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Registry No. (*S,S*)-1, 82468-65-3; (*S,S*)-2, 80656-07-1; (*S*)-NapEt·HClO$_4$, 82431-48-9; (*R*)-NapEt·HClO$_4$, 82456-17-5; (*S*)-AlaOMe·HCl, 2491-20-5; (*R*)-AlaOMe·HCl, 14316-06-4.

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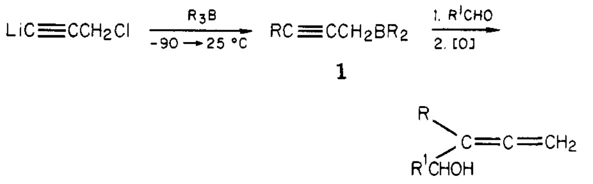
Preparation of Functionally Substituted Allenes from Methylacetylenes via Propargylic Lithium Alanate or Lithium Borate Intermediates

Summary: Propargylic lithium alanates or lithium borates react with allylic halides or with various carbonyl reagents in a highly regioselective manner to furnish 1,1-disubstituted allenes.

Sir: We herein report that addition of allylic halides or carbonyl reagents to readily accessible propargylic alanates or borates provides a convenient route to a variety of functionally substituted allenes. These are obtained in high yields and isomeric purities. Functionally substituted allenes are valuable synthetic intermediates and have been used as dienophiles in Diels–Alder reactions[1] and as substrates for 1,4-additions of organocuprates.[2]

Recently we have shown that propargylic boranes 1, derived from lithium chloropropargylide and trialkylboranes, react with aldehydes to afford α-allenic alcohols (eq 1).[3] Unfortunately, attempts to develop this reaction into a general synthesis for functionally substituted allenes using carbon electrophiles other than aldehydes have not been successful. Thus, in a search for ways to circumvent the synthetic limitations attendant with the use of 1, we have investigated the syntheses and reactions of the propargylic alanates 3 and borates 4.



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(1)

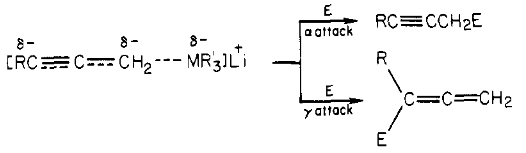
It has been well-established that conversion of triorganoalanes or triorganoboranes into the corresponding *ate* complexes results in an enhancement in their reactivity toward many electrophilic reagents.[4] In accord with this, we have now found that propargylic alanates and borates react readily with allylic halides[5] as well as with various carbonyl reagents. This provides the basis for an operationally simple procedure for preparing 1,1-disubstituted allenes bearing an α-functional group. Moreover, we have developed an efficient synthesis for the required organometallic *ate* complexes using the readily available 2-alkynes as precursors.

Metalation of 2-alkynes with *tert*-butyllithium in the presence of TMEDA (tetramethylethylenediamine) affords the corresponding lithium reagents 2 (eq 2).[6,7] Treatment of these with triisobutylalane or with tri-*sec*-butylborane furnishes the lithium alanates 3 or borates 4, respectively.[8] The assignments of propargylic structures to 3 and 4 are based on IR and NMR data obtained from reaction mixtures containing these organometallic intermediates.

$$\mathrm{RC{\equiv}CCH_3} \xrightarrow[\substack{\mathrm{Et_2O{-}TMEDA}\\ -78 \longrightarrow 0\,^\circ\mathrm{C}}]{t\text{-}\mathrm{C_4H_9Li}} \underset{\mathbf{2}}{[\mathrm{RC{\equiv}C{=}CH_2}]^-\mathrm{Li}^+} \xrightarrow{\mathrm{R^1_3M}} [\mathrm{RC{\equiv}CCH_2\overset{-}{M}R^1_3}]\overset{+}{\mathrm{Li}} \quad (2)$$

