

SOLVOLYTIC STUDIES OF STEREOISOMERIC TRICYCLO[4.2.0.0<sup>2,4</sup>]OCTAN-5-YL DERIVATIVES.

CONFORMATIONALLY DISTINGUISHABLE CYCLOPROPYLCARBINYL CATIONS

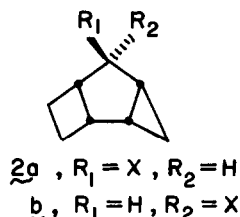
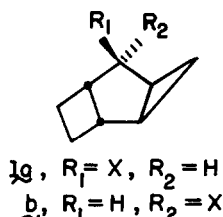
AND THE REACTIVITY CONSEQUENCES OF DIFFERING ORBITAL ALIGNMENTS

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(Received in USA 18 May 1973; received in UK for publication 13 July 1973)

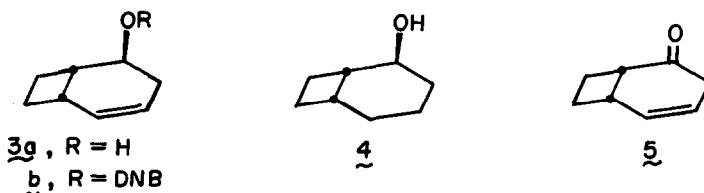
The accelerated solvolytic behavior of exo- and endo-bicyclo[3.1.0]alk-2-yl derivatives provides convincing evidence that comparable cyclopropyl participation accompanies ionization of both epimers.<sup>2</sup> The pair of isomers react at very similar rates ( $k_{\text{endo}}/k_{\text{exo}} = 1.3-1.5$  depending on the leaving group), the small discrepancy arising from ground state energy differences.<sup>2b</sup> Product studies have suggested further that a single conformationally stable minimum energy cyclopropylcarbinyll cation results, independent of the original relationship of the leaving group and cyclopropane ring.<sup>3</sup> This striking convergence to a single conformationally unique [3.1.0]bicyclic carbonium ion points to the existence of unique geometric effects in cyclopropylcarbinyll cation stabilization. In this connection, we have now assessed the solvolytic behavior of the four possible tricyclo[4.2.0.0<sup>2,4</sup>]octan-5-yl 3,5-dinitrobenzoates 1 and 2. Not only was noninterconvertibility of the resulting two homoallylic cations in evidence,<sup>5</sup> but that derived from 2a and 2b has been shown to exhibit alone a propensity for structural rearrangement to the cis-bicyclo[3.3.0]oct-6-en-2-yl system. This latter transformation constitutes a "double-barreled" expansion of both small rings present in 2.



Alcohols 1a-OH and 2b-OH were available from an earlier study.<sup>6</sup> Additionally, alcohol 1b-OH was obtained by LiAlH<sub>4</sub> reduction of the related ketone<sup>6</sup> and access to 2a-OH was gained by treatment of 2b-OH with aluminum isopropoxide in isopropyl alcohol containing acetone.<sup>7</sup> The set of four 3,5-dinitrobenzoates<sup>8</sup> were subjected to hydrolysis in acetone-water (80:20) and the relevant kinetic data are summarized in Table I. All four esters obeyed good first-

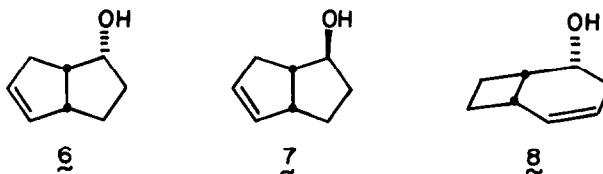
order kinetics and alkyl-oxygen cleavage was established by conducting comparable kinetic measurements in methanol-tetrahydrofuran (3:1) where only methyl ethers were isolated. To remove the possibility that starting esters 2a and 2b were rapidly interconverting (note similarity in rate) the solvolysis of 2a was interrupted at several points (e.g., 21%, 40%, etc. conversion). Nmr analysis of the recovered dinitrobenzoate revealed the total absence of detectable ( $\leq 3\%$ ) 2b.

