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Diastereoselectivity of allylboration of aromatic aldehydes with 1,6-bis(dipropylboryl)hexa-2,4-diene

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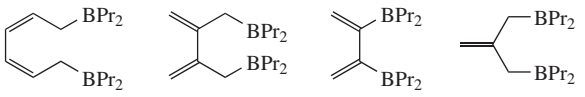
Allylboration of aromatic aldehydes with 1,6-bis(dipropylboryl)hexa-2,4-diene stereoselectively furnishes only two diastereomeric 1,4-diaryl-2,3-divinyl-1,4-diols with *threo*-configuration at C(2) and C(3).

Allylboration of organic compounds containing a double or triple bond with allylboranes and allylboronates[1] presents now a classical method for the formation of carbon–carbon bonds.[2] At the same time, reagents containing two 'allylic' boron atoms in one molecule such as compounds **1**–**4** have been less studied.



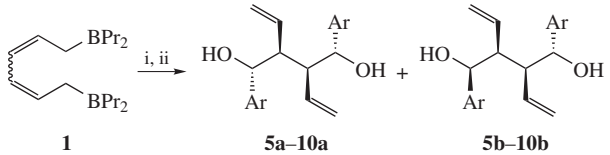
1 **2** **3** **4**

These derivatives are readily available *via* metallation–borylation of 1,5-hexadiene,[3] 2,3-dimethylbuta-1,3-diene,[4] methylidenecyclopropane[3] or isobutene,[5] respectively, and can serve as promising starting materials for the tandem allylation of carbonyl compounds.

Compound **1** exists as a 4:5 mixture of *E*,*E*- and *E*,*Z*-isomers, interconverting by sequential [1,3]-boron shifts.[3,6] Allylboration of ketones with **1** was previously demonstrated[6] to proceed with an excellent stereoselectivity to furnish the corresponding 2,3-divinyl-1,4-diols with *d*,*l*-configuration as a sole product. It was also mentioned[6] that the reaction of **1** with acetaldehyde after oxidation gave rise to a mixture of two diastereomeric diols, however, their relative configurations have not been established. Therefore, it was of interest to investigate in detail allylboration diastereoselectivity in the case of aldehydes, when four asymmetrical centres are formed.

Here, allylboration of aromatic aldehydes with 1,6-bis(dipropylboryl)hexa-2,4-diene **1**, as well as stereochemistry of the reaction and X-ray structure of derived diols are reported.

We employed the standardized protocol (–78 °C, diethyl ether) for allylboration of benzaldehydes containing electron-withdrawing or donating groups. Reactions of diallyldiborane **1** with benzaldehyde, 3,4-dimethoxy-, 4-methoxy-, 4-chloro-, 4-bromo-, and 3-nitrobenzaldehydes proceed readily at –78 to 20 °C, and after deboronation of initially formed borinates under oxidation (H_2O_2/OH^-) the corresponding 1,4-diaryl-2,3-divinyl-1,4-diols **5**–**10** were obtained in 69–87% overall yields† (Scheme 1, Table 1).



1 **5a–10a** **5b–10b**

Scheme 1 *Reagents and conditions*: i, ArCHO, 2.2 equiv., –78 °C to 20 °C; ii, H_2O_2, OH^-, 5 °C.

Table 1 Allylboration of ArCHO with compound **1**.

Entry	ArCHO	Products		
		Diol	**a**:**b** ratio[a]	Yield (%)[b]
1	PhCHO	**5**	37:63	69
2	4-$MeOC_6H_4CHO$	**6**	67:33	77
3	3,4-$(MeO)_2C_6H_3CHO$	**7**	85:15	79
4	4-ClC_6H_4CHO	**8**	44:56	87
5	4-BrC_6H_4CHO	**9**	42:58	82
6	3-$O_2NC_6H_4CHO$	**10**	27:73	71

[a]Isolated after chromatography. [b]Overall yield after chromatography in terms of borane.

According to ^{1}H NMR data the crude products in each case were the mixtures of only two isomers whose separation by column chromatography afforded pure diastereomers **5a**–**10a** and **5b**–**10b**.

