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SYNTHESIS OF STERICALLY DEMANDING 3-SILYLPYRIDINES AND THEIR USE IN ASYMMETRIC SYNTHESIS WITH CHIRAL *N*-ACYLIMINIUM IONS

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Abstract- A convenient one-pot procedure for the synthesis of sterically hindered 3-silylpyridines is reported. It is based on 3-lithiopyridine that is generated from commercially available 3-bromopyridine and subsequently trapped with silyl chlorides. 3-Triisopropylsilylpyridine was employed in an asymmetric electrophilic α-amidoalkylation reaction providing a chiral *N*-acyl-1,2-dihydropyridine in very high regio- and diastereoselectivity. Conjugate reduction of the diene moiety and removal of the chiral auxiliary led to the corresponding 1,2,3,6-tetrahydropyridine in enantiomerically pure form.

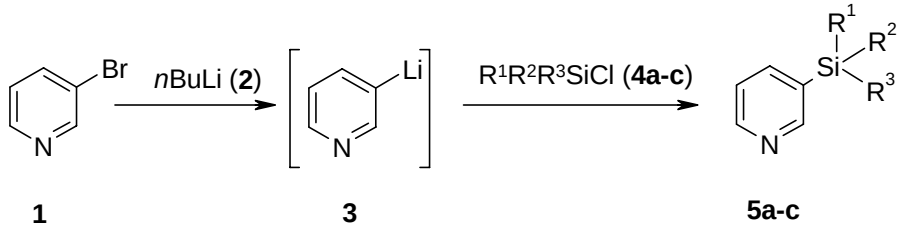
There is considerable interest in silyl substituted heterocycles, especially as precursors for multi step reactions, which are due to the usefulness and versatility of the silyl group in organic functional group transformation reactions.[1] In the total synthesis of the indolizidine alkaloide (±)-elaeokanine A reported by Comins *et al.*,[2] for example, 3-triisopropylsilylpyridine (**5a**) was employed as a precursor for the generation of an *N*-acylpyridinium ion. In this synthesis, the bulky triisopropylsilyl substituent was employed to control the regioselectivity of subsequent trapping reactions of the *N*-acylpyridinium ion with Grignard reagents.

So far, for the synthesis of 3-triisopropylsilylpyridine (**5a**) a two step sequence has been reported.[2] This is based on 2-chloropyridine, which is silylated in position 3 and subsequently liberated from the chloro substituent to provide **5a** in an overall yield of 42%. Interestingly, according to a publication of Anderson *et al.*,[3] 3-trimethylsilylpyridine as a related compound is accessible by a more simple sequence involving a halogen-metalexchange at 3-bromopyridine followed by a silylation reaction.

[#] Dedicated with the very best wishes to Prof. A.I. Meyers on the occasion of his 70th birthday

Thus, we wondered whether this one-pot procedure might be applicable to the synthesis of 3-triisopropylsilylpyridine (**5a**) and related silylpyridines with sterically demanding silyl groups as well. To this end, the present study was performed.

However, when the reaction was carried out in Et_2O according to the procedure of Anderson *et al.*[3] the yield of **5a** amounted to only 8% (see **Scheme 1** and **Table 1**). Since 3-lithiopyridine (**3**) as the intermediate in this reaction is insoluble in Et_2O forming a precipitate, we assumed, that this might be detrimental for trapping reactions of **3**, especially when sterically demanding reagents like triisopropylsilyl chloride (**4a**) are employed. Though the reaction mixture with 3-lithiopyridine (**3**) becomes homogenous upon addition of THF, this does not provide a solution for the aforementioned problem, as in this case an immediate decomposition of **3** occurs which is indicated by the color of the reaction mixture turning to black. However, by a simple change of the procedure we were able to significantly improve the yield of **5a**. When 3-lithiopyridine (**3**) was generated in Et_2O and premixed with 3-triisopropylsilyl chloride (**4a**) before THF was added to dissolve the 3-lithiopyridine (**3**), the yield rose to 67% (**Table 1**). Due to the synthetic potential of the 3-dimethylphenylsilyl substituent, which can be considered e.g. as a masked hydroxy group,[1] also the synthesis of 3-dimethylphenylsilylpyridine (**5b**) was performed. Compound (**5b**) has been mentioned so far only in a patent,[4] but no experimental details nor the yield or any other data have been provided. With the above procedure **5b** was obtained in a yield of 73%. However, whereas the addition of THF substantially increased the yield, when triisopropylsilyl chloride was employed, silylation with the more reactive dimethylphenylsilyl chloride also proceeded smoothly in Et_2O without THF as an additive (69%). Finally also the synthesis of 3-triphenylsilylpyridine (**5c**) was accomplished. In this case, however, the yield amounted to 62%, when the reaction was run in the absence of THF, whereas it deteriorated to 47%, when the latter was added to the final reaction mixture.



