

for 5 days. The reaction was quenched with the addition of 1 M hydrochloric acid (5 mL). The catalyst was removed by filtration and washed with dichloromethane. The filtrate was extracted with dichloromethane. The combined organic layers were dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was purified by silica gel TLC (AcOEt-hexane = 1:4, v/v as eluent), and subsequent bulb-to-bulb distillation afforded optically active secondary alcohol 3.

**Recovery of Catalyst 11.** The catalyst was collected from the reaction mixture by filtration and was stirred for 1 h in a

mixture of THF-2 M HCl (4:1, v/v). The catalyst was filtered and washed successively with water and dioxane. Then the catalyst was stirred again in a mixture of THF-2 M aqueous NaOH (4:1, v/v). The catalyst was filtered and washed successively with water, THF, and methanol. After drying in vacuo at 40 °C, the catalyst was reused in the enantioselective addition of dialkylzinc to aldehyde.

**Acknowledgment.** We thank the Saneyoshi Scholarship Foundation for partial financial support.

## Novel ( $\alpha,\beta$ -Epoxyalkyl)lithium Reagents via the Lithiation of Organyl-Substituted Epoxides<sup>1</sup>

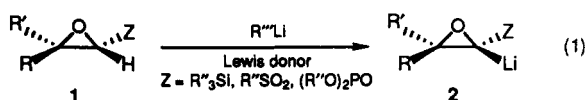
John J. Eisch\* and James E. Galle

Department of Chemistry, The State University of New York at Binghamton, Binghamton, New York 13901

Received February 26, 1990

A series of epoxides bearing unsaturated organyl groups attached directly to the epoxy group was found to have sufficient kinetic acidity to undergo clean lithiation at low temperatures. Epoxides of the type  $R_2C-CH(Un)O$ , where Un is aryl, vinylic, acetylenic, alkoxy-carbonyl, or cyano, were smoothly converted into  $R_2C-CLi(Un)O$  by either *t*-BuLi or LDA in the temperature range of -80 to -115 °C. The resulting ( $\alpha,\beta$ -epoxyalkyl)lithium reagents could be transformed into a variety of substituted epoxides, such as  $R_2C-CE(Un)O$ , where E = D,  $R_3Si$ ,  $R_3Sn$ , R, RCO,  $CO_2H$ , or  $COH(R)_2$ . In cases where Un is acyl, addition to the carbonyl, rather than lithiation, occurred preferentially. Attempted lithiations of aziridines and thiiranes led to extrusion of nitrogen and sulfur, respectively. Even the relatively stable  $R_2C-CLi(Un)O$  intermediates generated at <-90 °C underwent carbenoid-like decomposition at higher temperatures to yield isomerization and intermolecular-insertion products. Observation of these processes gives direct corroboration of reaction mechanisms proposed for the base-promoted isomerizations of epoxides.

The finding that ( $\alpha,\beta$ -epoxyalkyl)lithium compounds are readily available via the lithiation of a variety of  $\alpha$ -heteroatom-substituted epoxides (eq 1) has presented chemists with a versatile class of synthetic intermediates.<sup>2</sup> Especially



for the cases where triorganylsilyl groups are involved, the resulting ( $\alpha$ -silyl- $\alpha,\beta$ -epoxyalkyl)lithium reagents have commanded attention for the construction of carbon skeletons in a controlled, stereoselective fashion.<sup>2a,3</sup> The availability of such lithiated epoxides has thus enhanced considerably the already impressive potential of organo-silicon reagents in organic synthesis.<sup>4,5</sup>

Because of the significance of (epoxyalkyl)lithium reagents 2, we were interested to learn what other heteroatom substituents Z in 1 would also serve to acidify the  $\alpha$ -proton and, further, whether certain organyl groups (Z = vinyl, acetylenic, aryl, acyl, alkoxy-carbonyl, cyano, or alkyl) might serve a similar purpose. From previous extensive research on the base-promoted isomerizations of epoxides, there is ample evidence to support the transitory formation of  $\alpha$ -metalloepoxides in such transformations.<sup>6</sup> By conducting the lithiations of a series of  $\alpha$ -organyl-substituted epoxides at low temperatures, we hoped to generate and form synthetically useful derivatives of such labile intermediates. Some success in this endeavor would extend the availability of (epoxyalkyl)lithium reagents from solely  $\alpha$ -heteroatom-substituted epoxides to  $\alpha$ -organyl-substituted epoxides as well. We report here that these hopes have been largely realized.

## Results

**Organyl-Substituted Epoxides.** In order to investigate the acidifying character of various organic groups  $\alpha$  to the epoxide linkages ( $R''$  in eq 2), the compounds depicted in Scheme I were subjected to the action of the 1:1 complex of *tert*-butyllithium and TMEDA at temperatures of -80 to -115 °C.<sup>7</sup> After a suitable interval the reaction

(1) Part 8 of the series of publications devoted to "Functionalized Organolithium Reagents" and herewith established. Previous parts, Part 7: *J. Organomet. Chem.* 1988, 341, 293. Part 6: *J. Org. Chem.* 1985, 50, 3674. Part 5: *J. Organomet. Chem.* 1985, 285, 121. Part 4: *J. Org. Chem.* 1980, 45, 4534. Part 3: *J. Org. Chem.* 1979, 44, 3279. Part 2: *J. Organomet. Chem.* 1976, 121, C10. Part 1: *J. Am. Chem. Soc.* 1976, 98, 4646.

(2) (a) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* 1988, 341, 293. (b) Eisch, J. J.; Galle, J. E. *J. Org. Chem.* 1976, 41, 2615. (c) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* 1976, 121, C10. (d) Eisch, J. J.; Galle, J. E. *J. Am. Chem. Soc.* 1976, 98, 4646.

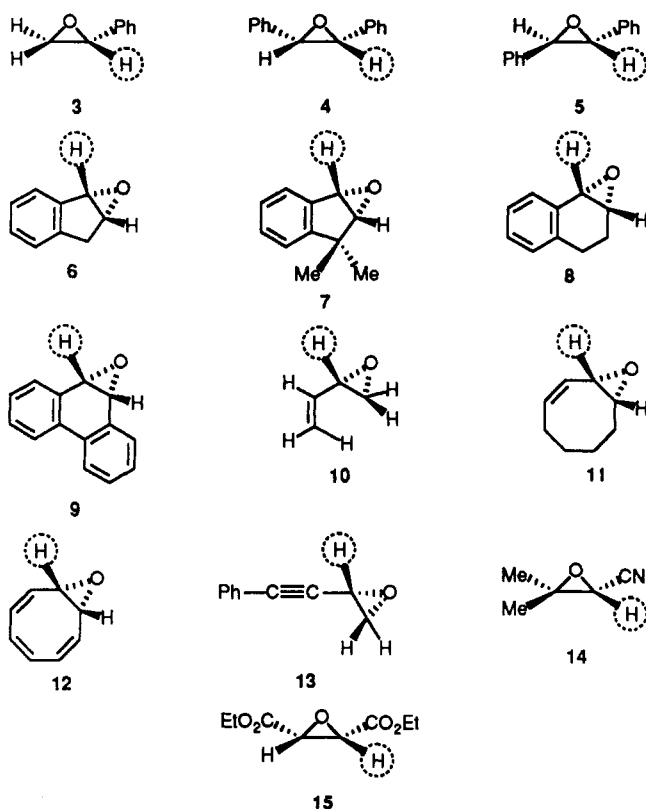
(3) Molander, G. A.; Mautner, K. *J. Org. Chem.* 1989, 54, 4042.

