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# Preparation and Reactions of Diorganocuprate Reagents Derived from 2-Lithio-3,3-diethoxypropene. Functionalized Reagents for the Transfer of an $\alpha$ Acrolein Carbanion Equivalent


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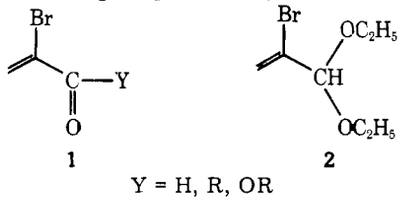
*Received December 4, 1975*


The preparation of several cuprate reagents from 2-lithio-3,3-diethoxypropene is described. The reactivity of these reagents is described with a variety of $\alpha,\beta$ unsaturated ketones to afford 1,4 adducts in moderate to excellent yields depending upon steric hindrance in the enone. Allylic halides couple but epoxides and saturated vinyl halides are unreactive. Enolate oxygenation experiments are described which allow introduction of an $\alpha$ oxygen via epoxidation of the derived enol trimethylsilyl ether. An interesting solvent effect is observed for this process. The use of ether affords $\alpha$-benzoyloxy ketones and methylene chloride the $\alpha$-trimethylsilyloxy ketone. Some model compound experiments suggest that this solvent effect might be general.


The application of organocopper chemistry to synthesis has seen an enormous amount of activity in the recent past. These organometallic reagents have found wide use for selective coupling and alkylation reactions,[2] conjugate addition to various $\alpha,\beta$ unsaturated carbonyl derivatives,[3,4] as well as acylation.[5] However, the majority of the activity has been directed toward the utilization of simple, readily available lithium reagents. Relatively little is known about the potential for successful formation and use of cuprate reagents containing highly functionalized ligands. Among the examples already documented is the work of the Syntex group on the transfer of the prostaglandin $\beta$ side chain,[6] as well as the work of Eaton[7] and Heathcock,[8] and that from our laboratories.[9,10]

One class of carbanions which would be particularly valuable would be those derived from $\alpha$-bromo acrylate derivatives (**1**). A number of potential applications including the synthesis of derivatives of the much sought after $\alpha$-methylene-$\gamma$-butyrolactones[11] were apparent. Marino's elegant use of $\alpha$-bromoacrylic ester[12] provides a valuable reagent in certain cases; however, this organometallic reagent seems to be of much lowered reactivity, and does not appear to undergo conjugate addition cleanly. Ficini[13] and later Depazay[14] prepared what appeared to be a more promising carbanion for complex formation by metalation of $\alpha$-bromoacrolein diethyl acetal (**2**). This reagent presumably would satisfy the requirements of complex formation in a more straightforward way and is presumably convertible to all the required oxidation states. After our studies of the complexes derived from this carbanion were nearly completed, two preliminary reports[15,16] of the formation of cuprate reagents derived from **2** appeared. We now report the results of our studies of the utility of these reagents.




**1** **2**

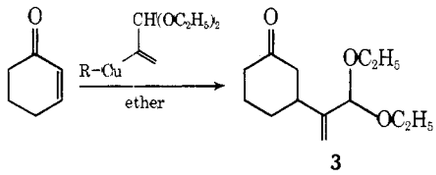
Y = H, R, OR

We found initially that the homogeneous diorganocuprate reagent derived from **2** and cuprous iodide in the usual fashion proved to be relatively difficult to handle, providing solutions which were not completely homogeneous. The reagent was indeed present as was demonstrated by its addition in moderate yield to 2-cyclohexen-1-one. We turned to the use of mixed reagents without further study in hopes of achieving the preparation of reagents soluble in the usual reaction media, ether and tetrahydrofuran (THF). Mixed diorganocuprate reagents were prepared utilizing *n*-pentynylcopper (**4**),[17] phenylthiocopper (**6**),[18] and *tert*-butylethynylcopper (**5**).[19] Only the latter reagent provided, reproducibly, a nicely soluble reagent. A similar conclusion was reached by Marino.[15]

All the reagents react with 2-cyclohexen-1-one to afford adduct **3** as shown in Table I. Ether appears to be a superior solvent to THF where applicable.

We then set out to determine the reactivity of the cuprate reagent (**5**) [R = $(CH_3)_3CC{\equiv}C-$] with various unsaturated ketones, halides, and epoxides. From the results in Table II, for enones, the reactivity seems comparable to most cuprate reagents. The branched ligand is sterically somewhat more demanding as can be seen by the reduction in yield as the substitution at the $\beta$ carbon increases. This effect is generally observed, but it is significant that moderate yields are obtained from quite hindered enones such as **7** and **8**. Other

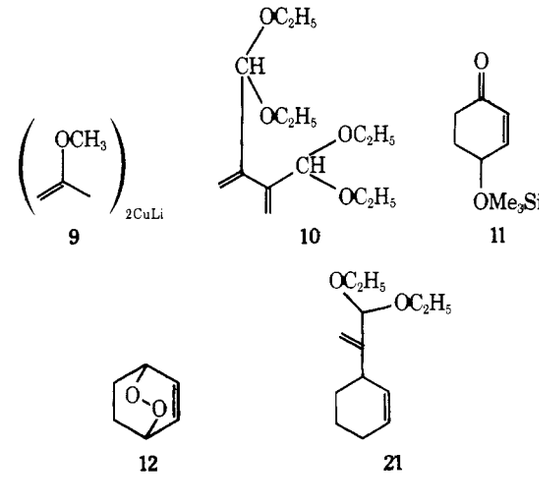
Table I




3

| | |
|---|---|
| 4, R = *n*-Pr-≡- | 65% |
| 5, R = $(CH_3)_3C$-≡- | 92% (85)[a] |
| 6, R = PhS- | 50% |

[a] Reaction conducted in anhydrous THF.



