Synthesis of Substituted *cis*-Cyclodecenes from Cyclooctanone

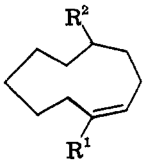
James A. Marshall and Charles J. V. Scanio

Department of Chemistry, Northwestern University, Evanston, Illinois

Received March 9, 1965

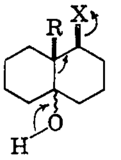
An efficient synthetic route to *cis*-cyclodecenes such as I has been developed. The key step in this sequence involves fragmentation of 1,3-diol monosulfonates **6**, **8**, **14**, and **15** with a suitable base. Preparation of these esters from dione **3** is described.

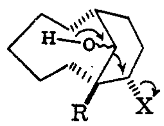
The discovery in recent years of a class of sesquiterpenes containing a ten-membered ring[1] has stimulated interest in the chemistry and synthesis of cyclodecane derivatives.[2] The present report discloses a straightforward synthetic pathway to the substituted *cis*-cyclodecenes exemplified by formula I.



I, $R^1 = H$; $R^2 = CH_2OH$, CHO, CO_2H
$R^1 = CH_3$; $R^2 = CH_2OH$

A communication[3] describing a fragmentation[4] of the bicyclo[4.4.0]decane carbon framework (scheme A) prompted our consideration of alternative bicyclic carbon skeletons which might yield a ten-membered ring *via* an analogous fragmentation route. We selected the bicyclo[5.3.1]undecane system for our initial studies (scheme B) because of the potential availability of the prerequisite diol derivatives and the applicability of the projected route to isoprenoid compounds.


A


B

The required starting material, bicyclo[5.3.1]undecane-8,11-dione (**3**, Chart I), was readily prepared by cyclization of methyl 3-(2-oxocyclooctyl)propanoate (**1**) using sodium hydride in 1,2-dimethoxyethane. Dione **3** was thus obtained as its sodio enolate which was neutralized with ethereal acetic acid to preclude cleavage of the labile 1,3-diketone system. Although **3** is a substituted cyclohexane-1,3-dione, its spectral properties fail to indicate the presence of enol II. The infrared spectrum displays strong sharp bands at 5.8 and 5.9 μ in accord with its formulation as both a cyclohexanone and a cyclooctanone.[5] The enol form II was anticipated because Prelog and co-workers[6] have shown that Bredt's rule need not apply to bicyclo[5.3.1]undecenones by preparing conjugated ketone III.

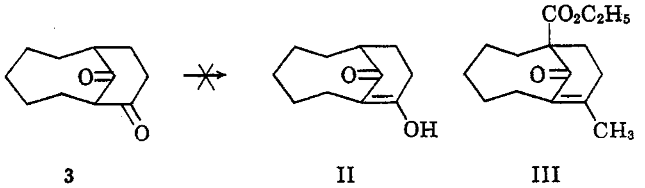
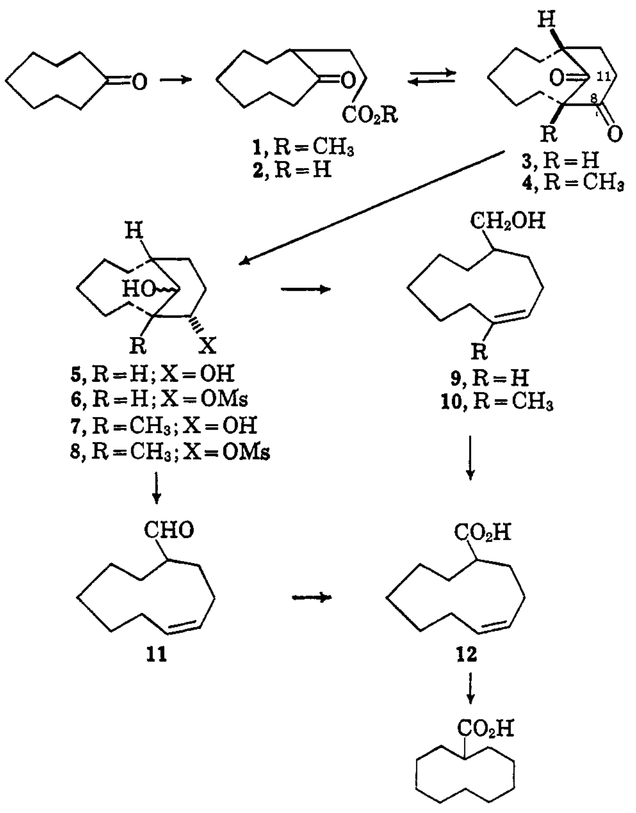

3 II III

Chart I


1, $R = CH_3$
2, $R = H$
3, $R = H$
4, $R = CH_3$
5, $R = H; X = OH$
6, $R = H; X = OMs$
7, $R = CH_3; X = OH$
8, $R = CH_3; X = OMs$
9, $R = H$
10, $R = CH_3$
11
12
13

Having demonstrated a reliable route to the requisite bicyclo[5.3.1]undecane framework we now consider functional modifications necessary for our application of scheme B.

