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DIASTEREOSELECTIVE ADDITION OF γ-METHOXY-ALLYLBORONATES TO ALDEHYDES

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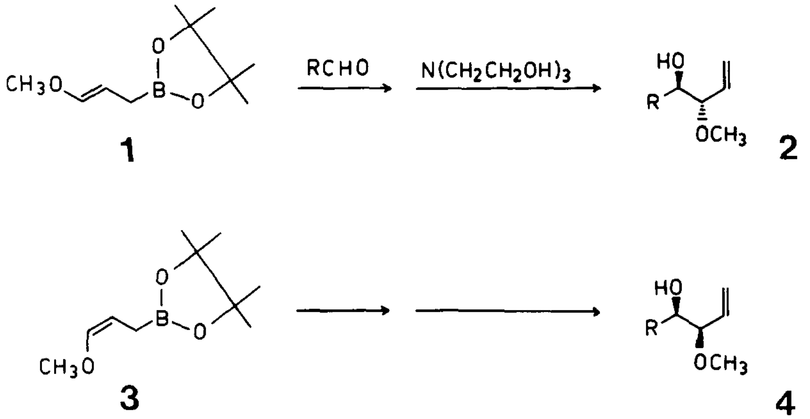
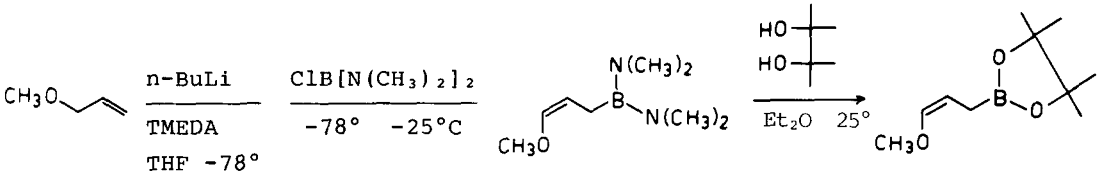
Summary: The E- and Z-γ-methoxy-allylboronates 1 and 3 add cleanly to aldehydes to give diastereoselectively the adducts 2 and 4.

The diastereoselective addition of E- and Z-γ-methoxy-allylboronates (1) and (3) to aldehydes forming methoxy-homoallylalcohols 2 and 4 could be of interest for the synthesis of highly oxygenated natural products such as carbohydrates or macrolide antibiotics. This reaction would supplement existing synthetic routes, which lead to vic-diol-derivatives by polar addition of α-oxygenated carb=anions [1,2] or enolates [3] to aldehydes. The question is, whether these established reactions are sufficiently diastereoselective, and also whether they could give access to either of the two expected diastereomers. So far high diastereoselectivity has been only occasionally observed in additions of alkoxy-allyl-metal compounds to aldehydes [2] depending on the metal or substituents used. Variable diastereoselectivity was recently reported for the addition of α-alkoxy enolate reagents to aldehydes [4]. We reasoned from the highly diastereoselective addition of crotyl- [5] and γ-alkylthio-allylboronates [6] to aldehydes, that γ-alkoxy-allylboronates should be ideal reagents for the



generation of either isomer of vic-diol-derivatives. Independent of our studies the reactions of the butyl and methyl Z-γ-methoxy-allylboronates similar to 3 with aldehydes to give 4 have been investigated by P.G.M. Wuts [7].

The Z-γ-methoxy-allylboronate 3 was obtained via Z-methoxy-allyl-lithium, generated by metalation of 3-methoxypropene with n-butyllithium/TMEDA instead of the more expensive s-butyllithium [2].



