### Metalation in 2-Thiophenesulfonamides

to 2-methyl-2-butene. The resulting products were compound **11b** (mp 145–145.5°), mass spectrum m/e 237 (molecular ion), and **12b** (mp 131.5–132°): mmr (CDCl<sub>3</sub>)  $\tau$  2.11–2.75 (4 H, aromatic), 6.35 (1 H, J = 9.0 Hz, CH), 7.58 (1 H, J = 7.0 Hz, CH), 8.70 (3 H, CH<sub>3</sub>), 8.88 (3 H, J = 7.0 Hz, CH<sub>3</sub>), 9.20 (3 H, CH<sub>3</sub>); mass spectrum m/e 237 (molecular ion).

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Registry No.—1a, 825-44-5; 1b, 41674-77-5; 2a, 41674-78-6; 2b, 41674-79-7; 3, 41674-80-0; 4, 156-59-2; 5, 156-60-5; 6-7, 41674-81-1; 8, 75-35-4; 9a, 41674-82-2; 11a, 41674-83-3; 11b, 41674-84-4; 12a, 41674-85-5; 12b, 41674-86-6; 3-deuteriothianaphthene, 15816-45-2; 3-bromothianaphthene, 7342-82-7; trichloroethylene, 79-01-6; 2-methyl-2-butene, 513-35-9.

# Directed Metalation Reactions. V.<sup>1</sup> Metalation and Rearrangement in Substituted 2-Thiophenesulfonamides

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Metalation of several 2-N, N-dialkylthiophenesulfonamides with n-butyllithium has revealed some diverse behavior. Whereas metalation of 5-trimethylsilyl-N, N-dimethyl-2-thiophenesulfonamide (1) gave 3 metalation only, metalation of the diethyl analog (4) produced 3 metalation accompanied by loss of the trimethylsilyl group when the lithio intermediate 4' was condensed with Dry Ice. When other reagents were condensed with 4', loss of the trimethylsilyl group was not observed and 3-substituted derivatives of 4 were produced. Moreover, when dimethylsulfonamide 1 was treated with n-butyllithium-TMEDA complex, a rearrangement ensued which produced 2-trimethylsilyl-4-N, N-dimethylthienylamine (3).

Ortho metalation of both N-methyl- and N-phenylbenzenesulfonamide has been demonstrated.<sup>2a</sup> Similarly, N,N-dimethylbenzenesulfonamide was found<sup>2b</sup> to undergo metalation ortho to the sulfonamide group and to give good yields of various condensation products. Such studies involving the metalation of thiophenesulfonamides have not been reported in the literature. However, it has been shown by Stoyanovitch and Fedorov<sup>3</sup> that *tert*-butyl 2-thienyl sulfone was dimetalated in the 3 and 5 positions with excess *n*-butyllithium. Similar results were anticipated in the metalation of the thiophenesulfonamides, but, as described below, other processes intervened at times.

Initial attempts to effect metalation of N,N-dimethyl-2-thiophenesulfonamide in the 3 or 3,5 positions were unsuccessful, metalation occurring only at the 5 position. This observation prompted the introduction of a blocking group into the 5 position of the thiophenesulfonamide with the result that 5-trimethylsilyl-N,Ndimethyl-2-thiophenesulfonamide (1) was prepared. Metalation of 1 with *n*-butyllithium followed by condensation of the lithio intermediate (1') with Dry Ice afforded a 10% yield of 5-trimethylsilyl-3-carboxyl-N,N-dimethyl-2-thiophenesulfonamide (2) (eq 1) and 75% recovery of starting material. An ir spectrum of 2 exhibited bands between 3000 and 2450 and at 1710



<sup>(1)</sup> For paper IV in this series, cf. D. W. Slocum and B. P. Koonsvitsky, J. Org. Chem., **38**, 1675 (1973).

