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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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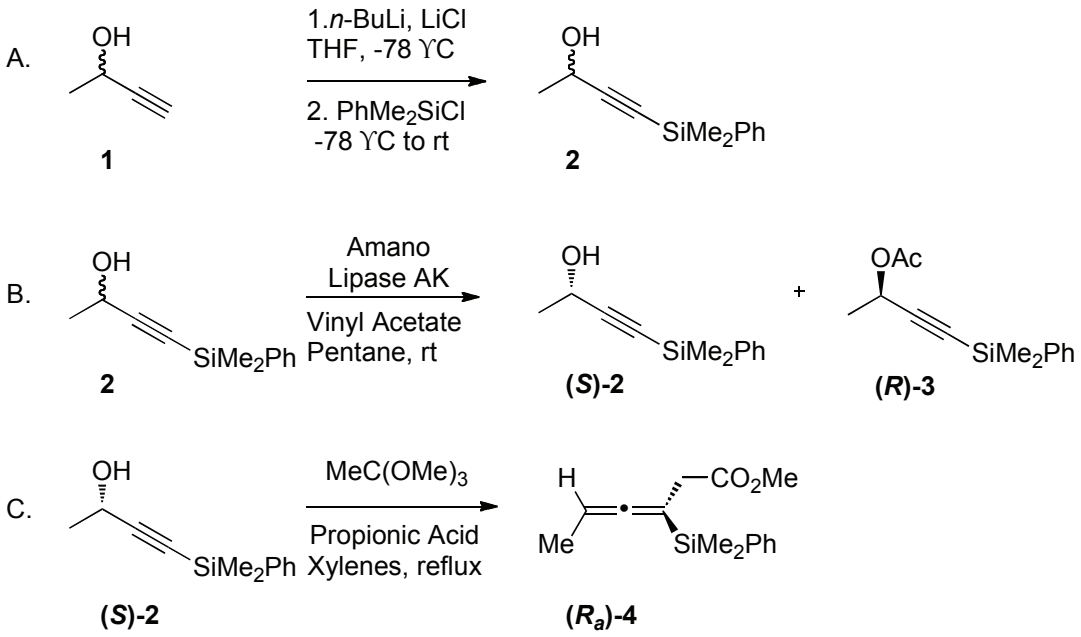
Preparation of (R_a)-Methyl 3-(dimethyl(phenyl)silyl)hexa-3,4-dienoate



Submitted by Ryan A. Brawn and James S. Panek.[1]
Checked by Francois Grillet and Kay M. Brummond.

1. Procedure

A. *(±)-4-(Dimethyl(phenyl)silyl)-but-3-yn-2-ol* (**2**). An oven-dried, one-necked, 500-mL, round-bottomed flask equipped with a 3-inch, egg-shaped, Teflon-coated magnetic stir bar and rubber septum is charged with flame-dried lithium chloride (6.36 g, 150 mmol, 2 equiv) (Notes 1 and 2). Tetrahydrofuran (150 mL) and 3-butyn-2-ol (**1**) (6.06 mL, 5.42 g, 75 mmol, 1 equiv) are added by syringe, and the flask is chilled to –78 °C in a dry ice/acetone bath. The rubber septum is replaced with a pressure-equalizing addition funnel and *n*-butyllithium (60 mL of a 2.5 M solution in hexanes, 150 mmol, 2 equiv) is transferred to the addition funnel using cannula techniques and then added dropwise to the cooled solution over 15 min. The solution is stirred for an additional 30 min at –78 °C (Note 3). The addition funnel is replaced with a rubber septum and chloro(dimethyl)phenylsilane (12.59 mL, 12.80 g, 75 mmol, 1 equiv) (Note 4) is added dropwise over 15 min via syringe, and the cloudy white mixture is stirred 14 h while warming

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slowly to room temperature. After cooling to 0 °C, the septum is removed and the cloudy yellow mixture is quenched by careful addition of 0.1 M HCl (100 mL, 10 mL portions added over 5 min) and stirred at room temperature for an additional 20 min. The reaction mixture is poured into a 1-L separatory funnel and extracted with diethyl ether (3 x 50 mL), and the combined organic layers are washed with water (25 mL) and brine (25 mL). The organic layer is dried with $MgSO_4$ (15 g), filtered, and concentrated under reduced pressure. Purification by column chromatography (Note 5) (10% ethyl acetate/hexanes) yields (±)-4-(dimethyl(phenyl)silyl)-but-3-yn-2-ol (**2**) (13.73 g, 67.2 mmol, 90% yield) as a pale yellow oil (Note 6).

B. *(S)-4-(Dimethyl(phenyl)silyl)-but-3-yn-2-ol* **(*S*)-2**. A single-necked, 250-mL, round-bottomed flask equipped with a rubber septum and a 3-inch, egg-shaped, Teflon-coated magnetic stir bar is charged with racemic 4-(dimethyl(phenyl)silyl)-but-3-yn-2-ol (15.03 g, 73.5 mmol, 1 equiv) and *n*-pentane (100 mL). Lipase AK Amano (4.5 g, 0.3 weight equiv) (Note 7) is added in one portion, followed by the addition of vinyl acetate by syringe (33.9 mL, 31.66 g, 367.7 mmol, 5 equiv). The resulting brown dispersion is stirred at room temperature and the reaction is monitored by ^{1}H NMR (Note 8). Upon completion the reaction mixture is filtered through a fritted funnel to remove the lipase, the precipitate is washed with diethyl ether (2 x 100 mL), and the clear filtrate is concentrated under reduced pressure. Purification of the residue by column chromatography (Note 9) (gradient elution 5%-20% ethyl acetate/hexanes) results in *(S)*-4-(dimethyl(phenyl)silyl)-but-3-yn-2-ol **(*S*)-2** (7.04 g, 34.4 mmol, 47% yield) as a clear yellow oil (Note 10). Also isolated is the (*R*)-acetate **(*R*)-3** (7.69 g, 31.2 mmol, 43% yield) (see discussion).

C. *(R_a)-Methyl 3-(dimethyl(phenyl)silyl)hexa-3,4-dienoate* (**R_a-4**). A single-necked, 250-mL, round-bottomed flask equipped with a rubber septum and a 3-inch, egg-shaped, Teflon-coated magnetic stir bar is charged with (*S*)-4-(dimethyl(phenyl)silyl)-but-3-yn-2-ol (***S*-2**) (6.61 g, 32.3 mmol, 1 equiv), trimethylorthoacetate (16.5 mL, 15.55 g, 129.3 mmol, 4 equiv) and xylenes (66 mL) (Note 11). Propionic acid (0.12 mL, 0.12 g, 1.62 mmol, 0.05 equiv) is added, and a reflux condenser is attached. The flask is placed in a pre-heated 160 °C oil bath and the solution is heated at reflux for 24 h (Note 12). Additional trimethylorthoacetate is added (8.2 mL, 7.77 g, 64.7 mmol, 2 equiv) by syringe, and the solution is refluxed for an additional 16 h. The pale yellow solution is cooled to room temperature, concentrated (Note 13) and purified by column chromatography (Note 14) (2% ethyl

acetate/hexanes) to give (*R*)-methyl 3-(dimethyl(phenyl)silyl)hexa-3,4-dienoate **(R_a)-4** (6.53 g, 25.1 mmol, 78% yield) as a light yellow oil (Note 15). The product is formed in >93% ee (Note 16).

2. Notes

1. Lithium chloride was flame dried under vacuum for 10 min. All glassware is dried overnight at 95 °C prior to use. All reactions are run under 1 atmosphere of argon. All solvents and reagents are added via syringe through a rubber septum. All reagents are purchased from Sigma Aldrich and used as received unless another vendor or method of purification is specified below. The purity of 3-butyn-2-ol used was 97%. Anhydrous 99.9%, inhibitor free tetrahydrofuran was purchased from Aldrich and purified with alumina using the Sol-Tek ST-002 solvent purification system directly before use. The submitters report that reagent grade tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl under an atmosphere of dry nitrogen.

2. The submitters report that the three-step reaction sequence can be performed on a 150-mmol scale with similar yields and stereocontrol.

3. Significant quantities of salts are formed during this reaction, so efficient stirring is crucial.

4. Phenyldimethylchlorosilane is purchased from Gelest and used as received.

5. The column was packed with 275 g of silica gel, then 500 mL of hexanes followed by 500 mL of 5% ethyl acetate/hexanes are used to elute unreacted silane (R_f = 0.95, 20% ethyl acetate/hexanes), followed by 4 L 10% ethyl acetate/hexanes . Fractions were collected using 50 mL test tubes, the product has an R_f = 0.40 in 20% ethyl acetate/hexanes, and stains strongly with potassium permanganate. Alcohol (**2**) exhibits the following characteristics: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.42 (s, 6 H), 1.49 (d, J = 6.6 Hz, 3 H), 1.96 (m, 1 H), 4.56 (m, 1 H), 7.37 − 7.39 (m, 3 H), 7.60 − 7.63 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: –1.0, 24.1, 58.6, 86.2, 109.4, 127.9, 129.4, 133.6, 136.6; IR (film) υ_{max} 3330, 3076, 2978, 2181, 1429 cm^{-1}; HRMS (CI, NH_3) *m/z* calcd for $C_{12}H_{17}OSi$ $[M+H]^+$ 205.1049, found: 205.1040; Anal. calcd. for $C_{12}H_{16}OSi$: C, 70.53, H, 7.89. Found: C, 70.30, H, 7.79.

