[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

The Synthesis of *d,l-β*-Santalene and *d,l-epi-β*-Santalene by Stereospecific Routes

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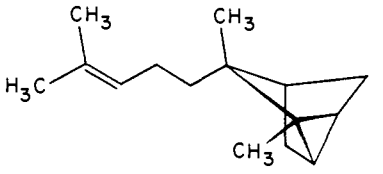
RECEIVED JANUARY 20, 1962

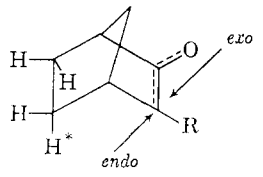
Simple stereospecific syntheses of *d,l-β*-santalene (V) and *d,l-epi-β*-santalene (VIII) from norcamphor are described. The hydrocarbon VIII has been found to occur together with V in a sample of "natural β-santalene" by use of vapor phase chromatographic and nuclear magnetic resonance measurements. The stereochemistry of the major component (V) of the natural mixture corresponds to that previously assigned to β-santalene by Ourisson.

In a previous article the synthesis of α-santalene (I), one of the main hydrocarbon components of East Indian sandalwood oil, was reported.[1] We describe here a sequel to this study, the synthesis of the isomeric companion hydrocarbon β-santalene (V). Specifically our objective was the development of a simple and direct route to β-santalene which would be highly stereoselective and, at the same time, allow independent assignment of configuration at the asymmetric carbon substituted by methyl and 4-methyl-3-pentenyl groups relative to the one and two carbon bridges.



I

The reaction sequence which was successfully employed for the synthesis is outlined in Fig. 1. The introduction of the exocyclic methylene group in V was accomplished using a carbonyl precursor which also served the purpose of allowing the placing of methyl and 4-methyl-3-pentenyl substituents by successive alkylation procedures. The crucial aspect of the synthesis is the stereochemistry of alkylation of the enolate derived from III. It had been anticipated that the attack on a bicyclo[2.2.1]heptenolate ion by an electrophilic alkylating agent would occur specifically from the *exo* direction because of strong steric shielding by the *endo* hydrogens of the two carbon bridge (especially H*)



This preference, expected to be almost independent of α-substitution in the enolate (*i.e.*, R), has manifested itself in the closely related addition reactions of bicyclo[2.2.1]heptene, *e.g.*, halogenation,[2,3] epoxidation,[4,5] hydroxylation,[4,6,7] oxymercuration,[8,9] diene addition,[10] 1,3-dipolar addition,[11] methylene addition[12] and sulfenium addition,[13,14] and also in addition to the trigonal carbon of bicyclo[2.2.1]-heptanone-2.[15,16]

The high stereospecificity of alkylation in the bicyclo[2.2.1]heptanone-2 system was confirmed at the outset of this investigation by a quantitative study of the methylation of the parent ketone II previously reported to yield 3-methylbicyclo-[2.2.1]heptanone-2[17] largely in the form having *exo* oriented methyl.[18,19] In our experiments the monomethylated ketone was produced by reaction of an ethereal solution of the sodium enolate (generated from sodium amide or tritylsodium on the ketone) with excess methyl iodide and was subjected to analysis by vapor phase chromatography which revealed the presence of 97% of the *exo* and at most 3% of the *endo* isomer. Equilibration of the methylated ketone (in boiling methanol with sodium methoxide catalyst) followed by vapor phase chromatographic analysis indicated that, in fact, the *exo* isomer is slightly less stable than the *endo* isomer (*Kexo/endo* ~ 0.9). Thus, it may be concluded that even with a small alkylating agent (probably a limiting case) *exo* attack predominates kinetically by a factor of more than 30.[20] All our findings are in consonance with this inference; thus, the alkylation or 3-methyl bicyclo[2.2.1]-heptenolate by 4-methyl-3-pentenyl chloride or iodide affords a single isomer. In view of the high stereo-specificity in this reaction, structure IV can be assigned with confidence to the product. The *d,l*-hydrocarbon V derived from IV was completely identical (except for optical rotation) with a sample of β-santalene which had been purified

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(3) J. D. Roberts, F. O. Johnson and R. A. Carboni, *ibid.*, **76**, 5692 (1954).

