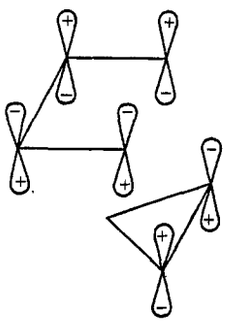
of an unfavorable increase in energy for the endo transition state as a result of secondary orbital interactions (**11**).[5] In **11**, a mixing of the highest occupied diene



11

orbital with the lowest unoccupied cyclopropene or azirine orbital occurs.

It is possible that the endo adduct **4** is formed to a small extent but is unstable and undergoes a retro Diels–Alder reaction.[9]

We are currently examining the possible dehydrative rearrangement of the azanorcarane **6** to the 2*H* azepine **8**.

Experimental Section

Reaction of 3-Methyl-2-phenyl-1-azirine with 1,3-Diphenylisobenzofuran. Formation of Exo Adduct 3.—A solution of 1.048 g (8 mmol) of 3-methyl-2-phenyl-1-azirine (**1**)[8,12] in 10 ml of toluene was treated with a solution of 1.620 g (6 mmol) of 1,3-diphenylisobenzofuran (**2**)[8] in 15 ml of toluene. The reaction mixture was heated under reflux for 18 hr and then chromatographed over silica gel. Unreacted 1,3-diphenylisobenzofuran was eluted with pentane and the adduct with 10% ether–pentane. Crystallization from ether–pentane gave the exo adduct **3** as white plates (1.75 g, 73%): mp 192–194°; nmr $\delta_{TMS}^{CDCl_3}$ 1.05 (d, J = 5.8 Hz, 3 H), 3.52 (q, J = 5.8 Hz, 1 H), 6.48–7.96 (m, 19 H).

Anal. Calcd for $C_{29}H_{23}NO$: C, 86.75; H, 5.77; N, 3.49. Found: C, 86.43; H, 5.51; N, 3.53.

Thermal Stability of Exo Adduct 3.—The adduct **3** in $CDCl_3$ was heated in a sealed nmr tube at 100° and the reaction was monitored by periodic nmr spectral determinations. Even after 1 week, about 85 ± 5% of **3** remained undestroyed.

3-Chloroethyl-4-hydroxy-1,3,4-triphenyl-3,4-dihydroisoquinoline (5).—A solution of 500 mg of the adduct **3** in 5 ml of anhydrous benzene was treated with 10 ml of a saturated solution of anhydrous HCl in benzene. The reaction mixture darkened immediately. After the mixture was stirred for 3 hr, the yellow crystalline compound that precipitated out (**5**·HCl) was collected (510 mg): mp 168°; nmr $\delta_{TMS}^{CD_3OD}$ 1.43 (d, J = 6.2 Hz, 3 H), 5.24 (s, broad, 2 H), 6.06 (q, J = 6.2 Hz, 1 H), 6.58–7.95 (19 H).

The product from the foregoing reaction was dissolved in 5 ml of methanol and treated with 20 ml of 2 *N* aqueous NaOH. The reaction mixture was diluted with 100 ml of water and extracted with benzene (3 × 50 ml). The combined organic extract was washed with water and dried (Na_2SO_4). The solution was concentrated and treated with pentane when pale yellow plates of the dihydroisoquinoline **5** crystallized out (335 mg, 76%): mp 178–180°; nmr $\delta_{TMS}^{CDCl_3}$ 1.28 (d, J = 6.2 Hz, 3 H), 4.10 (s, 1 H), 4.72 (q, J = 6.2 Hz, 1 H), 6.84–8.00 (m, 19 H).

Anal. Calcd for $C_{29}H_{24}NOCl$: C, 79.53; H, 5.52; N, 3.20. Found: C, 79.50; H, 5.32; N, 3.22.

Reductive Cleavage of Exo Adduct 3 with $LiAlH_4$. Isolation of Benzoazanorcarane (6).—A solution of 300 mg of the adduct **3** in 5 ml of anhydrous ether was reduced with $LiAlH_4$. Purification of the product by preparative layer chromatography on silica gel PF_{254} with 50% benzene–pentane as the developing solvent gave benzoazanorcarane (**6**) as a viscous, pale yellow oil which crystallized slowly from ether–pentane as pale yellow plates (280 mg, 93%): mp 85°; nmr $\delta_{TMS}^{CDCl_3}$ 0.95 (d, J = 5.5 Hz, 3 H), 2.32 (q, J = 5.5 Hz, 1 H), 2.52 (s, broad, 1 H), 5.69 (s, 1 H), 6.60–7.90 (m, 19 H).

