

A PREPARATION OF BROMOLEFINS FROM CARBONYL COMPOUNDS

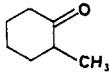
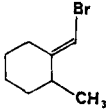
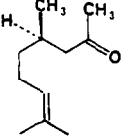
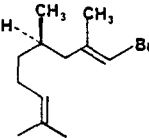
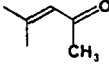
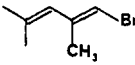
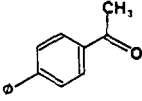
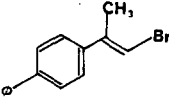
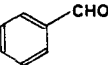
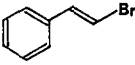
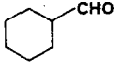
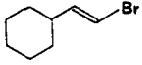
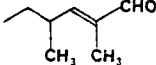
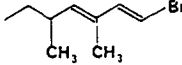
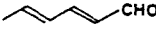
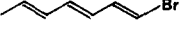
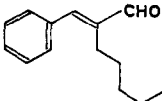
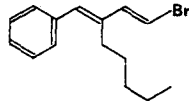
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Summary: A variety of 1-bromoalkenes are prepared by addition of dibromomethylithium to ketones and aldehydes followed by reductive elimination with zinc-acetic acid. The product *E/Z* ratios were determined, and halogen-lithium exchange with *t*-butyllithium was examined.

Considerable methodology is now available for the stereocontrolled preparation of vinylic bromides from acetylenic precursors.¹ However, possibilities for the transformation of ketones and aldehydes to bromoalkenes with inclusion of an additional carbon atom are quite limited. The Wittig reaction using bromomethylenetriphenylphosphorane generally fails with ketones, but proceeds with aldehydes affording the vinylbromides with some preference for the *Z*-geometry.² Mixtures of the expected bromides and terminal olefins are sometimes obtained resulting from halide-metal exchange during generation of the phosphorane. The α,β -epoxysilanes as prepared by Magnus and coworkers³ yield 1-bromoalkenes upon treatment with hydrogen bromide in ether.⁴ We have found that the alcohols obtained from addition of dibromomethylithium to aldehydes and ketones undergo reductive elimination to bromoalkenes upon treatment with zinc dust and glacial acetic acid in refluxing methylene chloride.

Results from a number of aldehyde and ketone substrates are shown in Table I. The methodology is particularly well-suited for the preparation of conjugated 1-bromoalkenes. Although the reactions generally displayed little stereoselectivity, the vinyl bromides obtained are excellent precursors to terminal acetylenes.⁵ Attempts to elicit improved stereocontrol of the reduction using sodium-amalgam, trifluoroacetic anhydride-sodium iodide and trimethylphosphite at reflux afforded only slightly altered *E/Z* product ratios with far less efficiency.

The dibromoalcohols were prepared by addition of a solution of lithium dicyclohexylamide in tetrahydrofuran to a mixture of dibromomethane and carbonyl compounds at -78°C in accordance with the literature procedure.⁶ The desired alcohols were characterized following purification by column chromatography on silica gel, and subsequent reduction with zinc dust (in excess) and glacial acetic acid (2 to 6 equivs) in methylene chloride at reflux provided the bromoolefins. The examples containing allylic and benzylic alcohols were reduced more rapidly, often with a slight initial exotherm, generally affording better yields. In all cases we noted that reduction slows and often

TABLE I	Carbonyl Compounds	Isolated Dibromoalcohols	Bromoalkenes	Reaction Time (hr)	Isolated yield ^a (E/Z Ratio)
1.		61%		18	68% (82:18) ^b
2.		68%		4	89% (55:45) ^c
3.		83%		12 ^d	62% (55:45)
4.		75%		10	76% (68:32)
5.		98%		0.3	95% (55:45)
6.		83%		6	75% (55:45)
7.		72%		4	93% (69:31)
8.		80%		0.5 ^e	75% (55:45)
9.		76%		0.5	90% (58:42) ^c

(a) *E/Z* ratios of purified bromoalkenes were determined by NMR integrations and glpc (glass column (6') packed with 15% OV-101 on chromosorb W resulted in elution of the *Z*-isomer followed by *E*-isomer in every case).

(b) *E* and *Z*-isomers were separated by preparative glpc for individual NMR characterization.

(c) *E* and *Z*-isomers were also separated by silica gel chromatography (Waters Prep-500A or thick tlc).