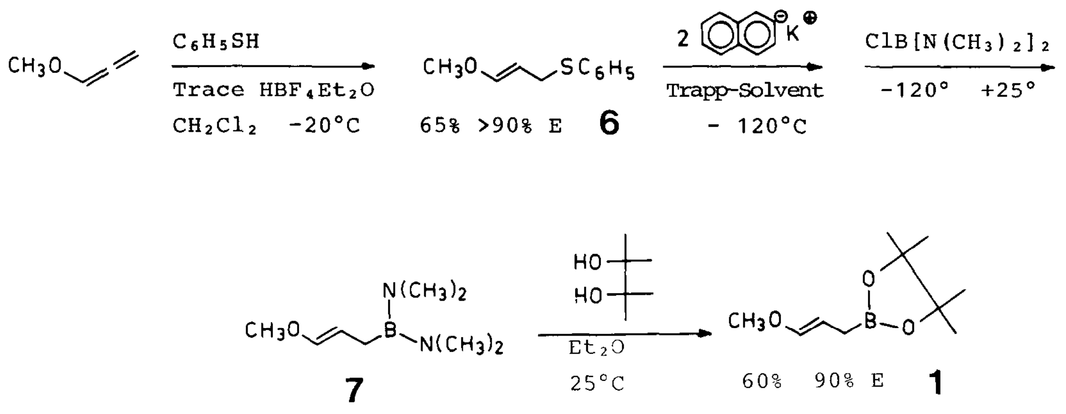
5 46 %

80% 3

It was advantageous to purify reagent 3 by filtration over a short plug of silica gel [8]. The addition of 3 (> 95% Z according to ^1H- and ^{13}C-NMR-spectra) to aldehydes proceeded during several days at 40 °C neat, or two weeks at reflux in pet. ether (40-60 °C). Apparently the pinacol boronates react more slowly than the corresponding butyl or methyl boronates [7], hence, for convenience a 30% molar excess of aldehyde was applied. After the usual workup with triethanolamine [5,6] the homoallylalcohols 4 [8] were obtained in good yield and good to excellent diastereoselectivity; see table. Since the relative configuration of 4 ($R = C_5H_{11}$) formed in a similar reaction has been rigorously established [7], and in view of the clearcut stereochemistry of other allylboronate additions [5,6,9], we have no doubts that the assigned relative configurations are correct, cf. table.

The corresponding reagent 1 with E-configuration required a different synthetic approach: By suitable choice of catalyst and temperature the highly exothermic addition of thiophenol to methoxyallene [10] could be conducted such that almost only pure E-6 resulted [8], although traces of the Z-isomer are noticeable in the ^{13}C- or ^1H-NMR-spectra.

Reduction of 6 by lithium naphthalenide, cf. [1b], followed by quenching with $ClB[N(CH_3)_2]_2$, led only to 5. Apparently the intermediate γ-methoxy-allyl-lithium is not configurationally stable and isomerizes (via the covalent allyl-lithium species?) to the more stable Z-isomer. This isomerization should be slower in the corresponding potassium compound [11]. Hence reduction of 6 with potassium-naphthalenide at low temperatures in the presence of $ClB[N(CH_3)_2]_2$ generated the diaminoborane 7 which alongside with naphthalene was separated



from the potassium thiophenoxide by vacuum transfer. This had to be done carefully, since after conversion of 7 into 1 traces of thiophenol cause rapid equilibration between 1 and 3. Crude 7 was converted into 1 [8)] which without separation from naphthalene was reacted with the aldehydes for three days at 25 °C in petrolether (40-60 °C). After workup with triethanolamine, naphthalene, the homoallylalcohols 2 [8)] and pinacol could easily be separated on silica gel by sequential elution with petroleumether and CH_2Cl_2. Again [6)] we benefited from the observation that the E-isomer 1 reacted more rapidly with aldehydes than the Z-isomer 3. Hence with 0.9 mol equiv. of the aldehydes the homoallylalcohols 2 formed, were essentially derived from the E-reagent 1, see table.

Entry	Allylboronate 1 : 3	Aldehyde	equiv.	Homoallylalcohols yield	2 : 4
1	89 : 11	C_6H_5CHO	0.9	87 %	95 : 5
2	89 : 11	CH_3CHO	0.9	76 %	95 : 5
3	89 : 11	CH_3CH_2CHO	0.9	68 %	95 : 5
4	89 : 11	$(CH_3)_2CHCHO$	0.9	77 %	>98 : <2
5	< 5 : >95	C_6H_5CHO	1.3	86 %	< 5 : >95
6	< 5 : >95	CH_3CHO	1.3	85 %	7 : 93
7	< 5 : >95	CH_3CH_2CHO	1.3	94 %	8 : 92
8	< 5 : >95	$(CH_3)_2CHCHO$	1.3	94 %	11 : 89

In summary we report that the E- and Z-γ-methoxy-allylboronates 1 and 3 are complementary reagents, each of which leads to a different diol-diastereomer upon reaction with an aldehyde.

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8) ^{1}H-NMR($CDCl_3$): 1:δ = 1.25 (s, 12H); 1.55 (broad d, 2H); 3.55 (s, 3H); 4.35 (dt, 1H); 5.85 (dt, J = 6.5 Hz, 1H); - 2:(R = C_6H_5): δ = 2.60 (broad s, 1H), 3.31 (s, 3H), 3.76 (m, 1H), 4.82 (d, J = 4.44 Hz, 1H), 5.14 - 5.28 (m, 2H), 5.59 - 5.68 (m, 1H), 7.33 (m, 5H); - 3: δ = 1.24 (s, 12H), 1.50 (broad d, 2H), 3.48 (s, 3H), 4.75 (dt, 1H), 6.26 (dt, J = 12.6 Hz, 1H); - 4 (R = C_6H_5): δ = 2.60 (broad s, 1H), 3.36 (s, 3H), 3.61 (m, 1H), 4.48 (d, J = 7.88 Hz, 1H), 5.03 - 5.18 (m, 2H), 5.47 - 5.56 (m, 1H), 7.33 (m, 5H); - 6: δ = 3.7 (s, 3H); 3.7 (d, 2H), 5.0 (dt, 1H), 6.6 (d, J = 13 Hz, 1H), 7.5 (m, 5H).
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