795. *Esters and Derivatives of* N-*Substituted Dithiocarbamic Acids and* O-*Alkyl Hydrogen Dithiocarbonates.*

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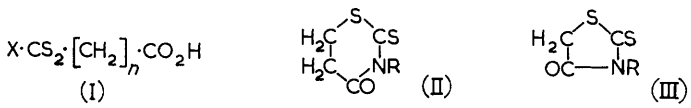
The preparation of a number of carboxyalkyl esters of *N*-substituted dithiocarbamic acids and *O*-alkyl hydrogen dithiocarbonates is described. β-(*N*-alkylthiocarbamoylthio)propionic acids (I; X = NHR, $n = 2$) were cyclised to 3-alkyltetrahydro-4-oxo-2-thiothiazines (II). The ultraviolet absorption spectra and stability of these compounds are compared with those of their *N*-aryl-substituted analogues.

FOR trial as fungicides a number of carboxyalkyl and carboxyalkenyl esters of *N*-substituted dithiocarbamic acids and similar derivatives of *O*-alkyl hydrogen dithiocarbonates have been prepared, together with some 3-alkyltetrahydro- and 3-alkyldihydro-4-oxo-2-thiothiazines. The preparation, stability, and ultraviolet absorption spectra of the carboxyalkenyl esters and their derivatives are to be discussed.[1]

All our ω-(*N*-alkylthiocarbamoylthio)alkanoic acids (I; X = NH_2, NHR, or NR_2) were synthesised by the interaction of ω-halogeno-alkanoic acids or the corresponding nitriles with salts of *N*-alkyldithiocarbamic acids. β-(Alkoxythiocarbonylthio)propionic acids (I; X = OR, $n = 2$), which previously have been prepared by the addition of *O*-alkyl hydrogen dithiocarbonates to propiolactone,[2] were prepared here by addition to acrylic acid. β-(*N*-Alkylthiocarbamoylthio)propionic acids (I; X = NHR, $n = 2$) were cyclised to 3-alkyltetrahydro-4-oxo-2-thiothiazines (II) by phosphorus trichloride. The preparation of compounds derived from *N*-aryldithiocarbamic acids has already been described.[3]



(I) (II) (III)

The instability of compounds derived from mono-*N*-substituted dithiocarbamic acids is thought to be important in their action as fungitoxicants.[4,5] The instability of thiazines, rhodanines, and certain esters of *N*-alkyldithiocarbamic acids has already received some attention.[5,6] In order to assess the contribution that instability makes to fungitoxicity, the fragmentation in an excess of absolute alcohol of some compounds was studied by observation of changes in the ultraviolet absorption spectra. In all cases the reaction was found to be unimolecular or pseudo-unimolecular.

Tetrahydro-4-oxo-2-thiothiazine and its 3-methyl homologue in absolute alcohol underwent ring fission forming products whose ultraviolet absorption spectra were identical with those of the corresponding β-(thiocarbamoylthio)propionic acids; since the ultraviolet absorption spectra of these acids are indistinguishable from those of their esters and the reaction took place in absolute alcohol, it is more probable that the products are ethyl β-(thiocarbamoylthio)propionates. 3-Methylrhodanine, on the other hand, was stable in solution. 3-Aryltetrahydro-4-oxo-2-thiothiazines also underwent rapid fragmentation, yielding aryl isothiocyanates. No evidence was found indicating the formation

[1] Garraway, *J.*, 1962, following paper.
[2] Farrar, *J. Org. Chem.*, 1958, **23**, 1065.
[3] Garraway, *J.*, 1961, 3733.
[4] Barratt and Horsfall, *Conn. Agr. Exp. Sta. Bull.*, 1947, **508**, 1; Cox, Sisler, and Spurr, *Science*, 1951, **114**, 643; Kerk and Klöpping, *Rec. Trav. chim.*, 1952, **71**, 1179; Ludwig and Thorn, *Plant Dis. Reports*, 1953, **37**, 121; Ludwig, Thorn, and Miller, *Canad. J. Bot.*, 1954, **32**, 48; Sijpesteijn and Kerk, *Biochim. Biophys. Acta*, 1954, **13**, 545; Ludwig, Thorn, and Unwin, *Canad. J. Bot.*, 1955, **33**, 42; Ludwig and Thorn, *Adv. Pest Control Res.*, 1960, **3**, 219.
[5] Kerk, *Mededel. Landbouwhogeschool Opzoekingsstas. Staat Gent*, 1956, **21**, 305.
[6] Kerk, *Rec. Trav. chim.*, 1955, **74**, 1262; Delaby, Damiens, and Seyden-Penne, *Compt. rend.*, 1956, **242**, 1482; Seyden-Penne, *Ann. Chim.* (*France*), 1958, **3**, 599.

