ORGANIC AND BIOLOGICAL CHEMISTRY

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

Hydroboration of Terpenes. II. The Hydroboration of α- and β-Pinene—The Absolute Configuration of the Dialkylborane from the Hydroboration of α-Pinene

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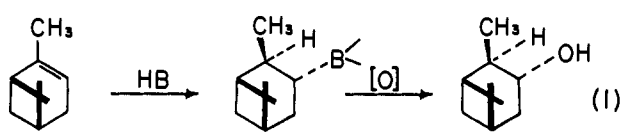
The hydroboration of (−)-β-pinene yields an organoborane which undergoes protonolysis with propionic acid to (−)-*cis*-pinane and oxidation with alkaline hydrogen peroxide to (−)-*cis*-myrtanol. After 1 hr. at 150° the initially formed organoborane is transformed into another product which undergoes protonolysis to (−)-*trans*-pinane and oxidation to (−)-*trans*-myrtanol. Consequently, hydroboration must involve addition of the boron–hydrogen bond to the carbon–carbon double bond from the side that is remote from the *gem*-dimethyl group to form the tris-(*cis*-myrtanyl)-borane, and the latter is rapidly isomerized at higher temperatures into the more stable tris-(*trans*-myrtanyl)-borane. (+)-α-Pinene undergoes hydroboration only to the dialkylborane stage. Protonolysis of the product yields (+)-*cis*-pinane. Consequently, here also the addition of the boron–hydrogen bond to the carbon–carbon double bond must proceed from the side away from the *gem*-dimethyl group. On the basis of the now well-substantiated *cis* addition of the boron–hydrogen bond, the organoborane must be diisocampheylborane and the alcohol obtained therefrom by oxidation must be isopinocampheol. This conclusion was confirmed by oxidation of isopinocampheol to isopinocamphone, followed by reduction with lithium trimethoxyaluminohydride to an isomeric alcohol, neoisopinocampheol. Consequently the reduction must also involve an approach of the reagent from the side away from the *gem*-dimethyl group. Neoisopinocampheyl methanesulfonate undergoes methanolysis at 25° at a rate ($k_1 = 5.85 \times 10^{-5}$ sec.$^{-1}$) three times that of isopinocampheyl methanesulfonate ($k_1 = 1.98 \times 10^{-5}$ sec.$^{-1}$) supporting the *cis* assignment of the hydroxyl and the C_2-methyl in neoisopinocampheol and the *cis* assignment of hydroxyl and hydrogen in isopinocampheol. Nuclear magnetic resonance spectra of the products were examined. It is concluded that all of the results are consistent only with a *cis* addition of the boron–hydrogen bond to α- and β-pinene from the less hindered direction (away from the *gem*-dimethyl group), with protonolysis and oxidation of the boron–carbon bond proceeding with retention of configuration. Since the absolute configurations of α-pinene and *cis*-pinane have been established, the absolute configuration of diisopinocampheylborane can be assigned.

The hydroboration reaction provides a convenient procedure for the conversion of olefinic structures into alcohols—without rearrangement and with the production of stereochemically defined structures. Thus, the addition of the boron–hydrogen bond to the carbon–carbon bond occurs anti-Markovnikov, placing the boron atom at the least substituted carbon atom of the double bond. Moreover, the available evidence supports the conclusion that the addition occurs in a pure *cis* manner, predominantly from the less hindered side of the molecule.[1]

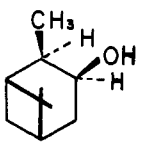
These characteristics should be very valuable in applying the hydroboration reaction to complex molecules, such as terpenes and steroids. In order to test the reliability of the above generalizations, we have undertaken the examination of the hydroboration of a number of representative terpenes. The selective hydroboration of myrcene was previously described.[2] In the present paper we examine critically the stereochemical aspects of the hydroboration of α- and β-pinene.

It was previously reported that α-pinene undergoes hydroboration–oxidation to form isopinocampheol, and this result was considered to support the proposed generalization that hydroboration involves an anti-Markovnikov, *cis* addition from the less hindered side of the double bond[3] (1).



(1)

The configuration for isopinocampheol (1) comes from the assignment by Schmidt,[4] who based it mainly on the Auwers–Skita rule. Unfortunately, Schmidt's assignment has recently been challenged by Bose[5] and by Hückel.[6] These workers agree that isopinocampheol belongs to the *cis*-pinane series, but they prefer the extreme *cis* configuration for the alcohol (2).



