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Article

Hyphenating the Curtius Rearrangement with Morita-Baylis-Hillman Adducts: Synthesis of Biologically Active Acyloins and Vicinal Aminoalcohols

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Um rearranjo de Curtius, utilizando adutos de Morita-Baylis-Hillman como substrato, foi realizado em uma sequência que permitiu a síntese de várias hidroxi-cetonas (aciloínas) com uma grande diversidade estrutural e com bons rendimentos globais. Por sua vez, essas aciloínas foram transformadas em 1,2-amino-alcoóis de configuração relativa *anti*, através de uma etapa de aminação redutiva altamente diastereosseletiva. A utilidade sintética dessas abordagens foi demonstrada através das sínteses totais da (±)-bupropiona, fármaco utilizado no tratamento na síndrome de abstinência de fumantes e da (±)-espisulosina, um potente agente anti-tumoral isolado inicialmente de uma fonte marinha.

Using Morita-Baylis-Hillman adducts as substrates, the Curtius rearrangement was performed in a sequence that allowed the synthesis of several hydroxy-ketones (acyloins) with great structural diversity and in good overall yields. These acyloins in turn were easily transformed into 1,2-*anti* aminoalcohols through a highly diastereoselective reductive amination step. The synthetic utility of these approaches was exemplified by performing the syntheses of (±)-bupropion, a drug used to treat the abstinence syndrome of smoker and (±)-spisulosine, a potent anti-tumoral compound originally isolated from a marine source.

Keywords: Curtius rearrangement, Morita-Baylis-Hillman, drugs, aminoalcohols, acyloins

Introduction

The formation of new C–N bonds by incorporation of a nitrogen atom into a molecule is a fundamental transformation in organic chemistry, since it allows accessing many valuable compounds.[1] Basically, this can be achieved by nucleophilic substitution reactions or by electrophilic amination reactions.[2]

A C–N bond can also be built through rearrangement reactions. For instance, Lossen,[3] Beckman,[4] Schmidt[5] and Curtius[6] rearrangements are processes which allow the efficient formation of a new C–N bond from carbonyl containing derivative compounds.

The Curtius rearrangement is a thermal decomposition of a carbonyl azide leading to an isocyanate. This stereospecific rearrangement provides carbamates or amines in good overall yields and selectivities. Unfortunately, this rearrangement has the drawback that low molar mass acyl azides present an explosion hazard.[7] This safety issue has limited the industrial use of this transformation until recently, when Am Ende *et al.*[8] reported a new experimental protocol, which enabled the use of this reaction under safer conditions even when conducted on a large scale. This and other protocols have revived interest in this rearrangement, particularly for industrial purposes.[9]

Regarding the potential of this rearrangement, our group has recently reported the preparation of some carbamates from Morita-Baylis-Hillman (MBH) adducts.[10] Curtius rearrangement would be the best way to achieve our target, since the carboxyl group in this structure is needed to perform this rearrangement. Thus, when an acid derived from a MBH adduct was treated with sodium azide, heated at reflux and treated subsequently with *t*-butanol, the corresponding ene-carbamate was formed in good overall yield. However, in some examples it was observed the occurrence of a byproduct (*ca.* 12-15%) which was characterized as being an acyloin (Scheme 1).

The acyloin formation was easily explained by the presence of water (tiny amount) in the *t*-BuOH used to transform the intermediate ene-isocyanate into the

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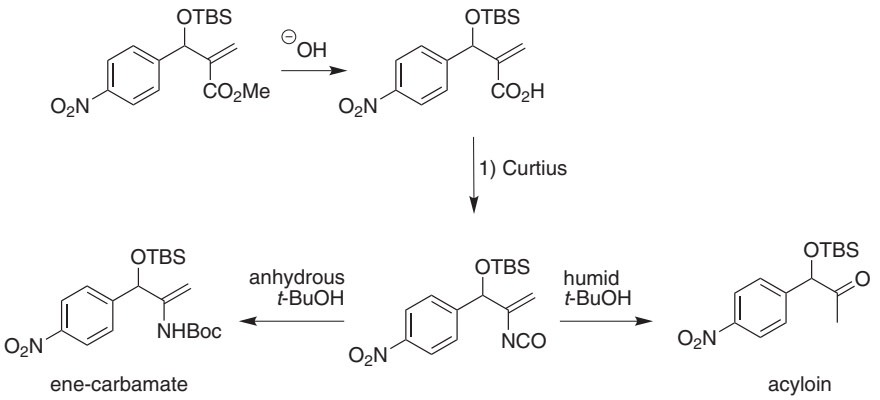


Scheme 1. Curtius rearrangement using Morita-Baylis-Hillman adduct as substrate.

corresponding ene-carbamate. This undesirable side reaction caught our attention, since α-hydroxyketones (acyloins) are structural motifs present in several biologically active compounds, in which the activity is closely associated with the presence of this structural pattern. Due to the synthetic and biological relevance of acyloins, several synthetic approaches have already been developed in order to prepare them. Conventionally, α-hydroxy ketones are prepared by the acyloin condensation reaction,[11] oxidation of enolates or double bonds,[12] or reduction of α-diketones or esters.[13] Recently, a method based on ketohydroxylation of alkenes was developed to give acyloins.[14] Alternatively, radical oxidation of a 1,3-dicarbonyl compound with cerium salts could also be used for the preparation of acyloins.[15] Most recently, a skeletal rearrangement of symmetrically α,α-disubstituted α-amino aldehyde has been reported as a new strategy for preparing acyloins.[16]

Beyond its biological importance, α-hydroxyketones are also an interesting synthetic platform that allows further chemical transformations. For instance, a α-hydroxyketone can be easily transformed into a α-aminoketone. This structural pattern is present in some commercial drugs, such as bupropion [(±)-α-t-butylamino-3-chloropropiophenone] (**1**, Figure 1), a potent synthetic inhibitor of dopamine reuptake with subtle noradrenergic reuptake.[17] Bupropion is an atypical antidepressant, which has been licensed by FDA to treat the abstinence syndrome of smokers.[18]

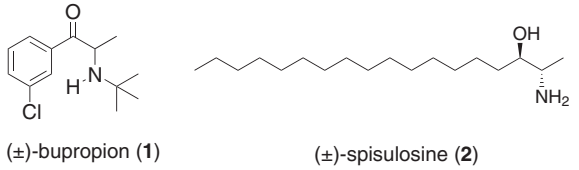


Figure 1. Molecular structures of bupropion and spisulosine.

Vicinal aminoalcohols (or 1,2-aminoalcohols) are structural units that currently occur in several biologically active compounds. They are also part of several chiral catalysts and new materials.

The biological and synthetic importances of this structural motif have stimulated the development of several methods to synthesize it, both in racemic and enantiomerically pure forms.[19] Classically, *syn*-1,2-aminoalcohols can be prepared in their racemic or asymmetric versions using the aminohydroxylation strategy developed by Sharpless *et al*.[20] Another efficient way to prepare vicinal aminoalcohols is by the opening of an epoxide ring with a suitable nitrogen source, such as amines or azide ions, to provide aminoalcohols or azidoalcohols, respectively.[21,22]

By using simple chemical transformations, α-hydroxyketones (acyloins) can also be used as substrates for the stereoselective preparation of 1,2-aminoalcohols.[23]

Spisulosine (**2**, Figure 1) is a sphingoid-type base which presents a long unsaturated alkyl chain (C_{15}) and a 1,2-aminoalcohol motif in an *anti* relationship.[24] This compound was isolated from extracts obtained from the clam *Spisula polynyma* and exhibits a promising activity against prostate cancer.[25]

In a research program directed towards the total synthesis of drugs from Morita-Baylis-Hillman adducts,[26] we describe herein the synthesis of α-hydroxyketones and their diastereoselective transformations into *anti*-1,2-aminoalcohols. To exemplify the synthetic utility of this approach, we also describe the syntheses of the drugs (+/-)-bupropion and (+/-)-spisulosine.

Results and Discussion

The present work began by preparing the MBH adducts, according to a procedure previously developed in our laboratory.[27] The strategy provides the corresponding adducts in good to high yields. The results are summarized in Table 1.

Initially, the Curtius rearrangement without protection of the secondary hydroxyl group was of interesting in this

Table 1. Morita-Baylis-Hillman adducts

Entry	Aldehyde	MBH adduct, yield / %[a]
1	2-nitrobenzaldehyde	**3**, 92
2	3-chlorobenzaldehyde	**4**, 89
3	benzaldehyde	**5**, 75
4	4-methoxybenzaldehyde	**6**, 77
5	3,4,5-trimethoxybenzaldehyde	**7**, 60
6	thiophenecarboxaldehyde	**8**, 90
7	2-fluorobenzaldehyde	**9**, 95
8	propanaldehyde	**10**, 80
9	hexanaldehyde[b]	**11**, 76
10	hexadecanaldehyde[c]	**12**, 60

[a]Yields refer to isolated and purified products; [b]MBH reaction was performed with excess of methyl acrylate in the presence of [bmim]PF_6 at 0 °C; [c]prepared by oxidation of commercial hexadecanol with PCC in refluxing dichloromethane in 95% yield.

work. So, adduct **3** was hydrolysed in the presence of LiOH in an acetonitrile:H_2O (1:1) mixture to give a hydroxyacid in almost quantitative yield (> 98%). When this acid was treated with ethyl chloroformate, extensive degradation of our starting material was observed by TLC analysis.

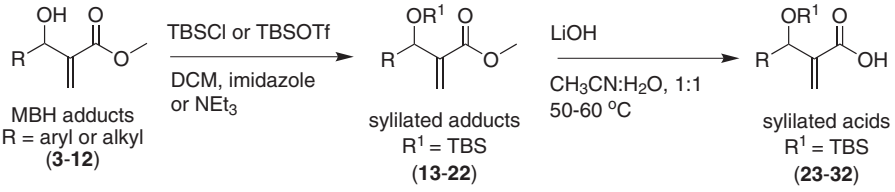
In an attempt to circumvent this issue, the secondary hydroxyl group of the MBH adducts was protected, before ester hydrolysis. Thus, adducts **3**-**12** were treated with TBSCl or TBSOTf in DMF or dichloromethane, in the presence of imidazole or triethylamine, respectively. The silylated adducts (**13**-**22**) were obtained in good to excellent yields. Soon after, ester hydrolysis was carried out with LiOH, in an acetonitrile:H_2O mixture at 60 °C to produce acids **23**-**32** in excellent yields. The results of these steps are summarized in Table 2.

The Curtius rearrangement was initiated using diphenylphosphoryl azide (DPPA).[28] This reagent is supposed to react with a carboxylic acid to provide an isocyanate in a single step. A solution of silyl-acid **23** in toluene was therefore treated with DPPA at reflux for 20 h. Unfortunately, it was unable to isolate any isocyanate. Instead, a complete destruction of the silylated acid was observed.

Because of this result, it was decided to perform the Curtius rearrangement by using a classical experimental protocol. Thus, an acetone solution of silylated acids was treated with ethyl chloroformate in the presence of triethylamine at 0 °C for 5 min. After that, sodium azide was added to the reaction mixture and this mixture was vigorously stirred for 2 h. The crude products were refluxed in dry toluene for 2 h to give the corresponding isocyanates, which finally were refluxed in water to furnish a set of acyloins in good overall yield (ranging from 35 to 50% for 3 steps). The results are summarized in Table 3.

Acyloins were obtained in good overall yield in three steps from Morita-Baylis-Hillman adducts. The strategy is simple and requires no special conditions such as low temperature, dry solvents or special catalysts. Moreover, it uses reagents which are routinely found in organic synthesis laboratories.

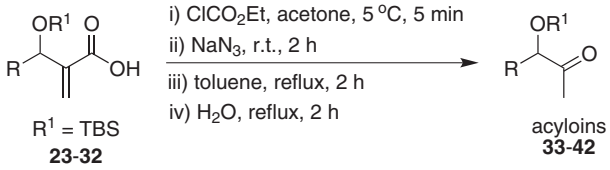
Table 2. Silylation and hydrolysis of Morita-Baylis-Hillman adducts



Entry	MBH adducts	Silylated adducts, yield / %[a]	Silylated acids, yield / %[a]
1	**3**	**13**, 97	**23**, 97
2	**4**	**14**, 99	**24**, 99
3	**5**	**15**, 99	**25**, 99
4	**6**	**16**, 99	**26**, 98
5	**7**	**17**, 99	**27**, 99
6	**8**	**18**, 90	**28**, 99
7	**9**	**19**, 85	**29**, 99
8	**10**	**20**, 85	**30**, 99
9	**11**	**21**, 99	**31**, 98
10	**12**	**22**, 70	**32**, 99[b]

[a]Yields refer to isolated and purified products; [b]methanol used as solvent and NaOH used as base instead of LiOH.

Table 3. Acyloins from Morita-Baylis-Hillman adducts



R^1 = TBS
23-32

acyloins
33-42

Entry	R	Acyloin	Yield / %[a,b]
1	2-nitrophenyl	**33**	46
2	3-chlorophenyl	**34**	45
3	phenyl	**35**	50
4	4-methoxyphenyl	**36**	48
5	3,4,5-trimethoxyphenyl	**37**	42
6	thienyl	**38**	44
7	2-fluorophenyl	**39**	41
8	ethyl	**40**	46
9	hexyl	**41**	42
10	hexadecanyl	**42**	40

[a]Yields refer to isolated and purified products; [b]overall yield (3 steps from silyl esters).

The bifunctional identity (one eletrophilic group and another nucleophilic) makes acyloins an important building block in organic synthesis. They can be converted into several different functional groups, such as alcohols, diols, epoxides, amines, hydroxylamines and haloketones. This synthetic versatility explains the frequent use of acyloins as building blocks for the synthesis of pharmaceutical compounds.[29]

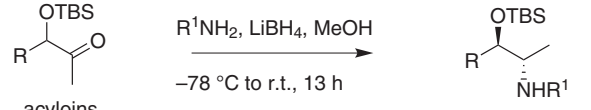
A ketone carbonyl group can be promptly transformed into an amine by a reductive amination reaction. Applications of this reaction are widespread in the pharmaceutical, agrochemical and chemical industries, and in materials science and biotechnology.[30-32]

Recently, Cabral *et al.*[33] have developed a simple method to perform a reductive amination, based on *in situ* formation of an iminium, followed by reduction with $LiBH_4$. Thus, this was viewed in the present work as an attractive opportunity to test this method to prepare vicinal aminoalcohols from our acyloins.

A methanol solution of **35** was treated with $LiBH_4$ in the presence of an excess of benzylamine (3 equiv.) at −72 °C to give aminoalcohol **46** in 83% yield and excellent 1,2-*anti* diastereoselectivity (97:3 d.r., *anti*:*syn*). This simple sequence has allowed the development of a highly diastereoselective synthesis of several different aminoalcohols in good yields. The results are summarized in Table 4.

For all cases examined, the vicinal aminoalcohols were obtained in good yields and with excellent diastereoselectivities. To confirm the 1,2-*anti* relative stereochemistry, the silyl protecting group of aminoalcohol **44** was removed by treatment with TBAF. The unprotected vicinal aminoalcohol **55** was reacted with triphosgene to

Table 4. Vicinal aminoalcohols from acyloins

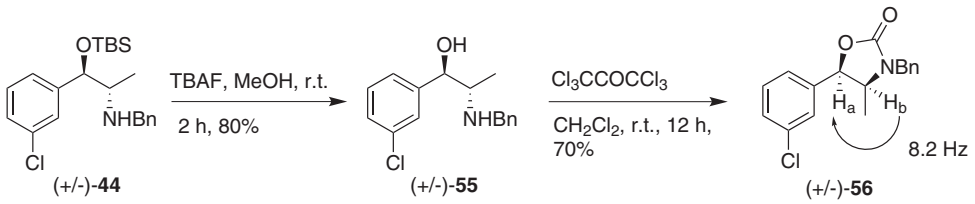


acyloins
34-35, **37-40**

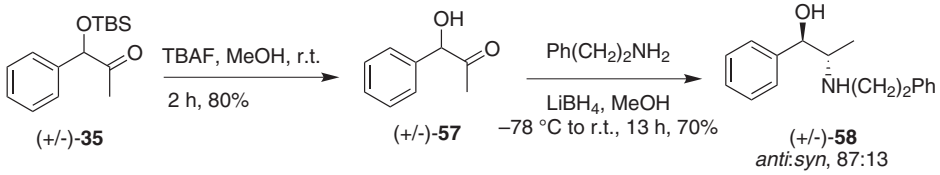
(+/-)-*anti*-
vicinal aminoalcohols (**43-54**)

Entry	Acyloin (R)	Amine (R^1)	Yield / %[a]	d.r.[b]
1	**34**, 3-chlorophenyl	phenethyl	**43**, 79	96:4
2	**34**, 3-chlorophenyl	benzyl	**44**, 77	92:8
3	**35**, phenyl	phenethyl	**45**, 85	> 95:5
4	**35**, phenyl	benzyl	**46**, 83	97:3
5	**35**, phenyl	allyl	**47**, 82	98:2
6	**35**, phenyl	cyclohexyl	**48**, 80	93:7
7	**37**, 3,4,5-trimethoxyphenyl	phenethyl	**49**, 81	> 95:5
8	**37**, 3,4,5-trimethoxyphenyl	allyl	**50**, 80	87:13
9	**38**, thienyl	phenethyl	**51**, 82	91:9
10	**39**, 2-fluorophenyl	phenethyl	**52**, 78	> 95:5
11	**40**, ethyl	phenethyl	**53**, 73	> 95:5
12	**40**, ethyl	decyl	**54**, 71	> 95:5

[a]Yields refer to isolated and purified products; [b]diastereoisomeric ratio was determined by analysis of the ^{1}H NMR spectra of the crude reaction mixture. The carbinolic proton shows a doublet with a coupling constant of 5 Hz for the *anti* relationship, while the *syn* product shows a coupling constant of 8.2 Hz.



Scheme 2. Relative stereochemistry assignment of the 1,2-*anti* aminoalcohol derivatives.



Scheme 3. Silyl protecting group and diastereoselectivity.

afford oxazolidinone **56**, in 70% yield (Scheme 2). The coupling constant between hydrogens H_a and H_b was found to be 8.2 Hz, which it is in agreement with typical coupling constants for a *cis* relationship in oxazolidinones formed from a 1,2-*anti* aminoalcohol (Scheme 2).[34]

The presence of a bulky protecting group on the secondary hydroxyl group might play an important role in the iminium reduction step. Most likely the hydride attack occurs at the opposite side from the protecting group. To experimentally validate this hypothesis, silylated acyloin **35** was treated with TBAF in methanol to provide acyloin **57** in 80% yield. A methanol solution of **57** at −72 °C was treated with $LiBH_4$ to afford aminoalcohol **58** in 70% yield and moderate diastereoselectivity (87:13 d.r.; *anti*:*syn*) (Scheme 3).

This result shows the effect of the silyl protecting group on the diastereoselectivity of the reduction step. Besides, the lithium atom could be complexed both with the nitrogen and the oxygen lone pairs (Figure 2). This arrangement allows the hydride to approach only from the less hindered side. The oxygen atom attached to the silicon of the TBS group has a low basicity, however it is still able to establish intramolecular hydrogen bonds in order to control stereoselectivities of reactions.[35]

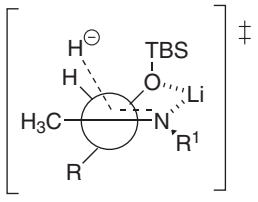


Figure 2. Rationalizing the diastereoselectivity.

The Curtius rearrangement carried out with MBH adducts has allowed the development of a new approach to prepare α-hydroxyketones, which have been used to prepare diastereoselective 1,2-*anti* vicinal aminoalcohols.

Searching to demonstrate the synthetic utility of these approaches, the total synthesis of two pharmacologically active compounds is now described. (±)-Bupropion (**1**, Figure 1) is an aminoketone acting on CNS.[36] This compound is commmercialized in its racemic form, since it racemizes very quickly in the body when administered in its enantiomerically pure form. Our target compound could be prepared from acyloin **34** (Figure 3). A 1,2-carbonyl transposition reaction is required to provide **59**, which can be converted uneventfully to (±)-**1**.[37]

A direct way to perform the required 1,2-carbonyl transposition was using the Lobry-de Bruyn-van Ekenstein transformation.[38] This reaction, currently used in carbohydrate chemistry, is essentially an enolization of a sugar having a hydrogen at the α-carbon to the carbonyl group and proceeds via an enediol intermediate. Some acyloins rearrange with positions exchanged under the influence of base in this transformation. To test this alternative, the TBS group of acyloin **34** was removed by treatment with TBAF in methanol for 12 h to give the corresponding unprotected acyloin in

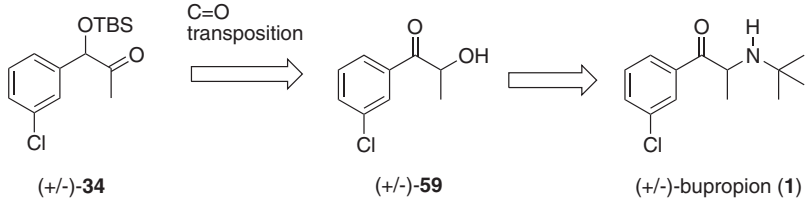


Figure 3. Synthesis of (±)-bupropion from acyloin **34**.

75% yield. A methanol solution of this acyloin was reacted with a 30% solution of NaOH at room temperature. As a result, an extensive acyloin degradation was observed even at lower temperatures (−5 and −10 °C). We also tested the Voight amination (formation of ketoamine by treatment of an acyloin with P_2O_5 in the presence of a primary amine), however this reaction also failed.[39]

Due to these results, the synthetic approach towards the synthesis of bupropion was changed. As an alternative, the required transposition could be done in three steps. Thus, carbonyl reduction of the acyloin (±)-**34** directly led to a monoprotected diol (±)-**60** in almost quantitative yield. TBS removal was performed in the presence of TBAF to afford diol (±)-**61** in 97% yield, as a mixture of diastereoisomers. Selective benzylic oxidation of (±)-**61** with IBX in DMSO expectedly led to the 1,2-carbonyl transposition product (±)-**59**, as the sole product, in 85% yield (3 steps, 81% overall yield, Scheme 4).

Bupropion, in its racemic version, was obtained in 7 steps from Morita-Baylis-Hillman **4**, in 27% overall yield. The sequence is facile to execute and can be scaled-up without problems.

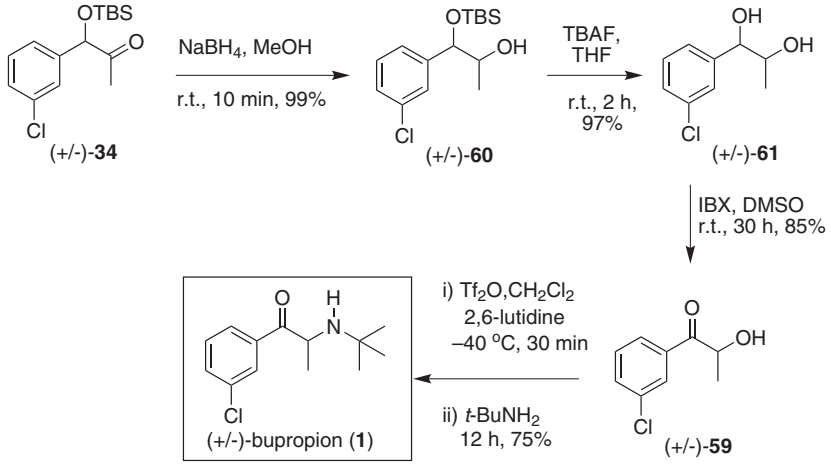
The synthetic methods described in this paper can be combined in order to synthesize spisulosine (**2**, Figure 1) as a racemate. This natural anti-tumoral compound can be prepared from acyloin **42**, using a diastereoselective reductive amination step (Scheme 5).

The diastereoselective total synthesis of spisulosine was accomplished from acyloin (±)-**42** using a very simple and direct sequence. Reductive amination of acyloin (±)-**42** was performed with an excess of benzylamine to give vicinal aminoalcohol (±)-**62**, with high *anti* diastereoselectivity (> 95:5, *anti*:*syn*), in 68% yield (Scheme 6). To quickly finish the synthesis, it was only necessary to remove the protecting groups (TBS and benzyl). For thus, a solution of (±)-**62** in methanol was acidified with some drops of concentrated HCl and the mixture was poured into a hydrogenating bottle containing 10% Pd on charcoal (10 mol%). To our surprise, after several hours at 60 psi, neither of the protecting groups was removed. Perhaps, the long carbon chain favoured the formation of mycelles, which could interact with the solid catalyst.

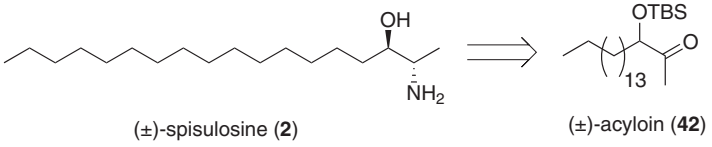
To solve this unexpected issue, a mixture of solvents for the hydrogenation reaction was used. Thus, a mixture of (±)-**62** in dichloromethane:acetic acid (1.5:1) in the presence of 10% Pd/C at 60 psi and 50 °C was shaken for 20 h to furnish the debenzylated aminoalcohol (±)-**63** in 87% yield.

Finally, the TBS group of (±)-**63** was removed by the treatment with concentrated HCl (0.1 mL) in a solution of dichoromethane:methanol (1:1; 1 mL) to give (±)-spisulosine (**2**) in 98% yield. All spectroscopic and physical data are identical to those described in literature for natural and synthetic spisulosine (Scheme 6).[24,40]

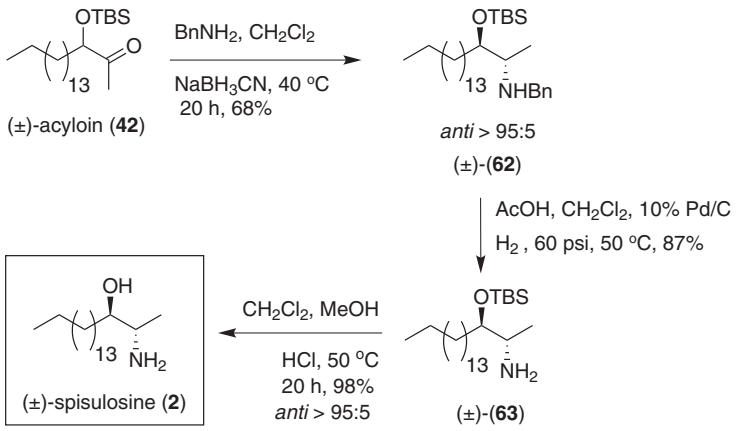
Spisulosine was synthetized in 7 steps from hexadecanal with an overall yield of 10%. The strategy is very simple and requires no special conditions such as low temperature or dry solvents. If the sequence begins with adduct **12** in its enantiomerically pure form, it would allow the



Scheme 4. Racemic total synthesis of bupropion from an acyloin.



Scheme 5. Retrosynthesis of spisulosine (**2**).



Scheme 6. Diastereoselective total synthesis of (+/-)-spisulosine from acyloin.

enantioselective synthesis of spisulosine. By using this strategy, spisulosine derivatives can also be synthesized using the sequence described herein.

Conclusions

In summary, the Curtius rearrangement coupled with Morita-Baylis-Hillman adducts as substrate has proven to be an alternative for the preparation of interesting building blocks for organic syntheses. This combination allowed the synthesis of a set of acyloins in good overall yields for three steps. Reductive amination of these acyloins gave vicinal aminoalcohols in good overall yields and with high diastereoselectivities, in favor of the 1,2-*anti* isomer. Moreover, we have demonstrated that these methods can be used in the synthesis of important pharmacologically active compounds. Thus, (±)-bupropion was prepared in 7 steps from a MBH adduct, in 27% overall yield. Using this strategy we also showed a highly diastereoselective total synthesis of (±)-spisulosine which was accomplished in 7 steps from hexadecanal with an overall yield of 10%.

Experimental

General procedure

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker at 250 and 62.5 MHz, respectively, or on an Inova instrument at 500 and 125 MHz, respectively. High resolution mass (HRMS) spectra were recorded using a Q-TOF Micromass equipment (Waters, UK). Manipulations and reactions were not performed under dry atmospheres or employing dry solvents, unless otherwise specified. In those cases CH_2Cl_2, DMF and triethylamine were dried over CaH_2 and distilled. Purification and separations by column chromatography were performed on silica gel, using normal or flash chromatography. Thin layer chromatography (TLC) was detected by spraying with 5% ethanolic phosphomolybdic acid and heating. All the Morita-Baylis-Hillman reactions were sonicated in an ultrasonic cleaner (81 W, 40 MHz).

General procedure for the synthesis of the Morita-Baylis-Hillman adducts

A mixture of aldehyde (3-10 mmol), methyl acrylate (excess, *ca.* 5 equiv.) and DABCO (0.65 equiv.) was sonicated in an ultrasound bath at 30 °C. Reaction evolution was followed by TLC analysis. For the preparation of the MBH adducts **10** and **12** the reaction was carried out using methyl acrylate (10 equiv.), ionic liquid ([bmim]BF_4; 5 drops) as an additive, at 50 °C with stirring. The excess of methyl acrylate was removed under vaccum. The crude residue was diluted in ethyl acetate (25 mL). The organic layer was washed with distilled water (15 mL), brine (2 × 15 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by flash silica gel column chromatography (ethyl acetate:hexanes, up to 30:70) to provide the MBH adducts in good to high yields.

*(±)-Methyl 2-[hydroxy(2-nitrophenyl)methyl]prop-2-enoate (**3**)*: 92% yield, pale yellow oil; IR (film) ν_{max}/cm^{-1}: 3469, 1716, 1630, 1528, 1352; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, *J* 1.2/8.2 Hz, 1H), 7.78 (d, 1H, *J* 7.9 Hz), 7.61-7.67 (m, 1H), 7.41-7.48 (m, 1H), 6.36 (s, 1H), 6.20 (s, 1H), 5.72 (s, 1H), 3.73 (s, 3H), 3.08 (s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.3, 148.2, 140.7, 136.0, 133.4, 128.8, 128.6, 126.4, 124.5, 67.6, 52.1; HRMS (ESI TOF) Calcd. for $C_{11}H_{11}NO_5$[M + Na^+]: 260.0529. Found: 260.0530.

*(±)-Methyl 2-[(3-chlorophenyl)(hydroxy)methyl] prop-2-enoate (**4**)*: 89% yield, colorless oil; IR (film) ν_{max}/cm^{-1}: 3452, 1711, 1433, 1282, 1151, 1041; ^{1}H NMR

(250 MHz, $CDCl_3$): δ 7.36 (s, 1H), 7.21-7.26 (m, 3H), 6.34 (s, 1H), 5.84 (s, 1H), 5.49 (s, 1H), 3.71 (s, 3H), 3.16 (s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.6, 143.4, 141.4, 134.3, 129.7, 127.9, 126.7, 124.8, 72.6, 52.1; HRMS (ESI TOF) Calcd. for $C_{11}H_{11}O_3Cl$ [M + Na^+]: 249.0294. Found: 249.0318.

*(±)-Methyl 2-[hydroxy(phenyl)methyl]prop-2-enoate (**5**)*: 75% yield, oil; IR (film) ν_{max}/cm^{-1}: 3448, 2949, 1711, 1446, 1270, 1155, 1041; ^1H NMR (250 MHz, $CDCl_3$): δ 7.21-7.37 (m, 5H), 6.31 (s, 1H), 5.86 (s, 1H), 5.52 (s, 1H), 3.65 (s, 3H), 3.45 (s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.7, 142.1, 141.4, 128.4, 127.8, 126.7, 125.8, 72.8, 51.9; HRMS (ESI TOF) Calcd. for $C_{11}H_{12}O_3$ [M + Na^+]: 215.0684. Found: 215.0811.

*(±)-Methyl 2-[hydroxy(4-methoxyphenyl)methyl]prop-2-enoate (**6**)*: 73% yield; amorphous solid; mp 70-72 °C; IR (KBr) ν_{max}/cm^{-1}: 3465, 1714, 1611, 1512, 1465, 1034; ^1H NMR (250 MHz, $CDCl_3$): δ 7.29 (d, 2H, *J* 8.5 Hz), 6.87 (d, 2H, *J* 8.5 Hz), 6.32 (s, 1H), 5.85 (s, 1H), 5.53 (s, 1H), 3.80 (s, 3H), 3.72 (s, 3H), 2.43 (s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.8, 159.2, 142.1, 133.4, 127.9, 125.7, 113.8, 72.8, 55.2, 51.9; HRMS (ESI TOF) Calcd. for $C_{12}H_{14}O_4$ [M + Na^+]: 245.0784. Found: 245.0780.

*(±)-Methyl 2-[hydroxy(3,4,5-trimethoxyphenyl)methyl] prop-2-enoate (**7**)*: 60% yield; amorphous solid; mp 121-123 ºC; IR (KBr) ν_{max}/cm^{-1}: 3464, 1712, 1613, 1514, 1463, 1036; ^1H NMR (250 MHz, $CDCl_3$): δ 6.54 (s, 2H), 6.27 (s, 1H), 5.81 (s, 1H), 5.44 (d, 1H, *J* 5.0 Hz), 3.78 (s, 6H), 3.77 (s, 3H), 3.69 (s, 3H), 3.35 (d, 1H, *J* 5.0 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.8, 153.1, 141.9, 137.2, 137.0, 125.9, 103.5, 72.9, 60.7, 55.9, 52.0; HRMS (ESI TOF) Calcd. for $C_{11}H_{11}O_3Cl$ [M + Na^+]: 305.0996. Found: 305.0989.

*(±)-Methyl 2-[hydroxy(thiophen-2-yl)methyl]prop-2-enoate (**8**)*: 90% yield; pale yellow oil; IR (film) ν_{max}/cm^{-1}: 3445, 2952, 1715, 1632; ^1H NMR (250 MHz, $CDCl_3$): δ 7.21 (dd, 1H, *J* 2.5/3.8 Hz), 6.90-6.93 (m, 2H), 6.32 (s, 1H), 5.95 (s, 1H), 5.73 (d, 1H, *J* 6,2 Hz), 3.73 (d, 1H, *J* 6.2 Hz), 3.70 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.5, 145.8, 141.5, 126.8, 126.0, 125.2, 124.8, 69.1, 52.0; HRMS (ESI TOF) Calcd. for $C_9H_{11}O_3S$ [M + H]$^+$: 199.0423. Found: 199.0417.

*(±)-Methyl 2-[(2-fluorophenyl)(hydroxy)methyl]prop-2-enoate (**9**)*: 95% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 3437, 1721; ^1H NMR (250 MHz, $CDCl_3$): δ 7.42 (dt, 1H, *J* 1.9/7.5 Hz), 7.21-7.28 (m, 1H), 7.10 (dt, 1H, *J* 1.2/7.5 Hz), 6.97-7.05 (m, 1H), 6.31 (s, 1H), 5.85 (d, 1H, *J* 5.5 Hz), 5.76 (s, 1H), 3.69 (s, 3H), 3.62 (d, 1H, *J* 5.5 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.7, 160.0 (d, *J* 245.5 Hz), 140.9, 129.4 (d, *J* 8.2 Hz), 128.4, 128.1 (d, *J* 3.7 Hz), 126.3, 124.1 (d, *J* 3.5 Hz), 115.3 (d, *J* 21.5 Hz), 66.7, 52.0; HRMS (ESI TOF) Calcd. for $C_{11}H_{12}FO_3$ [M + H]$^+$: 211.0765. Found: 211.0762.

*(±)-Methyl 3-hydroxy-2-methylenepentanoate (**10**)*: 80% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 3454, 2928, 2853, 1705, 1287, 1157; ^1H NMR (250 MHz, $CDCl_3$): δ 6.15 (s, 1H), 5.74 (s, 1H), 4.27 (q, 1H, *J* 5.7 Hz), 3.69 (s, 3H), 3.00 (d, 1H, *J* 5.7 Hz), 1.45-1.71 (m, 2H), 0.86 (t, 3H, *J* 7.4 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 167.0, 142.3, 124.9, 72.4, 51.7, 29.0, 9.9; HRMS (ESI TOF) Calcd. for $C_7H_{13}O_3$[M + H]$^+$: 145.0859. Found: 145.0856.

*(±)-Methyl 3-hydroxy-2-methylenenonanoate (**11**)*: 76% yield; amorphous solid; mp 131-132 ºC; IR (KBr) ν_{max}/cm^{-1}: 3452, 2929, 2855, 1707, 1290, 1155; ^1H NMR (500 MHz, $CDCl_3$): δ 6.20 (s, 1H), 5.78 (s, 1H), 4.37 (t, 1H, *J* 6.7 Hz), 3.77 (s, 3H), 1.54-1.71 (m, 2H), 1.19-1.50 (m, 8H), 0.86 (t, 3H, *J* 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 142.5, 124.9, 71.7, 51.8, 36.2, 31.7, 29.0, 25.7, 22.5, 14.0; HRMS (ESI TOF) Calcd. for $C_{11}H_{21}O_3$ [M + H]$^+$: 201.1485. Found: 201.1483.

*(±)-Methyl-3-hydroxy-2-methyleneoctadecanoate (**12**)*: 60% yield; amorphous solid; mp 43-45 °C; IR (film) ν_{max}/cm^{-1}: 3465, 2984, 2929, 2856, 1742, 1374, 1242, 1048; ^1H NMR (250 MHz, $CDCl_3$): δ 6.21 (s, 1H), 5.79 (t, 1H, *J* 1.0 Hz), 4.37 (q, 1H, *J* 6.5 Hz), 3.77 (s, 3H), 2.59 (d, 1H, *J* 6.5 Hz), 1.55-1.70 (m, 2H), 1.18-1.50 (m, 26H), 0.87 (t, 3H, *J* 6.9 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 167, 142.5, 124.9, 71.8, 51.8, 36.2, 31.9, 29.7, 29.63, 29.6, 29.5, 29.4, 29.3, 25.8, 22.7, 14.1; HRMS (ESI) Calcd. for $C_{20}H_{39}O_3$ [M + H]$^+$ 327.2894; Found 327.2877.

General procedure for the silylation of Morita-Baylis-Hillman adducts

A mixture of MBH adduct (1-3 mmol), imidazole (2.5 equiv.), TBSCl (1.5 equiv.) and a few drops of DMSO (to facilitate stirring), under argon atmosphere, was stirred at room temperature. After 2-4 h, the crude residue was diluted in ethyl acetate (25 mL). The organic layer was washed with distilled water (15 mL), brine (2 × 15 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude mixture was filtered through silica gel (ethyl acetate:hexanes, 30:70) to provide the silylated compounds in good to excellent yields.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](2-fluorophenyl)methyl}prop-2-enoate (**13**)*: 97% yield; pale yellow

oil; IR (film) ν_{max}/cm^{-1}: 2949, 2929, 2851, 1728, 1531, 1352, 1249, 1090, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.78 (d, 1H, *J* 8.0 Hz), 7.68 (d, 1H, *J* 8.0 Hz), 7.56 (t, 1H, *J* 7.5 Hz), 7.37 (t, 1H, *J* 7.5 Hz), 6.34 (s, 1H), 6.29 (s, 1H), 5.97 (s, 1H), 3.64 (s, 3H), 0.88 (s, 9H), 0.13 (s, 3H), –0.06 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 165.2, 148.2, 143.1, 137.5, 132.6, 129.6, 128.1, 125.0, 123.9, 66.7, 51.8, 25.7, 18.1, –5.1. HRMS (ESI TOF) Calcd. for $C_{17}H_{25}NO_5Si$ [M + Na$^+$]: 374.1394. Found: 374.1389.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](3-chlorophenyl)methyl}prop-2-enoate (**14**)*: > 99% yield; pale yellow oil; IR (film) ν_{max}/cm^{-1}: 2949, 2929, 2855, 1707, 1061, 841, 780; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.17-7.32 (m, 3H), 6.28 (s, 1H), 6.10 (s, 1H), 5.58 (s, 1H), 3.69 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), –0.08 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 166.1, 144.8, 143.4, 133.9, 129.3, 127.5, 127.0, 125.2, 124.4, 72.1, 51.7, 25.7, 18.1, –5.0; HRMS (ESI TOF) Calcd. for $C_{17}H_{25}ClO_3Si$ [M + Na$^+$]: 363.1154. Found: 363.1150.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](phenyl) methyl}prop-2-enoate (**15**)*: > 99% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2949, 2851, 1458, 1258, 1082; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.17-7.41 (m, 5H), 6.25 (s, 1H), 6.08 (s, 1H), 5.61 (s, 1H), 3.68 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), –0.11 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.4, 143.9, 142.6, 128.0, 127.3, 127.0, 123.8, 72.7, 51.6, 25.7, 18.1, –4.9; HRMS (ESI TOF) Calcd. for $C_{17}H_{26}O_3Si$ [M + Na$^+$]: 329.1543. Found: 329.1537.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](4-methoxyphenyl)methyl}prop-2-enoate (**16**)*: > 99% yield; amorphous solid; mp 112-114 ºC; IR (KBr) ν_{max}/cm^{-1}: 2949, 2929, 2851, 1715, 1507, 1245, 1047, 833, 771; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.27 (d, 2H, *J* 7.0 Hz), 6.82 (d, 2H, *J* 7.0 Hz), 6.22 (s, 1H), 6.06 (s, 1H), 5.56 (s, 1H), 3.78 (s, 3H), 3.67 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), –0.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 158.8, 144.1, 134.8, 128.2, 123.3, 113.4, 72.3, 55.1, 51.6, 25.7, 18.1, –4.9; HRMS (ESI TOF) Calcd. for $C_{18}H_{28}O_4Si$ [M + Na$^+$]: 359.1649. Found: 359.1647.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](3,4,5-trimethoxyphenyl)methyl}prop-2-enoate (**17**)*: 80% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2950, 2927, 2854, 1718, 1505, 1246, 1051; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.56 (s, 2H), 6.18 (t, 1H, *J* 1.1 Hz), 5.95 (t, 1H, *J* 1.5 Hz), 5.53 (s, 1H), 3.78 (s, 6H), 3.67 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), –0.10 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.5, 152.8, 143.9, 138.3, 137.0, 123.9, 103.7, 72.4, 60.7, 55.9, 51.6, 25.6, 18.1, –4.9, –5.1; HRMS (ESI TOF) Calcd. for $C_{20}H_{32}O_6Si$ [M + Na$^+$]: 419.1860. Found: 419.1855.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](thiophen-2-yl)methyl}prop-2-enoate (**18**)*: 90% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2954, 2930, 2857, 1723, 1632, 1256, 1082; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.18 (dd, 1H, *J* 5.0/1.3 Hz), 6.83-6.98 (m, 2H), 6.28 (t, 1H, *J* 1.1 Hz), 6.12 (t, 1H, *J* 1.5 Hz), 5.89 (s, 1H), 3.73 (s, 3H), 0.90 (s, 9H), 0.08 (s, 3H), –0.003 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.2, 147.3, 143.5, 126.3, 124.6, 124.4, 124.2, 68.4, 51.7, 25.7, 18.2, –5.1, –5.14; HRMS (ESI TOF) Calcd. for $C_{15}H_{24}O_3SSi$ [M + Na$^+$]: 335.1108. Found: 335.1107.

*(±)-Methyl 2-{[(tert-butyldimethylsilyl)oxy](2-fluorophenyl)methyl}prop-2-enoate (**19**)*: 85% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 1723; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.35 (dt, 1H, *J* 1.5/7.5 Hz), 7.16-7.28 (m, 1H), 6.95-7.14 (m, 2H), 6.34 (s, 1H), 6.07 (s, 1H), 5.95 (s, 1H), 3.66 (s, 3H), 0.87 (s, 9H), 0.08 (s, 3H), –0.09 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.0, 159.8 (d, *J* 245.7 Hz), 142.7, 129.5 (d, *J* 13.5 Hz), 129.1, 129.0 (d, *J* 6.8 Hz), 128.8, 124.8, 123.9 (d, *J* 3.5 Hz), 115.2 (d, *J* 22.2 Hz), 65.8, 51.6, 25.7, 18.1, –5.2, –5.3.

*(±)-Methyl 3-[(tert-butyldimethylsilyl)oxy]-2-methylidenepentanoate (**20**)*: 85% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2930, 2845, 1721; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.20-6.23 (m, 1H), 5.86-5.89 (m, 1H), 4.50-4.59 (m, 1H), 3.74 (s, 3H), 1.35-1.75 (m, 2H), 0.90 (s, 9H), 0.85 (t, 3H, *J* 7.4 Hz), 0.05 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.8, 143.6, 124.5, 71.0, 51.6, 30.3, 25.8, 18.1, 9.0, –4.8, –5.1; HRMS (ESI TOF) Calcd. for $C_{17}H_{25}FO_3Si$ [M + Na$^+$]: 347.1449 Found: 347.1445.

*(±)-Methyl 3-[(tert-butyldimethylsilyl)oxy]-2-methylidenenonanoate (**21**)*: > 99% yield; amorphous solid; mp 102-103 ºC; IR (film) ν_{max}/cm^{-1}: 2929, 2859, 1719, 1249, 1090, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.17-6.21 (m, 1H), 5.87-5.90 (m, 1H), 4.52-4.61 (m, 1H), 3.72 (s, 3H), 1.18-1.65 (m, 10H), 0.78-0.92 (m, 12H), 0.04 (s, 3H), –0.04 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.7, 144.1, 124.2, 70.2, 51.5, 37.8, 31.8, 29.1, 25.7, 24.9, 22.6, 18.1, 14.0, –4.8, –5.1; HRMS (ESI TOF) Calcd. for $C_{17}H_{34}O_3Si$ [M + Na$^+$]: 337.2169. Found: 337.2168.

*(±)-Methyl-3-[(tert-butyldimethylsilyl)oxy]-2-methyleneoctadecanoate (**22**)*: 70% yield; viscous colorless oil; IR (film) ν_{max}/cm^{-1}: 2926, 2855, 1722, 1463, 1257, 1092; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.19-6.21 (m, 1H), 5.90 (t, 1H, *J* 1.6 Hz), 4.56-4.61 (m, 1H), 3.75 (s, 3H),

1.18-1.63 (m, 28H), 0.81-0.93 (m, 12H), 0.05 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 166.7, 144.2, 124.2, 70.2, 51.6, 37.9, 31.9, 29.7, 29.63, 29.6, 29.55, 29.5, 29.3, 25.8, 22.7, 18.1, 14.1, –4.8, –5.1; HRMS (ESI TOF) Calcd. for $C_{26}H_{52}O_3Si$ [M + Na]$^+$: 463.3578. Found: 463.3572.

