(+)-**Selinane (7) from β-Selinene.**—β-Selinene (131 mg, 0.64 mmol) was hydrogenated in the presence of platinum/charcoal (100 mg) in 95% EtOH (50 ml) as described above, 2.14 equiv of hydrogen being consumed. Purification by gas chromatography on the OV-101 column at 148° afforded (+)-selinane, mol wt (mass spectrum) 208, optical rotation (95% EtOH) $[\alpha]^{25}D$ +10°. Spectral data: ir 2930, 1468, 1386, 1370, 1326, 1236, 1206, 1170, 1030, 974, 934, 918, 854 cm^{-1}; nmr δ 0.88 (s, 3 H), 0.88 (d, 6 H, J 6 Hz), 0.87 (d, 3 H, J = 6 Hz); mass spectrum *m/e* (rel intensity) 43 (100), 95 (65), 109 (60), 83 (54), 81 (52), 41 (47), 55 (43), 69 (40), 67 (37), 58 (25).

(−)-**Selinane from Paradisiol. A.**—A mixture of **9** and **10** (140 mg 0.63 mmol) was hydrogenated in the presence of 5% palladium/charcoal (100 mg) in acetic acid (40 ml) with 2.20 equiv of hydrogen being consumed. Work-up of the product in the usual manner gave a saturated hydrocarbon having identical ir, nmr, and mass spectra with (+)-selinane, optical rotation (95% EtOH), $[\alpha]^{25}D$ −16°.

B.—Dihydroparadisiol (palladium-catalyzed) (45 mg, 0.20 mmol) was dehydrated as described above. The resulting mixture of olefins (36 mg) was hydrogenated over 5% platinum/charcoal (25 mg) in 95% ethanol (30 ml) with 1.09 equiv of hydrogen being consumed. Work-up in the usual manner gave a compound identical with that made by method A.

Hydrocarbon 11 from Paradisiol.—A mixture of **9** and **10** (67 mg, 0.33 mmol) was reduced catalytically with 5% platinum/charcoal (44 mg) in 95% ethanol (20 ml), 2.31 equiv of hydrogen being consumed. The crude hydrogenation mixture was purified by gas chromatography as described above, giving **11** with the following spectral data: mol wt (mass spectrum) 208; ir 2930, 1460, 1386, 1366, 1282, 1170, 1108, 1080, 1038, 998, 976, 938, 904, 854 cm^{-1}; nmr δ 0.89 (s, 3 H), 0.91 (d, 3 H = 6 Hz), 0.88 (d, 3 H, J = 6 Hz), 0.85 (d, 3 H, J = 6 Hz); mass spectrum *m/e* (rel intensity) 93 (100), 107 (98), 41 (89), 79 (85), 55 (78), 67 (69), 82 (63), 69 (61), 81 (57), 43 (47).

Registry No.—**8**, 29969-75-3; **9**, 29868-52-8; **10**, 28290-23-5; **11**, 28290-24-6; dihydroparadisiol, 29868-51-7.

Acknowledgment.—The authors wish to thank Nancy Bennett for the nmr data and W. F. Haddon for the high-resolution mass spectral data.

Conformation of Valerane

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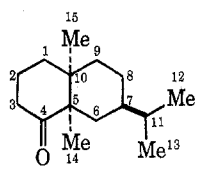
5β-Hydroxy-*cis*-9,10-dimethyl-2-decalone (**2**) which was shown to exist in the steroid cis conformation C was converted to 2α-acetyl-5β-hydroxy-*cis*-9,10-dimethyldecalin (**6**) and 2β-acetyl-5β-hydroxy-*cis*-9,10-dimethyldecalin (**7**). Through nmr spectral data and base equilibration, compounds **6** and **7** were assigned steroid cis conformations E and F, respectively. Through a sequence of reactions, decalin **6** was transformed to *dl*-valerane (**13**) and *dl*-7-isovalerane (**15**). The stereochemistry and conformation of the key intermediates were established by nmr studies. This investigation lends additional support for the conformation of the carbon skeleton of valeranone.

The natural product *l*-valeranone is one of the few known nonisoprenoid sesquiterpene ketones. After a great deal of experimentation by several groups of investigators its structure and absolute stereochemistry were finally established as shown in formula **1**.[1] It



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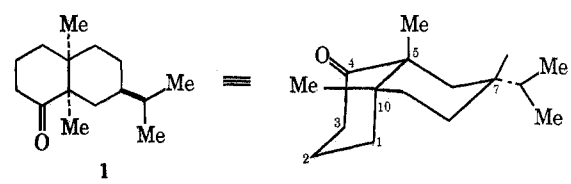
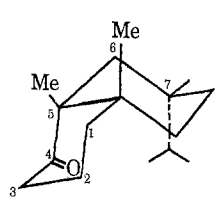
possesses an unusual carbon skeleton having two angular methyl groups in a cis-fused decalin ring system. The C-14 and C-15 methyl groups are α-oriented whereas the C-7 isopropyl group is β-oriented. The correctness of the proposed structure was substantiated by two different syntheses of *d*- and *l*-valeranones.[2,3] Subsequently other naturally occurring sesquiterpenoids structurally related to valeranone have been isolated from Japanese valerians.[1f] In view of the flexible nature of the cis decalin, valeranone could exist in at least two interchangeable all-chair conformations such as the "steroid" cis conformation A or the "nonsteroid" cis conformation B.

Hartshorn, *et al.*,[4] compared the optical rotatory dispersion curve of valeranone (*a*, −166) with those of 5β-



1 steroid cis A



nonsteroid cis B

methylcholestan-4-one (*a*, −75) and methyl 1-oxo-5β-etianate (*a*, −136) and suggested that the carbonyl group of valeranone is situated in the same relative en-

(1) (a) J. Kripinsky, M. Romanuk, V. Herout, and F. Šorm, *Collect. Czech. Chem. Commun.*, **28**, 3122 (1963); (b) E. Hohne, *ibid.*, **28**, 3128 (1963); (c) W. Klyne, S. C. Bhattacharyya, S. K. Paknikar, C. S. Narayanan, K. S. Kulkarni, J. Krepinsky, M. Romanuk, V. Herout, and F. Šorm, *Tetrahedron Lett.*, 1443 (1964); (d) K. S. Kulkarni, S. K. Paknikar, and S. C. Bhattacharyya, *Tetrahedron*, **20**, 1289 (1964); (e) H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro, and T. Takemoto, *Chem. Pharm. Bull.*, **11**, 1207 (1963); (f) H. Hikino, Y. Hikino, Y. Takeshita, K. Meguro, and T. Takemoto, *ibid.*, **13**, 1408 (1965).

(2) J. A. Marshall, W. I. Fanta, and G. L. Bundy, *Tetrahedron Lett.*, 4807 (1965).

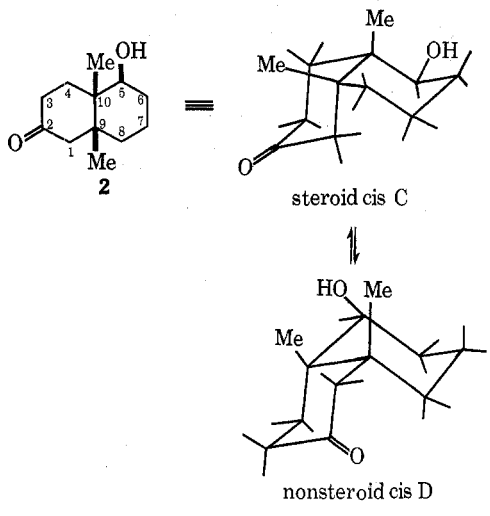
(3) E. Wenkert and D. A. Berges, *J. Amer. Chem. Soc.*, **89**, 2507 (1967).

