Pergamon

Tetrahedron Letters, Vol. 35, No. 48, pp. 8981-8984, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)02022-1

Photoinduced Rearrangement of Carbocyclic 2-Phenylthio-1,3-diols to Deoxysugars.

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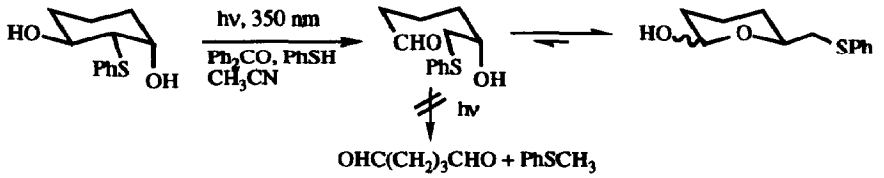
ABSTRACT: The present paper describes the rearrangement of carbocyclic 2-phenylthio-1,3-diols and 1,3,4-triols to tetra-, tri-, and dideoxysugars by a photoinduced electron transfer process.

Some time ago, we reported the photosensitized cleavage of 2-phenylthioalcohols as a synthetically useful indirect redox cleavage of the olefinic bond.[1] This transformation, which belongs to a growing class of reactions named photoinduced electron transfer-fragmentation reactions,[2] was developed in analogy to the photosensitized decarboxylation of arylamino-, phenylthio- or phenoxyacetic acids and the fragmentation of substituted 2-aminoethanols studied by Davidson[3] a number of years ago.

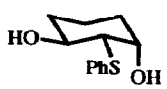
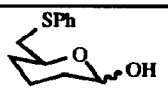
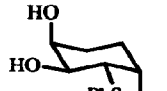
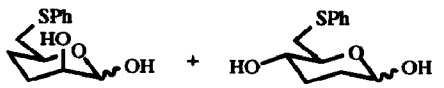
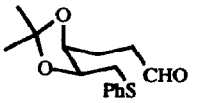
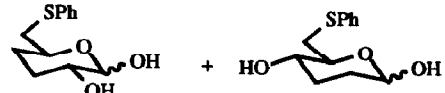
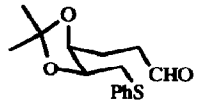
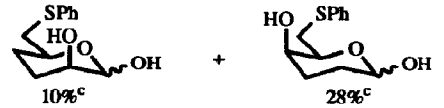
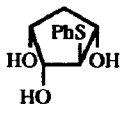
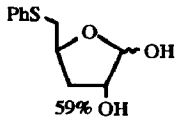
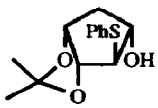
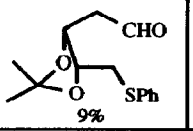
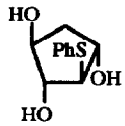
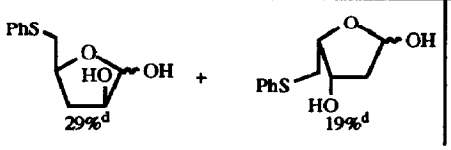
Recent studies of the above phenylthioalcohol system, as pertain to the influence of additional hydroxyl substituents and the effect of their stereochemistry on the course of reaction, have allowed us to uncover new reactivity patterns of synthetic and mechanistic interest.

Table 1 shows a series of carbocyclic 2-phenylthio-1,3-diols and 1,3,4-triols which have been submitted to benzophenone sensitized photolysis in acetonitrile to yield, beyond our expectations, a series of tetra-, tri-, and dideoxysugars. Indeed, and as shown below on the basis of our previously reported results,[1] the photolysis of 2-phenylthiocyclohexane-1,3-diol of entry 1 should have yielded some (if not solely) glutaraldehyde and thioanisole through sequencial redox cleavage of the *vicinal* phenylthioalcohol moieties. Instead however, the phenylthiohydroxyaldehyde generated by the first cleavage is protected from further efficient reaction by formation of an internal hemiacetal through ring-chain tautomerism and the structure thus formed corresponds to a deoxysugar. Because of the large number of natural products whose structures can be correlated to deoxysugars,[4]



this observation bears potential synthetic value and merits systematic investigation. Thus, entries 2 to 9 show that the rearrangement appears general leading to deoxypyranoses and furanoses with yields varying between ~40-65%, except in the case of entry 8 where the yield could not be raised under our standard conditions. More specifically, entry 2 shows that the introduction of an additional hydroxyl group in a *vicinal-cis* relationship to the equatorial alcohol flanking the phenylthio group, gives an almost totally regioselective rearrangement with cleavage on the diol side. Furthermore, this selectivity can be completely diverted to the other side (i.e. the lone

