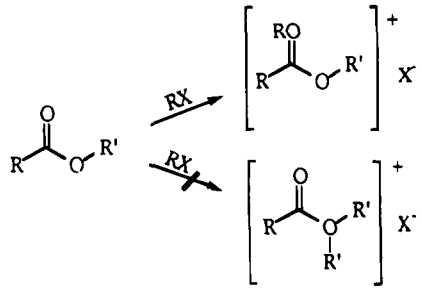
invoked for the "unimolecular acid hydrolysis with acyl oxygen fission" mechanism ($A_{ac}1$) in strong acidic media (Figure 1).[7]

The reactivity of *O*-acyl-*O*,*O*-dialkyloxonium ions (**2**) which correspond to alkyl oxygen alkylated esters were studied by Klages and Lukasczyk.[8] Klages and Mühlbauer[9] found that such species can be obtained by the reaction of acetyl chloride with antimony pentachloride/dimethyl ether complex at low temperatures (although no spectroscopic characterization of the structure was reported).



2

The alternative direct alkylation of the ether oxygen was unsuccessful due to the much greater nucleophilicity of the carbonyl oxygen.[8]



O-Acyl-*O*,*O*-dialkyloxonium ions were found to react as strong Friedel–Crafts acylating agents. Similar to acyl ion salts, they are able to acylate benzene in 20% yield over a period of 4 weeks at −20 °C.[8] This is in contrast to the isomeric 1,1-dimethoxyalkyl cations which do not acylate benzene or alkylbenzenes.

In the course of our continuing studies on the protosolvolytic activation of electrophiles to give superelectrophiles we showed that it is possible to protonate the nonbonded electron pair of trialkyloxonium ions. Moreover, even the small parent hydronium ion (H_3O^+) can be further protonated to form the corresponding *gitonic* onium dication,[10] wherein the charge cannot be efficiently delocalized. Departing from these results and focusing again on ester systems it is noted that in diprotonated esters charge can be more efficiently delocalized. Accordingly, a protosolvated dicationic intermediate should be more easily obtained with a protonated ester than with oxonium ions. Therefore, the object of the present study is to extend the concept of superelectrophilic activation to protonated esters and open up an unexplored possibility that in ester cleavage under superacidic conditions diprotolytic activation through superelectrophilic *gitonic* carboxonium dications is possible. Similar bidentate activation could be also considered for solid

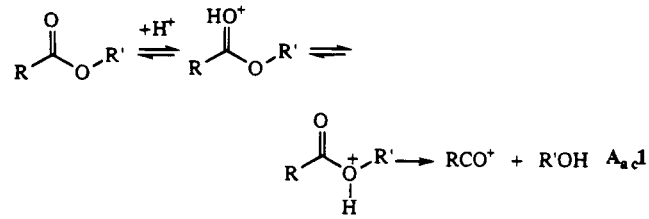
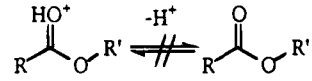


Figure 1. The $A_{ac}1$ mechanism of ester hydrolysis.

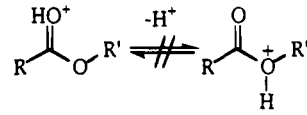
acids or even enzymatic systems. The term *gitonic*, *i.e.*, proximal, is used to differentiate from *distonic* (distant) dications.[1,11]

Results and Discussion

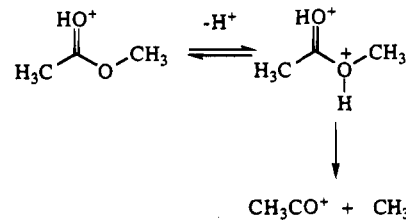
Esters, such as methyl acetate, are completely protonated in superacidic media, and deprotonation equilibria of such ions cannot be observed.



There is also no indication of a tautomerization equilibrium with the ether-oxygen protonated isomer.



However, protonated methyl acetate undergoes even at −78 °C in $FSO_3H/SbF_5/SO_2$ solution slow acyl oxygen cleavage to give acetyl cation and methyloxonium ion. This is indicative of further protolytic activation *via* superelectrophilic *gitonic* carboxonium dications. The cleavage is much accelerated when the temperature is raised to −20 °C.[4a]



Ethyl acetate in 4:1 M FSO_3H/SbF_5 was observed to undergo similar acyl–oxygen cleavage. However, in the significantly stronger 1:1 M FSO_3H/SbF_5 system, alkyl oxygen cleavage is observed giving protonated acetic acid and *tert*-butyl cation.[4a]

It was found that 1,1-dimethoxyethyl cation (methylated methylacetate) undergoes slow protolytic cleavage in superacidic media giving acetyl cation. The system was conveniently studied starting from trimethyl orthoacetate in $FSO_3H/SbF_5/SO_2$ solution. Protolytic cleavage gives the 1,1-dimethoxyethyl cation at −78 °C. Further protolysis occurs when the temperature is raised to −10 °C.

When 1,1-dimethoxyethyl cation is reacted with excess CD_3SO_3F:SbF_5 at −30 °C for a period of 2 weeks, it was found that slow methyl exchange at the methoxy oxygen occurs.[13a] ^{2}H-NMR of the reaction mixture indicated the presence of two different methoxy-d_3 groups (δ 4.44; 4.62 referenced to CD_3SO_3F, δ 4.00), corresponding to the two isomers **I** and **II** of 1,1-dimethoxy-d_3-ethyl cation. This exchange result supports further methylation of the dimethoxyethyl ion to a *gitonic*

(4) (a) Olah, G. A.; O'Brien, D. H.; White, A. M. *J. Am. Chem. Soc.* **1967**, *89*, 5694. (b) Hogeveen, H. *Recl. Trav. Chim.* **1967**, *86*, 80. (c) Diprotonated ketoesters were also observed: Olah, G. A.; Ku, A. T.; Sommer, J. *J Org. Chem.* **1970**, *35*, 2159.