3, $\mathrm{MR^1_3} = \mathrm{Al}(i\text{-}\mathrm{C_4H_9})_3$
4, $\mathrm{MR^1_3} = \mathrm{B}\text{-}(sec\text{-}\mathrm{C_4H_9})_3$

The propargylic moieties in 3 and 4 possess two potential nucleophilic sites. Attack of an electrophile "E" at the α carbon should afford a homopropargylic derivative, whereas attack at the γ carbon should produce, via bond transposition, an allenic compound (eq 3).[9]



(3)

Treatment of the propargylic alanate 3 (R = *n*-C$_4$H$_9$) in ether at −78 °C with allyl bromide, prenyl bromide (1-bromo-3-methyl-2-butene), or (*Z*)-1-chloro-2-heptene followed by warming the reaction mixture to room temperature furnished, after hydrolytic workup, the corresponding allyl allenes 5 containing less than 4% of the α-coupling product 6 (eq 4).[10] Interestingly, substituting the *n*-butyl group on the γ carbon in 3 by the larger cyclohexyl group resulted in only a small increase in α prenylation (Table I). It is important to note that the structures of the allyl allenes derived from 3 and prenyl bromide or (*Z*)-1-chloro-2-heptene are consistent with a direct S$_N$2 attack on the electrophiles by the organometallic reagent.

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(1) Kozikowski, A. P.; Floyd, W. C.; Kuniak, M. P. *J. Chem. Soc., Chem. Commun.* **1977**, 582. Ismail, A. M.; Hoffmann, H. M. R. *J. Org. Chem.* **1981**, *42*, 3549.

(2) Bertrant, M.; Gil, G.; Viala, J. *Tetrahedron Lett.* **1977**, 1785.

(3) Zweifel, G.; Backlund, S. J.; Leung, T. *J. Am. Chem. Soc.* **1978**, *100*, 5561.

(4) Negishi, E. "Organometallics in Organic Synthesis"; Wiley: New York, 1980.

(5) The reactions of 3 and 4 with methyl iodide were too sluggish to be synthetically useful.

(6) (a) For alternative procedures for lithiation of methylacetylenes see: Klein, T. in "The Chemistry of Carbon–Carbon Triple Bonds"; Patai, L., Ed.; Wiley: New York, 1978; Vol. 1. (b) Despo, A. D.; Chin, S. K.; Flood, T.; Peterson, P. E. *J. Am. Chem. Soc.* **1980**, *102*, 5120.

(7) The organolithium reagents 2 exist as equilibrium mixtures of allenic and propargylic isomers.[6a]

(8) Reactions of the organolithium reagents 2 with diisobutylchloroalane or with dialkylchloroboranes provides an efficient synthesis for trigonal propargylic alanes and boranes, respectively. These, upon treatment with aldehydes, afford nearly exclusively the corresponding α-allenic alcohols. Zweifel, G.; Hahn, G.; Pearson, N. R., unpublished results.

(9) Although the following discussion focuses on the propargylic alanates and borates, it is conceivable that in certain cases the corresponding isomeric allenic organometallics may compete with 3 and 4 for the electrophile. The possibility that these species, in concentrations too low for spectroscopic detection, are in equilibrium with the thermodynamically favored propargylic organometallics 3 and 4 cannot be precluded.

