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Silylcupration of Conjugated Alkynes and Copper-Hydride Reductions of Morita-Baylis-Hillman Adducts

A Thesis submitted in partial satisfaction of the requirements for the degree of

Master of Science in Chemistry

by

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December 2015

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Liming Zhang

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Bruce H. Lipshutz, Committee Chair

September 2015

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"Enantioselective Copper-Hydride Reductions of Morita-Baylis-Hillman Adducts" Linstadt, R. T. H.; **Peterson, C. A.**; Jette, C. I.; Lipshutz, B.H. *Manuscript in Preparation.*

"Stereoselective Silylcupration of Conjugated Alkynes in Water at Room Temperature" Linstadt, R. T. H.; **Peterson, C. A.**; Lippincott, D. J.; Jette, C. I.; Lipshutz, B. H.*Angew. Chem. Int. Ed.* **2014**, 126, 16, 4243-4247.

ABSTRACT

Stereoselective Silylcupration of Conjugated Alkynes and Copper-Hydride Reductions of Morita-Baylis-Hillman Adducts

by

Carl August Peterson

There currently exists a need for more extensive mild and greener bond forming reactions that allow for construction of sophisticated carbon frameworks. Vinylsilanes have proven themselves to be valuable intermediates in organic synthesis. Traditionally, these educts have been difficult to access requiring stoichiometric metals which often precudes their use on scale. Herein, we investigated the use of Suginome's reagent, $PhMe_2SiBpin$, in a commercially available surfactant TPGS-750-M to afford isomerically pure *(E)-β*-silyl-substituted carbonyl derivatives by way of a copper catalyzed silylcupration in water at room temperature.

Copper hydride has seen extensive use as both an asymmetric and achiral source of hydride for many decades. We were interested in investigating copper hydride's application toward Morita-Baylis-Hillman adducts given their possession of multiple electrophilic sites. We discovered that CuH could be used for tandem reductions of racemic MBH ketones lacking defined olefin geometry into valuable chiral allylic alcohol derivatives with defined stereochemistry.

Table of Contents

1. Stereoselective Silylcupration of Conjugated Alkynes

1.1 Introduction

It is currently of great interest to organic chemists to improve the efficiency of bond forming reactions. Recently in the Lipshutz group we have been keenly interested in providing access to valuable intermediates in an environmentally conscious way. We have achieved this through the use of the commercially available designer surfactant TPGS-750-M as the reaction medium. We discovered that micellar catalysis could be used to provide access to isomerically pure (*E*)-*β*-silyl-substituted alkynes. This was achieved by copper-catalyzed silylcupration of various alkynes bearing electron-withdrawing groups.

1.2 Background

1.2.1 Vinylsilanes

Vinylsilanes are highly valuable and have seen extensive use as intermediates in organic synthesis.[1,2] These intermediates have been utilized in Hiyama-Denmark couplings,[3] iododesilylation,[4] and Brook rearrangement/anion relay chemistry.[5] They also provide great potential for late stage functionalization in total synthesis as highlighted by the groups of Volchkov,[6] Nicolaou,[7] and Zakarian.[8]

Traditionally, these functional groups have been prepared through silylcupration by utilizing Flemings's cuprate.[9] This process involves stoichiometric amounts of copper, which entails waste disposal which tends to prohibit it's use on scale.[10] An alternative reagent was discovered by the Suginome group, $PhMe_2SiBpin$, that allows for nucleophilic organosilicon chemistry. It has previously been demonstrated in the Lipshutz group that the inclusion of water or a protic solvent increased the efficiency of copper-catalyzed reactions. It was reasoned that Suginome's silylborane would be a good candidate to perform in water with in situ transmetallation from boron to copper.

Several reactions have previously been developed based on silylboranes. These have been described in a review by Oestreich.[11] Past approaches functionalize ynolates or phosphonate esters by condensation to give *E*- or *Z*-*β*-silylenoates. These methods generally required multiple steps and lacked efficiency. A more atom-economical approach was developed by Trost using ruthenium catalysts to perform hydrosilylations of an activated alkyne to afford (*Z*)-*β*-vinylsilanes.[12] This was later extended to palladium catalysis which gave highly selective *α*-silylation of conjugated alkynes.[13] The Ferreira group published a method extending this work to include internal alkynes using platinum catalysts.[14]

Molander has most recently documented a copper-catalyzed addition of silicon to conjugated alkynes to afford (*E*)-*β*-silyl-substituted carbonyl derivatives.[15] This method unfortunately gives variable stereoselectivity and modest yields. It also requires the use of DMPU and operates at high temperatures in order to activate the disilane. We sought to adapt this and provide a complementary method to that of Trost to selectively provide access to (*E*)-*β*-silyl-substituted carbonyl derivatives.

1.3 Results and Discussion

1.3.1 Optimization of Copper Source and Catalyst Ligand

Studies were performed to determine the ideal conditions to afford the desired conjugate silylation reaction. The reaction was run with an ynoate using $PhMe_2SiBpin$ as the source of silicon, with catalytic amounts of a copper(I) salt and phosphine ligand. The commercially available surfactant TPGS-750-M in water served as the reaction medium. Under these conditions, the *E*-β-silylenoate was produced within minutes (Table 1). Reactions were performed to reveal that a copper(I) source is required. In the absence of copper no reaction took place, and likewise, replacing the Cu(I) salt with $Cu(OAc)_2$ lead to no conversion. Attempts to utilize either CuI or CuBr led to no conversion. The air stable copper(I) source, $CuF\cdot(PPh_3)_3\cdot 2MeOH$, gave the product in good yield and selectivity. Next, other ligands were tried, such as PPh_3 and TMEDA, which are much less expensive than BDP and gave similar results. The reaction rate was very slow when using ligandless CuOAc which confirms the need for a ligand on copper. The reaction concentration can be adjusted to 0.75 M leading to an even more facile outcome, with consumption of starting material in less than five minutes at room temperature.

Somewhat surprisingly, this reaction could be run "on water", where the reagents and copper catalyst were mixed together neat with only five equivalents of water. These "on water" reactions are limited to liquid substrates. The use of a surfactant provides greater flexibility by allowing for both solid and liquid substrates and also providing the opportunity for in-flask recycling of the reaction medium.

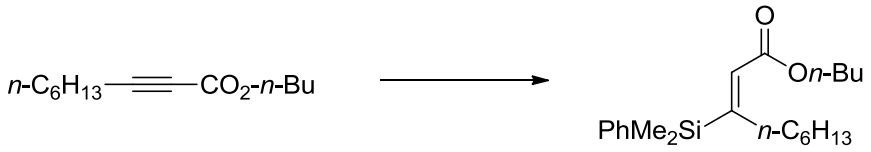
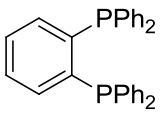


Table 1: Results of Optimization of Reaction Conditions

Cu Source (mol %)	Ligand (mol %)	Conc. [M]	Time (h)	Conv. (%)
none	BDP (3)	0.50	9	<2[b]
CuI (3)	BDP (3)	0.50	9	0[a]
CuBr (3)	BDP (3)	0.50	9	0[a]
CuF (3)[c]	BDP (3)	0.50	9	82[a]
$Cu(OAc)_2$-H_2O (3)	BDP (3)	0.50	9	0[b]
Cu(I)Oac (3)	none	0.50	1	44[b]
Cu(I)Oac (3)	BDP (3)	0.50	1	100[b]
Cu(I)OAc (3)	TMEDA (3)	0.75	6	98[b]
Cu(I)OAc (1)	PPh_3 (1)	0.75	5 min	100[b]
Cu(I)OAc (1)	PPh_3 (1)	neat[d]	5 min	100[b]

All reactions were run under an inert atmosphere in 2 wt. % aqueous solution of TPGS-750-M, with 1.25 equiv of $PhMe_2SiBpin$. [a]Conversion monitored by GCMS. [b]Conversion monitored by NMR on crude material. [c]Using CuF-$(PPh_3)_3$-2MeOH. [d]Using 5 equiv H_2O.

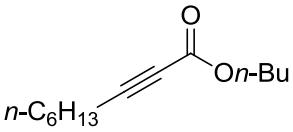
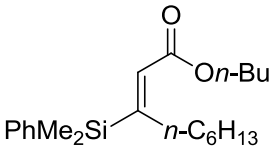
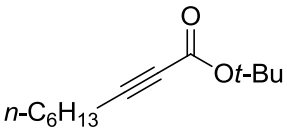
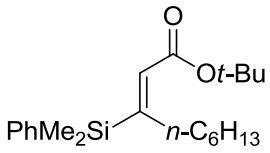
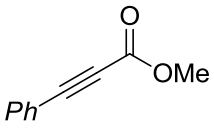
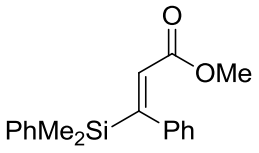
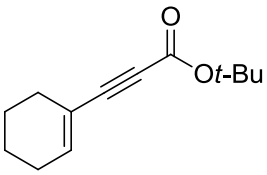
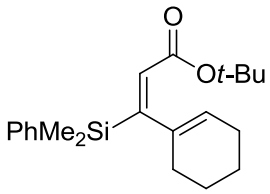
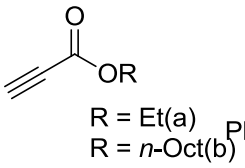
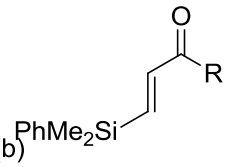
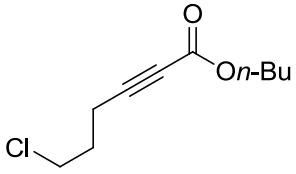
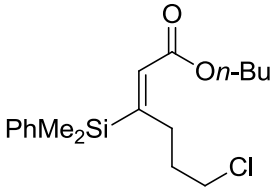


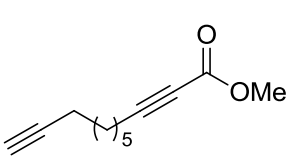
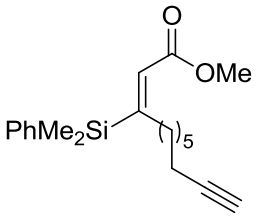
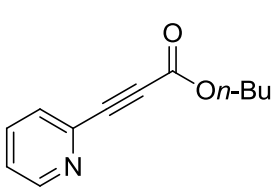
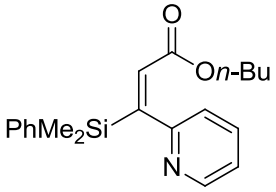
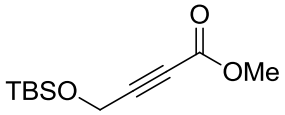
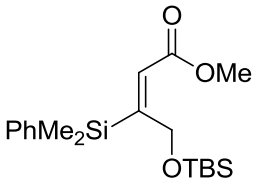
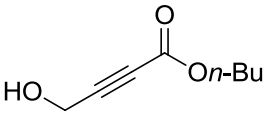
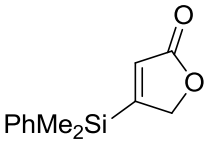
(BDP)

1.3.2 Reaction of Acetylenic Esters

Once the ideal copper salt and phosphine ligand had been selected, the scope of the reaction was investigated with a variety of acetylenic esters (Table 2). Alkyl esters, such as *n*-butyl, *t*-butyl and methyl gave little variation in yield or stereochemical outcome. In the case of extended conjugation, only the 1,4 addition product was formed. Terminal alkynes were completely *E*-selective. A product containing an alkyl chloride could be produced in slightly lower yield. By increasing the amount of copper catalyst to 5 mol % and two equivalents of $PhMe_2SiBpin$ the yield could be increased to 82% of the desired product. A ynoate with an additional terminal alkyne gave a product yield of 75%, the remaining mass balance was addition to the terminal alkyne and recovered starting material. A 2-pyridyl group was used to test the effect of internal chelation on the stereochemical outcome. The 2-pyridyl educt resulted in an acceptable 12:1 *E*-selectivity. In another interesting example, either a protected or free alcohol could be used, in the latter case spontaneous cyclization to the corresponding γ-lactone ensued.

Table 2: Substrate Scope of Acetylenic Esters

Ynoate	Product	Yield (%)	*E/Z*
		95	>20:1
		>95	>20:1
		>95	>20:1
		>95	>20:1
 R = Et(a) R = *n*-Oct(b)		75(a) 82(b)	>20:1 >20:1
		72 (82)[a]	>20:1 >20:1

		75	>20:1
		82	12:1
		88	>20:1
		70	>20:1

[a]With 5 mol % catalyst, 2 equiv $PhMe_2SiBpin$, overnight, at room temperature

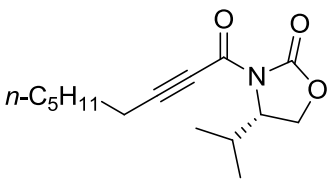
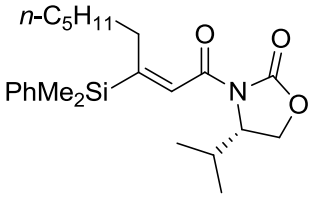
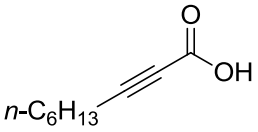
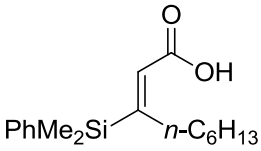
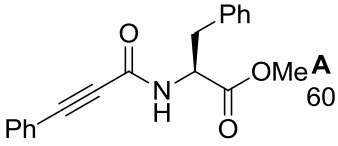
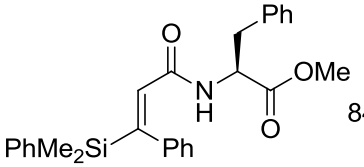
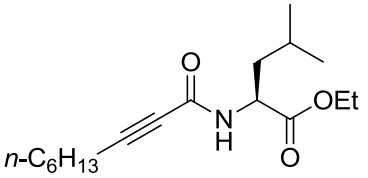
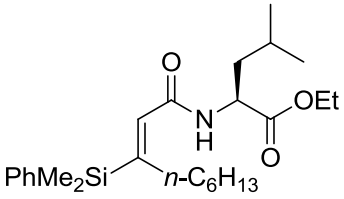
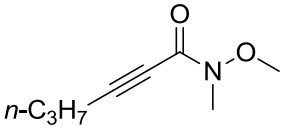
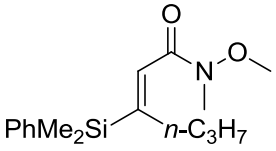
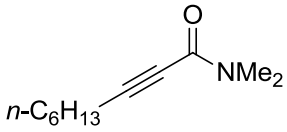
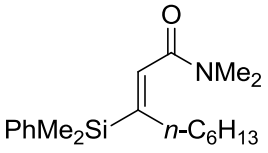
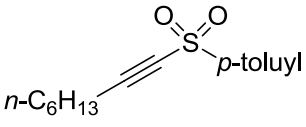
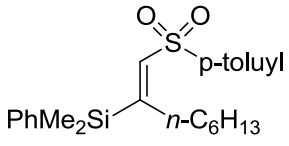
1.3.3 Reaction of alkynes with electron-withdrawing substituents

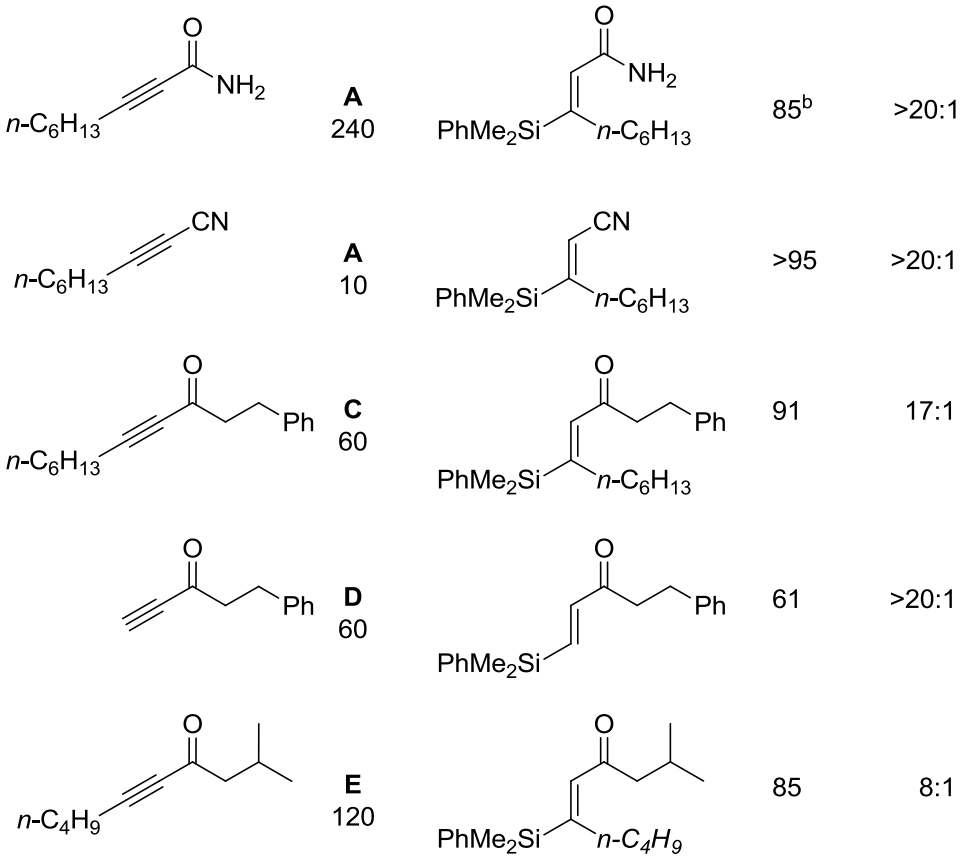
Alkynes with other electron-withdrawing groups were studied to further extend the scope of this silylation (Table 3). A acetylenic oxazolidinone could be used, giving predominantly the (*E*)-product in 70% yield, and the (*Z*) isomer (12%), which were easily separable by flash chromatography. The formation of the second isomer suggests that the O-chelated copper allenoate intermediate is stabilized prior to proteoquenching. An acetylenic acid could be utilized given the mild and neutral conditions of the reaction. Alkynyl peptides reacted successfully giving exclusively their *E*-isomers with

preserved stereochemistry of the peptide moiety. In the case of the alkynyl peptide bearing the phenylalanine methylester substituent the advantage of the use of a surfactant became apparent as solid crystalline reactants cannot be used "on water". Silylation of an acetylenic Weinreb amide provided a very desirable product, giving potential access to ketone or aldehyde derivatives. Tertiary and primary amides could be used with no loss in yield or selectivity. Acetylenic sulfone and nitrile underwent silylation easily giving >95% yield. This is an important example given that vinylic derivatives have been previously reported to be sluggish toward copper catalyzed silylation.[16]

Ketones were investigated but initially gave low 4:1 *E/Z* selectivity. Further optimization led to the use of tri(*p*-fluorophenyl)phosphine-complexed copper(I) acetate which afforded the product in a 17:1 *E/Z* mixture. The isobutyl ketone under the same conditions gave a much lower selectivity of 3:1 *E/Z*. Changing the ligand to BDP and performing the reaction in surfactant led to an acceptable 8:1 selectivity.

Table 3: Substrate Scope of Acetylenic Esters

Substrate	Conditions[a] Time (min.)	Product	Yield (%)	*E*/*Z*
	**A** 30		70 (*E*) 12 (*Z*)	
	**A** 30		84[b]	>20:1
	**A** 60		84[b]	>20:1
	**A** 30		88[b,c]	>20:1
	**B** 30		90[b]	>20:1
	**A** 30		78	>20:1
	**A** 360		>95	>20:1



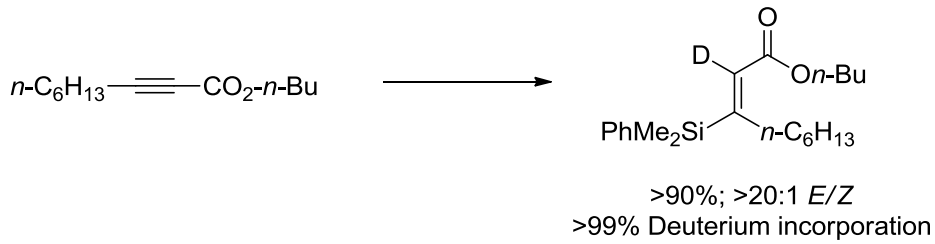
Conditions **A**: 1.25 equiv $PhMe_2SiBpin$, [0.75 M] 2 wt. % TPGS-750-M, 1 mol % PPh_3/CuOAc.
Conditions **B**: 1.25 equiv $PhMe_2SiBpin$, neat, 5 equiv H_2O, 1 mol % PPh_3/CuOAc.
Conditions **C**: 1.50 equiv $PhMe_2SiBpin$, on water, [0.3 M], 2 mol % (4-F-$C_6H_4)_3P$/CuOAc.
Conditions **D**: 1.00 equiv $PhMe_2SiBpin$ 2.00 equiv ynoate, [0.75 M] 2 wt. % TPGS-750-M, 1 mol % (4-F-$C_6H_4)_3P$/CuOAc.
Conditions **E**: 1.25 equiv $PhMe_2SiBpin$, 1 mol % BDP/CuOAc, [0.75 M] 2 wt. % TPGS-750-M, ice bath temperature.
[a]Unless stated otherwise, all reactions were performed at ambient temperature.
[b]Using 2 equiv $PhMe_2SiBpin$. [c]Quenching with 50% sat. aq. $NaHCO_3$.

1.3.4 Deuterium Incorporation

To further probe the mechanism, the reaction was run in an aqueous surfactant solution made from TPGS-750-M dissolved in D_2O. Deuterium incorporation was selective for the α-position. This implies that an α-vinylcopper(I) species is formed and

is protioquenched (Fig 1). Attempts to trap this postulated α-cuprio intermediate with electrophiles other than deuterium were unsuccessful.

Fig 1: Deuterium Incorporation

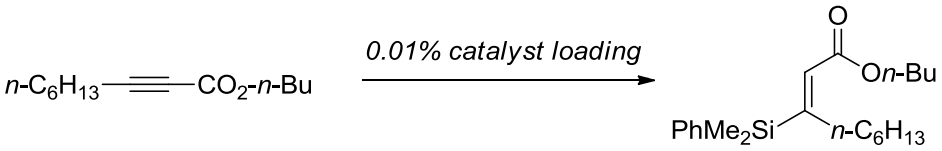


>90%; >20:1 *E/Z*
>99% Deuterium incorporation

1.3.5 Evaluation of Catalyst Loadings

In order to make this reaction more desirable for use on large scale by minimization of waste the catalyst loading was investigated. Due to the short reaction time of this reaction it was thought possible to significantly reduce the amount of copper used. The β-silylation was achieved with only 0.01 mol % catalyst-to-substrate loading (*i.e.*, S/C = 10,000:1), requiring 16 hours to reach complete conversion (Fig 2).

Fig 2: Low Catalyst Loading



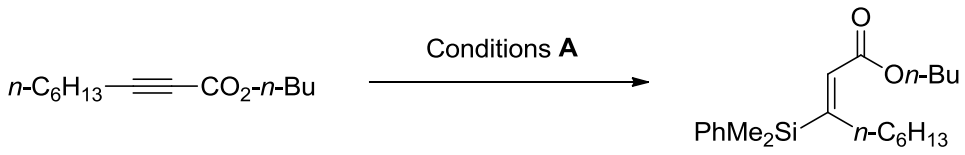
>90%; >20:1 *E/Z*

1.3.6 Recycling of Catalyst and Reaction Medium

For an even further reduction in waste, recycling of the aqueous reaction medium was performed. An in-flask extraction using a minimum amount of organic solvent removes the product. The reaction can be performed sequentially for at least six cycles (Fig 3)

without additional surfactant or copper catalyst. All runs gave excellent isolated yields (>90% yield for each) with no change in time of reaction or the purity of the product.

Fig 3: Recycling of Catalyst and Reaction Medium



Run 1: 94%; 2: 90%; 3: 90%; 4: 91%; 5: 95%; 6: 97%[a]

[a]Final run worked up on silica gel

1.3.7 Gram Scale Silylation and E Factor Analysis

To demonstrate the ability to scale this reaction, a gram scale example was run. All previous reactions were performed on a 0.1 to 0.4 mmol scale. It was found that starting with 0.83 g of an ynoate, 1.184 grams (86% yield) of product was afforded in less than 15 minutes. The remaining mass was recovered starting material.

To further evaluate the environmental greenness of this reaction an E Factor was calculated for this process. E Factors have become a commonly used metric to determine the environmental impact of a given reaction.[17] Depending on the industry involved they typically range from 5 to 100 and are defined as the ratio of the mass of waste to the mass of desired product formed. For the representative silylation from these studies the E Factors, based on solvent used, calculated are 4.2 (aqueous surfactant) or 2.1 (neat). Traditionally, only organic solvents, not water, were included in these calculations. Taking into account the water used in the reaction medium these values are slightly elevated to 8.5 and 2.4 respectively.

1.3.8 Conclusions

In conclusion, a new method was developed to give copper-catalyzed silylcuprations of electron deficient alkynes in water at room temperature. This gives access to isomerically pure (*E*)-*β*-silyl-substituted carbonyl derivatives in high yields. A high degree of compatibility with many electron-withdrawing groups was shown giving mainly the *E*-isomer.

2. Enantioselective Copper-Hydride Reductions of Morita-Baylis-Hillman Adducts

2.1 Introduction

Since its first reported synthesis and characterization by the group of Churchill and Osborn in 1971, copper(I) hydride has seen growing success for the reduction of electrophilic double bonds. It has been shown that reduction reactions could also be achieved using various sources of hydrides as well as its use catalytically.

2.2 Background

2.2.1 Copper Hydride

The first fully characterized example of a phosphine copper(I) hydride complex was reported in 1971 by Churchill, Osborn and coworkers.[18] Tetrameric copper(I) *tert*-butoxide in the presence of triphenylphosphine under hydrogenation conditions gave an orange crystalline solid (equation 1). This was identified by X-ray crystallography as a hexameric triphenylphosphine copper(I) hydride with six copper atoms at each position of a regular octahedron and one phosphine linked to each copper atom.

$$1/4\ [CuOBu\text{-}t]_4 + PPh_3 + H_2 \xrightarrow{THF} 1/6\ [CuH(PPh_3)]_6 + t\text{-}BuOH \quad (1)$$

The structure of the copper(I) hydride complex is highly ligand dependent. The published examples show that the structure and Cu/P stoichiometry is dependent on the ligand. When dppp (1,3-bis(diphenylphosphino)propane) is used the corresponding complex incorporated two copper atoms per diphosphine ligand.[19] When a triphos

(1,1,1-tris(diphenylphosphinomethyl)ethane) ligand is used, a dimeric hydride is isolated in which each copper atom is chelated by two phosphorus atoms from the triphos ligand.[20]

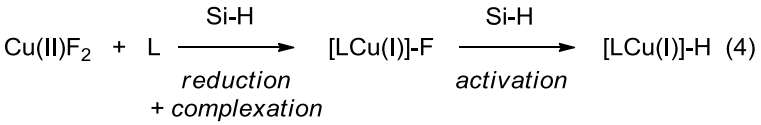
The initial procedure to generate hexameric copper(I) hydride involved the use of hydrogen and the air sensitive copper(I) *tert*-butoxide. In 1988 the Stryker group reported the first multi-gram scale preparation of copper(I) hydride (equation 2).[21]

$$CuCl + PPh_3 + NaOBu\text{-}t \xrightarrow[\text{toluene } C_6H_6]{H_2} 1/6\ [CuH(PPh_3)]_6 + t\text{-}BuOH + NaCl \quad (2)$$

This allows the copper alkoxide to be generated *in situ* from copper(I) chloride under a positive pressure of hydrogen (1 atm). Various copper(II) salts were investigated in addition to reducing agents to substitute the use of hydrogen. The most widely adopted method involves the use of copper(I) chloride and a chelating diphosphine which generates complex [LCu(I)]-Cl (equation 3). The Cu-Cl bond cannot be cleaved by a hydride source and requires further activation by ligand exchange with a hard ligand such as an alkoxide. The copper(I) alkoxide [LCu(I)]-OR that is sensitive can thus be generated and subsequently activated by the hydride source (silane) to generate the desired copper(I) hyride complex [LCu(I)]-H.

$$Cu(I)Cl + L \xrightarrow[\textit{complexation}]{} [LCu(I)]\text{-}Cl \xrightarrow[\textit{ligand exchange}]{RO^-} [LCu(I)]\text{-}OR \xrightarrow[\textit{activation}]{Si\text{-}H} [LCu(I)]\text{-}H \quad (3)$$

Copper(II) precursors bearing hard ligands such as fluoride were found to readily undergo activation by a stoichiometric reducing agent along with complexation with a phosphine ligand to afford the copper(I) hydride catalyst (equation 4).