Anal. Calcd for $C_{29}H_{25}NO$: C, 86.32; H, 6.24; N, 3.47. Found: C, 86.62; H, 6.41; N, 3.50.

Treatment of Benzoazanorcarane (6) with Anhydrous HCl in Benzene. Isolation of Isoquinoline (7).—A solution of 403 mg (1 mmol) of **6** in 20 ml of anhydrous benzene was treated with anhydrous HCl at reflux temperatures for 0.5 hr. The solution was concentrated and subjected to preparative layer chromatography using silica gel PF_{254} with 50% ether–pentane as the developing solvent. The isoquinoline (**7**) crystallized from ether–pentane as pale yellow plates (197 mg, 55%): mp 184–185; nmr $\delta_{TMS}^{CDCl_3}$ 7.08–8.18 (m, 19H).

Anal. Calcd for $C_{27}H_{19}N$: C, 90.72; H, 5.36; N, 3.92. Found: C, 90.79; H, 5.59; N, 3.83.

In a separate experiment the benzoazanorcarane (**6**) was treated with anhydrous HCl in benzene at 25°, and the precipitated white crystalline compound (**6** HCl) was collected: mp 178–181°; nmr $\delta_{TMS}^{CD_3OD}$ 1.45 (d, J = 5.8 Hz, 3 H), 5.12 (s, broad, 2 H), 5.94 (q, J = 5.8 Hz, 1 H), 6.60–8.13 (m, 20 H). Basification of this salt gave **6** quantitatively.

Reaction of 2,3-Diphenyl-1-azirine (9) with 1,3-Diphenylisobenzofuran. Formation of Exo Adduct 10.—A solution of 386 mg (2 mmol) of 2,3-diphenyl-1-azirine (**9**)[13] and 405 mg (1.5 mmol) of 1,3-diphenylisobenzofuran (**2**) was heated under reflux for 44 hr and then chromatographed using preparative plates (silica gel PF_{254}). Crystallization from ether–pentane gave the exo adduct **10** as white plates (490 mg, 70.5%): mp 198–200°; nmr $\delta_{TMS}^{CDCl_3}$ 4.52 (s, 1 H), 6.27–7.97 (m, 24 H).

Anal. Calcd for $C_{34}H_{25}NO$: C, 89.03; H, 5.00; N, 2.78. Found: C, 88.62; H, 5.22; N, 2.70.

Registry No.—**2**, 5471-63-6; **3**, 34806-16-1; **5**, 34806-17-2; **5** HCl, 34806-18-3; **6**, 34792-35-3; **6** HCl, 34792-36-4; **7**, 30081-56-2; **10**, 34806-20-7.

Acknowledgment.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 1871-G1), for partial support of this research.

(12) An excess of the azirine was used in all runs because of the instability of the azirines at elevated temperatures.

(13) A. Hassner and F. W. Fowler, *J. Amer. Chem. Soc.*, **90**, 2869 (1968).

Selectivity in the Reaction of Azodicarboxylate Esters with Sulfides[1]

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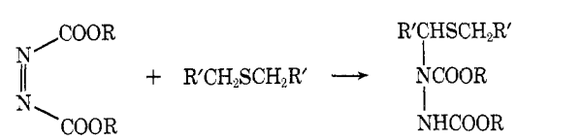
In the course of studies of other reactions which result in substitution at the α-carbon atom of sulfides, we have examined the reactions of azodicarboxylate esters with a number of sulfides. This reaction was used initially by Woodward in the synthesis of cephalosporin C.[2,3] The transformations, which proceed as

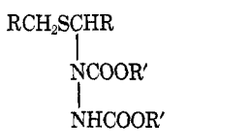


(1) Taken from the thesis of J. H. E. Martin submitted in partial fulfillment of the degree of Master of Science at the Polytechnic Institute of Brooklyn.

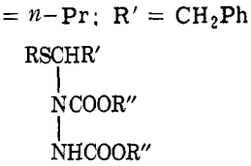
(2) R. B. Woodward, H. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, and H. Vorbruggen, *J. Amer. Chem. Soc.*, **88**, 852 (1966).

(3) R. B. Woodward, *Science*, **153**, 487 (1966).