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(16) S. Beckmann and R. Mezger, *Ber.*, **89**, 2738 (1956).

(17) O. Diels and K. Alder, *Ann.*, **486**, 202 (1931).

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(20) The possibility that the 3-*endo*-methyl-bicyclo[2.2.1]heptanone in the methylated product may have been formed by isomerization of the *exo* isomer and therefore that this figure should be considerably larger is not unlikely.

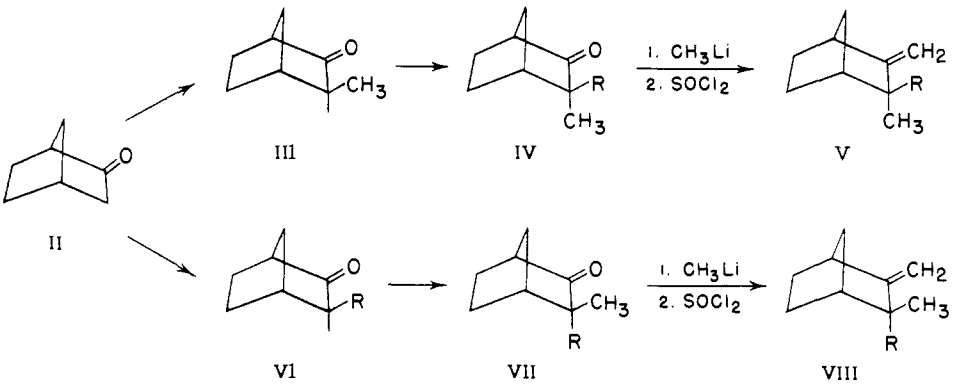

Fig. 1.—R = $CH_2CH_2CH{=}C(CH_3)_2$.

rigorously by gas chromatography to remove all but the major constituent. The total synthesis of *d,l*-β-santalene is thereby validated as is the previous assignment of stereochemistry.[21]

The sample of natural β-santalene,[22] b.p. 135–140° (10 mm.), $[\alpha]^{27}D$ + 73.94 (*C*, 11.67, $CHCl_3$), $n^{26}D$ 1.4940, from which pure V had been obtained was shown by vapor chromatographic analysis to have as the major impurity a component very similar to β-santalene (V). The unknown substance, present in the mixture with V in the ratio 15:85, respectively, was shown to be the epimer VIII of β-santalene, by comparison with synthetic material produced as shown in Fig. 1. It would appear, therefore, that what has been termed "β-santalene" is a mixture of substances with V in predominance and with lesser amounts of the epimer VIII; these substances are designated here as β-santalene (V) and *epi*-β-santalene (VIII).

The sequence of reactions leading to *epi*-β-santalene (VIII) is also stereospecific. Only one isomer was obtained from the alkylation of II by 4-methyl-3-pentenyl iodide and from the alkylation of VI with methyl iodide. Both the epimeric santalenes V and VIII could be distinguished clearly by vapor phase chromatography and by nuclear magnetic resonance spectroscopy and further, both the epimeric ketones IV and VII could be differentiated by the latter. It was thus possible to determine that the alkylation reactions leading to the ketones IV and VII were stereospecific out to the limits of analytical sensitivity and that, in these cases *exo* alkylation predominates by a factor greater than 30.

Acknowledgment.—We are grateful to the National Science Foundation for support of this investigation (G-9999).

