

malachite green chloride and dichloromercuri malachite green carbinol, the analysis would indicate 16% of dye and 84% of carbinol in the mixture.

Summary

1. The difficulties in the mercuration of basic

triphenylmethane dyes have been confirmed and explained.

2. Organic mercury derivatives of malachite green have been prepared by two separate methods.

POINT PLEASANT, NEW JERSEY

RECEIVED SEPTEMBER 10, 1940

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

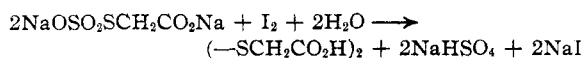
The Use of Bunte Salts in Synthesis. II. The Preparation of Derivatives of Mercapto Aliphatic Acids

BY GEORGE G. STONER AND GREGG DOUGHERTY

Sodium thiosulfate reacts with alkyl halides to form esters of the type RSSO_3Na , called Bunte salts.¹ These S-alkyl thiosulfates have been used for preparing neutral mercaptans,² disulfides,³ mercaptals⁴ and mercaptols.⁵

This paper describes the use of Bunte salts for directly preparing dicarboxylic acids which are disulfides, mercaptals and mercaptols.

Sodium thiosulfate and sodium chloroacetate formed disodium S-carboxymethyl thiosulfate which was converted by iodine and water directly to dithiodiacetic acid.



Similarly prepared were α, α' - and β, β' -dithiodipropionic acids. In the latter case this method was excellent by virtue of the striking insolubility of β, β' -dithiodipropionic acid. By hydrolyzing γ, γ' -dithiodibutyronitrile, γ, γ' -dithiodibutyric acid was obtained.

Eleven dibasic acids of the thioacetal type (see Table I) were prepared directly from carbonyl compounds and halogen-substituted aliphatic acids through Bunte salts. In each case the catalyst was six equivalents of acid per mole of disodium S-carboxyalkyl thiosulfate.

Experimental Part

Dithiodiacetic Acid.—Chloroacetic acid (9.5 g., 0.1 mole) was dissolved in 45 cc. of water, neutralized with anhydrous sodium carbonate and heated for one hour at 100° with a solution of 25 g. (0.1 mole) of sodium thiosulfate in 30 cc. of water. While hot, 12.7 g. (0.1 atom)

of iodine was added in small portions during a period of ten minutes while stirring. Any excess iodine was removed by passing sulfur dioxide into the cold solution momentarily. It was acidified with 3 cc. (0.05 mole) of concd. sulfuric acid and extracted with six 25-cc. portions of ether. After evaporation to dryness the residue was dissolved in 10 cc. of acetone, filtered into 100 cc. of toluene, and about 25 cc. of the solvent was distilled off. After standing at 25° for one day, 4.6 g. (50% yield) was obtained, equivalent weight calcd. 91.1, found 91.1. Recrystallization from carbon tetrachloride raised the m. p. from 102–103° to 106°.⁶

α, α' -Dithiodipropionic Acid.—This material was prepared from 15.3 g. (0.1 mole) of racemic α -bromopropionic acid in a way similar to that described above. At 5° it precipitated from the reaction solution as an oil in 57% yield (6.0 g.) in two days. After crystallization from ethanol-water and then from benzene the m. p. was 127–135°,⁷ equivalent weight calcd. 105.1, found 106.

β, β' -Dithiodipropionic Acid.—This compound was also similarly prepared from 10.9 g. (0.1 mole) of β -chloropropionic acid. It precipitated promptly when the reaction solution was cooled. After filtering, it was desiccated azeotropically by distilling considerable benzene from it to give 8.4 g. (80% yield). It was purified by dissolving it in 200 cc. of hot ethyl acetate, filtering this solution into 400 cc. of hot benzene and cooling. Within one hour 7.9 g. had crystallized, m. p. 154°,⁸ equivalent weight calcd. 105.1, found 105.5.