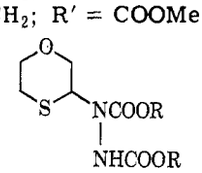
shown to produce derivatives of bicarbamic acid, were in general carried out by warming a mixture of sulfide and azo compound with or without added benzoyl peroxide, thus providing the derivatives I–III. However, for benzyl methyl sulfide, better yields were obtained using uv irradiation to realize the functionalization of the methylene group. A similar reaction has been carried out with ethers, but in this case irradiation was necessary to effect reaction.[4] In a competition experiment 1,4-oxathiane underwent reaction only adjacent to the sulfur atom. This may indicate that the initial complexation between azo acceptor and heteroatom donor is stabilized by polarizability interactions or that it involves selective hydrogen abstraction as an initiating step. In this regard radicals are



Ia, R = Ph; R′ = Me
b, R = Ph; R′ = CH_2Ph
c, R = *n*-Pr; R′ = Me
d, R = *n*-Pr; R′ = CH_2Ph



IIa, R = CH_3; R′ = Ph; R″ = Me
b, R = Me; R′ = Ph; R″ = CH_2Ph
c, R = $PhCH_2$; R′ = COOMe; R″ = Me
d, R = $PhCH_2$; R′ = COOMe; R″ = CH_2Ph

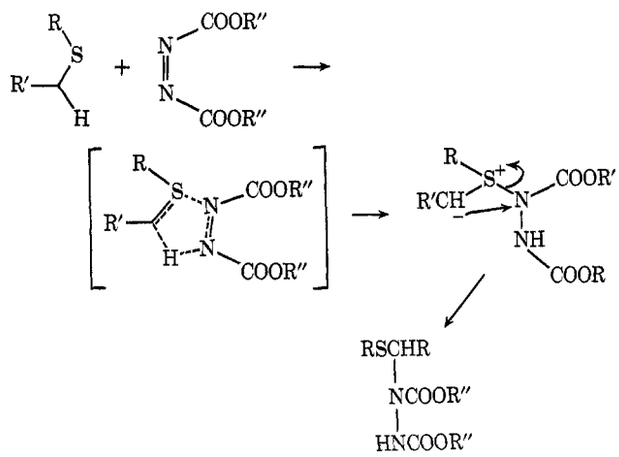


IIIa, R = Me
b, R = *t*-Bu

known to be better stabilized by adjacent sulfur than by adjacent oxygen.[5] The nature of the ester function did not seem to be an important factor; *tert*-butyl azodicarboxylate reacted with the same facility as the methyl ester. By contrast the reaction appears quite sensitive to substitution on the α carbon atom. Thus, di-*n*-butyl sulfide reacted readily, but di-*sec*-butyl sulfide failed to provide the bicarbamate esters under any conditions. The reactivity order for protons adjacent to sulfur appears to be CH_2COOR > benzyl > methyl, and this order is most consistent with proton removal to provide a transition state or intermediate with carbanionic character. A similar order of methylene reactivities was found by Tuleen for the chlorination of sulfides with *N*-chlorosuccinimide, and they arrived at a similar conclusion.[6] By contrast, in the Pummerer reaction of sulfoxides, methyl groups are attacked more easily than benzyl functions.[7]

(4) R. C. Cookson, I. D. R. Stevens, and C. T. Watts, *Chem. Commun.*, 259 (1965).
(5) C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press, New York, N. Y., 1962, p 27.
(6) D. L. Tuleen and T. B. Stephens, *J. Org. Chem.*, **34**, 31 (1969).
(7) C. R. Johnson, J. C. Sharp, and W. G. Phillips, *Tetrahedron Lett.*, 5299 (1967).

In view of the vacant bonding orbital of azodicarboxylic esters[8] and in concert with the original proposal by Woodward,[3] we consider that the association of sulfide with the azo linkage might be accompanied by proton transfer to generate an ylide in one step. Functionalization of the α position might take place by a nitrogen migration from the sulfur atom to the electron-rich ylide carbon atom similar to that initially suggested for the Pummerer reaction[9] as shown below. The expected low acidity of the hydrazine moiety makes unattractive a mechanism involving ejection of the $ROOCNH\bar{N}COOR$ function from the ylide and its subsequent attack on the sulfocarbonium ion thus formed.



