with 2 g of Amberlite H^+ ion exchange resin. The solvent was removed under reduced pressure to yield **11a** (190 mg, 0.550 mmol, 83%), mp 130 °C dec. ^1H NMR analysis of the mixture showed the ratio of anomers to be about 9:1 α/β: IR (KBr) 3515, 3417, 3100–2400 br, 1751, 1720, 1639, 1377, 1262, 1115; ^1H NMR (d_6-DMSO, α-anomer) δ 8.36 (d, J = 6.6, 1 H), 7.32 (s, 1 H), 7.07 (d, J = 3.9, 1 H), 7.03 (s, 1 H), 5.16 (t, J = 3.9, 1 H), 4.89 (t, J = 9.0, 1 H), 4.17 (d, J = 10, 1 H), 4.08 (q, J = 6.6, 1 H), 3.74 (m, 1 H), 3.63 (t, J = 9.6, 1 H), 2.04 (s, 3 H), 1.82 (s, 3 H), 1.15 (d, J = 6.6, 3 H); ^{13}C NMR (d_6-DMSO), 174.94, 169.75, 169.70, 169.10, 90.62, 76.51, 75.61, 71.56, 68.31, 53.62, 22.66, 20.70, 18.80; HRMS (FAB) calcd for $C_{13}H_{21}N_2O_9$ (M + 1) 349.1247, found 349.1248.

2-Acetamido-4-*O*-acetyl-2-deoxy-3-*O*-[(*R*)-1-(methoxycarbonyl)ethyl]-D-glucopyranosiduronic Acid (11b). Compound **10b** (1.2 g, 2.2 mmol) was dissolved in ethanol (150 mL) and was heated at 65 °C under nitrogen. Triethylamine (2.2 mL, 1.6 g, 15.8 mmol) and formic acid (0.83 mL, 18 mmol) were added, followed by 10% Pd/C (1.6 g). Vigorous evolution of gas was observed, which subsided after about 15 min. After 45 min, the mixture was cooled and filtered. The solvent was removed under reduced pressure, and the residue was taken up in methanol and treatd with Amberlite H^+ ion exchange resin. The methanol was removed with a rotary evaporator to yield **11b** (780 mg, 2.14 mmol, 97%) as a glass, which was used without further purification. ^1H NMR analysis indicated that the ratio of anomers was about 3:1 α/β: IR (KBr) 3400–2500 br, 3300, 1740, 1660, 1550, 1375, 1230, 1125; ^1H NMR (d_6-DMSO, α-anomer) δ 7.89 (m, 1 H), 5.75 (d, J = 3, 1 H), 5.04 (br s, 1 H), 4.79 (m, 1 H), 4.27 (m, 1 H), 4.19 (d, J = 8, 1 H), 3.71 (m, 2 H), 3.61 (s, 3 H), 3.43 (m, 1 H), 2.03 (s, 3 H), 1.81 (s, 3 H), 1.18 (d, J = 6, 3 H); ^{13}C NMR (d_6-DMSO) 172.78, 169.49, 169.29, 169.04, 90.85, 76.31, 75.46, 71.23, 68.02, 52.95, 51.81, 22.57, 20.56, 18.54. Anal. Calcd for $C_{14}H_{21}NO_{10}$: C, 46.28; H, 5.83; N, 3.86. Found: C, 46.53; H, 5.73; N, 3.31.

2-Acetamido-4-*O*-acetyl-3-*O*-[(*R*)-1-carbamoylethyl]-2-deoxy-D-glucopyranosiduronic Acid Benzyl Ester (1a). Compound **11a** (333 mg, 0.960 mmol) was dissolved in dry DMF (7 mL) under nitrogen. Sodium bicarbonate (160 mg, 1.91 mmol) was added, followed by benzyl bromide (0.22 mL, 325 mg, 1.91 mmol). The mixture was stirred at 45 °C for 18 h. The solvent was removed under reduced pressure, and the residue was triturated with acetone and filtered. The residue was then triturated with water and filtered again, and the solid was washed with acetone and dried in a vacuum oven at 40 °C to yield **1a** (372 mg, 0.85 mmol, 88%), mp 220 °C dec. ^1H NMR analysis of the mixture showed the ratio of anomers to be greater than 9:1 α/β: IR (KBr) 3429, 3312, 3300–3100 br, 1744, 1678, 1378, 1245, 1121; ^1H NMR (d_6-DMSO) δ 8.41 (d, J = 6.6, 1 H), 7.36 (m, 5 H), 7.31 (s, 1 H), 7.13 (br s, 2 H), 5.16 (d, J = 3.3, 1 H), 5.10 (d, J = 11.7, 1 H), 5.01 (d, J = 11.7, 1 H), 4.85 (t, J = 10, 1 H), 4.31 (d, J = 10, 1 H), 4.10 (q, J = 6.9, 1 H), 3.70 (m, 1 H), 3.63 (t, J = 9, 1 H), 1.88 (s, 3 H), 1.81 (s, 3 H), 1.13 (d, J = 6.9, 3 H); ^{13}C NMR (d_6-DMSO) 174.85, 169.74, 167.93, 135.23, 128.50, 128.39, 90.80, 76.54, 75.37, 71.51, 68.12, 66.74, 53.54, 22.61, 20.39, 18.77; mass spectrum m/z 439.1 (M + 1). Anal. Calcd for $C_{20}H_{26}N_2O_9$: C, 54.79; H, 5.98; N, 6.39. Found: C, 54.69; H, 6.00; N, 6.41.

2-Acetamido-4-*O*-acetyl-2-deoxy-3-*O*-[(*R*)-1-(methoxycarbonyl)ethyl]-D-glucopyranosiduronic Acid Benzyl Ester (1b). Compound **11b** (705 mg, 1.94 mmol) was dissolved in dry DMF (10 mL). Sodium bicarbonate (326 mg, 3.88 mmol) was added, followed by benzyl bromide (0.46 mL, 661.5 mg, 3.87 mmol). The mixture was stirred under nitrogen at 45 °C for 16 h. The mixture was cooled to room temperature, and most of the DMF was removed under reduced pressure. The residue was dissolved in ethyl acetate, washed (water, brine), dried over magnesium sulfate, filtered, and concentrated with a rotary evaporator. The residue was subjected to column chromatography on silica gel (40 g), eluting with ethyl acetate, to give **1b** (402 mg, 0.890 mmol, 46%), mp 55–58 °C: IR (KBr) 3330, 1740, 1660, 1550, 1375, 1230, 1125; ^1H NMR δ 7.98 (d, J = 2.4, 1 H), 7.32 (m, 5 H), 5.79 (s, 1 H), 5.12 (t, J = 7.5, 1 H), 5.10 (d, J = 12.3, 1 H), 5.01 (d, J = 12.3, 1 H), 4.53 (m, 1 H), 4.42 (d, J = 10, 1 H), 4.28 (q, J = 6.9, 1 H), 3.80 (m, 2 H), 3.75 (s, 3 H), 2.01 (s, 3 H), 1.80 (s, 3 H), 1.32 (d, J = 6.9, 3 H); ^{13}C NMR (d_6-DMSO) 172.77, 169.23, 169.21, 167.91, 135.24, 128.53, 91.06, 76.20, 75.53, 71.32, 68.03, 66.77, 52.93, 51.86, 22.60, 20.36, 18.57; HRMS (FAB) calcd for $C_{21}H_{28}NO_{10}$ (M + 1) 454.1713, found 454.1706.