Dione **3** was reduced to diol **5** only after prolonged treatment with excess sodium borohydride. A study of the reaction progress by infrared analysis of aliquots removed after various time intervals revealed complete reduction of the cyclohexanone (C-8) carbonyl group within several hours. However, reduction of the cyclooctanone (C-11) carbonyl group required 40 hr. for completion. This observation parallels the rela-

---

[1] A comprehensive review is presented by F. Šorm, *Pure Appl. Chem.*, **2**, 533 (1961).

[2] See J. Sicher [*Progr. Stereochem.*, **3**, 202 (1962)] for a review of work prior to 1962.

[3] P. S. Wharton, *J. Org. Chem.*, **26**, 481 (1961). An application of this general scheme to a bicyclo[4.3.0]nonane derivative has also been reported: E. J. Corey, R. B. Mitra, and H. Uda, *J. Am. Chem. Soc.*, **86**, 485 (1964).

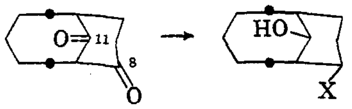
[4] C. A. Grob, IUPAC Kékulé Symposium, London, Sept. 1958, Butterworth and Co. (Publishers) Ltd., London, 1959, p. 114.

[5] Dimedone shows an enol-chelate band at 6.32 μ: D. F. Martin, M. Shamma, and W. C. Fernelius, *J. Am. Chem. Soc.*, **80**, 5851 (1958). The carbonyl group of cyclooctanone absorbs at 5.90 μ.

[6] V. Prelog, P. Barman, and M. Zimmermann, *Helv. Chim. Acta*, **32**, 1284 (1949).

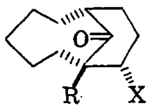
tive rates reported by Brown and Ichikawa[7] for reduction of cyclohexanone and cyclooctanone with sodium borohydride. Steric factors should augment intrinsic differences between the two carbonyl groups of dione **3**.

Synthesis of a fragmentable bicyclic precursor (scheme B) from dione **3** requires stereoselective reduction of the C-8 carbonyl grouping to the equatorial alcohol (*e.g.*, **5a**) in order to satisfy the rigorous *trans*-coplanar geometry required of the breaking bonds in the transition state.[4] Selective esterification of the C-8 alcohol function of diol **5** constitutes a second prerequisite of this scheme.



3

5a, X = OH
14, X = OTs
15, X = OMs



16, X = OH; R = H
17, X = OTs; R = H
18, X = OMs; R = H
19, X = OMs; R = CH_3

Molecular models support the assumption that the C-8 carbonyl group in dione **3** is not unusually hindered toward axial attack by an external nucleophile such as sodium borohydride. In fact, the diaxial geometry required of the cyclooctane ring fusion renders equatorial attack difficult. Therefore[8] the equatorial alcohol **5a** should constitute the major diol isomer. The configurational assignment at the 11-carbon in diol **5a** is somewhat tenuous owing to conformational uncertainties regarding the cyclooctane ring in the presumed intermediate ketol **16**. However, the configuration of C-11 should be inconsequential to the success of the fragmentation reaction[4] (scheme B). Evidence presented below confirms the validity of these *a priori* suppositions.

A crystalline diol (presumably **5a**) was obtained in 63% yield from the crude mixture of diols **5**. This crystalline diol afforded an oily monotosylate derivative (**14**, see below) which was oxidized to crystalline keto tosylate **17** in 94% yield. The monomesylate of diol **5a** was obtained as a crystalline compound, m.p. 110–115°, in 97% yield and therefore constitutes a more satisfactory derivative. Oxidation of this substance afforded keto mesylate **18**. Both ketone derivatives **17** and **18** exhibit a band at 5.90 μ indicative of a cyclooctanone carbonyl grouping. Thus, selective esterification of the C-8 alcohol of diol **5a** is established. The crystalline keto mesylate **18** was obtained in 78% yield from crude diol **5** thereby confirming the highly stereoselective nature of the reduction at C-8 in dione **3**.

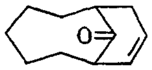
Tosylate **14** underwent facile fragmentation upon treatment with potassium *t*-butoxide giving *cis*-4-cyclodecenecarboxaldehyde (**11**). The structure of this aldehyde was confirmed by a strong band at 14 μ (*cis* HC=CH)[9] in its infrared spectrum and a doublet at 9.60 p.p.m. (CHC*H*O, J = 1 c.p.s.) in its n.m.r. spectrum. Additional proof of structure was provided by oxidation followed by hydrogenation whereupon cyclodecanecarboxylic acid, m.p. 50–51°, was obtained in 64% yield. The ease with which tosylate **14** undergoes fragmentation corroborates the stereochemistry of C-8 in diol **5**. The stereochemistry of the double bond in unsaturated aldehyde **11** can also be derived from mechanistic considerations.[4]

Aldehyde **11** is highly susceptible to oxidation, but a satisfactory yield was obtained when special precautions were taken to exclude air during the isolation procedure.

