General Procedure for the Hydroboration of Gaseous Olefins and Dienes.—One-tenth mole (13.0 g.) of crude trimethylamine *t*-butylborane was placed in a 50-ml. three-necked flask equipped with a gas inlet tube, reflux condenser, thermometer and magnetic stirrer. The system was flushed with the desired olefin or diene and the temperature of the reaction vessel slowly raised to 60° with stirring. At this point the pressure began to fall in the reaction vessel and a slow stream of olefin or diene was passed through the reaction mixture. Trimethylamine was observed at the gas bubbler which served as an outlet of the reflux condenser. After approximately 2 hours, trimethylamine ceased to be evolved and the reaction system was purged with nitrogen and cooled. The liquid products were transferred to a spinning-band distillation column and separated by distillation at reduced pressures. Air was excluded at all times. Table I presents the boiling points, yields and analyses of the products obtained.

General Procedure for the Hydroboration of Liquid Dienes.—The procedure employed here was identical to that described above with two exceptions. A Dry Ice cooled condenser was employed and the theoretical quantity of diene was added from a small dropping funnel in a slow stream of nitrogen. The cessation of trimethylamine evolution signaled the completion of the reaction.

The Preparation of 1-*t*-Butyl-1-bora-4-oxacyclohexane.—In a 100-ml. three-necked round-bottom flask was placed 22.5 g. (0.173 mole) of crude trimethylamine *t*-butylborane. The system was equipped with a Dry Ice cooled reflux condenser, a magnetic stirrer and a small pressure-equalized dropping funnel which carried a nitrogen inlet. The Dry Ice cooled condenser was attached to a gas bubbler which served as a seal to the atmosphere. Divinyl ether (12 g., 0.173 mole) was added to the dropping funnel, the system flushed with dry nitrogen and heating commenced. When the reaction mixture reached 60°, divinyl ether as added dropwise over a period of 3 hours. During the addition white crystals formed on the reflux condenser and the upper portions of the reaction flask. The reaction mixture was cooled to room temperature in a stream of nitrogen and 50 ml. of pentane was added through the reflux condenser. By cooling the resulting pentane solution to −80°, a large amount of crystalline product was collected by filtration in an air-free glove-box (m.p. 65–68°). The extreme reactivity of the product with air did not suggest this method of isolation for preparative use. As an alternative isolation

method, the pentane solution of product was distilled with a spinning-band distillation column and the product collected at 90° (56 mm.). The yield amounted to 17.0 g. or 70% of theory. Analysis for carbon and hydrogen was impossible due to the extreme air sensitivity of the product. However, two solutions of known concentration in benzene were prepared in the glove-box. These solutions were employed in a cryoscopic determination of the molecular weight (found 142 and 144, theory 140). Aliquots of these same benzene solutions were then analyzed.

Anal. Calcd., B: 7.73. Found: B, 7.72.

General Procedure for the Hydroboration of Terminal Acetylenes.—One-tenth mole (13.0 g.) of crude trimethylamine *t*-butylborane was dissolved in 75 ml. of purified tetrahydrofuran and employed in accordance with the general procedures described above. The reaction temperature was 60° in all cases and the products were isolated by distillation as described above.

Oxidation of *t*-Butyldi-(1-butenyl)-borane to *n*-Butyraldehyde.—Three grams of purified *t*-butyldi-(1-butenyl)-borane dissolved in 20 ml. of pure diethyl ether was added dropwise with cooling and stirring to a solution of 15 ml. of water, 5 ml. of 30% hydrogen peroxide and 2 ml. of 10% sodium hydroxide. Following the addition the mixture was stirred at 0° for 15 minutes, the ether layer separated and washed with saturated aqueous ferrous ammonium sulfate which contained 5% sulfuric acid. The ether layer was then treated with an equal volume of saturated alcoholic 2,4-dinitrophenylhydrazine hydrochloride and allowed to stand at room temperature overnight. Removal of solvent followed by chromatography on alumina with benzene solvent afforded 0.90 g. of *n*-butyraldehyde 2,4-dinitrophenylhydrazone (m.p. 121–122°) which was identical to an authentic sample in the infrared.

Nuclear Magnetic Resonance Measurements.—All nuclear magnetic resonance measurements were carried out on neat samples with benzene or trimethyl borate as an internal reference sealed in a capillary insert.

Hydroboration. IX. The Hydroboration of Cyclic and Bicyclic Olefins—Stereochemistry of the Hydroboration Reaction

BY HERBERT C. BROWN AND GEORGE ZWEIFEL[1]

RECEIVED JANUARY 25, 1961

The hydroboration of 1-methylcyclopentene, 1-methylcyclohexene and 1-phenylcyclohexene, followed by oxidation with alkaline hydrogen peroxide, yields the pure (>99%) *trans*-2-methylcyclopentanol, *trans*-2-methylcyclohexanol and *trans*-2-phenylcyclohexanol, corresponding to a pure *cis* hydration of the double bond. (However, 1-methylcyclooctene yielded several isomeric alcohols, presumably arising from a facile rearrangement of the organoborane formed initially.) That the stereochemistry of the reaction is not controlled by the stability of the product is revealed by the products obtained from 1,2-dimethylcyclopentene and 1,2-dimethylcyclohexene. In each case the alcohol obtained corresponds to a pure *cis* addition of the elements of water to the double bond, even though this results in the thermodynamically less stable isomer. Norbornene yields *exo*-norborneol. These results lead to the generalization that hydroboration proceeds through a *cis-anti*-Markownikoff addition of the boron–hydrogen bond to the carbon–carbon double bond, the reaction proceeding preferentially from the less hindered direction. In support of this generalization are the observations that hydroboration–oxidation converts α-pinene into isopinocampheol, β-pinene into *cis*-myrtanol, and camphene into *endo*-camphanol. 1-Methylcyclopentene and 1-methylcyclohexene are cleanly converted into 3-methylcyclopentene and 3-methylcyclohexene by (1) hydroboration, (2) oxidation, (3) tosylation and (4) elimination, providing a route of wide generality for the synthesis of 3-alkyl-cycloalkenes. In the hydroboration of 3-methylcyclopentene, 3-methylcyclohexene and 3,3-dimethylcyclohexene, diborane exhibits little selectivity between the two carbon atoms of the double bond, with only a modest selectivity exhibited by bis-3-methyl-2-butylborane. Hydroboration provides a valuable procedure for the synthesis of stereochemically defined alcohols.

The hydroboration of unsymmetrically substituted acyclic olefins, followed by oxidation with alkaline hydrogen peroxide, provides a convenient

synthetic route for the anti-Markownikoff hydration of double bonds.[2] It appeared that a study of

(1) Post-doctorate research assistant on a grant supported by the Ethyl Corporation, 1958–1959.

