

## Supporting Information

## The Total Synthesis of (–)-SNF4435C and (+)-SNF4435D

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## Index of Compounds

<i>Structure</i>	<i>Exp.</i>	<i>NMR spec.</i>	<i>Structure</i>	<i>Exp.</i>	<i>NMR spec.</i>
<b>4d</b>	S3	S28 ( <sup>1</sup> H), S29 ( <sup>13</sup> C)	<b>12</b>	S10	S46 ( <sup>1</sup> H), S47 ( <sup>13</sup> C)
<b>5d</b>	S4	S30 ( <sup>1</sup> H)	<b>13</b>	S11	S48 ( <sup>1</sup> H), S49 ( <sup>13</sup> C)
<b>mixed endo-8d, exo-9d</b>	S4	S31 ( <sup>1</sup> H)	<b>14</b>	S12	S50 ( <sup>1</sup> H), S51 ( <sup>13</sup> C)
<b>4f</b>	S5	S32 ( <sup>1</sup> H), S33 ( <sup>13</sup> C)	<b>15</b>	S12	S52 ( <sup>1</sup> H), S53 ( <sup>13</sup> C)
<b>5f</b>	S6	S34 ( <sup>1</sup> H), S35 ( <sup>13</sup> C)	<b>16</b>	S13	S54 ( <sup>1</sup> H), S55 ( <sup>13</sup> C)
<b>endo-8f</b>	S6	S36 ( <sup>1</sup> H), S37 ( <sup>13</sup> C)	<b>Mosher -16</b>	S13	S56 ( <sup>1</sup> H)
<b>exo-9f</b>	S6	S38 ( <sup>1</sup> H), S39 ( <sup>13</sup> C)	<b>Mosher – racemic 16</b>	S13	S57 ( <sup>1</sup> H)
<b>4g</b>	S7	S40 ( <sup>1</sup> H), S41 ( <sup>13</sup> C)	<b>17</b>	S14	S58 ( <sup>1</sup> H), S59 ( <sup>13</sup> C)
<b>5g</b>	S8	S42 ( <sup>1</sup> H)	<b>19</b>	S15	S60 ( <sup>1</sup> H), S61 ( <sup>13</sup> C)
<b>mixed endo-8g, endo- 8g', exo- 9g, exo- 9g'</b>	S9	S43 ( <sup>1</sup> H)	<b>20</b>	S15	S62 ( <sup>1</sup> H), S63 ( <sup>13</sup> C)
			<b>21</b>	S16	S64 ( <sup>1</sup> H), S65 ( <sup>13</sup> C)
			<b>22</b>	S17	S66 ( <sup>1</sup> H), S67 ( <sup>13</sup> C)
			<b>23</b>	S17	S68 ( <sup>1</sup> H)
<b>11</b>	S10	S44 ( <sup>1</sup> H), S45 ( <sup>13</sup> C)	<b>1a+1b</b>	S18	S69 ( <sup>1</sup> H)
			<b>1a</b>	S17	S70 ( <sup>1</sup> H), S71 ( <sup>13</sup> C)
			<b>1b</b>	S17	S72 ( <sup>1</sup> H), S73 ( <sup>13</sup> C)

## General Experimental Methods

- **Procedures**

All air- and moisture-sensitive reactions were performed under argon in oven-dried or flame-dried glassware. Solvents and solutions for air- and moisture-sensitive reactions were transferred via syringe or cannula with the maintenance of a positive pressure of an inert gas. Concentration of solutions was accomplished with a Buchi rotary evaporator evacuated by a water aspirator. In general, the residual solvent was removed on a vacuum line at 1-1.5 torr.

- **Reagents and Solvents**

Unless stated otherwise, commercially available reagents were used as supplied and solvents were dried over molecular sieves prior to use. HPLC grade hexane and HPLC grade ethyl acetate (EtOAc) were used in chromatography. Tetrahydrofuran (THF) and diethyl ether (Et<sub>2</sub>O) were distilled from sodium-benzophenone ketyl and dichloromethane was distilled from calcium hydride under argon gas. Diisopropylethylamine and triethylamine were distilled from sodium.

- **Chromatography**

All experiments were monitored by thin layer chromatography (TLC) performed on EM Science precoated silica gel 60<sub>F-254</sub> glass-supported plates with 0.25 mm thickness. Spots were visualized by exposure to ultraviolet (UV) light (254 nm) or to iodine vapor or by staining with a 10 % solution of phosphomolybdic acid (PMA) in ethanol and then heating. Flash chromatography was carried out with Fisher brand silica gel (170-400 mesh). Preparative thin layer chromatography (PrepTLC) was performed on EM Science precoated silica gel 60<sub>F-254</sub> glass-supported plates with 1.00 mm thickness.