Experimental Section

Materials and Procedures.—The esters of azodicarboxylic acid and the sulfides were obtained from Aldrich Chemical Co. and used without further purification. Tlc silica gel F_{254} plates, available from Brinkmann Instruments Inc., were used for all thin layer chromatography. Mass spectral data were obtained on an Associated Electric Industries MS9 instrument using a direct inlet. All nmr curves were obtained with a Varian A-60 spectrometer at 60 MHz. All melting points were obtained on a Fisher-Johns hot stage apparatus and are reported uncorrected. All pure samples were dried *in vacuo* at 56–57° for 16 hr before microanalysis. Solutions were allowed to cool slowly to 4° for all crystallizations.

The Photochemical Apparatus.—The photochemical apparatus consisted of a water-jacketed quartz irradiation vessel equipped with a bubbler for a continuous flow of nitrogen through the reaction chamber. A Hanovia 140-W mercury lamp was used as the source of ultraviolet light, and a General Electric 275-W sunlamp was used for reactions with visible light. Tap water was allowed to flow through the jacket for the dissipation of heat. The current of ultrahigh purity nitrogen through the reaction chamber served to keep the system free of oxygen and agitated.

Chromatography on Silica Gel.—The crude reaction mixtures and preparations from the interaction of azodicarboxylate esters and sulfides were purified by chromatography on silica gel. All columns were prepared in the same manner. Silica gel (Grade No. 62 from Davison Chemical Co., Baltimore, Md.) (100 g) was suspended in heptane–chloroform (1:1 by volume) and poured into a 1.25-in. glass column, after which the excess solvent was allowed to drain away. The preparations to be purified were dissolved or suspended in chloroform–heptane (1:1 by volume) and applied to the top of the column. The column was eluted first with chloroform–heptane (1:1 by volume), then successively with chloroform, chloroform–ethyl acetate (1:1 by volume), and finally ethyl acetate. Fractions (40 ml) were collected in erlenmeyer flasks and allowed to evaporate at room temperature. The presence of a peak in the infrared in the range 3200–3600

(8) F. Yoneda, K. Suzuki, and Y. Nitta, *J. Org. Chem.*, **32**, 727 (1967).
(9) F. G. Bordwell and B. M. Pitt, *J. Amer. Chem. Soc.*, **77**, 572 (1955).

cm^{-1} (NH) was used to determine which fractions were to be retained and worked up further.

Dimethyl [α-(Methylthio)benzyl]bicarbamate.—A solution of benzyl methyl sulfide (3 ml) and dimethyl azodicarboxylate (0.4 ml) was irradiated with a sun lamp in a Pyrex apparatus for 8 hr. The reaction mixture was concentrated *in vacuo* to about ½ volume, and hexane (15 ml) was added to the concentrate, leading to a white crystalline precipitate. The supernatant was decanted, and the residue was washed with several portions of fresh hexane. The air-dried product weighed 444 mg (48%). The air-dried solid was dissolved in carbon tetrachloride (7 ml), and hexane was added until a precipitate formed. The suspension was redissolved by heating over a steam cone and then allowed to cool slowly to 4°, giving 237 mg of dimethyl [α-(methylthio)-benzyl]bicarbamate as a white, crystalline solid: mp 126°; nmr (DMSO-d_6) δ 2.30 (s, 3), 3.67 (s, 1), 3.80 (s, 6), 6.54 (s, 1), 7.40 (m, 5); mass spectrum *m/e* (rel intensity) 284 (<1), 239 (2.3), 238 (17.4), 237 (100), 193 (27.9), 161 (26.7), 139 (8.0), 138 (11.0), 137 (125.6), 122 (5.8), 121 (12.8), 118 (15.1), 105 (8.1), 104 (18.6), 103 (12.8), 92 (5.2), 91 (16.9), 90 (19.8), 89 (3.5), 78 (5.8), 77 (18.6), 65 (6.4), 58 (5.8), 51 (5.8), m* at 157.1 (237 → 193), 134.3 (193 → 161); ir ν_{max} (KBr) 1510, 1670, 1750, 3350, 3450 cm^{-1}.

Anal. Calcd for $C_{12}H_{16}N_2O_4S$: C, 50.69; H, 5.64; N, 9.86; S, 11.28, mol wt, 284.3. Found: C, 50.77; H, 5.98; N, 9.99; S, 11.08; mol wt, 284 (mass spectrum).

