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An original catalytic synthesis of boriran-1-ols

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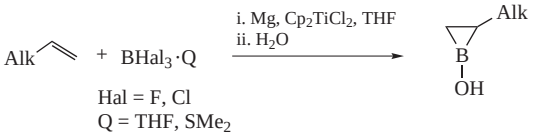
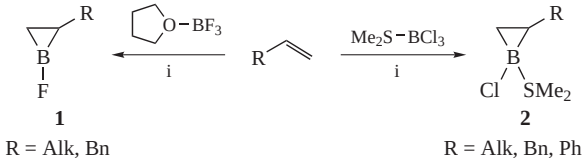
2-Alkylboriran-1-ols were obtained in a one-pot process by hydrolysis of 1-fluoro- and 1-chloroboriranes in 90–92% yield. The starting 1-haloboriranes were generated by cycloboration of α-olefins with $BCl_3·SMe_2$ or $BF_3·THF$ in the presence of Mg metal (acceptor of halogen ions) and Cp_2TiCl_2 catalyst.



Recently,[1] we have carried out direct catalytic cycloboration of α-olefins with molecular complexes of boron trihalides ($BF_3·THF$ and $BCl_3·SMe_2$) in the presence of Cp_2TiCl_2 catalyst. Under optimized reaction conditions (α-olefin : [B] : Mg = 1 : 2 : 4, 20 mol% Cp_2TiCl_2, THF, 20 °C, 14 h), the appropriate 1-fluoro- or 1-chloro-2-R-boriranes **1** and **2** were obtained (Scheme 1).

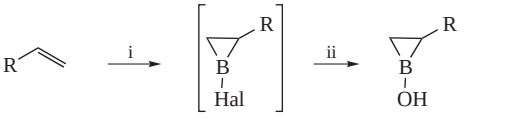


1 R = Alk, Bn

2 R = Alk, Bn, Ph

Scheme 1 *Reagents and conditions:* i, Mg, Cp_2TiCl_2 (20 mol%), THF, ~20 °C.

Considering that organoboron derivatives, in particular cyclic esters of boronic and borinic acids, are applied in clinical practice as anticancer, antiviral and antifungal drugs,[2] by analogy with the published results,[3] we attempted to perform the synthesis of previously undescribed boriran-1-ols from the above-mentioned 1-haloboriranes. The proposed idea lies in the possibility of obtaining diverse boriranes which can be in principle converted into the corresponding boriran-1-ols by the known method[3] excluding isolation of 1-haloboriranes from the reaction mixture. In this regard, we have synthesized 2-alkyl-1-fluoroboriranes **1a**,**b**, and 2-alkyl-1-chloroboriranes **2a**,**b**, which were hydrolyzed with H_2O without isolation from the reaction mixture (Scheme 2). As a result, boriran-1-ols **3a**,**b** have been isolated by vacuum distillation and identified by means of multinuclear ^{11}B, ^{19}F, ^{1}H and ^{13}C MNR spectroscopy.†



1a,**b** **2a**,**b**

3a R = *n*-C_6H_{13}, 90%

3b R = *n*-C_8H_{17}, 92%

1a Hal = F, R = *n*-C_6H_{13} **2a** Hal = Cl, R = *n*-C_6H_{13}

1b Hal = F, R = *n*-C_8H_{17} **2b** Hal = Cl, R = *n*-C_8H_{17}

Scheme 2 *Reagents and conditions:* i, $BF_3·THF$ (for **1a**,**b**) or $BCl_3·SMe_2$ (for **2a**,**b**), Mg, Cp_2TiCl_2 (20 mol%), THF, ~20 °C; ii, H_2O.

The absence of fluorine signals in ^{19}F NMR spectra confirms formation of boriranols **3a**,**b**, after completion of the hydrolysis of 1-fluoro-2-alkylboriranes **1a**,**b**, while the starting 1-fluoro-2-alkylborirans **1a**,**b** manifest singlets at δ_F –151.5 ppm.[1(a)] The signals of boron atoms for **3a**,**b** at δ_B ~32 ppm in ^{11}B NMR spectra were significantly shifted downfield as compared to the initial 1-fluoro-2-alkylboriranes **1a**,**b** (δ_B ~1 ppm[1(a)]). In the IR spectra of **3a**,**b**, absorption bands in the 3400 cm^{-1} region were observed thus indicating the presence of the OH group. The mass spectra of compounds **3a**,**b** contain the fragmentary ion peaks at *m*/*z* 112 [$C_8H_{18}O$ (octanol) – H_2O] for **3a** and 140 [$C_{10}H_{22}O$ (decanol) – H_2O] for **3b**, corresponding to the oxidation and hydrolysis products, arising from **3a**,**b** in the mass spectrometer.

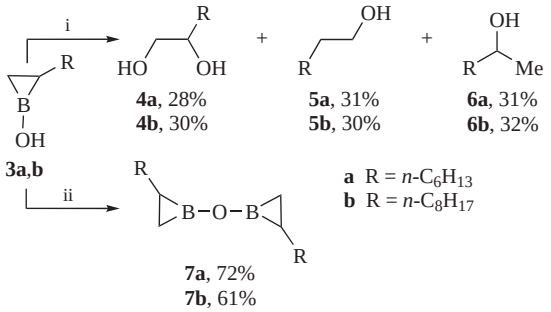
Similar results have been obtained from the reaction between water and 1-chloro-2-alkylboriranes **2a**,**b**. Based on the physicochemical characteristics and spectral data, the isolated compounds were identified as 2-alkylboriran-1-ols **3a**,**b**.

