# Hydrogen bonding-promoted efficient Ru-catalyzed ring-closing metathesis of steric demanding homoallyl 2-(hydroxymethyl)acrylates

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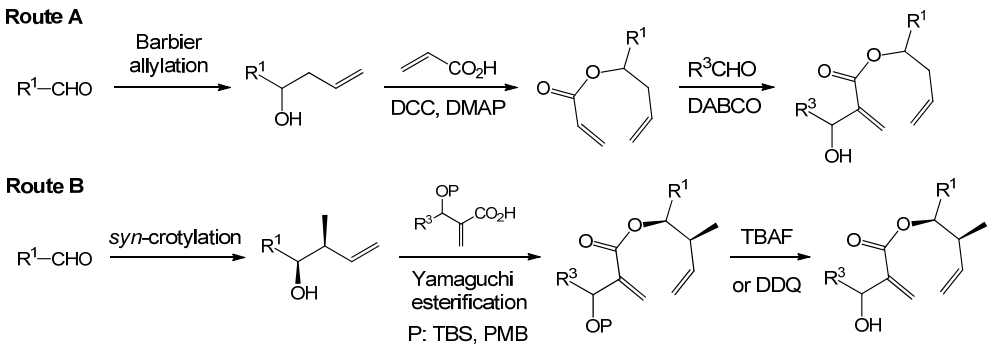
## ■ Synthesis of RCM substrates

### 1. General procedures for substrate synthesis

The substrates for the ring-closing metathesis reactions were prepared by using the following two routes. No attempts were made to optimize yields for substrate synthesis.




### 1.1. General procedures of Route A

1) Barbier reaction step

To a round-bottom flask containing a magnetic stir bar were added THF (50 mL), aldehyde (20 mmol) and zinc dust (10 mmol). The reaction vessel was cooled to 0 $^{o}$C in an ice bath. Allyl bromide (24 mmol) was added into the round-bottom flask, followed by saturated aqueous $NH_4Cl$ solution (1.0 mL). The reaction was allowed to warm to room temperature and stirred for 6 h. The reaction was quenched with $NH_4Cl$ solution (30 mL), filtered, and extracted with EtOAc. The organic phases were combined, washed with water and brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product obtained was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to give the homoallyllic alcohol in 75-90% yield.

2) Esterification step

To a round-bottom flask containing a magnetic stir bar were added anhydrous DCM (100 mL), acrylic acid (20 mmol), DCC (30 mmol) and DMAP (4 mmol). The reaction was allowed to stir at 0 $^{o}$C for 30 min. The homoallylic alcohol obtained above (10 mmol) was dissolved in DCM (3 mL) and added into the round-bottom flask. The reaction was allowed to stir at room temperature for 24 h, then the second portion of DCC (20 mmol) was added and the mixture stirred for another 24 h. The mixture was filtered through a pad of celite. The filtrate was washed with water and brine, dried over $Na_2SO_4$,

filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to give the homoallyl acrylate in 22-46% yield.

3) Baylis-Hillman reaction step

To a round-bottom flask containing a magnetic stir bar were added 1,4-dioxane (20 mL), homoallyl acrylate obtained above (2 mmol), aldehyde (5 mmol) and DABCO (2 mmol). The reaction was allowed to stir at room temperature for 2 days. The mixture was partitioned between EtOAc and water. The organic phases were separated, washed with water and brine, dried over $Na_2SO_4$, filtered, and concentrated under vacuum. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to give the homoallyl 2-(hydroxymethyl)acrylate in 68-86% yield.

**1.2. General procedures of Route B**

1) *syn*-Crotylation step

Roush's protocol for *syn*-crotylation was used. [1-3] To a suspension of powdered 4 Å molecular sieves (5.8 g) in anhydrous toluene (40 mL) under nitrogen was added the matched Roush's (*Z*)-crotylboronate (1.0 M in toluene, 16.5 ml, 16.5 mmol) freshly prepared from (S,S)- or (R,R)-diispropyl tartrate. The mixture was stirred at r.t. for 30 min, and then cooled to -80 $^{o}$C. A solution of aldehyde (9.7 mmol) in toluene (20 mL) was added dropwise over 20 min, and then the reaction was stirred at -80 $^{o}$C for 18 h. An aqueous solution of NaOH (1 N, 100 mL) was added. The resulted mixture was stirred at r.t. for 1 h, filtered through celite, and separated. The aqueous phase was extracted with $Et_2O$ (20 mL x 3). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the corresponding homoallylic alcohol. The yield and stereoselectivity for each substrate are: benzaldehyde, 86% yield, d.r. > 20:1, e.r. 1.7:1; (S)-glyceraldehyde acetonide, 74% yield, d.r. > 20:1; (2S)-5-(TBSO)-2-methoxypentanal, 93% yield, d.r. 5.5:1. [3]

2) Yamaguchi esterification step

The TBS-protected carboxylic acid (1.5 equiv. to the homoallylic alcohol) was dissolved in anhydrous DCM (0.1 M) under nitrogen. Triethylamine (6 equiv.) and 2,4,6-trichlorobenzoyl chloride (2.25 equiv.) were added at r.t. with stirring. After 1.5 hours, solutions of the homoallylic alcohol in

DCM and DMAP (0.5 equiv.) in DCM were added. The reaction was stirred at r.t. for 5 hours, and then was quenched by adding saturated aqueous solution of $Na_2CO_3$. The organic layer was separated, and the aqueous layer was extracted with DCM. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the ester as a mixture of stereoisomers in 76-85% yield.

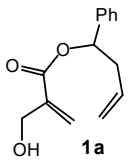
3) Deprotection step

Removal of TBS group: The above-obtained TBS-protected ester was disolved in THF and treated with tetrabutylammonium fluoride (1.00 M in THF, 1.5 equiv.) overnight. The reaction mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the desired alcohol in 81-87% yield.

Removal of PMB group: The above-obtained PMB-protected ester was disolved in a DCM-water mixture (DCM/water 1:0.05) and treated with DDQ (1.2 equiv.) for 2 h. The mixture was washed with saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with DCM. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate) to afford the desired alcohol in 85-90% yield.

## 2. Characterization of substrates

### 2.1. 1-Phenylbut-3-en-1-yl 2-(hydroxymethyl)acrylate (1a)

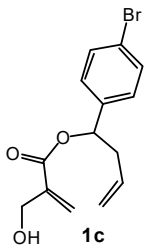


**1a**

Colorless oil. Yield: 18% (3 steps from benzaldehyde, Route A).

$^1$H-NMR (400 MHz, $CDCl_3$) δ 7.30-7.20 (m, 5H), 6.25 (bs, 1H), 5.82 (dd, *J* = 8.0, 5.5 Hz, 1H), 5.77 (dd, *J* = 2.5, 1.5 Hz, 1H), 5.71-5.60 (m, 1H), 5.06-4.98 (m, 2H), 4.25 (bs, 2H), 2.68-2.50 (m, 2H), 2.16 (bs, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 165.9, 141.3, 139.6, 133.3, 128.5, 128.3, 126.0, 125.7, 118.2, 73.5, 62.7, 38.6. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{14}H_{16}NaO_3$ 255.0992, found 255.0993. IR (KBr) ($cm^{-1}$) 3440, 2958, 2927, 1709, 1635, 1450, 1385, 1266, 1169, 1047, 814.

### 2.2. 1-(4-Bromophenyl)but-3-en-1-yl 2-(hydroxymethyl)acrylate (1c)

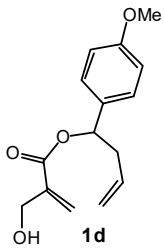


**1c**

Colorless oil. Yield: 30% (3 steps from *p*-bromobenzaldehyde, Route A).

$^{1}$H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.5 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 6.31 (s, 1H), 5.87 (bs, 1H), 5.85-5.80 (m, 1H), 5.75-5.63 (m, 1H), 5.13-5.06 (m, 2H), 4.32 (s, 2H), 2.73-2.54 (m, 2H), 2.23 (bs, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 164.3, 138.3, 137.8, 131.6, 130.7, 127.1, 125.2, 121.0, 117.7, 74.1, 61.4, 39.6. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{14}H_{15}BrNaO_3$ 333.0102, found 333.0095. IR (KBr) ($cm^{-1}$) 3432, 2928, 1714, 1642, 1490, 1265, 1160, 1053, 820.

### 2.3. 1-(4-Methoxyphenyl)but-3-en-1-yl 2-(hydroxymethyl)acrylate (1d)

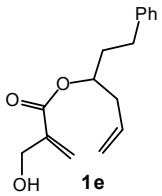


**1d**

Colorless oil. Yield: 29% (3 steps from *p*-methoxybenzldehyde, Route A).

$^{1}$H-NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 6.21 (s, 1H), 5.79-5.74 (m, 2H), 5.69-5.57 (m, 1H), 5.05-4.96 (m, 2H), 4.23 (s, 2H), 3.71 (s, 3H), 2.68-2.47 (m, 2H), 2.40 (bs, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 165.5, 159.4, 139.6, 133.3, 131.9, 127.9, 125.8, 118.2, 113.9, 75.5, 62.4, 55.3, 40.7. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{15}H_{18}NaO_4$ 285.1097, found 285.1089. IR (KBr) ($cm^{-1}$) 3466, 2937, 1715, 1614, 1515, 1252, 1170, 1051, 830.

### 2.4. 1-Phenylhex-5-en-3-yl 2-(hydroxymethyl)acrylate (1e)

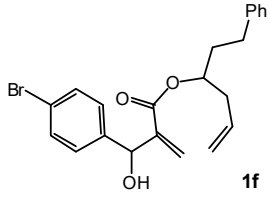


**1e**

Colorless oil. Yield: 25% (3 steps from hydrocinnamic aldehyde, Route A).

$^{1}$H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 2H), 7.11-7.14 (m, 3H), 6.25 (bs, 1H), 5.83-5.81 (m, 1H), 5.81-5.71 (m, 1H), 5.13-5.04 (m, 3H), 4.32 (bs, 2H), 2.73-2.58 (m, 2H), 2.47-2.35 (m, 2H), 2.32 (bs, 1H), 2.02-1.89 (m, 2H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 165.9, 141.3, 139.6, 133.3, 128.5, 128.3, 126.0, 125.7, 118.2, 73.6, 62.7, 38.6, 35.2, 31.7. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{16}H_{20}NaO_3$ 283.1305, found 283.1306. IR (KBr) ($cm^{-1}$) 3427, 2961, 2926, 1713, 1640, 1384, 1262, 1093, 1026, 805.

### 2.5. 1-Phenylhex-5-en-3-yl 2-((4-bromophenyl)(hydroxyl)methyl)acrylate (1f)

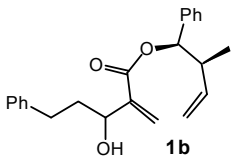


**1f**

Colorless oil. Yield: 20% (3 steps from hydrocinnamic aldehyde, Route A). Mixture of stereoisomers.

$^1$H-NMR (400 MHz, $CDCl_3$) δ 7.42-7.38 (m, 2H), 7.22-7.15 (m, 4H), 7.13-7.07 (m, 1H), 7.02-6.96 (m, 2H), 6.26 (bs, 1H), 5.75 (bd, *J* = 4.0 Hz, 1H), 5.64-5.48 (m, 1H), 5.40 (bd, *J* = 12.0 Hz, 1H), 5.00-4.88 (m, 3H), 3.04 (bs, 1H), 2.49-2.36 (m, 2H), 2.29-2.18 (m, 2H), 1.82-1.73 (m, 2H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ (164.72, 164.64), (140.77, 140.67), (140.11, 140.08), (139.52, 139.41), (132.03, 131.97), (130.53, 130.49), 127.44, (127.37, 127.23), 127.24, (125.24, 125.14), 124.98, (120.80, 120.71), 117.17, (72.76, 72.70), (71.96, 71.84), (37.51, 37.46), (34.11, 34.08), (30.55, 30.50). HRMS (ESI) $[M+Ma]^+$ calcd for $C_{22}H_{23}BrKO_3$ 453.0462, found 453.0456. IR (KBr) ($cm^{-1}$) 3427, 2956, 2925, 1711, 1631, 1486, 1401, 1263, 1155, 1034, 818.

**2.6. *syn*-2-Methyl-1-phenylbut-3-en-1-yl 3-hydroxy-2-methylene-5-phenylpentanoate (1b)**

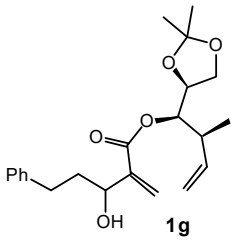


**1b**

Colorless oil. Yield: 61% (3 steps from benzaldehyde, Route B with TBS protection). Mixture of stereoisomers.

$[\alpha]^{25}_D$ = +18.3 (c 0.84, $CHCl_3$). $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.15 (m, 7H), 7.14-7.08 (m, 3H), 6.27 (s, 1H), 5.78-5.75 (m, 1H), 5.65 (t, *J* = 6.5 Hz, 1H), 5.62-5.53 (m, 1H), 4.9-4.88 (m, 2H), 4.35 (bs, 1H), 2.78-2.49 (m, 4H), 1.93-1.82 (m, 2H), 0.99 (d, *J* = 7.0 Hz, 1.5H), 0.98 (d, *J* = 7.0 Hz, 1.5H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ (165.64, 165.62), 142.68, (141.70, 141.68), 138.96, (138.58, 138.54), (128.54, 128.52), (128.44, 128.43), 128.24, 127.94, 126.95, 125.92, (125.28, 125.17), 115.95, (79.56, 79.52), 70.96, 42.97, 37.80, (32.15, 32.11), (15.31, 15.29). HRMS (ESI) $[M+Ma]^+$ calcd for $C_{23}H_{26}NaO_3$ 373.1780, found 373.1784. IR (KBr) ($cm^{-1}$) 3431, 2928, 2857, 1709, 1636, 1449, 1385, 1169, 1053, 812.

**2.7. (1*R*,2*S*)-1-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2-methylbut-3-en-1-yl 3-hydroxy-2-methylene-5-phenylpentanoate (1g)**



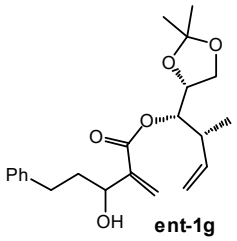
**1g**

Colorless oil. Yield: 60% (3 steps from (S)-glyceraldehyde acetonide, Route B with TBS protection). Mixture of stereoisomers.

$[\alpha]^{25}_D$ = -13.6 (*c* 3.60, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ 7.32-7.26 (m, 2H), 7.23-7.17 (m, 3H), 6.29 (bs, 0.6H), 6.27 (bs, 0.4H), 5.84 (s, 0.6H), 5.82 (s, 0.4H), 5.79-5.71 (m, 1H), 5.21-5.17 (m, 1H), 5.10-5.05 (m, 2H), 4.47-4.40 (m, 1H), 4.29-4.24 (m, 1H), 4.02-3.96 (m, 1H), 3.90-3.84 (m, 1H), 2.87-2.78 (m, 1H), 2.77-2.67 (m, 2H), 2.53-2.43 (m, 1H), 2.04-1.94 (m, 2H), 1.36 (s, 1.2H), 1.35 (s, 1.8H), 1.34 (s, 1.2H), 1.33 (s, 1.8H), 1.08 (d, *J* = 5.8 Hz,

1.8H), 1.07 (d, $J$ = 5.8 Hz, 1.2H). $^{13}$C-NMR (125 MHz, $CDCl_3$) δ (165.76, 165.75), (142.50, 142.33), (141.63, 141.60), (139.12, 139.11), (128.49, 128.46), (128.4, 125.90), (125.45, 125.25), (115.94, 115.93), (109.26, 109.25), 75.70, (75.02, 74.95), 71.19, 70.56, (65.21, 65.09), (39.61, 39.59), (37.74, 37.55), (32.14, 32.09), (26.44, 26.41), (25.12, 25.07), (15.45, 15.34). HR-MS (ESI) $[M+Ma]^+$ calcd for $C_{22}H_{30}NaO_5$ 397.1991, found 397.1997. IR (KBr) ($cm^{-1}$) 3431, 2929, 1718, 1622, 1427, 1266, 1167, 1079, 821.

**2.8. (1*S*,2*R*)-1-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2-methylbut-3-en-1-yl 3-hydroxy-2-methylene-5-phenylpentanoate (ent-1g)**

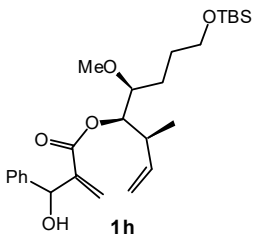


**ent-1g**

Colorless oil. Yield: 58% (3 steps from (R)-glyceraldehyde acetonide, Route B with TBS protection). Mixture of stereoisomers.

$[\alpha]_D^{25}$ = +21.5 (*c* 1.25, $CHCl_3$). $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.27-7.21 (m, 2H), 7.18-7.12 (m, 3H), 6.24-6.20 (m, 1H), 5.80-5.77 (m, 1H), 5.74-5.65 (m, 1H), 5.16-5.12 (m, 1H), 5.05-5.00 (m, 2H), 4.43-4.34 (m, 1H), 4.24-4.18 (m, 1H), 3.97-3.90 (m, 1H), 3.85-3.78 (m, 1H), 2.82-2.61 (m, 3H), 2.48-2.37 (m, 1H), 1.98-1.89 (m, 2H), 1.31 (s, 1.5H), 1.30 (s, 1.5H), 1.29 (s, 1.5H), 1.28 (s, 1.5H), 1.02 (d, $J$ = 7.0 Hz, 1.5H), 1.20 (d, $J$ = 7.0 Hz, 1.5H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ (164.75, 164.73), (141.55, 141.38), (140.63, 140.60), 138.12, (127.48, 127.45), 127.39, 124.88, (124.39, 124.20), 114.91, 108.24, 74.69, (74.01, 73.93), (70.12, 69.51), (64.22, 64.10), (38.58, 38.57), (36.75, 36.56), (31.11, 31.06), (25.43, 25.39). (24.12, 24.06), (14.41, 14.29). HRMS (ESI) $[M+H]^+$ calcd for $C_{22}H_{31}O_5$ 375.2166, found 375.2161. IR (KBr) ($cm^{-1}$) 3443, 2933, 2872, 1714, 1619, 1513, 1256, 1171, 1037, 828.

**2.9. (3*S*,4*R*,5*S*)-8-((*tert*-Butyldimethylsilyl)oxy)-5-methoxy-3-methyloct-1-en-4-yl 2-(hydroxyl(phenyl)methyl)acrylate (1h)**



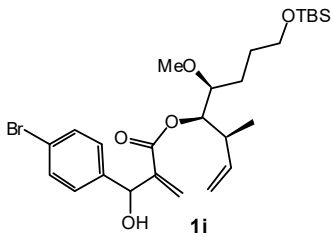
**1h**

Colorless oil. Yield: 68% (3 steps from (2S)-5-(TBSO)-2-methoxypentanal, Route B with PMB protection). Mixture of stereoisomers.

$[\alpha]_D^{25}$ = +25.1 (*c* 2.87, $CHCl_3$). $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.39-7.31 (m, 4H), 7.30-7.7.25 (m, 1H), 6.37-6.30 (m, 1H), 5.82-5.70 (m, 1H), 5.55 (bs, 1H), 5.52-5.36 (m, 1H), 5.28-5.15 (m, 1H), 5.10-4.94 (m, 1H), 3.64-3.50 (m, 2H), 3.36-3.29 (m, 3H), 3.26-3.16 (m, 1.7H), 3.10-3.05 (m, 0.3H), 2.45-2.14 (m, 2H), 1.69-1.60 (m, 1H), 1.60-1.55 (m, 3H),

1.55-1.43 (m, 2H), 1.42-1.32 (m, 1H), 8.88 (bs, 9H), 0.04 (bs, 6H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ (166.32, 166.23), 142.65, 141.67, 128.78, 128.16, 127.30, 126.99, 126.49, 125.42, 125.27, (82.03, 81.96), 81.17, (75.35, 75.20), 74.95, 73.82, 63.35, (58.55, 58.44), (33.60, 33.20), (29.22, 29.04), 27.78, (27.55, 27.47), (26.95, 26.87), 26.48, 26.35, (18.72, 18.29), 13.25, -4.90. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{26}H_{42}NaO_5Si$ 485.2699, found 485.2708. IR (KBr) ($cm^{-1}$) 3425, 2960, 1712, 1621, 1510, 1385, 1250, 1163, 1036, 817.

**2.10. (3*S*,4*R*,5*S*)-8-((*tert*-Butyldimethylsilyl)oxy)-5-methoxy-3-methyloct-1-en-4-yl 2-((4-bromo-phenyl)(hydroxy)methyl)acrylate (1i)**

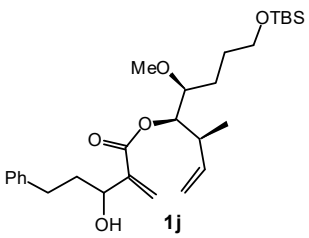


**1i**

Colorless oil. Yield: 62% (3 steps from (2S)-5-(TBSO)-2-methoxypentanal, Route B with PMB protection). Mixture of stereoisomers.

$[\alpha]_D^{25}$ = -32.7 (*c* 1.95, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.31 (bs, 1H), 5.68-5.59 (m, 1H), 5.65 (bs, 1H), 5.52 (d, *J* = 4.0 Hz, 1H), 5.11 (dd, *J* = 8.5, 3.5 Hz, 1H), 5.08-5.00 (m, 2H), 3.65-3.59 (m, 1H), 3.58-3.52 (m, 1H), 3.39 (d, *J* = 4.5 Hz, 1H), 3.30 (s, 3H), 3.30-3.24 (m, 1H), 2.48-2.39 (m, 1H), 1.71-1.62 (m, 2H), 1.52-1.36 (m, 2H), 0.89 (bs, 9H), 0.89-0.87 (m, 3H), 0.05 (bs, 6H). $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 166.4, 142.7, 140.6, 139.6, 131.9, 128.9, 126.6, 122.1, 116.2, 81.0, 76.2, 73.1, 63.3, 57.6, 39.6, 29.2, 26.4, 26.7, 18.7, 16.8, -4.9. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{26}H_{41}BrNaO_5Si$ 563.1804, found 563.1784. IR (KBr) ($cm^{-1}$) 3428, 2926, 1716, 1640, 1455, 1384, 1257, 1092, 807.

**2.11. (3*S*,4*R*,5*S*)-8-((*tert*-Butyldimethylsilyl)oxy)-5-methoxy-3-methyloct-1-en-4-yl 3-hydroxy-2-methylene-5-phenylpentanoate (1j)**



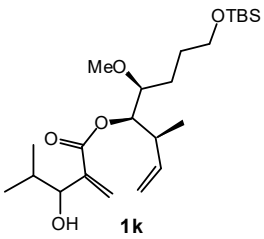
**1j**

Colorless oil. Yield: 62% (3 steps from (2S)-5-(TBSO)-2-methoxypentanal, Route B with PMB protection). Mixture of stereoisomers.

$[\alpha]_D^{25}$ = -6.0 (*c* 2.34, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ 7.31-7.26 (m, 2H), 7.23-7.16 (m, 3 H), 6.24 (bs, 1H), 5.82 (bs, 0.5 H), 5.80 (bs, 0.5 H), 5.76-5.65 (m, 1H), 5.20-5.15 (m, 1H), 5.13-5.03 (m, 2H), 4.45 (bs, 1 H), 3.68-3.54 (m, 2H), 3.38-3.28 (m, 1H), 3.34 (s, 1.5H), 3.33 (s, 1.5H), 2.88-2.77 (m, 1H), 2.75-2.65 (m, 1H), 2.57-2.47 (m, 1H), 2.05-1.90 (m, 2H),

1.75-1.66 (m, 2H), 1.55-1.40 (m, 2H), 1.04 (d, *J* = 6.5 Hz, 1.5H), 1.02 (d, *J* = 6.5 Hz, 1.5H), 0.90 (bs, 9 H), 0.05 (bs, 6 H). $^{13}$C-NMR (125 MHz, $CDCl_3$) δ (166.31, 166.13), (142.84, 142.73), 141.83, (139.50, 139.39), (128.55, 128.52), 128.41, (125.88, 125.86), (124.79, 124.72), (115.86, 115.81), 80.61, (75.33, 75.28), (71.07, 70.34), 63.03, (57.27, 57.25), 39.23, (37.97, 37.40), (32.16, 32.11), (28.91, 28.89), 25.99, (25.34, 25.23), 18.36, (16.60, 16.48), -5.24. HRMS (ESI) $[M+Na]^+$ calcd for $C_{26}H_{42}NaO_5Si$ 513.3012, found 513.3003. IR (KBr) ($cm^{-1}$) 3480, 2963, 2928, 1714, 1590, 1459, 1382, 1260, 1049, 804.

### 2.12. (3*S*,4*R*,5*S*)-8-((*tert*-Butyldimethylsilyl)oxy)-5-methoxy-3-methyloct-1-en-4-yl 3-hydroxy-4-methyl-2-methylenepentanoate (1k)



**1k**

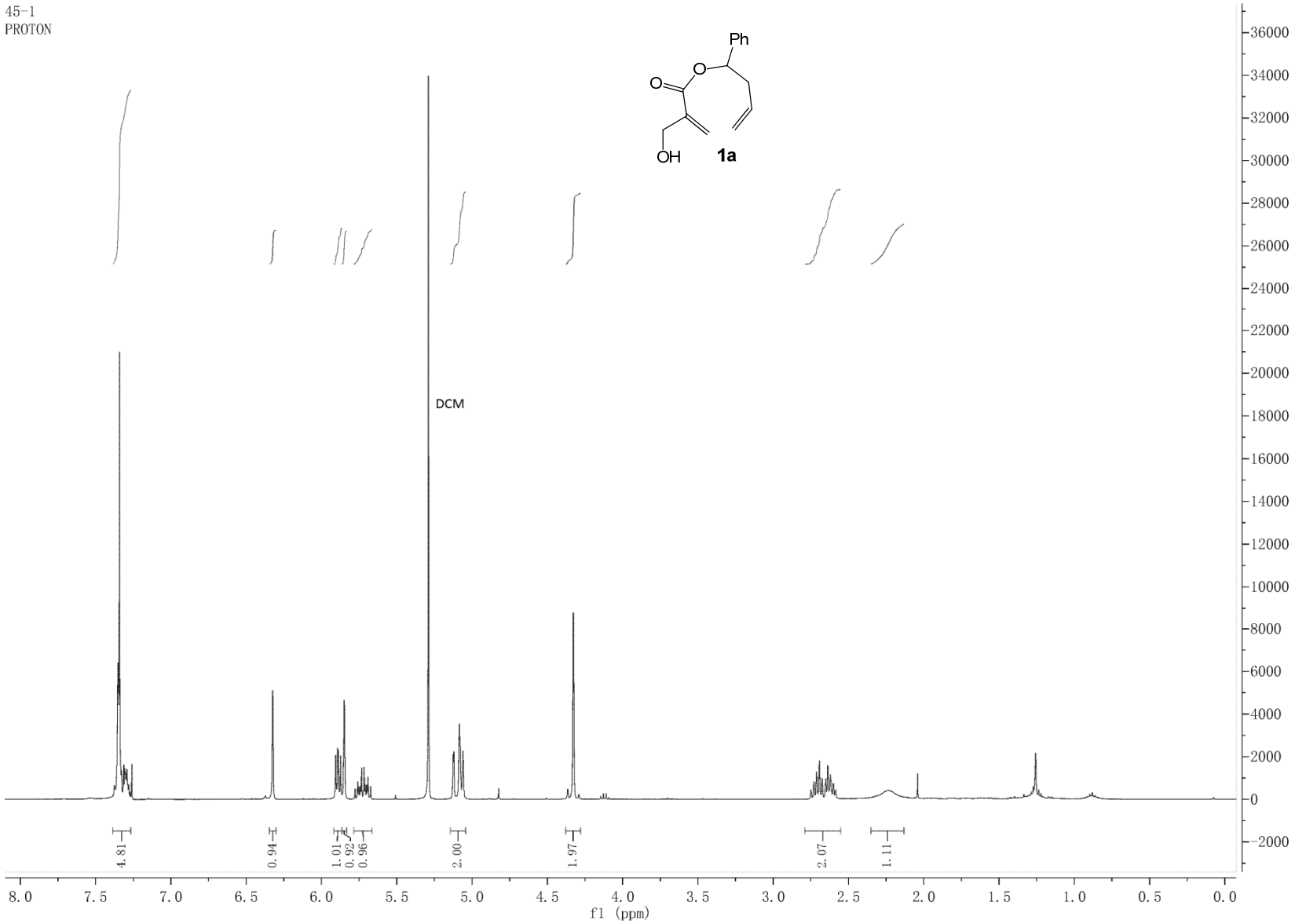
Colorless oil. Yield: 61% (3 steps from (2S)-5-(TBSO)-2-methoxypentanal, Route B with PMB protection). Mixture of stereoisomers.

