Reactions of Thiols with Metals. II. Low-Temperature Oxidation by Soluble Metal Salts[1]

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The homogeneous reaction of various thiols with ferric octanoate has been studied at low temperatures in xylene in the absence of molecular oxygen. An oxidation–reduction step occurs exclusively to produce disulfides and ferrous octanoate. Rate studies in xylene and acetone indicate that these reactions adhere to second-order kinetics. The reactions proceed with great rapidity even in nonpolar solvents. Rate constants for the oxidation of α-toluenethiol and 1-dodecanethiol varied from 7.50×10^{-1} to 5.83×10^{-2} l./mole/sec at 25°. Aromatic thiols are even more reactive and in more polar solvents accurate rate measurements could not be obtained. The radical nature of the reactions was also established by trapping the thiyl radicals with an olefin. The results are consistent with recent theories which indicate that metals are active oxidation catalysts at extremely low concentrations. Some limited studies with cupric octanoate are also reported. The latter metal cation appears to react in a more complex manner than ferric ions.

In a previous paper, it was demonstrated that insoluble metal oxides are capable of oxidizing thiols to disulfides in nonpolar media at low temperatures.[2] It was also established that the rate-determining step was adsorption of the thiols on the surface of the metal oxide. Oxidation studies in the presence of an olefin indicated that the reactions were radical in nature. We have now extended this study to the oxidation of thiols by soluble metal salts in xylene solution. Such a study is of interest since oxidation–reduction reactions between thiols and soluble metals have been primarily carried out in aqueous alkali.[3] Several recent studies, in addition to our metal oxide work, suggest that thiol-soluble metal reactions will occur under mild conditions. It has recently been demonstrated that ferric chloride is capable of monitoring the chain length in vinyl polymerizations.[4] This is due to reactions of type 1.

$$R_n \cdot + FeCl_3 \longrightarrow \text{polymer} + FeCl_2 \qquad (1)$$

Similarly, it has been demonstrated that cuprous chloride is an efficient catalyst for the selective (75–90%), low-temperature, autoxidative radical coupling of phenyl acetylene[5] and acetylenic alcohols.[6] More significant is the fact that potassium ferricyanide, ferric chloride, and cupric o-toluate are capable of oxidizing phenols

to phenoxy radicals.[7–10] The resulting radicals dimerize to give bissemiquinones. The latter finding suggested that oxidative coupling of thiols by soluble metals should proceed readily in nonpolar media.

Results

The ability of ferric octanoate [Fe(Oct)₃] and cupric octanoate [Cu(Oct)₂] to oxidize thiols at low temperatures (35–55°) in xylene has been studied. The solvent was degassed and stored in a nitrogen drybox; all reaction mixtures were prepared in a nitrogen drybox; and the reaction vessel was thoroughly sealed to prevent contact with oxygen during the course of the reaction. Initially, the ability of ferric octanoate to promote the oxidative coupling of a series of thiols was determined. The reaction conditions employed and the results obtained are summarized in Table I. 1-Dodecanethiol, 1-hexadecanethiol, α-toluenethiol, o-toluenethiol, and benzenethiol were oxidized to their corresponding disulfides in yields of 75–93% over reaction periods of 2–30 hr. Isolation of each disulfide was carried out in a nitrogen drybox according to the technique described in the Experimental Section. All yields recorded in Table I are based on the amount of isolated disulfide. The structure of each disulfide was substantiated by either its melting point and mixture melting point with an authentic sample or by glpc comparison of retention times.

(1) This is paper 6 in a series of studies on oxidation–reduction reactions in the presence of transition metal catalysts.

(2) T. J. Wallace, *J. Org. Chem.*, **31**, 1217 (1966).

(3) D. S. Tarbell, "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1960, Chapter 10.

(4) W. I. Bengough, S. A. MacIntosh, and I. C. Ross, *Nature*, **200**, 567 (1963).

(5) A. S. Hay, *J. Org. Chem.*, **25**, 1275 (1960).

(6) H. A. Stansbury and W. R. Proops, *ibid.*, **27**, 320 (1961).