of β-(*N*-arylthiocarbamoylthio)propionic acids as intermediates, these compounds undergoing rather slower decomposition to aryl isothiocyanates. 3-Arylrhodanines formed aryl isothiocyanates rather more rapidly than their thiazine analogues, but this was complicated by a secondary reaction thought to be with traces of acetaldehyde in the solvent. In general, the velocity constants of aryl-substituted compounds showed some dependence on the $\pm I$ effect of the nuclear substituent.

It appears, therefore, that the thiazole ring is potentially more stable than its thiazine analogue, possibly owing to the slightly strained nature of the latter. Instability in the thiazole ring of rhodanines is introduced by the presence of an aryl group at position 3. This is difficult to explain as the corresponding degree of instability is not introduced into thiazines and steric compression between the aromatic nucleus and the thion and the carbonyl group is thought, therefore, not to contribute to additional instability. Ring fission of 3-alkyltetrahydro-4-oxo-2-thiothiazines is probably initiated by the attack of a solvent molecule at the 4-carbon atom and terminated by combination of a proton with the nitrogen atom. The ring fission of the 3-aryl-rhodanines and -tetrahydro-4-oxo-2-thiothiazines proceeds similarly except that the electron gained by the intermediate is apparently no longer confined to the nitrogen atom; it is delocalised towards the thion-thio-grouping with stabilisation by the aromatic nucleus. This redirects the proton attack, resulting in fragmentation with formation of a thiol and aryl isothiocyanate. The close proximity of the carbonyl group, with its $+I$ effect, is probably sufficient to assist such a delocalisation in the intermediates formed from 3-arylrhodanines, thus hastening fragmentation. The instability of β-(*N*-arylthiocarbamoylthio)propionic acids is probably due to the labile nature of the hydrogen attached to the nitrogen atom, fragmentation proceeding as described above.

The intense ultraviolet absorption bands (log $\varepsilon > 3$) of all compounds in ethanol were recorded. Janssen [7] has discussed the ultraviolet absorption spectra of related compounds. All the carboxyalkyl esters of *N*-substituted dithiocarbamic and alkoxydithioformic acids exhibited the characteristic bands of their respective chromophores, which showed little difference in position and intensity from those for other esters. Increasing the size of the alkyl substituent caused the usual bathochromic shifts [1,7,8] which were somewhat larger for the dialkyl compounds. The larger wavelength interval between the two absorption bands of β-(thiocarbamoylthio)-propionic and -acrylic [1] acid suggests considerable tautomerism in compounds with an unsubstituted nitrogen atom. 3-Alkyltetrahydro-4-oxo-2-thiothiazines gave two bands, at longer wavelengths than for those of the parent acids, owing to resonance interaction with the carbonyl group. This shift is somewhat larger than for 3-alkylrhodanines, the size of the thiazine ring being more favourable for such resonance interactions.

The spectra of aryl-substituted compounds (Table 5) were more complex. In general, β-(*N*-arylthiocarbamoylthio)propionic acids gave two main bands, usually at longer wavelengths, indicating considerable resonance interaction between the chromophore and the aromatic nucleus. The assignment of the bands is probably the same as for the alkyl compounds, except for the long-wavelength band of β-(*N*-*p*-nitrophenylthiocarbamoylthio)propionic acid which has the features of a transition involving the substituted aromatic nucleus alone. The bands of *ortho*-substituted compounds were displaced hypsochromically, suggesting considerable steric interaction [9] with the sulphur atoms as steric interference with an amino-group is small.[10] The long-wavelength band of compounds having $+M$ nuclear substituents was never clearly defined and tended to occur at shorter wavelengths and to be less intense. This appears to correlate with the hyperconjugative effect of alkyl groups on electronic absorption spectra of thion compounds.