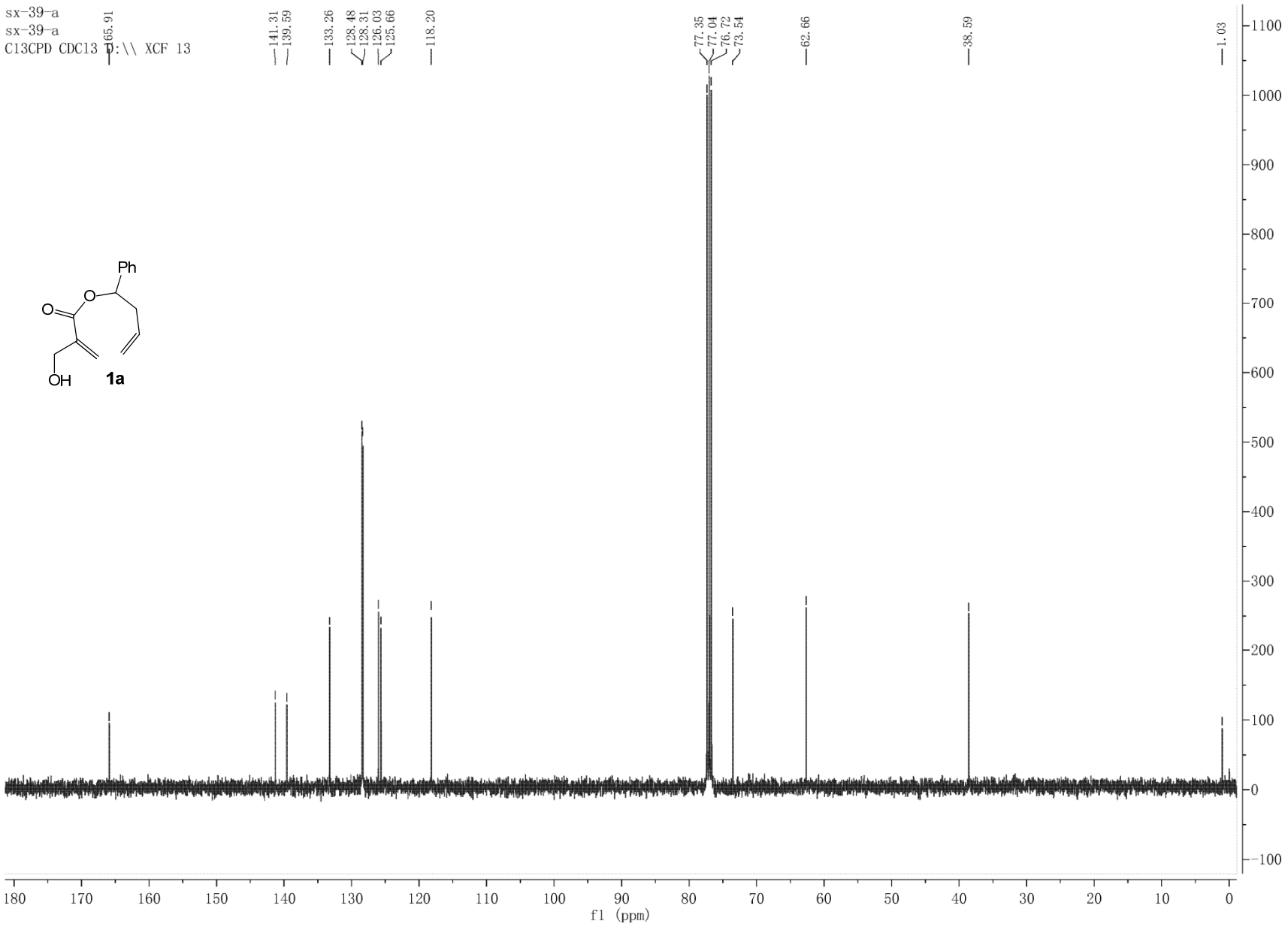
$^1$H-NMR (500 MHz, $CDCl_3$) δ 6.28 (s, 0.3H), 6.2 (s, 0.7H), 5.76-5.66 (m, 2H), 5.13 (dd, *J* = 7.5, 4.0 Hz, 0.7H), 5.11-5.01 (m, 2H), 4.99-4.92 (m, 0.3H), 4.05 (bs, 0.7H), 3.98 (bs, 0.3H), 3.67-3.53 (m, 2H), 3.39-3.27 (m, 1H), 3.36 (s, 0.9H), 3.32 (s, 2.1H), 2.80 (bs, 0.3H), 2.75-2.68 (m, 0.3H), 2.65 (bs, 0.7H), 2.58-2.50 (m, 0.7H), 1.97-1.87 (m, 1H), 1.72-1.38 (m, 4H), 1.03 (d, *J* = 6.5 Hz, 2.1H), 1.01-0.92 (m, 3.9H), 0.90-0.83 (m, 12H), 0.04 (s, 4.2H), 0.03 (s, 1.8H). $^{13}$C-NMR (125 MHz, $CDCl_3$) δ 166.74, 142.09, (140.43, 140.11), (126.68, 125.94), (116.14, 115.93), (80.97, 80.37), (79.11, 78.22), 75.85, (63.45, 63.29), (58.31, 57.59), (39.45, 39.38), (33.29, 33.07), (29.22, 28.83), 26.76, 26.34, 25.95, 20.04, (18.71, 18.48), (17.99, 17.84), 16.44, -4.90. HRMS (ESI) $[M+Ma]^+$ calcd for $C_{23}H_{44}NaO_5Si$ 451.2856, found 451.2859. IR (KBr) ($cm^{-1}$) 3447, 2926, 1712, 1623, 1485, 1402, 1257, 1161, 1012, 814.

## ■ References


1. W. R. Roush, K. Ando, D. B. Powers, A. D. Palkowitz, R. L. Halterman, *J. Am. Chem. Soc.*, 1990, **112**, 6339.
2. W. R. Roush, L. K. Hoong, M. A. J. Palmer, J. A. Straub, A. D. Palkowitz, *J. Org. Chem.*, 1990, **55**, 4117.
3. X. G. Liu, Z. L. Yang, Y. M. Li, F. Yang, L. Feng, N. Z. Wang, D. B. Ma, K. J. Chang, Y. H. Shen, *Tetrahedron*, 2014, **70**, 9522.

