with 10% ethyl acetate–hexane to give **10** (14 mg, 65%). Sublimation at 100 °C (8 torr) gave analytically pure sample **10**: mp 246 °C; IR (KBr) ν_{max} 2950, 1090 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.7–1.9 (4 H, m), 2.2–2.3 (2 H, br s), 2.9–3.0 (2 H, br s), 4.4–4.8 (4 H, m); ^{13}C NMR (25 MHz, $CDCl_3$) δ 86.5, 81.4, 56.9, 42.0, 36.2. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.36. Found: C, 73.10; H, 7.35.

Hexahydro-3,2,5-ethanylylidene-2*H*,3*H*-1,4-dioxacyclopenta[*cd*]pentalene (11). Pentacyclic bromide **8** (10 mg, 0.30 mmol) in 5 mL of dry toluene was placed in a three-necked round-bottomed flask under N_2. Tri-*n*-butylstannane (20 mg, 0.06 mmol) along with a catalytic amount of AIBN was added, and the reaction mixture was refluxed for 2 h. The reaction was worked up as described above. Sublimation of the residue at 80 °C (10 torr) furnished 3 mg of analytical sample **11**: mp 208 °C (lit.[1e] mp 213 °C); IR (KBr) ν_{max} 2900, 1090 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 1.2–2.2 (6 H, m), 2.9–3.1 (2 H, m), 4.2–4.4 (2 H, m), 4.4–4.6 (2 H, m); ^{13}C NMR (25 MHz, $CDCl_3$) δ 85.4, 78.8, 54.8, 38.2, 36.7.

Acknowledgment. K.R.R. thanks CSIR for a research fellowship. This research was supported through UGC special assistance and COSIST programs in organic chemistry.

2-Bornyllithium. Preparation, Characterization, and Use in Synthesis

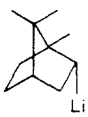
Gary W. Erickson and James L. Fry*

Bowman-Oddy Laboratories, Department of Chemistry,
The University of Toledo, Toledo, Ohio 43606

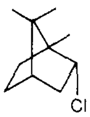
Received September 23, 1986

The use of chiral, nonracemic components derived from inexpensive naturally occurring materials to construct new molecules with high degrees of enantiomeric purity is an appealing synthetic strategy. The advantages of the use of such "chiral building blocks" have been discussed in depth.[1] We were interested in using an organometallic derivative of the 2-bornyl system in order to pursue the synthesis of some chiral organosilicon hydrides by this approach. In this note we describe our work with 2-bornyllithium (**1**).

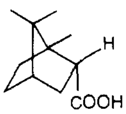
Perusal of the literature reveals that the Grignard reagent derived from 2-bornyl chloride (**2**) does not serve as a well-behaved synthetic intermediate. Treatment of 2-bornyl chloride with magnesium followed by carbonation is reported to lead to variable yields of mixtures of the diastereomeric boranecarboxylic (endo) and isobornanecarboxylic (exo) acids **3** and **4**, respectively, along with various hydrocarbon byproducts.[2] In addition, bornylmagnesium chloride tends to act as a reducing agent toward ketones instead of adding to them.[3] In view of these reports of low synthetic yields, variable degrees of diastereomeric purity, and the undesirable reducing properties of the 2-bornyl Grignard reagent, we decide to investigate the possibility of using the previously unreported 2-bornyllithium reagent in its place.



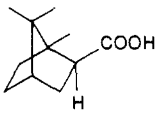
1



2



3



4

Results and Discussion

Initial attempts to prepare the organolithium reagent of bornyl chloride (prepared by hydrochlorination of α- or β-pinene) were run under argon at low temperatures (−30 to −45 °C) in diethyl ether by using lithium wire containing 1% sodium. The yields of bornyllithium in these initial reactions were estimated by GC analysis of the products obtained from the addition of reaction aliquots to dimethyldiethoxysilane. The yields of the desired dimethylbornylethoxysilane were very low, ranging from from 0 to 8%. The major products of the reaction were bornane and unreacted bornyl chloride. Considerable improvements in the yield of bornyllithium were obtained by using a very finely dispersed lithium sand containing 3–4% sodium and by carefully drying the bornyl chloride just prior to use. The bornyl chloride was dried by addition of benzene and then subsequent removal of the benzene by distillation at atmospheric pressure. This caused any residual water to be lost as an azeotrope. Small traces of remaining benzene did not pose any problems in later steps.