An alternative method for the fragmentation of tosylate **14** employed lithium aluminum hydride as a combined basic initiator and reducing agent; *cis*-4-cyclodecenylmethanol (**9**) was thus obtained in 78% yield. A similar reductive fragmentation of mesylate **15** afforded alcohol **9** in 70% yield. This latter reaction was notably slower than the analogous conversion of tosylate **14** to alcohol **9**. Aldehyde **11** undoubtedly intervenes in these transformations, but the excess lithium aluminum hydride causes subsequent reduction to the alcohol **9**. The greater ease of product isolation constitutes an advantage offered by this procedure over that employing potassium *t*-butoxide. A stereochemical advantage may also be envisioned if reduction of the intermediate aldehyde **11** is faster than its epimerization under these reaction conditions. Investigation of this point is forthcoming. The structure of alcohol **9** was ascertained from spectral properties and through oxidation to *cis*-4-cyclodecenecarboxylic acid (**12**).

Treatment of the crude diol mixture **5** with 1 equiv. of mesyl chloride in pyridine followed by reductive fragmentation of the crude mesylate afforded alcohol **9** in 70% yield. This conversion provides further proof for the stereoselective reduction of the C-8 carbonyl grouping of dione **3**.

Attempts to obtain acid **12** *via* fragmentation of keto tosylate **17** using potassium hydroxide in dioxane or methanol were unsuccessful.[10] An unsaturated cyclooctanone (presumably **20**) was obtained instead. This finding is concordant with the observation that the C-11 carbonyl grouping of dione **3** is but slowly reduced by sodium borohydride. Apparently addition of hydroxide to the carbonyl grouping of keto tosylate **17** is likewise slow.



20

The methylated cyclodecenylmethanol **10** was prepared prior to projected applications of the above methods to the synthesis of isoprenoid substances. Methylation of dione **3** using sodium hydride and methyl iodide afforded dione **4**. Reduction of dione **4** was smoothly effected by lithium aluminum hydride to give a crystalline mixture of diols **7** epimeric at C-11. Diol mixture **7** was converted to an oily monomesylate which was oxidized, without purification, to crystalline keto mesylate **19**. The band at 5.90 μ in the infrared spectrum of this material verified the presence of a cyclooctanone carbonyl group. The n.m.r. spectrum of keto mesylate **19** displayed a four-line

---

[7] H. C. Brown and K. Ichikawa, *Tetrahedron*, **1**, 221 (1957).

[8] *Cf.* W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956); J. C. Richer, *J. Org. Chem.*, **30**, 324 (1965).

[9] K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p. 24.

[10] This approach to fragmentative ring expansion was first applied by Stork and Landesman to the synthesis of 4-cyclooctanecarboxylic acid from the methiodide of 2-pyrrolidinobicyclo[3.3.1]nonan-9-one: G. Stork and H. Landesman, *J. Am. Chem. Soc.*, **78**, 5129 (1956). We were unable to prepare the analog (**16**, R = H; X = C_4H_8N) from cyclooctanone using this procedure.

pattern[11] at 4.57 p.p.m. due to the axial C-8 hydrogen, thus confirming the anticipated stereochemistry of this intermediate. The mixture of C-11 epimeric diol monomesylates **8** was converted to *cis*-5-methyl-4-cyclodecenylmethanol (**10**) in 88% yield through the action of lithium aluminum hydride in 1,2-dimethoxyethane.

Experimental[12]

Methyl 3-(2-Oxocyclooctyl)propanoate (1).—The pyrrolidine enamine of cyclooctanone was prepared according to Kuehne[13] except that toluene was used for the azeotrope procedure. The yield of the enamine, b.p. 79–81° (0.5 mm.), was 67.5%.

Alkylation of the cyclooctanone pyrrolidine enamine with methyl acrylate was accomplished by the procedure of Stork and co-workers.[14] The keto ester **1**, b.p. 94–95° (0.2 mm.), $n^{20}\text{D}$ 1.4756 [lit.[15] b.p. 152° (4 mm.), $n^{20}\text{D}$ 1.4754], was obtained in 64% yield: $\lambda_{\max}^{\text{film}}$ 5.75 (ester CO), 5.90 (cyclooctanone CO), 7.92, 8.30, and 8.51 μ.

Bicyclo[5.3.1]undecane-8,11-dione (3).—The mineral oil was removed from 12.0 g. of 51% sodium hydride dispersion through successive washings with benzene and 1,2-dimethoxyethane (DME). A stirred suspension of the resulting sodium hydride in 200 ml. of anhydrous DME containing 13.8 g. of keto ester **1** was heated at reflux for 12 hr.[12c] The resulting yellow paste was cooled and a solution containing 30 ml. of acetic acid in 200 ml. of anhydrous ether was carefully added. The mixture was washed with a small portion of water and the product was isolated with ether.[12b] The dione **3**, b.p. 95–98° (0.3 mm.), was obtained in 84% yield (13.4 g.): $\lambda_{\max}^{\text{film}}$ 5.80 (cyclohexanone CO), 5.90 (cyclooctanone CO), 7.40, 7.50, 7.60, 7.92, 8.15, 8.55, 8.79, 9.00, 9.41, and 9.80 μ. The analytical sample, b.p. 97–98° (0.3 mm.), $n^{20}\text{D}$ 1.5147, was obtained by redistillation.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.0; H, 8.7.