(4) M. P. Hartshorn, D. N. Kirk, and W. Klyne, *Tetrahedron Lett.*, 89 (1965).

vironment as in the steroid compounds and hence proposed the steroid cis conformation A. Hikino, *et al.*,[5] from a similar study of the optical rotatory dispersion data of valeranone and its monobromo derivative, also arrived at the conclusion that valeranone exists in conformation A.

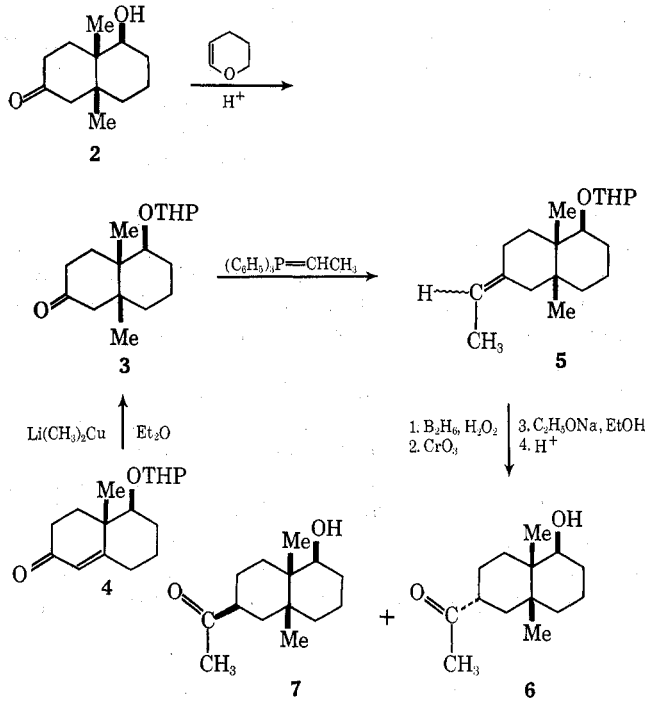
However, the above investigations failed to provide conclusive evidence about the conformation of the nonoxygenated ring, and it was assumed that this ring was in the chair form so as to keep the C-7 isopropyl group equatorial. Although this assumption was reasonable, we felt it desirable to provide unequivocal evidence for its conformation. In this study we have provided additional evidence for the conformation of valerane by unambiguous chemical methods and through nmr spectral data.

Recently we described the synthesis of 5β-hydroxy-*cis*-9,10-dimethyl-2-decalone (**2**).[6,7] From a detailed



nmr study we have demonstrated that decalone **2** was locked in the steroid cis conformation C.[6] The 5β-hydroxyl group in **2** exerts a strong 1,3-diaxial interaction with the C-9 methyl group in the nonsteroid conformation D and therefore it could conveniently assume the conformation C. Well-established procedures are available for stereospecific introduction of an equatorial substituent such as an isopropyl group through the carbonyl function in decalone **2**, and the 5β-hydroxyl group (or the bulky THP ether function) might greatly help to induce the molecule to adopt the steroid cis conformation. It was anticipated that in the nmr spectrum analysis of the resonance signal due to the methine proton adjacent to the C-5 hydroxyl might yield valuable information about the conformation of the products derived from ketone **2**. After having established that an equatorial isopropyl group had been introduced through the carbonyl function in decalone **2** and the steroid cis conformation validated, subsequent removal of the hydroxyl function should give *dl*-valerane. To avoid the 1,3-diaxial interaction with the angular methyl group at C-9 in the nonsteroid conformation, the equatorial isopropyl substituent will induce *dl*-valerane to assume the steroid cis conformation. The comparison of the nmr data of this racemic product with *l*-valerane, which was prepared earlier by Hikino, *et al.*,[1f] from natural *l*-valeranone, should provide conclusive evidence for the conformation of the ring containing the isopropyl group. The synthetic sequence employed is outlined in Scheme I. The 5β-hydroxyl group in decalone **2** was

SCHEME I



protected as a tetrahydropyranyl ether by reacting with dihydropyran in the presence of a catalytic amount of toluene-*p*-sulfonic acid to give **3**. Alternatively, by reacting the known tetrahydropyranyl ether derivative **4**[8] with lithium dimethylcopper[9] in ether, compound **3** was obtained in 75% yield. The decalone **3** was subjected to a Wittig reaction with ethylidenetriphenylphosphorane in dimethyl sulfoxide[10] at 50–60° to afford in high yield the 2-ethylidene compound **5** as a mixof the two geometrical isomers. Hydroboration of **5** with diborane in tetrahydrofuran solution followed by oxidation of the resulting organoborane with alkaline hydrogen peroxide[11] gave a mixture of two epimeric secondary alcohols, which without further purification were oxidized with 8 *N* chromic acid[12] to give a mixture of 2ξ-acetyl-9,10-*cis*-dimethyldecalin derivatives. Equilibration of this mixture with sodium ethoxide in ethanol and subsequent removal of the tetrahydropyranyl protecting group afforded two crystalline compounds **6** and **7** in 78% overall yield.[13] The equilibrated mixture consisted of 97.4% of compound **6** and 2.6% of compound **7** and they could be readily separated by column chromatography on alumina. The nmr spectra data of each of these isomeric products shed

(5) H. Hikino, Y. Takeshita, Y. Hikino, and Y. Takemoto, *Chem. Pharm. Bull.*, **13**, 626 (1965).

(6) P. N. Rao and J. E. Burdett, Jr., *J. Org. Chem.*, **34**, 1090 (1969).

(7) All structural formulas except **1**, **16**, and **17** designate only one enantiomorph of a racemic mixture.

(8) T. A. Spencer, T. D. Weaver, R. M. Villarica, R. J. Friary, J. Posler, and M. A. Schwartz, *J. Org. Chem.*, **33**, 712 (1968).

(9) (a) H. O. House, W. L. Respess, and G. M. Whitesides, *ibid.*, **31**, 3128 (1966); (b) J. A. Marshall and H. Roebke, *ibid.*, **33**, 840 (1968); (c) E. Piers and R. J. Keziere, *Can. J. Chem.*, **47**, 137 (1969).

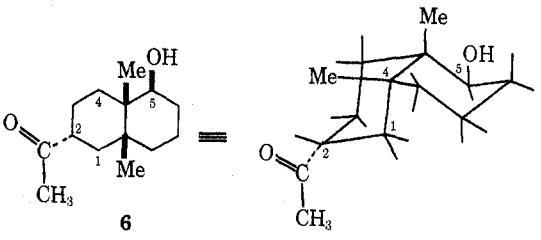
(10) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

(11) G. Zweifel and H. C. Brown, *Org. React.*, **13**, 1 (1963).