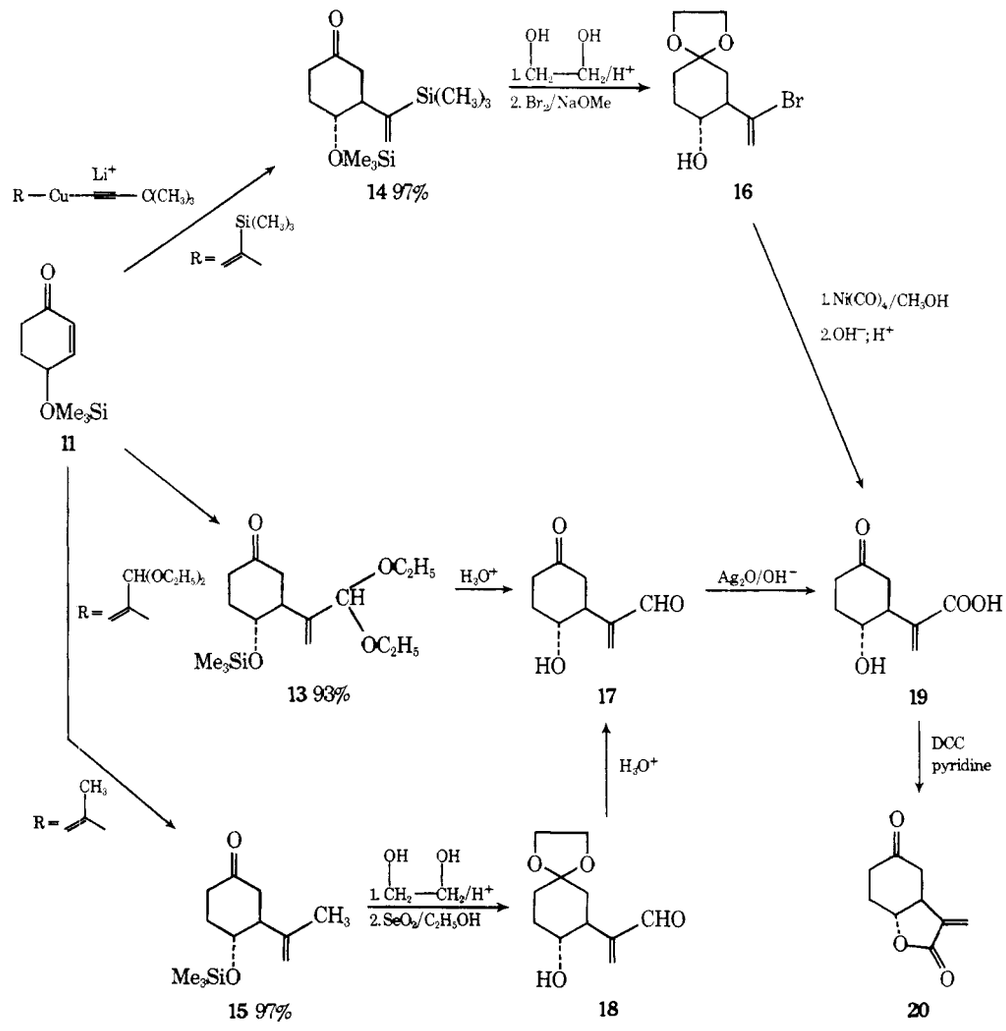

9 10 11

12 21

branched cuprate reagents such as **9** studied by ourselves[10] and Heathcock[8] fail to react appreciably when even a methyl is present at the $\beta$ position. Typical reaction conditions involve treatment of the substrate with 1.5 equiv of the mixed cuprate reagent at −78 °C, warming to −20 °C for 12 h, and warming to 0 °C for 4 h followed by workup [ammonium chloride–ammonium hydroxide solution (pH 10)]. The cases such as **4** and **5** (Table II) presented some purification problems due to the presence of significant amounts of symmetrical dimer **10**. When the reagent fails to react, the dimer **10** is produced exclusively, presumably via thermal decomposition of the reagent.

4-Hydroxy-2-cyclohexen-1-one trimethylsilyl ether (**11**) reacts extremely readily, producing exclusively the compound derived from addition trans to the 4-trimethylsiloxy group (**13**). The substrate enone (**11**) is prepared conveniently by oxidation of 1,3-cyclohexadiene with singlet oxygen[20] followed by treatment of the endoperoxide (**12**) with pyridine containing a catalytic amount of triethylamine and trimethylchlorosilane. For example, ketone **13** was obtained in 93% yield upon treatment of **11** with 1.5 equiv of cuprate **5** in ether at −78 to 0 °C. Several other substituted cuprates also afforded exclusively trans addition products upon reaction with **11** (Scheme I). Since considerable interest has been generated in the production of trans $\alpha$-methylene lactones, we proved the structure of the adducts and demonstrated the feasibility of each of these substituted vinyl groups as precursors of keto

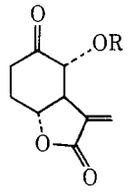
Scheme I



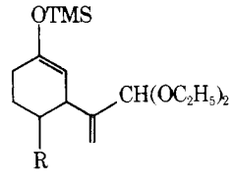
acid **19** and lactones such as **20.** The trans nature of each of the adducts is demonstrated by their conversion to **19** and the characteristic reluctance of this type of hydroxy acid to form the lactones. The corresponding cis lactones close spontaneously.[21]

The coupling reactions of cuprate **5** have also been investigated. Successful coupling with alkyl halides would lead to a variety of $\alpha$-substituted acrolein derivatives. Of particular interest were the reactions with vinyl halides which would provide access to derivatives of 2-formylbutadiene. We have found that reaction of the cuprate in excess (5–6 equiv) with allylic halide provides 1,4-dienes such as **21** in high yield (98%). However, remarkably, cuprate **5** does not react with primary and secondary vinyl bromides and iodides or a variety of aliphatic primary bromides and iodides, affording only dimer **10** upon prolonged reaction. A variety of solvent and temperatures were investigated without success. A similar selectivity was observed in one case, benzyl bromide, by Grieco.[16] This troublesome lack of reactivity, while severely limiting the generality, should allow the potentially useful selective coupling of an allylic bromide in preference to any other halide or tosylate in a multifunctional molecule. All attempts to open a variety of substituted epoxides were also unsuccessful.