(5) Wiberg, K. B.; Waldron, R. F. *J. Am. Chem. Soc.* **1991**, *113*, 7705.

(6) (a) White, A. M.; Olah, G. A. *J. Am. Chem. Soc.* **1969**, *91*, 2943. (b) Borsch, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5303.

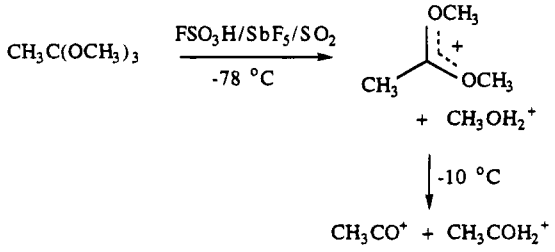
(7) Yates, K.; McClelland, R. A. *J. Am. Chem. Soc.* **1967**, *89*, 2686.

(8) Lukasczyk, G. Dissertation, TU Munich, 1961.

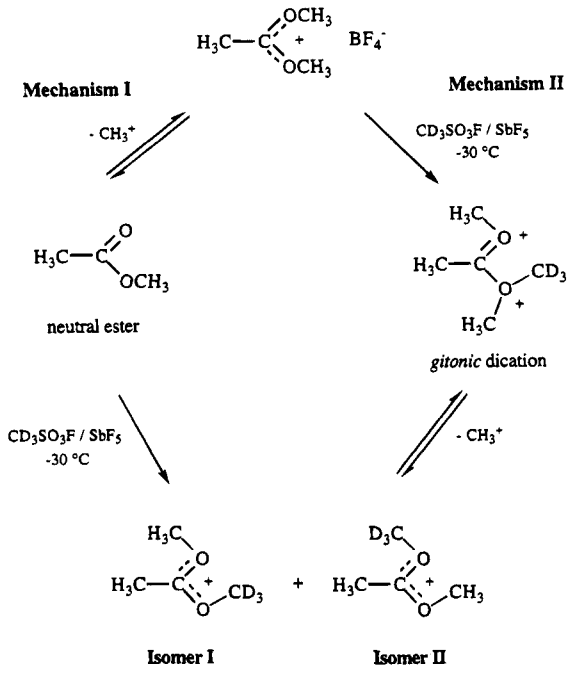
(9) Mühlbauer, E. Dissertation, TU Munich, 1957.

(10) Olah, G. A.; Prakash, G. K. S.; Barzaghi, M.; Lammertsma, K.; Schleyer, P. v. R.; Pople J. A. *J. Am. Chem. Soc.* **1986**, *108*, 1032.

(11) Olah, G. A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 767.

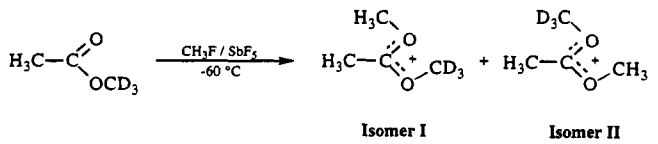


activated dication as an intermediate (mechanism II). Formation of two isomeric cations **I** and **II** by demethylation/remethylation reaction of 1,1-dimethoxyethyl cation through the neutral ester is, however, unlikely in the highly acidic medium (mechanism I).

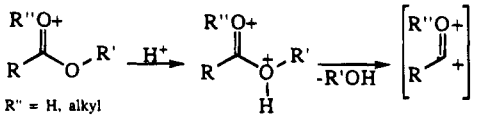


In fact, high acidity medium appears to be crucial for the methyl exchange reaction. When 1,1-dimethoxyethyl tetrafluoroborate was reacted with the relatively less acidic methylating system CD_3F/SbF_5 in SO_2 solution (involving $CH_3-O^+=S=O$) at −70 °C for 6 h, no exchange of the methyl groups could be observed by ^{2}H-NMR. The latter observation supports the formation of the *gitonic* dication under the former exchange conditions.

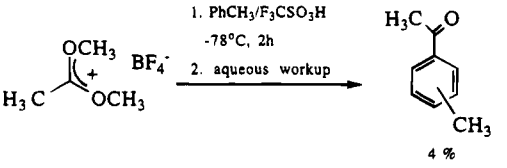
In order to confirm the chemical shifts of the methoxy-d_3 groups in isomers **I** and **II** of 1,1-dimethoxy-d_3-ethyl cation, methyl acetate-d_3 was reacted with excess CH_3F:SbF_5 in SO_2 to yield 1,1-dimethoxy-d_3-ethyl cation. When monitored by ^{2}H-NMR at −60 °C, two different methoxy-d_3 groups were detected at δ 4.43; 4.60, again corresponding to isomers **I** and **II** of 1,1-dimethoxy-d_3-ethyl cation as depicted below:



When 1,1-dimethoxyalkyl cations (*i.e.*, acyl oxygen methylated esters) and acyl oxygen protonated esters are further activated by protonation (protosolvation) of the alkyl oxygen, cleavage would not give the corresponding acyl cation directly. Rather a superelectrophilic, protonated or methylated acetyl dication with greatly enhanced reactivity would be formed. Therefore, superelectrophilic reactivity would be an indication for diprotonation or protosolvation of esters in superacidic media in the absence of a deprotonation (demethylation) equilibrium, *i.e.*, it would strongly suggest the involvement of *gitonic* carboxonium dications in a novel ester cleavage mechanism.



