However, since all runs were carried out in the same trifluoroacetic acid and reproducible rate constants were obtained for all the hydrocarbons, the comparison of rate constants within the series studied is valid.

Acknowledgments.—We thank the Research Committee of the New Zealand University Grants Committee for financial support. Part of the work was carried out at the Chemical Laboratory, University of Sussex, during the tenure (by G. J. W.) of a Leverhulme Visiting Fellowship.

Solvolysis of 2-(Δ^2-Cyclohexenyl)ethyl System

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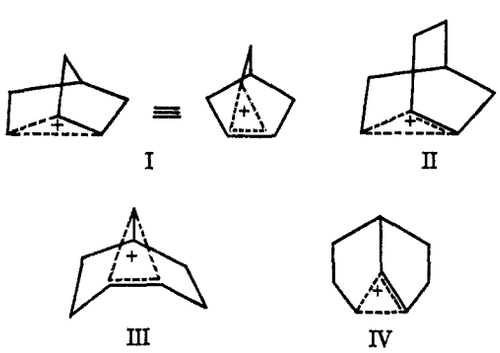
Received December 7, 1967

The field of π-electron participation in solvolytic displacement reactions of unsaturated sulfonate esters has grown rapidly in the last decade and has attracted the interest of many chemists both from the theoretical and synthetic point of view.[1]

Recently, it has been commonly accepted that one and the same bridged nonclassical ion can be generated by delocalization of either σ or π electrons. One criterion which has been frequently used to demonstrate the intervention of bridged ions is rate enhancement observed in solvolysis. Examples of this phenomenon include the 2-norbornyl nonclassical ion[2-4] I and the two isomeric nonclassical bicyclo[3.2.1]oct-2-yl cations[5,6] (II and III)[7] as well as the nonclassical bicyclo[3.3.0]oct-2-yl cation[8,9] (IV).



I II III IV

Such rate enhancement is not, however, the general rule for all compounds possessing a nonconjugated double bond. Thus Wilcox and Chibber[10] reported the absence of double bond interaction in the solvolysis of Δ^3-cyclohexenylcarbinyl derivatives. A similar conclusion was reached for 2-(Δ^2-cyclopentenyl)ethyl-,[11] 3-(Δ^1-cyclopentenyl)propyl-,[9] and 3-(Δ^3-cyclopentenyl)-propyl brosylates.[3]

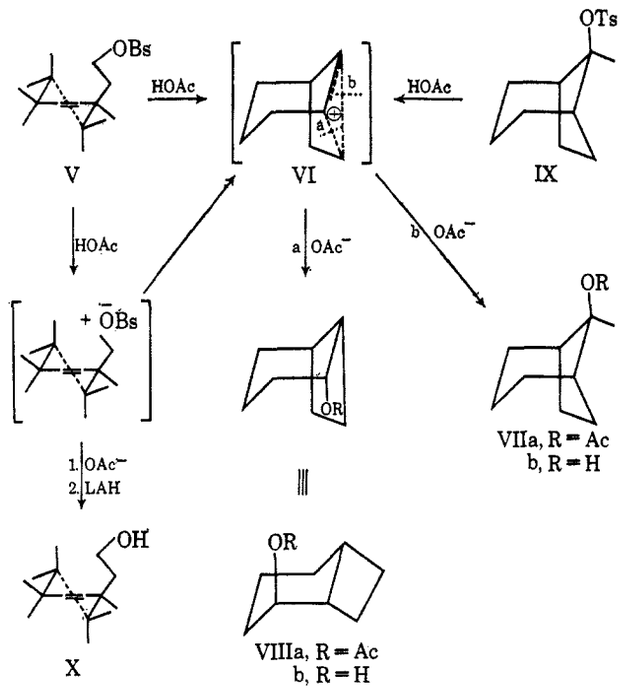


Figure 1.

In view of the general interest of double-bond interactions we wish to report the synthesis of 2-(Δ^2-cyclohexenyl)ethyl brosylate and its acetolysis along with the saturated analog.

Results and Discussion

2-(Δ^2-Cyclohexenyl)ethyl alcohol and the brosylate ester were prepared as outlined in the Experimental Section. The purity of the ester, which is a liquid at room temperature, was estimated from the infinity titer of kinetic runs to be better than 95–96%. The solvolysis was conducted in anhydrous acetic acid at two temperatures, and the first-order reactions were followed to about 60% reaction. The kinetic data are collected in Table I along with pertinent reference rates.