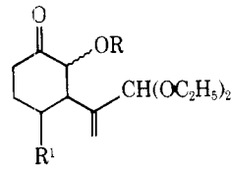
Finally, we have investigated the use of cuprate **5** for the production of dioxygenated lactones such as **22** and determined the potential for stereochemical control in these processes. Oxygenation patterns such as that present in **22** are



**22**



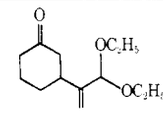
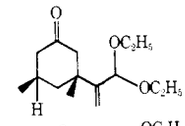
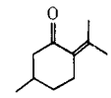
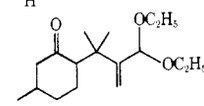
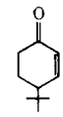
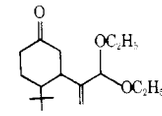
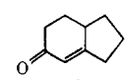
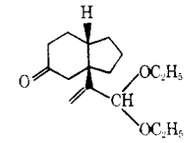
**23**, R = H
**34**, R = $OMe_3Si$



**24**, R = $CC_6H_4Cl$; $R^1$ = H
**25**, R = $Si(CH_3)_3$; $R^1$ = H
**26**, R = H; $R^1$ = H
**35**, R = $CC_6H_4Cl$; $R^1$ = $OMe_3Si$

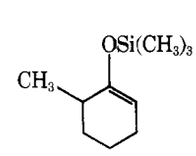
found in a number of naturally occurring terpenes.[22] Initially, our attempts focused upon the oxidation of the enolate formed from the conjugate addition of cuprate **5** to enones. Treatment of the intermediate enolate from the addition of cuprate **5** to 2-cyclohexen-1-one with oxygen,[23] lead tetraacetate,[24] or molybdenum peroxide,[25] all of which have been utilized to oxidize enolates to $\alpha$-oxygenated systems, were uniformly unsuccessful. Consequently, we turned to the use of the derived enol trimethylsilyl ether **23** which could be isolated in 75% yield by addition of trimethylchlorosilane and triethylamine to the enolate solution.[26] It is well known that enol ethers, upon oxidation with peracids, afford the $\alpha$-benzoyloxy ketone.[27] However, enol silyl ethers have been shown by Rubottom,[28] and more recently by Hassner,[29] to afford the $\alpha$-trimethylsiloxy ketones on treatment with peracids in nonpolar media. We have observed a rather remarkable solvent effect for this process. Treatment of silyl ether **23** with *m*-chloroperbenzoic acid in ether at 0 °C to room temperature affords the $\alpha$-*m*-chlorobenzoyloxy ketone (**24**) as a mixture

Table II

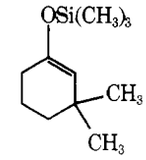
| | Substrate | Adduct | Yield,[a] % |
|---|---|---|---|
| 1 |  |  | 92 |
| 2 |  |  | 56 |
| 3 |  |  | 20 |
| 4 |  7 |  | 25 |
| 5 |  8 |  | 30 |

[a] Isolated yields of products purified by chromatography or distillation.

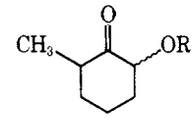
of cis and trans isomers (~1:1). Remarkably, upon treatment of **23** with the same peracid in methylene chloride only the trimethylsiloxy derivative (**25**) is obtained. Consequently it is possible to select either an acid-labile or non-acid-labile group by simply changing the solvent. Control experiments have demonstrated that the production of the benzoyloxy ketone does not proceed via the trimethylsiloxy compound. Exposure of **25** to ethereal *m*-chlorobenzoic acid results only in slow conversion of **25** to the hydroxy compound **26.** Furthermore, we have demonstrated that the products do not arise via the intermediacy of the ketone by conversion of enol silyl ethers **27** and **28** to the *m*-chlorobenzoates **29** and **30** in



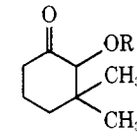
**27**



**28**



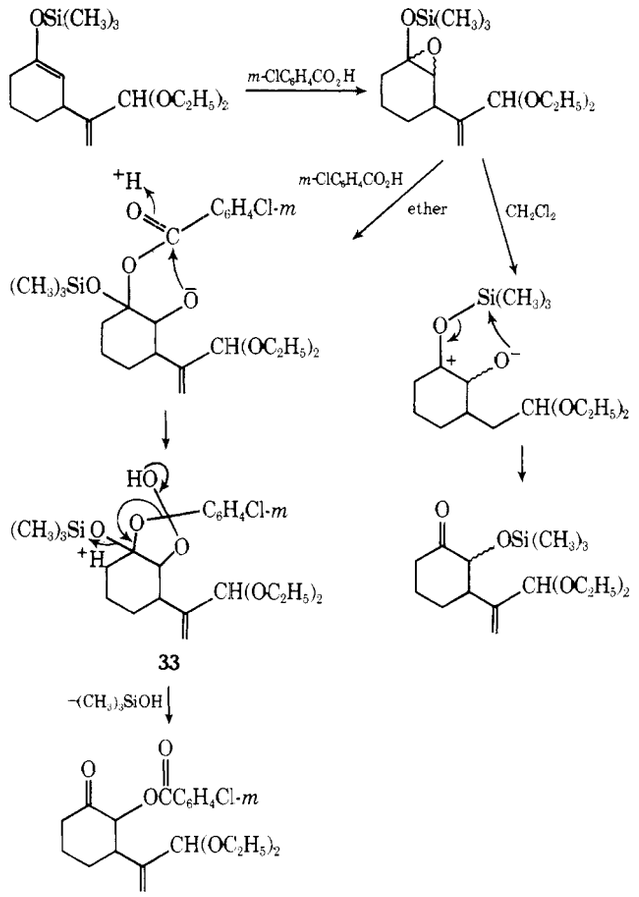
**29**, R = *m*-$ClC_6H_4C$
**31**, R = $Si(CH_3)_3$



**30**, R = *m*-$ClC_6H_4C$
**32**, R = $Si(CH_3)_3$

ether solvent and the silyl ethers **31** ad **32** in methylene chloride. It seems that the most plausible explanation for this effect is the enhanced nucleophilicity of the benzoic acid in ether due to higher basicity of ether. This increases the rate of attack of the benzoic acid upon the epoxy ether leading via intermediate **33** to benzoate. In nonpolar media internal transfer of silicon as postulated by Rubottom and Hassner[28,29] is much more rapid (Scheme II). Further experiments to clarify this are in progress. Extension of this process to enone **11** afforded silyl enol ether **34** in 62% yield accompanied by 36% of the ketone **13.** However, treatment of (**34**) with *m*-chloroper-

Scheme II




benzoic acid did not produce the desired benzoate (**35**). We could obtain only the hydrolysis product, ketone **13.**

## Summary

The preparation of mixed ligand cuprates from 2-lithio-1,1-diethoxy-2-propene is convenient with the *tert*-butylacetylene ligand preferred owing to enhanced solubilities. The cuprate reagent adds rapidly and in high yield to unhindered unsaturated ketones and sluggishly to more hindered enones. Considerable sensitivity of the reagent to steric congestion about the $\beta$ carbon of the enone is observed, although additions proceed with some hindered cases but the yields are lower. High selectivity for reaction with allylic halides is shown and this selectivity nicely complements the reactivity of the lithium reagent itself with alkyl halides.[14] We have demonstrated that this cuprate serves as an efficient precursor of trans $\alpha$-methylene lactones and that the addition of a single oxygen function is possible although presently not with high stereoselectivity or in the presence of a second oxygen function.

