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ARTICLE TYPE

Trimethylsilyl Chloride Promoted Synthesis of α -branched amines by Nucleophilic Addition of Organozinc Halides to Nitrones

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A general procedure for the nucleophilic addition of organozinc halides with nitrones in the presence of trimethylsilyl chloride has been developed. Trimethylsilyl chloride was found to be both an indispensable reaction promoter and a ready hydroxylamine protection agent in these reactions. The produced O-(trimethylsilyl)hydroxylamines can be easily reduced into corresponding amines just by a zinc-copper couple in saturated aqueous NH_4Cl solution.

α -Branched amines represent an important class of nitrogen containing compounds regarding their attractive biological and pharmacological activities. As for example, Remacemide is used for the treatment of acute ischemic stroke, epilepsy, Huntington's disease and Parkinson's disease.¹ Rivastigmine is a reversible cholinesterase inhibitor and is used to treat Alzheimer's disease.² In addition, α -Branched amines are highly valuable molecules in bioorganic chemistry as they are widely found in natural such as 2,5-dideoxy-2,5-imino-D-mannitol DMDP and 2,5-dideoxy-2,5-imino-DL-glycero-D-manno-heptitol (homo-DMDP) which are found to be efficient glycosidase inhibitors.³ Thus, efficient syntheses of a library of α -branched amines are of interest in both organic and medicinal chemistry.⁴

reagents are frequently deployed in these conversions due to their ready availability and high reactivity, especially when chiral nitrones⁶ or chiral catalysts⁷ were introduced, high yields as well as high stereoselectivities are always obtained. A large variety of natural and semi-natural products such as pyrrolizidines and indolizidines were successfully prepared via this protocol.⁸ However, Organozinc reagents, as a kind of less reactive yet more selective organometallic reagents,⁹ although extensively used in the reactions with carbonyl compounds, are less explored in reactions with imine derivatives, such as nitrones. A few reports have appeared in which some reactive organozinc species, such as diorganozinc¹⁰ or diorganozinc mediated alkynylation,¹¹ allylation,¹² vinylation¹³ and the Reformsky reaction¹⁴ are effective. However, to the best of our knowledge, a practical synthesis of α -branched amine derivatives by nucleophilic addition of nitrones with organozinc halides has not been reported to date.

Actually, organozinc halides are one of the most useful organometallic reagents that can be easily prepared by direct insertion of zinc metal into corresponding functionalized organic halides and are therefore considered as a "real kind of" functionalized organometallics.¹⁵ We were attracted by their wide application in synthetic chemistry, and have reported that reaction of benzylic zinc halides with aryl aldehydes under transition-metal-complex catalysis in the presence of trimethylsilyl chloride (TMSCl) leads to *trans*-stilbenes in high yield,¹⁶ whereas reaction of primary alkyl zinc halides with aromatic aldehydes under the same conditions gave α,α -dialkyltoluenes.¹⁷ To broaden the utility of organozinc reagents in organic synthesis, especially with the aim of exploring the utilization of organozinc halides as a mild and selectively functionalized nucleophile for the synthesis of α -branched amines, we report here an interesting TMSCl promoted nucleophilic addition reaction of organozinc halides with nitrones in which TMSCl was found to be both an indispensable reaction promoter and a ready hydroxylamine protection reagent.

Initially, the reaction of benzylzinc chloride **1a** and *N*-(4-methoxybenzylidene)aniline oxide **2a** was examined without any catalyst. Unfortunately, no reaction occurred at room temperature. When the reaction temperature was raised to 60 °C, the reaction proceeded sluggishly and after 6 hours, the nitrone **2a** had completely reacted and the corresponding hydroxylamine **3a** was obtained in 65% yield (Table 1, entries 1 and 2).

Fig 1. drugs and natural products of α -branched amine

The nucleophilic addition reaction of organometallic reagents to nitrones is a convenient and reliable procedure, and hence, is widely used in the synthesis of structurally variable α -branched amines.⁵ Grignard reagents and organolithium

Lewis acids can greatly enhance the reactivity of nitrones in various kinds of reactions such as 1, 3-dipolar cycloaddition¹⁸ and nucleophilic addition reactions.^{8b} When one equiv of TMSCl was added, the reaction proceeded slowly at room temperature and nitrone **2a** disappeared in six hours. However, hydroxylamine **3a** and the O-TMS hydroxylamine ether **4a** were formed in 78% overall yield (**3a/4a** 1:3). When 2 equivalents of TMSCl were added, the reaction proceeded quite quickly and cleanly. Nitrone **2a** reacted in only 30 minutes and the O-TMS hydroxylamine ether **4a** was obtained as the only product in 92% isolated yield (Table 1, entries 3 and 4).

With the preliminary success of the effect of trimethylsilyl chloride, several other organosilyl reagents were then screened. TMSBr, TMSI and TMSOTf worked in the same way in this reaction system. They all gave the desired silylated hydroxylamine derivatives **4a** cleanly with similar yield compared to TMSCl (entries 5-7). However, the widely used hydroxyl group protection reagents, *tert*-butyldimethylsilyl chloride (TBDMSCl) and *tert*-butyldiphenylsilyl chloride (TBDPSCI) were ineffective (entries 8, 9). When considering the price and availability of these trimethylsilyl compounds, TMSCl is the best choice and was selected in our following studies.

Table 1. Optimization of the reaction conditions^a

Entry	temp[°C]	time [h]	5 (equiv) ^b	3a/4a	yield [%] ^d
1	RT	12	-	-	0
2	60	6	-	1/0	65
3	RT	6	TMSCl (1.0)	1/3 ^c	78
4	RT	0.5	TMSCl (2.0)	1/0	92
5	RT	0.5	TMSBr (2.0)	1/0	88
6	RT	0.5	TMSI (2.0)	1/0	86
7	RT	0.5	TMSOTf (2.0)	1/0	91
8	RT	6	TBDMSCl (2.0)	-	-
9	RT	6	TBDPSCI (2.0)	-	-

^a Reaction conditions: nitrone **2a** (3 mmol) was treated with benzylic zinc chloride **1a** (4.5 mmol) and organosilyl halides in THF (15 mL) at room temperature under argon. ^b Amount of organosilyl halides was based on nitrone **2a**. ^c The ratio was determined by ¹H NMR spectra. ^d Isolated yields.

Attracted by this unexpected reactivity, we then investigated the efficacy of TMSCl on reactions of various benzylic zinc halides and α , *N*-diaryl nitrones. Different kinds of α , *N*-diaryl nitrones bearing both electron donating and electron withdrawing groups were subjected to the optimized reaction conditions (Table 2). The results showed that the reaction has broad applicability. *N*-phenyl nitrones bearing both electron-donating and electron-withdrawing groups on the C-phenyl rings reacted with benzylic zinc halide to give the corresponding O-silylated hydroxylamines in high to very high yields (Table 2, entries 1-11). Aromatic heterocyclic aldehydes derivated nitrones such as 3-thienyl and 2-furanyl substituted nitrones all reacted smoothly with benzylic zinc halides with the corresponding silylated hydroxylamine derivatives were obtained in high (Table 2, entries 9, 10, 12 and 18). Interestingly, hydroxyl substituents on the benzylidene ring of the nitrones do not require further protection as the desired O-

silylated hydroxylamine ethers were obtained in good yield when a 2.5 molar ratio of benzylic zinc chloride was added (Table 2, entries 7 and 11).

Encouraged by our success with benzylic zinc chlorides, we then investigated other organozinc reagents (Table 3). To our delight, other organozinc reagents (R^1ZnBr) selected, such as R^1 = aryl (entries 1-5, 15), hetero aromatics R^1 = 3-thienyl (entries 6-8) and alkyl zincs (entries 9-14) all gave the desired products in high yields (entries 1-15). Alkyl zinc halide species of both primary alkyl zinc halide (entries 9-12) and secondary alkyl zinc halide (entries 13, 14) can also be applied here. Halogens such as chloro, fluoro are tolerated in both organozinc halides and nitrones. However, nitrones bearing hydroxyl groups when subjected to organozinc reagents, were unreactive (entries 16 and 17). This is probably due to the strong electron donating effects of the phenolate, of the hydroxylated nitrone¹⁹ significantly reducing the electrophilicity of these nitrones so that only the more reactive organozinc species such as benzylic zinc halide can be used successfully.

Table 2. Reaction of benzylic zinc chlorides with α , *N*-diaryl nitrones^a

Reaction scheme showing the reaction of a benzylic zinc chloride (**1**) with a nitrone (**2**) in the presence of TMSCl at room temperature to form an O-TMS hydroxylamine ether (**4**).

