SYNTHESIS AND FLUORIDE PROMOTED WITTIG REARRANGEMENTS OF α-ALKOXYSILANES

Supporting Information

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Materials and Methods

Reactions were carried out in oven- or flame-dried glassware under nitrogen atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under nitrogen. Anhydrous dimethylformamide (DMF) was purchased from Aldrich and stored over freshly activated 4 Å molecular sieve powder. Cesium fluoride was dried under vacuum at 120 °C overnight. Cyclohexane, *n*-butyllithium, *t*-butyllithium were purchased from Aldrich. Except as otherwise indicated, all reactions were magnetically stirred and monitored by thin layer chromatography with Whatman 0.25-mm precoated silica gel plates. Flash chromatography was performed with silica gel 60 Å (particle size 230-400 Mesh ASTM) supplied by Whatman Inc. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Infrared spectra were recorded on a Nicolet IR/42. Proton and carbon NMR spectra were recorded on a Varian Gemini-300 spectrometer. Chemical shifts are reported relative to the residue peaks of solvent chloroform (δ 7.24 for ^{1}H and δ 77.0 for ^{13}C). High-resolution mass spectra were measured by the Mass Spectrometry Laboratory of the Department of Chemistry and Biochemistry at the University of South Carolina. Microanalyses were performed by Robertson Laboratories, Madison, NJ.

α-(Trimethylsilyl)benzyl alcohol (1a): A solution of benzyl alcohol (12 g, 0.11 mol) in 200 mL THF was cooled to 0 °C under nitrogen atmosphere. *n*-BuLi (1.6 M in hexanes, 75 mL, 0.12 mol) was added dropwise. After an additional 15 min 15 mL (0.12 mol) TMSCl was added dropwise while the solution was well stirred. The solution was stirred under nitrogen at 0 °C for 15 min before it was cooled to -76 °C . *t*-BuLi (1.7 M in hexanes, 82 mL, 0.14 mol) was than added dropwise. After an additional 1 hr during which the reaction temperature was allowed to rise to room temperature, the reaction was diluted with diethyl ether, quenched with saturated aqueous NH_4Cl and washed with water and brine. The organic phase was dried over $MgSO_4$ and concentrated. Distillation (0.3 mm Hg, 65-68 °C) gave 17.6 g (89%) of **1a** as a light yellow liquid. The spectroscopic data for **1a** were consistent with those previously reported

in the literature (Chuang, T.-H.; Fang, J.-M.; Jiaang, W.-T.; Tsai, Y.-M. *J. Org. Chem.* **1996**, *61*, 1794-1805).

α-(Trimethylsilyl)allyl alcohol (1b). Applying the procedure above to 10 g (0.17 mol) of allyl alcohol furnished 20 g crude product (**1b**) as a greenish yellow liquid in 89% yield which was used without further purification. The spectroscopic data for **1b** were consistent with those previously reported in the literature (Danheiser, R. L.; Fink, D. M.; Okano, K.; Tsai, Y.-M.; Szczepanski, S. W. *Org. Syn.* **1987**, *66*, 14-21).

α-(Trimethylsilyl)*n*-propyl alcohol (1c). A suspension of 0.1 g Pd on activated carbon (10%) in 10 mL EtOAc was purged with H_2 and stirred under 1 atm H_2 for 5 min. Then 0.8 g of α-(trimethylsilyl)allyl alcohol **1b** (6.2 mmol) was added via syringe and the mixture was stirred overnight at room temperature. The catalyst was then removed via filtration and the solvent was carefully distilled off to furnish 0.5 g crude product **1c** (62%) as a pale yellow liquid. The crude material was used without further purification, however an analytical sample was obtained by distillation (~180 °C oil bath; 1 atm) using a distillation head with a vacuum jacket. The spectroscopic data for **1c** were consistent with those previously reported in the literature (Soderquist, J. A.; Lee, S.-J. H. *Tetrahedron*, **1988**, *44*, 4033-4042).

Preparation of 2a and 2b. To a solution of α-(trimethylsilyl)benzyl alcohol **1a** (0.85 g, 4.7 mmol) in 50 mL cyclohexane was added the trichloroacetimidate of crotyl alcohol (2.0 g, 9.2 mmol). To the well stirred solution was added 0.1 mL TMSOTf in 1 mL cyclohexane via syringe. A white precipitate formed in several minutes. The reaction mixture was stirred at room temperature overnight before being filtered. The filtrate was diluted with petroleum ether, washed with saturated aqueous $NaHCO_3$, 1 N HCl, and brine. The organic phase was dried over $MgSO_4$ and concentrated. Silica gel chromatography (1% diethyl ether in pentane) furnished 740 mg (67%) of **2a** and 277 mg (25%) of **2b** as a 2:1 mixture of two diastereomers, all as colorless oils.

For **2a**: IR (thin film) 3024, 2959, 1600, 1450, 1248, 1051 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33-7.12 (m, 5 H), 5.60 (m, 2 H), 4.14 (s, 1 H), 4.09-4.01 (m, 1 H), 3.72-3.63 (m, 1 H), 1.73 (dd, *J* = 4.8, 1.0 Hz, 3 H), 0.0 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 128.6, 128.3, 128.0, 125.9, 125.5, 76.9, 71.1, 17.8, -3.9; HRMS (EI) *m/z* 233.1361 [$(M-H)^+$; calcd for $C_{14}H_{21}OSi$ 233.1362].

For **2b**: IR (thin film) 3024, 2928, 1450, 1248, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.18-7.13 and 7.33-7.26 (m, 5 H), 5.83 and 5.65 (ddd, *J* = 5.5, 10.4, 17.3 Hz and 7.7, 10.2, 17.3 Hz, 1 H), 5.23-4.98 (m, 2 H), 4.26 and 4.23 (s, 1 H), 3.88 and 3.74 (q, *J* = 6.32 and 6.32 Hz, 1 H), 1.20 and 1.23 (d, *J* = 6.30 and 6.30 Hz, 3 H), 0.00 and -0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3 and 142.2, 141.4 and 140.5, 127.9 and 127.8, 125.9 and 125.7, 125.4 and 125.4, 116.2 and 113.6, 75.5 and 75.0, 74.7 and 74.0, 22.4 and 22.2, -3.96 and -3.96; HRMS (EI) *m/z* 233.1356 [$(M-H)^+$; calcd for $C_{14}H_{22}OSi$ 233.1362].

Preparation of 2c: Applying the representative procedure above to 1.0 g (5.5 mmol) of **1 a** and 2.4 g (11 mmol) of the trichloroacetimidate of 2-methyl-2-propen-1-ol afforded after silica gel chromatography (1% diethyl ether in pentane) 0.71 g (55%) of **2c** as a colorless liquid. IR (thin film) 2959, 1769, 1451, 1248, 841 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.10 (m, 5 H), 4.89 (m, 2 H), 4.13 (s, 1 H), 3.81, (AB, Δ = 105.5 Hz, *J* = 12.4 Hz, 2 H), 1.74, (s, 3 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 141.4, 128.0, 125.9, 125.6, 111.8, 76.9, 74.1, 19.6, -3.9; GC/MS (EI) *m/z* 179.2, 77.0, 73.1.

Anal. Calcd for $C_{14}H_{22}OSi$: C, 71.75; H, 9.47; Found: C, 71.62; H, 9.39.

