Chapter 2

NICKEL-CATALYZED CROSS-COUPLINGS OF UNACTIVATED SECONDARY AND TERTIARY ALKYL BROMIDES WITH SILICON NUCLEOPHILES

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The work described was performed in collaboration with Dr. Yufan Liang, who performed mechanistic studies and contributed to the writing of the manuscript.

Abstract

The formation of C–C bonds from unactivated alkyl electrophiles has been extensively investigated, but methods to form analogous C–heteroatom bonds are far less developed. The first cross-coupling reaction of unactivated secondary and tertiary alkyl electrophiles to form C–Si bonds is described. Using a commercially available nickel complex $NiBr_2\cdot$diglyme, a variety of alkyl bromides efficiently undergo cross-coupling with silylzinc reagents at low temperature. This nickel-catalyzed silylation method represents a rare example of employing unactivated tertiary alkyl halides as electrophilic coupling partners. Additionally, the versatility of this reaction is demonstrated through compatibility with different classes of silicon nucleophiles. Stereochemical studies and relative reactivity experiments are consistent with the generation of a radical intermediate for C–X bond cleavage.

Introduction

Beyond their role as synthetic intermediates,[1] organosilicon compounds exhibit diverse applications in fields ranging from materials science[2] to agrochemistry[3] to medicinal chemistry.[4] Silicon-containing agrochemicals have reached broad commercial application due to their function as antifungals and insecticides. Furthermore, the introduction of silicon atoms as isosteres for carbon has become a strategy for tuning biological properties by medicinal chemists. However, the synthesis of these compounds is limited by several factors. Tetraorganosilanes are typically prepared either through the hydrosilylation of olefins (Figure 2.1(a)), where issues of reactivity (e.g., hindered substrates) and regioselectivity (e.g., 1,2-disubstituted olefins) can present significant challenges,[5,6] or through the reaction of an organic nucleophile with a silicon electrophile (Figure 2.1(b)),[7] for which general methods are limited to primary alkyl nucleophiles.[8] In principle, the coupling of an alkyl electrophile with a silicon nucleophile (Figure 2.1(c)) could provide a general approach for the synthesis of tetraorganosilanes; however, progress in developing this reaction has been rather limited, especially with respect to catalyzed processes. Indeed, to the best of our knowledge, catalyzed methods have been restricted to couplings of activated alkyl electrophiles (e.g., allylic, benzylic, and propargylic),[9] with the exception of two reports of the cross-coupling of unactivated primary alkyl electrophiles.[10,11]

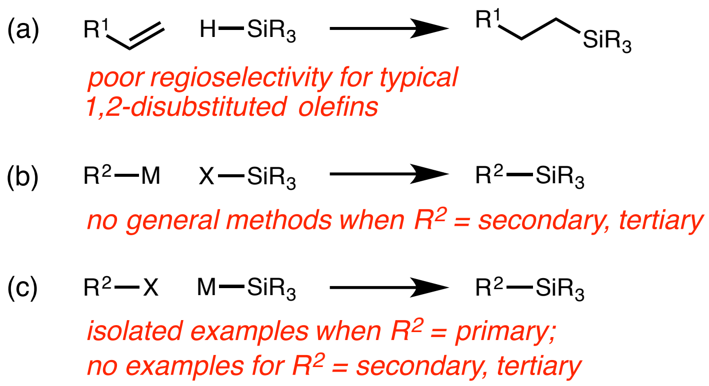
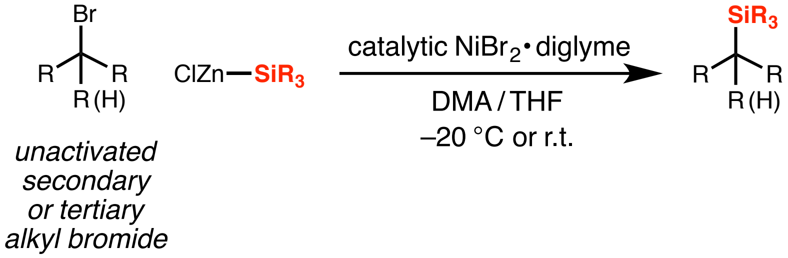


Figure 2.1. Three approaches to the synthesis of tetraorganosilanes.

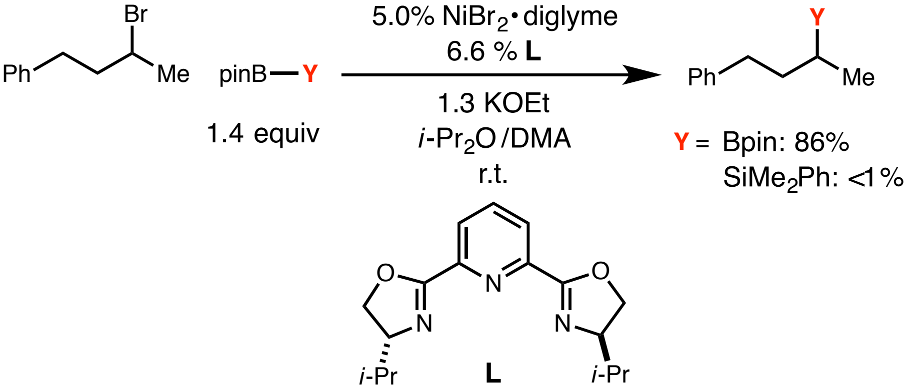
Over the past decade, significant progress has been made toward developing catalytic cross-coupling reactions of alkyl electrophiles to generate C–C bonds.[12] However, similar transformations to generate bonds to heteroatoms are far less common. As part of an ongoing effort to broaden the scope of cross-couplings of alkyl electrophiles, we recently reported our first nickel-catalyzed C–X bond-forming process, the Miyaura borylation of primary, secondary, and tertiary alkyl halides.[13,14] Drawing inspiration from this transformation, we turned our attention to a related silylation reaction. Specifically, we establish that a commercially available nickel catalyst, without an added ligand, catalyzes the cross-coupling of unactivated secondary and tertiary alkyl bromides with silylzinc nucleophiles (Eq. 2.1).



(2.1)

Reaction Optimization

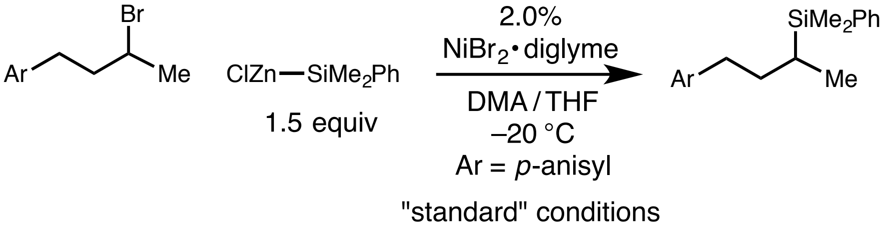
During initial studies, we applied our previously discovered borylation reaction conditions to an analogous silylation reaction involving a silylboron reagent, hoping to achieve similar reactivity.[13] Unfortunately, only trace levels of C−Si bond formation were detected (Eq. 2.2),[15] and further attempts to increase product yields with this nucleophile failed.



(2.2)

After exploring various reaction parameters with a monosilylzinc halide[16] serving as the nucleophile, we were delighted to find that $NiBr_2$·diglyme could catalyze the silylation reaction of a model unactivated secondary alkyl bromide with $PhMe_2Si$–ZnCl in good yield (Table 2.1, entry 1). As shown in Table 2.1, no C–Si bond formation is observed in the absence of $NiBr_2$·diglyme (entry 2). Under these conditions, other classes of silicon nucleophiles tested are not effective coupling partners (entries 3 and 4). Additionally, other selected transition metal complexes (Fe, Co, Cu, and Pd) are not able to facilitate the reaction (entries 5–8).[17] Without the use of DMA as a co-solvent, the reaction affords almost none of the desired product (entry 9).[18] A reduction in yield occurs when the reaction is performed with lower catalyst loading, less nucleophile, and at room temperature (entries 10–12). Interestingly, the silylation is only moderately sensitive to air (entry 13) and very tolerant of water (entry 14). This is the first nickel-catalyzed cross-coupling reaction of alkyl electrophiles reported by the Fu laboratory that does not use an added ligand.

Table 2.1. Silylation of a Model Unactivated Secondary Bromide: Effect of Reaction Parameters



entry	variation from the "standard" conditions	yield (%)[a]
1	none	84
2	no $NiBr_2$•diglyme	<1
3	Li–$SiMe_2Ph$, instead of ClZn–$SiMe_2Ph$	2
4	ClMg–$SiMe_2Ph$, instead of ClZn–$SiMe_2Ph$	1
5	$FeCl_2$, instead of $NiBr_2$•diglyme	<1
6	$CoCl_2$, instead of $NiBr_2$•diglyme	2
7	CuBr•SMe_2, instead of $NiBr_2$•diglyme	<1
8	$Pd(MeCN)_2Cl_2$, instead of $NiBr_2$•diglyme	<1
9	no DMA	1
10	0.5 mol% $NiBr_2$•diglyme	60
11	1.1 equiv ClZn–$SiMe_2Ph$	78
12	r.t., instead of –20 °C	73
13	under air in a closed vial	69
14	added H_2O (2.0 equiv)	78

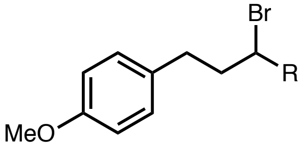
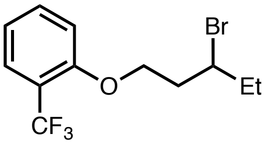
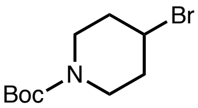
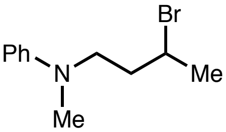
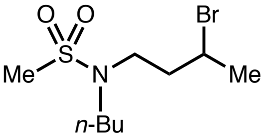
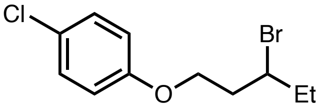
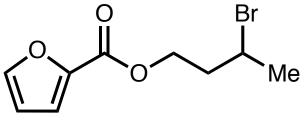
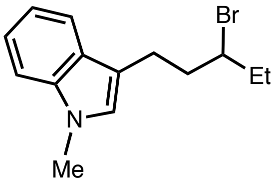
[a] Yields were deteremined by GC analysis with the aid of a calibrated standard (averages of two experiments).

Scope with Respect to the Electrophile

With the optimized conditions in hand, we next investigated the electrophile scope. The commercially available catalyst $NiBr_2$·diglyme can be used for the silylation of an array of unactivated secondary alkyl bromides at –20 ºC (Table 2.2). In addition to the model electrophile (entry 1) used for optimization, sterically hindered α-branched substrates such

Table 2.2. Silylation of Unactivated Secondary Alkyl Bromides: Scope

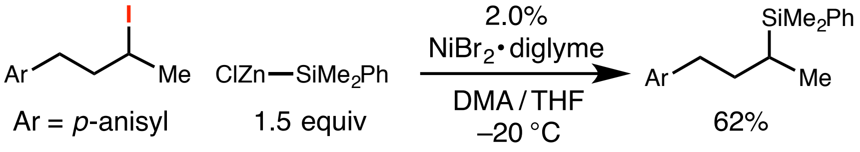
$$R_{alkyl}{-}Br \quad \underset{1.5\ \text{equiv}}{ClZn{-}SiMe_2Ph} \quad \xrightarrow[\substack{DMA/THF \\ -20\ ^{\circ}C}]{\substack{2.0\% \\ NiBr_2 \cdot diglyme}} \quad R_{alkyl}{-}SiMe_2Ph$$

entry	substrate		yield (%)[a]
		R=	
1		Me	79
2[b]		*i*-Pr	76
3[b]		*t*-Bu	68
4			61
5			74
6			76
7			78
8			65
9			75
10[b]			79

[a] Yields of purified products (averages of two experiments). [b] Catalyst loading: 5.0% $NiBr_2 \cdot$diglyme.

as an *iso*-propyl (entry 2) and even a *tert*-butyl (entry 3) substituted alkyl bromide are useful coupling partners. A variety of functional groups, including a trifluoromethyl group (entry 4), a carbamate (entry 5), a tertiary amine (entry 6), a sulfonamide (entry 7), and an aryl chloride (entry 8) are well suited for this reaction. Furthermore, heterocycles such as furan (entry 9) and indole (entry 10) enable efficient C–Si bond formation. These functionalized electrophiles include sensitive groups that are incompatible with the formation of alkyl nucleophiles used in the reaction shown in Figure 2.1(b).[19] Initial studies investigating an alkyl bromide containing thiophene, a secondary alkyl choride, and an alkyl tosylate showed that these are not useful coupling partners under the standard conditions.

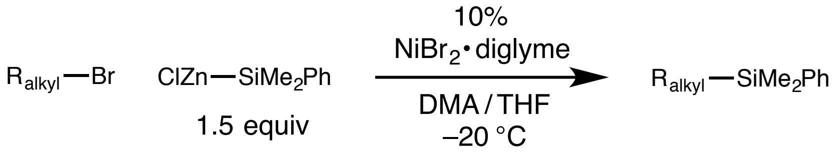
While the standard reaction conditions did not facilitate C–Si bond formation with secondary alkyl chlorides, an unactivated secondary alkyl iodide was an effective electrophile (Eq. 2.3).[20] Additionally, this method is adaptable to scale-up, and the cross-coupling reaction shown in Table 2.2, entry 1 can be performed with reduced catalyst loading (1% Ni) in 81% yield.

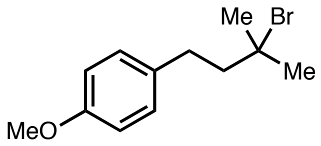
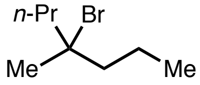
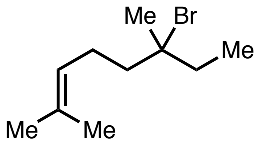
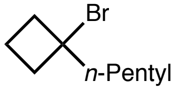
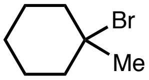
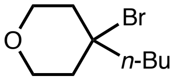


(2.3)

Tertiary alkyl electrophiles are known to be challenging substrates, and reports of unactivated tertiary alkyl electrophiles in cross-coupling reactions have been limited.[21] Thus, we were excited to find that the optimized conditions allow for the coupling of unactivated tertiary alkyl bromides (Table 2.3) in addition to secondary alkyl bromides. Both acyclic (entries 1–3) and cyclic (entries 4–6) substrates are compatible under the standard conditions. Furthermore, an alkyl bromide containing an olefin (entry 3) is demonstrated to be a suitable substrate.

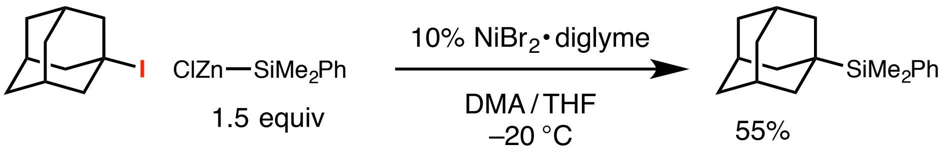
Table 2.3. Silylation of Unactivated Tertiary Alkyl Bromides: Scope



entry	substrate	yield (%)[a]
1		70
2		54
3		49
4		70
5		70
6[b]		74

[a] Yields of purified products (averages of two experiments). [b] Catalyst loading: 2.0% $NiBr_2$·diglyme.

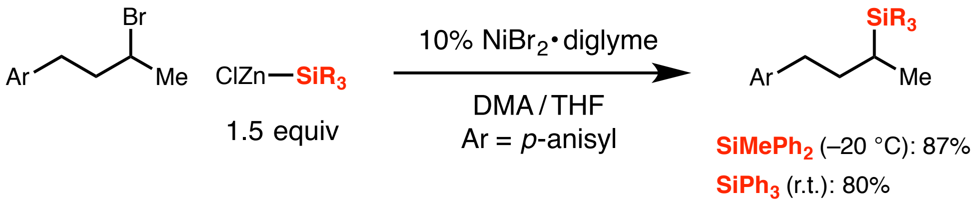
In addition to the tertiary alkyl bromides shown in Table 2.3, a preliminary attempt to silylate 3-iodoadamantane under the standard conditions provided a promising result toward the silylation of tertiary alkyl iodides (Eq. 2.4).



(2.4)

Scope with Respect to the Nucleophile

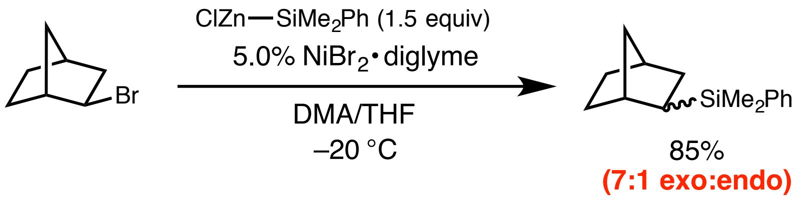
Following investigations demonstrating that the scope of this new silylation reaction is broad with respect to secondary and tertiary alkyl electrophiles, we next evaluated the compatibility of other silicon nucleophiles. The simple nickel catalyst facilitates C–Si bond formation with silylzinc reagents containing one, two, and three aryl substituents with high steric bulk in good yield (Eq. 2.5).[22]



(2.5)

Mechanistic Insights

Previous studies of nickel-catalyzed cross-couplings of unactivated alkyl halides to generate C–C and C–B bonds from the Fu laboratory have suggested that alkyl electrophiles can undergo oxidative addition to form alkyl radical intermediates.[13,23] Our studies of this new C–Si bond forming reaction suggest that oxidative addition occurs by a similar radical mechanism. In the reactions of *exo*- and *endo*-2-bromonorbornane, the same diastereomeric mixture of products is formed (7:1 exo:endo; each alkyl bromide remains a single stereoisomer at partial conversion), consistent with the formation of a common intermediate



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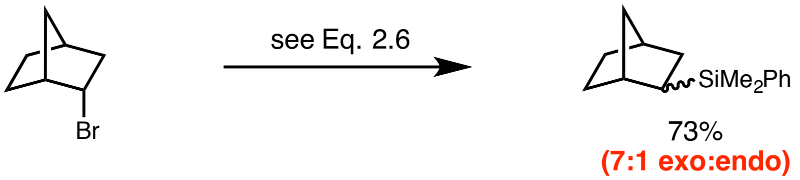
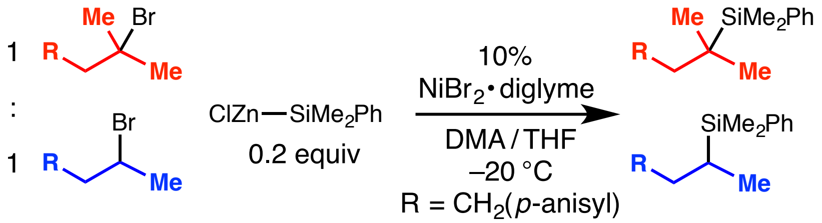


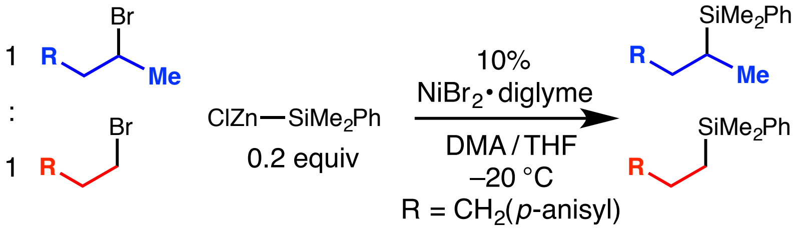
(2.7)

in the two reactions (Eqs. 2.6 and 2.7).[24] Furthermore, the addition of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO),[25] which rapidly traps alkyl radicals, inhibits C–Si bond formation under our standard conditions.