(4) Hudrlik, P. F. In *New Applications of Organosilicon Reagents in Organic Synthesis*; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; pp 127-159.

(5) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: New York, 1988; p 147.

(6) Crandall, J. K.; Apparu, M. *Org. React.* 1983, 29, 345.

(7) An even more powerful base for kinetically controlled lithiations, lithium diisopropylamide, proved advantageous with certain substrates (such as  $\alpha$ -cyanoalkyl epoxides) not cleanly responsive to *t*-BuLi-TMEDA.

Scheme I<sup>a</sup>

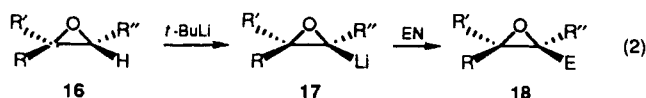
<sup>a</sup>The hydrogens encircled are exchanged for lithium in the lithiations with *t*-BuLi-TMEDA or with LDA. In the cases of compounds 6, 8, 9, and 12, further rearrangements ensue. Stable derivatives formed from the other  $\alpha$ -lithio epoxides are summarized in Table I.

Table I. Lithiations of  $\alpha$ -Organyl-Substituted Epoxides<sup>a</sup>

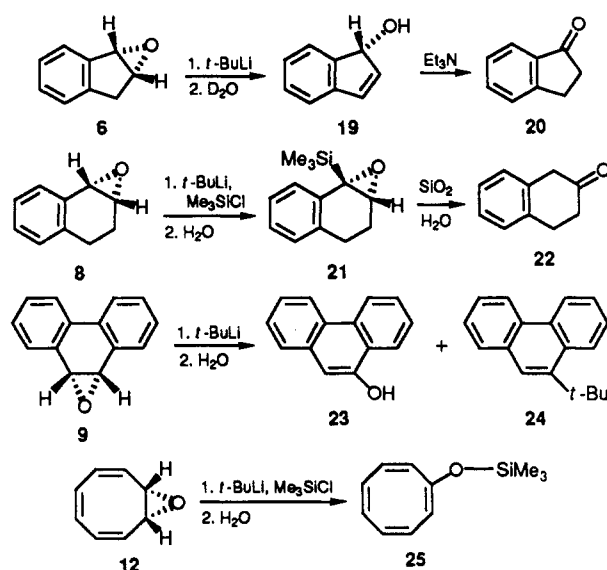
epoxide	$\alpha$ -substituent	derivative	yield, %
1,2-epoxy-1-phenylethane	phenyl	D	95
		Me <sub>3</sub> Si	96
		PhCO	65
<i>cis</i> -1,2-epoxy-1,2-diphenylethane	phenyl	Me <sub>3</sub> Si	94
		phenyl	91
<i>trans</i> -1,2-epoxy-1,2-diphenylethane	phenyl	Me <sub>3</sub> Si	70
1,2-epoxy-3,3-dimethylindan	phenyl	Me <sub>3</sub> Si	81
3,4-epoxy-1-butene	vinyl	PhCO	35
3,4-epoxy-1-cyclooctene	vinyl	Me <sub>3</sub> Si	45
		D	90
		Me <sub>3</sub> Si	95
3,4-epoxy-1-phenyl-1-butene	vinyl	PhCO	81
		Me <sub>3</sub> Si	65
1-cyano-1,2-epoxy-2-methylpropane <sup>b</sup>	cyano	Me <sub>3</sub> Si	95
diethyl 2,3-epoxysuccinate <sup>b</sup>	ethoxycarbonyl	Me <sub>3</sub> Si	70

<sup>a</sup> Except where noted otherwise, a complex of *tert*-butyllithium with TMEDA was the lithiating agent. <sup>b</sup> Lithium diisopropylamide was the lithiating agent in this case.

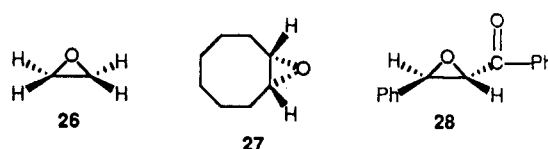
mixture was treated with D<sub>2</sub>O, chlorotrimethylsilane, or *N,N*-diethylbenzamide (EN in eq 2), in the expectation that the corresponding  $\alpha$ -deuterio,  $\alpha$ -trimethylsilyl, or  $\alpha$ -benzoyl derivative, respectively (E in eq 2), would form from the lithio product. Except for the lithiations of 6,



Scheme II

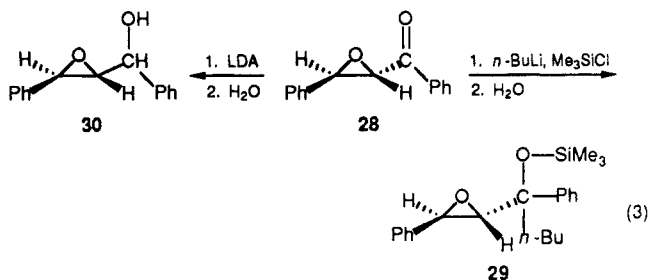


Scheme III



8, 9, and 12, such (epoxyalkyl)lithium reagents were produced and derivatized in good to excellent yields (Table I). In the case of the four exceptions, there is no doubt that similar lithiation occurred, but these intermediates underwent the well-known epoxide isomerizations,<sup>6</sup> even at  $-95$  to  $-110$  °C (Scheme II).