## Experimental Section

Melting points were determined on a Fisher-Johns or Thomas-Hoover melting point apparatus and are uncorrected. Nuclear magnetic resonance spectra were obtained on a Varian T-60 spectrometer and are reported in $\delta$ downfield from $Me_4Si$ (internal standard). Infrared (IR) spectra were obtained on a Perkin-Elmer 137 infrared spectrophotometer and are reported in reciprocal centimeters. Mass spectra (high and low resolution) were determined on an AEI MS-9 spectrometer. Reaction solvents such as ether and tetrahydrofuran (THF) were freshly distilled from lithium aluminum hydride under argon to obtain them anhydrous. All reactions involving organometallics were performed in flame-dried, septum capped apparatus under an argon atmosphere. All transfers were via syringe. The copper iodide used was purified by reprecipitation from concentrated potassium iodide after Norit treatment and dried at 100 °C under high vacuum for 12 h. *tert*-Butyllithium was obtained from Alfa Inorganics as ~0.5 M in pentane and used as received. All other commercial materials were purified as appropriate before use.

**Lithium (3,3-Dimethyl-1-butynyl)-1,1-diethoxy-2-propenylcuprate (5).** A solution of lithio-3,3-dimethyl-1-butyne [prepared from 3,3-dimethyl-1-butyne (0.240 g, 3 mmol) and methyllithium (1.5 mL, 3 mmol, 2.3 M in ether) at 0 °C in ether (4 mL) under argon] was added to a suspension of purified copper iodide (0.570 g, 3 mmol) in ether (4 mL) under argon at 0 °C and stirred at 15–20 °C for 15 min (red color). To a cold (−78 °C) solution of 1,1-diethoxy-2-bromopropene (0.527 g, 3 mmol) in ether (4 mL) under argon, *tert*-butyllithium (5.1 mL, 6 mmol, 1.25 M in hexane) was added dropwise in ~20 min and then stirred for 1.5 h. This solution was transferred by means of a precooled syringe to the above cooled (−78 °C) solution of copper 3,3-dimethyl-1-butyne (3 mmol) and stirred for 2 h. The temperature was then raised to −40 °C and the solution stirred for 30 min. The complete formation of cuprate **5** was assumed when the red color of the copper acetylide disappeared and it was also assumed that this solution contained 3 mmol of **5.**

**Lithium (3,3-Dimethyl-1-butynyl)-2-trimethylsilylvinylcuprate and lithium (3,3-dimethyl-1-butynyl)-2-propenylcuprate** were prepared analogously. Similar procedures were used to prepare these cuprates in THF.

**Preparation of 11 from Endoperoxide 12.** Endoperoxide (11.2 g, 0.1 mol), pyridine (20 mL), and a catalytic amount of triethylamine were stirred at room temperature for 12 h. When the endoperoxide was completely consumed (TLC), trimethylsilyl chloride (40 mL) was added slowly through a rubber septum and then stirred for 12 h (followed by TLC). Excess pyridine and trimethylsilyl chloride were removed in vacuo and ether (200 mL) was added. The solution was filtered and the filtrate concentrated. The concentrate was dissolved in ether (50 mL) and then passed through a small column of silica gel and the column further eluted with ether. The combined ether solution was concentrated and distilled to afford **11:** 15.5 g (85%); bp 70 °C (0.4 mm); NMR ($CDCl_3$) $\delta$ 0.23 (s, 9 H), 2.4 (m, 4 H), 4.63 (m, 1 H), 6.01 (dd, 1H, $J_2$ = 10 Hz), 6.98 (q, 1 H, $J$ = 1.2, 2, 10 Hz); IR (film) 1690, 1255, 1110 $cm^{-1}$; $M^+$ 184.

Anal. Calcd for $C_9H_{16}O_2Si$: C, 58.69; H, 8.69. Found: C, 60.04; H, 8.65.

***trans*-4-Trimethylsilyloxy-3-(1,1-diethoxy-2-propenyl)cyclohexanone (13).** To the cuprate **5** (3 mmol) in ether, a solution of enone **11** (0.368 g, 2 mmol) in ether (1 mL) was added dropwise at −78 °C, allowed to warm to −15 °C, and then kept at this temperature for 12 h. The reaction mixture was quenched with saturated ammonium chloride (10 mL) and then stirred for 5–10 min. The entire reaction mixture was transferred to a separatory funnel and ether (100 mL) was added. This two-phase mixture was extracted with ammonium hydroxide (20%, 2 × 10 mL). The organic layer was separated, and the aqueous phase extracted twice with ether (20 mL). The combined organic layers were extracted once with saturated sodium chloride and then dried over anhydrous magnesium sulfate. After filtration, the solvent was removed on a rotary evaporator. The residue was distilled (bulb to bulb) to afford **13:** 0.584 g (93%); bp 98 °C (1.0 mm); NMR ($CDCl_3$) $\delta$ 0.22 (s, 9 H), 1.3 (t, 6 H), 2.40 (m, 7 H), 3.55 (m, 4 H), 4.20 (m, 1 H), 4.95 (s, 1 H), 5.08 (s, 1 H), 5.32 (s, 1 H); IR (film) 1715, 1250, 1110, 1060, 1010, 880, 840 $cm^{-1}$; $M^+$ 314.

Anal. Calcd. for $C_{16}H_{30}O_4Si$: C, 61.14; H, 9.55. Found: C, 60.85; H, 9.61.

**3-(1,1-Diethoxy-2-propenyl)cyclohexanone.** To the cuprate **5** (3 mmol) in ether, a solution of 2-cyclohexen-1-one (0.196 g, 2 mmol) in ether (1 mL) was added dropwise at −78 °C under argon. After 2 h stirring (−78 °C), the solution attained a red color. The temperature was gradually raised to −20 °C (1 h) and then the mixture was quenched with saturated ammonium chloride (10 mL). The crude product was isolated according to the procedure described for **13.** Distillation (bulb-bulb) afforded the ketone 0.442 g (98%): NMR ($CDCl_3$) $\delta$ 1.2 (t, 6 H), 2.4 (m, 9 H), 3.5 (m, 4 H), 4.75 (s, 1 H), 5.10 (s, 1 H), 5.35 (s, 1 H); IR (film) 1710, 1450, 1230, 1110 $cm^{-1}$; $M^+$ 226.

