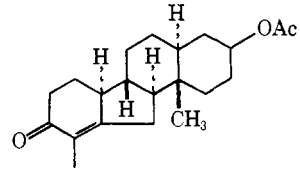
Making now the well-founded assumption that the enzyme prefers the antipode of VII possessing 10*R* configuration leads to the prediction of *anti-trans* stereochemistry for VII. This is in conformity with the X-ray crystal structure for *rac*-V, which latter incorporates these three centers unchanged as C-8, C-13, and C-14 by virtue of the synthetic route.

A further test for the preference of the enzyme for the 10*R* configuration involved the assignment of relative configuration at C-10 to the two isomeric pairs, *rac*-V and *rac*-VI derived from *rac*-VII. Both *rac*-V and *rac*-VI were shown from nmr data to possess rings B and C in *cis* fusion after conversion to IX and its enantiomer IXa, respectively, by the action of the *A. simplex* enzyme (4 hr and 5 days, respectively) followed by Dryden aromatization.[8] *rac*-V and *rac*-VI differ, therefore, only in their relative stereochemistry at C-10. The phenol IXa derived from *rac*-VI had CD $[\theta]_{230}$ −1600, $[\theta]_{280}$ positive. In comparison, estradiol (9α) showed $[\theta]_{233}$ +5900, $[\theta]_{283}$ −390, and 9β-estradiol has a negative Cotton effect near 230 nm and a positive one near 280 nm.[11] IX derived from the enantiomer of V had Cotton effects opposite to those of IXa. The preference of the dehydrogenase for the antipodes of V and VI, which possess the same chirality at C-10 (but opposite chirality at all remaining centers), again points up the importance of this center for enzyme selectivity. The above data define the absolute configuration of IX and IXa, and of V and VI and their enantiomers with the exception of that at C-10.[12] Applying now our rule that the enantiomers possessing 10*R* chirality are the preferred substrates for dehydrogenation, IXa must be derived from *rac*-VI, while its enantiomer IX has as its precursor *rac*-V. This defines the complete stereochemistry of V, VI, and their enantiomers, and is in full accord with the structure of *rac*-V as determined by X-ray crystallography.[8]

It is significant that the examples presented in this paper include tricyclic and tetracyclic systems, as well as systems containing five-membered rings. It should be pointed out that only when R = CH_3 (structure I) does the enzyme show complete specificity. When R = H it shows selectivity,[13] and when chirality at C-10 is eliminated as by introduction of a 9,10 double bond both enantiomers are attacked at equal rates.[8]

It was of interest to demonstrate that the 10*R* selectivity rule was valid for bicyclic systems as well. Dehydrogenation of *rac*-Δ^4-9-methyloctalin-3,8-dione followed by reisolation of the substrate showed the latter to have $[\alpha]_D$ −33°, and the 8-ol derived from it by $NaBH_4$ reduction[14] to possess θ_{318} +730. (9*R*)-Δ^4-9-Methyloctalin-3,8-dione has $[\alpha]^{EtOH}_D$ −130°,[15] and (8*S*,9*S*)-Δ^4-9-methyloctalin-3-on-8-ol shows a negative Cotton effect near 320 nm.[16] The 9*S* enantiomer (corresponding to 10*R* chirality in previous examples) is thus again preferentially dehydrogenated.[17]



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Acknowledgments. Support of this work by the National Institutes of Health is gratefully acknowledged. The authors thank Dr. S. C. Pan, Squibb Institute for Medical Research, for the acetone-dried *A. simplex* cells, Dr. E. P. Oliveto, Hoffmann-LaRoche, for samples of *rac*- and *l*-retrotestosterone, Dr. J. Kerwin, Smith Kline and French, for a sample of B-norestradiol, and Professor J. P. Kutney, University of British Columbia, for samples of *rac*- and (+)-Δ^{12}-3β-acetoxyetiojerven-17-one.

