Tetrahedron Letters,Vol.24,No.4,pp 419-422,1983 0040-4039/83/040419-04$03.00/0
Printed in Great Britain

THE PREPARATION β-KETOALDEHYDES[1]

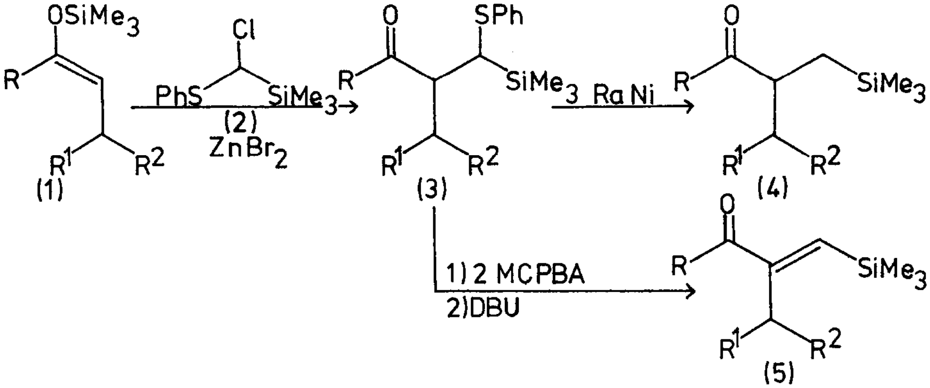
By David J. Ager

Department of Organic Chemistry, Robert Robinson Laboratories,
P.O. Box 147, Liverpool, L69 3BX[+].

Summary: β-Ketoaldehydes(7) were prepared by the addition of bromophenylthiotrimethylsilylmethane(6) to trimethylsilyl enol ethers(3) followed by a sila-Pummerer rearrangement and hydrolysis.

The phenylthiotrimethylsilyl group has been used to prepare aldehydes[2-4] and olefins[5] and has been introduced as phenylthiotrimethylsilylmethyllithium[2,3], 1-phenylthio-1-trimethylsilylethene[6] or from bis(phenylthio)acetals[5]. This paper describes the introduction of the group as bromophenylthiotrimethylsilylmethane.

Fleming and co-workers have found that chlorophenylthiotrimethylsilylmethane(2) reacts with trimethylsilyl enol ethers(1) in the presence of zinc bromide to give the β-phenylthio-β-trimethylsilylketones(3). These adducts have been used to synthesise β-trimethylsilylketones(4) by desulphurisation with Raney nickel[7] and β-trimethylsilylenones(5) by oxidation of the sulphur and elimination of the sulphone with DBU[8] (see scheme 1).

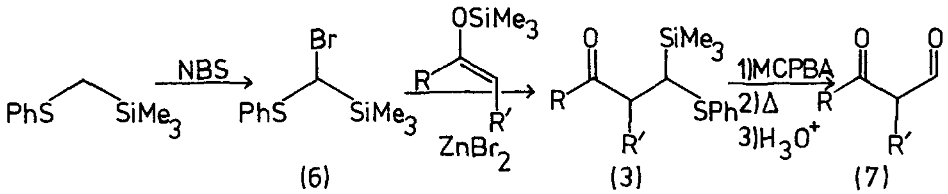


Scheme 1.

We have found that bromophenylthiotrimethylsilylmethane(6) can be used to prepare the adducts(3) in high yield. The bromo compound(6)

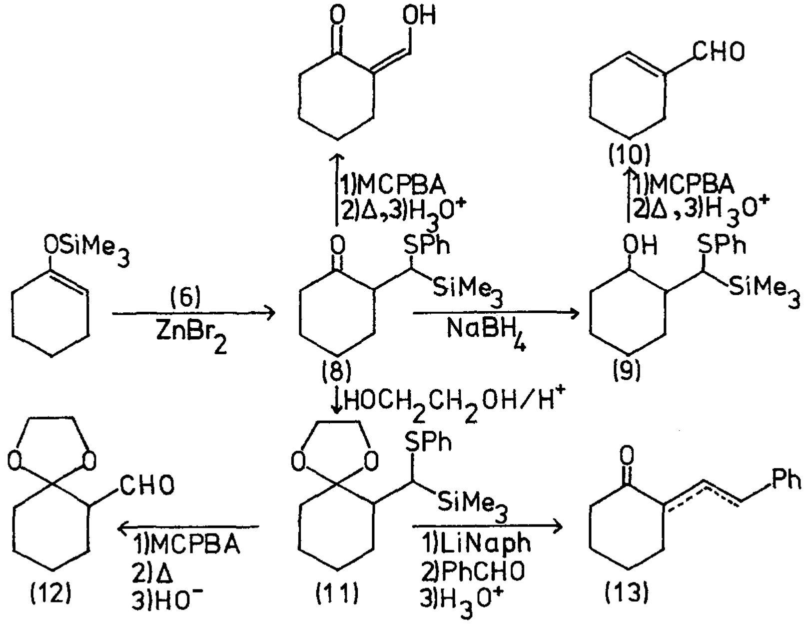
[+] Present address: Department of Chemistry, University of Toledo,
2801 W. Bancroft St., Toledo, Ohio 43606, U.S.A.

was prepared by heating phenylthiotrimethylsilylmethane and N-bromosuccinimide in carbon tetrachloride in the presence of a peroxide for 1h, in essentially quantitative yield (>95% by nmr). Reaction of (6) with trimethylsilyl enol ethers(1)[9] in the presence of zinc bromide gave the adducts(3) in good yields (see table)[10].



