Tetrahedron Letters No.18, pp. 2275-2280, 1968. Pergamon Press. Printed in Great Britain.

THE NUCLEOPHILIC EFFICIENCY OF REMOTE CYCLOPROPANE IN INTRAMOLECULAR DISPLACEMENT REACTIONS: SYNTHESIS AND ACETOLYSIS OF 2-(*TRANS*-3-BICYCLO[3.1.0]) ETHYL *p*-NITROBENZENESULFONATE

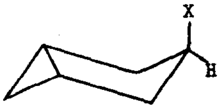
G. Dann Sargent
Department of Chemistry, Amherst College, Amherst, Massachusetts 01002

Robert L. Taylor, Wolfgang H. Demisch
Department of Chemistry, Princeton University, Princeton, New Jersey 08540

(Received in USA 9 January 1968)

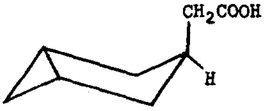
Over the past two decades, increasing attention has been devoted to the nucleophilicity of carbon-carbon bonding electrons. Essentially four types of nucleophile within this class have emerged: aromatic *pi* electrons, (1-3) carbon-carbon double bonds, (1,2,4) cyclopropane carbon-carbon *sigma* bonds, (1,2,5-8) and other carbon-carbon *sigma* bonds. (1,2,9) In the transition state for nucleophilic displacement, the first two types of nucleophile in this list are clearly capable of initiating either *pi* or *sigma* interaction. (9) The highly efficient cyclopropyl participation in cyclopropyl carbinyl systems appears to involve interaction between the cyclopropane ring and both lobes of the orbital at the electron deficient center. (7a,10,11) In this sense, this ion seems more akin to the allyl cation than, for example, to the 7-norbornenyl cation. (12) Since the cyclopropyl ring appears to be of comparable efficiency to a carbon-carbon double bond in stabilizing an incipient cationic center by *pi* or pseudo-*pi* participation, (1,2,5-8) the question arises whether a cyclopropane ring is also comparable in nucleophilicity to a structurally remote double bond whose interaction with an incipient cationic center must perforce be *sigma* in nature. We now communicate the results of an investigation designed to illuminate this point.

trans-3-Bicyclo[3.1.0]hexylcarboxylic acid (13) (Ia) was converted by the standard Arndt-Eistert sequence (Ia → Ib → Ic → II) to *trans*-3-bicyclo[3.1.0]hexylacetic acid (II), which in turn was reduced with $LiAlH_4$ to 2-(*trans*-3-bicyclo-[3.1.0]-hexyl)ethanol (IIIa). Treatment of IIIa with *p*-nitrobenzenefulfonyl chloride at 0° gave IIIb (m.p., 52.3 - 53.8°). *Anal.* Calcd. for $C_{14}H_{17}NO_5S$: C, 54.01; H, 5.50; N, 4.50; S, 10.30. Found: C, 54.12; H, 5.52; N, 4.64; S, 10.24.

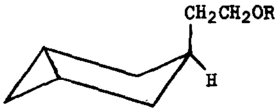


I

(a) X = COOH
(b) X = COCl
(c) X = $COCHN_2$



II



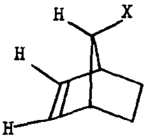
III

(a) R = H
(b) R = *p*-$C_6H_4(NO_2)SO_2^-$
(c) R = CH_3CO^-

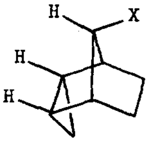
The observed first order rate constant for solvolysis of IIIb in anhydrous acetic acid containing excess sodium acetate at 100.85°C., followed kinetically by employing the standard ampoule technique and analyzing spectrophotometrically for unreacted ester, was $5.3 \pm 1.0 \times 10^{-5}$ sec.$^{-1}$.

Since this rate constant is virtually indistinguishable from those of the two model compounds 2-(cyclopentyl)ethyl *p*-nitrobenzenesulfonate (IV) (6.24×10^{-5} sec.$^{-1}$) (14) and 2-(3,4-dimethylcyclopentyl)ethyl *p*-nitrobenzenesulfonate (V) (5.17×10^{-5} sec.$^{-1}$), (15) this observation is inconsistent with any participation by the cyclopropane ring in the transition state for solvolysis of IIIb. This conclusion is reinforced by the fact that the product of solvolysis of IIIb was found to be indistinguishable from 2-(*trans*-3-bicyclo[3.1.0]hexyl)ethyl acetate (IIIc).

