Tetrahedron Letters, Vol 32, No 6, pp 815-818, 1991
Printed in Great Britain

0040-4039/91 $3 00 + 0
Pergamon Press plc

SYNTHETIC USEFULNESS OF SILYL THIOKETONES: FUNCTIONALIZATION OF THEIR PRIMARY ADDUCTS THROUGH DESILYLATION AND TRAPPING BY CARBON ELECTROPHILES

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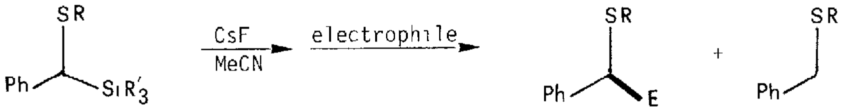
Summary Desilylation of either α-silyl sulphides or silyl dihydrothiopyrans (easily obtained from silyl thiones as primary adducts), when performed in the presence of carbon electrophiles (aldehydes or ketones), offers an easy entry to carbofunctionalised products

Synthetic methods in organic chemistry based on organosilicon intermediates have been widely used in recent years[1] Among these methods, an approach rests upon the fluorodesilylation of an appropriate silane leading to the generation of a nucleophilic carbon, able to be intercepted either by a proton or by a suitable carbon electrophile, with the formation of a new carbon-carbon bond[2-5]

As a part of our studies on the chemistry of silyl thioketones,[6] it has already been shown that they can be easily transformed into α-silyl sulphides through thiophilic addition of organometallic reagents or into 6-silyl 5,6-dihydrothiopyrans through cycloaddition with 1,3-dienes Protodesilylation of these primary adducts gives in nearly quantitative yield the products formally deriving from thioaldehydes

We report here our preliminary results concerning the desilylation of α-silyl sulphides **1a-d** and **2a-b** in the presence of carbonyl compounds as carbon electrophiles The procedure employed in order to minimise protodesilylation was the following cesium fluoride (CsF) flame dried under high vacuum (0 1 mm Hg) for 1 hour was treated with a solution containing the educt **1** or **2** and the carbonyl compound (molar ratio substrate electrophile 1 . 1 2) in anhydrous acetonitrile The results concerning the desilylation of **1** and **2** are reported in tables 1 and 2 respectively[7] Among the electrophiles tested, aromatic, not enolizable aldehydes gave the highest yield of addition products vs side protodesilylation For instance, p-tolualdehyde afforded the carbinols **3a,d,e**[8] in 56, 73 and 50% yield respectively from α-silyl sulphides **1a,b,** and **c** (table 1, entries 1,4,5) Similar results were found in the desilylation of **2a** (table 2, entry 1) Aliphatic, enolizable aldehydes gave lower yield of addition, with both **1a** and **2a** (table 1 entry 2, table 2 entry 2), this is in agreement with previous findings concerning fluorodesilylation in the presence of aldehydes as trapping agents[2c,5] Aliphatic ketones were

Table 1



3a–e

4a–c

1a R = Me R = Me
1b R = Ph ″
1c R = t-Bu
1d R = Ph R = Me,Ph,α-Np

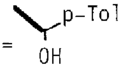
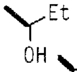
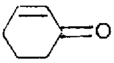
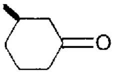
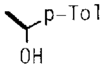
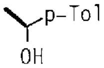
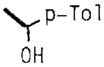
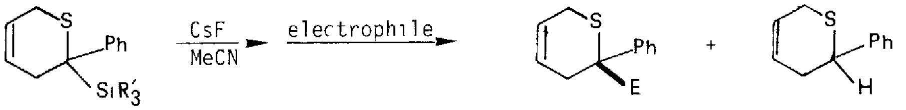
entry	educt (1)	electrophile	product (3)	Yields%			
1	1a	p-TolCHO	3a E = 	3a	$56^{a,b}$	4a	15
2	1a	EtCHO	3b E = 	3b	$26^{a,b}$	4a	27
3	1a		3c E = 	3c	20^{a}	4a	60
4	1b	p-TolCHO	3d E = 	3d	$73^{a,b}$	4b	24
5	1c	p-TolCHO	3e E = 	3e	$50^{a,b}$	4c	-
6	1d	p-TolCHO	3d E = 	3d	$45^{a,b}$	4b	40

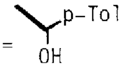
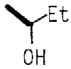
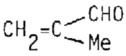
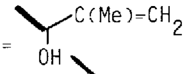
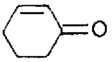
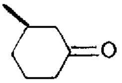
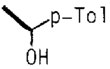
Table 2·



5a–e

6

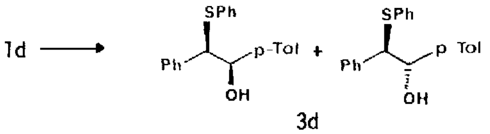
2a R = Me
2b R = Me,Ph,α-Np

entry	educt (2)	electrophile	product (5)	Yields%			
1	2a	p-TolCHO	5a E = 	5a	$70^{a,b}$	6	20
2	2a	EtCHO	5b E = 	5b	$54^{a,b}$	6	27
3	2a	 $CH_2=C(CHO)Me$	5c E = 	5c	$30^{a,b}$	6	17
4	2a		5d E = 	5d	40^{a}	6	48
5	2a	$PhCOCH_2Br$	5e E = $-CH_2COPh$	5e	15	6	20^{c}
6	2b	p-TolCHO	5a E = 	5a	45	6	15

