Hz), 8.20 (d, 1 H, J = 7.9 Hz); ^{13}C NMR 28.06, 31.00, 32.42, 36.14, 51.19, 55.68, 58.90, 61.99, 65.82, 66.15, 82.29, 88.50, 106.70, 121.87, 122.20, 124.75, 125.05, 125.81, 126.37, 128.20, 147.51, 151.36, 172.40, 174.52 ppm; IR ($CDCl_3$) 3400–2820 (br), 1730, 1600, 1465, 1372, 1265, 1230, 1160, 1090 cm^{-1}. Anal. Calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C, 64.70; H, 6.50.

8,13-Dimethoxy-1,14-dioxo-2-oxa-1,2,3,4,4a,5,6,6a,7,14,14a,14b-dodecahydro-4a,6a-epoxybenzo[*a*]naphthacene 18. With the procedure developed for 11, acid (0.627 g, 1.52 mmol) was converted to keto lactone 18. Recrystallization from acetone/hexane afforded 0.45 g (75%) of 18: mp 208–210 °C; 300-MHz ^{1}H NMR ($CDCl_3$) δ 2.05–2.19 (m, 4 H), 3.02 (d, 1 H, J = 8 Hz), 3.46 (d, 1 H, J = 18.9 Hz), 3.65 (d, 1 H, J = 18.9 Hz), 3.66 (d, 1 H, J = 8 Hz), 3.92 (s, 3 H), 3.98 (s, 3 H), 4.32–4.36 (m, 2 H), 7.52 (t, 1 H, J = 7 Hz), 7.61 (t, 1 H, J = 7 Hz), 8.04 (d, 1 H, J = 8.2 Hz), 8.27 (d, 1 H, J = 8.2 Hz); ^{13}C NMR 28.20, 28.75, 35.98, 36.54, 49.34, 61.20, 61.37, 63.95, 65.42. 84.26, 85.49, 121.78, 122.01, 124.61, 125.68, 126.20, 128.53, 128.60, 130.89, 148.42, 153.82, 171.50, 195.44 ppm; IR ($CDCl_3$) 2960, 1715, 1615, 1450, 1375, 1340, 1270, 1080, 1035 cm^{-1}. Anal. Calcd for $C_{23}H_{22}O_6$: C, 70.04; H, 5.62. Found: C, 69.90; H, 5.69.

4a,14-Dihydroxy-2-oxa-1,8,13-trioxo-1,2,3,4,4a,5,6,8,13,14b-decahydrobenzo[*a*]naphthacene (19). With the general oxidative demethylation procedure, keto lactone 18 (0.083 g, 0.21 mmol) was oxidized to quinone. The crude quinone was dissolved in 5 mL of acetone. After the addition of concentrated HCl (1 drop), the reaction mixture was stirred for 20 h. The yellow precipitate was filtered and washed with cold acetone to afford 0.023 g (30%) of 19 (mp 263–268 °C) as a mixture of diastereomers: 300-MHz ^{1}H NMR (Me_2SO-d_6) δ 1.99–2.48 (m, 4 H), 4.19 and 5.12 (2 s, 1 H), 4.43–4.64 (m, 2 H), 7.53 (s, 1 H), 7.92–7.98 (m, 2 H), 8.18–8.26 (m, 2 H), 13.01 (s, 1 H); MS, m/e 364, 346, 316, 302, 292, 275, 263; high-resolution mass spectrum for $C_{21}H_{16}O_6$ requires 364.0947; found 364.0960; FT IR (KBr) 3500, 1749, 1674, 1630, 1589, 1380, 1337, 1276, 1213, 1176, 1056, 1020, 943, 790, 717 cm^{-1}.

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Generation of (1-Alkoxycyclopropyl)lithium Reagents

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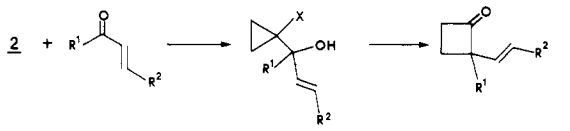
Various approaches to the generation of (1-alkoxycyclopropyl)lithium reagents were investigated. The syntheses of [1-(methoxymethoxy)cyclopropyl]tri-*n*-butylstannane, cyclopropyl 2,4,6-triisopropylbenzoate, and 1-bromo-1-ethoxycyclopropane were carried out and their conversions to the corresponding organolithium species were studied. The most convenient preparative-scale precursor of a (1-alkoxycyclopropyl)lithium reagent was found to be 1-bromo-1-ethoxycyclopropane.

Organometallic compounds bearing α-heteroatoms occupy a central position in synthetic organic chemistry, serving as nucleophilic latent precursors of a variety of functional groups. A large number of α-hetero-substituted organometallic reagents are known, with the most common being α-lithiated ethers, sulfides, selenides, silanes, phosphoranes, and alkyl halides (1, X = OR, SR, SeR, SiR_3, PR_2, Br, etc.).[1] The α-hetero-substituted cyclo-

1 2

propyllithium compounds (2) comprise a particularly interesting subclass of this family of organometallic reagents, since they play a key role in strategies developed for the synthesis of cyclobutanes[2,3] and cyclopentanes.[4]

In connection with a number of ongoing research projects in our group, we needed to prepare a variety of 2-alkenylcyclobutanones. Among all the known methods for the synthesis of cyclobutanones, the most convenient for our needs appeared to be the addition of an α-hetero-substituted cyclopropyllithium reagent to an enone or enal, followed by rearrangement of the adduct to a cyclobutanone (eq 1). Unfortunately, all of the available α-