It was now found that 1,1-dimethoxyethyl tetrafluoroborate acylates toluene, *albeit* in low 4% yield (*ortho*:*para* in 4:96 ratio)), in the presence of trifuoromethanesulfonic acid to give methyl acetophenones. Xylenes (*i.e.*, methylation products) were not observed. Without superacid catalysis no reaction between 1,1-dimethoxyethyl tetrafluoroborate and toluene was observed even at room temperature.



This suggests that the 1,1-dimethoxyethyl cation is protonated (protosolvated) by the superacid. Cleavage of the protonated dimethoxyethyl cation would lead to the superelectrophilic methylated acetyl cation. This activated species is then able to react with toluene. Enhanced acetylating ability of acetyl cation salts have been observed by Shudo[13b] in trifluoromethanesulfonic acid medium.

In order to rationalize the experimental results a series of *ab initio* calculations was carried out to explore the interaction of methyl acetate, as a model for esters in general, with protons and methyl cations to give mono- and diactivated species. Previously, a detailed study on the protonation and methylation of methyl acetate[5] and related systems[12] was reported. Departing from these well-known monoactivated methyl acetate species which were recalculated again at higher level of theory we report now the first calculational investigation of a new class of diactivated methyl acetates, whereby protons and methyl cations are used as model electrophiles.

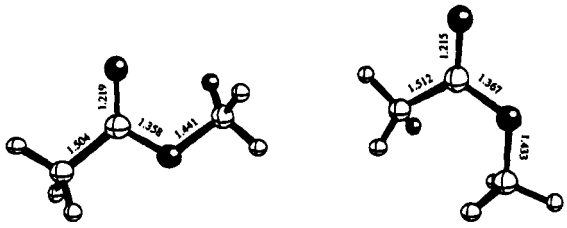
Diprotonated and dimethylated systems are characterized by a large number of conformational isomers which are derived (*vide infra*) as follows by assuming that the heavy atoms are approximately in the same plane.

All isomers were optimized at Hartree−Fock level with the HF/6-31G* basis set using gradient optimization techniques.[14] Then, the obtained structures were further optimized at the MP2/6-31G* level. Stationary points were characterized with frequency calculations at the MP2/6-31G*//MP2/6-31G* level. Zero point vibrational energies were scaled by a factor of 0.93, for the calculation of relative energy and proton affinities at 0 K, to account for the well-known systematic error at this level

(12) (a) Glaser, R.; Choy, G. S.-C. *J. Org. Chem.* **1992**, *57*, 4976. (b) Johansen, H.; Rettrup, S.; Jensen, B. *Theor. Chim. Acta* **1980**, *55*, 267.

(13) (a) About 4% deuteriated to protio methyl group exchange was observed. However, it is difficult correlate the exchange rate to acidity since measurements on the methylating ability of FSO_3CD_3/SbF_5 have not been established in quantitative terms. Further, the extremely slow exchange rate precludes any quantitative measurements. (b) Sato, Y.; Yato, M.; Ohwada, T.; Saito, S.; Shudo, K. *J. Am. Chem. Soc.* **1995**, *117*, 3037.

(14) (a) Broyden, C. G. *J. Math. Appl.* **1970**, *24*, 647. (b) Fletcher, R. *J.* **1970**, *13*, 370. (c) Goldfarb, D. *Math. Comp.* **1970**, *24*, 647. (d) Shanno, D. F. *J. Optim. Theory Appl.* **1985**, *46*, 87.



3 4

Figure 2. Selected parameters for **3** and **4** (MP2/6-31G*; bond length in Å).

of theory. No attempt was made to correct the proton affinities for 298 K due to the difficulty in treating methyl rotations with small barriers.[5] Single point calculations using fourth order Møller–Plesset perturbation theory[15] were carried out for MP2/6-31G* optimized structures with less than eight heavy atoms (MP4(SDTQ)/6-31G*//MP2/6-31G*). Relative energy based on MP4(SDTQ)/6-31G*//MP2/6-31G* + ZPE were calculated and given in the text unless denoted otherwise.

The neutral structures **3** and **4** of the **Z** and **E** isomer are separated by an energy difference of 8.5 kcal/mol with the **Z** form (**3**) being more stable.

Monoprotonation can occur at the acyl or alkyl oxygen position. Acyl oxygen monoprotonation of methyl acetate was previously a subject of theoretical investigation.[5] Also at the higher level employed in this study the acyl oxygen protonation gives the four possible isomers as stable minima. The global minimum for the monoprotonated methyl ester was found to be the acyl oxygen protonated syn_H-**Z** form **5** which is in line with experimental data. The energy difference between the different acyl protonated species is less than 5.4 kcal/mol with **7** being the least favorable conformation. The calculated proton affinity of **3** (to form **5**) is 194.5 kcal/mol and agrees very well with the experimental value of 197.8 kcal/mol.[15b]

The monoprotonation of the alkyl oxygen of methyl acetate, to give isomers **9** and **10**, lead to stationary points which are 15.4 and 16.6 kcal/mol less stable than **5**. In ether-oxygen protonated methyl acetate **9** and **10** the charge cannot be stabilized with adjacent donor orbitals as in case of acyl protonation. The onium center is further destabilized due to the electron withdrawing acyl substituents. This reflects the high preference for the initial acyl oxygen protonation and the unlikeliness of an efficient equilibrium between **5** and **9** in superacidic media.

