obtained. It melted at 105–107° alone and when mixed with authentic dibenzhydryl ether.

Attempted Self-Etherification of Triphenylcarbinol, Butyl Alcohol and Benzyl Alcohol.—In the triphenylcarbinol experiment a total of only 0.125 mole of the alcohol was used. Little, if any, reaction occurred until the catalyst concentration was increased to 0.064 molar. Twice the theoretical volume of water for etherification (*i. e.*, 100% of theory for alkylation) was then evolved over a period of eighteen hours. A 32% yield (9.75 g.) of triphenylmethane, instead of the expected tetraphenylmethane, was isolated. After four recrystallizations from benzene the product melted at 93–93.5° alone and when mixed with authentic triphenylmethane.[18] A mixture of solids which have not been characterized was isolated from the mother liquors.

No water was evolved when attempts were made to etherify *n*-butyl alcohol with itself.

One-fourth mole of benzyl alcohol and 0.128 molar catalyst was used in an attempt to form dibenzyl ether. A 99% yield of water, calculated for alkylation, was evolved in thirteen hours. A 66% yield of diphenylmethane (f. p. 25–25.2°) and a 17% yield of *m*-dibenzylbenzene (m. p. 58–58.5°) were isolated by distillation (lit. m. p. 58–59° for meta-, 78° for ortho- and 86° for para-dibenzylbenzene).

Alkylation of the solvent also occurred in an attempted etherification of benzyl alcohol with butyl alcohol. A 96% yield of water (calculated for etherification) was evolved in eighty hours at a catalyst concentration of 0.128 molar. Fractionation of the product gave a 40% yield of benzyl butyl ether and a 33% yield of diphenylmethane. The ether boiled at 113–113.5° (22 mm.), n^{25}_{D} 1.4892.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.50; H, 9.82. Found: C, 80.84; H, 10.01.

Summary

A study of the relative ease of formation of a number of ethers of triphenylcarbinol, benzhydrol, benzyl alcohol and butyl alcohol has been made. Certain transetherifications were also investigated. Both the etherifications and transetherifications were carried out and followed by a method which involved removal of the byproduct water by azeotropic distillation.

COLLEGE PARK, MD. RECEIVED[19] APRIL 4, 1949

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[18] The ease of reduction of triphenylcarbinol to triphenylmethane has been emphasized by Kauffman and Gromach, *Ber.*, **38**, 2706 (1905). The decomposition of ethers of triphenylcarbinol to triphenylmethane has been studied by Norris and Young, THIS JOURNAL, **52**, 753 (1930).

[19] Original manuscript received August 4, 1948.

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE]

Oxidation–Reduction Potentials of Thiol–Disulfide Systems. III. Substituted Thioureas and Compounds Containing Two Thioureido Groups

BY PAUL W. PREISLER

Organic compounds having -SH or -SS- constituent groups are frequently used for activation or inactivation of enzymatic processes. To increase the available selection of such reagents and to assist in a more systematic approach to the study of the mechanisms of the reactions involved, a number of thiol and dithiol compounds have been prepared and the equilibrium oxidation–reduction potentials with their corresponding disulfides have been measured.

Series of methyl and of ethyl substituted thioureas and various other thioureas were investigated. The thioureas were selected because the thiourea(RSH)–formamidine disulfide (RSSR) system had been shown to give stable reproducible potentials[1] which follow the theoretical mathematical equations applicable to systems of the type: 2 reductant = oxidant + 2 H.

A series of compounds containing two thiourea type (thioureido)-SH groups was also prepared. Oxidation of these groups might result in either a disulfide of the R-SS-R type in a chain series or in a disulfide with the -SS- in a ring structure or in a combination of both. The reversible oxidation of dithiobiuret (2-SH groups) to 3,5-diimino-1,2,4-dithiazolidine (-SS- in ring) gives stable potentials[2] following the mathematical equations of the systems of the type: reductant = oxidant + 2H. The potentials of the several members of this series which were determined indicate that the predominant oxidation is to form the ring structure.

