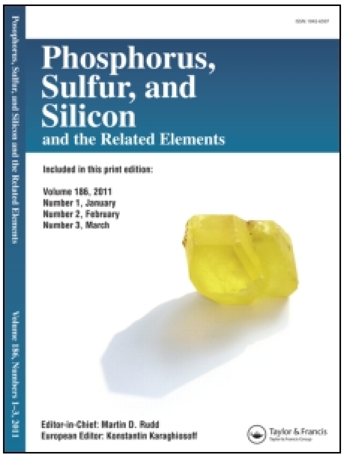

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AN ALTERNATE SYNTHESIS OF THE POTENT ANTIMUSCARINIC AGENT SILA-BIPERIDEN

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Sila-biperiden, **9x(*RS,SR*)**, i. e. racemic (Si*RS*, C2*SR*)-(*exo*-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl)silanol, the silicon analogue of the antimuscarinic agent biperiden, is prepared by a seven-step synthesis. The first step consists in the hydrosilylation of 5-*exo*-bromobicyclo[2.2.1]-hept-2-ene (**2**) with dichloro(phenyl)silane (**1**) in the presence of H_2PtCl_6. The product of the last synthetic step is a mixture of four *endo*- (**9n**) and four *exo*-diastereomers (**9x**) of (bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl)silanol and of the (tricyclo[2.2.1.0^{2,6}]hept-1-yl)silanol derivative **9t**. Eight-fold crystallization of the **9n/9x/9t**-mixture gave pure sila-biperiden (racemate) in an overall yield of 5.3%, which represents a more than 30-fold improvement over the earlier synthesis.

Keywords: Sila-pharmaca; Hydrosilylation; Elimination of hydrogen bromide; thermally and baseinduced

INTRODUCTION

Sila-biperiden, i. e. *rac*-(Si*RS*,C2*SR*)-(*exo*-bicyclo[2.2.1]hept-5-en-2-yl)phenyl (2-piperidinoethyl)silanol, **9x(*RS,SR*)** (Scheme 1), is a very potent antimuscarinic agent which has become an important pharmacological model compound.[1] This compound had so far only been obtained in very low yields in addition to its *endo*-analogue (*endo*-sila-biperiden).[2] In this paper we report a new synthesis of sila-biperiden, which furnishes sufficient quantities of **9x(*RS,SR*)** for experimental pharmacology. As hydrosilylations of halogen-substituted bicyclo [2.2.1]hept-2-ene have not been investigated so far,[3] we describe in some detail the hydrosilylation of 5-*exo*-bromobicyclo[2.2.1]-hept-2-ene (**2**) with dich-

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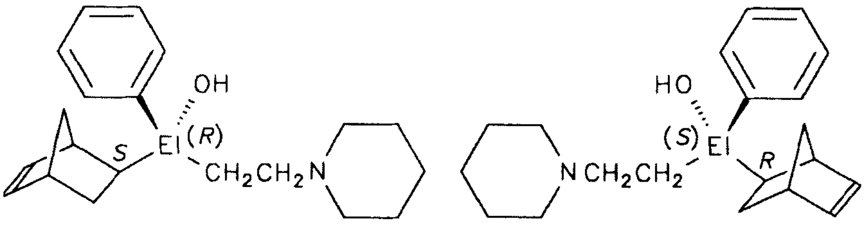


SCHEME 1 Enantiomers contained in biperiden[3] (El = C) and sila-biperiden (El = Si), **9x(*RS*,*SR*)**. Explicitly, **9x** consists of (Si*R*,C2*S*)-*exo*-**9** (left) and (Si*S*,C2*R*)-*exo*-**9** (right).

loro(phenyl)silane (**1**) and the properties of the intermediates and side products **3** and **4**.