Structure **1**: ArCH_2ZnX

Structure **2**: $\text{R}-\text{CH}=\text{N}^+\text{Ph}-\text{O}^-$

Structure **4**: $\text{R}-\text{CH}(\text{CH}_2\text{Ar})-\text{N}(\text{OTMS})\text{Ph}$

Entry	Ar	R	4	yield (%) ^b
1	Ph (1a)	4-CH ₃ OC ₆ H ₄ (2a)	4a	92
2	Ph (1a)	Ph (2b)	4b	90
3	Ph (1a)	2-ClC ₆ H ₄ (2c)	4c	76
4	Ph (1a)	4-ClC ₆ H ₄ (2d)	4d	94
5	Ph (1a)	2,4-Cl ₂ C ₆ H ₃ (2e)	4e	91
6	Ph (1a)	3,4,5-(CH ₃ O) ₃ C ₆ H ₂ (2f)	4f	85
7	Ph (1a)	3-HO-4-CH ₃ OC ₆ H ₃ (2g)	4g	66 ^c
8	Ph (1a)	4-CH ₃ C ₆ H ₄ (2h)	4h	86
9	Ph (1a)	3-thienyl (2i)	4i	86
10	Ph (1a)	2-furanyl (2j)	4j	74
11	Ph (1a)	4-HOC ₆ H ₄ (2k)	4k	56
12	4-Cl C ₆ H ₄ (1b)	3-thienyl (2i)	4l	79
13	4-Cl C ₆ H ₄ (1b)	Ph (2b)	4m	86
14	4-Cl C ₆ H ₄ (1b)	4-CH ₃ OC ₆ H ₄ (2a)	4n	88
15	4-Cl C ₆ H ₄ (1b)	3,4,5-(CH ₃ O) ₃ C ₆ H ₂ (2f)	4o	83
16	4-Cl C ₆ H ₄ (1b)	2,4-Cl ₂ C ₆ H ₃ (2e)	4p	82
17	2-ClC ₆ H ₄ (1c)	Ph (2b)	4q	66
18	2-naphthyl (1d)	4-ClC ₆ H ₄ (2c)	4r	72

^a Unless otherwise noted, the reaction was performed by employing benzylic zinc chloride (4.5 mmol), *N*, α -diphenyl nitrone (3 mmol) in THF (15 mL). ^b Isolated yield. ^c Benzylic zinc halide (2.5 equiv).

Although Grignard reagents can react readily with nitrones and give hydroxylamines in high yield,²⁰ our TMSCl promoted organozinc reagent method has some significant advantages. The organozinc reagent can be highly functionalized whereas functionalized Grignard reagents are not readily utilized. The most practical advantage of our protocol is that the reaction of Grignard reagents with nitrones leads only to hydroxylamines and since the hydroxylamine derivatives, especially *N*-substituted aromatic hydroxylamines are very air sensitive, they decompose readily^[20] and usually cannot be isolated in a pure form by quickly polymerizing after column chromatography. Thus, the synthesis, purification and characterization of hydroxylamines proved challenging. Even when these compounds were kept

under nitrogen in a deep freezer for several weeks, they were found to have decomposed as indicated by ^1H NMR analysis. However, in our protocol, the *O*-TMS hydroxylamine ethers are stable to air and can be kept in a refrigerator for months without any decomposition. We consider our protocol whereby TMSCl serves as a reaction promoter and a ready *N*-hydroxylamine protecting reagent is a significant improvement on the reaction of any other previously reported Grignard and diorganozinc methods.

Table 3. Reaction of various organozinc halides with nitrones^a

$\text{R}_1\text{ZnX} + \text{R}_2\text{C}=\text{N}^+\text{R}_3 \xrightarrow[\text{RT}]{\text{TMSCl}} \text{R}_2\text{C}(\text{R}_1)\text{N}(\text{R}_3)\text{OTMS}$					
Entry	6	R ¹	R ²	R ³	yield(%) ^b
1	6a	Ph	Ph	4-FC ₆ H ₄	84
2	6b	Ph	Ph	2-ClC ₆ H ₄	71
3	6c	Ph	Ph	3,4,5-(CH ₃ O) ₃ C ₆ H ₂	91
4	6d	Ph	Bn	Ph	88
5	6b	2-ClC ₆ H ₄	Ph	Ph	86
6	6e	3-Thenyl	Ph	2-ClC ₆ H ₄	76
7	6f	3-Thenyl	Ph	4-FC ₆ H ₄	87
8	6g	3-Thenyl	Ph	2,4-Cl ₂ C ₆ H ₃	92
9	6h	<i>n</i> -Hexyl	Ph	4-CH ₃ OC ₆ H ₄	73
10	6i	<i>n</i> -Hexyl	Ph	3,4,5-(CH ₃ O) ₃ C ₆ H ₂	79
11	6j	<i>n</i> -Hexyl	Ph	2-Thenyl	74
12	6k	<i>n</i> -Hexyl	Ph	2-ClC ₆ H ₄	66
13	6l	<i>s</i> -Butyl	Ph	4-CH ₃ C ₆ H ₅	54
14	6m	<i>s</i> -Butyl	Ph	4-CH ₃ OC ₆ H ₅	43
15	6n	1-naphthyl	Ph	4-CH ₃ C ₆ H ₅	73
16		ph	Ph	3-HO-4-CH ₃ OC ₆ H ₃	NR ^c
17		<i>n</i> -Hexyl	Ph	4-HOC ₆ H ₄	NR ^c

^a Unless otherwise noted, the reaction was performed by employing organozinc halide (4.5 mmol), N, α -diphenyl nitron (3 mmol) in THF (20 mL). ^b Isolated yield. ^c NR = No reaction.

The *O*-trimethylsilyl hydroxylamine ethers can be easily converted into corresponding amines by simply stirring the ethers with a zinc-copper couple in a saturated aqueous NH₄Cl at 50 °C for 1 hour. As illustrated in Scheme 1, the substrates **4a** and **4f** were reduced using this protocol to the corresponding amines in 77% and 72% isolated yields respectively.

Scheme 1. Reduction of *O*-TMS hydroxylamine ethers to amines

To test the application of our TMSCl promoted organozinc protocol for natural product synthesis, we prepared a cyclic nitron **9** from D-mannose²¹ (Scheme 2). Gratifyingly, **9** reacted with phenylzinc bromide, [no reaction without TMSCl] in the presence of two equivalents of TMSCl at room temperature to furnish the desired *O*-TMS-hydroxylamine ether **10** in 84% yield stereospecifically. Upon further stirring the reaction mixture at room temperature for 2 hours in saturated aqueous NH₄Cl solution and with zinc metal in the presence of catalytic amount of Cu(OAc)₂, **10** was completely reduced to the pyrrolidine **11** in 91% yield. Deprotection of **11** by catalytic hydrogenation in acid

solution gave the α -ethyl polyhydroxylated pyrrolidine **12** in quantitative yield which is a structural analogue of 2,5-dideoxy-2,5-imino-D-glycero-D-manno-heptitol (homo DMDP), a natural selective inhibitors of β -glucosidases.^{3b}

Scheme 2. Synthesis of branched polyhydroxylated pyrrolidine **12**

In conclusion, we have successfully developed a new method for the synthesis of substituted *O*-trimethylsilyl hydroxylamine ethers via a TMSCl-catalyzed nucleophilic addition of organozinc halides to nitrones. To the best of our knowledge, the present reaction is the first example of a TMSCl catalyzed nucleophilic addition reaction of organozinc reagents with nitrones whereby the TMSCl acts both as a reaction promoter and a good protection reagent for the sensitive *N*-hydroxylamine group. Furthermore, the *O*-TMS protected hydroxylamine ethers can be easily reduced by zinc to the corresponding amines. This protocol offers a practically useful method in natural products synthesis.

Notes and references

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Supporting Information

Trimethylsilyl Chloride Promoted Synthesis of α -branched amines by Nucleophilic Addition of Organozinc Halides to Nitrones

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General Experimental Section:

Analytic methods. All the reactions were carried out under argon atmosphere using standard Schlenk technique. ^1H NMR (400 MHz), and ^{13}C NMR (100 MHz) were recorded on Bruker AV400 NMR spectrometer with CDCl_3 as solvent. Chemical shifts of ^1H and ^{13}C NMR spectra are reported in parts per million (ppm) with TMS as an internal standard. All coupling constants (J values) were reported in Hertz (Hz). Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt), triplet (t), triplet of doublets (td), quartet (q), and multiplet (m). Column chromatography was performed on silica gel 300–400 mesh. Analytical thin-layer chromatography (TLC) was performed on pre-coated, glass-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance (254 nm). IR spectra were recorded as KBr disks on a Alpha Centauri FT-IR spectrometer. EI mass spectra and HRMS were done on QP-1000A GCMS spectrometer by EI ionization at 70 eV. ESI mass spectra were recorded on a Bruker Esquire 6000.

General preparation for chemicals. The substrates N-phenylhydroxylamine^[1] and N-benzyl hydroxylamine^[2] was prepared according to the known procedure. α ,N-diphenyl nitron derivatives were prepared from benzaldehydes and N-hydroxylamines following a modified literature procedure.^[3] Benzylic zinc halides were prepared following the Knochel's procedure.^[4] Arylic zinc halides and alkyl were prepared by transmetalation of corresponding Grignard reagents with ZnCl_2 and were titrated by standard procedure.^[5] All other reagents used are from commercial sources and used without any further purification.

General Procedure A: TMSCl promoted reaction of organozinc halides with nitrones

General procedure for the TMSCl promoted reaction of organozinc halides with nitrones. The organozinc halides were used immediately after preparation. TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was slowly added to a solution of organozinc halides (4.5 mmol) and nitron (3.0 mmol) in THF (10 mL) at room temperature. The reaction mixture was heated to 30 °C and stirred at this temperature for 4 h. After cooling to room temperature, the reaction solution was quenched with saturated NH_4Cl (10 mL), 20 mL of ethyl acetate was then added and the organic phase was separated, washed with 10 mL of water and then with 10 mL of brine. The water phase was extracted with ethyl acetate (2×10 mL). The combined organic phase was then dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography on silica gel with petroleum/ethyl acetate as eluent gave the protected O-trimethylsilyl hydroxylamine ethers.