(2)

Their arguments are based on conformational analysis[5] and on rate studies on the isopinocampheyl tosylate.[6]

Recent developments have made it especially important to know the exact configuration of the dialkylborane produced in the hydroboration of α-pinene. Thus this substance, derived from optically active α-pinene, permits the synthesis of optically active alcohols from olefins[7] and the resolution of racemic olefins.[8] Moreover, it has proved possible to correlate the configuration of the optically active alcohols produced *via* the reagent with the assumed structure of the reagent.[9] For these reasons it appeared especially desirable at this time to subject the hydroboration of α- and β-pinene to a critical examination.

Results and Discussion

Configuration of α- and β-Pinene.—Both dextro- and levorotatory α-pinene ($[\alpha]_D$ +47.6°, −47.9°, respectively) are readily available in reasonably high optical purity (~94%).[10] β-Pinene is also readily available in levorotatory form ($[\alpha]^{20}_D$ −21.1°)[11] and may readily be converted into levorotatory α-pinene without racemization by shaking with palladium hydrogenation catalyst in the presence of a little hydrogen.[12]

(1) For a summary of data and pertinent references, see H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(2) H. C. Brown, K. P. Singh, and B. J. Garner, *J. Organometal. Chem.*, **1**, 2 (1963).

(3) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **81**, 247 (1959); **83**, 2544 (1961).

(4) H. Schmidt, *Ber.*, **77**, 544 (1944).

(5) K. Bose, *J. Org. Chem.*, **20**, 1003 (1955).

(6) W. Hückel and D. S. Nag, *Ann.*, **645**, 101 (1961).

(7) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 486 (1961).

(8) H. C. Brown, N. R. Ayyangar, and G. Zweifel, *ibid.*, **84**, 4341 (1962).

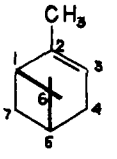
(9) G. Zweifel, N. R. Ayyangar, and H. C. Brown, *ibid.*, **84**, 4342 (1962).

(10) F. H. Thurber and R. C. Thielke, *ibid.*, **53**, 1030 (1931), report for (+)-α-pinene: $[\alpha]_D$ +51.5°.

(11) G. Dupont, *Ann. Chim.*, [x] **1**, 184 (1926), reports for (−)-β-pinene: $[\alpha]^{25}_D$ −22.4°.

(12) I. Richter and W. Wolff, *Ber.*, **59**, 1733 (1926).

The absolute configuration of (+)-α-pinene has been established[13,14] as 1R:5R (3).

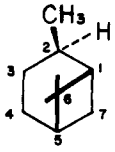


(1R:5R)-(+)-α-pinene

(3)

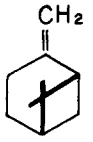
Hydroboration of (−)-β-Pinene.—β-Pinene readily undergoes hydroboration in the mole ratio, 3 β-pi ene/BH_3, to form the corresponding organoborane. The product, heated *in situ* with propionic acid to bring about the protonolysis of the boron substituent,[15] is converted into essentially pure *cis*-pinane ($[\alpha^{20}]D$ −19.3°).

The absolute configuration of (−)-*cis*-pinane (4) has been established as 1S:2R:5S through its conversion into (3R)-(+)-citronellol.[16] Consequently, (−)-β-pinene must have the configuration 1S:5S (5).



(1S:2R:5S)-(−)-cis-pinane

(4)



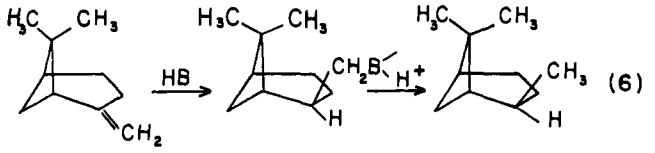
(1S:5S)-(−)-β-pinene

(5)

The results indicate that the hydrogen atom of the boron–hydrogen bond has become attached to the 2-position from the side away from the *gem*-dimethyl group to produce the less stable of the two possible derivatives.

The hydrogenation of β-pinene over platinum on carbon catalyst[17] produces *cis*-pinane containing 20% of the *trans* isomer. However, the hydroboration–protonolysis product was at least 98% pure by gas chromatographic examination. Consequently, it appears that hydroboration is more sensitive to steric control in this system than catalytic hydrogenation.

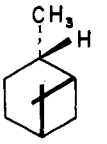
The observed reaction course may, therefore, be represented as involving a preferential attack from the less hindered side (6).



