Table I. 1,1-Bis(acylthio)alkane Synthesis[a]

$RCH(SCR)_2$ (R = O)

R	registry no.	bp, °C (torr)	mp, °C	% yield[b]
CH_3	20266-80-2	41 (0.002)		97
C_2H_5	67584-26-3	60 (0.002)		90
C_3H_7	67584-27-4	82 (0.003)		87
C_6H_5	13286-78-7		137–138	93

[a] Satisfactory analytical data (±0.4% for C, H, S) were reported for all new compounds listed in the table. [b] Calculated on the basis that 3 mol of thiol acid are consumed in the formation of 1 mol of alkane.

temperature for 8 h. This solid was identified by comparison of physical properties with an authentic sample of sulfur.

Thin-layer chromatographic monitoring of the reaction mixture on silica gel plates indicated that the thiolacetic acid had been consumed with concomitant appearance of a new band in the chromatogram. This product was subsequently isolated by distillation [bp 41 °C (0.002 torr)] and was tentatively identified as 1,1-bis(acetylthio)ethane (1) from NMR [($CDCl_3$) δ 2.4 (s, 6, $CH_3C(S)=O$), 3.8 (q, 1, HCS_2), 1.4 (d, 3, CH_3CS_2)], IR [(CCl_4) 1690 cm^{-1} (C=O)], mass spectral (M^+ 178), and elemental analysis data (eq 1). The structure was

$$CH_3COSH \xrightarrow{R_3N} \underset{\mathbf{1}}{CH_3CH(SCCH_3)_2} + S + H_2O \qquad (1)$$

verified by alternative preparation of 1 from 1,1-dimethoxyethane plus thiolacetic acid.[1] Thiol acid (3 mol) reacts in the presence of base to form the corresponding dithiolacylate. In the process, 1 mol of thiol acid is reduced to the aldehyde oxidation state with expulsion of elemental sulfur. Acetaldehyde could not be detected in the reaction mixture, suggesting that the reaction may not proceed by initial formation of an aldehyde intermediate. 1,1-Bis(acylthio)alkanes have been synthesized previously by reaction of *gem*-dithiols with acid anhydrides[2] and by reaction of *gem*-thiocyanates with thiol acids.[3]

The synthetic utility of this reaction was explored using several thiol acids. The yields and physical properties of the resulting 1,1-bis(acylthio)alkanes are shown in Table I. The reaction proceeded efficiently with all the thiol acids that were tested; so this reaction appears to be a useful synthetic route to symmetrical 1,1-bis(acylthio)alkanes and may, for some applications, be a useful pathway for reduction from the acid to aldehyde oxidation state.

Experimental Section

Thiol acids (0.15 mol) were dissolved in ether (75 mL) containing 0.15 mol of triethylamine or pyridine. The solutions were allowed to stand at room temperature for 8 h, after which time they were cooled to 0 °C in an ice bath. The orange precipitate that had formed was removed by filtration and the solution was then acidified with 10 mL of cold 10% hydrochloric acid solution followed by the addition of 10 mL of cold water. An oil separated and was taken up in 25 mL of ether. The aqueous layer was then extracted with three 25-mL portions of ether; the organic phases were combined and dried over anhydrous sodium sulfate. The ether was removed by distillation and the residue was distilled under reduced pressure.

Registry No.—Thiolacetic acid, 507-09-5; thiolpropionic acid, 1892-31-5; thiolbutyric acid, 3931-64-4; thiolbenzoic acid, 98-91-9.

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Another Pathway of the Reaction of Thionyl Chloride with Active Methylene Compounds. Reaction of Anthrone with Thionyl Chloride

