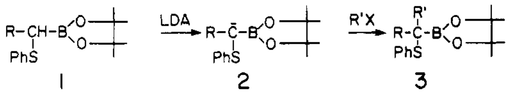
Carbanions from Deprotonation of α-(Phenylthio)alkaneboronic Esters

Sir:

The deprotonation of *gem*-diboronic esters[1] and the chemistry of (phenylthio)methyllithium[2,3] suggested the preparation of pinacol (phenylthio)methaneboronate (**1a**) and its deprotonation by lithium diisopropylamide (LDA) to the carbanion **2a**. This route to boron substituted carbanions is significantly easier and cheaper than those found previously,[1,4,5] and derivatives of **2a** show promise of versatile and useful synthetic chemistry.

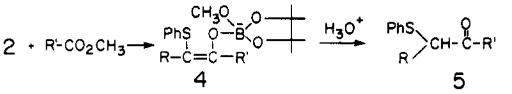
Alkylation of **2a** with primary alkyl halides proceeds efficiently, and the products (**3 = 1b, 1c**) may in turn be deprotonated and alkylated (eq 1). The new compounds obtained are summarized in Table I.[6]



(1)

a, R = H; b, R = CH_3; c, R = $CH_3(CH_2)_3$

Acylation of the carbanions **2** with methyl esters provides an efficient, regiospecific, general synthesis of α-(phenylthio) ketones (**5**) (eq 2) (Table II).[6] The synthetic utility of **5** is well established in other contexts.[7] The postulated boron enolate intermediate[1] **4** is consistent with the high yields of **5**.



(2)

Details and further results follow. (Phenylthio)methyllithium,[2] 1 mol in 800 mL of tetrahydrofuran (THF), was stirred at −70 °C during the dropwise addition of 1.1 mol of trimethyl borate. (All manipulations of carbanions were under argon.) Workup with aqueous acid and crystallization from ether/petroleum ether yielded 77–87% of (phenylthio)methaneboronic acid, mp 109–110 °C.[6] Treatment with the theoretical amount of pinacol in ether, followed by separation of water and distillation, yielded 96–98% of the pinacol ester **1a**, bp 108–110 °C (0.1 mm), mp 34–37 °C.[6] Solutions of **2a** were prepared by adding 1.25 g (5 mmol) of **1a** dropwise to 5 mmol of LDA (from diisopropylamine and 2 M butyllithium in hexane) and 10 mmol of tetramethylethylenediamine (TMEDA) in 50 mL of THF at 0 °C and stirring for 0.5–2 h. The precipitated lithium salt of **2a** + 1 THF (^{1}H NMR and elemental analysis[6]) resulted when 15 mmol of **1a** in 3 mL of THF was added to 15 mmol of LDA in 2 mL of THF and 20 mL of pentane was added at 0 °C, 80–85% after filtration and drying at 25 °C (0.1 mm). TMEDA decreased side reactions with solutions of **2a** but did not affect yields or composition of precipitated **2a** and was not used for making solutions of **2b** or **2c**. The 2,2-dimethyl-1,3-propanediol ester analogue of **1a**[6] was deprotonated and methylated in only 60% yield, and the ethylene glycol ester[6] failed.

Solutions of **2** treated with 1 equiv of alkyl halide at 0 °C and stirred for 1–3 h, 0–25 °C, followed by workup with dilute phosphoric acid, extraction with ether, and distillation, yielded α-(phenylthio)alkaneboronic esters (**3**) (Table I). Isopropyl bromide with precipitated **2a** at −70 °C, then 12 h at 25 °C in THF, gave ~42% **3**, 48% regenerated **1a**, by ^{1}H NMR analysis. Further exploration of secondary halides has not yet been carried out.

