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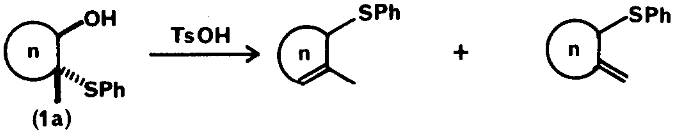
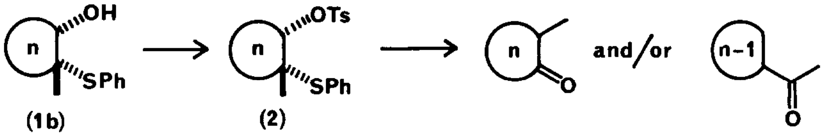
ALKYL MIGRATION INCLUDING RING CONTRACTION FROM A MIGRATION ORIGIN BEARING A PHENYLTHIO (PhS) GROUP

Malcolm Hannaby and Stuart Warren*
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW.

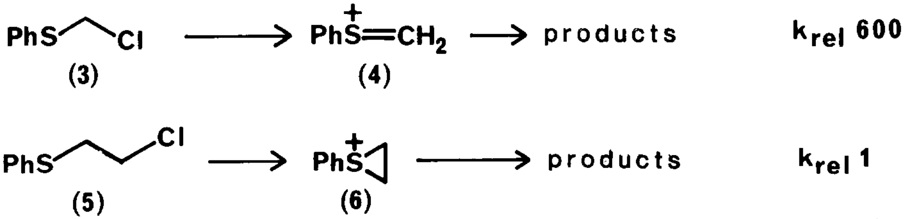
Alkyl shifts occur from tertary C atoms bearing a PhS group if PhS migration is prevented, but are retarded by the PhS group: the transition state has a cation-like migration terminus with little, if any, alkyl participation.

We have recently shown that rearrangement of alcohols (1a) occurs with migration of the PhS group from a tertiary migration origin [C-2 in (1)] via an episulphonium ion,[1] but that the diastereoisomers (1b) , with cis OH and PhS groups, did not react under these conditions. We now report that rearrangement of the cis tosylates (2) does occur with alkyl migration.





Electron-withdrawing groups such as diphenylphosphinoyl (Ph_2PO) migrate in preference to other substituents at a migration origin to avoid formation of an unstable α-Ph_2PO-cation.[2] In contrast, electron-donating groups such as PhS are known to stabilise an adjacent positive charge[3] and so might be expected to assist other groups to migrate, providing that the group itself (e.g. PhS) is prevented from migrating. Indeed, rates of hydrolysis of sulphides (3) and (5) suggest that this type of assistance via the ion (4) might be extremely efficient.[4] Though there are some examples of heteroatoms migrating from an origin bearing a PhS group,[5] the only examples of alkyl migration involve expansion of a three-membered ring.[6]



The alcohols (11b) and (11d) were prepared by stereoselective reduction of the corresponding α-PhS-ketones. Methylation of the α-PhS-ketone[7] (7) (KH, MeI) gave ketones (8a,b) as a 6:1 mixture of diastereoisomers, the major product (8a) resulting from axial attack by the electrophile.[8] Reversing the order of addition by sulphenylation of the thermodynamic silyl enol ether (9) gave the same ketones in a 1:1 mixture. The diastereoisomers (8a,b) were easily separated by flash chromatography.

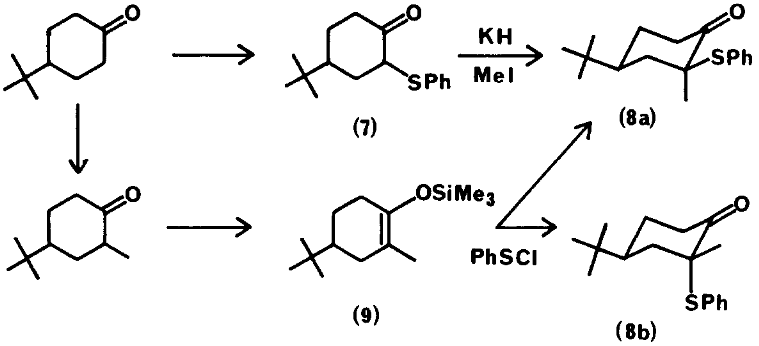
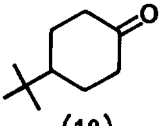