Inspired by the fact that unactivated *tertiary* alkyl electrophiles are effecting coupling partners under our standard conditions, we conducted competition experiments between a tertiary, a secondary, and a primary alkyl bromide (Eqs. 2.8 and 2.9). Electrophiles with higher degrees of substitution demonstrate higher levels of reactivity (tertiary > secondary > primary).[26] This result is consistent with the stability of the radical, rather than steric effects, being the dominant factor influencing relative reactivity, providing further evidence for the generation of a radical intermediate for the oxidative addition step.



(2.8)



(2.9)

Conclusion

We have described the first cross-coupling reaction of unactivated secondary and tertiary alkyl electrophiles to form C−Si bonds. Using only a commercially available nickel catalyst, we have observed efficient cross-coupling of a variety of silylzinc nucleophiles with both secondary and tertiary alkyl bromides, demonstrating good tolerance of both steric bulk as well as diverse functional groups. Competition experiments suggest that tertiary alkyl bromides are more reactive than secondary or primary alkyl bromides. Preliminary mechanistic studies are consistent with a radical mechanism for oxidative addition.

Experimental Section

General Information

Anhydrous THF was purified and dried using a solvent-purification system that contained activated alumina. The following reagents and solvents were purchased and used as received: lithium metal (granular, 4-10 mesh particle size, 99%; Aldrich), zinc chloride (≥98%; Aldrich), dimethylphenylchlorosilane (TCI), chloro(methyl)diphenylsilane (Aldrich), chlorotriphenylsilane (Acros), $NiBr_2{\cdot}$diglyme (Aldrich), dimethylacetamide (≥99%, over molecular sieves; Aldrich), triphenylphosphine (Aldrich), bromine (Aldrich), imidazole (Aldrich), LiBr (≥99%; Aldrich), and *N*-Boc-4-bromopiperidine (Aldrich). All other alkyl bromides were prepared from the corresponding alcohols according to General Procedure A or B.

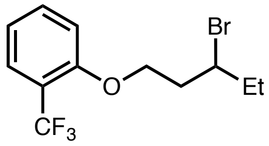
^{1}H and ^{13}C NMR spectroscopic data were collected on a Varian 500 MHz spectrometer at ambient temperature. GC analyses were obtained on an Agilent 6890 Series GC system with a DB-1 column (length 30 m, internal diameter 0.25 mm).

Preparation of Electrophiles

General Procedure A: Bromination of Secondary Alcohols.[27] Triphenylphosphine (1.3 equiv) and imidazole (1.3 equiv) were dissolved in dry CH_2Cl_2 (0.2 M), and the resulting solution was stirred at 0 °C under a nitrogen atmosphere. Bromine (1.3 equiv) was added dropwise, and the reaction mixture was stirred at 0 °C for 5 min. The alcohol was then added dropwise over 3 min. The reaction mixture was allowed to warm to r.t., and then it was stirred for 6–12 h. A saturated aqueous solution of NH_4Cl was added to the reaction mixture, which was then extracted two times with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by flash chromatography (Et_2O/hexane).

General Procedure B: Bromination of Tertiary Alcohols.[28] LiBr (2.0 equiv) was dissolved in 48 wt% aqueous HBr, and the resulting solution was cooled to 0 °C. The alcohol was added at 0 °C, and the reaction mixture was allowed to warm to r.t. and stirred for 3 h. The mixture was then diluted with Et_2O and washed once with each of the following: deionized water, saturated aqueous $NaHCO_3$ solution, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by distillation under reduced pressure.

The yields have not been optimized.



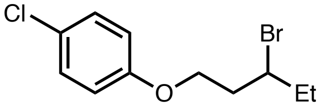
1-((3-Bromopentyl)oxy)-2-(trifluoromethyl)benzene. The bromide was prepared according to General Procedure A from the corresponding alcohol, 1-(2-(trifluoromethyl)phenoxy)pentan-3-ol. The product was purified by flash chromatography (0→2% Et_2O/hexane). Pale-yellow oil (1.42 g, 90%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 1H), 7.52 – 7.46 (m, 1H), 7.05 – 6.98 (m, 2H), 4.33 – 4.19 (m, 3H), 2.37 (dddd, 1H, J = 15.0, 8.4, 5.8, 3.4 Hz), 2.23 (ddt, 1H, J = 14.7, 10.0, 4.5 Hz), 2.03 – 1.87 (m, 2H), 1.10 (t, 3H, J = 7.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.6, 133.3, 127.1 (q, J = 5.2 Hz), 123.7 (q, J = 272.3 Hz), 120.1, 118.8 (q, J = 30.6 Hz), 112.8, 66.4, 55.9, 38.1, 32.4, 12.0.

FT-IR (film) 2971, 1608, 1495, 1460, 1322, 1276, 1258, 1116, 1057, 1037, 754 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{12}H_{14}{}^{79}BrF_3O$: 310, found: 310.



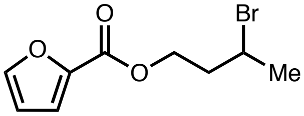
1-((3-Bromopentyl)oxy)-4-chlorobenzene. The bromide was prepared according to General Procedure A from the corresponding alcohol, 1-(4-chlorophenoxy)pentan-3-ol. The product was purified by flash chromatography (0→2% Et_2O/hexane). Pale-yellow oil (1.01 g, 92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.20 (m, 2H), 6.85 – 6.80 (m, 2H), 4.23 (ddt, 1H, J = 12.6, 8.1, 2.8), 4.17 – 4.08 (m, 2H), 2.35 – 2.25 (m, 1H), 2.25 – 2.15 (m, 1H), 2.01 – 1.85 (m, 2H), 1.10 (t, 3H, J = 7.3 Hz).

^{13}C NMR (126 MHz, CDCl$_3$) δ 157.3, 129.3, 125.7, 115.8, 66.1, 55.9, 38.1, 32.4, 12.0.

FT-IR (film) 2969, 2934, 2877, 1597, 1581, 1492, 1468, 1245, 823, 670 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{11}H_{14}{}^{79}BrClO$: 276, found: 276.



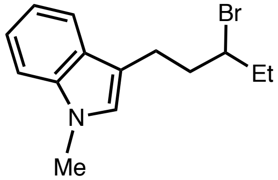
3-Bromobutyl furan-2-carboxylate. The bromide was prepared according to General Procedure A from the corresponding alcohol, 3-hydroxylbutyl furan-2-carboxylate. The product was purified by flash chromatography (10% EtOAc/hexane). Pale-yellow oil (1.34 g, 54%).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.57 (dd, 1H, *J* = 1.8, 0.9 Hz), 7.17 (dd, 1H, *J* = 3.5, 0.9 Hz), 6.51 (dd, 1H, *J* = 3.5, 1.7 Hz), 4.53 – 4.47 (m, 1H), 4.42 (ddd, 1H, *J* = 11.2, 7.9, 5.7 Hz), 4.27 (dqd, 1H, *J* = 9.0, 6.7, 4.5 Hz), 2.29 – 2.14 (m, 2H), 1.77 (d, 3H, *J* = 6.7 Hz).

^{13}C NMR (126 MHz, CDCl$_3$) δ 158.5, 146.4, 144.4, 118.1, 111.8, 62.9, 46.7, 39.7, 26.5.

FT-IR (film) 2969, 1724, 1473, 1296, 1179, 1116, 885, 761 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_9H_{11}{}^{79}BrO_3$: 246, found: 246.



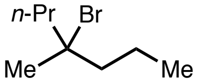
3-(3-Bromopentyl)-1-methyl-1*H*-indole. The bromide was prepared according to General Procedure A from the corresponding alcohol, 1-(1-methyl-1*H*-indol-3-yl)pentan-3-ol. The product was purified by flash chromatography (5→10% EtOAc/hexane). Pale-yellow oil (0.86 g, 34%).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.63 (dt, 1H, *J* = 7.9, 1.0 Hz), 7.33 – 7.30 (m, 1H), 7.27 – 7.23 (m, 1H), 7.15 – 7.10 (m, 1H), 6.91 (s, 1H), 4.03 (ddt, 1H, *J* = 8.6, 7.1, 5.2 Hz), 3.76 (s, 3H), 3.11 – 3.02 (m, 1H), 2.98 – 2.89 (m, 1H), 2.27 – 2.12 (m, 2H), 1.95 – 1.85 (m, 2H), 1.06 (t, 3H, *J* = 7.2 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.0, 127.7, 126.5, 121.5, 118.9, 118.6, 113.5, 109.2, 60.3, 39.3, 32.6, 32.3, 23.2, 12.0.

FT-IR (film) 2933, 1473, 1377, 1325, 1249, 802, 737 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{14}H_{18}{}^{79}BrN$: 279, found: 281 (M^++2).



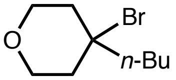
4-Bromo-4-methylheptane. The bromide was prepared according to General Procedure B from the corresponding alcohol, 4-methylheptan-4-ol. The product was distilled at 35 °C under reduced pressure (5 torr). Colorless oil (3.01 g, 81%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 1.87 – 1.72 (m, 4H), 1.70 (s, 3H), 1.56 – 1.45 (m, 4H), 0.94 (t, 6H, J = 7.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 74.1, 47.7, 31.5, 19.1, 14.1.

FT-IR (film) 2960, 2873, 1465, 1380, 1142, 1125, 806, 745 cm^{-1}.

MS (EI) *m/z* (M^+–Br) calcd for C_8H_{17}: 113, found: 113.



4-Bromo-4-butyltetrahydro-2*H*-pyran. The bromide was prepared according to General Procedure B from the corresponding alcohol, 4-butyltetrahydro-2*H*-pyran-4-ol. The product was distilled at 34 °C under reduced pressure (0.16 torr). Colorless oil (3.43 g, 88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.88 – 3.82 (m, 4H), 1.99 – 1.92 (m, 2H), 1.90 – 1.82 (m, 2H), 1.74 (ddd, 2H, J = 14.7, 9.2, 7.7 Hz), 1.59 – 1.51 (m, 2H), 1.41 – 1.31 (m, 2H), 0.94 (t, 3H, J = 7.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 72.6, 64.6, 46.8, 40.6, 26.6, 22.7, 14.0.

FT-IR (film) 2956, 2862, 1467, 1241, 1140, 1106, 1017, 857, 813, 637 cm^{-1}.

MS (EI) *m/z* (M^+–Br) calcd for $C_9H_{17}O$: 141, found: 141.

Nickel-Catalyzed Silylations of Unactivated Alkyl Halides

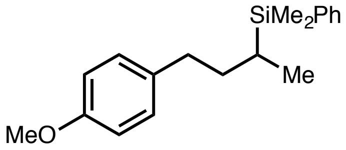
General procedure for the preparation of solutions of ClZn–SiMe$_2$Ph and ClZn–SiMePh$_2$.[29] An oven-dried 40-mL vial equipped with a magnetic stir bar was charged with elemental lithium (174 mg, 25 mmol, 2.5 equiv), closed with a PTFE septum cap, and placed under vacuum. The vial was refilled with argon, and this evacuation-refill cycle was repeated three times. THF (10 mL) was then added via syringe, an argon-filled balloon was attached to the vial, and the suspension was cooled to 0 °C. The chlorosilane (10 mmol, 1.0 equiv) was added via syringe, and then the reaction mixture was sonicated in an ice/water bath for 1 h, allowing the final bath temperature to reach ~10 °C. The mixture was then stirred under argon at 0 °C for 12 h. Next, the vial was warmed to r.t., and the supernatant was removed from the residual lithium metal and transferred via syringe to an oven-dried, septum-capped 40-mL vial equipped with a stir bar under a nitrogen atmosphere; the silyllithium was titrated against diphenylacetic acid according to Kofron's method.[30] In air, $ZnCl_2$ (dried with a heat gun under high vacuum for 20 min prior to the reaction; 1.0 equiv with respect to titrated silyllithium) was quickly weighed into an oven-dried 8-mL vial and placed under vacuum. The vial was refilled with nitrogen, and this evacuation-refill cycle was repeated three times. Dry THF was then added to form an ~1.2 M solution of $ZnCl_2$. This solution was added via syringe into a 40-mL vial equipped with a nitrogen-filled balloon that contained the silyllithium at 0 °C, and the reaction mixture was stirred at 0 °C for 30 min. After warming to r.t., the mixture was filtered under a nitrogen atmosphere by injecting it through a syringe filter directly into a nitrogen-filled, 20-mL scintillation vial sealed with a septum cap. The silylzinc solution (routinely formed as an ~0.4 M solution) was titrated using Knochel's method (at r.t.).[31]

These solutions of silylzinc halide reagents can be stored for 1 month without deterioration under an inert atmosphere at −35 °C.

Procedure for the preparation of a solution of $ClZn–SiPh_3$. An oven-dried 40-mL vial equipped with a magnetic stir bar was charged with elemental lithium (87 mg, 12.5 mmol, 2.5 equiv) and chlorotriphenylsilane (1.47 g, 5.0 mmol, 1.0 equiv), closed with a PTFE septum cap, and placed under vacuum. The vial was refilled with argon, and this evacuation-refill cycle was repeated three times. THF (10 mL) was then added via syringe, an argon-filled balloon was attached to the vial, and the suspension was cooled to 0 °C and sonicated in an ice/water bath for 2 h, allowing the final bath temperature to reach r.t. and forming a brownish-green slurry. The mixture was then stirred under argon at 0 °C for 12 h. Next, the vial was warmed to r.t. and transferred into a nitrogen-filled glovebox. The supernatant was removed from the residual lithium metal and filtered through a fritted funnel; the dark-green silyllithium was then titrated against diphenyl acetic acid. $ZnCl_2$ (dried with a heat gun under high vacuum for 20 min prior to the reaction; 1.0 equiv with respect to titrated silyllithium) was weighed in the glovebox into an oven-dried 8-mL vial, and dry THF was added to form an ~1.2 M solution of $ZnCl_2$. Outside of the glovebox, this solution was added via syringe into a 40-mL vial that contained the silyllithium at 0 °C, and the reaction mixture was stirred at this temperature for 30 min. After warming to r.t., the vial was transferred into the glovebox, and the reaction mixture was filtered by injecting it through a syringe filter. The silylzinc solution was titrated using Knochel's method for alkylzinc titration.[31]

General procedure for nickel-catalyzed silylations of unactivated alkyl halides. An oven-dried 20-mL vial equipped with a magnetic stir bar was charged with $NiBr_2$·diglyme (4.9 mg, 0.014 mmol) and sealed with a PTFE septum cap. The vial was placed under vacuum and refilled with nitrogen, and this evacuation-refill cycle was repeated three times. DMA (2.1 mL) was added via syringe, and the mixture was stirred vigorously at r.t. for 10 min. The alkyl bromide (0.7 mmol) was added via syringe, followed by stirring at r.t. for 5 min. A nitrogen-filled balloon was attached to the vial, which was then cooled to −20 °C. The mixture was stirred for 5 min, and then the solution of the silylzinc in THF (1.05 mmol, 1.5 equiv) was added, the balloon was removed, the puncture hole was covered with vacuum grease, and the reaction mixture was stirred at −20 °C for 6–24 h. The reaction was then quenched by the addition of ethanol (0.7 mL), followed by stirring for 1 min. The mixture was next allowed to warm to r.t., and then it was diluted with Et_2O (100 mL) and washed with deionized water (20 mL × 3). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography.

For electrophiles that are solids or are viscous liquids: The alkyl bromide (0.70 mmol) was weighed into an oven-dried 20-mL vial charged with a magnetic stir bar, which was then placed under vacuum. The vial was refilled with nitrogen, and this evacuation-refill cycle was repeated three times. The solution of $NiBr_2$·diglyme in DMA prepared as described above was added to the alkyl bromide, and the mixture was stirred vigorously at r.t. for 5 min. The procedure was then completed as described above.



(4-(4-Methoxyphenyl)butan-2-yl)dimethyl(phenyl)silane (Table 2.2, Entry 1). The title compound was synthesized according to the General Procedure, using 2.0 mol% $NiBr_2$·diglyme, from 1-(3-bromobutyl)-4-methoxybenzene (170 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (10→15% CH_2Cl_2/hexane). Colorless oil.

First run: 167 mg (80% yield). Second run: 164 mg (78% yield).

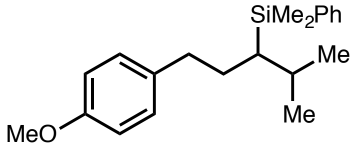
This compound was also prepared on a 4.5 mmol scale, using (1-(3-bromobutyl)-4-methoxybenzene (1.09 g, 4.50 mmol), the silylzinc reagent (0.46 M; 14.7 mL, 6.8 mmol, 1.5 equiv), and $NiBr_2$·diglyme (15.9 mg, 0.045 mmol; 1.0 mol%). Reaction time: 12 h. The title compound was isolated in 81% yield (1.09 g).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 2H), 7.39 – 7.33 (m, 3H), 7.06 – 7.02 (m, 2H), 6.84 – 6.80 (m, 2H), 3.80 (s, 3H), 2.72 (ddd, 1H, *J* = 14.4, 10.1, 4.8 Hz), 2.43 (ddd, 1H, *J* = 13.7, 9.7, 6.8 Hz), 1.79 (dddd, 1H, *J* = 16.7, 9.7, 6.5, 3.2 Hz), 1.46 – 1.34 (m, 1H), 1.05 – 1.00 (m, 3H), 0.96 – 0.87 (m, 1H), 0.26 (d, 6H, *J* = 4.6 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 138.6, 134.9, 133.9, 129.2, 128.8, 127.6, 113.7, 55.2, 33.91, 33.89, 18.7, 14.0, −4.7, −5.0.

FT-IR (film) 2952, 1512, 1246, 1112, 1038, 816, 701 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{19}H_{26}OSi$: 298, found: 298.



1-(4-Methoxyphenyl)-4-methylpentan-3-yl)dimethyl(phenyl)silane (Table 2.2, Entry 2). The title compound was synthesized according to the General Procedure, using 5.0 mol% $NiBr_2$·diglyme, from 1-(3-bromo-4-methylpentyl)-4-methoxybenzene (190 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (0→20% CH_2Cl_2/hexane). Colorless oil.

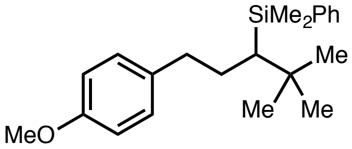
First run: 175 mg (76% yield). Second run: 173 mg (76% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.50 (m, 2H), 7.37 – 7.33 (m, 3H), 6.98 – 6.93 (m, 2H), 6.81 – 6.77 (m, 2H), 3.79 (s, 3H), 2.53 – 2.36 (m, 2H), 1.99 (ddq, 1H, *J* = 10.7, 6.9, 3.5 Hz), 1.72 – 1.63 (m, 2H), 0.96 (d, 3H, *J* = 6.8 Hz), 0.92 – 0.87 (m, 4H), 0.34 (d, 6H, *J* = 3.7 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 140.1, 135.0, 133.8, 129.2, 128.6, 127.6, 113.6, 55.2, 35.8, 32.6, 29.3, 28.6, 22.9, 21.3, −1.9, −2.7.

FT-IR (film) 2953, 1511, 1246, 1110, 1039, 820, 701 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{21}H_{30}OSi$: 326, found: 326.



(1-(4-Methoxyphenyl)-4,4-dimethylpentan-3-yl)dimethyl(phenyl)silane (Table 2.2, Entry 3). The title compound was synthesized according to the General Procedure, using 5.0 mol% $NiBr_2$·diglyme, from 1-(3-bromo-4,4-dimethylpentyl)-4-methoxybenzene (200 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (0→20% CH_2Cl_2/hexane). Colorless oil.