Product studies with 1a-ODNB and 1b-ODNB were carried out in both unbuffered and buffered (10% mole excess of 2,6-lutidine) solutions. In the first instance, both esters gave within experimental error an identical mixture of alcohol 3a (25%) and its internally returned ester 3b (55-60%). In confirmation of its structural assignment, 3a was catalytically hydrogenated to known alcohol 4<sup>9</sup> and oxidized to  $\beta,\gamma$ -unsaturated ketone 5. The buffered hydrolyses, conducted at 100° for ten half-lives, gave a 75:25 mixture of 3a and 1a-OH, together with 20% of 3b. Tricyclic alcohol 1a-OH does experience partial isomerization to 3a under these conditions



Comparable buffered hydrolyses of 2a-ODNB and 2b-ODNB gave, in contrast, a quite different spectrum of products consisting of 6 (30-34%), 7 (24%), 8 (33-41%), 2a-OH (4-5%), and 2b-OH (2.5%).<sup>10</sup> To establish the identity of 6 and 7, they were individually acetylated<sup>11</sup> and also oxidized to cis-bicyclo[3.3.0]oct-6-en-2-one which was synthesized independently by the method of Roberts and Gorham.<sup>12</sup> Alcohol 8 was prepared (92% stereoselectivity) by sodium borohydride reduction of 5, and together with 6 and 7, was shown to be stable under the reaction conditions.

The relative ionization rates of anti epimers 1 differ only by a factor of 3-4, again indicating little kinetic dependence on leaving group geometry. The essentially identical rate data for 2a-ODNB and 2b-ODNB are compatible in direction with the greater ground state strain in 2b-OH, RT ln 6.7, which is suggested from actual equilibration.<sup>7</sup> That these solvolyses give only cis-bicyclo[4.2.0]oct-4-en-2-ols with hydroxyl orientation inextricably linked to a specific tricyclic precursor geometry strongly implicates highly directed attack of solvent

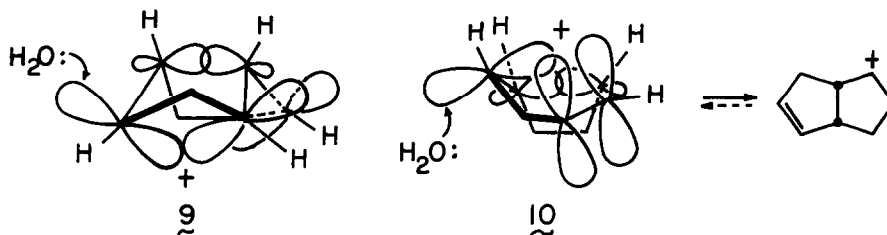


nucleophile. This stereospecificity in homoallylic alcohol formation can best be explained by intervention of carbocation intermediates 9 and 10, the relative orientation of the intramolecular 'cyclopropyl' bonding electrons directing solvent capture as shown.

Table I. Rates of Hydrolysis in 80% Aqueous Acetone

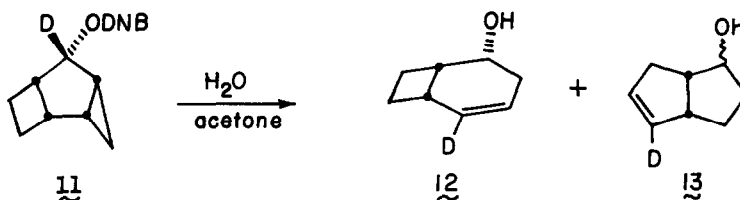
3,5-Dinitrobenzoate	Temp, °C	$10^5 k_1$ , sec <sup>-1</sup>	115° $k_{rel}$	$\Delta H^\ddagger$ , kcal/mol	$\Delta S^\ddagger$ , eu
<u>1a</u>	85.4	5.49	70	27.3	-2.5
	100.4	26.6			
	114.8	107.2			
<u>1b</u>	100.4	8.23	20	27.1	-5.3
	114.8	33.3			
	130.0	128.9			
<u>2a</u>	114.8	1.62	1	31	-0.37
	130.0	7.77			
<u>2b</u>	114.8	1.55	1	30	-3.4
	130.0	7.03			

The observation that only 2a-ODNB and 2b-ODNB give cis-bicyclo[3.3.0]oct-6-en-2-ols further corroborates the involvement of non-interconverting ions 9 and 10 in the product-forming steps. Molecular models show that in 10 stereoelectronic alignment of the homoallylic p orbital with the internal cyclobutane bond is highly favorable for 1,2 carbon shift. In the cation produced from 1 (i.e., 9), this p orbital is oriented out of plane.