Product Analysis.—Infrared analysis, vapor phase chromatography, and nuclear magnetic resonance techniques were used to determine product composition. Acetolysis products were reduced by lithium aluminum hydride to the corresponding alcohols and analyzed. Possible bicyclic products, *endo*-bicyclo[3.2.1]octanol-8 (VIIb) and *endo*-bicyclo[4.2.0]octanol-2 (VIIIb), which could have been formed if double-bond participation was significant, were looked for carefully and found to be absent within experimental error. Acetolysis of V gave only compound X (See Figure 1).

The slight decrease in the rate of acetolysis of V compared with the saturated analog is attributed to the double bond which destabilizes the transition state for solvolysis by inductively retarding the departure of the incipient anion. The ratio k_{satd}/k_{unsatd} = 1.73 agrees with that found by Wilcox[10] for the solvolysis of Δ^3-

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TABLE I
SPECIFIC RATE CONSTANTS AND ACTIVATION PARAMETERS[a]

Compd	Temp, °C ±0.05	k_1, sec^{-1}	ΔH^*, kcal/mol	ΔS^*, eu
2-(Δ^2-Cyclohexenyl)ethyl	75.00	2.02×10^{-6}		
p-bromobenzenesulfonate	95.00	1.71×10^{-5}	26.3	−8.8
2-Cyclohexylethyl	75.00	3.50×10^{-6}		
p-bromobenzenesulfonate[b]	95.00	4.02×10^{-5}	31.4	6.5
endo-Bicyclo[3.2.1]octyl	75.00	1.35×10^{-8}		
8-*p*-toluenesulfonate[c]	120.00	0.30×10^{-6}	31.9	−3.5
exo-Bicyclo[3.2.1]octyl-				
8-*p*-toluenesulfonate[c]	75.00	3.16×10^{-5}		

[a] All solvolyses were conducted in acetic acid. [b] Winstein reported a value of *ca.* 2×10^{-6} for k_1 at 75°.[2b] [c] Extrapolated: C. S. Foote and R. B. Woodword, *Tetrahedron*, **20**, 687 (1964).

cyclohexenyl carbinyl systems (1.68) where double-bond participation was excluded.

This result differs from that observed for 2-(Δ^3-cyclohexenyl)ethyl brosylate where rate enhancement and formation of bicyclic products was reported.[2b] Such difference can be rationalized by considering the interaction of the developing carbonium ion *para* orbital with the *para* orbitals of the double bond.[12] A symmetrical interaction in 2-(Δ^3-cyclohexenyl)ethyl cation can lead to a stabilized nonclassical ion. An unsymmetrical interaction predicted for 2-(Δ^2-cyclohexenyl)-ethyl cation can only lead to a classical ion as actually observed. A similar interaction between the π electrons of the double bond and a polar substituent in the side chain was recently postulated[13] for Δ^3-cyclohexene derivatives resulting from a preferential fixed conformation of the ring.

A bridged ion VI would be comparable to that expected from solvolysis of *endo*-bicyclo[3.2.1]octyl 8-tosylate (IX), resulting from σ delocalization, if it does occur. Fortunately, acetolysis of this system was recently studied[14] and the results excluded intervention of a bridged ion. The absence of σ delocalization in the *endo* isomer, as opposed to the *exo* isomer (see Table I), was attributed to increase in angle strain in formation of a bridged transition state. Consequently, it is not unreasonable to assume that the same argument holds good for acetolysis of V.

Furthermore, the value of k_s/k_Δ, the ratio of solvent to double-bond participation in 2-(Δ^2-cyclohexenyl)-ethyl system, can be roughly estimated following a procedure similar to that suggested by Wilcox.[10] Assuming that the difference in free energies between Δ^3- and Δ^2-cyclohexenylethyl systems equals the free energy difference in the related transition states for solvolysis of bicyclo[2.2.2]octyl-2- and *endo*-bicyclo-[3.2.1]octyl-8-tosylates, respectively, k_s/k_Δ was calculated to be *ca.* 10^5 or no significant double-bond participation in the 2-(Δ^2-cyclohexenyl)ethyl system.

