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REARRANGEMENT OF CYCLIC ALCOHOLS WITH AN ADJACENT PHENYLTHIO (PhS-) GROUP: MIGRATION OF A PhS GROUP AROUND A RING.

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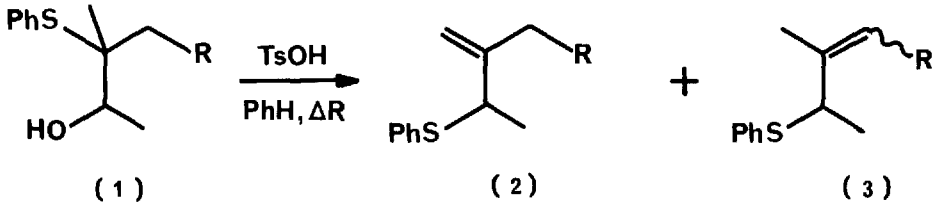
PhS migration around rings (size 5-15) gives allyl sulphides with a regioselectivity which varies with ring size.

We have recently shown[1] the effect of an adjacent phenylthio (PhS) group on the dehydration of a series of tertiary alcohols. We now report the rearrangement of an isomeric series of cyclic secondary alcohols (9), where PhS migration,[2] e.g. (1)-(3) is expected, illustrating the effect of ring sizes (n = 5-15) on sulphur participation. The β-hydroxy-sulphides (9) were prepared by sulphenylation of the corresponding cyclic ketone [either by (Method a) bromination of the ketone (4) and addition of sodium thiophenate or by (Method b) formation of the trimethyl silyl enol ether and addition of phenylsulphenyl chloride,[3]] and then methylation (KH, MeI).



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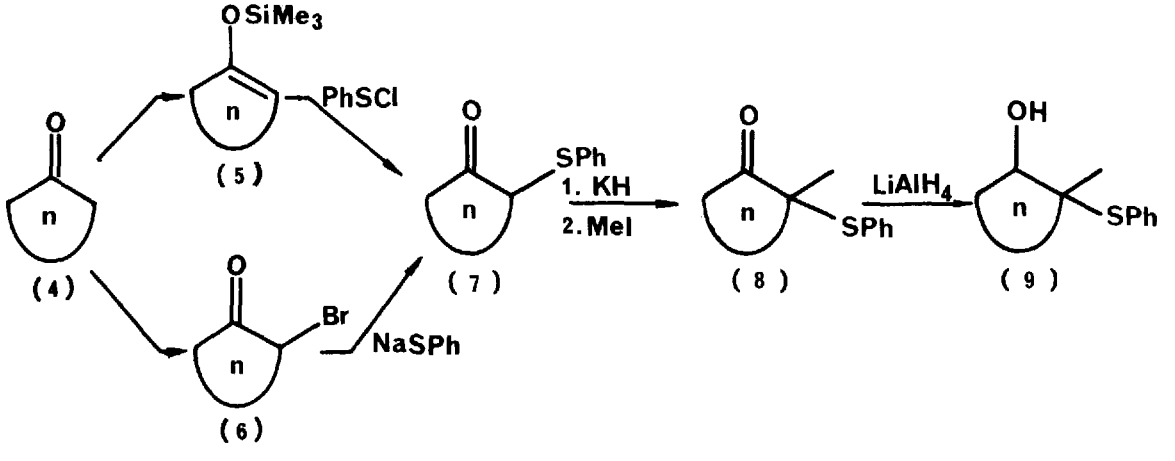
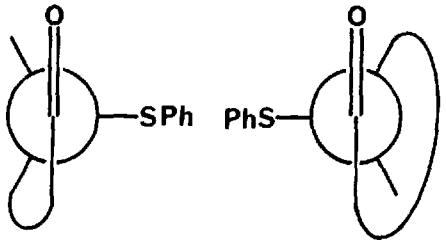


Reduction ($LiAlH_4$, Et_2O, 0 °C) produces a pair of diastereoisomers (Table 1). Small rings show relatively high selectivity [(8), n = 5, 6, > 7:1]

whereas medium and large rings produce only moderate diastereomeric ratios [(8), n = 7, 8, 15, < 2:1]. Such selectivities have been explained in terms of an electronic interaction between the σ^* orbital of the incipient bond and the adjacent high energy C-S σ bond.[3] In open chain molecules and presumably in very large rings, this is the same as Felkin's model,[5] with the medium-sized group [the ring for (11)] adjacent to the carbonyl group giving the trans-isomer as the major product of reduction. Small rings controlled by the same electronic interaction can adopt a similar conformation accommodating the shorter linking chain (10) and so giving the cis-isomer as the major product. Orbital alignment improves as ring size decreases: this change is reflected in an increased selectivity during reduction (12, 13). Force-field calculations[6] show that medium rings have a similar low energy conformation, however the anti face of the ketone is sterically hindered by the far side of the ring, so reaction must occur in some other less stereoselective conformation.