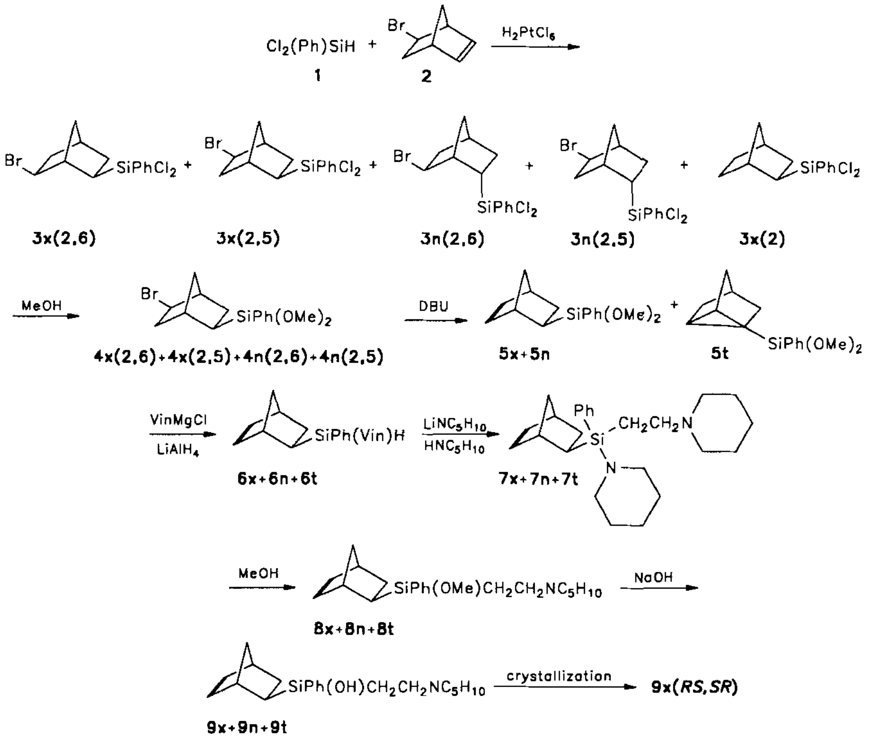
RESULTS AND DISCUSSION

Sila-biperiden is prepared by a seven step synthesis and subsequent eightfold recrystallisation in a total yield of 5.3%. Scheme 2 illustrates the synthetic pathway leading to **9x(*RS*,*SR*)**. Isomers are labeled **x** for *exo*, **n** for *endo*, and **t** for the corresponding derivatives of tricyclo[2.2.1.$0^{2,6}$]heptane. Silicon is connected to C-2 and bromine to C-5 or C-6 (cf. Scheme 5 in Experimental). For reasons of clarity, mostly the *exo*-isomers (**x**) and one tricyclic isomer (**5t**) are depicted in Scheme 2.

The first three steps of the synthesis are investigated in more detail. Hydrosilylation of 5-*exo*-bromobicyclo[2.2.1]hept-2-ene (**2**) with phenyldichlorosilane (**1**) in the presence of H_2PtCl_6 proceeds predominantly in the *exo* direction as had been observed also for the hydrosilylation of the parent bicyclo[2.2.1]hept-2-ene.[4] The isomeric composition of the resulting dichloro (norbornyl)phenylsilanes **3** is estimated by NMR after their conversion into the dimethyl esters **4**. Compounds **3x(2,6)**, **3x(2,5)**, **3n(2,6)** and **3n(2,5)** are obtained in low yields because the desired hydrosilylation is accompanied by side reactions. The first one of these is H/Br exchange in silane **1** to give bromosilane **11** while **2** is converted to **10**.

A similar H/Br exchange had been observed earlier as a side reaction in the hydrosilylation of allyl compounds,[5] while it is the only reaction when relatively bulky silanes are used.[6] When $PhCl_2SiH$ is replaced by $^{i}Bu(^{i}PrO)_2SiH$, **2** reacts exclusively according to Scheme 3.

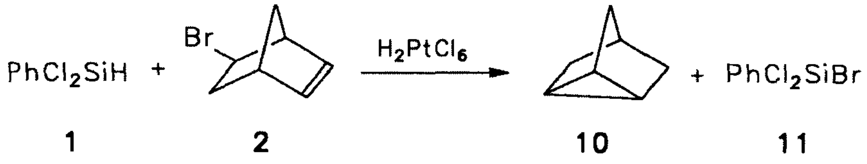
The second side reaction is isomerization. Although **2** is thermally stable up to 95 °C, it isomerizes to 3-bromotricyclo[2.2.1.$0^{2,6}$]heptane at this temperature in the presence of H_2PtCl_6. Thirdly, a considerable amount of *rac*-(C2*RS*)-(*exo*-



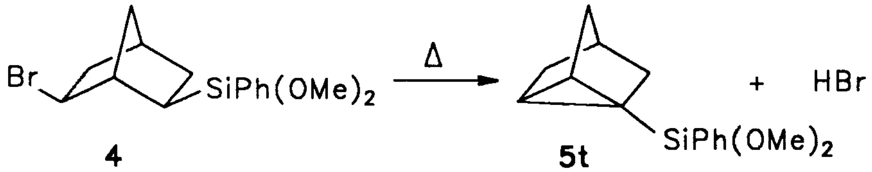
SCHEME 2 Reaction sequence for the synthesis of **9x(*RS,SR*)**. Configuration of **3**, **4** and **5**: *rac*-(C2*RS*)-*exo*, *rac*-(C2*RS*)-*endo*; of **6**, **7**, **8** and **9**: *rac*-(Si*RS*,C2*RS*)-*exo*, *rac*-(Si*SR*,C2*RS*)-*exo*, *rac*-(Si*RS*,C2*RS*)-*endo*, and *rac*-(Si*SR*,C2*RS*)-*endo*.

bicyclo[2.2.1]hept-2-yl)dichloro(phenyl)silane, **3x(2)**, is isolated. This product is studied more closely as its dimethoxy derivative.

Compounds **3x(2,6)**, **3x(2,5)**, **3n(2,6)**, and **3n(2,5)** are thermally stable and there is no change in isomer composition up to ca. 180 °C. Chlorohydrocarbons, in particular 1,2-dichloroethane, turn out to be the best solvents for the methanolysis of **3**. However, the reaction cannot be completed in this manner since only ca. 80% of the chlorine atoms are substituted. The remaining ones only



SCHEME 3 H/Br exchange in **1** as a side reaction in the hydrosilylation of **2**.



SCHEME 4 Formation of the (tricyclo[2.2.1.0^{2,6}]hept-1-yl)silane derivative **5t** upon thermal treatment of **4**.

react with methanol at low concentrations of triethylamine to neutralize the HCl formed. Other attempts to completely substitute the chlorine ligands by methoxy groups were unsuccessful. Methanolyses in ether or in boiling methanol caused siloxane formation. The use of sodium methoxide gave significant parallel HBr elimination leading mostly to tricyclo[2.2.1.0^{2,6}]heptane derivatives. Alcoholysis in the presence of a stoichiometric quantity of triethylamine also lead to HBr elimination with formation of tricyclo[2.2.1.0^{2,6}]heptane derivatives.