(2) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 2582 (1956); H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1136 (1957); H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **81**, 6423, 6428 (1959); H. C. Brown and G. Zweifel, *ibid.*, **82**, 4708 (1960).

the hydroboration of cyclic olefins might provide information on the stereochemistry of the hydroboration reaction. Accordingly, we undertook a study of the hydroboration of a number of representative cyclic and bicyclic olefins.[3,4]

Results

Hydroboration of 1-Substituted Cycloalkenes.—
The hydroboration of 2-methyl-2-butene proceeds rapidly only to the dialkylborane stage, forming bis-3-methyl-2-butylborane (disiamylborane) containing the boron atom on the less substituted of the two carbon atoms of the double bond (eq. 1).[2,5]

$$2C—\overset{\overset{\displaystyle C}{|}}{C}=C—C + \tfrac{1}{2}B_2H_6 \longrightarrow \quad B—H \quad (1)$$
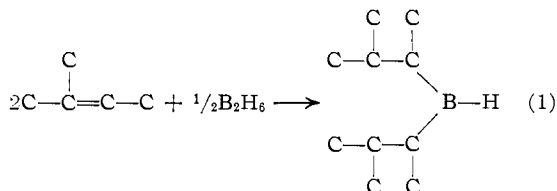
1-Methylcyclopentene and 1-methylcyclohexene are also trisubstituted olefins. It was not unexpected, therefore, that the hydroboration of these olefins proceeded rapidly to the dialkylborane stage, with further reaction being very slow. Oxidation of the products with alkaline hydrogen peroxide yielded the 2-methylcycloalkanols. Consequently, here also the addition occurs to place the boron atom at the less substituted of the two carbon atoms of the double bond.

Examination of the crude product from 1-methylcyclopentene by vapor phase chromatography (v.p.c.) utilizing a glycerol column revealed the presence of 1.5% of 1-methylcyclopentanol and 98.5% of trans-2-methylcyclopentanol. No evidence for the presence of the cis isomer was observed. Distillation yielded pure trans-2-methylcyclopentanol (b.p. 150–151°, n^{20}D 1.4505, 86% yield).

In the same way v.p.c. examination of the crude product from 1-methylcyclohexene revealed the presence of 1.5% of 1-methylcyclohexanol, 0.8% of cis-2-methylcyclohexanol[6] and 97.7% of trans-2-methylcyclohexanol (distilled: b.p. 166° at 741 mm., n^{20}D 1.4611, 85% yield).

We then applied this reaction to 1-methylcyclooctene, but encountered anomalous results. Examination (v.p.c.) of the product revealed the presence of three components. The results are compatible with an unusually facile isomerization of the 2-methylcyclooctylborane derivative presumably formed in the hydroboration stage.[7]

Application of the hydroboration–oxidation procedure to 1-phenylcyclohexene produced trans-2-phenylcyclohexanol (m.p. 55–57°, 79% yield).

(3) A preliminary Communication reporting our discovery of a pure cis hydration of the double bond was published earlier: H. C. Brown and G. Zweifel, J. Am. Chem. Soc., 81, 247 (1959).

(4) Since our original announcement (ref. 3), numerous applications of the reaction have been made to synthesize stereochemically defined alcohols. These will be summarized in the discussion of the stereochemistry of the reaction in the Discussion section.

(5) H. C. Brown and G. Zweifel, J. Am. Chem. Soc., 83, 1241 (1961).

(6) Tentative identification based only on the similarity in retention time with an authentic sample of cis-2-methylcyclohexanol. We were unable to achieve resolution on other columns to verify this tentative identification.

(7) Similar results have been observed by Professor A. C. Cope and his students. We shall shortly communicate the results of our studies of the isomerization of cycloalkylorganoboranes.

Hydroboration of 1,2-Dimethylcycloalkenes.—
Each of the above alcohols is the more stable of two possible isomers. Accordingly, it appeared desirable to examine the hydroboration of 1,2-dimethylcyclopentene and 1,2-dimethylcyclohexene. In these cases cis-hydration would result in the formation of the thermodynamically less stable isomer.

The hydroboration of 1,2-dimethylcyclopentene and -cyclohexene proceeds readily only to the monoalkylborane stage, presumably because of the large steric requirements of the tetraalkyl substituted olefins.[2] Fortunately, oxidation of the resulting organoborane proceeds readily.

In this way, these two olefins were converted into pure cis-1,2-dimethylcyclohexanol (b.p. 76–77° at 19 mm., m.p. 24–25°, 82% yield) and pure cis-1,2-dimethylcyclopentanol (b.p. 66–69° at 21 mm., m.p. 23–24°). Consequently, in these cases also the procedure results in a pure cis-hydration of the double bond.

Hydroboration of Bicyclic Olefins.—
The hydroboration of norbornene proceeded readily to the trialkylborane stage. Oxidation yielded a norborneol which by v.p.c. examination appeared to consist of at least 99% of the exo isomer. Recrystallization from petroleum ether yielded pure exo-norborneol (m.p. 126–127°, 85% yield).

This experiment suggested that hydroboration proceeds preferentially from the less hindered side of cyclic and bicyclic olefins with rigid structures. To test this possibility, the hydroboration of α- and β-pinene was examined.

The hydroboration of α-pinene proceeded to the dialkylborane stage. Oxidation of the organoborane provided isopinocampheol in high yield (m.p. 54–56°, [α]^{20}D −32.4°, 89% yield). The structure was confirmed by oxidation with chromic acid into isopinocamphone (b.p. 69–70° at 5 mm., n^{20}D 1.4745, αD + 11.1°, 74% yield). In the same way, β-pinene was converted into cis-myrtanol (b.p. 70–72° at 1 mm., n^{20}D 1.4910, [α]^{20}D −21°).

In both cases the products correspond to those expected on the basis of the proposed generalization.

Synthesis of 3-Alkylcycloalkenes.—
It has been demonstrated by Hückel that the tosylates from trans-2-cyclohexanol and -pentanol readily undergo elimination under extensive treatment with 4 N sodium isopropoxide in refluxing isopropyl alcohol to form 3-methylcyclohexene and 3-methylcyclopentene.[8] With the ready formation of trans-2-methylcyclohexanol and -cyclopentanol now possible, it appeared that this development made available a simple synthetic route to the 3-alkylcycloalkenes. Accordingly, we explored the elimination stage in the hope of developing a procedure which would be somewhat more convenient than that previously described.[8]

It was observed that treatment of trans-2-methylcyclohexyl and -2-methylcyclopentyl tosylates with sodium isoamylate in diglyme led to rapid elimination at temperatures of 120–140°. The olefins could be distilled directly out of the reaction mixture in a reaction time of approximately one hour.

(8) W. Hückel and H. D. Sauerland, Ber., 87, 1003 (1954).

In this way, there were obtained 3-methylcyclo-hexene (b.p. 99–100° at 745 mm., $n^{20}D$ 1.4420, yield 73%) and 3-methylcyclopentene (b.p. 65–66°, $n^{20}D$ 1.4208, yield 69%).

Directive Effects in the Hydroboration of 3-Alkylcycloalkenes.—It was of interest to explore the hydroboration of 3-methylcyclopentene, 3-methylcyclohexene and 3,3-dimethylcyclohexene in order to establish whether the methyl substituent is capable of exerting any directive effect on the hydroboration of the double bond.

