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Rearrangements of Phenylthio Substituted 1,n-Diols with Toluene-p-sulfonic Acid and with Toluene-p-sulfonyl Chloride

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Abstract: Rearrangement of a series of 1,n diols (n= 2 to 12), one OH group having an adjacent PhS group, under the two sets of conditions in the title, gives single compounds in high yield drawn from four possible classes of product. The effects of chain length help in our understanding of the mechanism of the rearrangements.

We have used phenylthio (PhS) migration in stereospecific syntheses¹ of substituted lactones, cyclic ethers, e.g. 3, and amines² and elaborated rules³ for the stereo- and regiochemical control of these rearrangements. We now report the effects of different chain lengths between the two hydroxyl groups in the diols 5 (1 is 5; n=3) during acid catalysed rearrangements and on a new reaction: the rearrangement of the same diols 5 on treatment with toluene-*p*-sulfonyl chloride in pyridine. The acid catalysed reaction gives products from the episulfonium ions 6 while the TsCl/pyridine reaction has the primary tosylate 4 as an intermediate which is not usually isolated.



The various possible products are illustrated in the Scheme. Using the same series (n=3) they are: the allylic sulfide 7, formed by the well known [1,2] PhS shift,¹ the allylic alcohol 8 formed by the unknown [1,5] PhS shift and the two cyclic ethers: 3 formed with PhS migration⁴ by a hybrid 7-endo- and 6-exo-tet cyclisation and 9 formed without PhS migration by a 5-exo-tet cyclisation. In fact the diol 1 gives 100% rearranged heterocycle 3 in acid solution and 98% unrearranged heterocycle 9 with TsCl/pyridine.



Scheme: Four possible products from the rearrangement of the diols 5.



The diol 5; n=1 was made from the aldehyde¹ 11 using a Sharpless racemic dihydroxylation⁵ to introduce the 1,2-diol. It rearranged to the allyl sulfide 13 (96%) in acid. In TsCl/pyridine however, it gave the epoxide 10 (80%) whose structure was independently confirmed by synthesis from the 2-PhS-aldehyde¹ 11, the starting material for all of the syntheses. Presumably the allyl sulfide 13 is formed via the episulfonium ion 6; n=1 and the epoxide is formed by a simple closure of the primary tosylate 4; n=1 in base.



When the epoxide 10 is subjected to the conditions of the acid-catalysed reactions, it too forms the allylic sulfide 13 by a [1,2] PhS shift 14 which must occur via the same episulfonium ion 6; n=1 and hence also via the remarkable oxaspiropentane transition state 15. The epoxide 10 can never be made by the acid catalysed rearrangement but is usefully formed in good yield as the kinetic product with TsCl/pyridine.



The homologous 1,3-diol 5; n=2, made by aldol methodology,¹ gives the expected¹ tetrahydrofuran (THF) 17 (99%) in acid via the episulfonium ion 6; n=2, but the unexpected product 16 (97%) of a [1,4] PhS shift via 19 and 18 with TsCl in pyridine. The same pair of reactions occurs stereospecifically on the syn or the anti-diols 22 to give the [1,4] PhS shift 21 or THF 23. We have previously observed [1,4] PhS shifts only with the assistance of two other PhS groups in the same molecule.⁶ The first two diols provide a representative of each of the four types of product: all are formed in very high yield.



The remaining diols were made in excellent overall yields [5; n=3 (99%), n=4 (85%), n=5 (89%), n=6 (99%), n=8 (87%) and n=11 (99%)] by addition of the appropriate protected lithium derivative of 25 (cf. n=3 introduced by Eaton⁷) to the aldehyde 11. Deprotection (HCl, H₂O, EtOH) was easily achieved without rearrangement. The 1,4-diol 5; n=3 is compound 1 whose rearrangement to the tetrahydropyran (THP) 3 is known.⁴ With TsCl/pyridine it gives instead the THF 9 in near quantitative yield. This reaction is simple ether formation, like the formation of the epoxide 10 from 5; n=1. With 5; n=4 we come to the only example of a mixture formed in the acid catalysed rearrangement: the unrearranged THP 26 and the rearranged allylic sulfide 27 are formed in a combined yield of only 72%. The rearranged heterocycle would be a less stable oxepin and this is not formed. Quantitative yields return with a Z-alkene in the chain 28 but again only the DHP 30 is produced: the intermediate 29 clearly has more conformations favourable for cyclisation than has 6; n=4. The TsCl/pyridine reaction on 5; n=4 gives the THP 26 as expected by simple ether closure.