Registry No. α-**1a**, 129392-02-5; β-**1a**, 129392-15-0; α-**1b**, 129392-08-1; β-**1b**, 129392-16-1; **2**, 66026-10-6; **3**, 69323-67-7; **4**, 15892-26-9; **5**, 62959-83-5; **6**, 129392-03-6; **7a**, 129392-04-7; **7b**, 129392-09-2; **9a**, 129392-05-8; **9b**, 129392-10-5; **10a**, 129392-06-9; **10b**, 129392-11-6; α-**11a**, 129392-07-0; β-**11a**, 129392-13-8; α-**11b**, 129392-12-7; β-**11b**, 129392-14-9; $NaIO_4$, 7790-28-5; *N*-acetyl-α-D-glucosamine, 10036-64-3; (*S*)-(−)-2-chloropropionic acid, 29617-66-1; ruthenium trichloride hydrate, 14898-67-0.

Supplementary Material Available: NMR spectra for compounds **1b**, **7a**, **9a**, and **11a** (8 pages). Ordering information is given on any current masthead page.

The 1,5-Addition Reaction of Lithium Diorganocuprates to Methylenecyclopropyl Ketones

Edward W. Thomas* and Jacqueline R. Szmuszkovicz[1]

Metabolic Diseases Research, The Upjohn Company, Kalamazoo, Michigan 49001

Received March 26, 1990

In the last two decades, methylenecyclopropane chemistry has been advanced by numerous synthetic[2] and mechanistic[3] studies. The biologically active natural product hypoglycin[4] contains this moiety. More recently, (methylenecyclopropyl)acetyl-CoA was synthesized as a tool to study enzyme-catalyzed reactions.[5] Despite all this research, few have investigated the reaction of nucleophiles with this ring system.[6]

Due to our interest in employing methylenecyclopropanes as 4-carbon synthons,[7] we viewed methylenecyclopropyl ketones **1a** and **1b** as intriguing substrates for nucleophilic substitution reactions. These compounds contain a monoactivated strained ring due to the exomethylene group, in contrast to other monoactivated cyclopropanes which will not undergo nucleophilic addition on a ring, unless the ring is part of a larger strained ring system.[8] Bertz has studied specifically the reaction of dialkylcuprates with cyclopropanes and also concluded that double activation of the ring is necessary for good yields, while only in special strained systems would monoactivated compounds undergo reaction.[9] Falck and Mioskoski found

(1) Taken in part from the senior thesis of J. R. Szmuszkovicz, Kalamazoo College, Kalamazoo, MI, 1987.

(2) (a) Noyori, R.; Hayashi, N.; Kato, M. *J. Am. Chem. Soc.* **1971**, *93*, 4948–4950. (b) Noyori, R.; Hayashi, N.; Kato, M. *Tetrahedron Lett.* **1973**, *11*, 2983–2984. (c) Binger, P.; Buch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77–151. (d) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1–20. (e) Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1989**, *111*, 7285–7286.

(3) (a) Noyori, R.; Yamakawa, M.; Takaya, H. *Tetrahedron Lett.* **1978**, 4823–4826. (b) Berson, J. A. In *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Academic Press: New York, 1980; pp 334–348. (c) Lazzars, M. G.; Harrison, J. J.; Rule, M.; Hilinski, E. F.; Berson, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 2233–2243.

(4) (a) Carbon, J. A.; Martin, W. B.; Swett, L. R. *J. Am. Chem. Soc.* **1958**, *80*, 1002. (b) Black, D. K.; Landor, S. R. *J. Chem. Soc. C* **1968**, 288–290. (c) Bressler, R.; Corredor, C.; Brendel, K. *Pharmacol. Rev.* **1969**, *21*, 105–130.

(5) Lenn, N. D.; Shih, Y.; Stankovich, M. T.; Liu, H. *J. Am. Chem. Soc.* **1989**, *111*, 3065–3067.

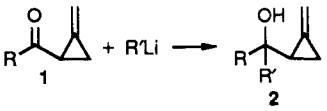
(6) (a) Goss, F. R.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc.* **1925**, *127*, 460–469. (b) Weber, A.; Neuenshwander, M. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 774–776. (c) Goldschmidt, Z.; Finkel, D. *J. Chem. Soc., Perkin Trans. 1* **1983**, 45–47. (d) For palladium activated systems, see: Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1988**, *44*, 5809–5820.

(7) (a) Thomas, E. W. *Tetrahedron Lett.* **1983**, *24*, 1467–1470. (b) Thomas, E. W. *Ibid.* **1983**, *24*, 2347–2350.

(8) For a review on the use of activated cyclopropanes in organic synthesis, see: Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66–72.

0022-3263/90/1955-6054$02.50/0

Table I. Organolithium Additions to Methylenecyclopropyl Ketones



2	R	R′	yield, %
a	C_6H_5	CH_3	94
a′	C_6H_5	$(CH_2)_3CH_3$	87
b	C_6H_{11}	CH_3	98
b′	C_6H_{11}	$(CH_2)_3CH_3$	77

one type of nucleophile ($Bu_2CuCNLi{\cdot}BF_3$) that reacts in moderate to good yields with monoactivated alkylcyclopropyl ketones.[10] These data indicated methylenecyclopropyl ketones would likely undergo a 1,5-addition reaction with one of these reagents, yet there exists little literature precedent to predict the regioselectivity of the reaction. The purpose of this report is to note the reaction of ketones **1a** and **1b** with lithium dialkylcuprates and their reaction products.

Ketones **1a** and **1b** were synthesized from the corresponding acids, which were treated at −78 °C with MeLi followed by (methylenecyclopropyl)lithium.[7a,11] As expected, reaction of these ketones with MeLi and BuLi afforded only 1,2-addition products with no evidence for 1,5-addition (Table I).