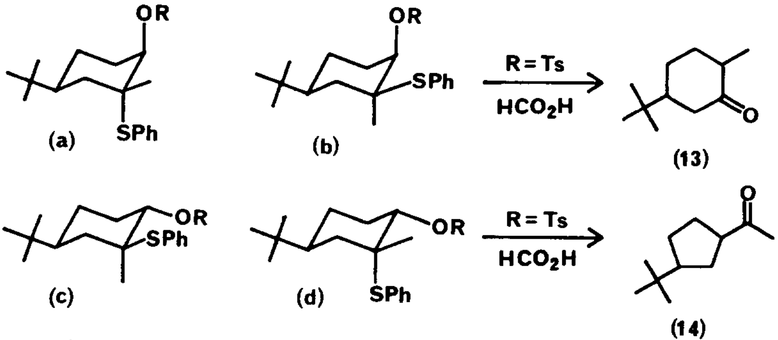
Table 1: Stereoselectivity in the Reduction of Ketones

	Product Ratios (axial:equatorial)		
Ketone	$LiAlH_4$	L-Selectride	$Zn(BH_4)_2$
(8a)	14:86	95:5	-
(8b)	0:100	7:93	1:99
(10)	9:91	96:4	-



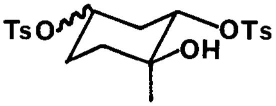
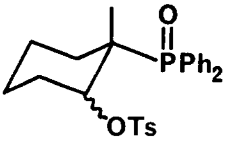
(10)

Reduction of these ketones with $LiAlH_4$ or $Zn(BH_4)_2$ gave predominantly the equatorial alcohols (11c,d) (table 1). L-Selectride reduction of ketone (8a), which has an equatorial PhS group, gave the axial alcohol (11b) as the major product.[9] However, ketone (8b), having an axial PhS group, gave predominantly the equatorial alcohol (11d) with this reagent, reduction occurring by axial attack. This reversal of selectivity may be due to interaction between the σ^* orbital of the incipient C-H bond and the high-energy σ orbital of the axial C-S bond[10] and steric hindrance from the axial PhS group.



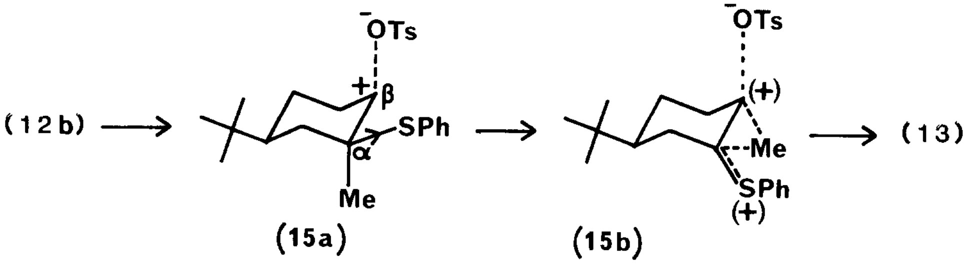
(11; R=H) (12; R=Ts)

Table 2: Half-lives of Solvolysis of Tosylates at 75 °C in HCO_2H (min).

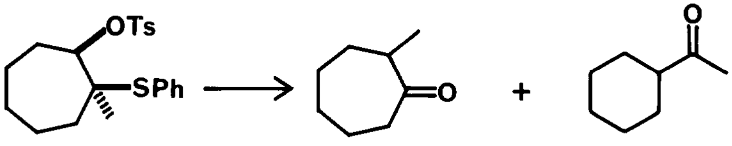
			(12b)	(12d)
0.42	2.0	(22; axial OTs) 15.2 (22; equatorial OTs) 25.8	36 ± 8	56 ± 16

Tosylation of alcohols (11b,d) went smoothly and in high yield, whereas the crowded environment of the hydroxyl group of (11c) prevented either tosylation or mesylation under a variety of conditions. Heating the tosylates (12b, d) in HCO_2H at 90 °C for 30 minutes gave, after aqueous work-up, the ketones (13, 14). Rearrangement had occurred with migration of the bond anti-peri-planar to the leaving group: tosylate (12b) with methyl migration and (12d) with ring contraction.

