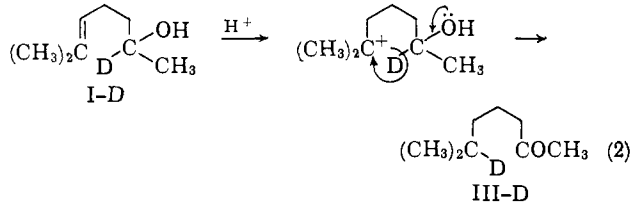
singlet (6 H) at τ 0.87. The mass spectrum was consistent with this structure, with the parent peak shifted completely to *m/e* 129, and peaks of considerably higher intensity, relative to the spectrum of the undeuterated ketone, at *m/e* 114, 97, 86, 72, 30, and 28.

Since both intra- and intermolecular hydride transfer are feasible, a crossover experiment was designed to determine which mechanism is operative in this case. A 1:2 mixture of alcohols I-D and II was heated in PPA and the ketonic products were isolated. Mass spectrometric examination of the methylheptanone showed it to be completely identical with the deuterated ketone III-D obtained above, with no detectable amount (<5%) of III. The reaction is consequently entirely intramolecular and may be described by the cyclic mechanism shown in eq. 2.



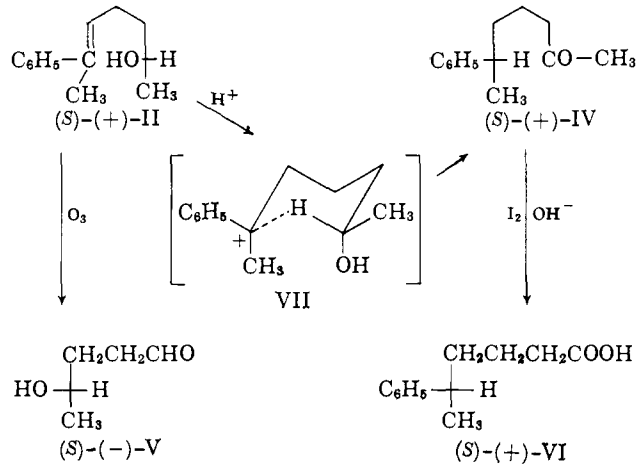
I-D

III-D (2)

It was anticipated that this isomerization, in common with other reactions involving six-membered cyclic transition states, would exhibit distinct stereospecificity. This expectation was realized by isomerizing the dextrorotatory isomer of 6-phenylhept-5-en-2-ol (II), $[\alpha]_D$ +16.9°, to 6-phenylheptanone-2 (IV, 63% yield), which proved to be optically active, $[\alpha]_D$ +2.3°. The oriented creation of a new asymmetric center simultaneous with the destruction of the original one is in accord with the demands of the cyclic transfer mechanism.

In order to determine the degree and direction of this specificity, II and IV were converted to compounds of known absolute configuration and optical purity. Ozonolysis of II, $[\alpha]_D$ +15.3°, gave (*S*)-(−)-4-hydroxyvaleraldehyde[7] (V), $[\alpha]_D$ −3.45°, while oxidation of (+)-IV with hypoiodite led to (*S*)-(+)-5-phenylcaproic acid (VI),[8] $[\alpha]_D$ +2.3°. These correlations establish first that, based on maximum rotations recorded in the literature, the reaction proceeds with an optical purity of 15%, and second that it proceeds in the steric direction shown. This result is in satisfying agreement with the prediction that the six-membered cycle would adopt a conformation resembling the cyclohexane chair (VII), with the phenyl at C-6 and the methyl at C-2 occupying equatorial positions, consonant with their larger steric requirements than methyl and hydroxyl, respectively.[11]

This discovery of an intramolecular 1,5-hydride transfer to a simple acyclic carbonium ion implies that this reaction should be much more common than heretofore realized. We are continuing studies on the



(*S*)-(+)-II

(*S*)-(+)-IV

VII

(*S*)-(−)-V

(*S*)-(+)-VI

stereochemistry of acid-catalyzed hydride transfer reactions.