(11) P. Crabbé, "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry," Holden-Day, San Francisco, Calif., 1965, p 293.

(12) The CD curves for recovered V and VI were also determined but their sign is of questionable value in determining absolute configuration, because of the influence of subtle conformational factors on the sign of the Cotton effects of steroidal α,β-unsaturated ketones (*cf.* G. Snatzke, *Tetrahedron*, **21**, 421 (1965)). V and VI were therefore oxidized to the corresponding diketones and the Cotton effect for the saturated keto group was determined as the difference between the CD curves for V and VI and their respective diketones. These Cotton effects should provide a safe indication of the absolute configuration of all centers other than C-10. The values for $\Delta\theta_{285}$ were −4900 and +400, respectively, which confirms the conclusions derived from the CD data for IX and IXa.

(13) This results in incomplete resolution and lower than maximal values for the ORD and CD peaks. This in no way alters the validity of the proposed procedure.

(14) C. H. Heathcock, R. A. Badger, and J. W. Patterson, Jr., *J. Amer. Chem. Soc.*, **89**, 4133 (1967).

(15) V. Prelog and W. Acklin, *Helv. Chim. Acta*, **39**, 748 (1956).

(16) C. Djerassi, J. Osiecki, and W. Herz, *J. Org. Chem.*, **22**, 1361 (1957).

(17) It was gratifying to find that *rac*-**1** (J. P. Kutney, J. Cable, W. A. F. Gladstone, H. W. Hanssen, E. J. Torupka, and W. D. C. Warnock, *J. Amer. Chem. Soc.*, **90**, 5332 (1968)) on dehydrogenation for 5 days left **1**, CD, θ_{248} +6300, θ_{318} −2200. Authentic **1** (W. F. Johns and I. Laos, *J. Org. Chem.*, **30**, 123 (1965)) had θ_{248} +45,700, θ_{318} −16,600.

Josef Fried, Michael J. Green, G. V. Nair

Ben May Laboratory for Cancer Research and the Departments of Chemistry and Biochemistry
University of Chicago, Chicago, Illinois 60637

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Stable Carbonium Ions. CIII.[1] Ring Contraction and Transannular Bond Formation in Medium-Ring Cycloalkyl Cations

Sir:

Solvolyses of medium-ring (eight- to eleven-membered) cycloalkyl derivatives occur at enhanced rates over the common-ring (five- to seven-membered) and large-ring (12+-membered) cycloalkyl derivatives. These results have been interpreted as due to relief of steric strain.[2] From labeling experiments, Prelog has shown that facile transannular hydride shifts occur after ionization but before solvent capture in the solvolyses.[2] Acetolysis of cyclodecyl tosylate yields mainly *cis*- and *trans*-cyclodecenes, in the ratio of 1:5. It was observed that decomposition of solid cyclodecyl tosylate also gave small amounts of deca-

(1) Part CII: G. A. Olah, J. M. Bollinger, and D. P. Kelly, *J. Amer. Chem. Soc.*, **92**, 1432 (1970).

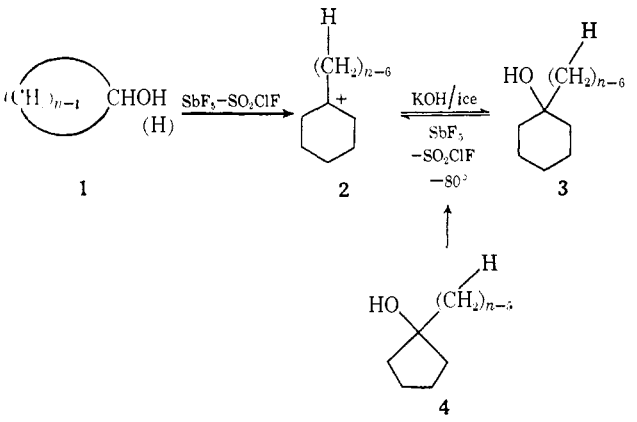
(2) (a) V. Prelog, *J. Chem. Soc.*, 420 (1950); (b) R. Heck and V. Prelog, *Helv. Chim. Acta*, **38**, 1541 (1955); (c) V. Prelog and J. G. Traynham in "Molecular Rearrangements," Part 1, P. deMayo, Ed., Wiley-Interscience, New York, N. Y., 1963, pp 593–615; (d) V. Prelog, *Rec. Chem. Progr.* **18**, 247 (1957); as in "Nonclassical Ions," P. D. Bartlett, Ed., W. A. Benjamin, New York, N. Y., 1965, pp 197–210; (e) V. Prelog, W. Küng, and T. Tomljenovic, *Helv. Chim. Acta*, **45**, 1352 (1962); (f) H. C. Brown and C. Ham, *J. Amer. Chem. Soc.*, **78**, 2735 (1956).

