Carbanions from α-Phenylthio Boronic Esters as Synthetic Intermediates

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(Phenylthio)methaneboronic acid (1) was easily prepared from (phenylthio)methyllithium and trimethyl borate and was converted to boronic esters 2. The pinacol ester **2b** was efficiently deprotonated by lithium diisopropylamide in tetrahydrofuran/ether/hexane to yield the lithio derivative 3 as its THF complex, an isolable though air-sensitive solid. Evidence was also obtained that 1 was C-lithiated as well as B-butylated by excess butyllithium. Reaction of 3 with primary alkyl halides yielded pinacol 1-(phenylthio)alkane-1-boronates 5, which could also be deprotonated with LDA and reacted with alkyl halides to introduce a second alkyl group. Reaction of 3 or lithiated 5 with carboxylic esters has efficiently yielded α-phenylthio ketones 9, providing a uniquely general and regiospecific synthesis of this useful class of compounds. With aldehydes and ketones, 3 or lithiated 5 behaves as Wittig reagents to provide high yields of enethiol ethers 12. Reaction of 3 or lithiated 5 with ethylene oxide resulted in a mixture of pinacol (hydroxyalkyl)boronic ester (15) and cyclic boronic half ester (16). Pinacol bromo(phenylthio)methaneboronate (18) was prepared by bromination of 3. Phenylmagnesium bromide converted 18 to pinacol phenyl(phenylthio)methaneboronate (20), but this type of transformation failed with cyclohexylmagnesium bromide or butyllithium. Conversion of pinacol 2-phenyl-1-(phenylthio)ethane-1-boronate (**5b**) to the 2-phenyl-1-iodoethane-1-boronate (22) was accomplished with methyl iodide and sodium iodide in DMF. Conversion of the difficultly hydrolyzable pinacol boronic ester group of **5b** to a diethanolamine ester (7) was also accomplished.

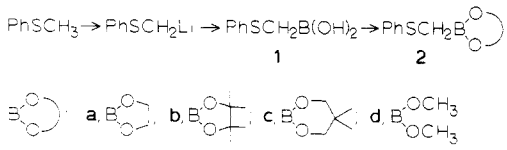
Introduction

Carbanions stabilized by adjacent boron have recently been generated by deprotonation of sterically hindered organoboron compounds with hindered lithium dialkylamides[1–4] and show promise as intermediates for organic synthesis. Prior to these discoveries, boron-substituted carbanions were accessible only through deboronation of compounds having three or four boronic ester groups[5,6] or two boronic ester and one or two group 4 metal substituents on the same carbon[7] or through deprotonation of carboranes[8] or a borabenzene anion precursor.[9] None of these earlier routes could provide carbanions at low enough cost to be considered for general synthetic organic purposes. The substantial improvement in synthetic practicality provided by the deprotonation of *gem*-diboronic esters[2] immediately suggested the possibility that pairing boron with another carbanion-stabilizing element might lead to some new and useful synthetic operations. The obvious choice of a second element was sulfur.

Deprotonation of organosulfur compounds has become a widely used route to carbanions for synthetic purposes. Examples include thioanisole,[10,11] dithiane,[12] cyclopropyl phenyl sulfide,[13] dimethyl sulfide,[14] $PhSCH_2SiMe_3$,[15] CH_3OCH_2SPh,[16] $CH_3SCH_2PO(OEt)_2$,[17] and $PhSCH_2CH(CH_3)_2$.[18] We expected that reaction of a suitable sulfur-substituted carbanion with trimethyl borate would lead to a sulfur-substituted boronic acid, which could be converted to a variety of boronic ester derivatives. With sufficient steric hindrance by the boronic ester group to prevent attack on boron by a sterically hindered lithium dialkylamide,[2] deprotonation of the carbon flanked by boron and sulfur would be expected.

Results

Synthesis of (Phenylthio)methaneboronic Esters. Treatment of (phenylthio)methyllithium[10] with trimethyl borate followed by aqueous workup efficiently yielded (phenylthio)methaneboronic acid (1), which was easily



converted to (phenylthio)methaneboronic esters (2) by standard methods. This very simple route to 2 is easily operable on a 1-mol scale, and involves less effort and potential hazard than the preparation of *gem*-diboronic esters.[6]

Deprotonation–Methylation Studies. Exploration to find conditions suitable for deprotonation of (phenylthio)methaneboronic esters (2) was aided by proton NMR

(1) Preliminary communication: Matteson, D. S.; Arne, K. *J. Am. Chem. Soc.* **1978**, *100*, 1325–1326.
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(4) Subsequent to our preliminary communication:[1] (a) Mendoza, A.; Matteson, D. S. *J. Org. Chem.* **1979**, *44*, 1352–1354. (b) Matteson, D. S.; Majumdar, D. *J. Chem. Soc., Chem. Commun.* **1980**, 39–40. (c) Wilson, J. W. *J. Organomet. Chem.* **1980**, *186*, 297–300.
(5) Matteson, D. S.; Moody, R. J. *J. Org. Chem.* **1980**, *45*, 1091–1095.
(6) (a) Matteson, D. S.; Hagelee, L. A. *J. Organomet. Chem.* **1975**, *93*, 21–32. (b) Matteson, D. S. "Gmelins Handbuch der Anorganischen Chemie", 8th ed., New Supplement Series; Niedenzu, K.; Buschbeck, K.-C., Eds.; Springer-Verlag: Berlin, 1977; Vol. 48, Part 16, pp 37–72. (c) Matteson, D. S. *Synthesis* **1975**, 147–158.
(7) (a) Matteson, D. S.; Larson, G. L. *J. Organomet. Chem.* **1973**, *57*, 225–230. (b) Matteson, D. S.; Wilcsek, R. J. *Ibid.* **1973**, *57*, 231–242. (c) Matteson, D. S.; Jesthi, P. K. *Ibid.* **1976**, *110*, 25–37.
(8) Grimes, R. N. "Carboranes"; Academic Press: New York, 1970; pp 66–68.
(9) Ashe, A. J., III; Shu, P. *J. Am. Chem. Soc.* **1971**, *93*, 1804–1805.
(10) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097–4099.
(11) Corey, E. J.; Jautelat, M. *Tetrahedron Lett.* **1968**, 5787–5788.
(12) House, H. O. "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin: Menlo Park, CA, 1972; pp 731–733.
(13) (a) Trost, B. M.; Keeley, D. E.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 3068–3070. (b) Trost, B. M.; Keeley, D. E.; Arndt, H. C.; Rigby, J. H.; Bogdanowicz, M. M. *Ibid.* **1977**, *99*, 3080–3087.
(14) Peterson, D. J. *J. Org. Chem.* **1967**, *32*, 1717–1720.
(15) Carey, F. A.; Court, A. S. *J. Org. Chem.* **1972**, *37*, 939–943.
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(17) Corey, E. J.; Schulman, J. I. *J. Org. Chem.* **1970**, *35*, 777–780.
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Table I. Exploration of Conditions for Deprotonation of Pinacol (Phenylthio)methaneboronate (2b) and Methylation to Pinacol 1-(Phenylthio)ethane-1-boronate (4)

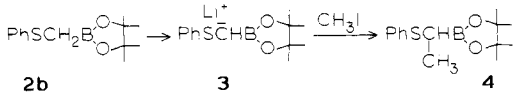
deprotonation conditions							products, % yields[a]		
base	equiv	other	equiv	solvent	T, °C	time, h	4	2b	$PhSCH_3$
LiTMP[b]	1			THF	25	5	70	15	10
LiTMP	1	DABCO[c]	1	THF	25	5	85	15	0
LiTMP	1	HMPA[d]	1	THF	25	21	45	45	5
LiTMP	1			ether	25	7	70	30	0
LiTMP	1	DABCO	1	ether	25	7	70	30	0
LiNRR′[e]	1			isooctane	−10	0.5	60	35	0
LiNRR′[e]	1.2	TMEDA[f]	1.2	THF	0	3	85	15	0
LDA[g]	1.2	TMEDA	1.2	THF	0	3	85	15	0
LiO-*t*-Bu	1	DABCO	2	THF	0	21	0	60	25
$LiCPh_3$	1			THF	25	14	0	100	0

[a] Estimated from the proton NMR spectrum. Where total is less than 100%, other products were present, including $PhSCH_2CH_3$. [b] Lithium 2,2,6,6-tetramethylpiperidide. [c] 1,4-Diazabicyclo[2.2.2]octane. [d] Hexamethylphosphoramide. [e] R = cyclohexyl, R′ = isopropyl. [f] 1,2-Bis(dimethylamino)ethane. [g] Lithium diisopropylamide.

analysis of the products. After each trial set of conditions for deprotonation of **2**, methyl iodide was added and allowed to react ~2 h at 20–25 °C, the mixture was worked up with aqueous acid, and the organic product was analyzed by proton NMR for $PhSCH_3$, SCH_2B, $SCH(CH_3B$, and SCH_2CH_3, each of which gave distinctive signals at 60 MHz.