■ **NMR spectra of RCM substrates and products**

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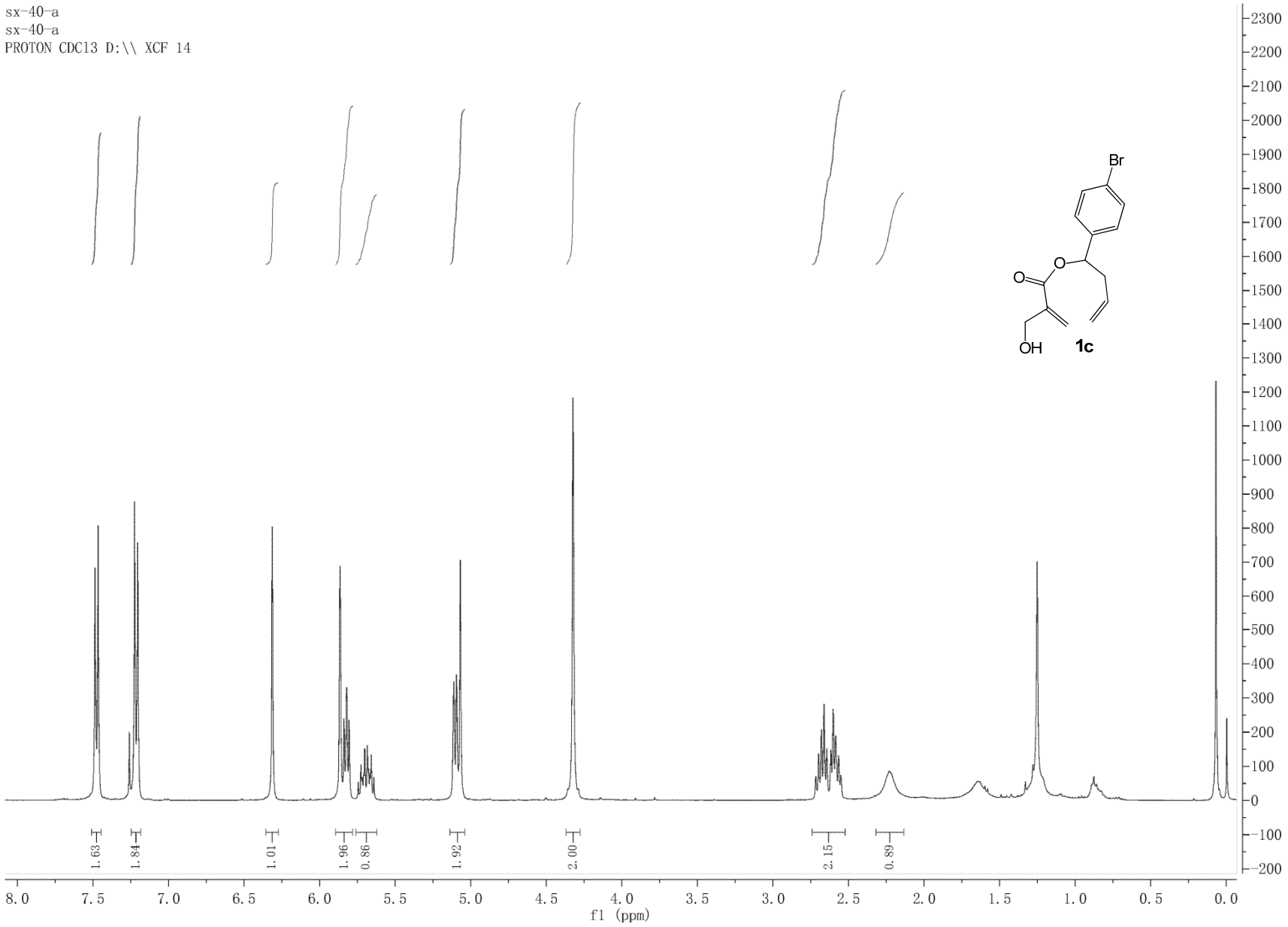
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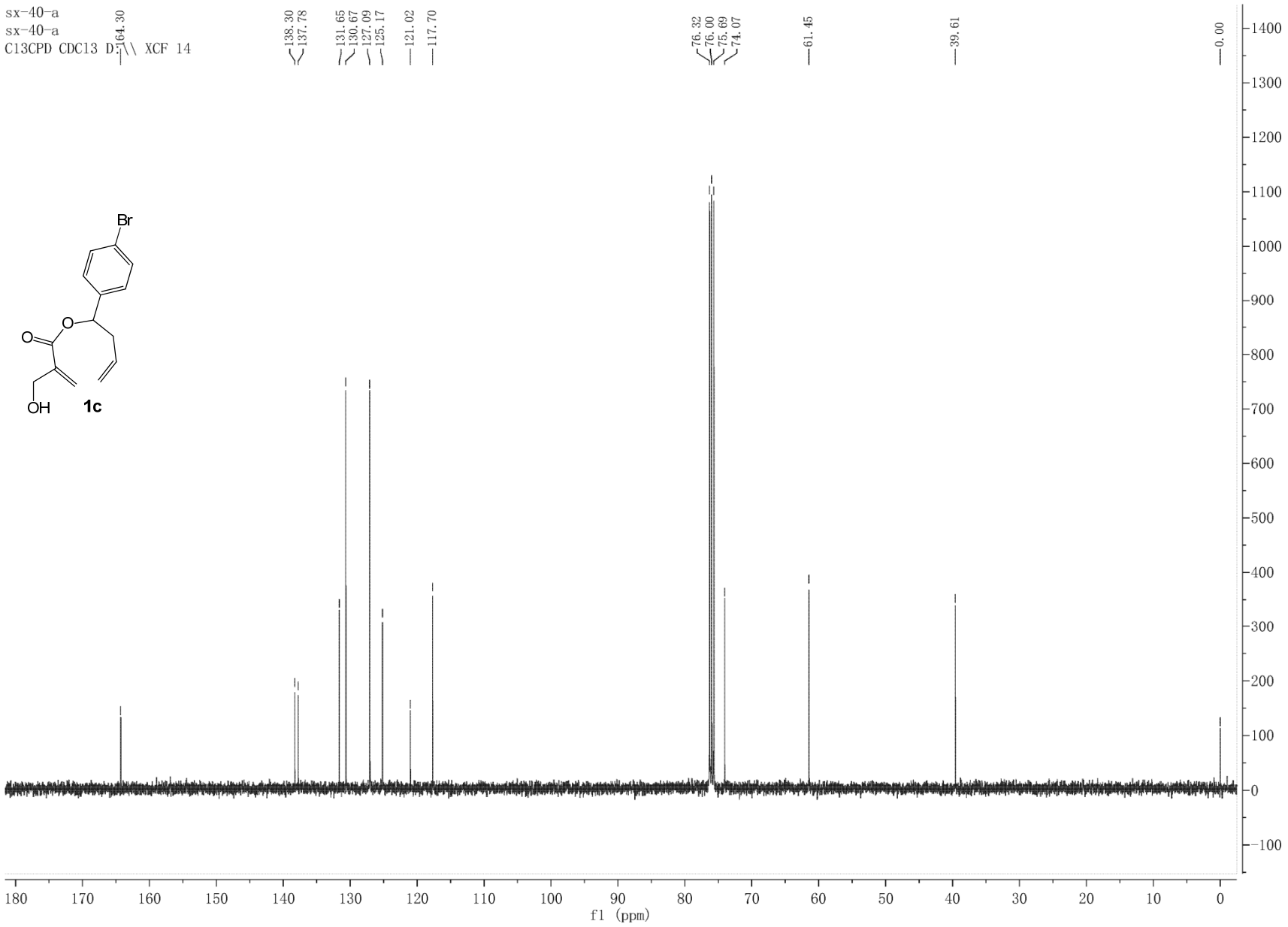
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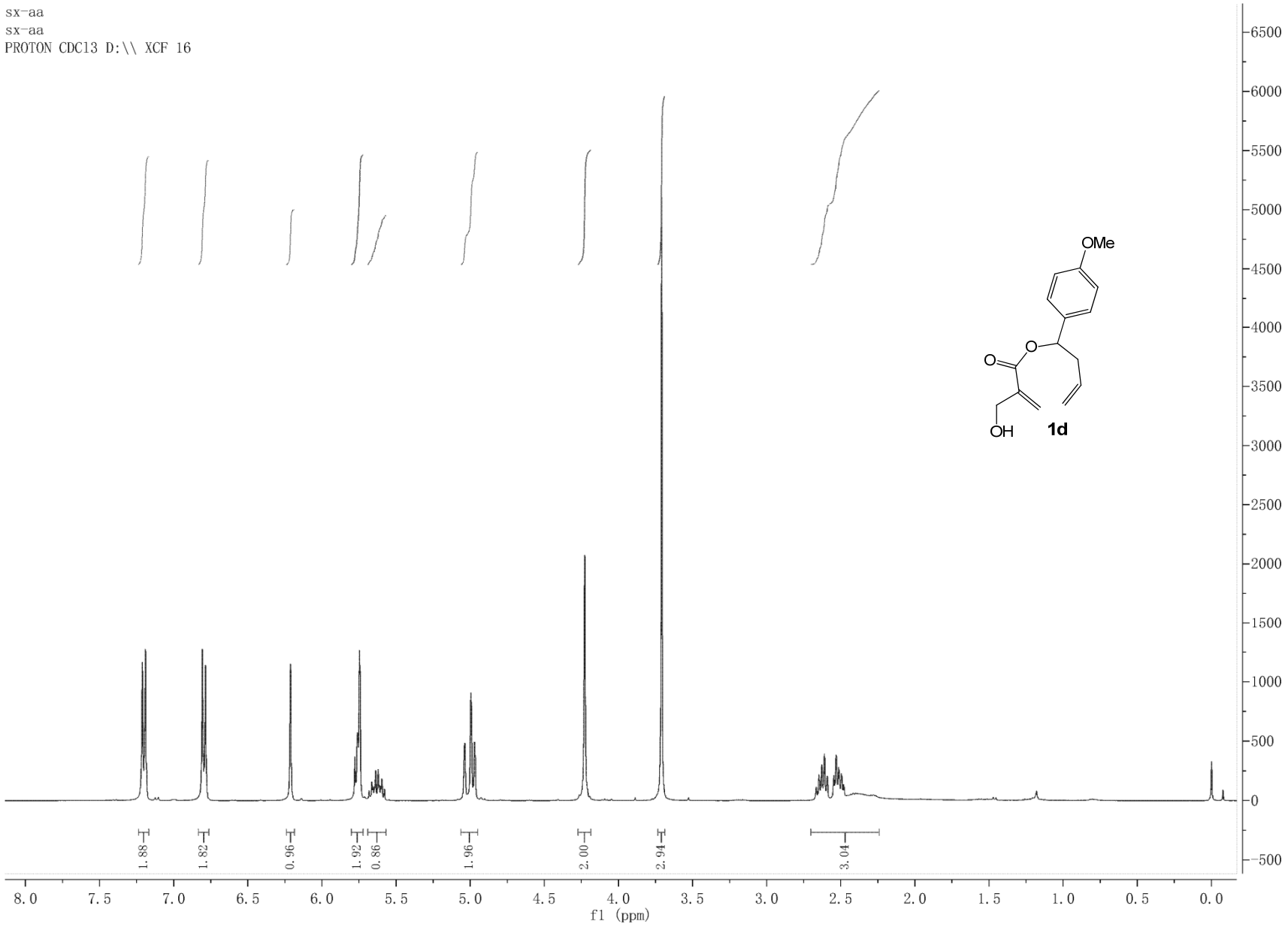
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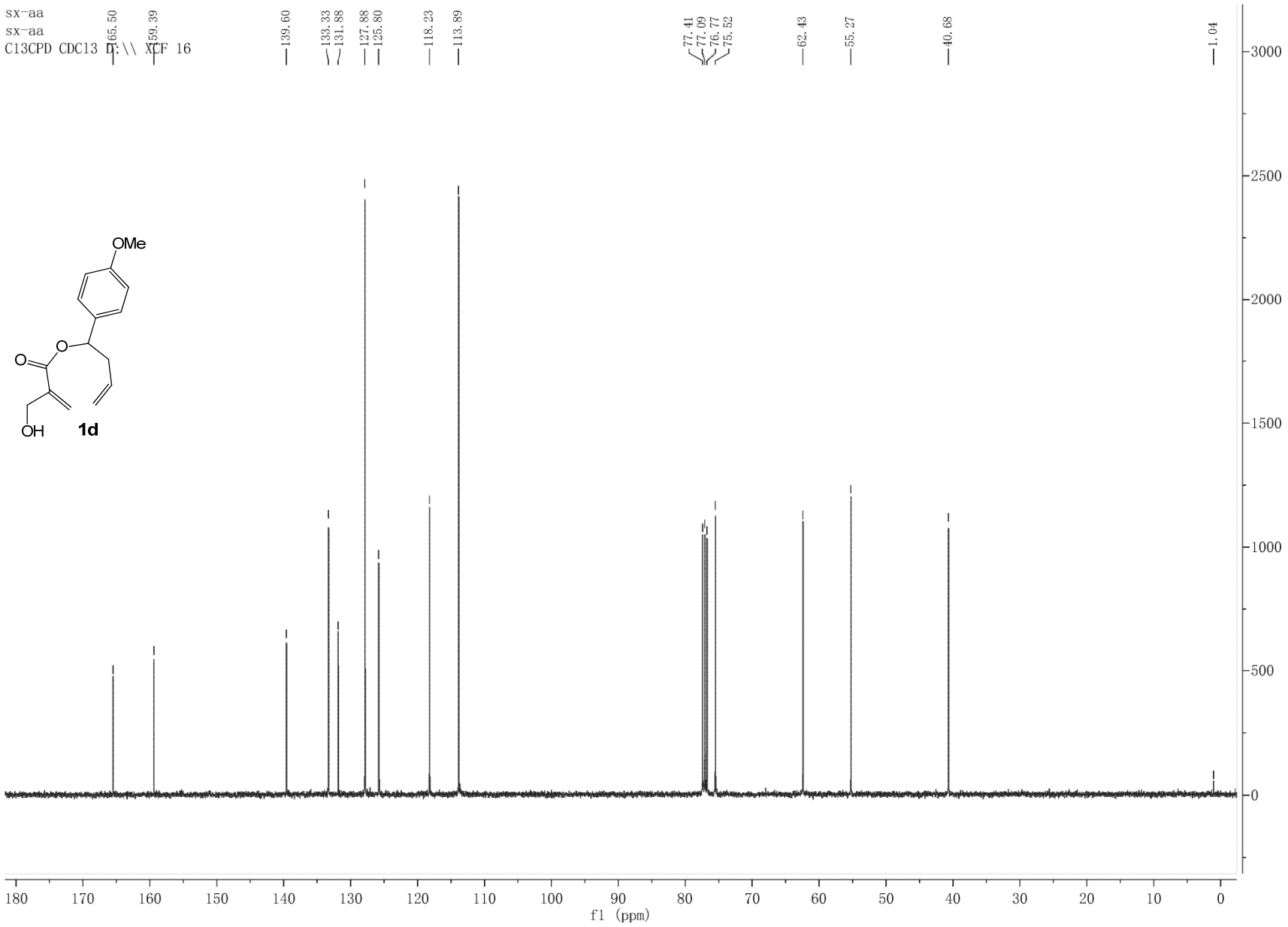
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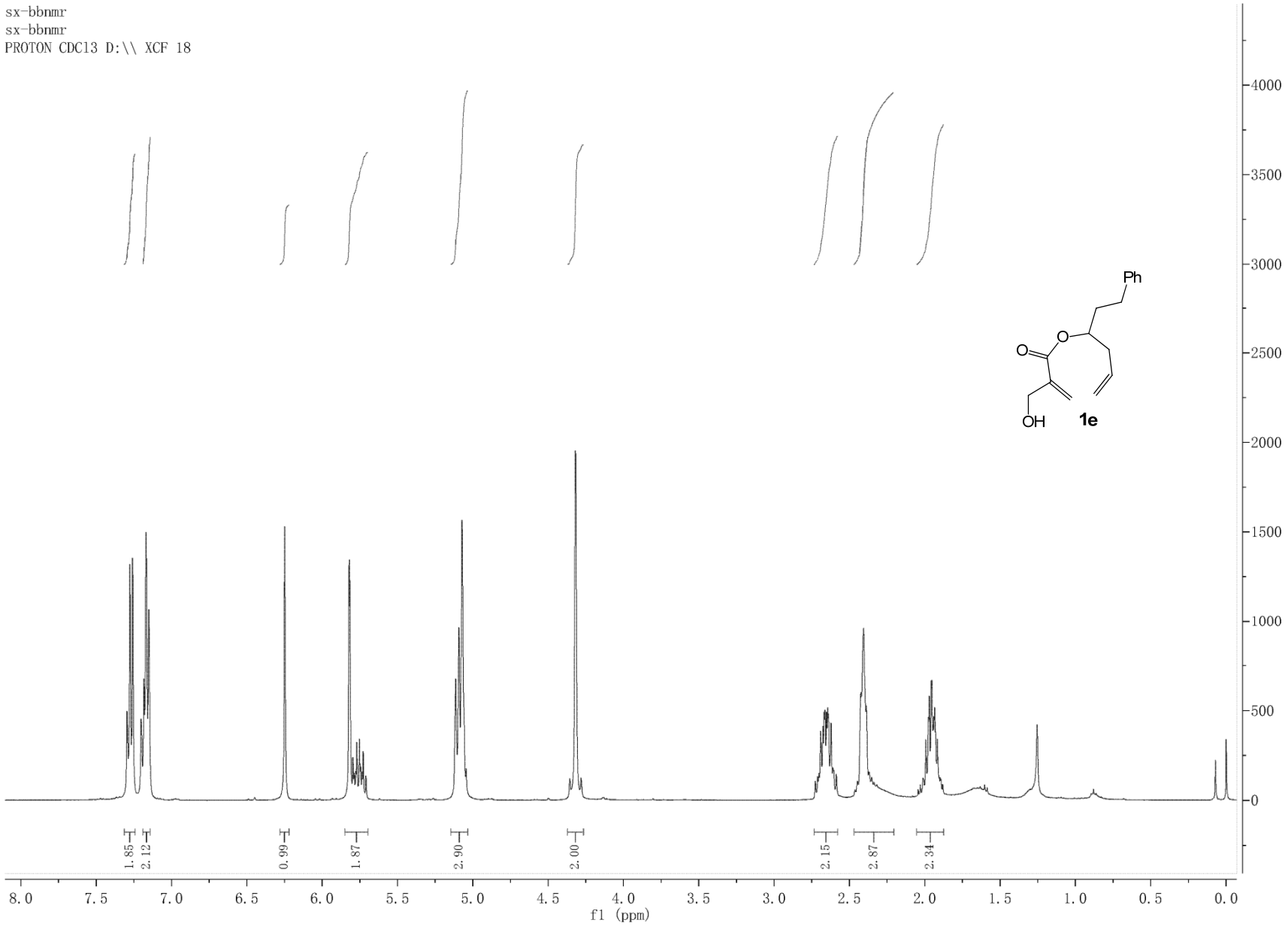
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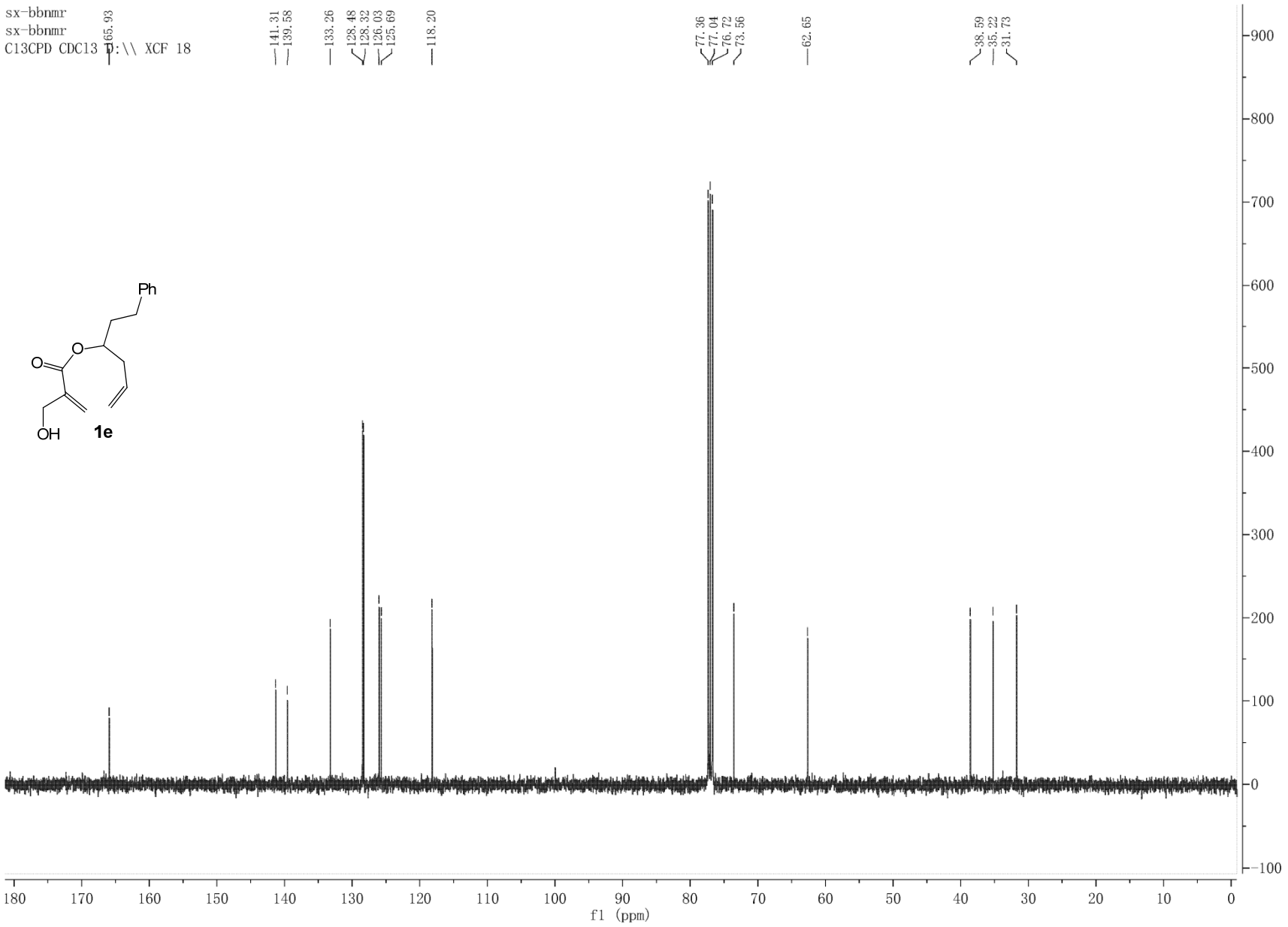
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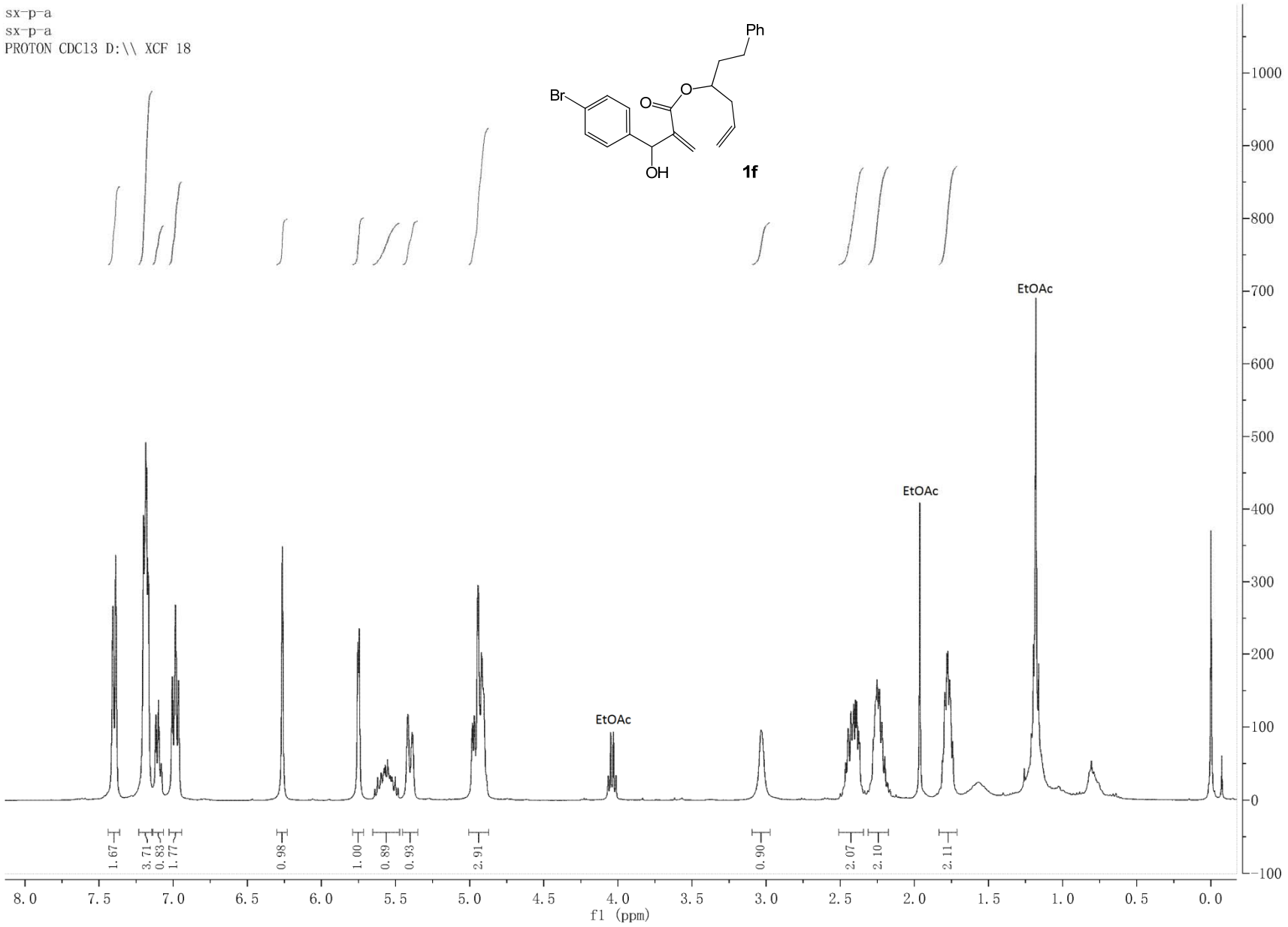
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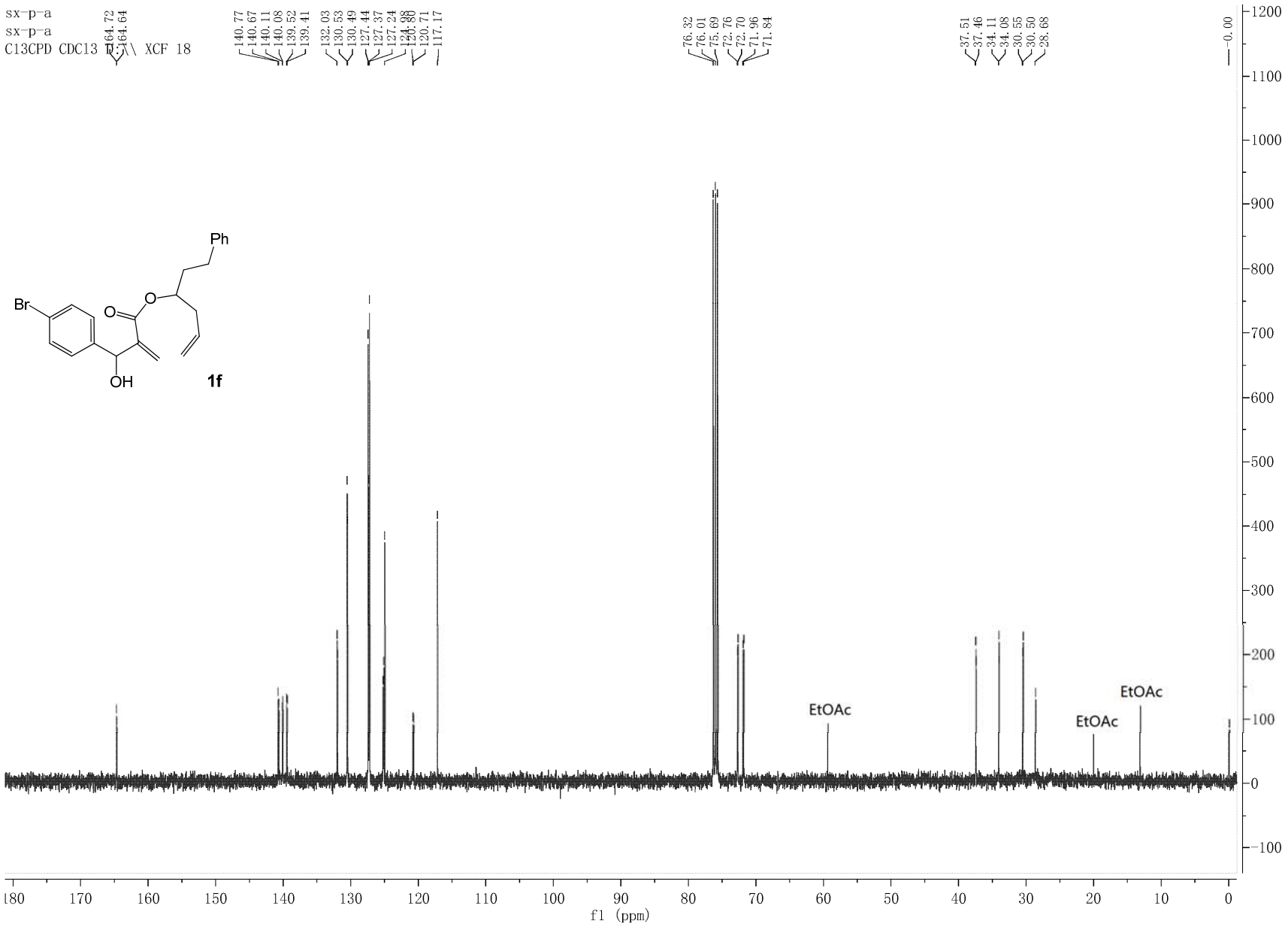
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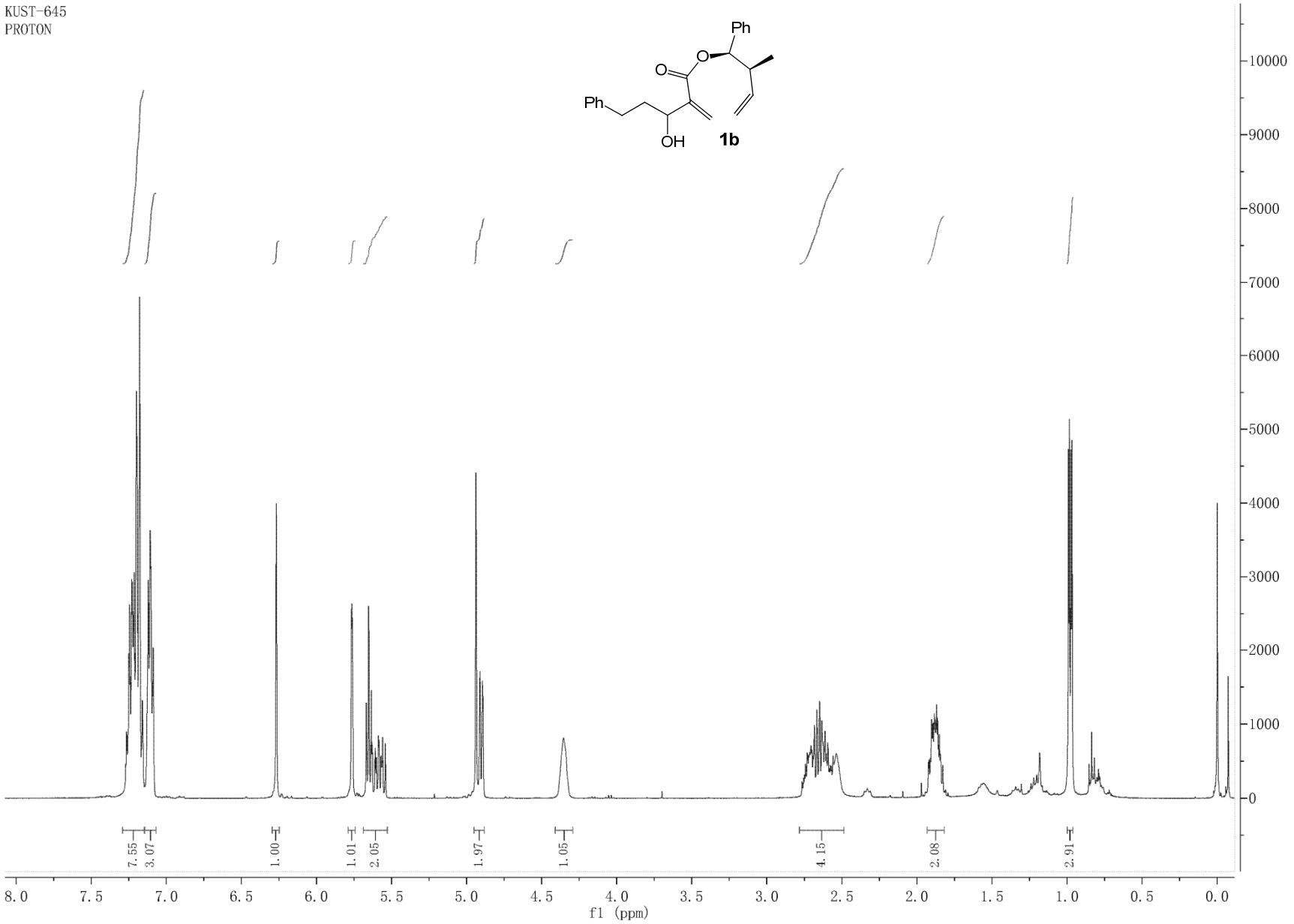
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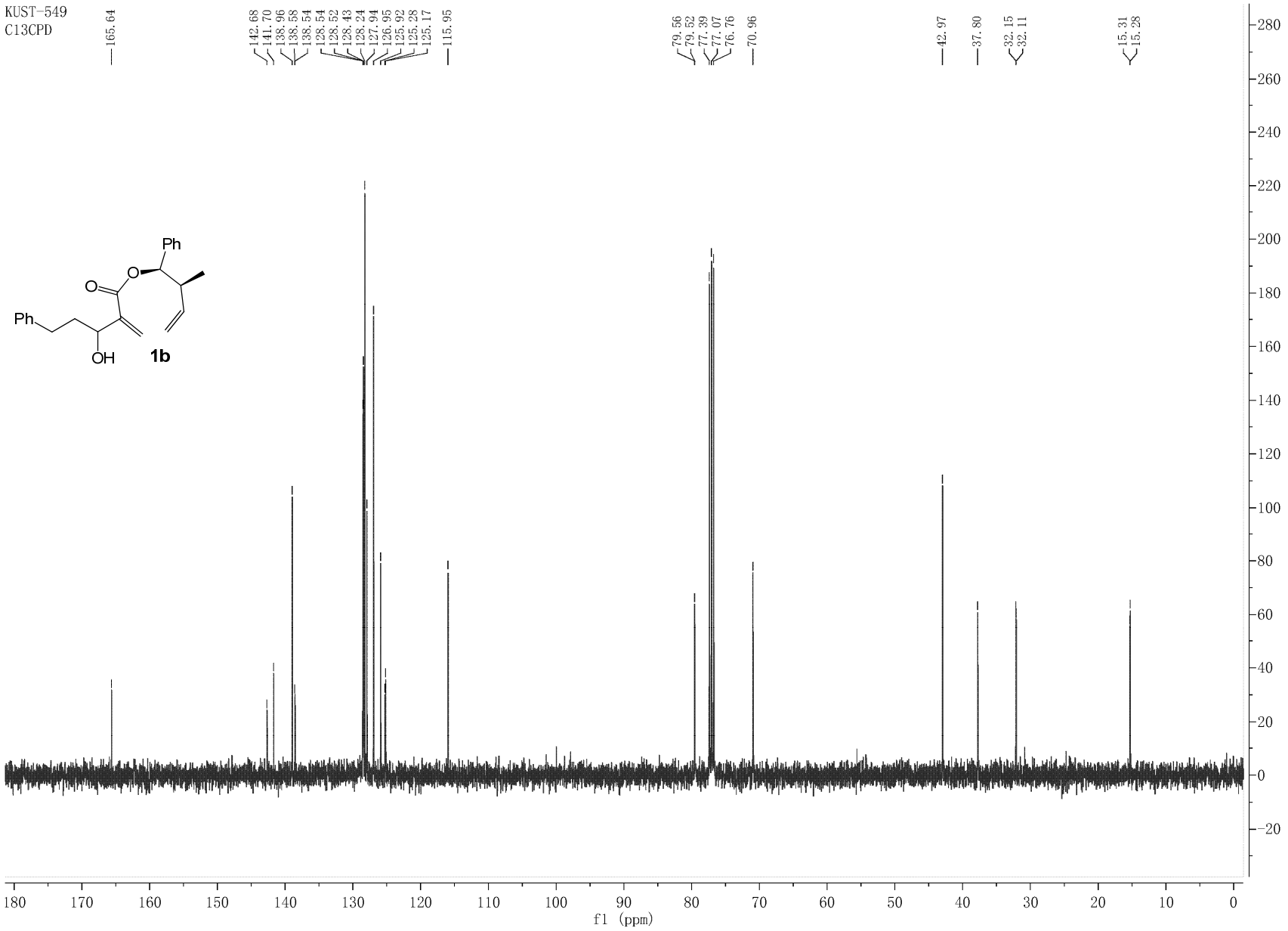
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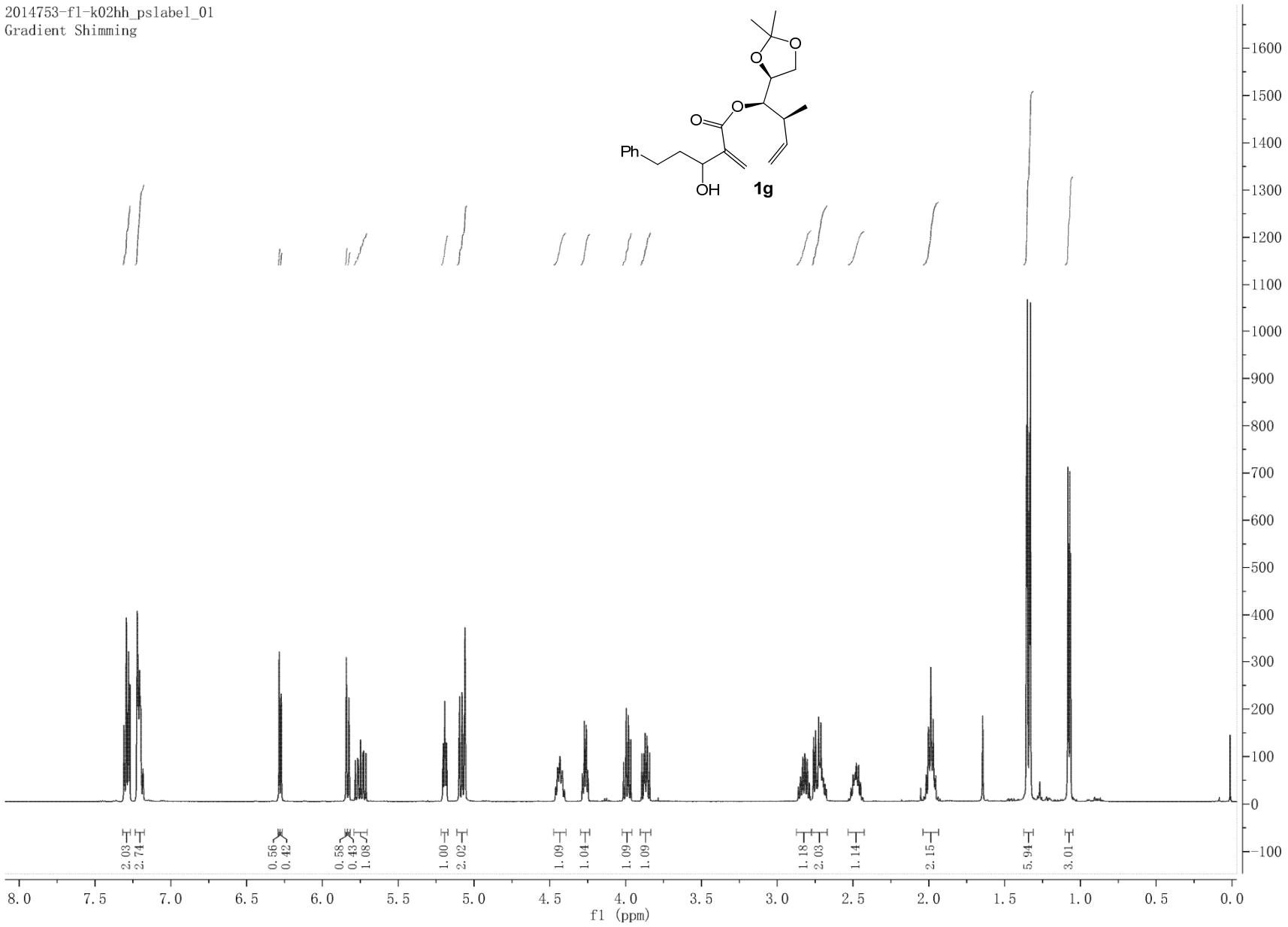
