2-Acetylthiomethyl-1,3-cyclohexanedione.—A solution of 1.1 g (0.01 mol) dihydroresorcinol and 2.1 g (0.01 mol) piperidinomethyl thioacetate hydrochloride dissolved in 50 ml of chloroform was refluxed for 1 hr. The chloroform solution was reduced to half its volume, and 100 ml of ether was added to precipitate piperidine hydrochloride, 1.55 g (100%). The solvent was removed to give an orange semisolid which was recrystallized from dichloromethane–petroleum ether (bp 63–68°) to yield 1.1 g (55%) of product, mp 132°. The nmr and ir spectra were as expected.

Anal. Calcd for $C_9H_{12}O_3S$: C, 54.00; H, 6.04. Found: C, 53.72; H, 5.94.

2-Phenylthiomethyl-5,5-dimethyl-1,3-cyclohexanedione.—To 25 ml of refluxing *p*-dioxane was added 2.4 g (0.01 mol) of N-phenylthiomethylpiperidine hydrochloride. Dimedone, 1.4 g (0.01 mol), was then added to the refluxing solution. Within 2 min, a white precipitate was observed. After cooling the reaction mixture, 1.1 g of piperidine hydrochloride was collected by filtration. The filtrate was poured into 100 ml of ice water and allowed to stand overnight. The precipitate was filtered and air-dried to yield 2.3 g (89%) of product. The solid was recrystallized from acetone–petroleum ether (bp 63–68°), mp 139°. The nmr and ir spectra were as expected.

Anal. Calcd for $C_{15}H_{18}O_2S$: C, 68.67; H, 6.91. Found: C, 68.65; H, 6.90.

Desulfurization Procedure.—Raney nickel, the catalyst, was prepared by the method of Pavlic and Adkins.[8] Examples of the general procedure follow.

2,5,5-Trimethyl-1,3-cyclohexanedione.—2-Benzoylthiomethyl-5,5-dimethyl-1,3-cyclohexanedione, 2.9 g (0.01 mol), was dissolved in 125 ml of ethyl acetate at 65–70°. About 20 g (wet weight) of Raney nickel was added to the solution with stirring and heated for 1 hr. The reaction mixture was filtered while hot and the residue was washed with three 50-ml portions of hot ethyl acetate. The washings and original filtrate were combined, and the solvent was removed to yield 0.96 g (62%) of product melting at 163–165° (lit.[9] mp 163°). An authentic sample was prepared by the method of Desai.[9] The melting point and infrared spectra were identical with those of the desulfurized product.

3-Methyl-4-hydroxycoumarin.—The above procedure was followed to desulfurate 2.1 g (0.0067 mol) of 3-benzoylthiomethyl-4-hydroxycoumarin dissolved in 80 ml of ethyl acetate using 14 g (wet weight) of Raney nickel. Upon removal of the solvent, 0.86 g (74%) of product was isolated and recrystallized from chloroform–carbon tetrachloride, mp 225–228° (lit.[10] mp 231°).

(8) A. A. Pavlic and H. Adkins, *J. Amer. Chem. Soc.*, **68**, 1471 (1946).

Registry No.—Hydroxymethyl thiobenzoate, 23853-33-0; **1a** (HI), 23853-34-1; **1b** (HCl), 876-24-4; **5** (methiodide), 23853-36-3; **5** (methochloride), 23853-37-4; **6b**, 23853-38-5; 2-benzoylthiomethyl-5,5-dimethyl-1,3-cyclohexanedione, 23853-39-6; 3-benzoylthiomethyl-2,4-pentanedione, 23853-40-9; 2-benzoylthiomethyl-2-phenylacetaldehyde (2,4-DNP), 23853-41-0; N-benzoylthiomethylbenzenesulfonamide, 23853-42-1; 3-benzoylthiomethyl-4-hydroxycoumarin, 23853-43-2; 2-acetylthiomethyl-5,5-dimethyl-1,3-cyclohexanedione, 23853-44-3; 2-acetylthiomethyl-1,3-cyclohexanedione, 23853-45-4; 2-phenylthiomethyl-5,5-dimethyl-1,3-cyclohexanedione, 23853-46-5.