The addition of dimethyl cuprate to the phenyl ketone **1a** in Et_2O afforded the 1,5-addition products listed in Table II. Compounds **3a** and **5a** were carefully separated on a silver nitrate impregnated silica gel column.[12] Even with a silver nitrate column, we could not separate **4a** as an impurity from **5a**. Authentic **4a** was prepared in 26% yield from **3a** by deprotonation, followed by kinetic quench with acetic acid[13] In the reaction, the enolate of **4a** is likely formed and upon quenching the more stable olefin **3a** (a 5:1 mixture of isomers) is also produced. The structure of the major product **5a** was confirmed by comparison to an authentic sample.[14] Compound **5a** arises formally from attack at the vinyl ring carbon, through most likely an addition–elimination mechanism. Although nucleophilic substitution reaction at a vinyl carbon is known, it is not common unless the substrate is activated.[15] By simply changing the solvent to THF in this reaction, no **5a** was detected, although a trace of the 1,2-adduct **2a** was isolated. In the reaction of dimethyl cuprate with cyclohexyl ketone **1b**, in Et_2O, the adducts **3b**, **4b**, and **5b** were formed (Table II). These compounds, as well as products from subsequent reactions, could be completely separated by silver nitrate chromatography.

Dibutyl cuprate selectively attacks the olefin ring carbon of **1a** to yield only butyl adduct **6a**, hydride substitution product **7a**, and dimer **8a**. Adduct **7a** may arise due to β-hydride elimination of the butyl organometallic reagent, a pathway not available to dimethyl cuprates. The formation of the dimer **8a** could be the result of coupling of vinyl cuprates which are unstable.[16] However, lowering the temperature of the reaction to −50 °C did not change the ratio of products. Conducting the reaction in THF favored the formation of **6a**. As has been observed for other organocopper reactions, the choice of solvent (Et_2O or THF) had a major influence on product ratios in these reactions.[17] The addition of dibutyl cuprate to alkyl ketone **1b** produced only compounds arising from addition to the olefin ring carbon (Table III).

Although the mechanism of organocuprate additions to unsaturated compounds remains an area of active research, House[18] and Casey[19] believe for 1,5-addition reactions the organocuprate acts as a nucleophile to open the strained cyclopropyl ring. While recognizing this, we believe the olefin and the cuprate may form a complex, as has been proposed for conjugate addition reactions,[20a,21] which serves to direct the nucleophilic addition as evidenced by the olefin substituted products in Table III. The reaction of **1a**, in Et_2O, with a higher order cuprate ($Bu_2CuCNLi{\cdot}BF_3$)[22] or a cuprate generated from $CuBr{\cdot}Me_2S$ produced the same results as listed in Table III. Although the addition of Me_3SiCl to cuprate reactions has been recently explored,[20] its addition to the reaction of **1a** and dibutyl cuprate optimized only the yield of **7a**.

In summary, we have demonstrated these readily available methylenecyclopropyl ketones reacted in moderate to high yields with dimethyl and dibutyl cuprates, although a number of products were formed. Of these reagents, dibutyl cuprate proved more selective by only adding to the olefin ring carbon of the alkyl or aryl ketones, **1a** or **1b**.

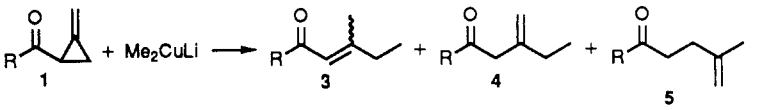
Experimental Section

^1H NMR spectra were recorded at 90 or 300 MHz. ^{13}C NMR spectra were recorded at 20 or 75 MHz. Melting points in open capillaries are uncorrected. Unless specified, all Burdick and Jackson solvents and reagents purchased from Aldrich Chemical Co. were used without further purification. THF and Et_2O were dried over molecular sieves.[23] $AgNO_3$-impregnated SiO_2 was prepared by dissolving the $AgNO_3$ in CH_3CN and adding SiO_2.[12] All compounds were dried over $MgSO_4$. The solvent was removed on a rotovap under house vacuum. Unless indicated otherwise, all products were obtained as colorless liquids.

2-Methylenecyclopropyl Phenyl Ketone (1a). Benzoic acid (12.2 g, 100 mmol) and THF (100 mL) were cooled to −78 °C. MeLi (77 mL, 100 mmol, 1.3 M in Et_2O) was added over 10 min. After an additional 0.5 h, the reaction was warmed to room temperature over 1.5 h. (Methylenecyclopropyl)lithium (200 mmol), generated under standard conditions[7a] from *n*-BuLi (134 mL, 200 mmol, 1.5 M in hexane) and methylenecyclopropane (20 mL, 320 mmol) in THF (200 mL), was added to the above reaction, which had been recooled to −78 °C. After the reaction was allowed to warm to room temperature, it was quenched by pouring into rapidly stirred H_2O. The aqueous portion was extracted with Et_2O (3 × 100 mL). The organic portion was dried and concentrated

(9) Bertz, S. H.: Dabbagh, G.; Cook, J. M.; Honkan, V. *J. Org. Chem.* **1984**, *49*, 1739–1743.
(10) Mioskowski, C.; Manna, S.; Falck, J. R. *Tetrahedron Lett.* **1983**, *24*, 5521–5524.
(11) For an alternate route see: Maurin, R.; Bertrand, M. *Bull. Soc. Chim. Fr.* **1970**, 2261–2270.
(12) Gupta, A. S.; Dev, S. *J. Chromatogr.* **1963**, *12*, 189–195.
(13) Zimmerman, H. E. *Acc. Chem. Res.* **1987**, *20*, 263–268.
(14) (a) Tsuda, T.; Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381–6384. (b) Tsuda, T.; Okada, M.; Nishi, S.; Saegusa, T. *J. Org. Chem.* **1986**, *51*, 421–426.
(15) (a) Patai, S.; Rappoport, Z. In *The Chemistry of Alkenes*; Patai, S., Ed.; Interscience: London, 1964: pp 525–546. (b) Fujisawa, T.; Sato, T.; Gotoh, Y.; Kawashima, M.; Kawara, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3555–3559.
(16) (a) Kluge, A. F.; Untch, K. G.; Fried, J. H. *J. Am. Chem. Soc.* **1972**, *94*, 7827–7832. (b) House, H. O.; Chu, C.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460–1469.
(17) Posner, G. H. *Org. React.* **1972**, *19*, 1–113.
(18) (a) House, H. O.; McDaniel, W. C.; Sieloff, R. F.; Vanderveer, D. *J. Org. Chem.* **1978**, *43*, 4316–4323. (b) House, H. O.; Prabhu, A. V.; Lee, L. F. *Ibid.* **1976**, *41*, 3067–3076.
(19) Casey, C. P.; Cesa, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 4236–4244.
(20) (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6019–6022. (b) Alexakis, A.; Berlan, J.; Besace, Y. *Ibid.* **1986**, *27*, 1047–1050.
(21) Bertz, S. H.; Smith, R. A. J. *J. Am. Chem. Soc.* **1989**, *111*, 8276–8277.
(22) For a review of higher order mixed organocuprates, see: Lipshutz, B. H. *Synthesis*, **1987**, 325–341.
(23) Burfield, D. R.; Gan, G.; Smithers, R. H. *J. Appl. Chem. Biotechnol.* **1978**, *28*, 23–30.