1 **3** **5a-c**

a: $R^1 = R^2 = R^3 = i$Pr
b: $R^1 = R^2$ = Me, R^3 = Ph
c: $R^1 = R^2 = R^3$ = Ph

Scheme 1

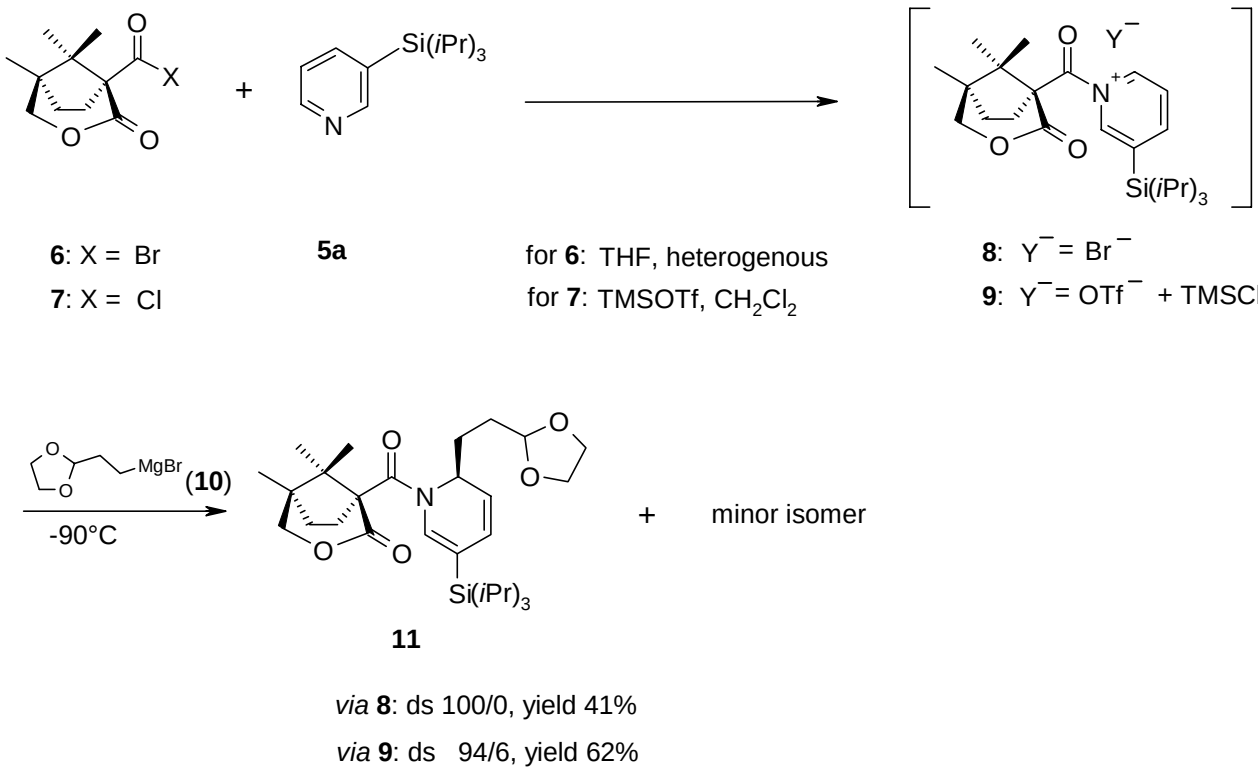
3-Bromopyridine (**1**)	*n*BuLi	$R^1R^2R^3SiCl$ (**4**)		silylation time (h)	yield (%) of **5**	
1.0 eq (0.4 M in Et_2O)	1.1 eq	**4a**	1.1 eq	66	**5a**	8
1.0 eq (0.4 M in THF)	″	″	1.1 eq	″	″	-
1.0 eq (0.27 M in Et_2O/THF)[a]	″	″	1.2 eq	″	″	67
1.0 eq (0.4 M in Et_2O)	″	**4b**	1.2 eq	19	**5b**	69
1.0 eq (0.27 M in Et_2O/THF)[a]	″	″	1.2 eq	″	″	73
1.0 eq (0.4 M in Et_2O)	″	**4c**	1.1 eq	66	**5c**	62
1.0 eq (0.27 M in Et_2O/THF)[a]	″	″	1.1 eq	″	″	47