(7) C. D. Cook and B. E. Norcross, *J. Am. Chem. Soc.*, **78**, 3797 (1956).

(8) H. Musso, *Angew. Chem.*, **75**, 965 (1963).

(9) G. S. Hammond, L. R. Mahoney, and U. S. Naudi, *J. Am. Chem. Soc.*, **85**, 737 (1963).

(10) W. W. Kaeding, *J. Org. Chem.*, **28**, 1063 (1963).

TABLE I
SUMMARY OF THIOL COUPLING REACTIONS PROMOTED BY FERRIC OCTANOATE[a]

Thiol, moles	Fe(Oct)₃, mole	Time, hr	Mole % yield[b] of disulfide	RSSR mp, °C	Lit.[c] mp, °C
1-Dodecane, 0.025	0.025	19	90	32	32
1-Dodecane, 0.005	0.005	2	93[d]	..	...
Benzene, 0.025	0.025	27	80	60	61
α-Toluene, 0.025	0.025	27	75	70	71
o-Toluene, 0.025	0.025	30	92[d]	..	...
1-Hexadecane, 0.025	0.025	23	80	54	53–55

[a] Reaction conditions: 50 ml of xylene, 55°, N₂, 1000 rpm. [b] Mole of RSSR isolated/theoretical moles × 100. [c] E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. III, Chemical Publishing Co., New York, N. Y., 1960, p 362, *et seq.* [d] Determined by glpc.

thiol under these conditions adhered to reasonable second-order behavior when plotted according to a conventional second-order rate expression (see Figure 1). From the observed rate constants (see Table III) it is obvious that these reactions are extremely fast. When the α-toluenethiol reaction was carried out at 55°, the rate could not be measured. The extremely rapid rate at 35° deterred us from attempting to measure the rate of disappearance of an aromatic thiol. However, the data suggest that the oxidation–reduction step is second order in nature. Rapidity of reaction also hindered us from obtaining precise data on solvent effects. Some approximate data for the per cent conversion of 1-dodecanethiol in dimethylformamide and octanoic acid at 35° is given in Table IV. Since 75% thiol conversion was observed in 60–75 sec, it is obvious that solvent polarity does accelerate these reactions, but the exact magnitude of this effect could not be assessed.

The final aspect of this study was concerned with the oxidation of various thiols by cupric octanoate in xylene

TABLE II
ADDITION REACTIONS OF 1-DODECANETHIOL TO 1-DODECENE[a] CATALYZED BY FERRIC OCTANOATE

1-C₁₂H₂₅SH, mole	Fe(Oct)₃, mole	RSH/ Fe(Oct)₃	Time, hr	% convn of 1-C₁₂H₂₅SH	RSSR, mole	RSR, mole	RSSR/ RSR	% selectivity[b] of RSR
0.01	0.01	1	19	~100	4.41 × 10⁻³	0.21 × 10⁻³	21	4.5
0.01	0.0025	4	18	61	2.23 × 10⁻³	0.41 × 10⁻³	5.4	15.5
0.01	0.0001	10	18	42	1.30 × 10⁻³	0.96 × 10⁻³	1.4	42.5
0.01	5 × 10⁻⁴	20	18	30	0.10 × 10⁻³	1.42 × 10⁻³	0.07	93.4
0.01[c]	0.01	1	20	85	4.47 × 10⁻³	None	...	...

[a] Reaction conditions: 50 ml of xylene, 35°, N₂, 1000 rpm, olefin/1-C₁₂H₂₅SH = 10. [b] Mole of RSR/mole of RSR + mole of RSSR × 100. [c] Blank run, *i.e.*, no olefin present.