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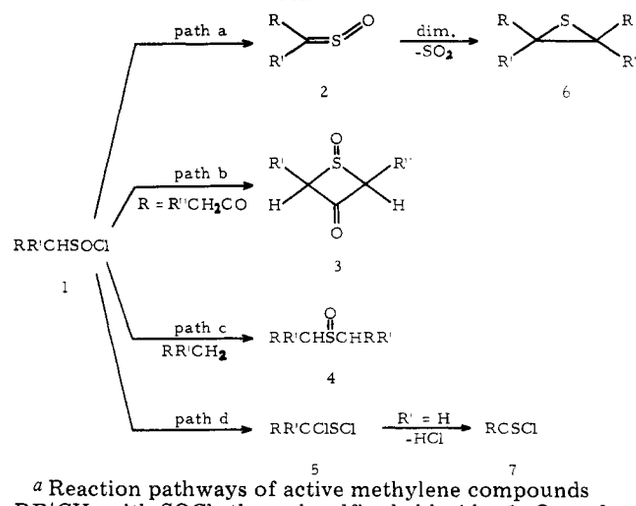
In the reaction of thionyl chloride and active methylene compounds, several pathways may be considered according to the amount of thionyl chloride employed and the structure of the substrate. Sulfinyl chlorides 1 (Scheme I), which had been believed to be primary products,[1] were isolated by Pizey and Symeonides.[2a] The chemical behavior of such sulfinyl chlorides in reaction medium includes the following: (a) intramolecular dehydrochlorination to give a sulfine (**2**, path a)[3] or a thietanone *S*-oxide (**3**, path b);[2a,b] (b) intermolecular dehydrochlorination to give a sulfoxide (**4**, path c);[3] or (c) Pummerer-type rearrangement, leading to an α-chlorosulfenyl chloride (**5**, path d).[4]

Paths a and b proceed with equimolar or slightly excessive amounts of thionyl chloride, while path c requires a half-molar amount of reagent and path d a large excess of reagent.[5] Formation of other products might be explained in terms of further chemical modifications; for instance, (a) olefins from malonates by Ireland and Pizey[6] are understandable in terms of dimerization and desulfurization of the sulfine via thiirane **6**[6,7] and (b) thioacyl chlorides **7** from acetophenone and other active methyl compounds are explained by dehydrochlorination of the sulfenyl chloride **5**.[8] However, one can find other examples in the literature which cannot be explained by these proposals. Takimoto and Krbechek[9] have reported that anthrone in hot thionyl chloride gave an unstable material of unknown structure which was converted to olefin **16** (Scheme II) by treatment with malononitrile. At first, we considered that this intermediate might be α-chlorosulfenyl chloride **17**, owing to our consideration that such sulfenyl chlorides might be easily converted to olefins when treated with a strong carbon acid via thiocarbonyl ylide and its electrocyclized thiirane.[10] However, our efforts to isolate it failed in spite of its expected stability.

When anthrone 8 was treated with 3 molar equiv of thionyl chloride at room temperature, a crystalline product was obtained quantitatively after vigorous evolution of hydrogen

Scheme I[a]



[a] Reaction pathways of active methylene compounds $RR'CH_2$ with $SOCl_2$ through sulfinyl chlorides 1. One of the substituents or both of them are π-accepting groups such as C=O, C=N, etc.

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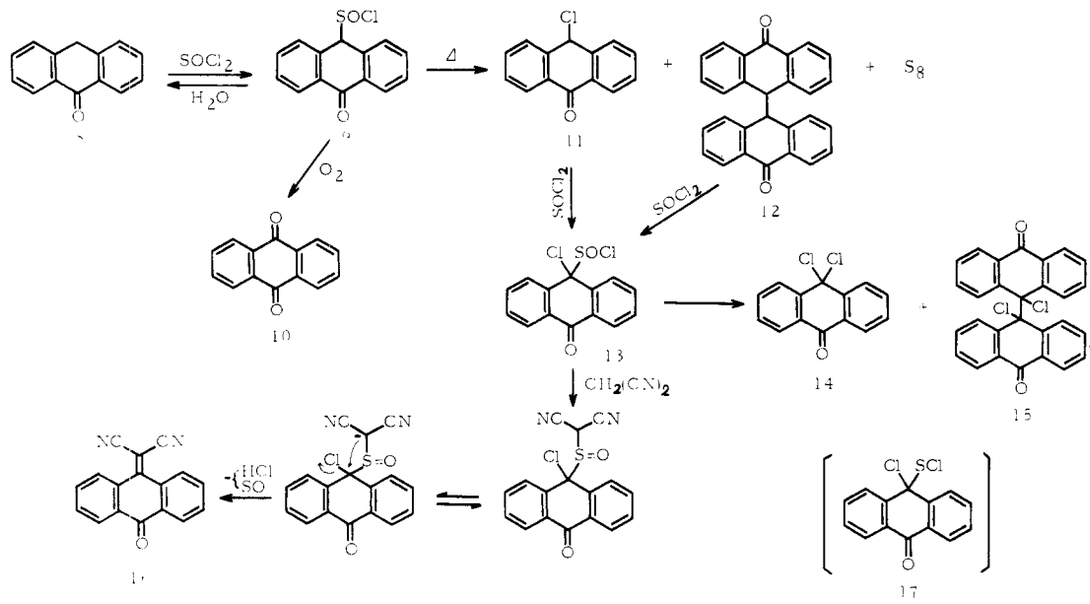
Scheme II