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

(13) The yield was based on the amount of pure material actually isolated.

considerable light on their conformation. In the spectrum of compound **6** the C-5 methine proton gave rise to an unresolved broad band centered at 4.03 ppm whose width at half-height (19 Hz) suggested the axial orientation.[14] Consequently, the hydroxyl group in this compound should be equatorially disposed. On the other hand, in the nmr spectrum of the isomeric compound **7**, the C-5 methine proton displayed a poorly resolved triplet centered at 3.38 ppm whose width at half-height (8 Hz) clearly indicated the equatorial orientation. As a result the hydroxyl group in compound **7** must have an axial configuration. An additional interesting feature of the nmr spectra of compounds **6** and **7** is that they both displayed one-proton signals as complex broad bands centered at 2.6 ($W_{1/2}$ = 23 Hz) and 2.5 ($W_{1/2}$ = 22 Hz) ppm, respectively. This may be attributed to the C-2 methine proton in **6** and **7** adjacent to the acetyl function. The large width at half-height in both these compounds again suggested the axial orientation of these protons, and hence the acetyl group in both **6** and **7** may be assigned equatorial orientation. Under the basic equilibration conditions the bulky acetyl group assumed the stable equatorial conformation in both compounds **6** and **7**. In view of the above evidence compounds **6** and **7** were assigned steroidal cis conformation E and nonsteroidal cis conformation F, respectively. In the two conformations E and F the 2-acetyl group has equatorial orientation, whereas the C-5 hydroxyl group in **6** is equatorial and the one in **7** is axial.

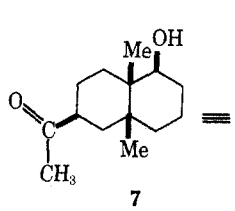


6

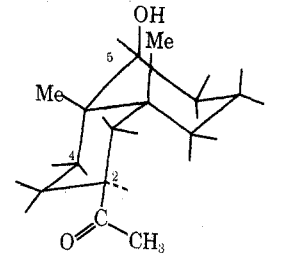
steroid cis E

C-2 H $W_{1/2}$ = 23 Hz

C-5 H $W_{1/2}$ = 19 Hz



7



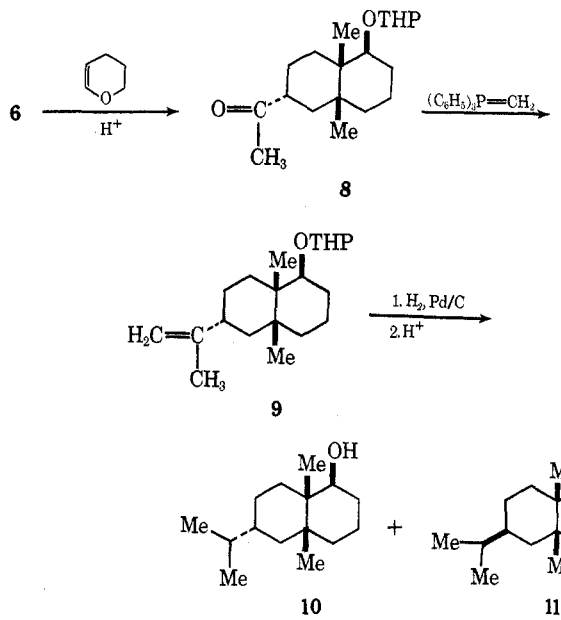
nonsteroid cis F

C-2 H $W_{1/2}$ = 22 Hz

C-5 H $W_{1/2}$ = 8 Hz

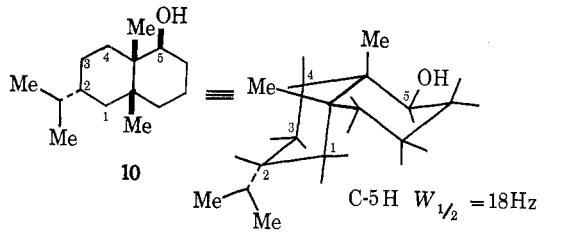
To gain additional information as to the ratio of the two isomers E and F at equilibrium, compounds **6** and **7** were separately equilibrated with ethanolic sodium ethoxide. Under these conditions compound **6** was epimerized to **7** *only in 3% yield, and 97% of the material was recovered unchanged, whereas compound* **7** *was epimerized to* **6** *in 97% yield and only 3% remained unchanged.* An examination of the Dreiding models revealed that the hydroxyl group in compound **7** exerts a strong 1,3-diaxial interaction with the C-9 methyl group in the nonsteroid conformation F and hence exists in low concentration at equilibrium. In the steroid conformation E, such interaction is minimal when both C-2 acetyl and C-5 hydroxyl groups assume the more stable equatorial orientation. These studies clearly support the stereochemistry assigned to compounds **6** and **7**.

Subsequent synthetic operations were carried out with **6**. Protection of the 5β-hydroxyl group in **6** was readily accomplished by reacting **6** with dihydropyran in the presence of a catalytic amount of toluene-*p*-sulfonic acid to give the tetrahydropyranyl ether **8**. Treatment of ketone **8** with methylenetriphenylphosphorane in dimethyl sulfoxide[10] gave the isopropenyl compound **9** in excellent yield. Catalytic hydrogenation of **9** in the presence of 5% palladium on carbon in ethyl acetate solution and then removal of the tetrahydropyranyl protecting group with ethanolic hydrochloric acid gave two crystalline compounds, **10** and **11**, in the approximate ratio of 24:1, which were separated on a column of alumina. In the nmr spectrum of the major compound **10** the C-5 methine proton appeared as a broad multiplet at 3.91 ppm whose width at half-height (18 Hz) indicated the axial orientation, and therefore the 5β-hydroxyl group must be equatorially disposed. In the isomeric minor product **11** the corresponding hydrogen was seen as a poorly resolved triplet centered at 3.28 ppm whose width at half-height (6 Hz) suggested an equatorial conformation, and consequently the 5β-hydroxy group in this compound must be axially oriented. We have therefore assigned the steroid cis conformation G for the major product **10** and the nonsteroid cis conformation H for the minor product **11** as shown.

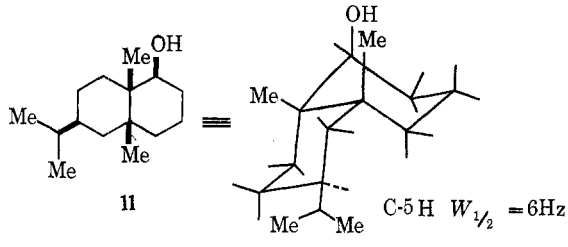


Although we have employed the stereochemically homogeneous compound **6**, the fact that we obtained a mixture of the two isomeric compounds **10** and **11** in the ratio of 24:1 after the Wittig reaction and catalytic hydrogenation needs some explanation. We have demonstrated (*vide supra*) that compound **6** under alkaline

(14) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, pp 78–81.



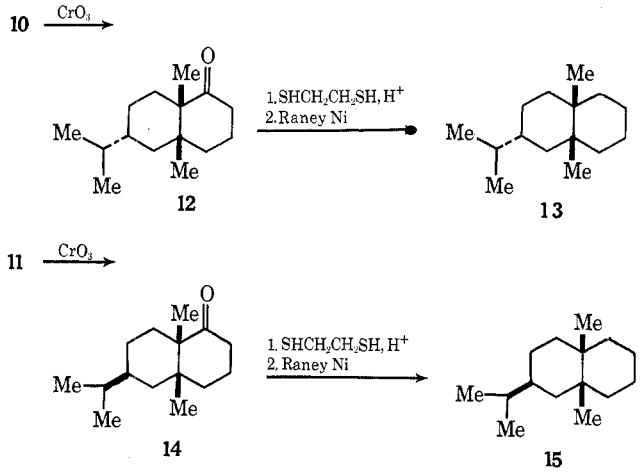
steroid cis G



nonsteroid cis H

conditions can equilibrate, and a very small amount (3%) of compound **7**, with nonsteroid cis conformation, can be obtained. Apparently under the alkaline Wittig reaction conditions the tetrahydropyranyl ether derivative **8** must have similarly epimerized to a small extent, resulting in formation of **11** with nonsteroid cis conformation. It was also possible that some inversion of the acetyl side chain of ketone **6** took place during the preparation of the tetrahydropyranyl ether.

