Reaction of 2-Norbornyl- and 3,3-Dimethyl-2-norbornylmagnesium Bromide with Acetone

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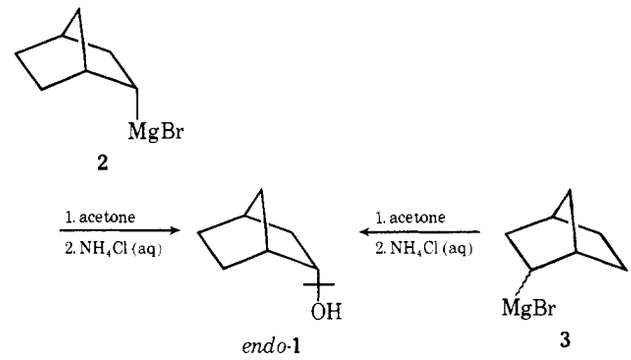
Attempts to determine the stereochemistry of electrophilic addition of acetone to two configurationally rigid Grignard reagents [2-norbornylmagnesium bromide (3) and 3,3-dimethyl-2-norbornylmagnesium bromide (9)] are described. Evidence is presented which suggests that the reaction of 9 with benzophenone proceeds via an electron-transfer pathway. In addition, results describing an improved synthesis of camphenilone and the stereospecific synthesis of *exo*-2-bromo-3,3-dimethylnorbornane are presented.

Despite its long-standing synthetic importance, a detailed understanding of the reaction of Grignard reagents with carbonyl compounds has only recently begun to emerge.[2,3] The products of such reactions indicate that several, frequently competitive reaction pathways are available: (a) direct 1,2-addition, (b) electron transfer, (c) reduction (when a β hydrogen is present in the Grignard reagent), and (d) enolization (if the ketone contains α protons).

The role of electron-transfer processes in the reaction of Grignard reagents with certain ketone substrates is well documented.[2,3] In general, however, it is believed that such processes play a relatively minor role in the overall addition of organomagnesium reagents to ketones, becoming important only when the structure of the ketone is such that its one-electron reduction results in a relatively stable ketyl. To be sure, the stability of the intermediate ketyl is an important point in considering the extent to which an electron-transfer component participates in the reaction of a ketone with a Grignard reagent. Such participation, however, cannot be ascertained with certitude by existing direct (ESR) or indirect (kinetic and product studies) evidence. In an effort to determine the extent, if any, that single-electron transfer processes are involved in such reactions, we have examined the reaction of two stereochemically rigid organomagnesium reagents with acetone, reasoning that a concerted reaction might be expected to lead to products with retained or inverted stereochemistry while a nonconcerted process such as electron transfer might be expected to yield, in general, products with loss of stereochemistry. Specifically, we chose to examine the reaction of acetone with *endo*- and *exo*-2-norbornyl- and *endo*- and *exo*-3,3-dimethyl-2-norbornylmagnesium bromide. Although our ultimate objective proved elusive, we describe here the procedures and results in the hope that others will benefit from these findings.

Results and Discussion

An equilibrium mixture of 2-norbornylmagnesium bromide (60% endo, 40% exo) was converted to *endo*-2-norbornylmagnesium bromide (>97% endo) by treatment with benzophenone according to published procedures.[4] The resulting mixture was allowed to react at 0 °C with an excess of dry acetone. Following an unexceptional workup, the sole addition product was isolated and its structure assigned as *endo*-1. This assignment is based on an interpretation of the ^{1}H NMR data in Table I and its comparison with prior studies of the ^{1}H NMR spectra of norbornanes.[5] Briefly, endo substitution in 2-substituted norbornanes is easily distinguishable from exo configuration on the basis of the magnitude of the vicinal coupling constant, with representative ranges for coupling constants in these configurations being $J_{2x,3x}$ = 4–12, $J_{2n,3n}$ = 4–7, and $J_{3x,3n}$ = 2–4 Hz. In addition, coupling between a bridgehead proton and its vicinal exo proton is significant ($J_{1,2x}$ = 2.5–4.5 Hz) while the corresponding coupling to the vicinal endo proton is small. Moreover, coupling between the endo proton at the 2 or 3 position and the anti-7 proton is significant ($J_{2n,7'}$ = 2–4 Hz) while the coupling to the corresponding exo proton ($J_{2x,7'}$) is small. Repetition of this experiment employing an equilibrium mixture of 2-norbornylmagnesium bromide produced the same epimeric distribution of 1 (i.e., >97% endo) in 48% yield.

