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A MILD AND SELECTIVE SYNTHESIS OF CYCLOPROPENE AND CYCLOPROPANE DERIVATIVES VIA CYCLIALLYLATION OF ALKENYLLITHIUMS[1]

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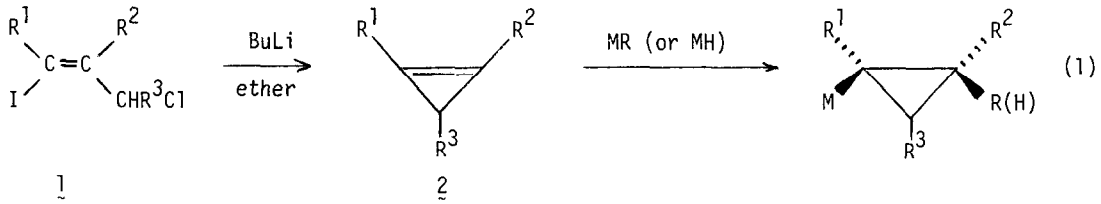
SUMMARY: Treatment of *cis*-1-iodo-3-chloro-1-propene derivatives, readily obtainable via trans addition of organometals to propargyl alcohols followed by iodinolysis and chlorination, with alkyllithiums, such as *t*-BuLi and *n*-BuLi, can proceed rapidly and cleanly even at -78°C to give in high yields cyclopropene derivatives, which undergo cis hydrometalation and carbometalation reactions more rapidly than the corresponding alkynes to produce cyclopropane derivatives.

Cyclopropenes are of interest from both theoretical and synthetic viewpoints. The heat of hydrogenation for the conversion of cyclopropene to cyclopropane is ca. 54 kcal/mole[2] and is considerably larger than that for the conversion of acetylene to ethylene (42 kcal/mole[2]), suggesting that cyclopropenes should be more reactive than the corresponding alkynes in hydrometalation, carbometalation, and other addition reactions. And yet, relatively little has been published on these reactions, presumably because relatively few satisfactory routes to cyclopropenes have been developed.

We now report that treatment of *cis*-1-iodo-3-chloropropene derivatives (1), readily obtainable via carbometalation of propargyl alcohols followed by iodinolysis and chlorination, with an alkyllithium, e.g., *t*-BuLi (2 equiv) or *n*-BuLi (1 equiv), can proceed rapidly and cleanly even at -78°C to give 1,2-disubstituted cyclopropenes in high yields (eq 1). However, the yields of 1-monosubstituted cyclopropenes are low. We further report that cyclopropenylsilanes react stereo- and regioselectively with organocoppers, allylzinc bromide, and diisobutylaluminum hydride (DIBAH) via clean cis addition placing the metal atom on the Si-bearing carbon atom (eq 1). These reactions are indeed considerably faster than the corresponding reactions of alkynylsilanes.

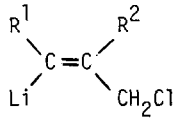


(1)

1 2

Cyclopropenes have been synthesized mostly via (i) carbenoid addition to alkynes,[2b,3] (ii) carbenoid rearrangement,[2b,4] and (iii) 1,2- or 1,3-elimination.[2b,5] However, the preparation of cyclopropenes via cycliallylation of alkenylmetals appears to be unprecedented, although the formation of 1-trimethylsilyl-2,2-dimethylcyclopropane by the reaction of 1-trimethylsilyl-3-

bromopropyne with $Me_3Al\text{-}Cl_2ZrCp_2$ reported by us[6] recently must have proceeded via 1-trimethylsilyl-2-methylcyclopropene. Furthermore, the conversion of 1 into 2 is exceedingly rapid and clean in cases where neither R^1 nor R^2 is H. Provided that 1 is prepared from the corresponding iodoalcohol purified by column chromatography (silica gel, 9:1 hexane-ethyl acetate), its treatment with either 2 equiv of *t*-BuLi or 1 equiv of *n*-BuLi cleanly gives 2, and its yield determined by ^1H NMR or GLC is uniformly high. Although it is reasonable to assume that 3 is an intermediate in the cyclization in an analogy with the corresponding cyclization reaction of 1-iodo-4-chloro-1-butenes,[7] our attempts to generate 3e by treatment of 1e with 1 equiv of *n*-BuLi in ether at -78°C and trap it with either D_2O-THF or MeOH at -78°C immediately after the addition of *n*-BuLi (<1 min) led only to the formation of 2e in 93% yield. Nevertheless, the nonformation of any double bond-rearranged product rules out the carbenoid rearrangement mechanism.



