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Direct synthesis of 4,4-disubstituted *N*-silyl-1,4-dihydropyridines

Jan Bräckow and Klaus T. Wanner*

Department Pharmazie-Zentrum für Pharmaforschung, Ludwig-Maximilians-Universität München, Butenandtstr. 7, Haus C, D-81377 München, Germany

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Abstract—An unprecedented method for the preparation of 4,4-disubstituted 1,4-dihydropyridines is presented. It is based on the trapping reaction of 4-substitued *N*-silylpyridinium ions. When performed with dialkylmagnesium reagents, such as $i\mathrm{Pr}_2\mathrm{Mg}$, silyl protected 4,4-disubstituted 1,4-dihydropyridines were obtained in up to quantitative yields. High 1,4-selectivity was found for sterically demanding nucleophiles, whereas small nucleophiles ($\mathrm{Me}_2\mathrm{Mg}$) tend to yield 1,2-addition-products. Grignard, dialkylzinc and organocopper reagents were found to give either no addition products or less favorable results. Reduction of the obtained 1,4-dihydropyridine with NaCNBH_3 in the presence of HCl, followed by treatment with *tert*-butyl dicarbonate provided the corresponding *N*-Boc protected piperidines with high yields.

1. Introduction

1,4-Dihydropyridines (DHP) constitute important classes of compounds, with many derivatives being found especially among natural products and bioactive agents.[1] Regioselective addition of nucleophilic reagents to *N*-acylpyridinium ions is a common method in the preparation of 1,2- and 1,4-dihydropyridines. When Grignard[2] or organotin[3] reagents are used mainly 2-substituted 1,2-dihydropyridines are formed. In contrast, the use of organotitanium[4] reagents and lithium–dialkylcuprates[5] leads almost exclusively to the formation of 4-substituted 1,4-dihydropyridines, which is also the case when Grignard and organozinc reagents admixed with copper(I) salts are employed.[6] The regioselectivity of the nucleophilic attack on the pyridinium cation is believed to follow the HSAB principle. According to this principle relatively hard nucleophiles are predicted to display a preference for the addition to the 2-position of the pyridine ring and relatively soft nucleophiles for the 4-position.[7] Whereas *N*-ayclpyridinium ions are widely used for nucleophilic addition reactions, related examples with *N*-silylpyridinium ions are scarce. According to the work of Akiba et al.[8] with *N*-silylpyridinium ions derived from pyridine, these intermediates are susceptible to nucleophilic addition reactions of Grignard reagents leading to 1,4-addition products with high regioselectivity. Similar results were found, for *N*-silylpyridinium ions derived methyl nicotinate.[9] Compared to *N*-silylpyridinium ions the 1,4-regioselectivity of related reactions of *N*-silylquinolinium[10] ions is poor, though it may be improved by increasing the bulk of the *N*-silyl moiety. It is well documented that the regioselectivity of addition reactions to *N*-acylpyridinium ions is strongly influenced by the substituents present on the pyridine ring: for example, when a substituent is present in the 4-position, nucleophiles almost exclusively add to the 2- and 6-position of the ring system.[11] However, corresponding data for *N*-silylpyridinium ions are still missing. So far, even the question whether 4-substituted *N*-silylpyridinium ions are susceptible to nucleophilic addition reactions at all has not been examined, although such trapping reactions might be synthetically quite useful. Actually, one would expect that the presence of a sterically demanding *N*-silyl group would shield the 2- and 6-position and thus force a nucleophile to add to the 4-position of the *N*-silylpyridinium ion even if a substituent is already present in this position. As a result 4,4-disubstituted *N*-silyl-1,4-dihydopyridines and finally, after desilylation, the parent compounds should be formed. So far, only a few scattered examples for the direct preparation of 4,4-disubstituted 1,4-dihydropyridines from activated pyridine derivatives are known. These are limited to *N*-alkyl- and *N*-acylpyridinium salts possessing an ester function in the 4-position, which when treated with alkyl or acyl halides and zinc give the 4,4-disubstituted products presumably by a radical process.[12] In addition to these examples 4-addition to 4-substituted pyridine derivatives has only been observed for intramolecular processes leading to spirocyclic compounds.[13] But usually multistep syntheses are required for the construction of 4,4-disubstituted 1,4-dihydropyridines.[14] We therefore thought it would be

Keywords: Dihydropyridines (DHP); Piperidines; Pyridinium salts; Dialkylmagnesium reagents.
* Corresponding author. Tel.: +49 89 218077249; fax: +49 89 218077247; e-mail: klaus.wanner@cup.uni-muenchen.de

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a highly rewarding endeavor to establish a method for the direct synthesis of 4,4-disubstituted 1,4-dihydropyridines from *N*-silylpyridinium ions. In the present paper, we report the successful implementation of this plan.

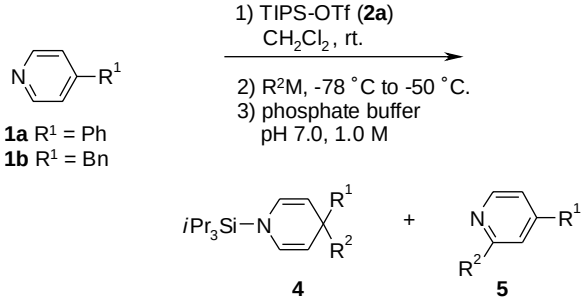
2. Results and discussion

Initial experiments were performed with pyridine **1a** (Table 1) and triisopropylsilyl triflate (TIPS triflate **2a**) as activating agent. The 4-phenyl group present in **1a** was chosen because of its inertness towards basic conditions and the TIPS group as it should efficiently shield the 2- and 6-position of the pyridine ring (Scheme 1). We were very pleased to find that upon treatment of **1a** with one equivalent of TIPS triflate at room temperature followed by 2 equiv of EtMgCl (2.0 M in Et_2O) at −78 °C the 4,4-disubstituted dihydropyridine **4a** was formed. Under optimized conditions the yield of **4a** amounted to 28%. Interestingly, **4a** was sufficiently stable for isolation, in contrast to the 1,2-addition product, which probably had already been oxidized during the quench reaction to give the aromatic species **5a**. But according to the ^{1}H NMR of the crude product only 1% of the latter was formed. Thus, the addition reaction had proceeded with a high regioselectivity in favor of the 1,4-addition. But unfortunately, even under optimized conditions 64% of the starting material **1a** were still present in the crude product (according to ^{1}H NMR).

When *n*BuMgCl (2.9 M in Et_2O) was used as a nucleophile, the corresponding 4-addition product **4b** was isolated in 34% (Table 1, entry 4). Interestingly, the reaction failed when Et_2O as solvent for the Grignard reagent (*n*BuMgCl) was replaced by THF. With BnMgCl, using again Et_2O as solvent (1.0 M) the reaction even came to completion and gave the 1,4-addition product **4c** in high yield (90%) and with good regioselectivity (Table 1, entry 7). Various other organometallic compounds as well as the pyridine derivative **1b** were checked for their suitability in this reaction. However, all of these reactions failed except for the ones employing higher order cuprates for which at least small amounts of the 1,4-addition products could be isolated or observed by ^{1}H NMR (Table 1, entries 10 and 11).