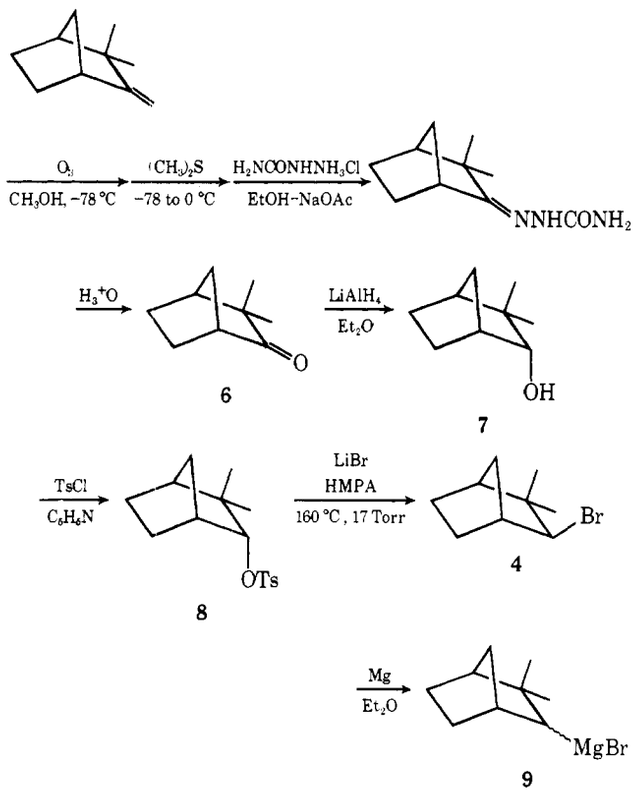


The failure to observe *exo*-1 in the product mixture resulting from the reaction of 2-norbornylmagnesium bromide with acetone is not a consequence of its instability under reaction or isolation conditions. This point was demonstrated by the fact that authentic *exo*-1, admixed with acetone and treated with 2-norbornylmagnesium bromide, could be isolated together with *endo*-1 by preparative GLC. The composition of this epimeric mixture was readily established by ^{1}H NMR analysis in the presence of the shift-inducing reagent Eu(fod)$_3$ as well as GLC analysis.

Because stereochemical conclusions based on a comparison of the starting and product geometries of differing geometrical (in contrast to optical) isomers are valid only in the demonstrated absence of processes leading to epimerically selective reactions (e.g., the kinetically favored or disfavored reaction of one epimer), the absence of any detectable quantity of *exo*-1 from the reaction of 3 with acetone precludes a conclusive statement regarding the stereochemistry of the carbon–carbon bond forming step in the reaction of 2-norbornylmagnesium bromide with acetone. Reasoning that the absence of *exo*-1 in the addition of 3 to acetone might, in view of the geometric considerations of the norbornyl system, result from a preference of *exo*-2-norbornylmagnesium bromide to participate in a reduction[6] rather than an addition process, we prepared and examined the reactions of 3,3-dimethyl-2-norbornylmagnesium bromide with acetone. The synthesis of the requisite bromide, 2-bromo-3,3-dimethylnorbornane (4), is outlined in Scheme I and merits brief discussion.

The preparation of camphenilone (6) has been reported by other workers.[7] The procedure described here provides a product of substantially improved purity with a considerable reduction in effort. The reduction of camphenilone with

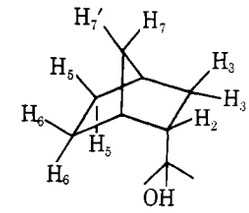
Scheme I



$LiAlH_4$ is sterospecific,[8] insofar as can be determined by ^1H NMR analysis, producing only *endo*-3,3-dimethylnorbornan-2-ol (*endo*-camphenilol, **7**). The conversion of **7** to its tosylate **8** was achieved by conventional procedures and requires no additional comment. The stereospecific conversion of **8** into *exo*-2-bromo-3,3-dimethylnorbornane (*exo*-**4**) was accomplished by reaction of **8** with anhydrous lithium bromide in HMPA at 160 °C under a reduced pressure. The stereospecific conversion of alkyl tosylates into the corresponding halide by treatment with LiX–HMPA is a established procedure.[9] However, the ability of LiX–HMPA to effect a stereospecific displacement at the 2 carbon on a 3,3-disubstituted norbornyl ring is noteworthy and suggests the remarkable and unique nucleophilic properties associated with this reagent mixture.

Varied attempts to prepare 3,3-dimethyl-2-norbornylmagnesium bromide (**9**) by classical procedures, i.e., by the direct reaction of **4** with magnesium turnings, produced, in substantial yield, a substance tentatively identified as bis(3,3-dimethyl-2-norbornane), presumably as a result of a Wurtz-like coupling process. These failures notwithstanding, solutions of 3,3-dimethyl-2-norbornylmagnesium bromide in ether were finally achieved by treating **4** with finely divided magnesium produced by the reaction of anhydrous magnesium bromide with sodium–potassium (78% K) alloy in refluxing ether. The epimeric distribution of an equilibrium mixture of **9** was established by a procedure developed to assay the isomer composition of 2-norbornylmagnesium bromide.[10] Thus, **9** is converted to 3,3-dimethyl-2-norbornyl(tri-*n*-butylphosphine)copper(I) (**10**), which on treatment with 3–5 equiv of methyllithium is converted to the corresponding methylate complex, **10a**. Oxidative coupling of **10a** with nitrobenzene at −78 °C yields 2,2,3-trimethylnorbornane (16% exo, 84% endo). A selective, albeit incomplete, epimer destruction of **9** can be achieved by treating it with a limiting quantity of benzophenone. Table II summarizes the epimer ratio produced by treating ether solutions of **9** with differing amounts of benzophenone at −78 °C.