(6)

Oxidation of the organoborane from (−)-β-pinene forms (−)-*cis*-myrtanol.[3,18] On the other hand, under the influence of heat (2.5 hr. at 125°) the initially formed organoborane undergoes isomerization to another derivative, oxidation of which yields (−)-*trans*-myrtanol.[18]

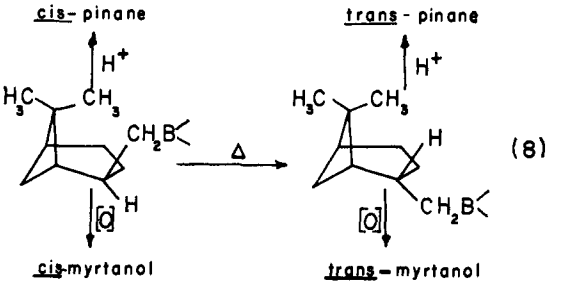
Protonolysis of the isomerized derivative converts the organoborane into essentially pure (−)-*trans*-pinane (7).



(1S:2S:5S)-(−)-trans-pinane

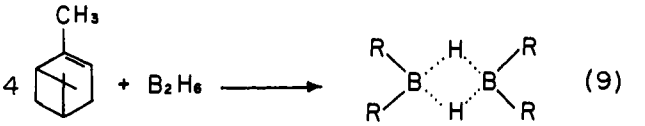
(7)

It is evident from these results that the addition of the boron–hydrogen moiety from the less hindered side places the resulting —$CH_2B<$ group in position where it is sterically crowded against the *gem*-dimethyl group. Under the influence of heat the molecule readily isomerizes into the thermodynamically more stable isomer which contains the above group in the *trans* relationship to the *gem*-dimethyl structure (8).



(8)

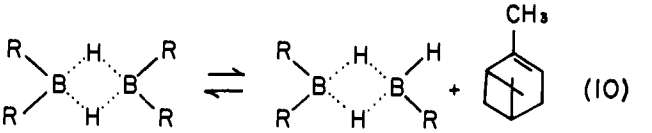
Hydroboration of α-Pinene.—The hydroboration of α-pinene at 0° proceeds to the dialkylborane stage, even with excess olefin present. The product is dimeric in tetrahydrofuran solution.[19] Consequently, the reaction proceeds to produce a *sym*-tetraalkyldiborane as a limit (9).



(9)

This product from (+)-α-pinene, previously assigned the structure tetraisopinocampheyldiborane, exhibits a rotation in tetrahydrofuran of $[\alpha]^{20}D$ −37.1°.[19]

In the absence of excess α-pinene, the product exhibits significant dissociation into triisopinocampheyldiborane and α-pinene[20] (10).



(10)

Thus, a 0.5 *M* solution in tetrahydrofuran shows the presence of 10% of the original quantity of α-pinene utilized to synthesize the derivative. The product is less soluble in diglyme and precipitates from solution when prepared at the usual concentrations. In this medium the amount of residual α-pinene is somewhat lower, 4%, presumably the result of the smaller quantity of the reagent which is in solution. For this reason, we have found it preferable to synthesize and utilize the reagent in diglyme solution.

(+)-α-Pinene was hydroborated in diglyme in the usual manner and the product was subjected to protonolysis.[15] Only half of the alkyl groups was recovered.[21] The product was pure (+)-*cis*-pinane. Consequently, in this case also the hydrogen of the

(13) For a summary of evidence and references dealing with the configuration of (+)-α-pinene, see J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5491 (1959).

(14) For the R–S configurational nomenclature, see R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

(15) H. C. Brown and K. J. Murray, *J. Am. Chem. Soc.*, **81**, 4108 (1959); *J. Org. Chem.*, **26**, 631 (1961).

(16) R. Rienäcker and G. Ohloff, *Angew. Chem.*, **73**, 240 (1961).

(17) C. A. Brown and H. C. Brown, *J. Am. Chem. Soc.*, **84**, 2829 (1962).

(18) J. C. Braun and G. S. Fisher, *Tetrahedron Letters*, **No. 21**, 9 (1960).

(19) H. C. Brown and G. J. Klender, *Inorg. Chem.*, **1**, 204 (1962).

(20) H. C. Brown and A. W. Moerikofer, *J. Am. Chem. Soc.*, **84**, 1478 (1962).

(21) It was previously observed that in the protonolysis of the organoborane from 2-norbornene that one alkyl group per boron atom resisted protonolysis under the usual conditions (ref. 15).

