agent.[19] Nitrogen was bubbled through the reaction mixture. After 1 hr. at room temperature, the chromate color had disappeared and 0.2 ml. more of standard chromate reagent was added. After 1 hr. the excess chromate was decomposed with aqueous sodium metabisulfite. The reaction mixture was diluted with water and was extracted with methylene chloride. The extracts were washed with dilute potassium hydroxide and with water and were dried over magnesium sulfate. Removal of the methylene chloride and drying afforded 0.196 g. of a foam. Crystallization from methanol yielded 0.120 g. (61.3%) of V, m.p. 238–240°, lit.[3] m.p. 243–246°. The infrared spectrum of V was identical with the spectrum of an authentic sample.[3]

3α,12α-Diacetoxy-5β,16-pregnen-20-one (I).—3α,12α-Diacetoxy-5β-Δ^{16}-pregnen-20-one was prepared according to the method reported by Adams, Patel, Petrow, and Stuart-Webb.[4] From 25 g. (0.0598 mole) of 3α,12α-diacetoxy-5β-pregnan-20-one, 4.1 g. (16.5%) of I was obtained, m.p. 198–199°, lit.[4] m.p. 190–192°.

3α,12α-Diacetoxy-2′-methyl-5β,16β,17α-(16,17-butanoandrost-2′-en)-4′-one (IIIb).—This reaction was conducted in the same manner as described for the preparation of IVa using 4.0 g. (9.6 mmoles) of 3α,12α-diacetoxy-5β,16-pregnen-20-one, 60 ml. of acetone, 38 ml. of water, and 6 g. of potassium hydroxide. The crude product was acetylated with acetic anhydride–pyridine at room temperature overnight. The usual work-up afforded 4.08 g. of a foam which was dissolved in benzene and chromatographed on 200 g. of Florisil. A fraction weighing 1.32 g. was eluted with benzene–2% methanol. Recrystallization from cyclohexane yielded 0.98 g. (22.4%) of IIIb, m.p. 213.5–214.5°. The analytical sample was recrystallized from isopropyl alcohol, m.p. 214–215°, $[\alpha]^{24}\text{D}$ +122°, $\lambda_{\max}^{CH_3OH}$ 235 mμ (ϵ 12,550); the infrared spectrum (methylene chloride) showed the presence of a strong band at 1720 (acetate carbonyl), conjugated ketone carbonyl peak at 1668, and a double bond peak at 1612 cm.$^{-1}$.

Anal. Calcd. for $C_{28}H_{40}O_5$: C, 73.65; H, 8.83. Found: C, 73.35; H, 8.75.

3β,12β-Diacetoxy-2′-methyl-5α,16β,17α-(16,17-butanoandrostan)-4′-one (VI).—To a solution of 0.525 g. (0.00157 mole) of the diacetate (IVb) in 50 ml. of methanol was added 0.25 g. of 5% palladium-on-carbon catalyst. The mixture was hydrogenated for 1 hr. at room temperature with stirring. The catalyst was filtered off, and the filtrate was evaporated to dryness *in vacuo* yielding 0.50 g. of colorless glass. Crystallization from petroleum ether afforded 0.30 g. of crystals that had m.p. 148–149.5°. The analytical sample crystallized from petroleum ether, m.p. 150–151°, $[\alpha]^{24}\text{D}$ +37°; the infrared spectrum (carbon disulfide) shows a peak at 1730–1735 (3β,12β-acetate carbonyls) and 1719 cm.$^{-1}$ (4′ ketone).

Anal. Calcd. for $C_{28}H_{42}O_5$: C, 73.32; H, 9.23. Found: C, 73.02; H, 9.28.

3β,12β-Diacetoxy-2′-methyl-5α,16β,17α-(16,17-butanoandrostan)-4′α-ol (VIIc).—To 0.25 g. of VI (0.005 mole) in 10 ml. of dry tetrahydrofuran was added 1.0 g. of lithium aluminum tri-*t*-butoxy hydride. The solution was allowed to stand overnight at room temperature. Aqueous acetic acid was added and the tetrahydrofuran removed *in vacuo* at room temperature. The residual suspension was extracted with ether and the extracts were washed with bicarbonate solution until neutral. After drying, the extracts were evaporated to dryness yielding 0.24 g. of a glass. Preparative thin layer chromatography on silica gel G (1:1:1 benzene–ethyl acetate–chloroform eluent) afforded 0.190 g. of colorless glass which was shown to be pure by analytical thin layer chromatography using three solvent systems: (a) 1:1:1 benzene–ethyl acetate–chloroform, R_f 0.69; (b) 3% isopropyl alcohol in benzene, R_f 0.32; (c) 15% acetone in petroleum ether, R_f 0.43. This material could not be obtained in crystalline form. An analytical sample was prepared by dissolving the glass in a small volume of benzene, freeze-drying, and drying the residual foam *in vacuo* over refluxing ethanol in an Abderhalden dryer. The infrared spectrum shows a strong hydroxyl band at 3575, a broad carbonyl band at 1730–1750, and C–O stretching bands at 1240 and 1220 cm.$^{-1}$; $[\alpha]^{24}\text{D}$ −70°.

Anal. Calcd. for $C_{28}H_{44}O_5$: C, 73.00; H, 9.63. Found: C, 73.07; H, 9.74.

2′-Methyl-5α,16β,17α-(16,17-butanoandrostane)-3β,12β,4′α-triol (VIIa).—A solution of the monohydroxy diacetate (VIIc, 0.140 g.) in 10 ml. of 10% methanolic potassium hydroxide was heated on a steam bath for 1 hr. After removal of the methanol *in vacuo*, water was added, and the resulting suspension was extracted with ether. On drying and evaporation to dryness, 0.126 g. of crystalline solid was obtained. The infrared spectrum shows no carbonyl band.

3β,4α-Diacetoxy-2′-methyl-5α,16β,17α-(16,17-butanoandrostan)-12β-ol.—Triol VIIa (0.1 g.) was dissolved in 2 ml. of acetic anhydride and 2 ml. of pyridine and allowed to stand at 25° overnight. The liquid was removed *in vacuo* yielding a mixture of crystals and glass. Trituration with methanol afforded 0.078 g. of crystals, m.p. 203–206°. The infrared spectrum was identical with that of a compound previously prepared.[3,15] The melting point of this compound was 205–207°. A mixture of this compound and an authentic sample of VIIb[3] melted at 203–207°.