Table I. Alkylation of Carbanions **2** with Alkyl Halides R'X to Form α-(Phenylthio)alkaneboronic Esters (**3**) (Eq 1)[a]

R	R'X	Bp of 3, °C (mm)	% yield
H	CH_3I	125 (0.7)	83,[b] 71[c]
H	n-C_4H_9Cl, -Br, -I	115–120 (0.1)	76–88,[b] 88[c,d]
H	t-$BuCH_2CH(CH_3)$-CH_2CH_2Br	160–165 (0.1)	58
H	$PhCH_2Br$	145–150 (0.05)	75[e]
H	$PhCH_2CH_2I$	176–180 (0.1)	72[f]
H	$PhOCH_2CH_2I$	146–150 (0.1)	71
CH_3	A[h]	174 (0.3)	71[g]
n-C_4H_9	CH_3I	136 (0.1)	70
n-C_4H_9	n-C_4H_9Br	150 (0.2)	67
n-C_4H_9	$PhCH_2Br$	183–185 (0.5)	78

[a] See note 6. [b] NMR estimate of **3** contained in mixture with 10% **1a.** [c] Pure **3** from precipitated **2a.** [d] From C_4H_9Br. [e] Requires redistilled $PhCH_2Br$ for best yield, first attained by Abel Mendoza. [f] We thank A. Mendoza for these data. [g] Yield 48% after 3 h, 71% after 12 h. [h] See structure below.

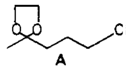


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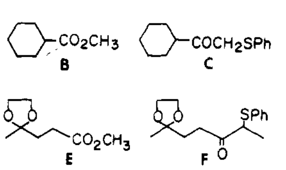
Table II. Acylation of Carbanions **2** with Methyl Esters and Other Reagents to form α-(Phenylthio) Ketones (**5**) (Eq 2)

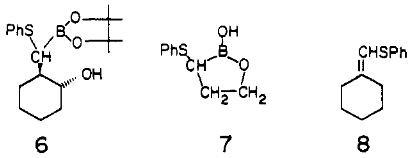
R of **2**	Acylating agent R'COX	Product **5**	% yield[a]
H	$CH_3CH_2CH_2$-CO_2CH_3	$CH_3CH_2CH_2COCH_2SPh$	82
H	B[e]	C[e]	80
H	$PhCO_2CH_3$	$PhCOCH_2SPh$[b]	75[b]
H	D[e]	$HO_2CCH_2CH_2COCH_2$-SPh[c]	74[c]
CH_3	$CH_3CH_2CH_2$-CO_2CH_3	$CH_3CH_2CH_2COCH$-$(SPh)CH_3$	81[d]
CH_3	$PhCO_2CH_3$	$PhCOCH(SPh)CH_3$	86
CH_3	E[e]	F[e]	66
n-C_4H_9	G[e]	$HOCH_2CH_2CH_2COCH$-$(SPh)C_4H_9$	50

[a] Yield of pure[6] chromatographed oil, except as noted. [b] Mp 53–54 °C, reported[8] mp 53–54 °C. [c] Yield from aqueous acid. Recrystallized from ether, mp 78–79 °C.[6] [d] Mixed reagents at −70 °C; when mixed at 0 °C, 63%. [e] See structures below.



Solutions of **2** with 0.8 equiv of methyl ester added at 0 °C and stirred overnight at 25 °C, followed by concentration, addition of pentane, washing with 3 M sodium hydroxide, then dilute acid and water, and chromatography on silica plates with pentane/ether, yielded α-(phenylthio) ketones (Table II). The workup for the acid product from succinic anhydride consisted of precipitation from aqueous acid. The present results may be contrasted to the previously reported reaction of α-lithioisobutyl phenyl sulfide with methyl benzoate, which yielded 46% α-(phenylthio)isobutyl phenyl ketone[9] and which has not been extended to esters having ionizable α protons.

