($CHCl_3$) 3580, 3210, 1705, (weak), 1650 cm^{-1}; NMR ($CDCl_3$) δ 1.0–2.7 [br m, 8, $-(CH_2)_4-$], 2.20 (s, 3, $NCOCH_3$), 5.19 (X part of ABX system, $J_{AX} + J_{BX}$ = 19 Hz, 1, $NCHCH_2$), 6.8–7.1 (br m, 4, aromatic), 9.24 (s, 1, OH); MS *m/e* 247 (M^+).

Anal. Calcd for $C_{14}H_{17}NO_3$: C,68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.87; N, 5.77.

4a-Acetoxy-10-acetyl-1,2,3,4,4a,10a-hexahydrophenoxazine (10). A sample of **9** (243 mg, 0.99 mmol) and *p*-toluenesulfonic acid (18 mg, dried by removal of water as a benzene azeotrope) were heated in 3.0 ml of acetic anhydride for 5 min at 80–90 °C. Solvent was removed in a manner similar to the method used in preparation of **9**. Preparative thin layer chromatography (silica gel, 20% EtOAc/$CHCl_3$, one development, R_f 0.49) gave 190 mg (66.4%) of colorless needles, mp 121–126 °C. Recrystallization from 50% ethanol–water gave colorless prisms: mp 126–127.5 °C; ir ($CHCl_3$) 1745, 1661 cm^{-1}; NMR ($CDCl_3$) δ 1.2–2.4 (br m, 8, aliphatic), 1.88 (s, 3, $NCOCH_3$), 2.26 (s, 3, $OCOCH_3$), 2.66 (br m, 1, NCH), 7.0 (m, 4, aromatic); MS *m/e* 289 (M^+).

Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N. 4.84. Found: C, 66.32; H, 6.92; N, 4.71.

10-Benzyl-1,2,3,4,4a,10a-hexahydro-4a-hydroxyphenoxazine (11). A solution of **8** (254 mg, 1.24 mmol) and benzyl bromide (1.0 ml) in 10 ml of acetone was heated under reflux with potassium carbonate (343 mg) for 13.5 h. After removal of solvent, the residue was partitioned between benzene and water. The organic phase was washed with water until neutral and the dried ($MgSO_4$) solution was filtered and concentrated. The residue was redissolved in benzene and filtered through an 8-cm column of alumina II. Removal of solvent afforded 150 mg (41%) of a colorless oil which appeared pure by TLC (R_f 0.40 on silica gel with chloroform): ir ($CHCl_3$) 3490, 2935, 1600 cm^{-1}; NMR ($CDCl_3$) δ 1.0–1.8 (m, 7, aliphatic), 2.20 [m, 1, $-OC(OH)CH$], 2.97 (m, 1, NCH), 3.64 (s, 1, OH), 4.18 and 4.54 (calculated shifts from AB quartet for benzylic protons), 6.8 (m, 4, aromatic), 7.3 (s, 5, aromatic); MS *m/e* 295 (M^+), 91 (tropylium).

4,4,10a-Trideuterio-1,2,3,4,4a,10a-hexahydro-4a-hydroxyphenoxazine (8-d_3). A sample of **8** (341 mg, 1.66 mmol) was added to a solution of sodium metal (0.2 g) in 10.0 ml of deuterium oxide and heated at reflux under nitrogen for 2 h. The reaction mixture was cooled to 10 °C, neutralized with glacial acetic acid, and extracted with 25 ml of chloroform. The organic phase was washed twice with water, dried ($MgSO_4$), and filtered through a column of silica gel (5 g) to remove traces of a polar contaminant. Removal of solvent gave 256 mg (74%) of a beige solid, mp 161–164 °C. Upon recrystallization from ethyl acetate and *n*-hexane, 128 mg of light pink crystals, mp 169–170 °C, were obtained: MS (14 eV) 4.4% d_5 (210), 13.9% d_4 (209), 46.5% d_3 (208), 26.6% d_2 (207), 4.7% d_1 (206), 3.9% d_0 (205).

4a-Acetyl-4,4,10a-trideuterio-1,2,3,4,4a,10a-hexahydrophenoxazine (9-d_3). A sample of 8-d_3 (111 mg, 0.53 mmol) was acetylated as for the undeuterated compound giving 71 mg (54%) of a pink, crystalline solid: mp 176–178.5 °C; NMR ($CDCl_3$) δ 1.0–2.2 [br m, 6, $-(CH_2)_3-$], 2.20 (s, 3, $NCOCH_3$), 6.8–7.1 (br m, 4, aromatic), 9.25 (s, 1, OH); MS (7 eV deuterated vs. 20 eV undeuterated) 8.5% d_4 (251), 51% d_3 (250), 32.5% d_2 (249), 5% d_1 (248), 3% d_0 (247).