2.2.2 1,2- and 1,4-Reductions Catalyzed by Copper Hydride

The need for new synthetic methods for forming chiral centers has driven the development of catalytic tools tremendously over the past 30 years. The use of α,β-unsaturated Michael acceptors has been an efficient way to construct tertiary centers of chirality. The carbophilic nature of copper means that hydrogen is introduced in a 1,4-addition, usually.

Shortly following the initial report on stoichiometric applications of $[CuH(PPh_3)]_6$ the first catalytic cycle was established[22] (Fig 4).

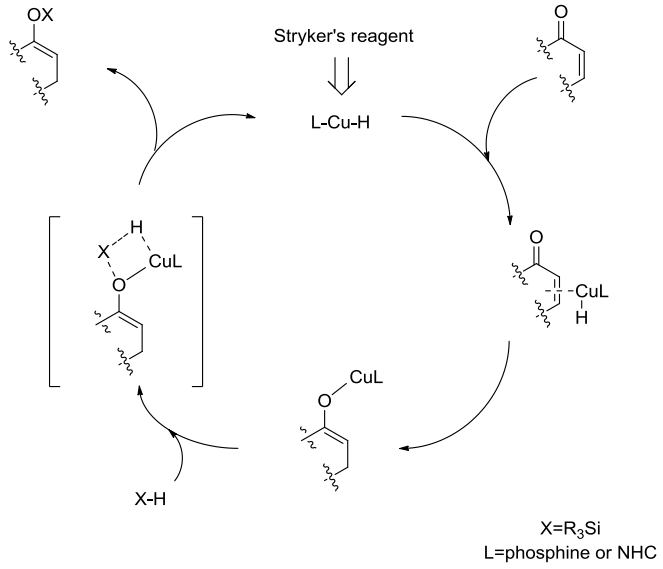


Fig 4. Proposed Catalytic Cycle for Conjugate Reductions

In the catalytic cycle, the carbophilic copper hydride reacts with the Michael acceptor to form a π-complex. Delivery of the hydride to the β-carbon atom to form the enolate, which undergoes a σ-bond metathesis with the stoichiometric hydride source. This regenerates catalytic copper(I) hydride and eliminates the enolate which tautomerizes to the product. One of the noteworthy challenges in the development of this methodology was that of β,β-disubstituted acyclic enones. The first breakthrough came from the Lipshutz group.[23] Asymmetric reductions employing the Josiphos ligand (R,S)-PPF-P(*t*-Bu)$_2$ developed by Solvias reduced acyclic α,β-unsaturated ketones and esters in good yields and excellent ee's. Doubly substituted enoates were also reduced selectively with a biaryl ligand developed by Takasago.[24]

The biaryl core of these ligands proved to be important. The core of the SEGPHOS ligand, which is biaryl, has a smaller dihedral angle (65^o) relative to several other commercially available biaryl ligands, including BINAP (73.5^o) and MeO-BIPHEP (68.6^o) in their Ru complexes.[25] This correlation holds true experimentally that the selectivity is directly tied to the dihedral hold with copper. One would expect, therefore, that stereocontrol would be heightened due to enhanced interactions between an equatorial aryl moiety on phosphorus and a substrate (Figure 5).

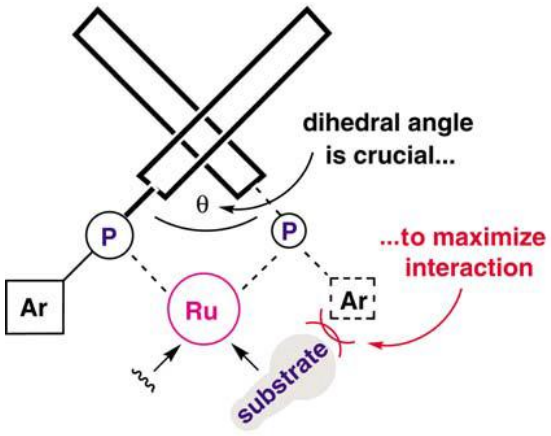


Figure 5. Substrate-catalyst interaction

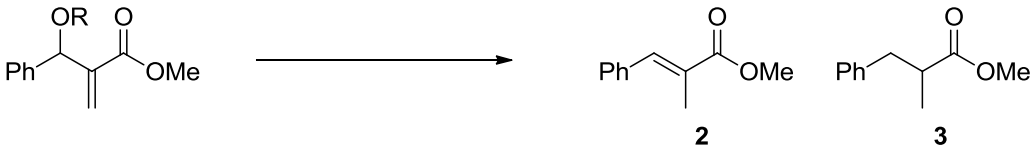
Another equally powerful ligand that proved valuable was the BIPHEP series of ligands developed by Roche. 3,5-Xyl-MeO-BIPHEP was found to reduce aryl ketones in good yield's and good ee's.[26] This ligand proved to be very general and the copper(I) hydride complex reduced several aryl and heteroaryl ketones affording ee's >90% when done at low temperatures (≤-50 ^{o}C). With the adoption of highly discriminating ligands in the BIPHEP, JOSIPHOS, and SEGPHOS series the problem of asymmetric hydrosilylation was essentially solved.

2.2.3 Copper-Hydride Reductions of Morita-Baylis-Hillman Adducts

Of note most recently was the extension of this chemistry to the framework of Morita-Baylis-Hillman adducts in the Lipshutz group. The aim of this work was to give access to enantioenriched chiral allylic alcohols with defined olefin geometry. As previously mentioned, catalytic copper-hydride mediated reductions have been

extensively developed in recent years allowing for highly enantio- and chemoselective 1,4- and 1,2-reductions under mild conditions for a diverse array of substrates. The question to be answered was could CuH deliver a hydride to the activated allylic site or in a 1,4-sense to the Michael acceptor. Given that CuH reductions are known to give rise to a O-Cu enolate following delivery of hydride, it was reasoned that the 1,4-addition pathway could either be trapped out as a silyl ketene acetal and further quenched, or undergo anti-elimination to give an enoate.

It was found that subjecting a MBH adduct to typical CuH conditions, only enoate and the overreduced ester were isolated. It was concluded that allylic substitution was far faster than 1,4-reduction. The reaction was optimized to eliminate the undesired pathway of overreduction as illustrated in table 3.

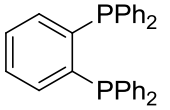


2 **3**

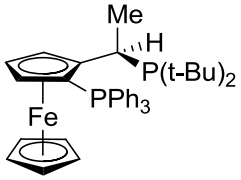
Table 3: Results of Optimization of Reaction Conditions

R	$Cu(OAc)_2$-H_2O (mol %)	ligand (mol %)	silane (H- equiv)	temp. (^oC)	time (h)	**2** (%)[b]	**3** (%)[b]
Ac	3 mol%	BDP (3)	DEMS (2)	r.t.	2	81 (8:1 *E/Z*)	18
Ac	0 mol%	none (0)	DEMS (2)	r.t.	18	0	0
Ac	0 mol%	BDP (3)	DEMS (2)	r.t.	72	0	0
Ac	3 mol%	BDP (3)	DEMS (2)	-25	13	80	7
Ac	3 mol%	L1 (3)	DEMS (2)	r.t.	2	69	5
Ac	3 mol%	L2 (3)	DEMS (2)	r.t.	2	21	0
Ac	3 mol%	L3b (3)	DEMS (2)	r.t.	2	22	1
Ac	3 mol%	L3a (3)	DEMS (2)	r.t.	2	100	0
Ac	3 mol%	L3a (3)	PMHS (4)	r.t.	2	100 (6:1 *E/Z*)	0
H	3 mol%	L3a (3)	PMHS (4)	r.t.	2	100 (>20:1 *E/Z*)	0

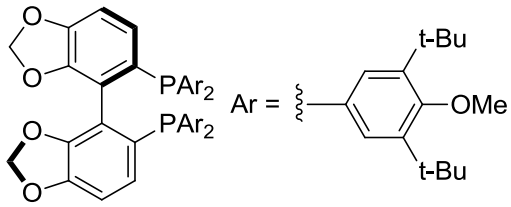
[a]Reactions were performed under an inert atmosphere at [0.4M] in TH
F. [b]Determined by GC-MS of the crude reaction mixture. [c]Determined by ^{1}H-NMR of the pure product. DEMS = diethoxymethylsilane. PMHS = polymethylhydrosiloxane.



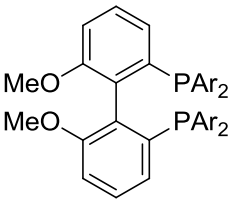
BDP



(*R,S*)-PPF-P(t-Bu)$_2$
L1



DTBM-SEGPHOS
L2



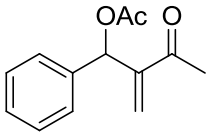
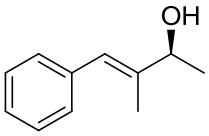
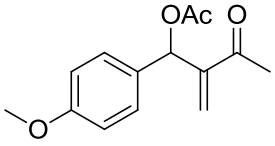
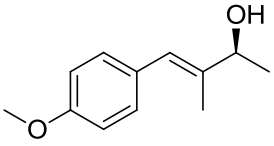
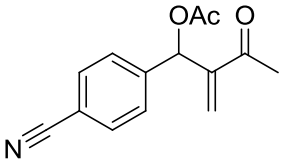
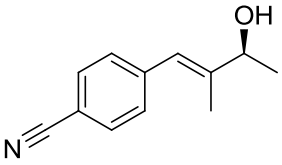
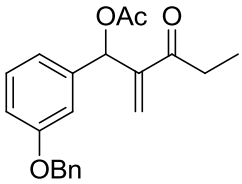
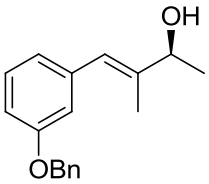
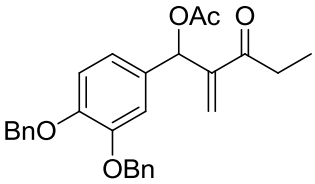
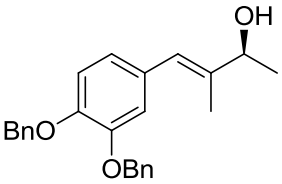
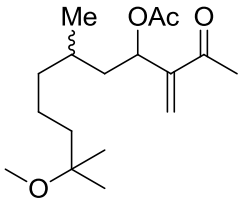
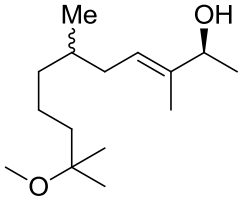
BIPHEP
L3 a (*R*) Ar = Phenyl
b (*R*) Ar = 3,5-*t*-Bu
c (*R*) Ar = 3,5-Xylyl

2.3 Results and Discussion

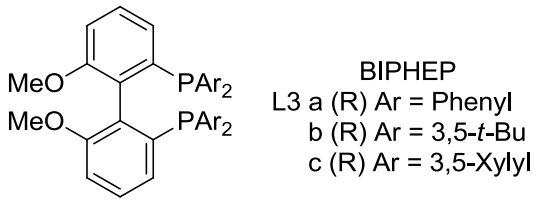
2.3.1 Scope of Tandem Allylic Substitution 1,2-Reduction of MBH Ketones

The scope of this tandem allylic substitution 1,2-reduction was examined using MBH ketones. Ketones possess an intriguing question of selectivity, given they have an α-substituent. If hydride could be directed to react in a similar way to the MBH esters outlined previously, then the unsaturated ketone product might be further reduced asymmetricaly in a 1,2-fashion. This was indeed the case and we were happy to report that electron rich, electron deficient and even the coordinating nitrile substrates were reduced efficiently and with great selectivity. It was also shown that this tandem reaction could be effectively run in surfactant solution, previously demonstrated in the group. This provided enhanced selectivity of 93% ee being run in TPGS-750-M in comparison to 76% ee in Et_2O at -25^{o}C.

Table 4: Substrate Scope

Substrate	Ligand time (h)	Product	Yield (% isolated)
	L3c 24		(92%) 93% ee[a] (91%) 76% ee
	L3c 24		(87%) 84% ee
	*ent*-L3c 24		(93%) 89% ee
	*ent*-L3c 24		(74%) 95% ee
	L3c 24		(92%) 99% ee
	*ent*-L3c 36		(70%) 22.1:16.5:1.5:1 d.r. (88% d.e.)

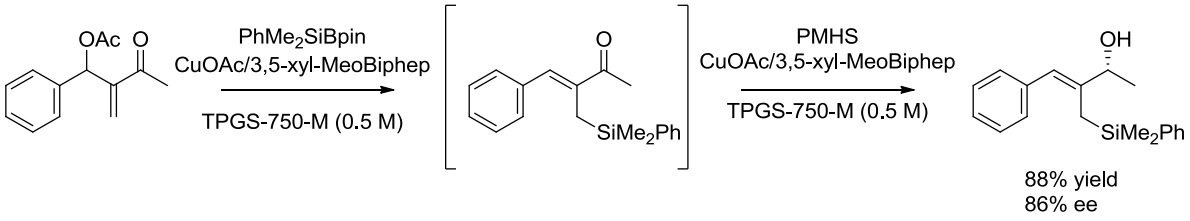
Unless otherwise noted reactions were performed at -25 ^{o}C in Et_2O. [a]Reaction was run in TPGS-750-M [0.25 M].



2.3.2 Tandem Silylation/1,2-Reduction

This method was extended to utilize previously published work. First, a 1,4-additon of silicon followed by formation of CuH in 1-pot so as to reduce the remaining carbonyl moiety. This initially proved difficult when using the nonracemic ligand DTBM-Segphos. It was found that the ligand was coordinated too strongly to copper and prevented the formation of active CuH. This problem was solved by either the addition of 0.25 equivalents of methyl acrylate, a scavenger to react with the remaining $PhMe_2SiBpin$, or complex atoms of CuH separately. Interestingly, it was found that 3,5-xyl-MeoBiphep does not suffer from this problem and must have a more labile interaction with copper, since addition of PMHS readily forms an active CuH species.

Fig 5: Tandem Allylic Silylation 1,2-Reduction



2.3.3 Conclusion

In conclusion, it has been demonstrated that MBH adducts can be efficiently transformed to chiral allylic alcohols by utilizing a highly controlled tandem reduction. This affords a highly valuable chiral allylic alcohol with defined stereochemistry.

3. Experimental Procedures

3.1 General Information

Unless otherwise noted, all reactions were performed under an atmosphere of argon. All commercially available reagents were used without further purification. A 2 wt % TPGS-750-M/H_2O solution was prepared by dissolving 4 g TPGS-750-M in 196 g water (HPLC grade), followed by degassing with argon. TPGS-750-M was made as previously described,[i] and is available from Sigma-Aldrich (catalog #733857). Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F_{254} plates (Merck, 0.25 mm thick). The developed chromatograms were analyzed by UV (lamp, 254 nm). Non-UV active compounds were developed using aqueous potassium permanganate ($KMnO_4$), Vanillin/H_2SO_4, Ceric Ammonium Molybdenate (CAM stain), or Seebach's stain. Flash chromatography was performed in glass columns using Silica Flassh® P60 (SiliCycle, 40-63 μm). GCMS data was recorded on a 5975C Mass Selective Detector coupled with a 7890A Gas Chromatograph (Agilent Technologies). A capillary column (HP-5MS cross- linked 5% phenylmethylpolysiloxanediphenyl, 30 m x 0.250 mm, 0.25 micron, Agilent Technologies) was employed. Helium was used as carrier gas at a constant flow of 1 mL/min. ^1H and ^{13}C NMR were recorded at 22 °C on a Varian UNITY INOVA Avance at 400, 500, or 600 MHz. Chemical shifts in ^1H NMR spectra are reported in parts per million (ppm) on the δ scale from an internal standard of residual chloroform (7.26 ppm) or dichloromethane (5.30 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sex = sextet, sep = septet, m = multiplet, br = broad w = weak), coupling constant in Hertz (Hz), and integration. Chemical shifts of ^{13}C NMR spectra are reported in ppm from the central peak of $CDCl_3$ (77.16 ppm) or the left peak of CD_2Cl_2

(53.84 ppm) on the δ scale. IR data was collected on an FTIR Perkin Elmer Spectrum Two UATR Two spectrum using $1cm^{-3}$ resolution: Chiral HPLC data were collected using a Shimadzu SPD-m20a Prominence diode array detector.

3.2 Procedures

3.2.1 Procedures of Stereoselective Silylcupration

3.2.1.1 Synthisis of Ynoates

Unsaturated esters were prepared according to the following general procedure. A flame dried RBF was charged with a stir bar and dry THF [0.1 M] and covered with a rubber septa under positive argon flow. The corresponding alkyne (1 equiv) was added through the septa via syringe and the flask was placed in a dry ice acetone/bath on a stir plate and stirred at -78 ˚C for 10 min. After 10 min a recently titrated solution of *n*-BuLi in hexanes (1.05 equiv) was added semi-dropwise. After the addition was complete, the mixture was stirred at -78 ˚C for 10 min, the flask was then raised a few inches above the level of solvent in the acetone bath and allowed to warm while stirring for 20 min. The flask was then resubmerged and allowed to recool to -78 ˚C. Once cooled, (1.1 equiv) of the corresponding chloroformate or carbonic anhydride was added dropwise. In the case of solid anhydrides (Boc_2O), addition was performed by dropwise addition through a cannula as a [0.5 M] solution in dry THF to the solution of lithiated alkyne. After the addition the cooling bath was removed and the solution was allowed to warm to ambient temperature while stirring for 2 h. The septa was then removed and the reaction was quenched by cautious addition of a saturated aqueous solution of ammonium chloride until bubbling ceased. The contents of the RBF were transferred to a separatory funnel and the RBF was

rinsed one time with Et_2O into the funnel. The mixture was diluted with Et_2O shaken and layers separated. On occasions where the layers did not readily separate a small quantity of DI water was added to the seperatory funnel. The aqueous layer was washed 3 more times with Et_2O, and the organic extracts were combined. The combined organic extracts were washed with saturated aqueous sodium bicarbonate, a small amount of DI water, brine, dried over sodium sulfate, filtered and concentrated by rotary evaporation. Samples were further purified by flash chromatography, eluting with 0-2% Et_2O/hexanes at a high rate of flow. The use of EtOAc/hexanes to elute led to inferior separations for most ynoates.

3.2.1.2 Synthesis of Suginome's Reagent: $PhMe_2SiBpin$

$PhMe_2SiBpin$ was prepared according to the procedure outlined by Sugimoto.[ii] The procedure was observed to work well with lithium wire as opposed to lithium shot, and can be done conveniently performing the lithium halogen exchange for 6-8 h at 0 ˚C as opposed to -5 ˚C for 18 h. Higher yields were observed when using HBpin as opposed to *i*-PrOBpin. Old samples of HBpin and *i*-PrOBpin led to unsatisfactory results and these reagents are best used fresh. The distillation of $PhMe_2SiBpin$ was performed in a bulb to bulb apparatus under high vacuum at 150 ˚C. Running the distillation under high vacuum at 125 ˚C led to longer distillation times by about 4-6 h and gave lower yields presumably due to thermal decomposition. Running the reaction with old samples of HBpin and *i*-PrOBpin were observed to generate up to 20% PhMe2Si-O-Bpin as confirmed by GCMS and NMR which could not be separated from the desired compound by distillation. However, samples that contained this impurity could be used in subsequent silylation without any disadvantage providing the mass of the impurity was taken into account in the corresponding molar equivalents calculation. $PhMe_2SiBpin$ was stored in a refrigerator in a Parafilm wrapped

vial under argon. Samples of the reagent stayed active for up to 6 weeks. Reagent was withdrawn from the vial under a blanket of argon. After some time the reagent was observed to turn from a clear liquid to a pale yellow color but this did not affect performance.

3.2.1.3 Procedure for reaction using .01 mol % catalyst

Prepared according to General Procedure **A** with the following modifications:
Due to the low amount of copper in the reaction, to prevent oxidation of the catalyst all starting materials were purged under vacuum and backfilled with argon 4-5 times. Surfactant solution, TPGS-750-M (2 wt. %), was thoroughly degassed with argon bubbling while stirring prior to use. 0.01 mol % CuOAc/PPh_3 were introduced into the reaction vessel by serial dilutions of a stock solution of a 1:1 CuOAc/PPh_3in THF. The appropriate volume of dilute CuOAc/PPh_3 was then transferred to the reaction vessel and evaporated under a positive flow of argon until the mass of the vial no longer changed. 0.13 mL of freshly degassed 2 wt % TPGS-750-M solution was added via syringe and the solution was let stir 15 min under a positive argon flow. Ynoate (**1**, 1 equiv) was added via syringe and let stir 5 min followed by addition of $PhMe_2SiBpin$ (1.25 equiv). The argon needle was removed and the septa was securely sealed with parafilm and stirred vigorously for 16 hours followed by standard workup.

3.2.1.4 Recycle Study

Prepared according to General Procedure **A** with the following modification.
All reactions run on 0.1 mmol scale. The reaction was worked up by addition via syringe of 0.2 mL hexane while remaining under argon atmosphere. The reaction was let stir for 30

sec and was subsequently let settle for an additional 30 sec until two separate layers formed. The hexane was removed via syringe. The extraction was performed a second time with 0.3 mL hexane. The organic extracts were combined and subsequently purified by flash chromatography. A second addition of ynoate (**1**, 1 equiv) was added and let stir 5 min, followed by addition of $PhMe_2SiBpin$ (1.25 equiv). The reaction was let stir 30 min. followed by extraction outlined previously. This was performed five times. The sixth reaction was pipetted onto a pad of silica and worked up according to the general procedure.

3.2.1.5 E Factor Calculations

Prepared on 0.1 mmol scale according to the procedure outlined above for recycling of the reaction medium.

Calculation For Conditions A:
E Factor = (Mass organic waste) / (Mass of pure product)
= (Mass hexanes)/ (Mass pure product)
= (131mg hexane)/ (31.8mg pure product)
= 4.2
Including water in the reaction medium
= (131mg hexane + 140mg water)/ (31.8mg pure)
= 8.5

E Factor study with Procedure **B** was followed with the following modifications. Prepared on 0.1 mmol scale with 5 equiv. HPLC Grade H_2O (degassed). After 30 min 100 mg silica was added to the reaction vessel and the sides were washed with .1 mL hexane, stirred for 1 min, concentrated under vacuum, loaded directly onto a flash column.

Calculation For Conditions **B**:
E Factor = (Mass organic waste) / (Mass of pure product)
= (Mass hexanes)/ (Mass pure product)
= (65.5mg hexane)/ (31.4mg pure product)
= 2.1
Including water in the reaction medium
= (65.5mg hexane + 9mg water)/ (31.4mg pure)
= 2.4

3.2.2 Procedures for Enantioselective Copper-Hydride Reductions

3.2.2.1 Synthesis of Morita-Baylis-Hillman Adducts

MBH adducts were prepared according to the following general procedure:

To a solution of aldehyde (1 equiv), methyl vinyl ketone (3 equiv) and tetrahydrothiophene (1.2 equiv) in DCM [0.2 M] at 0 ^{o}C was added $BF_3 \cdot OEt_2$ (1.5 equiv). After stirring for 30 min at this temperature Et_3N (1 equiv) was added to the mixture and stirred for a further 15 min while warming to rt. The solution was washed with dilute HCl, saturated $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo* to give the crude product which was purified by column chromatography.

3.2.2.2 Acetate Protection of Morita-Baylis-Hillman Adducts

MBH alcohol (1 equiv) in DCM [1 M] at -20 ^{o}C was added pyridine (1.3 equiv) followed by the addition of acetyl chloride (1.3 equiv). The solution was let stir 30 min warming to rt. Water was added (1:1 w/ DCM) to the reaction and let stir 5 min. Water was removed and the organic phase was washed with water (2x), brine and dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Followed by purification by flash chromatography.

3.2.2.3 Procedure of Tandem 1,4 1,2 Copper-Hydride Reduction

A conical 5 mL microwave vial containing a conical stir bar was charged with fine powdered $Cu(OAc)_2 \cdot H_2O$ (3 mol %) and (*R*)-3,5-Xyl-MeoBiphep (3 mol %). The vial was capped with a rubber septum and placed under an argon atmosphere, Et_2O (0.25 M) was added via

syringe. At rt, PMHS (9 H^- equiv) was introduced, resulting in a yellow solution after 45 min. The vial was then placed into a pre-cooled acetone bath at -25 ^oC and stirred for an additional 10 min. Liquid substrates were subsequently introduced via syringe. After TLC confirmed full conversion, the reaction was quenched at -25 ^oC by the addition of 0.5 mL sat. NH_4F/MeOH. The reaction vial was taken out of the cooling bath and warmed to rt. After filtration through SiO_2, the solvent was evaporated *in vacuo* and the crude reaction mixture purified by column chromatography on silica gel.

3.2.2.4 Procedure of Tandem Silylation 1,2 Reduction in Water

A conical 5 mL microwave vial containing a conical stir bar was charged with fine powdered Cu(I)OAc (3 mol %) and (R)-3,5-Xyl-MeoBiphep (3 mol %). The vial was capped with a rubber septum and placed under an argon atmosphere, TPGS-750-M [1 M] was added *via* syringe. At rt, the liquid substrates were introduced via syringe followed subsequently by $PhMe_2SiBpin$ (1.25 equiv).

After TLC confirmed full conversion a second conical microwave vial containing a conical stir bar was charged with fine powdered Cu(I)OAc (3 mol %) and (R)-3,5-Xyl-MeoBiphep (3 mol %). The vial was capped with a rubber septum and placed under an Argon Atmosphere, TPGS-750-M [1M] was added via syringe. PMHS (9 H^- equiv) was then added and let stir 15 min. This solution of preformed CuH was introduced to the previous microwave via syringe. After TLC confirmed full conversion, the reaction was quenched by the addition of 1 mL sat. NH_4F/H_2O. The reaction mixture was extracted with DCM (4x), washed with $NaHCO_3$, dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo*

and the crude reaction mixture purified by column chromatography on silica gel. The product was analyzed by analytical HPLC on a chiral stationary phase for the determination of ee.

Note: Care was taken quenching this reaction and was not allowed to stir more than 30 min to prevent desilylation of the product.

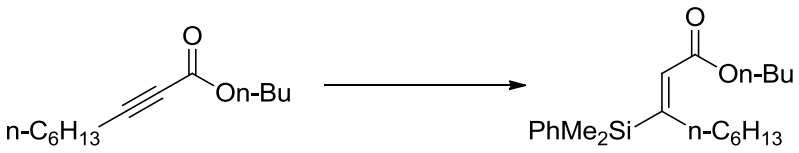
3.2.2.5 Procedure for Synthesis of Racemic Samples

A conical 5 mL microwave vial containing a conical stir bar was charged with fine powdered CuOAc (3 mol %) and BDP (3 mol %). The vial was capped with a rubber septum and placed under an argon atmosphere, Et_2O (0.25 M) was added *via* syringe. At rt, PMHS (1 H^- equiv) was introduced, resulting in a yellow solution after 45 min. Liquid substrates were subsequently introduced via syringe. After 2 h the reaction was quenched by the addition of 0.5 mL sat. NH_4F/MeOH. After filtration through SiO_2, the solvent was evaporated in vacuo and the crude reaction mixture purified by column chromatography on silica gel.
Flash chromatography eluting with 10% Et_2O/hexanes yielded as a colorless oil.

Subsequently, to a solution of $CeCl_3 \cdot 7H_2O$ in MeOH [0.4 M] was added ketone (1 equiv) and stirred 5 min. $NaBH_4$ was introduced and stirred until TLC indicated complete conversion.

3.3 Characterization of Products

(*E*)-Butyl 3-(dimethyl(phenyl)silyl)non-2-enoate



Prepared according to General Procedure **A** or **B**

Flash chromatography with 1% Et_2O/hexanes yielded (94%, procedure **A**) or (98%,

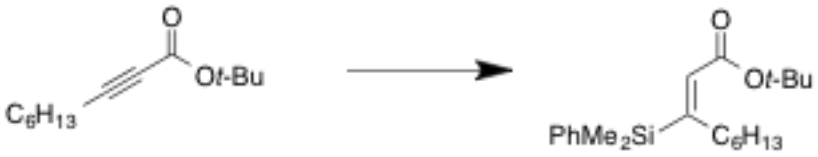
procedure **B**) of (*E*)-butyl 3-(dimethyl(phenyl)silyl)non-2-enoate as a clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.42 (s, 6H), 0.82-0.85 (t, *J* = 7.1 Hz, 3H), 0.92-0.95 (t, *J* = 7.4 Hz, 3H), 1.22-1.28 (m, 8H), 1.36-1.43 (m, 2H), 1.61-1.66 (m, 2H), 2.59-2.62 (m, 2H), 4.09-4.11 (t, *J* = 6.7 Hz, 2H), 7.30-7.40 (m, 3H), 7.49-7.52 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.07, 13.89, 14.20, 19.40, 22.73, 29.87, 29.97, 30.93, 31.69, 31.82, 63.92, 103.89, 128.03, 129.51, 134.18, 136.87, 164.32, 165.67.

