Tetrahedron Letters,Vol.23,No.23,pp 2399-2402,1982 0040-4039/82/232399-04$03.00/0
Printed in Great Britain

O-SILYLATED ENOLATE PHENYLTHIOALKYLATION: A NEW SYNTHESIS OF UNSATURATED 1,5-DICARBONYL COMPOUNDS.

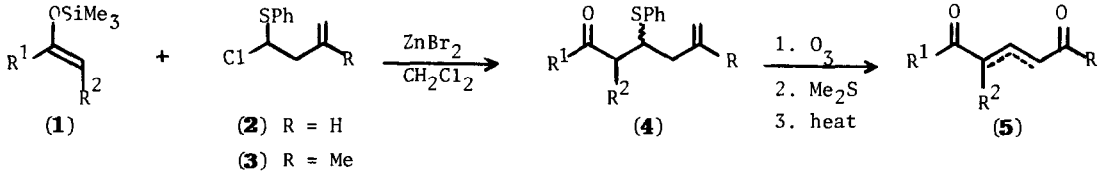
Hassan A. Khan and Ian Paterson*

Department of Chemistry, University College London,
20 Gordon Street, London WC1H OAJ, England.

Summary: The *O*-silylated enolates of ketones and esters can be phenylthioalkylated by the chlorides (**2**) and (**3**) under $ZnBr_2$-catalysis; ozonolysis and subsequent sulphoxide thermolysis then gives the corresponding unsaturated 1,5-dicarbonyl compounds.

O-Silylated enolates are, in many cases, useful alternatives to more electropositive metal enolates for the controlled α-substitution of carbonyl compounds.[1-3] For instance, they can be regiospecifically alkylated by α-chloroalkyl phenyl sulphides (PhSCHClR, R = H[2] or saturated alkyl[3]), in the presence of suitable Lewis acids, to give β-phenylthiocarbonyl compounds; reductive or oxidative sulphur-removal then leads to overall α-alkylation or α-alkylidenation.

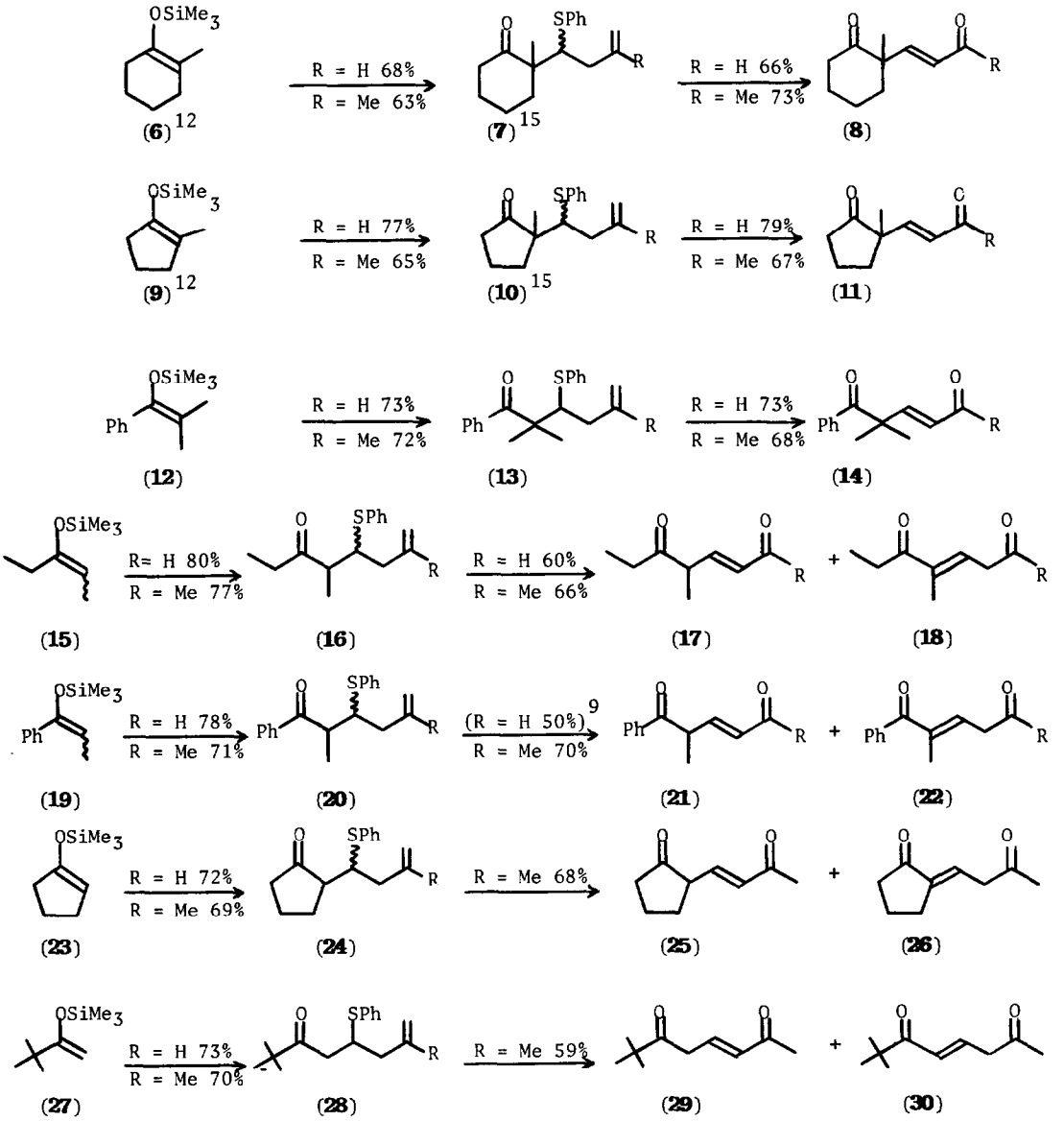
As an extension of this work, we now report a novel method for the synthesis of various unsaturated 1,5-dicarbonyl compounds, useful synthetic intermediates *inter alia* for heterocycle construction[4] and annulation.[5] Phenylthioalkylation of *O*-silylated enolates (**1**) with the unsaturated α-chloroalkyl phenyl sulphides (**2** and **3**), under mild $ZnBr_2$-catalysis, gives the homoallylsulphides (**4**, R = H and R = Me). These are then transformed into the corresponding unsaturated aldehydes (**4** → **5**, R = H) or methylketones (**4** → **5**, R = Me) by ozonolysis *with concomitant sulphur oxidation*, followed by easy sulphoxide cycloelimination. The overall transformation is, therefore, the synthetic equivalent of enolate Michael addition to $HC{\equiv}CCHO$ or $HC{\equiv}CCOCH_3$.[5]