Experimental

Methylation of Bicyclo[2.2.1]heptanone-2. A.—Bicyclo[2.2.1]heptanone-2 was converted to the sodio derivative using 1.5 equivalents of finely divided sodium amide with ether as solvent at reflux under high speed sitrring and with the passage of a stream of nitrogen through the reaction vessel to expel ammonia. Vigorous stirring and small particle size of the sodium amide are essential in order to minimize aldol condensation which occurs when enolate formation is slow. The suspension of sodium enolate was separated from unreacted sodium amide (sedimented at the bottom of the flask) and added to a 10-fold excess of methyl iodide in a small volume of ether. The mixture was heated under nitrogen at reflux until neutral. Addition of water, extraction with ether, concentration of the extract and distillation with a spinning band column yielded *exo*-3-methylbicyclo[2.2.1]heptanone-2, b.p. 67° (14 mm.),[17] after a forerun of bicyclo[2.2.1]heptanone-2. In addition, higher boiling fractions were obtained consisting of 3,3-dimethylbicyclo[2.2.1]heptanone-2. The average yield of III obtained in this way was 55%. The distilled product was shown to be at least 98% pure by vapor phase chromatography using a tricyanoethoxypropane (TCEP) column.[23] No significant amount of the *endo* isomer was detected. In agreement the n.m.r. spectrum (in $CDCl_3$) showed *exo*-methyl absorption as a doublet at 9.05 and 8.92τ, without detectable *endo*-methyl peaks (expected at 8.95 and 9.08τ; see below).

B.—In a three-necked flask fitted with a condenser was placed 4.4 g. (0.04 mole) of II dissolved in 15 ml. of dry dioxane. The air was completely replaced by nitrogen and there was added with stirring about 70 ml. (0.04 mole, 66.66 ml.) of a 0.6 *N* solution of triphenylmethyl sodium in ether using a syringe; a deep red color persisted at the end of addition indicative of an excess of the reagent. The mixture was allowed to stand for 2 minutes after which 22.27 g. (10 ml., 4-fold excess) of freshly distilled methyl iodide was added in a lot with stirring. There was immediate reaction in the cold and the solution turned yellow. This was stirred until it became completely neutral (10 hours) after which it was diluted with water and extracted with pentane. The pentane extract was washed with brine, dried and concentrated. The residue thus obtained was distilled using a small column (2″) to give 4 g. (81%) of methyl norcamphor (III) as a colorless liquid b.p. 33° (1 mm.). The compound showed characteristic infrared absorption (in CCl_4) at 5.7(s) and 7.28(nμ). Vapor phase chromatography of this product on a 10 ft. TCEP column (25% on Chromasorb) at 135° with a helium flow rate of 50 ml./min. gave two peaks with elution times of 62 min. and 72 min. 10 sec., respectively. The first peak due to compound III (the *exo* isomer) accounted for 97% of the product while the second peak (3%) was due to the *endo* isomer. In the n.m.r. spectrum (in CCl_4) the methyl protons appeared as a doublet at 8.917 and 9.05τ.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.00; H, 9.58.

Isomerization of III by Sodium Methoxide.—*exo*-3-Methylbicyclo[2.2.1]heptanone-2 (0.248 g., 0.002 mole) in a 20-ml. flask fitted with a condenser was treated with 3 ml. of 3% sodium methoxide in methanol. This was refluxed in an oil-bath under nitrogen for 4 hr., cooled, treated with 15 ml. of ice-water and extracted with pentane–methylene chloride mixture. The extracts were washed free of the alkali with ice-water, dried and concentrated carefully using a 10-inch column to give 0.23 g. (92.7%) of the mixture of isomers. This on vapor phase chromatography using a 10 ft. TCEP column (25% on Chromasorb) at 135° with a helium flow rate of 49 ml./min. gave two peaks with elution times of 62 min. 40 sec. and 73 min. 30 sec., respectively.

(21) G. Ourisson, *Bull. soc. chim. France*, 895 (1955).

(22) Kindly provided by Dr. S. C. Bhattacharyya, National Chemical Laboratory, Poona-8, India.

(23) H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **65**, 23 (1943).

