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[1,4] PHENYLTHIO SHIFTS OF 2,4,4-TRISPHENYLTHIOBUTANOLS

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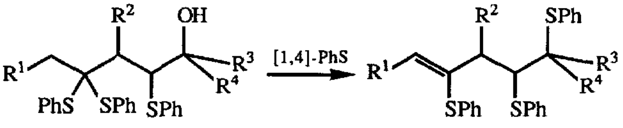
Summary. The title compounds (1) undergo a [1,4]-PhS shift to give an *E,Z* mixture of vinyl sulphides (2) with thionyl chloride but only the *Z* isomer if toluene-*p*-sulphonic acid is used. The reaction occurs only if another PhS group is present β to the hydroxyl. The starting materials (1) were available *via* Michael addition of dithioacetal nucleophiles (3) to methyl crotonate followed by α-sulphenylation.

We have shown[1] that 2,2-bisphenylthioethanols undergo [1,2] phenylthio (PhS) migration when treated with thionyl chloride and triethylamine under conditions of kinetic control and that the 2,3-bisphenylthiopropenes obtained isomerize by [1,3]-PhS shifts on exposure to light. Compounds having only one PhS group give allyl sulphides by similar acid-catalysed [1,2]- and photochemical [1,3]-PhS migrations on treatment with toluene-*p*-sulphonic acid (TsOH) under conditions of thermodynamic control.[2] We now report an unusual long-distance PhS shift,[3] a [1,4]-PhS migration of 2,4,4-trisphenylthiobutanols (1) to give vinyl sulphides (2) under these rearrangement conditions. We describe the extension of this [1,4]-PhS shift into substrates with a tertiary, secondary, or primary migration terminus, as well as the synthesis of the compounds used in this study.



(1) (2)

Dithioacetal nucleophiles are effective stereocontrol units in alkylations of acyclic and cyclic α,β-unsaturated esters[4] through the corresponding enolates. We have used the Michael addition of bisphenylthio acetal nucleophiles (3) followed by α-sulphenylation as the method to prepare the 2,4,4-triphenylthioesters (5), easily converted into the tertiary, secondary or primary alcohols required to study the [1,4]-PhS shift. Lithium derivatives of bisphenylthioacetals (3)[5] underwent conjugate addition to methyl crotonate in THF at low temperature (-78 °C) and the enolate (4) was silylated directly with chlorotrimethylsilane and triethylamine at -78 °C. The silyl enol ether was kept at room temperature for two hours, cooled to -78 °C, and sulphenylated with phenylsulphenyl chloride in THF solution[6], to give the methyl 2,4,4-trisphenylthioester *syn* -(5) as the major diastereomer. The results are summarized in the Table. The high diastereoselectivity of sulphenylation can be explained if the electrophile (PhSCl) attacks the less hindered face of the Houk conformation of the silyl enol ether (see note 7). The bulk of the dithioacetal unit and the lack of coordination by sulphur (it would have to form a seven-membered chelate) may also be responsible for the highly efficient 1,2-asymmetric induction in alkylations of enolates.[4a,8]

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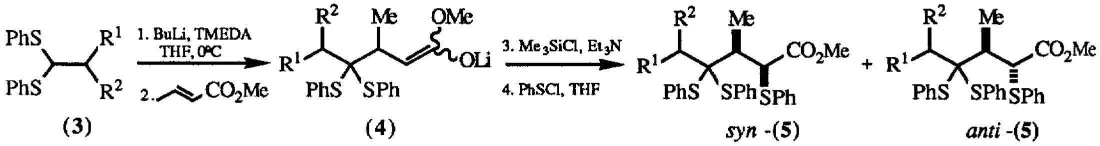
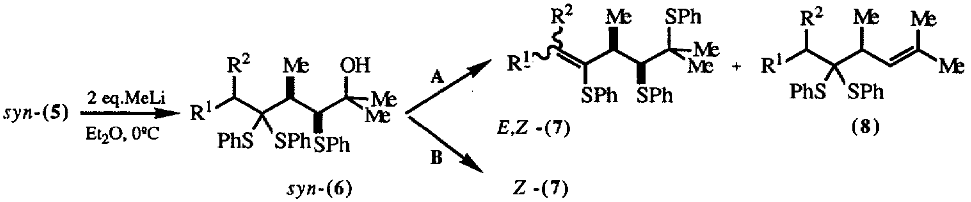


Addition of MeLi to *syn*-(**5**) gave tertiary alcohols *syn*-(**6**), which on treatment in the dark with thionyl chloride and triethylamine in carbon tetrachloride at 0 °C for a few minutes (Method A), gave in good yields the [1,4]-PhS shift product, an inseparable mixture of vinyl sulphides *E*-(**7**) and *Z*-(**7**) (50-65%), *E*-(**7**) being favoured. The other product was (**8**) (25-30%). Reaction of *syn*-(**6**) with TsOH in dichloromethane under reflux (method B) gave Z-(**7**) as the only product (50-60%). The results are summarized in the Table.