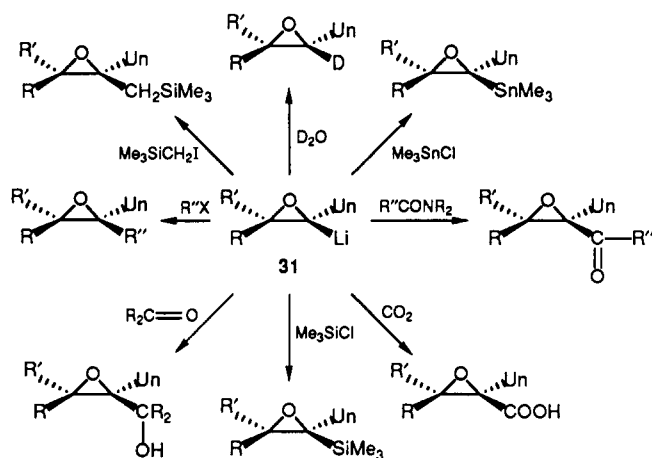
A second group of organyl-substituted epoxides, where the  $\alpha$ -substituent was hydrogen, alkyl, or acyl (exemplified by those in Scheme III), could not be lithiated by alkyl-lithium or lithium amide reagents cleanly at  $-95$  °C. In these cases, simple opening of the epoxide ring 26, isomerization to the ketone 27, or additions to the acyl group 28 predominated (eq 3).<sup>8</sup>



**Heteroatom-Substituted Aziridines and Thiiranes and Attendant Carbenoid Decomposition.** Attempted lithiations of aziridines, such as 1-phenyl-2-(trimethylsilyl)aziridine and 1-phenyl-2-(triphenylsilyl)aziridine with *tert*-butyllithium gave only products consistent with the decomposition of the initial 2-lithioaziridine (30) by a carbenoid  $\alpha$ -elimination, namely (1-*tert*-butylethenyl)-(triorganyl)silanes.<sup>2a</sup> On the other hand, attempted lithiation of 2-phenylthiirane (32) led, instead, to styrene; apparently, the previously described<sup>9</sup> thiophilic attack of

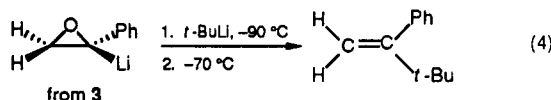
(8) A number of such reductions of carbonyl derivatives were observed by us as early as 1975. Indeed, magnesium diisopropylamide have just recently been shown to be an effective reagent for converting carbonyl compounds to alcohols: Sanchez, R.; Scott, W. *Tetrahedron Lett.* 1988, 29, 139.

Scheme IV



*tert*-butyllithium on sulfur is a lower energy pathway than  $\alpha$ -lithiation.

Finally, in two cases where the  $\alpha$ -lithiation of the epoxide could be quantitatively achieved at  $-80^\circ$  to  $-90^\circ$  C, namely with **3** and **11**, the lithium reagents were purposely allowed to warm up and undergo carbenoid decomposition (eq 4).<sup>10</sup>



### Discussion and Conclusions

From the foregoing findings it is evident that a single unsaturated organyl group (vinylic, acetylenic, aryl, alkoxycarbonyl, or cyano) directly attached to an epoxide (Un in Scheme IV) suffices to permit lithiation of the geminal carbon-hydrogen bond in high yield (Table I). The resulting ( $\alpha,\beta$ -epoxyalkyl)lithium reagents have sufficient kinetic stability at temperatures below  $-80^\circ$  C so that they can be smoothly converted into (clockwise in Scheme IV)  $\alpha$ -deuterio,  $\alpha$ -trialkylstannyl,  $\alpha$ -acyl,  $\alpha$ -carboxyl,  $\alpha$ -trimethylsilyl,  $\alpha$ -( $\alpha$ -hydroxyalkyl),  $\alpha$ -alkyl, or  $\alpha$ -trimethylsilylmethyl derivatives in good to excellent yields.<sup>11</sup> In those cases where any *cis*-*trans* isomerization of the lithiated epoxide **31** would have been observable, namely with **4**, **5** and **15**, no isomerization upon derivative formation was detected. The reactions summarized in Scheme IV thus appear to take place with retention of configuration at low temperatures. This finding generally conforms with the recent observations of Molander and Mautner on the reactions of aldehydes and ketones with  $\alpha$ -lithiated ( $\alpha,\beta$ -epoxyalkyl)silanes.<sup>9</sup> However, in their work some lithiated reagents did show the tendency to isomerize prior to their adding to ketonic substrates. Hence, in any synthetic application of these lithiated epoxides, the stereochemistry of any such derivative should be carefully monitored and corroborated.<sup>12</sup>

(9) Neureiter, N. P.; Bordwell, F. G. *J. Am. Chem. Soc.* **1959**, *81*, 578.

(10) Crandall, J. K.; Chang, L. H. *J. Org. Chem.* **1967**, *32*, 532.

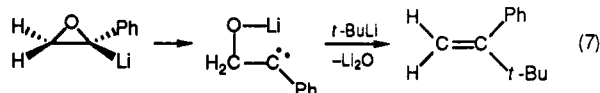
(11) Each of these derivatizing reactions has been carried out with two or more ( $\alpha,\beta$ -epoxyalkyl)lithium reagents of type **3** in research described here, in ref 2a, or in ref 3. Naturally, each derivatizing reaction has not been conducted on every reagent of type **31**.

(12) That such organolithium compounds maintain their configuration at low temperatures and are freely soluble in solvents of low polarity are experimental observations more in accord with the presence of polar, but covalent C-Li bonds in such (epoxyalkyl)lithium reagents. In light of this and other abundant structural evidence on the bonding in organolithium compounds (Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: Oxford, 1974), we judge that it is not accurate, and indeed misleading, to refer to such lithium reagents as "oxiranil anions", as do Molander and Mautner in ref 3.

Furthermore, this derivatization has other advantageous implications: through the lithiation of such unsaturated epoxides in the presence of chlorotrimethylsilane, a novel route to ( $\alpha,\beta$ -epoxyalkyl)silanes has thus been established. Since these silyl epoxides undergo a large number of useful transformations,<sup>5</sup> exemplified in eqs 5 and 6, the lithiation of epoxides awards a bonus in synthetic utility.



Finally, the generation of these  $\alpha$ -organyl-substituted (epoxyalkyl)lithium reagents at low temperatures provides a direct corroboration for the mechanisms proposed for base-promoted epoxide isomerizations.<sup>6</sup> In two individual cases, the lithiated epoxides from **3** and **11** were shown to undergo  $\alpha$ -elimination at higher temperatures and then to form products ascribable to intermolecular (eqs 4 and 7) and intramolecular carbenoid reactions, respectively.



Precisely such pathways have been proposed for these interesting isomerizations.<sup>6</sup> It is evident that the carbenoid intermediates are so high in energy that they react with the nearest accessible intramolecular group: that is obviously the transannular C-H in **11**. That *tert*-butyllithium captures the carbenoid in eq 7 supports the assumption that *tert*-butyllithium must be complexed with the epoxy lithium reagent and hence is intramolecularly accessible for reaction with the carbenoid.