γ, γ' -Dithiodibutyronitrile.— γ -Chlorobutyronitrile (10.4 g., 0.1 mole) was dissolved in 45 cc. of alcohol, refluxed and stirred on a steam-bath for two hours with a solution of 25 g. (0.1 mole) of sodium thiosulfate in 30 cc. of water. While hot, 12.7 g. (0.1 atom) of iodine was added and then the solution was cooled. The precipitated product was purified by refluxing in 40 cc. of alcohol with activated carbon, filtered, and reprecipitated as a colorless liquid by the addition of 200 cc. of water. After desiccation for forty hours at 1 mm. over phosphoric anhydride the yield

(1) Bunte, *Ber.*, **7**, 647 (1874).

(2) Price and Twiss, *J. Chem. Soc.*, **95**, 1727 (1909).

(3) Price and Twiss, *ibid.*, **93**, 1395, 1401, 1651 (1908); **95**, 1050, 1489, 1727 (1909); **97**, 1175 (1910); **105**, 36 (1914); *Ber.*, **41**, 4375 (1908).

(4) Westlake and Dougherty, *THIS JOURNAL*, **63**, 658 (1941).

(5) German patent 46,333, *Ber.*, **22**, 115 (1889).

(6) Biilmann, *Ann.*, **339**, 357 (1905), reported 107–108° (from ether and petroleum ether); Holmberg, *Z. anorg. Chem.*, **56**, 385 (1908), reported 108–109° (from ethyl acetate and benzene).

(7) Fredga, *Arkiv Kemi, Mineral. Geol.*, **12B**, No. 22 (1938), and **12A**, No. 13 (1937), reported 118–119° for the *meso* form and 148–149° for the racemate.

(8) Biilmann, *loc. cit.*, reported 155°.

TABLE I
 ACIDS OF THE THIOACETAL TYPE PREPARED BY THE USE OF SODIUM THIOSULFATE

| Starting materials | | Product | | | | | | |
|---------------------|-------------------------|---|----------------------|---|----------------|--|---------------------------|----------------------------|
| Carbonyl compound | Halo acids ^a | Name, acid | Obsd. | M. p., °C. Literature | Yield, pure, % | Formula | Sulfur, % Calcd. Found | Equiv. wt. Calcd. Found |
| Formaldehyde | A | (Methylenedithio)-diacetic | 126-127 | 128.5-129.5, ^b 129, ^c 120-125 ^d | 38 | C ₄ H ₆ O ₄ S ₂ | | 98.1 98.2 |
| Benzaldehyde | A | (Benzaldithio)-diacetic | 124 | 126-127 ^{b,d} , 124 ^e | 92 | C ₁₁ H ₁₂ O ₄ S ₂ | | 136.2 137 |
| 2-Nitrobenzaldehyde | A | (2-Nitrobenzaldithio)-diacetic | 124 | 122-123 ^e | 32 | C ₁₁ H ₁₁ NO ₆ S ₂ | | 158.7 159 |
| Acetone | A | (Isopropylidenedithio)-diacetic | 129 | 126-127, ^e 134-135 (cor.) ^f | 20 | C ₇ H ₁₂ O ₄ S ₂ | | 112.1 112 |
| Formaldehyde | B | α,α'-(Methylenedithio)-dipropionic | 149-152 ^g | 155-156 ^h | 12 | C ₇ H ₁₂ O ₄ S ₂ | | 112.1 114 |
| Benzaldehyde | B | α,α'-(Benzaldithio)-dipropionic | 149-150 ^g | 138-140 ^g | 12 | C ₁₂ H ₁₄ O ₄ S ₂ | | 150.2 152 |
| Acetone | B | α,α'-(Isopropylidenedithio)-dipropionic | 174 ^g | | 5 | C ₉ H ₁₆ O ₄ S ₂ | 25.41 25.1 | 128.2 126 |
| Butanone | B | α,α'-(Methylethylmethylene)-dithio]-dipropionic | 126-127 ^g | | 7 | C ₁₀ H ₁₈ O ₄ S ₂ | 24.07 24.2 | 133.2 132 |
| Formaldehyde | C | β,β'-(Methylenedithio)-dipropionic | 142 | | 13 | C ₇ H ₁₂ O ₄ S ₂ | 28.59 28.3 | 112.2 113 |
| Benzaldehyde | C | β,β'-(Benzaldithio)-dipropionic | 90 | | 13 | C ₁₂ H ₁₄ O ₄ S ₂ | 21.34 21.4 | 150.2 150 |
| Acetone | C | β,β'-(Isopropylidenedithio)-dipropionic | 70 | | 10 | C ₉ H ₁₆ O ₄ S ₂ | 25.41 25.5 | 128.2 125 |