The methoxy compounds **4** corresponding to **3x(2,6)**, **3x(2,5)**, **3n(2,6)** and **3n(2,5)** are thermally unstable and purification of **4** by distillation leads to substantial loss of material due to a side reaction (Scheme 4). The hydrogen bromide formed partially substitutes the Si-OMe groups. Isomers **4x(2,6)** and **4n(2,6)** react much faster according to Scheme 4 than do **4x(2,5)** and **4n(2,5)**. Extended heating of crude **4** therefore results in a mixture of **4x(2,5)** and **4n(2,5)** which proved to be thermally much more stable than raw product **4**. It is therefore sensible to evaporate volatile materials under very mild conditions and abstain from purifying **4** by distillation.

(Dimethoxy)phenyl(tricyclo[2.2.1.0^{2,6}]hept-1-yl)silane (**5t**) is not formed from **5x** or **5n** because *rac*-(C2*RS*)-(bicyclo[2.2.1]hept-5-en-2-yl)dimethoxy(phenyl) silane (**5n/5x**, *endo/exo* = 73:27) obtained by a different route[2] is stable up to 160 °C.

Treatment of **4** with DBU leads to elimination of HBr and formation of an isomeric mixture of **5x/5n** in the approximate ratio of 2–3. The proportion of **5t** formed amounts to 7–40%. The isomer distribution depends on the reaction conditions and on the diastereomer ratio of **4**. Compounds **4x(2,6)** and **4n(2,6)** are more reactive towards DBU and by HBr elimination furnish mainly **5t**. The thermal properties of the different isomers of **4** and the behaviour of **4** towards DBU can be explained by stabilization of α-silyl carbanions[7a,b] as well as of γ-silyl carbocations, especially in a W-arrangement.[7c] Although the intermediates **5–9** could not be separated from the tricyclo[2.2.1.0^{2,6}]heptane derivatives **5t-9t** by distillation, our suggested synthetic pathway is nevertheless suited for the preparation of sila-biperiden as the final product can be purified by crystallization.

The reaction of **5** with vinylmagnesium chloride and further with lithium aluminium hydride furnishes the isomeric mixture **6** containing impurities of the corresponding divinyl and dihydrido compounds. Separation of these impurities by distillation was not attempted as it would presumably have caused a substantial loss of **6x** and **6n**. **6x/6n** polymerize slowly when stored at room temperature. Treatment of **6** with an excess of piperidine and a catalytic amount of piperidine-lithiumamide furnishes mixture **7** in good yields. Reaction of **7** with excess methanol leads to a good yield of mixture **8**, which through catalysis by base gives the corresponding mixture **9** of silanols. Eightfold crystallisation from ether at −6 °C furnishes the *rac*-(Si*RS*,C2*SR*)-(*exo*-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl)silanol, **9x(*RS,SR*)**.

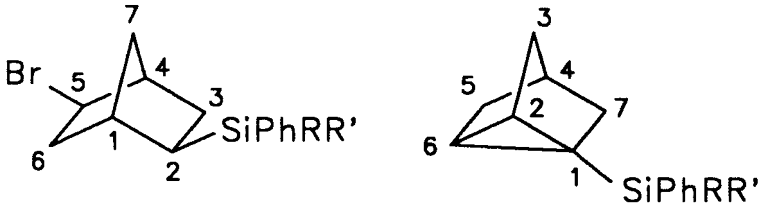
EXPERIMENTAL

All reactions were carried out under an atmosphere of argon. Dry solvents were used. The structures and compositions of the isomeric and diastereomeric mixtures **3–9**, prepared for the first time, were secured by MS, ^{1}H-, ^{13}C- and ^{29}Si-NMR investigations as well as by elemental analyses. Melting points (not corrected): Kofler hot-stage microscope. ^{1}H NMR spectra: solvent $CDCl_3$, int. standard $CHCl_3$ ($\delta = 7.25$), Bruker AC-250, AM-300 and AM-400; ^{13}C NMR spectra: solvent and int. standard $CDCl_3$ ($\delta = 77.05$), Bruker AC-250, AM-300 and AM-400; ^{29}Si NMR spectra: solvent $CDCl_3$, int. standard TMS ($\delta = 0$), Bruker AC-250. Signal assignments for **4x(2)**, **4x(2,5)**, **4n(2,5)** and **5t** were derived from H,H- and C,H-COSY and from homonuclear NOE difference experiments. Labelling of the carbon and hydrogen atoms in the bicyclo[2.2.1]heptane and the tricyclo[2.2.1.0^{2,6}]heptane derivates is shown in Scheme 5. *exo*-, *endo*-, *anti*- and *syn*-Hydrogens are labelled *x*, *n*, *a* and *s*, respectively.

5-exo-Bromobicyclo[2.2.1]hept-2-ene (**2**) was prepared according to Schmerling *et al.*[8] The sample obtained consisted of 83% *exo*-isomer, ca. 12% of 3-bromotricyclo[2.2.1.0^{2,6}]heptane and ca. 5% of 5-*endo*-bromobicyclo[2.2.1]hept-2-ene.