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[19] A solution of 26.72 g. of chromium trioxide in 23 ml. of concentrated sulfuric acid diluted with water to a volume of 100 ml. was used.

A Tautomeric Nitrile–Thiol Iminothiolactone System[1]

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Department of Chemistry, Washington State University, Pullman, Washington

Received August 8, 1963

An interesting type of ring-chain tautomerism has been studied. When Ia,b was reduced with sodium borohydride–aluminum chloride (3:1), its tautomeric character became apparent in that products corresponding to both the chain form, (1-aminomethyl-2-naphthyl)methanethiol (II, 17%), and ring form, 1,3-dihydronaphtho[1,2-*c*]thiophene (III, 48%), resulted. It was found that when the proportion of sodium borohydride–aluminum chloride was increased from 3:1 to 4:1, II was obtained as the sole product (51%). The structure of I in the solid state and in chloroform solution appears to be that of naphtho[1,2-*c*]thiophen-1(3*H*)-imine (Ib) as confirmed by infrared and n.m.r. spectra. The chemical properties of I under neutral and acidic reaction conditions also substantiate this structure (Ib). In agreement with the conditions of reduction, in basic media it is possible to demonstrate the chain tautomeric structure (Ia) by sulfide and disulfide formation.

Reduction of the substance Ia,b with sodium borohydride–aluminum chloride (3:1) resulted in a demonstration of its tautomeric character by the formation of (1-aminomethyl-2-naphthyl)methanethiol (II), and 1,3-dihydronaphtho[1,2-*c*]thiophene (III). The structure of II was confirmed by conversion to the amino disulfide, which subsequently was acetylated to a diacetyl compound. Structure III, a new sulfur heterocyclic system, was established simply by Raney nickel desulfurization to 1,2-dimethylnaphthalene. The hydrogenolysis by sodium borohydride of the imino group of Ib to form III may occur by the mechanism pro-

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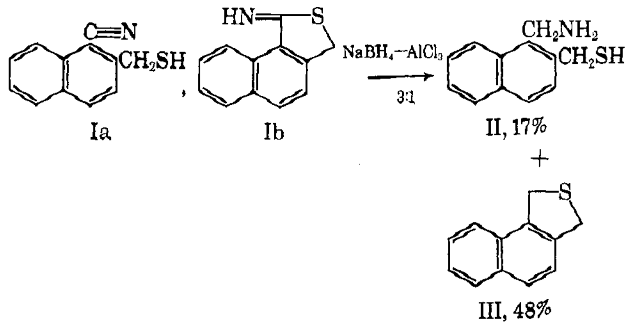
[1] Previously reported as a "Communication to the Editor," G. W. Stacy, A. J. Papa, and S. C. Ray, *J. Org. Chem.*, **26**, 4779 (1961); also presented in part before the Division of Organic Chemistry at the 140th National Meeting of the American Chemical Society, Chicago, Ill., September, 1961.

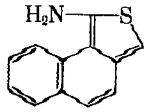
[2] In part abstracted from a thesis submitted by A. J. Papa in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Washington State University, January, 1961.



posed by Gaylord[3] for the hydrogenolysis of amides with lithium aluminum hydride.

Ring-chain tautomerism of *o*-cyanobenzyl mercaptans was observed by Day and Gabriel in 1890.[4] In the present work several new lines of evidence for this phenomenon have been developed for the related naphthalene derivative (Ia,b).

Actually, it is also necessary to consider a second cyclic tautomeric structure which involves the amino form Ic. Intuitively, one would favor this form less enthusiastically because of the quinoidal structure of higher energy; however, Boulton and Katritzky[5] have shown that various aminooxazoles exist predominately in the amino form. Also Howell, Quinones, and Hardy[6] demonstrated a similar situation for various 2-amino-4-oxazolidinones, while Gronowitz and Hoffman[7] have found that 2- and 3-aminothiophene exist in the amino rather than imino form.



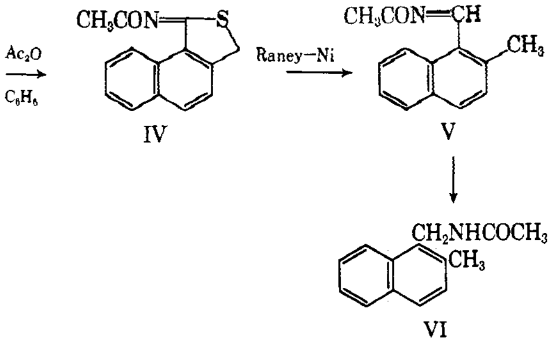
Ic

As with Boulton and Katritzky,[5] it appeared that here again a logical choice of structures could be accomplished by the use of n.m.r. and infrared spectra. Spectra of I in 10% solutions in chloroform and dioxane and a 5% solution of carbon tetrachloride were all found to have only one band at 3280 cm.$^{-1}$, which corresponded to the nitrogen–hydrogen stretching frequency of an imino group and verified structure Ib.[8] In addition, this material did not contain a band at 2500 cm.$^{-1}$ corresponding to the sulfur–hydrogen stretching frequency. On the other hand, 4-mercaptomethyl-1-naphthonitrile, 2-[(benzylthio)methyl]-1-naphthonitrile (XI), and 2-bromomethyl-1-naphthonitrile (XIV) showed the expected absorption bands.

To differentiate the possibilities of Ib *vs.* Ic, a sample was partially deuterated and an absorption spectrum of the resulting substance was determined. If a primary amino group were involved, then three new absorption bands in the region of 2600–2400 cm.$^{-1}$ would be anticipated.[5,9] On the other hand, if an imino group were primarily concerned, only one new stretching band would be observed. The infrared spectrum of the deuterated sample in dioxane contained only one new band at 2420 cm.$^{-1}$ in the nitrogen–deuterium stretching region, while the band at 3280 cm.$^{-1}$ was greatly decreased in intensity. Thus this constitutes strong evidence that Ib is the predominating structure.