(7) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **83**, 177 (1929), report $[\alpha]_D$ −7.8° for V.

(8) The absolute configuration of (+)-VI is assigned from its synthesis[9] from (+)-β-phenylbutyric acid; the correlation of (+)-β-phenylbutyric acid with (*R*)-(−)-hydratropic acid is summarized by J. H. Brewster and M. W. Kline, *J. Am. Chem. Soc.*, 74, 5180 (1952). Since 3-phenyl-1-bromobutane with $[\alpha]_D$ +6.03° gave VI with $[\alpha]_D$ +2.01°, and the highest recorded rotation of 3-phenyl-1-bromobutane[10] is 104.3°, the maximum rotation of VI is at least 34.8°.

(9) P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **93**, 749 (1931).

(10) D. J. Cram, *J. Am. Chem. Soc.*, 74, 2138 (1952).

(11) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 236.

(12) Alfred P. Sloan Foundation Research Fellow, 1963–1965.

(13) National Institutes of Health Predoctoral Fellow, 1964–1965.

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The Stereoselective Total Synthesis of Alantolactone

Sir:

Alantolactone (**15**) and its derivatives play a premier role in the structural elucidation of numerous eudesmane sesquiterpenes.[1] We delineate in this communication a stereoselective total synthesis of racemic alantolactone which confirms the structure[2] of the natural compound and illustrates an approach to related sesquiterpene lactones. The essential stages of the present synthesis involve: (1) construction of the carbocyclic framework *via* cationic olefin cyclization (**2** → **3**); (2) modification of the carbon framework by stereoselective photooxygenation of olefin **9** and dehydration of the related dihydro alcohol (**11** → **12**); (3) application of the recently discovered α-methylene-γ-butyrolactone synthesis (**12** → **15**).[3]

Alkylation of Hagemann's ester[4] with 4-bromobutene[5] using sodium hydride in refluxing toluene followed by saponification and thermal decarboxylation of the resulting keto acid afforded unsaturated ketone **1** [λ_{max}^{EtOH} 243 mμ (ε 12,000)]. Alcohol **2**, obtained by addition of ethereal methyllithium to ketone **1**, cyclized smoothly in formic acid under conditions employed by Johnson and co-workers for analogous compounds.[6] The resulting formate **3** was directly saponified and the alcohol **4** thus produced was oxidized with chromic acid reagent[7] giving octalone **5** whose structure was con-

(1) *Cf.* W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1960); W. Herz, G. Högenauer, and A. Romo de Vivar, *J. Org. Chem.*, **29**, 1700 (1964), and references therein; V. Benešová, V. Herout, and W. Klyne, *Collection Czech. Chem. Commun.*, 27, 498 (1962).

(2) J. A. Marshall and N. Cohen, *J. Org. Chem.*, **29**, 3727 (1964), and references therein.