IR: 2956, 2929, 2858, 1715, 1587, 1459, 1427, 1379, 1249, 1216, 1147, 1112, 1088, 998, 909, 832, 815, 699 cm^{-1}

***t*-Butyl (*E*)-3-(dimethyl(phenyl)silyl)non-2-enoate**



Prepared according to general procedure **B**

Flash Chromatography gradient elution 0-2% Et_2O/hexanes gave quantitative yield of *t*-butyl (*E*)-3-(dimethyl(phenyl)silyl)non-2-enoate as a clear oil; single isomer.

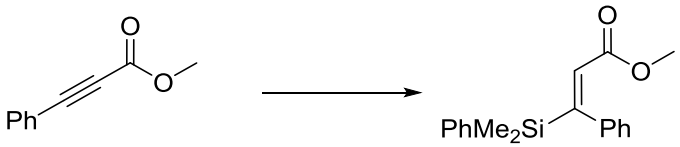
^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.41 (s, 6H), 0.84 (t, *J* = 7.5 Hz, 3H), 1.14-1.27 (m, 8H), 1.48 (s, 9H), 2.57 (t, *J* = 8 Hz, 2H), 5.98 (s, 1H), 7.34-7.39 (m, 3H), 7.50-7.52 (m, 2H)

^{13}C NMR (125MHz, $CDCl_3$) δ: -3.012, 14.192, 22.707, 28.365, 29.925, 31.485, 31.746, 80.192, 127.987, 129.427, 130.214, 134.209, 137.132, 161.43, 165.37

ESI-HRMS: Calcd. For $C_{21}H_{34}O_2Si$: 346.2328. Found: 369.2226 $(M+Na)^+$

IR: 3075, 2956, 2928, 2857, 1712, 1598, 1456, 1428, 1366, 1249, 1214, 1146, 832, 816, 773, 731, 699 cm^{-1}

Methyl (*E*)-3-(dimethyl(phenyl)silyl)-3-phenylacrylate



Prepared according to General Procedure **A**

Flash chromatography gradient elution with 1-2% Et_2O/hexanes yielded 98% of methyl (*E*)-3-(dimethyl(phenyl)silyl)-3-phenylacrylate as a colorless oil and as a single isomer.

TLC: 10% Et_2O/Hexanes R_f: 0.37 Stain: UV/$KMnO_4$

^1H NMR (500 MHz, $CDCl_3$) δ: 0.38 (s, 6H), 3.50 (s, 3H), 6.21 (s, 1H), 6.82-6.84 (m, 2H), 7.19-7.25 (m, 3H), 7.36-7.37 (m, 3H), 7.46-7.48 (m, 2H).

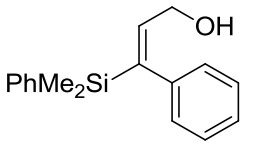
^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.69, 51.10, 125.86, 126.13, 127.74, 127.92, 128.75, 129.59, 134.21, 135.58, 140.96, 162.11, 165.47

IR: 3023, 2952, 1732, 1713, 1594, 1490, 1428, 1349, 1249, 1195, 1163, 1113, 1032, 942, 860, 831, 809, 779, 696 cm^{-1}

Absolute *E* stereochemistry for methyl (*E*)-3-(dimethyl(phenyl)silyl)-3-phenylacrylate was established by ^1H-^1H NOESY (600 MHz, $CDCl_3$) (see attached spectra) and suggested by the strong cross peak between the Si-Me and α-vinyl proton.

Additionally absolute *E* stereochemistry was further supported for Methyl (*E*)-3-(dimethyl(phenyl)silyl)-3-phenylacrylate by reduction to the known corresponding allylic alcohol using 2.2 equiv DIBAL-H in dry DCM 0.4 M at rt for 4 h to yield (*E*)-3-(dimethyl(phenyl)silyl)-3-phenylprop-2-en-1-ol as a colorless oil. Spectral data matches that

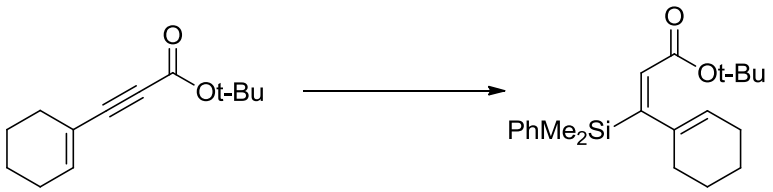
previously reported for the *E* isomer[iii], *and is inconsistent with that reported for the Z isomer.*[iv]



(*E*)-3-(Dimethyl(phenyl)silyl)-3-phenylprop-2-en-1-ol

^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.35 (s, 6H), 4.06 (d, *J* = 6.5 Hz), 6.16 (t, *J* = 6 Hz, 1H), 6.84 (m, *J* = 7 Hz, 2H), 7.15-7.25 (m, 3H), 7.32-7.39 (m, 3H), 7.48-7.50 (m, 2H)

Tert-butyl (*E*)-3-(cyclohex-1-en-1-yl)-3-(dimethyl(phenyl)silyl)acrylate



Prepared according to general procedure **B** on 0.4 mmol scale. Flash chromatography through a short (3 inch) silica column yielded 131 mg (95.6% isolated) of *t*-butyl (*E*)-3-(cyclohex-1-en-1-yl)-3-(dimethyl(phenyl)silyl)acrylate as a colorless oil, and as a single isomer.

R_f = .55 10% EtOAc/hexanes Stain: UV/$KMnO_4$

^{1}H NMR (500 MHz, CDCl3) δ: 0.40 (s, 6H), 1.45 (s, 9H), 1.54 (m, 4H), 1.84 (br, m, 2H), 2.00 (br, m, 2H), 5.09 (m, 1H), 5.87 (s, 1H), 7.33-7.37 (m, 3H), 7.50-7.52 (m, 2H)

^{13}C NMR (125MHz, CDCl3) δ: -3.14, 22.12, 22.87, 25.19, 28.32, 29.11, 80.34, 120.28, 127.85, 129.39, 130.06, 134.31, 136.94, 138.58, 160.51, 165.66

ESI-HRMS: Calcd. For $C_{21}H_{30}O_2Si$: 342.2015. Found: 365.1900 $(M+Na)^+$

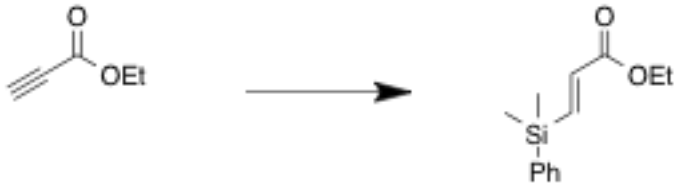
IR: 3070, 2929, 2834, 2210, 1718, 1704, 1588, 1427, 1390, 1349, 1247, 1145, 985, 808, 699 cm^{-1}

E stereochemistry was confirmed by ^{1}H-^{1}H NOESY (600 MHz, $CDCl_3$) (see attached spectra)

Key observations supporting the *E*- assignment are as follows:

1) Methyl groups on silicon gave a strong cross peak with the α-vinyl proton
2) The ring vinyl and the allylic ring protons gave a strong cross peak with *t*-buyl protons.
3) The absence of silicon methyl's coupling to the *t*-butyl protons which would be expected for the *Z* isomer
4) The absence of coupling between the silicon phenyl protons and *t*-butyl protons

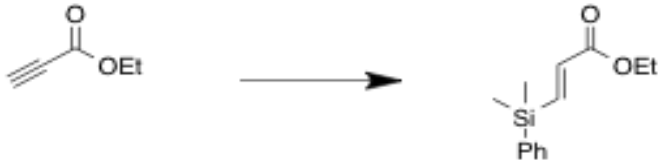
Ethyl (*E*)-3-(dimethyl(phenyl)silyl)acrylate



Prepared according to General Procedure **A** in 75% isolated yield as a single isomer. Spectral data matches that of previously reported for the *E* isomer.[v]

^{1}H NMR (500 MHz $CDCl_3$) δ: 0.42 (s, 6H), 1.30 (t, *J* = 12.5 Hz, 3H), 4.20 (q, *J* = 7 Hz, 2H), 6.29 (d, *J* = 19 Hz, 1H), 7.34-7.40 (m, 4H), 7.50-7.52 (m, 2H).

***n*-Octyl (*E*)-3-(dimethyl(phenyl)silyl)acrylate**



In a microwave vial under argon atmosphere, copper (I) acetate (0.5 mg, 0.004 mmol, 0.02 equiv), triphenylphosphine (1.1 mg, 0.004 mmol, 0.02 equiv), were added to 266.67 µL of TPGS-750-M**.** *n*-octyl propiolate (36.45 mg, 0.2 mmol, 1 equiv) was subsequently added followed immediately by dropwise addition of $PhMe_2SiBpin$ (0.25 mmol, 1.25 equiv). The solution was allowed to stir for 2 h, after which the reaction was diluted with CH_2Cl_2 and filtered through a pad of SiO_2. The solvent was removed by rotovap and the resulting crude product was further purified by flash chromatography, affording 50.4 mg (80%) of a colorless oil. *E* stereochemistry determined by J_{ab} frequency of the α-proton.

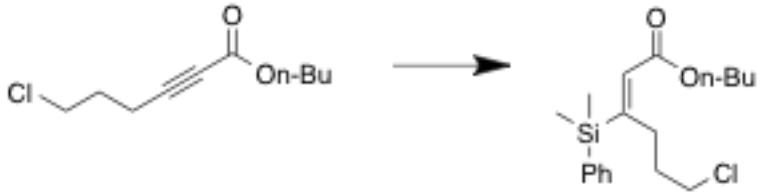
^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.52-7.34 (m, 6H), 6.29 (d, *J* = 12.5 Hz 1H), 4.15 (t, 2H), 1.69 (q, 2H), 1.38-1.26 (m, 10H), 0.90 (t, 3H), 0.42 (s, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.01, 147.41, 136.60, 135.52, 133.99, 129.64, 128.13, 65.00, 31.93, 30.47, 29.85, 29.37, 29.31, 28.79, 26.09, 22.78, 14.23, -3.02.

IR: 2956, 2925, 2856, 1725, 1430, 1304, 1249, 1221, 1165, 839, 996, 840, 817, 730, 698 cm^{-1}

EI-HRMS calcd for $C_{19}H_{30}O_2Si$ [M^+] = 318.2015, found 303.1784 [M-CH_3] $^+$

Butyl (*E*)-6-chloro-3-(dimethyl(phenyl)silyl)hex-2-enoate



Prepared according to general procedure **A**

Stirred for 4 h. Usual workup and flash chromatography gradient elution 0-2% Et_2O/hexanes yielded 82% of a colorless oil. Use of 5 mol % catalyst and 2 equiv $PhMe_2SiBpin$ gave 82% isolated yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.46 (s, 6H), 0.95 (t, *J* = 9 Hz, 3H), 1.43 (sex, *J* = 9.5 Hz, 2H), 1.66 (p, *J* = 8.5 Hz, 2H), 1.78 (m, *J* = 8 Hz, 2H), 2.75 (t, *J* = 10 Hz 2H), 3.48 (t, *J* = 8.5 Hz, 2H), 4.11 (t, *J* = 8.5 Hz, 2H), 6.12 (s, 1H), 7.51-7.36 (m, 5H),

^{13}C NMR (125MHz, $CDCl_3$) δ: -3.24, 13.88, 19.37, 29.18, 30.89, 32.57, 45.33, 64.10, 128.17, 129.08, 129.73, 134.17, 136.30, 162.81, 165.41

ESI-HRMS: Calcd. For $C_{18}H_{27}ClO_2Si$: 338.1469. Found: 361.1353 $(M+Na)^+$

IR: 3076, 2958, 2873, 1712, 1602, 1428, 1250, 1178, 1153, 1113, 1027, 833, 814, 775, 732, 699, 569, 469 cm^{-1}

Methyl (*E*)-3-(dimethyl(phenyl)silyl)undec-2-en-10-ynoate

Prepared according to General Procedure **A**
TLC: 10% EtOAc/hexanes R_f = 0.41 (product), 0.47 (impurity), Stain: UV/$KMnO_4$

Usual workup and flash chromatography gradient elution with 0-0.5% Et_2O/hexanes yielded 98 mg (75%) of product. Eluting with EtOAc/hexanes mixtures gave poor separations.

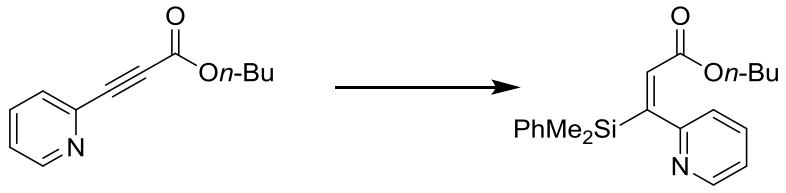
^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.43 (s, 6H), 1.23-1.35 (br, m, 6H), 1.45 (p, *J* = 7.5 Hz, 2H), 1.92, (t, *J* = 7.5 Hz, 1H), 2.13 (dt, *J* = 2.5, 7 Hz, 2H), 2.63 (t, *J* = 8.5 Hz, 2H), 3.69 (s, 3H), 6.07 (s, 1H), 7.32-7.40 (m, 3H), 7.47-7.57 (m, 2H)

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.13, 18.49, 28.51, 28.53, 29.61, 29.65, 31.71, 51.07, 68.17, 84.9, 127.59, 128.07, 129.58, 134.16, 136.68, 165.18, 165.76.

EI-HRMS: Calcd. For $C_{20}H_{28}O_2Si$: 328.1859. Found: 313.1638 $(M\text{-}CH_3)^+$

IR: 3306, 3070, 2935, 2858, 2122, 1718, 1602, 1428, 1346, 1249, 1193, 1170, 1112, 1044, 833, 817, 775, 732, 631, 468 cm^{-1}

Butyl (*E*)-3-(dimethyl(phenyl)silyl)-3-(pyridin-2-yl)acrylate (18)



Prepared according to General Procedure **A**

TLC: 40% EtOAc/hexanes R_f: 0.3, Stain: UV/$KMnO_4$

Flash chromatography elution with 20% EtOAc/hexanes yielded 82% as a yellow oil in a 12:1 *E/Z* ratio as determined according to the relative integrations of vinyl protons, providing sample was worked up, purified, and analyzed immediately.

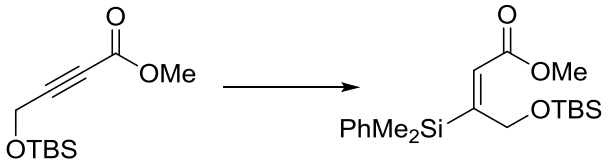
^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.42 (s, 6H), 0.79-0.82 (t, *J* = 7.4 Hz, 3H), 1.10-1.18 (sex, 2H), 1.31-1.37 (p, 2H), 3.88-3.90 (t, *J* = 6.6 Hz, 2H), 6.06 (s, *Z* (minor) isomer, 0.09H), 6.25 (s, *E* (major) isomer, 1H), 6.83-6.85 (d, *J* = 7.9 Hz, 1H), 7.08-7.11 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 8.55-8.56 (ddd, *J* = 4.9, 1.7, 1.1 Hz, 1H)

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.29, -3.27, 13.78, 19.14, 29.43, 30.51, 63.93, 64.36, 121.10, 121.72, 121.78, 128.07, 129.72, 130.66, 130.73, 134.10, 134.37, 135.51, 135.53, 135.77, 149.06, 160.18, 160.33, 165.30

IR: 3069, 2958, 2873, 1708, 1583, 1562, 1463, 1427, 1381, 1346, 1248, 1170, 1114, 1024, 834, 813, 792, 775, 699 cm^{-1}

ESI-HRMS: Calcd. For $C_{20}H_{25}NO_2Si$: 339.1655. Found: 362.1561 $(M+Na)^+$

Methyl (*E*)-4-((tert-butyldimethylsilyl)oxy)-3-(dimethyl(phenyl)silyl)but-2-enoate



Prepared according to General Procedure **A**

Flash chromatography gradient elution with 0-5% Et_2O/hexanes yielded 88% as a yellow oil.

TLC: 10% Et_2O/hexanes R_f: 0.53

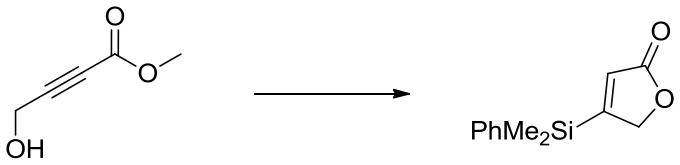
^1H NMR (500 MHz, $CDCl_3$) δ: -0.04 (s, 6H), 0.47 (s, 6H), 0.82 (s, 9H), 3.67 (s, 3H), 4.97 (d, *J* = 2.4 Hz, 2H), 5.87 (t, *J* = 2.4 Hz, 1H), 7.32-7.35 (m, 3H), 7.48-7.50 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -5.52, -1.57, 18.58, 26.19, 51.29, 65.73, 125.68, 127.86, 127.86, 129.12, 134.15, 138.11, 165.89, 157.60

IR: 2952, 2929, 2886, 2856, 1716, 1603, 1428, 1070, 1178, 833, 814, 775 cm^{-1}

EI-HRMS: For $C_{19}H_{32}O_3Si_2$: 364.1890. Found: 364.1884 ($M^{+\cdot}$)

4-(Dimethyl(phenyl)silyl)furan-2(5H)-one



Prepared according to General Procedure **A**

Flash chromatography gradient elution with 5-20% EtOAc/hexanes yielded 70% as a colorless oil.

TLC: 15% EtOAc/hexanes R_f: 0.24

^1H NMR (500 MHz, $CDCl_3$) δ: 0.53 (s, 6H), 4.87 (d, *J* = 2.1 Hz, 2H), 6.24 (t, *J* = 2.1 Hz, 1H), 7.39-7.49 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.42, 75.64, 128.55, 129.27, 130.44, 133.77, 134.16, 174.01

IR: 3070, 2959, 1777, 1743, 1339, 1428, 1245, 1164, 1111, 1056, 998, 833, 805, 780, 735, 780 cm^{-1}

ESI-HRMS: Calcd. For $C_{12}H_{14}O_2Si$: 218.0763. Found: 218.0766 ($M^{+\cdot}$)

(*S*,*E*)-3-(3-(Dimethyl(phenyl)silyl)non-2-enoyl)-4-isopropyloxazolidin-2-one

Prepared according to general procedure **A**

TLC 10% EtOAc/hexanes R_f: 0.29 (major, *E* isomer), 0.36 (minor, *Z* isomer) Staining with Seebach's Stain.

Flash Chromatography gradient elution 10-20% Et_2O/hexanes yielded 70% of *E* silylated oxazolidinone as a clear viscous oil. 12% of the corresponding *Z* isomer was also isolated.

Chromatography using EtOAc/hexanes caused isomers to elute with together.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.46 (s, 6H), 0.83 (t, *J* = 10 Hz, 3H), 0.90 (d, *J* = 5 Hz, 3H), 0.93 (d, *J* = 5 Hz, 3H), 1.11-1.30 (m, 8H), 2.41 (m, 1H), 2.52 (m, 2H). 4.21 (dd, *J* = 10, 5 Hz, 1H), 4.26 (t, *J* = 10 Hz, 1H), 4.48 (dt, *J* = 10, 5 Hz, 1H), 7.21 (s, 1H), 7.34-7.38 (m, 3H), 7.53-7.56 (m, 2H)

^{13}C NMR (125MHz, $CDCl_3$) δ: -3.12, -3.06, 14.20, 14.89, 18.23, 22.69, 28.64, 29.69, 29.88, 31.67, 32.45, 58.42, 63.42, 128.00, 128.27, 129.47, 134.25, 136.92, 154.02, 164.37, 164. 41

1H-1H NOESY (600 MHz, $CDCl_3$): See Attached

IR: 3070, 3054, 2957, 2927, 2856, 1776, 1679, 1587, 1486, 1464, 1427, 1384, 1372, 1299, 1242, 1199, 1112, 1022, 997, 971, 833, 813, 774, 732, 700, 632, 568, 469 cm^{-1}

ESI-HRMS: Calcd. For $C_{23}H_{35}NO_3Si$: 401.2386. Found: 424.2266 $(M+Na)^+$

***Z* - isomer:**

TLC: 10% EtOAc/Hexanes R_f = 0.36

^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.47 (d, *J* = 9 Hz, 6H), 0.73 (d, *J* = 6.6 Hz, 3H), 0.80 (d, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 1.26 (m, 6H), 1.43 (m, 2H), 2.03 (m, 1H), 2.35 (t, *J* = 7.8 Hz, 2H), 4.08 (s, 3H), 7.29 (m, 3H), 7.42 (s, 1H), 7.50 (m, 2H)

^{13}C NMR (125MHz, $CDCl_3$) δ: -1.45, -1.27, 14.21, 14.68, 18.07, 22.71, 28.34, 29.24, 29.51, 31.75, 39.42, 58.18, 63.35, 127.48, 128.56, 132.10, 134.00, 139.14, 154.05, 164.32, 165.74

IR: 3072, 2958, 2927, 2858, 1777, 1678, 1581, 1486, 1464, 1429, 1384, 1372, 1300, 1245, 1203, 1142, 1109, 1064, 1036, 976, 909, 836, 816, 774, 730, 701, 669, 647, 473 cm^{-1}

ESI-HRMS: Calcd. For $C_{23}H_{35}NO_3Si$: 401.2386. Found: 424.2286 $(M+Na)^+$

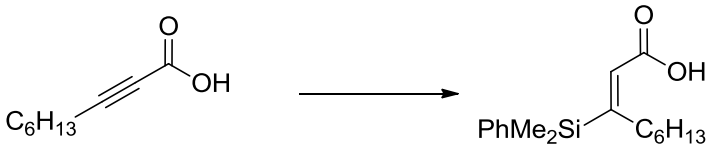
^1H-^{13}C GHSCQ: see attached spectra

^1H-^1H NOESY (600 MHz, CDCl3): see attached spectra:

Absolute configuration was determined for both compounds based on comparison of ^1H-^1H NOESY for both isomers. *E* stereochemistry was suggested by a strong cross peak of the silicon methyl's with the vinyl proton and the absence of a cross peak between the vinyl proton and allylic protons. Conversely, the *Z* isomer showed a strong cross peak between the vinyl and allylic protons and the absence of coupling between the silicon methyl's and the vinyl proton

^1H NMR of the Z isomer showed a puzzling singlet at 4.08 ppm integrating to 3 hydrogens, and the notable absence of the characteristic multiplets of the oxazolidone ring in the 4-4.5 ppm region. This would seem to suggest some sort of fragmentation/rearrangement resulting in the formation of an N, or O-methyl bond with concomitant opening of the oxazolidone ring, but this possibility is ruled out on the basis of several observations: 1) R_f values and staining are very similar by TLC; 2) The chirality is still intact as evidenced by the presence of diastereotopic doublets at 0.47 ppm, 0.73 ppm and 0.80 ppm; 3) HRMS confirms product is of the same mass as the *E* isomer; 4) GHSQC spectrum revealed that the apparent singlet results from the hydrogens of 2 carbons at 58.18 ppm and 63.35 ppm, respectively, which are substantially similar to the shifts observed for the ring carbons adjacent to N, and O in the *E* isomer at 58.42, and 63.42 ppm; 5) IR stretches are almost identical for both compounds; 6) 2D NOESY confirms that the geometry of the minor product is most likely the (*Z*) - isomer.

(*E*)-3-(Dimethyl(phenyl)silyl)non-2-enoic acid



Prepared according to General Procedure **A** using 2 equiv $PhMe_2SiBpin$

Flash chromatography with 10% EtOAc/hexanes yielded 84% as a colorless oil.

TLC: 10% EtOAc/hexanes R_f: 0.23

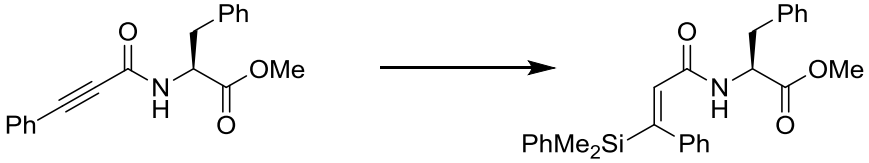
^1H NMR (500 MHz, $CDCl_3$) δ: 0.44 (s, 6H), 0.83-0.85 (t, *J* = 7.0 Hz, 3H), 1.17-1.28 (m, 8H), 2.62-2.65 (m, 2H), 6.08 (s, 1H), 7.35-7.40 (m, 3H), 7.54-7.55 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.16, 14.18, 22.64, 29.69, 29.84, 31.52, 31.91, 127.12, 127.84, 128.09, 129.38, 129.62, 133.14, 134.17, 136.49

IR: 2955, 2928, 2857, 1687, 1601, 1458, 1427, 1288, 1249, 1233, 819, 775, 730, 697 cm^{-1}

ESI-HRMS: Calcd. For $C_{17}H_{26}O_2Si$: 290.1702. Found: 313.1599 (M+Na)

***L*-Methyl (*E*)-(3-(dimethyl(phenyl)silyl)-3-phenylacryloyl)-phenylalaninate**



Prepared according to General Procedure **A** using 2 equivalents of $PhMe_2SiBpin$ and strirred for 1 h.

TLC: 20% EtOAc/hexanes R_f: 0.14

Flash chromatography elution with 20% EtOAc/hexanes yielded 84% as a yellow oil, and 15% recovered staring material.

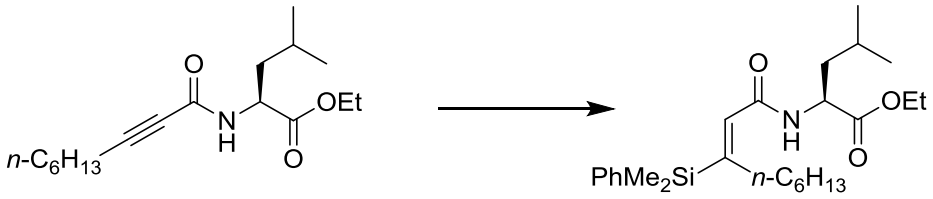
^1H NMR (500 MHz, $CDCl_3$) δ: 0.36 (d, *J* = 1.6 Hz, 6H), 2.70-2.79 (dq, *J* = 13.9, 6.1 Hz, 2H), 3.53 (s, 3H), 4.65-4.69 (dt, *J* = 7.5, 6.1 Hz, 1H), 5.60-5.62 (d, *J* = 7.5 Hz, 1H), 6.24 (s, 1H), 6.81-6.84 (m, 4H), 7.18-7.24 (m, 6H), 7.33-7.44 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.58, -3.56, 37.89, 52.16, 53.45, 126.59, 126.97, 126.99, 128.05, 128.51, 128.77, 129.21, 129.72, 133.66, 134.35, 135.72, 135.96, 139.82, 154.63, 165.52, 171.61.

ESI-HRMS: Calcd. For $C_{27}H_{29}NO_3Si$: 443.1917. Found: 466.1807 $(M+Na)^+$

IR : 3409, 3027, 2953, 1742, 1650, 1601, 1581, 1496, 1428, 1359, 1248, 1173, 1112, 1074, 935, 832, 811, 735 cm^{-1}

Ethyl (*E*)-(3-(dimethyl(phenyl)silyl)non-2-enoyl)-*L*-leucinate



Prepared according to General Procedure **A** using 1.5 equiv $PhMe_2SiBpin$ and stirred 1 h. Flash chromatography elution with 20% EtOAc/hexanes yielded 88% as a yellow oil.

^1H NMR (500 MHz, $CDCl_3$) δ: 0.41 (s, 6H), 0.81-0.84 (t, *J* = 7.1 Hz, 3H), 0.94-0.96 (t, *J* = 5.8 Hz, 6H), 1.13-1.24 (m, 6H), 1.26-1.29 (t, *J* = 7.1Hz, 6H), 1.51-1.57 (m, 2H), 1.62-1.67 (m, 2H), 2.57-2.60 (m, 2H), 4.16-4.21 (q, J = 7.1 Hz, 2H), 4.65-4.67 (dt, *J* = 8.7, 5.1 Hz, 1H), 5.77-5.79 (d, *J* = 8.4 Hz, 1H), 5.99 (s, 1H), 7.34-7.39 (m, 3H), 7.49-7.52 (m, 2H).

^{13}C NMR (500 MHz, $CDCl_3$) δ: -2.96, 14.21, 14.30, 22.23, 22.72, 22.93, 25.04, 29.91, 30.13, 31.59, 31.72, 42.10, 50.56, 61.44, 128.02, 129.45, 131.00, 134.23, 137.15, 158.37, 165.95, 173.46.