3-Methylcyclopentene was treated with diborane and oxidized to the corresponding methylcyclo-pentanols. We were unable to achieve resolution by v.p.c. analysis. Accordingly, the product was oxidized to the ketones and the latter examined. The v.p.c. analysis revealed the presence of 45% of 2-methyl- and 55% of 3-methylcyclopentanone. Similarly, 3-methylcyclohexene yielded 49% of 2-methyl- and 51% of 3-methylcyclohexanone. Finally, 3,3-dimethylcyclohexene yielded 50% of 2,2- and 50% of 3,3-dimethylcyclohexanol. Consequently, there is little directive influence of the 3-methyl groups on the hydroboration of these cyclic olefins.

We recently achieved considerable success in exerting steric control on the hydroboration of olefins with the bulky reagent, disiamylborane.[5] With this reagent, 3-methylcyclopentene yielded 40% of 2-methyl- and 60% of 3-methylcyclopentanone, 3-methylcyclohexene yielded 48% 2-methylcyclohexanone and 52% 3-methylcyclohexanone, and 3,3-dimethylcyclohexene yielded 40% 2,2- and 60% 3,3-dimethylcyclohexanol.

It proved possible subsequently to resolve the 2- and 3-methylcyclohexanols on a diglycerol capillary column. The analysis revealed the formation of 18% cis-2-, 30% trans-2-, 27% cis-3- and 25% trans-3-methylcyclohexanol.

Consequently, it appears that in contrast with the results achieved with acyclic olefins,[5] disiamyl-borane fails to exert any significant directive effect on the hydroboration of these simple olefins.

Discussion

These experiments establish that the hydroboration of 1-methylcyclopentene, 1-methylcyclohexene and 1-phenylcyclohexene, followed by oxidation with alkaline hydrogen peroxide, proceeds exceedingly cleanly stereochemically to give the pure trans-2-methylcyclopentanol, trans-2-methylcyclo-hexanol and trans-2-phenylcyclohexanol, corresponding to the anti-Markownikoff cis addition of the elements of water to the double bond (eq. 2–4).

In these cases the products are presumably the thermodynamically more stable isomers. However, the observation that 1,2-dimethylcyclopentene and 1,2-dimethylcyclohexene likewise undergo cis hydration (eq. 5–6) even though these products are presumably the thermodynamically less stable isomers, argues against the possibility that the stereochemical course of the reaction is controlled by product stability.

Finally the remarkable stereochemical cleanness of the reaction is an important argument for the reaction course being controlled by the reaction
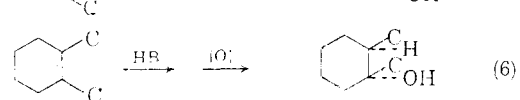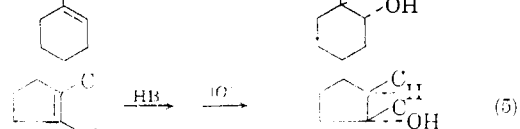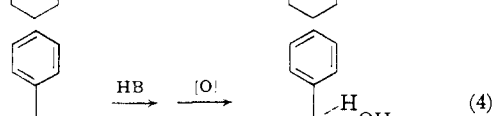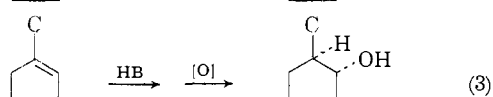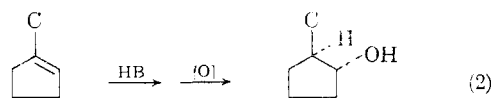

mechanism, and not by minor differences in the thermodynamic stabilities of the product.

Although the complete hydration corresponds to a clean cis hydration of the double bond, it is not possible from these results alone to draw conclusions as to the stereochemical characteristics of each stage in the reaction. Thus the results are consistent either with a cis addition of boron–hydrogen bond, followed by retention of configuration in the oxidation stage, or with a trans addition in the hydroboration step, with oxidation proceeding with inversion of configuration.

This question will be considered later in the paper.

Norbornene yields essentially pure exo-alcohol, with only traces of the endo isomer evident in the product (7).
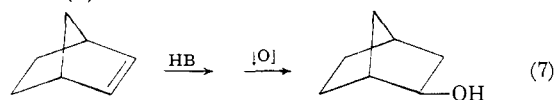
The very great predominance of exo-norborneol realized from norbornene led to the generalization that the hydroboration of olefins of rigid structure would proceed preferentially from the less hindered side of the double bond.[3]

The ready conversion of α-pinene to isopino-campheol is in complete accord with this generalization (8).
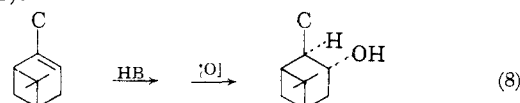
Similarly, β-pinene is converted into cis-myr-tanol (9) and camphene is converted into endo-camphenol (10).[9,10]
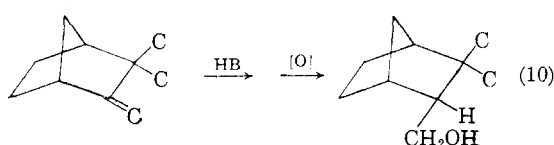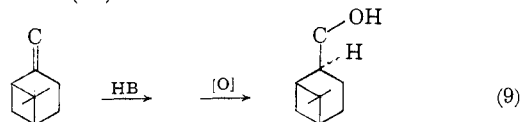
It is evident that this simple *cis* hydration of double bonds should find wide application in organic chemistry for the synthesis of stereochemically defined products. Thus, in the short time since our original announcement,[3] it has been utilized to convert a number of $\Delta^{1(9)}$-octalins into the corresponding decalols,[11] and steroids into the derived alcohols.[12,13] Winstein and his co-workers have utilized the reaction to convert *cis*- and *trans*-2-*p*-anisyl-2-butenes into the diastereomeric 3-*p*-anisyl-2-butanols.[14] Cristol and his co-workers converted *exo*-1,2-dihydrodicyclopentadiene into the corresponding *exo*-alcohol.[15] Finally, it has been utilized to convert isodrin into the *exo*-alcohol predicted on the basis of the above generalization.[16]

Since all of the data now available are in accord with the proposed generalization, it appears established that under non-isomerizing conditions the hydroboration–oxidation reaction involves a *cis* addition of the elements of water to the carbon–carbon double bond, the addition taking place anti-Markownikoff preferentially from the less hindered side.

In applying this procedure to the rigid bicyclic systems, such as norbornene or α-pinene, it is evident that the synthesis will produce only one of the two possible stereoisomers, that containing the hydroxyl group in the less hindered of the two arrangements. Fortunately, it is possible to circumvent this difficulty, thereby obtaining the other isomer. Thus oxidation of the alcohol produces the corresponding ketone and the latter is readily

(9) R. Dulou and Y. Chrétien-Bessière, *Bull. soc. chim. France*, 1362 (1959).

(10) R. Dulou and Y. Chrétien-Bessière (ref. 9) reported that the hydroboration–oxidation of β-pinene yielded *trans*-myrtanol, an apparent exception to our generalization and in conflict with our own experimental observations. However, this discrepancy has recently been resolved by J. C. Braun and G. S. Fisher, *Tetrahedron Letters*, No. 21, 9 (1960). They have demonstrated that upon heating, the initially formed organoborane isomerizes to a more stable derivative which yields *trans*-myrtanol on oxidation.

