

Enantioselective synthesis of α -hydroxysilanes by bioreduction of aroyltrimethylsilanes

PERKIN

Amauri F. Patrocínio, Ivan R. Corrêa Jr. and Paulo J. S. Moran*

Instituto de Química, Universidade Estadual de Campinas, 13083-970 Campinas, SP - Brazil

Received (in Cambridge, UK) 4th August 1999, Accepted 9th September 1999

Aromatic acylsilanes [Ar-CO-SiMe₃; Ar = C₆H₅, 4-ClC₆H₄, 2-, 3- and 4-OMeC₆H₄, 3,4-(OMe)₂C₆H₃ and 3,4-OCH₂OC₆H₃] were reduced by baker's yeast to optically active α -silyl alcohols in 20–70% yield and 43–88% ee. Comments are made on the influence of silicon in this bioreduction reaction.

Introduction

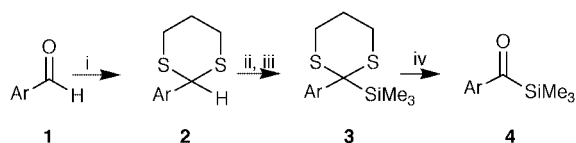
In view of the great importance of organosilicon compounds in synthetic organic chemistry, in particular the stereochemical control mediated by organosilicon moieties,¹ methodologies have been developed for the synthesis of chiral compounds containing silicon. α -Hydroxysilanes have been applied for this purpose² and in general are prepared by reduction of acylsilanes mediated by organoboranes.³

Baker's yeast (*Saccharomyces cerevisiae*) has been extensively applied for enantioselective reductions of pro-chiral ketones. It is known that acetophenone is acceptable as a substrate for baker's yeast, giving the optically active 1-phenylethanol in 15–45% yield and 69–89% ee,⁴ while other ketones like *tert*-butyl methyl ketone and *tert*-butyl phenyl ketone⁵ are not reduced. The lack of reactivity of these ketones may be due to enzyme–substrate steric interactions. In contrast, benzoyltrimethylsilane is reduced by baker's yeast, giving the corresponding optically active α -silyl alcohol.^{5b}

In this work we present the results of baker's yeast reduction of aromatic acylsilanes having substituent groups attached to the benzene ring.

Results and discussion

The aroylsilanes **4a–g** were prepared from the corresponding aldehydes **1** following the known dithiane route⁶ (Scheme 1).



Scheme 1 Reagents and conditions: (i) propane-1,3-dithiol, BF₃·OEt₂, CH₂Cl₂, 12 h, rt; (ii) *n*-BuLi, THF, 1 h, –23 °C; (iii) TMSCl, 1 h, 0 °C; (iv) HgCl₂, acetone–water (9 : 1), 8–15 h, rt.

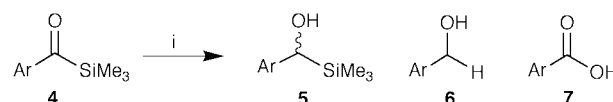
The yields of each step for the preparation of **4a–g** are summarised in Table 1. The reductions of aroylsilanes **4a–g** were performed by whole cells of *Saccharomyces cerevisiae* supported on montmorillonite K10, a system that has been shown to be efficient and has an additional advantage of needing only very simple work-up.⁷ Table 2 shows chemical yields and enantiomeric excesses of α -silyl alcohols **5a–g** and the yields of arylmethanols **6a–g** obtained as by-products in this bioreduction (Scheme 2).

It is known that the reduction rate of 4-substituted acetophenones by baker's yeast is decreased by electron-donating

Table 1 Obtained yields in each step of the preparation of aroyltrimethylsilanes **4a–g** from corresponding aldehydes **1a–g**

Aldehyde 1 Aryl group	1,3-Dithiane 2 Yield (%) ^a	Silyl-1,3-dithiane 3 Yield (%) ^a	Aroylsilane 4 Yield (%) ^b
a Ph	94	82	70
b 4-ClC ₆ H ₄	85	70	25
c 2-MeOC ₆ H ₄	93	90	65
d 3-MeOC ₆ H ₄	90	97	55
e 4-MeOC ₆ H ₄	91	90	91 ^c
f 3,4-(MeO) ₂ C ₆ H ₃	74	77	75
g 3,4-(OCH ₂ O)C ₆ H ₃	82	89	76

^a Isolated and purified by crystallisation in hexane. ^b Purified by liquid chromatography. ^c Isolated without further purification.



Scheme 2 Reagents and conditions: i, baker's yeast, montmorillonite K10, 48 h.

groups,¹⁰ and therefore 4-methoxy-¹⁰ and 3,4-methylenedioxyacetophenone¹¹ are not reduced by baker's yeast. In contrast, this work shows that aroyltrimethylsilanes **4c–g** are good substrates to be reduced by baker's yeast in spite of having electron-donating groups attached to the benzene ring.