Synthesis and characterization of products 4 and 6:

4a: N-(1-(4-methoxyphenyl)-2-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-methoxyphenyl) nitron **2a** (0.68 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.94 g, 2.4 mmol, 80 %) after purification on silica gel (10:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3424, 3062, 3028, 2958, 2836, 1609, 1487, 1453, 1249, 1207, 919; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.05 (s, 9H), 3.42 (dd, $J = 13.6, 10.7$ Hz, 1H), 3.53 (dd, $J = 13.8, 3.9$ Hz, 1H), 3.73 (s, 3H), 4.44 (dd, $J = 10.6, 3.9$ Hz, 1H), 6.70 (d, $J = 8.4$ Hz, 2H), 7.17 (dd, $J = 7.4, 0.9$ Hz, 3H), 7.24 (d, $J = 6.2$ Hz, 1H), 7.29 (t, $J = 13.7$ Hz, 6H), 7.40 (dd, $J = 10.8, 2.9$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): -0.5, 36.1, 55.0, 75.2, 112.8, 120.7, 123.3, 125.6, 128.0, 128.0, 129.2, 131.1, 139.4, 152.6, 158.7. MS (EI, 70 eV): m/z (%) = 211 (100), 391 (0.06, $[\text{M}]^+$); Anal. Calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_2\text{Si}$: C, 73.61; H, 7.46; N, 3.58. Found: C, 73.38; H, 6.96; N, 3.43.

4b: N-(1,2-diphenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was slowly added to a solution of N, α -diphenyl nitron **2b** (0.60 g, 3.0 mmol) and benzylzinc chloride (4.5 mmol) in 10 ml of THF at room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.90 g, 4.2 mmol, 83 %) after purification on silica gel (20:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3063, 3029, 2959, 1595, 1487, 1452, 1205, 878, 843; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.07 (s, 9H), 3.23-3.35 (m, 2H), 4.48 (q, $J = 4.0$ Hz, 1H), 6.93-7.02 (m, 3H), 7.11 (dt, $J = 7.2, 1.6$ Hz, 1H), 7.12-7.21 (m, 4H), 7.21-7.32 (m, 7H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): -0.5, 35.9,

75.8, 120.7, 123.5, 125.6, 127.2 127.5, 128.0, 128.1, 129.2, 130.1, 138.3, 139.3, 152.6. MS (EI, 70 eV): m/z (%) = 270 (100), 361 (1.0, $[M]^+$). Anal. Calcd for $C_{23}H_{27}NOSi$: C, 76.41; H, 7.53; N, 3.87. Found: C, 76.11; H, 7.22; N, 3.58.

4c: N-(1-(2-chlorophenyl)-2-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2-chlorophenyl) nitron **2c** (0.70 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.66 g, 1.7 mmol, 56 %) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3339, 3063, 3027, 1596, 1487, 1449, 1088, 1034, 921, 880; 1H NMR (400 MHz, $CDCl_3$) δ (ppm): -0.29 (s, 9H), 3.12 (dd, J = 14.6, 3.8 Hz, 1H), 3.32 (dd, J = 14.3, 11.4 Hz, 1H), 5.18 (dd, J = 11.2, 3.6 Hz, 1H), 6.86 (d, J = 6.8 Hz, 2H), 6.94 (tq, J = 7.2, 1.6 Hz, 2H), 6.98-7.08 (m, 3H), 7.14 (td, J = 7.6, 1.2 Hz, 1H), 7.16-7.28 (m, 5H), 7.56 (dd, J = 7.9, 1.7 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): -0.9, 32.6, 70.0, 119.6, 123.2, 125.7, 125.8, 128.0, 128.2, 128.6, 128.9, 131.0, 135.9, 136.1, 138.5, 152.7. MS (EI, 70 eV): m/z (%) = 304 (100), 395 (1.9, $[M]^+$). Anal. Calcd for $C_{23}H_{26}ClNOSi$: C, 69.76; H, 6.62; N, 3.54. Found: C, 70.04; H, 6.36; N, 3.33.

4d: N-(1-(4-chlorophenyl)-2-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-chlorophenyl) nitron **2d** (0.70 g, 3.0 mmol),

benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.97 g, 2.46 mmol, 82 %) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3028, 2960, 1596, 1490, 1250, 880, 844; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 0.02 (s, 9H), 3.26 (dd, $J = 13.6, 10.8$ Hz, 1H), 3.40 (dd, $J = 13.6, 4.0$ Hz, 1H), 4.49 (q, $J = 4.0$ Hz, 1H), 6.93-7.20 (m, 12H), 7.20-7.26 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm): -0.5, 36.7, 75.3, 120.8, 123.8, 125.9, 127.6, 128.1, 129.1, 131.3, 133.0, 136.6, 138.8, 152.4; MS (EI, 70 eV): m/z (%) = 304 (100), 395 (4.5, $[\text{M}]^+$). Anal. Calcd for $\text{C}_{23}\text{H}_{26}\text{ClNOSi}$: C, 69.76; H, 6.62; N, 3.54. Found: C, 69.93; H, 6.42; N, 3.75.

4e: N-(1-(2,4-dichlorophenyl)-2-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2,4-dichlorophenyl) nitron **2e** (0.80 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.92 g, 2.13 mmol, 71 %) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3029, 2959, 1593, 1488, 1451, 1250, 880, 843, 738, 698; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.01 (s, 9H), 3.36 (dd, $J = 14.4, 3.6$ Hz, 1H), 3.49 (dd, $J = 14.4, 11.2$ Hz, 1H), 5.36 (ddd, $J = 11.2, 4.0, 1.6$ Hz, 1H), 7.10 (d, $J = 8.0$ Hz, 2H), 7.15-7.30 (m, 4H), 7.36 (ddd, $J = 8.4, 3.2, 1.6$ Hz, 1H), 7.40-7.50 (m, 5H), 7.74 (dd, $J = 8.4, 1.5$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.9, 33.9, 69.4, 109.7, 110.1, 120.0, 123.5, 125.9, 128.1, 128.2, 128.9, 139.0, 141.5, 141.5, 152.1, 152.4. MS (EI, 70 eV): m/z (%) = 338 (100), 429 (1.8, $[\text{M}]^+$); Anal. Calcd for $\text{C}_{23}\text{H}_{25}\text{Cl}_2\text{NOSi}$: C, 64.18; H, 5.85; N, 3.25. Found: C, 63.87; H, 5.52; N, 3.07.

4f: N-phenyl-N-(2-phenyl-1-(3,4,5-trimethoxyphenyl)ethyl)-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3,4,5-trimethoxyphenyl) nitron **2f** (0.86 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was

stirred at this temperature for half an hour. The pure product was obtained as colorless oil (1.02 g, 2.25 mmol, 75%) after purification on silica gel (10:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2953, 2838, 1503, 1457, 1422, 1347, 1244, 1126, 1101, 922, 880, 844; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.13 (s, 9H), 3.11 (dd, $J = 13.7, 10.5$ Hz, 1H), 3.20 (dd, $J = 13.9, 3.9$ Hz, 1H), 3.59 (s, 6H), 3.68 (s, 3H), 4.30 (q, $J = 3.9$ Hz, 1H), 6.31 (s, 2H), 6.84-6.96 (m, 4H), 6.96-7.06 (m, 4H), 7.17 (t, $J = 8.4$ Hz, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.7, 36.0, 55.7, 60.5, 75.7, 107.0, 120.4, 123.3, 125.6, 127.8, 127.9, 128.9, 130.4, 137.1, 138.9, 152.0, 152.2. HRMS (ESI): calcd. for $\text{C}_{26}\text{H}_{34}\text{NO}_4\text{Si}$ $[\text{M}]^+$: 452.2257, found: 452.2258.

4g: 2-methoxy-5-(2-phenyl-1-(phenyl((trimethylsilyl)oxy)amino)ethyl)phenol

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 mL, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3-hydroxy-4-methoxyphenyl) nitron **2g** (0.73 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 mL of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.80 g, 1.98 mmol, 66%) after purification on silica gel (10:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3541, 3063, 3028, 2854, 1595, 1452, 1130, 1026, 987, 920, 872, 844; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.03 (s, 9H), 3.21 (dd, $J = 13.8, 10.7$ Hz, 1H), 3.29 (dd, $J = 13.8, 3.9$ Hz, 1H), 3.78 (s, 3H), 4.39 (dd, $J = 10.6, 4.0$ Hz, 1H), 5.47 (s, 1H), 6.54 (dd, $J = 8.0, 2.0$ Hz, 1H), 6.58 (d, $J = 8.4$ Hz, 1H), 6.90-7.06 (m, 4H), 7.06-7.12 (m, 3H), 7.16-7.22 (m, 3H), 7.24-7.30 (m, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 37.9, 55.6, 75.2, 109.4, 116.1, 120.6, 123.3, 125.6, 127.9, 128.0, 128.3, 129.1, 131.5, 139.3, 144.6, 145.6, 152.6; MS (EI, 70 eV): m/z (%) = 227 (100), 407 (0.6); Anal. Calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_3\text{Si}$: C, 70.72; H, 7.17; N, 3.44. Found: C, 70.48; H, 7.04; N, 3.25.

4h: N-phenyl-N-(2-phenyl-1-(p-tolyl)ethyl)-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(methylphenyl) nitron **2h** (0.63 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.86 g, 2.28 mmol, 76%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3027, 2958, 2924, 1595, 1487, 1250, 879, 843; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 0.31 (s, 9H), 2.27 (s, 3H), 3.25-3.45 (m, 2H), 4.49-4.58 (m, 1H), 6.90-7.40 (m, 14H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.6, 22.5, 36.1, 75.7, 120.5, 123.4, 125.7, 127.9, 129.0, 129.9, 133.6, 135.1, 137.2, 139.1, 141.6, 152.4. MS (EI, 70 eV): m/z (%) = 195 (100), 375 (0.58, $[\text{M}]^+$). Anal. Calcd for $\text{C}_{24}\text{H}_{29}\text{NOSi}$: C, 76.75; H, 7.78; N, 3.73. Found: C, 76.47; H, 7.84; N, 3.42.