Studies were next carried out to confirm the anticipated radical nature of these reactions. The reaction of 1-dodecanethiol with ferric octanoate was studied in the presence of 1-dodecene in xylene at 35° under a nitrogen atmosphere (Table II). In each reaction a 10/1 mole ratio of olefin to thiol was employed and the mole ratio of thiol to ferric octoate was varied from 1 to 20. Per cent thiol conversions and product yields were determined by glpc with the aid of an internal hydrocarbon standard. As the thiol/ferric octanoate ratio was increased from 1 to 20, thiol conversion for an 18–20-hr reaction period decreased from 100 to 30%. Dodecyl sulfide and disulfide were produced in each reaction. As shown, the sulfide was formed in 4 to 93% selectivity as the thiol/ferric octanoate ratio was increased. At the 20/1 ratio, it would appear that the reaction proceeds almost exclusively by a low-temperature, free-radical addition reaction. At a ratio of unity, the coupling reaction predominates over olefin addition which suggests that all radicals arise by a reaction with the metal salt. The latter was substantiated by the fact that essentially a quantitative yield of dodecyl disulfide was obtained in the absence of the olefin.

Kinetic studies on these reactions were next undertaken in an effort to obtain some information on the reaction order and rate-determining step. The reaction conditions used for three low-temperature kinetic experiments are summarized in Table III. In each experiment, equivalent mole quantities of thiol and ferric octanoate were employed. The disappearance of each

TABLE III
SUMMARY OF KINETIC DATA FOR THIOL OXIDATIONS BY FERRIC OCTANOATE

Thiol[a]	Temp, °C, ±0.1°	Solvent	Mole/l.	k, l./mole sec[b]
α-Toluene	35	Xylene	6.58 × 10⁻²	7.50 × 10⁻¹
1-Dodecane	55	Xylene	6.54 × 10⁻²	2.38 × 10⁻¹
1-Dodecane	35	Acetone	6.54 × 10⁻²	5.83 × 10⁻²

[a] Initial concentration of thiol and ferric octanoate was equivalent. [b] The average deviation in these rate constants was ±5%.

TABLE IV
EFFECT OF POLAR SOLVENTS ON REACTION RATE

Thiol, moles	Fe(Oct)₃, moles	Temp, °C	Solvent, ml	% thiol remaining	Time, sec
1-Dodecane, 5 × 10⁻³	5 × 10⁻³	35 ± 0.1	DMF, 75	23.4	75
1-Dodecane, 5 × 10⁻³	5 × 10⁻³	35 ± 0.1	Octanoic acid, 75	28.3	60

and these data are summarized in Table V. These reactions were more complex than those observed with ferric octanoate. In all reactions, both sulfide and disulfide were produced. The same result was obtained in two experiments with cupric naphthenate. The ratio of sulfide to disulfide varied from about 1 to 2. In the presence of 1-dodecene, the ratio was about 3 indicating that some olefin addition had occurred. The reaction of four disulfides with cupric octanoate was also studied. In each case, the corresponding monosulfide was produced.
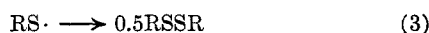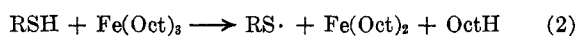
TABLE V

REACTIONS OF CUPRIC OCTANOATE WITH VARIOUS THIOLS AND DISULFIDES[a]

Reactant(s), mole	Cupric salt, moles	Reactant converted, %	Time, hr	RSSR, mole	RSR, mole
C_6H_5SH, 0.01	$Cu(Oct)_2$, 0.01	100	22.5	2.40×10^{-3}	2.61×10^{-3}
$1-C_{12}H_{25}SH$, 0.01	$Cu(Oct)_2$, 0.01	100	18.25	1.1×10^{-3}	2.6×10^{-3}
$1-C_{12}H_{25}SH$, 0.005	$Cu(Oct)_2$, 0.005	100	18	0.96×10^{-3}	1.77×10^{-3}
$1-C_8H_{17}SH$, 0.025	$Cu(Oct)_2$, 0.025	100	20	5.6×10^{-3}	6.1×10^{-3}
$1-C_{12}H_{25}SH$, 0.01 } $1-C_{12}H_{24}$, 0.10 }	$Cu(Oct)_2$, 0.01	100	18.5	0.85×10^{-3}	2.4×10^{-3}
$1-C_{12}H_{25}SH$, 0.005	$Cu(Naph)_2$, 0.005	100	18	0.46×10^{-3}	1.77×10^{-3}
$1-C_8H_{17}SH$, 0.005	$Cu(Naph)_2$, 0.005	100	18.5	0.56×10^{-3}	0.92×10^{-3}
$(1-C_{12}H_{25})_2S_2$, 0.0025	$Cu(Oct)_2$, 0.005	79	19	. . .	0.90×10^{-3}
$(1-C_8H_{17})_2S_2$, 0.0025	$Cu(Oct)_2$, 0.005	59	20.5	. . .	0.30×10^{-3}
$C_6H_5CH_2SH$, 0.005	$Cu(Oct)_2$, 0.005	100	18.5	1.0×10^{-3}	1.0×10^{-3}
$(C_6H_5CH_2)_2S_2$, 0.005	$Cu(Oct)_2$, 0.005	51	22	. . .	0.40×10^{-3}