General procedure for hydrolysis of silylated esters

To a solution of silylated MBH adduct (1-3 mmol) in a mixture of water:acetonitrile (1:1) was added LiOH (10 equiv.). The resulting solution was stirred for 4 h at 50-60 °C. Then, the solvents were removed under reduced pressure and the crude mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was filtered through silica gel (ethyl acetate as solvent) to provide the corresponding carboxylic acids in almost quantitative yields, for most cases > 99%.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](2-nitrophenyl) methyl}prop-2-enoic acid (**23**)*: 97% yield; viscous pale yellow oil; IR (film) ν_{max}/cm^{-1}: 2945, 2864, 2353, 1703, 1531, 1258, 1090, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.81 (d, 1H, *J* 8.0 Hz), 7.71 (d, 1H, *J* 8.0 Hz), 7.57 (t, 1H, *J* 7.5 Hz), 7.38 (t, 1H, *J* 7.5 Hz), 6.40 (s, 1H), 6.34 (s, 1H), 6.04 (s, 1H), 0.90 (s, 9H), 0.13 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.4, 148.1, 142.4, 137.3, 132.7, 129.5, 128.2, 127.2, 124.0, 66.6, 25.7, 18.1, –4.9; HRMS (ESI TOF) Calcd. for $C_{16}H_{23}NO_5Si$ [M + Na$^+$]: 360.1238. Found: 360.1237.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](3-chlorophenyl) methyl}prop-2-enoic acid (**24**)*: 99% yield; viscous colorless oil; IR (film) ν_{max}/cm^{-1}: 2949, 2929, 2851, 1691, 1437, 1254, 1074, 833, 780; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.34 (s, 1H), 7.18-7.29 (m, 3H), 6.43 (s, 1H), 6.19 (s, 1H), 5.54 (s, 1H), 0.88 (s, 9H), 0.06 (s, 3H), –0.07 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.1, 144.4, 142.6, 134.0, 129.4, 127.7, 127.0, 125.1, 71.9, 25.7, 18.1, –5.0; HRMS (ESI TOF) Calcd. for $C_{16}H_{23}O_3ClSi$ [M + Na$^+$]: 349.0918. Found: 349.1003.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](phenyl)methyl} prop-2-enoic acid (**25**)*: 99% yield; yellowish oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.20-7.41 (m, 5H), 6.39 (s, 1H), 6.13 (s, 1H), 5.58 (s, 1H), 0.88 (s, 9H), 0.07 (s, 3H), –0.07 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 169.8, 142.9, 141.9, 128.1, 127.6, 126.8, 126.4, 72.8, 25.7, 18.2, –5.0; HRMS (ESI TOF) Calcd. for $C_{16}H_{24}O_3Si$ [M + Na$^+$]: 315.1393. Found: 315.1338.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](4-methoxyphenyl) methyl}prop-2-enoic acid (**26**)*: 98% yield; viscous colorless oil; IR (film) ν_{max}/cm^{-1}: 2953, 2925, 2847, 1691, 1507, 1245, 1074, 837, 775; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.25 (d, 2H, *J* 7.0 Hz), 6.82 (d, 2H, *J* 7.0 Hz), 6.35 (s, 1H), 6.11 (s, 1H), 5.52 (s, 1H), 3.79 (s, 3H), 0.89 (s, 9H), 0.09 (s, 3H), -0.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 158.9, 143.1, 134.2, 128.1, 126.0, 113.5, 72.4, 55.2, 25.7, 18.1, –4.9, –5.1; HRMS (ESI TOF) Calcd. for $C_{17}H_{26}O_4Si$ [M + Na$^+$]: 345.1493. Found: 345.1490.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](3,4,5-trimethoxy-phenyl)methyl}prop-2-enoic acid (**27**)*: 99% yield; viscous oil; IR (film) ν_{max}/cm^{-1}: 2955, 2923, 2849, 1692, 1509, 1243, 1077; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.58 (s, 2H), 6.37 (s, 1H), 6.08 (s, 1H), 5.53 (s, 1H), 3.81 (s, 9H), 0.89 (s, 9H), 0.06 (s, 3H), –0.05 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.9, 152.8, 143.3, 137.9, 137.1, 126.4, 103.7, 72.3, 60.8, 56.0, 25.7, 18.2, –4.9, –5.1; HRMS (ESI TOF) Calcd. for $C_{19}H_{30}O_6Si$ [M + Na$^+$]: 405.1709. Found: 405.1566.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](thiophen-3-yl) methyl}prop-2-enoic acid (**28**)*: 99% yield; viscous colorless oil; IR (film) ν_{max}/cm^{-1}: 2959, 2931, 2857, 1691, 1459, 1259, 1074, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.20 (dd, 1H, *J* 5.0/1.3 Hz), 6.85-6.97 (m, 2H), 6.45 (t, 1H, *J* 1.0 Hz), 6.23 (t, 1H, *J* 1.3 Hz), 5.87 (s, 1H), 0.92 (s, 9H), 0.10 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 170.8, 146.9, 142.8, 126.9, 126.4, 124.8, 124.5, 68.3, 25.7, 18.2, –5.1, –5.14; HRMS (ESI TOF) Calcd. for $C_{14}H_{22}O_3SSi$ [M + Na$^+$]: 321.0957. Found: 321.0883.

*(±)-2-{[(tert-Butyldimethylsilyl)oxy](2-fluorophenyl) methyl}prop-2-enoic acid (**29**)*: 99% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2951, 2928, 2850, 1692, 1072, 832, 782; ^{1}H NMR (250 MHz, $CDCl_3$): δ 10.44 (s, 1H, COO<u>H</u>), 7.34 (dt, 1H, *J* 1.8/7.5 Hz), 7.18-7.29 (m, 1H), 6.95-7.15 (m, 2H), 6.47 (s, 1H), 6.16 (s, 1H), 5.92 (s, 1H), 0.87 (s, 9H), 0.09 (s, 3H), –0.08 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.0, 159.8 (d, *J* 246.1 Hz), 142.1, 129.3 (d, *J* 3.0 Hz), 129.1 (d, *J* 2.1 Hz), 128.8 (d, *J* 3.8 Hz), 127.3, 123.9 (d, *J* 3.5 Hz), 115.3 (d, *J* 22.0 Hz), 65.7, 51.6, 25.7, 18.1, –5.2, –5.24; HRMS (ESI TOF) Calcd. for $C_{16}H_{23}O_3FSi$ [M + Na$^+$]: 333.1298. Found: 333.1207.

*(±)-3-[(tert-Butyldimethylsilyl)oxy]-2-methylidene-pentanoic acid (**30**)*: fluid oil; 99% yield; IR (film) ν_{max}/cm^{-1}: 2923, 2854, 1691, 1253, 1084; ^{1}H NMR (250 MHz, $CDCl_3$): δ 11.60 (s, 1H, COO<u>H</u>), 6.41 (d, 1H, *J* 1.2 Hz), 6.00 (t, 1H, *J* 1.5 Hz), 4.55 (t, 1H, *J* 5.4 Hz), 1.41-1.80 (m, 2H), 0.78-1.00 (m, 12H), 0.08 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 171.6, 142.9, 127.2, 71.2, 30.3, 29.1,

25.7, 18.1, 9.1, −4.9, −5.1; HRMS (ESI TOF) Calcd. for $C_{12}H_{24}O_3Si$ [M + H$^+$]: 245.1573. Found: 245.1554.

*(±)-3-[(tert-Butyldimethylsilyl)oxy]-2-methylidenenonanoic acid (**31**)*: 98% yield; fluid oil; IR (film) ν_{max}/cm^{-1}: 2925, 2859, 1691, 1254, 1086, 833, 649; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.37 (s, 1H), 5.92 (s, 1H), 4.51-4.59 (m, 1H), 1.20-1.40 (m, 10H), 0.82-0.93 (m, 12H), 0.08 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$), δ: 170.6, 142.9, 126.9, 71.2, 37.7, 31.7, 29.1, 25.7, 25.0, 22.6, 18.1, 14.1, −5.0; HRMS (ESI TOF) Calcd. for $C_{16}H_{32}O_3Si$ [M + H$^+$]: 301.2199. Found: 301.2232.

*(±)-3-[(tert-Butyldimethylsilyl)oxy]-2-methyleneoctadecanoic acid (**32**)*: 99% yield; white solid; mp 45-47 °C; IR (film) ν_{max}/cm^{-1}: 2918, 2851, 1681, 1623, 1472, 1090, 838; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.34-6.36 (m, 1H), 5.86-5.88 (m, 1H), 4.53 (t, 1H, *J* 5.6 Hz), 1.45-1.63 (m, 2H), 1.18-1.39 (m, 26H), 0.83-0.93 (m, 12H), 0.1 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 169.7, 142.5, 126.8, 71.8, 37.6, 31.9, 29.7, 29.64, 29.6, 29.5, 29.5, 29.4, 29.3, 25.8, 25.1, 22.7, 18.1, 14.1, −4.8, −5.0; HRMS (ESI TOF) Calcd. for $C_{25}H_{50}O_3Si$ [M + H]$^+$: 427.3607. Found: 427.3599.

General procedure for the preparation of α-hydroxyketones (acyloins)

To a stirred 0.2 mol L^{-1} solution of carboxylic acid in acetone at 0 ºC was added triethylamine (2 equiv.) and ethyl chloroformate (1.5 equiv.). The mixture was stirred at 0 ºC and carbonate formation was observed by TLC after 5 min. After that, NaN_3 was added (2.5 equiv.). The resulting mixture was vigorously stirred for 2 h until the formation of a slightly apolar layer (acylazide formation). Then, the crude mixture was diluted in cold dichloromethane and washed with cold water. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. To this crude material, under an argon atmosphere, dry toluene (0.1 mol L^{-1}) was added and the mixture was refluxed for 2 h. The solvent was then removed under reduced pressure and the resulting product was diluted in water. The mixture was refluxed for 12 h. Then, the reaction mixture was coolled to room temperature and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by flash silica gel column chromatography (ethyl acetate:hexanes, up to 25:75) to provide the required acyloins. Yields refer to 3 steps from MBH adducts.

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(2-nitrophenyl)propan-2-one (**33**)*: 46% yield; pale yellow oil; IR (film) ν_{max}/cm^{-1}: 2953, 2933, 2851, 1728, 1527, 1343, 1254, 1102, 833; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.97-8.03 (m, 1H), 7.58-7.77 (m, 2H), 7.42-7.51 (m, 1H), 5.72 (s, 1H), 2.31 (s, 3H), 0.91 (s, 9H), 0.16 (s, 3H), −0.07 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 205.8, 147.7, 135.0, 133.2, 129.2, 128.8, 124.8, 26.3, 25.6, 18.1, −5.0; HRMS (ESI TOF) Calcd. for $C_{15}H_{23}O_4NSi$ [M + H$^+$]: 310.1475. Found: 310.1600.

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(3-chlorophenyl)propan-2-one (**34**)*: 45% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2953, 2929, 2864, 1719, 1470, 1258, 1111, 775; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.43 (s, 1H), 7.23-7.33 (m, 3H), 5.00 (s, 1H), 2.12 (s, 3H), 0.96 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 208.5, 140.7, 134.5, 129.8, 128.2, 125.9, 123.9, 80.6, 25.7, 23.9, 18.2, −4.9; HRMS (ESI TOF) Calcd. for $C_{15}H_{23}O_2ClSi$ [M + Na$^+$]: 321.1053. Found: 321.1056

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-phenylpropan-2-one (**35**)*: 50% yield; pale yellow oil; IR (film) ν_{max}/cm^{-1}: 2949, 2929, 2855, 1711, 1258, 1102, 865, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.25-7.45 (m, 5H), 5.04 (s, 1H), 2.11 (s, 3H), 0.96 (s, 9H), 0.10 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.1, 199.5, 138.6, 128.5, 128.0, 125.8, 81.2, 25.7, 23.9, 18.2, −4.9, −5.2; HRMS (ESI TOF) Calcd. for $C_{15}H_{24}O_2Si$ [M + H$^+$]: 265.1624. Found: 265.1685.

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(4-methoxyphenyl)propan-2-one (**36**)*: 48% yield; pale yellow oil; IR (film) ν_{max}/cm^{-1}: 2949, 2855, 1715, 1511, 1090, 841, 784; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.30 (d, 2H, *J* 6.7 Hz), 6.87 (d, 2H, *J* 6.7 Hz), 4.99 (s, 1H), 3.80 (s, 3H), 2.11 (s, 3H), 0.94 (s, 9H), 0.08 (s, 3H), −0.01 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 209.2, 159.4, 130.7, 127.1, 113.9, 80.8, 55.2, 25.7, 23.8, 18.2, −5.0; HRMS (ESI TOF) Calcd. for $C_{16}H_{26}O_3Si$ [M + Na$^+$]: 317.1549. Found: 317.1505.

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(3,4,5-trimethoxyphenyl)propan-2-one (**37**)*: 42% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2947, 2853, 1714, 1512, 1089, 843; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.65 (s, 2H), 4.95 (s, 1H), 3.75-3.88 (m, 9H), 2.10 (s, 3H), 0.95 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 208.8, 153.3, 137.5, 134.0, 102.4, 80.9, 60.8, 56.0, 25.7, 23.7, 18.2, −4.9, −5.1; HRMS (ESI TOF) Calcd. for $C_{18}H_{30}O_5Si$ [M + Na$^+$]: 377.1760. Found: 377.1657.

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(thiophen-2-yl)propan-2-one (**38**)*: 44% yield; pale yellow oil; IR (film)

ν_{max}/cm^{-1}: 2949, 2851, 1712, 1091; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.22-7.28 (m, 1H), 6.96-7.01 (m, 2H), 5.24 (s, 1H), 2.20 (s, 3H), 0.95 (s, 9H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 207.7, 153.3, 142.6, 127.1, 125.2, 124.3, 77.8, 25.6, 23.7, 18.2, −5.1, −5.2; HRMS (ESI TOF) Calcd. for $C_{13}H_{22}O_2SSi$ [M + Na$^+$]: 293.1007. Found: 293.0922.

*(±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(2-fluorophenyl) propan-2-one (**39**)*: 41% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2951, 1720, 1471, 1256, 1109; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.47 (dt, 1H, *J* 1.8/7.5 Hz), 7.23-7.35 (m, 1H), 7.15 (dt, 1H, *J* 1.2/7.5 Hz), 7.00-7.09 (m, 1H), 5.34 (s, 1H), 2.18 (s, 3H), 0.92 (s, 9H), 0.11 (s, 3H), −0.05 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 207.1, 159.8 (d, *J* 245.4 Hz), 129.8 (d, *J* 8.1 Hz), 128.2 (d, *J* 3.8 Hz), 126.6 (d, *J* 14.3 Hz), 124.3 (d, *J* 3.5 Hz), 115.4 (d, *J* 21.5 Hz), 74.9, 25.6, 24.9, 18.1, −5.1, −5.2; HRMS (ESI TOF) Calcd. for $C_{15}H_{23}O_2FSi$ [M + Na$^+$]: 305.1349. Found: 305.1284.

*(±)-3-[(tert-Butyldimethylsilyl)oxy]pentan-2-one (**40**)*: 46% yield; colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.90 (dd, 1H, *J* 5.6/6.5 Hz), 2.13 (s, 3H), 1.50-1.71 (m, 2H), 0.77-0.93 (m, 12H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 212.5, 79.9, 27.8, 25.3, 18.0, 9.1, −5.0, −5.1; HRMS (ESI TOF) Calcd. for $C_{11}H_{24}O_2Si$ [M + H$^+$]: 217.1624. Found: 217.1608.

*(±)-3-[(tert-Butyldimethylsilyl)oxy]nonan-2-one (**41**)*: 42% yield; pale yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.92-4.03 (m, 1H), 2.15 (s, 3H), 1.18-1.45 (m, 10H), 0.82-1.09 (m, 12H), 0.05 (s, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 212.8, 79.0, 34.8, 31.7, 29.2, 25.7, 25.2, 24.7, 22.6, 18.1, 14.1, −4.9; HRMS (ESI TOF) Calcd. for $C_{15}H_{32}O_2Si$ [M + Na$^+$]: 295.4887. Found: 295.4849.

*(±)-3-[(tert-Butyldimethylsilyl)oxy]octadecan-2-one (**42**)*: 40% yield; colorless viscous oil; IR (film) ν_{max}/cm^{-1}: 2926, 2855, 1719, 1465, 1253, 1104; ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.97 (dd, 1H, *J* 5.3/6.9 Hz), 2.15 (s, 3H), 1.46-1.55 (m, 2H), 1.17-1.40 (m, 26H), 0.83-0.97 (m, 12H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 212.7, 79.0, 34.8, 31.9, 29.7, 29.64, 29.6, 29.5, 29.4, 29.3, 25.7, 25.2, 24.7, 22.7, 18.1, 14.1, −5.0; HRMS (ESI TOF) Calcd. for $C_{24}H_{50}O_2Si$ [M + Na$^+$]: 421.3478. Found: 421.3453.

General procedure for the diastereoselective preparation of vicinal alcohols

To a 0.2 mol L^{-1} methanolic solution of acyloins was added an amine (3 equiv.). The resulting solution was vigorously stirred at room temperature for 1 h. After, the solution was cooled to −78 °C and $LiBH_4$ (1.2 equiv.) was added. The mixture was then warmed to room temperature and stirred for 12 h. Then, the medium was diluted with ethyl acetate (15 mL) and the organic phase was washed with water (5 × 7 mL), brine (10 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was purified through silica gel (solvent: hexanes:ethyl acetate, up to 65:35) to provide the corresponding vicinal aminoalcohols, in good yields and in high diastereoselectivities.

*(±)-1,2-anti-1-[(tert-Butyldimethylsilyl)oxy]-1-(3-chlorophenyl)propan-2-yl](2-phenylethyl)amine (**43**)*: 79% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2955, 2929, 2857, 1471, 1254, 1075, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.08-7.32 (m, 9H), 4.55 (d, 1H, *J* 4.7 Hz), 2.62-2.99 (m, 5H), 0.98 (d, 3H, *J* 6.4 Hz), 0.86 (s, 9H), −0.003 (s, 3H), −0.20 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 145.1, 139.9, 133.9, 129.2, 128.6, 128.4, 127.3, 126.8, 126.1, 124.8, 77.0, 59.7, 48.6, 36.5, 25.8, 18.1, 14.9, −4.6, −5.1; HRMS (ESI TOF) Calcd. for $C_{23}H_{34}ClNOSi$ [M + H$^+$]: 404.2177. Found: 404.1996.

*(±)-1,2-anti-Benzyl-[1-[(tert-butyldimethylsilyl)oxy]-1-(3-chlorophenyl)propan-2-yl]amine (**44**)*: 77% yield; yellowish oil. IR (film) ν_{max}/cm^{-1}: 2929, 2857, 1471, 1255, 1075, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.12-7.37 (m, 9H), 4.63 (d, 1H, *J* 4.8 Hz), 3.82 (d, 1H, *J* 13.5 Hz), 3.71 (d, 1H, *J* 13.5 Hz), 2.77 (dq, 1H, *J* 4.8/6.4 Hz), 1.02 (d, 3H, *J* 6.4 Hz), 0.89 (s, 9H), 0.05 (s, 3H), −0.16 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 145.2, 140.4, 133.9, 129.2, 128.3, 127.8, 127.3, 127.0, 126.8, 125.0, 77.1, 58.6, 51.0, 25.8, 18.1, 15.1, −4.6, −4.9; HRMS (ESI TOF) Calcd. for $C_{22}H_{32}ONClSi$ [M + H$^+$]: 390.2020. Found: 370.1797.

*(±)-1,2-anti-{1-[(tert-Butyldimethylsilyl)oxy]-1-phenylpropan-2-yl}(2-phenylethyl)amine (**45**)*: 85% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2928, 2857, 1453, 1255, 1063, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.09-7.32 (m, 10H), 4.58 (d, 1H, *J* 5.0 Hz), 2.61-2.99 (m, 5H), 1.02 (d, 3H, *J* 6.4 Hz), 0.86 (s, 9H), −0.001 (s, 3H), −0.22 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 142.9, 140.0, 128.6, 128.4, 127.9, 127.1, 126.7, 126.0, 77.6, 59.8, 48.7, 36.6, 25.8, 18.1, 15.1, −4.6, −5.1; HRMS (ESI TOF) Calcd. for $C_{23}H_{35}ONSi$ [M + H$^+$]: 370.2566. Found: 370.2747.

*(±)-1,2-anti-Benzyl({1-[(tert-butyldimethylsilyl)oxy]-1-phenylpropan-2-yl})amine (**46**)*: 83% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2956, 2929, 2857, 1493, 1254, 1063, 1028, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.12-7.38 (m,

10H), 4.64 (d, 1H, *J* 5.1 Hz), 3.81 (d, 1H, *J* 13.5 Hz), 3.72 (d, 1H, *J* 13.5 Hz), 2.80 (dq, 1H, *J* 5.1/6.4 Hz), 1.05 (d, 3H, *J* 6.4 Hz), 0.90 (s, 9H), 0.05 (s, 3H), –0.18 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 142.9, 140.6, 128.3, 127.9, 127.8, 127.1, 126.9, 126.7, 77.8, 58.7, 51.0, 25.8, 18.2, 15.4, –4.5, –5.0; HRMS (ESI TOF) Calcd. for $C_{22}H_{33}ONSi$ [M + H$^+$]: 356.2410. Found: 356.2561.

*(±)-1,2-anti-{1-[(tert-Butyldimethylsilyl)oxy]-1-phenylpropan-2-yl}(prop-2-en-1-yl)amine (**47**)*: 82% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2956, 2929, 2857, 1471, 1255, 1063, 867, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.17-7.42 (m, 5H), 5.73-5.95 (m, 1H), 5.00-5.21 (m, 2H), 4.65 (d, 1H, *J* 4.8 Hz), 3.12-3.39 (m, 2H), 2.80 (dq, 1H, *J* 4.8/6.4 Hz), 0.99 (d, 3H, *J* 6.4 Hz), 0.90 (s, 9H), 0.05 (s, 3H), –0.19 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 142.9, 137.0, 128.3, 127.9, 127.1, 126.7, 115.4, 77.3, 58.9, 49.6, 25.8, 18.2, 14.9, –4.5, –5.0; HRMS (ESI TOF) Calcd. for $C_{18}H_{31}ONSi$ [M + H$^+$]: 306.2253. Found: 306.2394.

*(±)-1,2-anti-N-{1-[(tert-Butyldimethylsilyl)oxy]-1-phenylpropan-2-yl}cyclohexanamine (**48**)*: 80% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2928, 2855, 1451, 1255, 1066, 862, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.15-7.40 (m, 5H), 4.61 (d, 1H, *J* 4.7 Hz), 2.89 (dq, 1H, *J* 4.7/6.3 Hz), 2.41-2.60 (m, 1H), 1.50-1.92 (m, 6H), 1.09-1.35 (m, 4H), 0.97 (d, 3H, *J* 6.3 Hz), 0.90 (s, 9H), 0.04 (s, 3H), –0.20 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 143.3, 127.8, 127.0, 77.5, 55.8, 52.9, 34.1, 33.1, 26.2, 25.6, 25.0, 24.9, 18.2, 15.5, –4.5, –5.0; HRMS (ESI TOF) Calcd. for $C_{21}H_{37}ONSi$ [M + H$^+$]: 348.2723. Found: 348.2834.

*(±)-1,2-anti-{1-[(tert-Butyldimethylsilyl)oxy]-1-(3,4,5-trimethoxyphenyl)propan-2-yl}(2-phenylethyl)amine (**49**)*: 81% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2933, 1592, 1455, 1321, 1128, 836, 776; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.05-7.27 (m, 5H), 6.48 (s, 2H), 4.45 (d, 1H, *J* 5.4 Hz), 3.84 (s, 3H), 3.81 (s, 6H), 2.62-3.00 (m, 5H), 1.05 (d, 3H, *J* 6.1 Hz), 0.86 (s, 9H), 0.01 (s, 3H), –0.19 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 152.8, 139.8, 138.6, 136.8, 128.5, 128.4, 126.1, 103.4, 77.9, 60.9, 59.9, 56.0, 48.6, 36.4, 25.8, 18.1, 15.3, –4.5, –5.1; HRMS (ESI TOF) Calcd. for $C_{26}H_{41}O_4NSi$ [M + H$^+$]: 460.2805. Found: 460.2871.

*(±)-1,2-anti-{1-[(tert-Butyldimethylsilyl)oxy]-1-(3,4,5-trimethoxyphenyl)propan-2-yl}(prop-2-en-1-yl)amine (**50**)*: 80% yield; colorless oil; IR (film) ν_{max}/cm^{-1}: 2930, 2857, 1592, 1420, 1330, 1130, 869, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 6.54 (s, 2H), 5.75-5.92 (m, 1H), 5.01-5.17 (m, 2H), 4.55 (d, 1H, *J* 5.0 Hz), 3.84 (s, 9H), 3.10-3.37 (m, 2H), 2.80 (dq, 1H, *J* 5.0/6.3 Hz), 1.03 (d, 3H, *J* 6.3 Hz), 0.91 (s, 9H), 0.06 (s, 3H), –0.14 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 152.8, 138.7, 136.9, 136.8, 115.4, 103.4, 77.6, 60.9, 59.0, 56.0, 49.6, 25.8, 18.2, 15.1, –4.5, –5.0; HRMS (ESI TOF) Calcd. for $C_{21}H_{37}O_4NSi$ [M + H$^+$]: 396.2570. Found: 396.2693.

*(±)-1,2-anti-{1-[(tert-Butyldimethylsilyl)oxy]-1-(thiophen-2-yl)propan-2-yl}(2-phenylethyl)amine (**51**)*: 82% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2955, 2929, 2857, 1471, 1253, 1075, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.09-7.27 (m, 6H), 6.80-6.93 (m, 2H), 4.76 (d, *J* 5.6 Hz, 1H), 2.63-2.99 (m, 5H), 1.08 (d, 3H, *J* 6.3 Hz), 0.85 (s, 9H), 0.02 (s, 3H), –0.15 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 146.9, 140.0, 128.6, 128.4, 126.002, 126.0, 124.5, 124.3, 74.7, 60.1, 48.7, 36.5, 25.7, 18.1, 15.9, –4.6, –5.1; HRMS (ESI TOF) Calcd. for $C_{21}H_{33}ONSSi$ [M + H$^+$]: 376.2130. Found: 376.2141.

*(±)-1,2-anti-{1-[(tert-Butyldimethylsilyl)oxy]-1-(2-fluorophenyl)propan-2-yl}(2-phenylethyl)amine (**52**)*: 78% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2857, 1486, 1254, 1033, 837; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.43 (dt, 1H, J_1 1.8, J_2 7.5 Hz), 7.05-7.35 (m, 8H), 6.90-7.01 (m, 1H), 5.07 (d, 1H, *J* 3.9 Hz), 2.62-2.99 (m, 5H), 0.97 (d, 3H, *J* 6.5 Hz), 0.87 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 159.4 (d, *J* 242.8 Hz), 140.2, 130.0 (d, *J* 13.3 Hz), 128.8 (m, C-Ar), 128.4 (m, C-Ar), 126.0, 123.7 (d, *J* 3.4 Hz), 114.8 (d, *J* 22.0 Hz), 70.0, 58.3, 48.7, 36.7, 25.8, 18.1, 14.8, –4.8, –5.2; HRMS (ESI TOF) Calcd. for $C_{23}H_{34}ONFSi$ [M + H$^+$]: 388.2472. Found: 388.2512.

*(±)-1,2-anti-{3-[(tert-Butyldimethylsilyl)oxy]pentan-2-yl}(2-phenylethyl)amine (**53**)*: 73% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2958, 2930, 2857, 1470, 1254, 1007, 835; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.12-7.37 (m, 5H), 3.49-3.60 (m, 1H), 2.60-2.99 (m, 5H), 1.38-1.52 (m, 2H), 0.98 (d, 3H, *J* 6.5 Hz), 0.78-0.90 (m, 12H), 0.03 (s, 3H), –0.01 (s, 3H); ^{13}C RMN (62.5 MHz, $CDCl_3$): δ 140.2, 128.7, 128.4, 126.1, 76.6, 56.9, 49.3, 36.9, 25.8, 25.3, 18.0, 15.0, 10.4, –4.4, –4.5; HRMS (ESI TOF) Calcd. for $C_{19}H_{35}ONSi$ [M + H$^+$]: 322.2566. Found: 322.2550.

*(±)-1,2-anti-{3-[(tert-Butyldimethylsilyl)oxy]pentan-2-yl}(decyl)amine (**54**)*: 71% yield; yellowish oil; IR (film) ν_{max}/cm^{-1}: 2958, 2928, 2855, 1463, 1254, 836; ^{1}H NMR (250 MHz, $CDCl_3$): δ 3.50-3.61 (m, 1H), 2.54-2.71 (m, 2H), 2.38-2.51 (m, 1H), 1.38-1.60 (m, 6H), 1.26 (br, 16H), 0.96 (d, 3H, *J* 6.5 Hz), 0.81-0.91 (m, 12H), 0.05 (s, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 76.6, 56.9, 47.8, 31.9, 30.4,

29.6, 29.5, 29.3, 27.5, 25.8, 25.2, 22.6, 18.1, 15.1, 14.1, 10.5, –4.4, –4.42; HRMS (ESI TOF) Calcd. for $C_{21}H_{47}NOSi$ [M + H^+]: 358.3505. Found: 358.3428.

*Synthesis of (±)-1-[(tert-Butyldimethylsilyl)oxy]-1-(3-chlorophenyl)propan-2-ol (**60**)*

To a solution of acyloin **34** (170 mg, 0.57 mmol) in anhydrous methanol (10 mL), under argon atmosphere and at 0 °C was added $NaBH_4$ (108.3 mg, 2.85 mmol). The resulting mixture was stirred for 10 min, after that 1 mL of water was added and the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate (15 mL) and the organic phase was washed with brine (5 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum to provide the alcohol **60**, in almost quantitative yield. Thus, it was used to the next step without purification. Colorless oil; IR (film) ν_{max}/cm^{-1}: 3448, 2949, 2933, 2851, 1462, 1254, 1070, 833, 775; ^{1}H NMR (250 MHz, $CDCl_3$): δ (mixture of diastereomers) 7.12-7.35 (m, 6H), 4.52 (d, *J* 4.7 Hz, H_a'), 4.28 (d, *J* 6.5 Hz, H_a), 3.80 (q, *J* 4.7 Hz, H_b'), 3.70 (q, *J* 6.5 Hz, H_b), 2.36 (s, 1H), 1.06 (d3H,, *J* 6.5 Hz, C$\underline{H}_3'$), 1.00, (d, 3H, *J* 6.5 Hz, C$\underline{H}_3$), 0.89 (s, 9H), 0.05 (s, 3H), –0.12 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ (diastereomeric mixture) 143.7, 143.3, 134.1, 133.9, 129.5, 129.3, 127.9, 127.7, 127.1, 125.2, 125.1, 80.0, 78.2, 72.4, 71.9, 25.8, 18.2, 18.1, 17.9, 17.6, –4.9; HRMS (ESI TOF) Calcd. for $C_{15}H_{25}ClO_2Si$ [M + H^+]: 301.1391. Found: 301.1577.

*Synthesis of (±)-1-(3-chlorophenyl)propane-1,2-diol (**61**)*

To a solution of alcohol (±)-**60** (100 mg, 0.34 mmol) in THF (6 mL) at 0° C was added a solution of TBAF (0.41 mL, 1 mol L^{-1} in toluene). The mixture was stirred for 5 min and was warmed to room temperature. After 2 h, a mixture of water (5 mL) and ethyl acetate (15 mL) was added to the reaction medium. The organic phase was separated, washed with brine (5 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was filtered through silica gel (solvent: ethyl acetate) to provide the diol (±)-**61**, in 97% yield. Colorless oil; IR (film) ν_{max}/cm^{-1}: 3395, 2978, 2876, 1569, 1426, 1082, 1037, 780, 694; ^{1}H NMR (250 MHz, $CDCl_3$): δ (diastereomeric mixture) 7.16-7.39 (m, 6H), 4.67 (d, *J* 4.0 Hz, H_a'), 4.33 (d, *J* 7.1 Hz, H_a), 3.92-4.07 (m, H_b'), 3.81 (q, *J* 7.1 Hz, H_b), 2.62 (s, 3H, O$\underline{H}$), 1.00-1.13 (m, 5H, C$\underline{H}_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (diastereomeric mixture) 143.1, 142.4, 134.4, 129.7, 129.5, 128.2, 127.8, 127.0, 126.7, 125.1, 124.8, 78.6, 77.2, 71.9, 71.0, 18.7, 16.9; HRMS (ESI TOF) Calcd. for $C_9H_{11}O_2Cl$ [M + Na^+]: 209.6252. Found: 209.6223.

*Synthesis of (±)-1-(3-chlorophenyl)-2-hydroxypropan-1-one (**59**)*

To a solution of diol (±)-**61** (70 mg, 0.38 mmol) in DMSO (1 mL) was slowly added 45% IBX (236.4 mg, 0.38 mmol) at room temperature. Caution: addition time 15 h, faster addition will give a diketone product. The mixture was stirred for 30 h. After that, the reaction medium was diluted with water (5 mL) and ethyl acetate (15 mL). The organic phase was separated, washed with brine (5 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was purified by silica gel column chromatography (solvent: hexanes:ethyl acetate, up to 60:40) to provide the acyloin (±)-**59**, in 85% yield. Yellowish oil; IR (film) ν_{max}/cm^{-1}: 3436, 2982, 2921, 2843, 1687, 1569, 1262, 1123, 1070, 1033, 739; ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.77-7.82 (m, 1H), 7.57-7.62 (m, 1H), 7.46 (t, 1H, *J* 7.9 Hz), 5.12 (q, 1H, *J* 7.0 Hz, C$\underline{H}$), 1.45 (d, 3H, *J* 7.0 Hz, C$\underline{H}_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 201.3, 135.3, 134.9, 133.9, 130.2, 128.7, 126.6, 77.2, 69.5, 22.1; HRMS (ESI TOF) Calcd. for $C_9H_9O_2Cl$ [M + Na^+]: 207.6093. Found: 207.6075.

*Synthesis of (±)-2-(tert-butylamino)-1-(3-chlorophenyl) propan-1-one (bupropion) (**1**)*

To a solution of acyloin (±)-**59** (30 mg, 0.16 mmol) in 3 mL of anhydrous CH_2Cl_2, at –78 °C, was added triflic anhydride (50 mg, 0.177 mmol, 29.81 µL) and 2,6-lutidine (26 mg, 0.24 mmol, 28.26 µL). The resulting mixture was cooled to –40 °C and stirred for 30 min. After that, the organic phase was washed with brine (5 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was immediately dissolved in dry CH_2Cl_2 and the solution was cooled to –40 °C. Then *tert*-butylamine (29.6 mg, 0.41 mmol, 42.5 µL) was added. The mixture was stirred for 2 h at –40 °C, warmed to 0 °C and kept at this final temperature for 12 h. After, the reaction medium was diluted with dichloromethane (10 mL). The organic phase was separated, washed with sodium bicarbonate (5 mL), water (5 mL), brine (5 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified through silica gel (solvent: hexanes:ethyl acetate, up to 60:40) to provide (±)-**1** as a white solid, in 75% yield; mp 233-234 °C (as hydrochloride;[41] 233-234 °C); ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.83-7.90 (m, 1H), 8.03-8.11 (m, 1H), 7.97-7.99 (m, 1H), 6.11 (q, 1H, *J* 7.0 Hz, C$\underline{H}$), 4.65 (s, 1H, N$\underline{H}$), 1.67 (t, 3H, *J* 7.0 Hz, C$\underline{H}_3$), 1.44 (s, 9H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 195.7, 136.0, 135.2, 133.5, 130.1, 128.6, 126.5, 71.9,

58.1, 30.3, 17.0; HRMS (ESI TOF) Calcd. for $C_{13}H_{18}OClN$ [M + Na^+]: 262.7309. Found: 262.7299.

*Synthesis of (±)-1,2-anti-benzyl({3-[(tert-butyldimethylsilyl)oxy]octadecan-2-yl})amine (**62**)*

To a stirred mixture of acyloin (±)-**42** (0.2 g, 0.502 mmol) and molecular sieves (4 Å) in anhydrous dichloromethane (3 mL), under an argon atmosphere, was added distilled benzylamine (0.268 g, 0.27 mL, 2.51 mmol). The resulting mixture was kept at 40 °C for 7 h. Then, the reaction was cooled to 0 °C and $NaBH_3CN$ (0.038 g, 0.6 mmol) was added in three small portions at 40 min. intervals. The reaction was warmed to room temperature and stirred for 12 h. The solvent was removed under reduced pressure and the residue was dissolved with ethyl acetate. The organic phase was filtered, washed with distilled water (3 × 10 mL), brine (15 mL), dried over anhydrous sodium sulfate and evaporated. The crude residue was purified by silica gel column chromatography (ethyl acetate:hexane, 25:75) to provide *anti* aminoalcohol **62** (0.19 g), as a viscous colorless oil, in 70% yield; IR (film) ν_{max}/cm^{-1}: 2925, 2854, 1463, 1254, 1030; ^1H NMR (250 MHz, $CDCl_3$): δ 7.22-7.32 (m, 5H), 3.89 (d, 1H, *J* 13.2 Hz), 3.67 (d, 1H, *J* 13.2 Hz), 3.54 (q, 1H, *J* 4.6 Hz), 2.69 (q, 1H, *J* 6.0 Hz), 1.32-1.48 (m, 2H), 1.17-1.35 (m, 26H), 1.02 (d, 3H, *J* 6.5 Hz), 0.82-0.92 (m, 12H), 0.04 (s, 3H), –0.02 (s, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 140.6, 128.3, 128.14, 128.1, 126.8, 75.4, 56.3, 51.5, 32.1, 31.9, 29.8, 29.7, 29.65, 29.6, 29.4, 26.1, 25.9, 22.7, 18.1, 15.2, 14.1, –4.3, –4.4; HRMS (ESI TOF) Calcd. for $C_{31}H_{59}NOSi$ [M + H]$^+$: 490.4439. Found: 490.4434.

*Synthesis of (±)-1,2-anti-[(2-aminooctadecan-3-yl)oxy](tert-butyl)dimethylsilane (**63**)*

To a stirred solution of aminoalcohol (±)-**62** (0.025 g, 0.05 mmol) in a mixture of dichloromethane (1.5 mL) and acetic acid (1.0 mL) was added 10% Pd/C (0.006 g). The resulting suspension was purged twice with hydrogen gas and kept under a hydrogen atmosphere. Then, the reaction was warmed at 50 °C and stirred for 20 h under hydrogen atmosphere. After that time, the reaction mixture was diluted with dichloromethane (10 mL) and the organic phase was washed with a saturated solution of $NaHCO_3$ (8 mL), dried over anhydrous sodium sulfate and evaporated. The crude residue was filtered over a plug of silica gel (dichloromethane:methanol, 97:3, as eluent) to provide silylated aminoalcohol (±)-**63** (0.018 g), as a viscous colorless oil, in 90% yield; IR (film) ν_{max}/cm^{-1}: 3409, 2926, 2855, 1682, 1465, 1255, 1084; ^1H NMR (250 MHz, $CDCl_3$): δ 3.45-3.60 (m, 1H), 2.85-2.99 (m, 1H), 1.10-1.45 (m, 28H), 1.01 (d, 3H, *J* 6.6 Hz), 0.80-0.91 (m, 12H), 0.0-0.10 (m, 6H); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 77.2, 56.3, 50.8, 31.9, 31.6, 29.8, 29.7, 29.6, 29.3, 25.9, 25.7, 22.7, 18.1, 17.9, 14.1, –4.3, –4.4; HRMS (ESI TOF) Calcd. for $C_{24}H_{53}NOSi$ [M + H]$^+$: 400.3964. Found: 400.3960.

*Synthesis of (±)-1,2-anti-2-aminooctadecan-3-ol (spisulosine) (**2**)*

To a stirred solution of aminoalcohol (±)-**63** (0.01 g, 0.025 mmol) in a mixture of dichloromethane (0.5 mL) and methanol (0.5 mL) was added a solution of concentrated hydrochloric acid (0.1 mL). The resulting mixture was warmed to 50 °C and stirred for 20 h. Then, the solvents were removed under reduced pressure and the residue was dissolved in dichloromethane (5 mL). To the stirred organic phase was added a saturated sodium bicarbonate solution (5 mL) and the resulting mixture was vigorously stirred for 30 min. The organic phase was separated, dried over anhydrous sodium sulfate and removed under reduced pressure. The crude residue was filtered over a plug of Florisil® to provide (±)-spisulosine (**1**, 7 mg), as a white solid, in 98% yield; mp 58-59 °C; IR (film) ν_{max}/cm^{-1}: 3348, 3297, 2955, 2919, 2851, 1607, 1471; ^1H NMR (250 MHz, $CDCl_3$): δ 3.39-3.47 (m, 1H), 2.88-3.06 (m, 1H), 1.64-1.88 (bs, 3H), 1.20-1.40 (m, 28H), 1.01 (d, 3H, *J* 6.5 Hz), 0.88 (t, 3H, *J* 7.0 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 74.7, 50.3, 32.4, 31.9, 29.8, 29.7, 29.6, 29.3, 26.2, 22.7, 16.8, 14.1; HRMS (ESI TOF) Calcd. for $C_{18}H_{40}NO$ [M + H]$^+$: 286.3110; Found 286.3088.

Supplementary Information

All the spectra of the synthesized compounds in this paper are available as supplementary file and are free of charge at http/jbcs.sbq.org.br as pdf file.

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Supplementary Information

Hyphenating the Curtius Rearrangement with Morita-Baylis-Hillman Adducts: Synthesis of Biologically Active Acyloins and Vicinal Aminoalcohols

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General

The ^{1}H and ^{13}C spectra were recorded on Bruker at 250 MHz and 62.5 MHz respectively. The ^{1}H and ^{13}C spectra were also recorded on Inova instrument at 500 MHz and 125 MHz, respectively. The high resolution mass spectra were recorded using a Q-TOF Micromass equipment (Waters, UK).

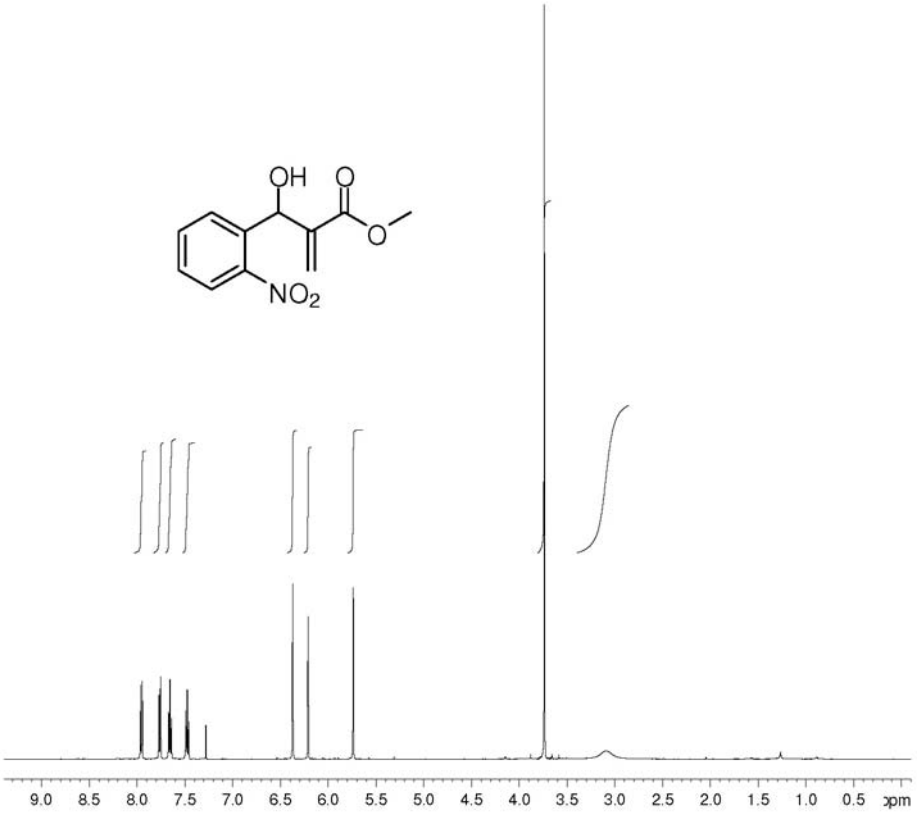

Figure S1. ^{1}H NMR ($CDCl_3$, 500 MHz) of MBH adduct **3**.

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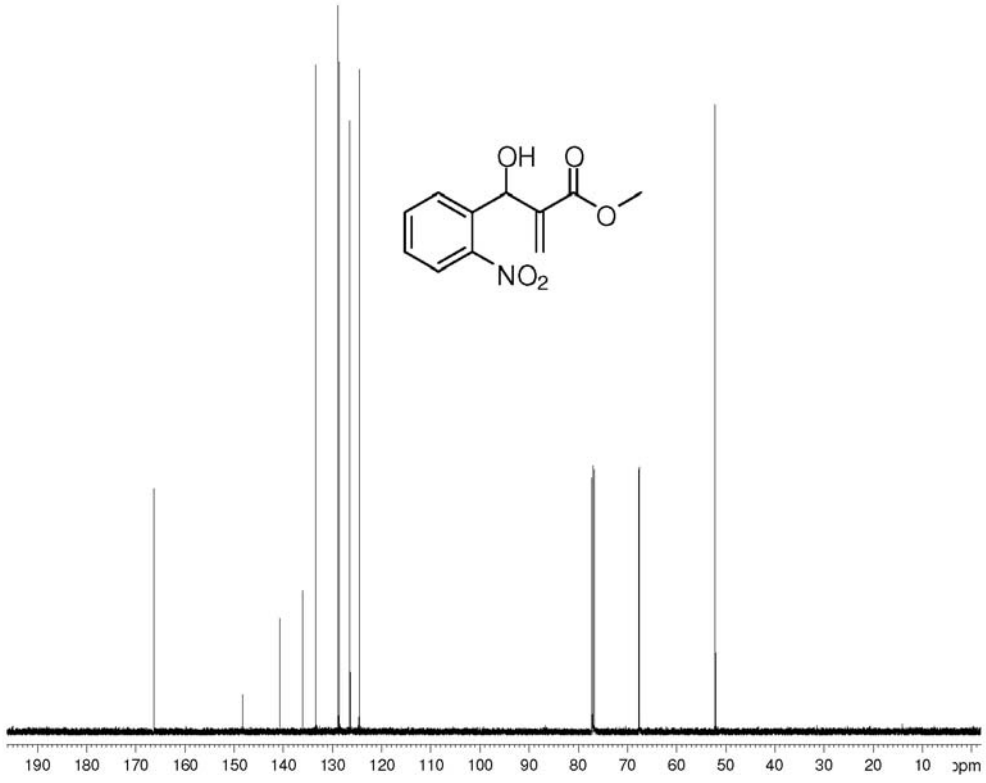

Figure S2. ^{13}C NMR ($CDCl_3$, 125 MHz) of MBH adduct **3**.

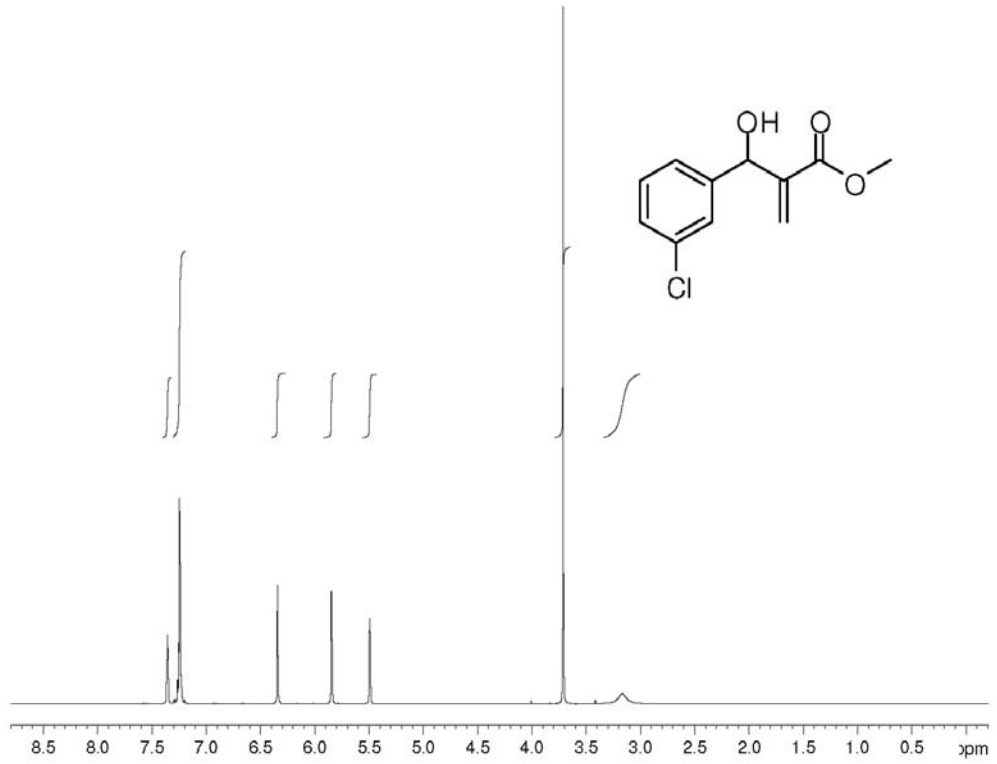

Figure S3. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **4**.