The first peak (due to the *exo* isomer III accounted for 47.4% of the mixture while the second, due to the *endo* isomer, accounted for 52.6% of the mixture. The infrared spectrum of the mixture of isomers showed characteristic absorption at 5.7(s) and 7.28(m) μ with considerable differences in the absorption in the region 6.5 to 12μ from that of pure III. In the n.m.r. spectrum (in CCl_4) of the mixture of isomers the methyl protons appeared as a pair of doublets at 8.917, 8.95, 9.05 and 9.083τ, respectively. In the n.m.r. spectrum (in CCl_4) of the pure *endo* isomer (collected by v.p.c.) the methyl protons appeared as a doublet at 8.95 and 9.083 τ, respectively. A similar equilibration under the conditions described above over a 24-hour reaction period afforded an identical mixture of *exo*- and *endo*-3-methylbicyclo-[2.2.1]heptanones.

4-Methyl-3-pentenyl chloride was prepared from cyclopropanecarboxylic acid *via* the methyl ester (prepared using diazomethane) by reaction with excess methyllithium to give cyclopropyldimethylcarbinol, b.p. 59–66° (155 mm.), followed by treatment with hydrochloric acid.[24] The chloride so obtained had b.p. 68° (98 mm.) and n.m.r. absorption consistent with the assigned structure including 2 methyl peaks at 8.38 and 8.32 τ and one olefin proton at 4.87 τ.

4-Methyl-3-pentenyl iodide was prepared from 11.85 g. (0.1 mole) of the above chloride and a saturated solution of 150 g. (1 mole) of anhydrous sodium iodide in dry acetone at reflux overnight. Distillation under vacuum gave 13.25 g. (63%) of the iodide, b.p. 65–66° (7 mm.). This compound showed characteristic infrared absorption (in CCl_4) at 6(w), 7.25(m) and 11.15(w) μ. Its ultraviolet spectrum had λ_{max}^{EtOH} 217 mμ, ε 6300.

***endo*-3-Methyl-*exo*-3-[4-methyl-3-pentenyl]-bicyclo-[2.2.1]heptanone-2 (IV).**—Finely ground sodium amide (1.585 g., 0.0406 mole) was transferred under nitrogen into a 100-ml. three-necked flask and covered with 40 ml. of freshly distilled dry tetrahydrofuran. A solution of 4.197 g. (0.0338 mole) of III in 15 ml. of tetrahydrofuran was added and the mixture was refluxed until evolution of ammonia has ceased. Then a solution of 6.503 g. (0.055 mole) of 4-methyl-3-pentenyl chloride in 15 ml. of tetrahydrofuran was added and the mixture was stirred at reflux under nitrogen for 48 hr. Most of the tetrahydrofuran was removed by distillation using a column, water was added and the reaction product was extracted with ether. After evaporation of the ether, starting chloride (2.70 g.) and methylnorcamphor (1.66 g.) were removed by distillation. The main fraction obtained by distillation, b.p. 100° (1.5 mm.), consisted of pure IV as shown by the n.m.r. (in CCl_4) spectrum which manifested one sharp methyl peak at 8.89 τ and 2 methyl peaks at 8.35 and 8.43 from the isopropylidine protons. The sharp peak at 8.92 τ characteristic of the tertiary methyl of epimer VII with *exo*-methyl grouping was completely absent, indicating that the above alkylation product IV (*endo*-methyl group) was formed stereospecifically.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.30; H, 10.72.