These conclusions are confirmed still further by the proton magnetic resonance spectrum at 60 Mc. The sample was run as a deuteriochloroform solution containing a small amount of tetramethylsilane as an internal reference. The spectrum showed three areas of resonance at δ = 4.3, 7.1–7.9, and 9.7–9.8 with an area ratio of 2:5:2. Again it was the imino structure (Ib) which is in complete agreement with the evidence. The signal at δ = 4.3 representing two protons could be assigned to the methylene group adjacent to the sulfur atom. In tetrahydrothiophene, the corresponding protons resonate at δ = 2.3,[10] and, in this case, they are adjacent to an aromatic system, are more acidic, and thus are at lower field.[11] The protons at positions 4–8 can be considered normal naphthalenic protons giving rise to the complicated signals at δ = 7.1–7.9. Naphthalene itself gives rise to proton absorption at δ = 7.5–7.7.[12] The broad peak at δ = 9.7 is due to the imino proton, and the multiplet at δ = 9.8 can be assigned to the α-proton of the naphthalene ring. This multiplicity is due to spin-coupling of the α-proton with β- and γ-protons. The peaks due to the α-proton have shifted out of the normal aromatic region to lower field, possibly because of a spatial effect of the iminothiophene group.

In acidic or neutral media, chemical evidence also reflects structure Ib. I behaves like an imine in that it readily forms a hydrochloride and can be acetylated. Conclusive evidence for the structure of the acetyl derivative (IV) was obtained by desulfurization with Raney nickel to N-[(2-methyl-1-naphthyl)methylene]-acetamide (V) which then was reduced with dimethylamine–borane to N-[(2-methyl-1-naphthyl)methyl]-acetamide (VI).



The structure of VI was confirmed by its alternate formation through a sodium borohydride–aluminum chloride reduction of 2-methyl-1-naphthonitrile and subsequent acetylation of the resulting amine with acetic anhydride. The identity of these products was indicated by comparison of their infrared spectra and by mixture melting point determination. Compound

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(3) N. G. Gaylord, *Experientia*, **10**, 166 (1954).

(4) A. W. Day and S. Gabriel, *Ber.*, **23**, 2478 (1890).

(5) A. J. Boulton and A. R. Katritzky, *Tetrahedron*, **12**, 51 (1961).

(6) C. F. Howell, N. Q. Quinones, and R. A. Hardy, *J. Org. Chem.*, **27**, 1686 (1962).

(7) S. Gronowitz and R. A. Hoffman, *Arkiv Kemi*, **16**, 499 (1960).

(8) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 263.

(9) H. M. Randall, N. Fuson, R. G. Fowler, and J. R. Dangl, "Infrared Determination of Organic Structures," D. Van Nostrand Co. Inc., New York, N. Y., 1949, p. 43.

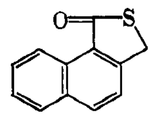
(10) H. S. Gutowsky, R. L. Rutledge, M. Tamres, and S. Searles, *J. Am. Chem. Soc.*, **76**, 4242 (1954).

(11) L. H. Meyer and H. S. Gutowsky, *J. Phys. Chem.*, **57**, 481 (1953).

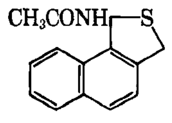
(12) H. J. Bernstein, W. G. Schneider, and J. A. Pople, *J. Chem. Phys.*, **26**, 957 (1957).

V also gives a positive reaction with bromine and potassium permanganate, tests which are characteristic for benzylidene amides of which a limited number have been mentioned in the literature.[13]

Substance I also underwent a facile acidic hydrolysis to form the expected thiolactone, naphtho[1,2-*c*]thiophen-1(3*H*)-one (VII). It is surprising to note that simple thiolactones are rare; a few examples have been cited by Reid.[14]



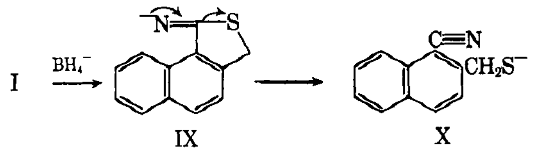
VII



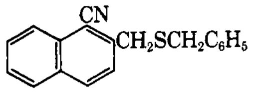
VIII

It was of interest to obtain the (1-aminomethyl-2-naphthyl)methanethiol (II) in good yield as a prospective antiradiation agent. Therefore, additional methods of reducing I were investigated. Since Brown and Subba Rao[15] had reported that nitriles show unusual reactivity toward diborane to give primary amines, it was thought that this might be a particularly suitable agent for the reduction of I. However, the objective was not realized, as a yield of only 11% of II was obtained. Dimethylamine–borane was investigated as a reducing agent, and, in this instance, the sulfur heterocycle (III) was obtained as the exclusive product in 59% yield. Reduction of the acetyl derivative (IV) with dimethylamine–borane led to a quantitative yield of 1,3-dihydro-1-acetamidonaphtho[1,2-*c*]thiophene (VIII).

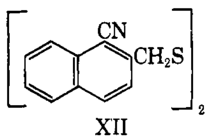
Re-examination of the circumstances surrounding the sodium borohydride–aluminum chloride reduction of I led to the speculation that possibly an increase in the basicity of the medium by adding more sodium borohydride to the reaction mixture might favor the formation of II. An increase in the concentration of the anion (X) would lead to an increased amount of II. Treatment of I with a 4:1 mixture of sodium borohydride–aluminum chloride led to II as the exclusive product in a yield of 51%. The fact that I behaves as the chain tautomer Ia under alkaline conditions was further demonstrated by the formation of sulfides. When I was treated with benzyl chloride in ethanolic sodium hydroxide solution, the corresponding sulfide derivative (XI) was obtained in excellent yield. In like manner, 2,4-dinitrochlorobenzene also formed a sulfide. The infrared spectra of these compounds showed strong absorption bands at 2220 cm.$^{-1}$ for the nitrile group, indicating that reaction had taken place at the sulfur atom rather than at the nitrogen (corresponding to Ib). The sulfide (XI) also was formed by reaction of 2-bromomethyl-1-naphthonitrile with α-toluenethiol in ethanolic sodium hydroxide. An attempt was made to debenzylate this compound with simultaneous reduction of the nitrile group by treatment with sodium in liquid ammonia, but only 1-aminomethyl-2-methylnaphthalene resulted. Compound I also formed disulfide XII when treated with hydrogen peroxide under alkaline conditions. Thus, a clear demonstration of the dual reactivity of I as both ring and chain tautomers has been accomplished.