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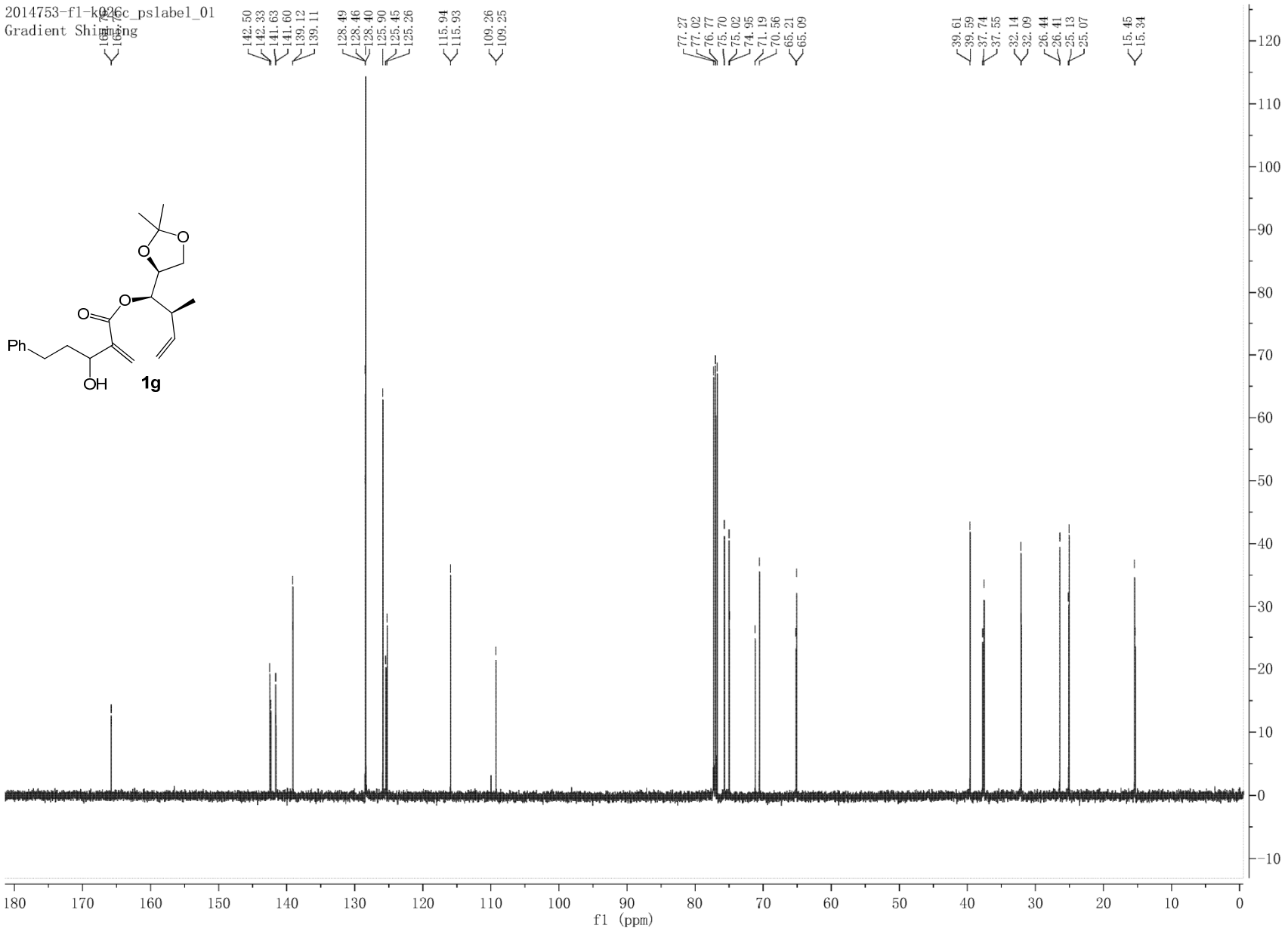
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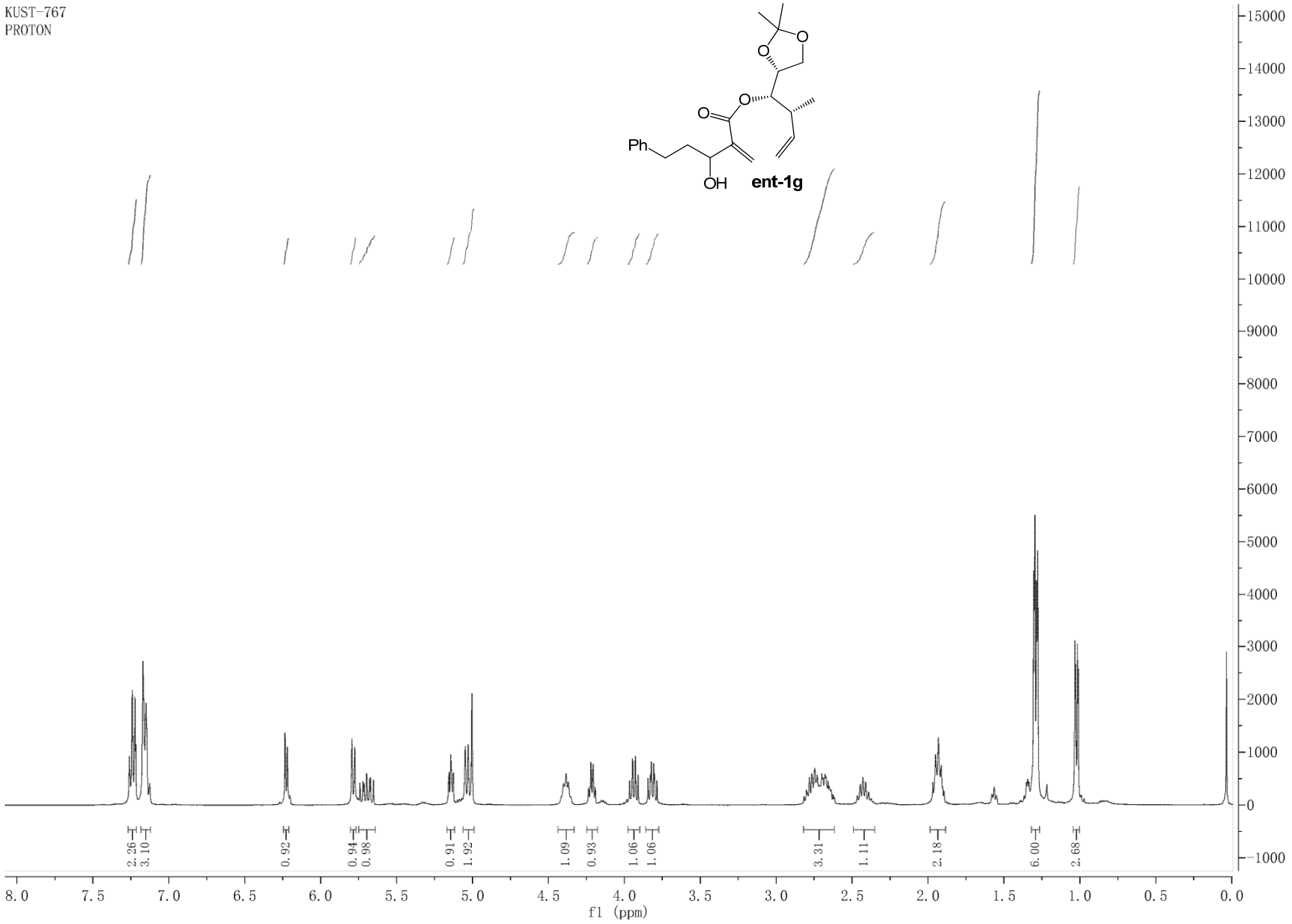
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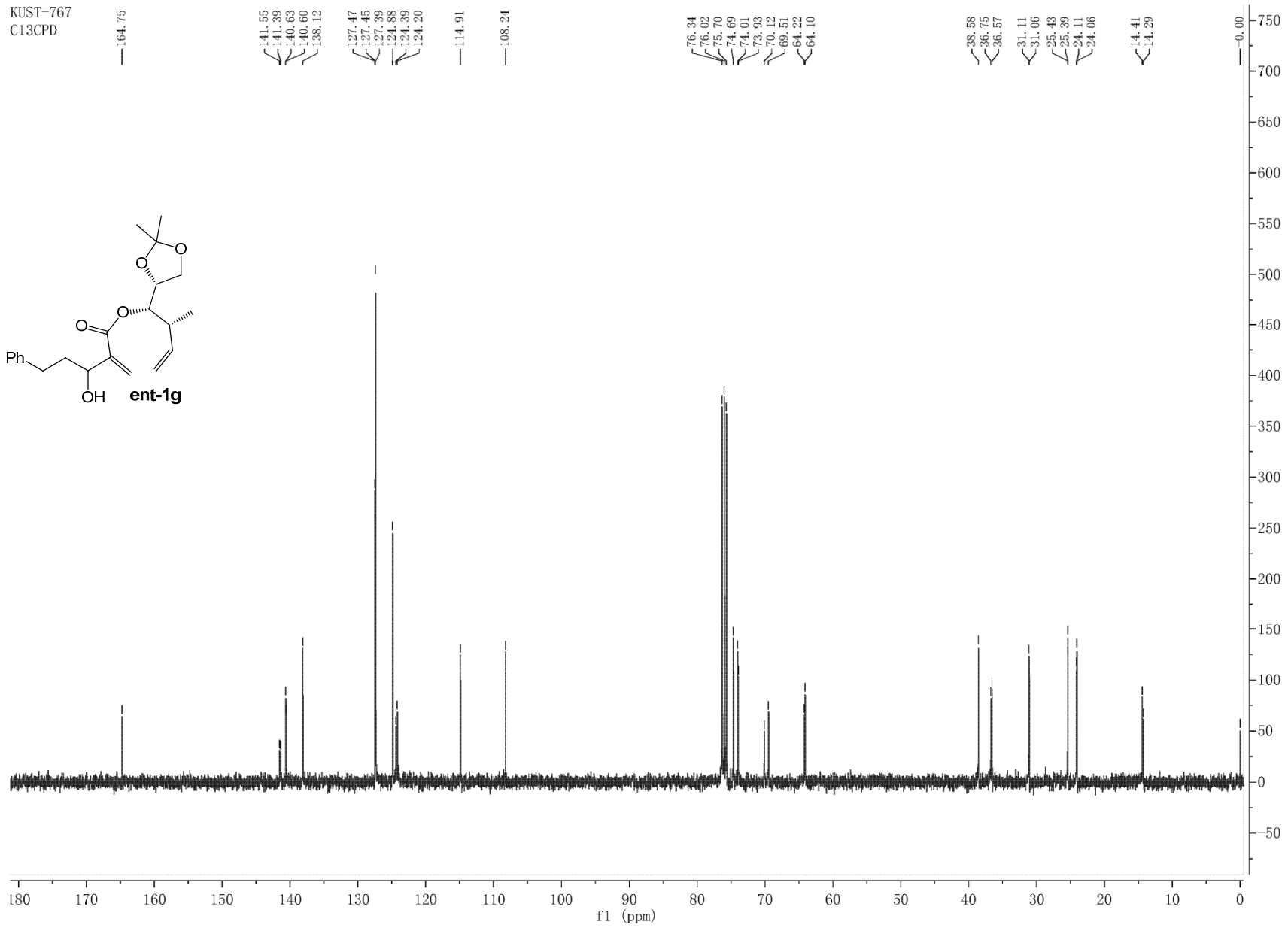
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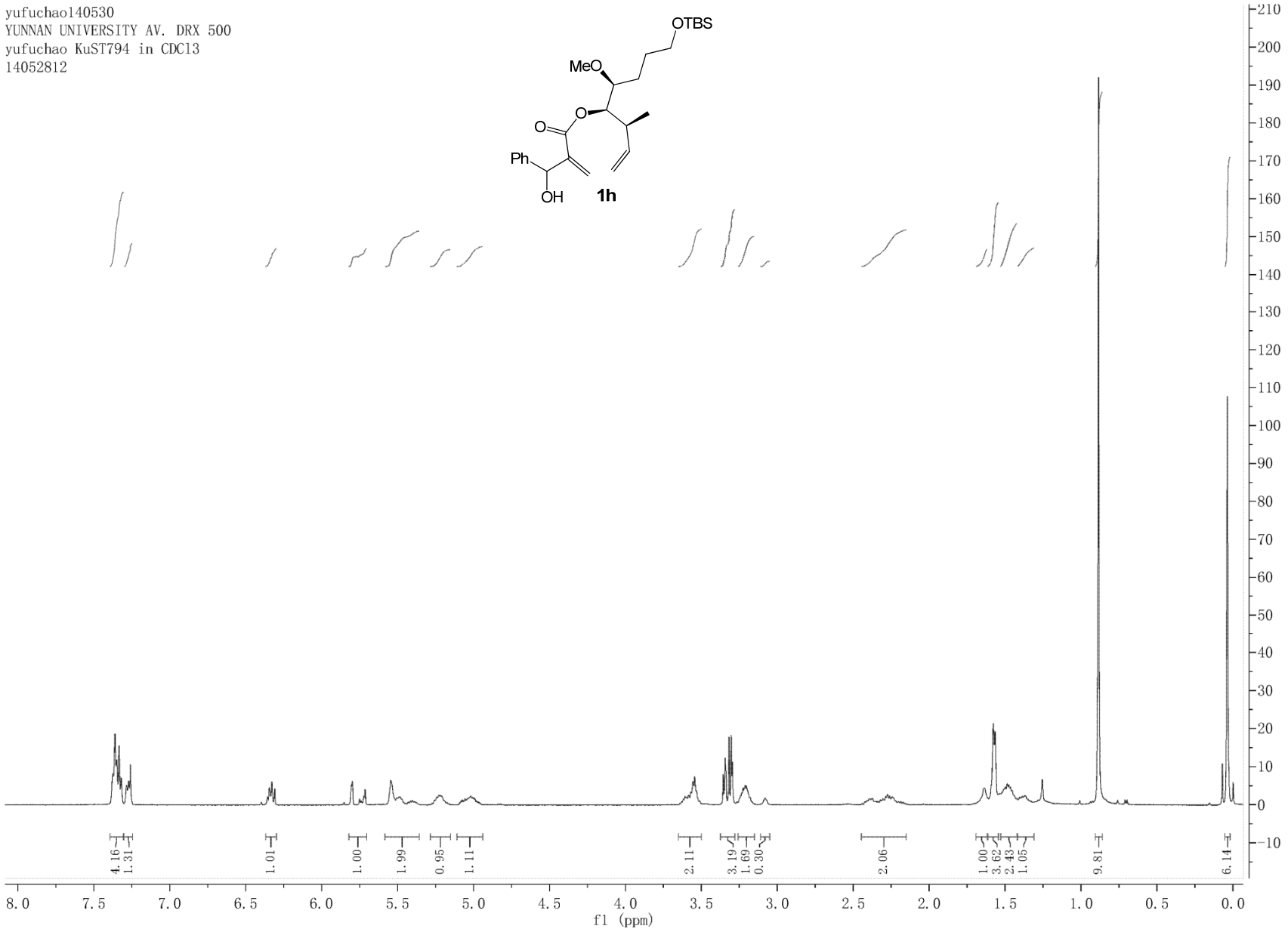
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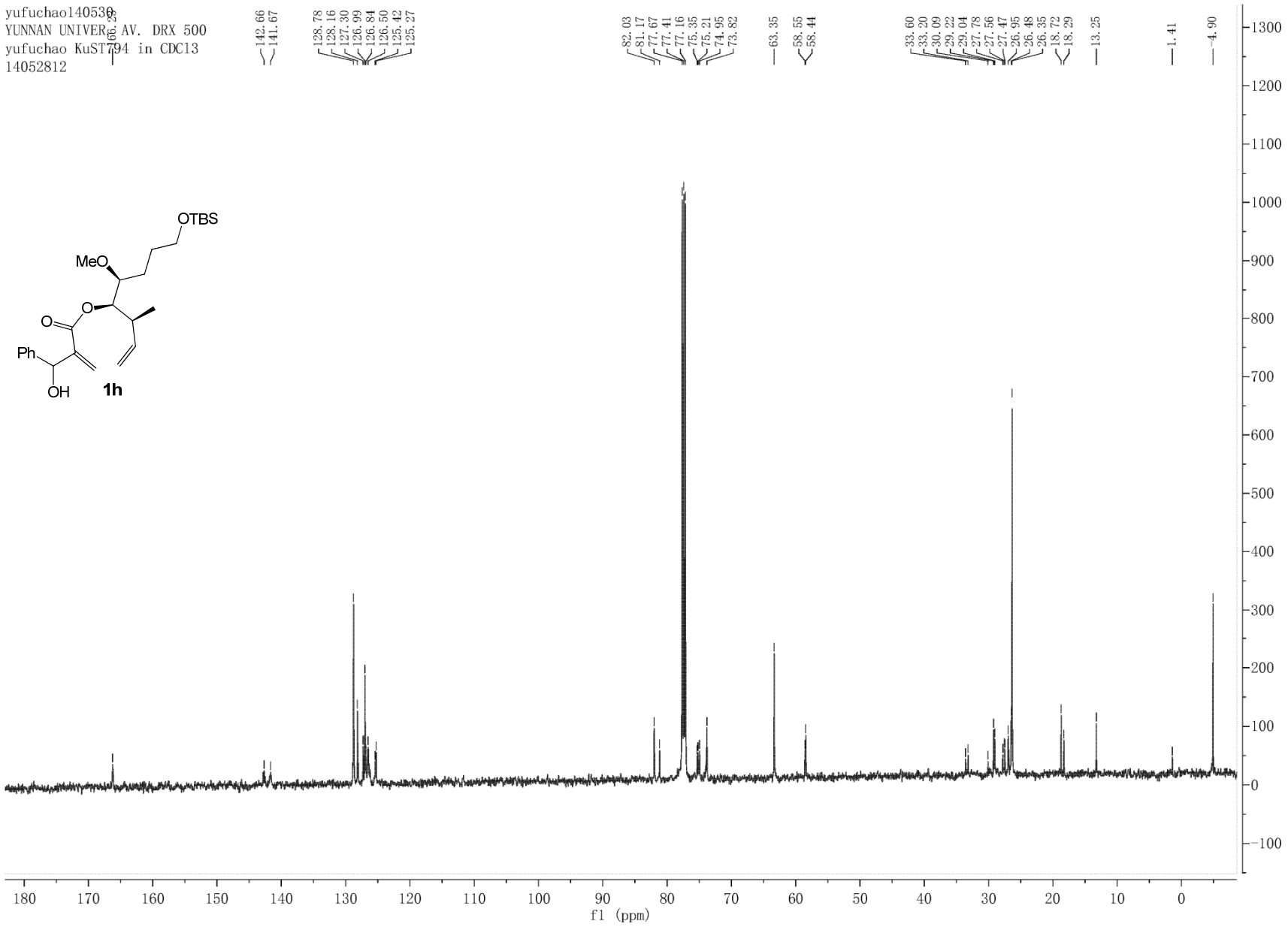
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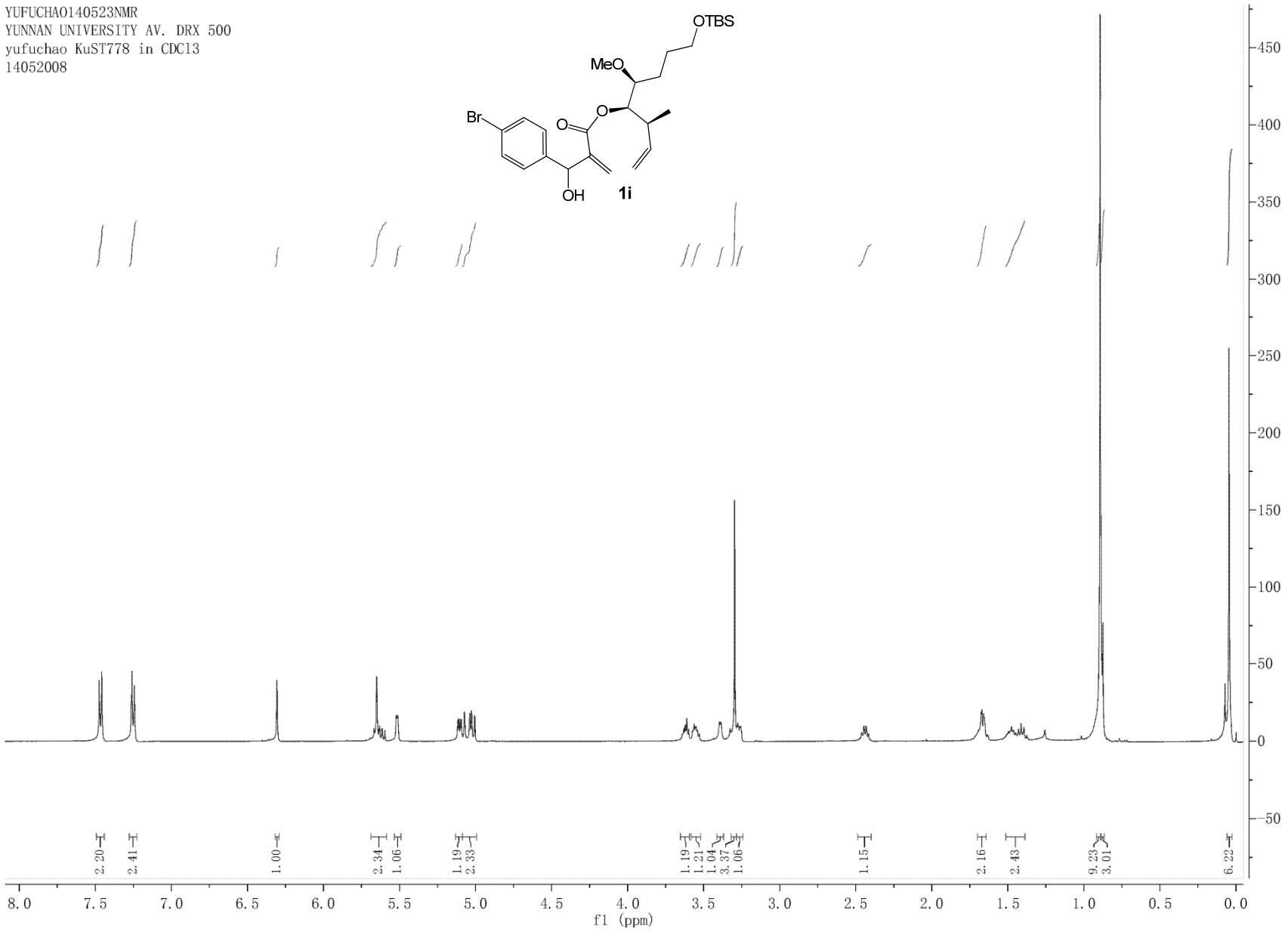
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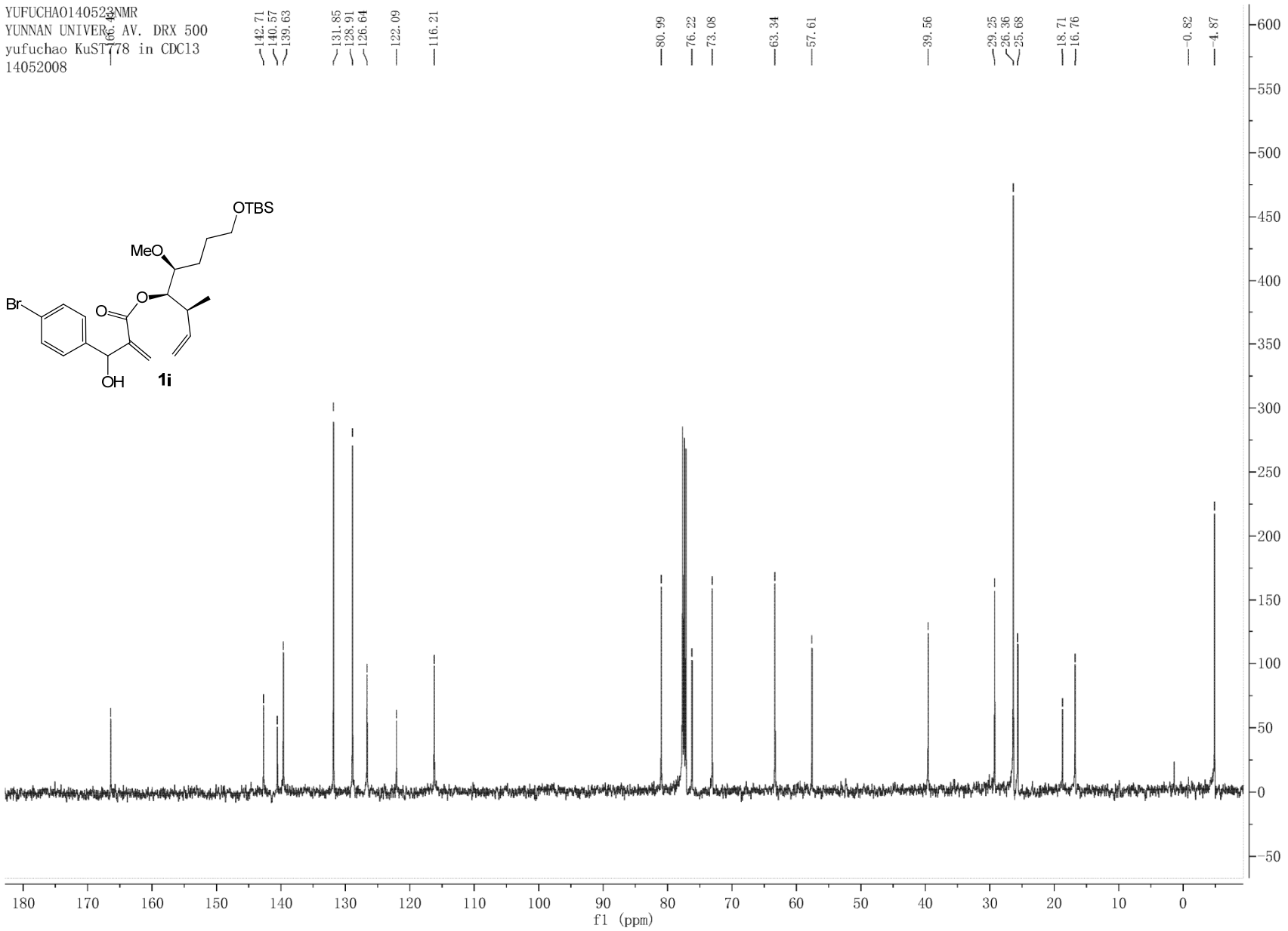
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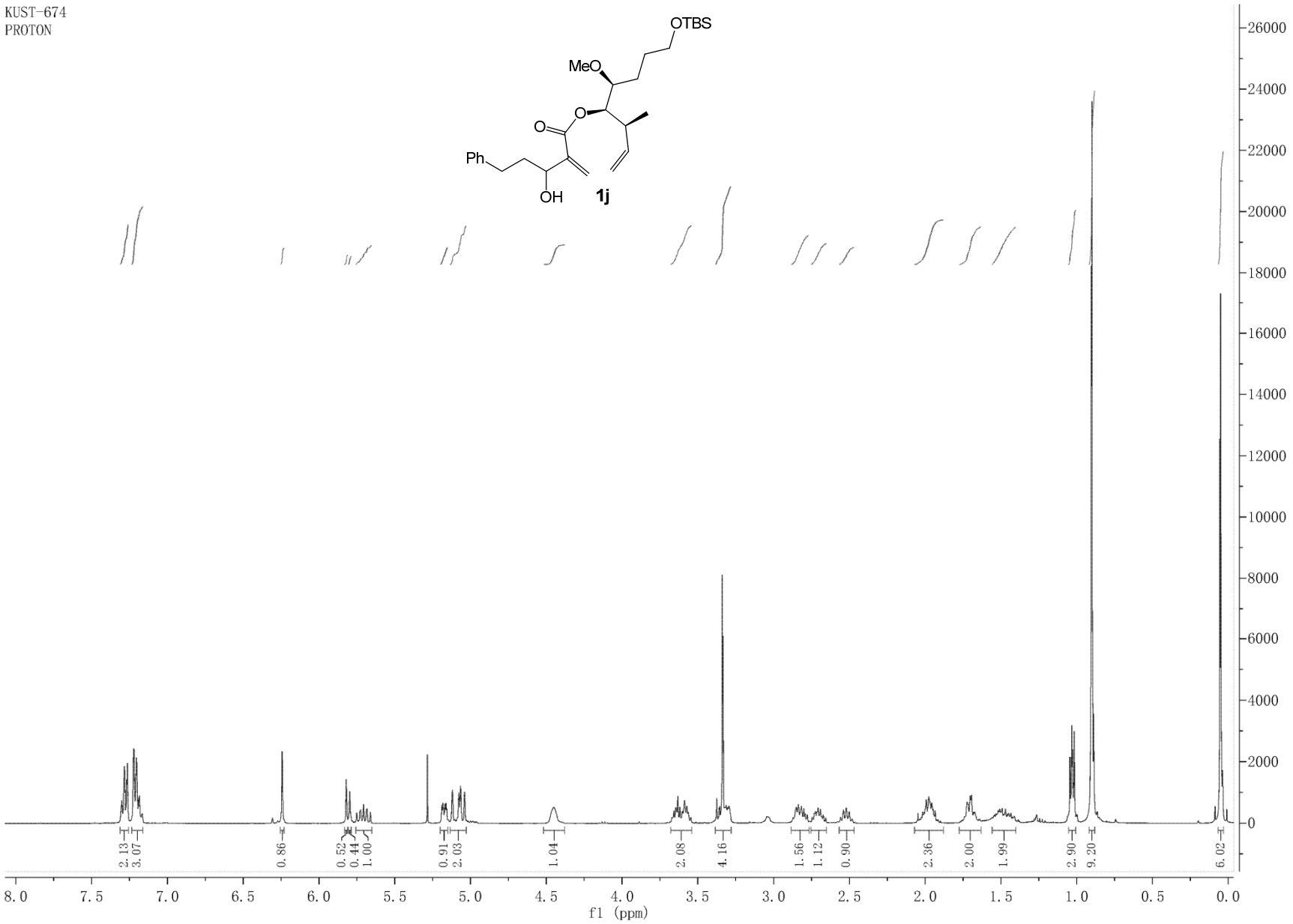
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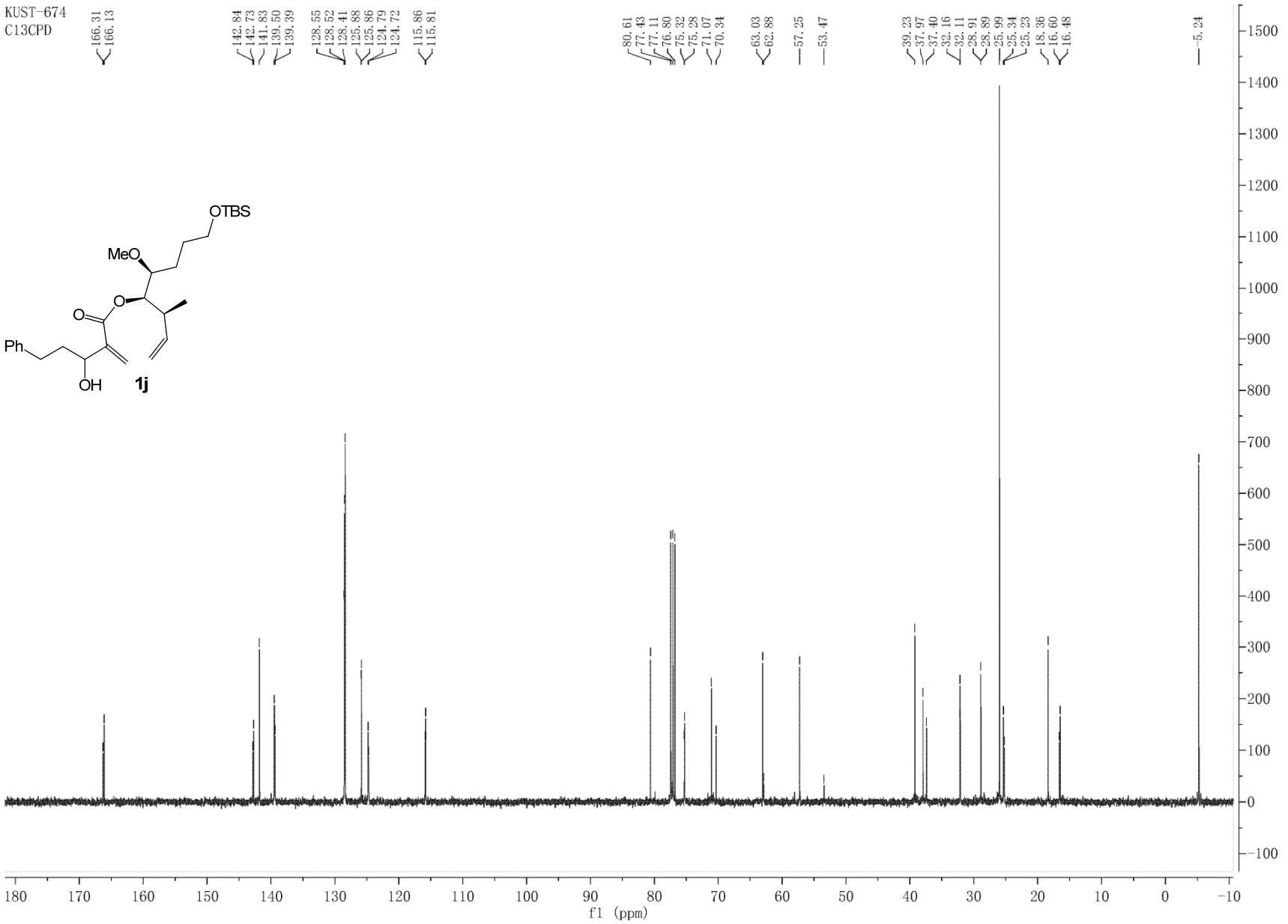
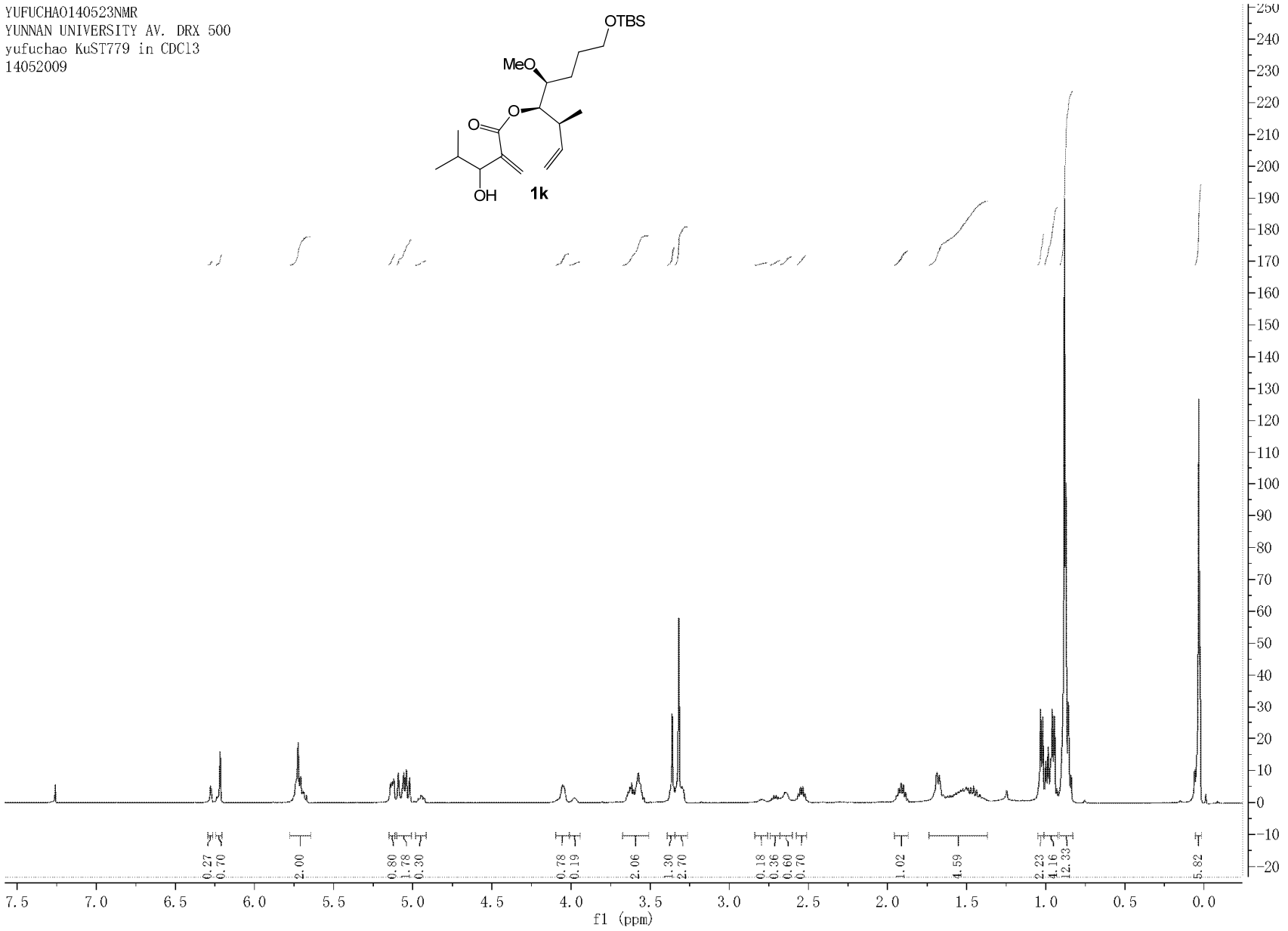
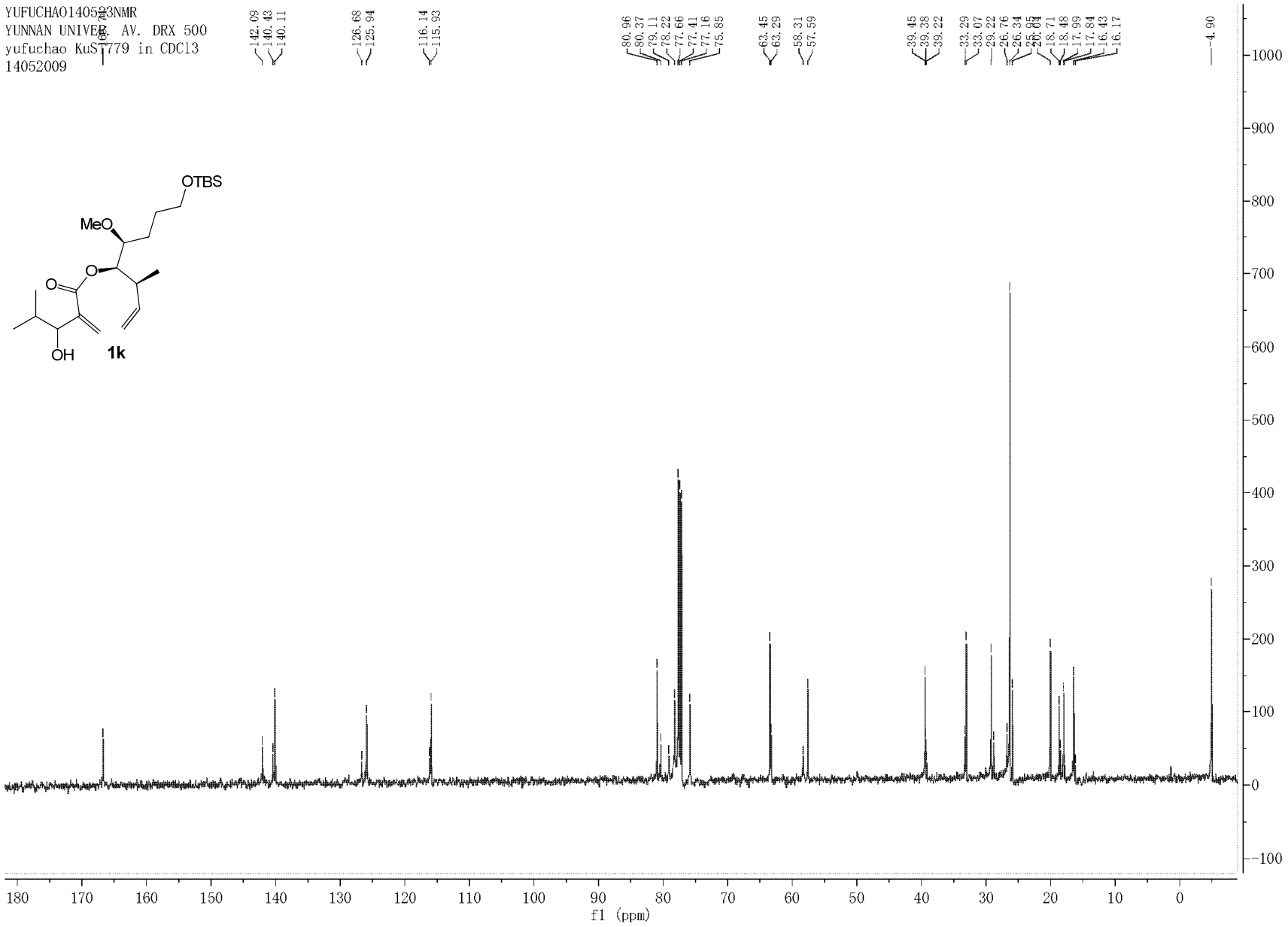
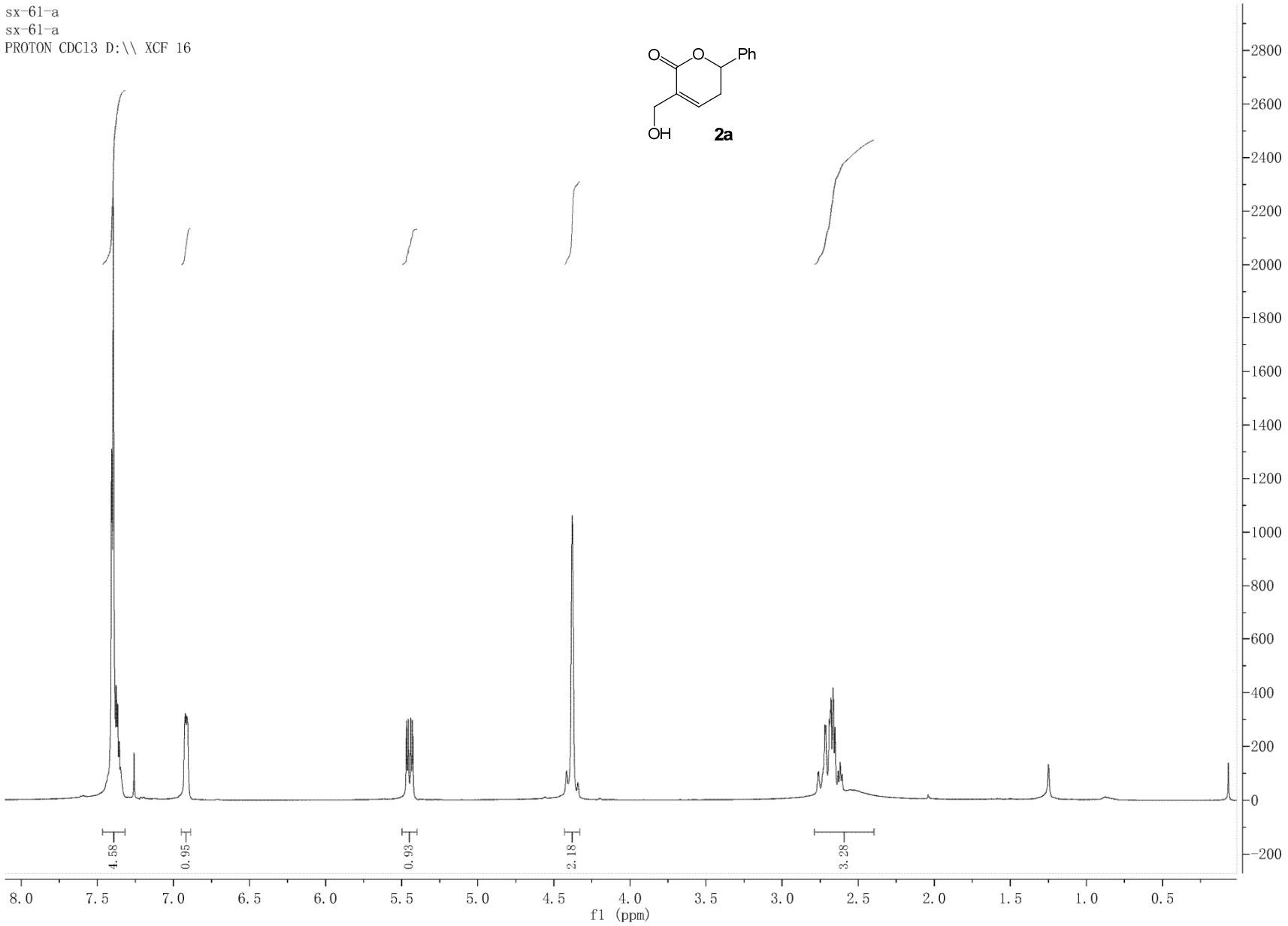
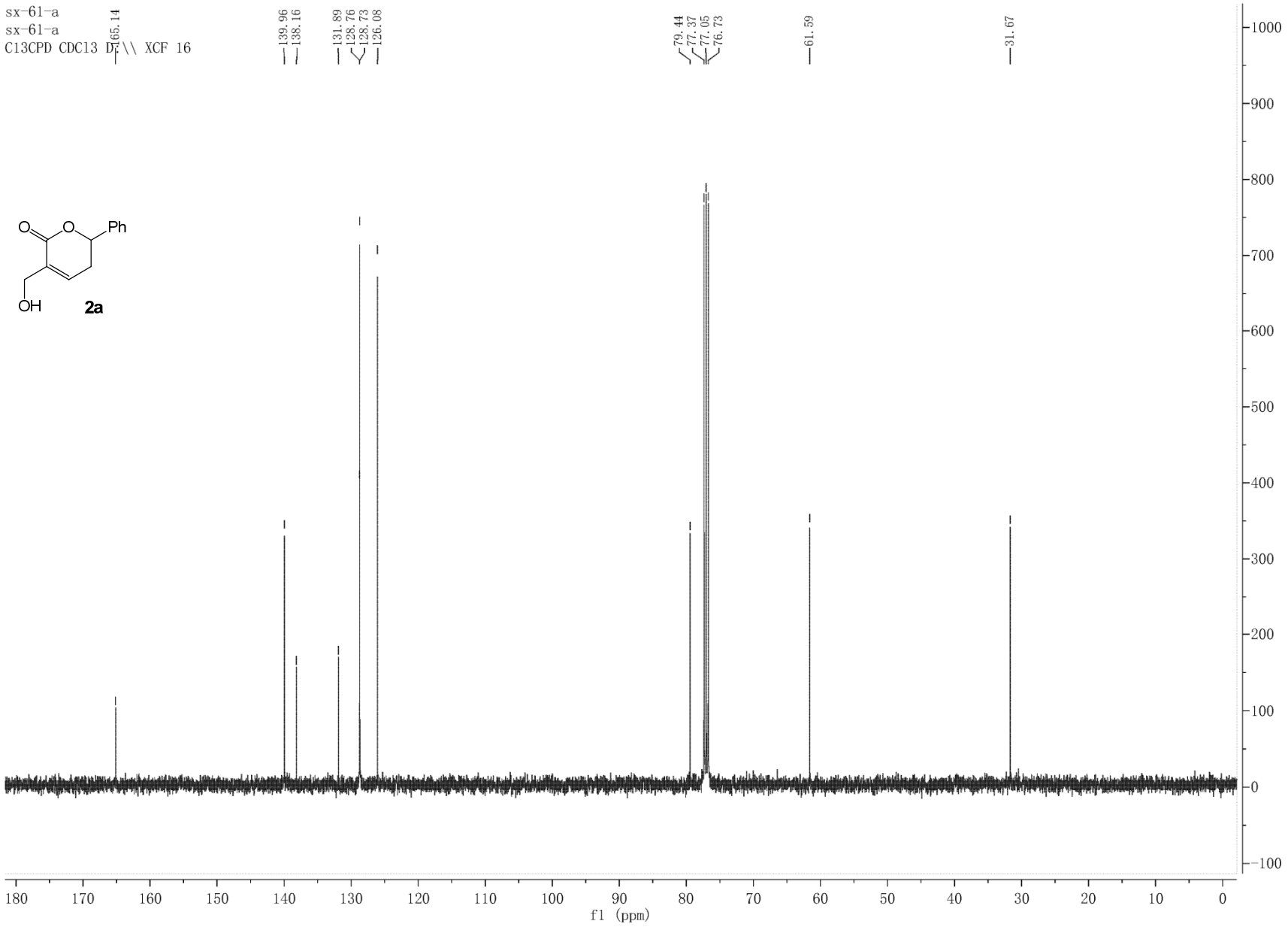
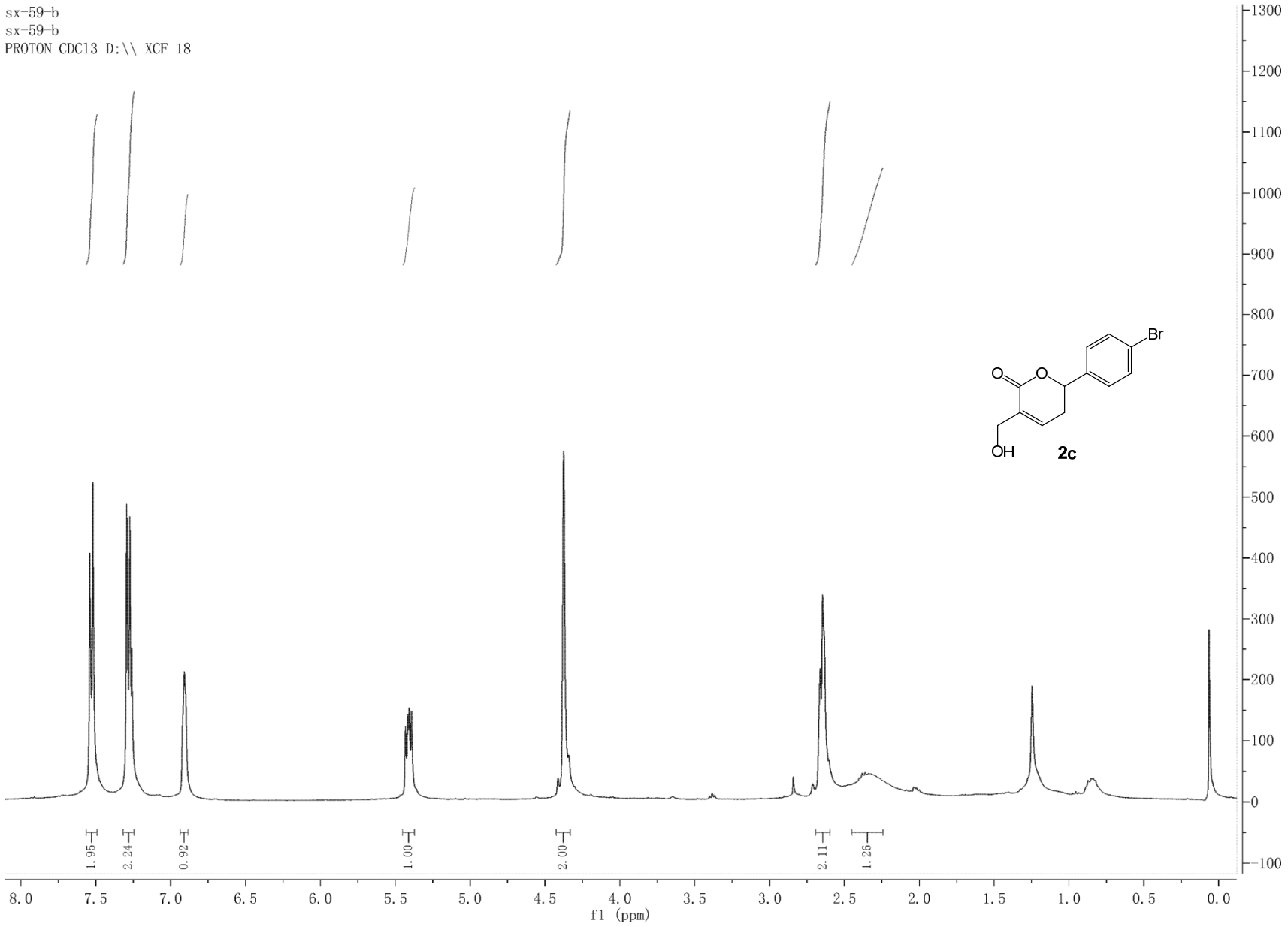