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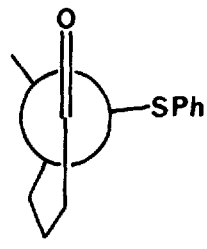

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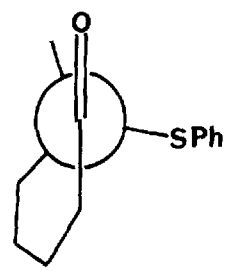
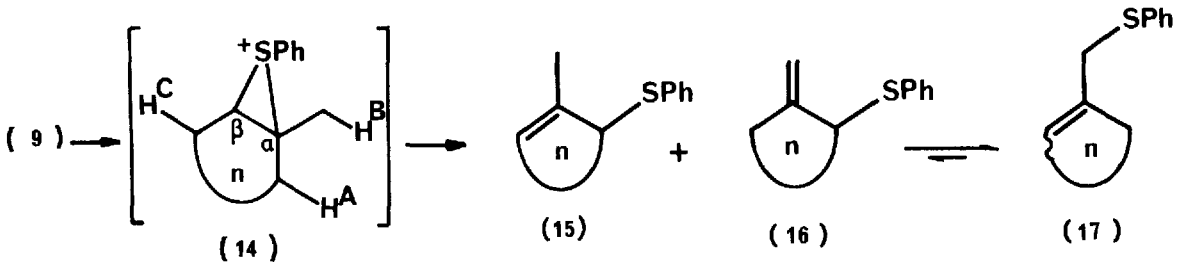


(13)

Rearrangement of the mixed cis- and trans-isomers of the β-PhS alcohols [(9, n=5-8), (10)] in refluxing benzene with catalytic amount of toluene-p-sulphonic acid (TsOH) gave recovered cis-alcohols (9) and allyl sulphides (15) and (16) by PhS shift from trans-alcohols (9). The exo-methylene compounds (16) were allowed to rearrange in daylight[7] to the more stable isomers (17) and the rearrangement products were isolated as mixtures of endocyclic allyl sulphides (Table 2). Both cis and trans 15-membered ring alcohols [(9), n=15] rearranged by PhS migration. Both 12-membered ring alcohols [(9), n=12] rearranged, but the cis-alcohol rearranged more slowly than the trans.

Table 1: Stereoselectivity of Reduction of α-PhS Cyclic Ketones (8)

Starting Material	n	Method (a or b)	Yield (7) (%)	Yield (8) (%)	Yield (9) (%)	cis:trans (9)
(4a)	5	a	32	70	100	20:1
(4b)	6	a	69	80	82	7:1
(4c)	7	a	35	47	100	3:1
(4d)	8	b	60	68	95	1.5:1
(4e)	10	b	50	60	95	2:1
(4f)	12	b	80	60	100	4:1
(4g)	15	b	64	94	90	2:1



Loss of H^A from the intermediate episulphonium ion (14) gives an endocyclic double bond (15), whereas loss of H^B gives the exocyclic allyl sulphide (16). Elimination of H^C does not occur presumably because the tertiary centre C^{α} is better able to stabilize a developing positive charge. Indeed force-field calculations show C^{α}-S to be longer than C^{β}-S (bond length C^{α}-S 1.898 A, C^{β}-S 1.806 A) supporting this suggestion.

The ratio of endocyclic to exocyclic elimination varied with ring size. Small ring trans-alcohols eliminated almost exclusively endo- and examination of the episulphonium ion [(14) n = 5,6] shows H^A is ideally orientated to eliminate. Larger ring trans-alcohols (n = 7-12) gave progressively more exo product (17). Loss of H^A would require either a very long chain (18) or an unfavourable transannular interaction (19). Cis-(9f) slowly rearranged to a mixture of exo and endo products: conformation (20) allowing loss of H^A. Both cis and trans-(9g) rearranged to (15, n = 15) via (18) and (20), now easily attained with such a long chain.