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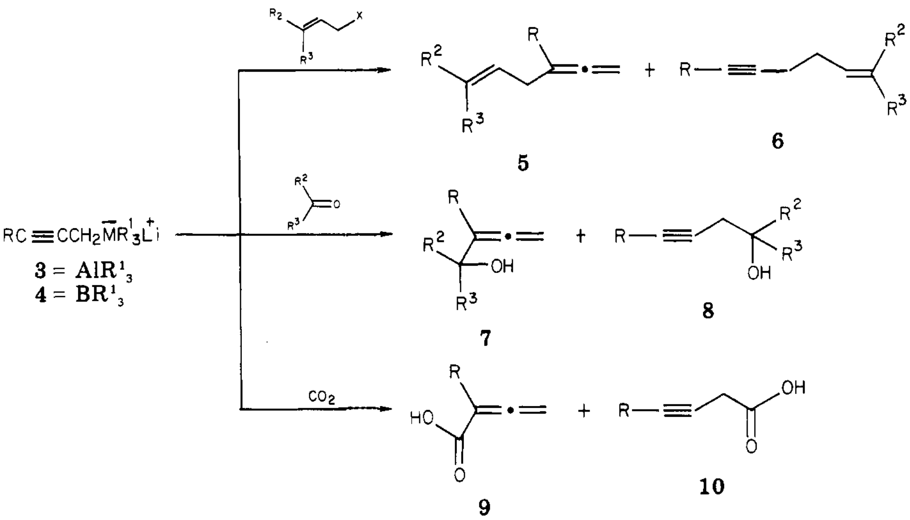

(4)

Table I. Products Derived from Coupling of RC≡CCH$_2$M Intermediates with Allylic Halides or with Carbonyl Reagents

RC≡CCH$_2$M[a]			product ratios, %		
M	R	electrophile[b] (E)	(R)(E)-C=C=CH$_2$	RC≡CCH$_2$E	yield,[c] %
AlR$_3$Li	n-C$_4$H$_9$	H$_2$C=CHCH$_2$Br	96	4	78
	n-C$_4$H$_9$	(CH$_3$)$_2$C=CHCH$_2$Br	99	1	84
	n-C$_4$H$_9$	(Z)-n-C$_4$H$_9$CH=CHCH$_2$Cl	97	3	(76)[d]
	c-C$_6$H$_{11}$	(CH$_3$)$_2$C=CHCH$_2$Br	95	5	(77)
	n-C$_4$H$_9$	H$_2$C=CHCHO	96	4[f]	80[e]
	n-C$_8$H$_{17}$	C$_2$H$_5$CHO	95	5	(94)
	t-C$_4$H$_9$	C$_2$H$_5$CHO	97	3	71
	n-C$_4$H$_9$	(CH$_3$)$_2$CO	95	5[f]	73[g]
	n-C$_4$H$_9$	CO$_2$	92	8	80
BR$_3$Li	n-C$_4$H$_9$	H$_2$C=CHCH$_2$Br	83	17	74[g]
	n-C$_4$H$_9$	(CH$_3$)$_2$C=CHCH$_2$Br	99	1	84
	n-C$_8$H$_{17}$	C$_2$H$_5$CHO	99	1	86
	t-C$_4$H$_9$	C$_2$H$_5$CHO	62	38	(21)
	n-C$_4$H$_9$	(CH$_3$)$_2$CO	48	52	(35)
	n-C$_4$H$_9$	CO$_2$	98	2	76
Li	n-C$_4$H$_9$	H$_2$C=CHCH$_2$Br	10	90	(62)
	n-C$_8$H$_{17}$	C$_2$H$_5$CHO	47	53	(87)
	n-C$_4$H$_9$	CO$_2$	80	20	79[h]

[a] AlR$_3$ = (i-C$_4$H$_9$)$_3$Al; BR$_3$ = (sec-C$_4$H$_9$)$_3$B. [b] The electrophile was added to the organometallic reagent at −78 °C and the reaction mixture was allowed to warm up to 25 °C prior to work up. [c] GLC yields are in parentheses. [d] The reaction mixture was maintained for 2 h at 25 °C prior to workup. [e] Only 1,2-addition was observed. [f] The structure of the acetylenic product has not been proven. [g] The reaction mixture was maintained for 16 h at 25 °C prior to workup. [h] The propargylic lithium was added at −78 °C to ether saturated with gaseous carbon dioxide.

In marked contrast to the high reactivity and regioselectivity observed with the alanate **3**, the corresponding reaction of allyl bromide with the borate **4** proceeded at a much slower rate and produced an 83:17 mixture of the allyl allene **5** and enyne **6**. It should be noted that treatment of the organolithium reagent **2** with allyl bromide afforded mainly enyne **6**, the α-coupling product. Nearly exclusive γ coupling was obtained, however, when the borate **4** was treated with the more reactive prenyl bromide.

