Triphenylmethyl tetrafluoroborate was prepared as described.[1] Separation of I from II and II from III after hydrolysis was based on the solubility of I and III in 5% aqueous NaOH. Where I and III occurred together, the relative amounts could be determined from the nmr spectrum of a solution of the mixture in CH_2Cl_2.

3,3,3-Triphenylpropionic acid (I) was identified by its melting point [179° (lit.[2] mp 178°)] and the nmr spectrum, which has been reported[5] and which was identical with an authentic sample.

3,3-Diphenylindanone (II) was identified by its melting point [131° (lit.[6] mp 132°)] and its nmr spectrum, which consisted of a singlet at δ 3.35 (CH_2) and a sharp singlet at δ 7.27 (phenyls) superimposed on a broad multiplet at δ 6.8–7.6 (acylated benzene ring).

Although the structure of III was not rigorously established, the following data are reasonably indicative. The nmr spectrum consisted of singlets at δ 1.21 (CH), 1.73 (CH_3), and 7.275 (phenyls). The δ 7.27 singlet is superimposed on a complex multiplet centered around δ 7.3, and there is another complex multiplet centered around δ 7.8. The two complex multiplets originate with the acyl-substituted ring. The areas were in the calculated ratios. Compound III dissolves in 5% NaOH and is precipitated by CO_2 in accord with the β-diketone structure. The infrared spectrum shows strong bands at 1600 and 1680 cm^{-1} in accord with two different keto groups. The mass spectrum exhibited a parent peak at m/e 326 in accord with a molecular weight of 326 and a dominant band at m/e 43 indicative of CH_3CO^+ and a CH_3CO substituent. Compound III could be recovered unchanged from solution in 96% H_2SO_4 for 2 min. The melting point of III was 164–166°.

A strong indication of the structure of III would have been deacetylation by alkali to II. Treatment of III with KOH in diethylene glycol at 230° for 15 min caused complete disappearance of III. The product mixture (after drowning and water washing) generated an nmr spectrum which consisted of relatively few sharp lines. However, the nmr bands of II accounted for only about 1% of the total area and the product mixture was not further investigated. Although it is believed that the trace of II came from III, the low yield diminishes the definitiveness of the experiment.

4,4,4-Triphenyl-2-butanone was identified by its melting point [142° (lit.[7] mp 141°)] and its nmr spectrum, which consisted of singlets at δ 1.78 (CH_3), 3.80 (CH_2), and 7.13 (phenyls) in the calculated ratios.

Registry No.—Acetic anhydride, 108-24-7; triphenylmethyl cation, 14699-91-3.

Acknowledgment.—Grateful acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation for support of this work.

(5) Sadtler Standard Spectra, Sadtler Research Laboratories, Philadelphia, Pa., 1967, nmr No. 428.

(6) C. Moureu, C. Dufraisse, and F. Baylocq, *Bull. Soc., Chim. Fr.*, [4] **43**, 1370 (1928).

(7) R. L. Garner and L. Hellerman, *J. Amer. Chem. Soc.*, **68**, 823 (1946).

Insertion Reaction of Carbon Disulfide with Sulfenamides

JOSEPH E. DUNBAR AND JOAN H. ROGERS

Edgar C. Britton Research Laboratory, The Dow Chemical Company, Midland, Michigan 48640

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Carbon disulfide is known to undergo "insertion reactions" with various nitrogen–carbon bonds,[1] nitrogen–trivalent phosphorus bonds,[2] nitrogen–trivalent arsenic bonds,[1,3] nitrogen–silicon bonds,[1,4] and nitrogen–transition metal bonds.[5] Simple insertion of carbon disulfide into the nitrogen–sulfur bond has not been reported, although E. S. Blake,[6] in an attempt to form trithiocarbonate compounds (I) by reaction of carbon disulfide with a secondary amine sulfide, obtained instead the tetraalkyl thiuram disulfide.

