Unexpectedly Facile Solvolysis of 3-Oxobicyclo[2.2.2]oct-1-yl Triflates: Through-Bond Interaction of the β-Carbonyl Lone Pair with the Cationic p Orbital

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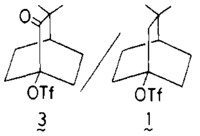
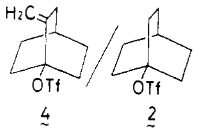
Summary: The title compounds solvolyze in 80% ethanol at 25 °C 10^3–10^4 times faster than predicted from the inductive effect of the carbonyl group, providing the first example of the through-bond interaction of the β-carbonyl lone pair with the cationic p orbital.

Sir: Many examples have been reported on the through-bond stabilization of incipient carbocations by the lone-pair electrons of amino nitrogen which is attached to the C(3) position (Scheme I).[1] On the other hand, there has never been described the similar stabilizing effect of a carbonyl lone pair (Scheme II), although its n–n orbital interaction in 1,2- and 1,4-diketones through σ bonds[2] has been attracting the interest of theoretical chemists. We now report the first example indicating that a β-carbonyl group positioned in an antiperiplanar arrangement with respect to the cationic p orbital behaves as an n donor.

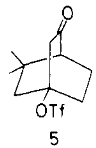
Previously, we reported that the rate of solvolysis of the bicyclo[2.2.2]oct-1-yl system is decelerated by the oxo or methylene substituent on the C(2) position by a respective factor of $10^{8.4}$ or $10^{3.9}$ in ethanol at 25 °C.[3] Since the π system is essentially perpendicular relative to the developing cationic p orbital, these decelerating effects have been ascribed to the purely inductive effect of the oxo and the methylene substituent at the C(2) position.[3] With a view to determining their attenuated inductive effects, the 3-oxo and 3-methylene derivatives **5**–**7** have been synthesized and their rates of solvolysis in 80% ethanol and products of methanolysis determined.[4] The rate data for **1**–**7** are summarized in Table I.



3 / 1 = $10^{-8.4}$ (EtOH, 25 °C)



4 / 2 = $10^{-3.9}$ (EtOH, 25 °C)



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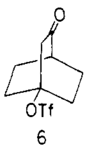

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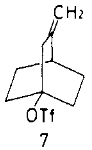

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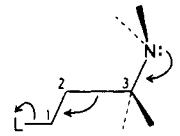
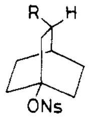
Scheme I



A marked difference is evident in the manner of attenuation of the inductive electron-withdrawing effect of the methylene and the oxo group. The oxo group on the C(2) position is markedly more electron withdrawing than the methylene group, as evidenced by the rate ratios of $10^{-9.1}$ for **3**/**1** and $10^{-3.9}$ for **4**/**2** in 80% ethanol at 25 °C. Surprisingly, when the oxo or the methylene group is attached to the C(3) position, their rate-decelerating effects are comparable, as indicated by the rate ratios $10^{-2.3}$ for **5**/**1** and $10^{-2.2}$ for **7**/**2**. A comparison of the rate of 3-oxobicyclo[2.2.2]oct-1-yl triflate (**6**) with that of the 3-methylene derivative **7** results in a rate ratio of 2.3 for **6**/**7**. This ratio increases to 6.2 in ethanolysis at 25 °C.[5] Apparently, the 3-oxo substituent is *less* electron withdrawing than the 3-methylene substituent toward the cationic center.