Table I. Coupling Constants for Dimethyl(*endo*-2-norbornyl)carbinol[a]



endo-1

$J_{1,2x}$[b]	$J_{2x,3x} = 12.5$
$J_{3x,3n} = 12.5$	$J_{3x,5x} = 2.5$
$J_{2x,3n} = 6.2$	$J_{3x,4} = 4.5$
$J_{3n,7'} = 2.3$	

[a] Spectra were recorded at 100 MHz in CCl_4 containing ~1:1 (molar) Eu(fod)$_3$:*endo*-1. Coupling constants (J) are in hertz. Coupling constant assignments were confirmed by decoupling. Notation: x = exo, n = endo. A complete assignment of the coupling constants for all ring protons was precluded by the overlap between several resonances. [b] Strong coupling was observed between H_1 and H_{2x} but its magnitude could not be accurately determined because of overlapping interference from $H_{7'}$.

Table II. The Distribution of *exo*- and *endo*-9 Produced by the Addition of Benzophenone to an Equilibrium Mixture of 9 in Ether at −78 °C

mmol 9	mmol benzophenone	Mol %[a] *exo*-9:*endo*-9	
0.92	0.00	16	84
1.4	0.59	37	63
1.8	1.1	49	51
2.2	1.7	56	44

[a] Determined by analysis of the ratio of *exo*- to *endo*-2,2,3-trimethylnorbornane. See text for a discussion of assay procedure.

Three conclusions are immediately obvious from the data in Table II. First, the epimer distribution in an equilibrium mixture of 3,3-dimethyl-2-norbornylmagnesium bromide contains a noticeably higher fraction of endo epimer than does an equilibrium mixture of 2-norbornylmagnesium bromide, indicating that the endo isomer is slightly more stable in **9** than in **2**. Second, in contrast to 2-norbornylmagnesium bromide,[4] it is the endo isomer of 3,3-dimethyl-2-norbornylmagnesium bromide which is preferentially destroyed in the reaction of **9** with benzophenone. Third, these results establish that the reduction of a Grignard reagent can proceed by a pathway other than β-hydrogen elimination[6] and strongly suggest that *electron transfer may also play a role.*

The magnitude of the difference between the epimer ratio of an equilibrium mixture and that of a selectively enhanced mixture of **9** (entry 4, Table II), although less than that possible for 2-norbornylmagnesium bromide, is nonetheless sufficient to permit a conclusive statement regarding the stereochemistry of the carbon–carbon bond forming step in its reaction with acetone. To our dismay, however, the reaction of **9** with acetone produced none of the expected addition product. While a detailed examination of this result has not been carried out, labeling experiments are consistent with the conclusion that enolization has become the dominant reaction pathway. Thus, addition of acetone to an ether solution of **9** produced a reaction mixture which, when hydrolyzed with deuterium oxide, yielded 2,2-dimethylnorbornane (<2% d_1). By comparison, the 2,2-dimethylnorbornane isolated from the

direct protonolysis of **9** with deuterium oxide exhibited >98% d_1 incorporation.[11]

In summary, an attempt to determine the extent to which electron transfer is involved in the reaction of Grignard reagents with simple ketones,[12] by determining the stereochemistry of the addition product resulting from the reaction of two different configurationally rigid organomagnesium reagents with acetone, has proven inconclusive because of the dominating influence of certain side reactions. In related studies, an improved procedure for the preparation of camphenilone, a stereospecific synthesis of *exo*-2-bromo-3,3-dimethylnorbornane (a useful precursor to other camphenil and apoisobornyl compounds),[8] and the preparation of a stereochemically rigid organomagnesium reagent devoid of β hydrogens have been described.

Experimental Section

Organometallic reagents were manipulated using standard procedures. Analytical GLC analyses were performed on a Hewlett-Packard Model 5750 instrument equipped with a flame-ionization detector, employing unexceptional internal standard techniques. Preparative GLC was carried out using a Hewlett-Packard Model 710 equipped with a thermal conductivity detector. Except where otherwise indicated, the desired separations were achieved using an 8-ft, 20% UC-W98 silicone rubber on Chromosorb P column. Pyridine was dried by distillation from calcium hydride under nitrogen. Diethyl ether and THF were distilled from $LiAlH_4$ under nitrogen. Methyllithium was purchased from Foote Mineral Co., and analyzed by the Gilman double titration method. Ozone was generated using a commercially available ozone generator (PSI Ozonizer Model LOA-2). Commercially available camphene (Technical grade, 80–85%), dimethyl sulfide, semicarbazide hydrochloride, and sodium acetate were used without further purification. Sodium–potassium alloy (78% K) was purchased from MSA Research Corp.

