New Synthesis of Butenolides and γ-Phenylthio Acrylic Esters

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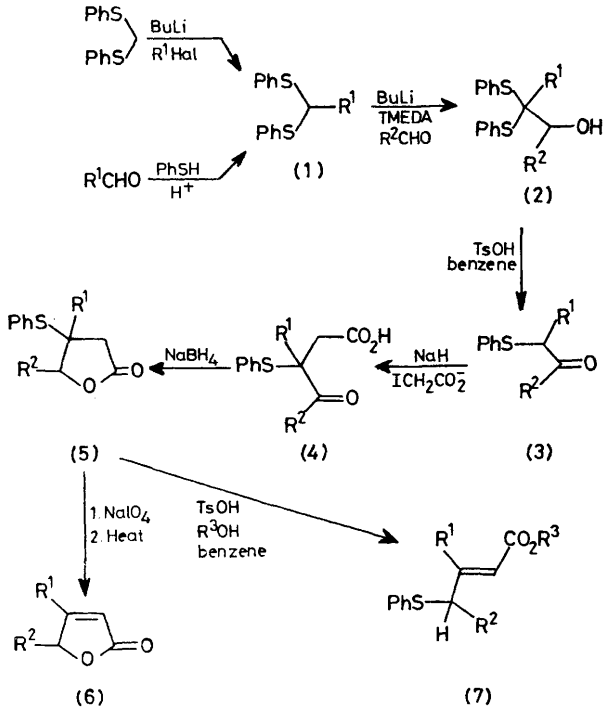
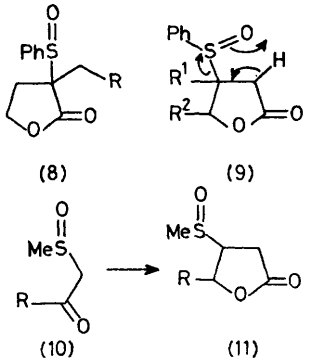
Summary β-Phenylthio-butanolides (**5**), synthesised from α-phenylthio-ketones in two steps, give the title compounds by oxidation and acid-catalysed rearrangement, respectively.

ONE important application of specific enol equivalents[1] is the synthesis of 1,4-dicarbonyl compounds[2] as in the alkylation of enamines with α-halogeno-ketones and esters.[3] α-Phenylthio-ketones (**3**) are specific enol equivalents in that they form enolate anions only on the phenylthio (PhS) side of the carbonyl group and that they no longer need to be made from the parent ketone; our convergent route[4] from the bis(phenylthio)acetals (**1**) gives single regioisomers (**3**) of whatever substitution pattern is needed.

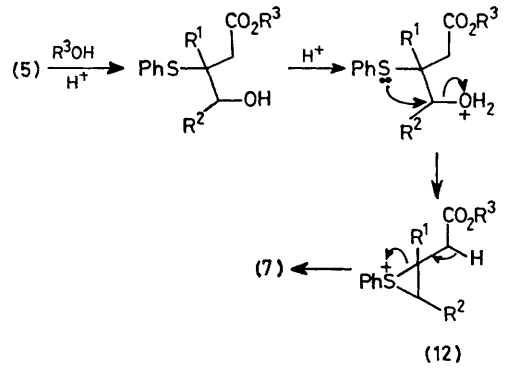


SCHEME 1

We now report that α-phenylthio-ketones (**3**) can be used as specific enol equivalents in a synthesis of 1,4-dicarbonyl compounds (Scheme 1) particularly suitable for making butenolides (**6**). Alkylation of the enolate anion (NaH, tetrahydrofuran) of (**3**) with iodoacetate *anion* gives high yields (>80%) of the crystalline acids (**4**) (α-halogeno-esters give lower yields of the corresponding esters). Borohydride reduction gives the lactones (**5**) directly (*e.g.*, $R^1 = H$, $R^2 = Me$, 98%; $R^1 = R^2 = Me$, 93%) and the butenolide synthesis is completed by formation ($NaIO_4$) and thermal decomposition (20—110 °C) of the sulphoxide. The sulphoxide elimination has been used before in butenolide syntheses[5] but usually on the other regioisomer (**8**). With our regioisomer, the elimination (**9**) is much faster and is totally regioselective as the proton to be lost is next to the carbonyl group and so the double bond is formed only inside the ring. This regioisomer has been used in one high-yielding butenolide synthesis[6] but the compounds (**11**) were derived *via* the ketones (**10**) from the acylation of dimethyl sulphoxide and had no substituents at the β carbon atom.



The lactones (**5**) also rearrange in acid solution in the presence of an alcohol [EtOH or Bu^nOH, toluene-*p*-sulphonic acid (TsOH) in benzene under reflux] with PhS migration to give γ-phenylthio-acrylic esters (**7**), presumably by the mechanism shown in Scheme 2. We have previously made allyl sulphides by PhS migration[7] but the reactions reported here show two new features. In one case we observed PhS migration between two secondary



(12)

SCHEME 2

centres (**7**, R^1 = H, R^2 = Me, R^3 = Et, 88% yield) and in another regioselectivity of double bond formation between two side chains [Et and CH_2CO_2Et in (**7**, $R^1 = R^3$ = Et, R^2 = Me), 64% yield]. Both reactions are controlled by the preferential loss of the relatively acidic proton next to the carbonyl group (**12**). PhS migrations between secondary centres may also be controlled by the preferential loss of a trimethylsilyl group.[8]

The γ-phenylthio-acrylic esters (**7**) produced in this reaction have activated protons on the γ carbon atom and we hope to use the anions of these compounds as regiospecific equivalents of the enols of α,β-unsaturated esters.†

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† For alternative approaches to this problem, see B. M. Trost and L. S. Melvin, *J. Amer. Chem. Soc.*, 1976, **98**, 1204; G. Stork and J. Benaim, *ibid.*, 1971, **93**, 5938; J. P. Marino and T. Kaneko, *Tetrahedron Letters*, 1973, 3971. The methylthio analogue of the unsubstituted ester (**7**, $R^1 = R^2$ = H, R^3 = Et) has been made from ethyl bromocrotonate (A. J. H. Labuschagne, J. S. Malherbe, C. J. Meyer, and D. F. Schneider, *Tetrahedron Letters*, 1976, 3571).

[1] G. Stork, *Pure Appl. Chem.*, 1975, **43**, 553.
[2] G. Rio and A. Lecas-Nawrocka, *Bull. Soc. chim. France*, 1976, 317.
[3] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, 1963, **85**, 207; L. Nilsson and C. Rappe, *Acta Chem. Scand.*, 1976, **B30**, 1000.
[4] P. Blatcher and S. Warren, *J.C.S. Chem. Comm.*, 1976, 1055.
[5] B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Amer. Chem. Soc.*, 1976, **98**, 4887, and references therein.
[6] P. A. Bartlett, *J. Amer. Chem. Soc.*, 1976, **98**, 3305; see also K. Iwai, H. Kosugi, A. Miyazaki, and H. Uda, *Synth. Comm.*, 1976, **6**, 357; P. A. Grieco and M. Miyashita, *J. Org. Chem.*, 1975, **40**, 1181.
[7] P. Brownbridge and S. Warren, *J.C.S. Chem. Comm.*, 1975, 820; *J.C.S. Perkin I*, 1977, 1131.
[8] P. Brownbridge, I. Fleming, A. Pearce, and S. Warren, *J.C.S. Chem. Comm.*, 1976, 751.