TABLE I

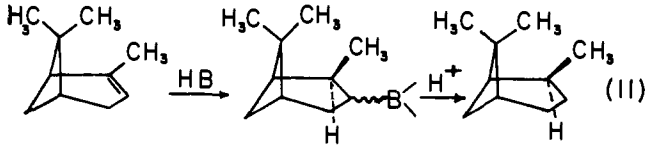
SUMMARY OF EXPERIMENTAL DATA FOR THE HYDROBORATION OF α- AND β-PINENE

Pinene	Rotation	Product	Rotation, deg.	Remark
β-	−	*cis*-Pinane	$\alpha^{20}D$ −19.3	Neat, 1 dm.
β-	−	*cis*-Myrtanol	$[\alpha]^{20}D$ −20.9	*c* 4, $CHCl_3$
β-	−	*trans*-Pinane[a]	$\alpha^{20}D$ −14.5	Neat, 1 dm.
β-	−	*trans*-Myrtanol[a,b]	$[\alpha]D$ −28.0	*c* 14.7, *p*-cymene
α-	+	*cis*-Pinane	$\alpha^{20}D$ +21.5	Neat, 1 dm.
α-	+	Isopinocampheol	$[\alpha]^{20}D$ −32.8	*c* 10, benzene
α-	−	*trans*-Myrtanol[a]	$[\alpha]^{20}D$ −28.5	*c* 4, $CHCl_3$
α-	+	*sym*-Tetraisopinocampheyldiborane[c]	$[\alpha]^{20}D$ −37.1	In tetrahydrofuran

[a] After isomerization of the initially produced organoborane. [b] Ref. 18. [c] Ref. 19.

boron–hydrogen bond has become attached to the 2-carbon of (+)-α-pinene (3) from the side away from the *gem*-dimethyl group.

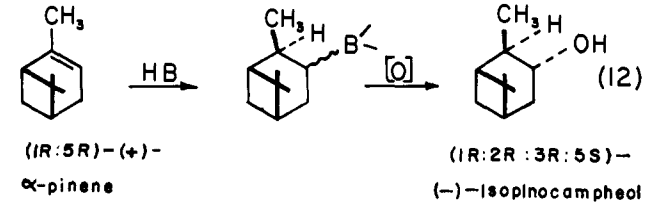
The *exo*-cyclic double bond in β-pinene is further removed and should be less influenced by the *gem*-dimethyl group than the *endo*-cyclic double bond in α-pinene. Consequently, if the *gem*-dimethyl group can control the hydroboration of β-pinene to proceed from the direction away from the *gem*-dimethyl group, it is not unexpected that this should also be the preferred direction of hydroboration in α-pinene (11).



It should be pointed out that (−)-β-pinene yields (−)-*cis*-pinane and (+)-α-pinene yields (+)-*cis*-pinane in these reactions. This confirms the conclusion advanced earlier that (−)-β-pinene (4) must be configurationally related to (−)-α-pinene.

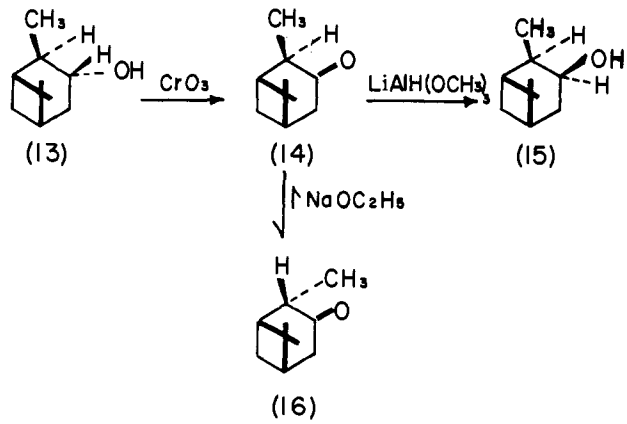
Oxidation of the hydroboration product yields an alcohol, m.p. 55–57°, $[\alpha]^{20}D$ −32.8° (*c* 10, benzene), m.p. acid phthalate ester 125–126°, m.p. 3,5-dinitrobenzoate 98–99°. There can be no doubt that this alcohol is identical with the isopinocampheol described by Schmidt.[4,22,23]

There remains the question of the configuration of the hydroxyl group in relation to the methyl group at C_2. The hydroboration–oxidation of a number of simple cyclic olefins,[3] such as 1-methylcyclopentene, 1-methylcyclohexene, 1-phenylcyclohexene, and 1,2-dimethylcyclohexene, as well as steroids, such as chlolesterol,[24] and acyclic olefins, such as *cis*- and *trans*-2-*p*-anisyl-2-butene,[25] results invariably in the product corresponding to a pure *cis* addition of the elements of water to the double bond. There appears to be no reason to expect an exception in the case of α-pinene. Consequently, it must be concluded that isopinocampheol has a *cis* relationship between the hydroxyl group and the hydrogen atom at C_2, confirming Schmidt's original assignment[4] (12).



