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Generation and alkylation of 2-boryl allylic sulfone anions[†]

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The deprotonation and electrophilic trapping of an allylic sulfone substituted at the 2 position by a pinacol boronate results in the formation of the corresponding alkylation products. The ability of the boronate ester to tolerate the sulfonyl carbanion suggests a broader application of the methodology to prepare a wide range of functionalized boronates.

The ability to form carbon–carbon bonds between the organoboron species and electrophilic partners has made Suzuki– Miyaura (SM) cross-coupling reaction a powerful methodology used throughout organic synthesis.¹ This has resulted in an explosion of syntheses utilizing the method, a wide availability of boronic acids and their derivatives, and continuing interest in the development of new routes to organoboron compounds.

Polyfunctional organoboron compounds offer unique opportunities for making value-added structures containing boron. This is especially important if the starting materials for such chemistry are inexpensive and the subsequent chemistry relatively simple. Recently, for example, Walsh has demonstrated the utility of a bifunctional boronate in palladium-catalyzed allylation chemistry, leading to more complex boronate-containing materials.²



We wanted to study the chemistry of compounds generically represented by **1**, ultimately to produce polyunsaturated systems *via* coupling reactions for the development of various synthetic methodologies involving pericyclic reactions. Our historic interest in sulfones led us to consider species like **2** and **3**, both of which are known compounds.^{3,4} Although the synthesis of **3** has been

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reported, very little chemistry associated with the substance has appeared.⁵ In addition to interests in coupling, we wondered what the anion chemistry of such a species might be. We report herein our preliminary results of studies in this context.

We were intrigued by the possibility that 3 might be deprotonated and further functionalized to give more complex boronates. The question was whether the boronate functional group would be compatible with a sulfonyl-stabilized carbanion, since the boron atom is not conjugated to the atom(s) bearing the negative charge. The literature was not exceptionally helpful in providing answers. However, some work by Whiting and co-workers in the early 1990s suggested that the possibility of performing the desired transformation was reasonable.⁶ This group reported that the boronate 4 could be deprotonated and alkylated with methyl iodide and other simple electrophiles like benzaldehyde (eqn (1)).



We began our studies with **3**. Although simple allylic sulfones are easily deprotonated and alkylated,⁷ it was not clear at the outset what we should expect with a nominally Lewis acidic atom in the molecule. While attempted deprotonation of **3** with *n*-BuLi resulted in decomposition, the corresponding reaction with amide bases was more promising. For example, treating **3** with excess LiHMDS followed by trapping with excess iodomethane afforded the dialkylation product **6** in 55% yield (eqn (2)). While we were pleased with this result, we desired controlled monoalkylation at this stage of our work. After considerable experimentation, we found that the best conditions for such a reaction involved simple deprotonation with a slight excess of LDA and electrophilic trapping to afford alkylation products

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Scheme 1 Synthesis of 7.

Table 1	Deprotonation	and alk	vlation of [•]	7

Entry	"R"	Product	Yield (%)
1	Ме	8a	70
2	Et	8b	60
3	nPr	8c	71
4	<i>n</i> Bu	8d	59
5	<i>n</i> -Heptyl	8e	53
6	Allyla	8f	44
7	Benzyl ^a	8g	44
8	3-Buten-1-vl	8ĥ	68
9	4-Penten-1-yl	8i	67
10	5-Hexen-1-vl	8j	66
11	4,6-Heptadien-1-yl	8ĸ	60
12	2-Phenyleth-1-yl	81	66
13	3-Phenylprop-1-yl	8m	65
14	3-(2-Iodophenyl)prop-1-yl	8n	73
15	SiMe ₃ ^b	80	62

 a The corresponding bromide was used. b The corresponding chloride was used.

in good yield. Since we occasionally observed deprotonation and trapping at the methyl group of **3**, as evidenced by spectroscopic examination of crude reaction mixtures, we conducted the bulk of our studies using its phenylsulfonyl analogue **7**, whose synthesis paralleled that of **3** (ref. 4) and is shown in Scheme 1. The results for the deprotonation and alkylation of **7** are summarized in Table **1**.