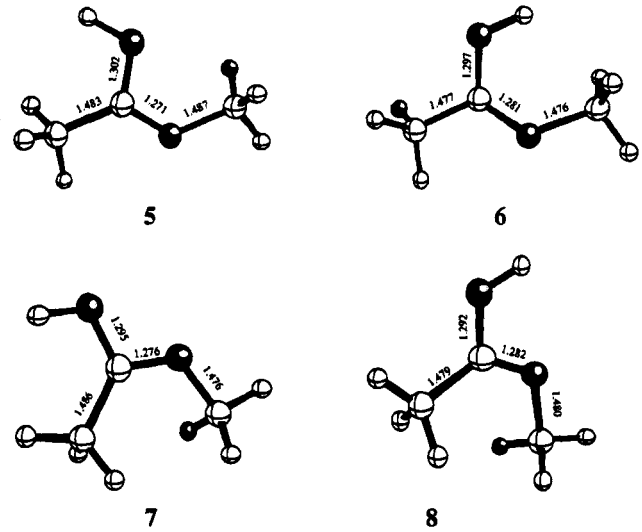
The monomethylation of the acyl oxygen gives all possible isomers as stable minima at the levels employed. The most stable isomer **13** is structurally similar to the global minimum for protonation (**5**), indicating that the 1,1-dimethoxyethyl cation is also in this respect an acceptable model for a protonated ester. The methylated structures **11**, **12**, and **13** are separated by an energy difference of less than 9.0 kcal/mol, with the sterically crowded isomer **12** being the least favorable structure.

Alkyl oxygen methylation gives **14** as a stable species that is 15.9 kcal/mol less stable than **13**. The unfavorable energetics of the alkyl oxygen methylated structure is in agreement with the experimentally observed inertness of the alkyl oxygen toward alkylation.

(15) (a) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618. (b) Binkley, J. S.; Pople, J. A. *Int. J. Quant. Chem.* **1975**, *9*, 229. (c) Pople, J. A.; Binkley, J. S.; Seeger, R. *Int. J. Quant. Chem.* **1976**, *S10*, 1. (b) Experimental proton affinity: Lias, S. G.; Liebman, F. J.; Levin, R. D.; *J. Phys. Chem. Ref. Data* **1984**, *13*, 695.

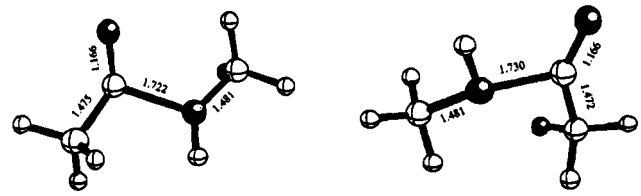
(16) Cohen, I.; Shulman, J.; Popowicz, A.; Ishida, T. *J. Labelled. Com. Radiopharm.* **1982**, *19*, 631.

(17) Currie, G. J.; Bowie, J. H.; Downard, K. M.; Sheldon, J. C. *J. Chem. Soc., Perkin Trans. 2.* **1989**, 1973.



5 6 7 8

Figure 3. Selected parameters for **5**–**8** (MP2/6-31G*; bond length in Å).

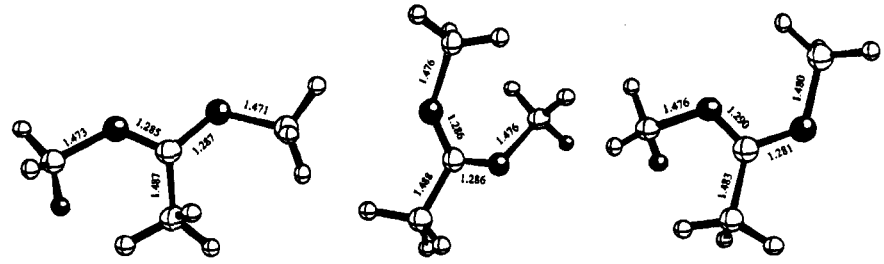


9 10

Figure 4. Selected parameters for **9** and **10** (MP2/6-31G*; bond length in Å).

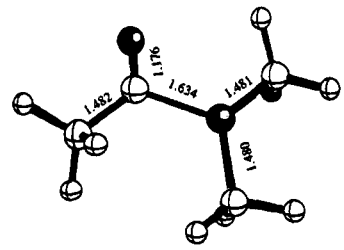
Diprotonation of methyl acetate gives formally two types of *gitonic* dication, *i.e.*, acyl oxygen diprotonated methyl acetate (**15** and **16**) and acyl–alkyl diprotonated methyl acetate (**17**–**20**). At Hartree–Fock level only structure **16** exists as a stable intermediate. However, when correlated levels are employed structures **15**–**20** exist as stable intermediates. Thermodynamically, the most stable diprotonated intermediate is syn_H-Z_H (**17**) which can be derived from the most stable monoprotonated syn_H-**Z** conformer **5** by ether oxygen protonation. The dication **17** is even 34.7 kcal/mol more stable than **5**. Accordingly, the energy difference between **9** and **17** is 50.1 kcal/mol. This means that the crucial structure **9** for the $A_{Ac}1$ cleavage of methyl acetate is 50.1 kcal/mol less stable than the crucial structure for the proposed ester cleavage mechanism involving a diprotonated *gitonic* methyl acetate. The calculated proton affinity of **5** to form **17** is 31.8 kcal/mol. Structurally, second protonation of **5** lengthens the carbon–oxygen bonds of the oxonium center and shortens the carbon–oxygen bond length of the acyl oxygen center. Assuming that lengthening of bonds increases the reactivity of the attached centers proton transfer, methyl transfer or the formation of a protoacetyl dication seem to be the preferred decomposition pathways in the gas phase. Proton transfer would simply reverse the diprotonation step. In the condensed phase formation of methyl cation is highly disfavored, whereby acylation *via* a protonated acetyl cation becomes the most favored observable process.