All melting points and boiling points are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 237 grating spectrophotometer. NMR spectra were determined with a Varian HA-100 NMR spectrometer. Mass spectra were determined on a Hitachi Perkin-Elmer RMU 6 mass spectrometer. Analytical analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Preparation of Anhydrous $MgCl_2$. Into a 1-L, three-neck flask equipped with a Teflon-coated magnetic stirrer bar, reflux condenser, and 250-mL addition funnel was placed 24.3 g (1.00 g-atom) of magnesium turnings. The entire system was flame dried under a flush of nitrogen and allowed to cool before adding 500 mL of THF. The addition funnel was charged with 120 mL (150 g, 1.52 mol) of 1,2-dichloroethane which was added slowly to the reaction vessel until reflux commenced, at which point the rate of addition was adjusted to maintain a gentle reflux. As the reaction continued a white precipitate of magnesium chloride formed. Following the completion of addition the reaction mixture was stirred for an additional 60 min and finally heated at reflux overnight. The resulting mixture was filtered under nitrogen and the magnesium chloride collected in a fritted glass funnel and subsequently dried at 150 °C (0.2 Torr) for 3 days. The yield of $MgCl_2$ was 95 g (100%).

Camphenilone (3,3-Dimethylbicyclo[2.2.1]heptan-2-one, 6). A solution of 200 g (1.18 mol) of technical grade camphene in 1500 mL of methanol was placed in a 3-L, one-neck flask. The flask was chilled in a dry ice–acetone bath and a gas dispersion tube (Kontes 956500), attached to a gas inlet adapter (Kontes 181000), was inserted. The solution was treated with ozone (inlet flow rate 7–8 L/min) for 8 h with care taken to maintain a bath temperature <−70 °C. The gas dispersion tube was removed and 150 mL of dimethyl sulfide added. The flask was removed from the bath and a Teflon-coated magnetic stirring bar carefully added. The resulting solution was allowed to warm gradually with stirring. At ~0 °C an exothermic reaction developed and the pot temperature rose rapidly to ~45 °C. After 4 h, the clear to light yellow solution was transferred to a 3-L, three-neck flask and the contents subjected to steam distillation. A total of 3.5 L of distillant was collected. The crude distillant was extracted with three 500-mL portions of petroleum ether (bp 30–60 °C) and the combined extracts dried over magnesium sulfate. The resulting solution was concentrated on a steam bath to yield 210–225 g of a pale yellow liquid. This material was transferred to a 1-L flask containing 350 mL of an ethanol–water mixture (60:1). The flask was equipped with a reflux condenser and a Teflon-coated magnetic stirrer bar. Semicarbazide hydrochloride (69.8 g, 0.630 mol) and sodium acetate (111 g, 1.36 mol) were added and the resulting mixture refluxed with stirring for 12 h, then cooled to 0 °C and the crystalline white solid collected by suction filtration, washed with 500 mL of water followed by 500 mL of petroleum ether, and air dried. The yield of camphenilone semicarbazone (mp 222–223 °C, lit.[12] 222–224 °C) was 34–37%, based on camphene, and it is sufficiently pure to be used directly in the following reaction. If necessary, it can be recrystallized from hot ethanol–water (2:1). Camphenilone semicarbazone (190 g, 0.970 mol) was placed in a 2-L flask. Water (650 mL), ethanol (650 mL, 95%), and hydrochloric acid (325 mL, 12 M) were added and the resulting mixture refluxed for 2 h and allowed to cool before adding 1000 mL of water. The oil that separated was extracted with four 500-mL portions of petroleum ether. The combined extracts were dried over magnesium sulfate and concentrated on a steam bath. The residual oil was transferred to a 250-mL flask which was fitted with a short-path, wide-bore distillation head. Vacuum distillation afforded 99 g (68–74% based on semicarbazone) of camphenilone [bp 40–50 °C (0.2 Torr); mp (sealed capillary) 38.0–39.5 °C, lit.[13] 38.4 °C].

***endo*-Camphenilol (*endo*-3,3-Dimethylnorbornan-2-ol, 7)** (mp 70–73 °C, lit.[8] 71–74.5 °C) was prepared by the reduction of camphenilone as described by Brown and co-workers.[8]