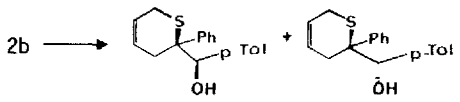
Notes a) as a mixture of diastereoisomers, b) variable amounts of product (up to 30%) were obtained as O-trimethylsilyl ether, c) in addition, starting 2a was recovered (20%), inert, whereas phenacyl bromide gave the product of halogen substitution **5e** in low yield (table 2, entry 5)[9]

The reaction with two kinds of α-ß-unsaturated carbonyl compounds (aldehydes and ketones) revealed a different chemoselectivity of the active species formed by cleavage of the carbon-silicon bond in either **1** or **2** This species, synthetically equivalent to an α-phenyl-α-thio carboanion, gave 1,2 addition to methacrolein, (table 2 entry 3), but 1,4 addition only to cyclohex-2-en-1-one (table 1 entry 3, table 2 entry 4) This result confirms precedent findings [2c] in fact, heteroacyl silanes also give 1,4 addition to cyclohexenone

The reaction here described offers an interesting probe to study the stereochemistry of carbodesilylation in fact, if desilylation in the presence of a carbon electrophile is accomplished on homochiral compounds **1d** or **2b**, deriving from a silyl thione chiral at silicon,[10] the resulting diastereomers **3** or **5** could be optically enriched Reaction of the optically active α-silyl sulphide **1d** with p-tolualdehyde in the presence of anhydrous CsF gave in 50% yield (table 1, entry 6) the optically active **3d** as a not racemic mixture of **syn/anti** isomers which were separated by preparative TLC The enantiomeric excess (e e) of both isomers (table 3) was determined by 1H NMR analysis in the presence of the chiral shift reagent Eu(hfc)3, following the signals at δ 4 35 (**syn 3d**) and 4 45 (**anti 3d**) of the protons α to the phenylthio group



3d



5a

Table 3[a]

entry	d e **1d**	**3d**	e e **syn**[b]	e e **anti**[b]	**syn/anti**
1	50		48 $[\alpha]_{546} = +69^{\circ}$	48 $[\alpha]_{546} = +53^{\circ}$	1/1 4
2	15		20 $[\alpha]_{546} = +21^{\circ}$	15 $[\alpha]_{546} = +18^{\circ}$	1/1 2

Table 4[a]

entry	d e **2b**	**5a**	e e **syn**[c]	e e **anti**[c]	**syn/anti**
1	50		10 $[\alpha]_{546} = -13\ 5^{\circ}$	7 $[\alpha]_{546} = -5\ 7^{\circ}$	1/1 4
2	28		7 $[\alpha] = 4\ 0^{\circ}$ (mixture)	5	1/1 3

a) Specific rotations measured at c = 1 in CH_2Cl_2

b) **syn/anti** relative stereochemistry assigned by comparison of NMR data with those of model compounds [12]

c) Relative configurations assigned by comparison with compounds **syn** and **anti 3d**

The e e of both **syn** and **anti** **3d** was found to be practically the same, within the experimental error, as the diastereomeric excess (d e) of the starting educt **1d** (Table 3, entries 1 and 2), leading to the conclusion that carbodesilylation of **1d** occurs without racemization at the asymmetric carbon When the same investigation was repeated on the optically active cyclic sulphide **2b**, product **5a** (Table 2, entry 7) was again formed as a not racemic mixture of diastereomers surprisingly, in this case the e e of both isomers was found to be much lower than the d e of the educt **2b**, ranging between 5 and 10% against a starting d e of either 50 or 30% (Table 4, entries 1 and 2) Hence, the preliminary conclusion is allowed that the stereochemical outcome of carbodesilylation may depend on the structure of the educt We observe here a partial racemization for the cyclic α-silyl sulphide **2b**, whereas protodesilylation of both compounds **1d** and **2b**[10] was found to occur with high stereoselectivity Previous results from the literature[11] showed that desilylation of various substrates in the presence of different electrophiles occurred, in general, with retention of relative configuration

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7 All new compounds, characterized by IR, 1H NMR and MS, gave correct spectral data

8 Products similar to **3a** and **3c** were obtained by Seebach following a different approach K H Geiss, D Seebach, B Seuring Chem Ber 1977, **110**, 1833

9 Other carbon electrophiles, like epoxides, chloroformiates, or α-haloacetals proved to be unreactive under the same reaction conditions In the presence of alkylating agents, like methyl iodide, the reaction follows another course, deriving from an intermediate sulfonium salt (unpublished results)

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(Received in UK 19 November 1990)