Tetrahedron Letters No. 34, pp 3205 - 3208.
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0040-4039/79/0815-3205$02.00/0

γ-SULPHENYLATION OF αβ-UNSATURATED ALDEHYDES, KETONES, AND ESTERS: THE USE OF *O*-SILYLATED DIENOLATES[1]

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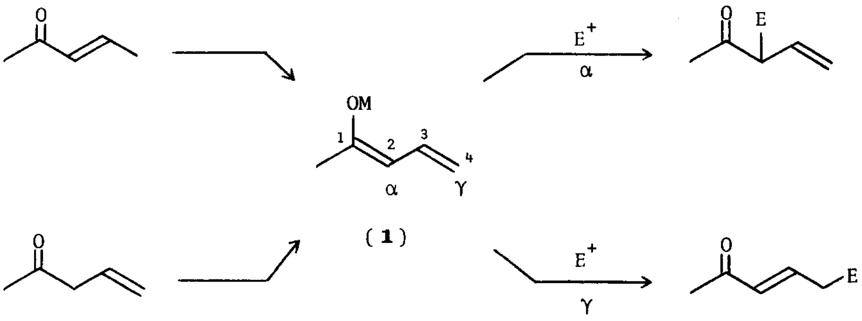
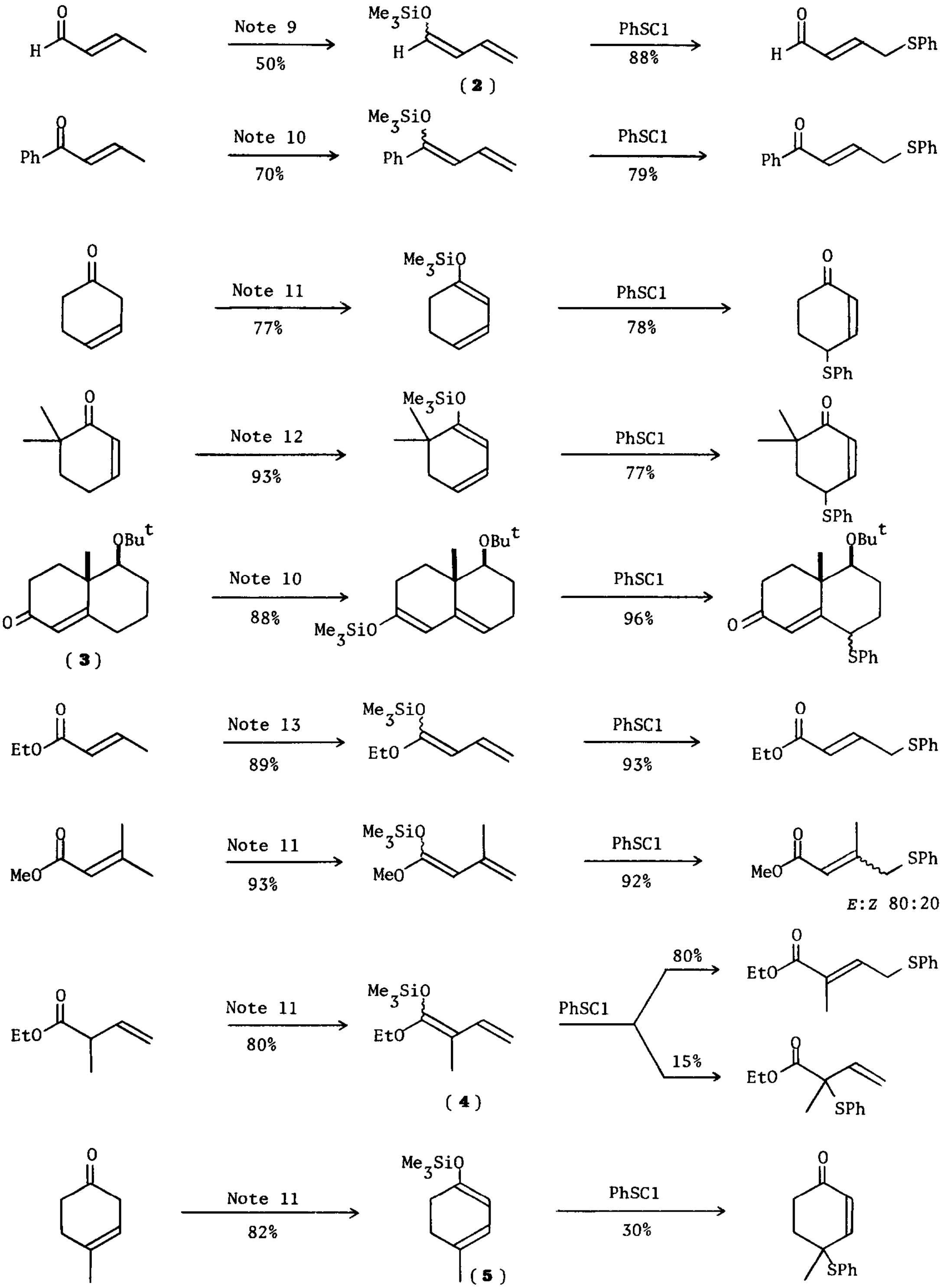
Summary: Phenyl sulphenyl chloride is a γ-selective electrophile in its reactions with *O*-silylated dienolates.