A preliminary study of the kinetics of solvolysis of 1-(Δ^2-cyclohexenyl)-2-chloropropane and its saturated analog in 70% aqueous acetone similarly showed absence of double bond participation ($k_{satd}/k_{unsatd} = 1.3$). These results will be reported later in detail.

It is noteworthy to point out a simple relationship that exists between rate enhancement and the position of the double bond relative to the leaving group. In all cases found in the literature, participation accompanied by rate enhancement is observed when the double bond in the cyclic system is separated from the carbon carrying the leaving group by an odd number of carbon atoms.[2b,3,7,9,11] Participation is, however, insignificant when the separation is by an even number of carbon atoms (see ref 3, 9, 10, 11, and present work).

(12) Kindly suggested by one of the referees.

(13) G. P. Kugatova-Shemyakina, *et al.*, *Tetrahedron*, **23**, 2721, 2987 (1967).

(14) See Table I, footnote *c*.

Experimental Section[15]

Diethyl Δ^2-Cyclohexenylmalonate.—To a solution of sodium (36.8 g, 1.6 g-atom) in absolute ethanol (600 ml) was added, while stirring under a nitrogen atmosphere, diethyl malonate (128 g, 0.8 mol) and then 1,2-dibromocyclohexane (121 g, 0.5 mol). The reaction mixture was heated at reflux for 15 hr and most of the alcohol was then removed. The residue was diluted with water (500 ml), extracted with three 100-ml portions of ether, and dried over anhydrous sodium sulfate. The solvent was removed and the residue was distilled *in vacuo* to give a colorless liquid (86 g, 71.5%): bp 136–137° (1 mm) (lit.[16] bp 87° (0.11 mm)).

Δ^2-Cyclohexenylmalonic Acid.—This was obtained in 71% yield by hydrolysis of the ester with methanolic potash. The acid crystallized from benzene in colorless plates: mp 167–169° (lit.[17] mp 165–167°).

Δ^2-Cyclohexenylacetic Acid.—Δ^2-Cyclohexenylmalonic acid (18.6 g, 0.1 mol) was heated in an oil bath up to 190°. The residue in the flask was distilled to give a colorless liquid (10.6 g, 75%): bp 116° (1 mm), n^{26}D 1.4828 (lit.[18] 125–127° (8 mm)).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.57; H, 8.57. Found: C, 68.56; H, 8.47.

Methyl (Δ^2-Cyclohexenyl)acetate.—This ester was prepared quantitatively by treating the preceding acid with the appropriate amount of diazomethane in ether: bp 67–69° (2 mm), n^{26}D 1.4731.

Anal. Calcd for $C_9H_{14}O_2$: C, 70.12; H, 9.09. Found: C, 70.24; H, 8.94.

2-(Δ^2-Cyclohexenyl)ethyl Alcohol.—Methyl (Δ^2-cyclohexenyl)-acetate (15.4 g) was reduced by lithium aluminum hydride in anhydrous ether (5-hr reflux) according to the usual procedure. The resulting alcohol (11.5 g, 92%), bp 100–101° (6 mm), was converted into the 3,5-dinitrobenzoate and crystallized from petroleum ether: mp 52–53°.

Anal. Calcd for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.00; N, 8.75. Found: C, 55.91; H, 5.28; N, 8.91.

Pure 2-(Δ^2-cyclohexenyl)ethyl alcohol was regenerated by alkaline hydrolysis of the 3,5-dinitrobenzoate derivative, followed by careful distillation through a 6-in. Vigreux column: bp 95–96° (2 mm); n^{26}D 1.4863.

(15) Melting points and boiling points are uncorrected. Microanalyses were performed by Alfred Bernhardt, West Germany. The infrared spectra were determined with a Unicam SP200 spectrophotometer. The vpc analyses were obtained with an Aerograph A-90 gas chromatograph, using a 10-ft column packed with 1% Carbowax on Chromosorb P, helium was used as a carrier gas. The nmr spectra were obtained with a Varian A-60 spectrometer. The petroleum ether used has bp 50–70°.

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Anal. Calcd for $C_8H_{14}O$: C, 76.19; H, 11.11. Found: C, 76.57; H, 10.95.