ESI-HRMS: Calcd. For $C_{25}H_{41}NO_3Si$: 431.2846. Found: 454.2751 $(M+Na)^+$

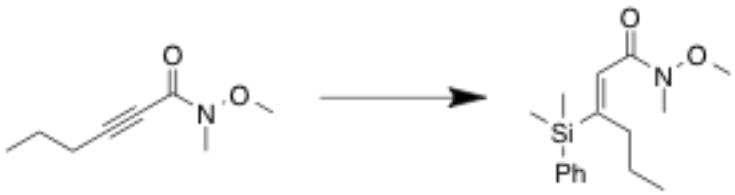
To check for possible erosion of chirality of the peptide during the silylation, an analytical sample was isomerized in ethanol with catalytic sodium ethoxide (20 mg/mL) for 30 min at RT. TLC showed a single spot with no decomposition of the product and the isomerized sample was purified via flash chromatography and was spectroscopically identical to the enantiopure sample. HPLC of pure compound directly after silylation showed only a single peak at 7.99 min, in contrast the isomerized sample showed the appearance of a second peak at 5.18 min, indicating that no isomerization occurred during the silylation.

Isomerized:
HPLC (Chiralcel OD-H 0.46 x 25 cm; 238 nm, 2% *i*-PrOH/hexanes; 1 ml/min; 1 mg/mL, 20 ul injection) t_R 5.18 (35.1%) and 7.99 min. (64.9%).

Enantiopure directly after silylation:

HPLC (Chiralcel OD-H 0.46 x 25 cm; 238 nm, 2% *i*-PrOH/hexanes; 1ml/min; 1 mg/mL, 20ul injection) t_R 7.99 min.

(*E*)-3-(Dimethyl(phenyl)silyl)-*N*-methoxy-*N*-methylhex-2-enamide



Prepared According to General procedure **B** using 2 equiv of $PhMe_2SiBpin$. The reaction was quenched with 50% sat. aq. $NaHCO_3$ and stirred for 15 min, before being poured onto a pad of silica and further purified. Flash chromatography gradient eluting 0-20% EtOAc/hexanes yielded 90% as a yellow oil. The α-proton displays a broad weakly integrating singlet on the ^{1}H NMR spectrum, however a similar trend was observed for the corresponding Weinreb amide of β-methyl cinnamic acid.

TLC 20% EtOAc/hexanes R_f: 0.39 Stain: $KMnO_4$, CAM

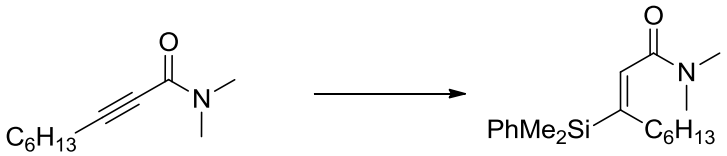
^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.43 (s, 6H), 0.88 (t, *J* = 7.5 Hz, 3H), 1.37 (sex, *J* = 3 Hz, 2H), 2.54 (t, *J* = 2.5 Hz, 2H), 3.18 (s, 3H), 3.57 (s, 3H), 6.44 (w, br, s, 1H), 7.33-7.44 (m, 3H), 7.50-7.55 (m, 2H)

^{13}C NMR (125MHz, $CDCl_3$) δ: -2.881, 14.687, 23.425, 29.826, 33.91, 61.446, 127.947, 128.474 (br, w), 129.368, 134.147, 137.472, 158.819 (br, w), 167.521.

IR: 3074, 2958, 2932, 2870, 1650, 1596, 1462,1427, 1406, 1375, 1248, 1112, 998, 832, 813, 772, 773, 700, 468 cm^{-1}

ESI-HRMS: Calcd. For $C_{16}H_{25}NO_2Si$: 291.1655 Found: 314.1541 $(M+Na)^+$

***(E)*-3-(Dimethyl(phenyl)silyl)-N,N-dimethylnon-2-enamide**



Prepared according to General Procedure **A**

Flash chromatography gradient elution with 5-20% EtOAc/hexanes yielded 78% as a colorless oil.

TLC: 10% EtOAc/hexanes R_f: 0.2

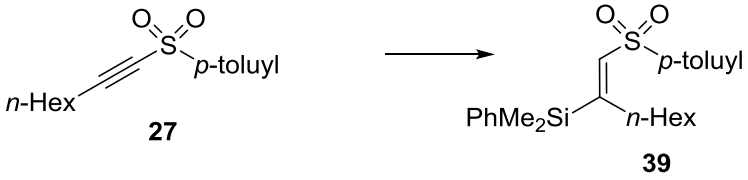
^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.42 (s, 6H), 0.81-0.84 (t, *J* = 7.1 Hz, 3H), 1.10-1.31 (m, 8H), 2.17-2.18 (d, *J* = 3.3 Hz, 1H), 2.27-2.30 (m, 2H), 2.94-2.96 (d, *J* = 6.5 Hz, 6H), 6.19 (s, 1H), 7.33-7.38 (m, 3H), 7.51-7.53 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -2.64, 14.21, 22.69, 29.43, 29.69, 29.75, 31.65, 32.25, 34.50, 37.85, 127.97, 129.32, 133.29, 134.12, 137.73, 150.81, 168.91.

IR: 2954, 2926, 2855, 1703, 1634, 1488, 1457, 1427, 1389, 1247, 1146, 1112, 1051, 998, 832, 813, 772, 732, 700 cm^{-1}

ESI-HRMS: Calcd. For $C_{19}H_{31}NOSi$: 317.5410. Found: 340.2066 $(M+Na)^+$

(*E*)-Dimethyl(phenyl)(1-tosyloct-1-en-2-yl)silane



Prepared according to general procedure **A** stirring for 6 hours. The reaction was filtered through a short plug of silica. Purification via column chromatography eluting with 20% Et_2O/hexanes afforded the product in 99% isolated yield.

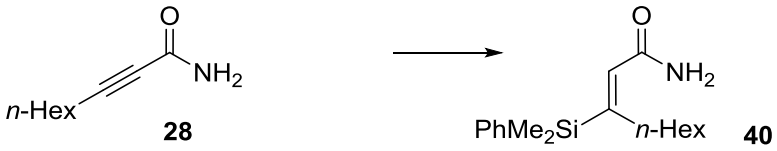
^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.40 (s, 6H), 0.82-0.85 (t, *J* = 7.0 Hz, 3H), 1.07-1.13 (m, 2H), 1.15-1.23 (m, 6H), 2.44 (s, 3H), 2.60-2.63 (t, *J* = 7.25 Hz, 2H), 6.46 (s, 1H), 7.31-7.42 (m, 7H), 7.77-7.78 (d, *J* = 8.0 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.14, 14.02, 21.60, 22.47, 29.48, 29.68, 30.32, 30.71, 31.37, 127.34, 128.03, 129.74, 129.75, 133.93, 135.45, 136.94, 139.37, 144.00, 161.39.

ESI-HRMS: Calculated for $[C_{23}H_{32}O_2SSi]^+$: 400.189. Found: 423.1773, $[M+Na^+]^+$.

IR: 3045, 2955.1, 2928.7, 2854.6, 1595.4, 1315, 1288.6, 1145.7, 817.7, 706.6 cm^{-1}

(*E*)-3-(Dimethyl(phenyl)sily)non-2-enamide



Prepared according to general procedure **A** using 2 equiv of $PhMe_2SiBpin$ and stirring for 6.5 h. The reaction was quenched with 50% sat. aq. $NaHCO_3$, stirred for 10 min and filtered through a short plug of silica. Purification via column chromatography afforded the product in 76.8 mg, 85% isolated yield.

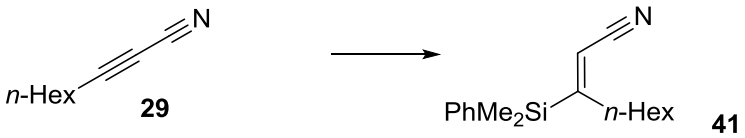
^1H NMR (500 MHz, $CDCl_3$) δ: 0.41 (s, 6H), 0.82-0.85 (t, *J* = 7.0, 3H), 1.17-1.33 (m, 8H), 2.59-2.62 (t, *J* = 7.75 Hz, 2H), 5.41 (s, 1H), 5.48 (s, 1H), 6.00 (s, 1H), 7.34-7.38 (m, 3H), 4.49-7.51 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.05, 14.05, 22.54, 29.71, 29.84, 31.40, 31.48, 127.88, 129.33, 130.08, 134.04, 136.92, 159.34, 168.14.

ESI-HRMS: Calculated for $[C_{17}H_{27}NOSi]$: 289.186. Found: 312.1747, $[M+Na^+]^+$.

IR: 3482, 3350.5, 3198, 2956, 2929.7, 2856.1, 1662.3, 1630.7, 1604.4, 1246.8, 1115.3, 810.26, 699.81 cm^{-1}

(*E*)-3-(Dimethyl(phenyl)silyl)non-2-enenitrile



Prepared according to general procedure **A**. The reaction was filtered through a short plug of silica. Purification via column chromatography eluting with 2% ether: hexanes afforded the product in 96% isolated yield.

TLC 2% Et2O/hexanes R_f: 0.26 Stain: I_2, $KMnO_4$.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.45 (s, 6H), 0.85-0.87 (t, *J* = 7.0 Hz, 3H), 1.16-1.30 (m, 6H), 1.31-1.38 (m, 2H), 2.47-2.50 (t, *J* = 7.75 Hz, 2H), 5.50 (s, 1H), 7.37-7.46 (m, 3H), 7.46-7.49 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: -3.36, 14.01, 22.46, 29.12, 29.25, 31.37, 35.29, 107.74, 115.96, 128.14, 129.87, 133.92, 135.19, 171.81.

ESI-HRMS: Calculated for $[C_{17}H_{25}NSi]^+$: 271.176. Found: 294.1643, $[M+Na^+]^+$.

IR: 3071.7, 2956, 2929.7, 2861.4, 2214.5, 1467.7, 1430.9, 1252, 1115.3, 815.52, 778.7, 736.63, 699.81, 478.93 cm^{-1}

(*E*)-5-(Dimethyl(phenyl)silyl)-1-phenylundec-4-en-3-one

Prepared according to general procedure **C**.

TLC: 20% Et_2O/hexanes R_f: 0.69, blue spots when staining with *p*-anisaldehyde. Starting material stains brown.

Flash chromatography gradient elution with 0-2% Et_2O/hexanes yielded 91% of (*E*)-5-(dimethyl(phenyl)silyl)-1-phenylundec-4-en-3-one as a clear oil in a 17:1 E/Z ratio as determined according to relative integrations of vinyl protons, providing sample was worked up, purified, and analyzed immediately, as the product was observed to isomerize over time.

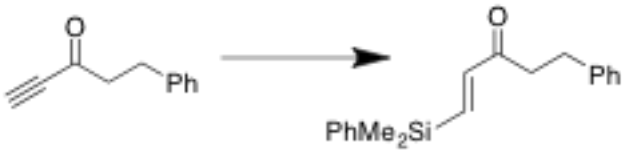
^{1}H NMR (500 MHz, CD_2Cl_2) δ: 0.38 (s, 6H), 0.85 (t, *J* = 6 Hz, 3H), 1.18-1.33 (m, 8H), 2.24 (t, *J* = 2 Hz, 2H), 2.69 (t, *J* = 5.5 Hz, 2H), 2.76 (t, *J* = 6 Hz, 2H), 6.38 (s, *Z* (minor) isomer, 0.06H), 6.74 (s, *E* (major) isomer, 1H), 7.07-7.37 (m, 8H), 7.46-7.51 (m, 2H)

^{13}C NMR (125MHz, CD_2Cl_2) δ: -1.88, 13.88, 22.61, 29.12, 29.65, 29.87, 31.63, 39.21, 44.54, 125.91, 127.36, 128.32, 128.35, 128.37, 133.79, 138.15, 138.15, 139.55, 141.47, 163.28 198.96

IR: 3074, 3026, 2955, 2927, 2856, 1686, 1572, 1497, 1454, 1406, 1361, 1245, 1110, 814, 775, 735, 666, 559, 473 cm^{-1}

EI-HRMS: Calcd. For $C_{25}H_{34}OSi$: 378.2379. Found: 363.2143 $(M-CH_3)^+$

(*E*)-1-(Dimethyl(phenyl)silyl)-5-phenylpent-1-en-3-one



In a 3 ml flame-dried microwave vial under argon, copper(I) acetate (0.25 mg, 2%) and tris(*p*-fluoro-triphenylphosphine) (0.65 mg, 2%) were stirred for 30 min in THF (0.1 ml), after which a vent needle was inserted and the THF was allowed to evaporate over 1 h. TPGS-750-M was immediately added to the vial followed by 5-phenylpent-1-yn-3-one (31.6 mg, 0.2 mmol, 2 equiv) and $PhMe_2SiBpin$ (26.22 mg, 0.1 mmol, 1 equiv) both added dropwise. The resulting mixture was allowed to stir for 1 h. It was then diluted with Et_2O and filtered through a pad of silica. The product was purified by flash chromatography (0.5-2% Et_2O/hexanes), yielding 18 mg of **43** (61%) as a colorless oil. *J* coupling of 14 Hz for vinyl protons confirms product is only the *E* isomer.

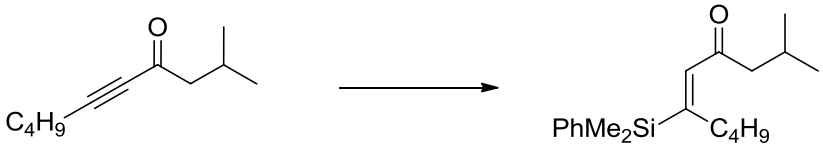
^{1}H NMR (500 MHz, CD_2Cl_2) δ: 0.45 (s, 6H), 2.83 (t, 2H), 2.91 (t, 2H), 6.54 (d, *J* = 14 Hz, 1H), 6.97 (d, *J* = 14 Hz, 1H), 7.12-7.59 (m, 10H)

^{13}C NMR (125MHz, CD_2Cl_2) δ: 200.0, 148.8, 142.3, 141.1, 139.7, 133.8, 128.9, 128.6, 128.5, 127.8, 126.2, 44.8, 30.5, 29.9.

IR: 3067, 3026, 2954, 2083, 1694, 1603, 1578, 1427, 1372, 1245, 1111, 1096, 817, 696 cm^{-1}

EI-HRMS Calcd. for $C_{19}H_{22}OSi$: 294.1440, Found: 279.1201 $(M-CH_3)^+$

***(E)*-6-(Dimethyl(phenyl)silyl)-2-methyldec-5-en-4-one**



Prepared according to General Procedure **A** using BDP in place of PPh_3 as the ligand. The metal and ligand were stirred at rt for 10 min and then placed in an ice bath and stirred for an additional 5 min. Substrate **32** (1 equiv) and $PhMe_2SiBpin$ (1.25 equiv) was then added stirred at 0 ^oC for 1 h. The reaction was removed from the cooling bath and allowed to warm to rt and monitored by TLC until completion.

Flash chromatography with 1% Et_2O/hexanes yielded 85% of **44** as a colorless oil (*E*/*Z* 8.14:1).

TLC: 1% Et_2O/hexanes R_f: 0.28

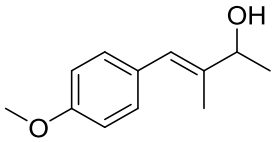
^1H NMR (500 MHz, $CDCl_3$) δ: 0.45 (s, 6H), 0.82-0.85 (m, 9H), 1.19-1.35 (m, 4H), 1.19-1.35 (m, 1H), 2.22-2.26 (m, 4H), 6.37 (s, *Z* (minor) isomer, 0.12H), 6.71-6.72 (s, *E* (major) isomer, 1H), 7.28-7.38 (m, 3H), 7.49-7.53 (m, 2H)

^{13}C NMR (125 MHz, $CDCl_3$) δ: -2.99, -1.64, 13.95, 22.62, 22.71, 25.15, 31.93, 31.98, 39.10, 52.25, 53.47, 127.48, 128.02, 128.49, 129.49, 133.96, 134.17, 135.66, 138.52, 139.55, 163.83, 200.0.

IR: 3069, 2956, 2930, 2871, 1684, 1571, 1465, 1427, 1404, 1365, 1244, 1153, 1109, 1062, 1030, 998, 815, 775, 735, 700, 666 cm^{-1}

EI-HRMS Calcd. For $C_{19}H_{30}OSi$: 302.2066. Found: 287.1840 $(M\text{-}CH_3)^+$

(*E*)-4-(4-Methoxyphenyl)-3-methylbut-3-en-2-ol



Prepared according to the General Procedure.

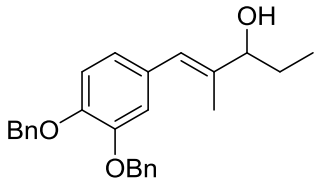
^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.35-1.36 (d, 3H), 1.87-1.88 (m, 3H), 3.81 (s, 3H), 4.35-4.39 (q, 1H), 6.45 (s, 1H), 6.87-6.88 (m, 2H), 7.21-7.26 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 13.5, 21.9, 55.4, 74.0, 114.7, 124.2, 130.2, 130.3, 140.0, 158.3.

EI-HRMS: Calcd. For $C_{12}H_{16}O_2$ $(M)^+$ 192.1150. Found: 192.1155

HPLC separation conditions CHIRALCEL AD-H, 244 nm, 5% IPA/hexane, 1 mL/min, t_R = 12.97 and 14.39 min, 84 % ee.

(*E*)-1-(3,4-bis(Benzyloxy)phenyl)-2-methylpent-1-en-3-ol



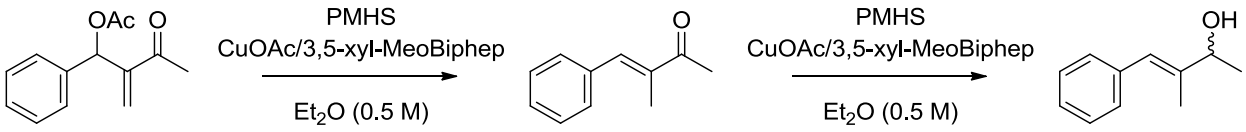
Prepared according to the General Procedure.

EI-HRMS: Calcd. For $C_{26}H_{28}O_3$ $(M)^+$: 388.2038. Found: 388.2038

HPLC separation conditions: Phenomenex Lux 5u Cellulose-2, 257 nm, 5% IPA/hexanes,

0.7 mL/min, t_R = 52.85 and 88.04 min, 99 % ee.

(*E*)-3-Methyl-4-phenylbut-3-en-2-ol



Prepared according to the General Procedure.

TLC: 30% EtOAc/hexanes R_f: 0.3

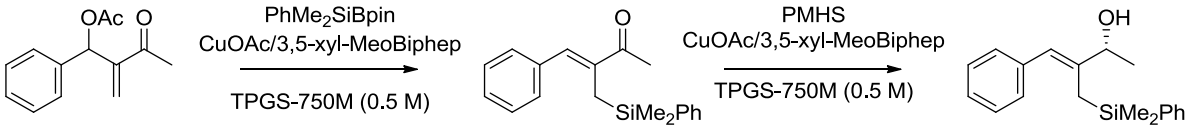
Flash chromatography eluting with 30% Et_2O/hexanes yielded as a colorless oil.

^1H NMR (500 MHz, $CDCl_3$) δ: 1.37-1.38 (d, 3H), 1.59 (s, 1H), 1.89 (s, 3H), 4.37-4.41 (q, 1H), 6.52 (s, 1H), 7.20-7.23 (m, 1H), 7.27-7.35 (m, 4H).

Spectra matches that of previously reported.[27]

HPLC separation conditions CHIRALCEL OD-H, 254 nm, 5% IPA/hexanes, 0.9 mL/min, t_R = 9.42 and 10.67 min, 93% ee.

(Z)-3-((Dimethyl(phenyl)silyl)methyl)-4-phenylbut-3-en-2-ol



Prepared according to the General Procedure.

TLC: 30% EtOAc/hexanes R_f = 0.24

Flash chromatography eluting with 30% Et_2O/hexanes yielded as a colorless oil.

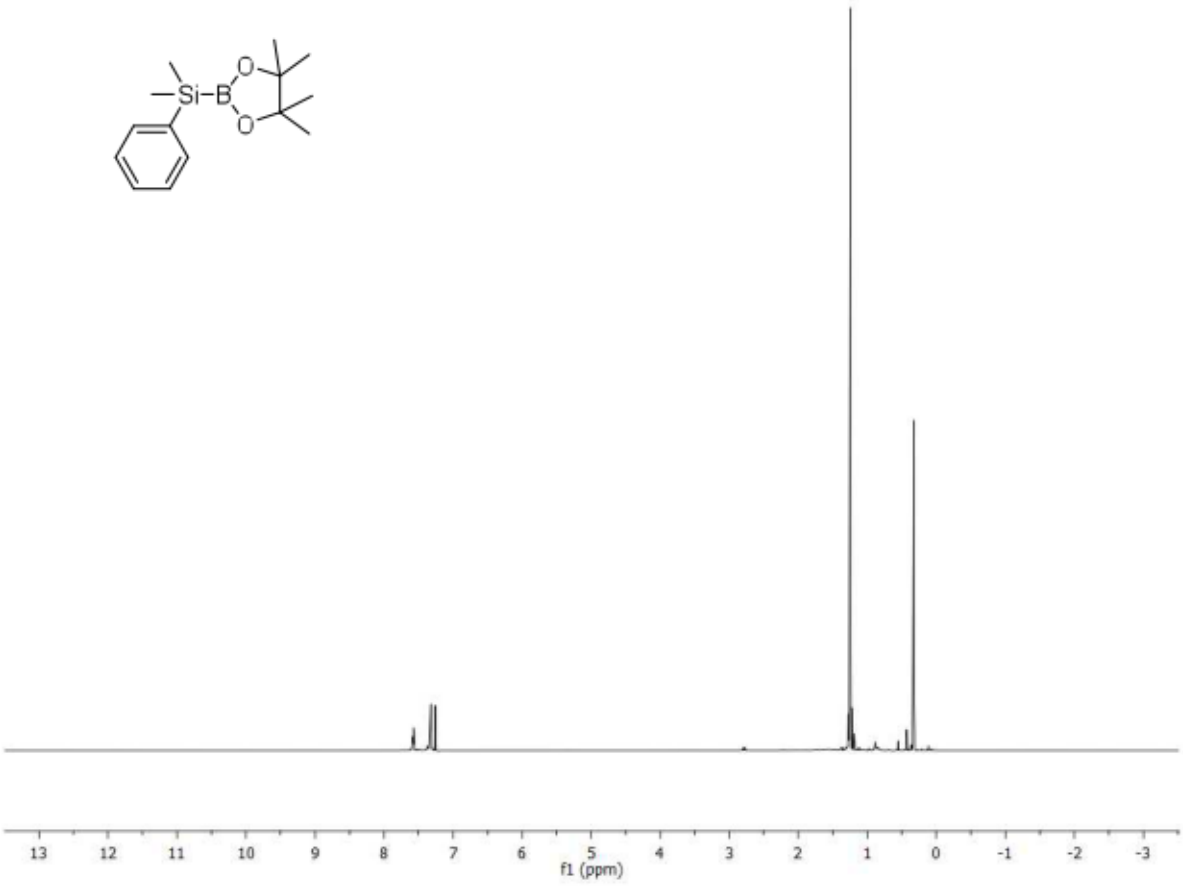
^1H NMR (500 MHz, $CDCl_3$) δ: 0.21-0.22 (d, 6H), 1.28-1.29 (d, 3H), 1.92-1.95 (m, 1H), 2.30-2.34 (m, 1H), 4.07-4.08 (m, 1H), 6.46 (s, 1H), 7.17-7.24 (m, 3H), 7.27-7.35 (m, 5H), 7.44-7.46 (m, 2H).

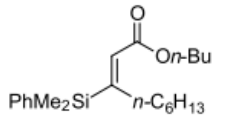
^{13}C NMR (125 MHz, $CDCl_3$) δ: -1.9, -1.8, 18.7, 22.7, 72.7, 121.2, 126.2, 128.0, 128.3, 128.9, 129.3, 133.7, 138.5, 139.2, 144.6.

HPLC separation conditions CHIRALCEL AD-H, 254 nm, 1% IPA/hexanes, 0.8 mL/min, t_R = 16.79 and 18.40 min, 87% ee.

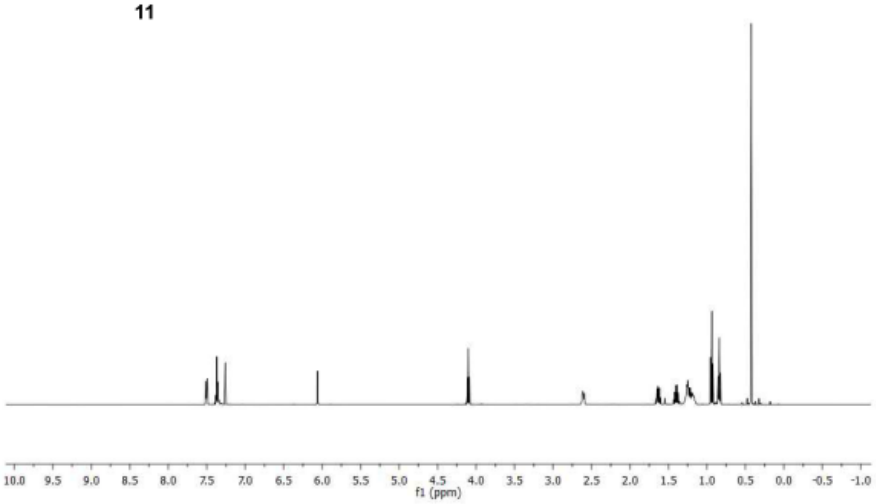
Stereoselective Silylcupration of Conjugated Alkynes in Water at Room Temperature

NMR Spectra:




O
On-Bu
PhMe2Si
n-C6H13

11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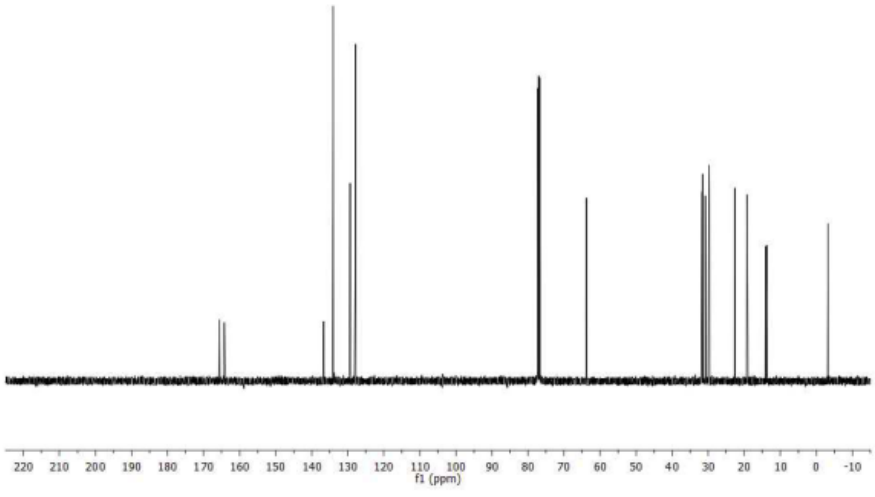
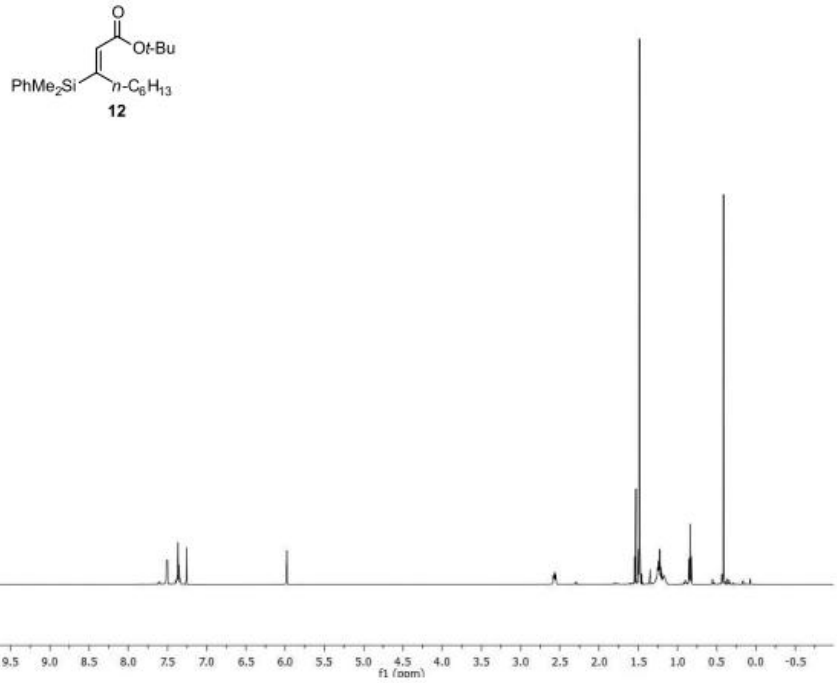
f1 (ppm)