Preparation of 2d: Applying the representative procedure above to 1.0 g (7.7 mmol) of **1 b** and 3.9 g (14 mmol) of the trichloroacetimidate of cinnamyl alcohol afforded after silica gel chromatography (1% diethyl ether in pentane) 1.25 g (67%) of **2d** as a colorless liquid. IR (thin film) 2959, 1628, 1451, 1248, 1030, 841 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45-7.20 (m, 5 H), 5.89-5.65 (m, 2 H), 5.35-5.15 (m, 2 H), 5.15-4.95 (m, 2 H), 4.85 (d, *J* = 8.2 Hz, 1 H), 3.94 (dt, *J* = 6.9, 1.4 Hz, 1 H), 0.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.4, 139.0, 137.2, 128.1, 127.0, 126.3, 117.4, 112.4, 80.8, 72.8, -3.9; HRMS (EI) *m/z* 246.1440 [(M^+); calcd for $C_{15}H_{22}OSi$ 246.1433].

Preparation of 2e: Applying the representative procedure above to 0.9 g (5 mmol) of **1a** and 2.5 g (10 mmol) benzyltrichloroacetimidate afforded after silica gel chromatography (1% diethyl ether in pentane) 0.7 g (52%) of **2e** as a colorless liquid. IR (thin film) 3027, 2959, 1496, 1451, 1248, 1059, 841 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.12 (m, 10 H), 4.46 (ABq, Δ = 124.5 Hz, J = 12.0 Hz, 2 H), 4.15 (s, 1 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.3, 139.1, 128.2, 128.17, 128.13, 127.7, 127.5, 127.3, 126.0, 125.9, 125.7, 77.2, 72.0, -3.93; GC/MS (EI) *m/z* 179.1, 163.2, 73.1.

Anal. Calcd for $C_{17}H_{22}OSi$: C, 75.52; H, 8.21; Found: C, 75.17; H, 7.98.

Preparation of 2f: Applying the representative procedure above to 1.0 g (5.5 mmol) of **1a** and 2.6 g (13 mmol) of the trichloroacetimidate of propargyl alcohol afforded after silica gel chromatography 0.78 g (64%) of **2f** as a colorless liquid. IR (thin film) 3308, 2959, 1767, 1450, 1248, 1059 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.10 (m, 5 H), 4.39 (s, 1 H), 4.08 (ABq, Δ = 87.0 Hz, J = 15.6, 2.1 Hz, 2 H), 2.38 (t, J = 2.4 Hz, 1 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 128.2, 126.1, 126.1, 80.5, 76.6, 73.7, 57.3, -4.0; HRMS [CI (NH_3)] *m/z* 236.1468 [$(M+NH_4)^+$; calcd for $C_{13}H_{22}NOSi$ 236.1471].

Preparation of 2g: Applying the representative procedure above to 0.9 g (6.8 mmol) of **1 b** and 3.5 g (14 mmol) benzyltrichloroacetimidate afforded after silica gel chromatography 0.8 g (53%) of **2 g** as a colorless liquid. IR (thin film) 3032, 2959, 1248, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43-7.25 (m, 5 H), 5.91-5.79 (m, 1 H), 5.15-5.07 (m, 2 H), 4.72 (d, J = 12.1 Hz, 1 H), 4.34 (d, J = 12.1 Hz, 1 H), 3.64 (dt, J = 7.14, 1.37 Hz, 1 H), 0.04 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 137.3, 128.2, 127.6, 127.2, 112.6, 75.9, 71.8, -3.98; HRMS (EI) *m/z* 220.1287 [$(M)^+$;calcd for $C_{13}H_{20}OSi$ 220.1283].

Preparation of 2h: Applying the representative procedure to 0.5 g (3.8 mmol) of **1c** and 2.5 g (10 mmol) benzyltrichloroacetimidate afforded after silica gel chromatography 0.52 g (63%) of **2h** as a colorless liquid. IR (thin film) 2959, 1454, 1248 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41-7.20 (m, 5 H), 4.52 (ABq, Δ = 48 Hz, J = 11.4 Hz, 2 H), 3.04 (dd, J = 7.5, 5.7 Hz, 1 H), 1.80-1.58 (m, 2 H), 1.01 (t, J = 7.2 Hz, 3

H), 0.07 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 128.2, 127.7, 127.3, 75.4, 73.4, 23.8, 11.7, -2.80; HRMS [CI (NH_3)] *m/z* 223.1514 [$(M+H)^+$; calcd for $C_{13}H_{23}OSi$ 223.1518].

Wittig rearrangement reaction of 2a with CsF. Preparation of 3: In a glove bag purged with nitrogen, CsF powder (ca. 100 mg) was suspended in DMF (4 mL). The resulting mixture was stirred for 5 min before **2a** (50 mg, 0.21 mmol) was added dropwise via syringe. The solution was stirred overnight at room temperature, before being diluted with diethyl ether, quenched with saturated aqueous NH_4Cl, washed with 0.1 N HCl, water, and then brine. The organic phase was dried over $MgSO_4$ and concentrated. Silica gel chromatography (5 to 10% diethyl ether in pentane gradient) afforded 28 mg (80%) of **3** as an inseparable mixture (1.2:1) of syn and anti diastereomers. The spectroscopic data were consistent with those previously reported (Kobayashi, S.; Nishio, K. *J. Org. Chem*. **1994**, *59*, 6620-6628; also see: Kang, S-K.; Kim, D-Y.; Hong, R-K.; Ho, P-S. *Synth. Commun*. **1996**, *26*, 1493-1498).

Wittig rearrangement reaction of 2b with CsF. Preparation of 4: Applying the Wittig rearrangement conditions above to 48 mg (0.20 mmol) of **2b** afforded after silica gel chromatography (10% diethyl ether in pentane) 20 mg (60%) of **4** as a colorless oil. The spectroscopic data were consistent with those previously reported in the literature (Kang, S-K.; Kim, D-Y.; Hong, R-K.; Ho, P-S. *Synth. Commun*. **1996**, *26(8)*, 1493-1498).

Wittig rearrangement reaction of 2c with CsF. Preparation of 5: Applying the Wittig rearrangement conditions above to 35 mg (0.15 mmol) of **2c** afforded after silica gel chromatography (10% diethyl ether in pentane) 19 mg (79%) of **5** as a colorless oil. The spectroscopic data were consistent with those previously reported in the literature (Kobayashi, S.; Nishio, K. *J. Org. Chem*. **1994**, *59*, 6620-6628).

Wittig rearrangement reaction of 2d with CsF. Preparation of 6 and 7: Applying the Wittig rearrangement conditions above to 45 mg (0.18 mmol) of **2d** afforded after silica gel chromatography (10% diethyl ether in pentane) 17 mg (54%) of **6** and 4 mg (13%) of **7** as an inseparable

