Aminolysis of Tertiary Alkyl Xanthates: a New Route to Dithiourethanes

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Summary Aminolysis of primary and secondary alkyl xanthate esters yields thioneurethanes (III), while dithiourethanes (IV) are formed, equally exclusively, by the aminolysis of tertiary alkyl xanthate esters.

THIOCARBONYL derivatives of amines have valuable analytical and synthetic uses, particularly in the amino-acid[1–5] and organometallic[6] fields. Their use in sequence analysis of polypeptides,[1] as intermediates in the preparation of volatile derivatives for the g.l.c. identification of amino acids,[2] and as chromophoric derivatives of chiral amines for o.r.d. and c.d. studies,[3] illustrates some analytical applications, while cyclisation products of analogously substituted amino acids are intermediates (*e.g. N*-thiocarboxylic anhydrides[4]) in newer methods of peptide synthesis.[4,5]

Whereas most methods of converting amines and amino acids into *N*-thioacyl, *N*-alkoxythiocarbonyl, and related thiocarbonyl derivatives involve their treatment with dithio-esters and similar compounds [*e.g.* xanthates (II)],[4] a lengthy two-step procedure is used[3a] for the conversion of amines into dithiourethanes (IV). We now report a simple new method for the preparation of dithiourethanes from amines, using a xanthate ester derived from a tertiary alcohol (II; R^3 = Bu^t or t-pentyl, R^4 = Me or Et). Previously,[4] the aminolysis of xanthate esters has been regarded as a high-yield route to thioneurethanes (III), facilitated by the expulsion of the good leaving group, the alkanethiolate anion. The aminolysis of xanthate esters derived from higher homologous alcohols has not been studied systematically before the present work, in which we show that the alternative reaction path, leading to dithiourethanes with the presumed expulsion of alkoxide anion, is followed by aminolysis of t-alkyl xanthate esters. An isolated precedent, the reaction of hydrazine with *S*-methyl t-butyl xanthate (II; R^3 = Bu^t, R^4 = Me), gives an oil, formulated[7] as the thioneurethane (III; $R^1 = NH_2$, R^2 = H, R^3 = Bu^t), and a crystalline product, $NH_2{\cdot}NH{\cdot}CS{\cdot}NH{\cdot}NH_2$; the present results provide a satisfactory

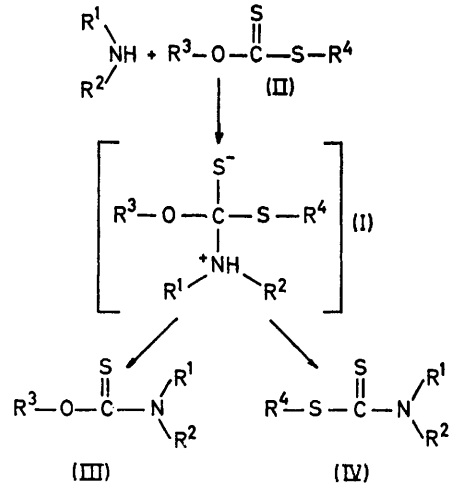
TABLE

Dithiourethanes (IV) *obtained by aminolysis of* S-*methyl and* S-*ethyl t-butyl* (*or t-pentyl*) *xanthates*

Amine	Dithiourethane		M.p. (°C)	Yield: %	C.d. data: $\Delta\epsilon$ (*ca.* 340 nm)
Dimethylamine	$RS{\cdot}CS{\cdot}NMe_2$	R = Me	47[a]	89	—
		R = Et	41—42	87	—
Piperidine	$MeS{\cdot}CS{\cdot}N[CH_2]_5$		32—34[a]	71	—
L-Alanine	(A)		85—87	24	−0·35 (Et_2O)
L-Leucine	(B)	R = Me	112	41	+1·06 (MeOH)
		R = Et	75	36	+1·78 (MeOH)
L-Proline	(C)	R = Me	94—96	60	+3·30 (Et_2O)
		R = Et	131—132	79	+1·57 (MeOH)
L-Thiazolidine-4-carboxylic acid	(D)		222[b]	79	+1·14 (MeOH)

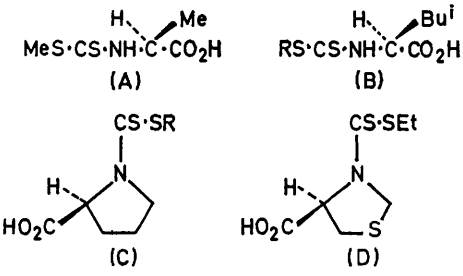
[a] In agreement with reported value, ref. 8 and L. Maier, *Helv. Chim. Acta*, 1970, **53**, 1216.
[b] M.p. (decomp.) and c.d. data refer to cyclohexylammonium salt.

interpretation of the formation of the latter product, since aminolysis of dithiourethanes is known[8] to give thioureas under such conditions.



SCHEME

In typical procedures, dithiourethanes are obtained by mixing the amine with *S*-methyl (or *S*-ethyl) t-butyl (or t-pentyl) xanthate,[9] or by dissolving an L-α-amino- or -imino-acid and the t-alkyl xanthate ester in 50% aqueous dioxan at pH 7—8, and working up after 12 h at room temp. Representative dithiourethanes prepared in this way (Table) were characterised by direct comparison with compounds obtained by reaction of the amine with carbon disulphide in alkaline solution, followed by alkylation with iodomethane or iodoethane, and supported by analytical and spectroscopic data for new compounds. In particular, L-α-amino- and -imino-acids gave products displaying a c.d. maximum centred near 340 nm, characteristic[3] of the dithiourethane chromophore, with $\Delta\epsilon$ values at least as large as those of the dithiourethanes prepared through the carbon disulphide–alkylation sequence, thus demonstrating high optical purity in the products of the one-step route.



The results suggest that the breakdown of the putative intermediate common to both reaction paths, shown in the Scheme, is determined by steric factors, the relief resulting from expulsion of a bulky alkoxy-group overriding the expulsion of the better leaving group, $-S\cdot R^4$. Yields of dithiourethanes by this route were low with primary amines (though in no case was a thione-ethane obtained), and high with secondary amines, tending to support the importance of steric factors in controlling reaction path. The recent report of the preparation of a sulphonyl analogue of a trithiocarbonate, *viz.* $R\cdot SO_2\cdot CS\cdot S\cdot R'$, states that these compounds yield dithiourethanes on aminolysis;[10] alkanesulphinate anion is evidently displaced here, in preference to the less bulky but more electronegative alkanethiolate anion, for steric reasons.

Our results suggest that t-alkyl xanthate esters may have additional synthetic applications, and that reactions of xanthates with nucleophiles may provide useful information on the breakdown of tetrahedral intermediates in analogous processes.

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