KUST-674
C13CPD
166.31
166.13
142.84
142.73
141.83
139.50
139.39
128.55
128.52
128.41
125.88
125.86
124.79
124.72
115.86
115.81
80.61
77.43
77.11
76.80
75.32
75.28
71.07
70.34
63.03
62.88
57.25
53.47
39.23
37.97
37.40
32.16
32.11
28.91
28.89
25.99
25.34
25.23
18.36
16.60
16.48
-5.24
OTBS
MeO
O
O
Ph
OH
1j
f1 (ppm)

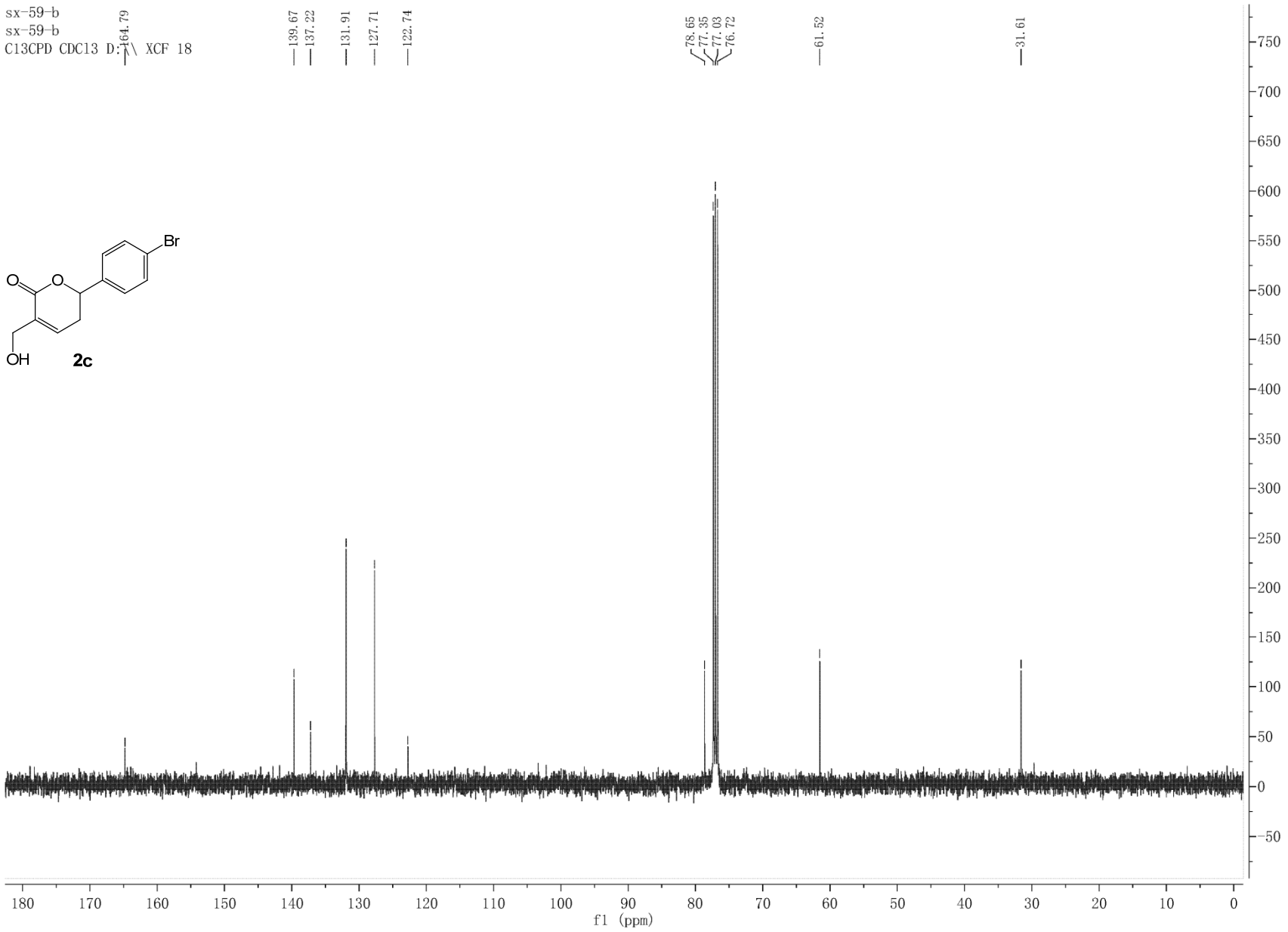

YUFUCHAO140523NMR
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST779 in CDCl3
14052009
OTBS
MeO
O
O
OH
1k
0.27
0.70
2.00
0.80
1.78
0.30
0.78
0.19
2.06
1.30
2.70
0.18
0.36
0.60
0.70
1.02
4.59
2.23
4.16
12.33
5.82
f1 (ppm)

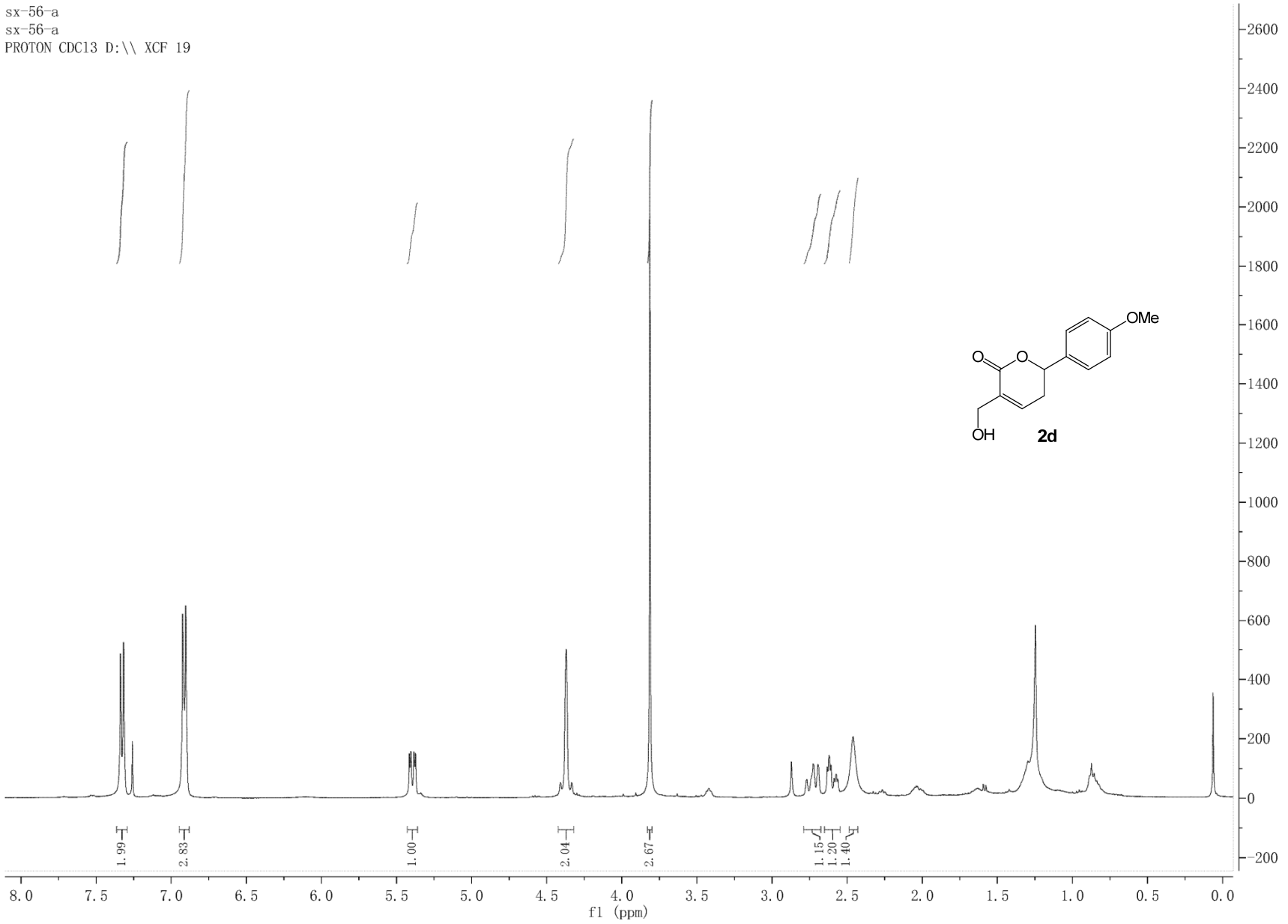

YUFUCHAO140523NMR
YUNNAN UNIVERS. AV. DRX 500
yufuchao KuST779 in CDCl3
14052009
142.09
140.43
140.11
126.68
125.94
116.14
115.93
80.96
80.37
79.11
78.22
77.66
77.41
77.16
75.85
63.45
63.29
58.31
57.59
39.45
39.38
39.22
33.29
33.07
29.22
26.76
26.34
25.95
25.82
18.71
18.48
17.99
17.84
16.43
16.17
-4.90
OTBS
MeO
O
O
OH
1k
f1 (ppm)

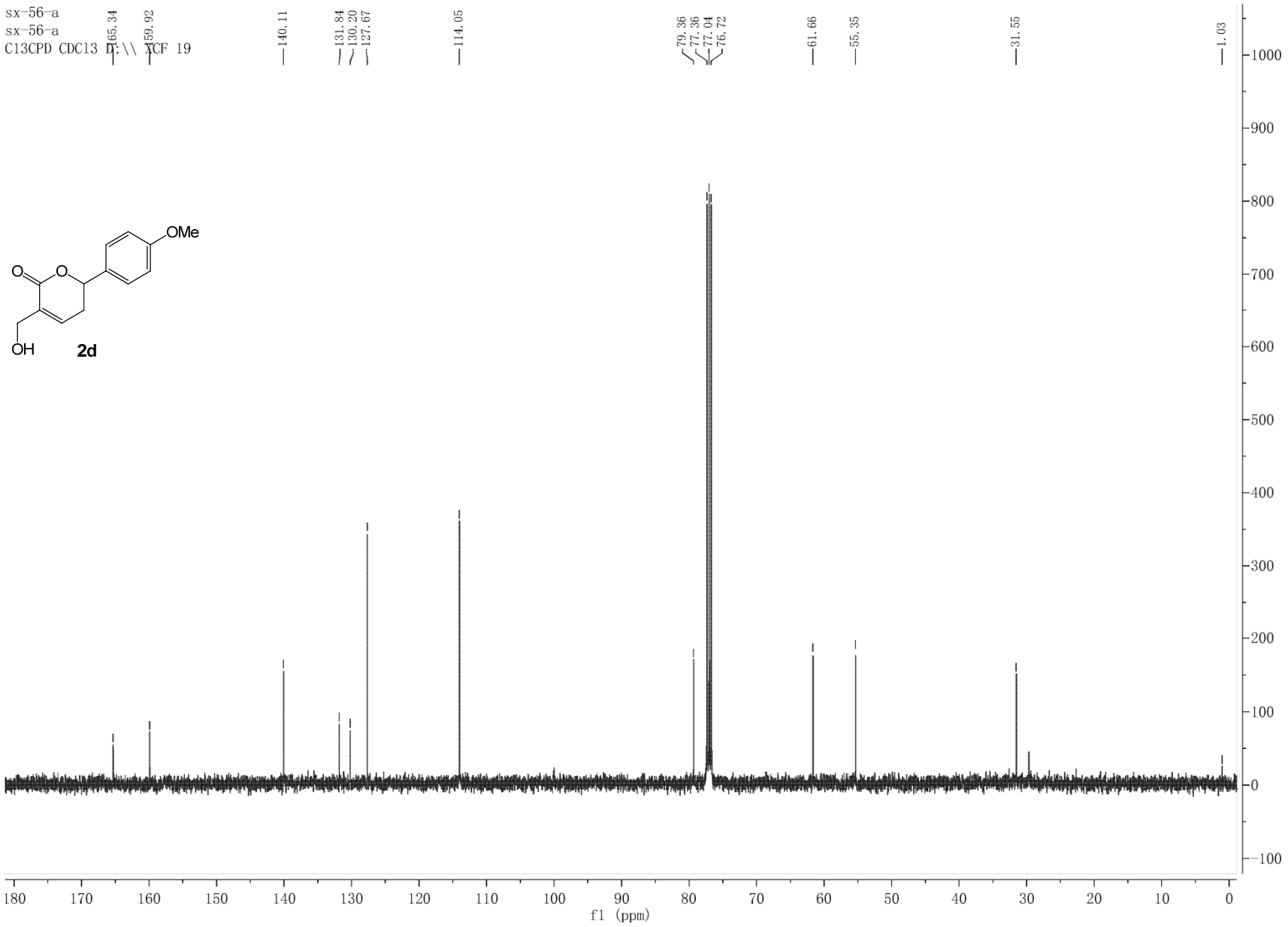

sx-61-a
sx-61-a
PROTON CDCl3 D:\\ XCF 16
O
O
Ph
OH
2a
4.58
0.95
0.93
2.18
3.28
f1 (ppm)

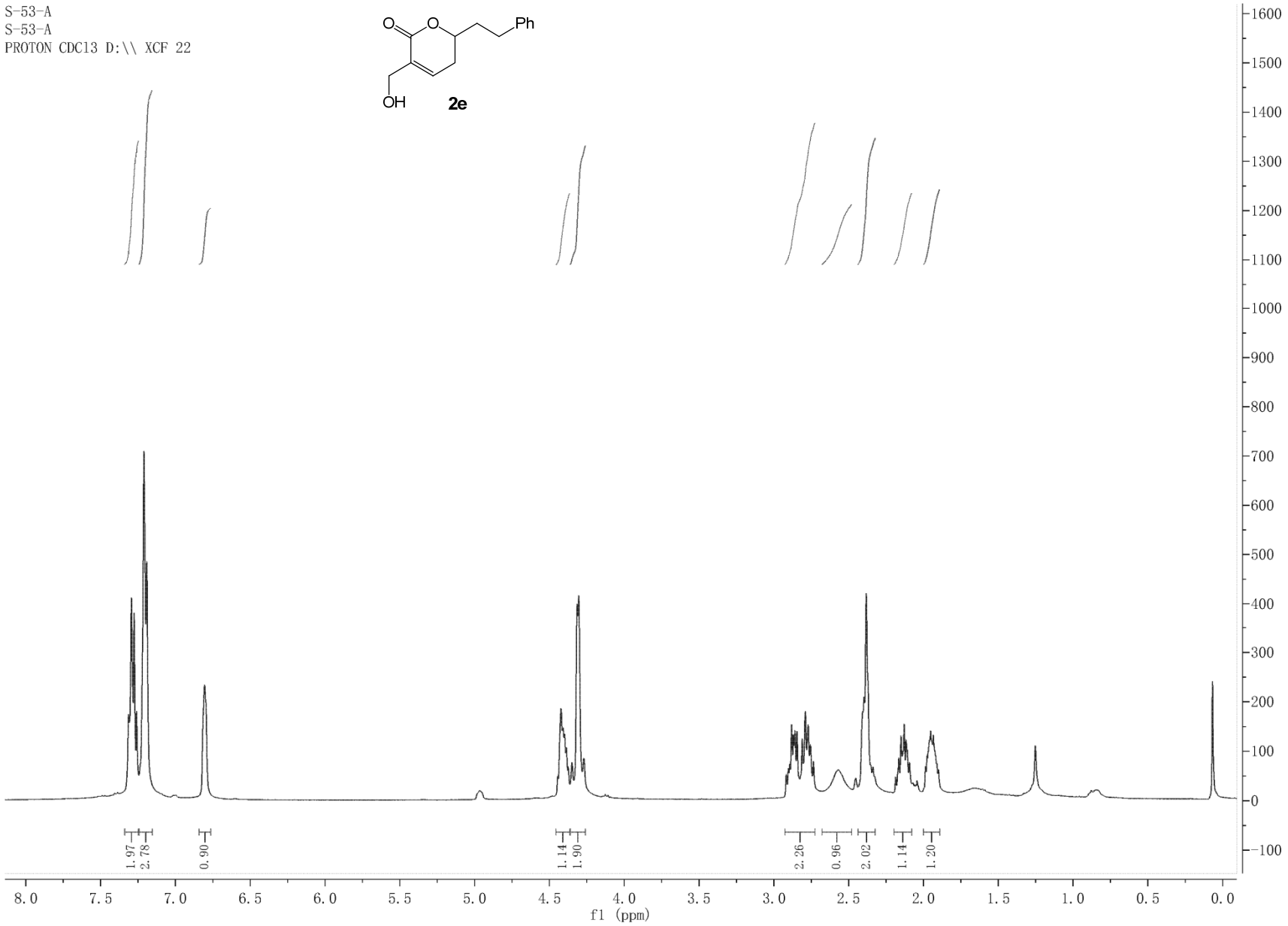

sx-61-a
sx-61-a
C13CPD CDCl3 D:\\ XCF 16
165.14
139.96
138.16
131.89
128.76
128.73
126.08
79.44
77.37
77.05
76.73
61.59
31.67
O
O
Ph
OH
2a
f1 (ppm)