Acyl oxygen diprotonation gives the *E*-isomer **16** as the most stable structure which is 3.5 kcal/mol less stable than **17**. The corresponding *Z*-isomer **15** is 7.1 kcal/mol les stable than **16** and 10.6 kcal/mol less stable than **17**. The structural changes of acyl oxygen diprotonation in **16** lead to lengthening of the acyl oxygen–carbon bond and shortening of the alkyl oxygen–carbon bond which is opposite to what is observed in case of **17**.



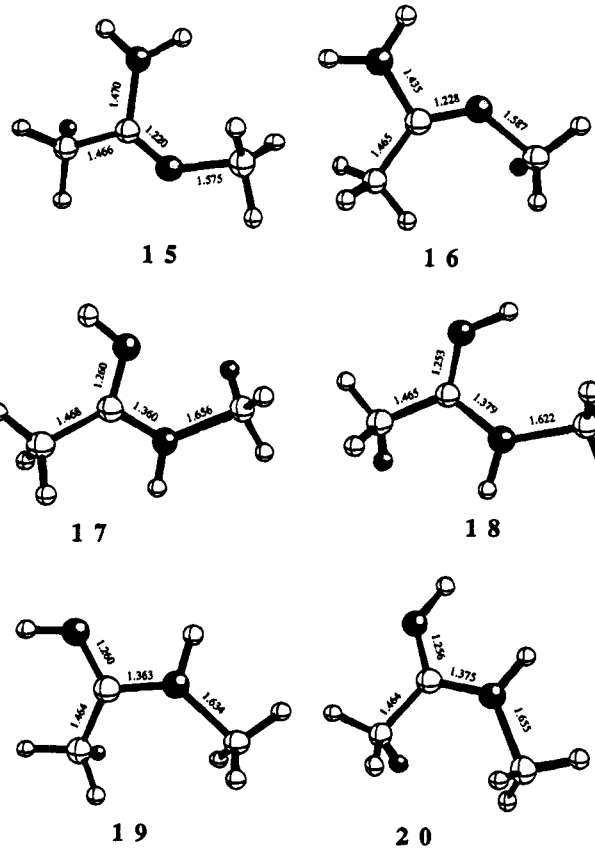
11 **12** **13**

Figure 5. Selected parameters for **11**–**13** (MP2/6-31G*; bond length in Å).



14

Figure 6. Selected parameters for **14** (MP2/6-31G*; bond length in Å).



15 **16**

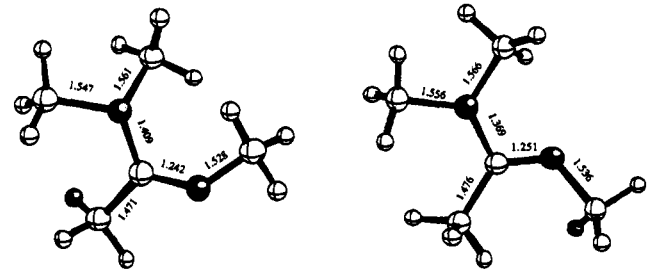
17 **18**

19 **20**

Figure 7. Selected parameters for **15**–**20** (MP2/6-31G*; bond length in Å).

The dimethylation of methyl acetate gives two stable isomers (**21** and **22**), whereby **22** is by 10.0 kcal/mol more stable than **21** (MP2/6-31G*//MP2/6-31G* + ZPE (HF/6-31G*//HF/6-31G*). The species **22** would be expected to be involved in the observed methyl exchange of 1,1-dimethoxyethyl cation.

Protonation of methylated methyl acetate, *i.e.*, protonation of 1,1-dimethoxyethyl cation, did not give any stationary points (**23**–**26**) at the Hartree–Fock level. Methyl elimination proved to be a very facile process at this level, and protonated acetic acid was obtained instead. However, at correlated levels isomers **23**–**26** exist as stable intermediates. The most stable intermediate turned out to be **23** which can be derived by protonation of the most stable methylated methyl acetate isomer **13**. The species **23** is 47.4 kcal/mol more stable than **13**. The presence of a thermodynamically favored protonated 1,1-dimethoxyethyl cation is in support of the observed acylation of toluene in superacidic media. Furthermore, oxygen protonation lengthens the acetyl carbon–oxygen bond and thereby facilitates cleavage.



21 **22**

Figure 8. Selected parameters for **21** and **22** (MP2/6-31G*; bond length in Å).