Acknowledgment.—The authors gratefully acknowledge support of this project by the National Institutes of Health Grants GM-9254 and GM-14,467.

(9) R. G. Desai, *J. Chem. Soc.*, 1079 (1932).
(10) K. Sen and P. Bagchi, *J. Org. Chem.*, **24**, 316 (1959).

Additions to Bicyclic Olefins. II. A Convenient Synthesis of Apobornene and Apocamphor[1]

HERBERT C. BROWN, JAMES H. KAWAKAMI,[1] AND SOICHI MISUMI[2]

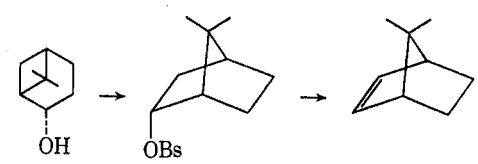
Richard B. Wetherill Laboratory, Purdue University, Lafayette, Indiana 47907

Received September 16, 1969

A convenient five-step synthesis of apobornene (7,7-dimethylnorbornene) from the readily available camphenilone (3,3-dimethylnorcamphor) has been developed in an overall yield of 30%. This procedure makes possible the synthesis of apobornene in relatively large quantities in purities of 98% or better. Through minor modifications the synthesis can be directed to the preparation of apocamphor.

A considerable quantity of pure apobornene (7,7-dimethylnorbornene) was required for our studies of the stereochemical aspects of additions to bicyclic systems.[3] The synthesis of apobornene has been described previously.[4,5] However, the procedures do not lend themselves to the preparation of apobornene in appreciable quantity or in the desired purity. Consequently, we undertook to develop a more satisfactory procedure.

The most direct procedure would be the Diels–Alder reaction of 5,5-dimethylcyclopentadiene with ethylene. However, the synthesis of the diene appeared to offer severe difficulties.[6] Another possibility was the conversion of β-nopinol into apobornyl brosylate,[7] followed by an elimination (eq 1). However, β-nopinol is not



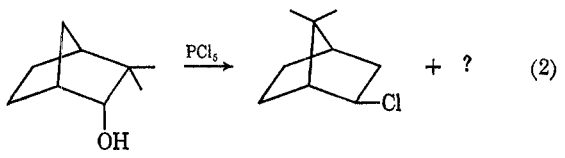
(1)

easily synthesized.[8] Solvolytic methods can be used to obtain apoisoborneol as a mixture with isomeric alcohols.[9] However, we observed that the isolation of pure alcohol on a large scale was quite time consuming.

After examining a number of such approaches we decided that the most convenient procedure appeared

(1) Graduate research assistant on grants (G 19878 and GP 6492 X) supported by the National Science Foundation.
(2) Postdoctorate research associate on Grant GM 10937 from the National Institutes of Health.
(3) H. C. Brown and J. H. Kawakami, *J. Amer. Chem. Soc.*, **92**, 1990 (1970).
(4) (a) G. Komppa and T. Hasselstrom, *Ann. Acad. Sci. Fenn. Ser. A9*, **24**, 3 (1925); (b) G. Komppa and T. Hasselstrom, *Ann.*, **497**, 116 (1932); (c) G. Komppa and R. H. Roschier, *ibid.*, **429**, 175 (1922).
(5) P. Lipp and J. Daniels, *Ber.*, **69**, 586, 2251 (1936).
(6) (a) C. F. Wilcox, Jr. and M. Mesirov, *J. Org. Chem.*, **25**, 1841 (1960); (b) R. S. Rouse and W. E. Tyler, *ibid.*, **26**, 3525 (1961).
(7) P. von R. Schleyer, W. E. Watts, and C. Cupas, *J. Amer. Chem. Soc.*, **86**, 2722 (1964).
(8) S. Winstein and N. J. Holness, *ibid.*, **77**, 3054 (1955).
(9) (a) See ref 8; (b) S. Beckmann and R. Bamberger, *Ann.*, **574**, 73 (1951); (c) Y. Chretien-Bessiere and J. P. Monthiard, *Compt. Rend.*, **258**, 937 (1964).

to be E2 elimination of the mixture of chlorides, presumably largely apoisobornyl chloride, produced in the reaction of phosphorus pentachloride with *endo*-camphenilol[9b] (eq 2). We hoped that we might then

