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ALKENE CARBOSULPHENYLATION AND CARBOSELENYLATION: THE USE OF ALLYLTRIMETHYLSILANE AND *O*-SILYLATED ENOLATES.

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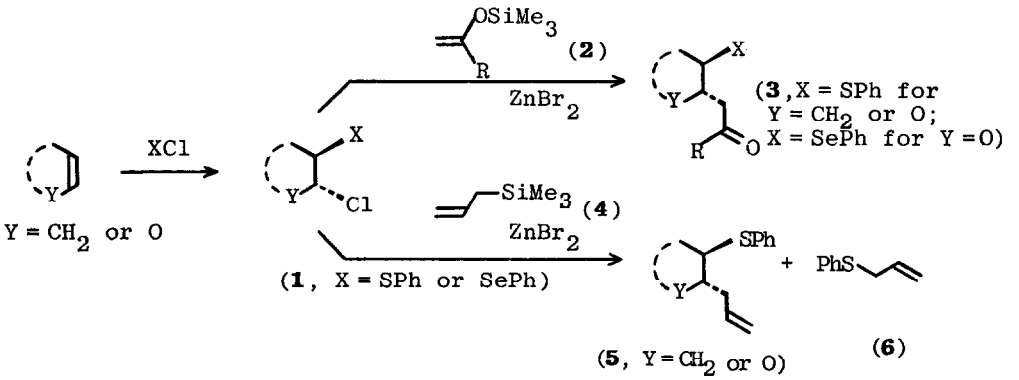
Summary: Allyltrimethylsilane, as well as *O*-silylated enolates, can be alkylated by the PhSCl adducts of alkenes and vinyl ethers (**1**, X=SPh); the PhSeCl analogues (**1**, X=SePh), however, are less useful for alkylation purposes due to competing nucleophilic attack at selenium.

The vicinal functionalisation of alkenes is an important area for the development of useful new synthetic methods, particularly when regio- and stereochemistry can be controlled. We recently reported that simple alkenes can be stereospecifically carbosulphenylated in an *anti*-fashion by reaction of their PhSCl adducts, under $ZnBr_2$-catalysis, with the *O*-silylated enolates of esters (**1** + **2** → **3**, X=SPh and Y=CH_2).[1] This new sulphur-mediated method[2] for the α-alkylation of carbonyl compounds works best with mono- and di-substituted alkenes, and most likely proceeds by nucleophilic attack at carbon in an intermediate episulphonium ion. In the case of tri- and tetra-substitutes alkenes, however, low alkylation yields were obtained and the favoured reaction was now attack at sulphur to give the α-phenylthio carbonyl compound.



We now report that many alkenes can be similarly carbosulphenylated by using allyltrimethylsilane[3] in reaction with β-chloroalkyl phenyl sulphides, as in **1** + **4** → **5**. Overall, this leads to the *anti*-addition of a synthetically versatile allyl group, together with a phenylthio group, to the olefinic carbons of the starting alkene. We also report our results[4] for additions to vinyl ethers. Using our general $ZnBr_2$-catalysed procedure,[1] *O*-silylated enolates and dienolates can be alkylated stereoselectively by both the PhSCl and PhSeCl adducts of vinyl ethers (e.g. **1** + **2** → **3**, X=SPh or SePh, for Y=O). The analogous selenium-mediated alkylations were unsuccessful, however, when using the PhSeCl adducts of alkenes (i.e. using **1**, X=SePh and Y=CH_2) due to competing selenylation of the nucleophile.

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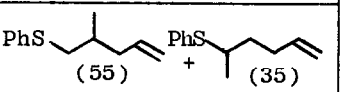
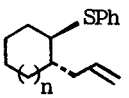
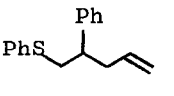
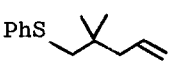
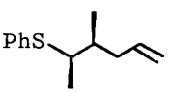
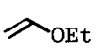
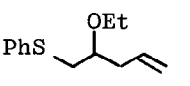
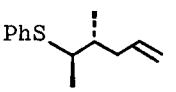
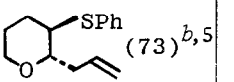
Some modification of our original experimental conditions[9] was required to obtain clean reaction of allyltrimethylsilane with a range of β-chlorosulphides to give the desired alkylation products. We eventually found that sublimed $ZnBr_2$ (0.25 equiv.) in dry nitromethane generally gave the best results (Table 1). Under these conditions, the formation of allylphenylsulphide (**6**), by competing sulphenylation of the allylsilane, was kept to a minimum (usually <10%).[5]

TABLE 1: Reaction (**1** + **4** → **5**) of allyltrimethylsilane (1.1 equiv.) with the PhSCl adducts of alkenes ($ZnBr_2$, 0.25 equiv.; CH_3NO_2, 20°C, 16h) and vinyl ethers ($ZnBr_2$, 0.05 equiv.; CH_2Cl_2, 20°C, 3h).

