Co-oxidation reactions in the benzenethiol-indene-2,5-dimethylpyrrole system in the presence and in the absence of tertiary alkyl primary amines. Primene 81-R (a mixture of C_{12-15} tertiary alkyl primary amines supplied by the Rohm and Haas Co.) was added to *n*-heptane solutions containing benzenethiol, indene, and 2,5-dimethylpyrrole. The test solutions (300 ml. each) were aerated for 6 hr. at room temperature and the following observations were made:

Benzenethiol, Indene, 2,5-Dimethylpyrrole, (Mole/L., Each)	Primene 81-R, (Mole/L.)	Thiol Oxidized, %	Peroxide Formed	Color of Solution	Precipitate, (G./100 Ml.)
0.30	Nil	68	Yes	Red	3.5 (Red oil)
0.30	0.03	56	No	Colorless	1.3 (Colorless crystals)[a]
0.01	Nil	75	Yes	Red	0.2 (Red solid)
0.01	0.001	53	No	Colorless	None

[a] Identified as *trans*-2-phenylmercapto-1-indanol.

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[CONTRIBUTION FROM THE CHEMICAL RESEARCH DEPARTMENT, MEDICINAL DIVISION, MALLINCKRODT CHEMICAL WORKS]

Preparation of Dithiooxamide Derivatives

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A number of *N,N'*-disubstituted dithiooxamides were synthesized by two methods: (1) reactions of aliphatic primary amines or the salts of amino acids with dithiooxamide; (2) treatment of an oxamide with phosphorus pentasulfide. *N,N'*-Disubstituted dithioxamides containing carboxyl or hydroxyl groups underwent esterification reactions without alteration of the thioamido grouping. Several polymeric dithiooxamides were obtained by the reactions of diamines with dithiooxamide. Limitations to the use of the first method in the preparation of *N,N'*-disubstituted dithiooxamides were found. Infrared spectra of *N,N'*-disubstituted dithiooxamides are reported for the first time and discussed.

Relatively few dithiooxamides are recorded in the chemical and patent literature, but an extraordinarily wide range of applications has been claimed for them. They have shown promise as effective metal deactivators in petroleum products.[2] They have been found to act as vulcanization accelerators.[3] Several of them have demonstrated inhibiting actions on certain bacteria[4] and dehydrogenases[5] Dithiooxamide itself has been used in the syntheses[6] of fluorescent 2,2'-dithiazoles that may be useful histological agents.[7] Dithiooxamides characteristically form stable metal complexes[8] that have been shown to act as color sources in duplicating processes[9,10] and as molecularly oriented, dichroic stains in light-polarizing films.[11] The versatility of this class of compounds has prompted us to synthesize a number of new dithiooxamide derivatives, many of which are listed in the tables. Three synthetic routes were utilized to obtain these compounds: (1) condensation of primary aliphatic amines with dithiooxamide; (2) treatment of oxamides with phosphorus pentasulfide; and (3) esterification of either *N,N'*-bis(carboxymethyl)dithioxamide or *N,N'*-bis(2-hydroxyethyl)-dithiooxamide.

The general reaction of unsubstituted thioamides with primary aliphatic amines under mild reaction conditions, referred to hereafter as the Wallach reaction,[12] has often been used to prepare *N*-alkyl-

(1) Present address: Morton Chemical Company, Woodstock, Ill.

(2) R. W. Watson and C. M. Loane (to the Standard Oil Co. of Indiana), U.S. Patent 2,484,257, Oct. 11, 1949.

(3) R. A. Naylor and E. O. Hook (to the American Cyanamid Co.), U.S. Patent 2,723,969, Nov. 15, 1955.

(4) K. Liebermeister, *Z. Naturforsch.*, 5B, 79 (1950); G. Hagelloch and K. Liebermeister, *Z. Naturforsch.*, 6B, 147 (1951).

(5) J. G. Miller and T. M. Brody, *J. Pharmacol. Exptl. Therap.*, 121, 43 (1957).

(6) P. Karrer and H. C. Sanz, *Helv. Chim. Acta*, 27, 219 (1944); P. Karrer and H. C. Sanz (to the Hoffman-LaRoche Co.), Swiss Patent 238,517, Nov. 1, 1945.

(7) P. Karrer, P. Leiser, and W. Graf, *Helv. Chim. Acta*, 27, 624 (1944).

(8) R. N. Hurd, G. De La Mater, G. C. McElheny, and L. V. Peiffer, *J. Am. Chem. Soc.*, 82, 4454 (1960). *Cf.* R. N. Hurd and G. De La Mater, *Chem. Revs.*, 61, 45 (1961), for a review of the literature on the reactions of amines with thioamides.

(9) C. S. Miller and B. L. Clark (to the Minnesota Mining and Manufacturing Co.), U.S. Patent 2,663,656, Dec. 22, 1953.

(10) Ditto, Inc., British Patent 802,170, Oct. 1, 1958.

(11) W. F. Amon, Jr., and M. W. Kane (to the Polaroid Corp.), U.S. Patent 2,505,085, April 25, 1950.

(12) O. Wallach, *Ann.*, 262, 357 (1891).

or *N*-aralkylthioamides and *N,N'*-dialkyl- or *N,N'*-diaralkyldithiooxamides.[4,12-14] The recent discovery[15] that monothiooxamide reacts with various alkylamines to form the corresponding *N*-alkylmonothiooxamides, $H_2NCOCSNHR$, illustrates that the thioamides undergo this reaction more readily than amides.