Table 1: [a] 0.4 M in Et_2O for the preparation of **3**, for silylation THF was added until a concentration of 0.27 M was achieved.

Trapping reactions of 1-phenoxycarbonyl-3-triisopropylsilylpyridinium salts have been found to proceed with complete regioselectivity with the nucleophile being directed to the C-6 position of the pyridinium moiety.[2] We thought to utilize this phenomenon for an asymmetric synthesis of chiral 6-substituted dihydro- or tetrahydropyridine derivatives. In addition, it was our intention to employ a synthetic strategy, which was first presented by us[5] and is based on chiral *N*-acyliminium ions exhibiting chiral *N*-acyl group as a chiral auxiliary. So far, the bicyclolactonecarboxylic acid underlying the acid halides (**6**) and (**7**) has turned out to be an efficient chiral auxiliary and as such has been successfully employed in the asymmetric synthesis of pyrrolidines, piperidines, 1,2,3,4-tetrahydroisoquinolines, 1,2,3,6-tetrahydropyridines and ß-carbolines derivatives.[6]

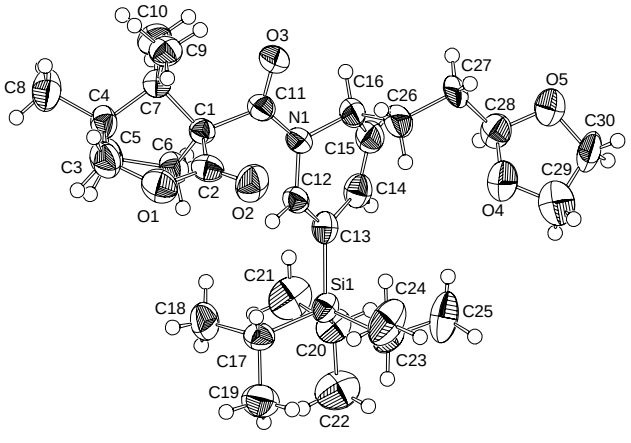
Thus, it has been selected for this study as well. As the target for this synthesis, compound (**13**) was chosen as it appeared to be of interest as a chiral building block in the construction of natural products, especially of quinolizidine and indolizidine alkaloids.

When 3-triisopropylsilylpyridine (**5a**) was treated with the acid bromide (**6**) in toluene, a precipitate occurred, indicating that the required chiral *N*-acylpyridinium salt (**8**) had formed. Upon addition of {[1,3]-dioxolan-2-ylethyl}magnesium bromide (**10**) at –90°C to this heterogenous mixture the desired 6-substituted *N*-acyl-1,6-dihydropyridine (**11**) was obtained. The yield amounted to 41% and the reaction had proceeded with complete regioselectivity and diastereoselectivity (100:0). According to a recent study,[6e] trapping reactions of *N*-acylpyridinium ions may be more efficient when performed under homogenous conditions in the presence of a suitable trialkylsilyl triflate, e.g. trimethylsilyl triflate (TMSOTf). These additives were found to shift the equilibria between the educts employed in the *N*-acyliminium ion formation and the *N*-acyliminium ion towards the side of the latter. Especially in the case of an unfavorable position of such equilibria this is of major importance for subsequent trapping reactions.



Scheme 2

In the present case, when the reaction was performed under the aforementioned conditions (with TMSOTf in CH_2Cl_2), where **9** as intermediate should form, the yield for **11** rose to 62%. As before, **11** was the only regioisomer formed and the diastereoselectivity was still very high, though it had slightly diminished to 94/6. Finally, in order to determine the stereochemistry an X-Ray analysis[7] of **11** was performed which established that **11** is of (*S*)-configuration at the newly created stereocenter of the pyridine ring (Figure 1).



