Attempts to obtain 2-(4-aminobenzenesulfonamido)-1,4-naphthoquinone by hydrolysis of X using (a) refluxing concentrated hydrochloric acid, or (b) refluxing 50% sulfuric acid, gave unchanged starting material as the only isolable material.

When the product X was subjected to acid hydrolysis as described for the quinones VII and IX, 2-amino-1,4-naphthoquinone (VIII) was obtained in 90% yield.

The Formation of 1,5,7,11-Tetrathiaspiro[5.5]undecane in the Reaction of Cyclic Trimethylene Trithiocarbonate with 2,2′-Iminodiethanol[1]

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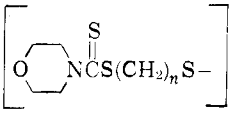
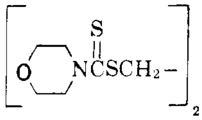
Ammonium dithiocarbamate and certain of its derivatives, including some with *S*-substitution, have been reported[2,3] to be effective in protecting mice from radiation-induced injury; Foye and Mickles[4] recently reported that a number of dithiocarbamates afforded significant protection to mice exposed to sub-lethal radiation dosage. Therefore, the products of the nucleophilic attack by secondary amines on cyclic ethylene trithiocarbonate—2-mercaptoethyl dithiocarbamates[5] and the corresponding disulfides[6]—should be evaluated as antiradiation agents. The corresponding propyl dithiocarbamates, which should be obtainable from cyclic trimethylene trithiocarbonate, are also of potential interest.

Attempting to use the literature procedures[6] described in general terms, we were unable to obtain the reported high yields (about 95%) of the dithiodiethylene *N,N*-disubstituted dithiocarbamates from the reaction of ethylene trithiocarbonate with dimethylamine and morpholine. The only pure product that we isolated from the reaction of equivalent amounts of ethylene trithiocarbonate and morpholine was not the expected dithiodiethylene 4-morpholinecarbodithioate (I) but ethylene 4-morpholinecarbodithioate (II). Ethylene esters such as II were previously identified as by-products of this general reaction and were obtained in increased yields by modifications of the original procedure; for example, by the addition of base.[7] The anomalous formation of these ethylene esters has been rationalized[7] as involving the base-catalyzed elimination of ethylene sulfide from 2-mercaptoethyl dithiocarbamates.[8] Durden, *et al.*,[9] apparently unaware that the products originally described as thiols[6] were later identified as disulfides,[5] recently demonstrated that the product they isolated in 40% yield from the reaction of ethylene trithiocarbonate with morpholine was the disulfide I. These observed variations in products and yields are apparently due in part to differences in isolation procedure. To make the disulfides in high yield we resorted to the alkylation of sodium dithiocarbamates with bis(2-chloroethyl) disulfide, an alternative procedure mentioned by Delaby, *et al.*[5]

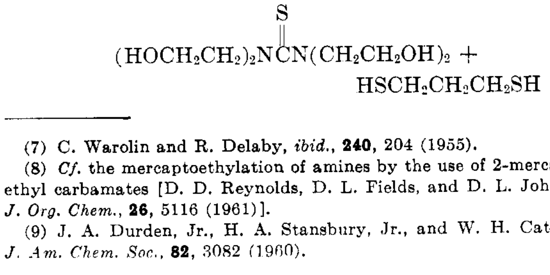


I. $n = 2$
IV. $n = 3$



II

Cyclic trimethylene trithiocarbonate (III) was opened with morpholine without difficulty to give 3 - mercaptopropyl 4 - morpholinecarbodithioate (92% pure by iodometric titration), which was subsequently oxidized by iodine to dithiodi(trimethylene) 4-morpholinecarbodithioate (IV). An attempt to prepare 3-mercaptopropyl bis(2-hydroxyethyl)dithiocarbamate (V) from III and 2,2′-iminodiethanol, however, led to the isolation in appreciable yield of a white crystalline compound, which has been identified as 1,5,7,11-tetrathiaspiro[5.5]undecane (VI) on the basis of elemental analysis, molecular weight, and the n.m.r. spectrum shown in Fig. 1. This spectrum, in conjunction with that of the starting material III, confirms the proposed structure as it shows two band systems in the region expected from methylene proton absorption (between 1.5 and 3.5 p.p.m.) whose areas are in a 2:1 ratio. The complex multiplet structure of each band system indicates strong spin coupling among adjacent methylene groups. The following sequence of reactions is proposed to explain the formation of VI:



$$\underset{\text{V}}{(HOCH_2CH_2)_2N\overset{S}{\overset{\|}{C}}SCH_2CH_2CH_2SH} \xrightarrow{(HOCH_2CH_2)_2NH} (HOCH_2CH_2)_2N\overset{S}{\overset{\|}{C}}N(CH_2CH_2OH)_2 + HSCH_2CH_2CH_2SH \quad (1)$$

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[1] This investigation was supported by the U.S. Army Medical Research and Development Command (Contract No. DA-49-193-MD-2028).

[2] P. Alexander, Z. M. Bacq, S. F. Cousens, M. Fox, A. Herve, and J. Lazar, *Radiation Res.*, **2**, 392 (1955).

[3] A. Phil and L. Eldjarn, *Pharmacol. Rev.*, **10**, 437 (1958).

[4] W. O. Foye and J. Mickles, Abstracts of the 141st National Meeting of the American Chemical Society, Washington, D.C., March, 1962, p. 30-N.

[5] R. Delaby, C. Warolin, P. Chabrier, and P. Piganiol, *Compt. rend.*, **232**, 1676(1951).

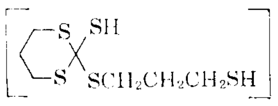
[6] R. Delaby, P. Piganiol, and C. Warolin, *ibid.*, **230**, 1671 (1950).

[7] C. Warolin and R. Delaby, *ibid.*, **240**, 204 (1955).

[8] *Cf.* the mercaptoethylation of amines by the use of 2-mercaptoethyl carbamates [D. D. Reynolds, D. L. Fields, and D. L. Johnson, *J. Org. Chem.*, **26**, 5116 (1961)].

[9] J. A. Durden, Jr., H. A. Stansbury, Jr., and W. H. Catlette, *J. Am. Chem. Soc.*, **82**, 3082 (1960).

$$HSCH_2CH_2CH_2SH + III \rightarrow$$



$$\rightarrow VI + H_2S \qquad (2)$$

The proposed formation of a thiourea in equation 1 finds support in the recently described preparation of 1,3-dibutyl-2-thiourea from ethylene trithiocarbonate and butylamine.[9] Although alkyl[10] and aryl[11] tetrathioorthocarbonates are known, VI is apparently the first example of a simple bicyclic tetrathioorthocarbonate, the tetracyclic 2,2′-spirobi(1,3-benzodithiole) has recently been described[12] as the probable product of a thermal decomposition of 1,2,3-benzothiadiazole in the presence of carbon disulfide.

Experimental

Dithiodiethylene Dimethyldithiocarbamate.—A solution of 670 mg. (4.40 mmoles) of sodium dimethyldithiocarbamate hemihydrate[13] in 4 ml. of ethyl alcohol was added to a solution of 380 mg. (2.10 mmoles) of bis(2-chloroethyl) disulfide[14] in 1 ml. of ethyl alcohol. The resulting mixture was stirred for 8 hr. and then allowed to stand for 2 days. The lower oily layer that had separated solidified when the sides of the flask were scratched with a glass rod. The mixture was poured into 75 ml. of water, and the solid that had formed was collected, washed with water and with ethyl alcohol, and dried *in vacuo* over phosphorus pentoxide; yield 662 mg. (92%), m.p. 86–87°[15] (lit.,[6] m.p. 86°).

Dithiodiethylene 4-Morpholinecarbodithioate (I).—A solution of 510 mg. (2.75 mmoles) of sodium 4-morpholinecarbodithioate[16] in 4 ml. of *N,N*-dimethylformamide was added to a solution of 240 mg. (1.25 mmoles) of bis(2-chloroethyl) disulfide[14] in 1 ml. of *N,N*-dimethylformamide; a solid precipitated within 1 min. The resulting mixture was stirred for 16 hr. at room temperature and then poured into 50 ml. of water. The gum initially formed slowly solidified on stirring to a white amorphous mass, which was collected, washed with water, and dried *in vacuo* over phosphorus pentoxide; yield 550 mg. (99%), m.p. 104–105°,[15] 105°.[17] Recrystallization of a 250-mg. sample from acetone gave 179 mg. of I as a white solid, m.p. 109°[17] (lit.,[6] m.p. 102°).