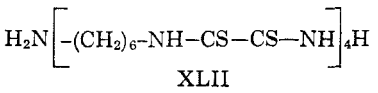
The preparative value of the Wallach reaction appears to be generally limited to the use of primary aliphatic amines. No *N,N'*-disubstituted dithiooxamide was isolated from reaction between dithiooxamide and any one of several secondary, aliphatic amines, including diethylamine,[16] diethanolamine, and piperidine.[17]

Dithiooxamide was found to be unreactive toward primary aromatic amines under the conditions of the Wallach reaction. This may be explained by the lower basicity of aromatic amines. Pyrrole, a secondary amine with aromatic properties, also was unreactive with dithiooxamide. Monoamino acids did not react with dithiooxamide as their neutral zwitterions. In the form of their salts, however, they readily gave rise to the *N,N'*-bis(carboxyalkyl)dithiooxamides listed in Table II. These observations are in accord with the results of studies on the reactions of thioformamide with amino acids, where it was found that only those amino acids that are basic (*i.e.* that contained free amino groups) reacted readily with thioformamide.[17]

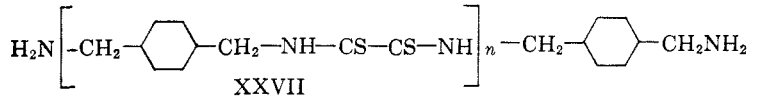
The Wallach reaction can result in the conversion of one *N,N'*-disubstituted dithiooxamide into another one. Thus, *N,N'*-dimethyldithiooxamide was transferred into the *N,N'*-dibutyl derivative by reaction with *n*-butylamine.[8] However, no reaction under the same conditions was observed between *N,N'*-dimethyldithiooxamide and cyclohexylamine. This latter result is in keeping with the behavior of cyclohexylamine in the preparation of V. Here, cyclohexylamine was observed to react more slowly with dithiooxamide than did primary amines without branching on their α-carbon atoms. Further, V was obtained in good yield only when the reaction mixture was warmed for an extended period. Steric hindrance of the nucleophilic attack of the amine at the thiocarbonyl carbon may be the explanation for the behavior of cyclohexylamine.

Evolution of hydrogen sulfide was noticed in all preparations of *N,N'*-disubstituted dithiooxamides *via* the Wallach reaction. Oxalamidines, $H_2N-C(=NR)-C(=NR)-NH_2$, were undoubtedly formed concurrently with hydrogen sulfide, but no effort was made to isolate them from the mother liquors.[18] Higher yields of the desired *N,N'*-disubstituted dithiooxamides were generally favored by mild reaction temperatures (*e.g.* usually below 50°).

Two primary aliphatic diamines reacted with dithiooxamide to yield pyridine-soluble products that are believed to be polymers of low molecular weight. Hexamethylenediamine and 1,4-cyclohexanebis(methylamine) reacted with dithiooxamide to yield pyridine-soluble, alcohol-insoluble polymers, XLII and XXVII, respectively. The application of the Wallach reaction to formation of



XLII



XXVII

polymers from α,ω-diamines has previously been noted.[2] The infrared spectrum of XXVII contained strong bands characteristic of primary aliphatic amino groups, suggesting that XXVII is a low molecular weight polymer terminating in such amino groups. The spectrum contained no bands attributable to the $-CSNH_2$ group.

Tetraethyldithiooxamide (XLI) and *p,p'*-dichlorodithiooxanilide (XL) were obtained by treatment of the corresponding oxamide and oxanilide, respectively, with phosphorus pentasulfide in boiling xylene. One failure of an oxanilide to react under these conditions was noted; on refluxing a xylene mixture of 4,4'-disulfooxanilide and phosphorus pentasulfide for eight hours, the oxanilide was unchanged. Failure of this reaction to occur may have been due to the insolubility of 4,4'-disulfooxanilide in refluxing xylene. It is not likely that lack of success was due to the presence of the electrophilic sulfo groups, since there have been reported examples in which an anilide with an electrophilic *p*-substituent was readily converted to the corresponding thioanilide under these conditions.[19]

In one experiment the product of an esterification, *N,N'*-bis(2-acetoxyethyl)dithiooxamide (XXXIX), was worked up in aqueous acidic medium without

(13) M. J. Schlatter, *J. Am. Chem. Soc.*, 64, 2722 (1942).

(14) H. M. Woodburn and C. E. Sroog, *J. Org. Chem.*, 17, 371 (1952).

(15) R. P. Welcher, M. E. Castellion, and V. P. Wystrach, *J. Am. Chem. Soc.*, 81, 2543 (1959).

(16) Diethylthioformamide was obtained by the reaction of formamide and phosphorus pentasulfide at elevated temperatures in the presence of diethylamine. K. Westphal and H. Andersag (to the Winthrop Chemical Co.), U.S. Patent 2,265,212, Dec. 9, 1941.

(17) Thioacetamide and piperidine have been reported to react in a nonpolar solvent, ether, to give *N*-(thioacetyl)-piperidine. F. Micheel, Z. Kraeminski, W. Himmelmann, and A. Kühlkamp, *Ann.*, 575, 90 (1952).

(18) Thioamides have often been used as sources of amidines. A. Bernthsen, *Ann.*, 184, 321 (1876); 192, 1 (1878).

(19) *N*-(4-Nitrophenyl)benzamide was readily converted in good yield to the corresponding thioamide under similar conditions. H. Rivier and J. Zeltner, *Helv. Chim. Acta*, 20, 691 (1937).

