3.6–3.85 (t, 2, OCH_2), and 1.85–2.20 (m, 7, CH_2CH_2 overlapping a singlet at 2.05, CH_3).

Anal. Calcd for $C_7H_{12}Cl_2O_2$: C, 42.3; H, 6.0. Found: C, 42.5; H, 6.2.

3,5-Dichloro-1-pentyl benzoate (**15b**) was prepared similarly in 74% yield, bp 131–135° (0.2 mm), $n^{20}{}_D$ 1.5288.

Anal. Calcd for $C_{12}H_{14}Cl_2O_2$: C, 55.4; H, 5.4; Cl, 26.9. Found: C, 55.2; H, 5.4; Cl, 26.8.

5-Chloropentyl Methanesulfonate.—A mixture of 128 g (1.49 mol) of tetrahydropyran, 114.5 g (1.0 mol) of methanesulfonyl chloride, and 10 g of anhydrous zinc chloride was refluxed under nitrogen for 3 hr. The reaction mixture was taken up in ether, washed with water, and dried, and the ether was removed. The residue was distilled to give 101.4 g (51%) of bright yellow oil, bp 121–124° (0.5 mm), which darkened rapidly: nmr ($CDCl_3$) δ 4.2 (t, 2, $SO_2OCH_2CH_2$), 3.6 (t, 2, $-CH_2Cl$), 3.0 (s, 3, CH_3SO_2O), and 1.3–2.15 (m, 6, $-CH_2CH_2CH_2-$).

3-Chloroglutaric Acid (**17**).—To 200 ml of concentrated nitric acid at 80° was added a few drops of **1**. After the reaction had initiated, the oxidation solution was cooled and 40 g (0.33 mol) of **1** was added dropwise at 30–40° over a 3-hr period. The reaction mixture was stirred an additional 18 hr at 20°, and the excess nitric acid was removed on a rotary evaporator at 20°. The resulting solid was dried over phosphorus pentoxide in a vacuum desiccator to give 52 g (95%) of colorless 3-chloroglutaric acid, mp 125–126° (lit.[12] mp 125–126°).

Anal. Calcd for $C_5H_7ClO_4$: C, 36.1; H, 4.2; Cl, 21.3; neut equiv, 83.3. Found: C, 36.2; H, 4.4; Cl, 21.5; neut equiv, 83.4.

Registry No.—**1**, 1768-64-5; **6**, 27070-15-1; **7**, 27070-16-2; **8**, 27070-17-3; **9**, 27070-18-4; **10**, 27070-19-5; **12**, 27070-20-8; **13b**, 27054-52-0; **14**, 27111-66-6; **15a**, 27070-21-9; **15b**, 27070-22-0; 3-methyl-3-phenyltetrahydropyran, 27070-23-1; 1,5-dibromo-3-phenylpentane, 27070-24-2; 5-chloropentyl methanesulfonate, 4337-21-7.

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The Redox Cleavage of the Sulfur–Sulfur Bond and Carbon–Sulfur Bond in Tetramethylthiuram Disulfide by *N*-Benzyl-1,4-dihydronicotinamide

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The interaction between *N*-benzyl-1,4-dihydronicotinamide and *N,N,N,'N'*-tetramethylthiuram disulfide in ethanol at room temperature in the dark has led to the formation of *N*-benzyl-3-carbamylpyridinium *N,N*-dimethyldithiocarbamate, carbon disulfide, and possibly *N,N*-dimethylperthiocarbamate. The mode of formation and the nature of these salts are discussed.

In an earlier study we have proposed[2] that the cleavage of the sulfur–sulfur bond in diphenyl disulfide by *N,N*-dimethylaniline and by ethanolamine may proceed by a one-electron transfer mechanism, analogous to the redox reaction between hydrogen peroxide and ferrous ion.[3] The corresponding thiyl radical, mercaptide ion, and amine cation radical are formed.[2]

$$ArS{-}SAr + R_3N\colon \rightleftarrows R_3N\cdot^{+}{-}{-}{-}ArS^- + ArS\cdot$$

In the extension of this study, we have examined the reactions between *N*-benzyl-1,4-dihydronicotinamide with *N,N,N',N'*-tetramethylthiuram disulfide and monosulfide and wish to report these findings.