***trans*-4-*tert*-Butyl-3-(1,1-diethoxy-2-propenyl)cyclohexanone.** To the cuprate **5** (3 mmol in THF) under argon a solution of 4-*tert*-butyl-2-cyclohexen-1-one (0.152 g, 1 mmol) in THF (1 mL) was slowly added at −78 °C and stirred for 3 h. The reaction mixture was left at −15 °C overnight and at 0 °C for 4 h. The reaction mixture was quenched with saturated ammonium chloride (10 mL) and worked up as described for compound **13** to afford a mixture of products. Preparative thick layer chromatography [silica gel, pentane–ether (1:1)] gave starting enone (0.025 g, 16.4%) and title compound: 0.060 g (25% based on recovered starting material; conversion 81%); NMR ($CDCl_3$) $\delta$ 1.00 (s, 9 H), 1.20 (t, 6 H), 2.32 (m, 8 H), 4.80 (s, 1 H), 5.12 (s, 1 H), 5.35 (s, 1 H); IR (film) 1710 $cm^{-1}$; $M^+$ 270.

**5-(1,1-Diethoxy-2-propenyl)hydrindan-3-one.** To the cuprate

5 (3 mmol) in THF, under argon, a solution of indenone (0.272 g, 2 mmol) was added at −78 °C, stirred for 2 h at −78 °C, and then kept at 0 °C for 36 h. The reaction mixture was quenched with saturated ammonium chloride (10 mL) and worked up as described for compound 13 to afford a mixture of compounds. Preparative thick layer chromatography on silica gel (ether–pentane, 1:2) gave starting enone (0.053 g, 20%) and title compound: 0.140 g (29%, based on recovered starting enone, 80.5% conversion); NMR ($CDCl_3$) δ 1.33 (t, 6 H), 2.35 (m, 13 H), 3.65 (m, 4 H), 4.95 (s, 1 H), 5.3 (s, 1 H), 5.98 (s, 1 H); IR (film) 1710, 1110, 1060 $cm^{-1}$; $M^+$ 266.

**3,5-Dimethyl-3-(1,1-diethoxy-2-propenyl)cyclohexanone.** To the cuprate 5 (3 mmol) in THF, under argon, a solution of 3,5-dimethyl-2-cyclohexen-1-one (0.248 g, 2 mmol) in THF (1 mL) was added at −78 °C and stirred for 3 h. The temperature was gradually raised to 0 °C (2 h) and then kept at 0 °C for 24 h. The reaction mixture was quenched with saturated ammonium chloride (10 mL) and then worked up as described for compound 13 to afford a mixture of products. This mixture was separated on preparative TLC (silica gel, ether–benzene, 1:3) to afford starting enone 0.090 g (36%) and the ketone (0.180 g, 55%); conversion 63%. NMR ($CDCl_3$) δ 1.3 (m, 12 H), 2.2 (m, 7 H), 4.90 (s, 1 H), 5.23 (s, 1 H), 5.6 (s, 1 H); IR (film) 1715, 1110, 1070 $cm^{-1}$; $M^+$ 254.

Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.86; H, 10.23. Found: C, 70.76; H, 10.29.

**1-Trimethylsilyloxy-3-(1,1-diethoxy-2-propenyl)-1-cyclohexene (23).** The reaction mixture, obtained from cuprate 5 (3 mmol) and cyclohex-2-en-1-one (0.196 g, 2 mmol) as described above for the compound 3, was quenched with purified trimethylsilyl chloride (3 mL) (added through a rubber septum with the help of a syringe), and then stirred for 2 h at room temperature. Dry pentane (30 mL) was added and the solution stirred for 5 min before filtering and washing with pentane (10 mL). The combined pentane solutions were concentrated on a rotary evaporator. A second portion of pentane (20 mL) was added and the mixture filtered and concentrated. This process was repeated until no more precipitate was formed on further addition of pentane. Column chromatography over silica gel, using benzene as eluent, afforded the silyl ether, 0.447 g (75%): bp 120 °C (0.5 mm) (bulb-to-bulb); NMR ($CDCl_3$) δ 0.2 (s, 9 H), 1.22 (d, 6 H), 2.0 (m, 7 H), 3.5 (m, 4 H), 4.8 (s, 2 H), 5.10 (d, 1 H, $J$ = 1 Hz), 5.3 (d, 1 H, $J$ = 1 Hz); IR (film) 1670, 1250, 1110, 1055, 910 $cm^{-1}$; $M^+$ 298.

***trans*-3-(1,1-Diethoxy-2-propenyl)-1,4-ditrimethylsilyloxy-1-cyclohexene (34).** The reaction mixture obtained from cuprate 5 (15 mmol) in THF and 11 (1.84 g, 10 mmol) according to the procedure described for the compound 34, was quenched with purified trimethylsilyl chloride (15 mL) and stirred for 3–4 h at room temperature (reaction was followed by TLC). Dry pentane (100 mL) was added and stirred for 5–10 min. The precipitate was filtered off and the solids washed with pentane (50 mL). The combined filtrates and washings were concentrated on a rotavapor. To the gummy residue pentane (50 mL) was further added and the precipitate was again filtered off. The filtrate was concentrated. This process was repeated until no more precipitate was separated on further addition of pentane. Column chromatography over silica gel using benzene–ether mixture (20:1) afforded 13 (1.10 g, 30%) and the enol ether (2.4 g, 62%): bp 120 °C (0.5 mm) (bulb-bulb); NMR ($CDCl_3$) δ 0.15 (s, 9 H), 0.20 (s, 9 H), 1.3 (t, 6 H), 3.6 (m, 5 H), 3.2 (m, 1 H), 3.6 (m, 4 H), 4.65 (d, 1 H, $J$ = 4 Hz) 4.88 (s, 1 H), 5.15 (d, 1 H, $J$ = 1 Hz), 54 (d, 1 H, $J$ = 1 Hz); IR (film) 1670, 1380, 1250, 1180, 1070, 910, 850 $cm^{-1}$; $M^+$ 386.