TABLE I

N,N'-DISUBSTITUTED DITHIOOXAMIDES

No.	RNHCSCSNHR R	Molecular Formula	Yield, %	Solvent[k]	M.P.	B.P.	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found	Chlorine, % Calcd.	Chlorine, % Found
				N,N'-Dialkyl-, *N,N'*-dicycloalkyl-, and *N,N'*-dialkenyldithiooxamides[a]								
I[b,d]	Isopropyl	$C_8H_{16}N_2S_2$	80	E	104.0–104.5[c]		13.73	13.03	31.37	31.90		
II[d]	Isobutyl	$C_{10}H_{20}N_2S_2$	57	E	32.5–33.5		12.05	11.93	27.59	27.60		
III[e,j]	Pentyl	$C_{12}H_{24}N_2S_2$	46		liquid[e]	139° (0.25 mm.)	10.76	10.60	24.62	24.34		
IV[j]	Hexyl	$C_{14}H_{28}N_2S_2$	40	E	16.4–18.0		9.71	9.43	22.23	22.50		
V[b,g]	Cyclohexyl	$C_{14}H_{24}N_2S_2$	67	E	149.0–149.5[f]		9.85	9.82	22.54	22.46		
VI[h]	Armeen-8D®	$C_{19.1}H_{38.2}N_2S_2$[h]	75	E	20		7.87	8.02	17.91	18.32		
VII[g]	Dodecyl	$C_{26}H_{52}N_2S_2$	92	E	50.3–51.3		6.13	5.60	14.03	14.20		
VIII[h]	Armeen-TD®	$C_{38.7}H_{79.2}N_2S_2$[h]	44	E	52–57		4.42	4.70	10.11	10.84		
IX[h]	Armeen-CD®	$C_{29.3}H_{58.6}N_2S_2$[h]	73	E	25–33		5.59	5.87	12.77	13.17		
X[g]	Octadecyl	$C_{38}H_{76}N_2S_2$	30	E	65.0–66.0		4.48	4.34	10.25	10.24		
XI	3-Hexylundecyl	$C_{28}H_{72}N_2S_2$	72			[i]	4.69	4.52	10.74	9.8[j]		
XII	1-Nonyldecyl	$C_{40}H_{90}N_2S_2$	37	M, E	40.0–41.0		4.29	4.45	9.81	9.30		
XIII	Allyl	$C_8H_{12}N_2S_2$	85				13.98	14.30	32.00	32.03		
				N,N'-Diaralkyldithiooxamides[a]								
XIV	Benzyl	$C_{16}H_{16}N_2S_2$	74	A	120.2–120.8[l]		9.33	9.08	21.34	21.28		
XV	D,L-α-Methylbenzyl	$C_{18}H_{20}N_2S_2$	59	E	52.8–94.5[n]		8.53	8.54	19.52	20.04		
XVI	*o*-Chlorobenzyl	$C_{16}H_{14}N_2S_2Cl_2$	52	B	131.0–132.0				17.36	16.98	19.20	19.04
XVII	*p*-Chlorobenzyl	$C_{16}H_{14}N_2S_2Cl_2$	60	B	164.5–166.5				17.36	17.10	19.20	19.02
XVIII	*p*-"Dodecyl"benzyl[m]	$C_{40}H_{64}N_2S_2$	78	[i]	[i]		4.39	4.86	10.06	9.43		
XIX[g]	Phenethyl	$C_{18}H_{20}N_2S_2$	69	E	115.0–115.7		8.55	8.40	19.52	19.95		
				N,N'-Diheterocyclicdithiooxamides[a]								
XX	Furfuryl	$C_{12}H_{12}N_2O_2S_2$	71	E	54.5–56.5		10.00	9.51	22.90	23.40		
XXI	2-Pyridylmethyl	$C_{14}H_{14}N_4S_2$	84	[i]	192.8–194.3		18.52	18.48[i]	21.21	21.40		
XXII	3-Pyridylmethyl	$C_{14}H_{14}N_4S_2$	54	[i]	185.5–187.5		18.52	19.18[i]	21.21	21.08		
				N,N'-Bis(aminoalkyl)dithiooxamides[a]								
XXIII	2-(Dimethylamino)ethyl	$C_{10}H_{22}N_4S_2$	57	E	97.6–98.2		21.35	21.02	24.44	24.15		
XXIV	3-(Dimethylamino)ethyl	$C_{16}H_{26}N_4S_2$	60	E	44.8–46.6		19.32	19.06	22.20	22.26		
XXV	2-(*N''*-Ethyl-*m*-toluidino)ethyl	$C_{24}H_{34}N_4S_2$	85	E	104.5–106.0		12.63	12.36	14.44	14.61		
XXVI[o]	2-(α-Naphthylamino)ethyl	$C_{26}H_{26}N_4S_2$	44	P	200.3–201.3		[o]	[o]	13.98	14.00		
				N,N'-Bis(hydroxyalkyl)- and *N,N'*-Bis(alkoxyalkyl)dithiooxamides[a]								
XXVIII	2-Hydroxypropyl	$C_8H_{16}N_2O_2S_2$	35	M, PE-E	98–101		11.85	11.47	27.13	27.70		
XXIX	Glucityl[39]	$C_{14}H_{28}N_2O_{10}S_2$	48	M[i]	154.4–155.4		6.23	6.13	14.23	14.14		
XXX	3-Methoxypropyl	$C_{10}H_{20}N_2O_2S_2$	74	M	44.0–46.5		10.59	10.28	24.25	24.19		

TABLE I (*Continued*)

No.	RNHCSCSNHR R	Molecular Formula	Yield, %	Solvent[k]	M.P.	B.P.	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found	Chlorine, % Calcd.	Chlorine, % Found
				Dithiooxamides Containing Ester Groups								
XXXVII	Carbethoxymethyl	$C_{10}H_{16}N_2O_4S_2$		E	131.5–133.5		9.58	9.64	21.93	21.52		
XXXVIII[p]	Dodecyloxycarbonylmethyl	$C_{30}H_{56}N_2O_4S_2$		[i]	93.4–94.8			[p]		[p]		
XXXIX	2-Acetoxyethyl	$C_{10}H_{16}N_2O_4S_2$		E	70.8–71.4		9.57	9.30	21.91	22.35		
				Dithiooxamides from Oxamides								
XL[s]		$C_{14}H_{10}N_2S_2Cl_2$	82	A-E	176.0–177.0[r]		8.21	8.05	18.79	18.91	20.78	20.26
XLI	$(C_2H_5)_2NCSCSN(C_2H_5)_2$	$C_{10}H_{20}N_2S_2$	35[q,i]	E	88–90		12.06	11.96	27.59	27.22		

