

2866, 1666, 1418  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{13}\text{H}_{21}\text{NO}$   $m/z$  207.1623, found  $m/z$  207.1627.

**36** (bp 65–75  $^{\circ}\text{C}$ , <1 mmHg):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , mixture of isomers)  $\delta$  0.83–0.89 (m, 6 H), 1.37–1.53 (m, 1 H), 1.73–2.24 (m), 2.30–2.82 (m), 3.29 (d, 2 H,  $J = 7.6$  Hz, **36a**), 3.38 (dd, 1 H,  $J = 7.0$ , 13.4 Hz, **36b**), 3.56 (dd, 1 H,  $J = 8.2$ , 13.4 Hz, **36b**), 4.78 (m, 1 H, **36b**);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  20.0, 20.1, 20.2, 21.0, 21.7, 26.2, 27.1, 28.4, 29.9, 30.4, 31.2, 32.0, 32.8, 33.2, 41.9, 50.1, 102.9, 115.6, 137.0, 144.1, 169.4, 170.1; IR (neat) 3010, 2963, 2934, 2903, 2872, 2849, 1688, 1660, 1633, 1466, 1406  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{19}\text{NO}$ : C, 74.57; H, 9.91; N, 7.25. Found: C, 74.13; H, 9.95; N, 7.19.

**39** (bp 55–65  $^{\circ}\text{C}$ , <1 mmHg):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.84 (d, 6 H,  $J = 6.7$  Hz), 0.98 (t, 3 H,  $J = 7.4$  Hz), 1.88 (m, 1 H), 2.00 (m, 2 H), 2.14 (t, 2 H,  $J = 7.9$  Hz), 2.44 (t, 2 H,  $J = 7.9$  Hz), 3.20 (d, 2 H,  $J = 7.5$  Hz), 5.68 (m, 1 H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  12.5, 20.0, 24.2, 26.9, 27.9, 31.6, 53.4, 121.5, 124.4, 169.5; IR (neat) 2964, 2842, 1639  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{11}\text{H}_{19}\text{NO}$ : C, 72.88; H, 10.56; N, 7.72. Found: C, 72.85; H, 9.87; N, 7.72.

**41** (bp 55–65  $^{\circ}\text{C}$ , <1 mmHg):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.86 (d, 6 H,  $J = 6.7$  Hz), 1.01 (t, 3 H,  $J = 7.4$  Hz), 1.18 (d, 3 H,  $J = 7.0$  Hz), 1.83–2.08 (m, 4 H), 2.26 (ddd, 1 H,  $J = 6.7$ , 16.4, 1.0 Hz), 2.48 (d quint, 1 H,  $J = 10.4$ , 7.0 Hz), 3.15 (dd, 1 H,  $J = 13.4$ , 7.4 Hz), 3.30 (dd, 1 H,  $J = 13.4$ , 7.6 Hz), 5.70 (s, 1 H);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  12.4, 15.9, 19.9, 20.0, 26.9, 27.8, 32.1, 35.3, 53.4, 120.1, 123.6, 172.6; IR (neat) 2964, 2932, 2872, 1662, 1458  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{12}\text{H}_{21}\text{NO}$   $m/z$  195.1623, found  $m/z$  195.1623.

**43** (bp 55–65  $^{\circ}\text{C}$ , <1 mmHg):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.87 (d, 6 H,  $J = 6.7$  Hz), 1.02 (m, 6 H), 1.92 (m, 1 H), 2.04 (m, 2 H), 2.23–2.36 (m, 2 H), 2.58 (m, 1 H), 3.01 (dd, 1 H,  $J = 13.4$ , 7.1 Hz), 3.46 (dd, 1 H,  $J = 13.4$ , 7.7 Hz), 5.63 (t, 1 H,  $J = 0.8$  Hz);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  12.7, 17.7, 19.9, 20.0, 24.8, 27.9, 29.8, 39.1, 53.2, 122.9, 125.9, 168.4; IR (neat) 2964, 2930, 2873, 1679, 1467, 1456, 1414  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{12}\text{H}_{21}\text{NO}$   $m/z$  195.1623, found  $m/z$  195.1630.

**46** (bp 85–95  $^{\circ}\text{C}$ , 3 mmHg):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.03 (t, 3 H,  $J = 7.4$  Hz), 1.13 (d, 6 H,  $J = 6.8$  Hz), 2.07 (bq, 2 H,  $J = 7.4$  Hz), 2.18 (bt, 2 H,  $J = 8.1$  Hz), 2.48 (dd, 2 H,  $J = 7.3$ , 8.7 Hz), 4.87 (sept, 1 H,  $J = 6.8$  Hz), 5.85 (quint, 1 H,  $J = 1.2$  Hz);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  12.4, 20.4, 23.5, 27.1, 31.6, 42.9,

117.7, 122.0, 168.1; IR (neat) 2968, 2934, 2898, 2877, 2842, 1657, 1463, 1437, 1410  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{10}\text{H}_{17}\text{NO}$   $m/z$  167.1310, found  $m/z$  167.1309.

**48** (bp 95–105  $^{\circ}\text{C}$ , 3 mmHg):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.97 (d, 3 H,  $J = 6.9$  Hz), 1.04 (t, 3 H,  $J = 7.4$  Hz), 1.10 (d, 3 H,  $J = 6.9$  Hz), 1.13 (d, 3 H,  $J = 6.9$  Hz), 2.02–2.11 (m, 2 H), 2.26 (m, 1 H), 2.26 (dd, 1 H,  $J = 3.8$ , 16.6 Hz), 2.57 (dd, 1 H,  $J = 16.6$ , 7.4 Hz), 4.87 (sept, 1 H,  $J = 6.9$  Hz), 5.76 (t, 1 H,  $J = 1.4$  Hz);  $^{13}\text{C}$  NMR (75.5 MHz,  $\text{CDCl}_3$ )  $\delta$  12.7, 17.5, 20.0, 20.6, 25.2, 29.1, 39.3, 42.8, 116.5, 127.3, 167.6; IR (neat) 2965, 2932, 2876, 1671, 1463, 1410  $\text{cm}^{-1}$ ; HRMS calcd for  $\text{C}_{10}\text{H}_{19}\text{NO}$   $m/z$  181.1466, found  $m/z$  181.1462.

**General Procedure for the Isomerization of Double Bonds and Hydrolysis of Enamides.** To a solution containing a mixture of enamide and lactam or mixture of double bond isomers (1 mmol in 10 mL of methanol) was added *p*-toluenesulfonic acid (0.2 mmol), and the reaction mixture was heated at reflux or stirred at ambient temperature until either the enamide was hydrolyzed or isomerization demonstrated no further change.

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**Supplementary Material Available:**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra for all reported compounds (66 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

## Aromatic Heteroannulation via Metalation–Cyclization of *N*-Acyl-2-chlorobenzenesulfonamides and *N*-Acylbenzenesulfonamides

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*N*-Acyl-2-chlorobenzenesulfonamides **7a–d** undergo competitive metal–halogen exchange and ortho-deprotonation or  $\alpha$ -deprotonation reactions when treated sequentially with sodium hydride and *n*-butyllithium. The *o*-lithio intermediates derived from metal–halogen exchange and ortho-deprotonation undergo cyclization to afford 3-substituted 1,2-benzisothiazole 1,1-dioxides **10a–d** and 3-substituted 7-chloro-1,2-benzisothiazole 1,1-dioxides **14a–d**, respectively. Reaction time–temperature data show evidence for the slow conversion of the lateral dianion of *N*-acetyl-2-chlorobenzenesulfonamide (**7a**) to the corresponding *N*,ortho-dialkali salt. 1,2-Benzisothiazole 1,1-dioxides **14a–d** were obtained in good yield and free from products resulting from metal–halogen exchange by treatment of sulfonamides **7a–d** with 2 equiv of LDA in THF. In the presence of 2 equiv of LDA, *N*-acylbenzenesulfonamides devoid of or containing only weakly acidic  $\alpha$ -hydrogens undergo  $\alpha$ -deprotonation–cyclization to afford the respective 1,2-benzisothiazole 1,1-dioxides.

