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Synthesis of a highly enantiomerically enriched silyllithium compound

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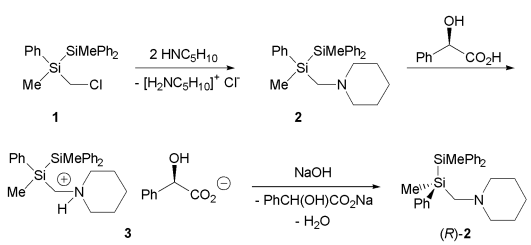
The highly enantiomerically enriched silyllithium compound lithiomethylphenyl(1-piperidinylmethyl)silane (4) reacts stereospecifically with chlorosilanes, but over a period of several hours slow racemization in solution at room temperature occurs, which can be supressed by a transmetalation reaction with $MgBr_2(thf)_4$.

Silyllithium compounds are useful reagents for the introduction of silylgroups in organic and organometallic systems[1a,b] and for the synthesis of complex polysilanes.[2] The preparation of lithiosilanes starting from chlorosilanes or disilanes is a well established method.[3a,b] Sommer *et al*. described the first synthesis of an optically active silyllithium compound by the cleavage of an enantiomerically enriched disilane[4] with lithium metal.[5] Corriu and coworkers also succeeded in the preparation of an optically active silyllithium system *via* a cobalt–lithium exchange reaction.[6a,b] The stability of configuration of the metallated silicon centre was estimated by NMR experiments[7] to be at least 100 kJ mol^{-1}. On the basis of these studies the configuration is expected to be stable at room temperature and the mechanism of racemization has been described in review articles[3a,8,9] and textbooks[10,11] as the inversion of a free silyl anion. A recent work by Kawakami and coworkers reports the synthesis of an enantiomerically enriched silyllithium system starting from enantiomerically enriched stannosilanes.[12] Here the authors report, for the first time, the racemization of a silyllithium compound but key intermediates and products have not been not characterized sufficiently. To our knowledge no preparation of a highly enantiomerically enriched silyllithium system (ee > 98%) starting from enantiomerically pure disilanes or chlorosilanes has been reported so far.

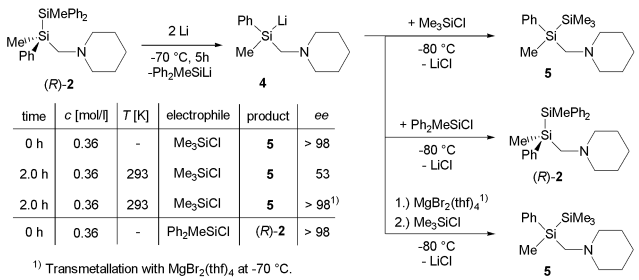
In this work we present an easy synthetic access to a highly enantiomerically enriched silyllithium compound. During our studies we discovered that this system racemizes in solution at room temperature. Closer observation shows an increase in stability by transmetalation reactions.

The starting material for our studies is the enantiomerically pure disilane (*R*)-**2**. From 1-(chloromethyl)-1,2-dimethyl-1,2,2-triphenyldisilane[13] (**1**) we were able to obtain 1,2-dimethyl-1,2,2-triphenyl-1-(1-piperidinylmethyl)disilane (**2**) in a yield of 75 % (Scheme 1).†



Scheme 1

Separation of the enantiomers was carried out using (*R*)-mandelic acid. The resulting enantiomerically pure disilane (*R*)-**2** could be isolated in a yield of 47% (yield relative to the amount of (*R*)-**2** in the diastereomeric salt). The ee-values were determined by ^{1}H NMR spectroscopy of **2** by addition of 3 equivalents of (*R*)-mandelic acid resulting in the separation of the resonance signals of the methyl groups and the $SiCH_2N$ group (AB-system). The ee-values of **5** were determined analogously. Evaluation of the absolute configuration at the silicon centre of (*R*)-**2** was performed by single crystal structure analysis of the diastereomeric salt (*R*)-**2**·(*R*)-mandelic acid, which crystallizes in the monoclinic crystal system (space group $P2_1$) with one equivalent of H_2O.‡



time	*c* [mol/l]	*T* [K]	electrophile	product	*ee*
0 h	0.36	-	Me_3SiCl	**5**	> 98
2.0 h	0.36	293	Me_3SiCl	**5**	53
2.0 h	0.36	293	Me_3SiCl	**5**	> 98[1)]
0 h	0.36	-	$Ph_2MeSiCl$	(*R*)-**2**	> 98

Scheme 2

In the experiments described below (Scheme 2), the enantiomerically pure disilane (*R*)-**2** was cleaved with lithium metal in THF at a temperature of −70 °C. The completeness of the cleavage reaction was established by GC-MS and ^{1}H NMR spectroscopy after the trapping reaction with Me_3SiCl. The resulting disilane **5** could be isolated with ee > 98%. Isolated solutions of lithiomethylphenyl(1-piperidinylmethyl)silane[14] (**4**) racemize within a few hours at temperatures between 0 and 20 °C, but a very slow decomposition of **4** was also observed. Due to this decomposition no exact determination of the reaction rate law was possible.