The expressive influence of silicon on the carbonyl group of acylsilanes was reported in many papers by Brook and in reviews.¹² It is known that the carbonyl group of an acylsilane has a considerable degree of single bond and polar character. This high degree of polarity of the carbonyl group should facilitate the hydride transfer performed by the NADH/NADPH-enzyme. In addition, although the trimethylsilyl (TMS) group's size is larger than that of the *tert*-butyl group, the abnormally long silicon–carbonyl carbon bond-length (1.92 Å)¹³ keeps the TMS group far from the reactive centre. Therefore, the steric effect of a TMS group may be sometimes less serious than that of a *tert*-butyl group.¹⁴ Only compound **4c**, which has a highly hindered carbonyl group, was not entirely converted after 48 h under the bioreduction conditions.

Taking into consideration the fact that an aryl moiety is bulkier than a TMS group, or at least gives a larger steric hindrance as established by *A*-value¹⁵ measurements, the baker's yeast reduction of the majority of our studied substrates followed Prelog's rule¹⁶ with “*re*-face attack” to provide the corresponding *S*-alcohols (Scheme 3). The moderate stereo-

Table 2 Bioreduction of acylsilanes mediated by baker's yeast immobilised onto montmorillonite K10 at 35 °C

	Aroylsilane 4 Aryl group	α -Hydroxysilane 5			ArCH ₂ OH 6	
		Yield (%) ^a	ee (%) ^b	[α] _D (c, CHCl ₃)	Conf. ^c	Yield (%)
a	Ph	60	84 ^d	-51.0 (1.5)	S ^e	10
b	4-ClC ₆ H ₄	70 ^f	86 ^d	-41.0 (2.0)	S	15
c	2-MeOC ₆ H ₄	20 ^g	79	+20.4 (2.5)	R	30
d	3-MeOC ₆ H ₄	46	88	-35.5 (1.2)	S	25
e	4-MeOC ₆ H ₄	45	44	-32.4 (2.0)	S	15
f	3,4-(MeO) ₂ C ₆ H ₃	50	43	-23.0 (2.0)	S	20
g	3,4-(OCH ₂ O)C ₆ H ₃	45	67	-21.9 (2.3)	S	15

^a Isolated and purified by TLC after 48 h of reaction. ^b Determined by ¹H NMR after derivatisation. ^c Proposed by Trost⁸ model. ^d Also determined by GC/MS analysis using a β -DEX™ 120 Capillary Column (Supelco). ^e This configuration was proposed by Mosher⁹ previously. ^f Total conversion after 24 h. ^g The acylsilane was 25% recovered after 48 h.

selectivities obtained in these biotransformations may be due to small size differences between TMS and Ar groups attached to the pro-chiral carbonylic carbon or may be due to competition between oxi-reductases. Benner¹⁷ has suggested, based on experimental data, that the less reactive carbonyl compounds can be reduced by the enzyme with NADH in the *syn* conformation, a stronger reducing agent than *anti*-NADH. In agreement, our results show that the more reactive aroylsilanes (**4a**, **4b** and **4d**) gave hydroxysilanes **5** with good ee (84–88%) while substrates **4e–g**, that have electron-donating groups attached to the aryl moiety, gave products **5** with poor ee (43–67%). Thus, these observations suggest that acylsilanes with low reactivity can undergo more competition between the enzymes with *anti*-NADH and *syn*-NADH providing moderated enantiomeric excesses. On the other hand, the less reactive 2-methoxybenzoyltrimethylsilane **4c** was reduced preferentially by the *syn*-NADH through the *si*-face, giving the (*R*)-(+)-alcohol **5c** (*anti*-Prelog) with good enantioselectivity (79%).

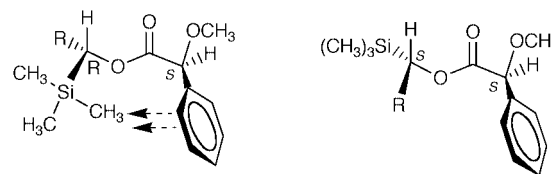
All the enantiomeric excesses were determined by ¹H NMR after derivatisation with (*S*)-(+)-mandelic acid, and with **5a** and **b** the ees were also determined by chiral GC/MS. The absolute configurations of **5a–g** were proposed by applying the model of Trost⁸ that has been frequently used for organosilicon compounds.^{3,18,19} Based on this model, the ¹H NMR signal of the TMS group of the *SR* diastereomer is more shielded due to the anisotropic effect of the phenyl group (see Fig. 1). In fact, we observed that the singlets of the TMS groups of diastereomeric mixtures were found about δ 0.18 from each other. When we analysed the silyl alcohol **5a**, which has the *S* configuration as established by Mosher⁹ for the negative optical rotation isomer, total agreement was observed. So, all the silyl alcohols **5** were analysed by the same form and we are proposing the *S* configuration for those optically active compounds with negative optical rotation. Only the aroylsilane **4c** was reduced to enantiomerically enriched (*R*)-(+)-isomer. The results of these analyses are in Table 3.

In this work, the yields of α -silyl alcohols **5** were moderated due to expressive competition reactions producing the corresponding desilylated arylmethanols **6** and carboxylic acids **7**. It was suggested¹⁹ that the phenylmethanol could be formed by Brook rearrangement²⁰ through the α -hydroxysilane. How-

Table 3 ¹H NMR chemical-shift of TMS group in mandelate ester derivatisation^a of compounds **5a–g**

α -Hydroxy-silane 5	δ_{SS}	δ_{SR}	SS:SR (%)
a	-0.09	-0.22	92.0:8.0
b	-0.06	-0.24	93.0:7.0
c	-0.06	-0.24	10.7:89.3
d	-0.04	-0.23	93.8:6.2
e	-0.05	-0.24	72.0:28.0
f	-0.02	-0.20	71.7:28.3
g	-0.06	-0.24	83.5:16.5

^a The esterifications were performed with (*S*)-(+)-mandelic acid, DCC, 4-DMAP over a period of 15 h, according to ref. 8.