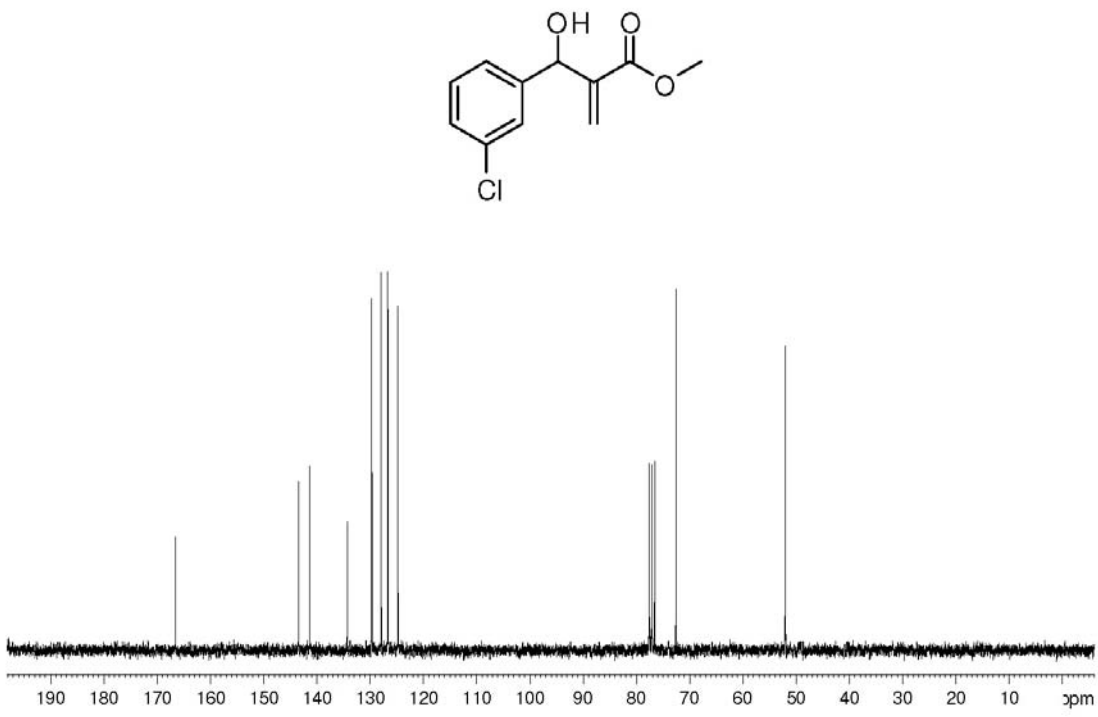

Figure S4. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **4**.

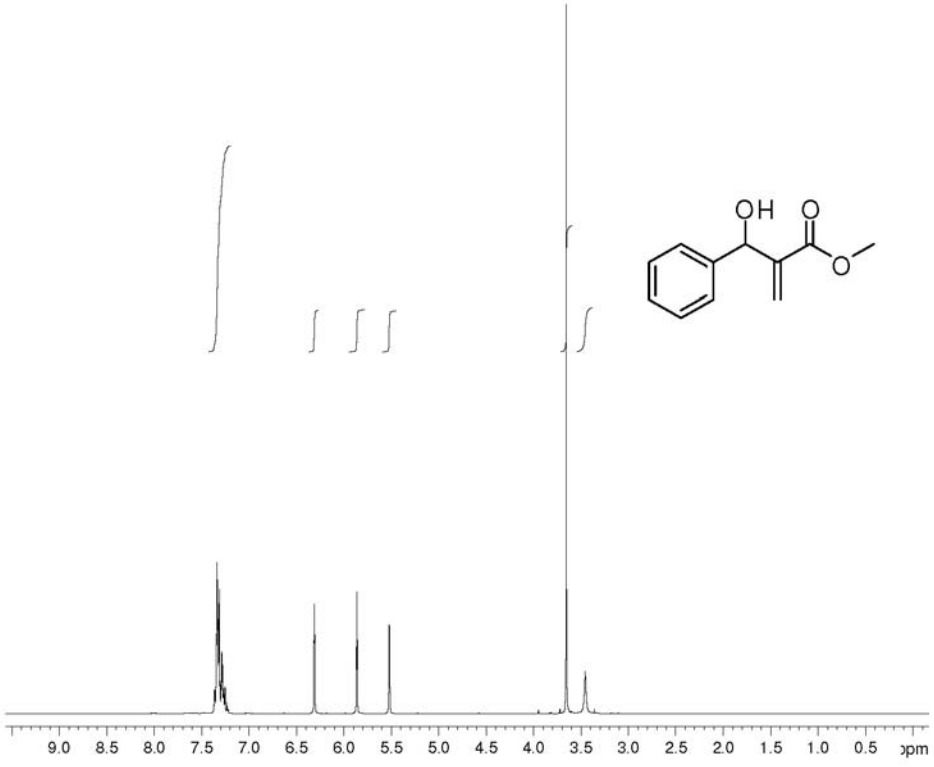

Figure S5. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **5**.

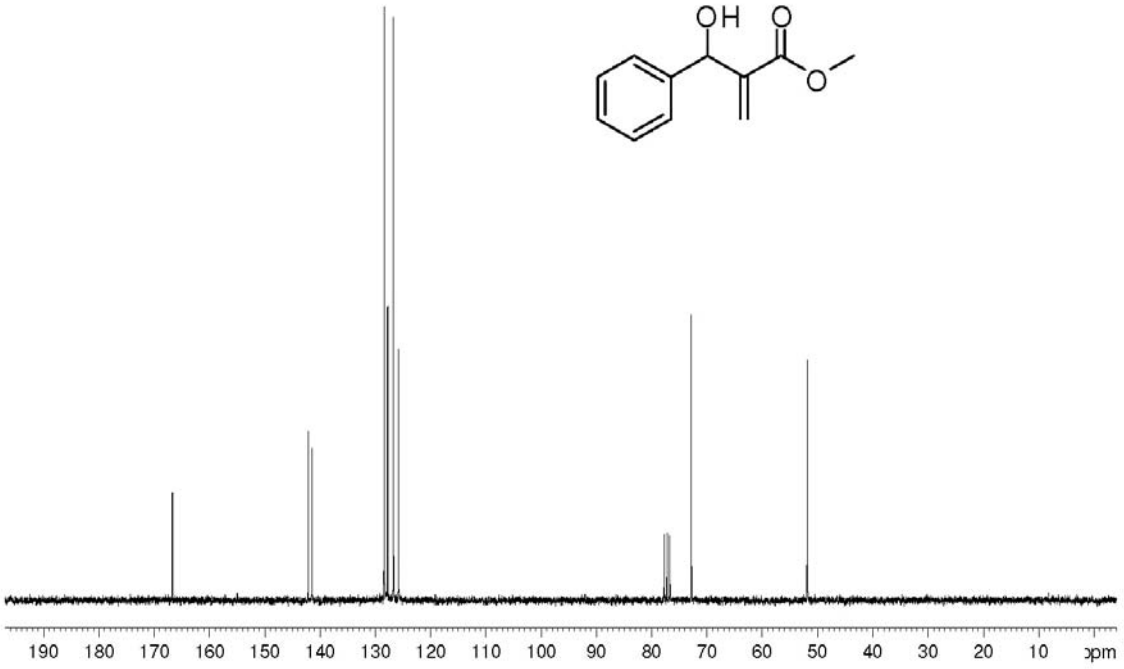

Figure S6. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **5**.

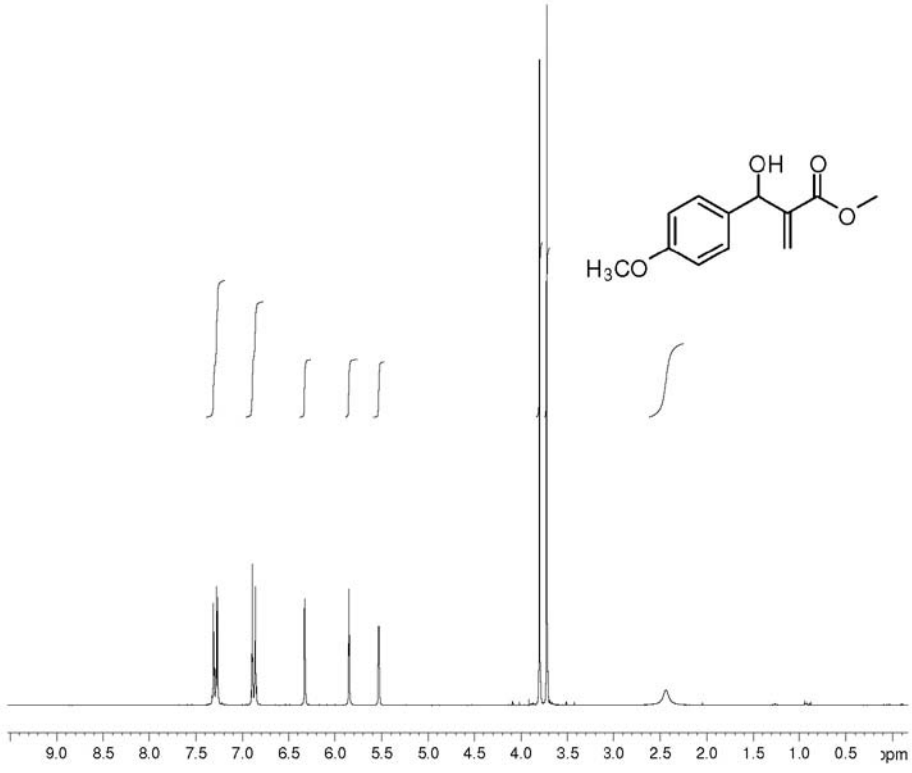

Figure S7. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **6**.

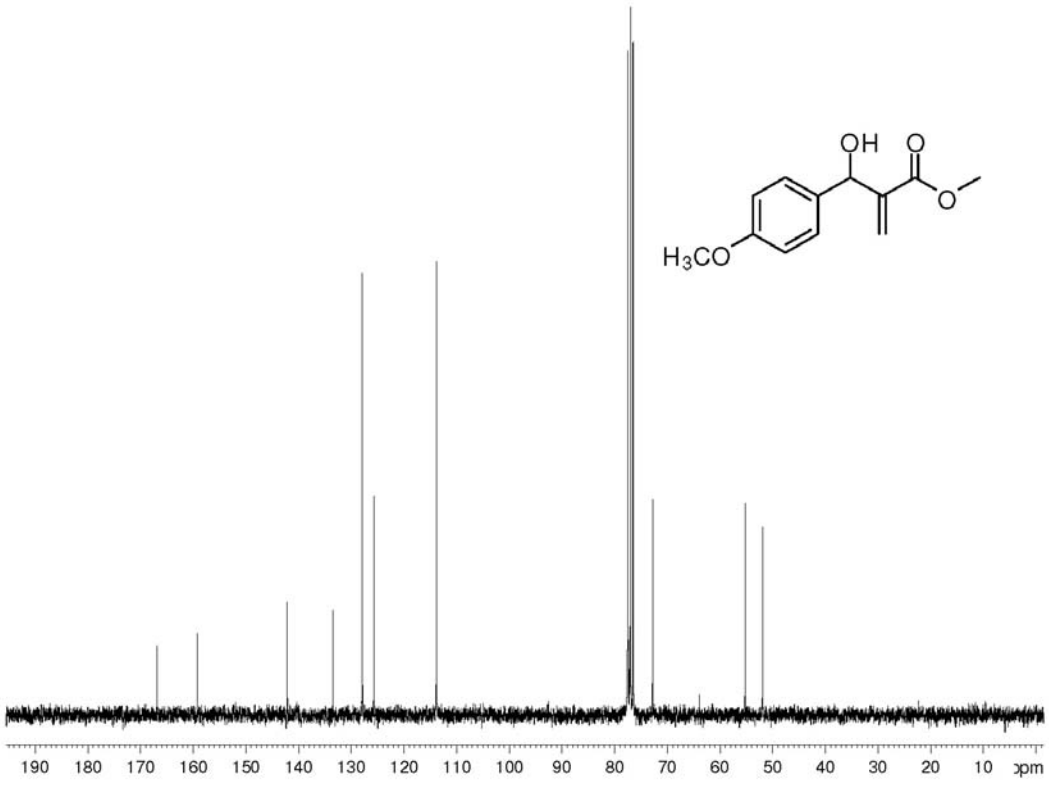

Figure S8. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **6**.

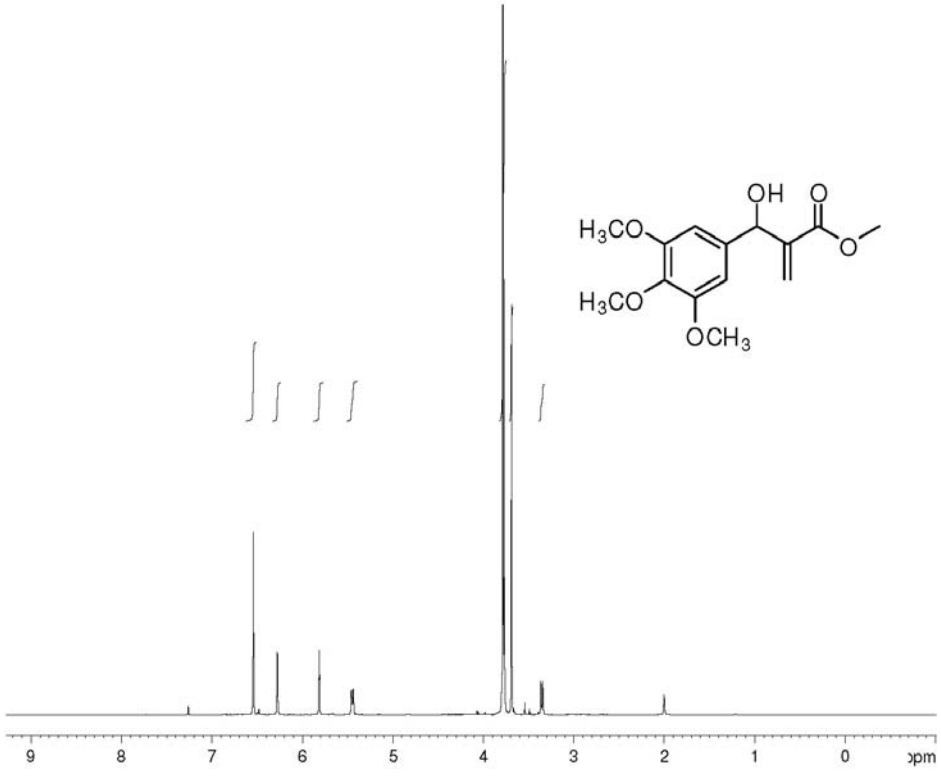

Figure S9. ^{1}H RMN ($CDCl_3$, 250 MHz) of MBH adduct **7**.

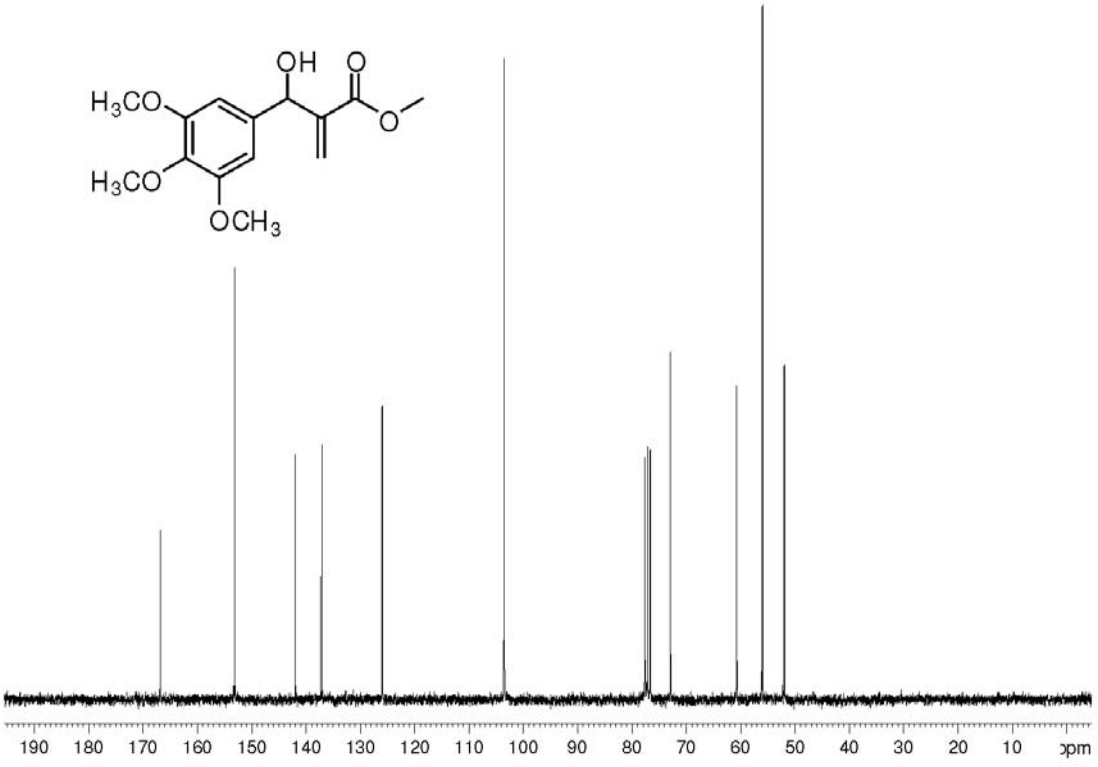

Figure S10. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **7**.

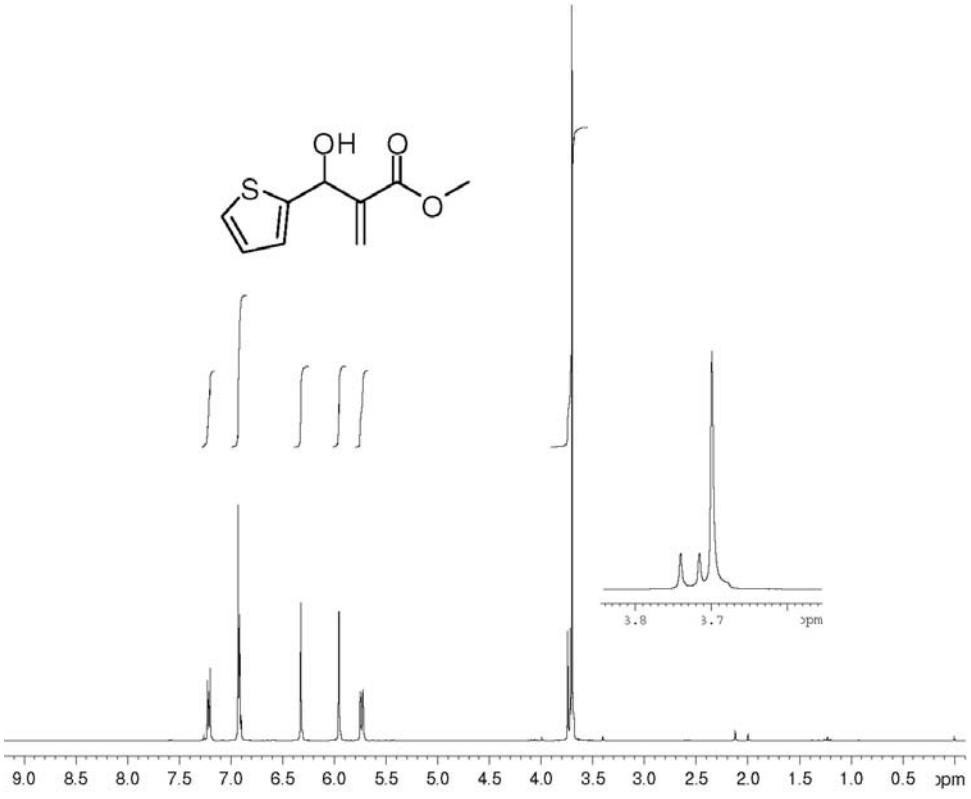

Figure S11. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **8**.

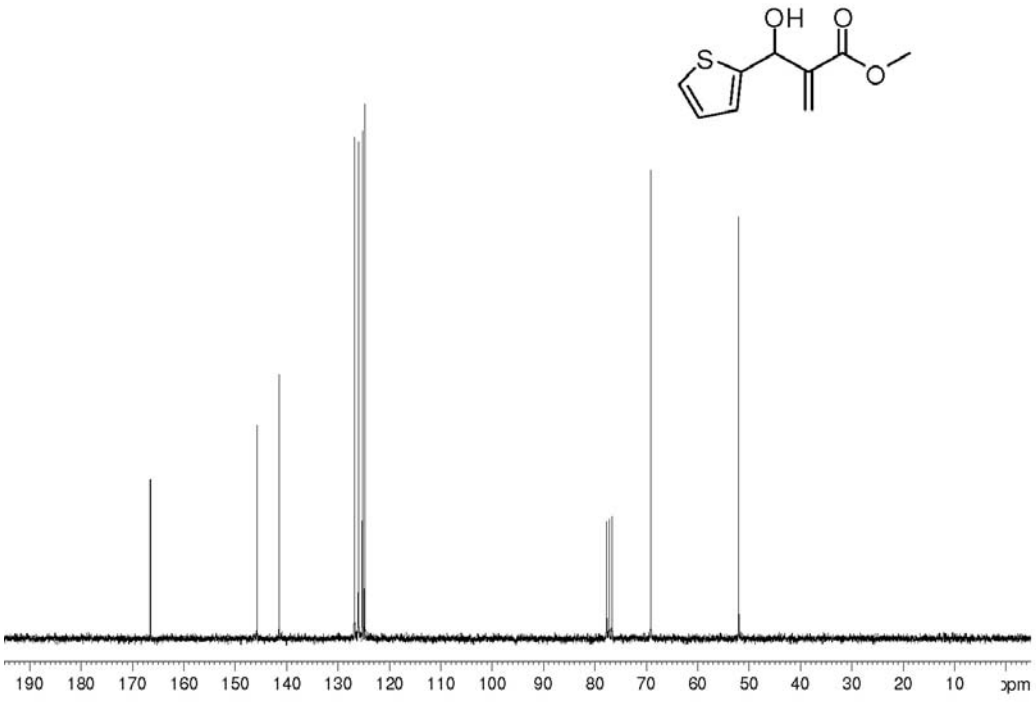

Figure S12. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **8**.

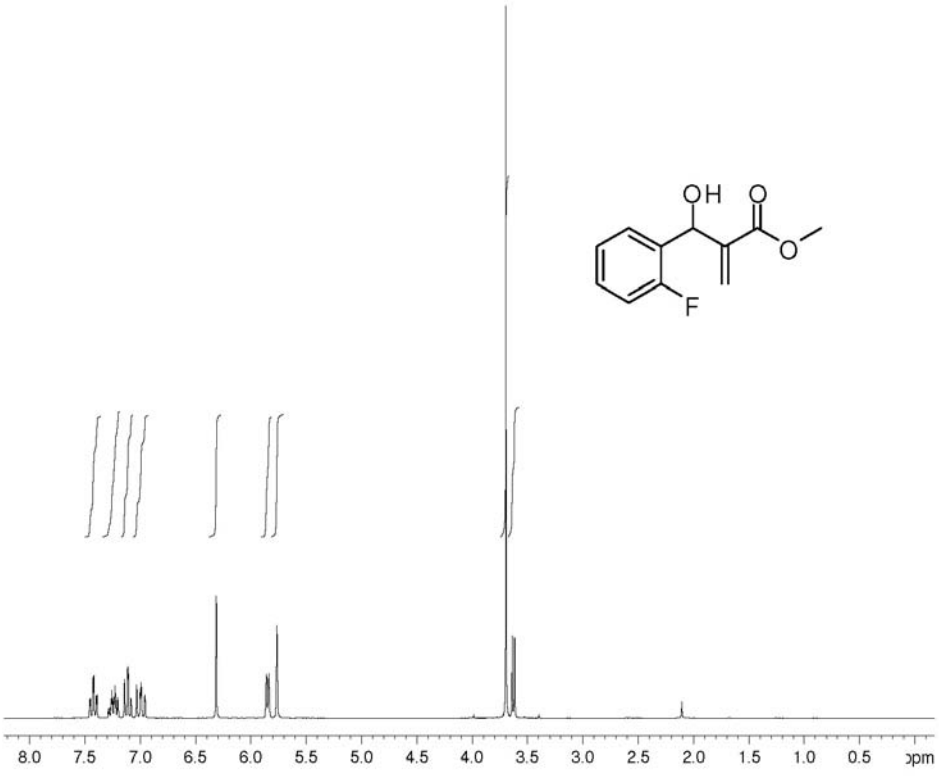

Figure S13. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **9**.

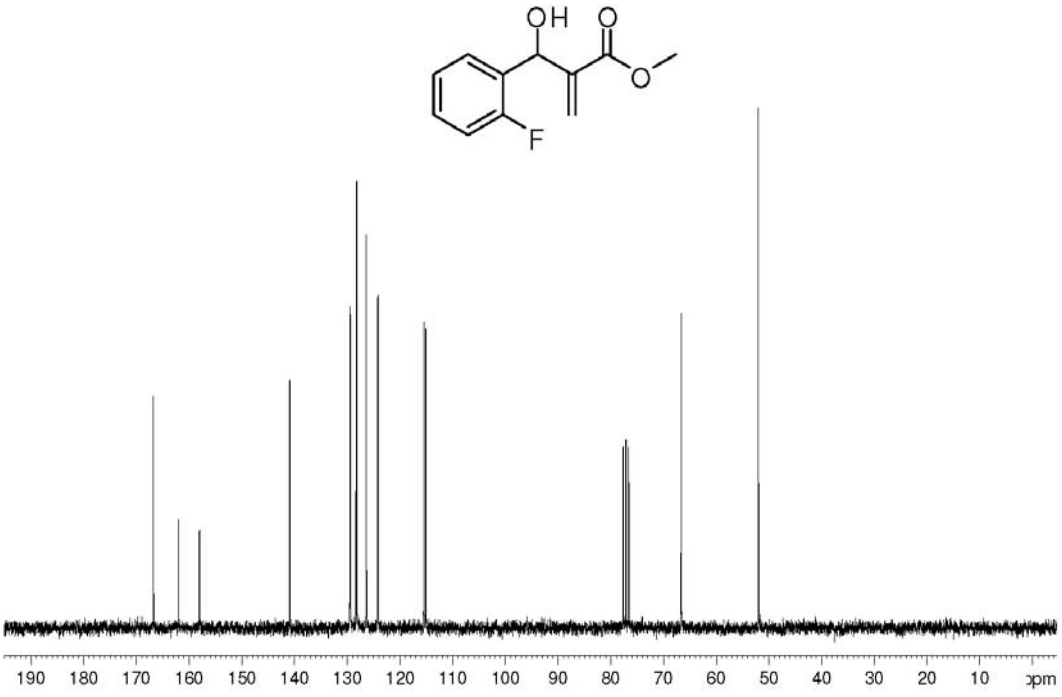

Figure S14. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **9**.

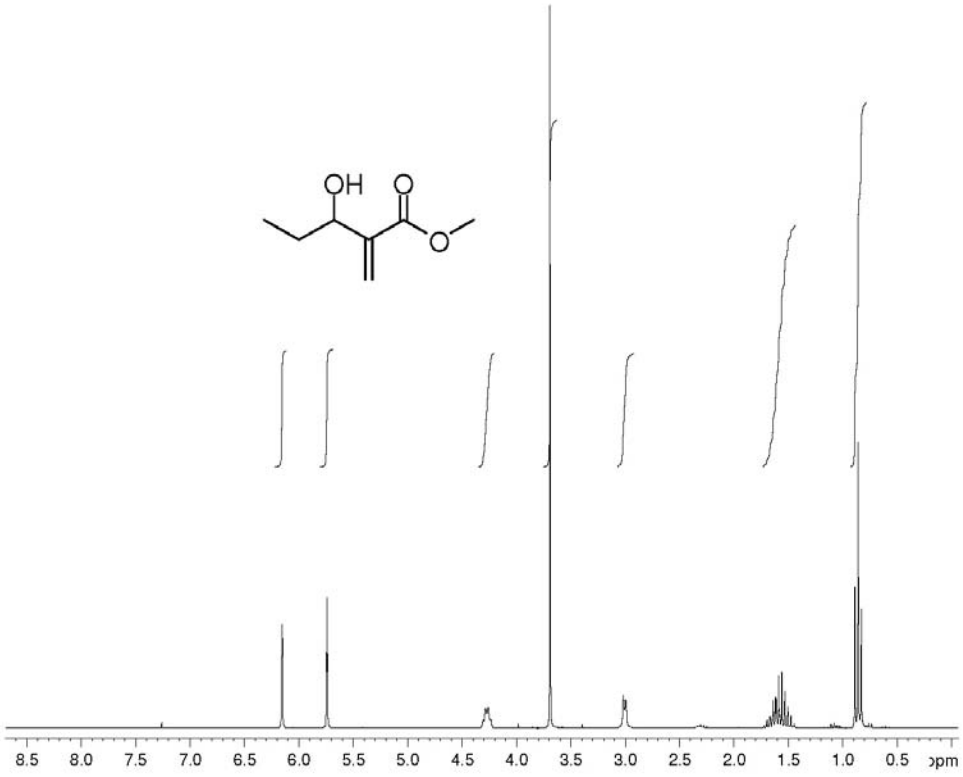

Figure S15. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **10**.

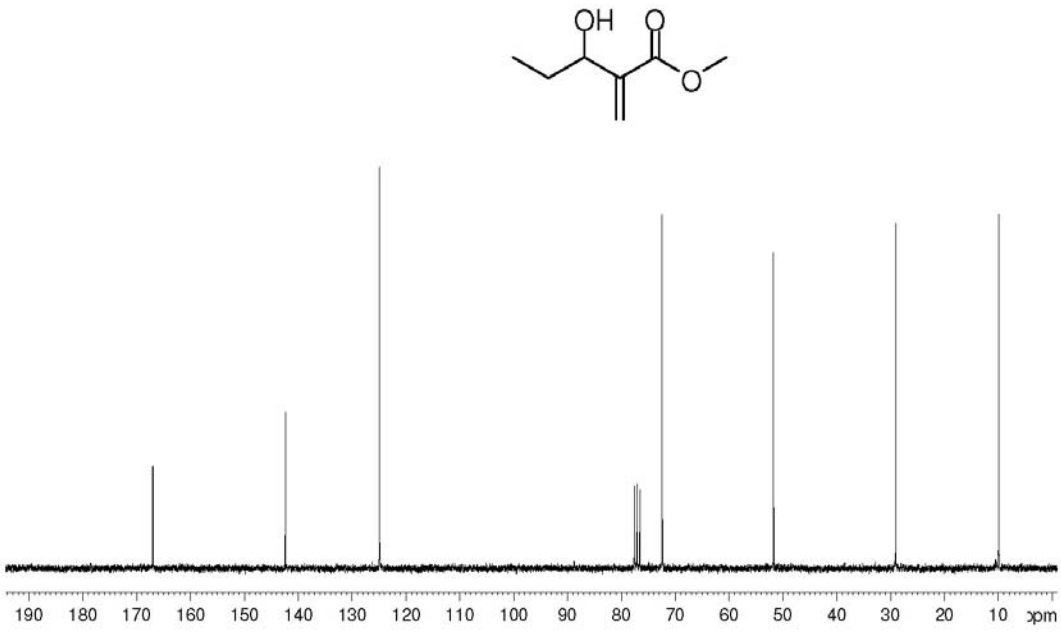

Figure S16. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of MBH adduct **10**.

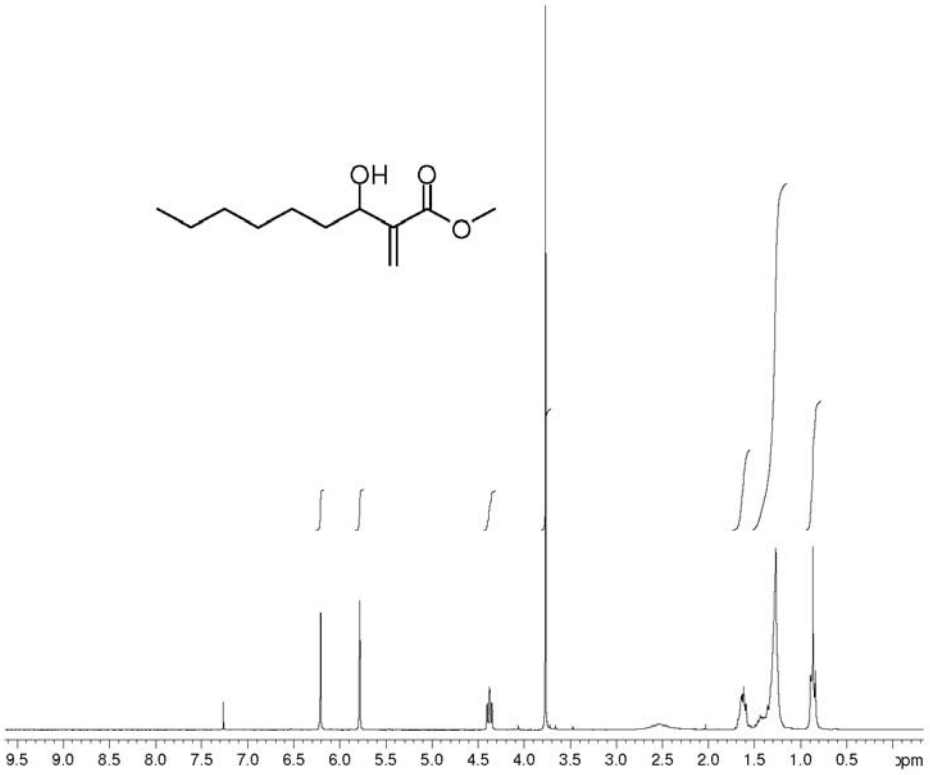

Figure S17. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **11**.

Figure S18. ^{13}C NMR ($CDCl_3$, 125 MHz) of MBH adduct **11**.

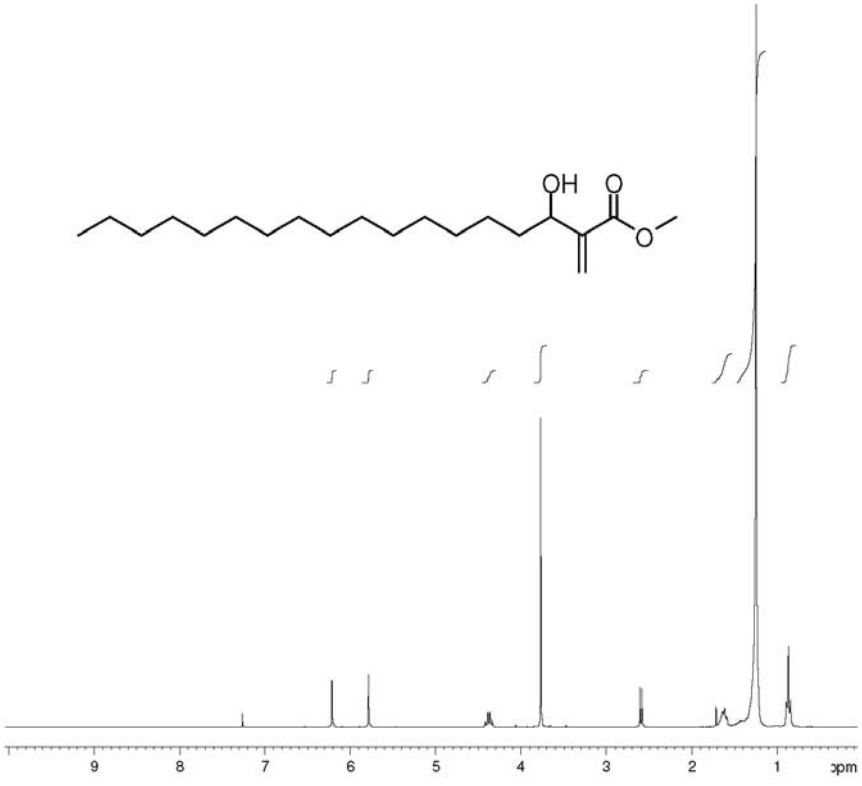

Figure S19. ^{1}H NMR ($CDCl_3$, 250 MHz) of MBH adduct **12**.

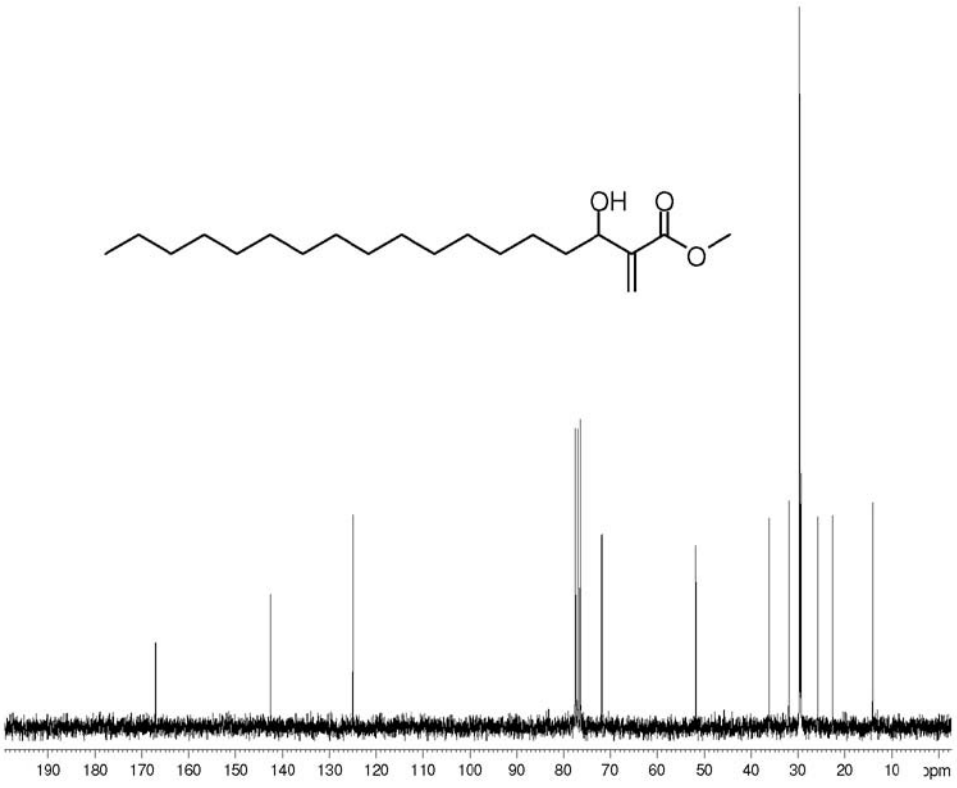

Figure S20. ^{13}C NMR ($CDCl_3$, 125 MHz) of MBH adduct **12**.

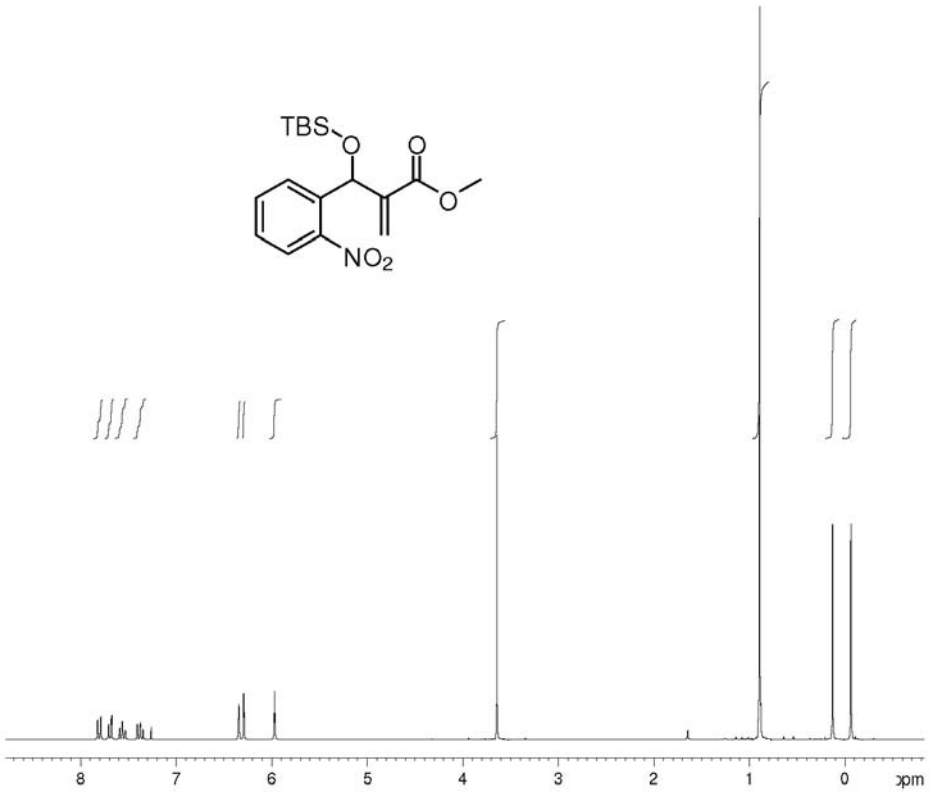

Figure S21. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **13**.

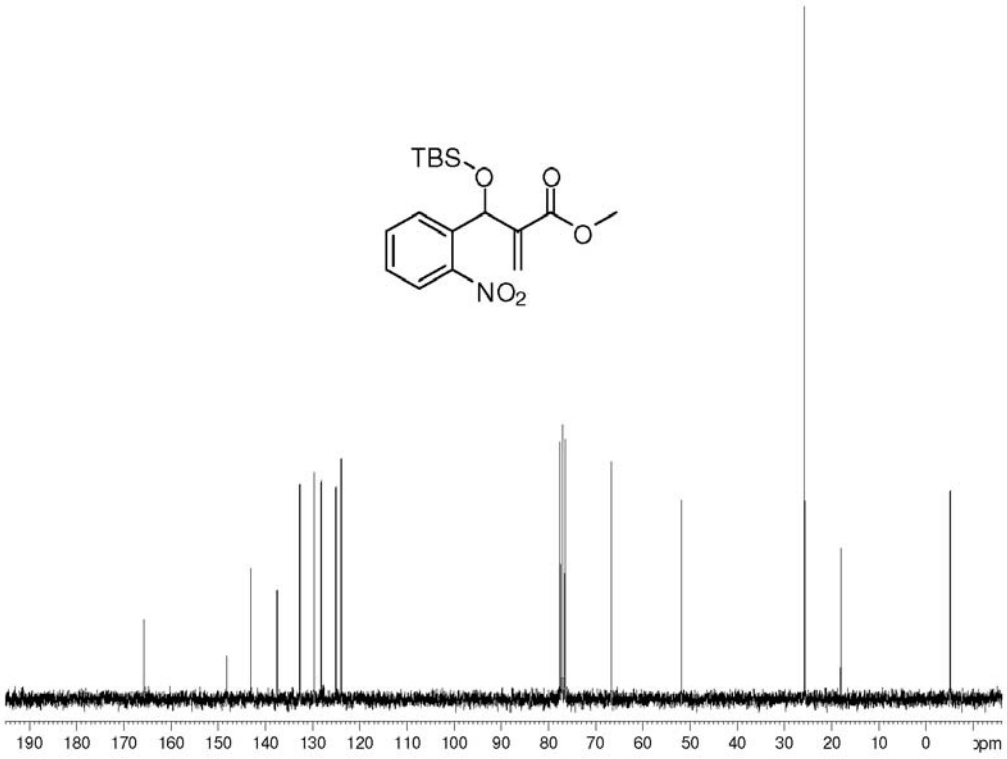

Figure S22. ^{13}C RMN ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **13**.

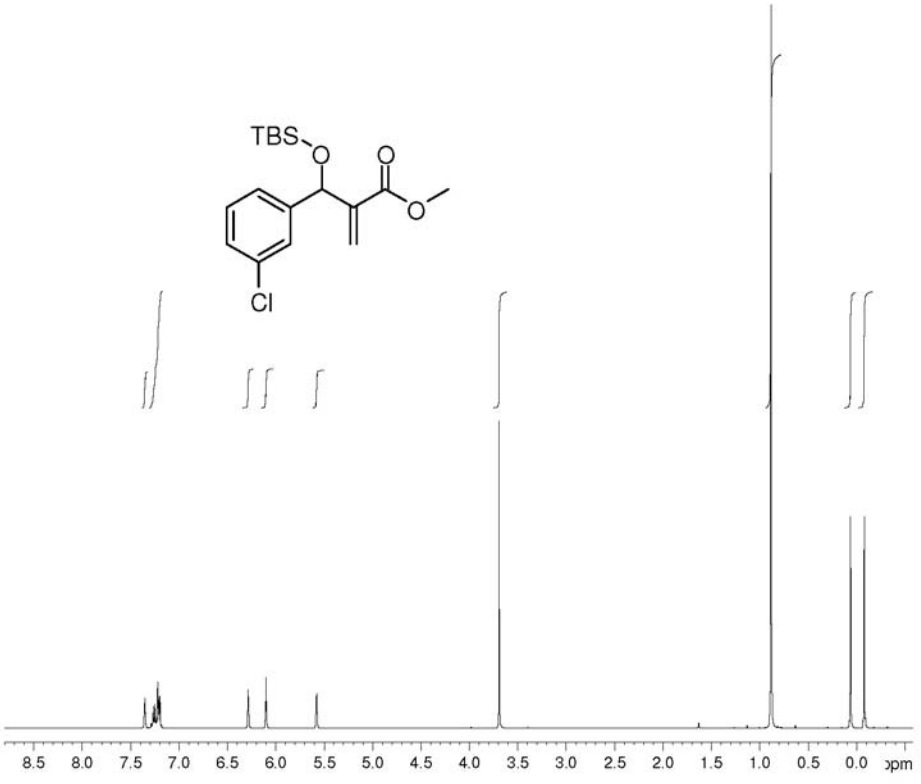

Figure S23. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **14**.

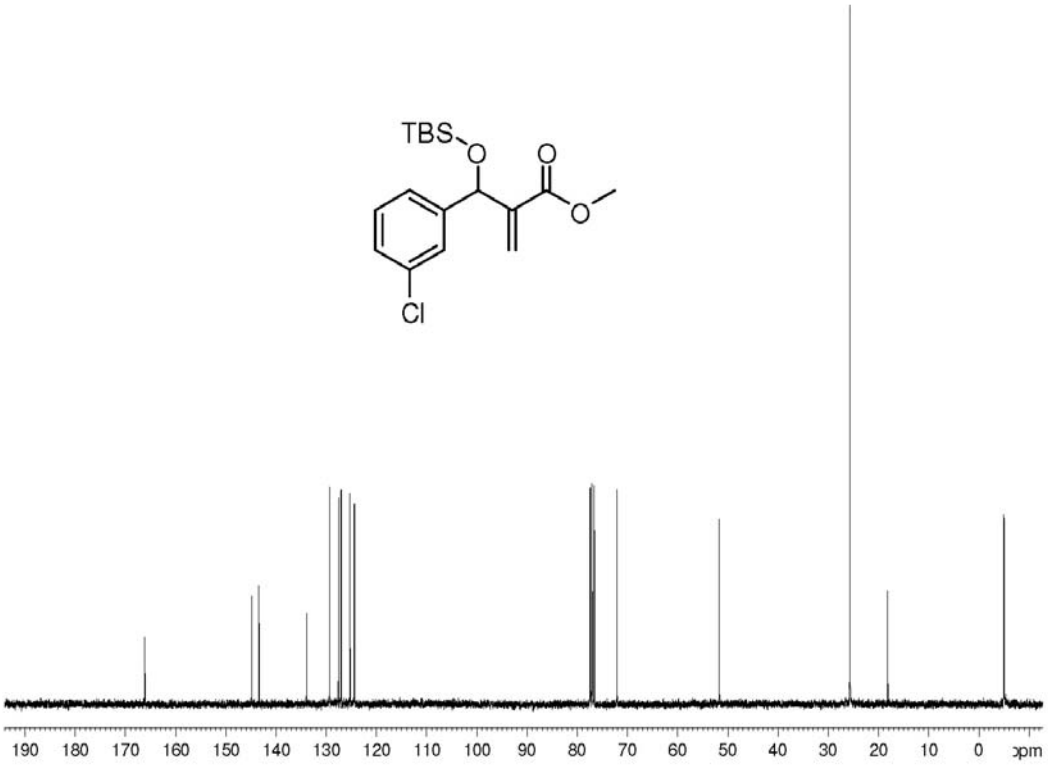

Figure S24. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **14**.