6. When the reaction was performed at half-scale, 6.9 g (90%) of product was isolated.

7. Lipase AK is purchased from Amano Enzyme Inc. The lipase is washed with diethyl ether (50 mL), filtered and air dried for 30 min immediately before use.

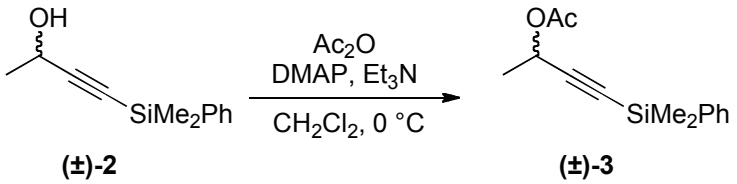
8. Small aliquots of the solution are removed and filtered through a cotton plug to remove traces of enzyme. The filtrate is concentrated under vacuum, and a ^{1}H NMR of the residue is taken. The reaction is judged complete when the integral ratios of the resonances for the protons alpha to the alcohol (δ 4.55) and alpha to the acetate (δ 5.52) are equal, typically requiring 15–20 h.

9. The column was packed with 400 g of silica gel. Elution with 2.5 L of 5% ethyl acetate/hexanes affords acetate **3** (R_f = 0.60, 20% ethyl acetate/hexanes). The first 1.0 L of eluent is collected in 250 mL fractions, followed by 50 mL fractions. Next, elution with 4.2 L of 10% ethyl acetate/hexanes is used to collect alcohol ((***S***)-**2**), 50 mL fractions are collected throughout, (R_f = 0.40 in 20% ethyl acetate/hexanes and stains strongly with potassium permanganate). Enantioenriched alcohol ((***S***)-**2**) exhibits the following characteristics: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.43 (s, 6 H), 1.47 (d, *J* = 6.6 Hz, 3 H), 1.93 (m, 1 H), 4.56 (m, 1 H), 7.26 − 7.40 (m, 3H), 7.62 − 7.63 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: -1.0, 24.1, 58.6, 86.3, 109.4, 127.9, 129.4, 133.6, 136.6; IR (film) υ_{max} 3342, 3064, 2982, 2177, 1429 cm^{-1}; HRMS (CI, NH_3) *m/z* calcd for $C_{12}H_{17}OSi$ $[M+H]^+$ 205.1049, found: 205.1051; Anal. calcd. for $C_{12}H_{16}OSi$: C, 70.53, H, 7.89. Found: C, 70.25, H, 7.97; $[\alpha]_D^{20}$–11.2 (c 5.5, CH_2Cl_2).

10. When the reaction was performed at half-scale, 3.31 g (49%) of product was isolated. The checkers established the enantiomeric purity of ((***S***)-**2**) by HPLC analysis (Note 17) run on a Chiralpak IB-3 column eluting in 0.5% 2-propanol/hexanes, with a 2.0 μL injection and a 1.0 mL/min flow rate. The alcohol has >98% ee. The peaks are visualized at 210 nm, with the racemic alcohol **2** exhibiting equal peaks with retention times of 11.6 and 12.6 min, and the enantioenriched alcohol ((***S***)-**2**) exhibiting a major peak with a retention time of 12.8 min (minor enantiomer has a retention time of 11.9 min). The submitters established the enantiomeric purity of the alcohol using a dilute solution (~0.2 mg/mL, it can be difficult to see baseline separation otherwise). HPLC is run on a ChiralCel OD column eluting in 1% 2-propanol /hexanes, with a 10 μL injection and a 1.0 mL/min flow rate. The alcohol has >95% ee. The peaks are visualized at 254 nm, with the racemic alcohol **2** exhibiting equal peaks with retention times of 18.1 and 19.5 min, and the enantioenriched alcohol ((***S***)-**2**) exhibiting a major peak with a

retention time of 19.2 min (minor enantiomer has a retention time of 18.4 min). Enantioenriched acetate ((***R***)-**3**) exhibits the following characteristics: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.42 (s, 6 H), 1.51 (d, J = 6.9 Hz, 3 H), 2.08 (s, 3 H), 5.51 (m, 1 H), 7.37 − 7.39 (m, 3 H), 7.60 − 7.63 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: –1.2, 20.7, 21.2, 60.3, 87.1, 105.3, 127.7, 129.3, 133.4, 136.2, 169.2; IR (film) υ_{max} 3068, 2991, 2954, 2178, 1744, 1434, 1364 cm^{-1}; HRMS (CI, NH_3) *m/z* calcd for $C_{14}H_{19}O_2Si$ $[M+H]^+$ 245.0998, found: 245.1018; Anal. calcd. for $C_{14}H_{18}O_2Si$: C, 68.25, H, 7.36. Found: C, 68.53, H, 7.21; $[\alpha]_D^{20}$+ 100 (7.4, CH_2Cl_2). Determination of the enantiomeric excess of the acetate required the synthesis of the racemic acetate (±)-**3** (Scheme 1).

Scheme 1. Acetylation of racemic alcohol



(±)-2 **(±)-3**

Alcohol **(±)-2** (523 mg, 2.56 mmol, 1 equiv) is dissolved in CH_2Cl_2 (10 mL) and 4-(dimethylamino)pyridine (32 mg, 0.256 mmol, 0.1 equiv), triethylamine (3.57 mL, 2.59 g, 25.6 mmol, 10 equiv) and acetic anhydride (1.2 mL, 1.31 g, 12.7 mmol, 5 equiv) are added in that order. The resulting solution is stirred at room temperature for 12 h, diluted with ammonium chloride (10 mL), filtered through a Celite plug and rinsed with CH_2Cl_2 (50 mL). The phases are separated and the aqueous layer is extracted with CH_2Cl_2 (2 x 30 mL). The combined organic layers are washed with brine (20 mL), dried over Na_2SO_4 (5 g), filtered, concentrated under reduced pressure and purified by flash chromatography (5% ethyl acetate/hexanes) to afford racemic acetate **(±)-3** (0.493 g, 78% yield) as a colorless oil. The checkers established enantiomeric purity by HPLC analysis (Note 17) run on a Chiralpak IB-3 column eluting in 0.2% 2-propanol/hexanes, with a 2.0 μL injection and a 0.3 mL/min flow rate. The acetate has >99% ee. The peaks are visualized at 210 nm, with the racemic acetate **(±)-3** exhibiting equal peaks with retention times of 10.0 and 11.6 min, and the enantioenriched alcohol (***R***)-**3** exhibiting a major peak with a retention time of 10.9 min; the minor enantiomer is not observed.

11. Both trimethylorthoacetate and xylenes are purchased from Aldrich and used without further purification.

12. It is critical that the bath temperature be kept at this temperature or the reaction will not go to completion.

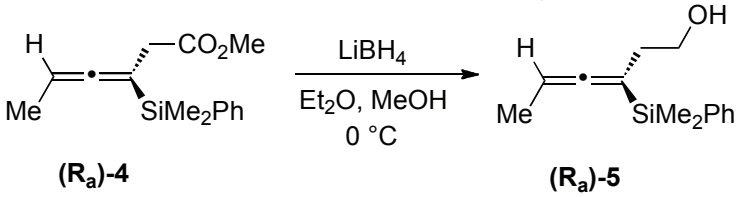
13. Most of the xylenes is removed using a rotary evaporator with the water bath heated to 60 °C and by using dry ice/acetone in the cooling trap, the remainder is removed during the chromatography purification step.

14. The column was packed with 150 g of silica gel. Hexanes (500 mL) was used to elute the xylenes (R_f = 1.0, 20% ethyl acetate/hexanes) then elution with 1.5 L of 2% ethyl acetate/hexanes afforded the product, which has an R_f = 0.85 in 20% ethyl acetate/hexanes, and stains strongly with potassium permanganate.

15. Enantiomerically enriched allenylsilane ((***R*****$_a$**)-**4**) exhibits the following characteristics: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.38 (s, 6 H), 1.64 (d, *J* = 7.2 Hz, 3 H), 2.93 (d, *J* = 1.6 Hz, 2 H), 3.55 (s, 3 H), 4.94 (m, 1 H), 7.34 − 7.36 (m, 3 H), 7.53 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: –3.0, –2.9, 13.2, 36.0, 51.4, 81.2, 88.4, 127.6, 129.0, 133.7, 137.4, 172.0, 209.4; IR (film) υ_{max} 2954, 1945, 1740, 1434 cm^{-1}; HRMS (EI$^+$) *m/z* calcd for $C_{15}H_{20}O_2Si$ $[M]^+$ 260.1233, found: 260.1252; $[\alpha]_D^{20}$–5.8 (c 5.7, CH_2Cl_2). When the reaction was performed at half-scale, 3.61 g (83%) of product was isolated. Purity (>98%) was established by HPLC analysis: ChiraCel OD column, eluent = *i*-PrOH/hexane = 0.5/99.5, flow = 1 mL/min, detection = 254 nm, injection volume : 20 μL, retention time = 4.39 mi (major isomer).