Oxidation of the major alcohol **10** with Jones reagent[12] gave the ketone **12** in almost quantitative yield. The oxygen function in ketone **12** was removed by first reacting it with ethanedithiol in the presence of boron fluoride etherate to give the 5-ethylene thioketal, which, without further purification, was desulfurized in acetone solution using deactivated Raney nickel[15] to give racemic valerane **13** in excellent yield. The natural *l*-valerane was prepared for comparison from *l*-valeranone[16]



as described by Hikino, *et al.*[1f] The infrared and nmr spectra of the synthetic material **13** were found to be identical with those of the authentic natural *l*-valerane.

Similarly, oxidation of the minor isomeric alcohol **11** with Jones' reagent gave the ketone **14** which was distinctly different from **12**. The infrared, nmr and gas chromatographic retention times of **14** were found to be different from those of the ketone **12**. Furthermore, ketone **12** gave a 2,4-dinitrophenylhydrazone, mp 177–179°, whereas the 2,4-dinitrophenylhydrazone obtained from **14** melted at 154–156°. Removal of the keto group in **14** through ethylene thioketal formation followed by Raney nickel reduction yielded the racemic hydrocarbon **15**. The infrared and nmr spectra of **15** differed considerably from those of compound **13**. The methyl and isopropyl peaks in the nmr spectra (Figures 1 and 2) are particularly helpful in establishing the identity of **13** with the natural product. Accordingly, **15** was designated as *dl*-7-isovalerane.[17]

These studies provide conclusive evidence that valerane exists in a steroid cis conformation with an equatorial isopropyl group and suggest conformation A for valeranone, in agreement with earlier assumptions.

In the nmr spectra of the epimeric pairs of 5β-hydroxy compounds **6** and **7** and **10** and **11**, we noted some interesting features. It has been stated that axial protons attached to hydroxyl-substituted carbon atoms resonate at higher field than the corresponding equatorial protons in the epimeric alcohol.[14] However, the characteristic chemical shifts of the epimeric alcohols, as summarized in Table I, show a reversal of the usual

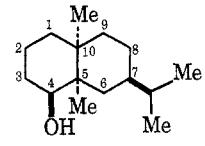
TABLE I

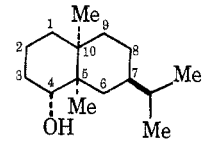
CHEMICAL SHIFTS AND LINE WIDTHS AT HALF-HEIGHT FOR C-5 PROTON ADJACENT TO OXYGEN FUNCTION IN *cis*-9,10-DIMETHYLDECALIN COMPOUNDS

Compd	Chemical shift (δ), ppm	Line width at half-height ($W_{1/2}$), Hz	Conformation of C-5 proton
6	4.03	19	Axial
7	3.38	8	Equatorial
10	3.91	18	Axial
11	3.28	6	Equatorial
16	3.59[a]	16[a]	Axial
17	3.25[a]	6[a]	Equatorial

[a] Data from Hikino, *et al.*[1f]

axial–equatorial relationship and present an exception to the rule. The epimeric alcohols **16** and **17** prepared





from natural *l*-valeranone by Hikino, *et al.*,[1f] also exhibit a similar reversal of axial–equatorial relationship. Similar exceptions have been reported earlier in the literature.[18] Although one could speculate that this anomaly may be due to long-range shielding effects associated with diamagnetic anisotropy, a clear understanding of this phenomenon is not possible at this time without further detailed study of other model compounds.

(15) (a) G. B. Spero and A. V. McIntosh, Jr., *J. Amer. Chem. Soc.*, **70**, 1907 (1948); (b) G. Rosenkranz, S. F. Kaufman, and J. Romo, *ibid.*, **71**, 3689 (1949); (c) P. N. Rao and H. R. Gollberg, *Tetrahedron*, **18**, 1251 (1962).

(16) The natural *l*-valeranone was kindly supplied by Dr. Hikino. The infrared and nmr spectra of *l*-valerane prepared in Japan were also kindly supplied by Dr. Hikino for our comparison of the product prepared in our laboratories.

(17) Valeranone skeleton numbering.

(18) (a) A. Nickon, M. A. Castle, R. Harada, C. E. Birkoff, and R. O. Williams, *J. Amer. Chem. Soc.*, **85**, 2185 (1963). (b) K. M. Wellman and F. G. Bordwell, *Tetrahedron Lett.*, 1703 (1963).

