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E- and Z-VINYLOXYBORANES (ALKENYL BORINATES): STEREOSELECTIVE FORMATION AND ALDOL CONDENSATION

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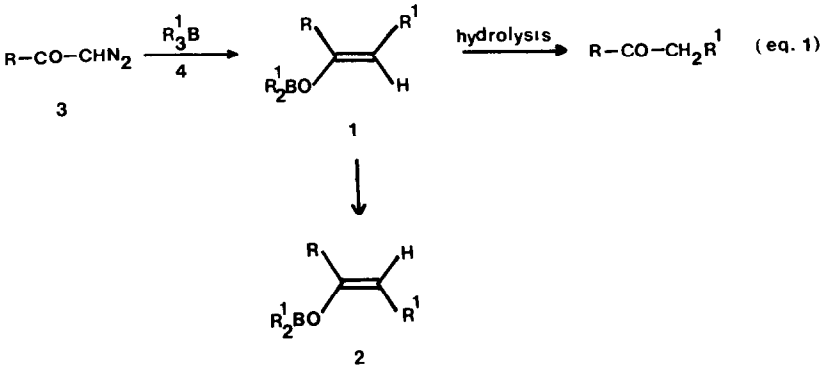
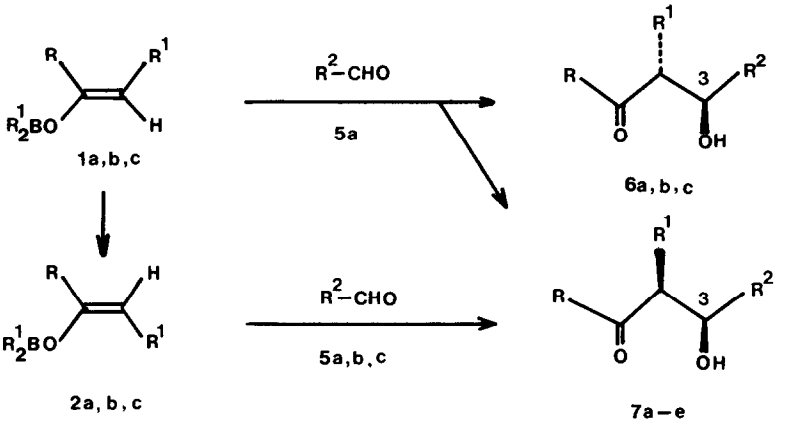
Vinyloxyboranes, intermediates of Hooz' reaction, are almost exclusively E-isomers which can be isomerized to the Z-isomers. Both isomers undergo stereoselective aldol condensations.

During our search for a general method that achieves a stereoselective aldol condensation,[1] some observations made earlier by Köster[2] suggested that the use of vinyloxyboranes (1, E-isomer; 2, Z-isomer) might provide a solution for this problem. We have closely examined several reported methods for the preparation of 1 and/or 2 and also the stereoselectivity of each isomer in the aldol reaction.[3] In this communication, we wish to describe two important observations: (1) that the vinyloxyboranes[4] which form as intermediates in Hooz' reaction (see equation 1)[5] are almost exclusively the E-isomers (1), and (2) that it is possible to isomerize 1 to the corresponding Z-isomers (2). With the stereo-defined vinyloxyboranes available, we are now able to clearly demonstrate that the Z-isomers (2) react with aldehydes to yield the erythro aldol product predominantly (≥ 95%)[6] and in excellent yields, whereas the E-isomers (1) react somewhat less stereoselectively (70-80%) but still provide good yields of the threo aldol product.



The preparation of 1a-c essentially follows the literature procedure.[5] Thus, after the dropwise (30 min) addition of a 1M solution of a diazoketone (3, 1 equiv) in THF to a 1M solution of tri-n-butylborane (4, 1 equiv) in the same solvent, the reaction mixture was stirred for 1 h at the temperature specified in Table 1 and then the solvent was removed (reduced pressure, room temperature) for NMR spectral measurements. The yields of 1a-c are near-quantitative and the spectral data are consistent with the vinyloxyborane structures (Table 1).



For 1a, b, c, R=CH_3, $C_6H_5CH_2$, C_6H_5, R^1=C_4H_9; for 2a, b, c, R=CH_3, $C_6H_5CH_2$, C_6H_5, R^1=C_4H_9; for 3a, b, c, R=CH_3, $C_6H_5CH_2$, C_6H_5; for 4, R=C_4H_9; for 5a, b, c, R^2=C_6H_5, C_2H_5, 2-C_3H_7; 6a, b, c, R=CH_3, $C_6H_5CH_2$, C_6H_5, R^1=C_4H_9, R^2=C_6H_5; for 7a, b, c, R=CH_3, $C_6H_5CH_2$, C_6H_5, R^1=C_4H_9, R^2=C_6H_5; for 7d, e, R=C_6H_5, R^1=C_4H_9, R^2=C_2H_5, 2-C_3H_7

Table 1. Reaction temperature for the preparation of and NMR spectra of 1a-c

	Reaction temp (°C)	^1H NMR spectrum[a]
1a	0	δ 0.7-1.6 (m, 25H), 1.65 (s, CH_3), 1.6-2.1 (m, 2H), 4.68 (tq, J=7.5 and ∿1.0 Hz, 1H)
1b	0	δ 0.7-1.7 (m, 25H) 1.8-2.3 (m, 2H), 3.30 (s, CH_2-C_6H_5), 4.70 (t, J=7.5 Hz, 1H), 7.1 (br s, C_6H_5)
1c	0	δ 0.8-1.7 (m, 25H), 1.9-2.5 (m, 2H), 5.10 (t, J=7.7 Hz, 1H), 7.0-7.6 (m, C_6H_5)

[a]One mmol of a sample in 0.15 ml of C_6D_6 was used for the measurement.