The diastereomeric purity of the bornyllithium produced from bornyl chloride (which was prepurified by preparative GC) was determined by carbonation with solid carbon dioxide of an aliquot of the reagent prepared in diethyl ether, a technique used before to establish the configuration of organometallic reagents.[4] The ^{1}H NMR spectrum of the resulting carboxylic acid product was consistent in all respects to a literature spectrum of bornanecarboxylic acid (**3**).[5] No evidence for the formation of isobornanecarboxylic acid (**4**) was present. The presence of any **4** would have been detected in the NMR spectrum by a triplet due to the α-methine hydrogen of **4** at δ 2.34.[6] The α-methine hydrogen in **3** appears as a distorted triplet farther downfield at δ 2.70. Additional evidence of the diastereomeric purity of product **3** came following methylation of the acid and analysis of the methyl ester by GC. Only a single methyl derivative was observed.

Another significant improvement in both the yield and ease of preparation of bornyllithium was attained through the use of refluxing anhydrous pentane as the reaction solvent. The yields, as determined by the Gilman double titration procedure using 1,2-dibromoethane to analyze for residual base,[7] ranged from 45 to 61% after reaction times of 6–12 h. These yields are believed to represent somewhat lower concentration values of bornyllithium than were actually present, since relatively large values were obtained for residual base content in the Gilman titration procedure. Residual base content is usually high only with organolithium reagents prepared in ethereal solvents where solvent cleavage can occur to give lithium alkoxides. The implication is that 1,2-dibromoethane is not reacting quantitatively with the organolithium reagent to give nonbasic products.

This belief was reinforced by the finding that both GC and isolated yields of the products derived from the reactions of bornyllithium solutions and either chlorodimethylsilane (1 equiv) or dichloromethylsilane (0.5 equiv) were often higher than the yields of bornyllithium given

---

[1] Scott, J. W. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds.; Academic Press, Inc.: New York, Vol. 4, 1984; pp 1–226.

[2] Riviere, C. *Ann. Chim.* (*Paris*) **1946**, *1*, 157. Vavon, G.; Riviere, C. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1941**, *213*, 1016. Walling, C.; Buckler, S. A. *J. Am. Chem. Soc.* **1955**, *77*, 6039.

[3] Bousett, R. *Bull. Soc. Chim. Fr.* **1955**, 210.

[4] Jensen, F. R.; Nakamaya, K. L. *J. Am. Chem. Soc.* **1966**, *88*, 3437. Glaze, W. H.; Selman, C. M. *J. Org. Chem.* **1968**, *33*, 1987. Glaze, W. H.; Selman, C. M. *J. Organomet. Chem.* **1968**, *11*, P3.

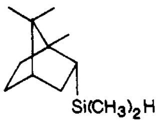
[5] Flautt, T. J.; Erman, W. F. *J. Am. Chem. Soc.* **1963**, *85*, 3212.

[6] Aul'chenko, I. S.; Gavrilova, T. F.; Kheifits, L. A. *J. Org. Chem. USSR* **1967**, *3*, 1593.

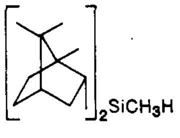
[7] Gilman, H.; Haubein, A. H. *J. Am. Chem. Soc.* **1944**, *66*, 1515. Gilman, H.; Cartledge, F. K. *J. Organomet. Chem.* **1964**, *2*, 447.

0022-3263/87/1952-0462$01.50/0

by the Gilman titration. Both bornyldimethylsilane (**5**) and dibornylmethylsilane (**6**) were obtained from these reactions and were fully characterized.