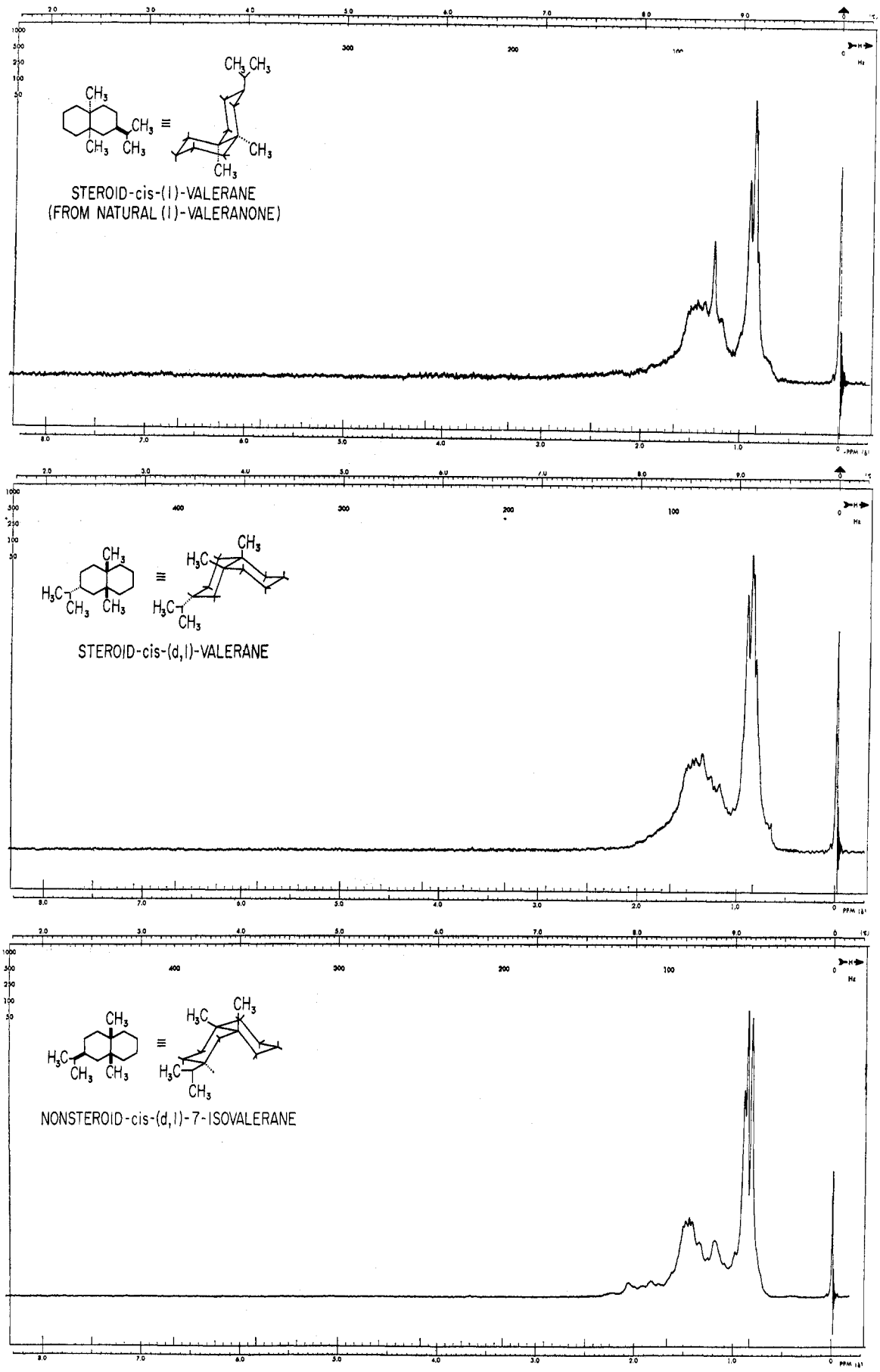


Figure 1.—Nmr spectra of **13**, **15**, and natural valerane in CCl_4.

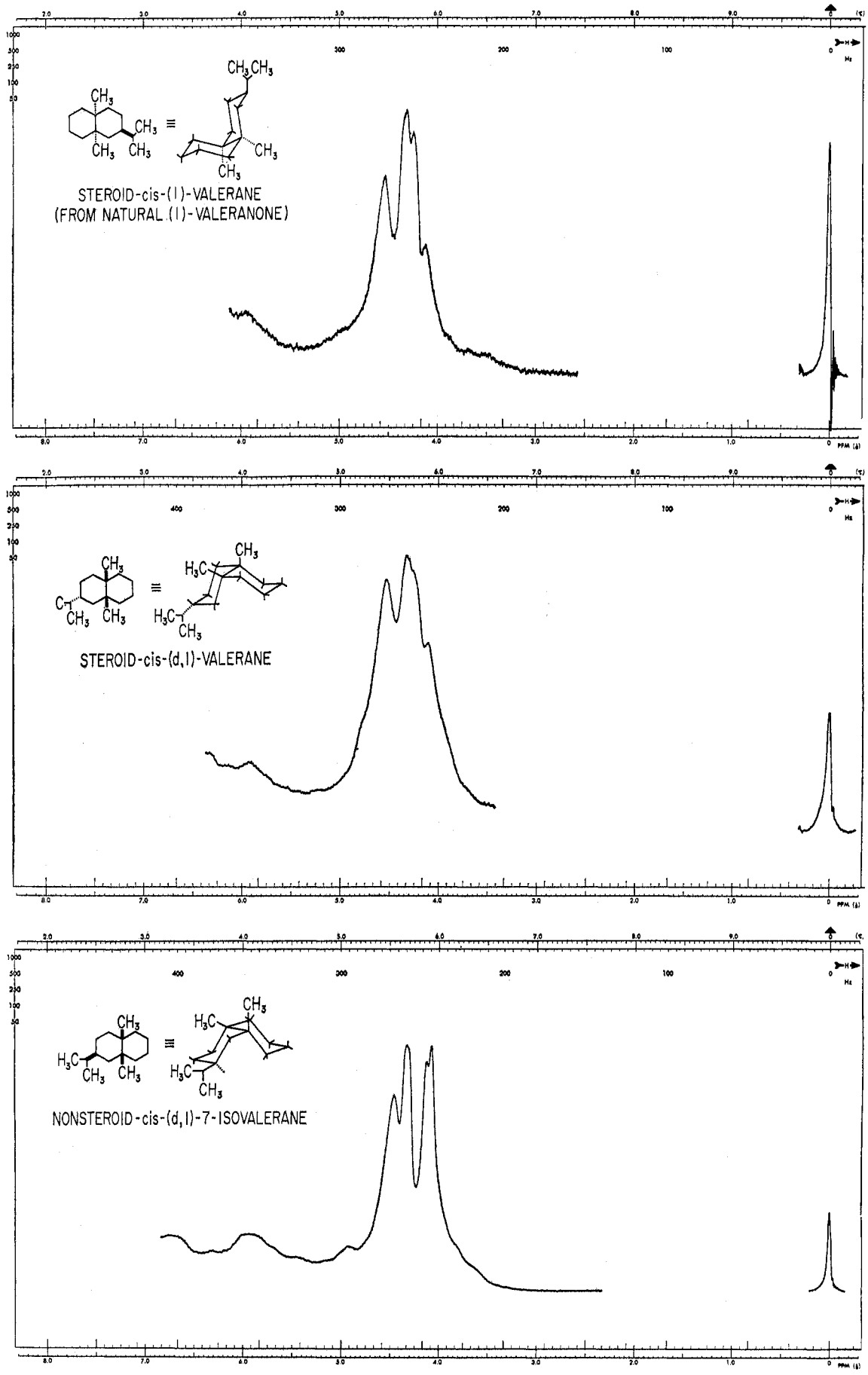


Figure 2.—Nmr spectra of isopropyl and methyl peaks of **13**, **15**, and natural valerane (0.1-Hz sweep time, 100-Hz sweep width).

Experimental Section[19]

5β-Tetrahydropyranyloxy-*cis*-9β,10β-dimethyl-2-decalone (3).[19]—To a solution of 5β-hydroxy-*cis*-9β,10β-dimethyl-2-decalone (2)[6] (2.87 g) in ether (50 ml), dihydropyran (2.5 ml) and toluene-*p*-sulfonic acid (50 mg) were added and the contents were stirred at room temperature for 4 hr. The reaction mixture was then washed with saturated sodium bicarbonate solution and saturated brine and dried (Na_2SO_4), and the solvent was evaporated. The resiude was then crystallized from petroleum ether to give **3** (3.8 g, 92%): mp 83–85°, $\nu_{max}^{CHCl_3}$ 2950, 2880, and 1710 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 0.92 (s, CH_3) and 1.0 (s, CH_3) ppm.

Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.80; H, 10.21.

Preparation of 3 from 5β-Tetrahydropyranyloxy-10β-methyl-1(9)-octal-2-one (4) by Conjugate Addition of Lithium Dimethylcopper.—A stirred suspension of cuprous iodide (68.7 g, 0.36 mol) in anhydrous ether (1000 ml) under an atmosphere of dry nitrogen was cooled to −25° by means of an external CCl_4–Dry Ice bath. To this mixture was added an ether solution of methyllithium until the yellow precipitate just disappeared (360 ml of 2 *M* concentration, 0.72 mol). A small amount of cuprous iodide was then added to bring back the yellow precipitate, thus ensuring that no excess methyllithium was present. A solution of ketone 4[8] (35 g, 0.132 mol) in dry ether (360 ml) was slowly added over a period of 20 min and the contents was stirred for 1 hr at −25°. The reaction mixture was then decomposed by pouring it into a rapidly stirred mixture of concentrated ammonium hydroxide (2 l.) and ice. The residue in the reaction flask was also treated with ice-cold ammonium hydroxide and ether and stirred until dissolved. The total combined aqueous–ether mixtures were transferred to a separatory funnel and the ether extract was separated, washed with brine, dried (Na_2SO_4), filtered, and evaporated. The residue was then diluted with petroleum ether and stored at −20° to give compound **3** (27.9 g), mp 83–85°. The mother liquor was passed through a column of alumina (365 g) and eluted with petroleum ether–benzene (8:2) to give an additional amount of **3** (3.4 g), mp 82–84°. The total yield of **3** amounted to approximately 75%. The product prepared by this method was found to be identical in all respects with that of the authentic sample described above.