Table 1. Rearrangement of Carbocycles to Deoxysugars.[a]

Entry[b]	Starting compound	Rearrangement product(s) and yield	shifts of diagnostic C_1 protons in $CDCl_3$
1		 64%	$H_{1\alpha}$ δ 4.69-4.74 (m, .55H) $H_{1\beta}$ δ 5.34 (s, .45H)
2		 63% + trace	2-OH: $H_{1\alpha}$ δ 4.69 (d, J= 7.0 Hz, .65H) $H_{1\beta}$ δ 5.11 (s, .35H) 4-OH: mixt. of C5 + C6 + open forms H_1 δ 4.80 (m, .13H); 5,28 (s, .19H); 5.47 (s, .36H); 5,56 (s, .20H); CHO: δ 9.48 (s, .12H).
3		 44%	CHO: δ 9.82 (t, J= 1,2 Hz) Hydrolysis gave 4-OH compound of entries 2 and 4
4		 48% + 17%	2-OH: $H_{1\alpha}$ δ 4.48 (d, J= 7.6 Hz, .54H) $H_{1\beta}$ δ 5.22 (d, J= 3.3 Hz, .46H) 4-OH: see entry 2
5		 62%	see entry 3
6		 10%[c] + 28%[c]	2-OH: see entry 2 4-OH: mixt. C5+C6+open forms H_1 δ 4.76 (s, .13H); 5.33 (s, .12H); 5.49 (s, .48H); 5.58-5.60 (m, .19H); CHO: 9.46 (s, trace)
7		 59%	$H_{1\alpha}$ δ 5.13 (s, .62H) $H_{1\beta}$ δ 5.20 (d, J=4,0 Hz, .38H) (in CD_3OD)
8		 9%	CHO: δ 9.71 (t, J= 1.8Hz) (in CD_3OD)
9		 29%[d] + 19%[d]	2-OH: $H_{1\alpha}$ δ 5.08 (d, J= 4,4 Hz, .34H) $H_{1\beta}$ δ 5.19 (s, .66H) 4-OH: H_1 δ 5.34 (m, .40H); 5.57 (m, .60H) (in CD_3OD)

[a]For a typical procedure see ref. 1. [b]All compounds prepared and isolated in this work were fully characterized by mass spectrometry and ^1H NMR with COSY 2D analysis. Starting diols and triols were all obtained by PhS-opening of precursor epoxyalcohols; triol of entry 6 was obtained as minor (13%) constituent in the preparation of triol of entry 2. [c]Yield determined by NMR but compounds isolated. [d]Yield determined by NMR.

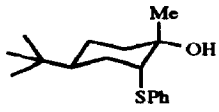
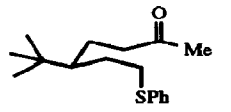
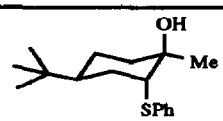
hydroxyl side) (entry 3), simply by forming the acetonide derivative of the *vic*-diol pryor to photolysis. Entry 4, where selectivity drops to ~3 : 1 still in favor of rearrangement on the *vic-cis*-diol side, shows (in comparison to entry 2) that both the presence of the *vic-cis*-diol and the stereochemistry of the lone hydroxyl flanking the phenylthio group on the other side affect the regioselectivity. Here again, protection of the *vic*-diol in the form of its acetonide (entry 5) pryor to photolysis, allows the rearrangement to be diverted totally to the other side.