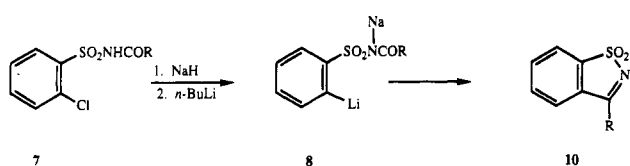
### Introduction

3-Substituted 1,2-benzisothiazole 1,1-dioxides **3** represent an important class of heterocycles with a broad range of biological activity. Compounds of this structural type have found application as diuretics,<sup>1–3</sup> hypotensive drugs,<sup>4</sup>

antimicrobial agents,<sup>5</sup> and agricultural fungicides.<sup>6,7</sup> A variety of synthetic strategies have been developed for

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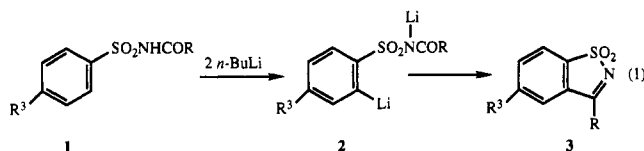
Scheme I



these compounds, the most direct of which involve treatment of saccharin with organolithium compounds<sup>8,9</sup> or Grignard reagents<sup>4,8,10,11</sup> to afford 3-alkyl- and 3-aryl-1,2-benzisothiazole 1,1-dioxides. Pseudosaccharin chloride has been used to prepare 3-aryl<sup>12</sup> and 3-alkoxy<sup>5-7,13</sup> derivatives. Oxidation of 1,2-benzisothiazoles with hydrogen peroxide<sup>3,14</sup> or perphthalic acid<sup>15</sup> yields the corresponding 1,1-dioxides. Numerous 3-aryl-1,2-benzisothiazole 1,1-dioxides have been prepared via cyclization reactions involving benzophenone<sup>16</sup> and appropriately substituted benzophenone derivatives<sup>1,2,11,17-20</sup> in which the heterocyclic moiety is constructed during the course of the reaction.

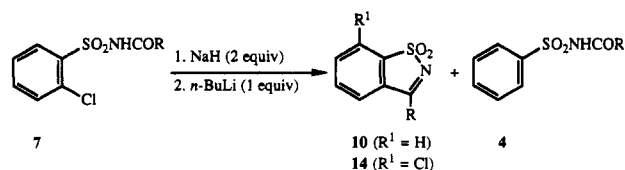
## Results and Discussion

Treatment of *N*-acylbenzenesulfonamides 1 with 2 equiv of *n*-BuLi has been reported by Abramovitch and co-workers<sup>8</sup> to afford low (<10%) yields of 3-methyl- and 3-aryl-1,2-benzisothiazole 1,1-dioxides 3 via *N*,*o*-dilithio derivatives 2 (eq 1). The poor yields observed in cycli-



zation reactions of *N*-acylbenzenesulfonamides containing acidic  $\alpha$ -hydrogens may be attributed to the fact that  $\alpha$ -deprotonation to give lateral 1,3-dianions such as 5 may be favored over formation of intermediates 2.<sup>21</sup> This was

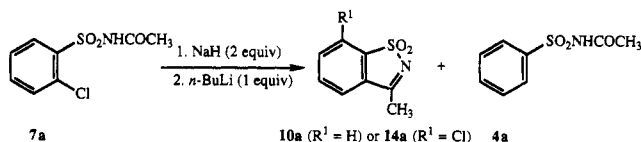
Table I. Distribution of Products for Reactions of *N*-Acylbenzenesulfonamides 7<sup>a</sup>



substrate	product (rel %) <sup>b</sup>			
7a, R = Me	10a (15)	14a (28)	4a (26)	7a (31)
7a <sup>c</sup>	10a (27)	14a (9)	4a (53)	7a (11)
7b, R = Et	10b (27)	14b (30)	4b (32)	7b (11)
7c, R = <i>i</i> -Pr	10c (59)	14c (41)		
7d, R = Ph	10d (32) <sup>d</sup>	14d (18) <sup>d</sup>		

<sup>a</sup> Each reaction was allowed to proceed for 1 h at  $-78^\circ\text{C}$ , then 1 h at  $-78$  to  $0^\circ\text{C}$ , and finally 1 h at  $0$  to  $25^\circ\text{C}$ . <sup>b</sup> Relative mol %, determined by NMR analysis of the crude product mixture. For isolated yields, see the Experimental Section. <sup>c</sup> Reaction with NaH (2 equiv)/*n*-BuLi (2 equiv). <sup>d</sup> Isolated yield after preparative TLC.

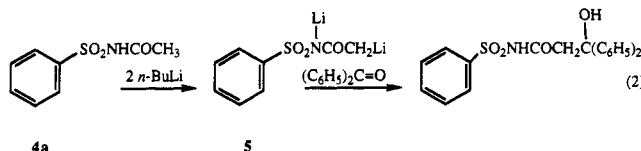
Table II. Variation in Product Distribution with Time and Temperature for the Reaction of *N*-Acetyl-2-chlorobenzenesulfonamide (7a) with NaH/*n*-BuLi



elapsed time, h	temp, $^\circ\text{C}$	rel % <sup>a</sup>			
		10a	14a	4a	7a
0.5	$-78$	13	27	22	38
1.0	$-78$	13	27	23	37
2.0	$-78$ to $0$	12	25	26	37
3.0	$0$ to $25$	12	29	25	34
6.0	$25$	12	41	23	24

<sup>a</sup> Relative mol %, determined by NMR analysis of the crude product mixture.

confirmed by our observation that, when *N*-acetylbenzenesulfonamide (4a) was treated with 2 equiv of *n*-BuLi, followed by addition of benzophenone, tertiary alcohol 6 was obtained in good yield, unaccompanied by detectable formation of the 1,2-benzisothiazole (eq 2).