A = $SOCl_2$, Et_3N, CCl_4, 0°C
B = TsOH, CH_2Cl_2

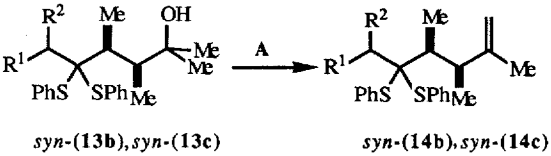
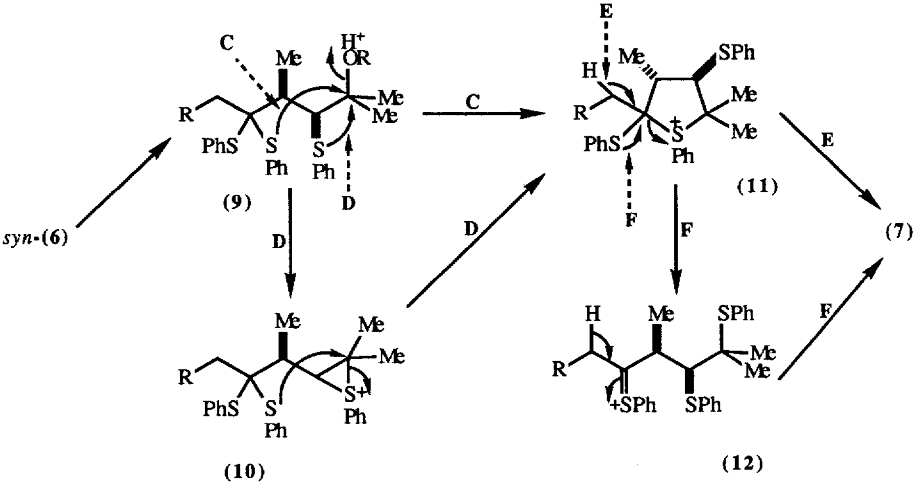


Table . Synthesis and Rearrangement of trisphenylthiobutanols (**6**).

Starting Material	R^1	R^2	*syn* -(**5**) : *anti* -(**5**)^a	Yields (%) *syn* -(**5**)^b	Yields (%) (**6**)^c	Rearrangement Method A (**7**)(%)	Rearrangement Method A *E* : *Z*	Rearrangement Method A (**8**)(%)	Rearrangement Method B *Z* -(**7**)(%)
(**3a**)	Me	H	78 : 22	40	64 (29)	52	57 : 48	25	55
(**3b**)	Me	Me	d	43	78	82	-	e	60
(**3c**)	Et	H	d	52	80	68	71 : 29	e	64
(**3d**)	CH_2=CH	H	86 : 14	60	42 (32)	f	f	25	f
(**3e**)	Pr	H	80 : 20	53	50 (39)	49	64 : 36	27	49
(**3f**)	PhCH_2-	H	65 : 40	65	40 (35)	52	69 : 31	34	47

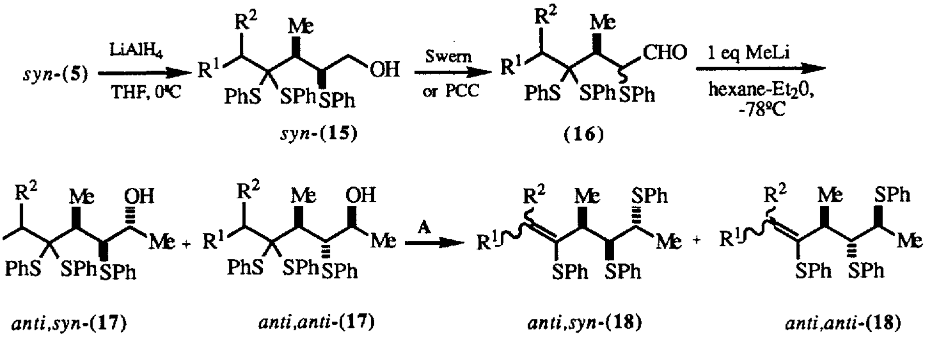
[a] *Syn* : *anti* ratios were determined by ^{1}H-NMR spectroscopy on the crude reaction mixture, stereochemistry established by coupling constants.[b] Isomers separated by flash column chromatography. [c] Yield of recovered *syn*-(**5**) in brackets. [d] Ratio not determined. [e] (**8b**) and (**8c**) were not isolated. [f] Mixture of products: (**7d**) not isolated.

