EVALUATION OF THE π -conjugative effect of the 2-methylene and the 2-oxo substituent on the stability of carbocations in the solvolysis of bicyclic bridgehead derivatives

Ken'ichi TAKEUCHI,* Fumio AKIYAMA, Keizo IKAI, Tadashi SHIBATA, and Midori KATO Department of Hydrocarbon Chemistry, Faculty of Engineering, Kyoto University, Sakyo-ku, Kyoto 606, Japan

<u>Abstract</u>. The incipient 2-methylenebicyclo[3.2.2]non-1-yl cation is stabilized by allylic conjugation by 4 kcal/mol compared with the more rigid 2-methylenebicyclo[2.2.2]oct-1-yl cation. In contrast to this, no appreciable stabilization due to carbonyl π -conjugation was detected in the 2-oxobicyclo[3.2.2]non-1-yl cation, indicating unimportance of π -conjugative stabilization in tertiary α -keto cations.

The cyano and carbonyl groups are strongly electron withdrawing (-I). However, in recent years considerable experimental and theoretical efforts have been made in evaluating the π -conjugative electron donation (+M) of these substituents toward cationic carbon (schemes 1 and 2).¹ As for the effect of the cyano substituent, solvolytic studies have been successfully applied, suggesting the conjugative nature between the cyano moiety and the cationic center (scheme 1).^{1a,b}



On the other hand, the solvolyses of α -keto substrates are hampered by various factors. First, the carbonyl group that is activated by a strongly electron withdrawing leaving group often undergoes carbonyl addition of solvent prior to solvolysis.^{1c,2} Secondly, the rate of solvolysis might be accelerated by participation of carbonyl oxygen positioned at the opposite side of the leaving group³ and by nucleophilic solvent assistance toward the highly electron deficient reaction center.^{1c,2a} Thirdly, when the rate of a tertiary α -keto substrate [R₁R₂CX-C(=0)R₃] is compared with that of a secondary alkyl substrate (R₁R₂CX-H) with a view to evaluating the electronic effect of the carbonyl group in comparison with that of hydrogen,^{1c} the rate of the former might involve enhancement by increased steric strain in the ground state.⁴ Fourthly, the substrate should not form encls during solvolysis. Therefore, in order to detect the carbonyl π -conjugative effect in solvolytic reactions, it is essential to utilize a system which is free from the above undesirable contributions.

The bridgehead substrates containing the oxo substituent at a vicinal position are free from carbonyl oxygen participation and nucleophilic solvent assistance from the rear side of the bridgehead carbon. In addition, with increase in the ring-size, the structure becomes more flexible and more susceptible to π -conjugation, with the steric circumstances around the reaction center essentially unchanged. With this in mind, we examined various systems and found that the 2-oxobicycloalkyl triflates 1 and 6 show typical S_N 1 behaviors.^{5,6} In order to confirm that the increased flexibility can enhance π -conjugation, it was also desired to examine the rates of solvolysis of the corresponding 2-methylene derivatives 2 and 7. Unfortunately, we were unable to synthesize 2. Therefore, the compound 3 was prepared and subject ed to solvolysis. The π -conjugative effect on the carbocation stability was evaluated by comparing the rate ratio k(7)/k(9) with k(3)/k(5) for the 2-methylene (or allylic) systems and k(6)/k(8) with k(1)/k(4) for the 2-oxo (or α -keto) systems.



The 2-oxo and 2-methylene bridgehead triflates (1, 3, and 6) and mesylate 7 were derived from the corresponding 1,2-diols which were prepared via acylative ring-expansion of bridgehead aldehydes following our previously reported method.^{7,8} The rates of ethanolysis were determined for the triflates or mesylates at 25.0°C. The rate of 8 was expected to be too fast to measure; therefore, it was estimated from the rate of 9 by using the rate ratio $k_{\text{OTF}}/k_{\text{OMs}} = 1.41 \times 10^6$ determined for the ethanolysis of 1-adamantyl triflate and mesylate at 25.0°C.⁹ The rate data are summarized in Table 1.

substrate			k ₁ /s ⁻¹		∆H [‡]	۵S †
No.	mp/°C ^b	25.0°C	50.0°C	75.0°C	kcalmol ⁻¹	eu
1	111.5-112	3.90×10 ^{-11c,d}	_	_	31.2	-1.4
3	oil	2.96×10^{-7c}	1.09×10 ⁻⁵	2.40×10 ⁻⁴	27.1	2.3
4	oil	8.99x10 ^{-3e}				
5	oil	2.14×10 ^{-3e}				
6	48-50	3.74×10 ⁻⁷	1.10×10 ⁻⁵		25.3	-3.1
7	62.5-63.5	7 . 17x10 ⁻⁶	1.86×10 ⁻⁴		24.3	-0.4
8		67f				
9	oil	4.75×10 ⁻⁵⁹			23.5	0.5