Hückel was led to propose a *cis* relationship between the hydroxyl group and the methyl at C_2 on the basis of the very fast rate of solvolysis that he observed for the tosylate.[6] He argued that the fast rate pointed to considerable steric assistance to the ionization. Unfortunately, he failed to extend the study to the neoisopinocampheol derivative. Consequently, it appeared desirable to undertake the synthesis of neoisopinocampheol and to compare the rate of solvolysis of its sulfonate ester with that of isopinocampheol.

Oxidation of (−)-isopinocampheol (13) with chromic acid gave (+)-isopinocamphone (14). Reduction of the ketone with lithium trimethoxyaluminohydride [$LiAlH(OCH_3)_3$], a reagent known to attack the carbonyl group preferentially from the less hindered side of the molecule,[26] gave (+)-neoisopinocampheol (15) in 96–97% isomeric purity.



Equilibration of isopinocamphone at 25° with sodium ethoxide[4] gave an 81:19 mixture of pinocamphone (16) and isopinocamphone. This is consistent with the argument that the approach from the *gem*-dimethyl direction is more congested than the approach from the opposite direction.

The two methanesulfonate esters were synthesized and solvolyzed in methanol at 25°. It was observed that the first-order rate constant for the solvolysis of the neoisopinocampheyl methanesulfonate, $k_1 = 5.85 \times 10^{-5}$ sec.$^{-1}$, exceeded by a factor of three the corresponding rate of solvolysis of the isopinocampheyl methanesulfonate, $k_1 = 1.98 \times 10^{-5}$ sec.$^{-1}$. These rate data would appear to support our conclusion that the hydroxyl and C_2-methyl have a *cis* relationship in neoisopinocampheol and a *trans* relationship in isopinocampheol.[27]

It should be mentioned that the organoborane from α-pinene readily isomerizes at 160° to yield a product which is converted by oxidation predominantly into *trans*-myrtanol.[28]

The results are summarized in Table I.

(22) Schmidt (ref. 4) reports for (−)-isopinocampheol m.p. 57°, $[\alpha]^{20}D$ −32°, m.p. acid phthalate ester 126°.

(23) Hückel and Nag (ref. 6) report for 3,5-dinitrobenzoate m.p. 99°.

(24) W. J. Wechter, *Chem. Ind.* (London), 294 (1959).

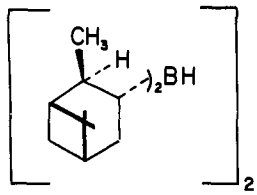
(25) E. L. Allred, J. Sonnenberg, and S. Winstein, *J. Org. Chem.*, **25**, 26 (1960).

(26) H. C. Brown and H. R. Deck, in print.

(27) F. J. Chloupek and G. Zweifel, to be published.

(28) A detailed study of the isomerization of organoboranes from cyclic and bicyclic olefins has been completed (H. C. Brown and G. Zweifel) and will shortly be reported.

There remains the question of assignment of boron at C_3 in the hydroboration product. All of the accumulated experience in the field is consistent only with the requirement that the hydroboration step involves a simple *cis* addition of the boron–hydrogen bond to the olefins, with the oxidation by alkaline hydrogen peroxide proceeding with complete retention of configuration.[29] No data have been made available which would appear to require modification of this conclusion. Consequently, the organoborane from (+)-α-pinene must be assigned the structure (−)-*sym*-tetraisopinocampheyldiborane[30] (17) with the absolute configuration (1R:2S:3R:5R) for each isopinocampheyl grouping.



(17)

(−)-Sym-Tetra-(1R:2S:3R:5R)-isopinocampheyl diborane

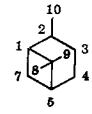
Nuclear Magnetic Resonance Spectra.—With the large number of configurationally defined products in hand, it appeared desirable to examine their nuclear magnetic resonance spectra. It was hoped that the spectra might reveal certain regularities that might assist in confirming the assignments and provide a basis for assignments in other related compounds with as yet unassigned configurations.

An n.m.r. study of isopinocamphone and pinocamphone was reported previously.[31] Their assignment for the methyl protons at C_8, C_9, and C_{10} was adopted for the present study.

The results are summarized in Table II.