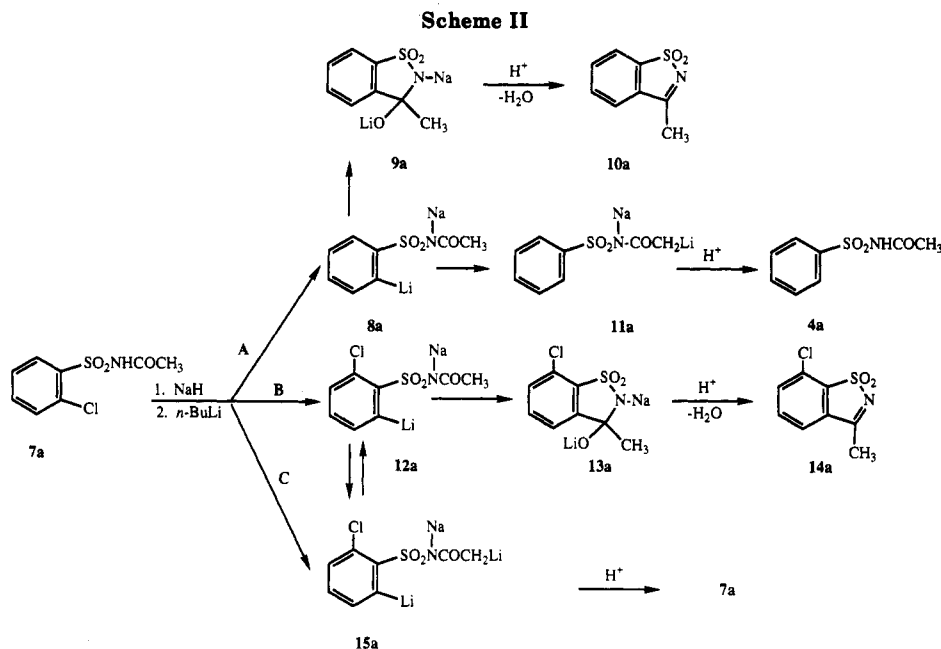


It occurred to us that an alternative approach to the synthesis of 1,2-benzisothiazole 1,1-dioxides 10 through *N*,*o*-dialkali intermediates like 2<sup>22</sup> might begin with *N*-acyl-2-chlorobenzenesulfonamides 7 (Scheme I). Thus, we anticipated that initial removal of the acidic NH proton of 7 with sodium hydride would lower the acidity of the  $\alpha$ -protons of the *N*-acyl group to the extent that subsequent addition of *n*-BuLi would give *N*,*ortho*-dialkali intermediates 8 rather than the corresponding lateral 1,3-dianion.<sup>22</sup>

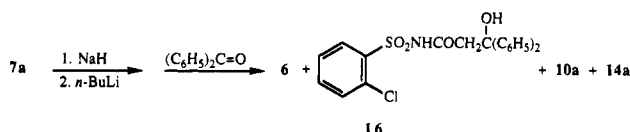
Using *N*-acetyl-2-chlorobenzenesulfonamide (7a) as a model compound, we have found that reaction of this

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substrate with sodium hydride (2 equiv) followed by *n*-BuLi (1 equiv) affords a mixture of metalated derivatives **8a**, **11a**, **12a**, and **15a** (Scheme II). The intermediacy of **8a** and **12a**, formed by metal-halogen exchange and ortho-lithiation, respectively, is supported by isolation of 3-methyl-1,2-benzisothiazole 1,1-dioxide (**10a**) and 3-methyl-7-chloro-1,2-benzisothiazole 1,1-dioxide (**14a**) (Table I). The reaction also yielded *N*-acetylbenzenesulfonamide (**4a**) and recovered **7a**, implicating formation of lateral dianions **11a** and **15a**. Further evidence for the coexistence of **11a** and **15a** was obtained by quenching a similar reaction with benzophenone which yielded a mixture of tertiary alcohols **6** (7%) and **16** (23%) after exposure of **7a** to NaH followed by *n*-BuLi at  $-78^\circ\text{C}$ .<sup>23</sup>



In an effort to elucidate details of the mechanism operating in the cyclization of **7a**, the effects of time and temperature on the distribution of products were studied (Table II). The data in Table II indicate that the product distribution remains essentially constant at temperatures between  $-78$  and  $0^\circ\text{C}$ . However, when the temperature of the reaction mixture is allowed to rise to  $25^\circ\text{C}$ , the yield of **14a** increases at the expense of recovered **7a**. A mechanism consistent with these results is outlined in Scheme II. It appears that **7a** is initially converted to a mixture of dianions **8a**, **12a**, and **15a** via routes A, B, and C, respectively. This assumption is supported by the fact that hydrolysis of the reaction mixture after 30 min exposure to *n*-BuLi at  $-78^\circ\text{C}$  afforded chloro compounds **14a** (route B, 27%) and unchanged **7a** (route C, 38%) and dehalogenated compounds **10a** and **4a** (route A, total 35%). Dianion **12a**, produced by ortho-lithiation, undergoes rapid cyclization to **13a**, which becomes **14a** after acid hydrolysis. Dianion **8a**, formed through metal-halogen exchange, suffers at least two fates, namely, cyclization to **9a**, the

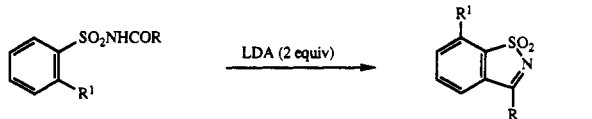
precursor to **10a**, and proton-metal exchange to form dianion **11a**, which upon subsequent protonation yields product **4a**. Support for the latter process was obtained through deuterium labeling experiments. Specifically, when (*N*-acetyl-*d*<sub>3</sub>)-2-chlorobenzenesulfonamide (**7a-d**<sub>3</sub>) was exposed to the same reaction conditions, ca. 22% of the obtained **4a** was found to contain a deuterium label at one of the equivalent ortho positions of the phenyl ring. As the reaction temperature is increased, **15a**, formed by initial  $\alpha$ -deprotonation of **7a** at  $-78^\circ\text{C}$ , begins to be converted to *o*-lithio derivative **12a** by proton-metal exchange. Consequently, the yield of **14a** increases at the expense of **7a** as **12a** undergoes irreversible cyclization. The case for a similar conversion of lateral dianion **11a** to *o*-lithio derivative **8a** cannot be made, however, since the ratio of **10a** to **4a** does not change with increasing reaction time and temperature. Apparently, the combined electron-withdrawing effects of the chloro and sulfonyl substituents render the ortho proton of **15a** more labile than the ortho protons of **11a**,<sup>24</sup> thereby facilitating the conversion of **15a** to **12a**.

Although the preceding study revealed some interesting aspects of the metalation of **7a** with *n*-BuLi, this reaction proved to be unsatisfactory as a preparative method for benzisothiazoles because of the low yields and difficult separation of **10a** and **14a**. Therefore, the reaction of **7a** was repeated using 2 equiv of *n*-BuLi, with the aim of eliminating chloro compounds **7a** and **14a** by converting them to **4a** and **10a**, respectively, through subsequent metal-halogen exchange involving dianions **13a** and **15a**. The product distribution from this reaction (Table I) shows that the yields of **7a** and **14a** were reduced by ca. two-thirds compared to yields obtained with 1 equiv of *n*-BuLi.

In order to assess the effect that the *N*-acyl group might exert on the composition of the product mixture, cyclization reactions of *N*-acyl-2-chlorobenzenesulfonamides **7b-d** were investigated. The results of these reactions are summarized in Table I. Treatment of *N*-propionyl-2-chlorobenzenesulfonamide (**7b**) with sodium hydride (2 equiv) followed by *n*-BuLi (1 equiv) afforded a mixture of

(23) Treatment of **7a** with 2 equiv of *n*-BuLi at  $-78^\circ\text{C}$  gave a similar ratio of the dilithio analogues of **11a** and **15a** as evidenced by production of **4a** and recovered **7a** in a ratio of 1:3.1 following hydrolysis of the reaction mixture.

(24) The  $^1\text{H}$  NMR chemical shift of the doublet for the more highly deshielded ortho proton of **7a** ( $\delta$  8.28) compared with that for the ortho protons of **4a** ( $\delta$  8.04) is consistent with this assumption.