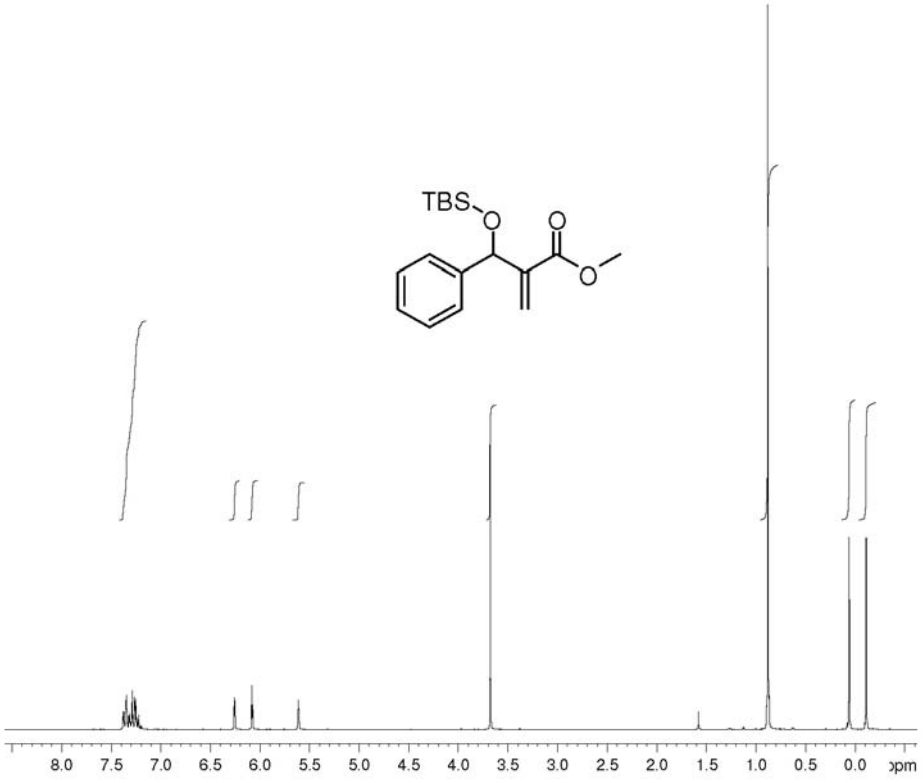

Figure S25. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **15**.

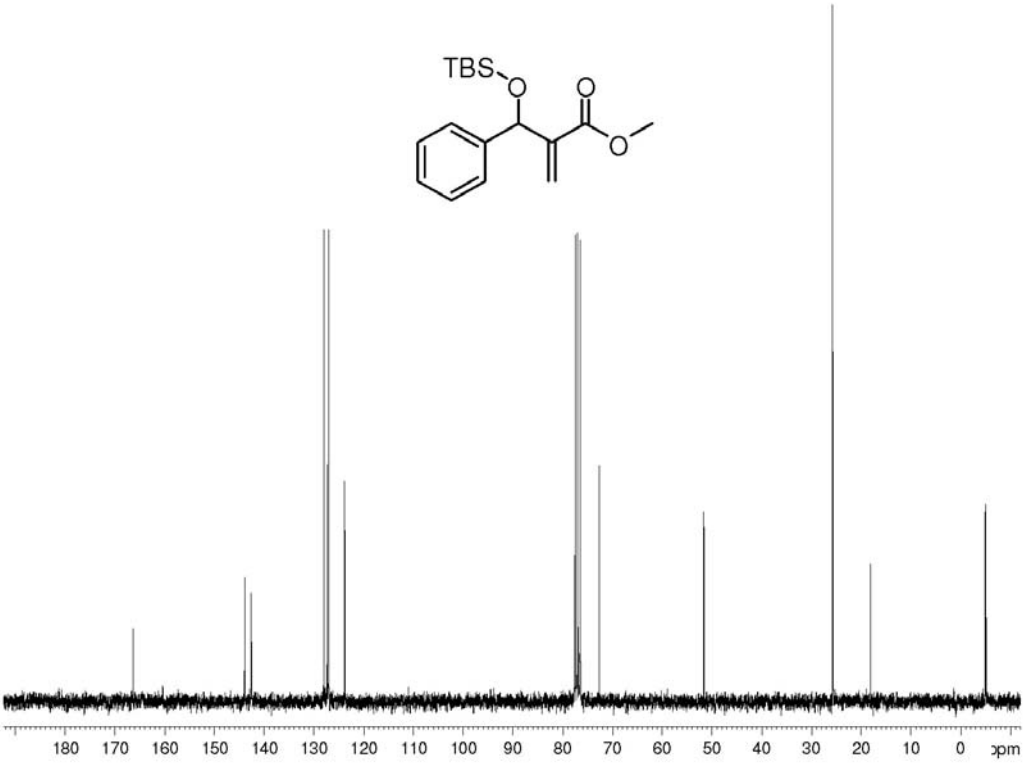

Figure S26. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **15**.

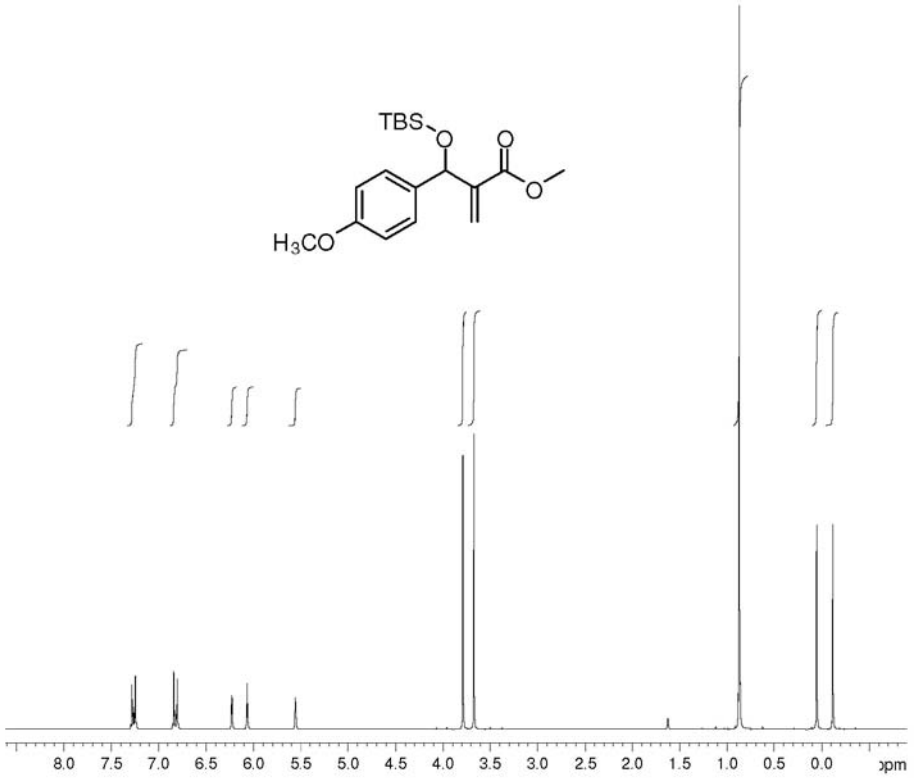

Figure S27. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **16**.

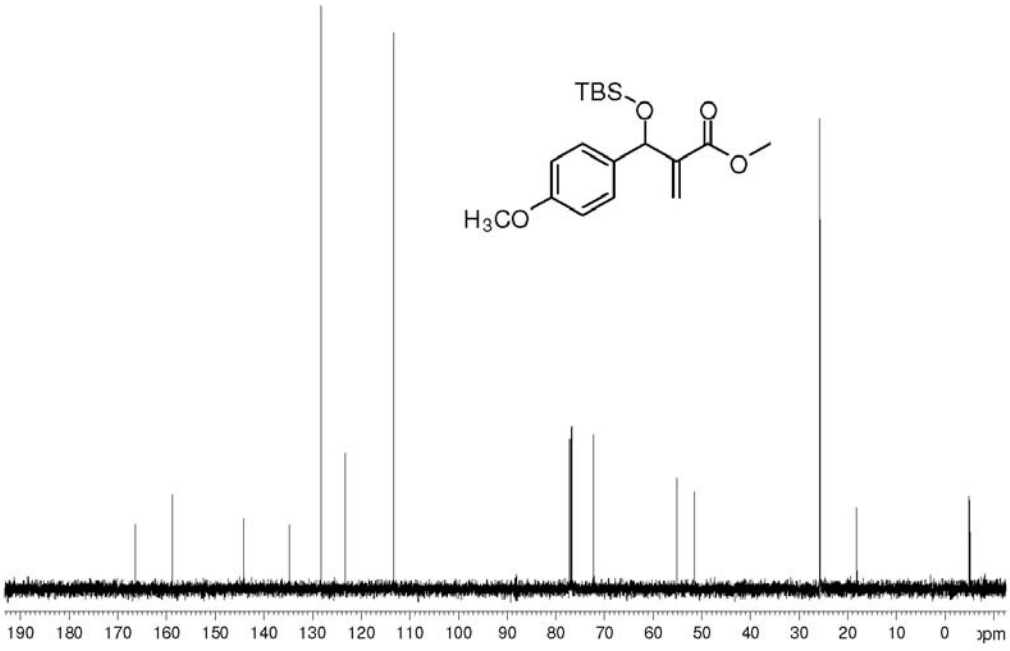

Figure S28. ^{13}C NMR ($CDCl_3$, 125 MHz) of silylated MBH adduct **16**.

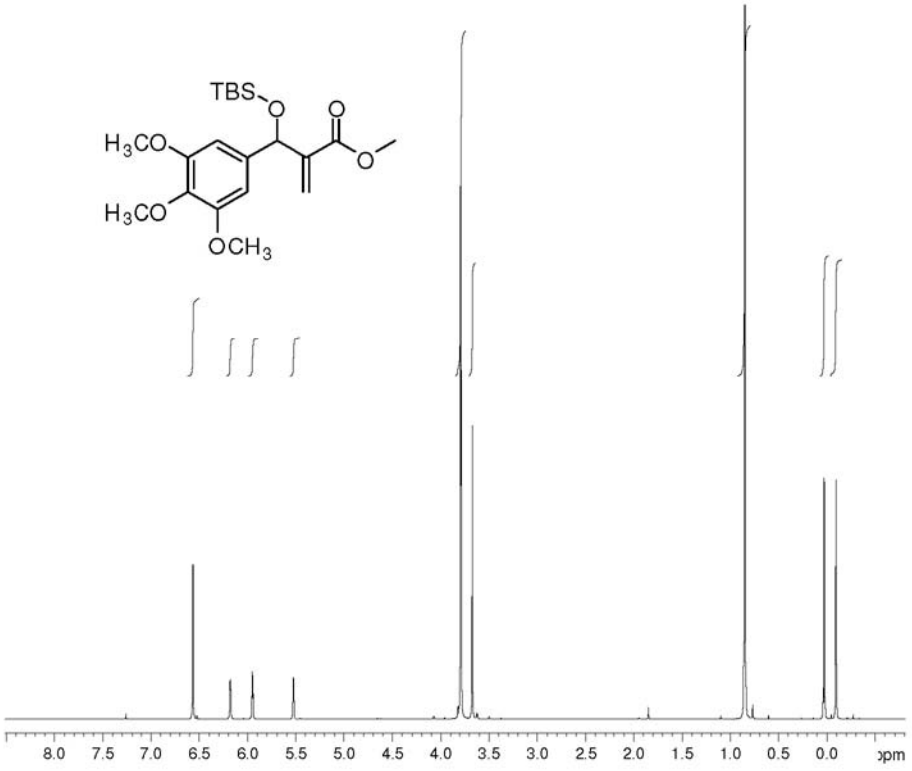

Figure S29. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **17**.

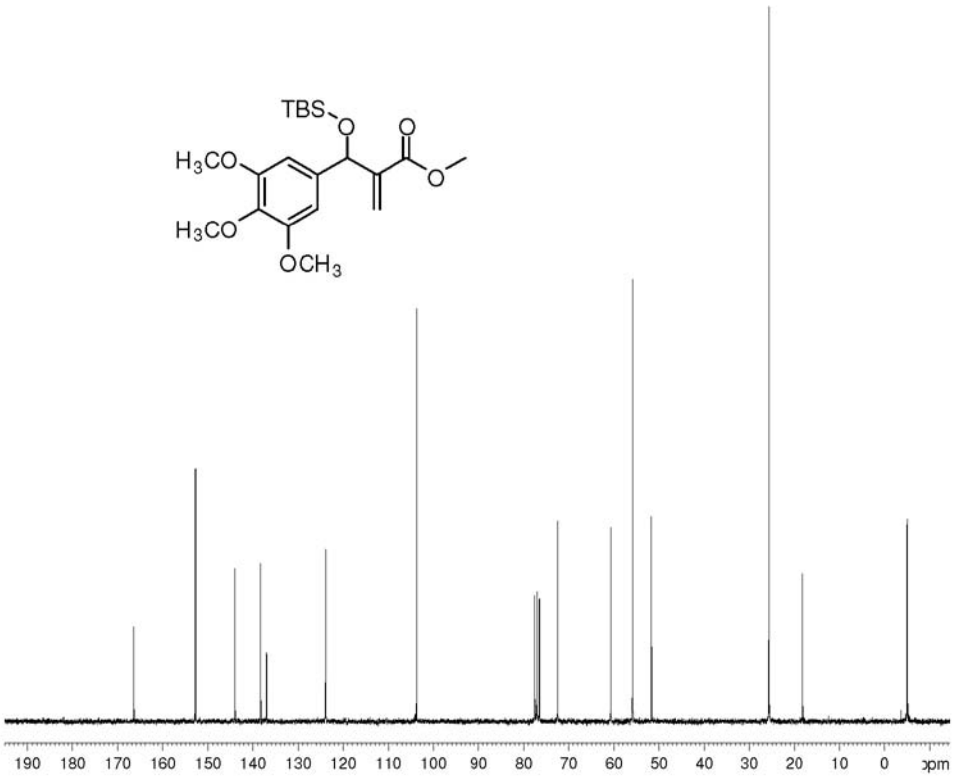

Figure S30. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **17**.

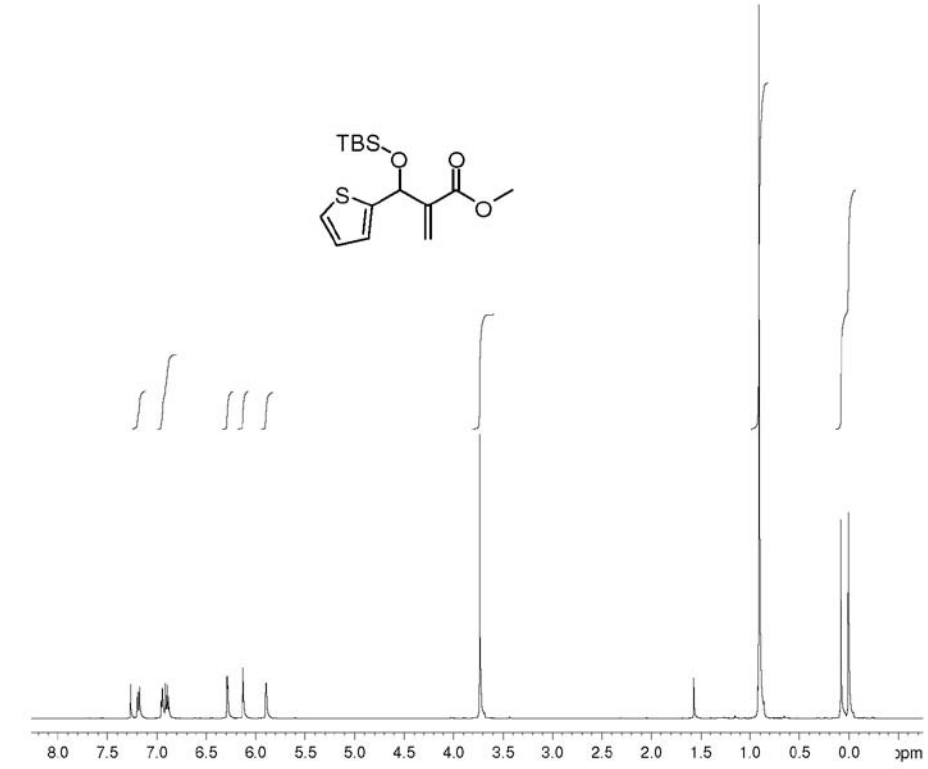

Figure S31. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **18**.

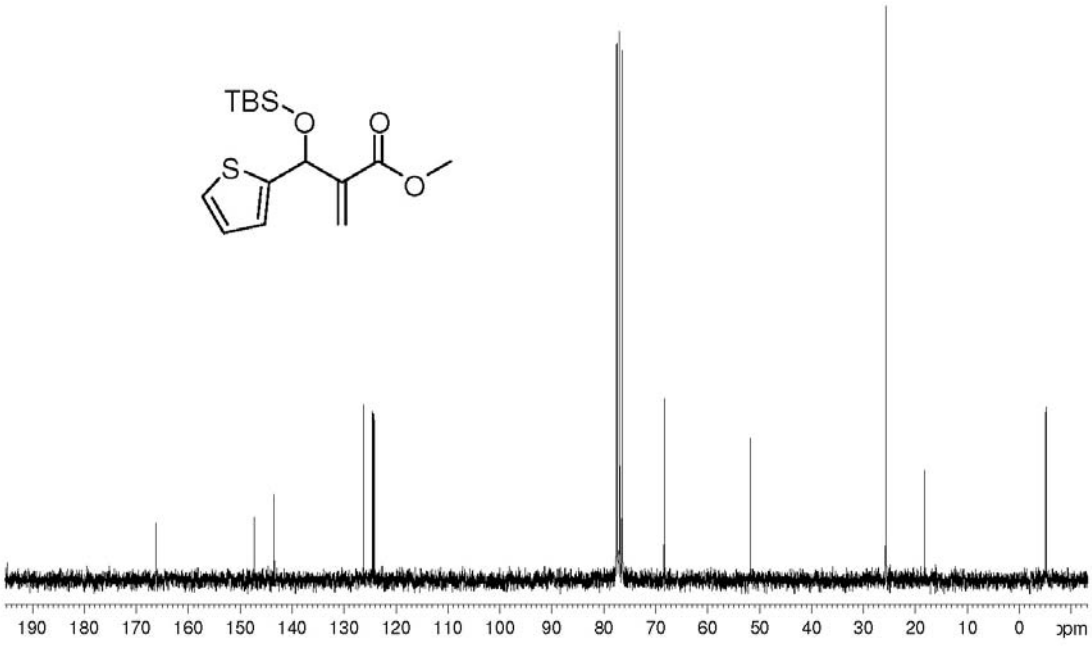

Figure S32. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **18**.

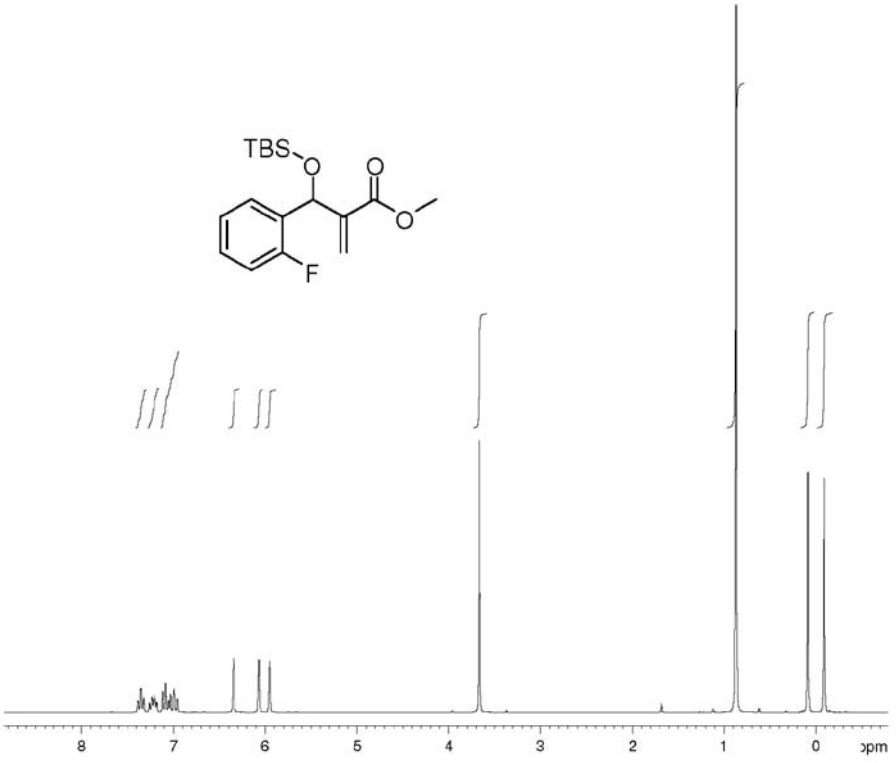

Figure S33. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **19**.

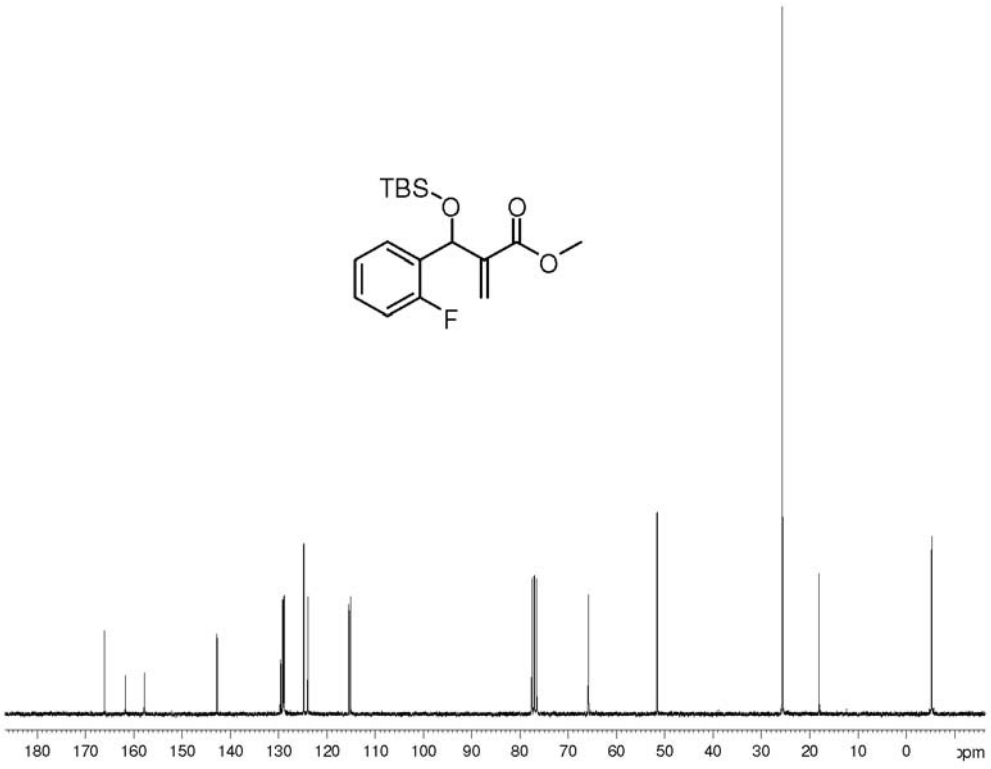

Figure S34. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **19**.

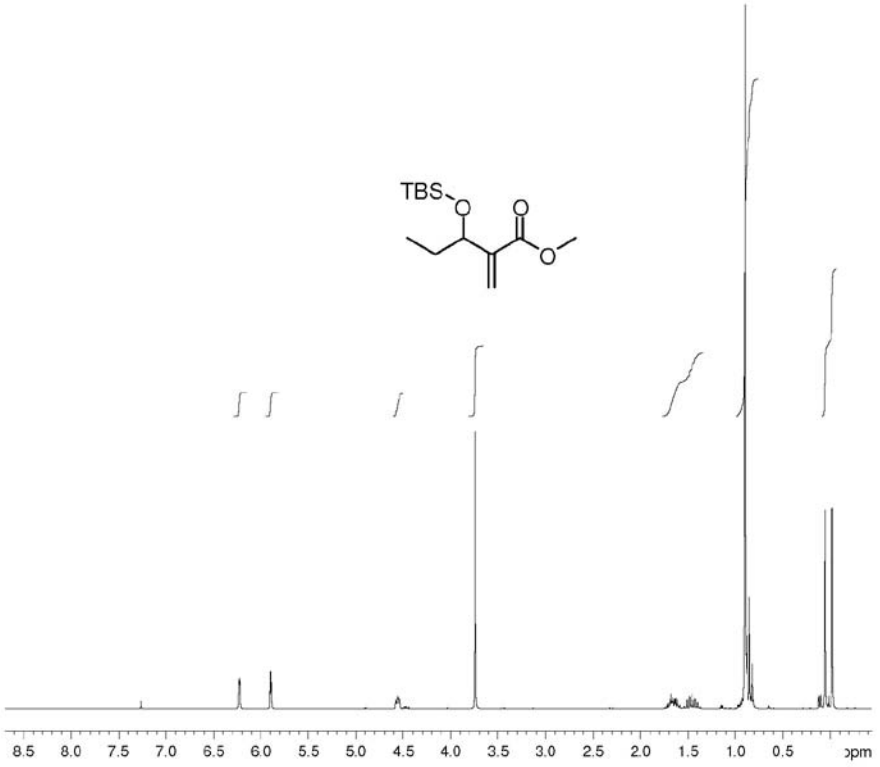

Figure S35. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **20**.

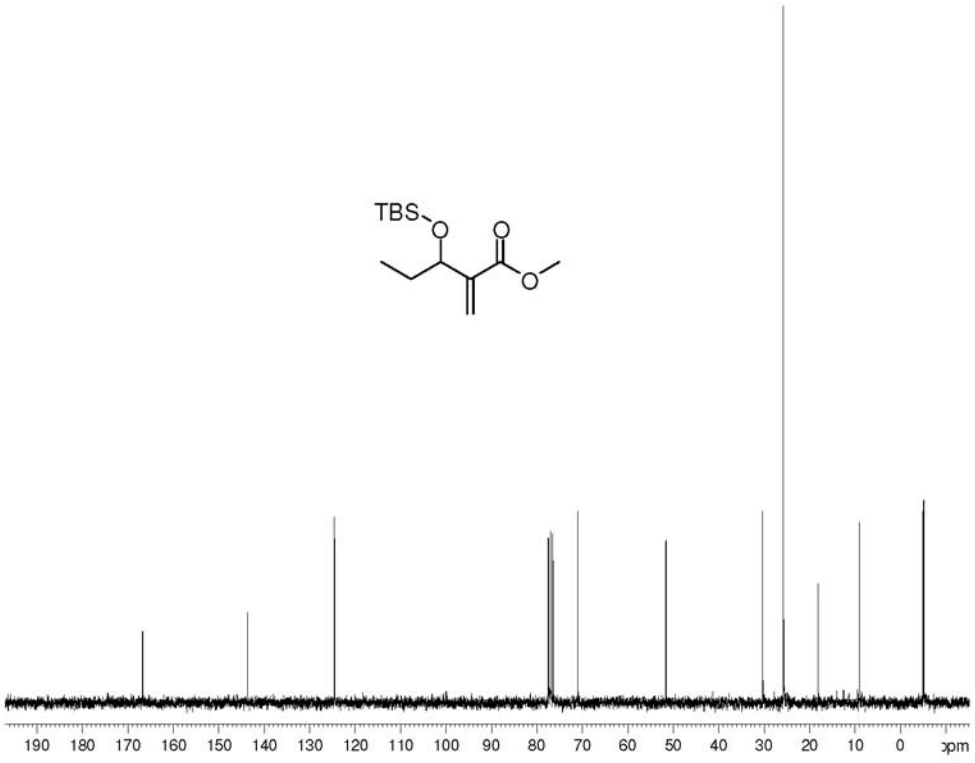

Figure S36. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **20**.

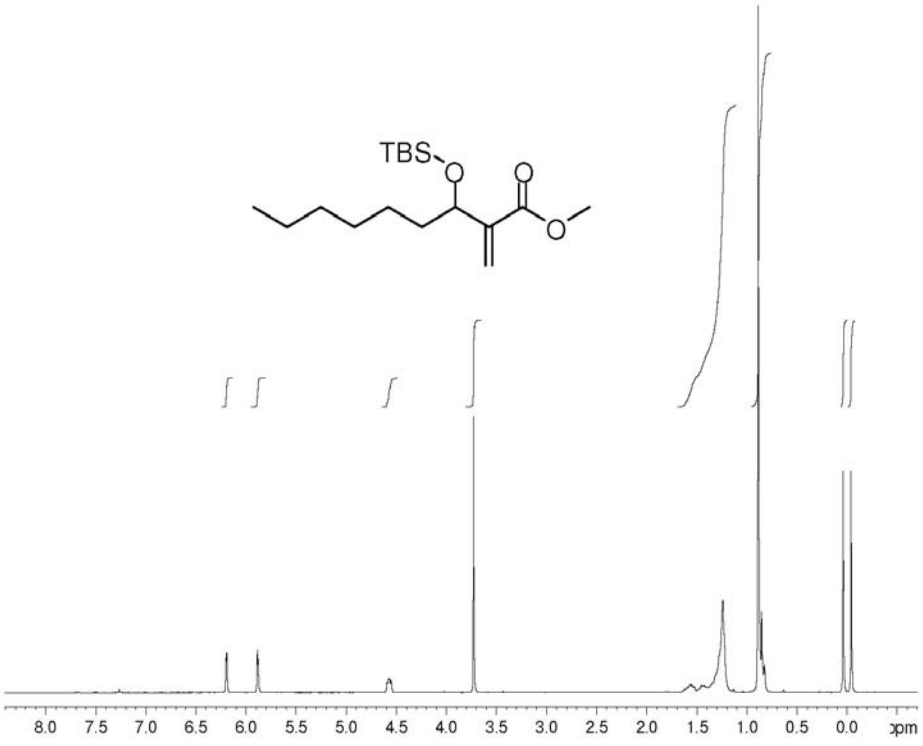

Figure S37. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **21**.

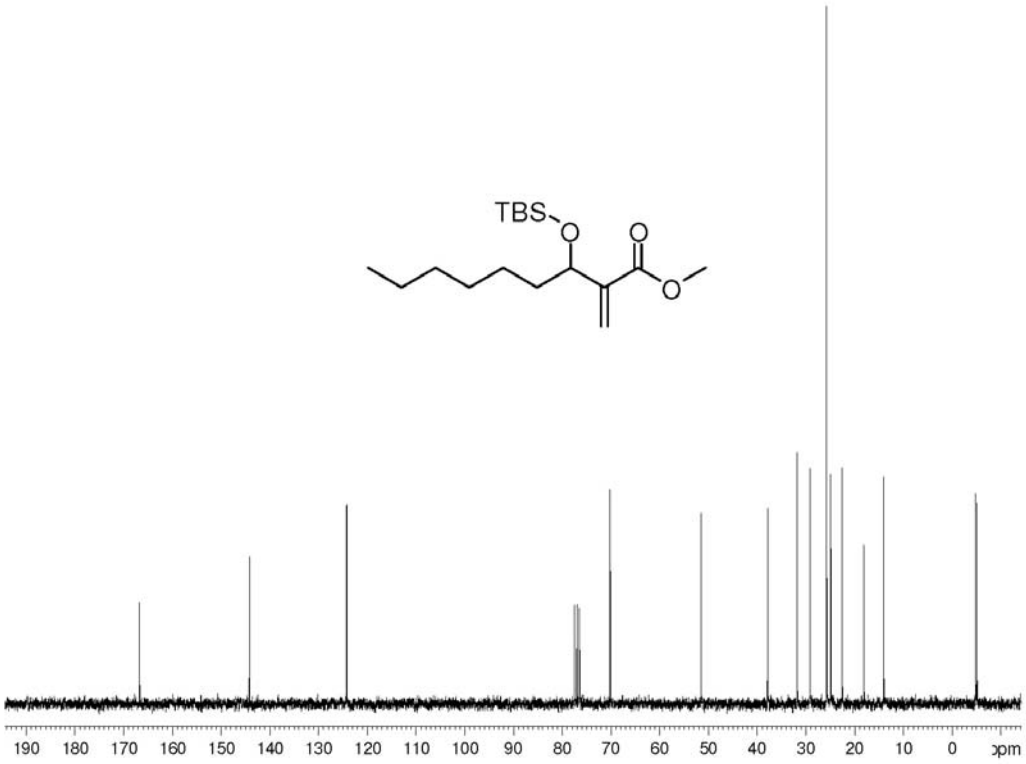

Figure S38. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **21**.

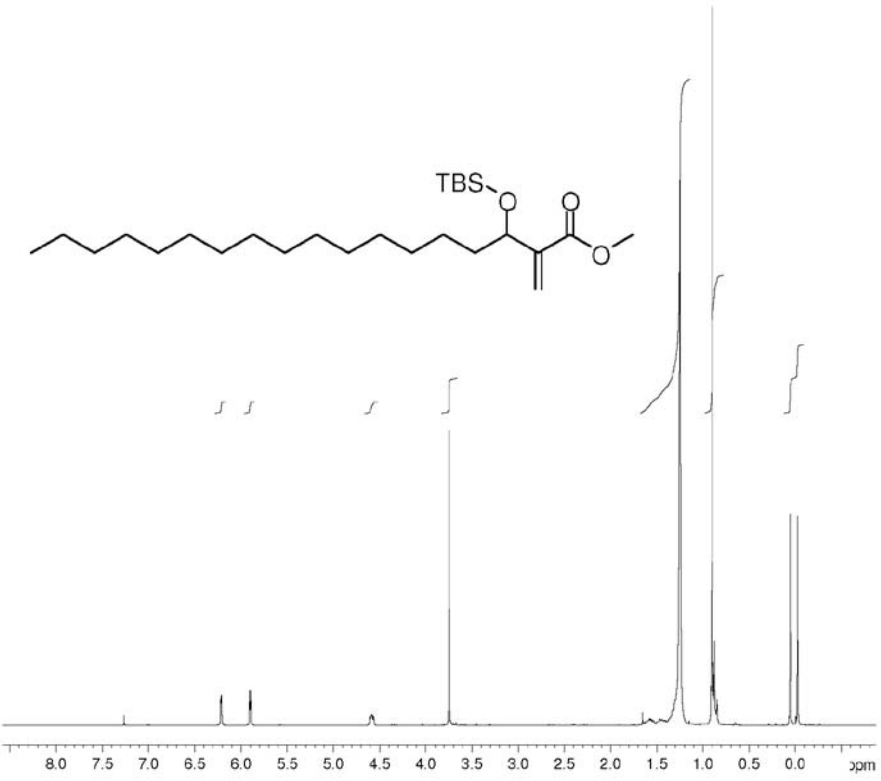

Figure S39. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated MBH adduct **22**.

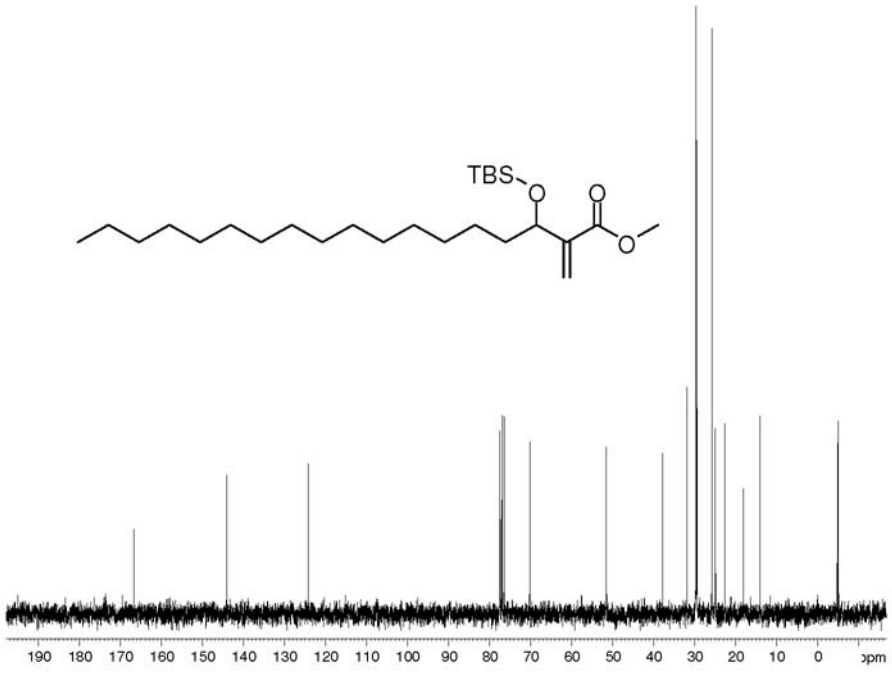

Figure S40. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated MBH adduct **22**.

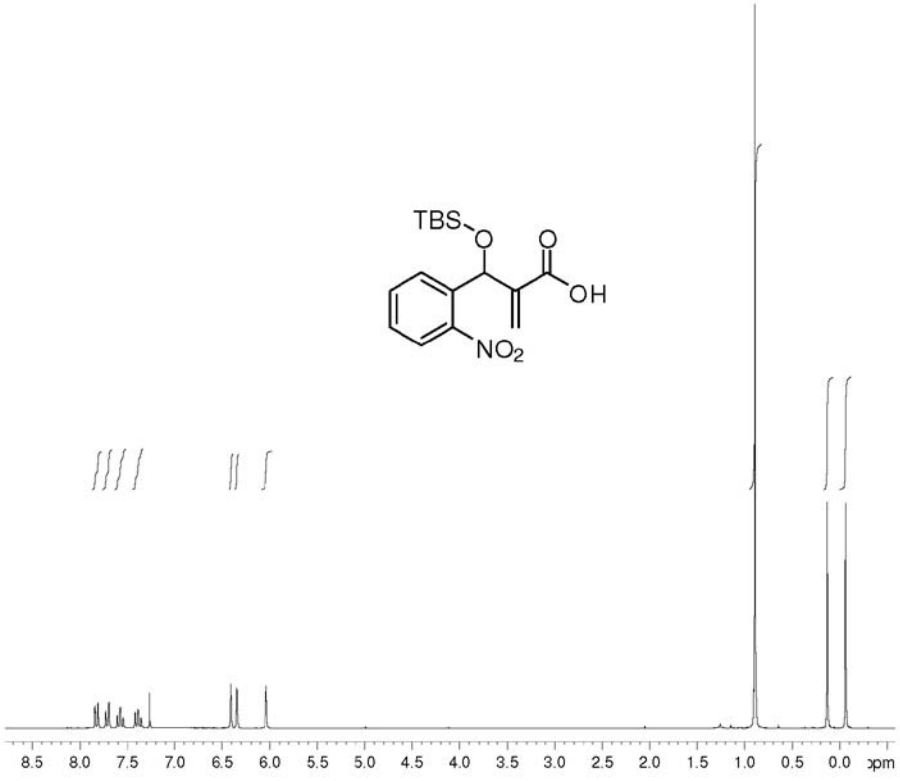

Figure S41. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **23**.

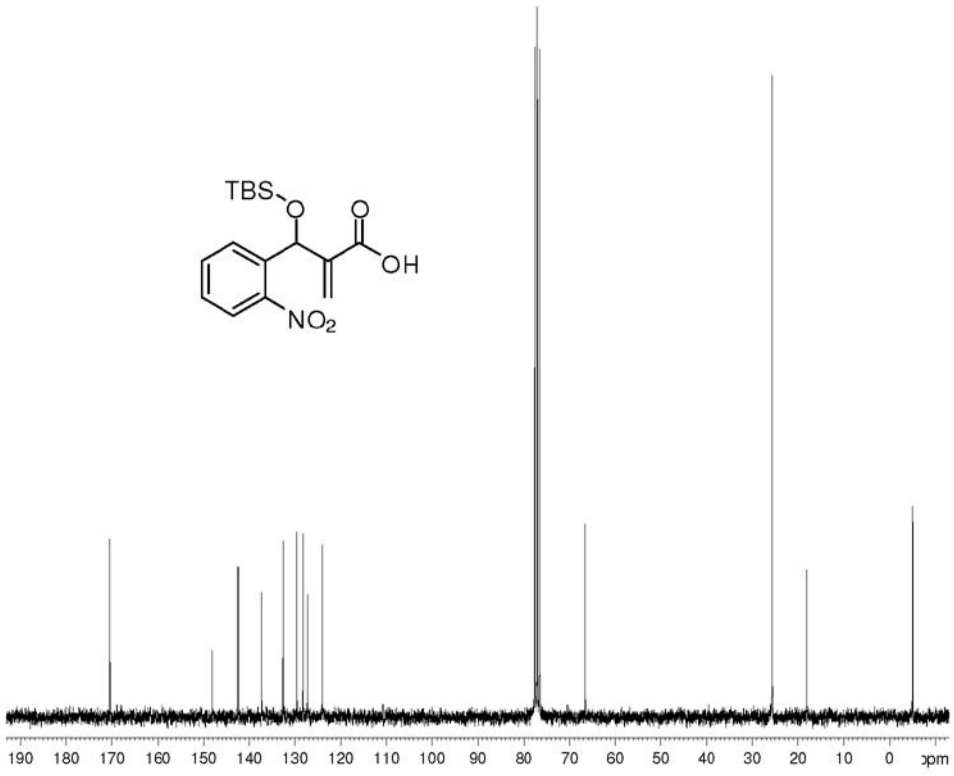

Figure S42. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **23**.

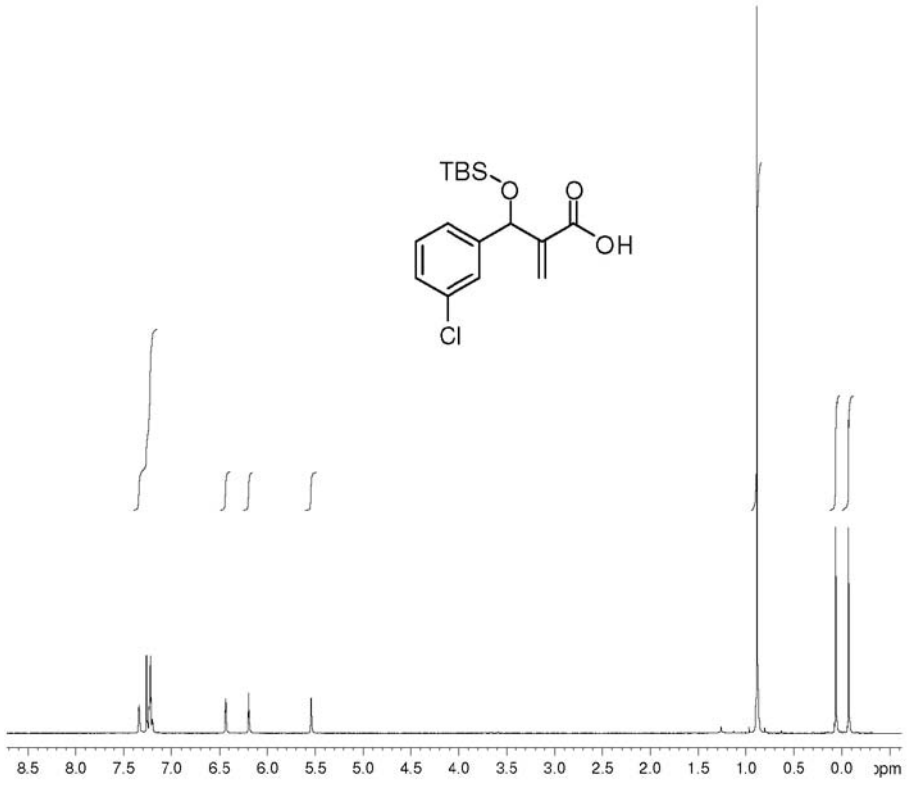

Figure S43. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **24**.

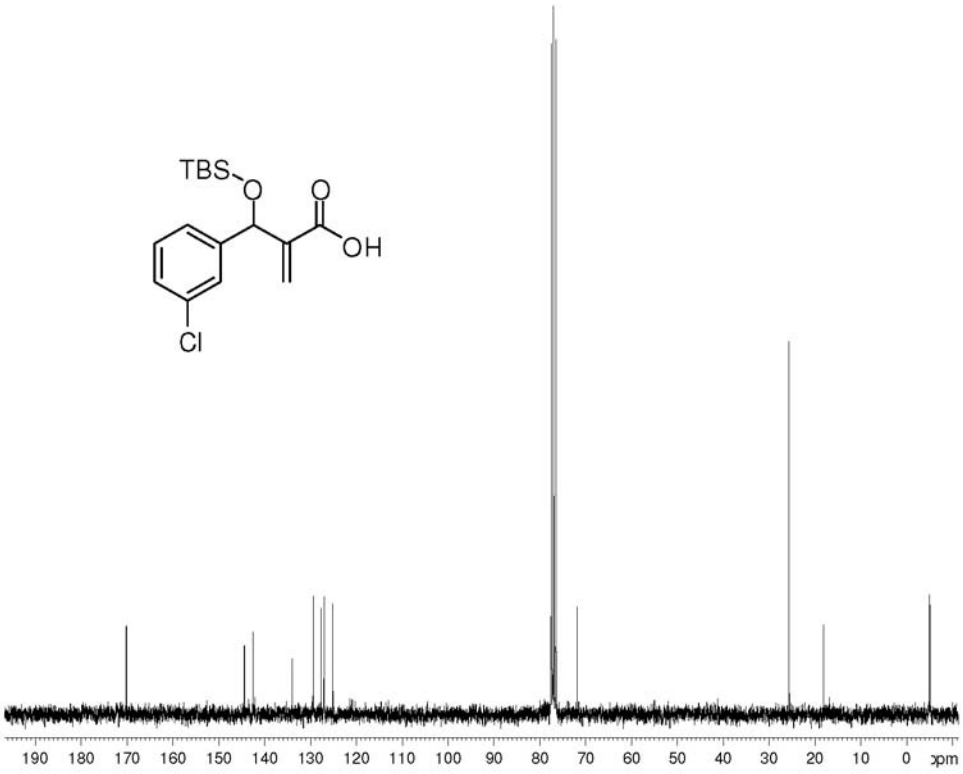

Figure S44. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **24**.

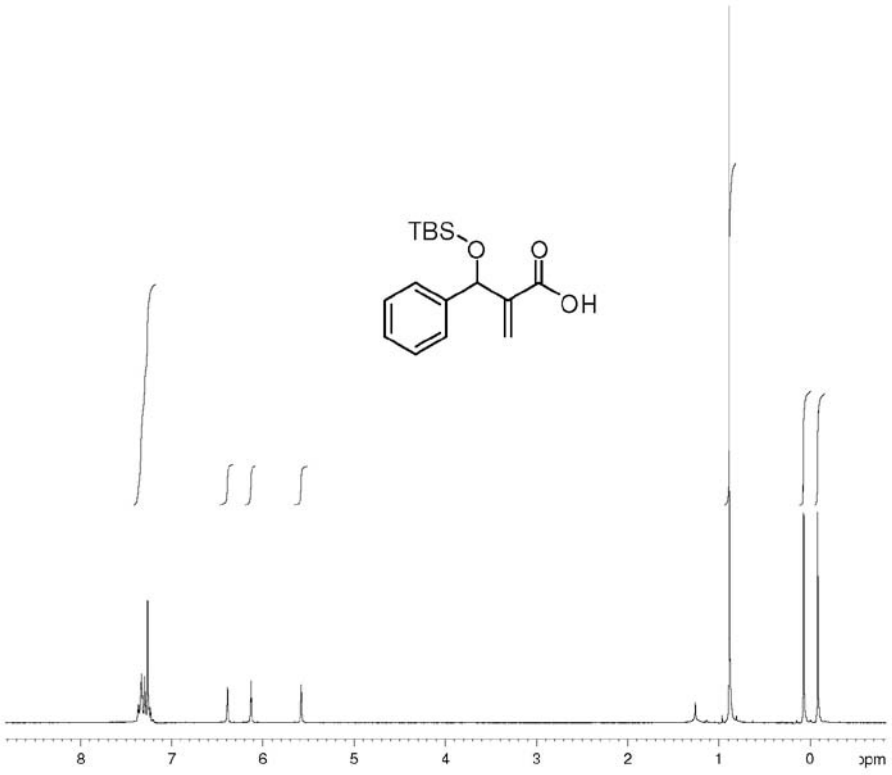

Figure S45. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **25**.