***endo*-Camphenilol Tosylate (8).** *p*-Toluenesulfonyl chloride (210 g, 1.10 mol) was placed in a three-neck, 1-L flask equipped with a Teflon-coated magnetic stirrer bar, a drying tube, and a 250-mL addition funnel containing 7.60 g (0.543 mol) of *endo*-camphenilol in 100 mL of pyridine. Pyridine (450 mL) was added to the reaction flask. The solution of camphenilol was added rapidly with stirring at room temperature. This mixture was stirred at ambient temperature for 3 days during which time a white precipitate of pyridine hydrochloride formed. The resulting mixture was poured into 1500 mL of ice–water which was then extracted with five 300-mL portions of methylene chloride. The combined organic layers were extracted with five 500-mL portions of cold 1.8 M H_2SO_4, followed by two 500-mL portions of a saturated aqueous solution of sodium bicarbonate, and dried ($MgSO_4$). Concentration of this solution under reduced pressure yielded 155 g of crude product. Recrystallization was achieved by dissolution in a minimal amount of petroleum ether at room temperature, treatment of this solution with decolorizing charcoal, gravity filtration, and finally slow cooling in a dry ice–acetone bath. The white, crystalline product was collected by suction filtration and vacuum dried to yield 115 g (72%) of **8**: mp 59.5–60.5 °C; ^1H NMR δ ($CDCl_3$) 7.50 (AB pattern, 4 H, aryl) 4.18 (d, 1 H, HCOTs), 2.43 (s, 3 H, CH_3), and 0.70–2.40 (complex, 16 H). Anal. Calcd for $C_{16}H_{22}O_3S$: C, 65.27; H, 7.53. Found: C, 65.37; H, 7.58.

***exo*-Camphenilyl Bromide (*exo*-2-Bromo-3,3-dimethylnorbornane, 4).** *Caution:* Hexamethylphosphorus triamide (HMPA) is a suspected carcinogen. This procedure should be carried out in a well-ventilated fume hood and appropriate precautions taken.

Into a 500-mL, one-necked flask equipped with a Teflon-coated stirrer bar and a short-path distillation head with 100-mL receiver was placed *endo*-camphenilyl tosylate (55.3 g, 0.187 mol), anhydrous lithium bromide (Research Organic/Inorganic, 26.3 g, 0.302 mol), and 200 mL of HMPA, distilled from calcium hydride under reduced pressure. Stirring was commenced as soon as possible and the pressure of the system was reduced to 16 Torr. The reaction flask was immersed in a oil bath heated to 160 °C and complete dissolution of all solids was soon noted. The volatiles that were produced as the reaction proceeded were collected in a chilled (−78 °C) receiver. Distillation was discontinued when the rate of distillant production slowed noticeably. The crude distillant (~80 mL) was added to 250 mL of petroleum ether and the resulting mixture extracted with four 250-mL portions of water, dried ($MgSO_4$), and concentrated on a steam bath. Fractionation of the residual liquid produced a forerun [6.62 g, bp 50–95 °C (17 Torr)] and a product-containing fraction [18.8 g, 50% yield, bp 100–101 °C (17 Torr)]. Fractionation of this material, which tends to solidify in the condenser, is aided by the use of a heat gun. *exo*-2-Bromo-3,3-dimethylnorbornane is a slushy semisolid at room temperature: ^1H NMR δ ($CDCl_3$) 3.60 (d, J = 2.0 Hz, 1 H, HCBr), 2.60–0.70 (complex, 15 H); *m/e* (rel intensity) 204 (7), 202 (7), and 67 (100).

2-Norbornylmagnesium bromide was prepared from *exo*-2-bromonorbornane using unexceptional procedures. Its stereochemistry was assayed by conversion to 2-methylnorbornane.[9]

***endo*-2-Norbornylmagnesium bromide** was prepared by the method of Jensen and Nakamaye.[4] Reference 9 describes the details of this procedure.

3,3-Dimethyl-2-norbornylmagnesium Bromide (9). Attempts to prepare **9** in ether by traditional methods yielded solutions with unusually low titer values. Examination of a hydrolyzed aliquot indicated that a substantial fraction of the starting bromide had been

converted to a hydrocarbon product, the mass spectrum of which was consistent with its assignment as bis-2-(3,3-dimethylnorbornane). Repetition of this procedure using 12.3 g (61.0 mmol) of **4**, 2.2 g (92 mg-atoms) of magnesium turnings, and 20 mL of THF produced higher yields of **9**. Unfortunately, the selective destruction of **9** (vide infra) could not be achieved in THF solution.

A general procedure for the preparation of ether solutions of **9** was ultimately achieved using an adaptation of the method described by Rieke and Bales[14] for preparing Grignard reagents from unreactive organic halides under mild conditions. Thus, into a 250-mL, flame-dried, three-neck flask equipped with a Teflon-coated magnetic stirrer bar and a reflux condenser were placed 9.87 g (104 mmol) of anhydrous magnesium chloride, 5.0 g of sodium–potassium (78% K) alloy, and ether (60 mL). The resulting mixture was refluxed for 96 h during which time the silvery, molten alloy was replaced by a fine, black precipitate. A solution of *exo*-**4** (7.70 g, 38.0 mmol) in ether was added dropwise at room temperature over a 4.5-h period with vigorous stirring. After an additional 1.5 h of stirring at ambient temperature, the reaction mixture was transferred to several flame-dried centrifuge tubes, each of which had been capped with a rubber septum. The reaction solids were compacted by centrifugation and the supernatant liquid transferred by cannula under a positive pressure of nitrogen to an appropriate storage container. The concentration (0.20 M as total base) was determined by titration against standardized 0.10 M HCl. Attempts to prepare higher concentrations of this Grignard in ether were uniformly unsuccessful.

