Pergamon

Tetrahedron Letters, Vol. 35, No. 30, pp. 5481-5484, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01035-8

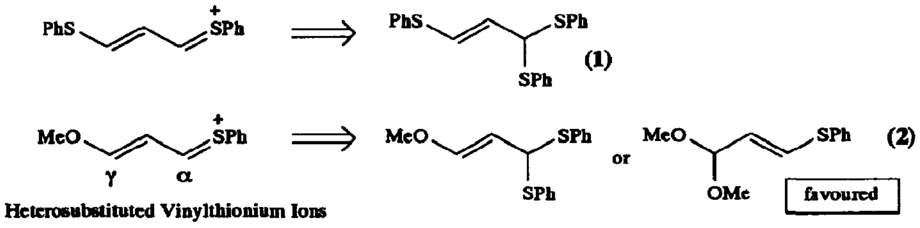
Regioselective Allylation of Enol Silyl Ethers with γ-Heterosubstituted Vinylthionium Ions.

Roger Hunter[a*], Joseph P. Michael[b] and Daryl S. Walter[b].

a:Department of Chemistry, University of Cape Town, Rondebosch 7700, South Africa.
b:Centre for Molecular Design, Department of Chemistry, University of the Witwatersrand,
Johannesburg 2001, South Africa.

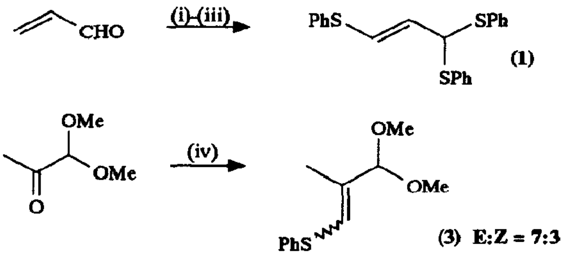
Abstract**: γ-Heterosubstituted vinylthionium ions regioselectively and diastereoselectively allylate enol silyl ethers. Intramolecular capture of a vinylthionium ion is used as a key step of a novel pentannulation sequence.**

We have recently reported[1] methodology for generation of carbon-substituted vinylthionium ions as useful allylating agents for enol silyl ethers, using tin tetrachloride ionisation of substituted 1,3- and 3,3-bis(phenylthio)propenes. We would now like to communicate our results on extension of this methodology to vinylthionium ions bearing alkoxy or phenylthio groups as γ-substituents, and to illustrate an application of the methodology to a pentannulation sequence. Scheme 1.



Scheme 1

Disconnection sequences illustrated in Scheme 1 revealed 1,3,3-tris(phenylthio)propene (1) and 3,3-dimethoxy-1-phenylthiopropene (2) to be desirable targets for the aforementioned vinylthionium ions. Compound (1) was prepared in a three step synthesis from acrolein in 40% overall yield via the following sequence: conjugate addition of thiophenol in the presence of triethylamine; N-chlorosuccinimide (NCS) chlorination α- to the sulfide accompanied by elimination to the vinyl sulfide on stirring at 0°C overnight; thioacetalisation using thiophenol and P_2O_5[2] in CH_2Cl_2. It was isolated as a pure (E)-isomer which was stable at room temperature indefinitely. By comparison, preparation of (2), via direct acetalisation of 3-phenylthioprop-2-enal or α-chlorination, acetalisation followed by dehydrochlorination of 3-phenylthiopropanal, proved unsuccessful. Therefore, the methyl analogue (3) was prepared instead and in 92% yield as a 7:3 E:Z mixture via Peterson olefination[3] of pyruvaldehyde dimethyl acetal. Scheme 2.



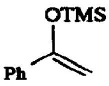
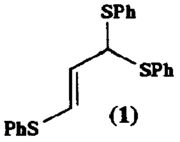
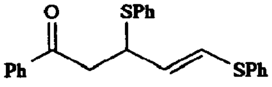
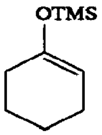
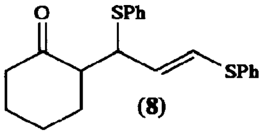
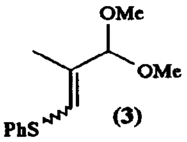
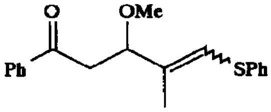
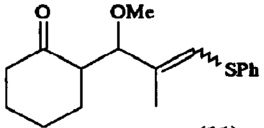
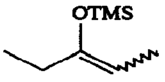
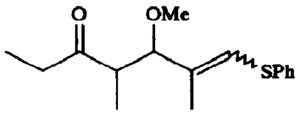
(i) PhSH / NEt_3 / CCl_4 / 0°C to RT
(ii) NCS / CCl_4 / 0°C to RT
(iii) PhSH(2eq) / P_2O_5 / CH_2Cl_2 / 0°C
(iv) PhSCH(Li)TMS / THF / 0°C to RT