TABLE II

CHEMICAL SHIFTS OF *cis*- AND *trans*-PINANE AND DERIVATIVES

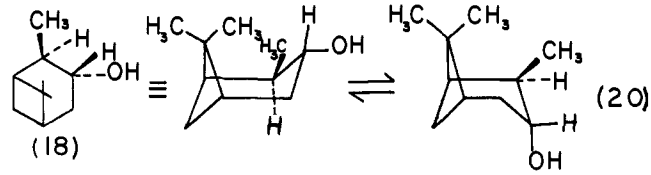


	τ-Values[a]				
	C_8-H_3	C_9-H_3	C_{10}-H_3[b]	C_3-H	C_3-OH
cis-Pinane	8.80	8.99	8.99		
trans-Pinane	8.80	9.18	9.17		
Isopinocamphone	8.68	9.13	8.85		
Pinocamphone	8.64	9.09	8.97		
Isopinocampheol	8.80	9.09	8.91	6.5	6.0
Neoisopinocampheol	8.82	8.94	8.93	5.69	6.87
cis-Myrtanol	8.82	9.03			
trans-Myrtanol	8.80	9.18			

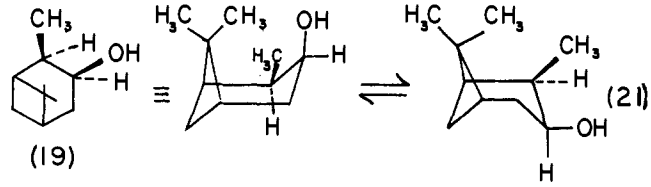
[a] Spectra at 60 Mc. in carbon tetrachloride with tetramethylsilane as reference. [b] $J_{2/10}$ = 6 to 8 c.p.s.; values obtained by first-order analysis.

Unfortunately, the results largely confirm the belief that the interpretations of long-range shielding effects are difficult to evaluate.[32]

The spectra of isopinocampheol (18) and neoisopinocampheol (19) reveal that the 8-methyl protons appear nearly at identical field strengths (τ 8.80 and 8.82). Likewise, the 10-methyl proton signals in both compounds occur nearly at the same field. This suggests that the spacial arrangement of the 10-methyl group relative to the 9-methyl may be similar in isopinocampheol and neoisopinocampheol with the probable absence of extreme conformations 20 and 21.

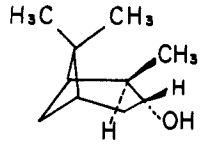


(18) (20)



(19) (21)

A planar conformation, 22 and 23, would account for the small chemical shifts observed for the 10-methyl and 9-methyl protons in 18 and 19.



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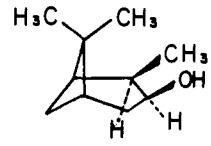

(23)

In isopinocampheol (22), the α-hydrogen at C_3 will be more shielded relative to the α-hydrogen in neoisopinocampheol (23). Therefore, the signal for the α-hydrogen in the former alcohol should occur at higher field. On the other hand, the hydroxyl proton in isopinocampheol should appear at lower field strength than the corresponding proton in neoisopinocampheol. The chemical shifts observed (Table II) favor a *trans* arrangement of the methyl group at C_2 and the hydroxyl group at C_3 in isopinocampheol.[33]

Conclusions

The results of this study fully confirm the earlier generalizations that the hydroboration reaction involves a simple anti-Markovnikov, *cis* addition of boron and hydrogen to the double bond predominantly from the less hindered side of the molecule. Oxidation by alkaline hydrogen peroxide serves to replace the boron substituent with complete retention of configuration. The hydroboration–oxidation of (+)-α-pinene produces (−)-isopinocampheol, with the absolute configuration (1R:2R:3R:5S). The organoborane formed in the hydroboration of (+)-α-pinene is (−)-*sym*-tetraisopinocampheyldiborane with the absolute configuration (1R:2S:3R:5R) for each of the alkyl groups.

Experimental

Materials.—(+)-α-Pinene, $[\alpha]^{20}D$ +47.6°, was a sample prepared from French turpentine and generously made available by Dr. R. A. Bankert of the Hercules Powder Co., Wilmington, Del. (−)-β-Pinene, $[\alpha]^{20}D$ −21.1°, is a commercial product available from the Glidden Co., Jacksonville, Fla. Solvents and reagents were purified as described in earlier papers.[3]

Preparation of (−)-*cis*-Pinane from (−)-β-Pinene.[34]—To 13.6 g. of (−)-β-pinene (0.100 mole, $[\alpha]^{20}D$ −21.1°) in 25 ml. of diglyme solution was added 30 ml. of a 1.00 *M* solution of sodium borohydride in diglyme. Hydroboration was achieved by adding 11.0 ml. of a 3.65 *M* solution of boron trifluoride in diglyme to the reaction mixture maintained at 0°. After 1 hr., 11 ml. of propionic acid was added to the reaction mixture and it was

(29) See ref. 1 for a detailed discussion of this point.

(30) In actual practice it is generally more convenient to refer to the reagent in its monomeric form, diisopinocampheylborane.

(31) R. L. Erskin and S. A. Knight, *Chem. Ind.* (London), 1160 (1960).

(32) N. Muller, private communication.