When water rather than acetic acid was used to destroy the excess sodium hydride and liberate dione **3** from its enolate, the yield was drastically decreased owing to the formation of the acidic cleavage product **2**. This keto acid, b.p. 130–135° (0.2 mm.), was obtained from keto ester **1** or dione **3** by mild alkaline hydrolysis.

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.8; H, 9.2.

Bicyclo[5.3.1]undecane-8α,11α-diol (5a).[12e]—A solution containing 10.8 g. of dione **3** and 3.4 g. of sodium borohydride in 250 ml. of absolute ethanol was stirred at room temperature for 40 hr.[12c] The reaction mixture was cautiously added to an ice–water mixture containing 6 ml. of acetic acid to decompose the excess sodium borohydride and diol **5** was isolated with ether.[12b] Recrystallization of the resulting solid from ether–hexane afforded 3.2 g., m.p. 115–115.5°. A second crop furnished an additional 3.8 g., m.p. 114–115° (63% over-all yield): $\lambda_{\max}^{\text{CHCl}_3}$ 2.79, 2.90 (OH), 7.92, 9.09, 9.23, 9.41, 9.72, and 9.92 μ. A residual 3.3 g. of oil, whose infrared spectrum was similar to that of the crystalline material, remained after removal of the solvent from the mother liquor. The analytical sample, m.p. 115–115.5°, was obtained after one recrystallization of the first crop from ether–hexane.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.8; H, 11.2.

The crystalline diol was converted to a diacetate, m.p. 66–67° from hexane.

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.1; H, 9.0.

Infrared analysis of an experiment performed under the conditions described above revealed a substantially faster decrease in the intensity of the 5.80-μ (cyclohexanone CO) band relative to the 5.90-μ (cyclooctanone CO) band. From these studies we infer that reduction of the cyclohexanone carbonyl group is complete within 2 hr. whereas the cyclooctanone carbonyl group requires 40 hr. before reduction is complete.

***cis*-4-Cyclodecenecarboxaldehyde (11).**—A solution of 3.60 g. of diol **5a** in 100 ml. of pyridine was cooled to 0° and 4.00 g. of *p*-toluenesulfonyl chloride was added portionwise under nitrogen over a 0.5-hr. period. The cooling bath was removed and the mixture was allowed to stand at room temperature for 4 days.[12c] The solution was poured onto ice and thoroughly extracted with ether, and the combined extracts were washed with water, 5% aqueous sulfuric acid, and saturated brine and dried over anhydrous magnesium sulfate. The oily residue which remained after removal of ether was chromatographed on 625 ml. of silicic acid.[16] Elution with 10% ether in benzene afforded 3.08 g. (46%) of oily tosylate **14**: $\lambda_{\max}^{\text{film}}$ 2.80 (OH), 6.22 (aromatic C=C), 8.40, 8.50, 8.82, 9.07, 9.21, 10.94, 11.20, 11.66, 11.85, 12.23, 13.11, and 13.60 μ.

Reaction times of 6 and 40 hr. at room temperature followed by chromatography afforded tosylate **14** in 31 and 39% yields, respectively.

To a solution of 923 mg. of chromatographed tosylate **14** in 26 ml. of dry *t*-butyl alcohol was added 6.8 ml. of 1.2 *M* potassium *t*-butoxide. The mixture was allowed to stand at room temperature for 0.5 hr. and was heated under reflux for an additional 0.5 hr.[12c] The cooled mixture was neutralized by addition of 0.4 ml. of concentrated hydrochloric acid followed by titration to the phenolphthalein end point with 0.10 *M* hydrochloric acid (6.0 ml. required). Solvent was removed from the neutral mixture on a rotary evaporator below 40° and the residue was transferred with hexane to a chromatographic column packed with 100 ml. of silicic acid.[16] Elution with 25% hexane in benzene afforded 272 mg. (61%) of colorless oil: $\lambda_{\max}^{\text{film}}$ 3.35 (C=CH), 3.70 (aldehyde CH), 5.80 (aldehyde CO), 14.00 (*cis* CH=CH), 6.59, 6.90, and 13.49 μ; $\delta_{\max}^{\text{CCl}_4}$ = 5.34–5.68 (H—C=C, complex multiplet) and 9.60 p.p.m. (H—C=O, doublet, J = 1 c.p.s.).

The semicarbazone derivative had m.p. 170–170.5° after three recrystallizations from methanol.

Anal. Calcd. for $C_{12}H_{21}N_3O$: C, 64.54; H, 9.48; N, 18.82. Found: C, 64.6; H, 9.5; N, 18.6.

Isolation by addition of water and extraction with ether[12b] furnished aldehyde **11** in 34% yield after chromatography on silicic acid.[16]

Bicyclo[5.3.1]undecane-8α,11α-diol[12e] Monomethanesulfonate (15).—The procedure of Eschenmoser, *et al.*,[17] was followed using 552 mg. of diol **5a** and 400 mg. of methanesulfonyl chloride in 1.5 ml. of dry pyridine. After standing for 12 hr. at room temperature,[12c] the reaction mixture was poured onto crushed ice and the product was isolated with ether,[12b] affording 786 mg. of yellow solid: $\lambda_{\max}^{\text{CCl}_4}$ 2.83 (OH), 7.40, 8.49, 8.90, 10.36, 10.70, 10.98, and 11.60 μ. Recrystallization from ethyl acetate–heptane gave 766 mg. (97%) of white solid, m.p. 110–115° dec. The analytical sample, m.p. 124–124.5° dec., was obtained after an additional five recrystallizations from the same solvent.