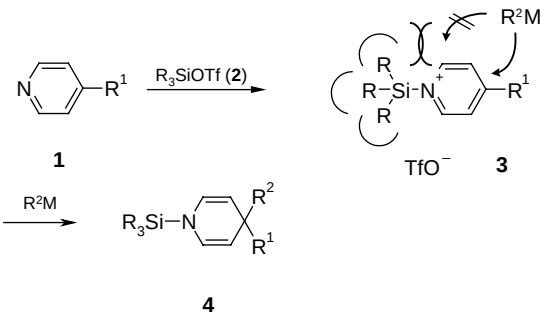
We speculated that the failure and the low yields observed for some of the trapping reactions of **3** using Grignard reagents were caused by the halide ions that had been introduced with the organometallic species. Due to their higher nucleophilicity compared to the triflate ion, the halide ion should shift the equilibrium between the *N*-silylpyridinium ion **3** and the free pyridine **1** towards the latter. This might hamper or even prevent trapping reactions of **3** especially when they are slow. To shed some light on this question we performed additional trapping reactions of **3** with ethyl and *n*-butyl Grignard reagents exhibiting bromide and iodide instead of chloride as counter ion. With EtMgBr the yield of **4a** improved to 44% (Table 1, entry 2) as compared to the addition reaction of EtMgCl

Table 1. Addition of various organometallic compounds to *N*-triisopropylsilylpyridinium ions



Entry	Start. mat.	R^2M[a]	Product	Yield **4** (%)[b]	Product ratio **4/5/1** (%)[c]
1	**1a** R^1=Ph	EtMgCl	**4a 5a**	28	35/1/64
2	**1a** R^1=Ph	EtMgBr	**4a 5a**	44	46/7/47
3	**1a** R^1=Ph	EtMgI	**4a 5a**	30	35/1/64
4	**1a** R^1=Ph	*n*BuMgCl[d]	**4b 5b**	34	36/11/53
5	**1a** R^1=Ph	*n*BuMgBr	**4b 5b**	20	27/4/69
6	**1a** R^1=Ph	*n*BuMgI	**4b 5b**	12	13/0/87
7	**1a** R^1=Ph	BnMgCl	**4c 5c**	90	90/10/0
8	**1a** R^1=Ph	PhMgBr	**4d 5d**	0	0/0/100
9	**1a** R^1=Ph	MeMgBr	**4e 5e**	0	0/0/100
10	**1a** R^1=Ph	$nBu_2CuCNLi_2$	**4b 5b**	11	nd[e]
11	**1a** R^1=Ph	$Me_2CuCNLi_2$	**4e 5e**	—[f]	3/0/97
12	**1a** R^1=Ph	Et_2Zn	**4a 5a**	0	0/0/100
13	**1a** R^1=Ph	*n*BuLi	**4b 5b**	0	0/0/100
14	**1b** R^1=Bn	EtMgBr	**4i 5i**	0	0/0/100
15	**1b** R^1=Bn	*n*BuMgCl	**4k 5k**	0	0/0/100

[a] In Et_2O.
[b] Isolated yield.
[c] According to ^{1}H NMR of the crude reaction product.
[d] With *n*BuMgCl in THF no reaction occurred.
[e] Not determined.
[f] Not isolated.



1 3 4

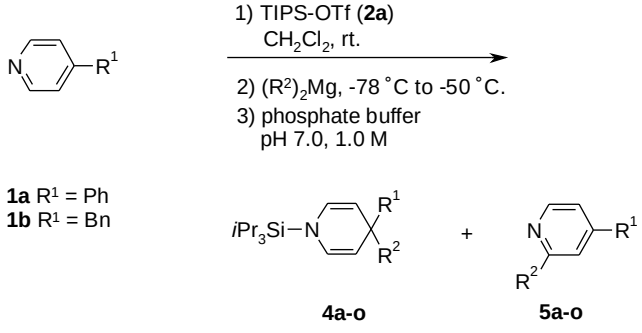
Scheme 1. Directing nucleophilic attack towards the 4-position of a pyridine nucleus.

(**4a**: 28%; Table 1, entry 1). However, using EtMgI a yield similar to the one of the addition reaction of EtMgCl was observed (30 vs 28%, compare Table 1, entries 3 and 1). In case of the addition of a *n*-butyl residue, the yield became distinctly lower when *n*BuMgBr instead of *n*BuMgCl was used, and showed a further drop when *n*BuMgI was employed (Table 1, entries 4–6). Although there was, obviously, no clear correlation between the yield of **4a** and the nucleophilicity of the counter ion of the Grignard reagent that could have supported our assumption, we thought it worth employing dialkylmagnesium derivatives as nucleophilic trapping reagents. The required magnesium compounds were prepared from Grignard reagents by precipitation of MgX_2.

When Et_2Mg (Table 2, entry 1) instead of ethyl Grignard reagents (Table 1, entry 1–3) was used the yield of the 4-addition product **4a** rose to 78%. Moreover, the regioselectivity was quite satisfactory (90/4; Table 2, entry 1). When using Bn_2Mg the yield, which had already been very high (Table 1, entry 7, 90%), remained more or less unaffected, while the regioselectivity (Table 2, entry 3; **4c/5c** 95/2) was significantly improved. Finally, employing iPr_2Mg the reaction proceeded with complete control of the regioselectivity providing the 4-addition product in 91% yield (Table 2, entry 6).

To uncover the impact of the *N*-silyl moiety on the outcome of the addition reactions experiments employing trimethylsilyl triflate **2b** and triphenylsilyl triflate **2c** as activating agents were performed. In case of trimethylsilyl triflate mediated trapping reactions employing Et_2Mg and Bn_2Mg as nucleophiles the results were far less satisfying both in respect to yield and regioselectivity (see Table 3, entries 1–2). But for the addition of iPr_2Mg regioselectivity and yield were only slightly diminished (see Table 3, entry 3). The most negative results had been yielded by the reaction of Et_2Mg. The addition products **4p** and **5a** were formed only in minute amounts and, interestingly, the regioselectivity had been inverted. In addition, all *N*-trimethylsilyl derivatives **4p–4r** were highly susceptible to hydrolysis and thus barley isolable. The use of the bulkier triphenylsilyl group gave some increased stability but for Et_2Mg and Bn_2Mg the yields of the desired product were distinctly

Table 2. Addition of various dialkylmagnesium reagents to *N*-triisopropylsilylpyridinium ions

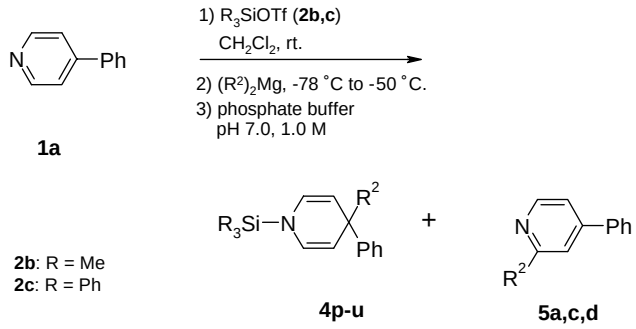


4a-o **5a-o**

Entry	Start. mat.	$(R^2)_2Mg$[a]	Product	Yield **4** (%)[b]	Product ratio **4/5/1** (%)[c]
1	**1a** R^1 = Ph	Et_2Mg	**4a 5a**	78	90/4/6
2	**1a** R^1 = Ph	nBu_2Mg	**4b 5b**	82	100/0/0
3	**1a** R^1 = Ph	Bn_2Mg	**4c 5c**	92	95/2/3
4	**1a** R^1 = Ph	Ph_2Mg	**4d 5d**	0	5/95[d]/0
5	**1a** R^1 = Ph	Me_2Mg	**4e 5e**	0	0/59/41
6	**1a** R^1 = Ph	iPr_2Mg	**4f 5f**	91	99/0/1
7	**1a** R^1 = Ph	tBu_2Mg	**4g 5g**	56	80/3/17[e]
8	**1a** R^1 = Ph	$Allyl_2Mg$	**4h 5h**	20	20/78[d]/2
9	**1b** R^1 = Bn	Et_2Mg	**4i 5i**	73	86/2/12
10	**1b** R^1 = Bn	nBu_2Mg	**4k 5k**	54	54/6/40
11	**1b** R^1 = Bn	Bn_2Mg	**4l 5l**	85	95/0/5
12	**1b** R^1 = Bn	iPr_2Mg	**4m 5m**	78	100/0/0
13	**1b** R^1 = Bn	tBu_2Mg	**4n 5n**	5	6/0/94[f]
14	**1b** R^1 = Bn	$Allyl_2Mg$	**4o 5o**	12	21/70/9

[a] After addition of the organomagnesium compound to the *N*-silylpyridinium ion at −78 °C the mixture was slowly warmed to −50 °C.
[b] Isolated yield.
[c] According to ^{1}H NMR of the crude reaction product.
[d] Sum of **5** and non oxidized 1,2-addition product, which were both present.
[e] Yield 63%, ratio 86/2/12 when addition performed by warming the mixture from −78 °C to room temperature.
[f] Yield 29%, ratio 32/0/68 when addition performed by warming the mixture from −78 °C to room temperature.