(33) For a summary of data on the chemical shift of substituted cyclohexanols, see E. L. Eliel, M. H. Gianni, and Th. H. Williams, *Tetrahedron Letters*, **No. 17**, 741 (1962).

(34) All hydroborations, isomerizations, and protonolyses were carried out under oxygen-free conditions (static nitrogen atmosphere).

heated under reflux for 2 hr. The reaction mixture was cooled to room temperature and sufficient 3 *N* sodium hydroxide added to ensure an excess. The upper phase was separated and washed with cold water to remove diglyme. There was obtained 12.4 g. of crude *cis*-pinane. Analysis of the crude product by gas chromatography (squalene column) indicated 98% *cis*-pinane, 2% *trans*-pinane. The crude product was purified by gas chromatography. The *cis*-pinane collected exhibited $n^{20}D$ 1.4624, $\alpha^{20}D$ −19.3° (1 dm.).

Preparation of (−)-*trans*-Pinane from (−)-β-Pinene.[34]—Under identical conditions described above, 13.6 g. of (−)-β-pinene was converted into the organoborane. The reaction mixture was then heated at 125° for 2.5 hr. to isomerize the product. The reaction mixture was cooled to room temperature, 11 ml. of propionic acid added, and the mixture heated for 2 hr. under reflux. The hydrocarbon product was isolated as for *cis*-pinane above. There was obtained 13.0 g. of crude product. Gas chromatographic examination indicated 98% *trans*- and 2% *cis*-pinane. The crude product was purified by gas chromatography on an acrylonitrile–glycerol column. The *trans*-pinane collected exhibited $n^{20}D$ 1.4610, $\alpha^{20}D$ −14.5° (1 dm.).

Preparation of *cis*-Pinane from (+)-α-Pinene.[34]—In a 200-ml. flask was placed 13.6 g. of (+)-α-pinene (0.10 mole, $[\alpha]^{20}D$ +47.6°) and 45 ml. of a 1.00 *M* solution of sodium borohydride in diglyme. Diborane was generated by adding to the reaction mixture 16.4 ml. of a 3.65 *M* solution of boron trifluoride in diglyme. The reaction flask was immersed in a water bath. The reaction was allowed to proceed for an additional 2 hr. at 20–25°. The excess hydride was destroyed by adding glycerol. The reaction mixture was treated with 11 ml. of propionic acid, then heated for 4 hr. under reflux. After cooling to room temperature, the reaction mixture was diluted with sufficient 3 *N* sodium hydroxide to ensure an excess of base. The upper layer was separated and washed with cold water to remove diglyme. Analysis of the crude product by gas chromatography (squalene column) indicated essentially pure *cis*-pinane. Preparative gas chromatography yielded 4.8 g., 35% yield, (+)-*cis*-pinane, $n^{20}D$ 1.4614, $\alpha^{20}D$ +21.5° (1 dm.).

Preparation of (−)-*cis*-Myrtanol from (−)-β-Pinene.[34]—β-Pinene was hydroborated and oxidized in the usual manner. The reaction product, *cis*-myrtanol, was purified by gas chromatography using a tris-(cyanoethoxy)-propane column to remove a very minor amount of the *trans* isomer. The purified product exhibited the constants $n^{20}D$ 1.4910, $[\alpha]^{20}D$ −20.9° (*c* 4, chloroform).

Preparation of (−)-Isopinocampheol.—In a 300-ml. flask, fitted with a dropping funnel, a reflux condenser, a nitrogen inlet tube, and a magnetically operated stirring bar, was placed 82.5 ml. of a 1.00 *M* solution of sodium borohydride in diglyme (10% excess), 27.2 g. of α-pinene (0.20 mole, $n^{20}D$ 1.4648, $[\alpha]^{20}D$ +47.6°) in 20 ml. of diglyme. The flask was immersed in a water bath and flushed with nitrogen. A static nitrogen atmosphere was then maintained. From the dropping funnel 14 ml. of boron trifluoride etherate (0.11 mole) was added dropwise to the stirred reaction mixture over a period of 30 min., keeping the temperature at 20 to 25°. The flask was permitted to remain for 1 hr. at this temperature. The excess of hydride was destroyed by the careful addition of 20 ml. of water. The organoborinic acid thus formed (R_2BOH) was oxidized at 30 to 50° by adding 22 ml. of 3 *N* sodium hydroxide, followed by the dropwise addition of 22 ml. of 30% hydrogen peroxide (vigorous reaction!). The flask was permitted to remain an additional hour at room temperature.