Anal. Calcd. for $C_{12}H_{22}O_4S$: C, 54.94; H, 8.45; S, 12.22. Found: C, 54.6; H, 8.5; S, 12.0.

***cis*-4-Cyclodecenylmethanol (9). A. By Reductive Fragmentation of Tosylate 14.**—To a solution of 109 mg. of lithium aluminum hydride in 5 ml. of dry 1,2-dimethoxyethane (DME) was added a solution of 480 mg. of tosylate **14** in 5 ml. of DME over a 0.5-hr. period. After 10 hr. at room temperature, the complex was decomposed with 0.20 ml. of water and 0.16 ml. of 10% sodium hydroxide. A 30-ml. portion of ether was added to assist granulation of the precipitate, and the mixture was stirred for 2 hr. and filtered. Solvent was removed from the filtrate leaving 212 mg. of yellow oil: $\lambda_{\max}^{\text{film}}$ 2.99 (OH), 14.05 (*cis* HC=CH), 9.48, 9.64, 9.79, and 10.29 μ. Distillation gave

---

[11] L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p. 90.

[12] (a) Melting points were deternined on a Fisher-Johns hot stage. (b) The isolation procedure consisted of thorough extraction and back extraction with the specified solvent, washing the combined extracts with saturated brine, and drying the extracts over anhydrous magnesium sulfate. The solvent was removed from the filtered extracts under reduced pressure on a steam bath. (c) The apparatus described by W. S. Johnson and W. P. Schneider [*Org. Syn.*, **30**, 18 (1950)] was used to maintain a nitrogen atmosphere over the reaction mixtures. (d) Microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, Ill. (e) The prefixes α and β designate the relative stereochemistry of an asymmetric center in a racemic substance. The prefix *dl* is omitted from the names of racemic materials.

[13] M. E. Kuehne, *J. Am. Chem. Soc.*, **81**, 5400 (1959).

[14] G. Stork, A. Brizzolara, H.Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 217 (1963).

[15] Z. Eckstein, A. Sacha, and W. Sobótka, *Roczniki Chem.*, **34**, 1329 (1960); *Chem. Abstr.*, **55**, 18722*d* (1961).

[16] H. Brockmann and H. Muxfeldt, *Ber.*, **89**, 1379 (1956).

[17] A. Eschenmoser and A. Frey, *Helv. Chim. Acta*, **35**, 1660 (1952).

185 mg. (78%) of colorless oil, b.p. 60–70° (bath temperature) at 0.05 mm.

Anal. Calcd. for $C_{11}H_{20}O$: C, 78.52; H, 11.98. Found: C, 78.6; H, 11.9.

B. **By Reductive Fragmentation of Mesylate 6.**—A solution containing 674 mg. of mesylate **6** (m.p. 110–115°) and 198 mg. of lithium aluminum hydride in 14 ml. of dry DME was stirred at room temperature for 10 hr. The product which was isolated as described above contained a significant amount of unreacted starting material as evidenced by the characteristic infrared band at 8.49 μ. Therefore, the crude material was heated under reflux with an additional 198 mg. of lithium aluminum hydride in 15 ml. of DME for 10 hr. Isolation of the product as described above followed by distillation afforded 303 mg. (70%) of colorless alcohol **9**, b.p. 60–70° (bath temperature) at 0.05 mm. The infrared spectrum of this material was identical with that of alcohol **9** prepared from tosylate **14**.

C. **From Dione 3 *via* Crude Diol 5 and Mesylate 6.**—A solution containing 1.09 g. of dione **3** and 0.34 g. of sodium borohydride in 35 ml. of ethanol was allowed to stand at room temperature for 56 hr. The diol was isolated as previously described and the entire crude sample was dissolved in 3 ml. of pyridine and treated with 0.665 g. of methanesulfonyl chloride for 2 hr. at 0° and 1 hr. at room temperature. The crude solid monomesylate (1.37 g., 93%) was isolated according to the procedure described above. A 0.901-g. sample of this crude mesylate was refluxed with 0.262 g. of lithium aluminum hydride in 20 ml. of 1,2-dimethoxyethane. The reaction mixture was treated according to the above procedure and 462 mg. (80%) of alcohol **9** was thus isolated. Distillation gave 403 mg. (70%), b.p. 60–70° (bath temperature) at 0.05 mm. The over-all yield of this material is therefore 65% based on dione **3**.

Bicyclo[5.3.1]undecan-8α-ol-11-one[12e] Toluenesulfonate (17).—A solution of 591 mg. of chromatographed tosylate **14** in 20 ml. of acetone was stirred at 0° and 0.45 ml. of Jones reagent[18] was added dropwise. After 10 min. the excess reagent was destroyed with 2-propanol, the mixture was filtered to remove insoluble salts, and the product was isolated from the filtrate with ether[12b] after addition of saturated brine. The yield of keto tosylate **17**, m.p. 115–117°, was 553 mg. (94%): $\lambda_{\max}^{\text{film}}$ 5.88 (cyclooctanone CO), 6.27 (aromatic C=C), 8.40, 8.50, 9.10, 10.30, 10.60, 11.10, 11.53, 11.94, and 15.03 μ. The analytical sample, m.p. 118–118.5°, was obtained after three recrystallizations from ethyl acetate–heptane.

