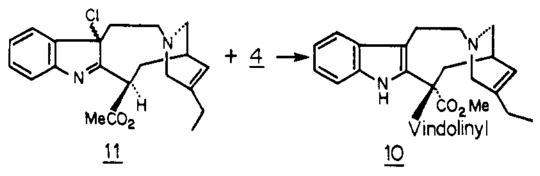
5–8 differ also in the stereochemistry at C_4' in that the former compounds have a 4′α-ethyl group while the synthetic dimers have a 4′β-ethyl group. Since the 4′-ethyl group would prefer the equatorial configuration, the conformation of the six-membered ring could be different between these two series of compounds. The relative insignificance of conformational changes in this part of the molecule to the overall effect on the CD data is revealed in the case of synthetic dimer **10** (Table I).[11] Chemical correlation[4] of **10** with **7** established its complete structure and absolute configuration. The signs of the Cotton effects in **10** are as expected for the unnatural stereochemistry at C_{18}'.



Finally the relative sensitivity of the CD effects to changes in chirality at C_{18}' are seen in the $\Delta^{1',18'}$-dimer **9.**[10] In the latter compound, the C_{18}' trigonal center decreases the angle of twist between the two chromophores and this results in a greatly decreased split Cotton effect.

As mentioned previously, work in this area of importance to the partial or total synthesis of antitumor alkaloids has required the X-ray diffraction for solution of the problem of C_{18}' stereochemistry. As the above results reveal it is now possible to monitor this dimerization reaction through observation of the CD spectrum and thereby provide a simple method for evaluating the chirality of compounds from future studies.

Although the above CD studies are based on an empirical correlation of the synthetic and natural dimers there is a theoretical basis for the observed changes in the CD curves. The "exciton chirality method" of Harada and Nakanishi,[12] which correlates signs of Cotton effects arising from dipolar interaction between aromatic chromophores with absolute configurations, is well documented and is based on molecular exciton theory.[13] In order to apply this method to the present case, however, it is necessary to know the polarization of the electronic transition moments involved. Unfortunately, this information is presently unavailable, so that further studies along this line are desirable.

Acknowledgments. This work was supported by the National Research Council of Canada (J.P.K.), by National Institutes of Health Grant No. CA-11095 (A.I.S), and by Contract NO1-CM-23223 (J.P.K.) from the Divison of Cancer Treatment, National Cancer Institute, National Institutes of Health, Department of Health, Education and Welfare, Bethesda, Md.

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Reaction of Lithium Vapor with Alkenes. A New Synthesis for Polylithium Compounds

Sir:

It has recently been reported that at elevated temperatures lithium vapor reacts with chlorocarbons[1] and with carbon vapor[2] to produce novel polylithium organic compounds. The reaction of excess lithium vapor with several alkenes has been studied and it has been found that both substitution of lithium for hydrogen and addition of lithium to the double bonds occur to produce polylithiated alkanes and alkenes.

A large excess of lithium (>15 g) was vaporized at 700–800° in an evacuated stainless steel reactor (Figure 1) with an inconel Knudsen cell (A) which was heated resistively. Simultaneously, the alkene was slowly vaporized into the circular tube (B) above the Knudsen cell. During the 30-min reaction period, products were collected as solids on the liquid nitrogen cooled cold finger (C). The pressure in the reactor during the reaction was approximately 10^{-3} Torr. After the reaction the contents of the reactor were warmed to room temperature and removed under argon.

The very reactive solids obtained from the reaction looked metallic but were very brittle. Frequently portions of the solid were colored, the hue varying from red to black. The products were carefully hydrolyzed by both H_2O and D_2O in a standard vacuum line to yield alkenes and alkanes which were identified by comparing ^1H NMR data, mass spectral fragmentation patterns and, if necessary, GLC retention times to authentic samples. The relative amount of lithiation was determined by low resolution mass spectroscopy (70 eV) of the deuterated alkenes recovered from the

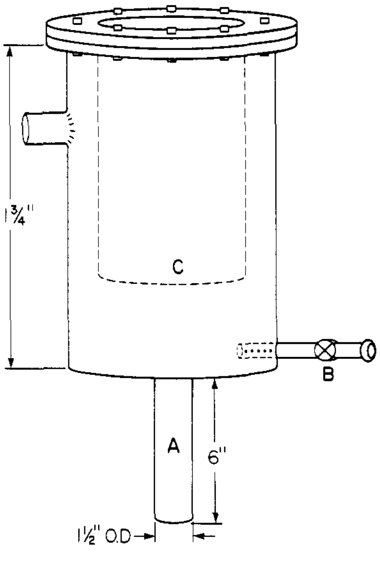
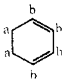
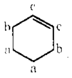


Figure 1. Inverted Dewar type reactor.