Experimental

The oxidation–reduction potential apparatus and procedure generally used for such measurements were employed. The potentials of platinum wire electrodes immersed in the test solution were measured against a saturated potassium chloride calomel half-cell connected by a saturated potassium chloride–4% agar bridge. A Leeds and Northrup Type K potentiometer and a No. 2420-C galvanometer were used. Liquid junction potentials were considered negligible. The electrode, vessel and calomel cell were kept in a water-bath at 30° and the test solution was deoxygenated and stirred with cylinder nitrogen gas previously purified by passing over hot copper. The recorded potentials have been converted into E_h values (normal hydrogen electrode taken as zero). The potentials of the two electrodes usually were within 0.001 volt and, after the first two minutes allowed for mixing and reaction, remained constant for several minutes except in a few systems where rapid decomposition of the oxidant obviously was taking place. In such cases the titration was performed more rapidly by measuring only the principal points: $^1/_4$, $^1/_2$ and $^3/_4$ oxidized (or reduced). Values in parentheses in the table are uncertain because of such decompositions.

The potentials of the systems were measured with mixtures prepared by titration of the reductants with 0.005 *N* thallic sulfate in *N* sulfuric acid or 0.1 *N* sulfuric acid containing 0.45 *M* potassium sulfate. From three to ten mixtures were made for each system at both acidities, always including those for 25, 50 and 75% total equivalents oxidized. The experimentally obtained values corresponded to the calculated to within 0.001 volt.

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[1] P. W. Preisler and L. Berger, THIS JOURNAL, **69**, 322 (1947).

[2] P. W. Preisler and M. M. Bateman, *ibid.*, **69**, 2632 (1947).

The solutions and reagents were made from commercial analytical grade chemicals. Potassium sulfate was added to the dilute sulfuric acid to increase the ionic strength. No correction was made for the difference in degree of ionization of sulfuric acid and potassium sulfate, the total molar concentration merely being made equal.

Thallic sulfate stock solutions were made by adding a weighed amount of thallic oxide to an amount of standard sulfuric acid which was equivalent to the oxide and that necessary for the desired final acid concentration. The acid was concentrated by boiling until the oxide had dissolved, after which the solution was diluted to proper final volume. In the solutions containing potassium sulfate and thallic sulfate, a precipitate sometimes formed after about an hour, probably a thallic–potassium sulfate similar to the alums. Therefore, solutions containing these substances were freshly prepared and used at once.

Substituted thioureas were prepared or obtained from sources indicated. All compounds (except the tetraethyl thiourea, which was a viscous liquid) were white crystalline solids. The melting points recorded are corrected values; those in parentheses are from the literature cited.

Unsymmetrical (N,N) dimethyl thiourea, m. p. 153–155° (158–159°),[3] and unsymmetrical (N,N) diethyl thiourea, m. p. 101–102° (101–102°),[3] were prepared from the corresponding substituted cyanamides[4] by saturating alcoholic solutions of the cyanamide simultaneously with both hydrogen sulfide and anhydrous ammonia.[3]

N-Ethyl thiourea, m. p. 110–111° (113°),[5] was prepared by the interaction of ethyl isothiocyanate and ammonia in ethanol; N,N,N′-triethyl thiourea, m. p. 45–46° (m. p. 46°),[6] from diethylamine and ethyl isothiocyanate.

Ethylenediamine in ethanol was treated with excess carbon disulfide to form N,N′-ethylene thiourea, m. p. 196–198° (197°).[7] Thiophosgene, prepared from perchloromethyl mercaptan[8] reacted with diethylamine in excess to form N,N,N′,N′-tetraethyl thiourea.[9]

N-Methyl thiourea,[10] m. p. 119–120° (118°),[11] N,N′-dimethyl thiourea,[10] m. p. 52–54° (51–52°),[12] N,N,N′-triethyl thiourea,[10] m. p. 85–86° (87–88°),[13] and N,N,-N′,N′-tetramethyl thiourea,[14] m. p. 76–77° (78°)[9] were prepared by other laboratories; and allyl thiourea,[15] m. p. 70–72° (m. p. 70°),[16] and N,N′-diethyl thiourea,[15] m. p. 76–77 (77°)[5] were purchased.