Several methods were investigated to effect the isomerization of 1a-c to 2a-c.[7] We found that when a catalytic amount of lithium phenoxide or pyridine was added to a solution of E-vinyloxyboranes 1a-c in benzene, smooth isomerization to the Z-isomers (2a-c) took place (Table 2). The stereochemical assignments of E to 1a-c and Z to 2a-c are based on the NMR spectral correlation proposed earlier for compounds of this type.[8]

A solution of each stereo-defined vinyloxyborane (0.5M, 1 equiv) and benzaldehyde (5a, 0.5M, 1.1 equiv) or other aldehydes in THF or toluene was allowed to stand at room temperature for 2 h, and subsequent hydrolysis of the resulting product with aqueous 30% H_2O_2 in methanol

provided the corresponding aldol. The stereochemistry assigned to each product is mainly based on the J value between the two protons attached to the chiral centers.[9] The results are summarized in Table 3.

Table 2. Reaction conditions for the conversion of 1 into 2 and NMR spectral data of 2a-c

	Reaction conditions	Yield of 2	^{1}H NMR Spectrum[a]
2a	$LiOC_6H_5$ (0.02 equiv) 16h, 22°	84	δ 0.7-1.6 (m, 25H), 1.71 (s, CH_3), 1.8-2.1 (m, 2H), 4.58 (br t, J=6.5 Hz, 1H)
2b	$LiOC_6H_5$ (0.02 equiv) 16h, 22°	81	δ 0.7-1.7 (m, 25H), 1.8-2.3 (m, 2H), 3.28 (s, 2H), 4.60 (t, J=7.0 Hz, 1H), 7.1 (br s, C_6H_5)
2c	Pyridine (0.50 equiv) 24h, 80° or $LiOC_6H_5$ (0.02 equiv) 8h, 50°	88	δ 0.8-1.7 (m, 25H), 1.9-2.5 (m, 2H), 5.40 (t, J=7.2 Hz, 1H), 7.0-7.6 (m, C_6H_5)

[a] One mmol of a sample in 0.15 ml of C_6D_6 was used for the measurement.

Table 3. Aldol condensation of 1 or 2

Reactant	Product[a]	erythro/threo ratio	combined[b] yield (%)
1a + 5a	6a and 7a	1:3	92
1b + 5a	6b and 7b	1:4	88
1c + 5a	6c and 7c	1:3	86
2a + 5a	7a	>20:1	90
2b + 5a	7b	>20:1	84
2c + 5a	7c	>20:1	85
2c + 5b	7d	>20:1	87
2c + 5c	7e	>20:1	86

[a] See footnote 10. [b] Yield is based on pure vinyloxyborane.

The above reaction sequence represents a net stereoselective conversion of a carboxylic acid (RCO_2H) into an erythro-aldol $R\text{-}CO\text{-}CHR^1\text{-}CH(OH)R^2$ and appears to be widely applicable to a variety of R, R^1, and R^2. In fact, several combinations of these parameters other than those in the Tables have been found to follow the general pattern, providing stereoselection in each step of the above sequence, although the complexity encountered in the NMR spectral analysis precluded definite stereochemical assignments to the products. A mixture of E- and Z-vinyloxyboranes produced by other methods such as the 1,4-addition of R_3B to vinylketones[2b],

and reactions of R_2BY with ketones[12] can now, in principle, be converted to the thermodynamically more stable Z-isomer in many cases, which renders the present methodology even more attractive. The mechanistic interpretation of the conversion 3 into 1 is only speculative at the present time.

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7. The isomerization of E- to Z-vinyloxyborane could also be readily effected with catalytic amounts (0.02 equiv) of lithium t-butoxide or even with water in some cases.

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9. Aldol products were reduced with $LiAlH_4$ to give a diastereoisomeric mixture of the diols. NMR spectra of the isopropylidine derivatives of the diols are also consistent with the assignments shown in Table 3.

10. NMR signals ($CDCl_3$) of C(3)-H of 6 or 7: 6a, δ 4.70 (d, J=8.7 Hz); 6b, δ 4.68 (d, J=7.4 Hz); 6c, δ 4.92 (d, J=7.5 Hz); 7a, δ 4.78 (d, J=6.8 Hz); 7b, δ 4.65 (d, J=6.5 Hz); 7c, δ 4.97 (d, J=5.5 Hz); 7d, δ 3.54 (ddd, J=4.7, 4.8, 8.2 Hz); 7e, δ 3.52 (dd, J=4.4, 6.5 Hz)

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