**Fig. 1** TMS group eclipsed (*RS*) and not eclipsed (*SS*) with phenyl group.

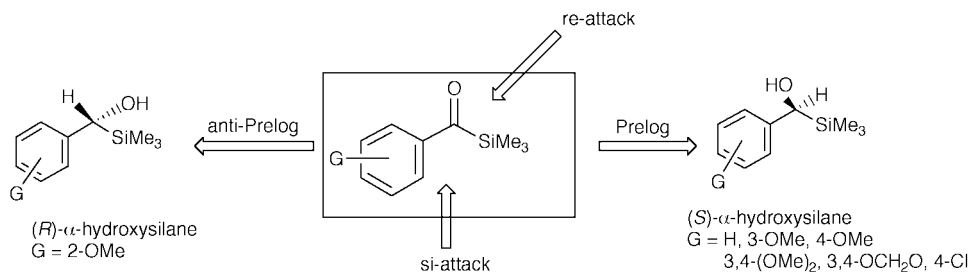
ever, we observed that the α -hydroxysilanes **5** are stable when submitted to the same conditions as those used with baker's yeast reaction mixture (see Experimental section). The mechanistic pathway for the formation of **6** and **7** needs further investigation and its elucidation is currently in progress.

Conclusion

The reduction of aroyltrimethylsilanes by baker's yeast proved to be a good method for the preparation of optically active silyl alcohols where the silicon moiety plays an important role in controlling the course of the reaction.

Experimental

Mps were measured on a Microquímica MQAFP-301 appar-

**Scheme 3** Stereoselective reduction of ketones **4** to alcohols **5**.

atus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1600 FT or Bomem MB series spectrophotometer. Column chromatography was performed with Silica gel-60. Mass spectra were obtained on a Shimadzu Class 5000 GC/MS system and the enantiomeric excesses were determined by GC analysis using a chiral column [stationary phase heptakis(2,6-dimethylpentan-3-yl)- β -cyclodextrin] or by ^1H NMR after derivatisation with (*S*)-(+)-mandelic acid as indicated in the text. NMR spectra were recorded on a Bruker AC 300P or Varian Gemini 300 spectrometer (300 and 75 MHz resonance frequencies for ^1H and ^{13}C , respectively) with CDCl_3 as solvent and CHCl_3 (δ_{H} 7.27) as internal standard; *J*-values are given in Hz. Elemental analyses were measured on a Perkin-Elmer 2400 CHN. Commercially available chemicals and solvents were used with further purification. Optical rotations were measured on a Polamat A, and $[\alpha]_{\text{D}}$ -values are given in units of 10^{-1} deg $\text{cm}^2 \text{g}^{-1}$.

All 1,3-dithianes **2**, 2-(trimethylsilyl)-1,3-dithianes **3**, and acylsilanes **4** were prepared according to a literature procedure.⁶ The following compounds have been described previously: 2-phenyl-1,3-dithiane **2a**,⁶ 2-phenyl-2-trimethylsilyl-1,3-dithiane **3a**,⁶ benzoyltrimethylsilane **4a**,⁶ 4-chlorobenzoyltrimethylsilane **4b**,²¹ 4-methoxybenzoyltrimethylsilane **4c**,²² 3,4-methylenedioxybenzoyltrimethylsilane **4g**,¹³ (*S*)-(-)- α -(trimethylsilyl)-benzenemethanol **5a**⁹ and 2-(3,4-methylenedioxyphenyl)-1,3-dithiane **2g**.²³

General procedure for the preparation of 2-aryl-1,3-dithianes **2**⁶

$\text{BF}_3 \cdot \text{OEt}_2$ (80.0 mmol) was added slowly to a stirred solution of aldehyde (20.0 mmol), propane-1,3-dithiol (20.5 mmol) in CH_2Cl_2 (50.0 cm^3) and molecular sieves (4 Å) (12–15 g) at 0 °C. The solution was stirred for 2 h at 0 °C and warmed to room temperature and was stirred for another 15 h. After that, aq. sodium bicarbonate was added, the product was extracted with CH_2Cl_2 (3 \times 40 cm^3), the organic phase was dried with MgSO_4 and the solvent was evaporated under reduced pressure. The product was purified by crystallisation in hexane.

General procedure for the preparation of 2-aryl-2-trimethylsilyl-1,3-dithianes **3**⁶

Under an Ar atmosphere, *n*-BuLi (21.0 mmol in hexane solution) was added cautiously over a period of 5 min to a stirred solution of a 2-aryl-1,3-dithiane **2** (20.0 mmol) in THF (50 cm^3) at -23 °C. After 1 h, the solution was warmed to 0 °C and then chlorotrimethylsilane (25.0 mmol) was added. The reaction mixture was stirred for another 1 h at 0 °C. After that water (50 cm^3) was added and then the product was extracted with CHCl_3 (3 \times 40 cm^3). The organic phase was dried, the solvent was evaporated under reduced pressure and the product purified by crystallisation in hexane.

