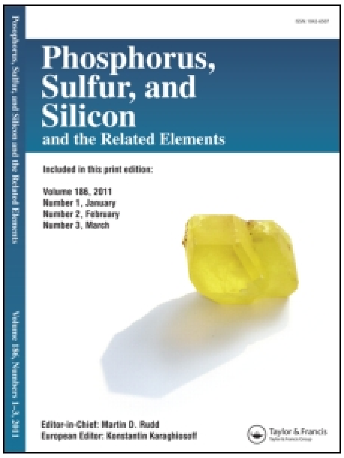

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α-(METHYLTHIO)BENZYL SULFONES AS SYNTHETIC INTERMEDIATES. III.[1] A NEW ROUTE TO *p*-SUBSTITUTED PHENYL ALKYL KETONES.[2]

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A versatile method of synthesis of *p*-substituted phenyl alkyl ketones, by decomposition of the alkylation products of the corresponding α-(methylthio)benzyl sulfones, is described. In a recent communication[1] we reported that α-methylthio-*p*-substituted benzyl sulfones (**1**) undergo thermal decomposition to give the corresponding *p*-substituted benzaldehydes.

$$\underset{\mathbf{1}}{p\text{-X—C}_6\text{H}_4\text{—CH(SMe)SO}_2\text{C}_6\text{H}_5} \xrightarrow{\Delta} p\text{-X—C}_6\text{H}_4\text{—CHO}$$

We wish to show now that α-methylthio-*p*-substituted benzyl sulfones (**1**) are also useful intermediates for the synthesis of *p*-substituted phenyl alkyl ketones. These compounds (Table I, **2a–i**) were obtained in good yields by a one pot reaction, which consisted of alkylation of (**1**) using NaH (1 equiv.) in DMSO and an appropriate alkyl halide (1 equiv.) at room temperature. The decomposition to ketones in some cases (**2d**, **e**, **g**, **h**) occurred spontaneously but in most cases only partially, additional heating up to 130 °C being necessary.

This method is superior to that reported for the synthesis of aliphatic ketones,[3] in which acid hydrolysis was employed, because it is also applicable to the syntheses of ketones containing acid sensitive functional groups (**2f**, **g**).

However, it should be observed that the results of the thermal decomposition are in close analogy to those for the acid hydrolysis procedure. Thus, benzylic α-alkylthio sulfones afford aromatic aldehydes and ketones by both procedures.[4] As for the corresponding aliphatic sulfones the observation that only ketones but not aldehydes can be obtained by acid hydrolysis[3] was also confirmed by our results of thermal decomposition.[5] Thus, α-methylthio-β-phenylethyl sulfone (**3**) did not give the corresponding aldehyde, but yielded, after alkylation, the expected ketone (**4**).

These results also indicate that the pyrolytic procedure is not limited to the benzylic *synthons*, and may be of general application to the synthesis of ketones.

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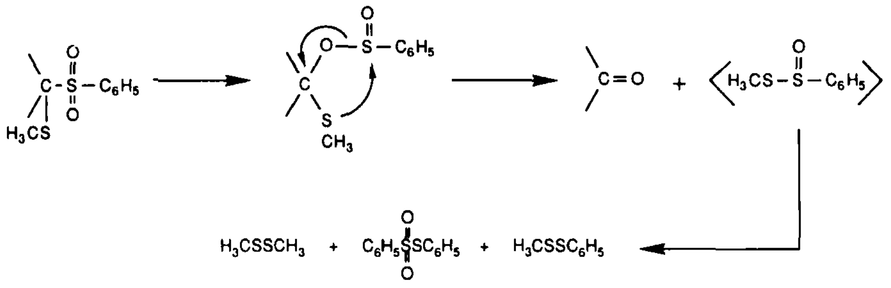
TABLE I

p-Substituted phenyl alkyl ketones from α-(methylthio)benzyl sulfones

Sulfones p-X—C_6H_4—CH(SMe)$SO_2C_6H_5$(**1**)	Alkylation reagents	Products (**2**)	Yields (%)
X = H	CH_3I	$C_6H_5COCH_3$ (**a**)	85
	C_2H_5I	$C_6H_5COC_2H_5$ (**b**)	83
	CH_3SCH_2Cl	$C_6H_5COCH_2SCH_3$ (**c**)	65
X = CH_3	CH_3I	p-CH_3—$C_6H_5COCH_3$ (**d**)	87
	$C_6H_5CH_2Br$	p-CH_3—$C_6H_4COCH_2C_6H_5$ (**e**)	76
	$C_2H_5O_2CCH_2Br$	p-$C_6H_4COCH_2CO_2C_2H_5$ (**f**)	57
	$(C_2H_5O)_2CHCH_2Br$	p-CH_3—$C_6H_4COCH_2CH(OC_2H_5)_2$ (**g**)	62
X = OCH_3	CH_3I	p-CH_3O—$C_6H_4COCH_3$ (**h**)	84
X = NO_2	CH_3I	p-NO_2—$C_6H_4COCH_3$ (**i**)	90

The mechanistic steps of the thermal decomposition of the α-(methylthio)benzyl sulfones have been suggested previously.[1] However, some further observations may be added. Thus, the identification of methyl phenyl disulfide and dimethyl disulfide and isolation of thiosulfonate, known decomposition products of thiosulfinate,[6,7] from the reaction mixture are evidence that the carbonyl group originates from the sulfone group. Therefore, a rearrangement of sulfone to sulfinic ester should occur in the first step. In fact, reverse rearrangement of sulfenates to sulfoxides[8-10] and of sulfinates to sulfones[11-14] have been reported, for which either ionic or intramolecular cyclic mechanisms have been proposed. It seems reasonable to suggest that, in the case of the α-methylthio-sulfones, the sulfone-sulfinate equilibrium is shifted irreversibly to the latter due to its rapid decomposition (see Scheme).

$$\begin{tikzcd} \underset{\mathbf{3}}{C_6H_5CH_2CH(SCH_3)SO_2C_6H_5} \arrow[r, "1.\ NaH/DMSO", "2.\ CH_3I"'] & C_6H_5CH_2C(CH_3)(SCH_3)SO_2C_6H_5 \arrow[d, "\Delta"] \\ & \underset{\mathbf{4}}{C_6H_5CH_2COCH_3} \end{tikzcd}$$



Our experimental data indicate, clearly, that for this thermal decomposition the presence of the α-sulfur atom but not the benzyl group is essential.

EXPERIMENTAL

Typical Procedure. To 0.030 g (0.75 mmol) of sodium hydride (60% in mineral oil), treated twice with 10 mL of dry benzene, were added 15 mL of dry DMSO and 0.208 g (0.75 mmol) of α-(methylthio)benzyl phenyl sulfone. After stirring for 25 min, 0.06 mL of chloromethyl methyl sulfide was added. The reaction mixture was stirred for 3 h, dropped into cold water and extracted three times with dichloromethane. The organic extract was washed three times with 20 mL of water and dried over magnesium sulfate. After removal of solvent, the oily residue was heated from 25 to 130 °C. The dark crude product was chromatographed on silica-gel-60, using hexane/acetone (4:1) as eluent. Pure ω-(methylthio)acetophenone[15] (0.081 g, 65%) was isolated. ^{1}H NMR ($CDCl_3$, TMS): δ2.10(3H, s); 3.58(2H, s); 7.15–8.00(5H, m).

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