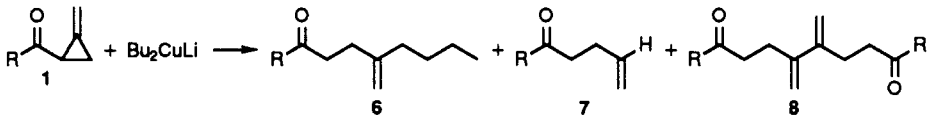
Table II. Addition of Dimethyl Cuprate to Methylenecyclopropyl Ketones



	R	solvent	temp, °C	ratio[a] 3	4	5	yield, %
a	C_6H_5	Et_2O	−10	8.0[b]	1.0	24.0	64
a	C_6H_5	THF	−10	8.0	1.0		80[c]
b	C_6H_{11}	Et_2O	−10	1.3[d]	1.9	1.0	58

[a] Ratios are based on isolated yields. [b] 5:1 mixture of *E* and *Z* isomers. [c] The other product isolated was **2a** (8%). [d] 2.4:1 mixture of *E* and *Z* isomers.

Table III. Addition of Dibutyl Cuprate to Methylenecyclopropyl Ketones



	R	solvent	temp, °C	ratio[a] 6	7	8	yield, %
a	C_6H_5	Et_2O	−30	3.0	2.4	1.0	96
	C_6H_5	Et_2O	−50	1.8	1.7	1.0	56
	C_6H_5	THF	−50	6.0	3.0	1.0	60
b	C_6H_{11}	Et_2O	−30	1.0	1.4	1.4	75

[a] Ratios are based on isolated yields.

in vacuo to 18.4 g. This was chromatographed on a Waters' Prep-500 (SiO_2 column) and eluted with 2% Et_2O in hexanes to yield 13.23 g. Bulb-to-bulb distillation (75–100 °C at 0.3 mm) of this in a Kugelrohr oven afforded **1a** (12.85 g, 81%): ^1H NMR ($CDCl_3$) δ 1.70–1.82 (m, 1 H, $=CCH_2$), 2.10–2.20 (m, 1 H, $=CCH_2$), 3.22–3.34 (m, 1 H, O=CCH), 5.40–5.55 (m, 2 H, $=CH_2$), 7.40–7.62 (m, 3 H, arom), 7.98–8.10 (m, 2 H, arom); ^{13}C NMR ($CDCl_3$) ppm 196.7 (s), 137.4 (s), 132.9 (s), 132.7 (d), 129.0 (d), 128.2 (d), 103.3 (t), 22.9 (d), 11.8 (t); IR (neat) 1816, 1783, 1675 (C=O), 1597, 1579 cm^{-1}; MS for $C_{11}H_{10}O$ *m/z* (relative intensity) 158 (M^+, 58), 157 (33), 129 (30), 115 (21), 105 (65), 77 (100). Anal. Calcd for $C_{11}H_{10}O$: C, 83.52; H, 6.37. Found: C, 83.73; H, 6.09.

Cyclohexyl Methylenecyclopropyl Ketone (1b). In a similar manner **1b** (11.93 g, 73%) was synthesized: distillation range 70–90 °C at 0.3 mm; ^1H NMR ($CDCl_3$) δ 1.10–2.10 (m, 12 H, CH_2), 2.39–2.50 (m, 1 H, O=CCH), 2.55–2.68 (m, 1 H, O=CCH), 5.30–5.52 (m, 2 H, $=CH_2$); ^{13}C NMR ($CDCl_3$) ppm 210.1 (s), 132.4 (s), 103.2 (t), 50.1 (d), 28.31 (t), 28.25 (t), 25.7 (t), 25.6 (t), 25.4 (t), 24.8 (d), 11.6 (t); IR (neat) 1762, 1739, 1696 (C=O), 1451, 1336, 1324 cm^{-1}; MS for $C_{11}H_{16}O$ *m/z* (relative intensity) 164 (M^+, 62), 149 (14), 121 (42), 109 (33), 83 (100), 81 (79). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.40; H, 9.90.

General Procedure for the Preparation of Alcohols 2. 1-(Methylenecyclopropyl)-1-phenylethanol (2a). Ketone **1a** (4.37 g, 27.6 mmol) and THF (80 mL) were cooled to −78 °C, and MeLi (27 mL, 43 mmol, 1.6 M in Et_2O) was added in one portion. The reaction was stirred for 1 h and was quenched by pouring into H_2O. The aqueous portion was extracted with Et_2O. The organic portions were combined, dried, and evaporated in vacuo to afford analytically pure **2a** (4.5 g, 94%) as an unseparated 4:1 mixture of diastereomers: ^1H NMR ($CDCl_3$) δ 1.05–1.30 (m, 2 H, CH_2), 1.54 (s, 3 H, CH_3), 1.78 (s, 1 H, OH), 1.91–2.19 (m, 1 H, CH), 5.30–5.60 (m, 2 H, $=CH_2$), 7.20–7.70 (m, 5 H, arom); ^{13}C NMR ($CDCl_3$) ppm (major diastereomer) 147.7 (s), 132.5 (s), 128.0 (d), 126.8 (d), 124.9 (d), 104.9 (t), 72.7 (s), 28.0 (q), 26.5 (d), 6.2 (t); IR (neat) 3434 (OH), 1602 cm^{-1}; MS for $C_{12}H_{14}O$ *m/z* (relative intensity) 174 (M^+, 0.2), 173 (0.6), 159 (4), 156 (3), 131 (100), 121 (39), 105 (37), 91 (42), 43 (100). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 83.02; H, 8.26.

α-Butyl-α-(methylenecyclopropyl)benzenemethanol (2a′): yield 87% (1.19 g) as an unseparated 3.3:1 mixture of diastereomers; ^1H NMR ($CDCl_3$) δ 0.80–0.95 (m, 3 H, CH_3), 1.00–1.40 (m, 6 H, CH_2), 1.59 (s, 1 H, OH), 1.70–1.84 (m, 0.4 H, $=CCH_2$), 1.84–1.96 (m, 1.6 H, $=CCH_2$), 2.00–2.10 (m, 0.2 H, CH), 2.10–2.20 (m, 0.8 H, CH), 5.25 (s, 0.8 H, $=CH_2$), 5.44 (s, 0.8 H, $=CH_2$), 5.50–5.60 (m, 0.4 H, $=CH_2$), 7.20–7.60 (m, 5 H, arom); ^{13}C NMR ($CDCl_3$) ppm (major diastereomer) 146.6 (s), 132.2 (s), 127.9 (d), 126.6 (d), 125.4 (d), 104.9 (t), 74.4 (s), 41.3 (t), 25.8 (t), 25.3 (d), 23.0 (t), 13.9 (q), 5.7 (t); IR (neat) 3555, 3473 (OH), 1676, 1600, 1447 cm^{-1}; MS for $C_{15}H_{20}O$ *m/z* (relative intensity) 216 (M^+, 1), 163 (89), 159 (93), 141 (33), 131 (89), 115 (24), 105 (86), 85 (100). Anal. Calcd for $C_{15}H_{20}O$: C, 83.29; H, 9.32. Found: C, 83.12; H, 9.18.

