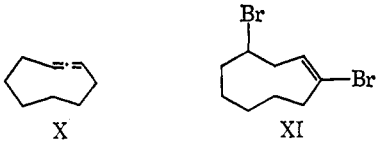
5.28 (dd) and 5.56 (dd, J = 5.5 and 10.5 Hz), 7.1–7.3 (m)] and the *cis* isomer IX (X = R = Br) [τ 3.93 (t, J = 9 Hz), 4.91 (dd, J = 5 and 12 Hz), 7.5–8.8 (m)]. The latter compound was identical with the main pyrolysis product of 9,9-dibromobicyclo[6.1.0]nonane[2b] (VII, X = Y = Br), thus suggesting that the pyrolysis conditions were too vigorous to allow the *trans* isomer VIII (X = R = Br) to be isolated.



X XI

Recently, Wedegaertner and Millam[17] reported that *trans*- and *cis*-2,3-dibromocyclononenes (VIII and IX, X = R = Br) were the products of bromine addition to cyclonona-1,2-diene (X). We have confirmed that the minor adduct (*ca.* 40%) is indeed *cis*-2,3-dibromocyclononene (IX, X = R = Br), but have shown[18] that the major adduct (*ca.* 60%) is *cis*-1,4-dibromocyclononene (XI) and not *trans*-2,3-dibromocyclononene, as previously reported.[17]

The facile $AgClO_4$-promoted ring-expansion reaction appears to be general. Furthermore, the reaction conditions described in this communication are appreciably milder than any which have previously been reported[1] for the solvolysis (in the presence or absence of Ag^+) or pyrolysis of halocarbene adducts of cyclic olefins. This has led to an increase in the synthetic potential of the ring-expansion reaction.

Acknowledgment. We thank Dr. Mark Baird for the gift of some starting materials.

(17) D. K. Wedegaertner and M. J. Millam, *J. Org. Chem.*, 33, 3943 (1968).

(18) The nmr spectrum of the major product [τ 4.17 (t, J 8.5 Hz, 1 H), 5.90 (m, 1 H), 7.1–7.7 (m, 4 H), 7.8–8.6 (m, 8 H)] corresponded closely to that reported by Wedegaertner and Millam;[17] however, it differed considerably from that of *trans*-2,3-dibromocyclononene and it seemed unlikely, both from the chemical shift (τ 5.90) and the multiplicity of its signal, that the methine proton was allylic. Double irradiation of the low-field part of the allylic region at τ 7.14 caused the triplet at τ 4.17 to collapse to a singlet and decreased the multiplicity of the signal at τ 5.90, which became virtually a triplet. These data suggested a partial structure $-CBr{=}CHCH_2CHBrCH_2-$ for this product and hence that it was either *cis*-1,4-dibromocyclononene (XI) or its *trans* isomer. The assignment of structure XI was confirmed by chemical evidence.

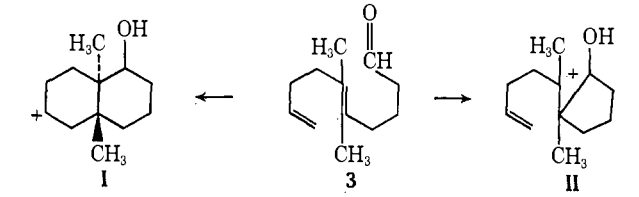
(19) Holder of a Science Research Council research studentship.

C. B. Reese, A. Shaw[19]
University Chemical Laboratory
Cambridge, England
Received January 2, 1970

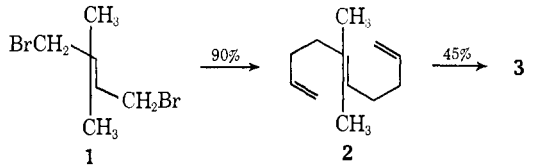
The Stereospecific Synthesis and Acid-Catalyzed Cyclization of 4,6-Dimethyl-*trans*-5,9-decadienal[1]

Sir:

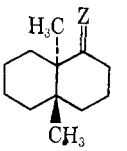
The elegant work from the laboratories of Johnson,[2a] Corey,[3] and van Tamelen[4] has reduced to laboratory practice certain aspects of the stereoselective synthesis and cyclization of squalene-like polyenes. The work of Johnson and coworkers,[2a] in particular, provides not only nonenzymic analogies that mimic the sterol biosynthetic processes but also practical synthetic procedures for the generation of *trans*-fused polycyclic systems from readily available acyclic precursors. It is the latter process that attracted our attention as a method for the generation[5] of the *trans*-13,14-dimethyl C/D ring system of such triterpenes as lanosterol and alnusenone. While such terpenoids arise in the enzymic squalene cyclization *via* a backbone rearrangement process, it appeared attractive to try to shortcut a portion of this natural process in the laboratory through the cyclization of the appropriate polyene system. Before such a synthetic program could realistically be planned, however, one further demonstration of the efficacy of the nonenzymic polyene cyclization process was necessary; namely, that the participation of an internal, tetrasubstituted double bond results in products derived from the formation of the decalin skeleton (I) in preference to those from the generation of the cyclopentane framework (II). While Johnson's work[2b,c] has shown that the cyclization of certain polyenic derivatives with internal disubstituted double bonds leads predominantly to products with the desired decalin skeleton, small amounts of cyclopentenyl derived products were also formed. In addition, these workers found that the formolysis of 6-methyl-5-heptenyl *p*-nitrobenzenesulfonate[2d] leads almost exclusively to the formation of cyclopentyl-type products as a result of the initial generation of the more stable, tertiary cyclopentyldimethyl carbonium ion. The similarity between the polyene derivatives logically desired for the triterpenoid syntheses envisaged here and the latter case above prompted an initial investigation of the mode of ring formation in the nonenzymic cyclization of a less complex model system best represented by 5,6-dimethyl-*trans*-5,9-decadienal (**3**).



I 3 II



1 2



4, Z = β-H, α-OH (38%)
5, Z = O (82%)
6, Z = H_2 (50%)
7, Z = β-H, α-OCO—⟨⟩—Br (90%)

(1) This research program was made possible by a grant (GP-7810) from the National Science Foundation. The X-ray work was supported by grants from the National Science Foundation (GB-6617X) and the National Institutes of Health (GM-12121). The authors gratefully acknowledge this support.

(2) (a) W. S. Johnson, *Accounts Chem. Res.*, 1, 1 (1968); (b) W. S. Johnson and J. K. Crandall, *J. Org. Chem.*, 30, 1785 (1965); (c) W. S. Johnson and R. B. Kinnel, *J. Amer. Chem. Soc.*, 88, 3861 (1966); (d) W. S. Johnson and R. Owyang, *ibid.*, 86, 5593 (1964).

(3) E. J. Corey, W. E. Russey, and P. R. Ortiz de Montellano, *ibid.*, 88, 4750 (1966).

(4) E. E. van Tamelen, *Accounts Chem. Res.*, 1, 111 (1968).

(5) For an alternate approach to this problem, see R. E. Ireland, D. A. Evans, D. Glover, G. M. Rubottom, and H. Young, *J. Org. Chem.*, 34, 3717 (1969).