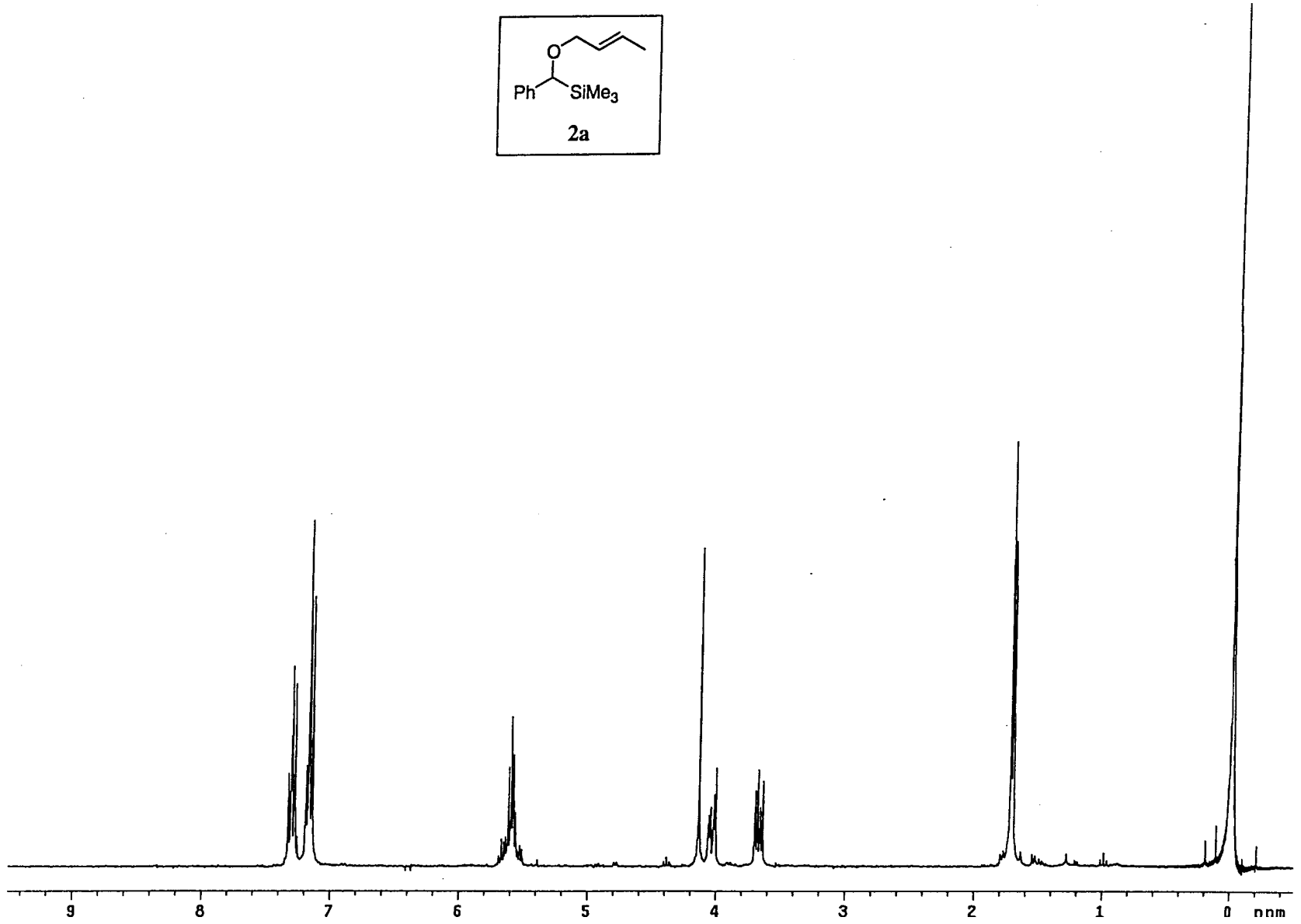
mixture (1:1) of syn and anti diastereomers. The spectroscopic data for these products were consistent with those previously reported in the literature (For **6** see: Enholm, E. J.; Satici, H.; Prasad, G. *J. Org. Chem.* **1990**, *55*, 324-329. For **7** see: Newman-Evans, R. H.; Simon, R.; Carpenter, B. K. *J. Org. Chem.* **1990**, *55,* 695-711).

Attempted Wittig rearrangement reaction of 2e with CsF. Preparation of 8: Applying the Wittig rearrangement conditions above to 71 mg (0.26 mmol) of **2e** afforded no Wittig rearrangement reaction product. Instead, after silica gel chromatography (1:5 diethyl ether in pentane) 43 mg of dibenzyl ether **8** was isolated in 82% yield. The spectroscopic data were consistent with those previously reported in the literature (Herzog, H.; Scharf, H.-D. *Synthesis* **1986**, 788-790).

Attempted Wittig rearrangement reaction of 2f with CsF. Preparation of 9: The Wittig rearrangement conditions above were applied to 110 mg (0.50 mmol) of **2f** but no rearrangement product was observed. Silica gel chromatography (1:20 diethyl ether in pentane) afforded 40 mg (54%) of desilylated compound **9**. The spectroscopic data of this product were consistent with those previously reported in the literature (Boger, D. L.; Palanki, M. S. S. *J. Am. Chem. Soc.* **1992**, *114*, 9318-9327).

Attempted Wittig rearrangement reaction of 2g with CsF. Preparation of 10 and 11: The Wittig rearrangement conditions above were applied to 88 mg (0.40 mmol) of **2g** but no Wittig was observed. Silica gel chromatography (1:50 diethyl ether in pentane) afforded 37 mg (63%) of **10** as an inseparable mixture of geometric isomers (*E:Z* 88:12) and 8 mg (14%) of **11**. The spectroscopic data were consistent with those previously reported in the literature (For **10** see: Dickinson, J. M.; Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1179-1184. For **11** see: Zimmerman, S. C.; Cramer, K. D.; Galan, A. A. *J. Org. Chem.* **1989**, *54*, 1256-1264).