[a] Reaction conditions: 50 ml of xylene, 35°, N_2, 100 rpm.

Discussion

The results summarized in Table I indicate that the reaction of thiols with ferric octanoate proceeds readily in xylene at mild conditions. Excellent yields of each disulfide were obtained. The disulfide most probably arises by an oxidation–reduction sequence between the thiol and ferric octanoate as shown in eq 2 and 3.

$$RSH + Fe(Oct)_3 \longrightarrow RS\cdot + Fe(Oct)_2 + OctH \quad (2)$$

$$RS\cdot \longrightarrow 0.5RSSR \quad (3)$$

The observed second-order kinetics (Figure 1) would indicate that reaction 2 is probably rate determining. The olefin addition studies with 1-dodecanethiol (Table II) establish unequivocally that the reaction is radical in nature. The sulfide must arise by a low-temperature, radical addition process involving thiyl radicals. Since sulfide selectivity increases as the thiol/ferric

$$RS\cdot + RCH\!\!=\!\!CH_2 \longrightarrow RSCH_2\dot{C}HR \quad (4)$$

$$RSCH_2\dot{C}HR + RSH \longrightarrow RSCH_2CH_2R + RS\cdot \quad (5)$$

octanoate ratio increases, the metal must function primarily as an initiator under these conditions. At a ratio of unity, the initial rate of thiyl radical production is so great that the dimerization step is maximized even though the olefin is in large excess. The rapid rate of thiyl radical production under these conditions also decreases the amount of thiol available for chain transfer (reaction 5).

The relatively high yields of disulfides and the radical nature of these reactions are not the major points of interest. Rather, we believe that the rapid rate observed in xylene is the most significant observation. Generally, it has been assumed that the oxidation of organic species by metal ions and complexes is most favorable in polar media.[11] Our results in dimethylformamide and octanoic acid are in agreement with this generalization. However, our rate studies indicate that these reactions are also extremely rapid in xylene. To date, this appears to be a unique observation. One possibly related study is that of Banks and co-workers.[12] In metal-catalyzed autoxidation studies on cyclohexene, these workers observed that Fe^{3+} and Cu^{2+} were more active catalysts in the olefin solution than in heptanoic acid solution. This could be due to the fact that the polar solvent is capable of stabilizing
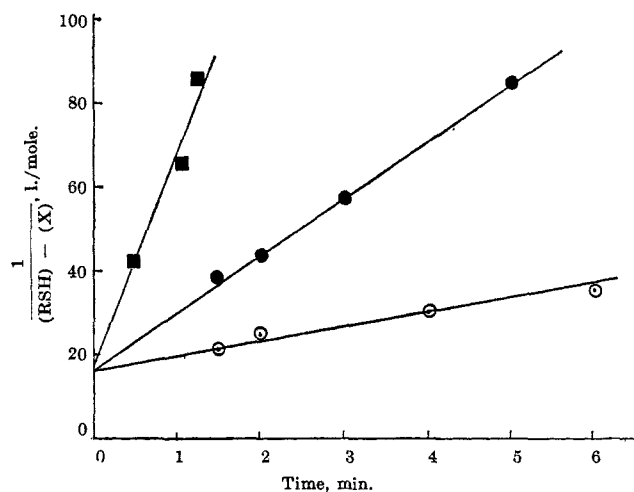

Figure 1.—Second-order rate plots for thiol oxidations by ferric octanoate: ■, $C_6H_5CH_2SH$ in xylene at 35°; ●, $1-C_{12}H_{25}SH$ in xylene at 55°; ⊙, $1-C_{12}H_{25}SH$ in acetone at 35°.

the higher oxidation states of these metals to a greater extent than the nonpolar solvent.