Table 3. Variation of the *N*-trialkylsilyl group in the trapping reactions of *N*-silylpyiridinium ions



Entry	R_3SiOTf	$(R^2)_2Mg$[a]	Product	Yield **4** (%)[b]	Product ratio **4/5/1** (%)[c]
1	Me_3SiOTf	Et_2Mg	**4p 5a**	0	1/4/95
2	Me_3SiOTf	Bn_2Mg	**4q 5c**	45	66/9/25
3	Me_3SiOTf	iPr_2Mg	**4r 5f**	90	91/2/7
4	Ph_3SiOTf	Et_2Mg	**4s 5a**	0	11/30/59
5	Ph_3SiOTf	Bn_2Mg	**4t 5c**	48	49/7/44
6	Ph_3SiOTf	iPr_2Mg	**4u 5f**	86	98/1/1

[a] After addition of the organomagnesium compound to the *N*-silylpyridinium ion at −78 °C the mixture was slowly warmed to −50 °C.
[b] Isolated yield.
[c] According to ^{1}H NMR of the crude reaction product.

lower than those obtained with TIPS triflate as activating agent (Table 3, entries 4–6). Additionally, with Et_2Mg a reversed selectivity in favor of **5a** was observed again (compare Table 2, entry 1 with Table 3, entry 4).

Consequently, for additional trapping reactions varying the diorganomagnesium compounds again, TIPS triflate was used for the activation of the pyridine moiety. In case of nBu_2Mg the 1,4-addition product **4b** was formed exclusively and in high yield (Table 2, entry 2). Even with tBu_2Mg the addition reaction proceeded smoothly providing **4g** in good yield and with high regioselectivity (Table 2, entry 7).

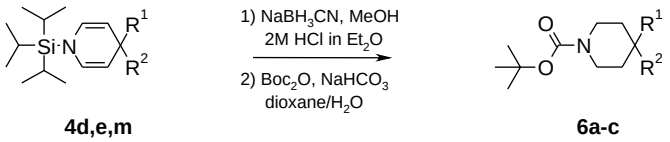
In contrast, Ph_2Mg, Me_2Mg and $allyl_2Mg$ with sterically less demanding residues reacted predominantly in the 2-position to yield the pyridine derivatives **5d**, **5e** and **5h** after aqueous workup as the major product (Table 2, entries 4, 5 and 8).

Additionally, a further set of experiments was performed with the pyridine derivative **1b**. The results of these trapping reactions closely paralleled those obtained for **1a**. The yield for the 4-addition product **4** obtained from **1b** was significantly lower only with tBu_2Mg (Table 2, entry 13, **4n**, 5%). But when the reaction was performed by increasing the temperature (from −78 °C) not only to −50 °C but to room temperature, the yield rose to 29% (ratio **4/5/1**=32/0/68). For the addition of tBu_2Mg to **1a** both the yield that had already been quite satisfying (from 56 to 63%) and the product ratio [from 80/3/17 to 86/2/12 (5/4/1)] improved slightly when the reaction temperature was allowed to reach room temperature. The insufficient outcome of the addition of tBu_2Mg to **1b** (yield 5%, see Table 2, entry 13) under standard conditions could be the result of a competing deprotonation reaction. It is obvious that the benzylic position of **1b** is highly acidic, which should be even more true for the *N*-silyl derivative of **1b**. Therefore, in case of the addition of tBu_2Mg to **1b** it also seems likely that a deprotonation reaction of the benzylic position occurs, which finally diminishes the yield of the addition product. Actually, it is quite intriguing that the reactivity of the benzylic position (in **1b**) had no or only a secondary effect on the other addition reactions performed with **1b**. The sharp drop in yield observed for the addition of tBu_2Mg is possibly due to its higher steric demand in addition to his higher basicity as compared to the other Grignard reagents.

At first sight one might be tempted to assume that the regioselectivity observed in the trapping reactions of **1a** and **1b** is a function of the softness, according to the HSAB principle, of the alkyl moiety of the organomagnesium compound used. Particularly, since relatively soft nucleophiles (such as Et_2Mg, nBu_2Mg, iPr_2Mg, tBu_2Mg) add preferentially to the 4-position of the pyridine ring, whereas harder nucleophiles ($allyl_2Mg$, Ph_2Mg) give mainly the respective 2-addition products. However, with Me_2Mg the 2-addition is more favored than with Ph_2Mg or $allyl_2Mg$ (see Table 2, entries 6–8), whereas according to the HSAB principle the opposite should be true. Therefore, it is more likely that the regioselectivity is dominated by the size and the steric demand of the nucleophile and depends only partly on the softness of the reagent. This is also indicated by the results of the trapping reaction with varying *N*-silyl groups according to which the size of the nucleophile as well as the steric demand of the *N*-silyl moiety play important roles for the regioselectivity.

The *N*-triisopropylsilyl-1,4-dihydropyridines prepared in this study were found to be sufficiently stable for isolation. Although, chromatography on standard silica gel columns caused considerable decomposition, the recovery of the materials was almost quantitative when aluminum oxide was used for purification (neutral, Brockmann activity III[15]).

Table 4.



4d,e,m **6a-c**

Entry	Start. mat.	Product	R^1	R^2	Yield **6** (%)[a]
1	**4f**	**6a**	Ph	*i*Pr	90
2	**4g**	**6b**	Ph	*t*Bu	95
3	**4m**	**6c**	Bn	*i*Pr	92

[a] Isolated yield.

Stored under nitrogen atmosphere at −20 °C the isolated *N*-triisopropylsilyl-1,4-dihydropyridines were stable for weeks.

Having established a highly efficient access to *N*-triisopropylsilyl-1,4-dihydropridines we set out to explore the utility of these compounds for the preparation of related 4,4-disubstituted piperidines. Interestingly, synthetic methods giving access to this class of compounds are still rare.[16]

It turned out that the desired transformation can be efficiently accomplished by treating the respective *N*-triisopropylsilyl-silyl-1,4-dihydropyridine in Et_2O with $NaCNBH_3$ and etheral HCl. Under these conditions not only a reduction of the double bonds but also, though not unexpected, a removal of the *N*-silyl group occurs. To allow for a more convenient isolation the formed amines were finally trapped with di-*tert*-butyl dicarbonate (Boc_2O) providing the corresponding Boc protected piperidine derivatives. Thus, from the *N*-silyl derivatives **4f**, **4g** and **4m** the corresponding piperidine derivatives **6a–c** were obtained in yields of ≥90%, which clearly demonstrates the efficiency of this approach (Table 4).

3. Conclusion

In summary, we have presented an easy and straightforward method for the preparation of 4,4-disubstituted 1,4-dihydropyridines with a wide variety of substituents. It is based on unprecedented trapping reactions of 4-substituted *N*-silylpyridinium ions with organomagnesium compounds. The obtained 4,4-disubstituted 1,4-dihydropyridines have been demonstrated to give rapid access to fully saturated 4,4-disubstituted piperidine derivatives, which adds a new method to the few existing for the preparation of piperidine derivatives with a quaternary carbon in 4-position. Further studies exploring the scope of the trapping reaction of *N*-silylpyridinum ions mentioned above for the synthesis of highly functionalized 1,4-dihydropyridines are in progress.

4. Experimental

4.1. General experimental

All reactions were performed using flame-dried glassware under N_2 atmosphere. All solvents were freshly dried using standard[17] procedures. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CD_2Cl_2 at 500 and 125 MHz, respectively. Infrared spectra were obtained on a Perkin-Elmer Model 1600 FTIR spectrometer. Microanalytical data for carbon, hydrogen and nitrogen were determined on a Heraeus Rapid Analyser and on a Elementar Vario EL Analyser. Flash chromatography was performed with 50–150 mesh aluminium oxide (neutral Brockmann activity III).

4.2. General procedure for the preparation of dialkylmagnesium reagents[18] (GP1)

Commercially available alkylmagnesium halide solutions in Et_2O or THF were diluted with Et_2O to yield 1.0 M stock solutions. 1,4-Dioxane (1.1 equiv) was added slowly to the mechanically stirred Grignard solution at room temperature. The heterogeneous solution was stirred over night to complete precipitation. The resulting suspensions were centrifuged to yield clear colorless R_2Mg solutions. Complete precipitation of magnesium halide was verified by addition of a few drops of 1,4-dioxane. The clear R_2Mg solutions were kept under nitrogen at 4 °C.