Dichloro(phenyl)silane (1) was prepared according to Metras *et al.*[9]

rac-(C2RS)-(5/6-exo-Bromobicyclo[2.2.1]hept-2-exo-yl)dichloro(phenyl) silane / rac-(C2RS)-(5/6-exo-bromobicyclo[2.2.1]hept-2-endo-yl)dichloro (phenyl) silane [**3x(2,5)**, **3x(2,6)**, **3n(2,5)**, **3n(2,6)**]: 89 mg (0.17 mmol) of hexachloroplatinic acid hydrate (Merck) were dissolved in 0.17 ml of isopropanol



SCHEME 5 Numbering scheme for (bicyclo[2.2.1]hept-2-yl)silane and (tricyclo[2.2.1.$0^{2,6}$]hept-1-yl)silane derivatives.

and left at room temperature for 2 h. This solution was added with vigorous stirring to 71.1 g (0.40 mol) of dichloro(phenyl)silane. Then 88.2 g (0.41 mol) of 5-*exo*-bromobicyclo[2.2.1]hept-2-ene (**2**) was added and the solution kept at 55 °C for 4 days. The brown liquid was distilled in vacuo through an electrically heated 30 cm Vigreux column. The following fractions were separated: a) tricyclo[2.2.1.$0^{2,6}$]heptane (**10**) in the cooling trap, identified by ^{1}H NMR; b) 20–80 °C/0.1–0.05 Torr: 26.8 g of a mixture of bromo(dichloro) phenylsilane (**11**) and 3-bromotricyclo[2.2.1.$0^{2,6}$]heptane; c) 90–130 °C/0.05 Torr: 12.1 g of a mixture of **3x(2)** (ca. 80%) and **3x(2,5)** + **3x(2,6)** + **3n(2,5)** + **3n(2,6)** (ca. 20%); d) 130–150 °C/0.05 Torr: 73.2 g of a mixture of **3x(2)** (ca. 20%) and **3x(2,5)** + **3x(2,6)** + **3n(2,5)** + **3n(2,6)** (ca. 80%). After fractional redistillation, fraction c yielded 8.4 g of *rac-(C2RS)-(exo-bicyclo[2.2.1]hept-2-yl)dichloro(phenyl)silane*, **3x(2)**, as a colourless liquid, bp. 97–102 °C/0.02 Torr. ^{1}H NMR: δ = 7.9 – 7.4 (m, 5H, C_6H_5), 2.7–2.3 (m, 2H, H-1,4), 2.2–1.2 (m, 9H). ^{13}C NMR: δ = 133.8 (C-*o*), 132.4 (C-*i*), 131.4 (C-*p*), 128.3 (C-*m*), 37.8 (C-1), 37.6 (C-7), 36.7 (C-4), 33.7 (C-6), 33.2 (C-2), 32.1 (C-3), 28.7 (C-5). ^{29}Si NMR: δ = 16.9. EI-MS: *m/z* 272 (12%, M^+), 93 (100%). **3x(2)** was further investigated after transformation into the dimethoxy derivative **4x(2)**. Fraction d after fractional redistillation gave 52.1 g (36.6%) of *rac-(C2RS)-(5/6-exo-bromobicylo[2.2.1]hept-2-exo-yl)-dichloro(phenyl)silane / rac-(C2RS)-(5/6-exo-bromobicyclo[2.2.1]-hept-2-endo-yl)-dichloro(phenyl)silane* [**3x(2,5)** + **3x(2,6)** + **3n(2,5)** + **3n(2,6)**], bp. 125–128 °C/0.02 Torr. ^{1}H NMR: δ = 7.83 – 7.41 (m, SiC_6H_5), 4.58–4.52 [m, CHBr(**n**)], 4.10–3.92 [m, CHBr(**x**)], 2.95–1.22 (m). EI-MS: *m/z* 350 (4%, M^+, $C_{13}H_{15}{}^{79}Br^{35}Cl^{37}ClSi$), 175 (100%, $C_6H_5SiCl_2$). $C_{13}H_{15}BrCl_2Si$(350.2), calc. C, 44.59; H, 4.32; Si, 8.02%; found C, 44.8; H, 4.4; Si, 8.0%.

rac-(C2RS)-(exo-Bicyclo[2.2.1]hept-2-yl)dimethoxy(phenyl)silane, [**4x(2)**]. This compound was obtained by methanolysis of **3x(2)** with an excess of methanol in 1,2-dichloroethane at room temperature. The solvent and volatile components were removed at reduced pressure and the residue was subjected to kugelrohr distillation (90 °C, 0.05 Torr). ^{1}H NMR: δ = 7.6 (m, H-*o*), 7.4 (m, H-*m/p*), 3.58 (s, OCH_3), 2.35 (br, H-1), 2.18 (br, H-4), 1.63 (dddd, H-3x), 1.53 (m, H-6x), 1.47 (m, H-5*x*), 1.40 (ddd, H-3*n*), 1.26 (m, H-6*n*), 1.19 (m, H-5*n*), 1.09 (dqi, H-7*s*), 1.03 (dqi, H-7*a*), 0.94 (ddd, H-2*n*); coupling constants [Hz]: $J_{1,6x}$ = 3.7, $J_{1,7a}$ = 1.8, $J_{1,7s}$ = 1.9, $J_{2n,3n}$ = 9.7, $J_{2n,3x}$ = 7.4, $J_{2n,7a}$ = 1.8,$J_{3n,3x}$ = 11.8, $J_{3n,7a}$ = 2.0, $J_{3x,4}$ = 4.3, $J_{3x,5x}$ = 2.7, $J_{4,5x}$ = 4.3, $J_{4,7a}$ = 1.8, $J_{4,7s}$ = 1.9, $J_{5n,7s}$ = 1.9, $J_{6n,7s}$ = 1.9, $J_{7a,7s}$ = 9.5 Hz. ^{13}C NMR: δ = 134.7 (d, 2 C, C-*o*), 132.8 (s, C-*i*), 129.9 (d, C-*p*), 127.8 (d, 2 C, C-*m*), 50.85, 50.84 (both q, 2 OCH_3), 37.8 (t, C-7), 37.4 (d, C-1), 36.7 (d, C-4), 33.8 (t, C-6), 31.5 (t, C-3), 29.0 (t, C-5), 26.5 (d, C-2). ^{29}Si NMR: δ = -19.2. EI-MS: *m/z* 262 (4%, M^+), 167 (100%, M^+-C_7H_{11}). $C_{15}H_{22}O_2Si$ (262.4), calc. C, 68.65; H, 8.45; Si, 10.70%; found: C, 68.8; H, 8.2, Si, 11.0%.