Table I. Hydrocarbon Chemical Shifts, $\tau \pm 0.02$ ppm

	From lithiated alkenes[a]				Reference compounds			
Compounds	H^A	H^B	H^C	$H^{D,E}$	H^A	H^B	H^C	$H^{D,E}$
Isobutene Products								
$(H^A{}_3C)_2C{=}CH_2{}^B$	8.34	5.42			8.38	5.44		
$(H^A{}_3C)_3CH^B$	9.14	. . .[b]			9.13	. . .		
2-Butene Products								
$H^A{}_3C(H^B)C{=}C(H)CH_3$	8.56[c]	4.90			8.47[d]	4.73[d]		
Cyclohexadiene Products								
 cyclohexadiene	7.90	4.16			7.86	4.17		
 cyclohexene	8.37	8.07	4.42		8.38	8.04[d]	4.41[d]	
cyclohexane	8.58				8.56[d]			
Butadiene Products								
$H^A{}_3CH^B{}_2C^HC{=}CH^DH^E$	9.03	7.95	. . .[e]	~5.08[f]	9.02	8.02	4.22	~5.10[f]
$H^A{}_3C(H^B)C{=}C(H)CH_3$	8.47[c]	4.70			8.47[d]	4.73[d]		

[a] If the polylithio products were hydrolyzed with D_2O, the resonances were further split by H–D coupling. [b] Very weak signal, the expected decet is further split by second-order effects. [c] Mixture of cis and trans isomers. [d] From reference 3. [e] Not observed. [f] The difference in the chemical shifts of these protons is very small.

reaction of the solids with D_2O. High resolution mass spectroscopy was used to determine accurately the composition of each low resolution peak. It was assumed that the parent ion peak intensities were proportional to the amount of the polylithioalkene originally present. The degree of lithiation was usually confirmed by reaction of the solids with chlorotrimethylsilane to yield the poly(trimethylsilyl) derivatives.

Isobutene, 1.5 g, was treated with lithium as described above; the solid was hydrolyzed with H_2O, and the resulting very volatile liquids were separated into two fractions using GLC. These fractions were regenerated isobutene in 26% yield based upon the amount of isobutene consumed, and isobutane in 4% yield. When the product was hydrolyzed with D_2O, the high resolution mass spectra (CEC21-110B mass spectrometer) of the isobutene fraction contained parent ion peaks for C_4H_7D (57.06897), $C_4H_6D_2$ (58.07459), $C_4H_5D_3$ (59.08079), and $C_4H_4D_4$ (60.08779) in the ratio of 10:4:3:1. This indicates the substitution of from one to four hydrogen atoms by lithium in isobutene. The low resolution mass spectra of the isobutene fraction also contained less intense parent ions due to the substitution of as many as seven of the original eight hydrogen atoms in the isobutene molecule. The mass spectrum of the products obtained from the reaction of Me_3SiCl with the solid indicated the presence of at least four trimethylsilyl groups on isobutene. The mass spectra of the deuterated isobutane fraction contained peaks at *m/e* 60–63 which indicates the presence of up to five deuterium atoms in the isobutane molecule. Figure 2 schematically presents the products from the reaction of the alkenes with lithium vapor. The two types of reactions represented are the stepwise replacement of hydrogen atoms by lithium and the saturation of the double bond to produce alkanes. Table I is a comparison of the ^1H NMR data of the hydrocarbons recovered from the hydrolysis reactions with data compiled from the literature or collected from standard samples. The ^1H NMR spectrum of the deuterated isobutene was integrated and the ratio of methyl protons to vinyl protons was found to be 6:1 indicating that substitution at the vinyl position is preferential.

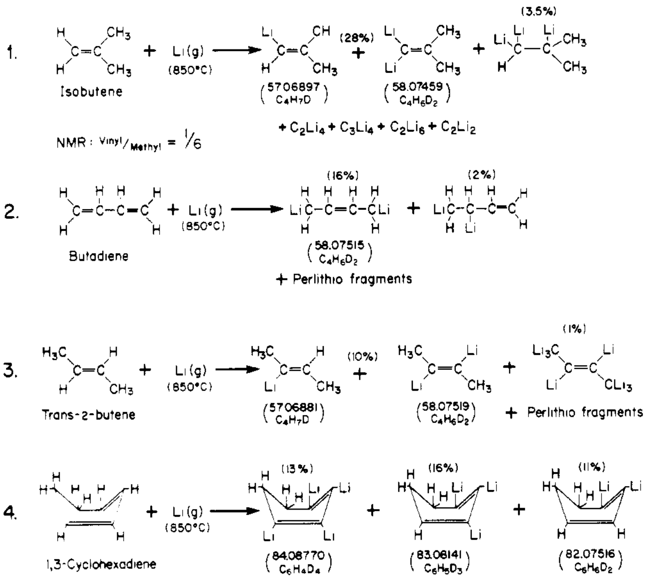


Figure 2. Major products of the reaction of lithium with alkenes.