The first attempts at deprotonation were made with the ethylene glycol ester **2a** and all failed totally. Bases tried included lithium 2,2,6,6-tetramethylpiperidide (LiTMP), *n*- and *tert*-butyllithium, and lithium *tert*-butoxide in tetrahydrofuran (THF). Additives, including hexamethylphosphoramide (HMPA), 1,4-diazabicyclo[2.2.2]octane (DABCO), or 1,2-bis(dimethylamino)ethane (TMEDA), did not help. The major product was always recovered (phenylthio)methaneboronic acid (**1**), often with lesser amounts of thioanisole ($PhSCH_3$) and sometimes ethyl phenyl sulfide ($PhSCH_2CH_3$). Thus, it appeared that these bases coordinate with the relatively unhindered boron atom of **2a** to form tetrahedral borates, which in some cases deboronate to a small extent to form $PhSCH_2Li$.

Successful deprotonation was immediately achieved with the sterically hindered pinacol ester **2b**. Pinacol lithio

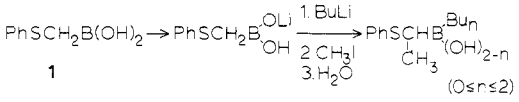


(phenylthio)methaneboronate (**3**) often precipitated from concentrated THF solutions and was readily methylated in situ to form pinacol 1-(phenylthio)ethane-1-boronate (**4**). Results are summarized in Table I. It may be noted that yields of **4** were generally good and not very sensitive to the base or conditions. The only failures encountered with the bases tested were with lithium *tert*-butoxide and triphenylmethyllithium.

Since lithium diisopropylamide (LDA) led to as high yields of **4** as any of the bases tested and is convenient and inexpensive, it was chosen for all further work. In some of the reactions where **3** was used in situ to be described in the remainder of this article, TMEDA was included as a lithium ion complexing agent, but its relevance is highly doubtful for reasons to be pointed out in the following section on the isolation of **3**. Early results seemed to indicate that the use of TMEDA or DABCO improved the yields of **4** somewhat, and this impression was reinforced by the finding in concurrent work that TMEDA was absolutely essential in the deprotonation of propanediol methanediboronate.[2]

Deprotonation of other (phenylthio)methaneboronic esters (**2**) was examined briefly, with LiTMP used as base and THF as solvent. Yields of methylated product from the 2,2-dimethyl-1,3-propanediol ester (**2c**) were 55–60% and yields from the dimethyl ester **2d**, zero. The propanediol ester[19] gave 45–50%. Thus, the steric hindrance to base attack at boron provided by the pinacol ester group appears to be essential.

An altogether different approach to deprotonation was explored briefly with some success. Treatment of (phenylthio)methaneboronic acid (**1**) with 3 equiv of *n*-butyl-



lithium in THF, with or without TMEDA, followed by methyl iodide resulted in 90% methylation, estimated by NMR. However, this C-methylation was incorporated into a mixture of B-butylated products. Less butyllithium gave less C-methylation and less B-butylation, and one equivalent yielded none of either. Attempts to deprotonate **1** with 3 equiv of LDA, sodium hydride, or lithium hydride led to no methylated product. The known deprotonation of carboxylate salts[20] provides a sort of precedent for the deprotonation of **1**. We were discouraged from further work on this system by the need for such a large excess of butyllithium and the inherent problem of dealing with a mixture of alkylborane products, even though the PhSCH(R)–B group of interest is common to all of them.

Isolation of Pinacol Lithio(phenylthio)methaneboronate (3). The precipitation of **3** during successful deprotonations of **2b** had been noted, and therefore the isolation and characterization of **3** were undertaken. The best yields of **3** precipitated from a mixture of THF, ether, and petroleum ether, and after the solid was collected under argon in a Schlenk apparatus and washed with additional solvent mixture, 80–85% yields of **3** as the monotetrahydrofuran complex were routinely obtained. Though this material is highly hygroscopic and sensitive to air, it yielded a satisfactory elemental analysis, and a solution in pyridine-d_5 showed the correct proton NMR spectrum for **3** (probably as an adduct with the solvent) with 1 mol of THF. If protected from air, solid **3**·THF appeared stable indefinitely.

Not all of the factors involved in the preparation of **3** are understood, and on a few occasions the precipitate proved fine or gummy and did not filter as rapidly as usual, with yields reduced to 60–70%. This problem was not

(19) Mendoza, A.; Matteson, D. S. *J. Organomet. Chem.* **1978**, *156*, 149–157.
(20) Creger, P. L. *J. Am. Chem. Soc.* **1967**, *89*, 2500–2501.

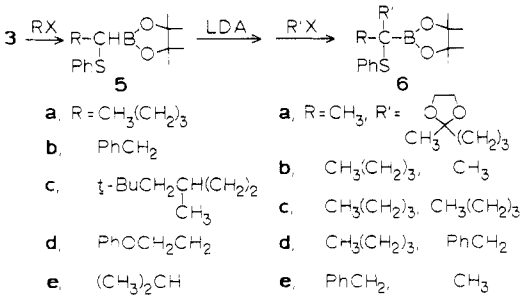
Table II. Alkylation of Pinacol Lithio(phenylthio)methaneboronate (3) with Alkyl Halides, RX, To Yield Pinacol 1-(Phenylthio)alkane-1-boronates 4 and 5

RX	method[a]	product	yield,[b] %
CH_3I	A	4	83[c]
CH_3I	B	4	84
n-C_4H_9Br	A	5a	80[c]
n-C_4H_9Br	B	5a	88
n-C_4H_9Cl	A	5a	76[c]
n-C_4H_9I	A	5a	79[c]
$(CH_3)_3CCH_2CH(CH_3)CH_2CH_2Br$	A	5c	58
$PhOCH_2CH_2Br$	A	5d	71
$PhCH_2Br$	A	5b	50–57
$PhCH_2Br$	B	5b	75[d]
$(CH_3)_2CHBr$	B	5e[e]	40[e]

[a] Method A is without isolation of 3, B is with isolation of 3, see text. [b] Distilled product. [c] Yield contained in a mixture with 10–12% of unconverted 2b. [d] We thank Abel Mendoza for this result. [e] Mixed with equal amount of 2b, not obtained pure.

frequent, and insufficient attention to excluding moisture is suspected. The presence or absence of TMEDA in the reaction mixture reproducibly showed no effect whatever on the yield of isolated 3, and TMEDA was not incorporated into the precipitate. Products prepared from isolated 3 were generally very pure and free from any unreacted boronic ester 2b.

Alkylations. As soon as the methylation studies had established that pinacol (phenylthio)methaneboronate (2b) could be deprotonated by LDA and the resulting lithio derivative 3 methylated in situ, alkylations with other primary halides were tried and found to yield pinacol 1-(phenylthio)alkane-1-boronates 5. Results are sum-



marized in Table II, "method A". It was later found that filtering and washing the precipitated lithio derivative 3 before alkylation led to improved yields and purities of 5, as shown in Table II, "method B". Isolation of 3 was crucial to obtaining a pure sample of the methylation product 4.

Even with isolated 3, secondary halides gave poor results. Isopropyl bromide yielded a 45/55 mixture of 5 and starting material 2b according to NMR analysis. 2-Pentyl bromide yielded only 10% of 5; 2-pentyl tosylate yielded 30–50% of 5.

Selected alkylation products (4, 5a, 5b) were tested for the possibility of a second deprotonation and alkylation. Deprotonation was readily accomplished with LDA in THF (without TMEDA). The lithio derivatives were all soluble in the reaction medium and were readily alkylated in situ to yield the dialkylated (phenylthio)methaneboronic esters 6, summarized in Table III. Little if any of the starting material 5 remained unconverted.