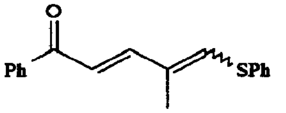
Scheme 2

The results of Lewis acid ($SnCl_4$ or $TiCl_4$) catalysed reaction of (1) and (3) with the enol silyl ethers of acetophenone (4), cyclohexanone (5) and pentan-3-one (6) (as a 3:1 Z:E mixture) are shown in Table 1 across the page. Several points deserve mentioning. Reaction of (1) independently with (4) and (5) gave the expected products (7) and (8) using three equivalents of $SnCl_4$ at -78°C in CH_2Cl_2. The use of excess Lewis acid had no detrimental effect on the reaction outcome in contrast to the case with 1,3- and 3,3-bis(phenylthio)propenes reported earlier[1], in which excess Lewis acid resulted in consumption of the γ-adducts (vinyl sulfides). Compound (8) was obtained as a (2:1) mixture of diastereomers[4], and (E)-vinyl sulfides were obtained exclusively as with the Pummerer methodology. Attempts to hydrolyse the vinyl sulfides (7) and (8) to the corresponding α,β-unsaturated aldehydes were unsuccessful. This methodology constitutes an electrophilic alternative to the carbanionic versions of Corey[5] and Cohen[6] for introduction of the useful 1,3-bis(phenylthio)propenyl fragment.

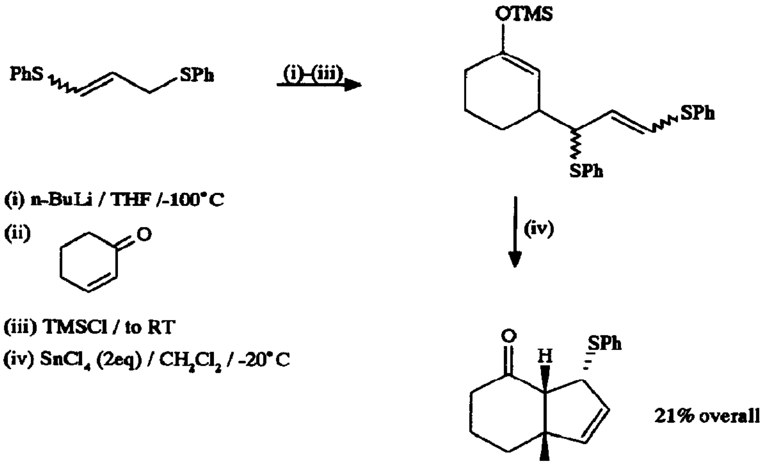
Reaction of (3) revealed a number of interesting features. Firstly, the reactions all occurred completely regioselectively at the oxygen-bearing carbon (γ-terminus, Scheme 1) with no evidence of any α-attack. The increase in E:Z ratio in all three cases lends support to the involvement of a 'free' vinylthionium ion which, in view of the regioselectivity, should be viewed more like a γ-substituted vinyloxocarbenium ion. $TiCl_4$ was used in all three cases as the Lewis acid in view of the Mukaiyama reaction[7]. An interesting feature of the reaction of (3) was that complete conversions could be achieved with less than a stoichiometric amount of Lewis acid when reactions of this type usually require a full equivalent of Lewis acid. In this regard, product (9) could be obtained exclusively in 74% yield with only 0.1 equivalents $TiCl_4$. In this case, higher concentrations of Lewis acid promoted elimination to the diene (10) which became the sole product above 2.5 equivalents $TiCl_4$. Similarly, the other products (11) and (12) could be obtained in high yield (0.5 eq.$TiCl_4$) but these showed a reluctance to eliminate even with excess Lewis acid. Since neither TMSCl nor $Ti(OPr)_4$ promoted the reaction, it is likely that $TiCl_4$ is truly catalytic here, being regenerated from TMSCl and $TiCl_3OMe$. Compound (11) was obtained as a single diastereomer (E:Z:9:1) while (12) was isolated as a 3:1 diastereomeric mixture (E:Z = 85:15) whose ratio was independent of the ratio of E/Z isomers used in the starting enol silyl ether of pentanone (6). Since simple acetals have been shown to react with enol silyl ethers using either TMSOTf[8] or $TiCl_4$[9] to give predominantly erythro (syn) diastereomers via acyclic transition states, it is likely that the major diastereomers in these reactions are the erythro forms. Table 1.