IX X

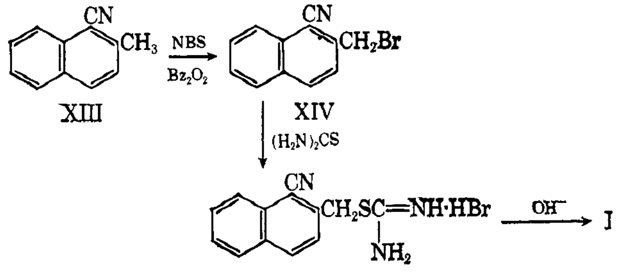


XI



XII

At this point, it is desirable to consider the synthetic procedures which led to II and its 1,4 isomer (XVII). Bromination of crude 2-methylnaphthalene in carbon tetrachloride solution gave 1-bromo-2-methylnaphthalene in a yield of 69%.[16] Conversion of this substance to 2-methyl-1-naphthonitrile (XIII) was readily accomplished by reaction with cuprous cyanide and pyridine, according to the procedure employed by Fuson, McKeever, and Behr.[17] However, purification of XIII was best accomplished with little loss by distillation under reduced pressure rather than recrystallization. Side-chain bromination of XIII with N-bromosuccinimide afforded XIV in excellent yield.[18] After numerous attempts at recrystallization from various solvents, it was discovered that carbon tetrachloride is quite specific for recrystallization of XIV with little loss in yield.



XIII XIV XV

The alkaline hydrolysis of isothiuronium salts is a well-known method for the introduction of a thiol group.[19] It appeared that the nitrile group could be preserved intact since the hydrolysis of aromatic nitriles is subject to marked steric inhibition by *ortho* substituents.[20] These objectives were realized; however, it is quite necessary to isolate the isothiuronium salt (XV) and purify it before proceeding with the hydrolysis with 5% sodium hydroxide solution.

In the analogous isomeric 1,4-series of naphthalene derivatives, the 1-bromo-4-methylnaphthalene was obtained in 29% yield by the method of Fieser, *et al.*,[21] employing potassium 1-methylnaphthalene-4-sulfonate. The intermediate 4-methyl-1-naphthonitrile was pre-

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(13) R. K. Mehra and K. C. Pandya, *Proc. Indian Acad. Sci.*, **10A**, 279, 285 (1939).

(14) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. I, Chemical Publishing Co., Inc., New York, N. Y., 1958, pp. 453, 454.

(15) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **82**, 681 (1960).

(16) (a) D. M. Hall and R. K. Mitchell, *J. Chem. Soc.*, 1375 (1951); (b) R. Adams and L. O. Binder, *J. Am. Chem. Soc.*, **63**, 2773 (1941).

(17) R. C. Fuson, C. H. McKeever, and L. C. Behr, *ibid.*, **63**, 2648 (1941).

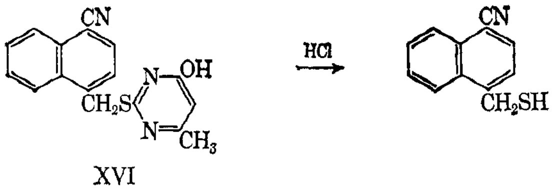
(18) M. S. Newman and A. I. Kosak, *J. Org. Chem.*, **14**, 375 (1949).

(19) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. I, Chemical Publishing Co., Inc., New York, N. Y., 1958, pp. 32–34.

(20) W. J. Hickinbottom, "Reactions of Organic Compounds," 3rd Ed., Longmans Green and Co., Ltd., New York, N. Y., 1957, p. 382.

(21) L. F. Fieser and D. M. Bowen, *J. Am. Chem. Soc.*, **62**, 2103 (1940).

pared according to the cuprous cyanide method.[17,22] Side-chain bromination of 4-methyl-1-naphthonitrile was accomplished in a yield of 71%. The 4-bromomethyl-1-naphthonitrile was converted to the corresponding thiol both by way of the intermediate isothiuronium salt and by a method described by Barkenbus,[23] which involves forming a readily hydrolyzable sulfide (XVI) with 6-methyl-2-thiouracil. The hydrolysis of the sulfide is accomplished by concentrated



XVI

hydrochloric acid, and again it appears that the nitrile group is not easily affected by strong acidic or alkaline conditions. The final product, (1-aminomethyl-4-naphthyl)methanethiol (XVII), was obtained in a 52% yield by reduction of the nitrile group with sodium borohydride–aluminum chloride.

Biological Evaluation.—The two aminomethylnaphthylmethanethiols (II and XVII), as well as the isothiuronium salts (XV and its isomer), were tested for possible antiradiation activity, but none of these compounds showed a substantial level.

Experimental[24]

Sodium Borohydride–Aluminum Chloride Reduction of Naphtho[1,2-*c*]thiophen-1(3*H*)-imine (Ib).—To 2.00 g. (0.01 mole) of I was added a solution of 280 mg. (7.5 mmoles) of sodium borohydride in 7.5 ml. of purified diglyme. A solution of 330 mg. (2.5 mmoles) of anhydrous aluminum chloride and 1.5 ml. of purified diglyme was added dropwise with stirring so that the temperature of the solution was maintained at 25°. After the addition was complete, the reaction mixture was stirred for 1 hr. at 25°, followed by heating on a steam bath for 15 min. The mixture was cooled and poured into a solution of 25 g. of crushed ice and 5 ml. of concentrated hydrochloric acid. After the mixture was stirred for 0.5 hr., 790 mg. (43%) of white flakes of III which separated was decanted along with the acidic solution from a tacky solid mass which remained. Recrystallization of the crude product from ethanol afforded pure 1,3-dihydronaphtho[1,2-*c*]thiophene (III); the yield was 640 mg. (34%), m.p. 111–112°.

Anal. Calcd. for $C_{12}H_{10}S$: C, 77.38; H, 5.41; S, 17.21. Found: C, 77.50; H, 5.23; S, 17.12.

The tacky solid was treated with 10 ml. of concentrated hydrochloric acid, filtered, and dried, yielding 700 mg. (29%). Washing with ether and crystallization from methanol–ether yielded 370 mg. (16%) of (**1-aminomethyl-2-naphthyl)methanethiol (II)** as a colorless hydrochloride, m.p. 219–220.5° dec.

Anal. Calcd. for $C_{12}H_{14}ClNS$: C, 60.11; H, 5.89; N, 5.84. Found: C, 59.91; H, 5.90; N, 5.87.

A later experiment gave yields of 48 and 17%, respectively, for the two products.

Desulfurization of 1,3-Dihydronaphtho[1,2-*c*]thiophene (III) with Raney Nickel.[25]—A solution of 1.90 g. (0.01 mole) of III in 150 ml. of absolute ethanol was heated under reflux with 10.0 g. of freshly prepared Raney nickel[26] for 3 hr. After the reaction mixture was allowed to stand overnight, the solution was filtered and then concentrated under reduced pressure. Distillation of the residue of 1,2-dimethylnaphthalene afforded 1.31 g. (84%) of a colorless oil, b.p. 125–126° (12 mm.). The picrate melted at 130–131° after two recrystallizations from methanol, lit.[27] m.p. 130–131°; the mixture melting point with the picrate of an authentic sample was 130–131°.

