

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

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Cyclic ethers with 5- to 7-membered rings are formed by sulphenioetherification 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 sulphenioetherification reaction using the stable, readily available⁴ 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.

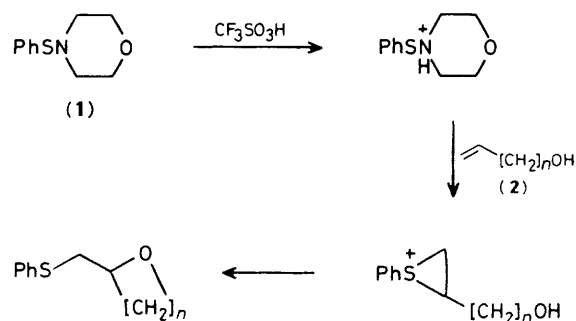


Table 1. Cyclic ether formation.

Alkenol	Cyclic ether	<i>n</i>	Yield (%) ^a
		3	95 ^{b,e}
		4 ⁹	96 ^b
			74 ^c , 78 ^b
			97 ^b , 97 ^c
			89 ^{b,f}
			47 ^{c,d}

^a Isolated yield of fully characterised products purified by flash column chromatography. ^b In MeCN. ^c In CH₂Cl₂. ^d Promotor CF₃SO₃SiMe₃. ^e *n*_D²⁰ 1.5718; lit. (W. E. Parham and L. D. Edwards, *J. Org. Chem.*, 1968, **33**, 4150); *n*_D²² 1.5702. ^f M.p. 54.5–55 °C (EtOH); lit.^{2d} m.p. 56–57 °C. ^g δ (CDCl₃) 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 (CDCl₃) 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 (CDCl₃) 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 benzene-thiol and 2,5-dihydrofuran⁷) 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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