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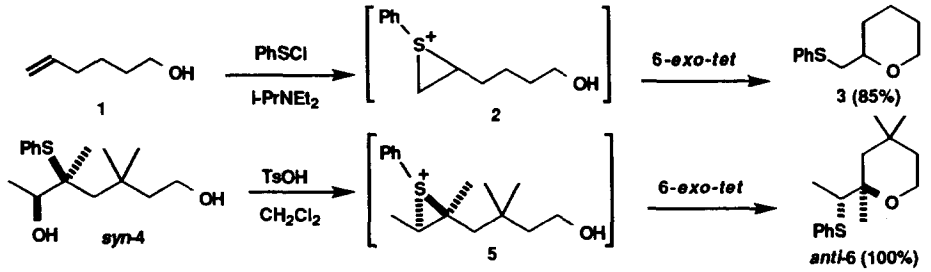
Reactions of Episulfonium Ions from the Sulfenylation of Alkenes and from Phenylthio Migration: Kinetic vs Thermodynamic Control

Paul Bird,[a] Jason Eames,[a] Alex G. Fallis,[b] Ray V. H. Jones,[c] Marc Roddis,[a] Claudio F. Sturino,[b] Susan O'Sullivan,[a] Stuart Warren,[a]* Martin S. Westwell[a] and Julia Worrall[a]

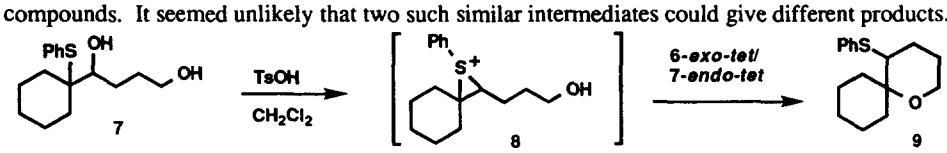
[a]University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW, England
[b]Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ontario, Canada K1N 6N5
[c]ZENECA Fine Chemicals Manufacturing Organisation, Earls Road, Grangemouth FK3 8XG, Scotland

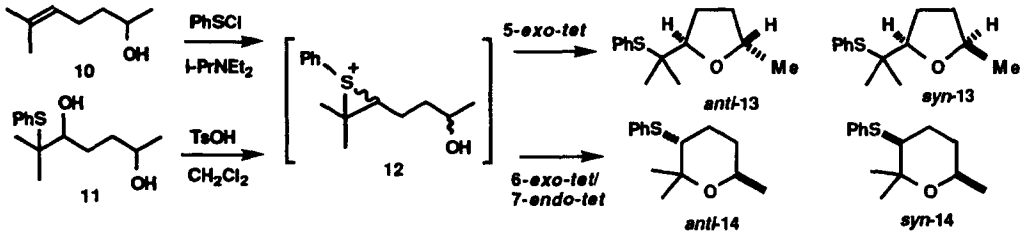
Abstract: The formation of the same cyclic ethers from the sulfenylation of unsaturated alcohols and from acid catalysed phenylthio migration on diols *via* the same intermediate can be explained by kinetic and thermodynamic control. Both reactions are synthetically useful. A result from a previous Tetrahedron Letter is corrected

The sulfenylation of unsaturated alcohols, e.g. **1**, gives cyclic ethers, e.g. **3**, (sulfenyletherification)[1,2] when the hydroxyl group attacks the intermediate episulfonium ion **2**. The rearrangement[3,4] of phenylthio (PhS) substituted diols, e.g. **4**, in acid solution gives the same type of intermediate **5** and similar cyclic ethers **6**. In almost all cases the rules[4] for both cyclisations are the same: (i) cyclisation occurs to the more substituted end of the episulfonium ion, (ii) a pure *exo* rather than hybrid *exo/endo* mode is preferred according to Baldwin's rules, (iii) the Thorpe-Ingold effect is important and (iv) developing *anti* stereochemistry in the new ring is preferred to *syn*. Thus the cyclisation of **1** to **3** and of *syn*-**4** to *anti*-**6**, both in high yield, clearly obey rules (i) and (ii) while rules (iii) and (iv) are unimportant. This letter reconciles an apparent conflict between rules (i) and (ii) with results from the two reactions in the one series of compounds where they are different.

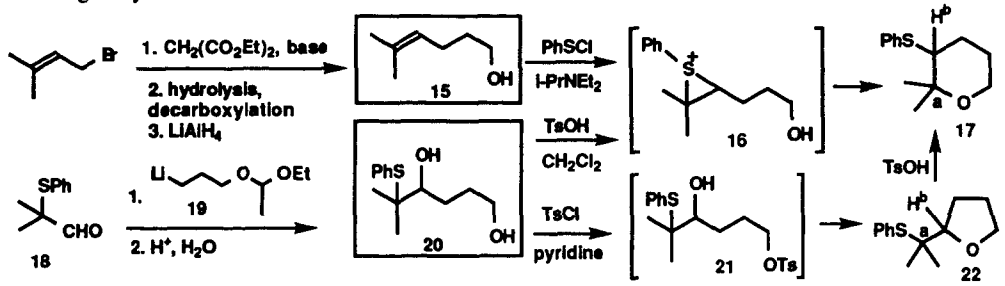


We had reported[4] that the diol **7** gave exclusively the THP **9** in 100% yield *via* the disfavoured hybrid 6-*exo*/7-*endo*-*tet* attack at the more substituted carbon atom of episulfonium ion **8**. We had also reported[1] that the alcohol **10** cyclised to a 1:1 mixture of the tetrahydrofuran[5] (THF) **13** and the tetrahydropyran (THP) **14** in 84% yield, through a very similar episulfonium ion **12**. We did not then discuss the stereochemistry of these compounds. It seemed unlikely that two such similar intermediates could give different products.