Dibenzyl [α-(Methylthio)benzyl]bicarbamate.—A solution of benzl methyl sulfide (1.5 ml) and dibenzyl azodicarboxylate (448 mg) was irradiated in a Pyrex vessel for 16 hr using a sunlamp. Petroleum ether–diethyl ether (1:1 by volume) was added to the reaction mixture and the resulting suspension was stored for 2 days at 4°. The resulting white, crystalline solid was collected on a filter, washed with fresh petroleum ether–diethyl ether solution, and air dried. The air-dried solid weighed 457 mg (69%). A portion (264 mg) was recrystallized from heptane–carbon tetrachloride (10:3 by volume) to give 208 mg of dibenzyl [α-(methylthio)benzyl]bicarbamate: mp 116–119°; nmr ($CDCl_3$) δ 2.20 (s, 3), 5.10 (s, 1), 5.20 (s, 4), 6.60 (s, 1), 7.30 (m, 15); ir ν_{max} (KBr) 1525, 1680, 1760, 3350, 3450 cm^{-1}.

Anal. Calcd for $C_{24}H_{24}N_2O_4S$: C, 66.06; H, 5.50; N, 6.42; S, 7.34; mol wt, 436.7. Found: C, 65.82; H, 5.53; N, 6.32; S, 6.82.

Using a mercury lamp and a quartz apparatus, a 60% yield was obtained.

Dimethyl (1,4-Oxathian-3-yl)bicarbamate.—A solution of 1,4-oxathiane (4 ml) and dimethyl azodicarboxylate (0.4 ml) was heated under reflux at 80° for 16 hr in the presence of 15 mg of benzoyl peroxide. A white, crystalline product (104 mg, 13%) was isolated by chromatography on silica gel. The material was recrystallized from heptane–chloroform (5:1), giving 53 mg of dimethyl (1,4-oxathian-3-yl)bicarbamate: mp 118–120°; nmr ($CDCl_3$) δ 2.70 (t, 2), 3.65 (s, 3), 3.70 (s, 3), 4.00 (m, 4), 5.20 (t, 3), 9.50 (s, 1); ir ν_{max} (KBr) 1540, 1720, 2950, 3300, 3350 cm^{-1}.

Anal. Calcd for $C_8H_{14}N_2O_5S$: C, 38.52; H, 5.64; N, 11.19; S, 12.81; mol wt, 250.3. Found: C, 37.92; H, 5.39; N, 11.04; S, 11.50.

Dimethyl [(Benzylthio)carboxymethyl]bicarbamate.—A solution of dimethyl azodicarboxylate (0.5 ml), methyl *S*-benzylthioglycollate (2.1 ml), and benzoyl peroxide (25 mg) was heated under reflux at 80° for 16 hr. The reaction was protected from atmospheric moisture by a calcium chloride drying tube. Chromatography on silica gel gave dimethyl [(benzylthio)carboxymethyl]bicarbamate (295 mg, 21%). The white solid was recrystallized from heptane–carbon tetrachloride (2:1) to give 124 mg of crystalline solid: mp 79–81°; nmr ($CDCl_3$) δ 3.65 (s, 6), 3.70 (s, 3), 3.90 (s, 2), 5.80 (s, 1), 7.30 (s, 5), and 9.50 (s, 1); ir ν_{max} (KBr) 1600, 1695, 1735, 2995, 3200, 3500 cm^{-1}; mass spectrum *m/e* (rel intensity) 344 (<1), 343 (<1), 342 (2.9), 283 (10.8), 235 (13.1), 234 (9.6), 222 (1.8), 221 (10.8), 220 (100), 195 (8.1), 175 (40), 161 (56.2), 147 (3.9), 146 (32.3), 143 (17.7), 135 (11.2), 123 (10.8), 122 (<1), 115 (38.5), 101 (7.8), 92 (24.3), 91 (111.7), 90 (6.2), 77 (6.2), 76 (16.2), 69 (3.2), 59 (32.3), 51 (5.3).

Anal. Calcd for $C_{14}H_{18}N_2O_6S$: C, 49.12; H, 5.30; N, 8.18; S, 9.36; mol wt, 342.3. Found: C, 49.01; H, 5.42; N, 8.19; S, 11.72; mol wt, 342 (mass spectrum).

