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DEHYDRATION OF ALCOHOLS WITH AN ADJACENT PHENYLTHIO (PhS) GROUP

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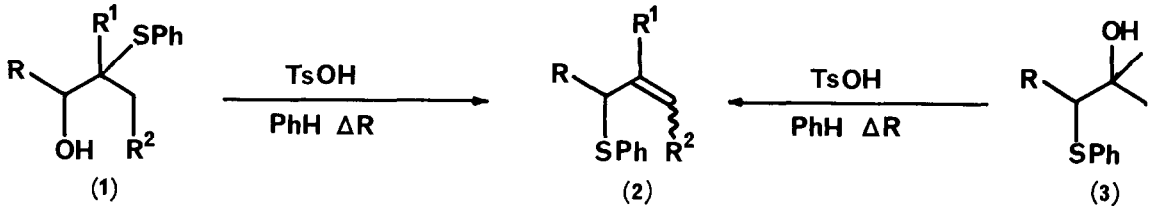
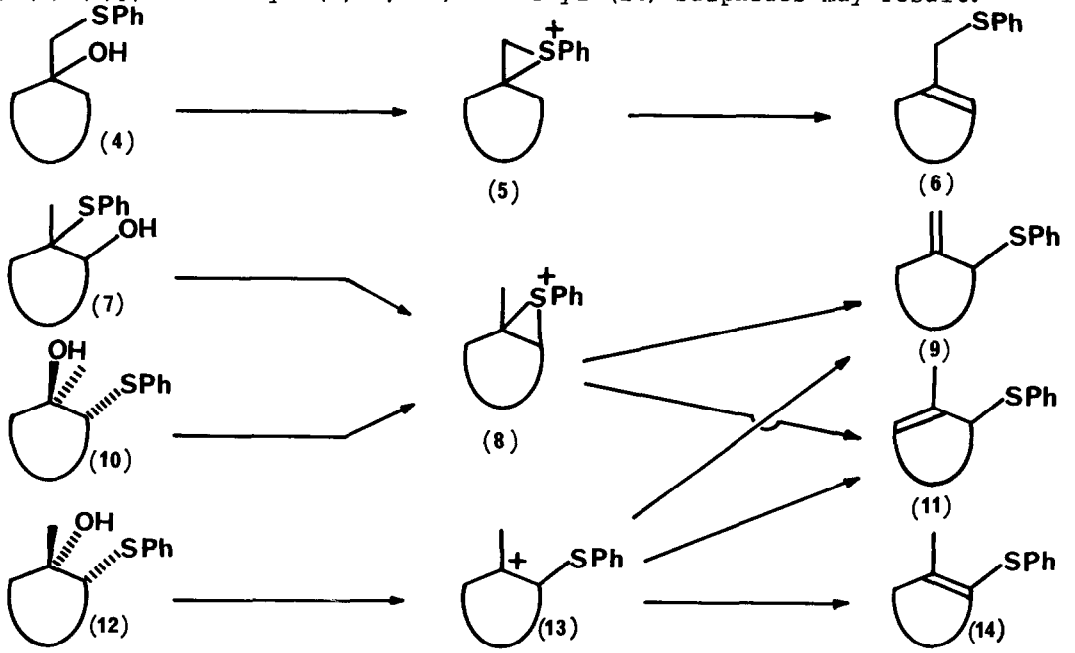
Rings produce particular constraints not experienced by acyclic systems. We have investigated how the change in conformational and steric factors caused by varying the ring size affects a reaction within cyclic systems.

Previous work[1] has shown that rearrangement of β-hydroxysulphides (1) leads to synthetically useful allyl sulphides (2). The isomeric tertiary alcohols[2] (3) undergo elimination to give the same product [(2); R^1=Me, R^2=H].