lin.[2e,f] Such transannular bond formation is much more facile in the corresponding unsaturated compounds, solvolysis of *cis*- and *trans*-5-cyclodecen-1-yl *p*-nitrobenzoates giving bicyclo[4.4.0]-1-decalols.[3] The latter have also been prepared by the action of lithium diethylamide on cyclodecene oxide.[4]

Previous studies of some cycloalkyl cations under long-lived ion conditions (where solvent capture is absent) have shown that the cyclobutyl cation is stabilized by σ delocalization,[5] the cyclopentyl cation by degeneracy *via* 1,2-hydride shifts,[6] and the cyclohexyl cation by ring contraction to the tertiary methylcyclopentyl cation.[7] We wish to report now the study of seven- to twelve-membered cycloalkyl cations in superacid media.

Dissolution of cycloheptanol **1** (n = 7) in SbF_5–SO_2ClF at −78° results in a clear yellow solution whose pmr spectrum exhibits broad signals at δ 4.28 (4 H, CH_2–C^+), 3.95 (3 H, CH_3–C^+), 2.58 (4 H, β-CH_2), and 2.25 (2 H, γ-CH_2) ppm. Identical spectra were obtained both from 1-methylcyclohexanol **3** (n = 7) and 1-ethylcyclopentanol **4** (n = 7), under the same conditions. Quenching of each solution in KOH–ice suspensions at low temperature gave one major product, 1-methylcyclohexanol, **3** (n = 7) (Scheme I).

Scheme I

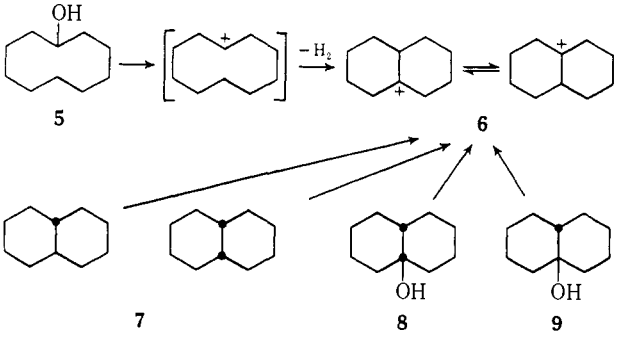


Similarly, cyclooctanol **1** (n = 8) in FSO_3H–SbF_5–SO_2ClF gave a solution with broad pmr absorptions at δ 4.15 (6 H, α-CH_2–C), 2.5–2.1 (6 H, β-, γ-CH_2), and 1.74 (3 H, triplet, CH_3) ppm. The same spectrum was also obtained from cyclooctane **1** (n = 8), methylcycloheptane, ethylcyclohexane (SbF_5–SO_2ClF), 1-ethylcyclohexanol **3** (n = 8), and 1-*n*-propylcyclopentanol **4** (n = 8) (FSO_3H–SbF_5–SO_2ClF) at −78°. The ion is thus identified as the tertiary 1-ethylcyclohexyl cation **2** (n = 8) confirmed by quenching each of the solutions at −78° to yield only[8] mixtures of 1-ethylcyclohexanol[9] and 1-methoxy-1-ethylcyclohexane, identical in all respects[10] with authentic materials.[11]

