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# The bora-ene reaction of sulfur dioxide and prop-2-ene-1-boronic esters. New route to sulfoxides

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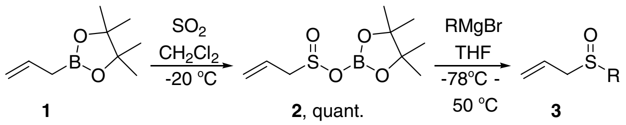
**Abstract**—A new one-pot synthesis of sulfoxides is presented. It involves the bora-ene reaction of sulfur dioxide and prop-2-ene-1-boronic esters, giving mixed anhydrides of sulfinic and boric acids. The latter react chemoselectively at the sulfur center with Grignard reagents in displacement reactions giving the corresponding prop-2-en-1-ylsulfoxides. Preliminary studies on the chirality transfer of enantiomerically enriched boronates to the sulfoxides are also presented.

Metallo-ene and H-ene reactions of Group 14 allylmetals have been studied extensively.[1,2] With sulfur dioxide as enophile, metallo-ene reactions have been reported for allyltrialkyltin compounds[1b] and allylgermanes.[3] We have reported the sila-ene reactions of allylsilanes and enoxysilanes.[4,5] The silyl prop-2-ene-1-sulfinates so-obtained can be converted in one-pot operations into polyfunctional sulfones, sulfonamides, and sulfonic esters.[4b] Although alk-2-ene-1-boronic esters are common synthetic intermediates,[6] their ene-reactions with $SO_2$ have never been reported.[7] We show here that alk-2-ene-1-boronic esters react readily with $SO_2$ generating mixed anhydride intermediates that can be reacted in situ with Grignard reagents giving the corresponding allylsulfoxides.

Preliminary studies with enantiomerically enriched boronates suggest that enantiomerically enriched allylsulfoxides might be obtained by this one-pot procedure. Sulfoxides are well recognized synthetic intermediates.[8] Others are bioactive compounds (e.g.: omeprazole and its ($S_s$)-enantiomer esomeprazole[9]) or natural products (e.g.: allium plants like garlic and onions[10]). Among the well studied applications of sulfoxides, one can mention the Mislow–Evans rearrangement,[11] their use as chiral auxiliaries,[12] and as intermediates in the synthesis of polypropionates.[13] Typical methods for the preparation of enantiomerically enriched sulfoxides use either asymmetric oxidation of nonsymmetrical sulfides,[14] or nucleophilic displacement of polar organometallic reagents to enantiomerically pure sulfinic esters.[15]

When triallylborane was exposed to sulfur dioxide at −80 °C, a very fast reaction was observed (NMR). Attempts to isolate the products of the reaction failed as quick decomposition occurred at room temperature. In contrast, a smooth reaction was observed when prop-2-ene-1-boronate **1** was treated with liquid $SO_2$ in $CH_2Cl_2$ at −20 °C (Scheme 1).

The intermediate 2-((allylsulfinyl)oxy)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2**) was not isolated, but characterized by its $^1H$ NMR and $^{13}C$ NMR spectra.[16] Low temperature evaporation of $SO_2$ and $CH_2Cl_2$ (−20 °C) gave an oil that was reacted directly with Grignard reagents in THF (Table 1) giving the corresponding allylsulfoxides **3** in moderate to good yields. The latter were fully characterized by their spectral data and by comparison with literature data.



**Scheme 1.** One-pot synthesis of allylsulfoxides derived from prop-2-ene-1-boronate of pinacol.

*Keywords*: Allylsulfoxide; Boronic ester; Chirality transfer; Ene-reaction; Grignard reagents.

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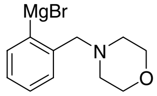
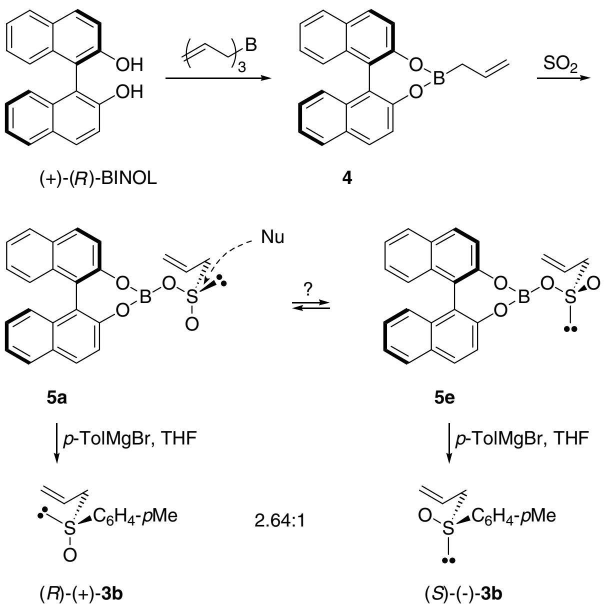
**Table 1.** Synthesis of allylsulfoxides **3** from allylboronate **1**

| Entry | RMgBr | Product (yield of isolated **3**)[b] |
|---|---|---|
| 1 | PhMgBr | **3a**[17] (62%) |
| 2 | 4-$MeC_6H_4MgBr$ | **3b**[11a](61%) |
| 3 | 3-$MeC_6H_4MgBr$ | **3c**[18] (48%) (60%)[a] |
| 4 | 1-NaphthylMgBr | **3d**[19] (50%) |
| 5 | 2,4,6-(*i*-Pr)$_3C_6H_2MgBr$ | **3e**[20] (36%) |
| 6 | BnMgCl | **3f**[21] (38%) (48%)[a] |
| 7 |  | **3g**[22] (46%) |

[a] In the presence of 20 mol % of $(CF_3SO_2)_2NSiMe_3$.
[b] All compounds gave expected elemental analyses.