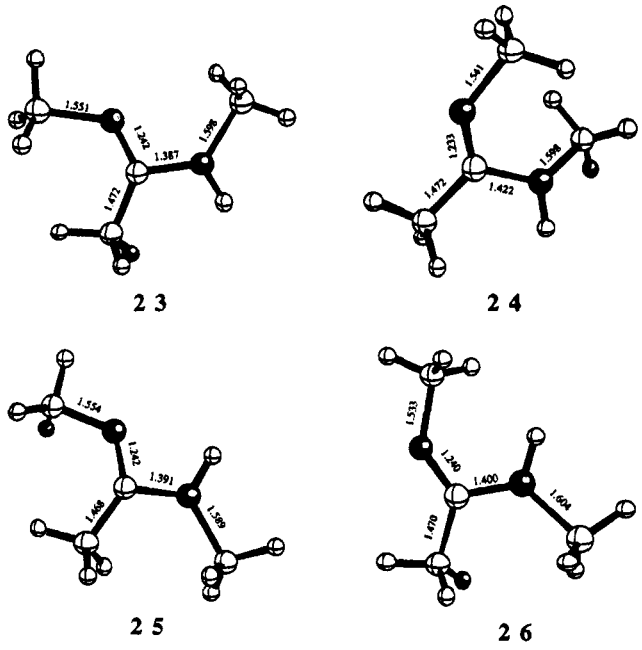
The alkyl oxygen methylation of the protonated ester resulted in two stable structures, **27** and **28**, which correspond to a complex between the protoacetyl dication and dimethyl ether, *i.e.*, protonated **14**. The energy difference between the *syn* and *anti* isomer is 8.5 kcal/mol. The proton affinity of **14** can be estimated from **27** to be 63.8 kcal/mol.

Conclusion

Protonation and methylation of the 1,1-dimethoxyethyl cation leads to *gitonic* carboxonium dications which are thermodynamically significantly more stable than the neutral esters. Activation of 1,1-dimethoxyethyl cation by further methylation was established by CH_3/CD_3 exchange studies in CD_3SO_3F:SbF_5 medium by ^{2}H-NMR spectroscopy. Involvement of protonated 1,1-dimethoxyethyl cation was inferred by its electrophilic reaction with toluene.

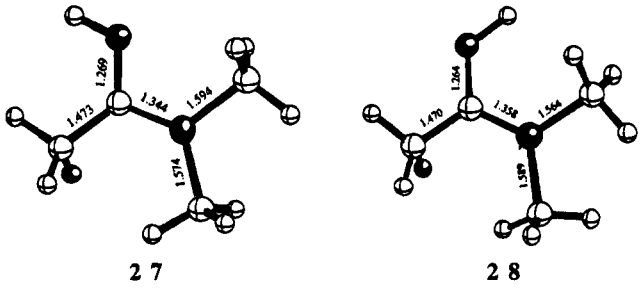
In the case of protonation, using *ab initio* molecular orbital theory, both first and second protonation turned out to be exothermic processes. Full protonation to form the corresponding dications cannot be excluded from our results. The rather large energy difference between the acyl oxygen (**9** and **10**) and the alkyl oxygen protonated ester (**5**) rules out any equilibrium between the two isomers in superacidic solution. The alternative diprotonation to form a *gitonic* carboxonium dication, *i.e.*, **16**, was found to be a thermodynamically more favorable process. The dissociation of structures **17**–**20** in the gas phase can be explained by kinetic instability. Related structures, however, can be stabilized in the condensed state by clustering with solvent molecules.

In the case of methylation, two stable isomers of methylated 1,1-dimethoxyethyl cation were found (**21** and **22**), whereby



2 3 2 4 2 5 2 6

Figure 9. Selected parameters for **23**–**26** (MP2/6-31G*; bond length in Å).



2 7 2 8

Figure 10. Selected parameters for **27** and **28** (MP2/6-31G*; bond length in Å).

22 is by 10.0 kcal/mol more stable than **21** (MP2/6-31G*//MP2/6-31G* + ZPE (HF/6-31G*//HF/6-31G*). The intermediacy of species (**22**) is possible in the observed methyl exchange in 1,1-dimethoxyethyl cation in FSO_3CD_3/SbF_5 medium.

Further interaction of the protonated ester, with the superacidic medium, supports the possibility for a novel mechanistic pathway of the ester cleavage in superacidic solution. In accordance with the Ingold nomenclature, the mechanism can be described as superacid assisted protolysis with acyl oxygen fission. It would be unimolecular if the diprotonated esters are intermediates and bimolecular if they are transition states.

Experimental Section

1,1-Dimethoxyethyl Tetrafluoroborate. In a flame dried Schlenk flask equipped with a septum trimethyl orthoacetate (5.0 mL, 4.72 g, 39.0 mmol) is dissolved in dichloromethane (5 mL) under magnetic stirring in nitrogen atmosphere. The temperature of the solution is then lowered to −78 °C and boron trifluoride etherate complex (5.5 mL, 6.3 g, 44.0 mmol) is added *via* syringe dropwise to the rapidly stirred solution. The mixture is warmed to 0 °C. After 90 min the reaction is complete, and the white solid is separated from the mother liquor at low temperature (−30 °C). The white product is washed with BF_3:Et_2O (2 × 2 mL), dry dichloromethane (2 × 5 mL); and dry pentane (2 × 5 mL) until it forms a hard white solid. After drying under vacuum 1,1-dimethoxyethyl tetrafluoroborate is obtained as white hygroscopic crystals which are stored and handled in a glovebox (6.24 g, 91% yield): ^{1}H-NMR (300 MHz/SO_2) δ 4.62 (s, 3H, OCH_3), 4.36 (s, 3H, OCH_3), 2.76 (s, 3H, CH_3); ^{13}C-NMR (75.4 MHz/SO_2) δ 192.8, 66.4, 63.1, 19.5.