β-Santalene (V).—To 400 ml. of a freshly prepared 1.2 *N* methyllithium solution in ether under nitrogen in a three-necked flask was added a solution of 2.54 g. of the ketone IV in 15 ml. of ether. The mixture was refluxed for 90 hours, decomposed by dropwise addition of water and worked up by separation of the ether layer and evaporation to give an oily product (2.76 g.) whose infrared spectrum showed no carbonyl absorption but strong absorption at 2.8μ due to hydroxyl. A portion of the crude hydroxy compound (1.535 g.) was dissolved in a mixture of 20 ml. of methylene chloride and treated at −5° with a solution of 5 ml. of thionyl chloride in 5 ml. of pyridine. After 10 minutes, 30 ml. of pentane was added followed by 132 ml. of 3 *N* hydrochloric acid. The pentane layer was separated, washed, dried and evaporated carefully after passage through a short column of alumina. Distillation of the residue afforded 1.10 g. (72% from the ketone IV) of β-santalene (V). The infrared and n.m.r. spectra of this material were identical with that of β-santalene of natural origin. The n.m.r. spectrum (in carbon tetrachloride) showed a sharp peak due to tertiary methyl at 8.97 τ, two peaks (not sharp) due to two methyl groups attached to double bond at 8.43 and 8.36 τ, sharp peaks at 5.60 and 5.32 τ due to the two olefinic methylene protons (J_{H-C-H} apparently almost 0) and a broader peak at *ca.* 5 τ due to the olefinic proton of the side chain. The characteristic peaks of *epi*-β-santalene were completely lacking. Vapor phase chromatographic analysis of samples of the above product and purified natural β-santalene on a 10-ft. tricyanoethoxypropane (TCEP) column (25% on Chromasorb) at 135° showed that these behaved identically (and that each was free of *epi*-β-santalene (VIII); see below). Pure natural β-santalene was obtained by small scale preparative gas chromatography on the 10-ft. TCEP column. The sample of "natural β-santalene"[22] showed two principal peaks in ratio 15:85 corresponding to VIII and V, respectively, in retention time. Further, the infrared and nuclear magnetic resonance spectra of the separated fractions were respectively identical with those of VIII and V.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.17; H, 11.83. Found: C, 88.15; H, 11.65.

3-[4-Methyl-3-pentenyl]-bicyclo[2.2.1]heptanone-2 (VI).—Into a 3-necked flask fitted with a condenser bearing a 3-way stopcock at the top, a ground glass stopper and a rubber stopple for syringe injection were placed a Teflon covered magnetic bar, 2.2. g. of bicyclo[2.2.1]heptanone-2 and 10 ml. of dry dioxane. The air in this system was replaced by nitrogen by alternate evacuation and admission of nitrogen through separate openings in the 3-way stopcock by changing its adjustment. To the stirred solution was added, using a syringe, about 35 ml. of 0.6 *N* triphenylmethylsodium, a sufficient excess so that a definite deep red color persisted at the end of the addition. After about 2 minutes, 16.8 g. (0.08 mole) of freshly distilled 2-methyl-5-iodopent-2-ene was added in one lot and the solution was heated to reflux (bath temp. 100°) with stirring. After working up the product in the usual way most of the triphenylmethane was removed by freezing a pentane solution, and the filtrate after concentration was chromatographed over 200 g. of alumina (grade II, Woelm) using a long column (0.7″ × 37″) with pentane. The first fraction (800 ml.) gave a mixture of the unreacted iodide and triphenylmethane. The second fraction (1.6 l.) gave 1.528 g. of the desired product VI and the last fraction (ether washings, 1 l.) gave 0.8525 g. of a mixture of VI and the aldol product from bicyclo[2.2.1]heptanone-2 from which 0.48 g. of VI was isolated by vapor phase chromatography, making a total weight of 2.008 g. of crude product. This on careful distillation gave 1.925 g. (50%) of VI as a clear liquid, b.p. 107–108° (1.4 mm.), $n^{24}D$ 1.4883. The compound had characteristic infrared absorption (in CCl_4) at 5.72(s), 6.03(w), 7.25(m) and 11.35(m) μ. Vapor phase chromatography of the ketone VI on a 4-foot silicone rubber column at 200° with a helium flow rate of 85 ml./min. indicated a retention time of 5 min. 15 sec. In the n.m.r. spectrum of VI (in CCl_4) the methyl protons appeared at 8.39 τ.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.11; H, 10.47.