Precipitated **2a** with 1 equiv of cyclohexene oxide at 25 °C overnight, followed by workup with aqueous acid and ether and concentration under vacuum, yielded 91% of an analytically pure residue of **6**,[6] shown to be the trans isomer by the characteristic[10] broad (~30 Hz) CHOD peak in the ^{1}H NMR spectrum ($CDCl_3/CD_3OD$) at δ 3.6. Ethylene oxide and **2a**



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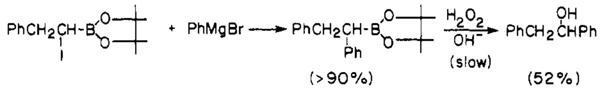
reacted similarly to yield 62% of the boronic ester, which was hydrolyzed with sodium borate in hot aqueous ethanol to the crystalline derivative **7**, mp 104–106 °C (from ether/petroleum ether).[6] Cyclohexanone with a solution of **2a** gave the enethiol ether **8**, 83% in crude product, 71% after treatment with aqueous ethanolic sodium borate and then sodium hydroxide to remove boron compounds and distillation. The yield of **8** from phenylthiomethyltrimethylsilane was 65%.[11] Enethiol ethers were also prepared from **2a** and butyrophenone, bp 130 °C (0.1 mm), 82%,[6] and from **2a** and benzophenone, mp 69–70 °C,[2] 71%.

One potential use of the α-(phenylthio)alkaneboronic esters (**3** and **6**) is as precursors of carbonyl compounds. The pinacol boronic ester group has proved unexpectedly resistant to hydrolysis or oxidation, but cleavage of **3a** with *N*-chlorosuccinimide under basic conditions has given high yields of hemithioacetals or dimethyl acetals.[12] Another use is the conversion of **1a** or **3a** ($R = C_4H_9$, CH_2Ph) to α-iodoalkaneboronic esters (70–77%) with methyl iodide and sodium iodide in dimethylformamide[3] for 3 days at 25 °C. α-Haloalkaneboronic esters are of interest for their carbon–carbon bond-forming reactions with Grignard or lithium reagents[13,14] and as precursors to boronic acids which may bind to enzymes.[15] Carbon–carbon bond formation has been demonstrated with the sequence illustrated (eq 3).


(3)

Acknowledgment. We thank the National Science Foundation for support, Grants No. MPS 75-19557 and CHE 77-11283.

References and Notes

(1) D. S. Matteson and R. J. Moody, *J. AM/ Chem. Soc.*, **99,** 3196 (1977).
(2) E. J. Corey and D. Seebach, *J. Org. Chem.*, **31,** 4097 (1966).
(3) E. J. Corey and M. Jautelat, *Tetrahedron Lett.*, 5787 (1968).
(4) D. S. Matteson, R. J. Moody, and P. K. Jesthi, *J. Am. Chem. Soc.*, **97,** 5608 (1975); D. S. Matteson, *Synthesis*, 147 (1975).
(5) M. W. Rathke and R. Kow, *J. Am. Chem. Soc.*, **94,** 6854 (1972); R. Kow and M. W. Rathke, *ibid.*, **95,** 2715 (1973).
(6) New compounds gave satisfactory analyses (C, H, S, and, if present, B and Li) and ^{1}H NMR spectra.
(7) B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, **98,** 4887 (1976).
(8) W. J. Kenny, J. A. Walsh, and D. A. Davenport, *J. Am. Chem. Soc.*, **83,** 4019 (1961).
(9) T. M. Dolak and T. A. Bryson, *Tetrahedron Lett.*, 1961 (1977).
(10) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964, pp 77–80.
(11) F. A. Carey and A. S. Court, *J. Org. Chem.*, **37,** 939 (1972).
(12) A. Mendoza and D. S. Matteson, unpublished work.
(13) D. S. Matteson and R. W. H. Mah, *J. Am. Chem. Soc.*, **85,** 2599 (1963).
(14) M. W. Rathke, E. Chao, and G. Wu, *J. Organomet. Chem.*, **122,** 145 (1976); H. C. Brown, N. R. DeLue, Y. Yamamoto, and K. Maruyama, *J. Org. Chem.*, **42,** 3252 (1977); H. C. Brown, N. R. De Lue, Y. Yamamoto, K. Maruyama, T. Kasahara, S. Murahashi, and A. Sonoda, *ibid.*, **42,** 4088 (1977).
(15) R. N. Lindquist and A. C. Nguyen, *J. Am. Chem. Soc.*, **99,** 6435 (1977).