16. To determine the enantiomeric excess of allenylsilane (***R*****$_a$**)-**4** the methyl ester was reduced to a primary alcohol using lithium borohydride (Scheme 2).

Scheme 2. Reduction of Methyl Ester



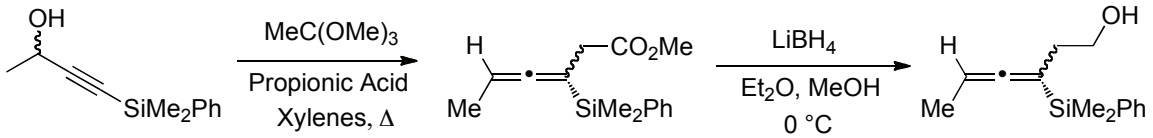
(R$_a$)-4 **(R$_a$)-5**

A single-necked, 25-mL round-bottomed flask equipped with a rubber septum and a 1-inch egg-shaped magnetic stir bar is charged with lithium borohydride (0.046 g, 2.12 mmol, 2 equiv), diethyl ether (3 mL) and methanol (0.2 mL). The resulting mixture is cooled to 0 °C and a solution of (***R*****$_a$**)-**4** (0.27 g, 1.06 mmol, 1 equiv) in diethyl ether (3 mL) is added. The

solution is stirred for 12 h while warming slowly to room temperature. Upon completion of the reaction, ethyl acetate (3 mL), acetone (3 mL) and water (10 mL) are added sequentially. The aqueous layer is separated and extracted with ethyl acetate (3 x 5 mL). The combined organic phases are washed with brine (10 mL), dried with sodium sulfate (200 mg), filtered and concentrated under reduced pressure. Purification over silica gel (4 g) using 100 mL of 10% ethyl acetate/hexanes results in (*R*)-3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-ol (***R***$_a$)-**5** (0.204 g, 0.880 mmol, 83%) as a colorless oil. The alcohol (***R***$_a$)-**5** exhibits the following characteristics: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.37 (s, 6 H), 1.58 (m, 1 H), 1.64 (d, *J* = 7.2 Hz, 3 H), 2.16–2.18 (m, 2 H), 3.67 (m, 2 H), 4.91 (m, 1 H), 7.35 − 7.36 (m, 3 H), 7.52 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: –3.2, –3.1, 13.8, 32.6, 62.2, 81.1, 91.7, 127.8, 129.2, 133.7, 137.9, 172.0, 207.3; IR (film) υ_{max} 3363, 3072, 2953, 2889, 1932, 1426, 1369 cm^{-1}; HRMS (EI+) *m/z* calcd for $C_{14}H_{20}OSi$ $[M]^+$ 232.1252, found: 232.1255; Anal. calcd. for $C_{14}H_{20}OSi$: C, 72.36, H, 8.67. Found: C, 71.77, H, 8.80; $[\alpha]_D^{20}$–18.6 (c 4.9, CH_2Cl_2); R_f= 0.25 in 5:1 hexanes/ethyl acetate.

The enantiomeric excess determination required the synthesis of the racemic alcohol **(±)-5**. The procedures used for the synthesis of the racemic compound were entirely analogous to the ones used to synthesize the enantiomerically enriched alcohol (***R***$_a$)-**5** (Scheme 3).

Scheme 3. Synthesis of the racemic alcohol



2 **(±)-4** **(±)-4**

The checkers established the enantiomeric purity by HPLC analysis (Note 17) run on a Chiralpak IB-3 column eluting in 0.5% 2-propanol/hexanes, with a 2.0 μL injection and a 1.0 mL/min flow rate. The alcohol has >93% ee. The peaks are visualized at 210 nm, with the racemic alcohol **(±)-5** exhibiting equal peaks with retention times of 14.2 and 15.8 min, and the enantioenriched alcohol (***R***$_a$)-**5** exhibiting a major peak with a retention time of 12.8 min (minor enantiomer has a retention time of 11.9 min).

The submitters established enantiomeric purity of the alcohol using a ChiralCel OD column eluting in 1% 2-propanol/hexanes with a 10 μL injection and a 1.0 mL/min flow rate. The peaks are visualized at 254 nm,

with the racemic alcohol **(±)-5** exhibiting equal peaks with retention times of 14.3 and 15.8 min, and the enantioenriched alcohol (***R**_a*)-**5** exhibiting a major peak with a retention time of 15.7 min (minor enantiomer has a retention time of 14.6 min).

17. Enantiomeric excess determinations reported by the checkers were performed by Chiral Technologies, Inc. The checkers and Organic Syntheses gratefully acknowledge their assistance.

Safety and Waste Disposal Information

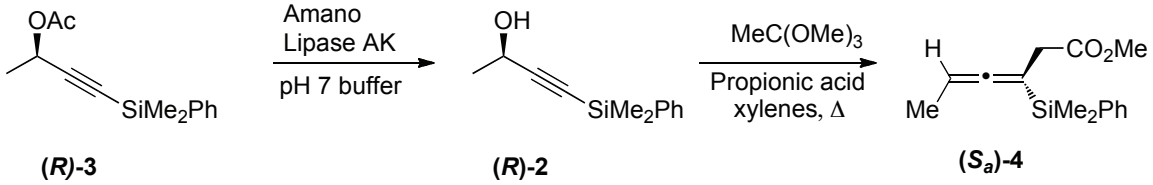
All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academies Press; Washington, DC, 2011.

3. Discussion

Allenylsilanes have proven to be versatile carbon nucleophiles for a variety of organic transformations.[2] In particular, chiral allenes have generated interest in the synthetic community due to the efficient transfer of the axial chirality in the allene into point chirality in the reaction products. Although allenylsilanes have proven to be effective nucleophiles for a variety of transformations, relatively few procedures exist for the multigram synthesis of highly enantioenriched reagents. Previous methods for the synthesis of chiral allenylsilane reagents typically use the S_N2' displacement strategy developed by Fleming.[3] A variety of other methods for the synthesis of enantioenriched allenylsilanes have begun to emerge in the literature, showing the increase in interest in these reagents.[4]

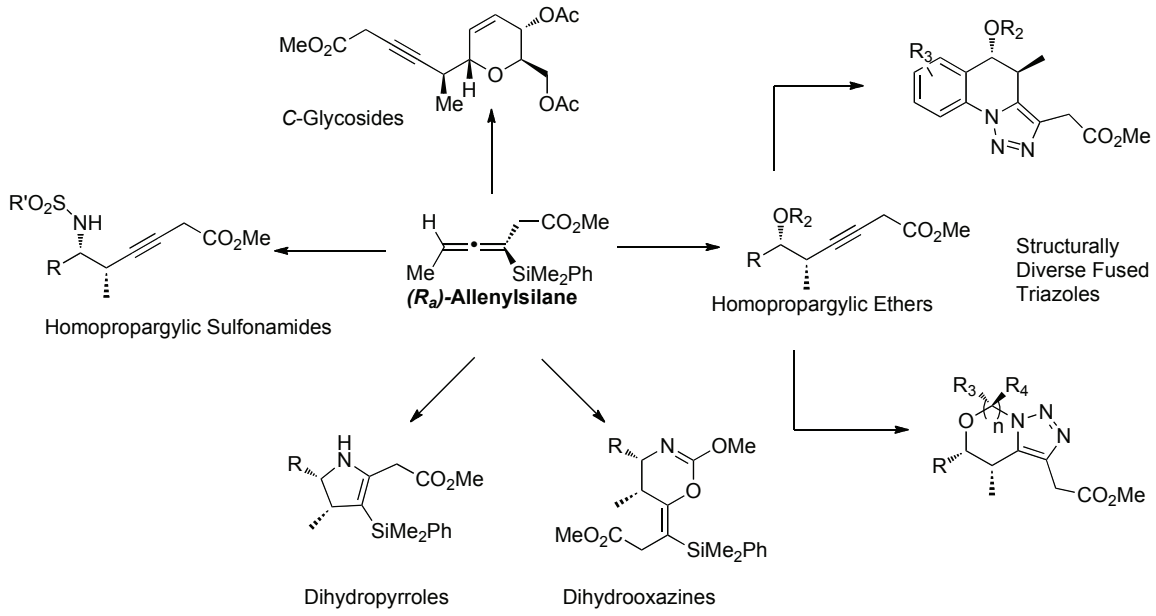
This submission details an efficient multi-gram synthesis of highly enantioenriched allenylsilanes. The allenes are formed in high yields with high levels of enantioselectivity by taking advantage of a C-selective silylation, followed by a lipase-catalyzed kinetic resolution, and a Johnson orthoester Claisen rearrangement. The (***R***) enantiomer of alcohol **2** can also be accessed by re-exposure of protected acetate (***R***)-**3** to the lipase in aqueous buffer, followed by the orthoester Claisen rearrangement, resulting in the (***S**_a*) enantiomer of allenylsilane **4** (Scheme 4).[5]

Scheme 4. Synthesis of allenylsilane (***S**_a*)-**4**.



