TABLE I

Tl(I) salt of	Product	Yield, %[a]	Bp(mm), °C	Lit. bp (mm), °C
Octanoic acid	1-Bromoheptane	98	70–75 (15)	62–65 (12)[b]
Decanoic acid	1-Bromononane	89	83–85 (10)	113 (27)[c]
Lauric acid	1-Bromoundecane	85	102–105 (2)	131–134 (15)[d]
Myristic acid	1-Bromotridecane	92	160–162 (5)	148–149 (9.5)[e]
Palmitic acid	1-Bromopentadecane	84	171–176 (5)	170–175 (8–10)[f]
Stearic acid	1-Bromoheptadecane	83	mp 27–29	mp 32[g]
β-Carbomethoxypropionic acid	Methyl β-bromopropionate	86	75–80 (22)	64–66 (18)[h]

[a] No attempt was made to optimize yields. All products were >98% pure as isolated, as determined by glpc. [b] J. Cason, M. J. Kalm, and R. H. Mills, *J. Org. Chem.*, **18**, 1670 (1953). [c] M. Tuot, *Bull. Soc. Chim. Fr.*, 363 (1946). [d] A. Lüttringhaus and D. Schade, *Chem. Ber.*, **74**, 1565 (1941). [e] H. Suida and F. Drahowzal, *ibid.*, **75**, 991 (1942). [f] T. N. Mehta, V. S. Mehta, and V. B. Thosar, *J. Ind. Chem. Soc., Ind. Ed.*, **3**, 137 (1940). [g] J. W. H. Oldham, *J. Chem. Soc.*, 100 (1950). [h] "Organic Syntheses," Coll. Vol. III, E. C. Hornung, Ed., John Wiley & Sons, Inc., New York, N. Y., 1955, p 576.

the yields of primary aliphatic bromides from about 30 to 85–95%.

Experimental Section

Melting points were determined on a Kofler hot stage apparatus and are uncorrected.[9] Infrared (ir) spectra were recorded on a Perkin-Elmer Model 325 grating spectrophotometer; the normal Nujol mull technique was used for solids; and liquids were recorded as liquid films. Gas–liquid phase chromatograms were recorded on a Perkin–Elmer Model 452 instrument, using a standard 1-m glass column with Apiezon L on Chromosorb as packing. Microanalyses were performed by Mr. D. L. Fyans. All glass apparatus was dried at 100° prior to use. Carbon tetrachloride and bromine were dried over phosphorus pentoxide.

Preparation of Thallium(I) Carboxylates.—Thallium(I) ethoxide[11] (0.09 mol) was pipetted into a stirred solution of the carboxylic acid (0.1 mol) in petroleum ether (100 ml, bp 60–80°). The salt precipitated immediately. Stirring was continued for 15 min, after which the solid was filtered, washed well with cold ether, and recrystallized from aqueous ethanol. The thallium(I) carboxylates were obtained in 90–98% yield as colorless needles.

Thallium(I) octanoate had mp 119–120°. *Anal.* Calcd for $C_8H_{15}O_2Tl$: C, 27.64; H, 4.35. Found: C, 27.60; H, 4.37.

Thallium(I) decanoate had mp 134–135°. *Anal.* Calcd for $C_{10}H_{19}O_2Tl$: C, 31.96; H, 5.08. Found: C, 31.66; H, 4.99.

Thallium(I) laurate had mp 119–120°. *Anal.* Calcd for $C_{12}H_{23}O_2Tl$: C, 35.72; H, 5.75. Found: C, 36.10; H, 6.20.

Thallium(I) myristate had mp 120–121°. *Anal.* Calcd for $C_{14}H_{27}O_2Tl$: C, 38.94; H, 6.30. Found: C, 38.50; H, 6.60.

Thallium(I) palmitate had mp 116–117° (lit.[12] mp 116–118°).

Thallium(I) stearate had mp 117–119° (lit.[13] mp 119°).

Reaction of Thallium(I) Carboxylates with Bromine. Preparation of *n*-Alkyl Bromides.—A solution of bromine (0.015 mol) in carbon tetrachloride (20 ml) was added dropwise during 15 min to a stirred suspension of the thallium(I) carboxylate (0.01 mol) in carbon tetrachloride. The resulting yellow solution was stirred and refluxed under nitrogen for 4 hr and cooled, the yellow inorganic salt was filtered off, and the filtrate was washed with aqueous sodium bisulfite solution followed by aqueous sodium bicarbonate solution and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, the residual oil was dissolved in chloroform, and the solution was passed through a short column of alumina to remove traces of thallium salts. Removal of the chloroform and distillation gave the *n*-alkyl bromides (Table I), whose identity was confirmed by comparison of infrared spectra and glpc retention times with those of genuine samples.