**Table III.** Cyclizations of *N*-Acylbenzenesulfonamides to 1,2-Benzisothiazole 1,1-Dioxides with LDA<sup>a</sup>


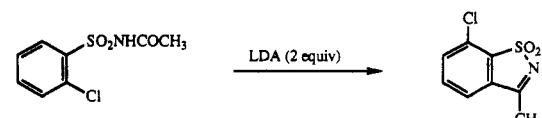
substrate	product	yield, <sup>b</sup> %	mp, <sup>c</sup> °C
4a, R = Me	10a	d	
4b, R = Et	10b	d	
4c, R = <i>i</i> -Pr	10c	58	87–88.5
4d, R = Ph	10d	80	166–167 <sup>e</sup>
7a, R = Me	14a	69	218.5–220
7b, R = Et	14b	65	144.5–145.5
7c, R = <i>i</i> -Pr	14c	74	143.5–144.5
7d, R = Ph	14d	86	219–220

<sup>a</sup> Each reaction was allowed to proceed for 1 h at –78 °C and then for an additional 4 h at –78 to 0 °C. <sup>b</sup> Isolated yield after recrystallization. <sup>c</sup> Spectral data and other details are given in the Experimental Section. <sup>d</sup> Starting material was recovered. <sup>e</sup> Lit.<sup>8</sup> mp 168 °C.

products similar to that described for 7a. However, the higher proportion of nonhalogenated products 4b and 10b in the reaction mixture of 7b compared with that of 7a suggests that metal–halogen exchange in 7b competes more effectively with deprotonation of the less acidic  $\alpha$ -hydrogens of the *N*-propionyl group. Reactions of *N*-isobutyryl-2-chlorobenzenesulfonamide (7c) and *N*-benzoyl-2-chlorobenzenesulfonamide (7d) gave mixtures of cyclized products and none of the corresponding benzenesulfonamides. Further reduction in the acidity of the  $\alpha$ -hydrogens of the *N*-acyl group of 7c compared with those of 7a and 7b apparently enables metal–halogen exchange and ortho-lithiation to predominate over  $\alpha$ -deprotonation. Sulfonamide 7d, which has no  $\alpha$ -hydrogens, can only react via cyclization.

In contrast to *n*-BuLi-induced metalation–cyclization reactions, which yielded product mixtures resulting from ortho-lithiation and metal–halogen exchange, reactions of *N*-acyl-2-chlorobenzenesulfonamides 7a–d with 2 equiv of LDA afforded a single benzisothiazole product. In general, these reactions which are summarized in Table III provide an efficient and convenient synthesis of 3-substituted 7-chloro-1,2-benzisothiazole 1,1-dioxides 14a–d. Not surprisingly, the highest yield of cyclized product was obtained with *N*-benzoyl-2-chlorobenzenesulfonamide (7d) for which interfering side-chain dilithiation is not possible. Cyclization reactions of sulfonamides with acidic  $\alpha$ -hydrogens were hampered by competing lateral dianion formation as demonstrated by the isolation of essentially equimolar amounts of tertiary alcohol 16 and benzisothiazole 14a following a benzophenone quench of the reaction of 7a with 2 equiv of LDA. This impediment to the cyclization of 7a could be largely overcome, however, by extending the reaction time at higher temperatures as illustrated by the data in Table IV. The same rationale presented earlier relative to intermediate dianions 12a and 15a may again be evoked to account for the slow conversion of 7a to 14a with increasing reaction time and temperature.

Attempted cyclization reactions of *N*-acetylbenzenesulfonamide (4a) and *N*-propionylbenzenesulfonamide (4b) using 2 equiv of LDA yielded only recovered starting material. Apparently, ortho-deprotonation, which effectively competed with  $\alpha$ -deprotonation in similar reactions of chloro analogues 7a and 7b, does not occur with 4a and 4b because of the lower acidity of their ortho protons. However, we have found that *N*-isobutyrylbenzene-

**Table IV.** Variation in Product Distribution with Time and Temperature for the Reaction of *N*-Acetyl-2-chlorobenzenesulfonamide (7a) with LDA


elapsed time, h	temp, °C	rel % <sup>a</sup>	
		14a	7a
0.5	–78	58	42
1.0	–78	55	45
2.0	–78 to 0	62	38
3.0	0–25	68	32
6.0	25	88	12

<sup>a</sup> Relative mol % determined by NMR analysis of the crude product mixtures.

sulfonamide (4c) and *N*-benzoylbenzenesulfonamide (4d) are converted to their *N*,ortho-dilithio salts by treatment with 2 equiv of LDA. These intermediates then undergo cyclization to 1,2-benzisothiazole 1,1-dioxides 10c and 10d, respectively, in satisfactory yields (Table III).

## Experimental Section

**General.** All commercial reagents were ACS certified. Solvents used in chromatography were distilled prior to use. Tetrahydrofuran (THF) was distilled from potassium/benzophenone ketyl and diisopropylamine was distilled from calcium hydride. Solutions of *n*-BuLi were periodically standardized against diphenylacetic acid.<sup>25</sup> Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. <sup>1</sup>H NMR spectra were recorded on either a Varian EM-390 spectrometer or a Bruker WP270 SY spectrometer. Mass spectra were determined by Kim Harich on a Varian MAT-112 mass spectrometer in the Department of Biochemistry and Nutrition at Virginia Tech. Elemental analyses were performed by Atlantic Microlaboratories, Inc., Norcross, GA. Analytical thin-layer chromatography (TLC) was performed using Eastman Chromatogram Sheets, Type 13181 (silica gel), with fluorescent indicator. Column chromatography was done using 60–200-mesh Davison silica gel or 150-mesh Aldrich basic, Brockman I, aluminum oxide at ambient pressure. Preparative thin-layer chromatography was performed using Analtech Precoated Plates, silica gel GF, 2000  $\mu$ m.

**Preparation of *N*-Acylbenzenesulfonamides.** The procedure of Fowkes and McClelland<sup>26</sup> was used to prepare *N*-acetylbenzenesulfonamide (4a), mp 124.5–126 °C (lit.<sup>26</sup> mp 127 °C), and *N*-acetyl-2-chlorobenzenesulfonamide (7a), mp 143–144 °C: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  2.11 (s, 3 H, CH<sub>3</sub>), 7.45–8.28 (m, 5 H, arom and NH). Anal. Calcd for C<sub>8</sub>H<sub>9</sub>NO<sub>3</sub>S: C, 41.12; H, 3.45; N, 5.99. Found: C, 41.20; H, 3.47; N, 6.03. (*N*-Acetyl-*d*<sub>3</sub>)-2-chlorobenzenesulfonamide (7a-*d*<sub>3</sub>) containing 80 atom % D by <sup>1</sup>H NMR analysis was prepared by the procedure of Abramovitch et al.<sup>8</sup> from 2-chlorobenzenesulfonamide and acetyl-*d*<sub>3</sub> chloride in pyridine.

*N*-Propionylbenzenesulfonamides 4b and 7b and *N*-isobutyrylbenzenesulfonamides 4c and 7c were prepared in the following manner: 0.88 g (22 mmol) of a 60% dispersion of NaH in mineral oil was placed in an oven-dried three-necked flask under N<sub>2</sub>. The mineral oil was removed by washing with hexane several times, and 10 mL of THF was added. A solution of 10 mmol of the benzenesulfonamide in 15 mL of THF was added dropwise and then stirred at room temperature for 1 h. The reaction mixture was cooled to –78 °C, and 11 mmol of the acyl halide was added. The solution was allowed to warm to room temperature over 2 h and then poured into 100 mL of a 10% HCl solution

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containing ice. The resulting solution was then extracted with  $\text{CHCl}_3$  (6  $\times$  25 mL). The  $\text{CHCl}_3$  extracts were dried and filtered, and the solvent was removed in vacuo to give the crude product, which was recrystallized from  $\text{CHCl}_3$ /hexane.