Entry	Alkene	Adduct (% yield[a])	Entry	Alkene	Adduct (yield[a])
1		n = 0 (91)	6[c]		
2		n = 1  (78)[b,5]	7		
3		n = 2 (50)	8		
4		 (92)	9		
5		 (40)	10		

[a] yields refer to isolated products throughout. [b] J_{vic} 11-12 Hz. [c] reaction conditions: 70°C, 16h.

In general, the results obtained for the stereo- and regiochemistry of this reaction are very similar to those for our earlier *O*-silylated enolate reactions.[1] Good yields of allylated *trans*-adducts were produced when using simple cycloalkenes (entries 1 - 3).[5] Moreover, the stereospecificity of addition was confirmed for *cis*- and *trans*-2-butene (entries 4 and 5): carbosulphenylation led to a single[6] but clearly different stereoisomer in each case. The β-chlorosulphide adducts of propene (entry 6) required more vigorous conditions than normal for complete reaction (70°C, 16h) and showed little regioselectivity, while the styrene adduct (entry 7) gave only the Markovnikov product of benzylic allylation. Allylation at the tertiary carbon in *iso*-butene (entry 8) also proceeded cleanly, however the use of tri- and tetra-substituted alkenes generally gave complex product mixtures in which allylphenylsulphide predominated. The present carbosulphenylation reaction using allyltrimethylsilane worked well with vinyl ethers (entries 9 and 10) to give the corresponding homoallyl ethers[5], with 3,4-dihydro-2*H*-pyran giving only the *trans*-stereoisomer.

Under $ZnBr_2$-catalysis, *O*-silylated enolates[7] of ketones and esters were found to be alkylated in good yield by the PhSCl adducts of vinyl ethers (**7**) (Table 2). The analogous PhSeCl adducts usually gave somewhat lower alkylation yields, again due mainly to competing

selenylation of the nucleophile leading to **9** (X=SePh). In both the sulphur and selenium series, dihydropyran gave only *trans*-adducts (J_{vic} 11-12 Hz) in all the cases examined (entries 4-6). The stereoselectivity observed with dihydrofuran (entry 7), however, was not as high; a mixture of *trans*- and *cis*-adducts was now obtained. In view of this non-stereospecificity,[8] it is unlikely that a bridged episulphonium ion is the sole product-determining intermediate, and the observed *trans* stereoselectivity is now probably simply a consequence of the preferred direction of attack on an open oxonium ion intermediate.

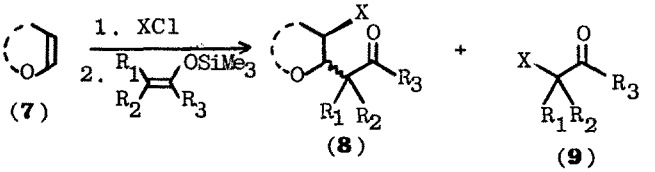
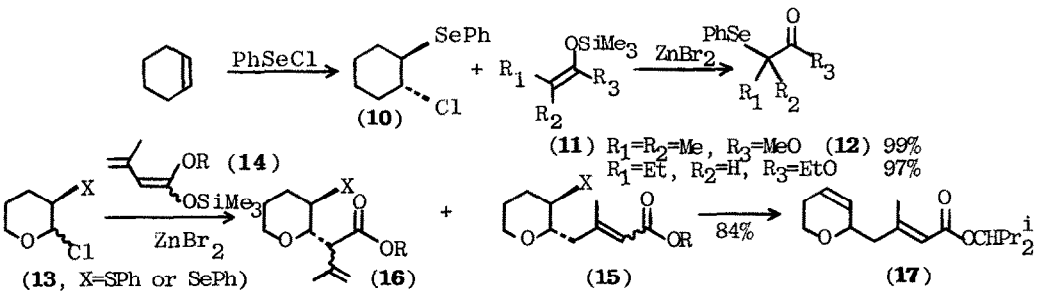


TABLE 2: Reaction of *O*-silylated enolates (1 equiv.) with PhSCl and PhSeCl adducts of vinyl ethers ($ZnBr_2$, *ca* 0.05 equiv.; CH_2Cl_2, 20°C, 0.5 — 3h).

Entry	(7)	R_1	R_2	R_3	(8)	X = SPh(%)	X = SePh(%)
1		H	H	Bu^t		82	50
2	EtO	H	Me	Et		52[a]	52[a]
3		Me	Me	MeO		96	71
4		H	H	Bu^t		59	36
5		Me	Me	MeO		73	76
6		Me	H	EtO		72[a]	40[a]
7		H	H	Bu^t	4:1	75	-

[a] pair of diastereomers



R	X = SPh γ : α	yield(%)	X = SePh γ : α	yield(%)
Me	65 : 35	76	80 : 20	50
Pr^i_2CH	>95 : <5	82	>95 : <5	55

Unfortunately, it appears carboselenylation using *O*-silylated enolates (as well as allyltrimethylsilane[5]) cannot at present be successfully applied to simple alkenes in the same way as is possible[1] for our analogous sulphur process. For example, the PhSeCl adduct (**10**) of cyclohexene, on $ZnBr_2$-catalysed reaction with *O*-silylated enolates (**11**), gave only the corresponding α-phenylseleno esters (**12**) by attack at selenium in preference to alkylation.[9]