Registry No.—Thallium(I) octanoate, 18993-50-5; thallium(I) decanoate, 18993-51-6; thallium(I) laurate, 18993-52-7; thallium(I) myristate, 18993-53-8.

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Some Extensions of the *ortho*-Lithiation Reaction[1]

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The *ortho*-lithiation reaction has been established to be of synthetic utility. Compounds of the type $Ar(CH_2)_nNR_2$ where $n = 0$, 1, and 2 have been *ortho* lithiated and the resultant carbanions treated with electrophiles.[2–4] Although substrates with active hydrogen are not commonly employed in these reactions, reports have appeared concerning the *ortho* lithiation of primary amines,[5] secondary amines,[6] and secondary sulfonamides.[7] The lithiation reaction has also been applied to sulfones[8] and thiophenes.[6,9–11] Now we wish to report our efforts along these lines including further studies of benzyl- and thenylamines.

Treatment of N,N-dimethylbenzylamine with *n*-butyllithium followed by condensation of the resulting carbanion with methyl borate afforded *o*-(dimethylaminomethyl)benzeneboronic anhydride (I), previously prepared by a different route.[12] At the time this work was completed, boron compounds had not been derived from similar lithiation-produced carbanions; such has since been reported.[13]

When a similar reaction was carried out using N-*n*-

(1) This investigation was supported in part by Public Health Service Research Grant CA-06587 from the National Cancer Institute.
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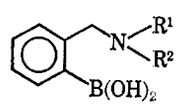
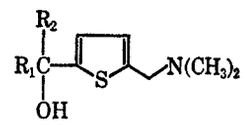
butylbenzylamine, a secondary amine with an active hydrogen, similar results were obtained. However, despite the fact that the reaction provided *ortho* substitution and boron-containing compounds (as evidenced by microanalyses, and nmr and ir spectral examination), we were unable to obtain the chief product, probably *o*-(*n*-butylaminomethyl)benzeneboronic acid (II), in a state of analytical purity. A foreshortened reaction with N-*n*-butylbenzylamine resulted in the formation of a boramide in high yield. Thus, in view of this result and the known relative acidities of NH as compared to CH, it is likely that N lithiation precedes C lithiation; the precursor to the boronic acid might be a dilithiated species.





I, $R_1 = R_2 = CH_3$ (as anhydride)
II, $R_1 = H$; $R_2 = n\text{-}C_4H_9$
III, $R_1 = H$; $R_2 = t\text{-}C_4H_9$
IV, $R_1 = R_2 = C_6H_5$
V, $R_1 = H$; $R_2 = C_6H_5$

The proclivity of thiophenes to lithiate in the α position suggests that N,N-dimethyl-2-thenylamine might lithiate in the 5 position, as do many 2-substituted thiophenes.[10,11] However, since canonical structures showing interaction between N and Li have been invoked to explain the tendency for benzyl systems to show *ortho* lithiation,[2] a parallel argument would lead to the prediction that, in the thiophene series, 3 substitution might result. Lithiation of N,N-dimethyl-2-thenylamine followed by condensation of the resulting carbanion with both benzaldehyde and benzophenone resulted in products which, on the basis of spectral data, we believe to be 2,5 disubstituted. This result indicates that resonance structures like those showing interaction between N and Li in the benzylamine series must be less important in the thiophene series than factors tending to favor α substitution. Unfortunately, a further test of this hypothesis, namely a parallel reaction with the corresponding 3-thenylamine, could not be completed before interruption of this work.

Experimental Section

Microanalyses were performed by Geller Microanalytical Laboratories, Saddle River, N. J., or Elek Microanalytical Laboratories, Torrance, Calif. Infrared spectra were determined with Beckman IR-5 or Perkin-Elmer 457 spectrophotometers. Melting points were determined in open capillary tubes with a calibrated Thomas–Hoover apparatus. Proton magnetic resonance spectra were determined with a Varian A-60 instrument.