11

Figure 1

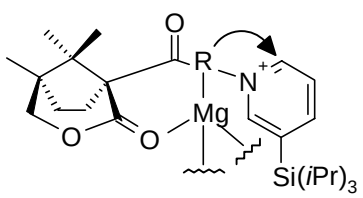


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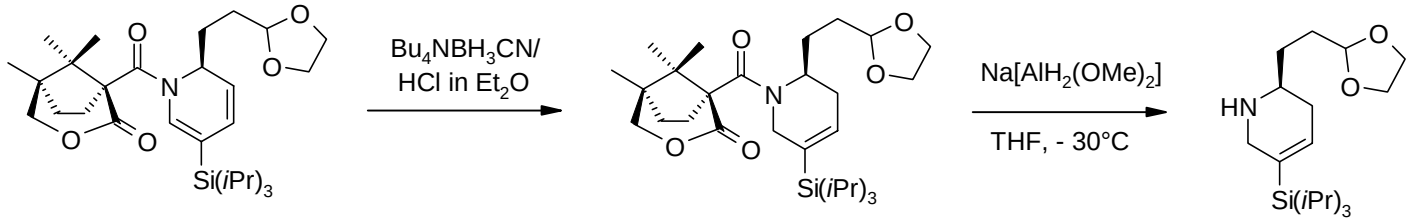
Figure 2

The asymmetric induction observed for the addition of **10** to the intermediate *N*-acyliminium ions (**8**) and (**9**), respectively, may be rationalized by a precomplexation mechanism that has been proposed already earlier for this type of chiral auxiliary.[6b] According to this model the addition of a nucleophile to the iminium ion takes place in an intramolecular fashion via a complex that is formed between the organometallic reagent and the carbonyl function of the chiral auxiliary (see Figure 2). In the present case, according to the stereochemistry found for the addition product (**11**), the transfer of the nucleophile to the iminium subunit has proceeded along the path indicated in **12**. However, depending on the nature of the organometallic reagent as well as of the *N*-acyliminium ion employed, the sense of the asymmetric induction may vary.[6]



11 **13** **14**

Scheme 3

The reduction of **11** to **13** could be best accomplished by treating a mixture of tetrabutylammonium cyanoborohydride and **11** in CH_2Cl_2 with HCl in Et_2O. This yielded **13** in 74%. Finally, to complete the synthesis of **13**, the chiral auxiliary had to be removed. This was performed by a reductive cleavage of the amide bond. Thus, when **13** was treated with $Na[AlH_2(OMe)_2]$ in THF at -25°C,[6e] the tetrahydropyridine (**14**) was obtained with a yield of 76%.

In summary, we have disclosed an efficient method for the synthesis of 3-silyl substituted pyridine derivatives (**5a-c**) from commercially available 3-bromopyridine (**1**) in a single step. By employing an asymmetric synthesis based on chiral *N*-acyliminium ions starting from **5b** the chiral building block (**14**) was obtained.

EXPERIMENTAL

All reactions were carried out in vacuum dried glassware under argon atmosphere. All reagents were used as commercially available. The solvents were dried and distilled. THF and Et_2O were freshly distilled from sodium metal/benzophenone ketyl prior to use. Melting points were determined on a Büchi melting point apparatus no. 510 (Dr. Tottoli) and are uncorrected. IR spectra were recorded with a Perkin Elmer FT-IR spectrophotometer Paragon 1000, and NMR spectra were obtained with a JEOL JNMR-GX 400

spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C) with TMS as internal standard. The NMR spectra were recalculated with NUTS, 2D version 5.097. MS spectra were recorded on a Hewlett Packard 5989 with 59980 B particle beam LC/MS interface. CHN-analyses were determined with an elemental analysator Rapid (Heraeus) and Vario EL (Elementar). TLC: Merck 60 F-254. Column chromatography (CC) was performed as flash chromatography with silica gel Merck 60 F-254 (0.040 – 0.063 mm). Analytical HPLC: L-6000 pump, L-4000 UV/Vis detector, D-7500 Chromato Integrator (Merck-Hitachi), column: LiChroCart® with Lichrospher® Si 60 cartridge (5 µm, 250 x 4 mm with precolumn 4 x 4 mm), (Merck). - Preparative HPLC: L-6000 pump, L-4000 UV/Vis, D-2000 Chromato Integrator (Merck-Hitachi), column: Hibar RT LiChrosorb® Si 60 (7 µm, 250 x 25 mm) (Merck).