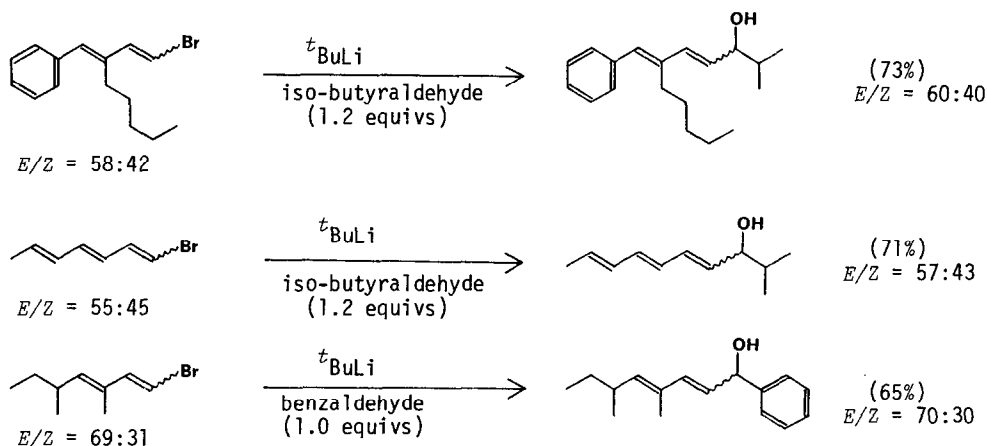
(d) Zinc in acetic acid at reflux.

(e) Reaction at 0°C.

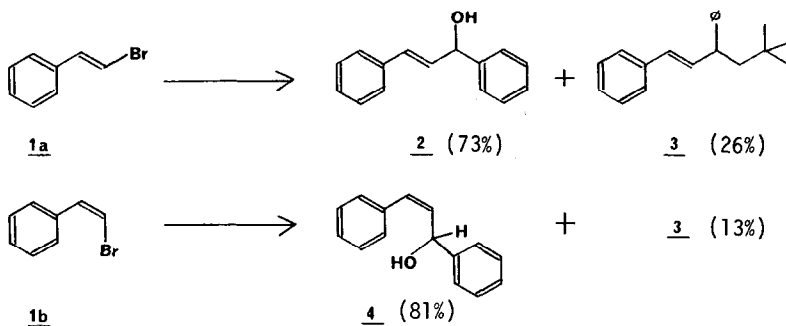
halts prior to complete consumption of the starting material. Additional amounts of zinc and acetic acid fail to provide further reaction. Workup and flash chromatography (silica gel) gave the pure 1-bromoalkenes (yields in Table I), and varying amounts of reisolated dibromoalcohols which can be cycled for a second reduction.

The trimethylsilyl ethers of some interesting 1,1-dibromo-2-hydroxyalkanes have been transformed to 1-bromoalkenes by metallation with *n*-butyllithium at -100°C ,⁷ however, similar treatment of alcohols without hydroxyl protection is reported to provide highly unstable lithium salts of 2-hydroxycarbenoids which readily rearrange to ketone enolates.⁸ Our results offer a direct non-basic alternative amenable to preparative scale.

In addition, we have examined the metallation of conjugated bromoolefins for application to synthetic problems underway in our laboratories using the *t*-butyllithium procedure as reported by Neumann and Seebach.⁹ The alkenyllithiums were generated using two equivalents of *t*-butyllithium¹⁰ at -120°C in a THF-pentane (1:1) solvent mixture under argon (1 hr). After complete consumption of vinylbromide, the reaction was warmed to -78°C and quenched by addition of aldehydes (20 mins). Some examples are illustrated below, and indicated the expected retention of olefin geometry.¹¹



A noteworthy side reaction was observed with the *E* and *Z*-bromostyrenes 1a and 1b which were individually submitted to halogen-lithium exchange (1:1/THF:pentane, -120°C , 1 hr) with *t*-butyllithium. Addition of benzaldehyde (-78°C) produced mainly the *E*-allylic alcohol 2 from 1a , and the *Z*-bromostyrene 1b gave the anticipated *Z*-allylic alcohol 3 (81%). However, both reactions produced the *E*-(*trans*)-alkene 3 (yields varied from 10-30%), which was formed at -120°C in the absence of benzaldehyde. This olefin appears to arise from generation of small quantities of styrene which adds *t*-butyllithium affording a benzylic anion followed by a second addition to the available bromostyrene and subsequent loss of bromide ion.¹² Indeed, when styrene (1 equiv) was added to the reaction mixture at -120°C the alkene 3 was obtained in 65% yield (based on starting bromoolefin).



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- The *tert*-butyllithium was purchased from Aldrich Chemical Company, Inc., and titrated prior to use.
- For these cases, the expected terminal olefins (protonation) were identified as the only additional products. In the first example, *E* and *Z*-bromides are separable and reactions cleanly yield a distinctive (*E/Z*) alcohol (by tlc and pmr) for each isomer. *E/Z* ratios of the purified alcohols were readily determined by NMR and glpc.
- All metallations were performed on 1 mmol scale under argon using flame-dried apparatus with dry, deoxygenated solvents and freshly chromatographed vinylbromides. The structure of alkene **3** was fully characterized by proton magnetic resonance (including decoupling experiments), carbon magnetic resonance data, mass spectral analysis, and ozonolysis which resulted in isolation of benzaldehyde and 2-phenyl-4,4-dimethylpentanal. Incorporation of deuterium was not observed in **3** after quenching experiments with D_2O (-78°C).

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