Dibenzyl [(Benzylthio)carboxymethyl]bicarbamate.—A solution of methyl *S*-benzylthioglycollate (2 ml) and dibenzyl azodicarboxylate (538 mg) was heated at 80° under reflux for 80 hr. The reaction mixture was chromatographed on silica gel to give a white solid weighing 272 mg (30%). The white solid was recrystallized from carbon tetrachloride–heptane (1:1 by volume) to dibenzyl [(benzylthio)carboxymethyl]bicarbamate weighing 132 mg: mp 85–88°; nmr ($CDCl_3$) δ 3.70 (s, 3), 4.05 (s, 2), 5.10 (s, 4), 5.95 (s, 1), 7.00 (s, 1), 7.33 (s, 15); ir ν_{max} (KBr) 1520, 1680, 1750, 3350, 3450 cm^{-1}.

Anal. Calcd for $C_{26}H_{26}N_2O_6S$: C, 63.14; H, 5.30; N, 5.67; S, 6.48; mol wt, 494.6. Found: C, 63.35; H, 5.45; N, 5.86; S, 6.12.

Di-*tert*-Butyl (1,4-Oxathian-3-yl)bicarbamate.—A solution of 1,4-thioxane (5 ml) and di-*tert*-butyl azodicarboxylate (530 mg) was heated under reflux at 80° for 20 hr. Chromatography on silica gel gave a white solid weighing 440 mg (54%). A portion was recrystallized from carbon tetrachloride to give 126 mg of di-*tert*-butyl (1,4-oxathian-3-yl)bicarbamate: mp 162–163°; nmr (DMSO-d_6) δ 1.40 (s, 18), 2.15 (t, 2), 3.80 (m, 4), 5.00 (m, 1), 8.50 and 8.96 (s, 1); ir ν_{max} (KBr) 1255, 1260, 1520, 1725, 1750, 3030, 3350, 3550 cm^{-1}.

Anal. Calcd for $C_{14}H_{26}N_2O_5S$: C, 50.30; H, 7.78; N, 8.38; S, 9.58. Found: C, 49.98; H, 7.70; N, 8.61; S, 7.69.

Dibenzyl [1-(Butylthio)butyl]bicarbamate.—A solution of *n*-butyl sulfide (10 ml) and dibenzyl azodicarboxylate (800 mg) was irradiated in the quartz apparatus with a mercury lamp for 24 hr. The reaction mixture was chromatographed on silica gel, yielding 1.13 g (95%) of a white waxy solid. This material was crystallized from 18 ml of carbon tetrachloride–heptane (1:5) to give 403 mg of dibenzyl [1-(butylthio)butyl]bicarbamate: mp 68–70°; nmr ($CDCl_3$) δ 0 to 1.80 (m, 14), 2.50 (t, 2), 5.10 (s, 4), 5.50 (m, 1), 6.80 (s, 1), 7.30 (s, 10); ir ν_{max} (KBr) 1310, 1410, 1460, 1515, 1665, 1720, 1740, 3350, 3550 cm^{-1}.

Anal. Calcd for $C_{24}H_{32}N_2O_4S$: C, 64.86; H, 7.21; N, 6.31; S, 7.21. Found: C, 64.88; H, 6.96; N, 6.25; S, 6.90.

Registry No.—Id, 34792-31-9; IIa, 34804-18-7; IIb, 34804-19-8; IIc, 34804-20-1; IId, 34804-21-2; IIIa, 34804-22-3; IIIb, 34804-23-4; benzyl methyl sulfide, 766-92-7; dimethyl azodicarboxylate, 2446-84-6; dibenzyl azodicarboxylate, 2449-05-0; 1,4-oxathiane, 15980-15-1; methyl *S*-benzylthioglycollate, 17277-59-7; di-*tert*-butyl azodicarboxylate, 870-50-8; *n*-butyl sulfide, 544-40-1.

Aminothiosulfonates

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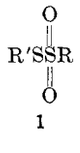
Interest in various biologically active properties of the thiolsulfonate moiety has prompted investigations of compounds containing this group in combination with groups bearing greater or lesser degrees of electronegativity. Thiolsulfonates **1** whose R′ groups



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consist of electron-withdrawing groups such as trichloromethyl[1,2] and trifluoromethyl[3] have been shown to exhibit biological and chemical properties different

(1) J. E. Dunbar and J. H. Rogers, *Tetrahedron Lett.*, 4291 (1965); *J. Org. Chem.*, **31**, 2842 (1966).

(2) B. G. Boldyrev and S. A. Kolesnikova, *Zh. Obshch. Khim.*, **35**, 198 (1965).

(3) J. P. Weidner and S. S. Block, *J. Med. Chem.*, **10**, 1167 (1967).