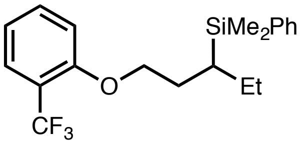
First run: 161 mg (68% yield). Second run: 161 mg (68% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.55 (m, 2H), 7.41 – 7.35 (m, 3H), 6.87 – 6.81 (m, 2H), 6.80 – 6.75 (m, 2H), 3.78 (s, 3H), 2.38 (ddd, 1H, *J* = 13.2, 11.5, 5.9 Hz), 2.09 (ddd, 1H, *J* = 13.2, 11.7, 5.6 Hz), 1.67 – 1.52 (m, 2H), 0.96 (s, 9H), 0.75 (dd, 1H, *J* = 4.9, 3.8 Hz), 0.43 (s, 3H), 0.38 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 141.0, 135.2, 134.0, 129.1, 128.5, 127.6, 113.6, 55.2, 38.76, 38.74, 34.8, 30.9, 30.6, 0.1, −2.0.

FT-IR (film) 2953, 1512, 1246, 816, 702 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{22}H_{32}OSi$: 340, found: 325 (M^+-CH_3).



Dimethyl(phenyl)(1-(2-(trifluoromethyl)phenoxy)pentan-3-yl)silane (Table 2.2, Entry 4). The title compound was synthesized according to the General Procedure, using 2.0 mol% NiBr$_2$·diglyme, from 1-((3-bromopentyl)oxy)-2-(trifluoromethyl)benzene (218 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil.

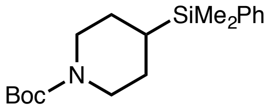
First run: 145 mg (57% yield). Second run: 166 mg (65% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.58 – 7.52 (m, 3H), 7.43 – 7.39 (m, 1H), 7.37 – 7.33 (m, 3H), 6.99 – 6.94 (m, 1H), 6.79 (d, 1H, *J* = 8.4 Hz), 3.97 – 3.92 (m, 2H), 1.99 (dtd, 1H, *J* = 14.3, 7.2, 5.1 Hz), 1.80 (ddt, 1H, *J* = 14.4, 8.3, 6.1 Hz), 1.61 (dqd, 1H, *J* = 14.0, 7.4, 5.1 Hz), 1.46 – 1.37 (m, 1H), 1.10 (ddt, 1H, *J* = 8.3, 7.1, 5.1 Hz), 0.93 (t, 3H, *J* = 7.4 Hz), 0.33 (d, 6H, *J* = 3.7 Hz).

^{13}C NMR (126 MHz, CDCl$_3$) δ 156.9 (d, *J* = 1.8 Hz), 138.8, 133.8, 133.1, 128.8, 127.7, 127.0 (q, *J* = 5.3 Hz), 127.8 (q, *J* = 272.3 Hz), 119.6, 118.7 (q, *J* = 30.5 Hz), 112.6, 67.9, 28.6, 22.9, 22.5, 13.8, −3.7, −4.2.

FT-IR (film) 2959, 1610, 1460, 1323, 1275, 1258, 1133, 1117, 1057, 1038, 830, 810, 755, 701 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{20}H_{25}F_3OSi$: 366, found: 351 (M$^+$−CH$_3$).



***tert*-Butyl 4-(dimethyl(phenyl)silyl)piperidine-1-carboxylate (Table 2.2, Entry 5).** The title compound was synthesized according to the General Procedure, using 2.0 mol% NiBr$_2$·diglyme, from *tert*-butyl 4-bromopiperidine-1-carboxylate (185 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (8:4:1 hexane/CH$_2$Cl$_2$/Et$_2$O). Colorless oil.

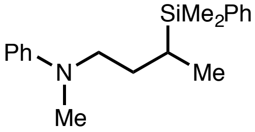
First run: 168 mg (75% yield). Second run: 162 mg (73% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.45 (m, 2H), 7.38 – 7.33 (m, 3H), 4.20 – 4.00 (br, 2H), 2.64 – 2.54 (m, 2H), 1.61 – 1.52 (m, 2H), 1.44 (s, 9H), 1.36 – 1.21 (m, 2H), 0.95 – 0.84 (m, 1H), 0.26 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 154.9, 137.5, 133.9, 129.0, 127.8, 79.1, 45.7, 28.5, 26.6, 23.9, −5.4.

FT-IR (film) 2928, 1693, 1427, 1248, 1167, 832, 809 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{18}H_{29}NO_2Si$: 319, found: 218 (M^+−Boc).



***N*-(3-(Dimethyl(phenyl)silyl)butyl)-*N*-methylaniline (Table 2.2, Entry 6)**. The title compound was synthesized according to the General Procedure, using 2.0 mol% $NiBr_2$·diglyme, from *N*-(3-bromobutyl)-*N*-methylaniline (170 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (10→20% CH_2Cl_2/hexane). Pale-yellow oil.

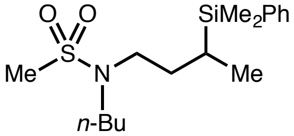
First run: 158 mg (76% yield). Second run: 160 mg (77% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.49 (m, 2H), 7.40 – 7.33 (m, 3H), 7.23 – 7.17 (m, 2H), 6.70 – 6.60 (m, 3H), 3.41 (ddd, 1H, J = 14.9, 10.6, 4.6 Hz), 3.19 (ddd, 1H, J = 14.5, 10.3, 6.0 Hz), 2.86 (s, 3H), 1.81 (dddd, 1H, J = 13.8, 10.6, 6.1, 3.4 Hz), 1.37 – 1.26 (m, 1H), 1.06 (d, 3H, J = 7.3 Hz), 0.93 – 0.85 (m, 1H), 0.28 (d, 6H, J = 2.9 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.4, 138.3, 133.9, 129.1, 128.9, 127.7, 115.9, 112.1, 52.2, 37.9, 28.4, 17.1, 14.4, −4.7, −5.1.

FT-IR (film) 2953, 1600, 1506, 1248, 1112, 833, 814, 746, 701, 691 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{19}H_{27}NSi$: 297, found: 297.



***N*-Butyl-*N*-(3-(dimethyl(phenyl)silyl)butyl)methanesulfonamide (Table 2.2, Entry 7)**. The title compound was synthesized according to the General Procedure, using

2.0 mol% $NiBr_2$·diglyme, from *N*-(3-bromobutyl)-*N*-butylmethanesulfonamide (200 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (25→35% Et_2O/hexane). Colorless oil.

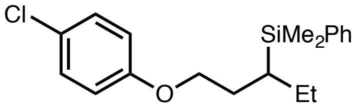
First run: 192 mg (80% yield). Second run: 182 mg (76% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 2H), 7.38 – 7.33 (m, 3H), 3.18 (ddd, 1H, *J* = 14.3, 9.9, 4.6 Hz), 3.13 – 2.96 (m, 3H), 2.74 (s, 3H), 1.75 (dddd, 1H, *J* = 13.4, 10.1, 6.8, 3.5 Hz), 1.52 – 1.40 (m, 2H), 1.33 – 1.20 (m, 3H), 0.99 (d, 3H, *J* = 7.3 Hz), 0.91 – 0.85 (m, 4H), 0.28 (d, 6H, *J* = 0.7 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.0, 133.9, 129.0, 127.8, 47.4, 47.0, 38.3, 30.8, 30.7, 19.9, 16.8, 14.0, 13.6, −4.7, −5.4.

FT-IR (film) 2956, 2869, 1334, 1249, 1146, 1112, 835, 816, 773, 702 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{17}H_{31}NO_2SSi$: 341, found: 326 ($M^+{-}CH_3$).



(1-(4-Chlorophenoxy)pentan-3-yl)dimethyl(phenyl)silane (Table 2.2, Entry 8). The title compound was synthesized according to the General Procedure, using 2.0 mol% $NiBr_2$·diglyme, from 1-((3-bromopentyl)oxy)-4-chlorobenzene (195 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (0→2% Et_2O/hexane). Colorless oil.

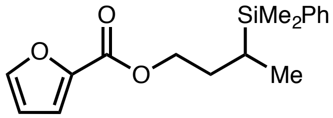
First run: 146 mg (63% yield). Second run: 156 mg (67% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 – 7.50 (m, 2H), 7.39 – 7.32 (m, 3H), 7.21 – 7.16 (m, 2H), 6.73 – 6.67 (m, 2H), 3.88 – 3.75 (m, 2H), 1.93 (dddd, 1H, *J* = 13.6, 8.2, 6.6, 5.1 Hz), 1.77 (dtd, 1H, *J* = 13.8, 8.0, 5.7 Hz), 1.61 (dqd, 1H, *J* = 13.9, 7.5, 5.0 Hz), 1.44 – 1.36 (m, 1H), 1.00 – 0.90 (m, 4H), 0.32 (d, 6H, *J* = 4.1 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 138.8, 133.8, 129.2, 128.9, 127.8, 125.3, 115.7, 67.9, 28.7, 23.7, 22.7, 13.9, −3.7, −4.2.

FT-IR (film) 2957, 1492, 1244, 823, 701 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{19}H_{25}ClOSi$: 332, found: 332.



3-(Dimethyl(phenyl)silyl)butyl furan-2-carboxylate (Table 2.2, Entry 9). The title compound was synthesized according to the General Procedure, using 2.0 mol% $NiBr_2$·diglyme, from 3-bromobutyl furan-2-carboxylate (173 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (10→15% CH_2Cl_2/hexane). Colorless oil.

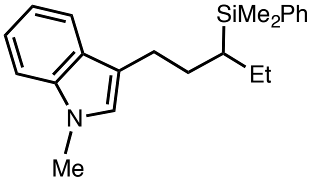
First run: 158 mg (75% yield). Second run: 158 mg (75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 – 7.56 (m, 1H), 7.53 – 7.48 (m, 2H), 7.38 – 7.33 (m, 3H), 7.14 (dd, 1H, J = 3.5, 0.9 Hz), 6.50 (dd, 1H, J = 3.5, 1.7 Hz), 4.40 – 4.22 (m, 2H), 2.01 – 1.91 (m, 1H), 1.54 – 1.41 (m, 1H), 1.09 – 1.00 (m, 4H), 0.29 (d, 6H, J = 4.2 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 146.1, 145.0, 137.9, 133.9, 129.0, 127.7, 117.6, 111.7, 64.3, 30.6, 15.9, 13.9, −4.9, −5.2.

FT-IR (film) 2956, 1728, 1475, 1295, 1180, 1117, 833, 815, 764, 702 cm^{-1}.

MS (EI) m/z (M^+) calcd for $C_{17}H_{22}O_3Si$: 302, found: 302.



3-(3-(Dimethyl(phenyl)silyl)pentyl)-1-methyl-1*H*-indole (Table 2.2, Entry 10). The title compound was synthesized according to the General Procedure, using 5.0 mol% $NiBr_2$·diglyme, from 3-(3-bromopentyl)-1-methyl-1*H*-indole (196 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (10→15% CH_2Cl_2/hexane). Pale-yellow oil.

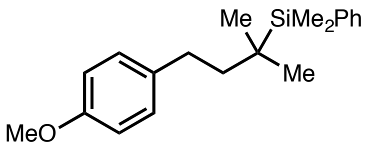
First run: 186 mg (79% yield). Second run: 185 mg (79% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 2H), 7.47 (dt, 1H, J = 7.9, 0.9 Hz), 7.40 – 7.34 (m, 3H), 7.30 – 7.27 (m, 1H), 7.24 – 7.20 (m, 1H), 7.10 – 7.07 (m, 1H), 6.72 (s, 1H), 3.73 (s, 3H), 2.79 (dddd, 1H, J = 14.6, 10.8, 5.1, 0.9 Hz), 2.65 (dddd, 1H, J = 14.5, 10.9, 6.0, 0.9 Hz), 1.89 (dddd, 1H, J = 13.7, 10.7, 6.0, 4.7 Hz), 1.79 – 1.62 (m, 2H), 1.56 – 1.45 (m, 1H), 1.01 – 0.90 (m, 4H), 0.33 (d, 6H, J = 3.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 139.5, 137.1, 133.9, 128.7, 128.0, 127.7, 125.8, 121.3, 119.1, 118.4, 115.7, 109.0, 32.5, 30.2, 27.1, 24.8, 22.4, 13.8, −3.5, −3.7.

FT-IR (film) 2955, 2929, 1484, 1472, 1426, 1376, 1325, 1247, 1111, 830, 810, 736, 701 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{22}H_{29}NSi$: 335, found: 335.



(4-(4-Methoxyphenyl)-2-methylbutan-2-yl)dimethyl(phenyl)silane (Table 2.3, Entry 1). The title compound was synthesized according to the General Procedure, using 10 mol% $NiBr_2$·diglyme, from 1-(3-bromo-3-methylbutyl)-4-methoxybenzene (180 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (10→20% CH_2Cl_2/hexane). Colorless oil.

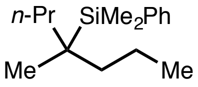
First run: 154 mg (70% yield). Second run: 150 mg (69% yield). The isolated product includes a small amount of a non-polar impurity that co-elutes with the desired product during column chromatography.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 2H), 7.42 – 7.33 (m, 3H), 7.07 – 7.01 (m, 2H), 6.87 – 6.78 (m, 2H), 3.79 (s, 3H), 2.51 – 2.44 (m, 2H), 1.58 – 1.50 (m, 2H), 0.99 (s, 6H), 0.32 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.5, 137.8, 135.6, 134.5, 129.1, 128.8, 127.5, 113.7, 55.2, 41.6, 29.2, 23.1, 20.1, −5.6.

FT-IR (film) 2953, 1512, 1246, 1039, 817, 770, 736, 701 cm^{-1}.

MS (EI) *m/z* (M^+) calcd for $C_{20}H_{28}OSi$: 312, found: 312.



Dimethyl(4-methylheptan-4-yl)(phenyl)silane (Table 2.3, Entry 2). The title compound was synthesized according to the General Procedure, using 10 mol% $NiBr_2$·diglyme, from 4-bromo-4-methylheptane (135 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil.

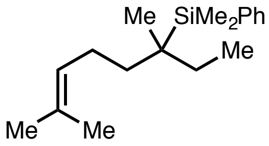
First run: 94 mg (54% yield). Second run: 92 mg (53% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.56 – 7.49 (m, 2H), 7.37 – 7.31 (m, 3H), 1.36 – 1.17 (m, 8H), 0.91 – 0.80 (m, 9H), 0.30 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 139.0, 134.5, 128.5, 127.4, 39.3, 24.0, 22.2, 17.5, 15.2, –4.1.

FT-IR (film) 2956, 2871, 1467, 1427, 1248, 1112, 816, 767, 735, 700 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{16}H_{28}Si$: 248, found: 248.



(3,7-Dimethyloct-6-en-3-yl)dimethyl(phenyl)silane (Table 2.3, Entry 3). The title compound was synthesized according to the General Procedure, using 10 mol% NiBr$_2$·diglyme, from 6-bromo-2,6-dimethyloct-2-ene (153 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil.

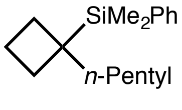
First run: 92 mg (48% yield). Second run: 95 mg (49% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.56 – 7.49 (m, 2H), 7.38 – 7.30 (m, 3H), 5.08 – 5.03 (m, 1H), 1.92 – 1.84 (m, 2H), 1.71 – 1.65 (m, 3H), 1.58 – 1.56 (m, 3H), 1.41 – 1.24 (m, 4H), 0.89 (s, 3H), 0.81 (t, 3H, J = 7.5 Hz), 0.32 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 138.9, 134.5, 130.8, 128.6, 127.4, 125.4, 36.0, 28.6, 25.7, 23.8, 23.0, 21.6, 17.6, 8.7, −4.1, −4.2.

FT-IR (film) 2960, 1460, 1427, 1377, 1248, 1110, 830, 811, 767, 735, 701 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{18}H_{30}Si$: 274, found: 274.



Dimethyl(1-pentylcyclobutyl)(phenyl)silane (Table 2.3, Entry 4). The title compound was synthesized according to the General Procedure, using 10 mol% NiBr$_2$·diglyme, from 1-bromo-1-pentylcyclobutane (144 mg, 0.70 mmol). Reaction time: 24

h. The product was purified by column chromatography on silica gel (hexane). Colorless oil.

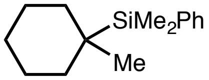
First run: 121 mg (66% yield). Second run: 132 mg (73% yield).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.58 – 7.53 (m, 2H), 7.39 – 7.32 (m, 3H), 2.13 – 2.05 (m, 2H), 1.93 – 1.76 (m, 3H), 1.70 – 1.59 (m, 1H), 1.51 – 1.42 (m, 2H), 1.31 – 1.15 (m, 6H), 0.86 (t, 3H, J = 7.1 Hz), 0.33 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 138.9, 134.1, 128.7, 127.5, 39.6, 32.9, 29.2, 28.3, 25.2, 22.6, 17.2, 14.1, −4.9.

FT-IR (film) 2924, 2853, 1247, 1112, 815, 699 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{17}H_{28}Si$: 260, found: 260.



Dimethyl(1-methylcyclohexyl)(phenyl)silane (Table 2.3, Entry 5). The title compound was synthesized according to the General Procedure, using 10 mol% NiBr$_2$·diglyme, from 1-bromo-1-methylcyclohexane (124 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil.

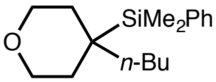
First run: 113 mg (69% yield). Second run: 118 mg (72% yield). The isolated product includes a small amount of a non-polar impurity that co-elutes with the desired product during column chromatography.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 – 7.48 (m, 2H), 7.38 – 7.32 (m, 3H), 1.65 – 1.56 (m, 1H), 1.55 – 1.40 (m, 4H), 1.40 – 1.26 (m, 4H), 1.17 – 1.05 (m, 1H), 0.95 (s, 3H), 0.27 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 137.7, 134.7, 128.6, 127.3, 31.9, 26.7, 20.3, 20.0, 17.9, −6.5.

FT-IR (film) 2916, 1426, 1246, 1106, 815, 766, 734, 699 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{15}H_{24}Si$: 232, found: 232.



(4-Butyltetrahydro-2*H*-pyran-4-yl)dimethyl(phenyl)silane (Table 2.3, Entry 6). The title compound was synthesized according to the General Procedure, using 2.0 mol% $NiBr_2$·diglyme, from 4-bromo-4-butyltetrahydro-2*H*-pyran (155 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (5→10% Et_2O/hexane). Colorless oil.

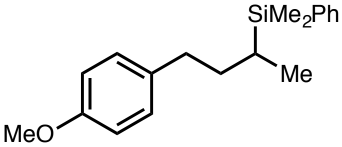
First run: 145 mg (75% yield). Second run: 142 mg (73% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 2H), 7.38 – 7.32 (m, 3H), 3.71 – 3.56 (m, 4H), 1.90 – 1.79 (m, 2H), 1.61 – 1.54 (m, 2H), 1.37 – 1.30 (m, 2H), 1.28 – 1.20 (m, 2H), 1.17 – 1.09 (m, 2H), 0.85 (t, 3H, J = 7.3 Hz), 0.32 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.9, 134.5, 128.9, 127.6, 62.6, 31.5, 30.6, 27.6, 23.8, 21.8, 14.0, −4.7.

FT-IR (film) 2953, 2931, 2858, 1427, 1249, 1105, 866, 826, 809, 767, 736, 701 cm^{-1}.

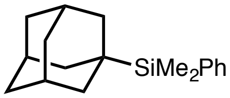
MS (EI) *m/z* (M^+) calcd for $C_{17}H_{28}OSi$: 276, found: 261 (M^+-CH_3).



(4-(4-Methoxyphenyl)butan-2-yl)dimethyl(phenyl)silane (Eq. 2.3). The title compound was synthesized according to the General Procedure, using 2.0 mol% $NiBr_2$·diglyme, from 1-(3-iodobutyl)-4-methoxybenzene (203 mg, 0.70 mmol). Reaction time: 6 h. The product was purified by column chromatography on silica gel (10→25% CH_2Cl_2/hexane). Colorless oil.

First run: 130 mg (62% yield). Second run: 130 mg (62% yield).

For the characterization data, see Table 2, Entry 1 (above).



(Adamantan-1-yl)dimethyl(phenyl)silane (Eq. 2.4). The title compound was synthesized according to the General Procedure, using 10 mol% $NiBr_2$·diglyme, from 1-iodoadamantane (183 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil.