Attempted Wittig rearrangement reaction of 2h with CsF. The Wittig rearrangement conditions above were applied to 50 mg of **2h** but no reaction was observed. The starting material was recovered in 81% yield.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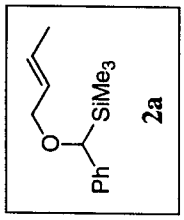
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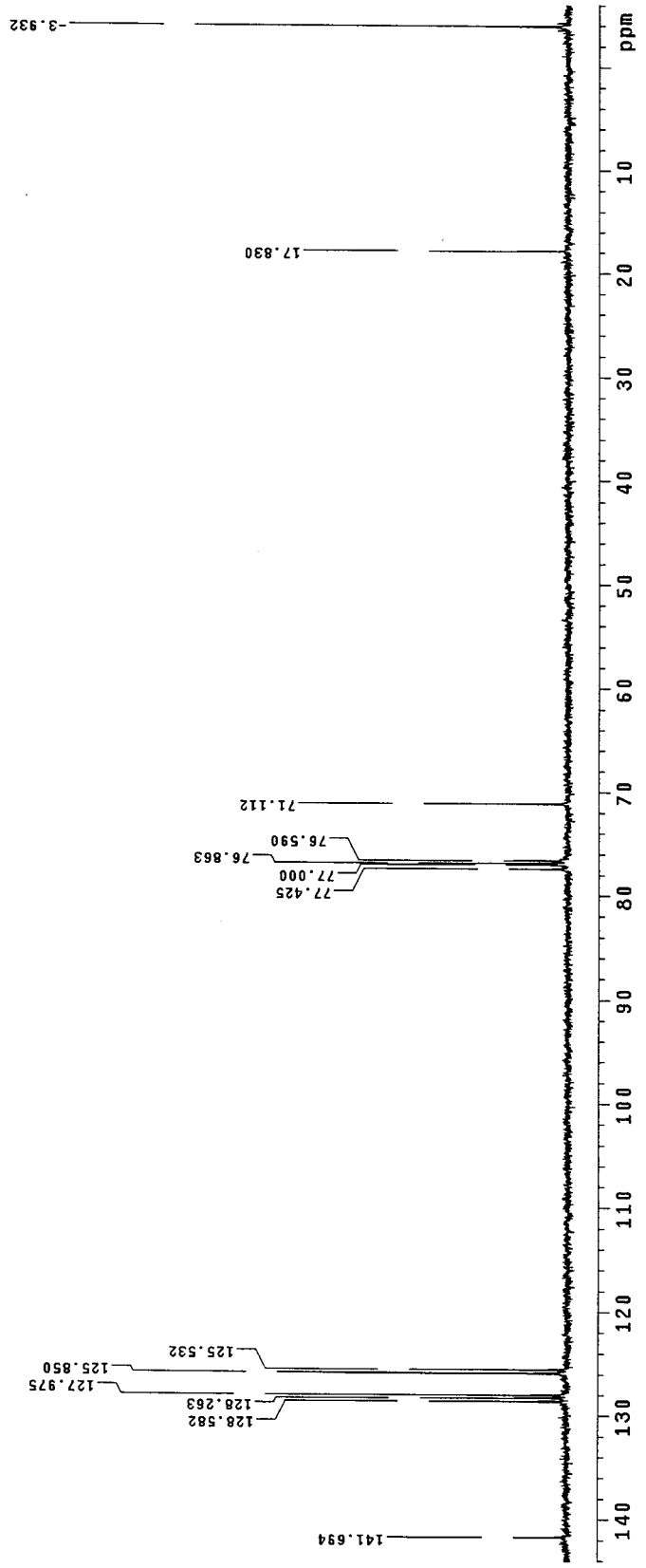
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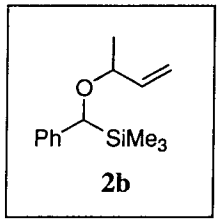
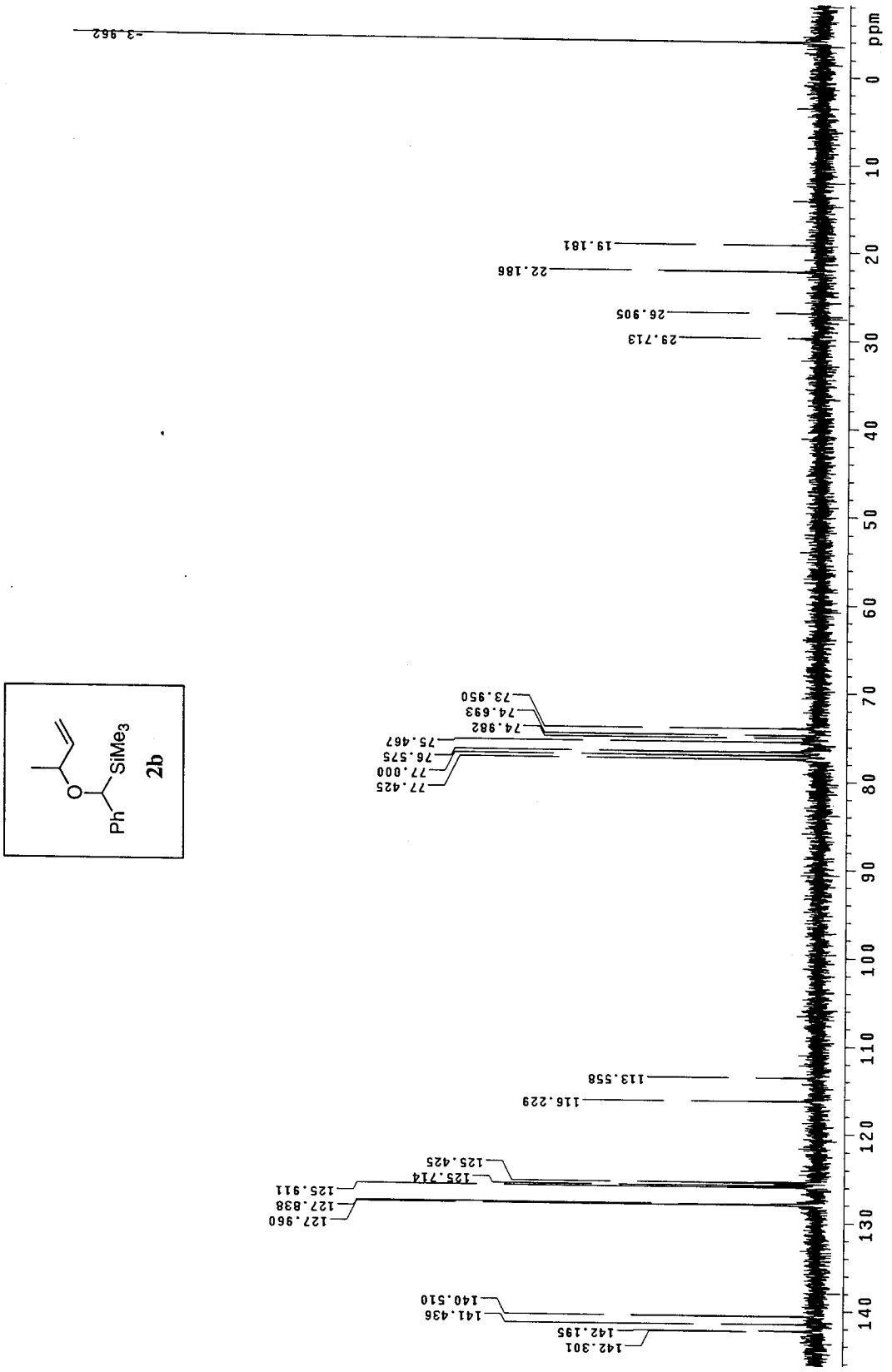


2b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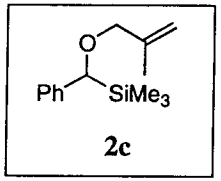