### Experimental Section

**Instrumentation and Analyses.** All melting points were measured with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded on Perkin-Elmer spectrophotometers, Models 457 and 283B, which were equipped with sodium chloride optics. Proton magnetic resonance spectra (<sup>1</sup>H NMR) were obtained with a Varian spectrometer, Model EM-360, on pure samples or on 10% solutions in pure deuterated solvents. The <sup>1</sup>H NMR data are reported on the  $\delta$  scale in parts per million with reference to internal tetramethylsilane, followed by peak multiplicities, relative proton intensities, and coupling constants in hertz. Mass spectral data (MS) were collected either with a Dupont instrument, Model 21-491B, or with a MS-902/CIS.2 instrument. The latter spectrometer was provided with a V6 Datasystem 2040 computerized recorder.

Gas-liquid-phase chromatographic analyses (GC) were carried out with an F&M temperature-programmed chromatograph, Model 720, equipped with dual 12-ft columns of a 10% UC-298 phase on a Chromosorb W support and with an electronic peak-area integrator. Thin-layer chromatographic analyses (TLC) were done on Eastman Chromagram Sheets, no. 13181, consisting of silica gel with fluorescent indicator.

**General Procedure.** All steps in the preparation, transfer, and main reactions of the organometallic reagents studied here were conducted under an atmosphere of anhydrous and oxygen-free nitrogen. All solvents and apparatus were likewise freed of traces of dissolved or adsorbed moisture and oxygen and then maintained under nitrogen. Methods and techniques for working under anhydrous and anaerobic conditions have been described previously.<sup>13</sup>

**Organometallic Reagents.** *tert*-Butyllithium in pentane solution and *n*-butyllithium in hexane were purchased from the Aldrich Chemical Co. and were analyzed just before use by the

(13) Eisch, J. J. *Organometallic Syntheses*; Academic Press: New York, 1981; Vol. 2, p 194.

Gilman double-titration procedure.<sup>14</sup>

Reaction media for organometallic reactions (diethyl ether, tetrahydrofuran, *N,N,N',N'*-tetramethylethylenediamine (TMEDA), toluene, and methylene chloride) were purified by standard procedures and then made anhydrous and deoxygenated by final distillation from appropriate drying agents under an argon atmosphere.<sup>13</sup>

**Starting Materials.** Many of the requisite olefins and some of the starting epoxides were readily available from commercial sources. The other epoxides of simple hydrocarbons could be prepared from the corresponding olefins by epoxidation with *m*-chloroperbenzoic acid in chloroform solution<sup>2b</sup> or by generating the halohydrin and treating the latter with concentrated aqueous base.<sup>15</sup> For olefins bearing electronegative substituents, such as acyl or cyano, epoxidation was achieved by means of alkaline hydrogen peroxide.<sup>2b</sup> All such epoxides have been described in the literature, and their spectral properties confirmed their identity. The two aziridines examined were prepared by known published procedures. In the few cases where the epoxide has not been previously described, details of its preparation and spectral properties are given.

**General Lithiation Procedures.** The most effective lithiating agent for epoxides bearing adjacent olefinic, acetylenic, or aryl substituents proved to be *tert*-butyllithium. As adjuvant solvent, TMEDA was most often advantageous, although the Trapp mixture (THF-Et<sub>2</sub>O-RH in a 3:1:1 ratio by volume)<sup>16</sup> or neat THF was especially useful at reaction temperature under -95 °C. Where the substituents adjacent to the epoxide were themselves capable of adding RLi (cyano, alkoxy-carbonyl, or acyl), then a solution of lithium diisopropylamide in THF (generated from *n*-butyllithium and the amine beforehand) was required for the best results.

To a solution of the epoxide (2.0–20 mmol) in the chosen solvent and cooled in the stated temperature bath was added dropwise 1.1 molar equiv of the specified lithiating agent. After the indicated reaction period over the given temperature range, the chemical quenching agent (D<sub>2</sub>O, Me<sub>3</sub>SiCl, or RCONR<sub>2</sub>) was introduced and a further reaction period was allowed for the reaction of any ( $\alpha,\beta$ -epoxyalkyl)lithium formed.

Further addition of water and diethyl ether, separation and washing of the resulting organic layer, drying of the organic layer over anhydrous CaSO<sub>4</sub>, solvent removal, and final purification and analysis of the organic residue gave the results described in the following individual sections.

**1,2-Epoxy-1-phenylethane (3).** (a) **Deuteration.** A 5.0-mmol sample of **3** in 20 mL of hexane was cooled to -90 °C and then treated with 8.0 mmol of *tert*-butyllithium in 30 mL of hexane containing 1.0 mL of TMEDA. After 2 h a solution of 2.0 mL of D<sub>2</sub>O (99.8%) in 50 mL of THF was added, and the temperature was held at -80 °C for 90 min. Usual workup and column chromatography on silica gel with elution by ether hexane (1:50, v:v) gave 79% of **3**, which by <sup>1</sup>H NMR spectroscopy was 95% deuteriated at the C<sub>1</sub>-position (quartet at 3.7 ppm). A small amount of 3,3-dimethyl-2-phenyl-1-butene (~5%) was also isolated.

(b) **Trimethylsilylation.** A solution of 10 mmol of **3** and 15 mmol of chlorotrimethylsilane in 100 mL of pentane was treated over 30 min at -90 °C with 12 mmol of the *tert*-butyllithium-TMEDA complex in 20 mL of pentane. After 30 min at -80 °C, the mixture was allowed to warm to 0 °C. The crude product (1.85 g, 96%) was essentially pure 1,2-epoxy-1-phenyl-1-(trimethylsilyl)ethane, as shown by <sup>1</sup>H NMR spectroscopy: <sup>1</sup>H NMR  $\delta$  0.11 (s, 9 H), 2.85 (d, 1 H, *J* = 6.0 Hz), 2.90 (d, 1 H), 7.25–7.35 (m, 5 H); after distillation, bp 115–120 °C (17 mmHg). Anal. Calcd for C<sub>11</sub>H<sub>16</sub>OSi: C, 68.69; H, 8.39. Found: C, 68.91; H, 8.24.