First run: 102 mg (54% yield). Second run: 105 mg (56% yield).

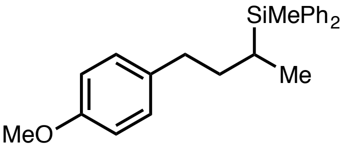
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 – 7.46 (m, 2H), 7.39 – 7.33 (m, 3H), 1.84 – 1.81 (m, 3H), 1.77 – 1.63 (m, 12H), 0.23 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.2, 134.6, 128.6, 127.3, 37.5, 37.1, 27.6, 21.5, −7.3.

FT-IR (film) 2896, 2843, 1426, 1252, 1115, 852, 827, 799, 764, 733, 699 cm^{-1}.

MS (ESI) *m/z* (M^+) calcd for $C_{18}H_{26}Si$: 270, found: 270.

The spectral data are in agreement with literature data.[32]



(4-(4-Methoxyphenyl)butan-2-yl)(methyl)diphenylsilane (Eq. 2.5). The title compound was synthesized according to the General Procedure, using 10 mol% $NiBr_2$·diglyme, from 1-(3-bromobutyl)-4-methoxybenzene (170 mg, 0.70 mmol) and a silylzinc reagent prepared from chloro(methyl)diphenylsilane. Reaction time: 24 h. The product was purified by column chromatography on silica gel (10→20% CH_2Cl_2/hexane). Colorless oil.

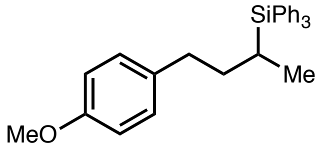
First run: 224 mg (89% yield). Second run: 216 mg (85% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.48 (m, 4H), 7.41 – 7.32 (m, 6H), 7.05 – 7.00 (m, 2H), 6.85 – 6.80 (m, 2H), 3.81 (s, 3H), 2.76 (ddd, 1H, J = 14.0, 9.6, 4.7 Hz), 2.47 (ddd, 1H, J = 13.7, 9.2, 7.4 Hz), 1.94 – 1.84 (m, 1H), 1.46 (dddd, 1H, J = 13.6, 10.8, 9.2, 4.7 Hz), 1.39 – 1.30 (m, 1H), 1.10 (d, 3H, J = 7.3 Hz), 0.54 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 136.5, 136.3, 134.81, 134.78, 134.6, 129.4, 129.03, 128.99, 127.71, 127.69, 113.6, 55.2, 33.77, 33.71, 16.8, 14.0, −6.4.

FT-IR (film) 3068, 2952, 2852, 1611, 1511, 1427, 1244, 1110, 1037, 785, 699 cm^{-1}.

MS (EI) *m/z* (M$^+$) calcd for $C_{24}H_{28}OSi$: 360, found: 360.



(4-(4-Methoxyphenyl)butan-2-yl)triphenylsilane (Eq. 2.5). The title compound was synthesized according to the General Procedure, using 10 mol% $NiBr_2$·diglyme, from 1-(3-bromobutyl)-4-methoxybenzene (170 mg, 0.70 mmol) and a silylzinc reagent prepared from chlorotriphenylsilane. Reaction time: 24 h; reaction temperature: r.t. The product was purified by column chromatography on silica gel (10→20% CH_2Cl_2/hexane). Colorless, viscous oil.

First run: 234 mg (79% yield). Second run: 236 mg (80% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.53 (m, 6H), 7.44 – 7.40 (m, 3H), 7.39 – 7.34 (m, 6H), 7.09 – 7.05 (m, 2H), 6.88 – 6.84 (m, 2H), 3.82 (s, 3H), 2.83 (ddd, 1H, J = 13.6, 9.0, 4.6 Hz), 2.56 (dt, 1H, J = 13.6, 8.3 Hz), 2.10 (dddd, 1H, J = 13.7, 9.0, 8.0, 2.3 Hz), 1.75 – 1.66 (m, 1H), 1.58 – 1.48 (m, 1H), 1.25 (d, 3H, J = 7.3 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 136.0, 134.5, 134.3, 129.5, 129.2, 127.7, 113.6, 55.2, 34.0, 33.6, 15.8, 14.3.

FT-IR (film) 3067, 2931, 1511, 1428, 1246, 1109, 741, 700 cm^{-1}.

MS (ESI) *m/z* (M$^+$) calcd for $C_{29}H_{30}OSi$: 422, found: 345 ($M^+-C_6H_5$).

(*exo*-Bicyclo[2.2.1]heptan-2-yl)dimethyl(phenyl)silane (Eq. 2.6) [65118-96-9]. The title compound was synthesized according to the General Procedure, using 5.0 mol% $NiBr_2$·diglyme, from *exo*-2-bromobicyclo[2.2.1]heptane (123 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil. The diastereoselectivity was determined by GC analysis of the unpurified cross-coupling product.

The major diastereomer was determined to be the exo isomer by comparing the ^{1}H NMR data with the data reported in the literature.[33] Additionally, after converting the product mixture to the corresponding bicyclo[2.2.1]heptan-2-ol via a Fleming oxidation,[34] the major alcohol product was confirmed to be the exo isomer by comparing with commercially available *exo*-bicyclo[2.2.1]heptan-2-ol.

First run: 136 mg (84% yield, exo/endo = 7:1). Second run: 137 mg (85% yield, exo/endo = 7:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (major, exo) 7.57 – 7.52 (m, 2H), 7.38 – 7.35 (m, 3H), 2.25 – 2.23 (m, 2H), 1.56 – 1.39 (m, 4H), 1.29 – 1.20 (m, 2H), 1.08 (m, 2H), 0.86 – 0.82 (m, 1H), 0.27 (s, 3H), 0.25 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (major, exo) 139.4, 133.9, 128.7, 127.6, 37.9, 37.8, 36.9, 34.3, 32.7, 28.9, 28.5, –4.06, –4.10.

FT-IR (film) 2947, 2865, 1427, 1246, 1113, 698 cm^{-1}.

MS (ESI) *m/z* (M^+) calcd for $C_{15}H_{22}Si$: 230, found: 230.

(*exo*-Bicyclo[2.2.1]heptan-2-yl)dimethyl(phenyl)silane (Eq. 2.7) [65118-96-9]. The title compound was synthesized according to the General Procedure, using 5.0 mol% catalyst loading, from *endo*-2-bromobicyclo[2.2.1]heptane (123 mg, 0.70 mmol). Reaction time: 24 h. The product was purified by column chromatography on silica gel (hexane). Colorless oil. The diastereoselectivity was determined by GC analysis of the unpurified cross-coupling product.

First run: 121 mg (75% yield, exo/endo = 7:1). Second run: 114 mg (71% yield, exo/endo = 7:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (major, exo) 7.56 – 7.52 (m, 2H), 7.38 – 7.35 (m, 3H), 2.25 – 2.23 (m, 2H), 1.57 – 1.39 (m, 4H), 1.29 – 1.20 (m, 2H), 1.08 (m, 2H), 0.86 – 0.81 (m, 1H), 0.27 (s, 3H), 0.25 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (major, exo) 139.3, 133.9, 128.7, 127.6, 37.9, 37.8, 36.9, 34.3, 32.7, 28.9, 28.5, –4.06, –4.10.

FT-IR (film) 2946, 2864, 1426, 1246, 1113, 698 cm^{-1}.

MS (ESI) *m/z* (M^+) calcd for $C_{15}H_{22}Si$: 230, found: 230.

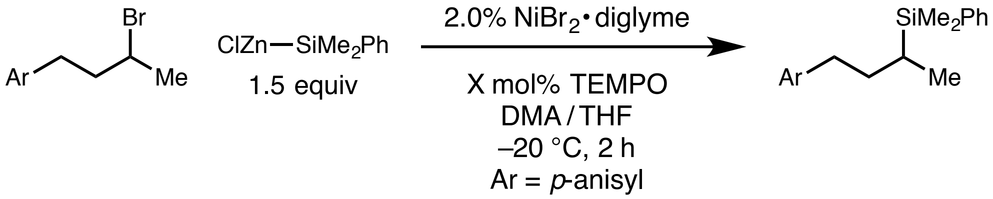
Competition Experiments (Eqs. 2.8 and 2.9). In a nitrogen-filled glovebox, $NiBr_2$·diglyme (3.5 mg, 0.010 mmol) was added to an oven-dried 4-mL vial equipped with a stir bar. DMA (0.3 mL) was added to the vial, and then the vial was closed with a PTFE septum cap and removed from the glovebox. The mixture was vigorously stirred at r.t. for 10 min, and then the two alkyl bromides (0.10 mmol each) were added to the vial via syringe, and the mixture was stirred at r.t. for 5 min. Next, the vial was cooled to –20 °C, and the reaction mixture was stirred for 5 min. Then, a solution of the silylzinc reagent (0.060 M; 0.33 mL, 0.020 mmol, 0.20 equiv) was added in one portion. The reaction mixture was stirred at −20 °C for 4 h, and then the reaction was quenched with ethanol (0.1 mL). *n*-Tetradecane (26 μL) was added to the vial as an internal standard, and the reaction mixture was analyzed via GC.

Effect of TEMPO

Entry 1 (no TEMPO): In a nitrogen-filled glovebox, $NiBr_2$·diglyme (7.0 mg, 0.020 mmol) was added to an oven-dried 4-mL vial equipped with a stir bar. DMA (3.0 mL) was added to the vial, and then the vial was closed with a PTFE septum cap. The mixture was vigorously stirred at r.t. for 10 min. Then, the stock solution of the catalyst (0.30 mL; 0.0020 mmol) was added to a 4-mL vial that contained the alkyl bromide (0.10 mmol) and a stir bar. The vial was closed with a PTFE septum cap and removed from the glovebox. The reaction mixture was stirred at r.t. for 5 min, and then the vial was cooled to –20 °C and the reaction mixture was stirred for an additional 5 min. A nitrogen-filled balloon was affixed to the vial. Next, a solution of the silylzinc reagent in THF (0.15 mmol, 1.5 equiv) was added, and the balloon was removed. The reaction mixture was stirred at –20 °C for 2 h, and then the reaction was quenched by the addition of ethanol (0.1 mL). The mixture was allowed to warm to r.t., *n*-tetradecane (26 μL) was added to the vial, and the reaction mixture was analyzed by GC.

Entries 2 and 3 (with TEMPO): In a nitrogen-filled glovebox, $NiBr_2$·diglyme (7.0 mg, 0.020 mmol) was added to an oven-dried 4-mL vial equipped with a stir bar. DMA (3.0 mL) was added to the vial, and then the vial was closed with a PTFE septum cap. The mixture was vigorously stirred at r.t. for 10 min. Then, the stock solution of the catalyst (0.30 mL; 0.0020 mmol) was added to a 4-mL vial that contained the alkyl bromide (0.10 mmol), TEMPO (1.6 mg, 0.010 mmol; or, 16 mg, 0.10 mmol), and a stir bar. The vial was closed with a PTFE septum cap and removed from the glovebox. The reaction mixture was stirred at r.t. for 5 min, and then the vial was cooled to –20 °C and the reaction mixture was stirred for an additional 5 min. A nitrogen-filled balloon was affixed to the vial. Next, a solution of the silylzinc reagent in THF (0.15 mmol, 1.5 equiv) was added, and the balloon was removed. The reaction mixture was stirred at –20 °C for 2 h, and then the reaction was quenched by the addition of ethanol (0.1 mL). The mixture was allowed to warm to r.t., *n*-tetradecane (26 μL) was added to the vial, and the reaction mixture was analyzed by GC.

Table 2.4 Effect of TEMPO



entry	X mol% TEMPO	yield (%)[a]
1	0	86
2	10	24
3	100	<2

[a] Yields were determined by GC analysis with the aid of a calibrated internal standard (average of two experiments).

^{1}H and ^{13}C NMR Spectra

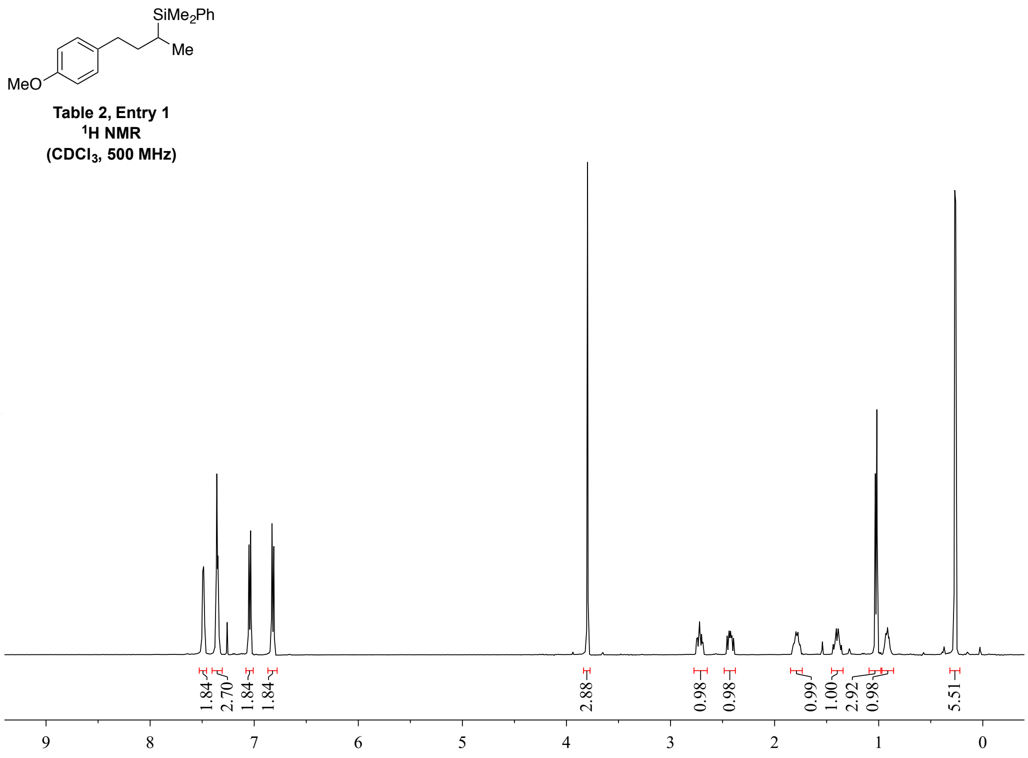


Table 2, Entry 1
^{1}H NMR
($CDCl_3$, 500 MHz)

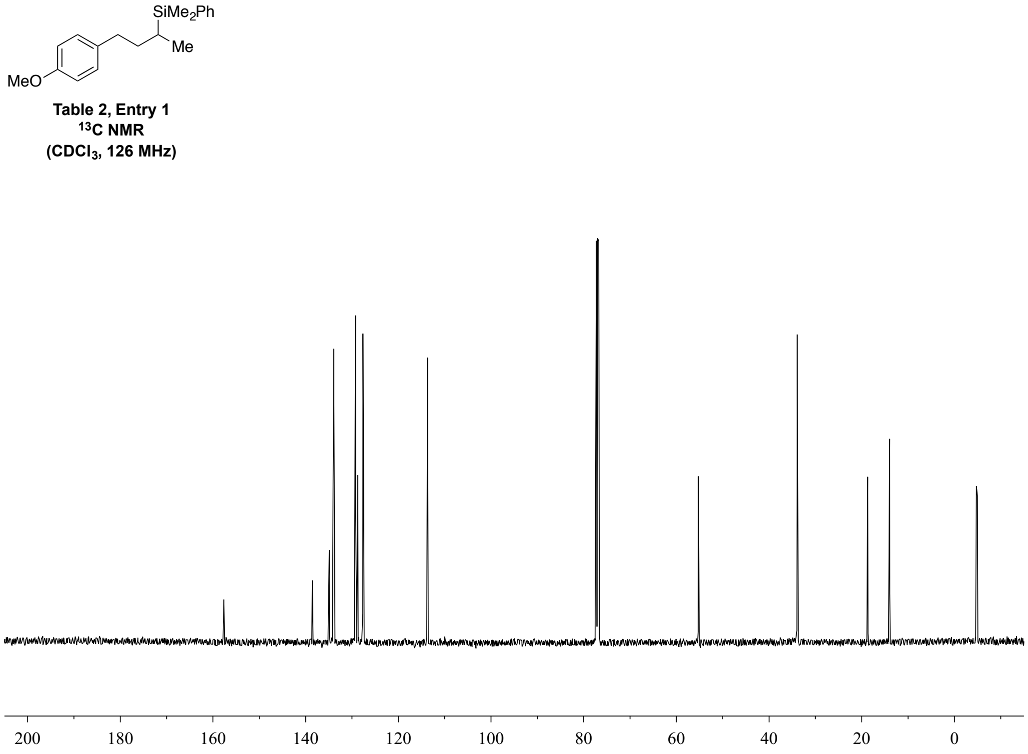


Table 2, Entry 1
^{13}C NMR
($CDCl_3$, 126 MHz)

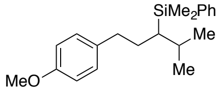
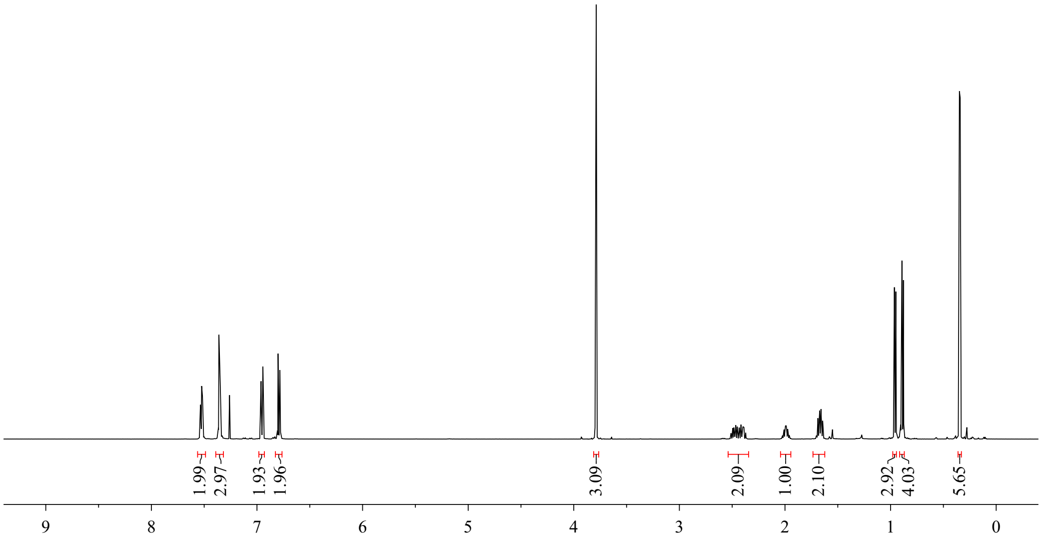


Table 2, Entry 2
^{1}H NMR
(CDCl$_3$, 500 MHz)



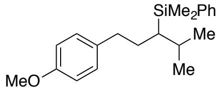
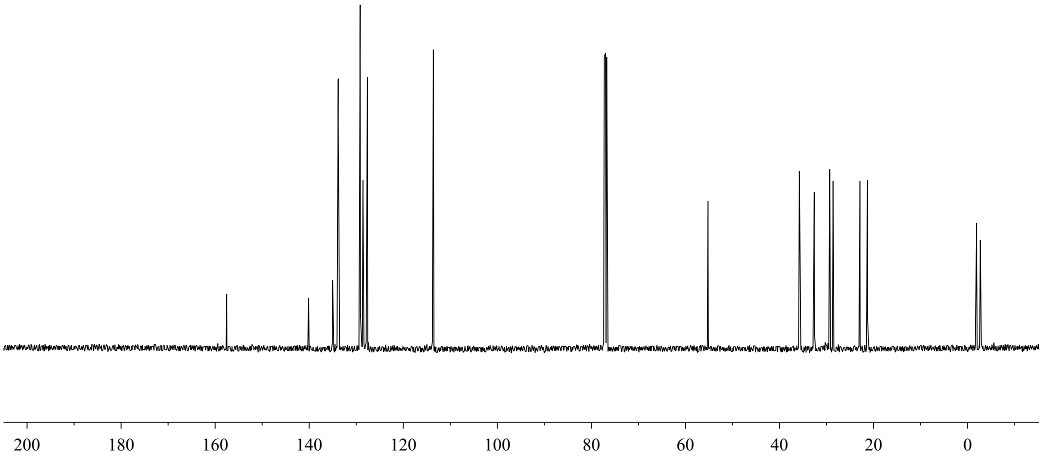