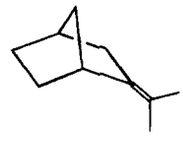
Determination of the Stereochemistry of 9. The epimeric composition of the Grignard reagent **9** in ether was determined by a procedure analogous to that described for 2-norbornylmagnesium bromide. Thus, **9** (8.0 mL, 0.18 M) and methyllithium (2.5 mL, 1.6 M) were added by syringe to a solution of bromo(tri-*n*-butylphosphine)-copper(I) dissolved in 3 mL of ether at −78 °C. The mixture was shaken vigorously for 1 min, then treated with nitrobenzene (1.0 mL) at −78 °C. The resulting mixture was hydrolyzed with concentrated hydrochloric acid (0.10 mL) and centrifuged and the yellow, supernatant liquid passed through a 0.5 × 3 cm column of neutral alumina. The eluent was concentrated and the epimeric mixture of 2,3,3-trimethylnorbornane collected. Reinjection onto a 24 ft × 0.125 in. Hi-Pak SE-30 column (Hewlett-Packard) indicated an epimer composition of 84% endo, 16% exo.

Selective Destruction of *endo*-9. Reaction of 9 with Benzophenone in Ether. An equilibrium mixture of 3,3-dimethyl-2-norbornylmagnesium bromide (8.0 mL, 0.18 M) was injected by syringe into a 40-mL, flame-dried centrifuge tube capped with a rubber septum and containing a Teflon-coated magnetic stirrer bar. The vessel was cooled to −78 °C and with vigorous shaking a solution of benzophenone (0.105 g, 0.589 mmol) in ether (3.0 mL) was added by syringe. The reaction mixture was stirred at ambient temperature for ca. 1 min. The precipitated solids were compacted by centrifugation and the clear red solution transferred by cannula to a clean, flame-dried centrifuge tube and stored at −78 °C until used. Analysis of the stereochemical composition of this material as described above indicated that it contained a 63% endo, 37% exo epimer distribution.

Reaction of *endo*-2-Norbornylmagnesium Bromide with Acetone. Into a 40-mL, flame-dried centrifuge tube capped with a rubber septum and equipped with a Teflon-coated magnetic stirrer bar was transferred by syringe 10 mL (8.0 mmol) of an ether solution of 2-norbornylmagnesium bromide. The vessel was cooled in an ice bath and, with vigorous stirring, anhydrous acetone (1.0 mL) was added dropwise over a 30-min period. The resulting mixture was stirred for an additional 30 min, then cautiously hydrolyzed by the addition of 1.0 mL of a saturated aqueous solution of ammonium chloride. After drying ($MgSO_4$), an additional 5 mL of ether was added and the mixture centrifuged. The clear supernatant solution was removed, concentrated to about one-half its volume, and subjected to GLC analysis. The last and next-to-the-last components to elute were identified, respectively, as the Wurtz-type coupling product 2,2′-bisnorbornane (M^+ 190) and dimethyl(*endo*-2-norbornyl)carbinol (*endo*-**1**, 48%). The IR of *endo*-**1** (CCl_4) exhibited two high-frequency vibrations at 3600 (sh, m) and 3470 cm^{-1} (br, m), characteristic, respectively, of nonassociated and associated ν (O–H). The ^1H NMR spectrum of a sample of *endo*-**1** collected from GLC showed δ (CCl_4) 0.96 (CH_3, s), 1.02 (CH_3, s), 1.09 (OH, s), and 0.80–1.60 (br, multiplet). The appearance of two nonequivalent methyl resonances results from their diastereotropic nature; the assignment of the O–H resonance was confirmed by the substantial dependence of its chemical shift and line width on solvent and concentration. A further analysis of the ^1H NMR spectrum of *endo*-**1** is given in Table I. Elemental analysis was carried out on a collected sample of *endo*-**1**. Anal. Calcd: C, 77.95; H, 11.69. Found: C, 77 90; H, 11.50.

In addition to the aforementioned products, a significant yield of norbornane and norbornene (identified by a comparison of GLC retention times and mass spectra) was also observed.

A further minor component present in an undetermined amount was also isolated by preparative GLC. It had IR (CCl_4) 2890 (C–H), 1440 (m), and 1365 cm^{-1} (m). Its ^1H NMR spectrum revealed δ (CCl_4) 1.20 (s), 1.50 (d, CH_3, J = 1.2 Hz), 1.65 (d, CH_3, J = 2.0 Hz), 2.35 (br, 1 H, bridgehead), 2.85 (br, 1 H, bridgehead), 0.80–2.20 (br, complex). The Raman spectrum of this material (neat) exhibited an intense, sharp band at 1689 cm^{-1}, the position and intensity of which are characteristic of the ν (C=C) observed in tetrasubstituted olefins. A mass spectrum of this compound showed *m/e* (rel intensity) 136 (12, M^+) 121, 107 (100), 93 (63), and 79 (59). Based on these spectroscopic data, this substance is tentatively identified as **11**, produced as a result of the dehydration of **1** during its isolation. The fact that the yield of **11** increases with increasing injection port, column, and detector temperature is consistent with this assignment.