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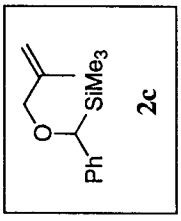
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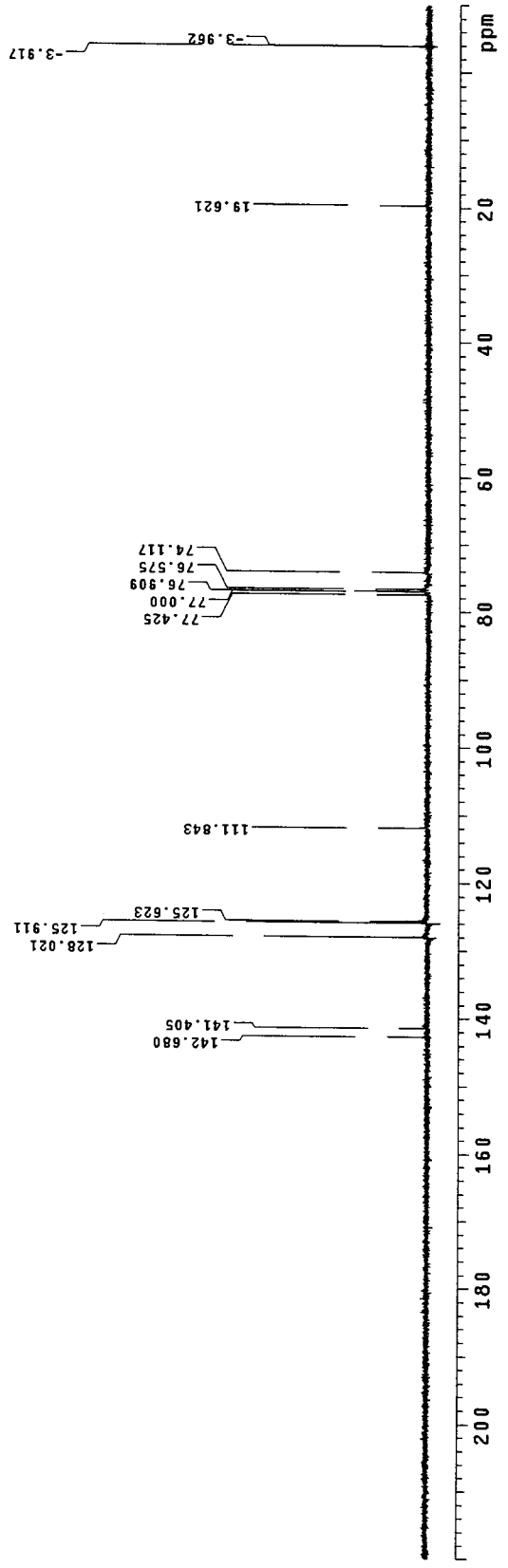
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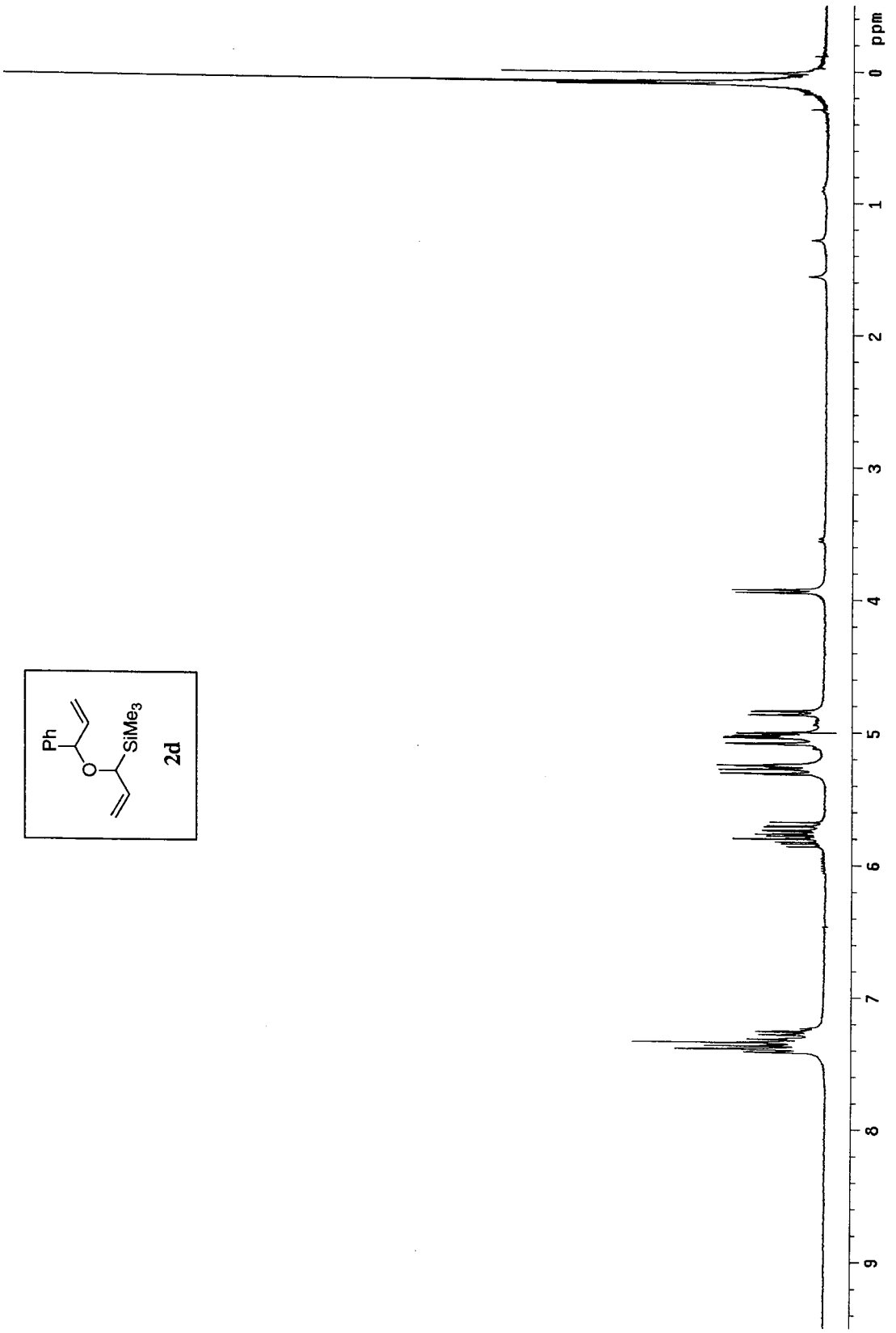
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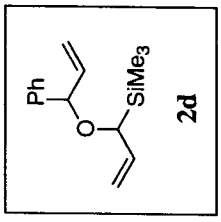
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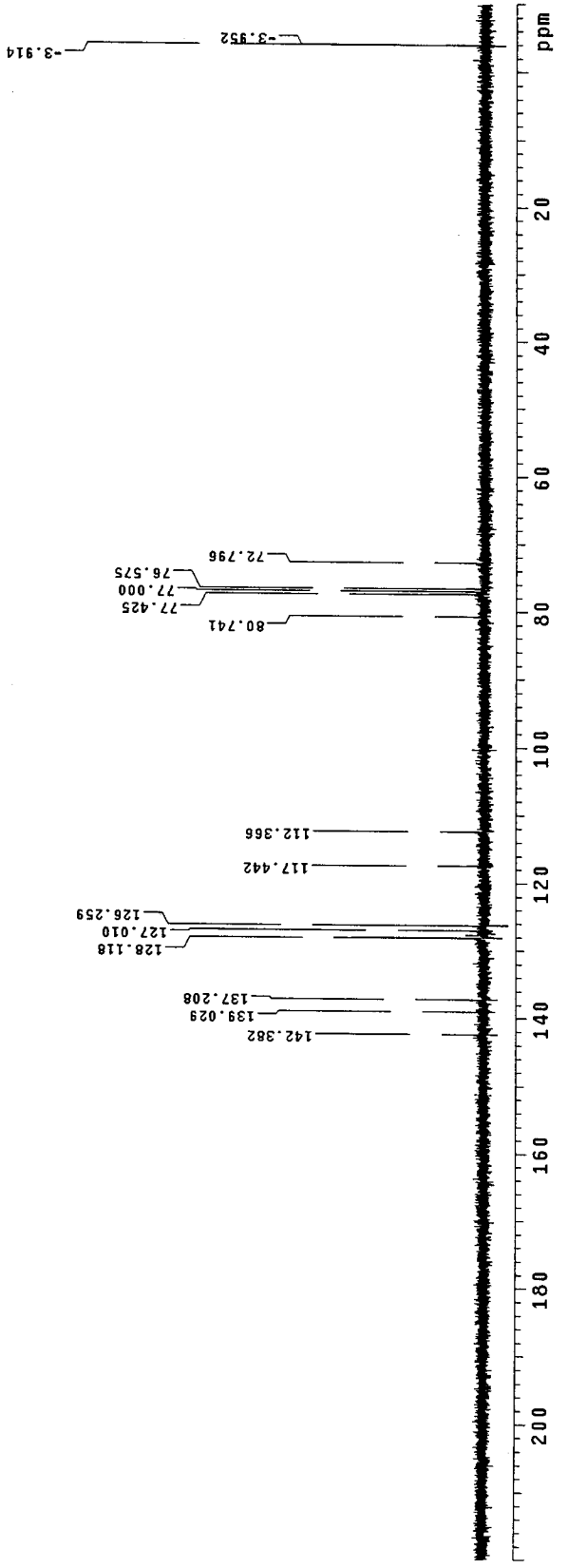
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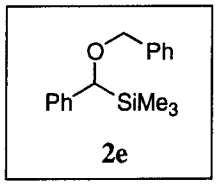

