Stereospecific Preparation of Trisubstituted Allylic Alcohols by Alkene Transfer from Boron to Zinc

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Abstract: (Z)-Trialkenylboranes, ($R^{1}HC=CR^{2}$)3B, easily prepared by hydroboration of the corresponding alkynes with BMS in THF, rapidly react with commercially available diethylzinc in hydrocarbon solvents, in either a 1:3 or 2:3 ratio of organoborane to organozinc, to yield an equilibrium mixture, favoring the migration of alkenyl groups from boron to zinc. Addition of an aldehyde to the 2:3 reaction mixture, in the presence of 10 mol % N-methylpiperidine, results in the exclusive transfer of both alkenyl groups from zinc, furnishing diastereomerically pure trisubstituted double bonds in allylic alcohols in good to excellent yields.

Dialkenylzincs represent an essentially unexplored class of organometallic compounds. In light of the emerging importance of the addition of dialkylzincs to aldehydes under asymmetric catalysis,¹ a means of preparing more functionalized dialkylzincs, amongst them dialkenylzincs, would greatly enhance the utility of this reaction. Since *in-situ* generated dialkylzincs from ZnCl₂ and an organometallic reagent are incompatible with the reaction conditions,² a method of preparing salt-free functionalized dialkylzincs would be highly desirable. A particularly important functional group is the allylic alcohol moiety. This would be attainable by the addition of a dialkenylzinc to an aldehyde, if the appropriate dialkenylzinc reagents were available.³ In this communication we describe our efforts primarily in preparing stereochemically defined and hitherto unknown dialkenylzincs and their subsequent reaction with aldehydes.

Access to stereodefined dialkenylzincs by a transmetallation sequence from the products of hydrometallation of alkynes was sought. Of the various hydrometallation and carbometallation reactions of alkynes,⁴ leading to stereospecifically defined metallated alkenes, the best and most general is probably that of a borane with a suitable alkyne.⁵ Transfer of the alkenyl group from boron to zinc would then give the desired dialkenylzinc.⁶ To optimize the reaction we initially studied the equilibrium between diethylzinc or dimethylzinc and (Z)-tri-4-octenylborane in various ratios and solvents. Equilibration between (alkenyl)₃B and R₂Zn can give rise to several species (eq 1).

$$R^{1} \xrightarrow{R^{2}}_{3B} + R^{3}_{2}Zn \xrightarrow{R^{2}}_{X} (R^{1} \xrightarrow{R^{2}}_{X})_{X}ZnR^{3}_{2\cdot X} + (R^{1} \xrightarrow{R^{2}}_{X})_{X}BR^{3}_{3\cdot X} (1)$$

Fortunately, all the boron containing species absorbed differently in their ¹¹B-NMR spectra, thus enabling determination of the extent of alkenyl transfer from boron.⁷ In addition, alkaline hydrolysis followed by oxidation of the equilibrium mixture gave an alkene from zinc and a ketone from boron.⁸ In practice we found

R^2 R^1 R^2 R^3 R^3 R^3 R^3						
R ¹	R ²	он Aldehyde	Allylic Alcohol ^c	Configuration	Time, h	Yield ^d ,%
C ₂ H ₅	C ₂ H ₅	cyclohexanecarboxaldehyde	ai Children Children	Е	12	65
C ₂ H ₅	C ₂ H ₅	4-chlorobenzaldehyde	Э́росі он	E	12	70
n-C ₃ H ₇	<i>n</i> -C ₃ H ₇	benzaldehyde		E	12	92
n-C ₃ H ₇	n-C ₃ H ₇	2-thiophenecarboxaldehyde	он	Е	3	80
n-C3H7	<i>n</i> -C ₃ H ₇	2-furaldehyde		Ε	4	93
n-C3H7	n-C3H7	propionaldehyde	OH OH	Ε	12	65
n-C ₃ H7	n-C ₃ H ₇	hydrocinnamaldehyde	∩ OH Me _s Si , , , , , , , , , , , , , , , , , , ,	E	12	67
n-C4H9	SiMe ₃	benzaldehyde	₅сд [№]	Z	12	68

Table I. Reaction of *in-situ* Generated^a Dialkenylzincs with Various Aldehydes^b.

^aUsing a 2:3 ratio of trialkenylboranes to diethylzinc. ^bFor experimental conditions, see Reference 14.^c All assigned structures are consistent with their ¹H-NMR and mass spectra. ^dIsolated yield of products based on aldehyde after column chromatography on silica gel.