Table 1. Total Energies (−Hartree) at Different Levels and Zero Point Energies (kcal/mol) of the Different Isomers of Neutral, Monoprotonated, Monomethylated, Diprotonated, and Dimethylated Methyl Acetate (**3**–**28**)

no.	HF/6-31G*// HF/6-31G*	MP2/6-31G*// MP2/6-31G* (ZPE)[a]	MP4(SDTQ)/ 6-31G*// MP2/6-31G*	rel energy[b]
3 (c_s)	266.836 83	267.573 24 (53.8)	267.635 06	0.0
4 (c_s)	266.821 84	267.559 14 (53.7)	267.621 33	8.5
5 (c_s)	267.164 74	267.890 26 (61.1)	267.954 72	0.0
6 (c_s)	267.158 51	267.883 96 (60.9)	267.948 51	3.7
7 (c_s)	267.155 60	267.881 48 (61.1)	267.946 12	5.4
8 (c_s)	267.163 31	267.888 65 (61.1)	267.953 17	1.0
9 (c_1)	267.123 94	267.862 74 (59.4)	267.927 45	15.4
10 (c_1)	267.121 38	267.861 16 (59.6)	267.925 85	16.6
11 (c_s)	306.189 12	307.043 33 (78.0)	307.125 50	6.2
12 (c_s)	306.186 01	307.038 65 (77.8)	307.120 95	8.9
13 (c_s)	306.199 70	307.053 69 (78.2)	307.135 73	0.0
14 (c_1)	306.158 23	307.026 55 (77.0)	307.108 42	15.9
15 (c_1)	*c*	267.932 57 (64.9)	267.999 20	10.6
16 (c_s)	267.222 39	267.944 57 (65.1)	267.010 79	3.5
17 (c_s)	*c*	267.950 90 (66.0)	267.017 76	0.0
18 (c_s)	*c*	267.935 94 (65.8)	267.002 88	9.1
19 (c_1)	*c*	267.948 20 (66.2)	267.014 98	2.0
20 (c_1)	*c*	267.934 63 (65.8)	267.001 77	9.8
21 (c_1)	345.320 46	346.296 68 (112.9)[d]		10.0
22 (c_1)	345.338 43	346.313 38 (113.4)[d]		0.0
23 (c_s)	*c*	307.134 42 (82.9)	307.218 81	0.0
24 (c_1)	*c*	307.116 84 (82.9)	307.201 57	10.8
25 (c_1)	*c*	307.132 82 (83.1)	307.217 23	1.2
26 (c_1)	*c*	307.120 64 (82.9)	307.205 37	8.4
27 (c_s)	306.288 06	307.133 67 (83.7)	307.218 35	1.1
28 (c_1)	306.272 98	307.119 61 (83.5)	307.204 47	9.6

[a] Zero point vibrational energies (ZPE) at the MP2/6-31G*//MP2/6-31G* level and scaled by a factor of 0.93. [b] Relative energies at the MP4(SDTQ)/6-31G*//MP2/6-31G* + ZPE level. [c] Dissociate at this level of optimization. [d] ZPE at the HF/6-31G*//HF/6-31G* level and scaled by a factor of 0.89.

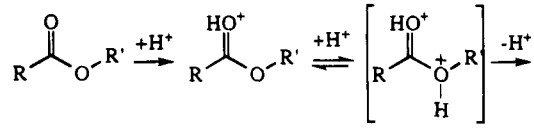


Figure 11. The proposed ester cleavage under superacidic conditions.

Reaction of 1,1-Dimethoxyethyl Tetrafluoroborate with Toluene. In a Schlenck flask equipped with a magnetic stirrer and a septum 1,1-dimethoxyethyl tetrafluoroborate (0.5 g, 2.3 mmol) is suspended in toluene (5.0 mL) under nitrogen atmosphere. Dichloromethane (5 mL) is then added *via* syringe, and the mixture is vigorously stirred at room temperature for 120 min. The reaction mixture was quenched with a few drops of aqueous bicarbonate solution and dried over Na_2SO_4. GC-MS analysis of the solution did not show any trace of ring acylated toluenes or other aromatic products.

Reaction of 1,1-Dimethoxyethyl Tetrafluoroborate with Toluene in Trifluoromethanesulfonic Acid. In a Schlenck flask equipped with a magnetic stirrer and a septum 1,1-dimethoxyethyl tetrafluoroborate (0.5 g, 2.3 mmol) is suspended in toluene (5.0 mL) under nitrogen athmosphere. The mixture is then cooled to −78 °C with a dry ice acetone bath. Subsequently, trifluoromethanesulfonic acid (5 mL) is carefully added *via* syringe to the vigorously stirred solution. The reaction mixture is kept at −78 °C for 120 min and is subsequently poured onto ice (15 g). Under these conditions the formation of decomposition products of toluene can be avoided. The mixture is neutralized with solid sodium bicarbonate while controlling the foaming by efficient stirring. The organic phase is separated, and the aqueous phase is extracted with dichloromethane (3 × 5 mL). The combined organic phases were dried over Na_2SO_4. Excess CH_2Cl_2 was evaporated under vacuum. GC-MS analysis of the organic layer shows methyl acetophenones as the high boiling reaction products in 4% yield (*ortho*: *para* in 4:96 ratio) with reference to toluene.

