Hydroboration of Terpenes. V. Isomerization of (+)-Sabinene to (−)-α-Thujene. Hydroboration of (+)-Sabinene and (+)-α-Thujene with Configurational Assignments for the Thujanols

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Received January 8, 1969

A revised nomenclature for various configurational thujanols is proposed. (+)-Sabinene readily isomerizes to an equilibrium mixture of 91% (−)-α-thujene (2) and 9% (+)-sabinene (1) under the influence of potassium *t*-butoxide in dimethyl sulfoxide, and this provides an improved synthetic route to (−)-α-thujene. Catalytic hydrogenation of (+)-α-thujene over platinum preferentially takes place away from the side of the cyclopropane ring to give chiefly (−)-*trans*-thujane (4) whereas catalytic hydrogenation of (+)-sabinene (1) takes place preferentially from the opposite side to give chiefly (−)-*cis*-thujane. Hydroboration of (+)-α-thujene takes place exclusively from the same direction as hydrogenation, *i.e.*, the side away from the cyclopropane ring. Hydroboration of sabinene also takes place from the side away from the cyclopropane ring, from the direction which is opposite to that taken in hydrogenation. The organoborane formed preferentially in the hydroboration of sabinene appears to be the thermodynamically more stable isomer, since it did not epimerize under isomerization conditions. A similar thermodynamic stability favoring the isomer with the mobile substituent (10-C) located on the side toward the cyclopropane ring is present in 10-thujaldehydes and 3-thujones. This unusual stability of the epimers which contain the substituents *cis* to the cyclopropane ring is interpreted in terms of a preferred existence of thujane derivatives in a boat conformation, rather than in the more usual planar or chair forms. The nmr spectra are subjected to a detailed analysis and provide support for these conformational assignments.

In our previous studies of the hydroboration of terpenes, *viz.*, α-pinene,[2] β-pinene,[2] 2-carene,[3] and 3-carenes,[4] only one side of the double bond was relatively free for reactions involving large steric requirements. Such steric effects controlled the direction taken by these reactions. The molecular models of α-thujene (2) and sabinene (1) indicate that both sides of the double bond are relatively accessible. However, a new feature is present in these systems. The double bond of both of these structures is in a position to conjugate with the cyclopropane ring. However, this ring is unsymmetrically situated with respect to the π electrons, so that the possibility exists that differences in such conjugation from the two sides may greatly affect the direction taken by the individual reactions. In order to explore this possibility a study was undertaken of the hydrogenation and hydroboration of thujene and sabinene. In the course of this work a new simple isomerization of the readily available sabinene to the relatively rare α-thujene was developed.

Nomenclature.—Previous investigations of the stereochemistry of the four naturally occurring thujyl alcohols and the corresponding thujones have been reviewed and the steric relationship between these compounds and the other members of the thujane group have been proposed and corrected by Norin[5,6] based on their chemical and spectroscopic properties. However, he retained the names assigned on the basis of the original erroneous structures. These new assignments have been further confirmed by other workers.[7-10] As in the case of stereoisomeric menthols, carvomenthols, caranols, and pinocampheols, the prefixes neo, iso, and neoiso have been applied to distinguish the different thujanols. However, considerable confusion has arisen in the application of these prefixes. For example, iso is used to indicate that methyl and cyclopropane are *cis* to each other in all thujyl alcohols and thujones,[5,6] but *cis* is also used to indicate that the methyl and isopropyl groups are *cis* to each other in the parent hydrocarbons.[9] Similarly neo is used to indicate that methyl and hydroxyl groups are *cis* to each other[5,6] in the "iso" series and *trans* to each other in the "normal" series.[5,6] It appears highly desirable to minimize the possibilities for such confusion by achieving uniformity between the thujyl derivatives and the related menthol, carvomenthol, pinocampheol, and caranol series. It is therefore proposed that iso or *cis* be used to indicate that methyl and isopropyl are *cis* to each other and that neo be used to indicate that methyl and hydroxyl are *cis* to each other, in accordance with the recommendation of Schroeter and Eliel[11] for the carvomenthol and related terpenes. This revision has been reviewed by Norin and Klein and has been approved by them.[12] To rule out any possible misunderstandings we have added the properties and the optical rotations of all four alcohols in Figure 1.

Results

Isomerization of (+)-Sabinene (1).—Savin oil contains (+)-sabinene of high optical purity in the hydrocarbon fraction and sabina acetate also of high optical purity, in the ester fraction. Consequently, (+)-sabinene is readily available in a state of high

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[2] G. Zweifel and H. C. Brown, *J. Amer. Chem. Soc.*, **86**, 393 (1964).

[3] S. P. Acharya and H. C. Brown, *ibid.*, **89**, 1925 (1967).

[4] H. C. Brown and A. Suzuki, *ibid.*, **89**, 1933 (1967).

[5] T. Norin, *Acta Chem. Scand.*, **16**, 640 (1962).

[6] M. S. Bergquist and T. Norin, *Arkiv Kemi*, **22**, 137 (1964).

[7] E. H. Massey, H. E. Smith, and A. W. Gordon, *J. Org. Chem.*, **31**, 684 (1966).

[8] H. E. Smith, J. C. D. Brand, E. H. Massey, and L. J. Durham, *ibid.*, **31**, 690 (1966).

[9] G. Ohloff, G. Uhde, A. F. Thomas, and E. sz. Kováts, *Tetrahedron*, **22**, 309 (1966).

[10] M. R. Cox, H. P. Koch, W. B. Whalley, M. B. Hursthouse, and D. Rogers, *Chem. Commun.*, 212 (1967).

[11] S. H. Schroeter and E. L. Eliel, *J. Org. Chem.*, **30**, 1 (1965).

[12] Private communications from T. Norin and E. Klein.

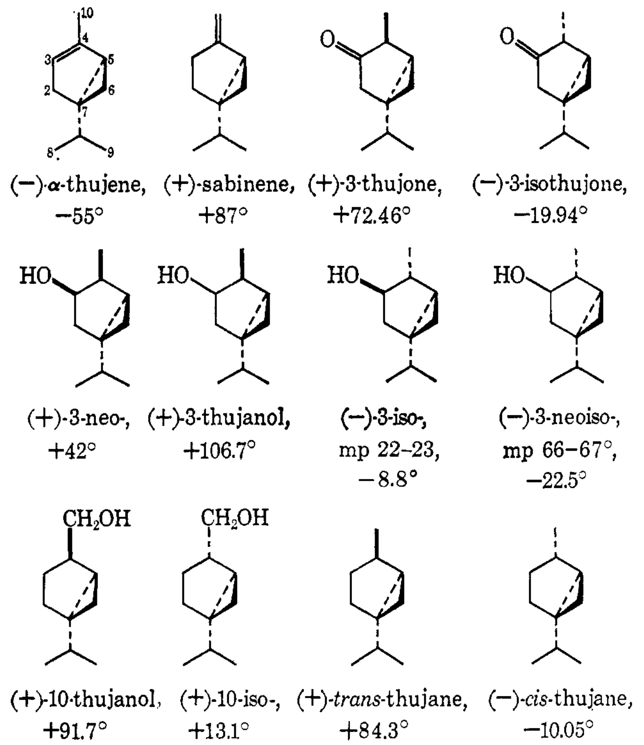

Figure 1.—Corrected nomenclature for thujane derivatives and rotations ([α]D).