From 1.57 g of benzenesulfonamide and 1.02 g of propionyl chloride was obtained 0.51 g (24%) of *N*-propionylbenzenesulfonamide (**4b**) as white crystals, mp 73.5–74.5 °C (lit.<sup>27</sup> mp 74–75 °C).

From 1.57 g of benzenesulfonamide and 1.17 g of isobutyryl chloride was obtained 1.76 g (78%) of *N*-isobutyrylbenzenesulfonamide (**4c**) as white crystals, mp 126–127 °C (lit.<sup>27</sup> mp 127–128.5 °C).

From 1.92 g of 2-chlorobenzenesulfonamide<sup>28</sup> and 1.02 g of propionyl chloride was obtained 1.65 g (67%) of *N*-propionyl-2-chlorobenzenesulfonamide (**7b**) as white plates after recrystallization, mp 134–135 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.10 (t,  $J$  = 7.4 Hz, 3 H,  $\text{CH}_3$ ), 2.38 (q,  $J$  = 7.4 Hz, 2 H,  $\text{CH}_2$ ), 7.45–8.32 (m, 5 H, arom and NH). Anal. Calcd for  $\text{C}_9\text{H}_{10}\text{NClO}_2\text{S}$ : C, 43.64; H, 4.07; N, 5.65. Found: C, 43.68; H, 4.07; N, 5.61.

From 1.92 g of 2-chlorobenzenesulfonamide and 1.17 g of isobutyryl chloride was obtained 1.85 g (70%) of *N*-isobutyryl-2-chlorobenzenesulfonamide (**7c**) as colorless prisms, mp 142.5–143.5 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.15 (d,  $J$  = 7.1 Hz, 6 H,  $\text{CH}_3$ ), 2.50 (sept,  $J$  = 7.1 Hz, 1 H, CH), 7.18–8.41 (m, 5 H, arom and NH). Anal. Calcd for  $\text{C}_{10}\text{H}_{12}\text{NClO}_2\text{S}$ : C, 45.89; H, 4.62; N, 5.35. Found: C, 45.86; H, 4.66; N, 5.33.

The procedure of Takatori and Ueda<sup>29</sup> was used to prepare *N*-benzoylbenzenesulfonamide (**4d**), mp 146.5–147.5 °C (lit.<sup>30</sup> mp 148 °C) and *N*-benzoyl-2-chlorobenzenesulfonamide (**7d**), mp 168.5–170 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  7.18–8.57 (m, 9 H, arom), 9.03 (s, 1 H, NH); EIMS  $m/e$  (rel intensity) 297 (0.4), 295 ( $M^+$ , 0.4), 196 (45.9), 130 (85.1), 128 (100.0), 113 (13.8), 111 (41.4), 105 (100.0), 77 (100.0).

**Procedure A. LDA Cyclizations.** To an oven-dried three-necked flask under a  $\text{N}_2$  atmosphere containing 20 mL of THF was added 0.60 g (0.98 mmol, 6 mmol) of diisopropylamine. This solution was cooled to –78 °C, and 3.85 mL (6 mmol) of 1.56 M *n*-BuLi in hexane was added slowly. The resulting solution was stirred at –78 °C for 30 min, and 2.81 mmol of the *N*-acylbenzenesulfonamide (**4** or **7**) in 5 mL of THF was added dropwise.

After being stirred for 1 h at –78 °C, the reaction mixture was warmed to room temperature and stirred an additional 4 h. The reaction was then quenched with the slow addition of 10 mL of water, and the THF was removed under reduced pressure. An additional 100 mL of water was added to the residue, and the aqueous layer was acidified with dilute HCl solution. After being stirred for several minutes, the aqueous solution was adjusted to pH 8 with dilute NaOH solution and then extracted with  $\text{CHCl}_3$  (3  $\times$  75 mL). The  $\text{CHCl}_3$  extract was washed with water, dried ( $\text{MgSO}_4$ ), and concentrated in vacuo to yield a residue (fraction A), which was purified by column chromatography on silica gel using  $\text{CHCl}_3$ . Recrystallization of the first major fraction from  $\text{CHCl}_3$ /hexane gave pure **10** or **14**. The aqueous layer was acidified with dilute HCl and extracted with  $\text{CHCl}_3$  (3  $\times$  75 mL). The  $\text{CHCl}_3$  extract was washed with water, dried ( $\text{MgSO}_4$ ), and concentrated in vacuo to yield a residue (fraction B). Purification was accomplished by chromatography on silica gel using EtOAc/MeOH (4:1) followed by recrystallization from EtOAc/hexane to give unreacted **4** or **7**.

**Procedure B. NaH/*n*-BuLi Cyclizations.** To an oven-dried three-necked flask kept under  $\text{N}_2$  was added 0.24 g (6 mmol, 2 equiv) of a 60% dispersion of NaH in mineral oil. The NaH was rinsed with hexanes several times, 20 mL of THF was added, and 2.81 mmol of the 2-chlorobenzenesulfonamide **7** in 5 mL of THF was added dropwise. The reaction mixture was allowed to stir for 30 min at room temperature and cooled to –78 °C, and 1.92 mL (3 mmol, 1 equiv) of 1.56 M *n*-BuLi was added dropwise. The reaction mixture was stirred 1 h at –78 °C, allowed to warm in an ice bath to 0 °C over a period of 1 h, and finally warmed to room temperature over 1 h. The reaction was quenched with 10

mL of water, the THF was removed under reduced pressure, and the residue was diluted to 75 mL with water. The aqueous layer was acidified with dilute HCl solution and then made slightly alkaline with dilute NaOH solution. The aqueous layer was extracted with  $\text{CHCl}_3$  (4  $\times$  60 mL), and the combined extracts were washed with water, dried ( $\text{MgSO}_4$ ), and reduced in vacuo to yield primarily cyclized products **10** or **14** (fraction A). The aqueous layer was acidified with dilute HCl solution and extracted with  $\text{CHCl}_3$  (4  $\times$  60 mL). The  $\text{CHCl}_3$  extract was washed with water, dried ( $\text{MgSO}_4$ ), and reduced in vacuo to yield a mixture of **4** or **7** (fraction B).

**Reactions of *N*-Acetyl-2-chlorobenzenesulfonamide (**7a**).** Procedure A afforded 0.07 g (11%) of recovered **7a** and 0.42 g (69%) of 3-methyl-7-chloro-1,2-benzisothiazole 1,1-dioxide (**14a**) as white crystals, mp 218.5–220 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  2.60 (s, 3 H,  $\text{CH}_3$ ), 7.15–7.62 (m, 3 H, arom); EIMS  $m/e$  (rel intensity) 217 (24.3), 215 ( $M^+$ , 62.1), 169 (22.9), 167 (72.9), 112 (32.9), 110 (90.7), 75 (100.0). Anal. Calcd for  $\text{C}_8\text{H}_6\text{NClO}_2\text{S}$ : C, 44.56; H, 2.80; N, 6.49. Found: C, 44.39; H, 2.85; N, 6.47.