(c) **Benzoylation.** A 20-mmol sample of **3** in 100 mL of pentane was treated at -90 °C with 22 mmol of the *tert*-butyllithium-TMEDA complex in 100 mL of pentane. After a 90-min reaction time at -85 °C the solution of 30 mmol of *N,N*-diethylbenzamide in 30 mL of THF was added rapidly. The suspension was warmed to -20 °C and worked up by hydrolysis. Column chromatography on silica gel and elution with a hex-

ane-ether gradient gave 65% of 90% pure 1-benzoyl-1,2-epoxy-1-phenylethane. Bulb-to-bulb distillation gave a pure sample: <sup>1</sup>H NMR  $\delta$  2.79 (s, 1 H, *J* = 6.0 Hz), 3.19 (s, 1 H), 7.03–7.45 (m, 8 H), 7.78–8.0 (m, 2 H). Anal. Calcd for C<sub>15</sub>H<sub>12</sub>O<sub>2</sub>: C, 80.04; H, 5.74. Found: C, 79.85; H, 5.72.

(d) **Carbenoid Fragmentation.** A solution of 3.0 mmol of **3** in 10 mL of THF were treated at -78 °C with 3.3 mmol of *tert*-butyllithium in pentane over a period of 2 min. The reaction solution, which immediately turned bright red, was stirred for a further 10 min at -78 °C and then quenched with D<sub>2</sub>O. Usual workup provided 420 mg of a 1:1 mixture of undeuteriated **3** and 3,3-dimethyl-2-phenyl-1-butene. The <sup>1</sup>H NMR spectrum of the latter product:  $\delta$  1.1 (s, 9 H), 4.70 (d, 2 H), 5.17 (d, 2 H), 7.2 (s, 5 H).

**cis-1,2-Epoxy-1,2-diphenylethane (4).** (a) **Trimethylsilylation.** A 5.0-mmol sample of **4** and 15 mmol of chlorotrimethylsilane in 75 mL of THF was treated at -95 °C with 12 mmol of *tert*-butyllithium in pentane. The mixture was allowed to approach -60 °C over 60 min and was then quenched with water. Usual workup gave a crude product that was essentially pure *cis*-1,2-epoxy-1,2-diphenyl-1-(trimethylsilyl)ethane (**35**). Column chromatography on silica gel and elution with an ether-hexane gradient yielded 1.27 g (94%) of **35**: <sup>1</sup>H NMR  $\delta$  0.10 (s, 9 H), 4.08 (s, 1 H), 6.88–7.02 (m, 10 H). Anal. Calcd for C<sub>17</sub>H<sub>20</sub>OSi: C, 76.07; H, 7.51. Found: C, 76.28; H, 7.73.

In order to ensure that the Me<sub>3</sub>Si group was attached to the epoxy group, and not to an aromatic ring, **35** was allowed to react with the 2,4-dinitrophenylhydrazine reagent.<sup>17</sup> From this reaction the 2,4-dinitrophenylhydrazone of benzoin was obtained, mp 203–204 °C.

(b) **Benzoylation.** A 5.0-mmol sample of **4** in 30 mL of THF was treated at -95 °C with 6.0 mmol of *tert*-butyllithium in pentane. The reaction was allowed to proceed for 60 min at -80 °C, the mixture was recooled to -95 °C, and 10 mmol of *N,N*-diethylbenzamide in 10 mL of THF introduced. After the mixture was allowed to warm to 0 °C, it was hydrolyzed. Usual column chromatographic purification yielded pure *cis*-1-benzoyl-1,2-diphenylethane (**36**), 1.37 g (91%), mp 83–84 °C (from methanol): <sup>1</sup>H NMR  $\delta$  4.48 (s, 1 H), 6.83–7.50 (m, 13 H), 7.97–8.20 (m, 2 H). Anal. Calcd for C<sub>21</sub>H<sub>16</sub>O<sub>2</sub>: C, 84.00; H, 5.37. Found: C, 84.05; H, 5.52.

**trans-1,2-Epoxy-1,2-diphenylethane (5).** A solution of 5.0 mmol of **5** and 15 mmol of chlorotrimethylsilane in 25 mL of THF was treated at -95 °C with 9 mmol of *tert*-butyllithium in pentane. The reaction mixture was allowed to come to -40 °C over 45 min and finally to 20 °C over 30 min. Usual workup gave a crude product that by <sup>1</sup>H NMR spectroscopy was a 30:70 mixture of **5** and *trans*-1,2-epoxy-1,2-diphenyl-1-(trimethylsilyl)ethane (**37**):  $\delta$  0.25 (s, 9 H), 3.76 (s, 1 H), 6.9–7.2 (m).

**1,2-Epoxyindan (6).** (a) **Attempted Deuteration.** A solution of 1 mmol of **6** in 40 mL of THF was treated at -95 °C with 11 mmol of *tert*-butyllithium in pentane. After 60 min at -95 °C a solution of D<sub>2</sub>O in THF was added. Usual hydrolytic workup yielded relatively pure 3-indenol (**19**) (<sup>1</sup>H NMR  $\delta$  3.84 (br s, 1 H), 4.80 (br s, 1 H), 6.1 (ctr dd, 1 H), 6.42 (ctr dd), 6.85–7.3 (m, 4 H)), which contained only a trace of **6**. Column chromatography and bulb-to-bulb distillation gave **19** that contained increasing amounts of 1-indanone. Indeed, treating **19** with a small amount of Et<sub>3</sub>N and allowing the samples to stand overnight converted alcohol **19** completely into 1-indanone. None of the products contained deuterium.

An analogous reaction of **6** with the *tert*-butyllithium-TMEDA complex at -90 °C gave, upon hydrolysis a mixture of 45% of epoxide **6**, 19% of alcohol **19** and 36% of 1-indanone.

(b) **Trimethylsilylation.** A solution of 10 mmol of **6** and 25 mmol of chlorotrimethylsilane in 20 mL of THF was treated at -95 °C with 22 mmol of *tert*-butyllithium over a period of 30 min. After being allowed to warm to -60 °C over a further 30 min, the mixture was hydrolyzed. The crude product seemed to be preponderantly 3-(trimethylsiloxy)-1-(trimethylsilyl)indene (**38**): <sup>1</sup>H NMR  $\delta$  0.10 (s, 9 H), 0.44 (s, 9 H), 3.30 (d, 1 H), 5.61 (d, 1 H), 7.15–7.50 (m, 4 H).

(14) Gilman, H.; Cartledge, F. R. *J. Organomet. Chem.* 1964, 2, 447.

(15) Kadesch, R. G.; *J. Am. Chem. Soc.* 1946, 68, 41.

(16) Köbrich, G.; Trapp, H. *Chem. Ber.* 1966, 99, 680.

(17) Shriner, R. L.; Fuson, R. C.; Curtin, D. Y. *The Systematic Identification of Organic Compounds*, 4th ed.; John Wiley & Sons: New York, 1956; p 111.

This compound was treated with potassium fluoride, benzyltrimethylammonium chloride, and methanol at 30 °C for 12 h to yield 1-indanone.

