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THE STEREOSPECIFIC CLEAVAGE OF NORTRICYCLANONE (1,2)

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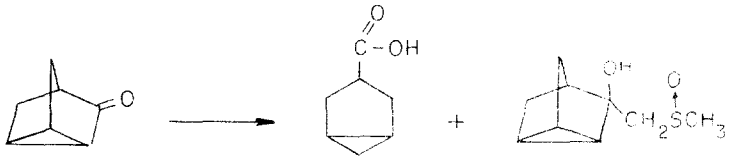
The elegant investigations of Cram and coworkers have firmly established the stereochemical control of various solvents in a variety of cleavage reactions (3). As a result of their studies the stereochemical ramifications of using dimethyl sulfoxide, as a solvent with high dissociating power, were defined. Dimethyl sulfoxide was found to be a "reaction media in which electrophilic substitution occurs with essentially complete racemization" (3).

While exploring the mechanistic route of the cleavage of non-enolizable ketones in dimethyl sulfoxide solution (4), we have found that the cleavage of nortricyclanone (I) in dimethyl sulfoxide solution is completely stereospecific and results in 100% retention of configuration. (5).

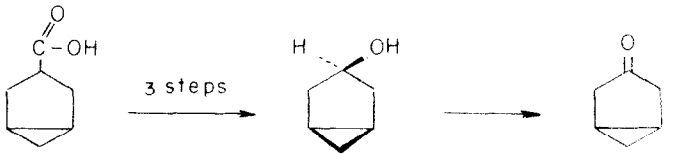
When I was added to a solution of 4 g. of sublimed potassium tert-butoxide in 11 ml. of dimethyl sulfoxide containing 0.19 g. of

water, rapid cleavage occurred at room temperature to give bicyclo-[3.1.0]hexane-3-carboxylic acid (II) (5), m.p. 30-31° in 65% yield. The dimethyl sulfoxide-nortricyclanone adduct, III, appears as the major by-product. The basic structure of II and the stereochemistry



I II III

of the acid function were established by chemical degradation. Treatment of II with methyl lithium gave the methylketone, IV. A Baeyer-

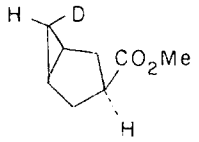


II V VII

Villiger reaction on IV followed by reduction with lithium aluminum hydride gave V. The alcohol, V, was converted to a tosylate, VI, m.p. 50.9-51.2° (lit. m.p. 50.6-50.8° for the tosylate of cis-3-bicyclo[3.1.0]hexanol) (6). Oxidation of V with Sarett's reagent gave VII. Bicyclo[3.1.0]hexan-3-one (VII) was identified as its 2,4-dini-

trophenylhydrazone which showed no melting point depression on mixing with an authentic sample (7). The stereochemical structure of V indicated that no epimerization of the carboxyl group took place in the cleavage reaction.

The stereochemical consequence of the reaction at the C-6 carbon was elucidated by carrying out the cleavage in perdeuterated solvent. Reaction of the deuterated acidic product with diazomethane gave VIII. The structure of VIII was established by nuclear magnetic



VIII

resonance spectroscopy. As shown in Fig. 1 the single methylene hydrogen (H_1) on the deuterated cyclopropyl ring appears as a triplet at 9.68τ with J_{13} = 8.0 cps. while the doublet due to the bridgehead hydrogens (H_3) appears at 8.79τ with J_{13} = 8.0 cps. This coupling constant of 8.0 cps. is only consistent with hydrogens H_1 and H_3 being cis (8,9,10). Additional evidence for the NMR based assignment of stereochemistry is obtained from the spectra of the non-deuterated acid and non-deuterated ester (Fig. 1). Both of these compounds show two sets of multiplets at high field (9.60 and 10.00τ for II) resulting from the H_1 and H_2 hydrogens coupling both with