In ^{1}H and ^{13}C NMR spectra of the **5a**–**10a**‡ isomers the only set of signals for both homoallylic fragments, indicating symmetrical structure of the molecules relative to C(2)–C(3) bond, is observed. According to well known regularities of aldehydes allylboration, (*E*)-2-butenyl boron compounds lead to *anti*-homoallylic alcohols[7] (*ca.* 70% of double bonds in a starting **1a** + **1b** have *E*-geometry); therefore, one could expect *d*,*l*-(*threo*)-configuration of C(2) and C(3), as it is observed in the reactions of **1** with ketones.[6] These data argue that relative configuration of stereogenic centres in 1,4-diaryl-2,3-divinyl-1,4-diols **5a**–**10a** is (1*R**,2*S**,3*S**,4*R**).

† *General procedure for the synthesis of compounds* **5**–**10**. To a cooled solution (–78 °C) of 1,6-bis(dipropylboryl)hexa-2,4-diene **1** (1 equiv.) in diethyl ether, a solution of aldehyde (2.2 equiv.) was added dropwise under argon. The temperature was slowly brought to 20 °C. Then the reaction mixture was cooled to 5 °C, consecutively treated by solution of NaOH (10%, 2.1 equiv.) and H_2O_2 (30%, 4.5 equiv.) and refluxed until complete deboronation (negative green-flame test of organic layer). The product was extracted with diethyl ether (3×20 ml). A combined organic layer was dried with Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The resulting crude product was purified by column chromatography on SiO_2 to give pure isomers **5a**–**10a** and **5b**–**10b**.

In ^{1}H and ^{13}C NMR spectra of isomers **5b**–**10b**, two non-equivalent homoallylic fragments are observed as two well-resolved sets of signals. One of two multiplets of H(2) and H(3) protons is low-field shifted (2.5–3.1 ppm) compared to corresponding δ value for H(2) in *anti*-homoallylic fragment (2.1–2.2 ppm), that indicates *syn*-stereochemistry of the second fragment and (1*R**,2*R**,3*R**,4*S**) relative configuration.[8] Complete assignment of signals in a molecule of **10b** was performed using 2D COSY, HSQC, qNOESY and HMBC spectra.[§]

Stereochemistry of compounds **8a**, **9a** and **6b** was ultimately proved by X-ray diffraction analysis (Figures 1–3, Table S1 in Online Supplementary Materials),[¶] which confirmed configuration (1*R**,2*S**,3*S**,4*R**) for **8a** and **9a** and (1*S**,2*S**,3*S**,4*R**) for **6b**. Note that in the case of **9a** two type of crystals were found (**9a** and **9a_2**, see Online Supplementary Materials); one of them crystallizes in the chiral space group *C*2 with four independent molecules. Since all of the independent molecules are characterized by the same configuration we may conclude that this particular solvate form of **9a** crystallizes as conglomerate, *i.e.*, mechanical mixture of opposite enantiomeric monocrystals.

The mutual disposition of vinyl groups in **8a**, **9a** and **6b** is almost the same [the torsion angle C(5)–C(2)–C(3)–C(7) varies in the range 44.7–59.7°] while conformation of C(1)–C(2)–C(3)–C(4) chain is changed from periplanar (torsion angle 23.8°) in **9a** to antiperiplanar in other crystals (torsion angle 154.5–172.1°). Depending on the substituent at the C(1) and C(4) atoms, molecules are assembled by H-bonds of moderate strength in different types of associates: chains in **9a** and **6b** and layers in **9a_2** and **8a**.

Formation of only two diastereomers containing four stereogenic centres can be explained in terms of rules of allylboration reactions with 2-butenylboranes.[7] Allylboration proceeds through a six-membered transition state, and two new C–C bonds are formed between carbonyl carbons and C-3, C-4 atoms of hexadiene system of **1**. Symmetrical **a**-isomers with two *anti*-homoallylic fragments are formally derived from *E*,*E*-**1a**, whereas

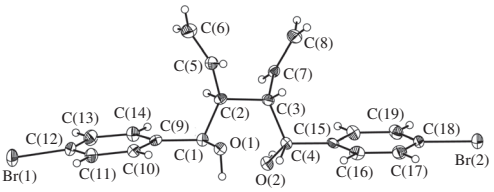


Figure 1 General view of molecule **9a** in representation of atoms by thermal ellipsoids (p = 50%).

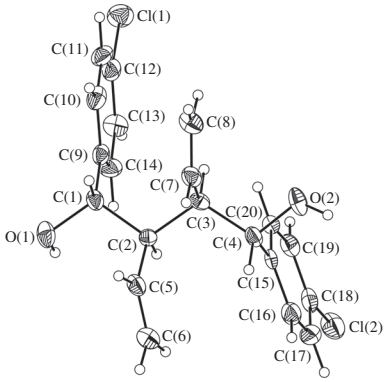


Figure 2 General view of molecule **8a** in representation of atoms by thermal ellipsoids (p = 50%).