Estimates of reaction half-lives showed that the rates of rearrangement of these tosylates were at least two orders of magnitude slower than the corresponding semi-pinacol or Wagner-Meerwein rearrangements[11] (table 2), and even slower than the reactions (elimination with or without hydride shift) found for the non-rearranging Ph_2PO compound (22). Far from encouraging rearrangement, the PhS group actually retards the reaction, though unlike the Ph_2PO group it permits the slow rearrangement of the alternative group. A recent X-ray crystallographic study[12] of the semi-pinacol rearrangement has shown that breaking of the C-OTs bond is well advanced as the transition state is approached, but little alkyl migration is evident. It seems that, during the rearrangement of (12b and d), through-bond destabilisation of the developing positive charge on C-β (15a) by the PhS group outweighs stabilisation of developing positive charge at C-α by sulphur as the transition state is approached: but after the transition state is passed, stabilisation of the developing positive charge on C-α (15b) by PhS becomes product determining.

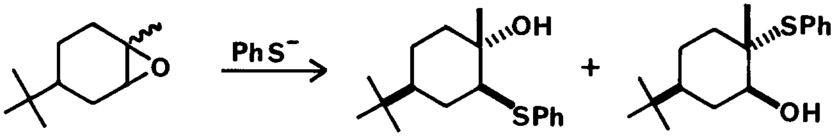


Rearrangement of the seven-membered ring tosylate (16) also occurred with alkyl migration. Although rigid enough to prevent PhS migration, the seven-membered ring is sufficiently flexible to allow either of the remaining groups at the migration origin to become anti-peri-planar to the leaving group resulting in a 4:1 mixture of alkyl migration (17) and ring contraction (18).

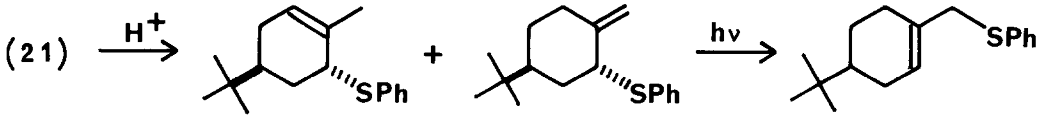


(16) (17) (18)

Although reduction of ketone (8b) failed to give the diaxially substituted alcohol (11a), trans diaxial opening of the epoxide (19) gave the isomeric secondary alcohol (21), which could be separated from the other product, the tertary alcohol (20). As expected, rearrangement of alcohol (21), which has a PhS group anti-peri-planar to the leaving group, occurred very easily with PhS migration to give a mixture of allyl sulphides.



(19) (20) (21)



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References

1. M. Hannaby and S. Warren, Tetrahedron Lett., 1986, **27**, (15602)
2. D. Howells and S. Warren, J. Chem. Soc., Perkin Trans. 2, 1973, 1645; 1974, 992; P. Brownbridge, P.K.G. Hodgson, R. Shepherd, and S. Warren, ibid., Perkin Trans. 1, 1976, 2024.
3. R.W. Taft, R.H. Martini, and F.W. Lampe, J. Am. Chem. Soc., 1965, **87**, 2490; W.P. Jencks and J.L. Jensen, ibid., 1979, **101**, 1476; G. Modena, G. Scorrano, and P. Venturello, J. Chem. Soc., Perkin Trans. 2, 1979, 1; R.A. McClelland, Can. J. Chem., 1977, **55**, 548.
4. E. Eliel, W.H. Pearson, L.M. Jewel, and A.C. Abatjoglou, Tetrahedron Lett., 1980, **21**, 331.
5. P. Blatcher, J.I. Grayson, and S. Warren, J. Chem. Soc., Chem. Commun., 1976, 547; C. Earnshaw, J.I. Grayson, and S. Warren, ibid., Perkin Trans. 1, 1979, 1506.
6. B.M. Trost and L.N. Jungheim, J. Am. Chem. Soc., 1980, **102**, 7910; J.H. Byers and T.A. Spencer, Tetrahedron Lett., 1985, **26**, 717.
7. M. Hannaby and S. Warren, Tetrahedron Lett., 1985, **26**, 3133.
8. H.O. House and M.J. Umer, J. Org. Chem., 1973, **38**, 1000.
9. S. Murai, Y. Kuroki, K. Hasegawa, and S. Tsutsumi, J. Chem.Soc., Chem. Commun., 1972, 946; I. Paterson and I. Fleming, Synthesis, 1979, 736.
10. A.S. Cieplak, J. Am. Chem. Soc., 1981, **103**, 4540.
11. A.P. Krapcho, J.E. McCullough, and K.V. Nahabedian, J. Org. Chem., 1965, **30**, 139; D.E. Orr and F.B. Johnson, Can. J. Chem., 1969, **47**, 47; see also S. Winstein and E. Grunwald, J. Am. Chem. Soc., 1948, **70**, 828.
12. M. Edwards, Ph.D. Thesis, Cambridge, 1985.

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