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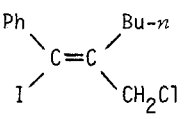
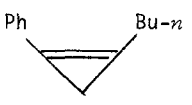
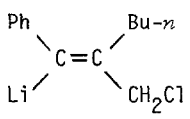


1e

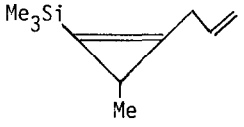


2e



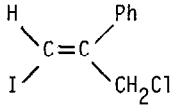
3e

Cyclopropenes prepared in this study are stable for at least a week at room temperature as 0.1 *M* solutions in ether and may be used directly in subsequent reactions. Upon concentration, however, those that are 3-unsubstituted rapidly decompose, although the 1,2,3-trisubstituted derivatives are more stable. Thus, for example, 2b was obtainable by concentration followed by bulb-to-bulb distillation at 50-55°C (15 mm) in 78% isolated yield, whereas attempts to isolate 2c by the same procedure led to its complete decomposition, even though its clean formation in essentially quantitative yield was indicated by GLC and ^1H NMR. Although it was feasible to distill 2c using *n*-hexadecane as a higher boiling diluent and trap it at -78°C in 58% yield, the other products have been identified and characterized as solutions by ^1H and ^{13}C NMR, IR, and MS after addition of $CDCl_3$ followed by evaporation of ether, and their yields have been determined by ^1H NMR using an internal standard, such as benzene.

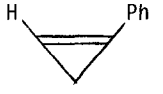


2b

2c



1i



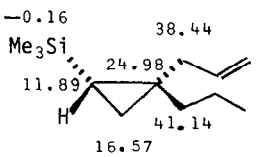
2i

The experimental results are summarized in Table I. In sharp contrast with the clean cyclization reaction of 1,2-disubstituted *cis*-1-iodo-3-chloropropenes, the corresponding reaction of monosubstituted derivatives gives a few unidentified byproducts along with the expected cyclopropenes formed in low yields. Thus, the yield of 2i obtained from 1i is only 46%.

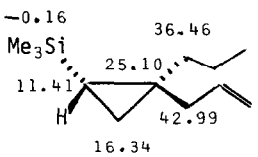
All *cis*-1-iodo-3-chloropropene derivatives (1) were prepared in high yields by sequentially treating the corresponding iodoalcohols with lithium diisopropylamide in THF-hexane (-78°C and then 0°C), CH_3SO_2Cl (-78°C to room temperature), and LiCl in DMF (room temperature).[8] The *cis*-iodoalcohols were, in turn, prepared by various known carbometalation[9] reactions of propargyl alcohols followed by iodinolysis. Introduction of a substituent in the C-3 position was

achieved via oxidation of iodoalcohols with pyridinium chlorochromate followed by methylation with MeMgBr. A representative cyclization procedure is as follows. To a solution of 0.66 g (2.0 mmol) of 1b in 18 mL of ether at -78°C was added 2.3 mL (4.0 mmol) of a 1.73 *M* solution of *t*-BuLi in pentane. After 30 min the reaction mixture was warmed to room temperature. GLC analysis (SE-30) of an aliquot quenched with aqueous NH_4Cl indicated the absence of the starting compound and a clean formation of a product. No other peaks were detectable in the product region. The reaction mixture was poured into aqueous NH_4Cl and extracted with pentane. The organic layer was washed with aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and distilled under nitrogen at 50-55°C (15 mm) to give 0.26 g (78% yield) of 2b. The generation of 2c from 0.95 g (3.0 mmol) of 1c was achieved analogously. However, its isolation required the following procedure. To the pentane extract, which had been worked up as above, were added 1.5 mL of *n*-hexadecane and 0.013 g (0.06 mmol) of 2,6-di-*t*-butyl-4-methylphenol as an antioxidant. The volatile solvents were removed at 0°C (5.5 mm), and the residue was bulb-to-bulb distilled at 0.4 mm (bath temperature 55°C) and trapped in a flask cooled at -78°C to give 0.27 g (58%) of 2c. After weighing, it was dissolved in $CDCl_3$ for spectroscopic characterization.