**1,2-Epoxy-3,3-dimethylindan (7).** (a) **Preparation.** Attempts to prepare 7 by the treatment of 100 mmol of 3,3-dimethylindene in 100 mL of chloroform with 100 mmol of *m*-chloroperbenzoic acid for 4 h at 25 °C yielded, instead, 3,3-dimethyl-2-indanone: <sup>1</sup>H NMR δ 1.25 (s, 6 H), 3.41 (s, 2 H), 6.95–7.3 (m, 4 H); IR (neat) ν 1855 cm<sup>-1</sup> (strong).

Hence, epoxidation under basic conditions was undertaken. Thus, a mixture of 122 mmol of the indene, 23 mL of benzonitrile, 29 mL of 30% hydrogen peroxide, 3.40 g of potassium bicarbonate, and 225 mL of methanol was heated at 45–55 °C for 2 h. The solvent was removed by evaporation, and the residue was treated with water and pentane. The dried and evaporated pentane layer was distilled to separate the benzonitrile from 7: bp 47–50 °C (0.1 mmHg); 15.9 g (82%); <sup>1</sup>H NMR δ 1.13 (s, 3 H), 1.33 (s, 3 H), 3.5 (d, 1 H, *J* = 2.6 Hz), 4.02 (d, 1 H), 6.9–7.4 (m, 4 H). Anal. Calcd for C<sub>11</sub>H<sub>12</sub>O: C, 82.05; H, 8.02. Found: C, 82.11; H, 8.15.

(b) **Trimethylsilylation.** A mixture of 20 mmol of 7 and 25 mmol of chlorotrimethylsilane in 100 mL of pentane was frozen to a suspension at -80 °C and then treated with 22 mmol of *tert*-butyllithium and TMEDA in pentane over 30 min.

The red reaction mixture was allowed to come to -55 °C and then over 30 min to -20 °C, where it was hydrolyzed. Usual workup provided a crude product in 81% yield, containing 19% of 7. Distillation at 56–60 °C (0.1 mmHg) yielded pure 1,2-epoxy-3,3-dimethyl-1-(trimethylsilyl)indan: <sup>1</sup>H NMR δ 0.33 (s, 9 H), 1.27 (s, 3 H), 1.49 (s, 3 H), 3.50 (s, 1 H), 7.1–7.2 (m, 4 H). Anal. Calcd for C<sub>14</sub>H<sub>20</sub>OSi: C, 72.45; H, 8.67. Found: C, 72.28; H, 8.60.

(c) **Benzylation.** A suspension of 20 mmol of 7 in 100 mL of pentane was treated at -95 °C with 24 mmol of the *tert*-butyllithium-TMEDA complex in pentane. The mixture was brought -80 °C for 60 min and then recooled -95 °C, where it was treated with 30 mmol of *N,N*-diethylbenzamide in 60 mL of THF. The mixture was warmed to -20 °C and after 30 min quenched with water. Usual workup and column chromatography on silica gel with an ether-hexane gradient gave 35% of 1-benzoyl-1,2-epoxy-3,3-dimethylindan: mp 97–99 °C (from methanol); <sup>1</sup>H NMR δ 1.25 (s, 3 H), 1.36 (s, 3 H), 3.76 (s, 1 H), 6.95–7.45 (m, 7 H), 7.85–8.10 (m, 2 H). Anal. Calcd for C<sub>18</sub>H<sub>16</sub>O<sub>2</sub>: C, 81.79; H, 6.10. Found: C, 81.88; H, 6.31.

**1,2-Epoxy-3,4-dihydronaphthalene (8).** (a) **Preparation.** A mixture of 100 mmol of 1,2-dihydronaphthalene (containing tetralin), 20 mL of benzonitrile, 26 mL of 30% hydrogen peroxide, and 3.4 g of potassium bicarbonate in 200 mL of methanol was heated for 2 h at 45–55 °C. After the usual workup the crude product was chromatographed on silica gel with an ether-hexane gradient to separate the epoxide (the crude product blackened on the column, so direct distillation may have given better yields). Subsequent distillation gave 58% of 8: bp 54–55 °C (0.1 mmHg); <sup>1</sup>H NMR δ 1.2–3.0 (m, 4 H), 3.3–3.7 (m, 2 H), 6.8–7.3 (m, 4 H). Anal. Calcd for C<sub>10</sub>H<sub>10</sub>O: C, 82.16; H, 6.90. Found: C, 82.12; H, 7.08.

(b) **Attempted Trimethylsilylation.** A solution of 35 mmol of 8 and 150 mmol of chlorotrimethylsilane in 300 mL of pentane was treated dropwise at -116 °C with 75 mmol of the *tert*-butyllithium-TMEDA complex over a period of 60 min. The mixture was allowed to react over a further 60 min at -60 °C. Usual workup yielded 9.0 g of product, which by <sup>1</sup>H NMR spectral examination contained no starting material nor 2-tetralone. However, after column chromatography on silica gel with an ether-hexane gradient the later fractions (~4.0 g) were shown to be 2-tetralone. The silyl derivative of 8 was thought to have decomposed on the column (blackening).

**9,10-Epoxy-9,10-dihydrophenanthrene (9).** (a) **Preparation.** A solution of 200 mmol of phenanthrene in 62 mL of dimethylformamide was treated with gaseous chlorine until 16 g were absorbed. After 20 min of additional stirring 300 mL of dry ether was added, and the deposited solid was collected by filtration. This solid was redissolved in a mixture of 100 mL of ether and 200 mL of water. Then solid KOH pellets (56 g) were added at such a rate that an ice bath kept the temperature below 25 °C. After stirring overnight, enough of a 1:1 mixture of ether and CH<sub>2</sub>Cl<sub>2</sub> was added to redissolve any precipitated solid. The separated organic layer was washed with water, dried with CaSO<sub>4</sub>,

and evaporated. Recrystallization of the residue from a hexane-CH<sub>2</sub>Cl<sub>2</sub> pair gave 9, mp 125–127 °C (if placed in bath at 120 °C), 35% yield.

(b) **Attempted Trimethylsilylation.** A mixture of 5 mmol of epoxide 9 and 10 mmol of Me<sub>3</sub>SiCl in a Trapp mixture (3:1:1 by volume of THF-ether-pentane<sup>16</sup>) at -120 °C was treated with *tert*-butyllithium over 60 min. After warming to 25 °C, hydrolysis and usual workup the crude product was analyzed by <sup>1</sup>H NMR spectroscopy. No signal was observed that indicated the presence of any Me<sub>3</sub>Si group. However, some 9-phenanthrol and 9-*tert*-butylphenanthrene<sup>18</sup> were isolated by column chromatography.