cm<sup>-1</sup> characteristic of a carboxyl group. In addition, its nmr spectrum showed a singlet at 7.66 ppm for the lone remaining thiophene ring proton and singlet peaks for the methyl groups attached to the sulfonamide group and silicon atom at 2.94 and 0.37 ppm, respectively. The site of metalation is postulated as being the 3 position, in analogy to the results for N,N-dimethylbenzenesulfonamide<sup>2</sup> and also as a result of a deuterium labeling experiment. When lithio intermediate 1' was quenched with D<sub>2</sub>O, a deuterated disubstituted thiophene resulted which exhibited attenuation of the more downfield signal, the signal which was assigned to the 3-position proton since it was adjacent to the highly deshielding sulfonamide group. A similar deshielding has been observed for SO<sub>2</sub>R derivatives of cymantrene and ferrocene.<sup>4</sup>

In order to possibly increase the yield of condensation product, sulfonamide 1 was metalated with *n*-butyllithium–N, N, N', N'-tetramethylethylenediamine (TM-EDA) at  $-30^{\circ}$  and condensed with Dry Ice. No carboxylic acid condensation product was isolated but rather a rearranged aminothiophene identified as 2-trimethylsilyl-N, N-dimethyl-4-thienylamine (3) was obtained in 39% yield (eq 2). Attempts to eliminate



Dry Ice from the reaction with substitution of ice water led to much lower yields of amine **3**. The structure of amine **3** was deduced from examination of its ir and nmr spectra. Its ir spectrum exhibited two bands at 2800 and 1250 cm<sup>-1</sup> characteristic of tertiary aryl amines,<sup>5</sup> whereas the intense sulfonamide bands at 1350 and

 <sup>(2) (</sup>a) H. Watanabe, R. L. Gay, and C. R. Hauser, J. Org. Chem., 33, 900 (1968); (b) H. Watanabe, R. A. Schwarz, C. R. Hauser, J. Lewis, and D. W. Slocum, Can. J. Chem., 47, 1543 (1969).

<sup>(3)</sup> F. M. Stoyanovitch and B. P. Fedorov, Khim. Geterotsikl. Soedin., 5, 823 (1967); Chem. Abstr., 69, 7119 (1968).

<sup>(4) (</sup>a) D. W. Slocum and C. R. Ernst, Organometal. Chem. Rev., Sect. A,
6, 283 (1970); (b) D. W. Slocum and C. R. Ernst, Advan. Organometal. Chem., 10, 79-114 (1972).

<sup>(5)</sup> K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, Calif., 1962, pp 38 and 40.

1160 cm<sup>-1</sup> were absent. The postulation of a 2,4 orientation of the substituents is based primarily on the compound's nmr spectrum, which exhibited a wellresolved AB pattern for the two ring protons. The observed coupling constant of 1.3 Hz for the two protons is reported to be characteristic of 2.4-disubstituted thiophenes.<sup>6</sup> A coupling constant of 1.5 Hz has recently been reported for a series of 2,4-thiophenediamines.<sup>7</sup>

Although the instability of thienylamines has long been recognized,<sup>8</sup> some stability is imparted to such systems if the amines are present in tertiary form. Thus, several examples of N, N-dialkyl-3-thienylamines have been reported,<sup>9,10</sup> and a unique series of 2,4tetraalkylthiophenediamines.<sup>7</sup> More to the point, N, Ndimethyl-3-thienvlamine has been prepared by a reductive method but the same technique failed to produce any of the 2 isomer.<sup>10</sup> Thus, the fact that amine 3 has the amine substituent in the  $\beta$  rather than the  $\alpha$  position appears to be consistent with current data for thienylamines.

A possible mechanism leading to the formation of amine 3 may begin with coordination of the lithiated intermediate with TMEDA as shown in Scheme I.



This, in turn, may enhance the carbanionic activity of the 3-position carbon-lithium bond sufficiently to effect a nucleophilic displacement reaction on nitrogen with the thiophenesulfinate anion functioning as a leaving Condensation with Dry Ice would not be group. expected to yield any stable product from the sulfinate intermediate but the subsequent hydrolysis step should yield the sulfinic acid derivative. Loss of SO<sub>2</sub> would then yield the rearrangement amine, 3. As mentioned previously, Dry Ice was not necessary for the production of amine 3, but yields were much poorer when it was omitted.