5



6

Bornyllithium appears to be one of the few organolithium reagents which can be prepared in good yield from the halide and lithium metal in pentane. The good synthetic yields as well as the high diastereomeric purity and the availability of both enantiomers from relatively inexpensive natural sources make bornyllithium a promising synthetic means of introducing a chiral substituent into many possible substrates.

Experimental Section

General Methods. Proton nuclear magnetic resonance spectra were obtained by using a Varian T-60A spectrometer. Unless otherwise indicated, the solvent used was $DCCl_3$ and chemical shifts were related to Me_4Si. Infrared spectra were obtained on either a Perkin-Elmer 137 or 621 spectrophotometer with CCl_4 solutions in 0.1-mm NaCl cells or with neat films. Gas chromatographic analyses were carried out on Varian Aerograph 90-P or Hewlett-Packard Model 5722A instruments using 6.4 mm × 2 m columns. Large-scale preparative separations were performed on a Hewlett-Packard Model 776 preparative gas chromatograph using 19 mm × 2 m columns. Optical rotations were measured on a Rudolph Research Model 26202 automatic digital polarimeter using 1.6 mm × 1 dm, 4 mm × 1 dm, and 3 mm × 1 dm (jacketed) tubes. Melting points (Thomas-Hoover apparatus) and boiling points are uncorrected. Elemental analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI. Solvent pentane was washed repeatedly, first with concentrated H_2SO_4, then with water, and dried over K_2CO_3 prior to distillation from $LiAlH_4$ just before use. Helium and argon gases were of "prepurified" grade and were further purified by passage through traps containing anhydrous $CaSO_4$ and Ascarite prior to introduction into reaction vessels.

Synthesis of 2-Bornyl Chloride (2). Bornyl chloride was prepared by bubbling dry HCl gas through a glass frit into a solution of 52.5 g (0.38 mol) of β-pinene (Aldrich), $[\alpha]^{26}_D$ $-23.7°$ (neat), in 20 mL of pentane at 0 °C for 6 h. The pentane was removed by using a rotary evaporator and the residue was then cooled to −30 to −40 °C. The resulting precipitate was isolated by suction filtration and dissolved in 80 mL of pentane. The solution was washed successively with saturated aqueous $NaHCO_3$ (2 × 20 mL), saturated aqueous NaCl, and then dried over anhydrous Na_2SO_4. Pentane was removed by rotary evaporation and the remaining white crystalline material was sublimed under reduced pressure to give 29.8 g (45% yield) of the desired product, (−)-**2**: mp 131–132 °C, $[\alpha]^{25}_D$ $-33.25°$ (*c* 2.00, Et_2O); lit.[8] mp 132 °C, $[\alpha]_D$ $-34.5°$ (Et_2O). This product was further purified by recrystallization from methanol. GC analysis of this product (20% Apiezon L, 160 °C) showed the presence of 8% of another component with a shorter retention time thought to be fenchyl chloride (vide infra). A portion of this product was purified by preparative GC (20% SE-30, 130 °C) for the lithiation–carbonation experiment. The ^1H NMR spectrum of **2** showed signals at δ 4.20 (1 H, m), 2.8–1.05 (7 H, overlapping signals), 1.0 (3 H, s), and 0.90 (6 H, s).

In a similar experiment, dry HCl was passed through α-pinene (Aldrich); $[\alpha]^{27}_D$ $-54.7°$ (*c* 8.07, $CHCl_3$), to give (+)-**2**, $[\alpha]^{27}_D$ $+25.45°$ (*c* 2.00, Et_2O), in 34% yield. It is of interest that regardless of which isomer of pinene was used, GC analysis of the crude product mixture showed that it contained 88% of **2** and 12% of another component. The structure of this impurity was not determined, but mechanistic considerations strongly favor fenchyl chloride.