Apparently, Dulou and Chrétien-Bessière inadvertently subjected the organoborane initially formed to temperatures sufficiently high to achieve isomerization prior to the oxidation stage.

A detailed study of the isomerization of organoboranes derived from cyclic olefins will shortly be reported by the present authors.

(11) F. Sondheimer and S. Wolfe, *Can. J. Chem.*, **37**, 1870 (1959).

(12) W. J. Wechter, *Chemistry & Industry*, 294 (1959).

(13) S. Wolfe, M. Nussim, Y. Mazur and F. Sondheimer, *J. Org. Chem.*, **24**, 1034 (1959); M. Nussim and F. Sondheimer, *Chemistry & Industry*, 400 (1960).

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

(15) S. Cristol, W. K. Seifert and S. B. Soloway, *J. Am. Chem. Soc.*, **82**, 2351 (1960).

(16) R. C. Cookson and E. Crundwell, *Chemistry & Industry*, 703 (1959); P. Bruck, D. Thompson and S. Winstein, *ibid.*, 405 (1960).

reduced with lithium aluminum hydride and its derivatives. Since these reducing agents prefer to attack from the less hindered side of the bicyclic system,[17,18] the reduction produces the epimer of the original alcohol (eq. 11, 12).

$$(11)$$

$$(12)$$
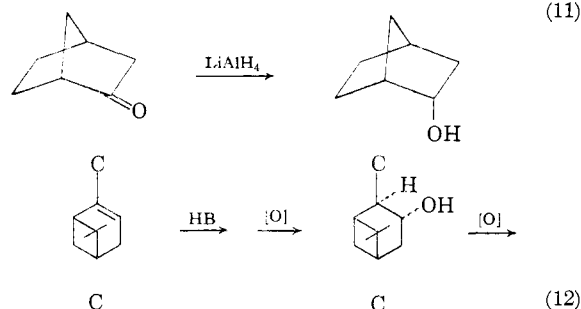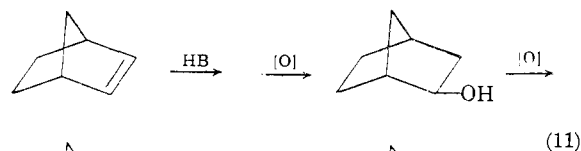
The observation that the hydroboration of 1-alkylcycloalkenes proceeds to yield the *trans*-2-alkylcycloalkanols, in conjunction with the preferential *trans* elimination of the 2-alkylcycloalkyl tosylates observed by Huckel,[8] suggests a convenient general synthesis of 3-alkylcycloalkenes (13).

$$(13)$$
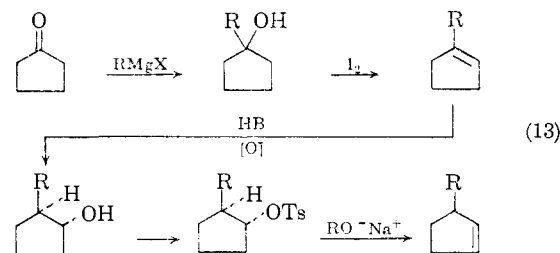
In the present study, this procedure was demonstrated for the synthesis of 3-methylcyclopentene and 3-methylcyclohexene. However, there does not appear to be any reason why it should not be generally applicable to the synthesis of 3-alkylcycloalkenes. Of course, the unusual characteristics of middle ring derivatives may introduce complications either in the hydroboration stage, as observed for 1-methylcyclooctene in the present study[7] or in the elimination stage, and thereby limit this synthesis somewhat.

In view of our success with acyclic olefins, it was disappointing to achieve so little control over the direction of hydroboration of 3-methylcyclopentene,[19] 3-methylcyclohexene and 3,3-dimethylcyclohexene. However, the results can be rationalized. Thus, with the methyl group situated in a *quasi*-
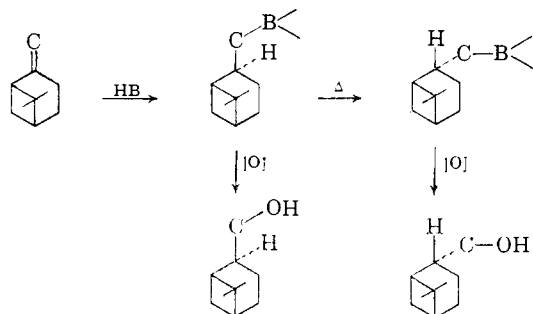
(17) S. Beckmann and R. Mezger, *Ber.*, **89**, 2738 (1956).

(18) O. H. Wheeler and J. L. Mateos, *Can. J. Chem.*, **36**, 1431 (1958).

(19) We previously observed that a 48:52 mixture of 3- and 4-methylcyclopentene was converted by disiamylborane into 82% 3- and 18% 2-methylcyclopentanol (ref. 5). This is not inconsistent with the present result if it is recognized that the 52% of 4-methyicyclopentene present in the mixture yields only 3-methylcyclopentanol.

equatorial position in the methylcyclohexene structure, there will be little steric influence on the direction of addition of the boron atom to the double bond (14). This is in accord with the observation that hydroboration proceeds 48% in the 2-position as compared to 52% in the 3-. There appears to be a slight preference for approach from the side more remote from the methyl group in the formation of 18% cis-2- and 30% trans-2-.

$$(14)$$
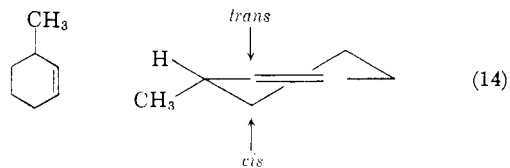
In the case of 3,3-dimethylcyclohexene, the methyl groups are both present in identical positions, which might be termed quasi-axial and quasi-equatorial (15). This brings about a larger preference for the 3-position, 40% 2- and 60% 3-. The smallness of the discrimination between the 2- and 3-positions is somewhat unexpected. However, this may arise from the flexibility of the half-chair form of the 3,3-dimethylcyclohexene structure, resulting in a simple conformational change which markedly reduces the steric interactions of the methyl group and the disiamylborane molecule in the transition state of the addition process.

$$(15)$$
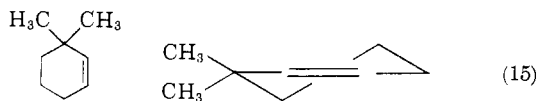
In a rigid system greater effects would be anticipated, and Professor Sondheimer has recently observed that treatment of Δ^1-cholestene with disiamylborane results in the predominant formation of cholestan-2α-ol, in contrast to the nearly 50:50 mixture of cholestan-1α-ol and cholestan-2α-ol realized with diborane.[20]

The question of the stereochemistry of the hydroboration stage remains to be considered. As was pointed out earlier, the mere fact that the over-all hydration corresponds to a clean cis hydration of the double bond does not permit one to draw conclusions as to the stereochemical characteristics of each stage in the reaction. The observed stereochemistry of the hydration reaction is consistent either with a cis addition of the boron–hydrogen bond, followed by retention of configuration in the oxidation stage, or with a trans addition in the hydroboration step, with the oxidation proceeding with inversion of configuration.

The results realized with norbornene favor the former alternative—cis addition and oxidation with retention.