Hydrolysis and Oxidation of Pinacol Esters. Typical unhindered boronic esters hydrolyze immediately on contact with water, but pinacol boronic esters do not. Their unusual stability permits chromatography, extrac-

Table III. Alkylation of Pinacol 1-(Phenylthio)alkane-1-boronates 4 and 5 by Deprotonation with LDA and Treatment with Alkyl Halides, R'X

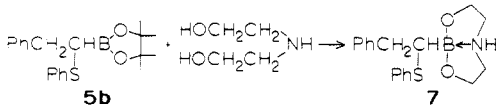
boronic ester	R	R'X	product	bp, °C (torr)	yield, %
4	CH_3	$CH_3C(O_2C_2H_4)(CH_2)_3Cl$	6a	174 (0.3)	71[a]
5a	n-Bu	CH_3I	6b	136 (0.1)	70
5a	n-Bu	n-BuBr	6c	150 (0.2)	67
5a	n-Bu	$PhCH_2Br$	6d	184 (0.5)	78
5b	$PhCH_2$	CH_3I	6e	160 (0.2)	77

[a] Reaction time 12 h, yield only 48% after 3 h.

tion, handling in air, and general treatment as stable organic compounds. The only inconvenience comes when it is time to run a carbon–boron bond-breaking reaction. For this purpose, it became desirable to find a way to cleave the pinacol efficiently from the boron.

Many pinacol boronic esters form rapidly at 20 °C from pinacol hydrate and the boronic acids, and the reverse process can be very slow only if the equilibrium constant for esterification is very high. Equilibria, including water/ether partitioning, appeared to be the major problem in a series of explorations of the hydrolysis of pinacol (phenylthio)methaneboronate (2b) by aqueous methanol containing aluminum chloride, phosphoric acid, or boric acid and ethanolamine, followed by dilution and extraction, all of which yielded 50–70% of boronic acid (1). Turning to a more sterically hindered and more relevant example, treatment of pinacol 1-(phenylthio)-2-phenylethane-1-boronate (5b) with methanol, boric acid, and ethanolamine followed by water/ether partitioning and crystallization from moist dichloromethane/petroleum ether yielded only 45% of the presumed boronic acid. Boiling 5b a few minutes in 2 M sulfuric acid in 1:1 water/tetramethylene sulfone, conditions vigorous enough to cause pinacol rearrangement, led to 58% of the presumed boronic acid, not enough for a good synthetic process.

Diethanolamine forms stable, crystalline, chelated esters with boronic acids.[21] Treatment of 5b with diethanolamine in 2-propanol/ether resulted in crystallization of analytically pure diethanolamine ester 7 (79–83%). This



solves the hydrolysis problem in principle, since diethanolamine esters are readily hydrolyzed by cold dilute acid, as was illustrated by the conversion of 2b to the diethanolamine ester (not characterized) to the boronic acid 1 in 70% overall yield. A more recent related example of diethanolamine ester hydrolysis has been reported.[22]

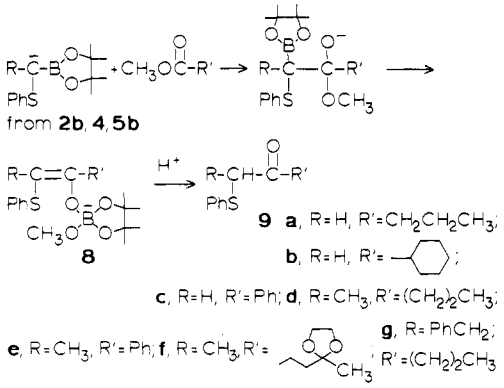
For oxidation of 5 to aldehyde equivalents, it is best to bypass the hydrolysis problem by using the facile reaction of 5 with N-chlorosuccinimide in methanol buffered with triethylamine, which yields monothioacetals or acetals.[19]

Several attempts to oxidize dialkylated (phenylthio)methaneboronic esters 6 to ketones have failed. For example, 6c was not attacked by sodium perborate[5] or hydrogen peroxide and sodium acetate[23] at 25 °C, and refluxing overnight with alkaline sodium perborate resulted mainly in protodeboronation to 5-(phenylthio)nonane ac-

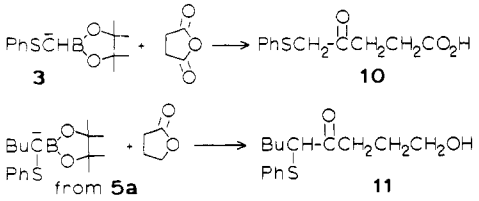
(21) Letsinger, R. L.; Skoog, I. J. Am. Chem. Soc. 1955, 77, 2491–2494.
(22) Matteson, D. S.; Ray, R. J. Am. Chem. Soc. 1980, 102, 7590–7591.
(23) Yamamoto, S.; Shiono, M.; Mukaiyama, T. Chem. Lett. 1973, 961–962.

cording to NMR evidence. *N*-Chlorosuccinimide in methanol[19] failed to attack **6d** even after extended reflux.

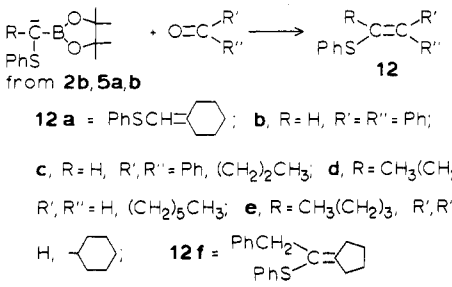
α-Phenylthio Ketones from Esters. By analogy to the acylation of carbanions from 1,1-diboronic esters with carboxylic esters to form ketones,[2] it was anticipated that acylation of the carbanions from 1-(phenylthio)alkane-1-boronic esters **2b**, **4**, and **5** with carboxylic esters would



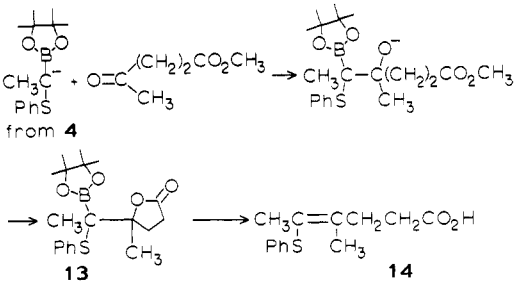
proceed by way of a postulated enol borate intermediate (**8**) to provide an efficient regiospecific synthesis of α-phenylthio ketones **9**, which are known to be useful synthetic intermediates.[24] These reactions worked very well, as shown in Table IV. Analogous acylation of **3** with succinic anhydride yielded the γ-keto acid **10**, and lithiated **5a** with γ-butyrolactone formed the γ-hydroxy ketone **11**.



Enethiol Ethers from Aldehydes and Ketones. Again by analogy to 1,1-diboronic ester chemistry,[2] it was expected that the carbanions derived from **2b**, **4**, and **5** would undergo Wittig type condensation with aldehydes and ketones, with elimination of boron to form enethiol ethers **12**. These reactions were also successful, as shown

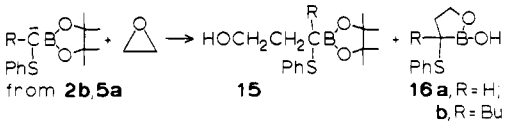


in Table V. On the basis of NMR spectra, it appeared that mixtures of *Z* and *E* isomers were obtained where possible. The reaction of lithiated **4** with methyl levulinate showed the expected preference for carbanion attack at the ketone group but provided a minor surprise in the total hydrolysis of the methyl ester. Perhaps an intermediate lactone (**13**) is formed, which undergoes elimination to form the salt of the isolated carboxylic acid (**14**). The major isomer of **14** crystallized, leaving an apparent mix-

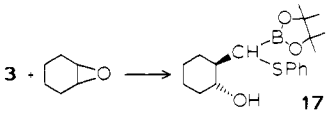


ture of isomers in the mother liquor.

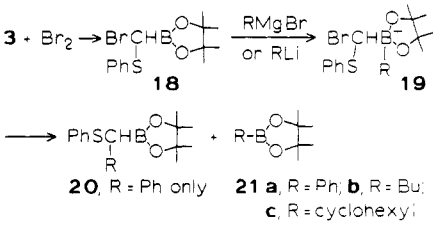
Epoxide Openings. Reaction of **3** or lithiated **5a** with



ethylene oxide occurred readily enough, but product isolation was complicated by partial hydrolysis of the initially formed pinacol boronic ester (**15**) to form a cyclic boronic half ester (**16**), which was the product isolated in each case. The investigation was not pursued to find a way to control the reaction to produce either pure **15** or pure **16**. However, reaction of **3** with cyclohexene oxide produced a single product (**17**), in which the hydroxyl group is not in a position to cyclize to the boronic ester group.