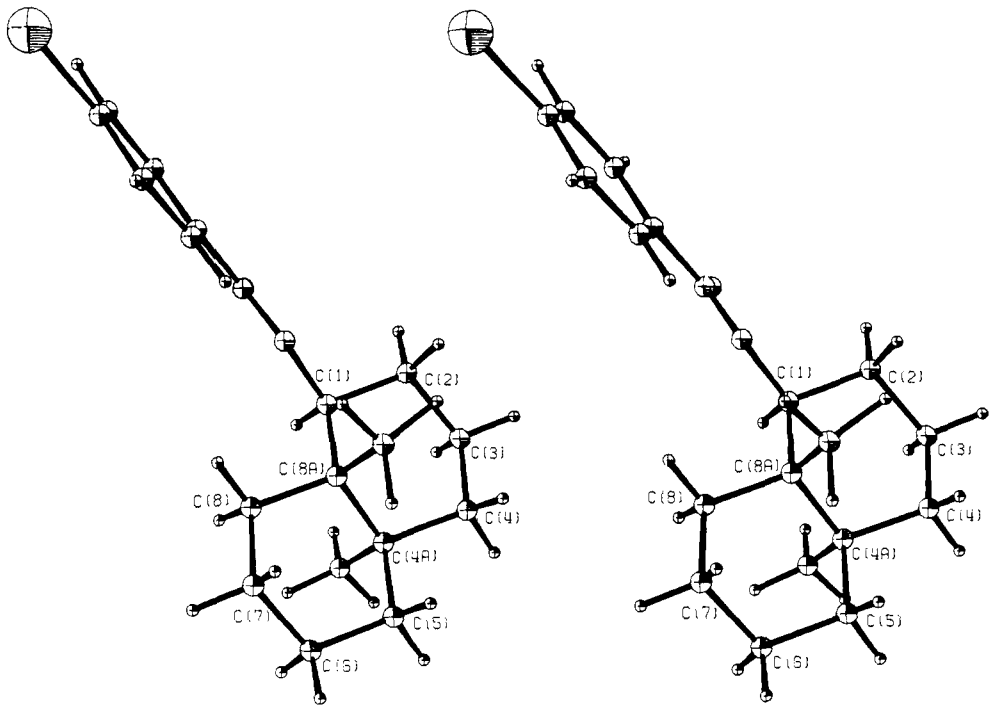


Figure 1. Stereoscopic plot of 4a,8a-dimethyl-*trans*-decal-1-yl *p*-bromobenzoate (7).

The starting material chosen for this work was the readily available dibromide **1**, for which the *trans* configuration had been established by extensive earlier work.[6] This bisallylic dibromide **1** proved to couple efficiently with several allylmagnesium halides and thereby provides an excellent stereoselective entry into the required 5,6-dimethyl-*trans*-5-decene skeleton. For the present work, the symmetrical triene **2**[7] was prepared in 90% yield with allylmagnesium chloride itself and then converted to the required aldehyde **3**[7] in 45% yield by monohydroboration with 1 equiv of disiamyl borane[8] and oxidation of the resulting dienol with Collins reagent.[9] This efficient, stereoselective scheme for the synthesis of polyenic derivatives that contain internal *trans*-dimethylated double bonds is based on the symmetry present in the initial intermediates and has been of value for the preparation of more complex analogs of potential utility for the triterpenoid syntheses themselves.

Cyclization experiments[2] were carried out in nitromethane at 0° for 10 min and stannic chloride was used as the catalyst. The initial product mixture from such treatment of the aldehyde **3** was subjected to catalytic hydrogenation (Pt–C_2H_5OH) without purification, and the saturated alcoholic products were isolated by a combination of direct crystallization and subsequent preparative thin layer chromatography of the mother liquors. The yield of the principal alcoholic product A (mp 115–117°)[7] ranged between 30 and 38% in a series of experiments. A second alcohol B (oil),[7] obtained in 5% yield in one experiment, was shown to be isomeric with the alcohol A about the hydroxyl-bearing carbon when oxidation of each substance with Collins reagent afforded the same ketone. The readily isolable alcohol A was used for subsequent structural work.

That the alcohol A was the product of a cyclization reaction that involved the central tetrasubstituted double bond was shown by the presence in the nmr (60 MHz) spectrum of two three-proton singlets at δ 0.96 and 1.0 which were assigned to the new quaternary methyl groups. The formation of a crystalline ketone[7] (mp 84–85°; $\lambda_{max}^{CCl_4}$ 5.85 μ) on oxidation[9] confirmed this fact, and the location of the carbonyl band in the infrared spectrum suggested the decalin structure **5**.[7] Evidence that, if the decalin skeleton was correct, the alcohol A did not belong to the *cis*-decalin series (and that isomerization of the central tetrasubstituted double bond had not occurred during cyclization) was readily obtained through the hydrocarbon **6**[7] (mp 97–98°). This hydrocarbon **6**, formed by Wolff–Kishner reduction of the ketone **5**, was different from 4a,8a-dimethyl-*cis*-decalin[7] (mp 88–91°), which was available by Wolff–Kishner reduction of the ketone of known[10a] stereochemistry obtained by conjugate addition of lithium dimethylcopper[10b] to 4a-methyl-1(8a)-octalin-2-one.[10a] Finally, unequivocal proof that the cyclization–hydrogenation sequence had produced 4a,8a-dimethyl-*trans*-1-decalol (**4**) as a major product was obtained through single-crystal X-ray structure analysis of the derived *p*-bromobenzoate **7**.[7] This derivative (mp 76–78°) crystallizes (petroleum ether, 30–60°) in the space group $P2_1/c$ with cell constants a = 7.075 ± 0.001, b = 25.062 ± 0.005, c = 10.312 ± 0.002 Å, and β = 106.08 ± 0.08°; D_{obsd} (flotation) = 1.38 g/cm³, D_{calcd} = 1.381 g/cm³; four molecules occur in the unit cell. The structure analysis was based on 1721 nonzero reflections,

(6) O. J. Sweeting and J. R. Johnson, *J. Amer. Chem. Soc.*, **68**, 1057 (1946).