[a] These compounds were prepared by the Wallach reaction. [b] Naylor and Hook prepared this compound by the reaction of glyoxal, sulfur, and the appropriate amine. [c] I: m.p. 101°.[3] [d] This compound was claimed[2] to result from heating to 200°F a mixture of the appropriate amine and dithiooxamide. No experimental details were given. [e] Wallach[12] reported that III was a solid (red prisms), m.p. 60°. [f] V: m.p. 145–147°[3]; m.p. 156–158°.[24] [g] This compound was claimed in poor yield by the reaction of the appropriate amine, sulfur, and a vinyl ether[24]. [h] Descriptions of Armeen® amines are given in Ref. 31. [i] See Experimental section. [j] n_D^{24}: III, 1.5533; IV, 1.5444. [k] Recrystallizing solvent: A = acetone, B = benzene, E = ethanol, M = methanol, P = 3-pentanone, PE-E = petroleum ether–ethanol. [l] XIV: m.p. 115°.[12] [m] The term "dodecyl" is used here in a statistical sense. See the Experimental section for information on the precursor (Conoco® DBCL) to XVIII. [n] The wide m.p. range of XV is a consequence of its two like asymmetric carbon atoms that give rise to racemic and *meso* forms. [o] Calcd.: C, 68.09; H, 5.71. Found: C, 67.86; H, 5.30. [p] Calcd.: C, 62.95; H, 9.78. Found: C, 62.98; H, 9.35. [q] Over-all yield from oxalyl chloride. [r] XL: m.p. 172°.[3,5] XL was reported[4] to result from the reaction of trichloroethylene, *p*-chloroaniline, and sulfur.

TABLE II

Dithiooxamides Containing Carboxyl Groups[a]

No.	RNHCSCSNHR R	Molecular Formula	Yield,[a] %	Aminoacid or Its Precursor	Solvent[d]	M.P.	Neutral Equivalent Calcd.	Neutral Equivalent Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
XXXI[b]	1-Carboxyethyl	$C_8H_{12}N_2O_4S_2$	32	α-Alanine	M	221–223 (d)[b]	132	130	10.60	10.32	24.26	23.80
XXXII	1-Carboxypropyl	$C_{10}H_{16}N_2O_4S_2$	59	D,L-α-Aminobutyric acid	Aq. M	219 (d)	146	150	9.58	9.07	21.93	22.34
XXXIII	3-Carboxypropyl	$C_{10}H_{16}N_2O_4S_2$	41	2-Pyrrolidone	E	161.0–162.5	146	141	9.58	9.60	21.93	21.86
XXXIV	1-Carboxybutyl	$C_{12}H_{20}N_2O_4S_2$	67	D,L-α-Aminovaleric acid	E	208.0–209.5	160	152	8.74	8.56	20.01	19.78
XXXV	5-Carboxypentyl	$C_{14}H_{24}N_2O_4S_2$	47	ε-Caprolactam[e]	A	137.5–139.0	174	172	8.04	7.32	18.40	18.19
XXXVI	2-Sodiosulfoethyl	$C_6H_{10}N_2Na_2O_6S_2$	99	Taurine	W	[c]			7.36	7.30	33.72	33.90

[a] Compounds XXXI–XXXVI (inc.) were prepared by reaction of dithiooxamide with the sodium salts of amino acids in water. [b] M. P. Doerner[25] similarly prepared XXXI, but reported a m.p. of 213–218°. [c] XXXVI, a salt, undergoes no decomposition below 300°. [d] Recrystallizing solvents: M = methanol. aq. M = aqueous methanol. E = ethanol. A = acetone. W = water. [e] ε-Caprolactam was hydrolyzed according to the procedure of Eck.[26]

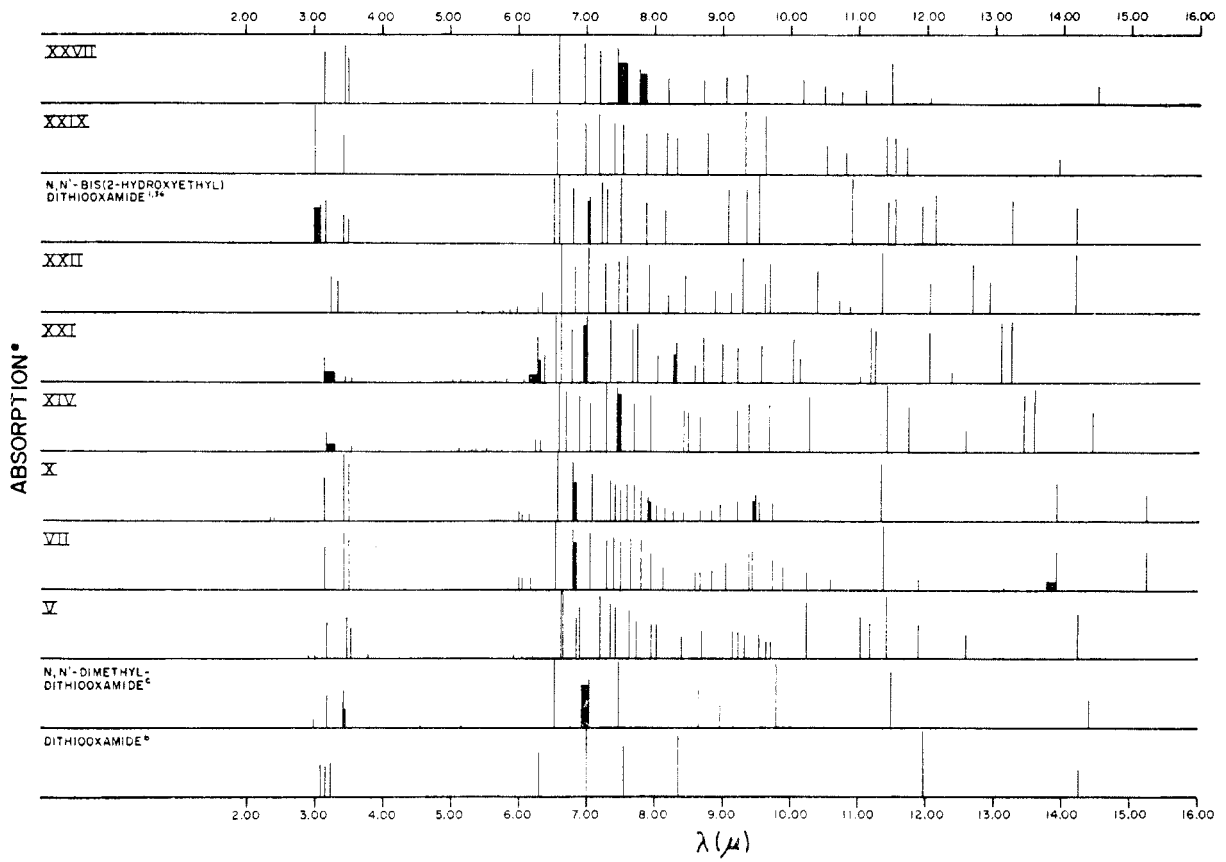


Fig. 1.[23] Infrared spectra of dithiooxamide samples prepared in KBr pellets. [a] Characteristic absorption bands for each spectrum. The heights of the vertical lines indicate the strengths of the absorption bands. Shoulders due to weak bands partially overlapping strong bands are indicated by black areas. [b] Dithiooxamide was prepared according to the procedure of G. DeLaMater, U. S. Patent 2,732,401. This spectrum, included for comparative purposes, was first reported by T. A. Scott, Jr., ref. 22c. [c] Ref. 12.