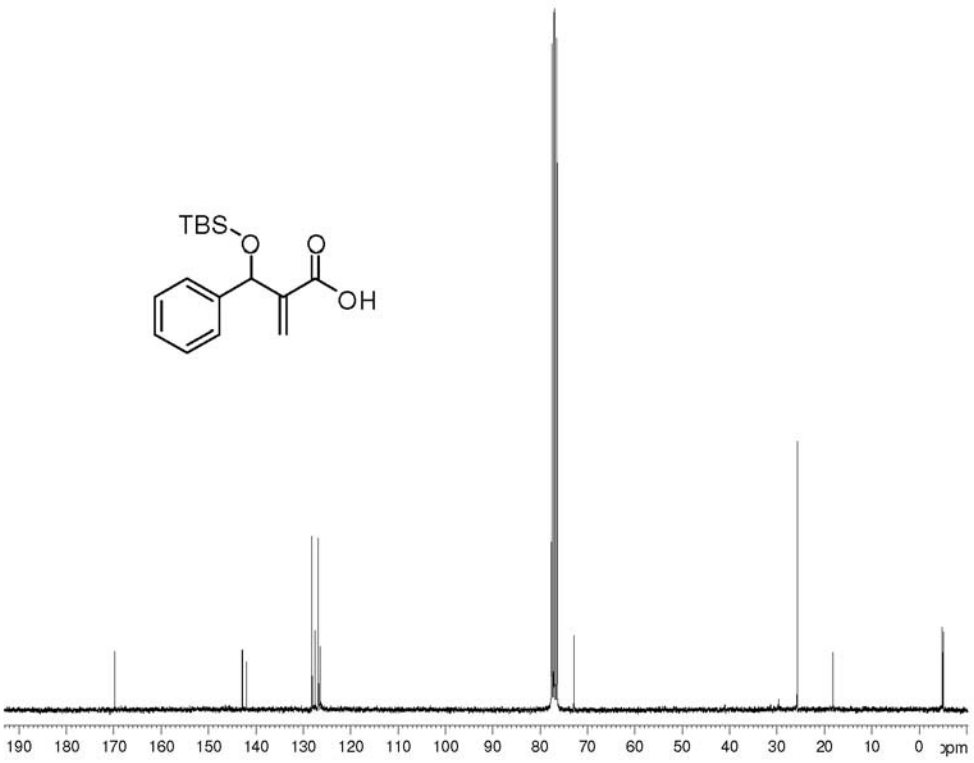

Figure S46. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **25**.

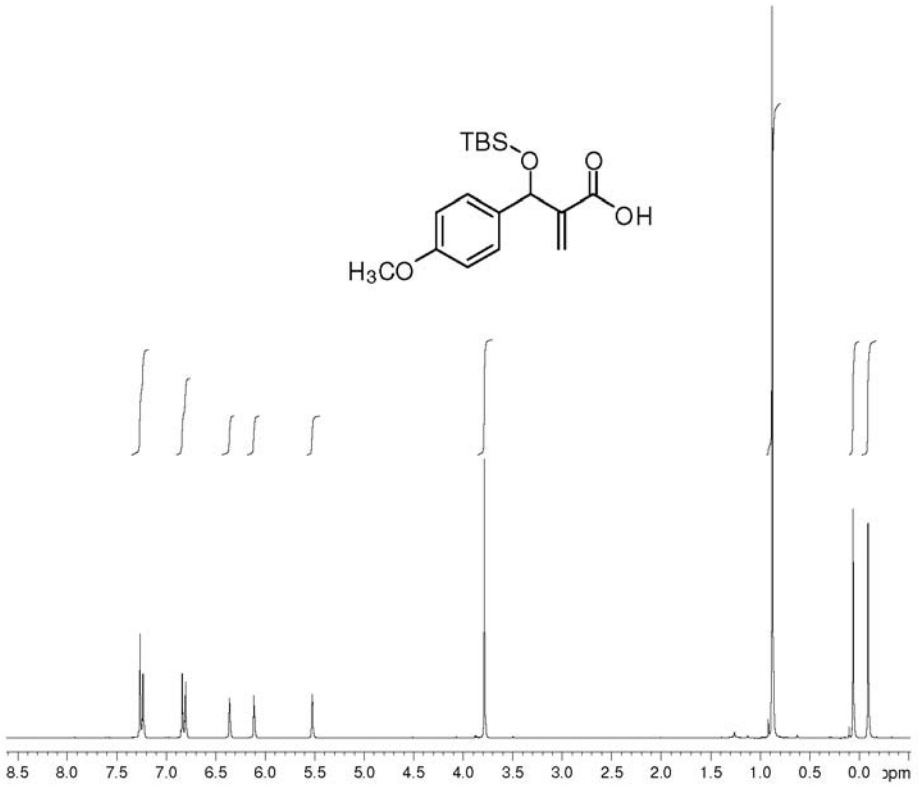

Figure S47. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **26**.

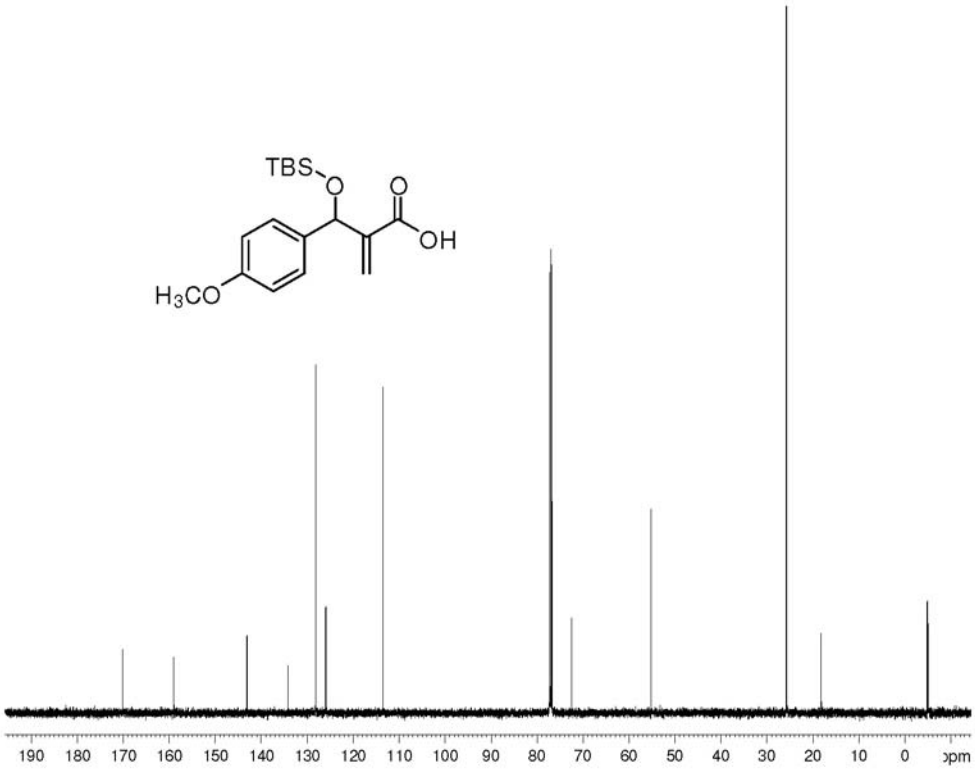

Figure S48. ^{13}C NMR ($CDCl_3$, 125 MHz) of silylated acid **26**.

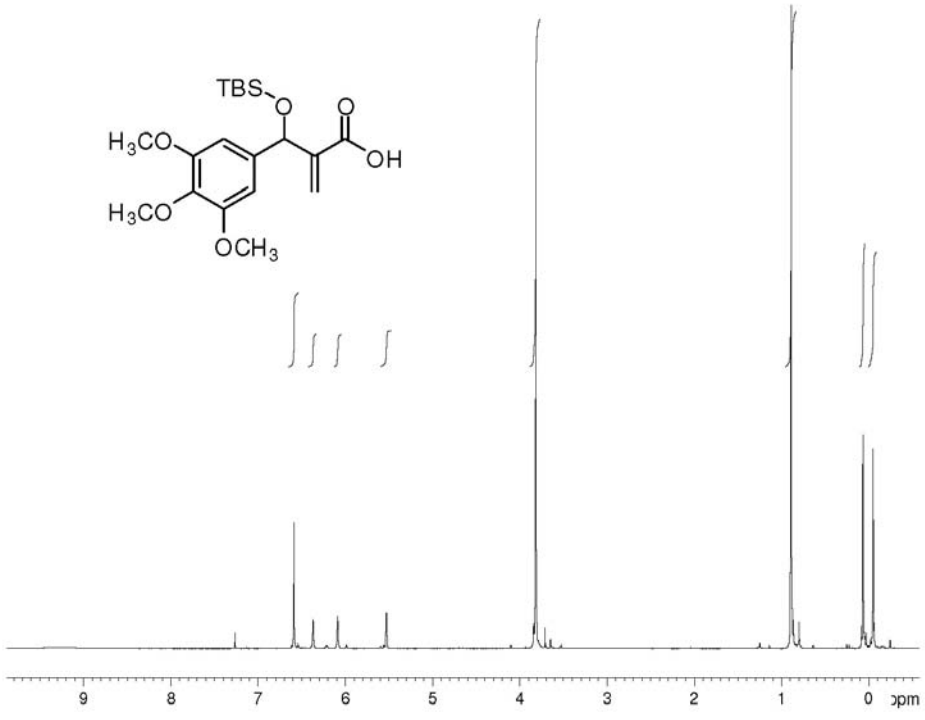

Figure S49. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **27**.

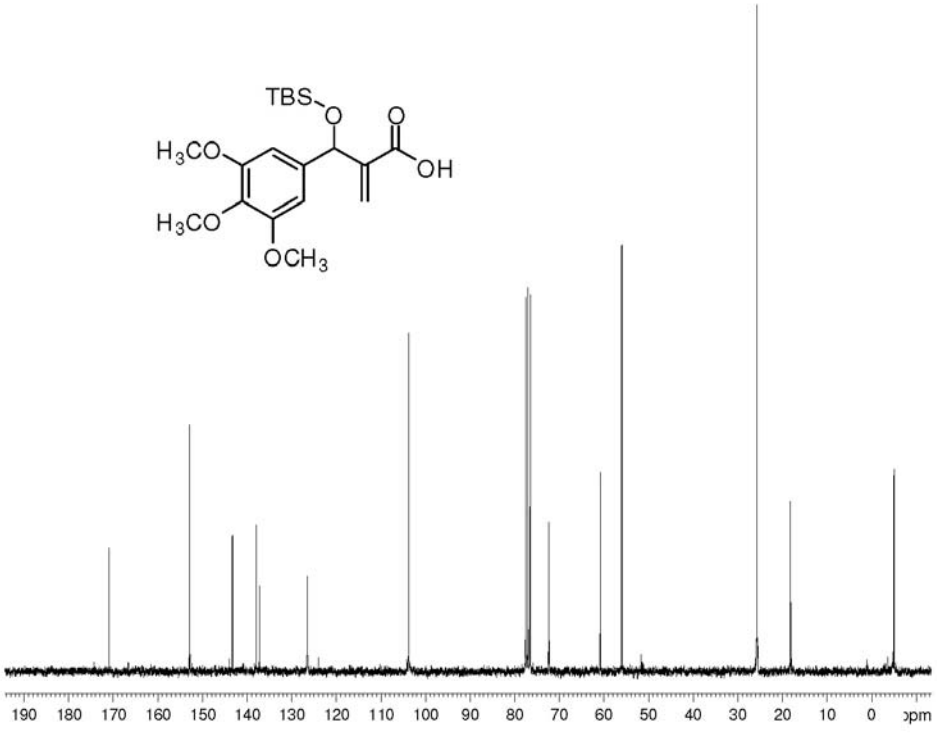

Figure S50. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **27**.

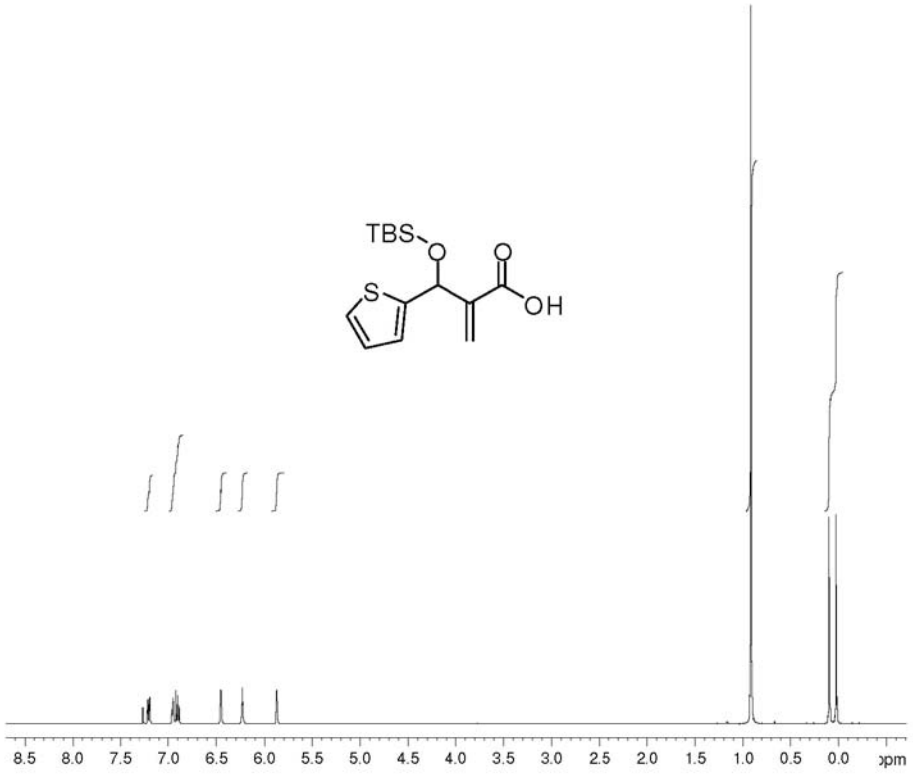

Figure S51. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **28**.

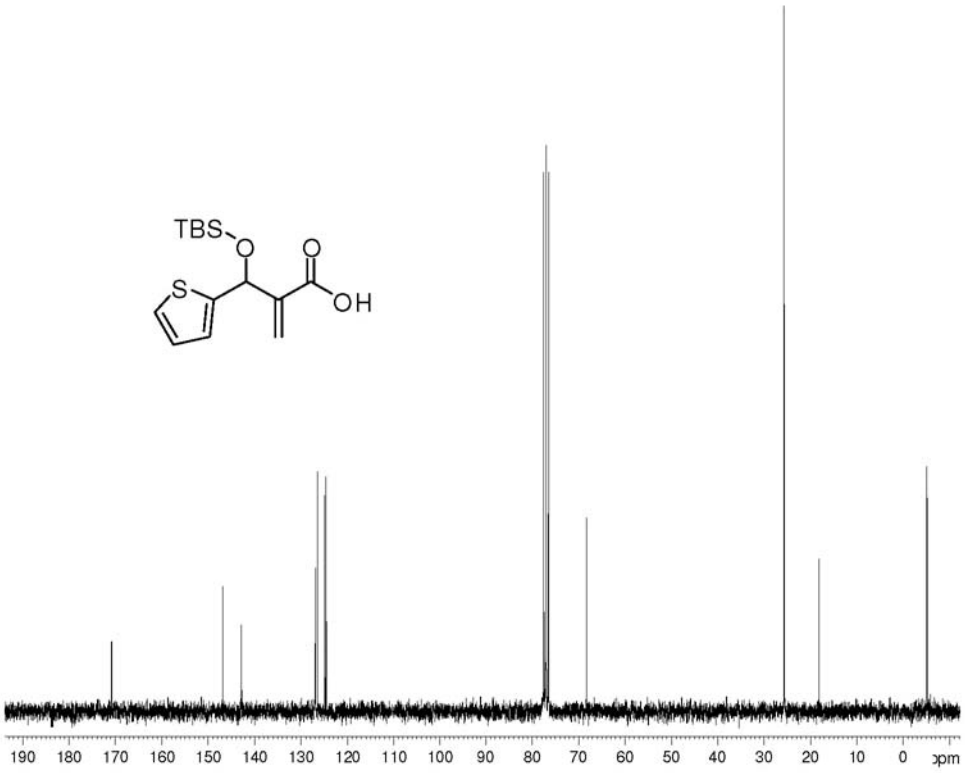

Figure S52. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silyated acid **28**.

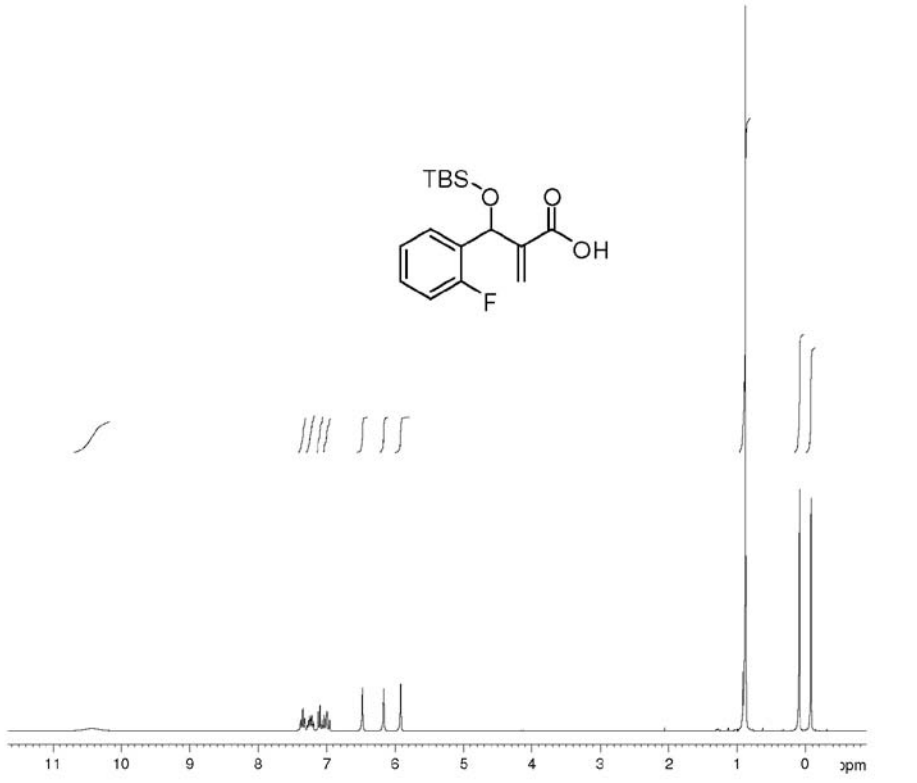

Figure S53. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **29**.

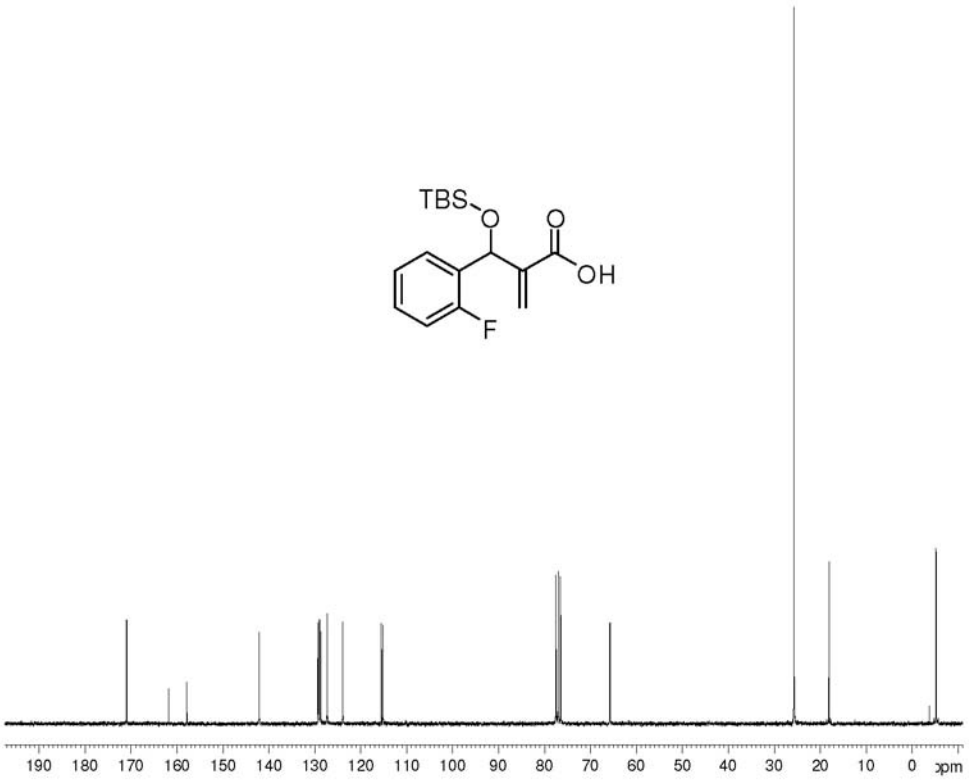

Figure S54. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **29**.

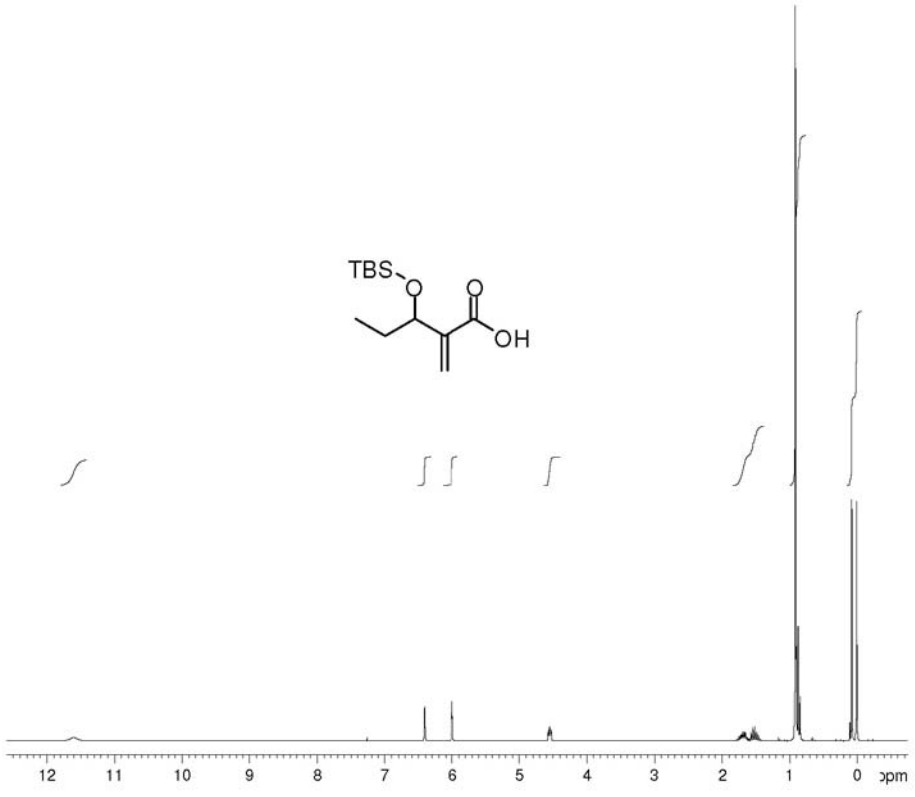

Figure S55. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **30**.

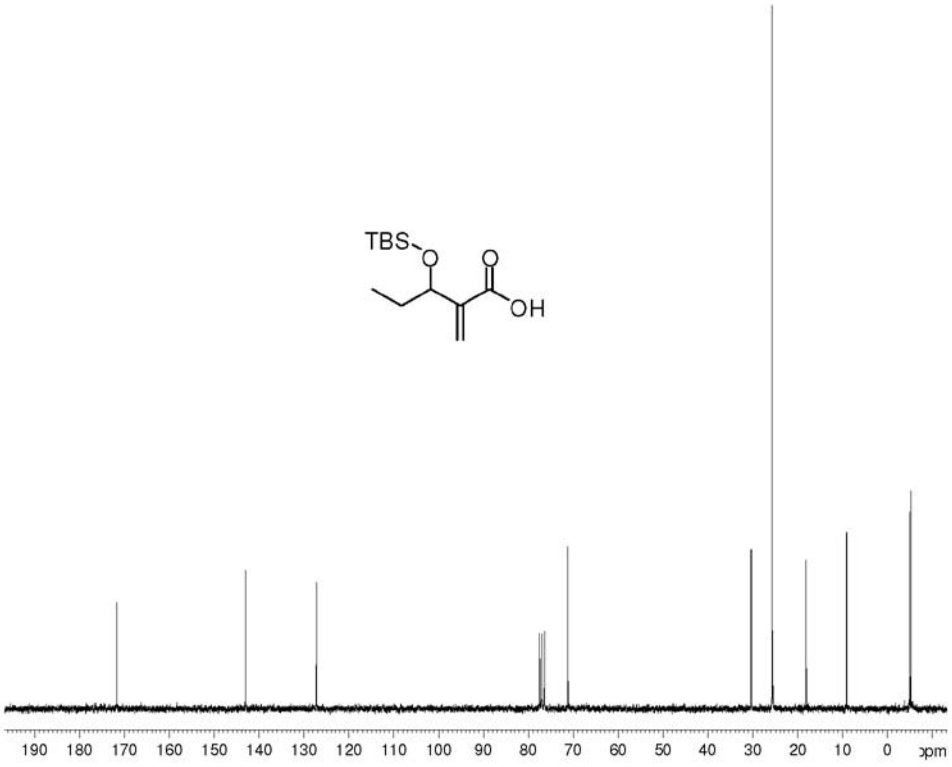

Figure S56. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **30**.

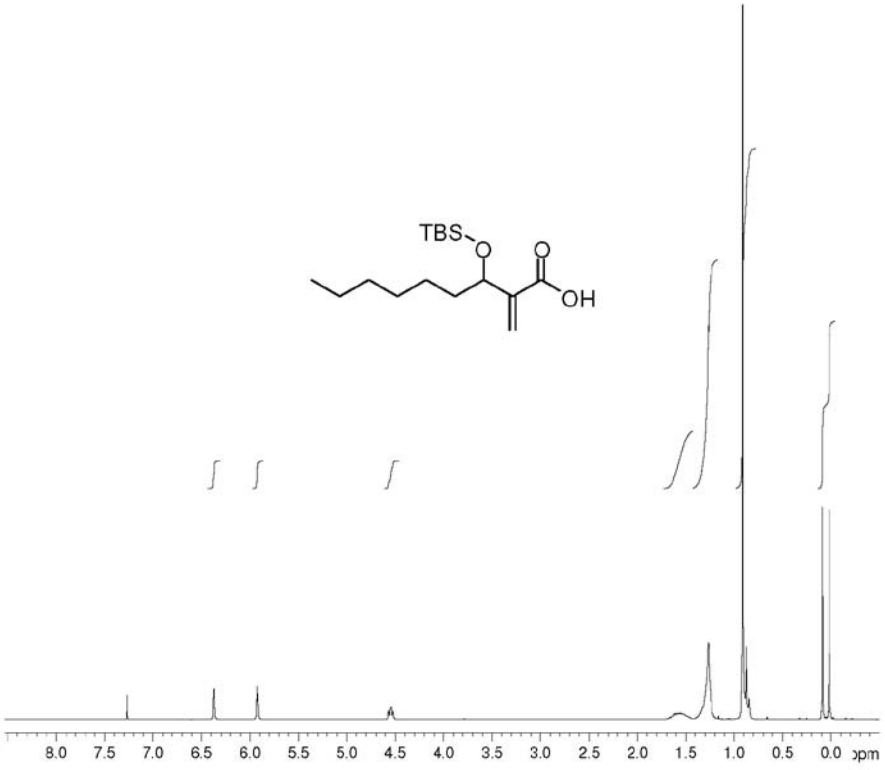

Figure S57. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **31**.

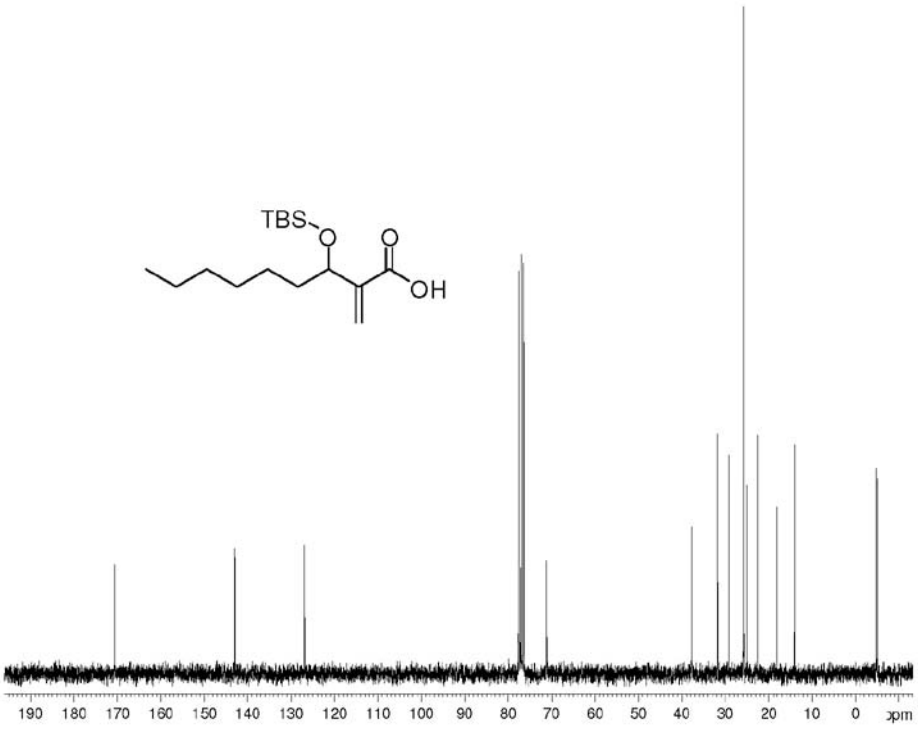

Figure S58. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **31**.

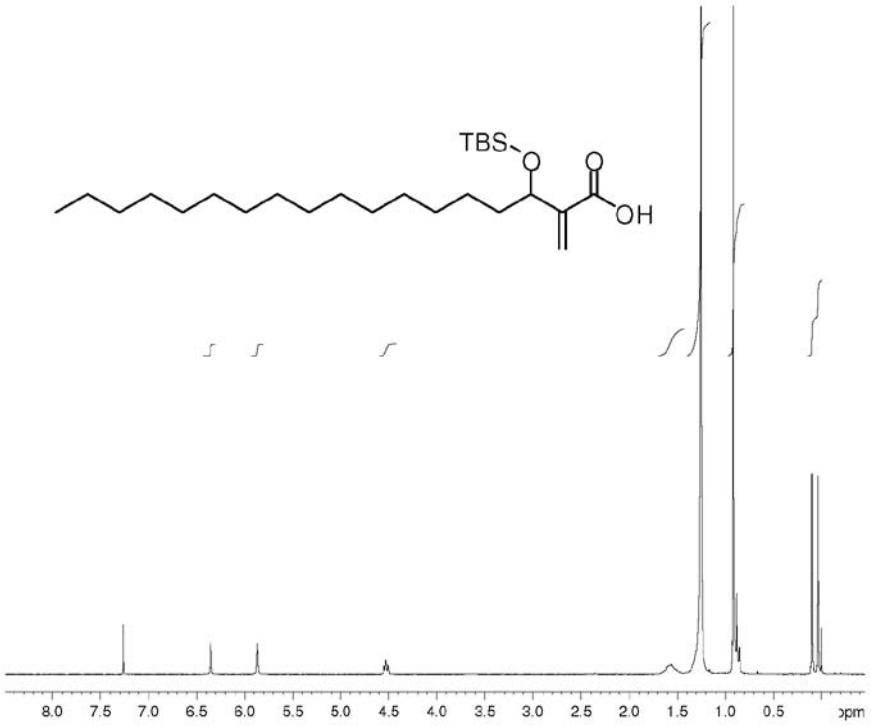

Figure S59. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated acid **32**.

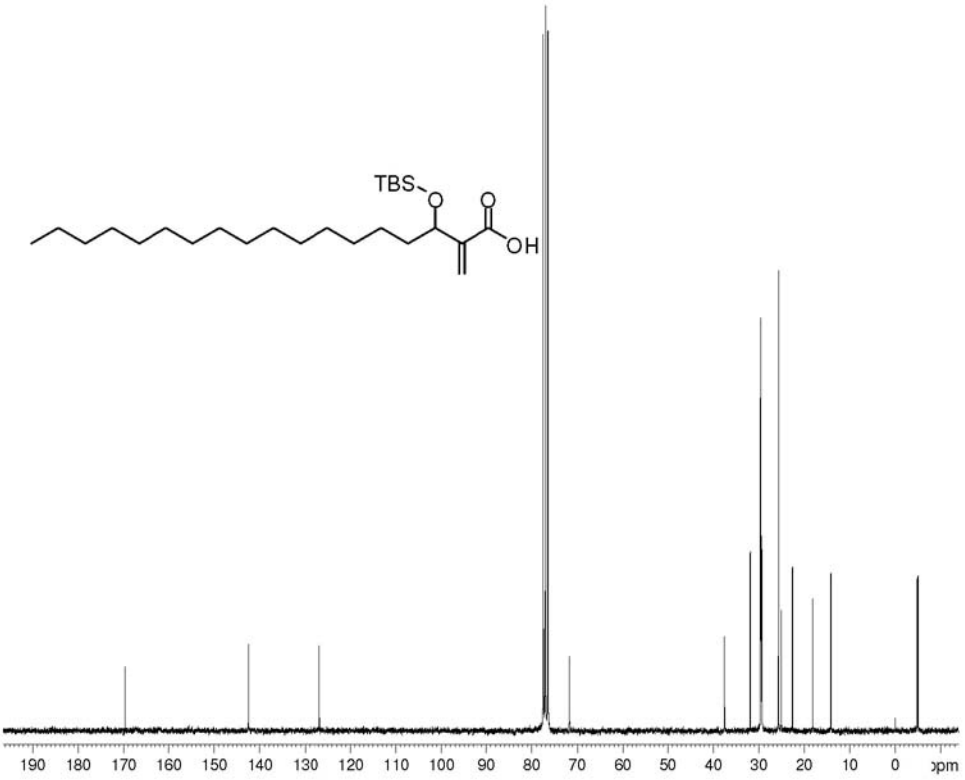

Figure S60. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated acid **32**.

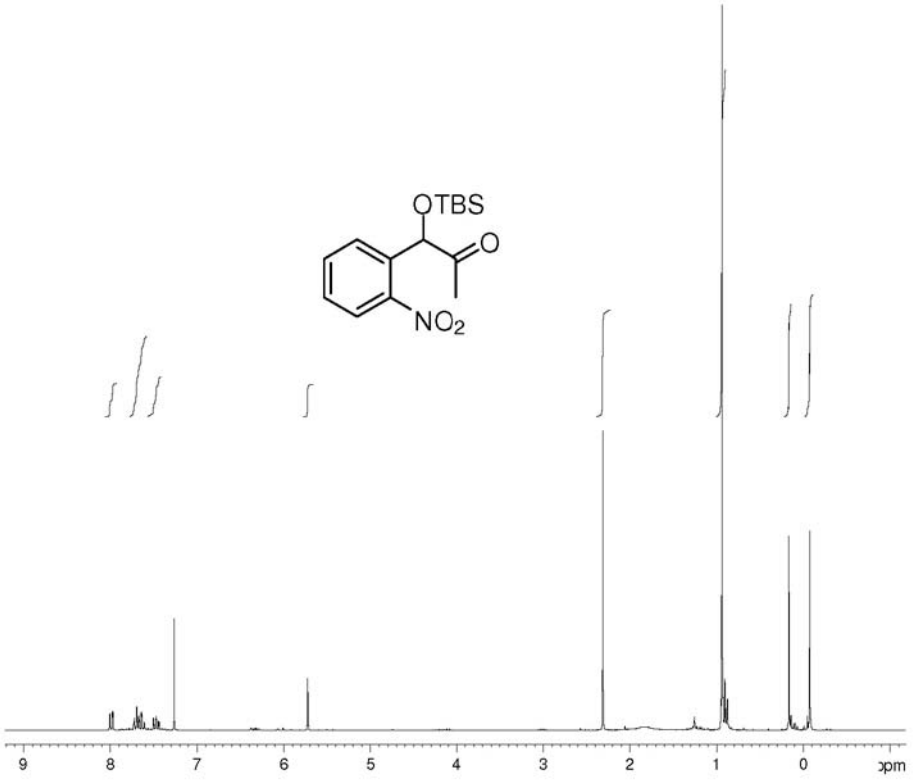

Figure S61. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **33**.

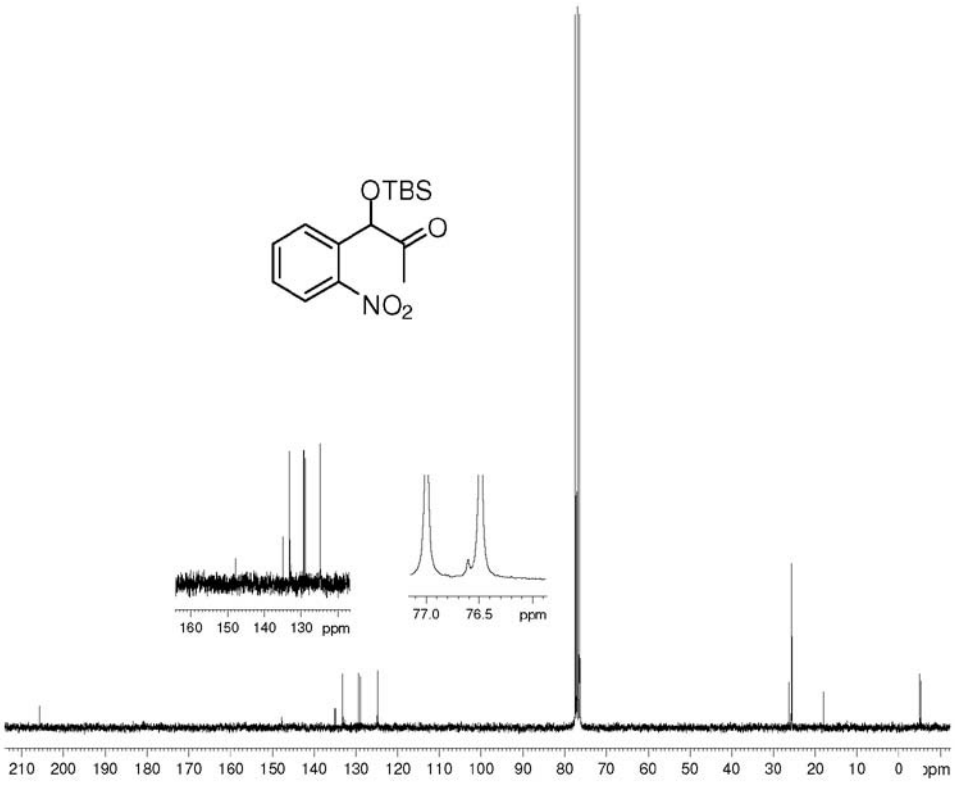

Figure S62. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **33**.

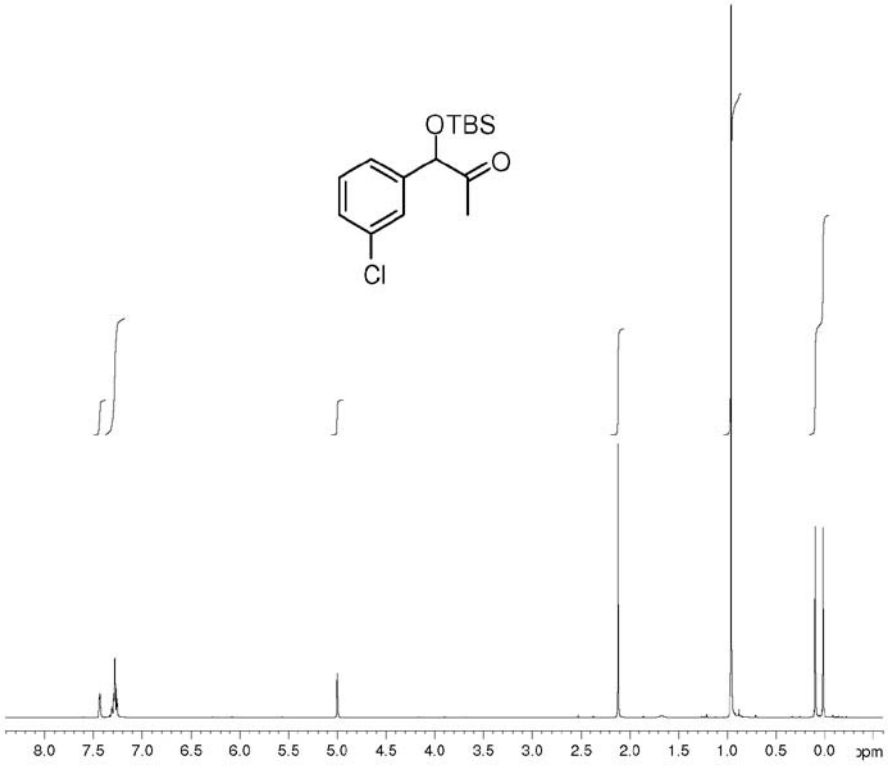

Figure S63. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **34**.

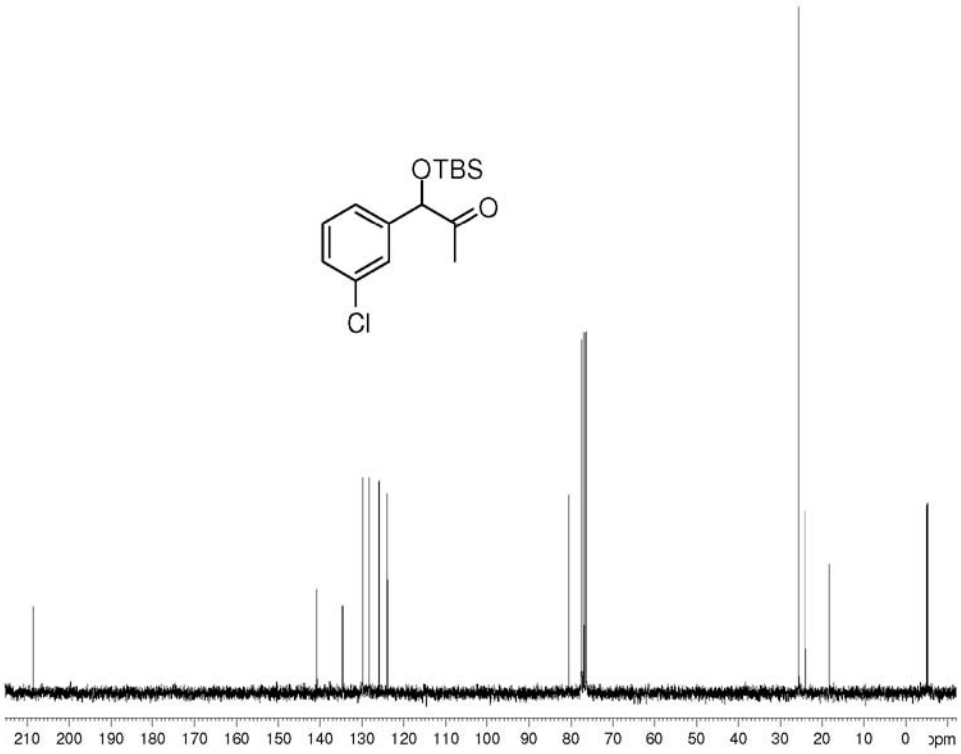

Figure S64. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **34**.

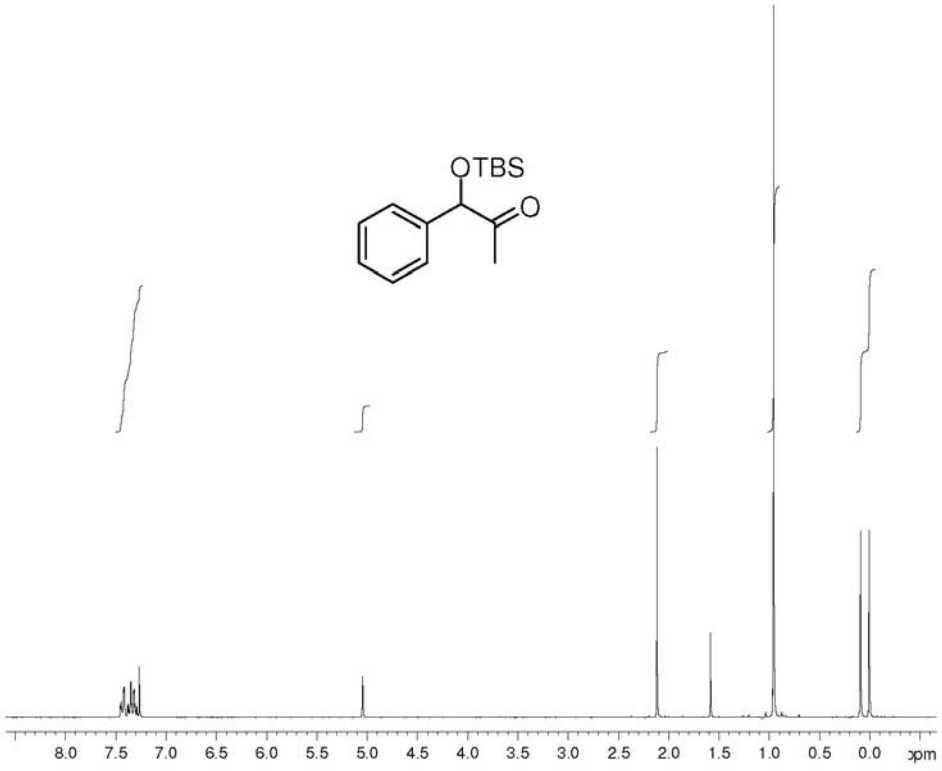

Figure S65. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **35**.

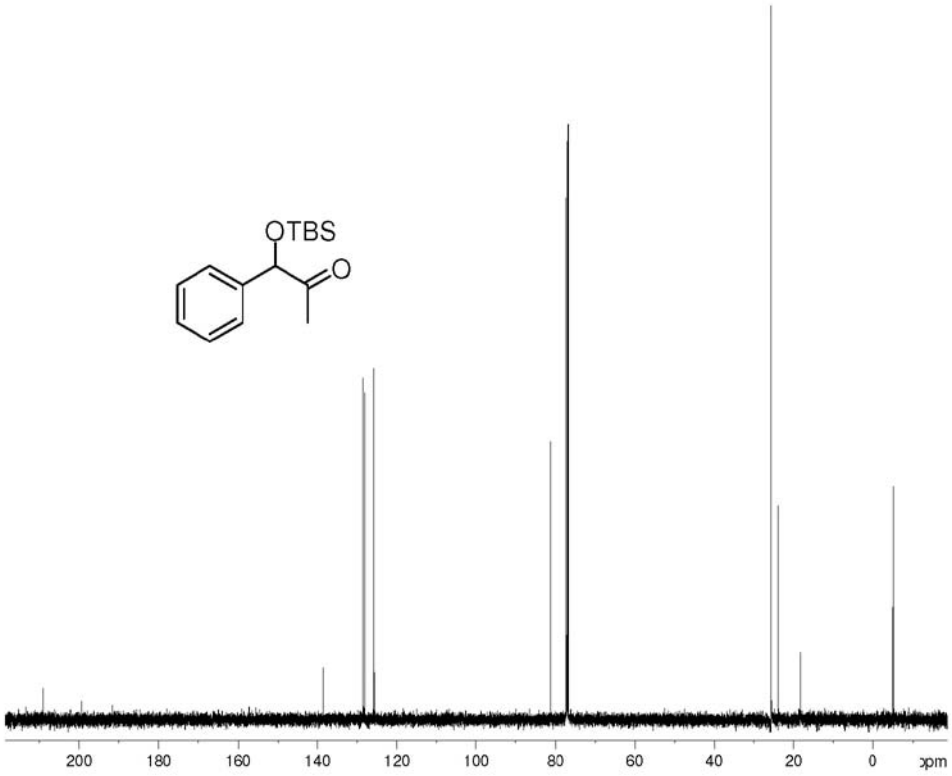

Figure S66. ^{13}C NMR ($CDCl_3$, 125 MHz) of acyloin **35**.

