On the relative migratory aptitudes of carbon and heteroatoms in borate complexes. A surprising α-thia effect

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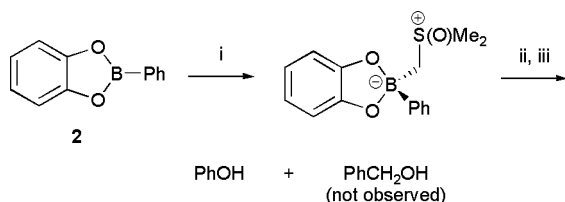
Dimethylsulfoxonium methylide reacts with dicyclohexyl(α-thiophenylmethyl)methylborane *via* 1,2-alkyl migration and alkyldithiaborolane *via* 1,2-sulfur migration.

Organoborane chemistry has played an important role in the construction of carbon–carbon bonds.[1,2] Many of these reactions involve formation of a tetrahedral "ate" complex followed by transfer of a carbon nucleophile to an acceptor. The transfer can be intermolecular, such as in the Suzuki reaction,[3,4] or intramolecular.[5,6] Examples of the latter include reactions of trialkylboranes with nucleophilic reagents such as ethyl bromoacetate,[7] α-chloroacetonitrile,[8] α-bromo ketones,[9] dihalomethyl lithium,[10] dimethylsulfoxonium methylide,[11] and various diazo compounds.[12] These reactions result in formation of new carbon–carbon bonds and several have achieved considerable synthetic importance. The atom-economy of these reactions may be increased by utilizing ligands on boron that allow the transfer of only a single carbon nucleophile. For example, *B*-alkyl 9-BBN, alkylboronate esters, and thexyldialkylboranes have been used to allow selective transfer of the alkyl substituent.[3]

Recently, trialkylboranes have been found to react with dimethylsulfoxonium methylide (**1**)[13] resulting in multiple insertions of methylene into the carbon–boron bond. Attempts at using oxygen ligands as blocking groups for homologation of alkyl boronic esters with ylide **1** were unsuccessful. For example, phenyl catechol boronate ester (**2**) was reacted with 1 equiv. of ylide **1** in toluene at 23 °C (Scheme 1) to form a borate complex (^{11}B NMR 9.6 ppm, toluene). Heating this complex in THF at 40 °C for 30 min followed by oxidation with H_2O_2 and NaOH produced only phenol. Benzyl alcohol, a product that would arise from homologation, was not observed. One possible explanation for the failure to observe phenyl migration is that the electron-deficient oxygen atoms remove electron density from the phenyl–boron σ bond, rendering it non-nucleophilic toward 1,2-migration. Sulfur has an electronegativity very similar to carbon and we surmised that ylide **1** complexes of alkyldithiaborolanes would allow sufficient electron density to reside at the remaining alkyl group to promote 1,2-migration (Fig. 1).
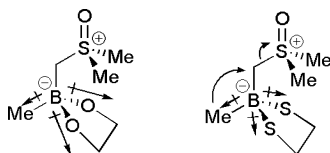
To test this hexyldithiaborolane (**3**),[14] dicyclohexylpentanethiaborane (**4**) and dicyclohexylethanethiaborane (**5**) were synthesized (Scheme 2).