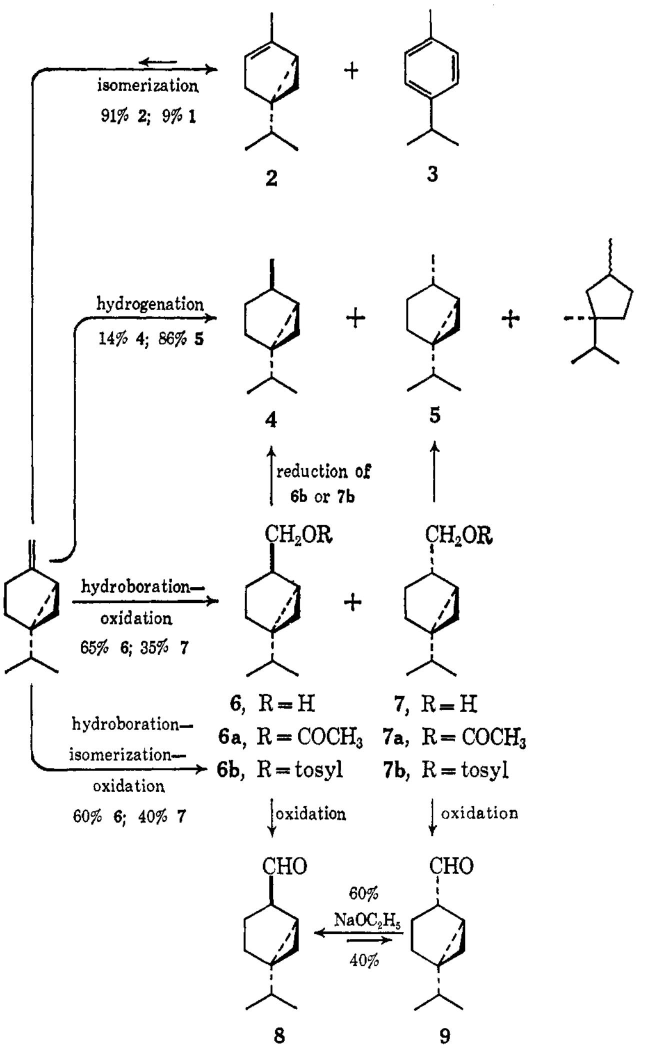

Figure 2.—Reactions of (+)-sabinene (1).

purity and its stability permits it to be stored for a considerable length of time. The situation is less favorable for α-thujene. It can be obtained by a Birch reduction of sabina acetate.[9] This gives the desired hydrocarbon predominantly with a ratio of sabinene to thujene of 15:85. Another but less satisfactory approach to α-thujene is the thermal decomposition of the thujyl xanthates[13] which gives α- and β-thujene in a ratio 30:70. A further difficulty is the fact that optically active α-thujene is difficult to store, since it undergoes racemization on standing[14] possibly through the same vinylcyclopropane mechanism postulated by Doering and Lambert[13] for the racemization at higher temperature. Consequently, it would be highly desirable to have a simple synthesis of optically active α-thujene available so that it could be prepared as needed.

Previously, we had observed that potassium *t*-butoxide in dimethyl sulfoxide provides a favorable simple route for the conversion of 3-carene into 2-carene.[3] We tested this procedure on (+)-sabinene and realized a rapid conversion into (−)-α-thujene of high optical activity. This procedure now makes (−)-α-thujene easily obtainable from the readily available (+)-sabinene (Figure 2).

Isomerization of (+)-sabinene by this procedure at 90° for 1.5 hr yielded an equilibrium mixture of 91% (−)-α-thujene and 9% (+)-sabinene. These are readily separated by column chromatography of a petroleum ether solution through a silicic acid–silver nitrate column, yielding pure (−)-α-thujene, $[\alpha]^{25}D$ −55°.

Ethylenediaminolithium, previously used for the isomerization of 3-carene to 2-carene,[15] was also applied to (+)-sabinene. Although essentially the same mixture of (+)-sabinene and (−)-α-thujene was realized, the product also contained considerable amounts of *p*-cymene (3). Consequently, we believe the potassium *t*-butoxide in dimethyl sulfoxide procedure is preferable.

An interesting feature is the presence of approximately 9% of sabinene at equilibrium. Both methylenecyclohexane and methylenecyclopentane isomerize almost completely to the endocyclic olefin at equilibrium.[16] A possible explanation is that a double bond in the bicyclic thujyl system is more strained than a similar double bond in the cyclopentane system, so that there exists a greater tendency in the thujyl system to move the double bond out to the exocyclic position. Such strain appears to be responsible for the presence of 92% of methylenenorbornane in an equilibrium mixture of that bicyclic olefin.[17] However, there is also the possibility that the better opportunity for conjugative interaction of the π electrons of the exocyclic double bonds of (+)-subinene with cyclopropane ring contributes to the enhanced stability of this exocyclic derivative.

Hydrogenation of (+)-Sabinene (1) and (+)-α-

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[13] W. E. Doering and J. B. Lambert, *Tetrahedron*, **19**, 1989 (1963).

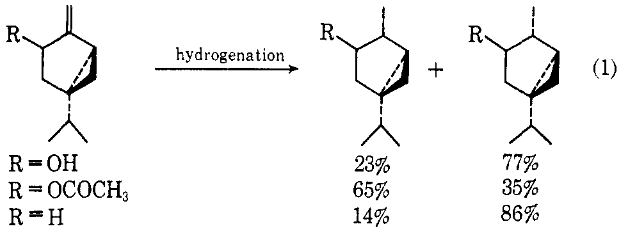
[14] J. L. Simonsen, "The Terpenes," Vol. 2, Oxford University Press, Cambridge, 1949, p 12; Vol. 3, 1952, p 533.

[15] G. Ohloff, K. H. Schulte-Elte, and W. Giersch, *Helv. Chim. Acta*, **48**, 1665 (1965).

[16] J. Herling, J. Shabtai, and E. Gil-Av, *J. Amer. Chem. Soc.*, **87**, 4107 (1965).

[17] S. Bank, C. A. Rowe, Jr., A. Schriesheim, and L. A. Nasland, *ibid.*, **89**, 6897 (1967); P. von R. Schleyer, S. Bank, W. F. Watts, and A. Schriesheim, private communication.

Thujene (2).—It has been reported that the catalytic hydrogenation of the alkenylcyclopropane system[5] in thujopsene, sabinene, thujene, sabinol, and sabina acetate on palladium gives the dihydro compounds under controlled conditions but, the products are always those obtained through a 1,4 addition of the hydrogen with the opening of the cyclopropane ring. However, simple addition of hydrogen to the double bond in sabinene[18] and thujene[19] has been achieved with platinum as the catalyst. Unfortunately, the stereochemistry of these products was not specified. Norin[5] reported that the hydrogenation of sabinol over supported platinum takes place predominantly from the cyclopropane side, whereas that of sabina acetate proceeds away from the cyclopropane ring as shown in eq 1.



We observed that hydrogenation of (+)-α-thujene over platinum at room temperature yielded considerable amounts of a tetrahydro derivative with the opening of the cyclopropane ring. However, hydrogenation at −20° avoided this side reaction and gave essentially pure dihydro derivative. The product was 85% (−)-*trans*-thujane (**4**), with minor amounts, 15%, of (+)-*cis*-thujane (**5**) (Figure 3). Thus the addition of hydrogen took place preferentially from the side away from the cyclopropane ring. On the other hand, (+)-sabinene underwent hydrogenation, under identical conditions from the cyclopropane side, to give 14% (+)-*trans*-thujane and 86% (−)-*cis*-thujane.

