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Through–Bond Interaction in the Trifluoroethanolysis of 4–Oxo–2_{eq}–adamantyl Triflate and Its Essential Vanishing in the Corresponding 2–Phenyl Substituted Trifluoroacetate

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Attachment of an oxo substituent on the 4–position of 2–adamantyl triflate alters the rate of trifluoroethanolysis at 25 °C by respective factors of $10^{-1.1}$ and $10^{-2.5}$ for 2_{eq}– and 2_{ax}–triflates, and $10^{-2.9}$ and $10^{-2.6}$ for the corresponding 2–phenyl–2_{eq}– and –2_{ax}–adamantyl trifluoroacetates, indicating the presence of through–bond interaction in the secondary equatorial and its essential vanishing in the 2–phenyl system. Product distributions agree with this notion.

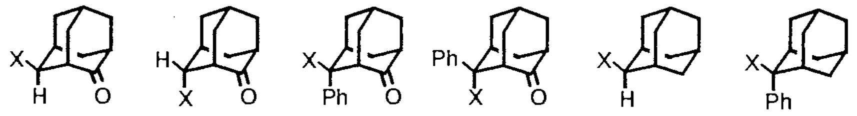
The stabilization of incipient carbocations by the lone pair of a hetero atom attached to the γ position was first demonstrated by Grob in 1960's for amino nitrogen, and the effect named the "frangomeric effect".1) A similar effect of carbonyl oxygen has been reported by Vogel and his coworkers since 1978 in the regioselective electrophilic additions to the C=C bond of bicyclo[2.2.1]hept–5–en–2–one and related enones, and the results have been explained in terms of through–bond n(CO) $\leftrightarrow$ σC(2)C(3) $\leftrightarrow$ pC(1)$^+$ hyperconjugative interaction in C(1)$^+$–C(2)–C(3)=O.2) This interpretation is based on Hoffmann's theory that the lone–pair of a carbonyl group interacts with the σ* orbital of adjacent C–C σ bond.3) Lajunen and his coworkers used this theory to rationalize the preferred protonation of bicyclo[2.2.1]hept–5–en–2–one on the C(5) position.4)

This sort of electronic effect would be best assessed quantitatively by using solvolysis. Recently, we found that 3–oxobicyclo[2.2.2]oct–1–yl triflate solvolyzes in 80% ethanol at 25 °C at a rate 10^3–10^4 faster than predicted from the inductive electron–withdrawing effect of the carbonyl group.5) The marked stabilization of the incipient 3–oxobicyclo[2.2.2]oct–1–yl cation was interpreted to show the above–mentioned through–bond interaction. Recent quantum mechanical calculations by Carrupt and Vogel confirmed our interpretation.6)

Evaluation of neighboring group participation in solvolysis by changing the electron demand of a cationic center is a familiar tool for physical organic chemists.7) We now report a successful use of this tool in the trifluoroethanolysis of 4–oxo–2_{eq}– and –2_{ax}–adamantyl triflates and 4–oxo–2–phenyl–2_{eq}– and –2_{ax}–adamantyl trifluoroacetates. The rate and product studies revealed the stabilization of the *secondary equatorial* transition state both in ionization and product formation steps by the through–bond n(CO) $\leftrightarrow$ σC(2)C(3) $\leftrightarrow$ pC(1)$^+$ interaction and its essential vanishing in the *tertiary* systems.

The alcohols **1-OH**,8,9) **2-OH**,8,9) and **6-OH**10) were prepared by the previously reported methods.

The tertiary keto alcohols **3-OH** and **4-OH** were synthesized as follows. Adamantane-2,4-dione[11] was treated with phenyllithium in ether and then the resulting mixture was separated over SiO_2 to give **3-OH** and **4-OH** in yields of 26 and 6%, respectively. The configuration at the C(4) position of **3-OH** and **4-OH** was determined by the X-ray crystal structure analysis of **3-OH**.[12] The triflates[9] and trifluoroacetates[13] were prepared in usual manners. The solvolysis in anhydrous TFE was conducted in the presence of 2,6-lutidine, and the rates were followed conductimetrically. The product distribution was determined by GLC(PEG20M) for the reaction mixture or ^{13}C NMR for the crude products after >10 half-lives.[14] The results are summarized in Tables 1 and 2.