Bromination. Isolation of the lithium salt **3** and bro-



mination at −78 °C in ether yielded pinacol bromo(phenylthio)methaneboronate (**18**), which could be purified on a small scale by molecular distillation. Treatment of crude **18** with phenylmagnesium bromide was expected to yield a *B*-phenyl borate complex (**19a**), which would rearrange to pinacol (phenylthio)phenylmethaneboronate (**20**) if it followed well-established precedent.[26,27] However, the yield of **20** was only 57% of impure material. A major byproduct based on NMR evidence was the cleavage product, pinacol phenylboronate (**21a**) (35%). When **18** was treated with butyllithium or cyclohexylmagnesium bromide, no alkyl migration product analogous to **20** could be detected, only the cleavage product **21b** or **21c** mixed with unidentified byproducts. Thus, the hope of establishing a synthetic route to 1-(phenylthio)alkane-1-boronic esters **5** not accessible by alkylation of **3** was not realized. However, an indirect route to this goal involving some analogous chemistry has been found more recently.[28]

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Table IV. Acylation of Lithiated Pinacol 1-(Phenylthio)alkane-1-boronates, $RCLi(SPh)BO_2C_2Me_4$, by Esters or an Anhydride To Yield α-Phenylthio Ketones, RCH(SPh)COR′, 9, 10, and 11

boronic ester	R	acylating agent $R'CO_2CH_3$ or other	product[a]	yield, %
2b	H	$CH_3(CH_2)_2CO_2CH_3$[b]	**9a**	82
2b	H	$c\text{-}C_6H_{11}CO_2CH_3$	**9b**	80
2b	H	$PhCO_2CH_3$[c]	**9c**[d]	75
2b	H	succinic anhydride	**10**[e]	74
4	CH_3	$CH_3(CH_2)_2CO_2CH_3$[f]	**9d**	81
4	CH_3	$PhCO_2CH_3$	**9e**	86
4	CH_3	$CH_3C(O_2C_2H_4)(CH_2)_2CO_2CH_3$[g]	**9f**[h]	66
5a	*n*-Bu	butyrolactone[i]	**11**	50
5b	$PhCH_2$	$CH_3(CH_2)_2CO_2CH_3$	**9g**[j]	82

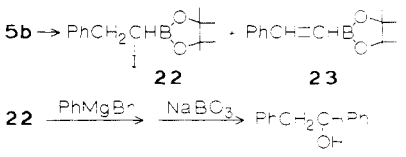
[a] Isolated by preparative TLC as analytically pure oils, except as noted. [b] Added dropwise over 30 min period at 35 °C. [c] Reacted with isolated **3**. [d] From aqueous ethanol, mp 53-54 °C (lit.[25] mp 53-54 °C). [e] From ether, mp 78-79 °C. [f] Added at −78 °C. Addition at 0 °C yielded only 63%. [g] Impurity present by NMR, may have lowered yield of **9f**. [h] Omitted washing with acid in order to preserve ketal. [i] Added dropwise at 40 °C, probably not optimum conditions. [j] Distilled, bp 161-163 °C (0.2 torr).

Table V. Wittig Condensation of Pinacol 1-Lithio-1-(phenylthio)alkane-1-boronates, $RCLi(SPh)BO_2C_2Me_4$, with Aldehydes or Ketones, R′COR″, To Yield Enethiol Ethers, R′R″C=C(SPh)R, 12 and 14

boronic ester	R	aldehyde or ketone	product	bp, °C (torr)	yield, %
2b	H	cyclohexanone	**12a**	110 (0.2)[a]	71
2b	H	PhCOPh	**12b**	cryst[b]	71
2b	H	$PhCOCH_2CH_2CH_3$	**12c**[c]	130 (0.1)	82
5a	*n*-Bu	$CH_3(CH_2)_5CHO$[d]	**12d**[c]	116 (0.1)	86
5a	*n*-Bu	$c\text{-}C_6H_{11}CHO$	**12e**[c]	136-139 (0.1)	84
4	CH_3	$CH_3COCH_2CH_2CO_2CH_3$	**14**[e]	cryst[e]	61
5b	$PhCH_2$	cyclopentanone	**12f**	156-158 (0.25)	81

[a] Lit.[15] bp 133 °C (1.1 torr). [b] From aqueous ethanol, mp 68-70 °C (lit.[10] mp 71 °C). [c] Mixture of *E* and *Z* isomers. [d] A 20% excess was used. [e] Note that the product is a free carboxylic acid. One isomer crystallized first from ether/petroleum ether, mp 83-85 °C. The second crop was a mixture of geometric isomers.

An α-Iodo Boronic Ester. 1-(Phenylthio)alkanes are readily converted to 1-iodoalkanes by methyl iodide and sodium iodide in dimethylformamide.[11] When pinacol 1-(phenylthio)-2-phenylethane-1-boronate (**5b**) was sub-



jected to the reported conditions, a low yield of pinacol 1-iodo-2-phenylethane-1-boronate (**22**) was obtained together with the 2-phenyletheneboronate (**23**). Reducing the temperature to 25 °C and extending the time to 3 days yielded mainly **22**, though analytical purity was not achieved. The structure of **22** was proved by replacement of the halide with phenylmagnesium bromide[26] followed by oxidation of the resulting pinacol 1,2-diphenylethaneboronate with sodium perborate[5] to yield 1,2-diphenylethanol.

Previous syntheses of α-halo boronic esters had been laborious[29] or restricted to α-branched carbon chains and other special structural types.[30] The method described here has been extended to provide the most convenient synthesis of iodomethaneboronic esters known to date.[31] However, for other general purposes this approach has been superseded by the recently developed homologation of boronic esters with dichloromethyllithium to yield α-chloro boronic esters.[22,28]

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Discussion

Our results show that pinacol (phenylthio)methaneboronate (**2b**) by way of its lithio derivative (**3**) can furnish a highly versatile connecting carbon for synthetic purposes. It is possible to classify **3** as a formyl anion equivalent, but **3** can also function as a Wittig reagent and, in the reaction with esters, as a new type of reagent entirely, a self-protecting source of $PhSCH_2^-$ for converting RCO_2CH_3 to $RCOCH_2SPh$ without further reaction of the ketone. Since **3** can be alkylated and the resulting 1-(phenylthio)alkane-1-boronic esters **5** can be lithiated and undergo a similar range of reactions, convergent syntheses can be designed in which two major fragments are ultimately joined to the central carbon provided by **3**.

Alkylation of **3** provides an efficient conversion of R–X to R–CHO by way of the monothioacetal $R\text{–}CH(SPh)OCH_3$ or acetal $R\text{–}CH(OCH_3)_2$.[19] There are a number of other good routes from R–X to R–CHO, including the well-known use of dithiane[12] and the use of a methanediboronic ester.[2] The route most closely related to that based on **3**, and perhaps the most competitive from the standpoint of efficiency and convenience, is that based on alkylation of lithiated $PhSCH_2SiMe_3$.[32] The use of **3** to convert R–X to $R\text{–}CH(SPh)OCH_3$ takes on added interest in view of the recent report that monothioacetals can be reduced to α-lithioalkyl methyl ethers, $R\text{–}CHLiOCH_3$.[33] A simpler alternative, described explicitly only in the case of alkylation by an allylic halide, might be the use of lithiated $PhSCH_2OCH_3$ to provide the monothioacetal directly.[16] The most useful application of the alkylation of **3** is likely to be to provide 1-(phenylthio)alkane-1-boronic esters **5** as synthetic intermediates for further carbon–carbon connections. Although this route to **5** is restricted to primary alkyl halides R–X, the general availa-

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bility of α-chloro boronic esters R–CHCl–B(OR′)$_2$ by homologation of R–B(OR′)$_2$ has made it possible to synthesize analogues of **5** containing branched alkyl groups R.[28]

The unique and most promising feature of α-phenylthio boronic ester chemistry is the condensation of **3** or lithiated **5** with carboxylic esters to yield α-phenylthio ketones **9**. The synthetic utility of this class of compounds has been demonstrated by Trost and co-workers.[24] However, the usual preparative route involves treatment of an enolate with diphenyl disulfide[24] and is therefore not regiospecific for unsymmetrical ketones. Our new route to **9** is regiospecific by nature and assembles the carbon skeleton in the same operation.

The boronic ester group provides vital activation and protection during the synthesis of **9**, even though it is lost in the process. It appears that the normal mode of reaction of (phenylthio)methyllithium, PhSCH$_2$Li, with carboxylic esters, R–CO$_2$CH$_3$, is double addition to form the carbinol, R–C(OH)(CH$_2$SPh)$_2$.[34] If the carboxyl group is sterically hindered, as in (CH$_3$)$_3$CCO$_2$CH$_3$ or poly(methyl methacrylate), it is possible to obtain the alkyl (phenylthio)methyl ketone, R–COCH$_2$SPh, in good yield at the cost of consuming two mols of the lithium reagent, the intermediate which protects the ketone being R–COCHLiSPh.[35] The α-phenylthio ketone has also been obtained from the reaction of lithiated isobutyl phenyl sulfide with methyl benzoate, though not in good yield.[18] Lithiation of higher homologues of PhSCH$_3$ requires special conditions,[18] and it is not clear from the published report whether this lithiation will work with any alkyl groups other than isobutyl or 2-methylalkyl. Thus, the general access to alkyl groups provided by deprotonation of **5** is significant, as is the comsumption of only 1 mol of **5** in the reaction to produce **9**.

