Cyclic Ether Formation with *N*-(Phenylthio)morpholine

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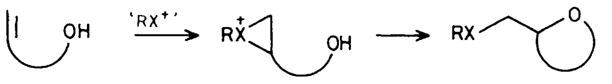
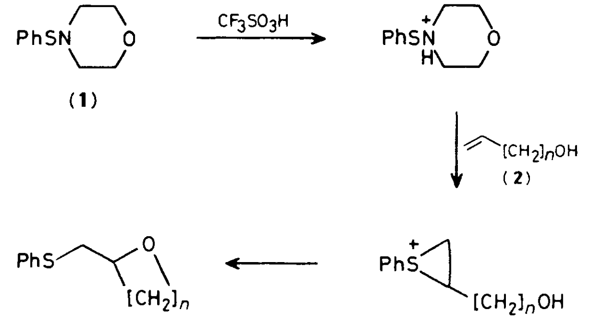
Cyclic ethers with 5- to 7-membered rings are formed by sulphenoetherification of unsaturated alcohols with *N*-(phenylthio)morpholine and trifluoromethanesulphonic acid.

Whilst the exact nature of episulphonium (and episelenonium) ions remains controversial,[1] there is no doubt that these intermediates are most useful in organic synthesis. Particularly notable are cyclization reactions in which an internal nucleophile is captured, such as 'sulpheno-/seleno-etherification' (Scheme 1).[2,3]

I now report a new sulphenoetherification reaction using the stable, readily available[4] sulphenamide, *N*-(phenylthio)-morpholine (**1**), which is operationally easy and produces cyclic ethers with rings of from five to seven members.[5] The cyclization is performed simply by adding one equivalent of

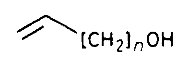
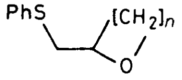
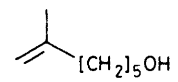
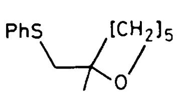
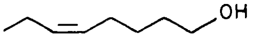
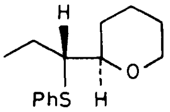
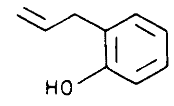
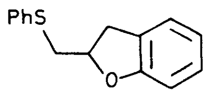
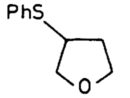


Scheme 1. X = S or Se.



Scheme 2

Table 1. Cyclic ether formation.

Alkenol	Cyclic ether	*n*	Yield (%)[a]
 (2)	 (6)	3 4[g]	95[b,e] 96[b]
	 (7)[h]		74[c], 78[b]
 (3)	 (4)[i]		97[b], 97[c]
			89[b,f]
(2), *n* = 2	 (5)		47[c,d]

[a] Isolated yield of fully characterised products purified by flash column chromatography. [b] In MeCN. [c] In CH_2Cl_2. [d] Promotor $CF_3SO_3SiMe_3$. [e] n_D^{16} 1.5718; lit. (W. E. Parham and L. D. Edwards, *J. Org. Chem.*, 1968, **33**, 4150), n_D^{22} 1.5702. [f] M.p. 54.5—55 °C (EtOH); lit.[2d] m.p. 56—57 °C. [g] δ ($CDCl_3$) 1.2—1.9 (6H, m), 2.93 and 3.08 (2H, ABX, J_{AB} 13.1, J_{AX} 5.8, J_{BX} 6.6 Hz), 3.35—3.5 (2H, m), 3.95—4.05 (1H, m), 7.1—7.4 (5H, m); *m/z* 208 (M^+), 124, 85. [h] δ ($CDCl_3$) 1.26 (3H, s), 1.4—1.9 (8H, m), 3.01, and 3.16 (2H, ABq, J_{AB} 12.5 Hz), 3.5—3.6 (2H, m), 7.1—7.4 (5H, m); *m/z* 236 (M^+), 123, 113. [i] δ ($CDCl_3$) 1.06 (3H, t, *J* 7.3 Hz), 1.4—1.95 (8H, m), 3.0—3.1 (1H, m), 3.35—3.5 (2H, m), 3.95—4.05 (1H, m), 7.1—7.4 (5H, m); *m/z* 236 (M^+), 152, 85.

the acid promotor (trifluoromethanesulphonic acid) to an equimolar mixture of (**1**) and the unsaturated alcohol (**2**) in dry acetonitrile or dichloromethane (2 mmol in 4 ml) at −20 °C (Scheme 2).[6]

Results are presented in Table 1. The *cis*-disubstituted alkenol (**3**) gives a single regio- and stereo-isomer (**4**) indicating *trans*-addition in the expected *exo* mode without any alkene isomerization.

It has not yet proved possible to induce four-membered ring formation by this method. Treatment of buten-3-en-1-ol (**2**, *n* = 2) under the above conditions gave only poorly characterized mixtures; changing the promotor to trimethylsilyl trifluoromethanesulphonate in dichloromethane resulted mainly in the *endo* cyclization product (**5**) (47%, identified by comparison with an authentic sample prepared from benzenethiol and 2,5-dihydrofuran[7]) rather than the 4-*exo-tet* product (**6**, *n* = 2). This mode of cyclization has precedent in some related reactions.[3,8]

The formation of the seven-membered ring ether (**7**) is particularly noteworthy in view of current interest in the synthesis of oxepane terpenes,[9] and application of this method to the synthesis of related natural products is in progress.

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