General procedure for the preparation of aroyltrimethylsilanes **4**⁶

The substrate 2-aryl-2-trimethylsilyl-1,3-dithiane **3** (10.0 mmol) was hydrolysed with HgCl_2 (15.0 mmol) and CaCO_3 or CdCO_3 (10.0 mmol) in aq. acetone (40 cm^3) for 8–15 h, at room temperature, to provide the corresponding aroylsilane **4**. The yellow compound was purified by column chromatography on silica using hexane as eluent.

General procedure for aroyltrimethylsilanes bioreduction

A mixture of dry baker's yeast (10 g), 2% aq. KCl (100 cm^3), sucrose (10 g) and montmorillonite K10 (10 g) was stirred at 35 °C. After 30 min the acylsilane **4** (1.2–1.6 mmol) was added and the mixture was stirred for 48 h. After this period, ethyl acetate was added over the reaction mixture and the mixture was vigorously stirred for 2 h. The solid was filtered off, the organic phase was separated and the aqueous phase was extracted with two 30 cm^3 portions of ethyl acetate. The organic

solutions were combined, and dried with MgSO_4 , and the solvent was evaporated at reduced pressure. The residue was purified by preparative TLC (silica gel; hexane and ethyl acetate).

2-(4-Chlorophenyl)-1,3-dithiane 2b. Obtained in 85% yield as a crystalline solid, mp 82.0–83.0 °C (Found: C, 51.5; H, 4.2. $\text{C}_{10}\text{H}_9\text{ClS}_2$ requires C, 52.0; H, 4.7%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1480, 1440, 1233; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 1.90–2.00 (1H, m), 2.15–2.22 (1H, m), 2.92 (2H, ddd, *J* 13.8, 4.3 and 2.9, H-eq), 3.10 (2H, ddd, 13.8, 9.5 and 3.2, H-ax), 5.15 (1H, s), 7.32 (2H, d, *J* 8.1), 7.43 (2H, d, *J* 8.1); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 24.9, 31.9, 50.5, 128.9, 129.1, 134.1, 137.6; *m/z* 230 (M^+ , 65%), 156 (100), 155 (94), 74 (93).

2-(2-Methoxyphenyl)-1,3-dithiane 2c. Obtained in 93% yield as a crystalline solid, mp 128.0–129.0 °C (Found: C, 58.8; H, 5.8. $\text{C}_{11}\text{H}_{14}\text{OS}_2$ requires C, 58.4; H, 6.2%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1595, 1430, 1244; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 1.90–2.00 (1H, m), 2.14–2.20 (1H, m), 2.85 (2H, ddd, *J* 15.2, 5.6, 3.5, H-eq), 3.15 (2H, ddd, *J* 15.2, 12.5, 3.2, H-ax), 3.85 (3H, s), 5.70 (1H, s), 6.87 (1H, d, *J* 8.3), 6.96 (1H, ddd, *J* 8.6, 8.6, 1.9), 7.26 (2H, ddd, *J* 8.3, 8.6, 2.1), 7.58 (2H, dd, *J* 8.6, 2.1); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 25.3, 32.4, 43.6, 55.7, 110.7, 121.0, 127.2, 129.1, 129.4, 155.4; *m/z* 226 (M^+ , 37%), 152 (100), 151 (94), 121 (34), 108 (17).

2-(3-Methoxyphenyl)-1,3-dithiane 2d. Obtained in 90% yield as a crystalline solid, mp 62.5–62.9 °C (Found: C, 57.9; H, 5.6%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1596, 1421, 1268, 702; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 1.84–2.21 (2H, m), 2.91 (2H, ddd, *J* 12.4, 4.4 and 3.4, H-eq), 3.06 (2H, ddd, *J* 12.4, 9.7 and 2.6, H-ax), 3.80 (3H, s), 5.15 (1H, s), 6.84 (1H, dd, *J* 7.3 and 2.5), 7.02–7.28 (3H, m); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 26.0, 32.0, 51.4, 55.2, 113.1, 114.4, 120.1, 129.8, 140.6, 159.9; *m/z* 226 (M^+ , 39%), 152 (100), 151 (54), 121 (21), 108 (39).

2-(4-Methoxyphenyl)-1,3-dithiane 2e. Obtained as a crystalline solid in 91% yield, mp 115.0–118.0 °C (Found: C, 59.0; H, 5.8%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1607, 1506, 1440, 1248; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 1.80–2.22 (2H, m), 2.90 (2H, ddd, *J* 15.1, 3.5, 3.0, H-eq), 3.07 (2H, ddd, *J* 15.1, 10.4, 2.8, H-ax), 3.80 (3H, s), 5.18 (1H, s), 6.90 (2H, d, *J* 8.6), 7.40 (2H, d, *J* 8.6); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 24.8, 24.7, 25.0, 46.7, 55.1, 113.7, 131.0, 132.3, 157.6; *m/z* 226 (M^+ , 42%), 152 (100), 151 (87), 121 (37), 108 (20).