Anal. Calcd. for $C_{18}H_{24}O_4S$: C, 64.26; H, 7.19; S, 9.53. Found: C, 64.5; H, 7.4; S, 9.3.

Bicyclo[5.3.1]undecan-8α-ol-11-one[12e] Methanesulfonate (18).—A solution of 421 mg. of crude diol monomesylate **6** (prepared from dione **3** in 93% yield without purification) in 20 ml. of acetone was oxidized with 0.4 ml. of Jones reagent[18] according to the procedure described above for keto tosylate **17**. The crude keto mesylate **18** solidified and was recrystallized from ether–hexane to give 324 mg. (78%): m.p. 88–90°; $\lambda_{\max}^{\text{CCl}_4}$ 5.88 (cyclooctanone CO), 7.32, 7.42, 7.98, 8.49, 10.38, 10.60, 11.10, 11.51, and 12.10 μ. A second crop yielded 25 mg., m.p. 87–89°. The analytical specimen, m.p. 90–91°, was obtained by two additional recrystallizations from ether–hexane.

Anal. Calcd. for $C_{12}H_{20}O_4S$: C, 55.36; H, 7.74; S, 12.32. Found: C, 55.6; H, 7.7; S, 12.4.

***cis*-4-Cyclodecenecarboxylic Acid (12).** A. **Oxidation of Aldehyde 11.**—To a stirred solution of 86.5 mg. of aldehyde **11** and 1.02 ml. of 10% aqueous silver nitrate in 5 ml. of ethanol was added dropwise 4.8 ml. of 2.5% aqueous sodium hydroxide solution. The mixture was stirred overnight and filtered, and the filtrate was concentrated under reduced pressure. Water was added, and the aqueous solution was washed with ether and acidified with 10% aqueous hydrochloric acid, and the liberated acid **12** was isolated with ether.[12b] The resulting oil was distilled affording 60 mg. (64%) of solid material, m.p. 79–81°, after one recrystallization from hexane: $\lambda_{\max}^{\text{film}}$ 3.2–3.7 (acid OH), 5.88 (CO), 14.03 (*cis* CH=CH), 6.79, 6.91, 7.05, 7.75, 7.92, and 8.07 μ.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.2; H, 9.9.

B. **Oxidation of Alcohol 9.**—To a stirred solution of 372 mg. of alcohol **9** in 30 ml. of acetone at 0° was added 1.1 ml. of Jones reagent.[18] The mixture was allowed to stir for 10 min. and the excess oxidizing agent was destroyed with 2-propanol. The mixture was diluted with water and the product was isolated with ether. Distillation of the crude oily material gave 350 mg. (87%) of solid acid **12** identified by its infrared spectrum. Recrystallization from hexane afforded 177 mg., m.p. 78–80°, undepressed upon admixture with acid prepared according to part A of this experiment. A second crop yielded 143 mg. of semisolid material.

Attempted Preparation of Acid 12 from Keto Tosylate 17.—A solution containing 253 mg. of keto tosylate **17** and 250 mg. of potassium hydroxide in 20 ml. of 3:1 dioxane–water was heated under reflux for 2 hr.[12c] The cooled mixture was extracted with ether, and the ether extracts were washed with brine and dried over anhydrous magnesium sulfate. The 101 mg. of crude neutral material thus obtained afforded 52 mg. of oil: b.p. 80–90° (bath temperature) at 0.07 mm.; $\lambda_{\max}^{\text{film}}$ 3.30 (HC=C), 5.89 (cyclooctanone CO), 7.24, 8.66, 8.91, 9.12, 10.35, 10.45, 10.83, 12.62, 13.01, and 13.78 μ. The n.m.r. spectrum of this material displayed multiplets centered at 6.05 and 5.73 p.p.m. (olefinic protons).

The aqueous alkaline phase yielded only 5 mg. of acidic material upon acidification and extraction with ether.

Cyclodecanecarboxylic Acid (13).—A solution of 143 mg. of acid **12** in 10 ml. of acetic acid was hydrogenated at atmospheric pressure over 25 mg. of platinum oxide. The mixture was filtered and the filtrate was distilled affording cyclodecanecarboxylic acid, b.p. 60–65° (bath temperature) at 0.05 mm., which solidified in the cold portion of the tube. This material was recrystallized twice from hexane giving 115 mg. (80%), m.p. 50–51° (lit.[19] m.p. 52°).