***exo*-3-Methyl-*endo*-3-[4-methyl-3-pentenyl]-bicyclo[2.2.1]-heptanone-2 (VII).**—In a flask, fitted with a condenser and a nitrogen system was taken 1 g. (0.0052 mole) of the ketone VI in 5 ml. of dry dioxane. The air was completely replaced by nitrogen and there was added with stirring about 10 ml. of 0.6 *N* triphenylmethylsodium in ether using a syringe. A deep red color persisted due to excess of the reagent. After 2 minutes, 4.43 g. (1.95 ml., 0.0312 mole) of freshly distilled methyl iodide was added. There was immediate reaction in the cold and the solution turned yellow. The reaction mixture was stirred for 2 days and worked up as above. There was obtained 0.89 g. (83%, crude) of the desired product VII which on distillation gave 0.7178 g. (67%) of VII as clear liquid, b.p. 95° (0.8 mm.), $n^{25}D$ 1.4850. The compound showed characteristic infrared absorption (in CCl_4) at 5.72(s), 6.02(w) 7.28(m) and 11.29-(m) μ. This compound on vapor phase chromatography on a 4-ft. silicone rubber column at 200° with a helium flow rate of 85 ml./min. gave a retention time of 6 min. 15 sec. In the n.m.r. spectrum (in CCl_4) of VII, the *exo*-methyl protons appeared as a sharp peak at 8.92 τ, the methyl protons of the side chain showed up as a rather wide peak at 8.22 τ and the olefinic proton appeared at 5.17 τ. The absence of a peak at 8.89 τ indicated that no appreciable amount of the epimer IV with the *endo*-methyl group was formed in this alkylation.

(24) T. A. Favorskaya and S. A. Fridman, *J. Gen. Chem. USSR*, **15**, 421 (1945).

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.45; H, 10.76.

epi-β-Santalene (VIII).—The ketone VII (0.7 g., 0.0034 mole) dissolved in 10 ml. of anhydrous ether was treated with 21.25 ml. (0.034 mole) of 1.6 *N* methyllithium solution in ether at reflux under nitrogen for 5 days. This was cooled in an ice-bath, hydrolyzed with ice-water and worked up in the usual way to give 0.69 g. (91.5%) of the desired hydroxy compound as a pale yellow liquid, showing infrared absorption at 2.71(w), 7.28(m) and 11.25(m) μ. A portion of this product (0.223 g.) dissolved in 5 ml. of anhydrous pyridine and 1 ml. of dry methylene chloride was cooled in an ice–salt-bath below 0°, and treated with a cooled solution of 1 ml. of pyridine and 1 ml. of thionyl chloride. At the end of the addition the brown mixture was kept at 0° for 10 minutes and then diluted with 10 ml. of pentane followed by 27 ml. of 3 *N* HCl (efficient cooling). The product was extracted with pentane, filtered through a column of alumina using pentane and distilled to give 0.14 g. (69%) of *epi-β*-santalene (VIII) as a colorless liquid. The compound showed infrared absorption (in carbon tetrachloride) at 3.2(w), 6.02(m) 7.26(m) and 11.3(s) μ and on vapor phase chromatography on a 10-ft. tricyanoethoxypropane column (25% on Chromasorb) at 135° with a helium flow rate of 33 ml./min. gave a retention time of 37 min. 20 sec. A mixture of the synthetic and the natural (isolated from natural β-santalene sample) *epi-β*-santalenes gave a single peak with the same retention time under the above conditions while pure β-santalene (both synthetic and natural) gave the retention time of 38 min. 55 sec. In the n.m.r. spectrum (in carbon tetrachloride) the *exo*-methyl proton appeared as a sharp single peak at 9 τ, the methyl proton of the side chain showed up as a single peak at 8.38 τ and the three olefinic protons showed up at 4.92 (side chain), 5.38 (terminal methylene) and 5.61 τ (terminal ethylene), respectively. In an n.m.r. spectrum of the mixture of pure β-santalene and the epimer VIII the protons due to *endo* (of β-santalene) and the *exo* (of epi-β-santalene) methyl groups appeared at 8.97 and at 9.00 τ, respectively, with a separation of 0.034 p.p.m. Furthermore, the absence of bands characteristic of β-santalene (V) in the n.m.r. spectrum of the product from the above reaction confirmed the vapor phase chromatographic analysis and supports the conclusion that the reactions leading to VII are stereo-specific.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Synthesis of *cis*- and *trans*-Derivatives of 1a-Carboxymethyl-8-methylhexahydrofluorenone[1a]

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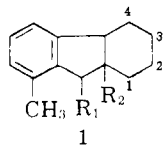
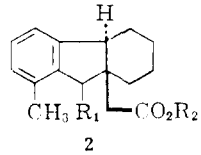
RECEIVED FEBRUARY 10, 1962

The previously described unsaturated acid **6** has been converted to the keto lactone **11**, a possible intermediate for the synthesis of allogibberic acid. Suitable transformations have transformed the keto acid **18a** to the unsaturated lactone **20** which yields both *cis*- (22) and *trans*- (21) hexahydrofluorenone derivatives on hydrogenation.