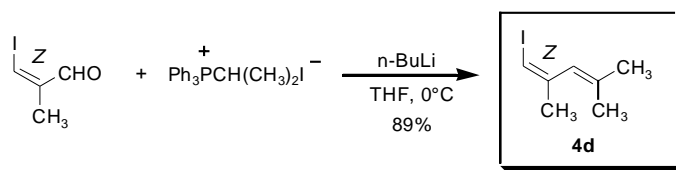
- **Physical and Spectroscopic Measurements**

Melting points were measured on a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer 1600 Series FT-IR instrument. Samples were scanned as neat liquids on sodium chloride (NaCl) salt plates. Frequencies are reported in reciprocal centimeters (cm<sup>-1</sup>). Nuclear magnetic resonance (NMR) spectra were recorded with a Varian Inova-600 (600 MHz for <sup>1</sup>H), Varian Inova-500 (500 MHz for <sup>1</sup>H), Varian Inova-400 (400 MHz for <sup>1</sup>H, 100 MHz for <sup>13</sup>C), or Gemini-2300 (300 MHz for <sup>1</sup>H, 75 MHz for <sup>13</sup>C) spectrometer. Chemical shifts for proton NMR are reported in parts per million (ppm) relative to the singlet at 7.26 ppm for chloroform-*d* or relative to the singlet at 7.15 ppm for benzene-*d*<sub>6</sub>. Chemical shifts for carbon NMR are reported in ppm with the center line of the triplet for chloroform-*d* set at 77.00 ppm. The following abbreviations are used in the experimental section for the description of <sup>1</sup>H-NMR spectra: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), doublet of doublets (dd), doublet of quartets (dq), and broad singlet (bs). For complex multiplets, the chemical shift is given for the center of the multiplet. Coupling constants, *J*, are reported in Hertz (Hz). High resolution mass spectra were obtained with a Kratos MS-80 spectrometer.

## • Materials Prepared by Literature Methods

(Z)-3-Iodo-2-methyl-2-propenal was prepared by the method of Larock.<sup>1</sup> (E, Z)-Iododiene **3** was best prepared by the Stork-Zhao procedure as modified by Beaudry and Trauner.<sup>2</sup> The Still-Gennari reagents, [bis-(2,2,2-trifluoroethoxy)-phosphoryl]-acetic acid ethyl ester<sup>3a,b</sup> and (2-oxo-tetrahydrofuran-3-yl)-phosphonic acid diethyl ester<sup>4</sup> were prepared by published methods. Methanesulfonic acid 4-(*tert*-butyldimethylsilanyloxy)-but-2-enyl ester was prepared by the method of Ziegler.<sup>5</sup> 2-Methyl-3-oxo-pentanoic acid ethyl ester was prepared by alkylation of the dianion of 2-methyl-3-oxo-butanoic acid ethyl ester.<sup>6</sup>

## • Experimental Procedures



**Diene 4d.** To a stirred suspension of isopropyltriphenylphosphonium iodide (2.76 g, 4.27 mmol) in THF (44 mL) was added n-BuLi (2.5 M in hexane, 1.71 mL, 4.27 mmol) at 0 °C. After 30 min, (Z)-3-iodo-2-methyl-2-propenal (560 mg, 2.85 mmol) in THF (26 mL) was added dropwise at 0 °C and the reaction mixture was stirred at rt for 2 h. Then it was quenched with satd aq  $\text{NH}_4\text{Cl}$  and extracted with  $\text{Et}_2\text{O}$ . The combined organic solution was washed with water and brine, dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The crude product was purified on silica gel with  $\text{Et}_2\text{O}$ /hexane (1/5) to give 566 mg (89 %) of a pale yellow oil.

$R_f$ : 0.7 ( $\text{Et}_2\text{O}$  /hexanes, 1/5)

$^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )

$\delta$  5.95 (t,  $J = 1.2$  Hz, 1H), 5.64 (s, 1H), 1.96 (d,  $J = 0.6$  Hz, 3H), 1.80 (d,  $J = 1.2$  Hz, 3H), 1.69 (d,  $J = 1.2$  Hz, 3H).

$^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )

$\delta$  145.3, 136.8, 127.2, 76.7, 26.4, 24.8, 20.0.

IR: (neat)

$\nu$  1100, 1034, 906  $\text{cm}^{-1}$

(1) Larock R. C.; Doty, M. J.; Han, X. *J. Org. Chem.*; **1999**, 64(24), 8770.