Consider the possibility that the hydroboration stage involves a trans addition of the boron–hydrogen bond to norbornene. In that event, we should anticipate that the boron atom would prefer the less hindered exo position. Oxidation with inversion of configuration would then produce endo-norborneol (eq. 16).

(20) F. Sondheimer and M. Nussim, J. Org. Chem., 26, 630 (1961).

$$(16)$$
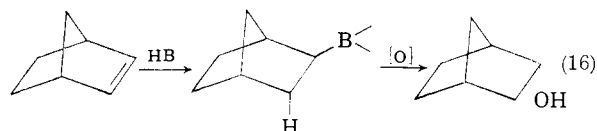
The formation of exo-norborneol is consistent with a cis addition in the hydroboration stage, placing the boron atom in the less hindered exo position, followed by oxidation of the organoborane with retention of configuration (eq. 17).

$$(17)$$
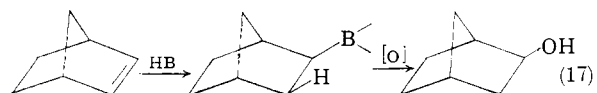
This conclusion is supported by a recent study of the hydroboration of norbornene with both diborane and hexadeuteriodiborane, followed by protonolysis and deuterolyses of the products (eq. 18, 19).

$$(18)$$

$$(19)$$
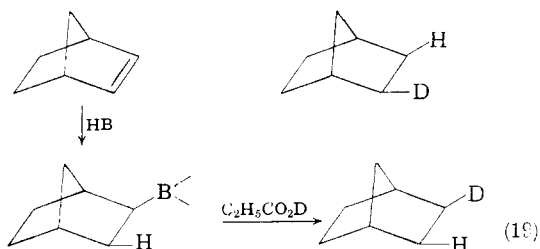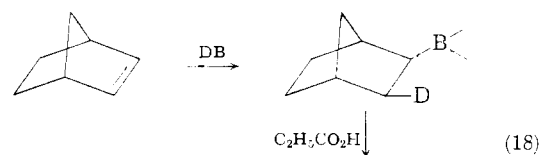
Examination of the products by n.m.r. spectroscopy clearly indicates that the monodeuterio derivatives are identical, with the deuterium atom occupying the exo position. This is consistent only with the proposed cis addition in the exo position in the hydroboration stage and with the protonolysis and deuterolysis proceeding with retention of configuration.[21]

Arguments can also be advanced to support the belief that the oxidation stage should proceed with retention of configuration.

A kinetic study of the reaction of trialkylboranes with hydrogen peroxide has not yet been reported. However, the related reaction of benzeneboronic acid with alkaline hydrogen peroxide has been the subject of a detailed investigation by Kuivila and his co-workers.[22] They have proposed the following mechanism for this reaction (20).

$$HO^- + H_2O_2 \rightleftharpoons H_2O + {}^-O_2H$$

$$(20)$$
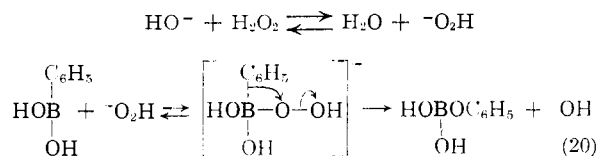
(21) H. C. Brown and K. J. Murray, ibid., 26, 631 (1961).

(22) H. G. Kuivila, J. Am. Chem. Soc., 76, 870 (1954); 77, 4014 (1955); H. G. Kuivila and R. A. Wiles, ibid., 77, 4830 (1955); H. G. Kuivila and A. G. Armour, ibid., 79, 5659 (1957).

An identical mechanism in three successive stages is consistent with the known facts about the oxidation of trialkylboranes with alkaline hydrogen peroxide.[12] This mechanism involves intermediates mechanistically similar to those postulated for the Hofmann, Curtius and Schmidt rearrangements, reactions which have been demonstrated repeatedly to proceed with retention of configuration in the migrating alkyl groups.[23]

Consequently, it appears safe to conclude that the hydroboration reaction proceeds *via* a *cis* four-center addition to the double bond, followed by oxidation with retention of configuration (21).

$$(21)$$
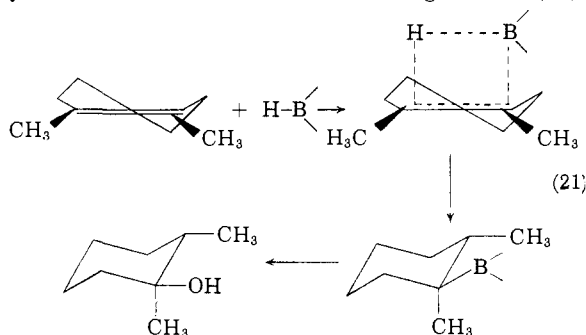
In conclusion, the simple *cis* addition of the boron–hydrogen bond to cyclic olefins provides an important new route to stereochemically defined derivatives. It may be anticipated that this reaction will play an increasingly important role in the synthesis of such derivatives.

Experimental Part

Materials.—Tetrahydrofuran was purified by distillation from lithium aluminum hydride. Diglyme (dimethyl ether of diethylene glycol), provided by the Ansul Chemical Co., was distilled under reduced pressure from lithium aluminum hydride. Boron trifluoride ethyl etherate was treated with a small quantity of ethyl ether (to ensure an excess of this component) and then distilled under reduced pressure to obtain a clear, colorless product. Sodium borohydride from Metal Hydrides Inc. (98%) was utilized without further purification.

1,2-Dimethylcyclopentene and 1,2-dimethylcyclohexene were provided by API Project 45. α- and β-pinene were from the Hercules Powder Co., and the norbornene from E. I. du Pont de Nemours Co. 2-Methyl-2-butene was obtained from the Phillips Petroleum Co. All other compounds were obtained from standard laboratory supply houses or synthesized by procedures indicated at the appropriate point.

trans-2-Methylcyclopentanol.—In a dry three-necked flask equipped with a thermometer, a condenser and a sintered glass dispersion tube, were placed 24.6 g., (0.3 mole) of 1-methylcyclopentene (b.p. 75–76° at 745 mm., n^{20}D 1.4326, synthesized *via* 1-methylcyclopentanol from cyclopentanone and methylmagnesium iodide) and 150 ml. of tetrahydrofuran. The dispersion tube was connected to the diborane generator. This generator consisted of a two-necked flask equipped with a pressure-equalized dropping funnel (serving alternately as an inlet for nitrogen gas) containing 4.75 g. of sodium borohydride in 125 ml. of diglyme (1.0 M solution). In the generator flask was placed 34.0 g. (0.24 mole) of boron trifluoride etherate (∼ 50% excess) and 30 ml. of diglyme. The air in the apparatus was displaced by nitrogen. Then the diborane, generated by dropwise addition of the sodium borohydride solution to the boron trifluoride etherate, was passed into the olefin–tetrahydrofuran solution (maintained at 0°) by initiating a slight flow of dry nitrogen through the generator. After completion of the sodium borohydride

addition (approximately 1 hour), the generator was heated for a second hour at 70–80°, maintaining a slight flow of nitrogen, to ensure the complete transfer of the diborane into the hydroboration flask.