Solutions of **4** left at room temperature for 2 h show reduced ee-values of 53% after trapping with Me_3SiCl. In order to determine stabilizing effects on the configuration at the silicon centre we performed a transmetalation reaction with $MgBr_2(thf)_4$ at −70 °C. After 2 h at room temperature no significant racemization of the resulting metallated silane could be observed (ee > 98%).

This increase of stability caused by the change of the metal is in contrast to the proposed mechanism of racemization for metalated silanes. Since the rate determining step of the racemization process is discussed in the literature[3a,8–11] as the inversion of the free silyl anion system no drastic effect by transmetalation should be expected. We are presently investigating the racemization process more closely by selective variation of the solvent, the metal and the concentration of the involved lithium compounds.

The results of cleavage of (*R*)-**2** to give **4**, followed by the trapping reaction with $Ph_2MeSiCl$ to give (*R*)-**2** (ee >98%), show that overall the configuration of the stereogenic silicon centre is retained (see Scheme 2), although it is not clear whether this is due to retention of the configuration at each step or through double inversion during the course of the reaction. Retention of configuration can also be observed if a transmetallation step with $MgBr_2(thf)_4$ is included in the reaction.

In summary, we were able to prove that it is possible to synthesize the highly enantiomerically enriched silyllithium

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compound **4** (ee > 98 %) in large amounts and to perform stereospecific reactions with chlorosilanes. Due to the observed racemization of **4** in solution, we believe that a thorough reassessment of previous work concerning optically active silyllithium species is in order.

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Notes and references

† All preparations were performed using standard Schlenk techniques in an argon atmosphere.

2: A solution of 45.8 g (125 mmol) 1-(chloromethyl)-1,2-dimethyl-1,2,2-triphenyldisilane (**1**) and 24.4 g (287 mmol) piperidine were heated under reflux in toluene (150 ml) for 18 h. After separation of salts and removing the solvent *in vacuo* the remaining product was purified by Kugelrohr distillation (T = 225 °C; $p = 10^{-2}$ mbar) giving 39.2 g (94.3 mmol, 75%) of **2**. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ 0.49 (s, 3H; $NCSiCH_3$), 0.66 (s, 3H; $NCSiSiCH_3$), 1.25–1.40 (m, 2H; $NCCCH_2$), 1.40–1.50 (m, 4H; $NCCH_2$), 2.15–2.30 (m, 4H; NCH_2C), 2.22, 2.36 (AB-system, J_{AB} 14.7 Hz, 2H; $SiCH_2N$), 7.20–7.55 (m, 15H; arom. H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C, $CDCl_3$): δ −4.8, −4.2 ($NCSiCH_3$, $NCSiSiCH_3$), 23.8 ($NCCCH_2$), 26.2 (2C; $NCCH_2$), 49.2 ($SiCH_2N$), 58.6 (2C; NCH_2C), 127.67, 127.72, 127.74 (6C; C-*m*), 128.6, 128.7, 128.8 (C-*p*), 134.5, 135.18, 135.23 (6C; C-*o*), 136.8, 137.1, 137.8 (C-*i*); ^{29}Si{^{1}H} NMR (59.6 MHz, $CDCl_3$, 25 °C, TMS): δ –23.3, –22.1; MS (EI, 70 eV): *m*/*z* (%): 218 (35) {[M − $SiCH_3(C_6H_5)_2$]$^+$}, 197 (11) [$SiCH_3(C_6H_5)_2^+$], 98 (100) [(H_2C=NC_5H_{10})$^+$].

(*R*)-**2**: (*R*)-**2**·(*R*)-mandelic acid·H_2O was crystallized from diethyl ether solutions of **2** with (*R*)-mandelic acid. Yield relative to the amount of (*R*)-**2** in the diastereomeric salt: 47%, *m*/*z* (%): 416 (100) [(M + H)$^+$]; mp 121 °C (decomp.). Disilane (*R*)-**2** was isolated using 2 M NaOH as a colourless liquid and purified by Kugelrohr distillation (T = 225 °C; $p = 10^{-2}$ mbar). The enantiomeric purity was verified by ^{1}H NMR spectroscopy by addition of 3 equiv. of (*R*)-mandelic acid. $[\alpha]_D^{25} = -7.3$ (c = 0.22, Et_2O).