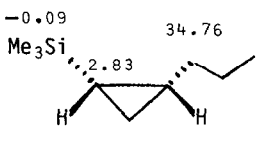
Concerning the stereochemistry of the addition of organometals to cyclopropenes, phenyllithium was shown to add to cyclopropene itself with >99% stereoselectivity but only in 3% yield.[4c] On the other hand, Grignard reagents[10a,10b] and borane[10c] have been shown to give cis addition products in good yields. Treatment of 2a, generated in situ, with *n*-PrCu·MgBr in ether for 1-2 h at -25°C gave, after protonolysis, a 65% isolated yield of 4a (>98% isomeric purity). Similarly, the reaction of 2c with 2 equiv of allylzinc bromide for 12 h at 22°C provided, after protonolysis, 4b (>98% isomeric purity) in 92% yield. The stereochemical assignments are based primarily on the facts that the ^{13}C NMR signals for the CH_2 carbon that is adjacent to the ring and cis to the Me_3Si group is shifted upfield relative to the trans CH_2 carbon due to the steric compression effect[11a] and that the off-resonance proton-decoupled ^{13}C NMR signals for the CH_2 carbons of the *n*-propyl group are broadened relative to that for the CH_2 carbon of the allyl group.[11b] The ^{13}C NMR chemical shifts of 4 and 5 are indicated in their structural formula. Treatment of 2c with DIBAH (2 equiv) in ether for 24 h at 22°C gave, after protonolysis, 5a (>98% isomeric purity) in 85% yield. On the other hand, its treatment with $LiAlH_4$ (2 molar equiv) in THF-ether for 36 h under reflux produced, after protonolysis, a 70:30 mixture of 5a and 5b in 95% yield. That the products before protonolysis are 1-(trimethylsilyl)cyclopropylmetal derivatives has been indicated by >90% D incorporation in the position α to Si upon quenching them with D_2O. When a 1:1 mixture of 2c and 1-pentynyltrimethylsilane was treated with 0.9 equiv (relative to each substrate) of *n*-PrCu·$MgBr_2$, allylzinc bromide, or DIBAH, 2c reacted selectively, with essentially 100% of 1-pentynyltrimethylsilane remaining unreacted, except in the DIBAH reaction in which the reactivity ratio of 2c to the alkynylsilane was ca. 5.



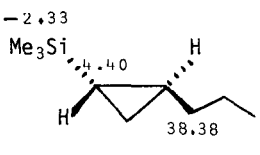
4a



4b



5a



5b

Table I. Preparation of Cyclopropenes by the Reaction of *cis*-1-Iodo-3-chloropropene Derivatives with Butyllithium[a]

Entry	Substituents in 1 and 2 R[1]	R[2]	R[3]	Yield[b] (%) of 2	IR[c] cm^{-1}	^1H NMR[d] ppm	^{13}C NMR[e] ppm
a	Me_3Si	Allyl	H	95	1795	0.71 (s)	6.48, 106.69, 133.32
b	Me_3Si	Allyl	Me	99 (78)	1800	1.22 (q)	14.18, 115.56, 141.30
c	Me_3Si	*n*-Pr	H	88 (58)	1795	0.61 (s)	6.16, 105.30, 135.25
d	Me_3Si	Ph	H	90	1800	1.05 (s)	5.67, 110.97, *f*
e[5c]	Ph	*n*-Bu	H	83	1830	1.20 (s)	7.12, 108.20, 115.23
f	*n*-Hex	Me	H	84	1870	0.79 (s)	8.13, 105.29, 110.18
g	*n*-Hex	Me	Me	70	1860	*g*	9.87, 113.27, 118.10
h	*n*-Hex	Allyl	H	90	1870	*g*	7.72, 107.42, 111.07
i	H	Ph	H	46[h]	—	—	—

[a]The reaction was carried out as described for the preparation of 2b in the text. [b]NMR yield based on 1. The number in parentheses is an isolated yield. [c]IR C=C stretching frequency for the cyclopropene ring. [d]Chemical shift of the ring methylene protons. [e]Chemical shifts of the ring carbons. [f]Not readily identifiable. [g]Not readily discernible. [h]Identified by its conversion into 2d.

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