This last step is lent some credence by a number of reports of the instability of aromatic sulfinic acids. For example, 2-thiophenesulfinic acid prepared from 2-thienyllithium and sulfur dioxide has been reported to

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(8) H. D. Hartough, "Thiophene and Its Derivatives," Interscience, New York, N. Y., 1952, pp 228-235.
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Chim. Pays-Bas, 83, 1160 (1964). (10) J. B. Sullivan and W. C. McCarthy, J. Org. Chem., 30, 662 (1965). be "somewhat unstable."<sup>11</sup> Moreover, all attempts to convert lithium 2-furansulfinate to the free sulfinic acid failed.<sup>11</sup> Benzyhydryllithium sulfinate upon acidification at 0° gave the free acid but this decomposed at  $25^{\circ}$ to sulfur dioxide and diphenylmethane.<sup>12</sup> Heating 2,4dinitrobenzenesulfonhydrazine (a reaction known to lead to sulfinic acids with other arylsulfonhydrazides) gave a quantitative yield of m-dinitrobenzene.<sup>13</sup>

Other possible rearrangement pathways were deemed less likely since they all would have given ring lithiated intermediates which under these conditions should have given a condensation product with Dry Ice-ether.

Further testing of the scope of this rearrangement was attempted by the metalation with n-butyllithium-TMEDA of 5-trimethylsilyl-N,N-diethyl-2-thiophenesulfonamide (4) with the idea of preparing the diethyl analog of 3. No rearrangement product was detected after this system was treated with Dry Ice. Rather directed metalation as observed for sulfonamide 1 with uncomplexed butyllithium occurred, accompained by loss of the trimethylsilyl group with the resulting isolation of a single product, 3-carboxyl-N,N-diethyl-2thiophenesulfonamide (5) in 44% yield (eq 3). The site



of metalation was ascertained from the product's nmr spectrum, which exhibited a well-resolved AB pattern for the two ring protons. The coupling constant of these protons was 4.9 Hz, which falls in the region reported for a large number of 2,3-disubstituted thiophenes.<sup>5</sup> Separate synthesis of the 2,5 isomer established unequivocally that this was not the structure of 5 (cf. Experimental Section).

The absence of rearrangement amine product could be associated with steric effects of the larger ethyl groups which may hinder close approach of the diethylamino group to the carbanionic site. Loss of the trimethylsilyl group could not be explained but was thought perhaps to be associated with the particular condensation reagent or work-up procedure. In order to explore this possibility, metalation of sulfonamide 4 with n-butyllithium-TMEDA was repeated but the lithio intermediate was hydrolyzed with D<sub>2</sub>O. Deuterated sulfonamide 4 was obtained in 70% recovery and with no loss of the trimethylsilyl group. Nmr integration indicated that one deuteron had been incorporated into the thiophene ring with the site of deuteration and, hence, of metalation being assigned the 3 position. Assignment of the site of deuteration was based on the nearly total attenuation of the downfield proton resonance. Of the two thiophene ring resonances this would correspond to the proton adjacent to the deshielding sulfonamide system.

The lithio intermediate of sulfonamide 4 was also

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#### METALATION IN 2-THIOPHENESULFONAMIDES

condensed with dimethylformamide to give an estimated 14% yield of the carboxaldehyde derivative.8 Again, no loss of the trimethylsilyl group was observed. Since the site of deuteration was in the 3 position, assignment of the carboxaldehyde functional group to the 3 position was deemed justified. Otherwise the structure 6 was supported by the usual spectral and analytical data but the compound was not obtained free of starting material.