4.3. General procedure for the preparation of 4,4-disubstituted *N*-silyl-1,4-dihydropyridines (GP2)

The corresponding 4-substituted pyridine was dissolved in CH_2Cl_2 and treated with 1.0 equiv TIPS triflate at room temperature. After stirring at ambient temperature for 15 min the colorless solution was cooled to −78 °C, followed by dropwise addition of a twofold excess of R_2Mg solution. The resulting yellow to deep red colored mixture was slowly warmed to −50 °C and quenched after the time given by addition of 2 ml phosphate buffer (pH 7, *c* 1.0 M). The aqueous layer was extracted with CH_2Cl_2 (4×7 ml). The combined organic layers were dried ($MgSO_4$), and concentrated in vacuo. Column chromatography at aluminum oxide (neutral, Brockmann activity III, pentane; addition of CH_2Cl_2 to dissolve side products was necessary in some cases) yielded the final product. The final compound was stored under N_2 atmosphere at −20 °C to avoid oxidation.

4.4. General procedure for the preparation of 4,4-disubstituted *N*-Boc protected piperidines (GP3)

The corresponding 4,4-disubstituted *N*-silyl-1,4-dihydropyridine was dissolved in CH_2Cl_2 and treated with 2.5 equiv of $NaBH_3CN$ in MeOH at room temperature. After addition of 5.0 equiv 2 M HCl in Et_2O the mixture was stirred for 1 h

at room temperature and subsequently quenched with aqueous 5 M KOH. The water phase was extracted with CH_2Cl_2. The raw material resulting from the combined organic layers was dissolved in a 1:1 mixture of dioxane and water containing $NaHCO_3$ and treated with 1.1 equiv of Boc_2O. After stirring over night the mixture was extracted with CH_2Cl_2. The organic extracts were concentrated and the resulting residue purified by CC on silica gel.

4.4.1. 4-Ethyl-4-phenyl-1-triisopropylsilyl-1,4-dihydropyridine (4a). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and Et_2Mg (1.0 ml, 0.5 M in Et_2O), reaction time 10 h.

Yield 66.6 mg (78%), colorless crystals, mp 59 °C. TLC R_f=0.69 (aluminum oxide 60 neutral, *n*-pentane). ^{1}H NMR ($CDCl_3$) δ=0.95 (t, J=7.5 Hz, 3H, CH_2CH_3), 1.11 (d, J=7.5 Hz, 18H, $CHCH_3$), 1.30 (sept, J=7.5 Hz, 3H, $CHCH_3$), 1.68 (q, J=7.5 Hz, 2H, CH_2CH_3), 4.36 (d, J=8.0 Hz, 2H, NCH=C*H*), 6.15 (d, J=8.0 Hz, 2H, NC*H*=CH), 7.12–7.16 (m, 1H, H_{aromat}), 7.30–7.34 (m, 2H, H_{aromat}), 7.40–7.43 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=10.0 (q), 11.4 (d), 17.9 (q), 35.0 (t), 42.2 (s), 106.1 (d, NC=*C*), 125.1 (d, C_{aromat}), 126.7 (d, N*C*=C), 128.0 (d, C_{aromat}), 128.2 (d, C_{aromat}), 152.6 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 324 (100) $[M+1]^+$, 312 (33), 157 (4), 147 (4). IR (film): $\tilde{\nu}$= 3054 cm^{-1}, 2984, 2304, 1423, 1265, 895, 746. Anal. Calcd for $C_{22}H_{35}NSi$ (341.62): C 77.35, H 10.33, N 4.10. Found C 77.33, H 10.39, N 4.05.

4.4.2. 4-*n*-Butyl-4-phenyl-1-triisopropylsilyl-1,4-dihydropyridine (4b). (A) According to GP2 from 4-phenylpyridine (**1a**, 77.6 mg, 0.5 mmol), TIPS triflate (153.2 mg, 134.8 µl, 0.5 mmol) in CH_2Cl_2 (4 ml) and Bu_2Mg (2.0 ml, 0.5 M in Et_2O), reaction time 10 h.

Yield 151.6 mg (82%), colorless crystals, mp 85–86 °C. TLC R_f=0.76 (aluminum oxide 60 neutral, *n*-pentane). ^{1}H NMR ($CDCl_3$) δ=0.92 (t, J=7.2 Hz, 3H, CH_3), 1.11 (d, J=7.4 Hz, 18H, CH_3), 1.28 (sept, J=7.4 Hz, 3H, $CH(CH_3)_2$), 1.31–1.39 (m, 4H, CH_2), 1.65 (m, 2H, CH_2), 4.40 (d, J=8.3 Hz, 2H, NCH=C*H*), 6.12 (d, J=8.3 Hz, 2H, NC*H*=CH), 7.14 (tt, J=7.2/1.1 Hz, 1H, H_{aromat}), 7.33 (m, 2H, H_{aromat}), 7.42 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=11.4 (d), 12.3 (q), 17.9 (q), 23.3 (t), 28.3 (t), 41.6 (s), 42.9 (t), 106.7 (d, NC=*C*), 125.1 (d, C_{aromat}), 126.6 (d, N*C*=C), 127.8 (d, C_{aromat}), 128.0 (d, C_{aromat}), 152.7 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 370 (100) $[M+1]^+$, 312 (53), 178 (7), 156 (6), 147 (5). IR (Film): $\tilde{\nu}$=3054 cm^{-1}, 2986, 2868, 2305, 1665, 1422, 1265, 895, 740, 705. Anal. Calcd for: $C_{27}H_{37}NSi$ (369.67): C 77.98, H 10.63, N 3.79. Found. C 77.98, H 10.73, N 3.79.

(B) A solution of 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol) in CH_2Cl_2 (2 ml) was treated with TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol), and stirred for 15 min at room temperature. After cooling to −78 °C the mixture was transferred via cannula to a prior prepared solution of $Bu_2CuCNLi_2$[19] (2.0 equiv) in Et_2O kept at −78 °C. Then the resulting red colored mixture was allowed to warm up to 0 °C. After 4 h it was quenched and worked up as described above. Yield of **4b**: 11%.

4.4.3. 4-Benzyl-4-phenyl-1-triisopropylsilyl-1,4-dihydropyridine (4c). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and Bn_2Mg (1.0 ml, 0.5 M in Et_2O), reaction time 10 h.

Yield 92.8 mg (92%), colorless crystals, mp 81 °C. TLC R_f=0.37 (aluminum oxide 60 neutral, *n*-pentane). ^{1}H NMR ($CDCl_3$) δ=0.95 (d, J=7.5 Hz, 18H, CH_3), 1.15 (sept, J=7.5 Hz, 3H, $CH(CH_3)_2$), 3.03 (s, 2H, CH_2), 4.51 (d, J=8.0 Hz, 2H, NCH=C*H*), 5.96 (d, J=8.0 Hz, 2H, NCH=C*H*), 7.09–7.15 (m, 3H, H_{aromat}), 7.16–7.20 (m, 3H, H_{aromat}), 7.38 (t, J=7.5 Hz, 2H, H_{aromat}), 7.49 (d, J=7.5 Hz, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=11.2 (d), 17.7 (q), 43.2 (s), 50.0 (t), 105.9 (d, NC=*C*), 125.3 (d, C_{aromat}), 125.5 (d, C_{aromat}), 126.7 (d, N*C*=C), 127.3 (d, C_{aromat}), 128.0 (d, C_{aromat}), 128.1 (d, C_{aromat}), 131.3 (d, C_{aromat}), 139.3 (s, C_{aromat}), 152.2 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 404 (100) $[M+1]^+$, 312 (84), 287 (12), 195 (22), 187 (11), 183 (6), 157 (6), 141 (7). IR (film): $\tilde{\nu}$= 3053 cm^{-1}, 2985, 2305, 1422, 1264, 895, 746, 706. Anal. Calcd for $C_{27}H_{37}NSi$ (403.69): C 80.33, H 9.24, N 3.47. Found C 80.34, H 9.26, N 3.41.

4.4.4. 4-Isopropyl-4-phenyl-1-triisopropylsilyl-1,4-dihydropyridine (4f). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and *i*Pr_2Mg (1.0 ml, 0.5 M in Et_2O), reaction time 4 h.