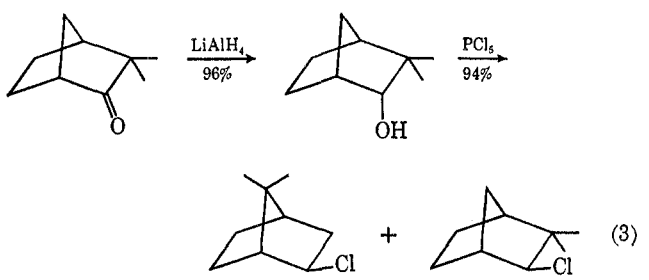


(2)

readily separate the desired olefin from the reaction mixture by fractional distillation or preparative gas chromatography. Although we encountered unexpected difficulties in this separation and isolation, we were able to solve the problems and achieve a convenient synthesis of apobornene in high purity and quantity. At the same time we developed a convenient procedure for the synthesis of apocamphor.

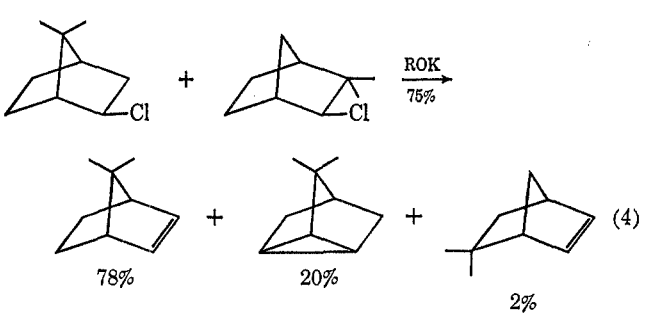
Results and Discussion

The present synthesis begins with camphenilone,[10] a compound readily available from the oxidation of camphene.[11] Reduction of camphenilone with lithium aluminum hydride gave a 96% yield of *endo*-camphenilol. The alcohol was treated with phosphorus pentachloride to produce a mixture of 64% apoisobornyl and 36% *exo*-camphenilyl chlorides in a yield of 94% (eq 3).



(3)

Experiments indicated that elimination with the potassium salt of 2-cyclohexylcyclohexanol in excess alcohol provided a highly satisfactory procedure. There was obtained a 75% yield of a mixture of apobornene (78%), apocyclene (20%), and 5,5-dimethylnorbornene (2%) (eq 4).



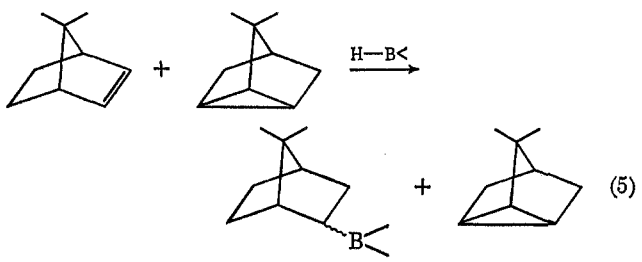
(4)

(10) The camphenilone was purchased in kilogram quantities from the Shawnee Chemicals Co., Springfield, Ohio.

(11) (a) W. Huckel, *Suomen Kemist.*, **B31**, 13 (1958); (b) P. S. Bailey, *Chem. Ber.*, **88**, 795 (1955); (c) P. D. Bartlett, E. R. Webster, E. E. Dills, H. G. Richey, Jr., *Ann.*, **623**, 217 (1959).

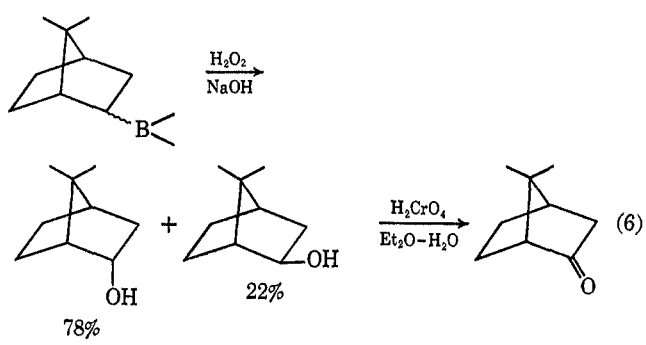
Here we encountered a major difficulty. The two hydrocarbons could not be separated by fractional distillation. Moreover, they could not be separated on a large number of preparative glpc columns examined. Surprisingly, even a silver nitrate column failed to achieve separation. Evidently the 7,7-dimethyl substituents block silver ion complexation from the *exo* direction, and complexation from the *endo* direction does not occur.[12]

Hydroboration of the reaction mixture[13] did achieve a selective reaction with apobornene and the apocyclene could be distilled away from the organoborane (eq 5).



