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Thioboration of α,β-Unsaturated Ketones and Aldehydes toward the Synthesis of β-Sulfido Carbonyl Compounds

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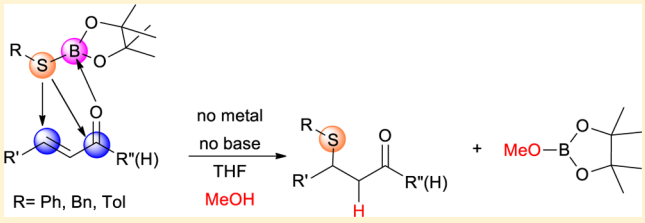
Supporting Information

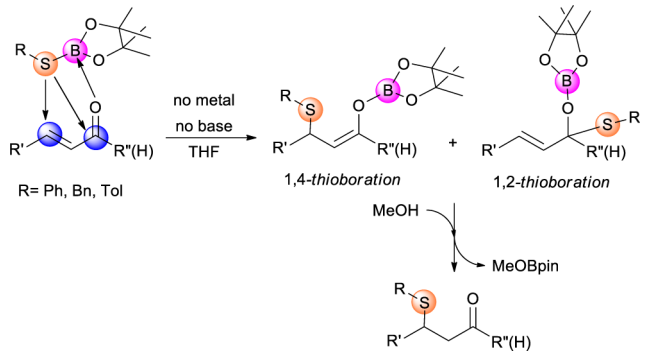
ABSTRACT: Herein a direct β-sulfido carbonyl compound synthesis by the easy activation of RS−Bpin reagents with α,β-unsaturated ketones and aldehydes is reported. This convenient methodology can be performed at room temperature with no other additives. The key point of this reactivity is based on the Lewis acidic properties of the boryl unit of the RS−Bpin reagent interacting with the C═O oxygen. Consequently, the SR unit becomes more nucleophilic and promotes the 1,4- versus the 1,2-addition, as a function of the involved substrate. The thioborated products can be further transformed into β-sulfido carbonyl compounds by addition of MeOH.



INTRODUCTION

The synthesis of β-sulfido carbonyl compounds and related compounds has been principally covered by the conjugate addition of thiols to α,β-unsaturated carbonyl compounds.[1] Metal catalysts and organocatalysts are required to activate both the substrate and the reagent and promote the formation of the C_β−S bond in a precise way,[2] particularly with asymmetric induction.[3] Despite the mild nucleophilicity of the sulfur moiety in thiol reagents,[4] the reaction conditions frequently lead to the formation of byproducts from side reactions such as self-condensation, polymerization, or rearrangements.[5] Pointing at the nature of the sulfur reagent, we focused our attention on thiodioxaborolanes, since they are easy to prepare[6] and the push−pull effect of the boryl unit might enhance the nucleophilic character of the interelement.[7] In that context, we have previously observed that alkoxides interact intermolecularly with pinB−Bpin and pinB−NR_2 bonds to deliver the Bpin or NR_2 moieties with enhanced nucleophilicity toward activated and nonactivated alkenes.[8,9] More recently, we have been able to observe that PhSe−Bpin can also be activated by Lewis bases, but the most remarkable circumstance is that the electron rich C═O of α,β-unsaturated ketones and aldehydes can activate the phenylselenium borane reagent, without the need for external Lewis bases or additives. This face to face reactivity is unusual, and theoretical calculations have demonstrated that this activation is more likely in B−E when E = Se > S > O.[10] With these data in mind, we became determined to demonstrate the efficient thioboration on α,β-unsaturated ketones and aldehydes that does not need catalysts or drastic reaction conditions and eventually provide an alternative synthesis toward β-sulfido carbonyl compounds, (Scheme 1).

Scheme 1. Postulated Substrate-Reagent Interaction To Promote 1,4- and 1,2-Thioboration and Protic Work-up Step towards β-Sulfido Carbonyl Compounds



RESULTS AND DISCUSSION

With the aim of activating PhS−Bpin (**1**)[11] and selectively transfering the PhS moiety to activated olefins, we first attempted the thioboration of 4-phenyl-3-buten-2-one (**2**). The reaction conditions entail substrate **2** (0.1 mmol scale) with an excess of **1** (for complete conversion) in 2 mL of THF,

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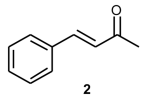
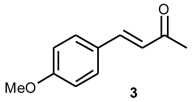
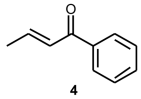
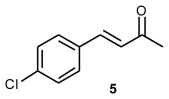
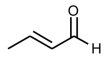
at room temperature. Within 16 h, the 1,4-thioborated intermediate (**2a**) was observed in 83% conversion, as a single regioisomer (Table 1, entry 1). When we extended the

Table 1. 1,4-Thioboration versus 1,2-Thioboration of Electron Deficient Ketones[a]

Entry	Substrate	Conv (%)	SPh OBpin R R' (%)[b]	OBpin SPh R R' (%)[b]
1	 **2**	83	99 (**2a**)	---
2	 **3**	99	99 (**3a**)	---
3	 **4**	99	99 (**4a**)	---
4	 **5**	97	99 (**5a**)	---
5	 **6**	99	30 (**6a**)	70(**6b**)
6	 **7**	99	---	99(**7b**)