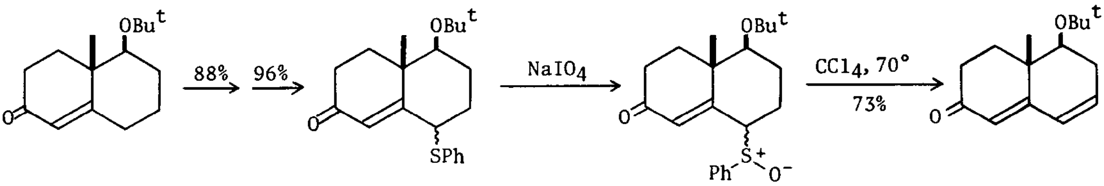
The lithium dienolates (**1**, M = Li) of αβ-unsaturated carbonyl compounds react with most electrophiles selectively at the α-position.[2] Various attempts to encourage attack at the γ-position have been reported,[3] but a general method is still lacking. We reasoned that γ-attack would be encouraged if the substituent (-OM in **1**) were made effectively less electron-donating: thus, in the extreme, with no substituent on C-1, the diene would undoubtedly react with electrophiles at C-4, not at C-2. Obvious candidates are the *O*-silylated dienolates or the *O*-acetylated dienolates. In this and the following paper, we report on the α- versus γ-selectivity of a range of *O*-silylated dienolates (**1**, M = $SiMe_3$) with various electrophiles, extending the work of Mukaiyama and Ishida,[4] who found high γ-selectivity in the Lewis acid-catalysed reactions of 1-trimethylsilyloxybutadiene (**2**) with acetals.



The effect of changing the metal from lithium to silicon is quite striking: sulphenylation, which is usually[5] but not always[6] α-selective with lithium dienolates, is highly γ-selective with the *O*-silylated dienolates of the αβ-unsaturated esters, ketones, and aldehyde shown in the diagrams below.[7] In only one case (**4**) was the product of α-attack detected, and in only one case (**5**) was the yield of γ-product so low that we cannot say that γ-attack is clearly the favoured reaction.[8]


Note 9
50%
(2)
PhSCl
88%
Note 10
70%
PhSCl
79%
Note 11
77%
PhSCl
78%
Note 12
93%
PhSCl
77%
(3)
Note 10
88%
PhSCl
96%
Note 13
89%
PhSCl
93%
Note 11
93%
PhSCl
92%
E:Z 80:20
Note 11
80%
(4)
PhSCl
80%
15%
Note 11
82%
(5)
PhSCl
30%

The products of these reactions, γ-sulphenylated enones, are useful, because they can be converted into 1,4-dicarbonyl compounds[14] and furans,[15] and their derived sulphones can be used to encourage γ-alkylation of αβ-unsaturated ketones[16] and esters.[17] Our method provides an alternative synthesis of γ-sulphenylenones to the method using allylic bromination followed by displacement of bromide by a sulphur nucleophile.[14,16,17] We find that the γ-sulphides provide a mild method for the extension of unsaturation: oxidation of the sulphide (**6**) to the sulphoxide (**7**) followed by gentle heating gave the dienone (**8**).



(**3**) (**6**) (**7**) (**8**)

In a typical procedure, phenyl sulphenyl chloride[18] (145 mg, 1 mmol) in dry dichloromethane (1 ml) was added to a stirred solution of the *O*-silylated dienolate (1 mmol) in dichloromethane (1 ml) at -78° under nitrogen. The colour was rapidly discharged. After 5 min, the solvent was evaporated and the products purified by preparative thin layer chromatography on silica gel eluting with dichloromethane.

NOTES and REFERENCES

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[6] C. N. Lam, J. M. Mellor, P. Picard, M. F. Rawlins, and J. H. A. Stibbard, *Tetrahedron Letters*, 4103 (1978). The observation by these authors that sulphenylation (and selenylation) can, in a special case, be γ-selective, coupled with their observation that alkylation of the same dien-

olate was still α-selective, is in line with our observation that phenyl sulphenyl chloride is more γ-selective than the alkylating agents described in the following paper.

[7] Sulphenylation of simple *O*-silylated enolates has been reported: S. Murai, Y. Kuroki, H. Hasegawa, and S. Tsutsumi, *J. C. S. Chem. Comm.*, 946 (1972). We find that our conditions, which differ principally in using a lower temperature, applied to simple unconjugated *O*-silylated enolates are generally superior to the sulphenylation of the corresponding lithium enolates, giving α-phenylthio ketones and esters in high yield and with an easy product separation. In particular, when the α-position is secondary, we see little, if any, disulphenylation.

[8] It is conceivable that α-attack was the kinetically favoured reaction, and that isomerisation to the γ-product followed. Such isomerisation in allyl phenyl sulphides is well known.[19] We found no sign of this pathway, and took care to avoid the light-catalysed reaction.

[9] This *O*-silylated dienolate was prepared (Me_3SiCl, Et_3N, benzene, reflux; non-aqueous work-up and purification by distillation)[20] by Dr. P. Gallagher of this department. We thank him for this gift.

[10] These *O*-silylated dienolates were prepared: Me_3SiCl, Et_3N, DMF, reflux,[21] with a neutral, aqueous work up, and chromatography on SiO_2 eluting with CH_2Cl_2. We thank Dr. P. Buchschacher, of Hoffmann La Roche, Basel, for a gift of the ketone (**3**).

[11] These *O*-silylated dienolates were prepared: 1.05 equivalents of LDA in THF at -78°, followed by 1.2 equivalents of Me_3SiCl from -78° to room temperature; non-aqueous work-up and purification by distillation. For βγ-enones as substrates in these conditions, see reference 22.

[12] These *O*-silylated dienolates were prepared as in note 11, except that they were purified by chromatography on SiO_2 eluting with CH_2Cl_2.

[13] This *O*-silylated dienolate was prepared by the method described in note 11, except that HMPA (1 equivalent) was added.[23]

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(Received in UK 8 June 1979)