Complications in the Reactions of Tris(thio)methyl-lithium Derivatives with δ-Valerolactone

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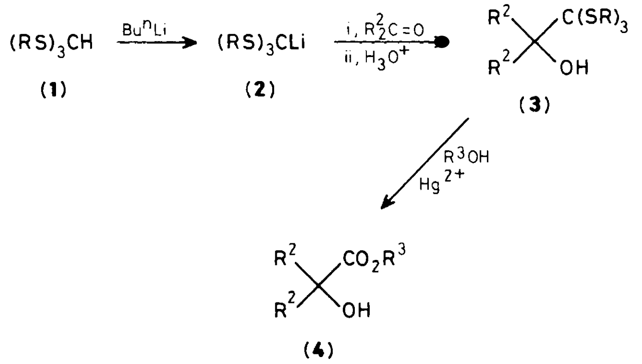
Reaction of tris(methylthio)methyl-lithium, tris(phenylthio)methyl-lithium, and 2-lithio-2-(methylthio)-1,3-dithiane with δ-valerolactone gives, respectively, 2-[bis(methylthio)methyl]tetrahydropyran-2-ol, phenyl tetrahydro-2-oxo-pyran-3-thiocarboxylate, and both 2-[2-(1,3-dithianyl)]tetrahydropyran-2-ol and 2-[2-(1,3-dithianyl)]tetrahydro-2-(methylthio)pyran-2-ol.

The addition of the lithio derivatives (**2**) of tris(thio)methanes (**1**) to aldehydes and ketones to give products of type (**3**) provides an excellent route for the synthesis of α-hydroxy carboxylic acids (**4**) and their derivatives (Scheme 1).[1] The potential of this reaction sequence has recently been expanded by its application to lactones of type (**5**) to give tetrahydropyran-2-ol derivatives (**6**) and (**7**) (Scheme 2).[2]†

We have now found that reaction of δ-valerolactone (**5**) itself with several tris(thio)methyl-lithium compounds can lead to products other than compounds of type (**6**). Thus treatment of (**5**) with an excess of tris(methylthio)methyl-lithium (**8**) followed by work-up with aqueous ammonium chloride as described[2] gave a 70% yield of a product, m.p. 43—45 °C, whose composition and spectra showed it to be a mixture of the tautomeric bis(methylthio) derivatives (**9a**) and (**9b**) in chloroform solution [in dimethyl sulphoxide only tautomer (**9b**) could be detected].‡

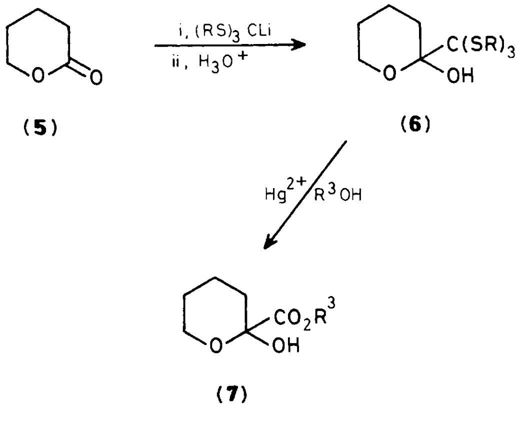
From treatment of (**5**) with tris(phenylthio)methyl-lithium (**10**) under similar conditions we have obtained the thio ester lactone (**11**), m.p. 63—65 °C, in 48% yield. In this case as in that of (**8**) we were unable to detect the formation of products of type (**3**).



Scheme 1

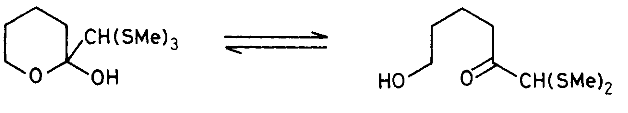
In the case of tris(thio)methyl compound (**12**) we have obtained products of both type (**3**) and type (**9**). Each exists in chloroform as a mixture of tautomers (**13a**)/(**13b**) and (**14a**)/(**14b**), respectively, analogous to the (**9a**)/(**9b**) mixture.

