Pergamon

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Tetrahedron Letters 44 (2003) 4451–4454

TETRAHEDRON LETTERS

Preparation of alcohols from sulfones and trialkylboranes

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Received 14 April 2003; revised 18 April 2003; accepted 19 April 2003

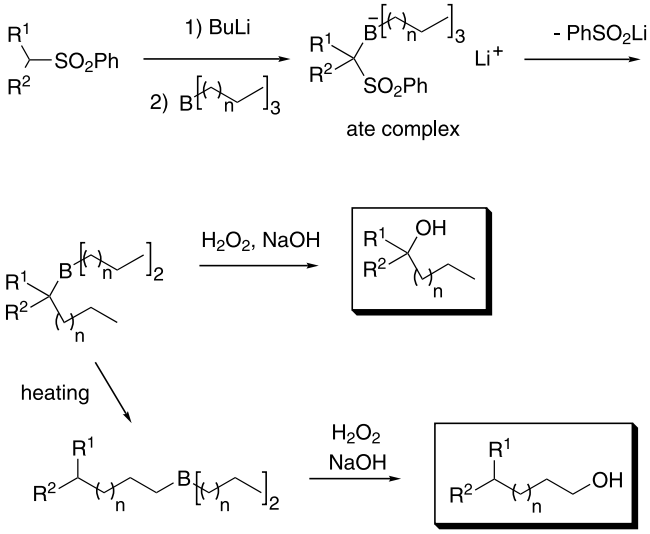
Abstract—The reaction of sulfone anions with trialkylboranes followed by thermal isomerization of the obtained boron compounds in the presence of excess borane–methyl sulfide complex and by alkaline hydroperoxide oxidation yields primary alcohols.

Boron compounds are versatile reagents which are widely employed as precursors for various functionalized organic compounds.[1] Many trialkylboranes are conveniently prepared by hydroboration of alkenes and several methods can be used to convert them to other boron compounds. Thus, thermal migration of organoboranes leads to less substituted trialkylboranes from isomeric, more substituted trialkylboranes.[2,3] Also, the reaction of an organoborane with a nucleophile bearing an α-leaving group can afford, after rearrangement of the initially formed ate complex, another boron compound, allowing the preparation of other functionalized products.[1] Nucleophiles that have been employed to achieve such a conversion include dihalomethane anions, dimethylsulfonium methylide, dimethylsulfoxonium methylide and diazo compounds.[4]

In 1981, Uguen reported the successful reaction of anions of sulfones substituted by a primary alkyl or allylic group with trialkylboranes, for the preparation of secondary alcohols.[5] This is of great interest since various sulfones can be easily prepared.[6] In order to broaden further the scope of this method, we envisioned to combine it with the thermal isomerization of organoboranes,[2] which allows a boron atom to migrate along a chain of carbon atoms (Scheme 1). In this letter, we describe our first results on this subject.

Several alkyl phenyl sulfones **1**, **2a**–**c** were prepared in good yields, as depicted in Scheme 2. These sulfones contain a common phenyl moiety, and differ by the absence or the presence of a R group in the sulfone α-position. This group was expected to have an influence on the reaction of the corresponding anion with boron compounds, as well as on the migration of the boron. Benzyl sulfones were not employed because they were reported to be less reactive than alkyl sulfones.

The reaction of the anions of the prepared sulfones with triethylborane were studied at first (Table 1). It was carried out in toluene rather than in THF, because the latter solvent would be expected to react with boron species at elevated temperatures. We observed that the reaction from **2a** proceeded very efficiently, leading,



Scheme 1.

Keywords: sulfone; borane; boron compound; alcohol.