Yield 81.0 mg (91%), colorless oil. TLC R_f=0.58 (aluminum oxide 60 neutral, *n*-pentane). ^{1}H NMR ($CDCl_3$) δ=0.82 (d, J=6.7 Hz, 6H, CH_3), 1.09 (d, J=7.4 Hz, 18H, $SiCH(CH_3)_2$), 1.26 (sept, J=7.4 Hz, 3H, $SiCH(CH_3)_2$), 2.07 (sept, J=6.7 Hz, 1H, $CH(CH_3)_2$), 4.97 (d, J=8.5 Hz, 2H, NCH=C*H*), 6.14 (d, J=8.5 Hz, 2H, NC*H*=CH), 7.13 (tt, J=7.2/1.4 Hz, 1H, H_{aromat}), 7.30–7.38 (m, 4H, H_{aromat}). ^{13}C NMR (125 MHz, $CDCl_3$, DEPT) δ= 11.4 (d), 17.8 (q), 17.9 (q), 37.4 (d), 45.5 (s), 104.2 (d, NC=*C*), 124.7 (d, C_{aromat}), 126.7 (d, C_{aromat}), 128.1 (d, C_{aromat}), 128.5 (d, N*C*H=CH)., 151.5 (s). MS (CI, CH_5^+); *m*/*z* (%): 356 (100) $[M+1]^+$, 312 (48), 235 (9), 189 (5), 184 (5), 157 (7), 147 (9). IR (film): $\tilde{\nu}$=3054 cm^{-1}, 2985, 2868, 2305, 1666, 1423, 1265, 895, 739, 706. Anal. Calcd for $C_{23}H_{37}NSi$ (355.64): C 77.68, H 10.49, N 3.94. Found C 74.64, H 10.65, N 3.93.

4.4.5. 4-*tert*-Butyl-4-phenyl-1-triisopropylsilyl-1,4-dihydropyridine (4g). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and *t*Bu_2Mg (1.0 ml, 0.5 M in Et_2O). After addition of the organometallic reagent the mixture was slowly warmed to room temperature, reaction time 10 h.

Yield 58.6 mg (63%), colorless crystals, mp 74 °C. TLC R_f=0.64 (aluminum oxide 60 neutral, *n*-pentane). ^{1}H NMR ($CDCl_3$) δ=0.86 (s, 9H, CH_3), 1.04 (d, J=7.4 Hz, 18H, $HCH(CH_3)_2$), 1.24 (sept, J=7.4 Hz, 3H, $CH(CH_3)_2$), 5.12 (d, J=8.5 Hz, 2H, NCH=C*H*), 6.11 (d, J=8.5 Hz, 2H, NC*H*=CH), 7.10 (t, J=7.4 Hz, 1H, H_{aromat}), 7.23–7.26 (m, 2H, H_{aromat}), 7.29–7.31 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=11.3 (d), 17.8 (q), 25.9 (q), 38.6 (s), 45.9 (s),

103.0 (d, NC=*C*), 124.7 (d, C_{aromat}), 127.0 (d, N*C*=C), 127.4 (d, C_{aromat}), 128.4 (d, C_{aromat}), 149.1 (s, C_{aromat}). MS (CI, CH_5^+); *m/z* (%): 370 (100) $[M+1]^+$, 312 (67), 292 (5), 184 (8), 156(12), 147 (9), 119 (6). IR (film): $\tilde{\nu}=3054\ cm^{-1}$, 2984, 2868, 2305, 1666, 1422, 1265, 895, 740, 706. Anal. Calcd for $C_{27}H_{37}NSi$ (369.67): C 77.98, H 10.63, N 3.79. Found C 77.80, H 10.65, N 3.72.

4.4.6. 4-Allyl-4-phenyl-1-triisopropylsilyl-1,4-dihydropyridine (4h). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and $allyl_2Mg$ (1.0 ml, 0.5 M in Et_2O), reaction time 2 h.

Yield 17.9 mg (20%), colorless oil. TLC $R_f=0.61$ (aluminum oxide 60 neutral, *n*-pentane). ^1H NMR ($CDCl_3$) $\delta=$ 1.10 (d, $J=7.5$ Hz, 18H, SiCH(CH_3)$_2$), 1.26 (sept, $J=$ 7.5 Hz, 3H, SiC*H*(CH_3)$_2$), 2.53 (d, $J=7.0$ Hz, 2H, CH_2), 4.46 (d, $J=8.0$ Hz, 2H, NCH=C*H*), 5.01–5.05 (m, 2H, CH=CH_2), 5.79–5.88 (m, 1H, C*H*=CH_2), 5.96 (d, $J=$ 8.0 Hz, 2H, NC*H*=CH), 7.16 (t, $J=7.5$ Hz, 1H, H_{aromat}), 7.34 (t, $J=7.5$ Hz, 2H, H_{aromat}), 7.42 (d, $J=7.5$ Hz, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) $\delta=11.4$ (d), 17.9 (q), 41.5 (s), 48.1 (t), 106.4 (d, NC=*C*), 116.2 (t, CH=*C*H_2), 125.2 (d, C_{aromat}), 126.7 (d, N*C*=C), 127.9 (d, C_{aromat}), 128.1 (d, C_{aromat}), 136.4 (*C*H=CH_2), 152.7 (s, C_{aromat}). MS (CI, CH_5^+); *m/z* (%): 354 (98) $[M+1]^+$, 312 (100), 236 (20), 184 (6), 156 (16), 147 (11). IR (film): $\tilde{\nu}=3053\ cm^{-1}$, 2985, 2304, 1665, 1421, 1265, 895, 739, 705. Anal. Calcd for $C_{23}H_{35}NSi$ (353.63): C 78.12, H 9.98, N 3.96. Found C 78.02, H 10.07, N 3.89.

4.4.7. 4-Benzyl-4-ethyl-1-triisopropylsilyl-1,4-dihydropyridine (4i). According to GP2 from 4-benzylpyridine (**1b**, 81.2 mg, 76.4 µl, 0.5 mmol), TIPS triflate (153.2 mg, 134.8 µl, 0.5 mmol) in CH_2Cl_2 (4 ml) and Et_2Mg (2.0 ml, 0.5 M in Et_2O), reaction time 10 h.

Yield 129.8 mg (73%), colorless oil. TLC $R_f=0.67$ (aluminum oxide 60 neutral, *n*-pentane). ^1H NMR ($CDCl_3$) $\delta=0.87$ (t, $J=7.4$ Hz, 3H, CH_2CH_3), 0.98 (d, $J=7.4$ Hz, 18H; CH(CH_3)$_2$), 1.16 (sept, $J=7.4$ Hz, 3H, C*H*(CH_3)$_2$), 1.23 (q, $J=7.4$ Hz, 2H, CH_2CH_3), 2.52 (s, 2H, CH_2Ph), 4.06 (d, $J=8.3$ Hz, 2H, NC*H*=CH), 5.96 (d, $J=$ 8.3 Hz, 2H, NCH=C*H*), 7.11–7.14 (m, 3H, H_{aromat}), 7.19–7.22 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) $\delta=$ 11.3 (d), 11.3 (q), 17.7 (q), 36.1 (t), 40.0 (s), 41.8 (t), 42.9 (t), 105.6 (d, NC=*C*), 125.3 (d, C_{aromat}), 127.2 (d, N*C*=C), 129.1 (d, C_{aromat}), 131.0 (d, C_{aromat}), 139.3 (s, C_{aromat}). MS (CI, CH_5^+); *m/z* (%): 356 (56) $[M+1]^+$, 264 (100), 147 (4). IR (film): $\tilde{\nu}=2958\ cm^{-1}$, 2867, 1671. Anal. Calcd for $C_{28}H_{39}NSi$ (355.64): C 77.68, H 10.49, N 3.94. Found C 77.58, H 10.63, N 3.89.

4.4.8. 4-Benzyl-4-*n*-butyl-1-triisopropylsilyl-1,4-dihydropyridine (4k). According to GP2 from 4-benzylpyridine (**1a**, 81.1 mg, 76.4 µl, 0.5 mmol), TIPS triflate (153.2 mg, 134.8 µl, 0.5 mmol) in CH_2Cl_2 (4 ml) and *n*Bu_2Mg (2.0 ml, 0.5 M in Et_2O), reaction time 5 h.