General procedure for the synthesis of 3-silylpyridines (**5a-5c**). 3-Bromopyridine (**1**) in Et_2O or THF was cooled to -78°C. *n*BuLi (1.6 M in hexane) was added dropwise giving 3-lithiopyridine as a yellow precipitate. After 45 min the respective silyl chloride (**4a**-**4c**) was added followed by THF, where indicated. After warming up to rt (30 min), the mixture was allowed to react the time given before it was quenched by the addition of phosphate buffer (pH 7, *c* = 1.0 M). Then the reaction mixture was extracted with CH_2Cl_2 and the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash chromatography.

3-(Triisopropylsilyl)pyridine (**5a**). A) According to the general procedure from 784 µL (1.27 g, 8.00 mmol) of 3-bromopyridine (**1**) in 20 mL of Et_2O, 5.5 mL (8.80 mmol, 1.1 eq) of *n*BuLi (1.6 M in hexane), 2033 µL (1.85 g, 8.80 mmol, 1.1 eq) of triisopropylsilyl chloride and 15 mL of THF. Silylation time: 66 h. Destillation (bp 103-105°C at 0.5 mm Hg) and purification of the crude product by CC (*n*-heptane/EtOAc = 80:20) yielded 1.254 g (67%) of compound (5a) as colorless crystals. Analytical data were in accordance with those in the literature.[2] mp. 38°C. - Anal. Calcd for $C_{14}H_{22}NSi$: C, 71.42; H, 10.70; N, 5.95. Found: C, 71.45; H, 10.85; N, 5.78.

B) According to the general procedure from 980 µL (1.588 g, 10.0 mmol) of 3-bromopyridine (**1**) in 25 mL of Et_2O, 6.8 mL (10.5 mmol, 1.1 eq) of *n*BuLi (1.6 M in hexane), 2224 µL (2.207 g, 10.5 mmol, 1.1 eq) of triisopropylsilyl chloride. Silylation time: 66 h. Destillation and purification of the crude product by CC (*n*-heptane/EtOAc = 80:20) yielded 188 mg (8%) of compound (**5a**).

3-Dimethylphenylsilylpyridine (**5b**). A) According to the general procedure from 392 µL (635 mg, 4.00 mmol) of 3-bromopyridine (**1**) in 10 mL of Et_2O, 2.8 mL (4.40 mmol, 1.1 eq) of *n*BuLi (1.6 M in hexane), 1017 µL (1043 mg, 4.40 mmol, 1.1 eq) of dimethylphenylsilyl chloride and 7.5 mL of THF. Silylation time: 19 h. Purification of the crude product by CC (*iso*-hexane/EtOAc = 80:20) yielded 620 mg (73%) of

compound (**5b**) as colorless oil. DC: R_f = 0.20 (*iso*-hexane/EtOAc = 80:20). - IR (film): $\tilde{\nu}$ = 2957 cm^{-1}, 1652, 1559, 1394, 1250, 1109, 818, 774, 700. - ^1H NMR ($CDCl_3$): δ = 0.59 ppm (s, 6 H, $Si(CH_3)_2$), 7.24 (dd, *J* = 7.9, 4.9 Hz, 1 H, NCH=C*H*), 7.75 (d, *J* = 7.9 Hz, 1 H, NCH=CHC*H*) 8.59 (d, *J* = 4.9 Hz, 1 H, NC*H*=CH), 8.70 (s, 1 H, NC*H*=CSi). - MS (70 eV); *m/z* (%): 214 (25) [M^+]. - Anal. Calcd for $C_{13}H_{15}NSi$: C, 73.18; H, 7.09; N, 6.57. Found: C, 72.91; H, 7.06; N, 6.49.