Following this argument to its conclusion requires that 11 solvolyze with formation of alcohols 12 and 13 in which deuterium is uniquely bonded to that trigonal carbon atom positioned adjacent to the ring fusion. Indeed, these isotopically labeled products are formed

with high site specificity. Unfortunately, in the case of 13 our data do not distinguish between an alternative ring opening pathway which gives access to 2,5-cyclooctadienyl-2-d



cations and their subsequent transannular cyclization. Notwithstanding, the results clearly show that cations 9 and 10 comprise separate and distinct potential energy minima.<sup>13</sup>

#### FOOTNOTES AND REFERENCES

1. (a) National Science Foundation Graduate Trainee, 1970-72; (b) National Science Foundation Undergraduate Research Participant, Summers 1969 and 1970.
2. (a) P.R. Brook, R.M. Ellam, and A.S. Bloss, *Chem. Commun.*, 425 (1968); (b) G.H. Schmid and A. Brown, *Tetrahedron Lett.*, 4695 (1968); (c) E.C. Friedrich and M.A. Saleh, *ibid.*, 1373 (1971); (d) E.C. Friedrich, M.A. Saleh, and S. Winstein, *J. Org. Chem.*, 38, 860 (1973); (e) E.C. Friedrich and M.A. Saleh, *J. Amer. Chem. Soc.*, 95, 2617 (1973).
3. Similar behavior has been observed with the *exo*- and *endo*-bicyclo[4.1.0]hept-2-yl ester systems [H.L. Goering and K.E. Rubenstein, *Abstr. 151st ACS Meeting*, March 28-3, 1966, p K011; L.E. Friedrich and G.B. Schuster, *Tetrahedron Lett.*, 3171 (1971)]. As the size of the larger ring is increased to 5-7 carbon atoms, the attendant enhancement of conformational flexibility (in the *cis* fused series) permits ionization to structurally distinct cationic intermediates.<sup>4</sup>
4. (a) A.C. Cope, S. Moon, and C.H. Park, *J. Amer. Chem. Soc.*, 84, 4850 (1962); (b) C.D. Poulter, E.C. Friedrich, and S. Winstein, *ibid.*, 92, 4274 (1970); (c) C.D. Poulter and S. Winstein, *ibid.*, 92, 4282 (1970).
5. For the pioneering work of noninterconverting homoallylic cations, consult: (a) S. Winstein and E.M. Kosower, *ibid.*, 81, 4399 (1959); (b) G.H. Whitham and J.A.F. Wickramasinghe, *J. Chem. Soc.*, 1655 (1964); (c) W.G. Dauben and L.E. Friedrich, *Tetrahedron Lett.*, 1755 (1967).
6. L.A. Paquette and O. Cox, *J. Amer. Chem. Soc.*, 89, 5633 (1967).
7. A.L. Wilds, *Organic Reactions*, 2, 178 (1944); F.F. Nelson, Ph.D. Dissertation, University of Wisconsin, 1960. This equilibration afforded an 87:13 mixture of 2a-OH and 2b-OH. Equilibrium was, however, not approached from both directions.
8. The mp's of the relevant ODNB derivatives are: 1a, 85-86°; 1b, 90.5-91.5°; 2a, 121-122°; 2b, 116.5-117°. Nmr spectra and combustion analyses were compatible with all new compounds described.
9. We thank Professor Peter K. Freeman for an authentic sample of this material.
10. These conditions have been separately shown to promote 25-30% conversion of 2a-OH and 2b-OH to a similar (but not identical) mixture of 6-8.
11. Sequential LiAlH<sub>4</sub> reduction and acetylation of *cis*-bicyclo[3.3.0]oct-6-en-2-one afforded predominantly (9% stereoselectivity) the acetate of 6.
12. J.D. Roberts and W.F. Gorham, *J. Amer. Chem. Soc.*, 74, 2278 (1952).
13. The partial support of this research by The Graduate School of The Ohio State University, The National Science Foundation, and Eli Lilly Company is gratefully acknowledged.