The reaction of 1.5 g of *trans*-2-butene with lithium, followed by deuterolysis, gave a 10% yield of deuterated 2-butenes. The mass spectra of these products contained parent ions for C_4H_7D (57.06881) and $C_4H_6D_2{}^+$ (58.07519) in a 3:2 ratio. A much less intense peak (~4%) for $C_4D_8{}^+$ (64.11280) indicates that all the hydrogen atoms were substituted with lithium in a small percentage of the starting 2-butene. In the deuterated hydrolysis products a parent peak for $C_4D_8H_2{}^+$ (66.12700) was found which indicates that in ~0.1% of the products lithium has added across the double bond. The ^1H NMR integral spectrum for the D_2O hydrolysis products (Table I) revealed a 12:1 ratio for the 1,4 to the 2,3 protons indicating preferential reaction at the unsaturated sites.

The reaction of 1.5 g of 1,3-cyclohexadiene with lithium gave polylithium compounds which yielded on hydrolysis 1,3-cyclohexadiene, cyclohexene, and cyclohexane in the ratio of 3:4:3. The total yield of the cyclic C_6 species was 54%. After hydrolysis with D_2O the mass spectra of the cyclohexadiene products contained parent ions for $C_6H_4D_4{}^+$ (84.08771), $C_6H_5D_3{}^+$ (83.08141), and $C_6H_6D_2{}^+$ (82.07516) in the relative intensities of 1.0:1.2:1.3. The lithiation was confirmed by derivation with Me_3SiCl; mass spectral peaks were observed for $C_6H_7SiMe_3{}^+$ (*m/e* 152), $C_6H_6(SiMe_3)_2{}^+$ (*m/e* 224), $C_6H_5(SiMe_3)_3{}^+$ (*m/e* 296), and $C_6H_4(SiMe_3)_4{}^+$ (*m/e* 368). Addition of lithium to one of the double bonds was indicated by mass spectral parent ions due to $C_6H_4D_6{}^+$ (*m/e* 88.1192) and to both double bonds by a molecular ion due to $C_6H_6D_6^+$ (*m/e* 90.13130) in the deuterated hydrolysis product.

In the preceding examples a large fraction of the products was derived from the replacement of hydrogen by lithium to yield polylithioalkenes. The reaction of 1,3-butadiene, however, yields compounds resulting from the addition of two lithium atoms to the double bonds of that compound. Thus, reaction of the lithiated products with H_2O did not regenerate butadiene, but instead gave a 10% yield of butenes. ^{1}H NMR spectra and GLC retention times indicated that the ratio of 1,4 addition to 1,2 addition was 8:1. Derivation with Me_3SiCl yielded a liquid possessing a small peak in the mass spectrum at *m/e* 200 having the appropriate isotopic distribution for a species with two silicon atoms (calcd mol wt for $Si_2C_{10}H_{24}$ is 200), and peaks with larger ion intensities at P − *n*-CH_3^+. One explanation for the dilithio product is the facile reaction of lithium with the diradical 2-butene produced from butadiene as the first step in the free radical polymerization of that compound.

In general both the mass spectra fragmentation patterns and the integrated ^{1}H NMR spectra indicated that substitution of the vinyl protons is preferred to substitution of the methyl protons. With the exception of butadiene it seems likely that the first reaction of alkenes with lithium is the substitution of a vinylic hydrogen with subsequent replacement of both vinyl and alkyl hydrogens. This last step is in competition with reactions in which lithium is added across the double bond. Under the reaction conditions (800°, gaseous alkali metal) fragmentation of the alkenes leads to C_3Li_4, C_2Li_6, C_2Li_4, and C_2Li_2 whose combined yields vary from 25 to 50%.