2-(3,4-Dimethoxyphenyl)-1,3-dithiane 2f. Obtained in 74% yield as a crystalline solid, mp 81.6–82.5 °C (Found: C, 56.8; H, 6.8. $\text{C}_{12}\text{H}_{16}\text{O}_2\text{S}_2$ requires C, 56.2; H, 6.3%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1595, 1578, 1256, 764; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 1.84–2.24 (2H, m), 2.90 (2H, ddd, *J* 15.0, 5.0, 3.5, H-eq), 3.06 (2H, ddd, *J* 15.0, 11.2, 2.5, H-ax), 3.86 (3H, s), 3.90 (3H, s), 5.13 (1H, s), 6.82 (1H, d, *J* 8.5), 7.01 (1H, s), 7.02 (1H, d, *J* 8.5); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 24.8, 33.9, 51.1, 55.8, 110.9, 111.2, 120.1, 131.8, 149.3; *m/z* 256 (M^+ , 43%), 182 (100), 151 (19).

2-(4-Chlorophenyl)-2-(trimethylsilyl)-1,3-dithiane 3b. Obtained in 70% yield as a crystalline solid, mp 90.0–92.0 °C (Found: C, 51.2; H, 5.9. $\text{C}_{13}\text{H}_{19}\text{ClS}_2\text{Si}$ requires C, 51.5; H, 6.3%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1480, 1433, 1420, 1083, 846; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 0.08 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.85–2.10 (2H, m), 2.42 (2H, ddd, *J* 13.8, 4.3, 2.9, H-eq), 2.78 (2H, ddd, *J* 13.8, 9.5, 3.2, H-ax), 7.32 (2H, d, *J* 8.2), 7.85 (2H, d, *J* 8.2); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ -4.0, 23.0, 25.0, 47.0, 128.5, 131.5, 139.5, 143.0; *m/z* 302 (M^+ , 7%), 267 (8), 229 (42), 194 (100), 155 (86), 73 (90).

2-(2-Methoxyphenyl)-2-(trimethylsilyl)-1,3-dithiane 3c. Obtained in 90% yield as a crystalline solid, mp 34.0–35.5 °C (Found: C, 56.8; H, 7.8. $\text{C}_{14}\text{H}_{22}\text{OS}_2\text{Si}$ requires C, 56.4; H, 7.4%); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1583, 1431, 1280, 1241, 842; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 0.11 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.85–2.10 (2H, m), 2.55 (2H,

ddd, J 14.4, 5.0, 3.0, H-eq), 2.59 (2H, ddd, J 14.4, 11.5 and 3.0, H-ax), 3.80 (3H, s), 6.90 (1H, d, J 8.0), 6.98 (1H, ddd, J 8.0, 7.8 and 1.4), 7.24 (1H, ddd, J 8.0, 7.8 and 1.4), 7.88 (1H, dd, J 7.8 and 1.9); δ_{C} (75 MHz; CDCl_3) -1.9, 24.9, 26.1, 43.5, 54.9, 112.3, 120.2, 127.6, 129.6, 132.5, 158.0; m/z 298 (M^+ , 16%), 283 (26), 225 (66), 193 (47), 151 (100), 73 (94).

2-(3-Methoxyphenyl)-2-(trimethylsilyl)-1,3-dithiane 3d.

Obtained in 97% yield as a crystalline solid, mp 46.0–47.0 °C (Found: C, 56.8; H, 6.9%); ν_{max} (KBr)/ cm^{-1} 1596, 1422, 1280, 1240, 842; δ_{H} (300 MHz; CDCl_3) 0.10 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.90–2.10 (2H, m), 2.44 (2H, ddd, J 13.7, 4.5, 3.0, H-eq), 2.80 (2H, ddd, J 13.7, 8.2, 2.5, H-ax), 3.83 (3H, s), 6.75 (1H, dd, J 8.1, 2.5), 7.25–7.55 (3H, m); δ_{C} (75 MHz; CDCl_3) -4.0, 25.0, 25.2, 47.5, 55.2, 110.6, 115.6, 122.3, 129.2, 142.5, 160.0; m/z 298 (M^+ , 12%), 283 (20), 225 (56), 193 (47), 151 (100), 73 (95).

2-(4-Methoxyphenyl)-2-(trimethylsilyl)-1,3-dithiane 3e.

Obtained in 90% yield as a crystalline solid, mp 79.8–81.0 °C (Found: C, 56.0; H, 6.7%); ν_{max} (KBr)/ cm^{-1} 1604, 499, 1460, 1289, 1242, 844; δ_{H} (300 MHz; CDCl_3) 0.20 (9H, s, $3 \times \text{CH}_3\text{Si}$), 1.82–2.30 (2H, m), 2.42 (2H, ddd, J 13.8, 3.3 and 2.8, H-eq), 2.78 (2H, ddd, J 13.8, 9.7 and 2.8, H-ax), 3.85 (3H, s), 6.90 (2H, d, J 9.2), 7.80 (2H, d, J 9.2); δ_{C} (75 MHz; CDCl_3) -4.3, 24.7, 25.0, 46.8, 55.1, 113.7, 131.0, 132.3, 157.6; m/z 298 (M^+ , 3%), 283 (24), 225 (53), 193 (36), 151 (100), 73 (77).

2-(3,4-Dimethoxyphenyl)-2-(trimethylsilyl)-1,3-dithiane 3f.