Hydroboration of (+)-α-Thujene.—(+)-α-Thujene readily undergoes hydroboration (Figure 3) to form the corresponding organoborane, converted by the usual hydrogen peroxide oxidation[20] into (−)-3-thujyl alcohol (**10**), n^{18}D 1.4603, $[\alpha]$D −46.7,[21] compared with the product from (−)-α-thujene,[9] n^{20}D 1.4602, $[\alpha]^{20}$D +114°. The structure of the product was confirmed by comparison with an authentic sample.[22] Isothujyl alcohol was not detected. This confirms that hydroboration of α-thujene essentially proceeds from the side away from the cyclopropane ring, in agreement with the indicated high sensitivity of the hydroboration reaction to steric requirements. Reduction of the tosylate of the thujyl alcohol with lithium aluminum hydride in ether gave pure (−)-*trans*-thujane (**4**), n^{20}D 1.4384, $[\alpha]^{28.5}$D −37.3, whereas that obtained from the hydrogenation of same (+)-α-thujene had n^{20}D 1.4376, $[\alpha]^{28}$D −29.3, the lower rotation corresponding to the presence of 15% (+)-*cis*-thujane. The oxidation of the alcohol by the ether–chromic acid procedure[23] gave pure (−)-thujone (**11**), n^{23}D 1.4538 and $[\alpha]$ −27.8°, which on epimerization with sodium ethoxide in ethanol at room temperature provided an equilibrium mixture, containing 68% (−)-thujone (**11**) and 32% (+)-isothujone (**12**), in satisfactory agreement with the 65:35 ratio reported earlier.[24] This indicates that in thujone the *cis* relationship between the 10-methyl group and the cyclopropane ring is thermodynamically more stable than the *trans* one, a case analogous to 4-isocaranone,[4] but differing from isopinocamphone[2] and 2-isocaranone.[3]

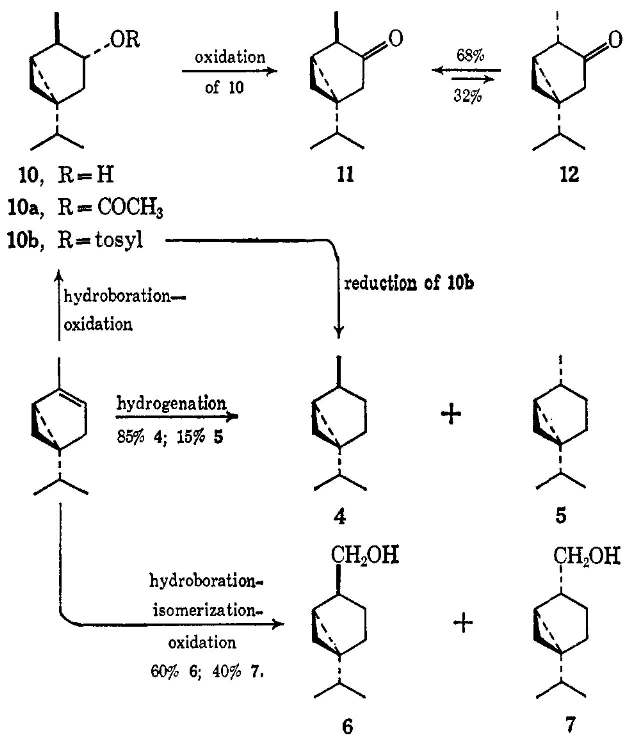


Figure 3.—Reactions of (+)-thujene.

Hydroboration of (+)-Sabinene.—Ohloff[9] hydroborated (+)-sabinene (**1**) and protonolyzed the organoborane with propionic acid for 2 hr and showed that hydroboration preferentially takes place away from the cyclopropane side to give 35% *cis*- and 65% *trans*-thujanes. Heating the organoborane for 2.5 hr at reflux in diglyme failed to epimerize the organoborane, contrary to the experience in the related pinane series.[2] In the later case, the organoborane from β-pinene undergoes protonolysis to give 98% *cis*- and 2% *trans*-pinane, but the isomerized organoborane gives the opposite, 2% *cis* and 98% *trans*.

This marked difference in the behavior of the organoboranes from β-pinene and sabinene in the isomerization reaction prompted us to examine this reaction in more detail. In order to avoid the possibility that the protonolysis reaction might be the cause of the apparent anomalous behavior of the organoborane in the isomerization reaction, we decided to proceed through oxidation to the alcohol (**6**, **7**), conversion into the tosylate (**6B**, **7B**) and reduction

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[18] N. Kizhner, *J. Russ. Phys. Chem. Soc.*, **43**, 1157 (1911).

[19] F. Richter, W. Wolff, and W. Presting, *Ber.*, **64**, 871 (1931).

[20] G. Zweifel and H. C. Brown, *Org. Reactions*, **13**, 1 (1963).

[21] The lower rotation of our product is a consequence of our original use of (+)-α-thujene from natural sources, kindly supplied by Dr. E. Klein of Dragoco. This was a material of relatively low optical purity, $[\alpha]$D +14.4°, compared with the material used by Ohloff, −49.5°, and that realized in our isomerization procedure, −55.0°. The new synthesis was developed only in the latter stages of this study, after we had exhausted our stock and could no longer obtain the natural material. All rotations reported in this paper for derivatives prepared from (+)-α-thujene were realized with the above material from natural sources.

[22] We are thankful to Dr. T. Norin of Kungl Tekniska Högskolon, Stockholm, Sweden, for a generous gift of the authentic thujyl alcohol and thujone.

[23] H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2952 (1961).

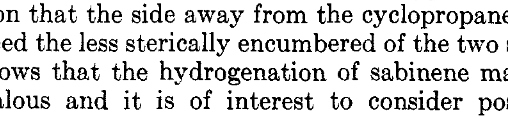
[24] A. G. Short and J. Read, *J. Chem. Soc.*, 2016 (1938).

with lithium aluminum hydride to the hydrocarbons (**4**, **5**) (Figure 2). As described earlier, an authentic sample of pure *trans*-thujane was available by the hydroboration–oxidation of thujene followed by the reduction of the tosylate of the alcohol thus produced. A mixture of *trans*- and *cis*-thujane was available from the hydrogenation of (+)-α-thujene, and (+)-sabinene. Consequently, it was possible to relate the alcohols from the hydroboration–oxidation of both thujene and sabinene by relating them to *cis*- and *trans*-thujanes.

Hydroboration of sabinene (Figure 2) proceeds to the trialkylborane stage. Oxidation by alkaline hydrogen peroxide gives two alcohols, **A** (**7**) and **B** (**6**), in the ratio 35:65, and hydroboration with disiamylborane (which usually is more sensitive to steric requirements), followed by oxidation gives the same alcohols in essentially the same ratio, 32:68. The corresponding acetates were separated by preparative glpc and were converted into the hydrocarbons. Hydrocarbon **5** from alcohol **A** had $n^{20}\text{D}$ 1.4390, $[\alpha]^{25}\text{D}$ −10.5, and was identical with *cis*-thujane by nmr and glpc. Hydrocarbon **4** from alcohol **B** had $n^{20}\text{D}$ 1.4367, $[\alpha]^{25}\text{D}$ +84.3, and corresponded by nmr and glpc with the *trans* component of the thujane mixtures obtained in the hydrogenation of thujene and sabinene. Therefore alcohol **A** must be the *cis* derivative and **B** must be the *trans* derivative. Hydroboration–isomerization–oxidation of both thujene and sabinene yields these two alcohols in the ratio of 41% *cis*/59% *trans*. It is also of interest that the corresponding aldehydes epimerize to give 40% *cis*/60% *trans*. Therefore we confirm Ohloff in that the isomerization procedure fails to epimerize the initially formed organoborane in the manner observed for β-pinene.