chloride and sulfur dioxide. This compound was assigned as sulfinyl chloride **9** by its spectroscopic analyses and reformation of anthrone on standing in air. In thionyl chloride at room temperature under argon, **9** did not undergo further reaction, while under air or oxygen it was oxidized to give anthraquinone. However, when **9** was heated at reflux temperature under argon in dioxane, it was converted into 41% of **11**, 38% of **12**, and 25% of free sulfur. These facts compelled us to consider that **11** and **12** were produced by rearrangement of free anthronyl radicals and chlorine radicals. Extrusion of sulfur monoxide was confirmed by isolation of free sulfur; the equilibrium of sulfur monoxide with sulfur and sulfur dioxide has been reported.[11]

On the other hand, when **9** was heated in thionyl chloride for 1 h, it afforded 51% of **14**, 12% of **15**, 32% of **12**, and a small amount of sulfur.[12] Under the same reaction conditions, **11** afforded **14** and **15** in a ratio of 4:1 and a trace of **12**. Furthermore, **12** gave similar results after prolonged heating for 5 h. These facts indicate that **9** in hot thionyl chloride undergoes thermal conversion to **11** and **12** during the early stage of the reaction, and then these intermediates react with thionyl chloride to give the final products. Thus, we carefully examined the reaction of **11** in hot thionyl chloride and observed the presence of another intermediate by silica gel TLC. This intermediate was fairly stable in thionyl chloride, but it could not be isolated since it underwent formation of the stable products **14** and **15** described above during the working up. The same intermediate was observed when **12** was heated in thionyl chloride. The NMR spectrum in thionyl chloride did not show any signals except aromatic protons. A reexamination of the experiment described in the report of Takimoto and Krbechek[9] was carried, and the conversion of this intermediate to the olefin **16** was actually proved. Consequently, we consider the structure of this material to be 10-chloro-10-chlorosulfinylanthrone (**13**). Production of the olefin **16** from this material and malononitrile may be explained reasonably in terms of the Ramberg–Bäcklund reaction shown in Scheme II.

Experimental Section

IR spectra were obtained as KBr tablets using a Hitachi EPR-50 spectrometer and are given in cm^{-1}. NMR spectra were determined in $CDCl_3$ on a JEOL PS-100 spectrometer. Microanalyses were performed by Microanalytical Center, T.C.P. TLC plates were made of Wako-gel B-O, and silica gel columns were made of Wako-gel C-200 (Wako Pure Chemical Industry, Osaka, Japan).

10-Chlorosulfinylanthrone (9). A solution of pyridine (0.02 mL) in $SOCl_2$ (3.0 mL) was added to powdered anthrone (1.0 g) in a round-bottom flask. After the vigorous evolution of HCl and SO_2 ceased, the crystalline product was collected and washed with a *n*-hexane–benzene mixture. Drying in vacuo at room temperature gave analytically pure needles (1.3 g): mp 260 °C dec; IR 1657 (C=O), 1254 (S=O) cm^{-1}; NMR δ 5.60 (s, 1 H), 7.59 (m, 6 H), 8.33 (m, 2 H). Anal. Calcd for $C_{14}H_9ClO_2S$: C, 60.76; H, 3.24. Found: C, 60.62; H, 3.33.

When this sample was allowed to stand in an atmospheric circumstance for 3 days, anthrone was recovered quantitatively (mp 155–157 °C). In $SOCl_2$ under air or an oxygen stream overnight, **9** was converted into anthraquinone (mp 285–287 °C) in 43% yield.

