Tetrahedron Letters, Vol.27, No.6, pp 757-760, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

ORGANIC SYNTHESIS WITH α-CHLOROSULPHIDES. CONVENIENT ROUTES TO PHENYLTHIOACETALS FROM α-DIAZOKETONES AND ALKYL PHENYL SULPHIDES VIA α-CHLOROSULPHIDES

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Summary α-Chloroalkyl phenyl sulphides, derived from either the action of benzenesulphenyl chloride on α-diazoketones or of N-chlorosuccinimide on alkyl phenyl sulphides, are converted into phenylthioacetals on exposure to thiophenol in the presence of zinc chloride.

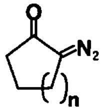
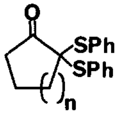
We have drawn attention in recent papers to the ease with which α-diazoketones react with benzenesulphenyl chloride and thiophenol, illustrating the efficacy of the reactions with convenient syntheses of α-(phenylthio)cycloalkenones, benzyl ketones, β-tetralones and α-(phenylthio) ketones,[1,2,3] Displacement of nitrogen from an α-diazoketone by benzenesulphenyl chloride represents an exceptionally mild and potentially regiospecific way of functionalising a ketone at the α-position with halogen and sulphur-containing substituents.[4,5] We have now developed simple extensions of the reaction which demonstrate that α-chlorosulphides from this and other sources are also useful intermediates for the synthesis of a wide variety of phenylthioacetals.

The diazoketone route provides access to acyl(phenylthio)acetals by reaction with benzenesulphenyl chloride followed by zinc chloride-catalysed addition of thiophenol (equation 1). Best yields were obtained when the first stage was conducted at low temperature (<0°C) in ether,

$$\mathrm{RCOCHN_2} \xrightarrow[\text{2. PhSH, ZnCl}_2]{\text{1. PhSCl}} \mathrm{RCOCH(SPh)_2} \qquad (1)$$

and the second stage, without purification of the chlorosulphide, in dichloromethane at room temperature. Examples of the sequence are summarised in Table 1; yields refer to analytically pure products whose structures have been confirmed by physical and spectroscopic data.[6] Both

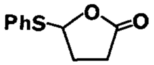
TABLE 2[a]

α-Diazoketone	α-Acyl (phenylthio)acetal (yield)	
1. $Ph(CH_2)_3COCHN_2$	$Ph(CH_2)_3COCH(SPh)_2$	(65%)
2. $PhSCH_2COCHN_2$	$PhSCH_2COCH(SPh)_2$	(76%)
3. $PhSO_2(CH_2)_3COCHN_2$	$PhSO_2(CH_2)_3COCH(SPh)_2$	(65%)
4. 		n = 1(58%) n = 2(67%)

[a] mole ratio of reactants. diazoketones: $PhSCl$:$PhSH$:$ZnCl_2$ = 1.0:1.0:1.0:1.2

acyclic and cyclic[7] phenylthioacetals can be obtained in this way, and additional sulphur-based functional groups can be easily incorporated into the diazoketone precursor, e.g. entries 2 and 3. Although the diazoketone-PhSCl route to α-chlorosulphides is useful, it is limited to the production of acyl derivatives. By far the most general route to α-chlorosulphides is NCS chlorination of alkyl sulphides. We have also combined the latter process with the thiophenol-zinc chloride reaction to convert a range of readily available sulphides bearing additional functionality into phenylthioacetals (equation 2). The first stage of the process was conducted in

$$PhSCH_2R \xrightarrow[2.\,PhSH,\,ZnCl_2]{1.\,NCS} (PhS)_2CHR \qquad (2)$$

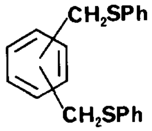
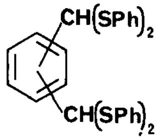
Sulphide	Phenylthioacetal (yield)	
1. $PhSCH_2CO_2Me$	$(PhS)_2CHCO_2Me$	(76%)
2. $PhSCH_2(CH_2)_9CO_2Me$	$(PhS)_2CH(CH_2)_9CO_2Me$	(71%)
3. $PhSCH_2CH_2CO_2Me$	$(PhS)_2CHCH_2CO_2Me$	(72%)
4. $PhSCHMeCO_2Me$	$(PhS)_2CMeCO_2Me_2$	(69%)
5. $PhSCH_2CH_2CO_2H$	$(PhS)_2CHCH_2CO_2H_2$	(62%)
6. $PhSCH_2CH_2CN$	$(PhS)_2CHCH_2CN$	(74%)
7. $PhSCH_2CH_2COMe$	$(PhS)_2CHCH_2COMe$	(64%)
8. 	$(PhS)_2CHCH_2CH_2CO_2H$	(64%)[8]

[a] mole ratio of reactants. sulphide:NCS:PhSH:$ZnCl_2$=1.0:1.0:1.0:2.0

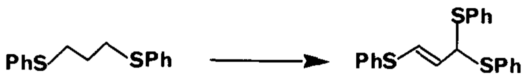
carbon tetrachloride at room temperature and, following removal of succinimide by filtration was completed by the addition of thiophenol and zinc chloride. Table 2 illustrates the efficient transformation of sulphides bearing ester, carbonyl, cyano and ketonic functional groups into the corresponding phenylthioacetals[9]. Entry 8 differs from the others in that NCS treatment is not involved; exposure of the lactone to thiophenol-zinc chloride produces the result indicated.

Through the use of symmetrical bis-sulphides it is possible to extend this methodology to the synthesis of a variety of bis(phenylthio)acetals as shown in Table 3. Interestingly, NCS chlorination of symmetrical bis-sulphides produces 1,X-dichlorides rather than 1,1-dichlorides. The conversion of 1,2-bis(phenylthio)ethane into 1,1,2,2-tetrakis(phenylthio)ethane (entry 1,n=0) is an illustrative example of the process. Similarly, the ortho, meta and para benzylic bis-sulphides in entry 2 are smoothly converted into bis-(phenylthio)acetals. Highly functionalised acetone derivatives are also accessible, 1,3-bis(phenylthio)acetone furnishing the tetra(phenylthio) derivative in entry 3. A further extension of the method which combines dehydrohalogenation of a chlorosulphide with thioacetal formation is the conversion of 1,3-bis(phenylthio)propane into the thioenol ether-thioacetal, m.p. 84-85°C (57% yield), in equation 3 on treatment with NCS followed by hot pyridine and thiophenol.

TABLE 3[a]

Bis-sulphide	Bis-(phenylthio)acetals (yield)
1. $PhSCH_2(CH_2)_nCH_2SPh$	$(PhS)_2CH(CH_2)_nCH(SPh)_2$
n=0,1,2,3	n=0(49%)[10];n=1(76%);n=2(65%)[11];n=3(77%)
2. 	
o,m,p	o(62%)[12], m(80%), p(75%)[13]
3. $PhSCH_2COCH_2SPh$	$(PhS)_2CHCOCH(SPh)_2$(56%)

[a] mole ratio of reactants:sulphide:NCS:PhSH:$ZnCl_2$=1.0:2.0:2.0:2.0.



(3)

Anions derived from (phenylthio)acetals have been used extensively in recent years as nucleophiles[14] and sources of carbenes[11]. The work described here offer new approaches to these co-compounds from readily available precursors.

References and Footnotes

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(Received in UK 21 November 1985)