This flask, disconnected from the generator, was permitted to stand for 2 hours at room temperature. Excess hydride (the hydroboration proceeds to the dialkylborane stage, R_2BH) was destroyed by the careful addition of 20 ml. of water. The organoborane was oxidized at 30–50° by adding 32 ml. of 3 N sodium hydroxide, followed by the dropwise addition of 32 ml. of 30% hydrogen peroxide (exothermic reaction!). The warm reaction mixture was stirred for an additional hour, then extracted with ether. The ether extract was washed, dried (over anhydrous magnesium sulfate), and analyzed by v.p.c. on a 1-meter glycerol column, followed by a 1-meter diglycerol column. The chromatogram indicated only traces of *cis*-2-methylcyclopentanol, 1.5% of 1-methylcyclopentanol and 98.5% of *trans*-2-methylcyclopentanol.

The solvents were removed by distillation and the product obtained by distillation through a small glass-spiral column. There was obtained 25.9 g. of *trans*-2-methylcyclopentanol (86% yield) b.p. 150–151° at 740 mm., n^{20}D 1.4505, m.p. 3,5-dinitrobenzoate 86–87° (lit.[8] b.p. 149–151° at 735 mm., n^{20}D 1.4501, m.p. 3,5-dinitrobenzoate 88°).

trans-2-Methylcyclohexanol.—The apparatus and procedure were identical with that described above. However, hydroboration of the 28.8 g. (0.3 mole) of 1-methylcyclohexene (b.p. 108° at 743 mm., n^{20}D 1.4508, synthesized *via* 1-methylcyclohexanol from cyclohexanone and the Grignard) resulted in the separation of a crystalline solid. This caused no difficulty, and the decomposition of the excess hydride and oxidation proceeded normally.

Analysis by v.p.c. of the dried ether extract (same columns as above) indicated the presence of 0.8% of a component corresponding in retention time to *cis*-2-methylcyclohexanol, 1.5% of 1-methylcyclohexanol and 97.7% of *trans*-2-methylcyclohexanol.

Distillation yielded 29.1 g. of *trans*-2-methylcyclohexanol (85% yield), b.p. 166° at 741 mm., n^{20}D 1.4611, m.p. 3,5-dinitrobenzoate 113–115° (lit.[24] b.p. 165° at 750 mm., n^{20}D 1.4616, m.p. 3,5-dinitrobenzoate 117°).

Hydroboration of 1-Methylcyclooctene.—Cyclooctanone (30 g., 0.24 mole) was treated with an equivalent quantity of methylmagnesium iodide. The 1-methylcyclooctanol was dehydrated without isolation by treatment with iodine to 1-methylcyclooctene.[25] The product, 19.5 g., 64% yield, was isolated by distillation through a small column: b.p. 164° at 740 mm., n^{20}D 1.4705 (lit.[25] b.p. 87–90° at 84 mm., n^{25}D 1.4682).

The olefin (12.4 g., 100 mmoles) in 50 ml. of tetrahydrofuran was treated at 0° with 30 mmoles of diborane. After 3 hours at room temperature, the excess of hydride was decomposed, and the organoborane was oxidized with 10 ml. of 3 N sodium hydroxide and 10 ml. of 30% hydrogen peroxide. Distillation of the ether extract gave 12.1 g., 85% yield, of product, b.p. 104–105° at 10 mm., n^{20}D 1.4798 (lit.[26] for 2-methylcyclooctanol: isomer A, b.p. 100–101° at 16 mm., n^{21}D 1.4750; isomer B, b.p. 103–104° at 16 mm., $n^{20.5}$D 1.4808); v.p.c. examination revealed the presence of three peaks, incompletely resolved.

trans-2-Phenylcyclohexanol.—1-Phenylcyclohexene, b.p. 70° at 0.4 mm., n^{20}D 1.5690, was synthesized by the usual Grignard-dehydration route. The olefin (7.9 g., 50 mmoles) in 50 ml. of tetrahydrofuran was treated with the diborane generated from 41 mmoles of sodium borohydride and 82 mmoles of boron trifluoride etherate (excess, allowing for the possible halting of the reaction at the monoalkylborane stage). The organoborane was treated with 6 ml. of 3 N sodium hydroxide, followed by 6 ml. of 30% hydrogen peroxide; v.p.c. analysis (carbowax 1500 column) indicated essentially pure *trans*-2-phenylcyclohexanol.

After removal of the solvents, the residue was crystallized from n-hexane, yielding 7.0 g. (79%) of *trans*-2-phenylcyclohexanol, m.p. 55–57° (lit.[27] m.p. 56–57°).

(23) For a summary of the evidence with pertinent literature references, see E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, Chapter 15.

(24) M. G. Vavon, A. Perlin and M. A. Horeau, *Bull. soc. chim. France*, **51**, 644 (1952); L. M. Jackman, A. K. Macbeth and J. A. Mills, *J. Chem. Soc.*, 117 (1949).

(25) A. C. Cope and H. C. Campbell, *J. Am. Chem. Soc.*, **74**, 179 (1952).

(26) M. Godchot and M. Cauquil, *Chim. and Ind.*, **29**, 1019 (1933).

(27) E. R. Alexander and A. Mudrak, *J. Am. Chem. Soc.*, **72**, 1810 (1950).

cis-1,2-Dimethylcyclohexanol.—1,2-Dimethylcyclohexene (99% pure, n^{20}D 1.4618, 22.0 g., 0.200 mole) was added to 150 ml. of tetrahydrofuran and treated with diborane from 0.165 mole of sodium borohydride and 0.33 mole of boron trifluoride etherate. Oxidation of the organoborane with 21 ml. of 3 *N* sodium hydroxide, followed by 21 ml. of 30% hydrogen peroxide, yielded 21.0 g. of *cis*-1,2-dimethylcyclohexanol (82% yield): b.p. 76–77° at 19 mm., m.p. 24–25° (lit.[28] b.p. 82.8° at 25 mm., m.p. 23.2°).

cis-1,2-Dimethylcyclopentanol.—Under similar conditions 1,2-dimethylcyclopentene was converted into *cis*-1,2-dimethylcyclopentanol: b.p. 66–68° at 21 mm., m.p. 23–24° (lit.[29] b.p. 62° at 17 mm., m.p. 24–26°).

exo-Norborneol.—Norbornene (b.p. 96–98° at 739 mm., m.p. 46–47°, 18.8 g., 0.200 mole) was dissolved in 100 ml. of tetrahydrofuran and treated with diborane from 0.055 mole of sodium borohydride and 0.11 mole of boron trifluoride etherate. (The hydroboration proceeds to the trialkylborane stage.) After oxidation with 21 ml. of 3 *N* sodium hydroxide and 21 ml. of 30% hydrogen peroxide, v.p.c. examination of the ether extract on a 150-foot polypropylene glycol capillary column indicated the formation of essentially pure *exo*-norborneol (~99%). Evaporation of the solvent yielded a residue which was recrystallized from 30–60° petroleum ether. There was obtained 19 g. of *exo*-norborneol, a yield of 85%. After sublimation the alcohol exhibited m.p. 126–127°, m.p. 3,5-dinitrobenzoate 104–105° (lit.[30] m.p. 128–129°, m.p. 3,5-dinitrobenzoate 105°).