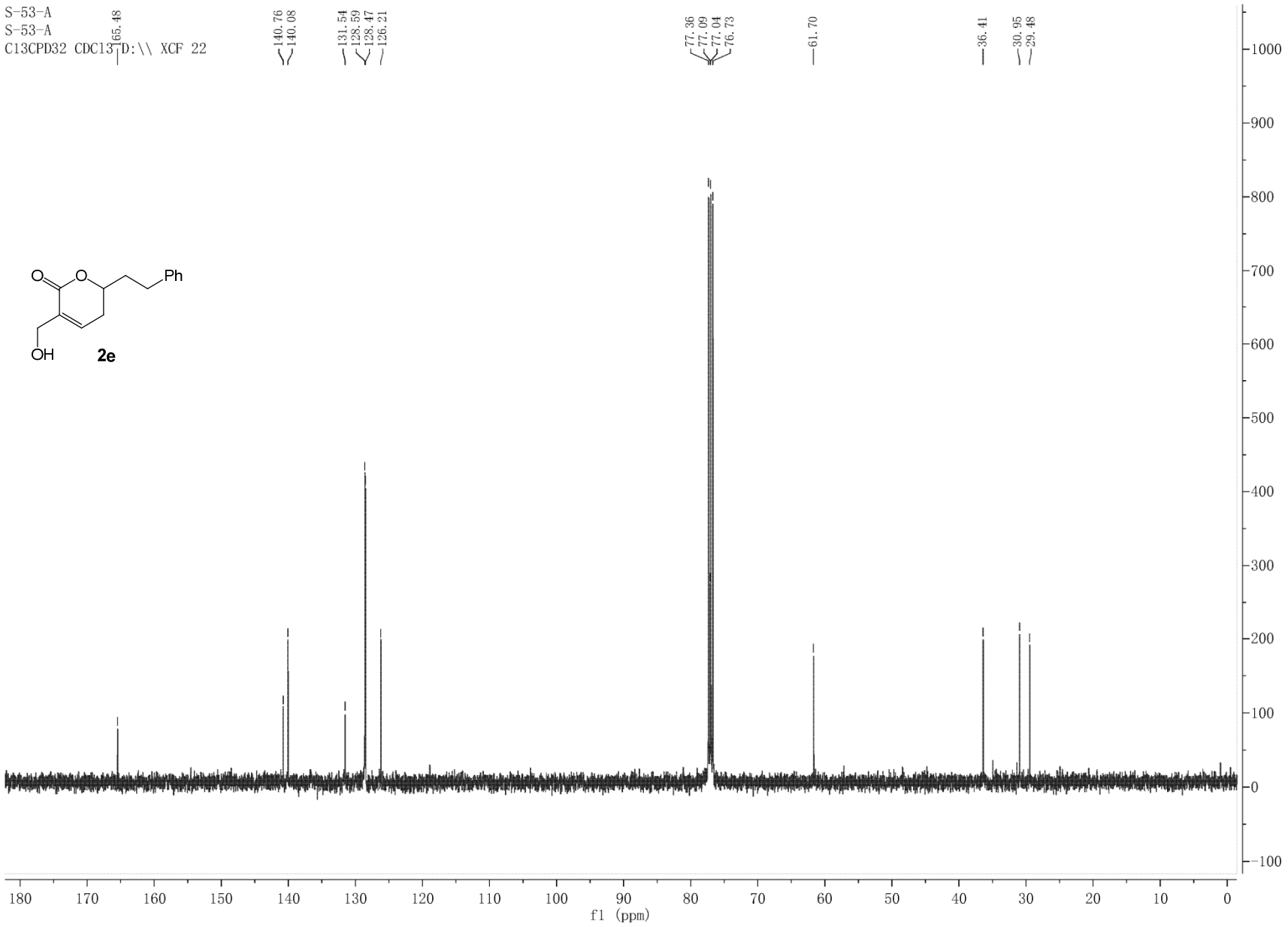

sx-59-b
sx-59-b
PROTON CDCl3 D:\\ XCF 18
Br
O
O
OH
2c
1.95
2.24
0.92
1.00
2.00
2.11
1.26
f1 (ppm)

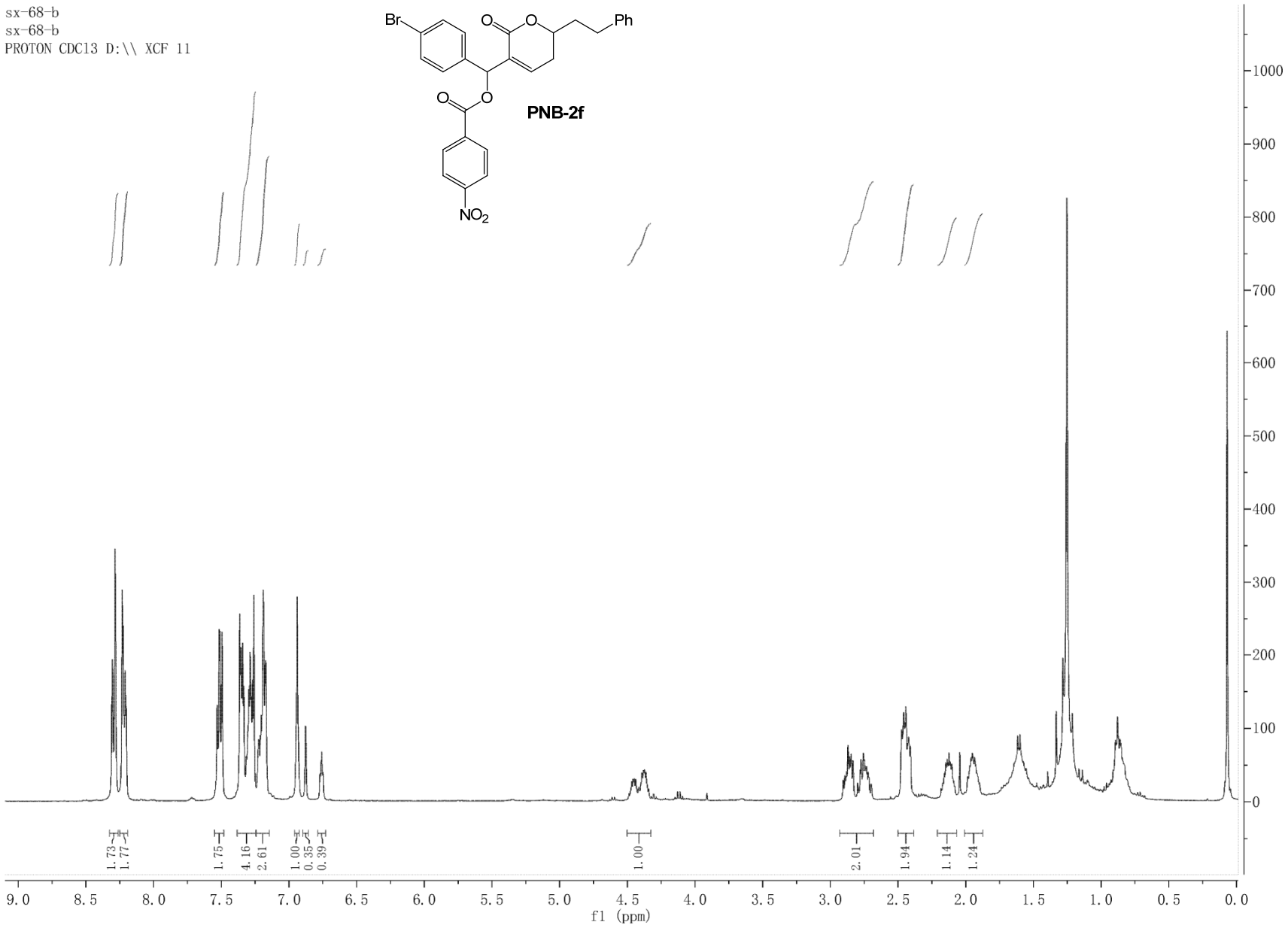

sx-59-b
sx-59-b
C13CPD CDCl3 D:\ XCF 18
164.79
139.67
137.22
131.91
127.71
122.74
78.65
77.35
77.03
76.72
61.52
31.61
Br
O
O
OH
2c
f1 (ppm)

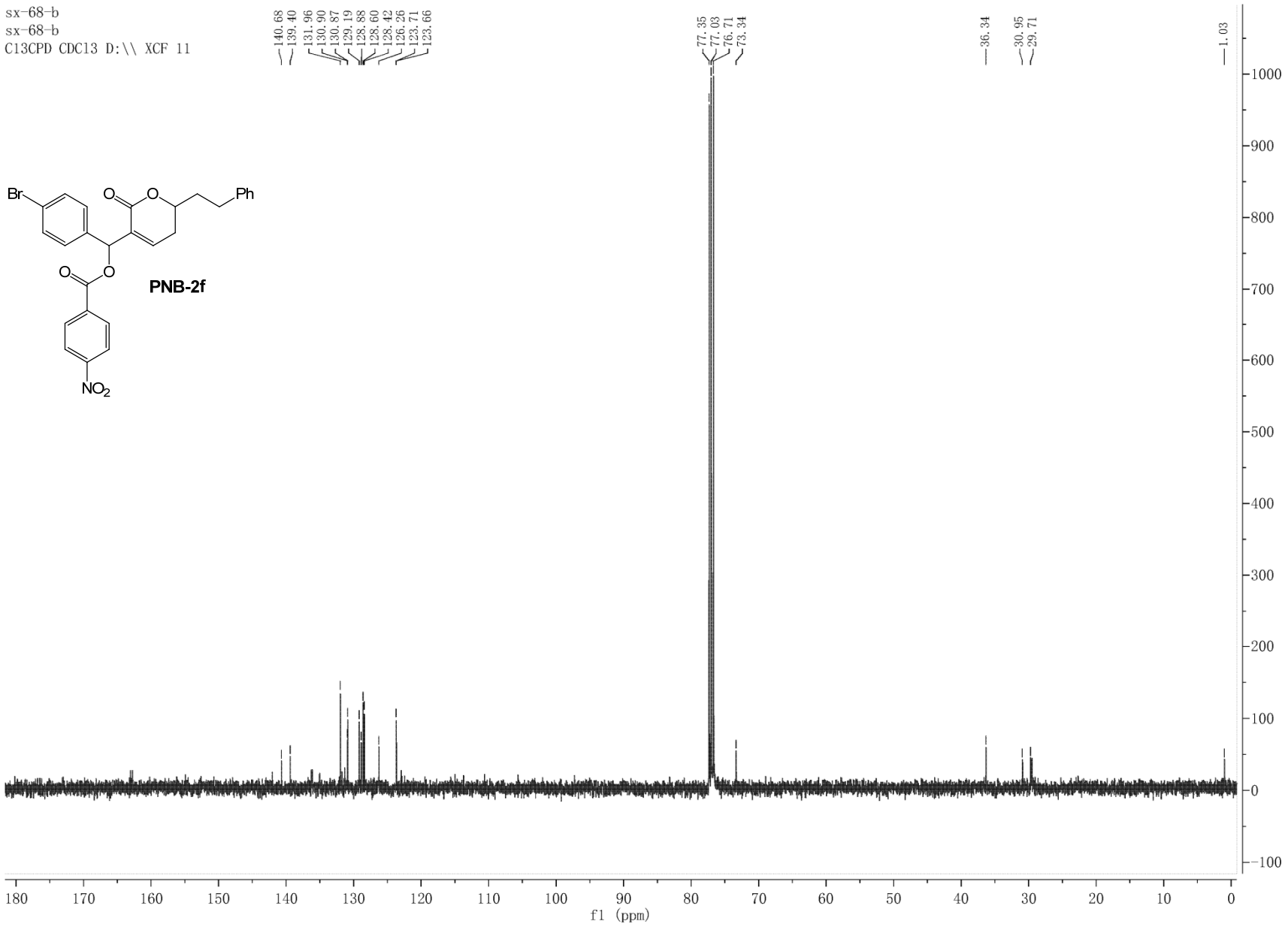

sx-56-a
sx-56-a
PROTON CDCl3 D:\\ XCF 19
OMe
O
O
OH
2d
1.99
2.83
1.00
2.04
2.67
1.15
1.20
1.40
f1 (ppm)

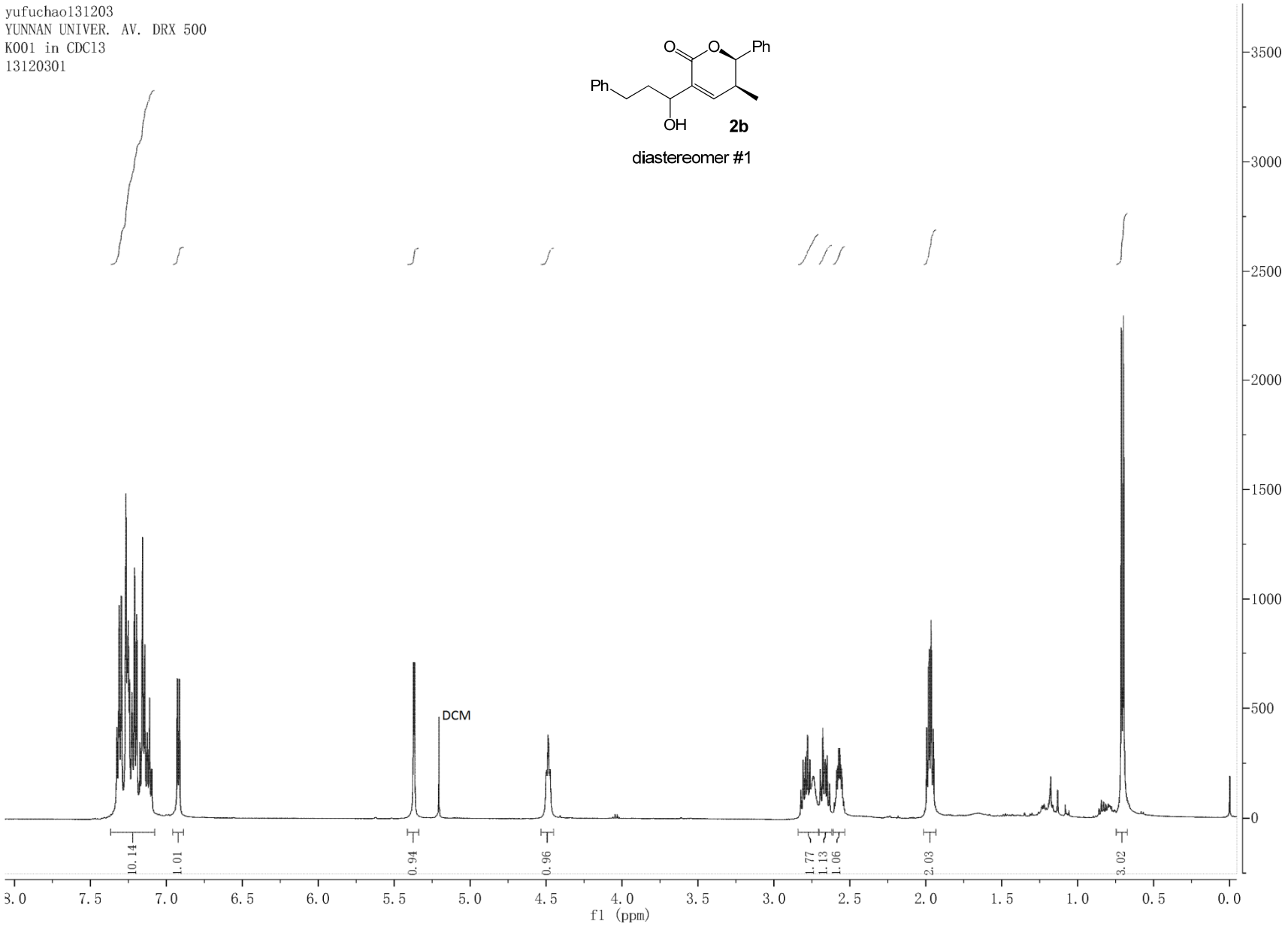

sx-56-a
sx-56-a
C13CPD CDC13 D:\\ XCF 19
165.34
159.92
140.11
131.84
130.20
127.67
114.05
79.36
77.36
77.04
76.72
61.66
55.35
31.55
1.03
OMe
O
O
OH
2d
f1 (ppm)

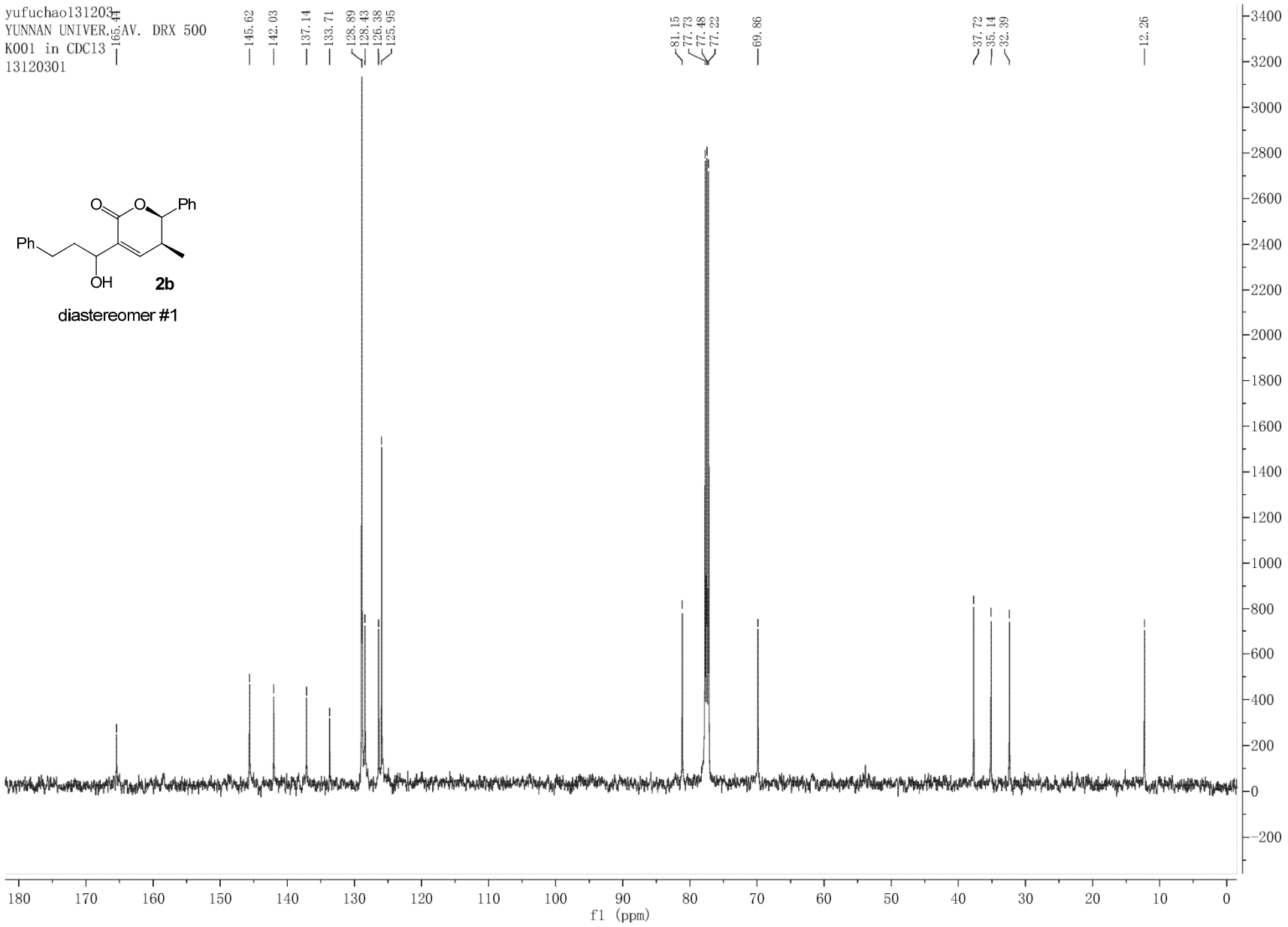

S-53-A
S-53-A
PROTON CDCl3 D:\\ XCF 22
O
O
Ph
OH
2e
1.97
2.78
0.90
1.14
1.90
2.26
0.96
2.02
1.14
1.20
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

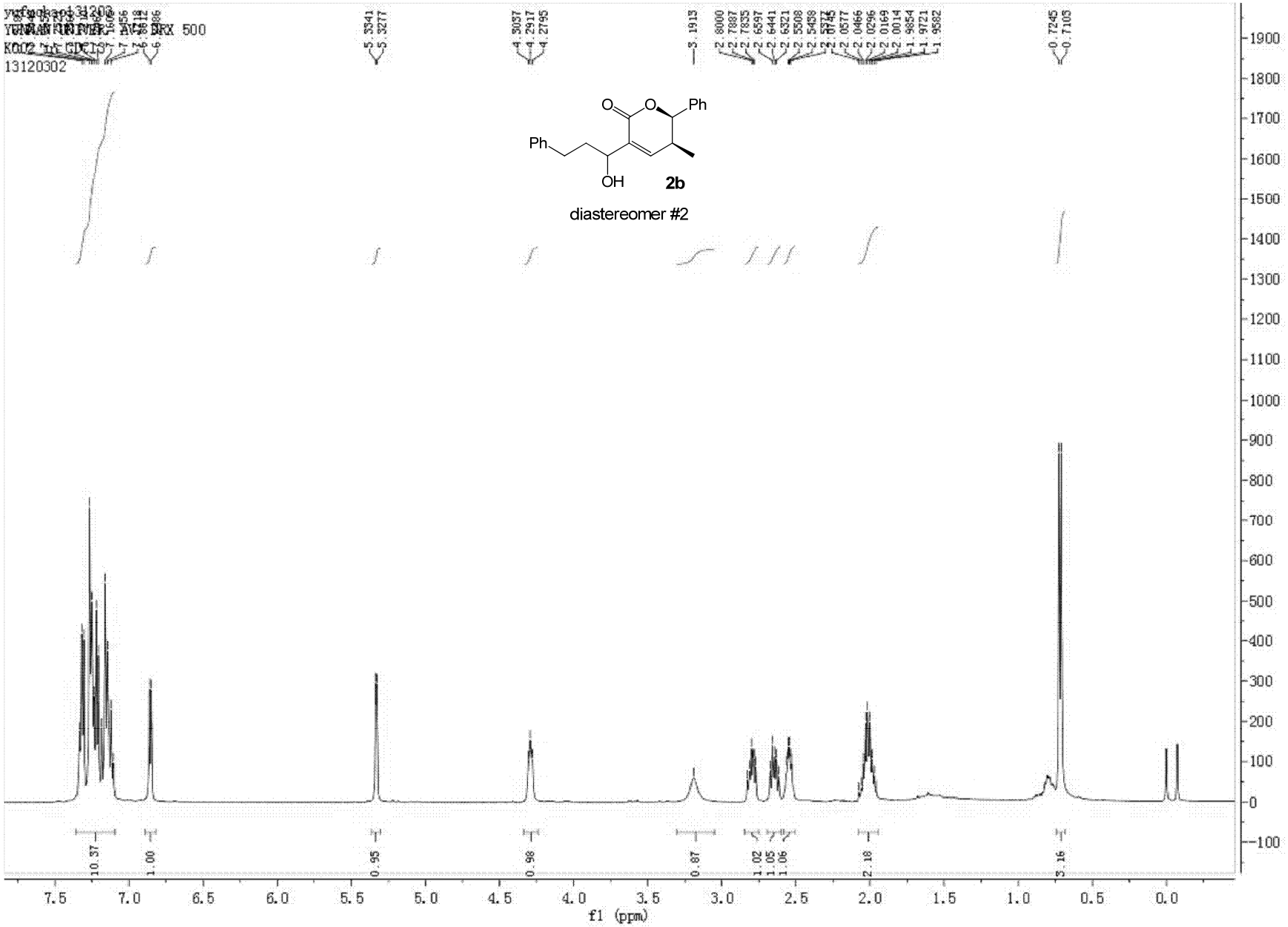

S-53-A
S-53-A
C13CPD32 CDC13 D:\\ XCF 22
165.48
140.76
140.08
131.54
128.59
128.47
126.21
77.36
77.09
77.04
76.73
61.70
36.41
30.95
29.48
O
O
Ph
OH
2e
f1 (ppm)

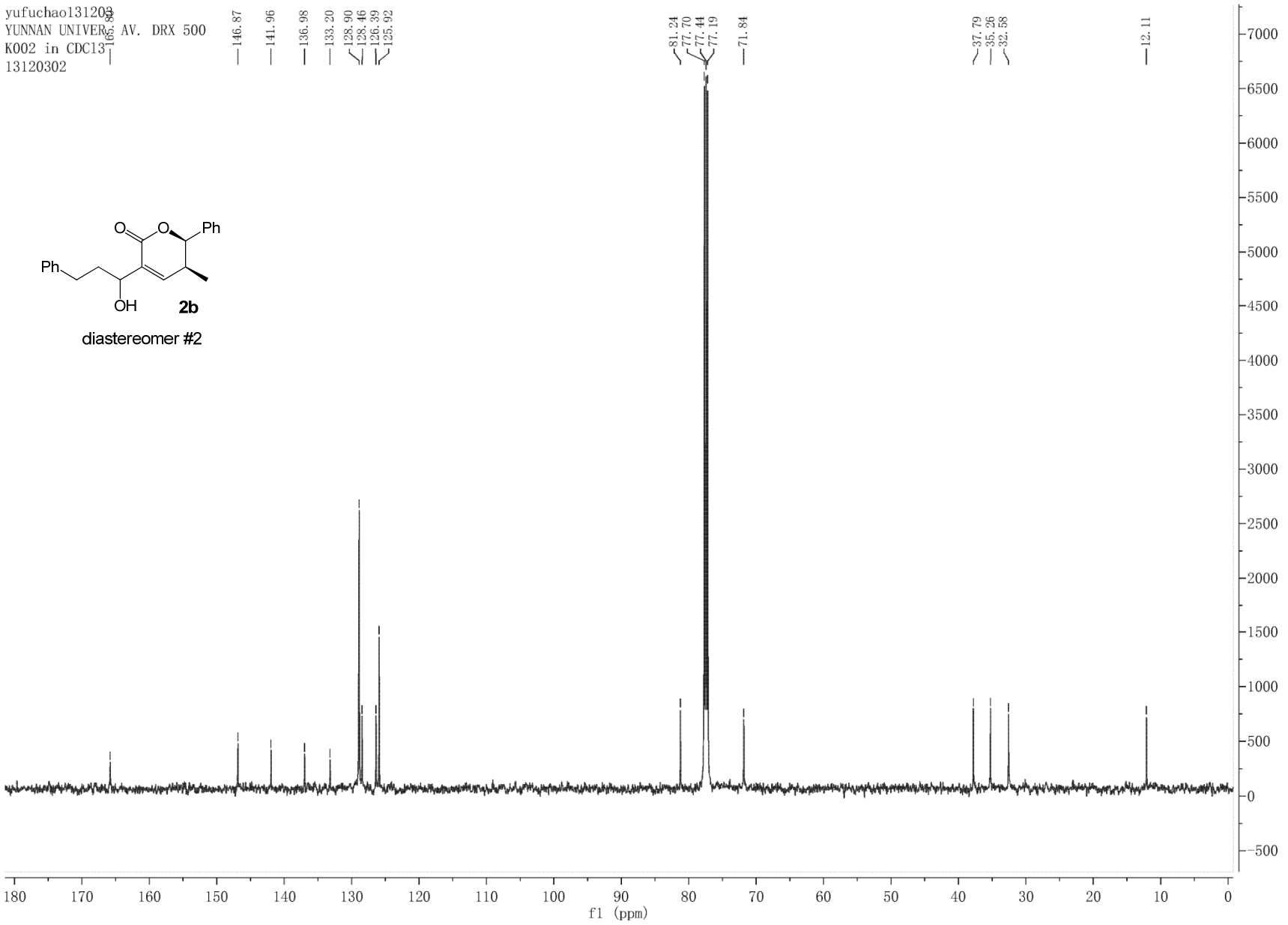

sx-68-b
sx-68-b
PROTON CDCl3 D:\\ XCF 11
Br
O
O
Ph
O
O
NO2
PNB-2f
1000
900
800
700
600
500
400
300
200
100
0
1.73
1.77
1.75
4.16
2.61
1.00
0.35
0.39
1.00
2.01
1.94
1.14
1.24
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