$$R_2NSCSNR_2$$
$$\|$$
$$S$$

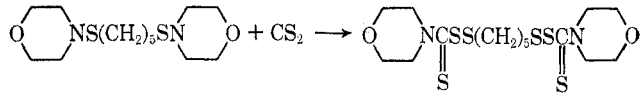
I

The present work demonstrates insertion of carbon disulfide into the nitrogen–sulfur bond of simple sulfenamides of secondary amines, resulting in the formation of aminecarbotrithioates (III and IV) in good yields (eq 1 and 2). This reaction constitutes a new procedure for the synthesis of aminecarbotrithioates. Known procedures involve reaction of aminecarbodithioate salts with sulfenyl halides,[7] Bunte salts,[8] sulfenyl thiocyanates,[9] and thiolsulfonates.[10]

$$RSNR'_2 + CS_2 \longrightarrow RSSCNR'_2 \quad (1)$$
$$\|$$
$$S$$

IIa–IIg IIIa–IIIg

a, R = CH_3; NR'_2 = piperidino
b, R = CH_3; NR'_2 = morpholino
c, R = allyl; NR'_2 = morpholino
d, R = CH_3; R' = C_2H_5
e, R = C_6H_5; NR'_2 = morpholino
f, R = $CH_3SCH_2CH_2$; NR'_2 = piperidino
g, R = $CH_3SCH_2CH_2$; R' = CH_3



IV (2)

Thus, the reaction of carbon disulfide and 1-(methylthio)piperidine (IIa) in ether solution at room temperature is complete in 5 min and afforded an 88% yield of methyl 1-piperidinecarbotrithioate (IIIa). These reactions are exceptionally clean, and purification procedures are made simple by the absence of by-products or of side reactions.

When R is electron-withdrawing, temperatures above the boiling point of carbon disulfide are required for reaction. Hence, the reaction of 4-(phenylthio)morpholine (IIe) with carbon disulfide to give phenyl 4-morpholinecarbotrithioate (IIIe) required heating at

(1) L. B. Clapp and J. W. Watjen, *J. Amer. Chem. Soc.*, **75**, 1490 (1953); N. Kreutzkamp and H. Y. Oei, *Arch. Pharm.* (Weinheim), **299**, 906 (1966); A. O. Fitton, A. Rigby, and R. J. Hurlock, *J. Chem. Soc., C*, 996 (1968); A. O. Fitton and A. Rigby, *ibid.*, 230 (1969).

(2) G. Oetel, H. Malz, and H. Holzschmidt, *Chem. Ber.*, **97**, 891 (1964).

(3) Von H.-J. Vetter and H. Nöth, *Z. Naturforsch.*, **19b**, 167 (1964).

(4) R. H. Cragg and M. F. Lappert, *J. Chem. Soc., A*, 82 (1966); E. A. V. Ebsworth, G. Rocktäschel, and J. C. Thompson, *ibid.*, 362 (1967).

(5) D. C. Bradley and M. H. Gitlitz, *Chem. Commun.*, 289 (1965).

(6) E. S. Blake, *J. Amer. Chem. Soc.*, **65**, 1267 (1943).

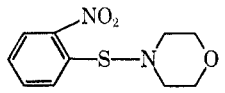
(7) J. Teppema, U. S. Patent 2,024,613 (1935); R. Ghosh, U. S. Patent 3,232,974 (1966), U. S. Patent 3,284,291 (1966).

(8) A. A. Watson, *J. Chem. Soc.*, 2100 (1964).

(9) M. Hunt, U. S. Patent 2,390,713 (1945).

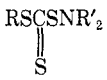
(10) J. E. Dunbar and J. H. Rogers, U. S. Patent pending; L. Field and J. D. Buckman, *J. Org. Chem.*, **33**, 3865 (1968).

75°. 4-(2-Nitrophenylthio)morpholine (V) failed to react with carbon disulfide in a sealed tube at 100° over a period of 5 hr.



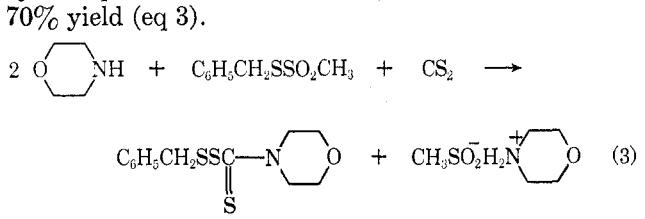
V

Insertion of carbon disulfide into the nitrogen–sulfur bond could conceivably result in the formation of a trithiocarbonate compound (VI). That the products are in fact aminecarbotrithioates was demonstrated by comparison of IIIe with an authentic sample of phenyl 4-morpholinecarbotrithioate prepared by the reaction of benzenesulfenyl chloride with sodium 4-morpholinecarbodithioate.