**2-(*trans*-2-Hydroxy-5-oxocyclohexyl)propenoic Acid Lactone (20).** A mixture of pyridine (2 mL), dicyclohexlcarbodiimide (0.640 g), and acid 19 (0.303 g. 1.65 mmol) was stirred for 24 h. (Reaction was followed by TLC.) Dry ether (15 mL) was added, the solution filtered, and the filtrate concentrated on a rotary evaporator. This process was repeated until no more precipitate was formed. Filtrate fractions were discarded and precipitate fractions were collected and extracted with chloroform (3 × 5 mL). The chloroform solution was filtered through a small silica gel column and washed with chloroform (10 mL). The chloroform was removed on a rotary evaporator to give a solid. Crystallization from chloroform–ether (1:10) afforded **20:** 0.150 g (55%); mp 149–150 °C; NMR ($CDCl_3$) δ 2.6 (m, 7 H), 4.22 (m, 1 H), 5.45 (d, 1 H, $J$ = 2 Hz), 6.2 (d, 1 H, $J$ = 2 Hz); IR (Nujol) 1750, 1715, 1425, 1260, 1150, 1130, 1015, 980 $cm^{-1}$; $M^+$ 166.

Anal. Calcd for $C_9H_{10}O_3$: C, 65.06; H, 6.02. Found: C, 65.33; H, 6.65.

**1-(1,1-Diethoxy-2-propenyl)-2-cyclohexene (21).** To the cuprate 5 (10 mmol in THF) under argon a solution of 1-bromo-2-cyclohexene (0.483 g, 3 mmol) in THF (2 mL) was added dropwise at −78 °C and then stirred for 2 h. The reaction mixture was kept at −15 °C for 12 h and then quenched with saturated ammonium chloride (10 mL). The product (21) was isolated according to the workup described for **13,** affording 0.617 g (98%): bp 130 °C (0.5 mm) (bulb to bulb); NMR ($CDCl_3$) δ 1.22 (t, 6 H), 2.0 (m, 6 H), 3.0 (m, 1 H), 3.6 (m, 4 H), 4.9 (s, 1 H), 5.18 (s, 1 H), 5.4 (s, 1 H), 5.8 (m, 2 H); IR (film) 1650, 1450, 1320, 1060, 920 $cm^{-1}$; $M^+$ 210.

**2-(*trans*-2-Hydroxy-5-oxocyclohexyl)propenaldehyde (17).** Ethanol (20 mL), water (10 mL), concentrated sulfuric acid (2 mL), and 13 (2.2 g, 9.7 mmol) were stirred at room temperature for 4 h. The alcohol was removed on a rotary evaporator and the solution neutralized with 5% sodium bicarbonate, then extracted with ether in a continuous extractor. The ether solution was dried over anhydrous magnesium sulfate and the solvent removed on a rotary evaporator. The residue was chromatographed over silica gel, first eluting with benzene (50 mL) which was discarded and then with ether (100 mL). Concentration of the ether fraction afforded pure aldehyde (1.15 g, 68%). Distillation caused polymerization. NMR ($CDCl_3$) δ 2.6 (m, 7 H), 4.17 (m, 1 H), 6.30 (s, 1 H), 6.48 (s, 1 H), 9.54 (s, 1 H); IR (film) 3400, 1715, 1705, 1430, 1240, 1075, 965 $cm^{-1}$; $M^+$ 168.

**2-(*trans*-2-Hydroxy-5-oxocyclohexyl)propenoic Acid (19).** To a mixture of ethanol (12 mL), water (12 mL), silver nitrate (0.890 g, 5.28 mmol), and the aldehyde 17 (0.82 g, 4.8 mmol), a solution of sodium hydroxide (1.1 g, 2.6 mmol, in 5 mL of water) was added dropwise at room temperature over 2 h and then stirred for 14 h. The mixture was filtered and acidified with 10% hydrochloric acid. The aqueous solution was extracted continuously with ether, and the ether solution dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a brown liquid which was passed through a small silica gel column in ether. The combined ether solutions were concentrated in vacuo to afford 19 (0.750 g, 85%) which was homogeneous by TLC. Distillation of 19 caused polymerization and it could not be crystallized. NMR ($CD_3COCD_3$-$D_2O$) δ 2.32 (m, 7 H), 4.3 (m, 1 H), 5.82 (s, 1 H), 6.5 (s, 1 H); IR (film) 3300, 3700 (broad), 1250 $cm^{-1}$; $M^+$ 184.

***trans*-4-Trimethylsiloxy-3-(1-trimethylsilylvinyl)cyclohexanone (14).** To the cuprate prepared from α-bromovinyltrimethylsilane as described for 5 above (3 mmol) in ether, at −78 °C, under argon, a solution of enone 11 (0.368 g, 2 mmol) in ether (1 mL) was added dropwise and stirred for 2 h. The temperature was gradually raised to −15 °C and kept for 12 h. The reaction mixture was then quenched with saturated ammonium chloride (10 mL) and worked up as described for compound 13 affording **14:** 0.520 g (97%); bp 95 °C (0.2 mm) (bulb-bulb); NMR ($CDCl_3$) δ 0.18 (s, 9 H), 0.22 (s, 9 H), 2.2 (m, 7 H), 4.2 (m, 1 H), 5.6 (d, 1 H, $J$ = 0.8 Hz), 5.7 (d, 1 H, $J$ = 0.8 Hz); IR (film) 1715 $cm^{-1}$; $M^+$ 268.

***trans*-8-Hydroxy-7-(1-trimethylsilylvinyl)-1,4-dioxaspiro[4.5]decane.** Ketone 14 (0.134 g, 0.5 mmol), ethylene glycol (0.031 g, 0.5 mmol), *p*-toluenesulfonic acid (a few crystals), and benzene were heated at reflux over a Dean-Stark apparatus for 12 h. The benzene solution was concentrated on a rotary evaporator and then ether (10 mL) was added. The ether solution was extracted with water and saturated sodium chloride solution, and then dried over anhydrous magnesium sulfate. After removal of the solvents on a rotary evaporator, the residue was distilled (bulb-bulb) to afford the ketal (0.100 g, 77%): bp 95 °C (0.2 mm); NMR ($CDCl_3$) δ 0.2 (s, 9 H), 1.8 (m, 7 H), 3.8 (m, 1 H), 4.0 (s, 4 H), 5.7 (d, 1 H, $J$ = 1 Hz), 5.9 (d, 1 H, $J$ = 1 Hz); IR (film) 3350, 1370, 1260, 1150, 1080, 920, 860 $cm^{-1}$; $M^+$ 256.