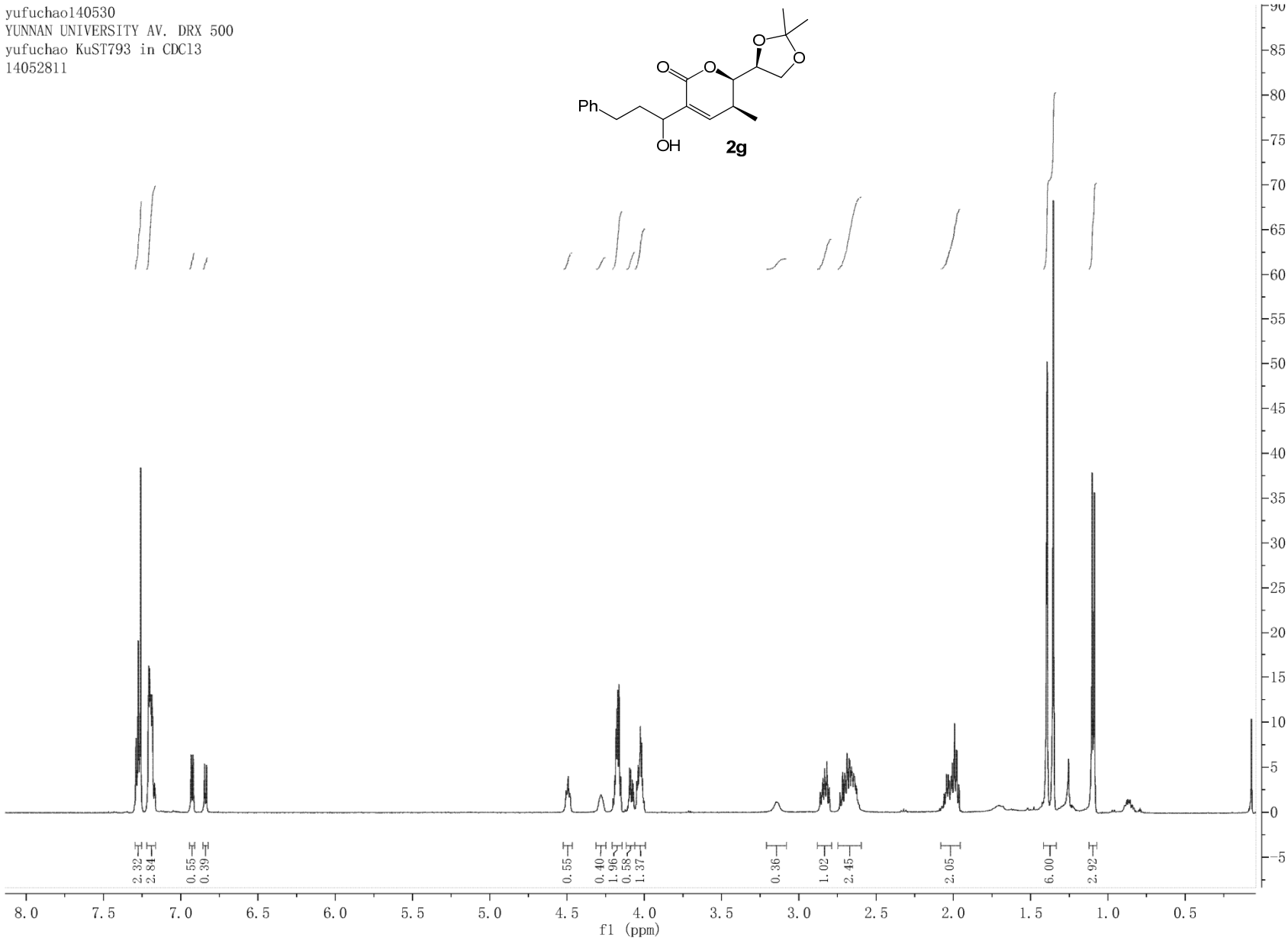

sx-68-b
sx-68-b
C13CPD CDCl3 D:\\ XCF 11
140.68
139.40
131.96
130.90
130.87
129.19
128.88
128.60
128.42
126.26
123.71
123.66
77.35
77.03
76.71
73.34
36.34
30.95
29.71
1.03
Br
O
O
Ph
O
O
NO2
PNB-2f
f1 (ppm)

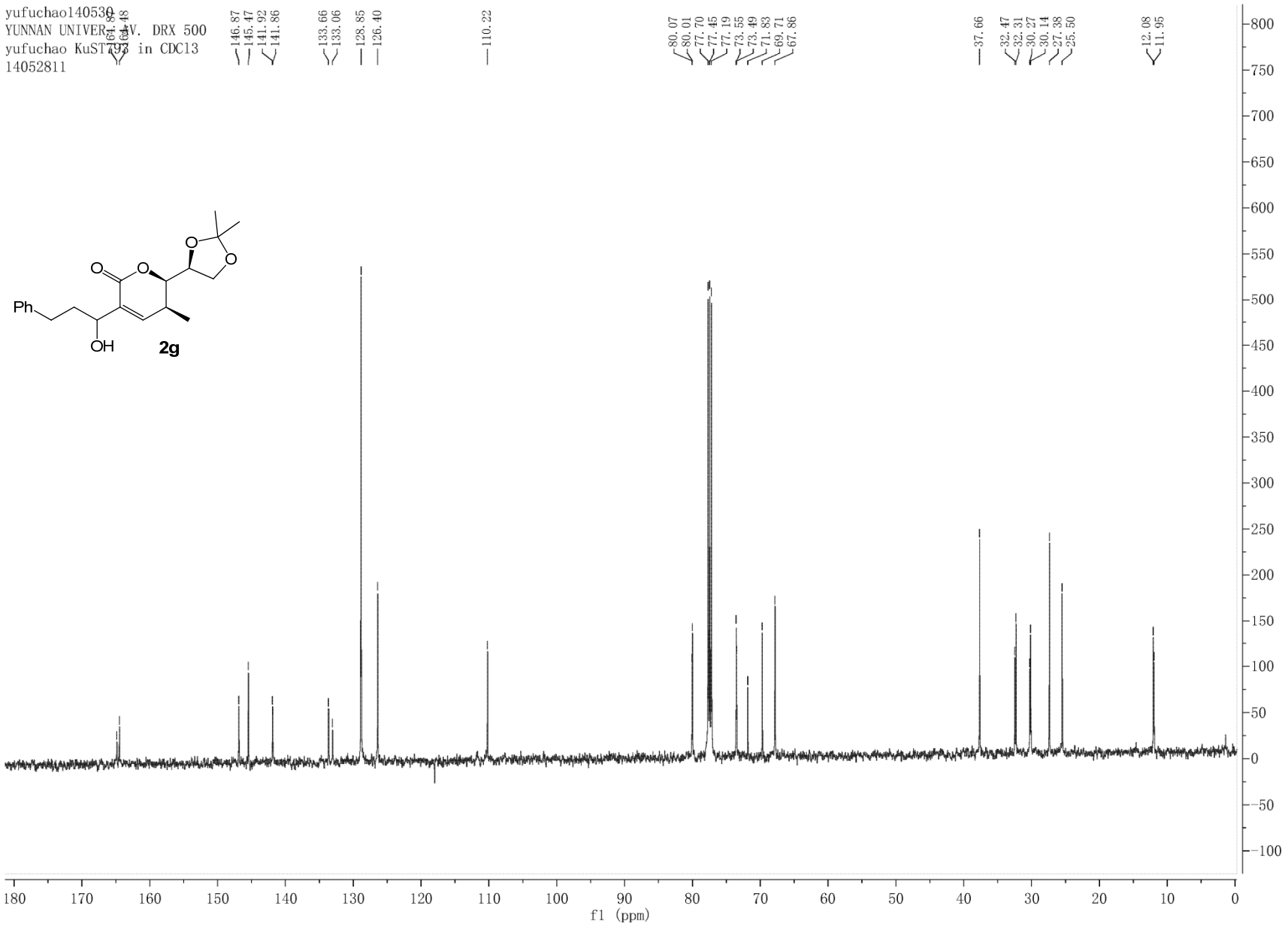

yufuchao131203
YUNNAN UNIVER. AV. DRX 500
K001 in CDCl3
13120301
Ph
OH
2b
diastereomer #1
DCM
10.14
1.01
0.94
0.96
1.77
1.13
1.06
2.03
3.02
f1 (ppm)

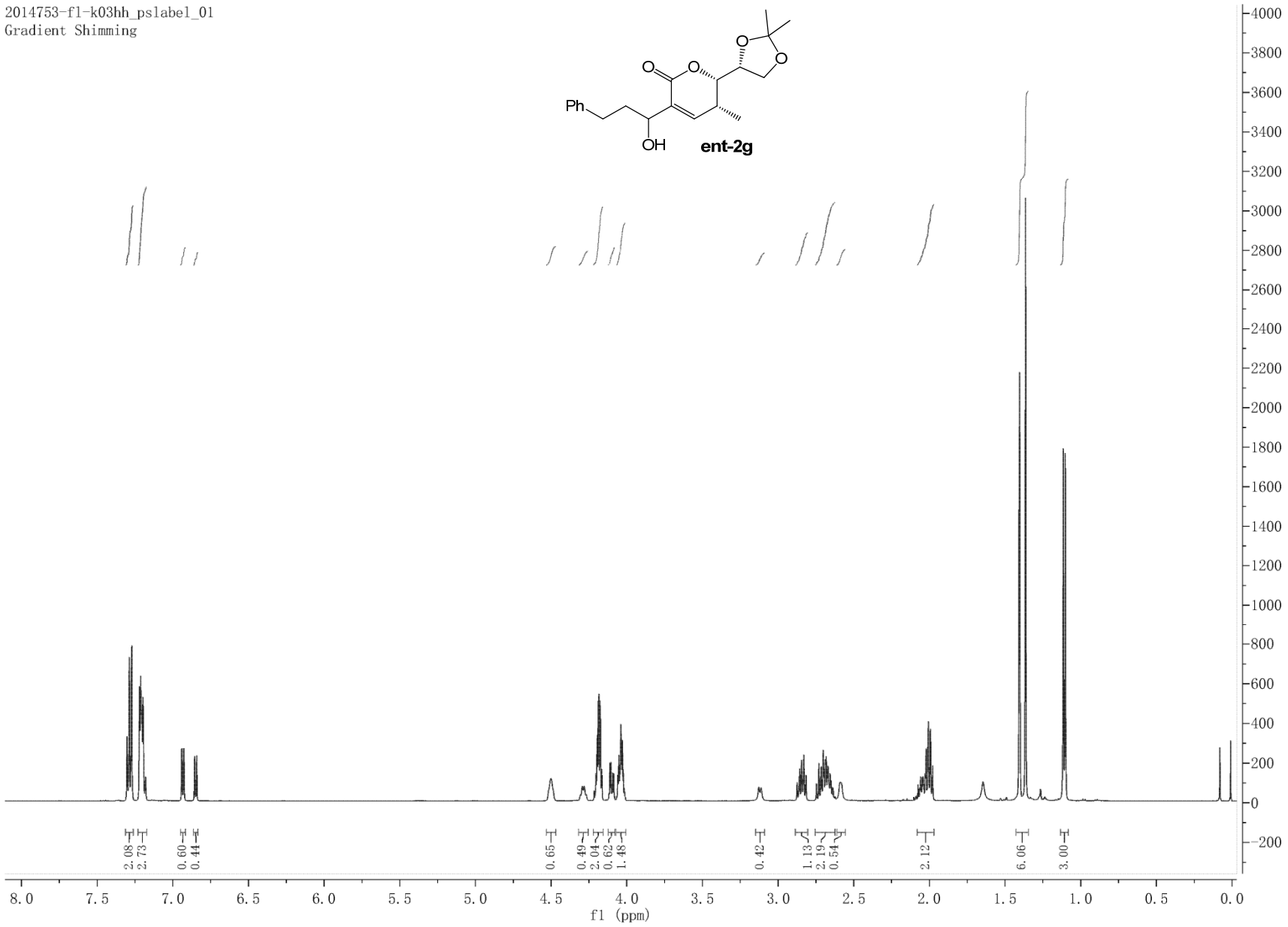

yufuchao131203
YUNNAN UNIVER.AV. DRX 500
K001 in CDC13
13120301
165.41
145.62
142.03
137.14
133.71
128.89
128.43
126.38
125.95
81.15
77.73
77.48
77.22
69.86
37.72
35.14
32.39
12.26
O
O
Ph
Ph
OH
2b
diastereomer #1
f1 (ppm)

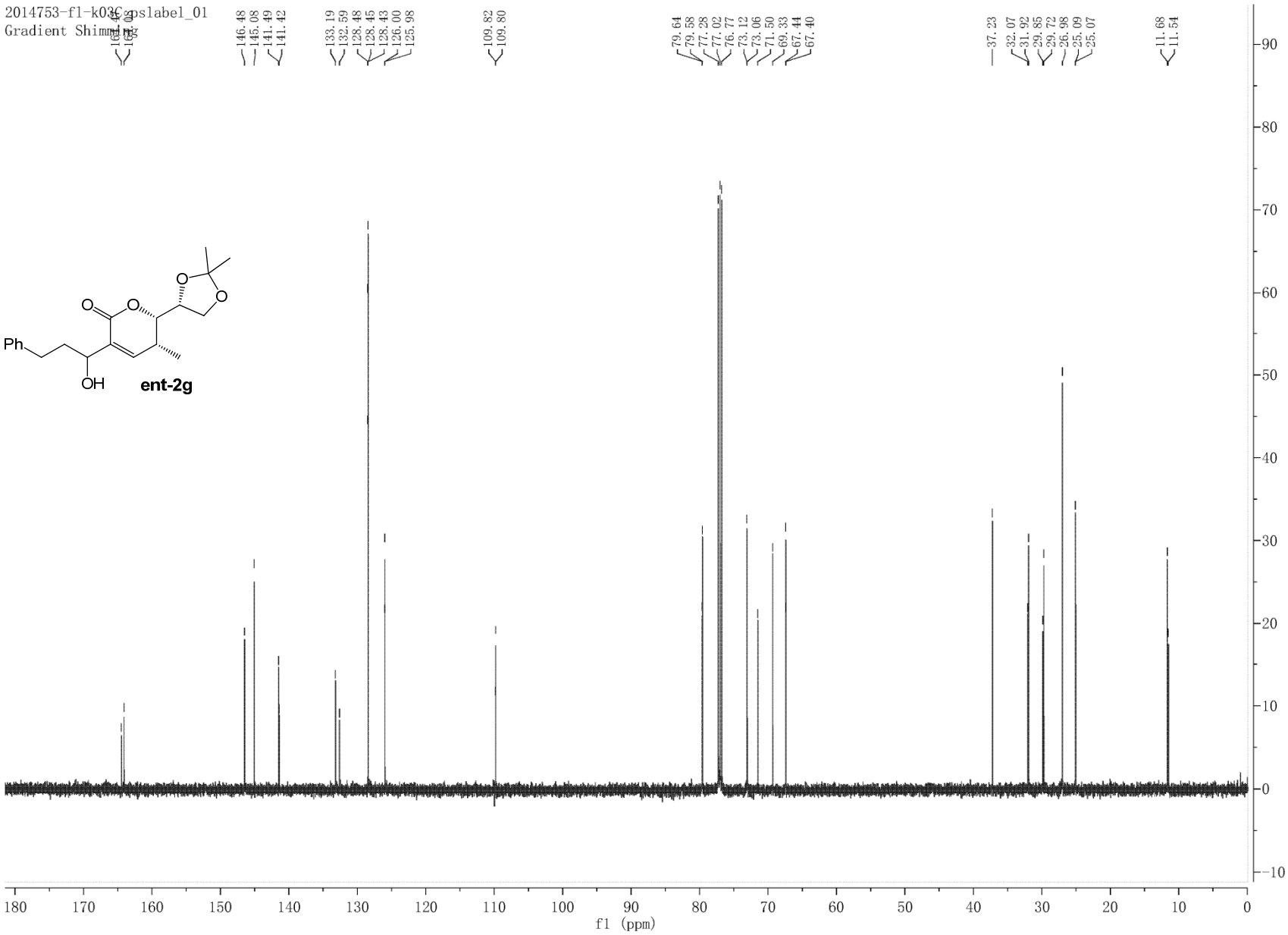

13120302
500
5.3341
5.3277
4.5037
4.2917
4.2795
3.1913
0.7245
0.7105
O
O
Ph
Ph
OH
2b
diastereomer #2
10.37
1.00
0.95
0.98
0.87
1.02
1.05
1.06
2.18
3.16
f1 (ppm)

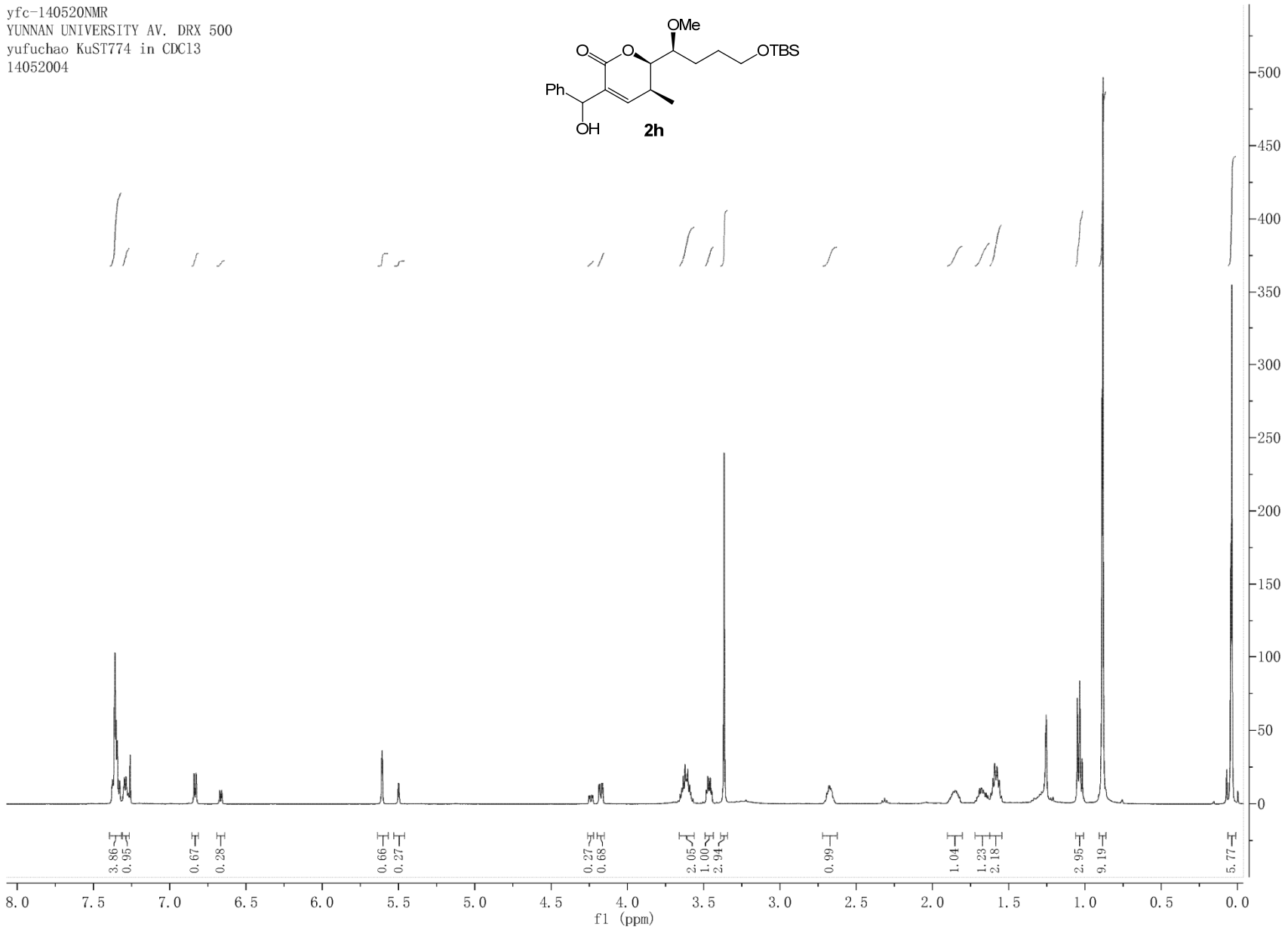

yufuchao131203
YUNNAN UNIVER. AV. DRX 500
K002 in CDC13
13120302
166.88
146.87
141.96
136.98
133.20
128.90
128.46
126.39
125.92
81.24
77.70
77.44
77.19
71.84
37.79
35.26
32.58
12.11
O
O
Ph
Ph
OH
2b
diastereomer #2
f1 (ppm)

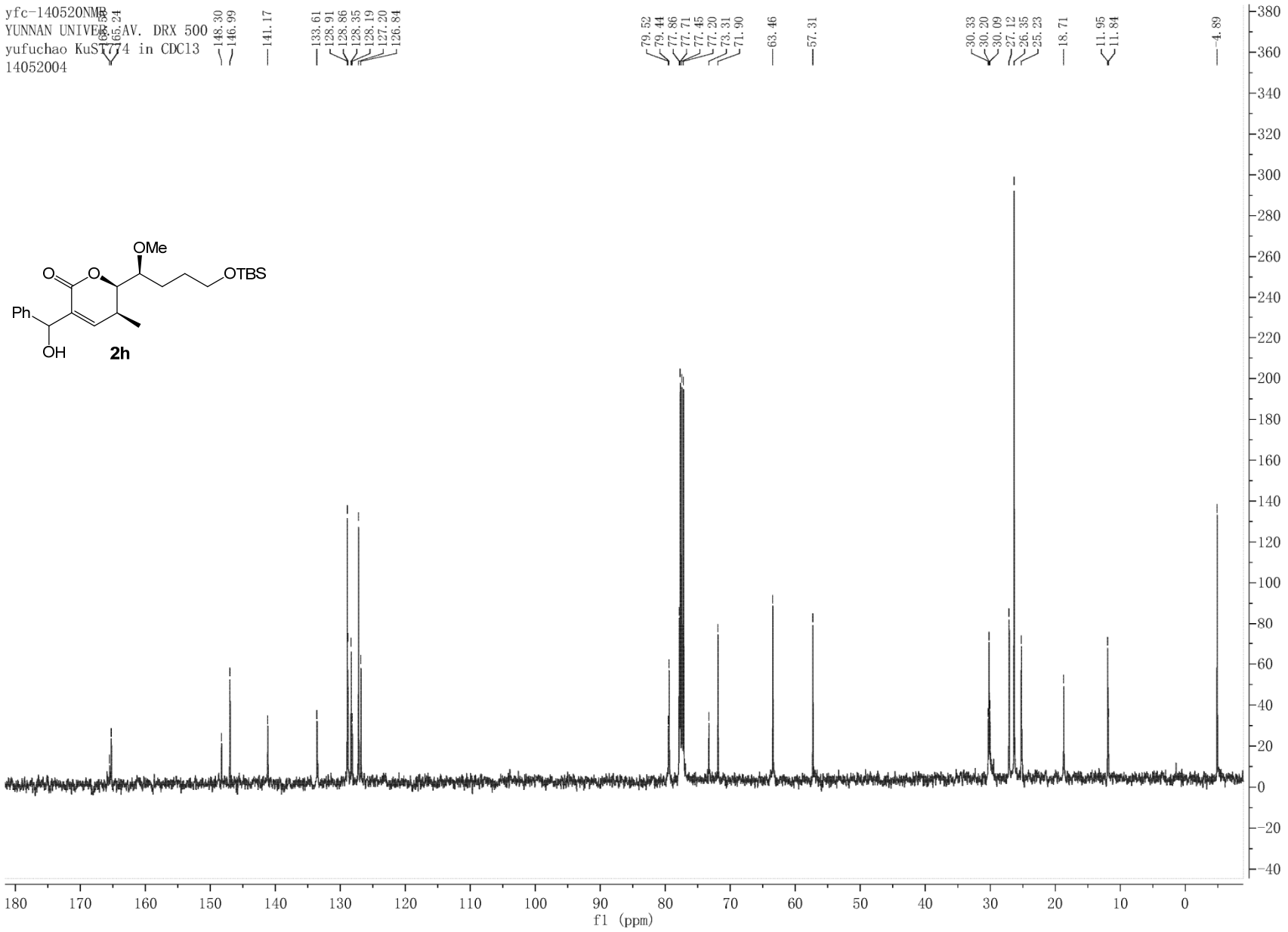

yufuchao140530
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST793 in CDCl3
14052811
Ph
OH
2g
2.32
2.84
0.55
0.39
0.55
0.40
1.96
0.58
1.37
0.36
1.02
2.45
2.05
6.00
2.92
f1 (ppm)

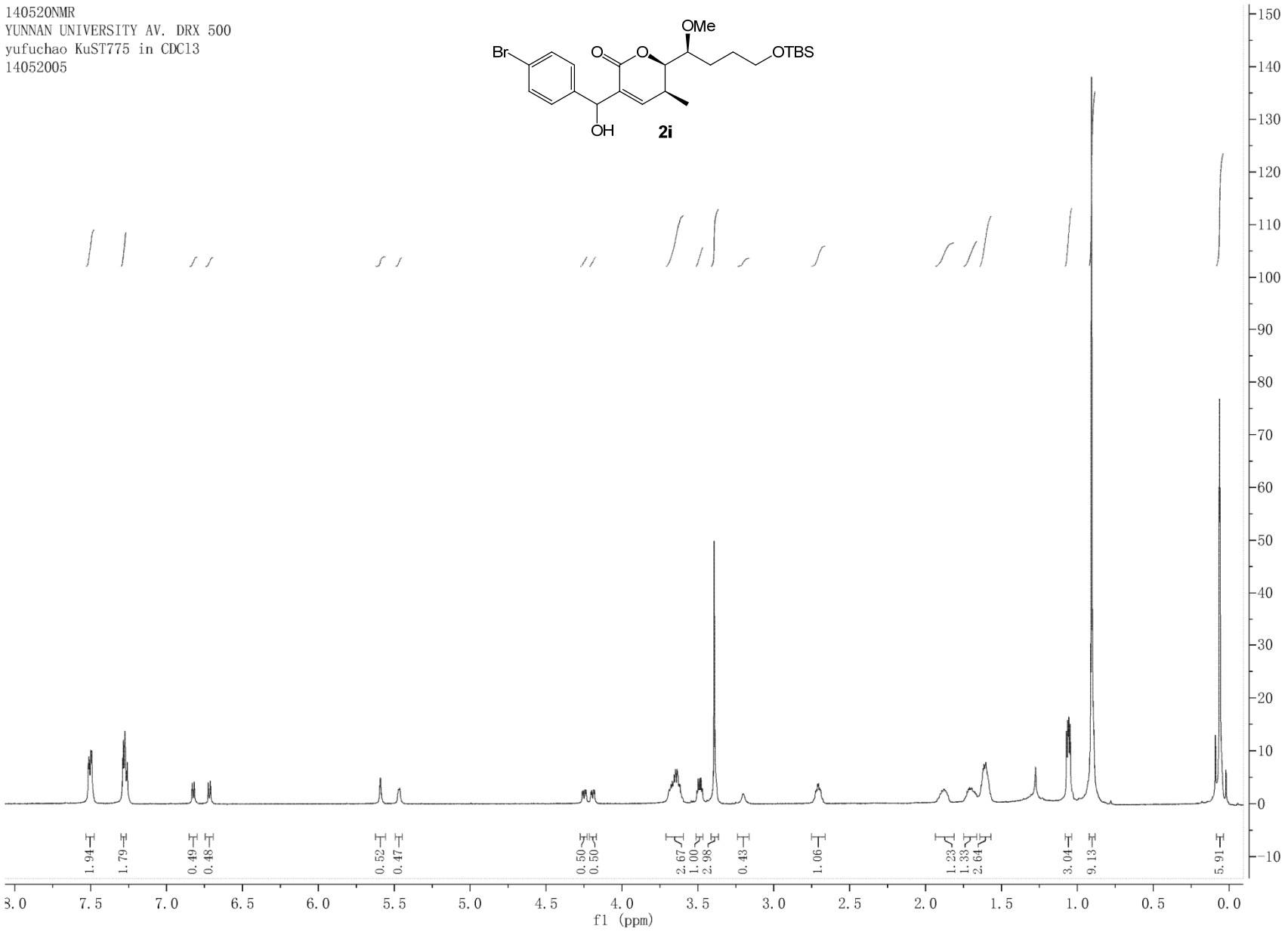

yufuchao140530
YUNNAN UNIVER. AV. DRX 500
yufuchao KuST[illegible] in CDC13
14052811
161.88
164.48
146.87
145.47
141.92
141.86
133.66
133.06
128.85
126.40
110.22
80.07
80.01
77.70
77.45
77.19
73.55
73.49
71.83
69.71
67.86
37.66
32.47
32.31
30.27
30.14
27.38
25.50
12.08
11.95
Ph
OH
2g
f1 (ppm)