2-Ethylidene-5β-tetrahydropyranyloxy-*cis*-9β,10β-dimethyldecalin (5).[19c]—The procedure of Corey, *et al.*,[10] was employed. A solution of sodium methylsulfinyl carbanion was prepared under nitrogen from sodium hydride (0.43 g, 0.018 mol) and dimethyl sulfoxide (12 ml). The solution was cooled in a cold water bath and stirred during the addition of ethyl triphenylphosphonium bromide (6.7 g, 0.018 mol) in dimethyl sulfoxide (30 ml), whereupon the characteristic color of the ethylidenephosphorane was produced. After the mixture was stirred at room temperature for 15 min, a solution of the ketone **3** (3.92 g, 0.014 mol) in dimethyl sulfoxide (10 ml) was added and stirring was continued at room temperature for 2 hr and then at 60–65° for an additional hour. The reaction mixture was cooled and poured into cold water (100 ml) and the product was isolated with hexane.[19b] The crude mixture was chromatographed on alumina (130 g) to remove the triphenylphosphine oxide. Elution with petroleum ether gave **5** (3.5 g, 86.5%). An analytical sample was prepared by short-path distillation at 10^{-4} mm, bath temperature 120°: $\nu_{max}^{CHCl_3}$ 2940, 2860, 1620, 1480, 1450, and 1390 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 0.83 (s, CH_3) and 0.88 (s, CH_3) ppm.

Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.02; H, 11.03. Found: C, 77.84; H, 11.20.

2α-Acetyl-5β-hydroxy-*cis*-9β,10β-dimethyldecalin (6) and 2β-Acetyl-5β-hydroxy-*cis*-9β,10β-dimethyldecalin (7).[19c] (i) **Hydroboration.**—A solution of tetrahydropyranyl ether **5** (24.4 g) in tetrahydrofuran (150 ml) was cooled to 0° and kept under nitrogen atmosphere. A solution of diborane in tetrahydrofuran[20] (164 ml, 1 *M* BH_3–THF complex) was added and the contents stirred at room temperature for 1 hr. Sodium hydroxide solution (235 ml, 10% solution) was added dropwise and the alkaline reaction mixture was brought to 0° once again. Hydrogen peroxide (164 ml, 30% solution) was then slowly added over a period of 20 min and the contents stirred for an additional hour; the reaction product was isolated with ethyl acetate.[19b] The crude product (24 g) exhibited hydroxyl absorption in the infrared spectrum and without further purification was oxidized with 8 *N* chromic acid.

(ii) **Oxidation of the Above Mixture of Alcohols with 8 *N* Chromic Acid.**[12]—The crude reaction product (24 g) from the above hydroboration experiment was dissolved in acetone (250 ml) and the contents was cooled to −5°. A solution of 8 *N* chromic acid[12] was added with stirring until the orange color persisted. The excess reagent was destroyed by the addition of a few drops of methanol and solid sodium bicarbonate was added to neutralize any excess acid. The mixture was filtered through Celite, the residual gummy solid was triturated with ethyl acetate, and the combined filtrates were concentrated under reduced pressure. The oxidation product was isolated with ethyl acetate[19b] to give a mixture of 2ξ-acetyl-*cis*-9β,10β-dimethyldecalin derivative (23.4 g). This crude product exhibited a strong carbonyl absorption at 1700 cm^{-1} in the infrared spectrum.

(iii) **Base-Catalyzed Equilibration of the Above 2ξ-Acetyl Compound.**—A solution of the above ketone (23.4 g) in ethanol (100 ml) was added to a solution of 1 *N* ethanolic sodium ethoxide (100 ml) and the contents was stirred at 60° for 18 hr under nitrogen atmosphere. The excess alkali was carefully neutralized with acetic acid and most of the ethanol was removed under reduced pressure. The product was isolated with ethyl acetate[19b] to yield an oil (23 g).

(iv) **Removal of the Tetrahydropyranyl Protecting Group and Separation of Ketones 6 and 7.**—The product from the above reaction was dissolved in ethanol (250 ml), and concentrated hydrochloric acid (5 ml) and water (2 ml) were added and stirred at room temperature overnight. Most of the ethanol was removed under reduced pressure and the product was isolated with ethyl acetate[19b] to give a thick gummy product (17.8 g) which, on crystallization from ether–petroleum ether, gave 2α-acetyl-5β-hydroxy-*cis*-9β,10β-dimethyldecalin (**6**) (9.1 g), mp 77–78°. The analytical sample crystallized from ether–hexane: mp 79–81°; $\nu_{max}^{CHCl_3}$ 3600, 2940, 2880, and 1700 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.03 (–CHOH, broad multiplet, $W_{1/2}$ = 19 Hz), 2.6 (>CHCOCH$_3$, broad multiplet, $W_{1/2}$ = 23 Hz), 2.13 (s, –COCH$_3$), 0.93 (s, CH_3), and 0.83 (s, CH_3) ppm.

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.83; H, 10.95.

The mother liquors were combined and chromatographed on alumina (270 g). Elution of the column with petroleum ether–benzene (1:1) gave 2β-acetyl-5β-hydroxy-*cis*-9β,10β-dimethyldecalin (**7**) (0.377 g) which crystallized from ether–hexane: mp 72–74°; $\nu_{max}^{CHCl_3}$ 3610, 2960, 2875, and 1705 cm^{-1}, $\delta_{TMS}^{CDCl_3}$ 3.38 (CHOH, poorly resolved triplet, $W_{1/2}$ = 8 Hz) 2.5 (>CHCOCH$_3$, broad multiplet, $W_{1/2}$ = 22 Hz), 2.05 (s, –COCH$_3$), 1.05 (s, CH_3), and 1.0 (s, CH_3) ppm.

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.74; H, 10.86.

Further elution of the column with benzene and benzene–ether (8:2) gave an additional amount of **6** (5.23 g). The total amount of 2α-acetyl product **6** obtained was 14.33 g. The 2β-acetyl product isolated amounted to 0.377 g. The overall yield of the combined 2ξ-acetyl product was 78.7%, of which 97.4% comprises **6** and 2.6% is compound **7**.

Base-Catalyzed Equilibration of 2α-Acetyl Product 6.—To a solution of 1 *N* ethanolic sodium ethoxide (25 ml) a solution of **6** (150 mg) in ethanol (5 ml) was added and the contents was stirred at 60° for 20 hr. The reaction mixture was neutralized with acetic acid and the alcohol was evaporated under reduced pressure. The equilibrated product was isolated with ethyl acetate.[19b] Thin-layer chromatographic examination (benzene–ether 1:1 solvent system) of a small sample from the total reaction product revealed the presence of a small amount of com-

(19) (a) All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer (Model 257) spectrometer. Nmr spectra were run in the specified solution using 2% TMS as internal standard on a Varian A-60A nmr spectrometer. Woelm neutral aluminum oxide activity III was employed for chromatography. Reagent grade silica gel G for tlc prepared by E. Merck was used for thin-layer chromatography in the specified solvent system. Petroleum ether employed was that of Mallinckrodt reagent grade, bp 30–60°. Microanalyses were carried out by Micro-Tech Laboratories, Skokie, Ill. (b) The following sequence describes a typical isolation procedure. The reaction mixture was treated with water and extracted with specified organic solvent. The solvent extract was washed with brine, dried over anhydrous sodium sulfate, and filtered, and the solvent was evaporated under reduced pressure on a Büchi rotary evaporator at 60–65°. The residue left in the flask was then purified as described. (c) The prefix *dl* is omitted from the names of racemic substances. The prefixes α and β are used to denote relative stereochemistry.