More quantitative evaluation of the unexpectedly fast rate of **5** is provided by locating the rate ratios **5**/**1** and **7**/**2** against **3**/**1** and **4**/**2**, respectively, in a logarithmic plot of the rate ratios **8**/**10** against **9**/**10** (Figure 1).[6] The rate data in 80% ethanol of the *p*-nitrobenzenesulfonates **8** and **9** have been reported by Grob and his co-workers for 10 substituents, and their rates have been found to be controlled by the inductive effect of the substituent R.[7]



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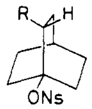

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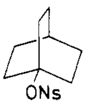

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As Figure 1 shows, the point for the methylene derivatives is fairly well accommodated to the plot, indicating that the methylene group may be treated as an ordinary electron-withdrawing substituent. On the contrary, the point for the oxo derivatives significantly deviates upward. The upward deviation is most reasonably attributed to the unexpectedly fast rate of **5**. The deviation from the regression line indicates a rate enhancement of $10^{4.2}$ in 80% ethanol at 25 °C. When a straight line passing through the points for R = H and methylene is used (see Figure 1), the enhancement is evaluated to be $10^{2.8}$. When the rate ratio **6**/**2** is plotted in the place of **5**/**1**, the acceleration of **6** is evaluated to be $10^{3.3}$–$10^{4.7}$. Since the 3-oxo substituent does not appear to exert any steric acceleration, the above rate enhancement of 10^3–10^4 should be electronic in origin. As the most probable contribution, we propose

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[1] (a) Grob, C. A.; Schiess, P. W. *Angew. Chem.* **1967**, *79*, 1. (b) Grob, C. A. *Ibid.* **1969**, *81*, 543.

[2] (a) Leonhard, N. J.; Laitnien, H. A.; Mottus, E. H. *J. Am. Chem. Soc.* **1953**, *75*, 3300. (b) Cowan, D. O.; Gleiter, R.; Hashmall, J. A.; Heilbronner, E.; Hornung, V. *Angew. Chem.* **1971**, *83*, 405. (c) Kroner, J.; Strack, W. *Ibid.* **1972**, *84*, 210. (d) Gleiter, R. *Ibid.* **1974**, *86*, 770. (e) Gleiter, R.; Jähne, G.; Oda, M.; Iyoda, M. *J. Org. Chem.* **1985**, *50*, 678.

[3] Takeuchi, K.; Akiyama, F.; Ikai, K.; Shibata, T.; Kato, M. *Tetrahedron Lett.* **1988**, *29*, 873.

[4] The new precursor alcohol (mp 158.5–159.5 °C) for **5** was prepared by following the method described in the literature: Cimarusti, C. M.; Wolinsky, J. *J. Am. Chem. Soc.* **1968**, *90*, 113. The new precursor alcohol (mp 57.0–58.0 °C) for **7** was derived from 3-oxobicyclo[2.2.2]octan-1-ol (Duddeck, H.; Wolff, P. *Org. Magn. Reson.* **1977**, *9*, 528) via protection of the hydroxyl group by trimethylsilylation followed by Wittig methylenation.

[5] The k_1's for **6** and **7** in ethanol containing 0.025 M 2,6-lutidine at 25.0 °C are 1.06×10^{-4} s^{-1} and 1.72×10^{-5} s^{-1}, respectively.

[6] The rate ratios were employed with a view to canceling out the effects of the methyl substituents and the leaving group.

[7] Bielmann, R.; Grob, C. A.; Küry, D.; Yao, G. W. *Helv. Chim. Acta* **1985**, *68*, 2158.

0022-3263/89/1954-3772$01.50/0

Table I. The Rates of Solvolysis of Various Bicyclo[2.2.2]oct-1-yl Triflates in 80% Ethanol at 25.0 °C[a]

compd[b]	k_1, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	relative rates		
1	6.0×10^{-1} [c]	19.4	5.4	1.0		
2	1.5×10^{-1} [c]	18.8	1.0		1.0	
3	4.5×10^{-10} [c]	30.6	1.3	$10^{-9.1}$		
4	1.99×10^{-5}	24.5	2.0		$10^{-3.9}$	
5	2.92×10^{-3}	20.9	0.0	$10^{-2.3}$		
6	2.43×10^{-3}	21.1	0.2		$10^{-1.8}$	2.3
7	1.06×10^{-3}	21.8	0.9		$10^{-2.2}$	1.0

[a] Buffered with 0.025 M 2,6-lutidine. [b] The crude, but essentially pure, liquid triflates 5–7 were used without purification after identification by ^{1}H and ^{13}C NMR. For other triflates, see ref 3. [c] Extrapolated from data at other temperatures.