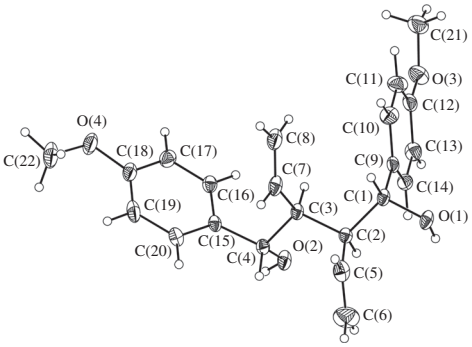


Figure 3 General view of molecule **6b** in representation of atoms by thermal ellipsoids (p = 50%).

b-isomers containing both *anti*- and *syn*-homoallylic fragments are formed from *E*,*Z*-**1b**. Relative configuration of C(2)–C(3) fragments in turn can be explained by the Felkin–Anh model for carbonyl addition because second allylboration proceeds between an aldehyde and borane with chiral centre at δ-carbon[9] (Scheme 2).

On the other hand, in almost all the cases diastereomeric ratio does not correspond to *E*,*E* and *E*,*Z* ratio in **1**. Thus, in case of aldehydes with electron-donating substituents in benzene ring (4-methoxy- or 3,4-dimethoxybenzaldehydes) the major product is formed predominantly from *E*,*E*-**1**. Obviously, diastereomeric ratio of products in the reaction discussed depends not only on the difference in the free energy of the transition state going to each product but also on the equilibrium constant of permanent allylic rearrangement (of **1** or allylborane formed after addition of one mole of aldehyde). Electron-deficient aldehydes (Table 1, entries 4–6) exhibited higher reactivity than electron-rich ones (Table 1, entries 2 and 3),[2(a),10] while *E*-butenylboranes are more reactive[11] and thermodynamically more stable than corresponding *Z*-isomers.[1,7]

In agreement with the above consideration, reaction of **1** with 3,4-dimethoxybenzaldehyde in a 1:1 molar ratio occurs diastereoselectively and after oxidation gives rise to a single diastereomer **7a** quantitatively in terms of aldehyde.

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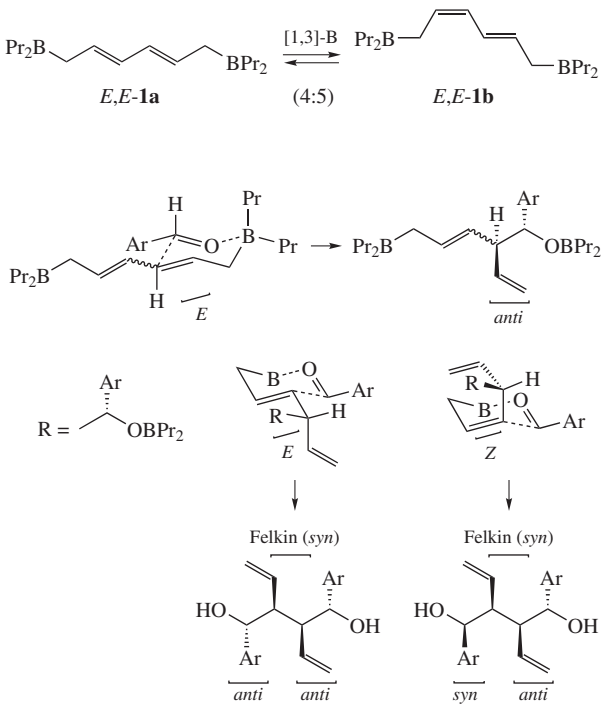
‡ For NMR data for all compounds, see Online Supplementary Materials. Representative NMR: *(1*R**,2*S**,3*S**,4*R**)-1,4-bis(3-nitrophenyl)-2,3-divinylbutane-1,4-diol* **10a**: yellow oil. ^{1}H NMR (200.13 MHz, $CDCl_3$) δ: 2.22 (dd, 2H, H-2, *J* 7.3, 7.3 Hz), 2.45 (s, 2H, OH), 4.72 (d, 2H, H-1, *J* 7.3 Hz), 5.16 (dd, 2H, H-6, *J* 15.6, 1.46 Hz), 5.41 (dd, 2H, H-6, *J* 10.4, 1.46 Hz), 5.97 (ddd, 2H, H-5, *J* 15.6, 10.4, 7.3 Hz), 7.47 and 8.09 (m, 4H, Ar). ^{13}C NMR ($CDCl_3$): 53.4 (C-2), 73.1 (C-1), 121.8 (C-6), 133.1 (C-5), 121.1, 122.9, 132.6, 133.8, 143.8, 148.1 (Ar). Found (%): C, 62.22; H, 5.05; N, 7.29. Calc. for $C_{20}H_{20}N_2O_2$ (%): C, 62.49; H, 5.24; N, 7.31.