As in the analogous reactions of propanediol lithiomethanediboronate with carboxylic esters,[2] we postulate that reactions of **3** or lithiated **5** with esters stop at the ketone stage because of rapid rearrangement of the initial adducts to stable boron enolates (**8**). Although the existence of **8** has not been proved and a few attempts to trap such an intermediate by alkylation have been inconclusive, **8** should be thermodynamically stable. Boron–oxygen bonds are 30–40 kcal/mol stronger than boron–carbon bonds if the boron is tricoordinate,[36] and on the basis of measured pK values,[37] coordination to methoxide will have a negligible effect. The exothermicity will be slightly diminished as a result of converting a keto structure B—C—C=O to an enol C=C—O—B. Intramolecular 1,3-suprafacial shift of boron is symmetry forbidden by the Woodward–Hoffmann rules if the boron is kept firmly tetracoordinate by the basicity of the ligands, but expulsion of alkoxide to provide a vacant orbital voids the symmetry restriction, and it seems likely that this or some other mechanism for formation of **8** will have a low activation energy.

The use of **3** or lithiated **5** as α-substituted Wittig reagents in condensations with aldehydes or ketones to produce enethiol ethers **12** also has considerable synthetic potential. Enethiol ethers can be unmasked to aldehydes or ketones, though the conditions are somewhat vigorous.[38] Allylic oxidation of enethiol ethers is a useful synthetic operation.[39] A prostaglandin synthesis utilizes enethiol ethers prepared by means of the Wittig reagent PhSCH=PPh$_3$.[40]

Our results suggest that α-phenylthio boronic esters may be the best reagents yet found for the Wittig route to enethiol ethers, but there are alternatives to consider. Yields from PhSCHLiSiMe$_3$,[15] PhSCH=PPh$_3$, or BuSCH=PPh$_3$[41] appear to average somewhat lower than ours, and RSC(CH$_3$)=PPh$_3$[41] is definitely inferior to lithiated **5**. Unprotected hydroxyl groups in sugars are tolerated by PhSCH=PPh$_3$,[42] a feature which our reagents cannot match. The phosphonate CH$_3$SCHLiPO(OEt)$_2$ can also undergo Wittig reactions but shows a tendency to promote aldol condensations.[17]

The reaction of ethylene oxide with **3** or **5a** appeared to proceed in high yield, but the mixture of **15** and **16** produced is a nuisance from a synthetic point of view. Presumably, this reaction could be adjusted to provide a single product if there were sufficient incentive. However, the silicon analogue of **3**, PhSCHLiSiMe$_3$, already gives high yields of pure products with epoxides.[32]

The use of an α-phenylthio boronic ester **5** as a source of RCHLiSPh by deboronation has been reported elsewhere.[4a] The temperature required was high enough to require immediate trapping of the anion, which was efficiently accomplished with methyl iodide, but further investigation did not seem warranted.

Other possible applications of α-(phenylthio)alkaneboronic ester chemistry remain to be explored. The inertness of the dialkylated series **6** discouraged us from trying to develop a ketone synthesis based on these compounds. However, new opportunities to make **6** may arise as a consequence of other recent synthetic developments,[22,28] and possibilities remain for oxidative or reductive cleavage of either the boron or the sulfur. Conjugate addition of **3** to α,β-unsaturated ketones and esters and conversion of **5** to α-phenylthio aldehydes have been accomplished recently and will be reported elsewhere.[43]

It may be concluded that α-phenylthio boronic esters are easily prepared and handled, that they are capable of undergoing some unique transformations, and that they are highly promising reagents for organic synthesis.

Experimental Section

General. Reactions were run under argon or nitrogen. Tetrahydrofuran (THF) and diethyl ether (ether) were distilled from sodium benzophenone ketyl. Other anhydrous solvents and reagents were distilled from calcium hydride. Butyllithium was 2 M in hexane, checked by titration with isopropyl alcohol with 1,10-phenanthroline as indicator.[44] Proton NMR spectra were recorded at 60 MHz with a Varian EM-360 instrument and are referred to internal tetramethylsilane.[45] Infrared spectra were recorded with a Beckman IR-5 or IR-18A. Glassware was dried at 130 °C for 1 h and flushed with argon during assembly. Extensive use was made of "Airless Ware" Schlenk type glassware from Kontes Glass Corp. Syringes and needles were used to transfer liquids. Elemental analyses were by Galbraith Laboratories, Knoxville, TN.

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(43) Ray, R.; Matteson, D. S., manuscript in preparation.
(44) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165–168.
(45) Recent recalibration of this instrument has indicated that all δ values were 2.7% too large (δ 0.2 at δ 7.5) at the time these measurements were made. A few spectra taken on a JEOL MH-100 also have yielded slightly smaller δ values than those tabulated.

Table VI. Physical Properties of Pinacol 1-(Phenylthio)alkane-1-boronates 4 and 5 from Alkylation of Pinacol (Phenylthio)methaneboronate (2b)

		NMR ($CDCl_3$),[a] δ				C		H		B		S	
compd	bp, °C (torr)	SCHB	R	CCH_3	C_6H_5S	calcd	found	calcd	found	calcd	found	calcd	found
4	125-127 (0.7)	2.99 q	1.36 d	1.20	7.50	63.65	63.41	8.01	8.09	4.09	3.95	12.14	12.05
5a	115-120 (0.1)	2.80 t	0.9 m, 1.5 m	1.21	7.42	66.67	66.74	8.89	8.97	3.53	3.45	10.47	10.42
5b	140-145 (0.05)	3.10 s	3.10 s, 7.35	1.14	7.35	70.59	70.72	7.41	7.42	3.18	3.08	9.42	9.57
5c	160-165 (0.3)	2.82 t	0.91 s (*t*-Bu), 0.6-1.9 m	1.23	7.47	70.20	70.44	9.91	10.01	2.87	2.85	8.52	8.49
5d	146-150 (0.1)	3.05 t	2.26 m, 4.16 t, 6.8-7.7 m	1.21	6.8-7.7	68.11	68.24	7.35	7.25	2.92	2.85	8.66	8.77
5e	115-117 (0.2)	2.63 d	1.1 obscured	1.17	7.3	not purified							

[a] Correct integrals were obtained (except for 5e). The pinacol CCH_3 appeared as a singlet and the C_6H_5S as a multiplet.

(Phenylthio)methaneboronic Acid (1). (Phenylthio)methyllithium was prepared by a modification of the published procedure[10] from thioanisole (1 mol) and 1,2-bis(dimethylamino)ethane (TMEDA) (1 mol) in THF (700 mL) treated with butyllithium (1 mol) at or below 20 °C and kept 1 h at 20 °C. The solution was cooled with a −78 °C bath and stirred during the dropwise addition of trimethyl borate (1.3 mol) over a period of 1 h. Stirring was continued overnight as the mixture warmed to 20 °C. The mixture was partially concentrated under vacuum, and the residue was treated with 130 mL of 85% phosphoric acid and 100 g of ice and the mixture then extracted with ether (3 × 300 mL). The organic phase was washed with water and concentrated under vacuum. The residue was recrystallized from moist ether/petroleum ether to yield 77–94% of 1 in two crops, mp 109–110 °C. Excessive drying of 1 should be avoided.[46] NMR (CD_3SOCD_3): δ 2.25 (s, 2, SCH_2B), 3.5 (s, 15 Hz wide at half height, 2, OH), 7.34 (m, 5, C_6H_5). Anal. Calcd for $C_7H_9BO_2S$: C, 50.04; H, 5.40; B, 6.43; S, 19.08. Found: C, 49.95; H, 5.52; B, 6.40; S, 18.99.

Ethylene Glycol (Phenylthio)methaneboronate (2a). Equimolar amounts of ethylene glycol and 1 were heated in benzene to distil the benzene–water azeotrope, the solution was concentrated, and the residue was crystallized from ether/petroleum ether, yielding 85% of 2, mp 65–66.5 °C. NMR ($CDCl_3$): δ 2.51 (s, 2, SCH_2B), 4.25 (s, 4, OCH_2), 7.26 (m, 5, C_6H_5). Anal. Calcd for $C_9H_{11}BO_2S$: C, 55.70; H, 5.71; B, 5.57; S, 16.52. Found: C, 55.70; H, 5.91; B, 5.70; S, 16.70.