VI

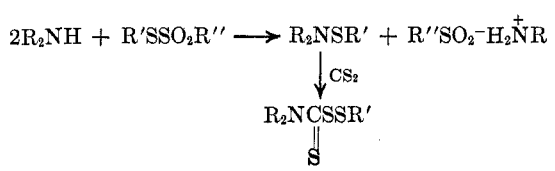
During the course of our investigation, it was learned that preparation of the sulfenamide intermediate is not necessary. When 2 equiv of morpholine was added dropwise to a solution of 1 equiv of benzyl methanethiolsulfonate in excess carbon disulfide, benzyl morpholinecarbotrithioate (VII) was obtained in 70% yield (eq 3).



(3)

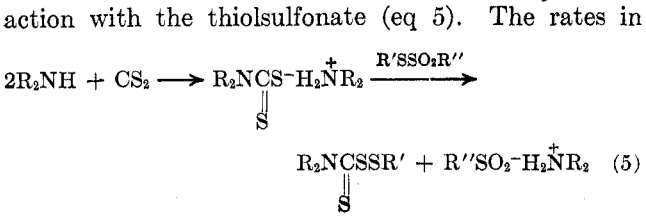
VII

In this case the aminecarbotrithioate can be formed by way of two different reaction paths. One route consists in the formation of the sulfenamide intermediate followed by its reaction with carbon disulfide (eq 4). The alternative route would involve initial



(4)

reaction of the amine with carbon disulfide to give the dithiocarbamate intermediate followed by its reaction with the thiolsulfonate (eq 5). The rates in



(5)

both initial steps are relatively fast in the absence of the third reactant; but in this case eq 5 would likely be the more important, considering the large concentration of carbon disulfide, although no rate studies have been made to establish this.

Experimental Section[11]

Methyl 1-Piperidinecarbotrithioate (IIIa).—Carbon disulfide (2 ml) was added to a solution of 2.14 g (0.0163 mol) of 1-(methylthio)piperidine[12] in 25 ml of ethyl ether, and the mixture was allowed to stand at room temperature for 5 min. The ether and excess carbon disulfide were removed by evaporation on the steam bath, and the residual oil was crystallized from petroleum ether (bp 60–70°) to give 2.97 g (88%) of the product as very pale yellow platelets: mp 47–48°; nmr ($CDCl_3$) δ 1.73 (br s, 6, $\overline{NCH_2CH_2CH_2CH_2CH_2}$), 2.50 (s, 3, CH_3), and 4.14 ppm (br s, 4, CH_2NCH_2).

Anal. Calcd for $C_7H_{13}NS_3$: C, 40.54; H, 6.32; N, 6.76. Found: C, 40.75; H, 6.08; N, 6.73.

Methyl 4-Morpholinecarbotrithioate (IIIb).—A solution of 15.2 g (0.114 mol) of 4-(methylthio)morpholine[12] in 50 ml of carbon disulfide was heated under reflux for 45 min and then allowed to stand at room temperature for 48 hr. The excess carbon disulfide was removed by evaporation *in vacuo*, leaving 23.4 g (98%) of pale yellow solid, mp 77–78.5°. Recrystallization from petroleum ether gave the pure substance as pale yellow crystals: mp 77.5–78.5°; nmr ($CDCl_3$) δ 2.48 (s, 3, CH_3), 3.80 (m, 4, CH_2OCH_2), and 4.17 ppm (m, 4, CH_2NCH_2).

Anal. Calcd for $C_6H_{11}NOS_3$: C, 34.42; H, 5.30; N, 6.69; S, 45.94. Found: C, 34.61; H, 5.56; N, 6.70; S, 46.23.

Allyl 4-Morpholinecarbotrithioate (IIIc).—4-(Allylthio)morpholine[12] (47.0 g, 0.295 mol) was added slowly to 250 ml of carbon disulfide with ice-bath cooling, the reaction being somewhat exothermic. After the addition was complete, the reaction mixture was heated under reflux for 4 hr. The excess carbon disulfide was removed by evaporation, and the remaining oil was crystallized from a mixture of petroleum ether and benzene, giving 57.5 g (83%) of the pure substance as pale yellow crystals, mp 28–29°.