[a]Thioboration carried out with α,β-unsaturated carbonyl substrate (0.1 mmol), PhS−Bpin (4.5 equiv), THF (2 mL), 25 °C, 16 h. [b]Regioselectivity determined by NMR spectroscopy.

thioboration reaction to other substrates such as 4-(4-methoxyphenyl)-3-buten-2-one (**3**), *trans*-1-phenyl-2-buten-1-one (**4**), and 4-(4-chlorophenyl)-3-buten-2-one (**5**), it was possible to observe a similar trend toward the quantitative 1,4-thioborated intermediate formation, (Table 1, entries 2−4, Figure 1).

However, the thioboration of the cyclic α,β-unsaturated ketone 2-cyclohexenone (**6**) gave a mixture of 1,4- and 1,2-thioborated products. The ^{1}H NMR spectra of the 2-cyclohexenone's crude thioboration reaction shows two different groups of signals in 7:3 ratio. The major signals are two doublets of triplets at 5.9 and 5.7 ppm that were correlated with

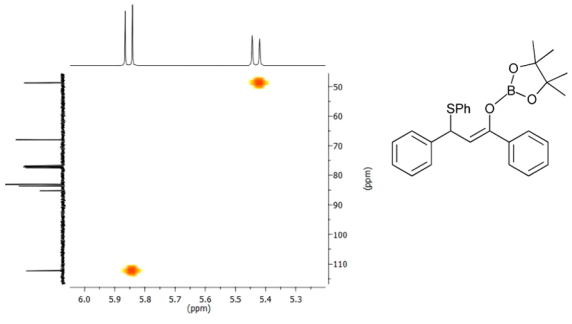


Figure 1. Enlargement of HSQC 2D in the reaction crude of chalcone.

two carbons at 130 ppm in the ^{13}C NMR spectra, in agreement with the formation of the 1,2-thioborated intermediate (**6b**) (Figure 2). The minor signals appeared at 5.4 and 3.9 ppm in the ^{1}H NMR spectra, which were correlated with an allylic and vinylic carbon, respectively, in the HSQC 2D NMR experiment (Figure 2). These data agreed with the minor formation of the 1,4-thioborated intermediate (**6a**). Interestingly, when the thioboration of the α,β-unsaturated aldehyde crotonaldehyde (**7**) was performed under the same reaction conditions, the unique thioborated intermediate observed was the 1,2-thioborated isomer (**7b**) (Figure 3). The signals appeared at 5.8 and 5.6 ppm correlated with two carbons at about 128 ppm, and the doublet at 5.9 ppm correlates with the carbon at 83 ppm, supporting that the aldehyde functional group has been transformed into −CH(OBpin)(SPh).

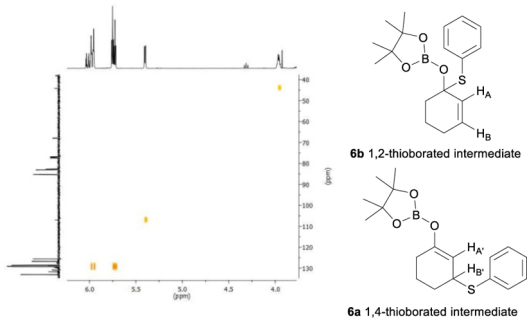


Figure 2. Enlargement of HSQC 2D of the thioboration of **6**.

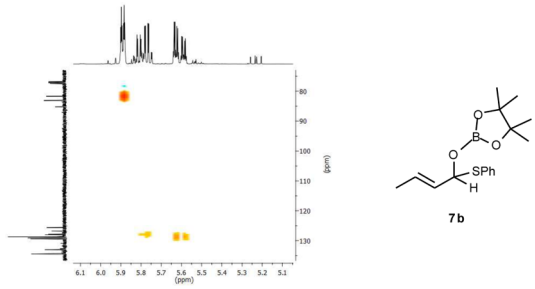


Figure 3. Enlargement of HSQC 2D of **7b** in the reaction crude.

After quantitative conversion of substrates **2**−**8** into thioborated products, the protic work up carried out with addition of MeOH (2 mL) provided the corresponding β-sulfido carbonyl compounds **2-SPh** to **8-SPh** (Table 2, entries 1−7). A plausible rearrangement of 1,2-thioborated intermediates **6b** and **7b** toward the β-sulfido carbonyl compounds seems to occur under the in situ protic work up. In order to discard the possible *in situ* formation of PhSH and direct interaction with the α,β-unsaturated carbonyl substrates, we ran the same reaction as in Table 2, entry 5, using PhSH instead of PhS−Bpin. As was expected, there is no β-sulfido cyclohexenone formation due to the lack of catalytic activation of the thiol. The thioboration of the less sterically hindered α,β-unsaturated substrates 1-penten-3-one (**9**), 3-hepten-2-one (**10**), and 3-nonene-2-one (**11**) required less of the PhS−Bpin reagent (1.1−3 equiv) to obtain quantitative conversion into the β-sulfido carbonyl compounds **9-SPh**, **10-SPh**, and **11-SPh** (Table 2, entries 8−10). When the thioboration of **10** was carried out in MeOH as the unique solvent, quantitative formation of the desired β-sulfido ketone was observed within 6