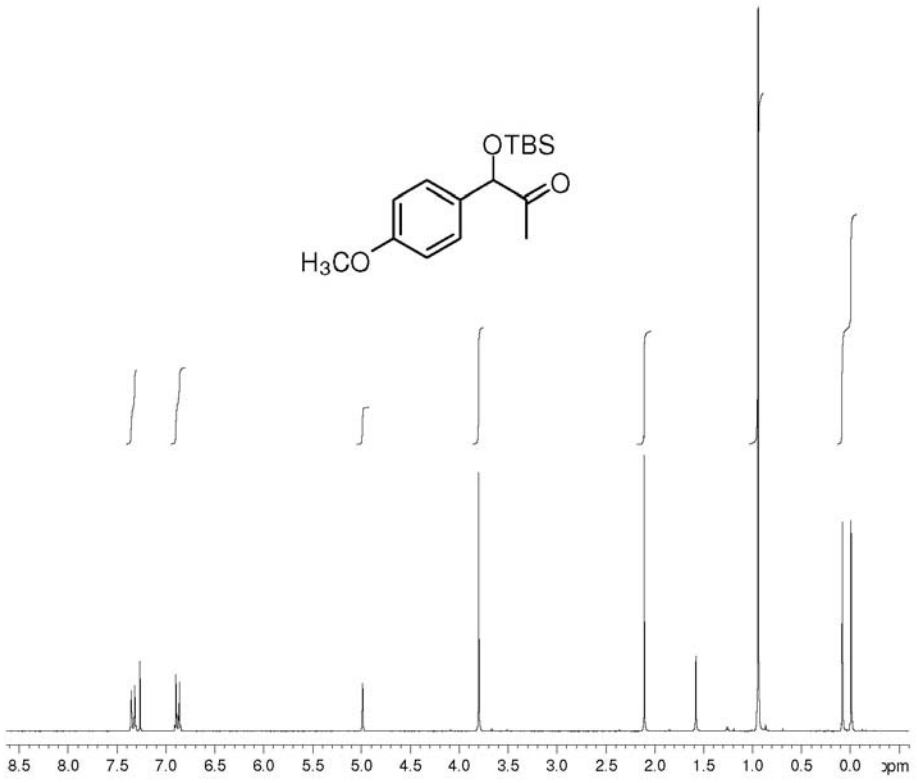

Figure S67. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **36**.

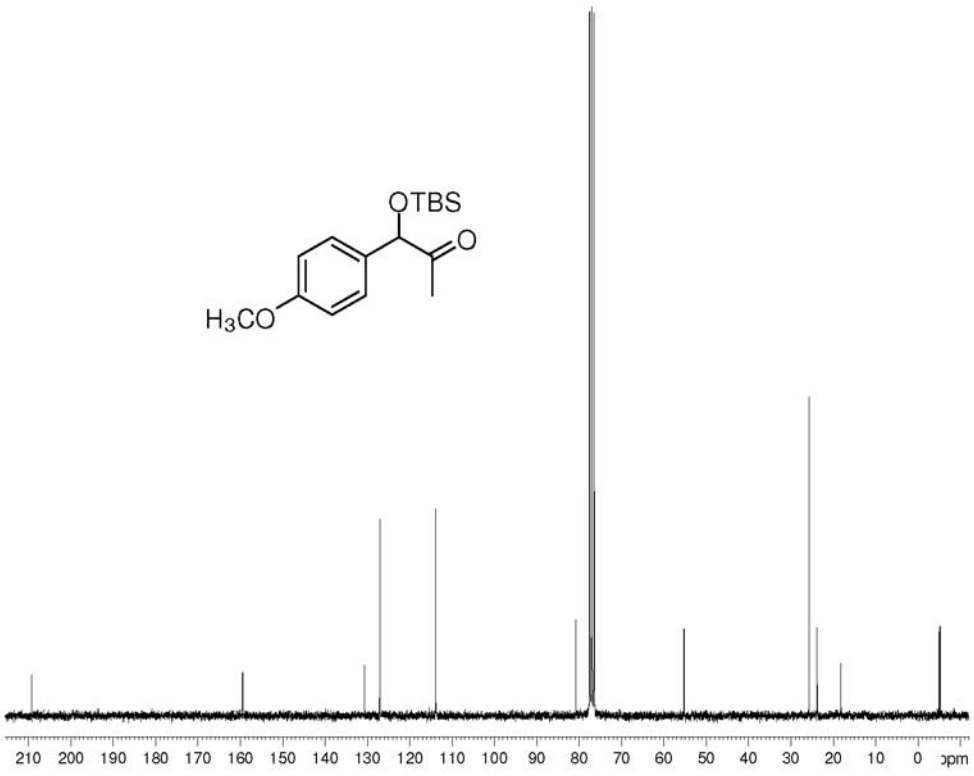

Figure S68. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **36**.

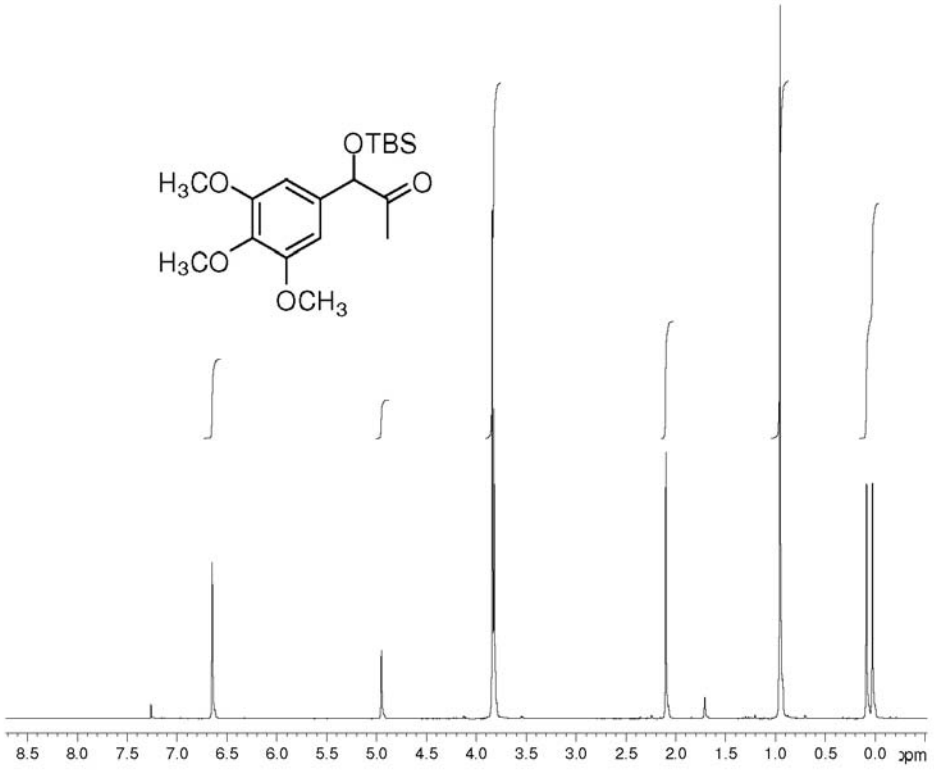

Figure S69. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **37**.

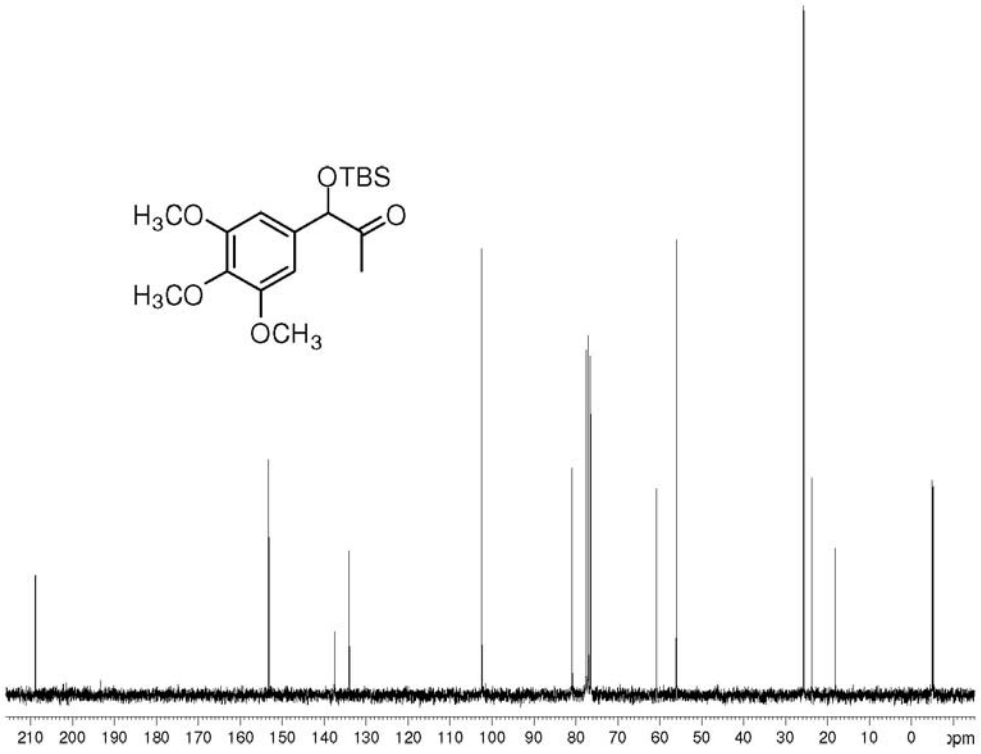

Figure S70. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **37**.

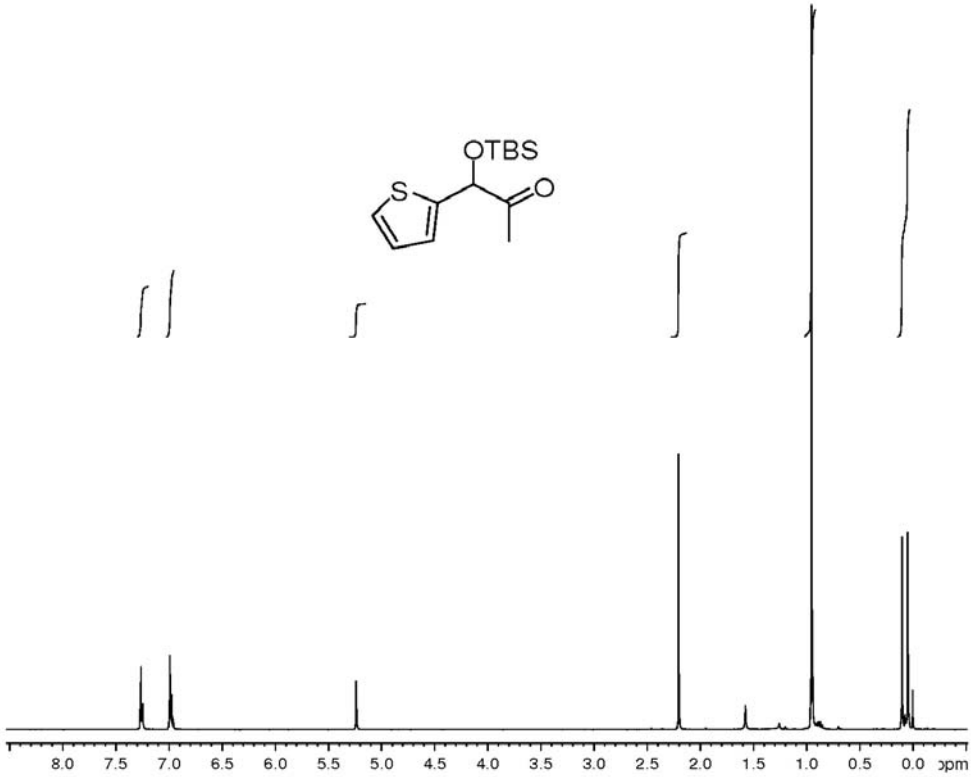

Figure S71. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **38**.

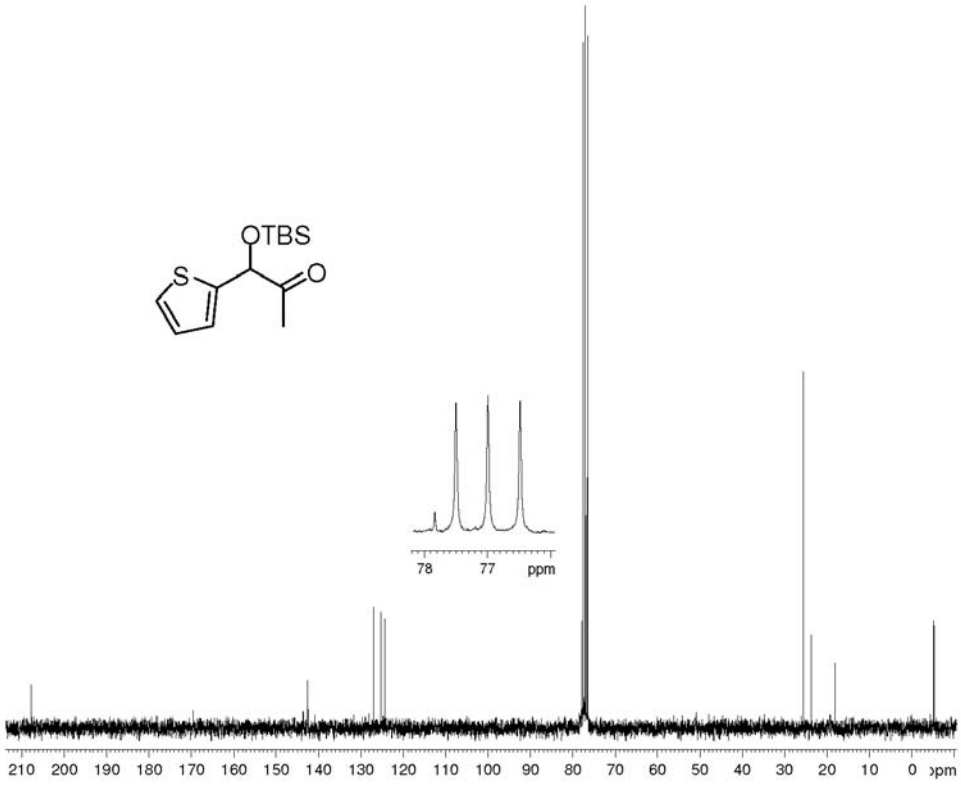

Figure S72. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **38**.

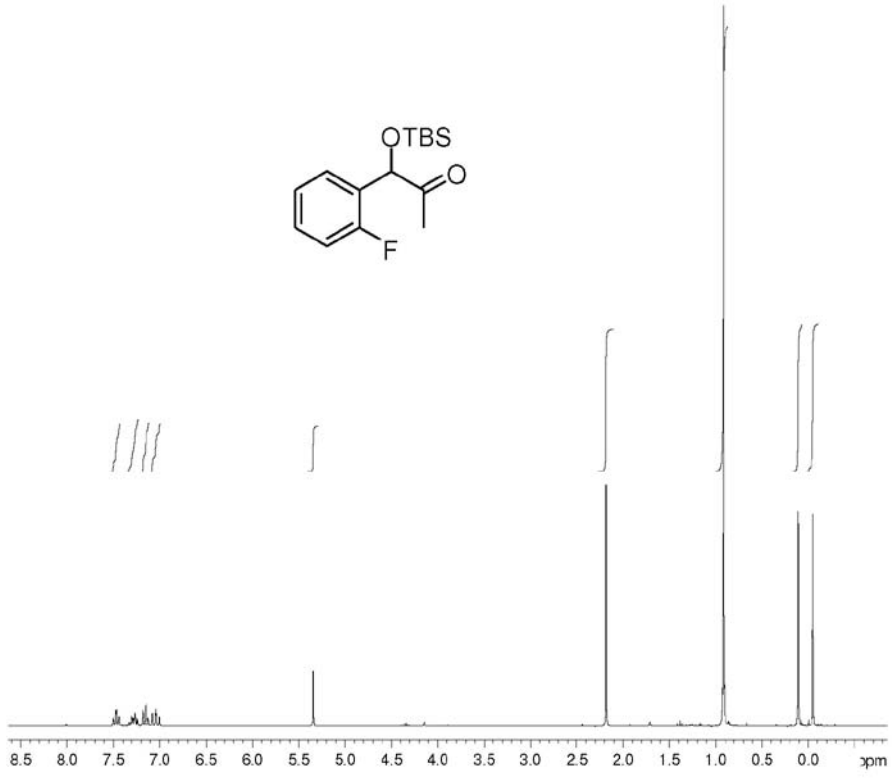

Figure S73. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **39**.

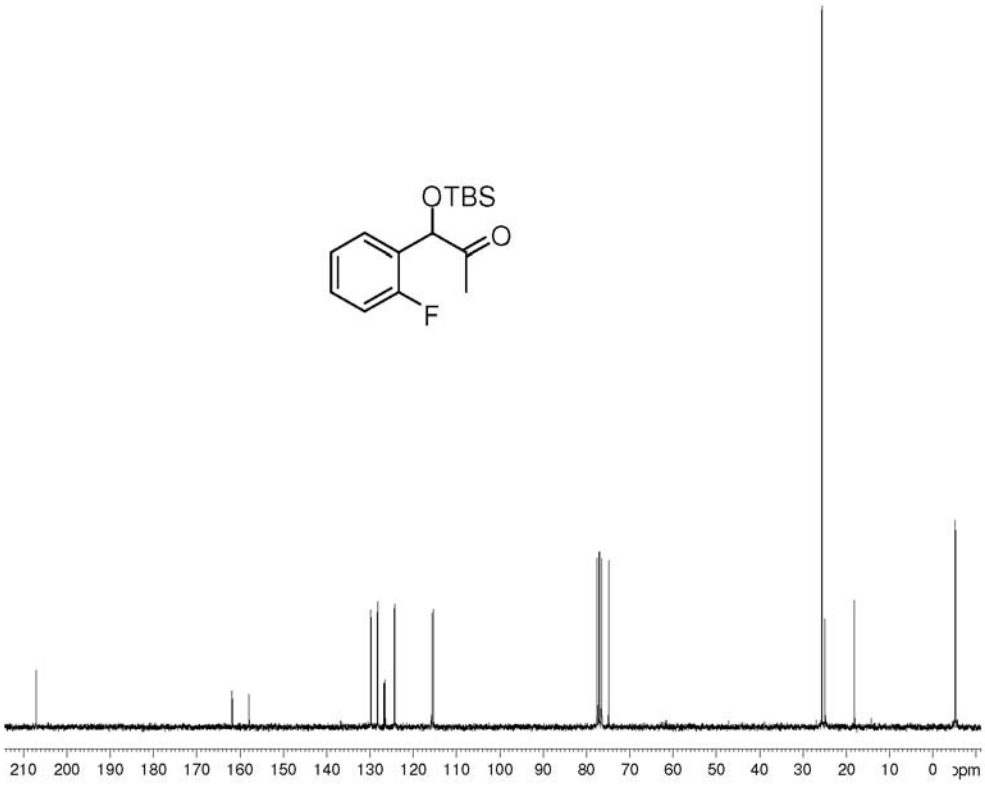

Figure S74. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **39**.

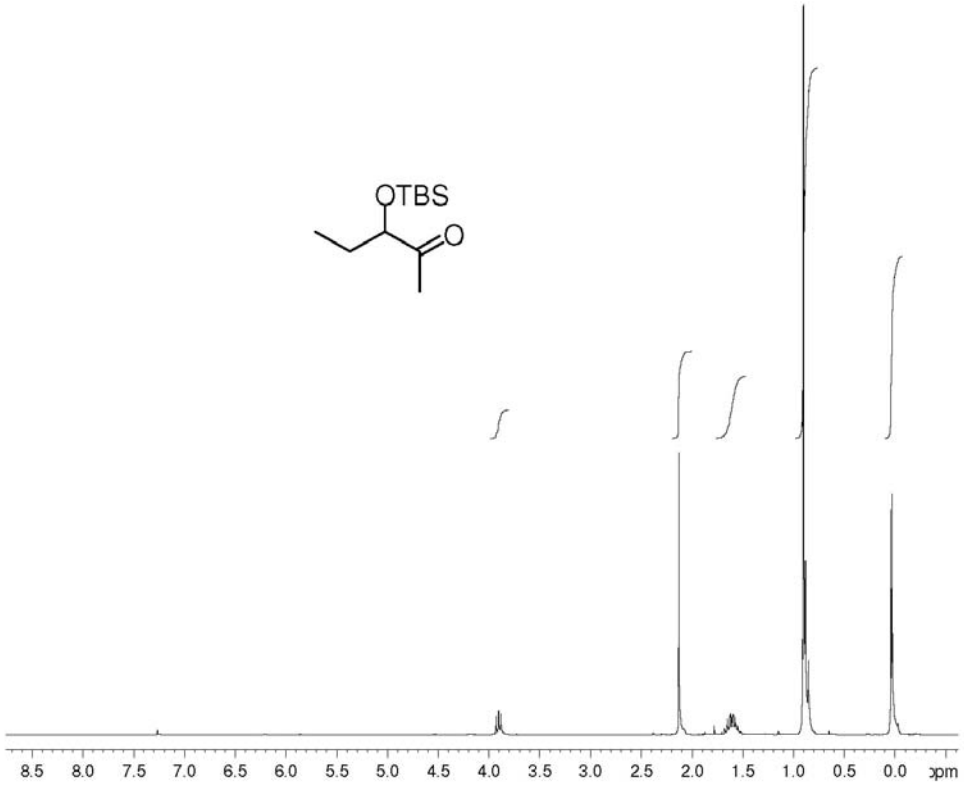

Figure S75. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **40**.

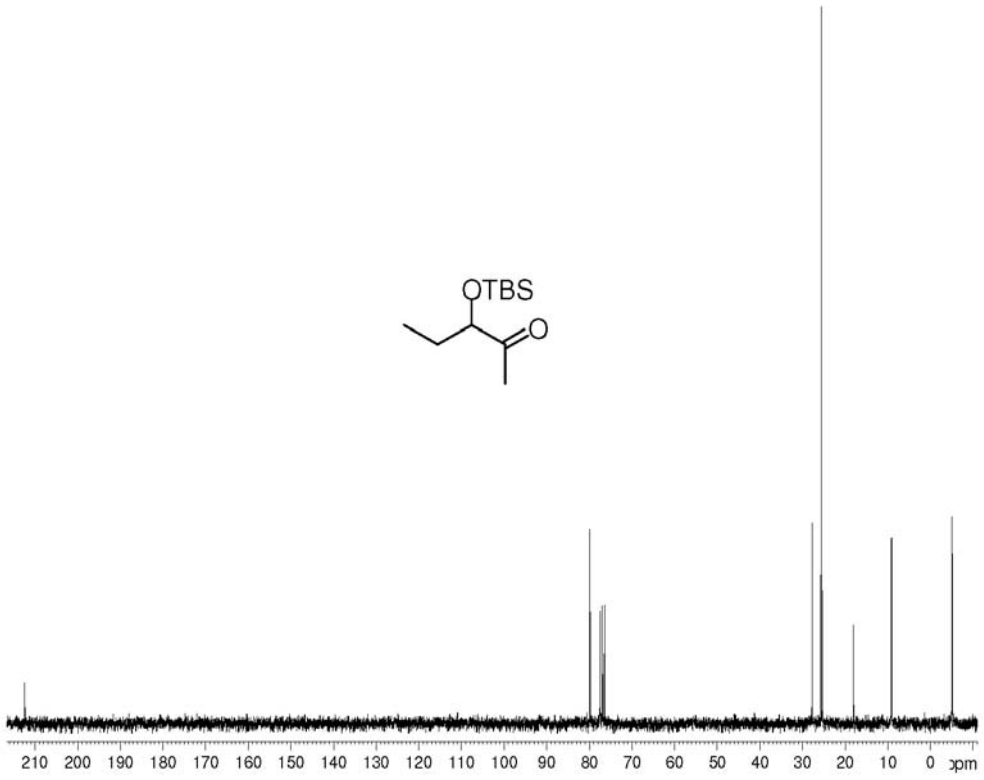

Figure S76. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **40**.

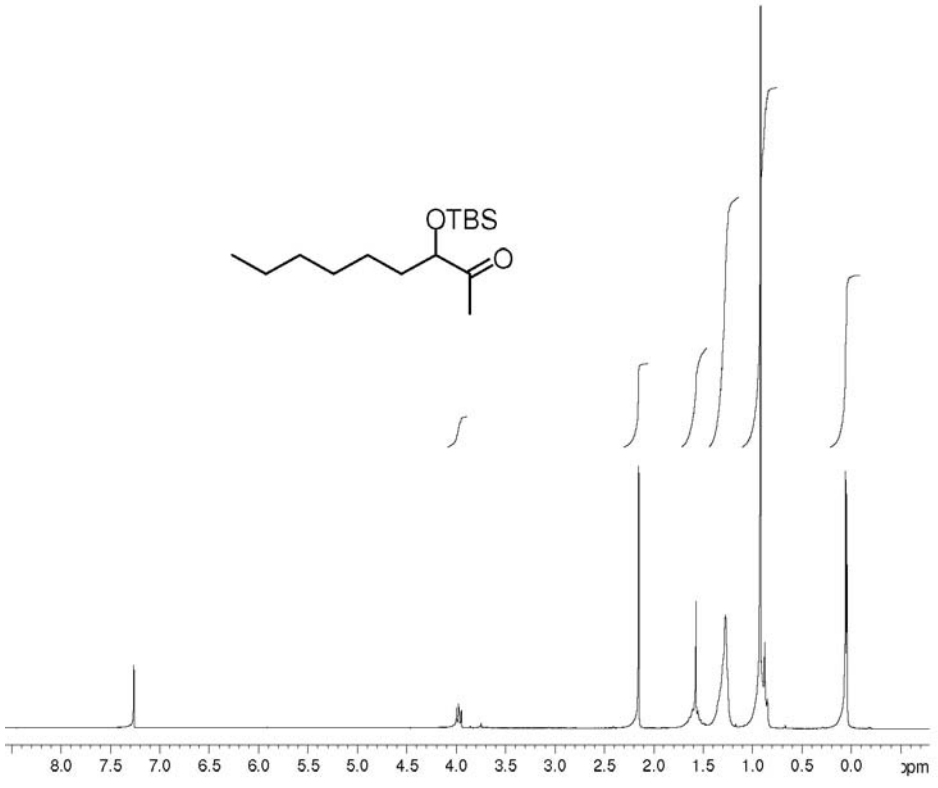

Figure S77. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **41**.

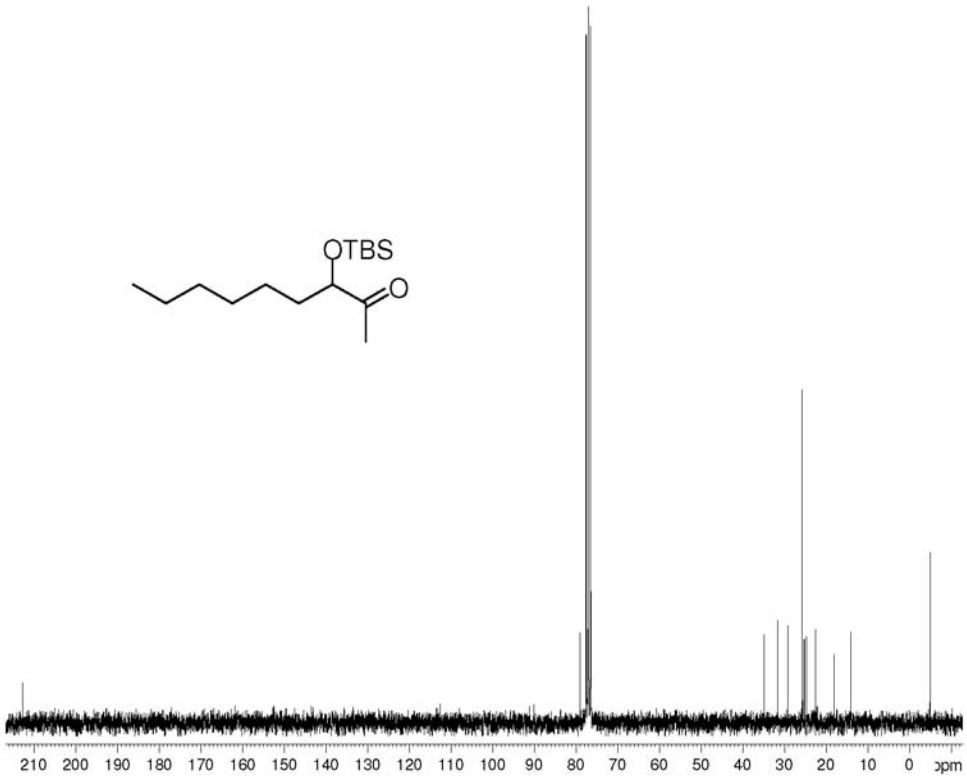

Figure S78. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **41**.

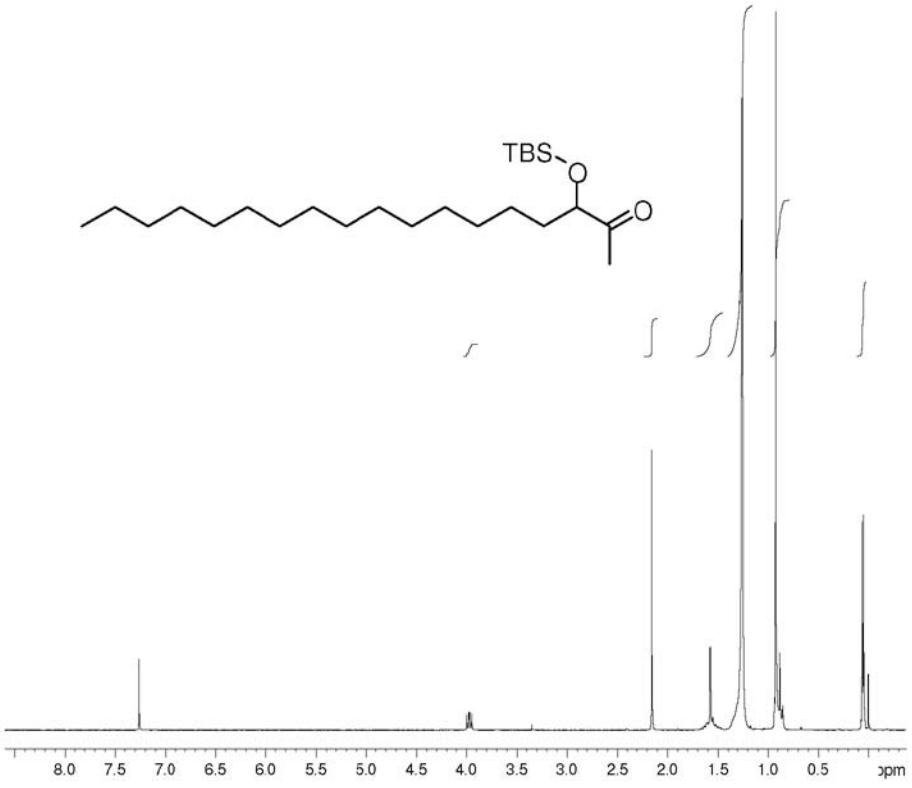

Figure S79. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **42**.

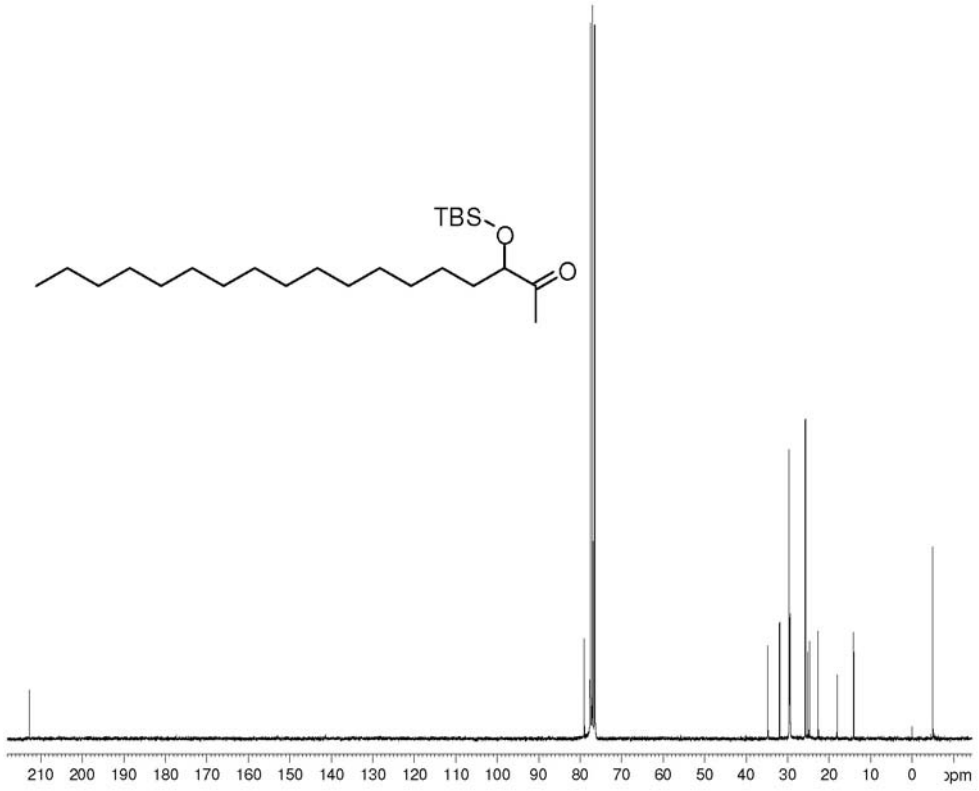

Figure S80. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of acyloin **41**.

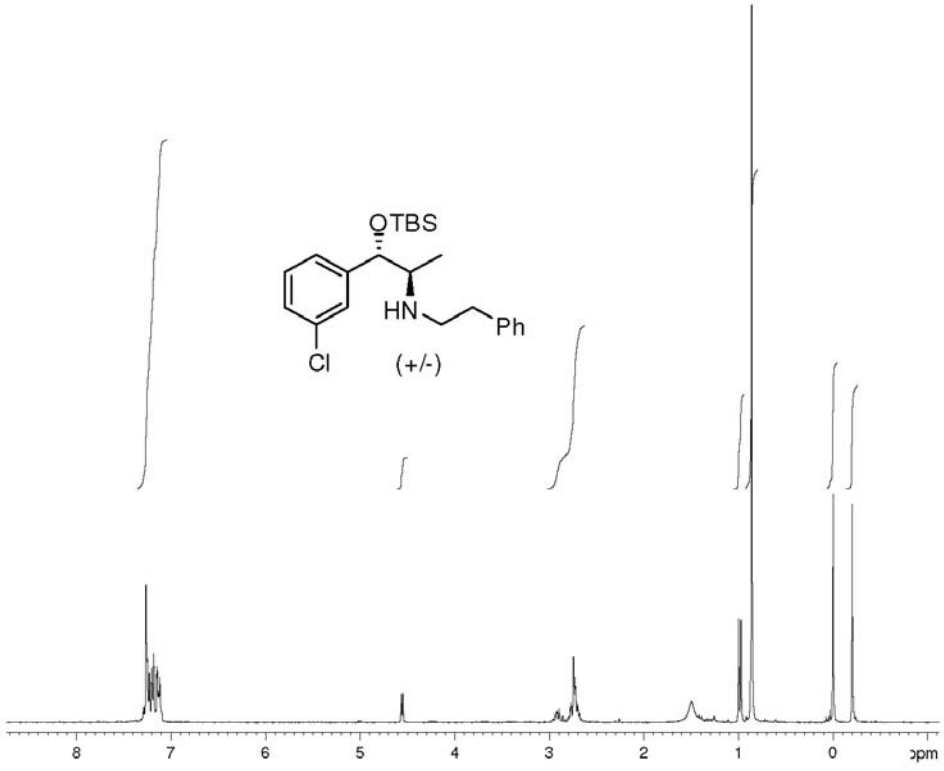

Figure S81. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **43**.

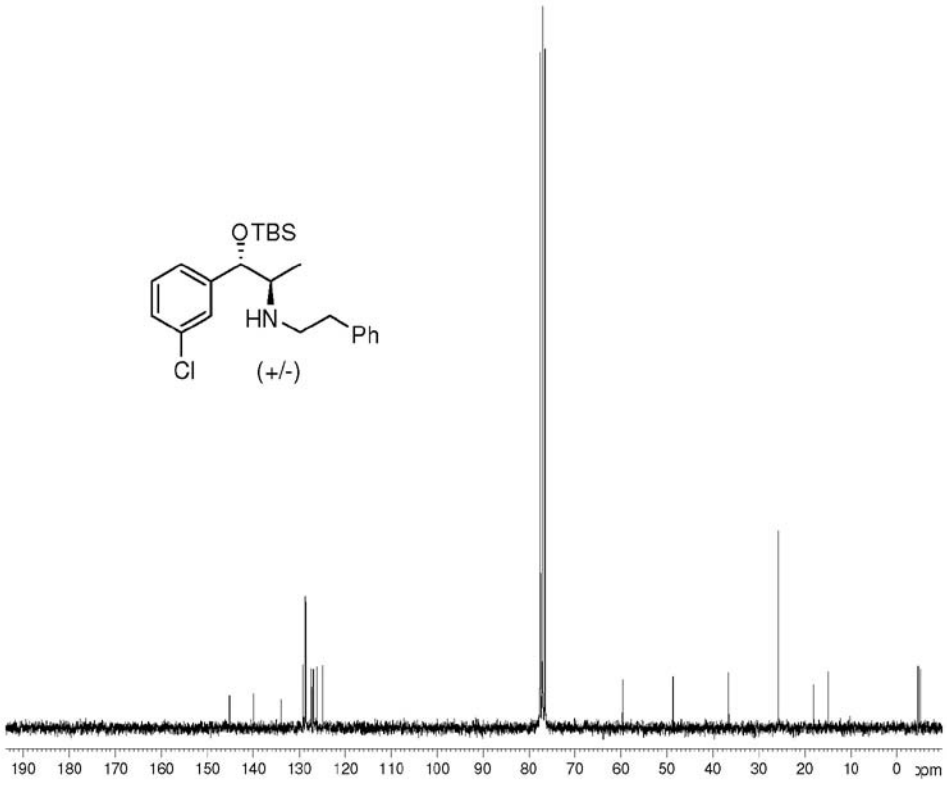

Figure S82. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **43**.

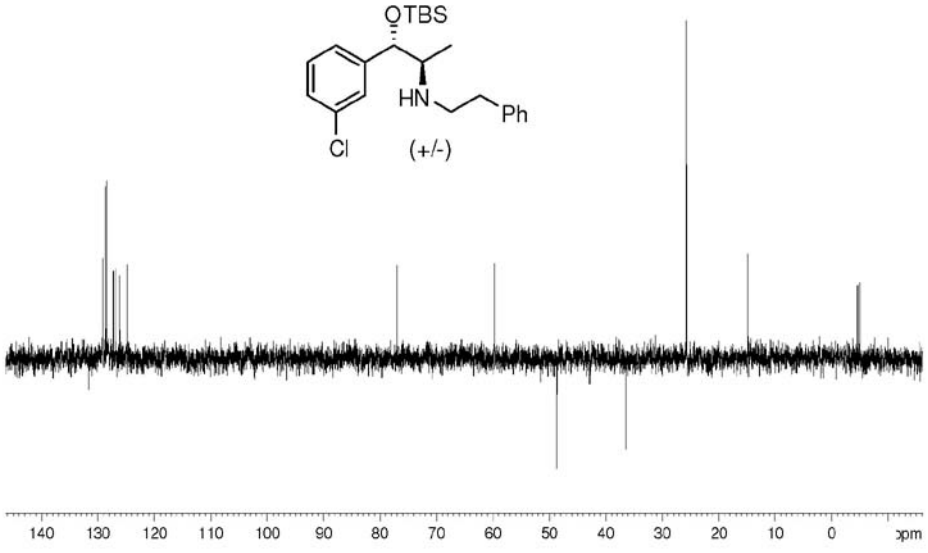

Figure S83. DEPT 135 ($CDCl_3$, 62.5 MHz) of of vicinal aminoalcohol **43**.

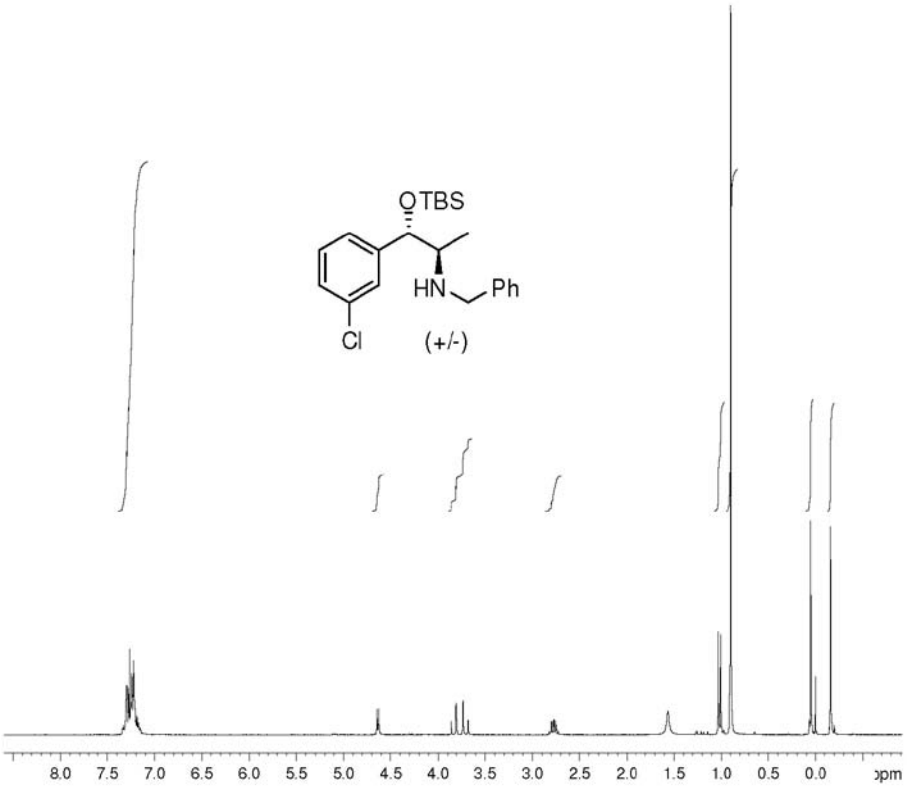

Figure S84. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **44**.

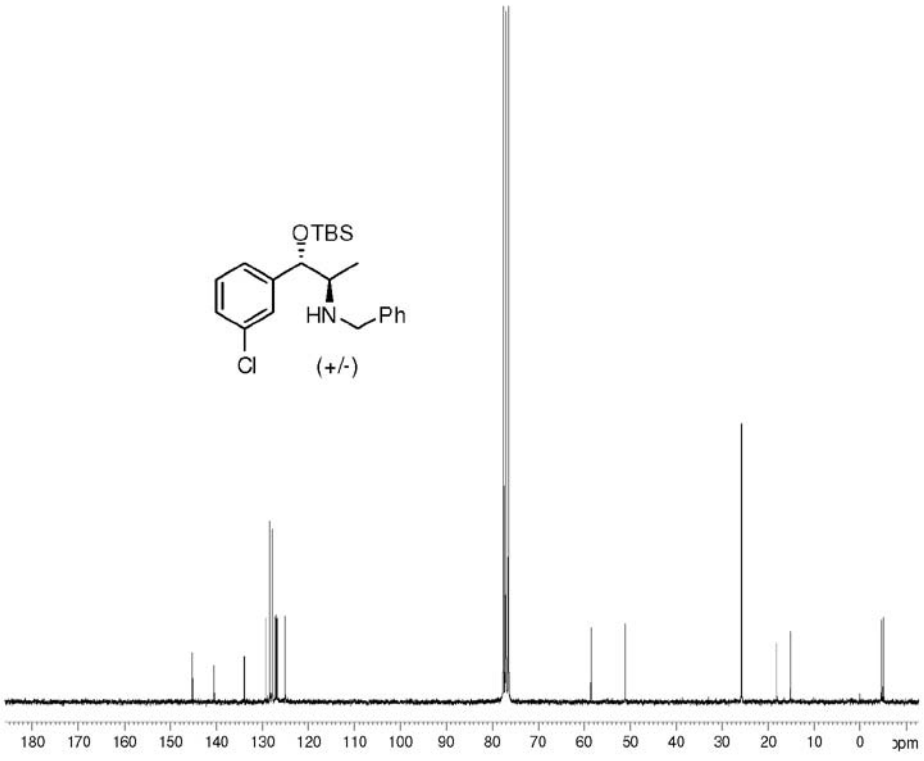

Figure S85. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **44**.

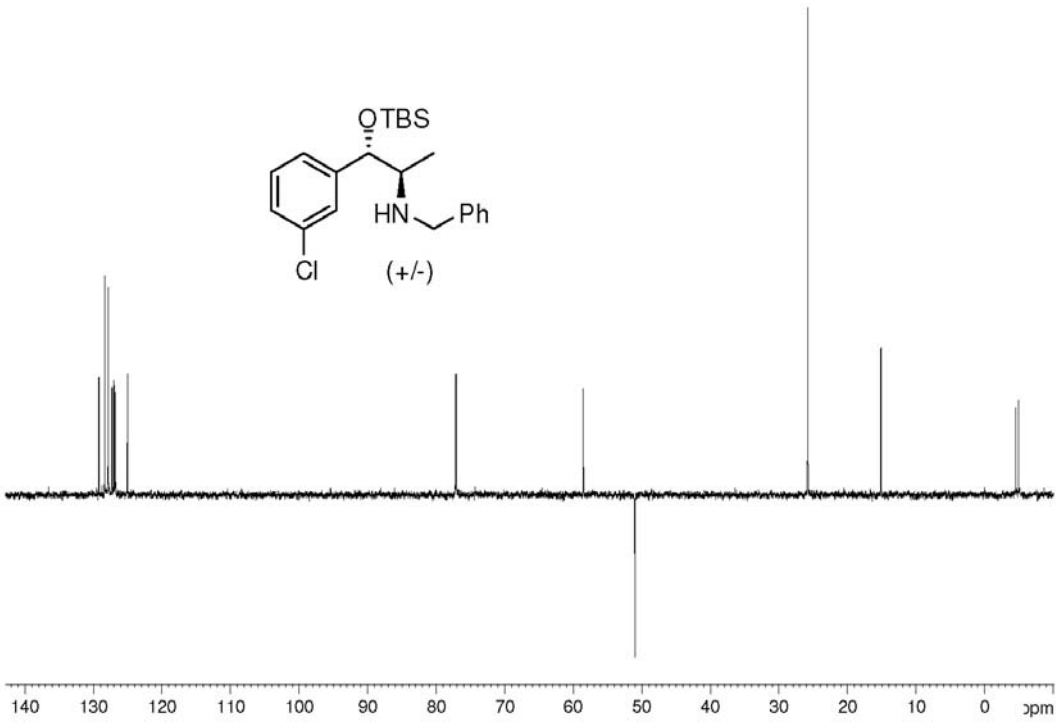

Figure S86. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **44**.

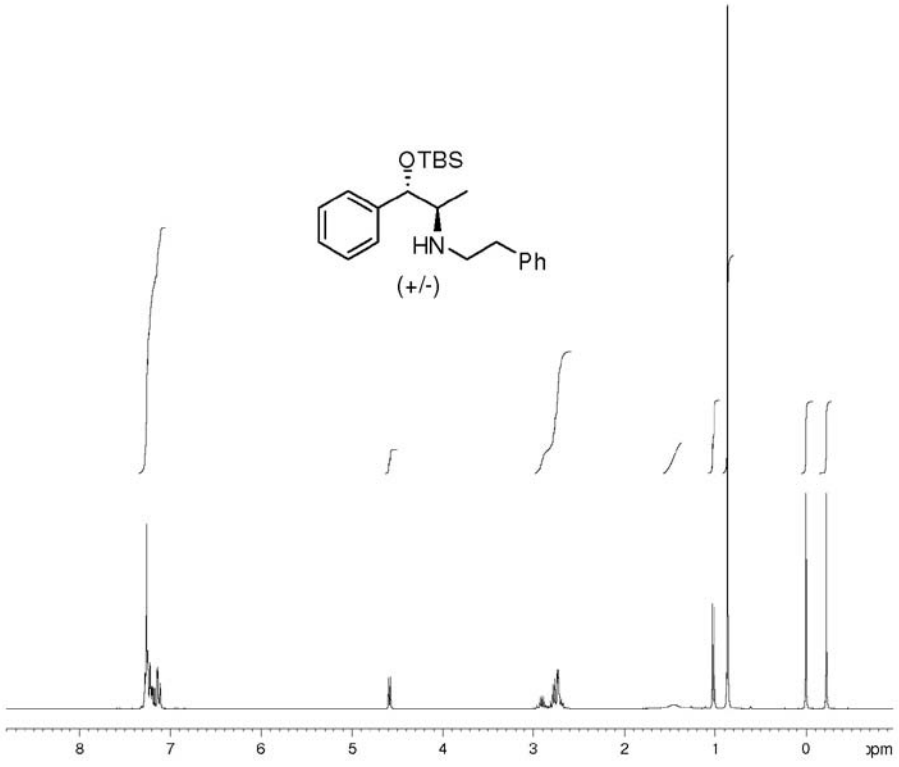

Figure S87.^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **45**.