The two alkylating agents (**2** and **3**) were prepared by chlorination of the respective homoallyl phenyl sulphides (NCS, CCl_4, 20°, 4h; >95%), each of which are readily accessible.[6,7] They reacted satisfactorily with *O*-silylated enolates in the presence of a catalytic amount of $ZnBr_2$[8] in CH_2Cl_2 at room temperature (15min - 1h), essentially identical conditions to those already developed for the simple phenylthioalkylation of ketones and

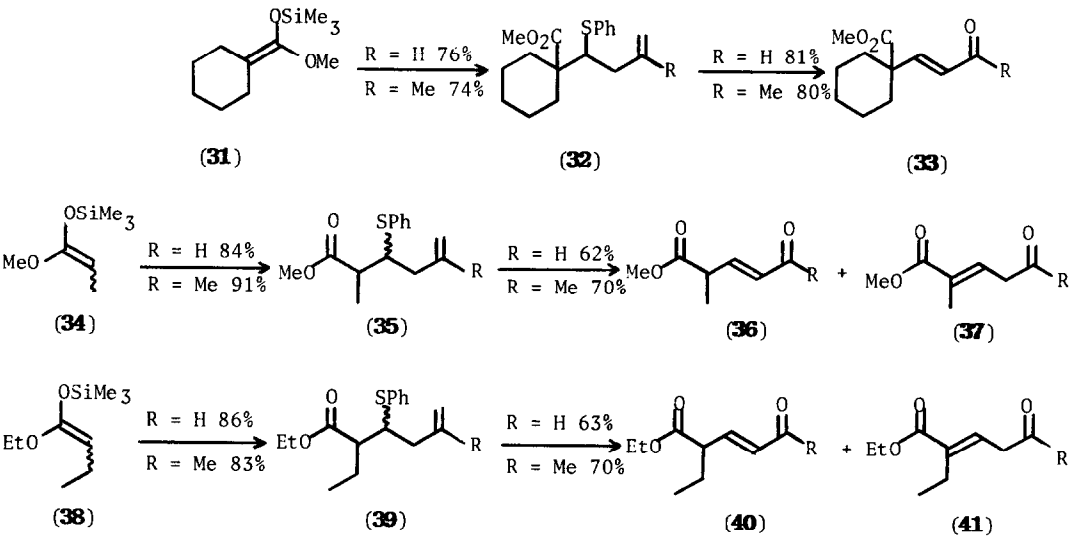
esters.[3] The new alkylation reactions, as summarised in diagrams **6** to **28** for ketone systems and **31** to **39** for ester systems, appear to be as general as phenylthiobutylation,[3] although yields are perhaps slightly lower.

Ozone treatment of the intermediate homoallylsulphide was best performed at -78° in CH_2Cl_2-MeOH (4:1) for systems derived from electrophile (**3**), and in Me_2CO for those derived from **2**, followed by normal Me_2S reduction (-78° → 20°). Substantial elimination of benzenesulphenic acid took place on warming up, and was completed by brief heating (CCl_4, 70°, 15min - 2h), to give the unsaturated 1,5-dicarbonyl compound. We have successfully prepared a range of unsaturated 1,5-diketones, ketoesters, and aldehydoesters using this procedure.