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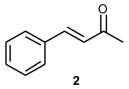
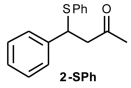
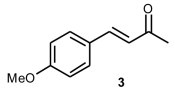
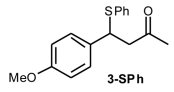
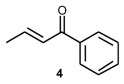
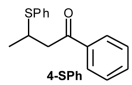
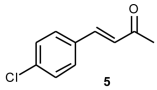
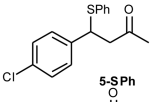
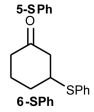
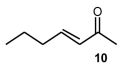
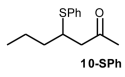
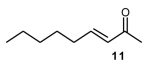
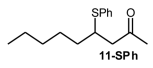
Table 2. Thioboration/Protonation of Electron Deficient Ketones[a]

Entry	Substrate	Product	Conv(%)[b]	IY(%)
1			76	64
2			78	70
3			88	72
4			87	75
5			78	70
6			87	80
7			82	78
8[c]			99	81
9[d]			99	80
10[d]			91	71

[a]Reaction conditions: α,β-unsaturated carbonyl substrate (0.1 mmol), PhS−Bpin (4.5 equiv), THF (2 mL), 25 °C, 16 h; addition MeOH (2 mL), 2 h. [b]Conversion calculated from an average of two assays. [c]PhS−Bpin (1.1 equiv). [d]PhS−Bpin (3 equiv).

h. We have noticed, in that case, that the use of MeOH as solvent reduces the reaction time.

In order to have a general picture of this boryl-assisted synthesis of β-sulfido carbonyl compounds, we considered the activation and reactivity of the analogue thiodioxaborolanes BnS−Bpin (**12a**) and TolS−Bpin (**12b**, Tol = 4-MeC_6H_4), which were also synthesized following the literature protocol.[6,11] Both sulfur boron compounds were characterized using multinuclear NMR spectroscopy and elemental analysis. To confirm the formation of these S−B bonded species, a single crystal X-ray diffraction study was carried out on **12b**, whereupon the molecular structure is shown in Figure 4. The B(1)−S(2) distance of 1.828(3) Å is similar to those found in an unusual hypervalent pentacoordinate boron compound bearing an anthracene backbone with B−S single bonds of 1.816(5) and 1.809(4) Å.[12] Likewise the S−B−O angles in **12b** are 126(2)° and 118.6(2)°, just slightly larger than those found in the related borothiolate osmium(II) complex [OsH(SBpin)-(η^2-H_2)(CO)(P^iPr_3)$_2$] at 113.86(11)°.[13] The C(3)−S(2)−B(1) angle of 104.09(14)° is only slightly compressed compared with a pure tetrahedral environment. Data derived

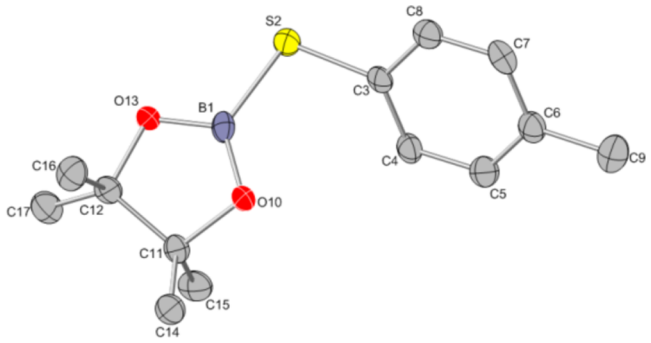


Figure 4. Molecular structure of **12b** with ellipsoids drawn at the 50% probability level and hydrogen atoms omitted for clarity.

from this study ultimately suggests that the B−S bond in **12b** is predominantly single and that negligible dative bonding from the sulfur lone pair to the boron empty orbital is occurring.

We became interested to evaluate the potential application of the thiodioxaborolanes BnS−Bpin (**12a**) and TolS−Bpin (**12b**, Tol = 4-MeC_6H_4), in comparison with PhS−Bpin (**1**). Selecting 3-nonene-2-one (**11**) and 4-hexen-3-one (**13**) as the Michael acceptors, we conducted the thioboration/protonation within 16 h at room temperature. The formation of the corresponding β-sulfido carbonyl compounds containing PhS and TolS were isolated up to 71% and 75%, respectively (Figure 5). Kinetic studies based on reaction progress