Table 2, Entry 2
^{13}C NMR
(CDCl$_3$, 126 MHz)



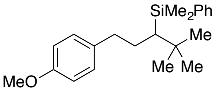
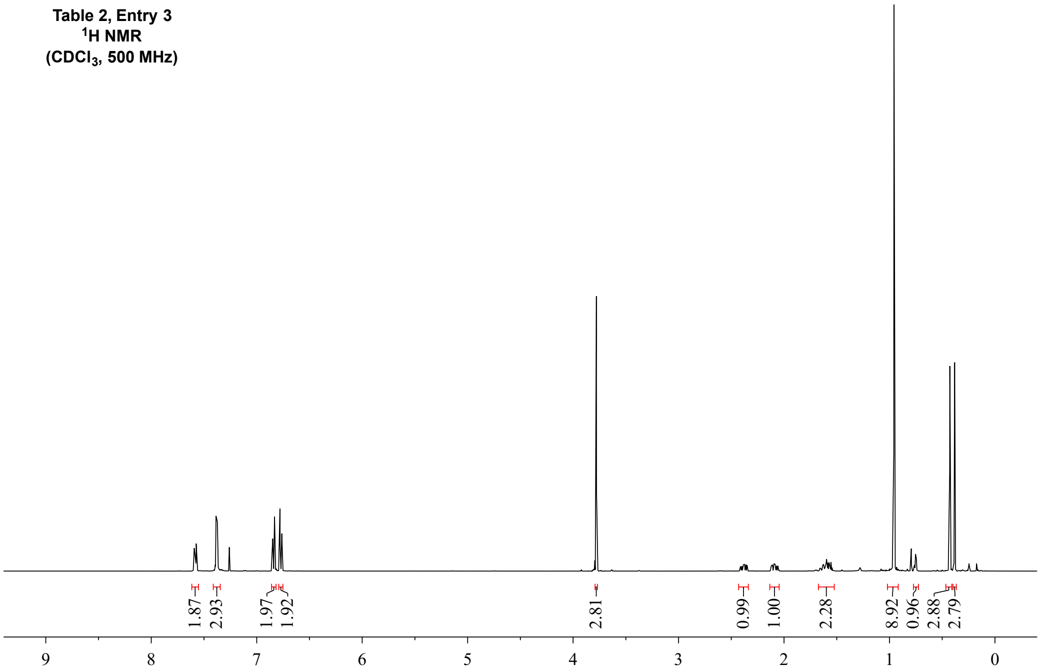


Table 2, Entry 3
^{1}H NMR
(CDCl$_3$, 500 MHz)



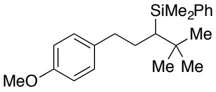
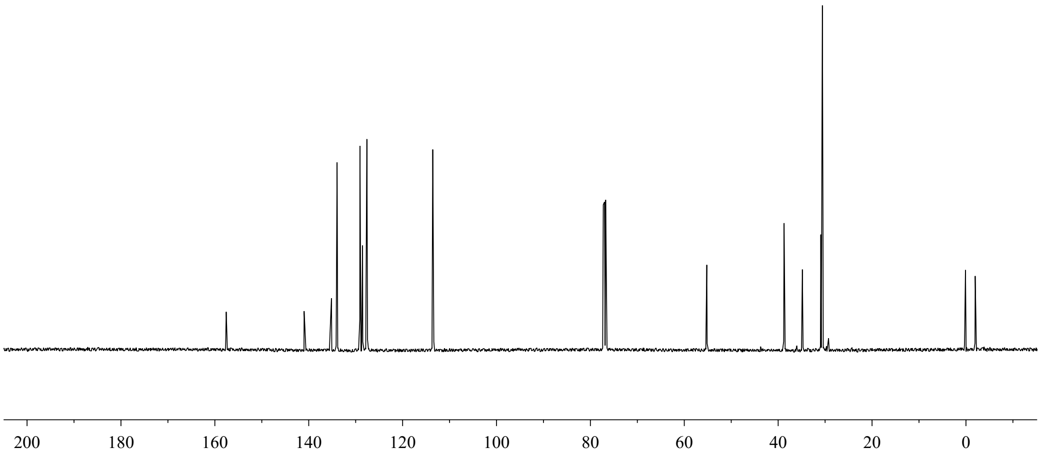


Table 2, Entry 3
^{13}C NMR
(CDCl$_3$, 126 MHz)



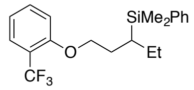
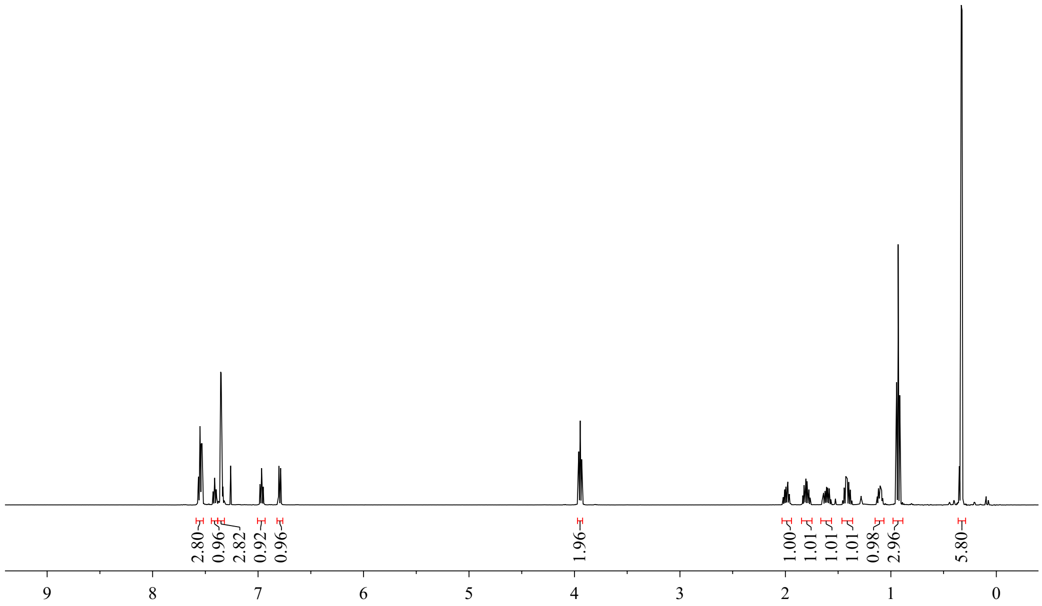


Table 2, Entry 4
^{1}H NMR
(CDCl$_3$, 500 MHz)



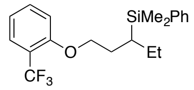
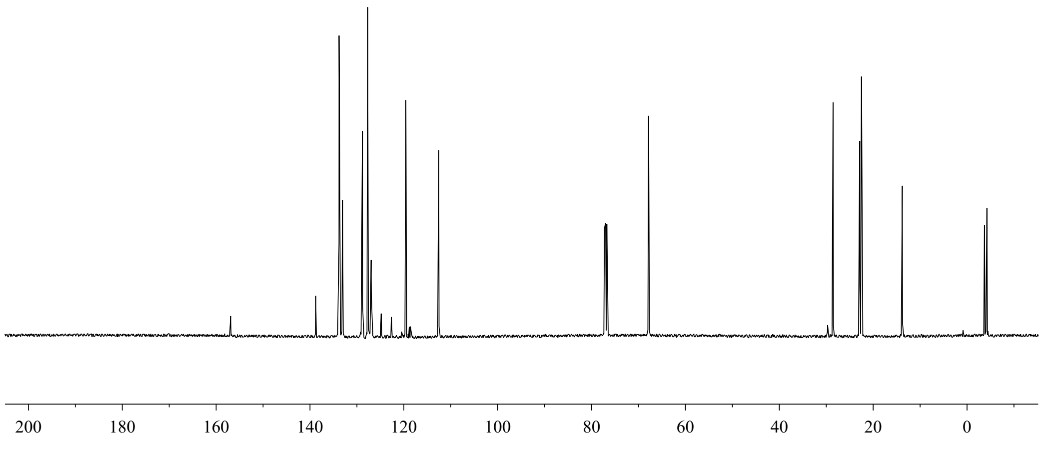


Table 2, Entry 4
^{13}C NMR
(CDCl$_3$, 126 MHz)



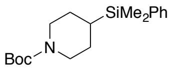
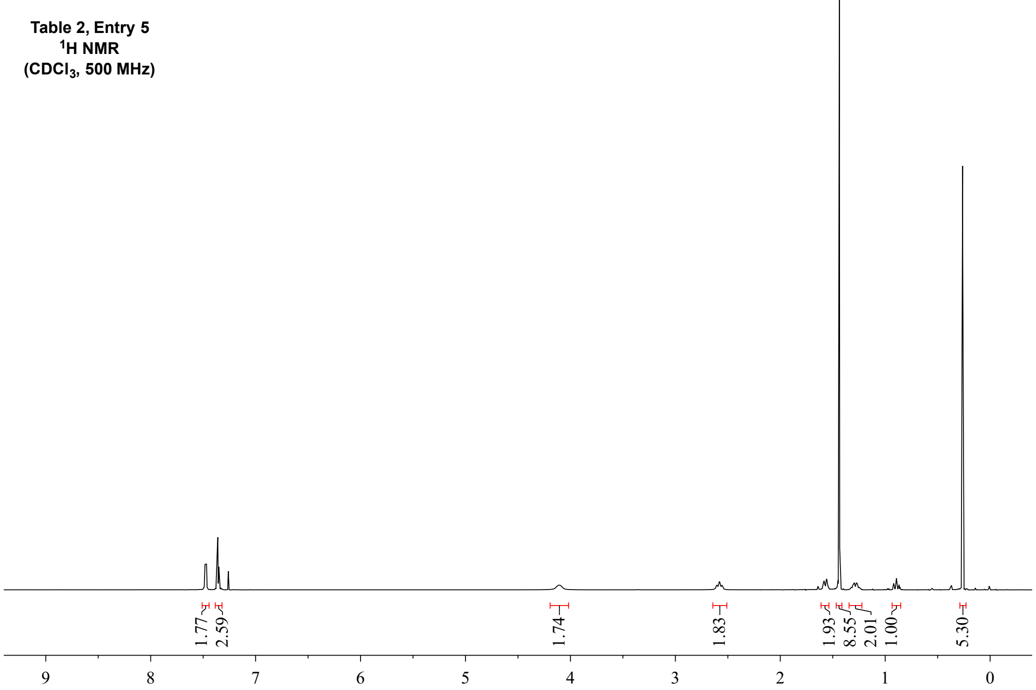


Table 2, Entry 5
^{1}H NMR
(CDCl$_3$, 500 MHz)



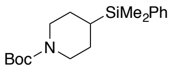
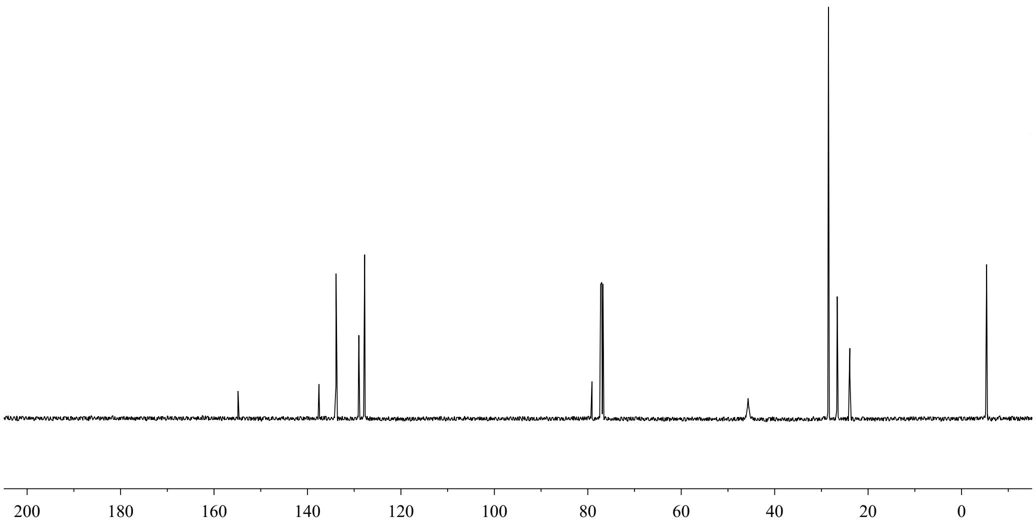


Table 2, Entry 5
^{13}C NMR
(CDCl$_3$, 126 MHz)



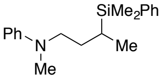
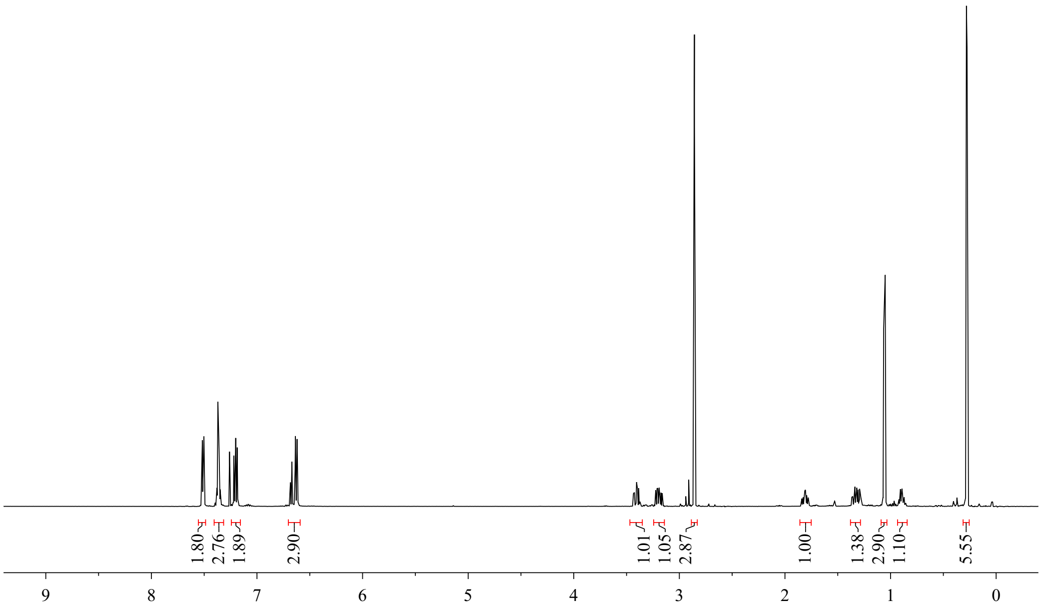


Table 2, Entry 6
^{1}H NMR
(CDCl$_3$, 500 MHz)



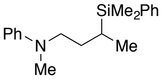
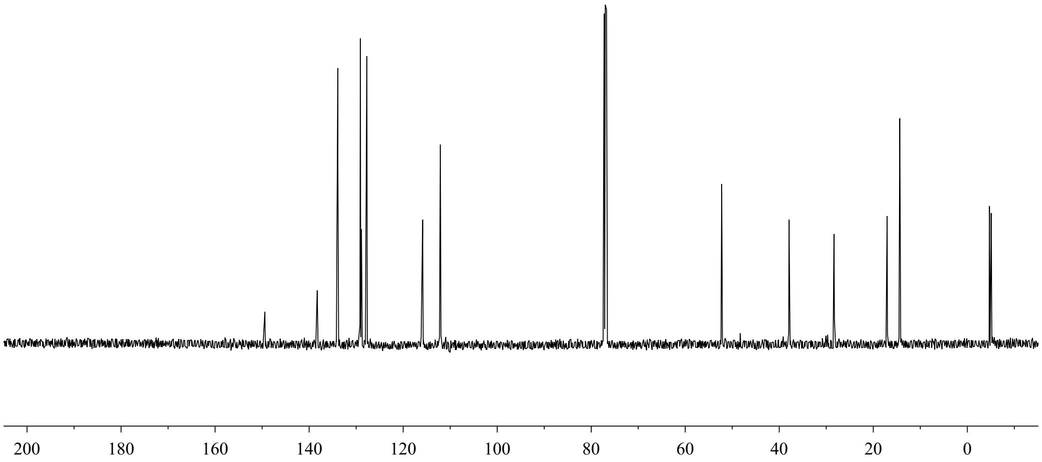


Table 2, Entry 6
^{13}C NMR
(CDCl$_3$, 126 MHz)



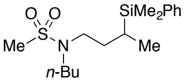
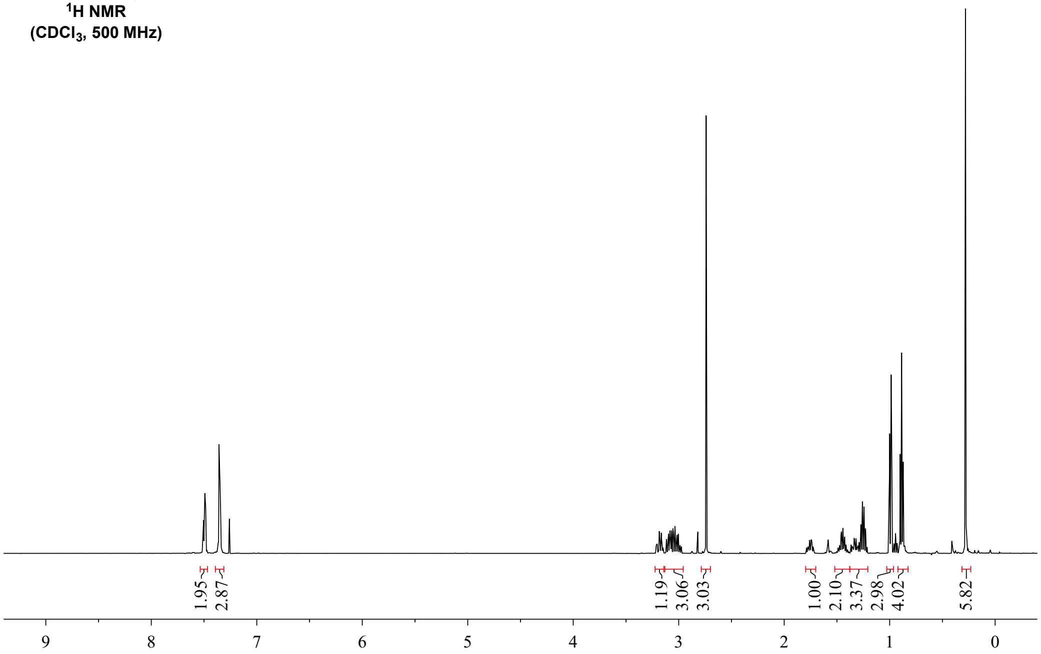


Table 2, Entry 7
^{1}H NMR
(CDCl$_3$, 500 MHz)