B) According to the general procedure from 98 µL (159 mg, 1.00 mmol) of 3-bromopyridine (**1**) in 2.5 mL Et_2O, 688 µL (1.10 mmol, 1.1 eq) of *n*BuLi (1.6 M in hexane), 183 µL (261 mg, 1.10 mmol, 1.1 eq) dimethylphenylsilyl chloride. Silylation time: 19 h. Purification by CC (*iso*-hexane/EtOAc = 80:20) yielded 147 mg (69%) of compound (**5b**).

3-Triphenylsilylpyridine (**5c**). A) According to the general procedure from 98 µL (159 mg, 1.00 mmol) of 3-bromopyridine (**1**) in 2.5 mL of Et_2O, 688 µL (1.10 mmol, 1.1 eq) of *n*BuLi (1.6 M in hexane), 324 mg (1.10 mmol, 1.1 eq) of triphenylsilyl chloride and 1.9 mL of THF. Silylation time: 66 h. Purification of the crude product by CC (*iso*-hexane/EtOAc = 70:30) yielded 156 mg (47%) of compound (**5c**) as colorless crystals. mp. 232°C - DC: R_f = 0.31 (*iso*-hexane/EtOAc = 70:30). - IR (KBr): $\tilde{\nu}$ = 1736 cm^{-1}, 1426, 1108, 726, 708, 697. - ^1H NMR ($CDCl_3$): δ = 7.28 (dd, *J* = 7.5, 5.0 Hz, 1 H, NCH=C*H*), 7.37 - 7.41 (m, 6 H, $H_{arom., meta}$), 7.42 - 7.48 (m, 3 H, $H_{arom., para}$), 7.52 - 7.58 (m, 6 H, $H_{arom., ortho}$), 7.82 (dt, *J* = 7.5, 1.8 Hz, 1 H, NCH=CHC*H*), 8.65 (dd, *J* = 5.0, 1.8 Hz, 1 H, NC*H*=CH), 8.74 (d, *J* = 1.8 Hz, 1 H, NC*H*=CSi). - MS (70 eV); *m/z* (%): 339 (7) [M^+]. - Anal. Calcd for $C_{23}H_{19}NSi$: C, 81.85; H, 5.67; N, 4.15. Found: C, 81.53; H, 5.76; N, 4.15.

B) According to the general procedure from 98 µL (159 mg, 1.00 mmol) of 3-bromopyridine (**1**) in 2.5 mL Et_2O, 688 µL (1.10 mmol, 1.1 eq) of *n*BuLi (1.6 M in hexane), 324 mg (1.10 mmol, 1.1 eq) of triphenylsilyl chloride. Silylation time: 66 h. Purification by CC (*iso*-hexane/EtOAc = 70:30) yielded 211 mg (62%) of compound (**5c**).

(1 *S*,5*R*)-1-[(*S*)-2-(2-[1,3]-Dioxolan-2-ylethyl)-5-triisopropylsilyl-1,2-dihydropyridin-1-ylcarbonyl]-5,8,8-trimethyl-3-oxabicyclo[3.2.1]octan-2-one (**11**). A) Acyl bromide (**6**) was prepared from 212 mg (1.00 mmol) of 5,8,8-trimethyl-2-oxo-3-oxabicyclo[3.2.1]octane-1-carboxylic acid[6b] in 10 mL of toluene, 100 µL (230 mg, 1.07 mmol, 1.07 eq) of oxalyl bromide and 2 µL of DMF at 40°C. After 4 h the solvent was removed *in vacuo*. The residue was dissolved in 2 mL of THF and 258 mg (1.10 mmol, 1.10 eq) triisopropylsilylpyridine (**5a**) in 4 mL of THF was added. The heterogenous reaction mixture was cooled to -90°C. After one hour 6 mL (6.00 mmol, 3.00 eq) of {[1,3]-dioxolan-2-ylethyl}magnesium bromide (**10**)[8] was added. The reaction mixture was stirred for 15 h before it was quenched (at -90°C) with phosphate buffer (pH = 7, *c* = 1.0 M). The resulting reaction mixture was extracted with CH_2Cl_2 and the

combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by CC (*n*-heptane/EtOAc = 70:30) and by preparative HPLC (*n*-heptane/EtOAc = 80:20; 12.0 mL/min; t_R = 25.79 min) yielded 178 mg (41%) of compound (**11**). Analytical HPLC (*n*-heptane/EtOAc = 80:20; 1.0 mL/min): t_R = 13.78 min. mp 125°C. - DC: R_f = 0.22 (*n*-heptane/EtOAc = 70:30). - $[\alpha]_D^{20}$ = +303.2° (*c* = 0.47, CH_2Cl_2). - IR (KBr): $\tilde{\nu}$ = 2942 cm^{-1}, 2866, 1718, 1655, 1541, 1309, 1222, 1130, 1053. - ^1H NMR (nitrobenzene-d_5, 140°C): δ = 0.90 (s, 3 H, CH_3), 1.01 - 1.19 (m, 27 H, 3 x C*H*$(CH_3)_2$, 3 x CH(C*H*$_3)_2$, 2 x CH_3), 1.83 - 2.06 (m, 6 H, CH_2CH_2, CH_2CH_2), 2.15 - 2.35 (m, 1 H, CH_2CH_2), 2.40 - 2.57 (m, 1 H, CH_2CH_2), 3.72-3.78 (m, 2 H, OCH_2CH_2O), 3.84-3.90 (m, 2 H, OCH_2CH_2O), 3.99 (d, *J* = 10.9 Hz, 1 H, OCH_2), 4.19 (d, *J* = 10.9 Hz, 1 H, OCH_2), 4.93 (t, *J* = 3.4 Hz, 1 H, OCHO), 5.03-5.09 (m, 1 H, NC*H*CH_2), 5.87 (dd, *J* = 9.4, 6.0 Hz, 1 H, NCHC*H*), 6.08 (d, *J* = 9.4 Hz, 1 H, NCH=CC*H*), 6.91 (s, 1 H, NC*H*=C). - MS (70 eV); *m/z* (%): 532 (1) [M^+], 430 (100), 195 (63), 167 (26), 139 (18). - Anal. Calcd for $C_{30}H_{49}NO_5Si$: C, 67.76; H, 9.29; N, 2.63. Found: C, 67.70; H, 9.44; N, 2.54.

B) Acyl chloride (**7**) was prepared from 106 mg (0.50 mmol) of 5,8,8-trimethyl-2-oxo-3-oxabicyclo[3.2.1]octane-1-carboxylic acid[6b] in 3.5 of mL CH_2Cl_2, 45 µL (67 mg, 0.53 mmol, 1.05 eq) of oxalyl chloride and 1 µL of DMF. After 2 h the solvent was removed *in vacuo*. The residue was dissolved in 1.25 mL of CH_2Cl_2 and 129 mg (0.55 mmol, 1.10 eq) of triisopropylsilylpyridine (**5a**) in 1.25 mL of CH_2Cl_2 was added. After one hour the reaction mixture was cooled to -90°C and 1.5 mL (1.50 mmol, 3.00 eq) of {[1,3]-dioxolan-2-ylethyl}magnesium bromide (**10**)[8] was added. The reaction mixture was stirred for 1 h before it was quenched (at -90°C) with phosphate buffer (pH = 7, *c* = 1.0 M). The resulting mixture was extracted with CH_2Cl_2 and the combined organic layers were dried (Mg_2SO_4) and concentrated *in vacuo*. Purification by CC (*n*-heptane/EtOAc = 80:20) yielded 164 mg (62%) of compound (**11**). Analytical HPLC (*n*-heptane/ EtOAc = 8:2, 1.0 ml/min): d.s. = 94/6; **11**: t_R = 13.6 min; minor isomer: t_R = 20.1 min.

(1*S*,5*R*)-1-[(*S*)-2-(2-[1,3]-Dioxolan-2-ylethyl)-5-triisopropylsilyl-1,2,3,6-tetrahydropyridin-1-ylcarbonyl]-5,8,8-trimethyl-3-oxabicyclo[3.2.1]octan-2-one (**13**). To a solution of 265 mg (0.94 mmol, 5.00 eq) of tetrabutylammonium cyanoborohydride and 100 mg (0.19 mmol) of **11** in 2 mL of CH_2Cl_2 2.09 mL (1.88 mmol, 10.0 eq) of HCl (0.9 M in ether) was added over a period of 1 1/2 h. Then, after 10 min phosphate buffer (pH = 7, c = 1.0) was added and the reaction mixture was extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by CC (*n*-heptane/EtOAc = 7:3) yielded 74 mg (74%) of **13** . Colorless crystals, mp 51-56°C. - TLC: R_f = 0.11 (*n*-heptane/EtOAc = 7:3). - $[\alpha]_D^{20}$ = +21.9° (c = 0.9 in CH_2Cl_2). - IR (KBr): $\tilde{\nu}$ = 2943 cm^{-1}, 2865, 1735, 1636, 1407, 1228, 1216, 1120, 1070, 1021, 882, 675. - ^1H NMR (nitrobenzene-d_5, 120°C): δ = 0.91 (s, 3 H, CH_3), 1.07-1.21 (m, 24 H, CH_3, CH_3CH CH_3), 1.43 (s, 3 H, CH_3), 1.77-2.03 (m, 6 H, CH_2CH_2), 2.19 (dd,