(1)

hetero-substituted cyclopropyllithium reagents suffer from some drawback. Problems with available reagents include failure to afford cyclobutanones from aldehydes,[5] formation of byproducts in the rearrangement step,[6] or conjugate addition to enones.[7]

The best currently available reagent of this type is (1-methoxycyclopropyl)lithium (4),[3] which cleanly undergoes 1,2-addition to enones to afford adducts which can be rearranged to 2-alkenylcyclobutanones in high yield under mild conditions. Generation of (1-methoxycyclopropyl)-lithium is accomplished by reductive desulfurization[8] of

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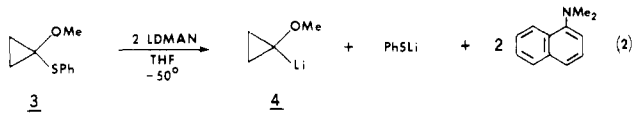
1-methoxy-1-(phenylthio)cyclopropane (3) with lithium 1-(dimethylamino)naphthalenide (LDMAN) (eq 2). We



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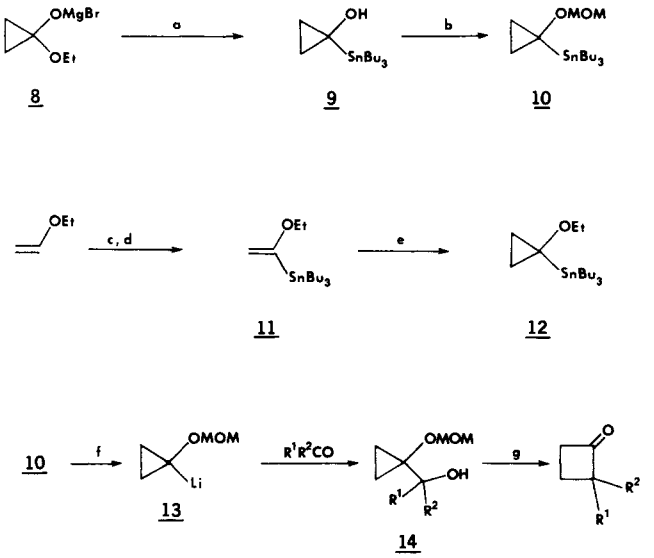
found this methodology, while elegant, to be impractical for our preparative needs, since reductive desulfurization requires rather careful control of experimental conditions and 1-methoxy-1-(phenylthio)cyclopropane requires a four-step synthesis from 1,3-dibromopropane. We therefore sought an alternative method for the generation of (1-alkoxycyclopropyl)lithium reagents.

Unlike many other α-hetero-substituted alkyllithium reagents, (α-alkoxyalkyl)lithium compounds are not generally accessible by direct deprotonation of dialkyl ethers. With the exception of some methyl ethers, tetrahydrofurans, and tetrahydropyrans,[9,10] the conditions required for deprotonation usually result in either decomposition of the (α-alkoxyalkyl)lithium species,[11,12] or, with higher alkyl ethers, competitive E2 elimination of alkoxide.[10,11] However, in addition to the quite general reductive desulfurization approach of Cohen,[3,8] there are several other methods for the generation of (α-alkoxyalkyl)lithium reagents which do not involve deprotonation of alkyl ethers. Specifically, these are transmetalation of organostannanes,[1a,13-15] deprotonation of hindered alkyl benzoates (followed by ester removal with LAH),[16,17] and metal–halogen exchange reactions of α-halo ethers.[18] We have investigated each of these methods for the generation of (1-alkoxycyclopropyl)lithium reagents, and we present our results herein.

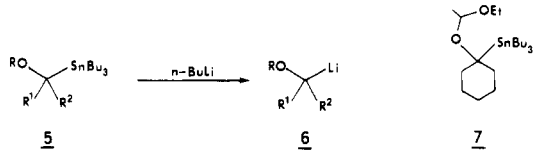
Results

(1-Alkoxycyclopropyl)tri-*n*-butylstannane. Transmetalation between (α-alkoxyalkyl)stannanes **5** and *n*-BuLi is one of the most general ways in which to generate (α-alkoxyalkyl)lithiums **6**. A number of workers[1a,13] have shown that simple (alkoxymethyl)lithium compounds could be prepared in this fashion (**6**, $R^1 = R^2 = H$), and Still[14] has extended this methodology to the preparation of primary (α-alkoxyalkyl)lithium compounds **6** (R^1 = H, R^2 = alkyl). At the time we undertook this investigation, there had been no examples of the formation of secondary (α-alkoxyalkyl)lithiums **6** (R^1, R^2 = alkyl) by this procedure and, in fact, Still had reported that attempted transmetalation of an (α-alkoxycyclohexyl)stannane (**7**) failed.[14]

Scheme I[a]



[a] (a) $Bu_3SnMgCl$, Et_2O, room temperature, 26 h, (or Bu_3SnLi, THF, room temperature, 24 h); (b) $(MeO)_2CH_2$, P_2O_5, room temperature, 30 min; (c) *t*-BuLi, THF, −78 °C; (d) Bu_3SnCl; (e) CH_2I_2, Et_2Zn, toluene, room temperature; (f) *n*-BuLi, THF, −78 °C; (g) catalytic HBF_4, Et_2O, room temperature.