(5)

Oxidation of the organoborane with alkaline hydrogen peroxide yielded a mixture of 78% apobornyl alcohol and 22% apoisobornyl alcohol,[4] free of any isomeric compounds. Oxidation of this mixture with chromic acid by the convenient two-phase procedure[14] gave pure apocamphor (eq 6).



(6)

We considered using the displacement reaction[15] as a means of regenerating the desired apobornene from the organoborane. However, a suggestion from Professor T. G. Traylor led us to try oxymercuration–deoxymercuration.[16] Fortunately, under the conditions employed, apocyclene does not undergo mercuration.[17] Consequently, reaction of the mixture with mercuric acetate in acetic acid, followed by dilution with aqueous

(12) A detailed study of this interesting feature was made and will be reported later.

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

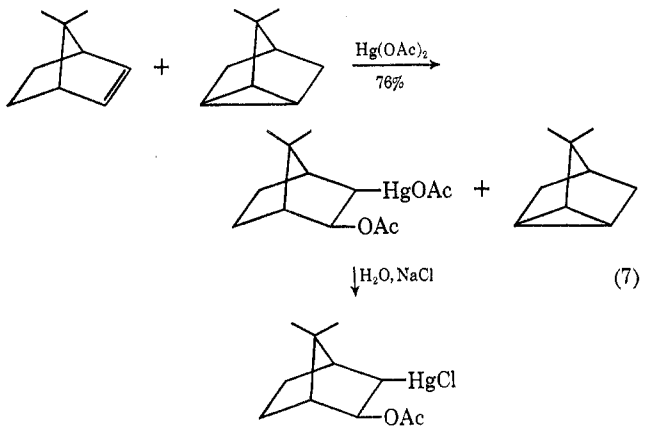
(14) H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, **83**, 2951 (1961).

(15) H. C. Brown, M. V. Bhatt, T. Munekata, and G. Zweifel, *ibid.*, **89**, 567 (1967).

(16) T. G. Traylor and S. Winstein, the 135th National Meeting of the American Chemical Society, Boston, Mass., April 1959, Abstracts, O-82.

(17) Cyclopropanes do undergo oxymercuration and in some cases the reaction is quite facile. For example, it has been reported that bicyclo-[2.1.0]pentane reacts with mercuric acetate in water to form the 1,3-addition compound: R. Y. Levina, V. N. Kostin, D. G. Kim, and T. K. Ustynyuk, *Zh. Obshch. Khim.*, **29**, 1956 (1959).

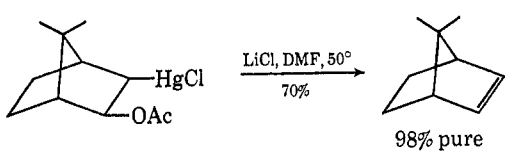
sodium chloride, precipitates the desired mercurichloride, free of apocyclene (eq 7).



(7)

We were anxious to avoid acidic deoxymercuration procedures,[18,19] to avoid possible isomerization of the product. Both lithium aluminum hydride and halide salts have been used to effect demercuration of such adducts.[16] Indeed, we observed that the use of lithium aluminum hydride in large excess does give good yields of apobornene along with a small amount of alcohol. However, although satisfactory for small-scale preparations, we considered the procedure hazardous for large-scale synthesis.

Consequently, we turned to demercuration with halide ion. A number of considerations led us to the use of lithium chloride in dimethylformamide. This worked ideally and provided apobornene in high purity (eq 8).