rac-(C2RS)-(5/6-exo-Bromobicyclo[2.2.1]hept-2-exo-yl)dimethoxy(phenyl) silane / rac-(C2RS)-(5/6-exo-bromobicyclo[2.2.1]hept-2-endo-yl)dimethoxy (phenyl)silane **(4, raw product)**. To a solution of 52.1g (0.15 mol) of **3x(2,5)** + **3x(2,6)** + **3n(2,5)** + **3n(2,6)** in 100 ml of 1,2-dichloroethane, into which a stream of argon was introduced, 9.5 g (0.35 mol) of methanol were added dropwise with stirring at room temperature within 3 h. Stirring was continued for 8 h at room temperature while introducing argon and then for 1 h under reflux. A sample taken showed the reaction to be 83% complete according to ^{1}H NMR. Another 2.1 g (0.07 mol) of methanol were added dropwise. While introducing argon stirring was continued for 12 h at room temperature and for 1 h under reflux. A renewed ^{1}H NMR measurement showed no further methanolysis had taken place. 6.0g (0.06 mol) of triethylamine were added, the precipitate was filtered off after 4h and the volatile components were cautiously removed from the filtrate under reduced pressure (up to 0.05 Torr) while keeping the bath temperature below 60 °C. Yield 50.5g (99 %) of a light yellowish liquid (**4-raw**). ^{1}H NMR: δ = 7.7–7.35 (m, C_6H_5), 4.54–4.48(?), 4.10–4.00(m, H-6*n* of **x2,6**), 4.05–3.95 (m, H-5*n* of **x2,5**), 3.92–3.88 (m, H-6*n* of **n2,6**), 3.90–3.85 (m, H-5*n* of **n2,5**), 3.622 (s, OCH_3 of **n2,6**), 3.609 u. 3.605 (s, OCH_3 of **x2,6**), 3.597 (s, OCH_3 of **x2,5**), 3.588 (s, OCH_3 of **n2,5**), 2.7–0.75 (m). ^{29}Si NMR: δ = -18.12 (**n2,6**), -18.42 (**n2,5**), -19.44 (**x2,5**), -20.87 (**x2,6**). EI-MS: *m/z* 342 u. 340 (2%, M^+), 167 (100%, $C_8H_{11}O_2Si$). $C_{15}H_{21}BrO_2Si$ (341.3), calc. C, 52.78; H, 6.20; Si, 8.22%; found C, 52.7; H, 6.3; Si, 8.2%. Isomer distribution according to integration of the OCH_3 resonances: 46% **4x(2,6)**, 34% **4x(2,5)**, 9% **4n(2,6)**, 9% **4n(2,5)**, according to the ^{29}Si signal intensities: 46% **4x(2,6)**, 34% **4x(2,5)**, 9% **4n(2,6)**, 11% **4n(2,5)**. Distillation: 43 g (0.13 mol) of **4-raw** material were fractionally distilled from a flask immersed in a silicon oil bath through a heated Vigreux column. The following fractions were separated: a) ca. 2 g of methanol and HBr (in the cooling trap), b) 3.2 g of a colourless liquid, bp. 125–140 °C/0.02 Torr, c) 26g of a colourless liquid, bp. 155–158 °C/0.1 Torr. Above a bath temperature of ca. 150 °C deterioration of the vaccum was noted; d) tarry residue. Fraction c was redistilled fractionally yielding e) 6.9 g of a colourless liquid, bp. 90–105 °C/0.05 Torr, (**5t**), f) 1.5 g of an intermediate fraction, bp. 105–115 °C/0.05 Torr, g) 15.2 g of a colourless liquid, bp. 140–145 °C/0.05 Torr (**4-dist**). No decrease of vacuum was noticed. Isomer distribution according to integration of the OCH$_3$ resonances: 32% **4x(2,6)**, 52% **4x(2,5)**, 5% **4n(2,6)**, 11% **4n(2,5)**, according to the ^{29}Si signal intensities: 30% **4x(2,6)**, 52% **4x(2,5)**, 8% **4n(2,6)**, 10% **4n(2,5)**; h) tarry residue.