***trans*-8-Hydroxy-7-(1-bromovinyl)-1,4-dioxaspiro[4.5]decane (16).** To a solution of the above ketal (0.095 g, 0.42 mmol) in methylene chloride (2 mL), a solution of bromine (0.067 g) in methylene chloride (1 mL) was added at 0 °C in 3 min. Immediately, the solvent was removed on rotary evaporator and the residue was dissolved in methanol (2 mL). This methanolic solution was added to freshly prepared sodium methoxide (0.020 g of sodium in 2 mL of methanol) and stirred for 3 h. The methanol was removed on a rotary evaporator and the residue neutralized with 0.1 N hydrochloric acid. The aqueous solution was repeatedly extracted with ether. The combined ether extracts were dried over anhydrous magnesium sulfate and filtered and the solvent removed on a rotary evaporator to give 0.115 g of gummy material. Column chromatography (silica gel–chloroform) afforded the liquid ketal 16 (0.050 g, 45%): NMR ($CDCl_3$) δ 1.8–2.6 (m, 7 H), 4.1 (s, 4 H), 4.2 (m, 1 H), 5.7 (d, 1 H, $J$ = 1 Hz), 5.9 (d, 1 H, $J$ = 1 Hz); IR (film) 1630, 1460, 1350, 1160, 1070, 1025, 950 $cm^{-1}$; $M^+$ 201.

***trans*-8-Hydroxy-7-(1-carbomethoxyvinyl)-1,4-dioxaspiro[4.5]decane.** To a solution of sodium methoxide (0.15 g in 2 mL of dry methanol) and nickel carbonyl (0.26 mL), a solution of 16 (0.05 g, 0.2 mmol) in methanol (2 mL) was added under argon with stirring. The reaction mixture was heated to 55 °C for 5 h and then saturated with carbon monoxide for 15 min. The residue was acidified with 0.1 N hydrochloric acid and then extracted with ether (5 × 10 mL). The combined ether fractions were washed with saturated sodium chloride and then dried over anhydrous magnesium sulfate. After the solvent

was removed in vacuo the residue was chromatographed over silica gel (chloroform) to afford the ketal ester as a liquid (0.02 g, 41.6%): NMR ($CDCl_3$) δ 1.8 (m, 7 H), 3.8 (s, 3 H), 4.1 (s, 4 H), 4.35 (m, 1 H), 5.9 (s, 1 H), 6.45 (s, 1 H); IR (film) 3445, 1695, 1520, 1445, 860 $cm^{-1}$; $M^+$ 242.

***trans*-3-(2-Propenyl)-4-trimethylsiloxycyclohexanone (15).** To the ethereal solution of the isopropenyl cuprate prepared as for **5** (3 mmol), under argon at −78 °C, a solution of 4-trimethylsiloxy-2-cyclohexen-1-one (0.368 g, 2 mmol) in ether (1 mL) was added and stirred for 2 h, then kept at −15 °C for 12 h and quenched with saturated ammonium chloride (10 mL). The workup described for the compound **13** afforded **15** (0.440 g, 97%): bp 100–105 °C (2.5 mm) (bulb-bulb); NMR ($CDCl_3$) δ 0.20 (s, 9 H), 1.8 (s, 3 H), 2.5 (m, 7 H), 4.2 (m, 1 H), 4.80 (s, 1 H), 4.95 (s, 1 H); IR (film) 1700, 1200, 1100, 845 $cm^{-1}$; $M^+$ 138.

***trans*-7-(2-Propenyl)-8-hydroxy-1,4-dioxaspiro[4.5]decane.** Ketone **15** (0.226 g, 1 mmol), ethylene glycol (0.062 g, 1 mmol), and *p*-toluenesulfonic acid (a few crystals) in benzene were refluxed under a Dean-Stark apparatus for 12 h. The benzene was evaporated and water (2 mL) was added. The mixture was extracted with ether (3 × 8 mL) and the ether extracts were washed with saturated sodium chloride. After drying the organic layer over anhydrous magnesium sulfate, the solvent was removed and the residue was distilled to afford the ketal (0.130 g, 66.5%): bp 140 °C (2.5 mm) (bulb-bulb); NMR ($CDCl_3$) δ 1.8 (m, 7 H), 2.1 (s, 3 H), 3.6 (m, 1 H), 4.0 (s, 6 H), 4.95 (s, 2 H); IR (film) 3450, 1380, 1245, 840 $cm^{-1}$; $M^+$ 198.

**Conversion of Ketal 15 to 2-(*trans*-2-Hydroxy-5-oxocyclohexyl)propenaldehyde.** Selenium dioxide (0.120 g, freshly sublimed), ethanol (3 mL), water (0.25 mL), and the above ketal (0.120 g, 0.6 mmol) were refluxed for 3 h. The solvent was evaporated and the residue extracted with ether (twice). The ether solution was dried and the solvent removed to afford a brown liquid which on chromatography (silica gel–benzene) afforded the aldehyde (0.020 g, 20%). The spectral properties of this material were identical with the spectra of the material prepared from **13**.

**2-(*m*-Chlorobenzoyloxy)cyclohexanone.** To a solution of 1-(trimethylsiloxy)cyclohexanone (0.340 g, 2 mmol) in dry ether (4 mL), a cold solution of *m*-chloroperbenzoic acid (0.516 g, 3 mmol) in dry ether (3 mL) was added at 0 °C and stirred for 10 min. The reaction mixture was passed through a column (1 × 8 cm) of alumina (neutral, activity I, Woelm) in ether and then concentrated in vacuo to afford the ketone (0.410 g, 81%): mp 152–153 °C (pentane); NMR ($CDCl_3$) δ 1.8–2.8 (m, 8 H), 5.5 (m, 1 H), 7.5 (m, 2 H), 8.1 (m, 2 H); IR (Nujol) 1730, 1720, 1315, 1230, 1215, 1125, 875, 750 $cm^{-1}$; $M^+$ 254, 252.

Anal. Calcd for $C_{13}H_{13}ClO_3$: C, 61.50; H, 5.15. Found: C, 61.67; H, 5.13.