Table 1. The Rates of Ethanolysis of Various Bridgehead Triflates and Mesylates.^a

^aThe rates were determined for 0.02M substrates in the presence of 0.025M 2,6-lutidine by titrating the generated acid with 0.01M KOH-EtOH in acetone to bromcresol green methyl red end point. ^bThe highly unstable liquid triflates **3**, **4**, and **5**, and mesylate **9** were used without purification after being identified by ¹³C NMR. The other new compounds showed satisfactory spectral and analytical data consistent with the proposed structures. ^CExtrapolated from data at other temperatures. ^dK₁ at 100.0°C, 1.90x10⁻⁶s⁻¹; k₁ at 125.0°C, 2.81x10⁻⁵s⁻¹. ^eDetermined conductimetrically for ca. 5x10⁻⁴M substrate. ^TEstimated by multiplying k₁ of **9** by a factor of 1.41x10⁶ (see text). ^gk₁ at 0.0°C, The 2-methylene derivative 3, where the π system is essentially perpendicularly oriented relative to the developing cationic p orbital, solvolyzes slower than the parent compound 5 by a factor of $10^{3.9}$. This value is comparable with that $(10^{4.2})$ determined for the acetolysis of 2-methylene-1-adamantyl and 1-adamantyl tosylates, the former solvolyzing slower than the latter.¹⁰ Since allylic conjugation is prohibited in the adamantyl system for geometric reasons, this deactivating factor of ca. 10^4 has been ascribed to the purely inductive effect (-1) of the methylene group.¹⁰ In the more flexible bicyclo[3.2.2]non-1-yl system, the 2-methylene derivative 7 solvolyzes slower than the parent compound 9 by a much smaller factor of $10^{0.8}$. The gain of $10^{3.1}$ (= $10^{3.9}/10^{0.8}$), which corresponds to ca. 4 kcalmol⁻¹, is reasonably attributed to the increase in allylic conjugation in the incipient carbocation from 7. It has been reported that when a fully conjugated allylic carbocation intermediate is formed, 2-methylene (or allylic) compounds solvolyze faster than unsubstituted model compounds by a factor of $10^2 - 10^{2.8}$.¹¹ Consequently, we estimate that the allylic conjugation is about 50% attained in the incipient carbocation from 7.

On the contrary, the rate ratio k(1)/k(4) of $10^{-8.4}$ is essentially identical with the ratio k(6)/k(8) (= $10^{-8.3}$).⁶ A reasonable interpretation of the marked contrast to the case of 2-methylene systems is that the π -conjugative stabilization may be unimportant in the incipient tertiary α -keto cation from 6. It has been proposed that π -conjugative stabilization of tertiary α -keto cations might amount to a solvolysis rate factor of $10^4 - 10^5$.^{12,13} If this is the case, the rate ratio k(6)/k(8) is expected to be greater than k(1)/k(4) by a factor of 10^2 in the light of realization of 50% allylic conjugation in the solvolysis of 7.

The S_N^1 nature of the solvolyses of 1 and 6 was provided by nicely linear mY_{OTf} relations¹⁴ in AcOH, EtOH, aq. EtOH (80, 60, and 50%), MeOH, and HCO₂H (1; m = 0.73, r = 0.996: 6; m = 0.77, r = 0.997).¹⁵ The products from the methanolysis of 1 and 6 in the presence of excess 2.6-lutidine were mostly rearranged. The major product from 1 was methyl 7.7-dimethylbicyclo-[2.2.1]heptane-1-carboxylate (11) (93%), accompanied by 10 (2.7%) and 12 (4.3%). On the other hand, 6 gave 1-(methoxymethyl)bicyclo[3.2.1]octan-2-one (15) (82%), 13 (17%), and 14 (1.0%). The predominant formation of the rearrangement products indicates marked destabilization of the 2-oxo substituted bridgehead carbocations from 1 and 6.¹⁶ In contrast to the behavior of 1 and 6, the 2-methylene compounds 3 and 7 gave only the corresponding bridgehead substitution products.



We are now extending the present methodology to other bicyclooctyl, bicyclononyl, and bicyclodecyl systems; the results will be reported in a full paper.