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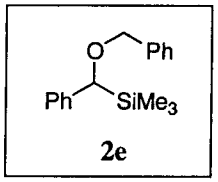

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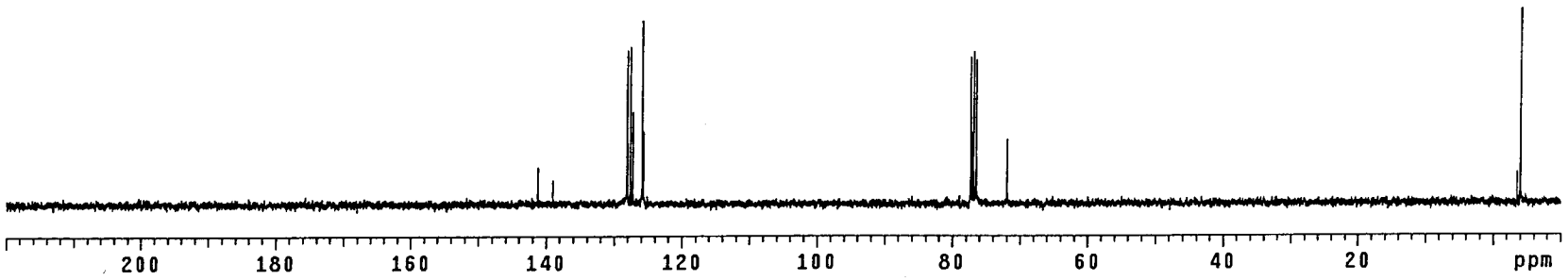