Anal. Calcd. for $C_{14}H_{24}N_2O_2S_6$: C, 37.81; H, 5.44. Found: C, 37.88; H, 5.44.

Ethylene 4-Morpholinecarbodithioate (II).—A solution of 3.00 g. (22.0 mmoles) of ethylene trithiocarbonate[18] in 1.92 g. (22.0 mmoles) of morpholine was stirred at 40° for 7 hr., the reaction mixture gradually solidifying. The crude solid thus formed was recrystallized from 1.1 l. of acetone with charcoal treatment to give 1.25 g. (32%) of white crystals, m.p. 230°,[17] after being dried *in vacuo* over phosphorus pentoxide. Recrystallization of a sample from 2-methoxyethanol afforded analytically pure II, m.p. 231°.[17,19]

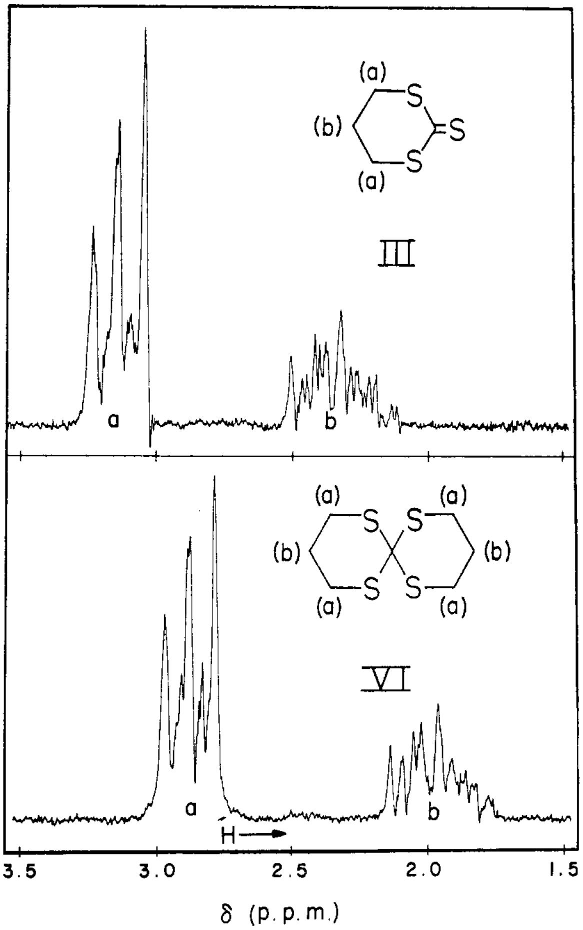


Fig. 1.—N.m.r. spectra of III and VI in carbon disulfide solution [*ca.* 20% (w./v.)] with δ in p.p.m. downfield from tetramethylsilane as internal reference; 60 Mc./sec.; R. F. field 0.06 milligauss.

Anal. Calcd. for $C_{12}H_{20}N_2O_2S_4$: C, 40.88; H, 5.72; S, 36.38. Found: C, 40.91; H, 5.86; S, 36.76.

In another experiment the same amounts of reactants were stirred at room temperature for 5 days under nitrogen. The resulting solid reaction mass was dissolved in 15 ml. of boiling 2-methoxyethanol. When cooled, the solution deposited 780 mg. (20%) of II as a white fluffy solid, m.p. 230°.[17]

3-Mercaptopropyl 4-Morpholinecarbodithioate and Dithiodi(trimethylene) 4-Morpholinecarbodithioate (IV).—A solution of 10.5 g. (70 mmoles) of trimethylene trithiocarbonate[20] and 6.1 g. (70 mmoles) of morpholine in 500 ml. of ethyl alcohol was refluxed under nitrogen for 5 hr. The solvent was removed by evaporation *in vacuo*, and the residual clear yellow viscous oil gave a 92% iodometric titer as 3-mercaptopropyl 4-morpholinecarbodithioate; yield 15.2 g. (85%, cor.).