excessive loss in yield due to hydrolysis of the thiocarbamido groups.[20,21]

The infrared spectra of a number of dithiooxamides are summarized in Figures 1 and 2. The spectra presented here are the first spectra known to us that have been published for *N,N'*-disubstituted dithiooxamides (with the exception of some metallic complexes of dithiooxamide[22a]). Comparison of these spectra shows the presence of two bands in each spectrum that may be due to vibrations of the —NCS group.[23] One band lies in the region 6.51–6.70 μ. The other band occurs in the region 11.09–11.51 μ in most of the spectra; in some cases, however, it is absent in this region, and when this occurs a band appears in the region 8.30–9.10 μ. These bands all represent strong absorptions. As the band in the 6.51–6.70 μ region moves to longer wave lengths the band in the 11.09–11.51 μ region moves to shorter wave lengths.

The spectrum of dithiooxamide has been studied[22c] recently, but, in general, the absorptions of the —NCS group remain one of the less-studied aspects of infrared spectroscopy. Several recent references are cited[22] that specify —NCS group assignments in other types of thioamides.

EXPERIMENTAL[27–29]

General procedure for the preparation of N,N'-disubstituted dithiooxamides listed in Table I by the Wallach reaction.[30]

(20) Dithiooxamide is hydrolyzed in boiling dilute hydrochloric acid to oxalic acid, ammonium chloride, and hydrogen sulfide. C. Völckel, *Ann.*, **38**, 314 (1941).

(21) In comparison, thiobenzoylglycine, $C_6H_5CSNHCH_2COOH$, was hydrolyzed in warm acid to hippuric acid, thiolbenzoic acid, glycine, and hydrogen sulfide. A. Kjaer, *Acta Chem. Scand.*, **4**, 1347 (1950).

(22) (*a*) J. R. Barceló, *Spectrochim. Acta*, **10**, 245 (1958). (*b*) M. Davies and W. J. Jones, *J. Chem. Soc.*, 955 (1958). (c) T. A. Scott, Jr., Ph. D. thesis, State College of Washington, 1957. (*d*) E. Spinner, *J. Org. Chem.*, **23**, 2037 (1958). These references cite additional literature on the subject of the infrared spectra of thioamides.

(23) We are indebted to Miss Ella M. Bettinger and Mr. B. D. Field, Department of Chemical Control, Mallinckrodt Chemical Works, for obtaining the spectra given in Figures 1 and 2, and for this discussion of the characteristics of these spectra.

(24) C. L. Levesque (to the Rohm & Haas Co.), U. S. Patent 2,525,075, Oct. 10, 1950; U. S. Patent 2,531,283, Nov. 21, 1950.

(25) M. P. Doerner (to The Dow Chemical Co.), U. S. Patent 2,830,058, April 8, 1958.

(26) J. C. Eck, *Org. Syntheses*, **17**, 7 (1937).

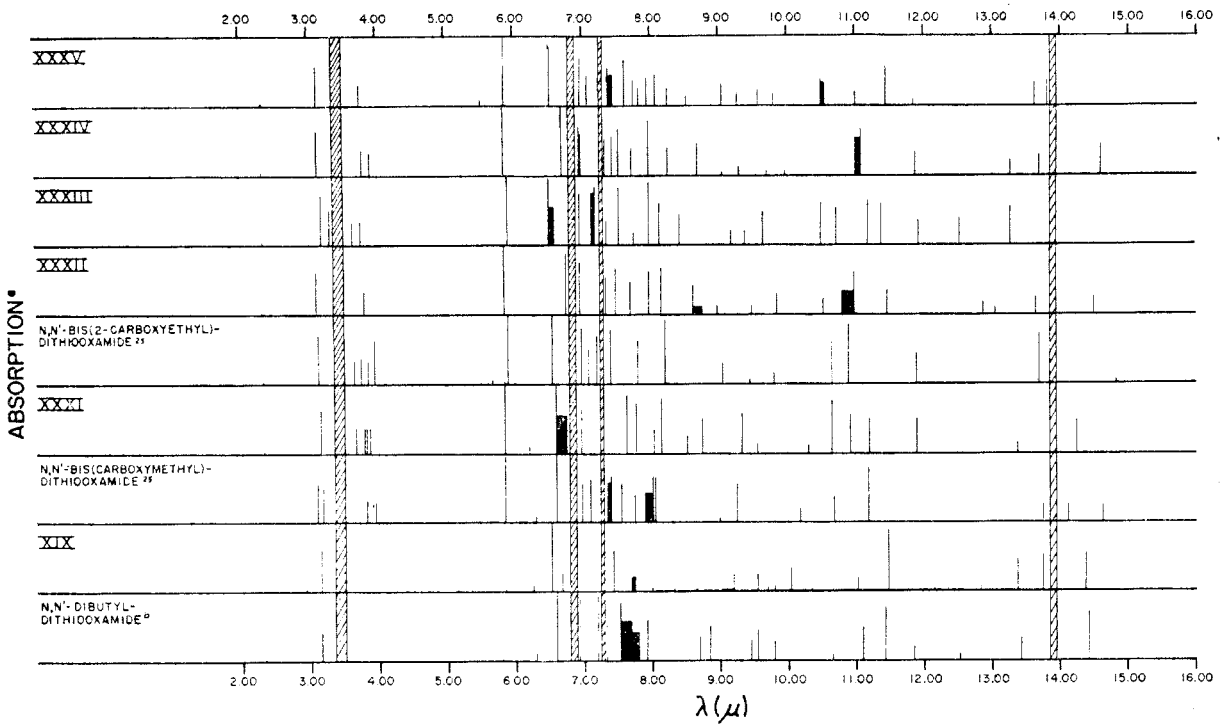


Fig. 2.[23] Infrared spectra of dithiooxamide samples prepared in Nujol® mulls. [a] Fig. 1, footnote *a*. [b] M. P. Doerner, U. S. Patent **2,772,309**. [c] The four shaded columns represent spectral regions where absorption due to Nujol® masks absorptions of the compounds.