Isopinocampheol.—α-Pinene (n^{20}D 1.4661, [α]^{20}D + 48°, 27.2 g., 0.200 mole) in 150 ml. of tetrahydrofuran was treated with diborane from 0.083 mole of sodium borohydride and 0.165 mole of boron trifluoride. The hydroboration proceeds to the dialkylborane stage and the latter partially separates as a white solid from the solution. After oxidation with 21 ml. of 3 *N* sodium hydroxide and 21 ml. of 30% hydrogen peroxide, the product was taken up in ether. Evaporation of the solvents left 27.5 g. of crystalline product, a yield of 89%.

The sublimed alcohol exhibited m.p. 54–56°, [α]^{20}D −32.4° (*c* 4 in benzene), m.p. acid phthalic ester 125–126° (lit. for *l*-isopinocampheol,[31] m.p. 57°, [α]^{20}D −32°, m.p. acid phthalic ester 126°).

Isopinocamphone.—Isopinocampheol (above), 17.0 g., 0.11 mole, was dissolved in 23 ml. of acetone. The flask was immersed in an ice-bath. A solution of chromic acid–sulfuric acid (7.5 g. of chromium(VI) oxide, 6.4 ml. of concentrated sulfuric acid and 20 ml. of water) was added to the reaction mixture over a period of 2 hours, maintaining the temperature at 3–4°.[32] The reaction was permitted to come to room temperature. After 2 hours, the mixture was treated with water and the product was extracted with ether. Distillation gave 12.3 g., 74%, of isopinocamphone, b.p. 69–70° at 5 mm., n^{20}D 1.4745, αD + 11.1° (lit.[33] b.p. 70° at 5 mm., n^{20}D 1.4748, αD +11°).

Treatment of isopinocamphone with lithium aluminum hydride yielded 20% isopinocampheol and 80% of a second product, presumably the epimeric neoisopinocampheol. Treatment of isopinocamphone with lithium trimethoxy-aluminohydride[34] yielded this latter substance (v.p.c. examination) almost exclusively, with only traces of isopinocampheol indicated.[35]

cis-Myrtanol.—β-Pinene (n^{20}D 1.4794, [α]^{20}D −21.2° 27.2 g., 0.200 mole) was hydroborated internally in diglyme with sodium borohydride and boron trifluoride etherate. (The reaction proceeds to the trialkylborane stage.) After oxidation the mixture was poured in water, the product taken up in ether, and the residual diglyme removed with several washings with ice-water. Distillation yielded 24.8

g., 81% yield, of *cis*-myrtanol: b.p. 70–72° at 1 mm., n^{20}D 1.4910, [α]^{26}D −21°, m.p. acid phthalate ester 128–129° (lit.[36] b.p. 113–113.8° at 14 mm., n^{20}D 1.4925, [α]D −24.5, m.p. acid phthalate ester 124.5–125.5°; m.p. of the acid phthalate ester of *trans*-myrtanol is reported as 108.5–109°).[37]

3-Methylcyclopentene.—*trans*-2-Methylcyclopentanol (synthesized as described above, 20 g., 0.200 mole) was converted into the tosyl ester by the usual pyridine procedure. The crude tosylate was added to a solution of sodium isoamylate–isoamyl alcohol in diglyme, prepared by adding 0.4 mole of sodium hydride (50% suspension in oil) to a mixture of 150 ml. of isoamyl alcohol and 150 ml. of diglyme. The reaction mixture was heated to 120–140° and the olefin formed distilled out of the reaction mixture as it formed. There was obtained 11.3 g., 69% of olefin, which on redistillation over sodium in a small column gave pure 3-methylcyclopentene, b.p. 65–66° at 745 mm., n^{20}D 1.4208 (lit.[38] b.p. 64.9°, n^{20}D 1.4207).

3-Methylcyclohexene.—In the same way 22.8 g., 0.200 mole, of *trans*-2-methylcyclohexanol was converted into the tosylate and the latter subjected to the elimination procedure. There was 14.1 g., 73% of the crude product, with the fractionated material exhibiting b.p. 99–100° at 745 mm., n^{20}D 1.4420 (lit.[39] b.p. 100–101°, n^{20}D 1.4435).

3,3-Dimethylcyclohexene.—2,2-Dimethylcyclohexanone, b.p. 169–170°, n^{20}D 1.4482 (lit.[40] b.p. 170–171°, $n^{18.5}$D 1.4492), was reduced with sodium borohydride in water. The product, 2,2-dimethylcyclohexanol, b.p. 180–181° at 742 mm., n^{20}D 1.4646, was converted to the tosyl ester. The crude ester, m.p. 65°, was subjected to the elimination reaction at 120–150°. The product was treated with a controlled quantity of lithium aluminum hydride to react with isoamyl alcohol which co-distilled and the olefin recovered by distillation under vacuum. Distillation in a Podbielniak micro column gave 3,3-dimethylcyclohexene, b.p. 115–116° at 745 mm., n^{20}D 1.4426 (lit.[41] b.p. 118–120° at 752 mm., n^{21}D 1.4439); v.p.c. analysis confirmed the purity of the product.

Hydroboration of the 3-Methylcycloalkenes with Diborane.—The olefin, 50 mmoles, in tetrahydrofuran solution was treated with a standard solution of diborane in tetrahydrofuran. The products were then oxidized to the alcohols and these examined to establish the isomeric distribution.

From 50 mmoles of 3-methylcyclopentene there was obtained 4.4 g., 88%, of methylcyclopentanols. None of the columns examined achieved a separation. Consequently, the alcohols were oxidized to the methylcyclopentanones by the Jones procedure[32] and the ether extract analyzed on a Ucon polar column. The yield of ketone indicated was 85%, with the analysis showing the presence of 45% of 2-methyl-cyclopentanone and 55% 3-methylcyclopentanone.

Similarly, 50 mmoles of 3-methylcyclohexene was converted into the 2- and 3-methylcyclohexanols. Since no resolution was achieved by the usual procedures, the material was converted into the ketone. Examination by v.p.c. on a Ucon polar column revealed the presence of 49% of 2- and 51% of 3-methylcyclohexanone.

Analysis by v.p.c. of the dimethylcyclohexanols was possible (Ucon polar column). These yielded 50% of 2,2-dimethylcyclohexanol and 50% 3,3-dimethylcyclohexanol.

Hydroboration of the 3-Methylcycloalkenes with Disiamylborane.—The reagent, 20 mmoles of disiamylborane, was prepared by treating 44 mmoles of 2-methyl-2-butene with 10 mmoles of diborane (generated internally) at 0°. To this reaction mixture was added 0.82 g., 10 mmoles, of 3-methylcyclopentene, the temperature permitted to come to 25° and allowed to remain there for approximately 24 hours. The organoborane was converted to the alcohol in the usual manner and the latter oxidized to the ketone[32]; v.p.c. analysis indicated the presence of 40% of 2-methylcyclopentanone and 60% of 3-methylcyclopentanone.

The same procedure was utilized to convert 3-methyl-

(28) G. Chiurdoglu, *Bull. soc. chim. Belg.*, **47**, 241 (1938).