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Preparation of *endo*-2,2,3-Trimethylnorbornane (15). Authentic **15** was synthesized by the sequence of reactions described below.

***exo*-2-Methylbicyclo[2.2.1]hept-5-ene-*cis,endo*-2,3-dicarboxylic acid (12)** was prepared in 88% yield by the literature procedure[15] (mp 129–130 °C, lit.[15] 122 °C).

***exo*-2-Methylbicyclo[2.2.1]hepta-*cis,endo*-2,3-dicarbinol (14).** Into a 250-mL flask equipped with a Dean-Stark trap was placed 5.0 g (25 mmol) of **12** and 100 mL of benzene. The mixture was refluxed for 24 h and the water that resulted removed periodically. The remaining solution was concentrated to dryness and the residual gummy solid purified by vacuum sublimation (80 °C, 0.1 Torr) to yield 2.3 g (60%) of *exo*-2-methylbicyclo[2.2.1]hept-5-enedicarboxylic anhydride (**12a**), mp 136.5–137.5 °C (sealed capillary). Reduction of **12a** (20 g, 0.10 mol) to *exo*-2-methylbicyclo[2.2.1]hepta-*cis,endo*-2,3-dicarboxylic anhydride (**13**) was achieved in quantitative yield in a Parr apparatus over PtO_2 catalyst suspended in ethyl acetate under a hydrogen atmosphere (40 psi). The catalyst was removed by filtration and the product isolated by concentrating the mother liquor to dryness, mp 134–135 °C.

Compound **13** (23 g, 0.11 mol) was dissolved in 150 mL of dry THF and this solution was placed in a 200-mL addition funnel and added dropwise to a solution of $LiAlH_4$ (26 g) dissolved in 300 mL of THF contained in a 500-mL flask equipped with a Teflon-coated stirrer. The flask was cooled to 0 °C and the reaction mixture stirred vigorously throughout the course of addition. The resulting mixture was subsequently refluxed (under nitrogen) for 7 days before destroying the excess $LiAlH_4$ by the cautious addition of ethyl acetate accompanied by cooling and stirring. Methanol was cautiously added until the evolution of gas subsided. The resulting thick paste was treated with 500 mL of 10% H_2SO_4 and the mixture extracted with five 300-mL portions of ether. The combined extracts were washed with 10% aqueous K_2CO_3, dried ($MgSO_4$), and concentrated in vacuo. The residual oil was subjected to a short-path distillation. The product, bp 116–120 °C (0.1 Torr), is a low-melting, gummy solid [IR (CCl_4) 3400 cm^{-1} (vs)] and is assigned the structure **14**. The isolated yield is 83%.

The ditosylate of the diol 14 was prepared by dissolving 15 g (90 mmol) of **14** in 20 mL of dry pyridine contained in a 250-mL flask. To this solution was added dropwise at 0 °C a solution of 49 g (0.26 mol) of *p*-toluenesulfonyl chloride dissolved in 50 mL of pyridine. A white solid soon appeared. The addition completed, the mixture was allowed to warm to room temperature and stir overnight, then treated with 50 mL of ice-cold water followed by 80 mL of ice-cold concentrated HCl. The resulting mixture was extracted with four 200-mL portions of CH_2Cl_2. The combined extracts were washed with 200 mL of a saturated aqueous solution of K_2CO_3, dried ($MgSO_4$), and concentrated to dryness under reduced pressure. The resulting oil was dissolved in a minimal amount of warm benzene. This solution was treated with petroleum ether until almost cloudy and placed in a refrigerator for 3 days. The white solid that formed was collected by suction filtration, air dried, and used directly in the next reaction.

Reduction of the Ditosylate of 14 with $LiAlH_4$. The crude tosylate obtained above (3.0 g) was dissolved in 20 mL of THF. This so-

lution was then added dropwise to a suspension of 0.5 g of $LiAlH_4$ in 50 mL of THF contained in a 100-mL flask. Vigorous stirring and cooling (0 °C) were maintained throughout the addition. The resulting mixture was refluxed for 24 h. The residual $LiAlH_4$ was cautiously destroyed and the reaction mixture poured into ice water and extracted with three 50-mL portions of ether. The combined extracts were dried ($MgSO_4$) and concentrated on a steam bath. GLC analysis on a 24 ft × 0.125 in. Hi-Pak SE-30 indicated two components in a 5:95 ratio (in order of increasing retention times). These peaks had identical retention times with those of the two components obtained from the reduction of camphene with hydrogen, the observed ratio in this instance being (in order of increasing retention times) 28:72. The latter peak to elute is, therefore, assigned as *endo*-2,2,3-trimethylnorbornane (**15**), and the former peak as *exo*-2,2,3-trimethylnorbornane.