The synthesis of 7 involved the addition of phenylsulfonyl iodide to the double bond in **9**, presumably by a radical mechanism. Elimination and presumably isomerization to the most thermodynamically favored system afforded 7 in good yield. Compound 7 is a crystalline solid. Interestingly, its solid state structure gave no indication of an interaction between the formally Lewis acidic boron atom and the oxygens of the sulfone group, though whether this situation changes in its conjugate base is not yet known.⁸



The deprotonation and subsequent alkylation of 7 proceeded smoothly using LDA in THF and primary iodides as electrophiles. Yields were fair to good in most cases, as shown in Table 1. Difficulties in handling allylic and benzylic iodides led us to use the corresponding bromides as electrophiles (Table 1, entries 6 and 7) and these were reasonably effective in producing the targeted alkylation products. A single allylic silane was also produced in moderate yield using TMSCl as the electrophile (Table 1, entry 15).

Attempts to use primary chlorides or bromides in the alkylation procedure were conducted using *n*-butyl electrophiles. While *n*-butyl bromide afforded some monoalkylation product, large amounts of starting material remained in the reaction mixture. For *n*-butyl chloride, the reaction was messy and the only clean compound that could be isolated was starting material.⁹ Secondary iodides, isobutyryl iodide and neopentyl iodide gave only starting material. Interestingly, solvents including dioxane, DME and toluene afforded no alkylation product, though it seemed to be the case from color changes that deprotonation of 7 was taking place. Solubility problems were encountered with diethyl ether and this solvent could not be used for the reaction.

The bases tested in the reaction included LiTMP, LiHMDS, LTBTA¹⁰ and even *n*-BuLi. All of these bases were effective to some degree in the alkylation process, but LDA was still superior, followed closely by LiHMDS (see ESI†). Concentration effects were interesting in that isolated yields were best at a concentration of 0.1 M and worse at both higher and lower concentrations. Thus, in the formation of **8c** at 0.025 M, the isolated yield was 27%; at 0.5 M, 42%. Even correcting for recovered starting material did not increase the yield significantly.¹¹

Deprotonation was conducted at -78 °C. Alkylation reactions proceeded at -78 °C, using *n*-propyl iodide as the electrophile, but were slow, affording a 1 : 0.7 ratio of **8c** : 7 after three hours. Good results were obtained from -30 °C to room temperature with respect to alkylation, but it proved most simple to begin the alkylation at -78 °C then remove the cooling bath and allow the reaction to proceed with gradual warming to, and stirring at, room temperature.

In conclusion, we have developed a method for the straightforward alkylation of borylated allylic sulfones, thus opening the door to the synthesis of a large number of new organoboron species. Further studies of the chemistry of the products should be fruitful in producing an even greater variety organoboron compounds. For example, treatment of 8h with the second generation Grubbs catalyst afforded the intramolecular ring-closing metathesis product 11 in 92% yield (Scheme 2).12 This compound could be further alkylated by treatment with LDA and the triflate 12 to afford a 1 : 0.55 mixture (by ¹H NMR) of regioisomers 13 and 14, respectively, which could be transformed to a single product by treatment with sodium phenyl sulfinate to afford 14 as the sole regioisomer.¹³ A preliminary coupling experiment with 11 was successful, but afforded 16 in relatively poor yield. Conversion of 11 to the corresponding potassium trifluoroborate¹⁴ improved the process. Thus, coupling of 17 with 15 led to 16 in 70% yield.

This chemistry can blossom into many facile ways to produce advanced organoboron species as well as other valueadded materials for synthesis.¹⁵ Exploration of the scope of the alkylation reaction, the other processes shown, as yet unexplored processes and their mechanisms, is ongoing. Additional results will be reported in due course.



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