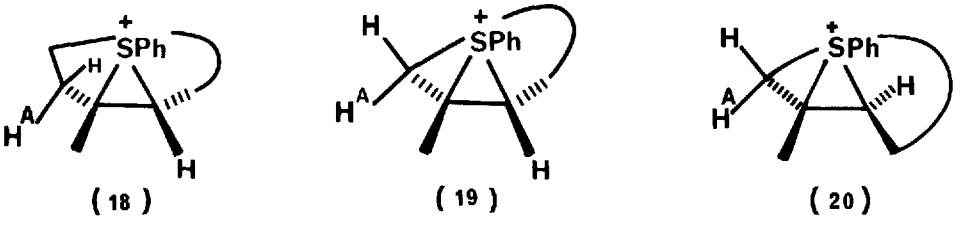


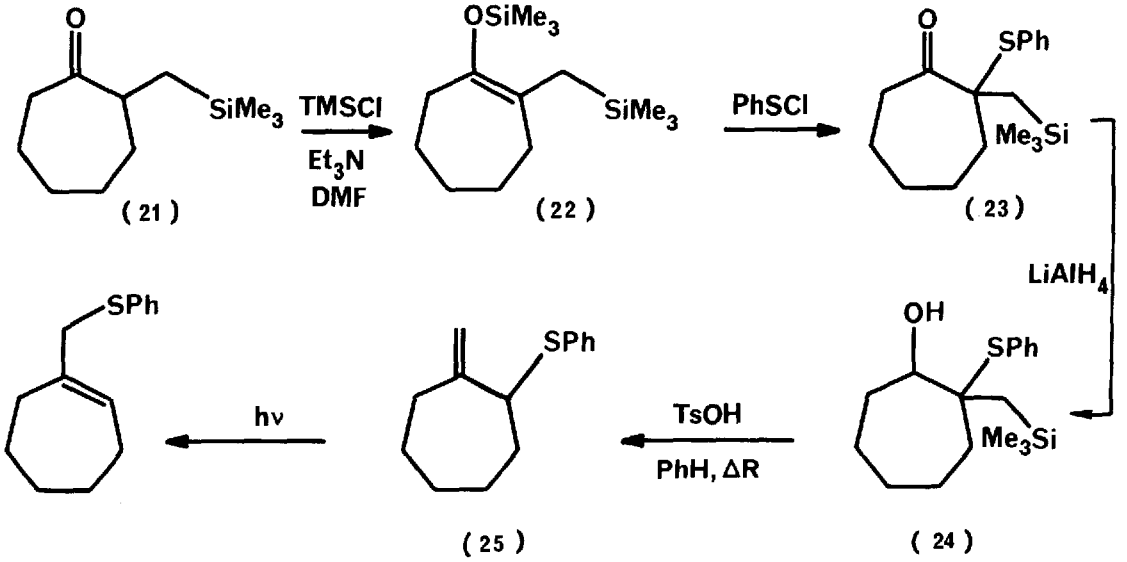
Table 2: Rearrangement of β-PhS Alcohols (9)

Starting Material		Yield	Product Ratios[a] (%)				endo:
	n	(%)	cis-(9)	(15)	(16)	(17)	exo
(9a)	5	83	95	4.5	0	0.5	9:1
(9b)	6	99	88	10	0	2	5:1
(9c)	7	76	51	39	0	10	4:1
(9d)	8	100[b]	60	0	40	0	0:1
(9d)	8	96	61	0	0	39	0:1
(9e)	10	99	49	25	0	26	1:1
(9f)	12	99	70	4	0	26	0.2:1
(9f)[c]	12	98	0	57	0	43	1.3:1
(9g)	15	99	0	92	8	0	11.5:1

a) Alcohol refluxed in benzene with cat. TsOH for 15 mins.
b) Isolated without exposure to light.
c) Reflux time 90 mins: cis-(9f) gives ca. 3:1 endo:exo.

One clear exception to this trend is the eight-membered ring [(9), n = 8] which rearranges to give exclusively the product of exo- elimination. Force-field calculations on the intermediate episulphonium ion show that in the eight-membered ring a conformation favourable for endo- elimination in the transition state (dihedral angle H^A-C-C-S, 180°) is energetically very unfavourable.

Silicon has been used in open chain compounds to control the regio-selectivity of PhS rearrangement,[8] and can be used to give the less favoured isomer. Alkylation of cycloheptanone with trimethylsilylmethyl iodide and formation of the thermodynamic silyl enol ether (22) allows access to the required β-hydroxy sulphide (24) which rearranges under normal conditions to give only the exocyclic allyl sulphide (25) (cf. Table 2).



(21) (22) (23) (24) (25)

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