α-Methyl-α-(methylenecyclopropyl)cyclohexanemethanol (2b): yield 98% (530 mg) as an unseparated 3.5:1 mixture of diastereomers; ^1H NMR ($CDCl_3$) δ 1.00–1.55 (m, 12 H, CH_2, CH_3), 1.61–1.75 (m, 2 H, $=CCH_2$), 1.76–2.00 (m, 4 H, OH, =CCH, OCCH, CH_{ax}), 5.39–5.56 (m, 2 H, $=CH_2$); ^{13}C NMR ($CDCl_3$) ppm (major diastereomer) 133.0 (s), 104.8 (t), 73.8 (s), 49.4 (d), 27.5 (t), 27.4 (t), 26.6 (t), 26.4 (t), 24.2 (d), 22.7 (q), 5.1 (t); IR (neat) 3475 (OH), 1451 cm^{-1}; MS for $C_{12}H_{20}O$ *m/z* (relative intensity) 165 (1), 127 (8), 109 (4), 97 (100), 83 (36). Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 79.68: H, 11.48.

α-Butyl-α-(methylenecyclopropyl)cyclohexanemethanol (2b′). The crude product was chromatographed on a Waters' Prep-500 (SiO_2, hexane/EtOAc, 19/1) to yield 922 mg (77%) of **2b′** as an unseparated 3:1 mixture of diastereomers: ^1H NMR ($CDCl_3$) δ 0.90–2.10 (m, 23 H), 5.32–5.58 (m, 2 H); ^{13}C NMR ($CDCl_3$) ppm (major diastereomer) 133.4, 105.4, 73.8, 46.2, 38.1, 27.5, 27.0, 26.9, 26.8, 26.6, 23.5, 23.4, 14.2, 4.8; IR (neat) 3493 (OH), 1742, 1448 cm^{-1}; MS for $C_{15}H_{26}O$ *m/z* (relative intensity) 207 (1), 169 (14), 165 (26), 139 (100), 83 (94). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.87; H, 11.47.

2-Methyl-1-butenyl Phenyl Ketone (3a) and 3-Methyl-3-buteny Phenyl Ketone (5a). Lithium dimethyl cuprate was generated from CuI (2.09 g, 11 mmol), in Et_2O (50 mL) at −10 °C, and MeLi (16.0 mL, 20 mmol, 1.25 M in Et_2O) over 1 h. To the clear solution, with some solid present, was added ketone **1a** (1.0 g, 6.3 mmol) dissolved in Et_2O (3 mL). The yellow mixture was stirred for 3 h. The reaction was quenched with saturated NH_4Cl (100 mL) and extracted with Et_2O (3 × 100 mL). The organic fractions were combined, dried, and evaporated in vacuo to yield 1.05 g. This was chromatographed (100 g of SiO_2/5% $AgNO_3$, 2.5% EtOAc in hexanes), and less pure fractions were rechromatographed on the same column to yield **3a** (130 mg, 12%), a mixture of **3a** + **5a** (1:1.3, 100 mg, 9%), and **5a** (470 mg, 43%, contaminated with a slight amount of **4a**) identical with authentic material. Data for **3a**, a 5:1 mixture of olefin isomers: ^1H NMR

($CDCl_3$) δ 1.16 (t, 3 H, J = 7.4 Hz, CH_3), 2.00 (s, minor isomer), 2.20 (s, 3 H, $=CCH_3$), 2.28 (q, 2 H, J = 7.4 Hz, $=CCH_2$), 2.63 (q, minor isomer), 6.73 (s, 1 H, =CH), 7.24–7.60 (m, 3 H, arom), 7.90–7.96 (m, 2 H, arom); ^{13}C NMR ($CDCl_3$) ppm for both isomers 191.9, 161.1, 139.4, 132.2, 128.4, 128.2, 120.7, 119.5, 34.3, 27.4, 25.1, 19.8, 12.6, 12.2; IR (neat) 1665, 1613, 1525, 1449 cm^{-1}; MS for $C_{12}H_{14}O$ m/z (relative intensity) 174 (M^+, 100), 173 (42), 159 (14), 145 (87), 127 (9), 105 (25), 97 (18). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.77; H, 8.05. Data for **5a** contaminated with 5% **4a**: ^1H NMR ($CDCl_3$) δ 1.86 (s, 3 H, CH_3), 2.45 (t, 2 H, J = 7.5 Hz, $=CCH_2$), 3.12 (t, 2 H, J = 7.5 Hz, $O=CCH_2$), 4.72 (s, 1 H, =CH), 4.77 (s, 1 H, =CH), 7.40–7.60 (m, 3 H, arom), 7.90–8.00 (m, 2 H, arom); ^{13}C NMR ($CDCl_3$) ppm 199.7, 144.7, 137.1, 133.0, 128.6, 128.1, 110.2, 36.9, 32.0, 22.7; IR (neat) 2969, 1687, 1650, 1598, 1450, 1202, 889, 745, 691 cm^{-1}; MS for $C_{12}H_{14}O$ m/z (relative intensity) 174 (M^+, 6), 159 (1), 145 (2), 106 (8), 105 (100), 77 (26). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.66; H, 8.09.