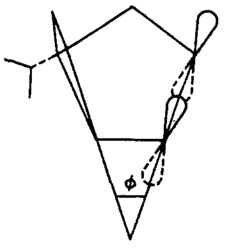
Discussion

In practically all systems previously examined, both hydrogenation and hydroboration takes place preferentially from the same direction, the least hindered side of the double bond. The same behavior is observed for α-thujene, with both hydroboration and hydrogenation taking place preferentially from the side away from the cyclopropane ring. In the case of sabinene we have a special feature appearing—hydroboration and hydrogenation take place from the opposite sides. We believe that in this case the hydroboration reaction is normal and takes place from the less hindered side of the double bond. An examination of the molecular models provides support for the position that the side away from the cyclopropane ring is indeed the less sterically encumbered of the two sides. It follows that the hydrogenation of sabinene may be anomalous and it is of interest to consider possible explanations.



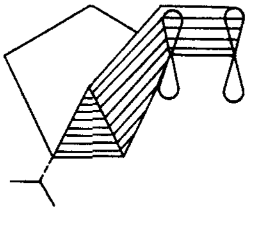
Hydrogenation on platinum catalysts is believed to proceed through the prior formation of a complex involving association of the π electrons of the double bond with the metal surface. Hydrogen associated with the metal surface then combines with the double bond from the same direction.[25]

It is generally accepted that the cyclopropane ring is rich in π character, approaching the π behavior of a double bond. Moreover, it is believed that the π-electron density[26] is at a maximum in the plane of the cyclopropane ring. In α-thujene the angle made by the cyclopropane ring with the π electrons of the double bond is unfavorable for conjugation (**2A**), whereas the possibilities for conjugation are much more favorable in sabinene (**1A**). It is our suggestion that such conjugation causes the sabinene molecule to associate with the platinum catalyst from the cyclopropane side in order to give this conjugated system maximum opportunity to interact with the platinum surface. This overcomes the usual steric preferences. In hydroboration, where such conjugation is unimportant, the reaction is controlled primarily by the ease of steric approach.



2A

electronic system making an angle φ in thujene



1A

maximum overlap in electronic system is possible from β-side in sabinene.

Anomolous Behavior of the 10-Thujyl Derivatives.—The equilibration of 3-thujone, the hydroboration–isomerization of thujene and sabinene, and the equilibration of 10-thujylaldehydes, all indicate that the thujyl system is more stable with the group in the 10 position situated *cis*, rather then *trans*, with respect to the cyclopropane ring. In the pinane case, however, it is the corresponding *trans* compounds[2] that are more stable. This unusual behavior could be explained if the assumption is made that the above thujyl derivatives prefer to exist in the boat form, thereby forcing the 10-methyl into equatorial conformation. In the usual chair form the 10-methyl group occupies the quasiaxial position. Support for this proposal is provided by a detailed study of the nmr spectra.

Spectroscopic Evidence.—Norin[6] postulated boat conformations for all thujane derivatives that he studied. This postulation now seems to be universal for all derivatives of the bicyclo[3.1.0]heptane series[27,28] and is now successfully extended to the 10-thujyl derivatives.

Proton H_D in 10-isothujanol (**7B**) appears as quartet with a coupling constant of 7 cps. On the other hand, the same proton in **6B** appears as a broad multiplet spread over 40 cps (Figures 4 and 5). If 10-isothujanol (**7B**) exists in a boat form, then no coupling

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(25) M. Freifelder, *Ann. N. Y. Acad. Sci.*, **145** (1), 5 (1967).

(26) C. Djerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).

(27) P. K. Freeman, M. F. Grostic, and F. A. Raymond, *J. Org. Chem.*, **30**, 771 (1965).

(28) W. G. Dauben and W. T. Wipke, *ibid.*, **32** 2977 (1967).

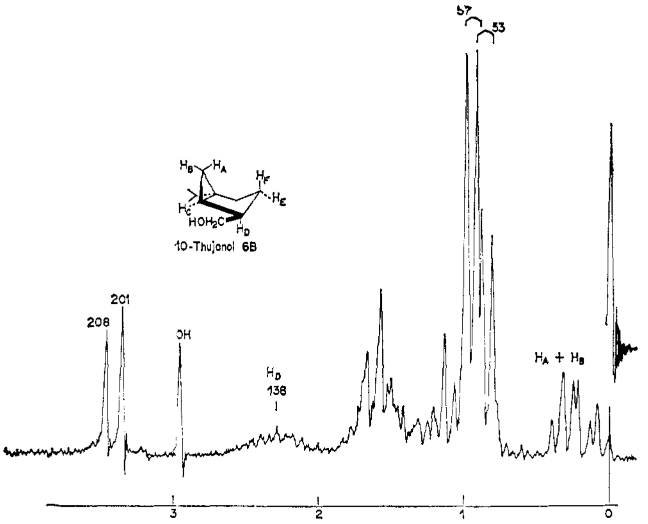


Figure 4.—Nmr spectrum of 10-thujanol (**6B**).

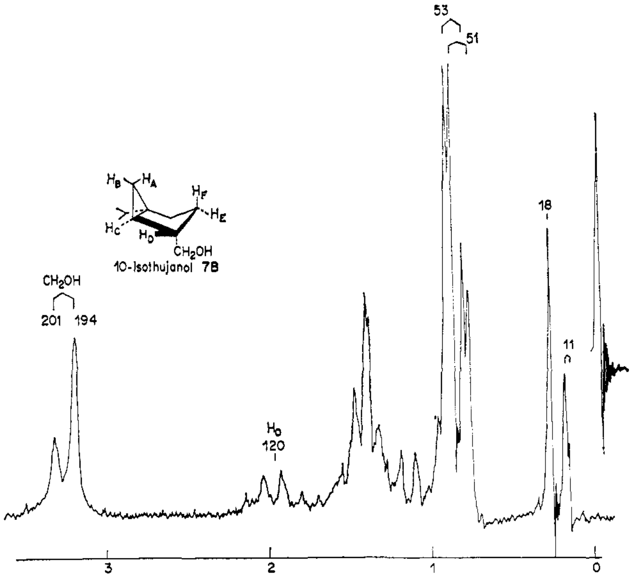
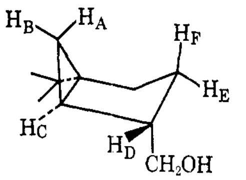
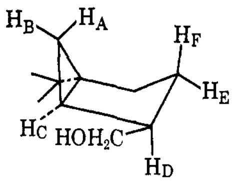


Figure 5.—Nmr spectrum of 10-isothujanol (**7B**).

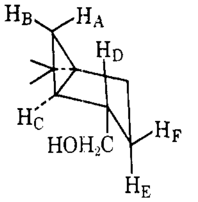
between H_D and H_C would be expected because the dihedral angle between these protons is 90°. Similarly,



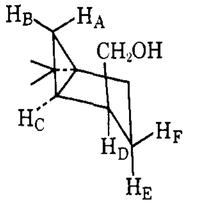
7B



6B



7C



6C

the dihedral angle between H_D and H_E protons is 90° and again no coupling between these two protons should be observed. Proton H_D can couple only with proton H_F, for the dihedral angle between these protons is 20°, and with protons of CH_2OH groups, with the result that the signal for H_D proton is a relatively narrow peak (half band width 24 cps). Similarly, in boat form of **6B**, proton H_D can couple with H_C (dihedral angle 20°), H_E (dihedral angle 20°), H_F (dihedral angle 110°), and the protons of CH_2OH group. Therefore the signal for this proton should be broad and it actually appears as a broad peak spread out over 40 cps.