N-Ethyl-N′-hydroxyethyl thiourea was prepared by mixing one volume of ethyl isothiocyanate with one volume of ethanol and then adding quite slowly, because considerable heat is evolved, 0.8 volume of ethanolamine. The mixture was cooled in an ice-bath and five volumes of ether was added. Fine white crystals formed which were filtered off and washed with chloroform and also ether and dried *in vacuo;* m. p. 74–75°.

Anal. Calcd. for $C_5H_{12}ON_2S$: C, 41.0; H, 8.17; N, 18.9. Found: C, 40.8, 40.7; H, 8.17, 8.20; N, 19.1, 19.0.

Straight-chain aliphatic compounds containing two thiourea type (thioureido) groups were prepared by the reaction of diamines with an excess of ethyl isothiocyanate.

N,N′-bis-(Ethylthioureido)-ethylenediamine, m. p. 129–130° (132°), resulted from the interaction of ethylenediamine and ethyl isothiocyanate in ethanol.[17]

N,N′-bis-(Ethylthioureido-)-trimethylenediamine was prepared by adding an excess of ethyl isothiocyanate to a solution of trimethylenediamine in twenty volumes of ethanol, refluxing for an hour and allowing to stand for several days. The ethanol and unreacted isothiocyanate were then distilled off on a steam-bath *in vacuo*. The oily residue was dissolved in boiling water containing a little hydrochloric acid and filtered. On cooling, an oily emulsion formed which crystallized after a few days. Three recrystallizations from very dilute hydrochloric acid gave fine white crystals; m. p. 126–127°.

Anal. Calcd. for $C_9H_{20}N_4S_2$: C, 43.6; H, 8.09; N, 22.6. Found: C, 43.5, 43.7; H, 8.09, 8.06; N, 22.4, 22.4.

N,N′-bis-(Ethylthioureido-)-tetramethylenediamine was prepared by adding an excess of ethyl isothiocyanate to a solution of tetramethylenediamine in ten volumes of ethanol. Heat was liberated and a white solid formed. After refluxing an hour, the solid was filtered off and washed thoroughly with ethanol; m. p. 173–174°.

Anal. Calcd. for $C_{10}H_{22}N_4S_2$: C, 45.8; H, 8.45; N, 21.4. Found: C, 45.6, 45.6; H, 8.25, 8.45; N, 21.2, 21.2.

The higher members of this series were not made because the low solubility of the other members indicated that their solubility would not be sufficient for satisfactory potential measurements.

Straight-chain nitrogen compounds containing two thioureido type groups were prepared by the reaction of ethyl isothiocyanate[18] or potassium thiocyanate[19] with hydrazine or its derivatives.

N,N′-bis-(Ethylthioureido-)-dimethylhydrazine was prepared by suspending N,N′-dimethylhydrazine dihydrochloride in twenty times the amount of absolute ethanol and adding a suspension of the calculated amount of lithium ethylate in absolute ethanol to neutralize the acid then followed by an excess of ethyl isothiocyanate. The mixture became yellow at first and was heated under reflux for two hours on a steam-bath. The ethanol and excess isothiocyanate were then distilled off under vacuum

TABLE I

E_0' OF SYSTEMS COMPOSED OF SUBSTITUTED THIOUREAS AND THEIR CORRESPONDING OXIDANTS

Reductant of system	E_0' (in N H_2SO_4) (pH = 0.37), volt	E_0' (in 0.1 N H_2SO_4, 0.45 M K_2SO_4) (pH = 1.95), volt
Thiourea	0.418	0.412
N-Methyl	.413	.406
N,N-Dimethyl	.439	.442
N,N′-Dimethyl	.460	.454
N,N,N′-Trimethyl	.511	(.499)
N,N,N′,N′-Tetramethyl	.445	.444
N-Ethyl	.409	.402
N,N-Diethyl	.432	.432
N,N′-Diethyl	.450	.448
N,N,N′-Triethyl	.503	(.496)
N,N,N′,N′-Tetraethyl	.438	.440
N-Ethyl-N′-hydroxyethyl	.469	.461
N-Allyl	.427	.427
N,N′-Ethylene	.496	.490
Quinhydrone (for pH detn.)	.677	.582

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[3] O. Wallach, *Ber.*, **32**, 1873 (1899).