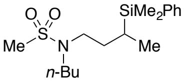
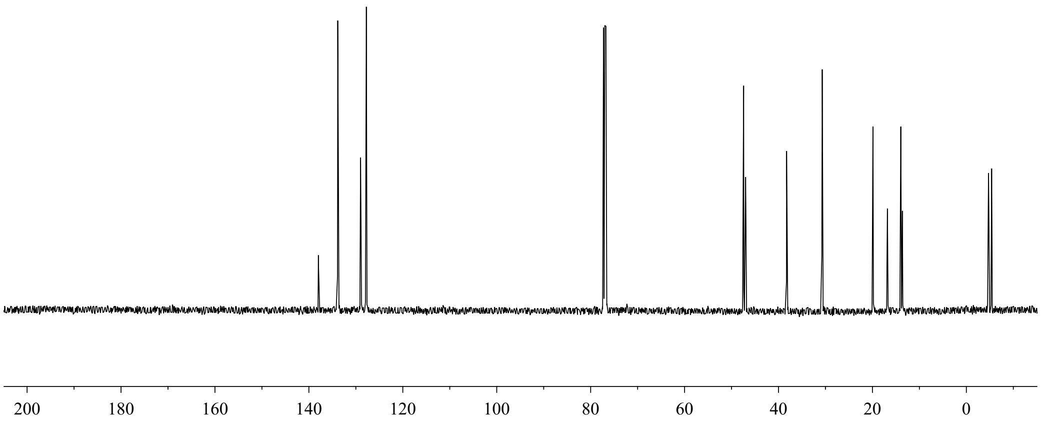


Table 2, Entry 7
^{13}C NMR
(CDCl$_3$, 126 MHz)



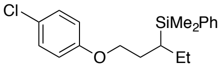
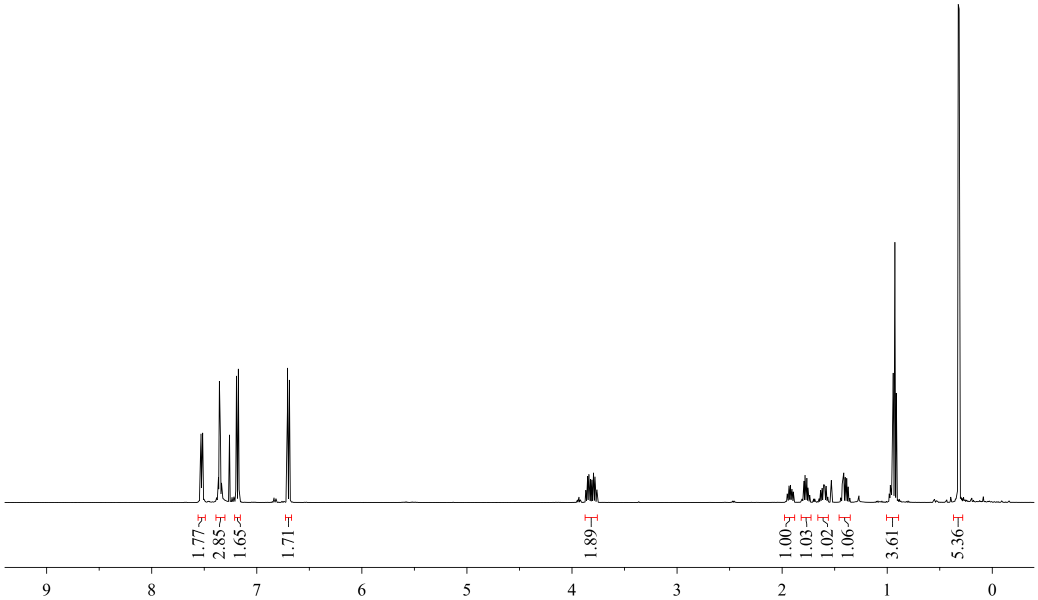


Table 2, Entry 8
^{1}H NMR
(CDCl$_3$, 500 MHz)



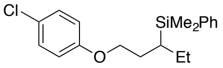
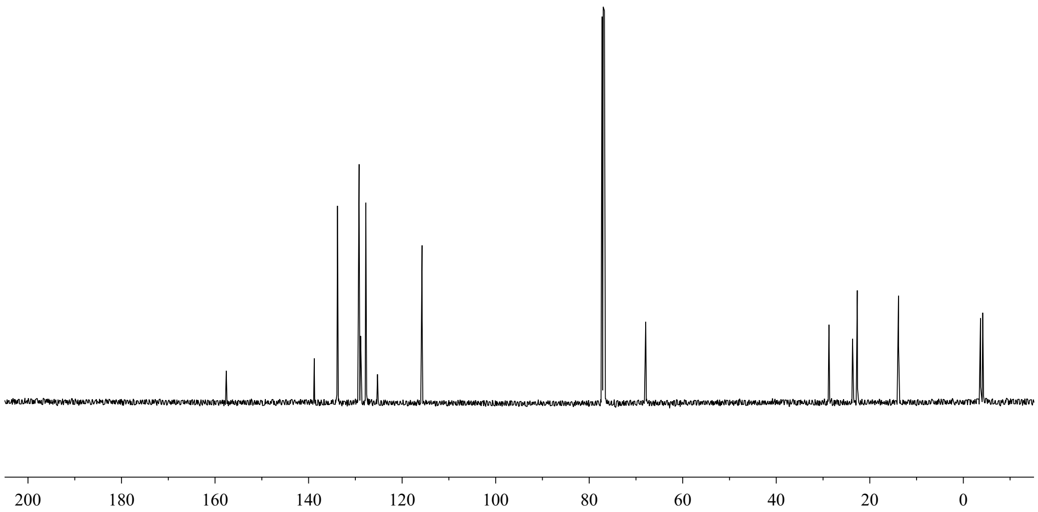


Table 2, Entry 8
^{13}C NMR
(CDCl$_3$, 126 MHz)



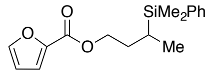
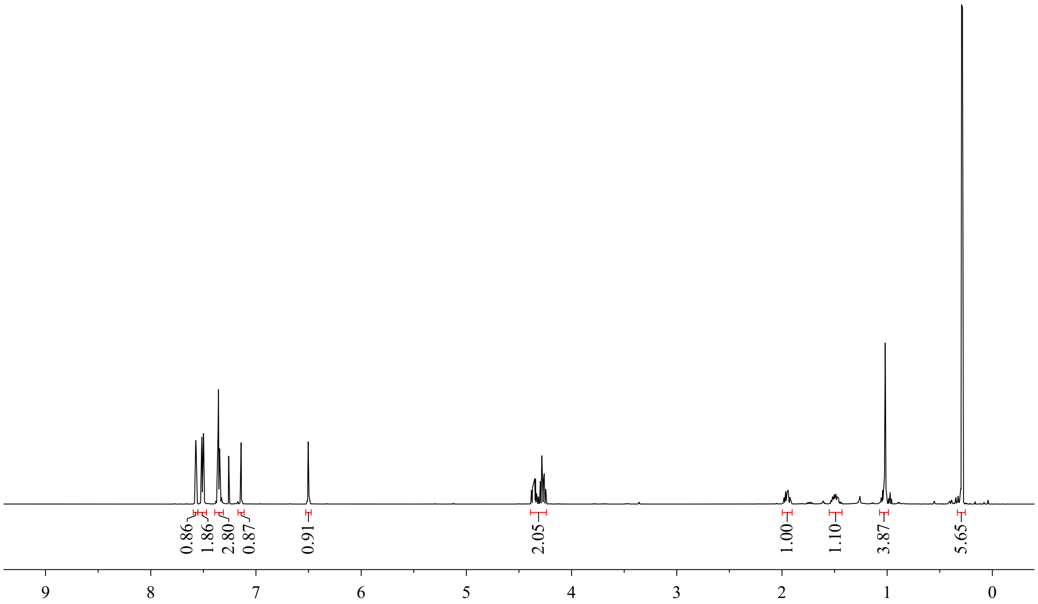


Table 2, Entry 9
^{1}H NMR
(CDCl$_3$, 500 MHz)



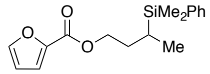
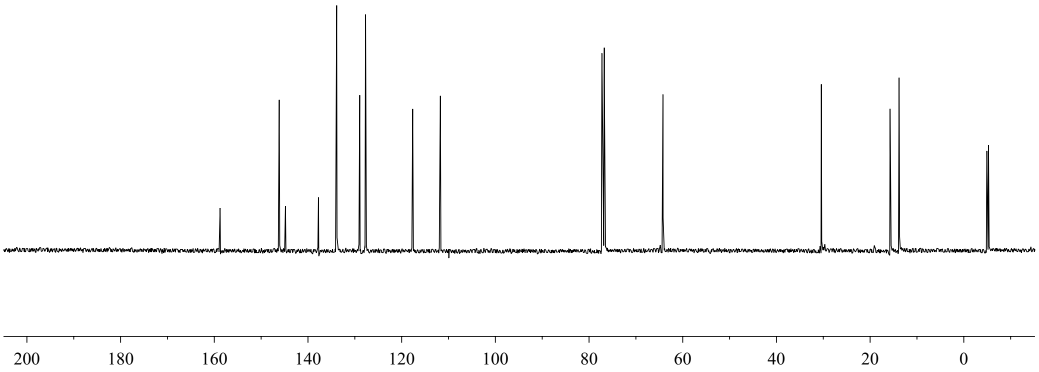


Table 2, Entry 9
^{13}C NMR
(CDCl$_3$, 126 MHz)



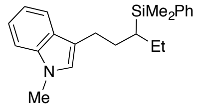
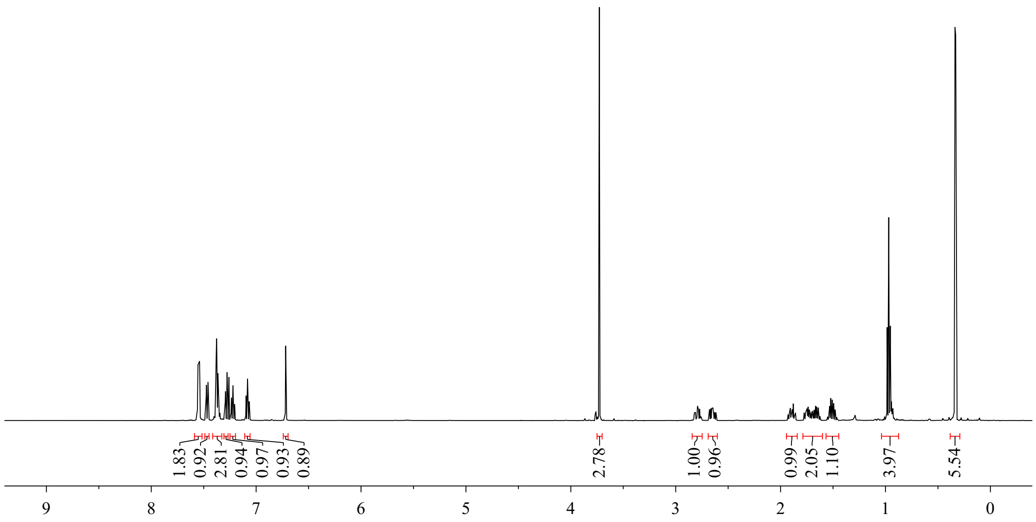


Table 2, Entry 10
^{1}H NMR
($CDCl_3$, 500 MHz)



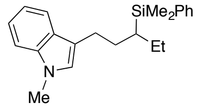
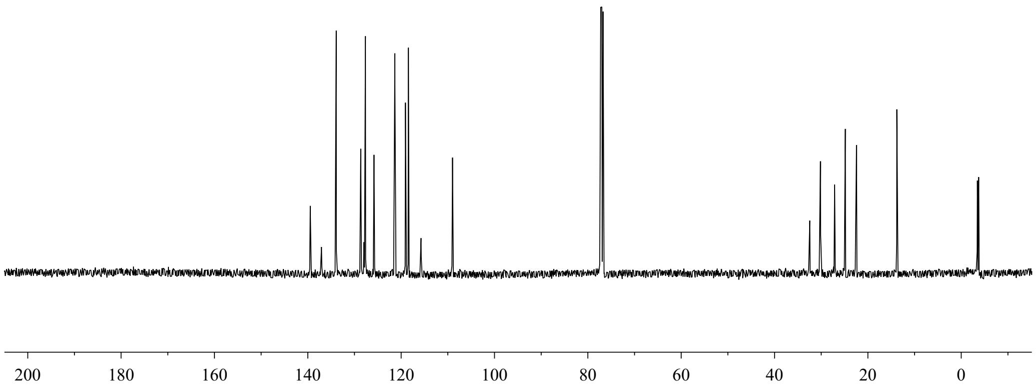
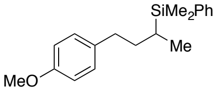
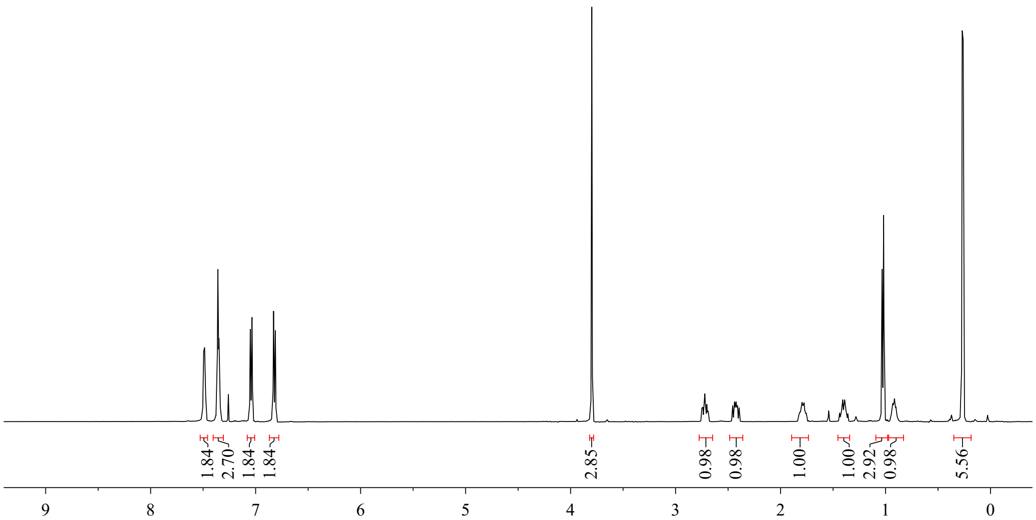


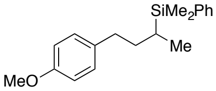
Table 2, Entry 10
^{13}C NMR
($CDCl_3$, 126 MHz)





Eq 3
^{1}H NMR
(CDCl$_3$, 500 MHz)





Eq 3
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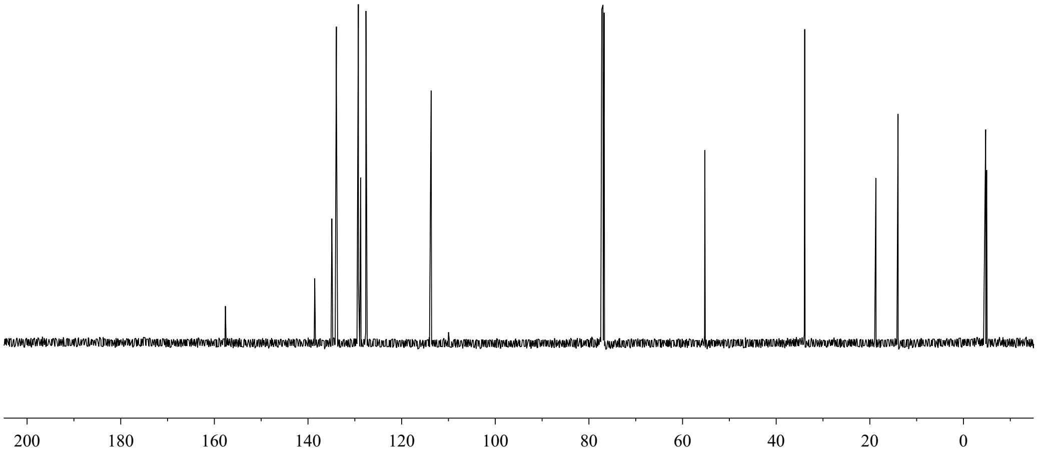


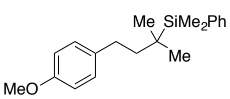
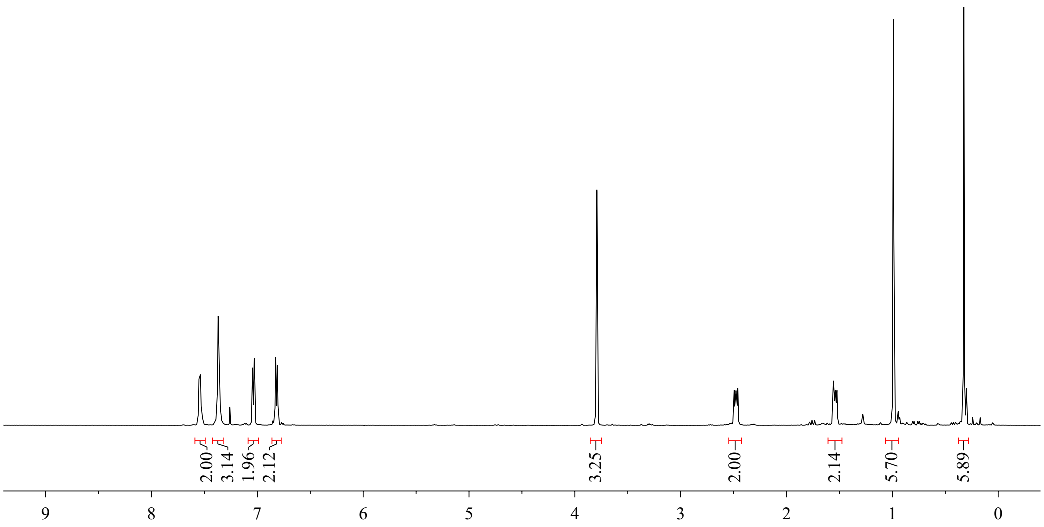


Table 3, Entry 1
^{1}H NMR
(CDCl$_3$, 500 MHz)



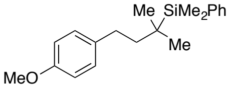
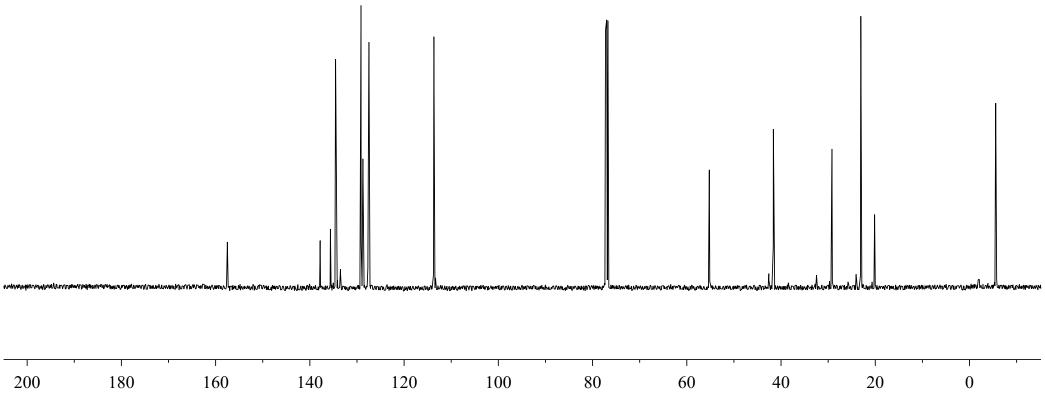


Table 3, Entry 1
^{13}C NMR
(CDCl$_3$, 126 MHz)