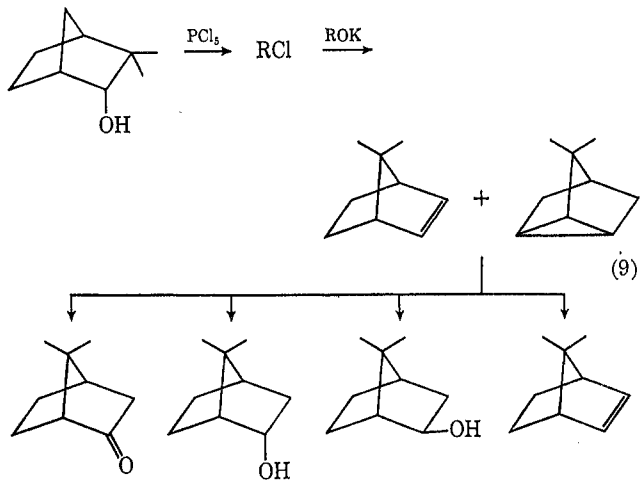


(8)

98% pure

Conclusions

The reaction of *endo*-camphenilol with phosphorus pentachloride, followed by elimination with the potassium salt of 2-cyclohexylcyclohexanol, provided a convenient route to an 80:20 mixture of apobornene and apocyclene. Oxymercuration–deoxymercuration provides pure apobornene. Oxymercuration–demercuration of the mixture provides pure apoisoborneol.[20] Finally, hydroboration oxidation provides a mixture of 78% apoborneol[21] and 22% apoisoborneol, with further oxidation yielding pure apocamphor (eq 9). Consequently, these procedures should greatly enhance the availability of these interesting intermediates.



Experimental Section

Purification of Camphenilone.—To a 500-ml flask fitted with a magnetic stirring bar and a 40 × 1 cm Vigreux column was added 333 g of 88% pure camphenilone[10] (12% camphene). Distillation at 223° until camphene was distilled out gave 247 g (74%) of 99% camphenilone, mp 41–43° (lit.[22] mp 38–39°). Analysis was on the Perkin–Elmer 154, 6 ft × 0.25 in. Carbowax 20M on 60–80 Chromosorb P, at 100°.

Preparation of *endo*-Camphenilol.—To a three-necked 3000-ml flask equipped with a mechanical stirrer and a reflux condenser was added 24.7 g (0.65 mol) of lithium aluminum hydride and 800 ml of anhydrous diethyl ether. With stirring, 247.3 g (1.79 mol) of camphenilone dissolved in 625 ml of ether was added from a pressure-equalized dropping funnel at such a rate to maintain a gentle reflux. After the addition was complete, the mixture was kept at reflux temperatures for a total reaction time of 4 hr. The excess hydride was destroyed with water at 0°, and 10% sodium hydroxide was added until the aluminum salts precipitated. The ether solution was decanted, and the ether was evaporated on the rotatory evaporator to give 224.5 g (90%) of camphenilol (predominantly *endo*-). In another preparation 100 g of camphenilone was converted into 97 g (96%) of camphenilol, mp 71–74.5° (lit.[22] mp 75–77°).

Conversion of *endo*-Camphenilol to a Mixture of Chlorides with Phosphorus Pentachloride.—To a 500 ml three-necked flask fitted with a mechanical stirrer, a pressure-equalized addition funnel (with tube leading to a sodium hydroxide solution to trap the generated hydrogen chloride), and a thermometer, was added 50.1 g (0.24 mol) of phosphorus pentachloride (Baker Analyzed), and 150 ml of petroleum ether (bp 35–37°). To this stirred slurry was added 28.2 g (0.202 mol) of *endo*-camphenilol dissolved in 200 ml of petroleum ether, at such a rate to keep the temperature between −5 to 0°. The addition time was about 45 min when a Dry Ice–acetone bath at −10° was employed. After the addition was completed, the reaction mixture was stirred vigorously for 5 min. The petroleum ether solution was decanted into a 2-l separatory funnel containing 300 g of crushed ice. Care was taken so that the unreacted phosphorus pentachloride (yellow solid) was not transferred. The flask was rinsed with 50 ml of petroleum ether, and the rinse was added to the funnel. (It is important that the temperature be kept near 0° or else the chlorides will isomerize. The presence of crushed ice in the separatory funnel during the work-up ensures this.) The aqueous layer was separated and the cloudy petroleum ether solution was washed twice with 500-ml portions of ice-cold water. Then the petroleum ether layer was washed with at least two 500-ml portions of ice-cold 2 *N* aqueous hydrochloric acid. (Vigorous shaking is necessary.) The washing was continued until no gas was evolved and the petroleum ether layer was clear and colorless. Then the organic layer was washed three times with a dilute solution of ice-cold potassium carbonate. Since it was difficult to remove all of the acid, the organic layer was dried over anhydrous potassium carbonate with stirring overnight at room temperature. The drying agent was filtered off and the solvent was removed at room temperature on the rotary evap-