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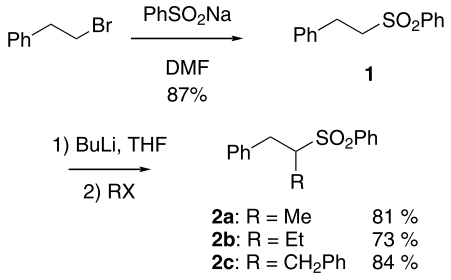
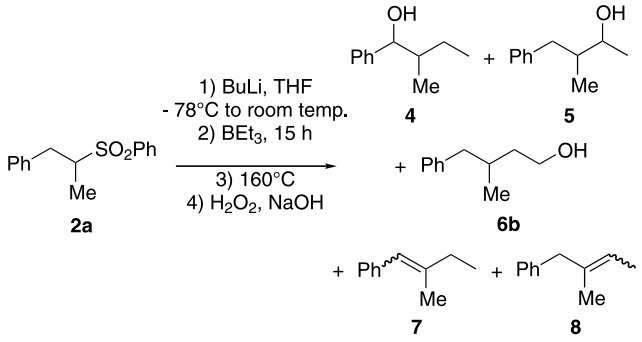
0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)01025-6



Scheme 2.



Scheme 3.

after 15 h at room temperature and subsequent oxidation, to alcohol **3b** in 78% yield. Higher temperatures were needed for the reactions using **1**, **2b** (50°C) and **2c** (80°C), which led to lower yields of the corresponding alcohols. The reaction from **2a** and tributyl- and trihexylborane worked also satisfactorily. It can be seen that this method provides an easy access to tertiary alcohols.

An evaluation of the combination of the reaction of the sulfone **2a** with triethylborane and of the thermal migration was then carried out. After proceeding as before for the first step, the mixture was heated at 160°C in toluene, in a heavy-walled pressure tube (Scheme 3). After 15 h and after usual oxidation, alcohol **6b**, which derives from the corresponding less substituted borane, was obtained in 61% yield. In another experiment under similar conditions, samples of the reaction mixture were oxidized after various times, and the proportions of alcohols evaluated by ^{1}H NMR (Table 2). It should be noted that alcohol **3b** that would result from the oxidation of the initially formed borane was not observed after 2 h heating, and that **4** and **5** are actually couples of diastereomers.

One drawback of this process is the presence of varying amounts of alkene by-products (such as **7** and **8** in the present instance) which in certain cases lowered significantly the yield of the expected alcohol. Alkenes are intermediates in the thermal isomerization of trialkylboranes which is thought to proceed through alternating dehydroboration to alkenes and dialkylboranes and then reaction of these compounds to more thermodynamically stable trialkylboranes.

Table 2. Distribution of alcohols **4**, **5**, **6b** after various heating times

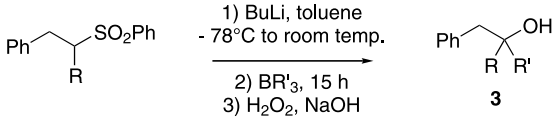
Entry	Reaction time (h)	Distribution of alcohols[a] (%)		
		4[b]	**5**[b]	**6b**
1	2	8	28	64
2	4	6	16	78
3	6	6	14	80

[a] From the ^{1}H NMR spectra of oxidized samples.
[b] Actually, two diastereomers.

In order not to obtain any alkene as product, borane (BH_3) was added to the mixture before heating. This also allowed to lessen the temperature needed for the thermal migration of boron. After several tries, we found that completion of the migration was obtained after heating at 120°C for several days in the presence of 9 equivalents of $BH_3{\cdot}SMe_2$ complex. The results are summarized in Table 3.

Reactions using triethylborane all afforded the expected alcohols, albeit after varying times of heating. Good yields were obtained from sulfones **2a** and **2b**, but compound **6d** was obtained from the sterically more

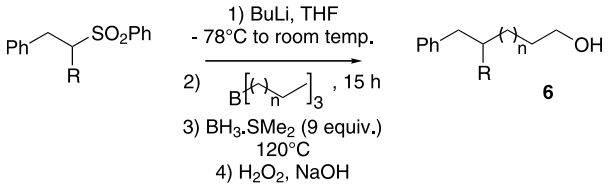
Table 1. Preparation of alcohols **3a**–**f**



Entry	Sulfone	R	R′	*T* (°C)	Yield[a] (%)	Alcohol[b]
1	**1**	H	Et	50	58	**3a**
2	**2a**	Me	Et	RT	78	**3b**
3	**2b**	Et	Et	50	54	**3c**
4	**2c**	CH_2Ph	Et	80	53	**3d**
5	**2a**	Me	Bu	RT	82	**3e**
6	**2a**	Me	Hex	RT	79	**3f**

[a] Yield of chromatographed product.
[b] See Ref. 7 for the description of spectroscopic characteristics of alcohols **3a**–**f**.