Yield 103.0 mg (54%), colorless crystals, mp 47 °C. TLC $R_f=0.68$ (aluminum oxide 60 neutral, *n*-pentane). ^1H NMR ($CDCl_3$) $\delta=0.89$ (t, $J=7.1$ Hz, 3H, CH_2CH_3), 0.98 (d, $J=7.3$ Hz, 18H, CH(CH_3)$_2$), 1.16 (sept, $J=7.6$ Hz, 3H, C*H*(CH_3)$_2$), 1.19–1.23 (m, 2H, CH_2), 1.27–1.34 (m, 4H, CH_2), 1.55 (s, 2H, CH_2Ph), 4.11 (d, $J=8.3$ Hz, 2H, NC*H*=CH), 5.92 (d, $J=8.3$ Hz, 2H, NCH=C*H*), 7.11–7.14 (m, 3H, H_{aromat}), 7.19–7.22 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) $\delta=11.3$ (q), 14.2 (d), 17.7 (q), 23.3 (t), 28.6 (t), 39.5 (s), 43.9 (t), 52.0 (t), 106.3 (d, NC=*C*), 125.3 (d, C_{aromat}), 127.2 (d, N*C*=C), 128.7 (d, C_{aromat}), 131.0 (d, C_{aromat}), 139.3 (s, C_{aromat}). MS (CI, CH_5^+); *m/z* (%): 384 (70) $[M+1]^+$, 292 (100), 147 (5). IR (film): $\tilde{\nu}=3053\ cm^{-1}$, 2960, 2867, 1668, 1288, 1265, 895, 737, 705. Anal. Calcd for $C_{28}H_{39}NSi$ (383.70): C 78.26, H 10.77, N 3.65. Found C 77.96, H 10.77, N 3.61.

4.4.9. 4-Dibenzyl-1-triisopropylsilyl-1,4-dihydropyridine (4l). According to GP2 from 4-benzylpyridine (**1b**, 40.6 mg, 38.2 µl, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and Bn_2Mg (1.0 ml, 0.5 M in Et_2O), reaction time 10 h.

Yield 88.8 mg (85%), colorless crystals, mp 101–102 °C. TLC $R_f=0.48$ (aluminum oxide 60 neutral, *n*-pentane). ^1H NMR ($CDCl_3$) $\delta=0.84$ (d, $J=7.4$ Hz, 18H, CH(CH_3)$_2$), 1.02 (sept, $J=7.4$ Hz, 3H, C*H*(CH_3)$_2$), 2.66 (s, 4H, CH_2), 4.18 (d, $J=8.3$ Hz, 2H, NCH=C*H*), 5.75 (d, $J=8.3$ Hz, 2H, NC*H*=CH), 7.11–7.16 (m, 6H, H_{aromat}), 7.19–7.22 (m, 4H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) $\delta=11.3$ (d), 17.5 (q), 41.5 (s), 51.5 (t), 105.7 (d, NC=*C*), 125.4 (d, C_{aromat}), 127.3 (d, N*C*=C), 128.8 (d, C_{aromat}), 131.0 (d, C_{aromat}), 139.6 (s, C_{aromat}). MS (CI, CH_5^+); *m/z* (%): 418 (48) $[M+1]^+$, 326 (100), 170 (7), 147 (8), 119 (7), 105 (11). IR (film): $\tilde{\nu}=3055\ cm^{-1}$, 2986, 1422, 1265, 896, 741, 706. Anal. Calcd for $C_{28}H_{39}NSi$ (417.72): C 80.51, H 9.41, N 3.35. Found C 80.34, H 9.26, N 3.31.

4.4.10. 4-Benzyl-4-isopropyl-1-triisopropylsilyl-1,4-dihydropyridine (4m). According to GP2 from 4-benzylpyridine (**1b**, 40.6 mg, 38.2 µl, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and *i*Pr_2Mg (1.0 ml, 0.5 M in Et_2O), reaction time 2 h.

Yield 71.8 mg (78%), colorless oil. TLC $R_f=0.70$ (aluminum oxide 60 neutral, *n*-pentane). ^1H NMR ($CDCl_3$) $\delta=$ 0.94 (d, $J=7.4$ Hz, 18H, SiCH(CH_3)$_2$), 0.95 (d, $J=6.9$ Hz, 6H, CH(CH_3)$_2$), 1.12 (sept, $J=7.4$ Hz, 3H, SiC*H*(CH_3)$_2$), 1.40 (sept, $J=6.9$ Hz, 1H, C*H*(CH_3)$_2$), 2.56 (s, 2H, CH_2Ph), 4.11 (d, $J=8.5$ Hz, 2H, NCH=C*H*), 5.89 (d, $J=8.3$ Hz, 2H, NC*H*=CH), 7.08–7.14 (m, 3H, H_{aromat}), 7.17–7.20 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) $\delta=11.3$ (d), 17.7 (q), 18.0 (q), 38.5 (d), 43.0 (s), 48.3 (t), 104.1 (d, NC=*C*), 125.2 (d, C_{aromat}), 127.1 (d, C_{aromat}), 129.0 (d, C_{aromat}), 131.0 (d, N*C*=C), 140.4 (s, C_{aromat}). MS (CI, CH_5^+); *m/z* (%): 370 (65) $[M+1]^+$, 326 (10), 278 (100), 147 (7), 122 (7). IR (film): $\tilde{\nu}=3054\ cm^{-1}$, 2985, 2867, 2305, 1668, 1422, 1265, 895, 740, 706. Anal. Calcd for $C_{24}H_{39}NSi$ (369.67): C 77.98, H 10.63, N 3.79. Found C 78.02, H 10.70, N 3.76.

4.4.11. 4-Benzyl-4-*tert*-butyl-1-triisopropylsilyl-1,4-dihydropyridine (4n). According to GP2 from 4-benzylpyridine (**1b**, 40.6 mg, 38.2 µl, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and *t*Bu_2Mg (1.0 ml, 0.5 M in Et_2O). After addition of the

organometallic reagents the mixture was slowly warmed to room temperature, reaction time 10 h.

Yield 28.1 mg (29%), colorless crystals, mp 74–75 °C. TLC R_f=0.69 (aluminum oxide 60 neutral, *n*-pentane). ^{1}H NMR ($CDCl_3$) δ=0.90 (d, J=7.3 Hz, 18H, SiCH(CH_3)$_2$), 0.97 (s, 9H, C(CH_3)$_3$), 1.08 (sept, J=7.6 Hz, 3H, SiC*H*(CH_3)$_2$), 2.54 (s, 2H, CH_2Ph), 4.26 (d, J=8.5 Hz, 2H, NCH=C*H*), 5.81 (d, J=8.5 Hz, 2H, NC*H*=CH), 7.05–7.10 (m, 3H, H_{aromat}), 7.14–7.18 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=11.2 (d), 17.6 (q), 25.3 (q), 38.4 (s), 43.4 (t), 45.4 (s), 103.3 (d, NC=*C*), 125.0 (d, C_{aromat}), 127.0 (d, C_{aromat}), 128.8 (d, C_{aromat}), 131.2 (d, N*C*=C), 141.6 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 384 (92) $[M+1]^+$, 326 (51), 292 (100), 170 (9), 157 (8), 147 (15). IR (film): $\tilde{\nu}$=3054 cm^{-1}, 2985, 1422, 895, 740, 706. Anal. Calcd for $C_{24}H_{39}NSi$ (383.70): C 78.22, H 10.77, N 3.65. Found C 78.22, H 10.55, N 3.57.

4.4.12. 4-Allyl-4-benzyl-1-triisopropylsilyl-1,4-dihydropyridine (4o). According to GP2 from 4-benzylpyridine (**1b**, 40.6 mg, 38.2 µl, 0.25 mmol), TIPS triflate (76.6 mg, 67.4 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and allyl$_2$Mg (1.0 ml, 0.5 M in Et_2O), reaction time 10 h.