Several attempts at acid hydrolysis of the thiophenetrimethylsilyl bond were attempted with the idea that the trimethylsilyl group would serve as a blocking group during the synthesis of 2,3-disubstituted thiophenes. All such attempts failed. Interestingly, cleavage of the trimethylsilyl-thiophene ring bond did occur upon carbonation of lithiated sulfonamide 4 but the reaction was not able to be generalized and at present remains inexplicable.

#### **Experimental Section**

n-Butyllithium (1.6 M in hexane) used in the following experiments was purchased from Foote Mineral Co. N, N, N', N'Tetramethylethylenediamine (TMEDA) was obtained from Aldrich Chemical Co. and stored over KOH pellets. The ether used as a reaction solvent was Matheson Coleman and Bell "absolute" grade and was stored over Linde 3A Molecular grade and was stored over Linde 3A Molecular Sieves or sodium metal.

Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn., and Alfred Bernhardt Laboratories, Mulheim, West Germany. Melting points were determined on a Hoover melting point apparatus and have been corrected. Ir spectra were obtained on a Perkin-Elmer Model 137 Infracord spectrometer using the 5.14- $\mu$  and 11.03- $\mu$  bands of polystyrene as ref-Nmr spectra were obtained on a Varian A-56/60 erences. spectrometer using tetramethylsilane (TMS) as an internal standard.

N, N-Dimethyl-2-thiophenesulfonamide.—2-Thiophenesulfonyl chloride was prepared in 24% yield from thiophene (25 ml, 0.32mol) and chlorosulfonic acid (100 g, 0.86 mol), according to the procedure of Blatt, et al.,<sup>14</sup> bp 58-60° (0.7 mm) [lit.<sup>14</sup> bp 99-101° (6.0 mm)]. The sulfonyl chloride (14 g, 0.77 mol) was then added dropwise to 100 ml of absolute dimethylamine with the reaction mixture kept at  $-20^{\circ}$ . After addition was complete, excess dimethylamine was boiled off on the steam bath, leaving a tancolored, crystalline material. The yield of N,N-dimethyl-2-thio-phenesulfonamide was 10.2 g (69%): mp 67-69°; ir 1360, 1160 cm<sup>-1</sup> (SO<sub>2</sub>N<); nmr (CDCl<sub>3</sub>) & 2.92 [s, 6, N(CH<sub>3</sub>)<sub>2</sub>], 7.42-8.10 (m, 3, aromatic CH).

Anal. Caled for C<sub>6</sub>H<sub>9</sub>NO<sub>2</sub>S<sub>2</sub>: C, 37.68; H, 4.74; N, 7.32. Found: C, 37.60; H, 4.64; N, 7.25.

6-Trimethylsilyl-N,N-dimethyl-2-thiophenesulfonamide (1).---N,N-Dimethyl-2-thiophenesulfonamide (5.7 g, 0.03 mol) was dissolved in 100 ml of dry THF under argon and 22.7 ml (0.036 mol) of 1.6 M n-butyllithium was added. After 20-min stirring, chlorotrimethylsilane (3.9 g, 0.036 mol) was added. The flask was tightly stoppered and the reaction mixture was stirred for 5 hr. Water was added and the organic layer was separated, combined with the ether extracts of the aqueous phase, dried over MgSO<sub>4</sub>, and stripped. The resultant brown solid was recrystallized from petroleum ether (bp  $30-60^{\circ}$ ) to give 3.24 g (41%) of 5trimethylsilyl-N,N-dimethyl-2-thiophenesulfonamide (1): mp 75-77°; ir 1350, 1160 cm<sup>-1</sup> (SO<sub>2</sub>N); nmr (CDCl<sub>3</sub>)  $\delta$  1.50 [s, 9, Si(CH<sub>3</sub>)<sub>8</sub>], 2.75 [s, 6, SO<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>], 7.21, 7.56 (AB,  $J_{34} = 3.5$  Hz, 2, aromatic CH).

Anal. Caled for C<sub>9</sub>H<sub>17</sub>O<sub>2</sub>NS<sub>2</sub>Si: C, 41.03; H, 6.50; N, 5.32. Found: C, 40.91; H, 6.62; N, 5.21.