Obtained in 77% yield as a crystalline solid, mp 96.2–97.0 °C (Found: C, 54.5; H, 7.8. $\text{C}_{15}\text{H}_{24}\text{O}_2\text{S}_2\text{Si}$ requires C, 54.8; H, 7.4%); ν_{max} (KBr)/ cm^{-1} 1603, 1588, 1260, 1228, 840; δ_{H} (300 MHz; CDCl_3) 0.06 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.90–2.10 (2H, m), 2.43 (2H, ddd, J 15.0, 4.2 and 3.5, H-eq), 2.81 (2H, ddd, J 15.0, 10.5 and 3.0, H-ax), 3.88 (3H, s), 3.89 (3H, s), 6.87 (1H, d, J 8.3), 7.42 (1H, dd, J 8.3 and 2.3), 7.48 (1H, d, J 2.3); δ_{C} (75 MHz; CDCl_3) -3.9, 25.1, 47.2, 55.9, 110.7, 113.0, 122.0, 132.7, 146.6, 148.6; m/z 328 (M^+ , 2%), 313 (97), 255 (65), 181 (100), 73 (59).

2-(3,4-Methylenedioxyphenyl)-2-(trimethylsilyl)-1,3-dithiane 3g.

Obtained as a crystalline solid in 89% yield, mp 123.0–125.0 °C (Found: C, 54.2; H, 6.0. $\text{C}_{14}\text{H}_{20}\text{O}_2\text{S}_2\text{Si}$ requires C, 53.8; H, 6.4%); ν_{max} (KBr)/ cm^{-1} 1604, 1471, 1246, 1232, 843; δ_{H} (300 MHz; CDCl_3) 0.10 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.84–2.30 (2H, m), 2.42 (2H, ddd, J 14.3, 5.1 and 2.9, H-eq), 2.80 (2H, ddd, J 14.3, 11.4 and 3.1, H-ax), 6.00 (2H, s), 6.81 (1H, d, J 8.2), 7.27 (1H, dd, J 8.2 and 1.9), 7.45 (1H, d, J 1.9); δ_{C} (75 MHz; CDCl_3) 4.2, 24.8, 47.1, 101.1, 107.9, 110.2, 123.2, 134.7, 145.4, 148.2; m/z 312 (M^+ , 16%), 239 (57), 165 (100), 73 (49).

2-Methoxybenzoyltrimethylsilane 4c. Obtained in 65% yield as a yellow oil (Found: C, 63.1; H, 7.3. $\text{C}_{11}\text{H}_{16}\text{O}_3\text{Si}$ requires C, 63.4; H, 7.7%); ν_{max} (film)/ cm^{-1} 1610, 1587, 1280, 841; δ_{H} (300 MHz; CDCl_3) 0.23 [9H, s, $(\text{CH}_3)_3\text{Si}$], 3.90 (3H, s), 6.90–7.05 (2H, m), 7.40–7.50 (2H, m); δ_{C} (75 MHz; CDCl_3) -2.5, 54.5, 110.7, 121.0, 126.9, 133.0, 133.4, 159.0, 237.9; m/z 208 (M^+ , 2%), 207 (4), 193 (7), 177 (2), 135 (44), 75 (100), 73 (90).

3-Methoxybenzoyltrimethylsilane 4d. Obtained in 55% yield as a yellow oil (Found: C, 63.0; H, 7.4%); ν_{max} (film)/ cm^{-1} 1614, 1579, 1260, 842; δ_{H} (300 MHz; CDCl_3) 0.40 [9H, s, $(\text{CH}_3)_3\text{Si}$], 3.85 (3H, s), 7.10–7.50 (4H, m); δ_{C} (75 MHz; CDCl_3) -0.1, 55.2, 110.4, 119.4, 121.3, 129.7, 142.8, 160.1, 235.6; m/z 208 (M^+ , 6%), 207 (4), 193 (4), 177 (20), 165 (44), 135 (14), 73 (100).

3,4-Dimethoxybenzoyltrimethylsilane 4f. Obtained in 75% yield as a yellow oil (Found: C, 60.1; H, 8.0. $\text{C}_{12}\text{H}_{18}\text{O}_3\text{Si}$ requires C, 60.5; H, 7.6%); ν_{max} (film)/ cm^{-1} 1573, 1508, 1413, 1260, 843; δ_{H} (300 MHz; CDCl_3) 0.38 [9H, s, $(\text{CH}_3)_3\text{Si}$], 3.91 (3H, s), 3.94

(3H, s), 6.94 (1H, d, J 8.4), 7.35 (1H, s), 7.55 (1H, d, J 8.4); δ_{C} (75 MHz; CDCl_3) -1.4, 55.7, 55.9, 107.7, 110.0, 124.4, 135.4, 149.5, 153.3, 233.1; m/z 238 (M^+ , 2%), 207 (50), 207 (7), 195 (40), 165 (37), 73 (100).

(S)-(-)-4-Chloro- α -(trimethylsilyl)benzenemethanol 5b.

Obtained as a colourless oil (Found: C, 55.4; H, 7.2. $\text{C}_{10}\text{H}_{15}\text{-ClOSi}$ requires C, 55.9; H, 7.0%); ν_{max} (film)/ cm^{-1} 3407, 1594, 1241, 1089, 836; δ_{H} (300 MHz; CDCl_3) 0.01 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.78 (1H, s), 4.50 (1H, s), 7.12 (2H, d, J 7.9), 7.27 (2H, d, J 7.9); δ_{C} (75 MHz; CDCl_3) -4.0, 70.0, 126.1, 128.4, 129.0, 131.0; m/z 214 (M^+ , 1%), 178 (4), 106 (78), 73 (100).