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Ot-Bu
PhMe2Si
n-C6H13
12
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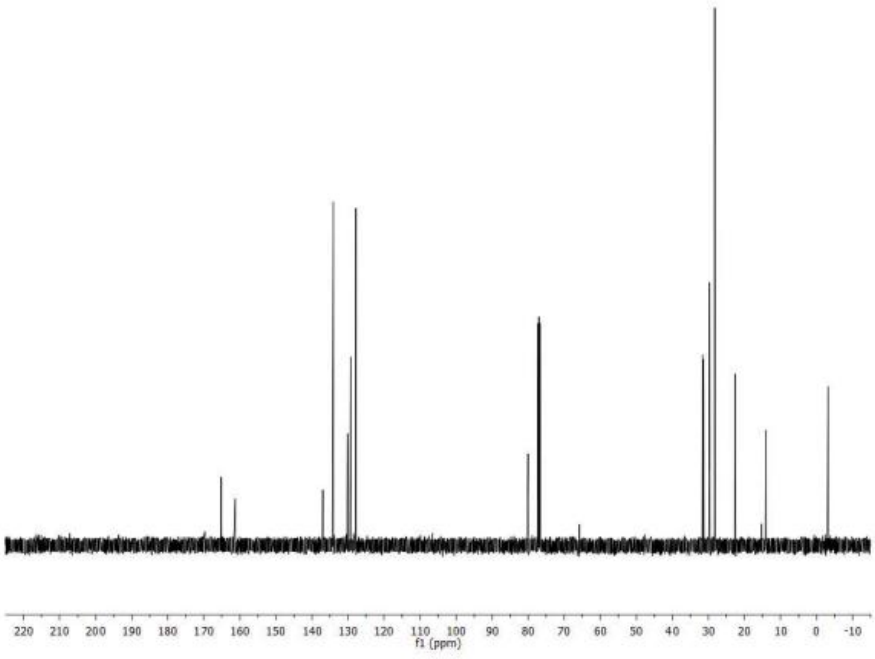
f1 (ppm)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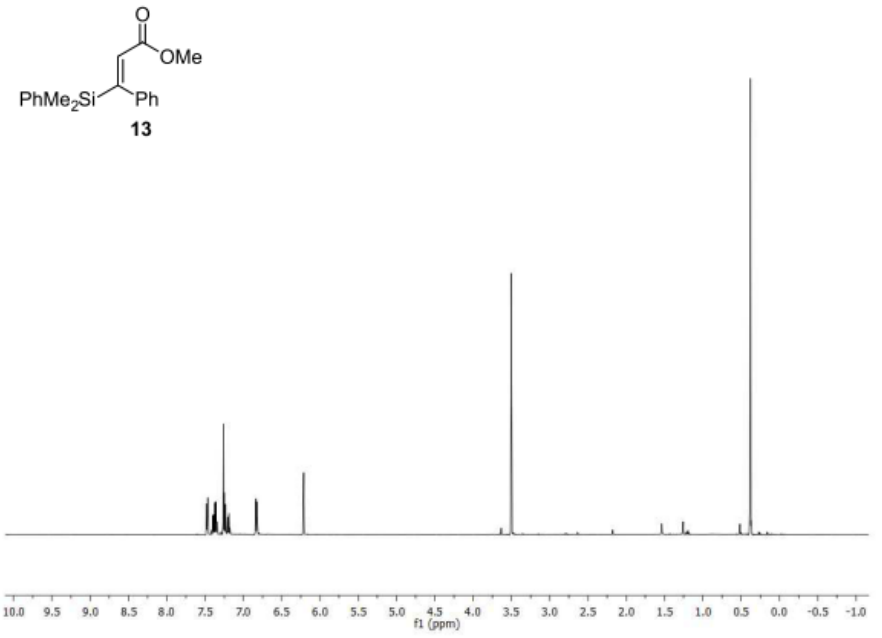
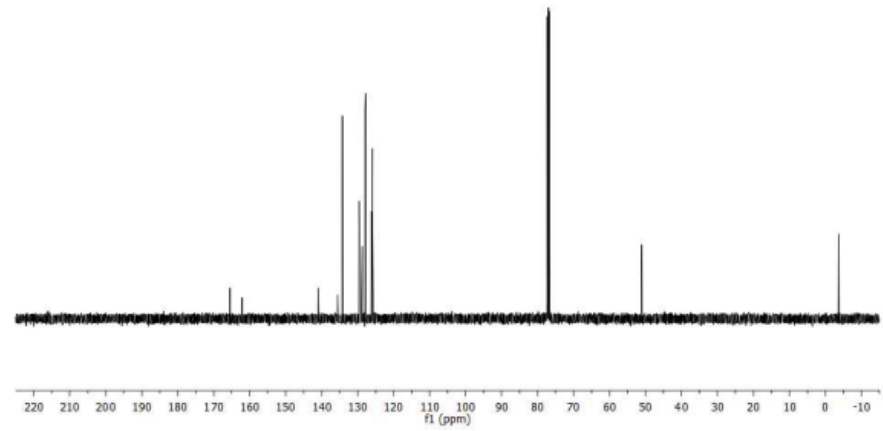
f1 (ppm)


O
OMe
PhMe2Si
Ph
13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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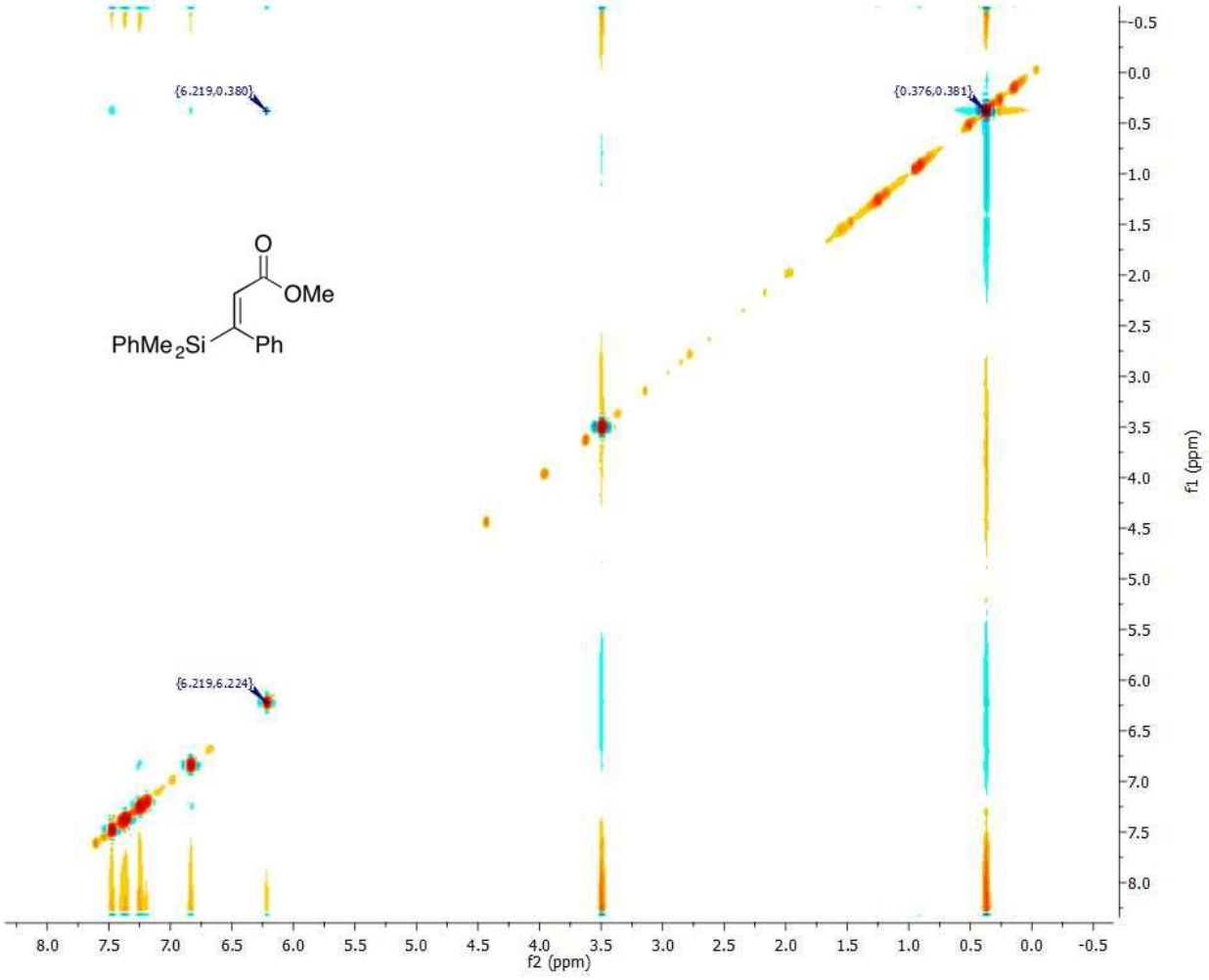
f1 (ppm)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{0.376,0.381}
{6.219,6.224}
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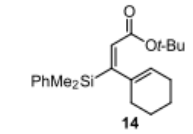
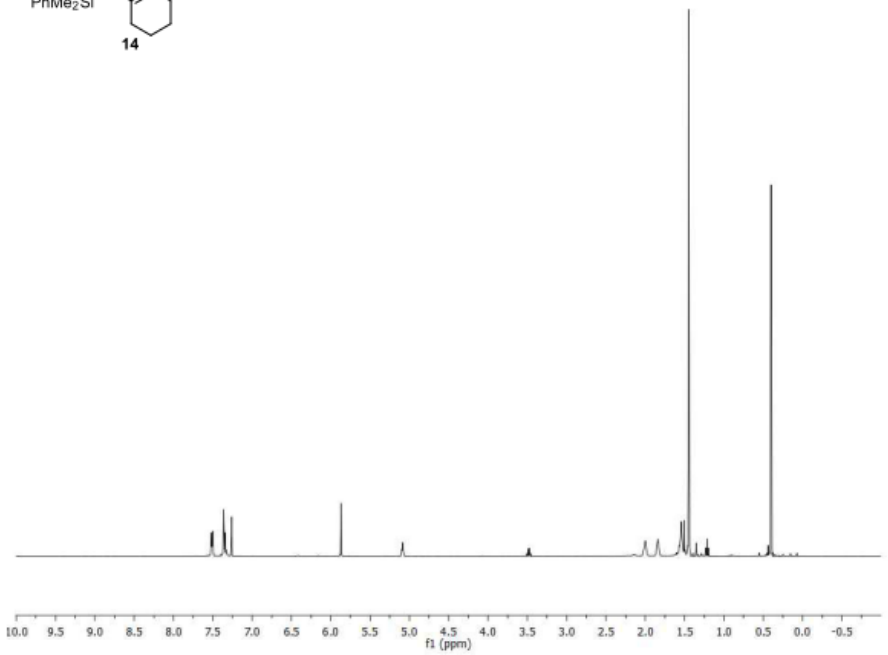
OMe
PhMe2Si
Ph
f2 (ppm)
f1 (ppm)


O
Ot-Bu
PhMe2Si

14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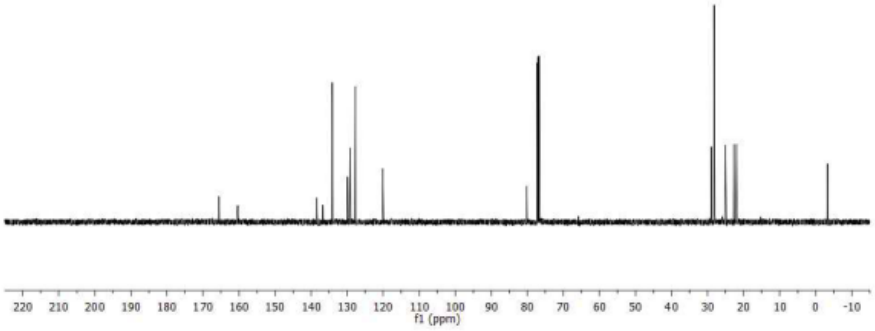
f1 (ppm)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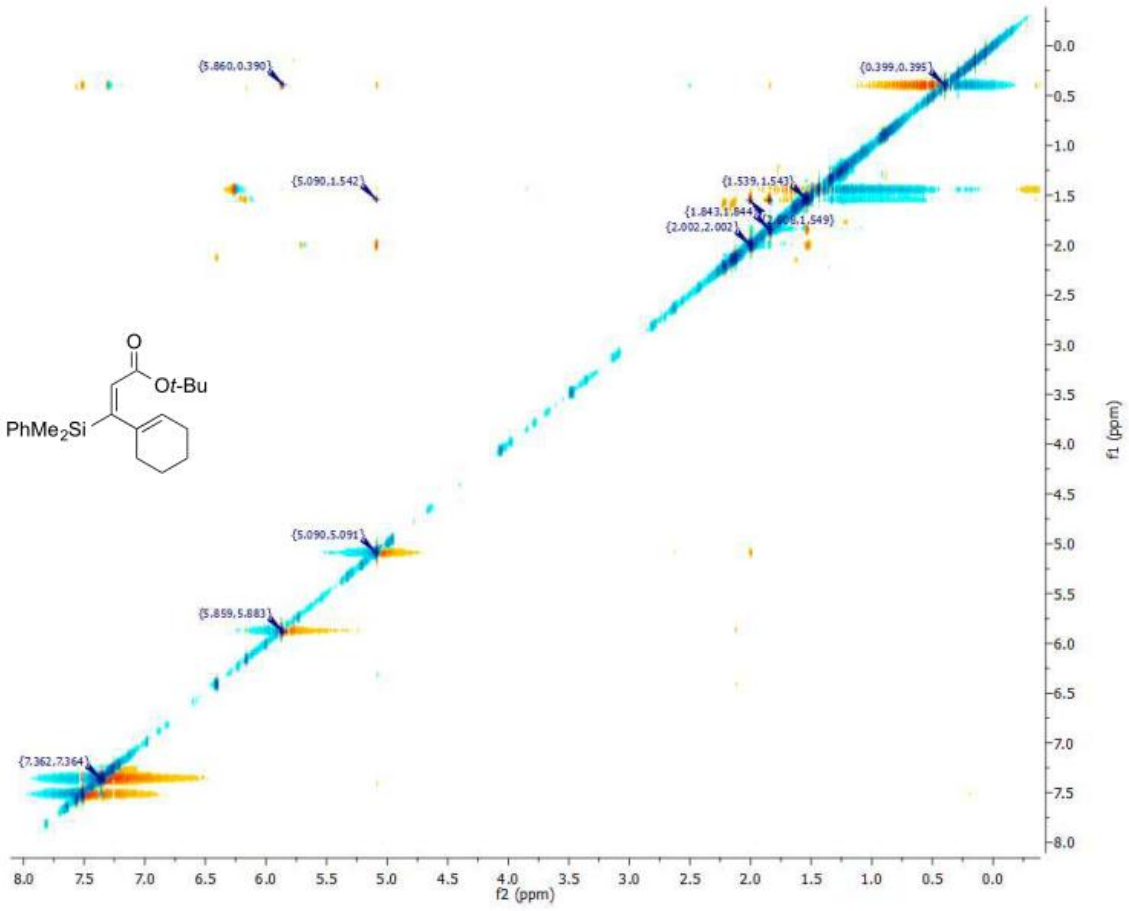
f1 (ppm)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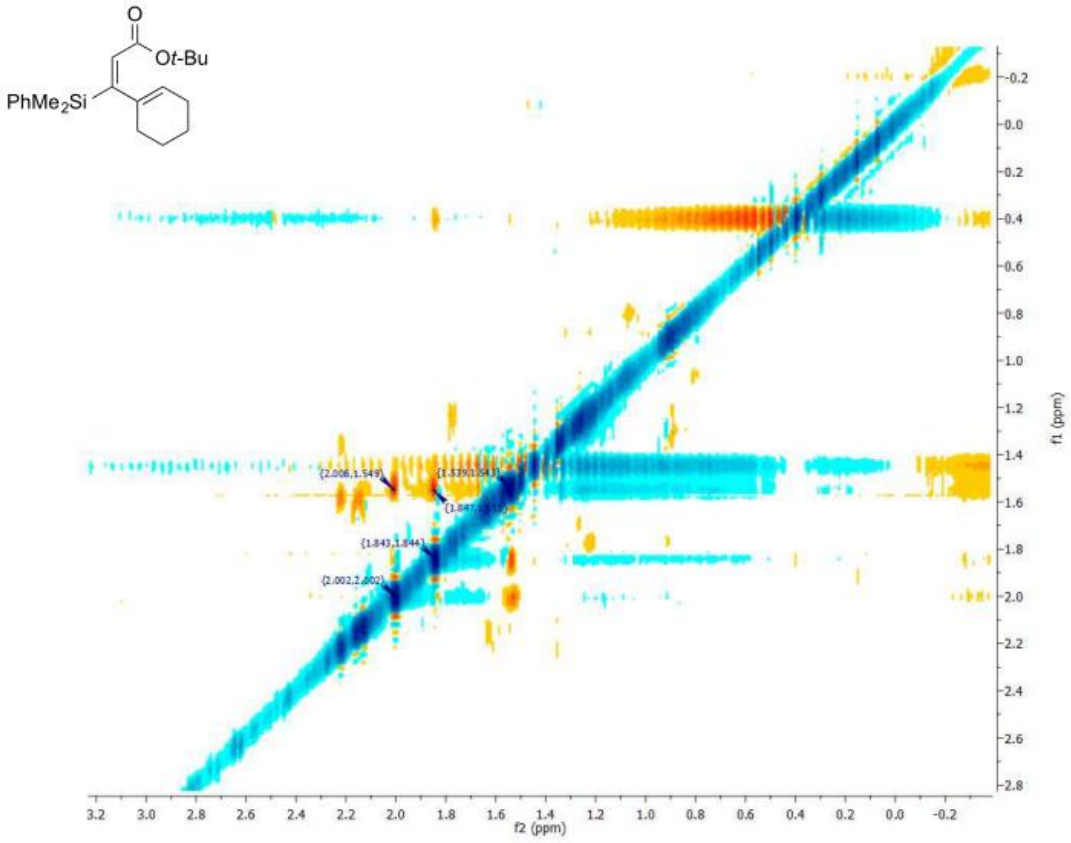
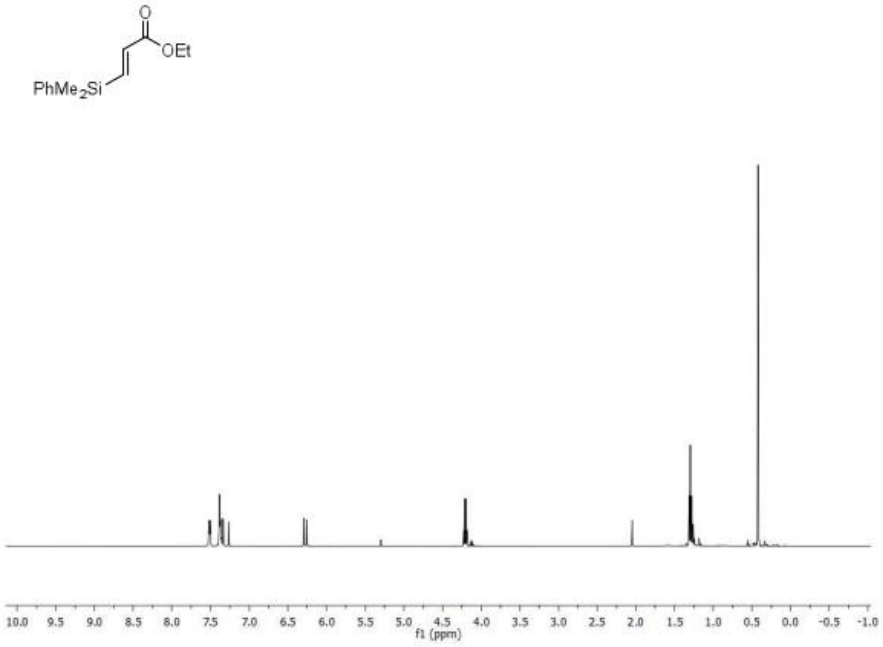
{5.090,1.542}
{1.539,1.543}
{1.843,1.844}
{2.002,2.002}
{1.549,1.549}
O
Ot-Bu
PhMe2Si
{5.090,5.091}
{5.859,5.883}
{7.362,7.364}
f2 (ppm)
f1 (ppm)


O
Ot-Bu
PhMe2Si
f2 (ppm)
f1 (ppm)


O
OEt
PhMe2Si
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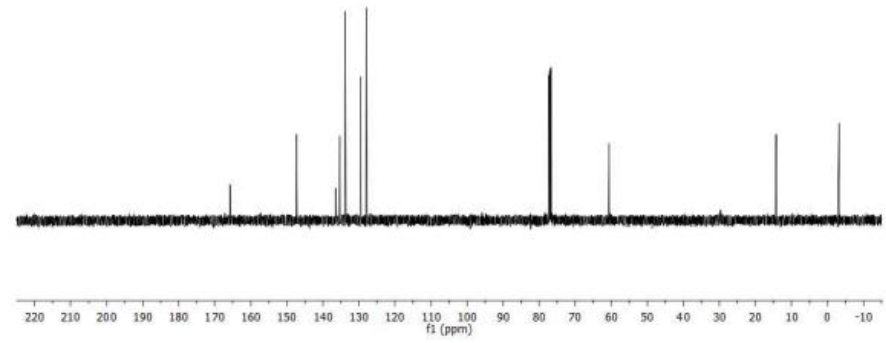
f1 (ppm)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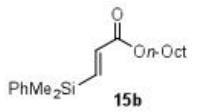
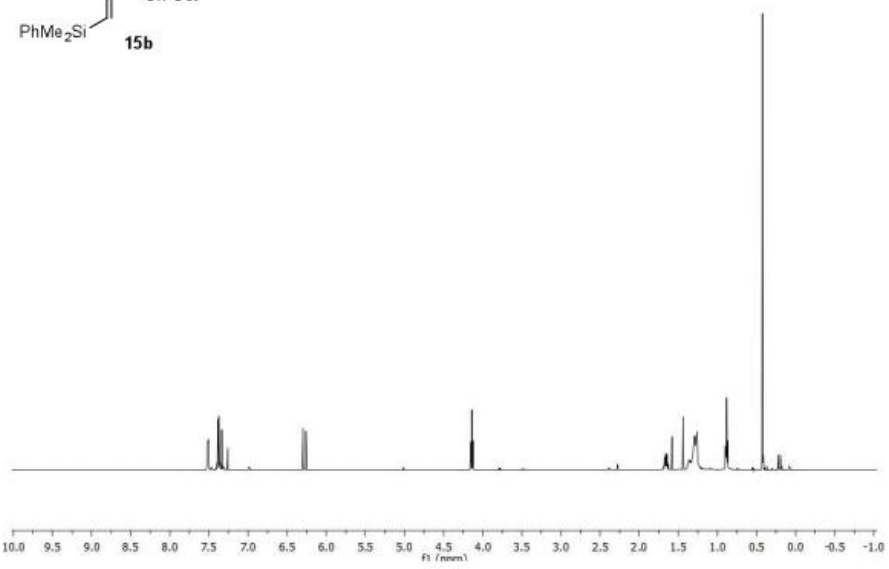
f1 (ppm)


O
On-Oct
PhMe2Si

15b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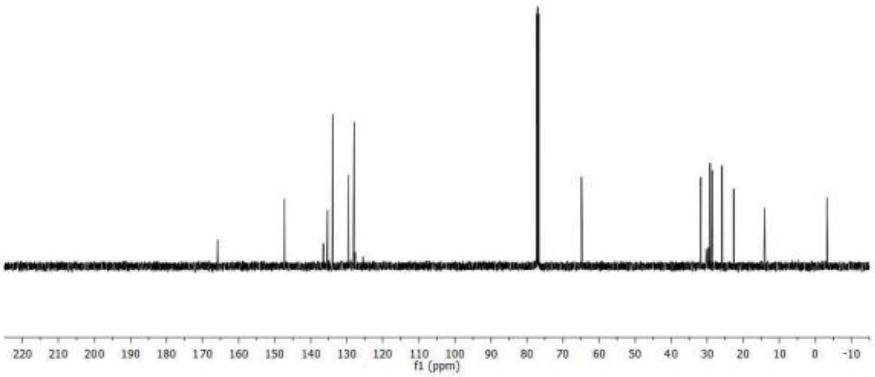
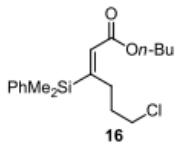
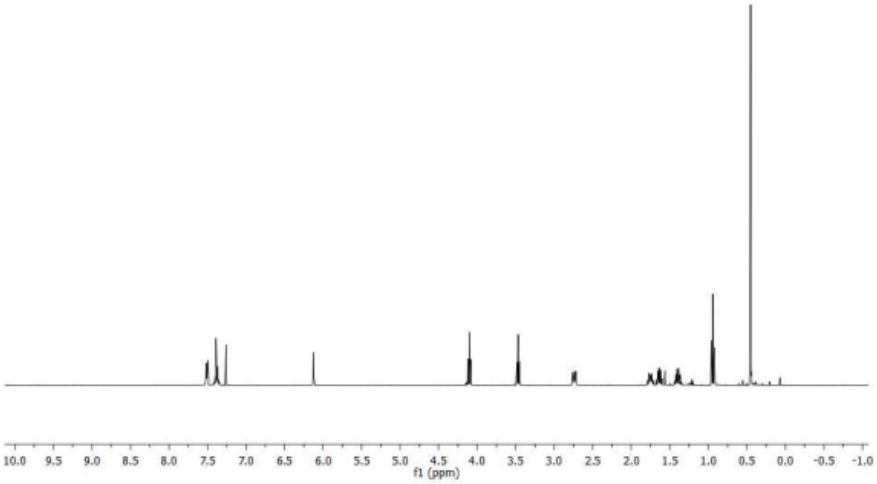
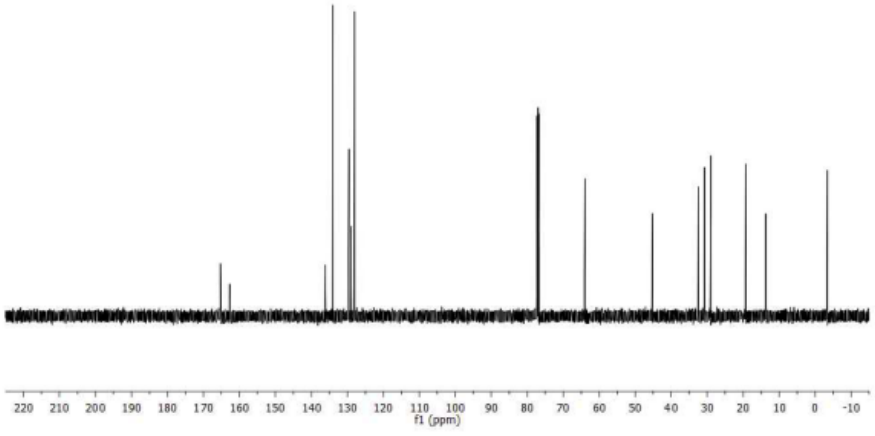
f1 (ppm)