The propargylic alanates **3** and borates **4** also exhibited differences both in reactivity and regioselectivity toward aldehydes and ketones. Thus, treatment of **3** with propanal yielded the corresponding α-allenic alcohols **7** containing less than 5% of the isomeric homopropargylic alcohols **8** (eq 4). On the other hand, reactions of the corresponding borates **4** with propanal exhibited significant decreases in γ selectivity and product yield with increasing shielding of the γ carbon (Table I).[11] Furthermore, treatment of **4** with acetone furnished a 48:52 mixture of **7** and **8** in low yield, whereas the corresponding reaction with the alanate **3** produced the α-allenic alcohol in 95% isomeric purity. Thus, the organoalanates provide greater flexibility in the choice of the propargylic component for the preparation of α-allenic alcohols than do the corresponding borates, and also offer a viable alternative to the propargylic borane route (eq 1).[3]

Especially attractive from a synthetic point of view was the prospect of preparing α-allenic carboxylic acids via the reactions of propargylic alanates and borates with carbon dioxide. It should be noted, however, that the trigonal propargylic alanes and boranes do not react with carbon dioxide. Thus, it was gratifying to find that treatment of the propargylic alanate **3** or borate **4** (R = n-C$_4$H$_9$) with carbon dioxide resulted in regioselective γ coupling and formation of the α-allenic acid **9** containing only a small amount of the isomeric acetylenic acid **10** (eq 4). On the other hand, the corresponding organolithium reagent **2**

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(10) Preferential γ allylation has also been observed in reactions of allylic halides with allylic aluminum and boron *ate* complexes. Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 6282. Yamamoto, Y.; Yatagai, H.; Maruyama, K. *Ibid.* **1981**, *103*, 1969.

(11) It is conceivable that the low yields of coupling product obtained from **4** (R = *tert*-butyl) and propanal may result from competing reduction of the aldehyde by β-hydride transfer from the *sec*-butyl moieties of boron. Such reductions have been previously observed in coupling reactions of allylic borates with allylic halides.[10]

coupled with carbon dioxide to produce an 80:20 mixture of the acids **9** and **10**.[12]

Although our primary goals in the present work were synthetic, the results provide important information regarding the factors that affect the regiochemistry of coupling reactions of propargylic alanates and borates with electrophiles. These factors are as follows: the nature of the metal center and hence the effective electron density at the α and γ carbons, the steric shielding of the α and γ carbons, and the reactivities of the electrophiles and their steric requirements. Also, preliminary investigations have revealed that replacement of the ether solvent employed in this study by tetrahydrofuran has a detrimental effect on both the regioselectivity of coupling as well as on the yield of coupling products.