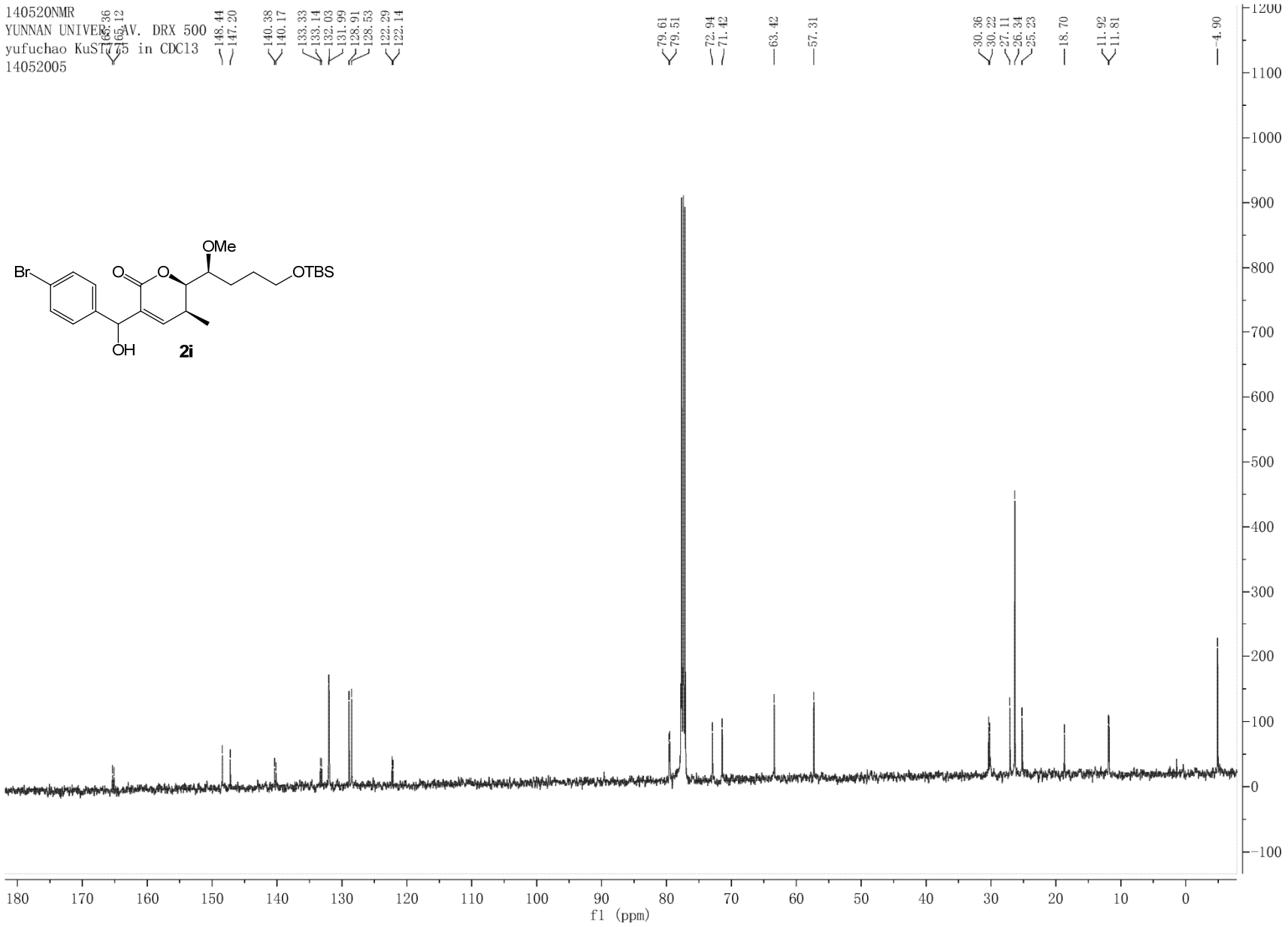

2014753-fl-k03hh_pslabel_01
Gradient Shimming
Ph
OH
ent-2g
2.08
2.73
0.60
0.44
0.65
0.49
2.04
0.62
1.48
0.42
1.13
2.19
0.54
2.12
6.06
3.00
f1 (ppm)

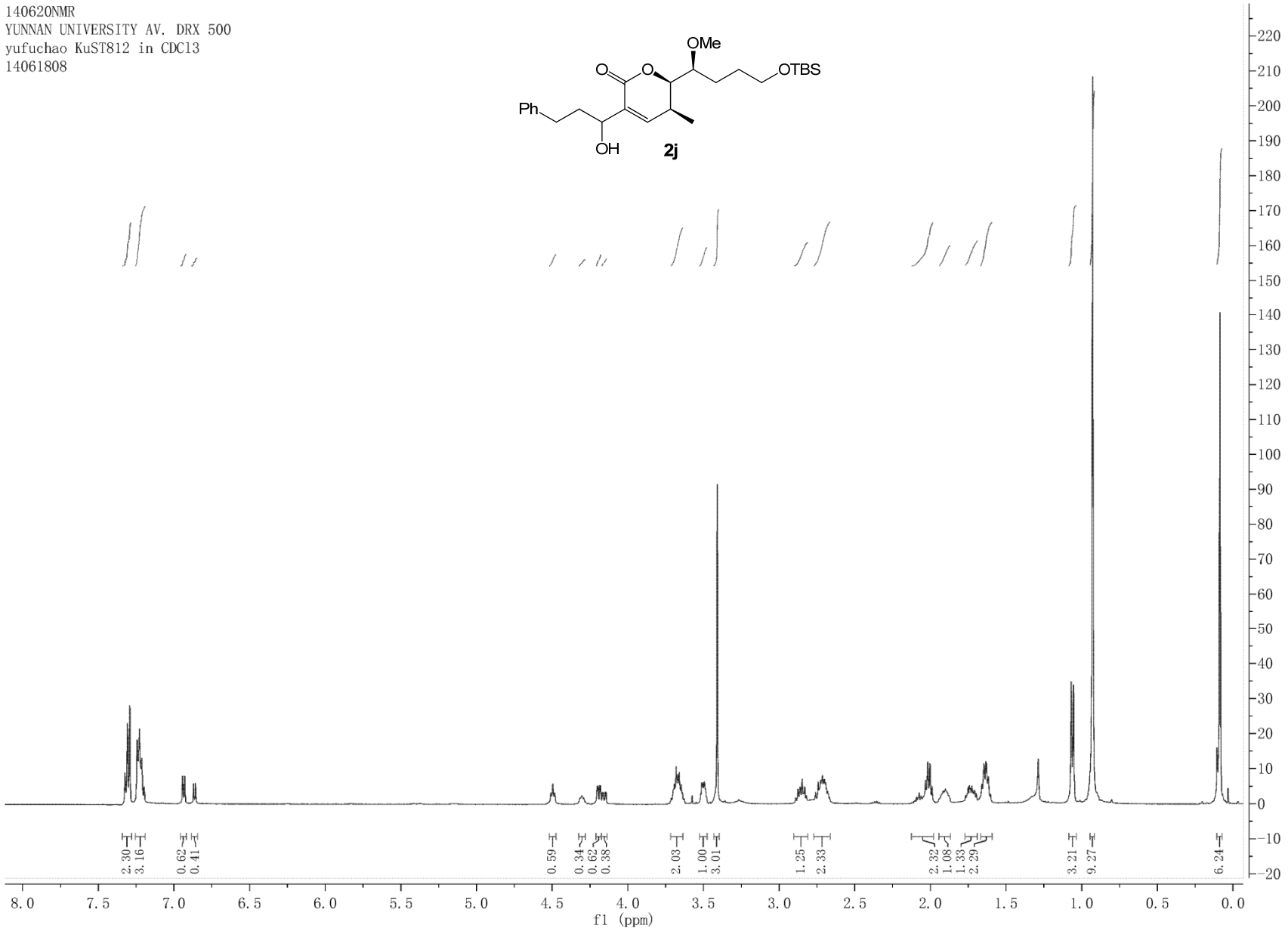

2014753-f1-k03C.apslabel_01
Gradient Shimming
166.42
166.29
146.48
145.08
141.49
141.42
133.19
132.59
128.48
128.45
128.43
126.00
125.98
109.82
109.80
79.64
79.58
77.28
77.02
76.77
73.12
73.06
71.50
69.33
67.44
67.40
37.23
32.07
31.92
29.85
29.72
26.98
25.09
25.07
11.68
11.54
Ph
OH
ent-2g
f1 (ppm)

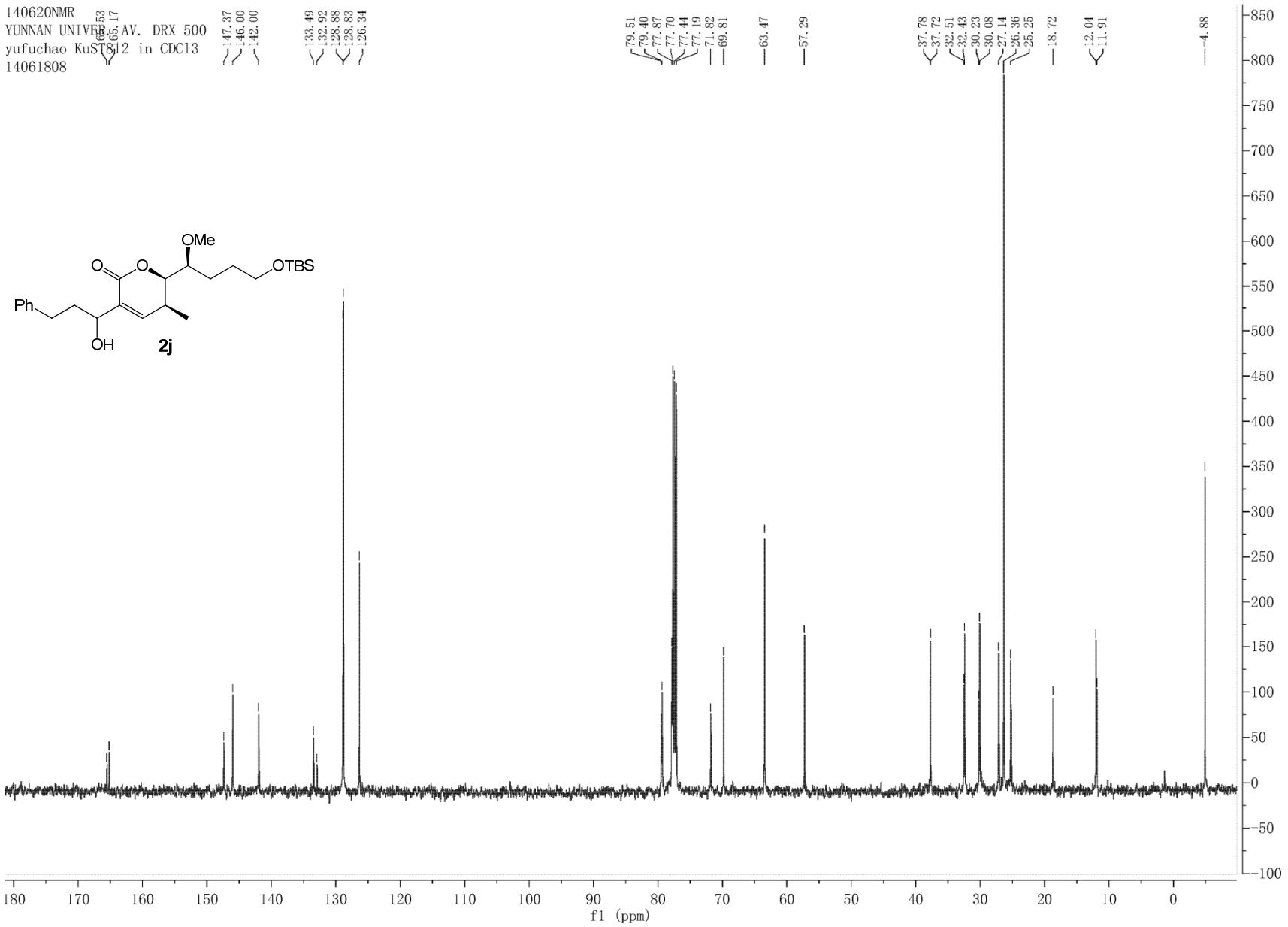

yfc-140520NMR
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST774 in CDCl3
14052004
OMe
OTBS
Ph
OH
2h
f1 (ppm)

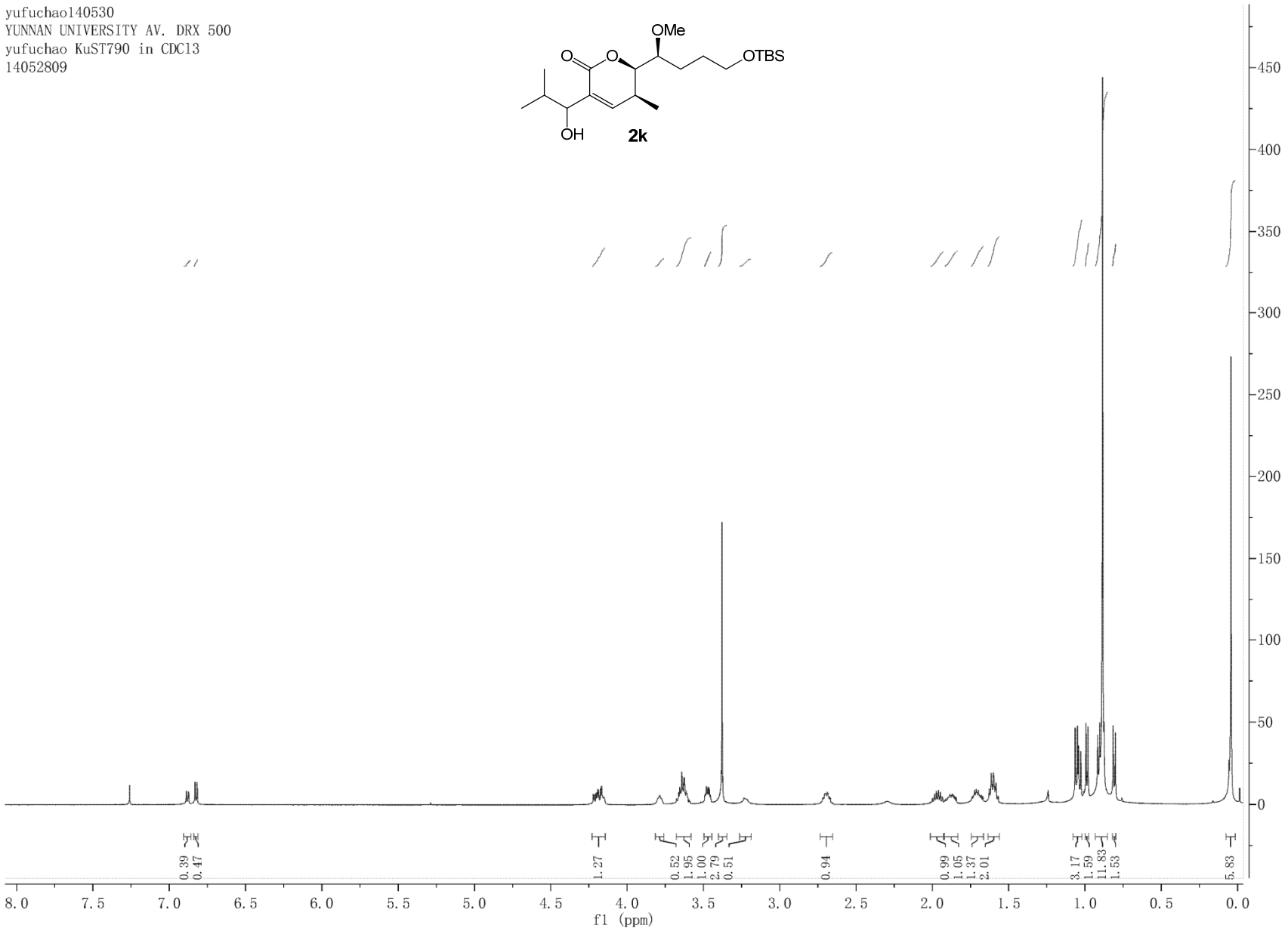

yfc-140520NMR
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST1714 in CDCl3
14052004
165.24
148.30
146.99
141.17
133.61
128.91
128.86
128.35
128.19
127.20
126.84
79.52
79.44
77.86
77.71
77.45
77.20
73.31
71.90
63.46
57.31
30.33
30.20
30.09
27.12
26.35
25.23
18.71
11.95
11.84
-4.89
OMe
OTBS
Ph
OH
2h
f1 (ppm)

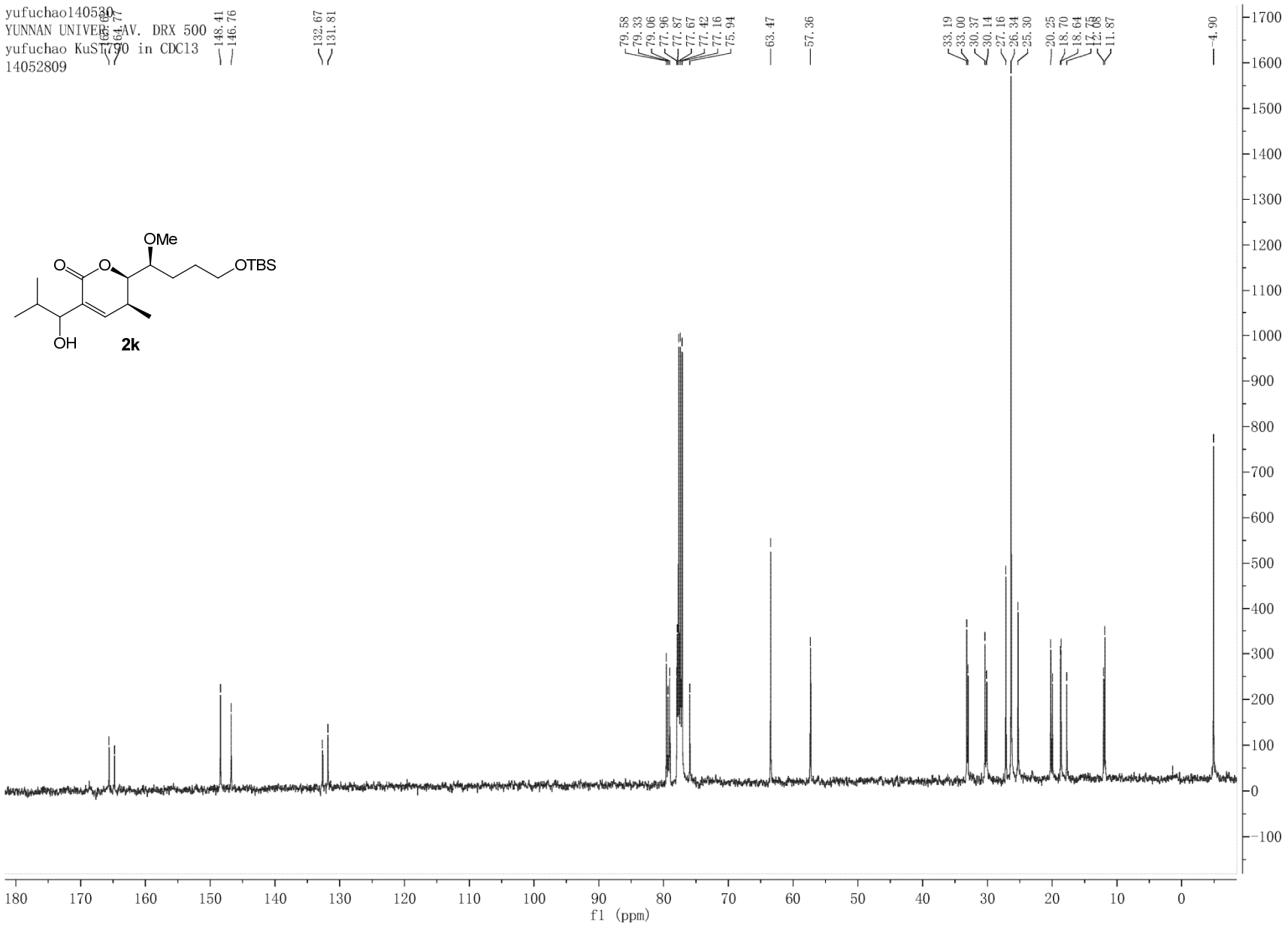

140520NMR
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST775 in CDCl3
14052005
Br
O
O
OMe
OTBS
OH
2i
1.94
1.79
0.49
0.48
0.52
0.47
0.50
0.50
2.67
1.00
2.98
0.43
1.06
1.23
1.33
2.64
3.04
9.13
5.91
f1 (ppm)

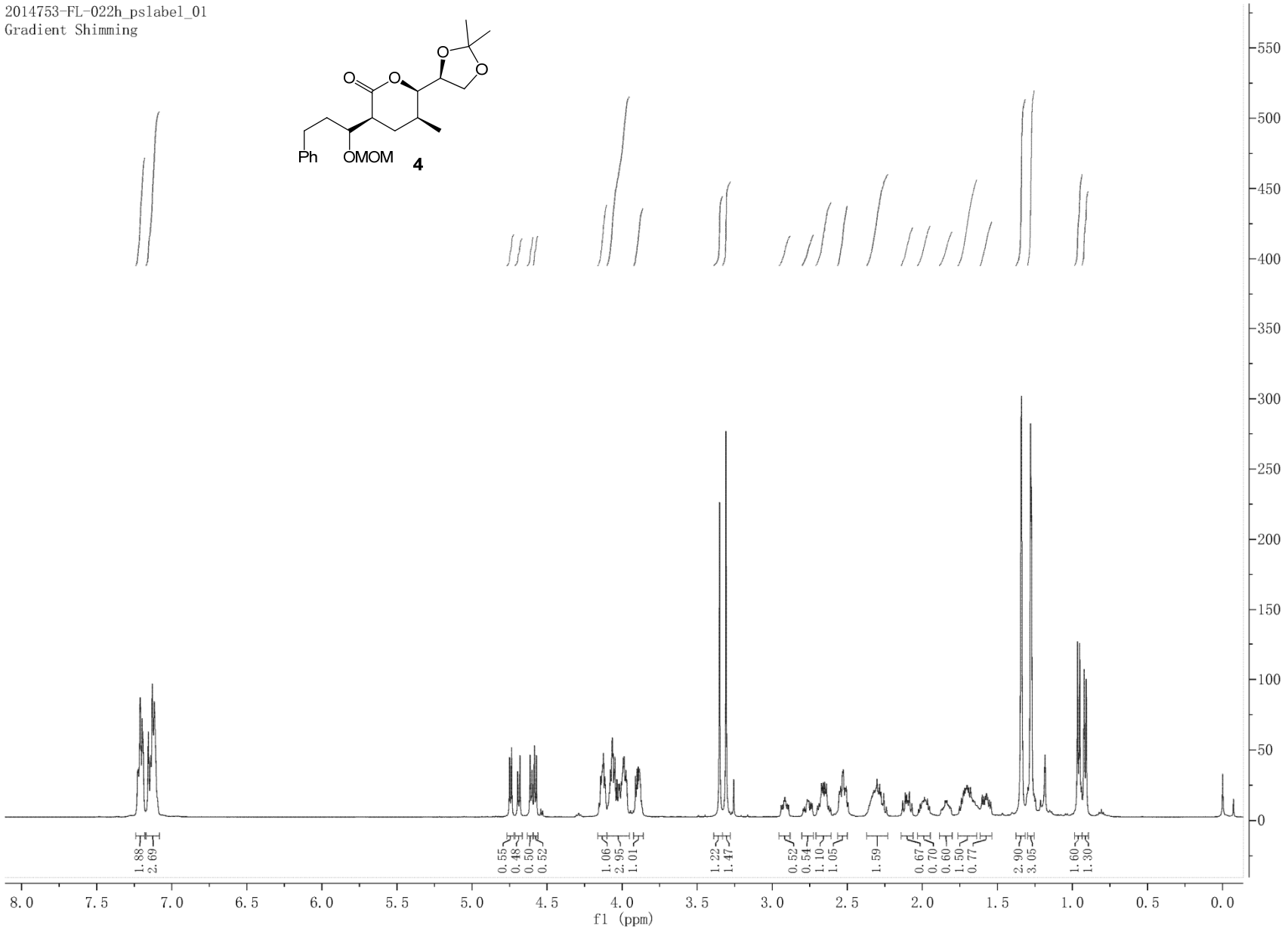

140520NMR
YUNNAN UNIVER.AV. DRX 500
yufuchao KuST[ ]5 in CDC13
14052005
165.36
165.12
148.44
147.20
140.38
140.17
133.33
133.14
132.03
131.99
128.91
128.53
122.29
122.14
79.61
79.51
72.94
71.42
63.42
57.31
30.36
30.22
27.11
26.34
25.23
18.70
11.92
11.81
-4.90
Br
O
O
OMe
OTBS
OH
2i
f1 (ppm)

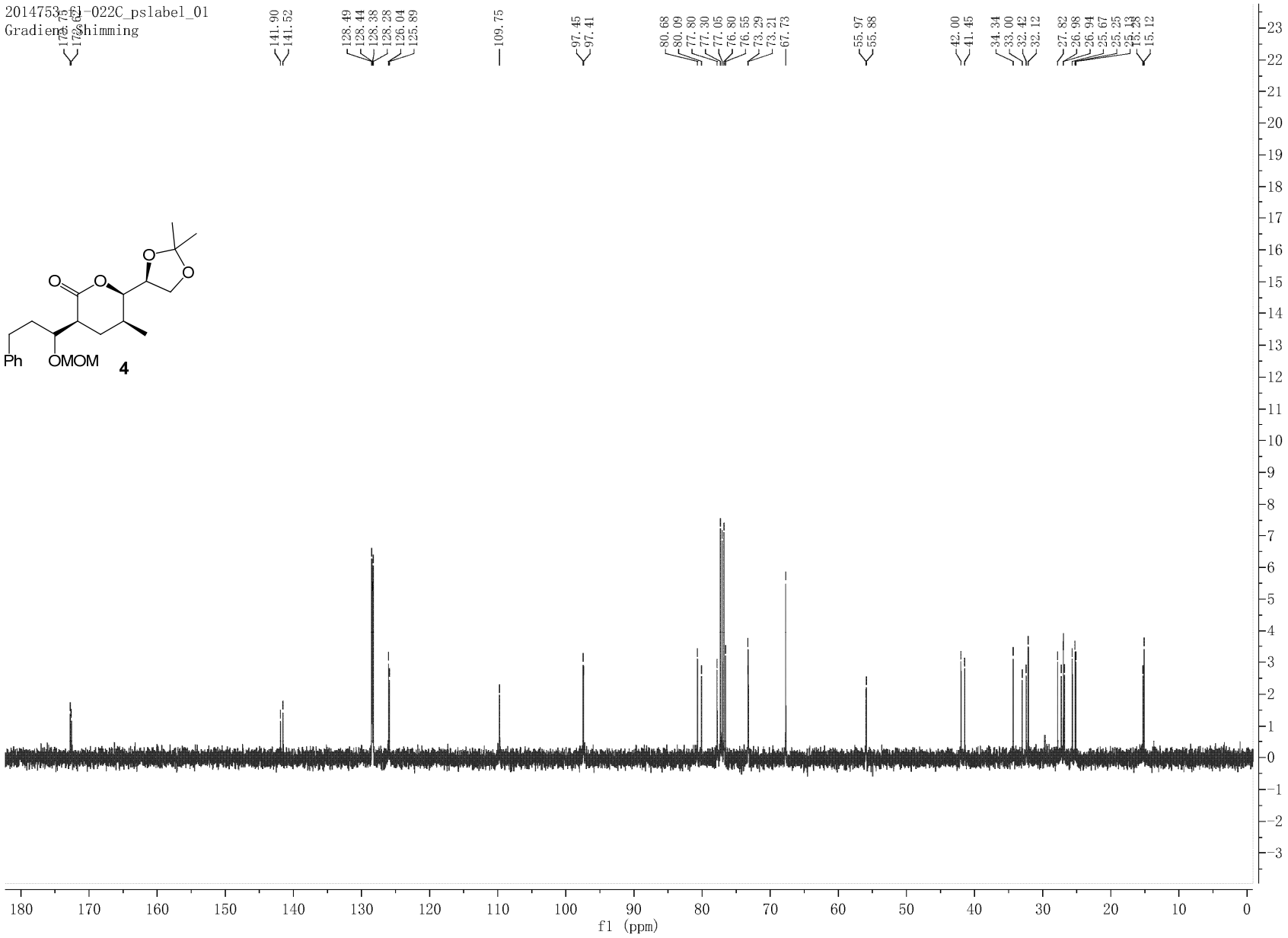

140620NMR
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST812 in CDCl3
14061808
OMe
OTBS
Ph
OH
2j
f1 (ppm)


140620NMR
YUNNAN UNIVER AV. DRX 500
yufuchao KuST812 in CDC13
14061808
166.53
165.17
147.37
146.00
142.00
133.49
132.92
128.88
128.83
126.34
79.51
79.40
77.87
77.70
77.44
77.19
71.82
69.81
63.47
57.29
37.78
37.72
32.51
32.43
30.23
30.08
27.14
26.36
25.25
18.72
12.04
11.91
-4.88
OMe
OTBS
Ph
OH
2j
f1 (ppm)


yufuchao140530
YUNNAN UNIVERSITY AV. DRX 500
yufuchao KuST790 in CDCl3
14052809
OMe
OTBS
O
O
OH
2k
f1 (ppm)


yufuchao140530
YUNNAN UNIVER. AV. DRX 500
yufuchao KuST790 in CDC13
14052809
148.41
146.76
132.67
131.81
79.58
79.33
79.06
77.96
77.87
77.67
77.42
77.16
75.94
63.47
57.36
33.19
33.00
30.37
30.14
27.16
26.34
25.30
20.25
18.70
18.64
17.75
17.08
11.87
4.90
OMe
OTBS
OH
2k
f1 (ppm)


2014753-FL-022h_pslabel_01
Gradient Shimming
O
O
O
O
Ph
OMOM
4
550
500
450
400
350
300
250
200
150
100
50
0
1.88
2.69
0.55
0.48
0.50
0.52
1.06
2.95
1.01
1.22
1.47
0.52
0.54
1.10
1.05
1.59
0.67
0.70
0.60
1.50
0.77
2.90
3.05
1.60
1.30
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


2014753-fj-022C_pslabel_01
Gradient Shimming
175.72
175.62
141.90
141.52
128.49
128.44
128.38
128.28
126.04
125.89
109.75
97.45
97.41
80.68
80.09
77.80
77.30
77.05
76.80
76.55
73.29
73.21
67.73
55.97
55.88
42.00
41.45
34.34
33.00
32.42
32.12
27.82
26.98
26.94
25.67
25.25
15.28
15.12
Ph
OMOM
4
f1 (ppm)