For the preparation of unsaturated 1,5-aldehydoketones, however, the method is usually restricted to blocked systems (e.g. **8**, **11**, and **14**; R = H); enolisable systems, when formed, did not survive chromatography and were best isolated by microdistillation (e.g. **17** and **18**; R = H).[9] The ozonolysis of **24** and **28** for R = H gave only polymeric materials with no identifiable aldehyde products.

In blocked, non-enolisable 1,5-dicarbonyl compounds (**8**, **11**, **14**, and **33**; R = H, Me) the products had exclusively E-stereochemistry. In all the remaining enolisable systems, there was generally significant (>5:1)[11] kinetic regioselectivity in sulphoxide elimination towards the disubstituted alkene isomer, while subsequent chromatographic isolation on SiO_2 usually led to equilibration towards the more stable trisubstituted alkene regioisomer. For example, the ratio of **17**:**18** (R = Me) after elimination (70°, 30min) was ~5:1 (^{1}H NMR),[10] which reversed to 1:15 after flash chromatography. Both regioisomers had E-stereochemistry in all cases examined.



The *O*-silylated enolates used were prepared by standard methods.[1-3] The $ZnBr_2$-phenylthioalkylation procedure was identical to that already described,[3] except that exactly one equivalent of electrophile (**2** or **3**)[13] was now used (c.f. 1.2 equivalents previously).[14] Typically, for the ozonolysis procedure, ozone (Wellsbach generator) was bubbled through a stirred solution of the homoallylsulphide (1 mmol) in CH_2Cl_2-MeOH (4:1, 10ml) or dry Me_2CO (10 ml) at -78° until the blue colour persisted, and then for a further 3 min. The solution was purged of excess O_3 by bubbling Ar through, Me_2S (1ml) was added, and the mixture allowed to warm to room temperature. The solvent was evaporated *in vacuo* to give usually a mixture of sulphoxides and eliminated products, which was then heated in CCl_4 (3ml) for 15min - 2h; flash chromatography on silica gel (or microdistillation) then gave the unsaturated 1,5-dicarbonyl compound.

In summary, this work further demonstrates the utility of *O*-silylated enolate phenylthioalkylation for the α-substitution of carbonyl compounds. The compatibility of these alkylations with other functionality in the α-chlorosulphide remains to be established.

We thank the S.E.R.C. for a Postdoctoral Research Assistantship (to H.A.K.).

NOTES AND REFERENCES

[1] J. K. Rasmussen, *Synthesis*, 91 (1977); I. Fleming in *"Comprehensive Organic Chemistry"*, Vol.3, D. H. R. Barton and W. D. Ollis, Pergamon Press (1979); E. W. Colvin, *Chem. Soc. Rev.*, **7**, 15 (1978)

[2] I. Paterson and I. Fleming, *Tetrahedron Letters*, 993 and 995 (1979).

[3] I. Paterson and I. Fleming, *ibid.*, 2179 (1979); for R = $SiMe_3$, see I. Fleming and S. Patel, *ibid.*, 2321 (1981).

[4] K. T. Potts, M. J. Cipullo, P. Ralli, and G. Theodoridis, *J. Amer. Chem. Soc.*, **103**, 3584 and 3585 (1981), and references therein.

[5] M. E. Jung, *Tetrahedron*, **32**, 3 (1976); R. B. Woodward and T. Singh, *J. Amer. Chem. Soc.*, **72**, 494 (1950).

[6] **2** was prepared from reaction of 1-bromo-3-butene with NaSPh (EtOH, 20°, 4h; 96%), or from allylbromide and $PhSCH_2Cu$ (TMEDA-THF, -78° → 20°; 2h, 80%).[7] **3** was prepared from 3-methyl-3-buten-1-ol *via* tosylation (TsCl-pyridine, 20°, 2h) followed by reaction with NaSPh (EtOH, 20°, 16h; 88% overall).

[7] E. J. Corey and M. Jautelat, *Tetrahedron Letters*, 5787 (1968).

[8] The $TiCl_4$-promoted reaction,[3] in this case, was much inferior to the $ZnBr_2$ procedure.

[9] Unsaturated aldehydoketones (**21** and **22**; R = H) could not be satisfactorily purified and the quoted yield is estimated from the NMR spectrum. All other yields are isolated yields.

[10] Microdistillation in the analogous aldehyde case gave **17**:**18** (R = H) in better than 10:1 ratio without equilibration occurring.

[11] The elimination regioselectivity was generally more pronounced in aldehyde cases, presumably reflecting the greater acidity of the aldehyde α-hydrogens over that of ester or ketone functions (see ref 10).

[12] **6**:regioisomer in the proportion 88:12; **9**:regioisomer 93:7.

[13] Compound **2** could be stored at -20° under N_2 for 2 - 3 months without deterioration, however, **3** could only be kept for ∿3 weeks under similar conditions.

[14] Concentration was important, 0.5 *M* (i.e. 2 ml CH_2Cl_2/mmol reactants) was found to be best.

[15] The amount of regioisomer produced in the alkylation was proportional to the amount of the corresponding silyl enol ether present in the starting material.[12]

(Received in UK 23 February 1982)