5 (ee > 98%): 750 mg (1.80 mmol) (*R*)-**2** were added to a suspension of 37.5 mg (5.40 mmol) lithium in THF (5.0 ml) at 0 °C. At the first change of colour the solution was immediately cooled to −70 °C and stirred for 5 h at this temperature. The brown solution of **4** was divided into five equal portions [five reactions were performed with one single portion (360 μmol) each]. One portion of **4** was added at −80 °C to a solution of 100 mg (920 μmol) Me_3SiCl in THF. Warming to room temperature and removing the solvent *in vacuo* lead to an oily residue, which was treated with 2 ml 2 M HCl. The byproducts were extracted with Et_2O. After neutralization to pH 12 the product **5** was extracted with Et_2O (70 mg, 240 μmol, 67%; ee > 98%). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ 0.08 (s, 9H; $NCSiSiCH_3$), 0.39 (s, 3H; $NCSiCH_3$), 1.25–1.40 (m, 2H; $NCCCH_2$), 1.45–1.55 (m, 4H; $NCCH_2$), 2.20−2.40 (m, 4H; NCH_2C), 2.22, 2.32 (AB-system, J_{AB} 14.6 Hz, 2H; $SiCH_2N$), 7.25–7.40 (m, 3H; arom. H), 7.45–7.55 (m, 2H; arom. H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C, $CDCl_3$): δ −5.6 ($NCSiCH_3$), −1.8 (3C; $NCSiSiCH_3$), 23.8 ($NCCCH_2$), 26.3 (2C; $NCCH_2$), 49.1 ($SiCH_2N$), 58.5 (2C; NCH_2C), 127.7 (2C; C-*m*), 128.3 (C-*p*), 134.1 (2C; C-*o*), 138.7 (C-*i*); ^{29}Si{^{1}H} NMR (59.6 MHz, $CDCl_3$, 25 °C, TMS): δ −23.3, −18.6; MS (EI, 70 eV): *m*/*z* (%): 276 (1) [(M – CH_3)$^+$], 218 (12) {[M − $Si(CH_3)_3$]$^+$}, 98 (100) (H_2C=$NC_5H_{10}^+$).

The enantiomeric purity was determined by ^{1}H NMR spectroscopy of **5** by addition of 3 equivalents of (*R*)-mandelic acid. $[\alpha]_D^{25} = -5.1$ (c = 0.22, Et_2O).

Trapping reactions to determine the stability of the configuration of **4** in solution: one of the remaining portions of the silyllithium solution **4** (c = 0.36 mol l^{-1}) from the synthesis of **5** was warmed to room temperature (T = 293 K). To another portion (360 μmol) of **4** 450 mg (952 μmol) $MgBr_2(thf)_4$ were added at −70 °C and the suspension warmed to room temperature. After 2 h the samples were trapped, as described in the synthesis of **5**, with Me_3SiCl and the ee-values were determined.

The reaction of **4** with $Ph_2MeSiCl$ (220 mg, 945 μmol) was performed analogously to the method described for **5** resulted in (*R*)-**2** (78 mg, 188 μmol, 52%; ee > 98%).

‡ *Crystal structure determination* of (*R*)-**2**·(*R*)-mandelic acid·H_2O (colourless crystals from Et_2O, 0.40 × 0.40 × 0.20 mm): $C_{34}H_{43}NO_4Si_2$, M = 585.89, monoclinic, space group $P2_1$ (no. 4), a = 9.886(2), b = 12.973(3), c = 13.140(3) Å, β = 107.83(3)°, U = 1604.2(6) Å^3, Z = 2, D_c = 1.213 Mg m^{-3}, Mo-Kα radiation, λ = 0.71073 Å, μ = 0.148 mm^{-1}. Measurements: Stoe IPDS diffractometer, T = 173 K. The structure was solved using direct and Fourier methods. 18908 reflections measured with θ in the range 2.26–25.99°, 6102 unique reflections; 5693 with $I > 2\sigma(I)$; refinement by full-matrix least-squares methods (based on F_o^2, SHELXL-93); anisotropic thermal parameters for all non-H atoms in the final cycles; H atoms were refined on a riding model in their ideal geometric positions; Flack parameter (−0,03(11)); R = 0.0524 [$I > 2\sigma(I)$], $wR(F_o^2)$ = 0.1416 (all data). SHELXS-86[15] and SHELXL-93[16] computer programs were used. CCDC reference number 162970. See http://www.rsc.org/suppdata/cc/b1/b111687h/ for crystallographic data in CIF or other electronic format.

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