A 7.70-g. sample of the crude thiol was dissolved in ethyl ether and titrated with 1 *N* iodine–potassium iodide solution to an iodine color end point. The yellow solid that precipitated was collected, washed with ether and then ethyl alcohol,

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(10) H. J. Backer and P. L. Stedehouder, *Rec. trav. chim.*, **52**, 923 (1933).

(11) H. J. Backer and P. L. Stedehouder, *ibid.*, **52**, 1039 (1933).

(12) R. Huisgen and V. Weberndörfer, *Experientia*, **17**, 566 (1961).

(13) M. Delépine, *Bull. soc. chim. France*, [4] **3**, 650 (1908).

(14) R. C. Fuson, C. C. Price, D. M. Burness, R. E. Foster, W. R. Hatchard, and R. D. Lipscomb, *J. Org. Chem.*, **11**, 487 (1946).

(15) Determined in a capillary and is uncorrected.

(16) This compound was prepared from morpholine, carbon disulfide, and aqueous sodium hydroxide in the conventional manner; the reaction mixture was evaporated to dryness *in vacuo* and the residue recrystallized from a concentrated aqueous solution and dried to constant weight *in vacuo* over phosphorus pentoxide at room temperature.

(17) Determined on a Kofler Heizbank.

(18) Cyclic ethylene trithiocarbonate was prepared from 1,2-dibromoethane by an adaptation of the method of W. Coltof [U.S. Patent 2,193,415 (March 12, 1940)]. Some of the ethylene ester used was purchased from L. Light and Co., Ltd., Colnbrook, Bucks, England.

(19) Warolin and Delaby[7] obtained II, m.p. 229°, by refluxing a benzene solution of 2-mercaptoethyl 1-piperidinecarbodithioate and morpholine.

(20) W. H. Mills and B. C. Saunders, *J. Chem. Soc.*, 537 (1931).

and dried *in vacuo*, and recrystallized from 900 ml. of ethyl alcohol; yield of IV as a pale yellow solid 6.84 g. (76%), m.p. 94–95°.[15]

Anal. Calcd. for $C_{16}H_{28}N_2O_2S_6$: C, 40.64; H, 5.97; S, 40.69. Found: C, 40.40; H, 5.88; S, 40.96.

1,5,7,11-Tetrathiaspiro[5.5]undecane (VI).—A solution of 2.1 g. (20 mmoles) of freshly distilled 2,2′-iminodiethanol in 50 ml. of ethyl alcohol was added to a solution of 3.0 g. (20 mmoles) of trimethylene trithiocarbonate[20] in 150 ml. of the same solvent. The resulting solution was evaporated under reduced pressure at 55–60° to a yellow oil, which was kept at this temperature for 3 hr. *in vacuo*. The white crystals that formed were collected, washed with cold propyl alcohol, and dried *in vacuo* over phosphorus pentoxide; yield 0.73 g. (33%),[21] m.p. 116°,[17] nitroprusside test for thiol negative (even after boiling briefly in dilute acid or base). Recrystallization from ethyl alcohol afforded a sample of VI for analysis as white crystals, m.p. 116–117°,[15] 117°;[17] ν_{max}^{KBr} (major bands) 2905 (s.), 1410 (s.), 1270 (s.), 1000 (m.), 905 (m.), 880 (s.), 770 (m.-s.), 740 (s.) cm.$^{-1}$. The n.m.r. spectrum (Fig. 1) was measured on a Varian A 60 n.m.r. spectrometer.

Anal. Calcd. for $C_7H_{12}S_4$: C, 37.46; H, 5.39; S, 57.15; mol. wt., 224. Found: C, 37.66; H, 5.39; S, 57.10; mol. wt., 230.

Acknowledgment.—The authors are indebted to Dr. W. C. Coburn, Jr., for determination and interpretation of the n.m.r. spectra; and to the Analytical Section of Southern Research Institute for the analyses reported.

[21] Additional crystals, not included in the yield figures, were deposited in the oily residue obtained by evaporation of the filtrate *in vacuo;* the residual oil gave a positive nitroprusside test. The crude oily thiols obtained from other runs also deposited crystals on long standing when seeded with VI.