Pinacol (Phenylthio)methaneboronate (2b). Pinacol or pinacol hydrate (1 mol) and 1 (1 mol) were stirred in ether (1 L) until the solids dissolved and two liquid phases remained. The phases were separated, the ether phase was washed with a little water and dried over magnesium sulfate, and 2b was distilled: bp 105–108 °C (0.1 torr); 89–97%. 2b may be kept indefinitely as a liquid, but cooling a pure sample to −78 °C and scratching induced crystallization; mp 33–36 °C. NMR ($CDCl_3$): δ 1.17 (s, 12, CCH_3), 2.38 (s, 2, SCH_2B), 7.30 (m, 5, C_6H_5). Anal. Calcd for $C_{13}H_{19}BO_2S$: C, 62.42; H, 7.66; B, 4.32; S, 12.82. Found: C, 62.65; H, 7.82; B, 4.14; S, 12.62.

2,2-Dimethyl-1,3-propanediol (Phenylthio)methaneboronate (2c). The azeotrope was distilled from an equimolar mixture of 2,2-dimethyl-1,3-propanediol and 1 in toluene, and 2c was distilled: bp 108–112 °C (0.3 torr); 87%. NMR ($CDCl_3$): δ 0.90 (s, 6, CCH_3), 2.36 (s, 2, SCH_2B), 3.64 (s, 4, OCH_2), 7.13–7.65 (m, 5, C_6H_5). Anal. Calcd for $C_{12}H_{17}BO_2S$: C, 61.04; H, 7.26; B, 4.58; S, 13.58. Found: C, 60.88; H, 7.36; B, 4.62; S, 13.34.

Dimethyl (Phenylthio)methaneboronate (2d). A 10% solution of 1 in 2,2-dimethoxypropane was distilled slowly to remove the esterification byproducts, acetone, and methanol, and 2d was distilled: bp 85–88 °C (0.5 torr); 88%. NMR ($CDCl_3$): δ 2.37 (s, 2, SCH_2B), 3.62 (s, 6, OCH_3), 7.15–7.8 (m, 5, C_6H_5). Anal. Calcd for $C_9H_{13}BO_2S$: C, 55.13; H, 6.68; B, 5.51; S, 16.35. Found: C, 55.30; H, 6.77; B, 5.51; S, 16.45.

Pinacol Lithio(phenylthio)methaneboronate (3). Butyllithium (15 mmol) in hexane was added dropwise to diisopropylamine (15.7 mmol) in THF (5 mL) stirred at 0 °C in a 100-mL Schlenk flask. A solution of pinacol (phenylthio)methaneboronate (2b) (15 mmol) in THF (5 mL) was added rapidly dropwise, yielding a white precipitate. Ether (10 mL) and light petroleum ether (10 mL) were added to complete precipitation. After 1 h of stirring at 0 °C, the mixture was cooled with a −78 °C bath and filtered. The collected 3 was washed with chilled (0 °C) ether and dried under vacuum (0.1 torr) 4 h at 25 °C, yield 80–85% as the complex with 1 mol of THF. Rigorous exclusion of air was maintained in all operations with 3. NMR (pyridine-d_5): δ 1.20 (s, 12, CCH_3), 1.7 (m, 4, OCH_2CH_2), 2.18 (s, 1, SCHB), 3.8 (m, 4, OCH_2CH_2), 7.55 (m, 5, C_6H_5). Anal. Calcd for $C_{17}H_{26}BLiO_3S$: C, 62.21; H, 7.98; B, 3.29; Li, 2.11; S, 9.77. Found: C, 62.34; H, 7.89; B, 3.26; Li, 2.09; S, 9.62.

Alkylation of Pinacol (Phenylthio)methaneboronate (2b). Method A. A solution of 5 mmol of diisopropylamine and 12 mmol of TMEDA in 50 mL of THF was treated with 5 mmol of butyllithium at 0 °C followed by 5 mmol of 2b. After 1 h at 0 °C the mixture was treated with 5 mmol of the selected alkyl halide and stirred at 20 °C 6–16 h. The mixture was treated with excess cold 10% phosphoric acid, and the product (4 or 5) was extracted with ether and distilled. Yields are listed in Table II. Physical properties are summarized in Table VI. **Method B.** Pinacol lithio(phenylthio)methaneboronate (3) was isolated as described in the preceding paragraph and transferred under argon to a reaction vessel with the aid of THF (2–5 mL/mmol of 3). The slurry was stirred at 0 °C, 1 equiv of alkyl halide was added, and stirring was continued 2–12 h at 20–25 °C. Excess cold 10% phosphoric acid was added, and the product (4 or 5) was extracted with ether and distilled. Yields are summarized in Table II and physical properties in Table VI.

Deprotonation of Pinacol 1-(Phenylthio)alkane-1-boronates 4, 5, and 2b. Butyllithium (5 mmol) was added to diisopropylamine (5 mmol) in THF (20–25 mL) with stirring at 0 °C. The selected pinacol 1-(phenylthio)alkane-1-boronate (4, 5, or 2b) (5 mmol) was injected from a syringe, either through a wide-bore needle or with the aid of a few milliliters of THF to reduce the viscosity. The mixture was stirred at least 2 h at 0 °C before use. Longer times up to 20 h gave the same results. Shorter times were not tried, except that 2b yields 3 rapidly.

Alkylation of Deprotonated 4 and 5 to Pinacol α-(Phenylthio)alkaneboronates (6). Deprotonation of 4 or 5 was carried out as described in the preceding paragraph. The selected alkyl halide (5 mmol) was added and the mixture was kept 2–4 h at room temperature. Aqueous 10% phosphoric acid was then added and the product (6) was extracted with ether and distilled. Yields and boiling points are recorded in Table III and proton NMR and analytical data in Table VII.

Acylation–Deboronation of Deprotonated 2b, 4, and 5 to α-Phenylthio Ketones 9, 10, and 11. Deprotonation of 2b, 4, or 5 was carried out in the usual manner (1-mmol scale) and 0.8 equiv of the selected methyl ester, anhydride, or lactone was injected at 0 °C. After 6–16 h at room temperature, the mixture was concentrated under vacuum. The residue was dissolved in pentane and washed with 3 M sodium hydroxide (30 mL for 1-mmol scale), 10% phosphoric acid (30 mL), and water (30 mL). The product (9, 11) was purified by chromatography on a silica gel plate with pentane/ether (20:1 or 10:1) as solvent. Yields are listed in Table IV, where some exceptions to the general procedure are also noted. The acid 10 was isolated by extraction from ether into aqueous sodium bicarbonate, which on acidification pre-

(46) Boronic acids may become air sensitive if dried to the point of boronic anhydride formation but are stable on storage if moist. Commercial samples of butaneboronic acid and others usually contain some water as a preservative.

Table VII. Proton NMR and Analytical Data for Pinacol α-(Phenylthio)alkaneboronates (6) Derived from Pinacol (Phenylthio)methaneboronate (2b) by Two Alkylations

	NMR ($CDCl_3$),[a] δ				C		H		B		S	
compd	R	R′	CCH_3	C_6H_5S	calcd	found	calcd	found	calcd	found	calcd	found
6a	CH_3 1.2 s[b]	1.23,[b] 1.5, 3.87 s	1.18	7.2–7.8	64.28	64.04	8.48	8.30	2.76	2.78	8.17	8.29
6b	Bu 0.9, 1.5 m	CH_3 1.24 s	1.19	7.3–7.7	67.50	67.46	9.13	9.10	3.38	3.47	10.01	10.26
6c	Bu 0.9, 1.5 m	Bu 0.9, 1.5 m	1.20	7.3–7.7	69.60	69.81	9.74	9.67	2.98	2.77	8.85	8.91
6d	Bu 0.9, 1.5 m	2.93 d, 3.11 d, 7.4[c]	1.16	7.3–7.7	73.85	73.74	6.97	7.17	2.77	2.54	8.21	7.96
6e	CH_3 1.17 s	2.86 d, 3.31 d, 7.4[c]	1.21, 1.23	7.3–7.9	71.19	71.38	7.68	7.78	3.05	3.35	9.05	8.85

[a] Correct integrals were obtained. Pinacol CCH_3 was a singlet, except that **6e** showed two closely spaced singlets. PhS appeared as a multiplet. [b] R′ is $CH_3C(O_2C_2H_4)(CH_2)_3$. One CH_3 appears at δ 1.23 on the side of the pinacol CCH_3; the other is obscured. [c] R′ is benzyl. The CH_2 appears as an AB pattern, J = 14 Hz and the C_6H_5 as a single peak in the midst of the PhS multiplet.