The reports by Westheimer and others on the oxidation of 1,4-dihydropyridines by certain carbonyl compounds[4,5] and by olefinic double bonds[6] and further on the oxidation of 1-alkyl-1,4-dihydronicotinamide by malachite green[7] and thiobenzophenone[8] have led to information relevant to the biological oxidation–reduction involving the coenzyme, nicotinamide–adenine nucleotide (NAD) and its reduced form (NADH).

These reactions appear to proceed by an ionic hydride transfer mechanism. However, free-radical mechanisms were not ruled out since *N*-alkyl-1,4-dihydronicotinamide reduces α,α-diphenyl-β-picrylhydrazyl[8] and quinone[9] which are indeed free-radical reactions. The free-radical mechanism has been further enhanced by other findings of Westheimer and coworkers on the photochemical reduction of bromotrichloromethane by derivatives of 1,4-dihydropyridine[10] and the isolation of stable pyridinyl free radicals by Kosower.[11] Another report on the oxidation of 3,5-dimethyl-2,4-dicarbethoxy-1,4-dihydropyridine by 2-mercaptobenzophenone suggests that a thiyl radical intermediate is involved in this transformation.[12]

Results and Discussion

Reduction of Tetramethylthiuram Disulfide (TMTD) with *N*-Benzyl-1,4-dihydronicotinamide.—*N*-Benzyl-1,4-dihydronicotinamide reacts with an equimolar quantity of TMTD in absolute ethanol at room temperature in the dark to afford two products with ultraviolet absorption maxima at 410 and 435 mμ, respectively. A trace amount of carbon disulfide was also

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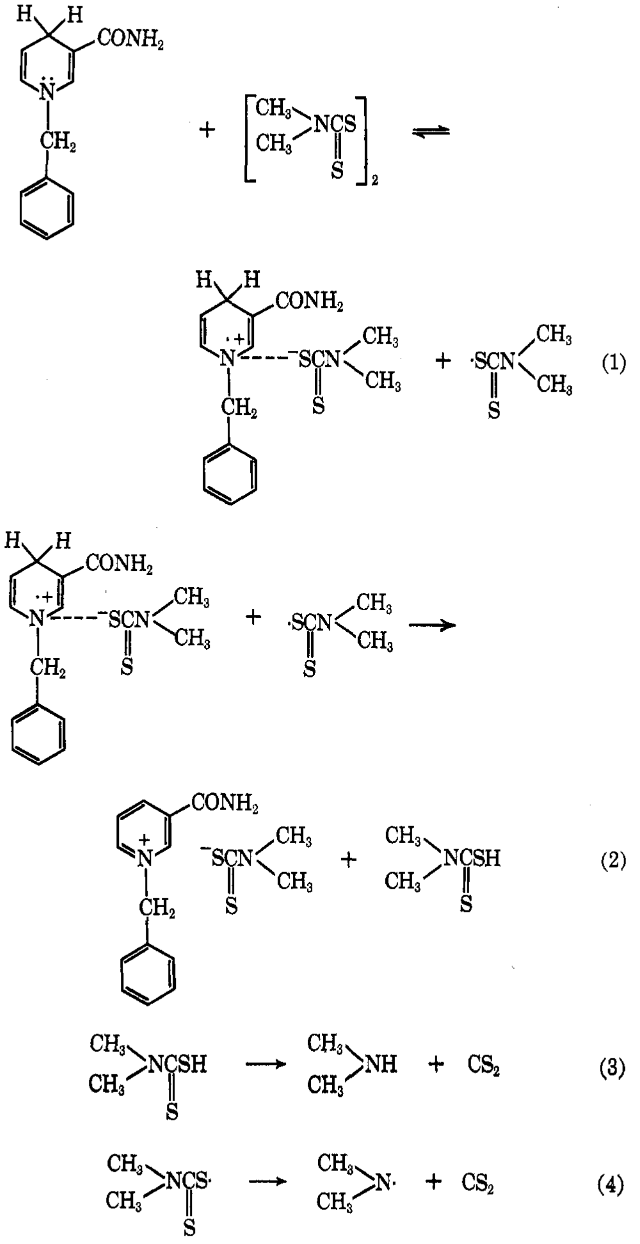
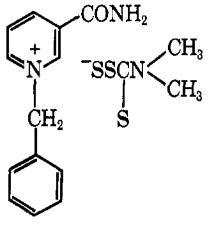
obtained. The compound with absorption maximum at 410 mμ was identified as *N*-benzyl-3-carbamylpyridinium *N*,*N*-dimethyldithiocarbamate. One can suggest a plausible mechanism for this reaction parallel to the one proposed for diphenyl disulfide and *N*,*N*-dimethylaniline.[2] Since this reaction can proceed at 25° in total darkness, one can assume that no prior homolytic dissociation of the sulfur–sulfur bond occurred.