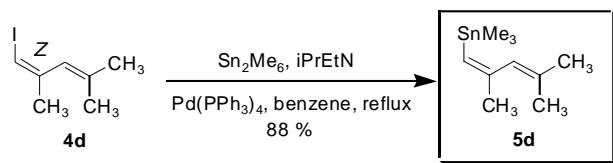
(2) Beaudry, C. M.; Trauner, D. *Org. Lett.* **2002**, 4, 2221.

(3) (a) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, 24, 4405.; (b) Tay, M. K.; About-Jaude, E.; Collignon, N.; Teulade, M. P.; Savignac, P. *Synth. Commun.* **1988**, 18(12), 1349.

(4) Murphy, J. A.; Rasheed, F.; Roome, S. J.; Scott, K. A.; Lewis, L. *J. Chem. Soc., Perkin Trans. 1*, **1998**, 15, 2331.

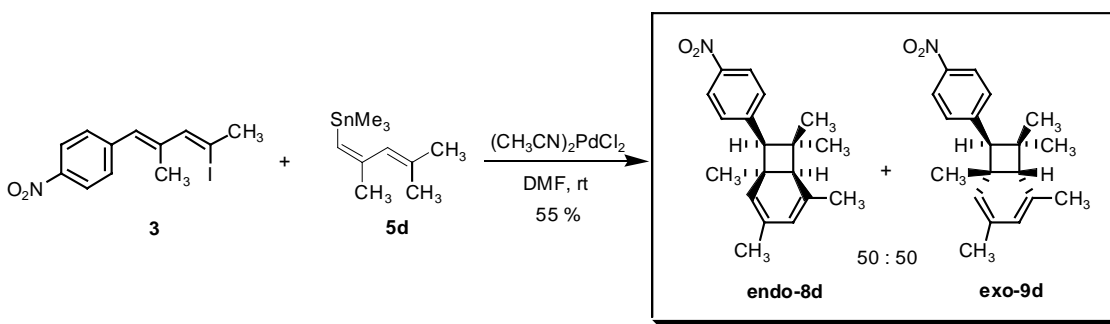
(5) Ziegler, F. E.; Lim, H. *J. Org. Chem.* **1984**, 49, 3278.

(6) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, 96, 1082.



**Vinyl stannane 5d.** To a stirred solution of diene **4d** (241 mg, 1.08 mmol) in dry benzene (11 mL) was added diisopropylethylamine (56.7  $\mu$ L, 0.324 mmol) and hexamethylditin (533  $\mu$ L, 1.62 mmol) and 5 mol% of tetrakis(triphenylphosphine)palladium (62.6 mg, 0.0542 mmol). The mixture was degassed with bubbling by an Ar stream for 10 min and then it was stirred at 80  $^{\circ}$ C for 12 h. The mixture was cooled to rt, and stirred with KF on Celite<sup>®</sup> (50/50 wt). The resulting suspension was filtered through Celite<sup>®</sup> and the filtrate was concentrated. The residue was purified further by chromatography on a short pad of basic alumina, eluted with Et<sub>2</sub>O/pentane (1/1). Concentration afforded a pale yellow oil 223 mg (88 %), sufficiently pure for use in the next step.

*R<sub>f</sub>*: 0.8 (EtOAc/hexanes, 1/10)  
<sup>1</sup>H NMR: (400 MHz, CDCl<sub>3</sub>, crude)  
 $\delta$  5.75 (s, 1H), 5.71 (t, *J* = 0.90 Hz, 1H), 1.96 (s, 3H), 1.73 (s, 3H), 1.67 (s, 3H), 0.20 (s, 9H).



**Endo-8d and Exo-9d.** To a solution of iododiene **3** (254 mg, 0.772 mmol) in dry DMF (8 mL) was added vinyl stannane **5d** (200 mg, 0.772 mmol) and 10 mol% (CH<sub>3</sub>CN)<sub>2</sub>PdCl<sub>2</sub> catalyst (20.0 mg, 0.0772 mmol) at rt. The reaction flask was wrapped by aluminum foil. After 16 h at rt, catalyst (10.0 mg, 0.0386 mmol) was added again, and the reaction was stirred for 6h more at rt. To remove trimethyltin iodide, the reaction was stirred with KF on Celite<sup>®</sup> (50/50 wt) for 2 h and filtered through Celite<sup>®</sup>. The resulting solution was washed with aq NaHCO<sub>3</sub> and the aqueous layer was extracted with Et<sub>2</sub>O. The combined organic solution was washed with water and brine, dried over anhydrous MgSO<sub>4</sub>, and concentrated. The crude product was purified further by column chromatography with Et<sub>2</sub>O/hexane (1/20) to give 126 mg (55 %) as a mixture of endo and exo products in a ratio of 1:1.<sup>7</sup>

<sup>7</sup> The <sup>1</sup>H-NMR spectrum of the mixture was deconvoluted by information derived from the nOe experiments so that individual peaks could be assigned to each component of the mixture.