Allenylsilanes **3** have been used as carbon nuclophiles in additions to oxonium ions to form homopropargylic ethers,[5] which can be used as a template for the formation of structurally and stereochemically diverse heterocycles containing a 1,2,3-triazole functionality.[6] In addition the allenylsilanes undergo additions to iminium ions, forming dihydropyrroles, dihydrooxazines and acyclic homopropargylic sulfonamides, with the reaction product determined by the nitrogen source used in iminium ion formation.[7] Stereoselective *C*-glycosidations allow for the formation of dihydropyran products with a side chain containing an internal alkyne.[8] Current work is focused on the development of a new methodology taking advantage of the axial chirality these reagents, as well as the application of this methodology to complex molecule synthesis (Scheme 5).

Scheme 5. Reactions products formed from enantioenriched allenylsilanes.



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02215. Email: panek@bu.edu. Funding for this work was provided by the NIH and through an AstraZeneca graduate fellowship to RAB.

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7. (a) Brawn, R. A.; Panek, J. S. *Org. Lett.* **2009**, *11*, 473–476. (b) Brawn, R. A.; Panek, J. S. *Org. Lett.* **2009**, *11*, 4362–4365.

8. Brawn, R. A.; Panek, J. S. *Org. Lett.* **2010**, *12*, 4624–4627.

Appendix
Chemical Abstracts Nomenclature; (Registry Number)

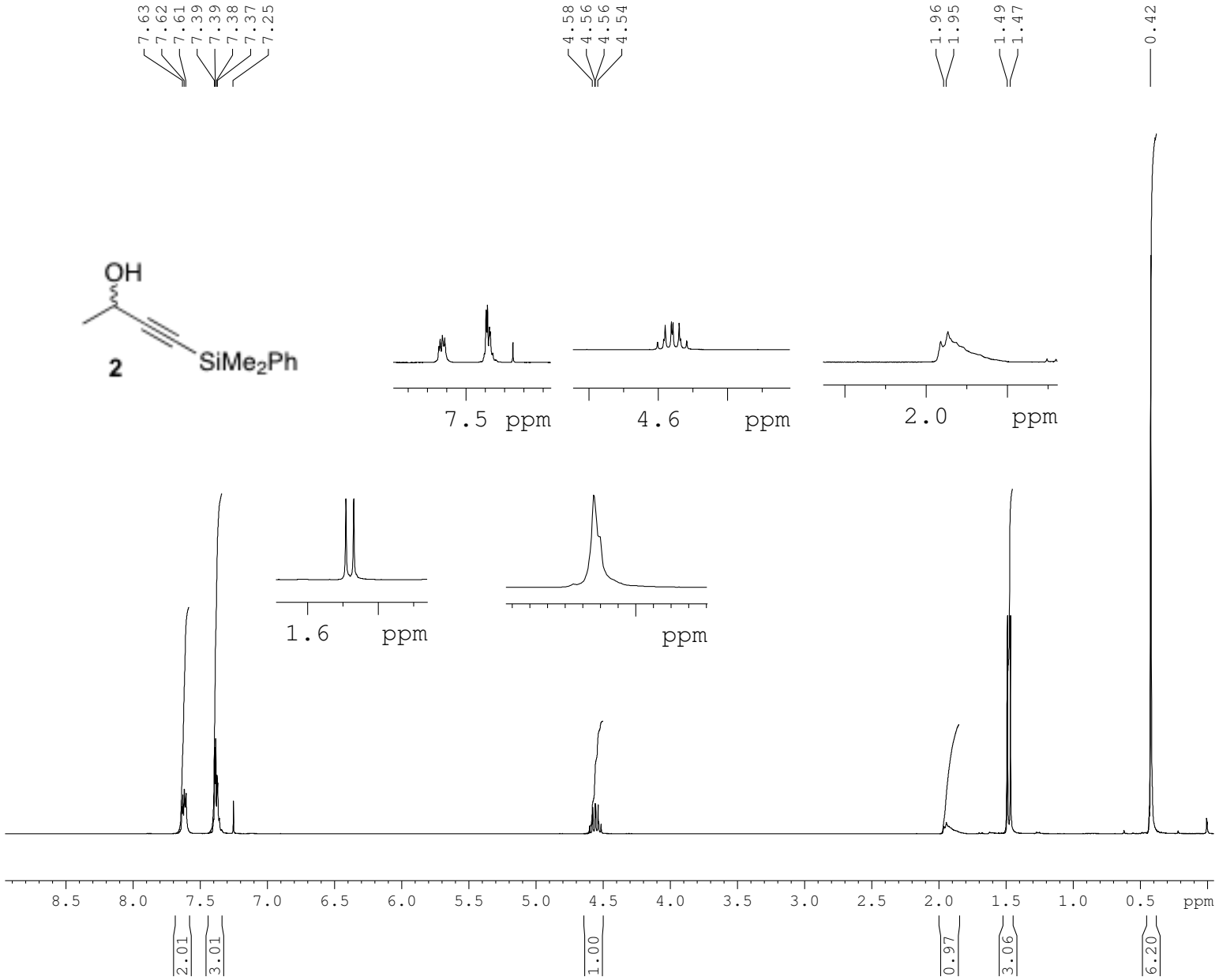
Lithium chloride; (7447-41-8)
3-butyn-2-ol; (2028-63-9)
n-Butyllithium; (109-72-8)
Chloro(dimethyl)phenylsilane; (768-33-2)
Vinyl Acetate; (108-05-4)
Trimethylorthoacetate; (1445-45-0)
Propionic Acid; (79-09-4)
Lithium Borohydride; (16949-15-8)
(±)-4-(Dimethyl(phenyl)silyl)-but-3-yn-2-ol; (115884-67-8)
(*S*)-4-(Dimethyl(phenyl)silyl)-but-3-yn-2-ol; (142697-17-4)
(*S*)-4-(Dimethyl(phenyl)silyl)-but-3-yn-2-yl acetate; (142611-82-3)
(R_a)-Methyl 3-(dimethyl(phenyl)silyl)hexa-3,4-dienoate; (945539-62-8)

James Panek was born in Buffalo NY in 1956. He earned a B.S. in Medicinal Chemistry, 1979, from the University at Buffalo (SUNY@Buffalo) and his Ph.D. in Medicinal Chemistry from the University of Kansas, 1984. He then pursued an NIH postdoctoral program at Yale University before joining the faculty at Boston University. Presently he serves as The Samour Family Professor of Chemistry. His research interests emphasize the field of synthetic organic chemistry, mainly in the area of acyclic stereocontrol with specific interest in the development of new reagents and new reaction methods. Ongoing studies in the area of natural product synthesis generate a complimentary research effort. Panek is also affiliated with the Center for Chemical Methodology and Library Development (CMLD) at Boston University.

Ryan Brawn was born in Camden, ME in 1980. He earned his BA in Biochemistry from Bowdoin College in 2003. He is currently finishing his Ph.D. in Organic Chemistry at Boston University in the Panek lab. His thesis work has focused on the development of enantioenriched allenylsilane reagents, and their use as carbon nucleophiles for a variety of stereocontrolled reactions. He is currently a postdoctoral fellowship at Pfizer, Groton CT and will begin work in the CVM group in Groton, CT in 2011.

Francois Grillet was born in 1982 in Saint Remy, France. He studied chemistry at the Ecole Nationale Supérieure de Chimie de Mulhouse where he received his engineer diploma in 2005. He then moved to Grenoble to carry out his Ph.D. under the supervision of Professor Andrew E. Greene working in the area of natural products synthesis. He is currently working as a post-doctoral fellow to apply the allenic Pauson-Khand reaction to the [5-7-5] ring system of 6,12-guaianolides in the group of Professor Kay Brummond at the University of Pittsburgh.