Registry No.—**1**, 533-60-8; **2**, 95-55-6; **8**, 60349-94-2; **8** HI, 60349-95-3; 8-d_3, 60349-96-4; **9**, 60349-97-5; 9-d_3, 60349-98-6; **10**, 60349-99-7; **11**, 60350-00-7; acetic anhydride, 108-24-7; benzyl bromide, 100-39-0.

Supplementary Material Available. The following crystallographic data: coordinates and anisotropic temperature factors for nonhydrogen atoms, distances, and angles (1 page). Ordering information is given on any current masthead page.

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Notes

An Improved Synthesis of Sulfamoyl Chlorides

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Sulfamoyl chlorides are important intermediates in the synthesis of sulfamate esters and unsymmetrical sulfamides. These latter compounds are useful in the synthesis of azo compounds[1] as well as certain biologically active chemicals.[2] Although many processes have been published for the synthesis of alkyl sulfamoyl chlorides,[3] only one method of preparation[4,5] is frequently cited as being useful on a laboratory scale.[6] This involves direct treatment of an amine hydrochloride with sulfuryl chloride either with[5] or without[4] a Lewis acid catalyst. The method is limited to simple alkyl amines[4,5] and is often characterized by long reaction times,[4,5] large excesses of reagent,[4,5] and low yields.[4] In addition, this procedure precludes the synthesis of those compounds bearing functionality sensitive to sulfuryl chloride. Aryl and alkenyl sulfamoyl chlorides are thus unobtainable by this route.[5]

In view of the above limitations we have developed an alternative synthesis which not only provides for the facile preparation of simple alkyl sulfamoyl chlorides, but also allows, for the first time, synthesis of monoaryl sulfamoyl chlorides.

In 1953 Bieber reported that treatment of isocyanates with an excess of neat, anhydrous sulfuric acid resulted in evolution of carbon dioxide and concomitant formation of the corresponding sulfamic acid.[7] On a preparative scale this reaction has been rendered more convenient by use of a highly polar solvent such as nitromethane and 1 equiv of fuming sulfuric acid. The reaction is instantaneous and the product precipitates as a crystalline solid. Filtration and recrystallization (if necessary) affords pure sulfamic acids in good to excellent yields. (See Table I.)

These acids are then slurried in benzene and treated with phosphorus pentachloride. Gentle warming initiates a vigorous reaction which produces the sulfamoyl chlorides as well as phosphorus oxychloride and hydrogen chloride.[8] After concentration the product may be purified by distillation or crystallization, although in most cases removal of the final traces of phosphorus oxychloride at high vacuum provides a product adequate for continued use.

$$RNCO + H_2SO_4 \cdot SO_3 \rightarrow RNHSO_3H$$

$$RNHSO_3H + PCl_5 \rightarrow RNHSO_2Cl$$

While the above method is effective for simple alkyl compounds, there are certain cases (e.g., R = *tert*-butyl and phenyl, entries 6 and 7 in Table I) where the use of fuming sulfuric acid is precluded. An alternate procedure is then effective. The salt of the sulfamic acid may be prepared by treatment of chlorosulfonic acid with an excess of the corresponding

Table I[a]

Entry	Sulfamic acid (salt)	Registry no.	% yield	Sulfamoyl chloride	Ref	% yield	Registry no.
1	CH_3NHSO_3H	4112-03-2	58	CH_3NHSO_2Cl	5	84	10438-96-7
2	$C_2H_5NHSO_3H$	4626-94-2	86	$C_2H_5NHSO_2Cl$	4	89	16548-07-5
3	n-$C_4H_9NHSO_3H$	39085-61-5	65	n-$C_4H_9NHSO_2Cl$	4	65	10305-43-8
4	i-$C_3H_7NHSO_3H$	42065-76-9	65	i-$C_3H_7NHSO_2Cl$	8	94	26118-67-2
5				c-$C_6H_{11}NHSO_2Cl$[b]	5	65	10314-35-9
6	t-$C_4H_9NHSO_3^- \cdot H_3N^+$-$t$-$C_4H_9$	60260-48-2	c	t-$C_4H_9NHSO_2Cl$	g	34[d]	33581-95-2
7				$C_6H_5NHSO_2Cl$[e]		f	60260-49-3

[a] All compounds had boiling points consistent with those in the literature, or satisfactory elemental analysis. Ed. [b] Starting sulfamic acid commercially available. [c] The salt was not isolated. [d] Yield based on starting amine. [e] From the sodium salt of phenylsulfamic acid; see ref 9. [f] Simple workup provided 90% material recovery. Attempts to purify further were attended by considerable decomposition. Immediate use of this crude material afforded adequate yields of products. [g] W. L Matier, W. T. Comer, and D. Deitchman, *J. Med. Chem.*, **15**, 538 (1972).