Thermal properties of 4. A sample (ca. 5 ml) of **4-distilled** material was stirred at 160 °C for 10 h. The volatile components were distilled off in a kugelrohr apparatus at 105 °C/0.05 Torr. 2 ml of methanol were added to the residue, the methanol removed and the product kugelrohr-distilled at 150 °C/0.05 Torr. Isomer distribution of the product, **4-heated** material, according to integration of the OCH$_3$ resonances: 11% **4x(2,6)**, 71% **4x(2,5)**, 17% **4n(2,5)**, according to the ^{29}Si signal intensities: 7% **4x(2,6)**, 63% **4x(2,5)**, 30% **4n(2,5)**.

rac-(C2RS)-(5-exo-Bromobicyclo[2.2.1]hept-2-exo-yl)dimethoxy(phenyl) silane (**4x2,5**). ^{1}H NMR: δ = 7.6 (m, H-*o*), 7.4 (m, H-*m/p*), 3.98 (td, H-5*n*), 3.597 (s, OCH$_3$), 2.52 (br.d, H-4), 2.43 (m, H-1), 2.10 (m, H-6*n*, H-6*x*), 1.79 (ddd, H-3*x*), 1.67 (dqi, H-7*a*), 1.43 (ddd, H-3*n*), 1.24 (dm, H-7*s*), 0.80 (ddd, H-2*n*). Coupling constants [Hz]: $J_{1,7a}$ = 1.9, $J_{2n,3n}$ = 9.9, $J_{2n,3x}$ = 6.9, $J_{2n,7a}$ = 1.8, $J_{3n,3x}$ = 12.9, $J_{3n,7a}$ = 2.3, $J_{3x,4}$ = 4.5, $J_{4,7a}$ = 1.9, $J_{5n,6n}$ + $J_{5n,6x}$ = 11.0, $J_{5n,7s}$ = 1.8, $J_{7a,7s}$ = 10.1 Hz. ^{13}C-NMR: δ = 134.6 (d, 2 C, C-*o*), 132.1 (s, C-*i*), 130.3 (d, C-*p*), 128.0 (d, 2 C, C-*m*), 53.5 (d, C-5), 51.0 (q, OCH$_3$), 48.2 (t, C-6), 47.0 (d, C-4), 38.5 (d, C-1), 34.9 (t, C-7), 29.2 (t, C-3), 25.7 (d, C-2).

rac-(C2RS)-(5-exo-bromobicyclo[2.2.1]hept-2-endo-yl)dimethoxy(phenyl) silane (**4n2,5**). ^{1}H NMR: δ = 7.6 (m,H-*o*), 7.4 (m, H-*m/p*), 3.87 (ddd, H-5*n*), 3.588 (s, OCH$_3$), 2.57 (br.d, H-4), 2.51 (ddd, H-6*n*), 2.40 (m, H-1), 1.93 (m, H-6*x*), 1.92 (dq, H-7*a*), 1.87 (td, H-3*x*), 1.41 (ddd, H-3*n*), 1.29 (m, H-7*s*), 1.20 (m, H-2*x*). Coupling constants [Hz]: $J_{1,7a}$ = 1.6, $J_{2x,3n}$ = 6.6, $J_{2x,3x}$ = 12.4, $J_{3n,3x}$ = 12.8, $J_{3n,7a}$ = 1.8, $J_{3x,4}$ = 5.1, $J_{4,7a}$ = 1.6, $J_{5n,6n}$ = 7.5, $J_{5n,6x}$ = 3.3, $J_{5n,7s}$ = 1.8, $J_{6n,6x}$ = 14.4, $J_{6n,7s}$ = 2.5, $J_{7a,7s}$ = 9.8 Hz. ^{13}C-NMR: δ = 134.4 (d, 2 C, C-*o*), 132.9 (s, C-*i*), 130.2 (d, C-*p*), 128.0 (d, 2 C, C-*m*), 54.1 (d, C-5), 51.0 (q, OCH$_3$), 47.3 (d, C-4), 42.0 (t, C-6), 39.7 (d, C-1), 38.5 (t, C-7), 29.2 (t, C-3), 25.5 (d, C-2).

The ^{13}C-NMR signals of **4x2,6** and **4n2,6** were assigned by comparison of the spectra of **4-raw** material and **4-heated** material. *rac-(C2RS)-(6-exo-Bromobicyclo[2.2.1]hept-2-exo-yl)dimethoxy(phenyl)silane* (**4x2,6**): ^{13}C NMR: δ = 134.6 (C-*o*), 131.7 (C-*i*), 130.2 (C-*p*), 127.9 (C-*m*), 56.1 (C-6), 50.9 (OCH$_3$), 46.8 (C-1), 43.3 (C-5), 37.2 (C-4), 34.8 (C-7), 29.8 (C-3), 25.3 (C-2). *rac-*

(C2RS)-(6-exo-Bromobicyclo[2.2.1]hept-2-endo-yl)dimethoxy(phenyl)silane (**4n2,6**): ^{13}C NMR: δ = 134.2 (C-*o*), 132.4 (C-*i*), 130.2 (C-*p*), 128.0 (C-*m*), 52.6 (C-6), 50.9 (OCH_3), 48.7 (C-1), 44.0 (C-5), 38.4 (C-7), 37.7 (C-4), 29.5 (C-3), 26.2 (C-2).

Dimethoxy(phenyl)tricyclo[2.2.1.0^{2,6}]hept-1-ylsilane (**5t**). ^1H NMR: δ = 7.65–7.60 (m, H-*o*), 7.40–7.31 (m, H-*m/p*), 3.56 (s, OCH_3), 2.00–1.95 (br. m; H-4), 1.30 (s, H-2,6), 1.24, 1.20 (AB system, J = 10.4 Hz, H-3,5), 1.20 (d, J = 1.6 Hz, H-7). ^{13}C NMR: δ = 134.3 (d, 2 C, C-*o*), 133.2 (s, C-*i*), 129.9 (d, C-*p*), 127.7 (d, 2 C, C-*m*), 50.6 (q, $^1J_{CH}$ = 142.5 Hz, OCH_3), 34.7 (t, $^1J_{CH}$ = 133 Hz, C-7), 33.0 (t, $^1J_{CH}$ = 133 Hz, 2 C, C-3/5), 29.8 (d, $^1J_{CH}$ = 147 Hz, C-4), 15.2 (d, $^1J_{CH}$ = 176 Hz, 2 C, C-2/6), 3.7 (s, C-1). ^{29}Si NMR: δ = −18.2. EI-MS: *m/z* 260(40%, M^+), 167(100%, M^+-C_7H_9). $C_{15}H_{20}O_2Si$ (260.4), calc. C, 69.15; H, 7.74; Si, 10.79%; found C, 69.5; H, 7.8; Si, 10.9%.