Reaction was initiated by the addition of one molar equivalent of dithiooxamide and two molar equivalents of a primary aliphatic amine to 95% ethanol stirred at room temperature in the flask. An easily stirred slurry, with a volume convenient for laboratory operations, was usually obtained by the use of 400 ml. of ethanol per 100 g. of dithiooxamide. The Wallach reactions were slightly exothermic, but in no case did the temperature of the reaction mixture rise above 35°. In the preparations of V and XXVI the yields were much improved if the reaction mixtures were warmed (50°) for several hours. The freshly-prepared slurries were stirred for several hours and then left to stand overnight at room temperature.

In the cases of the solid products, the appearance of the solid in each slurry changed gradually from that of dithiooxamide to that of the product. The solid products were filtered off and purified by recrystallization from the solvents given in the tables. Generally, recrystallization was accompanied by treatment with charcoal. All of the solid *N,N'*-disubstituted dithiooxamides were readily dried over phosphorus pentoxide *in vacuo* (0.1 mm.) in the course of a day. The lower melting ones were dried at room temperature, the higher melting ones at 65°. In the cases of the liquid *N,N'*-disubstituted dithiooxamides the reaction mixtures became homogeneous or the products separated as second liquid phases.

(27) Carbon, hydrogen, and Dumas nitrogen analyses were performed by the Clark Microanalytical Laboratory, Urbana, Ill. All other analytical results and the infrared spectra were obtained by the Department of Chemical Control, Mallinckrodt Chemical Works.

(28) All melting points are corrected.

(29) We are grateful to F. E. Borton for the preparation of X, P. J. Hartman for XXXV, D. E. Hudgin for V, and L. A. Patterson for XXIII and XXVI.

(30) Experimental details for the individual compounds of Tables I and II will be described only when they are in addition to the data given in the Tables and significantly different from the general procedure.

Important experimental details not covered in the general procedure or given in Table I are summarized below for individual compounds.

III.[12] The product, soluble in the mother liquor, was isolated and purified by vacuum distillation.

IV. The product, soluble in the mother liquor, was conveniently isolated by precipitation at 2°.

VI. Crude VI, obtained as a liquid layer under the mother liquor, was transformed into yellow crystals by alcohol dilution of the crude liquid following a chilling to induce precipitation.

XII. Crude XII, obtained as a viscous oil by removal of ethanol from the mother liquor, was transformed to a yellow solid by trituration with methanol.

XIII. This product was obtained as a liquid red residue by distillation of all material volatile below 140° (2.2 mm.) from the reaction mixture. Decomposition of XIII occurred below its boiling point *in vacuo*.

XXI. It was recrystallized from 5:1 methyl isobutyl ketone–dimethylformamide, dimethylformamide, pyridine, and finally from dimethylformamide to obtain analytically pure material as yellow needles. It was necessary to analyze for nitrogen by the Dumas method, as the Kjeldahl procedure gave unreproducible, low results with XXI.

XXII. Dimethylformamide and two recrystallizations from 7:1 methyl isobutyl ketone-dimethylformamide were necessary to obtain yellow-orange, analytically pure, material. Like XXI, this compound also could not be analyzed for nitrogen by the Kjeldahl method.

XXIV. Crude XXIV was obtained from the reaction mixture as an oily solid by dilution of the mixture with water.

XXVI. Unlike most dithiooxamides, XXVI was quite insoluble in ethanol. It was soluble in benzene, acetone, and 3-pentanone. The last-named proved to be the best solvent for purification of XXVI.

XXVIII. Crude XXVIII was obtained as an oily residue by evaporation of ethanol from the reaction mixture. This residue solidified on trituration with methanol.

N,N'-Bis(3-hexylundecyl)dithiooximide (XI). The synthesis of XI involved the following four steps, A–D (inc.):

A. *7-(Bromomethyl)pentadecane* (XLIII). This new bromide was prepared by the reaction of 2-hexyl-1-decanol (Enjay Hexadecyl Alcohol, MD-206) and phosphorus tribromide. The reaction conditions used were those of Noller and Dinsmore,[32] except that XLIII was isolated from the reaction mixture by neutralizing it with sodium carbonate, breaking the resulting emulsion and extracting XLIII with benzene, washing the extract with cold, concentrated hydrochloric acid and water, and distilling volatiles from the washed, dried extract. After a final distillation XLIII (b.p. 114–118° (0.5 mm.)) was obtained in 43% yield.

Anal. Calcd. for $C_{16}H_{33}Br$: Br, 26.17. Found: Br, 25.7.

B. *3-Hexylundecanonitrile* (XLIV). This new nitrile was prepared by the reaction of XLIII and potassium cyanide, using the reaction conditions of Ruhoff.[33] After reaction was complete, the mixture was filtered from a white solid and volatiles were distilled from the filtrate under reduced pressure. Two fractions were collected by distillation of the resulting oily residue. From 1.50 moles of XLIII: (1) 115–119° (0.5 mm.), 226 ml.; (2) 115–119° (0.1–0.2 min.), 96 ml.

Anal. Calcd. for $C_{17}H_{33}N$: N, 5.57. Found: N, 4.55, (fraction 1); 5.10, (fraction 2); Br, 2.3, (fraction 1); 1.0, (fraction 2).