Yield 10.8 mg (12%), colorless oil. TLC R_f=0.62 (aluminum oxide 60 neutral, *n*-pentane) ^{1}H NMR ($CDCl_3$) δ=0.98 (d, J=7.3 Hz, 18H, CH(CH_3)$_2$), 1.36 (sept, J=7.3 Hz, 3H, C*H*(CH_3)$_2$), 2.09 (dt, J=7.1/1.4 Hz, 2H, CH_2CH=CH$_2$), 2.57 (s, 2H, CH_2Ph), 4.17 (d, J=8.3 Hz, 2H, NC*H*=CH), 4.97–5.05 (m, 2H, CH=CH_2), 5.88–5.97 (m, 3H, C*H*=CH$_2$, NCH=C*H*), 7.12–7.15 (m, 3H, H_{aromat}), 7.20–7.23 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=11.3 (d), 17.7 (q), 36.4 (s), 49.1 (t), 50.9 (t), 105.9 (d, NC=*C*), 115.8 (t, CH=*C*H$_2$), 125.5 (d), 127.3 (d), 128.8 (d), 130.9 (d), 136.7 (d), 139.0 (s). MS (CI, CH_5^+); *m*/*z* (%): 368 (92) $[M+1]^+$, 326 (49), 276 (100), 236 (5), 147 (6). IR (film): $\tilde{\nu}$=3027 cm^{-1}, 2944, 2866, 2350, 1670, 1464, 1287, 1057. HRMS (70 eV) calcd for $C_{24}H_{37}NSi$ [M^+]: 367.2701. Found 367.2695.

4.4.13. 4-Benzyl-4-phenyl-1-trimethylsilyl-1,4-dihydropyridine (4q). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), TMS triflate (55.6 mg, 45.2 µl, 0.25 mmol) in CH_2Cl_2 (2 ml) and Bn$_2$Mg (1.0 ml, 0.5 M in Et_2O), reaction time 3 h.

Yield 36.1 mg (45%), colorless crystals, mp 51–52 °C. TLC R_f=0.9 (aluminum oxide 60 neutral, *n*-pentane/CH_2Cl_2 9:1). ^{1}H NMR ($CDCl_3$) δ=0.06 (s, 9H, Si(CH_3)$_3$), 3.04 (s, 2H, CH_2), 4.59 (d, J=8.2 Hz, 2H, NCH=C*H*), 5.98 (d, J=8.2 Hz, 2H, NC*H*=CH), 7.01–7.03 (m, 2H, H_{aromat}), 7.14–7.20 (m, 4H, H_{aromat}), 7.34–7.37 (m, 2H, H_{aromat}) 7.42–7.45 (m, 2H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=−1.2 (q), 43.1 (s), 50.7 (t), 106.5 (d, NC=*C*), 125.3 (d), 125.5 (d), 126.5 (d), 126.7 (d), 127.1 (d), 128.2 (d), 131.1 (d), 138.7 (s, C_{aromat}), 151.6 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 320 (88) $[M+1]^+$, 248 (19), 228 (100), 156 (28). IR (film): $\tilde{\nu}$=3024 cm^{-1}, 2952, 2359, 1666, 1598, 1293, 1253, 1098, 1036, 840, 735, 698. Anal. Calcd for $C_{17}H_{25}NSi$ (271.48): C 78.94, H 7.89, N 4.38. Found C 78.80, H 7.82, N 4.30.

4.4.14. 4-Isopropyl-4-phenyl-1-trimethylsilyl-1,4-dihydropyridine (4r). According to GP2 from 4-phenylpyridine (**1a**, 77.6 mg, 0.5 mmol), TMS triflate (111.2 mg, 90.4 µl, 0.5 mmol) in CH_2Cl_2 (2 ml) and *i*Pr$_2$Mg (2.0 ml, 0.5 M in Et_2O), reaction time 3 h.

Yield 122.1 mg (90%), colorless oil. TLC R_f=0.9 (aluminum oxide 60 neutral, *n*-pentane/CH_2Cl_2 9:1). ^{1}H NMR ($CDCl_3$) δ=0.19 (s, 9H, Si(CH_3)$_3$), 0.78 (d, J=6.6 Hz, 6H, CH(CH_3)$_2$), 2.01 (sept, J=6.6 Hz, 3H, C*H*(CH_3)$_2$), 4.55 (d, J=8.3 Hz, 2H, NCH=C*H*), 6.16 (d, J=8.5 Hz, 2H, NC*H*=CH), 7.08–7.12 (m, 1H, H_{aromat}), 7.28–7.33 (m, 4H, H_{aromat}). ^{13}C NMR ($CDCl_3$, DEPT) δ=−1.4 (q), 17.7 (q), 37.7 (d), 45.6 (s), 104.5 (d, NC=*C*), 124.8 (d, C_{aromat}), 126.6 (d, C_{aromat}), 127.3 (d, N*C*=C), 128.2 (d, C_{aromat}), 151.7 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 272 (100) $[M+1]^+$, 228 (85), 204 (6), 200 (11), 194 (5), 181 (8), 156 (7), 105 (9). IR (film): $\tilde{\nu}$=3053 cm^{-1}, 2956, 1667, 1598, 1295, 1253, 1092, 997, 843, 759. Anal. Calcd for $C_{17}H_{25}NSi$ (271.48): C 75.21, H 9.28, N 5.16. Found C 74.97, H 9.43, N 5.38.

4.4.15. 4-Benzyl-4-phenyl-1-triphenylsilyl-1,4-dihydropyridine (4t). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), triphenylsilyl triflate (1.0 ml, 0.25 M in CH_2Cl_2) in CH_2Cl_2 (2 ml) and Bn$_2$Mg (1.0 ml, 0.5 M in Et_2O), reaction time 3 h.

Yield 61.3 mg (48%), colorless crystals, mp 133–134 °C. TLC R_f=0.64 (aluminum oxide 60 neutral, *n*-pentane/CH_2Cl_2 9:1). ^{1}H NMR (CD_2Cl_2) δ=3.04 (s, 2H, CH_2Ph), 4.62 (d, J=8.5 Hz, 2H, NCH=C*H*), 5.95 (d, J=8.5 Hz, 2H, NC*H*=CH), 7.13–7.15 (m, 2H, H_{aromat}), 7.18–7.21 (m, 1H, H_{aromat}), 7.29–7.30 (m, 3H, H_{aromat}), 7.35–7.38 (m, 8H, H_{aromat}), 7.41–7.50 (m, 11H, H_{aromat}). ^{13}C NMR (CD_2Cl_2, DEPT) δ=43.5 (s), 50.1 (t), 107.2 (d, NC=*C*), 125.5 (d, C_{aromat}), 125.8 (d, C_{aromat}), 126.6 (d, N*C*=C), 127.4 (d, C_{aromat}), 128.0 (d, C_{aromat}), 128.1 (d, C_{aromat}), 128.2 (d, C_{aromat}), 130.3 (d, C_{aromat}), 131.4 (d, C_{aromat}), 132.0 (s, C_{aromat}), 135.9 (d, C_{aromat}), 139.4 (s, C_{aromat}), 151.9 (s, C_{aromat}). MS (EI); *m*/*z* (%): 505 (1) $[M^+]$, 414 (100), 259 (86), 181 (14), 105 (6), 91 (5). IR (Film): $\tilde{\nu}$=3428 cm^{-1}, 3022, 2343, 1667, 1428, 1288, 1114, 697. HRMS (70 eV) calcd for $C_{36}H_{31}NSi$ [M^+]: 505.2226. Found 505.2227.

4.4.16. 4-Isopropyl-4-phenyl-1-triphenylsilyl-1,4-dihydropyridine (4u). According to GP2 from 4-phenylpyridine (**1a**, 38.8 mg, 0.25 mmol), triphenylsilyl triflate (1.0 ml, 0.25 M in CH_2Cl_2) in CH_2Cl_2 (2 ml) and *i*Pr$_2$Mg (1.0 ml, 0.5 M in Et_2O), reaction time 3 h.

Yield 98.9 mg (86%), colorless oil. TLC R_f=0.66 (aluminum oxide 60 neutral, *n*-pentane/CH_2Cl_2 9:1). ^{1}H NMR (CD_2Cl_2) δ=0.86 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$), 2.09 (sept, J=6.9 Hz, 1H, C*H*(CH_3)$_2$), 4.62 (d, J=8.3 Hz, 2H, NCH=C*H*), 6.16 (d, J=8.3 Hz, 2H, NC*H*=CH), 7.13–7.16 (m, 1H, H_{aromat}), 7.33–7.37 (m, 4H, H_{aromat}), 7.40–7.43 (m, 6H, H_{aromat}), 7.46–7.50 (m, 3H, H_{aromat}), 7.62–7.64 (m, 6H, H_{aromat}). ^{13}C NMR (CD_2Cl_2, DEPT) δ=18.2 (q), 37.8 (d), 45.9 (s), 105.9 (d, NC=*C*), 125.3 (d, C_{aromat}), 126.9 (d, C_{aromat}), 128.4 (d, C_{aromat}), 128.5 (d, N*C*=C), 128.8 (d, C_{aromat}), 130.7 (d, C_{aromat}), 132.5 (s, C_{aromat}), 136.3 (d, C_{aromat}), 151.6 (s, C_{aromat}). MS (CI, CH_5^+); *m*/*z* (%): 458

(100) $[M+1]^+$, 414 (39), 380 (6), 259 (13). IR (film): $\tilde{\nu}=$ 3049 cm^{-1}, 2958, 1669, 1428, 1292, 1114, 699. HRMS (70 eV) calcd for $C_{32}H_{31}NSi$ $[M^+]$ 457.2226. Found 457.2231.