Metalation of 5-Trimethylsilyl-N,N-dimethyl-2-thiophenesulfonamide (1). A. With n-Butyllithium. Condensation with Dry Ice.—Sulfonamide 1 (2.00 g, 0.0076 mol) was dissolved in 75 ml of dry ether under argon and the solution was cooled to 0°; then 9.6 ml (0.015 mol) of 1.6 M n-butyllithium in hexane was added. After the reaction mixture was stirred for 6 hr at 0-4°,

(14) A. H. Blatt, S. Bach, and L. W. Kresch, J. Org. Chem., 22, 1693 (1957).

it was poured over a slurry of Dry Ice in ether. Water (100 ml) was later added to the suspension and the resulting two layers were separated. The aqueous layer was treated with 100 ml of 3 N HCl and extracted twice with ether. The ether extracts were combined, dried over MgSO4, and stripped to give a brown oil. Repeated washings of the oil with petroleum ether gave a brown solid. Recrystallization from 1:1 absolute ethanol-petroleum ether gave 0.23 g (9.8% yield) of 5-trimethylsilyl-3-carboxyl-N,N-dimethyl-2-thiophenesulfonamide (2), mp 119-121° dec.

The original ether layer was dried over MgSO4 and stripped to give 1.5 g (75%) of recovered material, mp 74-77°. The ir spectrum of the recovered material was identical with that of the sulfonamide 1. The ir spectrum of 2 showed bands at 3000-2450, 1710 (COOH), 1345, and 1150 cm<sup>-1</sup> (SO<sub>2</sub>N<); nmr (CD-Cl<sub>3</sub>)  $\delta$  0.37 [s, 9, Si(CH<sub>3</sub>)<sub>8</sub>], 2.94 [s, 6, SO<sub>2</sub>N(CH<sub>3</sub>)<sub>3</sub>], 7.66 (s, 1, aromatic CH), 10.70 (s, 1, COOH). Anal. Calcd for C<sub>10</sub>H<sub>17</sub>NO<sub>4</sub>S<sub>2</sub>Si: C, 39.06; H, 5.57; N, 4.56. Found: C, 39.48; H, 5.63; N, 4.67. B. With *n*-Butyllithium-TMEDA. Condensation with Dry

Ice.—Tetramethylethylenediamine (2.07 g, 0.0023 mol) was dissolved in 40 ml of 1:1 ether-hexane solution and treated with 1.28 ml (0.0023 mol) of 1.6 M n-butyllithium in hexane under argon. After being stirred for 15 min, the reaction mixture was cooled to  $-30^{\circ}$  and sulfonamide 1 (0.5 g, 0.0019 mol) was added. The stoppered flask was stirred for 5 hr at  $-30^{\circ}$ ; then the contents of the flask were poured over a slurry of Dry Ice in ether. After excess Dry Ice had evaporated, the white suspension was stirred with 100 ml of  $H_2O$  and the resulting two layers were separated. The aqueous layer was treated with 100 ml of 3 NHCl and extracted twice with ether; the combined ether extracts were dried over MgSO4 and stripped. No carboxylic acid product was obtained. The original ether layer was dried over  $MgSO_4$ and stripped to give a brown oil. Vacuum distillation of the crude oil gave 0.15 g (39%) of the rearranged amine, 2-trimethyl-silyl-N,N-dimethyl-4-thienylamine (3), bp 62-64° (1.5 mm), methiodide derivative mp 229-231°,

The following data support the structure of the rearranged amine 3: ir 2800 [N(CH<sub>3</sub>)<sub>2</sub>], 1250 cm<sup>-1</sup> (ArN<); nmr (CDCl<sub>3</sub>)  $\delta$  2.95 [s, 9, Si(CH<sub>3</sub>)<sub>s</sub>], 6.35 (d,  $J_{2,4}$  = 1.3 Hz, 1, aromatic CH), 7.05 (d,  $J_{2,4} = 1.3$  Hz, 1, aromatic CH); mass spectrum M<sup>+</sup> at m/e 199.