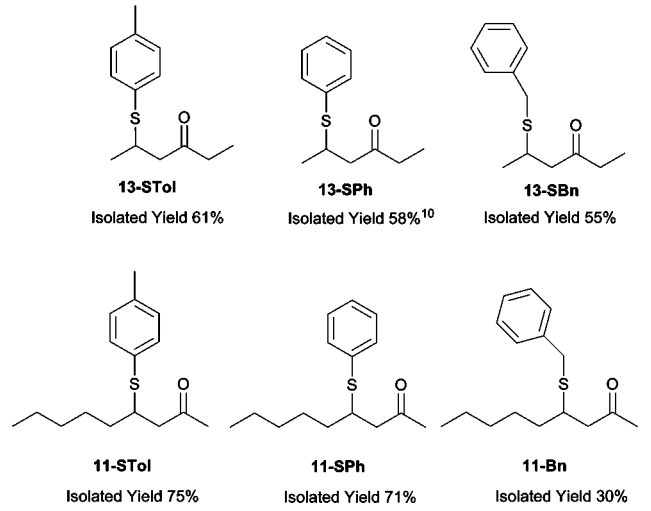


Figure 5. Comparative study of thioboration/protonation with thiodioxaborolanes PhS−Bpin (**1**), BnS−Bpin (**12a**), and TolS−Bpin (**12b**).

concentration profile analyzed by NMR spectroscopy provided a first order reaction for the substrate in the thioboration of **11** with **12a**.

Since we have recently unraveled the mechanism for the reaction of α,β-unsaturated carbonyl compounds with PhSe−Bpin species by means of DFT studies,[10] we envisaged a similar mechanistic behavior in the thioboration approach. Therefore, we postulate that the reaction occurs in three main steps, the first being the interaction of the carbonylic oxygen with the empty p orbital of the boron atom through a first transition state **TS1** and forming the corresponding intermediate **I1** (Figure 6). Two electrophilic positions can further receive the sulfido group: the carbonylic carbon, passing through the

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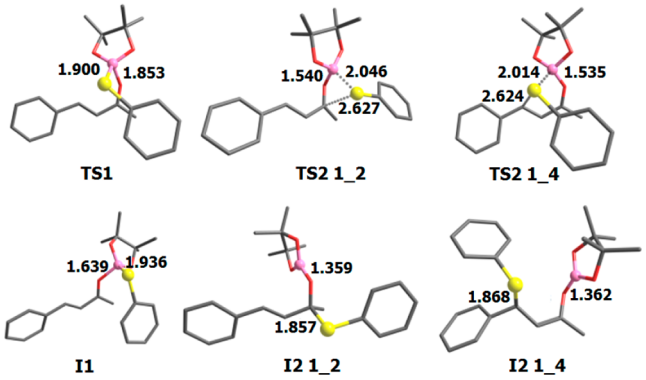

Figure 6. Optimized geometries of **TS1**, **I1**, **TS2-1_2**, **I2-1_2**, **TS2-1_4** and **I2-1_4** for the substrate 4-phenyl-3-buten-2-one (**2**) with the selected bond distances in Å.

transition state **TS2-1_2** or the C_β position through the **TS2-1_4** (Figure 6). These transition states give rise to the intermediates **I2-1_2** and **I2-1_4** (Figure 6), respectively, which finally undergo the protonation to give the corresponding β-sulfido carbonyl compounds and the byproduct HOBpin.

In order to clarify the different nucleophilic character of the thiodioxaborolanes used, we calculated the nucleophilicity index (N) based on relating the nucleophilicity to the computed highest occupied molecular orbital (HOMO) energy by the Kohn–Sham scheme[14] through the next formula introduced by Perez et al.[15]

$$N = E_{\mathrm{HOMO(Nu)}}(\mathrm{eV}) - E_{\mathrm{HOMO(TCE)}}(\mathrm{eV})$$

where tetracyanoethylene (TCE) is taken as reference. In this scale, the nucleophilicity index for TCE is N = 0.0 eV, presenting the lowest HOMO energy in a long series of organic molecules already considered. According to a same author's latter study[16] the nucleophiles can be classified as strong, N > 3.00 eV, moderate, 2.00 < N < 3.00 eV, and marginal, N < 2.00 eV. Table 3 collects the N values for the PhSe–Bpin, TolS–Bpin (TolS = 4-MeC$_6$H$_4$S), PhS–Bpin, PhO–Bpin, and BnS–Bpin species. Hence, the first four species have a strong nucleophilic character, whereas BnS–Bpin is considered as a moderate nucleophile. This is in agreement with the observed lower reactivity of the BnS–Bpin species compared with TolS–Bpin and PhS–Bpin. Also, they show the expected trend in nucleophilicity: Se > S > O. The N values for the intermediates **I1** formed in the reaction of the substrate 4-phenyl-3-buten-2-one (**2**) with TolS–Bpin, PhS–Bpin, and BnS–Bpin species are also collected in Table 3, confirming that its nucleophilicity is enhanced in relation to the reagents.

Table 3. Nucleophilicity Indexes (N) for Some X–Bpin Reagents and for the Intermediates I1 Formed on the Reaction of 4-Phenyl-3-buten-2-one (2) with TolS–Bpin, PhS–Bpin, and BnS–Bpin[a]

PhSe–Bpin	TolS–Bpin	PhS–Bpin	PhO–Bpin	BnS–Bpin	I1 TolS–Bpin	I1 PhS–Bpin	I1 BnS–Bpin
3.48	3.35	3.24	3.09	2.89	3.86	3.79	3.99

[a]All energies are in eV.