4i: N-phenyl-N-(2-phenyl-1-(thiophen-3-yl)ethyl)-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3-thienyl) nitron **2i** (0.61 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.88 g, 2.4 mmol, 80%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3028, 2959, 1596, 1488, 1452, 1304, 1250, 1203, 1080, 925, 878; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 0.20 (s, 9H), 3.34 (dd, J = 13.6, 10.8 Hz, 1H), 3.56 (dd, J = 13.6, 3.6 Hz, 1H), 4.90 (dd, J = 10.8, 4.0 Hz, 1H), 6.71 (s, 1H), 6.86 (dd, J = 5.2, 3.6 Hz, 1H), 7.10 (t, J = 13.2 Hz, 1H), 7.19 (t, J = 7.6 Hz, 2H), 7.20-7.26 (m, 6H), 7.26-7.34 (m, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): 0.8, 33.4, 78.7, 116.7, 119.9, 123.5, 125.9, 126.2, 128.2, 128.4, 129.1, 131.8, 133.6, 134.6, 136.7, 138.1, 152.4. MS (EI, 70 eV): m/z (%) = 187 (100), 367 (0.2, $[\text{M}]^+$); Anal. Calcd for $\text{C}_{21}\text{H}_{25}\text{NOSSi}$: C, 68.62; H, 6.86; N, 3.81; S, 8.72. Found: C, 68.36; H, 6.64; N, 3.48; S, 7.47.

4j: N-(1-(furan-2-yl)-2-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2-furanyl) nitron **2j** (0.56 g, 3.0 mmol), benzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.78 g, 2.4 mmol, 74%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2958, 2926, 1590, 1486, 1452, 1250, 878, 697; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.19 (s, 9H), 3.00-3.07 (m, 2H), 4.40 (q, $J = 7.2$ Hz, 1H), 5.95 (d, $J = 3.41$ Hz, 1H), 6.03-6.05 (m, 1H), 6.75-7.00 (m, 8H), 7.03-7.15 (m, 2H), 7.39-7.41 (m, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.8, 33.4, 69.5, 119.9, 123.5, 125.9, 126.2, 128.2, 128.8, 129.1, 131.8, 133.6, 134.6, 136.7, 138.1, 152.4. MS (EI, 70 eV): m/z (%) = 171 (100), 351 (0.6, $[\text{M}]^+$); Anal. Calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_2\text{Si}$: C, 71.75; H, 7.17; N, 3.98. Found: C, 71.57; H, 6.94; N, 3.88.

4k: 4-(2-(4-chlorophenyl)-1-(phenyl((trimethylsilyl)oxy)amino)ethyl)phenol

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-hydroxyphenyl) nitron **2k** (0.64 g, 3.0 mmol), 4-chlorobenzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.99 g, 2.4 mmol, 56%) after purification on silica gel (20:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3334, 3029, 2959, 2926, 1597, 1489, 1452, 921, 842; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.05 (s, 9H), 3.21 (dd, $J = 13.8, 10.7$ Hz, 1H), 3.29 (dd, $J = 13.8, 3.9$ Hz, 1H), 4.40 (dd, $J = 10.6, 4.0$ Hz, 1H), 5.40 (brs, 1H), 6.63 (dd, $J = 4.8, 2.0$ Hz, 1H), 6.92-7.12 (m, 11 H), 7.19 (dd, $J = 8.4, 7.2$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 36.1, 67.9, 75.2, 114.4, 120.7, 123.4, 125.6, 127.9, 128.0, 129.2, 130.3, 131.3, 139.4, 152.6, 154.9. MS (EI, 70 eV): m/z (%) = 197.15 (100), 412

(0.59, $[M+H]^+$); Anal. Calcd for $C_{23}H_{26}ClNO_2Si$: C, 67.05; H, 6.36; N, 3.40. Found: C, 66.83; H, 6.12; N, 3.16.

4l: N-(2-(4-chlorophenyl)-1-(thiophen-3-yl)ethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3-thienyl) nitron **2i** (0.61 g, 3.0 mmol), 4-chlorobenzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish syrup (0.95 g, 2.4 mmol, 79%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3067, 3029, 2959, 1593, 1490, 1449, 1407, 1250, 1204, 1094, 880, 847, 766, 698; 1H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.16 (s, 9H), 3.26 (dd, $J = 13.6, 10.8$ Hz, 1H), 3.41 (dd, $J = 13.2, 3.6$ Hz, 1H), 4.49 (dd, $J = 14.4, 3.6$ Hz, 1H), 6.50 (s, 1H), 6.95-7.25 (m, 12H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): -0.5, 38.6, 71.6, 120.2, 123.6, 125.2, 125.7, 127.2, 128.2, 130.4, 131.7, 137.4, 140.3, 152.1. MS (EI, 70 eV): m/z (%) = 276 (100), 401 (0.97, $[M]^+$); Anal. Calcd for $C_{21}H_{24}ClNOSSi$: C, 62.74; H, 6.02; N, 3.48. Found: C, 62.88; H, 5.78; N, 3.16.

4m: N-(2-(4-chlorophenyl)-1-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-phenyl nitron **2a** (0.59 g, 3.0 mmol), 4-chlorobenzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish syrup (0.90 g, 2.28 mmol, 76%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3063, 3028, 2967, 2926, 1596, 1489, 1452, 1406, 1375, 1300, 1256, 1207, 1169, 1095, 1028, 966, 930, 874; 1H NMR (400 MHz, $CDCl_3$) δ (ppm): -0.086 (s, 9H), 3.18-3.30 (m, 2H), 4.59 (q, $J = 4.8$ Hz, 1H), 6.86 (d, $J = 8.0$ Hz, 2H), 7.04 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 2H),

7.15-7.25 (m, 8H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.6, 35.3, 75.8, 120.7, 123.6, 127.5, 127.6, 128.1, 128.1, 130.0, 130.5, 131.4, 137.7, 138.0, 152.5. MS (EI, 70 eV): m/z (%): 270 (100), 395 (0.23, $[\text{M}]^+$); Anal. Calcd for $\text{C}_{23}\text{H}_{26}\text{ClNOSi}$: C, 69.76; H, 6.62; N, 3.54. Found: C, 69.58; H, 6.42; N, 3.43.

4n: N-(2-(4-chlorophenyl)-1-(4-methoxyphenyl)ethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-methoxyphenyl) nitron **2b** (0.68 g, 3.0 mmol), 4-chlorobenzylzinc chloride (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (0.99 g, 2.34 mmol, 78%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2957, 2926, 1596, 1489, 1452, 1406, 1251, 1207, 1169, 1095, 1028, 966, 874, 844; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 0.10 (s, 9H), 3.37 (dd, $J = 14.0, 3.2$ Hz, 1H), 3.48 (dd, $J = 13.6, 3.6$ Hz, 1H), 3.88 (s, 3H), 4.60 (dd, $J = 10.8, 4.0$ Hz, 1H), 6.86 (dd, $J = 6.4, 2.0$ Hz, 2H), 7.10-7.22 (m, 4H), 7.22-7.30 (m, 5H), 7.36 (dd, $J = 8.4, 7.2$ Hz, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 36.1, 55.0, 75.2, 112.8, 120.6, 123.3, 125.6, 127.9, 128.0, 129.1, 130.3, 131.0, 139.4, 152.6, 158.7. MS (ESI, m/z): 425.8 $[\text{M}]^+$; Anal. Calcd for $\text{C}_{24}\text{H}_{28}\text{ClNO}_2\text{Si}$: C, 67.66; H, 6.62; N, 3.29. Found: C, 67.45; H, 6.38; N, 3.08.

4o: N-(2-(4-chlorophenyl)-1-(3,4,5-trimethoxyphenyl)ethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 mL, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3, 4, 5-trimethoxyphenyl) nitron **2f** (0.68 g, 3.0 mmol), 4-chlorobenzylzinc chloride (4.5 mmol) in 10 mL of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (1.06 g, 2.34 mmol, 78%) after purification on silica gel (20:1 petroleum ether : EtOAc).

IR (KBr) ν (cm⁻¹): 3575, 3516, 3004, 2961, 1593, 1491, 1423, 1362, 1223, 1128, 1093, 1013, 924, 883, 846; ¹H NMR (400 MHz, CDCl₃) δ (ppm): -0.10 (s, 9H), 3.12 (dd, J = 13.6, 10.8 Hz, 1H), 3.20 (dd, J = 14.0, 4.0 Hz, 1H), 3.59 (s, 6H), 3.68 (s, 3H), 4.33 (dd, J = 6.4, 4.0 Hz, 1H), 6.31 (s, 2H), 6.82-6.96 (m, 2H), 6.98-7.04 (m, 4H), 7.09 (t, J = 8.4 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): -0.6, 35.5, 55.9, 60.6, 75.7, 107.2, 120.6, 123.6, 128.0, 130.3, 133.3, 137.6, 152.2. MS (EI, 70 eV): m/z (%) = 305 (100), 485 (0.2, [M]⁺); Anal. Calcd for C₂₆H₃₂ClNO₄Si: C, 64.24; H, 6.64; N, 2.88. Found: C, 63.96; H, 6.34; N, 2.64.