4-(dimethyl(phenyl)silyl)but-3-yn-2-ol



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TD	32768
SOLVENT	CDCl3
NS	7
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SWH	6188.119 Hz
FIDRES	0.188846 Hz
AQ	2.6477044 sec
RG	114
DW	80.800 usec
DE	6.50 usec
TE	296.3 K
D1	1.00000000 sec
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NUC1	1H
P1	13.20 usec
SI	32768
SF	300.2300108 MHz
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SSB	0
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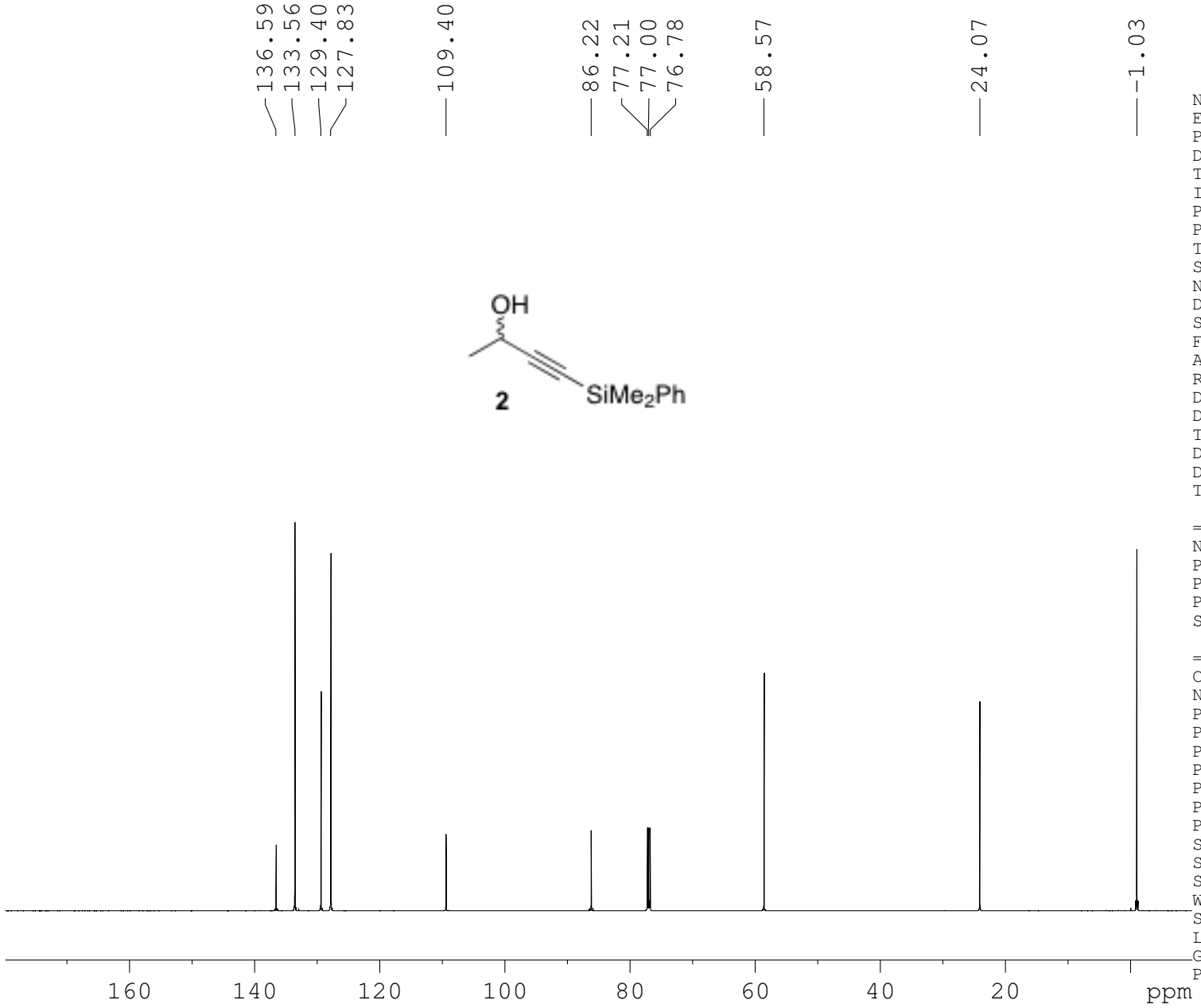
GB	0
PC	1.00

4-(dimethyl(phenyl)silyl)but-3-yn-2-ol

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TD                 65536
SOLVENT            CDCl3
NS                 22549
DS                     4
SWH            36057.691 Hz
FIDRES          0.550197 Hz
AQ              0.9088159 sec
RG                   203
DW                 13.867 usec
DE                  6.50 usec
TE                 293.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                 11.50 usec
PL1                 0.00 dB
PL1W         97.46119690 W
SFO1        151.1039906 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              70.00 usec
PL2                -2.00 dB
PL12               14.19 dB
PL13              120.00 dB
PL2W         19.70630455 W
PL12W         0.47381112 W
PL13W         0.00000000 W
SFO2        600.8724035 MHz
SI                 32768
SF          151.0889075 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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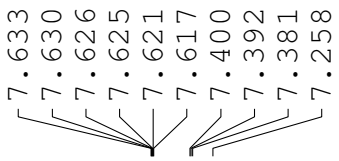
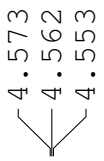
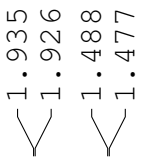
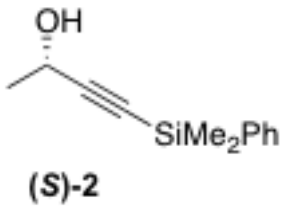
(S)-4-(dimethyl(phenyl)silyl)but-3-yn-2-ol