1-Aminomethyl-2-mercaptomethylnaphthalene (II).—To a solution of 6.00 g. (0.16 mole) of sodium borohydride in 90 ml. of purified diglyme was added 8.00 g. (0.04 mole) of I with stirring. While the temperature of the reaction was maintained between 80–90° by means of a steam bath, a freshly prepared solution of 5.20 g. (0.04 mole) of anhydrous aluminum chloride in 40 ml. of purified diglyme was introduced dropwise during a period of 15 min., and heating and stirring were continued for 2 hr. The cooled reaction mixture then was poured into 80 ml. of concentrated hydrochloric acid and 200 g. of crushed ice, evaporated to dryness under reduced pressure, and the residue was washed with water, dried, and then washed thoroughly with ether; the yield was 8.60 g. (90%). Crystallization from methanol–ether afforded 4.90 g. (51%) of white powder, m.p. 225–228° dec. Various samples of this compound, obtained by the same reaction, were found to melt over a range of 219–228° dec. However, the infrared spectrum was identical for each sample and, therefore, was used as the criterion of purity.

The infrared spectrum revealed bands that were assignable to -SH (2560 cm.$^{-1}$, w), -NH (3380 cm.$^{-1}$, m; 3150 cm.$^{-1}$, w), and a primary amine hydrochloride (2650 cm.$^{-1}$, m).

Bis([1-(aminomethyl)-2-naphthyl]methyl) Disulfide.—A solution of 1.20 g. (5.0 mmoles) of II in 20 ml. of glacial acetic acid was heated under reflux for 1 hr. with 1.20 g. (7.4 mmoles) of ferric chloride dissolved in 3 ml. of water. After chilling, the solid which separated from the reaction mixture was collected by filtration, washed with water, and dried, yielding 1.10 g. (92%). Recrystallization from methanol (Norit) afforded 850 mg. (71%) of colorless crystals, m.p. 277° dec.

Anal. Calcd. for $C_{24}H_{26}Cl_2N_2S_2$: C, 60.36; H, 5.49; N, 5.87; S, 13.43. Found: C, 60.18; H, 5.52; N, 5.81; S, 13.43.

Bis([1-(acetamidomethyl)-2-naphthyl]methyl) Disulfide.—To a suspension of 500 mg. (1.0 mmole) of the amino disulfide in 10 ml. of dry pyridine was added with stirring 230 mg. (2.2 mmoles) of acetic anhydride. The reaction mixture yielded 420 mg. (86%) of product, m.p. 243–244° dec. Recrystallization from glacial acetic acid afforded 370 mg. (76%) of white crystals, m.p. 244–245° dec.

Anal. Calcd. for $C_{28}H_{28}N_2O_2S_2$: C, 68.82; H, 5.78; N, 5.73; S, 13.12. Found: C, 68.63; H, 5.69; N, 5.67; S, 13.26.

Naphtho[1,2-*c*]thiophen-1(3*H*)-acetylimine (IV).—To a solution of 4.00 g. (0.02 mole) of I in 70 ml. of benzene was added 2.30 g. (0.022 mole) of acetic anhydride, along with one drop of concentrated sulfuric acid. The mixture was heated under reflux for 45 min. on a steam bath and then was cooled and filtered; the collected yellow crystals were washed with a small portion of cold benzene and dried, yielding 4.37 g. (92%), m.p. 187–188.5° dec. Recrystallization from methanol (Norit) afforded 3.58 g. (75%) of colorless needles, m.p. 189.5–191° dec.

Anal. Calcd. for $C_{14}H_{11}NOS$: C, 69.68; H, 4.60; N, 5.81; S, 13.29. Found: C, 69.90; H, 4.64; N, 5.75; S, 13.17.

N-[(2-Methyl-1-naphthyl)methylene]acetamide (V).—A solution of 2.40 g. (0.01 mole) of IV in 500 ml. of absolute ethanol was stirred overnight at room temperature with freshly prepared Raney nickel. The catalyst was removed by filtration, and the filtrate was evaporated to dryness under reduced pressure, yielding 1.80 g. (86%) of a white solid melting at 146–150°. Crystallization from acetone–water afforded 1.40 (67%) of colorless needles of V, melting at 163.5–164.5°.

Anal. Calcd. for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.47; H, 6.41; N, 6.58.

N-[(2-Methyl-1-naphthyl)methyl]acetamide (VI).—A solution of 1.10 g. (0.005 mole) of V and 0.59 g. (0.01 mole) of dimethylamine–borane[28] in 40 ml. of glacial acetic acid was stirred overnight at room temperature. The reaction mixture then was

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[22] H. G. Rule, *et al.*, *J. Chem. Soc.*, 1817 (1950).

[23] C. Barkenbus, E. B. Friedman, and R. K. Flege, *J. Am. Chem. Soc.*, **49**, 2549 (1927).

[24] The microanalytical work was performed by the Galbraith Laboratories, Knoxville, Tenn., and Weiler and Strauss Laboratories, Oxford, England. The absorption spectra were determined by means of a Beckman, Model IR-5, infrared spectrophotometer. The samples were in 10% chloroform solutions unless otherwise specified.

[25] The desulfurization procedure employed was similar to that described by Mozingo, *et al.*, for certain sulfides. R. Mozingo, D. E. Wolf, S. A. Harris, and K. Folkers, *J. Am. Chem. Soc.*, **65**, 1013 (1943).

[26] This was prepared from 30 g. of alloy, which was kept at 45–55° for 1 hr. after addition to the sodium hydroxide solution.

[27] M. C. Kloetzel, *J. Am. Chem. Soc.*, **62**, 1708 (1940).

[28] Dimethylamine-borane was obtained from the Callery Chemical Co., Pittsburgh 37, Pa.; J. H. Billman and J. W. McDowell, *J. Org. Chem.*, **26**, 1437 (1961).

heated on a steam bath for 1 hr., and most of the solvent was removed under reduced pressure. Pouring into water resulted in the separation of a solid which was collected by filtration, washed with water, and dried yielding 900 mg. (85%). Recrystallization from ethanol–water gave 750 mg. (71%) of VI, melting at 166.5–168°.