[7] Janssen, *Rec. Trav. chim.*, 1960, **79**, 454, 464.
[8] Svatěk, Zahradník, and Kjaer, *Acta Chem. Scand.*, 1959, **13**, 442; Zahradník, *Coll. Czech. Chem. Comm.*, 1959, **24**, 117.
[9] Braude, Sondheimer, and Forbes, *Nature*, 1954, **173**, 117.
[10] Wepster, *Rec. Trav. chim.*, 1957, **76**, 357; Forbes and Leckie, *Canad. J. Chem.*, 1958, **36**, 1371.

TABLE 1.

β-(*N*-Alkylthiocarbamoylthio)propionic acids (I; X = RR'N, *n* = 2).

R	R'	Method of prep.	M. p.	Yield (%)	Formula	Equiv. Found	Equiv. Reqd.	$\lambda_{max.}$ (mμ) and log ε			
H	H	A	124—125°	24	$C_4H_7NO_2S_2$	165·7	165·1	244	3·86	278	4·02
Me	H	A	85—86·5	39	$C_5H_9NO_2S_2$	180·8	179·1	250	3·92	273	4·01
Et	H	A	95—96	36	$C_6H_{11}NO_2S_2$	194·5	193·1	251	3·93	274	3·99
Pr^n	H	A	75—76	15	$C_7H_{13}NO_2S_2$	208·8	207·1	252	3·98	274	4·03
Pr^i	H	A	59·5—60·5	11	$C_7H_{13}NO_2S_2$	—	—*	253	3·93	274	3·98
Bu^n	H	A	83—84	27	$C_8H_{15}NO_2S_2$	221·9	221·1	253	3·99	275	4·03
Bu^i	H	A	75—77	25	$C_8H_{15}NO_2S_2$	221·2	221·1	252	3·96	274	4·01
Me	Me	A	143—145†	53	$C_6H_{11}NO_2S_2$	193·0	193·1	249	4·01	276	4·02
Et	Et	A	95—96	54	$C_8H_{15}NO_2S_2$	222·0	221·1	251	4·01	279	4·05
Pr^n	Pr^n	A	34·5—35·5	25	$C_{10}H_{19}NO_2S_2$	249·0	249·2	253	4·03	281	4·05
Pr^i	Pr^i	A	105—106	12	$C_{10}H_{19}NO_2S_2$	248·5	249·2	256	3·99	283	4·02
Bu^n	Bu^n	A	—‡	—	$C_{12}H_{23}NO_2S_2$	—	—	254	3·97	280	4·02
Bu^i	Bu^i	A	69·5—70·5	32	$C_{12}H_{23}NO_2S_2$	279·0	277·2	256	4·03	282	4·07
·[CH$_2$]$_4$·		A	169—170	36	$C_8H_{13}NO_2S_2$	220·6	219·1	249	4·06	276	4·08
·(CH$_2$)$_5$·		A	103·5—104·5	46	$C_9H_{15}NO_2S_2$	232·9	233·1	255	4·06	281	4·08

* Found: N, 6·9. Reqd.: N, 6·8% † Pluijgers (Thesis, Utrecht, 1959) gives m. p. 142—144°. ‡ Syrup, not purified.

TABLE 2.

ω-(*NN*-Dimethylthiocarbamoylthio)alkanecarboxylic acids (I; X = Me$_2$N).

n	Method of prep.	M. p.	Yield (%)	Formula	Equiv. Found	Equiv. Reqd.	$\lambda_{max.}$ (mμ) and log ε			
1	A	152—153°*	50	$C_5H_9NO_2S_2$	180·6	179·1	244	3·92	275	4·02
2	A	143—145*	53	$C_6H_{11}NO_2S_2$	193·0	193·1	249	4·01	276	4·02
3	B	96·5—98*	34	$C_7H_{13}NO_2S_2$	209·1	207·2	248	3·99	278	4·01
4	B	91·5—92·5	27	$C_8H_{15}NO_2S_2$	221·8	221·2	249	3·96	278	4·02
5	B	82—83·5	27	$C_9H_{17}NO_2S_2$	237·2	235·3	249	3·99	278	4·03
6	B	84—85	36	$C_{10}H_{19}NO_2S_2$	250·5	249·3	249	3·97	278	4·02

* Pluijgers (Thesis, Utrecht, 1959) gives m. p. (1) 145—146°, (2) 142—144°, (3) 96—97°.

TABLE 3.

β-(Alkoxythiocarbonylthio)propionic acids (I; X = RO, *n* = 2).