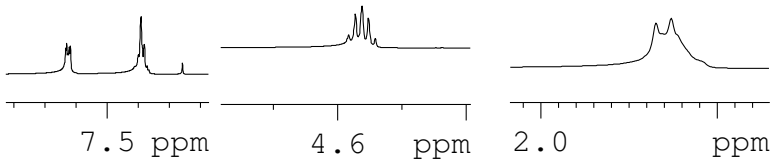


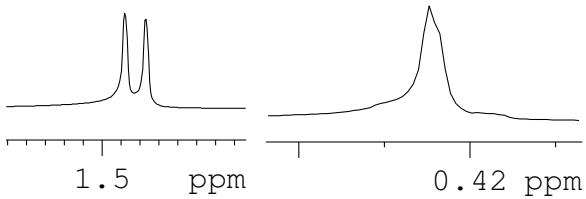


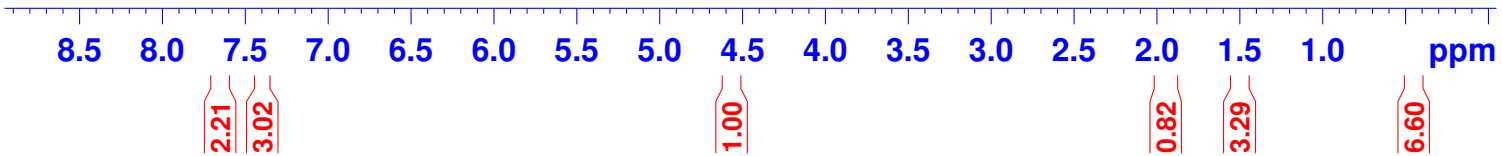




(*S*)-2







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TD	65536
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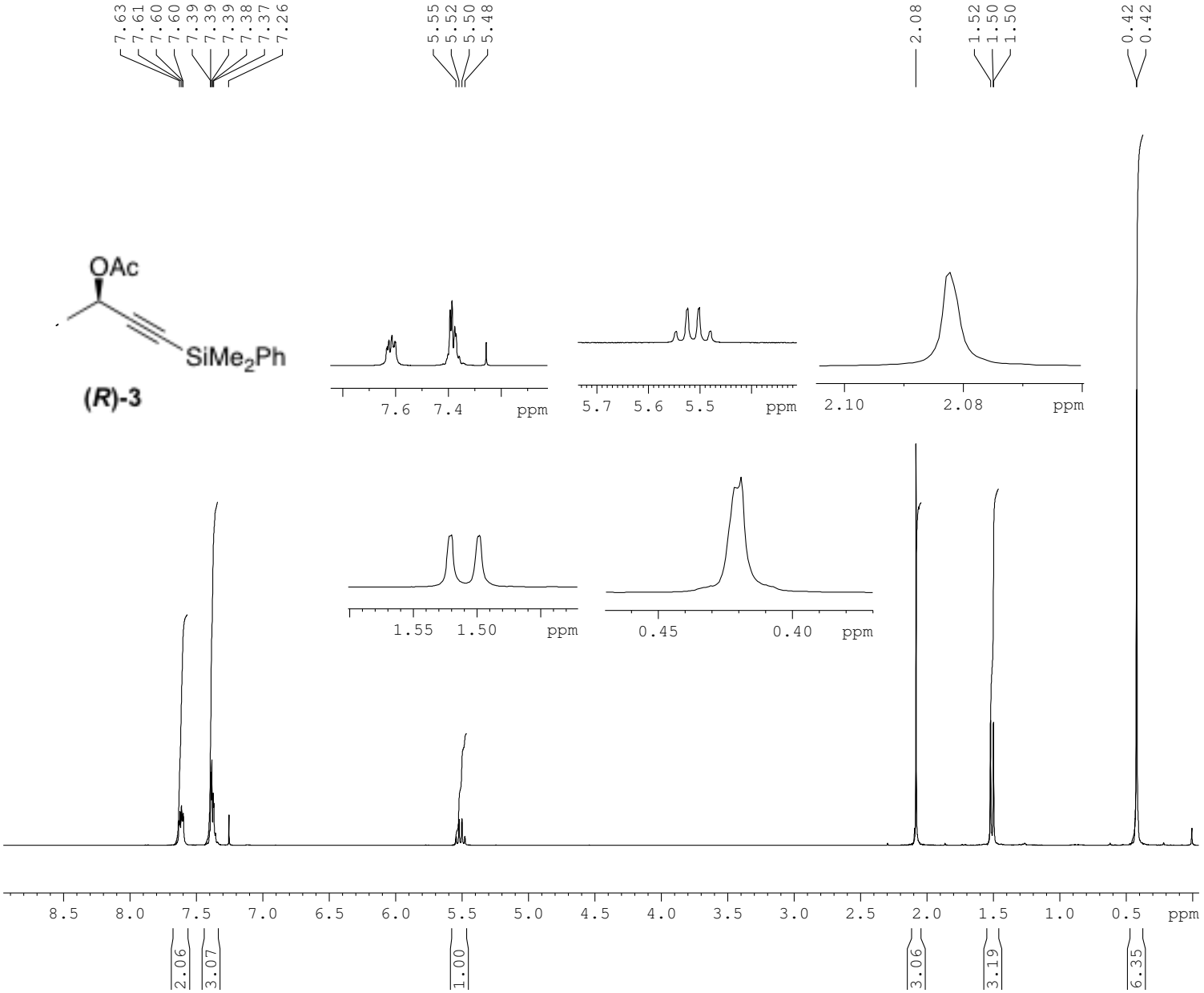
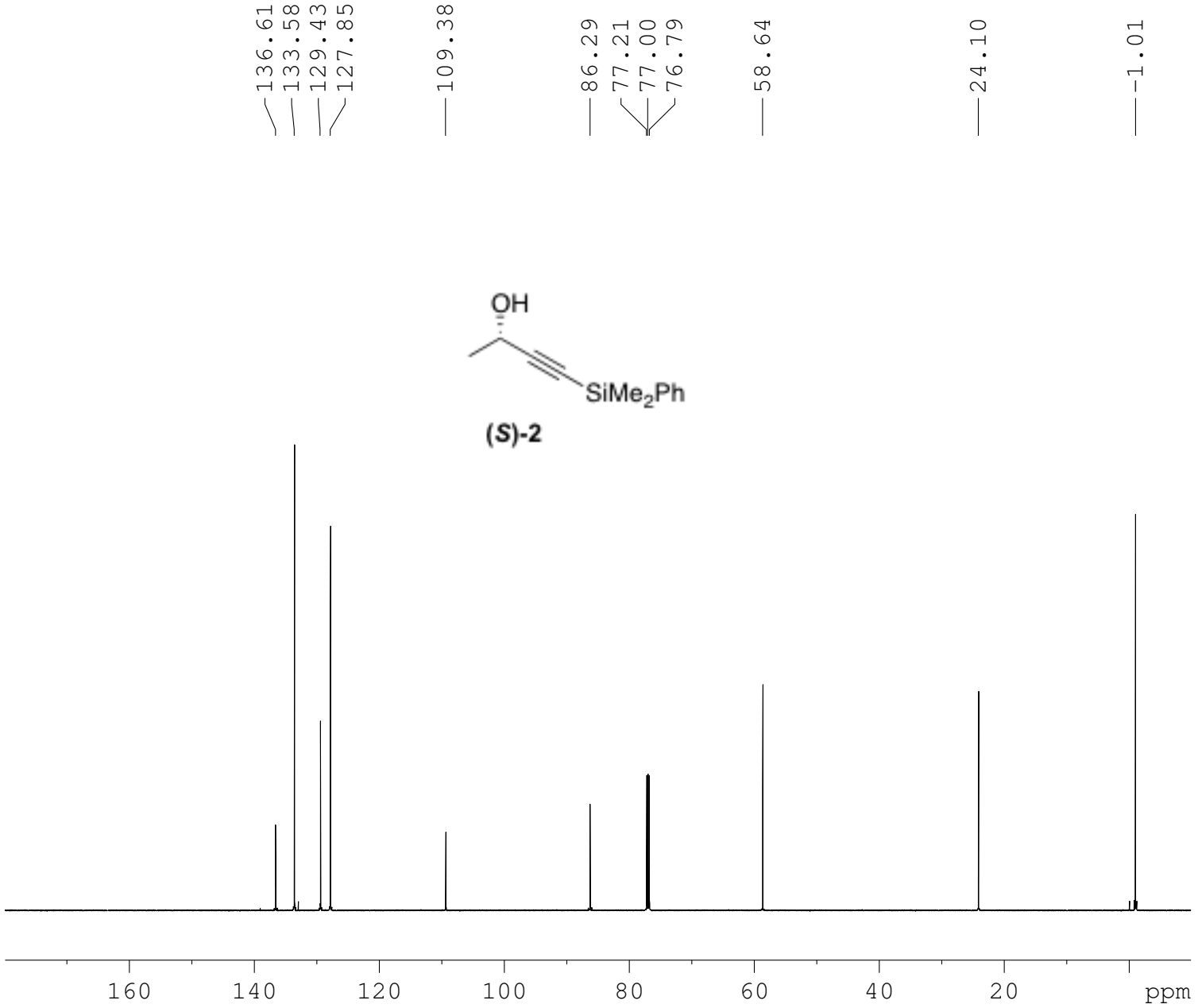
NS	15
DS	2
SWH	12335.526 Hz
FIDRES	0.188225 Hz
AQ	2.6564426 sec
RG	40.3
DW	40.533 use
DE	6.50 use
TE	293.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	1H
P1	10.86 use
PL1	-2.00 dB
PL1W	19.70630455 W
SFO1	600.8737106 MHz
SI	32768
SF	600.8700148 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

(R)-4-(dimethyl(phenyl)silyl)but-3-yn-2-yl acetate



NAME	FRGR007CF1 proton acetate
EXPNO	1
PROCNO	1
Date_	20110913
Time	7.26
INSTRUM	spect
PROBHD	5 mm Multinucl
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	8
DS	2
SWH	6188.119 Hz
FIDRES	0.188846 Hz
AQ	2.6477044 sec
RG	114
DW	80.800 usec
DE	6.50 usec
TE	296.2 K
D1	1.00000000 sec
======== CHANNEL f1 ========	
NUC1	1H
P1	13.20 usec
SI	32768
SF	300.2300104 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