(7) Satisfactory analytic and spectral data were obtained on all intermediates prepared.

(8) H. C. Brown and A. W. Moerikofer, *J. Amer. Chem. Soc.*, **85**, 2063 (1963).

(9) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).

(10) (a) J. A. Marshall, W. I. Fanta, and H. Roebke, *J. Org. Chem.*, **31**, 1016 (1966); (b) H. O. House, W. L. Respess, and G. M. Whitesides, *ibid.*, **31**, 3128 (1966).

collected on a General Electric–Datex diffractometer that used nickel-filtered copper radiation and a scintillation counter. The structure was solved by the usual heavy-atom methods based on bromine and full-matrix least-squares refinement of coordinates, isotropic temperature factors (bromine anisotropic), and scale factor reduced to R index to 10.6%. Hydrogen atoms were then located by a difference Fourier, and addition of these values to the structure-factor calculation and then application of anisotropic temperature factors and a second extinction factor[11] to the refinement reduced the R index to its final value of 5.6% (Figure 1).

This demonstration that the *trans*-decalin structure **4** is a major product of the acid-catalyzed cyclization of the dienal **3** is a rigorous test of the utility of the process, for the relatively low nucleophilicity of the terminal double bond might have resulted in the generation of mainly monocyclic material.[2b,c] Further work designed to incorporate the knowledge gained in this study in the triterpenoid synthetic problem itself is in progress.

(11) A. C. Larson, *Acta Crystallogr.*, 23, 664 (1967).

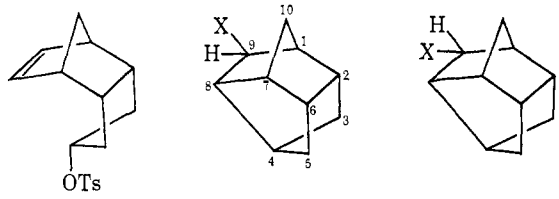
Robert E. Ireland, Marcia I. Dawson
Contribution No. 4018
The Gates and Crellin Laboratories of Chemistry
California Institute of Technology, Pasadena, California

Jon Bordner, Richard E. Dickerson
Norman Church Laboratories of Chemical Biology
California Institute of Technology, Pasadena, California 91109
Received February 23, 1970

Acetolysis of a Norbornyl-Type Tosylate. An Unusual *exo/endo* Rate Ratio

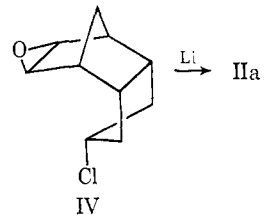
Sir:

For many years it has been found that *exo*-2-norbornyl-type tosylates containing no other functional groups solvolyze more rapidly than their *endo* isomer.[1] In norbornyl itself at 25° the *exo/endo* rate ratio for acetolysis is 280, for the tricyclo[3.2.1.0^{3,6}]octyl system it is 192, and for some substituted cases it is 10.[2] We wish to report an example of an *exo/endo* acetolysis rate ratio of less than one.



I — IIa, X = OH; b, X = OTs — IIIa, X = OH; b, X = OTs

Acetolysis of I (mp, alcohol 69.5–70.0°, tosylate 59–61°)[3,4] and saponification of the resulting acetate led to *exo*-tetracyclo[5.2.1.0.^{2,6}0^{4,8}]decan-9-ol (IIa; mp, alcohol 179–180°, tosylate 80–81°).[4] Oxidation with chromic acid[5] led to ketone (mp 184–185°)[4] and reduction of the ketone with lithium aluminum hydride led to IIIa (mp, alcohol 209–210°, tosylate 59–61°).[4] As a proof of structure of IIa an alternate synthesis was carried out by treating the chloro epoxide IV (mp 76–77°)[4] with lithium dispersion to close the ring.[2f,6] The alcohol product, obtained in 60% yield, was exactly identical with that from acetolysis of I. The nmr spectra were completely in agreement with structures