The formation of the bis(thio)methyl products of type (**9**) and (**14**) does not appear to be associated with the prior conversion of the lithio derivatives of the tris(thio)methanes to the corresponding bis(thio)methyl derivatives, since quenching of the lithio derivatives without addition of the lactone does not give significant amounts of the bis(thio)-methanes. We propose that (**9**) and (**14**) arise during work-up

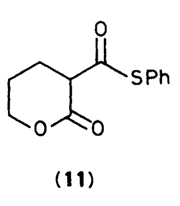


Scheme 2

$(RS)_3CLi$
(**8**) R = Me
(**10**) R = Ph



(**9a**) (**9b**)



(**11**)

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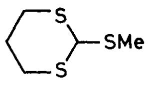
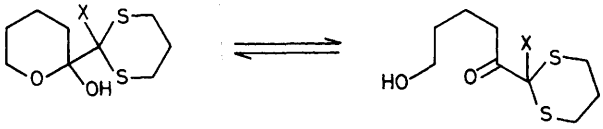
† Damon and Schlessinger[3] had earlier utilized the reaction of tris(methylthio)methyl-lithium (**8**) with an α,β-unsaturated γ-lactone: however, this leads to the 1,4 addition product.

‡ All new compounds were characterized by combustion analysis or mass spectral accurate mass measurements. They all had i.r., ^{1}H n.m.r., and ^{13}C n.m.r. spectra in accord with the structures assigned, *e.g.*, (**9b**): i.r. $\lambda_{max.}$(KBr) 3390 (m), 1701 (s) μm; ^{1}H n.m.r. δ (CD_3SOCD_3) 1.38 (m, 2H), 1.52 (m, 2H), 1.97 (s, 6H), 2.64 (m, 2H), 3.35 (m, 2H), 4.39 (m, 1H; absent after D_2O treatment), 4.92 (s, 1H); ^{13}C n.m.r. δ (CD_3SOCD_3) 11.9 (CH_3), 20.3 (CH_2), 31.8 (CH_2), 38.5 (CH_2), 60.0 (CH), 60.4 (CH_2), 202.3 (C=O); *m/z* 208 (2%), 109 (28), 108 (75), 107 (100), 101 (26).



(12)

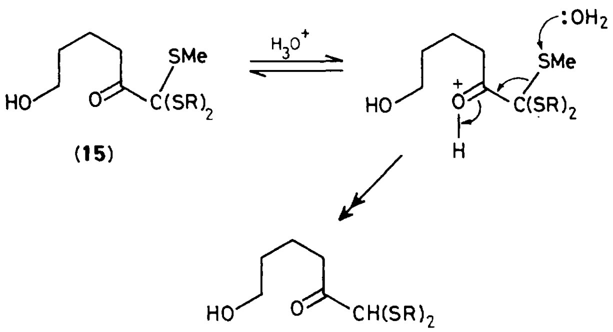


(13a) X = SMe **(13b)** X = SMe

(14a) X = H **(14b)** X = H

from the keto tautomers (**15**) of initially formed tris(thio)methyl products *via* the route shown in Scheme 3.

The route to (**11**) is more obscure. In this case the initially formed tris(phenylthio)methyl-lithium (**10**) is known to be relatively unstable[4] and the complication may result from reaction of its decomposition products with the lactone. Whatever the nature of the mechanisms for the formation of the various products that we have described, it is clear that synthetic applications of the type of reaction sequence shown in Scheme 2 must be undertaken with caution.§



Scheme 3

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§ It is probable that the nature of the products is very sensitive to the reaction and work-up conditions. We have attempted to duplicate the conditions referred to in ref. 2; however these were not described in detail for (**5**) and we have been unsuccessful in our attempts to obtain further details.