References and Notes

- 1. For reviews, see; a) P. G. Gassman and T. T. Tidwell, Acc. Chem. Res., 16, 279 (1983); b) T. T. Tidwell, Angew. Chem. Int. Ed. Engl., 23, 20 (1984); c) X. Creary, Acc. Chem. Res., 18, 3 (1985).
- 2. a) X. Creary, J. Am. Chem. Soc., 106, 5568 (1984); b) R. V. Hoffman, B. C. Jankowski, and C. S. Carr, J. Org. Chem., 51, 130 (1986).
- 3. Supporting evidence for the carbonyl oxygen participation has been reported: M. Maleki, A. C. Hopkinson, and E. Lee-Ruff, Tetrahedron Lett., 24, 4911 (1983). For an oppsite view, see; X. Creary, S. R. McDonald, and M. D. Eggers, Tetrahedron Lett., 26, 811 (1985).
- 4. MM2 calculations on t-butyl phenyl ketone and di-t-butyl ketone as models for the substrates used by Creary (ref 1c) indicated that their strain energies are 9.6 and 12.0 $kcalmol^{-1}$ greater than that of isobutane, respectively: unpublished results from this laboratory.
- 5. Presented in part at the 8th IUPAC Conference on Physical Organic Chemistry, Tokyo, Japan, August 24 - 29, 1986. Proceedings; K. Takeuchi, J. Kamata, T. Shibata, and K. Okamoto, Studies in Organic Chemistry, Vol. 31 (Edited by M. Kobayashi), pp. 303 - 310. Elsevier Science Publishers B. V., Amsterdam (1987).
- 6. 4-Oxo-3-homoadamantyl triflate also shows clean SN1 behaviors with the rate ratio to 3-homoadamantyl triflate of 10^{-8} , in ethanolysis at 25°C (see also ref 16). Contrarily, 2-oxo-1-adamantyl and 2-oxobicyclo[2.2.2]oct-1-yl triflates exhibited random mYOTf plots. suggesting intervention of mechanisms other than S_N1 solvolysis.
- 7. K. Takeuchi, I. Kitagawa, F. Akiyama, T. Shibata, M. Kato, and K. Okamoto, Synthesis, 1987, 612.
- 8. The synthetic route is illustrated below. The starting aldehydes used were 7,7-dimethylbicyclo[2.2.1]heptane-1-carbaldehyde, bicyclo[2.2.1]heptane-1-carbaldehyde, and bicyclo-[2.2.2]octane-1-carbaldehyde. The 1.2-diols were oxidized by silver carbonate on celite or Jones reagent in moderate yields. Since the oxidation of bicyclo[2.2.2]octane-1,2-dio1 with these reagents to the desired ketol proceeded in low yields (15 - 20%), it was derived from 1-methoxybicyclo[2.2.2]oct-5-en-2-one prepared by the Diels-Alder reaction of 1-methoxy-1,3-cyclohexadiene and 2-chloropropanenitrile in scaled-up preparations: D. A. Evans, W. L. Scott, and L. K. Truesdale, Tetrahedron Lett., 1972, 121. To convert 1hydroxybicyclo[2.2.2]octan-2-one to 2-methylenebicyclo[2.2.2]octan-1-ol the modified Wittig reaction was employed: R. Greenwald, M. Chaykovsky, and E. J. Corey, J. Org. Chem., 28, 1128 (1963). In the case of 1-hydroxybicyclo[3.2.2]nonan-2-one, the hydroxyl group had to be protected by trimethylsilylation prior to the Wittig reaction.



- 9. k1's/s⁻¹ (25.0°C) of ethanolysis of 1-adamantyl triflate and mesylate are 35.1 and 2.49x10⁻⁵, respectively: the detailed data will be reported shortly.
 10. a) B. R. Ree and J. C. Martin, J. Am. Chem. Soc., 92, 1660 (1970); b) V. Buss, R. Gleiter, and P. v. R. Schleyer, ibid., 93, 3927 (1971).
 11. A. Streitwieser, Jr., Solvolytic Displacement Reactions, p. 79. McGraw Hill, New York (1962); b) T. Tauti, J. Martiani, and S. Nichida, Bull Chem. Soc., Jun., 40, 2338 (1967);
- (1962); b) T. Tsuji, I. Moritani, and S. Nishida, Bull. Chem. Soc. Jpn., 40, 2338 (1967); c) C. F. Wilcox, Jr. and R. G. Jesaitis, Chem. Commun., **1967**, 1046. 12. X. Creary and C. C. Geiger, J. Am. Chem. Soc., **104**, 4151 (1982).
- 13. Ab initio calculations on the primary formylmethyl cation indicated small conjugative stabilization of 2.5 kcalmol-1: D. A. Dixon, R. A. Eades, R. Frey, P. G. Gassman, M. L. Hendewerk, M. N. Paddon-Row, and K. N. Houk, J. Am. Chem. Soc., 106, 3885 (1984).
- 14. For YOTF values, see; a) X. Creary and S. R. McDonald, J. Org. Chem., 50, 474 (1985); b) D. N. Kevill and S. W. Anderson, ibid., 50, 3330 (1985); c) T. W. Bentley and K. Roberts, ibid., 50, 4821 (1985).
- 15. The rate data will be reported in a full paper.
- 16. At the present stage, the only 2-oxo substituted bridgehead substrate that exclusively affords an unrearranged product is 4-oxo-3-homoadamantyl triflate, which gives a nicely linear mYOTF plot (m = 0.85; r = 0.998) (see also ref 6).

(Received in Japan 17 December 1987)