Procedure B gave 0.33 g of a white solid mixture composed largely of cyclized products **10a** and **14a** (fraction A) and 0.25 g of a viscous yellow oil containing compounds **4a** and **7a** (fraction B). The former mixture was separated by preparative TLC on silica gel using hexane/ $\text{CH}_2\text{Cl}_2$  (2:1) to give 0.17 g (28%) of **14a**, mp 217–219 °C, and 0.08 g (16%) of 3-methyl-1,2-benzisothiazole 1,1-dioxide (**10a**), mp 216–217.5 °C (lit.<sup>8</sup> mp 217 °C). Fraction B could not be separated by chromatography. Integration of the methyl signals of **4a** ( $\delta$  2.06) and **7a** ( $\delta$  2.11) in the <sup>1</sup>H NMR spectrum of this mixture revealed it to be a 1.2:1 mixture of **7a**:**4a**.

In a similar reaction of **7a** with 2 equiv of NaH and 2 equiv of *n*-BuLi was obtained 0.12 g (24%) of **10a**, mp 215–217 °C, by recrystallization of fraction A from  $\text{CHCl}_3$ /hexane.

**Reaction of (*N*-Acetyl-*d*<sub>3</sub>)-2-chlorobenzenesulfonamide.** Procedure B was followed except that the reaction mixture was quenched after 1 h at –78 °C with 10 mL of EtOH. Fraction A (0.30 g) and fraction B (0.18 g) were obtained as yellow solids. Fraction B was decolorized by column chromatography on silica gel with EtOAc. Analysis of the  $m/e$  = 77 and 78 peaks in the mass spectrum of this mixture indicated ca. 22% deuterium incorporation at one of the equivalent ortho positions of *N*-acetylbenzenesulfonamide.

**Reaction of *N*-Propionyl-2-chlorobenzenesulfonamide (**7b**).** Procedure A gave 0.10 g (14%) of recovered **7b** and 0.42 g (65%) of 3-ethyl-7-chloro-1,2-benzisothiazole 1,1-dioxide (**14b**) as white crystals, mp 144.5–145.5 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.38 (t,  $J$  = 7.2 Hz, 3 H,  $\text{CH}_3$ ), 2.97 (q,  $J$  = 7.2 Hz, 2 H,  $\text{CH}_2$ ), 7.54 (s, 3 H, arom); EIMS  $m/e$  (rel intensity) 231 (36.5), 230 (25.7), 229 ( $M^+$ , 100.0), 228 (41.5), 166 (11.5), 164 (30.1), 139 (10.9), 137 (33.2), 130 (33.2), 112 (8.3), 110 (24.0), 75 (39.9); HRMS  $m/e$  228.993 (calcd for  $\text{C}_9\text{H}_8\text{HClO}_2\text{S}$  228.996). Anal. Calcd for  $\text{C}_9\text{H}_8\text{NClO}_2\text{S}$ : C, 47.06; H, 3.51; N, 6.10. Found: C, 47.18; H, 3.56; N, 6.10.

Procedure B afforded 0.46 g of a pale yellow solid (fraction A) and 0.16 g of a viscous, yellow oil (fraction B). Column chromatography of fraction A on basic alumina using EtOAc gave 0.18 g (28%) of **14b**, mp 143–145 °C, and 0.12 g (22%) of 3-ethyl-1,2-benzisothiazole 1,1-dioxide<sup>31</sup> (**10b**), mp 128.5–130.5 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.45 (t,  $J$  = 7.2 Hz, 3 H,  $\text{CH}_3$ ), 3.04 (q,  $J$  = 7.2 Hz, 2 H,  $\text{CH}_2$ ), 7.62–7.89 (m, 4 H, arom); EIMS  $m/e$  (rel intensity) 195 ( $M^+$ , 100.0), 194 (31.4), 131 (7.8), 130 (62.5), 103 (44.4), 76 (39.4), 50 (21.8); HRMS  $m/e$  calcd for  $\text{C}_9\text{H}_8\text{NO}_2\text{S}$  195.035, found 195.034. The <sup>1</sup>H NMR spectrum of fraction B showed it to be mostly a mixture of **4b** and **7b**. Integration of the doublets for the H-2 and H-6 aromatic protons of **4b** ( $\delta$  8.06–8.10) and the H-6 proton of **7b** ( $\delta$  8.28–8.32) indicated a **4b**:**7b** ratio of 2.9:1.

**Reactions of *N*-Isobutyryl-2-chlorobenzenesulfonamide (**7c**).** Procedure A afforded 0.51 g (74%) of 3-isopropyl-7-chloro-1,2-benzisothiazole 1,1-dioxide (**14c**) as colorless crystals, mp 143.5–144.5 °C: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  1.42 (d,  $J$  = 6.9 Hz, 6 H,  $\text{CH}_3$ ), 3.32 (sept,  $J$  = 6.9 Hz, 1 H, CH), 7.64 (s, 3 H, arom); EIMS  $m/e$  (rel intensity) 245 (8.5), 243 ( $M^+$ , 228), 231 (3.8), 230

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(36.5), 229 (10.8), 228 (100.0), 139 (3.8), 137 (11.1), 75 (12.7); HRMS  $m/e$  243.017 (calcd for  $C_{10}H_{10}NClO_2S$  243.012). Anal. Calcd for  $C_{10}H_{10}NClO_2S$ : C, 49.28; H, 4.14; N, 5.75. Found: C, 49.18; H, 4.15; N, 5.75.

Procedure B yielded 0.62 g of a pale yellow solid (fraction A). Analysis of the  $^1H$  NMR spectrum of this mixture of 10c and 14c by comparing the integrals for the methyl protons, indicated a 1.4:1 ratio of 10c:14c. Separation of this mixture was achieved by preparative TLC with hexane/ $CH_2Cl_2$  (2:1) to give 0.21 g (30%) of 14c, mp 140–143 °C, and 0.19 g (32%) of 3-isopropyl-1,2-benzisothiazole 1,1-dioxide<sup>9</sup> (10c), mp 87–88.5 °C:  $^1H$  NMR ( $CDCl_3$ )  $\delta$  1.40 (d,  $J$  = 6.8 Hz, 6 H,  $CH_3$ ), 3.32 (sept,  $J$  = 6.8 Hz, 1 H, CH), 7.63–7.80 (m, 4 H, arom); EIMS  $m/e$  (rel intensity) 209 ( $M^+$ , 23.4), 194 (100.0), 144 (6.4), 130 (8.6), 103 (21.1), 76 (13.6). Anal. Calcd for  $C_{10}H_{11}NO_2S$ : C, 57.39; H, 5.30; N, 5.75. Found: C, 57.28; H, 5.32; N, 5.80.

**Reactions of *N*-Benzoyl-2-chlorobenzenesulfonamide (7d).** Procedure A yielded 0.67 g (86%) of 3-phenyl-7-chloro-1,2-benzisothiazole 1,1-dioxide (14d) as white crystals, mp 219–220 °C:  $^1H$  NMR ( $CDCl_3$ )  $\delta$  7.16–8.04 (m, arom); EIMS  $m/e$  (rel intensity) 279 (15.1), 277 ( $M^+$ , 36.2), 231 (5.1), 229 (13.9), 215 (31.3), 213 (100.0), 178 (94.5), 110 (14.2), 75 (45.2). Anal. Calcd for  $C_{13}H_9ClNO_2S$ : C, 56.22; H, 2.90; N, 5.04. Found: C, 56.00; H, 2.96; N, 4.99.