**Endo-8d**

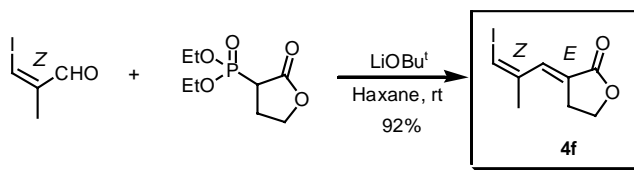
$R_f$ : 0.8 (EtOAc/hexanes, 1/10)  
 $^1\text{H NMR}$ : (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  8.12 (d,  $J = 7.8$  Hz, 2H), 7.48 (d,  $J = 7.8$  Hz, 2H), 5.50 (s, 1H), 5.05 (s, 1H), 3.31 (s, 1H), 2.40 (s, 1H), 1.71 (s, 3H), 1.67 (s, 3H), 1.235 (s, 3H), 1.232 (s, 3H), 0.99 (s, 3H).

**Exo-9d**

$R_f$ : 0.8 (EtOAc/hexanes, 1/10)  
 $^1\text{H NMR}$ : (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  8.14 (d,  $J = 7.8$  Hz, 2H), 7.41 (d,  $J = 7.8$  Hz, 1H), 5.56 (s, 1H), 5.12 (s, 1H), 3.29 (s, 1H), 2.44 (s, 1H), 1.71 (s, 3H), 1.68 (s, 3H), 1.20 (s, 3H), 1.11 (s, 3H), 1.03 (s, 3H).

**For mixture of endo-8d and exo-9d**

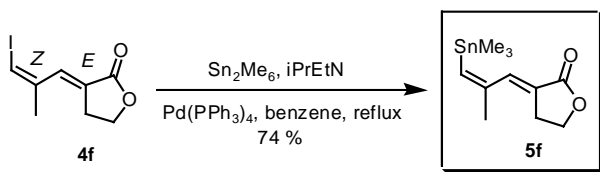
$\text{IR}$ : (neat)  
 $\nu$  2954, 2857, 1345, 1086  $\text{cm}^{-1}$   
 $\text{HRMS}$ : (FAB)  
 Calcd. for  $\text{C}_{19}\text{H}_{23}\text{NO}_2\text{Na}$   $[(M + \text{Na})]^+$  320.1626, found 320.1628.



**(E, Z)-Lactone 4f.** (2-Oxo-tetrahydrofuran-3-yl)phosphonic acid diethyl ester (1.39 g, 6.27 mmol) was added to dry hexane (7 mL). Ar was introduced and the mixture was stirred at room temperature. Lithium *tert*-butoxide (1.0 M in hexane, 6.27 mL, 6.27 mmol) was added in one portion via syringe. The solution became turbid, but no significant heating was observed. After 15 min, (Z)-3-iodo-2-methyl-2-propenal (820 mg, 4.18 mmol) in hexane (2 mL) was added dropwise over the course of 10 min via cannula. The solution became clear, and then was allowed to stir for an additional hour. It was quenched with water and the combined organic solution was washed with water, dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/10) to give 1.02 g (92 %) of a light yellowish white powder.

$R_f$ : 0.1 (EtOAc/hexanes, 1/5)  
 $^1\text{H NMR}$ : (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  7.40 (t,  $J = 2.7$  Hz, 1H), 6.62 (s, 1H), 4.39 (t,  $J = 7.2$  Hz, 2H), 3.12 (td,  $J = 7.2$  Hz,  $J = 2.7$  Hz, 2H), 2.13 (s, 3H).  
 $^{13}\text{C NMR}$ : (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  172.1, 141.1, 138.0, 126.9, 88.5, 65.4, 26.9, 23.1.  
 $\text{IR}$ : (neat)  
 $\nu$  2253, 1750, 1197, 1034  $\text{cm}^{-1}$   
 $\text{HRMS}$ : (FAB)

Calcd. for  $C_8H_9IO_2Na [(M + Na)]^+$  286.9545, found 286.9557.



**(E,Z)-Vinyl stannane 5f.** To a stirred solution of (E, Z)-lactone **4f** (134 mg, 0.507 mmol) in dry benzene (5.0 mL) was added diisopropylethylamine (26.5  $\mu$ L, 0.152 mmol) and hexamethylditin (216  $\mu$ L, 0.608 mmol) and 5 mol% of tetrakis(triphenylphosphine)palladium (29.3 mg, 0.0253 mmol). The mixture was degassed with bubbling by an Ar stream for 10 min and then was stirred at 80 °C for 12 h. The mixture was cooled to rt, and stirred with KF on Celite® (50/50 wt). The resulting suspension was filtered through Celite® and the filtrate was concentrated. The residue was purified further by chromatography on a short pad of basic alumina, eluted with  $Et_2O$ /pentane (1/5). Concentration afforded 113 mg (74 %) of a pale yellow oil, sufficiently pure for use in the next step.