Table 3. Preparation of alcohols **6a**–**g**



Entry	Sulfone	R	Borane	*n*	Time (days)	Yield[a] (%)	Alcohol[b]
1	**1**	H	BEt_3	0	3	50	**6a**
2	**2a**	Me	BEt_3	0	1.5	70	**6b**
3	**2b**	Et	BEt_3	0	4	74	**6c**
4	**2c**	CH_2Ph	BEt_3	0	4	26	**6d**
5	**1**	H	BBu_3	2	6	52	**6e**
6	**2a**	Me	BBu_3	2	5	78	**6f**
7	**2a**	Me	$BHex_3$	4	5	12	**6g**

[a] Yield of chromatographed product.
[b] See Ref. 8 for the description of spectroscopic characteristics of alcohols **6a**–**g**.

crowded sulfone **2c** in only 26% yield after 4 days at 120°C. Preparation of alcohols from tributylborane required longer reaction times under these conditions (entries 5, 6). Finally, after 5 days at 120°C, alcohol **6g**, derived from the sulfone **2a** and trihexylborane, was isolated in 12% yield, perhaps reflecting either a lower rate of deshydroboration or a lower reducing ability of dihexylborane formed initially by deshydroboration.

In conclusion, we have shown that the reaction of sulfone anions with trialkylboranes allows the efficient preparation of tertiary alcohols. The scope of this reaction was further extended by combining it with a thermal migration in the presence of excess borane. This should be of interest in the field of organic synthesis.

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7. Typical experimental procedure: To a solution of sulfone **2a** (200 mg, 0.77 mmol, 1 equiv.) in toluene (3 ml) at −78°C was added dropwise *n*-BuLi (0.34 ml of 2.5 M solution in hexanes, 0.85 mmol, 1.1 equiv.). The colorless solution became yellow immediately. The solution was stirred for 15 min at −78°C, then 15 min at room temperature. At −78°C, tributylborane (1.15 ml of 1 M solution in THF, 1.15 mmol, 1.5 equiv.) was added and the mixture was stirred 15 min at −78°C then at room temperature. After a certain time, the yellow solution lost its color and a white precipitate appeared. The mixture was stirred at room temperature for 15 h. At 0°C, 30% H_2O_2 (1.5 ml), 3N NaOH (1.5 ml) and EtOH (1.5 ml) were added. The solution was stirred for 6 h, then extracted with ether. The organic layers were washed with 1N HCl, dried over anhydrous $MgSO_4$ and concentrated by rotary-evaporation. Purification by column chromatography on silica gel (pentane/diethyl ether: 9/1) yielded alcohol **3e** (120.7 mg, 82%) as a colorless oil. Spectral data for compounds described in Table 1. Entry 1 (**3a**: 1-phenyl-2-butanol): IR (NaCl) $\nu = 3384, 2929, 1455, 974, 740, 699\ cm^{-1}$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.22 (m, 5H), 3.8–3.75 (m, 1H), 2.88 (dd, $J = 4.3$ Hz, $J = 13.4$ Hz, 1H), 2.66 (dd, $J = 8.5$ Hz, $J = 13.4$ Hz, 1H), 1.7–1.5 (m, 2H), 1.53 (broad s, 1H), 1.02 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 129.5, 128.6, 126.5, 74.1, 43.6, 29.7, 10.1. Entry 2 (**3b**: 2-methyl-1-phenyl-2-butanol): IR (NaCl) $\nu = 3438$, 2970, 1456, 1146, 928, 715 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.24 (m, 5H), 2.8 (d, $J = 13.4$ Hz, 1H), 2.74 (d, $J = 13.4$ Hz, 1H), 1.53 (q, $J = 7.3$ Hz, 2H), 1.29 (broad s,