Anal. Calcd for C<sub>9</sub>H<sub>17</sub>NSSi: C, 54.21; H, 8.59. Found: C, 54.12; H, 8.48.

5-Trimethylsilyl-N,N-diethyl-2-thiophenesulfonamide (4).-2-Thiophenesulfonyl chloride was prepared as described at the beginning of this Experimental Section. The sulfonyl chloride (9.0 g, 0.038 mol) was added dropwise to excess diethylamine (25 ml) with stirring. After the addition was completed, excess diethylamine was stripped, and the resulting white solid was washed with petroleum ether. The product was vacuum distilled at 1.3 mm to give a single fraction boiling between 99 and 102° which weighed 6.5 g (78%): ir 1330, 1155 cm<sup>-1</sup> (SO<sub>2</sub>N<); nmr (CDCl<sub>3</sub>)  $\delta$  1.25 (t, 6, CH<sub>3</sub>), 3.40 (q, 4, CH<sub>2</sub>), 7.33–7.97 (m, 3, aromatic CH).

Anal. Calcd for  $C_8H_{18}NO_2S_2$ : C, 43.81; H, 5.98; N, 6.39. Found: C, 43.78; H, 5.92; N, 6.27. The sulfonamide (6.5 g, 0.03 mol) was dissolved in 200 ml of

dry ether under argon and 22.7 ml (0.036 mol) of 1.6 M n-butyllithium was added. After 30-min stirring, chlorotrimethylsilane (7.8 ml, 0.72 mol) was added. The mixture was stirred for 20 min and hydrolyzed with  $H_2O$ , whereupon the ether layer was separated, washed once with  $H_2O$ , dried over MgSO<sub>4</sub>, and stripped. The resultant reddish-brown oil was vacuum distilled at 0.8 mm. A single fraction, bp 133-137°, was collected to give at 0.3 init: A single fraction, bp 135-137, was concrete to give 6.9 g (79%) of 5-trimethylsilyl-N,N-diethyl-2-thiophenesulfon-amide (4): ir 1345, 1150 cm<sup>-1</sup> (SO<sub>2</sub>N<); nmr (CDCl<sub>3</sub>)  $\delta$  0.35 [s, 9, Si(CH<sub>3</sub>)<sub>8</sub>], 1.17 (t, J = 7.0 Hz, 6, CH<sub>3</sub>), 3.22 (q, J = 7.0Hz, 4, CH<sub>2</sub>), 7.17 (d,  $J_{3,4} = 3.5$  Hz, 1, aromatic CH), 7.50 (d,  $J_{3,4} = 3.5$  Hz, 1, aromatic CH).

Anal. Calcd for C<sub>11</sub>H<sub>21</sub>NO<sub>2</sub>S<sub>2</sub>Si: C, 45.32; H, 7.26; N, 4.80. Found: C, 45.51; H, 7.25; N, 4.69. Metalation of 5-Trimethylsilyl-N,N-diethyl-2-thiophenesulfon-

amide (4) and Condensation with Electrophilic Reagents. A. Condensation with Dry Ice.-To a solution of TMEDA (0.56 g, 0.005 mol) in 45 ml of dry ether was added 3.1 ml (0.005 mol) of 1.6 M-n-butyllithium in hexane under argon. After 15-min stirring, the reaction mixture was cooled to  $0^{\circ}$  and sulfonamide 4 (1.27 g, 0.0045 mol) was added. The tightly stoppered flask was stirred for 6 hr at approximately  $-30^{\circ}$ , after which the contents of the flask was poured over a slurry of Dry Ice in ether. Water

(100 ml) was added, and the aqueous layer was separated, acidified with 100 ml of 10% HCl, and extracted twice with ether. The combined ether extracts were dried over MgSO4 and stripped to give 0.52 g (44%) of 3-carboxyl-N,N-diethyl-2-thiophenesulfonamide (5), mp 147-149°.