2-Methylenebutyl Phenyl Ketone (4a). A solution of LDA (generated from diisopropylamine (1.4 g, 14 mmol) in THF (30 mL) and n-butyllithium (9.24 mL, 14 mmol) was cooled to −78 °C. Ketone **3a** (2.2 g, 12.6 mmol), dissolved in THF (14 mL), was added to the LDA solution over 5 min. After 2 h the reaction was quenched with AcOH (1.4 mL). The mixture was brought to room temperature over 15 min, and saturated aqueous NH_4Cl (70 mL) was added. The mixture was extracted with Et_2O (3 × 120 mL). The organic layers were combined, dried, and concentrated in vacuo to 2.6 g. The mixture of olefins was chromatographed (400 g of $SiO_2/AgNO_3$ (2%), 2% EtOAc in hexanes) to yield **3a** (1.34 g, 61%) and **4a** (570 mg, 26%). Data for **4a**: ^1H NMR ($CDCl_3$) δ 1.06 (t, 3 H, J = 7.4 Hz, CH_3), 2.13 (q, 2 H, J = 7.4 Hz, CH_2), 3.70 (s, 2 H, $O=CCH_2$), 4.86 (d, 1 H, J = 1.1 Hz, =CH), 4.98 (d, 1 H, J = 0.7 Hz, =CH), 7.40–7.60 (m, 3 H, arom), 7.90–8.10 (m, 2 H, arom); ^{13}C NMR ($CDCl_3$) ppm 198.3, 145.2, 136.8, 128.5, 128.4, 112.6, 46.4, 29.1, 12.1; IR (neat) 1690, 1600, 1455 cm^{-1}; MS for $C_{12}H_{14}O$ m/z (relative intensity) 174 (M^+, 41), 173 (27), 172 (46), 159 (30), 145 (60), 129 (29), 115 (27), 105 (100), 77 (100).

Cyclohexyl 2-Methyl-1-butenyl Ketone (3b), Cyclohexyl 3-Methyl-3-butenyl Ketone (5b), and Cyclohexyl 2-Methylenebutanyl Ketone (4b). Lithium dimethyl cuprate was generated from CuI (8.4 g, 44 mmol), in Et_2O (200 mL) at −10 °C, and MeLi (64.0 mL, 80 mmol) over a 1-h period. Ketone **1b** (4.0 g, 24 mmol) dissolved in Et_2O (12 mL) was added to the clear solution of the cuprate. After 3 h the dark yellow slurry was quenched with saturated NH_4Cl (200 mL). The aqueous layer was extracted with Et_2O (3 × 200 mL). The organic portions were combined, dried, and concentrated in vacuo to 4.2 g of a mixture of three compounds. The compounds were chromatographed on a 5% $AgNO_3$ impregnated SiO_2 column (400 g, multiple elutions with 2% EtOAc in hexanes) to yield **3b** (0.95 g, 22%), **5b** (0.57 g, 13%), a mixture of **5b** and **4b** (0.42 g, 10%, **5b**:**4b** = 1:1.4), and **4b** (1.11 g, 26%). Data for **3b**, a 2.4:1 mixture of E and Z isomers: ^1H NMR ($CDCl_3$)δ 1.01–1.11 (m, 3 H, CH_3), 1.12–1.41 (m, 5 H), 1.62–1.89 (m, 5 H), 1.87 (d, 0.87 H, J = 1.3 Hz, $=CCH_3$, Z), 2.12 (d, 2.13 H, J = 1.2 Hz, $=CCH_3$, E), 2.15 (q, 1.4 H, J = 7.5 Hz, $=CCH_2$, E), 2.24–2.38 (m, 1 H, O=CCH), 2.56 (q, 0.6 H, J = 5.7 Hz, $=CCH_2$, Z), 6.05–6.11 (m, 1 H, =CH); ^{13}C NMR ($CDCl_3$) ppm (major isomer) 204.6, 160.3, 121.2, 51.7, 34.1, 28.7, 26.0, 25.8, 19.3, 12.1; IR (neat) 1685, 1619, 1450, 1146 cm^{-1}; MS for $C_{12}H_{20}O$ m/z (relative intensity) 180 (M^+, 17), 170 (3), 151 (4), 111 (17), 97 (100), 83 (61). Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 79.84; H, 11.08. Data for **5b**: ^1H NMR ($CDCl_3$) δ 1.11–1.45 (m, 5 H), 1.59–1.91 (m, 5 H), 1.73 (s, 3 H, CH_3), 2.26 (t, 2 H, J = 7.4 Hz, $=CCH_2$), 2.30–2.42 (m, 1 H, O=CCH), 2.56 (t, 2 H, J = 7.4 Hz, $O=CCH_2$), 4.65 (s, 1 H, =CH), 4.72 (s, 1 H, =CH); ^{13}C NMR ($CDCl_3$) ppm 213.5, 144.9, 109.9, 50.9, 38.8, 31.4, 28.5, 25.9, 25.7, 22.7; IR (neat) 1709, 1650, 1620, 1450 cm^{-1}; MS for $C_{12}H_{20}O$ m/z (relative intensity) 180 (M^+, 5), 165 (2), 139 (2), 125 (3), 111 (30), 97 (25), 83 (100). Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 80.05; H, 11.21. Data for **4b**: ^1H NMR ($CDCl_3$) δ 1.03 (t, 3 H, J = 7.4 Hz, CH_3), 1.10–1.41 (m, 5 H), 1.60–1.90 (m, 5 H), 2.03 (q, 2 H, J = 7.5 Hz, $=CCH_2$), 2.49–2.51 (m, 1 H, O=CCH), 3.16 (s, 2 H, $O=CCH_2$), 4.8 (s, 1 H, =CH), 4.91 (s, 1 H, =CH); ^{13}C NMR ($CDCl_3$) ppm 212.0, 144.9, 112.4, 50.1, 48.8, 29.0, 28.6, 25.9, 25.7, 12.0; IR (neat) 1709, 1646, 1450 cm^{-1}; MS for $C_{12}H_{20}O$ m/z (relative intensity) 180 (M^+, 27), 165 (2), 151 (4), 137 (2), 125 (5), 111 (16), 97 (100), 83 (27). Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 79.96; H, 11.07.