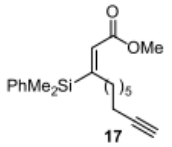

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
On-Bu
PhMe2Si
Cl

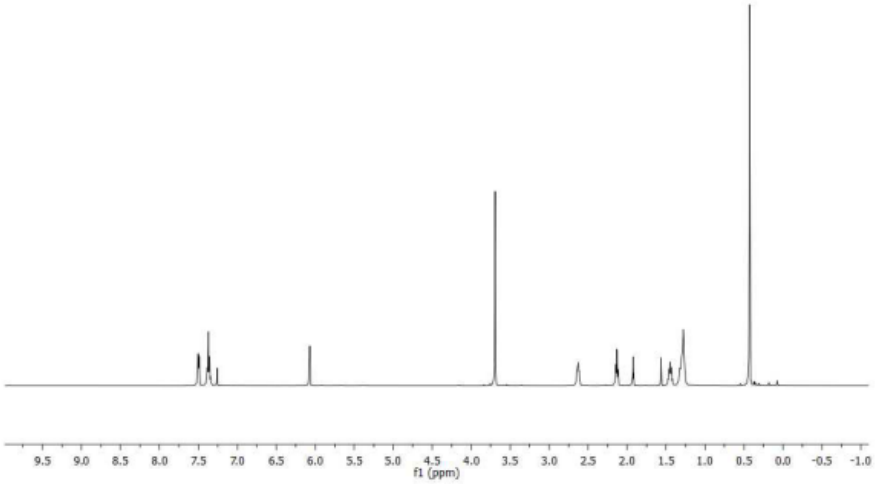
16

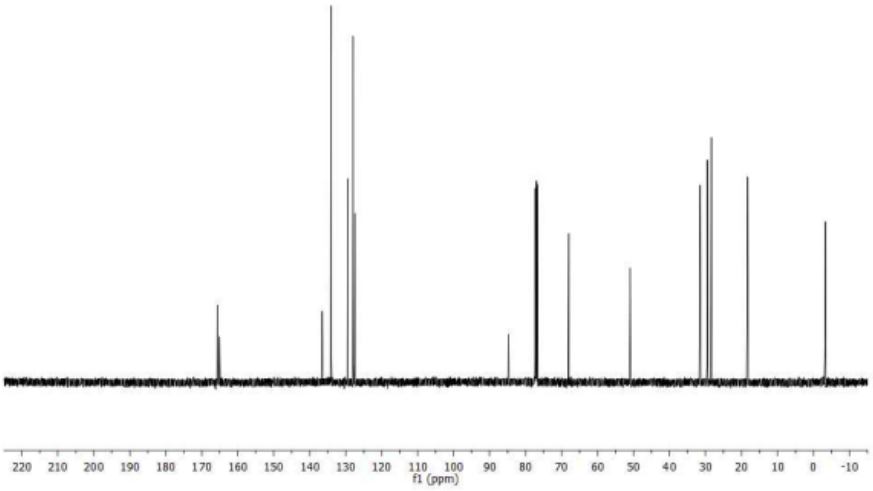

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

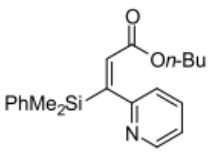

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OMe
PhMe2Si
5

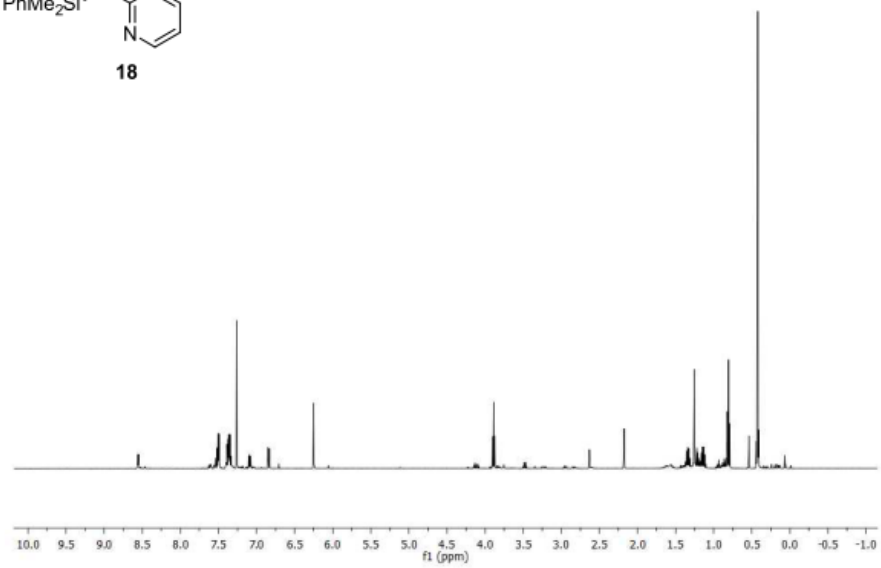
17

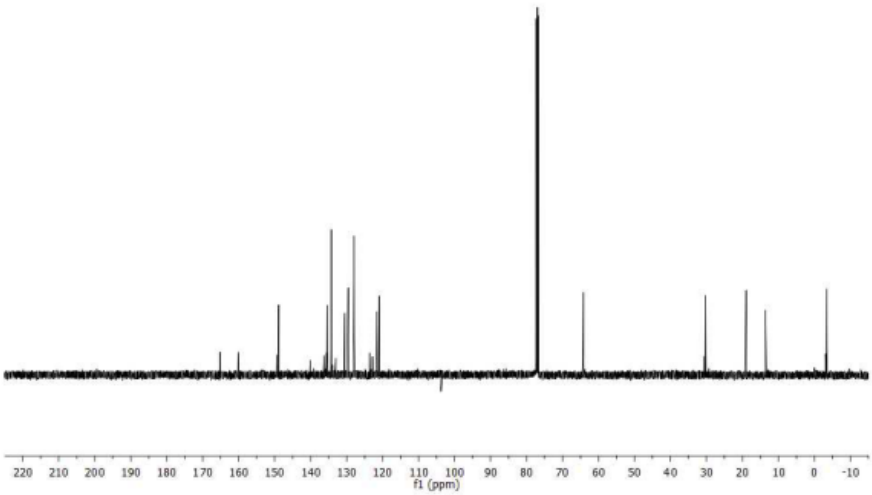

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

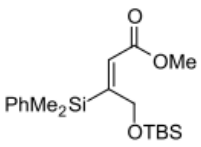

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
On-Bu
PhMe2Si
N

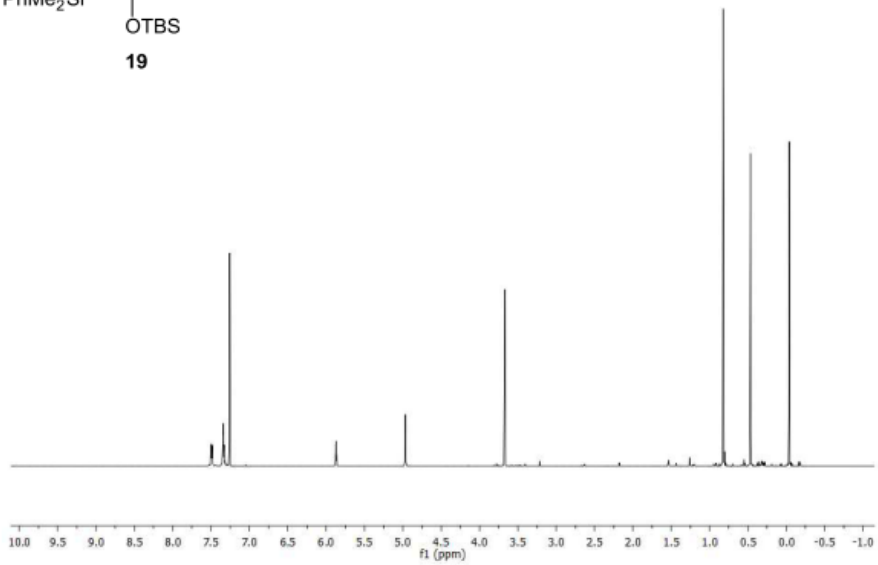
18

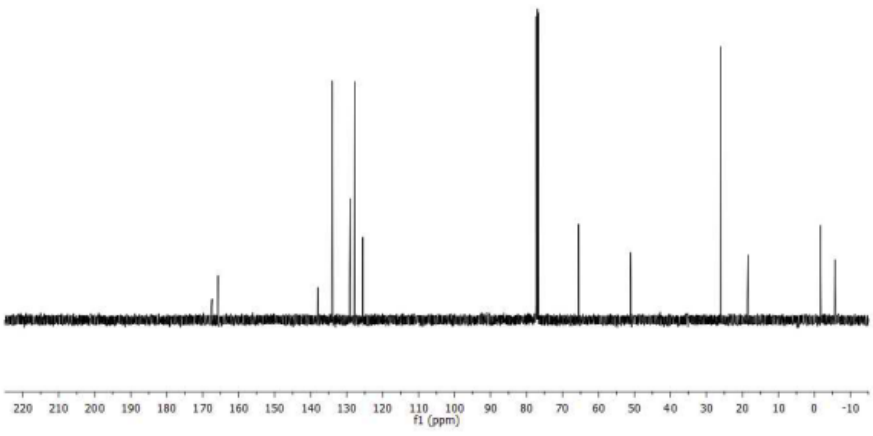

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

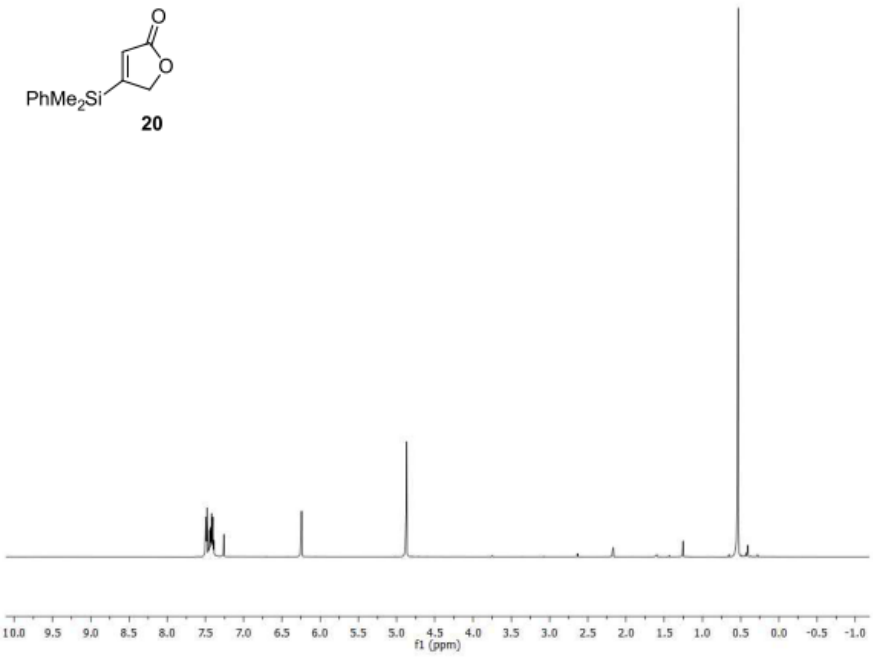

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

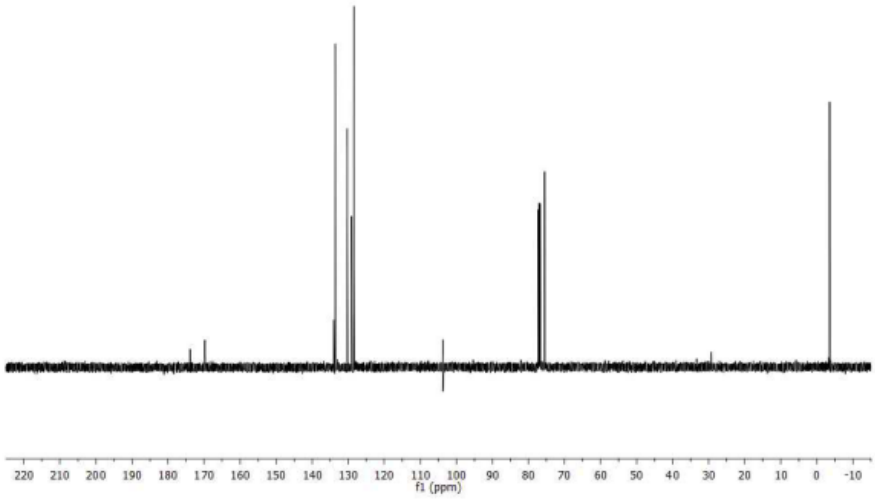

O
OMe
PhMe2Si
OTBS

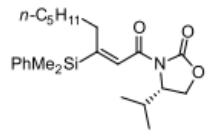
19


10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

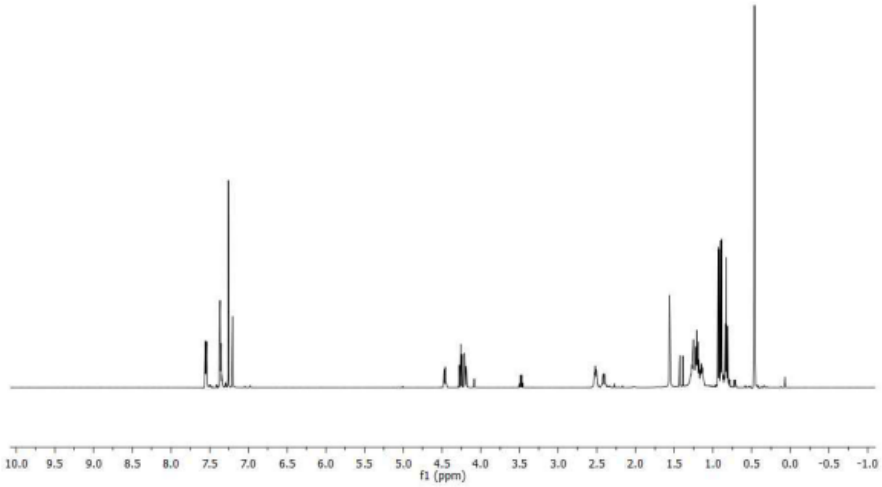

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

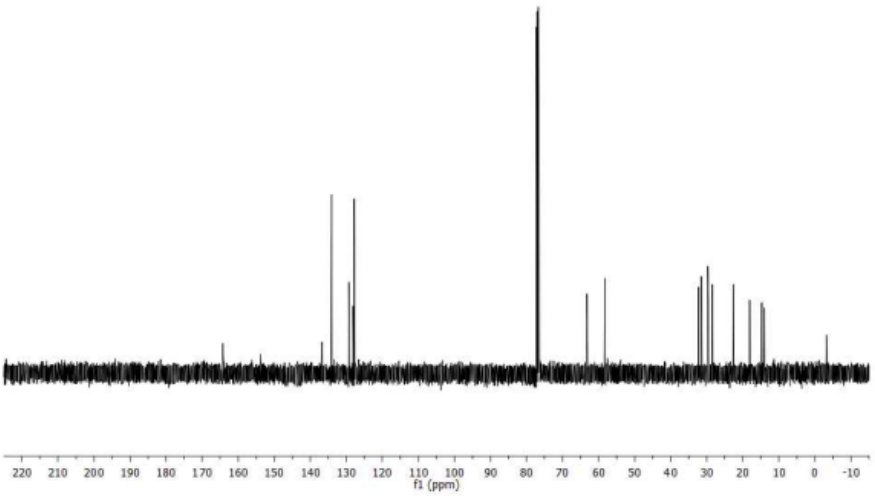

O
O
PhMe2Si
20
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

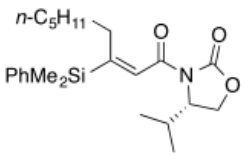

n-C5H11
PhMe2Si
O
O
N
O

(*E*)-33

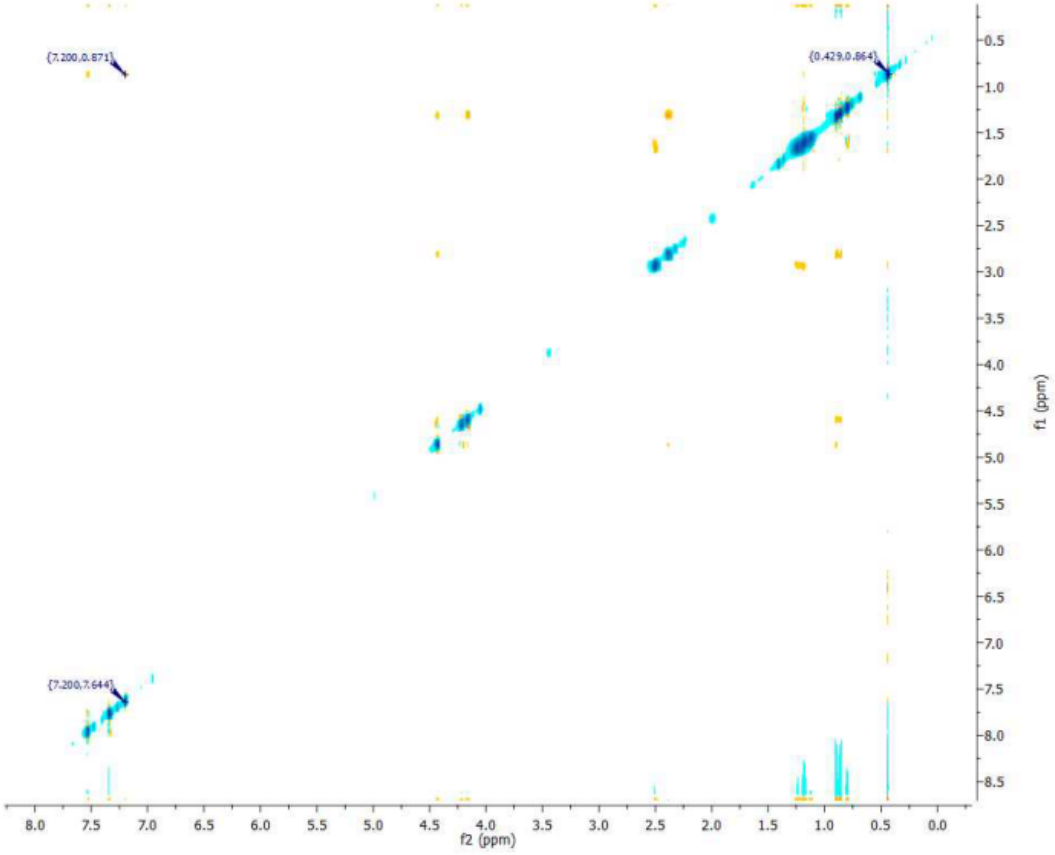

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

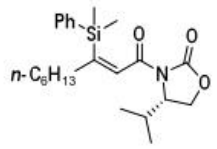

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2D-NOESY 1H-1H 600MHz:

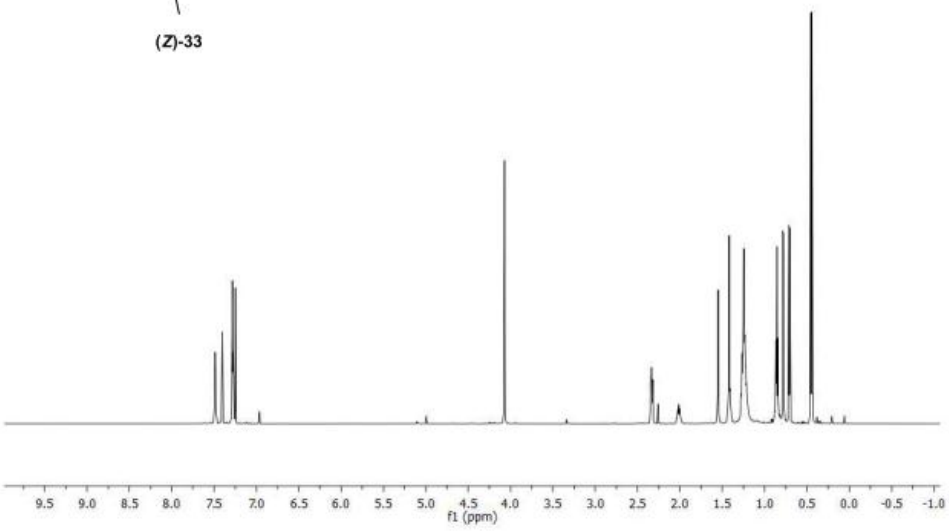


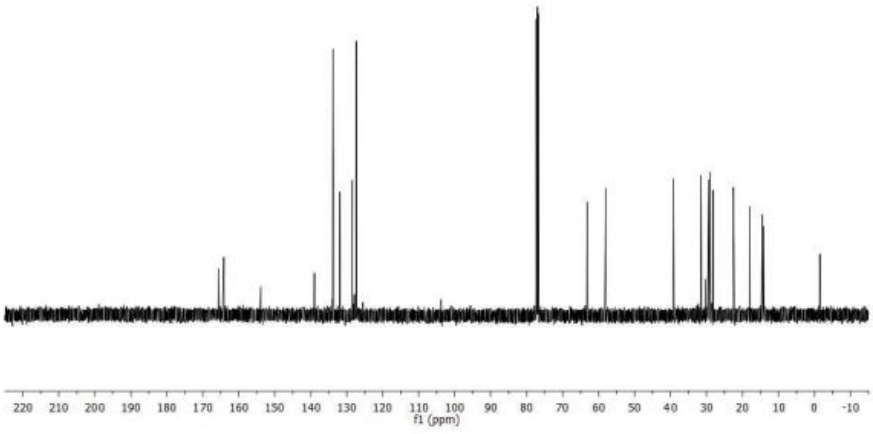
***(E)*-33**



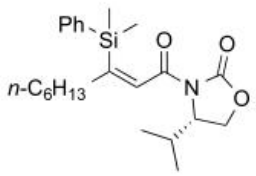

Ph
Si
O
O
N
O
n-C6H13

(*Z*)-33

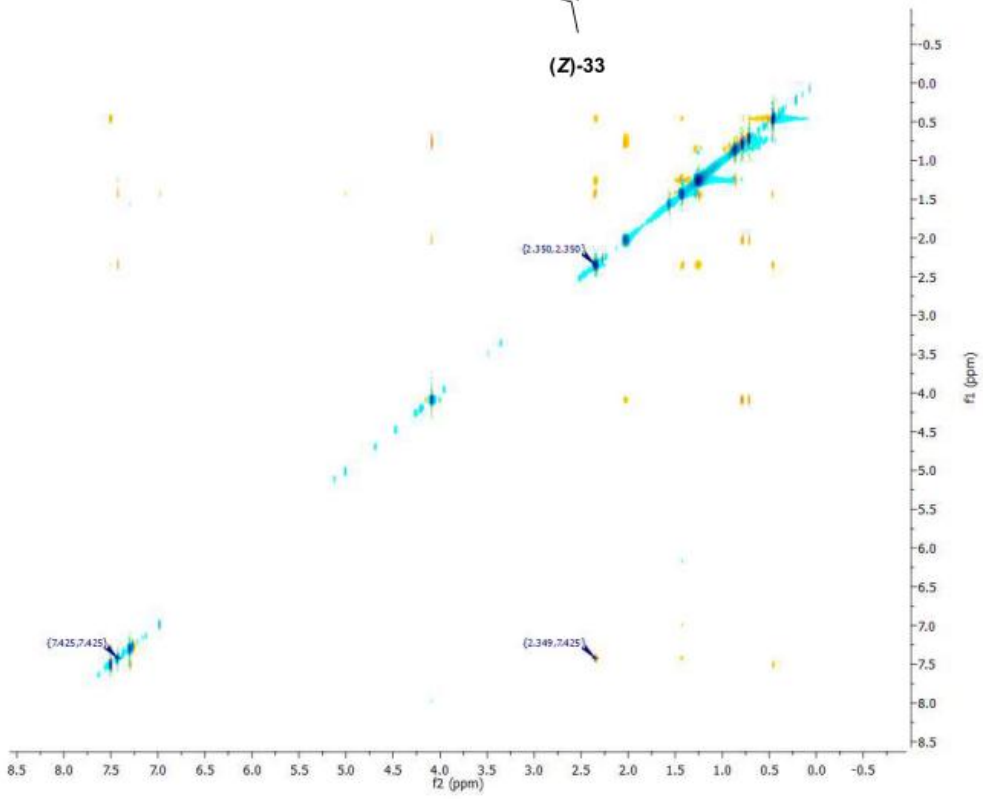

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

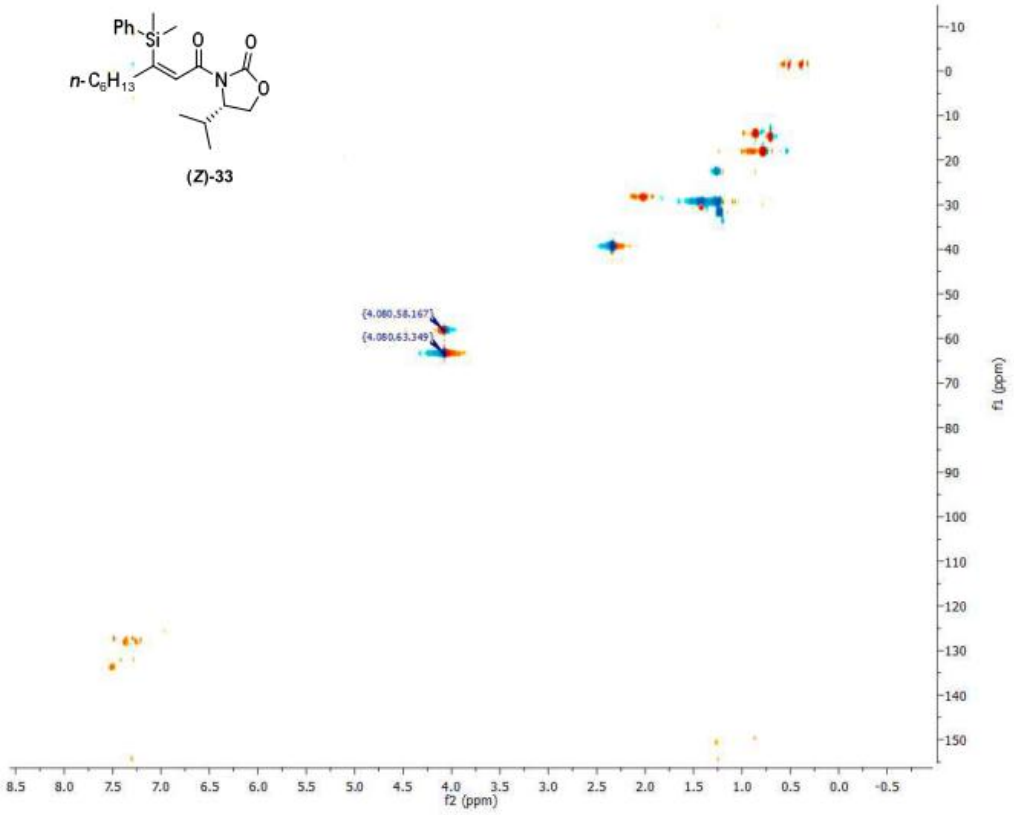

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

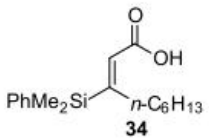
2D NOESY 1H-1H 600MHz:



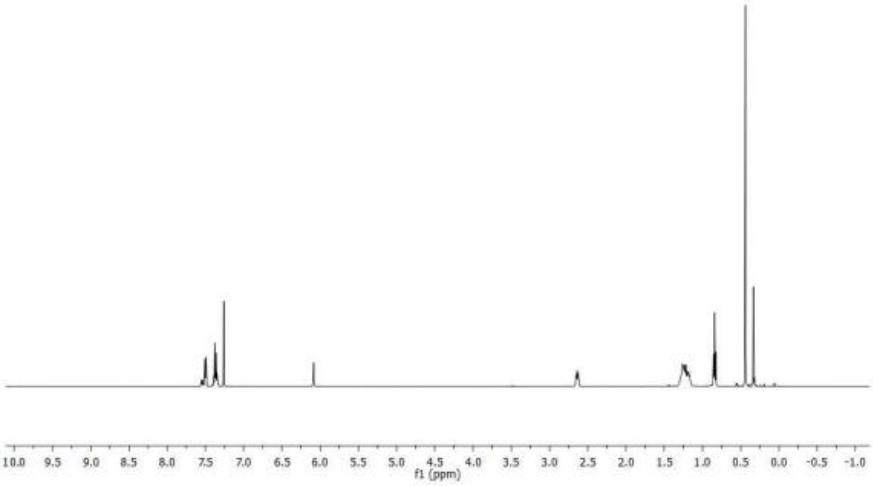
(Z)-33

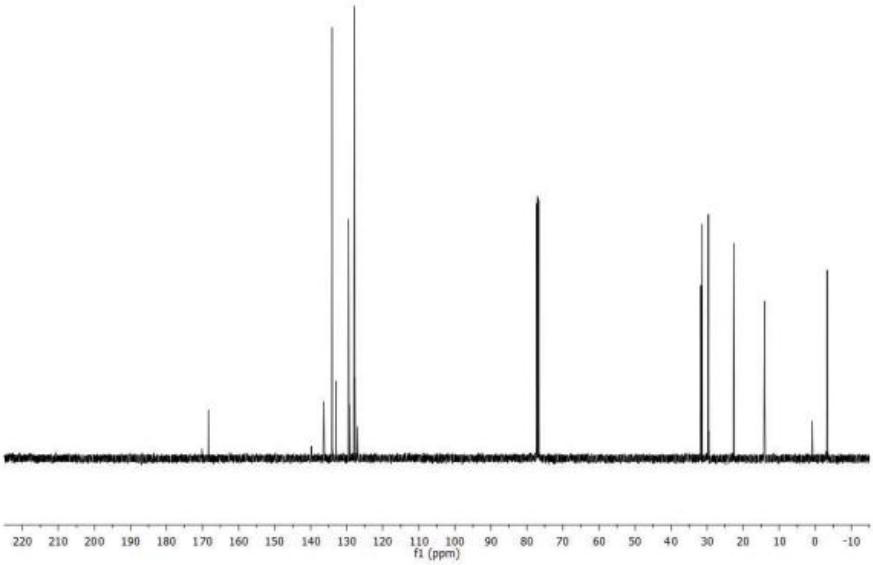


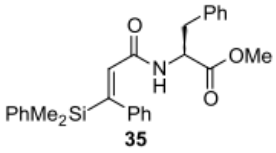

Ph
Si
O
O
N
O
n-C6H13
(Z)-33
{4.080,58.167}
{4.080,63.349}
f1 (ppm)
f2 (ppm)