(20) Available from Ventron Corp., Beverly, Mass.

pound **7**. The total product (150 mg) was then subjected to column chromatography on alumina (5 g). Elution of the column with petroleum ether–benzene (8:2) and (1:1) gave compound **7** (5 mg, 3.3%), mp 72–74°. A mixture melting point with authentic sample did not show depression and the infrared spectrum was found to be identical.

Further elution of the column with benzene and benzene–ether (8:2) gave unchanged **6** (143 mg), mp 79–81°, whose identity was established by comparing the infrared spectrum and mixture melting point determination.

Base-Catalyzed Equilibration of 2β-Acetyl Product 7.—A similar equilibration employing **7** (200 mg) and 1 *N* ethanolic sodium ethoxide (40 ml), after work-up and chromatographic separation as described above, gave **6** (193 mg, 97%), mp 78–80° and unchanged **7** (6 mg), mp 72–73°. The identity of these products was established through mixture melting point determination and by comparison of the infrared spectra.

2α-Acetyl-5β-tetrahydropyranyloxy-*cis*-9β,10β-dimethyldecalin (8).[19c]—To a solution of 2α-acetyl compound (12.1 g) in ether (250 ml), dihydropyran (5.2 ml) and toluene-*p*-sulfonic acid (300 mg) were added and the contents was stirred at room temperature for 18 hr. The ether solution was then washed with saturated sodium bicarbonate and brine and dried (Na_2SO_4), and the solvent was evaporated to give a viscous oil (16 g). The analytical sample was prepared by short-path distillation at 10^{-4} mm, bath temperature 125°: $\nu_{max}^{CHCl_3}$ 2940, 2880, and 1705 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 0.88 (s, CH_3), 0,95 (s, CH_3), and 2.15 (s, $-COCH_3$) ppm.

Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 73.72; H, 10.22.

2α-Isopropenyl-5β-tetrahydropyranyloxy-*cis*-9β,10β-dimethyldecalin (9).[19c]—A solution of methyltriphenylphosphonium bromide (5.36 g, 0.015 mol) in dimethyl sulfoxide (25 ml) was added under nitrogen atmosphere to a solution of dimethylsulfinylsodium[10] prepared from sodium hydride (0.36 g, 0.015 mol) and dimethyl sulfoxide (7.5 ml). The resulting yellow solution was stirred at room temperature for 0.5 hr and then a solution of ketone **8** (3.7 g, 0.012 mol) in dimethyl sulfoxide was added. The reaction mixture was stirred at 55° for 18 hr, cooled, diluted with water, and extracted with hexane. The combined hexane extracts were washed with aqueous dimethyl sulfoxide (50% solution) and water, dried (Na_2SO_4), and filtered, and the solvent was evaporated. The crude residue was then passed through a column of alumina (100 g) and eluted with petroleum ether to give **9** (2.94 g, 73%) as colorless mobile oil. The analytical sample was prepared by short-path distillation at 10^{-4} mm, bath temperature 130°: $\nu_{max}^{CHCl_3}$ 2940, 2860, and 1642 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 4.66 (d, J = 5 Hz, C=CH_2), 1.7 (s, C=CCH_3), 0.92 (s, CH_3), and 0.83 (s, CH_3) ppm.

Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.34; H, 11.43.

2α-Isopropyl-5β-hydroxy-*cis*-9β,10β-dimethyldecalin (10) and 2β-Isopropyl-5β-hydroxy-*cis*-9β,10β-dimethyldecalin (11).[19c] **(i) Hydrogenation**—A solution of **9** (15.9 g) in ethyl acetate (150 ml) was hydrogenated in the presence of 5% palladium on charcoal (1 g). The solution was filtered from the catalyst and the solvent was evaporated to give colorless viscous oil (15.9 g). The infrared and nmr spectra of this material indicated complete saturation.

(ii) Removal of the Tetrahydropyranyl Protecting Group and Separation of Alcohols 10 and 11—The hydrogenated product (15.9 g) was dissolved in 95% ethanol (150 ml), and concentrated hydrochloric acid (5 ml) was added; the mixture was stirred under nitrogen for 5 hr. The hydrochloric acid was neutralized with sodium hydroxide (5% solution) and most of the solvent was evaporated under reduced pressure; the product was isolated with ethyl acetate[19b] to give a mixture of **10** and **11** as a solid (10.6 g, 91%). Thin layer chromatographic examination (benzene–ether 8:2 solvent system) of a small sample revealed one major product with a small amount of another compound moving slightly ahead of it. The total solid was then crystallized from acetone–hexane to give pure **10** (4.2 g): mp 74–75°; $\nu_{max}^{CHCl_3}$ 3600, 2940, 2870, 1472, 1460, and 1018 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 3.91 (CHOH, broad multiplet, $W_{1/2}$ = 18 Hz), 0.9 (s, CH_3), 0.87 (d, J = 5 Hz, isopropyl), and 0.78 (s, CH_3) ppm.

Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.32; H, 12.56.

The residue (6.3 g) from the above mother liquor was subjected to very careful chromatography on alumina (190 g). Elution of the column with petroleum ether–benzene (8:2) gave pure **11** (0.39 g) which was crystallized from acetone: mp 75–77°; $\nu_{max}^{CHCl_3}$ 3618, 2980, 2880, 1470, and 980 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 3.28 (CHOH, poorly resolved triplet; $W_{1/2}$ = 6 Hz), 1.03 (s, CH_3), 0.98 (s, CH_3), and 0.87 (d, J = 5 Hz, isopropyl) ppm.

Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.44; H, 12.59.

Further elution of the column with petroleum ether containing gradual increments of benzene up to 1:1 gave an inseparable mixture of **10** and **11** (0.91 g). Finally, eluting the column with petroleum ether–benzene (1:1) and benzene gave an additional amount of pure **10** (5 g). The total amount of 2α-isopropyl compound **10** isolated from direct crystallization and chromatographic separation amounted to 9.2 g and the 2β-isopropyl compound **11** amounted to 0.39 g.

2α-Isopropyl-*cis*-9β,10β-dimethyl-5-decalone (12).[19c]—To a solution of **10** (1.34 g) in acetone (40 ml) 8 *N* chromic acid[12] was added with stirring until the orange color persisted. The excess reagent was destroyed by the addition of a few drops of methanol and solid sodium bicarbonate was added to neutralize any excess acid. The mixture was then filtered through Celite and the gummy residue was thoroughly washed with ethyl acetate. The combined filtrates were concentrated under reduced pressure and the oxidation product was isolated with ether.[19b] The crude product was purified by distillation at 0.35 mm, bath temperature 100°, to give **12** (1.28 g): $\nu_{max}^{CHCl_3}$ 2940, 2880, and 1700 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 1.03 (s, CH_3), 1.0 (s, CH_3), and 0.83 (d, J = 5 Hz, isopropyl) ppm.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.12; H, 11.59.

The 2,4-dinitrophenylhydrazone derivative of **12** was prepared by the standard procedure and was crystallized from ethyl acetate: mp 177–179°; ν_{max}^{KBr} 3320, 2940, 2880, 1630, 1600, 1530, and 1510 cm^{-1}.