(R)-(+)-2-Methoxy- α -(trimethylsilyl)benzenemethanol 5c.

Obtained as a white crystalline solid, mp 59–60 °C (Found: C, 62.7; H, 8.6. $\text{C}_{11}\text{H}_{18}\text{O}_2\text{Si}$ requires C, 62.8; H, 8.6%); ν_{max} (KBr)/ cm^{-1} 3347, 1592, 1400, 1238, 836; δ_{H} (300 MHz; CDCl_3) 0.05 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.90 (1H, s), 3.80 (3H, s), 4.85 (1H, s), 6.83 (1H, dd, J 8.3 and 1.0), 6.97 (1H, ddd, J 8.0, 8.0 and 1.2), 7.17 (1H ddd, J 8.3, 8.0 and 1.2), 7.28 (1H, dd, J 8.0 and 1.2); δ_{C} (75 MHz; CDCl_3) -3.7, 54.8, 65.4, 109.7, 120.6, 126.2, 126.5, 132.5, 155.2; m/z 210 (M^+ , 1%), 195 (26), 180 (15), 179 (40), 121 (18), 73 (100).

(S)-(-)-3-Methoxy- α -(trimethylsilyl)benzenemethanol 5d.

Obtained as a colourless oil (Found: C, 63.0; H, 8.6%); ν_{max} (film)/ cm^{-1} 3479, 1604, 1490, 1243, 841; δ_{H} (300 MHz; CDCl_3) 0.02 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.90 (1H, s), 3.80 (3H, s), 4.50 (1H, s), 6.70–7.30 (4H, m); δ_{C} (75 MHz; CDCl_3) -4.2, 55.1, 70.5, 110.4, 111.2, 117.4, 129.1, 146.2, 159.7; m/z 210 (M^+ , 13%), 195 (4), 179 (8), 121 (9), 73 (100).

(S)-(-)-4-Methoxy- α -(trimethylsilyl)benzenemethanol 5e.

Obtained as a colourless oil (Found: C, 62.5; H, 8.8%); ν_{max} (film)/ cm^{-1} 3441, 1581, 1415, 1245, 842; δ_{H} (300 MHz; CDCl_3) 0.01 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.70 (1H, s), 3.80 (3H, s), 4.48 (1H, s), 6.90 (2H, d, J 8.6), 7.10 (2H, d, J 8.6); δ_{C} (75 MHz; CDCl_3) -4.1, 55.2, 70.0, 113.6, 126.1, 136.3, 157.8; m/z 210 (M^+ , 7%), 195 (58), 167 (19), 120 (80), 73 (100).

(S)-(-)-3,4-Dimethoxy- α -(trimethylsilyl)benzenemethanol 5f.

Obtained as a colourless oil (Found: C, 59.4; H, 7.7. $\text{C}_{12}\text{H}_{20}\text{O}_3\text{Si}$ requires C, 60.0; H, 8.4%); ν_{max} (film)/ cm^{-1} 3503, 1513, 1414, 1259, 840; δ_{H} (300 MHz; CDCl_3) 0.01 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.85 (1H, s), 3.85 (6H, s), 4.40 (1H, s), 6.67 (1H, dd, J 8.1 and 1.8), 6.74 (1H, dd, J 1.8 and 1.8), 6.79 (1H, dd, J 8.1 and 1.8); δ_{C} (75 MHz; CDCl_3) -4.4, 55.6, 55.7, 70.1, 108.6, 111.1, 117.0, 137.0, 147.3, 149.0; m/z 240 (M^+ , 9%), 225 (76), 166 (29), 135 (23), 73 (100).

(S)-(-)-3,4-Methylenedioxy- α -(trimethylsilyl)benzenemethanol 5g. Obtained as a colourless oil (Found: C, 58.5; H, 6.8. $\text{C}_{11}\text{H}_{16}\text{O}_3\text{Si}$ requires C, 58.9; H, 7.2%); ν_{max} (film)/ cm^{-1} 3422, 1503, 1410, 1247, 841; δ_{H} (300 MHz; CDCl_3) 0.01 [9H, s, $(\text{CH}_3)_3\text{Si}$], 1.70 (1H, s), 4.43 (1H, s), 5.94 (2H, s), 6.62 (1H, dd, J 7.6, 1.1), 6.74 (1H, d, J 1.1), 6.77 (1H, d, J 7.6); δ_{C} (75 MHz; CDCl_3) -4.4, 70.4, 100.8, 106.0, 108.1, 118.0, 138.6, 146.0, 147.8; m/z 224 (M^+ , 31%), 151 (14), 134 (68), 73 (100).

Stability test of α -silyl alcohols

An α -silyl alcohol (90 mg, 0.43 mmol) was added to a mixture of dry baker's yeast (2.5 g), K10 (2.5 g), sucrose (2.5 g), and 2% aq. KCl (20 cm^3) and the mixture was stirred at 35 °C. After 48 h, the products were extracted and analysed by GC/MS. This test was performed with **5a**, **5c**, and **5d**.