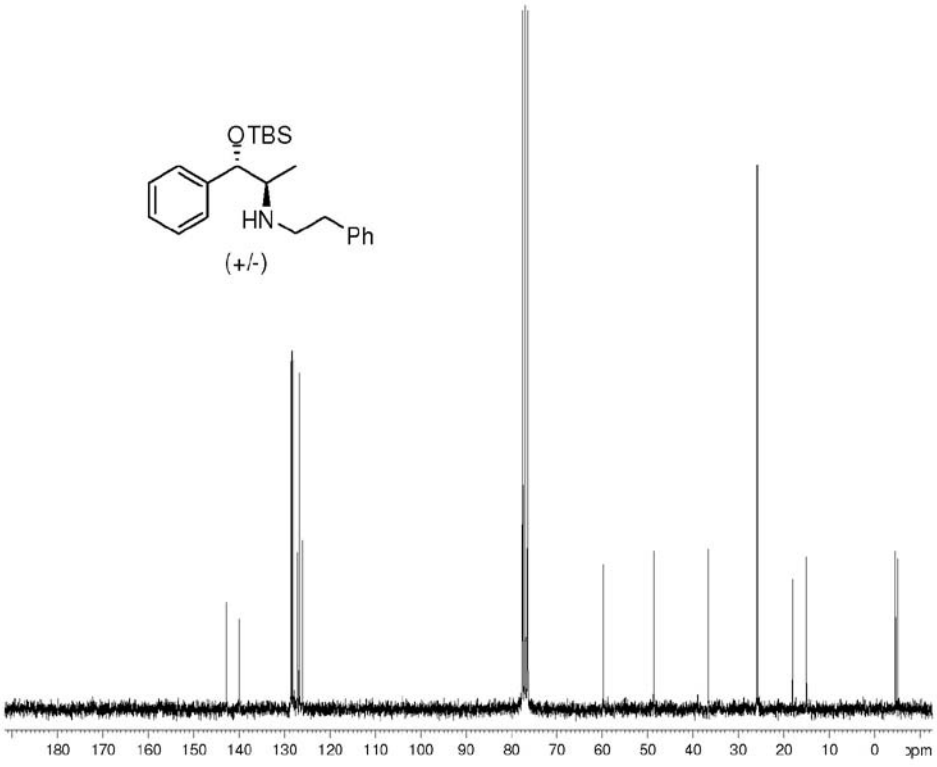

Figure S88. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **45**.

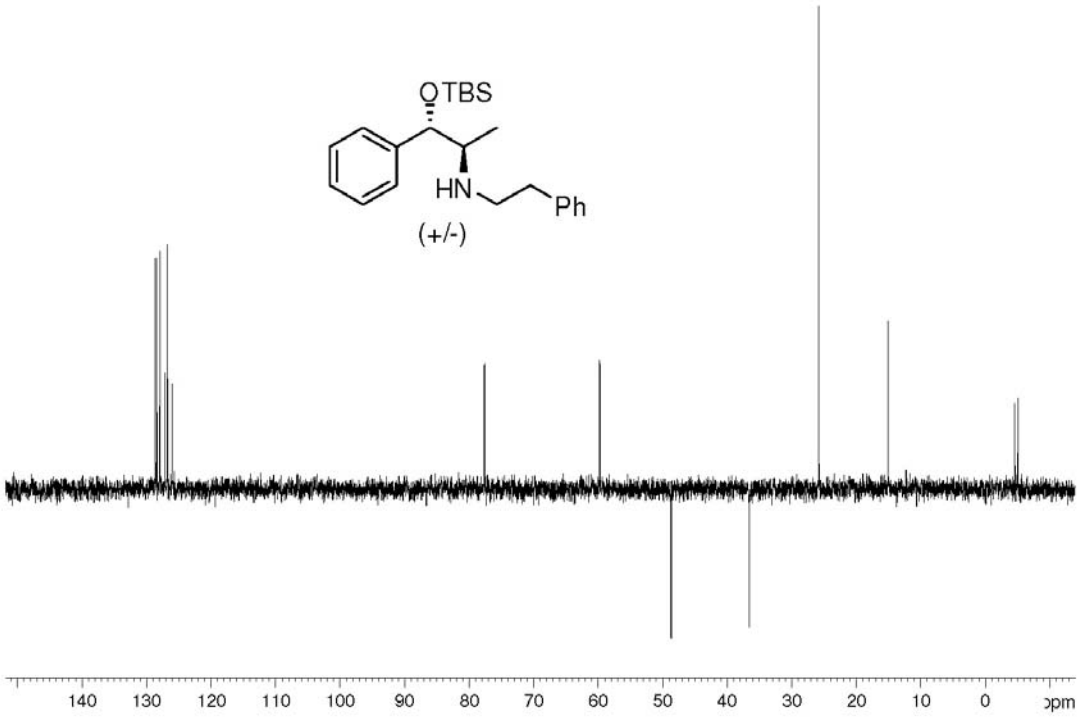

Figure S89. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **45**.

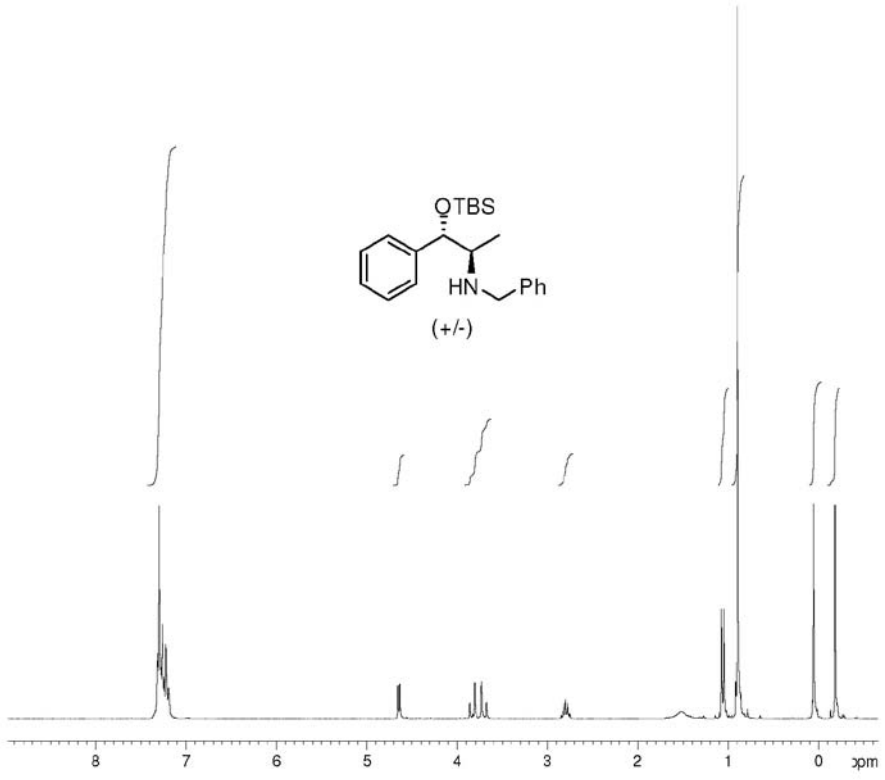

Figure S90. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **46**.

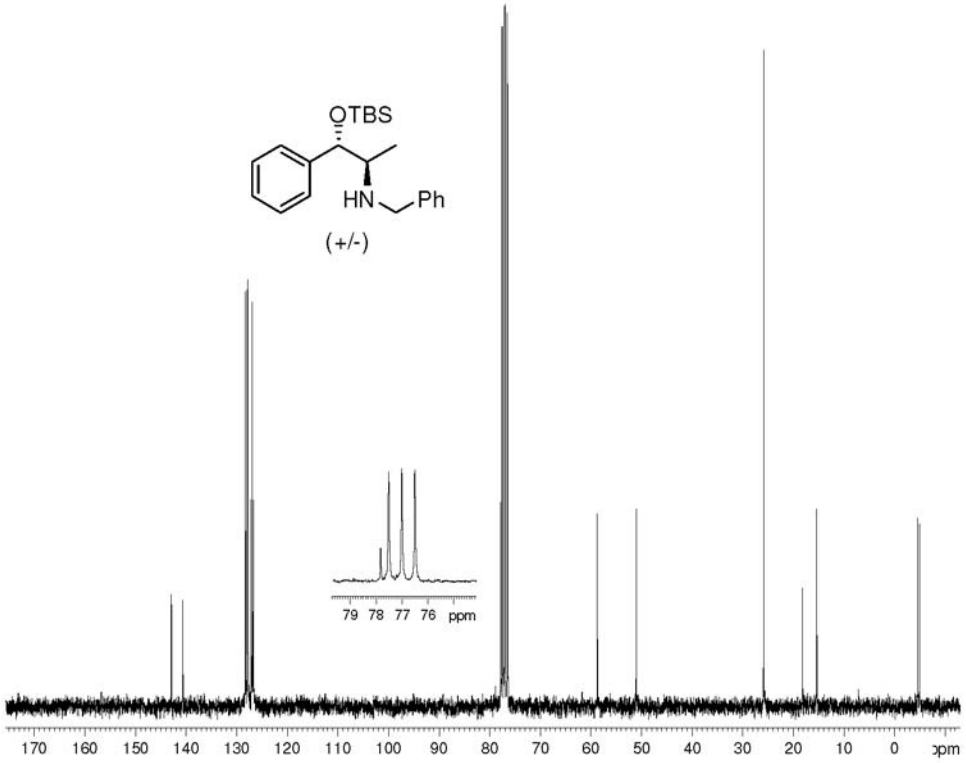

Figure S91. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **46**.

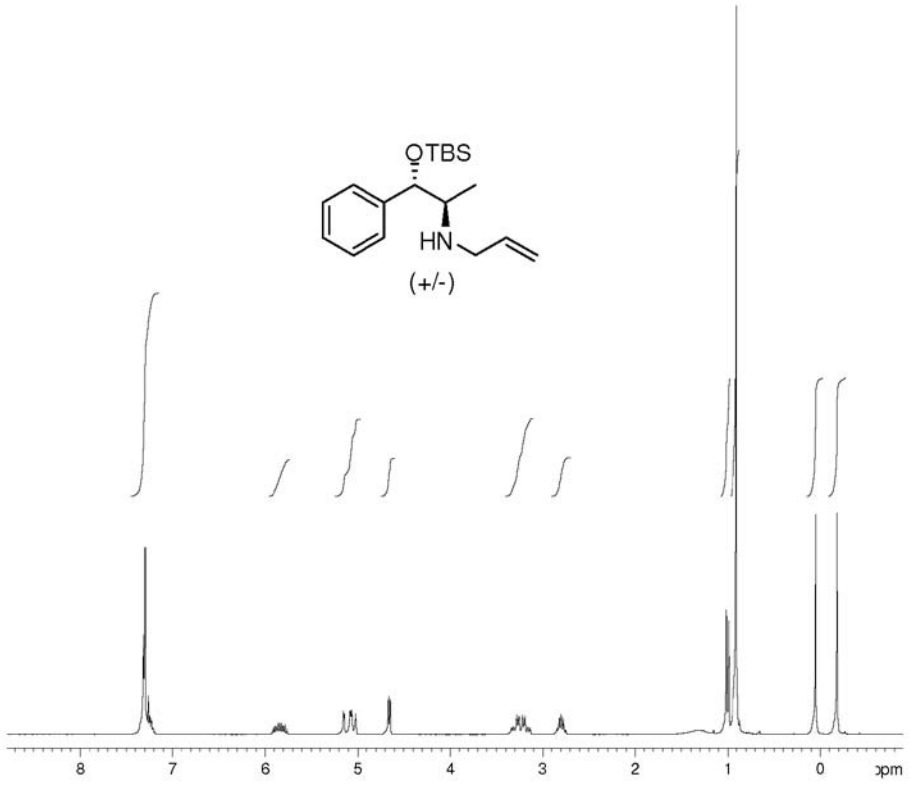

Figure S92. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **47**.

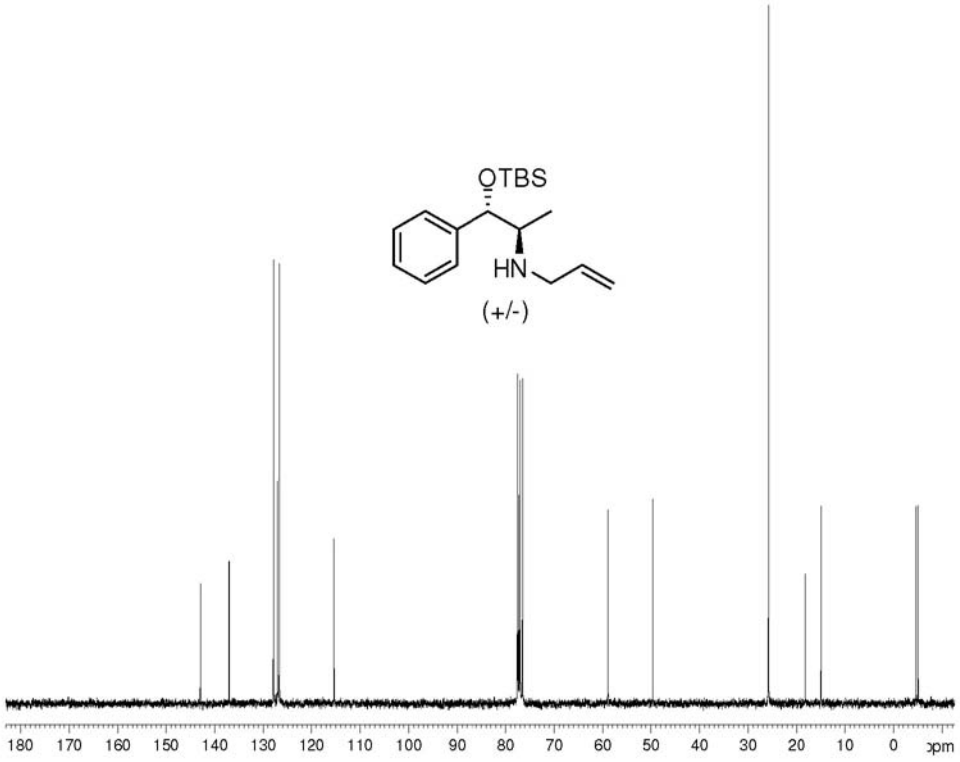

Figure S93. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **47**.

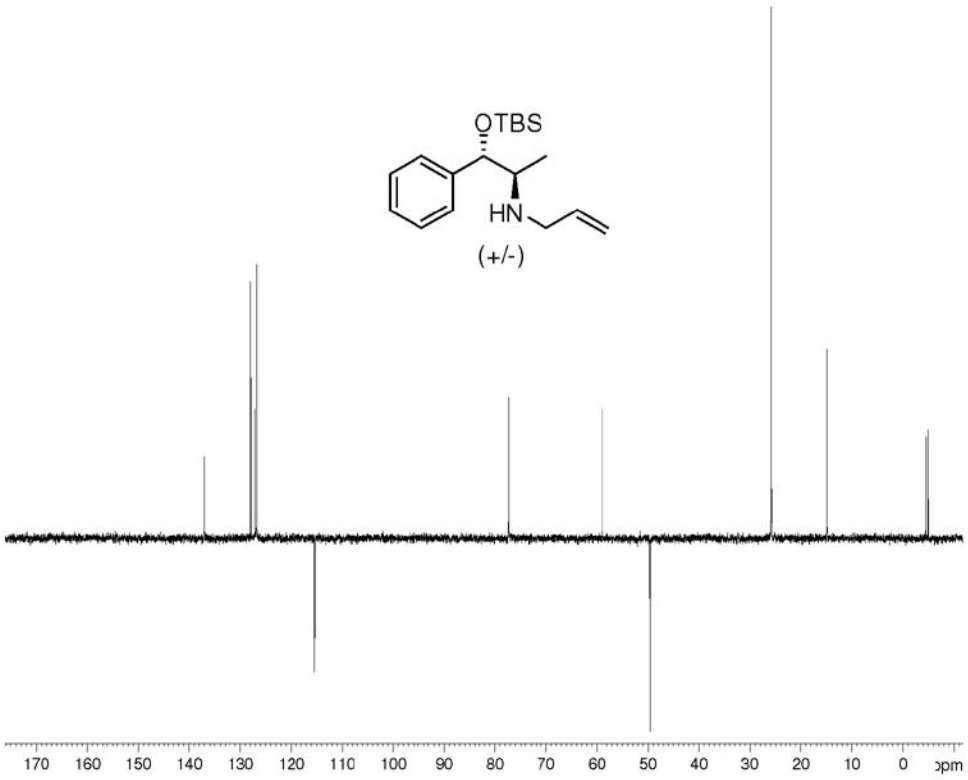

Figure S94. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **47**.

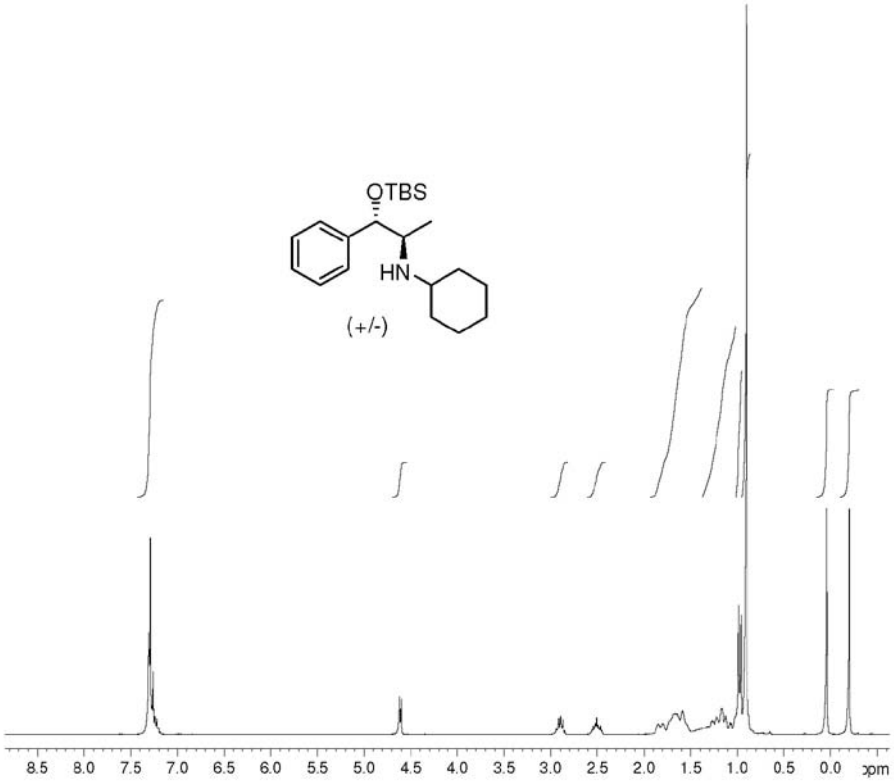

Figure S95. ^1H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **48**.

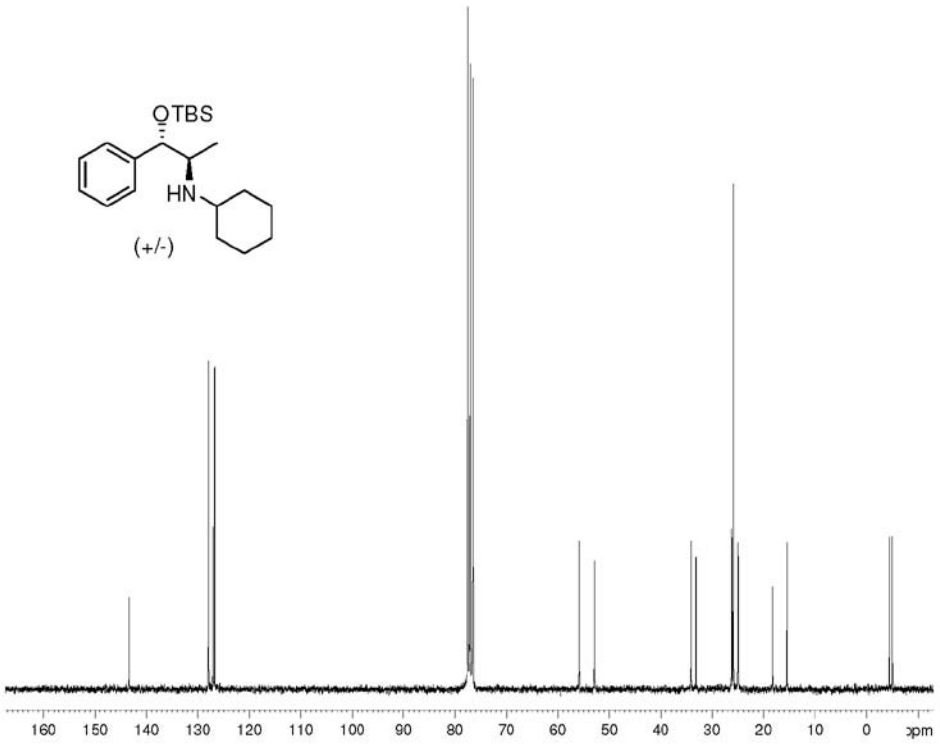

Figure S96. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **48**.

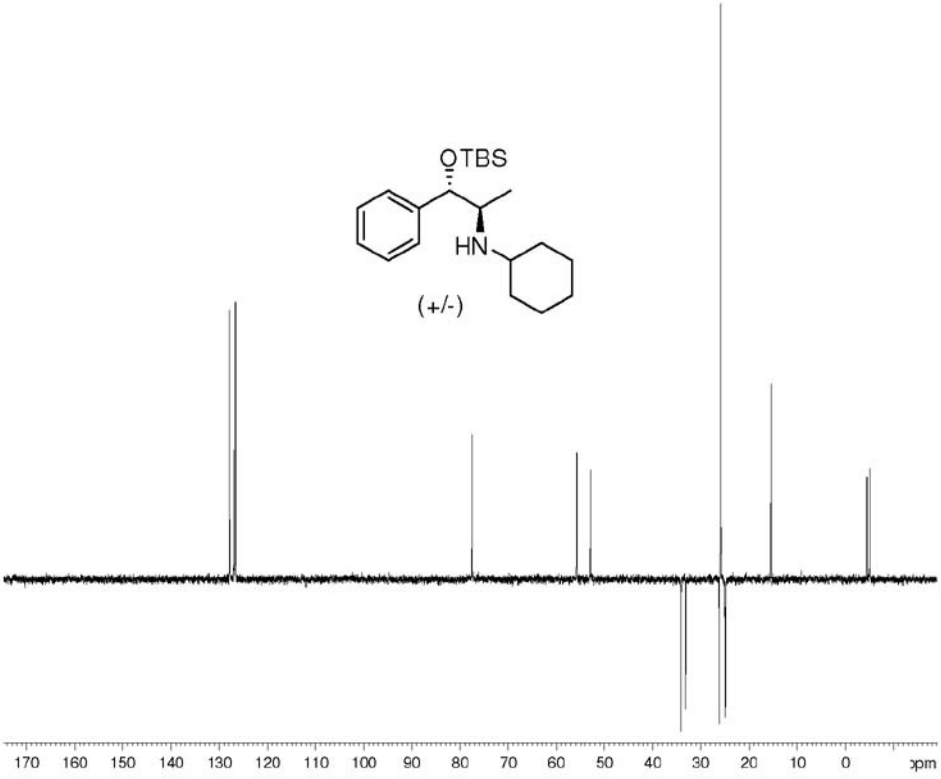

Figure S97. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **48**.

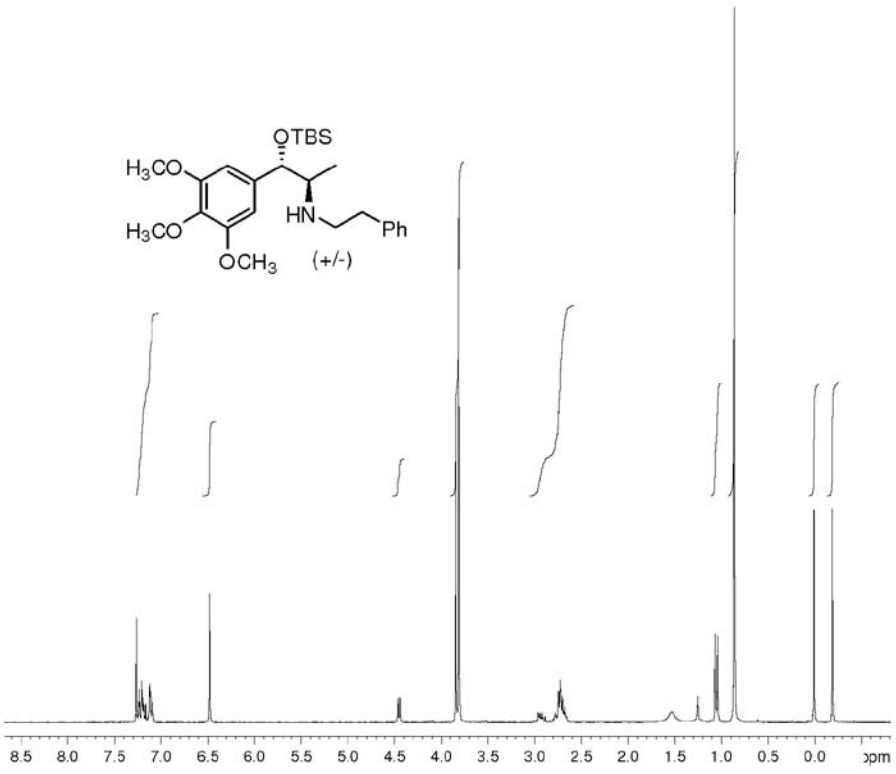

Figure S98. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalchol **49**.

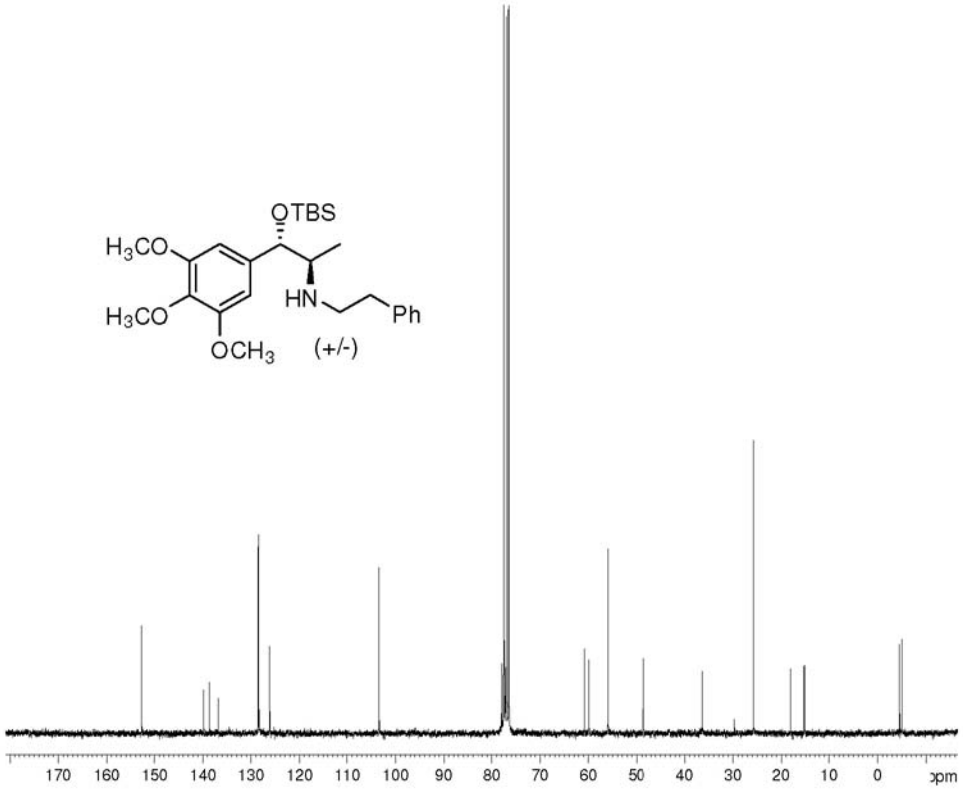

Figure S99. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **49**.

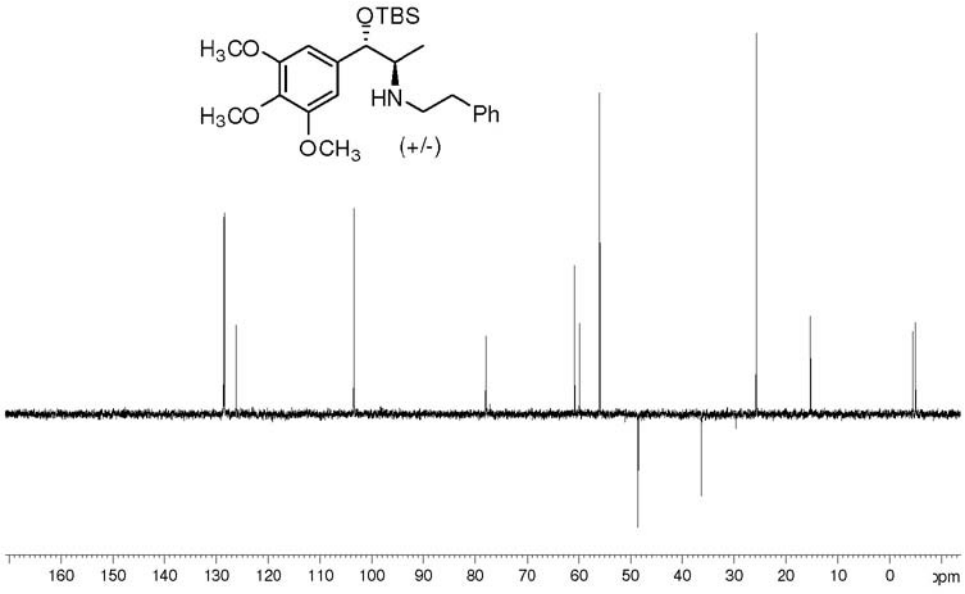

Figure S100. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **49**.

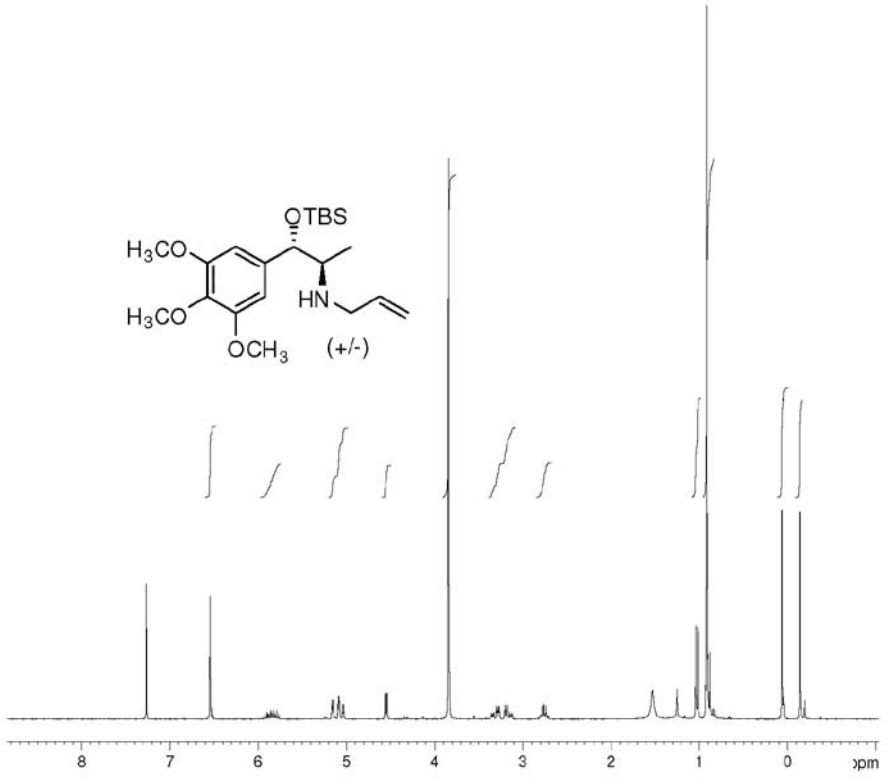

Figure S101. ^1H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **50**.

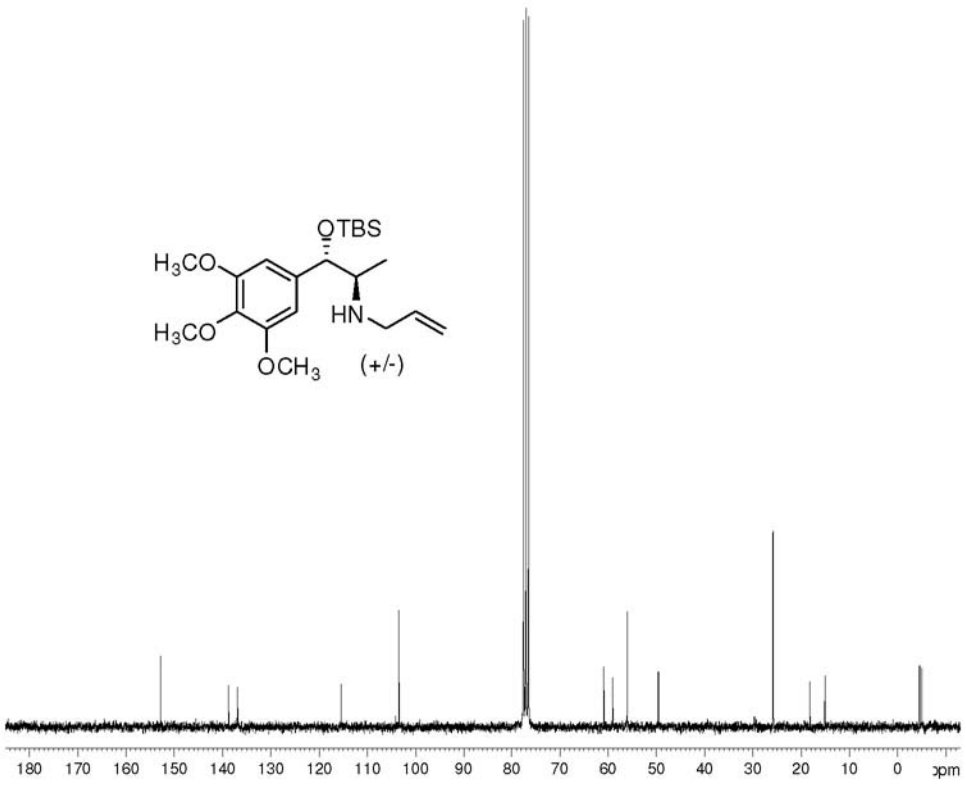

Figure S102. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **50**.

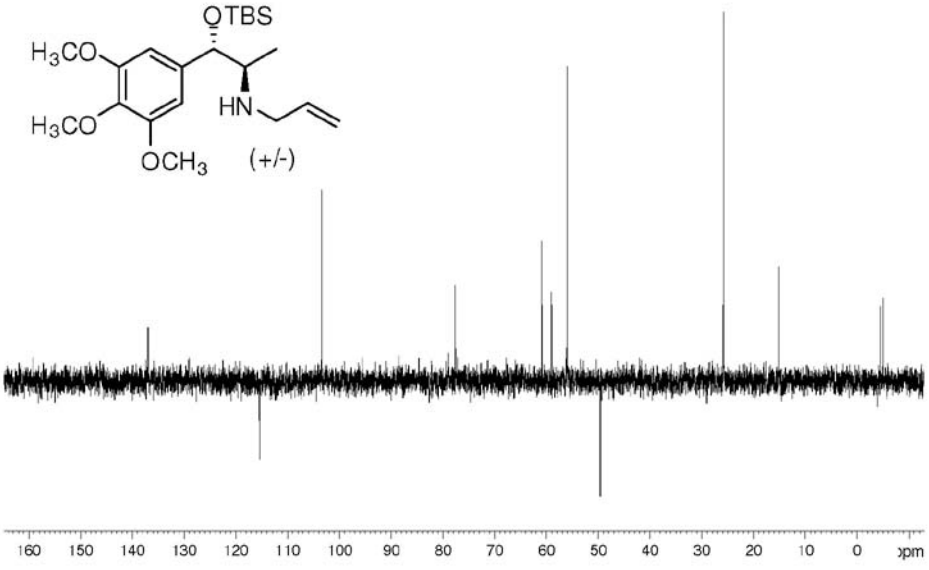

Figure S103. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicina aminoalcohol **50**.

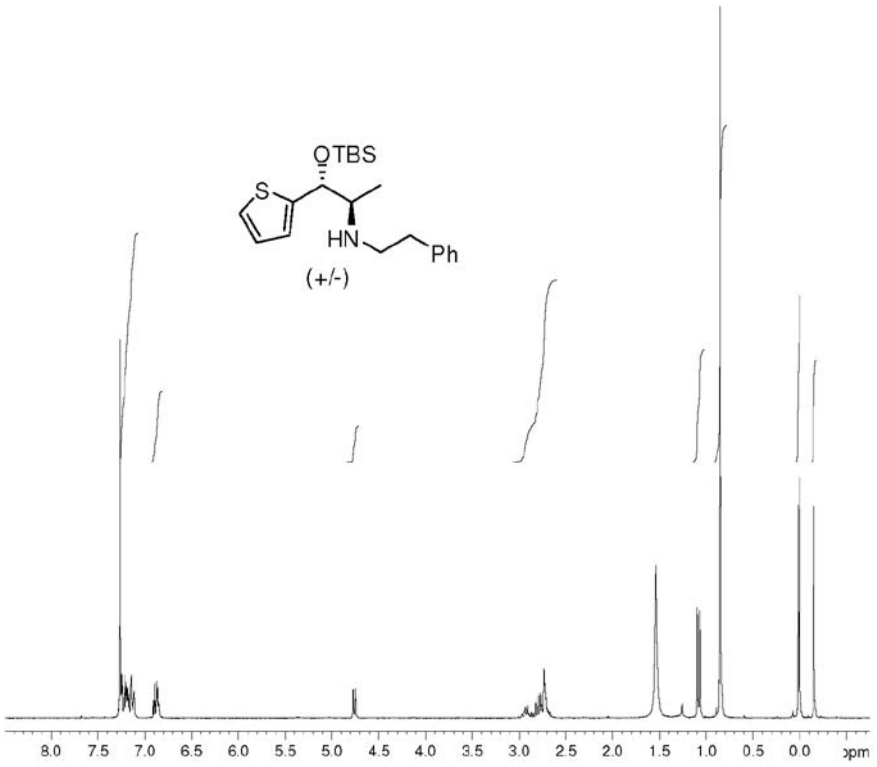

Figure S104. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **51**.

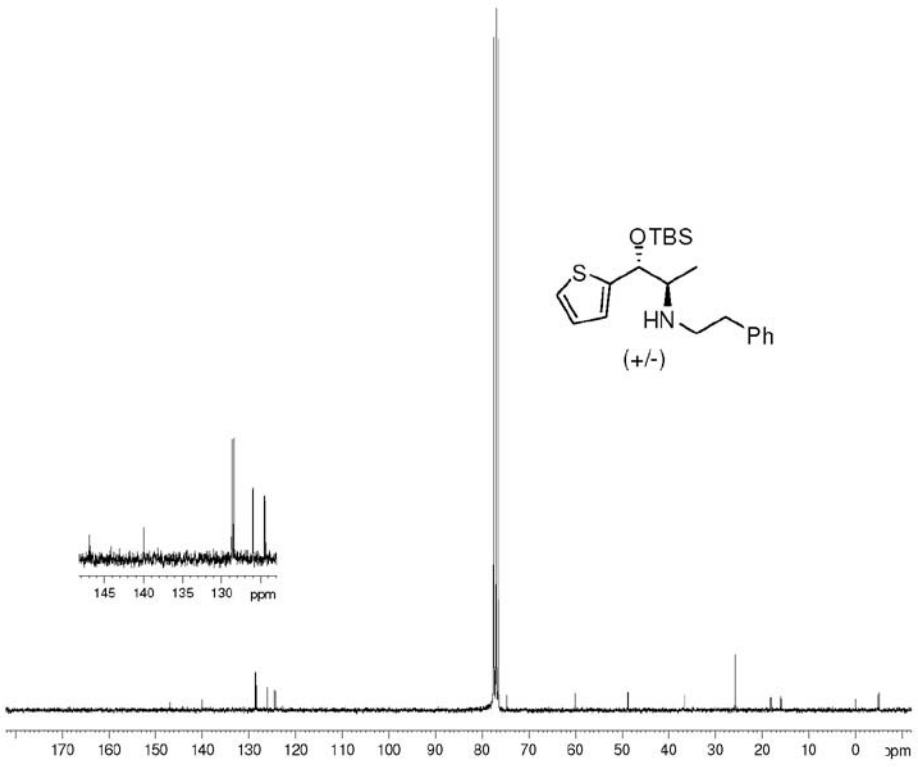

Figure S105. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **51**.

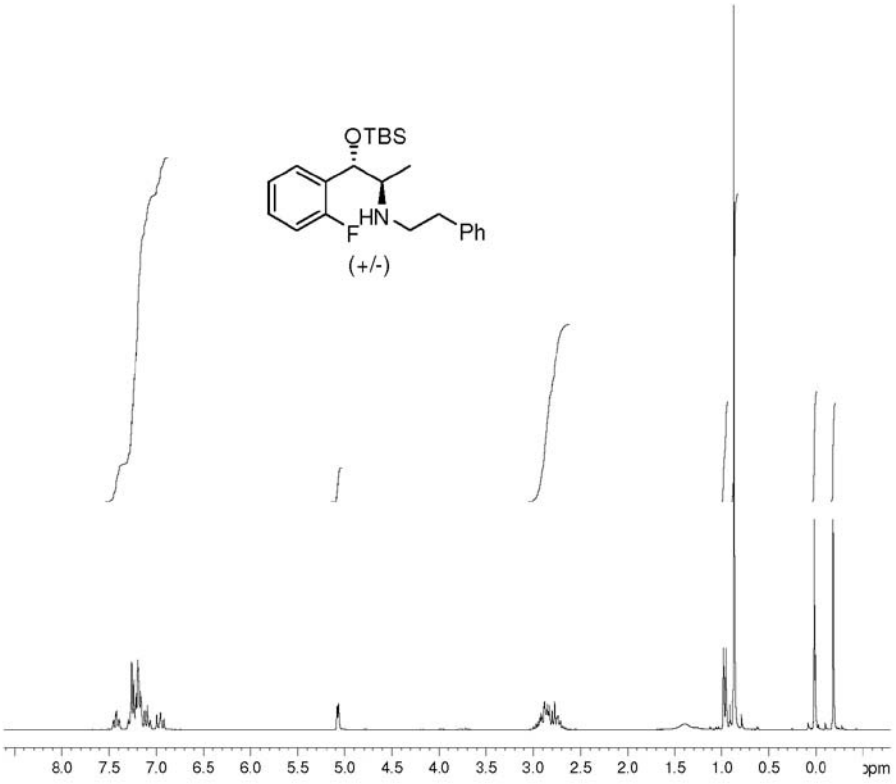

Figure S106. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **52**.

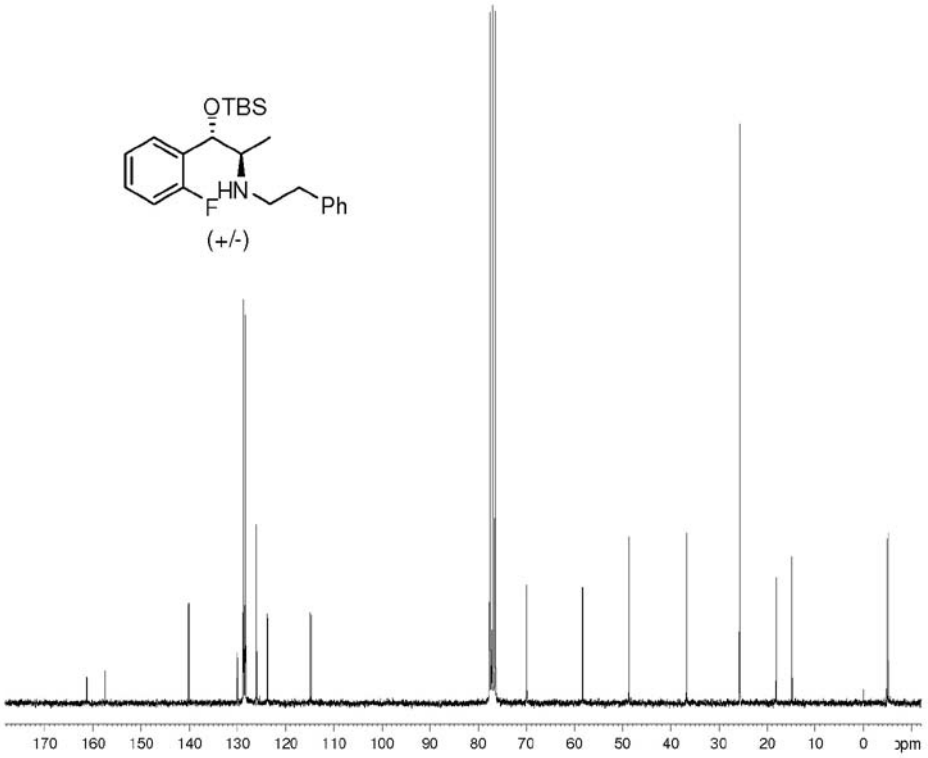

Figure S107. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **52**.

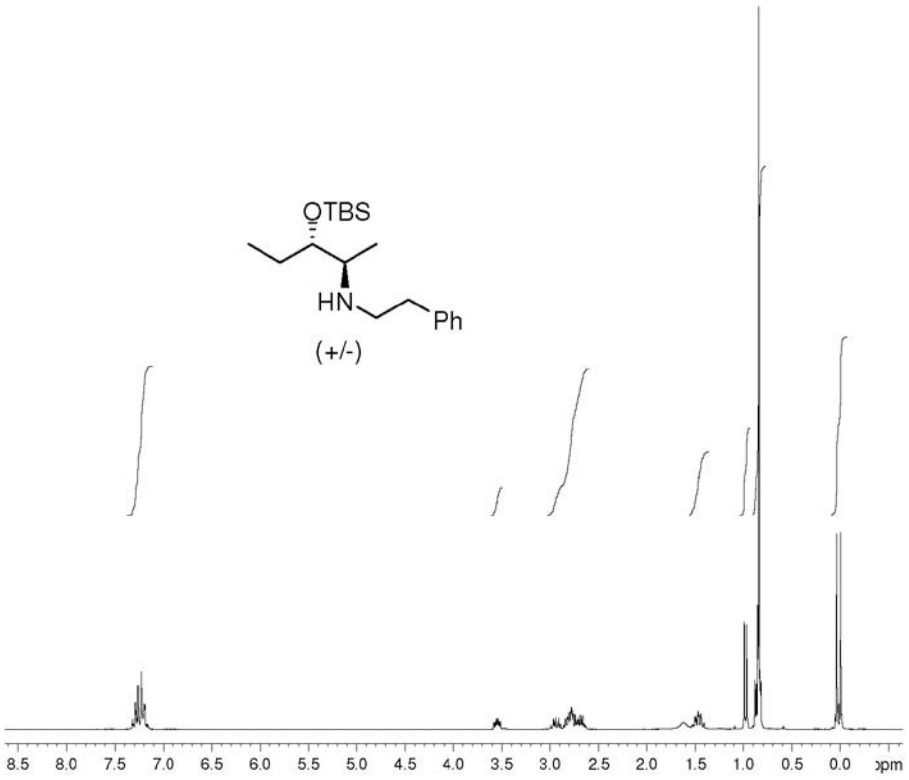

Figure S108. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **53**.