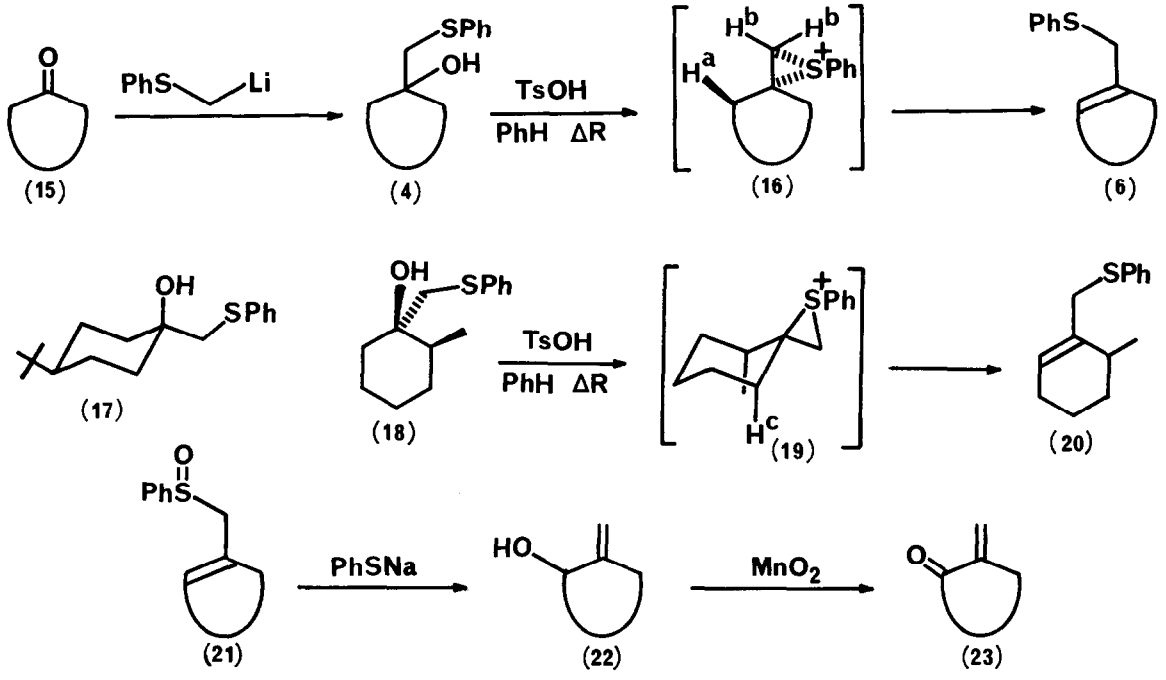


(1) (2) (3)

We now report the synthesis and dehydration of secondary alcohols (7), tertiary alcohols (4), and diastereoisomeric tertiary alcohols (10) and (12). Dehydration may occur with PhS migration [e.g. (7)-(8)-(9)] or without [(4)-(5)-(6)], and allyl (6, 9, 11) or vinyl (14) sulphides may result.



The first series of β-hydroxysulphides[3] (4) was prepared by the action of phenylthiomethyl-lithium[4] on the cyclic ketones (15). Elimination gave only the allyl sulphides (6) having an endocyclic double bond. This is because the formation of the episulphonium ion (16) is followed by loss of proton H^A. No vinyl sulphide was observed as neither of the protons H^B can achieve an antiperiplanar relationship to a C-S bond.



Addition of phenylthiomethyl-lithium to 4-t-butylcyclohexanone gave a 5:1 ratio of diastereoisomers in favour of the product (17) from equatorial attack,[3] though both diastereoisomers gave the same allyl sulphide on elimination. Addition to 2-methylcyclohexanone gave only one diastereoisomer probably again that from equatorial attack (18). Elimination was now regioselective giving only the allyl sulphide resulting from loss of the single available antiperiplanar proton (H^C in 19).

Table 1

Starting Materials		Yield of Isolated Products		
	n	(4)	(6)	(22)
(15a)	5	78%	100%	-
(15b)	6	81%	97.5%	72%[a]
(15c)	7	84%	-	-
(15d)	8	54%	97%	76%
(15e)	10	58%	100%	-
(15f)	12	90%	100%	53%
(15g)	15	88%	99%	60%

a. % yield by n.m.r.

Sodium periodate oxidation of the allyl sulphides (6) followed by [2,3] sigmatropic rearrangement of the sulphoxides (21) in the presence of a thiophile[5] gave the thermodynamically unstable exomethylene allylic alcohols[6] (22) in a better than 50% yield over 4 steps (Table 1). Mild oxidation with manganese dioxide gave the enones (23), [e.g. (23), n=8 in 98%]. Overall this represents a 1,2 carbonyl transposition with a one carbon homologation.

Addition of methyl-lithium to the α-(phenylthio)-ketones (24) gave the second series of β-hydroxysulphides (25), with the PhS group on the ring. Reaction occurs with high stereoselectivity particularly for medium rings (> 20:1, n=7, 8, 12) in favour of the cis alcohol (Table 2). This selectivity can be explained by a combination of both steric and electronic effects, the predominant isomer being formed by attack on the less sterically hindered face of the ketone opposite the bulky phenylthio group. Work on the reduction of ketones[7] suggests that the direction of attack is in part determined by interaction between the σ^* orbital of the incipient bond and an adjacent high energy σ orbital. Thus nucleophilic attack occurs preferentially anti to the C-S bond of the phenylthio group, leading to the cis isomer as the major product.