J = 17.7/5.2 Hz, 1 H, NCHC*H*$_2$), 2.44-2.56 (m, 1 H, CH_2CH_2), 2.59-2.77 (m, 1 H, CH_2CH_2), 2.78 (d, *J* = 17.7 Hz, 1 H, NCHC*H*$_2$), 3.74-3.87 (m, 3 H, OCH_2CH_2O, NCH_2), 3.88-4.02 (m, 2 H, OCH_2CH_2O), 3.99 (d, *J* = 10.9 Hz, 1 H, CH_2O), 4.20 (dd, *J* = 10.9, 1.6 Hz, 1 H, CH_2O), 4.53-4.78 (m, 2 H, NCH, NCH_2), 4.98 (t, *J* = 4.0 Hz, 1 H, OCHO), 6.13 (s, 1 H, C=CH). - MS (CI, CH_5^+); *m/z* (%): 534 (100) [M^++1], 490 (16), 338 (23). - Anal. Calcd for $C_{30}H_{51}NO_5Si$: C, 67.50; H, 9.63; N, 2.62; Found: C, 67.32; H, 9.76; N, 2.59.

(2*S*)-2-(2-[1,3]-Dioxolan-2-ylethyl)-5-triisopropylsilyl-1,2,3,6-tetrahydropyridine (**14**). 1.0 mL (1.0 mmol) of a $NaAlH_4$ solution (1.0 M in THF) and 81 µL (2.0 mmol) of $MeOH_{abs.}$ were stirred for 30 min. 140 µL (0.14 mmol, 1.8 eq) of the resulting $NaAlH_2(OMe)_2$ solution (1.0 M in THF) was added to 41 mg (0.08 mmol) of **13** in 1.0 mL of THF at -25°C. After 46 h the reaction mixture was quenched with phosphate buffer (pH = 7, *c* = 1.0 M) and extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by CC (*n*-heptane/EtOAc = 7:3 + 4% NMe_2Et) yielded 21 mg (76%) of **14**. Colorless oil. - TLC: R_f = 0.19 (*n*-heptane/EtOAc = 7:3 + 4% $NEtMe_2$). - $[\alpha]_D^{20}$ = +62.5° (c = 0.8 in CH_2Cl_2). - IR (film): $\tilde{\nu}$ = 2940 cm^{-1}, 2864, 1461, 1139, 1114, 1032, 882. - ^{1}H NMR (CD_2Cl_2): δ = 0.95-1.09 (m, 21 H, CH_3CHCH_3), 1.36-1.51 (m, 3 H, C*H*$_2$C*H*$_2$CH), 1.59-1.88 (m, 2 H, C*H*$_2$C*H*$_2$CH, NCHC*H*$_2$), 2.11 (d, *J* = 17.5 Hz, 1 H, NCHC*H*$_2$), 2.64 (dtd, *J* = 10.2, 6.7, 4.2, 1 H, NCH), 3.35-3.39 (m, 2 H, NCH_2), 3.77-3.83 (m, 2 H, OCH_2CH_2O), 3.88-3.94 (m, 2 H, OCH_2CH_2O), 4.83 (t, *J* = 4.7 Hz, 1 H, OCHO), 6.02 (dq, *J* = 4.4, 2.2, 1 H, C=CH). - MS (CI, CH_5^+); *m/z* (%): 340 (100) [M^++1]. - Anal. Calcd for $C_{19}H_{37}NO_2Si$: C, 67.20; H, 10.98; N, 4.12; Found: C, 67.03; H, 10.95; N, 3.88.

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