(c) **Carbenoid Decomposition.** A solution of 10 mmol of 9 in 50 mL of THF was treated at -78 °C with 11 mmol of *n*-butyllithium in hexane over 25 min. After warming to 25 °C the reaction mixture was worked up in the usual manner. The crude material was extracted with 5% aqueous KOH; acidification gave 42% of 9-phenanthrol, mp 151–153 °C. The base-insoluble material was chromatographed on silica gel with an ether-hexane gradient to give 7% of 9-phenanthrol and 20% of 9-*n*-butylphenanthrene, mp 79–81 °C (from hexane, lit.<sup>18</sup> mp 81 °C).

**3,4-Epoxy-1-butene (10).** (a) **Preparation.** The 4-bromo-3-buten-1-ol was prepared from butadiene, *N*-bromosuccinimide, and water, bp 65–70 °C (15 mmHg). Adding this to concentrated aqueous NaOH at 90 °C gave 10, bp 60–65 °C (15 mmHg).

(b) **Trimethylsilylation.** A solution of 30 mmol of 10 and 40 mmol of chlorotrimethylsilane in 125 mL of a Trapp mixture was treated at -110 °C with 35 mmol of *tert*-butyllithium. The mixture was allowed to warm to -50 °C over 60 min and then quenched. Usual workup and distillation provided 45% of 3,4-epoxy-3-(trimethylsilyl)-1-butene (39): bp 50–55 °C (45 mmHg); <sup>1</sup>H NMR δ 0.25 (s, 9 H), 2.60 (d, 1 H, *J* = 6.5 Hz), 2.85 (d, 1 H), 5.0–6.2 (m, 3 H). Anal. Calcd for C<sub>7</sub>H<sub>14</sub>OSi: C, 59.08; H, 9.92. Found: C, 59.25; H, 10.05.

**3,4-Epoxy-1-cyclooctene (11).** (a) **Preparation.** In a 250-mL distillation flask, equipped with head and descending condenser, were placed 300 mmol of 1,3-cyclooctadiene, 300 mmol of *tert*-butyl hydroperoxide, 100 mg of Mo(CO)<sub>6</sub>, 50 mL of toluene, and 25 mL of benzene. As the mixture was heated, a vigorous reaction commenced and was allowed to run its course. Any organic solvent that distilled over was returned to the flask; a Vigreux column was mounted on the flask, and the mixture was distilled until the head temperature reached 100 °C. The residual liquid was distilled at 15 mmHg, and the epoxide was collected: bp 60–65 °C (52%); <sup>1</sup>H NMR δ 1.0–2.5 (m, 8 H), 2.7–3.1 (m, 1 H), 3.1–3.3 (m, 1 H), 5.3–5.9 (m, 2 H).

(b) **Deuteration.** A mixture of 5 mmol of 11, 5.5 mmol of TMEDA, and 30 mL of pentane was treated at -90 °C with 5.5 mmol of *tert*-butyllithium over a period of 25 min. After 1 h the mixture was treated with D<sub>2</sub>O in THF. Usual workup gave a 95% recovery of 11, which by <sup>1</sup>H NMR analysis was 90% deuterated at C<sub>3</sub>.

(c) **Trimethylsilylation.** A mixture of 20 mmol of 11, 22 mmol of TMEDA, and 26 mmol of Me<sub>3</sub>SiCl was treated at -90 °C with 22 mmol of *tert*-butyllithium. After a reaction time similar to part b and workup, the crude product was essentially pure 3,4-epoxy-3-(trimethylsilyl)-1-cyclooctene (40): <sup>1</sup>H NMR δ 0.10 (s, 9 H), 1.0–2.3 (m, 8 H), 2.80–3.05 (m, 1 H), 5.3–5.75 (m, 2 H). Anal. Calcd for C<sub>11</sub>H<sub>20</sub>OSi: C, 67.28; H, 10.27. Found: C, 67.11; H, 10.06.

(d) **Benzylation.** On a scale as in part c the lithiated epoxide was treated at -90 °C with 25 mmol of *N,N*-diethylbenzamide in 50 mL of THF. Usual workup and column chromatography on silica gel with an ether-hexane gradient gave pure 3-benzoyl-3,4-epoxy-1-cyclooctene as an oil (81%): <sup>1</sup>H NMR δ 1.0–2.8 (m, 8 H), 3.0–3.3 (m, 1 H), 5.4–6.1 (m, 2 H), 7.2–7.45 (m, 3 H), 7.85–8.1 (m, 2 H). Anal. Calcd for C<sub>15</sub>H<sub>16</sub>O<sub>2</sub>: C, 78.92; H, 7.07. Found: C, 79.10; H, 7.02.

(e) **Carbenoid Decomposition.** Similar lithiations of 11, which were then allowed to come to 25 °C and stirred for 12 h, gave upon the usual workup up to 75% of pure bicyclo[3.3.0]-2-octen-8-ol, which was isolated by preparative gas chromatography and identified by mass and <sup>1</sup>H NMR spectral analyses.<sup>10</sup>

**7,8-Epoxy-1,3,5-cyclooctatriene (12).** (a) **Preparation.** This compound was prepared by the treatment of cyclooctatetraene

with *m*-chloroperbenzoic acid in  $\text{CHCl}_3$ : bp 68–71 °C (15 mmHg), 45%.

(b) **Attempted Trimethylsilylation.** A 10-mmol sample of 12 and 14 mmol of  $\text{Me}_3\text{SiCl}$  in 50 mL of the Trapp mixture were treated at –116 °C with 11 mmol of *tert*-butyllithium in pentane. After the usual reaction time and workup an 85% yield of 1-(trimethylsiloxy)-1,3,5,7-cyclooctatetraene was isolated:  $^1\text{H NMR}$   $\delta$  0.3 (s, 9 H), 5.2–5.85 (s, 7 H). By treatment with semicarbazide hydrochloride it was converted into the known semicarbazone of 2,4,6-cyclooctatrienone, mp 192–193 °C (lit.<sup>19</sup> mp 193 °C).

**3,4-Epoxy-1-phenyl-1-butyne (13).** (a) **Preparation.** Oxidation of 205 mmol of 1-phenyl-3-buten-1-yne with 350 mmol of benzonitrile and 450 mmol of 30% hydrogen peroxide in 5 g of  $\text{KHCO}_3$  and 250 mL of methanol at 60 °C gave 63% of 13: bp 55–60 °C (0.1 mmHg);  $^1\text{H NMR}$   $\delta$  2.76 (m, 2 H), 3.35 (t, 1 H), 7.0–7.35 (m, 5 H).