Thermal Decomposition of 9 in Dioxane. A solution of **9** (1.0 g) in dioxane (10 mL) was refluxed for 20 min under argon. The solvent was evaporated, and the residue was separated on a silica gel column (20 g) using a benzene–acetone (100:1) mixture. The first eluate contained 14 mg (25%) of S_8, and the second one contained 339 mg (41%) of 10-chloroanthrone (**11**), mp 223–224 °C dec (lit.[13] mp 225 °C). The third eluate contained 266 mg (38%) of bianthrone (**12**), mp 276–277 °C [keto form by NMR: δ 4.68 (s, 2 H), 6.75 (m, 4 H), 7.33 (m, 8 H), 7.84 (m, 4 H)] (lit.[14] mp 245–250 °C).

Reaction of 9 in Hot Thionyl Chloride. A solution of **9** (1.0 g) in $SOCl_2$ (10 mL) was heated at reflux for 1 h under argon. TLC developed with benzene showed two spots. A 0.5-mL amount of the mixture was worked up as follows. The more polar product (R_f 0.32) was assigned as bianthrone (**12**) by comparison with an authentic sample (R_f and IR). However, another product (R_f 0.45) could not be isolated. It was observed that this product was converted into two compounds by extraction, evaporation, and reexamination on TLC. The newly prepared compounds showed R_f values of 0.50 and 0.39.

The rest of the mixture was refluxed for another 4 h to give almost a single spot on TLC (R_f 0.45). The reagent was evaporated, and the residue was purified on a silica gel column (20 g) developed with a benzene–acetone (100:1) mixture. The first eluate contained 685 mg of 10,10-dichloroanthrone (**14**), which was recrystallized from benzene to give needles, mp 134–135 °C (lit.[15] mp 132–134 °C). The second eluate contained 148 mg of 10,10′-dichlorobianthrone (**15**), which was recrystallized from chloroform to give prisms: mp 240–241 °C; IR 1673 (C=O), 646 (C–Cl) cm^{-1}. Anal. Calcd for $C_{28}H_{16}O_2Cl_2$: C, 73.86; H, 3.54. Found: C, 73.74; H, 3.68.

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Registry No.—**8**, 90-44-8; **9**, 67673-27-2; **11**, 67673-28-3; **12**, 434-84-4; **13**, 67673-29-4; **14**, 38032-82-5; **15**, 38032-84-7; **16**, 10395-02-5; thionyl chloride, 7719-09-7.

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Synthesis of Carbamates of α-Amino Sulfonamides

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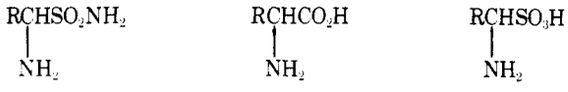
Based on the successful use of the sulfonamido group as a replacement for the carboxyl group in drugs such as the 4-aminobenzenesulfonamides, which are antimetabolites of 4-aminobenzoic acid,[1,2] and acetazolamide, which is a carbonic anhydrase inhibitor,[3] several investigators have suggested[4,5] that the α-amino sulfonamides (1) will be good antimetabol-



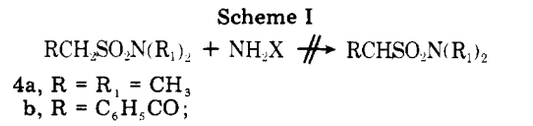
1 2 3

ites of the common amino acids (2). However, all previous attempts to prepare derivatives of the sulfonamides 1 have failed.[4-7] The moderately stable α-amino sulfonic acids (3) are known, but attempts to convert them or their *N*-acyl derivatives to sulfonamides have failed.[8] We now wish to report the first synthesis of carbamates of 1.

Results and Discussion

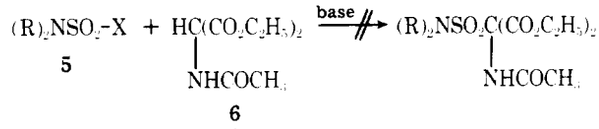
We first tried two general routes to 1 and derivatives of 1. Amination of carbanions of sulfonamides (4) as shown in Scheme I did not give amino sulfonamides. Treatment of **4a** with *n*-butyllithium in THF gave the carbanion which was treated with methyl benzoate to obtain **4b.** However, treatment of the carbanion from **4a** with a series of aminating agents gave only unchanged **4a** after workup. Our opinion is that the anion from **4a** is sufficiently basic to remove a proton from the aminating agents. With less basic carbanions, similar aminations are usually successful. Thus, we tried the amination of the anion of **4b,** which was generated with sodium hydride in DMF or with *n*-butyllithium in ether. The anion of **4b** should be of similar basicity to the anion of diethyl malonate, which can be successfully aminated.[9] Treatment of the anion from **4b** with a series of aminating agents did not furnish the amino sulfonamides. We do not know if the amino sulfonamides formed and decomposed under the basic conditions of these reactions. The amino sulfonamides bear a resem-