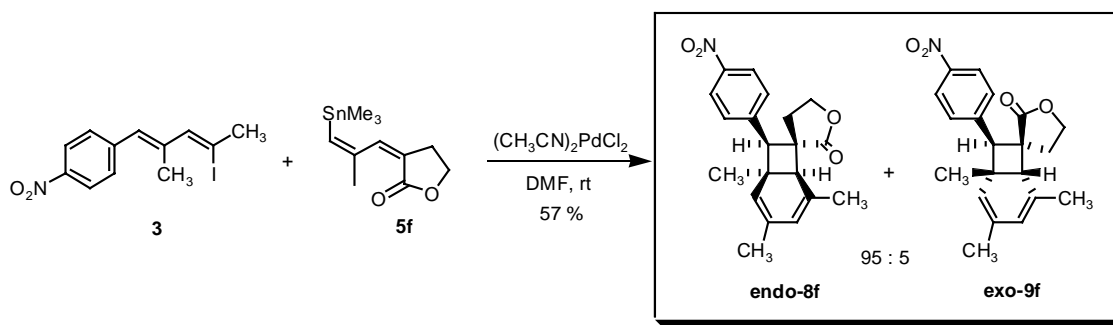
$R_f$ : 0.4 (Ethyl acetate/hexanes, 1/5)

$^1H$  NMR: (300 MHz,  $C_6D_6$ )

$\delta$  7.42 (t,  $J = 2.8$  Hz, 1H), 6.31 (s, 1H), 3.48 (t,  $J = 7.2$  Hz, 2H), 2.14 (td,  $J = 7.2$  Hz,  $J = 2.8$  Hz, 2H), 1.84 (s, 1H), 0.27 (s, 9H).

$^{13}C$  NMR: (100 MHz,  $C_6D_6$ )

$\delta$  171.6, 148.8, 146.3, 139.1, 124.0, 64.2, 26.1, 24.7, -8.6.



**Endo 8f and exo 9f.** To a solution of iododiene **3** (123 mg, 0.375 mmol) in dry DMF (4 mL) was added vinyl stannane **5f** (113 mg, 0.375 mmol) and 10 mol%  $(CH_3CN)_2PdCl_2$  catalyst (9.70 mg, 0.0375 mmol) at rt. The reaction flask was wrapped by aluminum foil. After 16 h at rt, catalyst (10.0 mg, 0.0386 mmol) was added again, the reaction was stirred further for 6h at rt. To remove trimethyltin iodide, the reaction was stirred with KF on Celite® (50/50 wt) for 2 h and filtered through Celite®. The resulting solution was washed with aq  $NaHCO_3$  and the aqueous layer was extracted with  $Et_2O$ . The combined

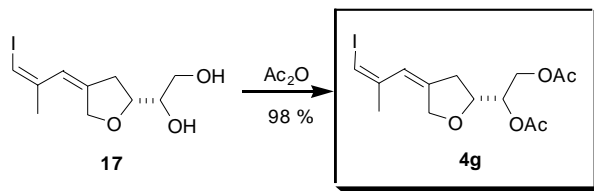
organic solution was washed with water and brine, dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The product was purified by column chromatography with  $\text{Et}_2\text{O}$ /pentane, 1/5 to give 73.6 mg of endo product and 3.8 mg of exo product (overall 57 %).

**endo-8f**

color: pale yellow crystal  
 $R_f$ : 0.3 ( $\text{Et}_2\text{O}$ /pentane, 1/5)  
 $^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  8.16 (d,  $J = 9$  Hz, 2H), 7.43 (d,  $J = 9$  Hz, 2H), 5.75 (s, 1H), 5.15 (s, 1H), 4.08 (s, 1H), 4.06 (m, 2H), 3.04 (s, 1H), 2.43 (m, 1H), 2.24 (m, 1H), 1.77 (s, 3H), 1.71 (s, 3H), 1.28 (s, 3H).  
 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  180.4, 147.3, 143.4, 131.0, 130.3, 129.5, 126.2, 123.6, 123.1, 66.7, 56.7, 51.4, 48.8, 43.9, 29.6, 25.4, 22.4.  
IR: (neat)  
 $\nu$  2983, 1751, 1515, 1344, 1109  $\text{cm}^{-1}$   
HRMS: (FAB)  
Calcd. for  $\text{C}_{20}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M} + \text{Na})]^+$  362.1368, found 362.1360.