The signal for H_D in **7B** (120 cps) is shifted upfield because it faces cyclopropane and the diamagnetic anisotropic effects of cyclopropane are operative. The corresponding signal in **6B** (138 cps) is shifted downfield because of the paramagnetic effects of the cyclopropane. Contrary to these observations, the signal for the carbinyl protons of CH_2OH is shifted upfield for **7B** (197.5 cps) and downfield for **6B** (204.5 cps). This may be due to the equatorial relationship of the CH_2OH group to both cyclopropane and cyclopentane in **6B** and to the axial relationship to the cyclopentane moiety in **7B**. The anisotropic effects of cyclopropane are operative only to H_D protons because of the proximity and not to the more distant carbinyl protons.

On the other hand, if 10-isothujanol (**7C**) and 10-thujanol (**6C**) are in the chair forms, the signal for H_D should be broader in **7C** than in **6C** and the chemical shift for the carbinyl protons of CH_2OH should be shifted upfield because now they face the cyclopropane ring and downfield in **7C** because they would be in an equatorial relationship to the cyclopropane and cyclopentane moieties. Since none of these characteristics is seen in the spectra, the 10-thujanol derivatives must exist in the boat form.

The stability of the boat form of thujane derivatives can be understood by considering the various nonbonded interactions. H_A will have two nonbonded interactions between 2-β-H and 4-β-CH_2OH or 4-β-H in **6C** and **7C**, instead of one in the boat form between H_A and H_F in **6B** and **7B**. In the boat form, 10-CH_3 or 10-CH_2OR will be in the equatorial conformation in **6B** and this is the reason why *cis* isomers (*cis* with respect to cyclopropane) are thermodynamically more stable than *trans*.

A similar pattern of nmr spectra is observed with all of the 10-thujanol derivatives, including the parent hydrocarbons. These results are summarized in Table I. Recently a detailed analysis was made of the nmr spectra of *cis*- and *trans*-thujanes.[29]

Experimental Section

Materials.—(+)-α-Thujene was a sample generously supplied by the Dragoco Co. This contained 15% α-pinene, but was used as such. This was also purified by using the Varian Autoprep from 85 to 96% purity and had $[\alpha]^{19}D$ + 14.4° (lit. + 37.7°,[14] −49.3° [9]), $n^{20}D$ 1.4568 (lit. 1.4502,[12] 1.4511[9]). The infrared spectra completely superimposed the published spectra (Sadtler ir spectra, no. 1089). (+)-Sabinene was a sample kindly made available by the International Flavors and Fragrances Inc. It was 95% pure, the impurities being 1.5% α-pinene and 3.5% α-thujene, and was used as such for all the reactions: $[\alpha]^{25}D$ +95° (*c* 20, CCl_4) (lit.[9] +87°), $n^{20}D$ 1.4692 (lit.[9] 1.4681). The infrared spectrum was identical with that of an authentic sample.[30]

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[29] A. Dieffenbacher and W. Philipsborn, *Helv. Chem. Acta*, **49**, 897 (1966).

[30] V. Herout, *Chem. Listy*, **46**, 438 (1952).

TABLE I

NMR SPECTRAL DATA[a] FOR THE THUJANE DERIVATIVES

	3-H	4-H	10-CH$_2$ or 10-CH$_3$	8-CH$_3$ or 9-CH$_3$	9-CH$_3$ or 8-CH$_3$	6-H$_A$	6-H$_B$	ArCH$_3$	OCOCH$_3$
α-Thujene (**2**)	4.87 (s)		1.72^b	0.89^c	0.93^c	0.7^d	0^d		
Sabinene (**1**)			4.44 (s) 4.57 (s)	0.90^c	0.96^c	0.66 (s)	0.58^e		
3-Thujanol (**10**)	3.22^f		0.87^c	0.97^c	1.01^c	−0.13–0.27^g			
3-Thujanol acetate (**10a**)	4.23^f		0.97^h	0.87^c	1.01^c	0.0–0.4^g			1.93 (s)
3-Thujanol tosylate (**10b**)	4.15^f		0.82^h	0.73^c	0.9^c	0.08–0.23^g		2.4 (s)	
10-Thujanol (**6**)		2.32^i	3.40^j	0.89^c	0.95^c	0.0–0.43^g			
10-Thujyl acetate (**6a**)		2.45^i	3.98^j	0.84^c	0.94^c	0.0–0.42^g			1.97 (s)
10-Isothujanol (**7**)		2.02^k	3.28^j	0.85^c	0.88^c	0.3 (s)	0.18^l		
10-Isothujanol acetate (**7a**)		2.2^k	3.89^j	0.83^c	0.95^c	0.34 (s)	0.23^l		1.98 (s)
cis-Thujane (**5**)		1.93^m	0.9^c	0.9^c	0.93^c	0.28 (s)	0.18^l		
trans-Thujane (**4**)			0.85^c	0.93^c	0.93^c	0.03–0.42^g			

[a] All spectra were taken on a Varian A-60A or JOL-60H instruments and the chemical shift is expressed in terms of δ units from tetramethylsilane. The letters in parentheses indicate singlet, doublet, quartet, and multiplet. [b] (q), J = 2 cps. [c] (d), J = 6.5 cps. [d] (q), J = 3 cps. [e] (d), J = 1.5 cps. [f] (q), J = 8 cps. [g] (m), AB pattern of an ABX system. [h] (d), J = 4.5 cps. [i] Broad peak spread over 40 cps. [j] (d), J = 7 cps. [k] (q), J = 7 cps broad peak spread over 24 cps. [l] (d), J = 1.5 cps. [m] Broad peak spread over 32 cps.

The purification of diglyme, tetrahydrofuran, and boron trifluoride–etherate and the preparation of diborane were carried out by the usual procedures.[20] The glpc analyses were made on a Hitachi gas chromatographic analyser KGL-2A with 45-m Golay columns of squalene (A), UC oil IB-550 X (B), Carbowax 20M (C), Ohukara gc analyzer GI-360 with 2-m packed columns of 15% Carbowax 20M on Diasolid (D), F & M Model 500 with 3-m packed columns of 20% Carbowax 20M on Chromosorb W (40/60) (E), F & M Prep Model 770 with 2.5- or 8-m packed columns of 15% Carbowax 20M on Chromosorb W (F and G), and Perkin-Elmer Model 226 with 45-m Golay columns of squalene (H), Carbowax 20M (I), and TCP (tricresyl phosphate) (J). The nmr spectra were taken on the JOL-60H or Varian A-60H. The infrared spectra were run on the Hitachi EPI-G2 or Perkin-Elmer Infracord Model 137.

Hydroboration–Oxidation of (+)-α-Thujene.—In a 250-ml three-necked flask equipped with a thermometer, condenser, pressure-equalizing dropping funnel, and side arm with a serum cap were placed 8.12 g of α-thujene (60 mmol) and 20 ml of tetrahydrofuran. The mixture was cooled to 0° and, under stirring, 27.5 ml of a 1.4 M solution of diborane in tetrahydrofuran (40 mmol of BH_3) was added dropwise. After 2 hr at 0° and 1 hr at 25°, the excess of hydride was destroyed by the careful addition of 1 ml of water in 1 ml of tetrahydrofuran. The reaction mixture was oxidized at 45–50° by adding 13.3 ml of 3 N sodium hydroxide (40 mmol) and 13.3 ml of 30% hydrogen peroxide. After 1 hr the mixture was saturated with potassium carbonate, the tetrahydrofuran layer separated, and the aqueous phase extracted with ether,; combined extracts were dried over $MgSO_4$ and distilled to give 7.2 g of the alcohols, bp 89° (3.2 mm), a yield of 83%. Isopinocampheol and thujyl alcohol were difficult to separate by glpc, but their acetates were easily separable.