(b) **Trimethylsilylation.** The epoxide (50 mmol) and  $\text{Me}_3\text{SiCl}$  (100 mmol) dissolved in 180 mL of the Trapp mixture were treated at –110 °C with 75 mmol of *tert*-butyllithium. Usual reaction time and workup gave a crude product containing no 13. Distillation and subsequent column chromatography gave 65% of 3,4-epoxy-1-phenyl-3-(trimethylsilyl)-1-butyne:  $^1\text{H NMR}$   $\delta$  0.32 (s, 9 H), 2.89 (d, 1 H,  $J = 6.5$  Hz), 3.20 (d, 1 H), 7.2–7.4 (m, 5 H). Anal. Calcd for  $\text{C}_{13}\text{H}_{16}\text{OSi}$ : C, 67.20; H, 6.94. Found: C, 67.45; H, 6.69.

**1-Cyano-1,2-epoxy-2-methylpropane (14).** A solution of 10 mmol of 14 and 11 mmol of  $\text{Me}_3\text{SiCl}$  in 20 mL of the Trapp mixture was treated at –110 °C with 10 mmol of lithium diisopropylamide in hexane over 10 min. The mixture was allowed

to warm to –80 °C over 45 min and then rapidly to 0 °C and hydrolyzed. Usual workup gave essentially pure 1-cyano-1,2-epoxy-2-methyl-1-(trimethylsilyl)propane (41) in 95% yield:  $^1\text{H NMR}$   $\delta$  0.3 (s, 9 H), 1.35 (s, 3 H), 1.60 (s, 3 H). Anal. Calcd for  $\text{C}_8\text{H}_{15}\text{NOSi}$ : C, 59.60; H, 8.34. Found: C, 59.85; H, 8.10.

**Diethyl *cis*-2,3-Epoxy succinate (15).** A solution of 150 mmol of 15 and 180 mmol of  $\text{Me}_3\text{SiCl}$  in 250 mL of the Trapp mixture was treated at –110 °C with 180 mmol of lithium diisopropylamide in a dropwise manner over 60 min. The mixture was then warmed to –40 °C and hydrolyzed. By  $^1\text{H NMR}$  analysis the crude product contained 10% of 15, 4% of the disilylated (42), product, and 86% of the monosilylated (43) product. By fractional distillation the diethyl 2,3-epoxy-2-(trimethylsilyl)succinate (43) was isolated (70%): bp 83–85 °C (0.05 mmHg);  $^1\text{H NMR}$   $\delta$  0.19 (s, 9 H), 1.3 (t, 6 H,  $J = 7$  Hz), 3.33 (s, 1 H), 4.17 (q, 4 H). Anal. Calcd for  $\text{C}_{11}\text{H}_{20}\text{O}_5\text{Si}$ : C, 50.75; H, 7.74. Found: C, 50.70; H, 7.65.

**Unsuccessful Lithiations.** Ethylene oxide with  $\text{Me}_3\text{SiCl}$  and *tert*-butyllithium gave the straightforward ring-opened product, *t*-BuCH<sub>2</sub>CH<sub>2</sub>OSiMe<sub>3</sub>; 1,2-epoxycyclooctane with  $\text{Me}_3\text{SiCl}$  and *tert*-butyllithium gave a small amount of silylation (10%); *trans*-2,3-epoxy-1,3-diphenyl-1-propanone with LDA gave the reduced product, 2,3-epoxy-1,3-diphenyl-1-propanol and with *n*-butyllithium and  $\text{Me}_3\text{SiCl}$  gave 1,2-epoxy-1,3-diphenyl-3-(trimethylsiloxy)heptane; 1-phenyl-2-(trimethylsilyl)aziridine with the *tert*-butyllithium–TMEDA complex gave some 2-(trimethylsilyl)-3,3-dimethyl-2-butene; 2-phenylthiirane with *tert*-butyllithium gave some styrene.

**Acknowledgment.** We are grateful for the support of this research through Grants CA-14540 and CA-28335 from the Public Health Service.

(19) Cope, A. C.; Tiffany, B. D. *J. Am. Chem. Soc.* 1951, 73, 4158.

## Substrate Leaving Group Control of the Enantioselectivity in the Palladium-Catalyzed Asymmetric Allylic Substitution of 4-Alkyl-1-vinylcyclohexyl Derivatives

Jean-Claude Fiaud\* and Jean-Yves Legros

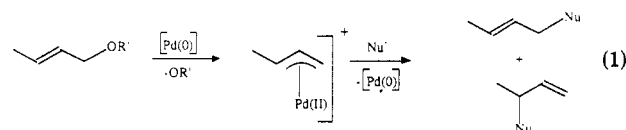
Laboratoire de Synthèse Asymétrique, CNRS URA 255, Université de Paris-Sud, 91405 Orsay Cedex, France

Received January 3, 1990

The strong influence of the nature of the leaving group in allylic derivatives in their enantioselective Pd-catalyzed substitution by nucleophile is reported. Analysis of the stereochemical course of the Pd-catalyzed substitution of achiral *trans*-4-*tert*-butyl-1-vinylcyclohexyl derivatives with nucleophiles indicates the enantioselective step to be oxidative addition of the allylic substrate onto the chiral Pd complex. The asymmetric induction may be understood as the result of the selection by the chiral Pd catalyst between two reactive enantiomeric conformations of the allylic substrate and, hence, was shown to be strongly dependent upon reaction conditions and especially upon the nature of the substrate leaving group. Indeed, dimethyl 2-[(4-*tert*-butylcyclohexylidene)methyl]malonate (4) was synthesized with 27, 48, and 78% ee through Pd-catalyzed reaction of sodium dimethyl malonate in THF with *trans*-4-*tert*-butyl-1-vinylcyclohexyl carbonate (1c), acetate (1a) and 4-methoxybenzoate (1h), respectively, in the presence of BINAP as the chiral ligand. In dioxane, 4 was produced from 4-methoxybenzoate 1h with 90% ee.

### Introduction

The palladium-catalyzed allylic substitution reaction has been thoroughly studied and has received wide study for asymmetric synthesis.<sup>1</sup> This reaction is considered to proceed in two steps (eq 1). The initial oxidative addition of the allylic substrate to a  $\text{Pd}^0$  complex produces an  $\eta^3$ -allyl complex, which is then attacked by a nucleophile.



[Pd(0)] = palladium(0)-phosphine complex

In preceding papers,<sup>2,3</sup> we described the asymmetric synthesis of chiral 4-substituted cyclohexylidene com-

(1) Consiglio, G.; Waymouth, R. M. *Chem. Rev.* 1989, 89, 257, and references herein.

(2) Fiaud, J. C.; Legros, J. Y. *Tetrahedron Lett.* 1988, 29, 2959.