Scheme 2 collects the relative Gibbs free energies of the species involved in the thioboration of 4-phenyl-3-buten-2-one (**2**) through 1,2- and 1,4-addition with PhS–Bpin, as well as the 1,4-addition with TolS–Bpin and BnS–Bpin. It can be observed that for the 1,2-addition of the PhS–Bpin reagent the activation free energies of both the **TS2-1_2** ($\Delta G^{\ddagger}_{\mathrm{TS2\text{-}1\_2}}$ = 20.1 kcal·mol^{-1}) and **TS3-1_2** ($\Delta G^{\ddagger}_{\mathrm{TS3\text{-}1_4}}$ = 18.6 kcal·mol^{-1}) are higher than the corresponding ones for the 1,4-addition pathway ($\Delta G^{\ddagger}_{\mathrm{TS2\text{-}1_4}}$ = 13.5 kcal·mol^{-1} and $\Delta G^{\ddagger}_{\mathrm{TS3\text{-}1\_4}}$ = 10.3 kcal·mol^{-1}, respectively). Also, the intermediate **I2-1_2** ($\Delta G_{\mathrm{I2\text{-}1_2}}$ = −7.8 kcal·mol^{-1}) is less stable than the corresponding **I2-1_4** ($\Delta G_{\mathrm{I2\text{-}1_4}}$ = −11.3 kcal·mol^{-1}) and the formation of the product **P-1_2** ($\Delta G_{\mathrm{P\text{-}1_2}}$ = −10.3 kcal·mol^{-1}) is less favored than the formation of the **P-1_4** ($\Delta G_{\mathrm{P\text{-}1_4}}$ = −25.3 kcal·mol^{-1}). Thus, we only display herein the 1,4-addition pathway for the TolS–Bpin and BnS–Bpin, which show the same behavior. The thiodioxaborolane BnS–Bpin is less reactive than the other two reagents by the fact that all the activation energies $\Delta G^{\ddagger}_{\mathrm{TS1}}$, $\Delta G^{\ddagger}_{\mathrm{TS2\text{-}1\_4}}$, and $\Delta G^{\ddagger}_{\mathrm{TS3\text{-}1\_4}}$ are higher as well as the corresponding intermediates ΔG_{I1} and $\Delta G_{\mathrm{I2\text{-}1\_4}}$. Note also that the computed values for the TolS–Bpin and PhS–Bpin reactions are very similar, the TolS–Bpin being slightly more reactive.

We also computed the reaction pathway for the thioboration reaction of substrate 2-cyclohexenone (**6**) with PhS–Bpin. In this case, the initial step based on the interaction of the carbonylic oxygen with the empty p orbital of the boron atom is the same as described above, but after the first transition state **TS1** ($\Delta G^{\ddagger}_{\mathrm{TS1}}$ = 9.7 kcal·mol^{-1}) and the formation of the intermediate **I1** (ΔG_{I1} = 8.4 kcal·mol^{-1}), the 1,2-addition takes place trough a **TS2-1_2** ($\Delta G^{\ddagger}_{\mathrm{TS2}}$ = 18.1 kcal·mol^{-1}) giving the 1,2-addition intermediate **I2-1_2** (**6b**) (ΔG_{I2} = −9.5 kcal·mol^{-1}). However, despite many efforts, the transition states corresponding to a direct 1,4-addition or an interconversion from 1,2- to 1,4-addition intermediates were not located. The *trans* disposition of the double bond in the 2-cyclohexenone substrate prevents the direct 1,4-addition because of geometric restraints. It is worth mentioning that during the course of these investigations aimed at characterizing the evolution of the 1,2-addition intermediate, when we introduced water (or methanol) as protonation agents, the models evolved directly to the formation of the final 1,4-product and BpinOH (or BpinOMe). Thus, we think that the interconversion from 1,2- to 1,4-addition intermediates does not take place directly but is coupled with the final protonation step. In any case, our results justify the observation of the 1,2-addition intermediate in the reaction crude. A very recent report on phosphinoboration of aldehydes and α,β-unsaturated aldehydes has also proved the preferred 1,2 addition intermediates.[12]

We conclude that the synthesis of β-sulfido carbonyl compounds can be achieved through a direct thioboration/protonation, where the PhS, TolS, and BnS moieties can be delivered from the thiodioxaborolanes PhS–Bpin, 4-MeC$_6$H$_4$S–Bpin, and BnS–Bpin by the simple activation of the Bpin moiety with a carbonyl group. This strategy is performed at room temperature in the absence of any catalyst. The thioboration generates 1,4-addition as well as 1,2-addition intermediates, depending on the structural nature of the substrate. Protic workup delivers the corresponding β-sulfido carbonyl compounds in good isolated yields. From the thiodioxaborolanes studied, the BnS–Bpin is less activated presumably because of the lack of electron delocalization from sulfur, making the boron atom less Lewis acidic. DFT-based studies provide a suitable mechanism for the reaction and a useful tool to analyze the change in the nucleophilicity of the