o-(Dimethylaminomethyl)benzeneboronic Anhydride.—A solution containing 135 mmol of N,N-dimethylbenzylamine and 178 mmol of a 1.6 *N* *n*-hexane solution of *n*-butyllithium was prepared in 100 ml of dry tetrahydrofuran. The reactants were stirred magnetically for 6 hr at 25–45° under an atmosphere of dry nitrogen. The resulting dark red solution was transferred under nitrogen and added slowly to 238 mmol of anhydrous methyl borate in 50 ml of THF, with cooling. At the completion of the reaction, 100 ml of water was added, the THF phase was decanted and concentrated *in vacuo* to 80 ml, and then 100 ml of low-boiling petroleum ether (bp 30–60°) was added. Trituration provided white crystals which were recrystallized repeatedly from toluene to provide 13.2 mmol of anhydride I (9.8% yield based upon amine taken) with an ir spectrum completely identical with that reported for authentic material.[14]

Tris(N-*n*-butylbenzylamino)boron.—When the same metalation was conducted upon N-*n*-butylbenzylamine with a greater ratio of *n*-butyllithium (to account for the active hydrogen of the secondary amine) for about the same length of time, and excess methyl borate was added to the resulting red solution, a simple boramide was formed in high yield (81%). Several recrystallizations (ether–ethanol) provided pure tris(N-*n*-butylbenzylamino)boron identical in all respects with an authentic sample prepared by the Grignard reaction,[15] mp 115.2–115.8°. The lithiation route proved comparable in convenience to the Grignard route for the preparation of this novel boramide. The boramide showed good resistance to hydrolysis.

Anal. Calcd for $C_{33}H_{45}BN_3$: C, 80.14; H, 9.17; N, 8.50. Found: C, 79.84; H, 9.89; N, 8.40.

When the above metalation was conducted for 12 hr, *o*-(*n*-butylaminomethyl)benzeneboronic acid was obtained in low yield. It was not satisfactorily purified. However, spectral data indicated that boronic acid II was at hand. For example, nmr spectra for *n*-butyl isomer II were analogous to those obtained for the previously reported *t*-butyl isomer III.[16] As noted previously, no appreciable tendency for ring closure to the 1,2-boraazaindanyl ring system by cyclodehydration was detected.[16]

Metalation of N,N-Dimethyl-2-thenylamine.—Prepared from 2-thenaldehyde[17] by the method of Smith and McDonald,[18] the amine was metalated similarly to the benzylamines (*e.g.*, 59 mequiv of amine, 75 mequiv of *n*-butyllithium). The lithiated amine was treated as follows.

Reaction with Benzophenone.—The lithiated amine (1.0 equiv) was added over a 5-min period to an ether solution of benzophenone (1.4 equiv). After 15 min of stirring, the reaction mixture was quenched with water and organic solvents were removed *in vacuo*. The reaction product was extracted into ether; it crystallized when the ether was replaced with *n*-heptane. The recrystallized yield (aqueous ethanol) of 2-(α-benzhydryl)-5-dimethylaminomethylthiophene (IV) was 47%, mp 140.2–141.7°, white plates.

Anal. Calcd for $C_{20}H_{21}NOS$: C, 74.27; H, 6.54; N, 4.33; S, 9.91. Found: C, 74.24; H, 6.68; N, 4.32; S, 9.94.

This carbinol showed ir and nmr spectra completely consonant with the assigned structure. On the basis of a strong band at 797 cm^{-1} in the infrared region (2,5-disubstituted thiophene) and the coupling constant between the two thiophene ring protons, δ 6.6 and 6.8, J_{34} = 3.7 Hz, the product was shown to be the 2,5 isomer.[19]

Reaction with Benzaldehyde.—A solution of benzaldehyde in ether (1.5 equiv) was added quickly to the lithiated amine (1.0 equiv). The exotherm was allowed to subside and the reaction mixture was stirred for 30 min, after which it was quenched with water. All solvents were removed *in vacuo* and the resultant residue extracted into *n*-heptane, from which it crystallized. The yield of (5-dimethylaminomethyl)-2-thenyl-α-benzyl alcohol (V) was 50%, mp 79–83°. Further recrystallization from ethanol, from water, and then from *n*-heptane yielded an analytical sample, mp 83.5–84.0°.

Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66; S, 12.96. Found: C, 68.33; H, 6.95; N, 5.54; S, 12.78.

Similarly, a strong absorption band in the infrared region at 788 cm^{-1} (2,5-disubstituted thiophene) and the coupling constant for the two thiophene ring protons, δ 6.5 and 6.6, J_{34} = 3.5 Hz,[19] indicated the product was the 2,5 isomer.

Registry No.—IV, 18936-26-0; V, 18936-27-1.

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