The original ether layer was dried over MgSO4 and stripped to give 0.30 g (22% recovery) of starting material whose ir spectrum was superimposable on that of sulfonamide 4.

The ir spectrum of compound 5 (Nujol) exhibited bands at 3000–2450, 1715 (COOH), 1340, 1140 cm<sup>-1</sup> (–SO<sub>2</sub>N<); nmr (DMSO- $d_6$ )  $\delta$  1.07 (t, 6, CH<sub>3</sub>), 3.40 (q, 4, CH<sub>2</sub>), 7.55, 8.05

(DMSO-a<sub>6</sub>) o 1.07 (t, 0, OH<sub>3</sub>), 5.40 (q, ±, OH<sub>2</sub>), 1.07 (AB,  $J_{AB} = 4.9$  Hz, 2, aromatic CH). Anal. Caled for C<sub>9</sub>H<sub>13</sub>NO<sub>4</sub>S<sub>2</sub>: C, 41.05; H, 4.98; N, 5.32. Found: C, 41.03 (41.40); H, 5.01; N, 4.79 (4.96). Metalation of N,N-Diethyl-2-thiophenesulfonamide.—To a

solution of N,N-diethyl-2-thiophenesulfonamide (2.0 g, 0.0093 mol) in 50 ml of dry ether under argon was added 6.3 ml (0.01 mol) of 1.6 M n-butyllithium with stirring. After 1 hr, the contents of the reaction flask was quickly added to a slurry of excess Dry Ice in ether. The mixture was later hydrolyzed with 100 ml of water. Solid NaOH was added until the mixture was strongly basic. The aqueous layer was separated, washed once with ether, and then neutralized with 10% HCl. Ether extracts of the neutralized aqueous layer were dried over MgSO4 and stripped to give 1.97 g (82%) of 5-carboxyl-N,N-diethyl-2-thiophenesulfonamide. Recrystallization from dry ether gave an analytical sample: mp 128–130°; ir (Nujol) 2700–2450, 1700 (COOH), 1360, 1145 cm<sup>-1</sup> ( $-SO_{2}N <$ ). Anal. Calcd for  $C_{9}H_{18}NO_{4}S_{2}$ : C, 41.05; H, 4.98; N, 5.32. Found: C, 41.04; H, 4.89; N, 5.14.

B. Condensation with Deuterium Oxide.-Lithio intermediate 4' was prepared as described at the beginning of this section using 2.0 g (0.007 mol) of sulfonamide 4, 5.0 ml (0.008 mol) of 1.6 M *n*-butyllithium in hexane, and 0.90 g (0.008 mol) of TMEDA. After being stirred for 6 hr, the reaction mixture was hydrolyzed with 1.0 ml of  $D_2O$ . The ether layer was separated, washed with H<sub>2</sub>O, dried over MgSO<sub>4</sub>, and stripped. The resulting oil was vacuum distilled to give 1.4 g (70% recovery of material), bp 130-132° (0.65 mm). An nmr spectrum indicated that 1.0 deuterium atom was incorporated into the aromatic ring by the absence of a proton resonance corresponding to the chemical shift of the downfield ring proton  $(\delta 7.50)$  in the undeuterated sulfonamide 4. The ir spectrum of deuterated sulfonamide 4 was identical with that of the starting material. The C-D stretching vibration that should be present for this compound was not in evidence on an instrument with the sensitivity of the Infracord 137.