C. *3-Hexylundecylamine* (XIV). This new amine was obtained by lithium aluminum hydride reduction of XLIV according to the procedure of Amundsen and Nelson.[34] A 66% yield of XIV, b.p. 117–123° (0.65–0.85 mm.), $n^{25.5}_D$ 1.4497, was obtained.

Anal. Calcd. for $C_{17}H_{37}N$: N, 5.48. Found: N, 5.03.

D. *N,N'-Bis(3-hexylundecyl)dithiooxamide* (XI). A portion of the product separated as a liquid layer, and the remainder could be obtained by ether extraction of the mother liquor. The infrared spectrum of charcoal-purified XI showed slight contamination with XIV. The low sulfur analysis may be correlated with the appearance of infrared carbonyl absorption on the basis of hydrolysis.

N,N'-Bis(p-"dodecyl"benzyl)dithiooxamide (XVIII). The synthesis of XVIII involved the preparation of XLVII:

A. *N-(p-"Dodecyl"benzyl)phthalimide* (XLVI). The term "dodecyl" in the names of compounds XVIII, XLVI, and XLVII is placed in quotation marks to denote that it is being used in a statistical sense. This usage stems from the nature of the starting material, *p*-"dodecyl"benzyl chloride (Conoco® DBCL),[35] which is a mixture of products obtained by chloromethylation of "dodecyl"benzene.[36] "Dodecyl"-benzene is prepared by alkylation of benzene with "dodecene." "Dodecene" is a statistical mixture of polymers obtained by polymerization of propylene. The "dodecyl" group contains very little unsaturation and is attached to the benzene ring primarily at nonterminal positions.

XLVI was obtained in 86% yield from the reaction of *p*-"dodecyl"benzyl chloride and potassium phthalimide,[37] using Sheehan and Balhofers' modification of the Gabriel synthesis.[38] The product was a light yellow oil (347 g., 86%) that could not be crystallized. The infrared spectrum of this oil showed that it was slightly contaminated with dimethylformamide and very slightly so with chloroform. The presence of nitrogen and chlorine was also shown by sodium fusion tests.

B. *p-"Dodecyl"benzylamine* (XLVII). To a refluxing methanolic solution (250 ml.) of XLVI (347 g., 0.87 mole) was added 102 g. (1.73 moles) of 85% hydrazine hydrate solution, causing immediate precipitation of a white solid. The solid was filtered and washed with water. The wash solution was added to the mother liquor, causing separation into aqueous and organic liquid layers. The organic layer was separated, diluted with 250 ml. of methanol, and refluxed with an additional 1.73 moles of 85% hydrazine reagent. Again, a white solid precipitated. The solids were combined and dissolved in dilute hydrochloric acid. On warming the acidic solution, phthalhydrazide, m.p. 340–343° (corr.), precipitated. The acidic filtrate from phthalhydrazide was neutralized and extracted with ether. The combined ether extracts were dried, and then stripped of ether to give 105 g. of brown oil.

The oil was then distilled *in vacuo* through a heated column packed with Raschig rings. Three fractions of distillate were collected: (1), 115–128° (0.03–0.05 mm.), 36.0 g.; (2), 129–136° (0.06–0.08 mm.), 20.7 g.; (3), 124–144° (0.04–0.06 mm.), 12.1 g. A viscous residue (16.7 g.) remained.

The three fractions had similar refractive indices (n^{25}_D 1.5015–1.5059). Their infrared spectra indicated that they consisted primarily of XLVII. All three fractions gave positive Hinsberg tests for primary amines and faint positive tests for halogen by the sodium fusion method.

N,N'-Diglucityldithiooxamide (XXIX).[39] Glucamine was obtained in 93% yield by passage of an aqueous solution of glucamine oxalate[40] through an Amberlite® IRA-401 column prepared in the OH— form. The glucamine solution, collected under a nitrogen atmosphere, was concentrated to a small volume. Glucamine, m.p. 125–127°, precipitated after dilution of the concentrate with methanol and chilling the methanolic solution.

XXIX was prepared according to the general procedure. The crude product was isolated by adding to the reaction mixture enough methanol to bring it to the point of incipient precipitation; on chilling the saturated solution, crude, yellow XXIX precipitated.

XXIX possessed unusual solubility characteristics for a dithiooxamide. It was soluble in water, ethylene glycol and Cellosolve, but relatively insoluble in methanol, ethanol, ether, carbon tetrachloride and toluene.

General procedure for the preparation of dithiooxamides containing carboxyl groups.[30] An aqueous solution of two molar equivalents of an amino acid was first neutralized with a common inorganic base, and then treated with one molar equivalent of dithiooxamide. The resulting slurry was stirred and warmed to 50–60° until the bulk of the solid material had gone into solution. After cooling, the mixture was filtered from a small amount of solid material and the filtrate acidified with hydrochloric acid. Acidification caused precipitation of the crude product. The crude product was first purified by dissolving it in a warm alkaline solution containing charcoal, filtering the basic solution, and then acidifying the filtrate to precipitate the product. The product was then recrystallized from the solvent given in Table II.

N,N'-Bis(carbethoxymethyl)dithiooxamide (XXXVII). A mixture of *N,N'*-bis(carboxymethyl)dithiooxamide[25] (70.9 g., 0.30 mole), ethanol (400 ml.) and concd. sulfuric acid (7 ml.) was refluxed for 1 hr. On cooling the black reaction mixture, the crude, brown product precipitated. The mixture

(31) *The Chemistry of Fatty Amines,* Armour and Company, 1957, Table I, page 3.

(32) C. R. Noller and R. Dinsmore, *Org. Syntheses,* **Coll. Vol. II,** 358 (1943).

(33) J. R. Ruhoff, *Org. Syntheses,* **Coll. Vol. II,** 292 (1943).

(34) L. H. Amundsen and L. S. Nelson, *J. Am. Chem. Soc.,* **73,** 242 (1951).

(35) Trademark registered by the Continental Oil Company.

(36) The authors are grateful to Dr. James Kirk, Research and Development Laboratories, Continental Oil Company, Ponca City, Okla., for this information.