**exo-9f**

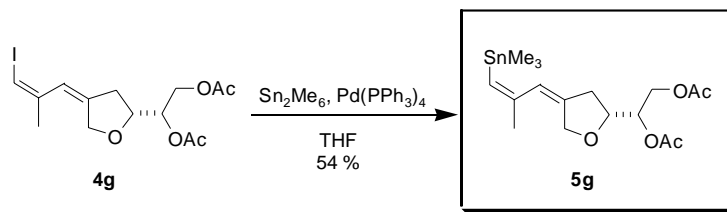
color: pale yellow crystal  
 $R_f$ : 0.2 ( $\text{Et}_2\text{O}$ /pentane, 1/5)  
 $^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  
 $\delta$  8.15 (d,  $J = 9$  Hz, 2H), 7.54 (d,  $J = 9$  Hz, 2H), 5.66 (s, 1H), 5.18 (s, 1H), 4.21 (m, 1H), 4.03 (m, 2H), 3.55 (s, 1H), 3.45 (s, 1H), 2.46 (m, 2H), 1.76 (s, 3H), 1.69 (s, 3H), 0.92 (s, 3H).  
 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  176.1, 146.9, 144.6, 130.7, 130.1, 128.4, 126.0, 124.2, 123.1, 64.7, 62.5, 52.5, 46.4, 35.0, 23.7, 22.0, 21.8.  
IR: (neat)  
 $\nu$  2993, 1765, 1519, 1348, 1206  $\text{cm}^{-1}$   
HRMS: (FAB)  
Calcd. for  $\text{C}_{20}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M} + \text{Na})]^+$  362.1368, found 362.1361.



**(Z,Z)-Acetate 4g.** To a stirred solution of diol **17** (170mg, 0.547 mmol) in  $\text{CH}_2\text{Cl}_2$  (2.2 mL) were added DMAP (133 mg, 0.109 mmol) and pyridine (245  $\mu\text{L}$ , 3.01 mmol). After 10 min, acetic anhydride (108  $\mu\text{L}$ , 1.14 mmol) was added to the mixture at rt. After stirring for 1 h, the reaction was quenched by addition of  $\text{H}_2\text{O}$ , and the organic solution

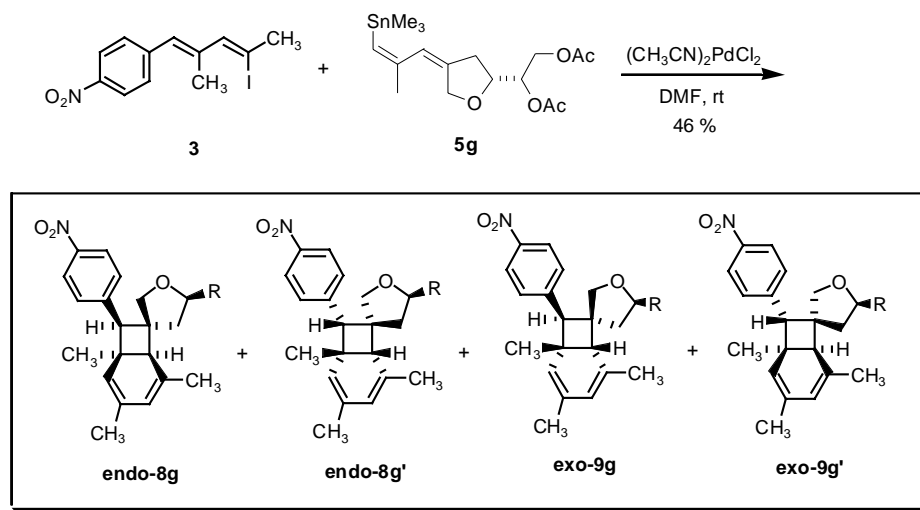
was washed with 10 % HCl, H<sub>2</sub>O, satd aq NaHCO<sub>3</sub>, and brine. The combined organic solution was dried over anhydrous MgSO<sub>4</sub>, and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/5) to give 216 mg (98 %) of a colorless oil.