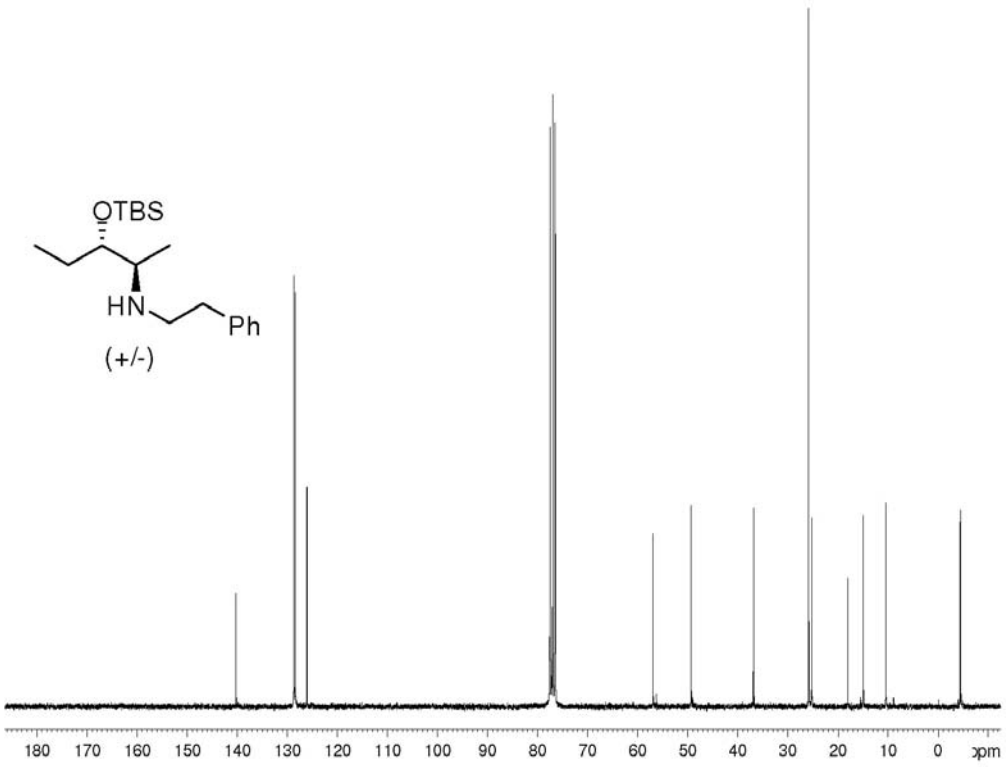

Figure S109. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **53**.

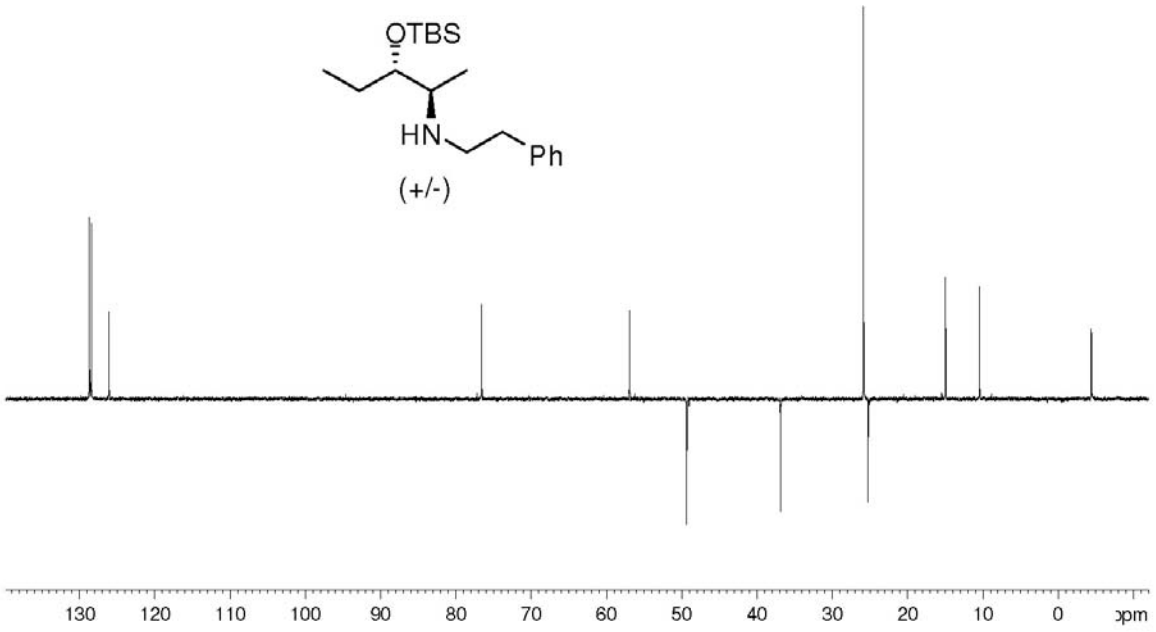

Figure S110. DEPT 135 ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **53**.

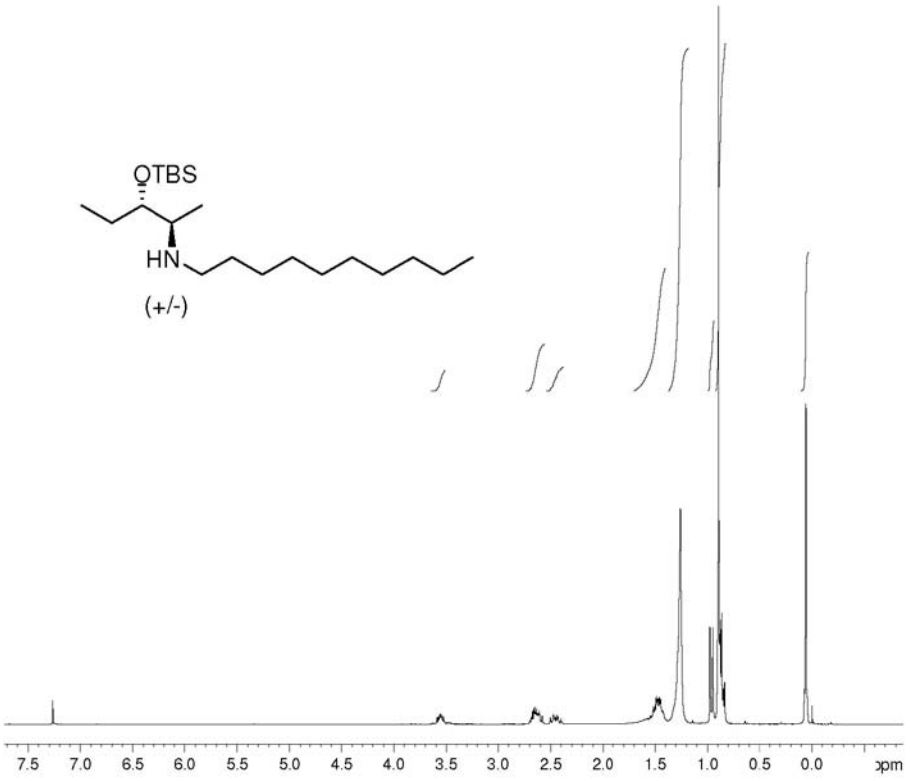

Figure S111. ^1H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **54**.

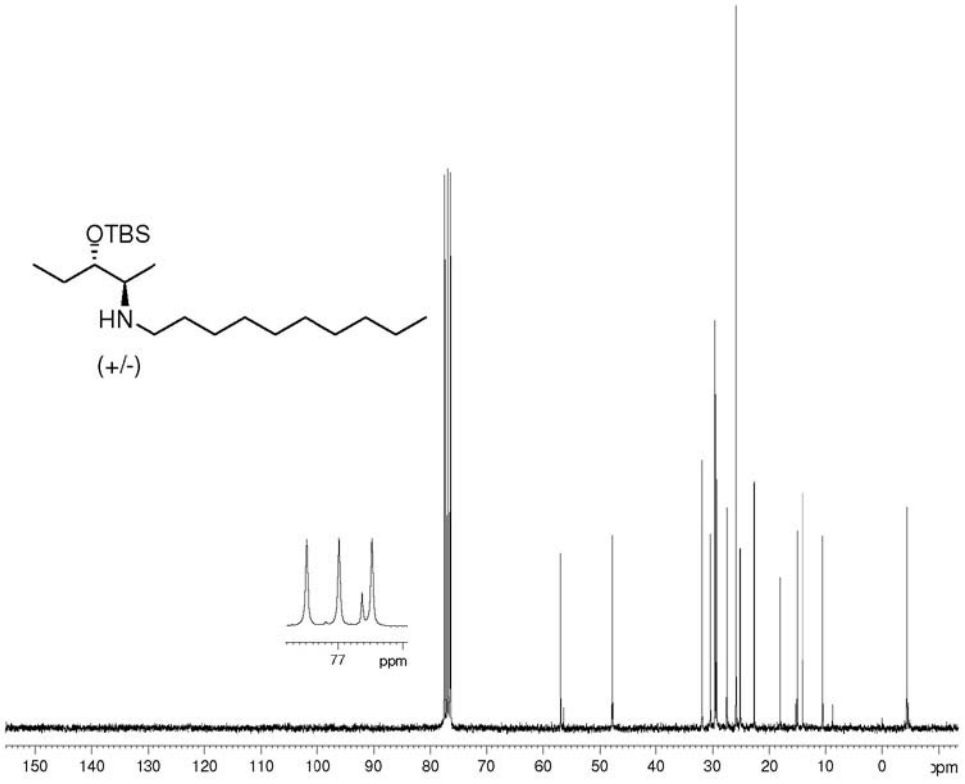

Figure S112. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **54**.

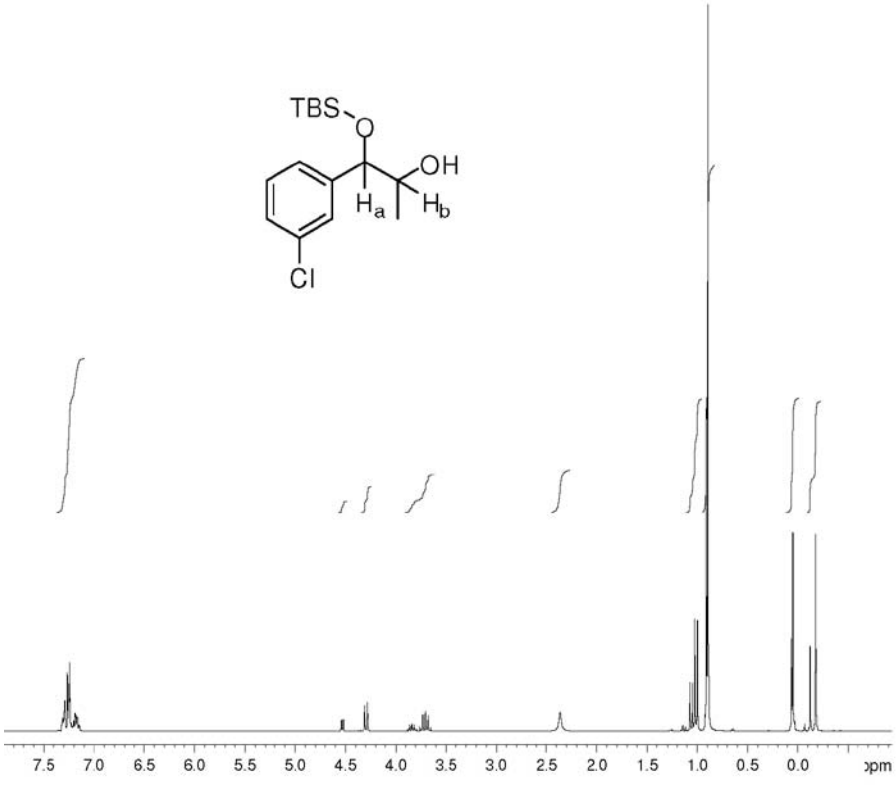

Figure S113. ^{1}H NMR ($CDCl_3$, 250 MHz) of monosilylated diol **60**.

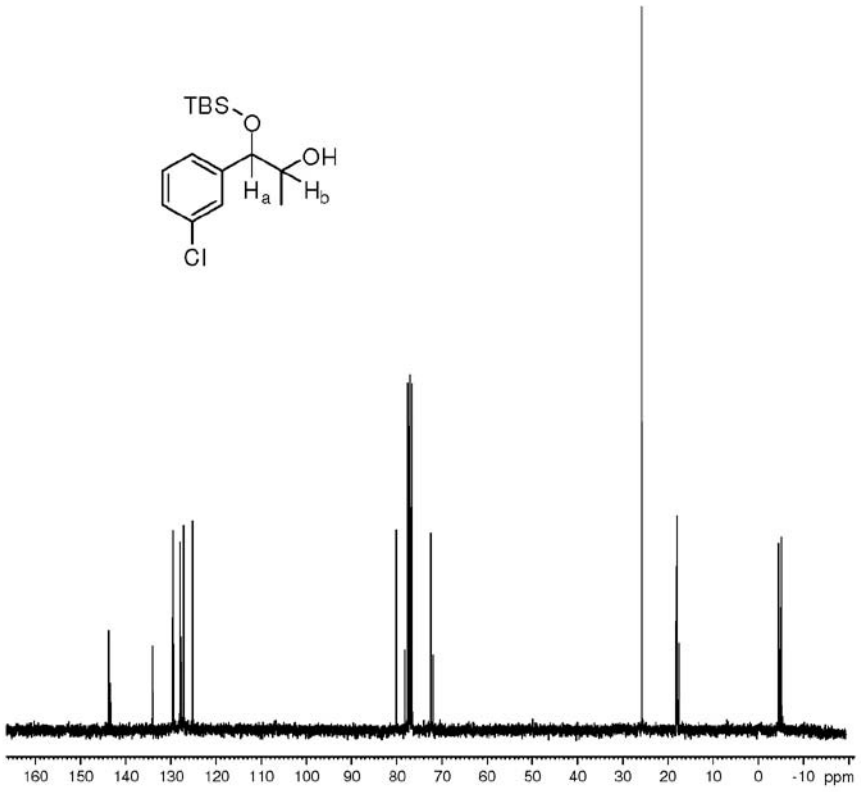

Figure S114. ^{13}C NMR ($CDCl_3$, 75.4 MHz) of monosilylated diol **60**.

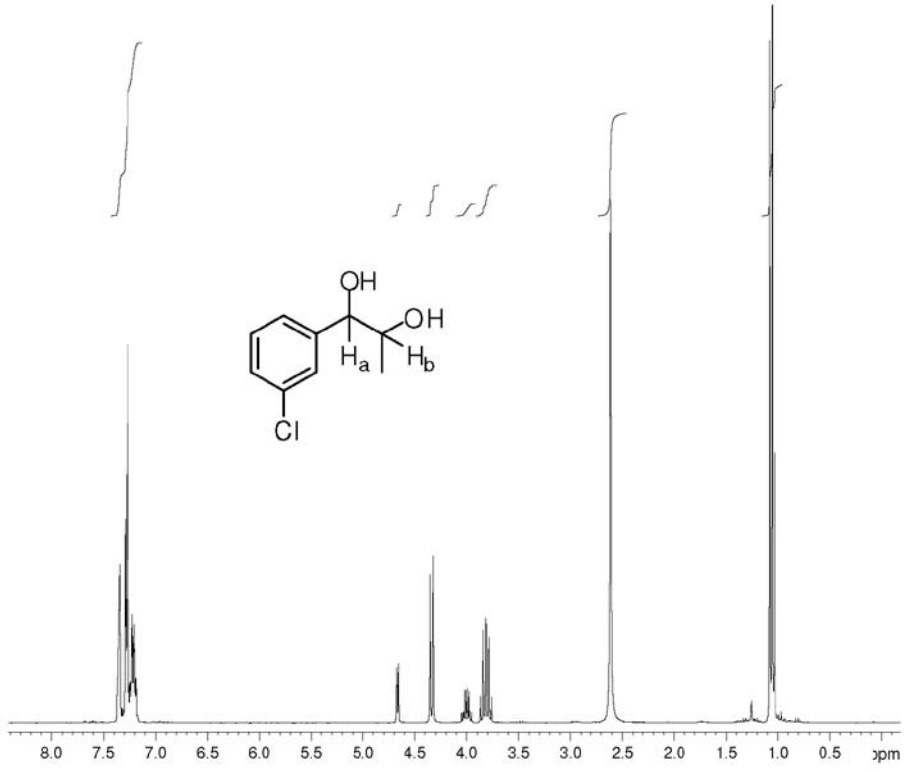

Figure S115. ^{1}H NMR ($CDCl_3$, 250 MHz) of diol **61**.

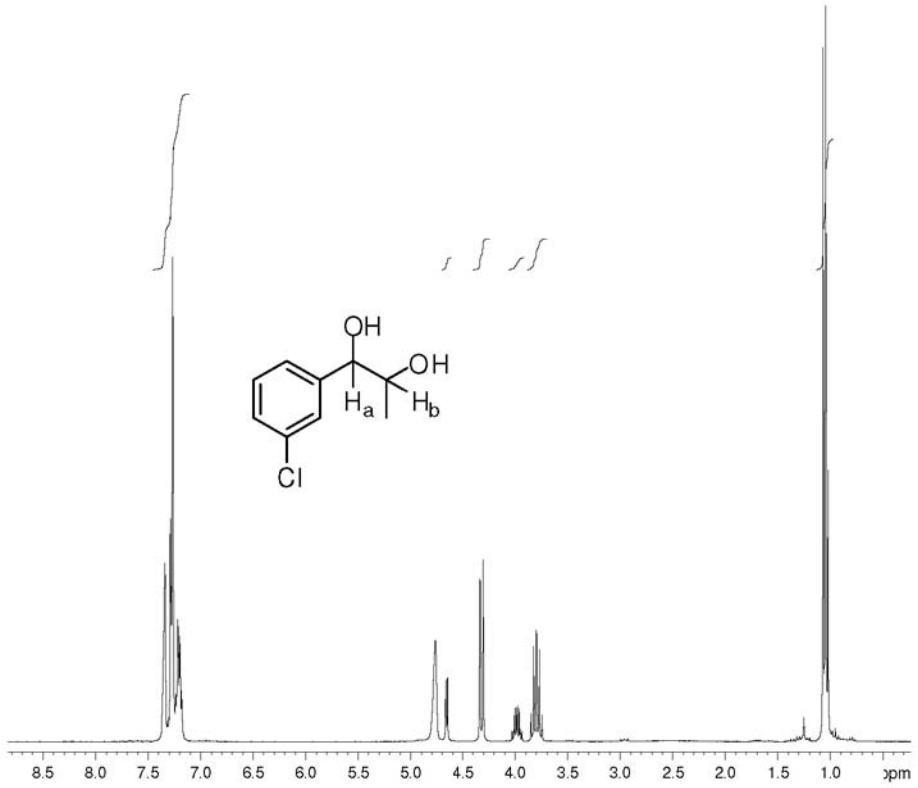

Figure S116. ^{1}H NMR ($CDCl_3$ + 2 drops of D_2O, 250 MHz) of diol **61**.

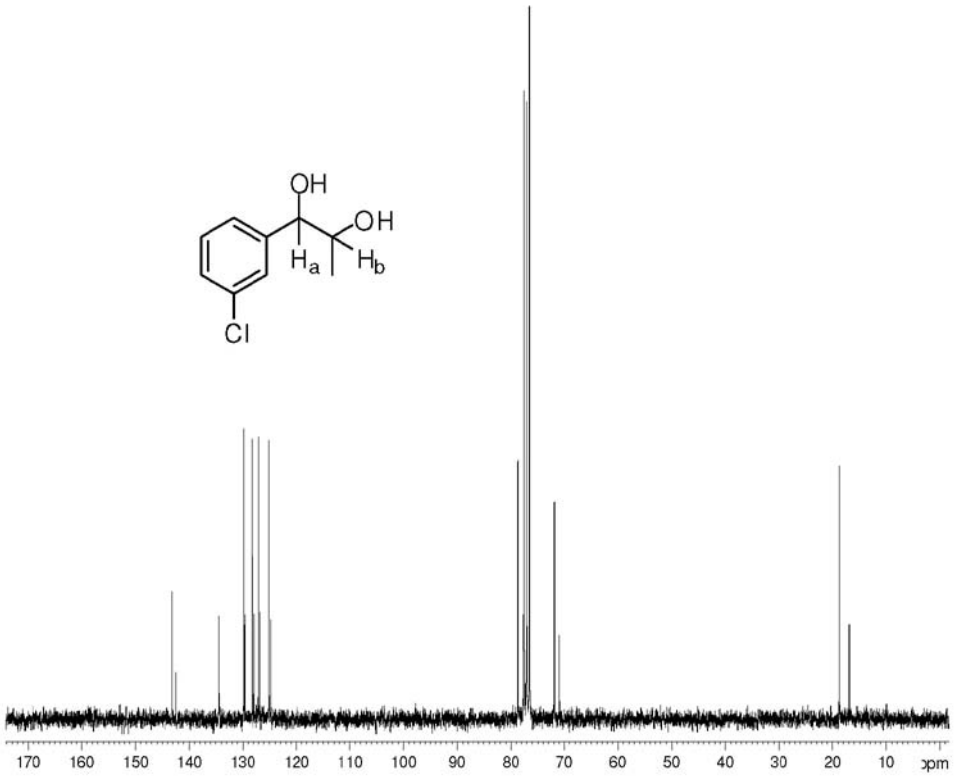

Figure S117. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of diol **61**.

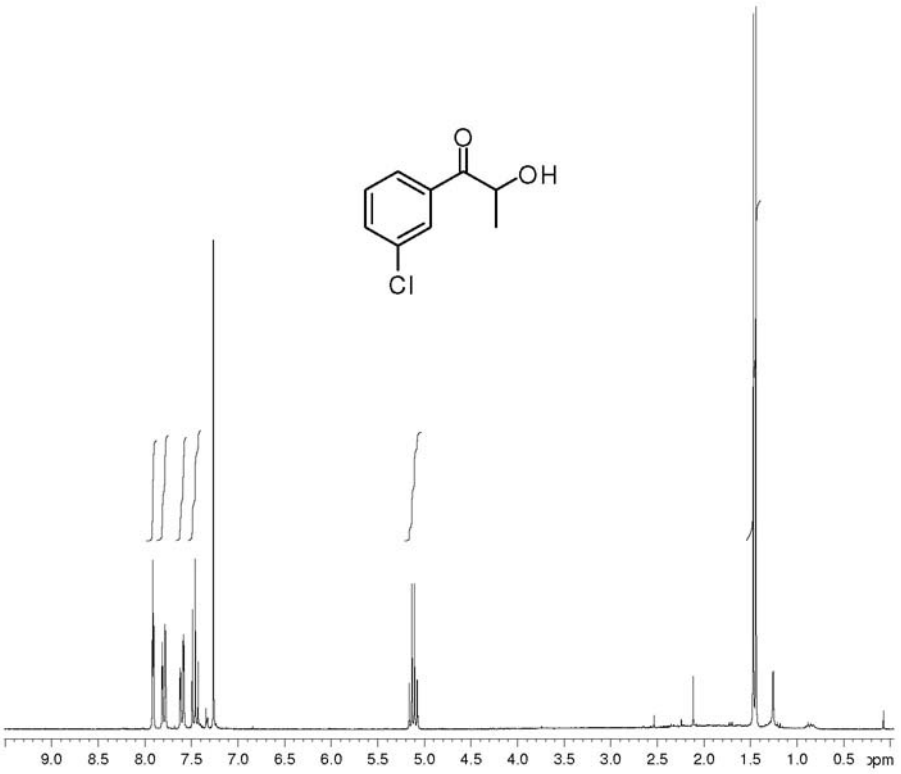

Figure S118. ^{1}H NMR ($CDCl_3$, 250 MHz) of acyloin **59**.

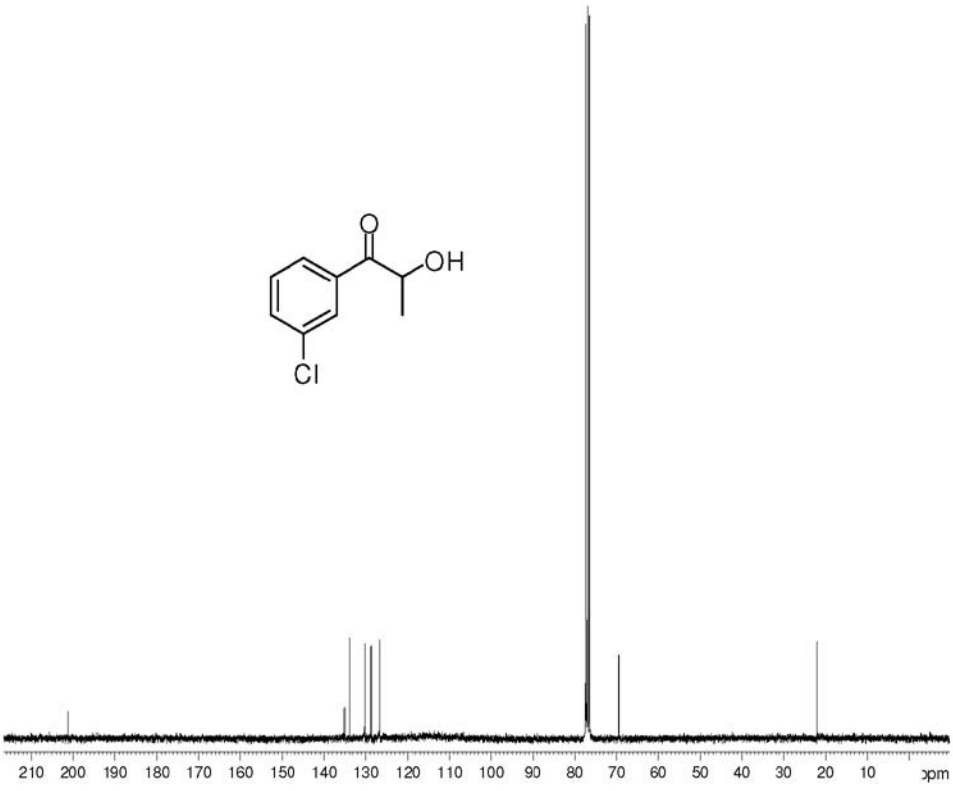

Figure S119. ^{13}C NMR ($CDCl_3$, 75.4 MHz) of acyloin **59**.

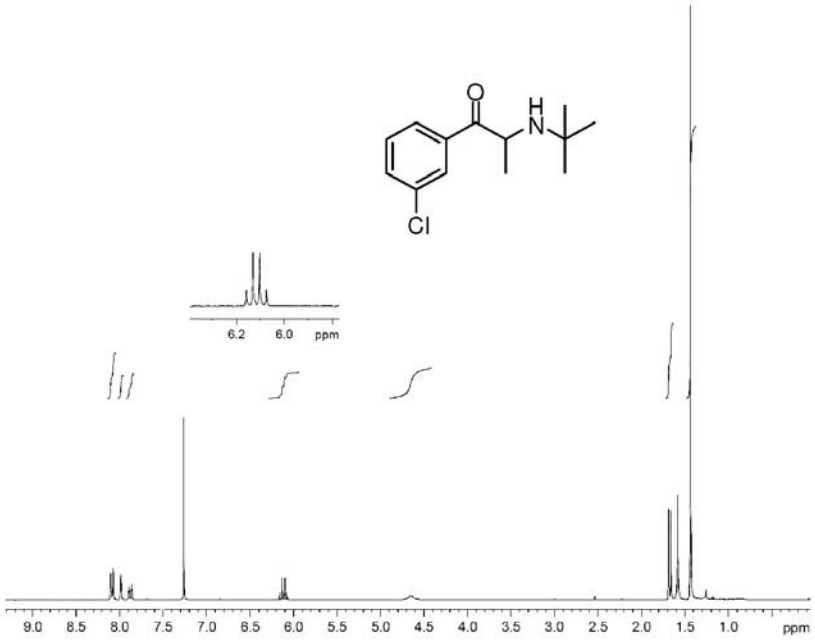

Figure S120. ^{1}H NMR ($CDCl_3$, 250 MHz) of bupropion (**1**).

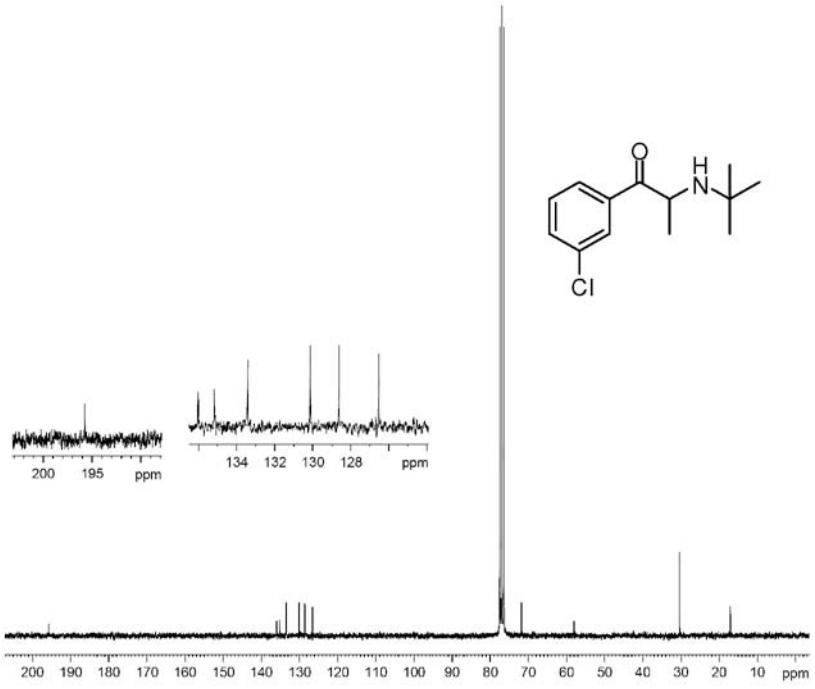

Figure S121. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of bupropion (**1**).

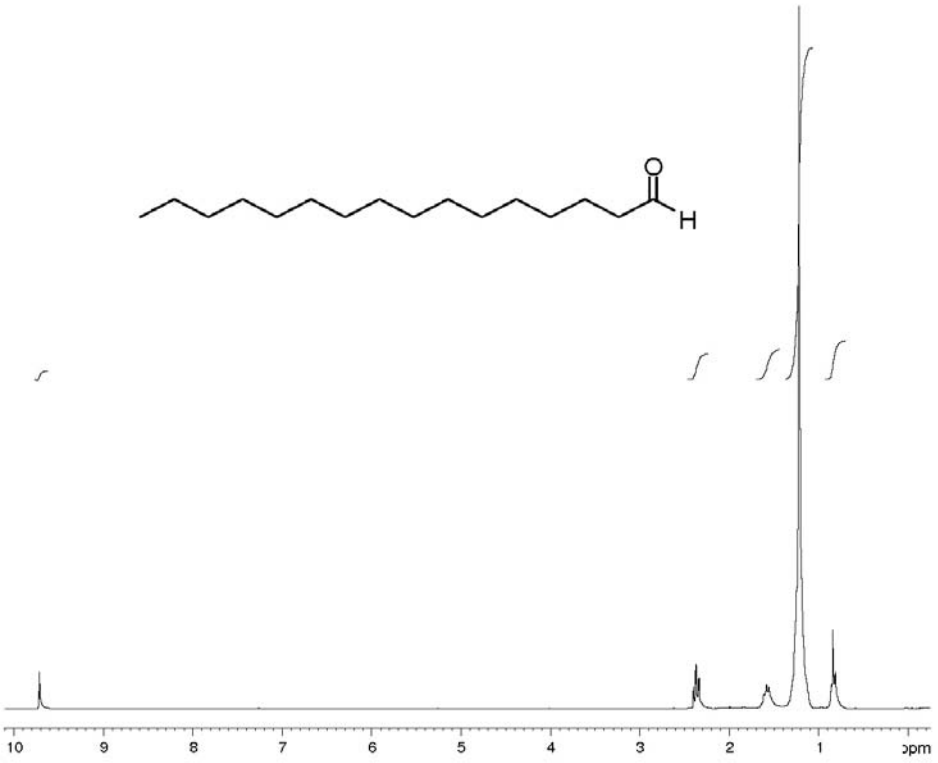

Figure S122. ^{1}H NMR ($CDCl_3$, 250 MHz) of hexadecanal.

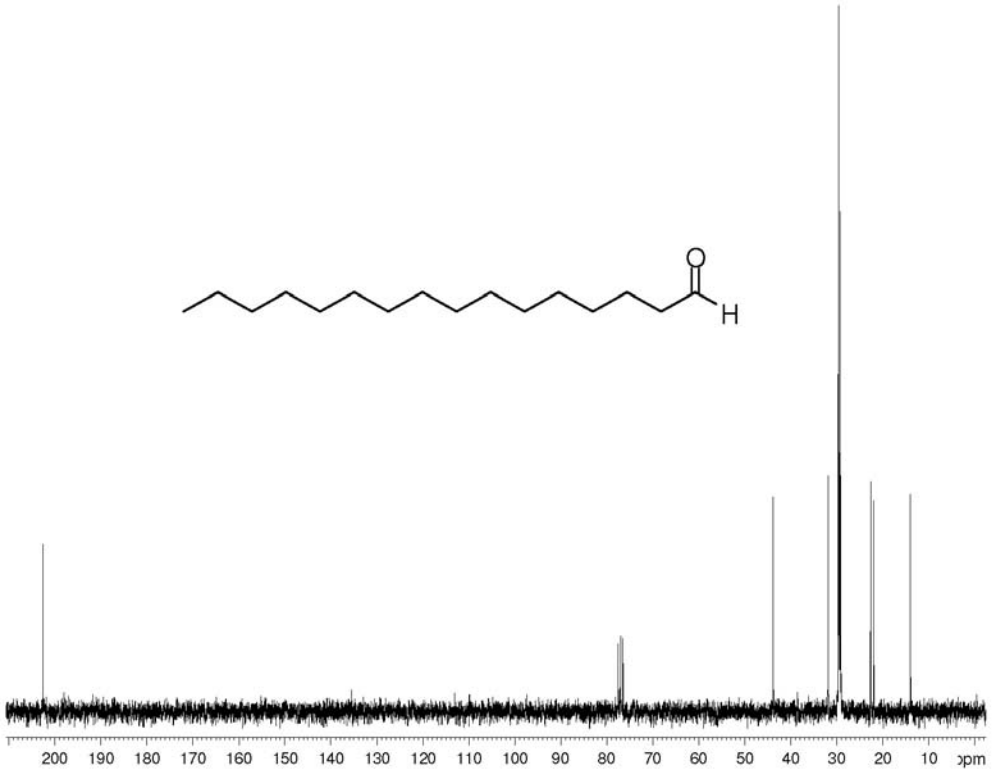

Figure S123. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of hexadecanal.

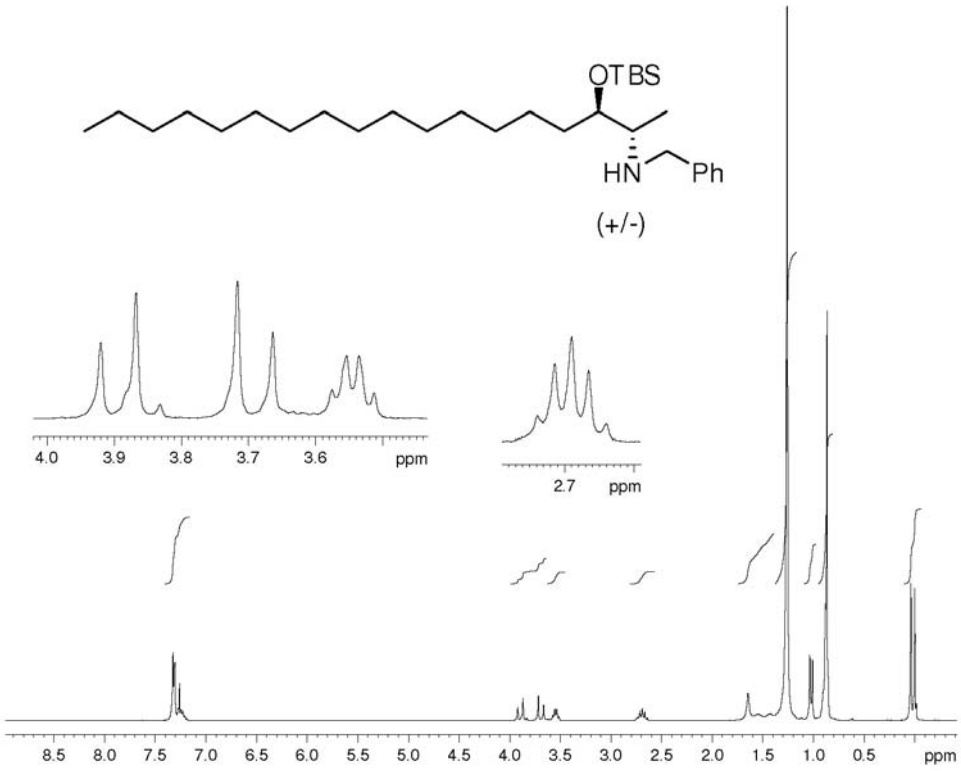

Figure S124. ^{1}H NMR ($CDCl_3$, 250 MHz) of vicinal aminoalcohol **62**.

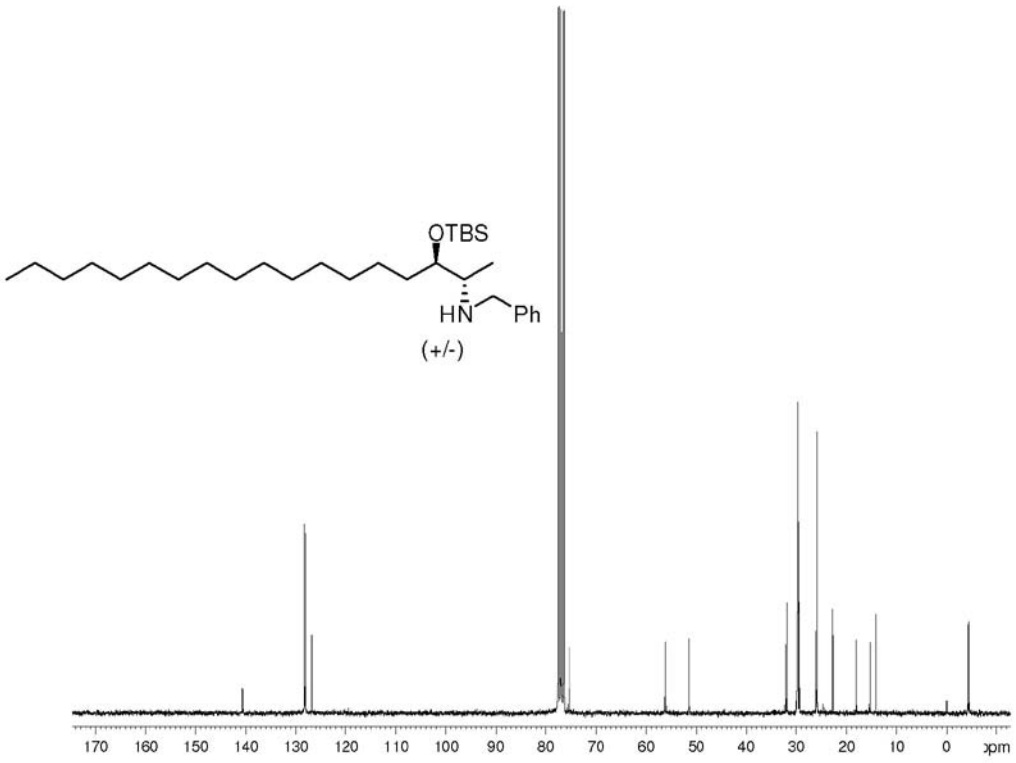

Figure S125. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of vicinal aminoalcohol **62**.

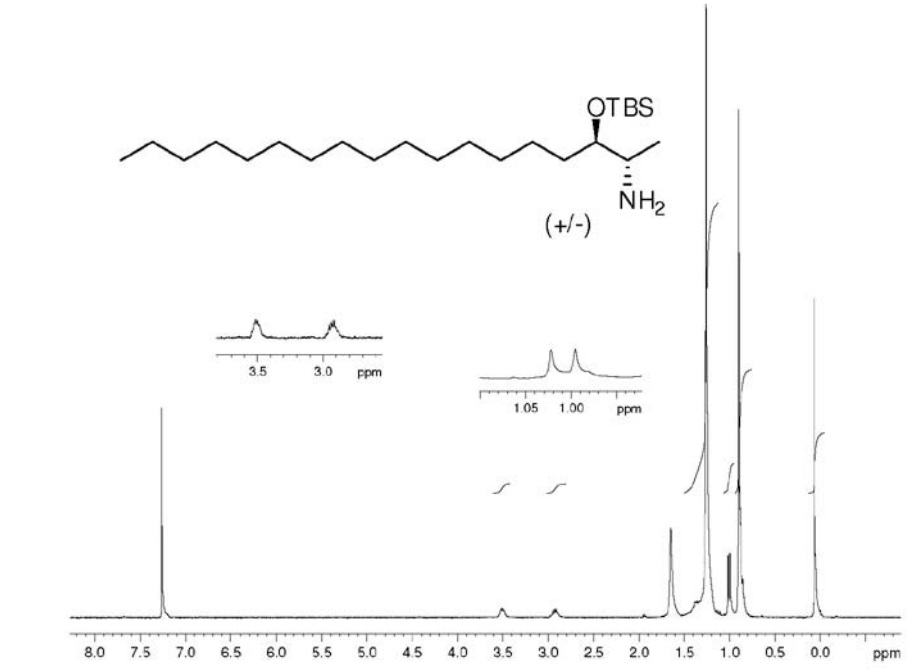

Figure S126. ^{1}H NMR ($CDCl_3$, 250 MHz) of silylated aminoalcohol **63**.

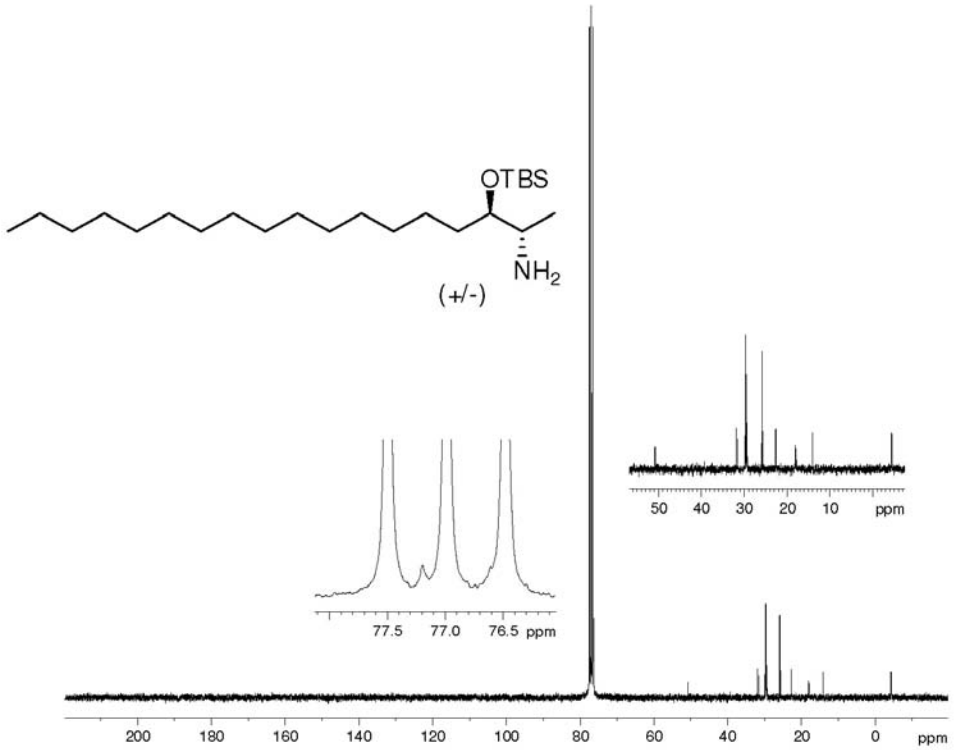

Figure S127. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of silylated aminoalcohol **63**.

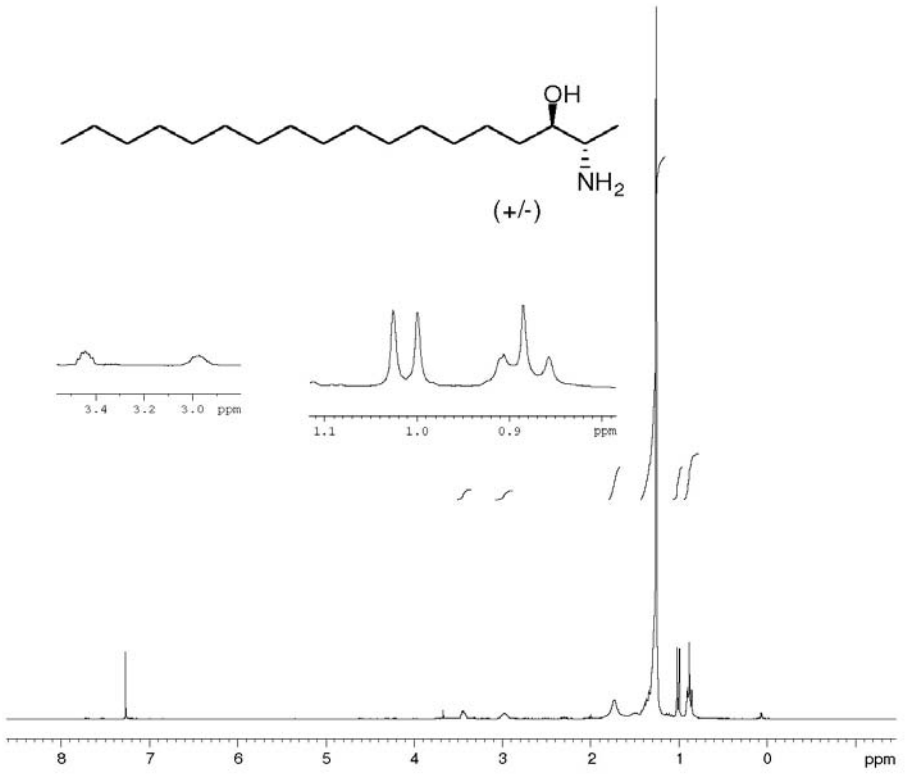

Figure S128. ^{1}H NMR ($CDCl_3$, 250 MHz) of spisulosine (**2**).

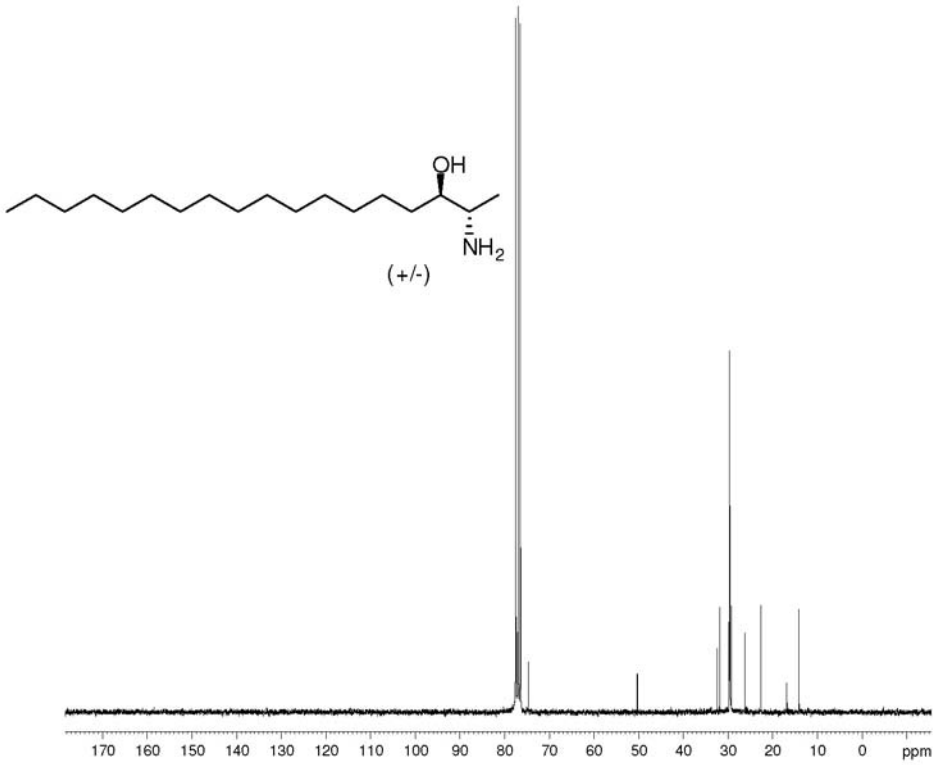

Figure S129. ^{13}C NMR ($CDCl_3$, 62.5 MHz) of spisulosine (**2**).