(29) L. V. Trevoy and W. G. Brown, *J. Am. Chem. Soc.*, **71**, 1675 (1949).

(30) K. Alder and H. F. Rickert, *Ann.*, **543**, 1 (1939).

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

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

(33) H. Schmidt, *Chem. Zentr.*, **113** [I], 2531 (1942).

(34) H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **80**, 5372 (1958).

(35) A detailed study of the utility of these substituted lithium aluminum hydrides for steric control of the reduction of bicyclic ketones will be reported shortly with Mr. C. P. Garg.

(36) G. Dupont and W. Zacharewiez, *Compt. rend.*, **199**, 365 (1934).

(37) We wish to express our appreciation to Dr. M. V. Bhatt who carried out this particular synthesis.

(38) G. Crane, C. E. Boord and A. L. Henne, *J. Am. Chem. Soc.*, **67**, 1237 (1945).

(39) W. Hückel and A. Hubele, *Ann.*, **613**, 27 (1958).

(40) F. E. King, T. J. King and J. G. Topliss, *J. Chem. Soc.*, 919 (1957).

(41) N. D. Zelinsky, K. Packendorff and E. B. Chochlowa, *Ber.*, **68**, 98 (1935).

cyclohexene into the corresponding alcohols. Although our original experiments required oxidation to the ketones for analysis, it proved possible to resolve the alcohols on a 150-foot diglycerol capillary column at 54°; 18% cis-2-, 30% trans-2-, 27% cis-3-, and 25% trans-3-methylcyclohexanol.

An identical procedure applied to 1.10 g. (10 mmoles) of 3,3-dimethylcyclohexene revealed the presence of 40% of 2,2-dimethylcyclohexanol and 60% of 3,3-dimethylcyclohexanol (Ucon polar column).

The Cyclic Trimerization of Acetylenes Over a Ziegler Catalyst

BY EUGENE F. LUTZ

Acetylene and six substituted acetylenes have been trimerized successfully over a Ziegler catalyst to benzene and substituted benzenes in good yields. The evidence obtained here shows that the polymerization of acetylenes proceeds by a mechanism different from that generally accepted for the polymerization of α-olefins in this catalyst system.

Introduction and Results

Although considerable effort has been devoted to the study of the polymerization of α-olefins over Ziegler catalysts,[1] very little has been published concerning the polymerization of acetylenes over these highly reactive and selective complexes. Three publications, one a patent, by Giulio Natta and co-workers,[2] describe the formation of high molecular weight polymers from acetylene,[2ab] phenylacetylene,[2a] 1-butyne[2a] and 1-hexyne[2c] over AlR₃– TiX₄ organometallic complex catalysts. Natta presents evidence indicating that the polymers formed are long chains of alternating single and double bonds.

More recently Franzus, et al.,[3] have shown that disubstituted acetylenes can be trimerized to hexasubstituted benzenes by regulating the ratio of (i-Bu)₃Al to TiCl₄ in the organometallic catalyst. These results are similar to those reported by Zeiss and co-workers[4] in the cyclic trimerization of internal acetylenes over organochromium[5] catalysts.

The literature to date suggests that monoalkylacetylenes are far too reactive to undergo cyclic trimerization and instead react very rapidly to form high molecular weight polymers. We have found, however, that in spite of their high reactivity, acetylene and monoalkylacetylenes can be trimerized over a Ziegler-type catalyst to benzene and trialkylbenzenes, respectively, by use of high

(1) See G. Natta and I. Pasquon in D. D. Eley, P. W. Selwood and Paul B. Weisz, "Advances in Catalysis and Related Subjects," Academic Press, Inc.. New York, N. Y., 1959, Vol. XI, pp. 1–66, for review and leading references.

(2) (a) G. Natta, P. Pino and G. Mazzanti. Italian Patent 530,753, July 15, 1955 (C. A., 52, 15128b (1958)); (b) G. Natta, G. Mazzanti and P. Corradini, Atti Accad. nazl. Lincei Rend. Classe sci. fiz. mat. e nat., 25, 3 (1958) (C. A., 53, 13985i (1959)); (c) G. Natta, G. Mazzanti, G. Pregaglia and M. Peraldo, Gazz. chim. ital., 89, 465 (1959) (C. A., 54, 11967i (1960)).

(3) B. Franzus, P. J. Canterion and R. A. Wickliffe, J. Am. Chem. Soc., 81, 1514 (1959).

(4) H. Zeiss in "Organometallic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1960, pp. 411–421.

(5) G. Wilke and M. Kroner, Angew. Chem.. 71. 574 (1959), obtained a bis-(hexamethylbenzene)-chromium complex from the reaction of 2-butyne over a Ziegler catalyst prepared from AlEt₃ and CrO₂Cl₂.

dilution techniques, i.e., a large volume of solvent, small catalyst particle size, efficient stirring and low reactant concentration.

$$3R-C{\equiv}C-R' \xrightarrow{\text{AlEt}_3\text{-TiCl}_4}$$

Ia, R = H; R' = H
Ib, R = alkyl, R' = H
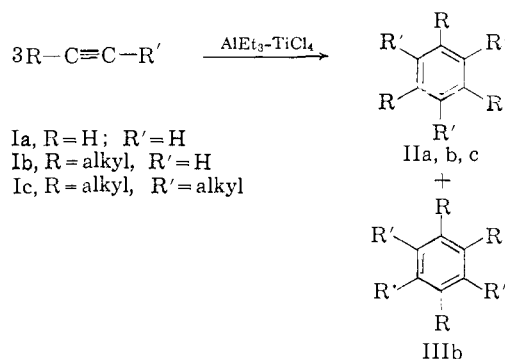Ic, R = alkyl, R' = alkyl

IIa, b, c

+

IIIb

Table I lists the acetylenes that have been trimerized to aromatic hydrocarbons in this Laboratory. This technique offers a convenient method for synthesizing substituted benzenes not readily available by other methods or from other sources.

TABLE I

ACETYLENES USED AND PRODUCTS OBTAINED

Substitution	Reacn. temp., °C.	Trimer	Yield, %	High polymer, % [c]
None	23–39[a,b]	Benzene	49.1	24.1
Methyl	23–36[a]	Mesitylene	40.4	9.3
		Pseudocumene	21.1	
Ethyl	23–30[a]	1,3,5-Triethylbenzene	35.5	7.3
		1,2,4-Triethylbenzene	17.0	
Butyl	24–32[a]	1,3,5-Tributylbenzene	59.8	..
Dimethyl	23–34[a]	Hexamethylbenzene	80.2	2.2[d]
Diethyl	24–32[a]	Hexaethylbenzene	76.5	..
Dibutyl	~86	Hexabutylbenzene[f]	52.2[e]	4.6[d]

[a] Reactions were exothermic, producing an 11–16° rise in temperature. [b] The temperature gradually dropped toward the end of the reaction, indicating a loss of catalyst activity. [c] Estimated by subtracting the weight of the organometallic catalyst from the total weight of the solids obtained from reaction; see Experimental for details. [d] Because of the reaction workup used, this represents the upper limit of high polymer formation; see the Experimental for further discussion. [e] A small amount of another product, perhaps a dimer, also was obtained. [f] This appears to be the first synthesis of this compound.