$R_f$ : 0.7 (EtOAc/hexanes, 1/1)  
<sup>1</sup>H NMR: (400 MHz, CDCl<sub>3</sub>)  
 $\delta$  6.24 (s, 1H), 6.01 (s, 1H), 5.10 (dt,  $J$  = 5.9 Hz, 3.1 Hz, 1H), 4.62 (d,  $J$  = 14 Hz, 1H), 4.46 (d,  $J$  = 14 Hz, 1H), 4.42 (dd,  $J$  = 12 Hz, 3.1 Hz, 1H), 4.09 (m, 2H), 2.78 (dd,  $J$  = 16 Hz, 5.9 Hz, 1H), 2.60 (dd,  $J$  = 16 Hz, 7.5 Hz, 1H), 2.07 (s, 3H), 2.04 (s, 3H), 1.96 (s, 3H).  
<sup>13</sup>C NMR: (100 MHz, CDCl<sub>3</sub>)  
 $\delta$  170.5, 170.0, 142.8, 141.6, 123.6, 78.5, 76.0, 72.0, 69.2, 62.6, 37.1, 22.9, 20.8, 20.7.  
 IR: (neat)  
 $\nu$  2960, 2859, 1744, 1370, 1222, 1062 cm<sup>-1</sup>  
 HRMS: (ESI-MS)  
 Calcd. for C<sub>14</sub>H<sub>20</sub>IO<sub>5</sub> [(M + H)]<sup>+</sup> 395.0355, found 395.0362.



**(Z,Z)-Vinyl stannane 5g.** To a stirred solution of (Z,Z)-acetate **4g** (216 mg, 0.537 mmol) in dry THF (3.4 mL) was added hexamethylditin (211  $\mu$ L, 0.644 mmol) and 5 mol% of tetrakis(triphenylphosphine)palladium (31.0 mg, 0.0268 mmol). The mixture was degassed with bubbling by an Ar stream for 10 min and then was heated to 80 °C for 10 h. The mixture was cooled to rt, and stirred with KF on Celite<sup>®</sup> (50/50 wt). The resulting suspension was filtered through Celite<sup>®</sup> and the filtrate was concentrated. The residue was purified by chromatography on a short pad of basic alumina, eluted with Et<sub>2</sub>O/pentane (1/5). Concentration of the eluent afforded a pale yellow oil 123 mg (54 %), sufficiently pure for use in the next step.

$R_f$ : 0.5 (Ethyl acetate/hexanes, 1/5)  
<sup>1</sup>H NMR: (400 MHz, C<sub>6</sub>D<sub>6</sub>)  
 $\delta$  6.10 (t,  $J$  = 2.3 Hz, 1H), 5.78 (s, 1H), 5.31 (dt,  $J$  = 6.4 Hz, 2.7 Hz, 1H), 4.57 (dd,  $J$  = 12 Hz, 2.7 Hz, 1H), 4.47 (d,  $J$  = 14 Hz, 1H), 4.31 (d,  $J$  = 14 Hz, 1H), 4.15 (m,  $J$  = 5.5 Hz, 1H), 3.89 (q,  $J$  = 7 Hz, 1H), 2.46 (t,  $J$  = 5.5 Hz, 2H), 1.82 (s, 3H), 1.69 (s, 3H), 1.67 (s, 3H), 0.20 (s, 9H).



**Endo 8g, 8g' and exo 9g, 9g'.** To a solution of iododiene **3** (93.3 mg, 0.284 mmol) in dry DMF (2.8 mL) was added vinyl stannane **5g** (124 mg, 0.284 mmol) and 10 mol%  $(\text{CH}_3\text{CN})_2\text{PdCl}_2$  catalyst (7.35 mg, 0.0284 mmol) at rt. The reaction flask was wrapped by aluminum foil. After 16 h at rt, catalyst (3.68 mg, 0.0142 mmol) was added again and the reaction was stirred for 6 h at rt. To remove trimethyltin iodide, the reaction was stirred with KF on Celite<sup>®</sup> (50/50 wt) for 2 h and filtered through Celite<sup>®</sup>. The resulting solution was washed with aq  $\text{NaHCO}_3$  and the aqueous layer was extracted with  $\text{Et}_2\text{O}$ . The combined organic solution was washed with water and brine, dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The crude product was purified further by column chromatography with  $\text{Et}_2\text{O}$ /pentane, 1/10 to give 61 mg (46 %) of a mixture of endo and exo products in a ratio of 82:18 (49% and 33% of each endo isomer and 18% of total two minor exo isomers).<sup>8</sup>

$R_f$ : 0.3 (Ethyl acetate/hexanes, 1/10)

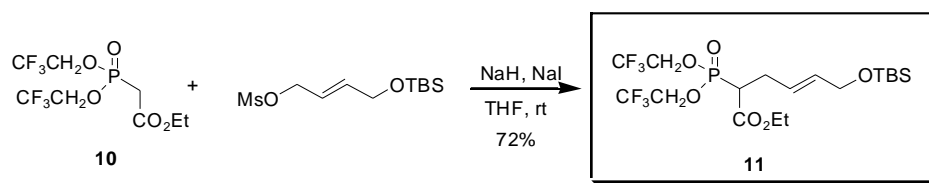
<sup>1</sup>H NMR: (400 MHz,  $\text{C}_6\text{D}_6$ )