that a rapid equilibrium was established in hexanes. In the 2:3 ratio of boron to zinc, preferential formation of dialkenylzinc occurred, while in the 1:3 ratio the mixed alkenyl(alkyl)zinc species dominated.⁹ Equilibration in THF was very slow, requiring about 24 h, while in ethyl ether equilibration was attained after 7 h. The stereochemistry of the double bond attached to zinc could be readily determined by hydrolysis followed by analysis of the liberated alkene. In the case of di-(4-octenyl)zinc, hydrolysis yielded 4-octene in a *cis/trans* ratio of 98.5:1.5, the same ratio as obtained from solvolysis of (Z)-tri-4-octenylborane. Thus the migration of the alkenyl group from boron to zinc occurred with complete retention of the stereochemistry around the carbon-carbon double bond, leading to (E)-1-alkenylzinc species. The stability of the alkenylzinc species varied with the boron:zinc ratio and the steric requirements of the group attached to the α -carbon of the double bond. In general the alkenyl(alkyl)zinc species were more stable than the dialkenylzincs in solution, presumably due to the more facile intramolecular coupling of the latter. Solutions of either (E)-di-(4-octenyl)zinc or (E)-di-(3-hexenyl)zinc were stable in hexanes for 24 h at 0 °C. However, at 25° C coloration of the solutions occurred

with deposition of zinc.¹⁰ In the case of the trimethylsilyl derivative¹¹ decomposition occurred rapidly, even at 0 °C. In all cases, stability of the alkenylzincs could be greatly enhanced by adding THF after equilibrium was attained.

Since the migration of the alkenyl group from boron to zinc proceeded with complete retention of stereochemistry, the subsequent reaction of the alkenylzinc species with aldehydes was expected to provide access to stereospecifically defined trisubstituted allylic alcohols.¹² Molar solutions of (E)-tri-(4-octenyl)borane and either Me₂Zn or Et₂Zn were mixed in various stoichiometries and treated with benzaldehyde in the presence of 10 mol % N-methylpiperidine.¹³ Reactions were monitored either by TLC or GC and terminated at the appropriate time by quenching with saturated ammonium chloride solution. The crude reaction mixtures were then analyzed by ¹H-NMR. Two products could be detected (eq 2), that of transfer of the alkenyl group 1, or that of the alkyl group migration 2.



The best ratio of alkenyl vs alkyl group transfer was obtained with diethylzinc in a 2:3 ratio of boron to zinc. Under these conditions alkenyl transfer from boron to zinc proceeded to place both alkenyl groups on zinc with subsequent exclusive migration of the alkenyl group to aldehyde. A 1:3 ratio of Et₂Zn to borane resulted in no selectivity of transfer. With dimethylzinc, the best results were obtained in a 1:3 ratio of boron to zinc. whereas a 2:3 ration of that reagent led to a complex mixture from which no products could be isolated. Increasing the reaction temperature resulted in reduced selectivity. The use of ether was not advantageous, and only served to slow the reaction. Based on these results a standard set of condition was selected, namely hexanes as solvent, diethylzinc to borane ratio of 2:3 and a reaction temperature of 0 °C. The reaction was found to proceed well with a variety of aldehydes (Table I).14 In all cases pure trisubstituted allylic alcohols were isolated in good to excellent yields. In general aromatic aldehydes gave higher yields. 2-Furaldehyde and 2-thiophenecarboxaldehyde were especially reactive and the reactions were complete in 3 and 4 h respectively. The yields, especially for the aromatic aldehydes, indicate that both alkenyl groups transfer from zinc. This is different from dialkyl species where only one group transfers to aldehydes, but is similar to the reaction of diallylzinc with aldehydes in which both groups transfer. The extension to asymmetric synthesis by use of appropriate catalysts is currently being investigated, as are other interesting reactions of this relatively unexplored class of organometallic reagents.

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(7) The absorbances for the various species are: R₃B, 85 ppm; (alkenyl)BR₂, 76 ppm; (alkenyl)₂BR, 70 ppm; (alkenyl)₃B, 65 ppm, relative to BF₃ etherate.

(8) The zinc-carbon bond is readily hydrolysed while the boron-carbon bond is stable to hydrolysis. Oxidation, however, yields a ketone from the boron-carbon double bond. GC analysis of the alkene/ketone ratio corroborated the ¹¹B-NMR data for alkenyl transfer.

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(13) Tertiary amines greatly accelerate the reaction. The exact nature of the catalyst is unknown. Under the reaction conditions N-methylpiperidine does not coordinate with the liberated Et₃B. Srebnik, M. Unpublished results.

(14) The preparation of (E)-1-phenyl-2-propyl-2-hexen-1-ol is typical. A dry nitrogen- flushed 50 mL round bottom flask fitted with a side arm capped with a rubber septum, was charged with (Z)-tri-4- octenylborane, (2 mL, 1 M in hexanes), and cooled to $0 \, ^{\circ}$ C with stirring. To the stirred solution, diethylzinc, (3 mL, 1 M in hexanes), was added by syringe. The mixture was stirred for 5 min after which N-

methylpiperidine, $(35 \ \mu\text{L}, 5 \ \text{mol} \%)$ followed by benzaldehyde (0.51 mL, 5 mmol) were added. A deep yellow color formed which gradually lightened during the course of the reaction. After stirring 12 h the reaction was brought to room temperature and all volatiles were removed under reduced pressure. The viscous oil was treated with a saturated solution of ammonium chloride, extracted with ethyl ether, dried and, after removal of volatiles followed by chromatography on silica gel (ethyl ether:hexanes, 90:10) pure (E)-1-phenyl-2-propyl-2-hexen-1-ol was obtained. Yield: 1.0 g, 4.6 mmol, 92 % based on benzaldehyde.