(−)-Thujyl Acetate (10a).—The mixture of thujyl alcohol and isopinocampheol (7.2 g, 50 mmol) was dissolved in 11 ml of pyridine and 5.6 ml of acetic anhydride (6 g, 60 mmol) was added and allowed to stand at room temperature overnight. The nmr analysis of this mixture indicated 90% acetylation. Pyridine and acetic anhydride were removed by distillation under reduced pressure at room temperature and the residue was distilled to give 7.8 g of acetates, bp 100–105° (5 mm), a yield of 82%. Thujyl acetate (85%, t_r 80 min) and isopinocampheol acetate, (15% t_r 105 min) were separated on column G at 200°. Pure thujyl acetate had bp 75° (2 mm); $n^{20}D$ 1.4475; $[\alpha]^{24}D$ −58° (c 20, CCl_4).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 74.43; H, 10.27. Found: C, 74.40; H, 10.65.

(−)-Thujyl Alcohol (10).—Thujyl acetate (2.52 g, 12.8 mmol) was allowed to react with 6.5 ml of lithium aluminum hydride in tetrahydrofuran (2.0 M, 13 mmol) overnight. Residual hydride was decomposed with water, a saturated solution of potassium sodium tartrate (6.5 ml) added, the supernatant tetrahydrofuran layer separated, and the aqueous layer extracted with ether. The combined extracts were dried over $MgSO_4$ and distilled to give 1.69 g of thujyl alcohol: bp 72° (1.8 mm); $n^{20}D$ 1.4603; $[\alpha]^{28.5}D$ −46.7 (c 20, CCl_4). Its infrared and nmr spectra were completely superimposable with those of the authentic samples.[22]

(+)-*trans*-Thujane (4).—Thujyl alcohol (0.79 g, 5 mmol) and 5 ml of dry pyridine were mixed. Then 0.95 g of freshly sublimed *p*-toluenesulfonyl chloride (5 mmol) was added at 0° with stirring. The mixture was placed in cold room (0°) for 24 hr. Analysis of the supernatant liquid by nmr indicated 89% tosylation. It was filtered to remove pyridine hydrochloride and the filtrate was evaporated to dryness at 1 mm. The dry product was treated with an ethereal solution of lithium aluminum hydride (7.5 ml of 2 M, 15 mmol) cautiously and left for 2 days with stirring under a nitrogen atmosphere. An insoluble white precipitate formed, ether was removed, and the product was collected at 90° (1 mm) in a Dry Ice cooled trap. Pure *trans*-thujane was isolated by glpc on column E. The yield was 0.310 g (45%); $n^{20}D$ 1.4384; $[\alpha]^{28.5}D$ −37.3° (c 10, CCl_4). Its infrared and nmr spectra were identical with those of the hydrocarbon from the alcohol B, the major alcohol obtained in the hydroboration–oxidation of (+)-sabinene.

(−)-3-Thujone (11).—(−)-3-Thujyl alcohol (10) and ether (2 ml) were treated with aqueous chromic acid in the usual manner.[23] A pure sample of (−)-3-thujone was obtained by glpc on column D: $n^{27}D$ 1.4538 (lit.[24] 1.4508); $[\alpha]$ −27.8° lit.[24] +73.4°). The infrared and nmr spectra were consistent with those of the authentic samples.[22]

Equilibration of (−)-3-Thujone (11) and (+)-Isothujone (12).—(−)-3-Thujone (1 mmol) was added to sodium ethoxide solution (1 ml, 1 M) and stirred at 25°. The progress of the equilibrations was studied by glpc analysis by removing aliquots, extracting the ketones with pentane, and neutralizing the alkali with 1% hydrochloric acid. The results are [time in minutes, per cent (−)-3-thujone] 0, 100; 30, 67.4; 60, 67.7; 120, 68.4.

Catalytic Hydrogenations. A. (+)-α-Thujene on Palladium.—(+)-α-Thujene (0.65 g) in 15 ml of ethanol was hydrogenated over palladium black catalyst (0.2 g) at 25°. After 60 min, the absorption of hydrogen had stopped, and 2 mol equiv of hydrogen had been consumed. The reaction mixture was filtered, diluted with water, and extracted with ether. The ether solution was dried and distilled. Glpc analysis on column A showed a single peak. However no attempt was made to determine whether it was a *cis*- or *trans*-cyclopentane derivative or a mixture of both. The isolated sample by glpc had $[\alpha]D$ −5.40°, $n^{18}D$ 1.4339; nmr, no cyclopropane protons between δ 0 and 0.78 from tetramethylsilane and no olefinic protons.

Anal. Calcd for $C_{10}H_{20}$: C, 85.63; H, 14.38. Found: C, 85.99; H, 14.09.

B. **(+)-α-Thujene on Platinum at −20°.**—In a Brown□ microhydrogenator was placed 0.1 g of platinum dioxide, 0.2 g of Darco, and 2 ml of diethyl ether. The catalyst was formed with hydrogen from the generator, which contained 2 ml of glacial acetic acid in the flask and sodium borohydride solution (1.197 M in H^-) in the buret. The mixture was allowed to stand for 5 min to ensure that there was no further absorption of hydrogen. The flask was cooled to −20°, using a Dry Ice–carbon tetrachloride slush. Thujene (1 ml, 0.845 g, 6.2 mmol) was added slowly and the absorption of hydrogen followed by the utilization of sodium borohydride solution: 1.8 ml, 5.72 mmol, over 45 min. The reaction was allowed to continue for a total of 2 hr, but there was no further hydrogen consumption, indicating a clean hydrogenation to a dihydro derivative.[31] The solution was separated from the catalyst and dried over $MgSO_4$. Glpc analysis on column E at 50° indicated two components. The second component (17%) was identified as α-pinene by comparison with an authentic nmr spectrum. The first component on columns H and I gave a single peak but on column J gave two peaks at 50° with 10-lb helium pressure: 85% *trans*-thujane (t_r 10 min) and 15% *cis*-thujane (t_r 11 min). The nmr spectra of the compound indicated the presence of cyclopropane protons δ 0–0.3 (m), but no olefinic protons. It had $[\alpha]^{28}\mathrm{D}$ −29.3° (*c* 20, CCl_4), $n^{20}\mathrm{D}$ 1.4376.

C. (+)-α-Thujene on Platinum at Room Temperature.—When the hydrogenation was done at room temperature using the Brown□ microhydrogenator under identical conditions and the product analyzed by glpc on column J, three compounds were obtained, 68% *trans*-thujane **4** (t_r 10 min), 14% tetrahydrothujane (t_r 10.5 min), and 18% *cis*-thujane **5** (t_r 11 min.)

D. (+)-Sabinene on Platinum at −20°.—Hydrogenation was done exactly as described for (+)-α-thujene, using exactly the same quantities, but the hydrogenation was over in 20 min. The glpc analysis on column J indicated the presence of two compounds: 15% *trans*-thujane (t_r 10 min) and 85% *cis*-thujane (t_r 11 min). The nmr spectrum of the product indicated the presence of cyclopropane protons at δ 0–0.7 (m), but no olefinic protons. It had $[\alpha]^{27}\mathrm{D}$ +9.17 (*c* 20, CCl_4), $n^{20}\mathrm{D}$ 1.4390.