rac-(C2RS)-(endo-Bicyclo[2.2.1]hept-5-en-2-yl)dimethoxy(phenyl)silane / rac-(C2RS)-(exo-bicyclo[2.2.1]hept-5-en-2-yl)dimethoxy(phenyl)silane / dimethoxy(phenyl)tricyclo[2.2.1.0^{2,6}]hept-1-ylsilane, **5** (= **5n** + **5x** + **5t**). A solution of 92.3 g (0.27 mol) of **4-raw** material and 48.0 g (0.32 mol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was kept at 73 °C for 13 days. The solid contents of the flask were then shaken with 100ml of toluene, the precipitate was filtered off and washed with 50 ml of toluene. Filtrate and washing solution were combined and the volatile components removed at reduced pressure (20 Torr). The residue was fractionally distilled in vacuo through a 15 cm Vigreux column. The following fractions were obtained: a) 55–65 °C/0.05 Torr: 9.4 g of DBU; b) 100–105 °C/0.05 Torr: 49.6 g of a mixture of DBU and **5** (= **5x** + **5n** + **5t**); c) residue: 22.5 g of a mixture of **4** and tarry components. It was possible to obtain more **5** by treating this residue again with DBU.

Fraction b was dissolved in ca. 100 ml of hexane, washed twice with 50 ml of water and dried with calcium hydride. After evaporation of hexane, the residue was distilled in a kugelrohr apparatus. Yield 44.5 g (63.1 %) of a colourless liquid, bp. 85 °C/0.01 Torr. Spectral assignments as in our earlier work[2] and as for **5t**. From the ^1H-NMR spectra the isomer composition was determined as follows: from the OCH_3 signals: 52% **5x**, 19% **5n**, 29% **5t**; from the H-5,6 resonances: 51% **5x**, 18% **5n**, 31% **5t**. EI-MS: *m/z* 260 (17%, M^+), 167 (100%, M^+-C_7H_9). $C_{15}H_{20}O_2Si$ (260.4), calc. C, 69.15; H, 7.74; Si, 10.79; found C, 69.1; H, 7.9; Si, 10.8. Elimination of HBr from **4-heated** material furnished **5** with an isomer distribution of 65% **5x**, 28% **5n**, 7% **5t**.

rac-(SiRS,C2RS)-(endo-Bicyclo[2.2.1]hept-5-en-2-yl)phenyl(vinyl)silane / rac-(SiRS,C2SR)-(endo-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(vinyl)silane / rac-(SiRS,C2RS)-(exo-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(vinyl)silane / rac-(SiRS, C2SR)-(exo-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(vinyl)silane / rac-(SiRS)-phenyl *(tricyclo[2.2.1.0^{2,6}]hept-1-yl)vinylsilane* **6** (**6n** + **6x** + **6t**). Following Ramdsen *et al.*,[10] a vinylmagnesium chloride solution was prepared from 48.0 g (2.0 mol) of magnesium and 125.0 g (2.0 mol) of vinyl chloride in 625 ml of tetrahydrofuran. Over a period of 2 h, 170 ml of this vinylmagnesium chloride solution were added dropwise at room temperature to a solution of 89.3g (0.34 mol) of **5** in 250 ml of ether while monitoring the reaction by ^{1}H NMR or GC. The solution was stirred under reflux for 1h and left for 12h. The precipitate was filtered off and the volatile components were removed from the filtrate under reduced pressure. The residue was distilled in a kugelrohr apparatus to give 79.1 g (91.1 %) of a colourless liquid, bp. 100 °C/0.05 Torr. To a solution of 77.1g (0.30 mol) of this liquid in 150 ml of ether 6.2g (0.16 mol) of $LiAlH_4$ were added in portions. The mixture was stirred for 6 h under reflux, another 5.1g (0.13 mol) of $LiAlH_4$ were added and stirring under reflux was continued for a further 12 h. The precipitate was filtered off with a reversed frit and washed twice with 50 ml of ether. The filtrate and the washing solution were combined and 100 ml of a 10 per cent ammonium chloride solution were added slowly with vigorous stirring. The resulting precipitate was filtered off and washed twice with 30 ml of ether. The combined filtrate and washing solution were dried with magnesium sulfate and then with calcium hydride. The volatile components were removed and the residue was distilled in a kugelrohr apparatus. Yield: 56.2 g (74%) of a colourless liquid, bp. 100 °C/0.05 Torr, isomer composition according to the integrals of the Si-H resonances: 61% **6x**, 24% **6n**, 15% **6t**, according to the ^{29}Si signal intensities: 66% **6x**, 22% **6n**, 12% **6t**. ^{1}H NMR: assignments as in ref.^{2}, additionally for **6t**: δ = 4.70 (d, J = 2.8 Hz, SiH), 2.15–2.10 (br. m). ^{13}C NMR: as in ref.^{2}, some additional resonances of **6t**. ^{29}Si NMR: as in ref.^{2}, additionally $\delta = -17.0$ (**6t**). EI-MS: *m/z* 226 (16%, M^+), 66 (100%, C_5H_6). $C_{15}H_{18}Si$ (226.4), calc. C, 79.58; H, 8.01; Si, 12.41%; found C, 79.0; H, 8.5; Si, 11.1%.