amine.[9] Treatment of a benzene slurry of these salts with PCl_5 as described above provides the desired compounds.[10]

$$3RNH_2 + ClSO_3H \rightarrow RNHSO_3^- \cdot H_3N^+R$$

$$RNHSO_3^- \cdot H_3N^+R \xrightarrow{PCl_5} RNHSO_2Cl$$

The previously unreported phenylsulfamoyl chloride thus obtained had limited stability. Bulb-to-bulb distillation of the crude reaction mixture resulted in considerable decomposition but did afford a product which recrystallized from carbon disulfide to afford an analytical sample. Treatment of the crude reaction mixture with excess isopropylamine provided N-isopropyl-N'-phenylsulfamide, identical with the product obtained from aniline and isopropylsulfamoyl chloride. Allowing the crude acid chloride to stand for any length of time resulted in significantly lower yields of products.

In summary, the method described above provides a synthesis of sulfamoyl chlorides that is fast, efficient, economical, and uncomplicated by side reactions. The starting materials are readily available and the conditions employed are quite mild, thereby allowing synthesis of more functionally diverse compounds than was previously possible.

Experimental Section[11]

General Procedure for the Preparation of Sulfamic Acids.[7] To a stirred solution of 100 g of 15% fuming sulfuric acid in 250 ml of nitromethane was added dropwise 1 mol of the appropriate isocyanate. An ice bath maintained the temperature at 25–30 °C. After addition the resulting suspension was refluxed for 0.5 h, then cooled and filtered. The collected crystalline acid was washed with ether and air dried.

General Procedure for the Preparation of Sulfamoyl Chlorides. To a stirred suspension of 1 molar equiv of the appropriate sulfamic acid in a suitable amount of benzene was added 1 molar equiv of phosphorus pentachloride. After gentle warming initiated a vigorous reaction, an ice bath was used to control the rate of reaction. After gas evolution had ceased the resulting solution was refluxed for 0.5 h, cooled, and concentrated in vacuo. Distillation at reduced pressure afforded the product.

***N*-*tert*-Butylsulfamoyl Chloride.** To a stirred solution of 43.8 g (0.6 mol) of *tert*-butylamine in 500 ml of methylene chloride, cooled to 0 °C in an ice/salt bath, was cautiously added 23.3 g (0.2 mol) of chlorosulfonic acid. After addition was complete, the resulting suspension was stirred for 0.5 h at room temperature and then filtered. The collected solids were air dried, then slurried in a convenient amount of benzene and treated with 41.6 g (0.2 mol) of phosphorus pentachloride. After the mildly exothermic reaction subsided, the solution was refluxed for 1 h. After cooling the mixture was filtered, and the filtrate was concentrated in vacuo. Distillation afforded the product as a colorless oil which crystallized on standing, bp 76–78 °C (0.6 mm).

***N*-Phenylsulfamoyl Chloride.** A slurry of 14.95 g (0.077 mol) of sodium N-phenylsulfamate and 15.95 g (0.077 mol) of phosphorus pentachloride in 250 ml of benzene was refluxed for 21 h. After cooling, the reaction mixture was cooled and filtered. The filtrate was concentrated in vacuo to afford 13.8 g (94%) of a crude yellow oil. A 1-g portion of this oil was subjected to evaporative bulb-to-bulb distillation (0.05 mm, oven temperature 110 °C) and provided 0.42 g of a yellow solid. Recrystallization from CS_2 gave pale yellow crystals, mp 69–70 °C.

Anal. Calcd for $C_6H_6ClNO_2S$: C, 37.60; H, 3.16; N, 7.31. Found: C, 37.82; H, 3.25; N, 7.41.

Registry No.—RNCO (R = CH_3), 624-83-9; RNCO (R = C_2H_5), 109-90-0; RNCO (R = n-C_4H_9), 111-36-4; RNCO (R = i-C_3H_7), 1795-48-8; cyclohexylsulfamic acid, 100-88-9; sodium phenylsulfamate, 15790-84-8; sulfuric acid, 7664-93-9; phosphorus pentachloride, 10026-13-8; *tert*-butylamine, 75-64-9; chlorosulfonic acid, 7790-94-5.

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Ortho Lithiation of Thiobenzamides

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Access to ortho-substituted derivatives of benzoic acids, in particular to those bearing one or more additional ring substituents, has been rather limited and was largely based on oxidative degradation, or Sandmeyer-type reactions of the