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However, we reasoned that the higher acidity of cyclopropanes relative to their acylic analogues[19] would lower the kinetic barrier to formation of an (α-alkoxycyclopropyl)lithium compound. As described below, this indeed was the observed result. Since our observations were made, Macdonald and McGarvey[15] have also reported that secondary (α-alkoxyalkyl)lithium compounds can be prepared by transmetalation of the corresponding (α-alkoxyalkyl)-stannanes if DME is used as solvent.

In principle, the required (α-alkoxycyclopropyl)stannane could be prepared by addition of (tri-*n*-butylstannyl)lithium to cyclopropanone, itself available by the addition of diazomethane to ketene.[20] However, we judged the preparation of cyclopropanone to be too inconvenient and potentially dangerous for scale-up, and we sought an alternative approach.

Several workers[21-23] have shown that 1-ethoxycyclopropanol can serve as a synthetic equivalent of cyclopropanone. A variety of organometallic reagents undergo addition to 1-ethoxycyclopropanol, and the reaction is facilitated if the hemiketal is first reacted with methyl-

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magnesium bromide to form the magnesium alkoxide. It seemed reasonable then that an (α-alkoxycyclopropyl)-stannane might be prepared by reaction of the magnesium alkoxide of 1-ethoxycyclopropanol with a tri-*n*-butylstannyl anion.

Reaction of (tri-*n*-butylstannyl)lithium (prepared from tri-*n*-butylstannane and LDA in THF[14]) with the magnesium salt of 1-ethoxycyclopropanol (**8**) proceeded very slowly to afford low yields of (1-hydroxycyclopropyl)-stannane (**9**, Scheme I). Generally, complete disappearance of the starting cyclopropyl hemiketal required reaction for 24 h at room temperature in THF. Since compound **9** was anticipated to be rather unstable, it was not purified, but was instead immediately protected as its MOM ether **10** by reaction with dimethoxymethane and P_2O_5.[24] Unfortunately, maximum optimized overall yields of **10** were only 28–33%. Similar results were obtained upon substitution of (tri-*n*-butylstannyl)magnesium chloride in Et_2O (from tri-*n*-butylstannane and cyclohexylmagnesium chloride[25]) for (tri-*n*-butylstannyl)lithium. Since TLC evidence indicated that the protection step proceeded in essentially quantitative yield, the low overall yield of **10** must be due to inefficient formation of the alcohol **9**, presumably due to competitive decomposition of the (tri-*n*-butylstannyl)lithium.[26]

As an alternative route to an (α-alkoxycyclopropyl)-stannane, we have also considered the cyclopropanation of (1-ethoxyethenyl)tri-*n*-butylstannane (**11**). Seyferth has reported[27] that standard Simmons–Smith reaction (Zn–Cu, CH_2I_2) of vinyltrimethylstannane led to the desired cyclopropyltrimethylstannane in low yield accompanied by various other tetraalkylstannanes produced by redistribution of the stannyl alkyl substituents. It was demonstrated that the zinc iodide produced in the Simmons–Smith reaction was responsible for this redistribution. Corey however has recently reported[28] that addition of diisopropylethyl amine to the cyclopropanation reaction suppressed the alkyl substituent redistribution, presumably by complexation with the zinc iodide. We thus were hopeful that the cyclopropanation of (1-ethoxyethenyl)-tri-*n*-butylstannane could be successfully accomplished.

Treatment of (1-ethoxyethenyl)lithium[29] with tri-*n*-butylstannyl chloride in THF afforded the vinyl stannane **11** in 97% yield (Scheme I).[30] The cyclopropanation of **11** under modified Simmons–Smith conditions (using diethylzinc rather than Zn–Cu couple) was investigated, since these modified conditions were reported to be particularly useful for cyclopropanation of vinyl ethers.[31] Unfortunately, however, reaction of **11** with diethylzinc and CH_2I_2 afforded the cyclopropane **12** in only 20% yield along with a great deal of polymeric material. Addition of diisopropylethylamine to the reaction mixture had no effect on the yield. Since this route offered no advantage over that previously described, it was not further investigated.

Once in hand, it was found that [1-(methoxymethoxy)cyclopropyl]tri-*n*-butylstannane (**10**) underwent smooth transmetalation with *n*-BuLi within seconds at −78 °C in THF. This is to be contrasted with the much slower transmetalation observed with other secondary (α-alkoxyalkyl)stannanes in THF[15] and presumably reflects the lower basicity of pyramidal cyclopropyl carbanions.[19] Reaction of the derived organolithium reagent **13** with a variety of carbonyl compounds occurred smoothly to afford adducts **14** which, in keeping with the observations of Cohen,[3] could be cleanly and easily rearranged to cyclobutanones (Scheme I). Table I lists several of the cyclobutanones prepared from **10**. In most of the cases, some of the starting carbonyl compound was recovered, presumably due to competitive proton transfer and enolate formation. The yields in Table I would be somewhat higher if they were based on recovered starting material.

Table I. Cyclobutanone Synthesis via [1-(Methoxymethoxy)cyclopropyl]lithium (13)

carbonyl compd	cyclobutanone produced	overall yield (%)	lit synth
		57	a
		51	b
		63	b
		45	b
		68	c

[a] Reference 3. [b] Reference 2. [c] Reference 38.