For additional confirmation of these structures, 2-alkylboriran-1-ols **3a**,**b** were oxidized with H_2O_2/NaOH in accordance with known techniques.[1,4] The corresponding alkanediols **4a**,**b** and

† *Synthesis of 2-alkylboriran-1-ols* **3a**,**b** (*general procedure*). Water (2 ml) was added to a solution of **1** or **2** borirane (10 mmol; for their synthesis see ref. 1) in THF (20 ml) and the mixture was stirred for 3 h. The organic layer was separated, the aqueous one was extracted with diethyl ether (2 × 10 ml), the extracts were combined with the organic phase. The solvent was evaporated and the residue was distilled under reduced pressure.

2-Hexylboriran-1-ol **3a**: isolated yield 1.26 g (90%), gray liquid, bp 90 °C (5 Torr). IR (film, ν/cm^{-1}): 3470, 2951, 2948, 2922, 2850, 1603, 1448, 1376, 1356, 1325, 1263, 1189, 1032, 893, 810, 766, 721, 670, 649. ^{1}H NMR, δ: 0.90 (t, 3H, Me, *J* 6.4 Hz), 1.20–1.65 (m, 8H, 4CH_2). ^{13}C NMR, δ: 14.06, 22.63, 29.24, 29.30, 31.80. ^{11}B NMR, δ: 32.14. In the ^{1}H and ^{13}C spectra signals of protons and carbon atoms directly attached to the boron atom [B–C^2H, C^3H_2 (cycle)] and C^4H_2 were not detected.

2-Octylboriran-1-ol **3b**: isolated yield 1.55 g (92%), gray liquid, bp 115 °C (5 Torr). IR (film, ν/cm^{-1}): 3466, 2956, 2924, 2854, 1717, 1619, 1467, 1376, 1321, 1260, 1217, 1032, 893, 804, 760, 720, 668. ^{1}H NMR, δ: 0.90 (t, 3H, Me, *J* 6.8 Hz), 1.20–1.50 (m, 12H, 6CH_2). ^{13}C NMR, δ: 14.10, 22.68, 29.35, 29.42, 29.61, 29.65, 31.90. ^{11}B NMR, δ: 32.12. In the ^{1}H and ^{13}C spectra signals of protons and carbon atoms directly attached to the boron atom [C^2H, C^3H_2 (cycle)] and C^4H_2 were not detected.



Scheme 3 *Reagents and conditions:* i, H_2O_2, OH^-, 0 °C; ii, $MgSO_4$, ~20 °C, neat, 24 h.

alkanols **5a**,**b** and **6a**,**b** have been obtained in 82–85% total yield (Scheme 3), their spectra were close to the published ones.[5]

We have found that boriranols **3a**,**b** at room temperature are partially converted into the corresponding diboroxanes **7a**,**b** (see Scheme 3). While storing compounds **3a**,**b** in the presence of anhydrous $MgSO_4$ for 24 h, almost complete transformation into anhydrides **7a**,**b** occurs.‡ In the ^{11}B NMR spectra of the latter, the signals of boron atom at ~18 ppm are shifted upfield compared to the parent boriranols **3a**,**b** (δ_B ~32 ppm). Molecular weight of dibroxanes **7a**,**b** was evaluated by the cryoscopy method[6] since they are easily destroyed under the conditions of the mass spectrometric analysis.

In summary, we have elaborated a new one-pot synthesis of previously undescribed 2-alkylboriran-1-ols in 90–92% yield. The method is based on the use of the catalytic cycloboration reaction of α-olefins[1] with complexes of boron trihalides (BF_3·THF and BCl_3·SMe_2) in the presence of metallic Mg (halogen ion acceptor) and Cp_2TiCl_2 catalyst leading to 1-fluoro- and 1-chloroboriranes, which are further subjected to hydrolysis.

We believe that the developed approach has a great synthetic potential for the production of diverse boriran-1-ols, which can serve as precursors in the creation of modern selective medicines.

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‡ *Diboroxanes* **7a**,**b**. A solution of boriranol **3a**,**b** (0.5 mmol) in $CDCl_3$ (0.5 ml) was treated with anhydrous $MgSO_4$ (50 mg) for 24 h. Yields of compounds **7a**,**b** were determined from the integrated intensity of the signals of boron atoms in the ^{11}B NMR spectrum.

1,1'-Oxybis(2-hexylborirane) **7a**. Yield 72%. ^1H NMR, δ: 0.90 (t, 6H, 2Me, *J* 6.2 Hz), 1.21–1.50 (m, 16H, 8CH_2). ^{13}C NMR, δ: 14.07, 22.63, 29.24, 29.31, 31.80. ^{11}B NMR, δ: 18.62. In the ^1H and ^{13}C spectra signals of protons and carbon atoms directly attached to the boron atom [C^2H, $C^{2'}H$, C^3H_2, $C^{3'}H_2$ (cycle)] and C^4H_2, $C^{4'}H_2$ were not detected.

1,1'-Oxybis(2-octylborirane) **7b**. Yield 61%. ^1H NMR, δ: 0.89 (t, 6H, 2Me, *J* 6.8 Hz), 1.20–1.50 (m, 24H, 12CH_2). ^{13}C NMR, δ: 14.09, 22.67, 29.34, 29.49, 29.61, 29.64, 31.91. ^{11}B NMR, δ: 18.34. In the ^1H and ^{13}C spectra signals of protons and carbon atoms directly attached to the boron atom [C^2H, $C^{2'}H$, C^3H_2, $C^{3'}H_2$ (cycle)] and C^4H_2, $C^{4'}H_2$ were not detected.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2018.11.003.

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