Entry 6, where the *vic*-diol is now *trans* with respect to entry 4 where it was *cis*, shows a reversal of selectivity with a ~3 : 1 ratio now favoring rearrangement on the lone hydroxyl side. This demonstrates that, not only the presence of the *vic*-diol has an effect on selectivity, but also its stereochemistry.

The last three entries show the same general trend in the five membered ring series. Indeed, entry 7, which displays the same stereochemistry pattern as entry 4, shows totally regioselective rearrangement on the *vic-cis*-diol side whereas in entry 4 it was ~3 : 1. Here again, the regioselectivity can be reversed (entry 8) but with a very poor yield of 9% and large amounts (~60%) of starting material being recovered. The final entry (9) shows the reactivity of a model compound where the stereochemistry of the *vic*-diol is now *trans* with respect to entry 7. This stereochemistry pattern is the same as that displayed in entry 6 where the results were ~3 : 1 in favor of rearrangement on the lone hydroxyl side whereas in entry 9 the ratio is ~3 : 2 in favor of the diol side. This variation in selectivity might well be due to conformational inhomogeneities or differences in dihedral angles in the 5-membered ring series.

In order to gain deeper insight into the influence on regioselectivity of the stereochemistry of the lone hydroxyl flanking the phenylthio group, the four stereoisomers represented in table 2 were studied to establish

Table 2. Influence of Stereochemistry on Relative Reactivities.[a]

Entry[b]	Starting compound	Cleavage product and yield[c]
A		 80%
B		" " " " " 40%
C		" " " " " 28%
D		" " " " " <4%

[a]Four solutions, each containing 0,1 mmol of stereoisomer and 0,1 mmol of benzophenone in 1 mL deuterated and degassed acetonitrile, are irradiated at 350 nm under argon in four NMR tubes using a Rayonet apparatus equiped with a Merry-go-Round adaptor. [b]see b) table 1. [c]Determined by NMR.

their relative reactivities. The first observation is that the *cis* relationship of the axial hydroxyl group to the equatorial phenylthio group (entry C) is less favorable to cleavage than the *trans* with an equatorial hydroxyl (entry B). This trend correlates nicely with the observations of entries 2 and 4 of table 1. Secondly, it stands out that the greatest differences in reactivities occur with the pair of stereoisomers having an axial phenylthio group. Indeed, the *cis* isomer (entry A) is >20 times more reactive than the *trans* diaxial isomer (entry D). This very result, in comparison to the other three of the table, indicates that the reaction most probably proceeds *via* a contact radical ion pair[1,3c] (or close to it) between the sulfide moiety and benzophenone where the most efficient cleavage takes place when deprotonation of the hydroxyl by the radical anion can occur before back electron transfer. Calculations have shown that appreciable weakening of sigma bonds β to hydroxyls results upon deprotonation and this effect has been related to the dramatic rate accelerations in the oxyanion Cope rearrangement.[5] These facts however, should not preclude the possibility, albeit less efficient , of cleavage when deprotonation cannot take place or in the case of O-alkyl derivatives, providing that a lone pair can be oriented antiperiplanar to the bond to be broken as demonstrated by Arnold in the case of 2-phenylcycloalkylethers.[6]

In conclusion, the present results demonstrate that various substituted cyclic 2-phenylthio-1,3-diols are rearranged to deoxysugars under sensitized photolysis conditions. It is also apparent that in unsymmetrical cases the regioselectivity of the rearrangement is influenced by substituent and stereoelectronic effects and stereochemical relationships. For instance, entries 2, 4, 6, 7 and 9 show that cleavage seems preferred on the *vic*-diol side of the phenylthio group when this diol is in a *cis* configuration but this selectivity is modulated by the stereochemistry of the lone hydroxyl group and the ring size.

The origin of selectivity and the *cis*-effect in this new rearrangement as well as its application as synthetic methodology are under active investigation in our laboratory and will be reported in due course.

ACKNOWLEDGMENTS

Financial support from NSERC, FCAR and Bio-Méga in the form of grants and/or fellowships is gratefully ackowledged.

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(*Received in USA* 15 *August* 1994; *revised* 3 *October* 1994; *accepted* 7 *October* 1994)