The rapidity of the oxidation–reduction reaction between thiols and ferric ions is also directly related to recent theories on the activity of metals in autoxidation reactions. Uri[13] has advanced the hypothesis that all autoxidation reactions are catalyzed by trace metals. A general conclusion is that metals may be active catalysts at concentrations as low as 10^{-7}–10^{-9} moles/l. Assuming that our second-order kinetics are valid, we have estimated the half-lives for the α-toluenethiol (35°) and 1-dodecanethiol (55°) oxidation reactions by Fe^{3+} at concentrations of 10^{-5}–10^{-7} moles/l. These results are summarized in Table VI. As indicated, reaction half-lives at these concentrations would vary from 2 days to 16 months in xylene and this is in good agreement with the conclusions of Uri.

TABLE VI

CALCULATED REACTION HALF-LIVES AS A FUNCTION OF CONCENTRATION

Thiol (°C)	Concn, moles/l	Half-life
α-Toluene (35)	10^{-5}	2 days
	10^{-7}	5 months
1-Dodecane (55)	10^{-5}	5 days
	10^{-7}	16 months

(11) For a review, see R. G. R. Bacon, Chem. Ind. (London), 19 (1962).

(12) G. L. Banks, et al., Nature, 174, 274 (1954).

(13) N. Uri, Advances in Chemistry Series, 36, American Chemical Society, Washington, D. C., 1962, Chapter 10, p 102, et seq.

Some comments on the results of our studies with cupric octanoate should also be made. In the presence of this metal, both sulfide and disulfide were produced from the thiols studied. Limited studies also indicate that disulfides react with cupric ions to produce sulfides. Obviously, disulfides must arise by the oxidation–reduction step. An alternative reaction path is the formation of unstable cupric thiolates which can decompose to cupric sulfide and sulfide (reaction 6)

$$Cu(SR)_2 \longrightarrow CuS + RSR \qquad (6)$$

For the disulfide, such intermediates could be produced by electrophilic attack of cupric ions on the disulfide linkage. At this point, such reactions are only possibilities. Our results clearly establish the need for further work in this area and demonstrate that the nature and complexity of the reaction may vary with the metal cation in question.

Experimental Section

Reagents.—1-Dodecanethiol, o-toluenethiol, and 1-hexadecanethiol were obtained from Columbia Organic Chemicals. Benzenethiol and α-toluenethiol were obtained from Evans Chemetics, Inc. Temperature-programmed gas chromatographic analyses on a 2-ft silicone rubber column (30 wt % silicone rubber on Chromosorb W) between 75 and 250° indicated that each thiol was at least 98% pure. All thiols were stored in a nitrogen drybox on a continuous basis. Ferric octanoate and cupric octanoate were purchased from the Shepherd Chemical Co. (Cincinnati, Ohio) as the ultrapure reagents. A suspension of cupric naphthenate (8% by weight) was generously supplied by Heyden Newport Chemical Corp.

Synthesis of Authentic Disulfides.—All authentic disulfides were synthesized from their corresponding thiols using the oxidation technique recently described by Wallace.[14] The thiol is added to an excess of dimethyl sulfoxide (DMSO) and the reaction mixture is heated at 100–160° overnight. The sulfoxide reduction product, dimethyl sulfide, easily distils from the reaction mixture as the reaction progresses because of its low boiling point (34°). On standing, the disulfides precipitate and may easily be purified by recrystallization from acetone or ethanol. The melting point of each disulfide synthesized by this technique agreed with that tabulated in Reid.[15]