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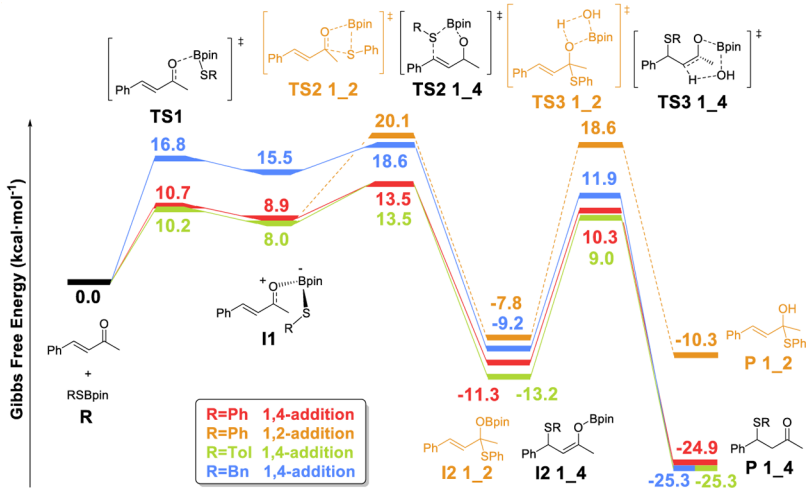
Scheme 2. Relative Gibbs Free Energies for the Reaction Pathway of the 1,2- and 1,4-Addition of the RS−Bpin Reagents to the Substrate 4-Phenyl-3-buten-2-one (2)[a]



[a]All energies are in kcal·mol^{-1}.

reagents by the modification of the substituent on the RS moieties.

EXPERIMENTAL SECTION

Synthesis of PhS−Bpin (1), BnS−Bpin (12a), and TolS−Bpin (12b) and X-ray data for 12b. To a toluene (10 mL) solution of the corresponding RSH (2.50 g, 20.13 mmol) and pinacolborane (2.60 g, 20.33 mmol) was added $RhCl(PPh_3)_3$ (4 mg, 0.0040 mmol, 0.02 mol %) as a solid. The reaction was allowed to proceed for 18 h, at which point solvent was removed under vacuum to give an off-white solid.[6,11] The solid was dissolved in Et_2O (4 mL) and stored at −30 °C. The resulting precipitate was collected by suction filtration to afford **1**, **12a**, and **12b** as a white solid. Compounds **1** and **12a** were previously reported.[11] Yield for **12b**: 4.68 g (93%). Spectroscopic NMR data for **12b** (in $CDCl_3$): ^{1}H δ 7.36 (d, J = 8.2 Hz, 2H, Ar), 7.07 (d, J = 8.2 Hz, 2H, Ar), 2.31 (s, 3H, CH_3), 1.29 (s, 12H, pin); ^{11}B δ 32 (br); ^{13}C{^{1}H} δ 136.7, 133.1, 129.6, 126.0, 85.2, 24.6, 21.2. Anal. Calcd for $C_{13}H_{19}BO_2S$ (250.16): C, 62.41; H, 7.66. Found: C, 62.22; H, 7.31.

General Method for β-Sulfonylation of α,β-Unsaturated Ketones and Aldehydes with PhS−Bpin (1), BnS−Bpin (12a), and TolS−Bpin (12b). The sulfur reagent, PhS−Bpin (**1**), BnS−Bpin (**12a**), or TolS−Bpin (**12b**) (1.1−4.5 equiv), was weighed and transferred into an oven-dried Schlenk tube inside the glovebox. The corresponding substrate (0.10 mmol) was introduced in the Schlenk tube under argon, and dry THF (2 mL) was added. The mixture was stirred for 16 h at room temperature. The solvent was removed under vacuum, and the resulting residue was analyzed by ^{1}H NMR. When the 1,2 or the 1,4 intermediates were detected by ^{1}H NMR, a methanolysis was carried out. The content of the NMR tube was added into a Schlenk with 2 mL of DCM and excess of MeOH (0.05 mL). The reaction was stirred for 2 h at room temperature. The solvent was removed under vacuum, and the resulting residue was analyzed by ^{1}H NMR. Conversion was determined by correlation of the integrals of the protons of the product and the substrate. The products, β-(phenylthio), β-(benzylthio), or β-(p-tolylthio) substituted ketone or aldehyde were purified by flash chromatography using a silica gel column and the mixture of petroleum ether and ethyl acetate adequate for each case.

*4-Phenyl-4-phenylthio-2-butanone (**2-SPh**).* Yield for **2-SPh**: 16.4 mg (64%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31−7.25 (m, 6H), 7.25−7.18 (m, 4H), 4.71 (dd, J = 8.0, 6.6 Hz, 1H), 3.09 (dd, J = 16.2, 7.3 Hz, 1H), 3.03 (dd, J = 16.3, 6.0 Hz, 1H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 205.7, 141.1, 134.1, 133.0, 129.0, 128.6, 127.8, 127.8, 127.6, 49.6, 48.1, 30.9. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{16}SO$ 257.3753; found 257.0993; [M + Na]$^+$ calcd for $C_{16}H_{16}SO$ 279.3512; found 279.0812.