(18) (a) M. M. Kreevoy and M. A. Turner, *J. Org. Chem.*, **29**, 1639 (1964); (b) M. M. Kreevoy, R. A. Kretchmer, G. E. Stokker, and A. K. Ahmed, *ibid.*, **28**, 3184 (1963).

(19) M. J. Abercrombie, A. Rodgman, K. R. Bharucha, and G. F. Wright, *Can. J. Chem.*, **37**, 1328 (1959).

(20) H. C. Brown, J. H. Kawakami, and S. Ikegami, *J. Amer. Chem. Soc.*, **89**, 1525 (1967).

(21) Although we did not attempt to separate these compounds, it is known that one can isolate the less reactive component of such mixtures (*i.e.*, isoborneol) through partial hydrolysis of the tosylates.

(22) W. Hückel, *Ann.*, **549**, 186 (1941).

orator (water aspirator vacuum) to give 30 g (94%) of a semisolid mixture of chlorides. The structures were assigned from their nmr spectrum in carbon tetrachloride. The proton adjacent to the chlorine exhibited a quartet at δ 3.9 ppm for 7,7-dimethyl-2-*exo*-norbornyl chloride (64%). The methyl resonances were at δ 1.0 and 1.33 ppm. In the minor isomer, the α-methine proton gave a doublet at δ 2.52 and methyl resonances at 1.06 and 1.1 ppm. These are consistent with 3,3-dimethyl-2-*exo*-norbornyl chloride (36%).[23]

Dehydrohalogenation of the Chlorides.—To a 200-ml one-necked flask fitted with a magnetic stirring bar and reflux condenser was added 100 g of 2-cyclohexylcyclohexanol (Dow Chemical Co.) and 11.7 g (0.3 g-atom) of potassium metal under a static pressure of nitrogen. The mixture was heated with stirring to 200° in 1 hr. The potassium reacts completely in 2 hr. (A powerful magnetic stirrer should be used.) The reaction mixture was cooled to 50° (solidification occurs), and then 30 g (0.189 mol) of chlorides was added (no solvent was used for the transfer). The reflux condenser was replaced with a Vigreux column (40 × 1 cm) maintained at 120° with a heating tape. A hot-water-heated condenser was connected to the Vigreux column, and an adapter (no narrow inside tube) was connected to the condenser. A three-necked flask fitted with a reflux condenser was used to collect the product. The mixture was then heated with stirring to 170° in about 1 hr. Initially some solvent remaining in the chloride distilled over. This can be removed with a pipet. At about 170° (oil-bath temperature), the apobornene and apocyclene starts to distil over. Within 2–3 hr (bath temperature 250°), there was obtained 17.3 g (75%) of a white semisolid. Analysis on the Perkin-Elmer Model 226 gas chromatograph on a 150 ft × 0.01 in. Golay column with Ucon LB 550X at 70° indicated 2% 5,5-dimethylnorbornene, 78% apobornene, and 20% apocyclene, in the order of increasing retention time.