1-Methylbicyclo[5.3.1]undecane-8,11-dione (4).—The mineral oil was removed from 3.6 g. of 51% sodium hydride dispersion by successive washing with benzene and 1,2-dimethoxyethane (DME). A stirred mixture containing the resulting sodium hydride and 12.34 g. of dione **3** in 150 ml. of dry DME was refluxed for 6 hr.[12c] The resulting white slurry of the enolate was cooled to room temperature and 10.2 g. of anhydrous, methanol-free methyl iodide[20] was added dropwise over a 15-min. period. The reaction mixture was stirred at room temperature for 10 hr. and the resulting clear solution was filtered to remove a small amount of sodium hydride. The filtrate was concentrated under reduced pressure until sodium iodide precipitated, enough water to dissolve the precipitate was added, and the product was isolated with ether.[12b] Distillation afforded 9.29 g. (70%) of dione **4**: b.p. 86–88° (0.3 mm.); $n^{20}\text{D}$ 1.5099; $\lambda_{\max}^{\text{film}}$ 5.81 (cyclohexanone CO), 5.92 (cyclooctanone CO), 7.29, 7.91, 8.05, 8.14, 8.40, 11.01, 11.42, 11.79, 12.06, and 12.41 μ; $\delta_{\text{TMS}}^{\text{CCl}_4}$ = 1.10 p.p.m. (C-1 CH_3).

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.9; H, 9.5.

1β-Methylbicyclo[5.3.1]undecane-8α,11-diol (7).[12e]—A solution containing 4.85 g. of dione **4** and 1.90 g. of lithium aluminum hydride in 150 ml. of ether was stirred at room temperature for 10 hr. The mixture was carefully treated with 3.8 ml. of water and 3.04 ml. of 10% aqueous sodium hydroxide and stirring was continued until the salts became granular. The mixture was filtered and the solvent was removed from the filtrate affording 4.85 g. (98%) of crude solid which was recrystallized from ether–hexane to yield 4.51 g. of white needles: m.p. 95–106°; $\lambda_{\max}^{\text{CHCl}_3}$ 2.78, 2.90 (OH), 9.24, 9.93, and 10.27 μ. Four successive recrystallizations from ether–hexane failed to provide sharply melting material and therefore a sample, m.p. 107–113°, was submitted for combustion analysis.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.6; H, 11.2.

1β-Methylbicyclo[5.3.1]undecan-8α-ol-11-one[12e] Methanesulfonate (19).—A solution of 231 mg. of methanesulfonyl chloride in 1 ml. of dry pyridine was added dropwise to a stirred, cooled solution of 396 mg. of diol **7** (m.p. 95–106°) in 2 ml. of dry pyridine.[17] The mixture was stirred at 0° for 3 hr. and allowed to warm to room temperature during an additional 1 hr.[12c] A 1–2-g. portion of ice was added and, after 5 min., the mixture was poured into water and the mesylate **8** was isolated with ether,[12b] affording 539 mg. (98%) of oily material: $\lambda_{\max}^{\text{film}}$

---

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

[19] A. Blomquist and F. Schlaefer, *J. Am. Chem. Soc.*, **83**, 4547 (1961), and references cited therein.

[20] Distilled from calcium hydride. When methyl iodide was used without purification, material resulting from cleavage of dione **4** *via* the addition of methoxide to the C-8 carbonyl group was formed.

2.82 (OH), 7.44, 7.50, 8.53, 10.80, 11.45, 12.00, 12.71, and 13.63 μ.

The crude mesylate (366 mg.) in 15 ml. of acetone was cooled to 0° and treated with 0.33 ml. of Jones reagent.[18] Isolation with ether[12b] as described above for keto tosylate **17** afforded 304 mg. of crude crystalline keto mesylate **19**: $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.90 (cyclooctanone CO), 7.40, 7.50, 8.52, 10.56, 10.82, and 11.47. Recrystallization from ethyl acetate–heptane afforded 230 mg. (65%) of white solid, m.p. 127–129°. Prolonged heating during the recrystallization procedure caused decomposition of this material as evidenced by deep yellow coloration of the solution. The analytical specimen, m.p. 128–129°, was obtained after three recrystallizations from ethyl acetate–heptane: $\delta_{\max}^{\mathrm{CCl_4}} = 4.57$ (H-8, X of ABX, $J_{\mathrm{AX}} = 10$ c.p.s., $J_{\mathrm{BX}} = 6$ c.p.s.),[11] 3.08 (CH_3SO_3), and 1.16 p.p.m. (C-1 CH_3).

Anal. Calcd. for $C_{13}H_{22}O_4S$: C, 56.91; H, 8.08; S, 11.69. Found: C, 57.1; H, 8.0; S, 11.6.

cis-**5-Methyl-4-cyclodecenylmethanol (10)**.—The mesylate **8** was prepared from 792 mg. of diol **7** (m.p. 95–105°) as described above. A solution containing the entire crude mesylate and 0.30 g. of lithium aluminum hydride in 24 ml. of anhydrous 1,2-dimethoxyethane was stirred under reflux for 10 hr. The mixture was treated carefully with 0.6 ml. of water and 0.48 ml. of 10% aqueous sodium hydroxide and the salts were removed by filtration after addition of ether. Distillation gave 0.64 g. (88%) of alcohol **10**: b.p. 85–90° (bath temperature) at 0.05 mm.; $\lambda_{\max}^{\mathrm{film}}$ 2.98 (OH), 6.76, 6.90, 9.48, 9.85, 10.30, 11.76, and 12.54 μ; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}} = 5.05–5.4$ (H-4, multiplet centered at 5.25), 3.5 (HO), 3.37 ($CHCH_2OH$, doublet, $J = 5$ c.p.s.), and 1.67 p.p.m. ($CH_3C{=}C$).