It is not clear whether the carbon disulfide is formed from the hypothetical dithiocarbamic acid as reported previously[13] or from the thiyl radical. The low yield of carbon disulfide and our failure to detect dimethylamine are consistent with reports that TMTD undergoes rather complicated decompositions leading to numerous minor products.[14] We have perhaps detected only a few of the major products of this reaction. The fact that this pyridinium salt absorbs at much longer wavelengths, 410 mμ, compared with the expected λ_{max} at 265 mμ for other pyridinium ion salts suggests that this pyridinium salt is not a typical one but resembles *N*-methylpyridinium iodide, a known charge-transfer complex species[15] which possesses an ultraviolet absorption maximum at much longer wavelength than 265 mμ. We were unable to isolate and identify the compound with absorption maximum at 435 mμ because it decomposes on exposure to air. We tentatively suggest that the product with absorption maximum at 435 mμ is *N*-benzyl-3-carbamylpyridinium dimethylperthiocarbamate, arising from cleavage of the carbon–sulfur bond in TMTD. It has been reported that TMTD undergoes homolytic cleavage of the sulfur–sulfur bond thermally or photochemically to form thiyl radicals[16] and also the cleavage of the carbon–sulfur bond to give a carbon radical and a thiyl radical.[17]



A comparison of bond dissociation energies between carbon–sulfur and sulfur–sulfur bonds offers a partial explanation for this reaction. In organic peroxides, the oxygen–oxygen bond is considerably weaker than the carbon–oxygen bond, and, in their decomposition, oxygen–oxygen bond rupture becomes the sole primary reaction. In organic disulfides, the carbon–sulfur bond and sulfur–sulfur bonds are cited to be nearly equal in strength.[18]

It is not surprising that decomposition of disulfides follows a more complex route than that of peroxide, and it is not unreasonable to suggest that the cleavage of the sulfur–sulfur bond and carbon–sulfur bond in TMTD under the attack of *N*-benzyl-1,4-dihydronicotinamide happens concurrently, leading to both *N*-benzyl-3-carbamylpyridinium dimethyldithiocarbamate and dimethylperthiocarbamate.

More pertinent information is obtained by treating *N*-benzyl-1,4-dihydronicotinamide with *N*,*N*,*N'*,*N'*-tetramethylthiuram monosulfide (TMTM). In this reaction, only *N*-benzyl-3-carbamylpyridinium *N*,*N*-dimethyldithiocarbamate, with λ_{max} at 410 mμ, was obtained. The other compound absorbing at 435 mμ is completely missing. It is known that TMTM initiates free-radical polymerization of methyl methacrylate under heat or photolysis by homolytic cleavage of the carbon–sulfur bond.[16] It appears reasonable that the reduction of TMTM by *N*-benzyl-1,4-dihydronicotinamide should occur at the same site. The longer absorption maximum for the perthiocarbamate salt than that of the dithiocarbamate may result because the dithiocarbamate ion is more stabilized by resonance and

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may have a higher ionization potential,[19] and more energy should be required to remove the electron from one of the sulfur atoms to the pyridine ring than in the case of perthiocarbamate. It seems unlikely that either the dithiocarbamate or perthiocarbamate ion add to the pyridinium ring to produce the dihydropyridinine analog, in a reaction analogous to the attack by other nucleophiles.[20] All such addition products have absorption maxima in the 340–360-mμ region in their ultraviolet absorption spectra, similar to the dihydropyridine compound. The products from reactions of TMTD and TMTM with *N*-benzyl-1,4-dihydronicotinamide do not absorb in this region.