The Structure of Ceanothic Acid[1]

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The medicinal plant *Ceanothus americanus*, fam. *Rhamnaceae* (Jersey Tea), has until quite recently escaped thorough chemical investigation although it has been known to contain numerous compounds of unknown structure.[2] During the last two years four groups have reported work on this plant.[1,3–5] Roscoe and Hall[3] have noted the presence of eight alkaloids in the root bark while others[1,4,5] have investigated the nonalkaloid fractions of the plant.

De Mayo[4] as well as this writer,[1] have been able to confirm the presence of ceanothic acid as first reported by Julian, Pikl, and Dowson[6] in 1938. Ceanothic acid was described by Julian as a hydroxy dicarboxylic acid in which both carboxyl groups were hindered. On melting it lost one equivalent of carbon dioxide and also one of water.

In this paper experiments are reported leading to structure Ia for ceanothic acid. For the sake of simplicity the entire discussion will be presented in terms of the eventually established structure.

An improved extraction procedure led to the easy separation of ceanothic acid, m.p. 356–358°, $[\alpha]_D$ +38°. Dimethyl ceanothate (Ib) showed an average molecular weight of 503 (Rast). Equivalent weight value of 248 was obtained for the free acid by titration using alkali; ceanothic acid is therefore dibasic. The infrared spectra of Ia and of Ib suggested the presence of a vinylidene group (1642 and 885 cm.$^{-1}$). On catalytic hydrogenation Ib absorbs one mole of hydrogen giving dimethyl dihydroceanothate (II) in which these two bands have disappeared. Repeated analyses of all compounds fitted a $C_{30}H_{46}O_5$ formula for ceanothic acid. Such an empirical formula requires a pentacyclic skeleton. On boiling with acid[7] followed by esterification of the remaining free carboxyl group Ia gave III which has a five-membered lactone (ν_{max} 1770 cm.$^{-1}$) but no vinylidene group. A reaction of this type is well known in the lupeol series.[7] In view of the empirical formula, the presence of the vinylidene group and the nature of the lactonization reaction (Ia → III) it seemed plausible that ceanothic acid is a triterpene of the lupeol group. The hydroxyl group, known to be present in the molecule, was assumed, on the basis of rather abundant analogies, to occupy the C-3 position. One of the carboxylic groups could be placed at C-17, in view of the lactonization reaction.

The simultaneous dehydration and decarboxylation occurring at the melting point of ceanothic acid[6] suggested that the second carboxyl group is located beta to the hydroxyl group. Indeed oxidation of the hydroxyl group to a ketone, gave a keto monocarboxylic acid (IVa), presumably obtained on decarboxylation of a labile β-keto acid intermediate. The infrared spectrum of this substance showed the presence of the vinylidene group (1640 and 882 cm.$^{-1}$) and of two bands in the carbonyl region at 1740 and 1720 cm.$^{-1}$. The 1740-cm.$^{-1}$ band suggested a five-membered ring ketone.

The triterpene emmolic acid was isolated in 1958 by Simes and coworkers[8] from *Emmenospermum alphitonioides* F. *Muell* (fam. Rhamnaceae)

[1] Preliminary communication: R. Mechoulam, *Chem. Ind.* (London), 1835 (1961).

[2] For leading references to work prior to 1960 see ref. 3 and 5.

[3] C. W. Roscoe and N. A. Hall, *J. Am. Pharm. Assoc., Sci. Ed.*, **49**, 108 (1960).

[4] P. de Mayo and A. N. Starratt, *Tetrahedron Letters*, **7**, 259 (1961).

[5] R. A. Abramovitch and G. Tertzakian, *Can. J. Chem.*, **39**, 1733 (1961).

[6] P. L. Julian, J. Pikl, and R. Dowson, *J. Am. Chem. Soc.*, **60**, 77 (1938).

[7] *Cf.* V. Bruckner, J. Kovács, and I. Koczka, *J. Chem. Soc.*, 951 (1948); G. S. Davy, T. G. Halsall, and E. R. H. Jones, *ibid.*, 2696 (1951).

[8] J. P. Boyer, R. A. Eade, H. Locksley, and J. J. H. Simes, *Austr. J. Chem.*, **11**, 236 (1958).