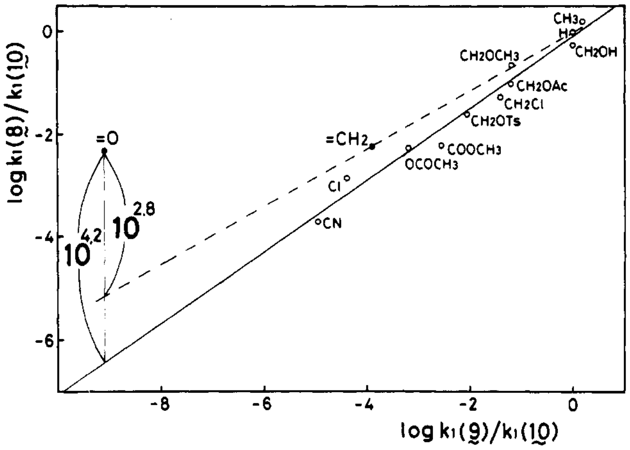
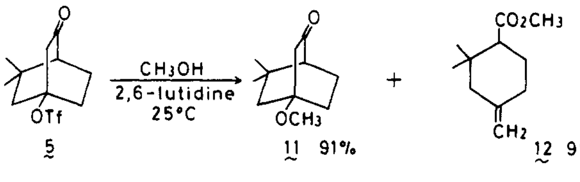


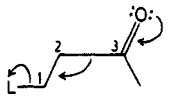
Figure 1. A plot of log $k_1(8)/k_1(10)$ vs log $k_1(9)/k_1(10)$ for the solvolysis in 80% ethanol at 25 °C. The closed circles indicated by =O and =CH$_2$ stand for the plots of log $k_1(5)/k_1(1)$ vs log $k_1(3)/k_1(1)$ and log $k_1(7)/k_1(2)$ vs log $k_1(4)/k_1(2)$, respectively. For the rate data of 8–10, see ref 7.

the through-bond electron donation from the carbonyl lone pair to the developing cationic p orbital.

A piece of evidence indicating the weakened C(2)–C(3) σ bond (Scheme II) has been provided by the formation of the fragmentation product 12 (9%) besides the normal substitution product 11 (91%) in methanolysis at 25 °C in the presence of excess 2,6-lutidine.[8]



Scheme II



Nonintervention of the carbonyl addition of solvent was evidenced by no incorporation of ^{18}O in the carbonyl group of the produced methyl ether 11 when solvolysis was conducted in 90% methanol–10% H$_2{}^{18}$O (27 atom % ^{18}O) in the presence of excess 2,6-lutidine for 10 half-lives at 25 °C.[9] Possible enolization of the substrate 5 prior to ionization was also refuted by no incorporation of deuterium (<5% by ^{1}H NMR) in the C(2) position of the product 11 (methyl-d_3 ether) from solvolysis in methanol-d_4.

In conclusion, the present rate and product studies indicate for the first time the through-bond stabilization of a carbocation by the β-carbonyl lone pair in the antiperiplanar arrangement. A study concerning whether the antiperiplanar arrangement would be a prerequisite condition is under way.

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(8) A similar fragmentation has been reported for the reaction of 4-methyl-3-oxobicyclo[2.2.2]oct-1-yl tosylate with titanium tetrachloride to give 4-methylene-1-methylcyclohexanecarbonyl chloride in trace amounts: Kraus, W.; Gräf, H.-D. *Angew. Chem.* **1975**, *87*, 878. The methanolysis of 7 gave the corresponding methyl ether as a single product.

(9) Investigation of the M + 2 peak in a mass spectrum of 11 showed 0.5% exchange if any. A preliminary examination on 11 enriched at the carbonyl oxygen (27 atom % ^{18}O) showed no exchange of the oxygen during workup.