3-Methyleneheptyl Phenyl Ketone (6a), 3-Butenyl Phenyl Ketone (7a), and 4,5-Dimethylene-1,8-diphenyloctane-1,8-dione (8a): Lithium dibutyl cuprate was generated from CuI (2.1 g, 11 mmol), in Et_2O (50 mL) at −30 °C, and n-butyllithium (13.3 mL, 20.0 mmol, 1.5 M in hexane) over 1.5 h. Ketone **1a** (1.0 g, 6.3 mmol), dissolved in Et_2O (4 mL), was added to the cuprate. After 3 h the reaction was quenched with saturated aqueous NH_4Cl (100 mL), and the aqueous layer was extracted with Et_2O (3 × 100 mL) and CH_2Cl_2 (100 mL). The organic portions were combined, dried, and concentrated in vacuo to 1.3 g. The semisolid was swirled with hexane/EtOAc, 30/1, and filtered to yield 190 mg of a white solid. This was chroamtographed (SiO_2, CH_2Cl_2) on a Waters' Prep-500 to afford **8a** (150 mg, 15%): mp 136 °C; ^1H NMR ($CDCl_3$) δ 2.73 (t, 4 H, J = 8.1 Hz, $=CCH_2$), 3.15 (t, 4 H, J = 7.9 Hz, $O=CCH_2$), 5.07 (s, 2 H, =CH), 5.18 (s, 2 H, =CH), 7.40–7.50 (m, 4 H, arom), 7.50–7.60 (m, 2 H, arom), 7.90–8.00 (m, 4 H, arom); ^{13}C NMR ($CDCl_3$) ppm 199.6, 146.2, 137.1, 133.0, 128.6, 128.1, 112.8, 37.8, 28.7; IR (mineral oil mull) 1685, 1595, 1282, 1205 cm^{-1}; MS for $C_{22}H_{22}O_2$, m/z (relative intensity) 318 (M^+, 3), 290 (3), 213 (6), 196 (11), 185 (7), 105 (100), 77 (70). A small amount of **8a** (16 mg) was sublimed (120 °C at 0.05 mm) to yield pure **8a** (15 mg): mp 136–137 °C. Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.97. Found: C, 83.05; H, 7.18. The filtrate from above was concentrated to 980 mg. This was chromatographed (200 g of 5% $AgNO_3/SiO_2$: hexane/EtOAc, 30/1) to yield **6a** (620 mg, 45%) followed by **7a** (360 mg, 36%). Data for **6a**: ^1H NMR ($CDCl_3$) δ 0.91 (t, 3 H, J = 7.2 Hz, CH_3), 1.22–1.50 (m, 4 H), 2.08 (t, 2 H, J = 7.5 Hz, $=CCH_2$), 2.45 (t, 2 H, J = 7.7 Hz, $O=CCH_2CH_2$), 3.12 (t, 2 H, J = 7.7 Hz, $O=CCH_2$), 4.74 (s, 1 H, =CH), 4.77 (s, 1 H, =CH), 7.40–7.60 (m, 3 H, arom), 7.90–8.01 (m, 2 H, arom); ^{13}C NMR ($CDCl_3$) ppm 199.7, 148.9, 137.2, 132.9, 128.6, 128.1, 109.1, 37.1, 36.2, 30.2, 30.1, 22.5, 14.0; IR (neat) 1689, 1645, 1598, 1450 cm^{-1}; MS for $C_{15}H_{20}O$ m/z (relative intensity) 261 (M^+, 0.08), 187 (1), 173 (1), 159 (1), 120 (7), 105 (100), 77 (31). Anal. Calcd for $C_{15}H_{20}O$: C, 83.29; H. 9.32. Found: C, 82.90; H, 9.17. Corrected for 0.21% H_2O. Data for **7a**: ^1H NMR ($CDCl_3$) δ 2.50 (dt, 2 H, J = 7.9 Hz, J = 7.2 Hz, $=CCH_2$), 3.09 (t, 2 H, J = 7.4 Hz, $O=CCH_2$), 4.95–5.15 (m, 2 H, $=CH_2$), 5.81–6.00 (m, 1 H, =CH), 7.40–7.61 (m, 3 H, arom), 7.90–8.05 (m, 2 H, arom); ^{13}C NMR ($CDCl_3$) ppm 199.4, 137.3, 137.1, 133.0, 128.6, 128.1, 115.3, 37.8, 28.2; IR (neat) 1688, 1641, 1598, 1450 cm^{-1}; MS for $C_{11}H_{12}O$, m/z (relative intensity) 160 (M^+, 4), 158 (14), 144 (3), 129 (7), 115 (12), 105 (100), 77 (53). Anal. Calcd for $C_{11}H_{12}O$: C, 82.47; H, 7.55. Found: C, 82.36; H, 7.60.

Cyclohexyl 3-Methyleneheptyl Ketone (6b), Cyclohexyl 3-Butenyl Ketone (7b), and 1,8-Dicyclohexyl-4,5-dimethyleneheptane-1,8-dione (8b). Lithium dibutyl cuprate was prepared from CuI (4.2 g, 22 mmol) in Et_2O (100 mL) and n-BuLi (26.6 mL, 40 mmol, 1.5 M in hexane) by stirring for 1 h at −30 °C. Ketone **1b** (2.0 g, 12.2 mmol), dissolved in Et_2O (5 mL), was added to the brown reaction. After 5 h the starting material was consumed and the reaction was quenched with saturated NH_4Cl (200 mL). The aqueous portion was extracted with Et_2O (3 × 100 mL), and the organic layer was combined, dried, and evaporated in vacuo to yield 3.0 g of crude material. Chromatography of this material on a Waters' Prep-500 (SiO_2, hexane/EtOAc, 30/1) afforded a mixture of **6b** and **7b** and pure **8b** (550 mg, 27%). Careful rechromatography of **6b** and **7b** under similar conditions afforded **6b** (500 mg, 18%), a mix of **6b** and **7b** (90 mg, 1:1), and **7b** (530 mg, 26%). Data for **6b**: ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, J = 6 Hz, CH_3), 1.10–1.50 (m, 9 H), 1.62–1.71 (m, 1 H), 1.71–1.91 (m, 4 H), 2.01 (t, 2 H, J = 7.5 Hz, $=CCH_2$), 2.26 (t, 2 H, J = 7.7 Hz, $O=CCH_2CH_2$), 2.31–2.42 (m, 1 H, O=CCH), 2.58 (t, 2 H, J = 7.7 Hz, $O=CCH_2$), 4.66 (s, 1 H, =CH), 4.72 (s, 1 H, =CH); ^{13}C NMR ($CDCl_3$) ppm 213.5, 149.0, 108.7, 50.9, 39.0, 36.2, 30.0, 29.6, 28.6, 25.9, 25.7, 22.5, 14.0; IR (neat) 1710, 1645, 1450 cm^{-1}; MS for $C_{15}H_{26}O$, m/z (relative intensity) 222 (M^+, 12), 205 (0.4), 167 (1), 139 (4), 111 (32), 83 (100). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.05; H, 11.62. Data for **7b**: ^1H NMR ($CDCl_3$) δ 1.09–1.49 (m, 5 H), 1.51–1.84 (m, 5 H), 2.20–2.43 (m, 3 H), 2.54 (t, 2 H, J = 7.2 Hz, $O=CCH_2$), 4.90–5.10 (m, 2 H, $=CH_2$), 5.71–5.90 (m, 1 H, =CH); ^{13}C NMR ($CDCl_3$) ppm 213.3, 137.5, 115.0, 50.9, 39.7, 28.5, 27.7, 25.9, 25.7; IR (neat) 1709, 1642,

1450 cm^{-1}; MS for $C_{11}H_{18}O$ m/z (relative intensity) 166 (M^+, 11), 137 (0.5), 124 (0.5), 111 (64), 83 (100), 55 (81). Anal. Calcd for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.55; H, 11.08. Data for **8b**: ^{1}H NMR ($CDCl_3$) δ 1.10-1.50 (m, 10 H), 1.51-1.95 (m, 10 H), 2.18-2.69 (m, 10 H), 4.96 (m, 2 H, =CH), 5.07 (m, 2 H, =CH); ^{13}C NMR ($CDCl_3$) ppm 213.3, 146.2, 112.5, 50.9, 39.7, 28.5, 28.0, 25.9, 25.7; IR (mineral oil mull) 1703, 1590, 1445, 1395, 1389 cm^{-1}; MS for $C_{22}H_{34}O_2$ m/z (relative intensity) 330 (M^+, 7), 315 (1), 312 (2), 247 (3), 229 (2), 219 (14), 202 (8), 191 (9), 111 (33), 83 (100), 55 (30). Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.59; H, 10.66.