Preparation of Lithium Sand Containing 3–4% Sodium. The basic approach of Bartlett and Lefferts for making finely dispersed lithium sand was used.[9] (Use caution!) To an oven-dried 250-mL, three-necked flask fitted with an He/Ar gas inlet and Herschberg stirrer was added 75 mL of mineral oil. The oil was degassed by bubbling helium or argon through it for 2 h. High-purity lithium metal (20 g, 2.89 mol) was then introduced and heated to its melting point. Sodium (0.6–0.8 g) was added and vigorous stirring of the flask contents was initiated. Oleic acid (4–5 drops) was then added and rapid stirring was maintained for 20 min at an internal pot temperature of 215 °C. The lithium sand was allowed to cool (stirring maintained) and then was placed in a separatory funnel where the mineral oil was removed and replaced with a fresh quantity. The sand was stored with the oil under helium or argon and washed with the reaction solvent just prior to use. Extended periods of storage did not seem to affect the properties of this material.

Preparation of Bornanecarboxylic Acid (3). To a three-necked flask fitted with Herschberg stirrer, condenser, addition funnel, and helium inlet was added 0.28 g (0.04 mol) of lithium sand containing 4% sodium. The lithium sand was washed with pentane and then 20 mL of anhydrous diethyl ether was added. The organolithium reaction was initiated at room temperature by the addition of a 5-mL portion of a solution of 1.90 g (0.011 mol) of GC-purified (−)-**2** in 20 mL of ether. After the reaction mixture had become cloudy, the remaining solution of **2** was added to the flask which was now maintained at a temperature of −30 to −45 °C. The reaction mixture was stirred at that temperature for 3 h and then an excess of finely ground solid carbon dioxide was added. After the excess carbon dioxide had been allowed to sublime away, the reaction mixture was acidified by addition of 6 M hydrochloric acid. The organic layer was then separated and washed three times with dilute aqueous KOH. Acidification of the combined aqueous extracts with dilute hydrochloric acid resulted in the formation of a white precipitate. The acidified suspension was extracted with pentane and the extracts were combined and dried over anhydrous Na_2SO_4. The solvent was removed on a rotary evaporator to yield 0.80 g (40%) of a white solid, mp 64–67 °C (lit.[5] mp 90.8–92.6 °C). The IR spectrum (CCl_4) of the crude material showed characteristic bands at 3000, 1720, 1240, and 940 cm^{-1}. The ^1H NMR spectrum (CCl_4) of this crude product was also in agreement with the published spectrum for bornanecarboxylic acid (**3**).[5] The spectrum displayed signals at δ 2.70 (1 H, br t), 2.0–1.10 (7 H, overlapping signals), 1.05 (3 H, s), and 0.90 (6 H, s). There was no evidence for the formation of any isobornanecarboxylic acid (**4**).[6] As a check, 0.25 g (1.4 mmol) of the crude acid was converted to the methyl ester with trimethyloxonium tetrafluoroborate following the method of Raber and Gariano.[10] GC analysis (4% SE-30, 145 °C) of the crude methyl ester reaction mixture showed only a single peak. The ^1H NMR spectrum ($CDCl_3$) of the methyl ester showed signals at δ 3.60 (3 H, s), 2.60 (1 H, distorted triplet), 1.95–1.10 (7 H, overlapping signals), 0.98 (3 H, s), and 0.82 (6 H, s).

General Procedure for the Preparation of Bornyllithium (1). In a typical preparation, excess lithium sand containing 3–4% sodium was added to a specially constructed three-necked, round-bottomed flask which had a course glass frit located on the bottom. Extending from the bottom of the frit and continuing up the outside of the flask was a piece of glass tubing fitted with a three-way Teflon-brand stopcock. The flask was also equipped with an addition funnel, Herschberg stirrer, helium/argon inlet, and condenser. Teflon-brand sleeves were used instead of stopcock grease on all ground-glass joints. The lithium sand was washed by the introduction of a portion of pentane. The pentane was then removed via the glass frit and side arm by subjecting the flask to positive internal pressure. A fresh quantity of pentane (1 mL per 1.8 mmol of halide) was added to the flask and then bornyl chloride in pentane (1 mL per 1.5 mmol of halide) was added dropwise to the stirred pentane–lithium mixture at reflux. Prior to this, the bornyl chloride had been dried by dissolving it in dry benzene followed by distillation of the benzene in order to remove any residual moisture as the minimum boiling azeotrope. In addition, 1 drop of Red-Al (Aldrich) was added both

---

[8] Thurber, F. H.; Thielke, R. C. *J. Am. Chem. Soc.* **1931**, *53*, 1032.