Thus we had found that **10** was indeed a suitable precursor for an (α-alkoxycyclopropyl)lithium reagent. However, the difficulties experienced in the preparation of **10** (or **12**) led us to explore other avenues of approach to the desired organolithium compounds.

Cyclopropyl 2,4,6-Triisopropylbenzoate. As previously discussed, direct deprotonation of alkyl ethers to produce (α-alkoxyalkyl)lithium reagents has only been successful with methyl ethers, tetrahydrofurans, and tetrahydropyrans.[9,10] Direct deprotonation of alkyl esters is however considerably easier than that of alkyl ethers, due to stabilization of the carbanion by the ester dipole. In particular, it has been shown by Beak[16] and Seebach[17] that methyl and ethyl benzoates with bulky aromatic substituents can be metalated with *sec*-BuLi/TMEDA complex at −78 °C in THF. The resulting [(benzoyloxy)alkyl]lithium species reacts with a variety of electrophiles, and the bulky ester can be subsequently removed with LAH. Although no examples of the metalation of secondary alkyl (e.g., isopropyl) benzoates have been reported, we felt that the increased acidity of cyclopropyl protons[19] should make this deprotonation relatively facile.

Cyclopropyl 2,4,6-triisopropylbenzoate (**15**) was easily synthesized by reaction of cyclopropanol with 2,4,6-triisopropylbenzoyl chloride in triethylamine containing a catalytic amount of 4-(dimethylamino)pyridine. Treatment of this ester with *sec*-BuLi/TMEDA for 6 h in THF at −78 °C resulted in essentially complete deprotonation (Scheme II). This was confirmed by quenching the anion

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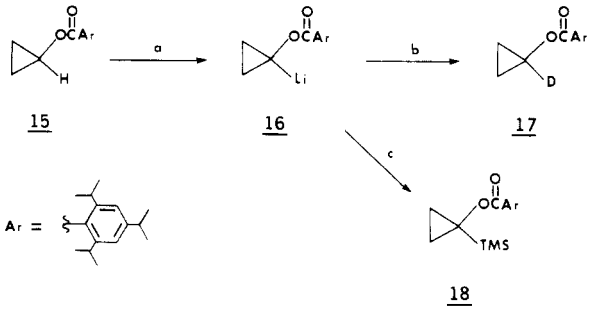
Scheme II[a]



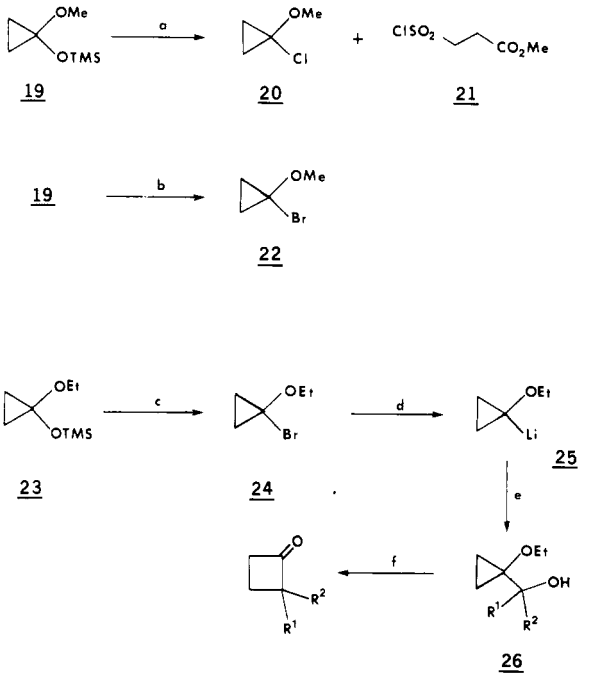
[a] (a) *sec*-BuLi/TMEDA, THF, −78 °C, 6 h; (b) D_2O; (c) Me_3SiCl.

16 with CH_3CO_2D to afford a 92% yield of deuteriocyclopropyl ester **17** which was at least 90% deuterated at the cyclopropyl carbon by NMR analysis. Similarly, treatment of the anion with Me_3SiCl afforded a 68% yield of (1-trimethylsilyl)cyclopropyl 2,4,6-triisopropylbenzoate (**18**). Unfortunately, the [1-(benzoyloxy)cyclopropyl]lithium species **16** failed to undergo reaction with cyclohexenone at temperatures between −78 °C and 25 °C and therefore further reactions of this organolithium were not pursued. The lack of reactivity toward cyclohexenone is probably due to steric hindrance, although competitive proton transfer from the ketone to the organolithium compound cannot be ruled out.[16b]

1-Bromo-1-ethoxycyclopropane. The final method we investigated for the generation of an (α-alkoxycyclopropyl)lithium reagent was the metal–halogen exchange between a 1-alkoxy-1-halocyclopropane and *t*-BuLi. Although several examples are known[18] of the reaction of chloromethyl ethers with various metals to afford the corresponding organometallic reagents, the metal–halogen exchange between an α-haloalkyl ether and *t*-BuLi has apparently not been studied. In addition, no examples exist of the generation of primary or secondary α-alkoxyalkyl organometallic reagents from the corresponding halides. Despite these uncertainties, it seemed likely that the metal–halogen exchange reaction would proceed smoothly. In contrast, on the basis of literature reports, it seemed possible that the synthesis of an appropriate 1-alkoxy-1-halocyclopropane precursor would be problematic.