Anal. Calcd for $C_{21}H_{30}O_4N_4$: C, 62.67; H, 7.51. Found: C, 62.71; H, 7.52.

2β-Isopropyl-*cis*-9β,10β-dimethyl-5-decalone (14).[19c]—2β-Isopropyl compound **11** (450 mg) in acetone solution (10 ml) was oxidized with 8 *N* chromic acid[12] as described above, and the product was purified by distillation at 0.7 mm, bath temperature 110°, to give **14** (410 mg): $\nu_{max}^{CHCl_3}$ 2980, 2880, and 1700 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.97 (s, CH_3), 0.89 (d, J = 5 Hz, isopropyl), and 0.80 (s, CH_3) ppm.

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.25; H, 11.57.

The 2,4-dinitrophenylhydrazone derivative of **14** was crystallized from ethyl acetate: mp 154–156°; ν_{max}^{KBr} 3220, 2960, 2880, 1628, 1600, 1530, and 1512 cm^{-1}.

Anal. Calcd for $C_{21}H_{30}O_4N_4$: C, 62.67; H, 7.51. Found: C, 62.70; H, 7.55.

Gas chromatographic analysis[21] indicated that ketone **12** was less polar compared to **14** and the retention times were 8.2 and 10.3 min, respectively.

2α-Isopropyl-*cis*-9β,10β-dimethyldecalin (Racemic Valerane) (13).[19c]—To a solution of the decalone **12** (230 mg) in ethanedithiol (0.5 ml), boron trifluoride etherate (0.5 ml) was added and the contents was stirred at room temperature overnight and then warmed for 4 hr at 70–75°. The crude ethylenethioketal derivative was isolated with ether[19b] and the infrared spectrum indicated the absence of carbonyl group. Without further purification the ethylene thioketal derivative was subjected to desulfurization with deactivated Raney nickel catalyst (W-2, two level teaspoonfuls)[15] in acetone solution (100 ml). After 4.5 hr of refluxing, the acetone solution was filtered from the catalyst, the solvent was evaporated, and the residue (202 mg) was purified by short-path distillation at 2 mm, bath temperature 105°, to give analytically pure compound **13** (127 mg): $\nu_{max}^{CHCl_3}$ 2940, 2880, 1530, 1510, 1400, and 1382 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.87 (s, CH_3), 0.86 (d, J = 5 Hz, isopropyl), and 0.85 (s, CH_3) ppm.

Anal. Calcd for $C_{15}H_{28}$: C, 86.46; H, 13.54. Found: C, 86.37; H, 13.37.

2β-Isopropyl-*cis*-9β,10β-dimethyldecalin (Racemic 7-Isovalerane[17]) (15).[19c]—To a solution of the decalone **14** (375 mg) in ethanedithiol (1 ml), boron trifluoride etherate (1 ml) was added and the contents was stirred at room temperature overnight. The ethylene thioketal derivative was isolated with ether[19b] and

(21) Aerograph Model (90 P3) with a 0.25-in. × 10-ft column of 10% UCON 75H 90,000 polar on 60–80 Gas Pack W was employed at 192° with a helium flow rate of 52 cc/min.

subjected to desulfurization with deactivated Raney nickel (two level teaspoonfuls)[15] in acetone solution (100 ml) as described above. Purification of **15** through short-path distillation at 2.5 mm, bath temperature 105°, gave analytically pure product (187 mg): $\nu_{max}^{CHCl_3}$ 2940, 2880, 1520, 1500, 1400, and 1380 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.87 (s, CH_3), 0.85 (d, J = 5 Hz, isopropyl), and 0.82 (s, CH_3) ppm.

Natural Valerane from *l*-Valeranone.—This product was prepared from natural valeranone (120 mg) essentially as described by Hikino, *et al.*,[1f] and the identity of the product prepared in our laboratories was established by comparison of infrared and nmr spectra of material prepared in Japan.[16]

Registry No.—**3**, 29969-74-2; **5**, 29863-73-8; **6**, 29863-74-9; **7**, 29863-75-0; **8**, 29862-76-1; **9**, 29863-77-2; **10**, 29863-78-3; **11**, 29863-79-4; **12**, 29863-80-7; **12** 2,4-DNP, 29863-81-8; **13**, 29863-82-9; **14**, 30008-94-7; **14** 2,4-DNP, 29863-83-0; **15**, 29863-84-1.

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Acetylation of Pinane

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When pinane was treated with acetyl chloride and aluminum chloride under Friedel–Crafts conditions, an unstable product, 2-acetyl-1-chloro-4-isopropyl-1-methylcyclohexane, was formed. This product was transformed to a mixture of acetyl-4-isopropyl-1-methylcyclohexenes by loss of HCl. The stereochemistry of the products and its bearing on the mechanism of the Kondakov reaction is discussed.

Although the chemistry of the pinenes has been extensively studied,[1] relatively little has been learned about the saturated hydrocarbon, pinane. The pinane molecule is quite stable and its potentially labile cyclobutane ring is resistant to most oxidizing agents and mineral acids. It reacts only slowly with hydrogen bromide at 230°.[2]

Whereas free-radical type reactions of pinane have been reported,[3-8] reactions of pinane by ionic mechanisms have not. However, the acetylation of saturated hydrocarbons with acetyl chloride in the presence of aluminum chloride is known[9-11] and offers a feasible route toward functionalizing pinane. We have investigated this reaction and present here the results of our work.

When an ethylene dichloride solution of the complex formed between acetyl chloride and aluminum chloride was added to pinane (**1**), a mixture of chloro ketones **5** was produced. The chloro ketones lost HCl slowly on standing. Upon heating, HCl was evolved more rapidly and the product formed was the α,β-unsaturated ketone **8**. When submitted to glc analysis, HCl was again lost but the products eluted were the β,γ-unsaturated ketones **6** and **7** plus a small amount of **8**.

That the chloro ketones formed are 2-acetyl-1-chloro-4-isopropyl-1-methylcyclohexanes (**5**) was supported by the fact that the same products were formed by adding acetyl chloride to 1-*p*-menthene. Also, the unsaturated ketones eluted from the glc were identical with those prepared by the acetylation of 1-*p*-menthene with acetic anhydride.

The nmr spectra of crude and distilled fractions of the β-chloro ketone **5** revealed that it was a mixture of at least two principal isomers **5a** and **5b**. One isomer (which dominated the earlier fractions of the distilled crude) showed a broad multiplet at τ 6.83 (*ca.* 12-Hz wide, $>CHCOCH_3$), sharp singlets at τ 7.82 (CH_3CO) and 8.35 [$>C(Cl)CH_3$], and a doublet at τ 9.22 (J = 5.5 Hz, $-<\begin{matrix}CH_3\\CH_3\end{matrix}$). The nmr of later fractions showed additional peaks at τ 7.30 (*ca.* 17-Hz wide, $>CHCOCH_3$), a sharp singlet at τ 7.77 (CH_3CO), and a doublet at τ 9.26 (J = 5.5 Hz, $-<\begin{matrix}CH_3\\CH_3\end{matrix}$) assigned to a second isomer. The signals for the methine protons α to the carbonyl indicated that this proton was equatorial in the lower boiling isomer **5a** (less broad and further downfield from TMS) and was axial in the higher boiling isomer **5b** (signal at higher field and broader due to diaxial coupling).[12]

In accord with the above, it was found that **5a** decomposed on glc to a β,γ-unsaturated ketone **6** in which the acetyl group is quasiaxial while isomer **5b** decomposed to a β,γ-unsaturated ketone **7** in which the acetyl

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