X=OH	**1-OH**	**2-OH**	**3-OH**	**4-OH**	**5-OH**	**6-OH**
X=OTf or OTFA	**1-OTf**	**2-OTf**	**3-OTFA**	**4-OTFA**	**5-OTf**	**6-OTFA**
X=OCH_2CF_3	**1-OTFE**	**2-OTFE**	**3-OTFE**	**4-OTFE**		

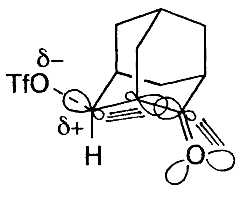
Table 1. The Rates of Trifluoroethanolysis of Various Triflates and Trifluoroacetates at 25 °C

Substrate	k / s^{-1}	$\Delta H^{\ddagger}_{298}$ / kJ mol^{-1}	$\Delta S^{\ddagger}_{298}$ /J K^{-1} mol^{-1}	Relative rate	k_{eq} / k_{ax}
1-OTf	$1.10\text{X}10^{-2}$ a)	86.2	6.3	$10^{-1.1}$	23.9
2-OTf	$4.60\text{X}10^{-4}$ a)	91.2	-2.9	$10^{-2.5}$	
5-OTf	0.15 b)	76.6 b)	-3.8 b)	1.0	
3-OTFA	$1.17\text{X}10^{-2}$ a)	84.5	1.9	$10^{-2.9}$	0.61
4-OTFA	$1.92\text{X}10^{-2}$ a)	80.8	6.3	$10^{-2.6}$	
6-OTFA	8.4 c)	69.5	6.3	1.0	

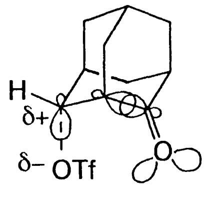
a) Determined conductimetrically within an experimental error of ±1% (r>0.999) by using $2\text{X}10^{-4}$ mol dm^{-3} of the substrate and $1.2\text{X}10^{-3}$ mol dm^{-3} of 2,6-lutidine. b) In 97% TFE; reference 15.
c) Extrapolated from data at lower temperatures.

The rate ratio of $10^{-1.1}$ for **1-OTf/5-OTf** is greater than those ($10^{-2.9}$-$10^{-2.5}$) for **2-OTf/5-OTf**, **3-OTFA/6-OTFA**, and **4-OTFA/6-OTFA** by factors of $10^{1.4}$-$10^{1.8}$, showing that the rate-decelerating effect of the oxo substituent in **1-OTf** is exceptionally small. Furthermore, the equatorial/axial rate ratio is 23.9 for the secondary pair (**1-OTf/2-OTf**), whereas it is only 0.61 for the tertiary one (**3-OTFA/4-OTFA**). These results are most reasonably interpreted to suggest the through-bond stabilization of the transition state in the ionization of secondary equatorial **1-OTf** (Scheme 1) and its essential absence in the case of tertiary equatorial **3-OTFA**. Although **1-OTf** has a favorable geometry to assume overlap arrangement of the carbonyl lone pair, C-C σ bond, and cationic p orbital, it is not the case with **2-OTf** (Scheme 2). Most probably, this geometric dissimilarity is reflected to the greater rate ratio for **1-OTf/5-OTf** ($10^{-1.1}$) than for **2-OTf/5-OTf** ($10^{-2.5}$).

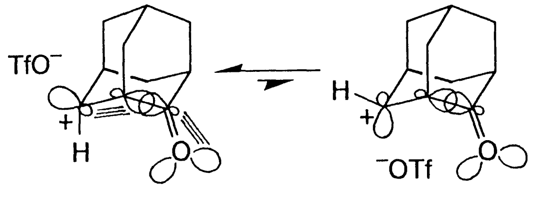
For the above-mentioned geometric reasons, we attribute the rate enhancement for **1-OTf** by a factor of 23.9 as compared with **2-OTf** to the through-bond stabilization of the transition state in **1-OTf**.[16] However, this factor is much smaller than 10^3-10^4 which was estimated in the solvolysis of 3-oxobicyclo[2.2.2]oct-1-yl triflate. This large discrepancy suggests that efficient through-bond interaction is effected by the antiperiplanar arrangement of the carbonyl lone pair, C–C σ bond, and cationic p orbital, which can be attained in the incipient 3-oxobicyclo[2.2.2]oct-1-yl cation. On the other hand, in the transition state from **1–OTf** the cationic p orbital is tilted from the C–C=O plane by approximately 60°.



Scheme 1.



Scheme 2.



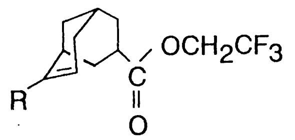
Scheme 3.

The effect of the through-bond interaction is also reflected in the product distributions. Both **1–OTf** and **2–OTf** gave the equatorial product **1–OTFE** in greater amounts than the axial product **2–OTFE**, with the **1–OTFE:2–OTFE** ratio 35:10 from **1–OTf** and 51:3.2 from **2–OTf** (Table 2).[17] The results may be explained by assuming that the equatorial ion pair is in equilibrium with the axial ion pair and that the former is favored being stabilized by the through-bond interaction.[18] The formation of a good deal of fragmentation product **7**[19] is attributable to the weakened C–C=O σ bond in the equatorial ion pair intermediate.