Attempts to use TMTD and TMTM with *N*-benzyl-1,4-dihydronicotinamide as a redox couple to initiate free-radical polymerization of ethyl acrylate or acrylonitrile were unsuccessful. A possible explanation for this result is that both 1,4-dihydropyridine and the cation radical are effective hydrogen donors and therefore scavenge the growing polymer chain.

The reactions which were carried out in acetone as solvent did not produce 2-propanol or pinacol. The thiyl radical produced by the redox cleavage of the disulfide bond is apparently a better acceptor of hydrogen atom from the 1,4-dihydropyridine than the carbonyl group in acetone.

Experimental Section[21]

Reagents.—*N*-Benzyl-1,4-dihydronicotinamide was prepared according to the method of Karrer and Stare.[22] Nicotinamide (Eastman, mp 129–130°, 10 g, 0.08 mol) was refluxed with 100 ml (0.87 mol) of benzyl chloride (Eastman, bp 179°) for 2 hr. The mixture was filtered hot and the solid was washed three times with 15 ml of ether. The yield of the crude *N*-benzyl-3-carbamylpyridinium chloride was 15 g, mp 234°. The reduction of this salt to *N*-benzyl-1,4-dihydronicotinamide was carried out following the procedure of Westheimer[7] and coworkers. Ten grams of the salt was shaken with 13.8 g of sodium carbonate and 25 g of sodium dithionite (Merck) in 150 ml of water for 10 min. The yellow crystals were filtered and recrystallized from the ethanol–water mixture: 4 g; mp 115–119° (lit.[22] 115–123°); λ_{max} 350 mμ (ε 7220).

***N*,*N*,*N'*,*N'*-Tetramethylthiuram monosulfide**, TMTM (Eastman), was recrystallized from ethanol, mp 106–108° (lit.[23] 108–110°).

***N*,*N*,*N'*,*N'*-Tetramethylthiuram disulfide**, TMTD (Eastman), was recrystallized from ethanol, mp 153–154° (lit.[24] 145–146°).

***N*-Benzyl-3-carbamylpyridinium *N*,*N*-dimethyldithiocarbamate** was prepared by reacting 1.4 g (1×10^{-2} mol) of sodium *N*,*N*-dimethyldithiocarbamate (Eastman) and 1.9 g (1×10^{-2} mol) of *N*-benzyl-3-carbamylpyridinium chloride in 50 ml of acetone. A yellow-colored solution and a precipitate were produced instantly when the two reagents were mixed in acetone. The solid was separated and extracted three times with 50-ml portions of acetone. The acetone solution upon concentration under reduced pressure afforded 1.51 g (~55%) of a yellow solid: mp 245–250° dec; λ_{max} 410 mμ (ε 1700) in ethanol. The analytical sample was recrystallized from ethanol, mp 248–250° dec.

Anal. Calcd for $C_{16}H_9N_3OS_2$: C, 57.6; H, 5.8; N, 12.6. Found: C, 57.7; H, 5.82; N, 12.63.

Reactions. TMTD and *N*-Benzyl-1,4-dihydronicotinamide.—Equal moles (5×10^{-3} mol) of each reactant were dissolved in 100 ml of absolute ethanol, and the solution was allowed to stand in the dark at 25° under nitrogen atmosphere. The reactions were carried out in duplicate, and each experiment was accompanied by a blank run where only the *N*-benzyl-1,4-dihydronicotinamide or TMTD was present under identical experimental conditions. The progress of the reactions and of the blank was followed by withdrawing an aliquot with a syringe at regular time intervals and noting the gradual decrease in absorbance of dihydropyridine at 350 mμ on a Beckman Model D.B. spectrophotometer. No attempt was made to follow the kinetics, but the half-life of the reaction was estimated to be ~6 days. The yield of the product with absorption maximum at 410 mμ (ε 1700) was estimated to be 67% from absorbance measurement. The yield of carbon disulfide, ~1%, was obtained by gas chromatographic analysis (Wilkens Aerograph, Model A-90-P, helium as carrier gas, 35 psi, flow rate 60 ml/min; column 20% Carbowax 20M on Chromosorb W 60–80; column temperature, 73°; injector, 148°; and detector, 282°). Effort directed to detect dimethylamine was not fruitful in any of the experiments. In the control runs, gas chromatography was sensitive enough to detect a minimum concentration of 1×10^{-5} mol of dimethylamine which corresponds to 0.1% yield.