*4-(4-Methoxyphenyl)-4-phenylthio-2-butanone (**3-SPh**).* Yield for **3-SPh**: 20.0 mg (70%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm):7.31−7.16 (m, 7H), 6.81−6.76 (m, 2H), 4.68 (dd, J = 8.3, 6.4 Hz, 1H), 3.77 (s, 3H), 3.05 (dd, J = 17.0, 8.5 Hz, 1H), 2.99 (dd, J = 16.9, 6.5 Hz, 1H), 2.05 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 205.9, 158.9, 134.3, 133.0, 132.9, 129.0, 128.9, 127.6, 114.0, 55.4, 49.9, 47.6, 30.9. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{17}H_{18}SO_2$ 309.0974; found 309.0927.

*1-Phenyl-4-phenylthio-1-butanone (**4-SPh**).* Yield for **4-SPh**: 18.5 mg (72%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.87−7.84 (m, 2H), 7.54−7.48 (m, 1H), 7.43−7.37 (m, 4H), 7.28−7.17 (m, 3H), 3.87 (dqd, J = 9.0, 6.7, 4.6 Hz, 1H), 3.25 (dd, J = 16.9, 4.5 Hz, 1H), 3.06 (dd, J = 16.9, 9.0 Hz, 1H), 1.32 (d, J = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 198.2, 136.9, 134.5, 133.4, 132.4, 129.1, 128.8, 128.2, 127.4, 45.6, 38.8, 21.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{16}SO$ 257.3753; found 257.1065; [M + Na]$^+$ calcd for $C_{16}H_{16}SO$ 279.0892; found 279.0812.

*4-(4-Chlorophenyl)-4-phenylthio-2-butanone (**5-SPh**).* Yield for **5-SPh**: 21.8 mg (75%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31−7.18 (m, 9H), 4.69 (t, J = 7.3 Hz, 1H), 3.05 (d, J = 7.3 Hz, 2H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 205.3, 139.8, 133.6, 133.2, 133.2, 129.2, 129.1, 128.7, 128.0, 49.4, 47.5, 30.8. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{16}H_{15}SOCl$ 313.0426; found 313.0429.

*3-Phenylthio-1-cyclohexanone (**6-SPh**).* Yield for **6-SPh**: 14.4 mg (70%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.45−7.40 (m, 2H), 7.34−7.27 (m, 3H), 3.43 (tdd, J = 10.4, 4.5, 3.4 Hz, 1H), 2.69 (ddt, J = 14.2, 4.4, 1.6 Hz, 1H), 2.41−2.26 (m, 3H), 2.21−2.09 (m, 2H), 1.80−1.64 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 208.9, 133.4, 133.1, 129.2, 127.9, 47.9, 46.3, 41.0, 31.4, 24.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{12}H_{14}SO$ 207.0816; found 207.0845; [M + Na]$^+$ calcd for $C_{12}H_{14}SO$ 229.0745; found 229.0663.

*3-Phenylthiobutanal (**7-SPh**).* Yield for **7-SPh**: 14.4 mg (80%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.76 (t, J = 1.7 Hz, 1H), 7.45−7.41 (m, 2H), 7.35−7.27 (m, 3H), 3.75−3.65 (m, 1H), 2.71 (ddd, J = 17.3, 6.0, 1.8 Hz, 1H), 2.59 (ddd, J = 17.3, 7.6, 1.7 Hz, 1H), 1.37−1.34 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 200.7, 137.8, 133.1, 129.2, 127.8, 50.2, 37.7, 21.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{10}H_{12}SO$ 181.0784; found 181.0534.

*3-Phenylthio-1-cyclopentanone (**8-SPh**).* Yield for **8-SPh**: 15.0 mg (78%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44−7.37 (m, 2H), 7.35−7.26 (m, 3H), 3.94−3.86 (m, 1H), 2.65−2.44 (m, 4H), 2.40−2.13 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 216.7,

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134.4, 132.2, 129.3, 127.7, 45.4, 43.6, 37.0, 29.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{12}SO$ 193.0726; found 193.0668.

*1-Phenylthio-3-butanone (**9-SPh**).* Yield for **9-SPh**: 15.7 mg (81%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.35−7.26 (m, 4H), 7.22−7.17 (m, 1H), 3.15 (t, J = 7.3 Hz, 2H), 2.73 (t, J = 7.3 Hz, 2H), 2.42 (q, J = 7.3 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 209.6, 135.9, 129.6, 129.2, 126.4, 41.9, 36.4, 27.7, 7.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_{14}SO$ 195.0876; found 195.0835.

*4-Phenylthio-2-heptanone (**10-SPh**).* Yield for **10-SPh**: 17.8 mg (80%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.42−7.38 (m, 2H), 7.33−7.21 (m, 3H), 3.64−3.56 (m, 1H), 2.72 (dd, J = 17.2, 6.1 Hz, 1H), 2.63 (dd, J = 17.2, 7.4 Hz, 1H), 2.13 (s, 3H), 1.57−1.42 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 207.1, 134.6, 132.5, 129.1, 127.3, 49.3, 43.6, 37.1, 30.9, 20.3, 14.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{18}SO$ 223.1216; found 223.1142; $[M + Na]^+$ calcd for $C_{13}H_{18}SO$ 245.1089; found 245.0964.