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.86; H, 7.07; N, 6.57. Found: C, 79.08; H, 7.10; N, 6.58.

The infrared absorption spectrum indicated bands assignable to NH stretching vibration (3350 cm.$^{-1}$, w), C=O stretching vibration (1665 cm.$^{-1}$, s), and amide band (1510 cm.$^{-1}$, s).

A mixture melting point determination and an infrared spectrum of the above compound showed it to be identical with that of a sample prepared from 1-aminomethyl-2-methylnaphthalene by acetylation with acetic anhydride.

1-Aminomethyl-2-methylnaphthalene.—To a solution of 1.50 g. (0.04 mole) of sodium borohydride and 8.40 g. (0.05 mole) of XIII in 40 ml. of purified diglyme was added a solution of 1.50 g. (0.011 mole) of anhydrous aluminum chloride in 5 ml. of purified diglyme with stirring over a period of 0.5 hr. The mixture was allowed to stir overnight and then for 2 hr. with heating on a steam bath. Evaporation of the reaction mixture to dryness under reduced pressure gave a white residue which was dissolved in boiling 30% sodium hydroxide solution. The pale yellow oil which separated from the cooled alkaline solution was extracted with four 50-ml. portions of ether and the combined ether extracts were dried over anhydrous sodium sulfate. Dry hydrogen chloride was passed through the ether solution, and the product was collected by filtration, yielding 5.70 g. (55%). Recrystallization from ethanol afforded 4.80 g. (45%) of white powder melting at 315° dec., lit.[29] m.p. 290°.

Anal. Calcd. for $C_{12}H_{14}ClN$: C, 69.39; H, 6.79; N, 6.74. Found: C, 69.52; H, 6.61; N, 6.82.

Naphtho[1,2-*c*]thiophen-1(3*H*)-one (VII).—A solution of 500 mg. (2.5 mmoles) of naphtho[1,2-*c*]thiophen-1(3*H*)-imine (I) in 20 ml. of 6 *N* hydrochloric acid was heated under reflux for 1.5 hr. The solid was collected by filtration, washed with water, and dried yielding 500 mg. (100%). Recrystallization from ethanol afforded 300 mg. (60%) of fine, white needles, m.p. 144.5–145°.

Anal. Calcd. for $C_{12}H_8OS$: C, 71.97; H, 4.03; S, 16.01. Found: C, 72.22; H, 4.04; S, 16.00.

The infrared absorption spectrum revealed a strong band attributed to a thiolactone at 1670 cm.$^{-1}$.

Dimethylamine–Borane Reduction of I.—A solution of 1.00 g. (5.0 mmoles) of I and 590 mg. (1.0 mmole) of dimethylamine-borane in 40 ml. of glacial acetic acid was stirred overnight at room temperature. The reaction mixture then was heated on a steam bath at 80–90° for 1 hr. and poured into 300 ml. of ice-water. The crude product which separated was collected by filtration, washed with water, and dried, yielding 550 mg. (59%). Recrystallization from ethanol (Norit) afforded 430 mg. (46%) of III, m.p. 110–111° (mixture melting point with the product obtained from the sodium borohydride–aluminum chloride reduction of I was 110–111°).

1,3-Dihydro-1-acetamidonaphtho[1,2-*c*]thiophene (VIII).—A solution of 1.20 g. (5.0 mmoles) of IV and 590 mg. (1.0 mmole) of dimethylamine–borane in 40 ml. of glacial acetic acid was stirred overnight at room temperature and then for 2 hr. at 80–90°. The cooled reaction mixture was poured into water, and the crude product which separated was collected, washed thoroughly with water, and dried, yielding 1.20 g. (100%) of yellow crystals of VIII, m.p. 209–211° dec. Recrystallization from ethanol (Norit) afforded 900 mg. (75%) of shining white needles, m.p. 217–219° dec.

Anal Calcd. for $C_{14}H_{13}NOS$: C, 69.11; H, 5.39; N, 5.76. Found: C, 69.27; H, 5.57; N, 5.83.

2-Bromomethyl-1-naphthonitrile (XIV).—A mixture of 16.7 g. (0.10 mole) of XIII, 16.9 g. (0.095 mole) of N-bromosuccinimide, and 0.50 g. of benzoyl peroxide in 100 ml. of carbon tetrachloride was heated under reflux for 3 hr. The warm reaction mixture was filtered after the addition of 100 ml. of carbon tetrachloride, and the residual succinimide, which had risen to the surface of the liquid, was removed by filtration and washed with 20 ml. of carbon tetrachloride; 9.23 g. (98%) of succinimide was obtained. After chilling, crystals from the filtrate were filtered off to give 16.0 g. (65%) of colorless needles, m.p. 97–100°. Concentration of the filtrate gave an additional 5.10 g.; the total yield was 21.1 g. (86%). When the product was recrystallized twice from carbon tetrachloride, 17.5 g. (71%) of purified material was obtained, m.p. 101–102.5°. The infrared spectrum showed a strong band at 2220 cm.$^{-1}$, which was assignable to C≡N.

Anal. Calcd. for $C_{12}H_8BrN$: C, 58.56; H, 3.28; N, 5.69. Found: C, 58.72; H, 3.28; N, 5.73.

2-[(1-Cyano-2-naphthyl)methyl]-2-thioisourea Hydrobromide (XV).—A mixture of 24.6 g. (0.10 mole) of XIV and 7.60 g. (0.10 mole) of thiourea in 300 ml. of ethanol was heated under reflux for 3 hr.; the mixture then was concentrated to a small volume under reduced pressure. Chilling and filtration gave 27.0 g. (84%) of a yellow solid, m.p. 218–222° dec. Addition of ether to the filtrate resulted in the further separation of 3.40 g. of product; the total yield was 30.4 g. (94%). Two recrystallizations from ethanol (Norit) gave 25.0 g. (78%) of colorless crystals, m.p. 225–227° dec.

Anal. Calcd. for $C_{13}H_{12}BrN_3S$: C, 48.45; H, 3.75; N, 13.04; S, 9.95. Found: C, 48.17; H, 3.58; N, 12.76; S, 9.81.