Procedure B afforded, after preparative TLC of fraction A with hexane/ $CH_2Cl_2$  (1:1), 0.14 g (18%) of 14d, mp 215–218 °C, and 0.22 g (32%) of 3-phenyl-1,2-benzisothiazole 1,1-dioxide (10d), mp 164–167 °C (lit.<sup>8</sup> mp 168 °C).

**Reaction of *N*-Isobutrylbenzenesulfonamide (4c) with 2 equiv of LDA.** Procedure A gave 0.34 g (58%) of 10c from fraction A and 0.24 g (38%) of 4c from fraction B.

**Reaction of *N*-Benzoylbenzenesulfonamide (4d) with 2 equiv of LDA.** Procedure A yielded 0.55 g (80%) of 10d from fraction A and 0.02 g (3%) of 4d from fraction B.

**Rate Study of the Reaction of *N*-Acetyl-2-chlorobenzenesulfonamide (7a) with 2 equiv of NaH and 1 equiv of *n*-BuLi.** Sodium hydride (0.44 g of a 60% dispersion, 11 mmol) was washed with hexane and introduced into a three-necked, 250-mL flask maintained under a dry  $N_2$  atmosphere and equipped with a magnetic stirrer, an addition funnel, and a rubber septum (to facilitate sample removal). THF (100 mL) was added to make a slurry, and while the slurry was stirred 1.17 g (5 mmol) of 7a in 20 mL of THF was added. After being stirred for 1 h at room temperature, the mixture was cooled to –78 °C and 2.45 mL (5.5 mmol) of 2.25 M *n*-BuLi in hexane was added over a 1-min period. Timing was begun with the addition of the last drop of *n*-BuLi solution.

Samples were withdrawn (15 mL each) at 30 min and 1 h, and then the reaction vessel was warmed in an ice bath to 0 °C. After another 1 h in the ice bath, the third sample was taken. The ice bath was removed, and after an additional 1 h, sample 4 was removed at room temperature. Finally, the fifth sample was taken following another 3-h reaction period at room temperature.

Each of the samples was processed as follows: after quenching in 20 mL of  $H_2O$  and acidifying with dilute HCl, the THF was evaporated and the aqueous solution was extracted with  $CHCl_3$  (3  $\times$  40 mL). The combined  $CHCl_3$  extracts were then washed with  $H_2O$  and dried ( $MgSO_4$ ).  $^1H$  NMR analyses were performed on the five samples and the distributions of the four major components were determined, based on the integration of the four different signals attributable to the  $CH_3$  absorptions of 4a, 7a, 10a, and 14a. These results are shown in Table II.

**Rate Study of the Reaction of *N*-Acetyl-2-chlorobenzenesulfonamide (7a) with 2 equiv of LDA.** Diisopropylamine (1.22 g, 1.69 mL, 12 mmol) was introduced into an oven-dried, three-necked, 250-mL flask containing 120 mL of freshly distilled anhydrous THF and equipped with a magnetic stirrer, an addition funnel, and a rubber septum. The flask was maintained under a  $N_2$  atmosphere while the solution was cooled to –78 °C in a dry ice/acetone bath, and 4.89 mL (11 mmol) of 2.25 M *n*-BuLi in hexane was added via a syringe. After stirring for 90 min at –78 °C, it was assumed that the solution contained 11 mmol of lithium diisopropylamide. At this point, 1.17 g (5 mmol) of 7a in 10 mL of THF was added. Timing was started when the last drop of the solution had been added. Samples were withdrawn and processed as described in the previous section.

The results are tabulated in Table III.

**Reaction of *N*-Acetylbenzenesulfonamide (4a) with 2 equiv of LDA, Followed by Benzophenone.** To an oven-dried three-necked flask containing 40 mL of THF and equipped with a magnetic stirrer and an addition funnel was added 1.6 g (16 mmol) of diisopropylamine. The solution was cooled to –78 °C in a dry ice/acetone bath under  $N_2$ , and 9.1 mL (16 mmol) of a 1.76 M solution of *n*-BuLi in hexane was added dropwise. The solution was allowed to stir for 15 min at –78 °C, and 1.49 g (7.5 mmol) of 4a in 10 mL of THF was added dropwise. The resulting solution was stirred for 30 min at –78 °C and then allowed to warm to 0 °C. A solution of 1.46 g (8 mmol) of benzophenone in 10 mL of THF was then added dropwise and stirred for 2 h at 0 °C. The reaction was quenched by the addition of 50 mL of 2 N HCl solution. The aqueous layer was extracted with  $CHCl_3$  (5  $\times$  50 mL). The  $CHCl_3$  extracts were combined, dried ( $MgSO_4$ ), and filtered, and the solvent was removed in vacuo. The crude residue was chromatographed on silica gel with  $CHCl_3$  to give 0.50 g of recovered benzophenone. Further elution with EtOAc afforded 0.29 g (19%) of recovered 4a and 1.86 g (65%) of *N*-(benzenesulfonyl)- $\beta,\beta$ -diphenyl- $\beta$ -hydroxypropionamide (6) as white crystals: mp 147–149 °C:  $^1H$  NMR ( $CDCl_3$ )  $\delta$  3.23 (s, 2 H,  $CH_2$ ), 4.28 (br s, 1 H, OH), 7.22–7.54 (m, 13 H, arom), 7.66–7.70 (overlapping d's, 2 H, H-2 and H-6 arom). Anal. Calcd for  $C_{21}H_{19}NO_4S$ : C, 66.12; H, 5.02; N, 3.67. Found: C, 66.15; H, 4.96; N, 3.72.

When this reaction was performed using 2 equiv of *n*-BuLi as the base under the same conditions, there was obtained after chromatography 0.19 g of benzophenone, 0.12 g (7%) of recovered 4a, and 2.29 g (80%) of 6.

**Reaction of *N*-Acetyl-2-chlorobenzenesulfonamide (7a) with 2 equiv of LDA, Followed by Benzophenone.** Diisopropylamine (1.22 g, 1.69 mL, 12 mmol) was introduced into an oven-dried, 250-mL three-necked flask containing 100 mL of anhydrous THF under  $N_2$ . The solution was cooled to –78 °C, and 4.89 mL (11 mmol) of 2.25 M *n*-BuLi in hexane was added. After the solution was stirred for 30 min at –78 °C, 1.17 g (5 mmol) of 7a in 10 mL of THF was added rapidly. The solution was then stirred for 15 min, and 0.95 g (5.2 mmol) of benzophenone in 10 mL of THF was added. The reaction mixture was then stirred for 30 min at –78 °C, warmed gradually to room temperature, and then stirred an additional 1 h. Water (10 mL) was then added dropwise to quench the reaction. The THF was evaporated under reduced pressure, and 100 mL of water was added to the residue. The solution was processed according to procedure A. Column chromatography of fraction A on silica gel with  $CH_2Cl_2$  gave 0.25 g of recovered benzophenone, and then elution with  $CH_2Cl_2$ /EtOAc (1:1) gave 0.43 g (40%) of 14a. Recrystallization of fraction B from  $CHCl_3$ /hexane afforded 0.94 g (45%) of *N*-(2-chlorophenyl)sulfonyl]- $\beta,\beta$ -diphenyl- $\beta$ -hydroxypropionamide (16) as white flakes: mp 152–154 °C:  $^1H$  NMR ( $CDCl_3$ )  $\delta$  3.23 (s, 2 H,  $CH_2$ ), 3.96 (br s, 1 H, OH), 7.23–7.50 (m, 13 H, arom), 8.07–8.11 (d, 1 H, H-6, arom). Anal. Calcd for  $C_{21}H_{18}ClNO_4S$ : C, 60.65; H, 4.36; N, 3.37. Found: C, 60.67; H, 4.37; N, 3.36.