E. (+)-Sabinene on Platinum at Room Temperature.—Like (+)-thujene, (+)-sabinene also gave three products at room temperature: *cis*-thujane, 62%, tetrahydrothujane, 25%, and *trans*-thujane, 13%.

F. (+)-Sabinene on Palladium at Room Temperature.—The hydrogenation was over within 40 min and the hydrogen consumed corresponded to 2 mmol for each mole of (+)-sabinene. Glpc analysis showed a single peak on column J.

Isomerization of (+)-Sabinene (1) to (−)-α-Thujene (2). A. With Ethylenediaminolithium.—The reagent was prepared as described earlier[3] using lithium (0.7 g) and ethylenediamine (30 ml). To the reagent (3 ml) was added 1 ml of sabinene (0.845 g) and this was allowed to stir overnight at room temperature. Water (3 ml) was added and the mixture extracted with pentane. Glpc analysis of the pentane extract on column H indicated that it is a mixture of three components: 68% α-thujene (t_r 18.5 min), 7% sabinene (t_r 23 min), and 25% *p*-cymene (t_r 29.5 min). Nmr analysis of the product indicated the presence of 10% conjugated diene, probably in the aromatic fraction: 75% sabinene and thujene, 10% unknown conjugated diene (330 cps), and 15% aromatics (408 cps).

B. With Potassium *t*-Butoxide in Dimethyl Sulfoxide.—A round-bottomed flask, fitted with a side arm with a serum cap, was flushed with nitrogen, and then potassium *t*-butoxide in dimethyl sulfoxide (2 *M*, 5 ml) was added, followed by sabinene (1.7 ml, 10 mmol) in 5 ml of dimethyl sulfoxide. The mixture was heated to 90°. At appropriate intervals 50-μl aliquots were removed and examined by glpc on column E at 79°, isothermally. The time in minutes and the per cent α-thujene formed were as follows: 5, 40; 10, 50; 20, 76; 30, 83; 40, 87; 50, 88; 60, 90; 70, 91; 80, 91; 120, 91; 150, 91. No aromatics formed, as indicated by glpc and nmr. The reaction mixture was decomposed with 5 ml of water and extracted with four 10-ml portions of pentane dried over $MgSO_4$, and passed through a column of silicic acid impregnated with silver nitrate (15%). It was further eluted with pentane (100 ml). Pure α-thujene was then isolated by distilling the solvent. Its infrared and nmr spectra were identical with those of the authentic samples, $n^{20}\mathrm{D}$ 1.4512, $[\alpha]^{28.5}\mathrm{D}$ −55 (*c* 20, CCl_4). Hence the Dragaco sample of (+)-α-thujene used in the present study and the sample obtained by isomerization of (+)-sabinene are optical antipodes.

Hydroboration–Oxidation of (+)-Sabinene.—Under the same conditions as described for α-thujene, sabinene (1.73 g) was hydroborated by diborane in tetrahydrofuran (4.4 ml of 1.82 *M* in BH_3) and then oxidized by alkaline hydrogen peroxide. It was shown by glpc on column C that the yield of the primary alcohols A and B was 93% and the distribution was 35:65. In the hope of getting more stereoselectivity, the hydroboration was carried out with disiamylborane. The reagent disiamylborane was prepared as described earlier[20] using 14.7 g of 2-methyl-2-butene (210 mmol) and 69 ml of diborane in tetrahydrofuran (1.45 *M* in BH_3, 100 mmol). Sabinene (9.52 g, 70 mmol) was then added to the well-stirred solution of disiamylborane at 0°. The progress of the reaction was studied by removing 1-ml aliquots of the solution and examining it for residual hydride. Within 1 hr 19% of the reaction was over. After 2 hr, at 0°, the reaction mixture was decomposed with water, oxidized with 35 ml of sodium hydroxide (3 *N*) and 35 ml of hydrogen peroxide (30%) at 35–40°, and extracted with ether. The combined extracts were dried over $MgSO_4$ and distilled. The product, 9.2 g, a yield of 90%, contained 32% alcohol **A** and 68% alcohol **B** and had the following properties: $n^{18}\mathrm{D}$ 1.4652 and $[\alpha]\mathrm{D}$ +51.6°. These alcohols gave ill-resolved peaks on glpc and hence could not be separated.

Separation of Alcohols A and B. A. Monophthalate Method.—The mixture of alcohols (2.4 g), freshly distilled phthalic anhydride (2.36 g), and dry pyridine (5 ml) was heated at 100° for 5 hr, and then poured into 30 ml of sodium carbonate solution (5%). Neutral compounds were extracted with petroleum ether. The aqueous phase was acidified to congo red with 30% sulfuric acid. The solid was extracted with ether. The extract was washed with brine and dried over Na_2SO_4. Repeated crystallization from petroleum ether and methanol gave a solid, mp 93.8–94.6°, $[\alpha]\mathrm{D}$ +79.2°.

Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.54; H, 7.39.

The purified acid phthalate (0.156 g), dissolved in alcoholic potassium hydroxide (potassium hydroxide, 0.152 g, and ethanol, 5 ml), was heated at reflux for 1 hr, and steam distilled. The distillate was extracted with ether and dried over $MgSO_4$ and distilled. It was found by glpc to be alcohol **B** uncontaminated with alcohol **A**.

Acetate Method.—The mixture of alcohols A and B (7.2 g, 48 mmol), 11 ml of pyridine, and 6 g of acetic anhydride (60 mmol) were mixed and left overnight. It was worked up as described earlier for thujyl acetate. Distillation at 100° (4 mm) gave 7.18 g of the acetate mixture. These acetates (4.8 g) were then separated by preparative glpc on column G at 200° by injecting 200 μl at a time. Three fractions were collected: first fraction, acetate of alcohol **A**, 100% pure by glpc and nmr (0.758 g, t_r 128 min); second fraction, a 50:50 mixture of acetates of alcohol A and B (0.720 g); and a third fraction, acetate of alcohol B, 100% pure by glpc and nmr (1.324 g, t_r 138 min).

Acetate of Alcohol A (7a).—It had bp 82° (2 mm); $n^{22.5}\mathrm{D}$ 1.4525; $[\alpha]^{22.5}\mathrm{D}$ +54° (c 10, THF), +6.10 (neat 1 dm).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 74.43; H, 10.27. Found: C, 74.40; H, 10.65.

Acetate of Alcohol B (6b).—It had bp 82° (2 mm); $n^{22.5}\mathrm{D}$ 1.4520; $[\alpha]^{27}\mathrm{D}$ +76.9° (*c* 10, THF), +75.27 (neat).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 74.43; H, 10.27. Found: C, 74.73; H, 10.35.

Alcohol A.—10-Isothujanol (7) was obtained in 90% yield by the lithium aluminum hydride reduction of the acetate of alcohol **A** (0.650 g) using the same procedure as described earlier. It had bp 80–81° (1.8 mm); $n^{30}\mathrm{D}$ 1.4656; $[\alpha]^{24.5}\mathrm{D}$ +13.1° (*c* 20, CCl_4).

Alcohol B.—10-Thujanol (6) was also prepared in 92% yield by the above procedure. It had bp 80–81° (1.8 mm); $n^{20}\mathrm{D}$ 1.4636; $[\alpha]^{24.5}\mathrm{D}$ +91.7° (*c* 20, CCl_4).