Vpc analysis showed that the alcohol was more than 99% pure. The infrared spectrum showed absorptions at $\nu_{max}^{CCl_4}$ 3400 (OH), 2960 (CH), 1645 (CH=CH), and 1050 cm^{-1} (CO). The nmr (CCl_4) spectrum showed peaks at τ 9.0–8.1, complex multiplet (9 $C_4H_7CH_2$); 6.47, triplet, J = 6.5 cps (2 $-OCH_2CH_2-$); 5.45, singlet (1 OH); 4.52, (2 CH=CH).

2-(Δ^2-Cyclohexenyl)ethyl *p*-Bromobenzenesulfonate.—Attempts to prepare this brosylate by the common method[19] gave back the alcohol and the acid chloride. Consequently, the alkoxide of the alcohol was prepared (0.69 g of sodium and 3.84 g of alcohol) in anhydrous ether under a nitrogen atmosphere. A solution of *p*-bromobenzenesulfonyl chloride (7.68 g) in anhydrous ether was added dropwise while cooling to −5°. The reaction mixture was stirred for 2 hr at this temperature and then for an additional 6 hr at room temperature. It was then left overnight, the ether solution was filtered, the solvent was removed and the residue was pumped at 0.5 mm for 30 min to remove any volatile products. The crude ester (9.5 g, 91.5%) was purified by several crystallizations, at low temperature, from petroleum ether: mp 10–11°; ir, $\nu_{max}^{CCl_4}$ 2930 (CH_2), 1650 (C=C), 1575 and 1460 (aromatic H), 1395 and 1190 cm^{-1} (OSO_2); nmr ($CDCl_3$), τ 9.0–8.2 (complex multiplet, 9 $C_4H_7CH_2$), 5.87 (triplet, J = 6.5 cps, 2 $-OCH_2CH_2-$), 4.50 (quartet, 2 CH=CH), 2.32 (multiplet, 4 aromatic H).

Ethyl cyclohexylidenecyanoacetate was prepared in 74% yield following Cope's procedure:[20] bp 150–151° (9 mm) (lit.[20] bp 150–151° (9 mm)); $n^{25}D$ 1.4980.

Ethyl cyclohexylcyanoacetate was prepared in 89% yield by catalytic reduction of ethyl cyclohexylidenecyanoacetate in the presence of Pd–C catalyst: bp 144–146° (7 mm); $n^{25}D$ 1.4640.

Cyclohexylacetic acid was prepared in 73% yield by refluxing ethyl cyclohexylcyanoacetate with concentrated hydrochloric acid for 20 hr. Working up the reaction mixture and distillation gave the acid: bp 116–118° (1 mm) (lit.[21] bp 135° (13 mm)); $n^{24}D$ 1.4682.

Ethyl Cyclohexylacetate.—Cyclohexylacetic acid was converted into the ethyl ester according to the usual procedure: bp 82–85° (2 mm) (lit.[21] bp 100° (17 mm)).

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.58; H, 10.58. Found: C, 70.49; H, 10.59.

2-Cyclohexylethyl alcohol was prepared in 94% yield by lithium aluminum hydride reduction of ethyl cyclohexylacetate according to the usual procedure, bp 100–102° (9 mm). The alcohol was converted into the 3,5-dinitrobenzoate derivative, crystallized from petroleum ether: mp 71° (lit.[22] 71–72°).

Anal. Calcd for $C_{15}H_{18}N_2O_6$: C, 55.90; H, 5.59; N, 8.69. Found: C, 55.84; H, 5.53; N, 8.92.

The pure alcohol was regenerated by alkaline hydrolysis of the 3,5-dinitrobenzoate followed by careful distillation through a 6-in. Vigreux column: bp 100–101° (8 mm); $n^{26}D$ 1.4660 (lit.[23] bp 85–87° (6 mm), $n^{20}D$ 1.4670). Vpc analysis showed that the alcohol was homogenous: ir, $\nu_{max}^{CCl_4}$ 3450 (OH), 2975 (CH), and 1055 cm^{-1} (CO); nmr (CCl_4), τ 9.0–8.2 (complex multiplet, 13 $C_6H_{11}CH_2$), 6.5 (triplet, J = 6.5 cps, 2 $-OCH_2CH_2-$), 5.52 (singlet, 1 OH).