In continuing our studies[2] of synthetic approaches to the gibberellins[3] and their degradation products, we desired synthetic routes to hexahydrofluorenones **1** containing an oxygen function at C_2 and to 1a-substituted hexahydrofluorenones (*e.g.*, **2**) having a *trans* fusion of the alicyclic rings. This paper describes solutions to these objectives as well as improved synthesis of several previously described[2c,d] intermediates. The previously described[2c] intermediates **3** and **4** were transformed to the diketo lactone **11** as indicated in Chart I.



1



2

The conversion of the unsaturated acid **6** to the iodo-*cis*-γ-lactone **9** is the result which would be predicted on steric grounds assuming a transition state involving *trans* copolanar addition to the carbon–carbon double bond.[4,5] The further transformation of the iodo lactone **9** to the epoxy ester **8** permits the assignment of the indicated configuration to the epoxy ester.[6] The fact that reaction of the epoxy ester **8** with aqueous acid produced two isomeric hydroxy lactones **10**, each of which produced the same diketo lactone **11** on oxidation, indicates either that the hydroxy lactones **10** differ in stereochemistry only at C2 or that one of the two diketo lactones **11** initially formed was epimerized under the mild oxidizing conditions[7] employed. The latter explanation is more probable if the usual[5] *trans* diaxial opening of the epoxide ring occurred prior to the formation of the hydroxy lactones **10** and both chair conformations of the epoxy ester **8** are of comparable energy. Although the abnormally high cyclohexanone carbonyl stretching frequency (1735 $cm.^{-1}$) in the infrared indicates that the preferred conformation of the diketo lactone **11** places the ethereal lactone oxygen atom on a equatorial bond, our data do not permit an unambiguous stereochemical assignment at C2 of the diketo lactone **11** to be made. However, the n.m.r. spectrum of (see Experimental) of this lactone **11** does exclude the alternative formulation **12** for this product

Reaction of keto acid **6** with sodium borohydride produced the *trans* hydroxy acid **13a** which was

(1) (a) This research has been supported by National Science Foundation Grant No. G-9486; (b) National Institutes of Health Predoctoral Fellow, 1960–1962; (c) National Research Council Postdoctoral Fellow, 1960–1961.

(2) (a) H. O. House, V. Paragamian, R. S. Ro and D. J. Wluka, *J. Am. Chem. Soc.*, **82**, 1452, 1457 (1960); (b) H. O. House, W. F. Gannon, R. S. Ro and D. J. Wluka, *ibid.*, **82**, 1463 (1960); (c) H. O. House, V. Paragamian and D. J. Wluka, *ibid.*, **82**, 2561 (1960); (d) **83**, 2714 (1961).

(3) For a recent review, see J. F. Grove, *Quart. Revs.*, **15**, 56 (1961).

(4) For discussion of an analogous iodolactonization, see A. W. Burgstahler and I. C. Nordin, *J. Am. Chem. Soc.*, **83**, 198 (1961).

(5) D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 44 (1956).

(6) The formation of only the same epoxy ester **8** by direct reaction of the unsaturated ester **7** with peracetic acid appears to be another example of an addition reaction stereodirected by a nearby functional group. For discussion and leading references see H. B. Henbest and B. Nicholls, *Proc. Chem. Soc.*, 225 (1958).

(7) A. Bowers, T. G. Halsall, E. R. H. Jones and A. J. Lewis, *J. Chem. Soc.*, 2548 (1953).