O
OH
PhMe2Si
n-C6H13

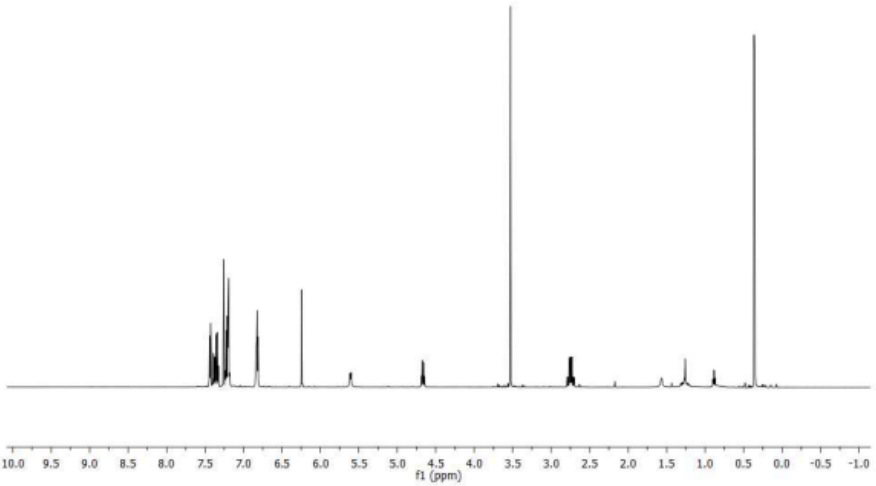
34

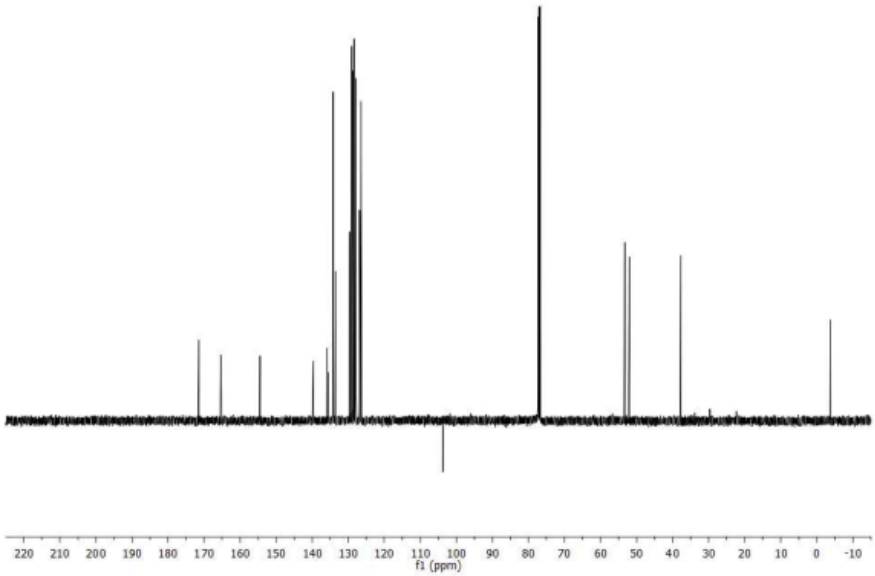

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

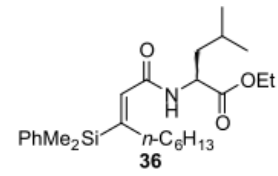

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Ph
O
N
H
OMe
O
PhMe2Si
Ph

35

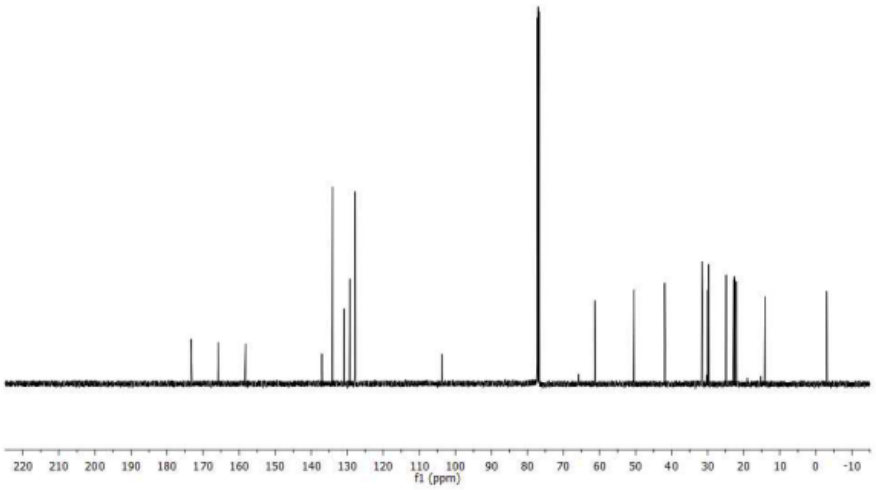

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

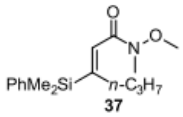

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OEt
O
PhMe2Si
n-C6H13

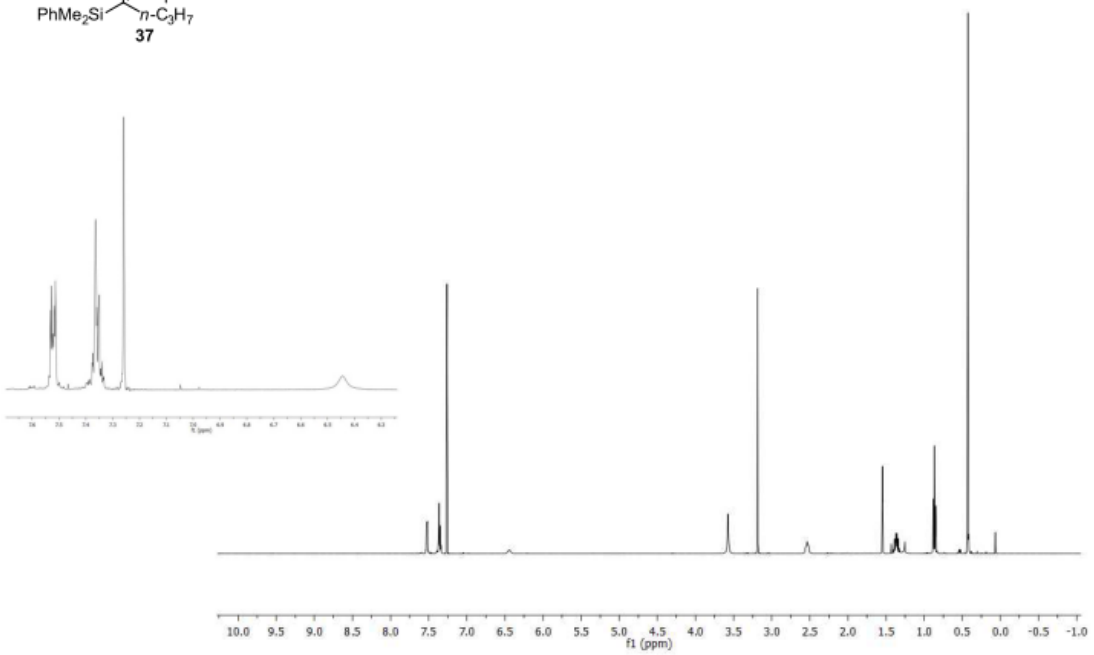
36

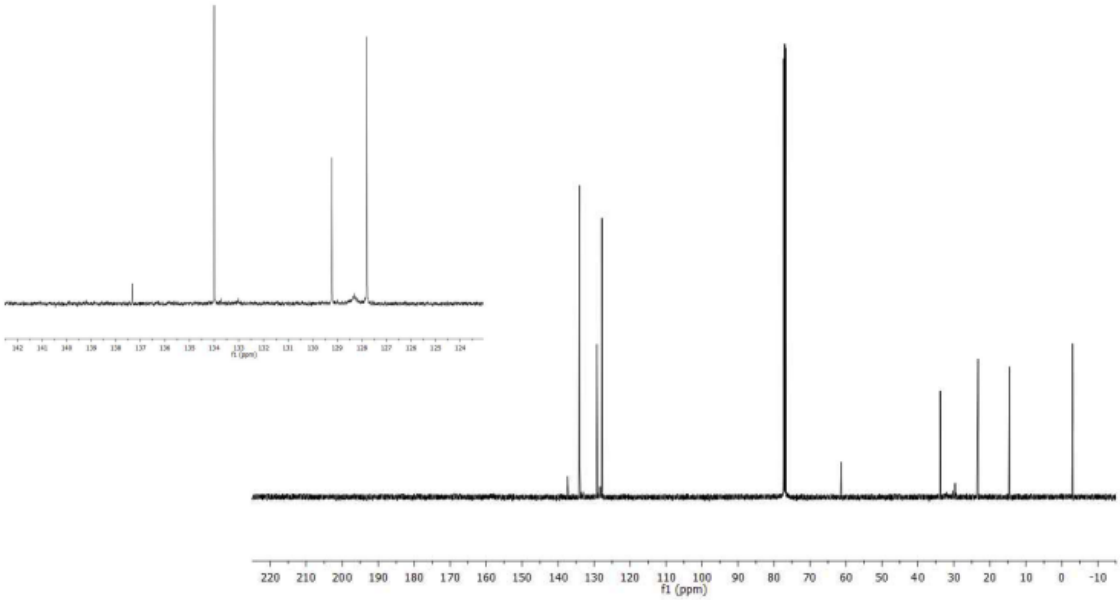
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

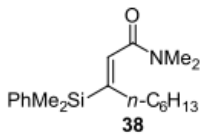

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
O
PhMe2Si
n-C3H7

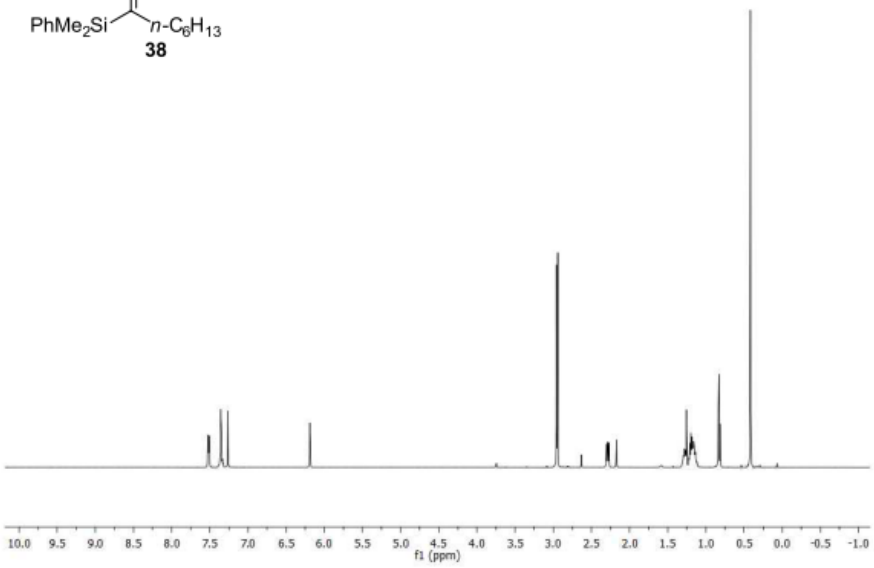
37

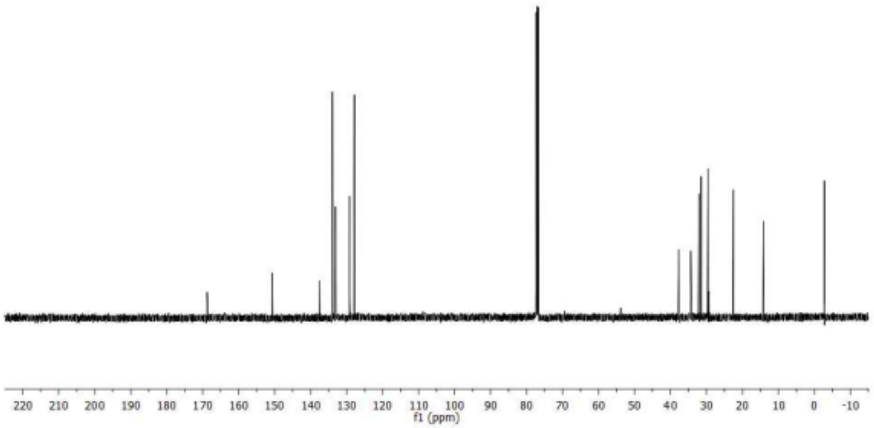

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

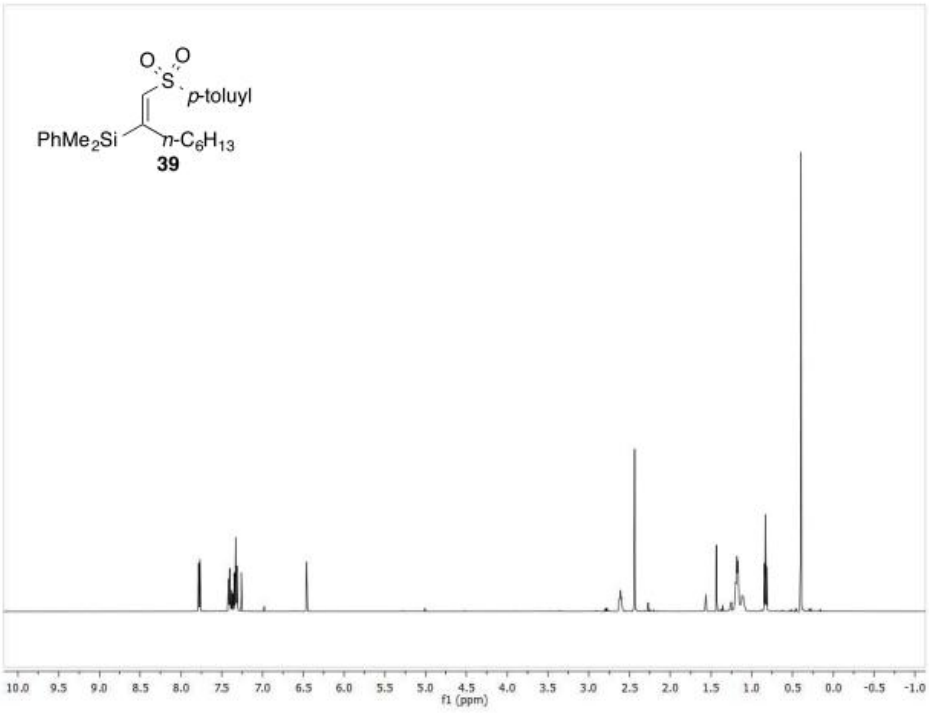

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

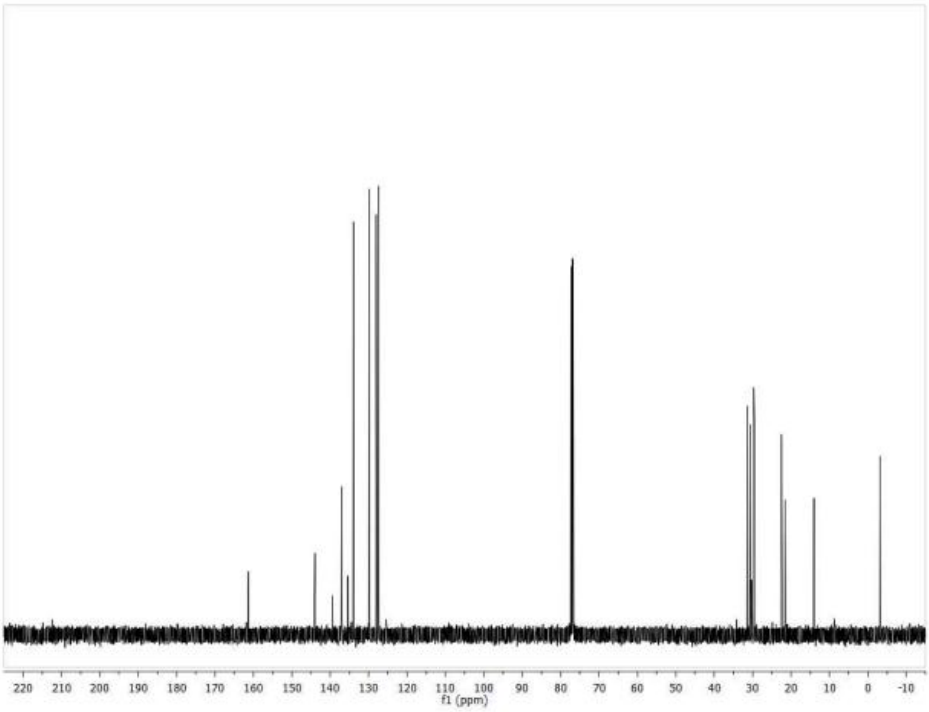

O
NMe2
PhMe2Si
n-C6H13

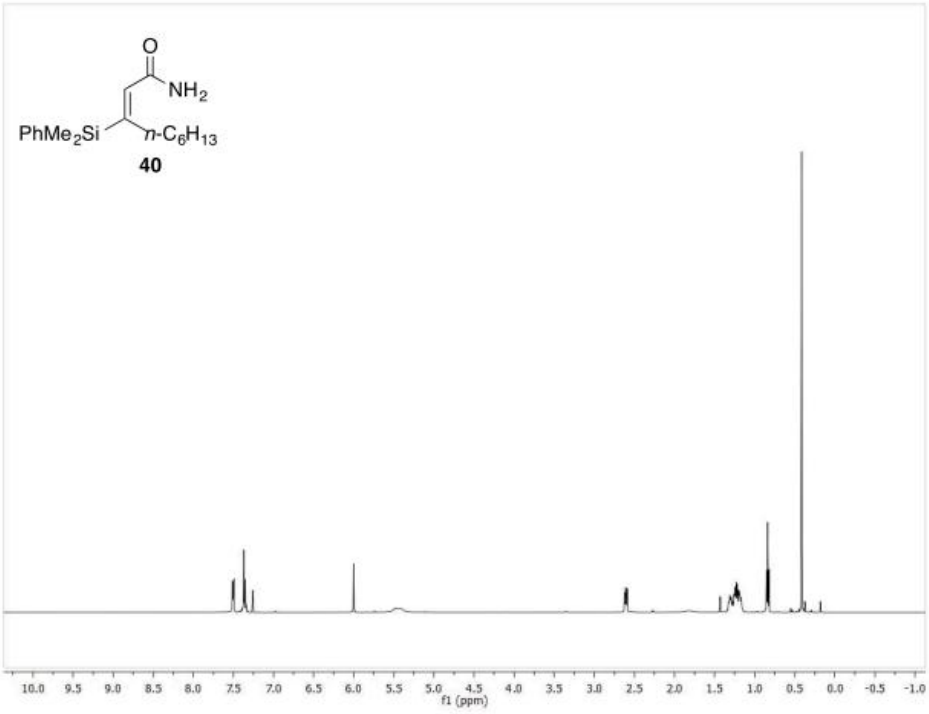
38

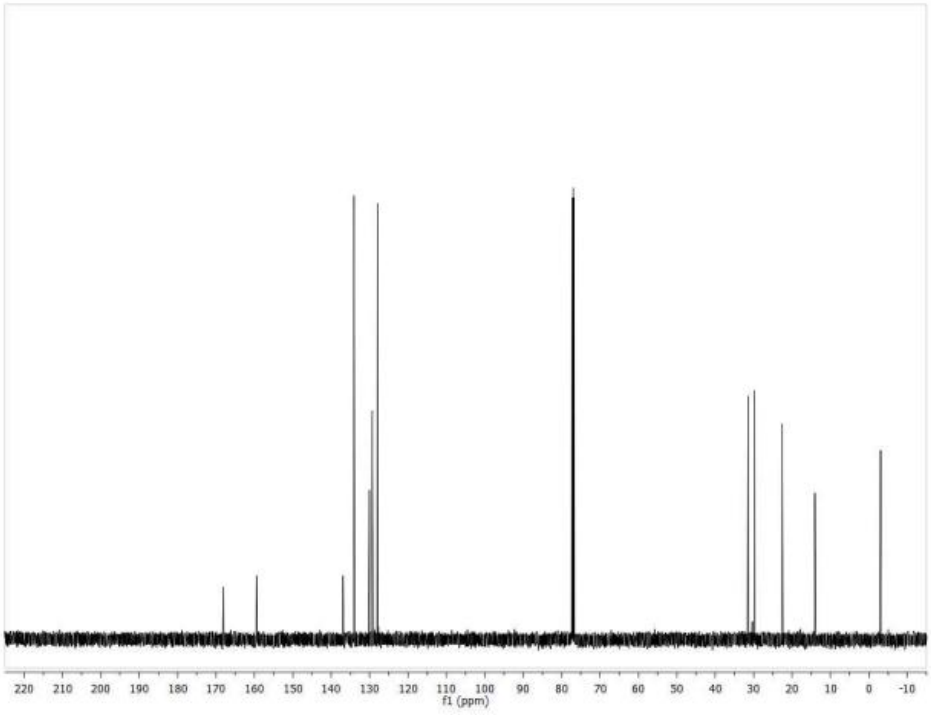

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

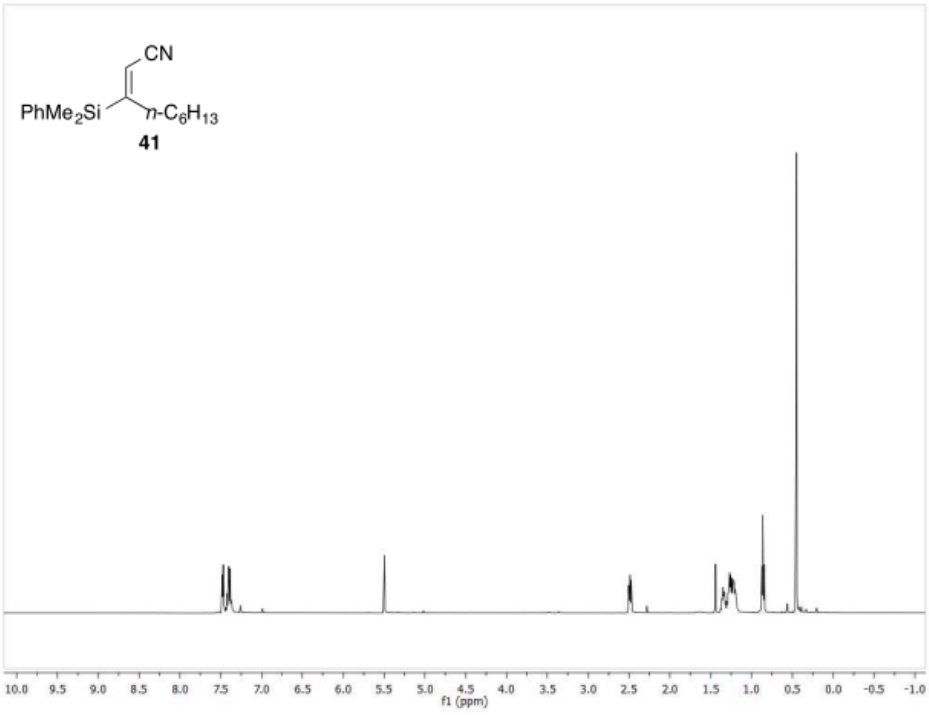

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

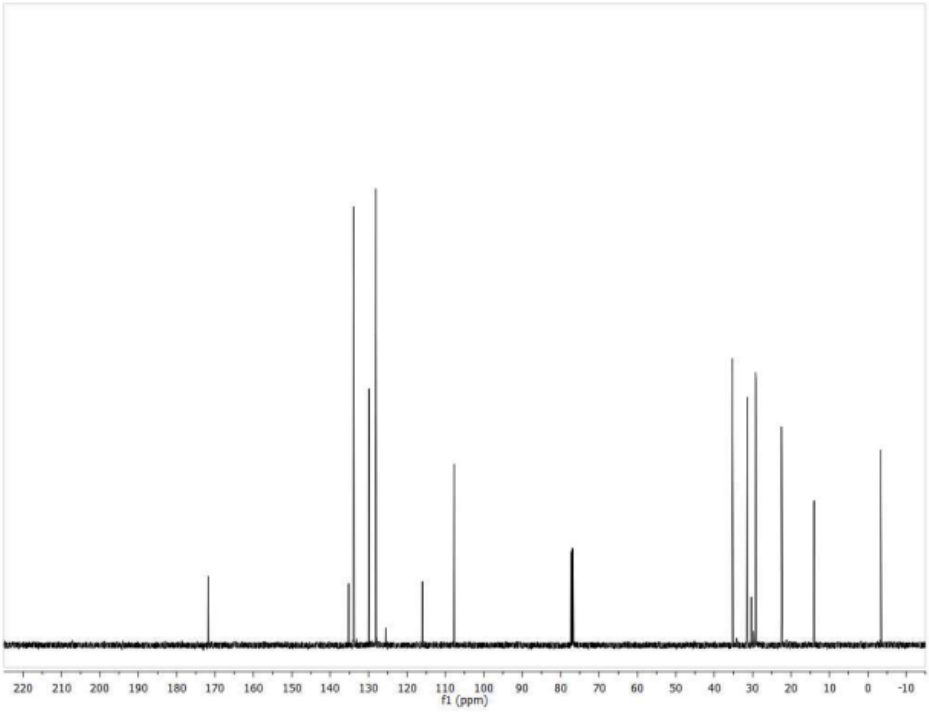

O
O
S
p-toluyl
PhMe2Si
n-C6H13
39
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

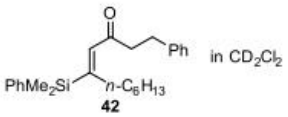

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
NH2
PhMe2Si
n-C6H13
40
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