4.4.17. 2,4-Diphenyl-pyridine (5d). According to GP2 from 4-phenylpyridine (**1a**, 77.6 mg, 0.5 mmol), TIPS triflate (153.2 mg, 134.8 µl, 0.5 mmol) in CH_2Cl_2 (4 ml) and Ph_2Mg (4.0 ml, 0.25 M in Et_2O), the reaction mixture was warmed to room temperature during 12 h. The reaction was quenched by addition of 2 ml 2 M HCl. The mixture was stirred for 15 min, before adding 3 ml, 2 M NaOH solution and extraction with CH_2Cl_2. The crude product was purified by CC on silica gel.

Yield 47.9 mg (41%), colorless oil. TLC $R_f=0.24$ (SiO_2, *n*-pentane/EtOAc 95:5). ^1H NMR ($CDCl_3$) $\delta=7.43$–7.55 (m, 7H, H_{aromat}), 7.71 (d, $J=7.0$ Hz, 2H, H_{aromat}), 7.95 (s, 1H, H_{aromat}), 8.06 (d, $J=7.0$ Hz, 2H, H_{aromat}), 8.76 (d, $J=$ 5.3 Hz, 1H, NC*H*=CH). HRMS (70 eV) calcd for $C_{17}H_{13}N$ $[M^+]$ 231.1048. Found 231.1036. Spectroscopic data for ^1H, ^{13}C NMR and IR are in accordance with those previously published.[20]

4.4.18. 4-Isopropyl-4-phenyl-piperidine-1-carboxylic acid *tert*-butyl ester (6a). According to GP3 from **4d** (150.8 mg, 0.424 mmol), $NaBH_3CN$ (66.6 mg, 1.06 mmol) in MeOH (3 ml), HCl 2 M in Et_2O (2.12 ml) and Boc_2O (101.9 mg, 0.467 mmol).

Yield 115.3 mg (90%), colorless crystals, mp 83–84 °C. TLC $R_f=0.28$ (SiO_2, *n*-pentane/EtOAc 95:5). ^1H NMR (500 MHz, $C_2D_2Cl_4$, 80 °C) $\delta=0.75$ (d, $J=6.6$ Hz, 6H, $CH(CH_3)_2$), 1.46 (s, 9H, $C(CH_3)_3$), 1.66–1.72 (m, 3H, $CH(CH_3)_2$ and NCH_2CH_2), 2.28–231 (m, 2H, NCH_2CH_2), 2.79–2.84 (m, 2H, NCH_2), 3.85–3.88 (m, 2H, NCH_2), 7.23–7.28 (m, 3H, H_{aromat}), 7.35–7.38 (m, 2H, H_{aromat}). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, DEPT, 80 °C) $\delta=17.3$ (q, CH_3), 28.6 (q, CH_3), 32.7 (t, CH_2), 38.5 (d, *C*H), 40.7 (t, CH_2), 43.5 (s), 79.0 (s), 125.8 (d, C_{aromat}), 128.0 (d, C_{aromat}), 128.4 (d, C_{aromat}), 141.5 (s, C_{aromat}), 155.0 (s, CO). MS (CI, CH_5^+); *m*/*z* (%): 304 (6) $[M+1]^+$, 248 (100), 204 (13). IR (KBr): $\tilde{\nu}=2972$ cm^{-1}, 2867, 1685. Anal. Calcd for $C_{19}H_{29}NO_2$ (303.45): C 75.21, H 9.63, N 4.62. Found C 75.15, H 9.77, N 4.61.

4.4.19. 4-*tert*-Butyl-4-phenyl-piperidine-1-carboxylic acid *tert*-butyl ester (6b). According to GP3 from **4e** (91.9 mg, 0.249 mmol), $NaBH_3CN$ (39.1 mg, 0.622 mmol) in MeOH (2 ml), HCl 2 M in Et_2O (1.24 ml) and Boc_2O (59.8 mg, 0.274 mmol).

Yield 75.9 mg (95%), colorless crystals, mp 107 °C. TLC $R_f=0.28$ (SiO_2, *n*-pentane/EtOAc 95:5). ^1H NMR (500 MHz, $C_2D_2Cl_4$, 80 °C) $\delta=0.85$ (s, 9H, $C(CH_3)_3$), 1.45 (s, 9H, $OC(CH_3)_3$), 1.77–1.83 (m, 2H, NCH_2CH_2), 2.30–2.33 (m, 2H, NCH_2CH_2), 2.61–2.66 (m, 2H, NCH_2), 3.92–3.95 (m, 2H, NCH_2), 7.23–7.28 (m, 3H, H_{aromat}), 7.34–7.37 (m, 2H, H_{aromat}). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, DEPT, 80 °C) $\delta=26.1$ (q, CH_3), 28.6 (q, CH_3), 29.3 (t, CH_2), 36.1 (s), 40.9 (t, CH_2), 43.4 (s), 78.9 (s), 125.8 (d, C_{aromat}), 127.6 (d, C_{aromat}), 129.9 (d, C_{aromat}), 139.8 (s, C_{aromat}), 155.0 (s, CO). MS (CI, CH_5^+); *m*/*z* (%): 318 (12) $[M+1]^+$, 262 (100), 218 (13). IR (KBr): $\tilde{\nu}=2968$ cm^{-1}, 2872, 1689. Anal. Calcd for $C_{20}H_{31}NO_2$ (317.48): C 75.67, H 9.84, N 4.41. Found C 75.53, H 9.91, N 4.40.

4.4.20. 4-Benzyl-4-isopropyl-piperidine-1-carboxylic acid *tert*-butyl ester (6c). According to GP3 from **4m** (151.1 mg, 0.409 mmol), $NaBH_3CN$ (64.1 mg, 1.02 mmol) in MeOH (3 ml), HCl 2 M in Et_2O (1.28 ml) and Boc_2O (98.2 mg, 0.450 mmol).

Yield 120 mg (92%), colorless crystals, mp 84–85 °C. TLC $R_f=0.34$ (SiO_2, *n*-pentane/EtOAc 95:5). ^1H NMR (400 MHz, $C_2D_2Cl_4$, 100 °C) $\delta=0.96$ (d, $J=6.8$ Hz, 6H, $CH(CH_3)_2$), 1.34–1.39 (m, 2H, NCH_2CH_2), 1.46 (s, 9H, $C(CH_3)_3$), 1.57–1.62 (m, 2H, NCH_2CH_2), 1.97 (sept, $J=$ 6.8 Hz, 1H, $CH(CH_3)_2$), 2.69 (s, 2H, CH_2Ph), 3.38–3.50 (m, 4H, NCH_2), 7.15–7.32 (m, 5H, H_{aromat}). ^{13}C NMR (100 MHz, $C_2D_2Cl_4$, DEPT, 100 °C) $\delta=16.7$ (q, CH_3), 28.6 (q, CH_3), 30.1 (d, *C*H), 31.0 (t, CH_2), 37.3 (s), 38.8 (t, CH_2Ph), 39.8 (t, NCH_2), 79.0 (s), 126.0 (d, C_{aromat}), 127.9 (d, C_{aromat}), 130.9 (d, C_{aromat}), 138.8 (s, C_{aromat}), 155.2 (s, CO). MS (CI, CH_5^+); *m*/*z* (%): 318 (2) $[M+1]^+$, 262 (100), 218 (11). IR (KBr): $\tilde{\nu}=2973$ cm^{-1}, 1679, 1418, 1155. Anal. Calcd for $C_{20}H_{31}NO_2$ (317.48): C 75.50, H 9.89, N 4.42. Found C 75.23, H 9.96, N 4.42.

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