Naphtho[1,2-*c*]thiophen-1(3*H*)-imine (2-Mercaptomethyl-1-naphthonitrile) (I).—A suspension of 32.2 g. (0.10 mole) of XV in 250 ml. of 5% sodium hydroxide solution was heated on a steam bath until the solid had completely dissolved (15 min.). The reaction mixture then was chilled, and the solid which separated was collected by filtration, washed with water until it gave a neutral test with litmus, and dried, yielding 17.6 g. (88%), m.p. 103–105° dec. Recrystallization was accomplished by dissolving the product in hot ethanol and then adding water until precipitation of the solid just began. Cooling resulted in the separation of 16.2 g. (81%) of colorless crystals, m.p. 105–106° dec.

Anal. Calcd. for $C_{12}H_9NS$: C, 72.33; H, 4.55; N, 7.03; S, 16.09. Found: C, 72.34; H, 4.79; 7.11; S, 15.92.

The infrared absorption spectrum revealed bands that were assignable to free NH stretching absorption (3220 cm.$^{-1}$, w), NH deformation vibration (1510 cm.$^{-1}$, s), and conjugated C=N and C=C linkages (1595 cm.$^{-1}$, s; 1640 cm.$^{-1}$, m).

A 2,4-Dinitrophenyl sulfide derivative was prepared from 600 mg. (3.0 mmoles) of I. The product amounted to 960 mg. (88%) of a yellow solid, m.p. 234–235°. The infrared spectrum showed a band at 2220 cm.$^{-1}$, which was assignable to C≡N.

Anal. Calcd. for $C_{18}H_{11}N_3O_4S$: C, 59.15; H, 3.04; N, 11.50; S, 8.78. Found: C, 59.38; H, 3.28; N, 11.72; S, 9.00.

The treatment of an acetone solution of I with dry hydrogen chloride resulted in the separation of **naphtho[1,2-*c*]thiophen-1(3*H*)-imine hydrochloride**, m.p. 240° dec.

Anal. Calcd. for $C_{12}H_{10}ClNS$: C, 61.14; H, 4.28; S, 13.60; Cl, 15.04. Found: C, 61.18; H, 4.21; S, 13.73; Cl, 15.27.

2-[(Benzylthio)methyl]-1-naphthonitrile (XI).—To a solution of 3.00 g. (0.13 g.-atom) of sodium metal dissolved in 100 ml. of absolute ethanol was added slowly during a period of 10 min. 12.4 g. (0.10 mole) of α-toluenethiol. Next, 24.6 g. (0.10 mole) of 2-bromomethyl-1-naphthonitrile (XIV) was introduced over a period of 45 min., and, after the reaction mixture had been allowed to stand overnight, it was heated for 2 hr. on a steam bath under gentle reflux. While still hot, the reaction mixture was filtered, and the filtrate was chilled, yielding 24.2 g. of colorless product. Concentration of the filtrate gave an additional 2.40 g.; the total yield was 26.6 g. (92%). Recrystallization from 95% ethanol (Norit) gave 23.2 g. (80%) of colorless crystals, m.p. 55°.

Anal. Calcd. for $C_{19}H_{15}NS$: C, 78.86; H, 5.23; S, 11.08. Found: C, 78.75; H, 5.32; S, 11.23.

The infrared absorption spectrum showed a band assignable to C≡N (2220 cm.$^{-1}$, s).

Compound XI also was prepared from naphtho[1,2-*c*]thiophen-1(3*H*)-imine (I). To a solution of 600 mg. (3.0 mmoles) of I in 20 ml. of ethanol was added a solution of 120 mg. (3.0 mmoles) of sodium hydroxide in 2 ml. of water. This mixture was added to a solution of 380 mg. (3.0 mmoles) of benzyl chloride in 10 ml. of ethanol and heated under reflux for 4 hr. After the reaction mixture had been cooled and filtered to remove the sodium chloride, it was evaporated to dryness at atmospheric pressure and room temperature. The resulting residue was washed thoroughly with water and then with a small, cold portion of ethanol; the yield was 600 mg. (69%), m.p. 52–53°. Two recrystallizations from heptane and ethanol afforded 430 mg. (50%) of colorless needles, m.p. 53.5–54.5° (mixture melting point with the product obtained from the reaction of XIV and benzyl mercaptan was 54.5–55.5°), and the infrared spectra of the two specimens were identical.

Bis[(1-cyano-2-naphthyl)methyl] Disulfide (XII).—To a solution of 2.00 g. (0.01 mole) of (I) and 0.90 g. (0.023 mole) of

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[29] S. J. Angyal, P. J. Morris, R. C. Rassack, and J. A. Waterer, *J. Chem. Soc.*, 2704 (1949).

sodium hydroxide in 30 ml. of water at 80–90° was added 4 ml. at 30% hydrogen peroxide dropwise over a period of 0.5 hr. with vigorous stirring. The reaction mixture was stirred for 1 hr. more and then cooled. The crude product was collected by filtration and washed thoroughly with water and then with a 30-ml. portion of ethanol; the yield was 2.00 g. (100%), m.p. 190–192°. Three recrystallizations from glacial acetic acid afforded 1.70 g. (86%), m.p. 192.5–193°.

Anal. Calcd. for $C_{24}H_{16}N_2S_2$: C, 72.70; H, 4.07; S, 16.17. Found: C, 72.62; H, 4.15; S, 16.35.

1-Aminomethyl-2-benzylthiomethylnaphthalene.—To a solution of 280 mg. (7.5 mmoles) of sodium borohydride in 8 ml. of purified diglyme was added 3.00 g. (0.01 mole) of XI slowly with stirring. After addition was complete, a solution of 330 mg. (2.5 mmoles) of anhydrous aluminum chloride in 1.5 ml. of purified diglyme was added dropwise over a period of 20 min.; stirring was continued for 1 hr. at room temperature and then for 1 hr. at 80–90° while heating on a steam bath. The cooled reaction mixture then was poured into a mixture of 25 g. of crushed ice in 10 ml. of concentrated hydrochloric acid and was allowed to stand for 36 hr. at room temperature. The crude product was collected by filtration and washed with one 10-ml. portion of cold water and then with two 15-ml. portions of ether to yield 2.50 g. (76%), m.p. 190–193° dec. Apparent ease of oxidation of this compound resulted in poor analytical results. Because of these difficulties, it was analyzed as an acetyl derivative.

N-[(2-Benzylthiomethyl-1-naphthyl)methyl]acetamide.—To a warm solution of 2.60 g. (8.0 mmoles) of 1-aminomethyl-2-benzylthiomethylnaphthalene in 20 ml. of dry pyridine was added slowly with stirring 1.00 g. (0.013 mole) of acetyl chloride. The mixture was stirred overnight at room temperature and then at 85–90° for 2 hr. Pouring the reaction mixture into water afforded a crystalline product which was collected by filtration, washed with water, and, dried, yielding 2.70 g. (100%). Recrystallization from ethanol (Norit) yielded 2.50 g. (93%), m.p. 124.5–126°.

