REGIOSELECTIVITY IN THE FORMATION OF CYCLIC SULPHONES FROM 4- AND 5-ALKENESULPHONYL CHLORIDES

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<u>Abstract</u>. Alk-4-enesulphonyl chlorides and alk-5-enesulphonyl chlorides cyclise under free radical conditions mainly in the <u>endo</u> mode to give tetrahydrothiopyran-1,1-dioxide and thiepane-1,1-dioxide respectively.

Sulphonyl radicals, RSO₂[•], generated from sulphonyl chlorides, readily undergo intermolecular addition to alkenes to give sulphones.¹⁻³ However, the intramolecular cyclisation reaction, which is a potential route to cyclic β -chloro sulphones, has scarcely been investigated. Unsaturated sulphonyl radicals were proposed as intermediates in the reactions of pentenylcobaloximes with trichloromethanesulphonyl chloride⁴ and sulphur dioxide.⁵ Cyclisation in the <u>endo</u> mode to give six-membered ring tetrahydrothiopyran-1,1-dioxides was observed.

We generated the archetype pentenesulphonyl radical 2 by treatment of pent-4-enesulphonyl chloride, 1, with photochemically produced trimethyltin radicals, in the cavity of an EPR spectrometer. Radical 2 was observed in the temperature range 240-370 K but no cyclised species were detected at higher temperatures.



Reduction of 1 with tri-n-butyltin hydride using photochemical initiation at 170 °C gave mainly pent-4-enesulphinic acid; 3, probably produced when radical 2 abstracts hydrogen from the organotin hydride. However, treatment of 1 with various alternative radical initiator systems (Table) led to the formation of significant amounts of 3-chlorotetrahydrothiopyran-1,1-dioxide, 7. That cyclisation

occurs mainly in the <u>endo</u> mode to give the 6-membered ring radical, 6, was established from the ¹H and ¹³C NMR spectra of 7 and by dehydrochlorination of 7 with DBU to give the dihydrothiopyran-1,1-dioxide 9. Minor amounts of 2-chloromethyltetrahydrothiophene-1,1-dioxide 5 were obtained, the ratio [7]:[5] being ca. 8:1 (Table)

Products of F	actions of Pent-	t-4-enesulphonyl Chloride 1.			
Initiator	т∕⁰С	Yield ^a mol %	Rel. Yie 7	elds (%) 8	5
CuCl ₂ /AIBN	150	12	100	-	
n .	75	nd	88	-	12
RuCl ₂ (Ph ₃ P) ₃	170	15	100	-	-
Bu3SnH/AIBN/C6H6	80	nd	74	26	-
(Bun3Sn)2/AIBN/PhBut	45	nd	77	12	11
Ph3SiH/hv ^b SnMe ₃	170	nd	78	14	8
(II) /hv ^c	170	18	91	-	ç

^a Yield of cyclised products after prep. TLC. ^b For method see ref. 6. ^c For method see ref. 7. nd = not determined.

In the Cu^{II} and Ru^{II} catalysed reactions, 7 was the main product, together with some polymer. It is likely, however, that 2 loses SO₂, under the reaction conditions, to give pentenyl radicals. The volatile products formed in this way easily escape and this accounts for the low yields of cyclic sulphones. Traces of 4 were observed in the Cu^{II} catalysed reaction. The reductions of 1 with Bu₃SnH or Ph₃SiH gave 7 together with 8, the proportions depending on temperature. Treatment of 7 with Bu₃SnH gave 8 and therefore this product may be formed directly from radical 6 and as a secondary product from 7.

In the Cu^{II} catalysed reaction of hex-5-enesulphonyl chloride, 10, at 150°C only chloromethylcyclopentane, 12, formed by sulphur dioxide loss from the intermediate sulphonyl radical 11, was observed. However, in the Bu₃SnH reduction of 10 at low



temperatures, the product of <u>endo</u> cyclisation, i.e. thiepane-1,1-dioxide, 14, was obtained in low yield.

The mechanism of the Cu^{II} catalysed reactions is thought to involve chlorine atom transfer from the CuCl₂ by the adduct radical^{1,2,8}, equ. (1):

$$SO_2CH_2CH' + CuCl_2 \longrightarrow SO_2CH_2CHCl + CuCl (1)$$

 $CuCl + RSO_2Cl - CuCl_2 + RSO_2^{-1}$

In the Ru^{II} catalysed process chlorine atom transfer is believed to occur from Ru^{III} chloride^{9,10}. In our reductions of 1 with Bu₃SnH and Ph₃SiH the main product was the chloro-sulphone 7. This indicates that chlorine atom transfer must occur very rapidly from the sulphonyl chloride, equ. (2).

$$SO_2CH_2CH' + RSO_2Cl \longrightarrow SO_2CH_2CHCl + RSO_2'$$
 (2)

i.e. reaction (2) must compete effectively with hydrogen atom transfer from Bu₃SnH, which is known to be very fast.¹¹

Radicals centred on carbon, nitrogen and oxygen with pent-4-enyl substituents preferentially cyclise in the <u>exo</u> mode to give 5-membered ring products.^{12,13} The sulphonyl radicals 2 and 10 provide a contrast in that <u>endo</u> cyclisation is preferred. Radicals centred on second row elements generally show lower regioselectivity in cyclisation.¹³ For example, thiyl radicals give both <u>exo</u> and <u>endo</u> products depending on reaction circumstances.^{13,14}

That the regioselectivity of alkenesulphonyl radicals can change in favour of <u>exo</u> cyclisation was shown by the reaction of the sulphonyl chloride 15 with CuCl₂ or Ph₃SiH. This gave exclusively the bicyclic sulphone 18 by <u>exo</u> cyclisation to 17 as shown below. In the Ph₃SiH reduction, 3-ethylcyclohexene was a major by-product which was



probably formed by loss of SO₂ from the sulphonyl radical 16. The surprising preference of 16 for 5-membered ring formation can be attributed to two factors. Firstly, in the half-chair conformation of radical 16 the sulphonylethyl group will preferentially occupy a quasi-equatorial orientation. Models indicate that the radical centre is much better placed for 5-membered ring formation in this conformation. Secondly, it is known that hexenyl radicals with *cis* substituents on the terminal

carbon of the double bond show an even greater preference for 5-membered ring formation than hex-5-enyl itself;¹³ probably because of increased steric interaction, in the transition state for 6-membered ring formation, between the *cis* substituent and the hydrogens on C β . A similar effect would operate in the transition state for 6-membered ring formation from the quasi-axial (and quasi-equatorial) conformation of radical 16.

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