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Reaction of Lithium Ethynyl- and Ethenyltrialkylborates with Acid. A Valuable Route to the Markovnikov Alkenyl- and Alkylboranes

Sir:

Monolithium acetylide and vinyllithium react rapidly with trialkylboranes to produce the lithium ethynyl- and ethenyltrialkylborates, respectively (eq 1 and 2).

$$R_3B + LiC{\equiv}CH \longrightarrow [R_3BC{\equiv}CH]Li \qquad (1)$$

$$R_3B + LiCH{=}CH_2 \longrightarrow [R_3BCH{=}CH_2]Li \qquad (2)$$

Protonation of these species with concentrated hydrochloric acid at low temperature (eq 3 and 4) provides directly the borane species with the opposite regiochemistry from that realized in hydroboration of terminal acetylenes[1] or olefins.[2]

Lithium 1-alkynyltrialkylborates react with a variety of electrophiles to induce an alkyl group migration from boron

Table I. Protonation and Oxidation of Lithium Ethynyltrialkylborates

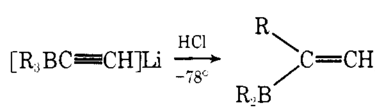
Alkylborane	Ketone	% yield[a]
Tri-*n*-butylborane	2-Hexanone	78
Triisobutylborane	4-Methyl-2-pentanone	90
Tricyclopentylborane	Cyclopentylethanone	70
Tricyclohexylborane	Cyclohexylethanone	77

[a] By BPC. All reactions were run on a 5-mmol scale.

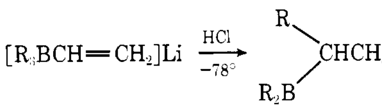
Table II. Protonation and Oxidation of Lithium Ethenyltrialkylborates

Alkylborane	Alcohol	% yield[a]
Tri-*n*-butylborane	2-Hexanol	91
Tri-*sec*-butylborane	3-Methyl-2-pentanol	87[c]
Triisobutylborane	4-Methyl-2-pentanol	87[c]
Tricyclopentylborane	1-Cyclopentylethanol	90[c]
Tricyclohexylborane	1-Cyclohexylethanol	93[c]
Tri-*exo*-norbornylborane	1-(2-Norbornyl)ethanol[b]	94[c]

[a] By VPC. All reactions were run on a 5-mmol scale. [b] Preliminary investigation revealed that the product was essentially the pure exo isomer. [c] These reactions were stirred with acid for 1 hr at −78° and for 2 hr at room temperature prior to oxidation.

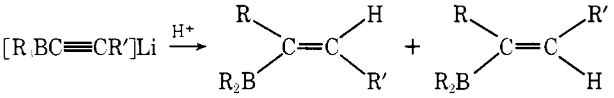


$$[R_3BC{\equiv}CH]Li \xrightarrow[-78^\circ]{HCl} (R)(R_2B)C{=}CH_2 \qquad (3)$$



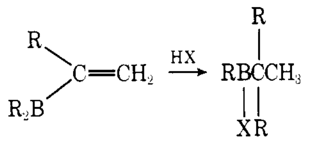
$$[R_3BCH{=}CH_2]Li \xrightarrow[-78^\circ]{HCl} (R)(R_2B)CHCH_3 \qquad (4)$$

to carbon.[3] Protonation, for example, produces a mixture of cis and trans alkenylboranes[3a,4] (eq 5). Protonation of the



$$[R_3BC{\equiv}CR']Li \xrightarrow{H^+} (R)(R_2B)C{=}C(H)(R') + (R)(R_2B)C{=}C(R')(H) \qquad (5)$$

parent compound, lithium ethynyltrialkylborate, would be expected to give the Markovnikov alkenylborane (eq 3). However, only low yields (55%) of the expected ketone are realized upon protonation with a variety of acids followed by oxidation of the intermediate organoborane. Investigation revealed that the alkenylborane initially produced undergoes a facile second alkyl group migration[5] (eq 6).



$$(R)(R_2B)C{=}CH_2 \xrightarrow{HX} RB(X)C(R)(R)CH_3 \qquad (6)$$

We discovered that the second migration can be stopped by adding base to the solution at −78° prior to bringing the solution to room temperature. Oxidation with alkaline hydrogen peroxide then produces good yields of the ketone (Table I).

In a similar manner, vinyllithium adds to trialkylboranes (eq 2) and the resulting complex undergoes protonation by concentrated hydrochloric acid at −78° (eq 4). After warming to room temperature, the acid may be neutralized and the borane oxidized to the Markovnikov alcohol (Table II).

This simple process, along with hydroboration, permits the production of either the Markovnikov or the anti-Markovnikov organoborane. For example, cyclohexylethyne may be hydroborated with dicyclohexylborane to produce regiospecifically the terminal (anti-Markovnikov) alkylborane[1] (eq 7) (vinyl proton NMR (CCl_4, Me_4Si) δ 6.15 (d, J = 18 Hz), 6.70 (dd, J = 18 Hz, J = 5.6 Hz)). Such alk-