2-Cyclohexylethyl *p*-bromobenzenesulfonate was prepared following the procedure employed for the unsaturated ester. The crude product (92% yield) was purified by crystallization from petroleum ether: mp 36° (lit.[2b] mp 37°); ir, $\nu_{max}^{CCl_4}$ 2950 (CH_2), 1645 (C=C), 1580 and 1460 (aromatic H), 1393 and 1190 cm^{-1} (OSO_2); nmr ($CDCl_3$), τ 9–8.2 (complex multiplet, 13 $C_6H_{11}CH_2$), 5.95 (triplet, J = 6.5 cps, 2 $-OCH_2CH_2-$), 2.32 (multiplet, 4 aromatic H).

Product Analysis.—The pure brosylate ester (0.035 mol) was allowed to react in anhydrous acetic acid (500 ml) containing sodium acetate (0.048 mol) for about 14 half-lives. The cooled solution was diluted with 2 l. of water and extracted three times with 200-ml portions of ether. The aqueous layer was diluted again with water, and extracted with ether. The combined ether extract was washed with water, allowed to stand for 2 hr over anhydrous sodium carbonate, and then dried over anhydrous sodium sulfate. The solvent was stripped carefully and the residue was distilled without an attempt at fractionation. The unsaturated ester gave a colorless liquid (91%) with bp 93–102° (2 mm), and the saturated ester gave a colorless liquid (89.5%) with bp 95–103° (3 mm).

Reduction of the Acetolysis Product.—To a slurry of lithium aluminum hydride (1.2 g) in anhydrous ether (30 ml) was added a solution of the solvolysis acetate (0.018 mol) in anhydrous ether. The mixture was refluxed with stirring for 5 hr and left overnight at room temperature. The reaction mixture was decomposed with wet ether and worked up in the usual manner to give the corresponding solvolysis alcohol. The alcohols were purified by distillation without fractionation and subjected to analysis.

Analysis of the Solvolysis Alcohols.—Vpc analysis of the solvolysis alcohol from the unsaturated brosylate showed that it was identical with pure 2-(Δ^2-cyclohexenyl)ethyl alcohol. Similarly the solvolysis alcohol from the saturated brosylate was identical with pure 2-cyclohexylethyl alcohol. Infrared and nmr spectra of the alcohol from the unsaturated brosylate were superimposable upon those of a pure sample: 3,5-dinitrobenzoate, mp 52–53° (from petroleum ether), undepressed when admixed with an authentic sample.

Rate Measurements.—The reagents used were purified and standardized as described in ref 5a. Titrations were carried out with 5-ml microburets using methyl violet indicator (saturated solution in chlorobenzene) and the end point was approached from the acid side. The compound to be solvolyzed was weighed into a volumetric flask and brought up to the mark with sodium acetate solution (0.03–0.04 *M*). The amount of material used was calculated so that the solution would still contain sodium acetate at the end of the reaction. The ampoule technique was employed throughout the rate measurements.

First-order rate constants k (where $k = 1/t \ln (a/a - x)$, a is the initial concentration in moles per liter of the material, t is the elapsed time, and x is the concentration of consumed base) were calculated. A plot of log $(a - x)$ *vs.* t for the solvolysis of the brosylate esters at different temperatures gave straight lines.

Registry No.— Methyl (Δ^2-cyclohexenyl)acetate, 16423-29-3; 2-(Δ^2-cyclohexenyl)ethyl alcohol, 16452-34-9; 2-(Δ^2-cyclohexenyl)ethyl *p*-bromobenzenesulfonate, 16423-30-6; ethyl cyclohexylcyanoacetate, 3212-50-1; 2-cyclohexylethyl *p*-bromobenzenesulfonate, 16423-32-8; Δ^2-cyclohexenylacetic acid, 3675-31-8; 2-(Δ^2-cyclohexenyl)ethyl alcohol 3,5-dinitrobenzoate, 16423-40-8.

Acknowledgment.—The authors thank Professor Y. Iskander, Head of the Chemistry Department and Professor of physical organic chemistry, for the facilities he provided and for many helpful discussions. We are grateful to Professor Leo A. Paquette of the Chemistry Department, The Ohio State University, Columbus, Ohio, for the use, by A. A. Y.,[24] of his laboratory's facilities for nmr and vpc work.

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Synthesis of 2-Methyladenosine and Its 5′-Phosphate

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Received January 29, 1968

In recent years, a number of methylated purine nucleosides have been detected in transfer ribonucleic acid (RNA) as minor components, and the detection of