Cyclononanol **1** (n = 9) when dissolved in FSO_3H–SbF_5–SO_2ClF at −78° yields a pale yellow solution with pmr absorptions at δ 4.13 (6 H, α-CH_2), 2.1–2.8 (8 H, β-,γ-CH_2), and 1.44 (3 H, triplet, CH_3) ppm. The same spectrum was obtained from 1-*n*-propylcyclohexanol (**3**, n = 9) and 1-*n*-butylcyclopentanol (**4**, n, = 9) (FSO_3H–SbF_5–SO_2ClF) at −78°. Quench products (H_2O–K_2CO_3) from the ion solutions consisted of mixtures of 1-*n*-propylcyclohexene and *n*-propylidenecyclohexane which were identical in all respects with authentic materials;[12] the ion thus is identified as the tertiary 1-*n*-propylcyclohexyl cation **2** (n = 9).

When cyclodecanol **5** is added to FSO_3H–SbF_5–SO_2ClF at −78°, effervescence of hydrogen[13] occurs to give a pale yellow solution. The pmr spectrum of this solution (δ 4.0 (1 H), 3.4 (8 H, α-CH_2), and 2.4 (8 H, β-CH_2) ppm) is identical with that of the 91,0 equilibrating bridgehead decalyl ion **6**, previously obtained by hydride abstraction[14] of decalin.[15] The 1,2-hydride shift still occurs at −130°. Ion **6** is also obtained by dissolving *cis*- (**8**) or *trans*-9-decalol (**9**) in the same acid system (Scheme II). We found no

Scheme II



evidence of a cyclodecyl ion[16] or ring contraction to a substituted monocyclic ion. Quenching solutions of the ion in KOH–ice or MeOH–MeONa suspensions at low temperature yielded *cis*- and *trans*-9-decalols and/or their methyl ethers, identified by pmr and glc comparisons with authentic materials.[17]

It was recently suggested from a study of the solvolysis products of *cis*- and *trans*-9-chlorodecalin and 4-cyclohexenylbutyl tosylate that the carbonium ions formed

(3) H. L. Goering and W. D. Closson, *J. Amer. Chem. Soc.*, **83**, 3511 (1961). Kinetic data are also given for cyclodecyl *p*-nitrobenzoate, but no product identification.

(4) A. C. Cope, M. Brown, and H. H. Lee, *ibid.*, **80**, 2855 (1958).

(5) G. A. Olah, D. P. Kelly, C. L. Jeuell, and R. D. Porter, *ibid.*, **92**, 2544 (1970).

(6) G. A. Olah and A. M. White, *ibid.*, **91**, 5801 (1969).

(7) G. A. Olah, J. M. Bollinger, J. Lukas, and C. Cupas, *ibid.*, **89**, 2692 (1967).

(8) *Ca.* 85% by glc analysis.

(9) Quenching of ion solutions prepared from carbinol precursors in MeOH–NaOMe always results in the formation of some carbinol products due to the relatively high concentration of H_3O^+ in the ion solution.

(10) Nmr, glc, ir, and mass spectra.

(11) 1-Methoxy-1-ethylcyclohexane was prepared from the carbinol by NaH–MeI according to C. W. Hurd and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*,74, 5252 (1952); pmr, δ 3.12 (s, 3 H, OCH_3), 1.46 (m, 12 H), and 0.83, (t, 3 H, CH_3); ir ν_{C-O} 1080 cm^{-1}.

(12) A mixture of 1-*n*-propylcyclohexene (91%) and *n*-propylidenecyclohexane (9%) was prepared by zinc chloride dehydration of 1-*n*-propylcyclohexanol.

(13) Identified by mass spectroscopy (J. Shen).