(+)-*trans*-Thujane (4).—Alcohol **B** (0.308 g, 2 mmol), pyridine (2 ml), and *p*-tolylsulphonyl chloride (0.396 g, 2 mmol) were mixed and allowed to react at 0° for 24 hr. The reaction mixture was filtered and the filtrate was evaporated to dryness at 1 mm. To the residue was added lithium aluminum hydride in diethyl ether (5 ml, 2 *M*) and allowed to react at room temperature for 48 hr. It was worked out as described earlier for (−)-*trans*-thujane from thujyl alcohol. Hydrocarbon (0.170 g, 62%) was collected by glpc on column E and was identical by nmr and glpc with that obtained from thujyl alcohol *via* the tosylate reduction, and also corresponded to the major hydrocarbon obtained in the hydrogenation of α-thujene at −20°. Hence the alcohol **B** is 10-thujanol (**6**). The hydrocarbon had $n^{20}\mathrm{D}$ 1.4367 and $[\alpha]^{25}\mathrm{D}$ +84.3° (*c* 20, CCl_4).

Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.70; H, 13.41.

(−)-*cis*-Thujane (5) was prepared in 57% yield from alcohol using identical conditions. This hydrocarbon was identical with

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(31) We are indebted to Dr. Charles A. Brown for disclosing to us the results of his studies of low temperature hydrogenation.

the minor hydrocarbon obtained during hydrogenation of (+)-thujene at −20° and with the major hydrocarbon obtained during the hydrogenation of (+)-sabinene at −20° by glpc and nmr. This compound had $n^{20}\mathrm{D}$ 1.4390; $[\alpha]^{28.5}\mathrm{D}$ −10.05° (*c* 20, CCl_4).

Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 87.04; H, 12.86.

Hydroboration–Isomerization–Oxidation of (+)-α-Thujene.—After hydroboration of α-thujene (0.085 g) with diborane in tetrahydrofuran (0.2 ml, 2.43 *M* in BH_3), diglyme, 2 ml, was added and tetrahydrofuran was removed under vacuum. The reaction mixture was then heated at 170–175° for 2.5 hr, oxidized by alkaline hydrogen peroxide, and analyzed by glpc on column D which indicated the ratio of alcohol **A** to alcohol **B** to be 40:60.

Hydroboration–Isomerization–Oxidation of (+)-Sabinene.—To a mixture of (+)-sabinene (0.1 g) in diglyme (0.5 ml) and sodium borohydride solution in diglyme (1.0 *M*, 0.9 ml) was added at 0° boron trifluoride–diglymate (3.65 *M*, 0.33 ml). The solution was stirred for 2 hr. It was heated at 150–160° for 2.5 hr and oxidized as usual. When analyzed by glpc on column D, the ratio of alcohol **A** to **B** was 40:60.

Oxidation of 10-Thujanol with Chromic Acid.—10-Thujanol (0.1 g) was oxidized with chromic acid under the same conditions as described for thujyl alcohol. Glpc analysis on column A indicated 47% yield of the aldehydes, the ratio of 10-thujylaldehyde (**8**) (t_r 5.0 min) to 10-isothujylaldehyde (**9**) (t_r 4.1) being 97:3. 10-Thujylaldehyde was obtained by preparative glpc. Although a pure analytical sample of 10-thujylaldehyde was not obtained, it was characterized by reducing it back to 10-thujanol with sodium borohydride.

Oxidation of 10-Isothujyl Alcohol with Chromic Acid.—10-Isothujyl alcohol was oxidized under the same conditions as above. The compound gave back pure 10-isothujanol on reduction with sodium borohydride.

Equilibration of 10-Thujylaldehyde.—A mixture of 85% pure 10-thujylaldehyde and 15% 10-isothujylaldehyde (40 mg) was added to sodium ethoxide solution (0.5 *M*, 1 ml) in ethanol. It was stirred at 25° and the progress of the reaction was studied by removing aliquots and neutralizing it with 1% hydrochloric acid. The pentane extract of the neutralized reaction mixture was then analyzed by glpc on column D. The results are (time in minute and per cent thujylaldehyde) 0.85; 30, 76; 60, 63; 120, 59; 200, 59.

Registry No.—(+)-Sabinene, 2009-00-9; (−)-α-thujene, 3917-48-4; (+)-*trans*-thujane, 5523-91-1; (−)-*cis*-thujane, 4423-90-0; (+)-10-thujanol, 20-126-25-4; (+)-10-thujanol acetate, 20-126-26-5; (+)-10-isothujanol, 20-126-27-6; (+)-10-thujanol acid phthalate, 20147-89-1; (+)-10-isothujanol acetate, 20-126-28-7; (−)-3-thujanol, 20-126-29-8; (−)-3-thujanol acetate, 20-126-30-1; 3-thujanol tosylate, 20-126-31-2; (+)-α-thujene, 563-34-8; (−)-*trans*-thujane, 20126-20-9; (+)-*cis*-thujane, 7712-66-5.

The Preparation and Chemistry of 9β-Estr-4-en-3-ones

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Received March 3, 1969

Hydrogenation of 17α-substituted estra-4,9(10)-dien-3-ones gave the corresponding 9β-estr-4-en-3-one accompanied by the 10α isomer. Because of inherent strain, the 9β-estr-4-en-3-ones readily isomerized under mild acid or base conditions to yield the analogous 9β-estr-5(10)-en-3-ones; more vigorous conditions resulted in epimerization to the 9β,10α-estr-4-en-3-ones. Reduction of 17β-hydroxy-17α-methyl-9β-estr-4-en-3-one with Li-NH_3 yielded 17β-hydroxy-17α-methyl-5α,9β,10β-estran-3-one.

The preparation of steroids having natural configurations at various ring juncture carbons continues to be a challenge to the synthetic chemist.[1] Although the 9β C_{19} steroid analogs have been prepared,[2] the corresponding 19-nor compounds have not been reported. In an earlier study, the hydrogenation of 17β-hydroxyestra-4,9(10)-dien-3-one to give unnatural 10α,19-nor steroids was described.[1c] As the C_{17} substituent of the dienone was varied, increasing amounts of a new isomer were obtained; changes in catalyst and in solvent also resulted in increased yields of this new isomer.

As an example, when 17β-hydroxy-17α-methylestra-4,9(10)-dien-3-one[3] was hydrogenated in EtOH with Pd–$SrCO_3$ catalyst,[4] there was obtained after fractional crystallization a 26% yield of 17β-hydroxy-17α-methyl-10α-estr-4-en-3-one (**1**) and an 18% yield of the new isomer, 17β-hydroxy-17α-methyl-9β-estr-4-en-3-one (**2**). The structure of **2** was assigned on the basis of spectral studies and chemical transformation. The presence of an α,β-unsaturated ketone was indicated by the uv and ir data. Also, the nmr supported the assignment as an isomeric 19-nor-4-en-3-one, since it revealed the presence of the 4 proton as a broadened singlet at δ 5.86 and the 17- and 18-methyl protons as singlets at δ 1.23 and 1.00, respectively. The 18-methyl proton resonance of the isomeric ketone **1** was at δ 0.82.

Examination of molecular models indicates that the 9β stereochemistry necessitates the presence of a boat conformation in one of the rings; the B ring is generally assigned this conformation since the flexible terminal A ring can assume a conformation which will minimize some of the resultant strain interactions. This conformation is consistent with the nmr data, since the C_{18} angular methyl group would be expected to be deshielded because it is situated on the convex β surface of the molecule.

The circular dichroism (CD) spectrum of **2** exhibits a positive Cotton effect in the long-wavelength region and a negative Cotton effect in the π–π^* region. This curve is similar to the CD spectrum of 17β-hydroxy-9β,10α-estr-4-en-3-one, except that the short-wavelength Cotton effect is less intense.[5] Because of this lower intensity, the chirality of the chromophore appears to be more nearly planar in the predominant conformer, a situation similar to that with the 9α,10α-estr-4-en-3-

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