Table 1

Enol Silyl Ether	Acetal	Product	Yield% / a / b
 (4)		 (7)	67 / (E) / -
 (5)	"		73 / (E) / 2:1
(4)		 (9)	74 / 5:1 / - [c]
(5)	"	 (11)	82 / 9:1 / 100:0
 (6) (E):(Z) = 1:3	"	 (12)	77 / 85:15 / 3:1

a is (E):(Z) ratio
b is diastereomeric ratio
c: Diene  (10) also obtained - see text

Application of the methodology to a pentannulation[10] sequence was accomplished using a conjugate addition-trapping strategy[11]. Scheme 3. Addition of the anion of 1,3-bis(phenylthio)propene to cyclohexenone[6] at -100°C in THF followed by enolate quenching with chlorotrimethylsilane gave the intermediate enol silyl ether which could not be purified. However, replacement of the THF with CH_2Cl_2 followed by intramolecular cyclisation via the vinylthionium ion using $SnCl_4$ at -20°C as before afforded cis-3-phenylthio-3, 3a, 5, 6, 7, 7a-hexahydro-4H-inden-4-one in 21% overall yield, isolated almost exclusively (> 85:15) as a single diastereomer as determined by ^1H and ^{13}C NMR. Its relative configuration was established as (3R*, 3aR*, 7aS*) by comparing the coupling constants $J_{H3\text{-}H3a}$ and $J_{H3a\text{-}H7a}$ with those from computer modelling using the modelling programme ALCHEMY[12]. The ring junction stereochemistry was assigned cis on the basis of an NOE experiment. Hence, this annulation complements existing strategies using bifunctional reagents[13].



Scheme 3

In conclusion, these examples illustrate further application of substituted vinylthionium ions in synthesis.

References

1. Hunter, R.; Michael, J.P.; Walter, D.S. *Tetrahedron Lett.* **1992**, 33, 5413.
2. For other, related preparative methods see: a) Cohen, T.; Bennett, D.A.; Mura Jr., A.J. *J. Org. Chem.* **1976**, 41, 2506; (b) Cohen, T.; Mura Jr., A.J.; Shull, D.W.; Fogel, E.R.; Ruffner, R.J.; Falck, J.R. *J.Org. Chem.* **1976**, 41, 3218.
3. a) Peterson, D.J. *J. Org. Chem.* **1968**, 33, 780; b) Ager, D.J. *J.C.S. Perkin Trans. 1* **1983**, **1**, 1131.
4. The same ratio (2:1) was obtained via reaction of 3-phenylsulfinyl-1-phenylthiopropene with (**5**) under Pummerer conditions implying that both reactions proceed via a 'free' vinylthionium ion.
5. Corey, E.J.; Erickson, B.W.; Noyori, R. *J. Am. Chem. Soc.* **1971**, 93, 1724.
6. Myers, M.R.; Cohen, T. *J. Org. Chem.* **1989**, 54, 1290.
7. Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043.
8. Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, 102, 3248.
9. Mukaiyama, T.; Hayashi, M. *Chem. Lett.* **1974**, 15.
10. Hudlicky, T.; Price, J.D. *Chem. Rev.* **1989**, 89, 1467.
11. De Lombaert, S.; Nemery, I.; Roekens, B.; Carretero, J.C.; Kimmel, T.; Ghosez, L. *Tetrahedron Lett.* **1986**, 27, 5099.
12. Alchemy II (Tripos associates inc.) in conjunction with the Karplus equation: Pretsch, E.; Seibl, J.; Simon, W.; Clerc, T. *Spectral Data for Structure Determination of Organic Compounds*, Springer-Verlag, Berlin, Heidelberg, H25 (1983).
13. a) Trost, B. M. *Angew. Chem. Int. Ed. Engl.* **1986**, 25, 1; b) Piers, E.; Marais, P.C. *J. Org. Chem.* **1990**, 55, 3454.

(*Received in UK* 8 *April* 1994; *revised* 26 *May* 1994; *accepted* 27 *May* 1994)