Thiaborane **4** was reacted with ylide **1** (1 equiv.) in Et_2O at 0 °C for 1 h (Scheme 3) and oxidized with trimethylamine-*N*-oxide dihydrate (TAO·2H_2O). The crude reaction mixture was analyzed by GCMS and found to contain cyclohexanol (**6**) and methyl pentyl sulfide (**7**). Cyclohexylmethanol, which would arise from 1,2-migration of the cyclohexyl group, was not observed. Methyl pentyl sulfide (**7**) arises from *S*-1,2-migration followed by hydrolysis with water[14] introduced by the oxidizing reagent. This result indicates that sulfur migrates in preference to carbon (2°) in the intermediate "ate" complex. This result is consistent with previous findings.[15]
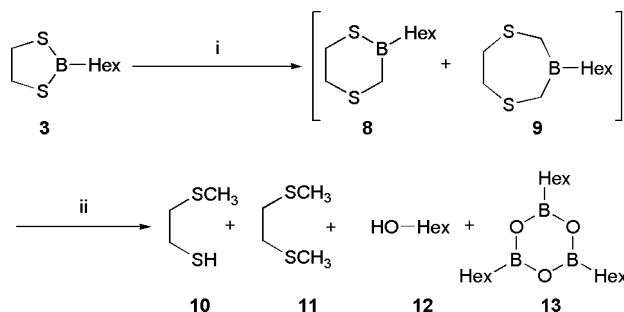
This finding was further supported by the following observation. Hexyldithiaborolane (**3**) was reacted with ylide **1** (1 equiv.) and oxidized with TAO·2H_2O (3 equiv.). The crude reaction was analyzed by GCMS and the relative, uncorrected areas for the products were monohomologated **10** (5.5%), bishomologated **11** (2.9%), hexanol (**12**) (77%), and hexylboroxine (**13**) (9.4%) (Scheme 4). Products **10** and **11** are derived from the hydrolysis of intermediate organoboranes **8** and **9**, which arise from one and two *S*-1,2-migrations. Hexylboroxine (**13**) arises from the condensation of hexylboronic acid, an unoxidized borane that is derived from hydrolysis of unreacted starting material or **8** or **9**. Heptanol, the product from 1,2-hexyl migration, was not detected. The exclusive
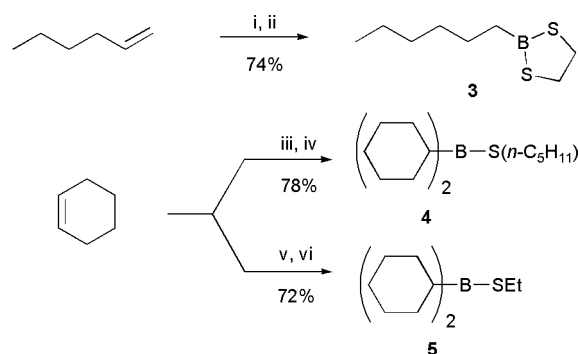
Scheme 2 *Reagents and conditions*: i, $Br_2BH·SMe_2$, CH_2Cl_2, 0–24 °C, 2 h; ii, $LiSCH_2CH_2SLi$, 0–24 °C, 18 h; iii, $BrBH_2·SMe_2$, THF, 0–23 °C, 2 h; iv, PenSH, 0–23 °C, 12 h; v, $BH_3·SMe_2$, THF, 0 °C, 15 min; vi, EtSH, 23 °C, 17 h.
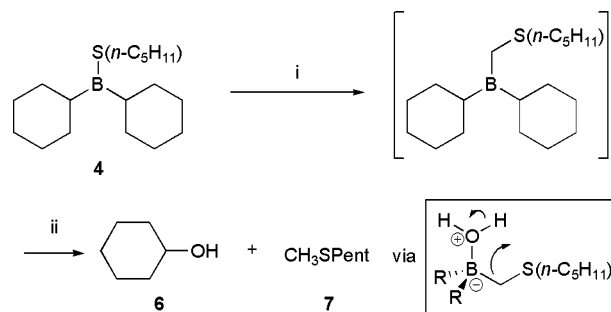
Scheme 3 *Reagents and conditions*: i, ylide **1** (1 equiv.), Et_2O, 0–25 °C, 1 h; ii, TAO·2H_2O (6 equiv.), 25 °C, 12 h.

PhOH   +   PhCH₂OH
(not observed)

Scheme 1 *Reagents and conditions*: i, ylide **1**, toluene, 23 °C; ii, 40 °C, 30 min, THF; iii, H_2O_2, NaOH, 23 °C, 2 h.

Fig. 1

Scheme 4 *Reagents and conditions*: i, ylide **1** (1 equiv.), toluene, 0–24 °C, 30 min; ii, TAO·2H$_2$O (3 equiv.), 60 °C, 2 h.

formation of products from 1,2-*S*-migration and the failure to detect 1-heptanol demonstrate that the migratory aptitude of sulfur is greater than carbon. In neither case were multiple methylene insertions in the same chain observed.

The reaction of thiaborane **5** and dithiaborolane **3** with an excess of ylide **1** was studied in order to determine the relative migratory aptitudes of alkyl *vs.* α-thiomethylene ligands. For example, thiaborane **5** was added to ylide **1** (10 equiv.) at 60 °C, then oxidized with basic hydrogen peroxide. The products, which were purified by chromatography and analyzed by GCMS, consisted of a distribution of cyclohexyl-terminated alcohols with an experimental degree of polymerization, DP_{exp} = 5.1, and polydispersity, PDI = 1.02 (Fig. 2). Similarly, hexyldithiaborolane **3** was added to ylide **1** (8.7 equiv.) at 50 °C and oxidized with basic hydrogen peroxide. Following chromatographic purification, the GCMS revealed a distribution of straight-chain alcohols (DP_{exp} = 5.2, PDI = 1.03).