Elimination of these cis isomers of small and medium ring alcohols [(25), n=5 to 8] leads to a mixture of allyl and vinyl sulphides, by proton loss endo (14,11) and exo (9) to the ring followed by photochemically induced [1,3] phenylthio shift[8] to the more thermodynamically stable isomer (6).

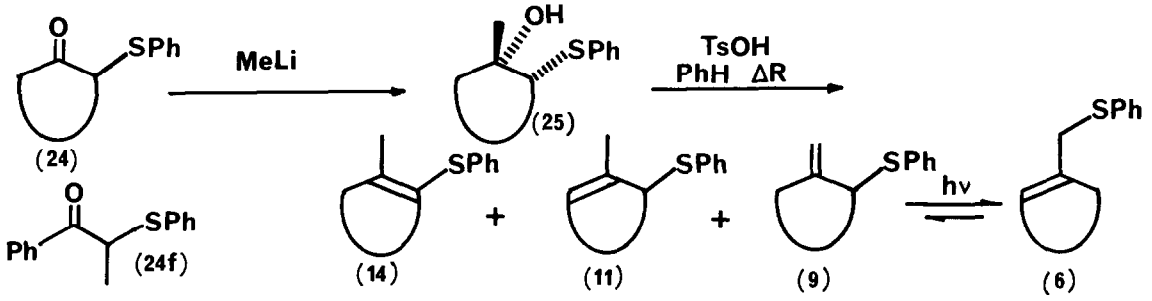


Table 2

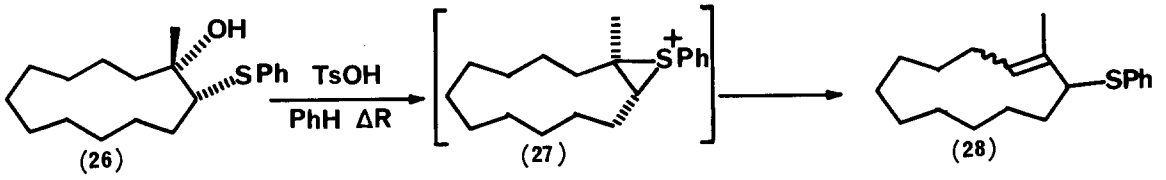
Starting Material	n	yield[a] (25)	cis/trans	Yield of Products (14)	(11)	(6)
(24a)	5	75%	8:1	b	b	b
(24b)	6	100%	7:1	c	c	c
(24c)	7	82%	>20:1	-	-	-
(24d)	8	100%	>20:1	20	40	40%
(24e)	12	78%	27:1	0	100	0%
(24f)	-	93%	2:1	0	0	100%

a. based on recovered starting material.

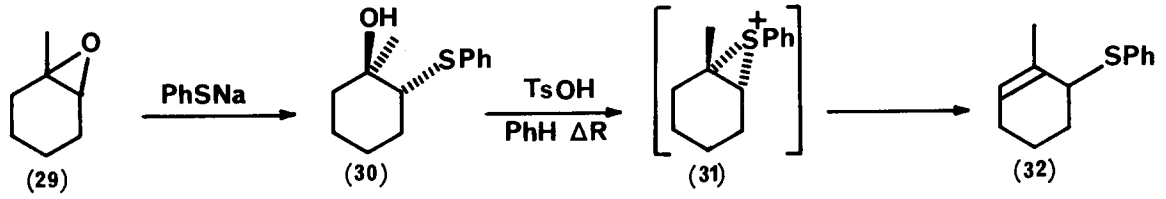
b. Decomposed.

c. Complex mixture.

The lack of regioselectivity shown in this reaction suggests product formation via the open carbonium ion (13), as the episulphonium ion (8) would require an unfavourable trans arrangement of the chain. However, the twelve-membered ring is sufficiently flexible to allow formation of the episulphonium ion (27) and hence gives only an E and Z mixture of the endocyclic allyl sulphides (28).



Opening of 1-methyl cyclohexene oxide (29) with sodium thiophenolate[9] allowed access to the epimeric trans alcohol (30). Elimination can now occur via the episulphonium ion with the chain arranged cis and gives only the endocyclic allyl sulphide [(11), n=6], in marked contrast to the cis isomer (25).



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