[9] Bartlett, P. D.; Lefferts, E. B. *J. Am. Chem. Soc.* **1955**, *77*, 2804.

[10] Raber, D. J.; Gariano, P. *Tetrahedron Lett.* **1971**, 4741.

to the bornyl chloride solution and to the lithium in the flask just before the reaction was begun. As the halide was added, the initially clear mixture acquired a purple color. In addition, the lithium sand, which initially had a very silvery luster, took on a black coating and sank to the bottom of the flask. When this happened, additional portions of lithium were added, up to a total of about 250% of the theoretically required amount. After completion of the addition of halide, the mixture was held at reflux for 2–10 h. The solution of bornyllithium was then transferred under positive internal flask pressure via the frit and side arm to a graduated addition funnel. The addition funnel was itself attached to another three-necked reaction flask equipped with dry nitrogen inlet, magnetic stirrer, and condenser. The yield of the bornyllithium was then determined by Gilman double titration of an aliquot using 1,2-dibromoethane.[7] The yields given by this method were in the range of 45 to 61%. Following this, the bornyllithium solution was introduced into the second vessel for reaction with an appropriate substrate.

Synthesis of (−)-Bornyldimethylsilane. Bornyllithium was prepared as described above from the reaction of 6.2 g (36 mmol) of (−)-bornyl chloride and ca. 1 g of lithium sand. The bornyl chloride addition took 4 h and the mixture was then held at reflux for 10 h. The bornyllithium solution was then added to 10 g (58 mmol) of chlorodimethylsilane (Petrarch) in 25 mL of anhydrous ether. The reaction solution was stirred for 2 h and then quenched with water. The organic layer was separated and washed with water (4 × 30 mL) and saturated aqueous sodium chloride solution and then dried over anhydrous Na_2SO_4. Pentane and diethyl ether were removed by rotary evaporation. GC analysis (15% FFAP, 155 °C) of the oil remaining showed it to consist of 15% unreacted 2 and 85% of the desired product. Purification by preparative GC (20% Carbowax 20M, 85 °C) gave the final product, an oil, α^{27}_{D} −20.91° (*l* 1 dm, neat). The IR spectrum (CCl_4) showed prominent absorption of Si-H at 2150 cm^{-1}. The ^{1}H NMR spectrum showed signals at δ 3.8 (1 SiH, multiplet), 2.0–0.9 (8 H, overlapping signals), 0.8 (9 H, br s), and at 0.05 (6 H, two sets of doublets resulting from the two diastereotopic Me groups on Si). Anal. Calcd for $SiC_{12}H_{24}$: Si, 14.26; C, 73.38; H, 12.32. Found: C, 73.43; H, 12.31.

Synthesis of (−)-Dibornylmethylsilane. Bornyllithium was prepared as described above from the reaction of 30.03 g (170 mmol) of (−)-bornyl chloride and 7.7 g of lithium sand. After the bornyl chloride addition, the mixture was held at reflux for 6 h and then stirred at room temperature for an additional 12 h. Dichloromethylsilane (Petrarch), 10.0 g (87 mmol), was then added dropwise with cooling directly to the bornyllithium solution. The resulting mixture was held at reflux for 1 h and then cautiously quenched with water. The organic layer was separated, washed with water (4 × 65 mL), and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and subsequent Kugelrohr distillation (100–125 °C/0.5 torr) yielded 19.42 g (70%) of the desired product as an oil, $[\alpha]^{24.5}_{D}$ −32.67° (*c* 10.3, EtOH). The IR spectrum (neat film) showed major absorptions at 2950, 2880, 2100, 1460, 1385, 1365, 1250, 1105, 1090, 1025, 960, 920, 880, 840, 820, and 790 cm^{-1}. The ^{1}H NMR spectrum showed signals at δ 4.0 (1 SiH, multiplet), 2.18–1.10 (16 H, overlapping signals), 1.0 (18 H, br s), and 0.38 (3 H, d). Anal. Calcd for $SiC_{21}H_{38}$: Si, 8.82; C, 79.16; H, 12.02. Found: C, 79.15; H, 12.07.