For example, although 1-chloro-1-methoxycyclopropane (**20**) has been prepared by reaction of $SOCl_2$ with 1-methoxy-1-(trimethylsiloxy)cyclopropane (**19**), the isolated yield of product was only 15%, and a significant amount of the ring-opened ester **21** was also produced (Scheme III).[32] 1-Bromo-1-methoxycyclopropane (**22**) has been prepared in unspecified yield from the same ketal by reaction with PBr_3 in pyridine,[33] but we were unable to repeat this procedure. We were pleased to find, however, that 1-bromo-1-ethoxycyclopropane (**24**) is formed cleanly upon reaction of 1-ethoxy-1-(trimethylsiloxy)cyclopropane (**23**) with PBr_3 in the absence of pyridine. NMR analysis of the reaction mixture after 6 h at 25 °C shows quantitative conversion to product, with no contamination by ring-opened byproducts. Upon suitable workup, 1-bromo-1-ethoxycyclopropane can be isolated in 65–75% yield. This compound is rather unstable at room temperature but can be stored at −20 °C for at least 2 months.

Scheme III[a]



[a] (a) $SOCl_2$; (b) PBr_3, pyridine; (c) PBr_3, room temperature, 6 h; (d) *t*-BuLi, Et_2O, −78 °C; (e) R^1R^2CO; (f) catalytic HBF_4, Et_2O, room temperature.

Since 1-ethoxy-1-(trimethylsiloxy)cyclopropane is easily prepared in one step from commercially available and inexpensive ethyl 3-chloropropionate,[34] this overall synthesis of 1-bromo-1-ethoxycyclopropane is very convenient and suitable for large-scale preparative needs.[35]

Addition of 1-bromo-1-ethoxycyclopropane to *t*-BuLi (2 equiv) in Et_2O at −78 °C results in an immediate and exothermic metal–halogen exchange to form the organolithium compound **25**. The exchange can also be accomplished with *n*-BuLi, but only at temperatures near 0 °C, where competitive decomposition of the organolithium compound occurs. As expected by analogy to (1-methoxycyclopropyl)lithium, **25** adds cleanly to a variety of aldehydes and ketones in excellent yields, and the derived adducts **26** can be cleanly rearranged to cyclobutanones in very high overall yields.[36] Representative cyclobutanone syntheses are presented in Table II, and spectral data are included in the Experimental Section for the two new cyclobutanones (**27** and **28**). In keeping with Cohen's observations,[3] we have found that (1-ethoxycyclopropyl)lithium is particularly well suited for the preparation of 2-alkenylcyclobutanones.

Conclusions

We have examined three ways of generating (1-alkoxycyclopropyl)lithium reagents which provide alternatives to the reductive desulfurization of 1-methoxy-1-(phenylthio)cyclopropane. Transmetalation of [1-(methoxymethoxy)cyclopropyl] tri-*n*-butylstannane proceeds smoothly in THF at low temperature, but the utility of this method is compromised by the relative inaccessibilility of the starting cyclopropylstannane. Direct deprotonation

(32) Jorritsma, R.; Steinberg, H.; de Boer, T.J. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 194. van der Vecht, J. R.; Steinberg, H.; de Boer, T.J. *Ibid.* **1977**, *96*, 313.

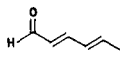
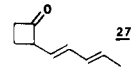
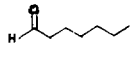
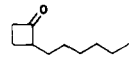
(33) van Tilborg, M. W. E. M.; van Doorn, R.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1979**, *101*, 7617.

(34) Ruhlmann, K. *Synthesis* **1971**, 236. Salaün, J.; Margeurite, J. *Organic Syntheses* **1984**, *63*, 147.

(35) A variety of substituted 1-chloro-1-methoxycyclopropanes have also been synthesized by reaction of chloromethoxycarbene with various alkenes: Smith, N. P.; Stevens, I. D. R. *Tetrahedron Lett.* **1978**, 1931. Moss, R. A.; Shieh, W.-C. *Ibid.* **1978**, 1935.

(36) This aspect of our work has already been reported in preliminary form. See ref 6b.

Table II. Cyclobutanone Synthesis via (1-Ethoxycyclopropyl)lithium (25)

carbonyl compd	cyclobutanone produced	overall yield (%)	lit synth
		69	a
		83	a
		78	b
		81	a
	 27	91	—
		82	c
		81	d
	 28	81	—

[a] Reference 2. [b] Reference 3. [c] Reference 39. [d] Reference 38.

of cyclopropyl 2,4,6-triisopropylbenzoate can be easily accomplished with *sec*-BuLi/TMEDA, but the derived organolithium compound does not react with enones such as cyclohexenone, presumably due to steric hindrance or competitive enolization of the enone. In contrast, 1-bromo-1-ethoxycyclopropane has been found to be an extremely convenient precursor of a reactive (1-alkoxycyclopropyl)lithium reagent. Metal–halogen exchange between 1-bromo-1-ethoxycyclopropane and *t*-BuLi occurs rapidly at low temperature, and the derived organolithium compound reacts cleanly with a variety of aldehydes and ketones. In addition, 1-bromo-1-ethoxycyclopropane is available on a preparative scale via a short synthesis from inexpensive starting materials. Studies of the reaction of (1-ethoxycyclopropyl)lithium with other electrophiles to afford useful 1-alkoxycyclopropyl derivatives are currently underway.