Anal. Calcd. for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18. Found: C, 75.31; H, 6.47; N, 4.27.

4-Bromomethyl-1-naphthonitrile.—A mixture of 40.0 g. (0.24 mole) of 4-methyl-1-naphthonitrile, 43.0 g. (0.24 mole) of N-bromosuccinimide, and 0.8 g. of benzoyl peroxide in 200 ml. of carbon tetrachloride was heated under reflux with stirring for 4 hr. The reaction mixture was cooled and filtered, and the residue was washed thoroughly with water and dried; crystallization yielded 42.0 g. (71%) of fine, colorless needles, m.p. 134.5°.

Anal. Calcd. for $C_{12}H_8BrN$: C, 58.55; H, 3.29; Br, 32.47; N, 5.69. Found: C, 58.38; H, 3.81; Br, 32.51; N, 5.74.

4-[(4-Hydroxy-6-methyl-2-pyrimidinyl)thio]methyl-1-naphthonitrile (XVI).—To a solution of 4 70 g. (0.20 g.-atom) of sodium in 300 ml. of ethanol was added with stirring 29.0 g. (2.20 moles) of 6-hydroxy-4-methyl-2-thiopyrimidine.[30] The mixture was stirred vigorously and heated on an oil bath for 5 hr. at 110–120°. After the reaction mixture had been cooled to room temperature, 50.0 g. (0.20 mole) of 4-bromomethyl-1-naphthonitrile was added in three portions at short intervals to permit proper mixing, and the resulting mixture was heated and stirred for 12 hr.

The crystalline mass was removed by filtration, washed with water, and recrystallized from glacial acetic acid to yield 60.0 g. (96%) of flaky microneedles, m.p. 256.5°.

Anal. Calcd. for $C_{17}H_{13}N_3OS$: C, 66.42; H, 4.26; N, 13.67; S, 10.43. Found: C, 66.73; H, 4.41; N, 13.60; S, 10.37.

4-[(1-Cyano-4-naphthyl)methyl]-2-thioisourea Hydrobromide.—A mixture of 24.6 g. (0.10 mole) of 4-bromomethyl-1-naphthonitrile, 7.60 g. (0.10 mole) of thiourea, and 300 ml. of absolute ethanol was refluxed with stirring for 3 hr. After cooling and filtration, there was obtained 27.5 g. (85%) of white, glistening needles, m.p. 227°. The filtrate on concentration furnished an additional amount of 3.50 g. (11%); this was crystallized twice from ethanol to give white needles, m.p. 227°.

Anal. Calcd. for $C_{13}H_{12}BrN_3S$: C, 48.45; H, 3.75; Br, 24.79. Found: C, 48.54; H, 3.66; Br, 24.70.

4-Mercaptomethyl-1-naphthonitrile.—A mixture of 30.0 g. (0.098 mole) of the above pyrimidine derivative, 160 ml. of concentrated hydrochloric acid, and 200 ml. of water was allowed to stand overnight. The mixture was heated initially at a low temperature to avoid serious loss of solid by frothing through the condenser. After 4 hr., the frothing had subsided and heating was increased to the reflux temperature where hydrolysis occurred rapidly. Refluxing and stirring were continued until almost no solid was observed on the surface of the mixture (*ca.* 3 hr.). The reaction mixture was cooled and extracted with 2.5 l. of ether. The ether solution was filtered, washed with 5% sodium carbonate solution and then with water, and finally dried over anhydrous sodium sulfate. The solution was concentrated to 100 ml. at which point 14.0 g. (72%) of stout needles separated, m.p. 95.5–97.5°. An analytical sample was prepared by four recrystallizations from ether, m.p. 97–98°.

This substance also was prepared from 25.0 g. (0.081 mole) of 4-[(1-cyano-4-naphthyl)methyl]-2-thiourea hydrobromide suspended in 200 ml. of 5% sodium hydroxide solution by heating in a water bath for 0.5 hr.

Anal. Calcd. for $C_{12}H_9NS$: C, 72.31; H, 4.55; S, 16.09. Found: C, 72.19; H, 4.93; S, 15.91.

(1-Aminomethyl-4-naphthyl)methanethiol (XVII).—At the temperature of an ice–salt freezing bath, a solution of 24.5 g. (0.123 mole) of 4-mercaptomethyl-1-naphthonitrile in 100 ml. of dry, purified diglyme was stirred vigorously for 5 min. with 4.80 g. (0.13 mole, twice required amount) of commercial sodium borohydride under anhydrous conditions. After 10 min., a cooled suspension of 5.50 g. (0.043 mole) of anhydrous, sublimed aluminum chloride in 50 ml. of diglyme was added over 2 hr. with stirring. This was allowed to stand at room temperature for 3 hr., then most of the diglyme was removed under reduced pressure, and the residue was treated in the cold with a mixture of 75 ml. of concentrated hydrochloric acid and 75 ml. water. The solid was filtered, washed with 150 ml. of 6 *N* hydrochloric acid, and dried, yielding 28.0 g. (95%), m.p. 250–260° dec.

To 10.0 g. of above hydrochloride suspended in 100 ml. water, 10 ml. of ammonium hydroxide solution was added. After thorough mixing, the resulting gummy material was taken up in benzene. The benzene solution was filtered, washed with dilute ammonium hydroxide, and then with water. The solution was concentrated to 60 ml. and saturated with anhydrous hydrogen chloride in the cold. The white precipitated hydrochloride was filtered and dried, yielding 8.50 g. It was then recrystallized twice from methanol, yielding 5.50 g. (52%), m.p. 262–263° dec.

The infrared absorption spectrum (potassium bromide pellet) showed bands that were assignable to NH stretching frequency (3400 cm.$^{-1}$, s; 1600 cm.$^{-1}$, s; 1105 cm.$^{-1}$, m) and SH (2555 cm.$^{-1}$, m).

Anal. Calcd. for $C_{12}H_{14}ClNS$: C, 60.10; H, 5.88; Cl, 14.79; S, 13.37. Found: C, 60.22; H, 5.80; Cl, 14.79; S, 13.33.

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[30] H. M. Foster and H. R. Snyder, *Org. Syn.*, **35**, 80 (1955).