R	Method of prep.	M. p.*	Yield (%)	Formula	Equiv. Found	Equiv. Reqd.	$\lambda_{max.}$ (mμ) and log ε			
Me	A	†	19	$C_5H_8O_3S_2$	183·3	180·1	~220	—	280	4·01
Et	C	70—71°	33	$C_6H_{10}O_3S_2$	195·2	194·1	~220	—	282	4·09
Pr^n	C	53—55	24	$C_7H_{12}O_3S_2$	209·8	208·1	~220	—	281	4·10
Pr^i	C	42—43	34	$C_7H_{12}O_3S_2$	209·2	208·1	~220	—	282	4·10
Bu^n	C	37—38	18	$C_8H_{14}O_3S_2$	223·7	222·1	~220	—	282	4·11
Bu^i	C	53—54·5	34	$C_8H_{14}O_3S_2$	222·1	222·1	~220	—	282	4·11

* Farrar (*J. Org. Chem.*, 1958, **23**, 1065) gives: Me, syrup; Et, m. p. 70—71°; Pr^n, m. p. 50—53°; Bu^n, syrup. † B. p. 139°/0·7 mm.

TABLE 4.

3-Alkyltetrahydro-4-oxo-2-thiothiazines (II).

R	Method of prep.	M. p.	Yield (%)	Formula	Nitrogen (%) Found	Nitrogen (%) Reqd.	$\lambda_{max.}$ (mμ) and log ε			
H	D	120—121° *	10	$C_4H_5NOS_2$	9·5	9·5 ¶	258	4·12	309	4·14
Me	D	80·5—81·5	41	$C_5H_7NOS_2$	8·9	8·7	266	4·12	310	4·01
Et	D	65—66 †	40	$C_6H_9NOS_2$	7·8	8·0	268	4·16	313	4·11
Pr^n	D	25·5—26·5	55	$C_7H_{11}NOS_2$	7·5	7·4	269	4·16	313	4·11
Pr^i	D	47—49	65	$C_7H_{11}NOS_2$	7·4	7·4	269	4·11	314	4·06
Bu^n	D	‡	37	$C_8H_{13}NOS_2$	6·5	6·9	269	4·13	315	4·09
Bu^t	D	§	20	$C_8H_{13}NOS_2$	6·5	6·9	269	4·14	313	4·09

* Gresham, Jansen, and Shaver (*J. Amer. Chem. Soc.*, 1948, **70**, 1001) give m. p. 119—120°. † *Idem* (*ibid.*) give m. p. 65—66°. ‡ B. p. ~159—161°/3 mm. § B. p. ~142—143/1 mm. ¶ N-*Methylrhodanine* (III; R = Me), m. p. 69—70·5° (Found: N, 9·7. $C_4H_5NOS_2$ requires N, 9·5%), $\lambda_{max.}$ 259, 293 (log ε 4·20, 4·22).

TABLE 5.

Ultraviolet absorption maxima of aryl-substituted compounds ($\lambda_{max.}$ in mμ; also log ε).

	Acids (I; X = R·NH; n = 2)						Thiazines (II)				Rhodanines (III)			
C_6H_5	210—220	?	282	4·18	310 *	4·11	264	4·10	314	4·09	258	4·04	295	4·15
p-Me·C_6H_4	210—220	?	281	4·22	312 *	4·10	263	4·06	313	4·08	258	3·98	295	4·16
o-Cl·C_6H_4	—	—	250	3·93	281	4·08	—	—	—	—	—	—	—	—
m-Cl·C_6H_4	215—225	?	285	4·23	313 *	4·13	—	—	—	—	—	—	—	—
p-Cl·C_6H_4	215—225	?	283	4·25	318 *	4·08	262	4·17	314	4·16	257	4·05	296	4·16
2,4-$Cl_2C_6H_3$	—	—	258	4·04	278	4·12	259	4·17	312	4·08	253	4·11	294	4·19
m-NO_2·C_6H_4	~240	?	—	283	4·34	—	—	—	—	—	—	—	—	—
p-NO_2·C_6H_4	230—240	?	305	4·13	346	4·21	262	4·00	312	3·97	256	4·10	298	4·17
p-MeO_2C·C_6H_4	230—240	?	293	4·29	320	4·31	—	—	—	—	—	—	—	—
p-HO·C_6H_4	—	—	281	4·20	305 *	3·94	—	—	—	—	—	—	—	—
p-MeO·C_6H_4	—	—	282	4·20	305 *	3·49	—	—	—	—	—	—	—	—

* Shoulder.