Scheme I



4a, R = R_1 = CH_3
b, R = C_6H_5CO; R_1 = CH_3
X = Cl, 2,4-dinitrophenoxy, methoxy, and 2,4,6-trimethylbenzenesulfonyloxy

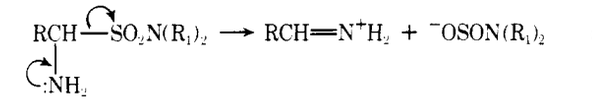
Scheme II



5 6

X = Cl and 4-nitrophenoxy; R = CH_3 and H

blance to cyanohydrins and bisulfite addition products and may decompose as shown in eq. 1.



(1)

Treatment of diethyl acetamidomalonate (**6**) with sulfamoyl chlorides (**5**) in the presence of bases such as sodium hydride, potassium *tert*-butoxide, or triethylamine in solvents such as benzene, ether, dimethoxyethane, acetonitrile, *tert*-butyl alcohol, or DMF did not give the amino sulfonamides. This method, which is shown in Scheme II, gave only unchanged **6.**

As shown in Scheme III, the Curtius rearrangement gave carbamates of amino sulfonamides (**14**).

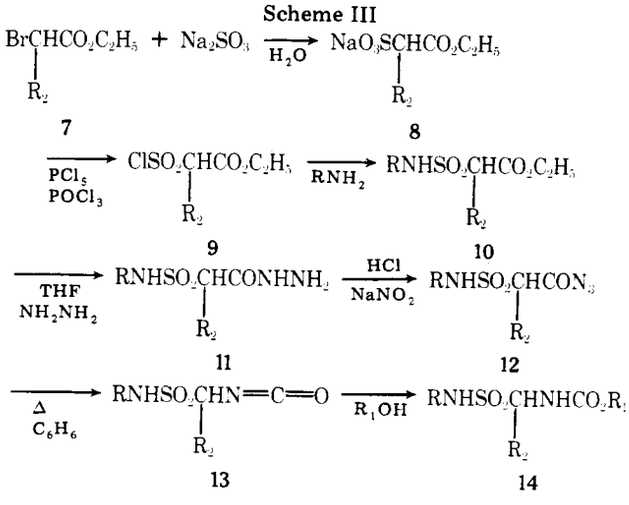
All of the steps in Scheme III proceeded well except the diazotization of **11** and the rearrangement of **12.** The diazotization has only been conducted with hydrochloric acid and sodium nitrite. Other methods of preparing the azides **12** have not been explored. When R = R_2 = H, **11a** was converted to **14a** in 21% yield. When R = *t*-Bu and R_2 = H, **11b** was converted to **14d** in 36% yield. When R_2 was methyl and R was H, the rearrangement of **12** gave only an intractable tar.

In general, the azides **12** and the isocyanates **13** were not isolated; however, **12,** where R and R_2 = H, was isolated. Both infrared and NMR spectra were obtained for the crystalline azide, but the stability of the compound was poor and additional data were not obtained.

Using the method shown in Scheme III, the sulfamoyl carboxylic acid esters (**10**), the sulfamoyl acid hydrazides (**11**), and the carbamates (**14**) shown in Table I were prepared.

A number of methods were tried for converting the carbamates to the free amino sulfonamides. Compound **14a** was heated with 10% hydrochloric acid; however, the only product was a high melting solid which did not have infrared absorption for the SO_2 group. Attempted hydrolysis of **14a** with 30% sodium hydroxide and barium hydroxide did not give an isolable product. Treatment of the isocyanate **13** (R = R_2 = H) with hydrochloric acid gave only ammonium chloride as an isolable product. Catalytic hydrogenation of **14b** and **14e** using palladium on carbon, palladium black, palladium hydroxide on carbon, and Raney nickel in solvents such as ethanol, gla-

Scheme III



7 8 9 10 11 12 13 14

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