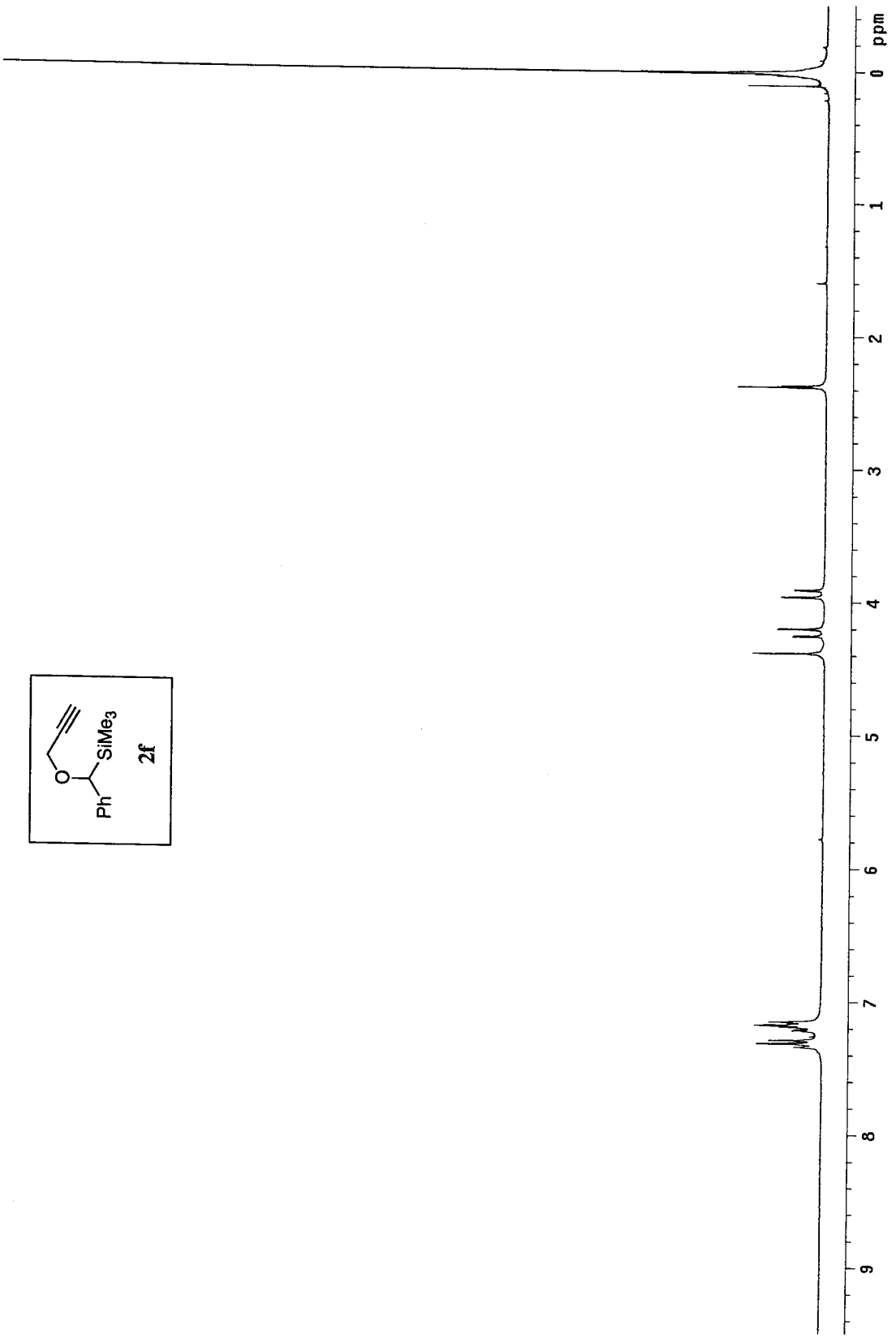
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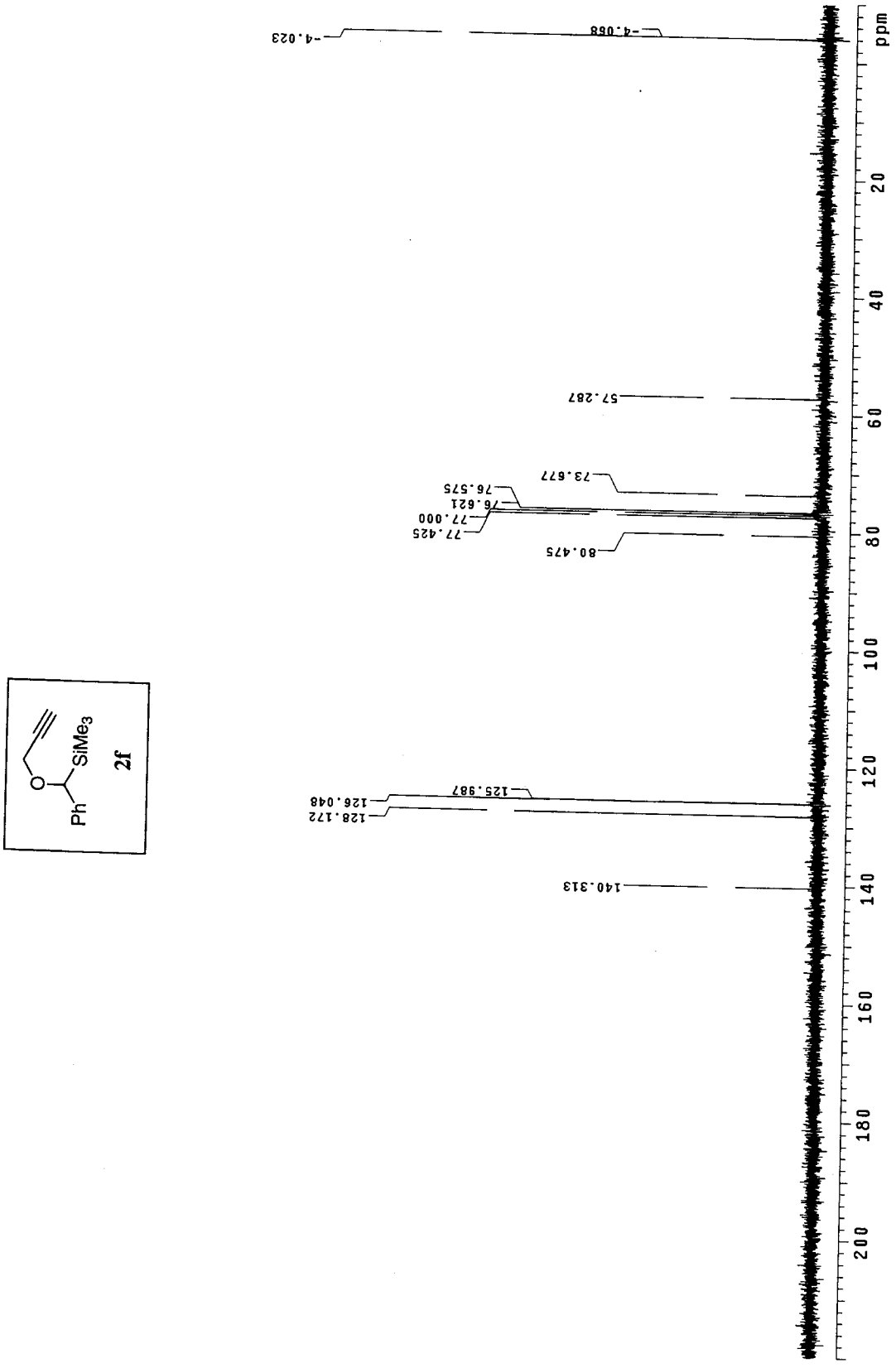
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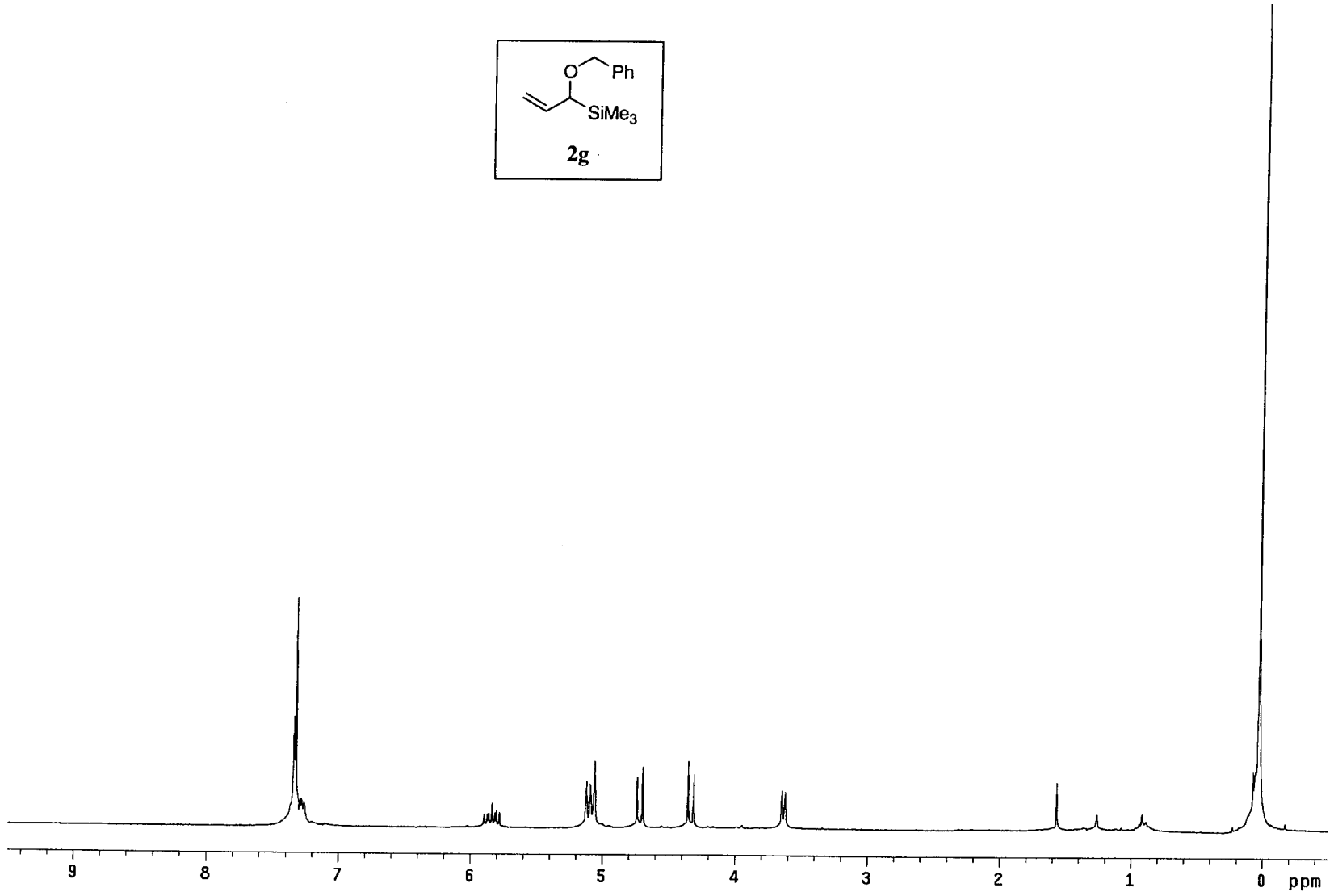
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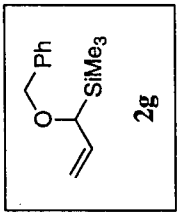
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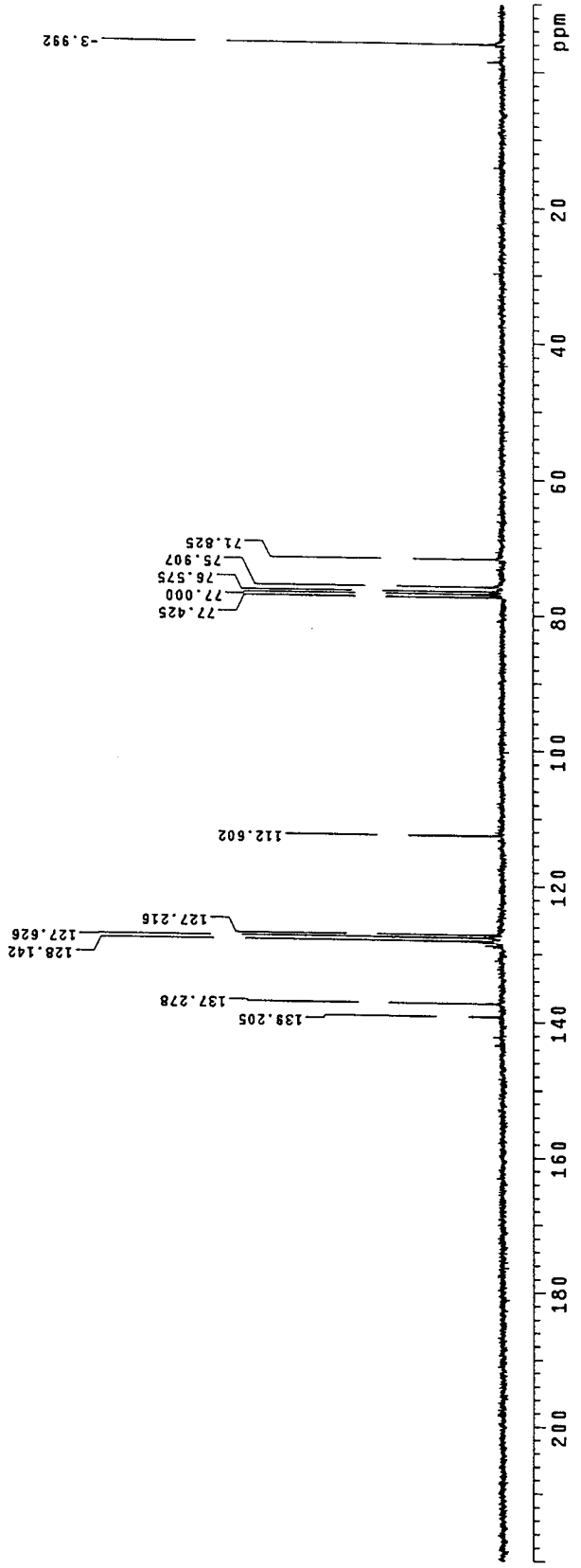
O