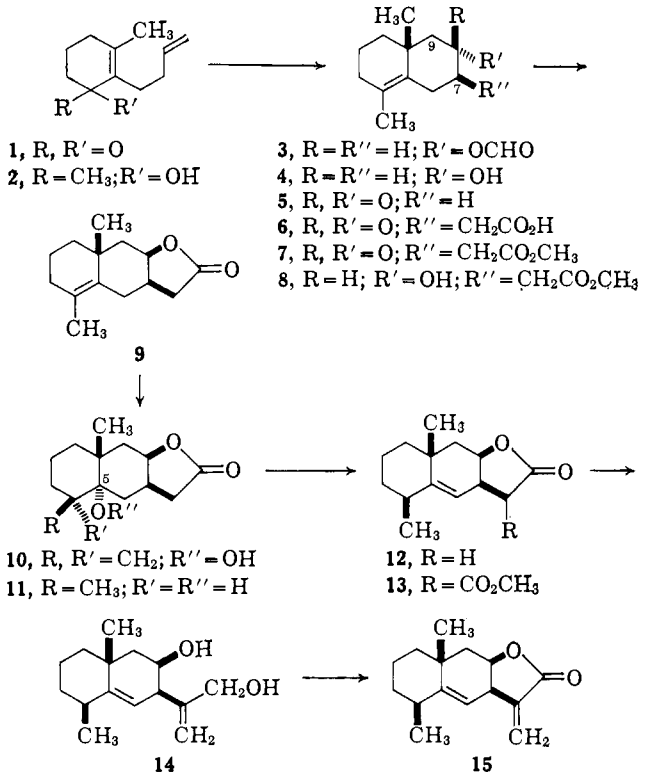
(3) J. A. Marshall and N. Cohen, *Tetrahedron Letters*, No. 30, 1997 (1964).

(4) A. J. B. Edgar, S. H. Harper, and M. A. Kazi, *J. Chem. Soc.*, 1083 (1957).

(5) R. P. Linstead and H. N. Rydon, *ibid.*, 1995 (1934).

(6) W. S. Johnson, W. H. Lunn, and K. Fitzi, *J. Am. Chem. Soc.*, **86**, 1972 (1964).

(7) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).



firmed by its n.m.r. spectrum [$\delta_{TMS}^{CCl_4}$ 1.69 (vinyl CH_3), 1.00 p.p.m. (angular CH_3); essential absence of absorption in the range 5–7 p.p.m. (vinyl H)].

Alkylation of octalone **5** with ethyl bromoacetate *via* the Stork enamine procedure[8] and saponification of the crude product afforded keto acid **6** (m.p. 128–130°) in 53% over-all yield (70% crude yield). The n.m.r. spectrum of the pyrrolidine enamine [$\delta_{TMS}^{CCl_4}$ 4.05 p.p.m. (vinyl H; half-height line width = 10 c.p.s.)] derived from octalone **5** provided assurance that the Δ^7-isomer was the predominant species. Had the Δ^8-isomer been the predominant enamine a relatively sharp[9] (half-height line width < 4 c.p.s.) vinyl hydrogen signal would be expected. The high yield of C-alkylation product **6** constitutes additional evidence for this conclusion since steric effects should render alkylation difficult at C-9 and thus cause the Δ^8-enamine isomer to alkylate principally on the nitrogen atom.[8]

Keto acid **6** was esterified (diazomethane) and the keto ester **7** was reduced with methanolic potassium borohydride giving lactone **9** (λ_{max}^{film} 5.63 μ) directly in 75% yield. The remainder of the material consisted of hydroxy ester **8** which was readily separated from lactone **9** by chromatography and oxidized to keto ester **7** in high yield, thus increasing the over-all yield of lactone **9**.

Photooxygenation of unsaturated lactone **9** according to the procedure of Nickon and Bagli[10] afforded hydroperoxide **10** [m.p. 117.5–118.5°; $\lambda_{max}^{CHCl_3}$ (μ) 2.86, 3.00 (OOH), 5.67 (lactone CO), and 6.08, 11.0 (C=CH_2); $\delta_{TMS}^{CHCl_3}$ 5.19, 4.88 p.p.m. (C=CH_2)]. The stereochemistry of the newly formed asymmetric center at C-5 in **10** is assigned by analogy with the stereochemical preference for α-attack by oxygen on steroidal olefins under comparable conditions. The marked tendency toward abstraction of a primary (*vs.* secondary) allylic hydrogen cannot be explained at present. Whether this preference results from steric or electronic factors is currently under investigation.

Since recrystallization caused its partial decomposition, hydroperoxide **10** was reduced directly to alcohol **11** [m.p. 183.5–184.5°; $\lambda_{max}^{CHCl_3}$ (μ) 2.79, 2.86 (OH), and 5.68 (lactone CO)] by hydrogenation over platinum in acetic acid.