The reaction mixture was taken up with 150 ml. of ether, and the ether extract was washed five times with equal amounts of ice water to remove diglyme. The ether extract was dried over anhydrous magnesium sulfate. The product obtained after removal of the ether was crystallized from a small amount of petroleum ether (35–37°). There was obtained 24.3 g., 79% yield, of isopinocampheol, m.p. 55–57°, $[\alpha]^{20}D$ −32.8° (*c* 10, benzene), m.p. acid phthalate 125–126°, m.p. 3,5-dinitrobenzoate 98–99°.

Preparation of Neoisopinocampheol.—Isopinocampheol was oxidized by the procedure of Brown and Garg[35] to yield isopinocamphone, b.p. 54–56° at 1 mm., $n^{20}D$ 1.4745, $\alpha^{20}D$ +10.3° (1 dm).[36]

Isopinocamphone (4.0 g., 26.3 mmoles) was added to 100 ml. of tetrahydrofuran containing 58 mmoles of lithium trimethoxyaluminohydride.[26] The product was purified by gas chromatography on a Carbowax 20M column. The neoisopinocampheol isolated, 2.1 g., exhibited m.p. 45–47°, $[\alpha]^{20}D$ +36° (*c* 3, benzene); m.p. 3,5-dinitrobenzoate 102–103°.[37]

A sample of (+)-isopinocamphone, 6.0 g., was added to a solution of 1.25 g. of sodium in 40 ml. of ethanol. After 24 hr. at 25°, the product was isolated by steam distillation. Gas chromatographic examination revealed 81% pinocamphone and 19% isopinocamphone.

Acknowledgment.—We are greatly indebted to Dr. R. A. Bankert of the Hercules Powder Co., Wilmington, Del., for a generous gift of (+)-α-pinene, and to the Glidden Co., Jacksonville, Fla., for a gift of (−)-β-pinene.

(35) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).
(36) Schmidt (ref. 4) reports $n^{20}D$ 1.4748, αD +10.5° for isopinocamphone.
(37) Schmidt (ref. 4) reports m.p. 48°, $[\alpha]D$ +36° for neoisopinocampheol.

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY, LAFAYETTE, IND.]

Hydroboration. XVIII. The Reaction of Diisopinocampheylborane with Representative *cis*-Acyclic, Cyclic, and Bicyclic Olefins. A Convenient Synthesis of Optically Active Alcohols and Olefins of High Optical Purity and Established Configuration

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Optically active diisopinocampheylborane, readily synthesized by the hydroboration of optically active α-pinene, reacts readily with *cis*-2-butene to yield diisopinocampheyl-2-butylborane. Oxidation with alkaline hydrogen peroxide yields isopinocampheol and 2-butanol, the latter in optical purity of 87%. (+)-α-Pinene yields (−)-2-butanol ($[\alpha]D$ −11.8°); (−)-α-pinene yields (+)-2-butanol ($[\alpha]D$ +11.7°). The reaction appears to be general for a number of *cis*-acyclic, cyclic, and bicyclic olefins, and it has been applied to *cis*-2-butene, *cis*-2-pentene, *cis*-3-hexene, *cis*-4-methyl-2-pentene, and norbornene. The alcohols realized exhibit optical purities in the range of 65 to 91%. Treatment of an excess of an olefin racemate with the reagent results in the preferential reaction of one of the components. In this way, racemic mixtures of 3-methylcyclopentene, 3-ethylcyclopentene, and 1-methylnorbornene have been converted into optically active olefin products. The absolute configuration of diisopinocampheylborane may be deduced from the known configuration of α-pinene. On the basis of a simple model for the hydroboration step it is possible to predict the absolute configuration of the optically active alcohols and olefins obtained in this asymmetric synthesis.

Dialkylboranes, readily accessible *via* hydroboration of hindered olefins, exhibit an unusually high selectivity for olefins with different structural features.[2] In view of these properties, it appeared possible that dialkylboranes derived from optically active terpenes or steroids might convert olefins into organoborane moieties capable of being transformed into optically active derivatives. Preliminary experiments indicated that diisopinocampheylborane, derived from the hydroboration of optically active α-pinene, is a highly selective hydroborating agent[2] and exhibits a remarkable asymmetric stereoselectivity when applied to the hydroboration of *cis*-olefins[3] and for the reduction of ketones.[4]

The subject matter of the present paper deals with a detailed study of the applicability of optically active

(1) Postdoctorate research associate on a grant provided by the National Science Foundation (G19878).
(2) G. Zweifel, N. R. Ayyangar, and H. C. Brown, *J. Am. Chem. Soc.*, **85**, 2072 (1963).
(3) A preliminary communication reporting this discovery was published earlier: H. C. Brown and G. Zweifel, *ibid.*, **83**, 486 (1961).
(4) H. C. Brown and D. B. Bigley, *ibid.*, **83**, 3166 (1961).