[4] Obtained through the courtesy of the American Cyanamid Company, Rockefeller Plaza, New York.

[5] A. W. Hofmann, *Ber.*, **1**, 27 (1868); **18**, 2788 (1885).

[6] N. Kurnakow, *J. prakt. Chem.*, [2] **50**, 500 (1894).

[7] W. Schacht, *Arch. Pharm.*, **235**, 442 (1897).

[8] Obtained through the courtesy of the J. T. Baker Chemical Company, Phillipsburg, N. J.

[9] M. Delépine, *Bull. soc. chim. France*, [4] **7**, 989 (1910).

[10] Obtained through the courtesy of Dr. Edwin B. Astwood, Pratt Diagnostic Hospital, Boston, Mass.

[11] R. Andreasch, *Monatsh.*, **2**, 277 (1881).

[12] A. E. Dixon, *J. Chem. Soc.*, **67**, 328 (1893).

[13] A. E. Dixon, *ibid.*, **67**, 557 (1895).

[14] Obtained through courtesy of American Cyanamid Company, Stamford, Conn.

[15] Purchased from Eastman Kodak Company, Rochester, N. Y.

[16] J. Dumas and J. Pelouze, *Ann.*, **10**, 326 (1834).

[17] H. Nägele, *Monatsh.*, **33**, 958 (1912).

[18] M. Busch and H. Lotz, *J. prakt. Chem.*, [2] **90**, 262 (1914).

[19] M. Freund and S. Wischewianski, *Ber.*, **26**, 2877 (1893).

TABLE II

E_0' OF SYSTEMS COMPOSED OF COMPOUNDS CONTAINING TWO –SH IN REDUCTANT AND FORMING CYCLIC OXIDANT

Reductant	E_0' (in N H_2SO_4) (pH = 0.37)	E_0' (in 0.1 N H_2SO_4, 0.45 M K_2SO_4) (pH = 1.95)
$H_2N\cdot C{=}S\cdot C{=}S\cdot NH_2$	Oxidant decomposes	
$H_2N\cdot C{=}S\cdot NH\cdot C{=}S\cdot NH_2$	0.243	0.196
$H_2N\cdot C{=}S\cdot NHNH\cdot C{=}S\cdot NH_2$	Oxidant decomposes	
$C_2H_5NH\cdot C{=}S\cdot NHNH\cdot C{=}S\cdot NHC_2H_5$	Oxidant decomposes	
$C_2H_5NH\cdot C{=}S\cdot NCH_3NCH_3\cdot C{=}S\cdot NHC_2H_5$	Oxidant decomposes	
$C_2H_5NH\cdot C{=}S\cdot NHCH_2NH\cdot C{=}S\cdot NHC_2H_5$	Unavailable	
$C_2H_5NH\cdot C{=}S\cdot NH(CH_2)_2NH\cdot C{=}S\cdot NHC_2H_5$	0.499	.501
$C_2H_5NH\cdot C{=}S\cdot NH(CH_2)_3NH\cdot C{=}S\cdot NHC_2H_5$	.448	.449
$C_2H_5NH\cdot C{=}S\cdot NH(CH_2)_4NH\cdot C{=}S\cdot NHC_2H_5$	.498	Oxidant decomposes

on the steam-bath. The white residue was dissolved in boiling water containing a little hydrochloric acid and filtered. A slight cloudiness was present, probably sulfur, and after cooling slowly, crystals formed. The material may be recrystallized from acidified aqueous solutions; m. p. 145–146°.

Anal. Calcd. for $C_8H_{18}N_4S_2$: S, 27.3. Found: S, 26.9, 26.8.

Discussion

The E_0' for the individual thiourea systems shown in Table I were calculated from the data by the equation

$$E_h = E_0' + 0.030 \log \frac{[R{-}SS{-}R]}{[R{-}SH]^2}$$

The E_0' for the systems shown in Table II whose reductant has two -SH groups (thioureido-) were calculated by the equation

$$E_h = E_0' + 0.030 \log \frac{[R = ({-}SS{-})]}{[R = ({-}SH)_2]}$$

The E_0' for each system shows no significant difference for the change in pH from 0.38 to 1.95, thereby indicating that there are no ionization constants near or within this zone and that the predominating ionic species of the systems are an un-ionized reductant and a ++ charged oxidant.