Acknowledgements

We are grateful to FAPESP and CNPq for financial assistance.

References

- 1 I. Fleming, A. Barbero and D. Walter, *Chem. Rev.*, 1997, **97**, 2063; T. H. Chan and D. Wang, *Chem. Rev.*, 1992, **92**, 995; R. A. N. C. Crump, I. Fleming, J. H. M. Hill, D. Parker, N. L. Reddy and D. Waterson, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3277.
- 2 A. R. Bassindale, A. G. Brook, P. F. Jones and J. M. Lennon, *Can. J. Chem.*, 1975, **53**, 332; J. D. Buynak, J. B. Strikland, T. Hurd and A. Pan, *J. Chem. Soc., Chem. Commun.*, 1989, 89; J. D. Buynak, J. B. Strikland, G. W. Lamb, D. Khasnis, S. Modi, D. Williams and H. Zhang, *J. Org. Chem.*, 1991, **56**, 7076; K. Sakaguchi, H. Mano and Y. Ohfuné, *Tetrahedron Lett.*, 1998, **39**, 4311.
- 3 J. A. Soderquist, C. L. Anderson, E. I. Miranda and I. Rivera, *Tetrahedron Lett.*, 1990, **31**, 4677.
- 4 R. MacLeod, H. Prosser, L. Fikentscher, J. Lanyi and H. S. Mosher, *Biochemistry*, 1964, **3**, 838.
- 5 (a) R. Czuc and B. Glanzer, *Chem. Rev.*, 1991, **91**, 49; (b) Y. Yamazaki and H. Kobayashi, *Chem. Express*, 1993, **8**, 97.
- 6 E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1965, **4**, 1075; A. G. Brook, J. M. Duff, P. F. Jones and N. R. Davis, *J. Am. Chem. Soc.*, 1967, **89**, 431; E. J. Corey, D. Seebach and R. Freedman, *J. Am. Chem. Soc.*, 1967, **89**, 434.
- 7 A. E. P. Sorrilha, M. Marques, I. Joeques, P. J. S. Moran and J. A. R. Rodrigues, *BioMed. Chem. Lett.*, 1992, **2**, 191; O. C. Kreutz, P. J. S. Moran and J. A. R. Rodrigues, *Tetrahedron: Asymmetry*, 1997, **8**, 2649.
- 8 B. M. Trost, J. L. Belletire, S. Godleski, G. J. D. Peddle, N. V. Schwartz and C. M. Warner, *J. Org. Chem.*, 1986, **51**, 2370.
- 9 M. S. Biernbaum and H. S. J. Mosher, *J. Org. Chem.*, 1971, **36**, 3168; *J. Am. Chem. Soc.*, 1971, **93**, 6221.
- 10 G. Eichberger, K. Faber and H. Griengl, *Monatsh. Chem.*, 1985, **116**, 1233.
- 11 R. Wendhausen, P. J. S. Moran, I. Joeques and J. A. R. Rodrigues, *J. Mol. Catal. B: Enzym.*, 1998, **5**, 69.
- 12 A. G. Brook, *Adv. Organomet. Chem.*, 1968, **7**, 95; A. G. Brook, M. A. Quigley, G. J. D. Peddle, N. V. Schwartz and C. M. Warner, *J. Am. Chem. Soc.*, 1960, **82**, 5102; P. C. B. Page, S. S. Klair and S. Rosenthal, *Chem. Soc. Rev.*, 1990, **19**, 147; A. Ricci and A. Degl'Innocenti, *Synthesis*, 1989, 647.
- 13 P. F. Cirillo and J. S. Panek, *Tetrahedron Lett.*, 1991, **32**, 457.
- 14 I. Fleming, in *Comprehensive Organic Chemistry*, ed. D. Barton and W. D. Ollis, Pergamon Press, Oxford, 1979, vol. 3, p. 541.
- 15 M. E. Squillacote and J. M. Neth, *J. Am. Chem. Soc.*, 1987, **109**, 198; W. Kitching, H. A. Olszowy and G. M. Drew, *J. Org. Chem.*, 1982, **47**, 5155.
- 16 V. Prelog, *Pure Appl. Chem.*, 1964, **9**, 119.
- 17 S. A. Benner, *Experientia*, 1982, **38**, 633; P. Deslongchamps, *Stereo-electronic Effects in Organic Chemistry*, Pergamon Press, Oxford, 1983, p. 340.
- 18 R. Linderman and A. Ghannam, *J. Am. Chem. Soc.*, 1990, **112**, 2392.
- 19 R. J. Linderman, A. Ghannam and I. Badejo, *J. Org. Chem.*, 1991, **56**, 5213.
- 20 A. G. Brook, *J. Am. Chem. Soc.*, 1958, **80**, 1886.
- 21 K. Yamamoto, S. Suzuki and J. Tsuji, *Tetrahedron Lett.*, 1980, **21**, 1653.
- 22 A. Capperucci, A. Degl'Innocenti, C. Faggi and A. Ricci, *J. Org. Chem.*, 1988, **53**, 3612.
- 23 D. Seebach, H. F. Leitz and V. Ehrig, *Chem. Ber.*, 1975, **108**, 1924.

Paper 9/06335H