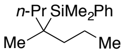
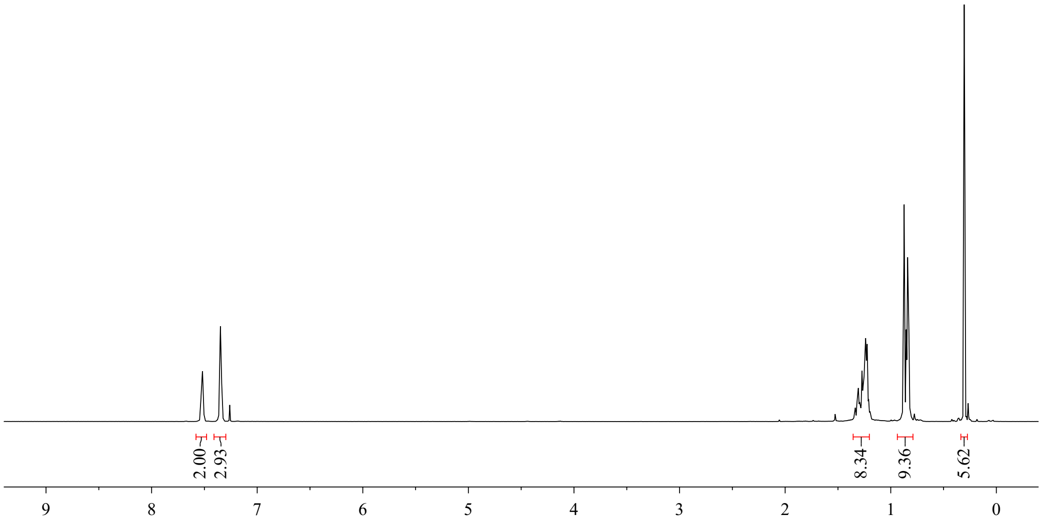


Table 3, Entry 2
^{1}H NMR
(CDCl$_3$, 500 MHz)



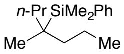
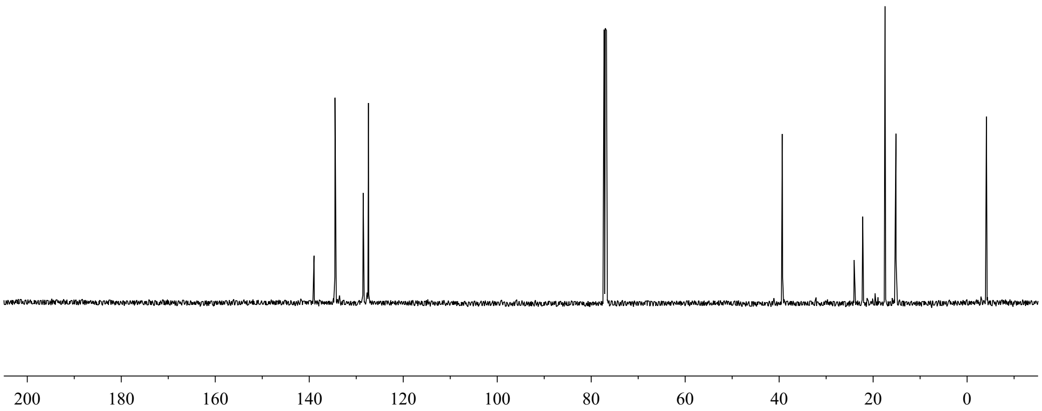


Table 3, Entry 2
^{13}C NMR
(CDCl$_3$, 126 MHz)



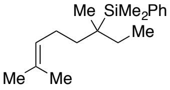
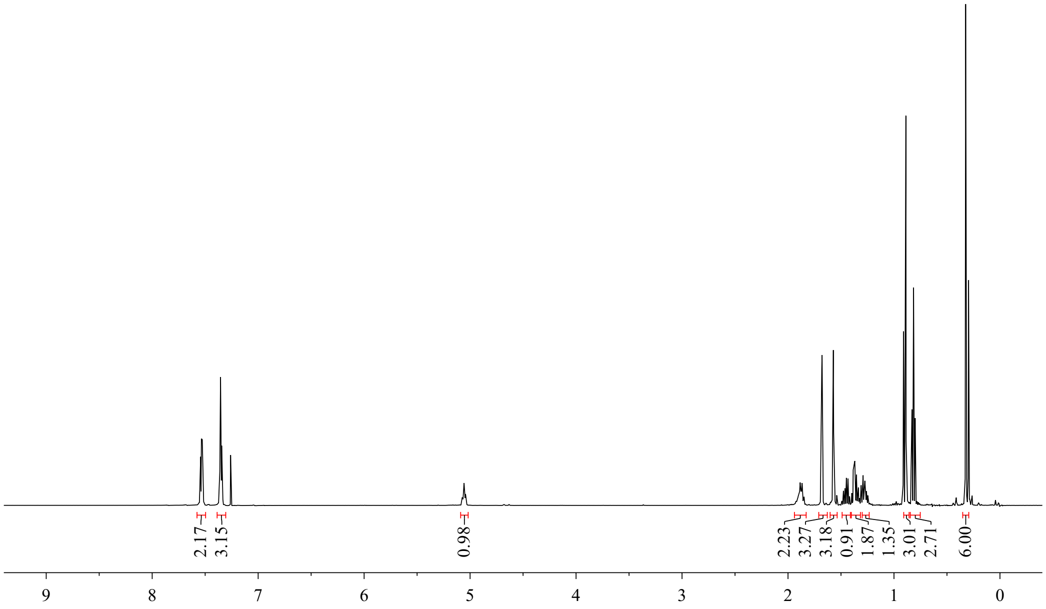


Table 3, Entry 3
^{1}H NMR
(CDCl$_3$, 500 MHz)



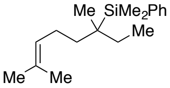
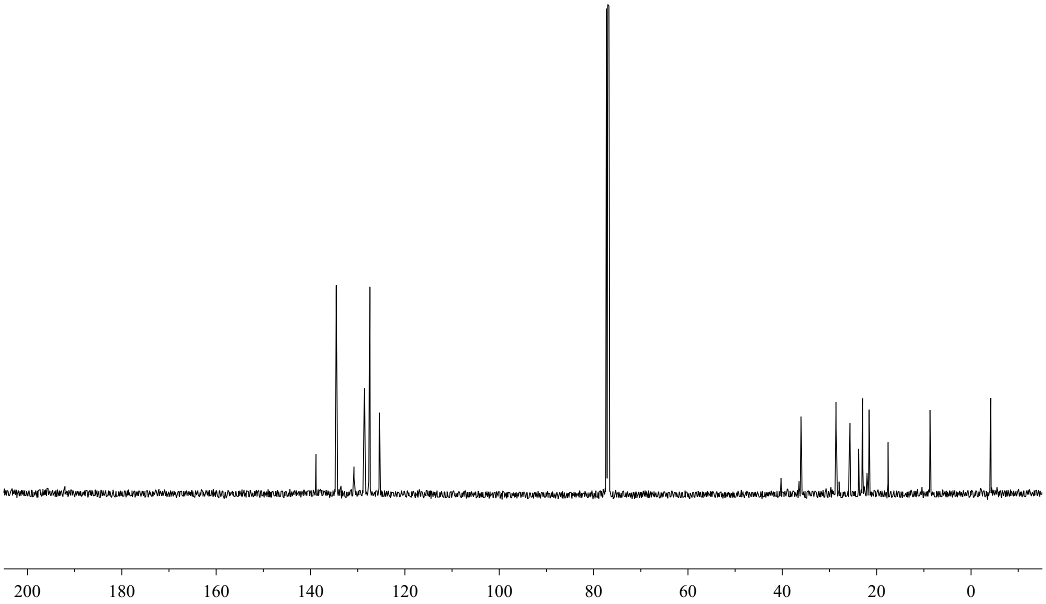


Table 3, Entry 3
^{13}C NMR
(CDCl$_3$, 126 MHz)



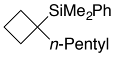
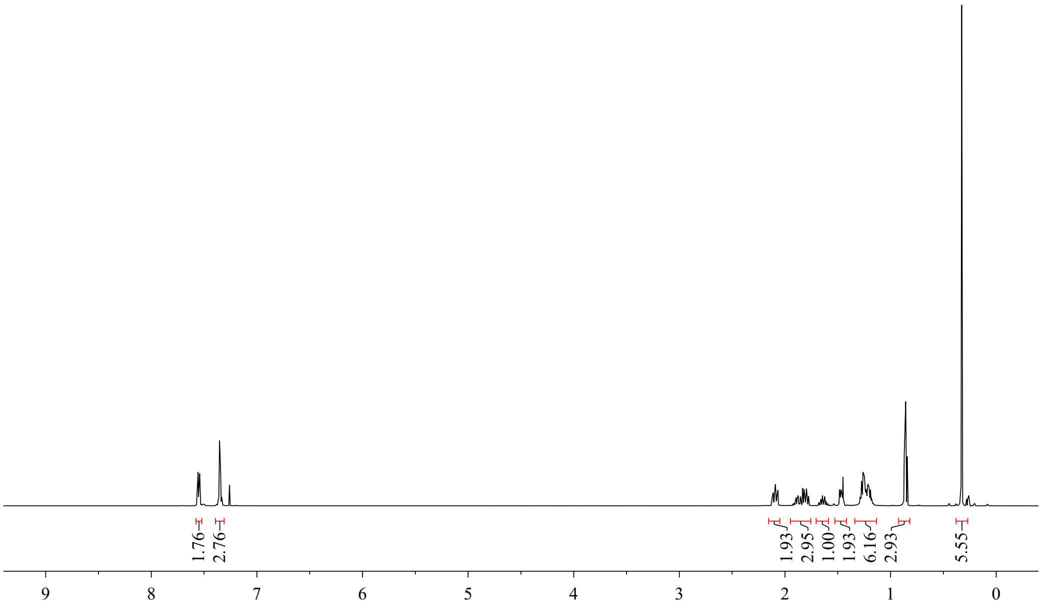


Table 3, Entry 4
^{1}H NMR
(CDCl$_3$, 500 MHz)



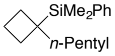
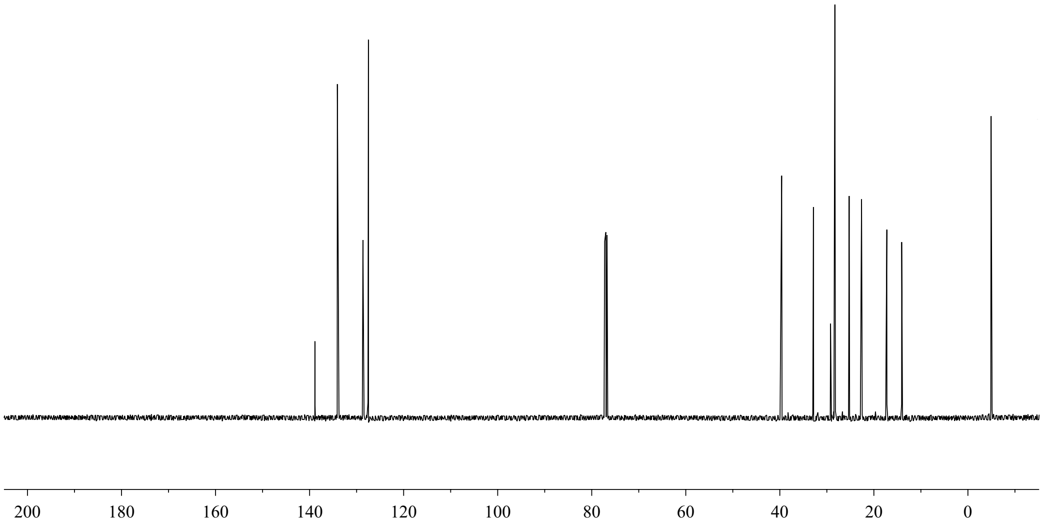


Table 3, Entry 4
^{13}C NMR
(CDCl$_3$, 126 MHz)



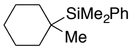
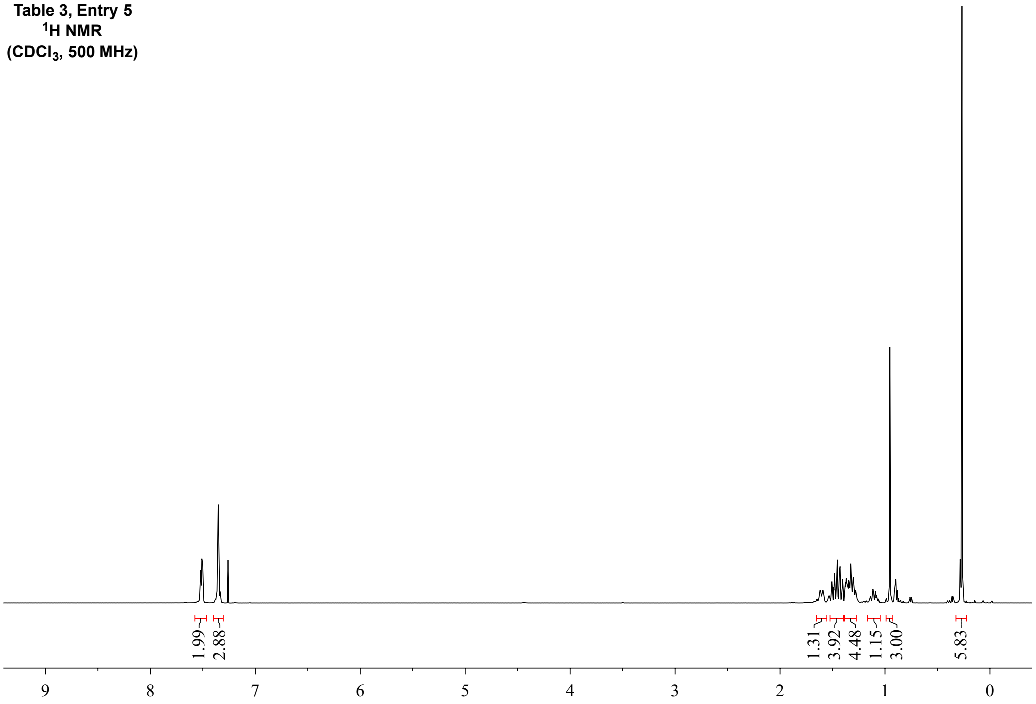


Table 3, Entry 5
^{1}H NMR
(CDCl$_3$, 500 MHz)



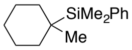
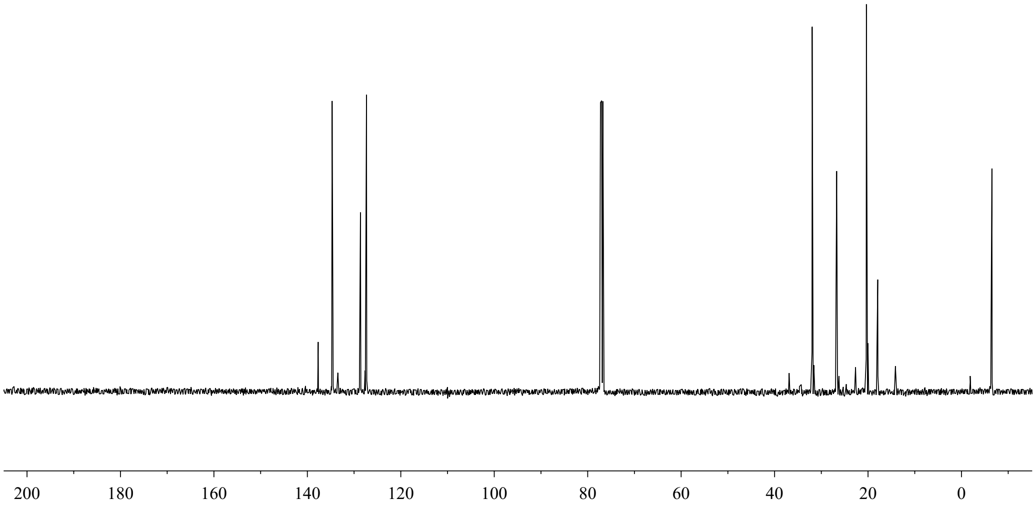


Table 3, Entry 5
^{13}C NMR
(CDCl$_3$, 126 MHz)



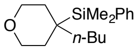
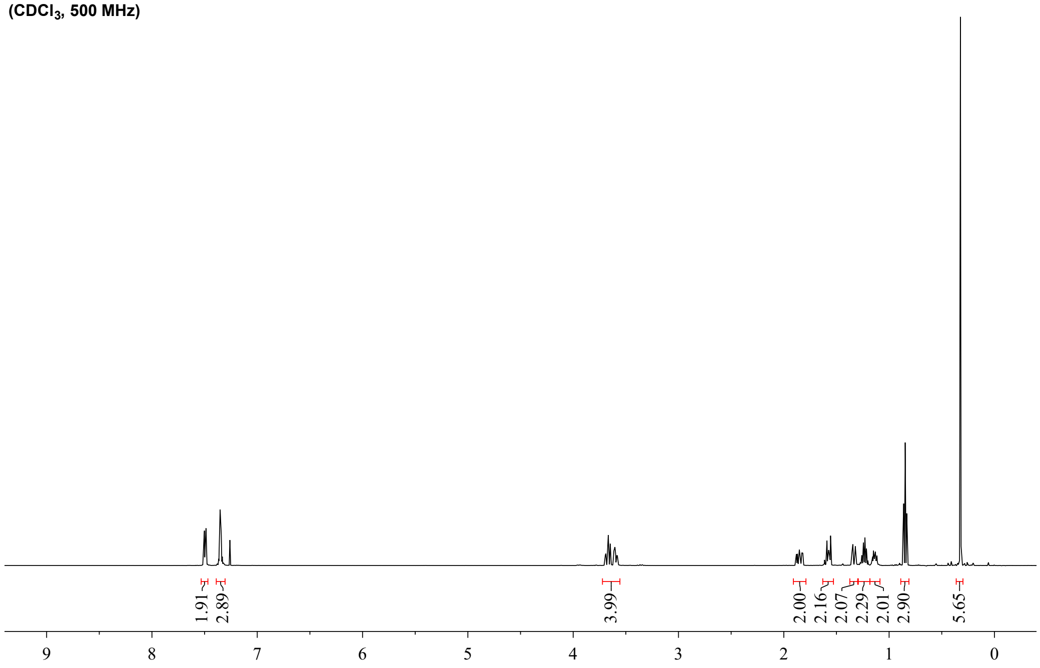


Table 3, Entry 6
^{1}H NMR
(CDCl$_3$, 500 MHz)