(14) It has been known for some time in our laboratories that SbF_5 (neat or diluted with SO_2ClF) is a very suitable solvent medium to form stable carbonium ions from hydrocarbons. These reactions are, however, always accompanied by formation of H_2, and/or protolytic C–C bond cleavage reactions. H_2 formed can reduce antimony pentafluoride to antimony trifluoride and hydrogen fluoride. Thus hydride abstraction by SbF_5 is not considered to take place by the Lewis acid itself, but as a protolytic process by SbF_5 and ubiquitous proton acid impurities.

(15) G. A. Olah and J. Lukas, *J. Amer. Chem. Soc.*, 90, 933 (1968).

(16) Such an ion would be expected to exhibit a single pmr absorption at *ca.* δ 4 ppm due to rapid degenerate 1,2-hydride shifts, as is observed in the cyclopentyl cation, ref 6.

(17) We are indebted to Professor R. Fort for samples of *cis*- and *trans*-9-decalols from which the methyl ethers were prepared by a modification (refluxing THF for 2 days) of Hurd and Saunders:[11] *cis*-9-methoxydecalin nmr δ ($CDCl_3$) 3.16 (s, 3 H, OCH_3) and 1.52 (m, broad, 17 H); ir ν_{C-O} 1080 cm^{-1}; *trans*-9-methoxydecalin nmr δ ($CDCl_3$) 3.07 (s, 3 H, OCH_3), 1.95–1.0 (m, 17 H); ir ν_{C-O} 1075 cm^{-1}.

are not identical, but *cis*- and *trans*-decalyl ions, the latter being 1.4 kcal mol^{-1} more stable.[18] Because we obtained the same pmr spectrum from both *cis* and *trans* precursors, separate ionic species were not apparent even at temperatures as low as $-130°$. Quenching of the ion solutions prepared from either *cis*- or *trans*-9-decalol yielded mixtures in which the isomer distributions were the same; that is *cis*–*trans*, 2:1. This could reflect the faster rate of quenching of the *cis* isomer under our conditions, or the higher stability of the *cis*-decalyl ion. If the *trans*-decalyl ion were more stable under our conditions and the rates of quenching were identical for both isomers, then this ratio would be reversed.

Cycloundecanol **1** (n = 11) when dissolved in FSO_3H–SbF_5–SO_2ClF at $-78°$ yields the 1-*n*-pentylcyclohexyl tertiary cation **2** (n = 11); pmr absorptions at δ 4.28 (6 H, α-CH_2), 1.5–3.0 (12 H, CH_2), and 1.3 (3 H, CH_3). The same spectrum was also obtained from 1-*n*-pentylcyclohexanol and 1-*n*-hexylcyclopentanol.

Similarly, cyclododecanol **1** (n = 12) when dissolved in FSO_3H–SbF_5–SO_2 at $-78°$ yields the 1-*n*-hexylcyclohexyl tertiary cation **2** (n = 12); pmr absorptions at δ 4.29 (6 H, α-CH_2), 1.4–2.9 (14 H, CH_2), and 1.2 (3 H, CH_3). An identical spectrum was also obtained from 1-*n*-hexylcyclohexanol.

Quench products from the 1-*n*-pentyl- and 1-*n*-hexylcyclohexyl cations were complex mixtures, indicating further rearrangement of the initially formed ions. The spectra of the ions, however, are identical with those of the 1-ethyl- and 1-*n*-propylcyclohexyl cation, with the exception of one peak in the β-, γ-CH_2 region.

It should be noted that the 1-alkylcyclohexyl ions reported in this communication are those formed at low temperature, generally at $-78°$. Subsequent rearrangements take place at higher temperatures predominantly to alkylcyclopentyl cations which are under investigation.

Acknowledgment. Support of this work by grants from the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, are gratefully acknowledged.

(18) A. F. Boschung, M. Geisel, and C. A. Grob, *Tetrahedron Lett.*, 5169 (1968); see also R. Fort and R. E. Hornisch, *Chem. Commun.*, 11 (1969).