IV

IIa,b and IIIa,b. For II the dihedral angle that the methine hydrogen makes with adjacent protons on C_1 and C_8 is 70 and 90°, respectively, leading to a calculated[7] coupling constant of less than 1 Hz in both cases. The observed spectrum exhibits a broadened singlet for the methine hydrogen in both alcohol and tosylate (IIa has a width at half-height of 4 Hz, IIb has a width of 5 Hz). This is very similar to the spectrum reported for *exo*-tricyclo[3.2.1.0^{3,6}]octan-2-ol.[2f] The methine hydrogen of III makes a dihedral angle with the C_1 and C_8 protons of 60 and 27° leading to calculated coupling constants of less than 2 and 6.5 Hz, respectively. The experimental spectra show a broadened doublet with J of 6 Hz for both alcohol and tosylate. The similarities in the nmr spectrum of alcohols and tosylates suggest that ion-pair formation and internal return[8] had not occurred in the preparation of IIb and IIIb. As an additional precaution we treated IIb with sodium and naphthalene in tetrahydrofuran.[9] Alcohol in 85% yield was recovered which showed no signs of skeletal rearrangement.[10]

Also, of interest are the rates of chromic acid oxidation of the two alcohols. In 40% aqueous acetic acid at 25° ($1.79 \times 10^{-3}M$ in chromic acid and $2.68 \times 10^{-3}M$ in alcohol) the rates of oxidation were 3.50×10^{-3} l. mol^{-1} sec^{-1} for IIa and 0.257 l. mol^{-1} sec^{-1} for IIIa. The *endo* alcohol is being oxidized faster by a factor of 73 than the *exo*, a ΔF difference of 2.54 kcal/mol. This rate ratio is similar to that observed for the *endo*-5,6-trimethylene-2-norbornanols where the rate ratio is 151.[11] This is very reasonable since models

(1) This behavior does not necessarily hold true where there are other functional groups: P. G. Gassman and J. L. Marshall, *Tetrahedron Lett.*, 2429, 2433 (1968); *J. Amer. Chem. Soc.*, 88, 2822 (1966).

(2) For discussion see: (a) J. A. Berson in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963, pp 111–232; (b) H. C. Brown, *Chem. Eng. News*, 45 (7), 87 (1967); *Chem. Brit.*, 2, 199 (1966); (c) G. D. Sargent, *Quart. Rev., Chem. Soc.*, 20, 301 (1966); (d) E. J. Corey and R. S. Glass, *J. Amer. Chem. Soc.*, 89, 2600 (1967); (e) P. v. R. Schleyer, M. M. Donaldson, and W. E. Watts, *ibid.*, 87, 375 (1965); (f) R. R. Sauers, R. A. Parent, and S. B. Damle, *ibid.*, 88, 2257 (1966).

(3) Prepared by an extension and modification of work of T. H. Webb, Ph.D. Thesis, Duke University, Durham, N. C., 1962; *Diss. Abstr.*, 23, 449 (1962).

(4) All new compounds gave a satisfactory elemental analysis. Experimental details will be reported shortly in the full paper.

(5) S. J. Cristol, R. M. Sequeira, and G. O. Mayo, *J. Amer. Chem. Soc.*, 90, 5564 (1968).

(6) R. R. Sauers, R. M. Hawthorne, and B. I. Dentz, *J. Org. Chem.*, 32, 4071 (1967).

(7) M. Karplus, *J. Chem. Phys.*, 30, 11 (1959).

(8) E. C. Friedrich and S. Winstein, *J. Amer. Chem. Soc.*, 86, 2721 (1964); P. v. R. Schleyer, W. E. Watts, and C. Cupas, *ibid.*, 86, 2722 (1964).

(9) W. D. Closson, P. Wriede, and S. Bank, *ibid.*, 88, 1581 (1966).

(10) Although a small amount of epimerization had occurred, estimated by infrared spectroscopy to be about 15%. There are major differences in the infrared and nmr spectra of the epimeric alcohols and tosylates. We believe that there was less than 5% of epimeric impurity (IIIb) in the sample of tosylate (IIb) used for this experiment.