4p: N-(2-(4-chlorophenyl)-1-(2,4-dichlorophenyl)ethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 mL, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2,4-dichlorophenyl) nitron **2e** (0.68 g, 3.0 mmol), 4-chlorobenzylzinc chloride (4.5 mmol) in 10 mL of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (1.14 g, 2.46 mmol, 82%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm⁻¹): 2958, 2926, 1591, 1489, 1452, 1250, 897, 848; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 0.00 (s, 9H), 3.33 (dd, J = 14.0, 4.0 Hz, 1H), 3.48 (dd, J = 14.0, 11.2 Hz, 1H), 5.31 (dd, J = 11.6, 4.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 7.35-7.54 (m, 3H), 7.56-7.61 (m, 6H), 7.76 (d, J = 8.4 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): -0.9, 33.0, 69.6, 119.9, 123.7, 126.2, 128.3, 128.4, 129.8, 131.7, 133.8, 134.3, 136.6, 152.3, 130.2. MS (EI, 70 eV): m/z (%) = 338 (100), 463 (3.9, [M]⁺); Anal. Calcd for C₂₃H₂₄Cl₃NOSi: C, 59.42; H, 5.20; N, 3.01. Found: C, 59.24; H, 4.96; N, 2.68.

4q: (S)-4-(2-(4-chlorophenyl)-1-(phenyl((trimethylsilyl)oxy)amino)ethyl)phenol

According to general procedure A: A solution of **TMSCl** (0.65 g, 0.78 ml, 6.0 mmol) in **THF** (5 mL) was added slowly to a mixture of **N**-phenyl-**C**-phenyl nitron **2a** (0.59 g, 3.0 mmol), 2-chlorobenzylzinc bromide (4.5 mmol) in 10 ml of **THF** under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (0.78 g, 1.98 mmol, 66%) after purification on silica gel (50:1 petroleum ether : **EtOAc**).

IR (KBr) ν (cm^{-1}): 3334, 3030, 2959, 1597, 1490, 1453, 1251, 921, 842; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.08 (s, 9H), 3.23 (dd, $J = 13.79, 3.5$ Hz, 1H), 3.65 (dd, $J = 13.80, 11.36$ Hz, 1H), 5.27 (dd, $J = 11.2, 3.6$ Hz, 1H), 6.72 (d, $J = 8.0$ Hz, 1H), 6.95-7.15 (m, 7H), 7.20-7.40 (m, 5H), 7.68 (dd, $J = 7.7, 1.6$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.4, 33.6, 66.9, 117.7, 119.6, 120.1, 122.6, 125.4, 127.9, 128.0, 129.2, 130.7, 139.6, 153.3, 154.4. MS (EI, 70 eV): m/z (%) = 197 (100), 395 (0.02, $[\text{M}]^+$); Anal. Calcd for $\text{C}_{23}\text{H}_{26}\text{ClNOSi}$: C, 69.76; H, 6.62; N, 3.54. Found: C, 69.54; H, 6.46; N, 3.44.

4r: N-(1-(2-chlorophenyl)-2-(4-chlorophenyl)ethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of **TMSCl** (0.65 g, 0.78 ml, 6.0 mmol) in **THF** (5 mL) was added slowly to a mixture of **N**-phenyl-**C**-(4-chlorophenyl) nitron **2d** (0.70 g, 3.0 mmol), 1-naphthylzinc bromide (4.5 mmol) in 10 ml of **THF** under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish syrup (0.83 g, 1.86 mmol, 62%) after purification on silica gel (30:1 petroleum ether : **EtOAc**).

IR (KBr) ν (cm^{-1}): 2923, 2852, 1591, 1489, 1456, 1420, 1330, 1244, 1184, 1128, 1011, 928, 887; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.06 (s, 9H), 3.26 (dd, $J = 14.4, 3.2$ Hz, 1H), 3.50 (dd, $J = 14.4, 12$ Hz, 1H), 5.44 (dt, $J = 10.8, 3.2$ Hz, 1H), 6.94 (dd, $J = 6.8, 1.2$ Hz, 2H), 7.05-7.15 (m, 4H), 7.21 (t, $J = 7.6$ Hz, 1H), 7.25-7.50 (m, 8H), 7.72 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.8, 36.9, 69.9, 119.7, 123.3, 125.9, 128.3, 129.4, 129.7, 130.2, 131.4, 135.6, 137.0, 152.5. MS (EI, 70 eV):

m/z (%) = 304 (100), 445 (0.04, $[M]^+$); Anal. Calcd for $C_{27}H_{28}ClNOSi$: C, 72.70; H, 6.33; N, 3.14. Found: C, 72.45; H, 6.08; N, 2.86.

6a: (S)-N-(1-(4-methoxyphenyl)-2-phenylethyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-fluorophenyl) nitron **2l** (0.65 g, 3.0 mmol), phenylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish syrup (0.81 g, 2.22 mmol, 74%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3459, 2923, 2852, 1598, 1506, 1250, 1222, 1027, 843, 756; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.14 (s, 9H), 5.71 (s, 1H), 6.82 (dd, $J = 3.6, 2.0$ Hz, 1H), 6.86 (tt, $J = 3.6, 2.0$ Hz, 1H), 6.92-7.02 (m, 4H), 7.08-7.18 (m, 5H), 7.23 (dd, $J = 5.2, 1.2$ Hz, 1H), 7.42 (dd, $J = 8.4, 6.0$ Hz, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.7, 73.5, 114.5, 114.7, 120.4, 123.7, 125.8, 127.6, 128.1, 131.4, 135.4, 140.6, 152.2, 162.2 (d, $J = 245$ Hz); MS (ESI, m/z): 366.0 $[M+H]^+$; Anal. Calcd for $C_{22}H_{24}FNOSi$: C, 72.29; H, 6.62; N, 3.83. Found: C, 72.54; H, 6.44; N, 3.74.

6b: N-((2-chlorophenyl)(phenyl)methyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2-chlorophenyl) nitron **2c** (0.70 g, 3.0 mmol), phenylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (0.81 g, 2.13 mmol, 71%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3450, 2957, 2924, 1593, 1486, 1444, 1249, 840, 754, 694; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.22 (s, 9H), 6.19 (s, 1H), 6.88 (tt, $J = 7.6$ Hz, 1H), 7.10-7.35 (m, 10 H), 7.47 dd, $J =$

8.0, 1.6 Hz, 2H), 7.77 (dd, $J = 8.0, 2.0$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.8, 72.3, 119.8, 122.9, 126.1, 127.2, 127.9, 128.1, 128.3, 129.3, 130.2, 132.1, 134.5, 137.8, 139.0, 152.6; MS (ESI, m/z): 382.0 $[\text{M}+\text{H}]^+$; Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{ClNOSi}$: C, 69.18; H, 6.33; N, 3.67. Found: C, 69.06; H, 6.23; N, 3.42.

6c: N-phenyl-N-(phenyl(3,4,5-trimethoxyphenyl)methyl)-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3,4,5-trimethoxyphenyl) nitron **2f** (0.86 g, 3.0 mmol), phenylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (1.19 g, 2.73 mmol, 91%) after purification on silica gel (20:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2923, 2852, 1591, 1456, 1244, 1128, 842; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.01(s, 9H), 3.87 (s, 6H), 3.92 (s, 3H), 5.69 (s, 1H), 6.75 (s, 2H), 7.01-7.02 (m, 1H), 7.39-7.51 (m, 4H), 7.32-7.38 (m, 3H), 7.54 (d, $J = 6.8$ Hz, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 55.9, 76.7, 120.6, 123.4, 127.1, 127.7, 127.9, 129.8, 135.1, 137.0, 139.7, 152.5, 152.7. MS (ESI, m/z): 436.3 $[\text{M}-\text{H}]^-$; Anal. Calcd for $\text{C}_{25}\text{H}_{31}\text{NO}_4\text{Si}$: C, 68.62; H, 7.14; N, 3.20. Found: C, 68.34; H, 6.88; N, 3.16.

6d: N-benzhydryl-N-benzyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-benzyl-C-phenyl nitron **2m** (0.63 g, 3.0 mmol), phenylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (0.79 g, 2.19 mmol, 73%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3028, 2924, 2851, 1598, 1456, 1247, 1126, 844; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.08 (s, 9H), 4.04 (d, $J = 14.8$ Hz, 1H), 4.24 (d, $J = 14.8$ Hz, 1H), 6.38 (s, 1H), 6.95-7.26 (m, 15H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -1.1, 65.2, 69.6, 119.6, 123.2, 125.7, 126.2, 128.0, 128.1,

128.0, 129.5, 132.2, 134.7, 137.6, 138.6, 152.4. MS (ESI, m/z): 361.8 $[M+H]^+$, Anal. Calcd for $C_{23}H_{27}NOSi$: C, 76.41; H, 7.53; N, 3.87. Found: C, 76.38; H, 7.36; N, 3.64.

6e: N-((2-chlorophenyl)(thiophen-3-yl)methyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2-chlorophenyl) nitron **2c** (0.70 g, 3.0 mmol), 3-thienylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish syrup (0.88 g, 2.28 mmol, 76%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3452, 2958, 1592, 1484, 1251, 895, 842, 754, 700; 1H NMR (400 MHz, $CDCl_3$) δ (ppm): -0.24 (s, 9H), 6.38 (s, 1H), 6.84 (dd, $J = 5.2, 3.6$ Hz, 2H), 6.92 (dd, $J = 6.8, 3.6$ Hz, 1H), 7.12-7.26 (m, 5H), 7.29 (dd, $J = 8.8, 1.2$ Hz, 2H), 7.36-7.42 (m, 1H), 7.64-7.70 (m, 1H). ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): -1.1, 69.5, 119.6, 123.2, 125.7, 125.8, 126.2, 128.0, 128.1, 129.5, 132.2, 134.7, 137.6, 138.6, 152.4. MS (ESI, m/z): 387.8 $[M+H]^+$. Anal. Calcd for $C_{20}H_{22}ClNOSSi$: C, 61.91; H, 5.72; N, 3.61. Found: C, 61.77; H, 5.42; N, 3.46.