Preparation of Authentic *exo*-1 and *endo*-1. *exo*-2-Norbornanecarboxylic acid[16] was converted to the corresponding acid chloride [bp 80–81 °C (10 Torr), lit.[17] 84 °C (15 Torr)] by treatment with thionyl chloride.

exo-2-Norbornanecarboxylic acid chloride (12.2 g, 77.0 mmol) was placed in a 1-L, three-necked, flame-dried flask equipped with an addition funnel, reflux condenser, and Teflon-coated magnetic stirrer bar. Dry ether (200 mL) was added. The addition funnel was charged with 200 mL (0.260 mol) of a solution of methyllithium in ether, which was added under a static head of nitrogen at a rate sufficient to maintain a gentle reflux. At the completion of addition the resulting mixture was refluxed for 45 min, then cautiously hydrolyzed with 50 mL of water followed by 50 mL of 6 M HCl. The layers were separated, and the aqueous layer extracted with three 125-mL portions of ether. The combined organic layers were washed with 250 mL of a saturated aqueous solution of $NaHCO_3$, dried ($MgSO_4$), and concentrated under reduced pressure to give 12.4 g of a dark brown, viscous oil. This material was subjected to chromatography through a 2.3 × 48.5 cm column of alumina (neutral, Fischer chromatography grade). Elution was achieved by treatment with 200 mL of petroleum ether followed by elution with 200 mL of a 1:9 (v/v) mixture of diethyl ether–petroleum ether and finally by 200 mL of diethyl ether. The material of interest eluted with the diethyl ether containing fractions. These were collected and concentrated under reduced pressure. The residual viscous oil (5.6 g) was distilled [bp 93–95 °C (13 Torr)] to give 3.8 g (32%) of material with the empirical formula $C_{10}H_{18}O$: IR (neat) 3450 (br, OH), 2940 cm^{-1}.

The ^1H NMR spectrum of this material in CCl_4, observed in the presence of the shift-inducing reagent $Eu(fod)_3$, revealed two isomers, one of which moved considerably more rapidly downfield than the other upon sequential addition of $Eu(fod)_3$. A comparison of these spectra with that of the *endo*-1 isolated from the reaction of norbornylmagnesium bromide with acetone established that one component was in fact *endo*-1, which we conclude formed as a result of epimerization in the course of the reaction of *exo*-2-norbornanecarboxylic acid chloride with methyllithium. The remaining component is, by exclusion, assigned the structure *exo*-1. Component analysis can also be achieved on 24 ft × 0.125 in. Hi-Pak Carbowax column (Hewlett-Packard). Under these conditions the endo isomer elutes first.

Registry No.—*endo*-1, 61723-39-5; *exo*-1, 61723-40-8; *endo*-3, 13058-87-2; **4**, 61723-41-9; **7**, 640-54-0; **8**, 23887-56-1; *endo*-**9**, 61723-42-0; *exo*-**9**, 61723-43-1; **11**, 4696-14-4; **12**, 28871-71-8; **12a**, 18310-60-6; **13**, 1873-09-2; **14**, 18310-62-8; **14** ditosylate, 61723-44-2; *p*-toluenesulfonyl chloride, 98-59-9; acetone, 67-64-1; *exo*-2-norbornanecarboxylic acid chloride, 1195-11-5.

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Reduction of Some 7-Norbornenols with Lithium Aluminum Hydride–Aluminum Chloride

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Reduction of a mixture of 7-phenyl-7-norbornenols with $LiAlH_4$–$AlCl_3$ gave 7-*syn*-phenylnorbornene (70%) and 7-phenyltricyclo[4.1.0.$0^{3,7}$]heptane (30%). Tricyclic hydrocarbon with deuterium incorporation exclusively at the endo-2 position was formed when the alcohol mixture reacted with $LiAlD_4$–$AlCl_3$. Reduction of a 7-*p*-anisyl-7-norbornenol mixture afforded 7-*syn*-*p*-anisylnorbornene (62%), 7-*anti*-*p*-anisylnorbornene (32%), and 7-*p*-anisyltricyclo[4.1.0.$0^{3,7}$]heptane (6%). Reduction of 7-*syn*-norbornenol proceeded to 7-norbornanol, whereas 7-*anti*-norbornenol was unaffected by the reduction medium.

In the course of our research on arylnorbornyl derivatives[1] a route to the alcohol 7-*syn*-phenyl-2-*endo*-norbornanol (**1**) was desired. A possible precursor to **1** is the alkene, 7-*syn*-phenylnorbornene (**2a**). Phenyllithium addition to 7-norbornenone gave a 64% *anti*-phenyl:36% *syn*-phenyl ratio of the unsaturated alcohols, **3a** and **4a**, respectively. Treat-