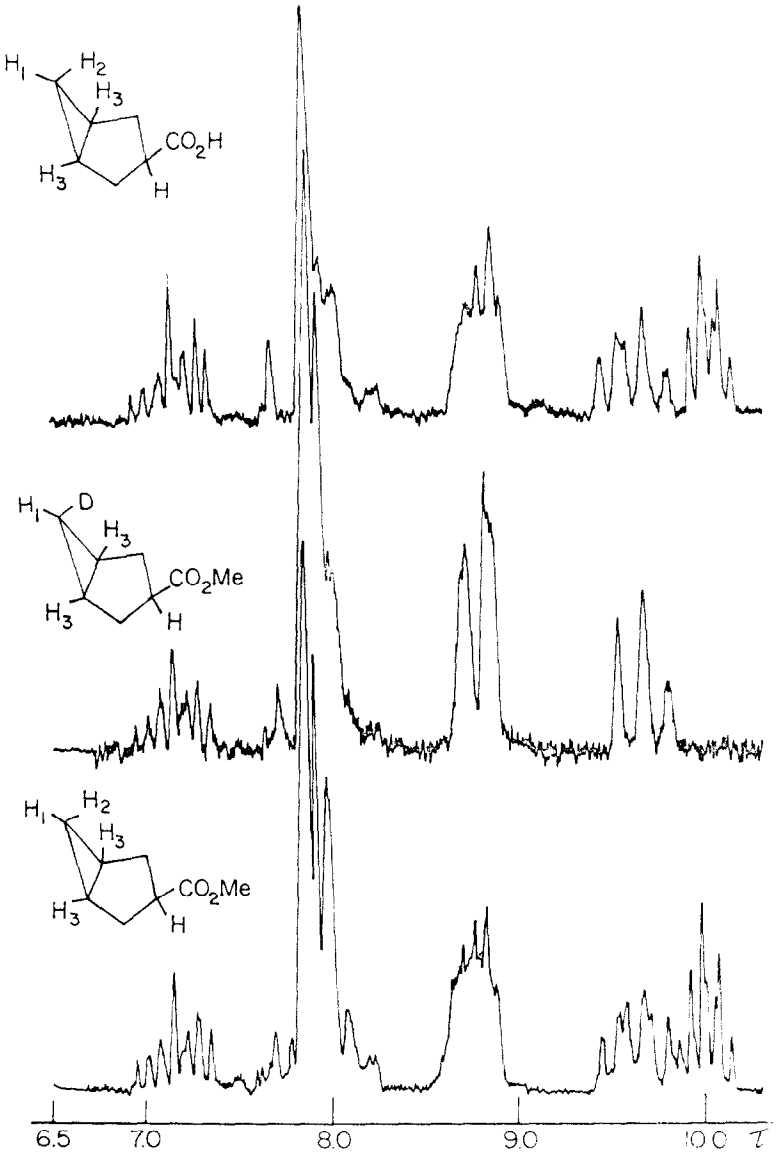


Fig. 1 Nuclear Magnetic Resonance Spectra (60 Mc.) on Varian Model A-60 Spectrometer.

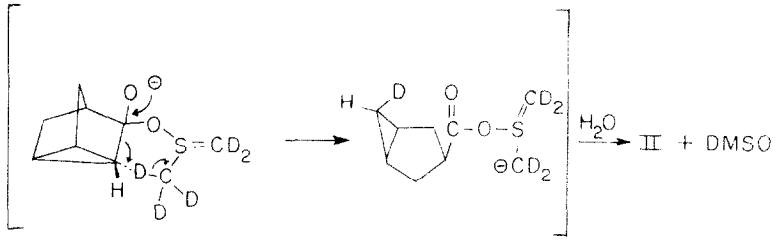
the two H_3 protons and with each other. The spectrum of II shows that whereas J_{13} is 8.0 cps. (the same as J_{13} in both the deuterated and non-deuterated esters), J_{23} is 4.1 cps. This small coupling constant is as expected for H_2 trans to H_3. The geminal coupling constant, J_{12}, is 5.5 cps., again approximately as predicted for geminal cyclopropyl hydrogens (8,9,10). The integrated ratios of the deuterated methyl ester ($H_1 : H_2 : H_3 :: 0.93 : 0.00 : 2.04$) and the non-deuterated carboxylic acid ($H_1 : H_2 : H_3 :: 1.05 : 1.05 : 1.99$) clearly illustrated the degree of stereospecificity of the cleavage reaction at the C-6 carbon.

The mechanistic implications of the complete retention of stereochemistry in the cleavage of nortricyclanone are complex. Two alternative rationalizations seem to be available; either the cleavage yields a cyclopropyl carbanion which undergoes no racemization, or the cleavage proceeds through a cyclic mechanism.

In postulating the generation of a non-racemizing cyclopropyl carbanion the investigations of Walborsky and Impastato on the Haller-Bauer cleavage of 1-benzoyl-1-methyl-2,2-diphenylcyclopropane must be considered. These authors first postulated a cyclic mechanism for their stereospecific Haller-Bauer reaction (11), but later revised their postulate to favor the formation of a non-racemizing cyclopropyl carbanion (12). Since the cleavage was run in toluene the latter mechanism seems probable.

In our cleavage the solvent system was extremely "non-asymmetric" in comparison to toluene (3). In view of Cram's studies, the complete retention of stereochemistry in dimethyl sulfoxide solution, even in the case of a cyclopropyl carbanion, would be quite surprising. However this possibility cannot be ruled out on the basis of our present results.

The alternate rational for complete retention of stereochemistry the existence of a cyclic transition state, requires consideration. Initial attack by hydroxide followed by a four-center concerted cleavage seems unlikely since an equivalence of water and tert-butoxide (complete conversion of the base to hydroxide) gives no cleavage. A more probable mode of internal proton transfer could occur through a six membered transition state if the initial attack was by the nucleophilic oxygen of the dimethyl sulfoxide anion to yield IX as illustrated below. Hydrolysis of the cleaved intermediate during the aqueous workup would yield II and dimethyl sulfoxide.



IX

Experiments aimed at discerning whether the stereospecificity of this facile cleavage is due to a stable cyclopropyl carbanion or to an intramolecular proton transfer are in progress (13).

REFERENCES

1. Presented in part before the Division of Organic Chemistry, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April, 1964; Abstracts, p. 7N.

2. We are indebted to the National Science Foundation for partial support of this research.

3. For a leading reference see D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, J. Amer. Chem. Soc., 81, 5774 (1959).

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7. We are indebted to Professor S. Winstein for an authentic sample of the 2,4-dinitrophenylhydrazone of bicyclo[3.1.0]hexan-3-one.

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13. It has been suggested by a referee that the two alternative mechanisms which have been proposed might be superimposed. This requires initial attack on the carbonyl to give a stabilized cyclopropyl carbanion which is then protonated by an intramolecular proton source. On the basis of our present results we cannot rule out this possibility.