Alcohol **11** upon treatment with thionyl chloride in pyridine[11] gave unsaturated lactone **12** [m.p. 90–91°; $\delta_{TMS}^{CCl_4}$ 5.23 (H-6; doublet, J = 3 c.p.s.), 4.82 (CH–O–), 1.29 (angular CH_3), and 1.19 p.p.m. (C-4 CH_3 doublet, J = 7 c.p.s.)][12] in 75% yield. Carbomethoxylation of lactone **12** using sodium hydride in dimethyl carbonate followed by reduction of the resulting enolate of lactone ester **13** (not isolated) with lithium aluminum hydride in 1,2-dimethoxyethane after removal of the excess dimethyl carbonate yielded diol **14** [m.p. 150.5–151°; $\lambda_{max}^{CHCl_3}$ (μ) 3.0, 6.08, and 10.87; $\delta_{TMS}^{CHCl_3}$ 5.46, 5.13 (C=CH_2), and 5.34 p.p.m. (H-6, doublet, J = 5 c.p.s.)]. Oxidation of diol **14** with manganese dioxide[13] in benzene afforded racemic alantolactone, m.p. 58–59°, whose identity with (+)-alantolactone[14] was established by superimposition of their richly detailed infrared spectra. Additional confirmation of identity was provided by t.l.c. mobility and gas chromatographic retention times (peak enhancement).

Acknowledgment. We thank the Public Health Service for support of this work through a Research Grant (AI-04965, National Institute of Allergy and Infectious Diseases) and a Fellowship (5-Fl-Gm-19,839).

(8) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963); J. Szmuszkovicz, *Advan. Org. Chem.*, **4**, 1 (1963).

(9) Allylic 1,3-coupling often causes peak broadening. *Cf.* T. A. Wittstruck, S. K. Malhotra, and H. J. Ringold, *J. Am. Chem. Soc.*, **85**, 1699 (1963).

(10) A. Nickon and J. F. Bagli, *ibid.*, **83**, 1498 (1961).

(11) *Cf.* V. Benešová, V. Herout, and F. Sǒrm, *Collection Czech. Chem. Commun.*, **26**, 1350 (1961).

(12) Compare with the published spectrum of alantolactone (ref. 2).

(13) O. Mancera, G. Rosenkranz, and F. Sondheimer, *J. Chem. Soc.*, 2189 (1953).

(14) Obtained from Chemical Procurement Inc. and purified by crystallization and chromatography to give material of m.p. 76–77°. *Cf.* ref. 2.

(15) Fellow of the National Institute of General Medical Sciences, Public Health Service, 1963–1965.

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Tetramethylcyclopropanone. I. Isolation and Characterization

Sir:

A number of attempts to prepare cyclopropanones have been reported in the chemical literature.[1,2] In general, derivatives of cyclopropanones but not the cyclopropanones themselves were isolated. However, a number of unsubstantiated reports of stable cyclo-

(1) Recently successful syntheses of hetero analogs of cylopropanones have been reported: (a) F. D. Greene and J. C. Stowell, *J. Am. Chem. Soc.*, **86**, 3569 (1964); (b) H. E. Baumgarten, *ibid.*, **84**, 4975 (1962); (c) *ibid.*, **85**, 3303 (1965); (d) J. C. Sheehan and I. Lengyel, *ibid.*, **86**, 746, 1356 (1964).

(2) (a) P. Lipp and R. Koster, *Ber.*, **64**, 2823 (1931); (b) P. Lipp, J. Buchkremer, and H. Seeles, *Ann.*, **499**, 1 (1932); (c) A. Kende, Ph.D. Dissertation, Harvard University, Cambridge, Mass., 1957; (d) W. L. Mock, Ph.D. Dissertation, Harvard University, Cambridge, Mass., 1965.