§ *(1*R**,2*R**,3*R**,4*S**)-1,4-bis(3-nitrophenyl)-2,3-divinylbutane-1,4-diol* **10b**: yellow oil. ^{1}H–^{1}H COSY (600.13 MHz, $CDCl_3$) δ: 2.26 (ddd, 1H, H-3, *J* 10.8, 10.2, 9.0 Hz), 2.47 and 2.57 (both s, 1H, OH), 3.08 (ddd, 1H, H-2, *J* 10.2, 10.2, 7.8 Hz), 4.63 (d, 1H, H-8A, *J* 16.8 Hz), 4.67 (d, 1H, H-4, *J* 9.0 Hz), 4.77 (d, 1H, H-1, *J* 7.8 Hz), 5.02 (d, 1H, H-8B, *J* 10.8 Hz), 5.32 (d, 1H, H-6A, *J* 16.8 Hz), 5.43 (d, 1H, H-6B, *J* 10.2 Hz), 5.66 (ddd, 1H, H-7, *J* 16.8, 10.8, 10.8 Hz), 5.97 (ddd, 1H, H-5, *J* 16.8, 10.2, 10.2 Hz), 7.41 [t, 1H, H-5 (4-Ar), *J* 7.8 Hz], 7.47 [d, 1H, H-6 (4-Ar), *J* 7.8 Hz], 7.52 [t, 1H, H-5 (1-Ar), *J* 7.8 Hz], 7.67 [d, 1H, H-6 (4-Ar), *J* 7.2 Hz], 7.96 [s, 1H, H-2 (4-Ar)], 8.04 [d, 1H, H-4 (4-Ar), *J* 7.8 Hz], 8.14 [d, 1H, H-5 (1-Ar), *J* 7.8 Hz], 8.17 [s, 1H, H-2 (1-Ar)]. ^{13}C NMR ($CDCl_3$, 150.90 MHz) δ: 52.09 (C-2), 53.35 (C-3), 74.41 (C-1), 74.48 (C-4), 120.47 (C-8), 121.94 (C-6), 134.07 (C-5), 134.39 (C-7), 128.81 [C-5 (4-Ar)], 132.87 [C-6 (4-Ar)], 129.25 [C-5 (1-Ar)], 133.22 [C-6 (1-Ar)], 121.80 [C-2 (4-Ar)], 122.80 [C-2 (1-Ar)], 122.58 [C-4 (4-Ar)], 122.78 [C-4 (1-Ar)], 144.11 [C-1 (1-Ar)], 144.99 [C-1 (4-Ar)], 148.04 [C-3 (4-Ar)], 148.27 [C-3 (1-Ar)]. Found (%): C, 62.32; H, 5.09; N, 7.23. Calc. for $C_{20}H_{20}N_2O_2$ (%): C, 62.49; H, 5.24; N, 7.29.

¶ Details of crystal structure refinement and crystal data are summarized in Online Supplementary Materials.

CCDC 783976–783979 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2011.



Scheme 2

In summary, the data obtained show that reaction of aromatic aldehydes with sophisticated 1,6-bis(dipropylboryl)hexa-2,4-diene **1** displays excellent diastereoselectivity regarding to C(2)–C(3) relative configuration in 1,4-diaryl-2,3-divinyl-1,4-diols formed and moderate selectivity regarding to homoallylic fragments C(1)–C(2) and C(3)–C(4). The latter, however, is attributed to the dynamic nature of borane itself (interconversion of *E*,*E*- and *E*,*Z*-isomers) and electronic properties of aldehyde aryl substituent. The reaction outcome can be explained in terms of stereoresults inherent for simplest allylboranes.[7]

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2011.01.001.

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