**Reaction of *N*-Acetyl-2-chlorobenzenesulfonamide (7a) with 2 equiv of NaH and 1 equiv of *n*-BuLi, Followed by Benzophenone.** Sodium hydride (0.44 g of a 60% dispersion, 11 mmol) was washed with hexane and introduced into a 250-mL, three-necked flask under  $N_2$  and equipped with a magnetic stirrer and an addition funnel. A slurry was made by the addition of 75 mL of THF, and 1.17 g (5 mmol) of 7a in 15 mL of THF was added dropwise and stirred at room temperature for 1 h. The mixture was cooled to –78 °C, and 2.44 mL (5.5 mmol) of 2.25 M *n*-BuLi in hexane was added dropwise. After 15 min at –78 °C, 0.95 g (5.2 mmol) of benzophenone in 10 mL of THF was added. The solution was then stirred for 30 min at –78 °C, gradually warmed to room temperature, and stirred for an additional 1 h. As the benzophenone was added, the initial yellow color rapidly changed to a pale green color. As stirring was continued the yellow color returned and finally became pale green. Water (10 mL) was then added to quench the reaction, the THF was evaporated under reduced pressure, and 100 mL of water was added to the residue. This solution was processed as described in procedure B. Fraction A was chromatographed on silica gel with  $CH_2Cl_2$  to remove 0.40 g of benzophenone. The eluant was changed to  $CH_2Cl_2$ /EtOAc (1:1), and 0.569 g of the cyclized



product mixture was obtained. NMR yields of this mixture converted to 0.163 g (18%) of 10a and 0.406 g (38%) of 14a. Fraction B weighed 0.589 g and consisted of a mixture of condensation products 6 and 16; NMR yields converted to 0.466 g (23%) of 16 and 0.123 g (7%) of 6.

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**Registry No.** 4a, 5661-14-3; 4b, 7242-83-3; 4c, 7242-84-4; 4d, 3559-04-4; 7a, 143105-03-7; 7a-d<sub>3</sub>, 143105-04-8; 7b, 143105-05-9; 7c, 143105-06-0; 7d, 143105-07-1; 10a, 34989-82-7; 10b, 61798-56-9; 10c, 84108-97-4; 10d, 53440-57-6; 14a, 143105-08-2; 14b, 143105-09-3; 14c, 143105-10-6; 14d, 143105-11-7; PhSO<sub>2</sub>NH<sub>2</sub>, 98-10-2; o-ClC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NH<sub>2</sub>, 6961-82-6.

## Reactions of Aldehydes with Cesium Fluoroxysulfate

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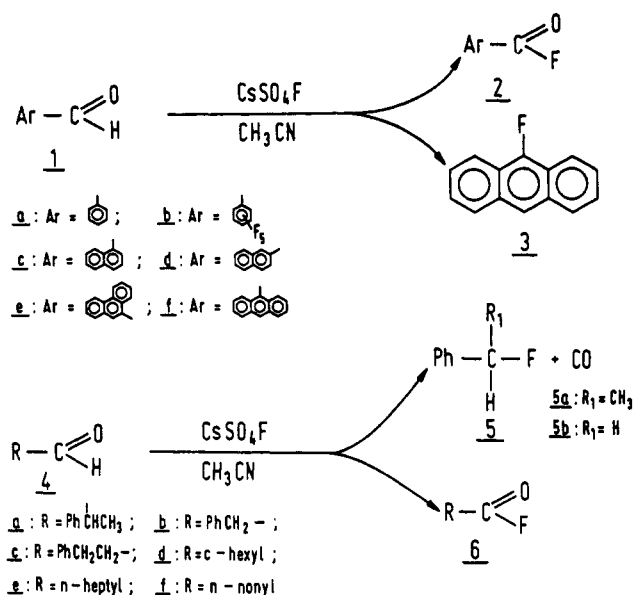
Various aromatic and aliphatic aldehydes reacted at 35–40 °C in CH<sub>3</sub>CN with CsSO<sub>4</sub>F giving acid fluorides in a good yield. In some cases formation of fluorohydrocarbons was also observed. Hammett correlation analysis of the transformation of various substituted benzaldehydes (*p*-OCH<sub>3</sub>, *p*-CH<sub>3</sub>, *p*-F, *p*-CF<sub>3</sub>, *m*-NO<sub>2</sub>) gave the reaction constant  $\rho^+ = -0.38$ . Solvent polarity strongly influenced the conversion of aldehydes into acid fluorides, being in acetonitrile almost quantitative and completely halted in CH<sub>2</sub>Cl<sub>2</sub>, *n*-hexane, or tetrahydrofuran. The presence of nitrobenzene, often used as a radical scavenger, considerably reduced the acid fluoride formation. Based on experimental observations was concluded that the main intermediates involved in the conversion of aldehydes into acid fluorides with CsSO<sub>4</sub>F must be of a radical nature.

The reactions of cesium fluoroxysulfate (CsSO<sub>4</sub>F) with organic compounds strongly depend on the type of organic molecules and the functional groups present. Alkenes<sup>1</sup> and alkynes<sup>2</sup> readily reacted with CsSO<sub>4</sub>F to yield addition or addition–elimination products, depending on reaction conditions. Fluorofunctionalization of activated aromatics<sup>3</sup> and saturated hydrocarbons,<sup>4</sup> as well as  $\alpha$ -carbonyl<sup>5</sup> or benzylic carbon atoms,<sup>6</sup> was also achieved under mild reaction conditions, while molecules containing a sulfur or phosphorus atom was transformed into the corresponding sulfoxides, sulfones, or phosphine oxides,<sup>7</sup> which could be explained by the fact that CsSO<sub>4</sub>F possess two reactive centers.<sup>8</sup>

It is known that aldehydes are very sensitive to oxygen and other oxidants transforming into acids or even peracids.<sup>9</sup> Reactions of aldehydes, having an  $\alpha$ -hydrogen, with halogens (chlorine or bromine) resulted in  $\alpha$ -halo-substituted aldehydes, while there are only few reports on direct conversion of aldehydes to acid chlorides or bromides<sup>10</sup> and none on direct conversion of aldehydes to acid fluorides.

We now report our investigation on the reaction of

Scheme I



CsSO<sub>4</sub>F with aromatic and aliphatic aldehydes.

## Results and Discussion

In a typical experiment 1 mmol of benzaldehyde 1a was dissolved in 2 mL of freshly distilled and oxygen-free CH<sub>3</sub>CN, CsSO<sub>4</sub>F (1.1 mmol) was introduced in a solution kept under inert atmosphere, and the reaction suspension was stirred for 1 h at 35–40 °C. The crude reaction mixture, isolated as cited in the Experimental Section, was analyzed and the high-yield formation of benzoyl fluoride as the sole product was confirmed. Furthermore, we have studied the effect of the structure of the aromatic nucleus on the course of the reaction and found that pentafluorobenzaldehyde (1b, Scheme I), 1- and 2-naphthyl

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