Anal. Calcd for $C_8H_{13}NOS_3$: C, 40.82; H, 5.57; N, 5.95. Found: C, 40.75; H, 5.88; N, 6.16.

Methyl Diethylaminecarbotrithioate (IIId).—The procedure was the same as that for the preparation of IIIc, using 9.6 g (0.080 mol) of N-(methylthio)diethylamine[13] and 75 ml of carbon disulfide. The crude product (11.8 g of amber oil, 76%) was crystallized at low temperature from a mixture of petroleum ether and diethyl ether to give the pure substance as a yellow solid melting below room temperature: $n^{25}D$ 1.6118; nmr ($CDCl_3$) δ 1.32 (t, 6, J = 7 Hz, CH_2CH_3), 2.50 (s, 3, SCH_3), and 3.89 ppm (m, 4, CH_2CH_3).

Anal. Calcd for $C_6H_{13}NS_3$: C, 36.89; H, 6.71; S, 49.23. Found: C, 37.5; H, 6.91; S, 49.57.

Phenyl 4-Morpholinecarbotrithioate (IIIe).—A solution of 11.0 g (0.0564 mol) of 4-(phenylthio)morpholine[14] in 100 ml of carbon disulfide was heated in a sealed tube at 75° for 4 hr. The reaction mixture was cooled and excess carbon disulfide was removed by evaporation *in vacuo*, leaving a light yellow oil which crystallized when cooled below 0°. Two recrystallizations from methanol gave the pure substance as 5.5 g (36%) of pale yellow crystals: mp 59.5–61°; nmr ($CDCl_3$) δ 3.77 (m, 4, CH_2OCH_2), 4.19 (m, 4, CH_2NCH_2), 7.26 (m, 3, 3,4,5-phenyl protons), and 7.56 ppm (m, 2, 2,6-phenyl protons).

Anal. Calcd for $C_{11}H_{13}NOS_3$: C, 48.68; H, 4.83; N, 5.16. Found: C, 48.8; H, 4.86; N, 4.95.

4-(2-Nitrophenylthio)morpholine[12] failed to react with carbon disulfide in a sealed tube at 100° over a period of 5 hr.

Phenyl 4-Morpholinecarbotrithioate (IIIe). Sulfenyl Chloride Method.—Sodium 4-morpholinecarbodithioate (12.5 g, 0.0675 mol) was slowly added to a solution of benzenesulfenyl chloride (prepared by the chlorination of 7.8 g of benzenethiol in carbon tetrachloride) in 250 ml of diethyl ether, keeping the temperature below 15° by means of an ice bath. After the addition was complete, the ice bath was removed and the mixture was stirred until it reached room temperature. More ether (200 ml) was then added, and the sodium chloride by-product was removed by filtration. The ether was removed from the filtrate *in vacuo*, leaving 14.0 g (77%) of pale yellow oil which was crystallized from methanol to give the pure substance as pale yellow crystals, mp 58–60°. The infrared spectrum of this substance was identical with that of the product in the foregoing experiment.

Anal. Calcd for $C_{11}H_{13}NOS_3$: C, 48.68; H, 4.83; N, 5.16. Found: C, 48.7; H, 5.01; N, 5.36.

1-[2-(Methylthio)ethylthio]piperidine.—Piperidine (36.5 g,

(11) All melting points are uncorrected. Nmr spectra were recorded on a Varian 60 spectrometer.

(12) J. E. Dunbar and J. H. Rogers, *J. Org. Chem.*, **31**, 2842 (1966).

(13) H. J. Backer, *Rec. Trav. Chim. Pays-Bas*, **70**, 254 (1951).

(14) R. C. Kinstler, U. S. Patent 2,840,556 (1958).