Mechanisms for [1,4]-PhS migration are summarized in Scheme 1 and we suggest a route *via* the five-membered ring intermediate (**11**).[9] Formation of (**11**) could occur by [1,4] participation by one PhS group of the bisphenylthio group with the loss of OR (route C) or by initial [1,2] formation of an episulphonium ion (**10**), which would decompose by attack of the sulphur atom of the dithioacetal unit (route D). Route C precludes the assistance of the PhS group β to the OH, while route D can be rationalized on the basis that no [1,2]-PhS migration "uphill" (secondary origin to tertiary terminus) *via* an episulphonium ion (**10**) has been observed.[2,10] To test the participation of the β-PhS group, tertiary alcohols lacking this group (**13**)[11] were submitted to the rearrangement conditions. No [1,4]-PhS shift occurred, the dehydration product (**14**) alone being formed. Other evidence for route D came from the by-product (**8**), formed by sulphur extrusion from (**10**). Cleavage of the C-H bond can occur from (**11**) (route E) or from the rearranged cation (**12**) (route F). Formation of mixtures rich in the less stable *E* -(**7**) using method A suggests that under these conditions route E should be preferred, as the transition state from (**12**) would so closely resemble the products (**7**) that Z-(**7**) should be favoured[1]. Under acidic conditions both routes may be possible.



Scheme 1

To study the scope of the [1,4]-PhS shift, primary and secondary alcohols were prepared. Reduction of syn-(**5**) gave primary alcohols *syn*-(**15**) but attempted rearrangement always gave complex mixtures of products. Oxidation of *syn* -(**15**) (Swern, PCC or PDC)[12] gave a mixture of diastereomeric aldehydes (**16**) favouring the *syn* isomer. The loss of stereochemical integrity is probably due to enolization of the α-PhS aldehyde under the reaction conditions. Addition of MeLi to (**16**) gave an inseparable mixture of the two Felkin secondary alcohols *anti,syn*- and *anti,anti*-(**17**).[13,14] For (**17**), the [1,4]-PhS shift occurred successfully only by method A when vinyl sulphides (**18**) (55%) were obtained. Previously, secondary to secondary PhS shifts have been found with [1,4] hydroxyl participation in the formation of tetrahydrofurans.[15]



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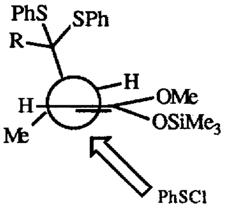

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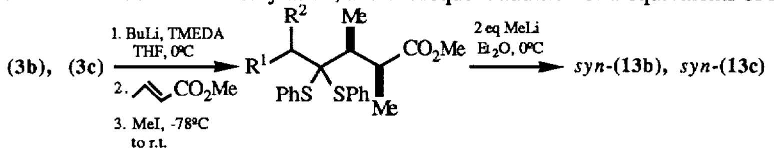
11. Tertiary alcohols (**13b**) and (**13c**) were available by 1,4-addition of bisphenylthioacetal anions (**3**) to methyl crotonate in tandem with methylation, and subsequent addition of 2 equivalents of MeLi.



12. a) K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651. Swern oxidation was performed at -78 ºC only for 15 minutes. Longer periods or higher temperatures favoured the loss of stereochemical integrity; b) E.J. Corey and G. Schmidt, *Tetrahedron Lett.*, 1979, 399 and refs. therein cited. The use of PCC or PDC gave slightly lower diastereomeric ratios but poor yields (30-40%).
13. The *syn* and *anti* convention suggested by Masamune is used: the first *syn* or *anti* refers to the relationship of OH and PhS or PhS and PhS in the 2,3 positions and the second to the PhS and Me in the 3,4 positions when the chain is drawn in its extended form. S. Masamune, S.A. Ali, D.L. Snitman, and D.S. Garvey, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 557; S. Masamune, W.Choy, J.S. Petersen, and L.R.Sita, *ibid.*, 1985, **24**, 1.
14. The corresponding *anti,syn*- and *anti,anti*-benzoates [$(PhCO)_2O$, DMAP, CH_2Cl_2] were separated by flash column chromatography on silica gel and then stereochemistry was assigned by n.m.r. We assume that the [1,4]PhS shift occurs with retention as inversion occurs in both the [1,2] and the [1,4] steps. These experiments show that it is stereospecific, but cannot definitely say in what sense.
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