Table 2. Product Distributions in the Trifluoroethanolysis of **1-OTf**, **2-OTf**, **3-OTFA**, and **4-OTFA** at 25 °C

Substrate	Equatorial product / %		Axial product / %		Fragmentation product / %	
	1-OTFE	**3-OTFE**	**2-OTFE**	**4-OTFE**	**7**	**8**
1-OTf [a]	35		10		52	
2-OTf [a]	51		3.2		44	
3-OTFA [b]		18		82		0
4-OTFA [b]		17		83		0

a) The product ratio was determined by GLC within an experimental error ±0.5%.
b) The product ratio was determined by ^{13}C NMR within an experimental error ±3%.



7 (R=H)
8 (R=Ph)

In contrast to the secondary substrates, the tertiary substrates, **3–OTFA** and **4–OTFA**, did not give any detectable amounts of the fragmentation product **8**. This finding strongly supports the essential vanishing of the through-bond interaction in the tertiary carbocation intermediate that is stabilized by the phenyl substituent. It is also notable that the equatorial:axial product ratio (**3–OTFE:4–OTFE**) is nearly 2:8 irrespective of the starting trifluoroacetate. Presumably, the axial side of the intermediate carbocation is less hindered because of the absence of one axial hydrogen through the substitution with the oxo group.

In conclusion, the tool of changing the electron demand has been successfully applied for the first time to the proof of the through-bond interaction of a carbonyl lone pair with a cationic p orbital. This effect plays an important role in controlling the equatorial:axial rate and product ratios in the solvolysis of the secondary 4-oxo-2-adamantyl derivatives, but it essentially vanishes in the tertiary 4-oxo-2-phenyl-2-adamantyl system. In this sense, the adamantyl system is appropriate to examine the importance of the through-bond interaction and the study along this line is in progress.

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12) The details of crystal data will be reported in a full paper. **3–OH**: mp 90–91 °C; ^{13}C NMR ($CDCl_3$) δ 26.2, 30.9, 31.3, 36.3, 37.1, 40.3, 45.1, 55.7, 77.0, 125.5, 127.3, 128.2, 145.3, 217.4. **4–OH**: mp 132.5–133.5 °C; ^{13}C NMR ($CDCl_3$) δ 26.5, 33.2, 33.5, 35.0, 36.6, 39.2, 45.5, 55.6, 79.5, 125.4, 127.9, 128.9, 142.7, 216.5.

13) **3–OTFA**: mp 116–118 °C; ^{13}C NMR ($CDCl_3$) δ 25.9, 29.9, 31.7, 36.4, 37.2, 40.0, 45.1, 51.7, 90.8, 114.0 (q, J=287 Hz), 126.2, 128.5, 128.8, 138.9, 154.5 (q, J=42 Hz), 213.6. **4–OTFA**: mp 110–112 °C; ^{13}C NMR ($CDCl_3$) δ 26.2, 32.9, 33.0, 33.3, 36.3, 38.9, 44.9, 53.0, 94.5, 113.8 (q, J=287 Hz), 127.2, 128.5, 129.2, 135.2, 154.5 (q, J=42 Hz), 212.8. **6–OTFA**: very unstable solid; ^{13}C NMR ($CDCl_3$) δ 26.2, 27.0, 33.0, 33.5, 34.4, 37.2, 92.7, 114.3 (q, J=287 Hz), 127.3, 128.1, 128.5, 137.6, 154.9 (q, J=41 Hz).

14) The isomeric trifluoroethyl ethers were separated from each other and unambiguously identified by comparing their ^{13}C NMR spectra with those of the corresponding alcohols. The spectral data will be reported in a full paper.

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16) The difference in the ground state stability may not be an important factor for the **1–OTf/2–OTf** rate ratio since MM2 calculations for **1–OH** and **2–OH** as surrogates showed that **1–OH** is only 0.8 kJ mol^{-1} less stable than **2–OH**. The MM2(87) program was obtained from QCPE.

17) The different product ratios may be rationalized by possible intervention of S_N2(intermediate) mechanism since the methanolysis of **2–OTf** predominantly afforded the inversion product; see:Ref. 9.

18) Ab initio calculations suggested that the 2–adamantyl cation may exist as a pair of rapidly equilibrating structures with nonplanarity at the cation center; see: R. Dutler, A. Rauk, T. S. Sorensen, and S. M. Whitworth, *J. Am. Chem. Soc.*, **111**, 9024 (1989).

19) **7**: oil; ^{13}C NMR ($CDCl_3$) δ 26.2, 28.3, 29.6, 31.2, 31.4, 31.7, 35.7, 60.2 (q, J=36 Hz), 123.3 (q, J=277 Hz), 128.9, 130.3, 173.7.

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