TABLE 6.

Velocity constants (10^{-4} min.$^{-1}$) for the fragmentation for various *N*-alkyl and *N*-aryl compounds in absolute alcohol at 26°.

R:	H	Me	Ph	*p*-Me·C_6H_4	*p*-Cl·C_6H_4	2,4-$Cl_2C_6H_3$	*p*-NO_2·C_6H_4
Acids (I; X = R·NH; n = 2)	Stable	Stable	1·35	0·76	1·60	2·38	3·93
Thiazines (II)	10·0	43·0	14·3	9·7	41·9	30·5	41·8
Rhodanines (III)	—	Stable	39·0	65·0	270	235	167

The effects can be understood by assuming a transition crudely represented by $^{-}C(\cdot S^{-}){:}N^{+}\!\!\swarrow \longleftrightarrow {}^{-}C({:}S)\cdot N\!\!\swarrow$, although this can hardly operate by direct conjugation of the aromatic nucleus or group with the chromophore.

3-Aryl-tetrahydro-4-oxo-2-thiothiazines and -rhodanines gave very similar absorption spectra to their alkyl analogues, indicating absence of resonance interaction with the aromatic nucleus owing to steric interactions.

Carboxyalkyl esters derived from alkoxydithioformic acid were fungitoxic; derivatives of *N*-alkyldithiocarbamic acid were less so. Some *N*-aryl compounds had high fungitoxicity. Details will be published elsewhere.

Experimental

The *products* and the methods used in their preparation are listed in Tables 1—4. The following are examples of the methods.

β-(NN-*Dimethylthiocarbamoylthio*)*propionic Acid* (I; X = Me_2N, *n* = 2) (*Method* A).—Sodium dimethyldithiocarbamate (1·8 g.) was dissolved in water (40 ml.). Sodium β-chloropropionate (1·3 g.) in water (10 ml.) was added and the solution heated on a water-bath for 1 hr. After cooling, the solution was acidified, and the *product* filtered off and obtained as colourless needles by recrystallisation from water.

7-(NN-*Dimethylthiocarbamoylthio*)*heptanoic Acid* (I; X = Me_2N, *n* = 6) (*Method* B).—Sodium dimethyldithiocarbamate (1·8 g.) was refluxed with 7-bromoheptanonitrile (1·9 g.) in ethanol (25 ml.) for ½ hr. The ethanol was removed, water (20 ml.) added, and the oil extracted into ether. After removal of the ether, the nitrile was hydrolysed with hot concentrated hydrochloric acid (25 ml.) for 3 hr. The solution was cooled, and the *product* filtered off and recrystallised from 3 : 17 benzene–light petroleum as colourless plates.

β-(*Ethoxythiocarbonylthio*)*propionic acid* (I; X = EtO, *n* = 2) (*Method* C).—Potassium *O*-ethyl xanthate (1·6 g.) was dissolved in methyl alcohol (25 ml.), and acrylic acid (1·4 ml.) added slowly with cooling. The solvent was removed with air and the residue washed with water and dried. Crystallisation from light petroleum yielded the *product* as colourless needles.

Tetrahydro-3-methyl-4-oxo-2-thiothiazine (II; R = Me) (*Method* D).—β-(*N*-Methylthiocarbamoylthio)propionic acid (0·4 g.) was refluxed for 1 hr. with phosphorus trichloride (2·5 ml.). The excess phosphorus trichloride was removed by a stream of air and the residue extracted with ether. The ether was removed after being washed with sodium hydrogen carbonate solution, and the residue recrystallised from water as yellow plates.

The ultraviolet absorption spectra of all compounds in absolute alcohol were plotted in a S.P. 500 Unicam ultraviolet spectrophotometer.

The stabilities of the compounds were determined by plotting their ultraviolet absorption spectra at intervals. A solution (3—5 × 10^{-6}M) in absolute alcohol was kept in a thermostat-bath at 26·0° ± 0·2°. Samples were withdrawn at intervals and the absorption spectra plotted. From the plot of log I_0/I against time at a suitable wavelength, the slopes were measured and plotted against log I_0/I on a second graph from which the value of the velocity constant (k) for the fragmentation reaction was obtained. Results are shown in Table 6.

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