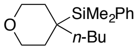
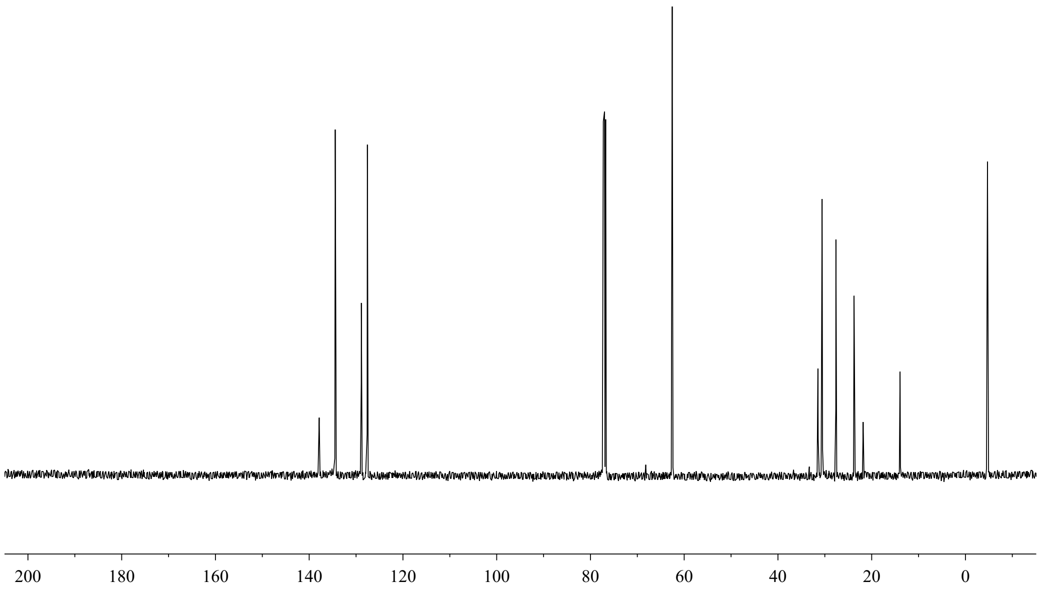
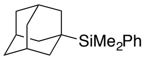
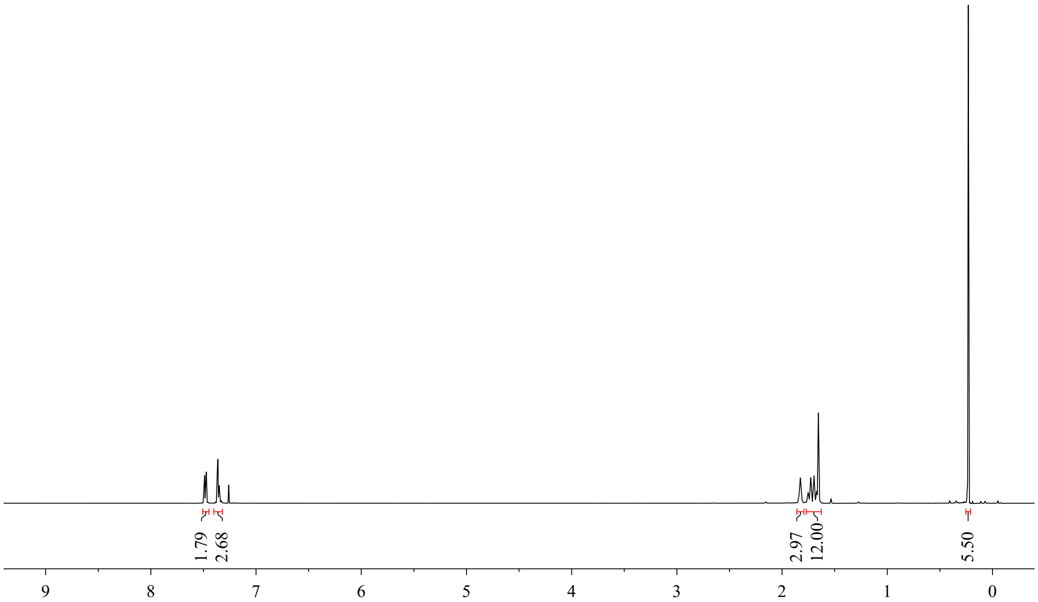


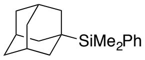
Table 3, Entry 6
^{13}C NMR
(CDCl$_3$, 126 MHz)



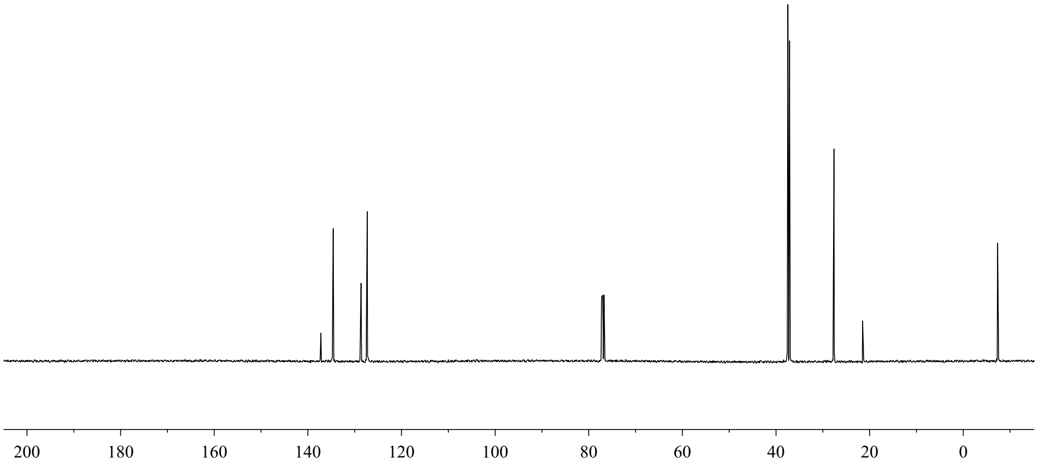


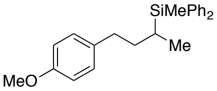
Eq 4
^{1}H NMR
(CDCl$_3$, 500 MHz)



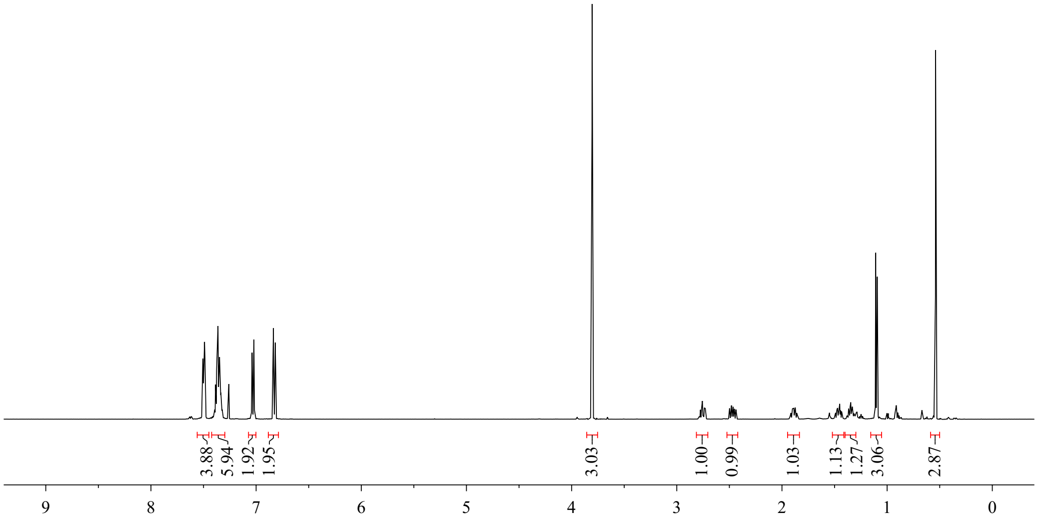


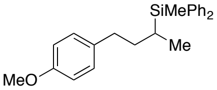
Eq 4
^{13}C NMR
(CDCl$_3$, 126 MHz)



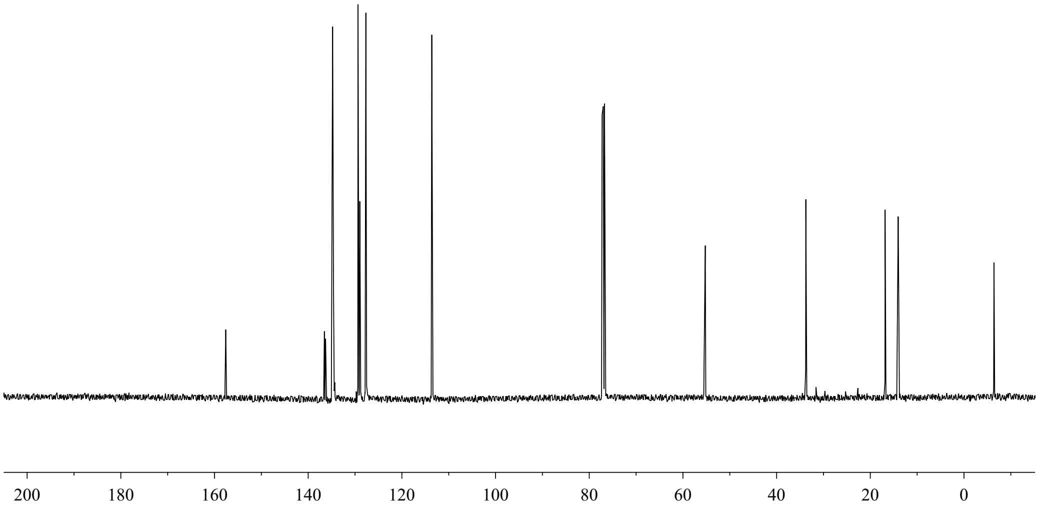


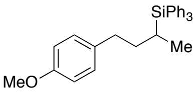
Eq 5
^{1}H NMR
(CDCl$_3$, 500 MHz)



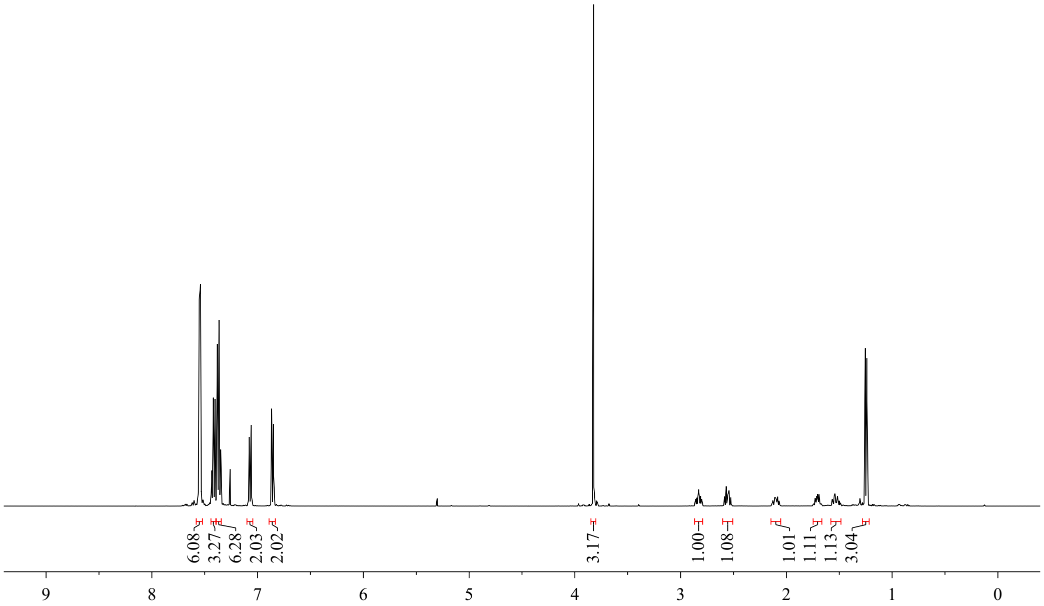


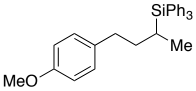
Eq 5
^{13}C NMR
(CDCl$_3$, 126 MHz)



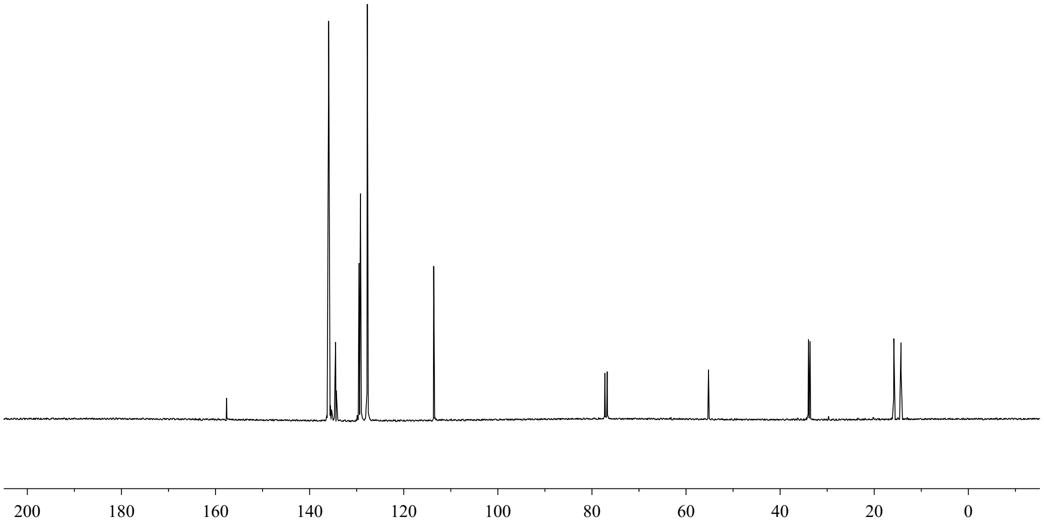


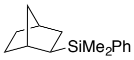
Eq 5
^{1}H NMR
(CDCl$_3$, 500 MHz)



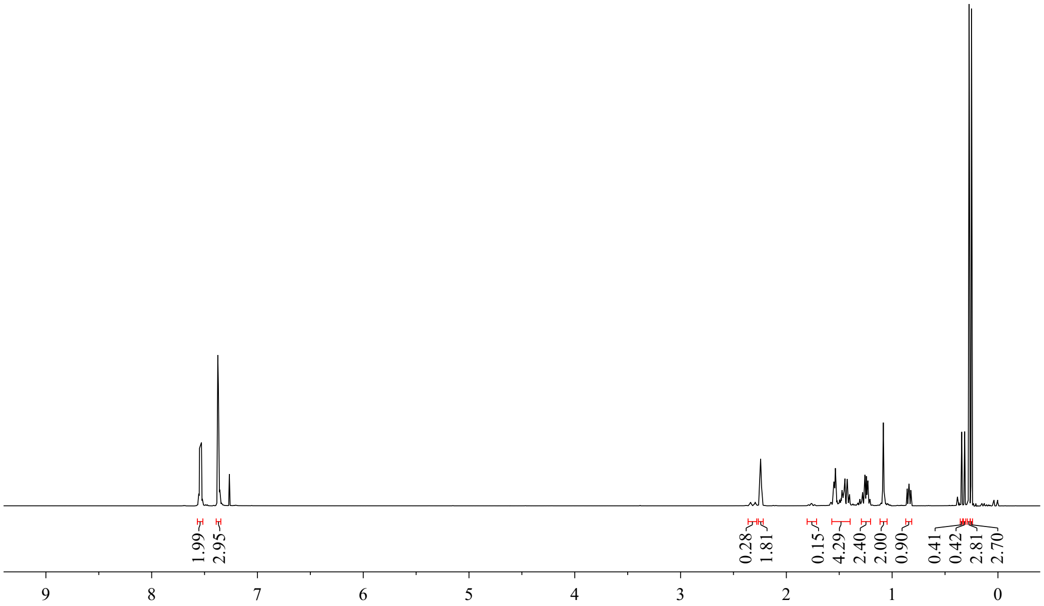


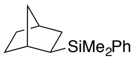
Eq 5
^{13}C NMR
(CDCl$_3$, 126 MHz)



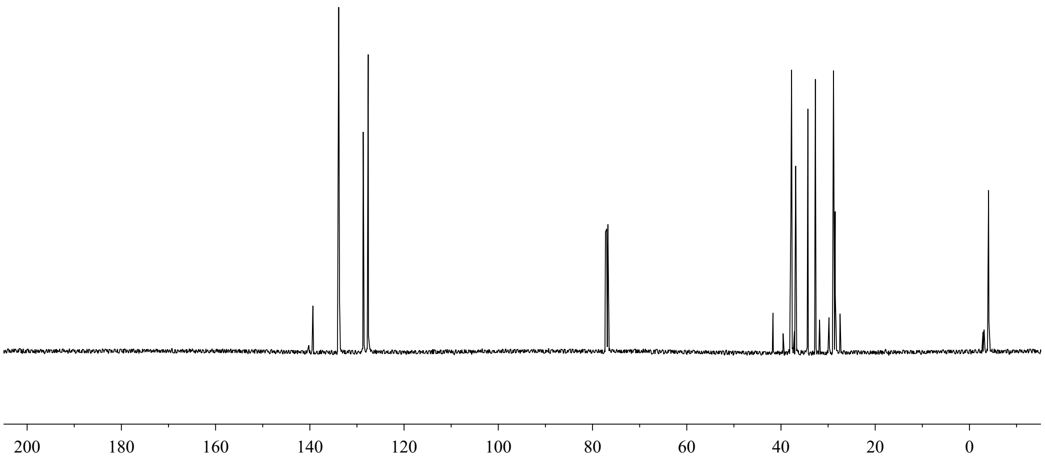


Eq 6
7:1 exo/endo
^{1}H NMR
(CDCl$_3$, 500 MHz)

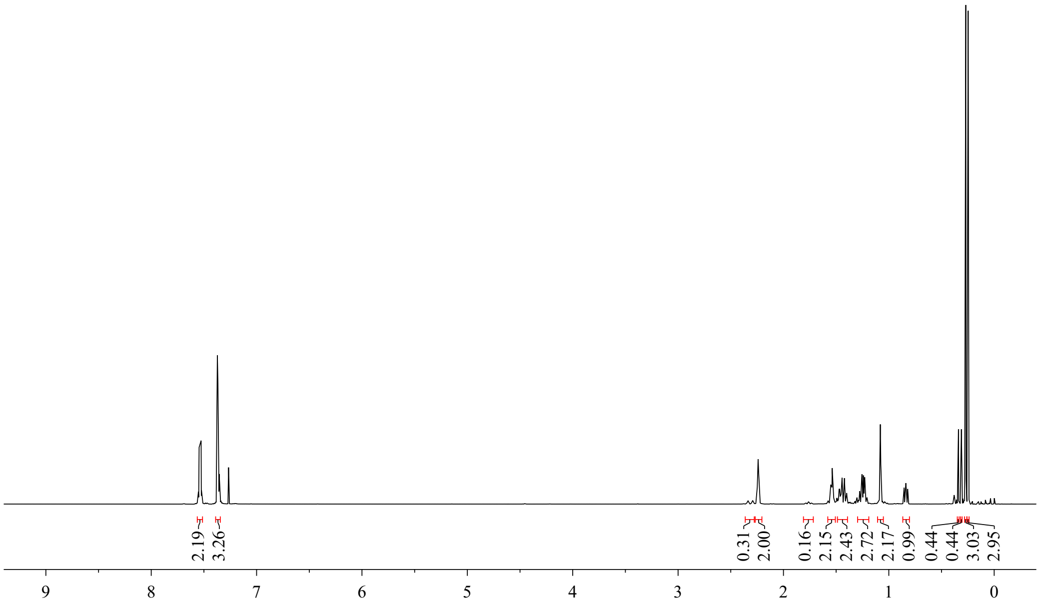




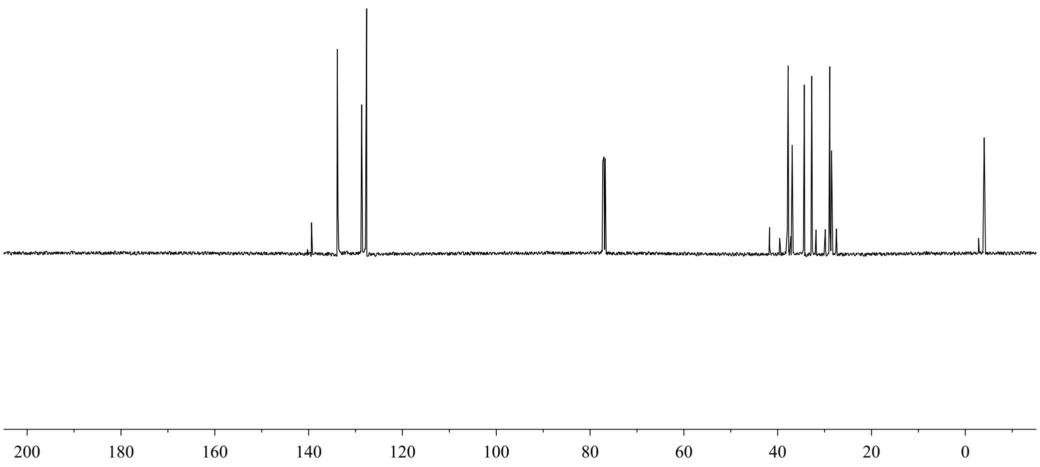
Eq 6
7:1 exo/endo
^{13}C NMR
(CDCl$_3$, 126 MHz)



Eq 7
7:1 exo/endo
^{1}H NMR
(CDCl$_3$, 500 MHz)



Eq 7
7:1 exo/endo
^{13}C NMR
(CDCl$_3$, 126 MHz)



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