We have now reinvestigated both reactions, forming the identical episulfonium ion **12** from the unsaturated alcohol **10** and the diol **11** and we report that the two reactions in fact give the same products and follow the same rules. We first studied the simpler compounds **15** and **20** without the extra methyl group, as there is no stereochemistry to cause confusion, made by the routes in Scheme 1. We found that both the sulfenylation of the unsaturated alcohol **15** and the acid catalysed rearrangement of the diol **20** gave the same product in good yield: the THP **17**. Attack occurs at the more substituted carbon atom of **16**.



Scheme 1: Synthesis and rearrangement of unsaturated alcohol **15** and the diol **20**.

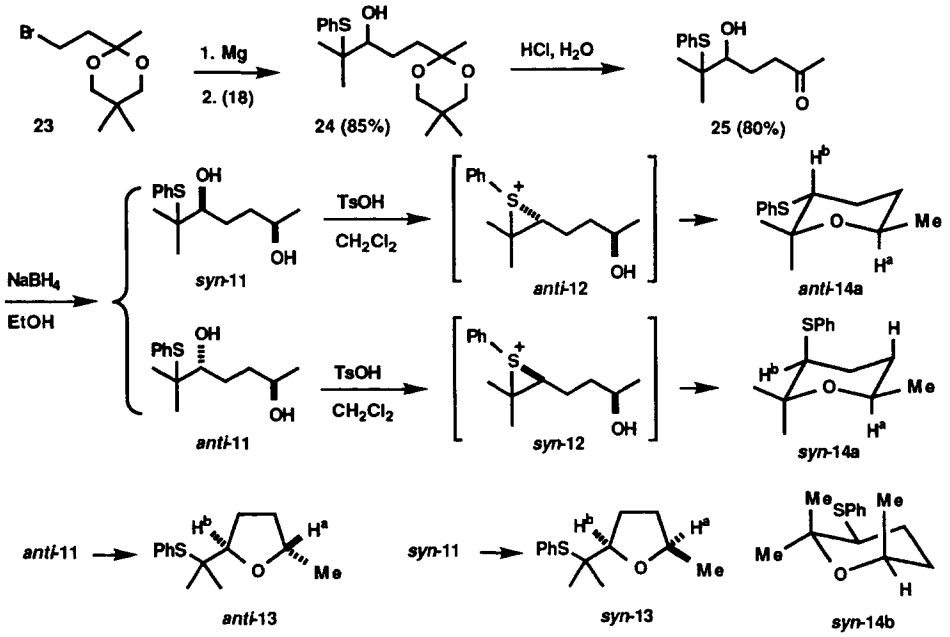
The identification of **17** as a THP was made easier because we had prepared[6] the alternative product, the THF **22**, by treatment of the same diol **20** with toluene-*p*-sulfonyl chloride in pyridine. The ^{1}H NMR spectrum of **22** includes (Table 1) a triplet (J = 7 Hz) for OC*H*, as $J_{syn} = J_{anti}$ in these THFs. The THP **17** by contrast has a double doublet for PhSC*H* with typical axial/axial and axial/equatorial coupling constants. In the ^{13}C spectra, the THF has a quaternary carbon[7] next to PhS (δ 51.7) and a CH group next to oxygen (δ 85.1), while the THP has a quaternary carbon[7] next to oxygen (δ 75.2) and a CH group next to PhS (δ 55.2). In the mass spectrum, the THF **22** fragments between the ring and the $PhSCMe_2$ group, both fragments being observed. No such fragmentation is possible with the THP **17** which gives $PhSC_2H_3$ as the base peak. The formation of the THP as sole product from the acid catalysed reaction is inevitable because the THF **22** rearranged to the THP **17** under the conditions of the reaction[10] and the THP is the thermodynamic product.

We could now proceed to the system under study. The diol **11** required for the key episulfonium ion **12** was made (Scheme 2) as a 1:1 mixture of diastereoisomers from the acetal[8] **23** via the hydroxyketone **25**. Rearrangement of the mixture (which we could not separate) with TsOH in refluxing CH_2Cl_2 for two hours gave a 1:1 mixture of two compounds and a trace of the third. Re-examination of the sulfenylation of the alcohol **7** showed that it too gave the same *three* products. These were identified (Table 1) as the THP *anti*-**14**, the THP *syn*-**14** and a trace of the THF *syn*-**13**. In the mass spectrum, both THPs gave the characteristic $PhSC_2H_3$ as base peak and failed to fragment between the $PhSCMe_2$ group and the rest of the molecule. The THP *anti*-**14a** was easily identified from its ^{13}C NMR spectrum (Table 1) and because H^b (next to PhS, δ 3.02 ppm) was clearly an axial proton on a six-membered ring [double doublet with large axial/axial (J 12.3 Hz) and small axial/equatorial (J 4.4 Hz) coupling constants].