6f: N-((4-fluorophenyl)(thiophen-3-yl)methyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-fluorophenyl) nitron **2l** (0.65 g, 3.0 mmol), 3-thienylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish syrup (0.86 g, 2.31 mmol, 77%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3447, 2955, 2924, 1598, 1510, 1256, 1231, 844, 758, 690; 1H NMR (400 MHz, $CDCl_3$) δ (ppm): -0.14 (s, 9H), 5.71 (s, 1H), 6.82 (dd, $J = 2.8, 0.8$ Hz, 2H), 6.86 (dd, $J = 5.2, 3.6$ Hz, 1H), 6.92-7.02 (m, 3H), 7.08-7.18 (m, 4H), 7.22 (dd, $J = 5.2, 0.8$ Hz, 1H), 7.42 (dd, $J = 8.4, 5.2$ Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): -0.9, 73.5, 114.6 (d, $J = 21$ Hz, 2C), 120.4, 123.7, 125.8,

127.6, 128.1, 131.4, 131.5, 135.4, 140.6, 152.2, 162.2 (d, $J = 245.0$ Hz, 1C); MS (ESI, m/z): 371.8 $[M+H]^+$; Anal. Calcd for $C_{20}H_{22}FNOSSi$: C, 64.65; H, 5.97; N, 3.77. Found: C, 64.57; H, 5.76; N, 3.54.

6g: N-((2,4-dichlorophenyl)(thiophen-3-yl)methyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2,4-dichlorophenyl) nitron **2e** (0.80 g, 3.0 mmol), 3-thienylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless syrup (1.04 g, 2.46 mmol, 82%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3442, 2961, 1637, 1590, 1485, 1381, 1252, 843, 748, 693; 1H NMR (400 MHz, $CDCl_3$) δ (ppm): -0.21 (s, 9H), 6.30 (s, 1H), 6.85 (dd, $J = 5.2, 3.6$ Hz, 2H), 6.89 (d, $J = 2.8$ Hz, 1H), 6.94 (t, $J = 7.2$ Hz, 1H), 7.15-7.23 (m, 4H), 7.26 (d, $J = 7.8$ Hz, 1H), 7.40 (d, $J = 2.0$ Hz, 1H), 7.63 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): -1.0, 69.0, 119.7, 123.5, 125.9, 126.1, 126.5, 128.1, 128.1, 129.2, 132.9, 133.9, 135.3, 136.2, 138.4, 152.1; MS (ESI, m/z): 421.7 $[M+H]^+$; Anal. Calcd for $C_{20}H_{21}Cl_2NOSSi$: C, 56.86; H, 5.01; N, 3.32. Found: C, 56.64; H, 4.88; N, 3.14.

6h: N-(1-(4-methoxyphenyl)octyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-methoxyphenyl) nitron **2b** (0.68 g, 3.0 mmol), 1-hexylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (0.84 g, 2.19 mmol, 73%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2955, 2928, 2857, 1608, 1512, 1485, 1301, 1249, 1177, 1035, 877, 842, 759, 698; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.06 (s, 9H), 0.83 (t, J = 6.8 Hz, 3H), 1.10-1.30 (m, 8H), 1.91 (t, J = 8.0 Hz, 2H), 3.77 (s, 3H), 4.08 (t, J = 6.4 Hz, 1H), 6.76 (dd, J = 8.8, 2.4 Hz, 2H), 6.90-7.00 (m, 3H), 7.04 (dd, J = 8.8, 2.4 Hz, 2H), 7.10-7.20 (m, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 14.0, 22.6, 26.8, 29.3, 30.5, 31.7, 55.1, 73.8, 112.8, 120.7, 123.1, 127.8, 130.8, 131.1, 153.0, 158.6; MS (ESI, m/z): 385.9 $[\text{M}+\text{H}]^+$; Anal. Calcd for $\text{C}_{23}\text{H}_{35}\text{NO}_2\text{Si}$: C, 71.64; H, 9.15; N, 3.63. Found: C, 71.46; H, 8.92; N, 3.51.

6i: N-phenyl-N-(1-(3,4,5-trimethoxyphenyl)octyl)-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3,4,5-trimethoxyphenyl) nitron **2f** (0.86 g, 3.0 mmol), 1-hexylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as colorless oil (1.06 g, 2.37 mmol, 79%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2953, 2931, 2857, 1591, 1506, 1460, 1331, 1244, 1130, 1021, 878, 843, 763, 698; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.46 (s, 9H), 0.84 (t, J = 7.2 Hz, 3H), 1.10-1.30 (m, 8H), 1.80-1.95 (m, 2H), 3.74(s, 6H), 3.82 (s, 3H), 4.03 (dd, J = 8.8, 6.0 Hz, 1H), 6.31 (s, 2H), 6.92-7.03 (m, 3H), 7.17 (t, J = 8.4 Hz, 2H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 14.0, 22.6, 26.8, 29.3, 30.6, 31.7, 56.0, 60.8, 74.7, 106.9, 120.8, 123.3, 127.8, 134.3, 137.2, 152.2, 152.8; MS (ESI, m/z): 445.1 $[\text{M}]^+$; Anal. Calcd for $\text{C}_{25}\text{H}_{39}\text{NO}_4\text{Si}$: C, 67.37; H, 8.82; N, 3.14. Found: C, 67.24; H, 8.65; N, 2.86.

6j: N-phenyl-N-(1-(thiophen-3-yl)octyl)-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(3-thienyl) nitron **2i** (0.61 g, 3.0 mmol), 1-hexylzinc

bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.80 g, 2.22 mmol, 74%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3435, 2954, 2926, 2856, 1595, 1486, 1454, 1308, 1250, 922, 876, 843, 760, 696; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 0.02 (s, 9H), 0.85 (t, $J = 6.8$ Hz, 3H), 1.15-1.35 (m, 8H), 1.80-2.06 (m, 2H), 4.41 (dd, $J = 9.2, 5.2$ Hz, 1H), 6.61 (d, $J = 2.4$ Hz, 1H), 6.83 (dd, $J = 5.1, 3.5$ Hz, 1H), 6.92-7.01 (m, 3H), 7.13-7.20 (m, 3H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.5, 14.0, 22.6, 26.9, 29.1, 31.7, 70.1, 120.2, 123.2, 124.7, 125.5, 126.4, 127.9, 152.6; MS (ESI, m/z): 362.0 $[\text{M}+\text{H}]^+$; Anal. Calcd for $\text{C}_{20}\text{H}_{31}\text{NOSSi}$: C, 66.43; H, 8.64; N, 3.87. Found: C, 66.23; H, 8.46; N, 3.76.

6k: (R)-N-(1-(2-chlorophenyl)octyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(2-chlorophenyl) nitron **2c** (0.70 g, 3.0 mmol), 1-hexylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.77 g, 1.98 mmol, 66%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 2954, 2925, 2856, 1595, 1485, 1446, 1250, 1036, 904, 877, 843, 754, 697; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.23 (s, 9H), 0.88 (t, $J = 7.2$ Hz, 3H), .95-1.22 (m, 8H), 1.76-1.83 (m, 1H), 2.00-2.13 (m, 1H), 4.84 (dd, $J = 10.8, 4.4$ Hz, 1H), 6.92-7.03 (m, 1H), 7.15-7.28 (m, 6H), 7.34 (dd, $J = 7.6, 1.2$ Hz, 1H), 7.48 (dd, $J = 7.6, 1.2$ Hz, 1H); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.9, 14.0, 22.5, 26.3, 29.1, 29.7, 31.6, 68.8, 119.9, 122.9, 126.0, 128.1, 128.4, 129.3, 130.6, 136.1, 136.9, 152.9; MS (ESI, m/z): 390.2 $[\text{M}+\text{H}]^+$; Anal. Calcd for $\text{C}_{22}\text{H}_{32}\text{ClNOSi}$: C, 67.75; H, 8.27; N, 3.59. Found: C, 67.46; H, 8.09; N, 3.64.

6l: N-((2-methyl-1-(p-tolyl)butyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-(4-methylbenzylidene)aniline oxide **2h** (0.63 g, 3.0 mmol), 2-butylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.55 g, 1.62 mmol, 54%) after purification on silica gel (50:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3394, 2961, 2924, 2873, 1595, 1485, 1451, 1250, 922, 887, 843, 758, 696; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 0.06 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.07 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.64 (d, $J = 6.8$ Hz, 3H, CH_3), 0.77 (t, $J = 6.4$ Hz, 3H, CH_3), 0.80-0.92 (m, 2H, CH_2), 1.04 (t, $J = 7.2$ Hz, 3H, CH_3), 1.20-1.30 (m, 2H, CH_2), 1.34 (d, $J = 6.4$ Hz, 3H, CH_3), 2.05-2.20 (m, 1H, CH), 2.27 (s, 6H, $2 \times \text{CH}_3$), 2.30-2.40 (m, 1H, CH), 3.72 (d, $J = 2.0$ Hz, 1H, CH), 3.74 (d, $J = 2.0$, 1H, CH), 6.75 (dd, $J = 8.0, 2.8$ Hz, 4H, ArH), 6.85 (dd, $J = 7.6, 2.0$ Hz, 4H, ArH), 6.88-6.96 (m, 6H, ArH), 7.18 (t, $J = 7.6$ Hz, 4H, ArH); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.1, 0.0, 10.7, 11.2, 16.5, 17.6, 26.4, 27.1, 35.2, 35.3, 80.5, 80.7, 120.2, 120.4, 122.7, 122.4, 127.4, 127.5, 130.3, 130.4, 132.9, 133.1, 136.2, 136.2, 153.5, 153.6; MS (ESI, m/z): 342.1 $[\text{M}]^+$; Anal. Calcd for $\text{C}_{21}\text{H}_{31}\text{NOSi}$: C, 73.84; H, 9.15; N, 4.10. Found: C, 73.69; H, 9.06; N, 3.89.