1H), 1.15 (s, 3H), 0.99 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7, 130.6, 128.2, 126.4, 72.7, 47.6, 34.2, 26, 8.4. Entry 3 (**3c**: 3-benzyl-3-pentanol): IR (NaCl) $\nu=$ 3464, 2965, 1455, 1137, 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.23 (m, 5H), 2.76 (s, 2H), 1.48 (q, $J=7.3$ Hz, 4H), 1.21 (broad s, 1H), 0.94 (t, $J=7.3$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.9, 130.5, 128.2, 126.3, 75.5, 47.8, 30.4, 7.9. Entry 4 (**3d**: 1,1-dibenzyl-1-propanol): IR (NaCl) $\nu=3570$, 2935, 1452, 1115, 1026, 750, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.26 (m, 10H), 2.84 (s, 4H), 1.41 (q, $J=7.3$ Hz, 2H), 1.36 (broad s, 1H), 1.05 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 130.6, 128.0, 126.3, 74.4, 44.8, 30.6, 8.3. Entry 5 (**3e**: 2-methyl-1-phenyl-2-hexanol): IR (NaCl) $\nu=3438$, 2934, 1457, 1376, 1144, 730, 701; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.22 (m, 5H), 2.81 (d, $J=13.4$ Hz, 1H), 2.74 (d, $J=13.4$ Hz, 1H), 1.50–1.35 (m, 7H), 1.16 (s, 3H), 0.96 (t, $J=6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 130.5, 128.1, 126.3, 72.4, 47.9, 41.5, 26.5, 26.2, 23.2, 14.1. Entry 6 (**3f**: 2-methyl-1-phenyl-2-octanol): IR (NaCl) $\nu=$ 3440, 2930, 1458, 1137, 931, 701; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.22 (m, 5H), 2.81 (d, $J=12.8$ Hz, 1H), 2.74 (d, $J=12.8$ Hz, 1H), 1.42–1.33 (m, 11H), 1.17 (s, 3H), 0.93 (t, $J=6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 130.4, 129.9, 126.2, 72.4, 47.9, 41.8, 31.8, 29.8, 26.3, 23.9, 22.5, 13.9.

8. Typical experimental procedure: In a heavy-walled pressure tube, at −78°C, *n*-BuLi (0.34 ml of 2.5 M solution in hexanes, 0.85 mmol, 1.1 equiv.) was added dropwise to a solution of sulfone **2a** (200 mg, 0.77 mmol, 1 equiv.) in toluene (3 ml). The colorless solution became yellow immediately. The solution was stirred 15 min at −78°C, then 15 min at room temperature. At −78°C, tributylborane (1.15 ml of 1 M solution in THF, 1.15 mmol, 1.5 equiv.) was added and the mixture was stirred for 15 min at −78°C then at room temperature. After some time, the yellow solution lost its color and a white precipitate appeared. The mixture was stirred at room temperature for 15 h. Then $BH_3{\cdot}SMe_2$ complex (3.5 ml of 2 M solution in THF, 6.93 mmol, 9 equiv.) was added. The tube was tightly closed and heated at 120°C for 5 days. At 0°C, 30% H_2O_2 (1.5 ml), 3N NaOH (1.5 ml) and EtOH (1.5 ml) were added. The solution was stirred for 6 h, then extracted with ether. The organic layers were washed with 1N HCl, dried over anhydrous $MgSO_4$ and concentrated by rotary-evaporation. Purification by column chromatography on silica gel (pentane/diethyl ether: 9/1) yielded alcohol **6f** (115.8 mg, 78%) as a colorless oil.