Table 1: Identification of THFs and THPs by ^{13}C and ^{1}H NMR and Mass spectra

δ (ppm) or *J* (Hz) or Mass Spectrum	Tetrahydrofurans			Tetrahydropyrans		
	22	***anti*-13**	***syn*-13**	**17**	***anti*-14**	***syn*-14**
δ quaternary[7] C^a	(C-S) 51.7			(C-O) 75.2	78.2	74.5
δ tertiary[7] C^b	(C-O) 85.1			(C-S) 55.2	53.1	55.0
δ H^b	3.78 (t)	3.95 (t)	3.78 (t)	3.07 (dd)	3.02 (dd)	3.20 (t)
J_{syn} H^b	7.0	6.0	7.05	11.75	12.3	3.4
J_{anti} H^b	7.0	6.0	7.05	4.1	4.4	3.4
151.1 ($PhSCMe_2^+$)	100%			0%	0%	0%
M – 151	40%			0%	0%	0%
136.0 ($PhSC_2H_3$)	0%			100%	100%	100%

We had previously identified the THP *syn*-**14** as the THF *anti*-**13**. In fact this THP has an axial PhS group (*syn*-**14a**) rather than an axial methyl group (*syn* **14b**) both because PhS has a smaller A value[9] (0.80) than has a methyl group (1.70) and because of the bad 1,3-diaxial interaction between two methyl groups in *syn*-**14b**. The equatorial proton appears as a THF-like triplet, but the coupling constant is 3.5 Hz, rather than 6-7 typical for a THF. We were fortunately able to make larger amounts of both THFs when we attempted to prepare cyclic sulfites[10] ($Et_3N/SOCl_2$) from the mixed diols **11**. The THFs both have triplets for H^b: at δ 3.90 ppm, J = 6 Hz for *anti*-**13** and at δ 3.78 ppm, J = 7 Hz for *syn*-**13**. In addition the ^{13}C spectra for all four compounds are characteristic with quaternary carbons next to PhS for the THFs and next to oxygen for the THPs (Table 1). Both reactions give the same products and cyclisation occurs almost exclusively at the more substituted end of the episulfonium ion **12**.

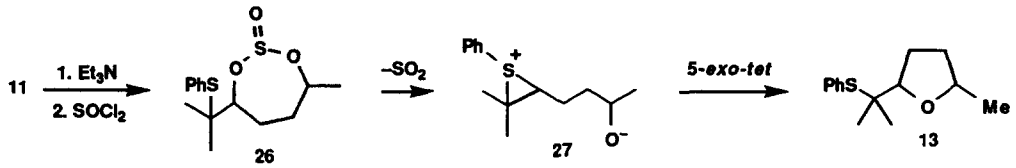


Scheme 2: Synthesis and Rearrangement of the Diol **11**.

Cyclisation of the episulfonium ion **12** is stereospecific: *syn*-**12** would give both *syn*-THF **13** and *syn*-THP **14** whilst *anti*-**12** would give both *anti*-THF **13** and *anti*-THP **14**. The THPs **14** are the thermodynamic products of both reactions. After five hours with TsOH in CH_2Cl_2 *anti*-**11** gives only *anti*-**14** while *syn*-**11** gives a 95:5 ratio of THP:THF. By reducing the time of reflux or the temperature we can approach kinetic control (Table 2) but this is finally achieved only by treatment with Et_3N followed by $SOCl_2$ so that the cyclic sulfite **26** is formed and decomposed in the presence of base and equilibration of THF to THP by acid cannot occur. Even then, the THP dominates in the *anti* series though the THF dominates in the *syn* series where 5-*exo*-*tet* closure of the zwitterion **27** finally becomes more favourable than THP formation. Sulfenyletherification of **10** also gives only *anti*-**14** and a 95:5 ratio of *syn*-**14**:*syn*-**13**. It seems after all that both sulfenyletherification and diol rearrangement give the same products from the same intermediates in all classes of compounds so far investigated and that both are under thermodynamic control.

Table 2: Kinetic and Thermodynamic Control in the formation of THFs and THPs

Reaction Conditions	Product Ratio THF:THP	
	anti-**13** : *anti*-**14**	*syn*-**13** : *syn*-**14**
Kinetic: 1. Et_3N, CH_2Cl_2; 2. $SOCl_2$	**39 : 61**	**72 : 28**
TsOH, CH_2Cl_2, 2h, room temperature	9 : 91	44 : 56
TsOH, CH_2Cl_2, 20 min, reflux	3 : 97	15 : 85
TsOH, CH_2Cl_2, 2h, reflux	<2 : >98	10 : 90
Thermodynamic: TsOH, CH_2Cl_2, 5 h, reflux	**<1 : >99**	**5 : 95**



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References and Notes.

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