0.429 mol) was added to a solution of 20.0 g (0.107 mol) of 2-(methylthio)ethyl methanethiolsulfonate[12] in 200 ml of absolute ethyl ether with stirring. The reaction mixture was allowed to stand at room temperature for 15 hr and was thereafter filtered to remove the by-product piperidinium methanesulfinate. The ether was removed from the filtrate by evaporation *in vacuo*, leaving a residue of crude product and excess piperidine. The residue was stirred with water and extracted with methylene chloride. The extract was dried over anhydrous magnesium sulfate; and, after removal of the solvent by evaporation, the residue was fractionated, giving the pure product as 16.5 g (80%) of colorless liquid: bp 76–82° (0.6 mm); $n^{25}D$ 1.5345.

Anal. Calcd for $C_8H_{17}NS_2$: C, 50.21; H, 8.96; N, 7.32. Found: C, 50.4; H, 8.77; N, 7.54.

2-(Methylthio)ethyl 1-Piperidinecarbotrithioate (IIIf).—The procedure was the same as that used for the preparation of IIIc, using 12.7 g (0.0665 mol) of 1-[2-(methylthio)ethylthio]piperidine and 100 ml of carbon disulfide. The crude product was obtained as 13.7 g (77%) of yellow crystals, mp 42–43.5°. Recrystallization from 2-propanol gave the pure substance as colorless crystals: mp 44°; nmr ($CDCl_3$) δ 1.73 (br s, 6, $NCH_2CH_2CH_2CH_2CH_2$), 2.13 (s, 3, SCH_3), 2.94 (m, 4, SCH_2CH_2S), and 4.14 ppm (s, 4, CH_2NCH_2).

Anal. Calcd for $C_9H_{17}NS_4$: C, 40.41; H, 6.41; N, 5.24. Found: C, 40.45; H, 6.37; N, 5.23.

N-[2-(Methylthio)ethylthio]dimethylamine.—An excess of anhydrous dimethylamine gas was passed through a solution of 37.2 g (0.200 mol) of 2-(methylthio)ethyl methanethiolsulfonate[12] in 300 ml of absolute ethyl ether at room temperature with stirring over a period of 30 min. The precipitated by-product, dimethylammonium methanesulfinate, was removed by filtration, and the ether filtrate was washed with water and dried over anhydrous magnesium sulfate. The ether was removed by evaporation *in vacuo*, and the residual oil was fractionated to give the pure product as 24.8 g (82%) of colorless oil: bp 41° (0.6 mm); $n^{25}D$ 1.5148.

Anal. Calcd for $C_5H_{13}NS_2$: C, 39.69; H, 8.66; N, 9.26. Found: C, 39.8; H, 8.48; N, 9.00.

2-(Methylthio)ethyl Dimethylaminecarbotrithioate (IIIg).—The procedure was the same as that for IIIc, using 15.1 g (0.100 mol) of N-[2-(methylthio)ethylthio]dimethylamine and 100 ml of carbon disulfide. The crystalline crude product was recrystallized from methanol to give 20.2 g (89%) of the pure substance as colorless needles: mp 35.5–36.5°; nmr ($CDCl_3$) δ 2.13 (s, 3, SCH_3), 2.93 (m, 4, CH_2CH_2), and 3.53 ppm [s, 6, $N(CH_3)_2$].

Anal. Calcd for $C_6H_{13}NS_4$: C, 31.69; H, 5.76; N, 6.16. Found: C, 31.7; H, 6.00; N, 5.93.

Registry No.—Carbon disulfide, 75-150; 1-[2-(methylthio)ethylthio]piperidine, 22158-14-1; N-[2-(methylthio)ethylthio]dimethylamine, 22158-16-3; IIIa, 22158-09-4; IIIb, 22158-10-7; IIIc, 22158-11-8; IIId, 22158-12-9; IIIe, 22158-13-0; IIIf, 22158,15-2; IIIg, 22158-17-4.

Acknowledgment.—The authors wish to express their appreciation for the technical assistance of Mrs. Betty H. Tarnowski.