(S)-4-(dimethyl(phenyl)silyl)but-3-yn-2-ol



NAME	FRGR004CAEcarbon
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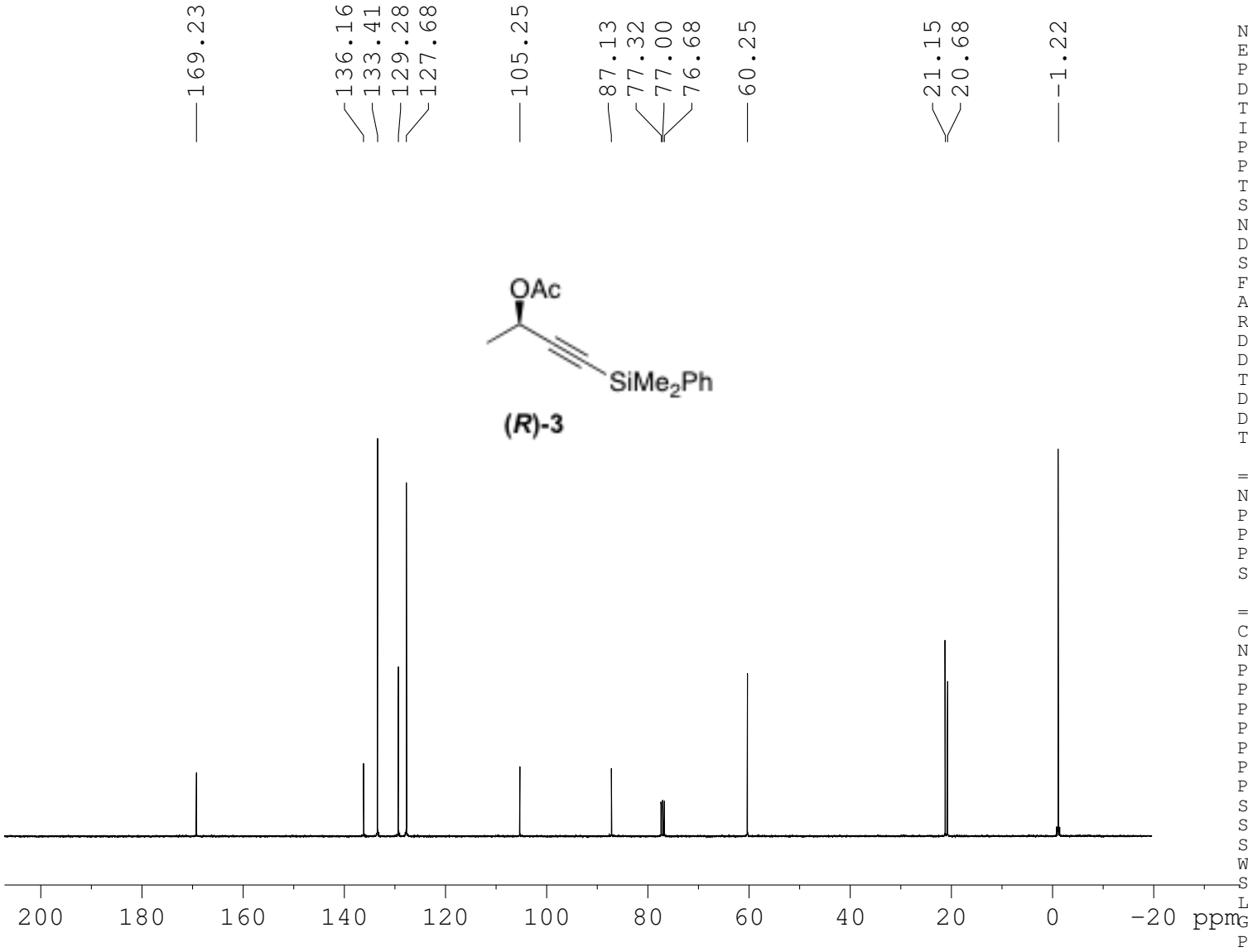
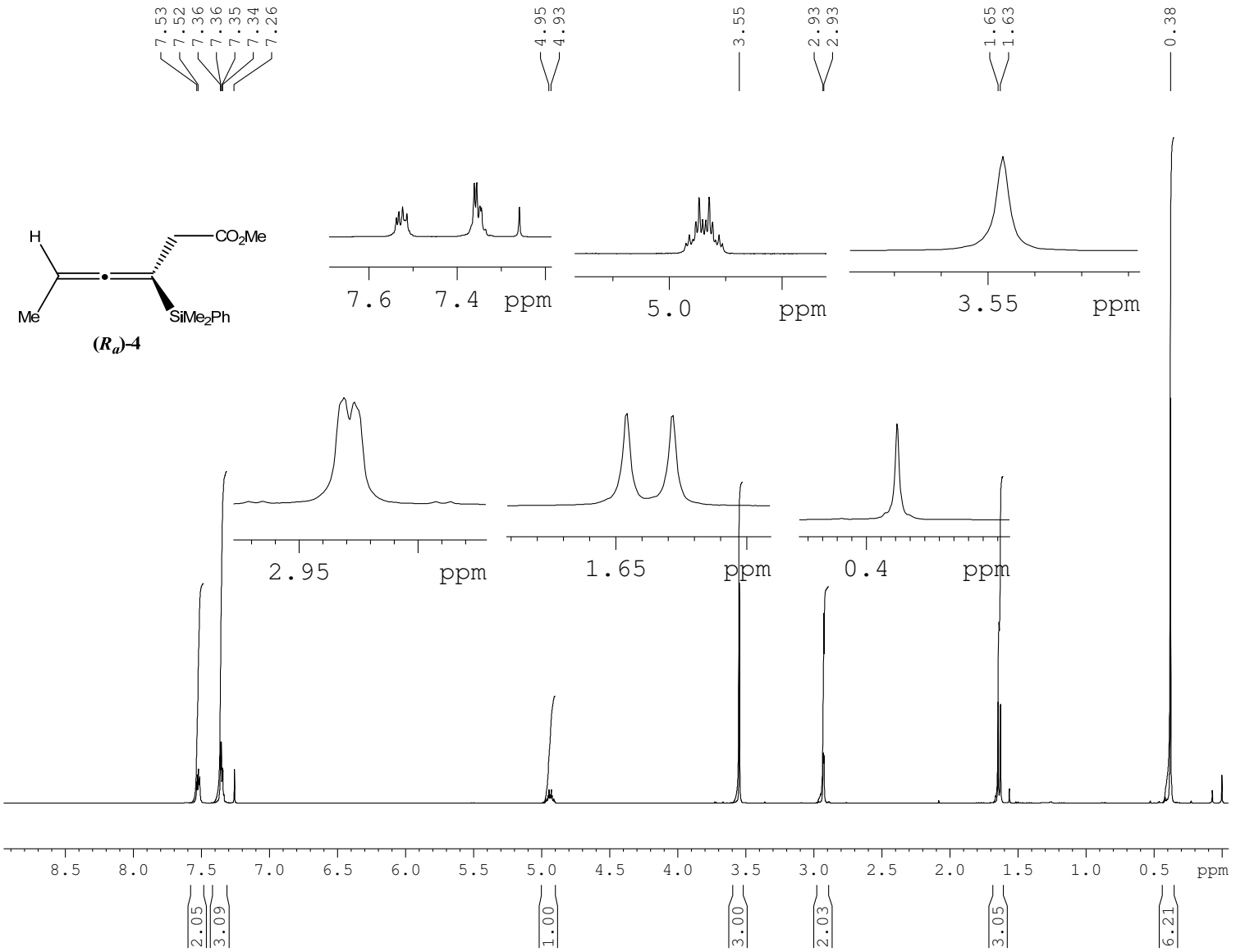
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	743
DS	4
SWH	36057.691 Hz
FIDRES	0.550197 Hz
AQ	0.9088159 sec
RG	203
DW	13.867 usec
DE	6.50 usec
TE	293.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	11.50 usec
PL1	0.00 dB
PL1W	97.46119690 W
SFO1	151.1039906 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-2.00 dB
PL12	14.19 dB
PL13	120.00 dB
PL2W	19.70630455 W
PL12W	0.47381112 W
PL13W	0.00000000 W
SFO2	600.8724035 MHz
SI	32768
SF	151.0889017 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

(R)-4-(dimethyl(phenyl)silyl)but-3-yn-2-yl acetate



NAME	FRGR007CF1carbon
EXPNO	1
PROCNO	1
Date_	20110913
Time	8.16
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	42
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	296.9 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	10.00 usec
PL1	-1.59 dB
PL1W	51.07626343 W
SFO1	100.6479773 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	75.00 usec
PL2	-1.00 dB
PL12	13.39 dB
PL13	20.00 dB
PL2W	11.09959412 W
PL12W	0.40393090 W
PL13W	0.08816721 W
SFO2	400.2316009 MHz
SI	32768
SF	100.6379478 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

(R)-methyl-3-(dimethyl(phenyl)silyl)hexa-3,4-dienoate



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EXPNO	1
PROCNO	1
Date_	20110919
Time	7.50
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	4
DS	2
SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	128
DW	60.800 usec
DE	6.50 usec
TE	295.3 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.31 usec
PL1	-1.00 dB
PL1W	11.09959412 W
SFO1	400.2324716 MHz
SI	32768
SF	400.2300132 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

(R)-methyl-3-(dimethyl(phenyl)silyl)hexa-3,4-dienoate

209.40
172.01
137.44
133.73
129.03
127.63
88.42
81.22
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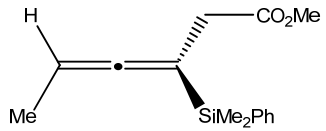
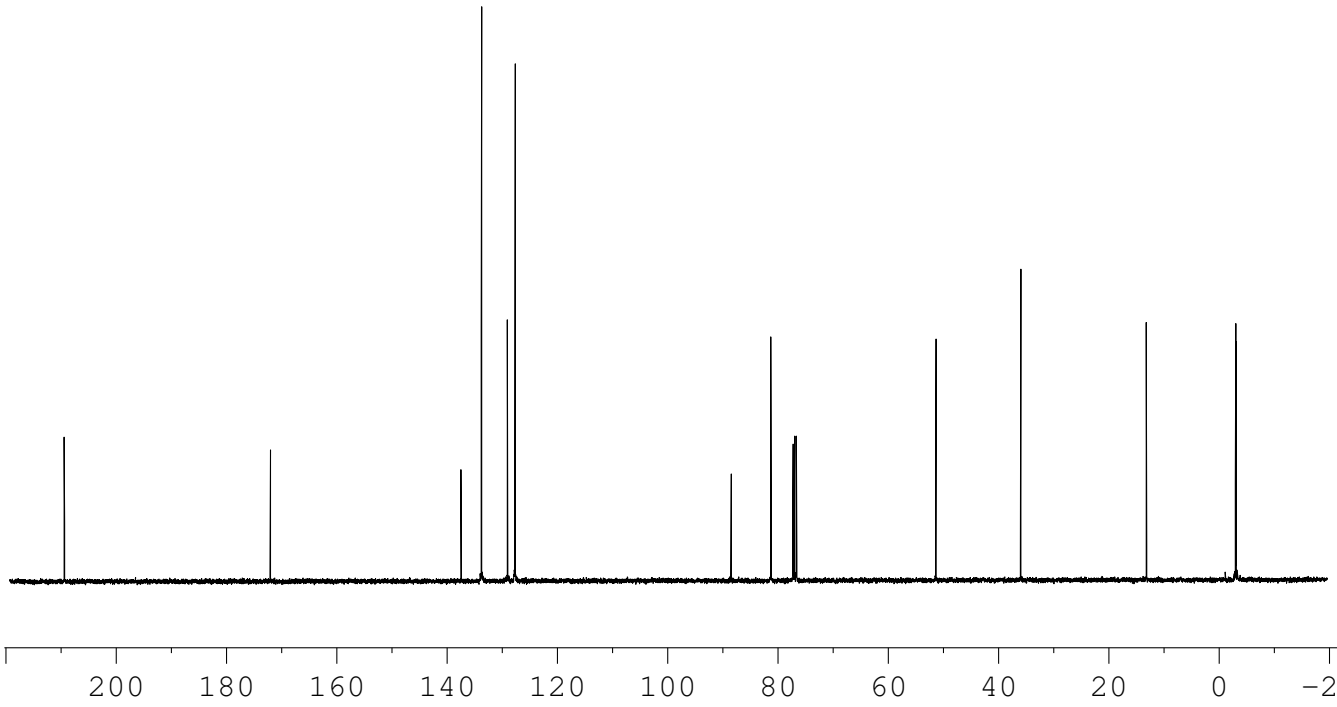
76.68
51.39
36.00
13.21
-2.97
-3.07