2g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77.000
77.425
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ppm
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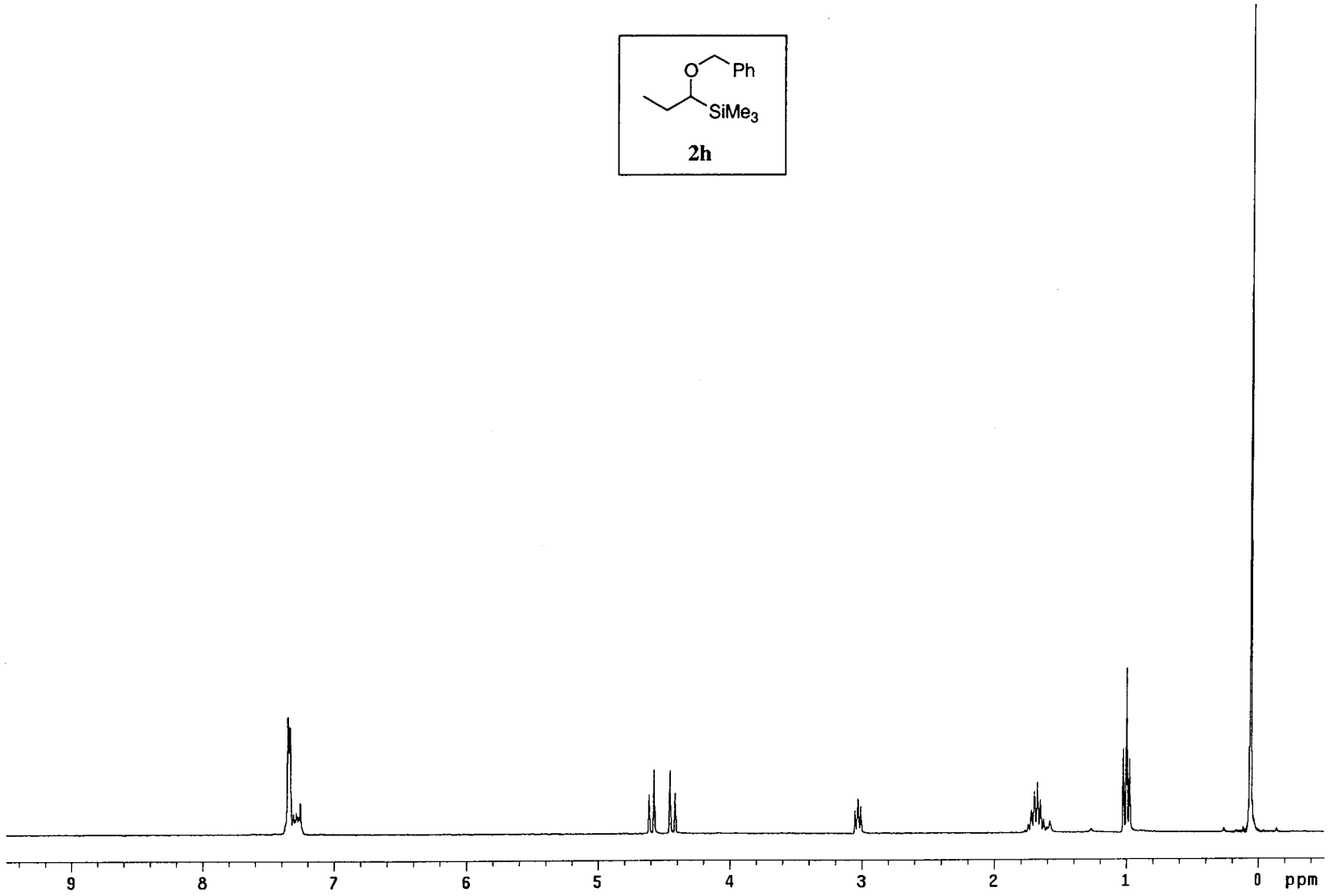
40
60
80
100
120
140
160
180
200


O
Ph
SiMe3
2h
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8
7
6
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4
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2
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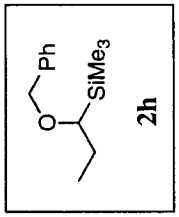
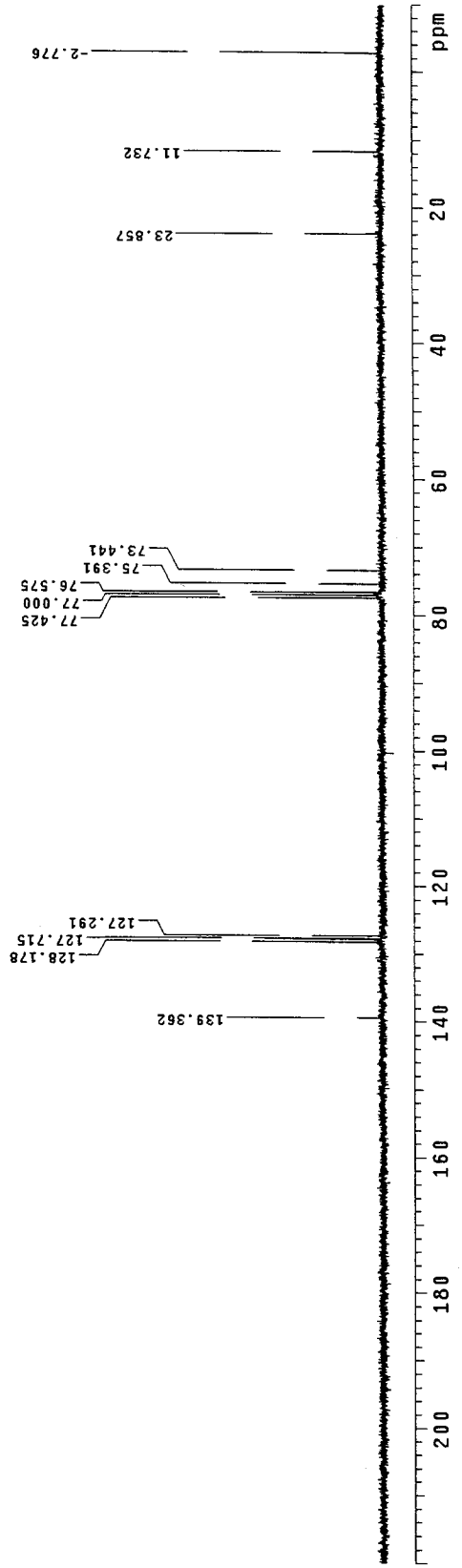

Ph
SiMe3
O
2h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40
60
80
100
120
140
160
180
200