For the methyl series, the E_0' of the N-monomethyl derivative is slightly lower than that of thiourea itself. As the number of methyl groups is increased, E_0' at first becomes progressively higher, the order being N-mono-, N,N-di, N,N′-di-, N,N,N′-tri, then becomes considerably lower for N,N,N′,N′-tetra-. The ethyl series makes similar variations but not to the same degree as the methyl. A regular progression of the E_0' to higher values as more groups were introduced would have been expected from structural considerations. No analogous variations for such substitutions were found for any systems previously reported in the literature.

A comparison of the E_0' reported[20] for the systems whose reductants are thiourea, N,N′-methyl thiourea, N,N,N′,N-tetramethyl thiourea, and ethylene thiourea, which were calculated from their equilibria with the iodine–iodide system at pH 2.0, shows the same relative order and position on the oxidation–reduction potential scale for the various individual systems as found by the direct potentiometric measurement.

The oxidants of most of the thiourea systems are not stable in solutions of much lower acidity than the normal acid employed, so that their use as substitute reagents for formamidine disulfide has no particular advantage except when E_0' differences are desirable. The ring type disulfides also are relatively unstable in solutions less acid than pH 2. The E_0' of the systems forming ring disulfide oxidants from reductants containing two thiourea type (thioureido-) groups is of the same order as that of the thiourea–formamidine disulfide system. The general energy level of the equilibrium of the oxidation of 2-SH to -SS- is apparently the same whether the disulfide is straight-chain or cyclic.

The largest cyclic disulfide oxidant studied contained six C atoms and two N atoms in the ring in addition to the two S.

The hydrazine derivatives, whose oxidants would be cyclic structures with two adjacent nitrogens in the ring, were prepared, but the oxidants were too unstable for satisfactory measurement of potentials.

One important difference between the two types of systems is in the effect upon the potential by simple dilution of a fixed mixture of oxidant and reductant without change in the ratio of their concentrations. The potential of the thiourea type system increases 0.030 volt for each tenfold decrease in total concentration because the reductant affects the potential in proportion to the square of its concentration. The potentials of the systems forming ring type disulfide oxidants do not change with total concentration.

Because of this difference in behavior, when a system of one type reacts with the other type at a particular pH, the relation between the two depends not only upon the relative E_0' values but also upon the total concentration of each system as well. Thus a fixed ratio of oxidant and reductant of one system might be oxidizing toward a fixed ratio of another system at one total concentration and reducing at another. This relationship should be useful in determining the type

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[20] J. F. Bone and P. H. Bell, presented at the April, 1947, meeting of the American Chemical Society, Atlantic City, N. J.

of oxidant (straight-chain or cyclic) of a particular system.

Summary

The oxidation–reduction potentials of systems whose reductants are substituted thioureas have been measured in acid solutions and the E_0' determined.

Compounds whose reductants contain two thiourea type (thioureido-) groups have also been measured. Their oxidants are cyclic disulfides: the largest ring oxidant studied contained eight atoms and the two S atoms.

ST. LOUIS, MISSOURI RECEIVED DECEMBER 18, 1948

[CONTRIBUTION FROM THE WOOD CHEMISTRY LABORATORY OF THE DIVISION OF FORESTRY, UNIVERSITY OF MINNESOTA]

Hydrogen Bonding and the Swelling of Wood in Various Organic Liquids[1,2]

BY AMAR NATH NAYER AND RALPH L. HOSSFELD

Many attempts have been made to account for the swelling of wood, cellulose, and other colloidal substances when in contact with swelling agents. By and large, the net result has been the development of general theories based on the Donnan equilibrium,[3] adsorption of ions and their associated sphere of water of hydration,[4] and selective adsorption of ions with a resulting repulsion of colloidal surfaces of like charge.[5] Other workers have attempted more specifically to relate the phenomenon of swelling to the dielectric constant[6] and to the zeta potential[7] of the swelling liquid with respect to wood and cellulose. According to Stamm, however, none of these theories will adequately explain the swelling of wood in all the many types of swelling agents which have been studied.[8]