Comparison of the solvolytic reactivity of IIIb with that of 2-(Δ^3-cyclopentenyl)ethyl *p*-nitrobenzenesulfonate (VI) (4.60×10^{-3} sec.$^{-1}$) (14) demonstrates that in this system a carbon-carbon double bond is *at least* eighty-seven times more efficient than a cyclopropane ring in stabilizing the transition state for nucleophilic displacement. This observation contrasts strongly with reports, (16,17) which appeared after the completion of the present investigation, that *endo-anti*-8-tricyclo[3.2.1.0(2,4)]octyl *p*-nitrobenzoate (VIII) undergoes solvolysis in 60% aqueous acetone at a rate enhanced by a factor of 10^3-10^4 over that of *anti*-7-bicyclo[2.2.1]hept-2-ene *p*-nitrobenzoate (VII). The nucleophilicity of a cyclopropane ring relative to that of a carbon-carbon double bond is thus seen to be less by at least a factor of 10^5-10^6 in the cyclopentylethyl system than in the bicyclo[2.2.1]heptyl system. This represents a relative destabilization of the transition state for cyclopropane participation by 8.5 - 10.3 kcal./mole (at 100°C.).



VII



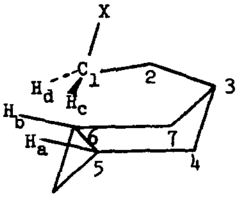
VIII

$X = p\text{-}NO_2(C_6H_4)COO^-$

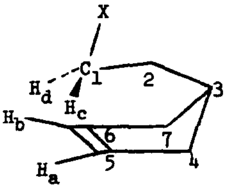
On the basis of these results, we must demur from the generalization: "It seems clear that as a participating group in solvolytic reactions cyclopropane is more effective than vinyl." (17) We note rather that as a participating group cyclopropane is remarkably more sensitive to environmental factors than is vinyl. On analysis, there emerge at least two plausible explanations for the enormous variance in the relative reactivity of the cyclopropane ring in the two systems here contrasted.

First, cyclopropane participation may involve a transition state in which at least a portion of the ground state steric strain associated with the three-membered ring is relieved. Since the cyclopropane ring in VIII suffers greater angle, non-bonded, and torsional (18) strain than its counterpart in IIIb, its greater efficiency as a nucleophile may derive from enhanced relief of strain in the transition state. This would represent a case of steric acceleration of solvolysis.

Second, the transition state for cyclopropane participation in the solvolysis of IIIb is destabilized by adverse non-bonded interactions not present in the transition state for solvolysis of VIII. Since our touchstone for the efficiency of cyclopropane participation in these two systems is the nucleophilic reactivity of a carbon-carbon double bond, this point is best illustrated by contrasting the reactive conformation for solvolysis of IIIb with (hypothetical) cyclopropane participation with that of VI with double bond participation.



IIIb



VI

X = p-$NO_2(C_6H_4)SO_3^-$

For both systems it is clear that as C_1 is brought progressively closer to C_5 and C_6, the non-bonded distance between the two hydrogen atoms bound to C_1 and the two hydrogen atoms labeled a and b decreases. Since the dihedral angle between plane $H_aC_5C_6H_b$ and plane $C_4C_5C_6C_7$ is less in IIIb than in VI, for any given C_1-C_5 (C_1-C_6) distance the H_a-H_c (H_b-H_d) distances are less in IIIb than in VI. Use of molecular scale models allows one to estimate the mutual dependence of the hydrogen-hydrogen non-bonded distance on the carbon-carbon non-bonded distance for both systems; by applying the non-bonded hydrogen-hydrogen potential function of Hendrickson, (19) one can characterize each carbon-carbon distance by an approximate non-bonded repulsion energy (Table I).

TABLE I

H-H Non-bonded Distances and Repulsion Energies as a Function of C_1-C_5 Non-bonded Distances for Conformations of IIIb and VI Suitable for Intramolecular Nucleophilic Displacement

	Non-Bonded Distances (A.)		Non-Bonded Repulsion Energies (kcal./mole)		
C_1-C_5	$(H_a$-$H_c)_{IIIb}$	$(H_a$-$H_c)_{VI}$	E_{IIIb}	E_{VI}	$(E_{IIIb}$-$E_{VI})$
2.55	1.70	2.20	2.2	0	2.2
2.45	1.55	2.00	6.0	0.2	5.8
2.30	1.40	1.80	9.0	1.8	7.8

It is immediately apparent that as long as the transition state is no less intimate for cyclopropane participation than for double bond participation, relative steric destabilization to cyclopropane participation will occur at carbon-carbon distances less than 2.6 A. Since the *ground state* C_2-C_8 distance in VIII is approximately 2.3 A, one can state with certainty that the activation energy required to bring IIIb into a reactive conformation must exceed that for VI by at least 15.6 (2 x 7.8) kcal./mole.

No such activation energy differential exists for solvolysis of VII and VIII. The peculiar geometry of the bicycloheptyl nucleus serves to eliminate completely the two severe non-bonded interactions present in the reactive conformation for IIIb. This very special element of molecular geometry must certainly play a most significant, and perhaps controlling, role in the dramatic participation by cyclopropane in the solvolysis of VIII. Whether *sigma* participation by cyclopropane is at all feasible in the absence of this special feature appears open to considerable doubt. (20)

Acknowledgment. The financial support of this investigation by the National Science Foundation (GP-5293, GP-6645) is gratefully acknowledged.

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