When alkyllithium, organozinc, or organocopper were engaged instead of the Grignard reagents, sluggish reactions were observed and the corresponding allylsulfoxides were not formed. It is noteworthy that the Grignard reagents prefer the sulfur electrophilic center rather than the boron center, in most cases. Attempts to catalyze the nucleophilic displacements with Lewis acids such as $LiClO_4$ or $Me_2AlCl$ did not improve the yields of the reactions. In contrast, addition of 20% $(CF_3SO_2)_2NSiMe_3$ slightly accelerated nucleophilic displacements and gave 10–15% higher yield of expected sulfoxides **3c** and **3f**.

We then explored the possibility of a chirality transfer between enantiomerically enriched allylboronates to the corresponding allylsulfoxides. For that were reacted the enantiomerically pure allylboronate **4**, derived from triallylborane[23] and (*R*)-(+)-BINOL (Scheme 2),[24] with sulfur dioxide. In pure $SO_2$, the bora-ene reaction of **4** occurred rapidly already at −50 °C. After evaporation of the excess of $SO_2$, the crude mixed anhydride **5** was not isolated but reacted directly with *p*-tolylmagnesium bromide in THF solution at 20 °C. After purification by column chromatography on silica gel, a 21–60% yield of the known allylsulfoxide (+)-**3b**[11a] was obtained. In the presence of $Eu(hfc)_3$, the $^1H$ NMR spectrum of (+)-**3b** showed an enantiomeric excess of 45% corresponding to a 2.64:1 mixture of **5a** and **5e** that would have reacted with complete inversion of configuration of the sulfur center[25] by displacement with the Grignard reagent.



**Scheme 2.** Incomplete chiral transfer from allylboronate to the allylsulfoxide.

The origin of the chirality transfer from **4** to **3b** deserves further studies that will be reported in due course. For the moment it raises several questions such as: what is the diastereoselectivity of the bora-ene reaction of $SO_2$? There are two possible modes of attack of $SO_2$ onto allylboranate **4** depending on whether the 'spectator' S=O bond of $SO_2$ that is not engaged in the boron transfer sits in a pseudo-axial or pseudo-equatorial position in the transition state.

The degree of chirality transfer depends on the proportion of **5a** and **5e** formed under conditions of kinetic control and upon the rate constant ratio of the nucleophilic displacements of **5a** and **5e** by the Grignard reagents. One assumes that these displacements occur with complete inversion at the sulfur center as found in related cases.[25] The degree of chirality transfer will depend upon the configurational stability of the mixed anhydrides **5a** and **5e**. We cannot exclude an allylic rearrangement with inversion at the sulfur centers of **5a** and **5e** that would equilibrate these two diastereomers ([1*i*,3*s*]-sigmatropic shift[26]). If such equilibrium should be fast compared with the reaction with the Grignard reagents, it would lead to a lower degree of chirality transfer, or to an increase of it, should one find chiral auxiliaries different from BINOL and leading to a relatively large free energy difference between **5a** and **5e**.

In order to gain more information about the diastereoselectivity of the bora-ene reaction of $SO_2$ we prepared the boronate **6**[27] from (+)-α-pinene (Scheme 3) and let it react with an excess of $SO_2$ in $CH_2Cl_2$ at −78 °C for 0.5 h, and then at −35 °C for 1.5 h. After evaporation of the excess of $SO_2$ and the solvent, the 2.3:1 mixture of mixed anhydride **7** and **8** ($^1H$ NMR) was dissolved in THF and reacted with *p*-tolylMgBr at −78 °C for 1 h, then at −50 °C for 3 h. Work-up with aqueous $NH_4Cl$ and extraction with ether gave a 3.2:1 mixture (30–50% yield) of sulfoxides (−)-**9** and **10** that could be separated by column chromatography on silica gel. Pure (−)-**9** was obtained by recrystallization from $EtOH/H_2O$. The relative *endo* configuration of the sulfoxide moiety of (−)-**9**[28] and **10**[29] was proven by their 2D-NOESY $^1H$ NMR spectra that showed the expected cross-peaks for the signals of protons H–C(3)/*syn*-Me–C(6) and Ha–C(4)/*syn*-Me–C(6), and by the vicinal coupling constants $^3J$(H(3)–Ha(4)) (9.0 Hz for **10**). The absolute configuration of (−)-**9** was proven unambiguously by X-ray diffraction studies[30] (Fig. 1).

These results can be interpreted in terms of a preferred *exo*-face attack of **6** with the 'spectator' S=O bond of