George A. Olah, David P. Kelly, Robert G. Johanson
Department of Chemistry, Case Western Reserve University
Cleveland, Ohio 44106
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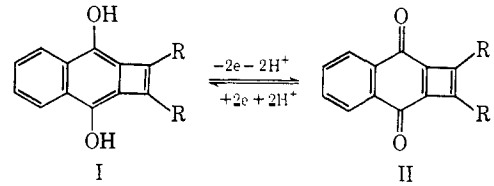
Electrochemical Evidence for the Antiaromaticity of Cyclobutadiene[1]

Sir:

The early simple conclusion that such 4π-electron systems as cyclobutadiene[2] are not aromatic has given way recently to indications that they are in fact antiaromatic,[3] *i.e.*, destabilized by conjugation. The type of evidence available involves rates or (preferably) equilibrium constants for the conversion of a saturated carbon into a trigonal atom, with consequent completion of the cyclic 4π-electron conjugated system. However, such a change generally involves an increase in strain as well as in electronic interactions; while a change in strain has been excluded[3a,b] as a major component in the apparent antiaromaticity of the cyclopropenyl anion, it was not ruled out as a factor in the antiaromaticity we have recently reported[3d] for a cyclobutadiene derivative. We now wish to describe evidence for the antiaromaticity of cyclobutadiene in which the antiaromatic interaction is brought in by an electron redistribution accompanied by only negligible changes in strain energy.

The system examined involves reversible oxidation of the hydroquinone Ia to the quinone IIa. Because of the low β–β' bond order in a naphthalene such as I, and the essentially full double bond in II, there

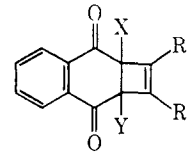


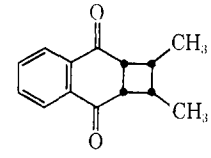
I II

a, R = C_6H_5
b, R = CH_3

is a considerable increase in the cyclobutadiene character of the system in converting I to II, but only a slight geometric change. We have examined and corrected for any geometric effects by using a cyclobutenonaphthohydroquinone Vb as a model for the cyclobutadieno derivative Ia.

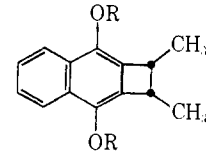
Irradiation of 2-butyne with naphthoquinone affords a 6% yield of the adduct IIIa,[4] which has recently been reported elsewhere.[5] This compound was con-





IIIa, X = Y = H; R = CH_3
b, X = Y = H; R = C_6H_5
c, X = Y = CH_3; R = C_6H_5
d, X = H; Y = Cl; R = C_6H_5

IV



Va, R = $COCH_3$
b, R = H

verted with ethylene glycol to the bisketal[4] of IIIa, mp 178–180°, and the cyclobutene double bond was hydrogenated over Pt to afford the bisketal[4] of IV,

(1) Taken in part from the Ph.D. Thesis of Robert Grubbs, Columbia University, 1968. Much of this material was described at the National Organic Chemistry Symposium, Salt Lake City, Utah, 1969. Support of this work by the National Institutes of Health, and technical help by Dr. K. Balasubramanian and Mr. William Chu, are gratefully acknowledged.

(2) M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

(3) (a) R. Breslow, J. Brown, and J. Gajewski, *J. Amer. Chem. Soc.*, **89**, 4383 (1967); (b) R. Breslow and M. Douek, *ibid.*, **90**, 2698 (1968); (c) R. Breslow and K. Balasubramanian, *ibid.*, **91**, 5182 (1969); R. Breslow and W. Chu, *ibid.*, **92**, 2165 (1970); (d) R. Breslow and W. Washburn, *ibid.*, **92**, 427 (1970).

(4) New compounds were characterized by satisfactory spectra, mass spectra, and in most cases C and H analyses.

(5) S. Farid, W. Kothe, and G. Pfundt, *Tetrahedron Lett.*, 4147 (1968).