6m: N-((4-methoxyphenyl)-2-methylbutyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-methoxyphenyl) nitron **2b** (0.68 g, 3.0 mmol), 2-butylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.58 g, 1.62 mmol, 54%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3375, 2958, 2924, 2854, 1597, 1488, 1462, 1246, 1032, 922, 888, 842, 753, 696; ^1H NMR (400 MHz, CDCl_3) δ (ppm): -0.04 (s, 9H, $\text{Si}(\text{CH}_3)_3$), -0.08 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 0.64 (d, $J = 6.8$ Hz, 3H, CH_3), 0.76 (t, $J = 6.4$ Hz, 3H, CH_3), 0.82-0.92 (m, 2H, CH_2), 1.04 (t, $J = 7.2$ Hz, 3H, CH_3), 1.20-1.30 (m, 2H, CH_2), 1.34 (d, $J = 6.4$ Hz, 3H, CH_3), 2.05-2.44 (m, 2H, CH), 3.20 (s, 3H, OCH_3), 3.22 (s, 3H, OCH_3), 4.51 (d, $J = 4.0$ Hz, 1H, CH), 4.54 (d, $J = 4.0$, 1H, CH), 6.60-6.68 (m, 4H, ArH), 6.80-6.95 (m, 8H, ArH), 7.05-7.18 (m, 6H, ArH); ^{13}C NMR (100MHz, CDCl_3) δ (ppm): -0.1, -0.1, 10.6, 11.1, 16.1, 17.8, 26.2, 29.7, 34.7, 34.9, 55.3, 110.4, 119.1, 119.7, 120.0, 122.2, 122.3, 127.4, 127.4, 131.4,

131.6, 154.3, 157.9; MS (ESI, m/z): 358.1, $[M+H]^+$; Anal. Calcd for $C_{21}H_{31}NO_2Si$: C, 70.54; H, 8.74; N, 3.92. Found: C, 70.89; H, 8.68; N, 3.64.

6n: N-(naphthalen-1-yl(p-tolyl)methyl)-N-phenyl-O-(trimethylsilyl)hydroxylamine

According to general procedure A: A solution of TMSCl (0.65 g, 0.78 ml, 6.0 mmol) in THF (5 mL) was added slowly to a mixture of N-phenyl-C-(4-methylphenyl) nitron **2h** (0.63 g, 3.0 mmol), 1-naphthylzinc bromide (4.5 mmol) in 10 ml of THF under room temperature. The reaction mixture was stirred at this temperature for half an hour. The pure product was obtained as yellowish oil (0.90 g, 2.19 mmol, 73%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3401, 2925, 1595, 1510, 1487, 1451, 1330, 1250, 1130, 916, 897, 843, 779, 752, 694. 1H NMR (400 MHz, $CDCl_3$) δ (ppm): -0.35 (s, 9H), 2.26 (s, 3H), 6.50 (s, 1H), 6.85 (tt, $J = 7.2, 0.9$ Hz, 1H), 7.01 (d, $J = 8.0$ Hz, 2H), 7.15 (tt, $J = 7.2, 0.9$ Hz, 2H), 7.26 (dd, $J = 8.8, 0.9$ Hz, 2H), 7.34-7.50 (m, 5H), 7.72 (t, $J = 8.0$ Hz, 2H), 7.81 (d, $J = 8.0$, 1H), 8.26 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): -0.7, 21.1, 29.7, 71.8, 119.1, 122.4, 123.7, 125.0, 125.9, 127.8, 128.2, 128.5, 128.6, 128.7, 130.2, 132.8, 136.2, 136.5, 136.6, 153.1; MS (ESI, m/z): 411.9 $[M]^+$; Anal. Calcd for $C_{27}H_{29}NOSi$: C, 78.79; H, 7.10; N, 3.89. Found: C, 78.64; H, 6.84; N, 3.26.

General procedure B: Reduction of O-trimethylsilyl hydroxylamines into amine.

The O-trimethylsilyl hydroxylamine (2 mmol) was dissolved into a 2:1 solution of EtOH and sat. aq. NH_4Cl (20 mL) in a 50 mL round bottomed flask. $Cu(OAc)_2$ powder (40 mg, 0.2 mmol) and Zn (260 mg, 4 mmol) were added and the mixture is stirred and heated under nitrogen atmosphere at 50 °C for several hours until the hydroxylime was completely consumed (TLC control). The mixture was cooled, filtered over Celite and concentrated. Then, a sat. Na_2CO_3 solution (15 mL) was added and the product is extracted with ethyl acetate (3x15 mL). The organic phase is dried over anhydrous Na_2SO_4 , then filtered and concentrated to afford the desired amine, which was then purified by flash column chromatography.

8a: N-(1-(4-methoxyphenyl)-2-phenylethyl)aniline

According to general procedure B: The O-trimethylsilyl hydroxylamine **5b** (0.78g, 2 mmol) was dissolved into a 2:1 solution of EtOH and sat. aq. NH_4Cl (20 mL) in a 50 mL round bottomed flask. Cu(OAc)_2 powder (40 mg, 0.2 mmol) and Zn (260 mg, 4 mmol) were added and the mixture is stirred and heated under nitrogen atmosphere at room temperature for 2 hours. The pure product was obtained as yellowish syrup (0.46 g, 1.54 mmol, 77%) after purification on silica gel (30:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3409, 2953, 2919, 2850, 1602, 1507, 1245, 1223; ^1H NMR (400 MHz, CDCl_3) δ (ppm): 3.30 (dd, $J = 14.0, 8.0$ Hz, 1H), 3.10 (dd, $J = 14.0, 5.6$ Hz, 1H), 3.7 (s, 3H), 4.09 (s, 1H), 4.54 (t, $J = 6.8$ Hz, 1H), 6.46 (d, $J = 8.4$ Hz, 2H), 6.62 (td, $J = 7.6, 0.9$ Hz, 1H), 6.83 (d, $J = 8.4$ Hz, 2H), 7.05 (t, $J = 7.2$ Hz, 2H), 7.10 (d, $J = 7.6$ Hz, 2H), 7.15-7.30 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) : 29.7, 45.1, 55.1, 58.6, 113.6, 113.8, 117.4, 126.6, 127.4, 128.4, 128.9, 129.2, 135.2, 137.7, 147.2, 158.5. HR-MS (ESI) calcd for $\text{C}_{21}\text{H}_{22}\text{NO}$ $[\text{M}+\text{H}]^+$: 304.4055; found 304.4056.

8b: N-(2-phenyl-1-(3,4,5-trimethoxyphenyl)ethyl)aniline

According to general procedure B: The O-trimethylsilyl hydroxylamine **5f** (0.90g, 2 mmol) was dissolved into a 2:1 solution of EtOH and sat. aq. NH_4Cl (20 mL) in a 50 mL round bottomed flask. Cu(OAc)_2 powder (40 mg, 0.2 mmol) and Zn (260 mg, 4 mmol) were added and the mixture is stirred and heated under nitrogen atmosphere at room temperature for 2 hours. The pure product was obtained as yellowish syrup (0.52 g, 1.44 mmol, 72%) after purification on silica gel (20:1 petroleum ether : EtOAc).

IR (KBr) ν (cm^{-1}): 3391, 3057, 2924, 1599, 1504, 1234, 1126, 1028, 1008, 981; ^1H NMR (400 MHz, CDCl_3), δ (ppm): 3.03 (dd, $J = 13.7, 10.5$ Hz, 1H), 3.09 (dd, $J = 13.9, 5.9$ Hz, 1H), 3.78 (s, 6H), 3.83 (s, 3H), 4.09 (s, 1H), 4.56 (t, $J = 13.9$ Hz, 1H), 6.46-6.40 (m, 2H), 6.51 (s, 2H), 7.05-7.14 (m, 4H), 7.21-7.30 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3), δ (ppm): 45.2, 56.0, 59.8, 65.3, 103.1, 113.7, 126.7, 126.9, 127.6, 128.6, 129.0, 129.2, 137.5, 139.2, 147.3, 153.2. HR-MS (ESI) calcd for $\text{C}_{23}\text{H}_{26}\text{NO}_3$: $[\text{M}+\text{H}]^+$: 364.1913; found 364.1914.

10. (2R, 3R, 4S, 5S)- N-trimethylsiloxy-2-vinyl-3,4-O-isopropylidene-5-[(R)-2,2-dimethyl-1,3-dioxolan-4-yl]pyrrolidine.