Methyl *p*-Toluenesulfonate-d_3.[16] The synthesis of methyl tosylate is carried out in a 500 mL round-bottom flask fitted with a Teflon coated stirring rod. The temperature of −40 °C was maintained with a cryostat. Methanol-d^4 (5.0 mL, 4.4 g, 123.0 mmol) is mixed with tosyl chloride (23.5 g, 1 equiv). Pyridine (90 mL) is then added slowly over a period of 2 h under rapid stirring. The stirring at −40 °C is continued for 60 min. Excess pyridine is then neutralized with ice-cold 5 N H_2SO_4 while the temperature of the product mixture is maintained below 20 °C. The crystallized methyl tosylate is vacuum filtered and stored in the refrigerator to prevent decomposition (6.47 g, 78% yield): mp 27.8 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.90, 7.40 (dd, 4H, H_{arom}), 2.47 (s, 3H, CH_3). ^{13}C-NMR (75.4 MHz, $CDCl_3$) δ 144.9, 132.0, 129.7, 127.9, 56.1, 21.5; GC-MS (50 eV) 91 (100), 155 (46), 189 (40, [M^+]).

Methyl Fluoride-d_3.[16] The reaction was carried out in a 200 mL three necked flask equipped with an inert gas inlet and a reflux condenser which is topped with a gas outlet. A sand bath was used to heat the reaction mixture. The tubing attached to the reflux condenser is connected to a wash bottle, a glass tube filled with calcium chloride, another glass tube filled with phosphorous pentoxide, and a cooling spiral. Finally a small glass tube (25 mL capacity) was used to condense the product at liquid nitrogen temperature. The internal pressure of the system is maintained at about 150 Torr by bleeding the gaseous product through a needle valve into a series of traps which were connected to a mechanical pump. Methyl-d^3 tosylate (5.0 g, 26.4 mmol) is mixed with anhydrous potassium fluoride (dried at 250 °C under high vacuum in the presence of P_2O_5 for 3 days) in the reaction flask, which was maintained at 230 °C for 7 h. After the methyl fluoride is trapped at liquid nitrogen temperature bulb-to bulb distillation was performed several times to remove impurities (0.71g 73% yield): ^{2}H-NMR (48.3 MHz, SbF_5:SO_2) δ 5.25 (s, 3D, CD_3), 4.35 (s, 3D, CD_3); GC-MS (50 eV) 16 (12), 18 (20).

Methyl Acetate-d_3. Methanol-d_4 (4.1 mL, 0.1 mol) in 30 mL dry pyridine was placed into a Schlenk flask under nitrogen atmosphere, and 7.1 mL (0.1 mol) freshly distilled acetyl chloride was slowly added to the mixture under ice-cooling. The product was distilled under nitrogen atmosphere to yield methyl acetate-d_3: colorless liquid, bp 58.5 °C; 5.4 g, 71% yield; ^{1}H-NMR (300 MHz/$CDCl_3$) δ 2.06 (t, CH_3); ^{13}C-NMR (75.4 MHz/$CDCl_3$) δ 77.02, 50.75, 20.55.

Methyl Exchange of 1,1-Dimethoxyethyl Tetrafluoroborate with CD_3SO_3F/SbF_5. 1,1-Dimethoxyethyl tetrafluoroborate (30 mg) is dissolved at −78 °C in a 1:1 solution of CD_3SO_3F/SbF_5 in an NMR tube. After the mixture was characterized by NMR spectroscopy, the NMR tube was stored at −20 °C for a period of 2 weeks. The sample was periodically analyzed by ^{1}H- and ^{2}H-NMR spectroscopy. After 2 weeks ^{2}H-NMR data indicated slow methyl/methyl-d_3 exchange: ^{1}H-NMR (300 MHz, CD_3SO_3F:SbF_5) after 2 weeks δ 2.76 (CH_3), 4.41 (OCH_3), 4.64 (OCH_3); ^{2}H-NMR (48.3 MHz, CD_3SO_3F:SbF_5) after 1 h δ 4.0 (tentatively set to CD_3SO_3F), after 2 weeks, δ 4.0 (CD_3SO_3F), 4.44 (OCD_3), 4.62 (OCD_3).

Methylation of Methyl Acetate-d_3 with CH_3F:SbF_5 in SO_2 as Solvent. Methyl acetate-d_3 (30 mg) was reacted with excess CH_3F:SbF_5:SO_2 at −78 °C in an NMR tube to yield 1,1-dimethoxy-d_3-ethyl cation: ^{1}H-NMR (300 MHz, −60 °C, CH_3F:SbF_5:SO_2) δ 2.76 (CH_3), 4.39 (OCH_3), 4.62 (OCH_3); ^{2}H-NMR (48.3 MHz, CD_3SO_3F:SbF_5) δ 4.43 (OCD_3), 4.60 (OCD_3).

Methyl Exchange of 1,1-Dimethoxyethyl Tetrafluoroborate with CH_3F/SbF_5. 1,1-Dimethoxyethyl tetrafluoroborate (30 mg) was dissolved at −78 °C in SO_2 in a NMR tube. SbF_5 is subsequently added to the vigorously stirred solution. After the mixture was characterized by NMR spectroscopy methyl fluoride-d_3 is introduced into the tube, and the reaction is monitored by ^{13}C-NMR at −78 °C using an acetone capillary as external standard. No exchange was observed under these conditions.

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