In the blank runs, TMTD alone in ethanol was stable over a period of 5 weeks and *N*-benzyl-1,4-dihydronicotinamide showed no significant change in absorbance after 4 weeks.

***N*-Benzyl-3-carbamylpyridinium Dimethylthiocarbamate.**—In another run, a mixture of 1.2 g (5×10^{-3} mol) of TMTD and 1.07 g (5×10^{-3} mol) of *N*-benzyl-1,4-dihydronicotinamide in 100 ml of ethanol was allowed to stand for a period of 6 weeks under nitrogen at 25° in the dark. The mixture upon concentration by evaporation under reduced pressure furnished a yellow solid in 43% yield (0.72 g). Analytical sample after recrystallization from ethanol melted with decomposition at 249–250° with gas evolution and its ultraviolet absorption maximum in ethanol was 410 mμ (ε 1700).

Anal. Calcd for $C_{16}H_9N_3OS_2$: C, 57.7; H, 5.8; N, 12.6. Found: C, 57.4; H, 5.89; N, 12.64.

A mixture melting point with an authentic sample of *N*-benzyl-3-carbamylpyridinium *N*,*N*-dimethyldithiocarbamate prepared from sodium *N*,*N*-dimethyldithiocarbamate and *N*-benzyl-3-carbamylpyridinium chloride showed no depression.

Concentration of the mother liquor afforded a low-melting, viscous material but it deteriorated upon exposure to air. Effort directed to solidify this oily substance was not successful.

TMTM and *N*-Benzyl-1,4-dihydronicotinamide.—When a mixture of 1.02 g (5×10^{-3} mol) of TMTM and 1.07 g (5×10^{-3} mol) of *N*-benzyl-1,4-dihydronicotinamide in 100 ml of ethanol was allowed to stand in the dark under nitrogen atmosphere at 25° for 6 weeks, it gave a 65% yield of *N*-benzyl-3-carbamylpyridinium dimethyldithiocarbamate from absorbance measurement at 410 mμ. No band absorbing at 435 mμ was detected. In the blank run, TMTM was stable under identical conditions for a period of 2 months. In this and subsequent repeated runs under identical or different conditions, the yield of carbon disulfide was always nil.

Attempted Polymerization of Vinyl Monomers by TMTD and *N*-Benzyl-1,4-dihydronicotinamide.—Attempts were made to induce polymerization of acrylonitrile and ethyl acrylate with TMTD and *N*-benzyl-1,4-dihydronicotinamide. In a typical run, a solution of equal moles (5×10^{-5} mol) of TMTD and *N*-benzyl-1,4-dihydronicotinamide in 10 ml of ethyl acrylate was allowed to stand under nitrogen at 37° for 3 weeks. By that time, the 350-mμ absorbance peak due to the dihydronicotinamide had vanished. However, when the reaction mixture was diluted with excess methanol, no polymeric substance was obtained.

Attempted Reduction of Acetone to Isopropyl Alcohol by *N*-Benzyl-1,4-dihydronicotinamide and TMTD.—A series of reactions between TMTD and *N*-benzyl-1,4-dihydronicotinamide were run in reagent grade acetone in the dark and room light. Gas-phase chromatographic analysis was unable to detect any isopropyl alcohol in any of the experiments.

Registry No.—*N*-Benzyl-1,4-dihydronicotinamide, 952-92-1; *N*,*N*,*N'*,*N'*-tetramethylthiuram disulfide, 137-26-8; *N*-benzyl-3-carbamylpyridinium *N*,*N*-dimethyldithiocarbamate, 27192-77-4.

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