Tandem Michael Reactions for the Construction of Highly Functionalized Five-Membered Rings

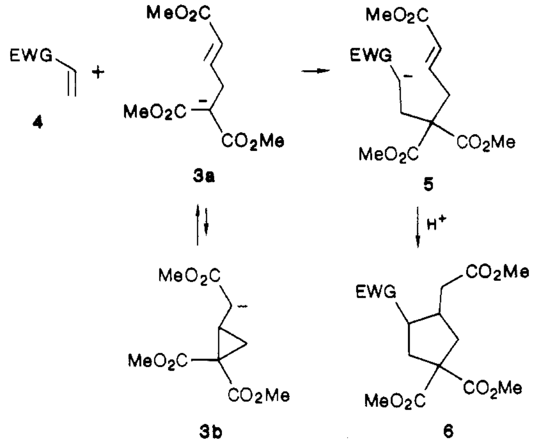
Richard A. Bunce,* Eric J. Wamsley,[1] Joey D. Pierce,[1]
A. Joe Shellhammer, Jr.,[1] and Raymond E. Drumright[1]

Department of Chemistry, Oklahoma State University,
Stillwater, Oklahoma 74078-0447

Received September 4, 1986

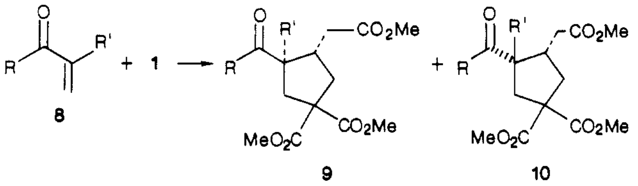
A perpetual goal of synthetic organic chemists is the development of more efficient methods for carrying out multistep transformations. Recently, several groups[2] have reported variants of a Michael–Michael ring closure procedure for the preparation of functionalized cyclohexane derivatives. In light of these reports, we describe an approach to highly functionalized five-membered rings involving a one-pot tandem Michael reaction sequence.

Scheme I[a]



[a] EWG = electron-withdrawing group.

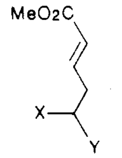
Table I. Addition of 1 to Acyclic Enones



enone	R	R′	9:10[a]	% yield (9 + 10)
8a	CH_3	H	>50:1	65
8b	CH_3	CH_3	5:2	73
8c	Ph	H	>50:1	81
8d	Ph	CH_3	18:1	83

[a] Ratios estimated by GC and NMR integration.

In designing reagents for tandem Michael reactions, it was necessary to position both a Michael donor and an acceptor moiety in the same molecule. To prevent intramolecular closure, the separation of these two subunits must be less than three carbons such that developing ring strain deters cyclization. Considering these criteria, compounds 1 and 2 were sought. Deprotonation of 1 would lead to a stabilized anion (**3a**) which would exist in equilibrium[3] with the less stable ring-closed anion **3b** (see



1 (X=Y=CO_2Me)
2 (X=Y=SO_2Me)

---

[1] Undergraduate Research Participants: E.J.W. (1985–1986); J.D.P. (Summer 1986); A.J.S. (1984–1986); R.E.D. (1985–1986).

[2] (a) Posner, G. H.; Lu, S.-B.; Asirvatham, E.; Silversmith, E. F.; Shulman, E. M. *J. Am. Chem. Soc.* **1986**, *108*, 511. (b) Danishefsky, S.; Harrison, P.; Silvestri, M.; Segmuller, B. *J. Org. Chem.* **1984**, *49*, 1319.

[3] Similar equilibria have been observed and studied previously: (a) Danishefsky, S.; Tsai, M. Y.; Dynak, J. *J. Chem. Soc., Chem. Commum.* **1975**, 7. (b) Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66.

0022-3263/87/1952-0464$01.50/0