Scheme 2.

As the phenylthiotrimethylsilyl group is a masked aldehyde (vide supra), the β-phenylthio-β-trimethylsilylketones(3) were converted to the corresponding β-ketoaldehydes(7) using the previously reported procedure[3].



Scheme 3.

Table

Reactions of bromophenylthiotrimethylsilylmethane(6) with trimethylsilyl enol ethers(1).

Enol ether(1)		Yield (%)[a]	
R=	R'=	(3)	(7)[b]
$-(CH_2)_3-$		69	65
$-(CH_2)_4-$		79[c]	72
Et	Me	82	69
Ph	H	77	78
$^nC_5H_{11}$	^nBu	71	62

[a] All new compounds have been characterised.

[b] Yield from (3).

[c] 84% when phenylthiotrimethylsilylmethyl chloride was used; see reference 8.

The phenylthiotrimethylsilyl group allows selective protection of the aldehyde or ketone functionality in the β-ketoaldehydes and some of these reactions were investigated using 2-(phenylthiotrimethylsilylmethyl)cyclohexanone(8) as the model compound[11]. The results are summarised in scheme 3. The ketone was reduced with sodium borohydride in ethanol to give the alcohol(9)[12]. Oxidation of (9) with m-chloroperoxybenzoic acid(MCPBA) in dichloromethane cleanly gave the sulphoxide which underwent the sila-Pummerer rearrangement to the O-trimethylsilylphenylthioacetal and gave, after acid hydrolysis, the enal(10) in an overall yield of 42% from (9). The ketone(8) could be protected as the ethylene glycol ketal(11) and the sila-Pummerer reaction, with basic hydrolysis gave the ethylene glycol ketal of the β-ketoaldehyde(12) in 65% yield. The phenylthio group of (11) was reacted with lithium naphthalenide in THF at -78°C[13] and then benzaldehyde to give, after acidic work-up, which also hydrolysed the ketal, the olefins(13)[14] *via* the Peterson reaction[5,15] in 61% yield.

The author wishes to thank Prof. R.C. Cookson FRS (University of Southampton) and Dr. Ian Fleming (University of Cambridge) for their help and encouragement.

References and notes.

1. Part of this work was carried out at the Department of Chemistry, The University, Southampton, SO9 5NH. An SRC postdoctoral fellowship is acknowledged.
2. P.J. Kocienski, Tetrahedron Lett., 1980, 21, 1559.
3. D.J. Ager and R.C. Cookson, Tetrahedron Lett., 1980, 21, 1677.
4. I. Cutting and P.J. Parsons, Tetrahedron Lett., 1981, 22, 2021.
5. D.J. Ager, Tetrahedron Lett., 1981, 22, 2923.
6. D.J. Ager, Tetrahedron Lett., 1981, 22, 587.
7. I. Fleming, Chem. Soc. Rev., 1981, 10, 83.
   I. Fleming and S.K. Patel, Tetrahedron Lett., 1981, 22, 2321.
8. I. Fleming and D.A. Perry, Tetrahedron, 1981, 37, 4027.
9. These preparations were carried out using one of the standard methods:-
   G. Stork and P.F. Hudrlik, J. Am. Chem. Soc., 1968, 90, 4462.
   G. Stork and P.F. Hudrlik, J. Am. Chem. Soc., 1968, 90, 4464.
   H.O. House, L.J. Czuba, M. Gall and H.D. Olmstead, J. Org. Chem., 1969, 34, 2324.
10. C.f. I. Paterson and I. Fleming, Tetrahedron Lett., 1979, 993.
    I. Paterson and I. Fleming, Tetrahedron Lett., 1979, 995.
    I. Paterson and I. Fleming, Tetrahedron Lett., 1979, 2179.
11. The mixture of diastereoisomers obtained from the condensation reaction was used for these studies.
12. This compound, again as a mixture of diastereoisomers, has been prepared by the reaction of phenylthiotrimethylsilylmethyllithium with cyclohexene oxide. See reference 3 and D.J. Ager, Tetrahedron Lett., 1981, 22, 2803.
13. C.G. Screttas and M. Micha-Screttas, J. Org. Chem., 1979, 44, 713.
    T. Cohen, W.M. Daniewski and R.B. Wiesenfeld, Tetrahedron Lett., 1978, 4665.
14. Both isomers were detected.
15. D.J. Peterson, J. Org. Chem., 1968, 33, 780.

(Received in UK 17 November 1982)