Experimental Section

General Methods. Proton nuclear magnetic resonance (NMR) spectra were measured on a Varian EM-390 spectrometer, or, where specified, on a JEOL FX-270 spectrometer, and all shifts are reported downfield from an internal Me_4Si or $CHCl_3$ standard. Infrared (IR) spectra were recorded with a Perkin-Elmer Model 283 spectrophotometer. Mass spectra (MS) were measured with a Hewlett-Packard HP5985 GC/MS system. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, IL, or by Galbraith Laboratories, Knoxville, TN.

Dry tetrahydrofuran (THF) and diethyl ether (Et_2O) were obtained by distillation from sodium benzophenone.

[1-(Methoxymethoxy)cyclopropyl]tri-*n*-butylstannane (10). A suspension of the magnesium salt of 1-ethoxycyclopropanol[21] (10.5 g, 10 mmol) was prepared in 65 mL of dry Et_2O at 0 °C according to Brown and Rao.[23] To this magnetically stirred suspension was added a chilled solution of (tri-*n*-butylstannyl)-magnesium chloride prepared from tri-*n*-butylstannane (Aldrich, 4.1 mL, 4.4 g, 15 mmol) according to Albert and Neumann.[25] After 10 min at 0 °C, the suspension was stirred at room temperature for 26 h. Addition of saturated aqueous NH_4Cl (10 mL), aqueous KF (1.6 g in 20 mL of water), and pentane (50 mL) to the reaction mixture produced an emulsion which was filtered through Celite. The phases were separated, and the aqueous phase was extracted with three 50-mL portions of pentane. The combined organic phases were washed with brine, dried with $MgSO_4$, and concentrated under aspirator vacuum to afford crude (1-hydroxycyclopropyl)tri-*n*-butylstannane (**9**) as a yellow liquid. This material was not usually purified before conversion to **10**, but a small purified sample gave the following spectral data: IR (neat) 3340 (m), 3070 (w), 2930 (s), 2850 (s), 1450 (m), 1165 (m), 1015 (m) cm^{-1}; 270-MHz ^1H NMR (C_6D_6) δ 1.57 (m, 6 H), 1.35 (m, 7 H), 0.92 (m, 15 H), 0.70 (m, 2 H), 0.44 (m, 2 H).

This crude material was dissolved in 15 mL of dimethoxymethane which had been freed of methanol and water by repeated (3–4 times) distillation from P_2O_5. Powdered P_2O_5 (3 g, 20 mmol) was added at room temperature to this stirred solution, and, after 30 min, the reaction was diluted with 20 mL of Et_2O and then poured into saturated aqueous Na_2CO_3 (10 mL). The remaining viscous black residue was dissolved by careful addition of Et_2O (30 mL) and saturated aqueous Na_2CO_3 (30 mL). The aqueous and organic phases were combined, shaken, and separated, and the aqueous phase was extracted with three 50-mL portions of Et_2O. The combined organic phases were washed with brine, dried with $MgSO_4$, and concentrated under aspirator vacuum to afford 5.9 g of a brown oil. This material was distilled by Kugelrohr at 60–110 °C (0.005 torr) to give 1.74 g of a yellow liquid. Chromatography on silica gel with hexane and then 0.5% ethyl acetate in hexane afforded 1.18 g of **10** (30% yield): IR (CCl_4) 3075 (w), 2920 (s), 2850 (s), 1465 (m), 1155 (m), 1085 (m) 1050 (s) cm^{-1}; ^1H NMR (CCl_4) δ 4.46 (s, 2 H), 3.28 (s, 3 H), 1.80–0.25 (m, 31 H). Anal. Calcd for $C_{17}H_{36}O_2Sn$: C, 52.20; H, 9.28. Found: C, 52.20; H, 9.28.

(1-Ethoxyethenyl)tri-*n*-butylstannane (11).[30] A solution of *t*-BuLi in pentane (Aldrich, 2.6 M, 5.6 mL, 15 mmol) was added dropwise to a stirred, −78 °C solution of ethyl vinyl ether (distilled under N_2, 2.8 mL, 29 mmol) in THF (20 mL) over 5 min.[29] The resulting suspension was stirred at −78 °C for 90 min and then warmed to 0 °C over 50 min and stirred at 0 °C for 30 min. This solution of (1-ethoxyvinyl)lithium was then cooled to −78 °C and tri-*n*-butylchlorostannane (Aldrich, 2.8 mL, 9.9 mmol) was added dropwise over 5 min. After being stirred for 20 min at −78 °C, the reaction mixture was warmed to room temperature and quenched with water (5 mL). Hexane (100 mL) was added to the reaction mixture, the phases were shaken and separated, and the organic phase was washed with three 5-mL portions of water and one 5-mL portion of brine. After filtration through Na_2SO_4 and concentration under aspirator vacuum, the residue was Kugelrohr distilled at 75–85 °C (0.005 torr) to afford 3.48 g (97% yield) of 11 as a colorless liquid: IR (neat) 3080 (w), 2930 (s), 2860 (s), 1570 (m), 1180 (s), 1040 (s), 810 (m) cm^{-1}; ^1H NMR (C_6D_6) δ 4.75 (d, 1 H, J = 2 Hz), 4.24 (d, 1 H, J = 2 Hz), 3.58 (q, 2 H, J = 7 Hz), 2.0–0.8 (m, 30 H).