According to general procedure A: A solution of TMSCl (0.73 g, 0.88 ml, 6.76 mmol) in THF (5 mL) was added slowly to a mixture of nitrone **9** Nitrone (0.87g, 3.38 mmol) was dissolved in 20 ml THF and the resulting mixture was cooled in a ice-water bath under argone. A solution of zinc chloride (0.70 g, 5.15 mmol) in THF (10 ml) was vinylzinc bromide (1.6M, 3.17 ml, 5.07 mmol, 1.5 eq.) was added dropwise. The reaction mixture was stirred 1 hour at room temperature, TLC showed that all the starting material was consumed. Saturated ammonium chloride (20 ml) was added, the resulting mixture was extracted with ethyl acetate (3×20ml). the organic mixture was dried (Na_2SO_4), and the solvent was evaporated to give a syrup which was chromatography to give the titled compound (1.01 g, 84%)

$[\alpha]_D^{20} = +7.10$ ($c = 0.87$, CHCl_3), IR $\nu(\text{cm}^{-1})$: 2987, 2937, 1647, 1381, 1258, 1212, 1071. ^1H NMR (CDCl_3) δ (ppm): -0.04 (9H, TMS), 1.22, 1.29, 1.41, 1.47 ($4 \times s$, 12H, CH_3), 3.06 (dd, $J = 6.2, 4.6$ Hz, 1H, H-5), 3.34 (dd, $J = 6.3, 6.3$ Hz, 1H, H-2), 3.90 (dd, $J = 7.8, 5.1$ Hz, 1H, H-4'), 4.04 (dd, $J = 9.2, 6.4$ Hz, 1H, H-4'), 4.16-4.28 (m, 2H, H-3 and H-4), 4.33 (dd, $J = 12.3, 7.2$ Hz, 1H, H-5'), 5.22 (d, $J = 10.2$ Hz, 1H, $\text{CH}_2=\text{CH}$), 5.34 (d, $J = 17.1$ Hz, 1H, $\text{CH}_2=\text{CH}$), 5.80-5.94 (m, 1H, $\text{CH}_2=\text{CH}$). ^{13}C NMR (CDCl_3) δ (ppm): -1.08, 25.13 (CH_3), 25.18 (CH_3), 26.46 (CH_3), 27.21 (CH_3), 66.18 (C-4'), 74.19 (C-5'), 75.91 (C-2), 76.35 (C-5), 77.43 (C-4), 80.31 (C-3), 109.87 (Me_2CO), 113.80 (Me_2CO), 118.98 ($\text{CH}_2=\text{CH}$), 136.00 ($\text{CH}_2=\text{CH}$). HR-MS (ESI): Calcd for $\text{C}_{17}\text{H}_{32}\text{NO}_5\text{Si}$ $[\text{M}+\text{H}]^+$: 358.2050; found 358.2053.

11. (2R, 3R, 4S, 5S)-2-vinyl-3,4-O-isopropylidene-5-[(R)-2,2-dimethyl-1,3-dioxolan-4-yl]pyrrolidine

Compound **10** (1.01g, 2.82 mmol) was dissolved in a solution of 20 ml of dichloromethane. 20ml of saturated NH_4Cl solution, zinc powder (1.2 g, 18 mmol) and Cu(OAc)_2 (360 mg, 1.8 mmol) were then added and the mixture was stirred at room temperature for 2 hours. TLC showed that all the starting material was exhausted. The organic solution was separated and the aqueous phase was extracted with dichloromethane (20 mL). The organic phases were collected and washed with brine, dried (MgSO_4) and concentrated. The pure product (0.69 g, 91%) was obtained after column chromatography using ethyl acetate/petroleum ether (5/1, v/v) as the eluant. $R_f = 0.47$ (ethyl acetate/petroleum ether 1/4). $[\alpha]_D^{20} = +4.1$ (c = 2.4, CHCl_3), IR $\nu(\text{cm}^{-1})$: 3339, 2986, 2936, 1645, 1385, 1375, 1210, 1071. ^1H NMR (CDCl_3) δ (ppm): 1.29 (s, 3H), 1.37 (s, 3H), 1.49 (s, 3H), 1.54 (s, 3H), 2.51 (brs, 1H), 3.14 (dd, $J = 6.3, 4.8$ Hz, 1H), 3.42 (t, $J = 6.6$ Hz, 1H), 3.94 (dd, $J = 7.8, 4.5$ Hz, 1H), 4.09 (dd, $J = 9.0, 6.9$ Hz, 1H), 4.19-4.29 (m, 2H), 4.35 (q, $J = 6.3$ Hz, 1H), 5.28 (d, $J = 10.5$ Hz, 1H), 5.38 (d, $J = 17.4$ Hz, 1H), 5.78-5.95 (m, 1H). ^{13}C NMR (CDCl_3) δ (ppm): 25.12, 25.19, 26.49, 27.22, 66.22, 74.21, 75.94, 76.38, 77.42, 80.28, 109.92, 113.85, 119.12, 135.97. HRMS m/z : calcd for $\text{C}_{14}\text{H}_{24}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 270.1705, found: 270.1699.

12. (2S, 3S, 4R, 5R)-2-[(R)-2,2-dimethyl-1,3-dioxolan-4-yl]-3,4-isopropylidenedideoxy-5-ethylpyrrolidine.

Amine **11** (160 mg, 0.39 mmol) was dissolved in 30 ml of methanol and 8 drops of concentrated hydrochloric acid. palladium-carbon (10%, 50 mg) was then added and the mixture was stirred under hydrogen atmosphere over night. the solid was filter off and the filtration was concentrated to give the desired product 76 mg, yield 100%.

$[\alpha]_D^{20} = -9.34$ (c = 1.07 CHCl_3), IR $\nu(\text{cm}^{-1})$: 3634 (br), 3290 (br), 2937 (m), 1583 (m), 1407 (s), 1349 (m), 1328 (m), 1239 (m), 1102 (vs), 1064 (vs), 957 (w); ^1H NMR (D_2O) δ (ppm): 0.95 (t, $J = 7.3$ Hz, 3H, CH_3), 1.63-1.76 (m, 2H, CH_2), 3.36 (q, $J = 7.1$ Hz, 1H, H-5), 3.49 (t, $J = 5.9$ Hz, 1H, H-2), 3.56 (dd, $J = 11.8, 5.3$ Hz, 1H, H-5'), 3.65 (dd, $J = 12.0, 3.8$ Hz, 1H, H-5'), 3.90 (dd, $J = 9.7, 4.4$ Hz, 1H, H-4'),

3.97 (t, $J = 5.3$ Hz, 1H, H-4), 4.15 (t, $J = 6.0$ Hz, 1H, H-3). ^{13}C NMR (D_2O) δ (ppm): 9.80 (CH_3), 22.76 (CH_2), 62.85 ($\text{C}5'$), 63.80 (C-5), 64.63 (C-2), 68.05 (C-4'), 70.51 (C-3), 72.52 (C-4).

HRMS m/z : calcd for $\text{C}_8\text{H}_{18}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 192.1236, found: 192.1229.

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Cover Letter

Dear Editors and Referees:

I am very glad to submit our manuscript to Organic & Biomolecular Chemistry. In this manuscript entitled with *Trimethylsilyl Chloride Promoted Synthesis of α -branched amines by Nucleophilic Addition of Organozinc Halides to Nitrones*, we reported a novel TMSCl promoted addition reaction of organozinc halides with *N*, α -diphenyl nitrones. The importance of this work can be viewed as follows:

Nitrones are easily available starting material for the synthesis of structurally variable amines either by 1,3-dipolar cycloaddition reaction or by nucleophilic addition reactions. The nucleophilic addition reaction of Grignards or Organolithium reagents with nitrones are explored widely and used frequently in the synthesis of amines. However, organozinc reagents are rarely used in these areas with the exception of diorganozinc reagents or some diorganozinc induced reactions. The organozinc halides, owing to their low nucleophilicities, are not employed in these reactions to date. We here **first report** a novel TMSCl promoted addition reaction of organozinc halides with nitrones, in which **TMSCl were shown to be both a necessary reactant and a ready hydroxylamine protecting reagent**.

With the presence of TMSCl, organozinc halides reacted with nitrones readily and easily in high yield under very mild reaction condition, however, without TMSCl, this type of reaction did not proceed under this condition. Even when the temperature was elevated, the produced hydroxylamines are easily decomposed under air condition, and thus very low yield obtained. Our TMSCl promoted methods have advantages over the traditional organometallic methods are that:

1. TMSCl is the promotor, thus these reactions can be proceeded under very mild conditions.
2. The obtained hudroxylamines were protected in situ by TMSCl, and thus led to very yields.
3. Oganozinc halides can be highly functionalized, thus our method can be used into construction of highly functionalized molecules.

The produced O-trimethylsilyl hydroxylamines can be easily reduced to corresponding amines by a zinc metal in the presence of $\text{Cu}(\text{OAc})_2$ in NH_4Cl solution.

4. This method was shown can be successfully used in natural product synthesis such as in the synthesis of polyhydroxylated pyrrolidines.

Please consider our manuscript and we would greatly appreciate if there are some suggestions on our work.

Best wishes,

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**Trimethylsilyl Chloride Promoted
Synthesis of α -branched amines by
Nucleophilic Addition of
Organozinc Halides to Nitrones**

Ying Fu, Yanhua Liu, Yaojuan
Chen, Helmut M. Hügel, Danfeng
Huang and Yulai Hu

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Activation and protection: The activation of nitron 1,3-dipole is a highly desirable when they were attributed to weak nucleophiles such as organozinc reagents. Gratifying, TMSCl was found to be both an indispensable reaction promoter and a ready hydroxylamine protection reagent in these reactions.