C. Condensation with Dimethylformamide.-To a solution of TMEDA (0.70 g, 0.006 mol) in 30 ml of dry ether was added 3.8 ml (0.006 mol) of 1.6 M n-butyllithium in hexane under argon. After being stirred for 15 min, the reaction mixture was cooled to 0°, sulfonamide 4 (1.45 g, 0.005 mol) was added, and the mixture was stirred for 24 hr at  $0-4^{\circ}$ . Dimethylformamide (0.88 g, 0.012 mol) was added to the mixture and stirred for 6 hr. After the reaction mixture was hydrolyzed, the ether layer was separated, combined with ether extracts of the aqueous layer, dried over MgSO4, and stripped. Vacuum distillation of the resultant crude oil gave 0.10 g of a yellow oil boiling at 80-82 (1.25 mm) and 0.39 g of a product mixture boiling at 156° (1.25 mm)mm). Ir and nmr spectra for the first fraction did not conform with any predicted product or products; ir spectrum showed bands at 2910, 1240, 1000, 833, and 745 cm<sup>-1</sup>; nmr (CDCl<sub>3</sub>)  $\delta$ 1.05-1.53 (m, 8.5 H), 2.40-3.00 (m, 2.2 H), 6.76 (s, 1, aromatic CH).

An nmr analysis of the second fraction showed it to be 43%starting sulfonamide 4 and 57% 5-trimethylsilyl-3-formyl-2-N,N-diethylthiophenesulfonamide (6) by comparison of the relative peak areas at 7.50 ppm for 4 and 10.30 ppm for compound 6. The nmr data corresponded to 12% recovery and a 14% yield, respectively, of the two compounds. An ir spectrum for the mixture showed bands at 1695 (C=O), 1330, and 1140 cm<sup>-1</sup> (SO<sub>2</sub>N); nmr (CCl<sub>4</sub>)  $\delta$  0.37 [s, unresolved, Si(CH<sub>3</sub>)<sub>8</sub>], 1.20 (t, unresolved, CH<sub>3</sub>), 3.27 (q, unresolved, CH<sub>2</sub>), 7.50 (d,  $J_{34}$  = 3.5Hz, aromatic CH), 7.58 (s, aromatic CH), 10.30 (s, CHO).

An unsuccessful attempt was made to separate the mixture on a 30-ft preparative scale gas chromatographic column containing Carbowax 4000.

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**Registry No.**—1, 41895-02-7; 2, 41895-03-8; 3, 41895-04-9; 3 methiodide derivative, 41895-05-0; 4, 41895-06-1; deuterated 4, 41895-07-2; 5, 41895-08-3; 6, 41895-09-4; N,N-dimethyl-2thiophenesulfonamide, 41895-10-7; dimethylamine, 124-40-3; chlorotrimethylsilane, 75-77-4; diethylamine, 109-89-7; N,N-5-carboxy-N,Ndiethyl-2-thiophenesulfonamide, 41895-11-8; diethyl-2-thiophenesulfonamide, 41895-12-9: dimethylformamide, 68-12-2.

## **Complexation as a Factor in Metalation Reactions.** Metalation of 1-Methoxy-2-phenoxyethane

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The effect of side-chain chelation on the rate of metalation of anyl rings by n-butyllithium was investigated by allowing anisole and 1-methoxy-2-phenoxyethane (MPE) to compete for excess base. The ratio of MPE to ani-sole metalation was found to be 13.9:1 and 14.4:1 in ether and hexane, respectively. MPE gave phenol and phenyl vinyl ether as minor products during the reaction. Labeling experiments showed the phenol to be derived from both inter- and intramolecular routes. Evidence for a 2:1 complex between n-butyllithium and MPE was presented.

The metalation reaction continues to attract attention both with regard to the mechanism of proton removal as well as synthetic utility.<sup>1</sup> In the latter context we became interested in the relative importance of heteroatom chelation as a directing and activating influence during the metalation of aromatics. Here we report a quantitation of this effect for oxygen in the metalation of benzene rings by *n*-butyllithium.

During the past few years evidence has been accumulating which clearly shows that heteroatoms either in the solvent or on reactants enhance the reactivity of lithium alkyls and influence site selection for proton removal. Thus, while generally unreactive to n-butyllithium, benzene can be quantitatively metalated by this base in the presence of simple tertiary amines.<sup>2</sup> Good chelating bases such as sparteine or

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