Recently Gordy[9,10] made use of the infrared absorption in studying the phenomenon of hydrogen bonding. He measured the wave length of the characteristic absorption band corresponding to the OD vibration in MeOD dissolved in benzene. In certain solvents, other than benzene, he observed a shift ($\Delta\mu$) in this wave length and attributed this shift to the formation of hydrogen bonds (actually deuterium bonds) between methyl alcohol and the solvent. The fact that Gordy found a very large value for $\Delta\mu$ in pyridine and the fact that pyridine is known to swell wood very appreciably, suggested that hydrogen bonding between hydroxyl groups in wood and added liquids may account for the swelling of wood in these liquids.

The relationship between the $\Delta\mu$ for the compounds as determined by Gordy and the degree of swelling of maple wood in these same compounds is shown in Fig. 1. It is apparent that a majority of the data indicates a direct relationship between the degree of swelling and the hydrogen bonding as determined by Gordy. Most notable exceptions to the relationship are the data for di-*n*-butylamine, tri-*n*-butylamine, N-methylaniline, N-dimethylaniline, quinoline and quinaldine.

In explanation of these exceptions, there is much evidence that molecular size might be an important factor.[7,11,12,13,14] However, determination of the swelling of maple wood by several homologous series of amines indicated that molecular structure as well as size might be important. In the series of methyl pyridines, the position of the methyl group was found to affect the swelling although the molecular size of the swelling agents was not greatly different.

The work of Brown and Barbaras[15] has shown, however, that the steric hindrance offered by a methyl group in the 2-position of pyridine decreased the stability of the resulting association compound with trimethyl boron. They have also shown that the steric effect in association compounds of trimethyl boron with secondary and tertiary aliphatic amines is in the order of increasing substitution on the nitrogen atom. Steric hindrance appears, therefore, to be a large factor in the strength of association between donor and acceptor atoms.

The majority of the OH groups in the cellulose molecule of wood may be in effect those of a substituted methyl alcohol R-(CHOH)-R′ where R and R′ represent portions of the cellulose molecule and as such would be subject to steric hindrance. It would, therefore, be predicted from Gordy's work that piperidine should be capable of swelling wood to a greater extent than pyridine and that 2-picoline should fall between these two.

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[1] From a thesis by A. N. Nayer presented to the Graduate Faculty of the University of Minnesota in partial fulfillment of the requirements for the Ph.D. degree, March, 1948.

[2] Paper No. 2457 in the Scientific Journal Series of the Minnesota Agricultural Experiment Station, St. Paul, Minnesota.

[3] Proctor and Wilson, *J. Chem. Soc.*, **109**, 307 (1916).

[4] Pauli and Handkowsky, *Biochem. Z.*, **18**, 340 (1909).

[5] Tarkow, Stamm and Erickson, Mimeo Report No. 1593, U. S. Forest Prod. Lab., Madison, Wis., 1946.

[6] De Bruyn, *Nature*, **142**, 570 (1938).

[7] Stamm, *Ind. Eng. Chem.*, **27**, 401 (1935).

[8] Stamm, "Wood Chemistry," A. C. S. Monograph No. 97, edited by Wise, Reinhold, New York, 1944, Chapter 13.

[9] Gordy, *J. Chem. Phys.*, **7**, 93 (1939).

[10] Gordy and Stanford, *ibid.*, **9**, 204 (1941).

[11] Davis, Barry, Peterson and King, THIS JOURNAL, **65**, 1294 (1943).

[12] Erickson and Rees, *J. Agr. Research*, **60**, 593 (1940).

[13] Kress and Bialkowski, *Paper Trade J.*, **93**, No. 20, 35 (1931).

[14] Sheppard and Newsome, *J. Phys. Chem.*, **36**, 2306 (1932).

[15] Brown and Barbaras, THIS JOURNAL, **69**, 1137 (1947).