(R_a)-4



NAME	FRGR008CANAcarbon
EXPNO	1
PROCNO	1
Date_	20110919
Time	8.10
INSTRUM	spect
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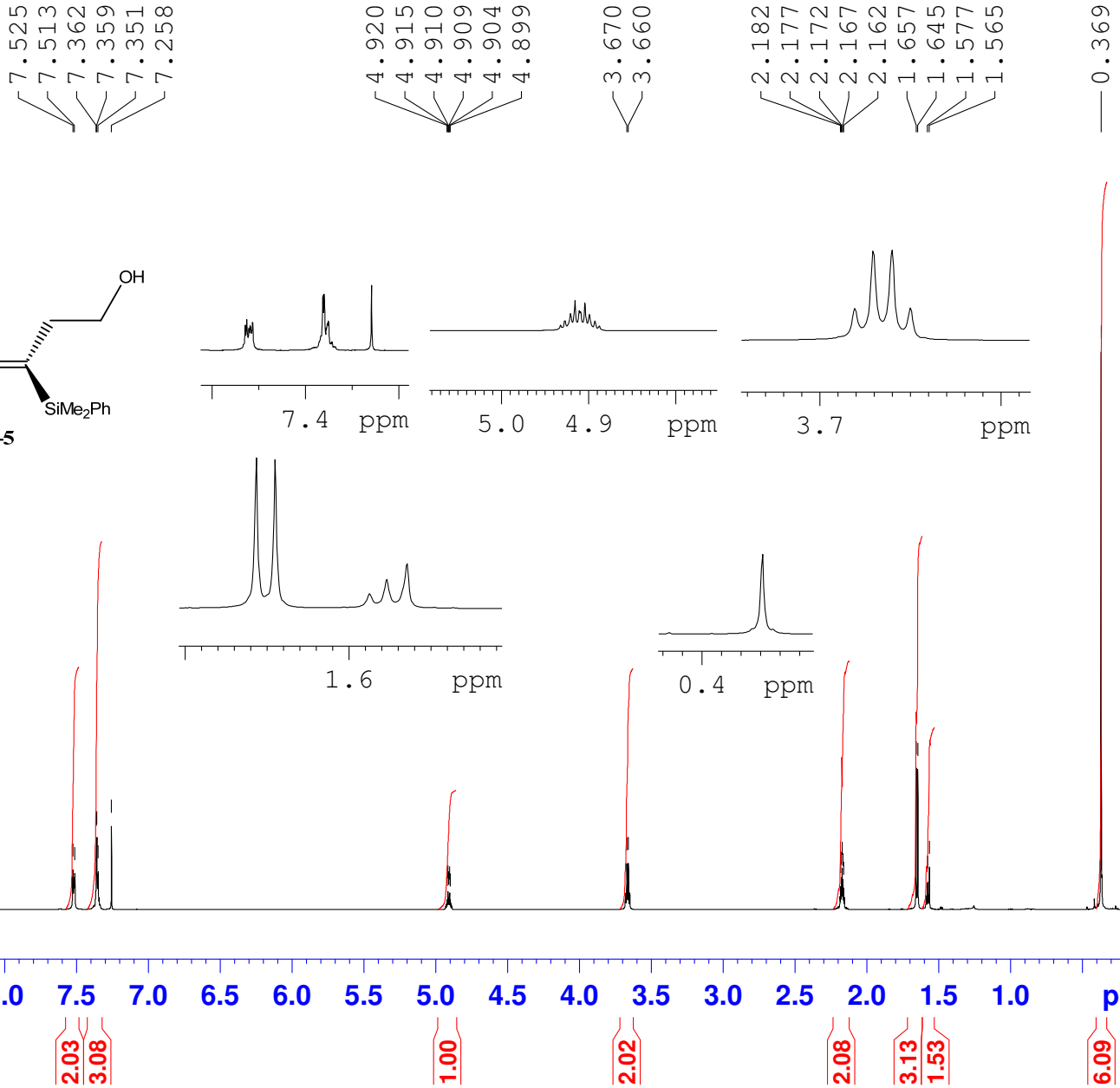
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	43
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.8 K
D1	3.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	10.00 usec
PL1	-1.59 dB
PL1W	51.07626343 W
SFO1	100.6479773 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	75.00 usec
PL2	-1.00 dB
PL12	13.39 dB
PL13	20.00 dB
PL2W	11.09959412 W
PL12W	0.40393090 W
PL13W	0.08816721 W
SFO2	400.2316009 MHz
SI	32768
SF	100.6379306 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

(Ra)-5 : 3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-ol



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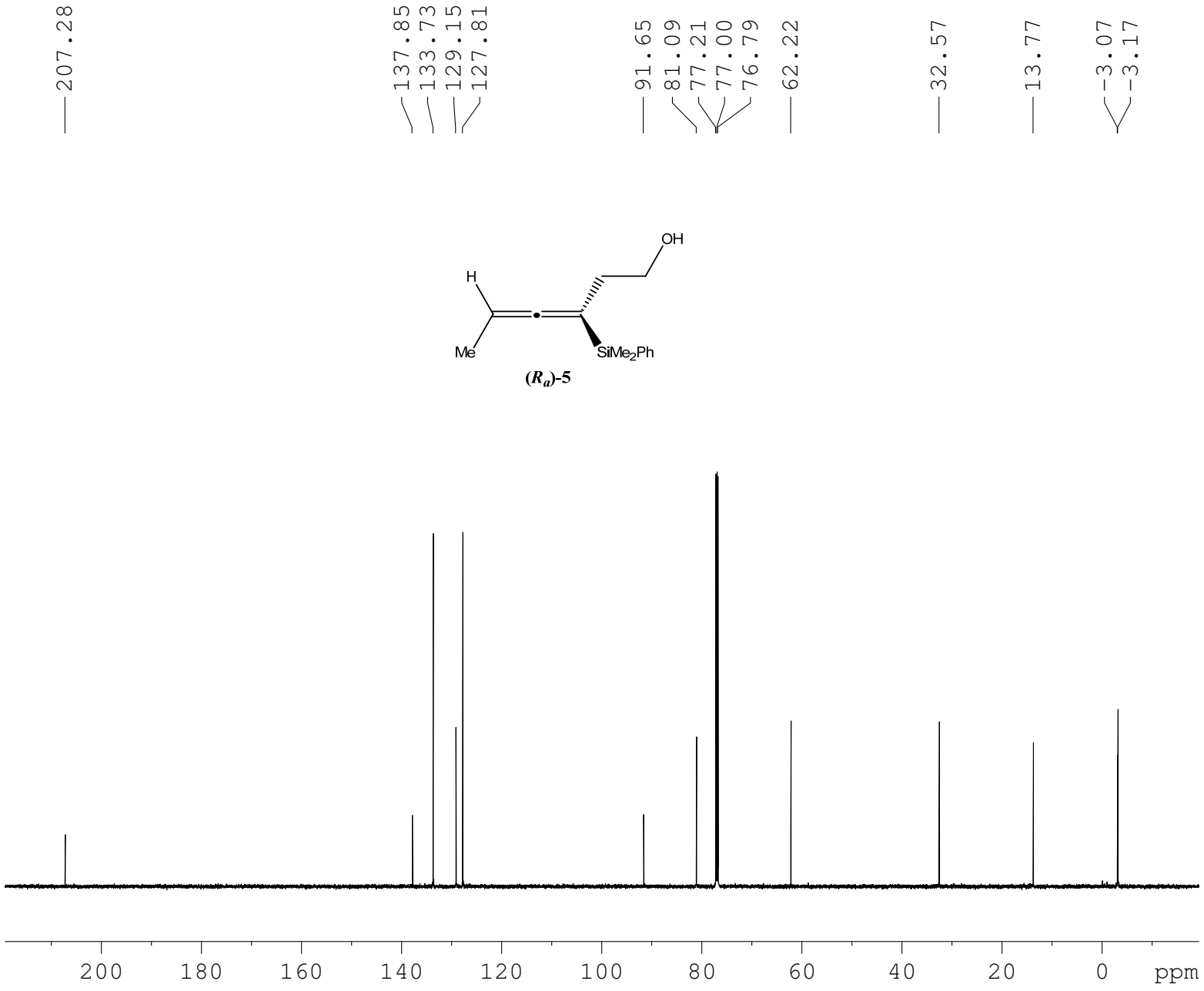
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12335.526 Hz
FIDRES	0.188225 Hz
AQ	2.6564426 sec
RG	71.8
DW	40.533 usec
DE	6.50 usec
TE	295.8 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	10.86 usec
PL1	-2.00 dB
PL1W	19.70630455 W
SFO1	600.8737106 MHz
SI	32768
SF	600.8700145 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

3-(dimethyl(phenyl)silyl)hexa-3,4-dien-1-ol



(R_a)-5

NAME	FRGR016CANAcarbon
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PROCNO	1
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Time	14.51
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	527
DS	4
SWH	36057.691 Hz
FIDRES	0.550197 Hz
AQ	0.9088159 sec
RG	203
DW	13.867 usec
DE	6.50 usec
TE	294.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	11.50 usec
PL1	0.00 dB
PL1W	97.46119690 W
SFO1	151.1039906 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-2.00 dB
PL12	14.19 dB
PL13	120.00 dB
PL2W	19.70630455 W
PL12W	0.47381112 W
PL13W	0.00000000 W
SFO2	600.8724035 MHz
SI	32768
SF	151.0888889 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40