Finally, we have examined the reactions of the *O*-silylated dienolates (**14**, R=Me and Pr^i_2CH)[10] with both the PhSCl and PhSeCl adducts of dihydropyran (**13**, X=SPh and SePh).[8a] The dienolate (**12**, R=Me) gave mixtures of γ- and α-alkylated products (**15** and **16** respectively). However, the more sterically demanding dienolate (**14**, R=Pr^i_2CH) showed very high regioselectivity (>20:1) for the γ-product (**15**) in both the sulphur and selenium series. For the PhS-containing system, the major *E*-stereoisomer of **15** (R=Pr^i_2CH) could be isolated by flash chromatography in 62% yield. Standard sulphur oxidation ($NaIO_4$, aq-MeOH; 20°C, 16h) followed by sulphoxide thermolysis (Cl_2CCCl_2, 120°C, 30h) then gave diene (**17**) in high yield. We propose to use this sequence (or the analogous selenium procedure) in a convergent approach to the synthesis of the pseudomonic acid series of antibiotics.[11]

The β-chlorosulphides and β-chloroselenides used were prepared by addition of a solution (1*M* in CH_2Cl_2) of PhSCl or PhSeCl (2.0 ml, 2 mmol) to a solution of the appropriate alkene or vinyl ether (2.1 mmol) in dry CH_2Cl_2 (2ml) at -78°C under Ar, and then warming to room temperature. While the PhSCl adducts of simple alkenes could usually be isolated and stored until required, the vinyl ether adducts were unstable and were used directly. All the PhSeCl adducts prepared were used immediately *in situ* as CH_2Cl_2 solutions.

In a typical allylsilane reaction, dry sublimed $ZnBr_2$ (113 mg, 0.5 mmol) was added to a stirred solution of allyltrimethylsilane (0.35 ml, 2.2 mmol) and the preformed β-chloroalkylphenylsulphide (2 mmol) in dry CH_3NO_2 (4 ml) under Ar. After 16h, the resulting yellow solution was poured into water and extracted with dichloromethane. The separated organic layer was dried ($MgSO_4$) and then concentrated *in vacuo* to give the crude alkylation product, which was purified by chromatography (SiO_2, 1% Et_2O/petrol) and/or bulb-to-bulb distillation.

For the *O*-silylated enolate alkylations, the *O*-silylated enolate (2 mmol) was added to a stirred solution of freshly prepared β-chlorosulphide or β-chloroselenide (2 mmol) in dry CH_2Cl_2 (4 ml), followed directly by a catalytic amount of dry $ZnBr_2$ (*ca* 20 mg). After 0.5-3h, the reaction was poured into saturated $NaHCO_3$ solution, and worked-up as before. This latter procedure was also followed for entries 10 and 11 (Table 1) in the allylsilane reactions.

NOTES AND REFERENCES

[1] S. K. Patel and I. Paterson, *Tetrahedron Letters*, *24*, 1315 (1983).

[2] For an alternative procedure using ArSCl adducts with $TiCl_4$ or $AgBF_4$ as Lewis acid, see: M. A. Ibraginov and W. A. Smit, *ibid*, *24*, 961 (1983).

[3] T. H. Chan and I. Fleming, *Synthesis*, 761 (1979).

[4] Ibraginov and Smit (ref.2) have independently reported on the alkylation of aldehydes and ketones with the ArSCl adducts of vinyl ethers using $TiCl_4$ (1 equiv.) and 2 equivalents of silyl enol ether. Our alternative method using catalytic $ZnBr_2$ is noteworthy, since it is milder, more economical (uses equimolar amounts of both reactants), and works well for ester substrates.

[5] The equivalent selenium reactions using allyltrimethylsilane gave a high yield of allylphenylselenide with little or no sign of alkylation products. Nucleophilic attack at the more electropositive selenium is apparently now more strongly favoured over attack at carbon.

[6] Isomeric purity was determined by ^{13}C- and ^1H-NMR (200 MHz). Isomer ratios in alkylations were measured by ^1H-NMR of the crude product mixtures and confirmed by weighing the chromatographically separated components.

[7] P. Brownbridge, *Synthesis*, 1 (1983); J. K. Rasmussen, *ibid*, 91 (1977).

[8] The initial addition of PhSeCl and PhSCl to vinyl ethers is also sometimes non-stereospecific, although high *trans*-stereoselectivity is usually observed, see: (a) D. G. Garratt, *Canad. J. Chem.*, *56*, 2184 (1978) and (b) K. Toyoshima, T. Okuyama, and T. Fueno, *J. Org. Chem.*, *43*, 2789 (1978).

[9] We thank Barry Langham (Wyeth) for assistance in this work.

[10] I. Fleming, J. Goldhill, and I. Paterson, *Tetrahedron Letters*, 3209 (1979).

[11] For some examples of synthetic efforts in this area, see: G. W. J. Fleet, M. J. Gough, and T. K. M. Shing, *ibid*, *24*, 3661 (1983) and references therein.

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