(1-Ethoxycyclopropyl)tri-*n*-butylstannane (12). Diethylzinc in toluene (Aldrich, 13%, 0.72 mL, 1.0 mmol) was added with stirring to 11 (0.37 g, 1.0 mmol) at room temperature under nitrogen. Diiodomethane (Aldrich, twice distilled, 0.12 mL, 1.5 mmol) was then added dropwise under nitrogen. The reaction flask was purged with air[31b] and allowed to stand at room temperature for 24 h. Hexane (20 mL) and 1 M HCl (1.5 mL) were added, the phases were shaken and separated, and the organic phase was washed with water (1 mL) and brine (1 mL). After being dried with $MgSO_4$, the hexane solution was concentrated under aspirator vacuum, and the residue was flash chromatographed with hexane and then 1% ethyl acetate in hexane. (1-Ethoxycyclopropyl)tri-*n*-butylstannane (**12**) was isolated as a colorless liquid (0.076 g, 20% yield): IR (neat) 3070 (w), 2920 (s), 2860 (s), 1455 (m), 1175 (m), 1120 (m), 1065 (s) cm^{-1}; 270-MHz ^1H NMR (C_6D_6) δ 3.38 (q, 2 H, J = 7 Hz), 1.58 (m, 6 H), 1.37 (m, 6 H), 1.10 (t, 3 H, J = 7 Hz), 1.05–0.80 (m, 17 H), 0.45 (m, 2 H); MS (15 eV), m/e 376 (M^+, Sn^{120}), 319 (base), 291, 235, 179, 165, 85.

General Procedure for Cyclobutanone Synthesis via [1-(Methoxymethoxy)cyclopropyl]lithium (13). To a stirred solution of stannane **10** (0.478 g, 1.22 mmol) in 3 mL of dry THF

at −78 °C was added *n*-BuLi (Aldrich, 1.6 M in hexane, 0.76 mL, 1.2 mmol), and the resulting solution was stirred for 5 min at −78 °C. A solution of aldehyde or ketone (1.0 mmol) in 5 mL of dry THF chilled to −78 °C was added via cannula over 1 min. After being stirred an additional 20 min at −78 °C the reaction was quenched by the addition of 0.5 mL of saturated aqueous NH_4Cl. The resulting suspension was warmed to room temperature, the aqueous phase was removed by pipette, and 0.6 mL of 48% aqueous HBF_4 was added. The resulting solution was stirred overnight at room temperature and then diluted with 10 mL of Et_2O. Saturated aqueous $NaHCO_3$ (2 mL) was carefully added to the reaction, followed by enough solid Na_2CO_3 to bring the aqueous phase to pH 8. The phases were separated, and the aqueous phase was extracted with two 5-mL portions of Et_2O. The combined organic phases were washed with brine, dried with $MgSO_4$, and concentrated under aspirator vacuum. The cyclobutanone was then purified by flash chromatography on silica gel or by distillation.

Cyclopropyl 2,4,6-Triisopropylbenzoate (15). To a solution of cyclopropanol[21] (0.55 g, 9.5 mmol) in Et_3N (5 mL) was added 2,4,6-triisopropylbenzoyl chloride[37] (1.78 g, 6.6 mmol) and 4-(dimethylamino)pyridine (10 mg, 0.082 mmol), and the mixture was stirred at room temperature for 72 h. The reaction was worked up by addition of water (10 mL) and extraction with three 15-mL portions of Et_2O. The combined organic phases were washed successively with two 15-mL portions of 1 M HCl, two 15-mL portions of saturated aqueous $NaHCO_3$, and 15 mL of brine. After drying with $MgSO_4$, the organic phases were concentrated under aspirator vacuum. The crude product was purified by flash chromatography with 10% ethyl acetate in hexane to afford 1.75 g (65% yield) of **15**: IR (CCl_4) 2960 (s), 2930 (m), 2870 (m), 1735 (s), 1460 (m), 1250 (s), 1150 (s), 1075 (s) cm^{-1}; ^1H NMR (CCl_4) δ 6.85 (s, 2 H), 4.20 (m, 1 H), 2.75 (m, 3 H), 1.20 (d, 18 H, J = 7 Hz), 0.60 (m, 4 H). Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.16; H, 9.72. Found: C, 79.16; H, 10.12.

1-(Trimethylsilyl)cyclopropyl 2,4,6-Triisopropylbenzoate (18). To a stirred solution of TMEDA (0.50 mL, 0.39 g, 3.3 mmol) in THF (1.5 mL) was added *sec*-BuLi (Aldrich, 1 M in cyclohexane, 1.4 mL, 1.4 mmol) at −78 °C under N_2. Ester **15** (0.16 g, 0.57 mmol) was added as a solution in 2 mL of THF. This reaction was stirred at −78 °C for 6 h, and then a solution of Me_3SiCl (Aldrich, 1.0 mL, 0.86 g, 7.9 mmol) in THF (1 mL) was added. After stirring an additional 3 h at −78 °C, the reaction was allowed to warm to room temperature, diluted with Et_2O (15 mL), and washed with two 15-mL portions of water. The aqueous phase was separated and then extracted with two 15-mL portions of Et_2O. The combined organic phases were washed with two 15-mL portions of 1 M HCl, two 15-mL portions of saturated aqueous $NaHCO_3$, and 15 mL of brine. After drying with $MgSO_4$, the combined organic phases were concentrated under aspirator vacuum. The residue was purified by flash chromatography on silica gel with 10% ethyl acetate in hexane to afford 0.14 g (68% yield) of **18**: IR (CCl_4) 2960 (s), 1725 (s), 1460 (m), 1250 (s), 1075 (m), 840 (s) cm^{-1}; ^1H NMR (CCl_4) δ 6.85 (s, 2 H), 2.80 (m, 3 H), 1.20 (d, 18 H, J = 7 Hz), 0.80 (m, 4 H), 0.05 (s, 9 H); MS (70 eV), m/e 362 (M + 2), 345, 319, 305, 231 (base), 73.