Acknowledgment. We wish to thank the Upjohn Company's Physical and Analytical Chemistry Unit for elemental analyses, mass spectra, and IR spectroscopy.

Preparation of 1-Substituted Bicyclo[2.2.1]heptanes by Anionic Cyclization of a 5-Hexen-1-yllithium

William F. Bailey* and Atmaram D. Khanolkar

Department of Chemistry, University of Connecticut, Storrs, Connecticut 06269-3060

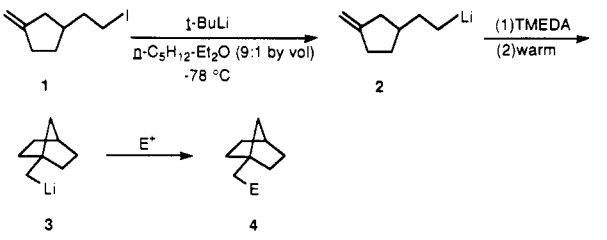
Received March 26, 1990

The facile regiospecific isomerization of a 5-hexen-1-yllithium to a (cyclopentyl)methyllithium at room temperature[1] provides a convenient route to functionalized cyclopentylmethyl-containing products.[2-4] As shown below, the precursor olefinic alkyllithiums may be easily prepared in high yield by low-temperature lithium-iodine exchange between an olefinic alkyl iodide and *tert*-butyllithium (*t*-BuLi)[5,6] and the organometallic formed upon 5-*exo*-*trig* cyclization may be functionalized by reaction with any of a variety of electrophiles. Herein we report that this methodology may be used to advantage for the preparation of 1-substituted bicyclo[2.2.1]heptanes via cyclization of the olefinic alkyllithium derived from readily available 3-(2-iodoethyl)-1-methylenecyclopentane (**1**). The two-step, one-pot synthetic sequence is summarized in Scheme I.

The synthesis of the requisite iodide, **1**, which is easily accomplished in straightforward fashion (Scheme II) from 2-cyclopenten-1-one,[7] is detailed in the Experimental Section.

Treatment of a 0.1 M solution of **1** in *n*-pentane-diethyl ether (3:2 by volume) at -78 °C with 2.2 equiv of *t*-BuLi following our general protocol for low-temperature lithium-iodine interchange[5] serves to generate cleanly the corresponding olefinic alkyllithium (**2**) as demonstrated by the fact that quench of such a reaction mixture with methanol at -78 °C affords 3-ethyl-1-methylenecyclopentane in virtually quantitative yield.

Scheme I



Scheme II

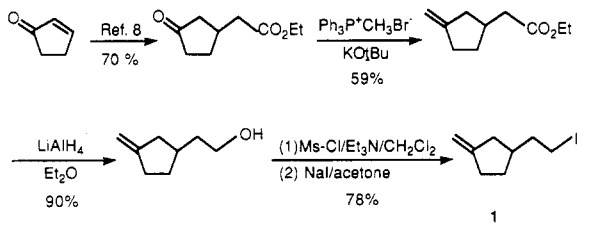
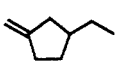
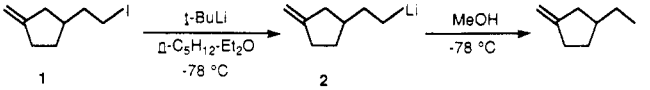


Table I. Exploratory Cyclizations of Organolithium 2[a]

entry	solvent system[b]	time, min	products, % relative yield (% d)[c]	
				
1	2:3	6	96	4 (100)
2	2:3	11	76	24 (88)
3	2:3	20	37	63 (80)
4	2:3	60	18	82 (55)
5	9:1	20	40	60
6	9:1	30	29	71
7	9:1	40	18	82 (86)
8	9:1	60	17	83 (70)

[a] TMEDA (2.2 equiv) was added at -78 °C to a solution of olefinic alkyllithium **2**, generated by lithium-iodine exchange between **1** and *t*-BuLi, the mixture was stirred for 5 min at -78 °C and then allowed to warm for the specified period of time before addition of MeOH (or MeOD). [b] Relative proportions by volume of *n*-pentane-diethyl ether used for the exchange reaction. [c] Percent incorporation of deuterium upon quench with MeOD.



Although the isomerization of **2** to (1-norbornylmethyl)lithium (**3**) is a thermodynamically favorable process, since it produces a C-C σ-bond (bond energy ca. 88 kcal/mol) at the expense of a C=C π-bond (π-bond energy *ca.* 60 kcal/mol), the reaction is, not surprisingly, much slower than the conversion of 5-hexen-1-yllithium to (cyclopentylmethyl)lithium.[1] Indeed, at the inception of this study it was not clear that the cyclization of **2** to **3**, which involves both the generation of a quaternary center and the introduction of additional ring strain, would be competitive with reactions that consume anions such as proton abstraction from solvent and oxidation with adventitious oxygen. In fact, **2** does not cyclize to an appreciable extent when allowed to stand at room temperature in pentane-ether solution and the addition of 2.2 equiv of dry, deoxygenated *N,N,N',N'*-tetramethylethylenediamine (TMEDA) is required to facilitate the isomerization.[2] Optimal conditions for the cyclization of **2** to **3** were established in a series of experiments, summarized in Table I, that involved quenching the reaction

(1) Bailey, W. F.; Patricia, J. J.; DelGobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* **1985**, *50*, 1999.
(2) (a) Bailey, W. F.; Nurmi, T. T.; Patricia, J. J.; Wang, W. *J. Am. Chem. Soc.* **1987**, *109*, 2442. (b) Bailey, W. F.; Rossi, K. *J. Am. Chem. Soc.* **1989**, *111*, 765.
(3) Chamberlin, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 4788 and references therein.
(4) Cooke, M. P., Jr.; Widener, R. K. *J. Org. Chem.* **1987**, *52*, 1381 and references therein.
(5) Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.*, submitted.
(6) Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1.
(7) Vogel, A. *Textbook of Practical Organic Chemistry*, 4th ed.; Longman: New York, 1978; p 870.
(8) McMurry, J. E.; Andrus, W. A.; Musser, J. H. *Synth. Commun.* **1978**, *8*, 53.

0022-3263/90/1955-6058$02.50/0