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Additions and Corrections

Flash Photolysis of Na^+, $C^-(Ph)_2CH_2CH_2C^-(Ph)_2,Na^+$. Redox Potential of 1,1-Diphenylethylene and Rate Constant of Dimerization of Its Radical Anion [*J. Am. Chem. Soc.*, 99, 4612 (1977)]. By H. C. WANG, E. D. LILLIE, S. SLOMKOWSKI, G. LEVIN, and M. SZWARC,* Department of Chemistry, State University of New York, College of Environmental Science and Forestry, Syracuse, New York 13210.

Because of an inadvertent error, the "wrong" Figure 7 was published. The correct figure is presented here.

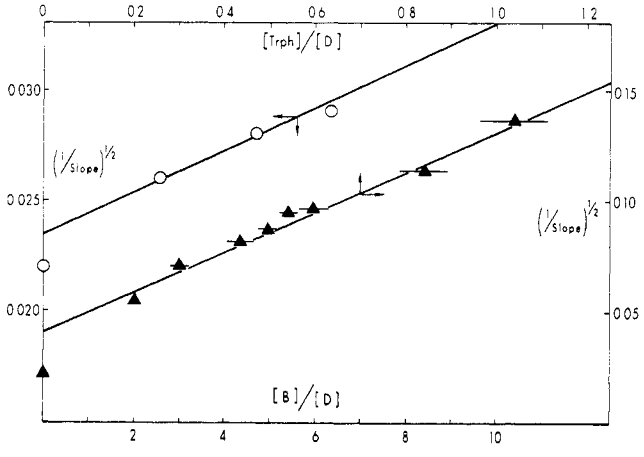

Figure 7. The square root of reciprocals of the corrected slopes of the lines $1/\Delta$(OD 470) vs. time (see caption to Figure 6) plotted as functions of [Trph]/[D] (triangles) or [B]/[D] (circles).

Cyclic Peptides. 17. Metal and Amino Acid Complexes of *cyclo*(Pro-Gly)$_4$ and Analogues Studies by Nuclear Magnetic Resonance and Circular Dichroism" [*J. Am. Chem. Soc.*, 99, 4788 (1977)]. By VINCENT MADISON, CHARLES M. DEBER, and ELKAN R. BLOUT,* Department of Biological Chemistry, Harvard Medical School, Boston, Massachusetts 02115.

Page 4790, first column, 15th line from the bottom: Read "the molecular weight of *cyclo*(Pro-Gly)$_1$", rather than "the molecular weight of *cyclo*(Pro-Gly)$_2$".

Page 4797, first column, line 12: Change "Table IV" to read "Table II".

Page 4797, column 2, third paragraph, line 14: Change "Table VIII" to read "Table IV".

Page 4797, fourth paragraph, lines 11 and 12: Change "Figure 4 and Table X" to read "Figure 2 and Table XI".

Application of Linear Dichroism to the Analysis of Electronic Absorption Spectra of Biphenyl, Fluorene, 9,9′-Spirobifluorene, and [6.6]Vespirene. Interpretation of the Circular Dichroism Spectrum of [6.6]Vespirene [*J. Am. Chem. Soc.*, 99, 6861 (1977)]. By JACOB SAGIV,* AMNON YOGEV, and YEHUDA MAZUR, Department of Isotopes and Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel.

Page 6868, column 1, line 1 should be: ". . . fluorene transitions lead to *z*- and *y*-polarized exciton pairs having opposite sign in the CD spectrum, while the transversal *x*-polarized bands . . .".