Table VIII. Proton NMR and Analytical Data for α-Phenylthio Ketones, RCH(SPh)COR′, 9, 10, and 11

	NMR ($CDCl_3$),[a] δ				C		H		S	
compd	R	CHSPh[b]	COCH of R′	other R′	calcd	found	calcd	found	calcd	found
9a	H 3.72 s	3.72 s	2.58 t	CH_2 1.65 m, CH_3 0.87 t	68.00	68.26	7.26	7.02	16.50	16.31
9b	H 3.79 s	3.79 s	2.7 m	$(CH_2)_5$ 1.2–1.9 m	71.75	71.61	7.74	7.69	13.68	13.38
9d	CH_3 1.41 d	3.85 q	2.63 t	CH_2 1.6 m, CH_3 0.90 t	69.19	69.40	7.74	7.77	15.39	15.10
9e	CH_3 1.48 d	4.61 q	none	Ph 7.2–7.7, 8.0–8.2 m	74.34	74.14	5.82	5.98	13.23	13.07
9f	CH_3 1.42 d	3.85 m	2.76 m	1.99 m, 3.95 s, 1.32 s[c]	64.26	64.51	7.19	7.36	11.44	11.23
9g[d]	C_6H_5 7.15 s[b] CH_2 3.03 m	3.82 t	2.30 m	CH_2 1.46 m, CH_3 0.80 t	76.01	76.43	7.09	6.92	11.27	11.14
10	H 3.79 s	3.79 s	2.85 m	2.85 m, CO_2H 7.8 s	58.91	59.15	5.39	5.50	14.30	14.33
11	Bu 0.85, 1.5 m	3.65 m	2.67 m	1.85 m, 3.65 m[e]	67.63	68.04	8.32	8.34	12.04	12.22

[a] Satisfactory integrals were obtained. [b] The SC_6H_5 absorption was a single peak near δ 7.4 in all cases, except for **9g**, the spectrum of which was redetermined after the instrument was recalibrated, δ 7.25. [c] Peaks for CH_2, $C(O_2C_2H_4)$, CH_3, respectively. [d] IR: (C=O, 1700 cm^{-1}. [e] Peaks for CH_2, CH_2O, respectively, OH obscured.

Table IX. Proton NMR and Analytical Data for Enethiol Ethers, PhSCR=CR′R″, 12 and 14

	NMR ($CDCl_3$),[a] δ			C		H		S	
compd	R	R′	R″	calcd	found	calcd	found	calcd	found
12c	H 6.36, 6.57[b]	Ph 7.4	CH_2 2.6 m, CH_2 1.4 m, CH_3 0.88 m	80.26	80.07	7.13	7.20	12.60	12.73
12d[c]	Bu 0.9, 1.3 m 2.2 m	H 5.83 m[c]	$(CH_2)_5$ 1.3 m, 2.2 m, CH_3 0.9 m	78.20	78.30	10.21	10.14	11.60	11.56
12e[d]	Bu 0.85, 1.4 m	H 5.78, 5.91 s	$(CH_2)_5$ 1.3–1.7, CH 2.7 m	78.77	78.66	9.55	9.71	11.68	11.53
12f	C_6H_5 7.33 s CH_2 3.63 s	CH_2 1.78, 2.58 m		81.38	81.47	7.19	7.31	11.43	11.23
14	CH_3 2.02 s	CH_3 2.05 s	$(CH_2)_2$ 2.61 s CO_2H 12.0 s	66.07	66.08	6.82	6.83	13.57	13.57

[a] Satisfactory integrals were obtained. The PhS peak appeared as a singlet at δ 7.35–7.45. [b] The two C=CH peaks of approximately equal size imply two geometric isomers. [c] Spectrum taken after recalibration of NMR instrument, PhS at δ 7.17. The C=CH absorption appears as two overlapping triplets 2 Hz apart, perhaps resulting from two geometric isomers in nearly equal amounts.

cipitated some **10**, the remainder being recovered by extraction with ether. Proton NMR and analytical data for the new compounds are listed in Table VIII.

Enethiol Ethers 12 and 14 from Deprotonated Boronic Esters 2b, 4, and 5 and Aldehydes or Ketones. The deprotonation of **2b**, **4**, or **5** was carried out in the usual manner (5-mmol scale). The mixture was cooled to −78 °C before the aldehyde or ketone (4–5 mmol) was injected, then allowed to warm slowly to 20 °C, and stirred 12–16 h. Pentane (50 mL) was added, and the mixture was extracted successively with 3 M sodium hydroxide (50 mL), 10% phosphoric acid (50 mL), and water. The organic phase was concentrated, and the product **12** was distilled or recrystallized. The acidic product **14** was found on acidification of the sodium hydroxide extract, and was purified by way of extraction into sodium bicarbonate. Recrystallization from ether/petroleum ether yielded 26% of **14** and 35% of a second crop containing **14** and its geometric isomer according to NMR analysis. Yields and boiling or melting points are summarized in Table V and proton NMR and analytical data for the new compounds in Table IX. NMR spectra in agreement with the published data were obtained for **12a**[15] and **12b**.[10]

2-Hydroxy-3-(phenylthio)-1,2-oxaborolane (16a). Deprotonation of **2b** (50 mmol) was carried out in the usual manner. The mixture was cooled to −78 °C, and ethylene oxide (57 mmol) was introduced by distillation through a double-ended needle. The mixture was allowed to warm slowly to 20 °C, stirred 16 h, concentrated, and treated with ether and 10% phosphoric acid. Analysis of the ether extract by NMR indicated a mixture of pinacol 3-hydroxy-1-(phenylthio)propane-1-boronate (**15a**) and its hydrolysis product (**16a**), which was refluxed overnight with boric acid (6 g) and sodium borate (6 g) in water (50 mL) in an attempt to complete the hydrolysis. Crystallization from ether/petroleum ether, with repetition of the hydrolysis on the mother liquor to produce a second crop, yielded 39% of **16a**, mp 104–106 °C. NMR ($CDCl_3$): δ 1.98 (m, CCH_2C), 2.35 (m, SCHB), 4.01 (m, CH_2O), 5.3 (br, OH), 7.29 (m, C_6H_5). Anal. Calcd for $C_9H_{11}BO_2S$: C, 55.70; H, 5.71; B, 5.57; S, 16.52. Found: C, 55.68; H, 5.64; B, 5.39; S, 16.73.

3-Butyl-2-methoxy-3-(phenylthio)-1,2-oxaborolane (Methyl Ester of 16b). The procedure used to make **16a** was followed

with **5a** in place of **2b**, up to the point where a mixture of **15b** and **16b** was first obtained. Attempted separation of the pinacol by steam distillation resulted in distillation of all of the product. Chromatography on silica yielded a fraction which appeared to be largely **16b** by NMR analysis. This was converted to the methyl ester of **16b** by treatment with 2,2-dimethoxypropane and distillation: bp 115 °C (0.4 torr); 15%. NMR ($CDCl_3$): δ 0.91 (m, 3, CH_3), 1.1–2.2 (m, 8, CCH_2C), 3.57 (s, 3, OCH_3), 4.2 (m, 2, CH_2O), 7.3–7.8 (m, 5, C_6H_5). Anal. Calcd for $C_{14}H_{21}BO_2S$: C, 63.65; H, 8.01; B, 4.09; S, 12.14. Found: C, 63.73; H, 8.09; B, 3.97; S, 12.13.

Pinacol (*trans*-2-Hydroxycyclohexyl)(phenylthio)methaneboronate (17). The lithium salt **3** (12 mmol) in THF (20 mL) was treated with cyclohexene oxide (12 mmol) at 0 °C and stirred 20 h at 25 °C. The solution was concentrated, water (75 mL) was added, and the product **17** was extracted into ether, washed with water, and isolated by concentration under vacuum as a viscous oil (diastereoisomers probable), 91%, analytically pure. NMR ($CDCl_3$): δ 1.22 (s, 12, CCH_3), 0.9–2.4 (m, 9, $(CH_2)_4CH$), 2.83 (d, 1, SCHB), 3.33 (s, 1, OH), 3.65 (br, 1, CHOH), 7.43 (s, 5, C_6H_5). NMR (CD_3OD): δ 1.20, 1.25 (s, s, 12, CCH_3), 0.9–2.4 (m, 9, $(CH_2)_4CH$), 2.83 (d, 1, SCHB), 3.46 (br, 1, CHOD), 5.3 (s, CD_3OH), 7–7.4 (m, 5, C_6H_5). Anal. Calcd for $C_{19}H_{29}BO_3S$: C, 65.52; H, 8.39; B, 3.10; S, 9.21. Found: C, 65.66; H, 8.15; B, 3.17; S, 9.48. Further evidence in support of structure **17** was obtained by *N*-chlorosuccinimide oxidation in methanol[19] to the dimethyl ketal, which was converted to *trans*-2-hydroxycyclohexanecarboxaldehyde 2,4-dinitrophenylhydrazone, which was characterized only by 100-MHz proton NMR (CD_3SOCD_3 + CD_3OD): δ 1.3 (m, 6, $(CH_2)_3$), 1.8 (m, 3, CHCOH), 3.43 (unresolved m, 25–30 Hz wide at a half-height, 1, CHOD), 3.9 (CD_3OH), 7.92, 8.36, 8.91 (m, 1 each, $C_6H_3(NO_2)_2$), 8.02 (d, J = 5 Hz, 1, N=CHCH). The broad CHOH absorption of **17** and the derived 2,4-DNP is characteristic of trans-2-substituted cyclohexanols.[47]