When the chain is longer, the TsCl/pyridine reaction finally gives primary tosylate 31 as neither cyclic ether formation nor a [1,7] PhS shift is favourable. The acid catalysed reaction forms only allylic sulfide, e.g. 32, with n=5, 6, 8, or 11 as the alternative would be a unfavourable medium ring heterocycle. Allylic sulfides of this kind have been used¹ to make allylic alcohols by the [2,3] sigmatropic rearrangement of the corresponding sulfoxides. The allylic sulfides 13 and 32 as well as those with longer chain lengths can be made without the protection of the primary alcohol needed in other published examples.^{1,3,4}

The table summarises these remarkably diverse reactions. The allylic sulfide is formed in the acid catalysed reactions when the chain is too short (n=1) or too long (n>4) to cyclise. The rearranged heterocycles are formed if the ring size is 5 or 6, but not otherwise. In the TsCl/pyridine reactions, the three-membered heterocycle 10 can also be formed, but this is unstable under the conditions of the acid-catalysed rearrangement. The only PhS migrations found are the [1,2] and [1,4] shifts via three and five-membered ring intermediates. Previous studies⁸ on PhS participation in the solvolysis of primary tosylates have shown that it is at least two orders of magnitude more efficient via three- and five-membered rings than via six-membered rings. It is not surprising therefore that participation by the secondary OH group to form the THF

9 is preferred to PhS participation in the reaction of 5; n=4 with TsCl/pyridine. By choice of starting material and rearrangement conditions, any of the five or six-membered cyclic ethers or (with protection if n=2, 3 or 4) the allylic sulfides 7 can be made in high yield.

	Product from TsCl/pyridine		Product from TsOH/CH ₂ Cl ₂	
Starting Material	Product Type ^a	Compound (yield)	Product Type ^a	Compound (yield)
5 ; n=1	Unrearranged heterocycle	10 (80%)	Allylic sulfide	13 (98%)
5 ; n=2	[1,4] PhS shift	16 (97%)	Rearranged heterocycle	17 (99%)
anti-22	[1,4] PhS shift	anti-21 (99%)	Rearranged heterocycle	anti-23 (98%)
syn-22	[1,4] PhS shift	syn-21 (99%)	Rearranged heterocycle	syn-23 (98%)
5; n=3 (= 1)	Unrearranged heterocycle	9 (98%)	Rearranged heterocycle	3 (100%)
5; n=4	Unrearranged heterocycle	26 (98%)	Unrearranged heterocycle Allylic sulfide	26 (59%) 27 (13%)
Z-28	-	-	Unrearranged heterocycle	30 (98%)
5 ; n=5	Primary tosylate	31 (90%)	Allylic sulfide	32 (95%)
5; n=6	-	-	Allylic sulfide	7; n=6 (99%)
5 ; n=8	-	•	Allylic sulfide	7; n=8 (95%)
5; n=11	_	-	Allylic sulfide	7; n=11 (95%)

Table: Products from the Rearrangement of Diols 5 with TsCl/pyridine and with TsOH/CH₂Cl₂.

^aRearrangement means PhS migration: "rearranged" heterocycles are of type 3 and "unrearranged" of type 9.

Typical procedures: Acid-catalysed rearrangement.- A solution of the diol 5 (1 mmol) and toluenep-sulfonic acid (0.2 mmol) in dichloromethane (2.5 cm^3) was heated under reflux for five minutes. The solution was filtered through silica with dichloromethane as eluent. The filtrate was evaporated under reduced pressure. Column chromatography of the residue on silica eluting with light petroleum, b.p. 40-60 °C/ether (9:1) gave the product as an oil.

Rearrangement with TsCl.- The diol 5 (1 mmol) and toluene-*p*-sulfonyl chloride (1.1 mmol) were stirred in dry pyridine (3 cm³) at room temperature under argon for 48 hours. Aqueous HCl (3 molar, 2 cm³) was added and the mixture extracted with ether (3 x 10 cm³). The combined ether extracts were dried (MgSO₄) and evaporated under reduced pressure. Column chromatography of the residue on silica eluting with light petroleum, b.p. 40-60 °C/ether (9:1) gave the product as an oil.

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