General Procedure For Thiol-Soluble Metal Coupling Reactions.—A general procedure was employed for the thiol-soluble metal reactions listed in Tables I and V. The desired quantity of metal salt and degassed solvent were placed in a 100-ml four-necked flask in a nitrogen drybox. The flask was equipped with a sealed paddle stirrer. A tight-fitting, self-sealing Neoprene diaphragm was inserted into each neck of the flask. The diaphragm extended down from the neck of the flask and further sealing was accomplished by wrapping a heavy piece of copper wire around the outside of the diaphragm. This arrangement provided double protection against contamination by air. The sealed flask was then removed from the drybox and transferred to a constant-temperature bath. When thermal equilibrium was reached, a mixture of prethermostated thiol and internal standard was injected into the reaction flask and stirring was simultaneously initiated at 1000 rpm. Completeness of reaction or extent of reaction was determined by gc analysis using the internal hydrocarbon standard and predetermined molar response

factors.[16] Since the reactions were fast, aliquots were injected into pentane (at −30°) prior to analysis by gas chromatography. Upon termination of the reaction, the reaction flask was transferred to the nitrogen drybox, the mixture was filtered to remove the hydrocarbon layer, the inorganic layer (Fe(Oct)_2) was washed with xylene (3 volume excess) to remove any adsorbed or occluded product, and the filtrates were combined. Subsequent dilution with ethanol and storage in a cold box (0°) precipitated the disulfides which were collected by filtration and dried to a constant weight. The structure of each disulfide was confirmed by either its melting point and mixture melting point with the authentic disulfides prepared above or by gc comparison of retention times with that of the authentic compound. It should be noted that all disulfide yields were based on the amount of isolated product. Hence, the yields shown in the tables represent minimum values.

Thiol Addition Reactions To 1-Dodecene.—Reaction mixtures in the 1-dodecanethiol addition reactions to 1-dodecene were prepared in the manner described above. In these studies, a 10/1 mole ratio of olefin to thiol was employed and the mole ratio of thiol to metal salt was varied as shown in Tables II and V. Cetane (0.01 mole) was added at the beginning of each reaction as an internal standard for gc analysis. Using predetermined molar response factors, it was then possible to compute the amount of thiol converted and the amount of sulfide and disulfide formed from each peak on the gas chromatograph at the end of the reaction. The glpc unit employed in these analyses was an F & M Model No. 609 flame ionization gas chromatograph equipped with a Minneapolis Honeywell recorder and a Disc Integrator (Model No. 201). The injection port of the unit was maintained at 305° and the inlet pressure of helium was 36 psig. The block of the detector was maintained at a constant temperature of 245°. The helium flow through the column was 100 ml/min when measured at room temperature with a flow meter. All quantitative data were obtained on a 3-ft, 20 wt % Carbowax (20 mm) on Chromosorb W column (0.25-in. stainless steel tubing). This column gave excellent separation of all mixtures used in the present study.[17]

Related Gas Chromatography Data.—In the above studies and in the rate studies listed in Tables III and IV, a series of molar response factors between the compound(s) of interest and its corresponding internal standard were computed. These values are summarized in Table VII.

TABLE VII

SUMMARY OF GAS CHROMATOGRAPHIC CONDITIONS

Reactant measured	Internal standard	Response factor	Preferred column temp, °C
1-Dodecanethiol	Cetane	1.41	185
Dodecyl sulfide	Cetane	1.20	225
Dodecyl disulfide	Cetane		290
α-Toluenethiol	Diphenylmethane	1.87	200
Benzenethiol	Toluene	1.15	200
o-Toluenethiol	o-Xylene	1.24	210

The competition studies on coupling and olefin addition reactions were carried out with 1-dodecanethiol because of the thermal stability of the resulting disulfide.

(14) T. J. Wallace, *J. Am. Chem. Soc.*, **86**, 2018 (1964).
(15) E. E. Reid, "Organic Chemistry of Bivalent Sulfur Compounds," III, Chemical Publishing Co., New York, N. Y., 1960, p 395.

(16) For a discussion on the significance of molar response factors, see A. E. Messner, D. M. Rosie, and P. A. Argabright, *Anal. Chem.*, **31**, 230 (1959).
(17) For other applications, see T. J. Wallace and J. J. Mahon, *Nature*, **201**, 816 (1964).