These results establish that upon reaction of ylide **1** with thia- and dithiaborolanes, *S*-1,2-migration is preferred over alkyl migration. Additional equivalents of ylide **1** coordinate and react by *C*-1,2-migration to afford cyclohexyl- and *n*-hexyl-terminated alcohols. Thus the α-thio ligand serves as a blocking group for 1,2-migration (Fig. 3).

B3LYP calculations for the Me$_2$BCH$_2$SMe·ylide complex (Fig. 3) support this hypothesis. The two possible transition state
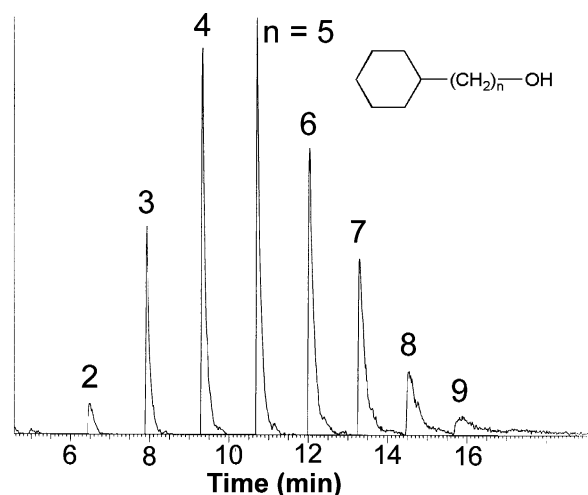

Fig. 2 GC of α-cyclohexyl-ω-hydroxypolymethylene formed from thiaborane **5** and ylide **1** (10 equiv.) at 60 °C in toluene.
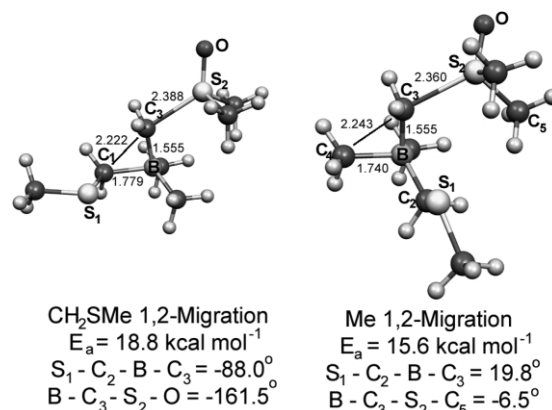

CH$_2$SMe 1,2-Migration
E_a = 18.8 kcal mol^{-1}
S$_1$ - C$_2$ - B - C$_3$ = -88.0°
B - C$_3$ - S$_2$ - O = -161.5°

Me 1,2-Migration
E_a = 15.6 kcal mol^{-1}
S$_1$ - C$_2$ - B - C$_3$ = 19.8°
B - C$_3$ - S$_2$ - C$_5$ = -6.5°

Fig. 3 B3LYP transition-state structures for Me$_2$BCH$_2$SMe·ylide complex. Distances are in Å.

structures were found for methyl 1,2-migration (E_a = 15.6 kcal mol^{-1}) and CH$_2$SMe 1,2-migration (E_a = 18.8 kcal mol^{-1}). The lower activation energy for 1,2-methyl migration is in agreement with the experimental results for preferential cyclohexyl and *n*-alkyl 1,2-migration of thiaboranes **3** and **5** compared with CH$_2$SEt 1,2-migration.

Oxygen has been used as a ligand on boron to affect the selective transfer of alkyl or aryl groups in carbon–carbon bond forming reactions. Sulfur ligands have not enjoyed the same benefit, perhaps due to their preferential migration over alkyl groups, as demonstrated by this work. The discovery that α-thia methylene ligands can serve as blocking groups in the reaction of boranes with ylides is novel. It is envisioned that α-thia methylene ligands may be utilized for a broad range of other boron-mediated carbon–carbon bond forming reactions.

Notes and references

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