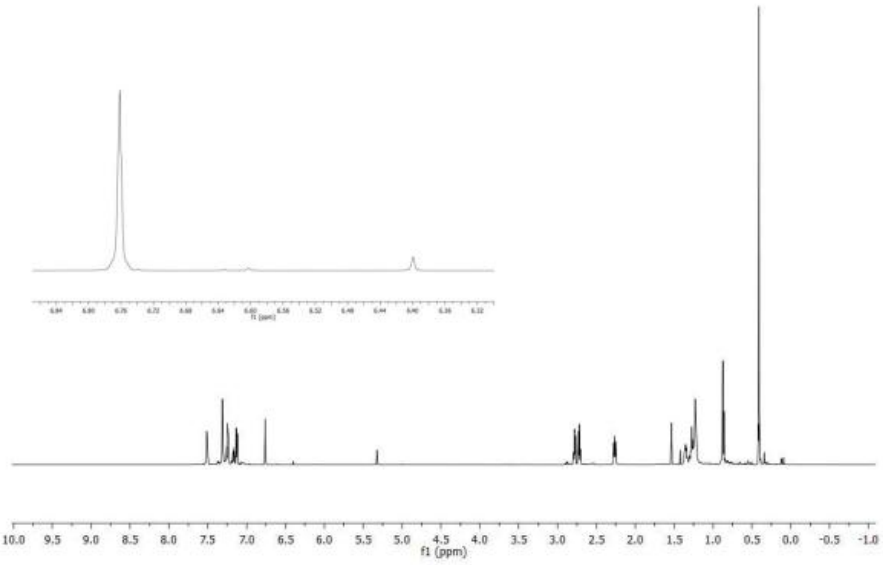

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

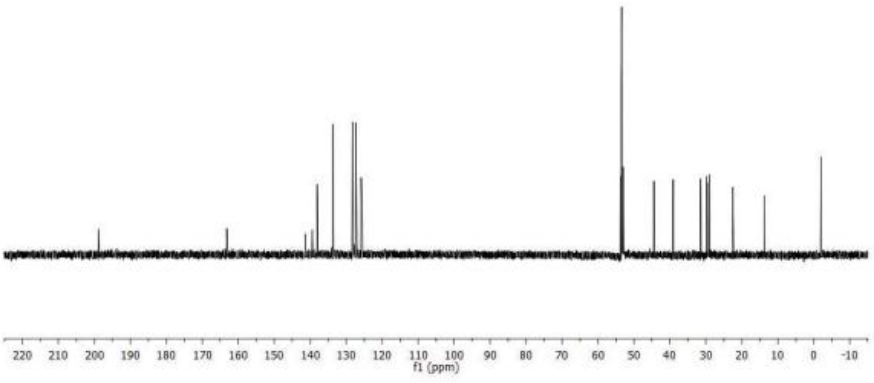

CN
PhMe2Si
n-C6H13
41
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

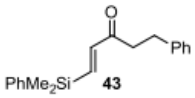

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Ph
PhMe2Si
n-C6H13

42 in CD_2Cl_2

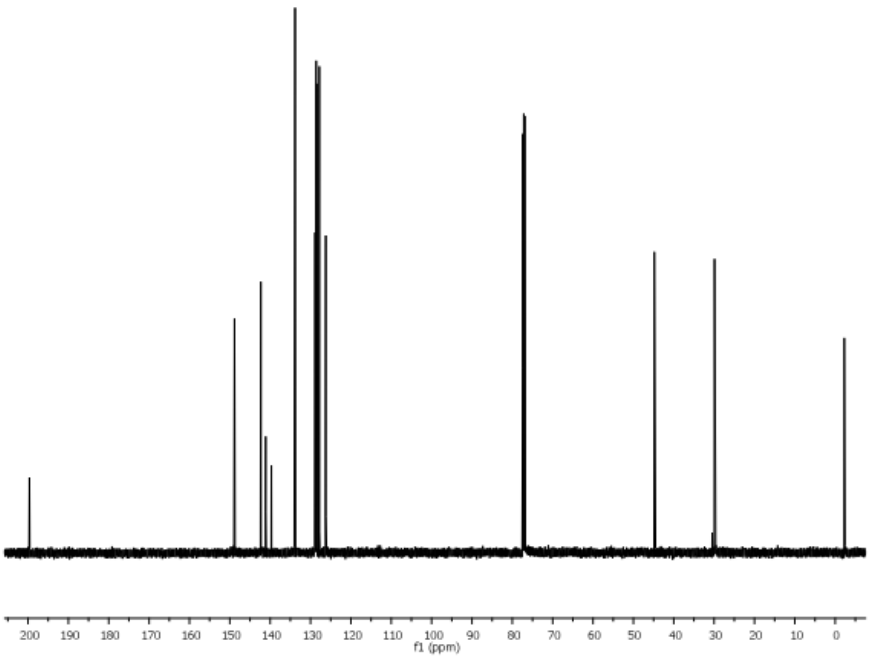

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

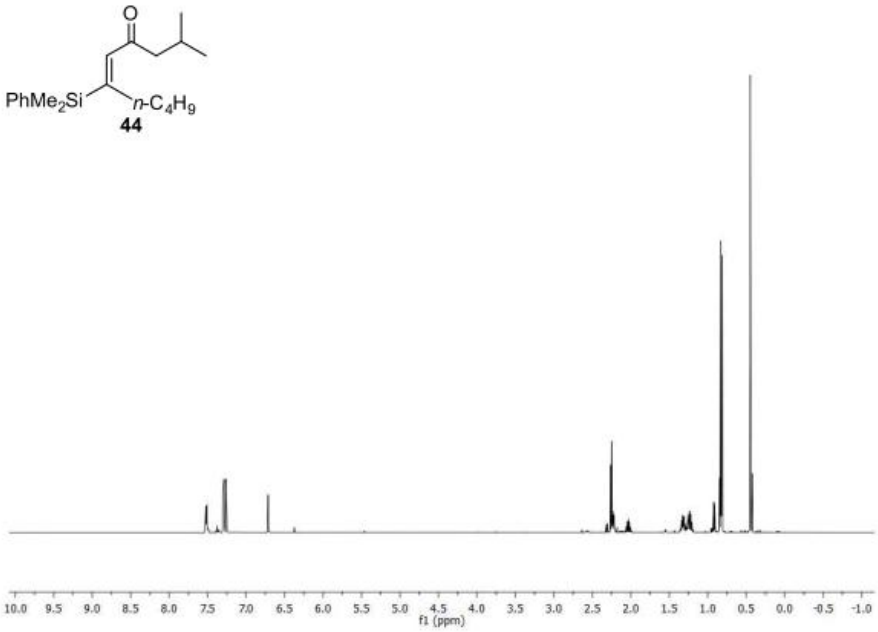

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

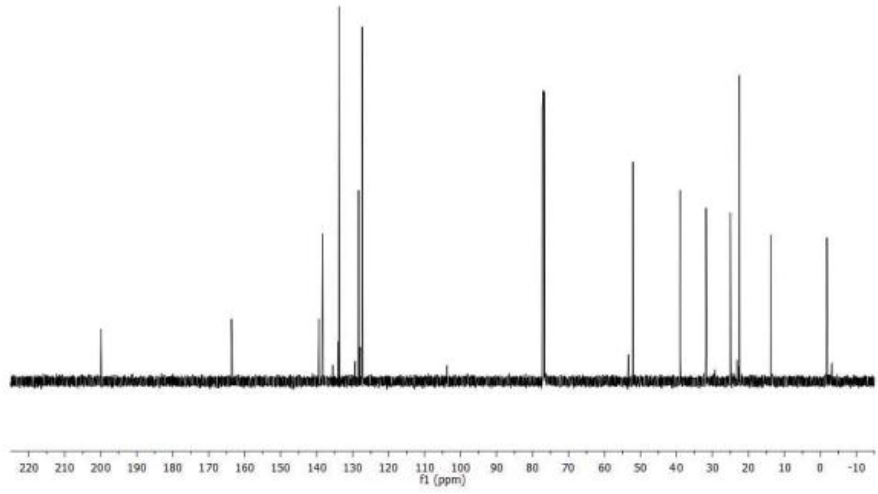

O
Ph
PhMe2Si

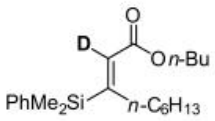
43

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

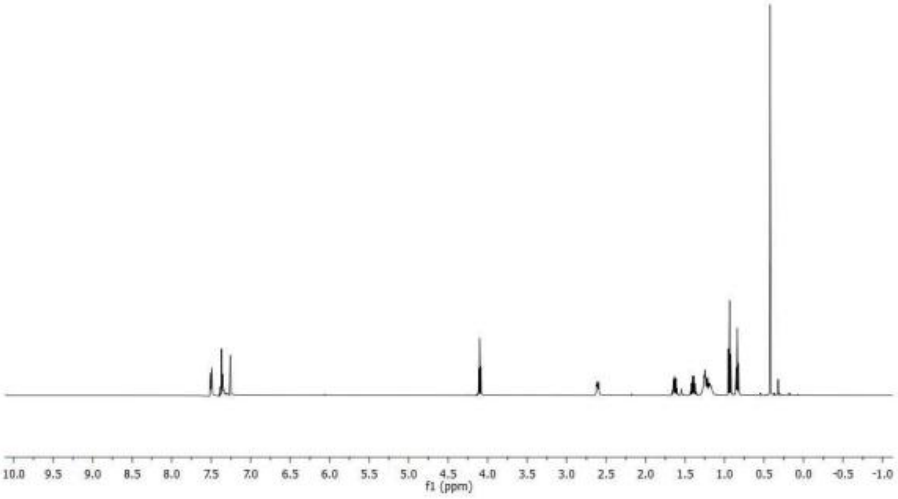

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

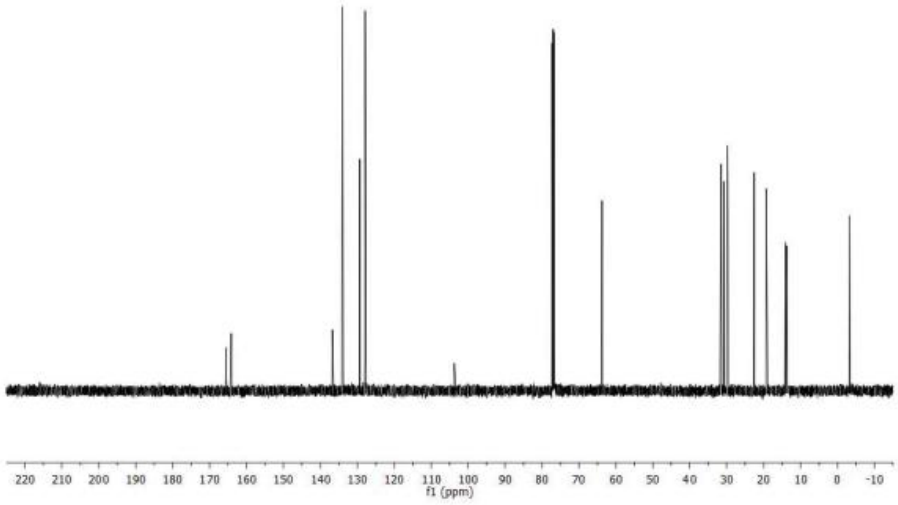

O
PhMe2Si
n-C4H9
44
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
D
O*n*-Bu
PhMe$_2$Si
n-C$_6$H$_{13}$

45


10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

==== Shimadzu LCsolution Analysis Report ====

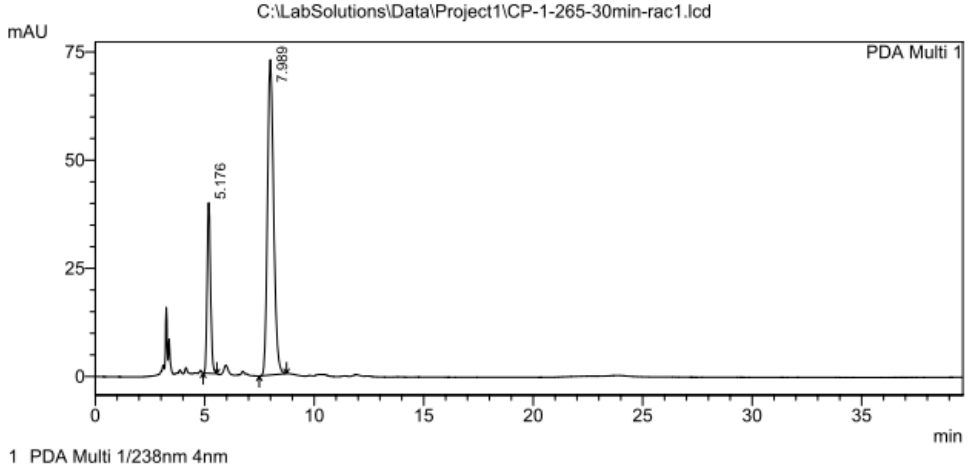
C:\LabSolutions\Data\Project1\CP-1-265-30min-rac1.lcd

Acquired by	: Admin
Sample Name	: CP-1-265-30min-rac
Sample ID	: CP-1-265-30min-rac
Vail #	:
Injection Volume	: 20 uL
Data File Name	: CP-1-265-30min-rac1.lcd
Method File Name	: ath-OD-H-analytical 0.46cm x 25cm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/4/2013 8:10:32 PM
Data Processed	: 12/4/2013 8:50:12 PM

rac-36

<Chromatogram>

C:\LabSolutions\Data\Project1\CP-1-265-30min-rac1.lcd



1 PDA Multi 1/238nm 4nm

PeakTable

PDA Ch1 238nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.176	429677	39422	23.161	35.113
2	7.989	1425496	72848	76.839	64.887
Total		1855172	112270	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

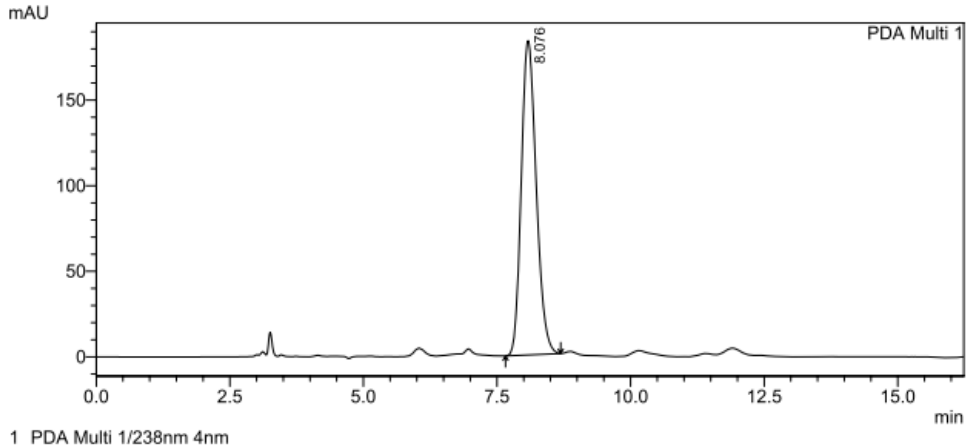
D:\final draftz\CP-1-265-standardnew1.lcd

Acquired by	: Admin
Sample Name	: CP-1-265-standardnew
Sample ID	: CP-1-265-standardnew
Vail #	:
Injection Volume	: 20 uL
Data File Name	: CP-1-265-standardnew1.lcd
Method File Name	: ath-OD-H-analytical 0.46cm x 25cm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 12/4/2013 7:52:30 PM
Data Processed	: 12/5/2013 2:06:55 PM

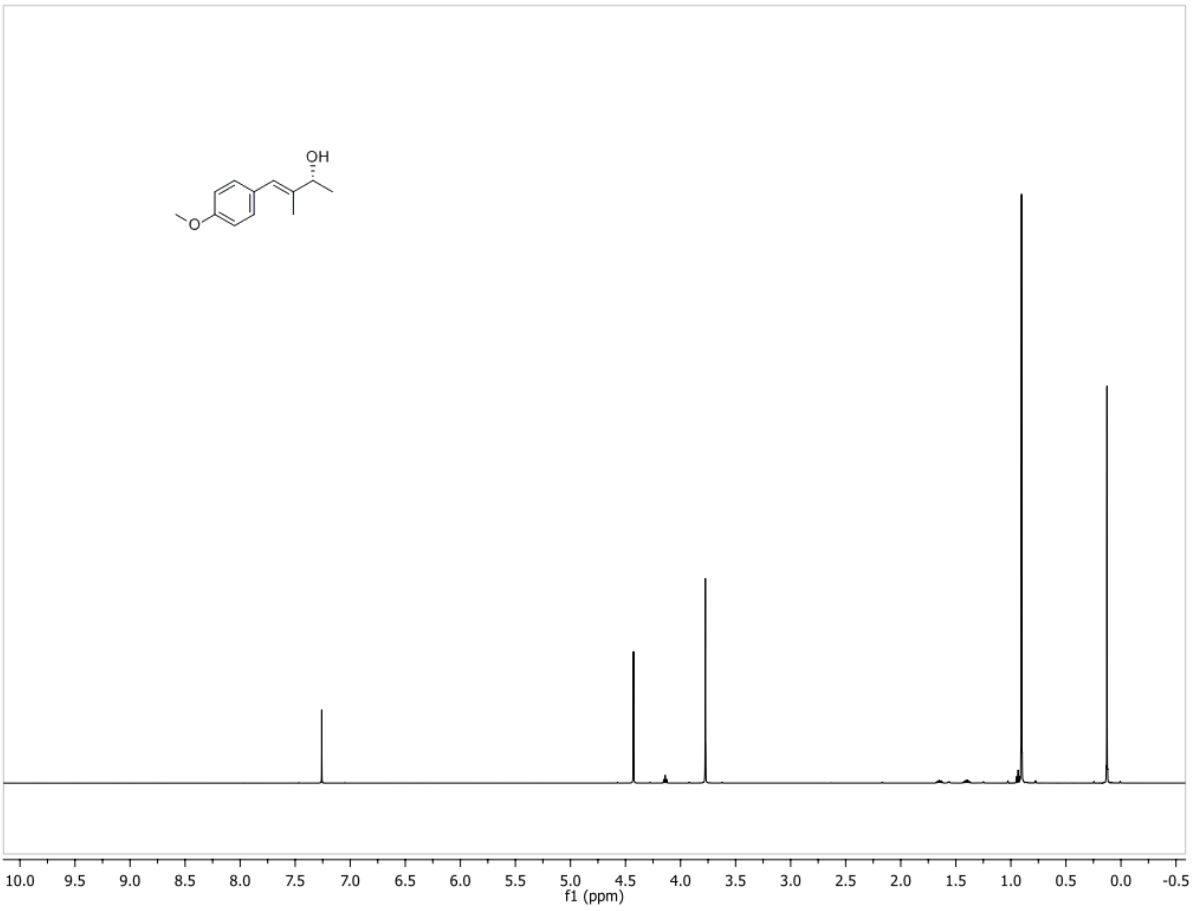
pure 36 after silylation

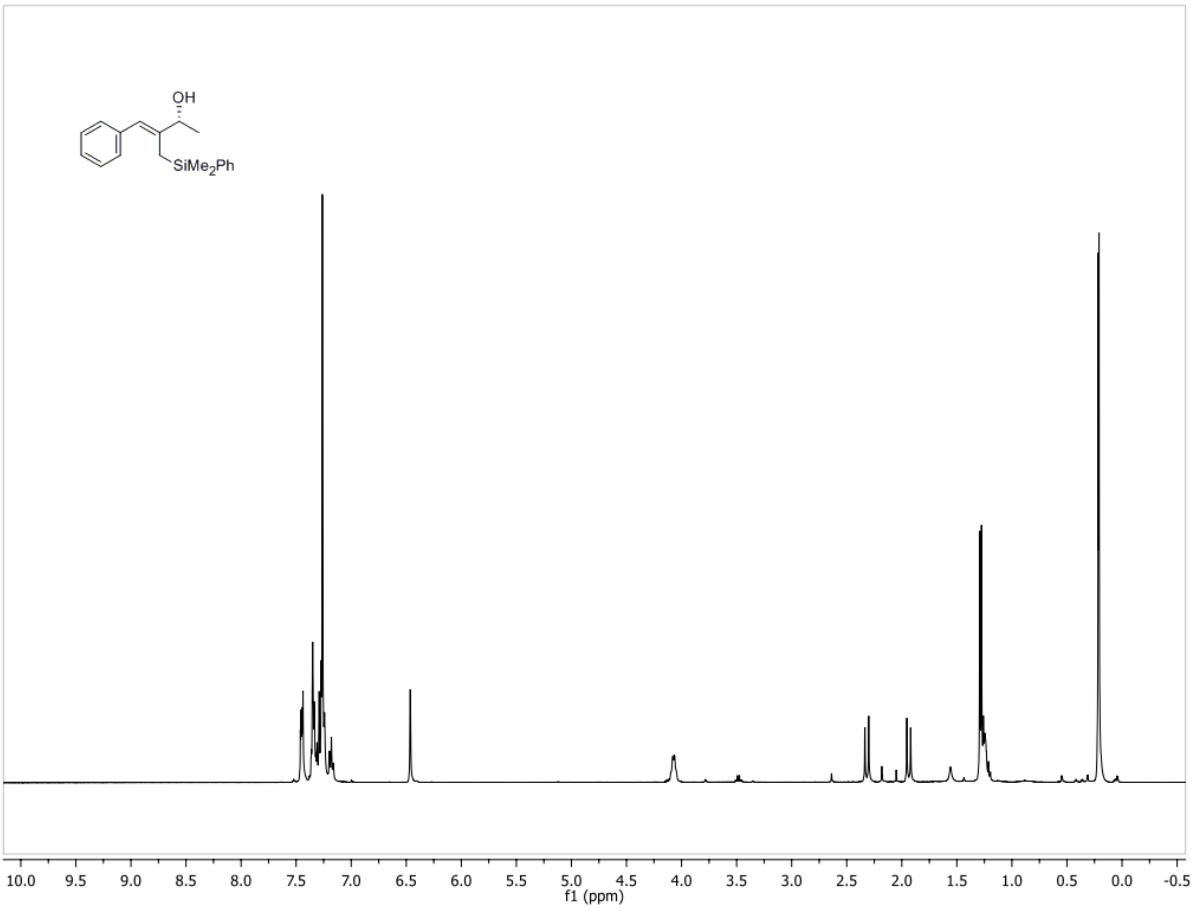
<Chromatogram>

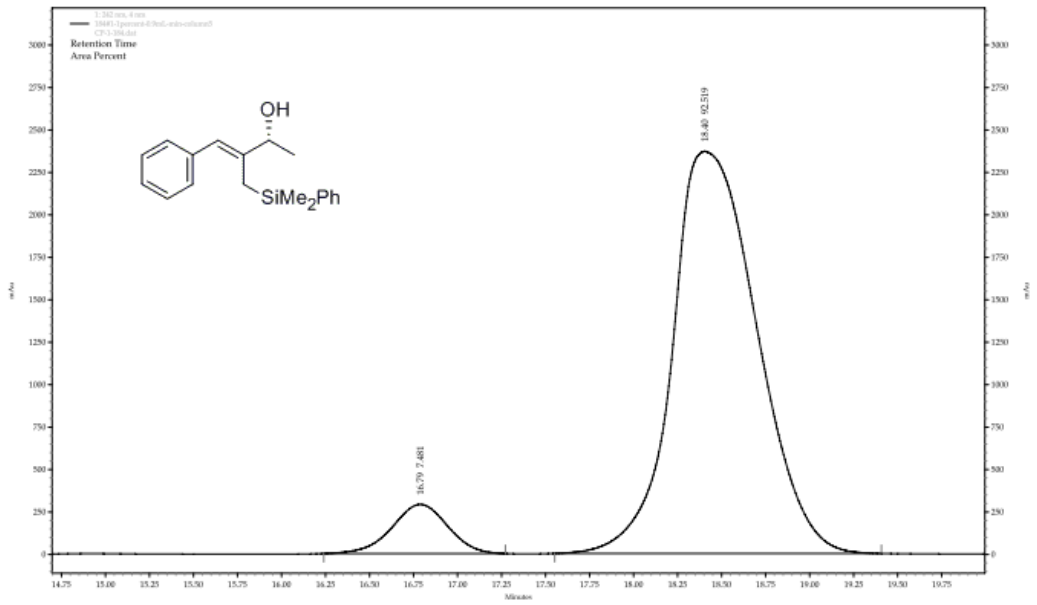
D:\final draftz\CP-1-265-standardnew1.lcd



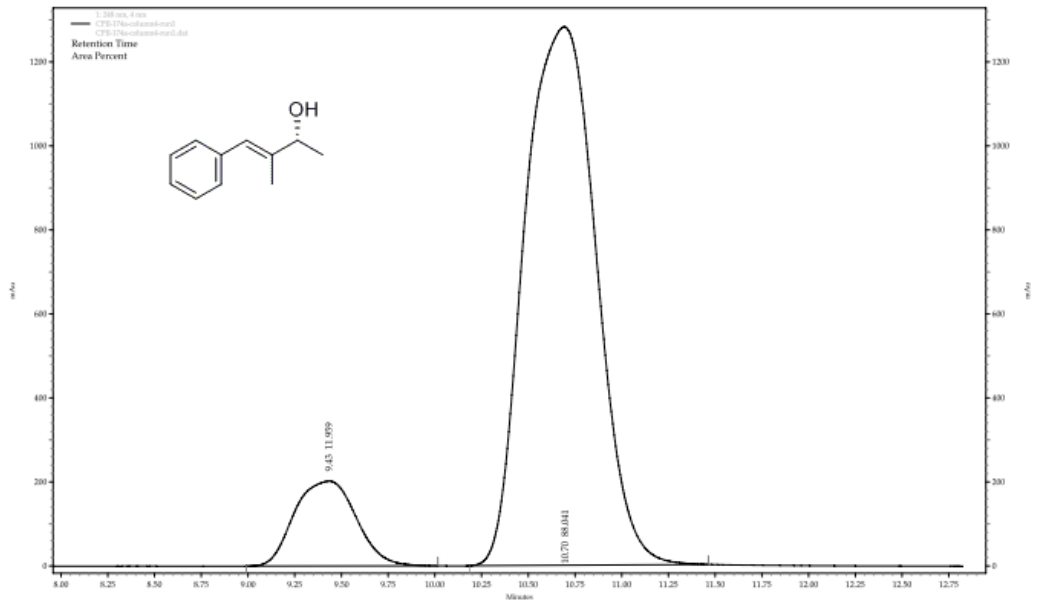
1 PDA Multi 1/238nm 4nm


OH
O
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

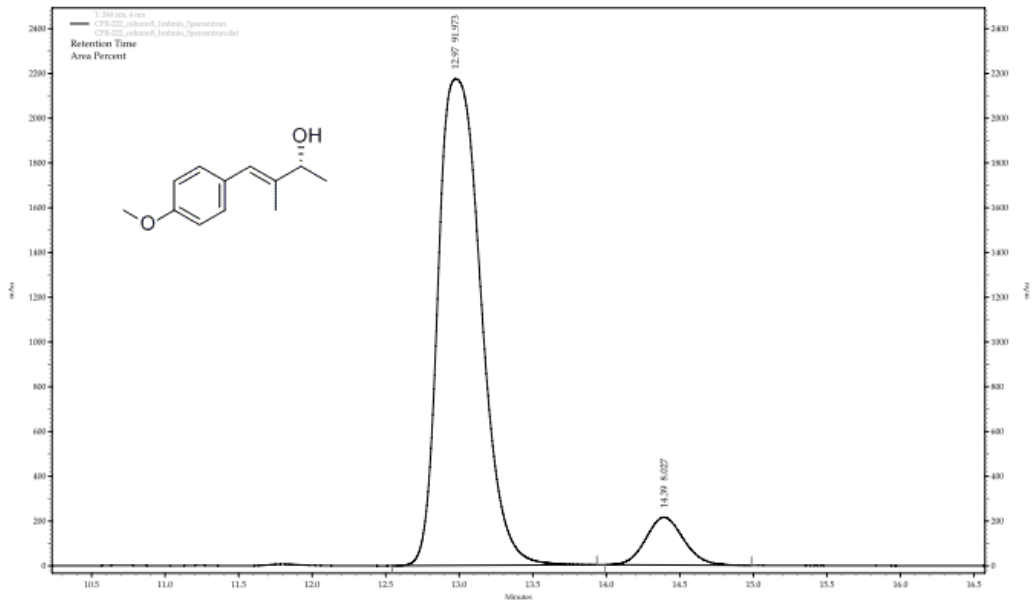

OH
SiMe2Ph
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



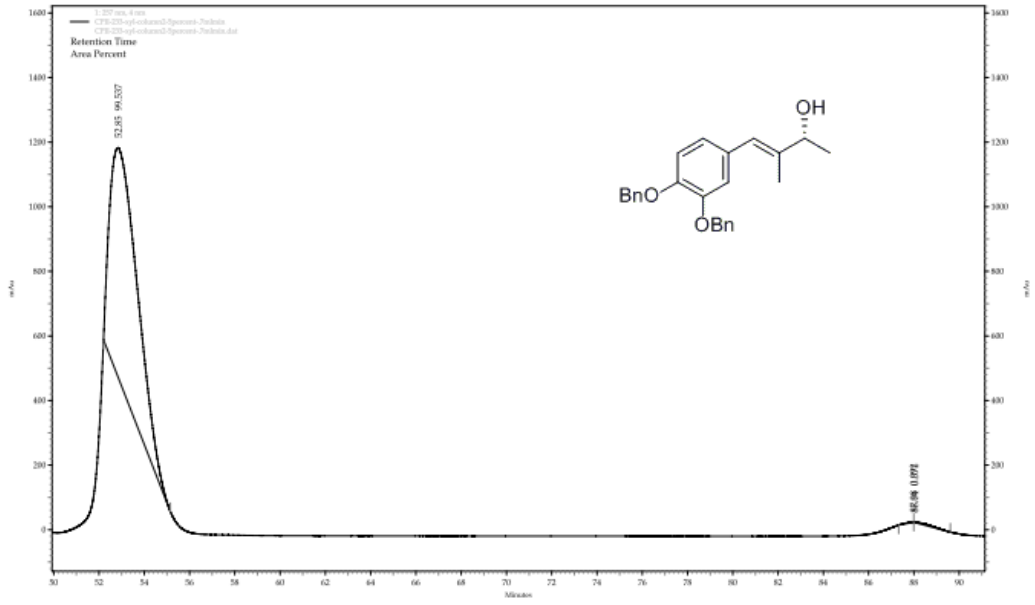
—— C:\EZStart\Projects\Default\Data\RASTASOLJA!\CP-1-184.dat, 1: 242 nm, 4 nm



—— C:\EZStart\Projects\Default\Data\RASTASOLJA!\CPII-174a-column4-run1.dat, 1: 248 nm, 4 nm



—— C:\EZStart\Projects\Default\Data\RASTASOLJA!\CPII-222_column5_1mlmin_5percentrun.dat, 1: 244 nm, 4 nm



—— C:\EZStart\Projects\Default\Data\RASTASOLJA!\CPII-233-xyl-column2-5percent-.7mlmin.dat, 1: 257 nm, 4 nm

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