rac-(SiRS,C2RS)-(endo-Bicyclo[2.2.1]hept-5-en-2-yl)phenyl(piperidino)(2-piperidinoethyl)silane / rac-(SiRS,C2SR)-(endo-bicyclo[2.2.1]hept-5-en-2-yl) phenyl(piperidino)(2-piperidinoethyl)silane / rac-(SiRS,C2RS)-(exo-bicyclo [2.2.1]hept-5-en-2-yl)phenyl(piperidino)(2-piperidinoethyl)silane / rac-(SiRS,C2SR)-(exo-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(piperidino)(2-piperidinoethyl)silane / rac-(SiRS)-phenyl(piperidino)-(2-piperidinoethyl)(tricyclo [2.2.1.0^{2,6}]hept-1-yl)silane **7** (= **7n** + **7x** + **7t**). Similar to ref.^{2} 90.2 g (96%) of a colourless liquid (**7**), bp. 200 °C/0.02 Torr (kugelrohr), were obtained from 74.9 g (0.88 mol) of piperidine and 55.1 g (0.24 mol) of **6**. ^{1}H NMR and ^{13}C NMR similar to ref.^{2}. ^{29}Si NMR: as in ref.^{2}, additionally $\delta = -3.4$ (**7t**). EI-MS: *m/z*, 394 (7%, M^+), 309 (100%, $C_{20}H_{27}NSi$). $C_{25}H_{38}N_2Si$ (394.7), calc. C, 76.08; H, 9.71; Si, 7.11%; found C, 76.7; H, 9.8; Si, 7.1%.

rac-(SiRS,C2RS)-(endo-Bicyclo[2.2.1]hept-5-en-2-yl)methoxy(phenyl)(2-piperidinoethyl)silane / rac-(SiRS,C2SR)-(endo-bicyclo[2.2.1]hept-5-en-2-yl) methoxy(phenyl)(2-piperidinoethyl)silane / rac-(SiRS,C2RS)-(exo-bicyclo[2.2.1] hept-5-en-2-yl)methoxy(phenyl)(2-piperidinoethyl)silane / rac-(SiRS,C2SR)-(exo-bicyclo[2.2.1]hept-5-en-2-yl)methoxy(phenyl)(2-piperidinoethyl)silane / rac-(SiRS)-methoxy(phenyl)-2-piperidinoethyl-(tricyclo[2.2.1.0^{2,6}*]hept-1-yl) silane* **8** (= **8n** + **8x** + **8t**). Similarly to ref.[2] 64.1 g (85%) of a colourless liquid, **8**, bp. 185 °C/0.05 Torr (kugelrohr), are obtained from 88.1 g (0.22 mol) of **7**. Isomer distribution according to integration of the $\mathrm{SiOC}H_3$ signals: 67% **8x**, 19% **8n**, 14% **8t**. ^{1}H NMR: Assignments as in ref.[2], additionally $\delta = 3.47$ (s, OCH_3 of **8t**). ^{13}C NMR: as in ref.[2], additionally some signals of **8t**. ^{29}Si NMR: as in ref.[2], additionally $\delta = 5.05$ (**8t**). EI-MS: *m/z* 341 (10%, M^+), 98 (100%, $C_6H_{12}N$). $C_{21}H_{31}NOSi$ (341.6), calc. C, 73.84; H, 9.15; Si, 8.22%; found C, 73.6; H, 9.2; Si, 8.4%.

rac-(SiRS,C2RS)-(endo-Bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl)silanol / rac-(SiRS,C2SR)-(endo-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl)silanol / rac-(SiRS,C2RS)-(exo-bicyclo[2.2.1]hept-5-en-2-yl) phenyl(2-piperidinoethyl)silanol / rac-(SiRS,C2SR)-(exo-bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl)silanol / rac-(SiRS)-phenyl(2-piperidinoethyl)-(tricyclo[2.2.1.0^{2,6}*]hept-1-yl)silanol* **9** (= **9n** + **9x** + **9t**). To a solution of 61.5 g (0.18 mol) of **7** in 1750 ml of THF were added dropwise under vigorous stirring 250 ml of 0.1 M NaOH (0.025 mol). The solution became turbid. Stirring was continued for 10 h at 40 °C and for 12 h at room temperature. The solution became clear. 400 ml of hexane were added, the aqueous solution was removed with a separation funnel and the organic layer washed four times with 50 ml of water and then dried with magnesium sulfate. The volatile components were removed at reduced pressure and room temperature. This left 58.6 g (99 %) of **9**, a honey-like substance.

rac-(SiRS,C2SR)-(exo-Bicyclo[2.2.1]hept-5-en-2-yl)phenyl(2-piperidinoethyl) silanol [**9x(*RS,SR*)**]. Eightfold crystallization was carried out from ether at −6 °C. 58.1 g of **9** yielded 5.3 g of **9x(*RS,SR*)**, mp. 100–102 °C. By repeating the crystallization procedure another 2.8g of **9x(*RS,SR*)** could be obtained. Total yield of the crystallizations, ca. 42 %. For IR-, NMR- and EI-MS-data of **9x(*RS,SR*)**, see ref.[2]

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