Pinacol Bromo(phenylthio)methaneboronate (18). The lithiated boronic ester **3** was isolated (12 mmol), and a suspension in ether (60 mL) was stirred at −78 °C during the dropwise addition of just enough bromine (10.3 mmol) to produce a persistent yellow color. The mixture was warmed to 20 °C and concentrated under vacuum. The residue was taken up in 25 mL of petroleum ether, and the precipitated lithium bromide was filtered. Concentration under vacuum yielded a residue of **18**. A small sample was purified by molecular distillation at 140–170 °C (0.1–0.5 torr). NMR ($CDCl_3$): δ 1.25 (s, 12, CCH_3), 5.03 (s, 1, SCHBrB), 7.47 (m, 5, C_6H_5). Anal. Calcd for $C_{13}H_{18}BBrO_2S$: C, 47.45; H, 5.51; B, 3.29; Br, 24.28; S, 9.74. Found: C, 47.61; H, 5.49; B, 3.41; Br, 24.03; S, 9.60.

Pinacol Phenyl(phenylthio)methaneboronate (20). The bromination of **3** was carried out as described in the preceding paragraph, and with the mixture still at −78 °C, an equivalent amount of phenylmagnesium bromide was added. After 16 h at 20 °C, the mixture was concentrated and worked up with 10% phosphoric acid and ether. Distillation yielded pinacol phenylboronate (**21a**), bp 90–110 °C (0.25 torr), 33% identified by NMR, and pinacol phenyl(phenylthio)methaneboronate (**20**), bp 145–150 °C (0.2 torr), 57%. NMR ($CDCl_3$): δ 1.26 (s, 12, CCH_3), 4.06 (s, 1, PhCH(SPh)B), 7.36 (m, 10, C_6H_5). Anal. $C_{19}H_{23}BO_2S$: C, 69.95: H, 7.11; B, 3.31% S, 9.83. Found: C, 69.45; H, 7.13; B, 3.09; S, 11.71.

Pinacol 1-Iodo-2-phenylethane-1-boronate (22). A solution of 3.40 g (10 mmol) of **5b**, 2 g of sodium iodide, and 7 mL of methyl iodide in 25 mL of dimethyl formamide was kept in the dark at 20–25 °C for 66 h. Ether (100 mL) and pentane (100 mL) were added, and the mixture was washed with water (3 × 100 mL). Distillation yielded 84% of **22**, not analytically pure even after redistribution, bp 98–99 °C (0.05 torr). 100-MHz NMR ($CDCl_3$): δ 1.20 (s, 12, CCH_3), 3.24 (m, 3, CH_2CH), 7.24 (s, 5, C_6H_5). Anal. Calcd for $C_{14}H_{20}BIO_2$: C, 46.97; H, 5.63; B, 3.02; I, 35.45. Found: C, 49.83; H, 5.76; B, 2.78; I, 33.22. Although the presence of pinacol 2-phenylethene-1-boronate (**23**) was not evident in the NMR spectrum, when the reaction of **5b** with methyl iodide was carried out with heating according to the model procedure,[11] the major product was **23** as indicated by the characteristic vinylic proton doublet near δ 5.6.[2,7c]

1,2-Diphenylethanol. Treatment of **22** in THF at −78 °C with 1 equiv of phenylmagnesium bromide was followed by standing at 20 °C overnight, workup with acid and ether, and oxidation with alkaline sodium perborate 2 days at 20 °C, which yielded the theoretical amount of 1,2-diphenylethanol. The NMR spectrum was identical with that of an authentic sample prepared from benzaldehyde and phenylmagnesium bromide, except that the crude sample contained about 3% pinacol. Recrystallization from ethanol/water yielded 52%.

Diethanolamine 2-Phenyl-1-(phenylthio)ethane-1-boronate (7). A solution of 2.5 mmol of the pinacol ester **5b** in 10 mL of ether was mixed with a solution of 2.7 mmol of diethanolamine in 5 mL of 2-propanol at 20 °C. After 1–3 days the crystalline **7** was collected: 82–83%: mp 190–192 °C. Anal. Calcd for $C_{18}H_{22}BNO_2S$: C, 66.07; H, 6.78; B, 3.30; N, 4.28; S, 9.80. Found: C, 65.92; H, 6.84; B, 3.46; N, 4.28; S, 9.44.

Deprotonation of (Phenylthio)methaneboronic Acid (1). Butyllithium (15 mmol) was added to a solution of **1** (5 mmol) in THF (30 mL) at −78 °C. The mixture was allowed to warm to 20 °C, then cooled to −78 °C and treated with methyl iodide (15 mmol), warmed to 20 °C for 2 h, treated with 10% phosphoric acid, extracted with ether, and concentrated. NMR analysis of the residue indicated that the ratio of $SCH(CH_3)B$ to SCH_2B groups was about 9:1 and that there was a large proportion of material which contained one or two *B*-butyl groups.

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Registry No. **1**, 67975-88-6; **2a**, 72824-03-4; **2b**, 66080-23-7; **2c**, 79121-30-5; **2d**, 79121-31-6; **3**, 66080-26-0; **4**, 66080-24-8; **5a**, 66080-25-9; **5b**, 66080-30-6; **5c**, 66080-29-3; **5d**, 66080-32-8; **5e**, 79121-32-7; **6a**, 66080-33-9; **6b**, 66080-34-0; **6c**, 66080-35-1; **6d**, 66080-36-2; **6e**, 79121-33-8; **7**, 79121-12-3; **9a**, 38793-73-6; **9b**, 79121-34-9; **9c**, 16222-10-9; **9d**, 66080-38-4; **9e**, 28403-86-3; **9f**, 66080-39-5; **9g**, 79121-35-0; **10**, 66080-37-3; **11**, 66080-40-8; **12a**, 33521-88-9; **12b**, 13112-46-4; **12c** (*E*), 79121-36-1; **12c** (*Z*), 79121-37-2; **12d**, 79121-38-3; **12e** (*E*), 79121-39-4; **12e** (*Z*), 79121-40-7; **12f**, 79121-41-8; **14**, 79121-42-9; **15a**, 79121-43-0; **16a**, 66080-42-0; **16b**, Me ester, 79121-44-1; **17**, 66080-41-9; **18**, 79121-45-2; **20**, 79121-46-3; **21a**, 24388-23-6; **22**, 79121-47-4; **23**, 78782-27-1; CH_3I, 74-88-4; *n*-BuBr, 109-65-9; *n*-BuCl, 109-69-3; *n*-BuI, 542-69-8; $(CH_3)_3CCH_2CH(CH_3)CH_2CH_2Br$, 50915-80-5; $PhOCH_2CH_2Br$, 589-10-6; $PhCH_2Br$, 100-39-0; $(CH_3)_2CHBr$, 75-26-3; $CH_3C(O_2C_2H_4)(CH_2)_3Cl$, 5978-08-5; $CH_3(CH_2)_2CO_2CH_3$, 623-42-7; c-$C_6H_{11}CO_2CH_3$, 4630-82-4; $PhCO_2CH_3$, 93-58-3; succinic anhydride, 108-30-5; $CH_3C(O_2C_2H_4)(CH_2)_2CO_2CH_3$, 35351-33-8; butyrolactone, 96-48-0; cyclohexanone, 108-94-1; PhCOPh, 119-61-9; $PhCOCH_2CH_2CH_3$, 495-40-9; $CH_3(CH_2)_5CHO$, 111-71-7; c-$C_6H_{11}CHO$, 2043-61-0; $CH_3COCH_2CH_2CO_2CH_3$, 624-45-3; cyclopentanone, 120-92-3; *trans*-2-hydroxycyclohexanecarboxaldehyde 2,4-dinitrophenylhydrazone, 79121-48-5; (phenylthio)methyllithium, 13307-75-0; trimethyl borate, 121-43-7.

(47) Bhacca, N. S.; Williams, D. H. "Application of NMR Spectroscopy in Organic Chemistry"; Holden-Day: San Francisco, 1964; pp 77–80.