Oxymercuration of Apobornene.—To a 100-ml round-bottom flask equipped with a magnetic stirring bar was added 15.9 g (50 mmol) of mercuric acetate and 50 ml of glacial acetic acid. To this stirred slurry was added 7.65 g of the apobornene–apocyclene mixture or 6.1 g (50 mmol) of apobornene. The mercuric acetate dissolves very quickly to form a pale yellow solution. After 3 hr at room temperature, the reaction mixture was poured into a stirred 200 ml of 1 *M* sodium chloride solution at room temperature. A white precipitate forms immediately. (If an oil forms, scratching with a glass rod induces crystallization.) After stirring for about 30 min, the product was filtered, crushed, washed well with cold water and pentane, and dried under vacuum at 1 mm overnight to give 18.7 g of the adduct (90%), mp 109–112°. Recrystallization by dissolving 15 g of the mercurial in 40 ml of hot absolute ethanol gave 12.6 g (84%) of pure mercurial, mp 121–121.5°. *Anal.* Calcd for $C_{11}H_{17}O_2HgCl$: C, 31.64; H, 4.11. Found: C, 31.41; H, 3.94.

(23) J. C. Davis, Jr., and T. V. Van Auken, *J. Amer. Chem. Soc.*, **87**, 3900 (1965), and references cited therein.

Deoxymercuration of the Apobornene Adduct.—To a 200-ml flask equipped with a magnetic stirring bar was added 20.9 g (50 mmol) of the mercurial and 100 ml of anhydrous dimethylformamide. The reaction mixture was warmed to 50° under nitrogen and 9.5 g (0.22 mol) of lithium chloride was added. After 6 hr at 50°, the reaction mixture was cooled, 25 ml of petroleum ether (bp 35–37°) was added, and the mixture was stirred well. Then the mixture was transferred to a separatory funnel containing 250 ml of water and shaken vigorously. Some emulsion and solid were separated, and the organic layer was washed twice with water and dried over magnesium sulfate. The solvent was distilled off through a 40 × 1 cm Vigreux column until some apobornylene started to distil. There was obtained 4.3 g (70%) of 98% apobornene and 2% 5,5-dimethylnorbornene, which had mp 46–47° (lit.[5d] mp 38°). The pmr spectrum in carbon tetrachloride exhibited a vinyl triplet at δ 5.9 (J = 1.5 Hz) and methyl protons at 0.90 and δ 0.95 ppm. *Anal.* Calcd for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.27; H, 11.52.

Apocyclene and Apobornene.—Apocyclene was prepared from the hydrazone of camphenilone, mp 40–41° (lit.[5b] mp 41–42°). The pmr spectrum displayed a methyl singlet at δ 0.90 ppm. 5,5-Dimethylnorbornene was obtained from Professor D. E. McGreer[24] who prepared it by the method of Berson.[25]

Synthesis of Apocamphor *via* Hydroboration.—To 11.2 ml (75 mol of hydride) solution of 1.13 *M* borane in tetrahydrofuran at 0° was added 4.88 g (40 mol) of 78% pure apobornene (20% apocyclene and 2% 5,5-dimethylnorbornene). The reaction mixture was stirred overnight under nitrogen at 25°. Decomposition of the excess hydride with water and oxidation with 10 ml of 30% hydrogen peroxide and 10 ml of 3 *M* sodium hydroxide at 40° in 2 hr gave 5.88 g (105%) of alcohol after the solvent and apocyclene were removed under vacuum. Oxidation by chromic acid, using the convenient ethyl ether–water two-phase method,[14] at 25° [20 ml of chromic acid solution prepared from 4.0 g (13.4 mol) of sodium dichromate dihydrate and 3 ml of 96% sulfuric acid] for 2 hr gave a 61% yield of apocamphor[26] by glpc, mp 108–110° (lit.[27] mp 109–110°).

Registry No.—*endo*-Camphenilol, 640-54-0; 7,7-dimethyl-2-*exo*-norbornyl chloride, 23758-28-3; 3,3-dimethyl-2-*exo*-norbornyl chloride, 22768-97-4; apobornene, 6541-60-2; mercurial, 23758-30-7; apocamphor, 10218-05-0.

(24) D. E. McGreer, *Can. J. Chem.*, **40**, 1554 (1962).

(25) J. A. Berson, *et al.*, *J. Amer. Chem. Soc.*, **83**, 3986 (1961).

(26) A modified procedure by using 100% excess of chromic acid at 0° for 15 min with vigorous stirring gave 80% isolation yield of apocamphor. A detailed discussion of this modified procedure will be reported in a manuscript now in preparation.

(27) G. Komppa and S. V. Hintikka, *Ber.*, **47**, 936 (1914).