1-Bromo-1-ethoxycyclopropane (24). 1-Ethoxy-1-(trimethylsiloxy)cyclopropane[34] (26.0 g, 30.2 mL, 0.149 mol) and PBr_3 (31.7 g, 11.0 mL, 0.117 mol) were mixed without solvent at 0 °C, and the resulting solution was stirred at room temperature for 6 h. Kugelrohr distillation (60 °C, 25 torr) afforded a mixture of **24** and Me_3SiBr. This mixture was diluted with pentane (150 mL), chilled to −20 °C, and then carefully treated with cold saturated aqueous Na_2CO_3 (100 mL) (*Caution! Vigorous gas evolution!*). The phases were carefully shaken and separated, and the aqueous phase was washed with two 75-mL portions of pentane. The combined organic phases were dried with $MgSO_4$ and concentrated by distillation of the pentane at atmospheric pressure. The residue was distilled under aspirator vacuum to afford 18.0 g (73% yield) of **24** (bp_{25} 48–50 °C). 1-Bromo-1-ethoxycyclopropane is somewhat unstable at room temperature but can be stored for at least 2 months at −20 °C without decomposition: IR (neat) 3100 (w), 2980 (s), 2930 (m), 2880 (m), 1440 (m), 1300 (s), 1155 (s), 1055 (s), 790 (s) cm^{-1}; ^1H NMR (CCl_4) δ 3.60 (q, 2 H, J = 7 Hz), 1.15 (m, 7 H); MS (15 eV), m/e 164/166 (M^+), 136/138 (base), 85, 57.

General Procedure for Synthesis of Cyclobutanones via (1-Ethoxycyclopropyl)lithium. To 5 mL of dry Et_2O at −78 °C was added *t*-BuLi (Aldrich, 2.35 M in pentane, 1.30 mL, 3.00 mmol) followed by **24** (0.264 g, 0.197 mL, 1.60 mmol). After 5 min at −78 °C, 1.00 mmol of an aldehyde or ketone was added as a solution in 2 mL of dry Et_2O (pre-cooled to −78 °C) via stainless steel cannula using nitrogen pressure. After an additional 10 min at −78 °C, the reaction was warmed to 0 °C in an ice bath and then quenched with 1 mL of saturated aqueous NH_4Cl. The phases were separated, and the aqueous phase was extracted with two 5-mL portions of Et_2O. The combined organic phases were dried with $MgSO_4$ and condensed under aspirator vacuum. The cyclopropyl carbinol thus obtained was freed from traces of inorganic salts by filtration through a small amount of silica gel using 10% ethyl acetate in hexane as solvent.

To a solution of the cyclopropylcarbinol in 10 mL of Et_2O was added 0.5 to 4.0 equiv of 48% aqueous HBF_4.[6b] The progress of the rearrangement was followed by TLC analysis and complete rearrangement required from 10 min to 48 h depending on the structure of the adduct.[6b] After rearrangement was complete, 1.2 equiv of 1 M Na_2CO_3 (based on the amount of HBF_4 used) and an equal volume of brine were added to the reaction, and the phase were shaken and separated. The aqueous phase was extracted with two 5-mL portions of Et_2O, and the combined organic phases were dried with $MgSO_4$ and concentrated under aspirator vacuum. The cyclobutanone was then purified by Kugelrohr distillation or flash chromatography.

2-[(*Z*,*Z*)-1,3-Pentadienyl]cyclobutanone (27). Cyclobutanone **27** was prepared by the procedure given above. This cyclobutanone is rather unstable and decomposes even at −20 °C in a matter of weeks; bp_3 80–85 °C; IR (neat) 3015 (m), 2960 (s), 2880 (m), 1780 (s), 1655 (w), 1615 (w), 1445 (m), 1060 (s), 985 (s) cm^{-1}; ^1H NMR (CCl_4) δ 6.4–5.2 (m, 4 H), 3.87 (br q, 1 H, J = 8 Hz), 2.95 (m, 2 H), 2.45–1.75 (m, 2 H), 1.75 (d, 3 H, J = 7 Hz); MS (70 eV), m/e 136 (M^+), 94 (base), 79.

2-Hexylcyclobutanone (28). Cyclobutanone **28** was prepared by the procedure given above; bp_3 75–78 °C, IR (neat) 2925 (s), 2855 (s), 1780 (s), 1460 (m), 1090 (m), 1070 (m) cm^{-1}; ^1H NMR (CCl_4) δ 3.19 (m, 1 H), 2.88 (m, 2 H), 2.15 (m, 1 H), 1.60 (m, 1 H), 1.29 (br s, 10 H), 0.89 (m, 3 H); MS (15 eV) m/e 154 (M^+), 126, 111, 98 (base), 84, 70, 56, 43.

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(38) Johnson, C. R.; Janiga, E. R. *J. Am. Chem. Soc.* **1973**, *95*, 7692.
(39) Halazy, S.; Zutterman, F.; Krief, A. *Tetrahedron Lett.* **1982**, *23*, 4385.