^a Symbols for halogen-substituted acids: A, chloroacetic acid; B, racemic-α-bromopropionic acid; C, β-chloropropionic acid. ^b Holmberg and Mattison, *Ann.*, **353**, 123 (1907). ^c Larsson, *Svensk Kem. Tids.*, **51**, 42 (1939). ^d Holmberg, *Ing. Vetensk. Akad. Handl.*, No. **103**, 5 (1930). ^e Bongartz, *Ber.*, **19**, 1932 (1886); **21**, 479 (1888). ^f Shriner, Cross and Dobratz, *This Journal*, **61**, 2002 (1939). ^g These temperatures are not of much significance because derivatives of α-mercaptopropionic acid were obtained as unresolved mixtures of several optically isomeric compounds, the proportions of which varied with recrystallization. ^h M. p. of the racemic compound, Fredga, *Arkiv. Kemi, Mineral. Geol.*, **12A**, No. 15 (1937).

was 7 g. (70%); d_{20}^{20} 1.270, n_D^{20} 1.606, molecular refraction calcd. 54.88, obsd. 54.4.

Anal. Calcd. for C₈H₁₂N₂S₂: S, 32.01. Found: S, 32.2.

γ,γ'-Dithiodibutyric Acid.—γ,γ'-Dithiodibutyronitrile (5 g., 0.025 mole) was refluxed for two hours with 21 cc. (0.25 mole) of concd. hydrochloric acid. The solution was decanted while hot from some tarry residue. The product crystallized immediately after cooling, and after recrystallization from 30 cc. of water, a yield of 1.2 g. (20%), m. p. 103-105°, was obtained,⁹ equivalent weight calcd. 119.2, found 120.

Mercaptal- and Mercaptol-Acids.—One decimole of halogen-substituted acid (see Table I) was neutralized in 45 cc. of water with sodium carbonate and heated for one hour at 100° with a solution of 25 g. (0.1 mole) of sodium thiosulfate in 30 cc. of water. After cooling, 50 cc. (0.6 mole) of concd. hydrochloric acid was added, and about

1 g. of sodium chloride was filtered off. The solution was refluxed ten hours with 0.1 mole (100% excess) of carbonyl compound, except when aromatic aldehydes were involved, only 0.4 mole, or 80% of the theoretical amount was added. The products were sufficiently insoluble to crystallize directly from the reaction solutions at 5° in three days, except methylenedithiodiacetic acid which was extracted with ether. For purification, the precipitated material was dissolved in 20 cc. of acetone, filtered into 130 cc. of benzene, concentrated somewhat, and after one day at 5° the product crystallized upon scratching the inside of the flask. Derived benzaldehydes were recrystallized from 400 cc. of water. See Table I for other data.

Summary

Bunte salts were used for preparing four disulfides, seven mercaptals and four mercaptols, all dicarboxylic acids, by a direct method from appropriate halogen-substituted acids.

(9) Brand, Block and Cahill, *J. Biol. Chem.*, **119**, 689 (1937), reported 106-107°; Gabriel, *Ber.*, **23**, 2489 (1890), reported 107-108°.