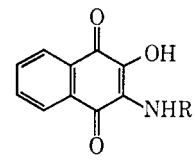
Synthesis of 2-Alkylamino-3-hydroxy-1,4-naphthoquinones[1]

EUGENE G. PODREBARAC AND C. C. CHENG

Midwest Research Institute, Kansas City, Missouri 64110

Received May 13, 1969

Although numerous 1,4-naphthoquinones have been synthesized and investigated, 2-alkylamino-3-hydroxy-1,4-naphthoquinones (I) have not been reported in the literature. The importance of compounds of type I can be exemplified by the interesting biological activities associated with many 3-alkyl- and 3-alkenyl-substituted derivatives of lawsone (2-hydroxy-1,4-naphthoquinone)[2] and arylamino-1,4-naphthoquinones.[3] Further need for a study of compounds of this type is illustrated by the observation that the *ortho*-amino quinoid unit is present in many antitumor antibiotics such as actinomycins, mitomycin C, porfiromycin, and streptonigrin.[4]



I

In connection with a study of the Mannich reaction of lawsone, the synthesis of 2-alkylamino-3-hydroxy-1,4-naphthoquinones was attempted by Dalgliesh[5] some 20 years ago. The methods involved treatment of lawsone with an amine, the reaction of amines with 2,3-dichloro-1,4-naphthoquinone followed by hydrolysis, and the rearrangement of aminonaphthoquinone oxide. None of these procedures proved to be successful. Certain 2-arylamino-3-hydroxy-1,4-naphthoquinones have been obtained by treatment of naphthoquinone oxide[2a] with aromatic amines[6] or by heating a mixture of aniline and 2-chloro-3-hydroxy-1,4-naphthoquinone.[7] When these reaction conditions were used in this laboratory for the preparation of the corresponding aliphatic amino compounds, the desired product could not be isolated. In addition, the product could not be prepared by the catalytic reduction of a mixture of the nitro compound II and the appropriate aldehyde.[8]

Compounds of type I were successfully prepared by the following general method. 2-Hydroxy-3-nitro-1,4-naphthoquinone[9] (II), prepared by the treatment of 2,3-dichloro-1,4-naphthoquinone with sodium nitrite,[10] was hydrogenated in glacial acetic acid in the presence of Adam's catalyst. To the intermediate 2-amino-1,3,4-trihydroxynaphthalene (III), *in situ*, was added the appropriate acyl chloride. The resulting reaction mixture was oxidized in air to yield the 2-acylamido-3-hydroxy-1,4-naphthoquinone (IV), which was readily reduced to the desired compound I with lithium aluminum hydride.

(1) This investigation was supported by the Cancer Chemotherapy National Service Center, National Cancer Institute, of the National Institutes of Health, U. S. Public Health Service, Contract No. PH-43-65-94.

(2) See, *e.g.*, (a) L. F. Fieser, *et al.*, *J. Amer. Chem. Soc.*, **70**, 3151, 3156, 3165, 3174, 3212, 3215, 3228, 3232, 3237 (1948); (b) M. T. Leffler and R. J. Hathaway, *ibid.*, **70**, 3222 (1948); (c) H. E. Zaugg, R. T. Rapala, and M. T. Leffler, *ibid.*, **70**, 3224 (1948); (d) P. Truitt, F. Mahon, O. Platas, R. L. Hall, and T. E. Eris, *J. Org. Chem.*, **25**, 962 (1960); (e) D. A. Berberian and R. G. Slighter, Jr., *J. Parasitol.*, **54**, 999 (1968); (f) D. A. Berberian, R. G. Slighter, Jr., and H. W. Freele, *ibid.*, **54**, 1181 (1968); (g) K. V. Rao, T. J. McBride, and J. J. Oleson, *Cancer Res.*, **28**, 1952 (1968).

(3) N. P. Buu-Hoï, *Bull. Soc. Chim. Fr.*, **11**, 578 (1944).

(4) K. V. Rao, K. Biemann, and R. B. Woodward, *J. Amer. Chem. Soc.*, **85**, 2532 (1963).

(5) C. E. Dalgliesh, *ibid.*, **71**, 1697 (1949).

(6) I. F. Vladimirtsev, *Zh. Obshch. Khim*, **30**, 2670 (1960).

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(8) R. T. Major, *ibid.*, **53**, 1901 (1931).

(9) T. Diehl and V. Merz, *Ber.*, **11**, 1314 (1878).

(10) (a) F. Kehrmann and O. Weichardt, *J. Prakt. Chem.*, [2] **40**, 179 (1889); (b) A. Inoue, N. Kuroki, and K. Konishi, *Yûki Gôsei Kagaku Kyôkai Shi*, **17**, 714 (1959); *Chem. Abstr.*, **54**, 4504e (1960).