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Registry No. 2 (R = *n*-C_4H_9), 82511-26-0; **2** (R = *n*-C_8H_{17}), 82511-27-1; **3** (R = *n*-C_4H_9), 82511-37-3; **3** (R = c-C_6H_{11}), 82511-38-4; **3** (R = *n*-C_8H_{17}), 82511-39-5; **3** (R = *t*-C_4H_9), 82511-40-8; **4** (R = *n*-C_4H_9), 82511-41-9; **4** (R = *n*-C_8H_{17}), 82511-42-0; **4** (R = *t*-C_4H_9), 82511-43-1; **5** (R = *n*-C_4H_9;R^2 = R^3 = H), 82511-28-2; **5** (R = *n*-C_4H_9;R^2 = R^3 = CH_3), 82511-29-3; (*Z*)-**5** (R = *n*-C_4H_9;R^2 = *n*-C_4H_9;R^3 = H), 82511-30-6; **5** (R = c-$C_6H_1$1;R^2 = R^3 = CH_3), 82511-31-7; **6** (R = *n*-C_4H_9;R^2 = R^3 = H), 82511-32-8; **7** (R = *n*-C_4H_9;R^2 = $CH{=}CH_2$;R^3 = H), 82511-33-9; **7** (R = *n*-C_8H_{17};R^2 = C_2H_5;R^3 = H), 82511-34-0; **7** (R = *t*-C_4H_9;R^2 = C_2H_5;R^3 = H), 82511-35-1; **7** (R = *n*-C_4H_9;R^2 = R^3 = CH_3), 867-94-7; **8** (R = *t*-C_4H_9;R^2 = C_2H_5;R^3 = H), 82511-36-2; **8** (R = *n*-C_4H_9;R^2 = R^3 = CH_3), 871-40-9; **9** (R = *n*-C_4H_9), 5665-73-6; $H_2C{=}CHCH_2Br$, 106-95-6; $(CH_3)_2C{=}CHCH_2Br$, 870-63-3; (*Z*)-*n*-$C_4H_9CH{=}CHCH_2Cl$, 55638-53-4; $H_2C{=}CHCHO$, 107-02-8; C_2H_5CHO, 123-38-6; $(CH_3)_2CO$, 67-64-1; CO_2, 124-38-9.

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[12] A representative procedure for the preparation of 3-carboxy-1,2-heptadiene (**9**, R = *n*-C_4H_9) is as follows. A solution of *tert*-butyllithium (5.1 mL, 10.5 mmol) in *n*-pentane was placed into a 50-mL, two-necked, round-bottomed flask equipped with a nitrogen-inlet tube, thermometer, and magnetic stirrer. The pentane was removed under reduced pressure at room temperature and the white, solid *tert*-butyllithium formed was cooled to −78 °C and dissolved in anhydrous ether (10 mL). After sequential addition of TMEDA (1.16 g, 10.0 mmol) and 2-heptyne (0.96 g, 10.0 mmol), the resultant yellow slurry was gradually warmed to 0 °C and stirred for an additional hour at this temperature. The yellow solution containing the lithium reagent **2** (R = *n*-C_4H_9) was cooled to −78 °C, treated with an ethereal solution of tri-*sec*-butylborane (11.0 mL, 11.0 mmol; Aldrich Chemicals)[13] and then allowed to warm up to 0 °C. The propargylic borate **4** solution obtained was cooled to −78 °C and then carbonated by introducing a steady stream of dry carbon dioxide. The mixture was maintained for 15 min at −78 °C and then was slowly brought to room temperature while the addition of carbon dioxide was maintained continually. The tri-*sec*-butylborane byproduct was oxidized at 35–40 °C by adding 6 N sodium hydroxide (5 mL) and 30% hydrogen peroxide (8.0 mL)[14] and stirring at ambient temperature for 30 min. The resultant aqueous phase was separated, extracted with ether, and the ethereal extract washed with 3 N sodium hydroxide (15 mL). The aqueous phase and washings were combined and then acidified with concentrated hydrochloric acid. The precipitated acid was extracted into ether and the ether was washed with 10% hydrochloric acid and with saturated aqueous sodium chloride. Drying and removal of the solvent yielded 1.1 g (76%) of 3-carboxy-1,2-heptadiene: mp 70–71 °C.

[13] For preparation of the propargylic alanate **3**, triisobutylalane (neat, 11 mmol, 2.8 mL; Texas Alkyls) was added to the organolithium reagent **2** in ether at −78 °C. The reaction mixture was stirred for 30 min and then was treated at this temperature with the electrophile. Alternatively, a 2 M solution of triisobutylalane in ether, prepared by replacing the benzene from a solution of (*i*-$C_4H_9)_3Al$–benzene (Aldrich Chemicals) with ether at 0 °C, may be employed.

[14] Since utilization of the propargylic alanate does not require an oxidative workup, the reaction mixture was brought to room temperature and then poured slowly into chilled, vigorously stirred 10% hydrochloric acid.