Spectral data for compounds described in Table 2: Entry 1 (**6a**: 4-phenyl-1-butanol): IR (NaCl) $\nu=3339$, 2934, 1453, 1061, 745, 698; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.14 (m, 5H), 3.53 (t, $J=6.4$ Hz, 2H), 2.57 (t, $J=7.3$ Hz, 2H), 1.67–1.51 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 128.3, 128.2, 125.6, 62.5, 35.5, 32.2, 27.4. Entry 2 (**6b**: 3-methyl-4-phenyl-1-butanol): IR (NaCl) $\nu=3341$, 2924, 1454, 1055, 737, 699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.5–7.3 (m, 5H), 3.94–3.80 (m, 2H), 2.73 (dd, $J=6.1$ Hz, $J=13.4$ Hz, 1H), 2.54 (dd, $J=7.9$ Hz, $J=13.4$ Hz, 1H), 2.04–1.95 (m, 1H), 1.9–1.8 (m, 1H), 1.66–1.55 (m, 1H), 1.37 (broad s, 1H), 1.08 (d, $J=6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1, 129.3, 128.3, 125.9, 61.2, 43.9, 39.5, 31.7, 19.6. Entry 3 (**6c**: 3-benzyl-1-pentanol): IR (NaCl) $\nu=3340$, 2928, 1426, 1058, 734, 699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.16 (m, 5H), 3.68–3.65 (m, 2H), 2.63 (dd, $J=7.3$ Hz, $J=13.4$ Hz, 1H), 2.53 (dd, $J=7.3$ Hz, $J=13.4$ Hz, 1H), 1.8–1.65 (m, 1H), 1.6–1.53 (m, 2H), 1.40 (broad s, 1H), 1.38–1.25 (m, 2H), 0.93 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.2, 129.1, 128.1, 125.7, 61.1, 40.2, 36.0, 25.8, 10.7, 3.60. Entry 4 (**6d**: 3,3-dibenzyl-1-propanol): IR (NaCl) $\nu=3338$, 3026, 2926, 1600, 1451, 1047, 746, 699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.15 (m, 10H), 3.64 (t, $J=6.7$ Hz, 2H), 2.75–2.50 (m, 4H), 2.25–2.05 (m, 1H), 1.57 (dt, $J=6.1$ Hz, $J=6.7$ Hz, 1H), 1.25 (m, 2H), 1.24 (broad s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 129.1, 128.2, 125.8, 60.8, 40.5, 38.6, 36.1. Entry 5 (**6e**: 6-phenyl-1-hexanol): IR (NaCl) $\nu=3338$, 2930, 1455, 1054, 745, 698; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.21 (m, 5H), 3.64 (t, $J=6.6$ Hz, 2H), 2.64 (t, $J=7.9$ Hz, 2H), 1.8–1.4 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.9, 128.3, 128.2, 125.5, 62.8, 35.8, 32.6, 31.3, 29.0, 25.5. Entry 6 (**6f**: 5-methyl-6-phenyl-1-hexanol): IR (NaCl) $\nu=$ 3338, 2928, 1455, 1053, 739, 699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.3–7.15 (m, 5H), 3.64 (t, $J=6.1$ Hz, 2H), 2.66 (dd, $J=6.1$ Hz, $J=13.4$ Hz, 1H), 2.40 (dd, $J=8.5$ Hz, $J=13.4$ Hz, 1H), 1.85–1.80 (m, 1H), 1.84 (broad s, 1H), 1.60–1.20 (m, 6H), 0.9 (d, $J=6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.3, 129.0, 127.9, 125.5, 62.7, 43.5, 36.3, 34.8, 32.8, 23.2, 19.2. Entry 7 (**6g**: 7-methyl-8-phenyl-1-octanol): IR (NaCl) $\nu=3335$, 2927, 1456, 1055, 738, 699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.14 (m, 5H), 3.65 (t, $J=6.7$ Hz, 2H), 2.64 (dd, $J=6.1$ Hz, $J=13.4$ Hz, 1H), 2.37 (dd, $J=7.9$ Hz, $J=13.4$ Hz, 1H), 1.75–1.65 (m, 1H), 1.60–1.58 (m, 2H), 1.57–1.34 (m, 9H), 0.86 (d, $J=6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 129.1, 128.0, 125.5, 63.0, 43.7, 36.6, 34.9, 32.7, 29.6, 27.0, 25.7, 19.4.