*4-Phenylthio-2-nonanone (**11-SPh**).* Yield for **11-SPh**: 17.7 mg (71%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.39−7.34 (m, 2H), 7.29−7.17 (m, 3H), 3.55 (m, 1H), 2.68 (dd, J = 17.2, 6.2 Hz, 1H), 2.60 (dd, J = 17.2, 7.4 Hz, 1H), 2.09 (s, 3H), 1.54−1.38 (m, 4H), 1.26−1.20 (m, 4H), 0.84 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 207.0, 134.7, 132.5, 129.1, 127.3, 49.3, 43.9, 34.9, 31.7, 30.8, 26.7, 22.7, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{22}SO$ 251.1547; found 251.1462; $[M + Na]^+$ calcd for $C_{15}H_{22}SO$ 273.1335; found 273.1279.

*4-Benzylthio-2-nonanone (**11-SBn**).* Yield for **11-SBn**: 8.0 mg (30%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.29−7.21 (m, 4H), 7.21−7.15 (m, 1H), 3.67 (d, J = 1.4 Hz, 2H), 2.98 (p, J = 6.8 Hz, 1H), 2.61 (dd, J = 16.8, 7.1 Hz, 1H), 2.53 (dd, J = 16.8, 6.7 Hz, 1H), 2.03 (s, 3H), 1.42 (dd, J = 7.6, 6.5 Hz, 2H), 1.31−1.17 (m, 6H), 0.80 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 207.1, 138.6, 129.0, 128.6, 127.1, 49.8, 40.5, 35.9, 35.2, 31.7, 30.7, 26.4, 22.7, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{24}SO$ 265.1657; found 265.1723.

*4-(p-Tolylthio)nonan-2-one (**11-STol**).* Yield for **11-STol**: 19.8 mg (75%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.31 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 7.8 Hz, 2H), 3.53−3.45 (m, 1H), 2.69 (dd, J = 17.0, 6.3 Hz, 1H), 2.59 (dd, J = 17.0, 7.4 Hz, 1H), 2.33 (s, 3H), 2.12 (s, 3H), 1.57−1.44 (m, 4H), 1.32−1.26 (m, 4H), 0.87 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 207.1, 137.6, 133.3, 130.6, 129.8, 49.3, 44.3, 34.8, 31.7, 30.8, 26.7, 22.7, 21.3, 14.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{24}SO$ 265.1626; found 265.1624.

*5-Benzylthio-3-hexanone (**13-SBn**).* Yield for **13-SBn**: 12.2 mg (55%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.34−7.28 (m, 4H), 7.26−7.20 (m, 1H), 3.76 (s, 2H), 3.23−3.13 (m, 1H), 2.66 (dd, J = 16.6, 6.0 Hz, 1H), 2.50 (dd, J = 16.6, 8.0 Hz, 1H), 2.36 (qd, J = 7.3, 2.2 Hz, 2H), 1.26 (d, J = 6.7 Hz, 3H), 1.02 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 209.4, 138.5, 128.9, 128.7, 127.2, 49.7, 36.7, 35.7, 35.2, 21.7, 7.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{18}SO$ 223.1215; found 223.1153; $[M + Na]^+$ calcd for $C_{13}H_{18}SO$ 245.1062; found 245.0971.

*5-(p-Tolylthio)hexan-3-one (**13-STol**).* Yield for **13-STol**: 13.5 mg (61%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.32 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 3.69−3.59 (m, 1H), 2.71 (dd, J = 16.8, 5.4 Hz, 1H), 2.51 (dd, J = 16.8, 8.5 Hz, 1H), 2.40 (qd, J = 7.3, 2.4 Hz, 2H), 2.33 (s, 3H), 1.26 (d, J = 6.6 Hz, 3H), 1.03 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 209.5, 137.7, 133.2, 130.5, 129.8, 49.3, 38.9, 36.8, 21.3, 21.2, 7.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{18}SO$ 223.1215; found 223.1161.

Computational Details. All calculations were carried out by using the Gaussian 09 package[13] with the hybrid M06-2X functional.[14] The standard 6-311G** basis set was used to describe the H, C, B, O, S, and Se atoms.[15] Full geometry optimizations were performed without constraints. The nature of the stationary points encountered was characterized either as minima or as transition states by means of harmonic vibrational frequencies analysis. The zero-point, thermal, and entropy corrections were evaluated to compute enthalpies and Gibbs free energies (T = 298 K, p = 1 bar). Single points with the functional B3LYP[16] were computed with the same basis set. Hydrogens have been omitted for clarity in the graphic representation of the geometries.

■ ASSOCIATED CONTENT

Supporting Information

X-ray diffraction study for **12b**, general method for β-sulfonylation of α,β-unsaturated ketones and aldehyde, ^1H and ^{13}C NMR of products, computational details, functional comparison, computed nucleophilicity indexes (N), structures and electronic energies of the involved species, and kinetic studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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