(37) P. L. Salzberg and J. V. Supniewski, *Org. Syntheses,* **Coll. Vol. I,** 2nd ed., 119.

(38) J. C. Sheehan and W. A. Balhofer, *J. Am. Chem. Soc.,* **72,** 2786 (1950).

(39) The term "glucityl" refers to the residue, $HOCH_2(CHOH)_4CH_2$—, obtained from glucamine.

(40) The authors are indebted to Dr. Albert Elder and Dr. G. N. Bollenback, Research Department, Corn Products Co., Argo, Ill., for a supply of glucamine oxalate.

was neutralized with triethylamine (18 ml.), and the solvent removed by distillation. The brown solid residue was purified by treatment with charcoal in hot ethanolic solution and recrystallization from ethanol.

N,N'-Bis(dodecyloxycarbonylmethyl)dithiooxamide (XXXVIII). A mixture of *N,N'*-bis(carboxymethyl)dithiooxamide[25] (23.6 g., 0.1 mole), 1-dodecanol (60 g., 0.3 mole) and hydrogen chloride (4.6 g.) was warmed (40–60°) for 1 hr. with frequent stirring. As it thickened it was diluted with 100 ml. of ethylene dichloride. From the mother liquor, separated by decantation and filtration at 25°, were obtained three more small crops by adding hydrogen chloride (*ca.* 5 g.) to the liquor and warming it for 45 min. at 40–60° for each crop. The combined solids were mixed with 1-dodecanol (150 ml.), and hydrogen chloride (5 g.) and then heated on the steam bath for 90 min. On cooling to 25° the liquor was removed by decanting and filtering. The filter cake was washed with ethanol (500 ml.) to remove 1-dodecanol, then crystallized from 700 ml. of 5:2 ethanol-ethylene dichloride to yield pure XXXVIII (42.6 g.) as lustrous, light orange plates.

N,N'-Bis(2-acetoxyethyl)dithiooxamide (XXXIX). *N,N'*-Bis(2-hydroxyethyl)dithiooxamide[2,41] (5.00 g., 0.018 mole) was dissolved in warm acetic anhydride (105 ml.). A drop of concentrated sulfuric acid was added, and the solution warmed for several minutes on the steam bath. It was then poured into 1 l. of ice water, whereupon the product gradually precipitated on hydrolysis of the excess anhydride. The crude material was recrystallized from ethanol to give 5.00 g. of XXXIX as bright yellow needles.

p,p'-Dichlorodithiooxanilide (XL).[4] Phosphorus pentasulfide (4.8 g., 0.02 mole) was added in small increments to a refluxing xylene solution (170 ml.) of *p,p'*-dichlorooxanilide[42] (10.0 g., 0.03 mole). The resulting mixture was refluxed for 5.5 hr. On cooling the reaction mixture, crude brown XL (9.0 g.) precipitated and was collected. By extraction of the mother liquor with 4% sodium hydroxide solution, followed by acidlfication of the extract with acetic acid, an additional 2.0 g. of crude XL was obtained. Pure XL was obtained by recrystallization of the crude material from an acetone-alcohol solvent mixture.

Tetraethyldithiooxamide (XLI). Tetraethyloxamide[43] was prepared by the slow addition of oxalyl chloride (86 ml., 1.0 mole) to a benzene solution (1000 ml.) of diethylamine (412 ml., 4.0 moles). After the reaction mixture had stood for several hours, diethylamine hydrochloride (88%, 193 g.) was filtered, and benzene was distilled *in vacuo* from the filtrate to leave 200 g. of crude brown oily tetraethyloxamide.

Phosphorus pentasulfide (89 g., 0.40 mole) was added in small increments to a refluxing xylene solution (1000 ml.) of this oil (200 g.). After the reaction mixture had been refluxed for 4 hr., it was cooled and filtered from a black, tarry residue. Xylene was removed *in vacuo* from the filtrate, whereupon crude XLI crystallized. The crude material was purified by treatment in hot ethanolic solution with charcoal and recrystallization from ethanol. Pure XLI was white, unlike any of the *N,N'*-disubstituted dithiooxamides reported in this study.

Polymeric product of reaction between dithiooxamide and hexamethylenediamine (XLII). A warm (50°) slurry of dithiooxamide (12.0 g., 0.10 mole) and hexamethylenediamine (11.6 g., 0.10 mole) in 200 ml. of ethanol was stirred for 3 hr., during which time the color of the mixture deepened from orange to tan. On cooling, 19.6 g. of crude XLII was collected by filtration. Crude XLII was recrystallized from a pyridine-ethanol solution to give pure XLII, m.p. 98–99°. XLII was insoluble in hot, concentrated hydrochloric acid and 50% alkali at room temperature.

Anal. Calcd. for $C_{32}H_{59}N_9S_8$: N, 15.25; S, 31.02. Found: N, 15.38; S, 31.32.

Polymeric product of reaction between dithiooxamide and 1,4-cyclohexanebis(methylamine) (XXVII). Warm, molten 1,4-cyclohexanebis(methylamine) (100 g., 0.70 mole) was added to a stirred ethanolic slurry (300 ml.) of dithiooxamide (84.5 g., 0.70 mole) over a period of 20 min., during which time the color of the mixture lightened to a pale yellow and the mixture became so thick as to be nearly unstirrable. Ethanol (225 ml.) was added, and the stirred mixture warmed to 54° for 1 hr. After cooling, the crude brown product was filtered. An aliquot (28 g.) of the crude XXVII was Soxhlet-extracted with ethanol for 2 days to obtain purified XXVII, which did not melt below 300°.

Anal. Calcd. for $C_{38}H_{66}N_8S_6$: N, 13.53; S, 23.24. Found: N, 14.25; S, 24.86.

XXVII had birefringence that disappeared on heating the solid to 200°, and which reappeared on cooling. XXVII did not melt, in the sense of becoming fluid, when heated to its decomposition point above 400°. However, a thin layer of XXVII, when heated to about 300° and subjected to moderate pressure, formed a film having a small measure of flexibility and toughness.

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(43) R. Barré, *Compt. rend.*, **185**, 1051 (1927).