Anal. Calcd. for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.8; H, 12.2.

The methanesulfonate derivative, m.p. 50–52° (after crystallization from ether-hexane), was prepared[17] in 70% yield.

Anal. Calcd. for $C_{13}H_{24}O_3S$: C, 59.96; H, 9.29; S, 12.31. Found: C, 60.0; H, 9.2; S, 12.1.

Acknowledgment.—We acknowledge with pleasure the financial support of a National Science Foundation Institutional Grant. C. J. V. S. expresses gratitude to the National Science Foundation for a summer fellowship (1964) and to the Ethyl Corporation for a fellowship (1963–1964).

Products from the Hydroformylation of Cyclohexene Oxide[1]

L. ROOS,[2a] R. W. GOETZ, AND M. ORCHIN[2b]

Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221

Received March 30, 1965

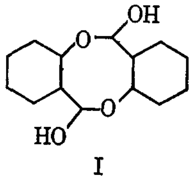
The major product resulting from the stoichiometric hydroformylation of cyclohexene oxide is not the expected 2-hydroxycyclohexanecarboxaldehyde but its dimer. A study of the chemical and spectroscopic properties of the dimer and its conversion products showed it to be a cyclic hemiacetal of structure II with all-*trans* stereochemistry. The hemiacetal was shown to be in equilibrium with the open hydroxycarboxaldehyde III. Catalytic hydroformylation under optimum conditions gave over a 40% yield of II.

The hydroformylation of epoxides has been reported to result in the formation of β-hydroxy esters, β-hydroxyaldehydes, and cobalt β-hydroxycarbonyls.[3–8] The only product reported to be formed from the hydroformylation of cyclohexene oxide is 2-hydroxycyclohexylcarbonylcobalt tetracarbonyl, which was isolated as the triphenylphosphine derivative; cleavage of this complex with iodine and methanol gave only methyl *trans*-2-hydroxycyclohexanecarboxylate.[5] Our investigation of this reaction, which was underway when the literature report appeared, indicated that the reaction was more complex, and that under certain conditions the major product was not the reported one. Furthermore, because yields were not reported and because other work[9] indicated *cis* addition, conclusions regarding the stereochemical course of the reaction are open to question.

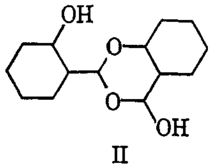
Results and Discussion of the Stoichiometric Hydroformylation

When cyclohexene oxide was treated with cobalt hydrocarbonyl under the usual conditions of the stoichiometric hydroformylation,[10] a slow uptake of carbon monoxide was observed, followed by the precipitation of a brown material. Recrystallization of this material led to a white needlelike crystalline compound, the analysis of which corresponded to that expected for the hexahydrosalicylaldehyde. However, the molecular weight of this material in benzene showed it to be dimeric; furthermore, the infrared spectrum of a halocarbon mull showed no carbonyl band. Since no mention of either hexahydrosalicylaldehyde or its dimer appears in the literature,[11] we decided to study the chemistry and the structure of this compound.

The molecular weight of the compound, the absence of carbonyl, its ultimate analysis, and the nature of the hydroformylation reaction suggested at least two structures. Although two hydroxyl groups are present



I



II

in each structure, those of structure II are nonequivalent. The n.m.r. and infrared spectra show the presence of two hydroxyl groups in totally different environments. A Stuart model indicates considerable steric interference in structure I, and thus the skeletal structure of II appears most likely.

---

[1] This work was performed in part under a grant (APSP-16,461) from the Division of Air Pollution, Bureau of State Services, U. S. Public Health Service.

[2] (a) Public Health Service Predoctoral Fellow, 1962–1965; (b) to whom inquiries should be addressed.

[3] J. L. Eisenmann, R. L. Yarmartino, and J. F. Howard, Jr., *J. Org. Chem.*, **26**, 2102 (1961).

[4] J. L. Eisenmann, *ibid.*, **27**, 2706 (1962).

[5] R. F. Heck, *J. Am. Chem. Soc.*, **85**, 1460 (1963).

[6] Y. Takegami, C. Yokokawa, Y. Watanabe, and H. Masada, *Bull. Chem. Soc. Japan*, **37**, 672 (1964).

[7] C. Yokokawa, Y. Watanabe, and Y. Takegami, *ibid.*, **37**, 677 (1964).

[8] C. Yokokawa, Y. Takegami, and Y. Watanabe, *ibid.*, **37**, 935 (1964).

[9] A. Rosenthal and D. Abson, *Can. J. Chem.*, **42**, 1811 (1964).

[10] G. Karapinka and M. Orchin, *J. Org. Chem.*, **26**, 4187 (1961).

[11] A compound having very similar physical and chemical properties, but described as 1-hydroxyhexahydrobenzaldehyde, appears in the literature: E. D. Venus-Danilova, *J. Gen. Chem. USSR*, **6**, 1863 (1936); *Chem. Abstr.*, **31**, 4281 (1937).