**2-(*m*-Chlorobenzoyloxy)-6-methylcyclohexanone (29).** To a cold solution of 1-(trimethylsiloxy)-6-methyl-1-cyclohexene (0.366 g, 2 mmol) dry ether (4 mL) was added at 0 °C and stirred for 10 min. The reaction mixture was then passed through a small column of alumina (neutral, activity I, Woelm) in ether (30 mL). The combined ether fractions were concentrated on a rotary evaporator to afford **29** (0.250 g, 50%) which could not be crystallized: NMR ($CDCl_3$) 1.1 (d, 3 H), 2.2 (m, 7 H), 4.3 (m, 1 H), 7.8 (m, 4 H); IR (film) 1720, 1450, 1250, 1120, 1000, 845 $cm^{-1}$; $M^+$ 268, 266.

**2-(*m*-Chlorobenzoyloxy)-3,3-dimethylcyclohexanone (30).** To a cold solution of 1-(trimethylsiloxy)-3,3-dimethyl-1-cyclohexene (0.396 g, 2 mmol) in dry ether (4 mL), a cold solution of *m*-chloroperbenzoic acid (0.516 g, 3 mmol) in dry ether (3 mL) was added at 0 °C and then stirred for 10 min. The reaction mixture was then passed through a small column of alumina (neutral, activity I, Woelm) in ether (30 mL). The combined ether fractions were concentrated on a rotary evaporator. The NMR spectrum showed the presence of the ketone resulting from the hydrolysis of the starting material. Chromatography on silica gel using a pentane–ether mixture afforded semisolid **30** (0.410 g, 73%). This material was homogeneous on TLC. NMR ($CDCl_3$) δ 1.1 (s, 3 H), 1.24 (s, 3 H), 2.1 (m, 6 H), 5.2 (s, 1 H), 2.6 (m, 2 H), 8.1 (m, 2 H); IR (film) 1720 (b), 1370, 1250, 1120 $cm^{-1}$; $M^+$ 282, 280.

Anal. Calcd for $C_{15}H_{17}O_3Cl$: C, 64.28; H, 6.07. Found: C, 64.15; H, 6.07.

**2-Trimethylsilyloxy-3-(1,1-diethoxy-2-propenyl)cyclohexanone (25).** Utilizing the procedure of Hassner,[29] silyl enol ether **23** (48 mg, 0.28 mmol) afforded ketone 25 (40 mg, 80%). TLC and VPC analysis showed a mixture of two epimeric substances (~1:1): NMR ($CDCl_3$) δ 0.2 (s, 9 H), 1.25 (d, 6 H) 2.0 [m (br), 7 H], 3.85 (m, 4 H), 4.5 [s (br), 1 H], 5.0 (s, 1 H), 5.28 (s, 1 H), 5.5 (s, 1 H); IR (film) 1720, 1250, 1105, 1050, 835 $cm^{-1}$, $M^+$ 314.

**2-(*m*-Chlorobenzoyloxy)-3-(1,1-diethoxy-2-propenyl)cyclohexanone (24).** To a cold solution (0 °C) of 1-trimethylsiloxy-3-(1,1-diethoxy-2-propenyl)-1-cyclohexene (0.149 g, 0.5 mmol) in dry ether (1 mL) was added a solution of *m*-chloroperbenzoic acid (0.130 g, 0.75 mmol) in ether (1 mL). The mixture was stirred for a total of 1.5 h during warming to room temperature. The total reaction mixture was applied to a small column of alumina and eluted with ether (20 mL). Removal of the solvent gave ketone **25** (95 mg, 50%) as a mixture of isomers (~1:2): NMR ($CDCl_3$) δ 1.25 (m, 6 H), 2.5 (m, 7 H), 3.8 (m, 4 H), 4.8 (m, 1 H), 5.2–5.6 (m, 3 H), 7.5–8.1 (m, 4 H); IR (film) 1720, 1275, 1250, 1110, 1050, 750 $cm^{-1}$; $M^+$ 382, 380.

**Acknowledgment.** The authors wish to thank the National Cancer Institute of the NIH for the award of a research grant in support of this work (CA 17154) and for the granting of a Career Development Award (CA-00273) to one of us (Robert K. Boeckman, Jr.).

**Registry No.**—**3,** 57428-13-4; **5,** 58419-23-1; **7,** 937-07-5; **8,** 1489-28-7; **11,** 61543-59-7; **12,** 6671-70-1; **13,** 61543-60-0; **14,** 61543-61-1; **15,** 61543-62-2; **16,** 61543-63-3; **17,** 61543-64-4; **19,** 61543-65-5; **20,** 61543-66-6; **21,** 57428-10-1; **23,** 61543-67-7; *cis*-**24,** 61543-68-8; *trans*-**24,** 61543-69-9; *cis*-**25,** 61543-70-2; *trans*-**25,** 61543-71-3; **27,** 19980-33-7; **28,** 61175-92-6; *cis*-**29,** 61543-72-4; *trans*-**29,** 61543-73-5; **30,** 61543-74-6; **34,** 61543-75-7; lithio 3,3-dimethyl-1-butyne, 37892-71-0; copper iodide, 7681-65-4; 1,1-diethoxy-2-bromopropene, 61543-76-8; lithium (3,3-dimethyl-1-butynyl)-2-trimethylsilylvinyl cuprate, 61544-10-3; lithium (3,3-dimethyl-1-butynyl)-2-propenyl cuprate, 61544-09-0; trimethylsilyl chloride, 75-77-4; 2-cyclohexen-1-one, 930-68-7; *trans*-4-*tert*-butyl-3-(1,1-diethoxy-2-propenyl) cyclohexanone, 61543-77-9; 5-(1,1-diethoxy-2-propenyl)hydrindan-3-one, 61543-78-0; 3,5-dimethyl-3-(1,1-diethoxy-2-propenyl)cyclohexanone, 61543-79-1; 3,5-dimethyl-2-cyclohexen-1-one, 1123-09-7; 1-bromo-2-cyclohexene, 1521-51-3; *trans*-8-hydroxy-7-(1-carbomethoxyvinyl)-1,4-dioxaspiro[4.5]decane, 61543-80-4; sodium methoxide, 124-41-4; *trans*-7-(2-propenyl)-8-hydroxy-1,4-dioxaspiro[4.5]decane, 61543-81-5; ethylene glycol, 107-21-1; *trans*-8-hydroxy-7-(1-trimethylsilylvinyl)-1,4-dioxaspiro[4.5]decane, 61543-82-6; 2-(*m*-chlorobenzoyl)cyclohexanone, 61543-83-7; *m*-chloroperbenzoic acid, 937-14-4.

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