$\delta$  8.18 (m+d,  $J = 8.7$  Hz, 2H), 7.45, (d,  $J = 8.7$  Hz, 0.98H), 7.40 (d,  $J = 8.7$  Hz, 0.66H), 7.35 (d,  $J = 8.4$  Hz, 0.36H), 5.69 and 5.67 (2s, 0.18H), 5.62 (s, 0.33H), 5.57 (s, 0.49H), 5.19 (s, 0.18H), 5.04 (td,  $J = 6.4$  Hz,  $J = 3.2$  Hz, 0.49H), 4.97 (td,  $J = 6.4$  Hz,  $J = 3.2$  Hz, 0.33H), 4.89 (s, 0.49H), 4.83 (s, 0.33H), 4.33 (m, 1H), 3.95 (m, 4H), 3.66 (s, 0.33H), 3.59 (s, 0.44H), 3.42 and 3.33 (2s, 0.18H), 2.87 and 2.85 (2s, 0.18H), 2.75 (s, 0.49H), 2.65 (s, 0.33H), 2.53 (m, 0.18H), 2.17 (m, 0.82H), 2.08-2.00 (m+s, 8H), 1.76-1.68 (vinylmethyl groups, 6H), 1.25 (2s, 3H).

HRMS: (FAB)

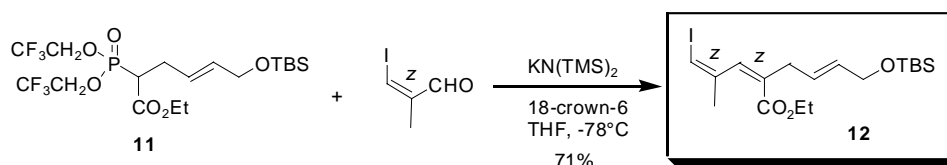
Calcd. for  $\text{C}_{26}\text{H}_{31}\text{NO}_7\text{Na}$   $[(M + \text{Na})]^+$  492.1998, found 492.1990.

<sup>8</sup> The <sup>1</sup>H-NMR spectrum of the mixture was detangled by information derived from the nOe experiments so that individual peaks could be assigned to each component of the mixture.



**Still-Gennari reagent 11.** To a stirred suspension of sodium hydride, NaH (37.0 mg, 1.46 mmol) in anhydrous DMF (3.00 mL) was added dropwise a solution of [bis-(2,2,2-trifluoroethoxy)-phosphoryl]-acetic acid ethyl ester (487 mg, 1.60 mmol) in THF (3.00 mL) at 0 °C. After stirring for 1 h at rt, methanesulfonic acid 4-(*tert*-butyldimethylsilyloxy)-but-2-enyl ester (374 mg, 1.33 mmol) was added dropwise and NaI (100 mg, 0.66 mmol) was added at rt. The resulting mixture was stirred for 24 h at rt under Ar atmosphere, then quenched with H<sub>2</sub>O and extracted with diethyl ether. The combined organic solution was washed with water and brine, and then dried over anh. MgSO<sub>4</sub>, and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/5) to give 494 mg (72 %) of a colorless oil.

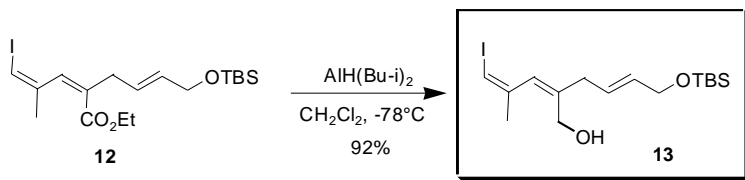
*R<sub>f</sub>*: 0.3 (EtOAc/hexanes, 1/5)  
 HNMR: (600 MHz, CDCl<sub>3</sub>)  
 $\delta$  5.87 (m, 2H), 4.43 (m, 4H), 4.21 (q, 2H), 4.17 (m, 2H), 3.26 (m, 1H), 2.74 (m, 2H), 1.33 (t, 3H), 0.93 (s, 9H), 0.10 (s, 6H).  
<sup>13</sup>C NMR: (100 MHz, CDCl<sub>3</sub>)  
 $\delta$  167.2, 133.0, 124.4 (d), 62.9 (m), 46.5, 44.3, 29.4 (d), 25.6, 13.6, -5.62.  
 IR: (neat)  
 $\nu$  2983, 1738, 1462, 1362, 1257, 1123, 1022, 973, 837 cm<sup>-1</sup>  
 HRMS: (ESI-MS)  
 Calcd. for C<sub>18</sub>H<sub>32</sub>F<sub>6</sub>O<sub>6</sub>PSi [(M + H)]<sup>+</sup> 517.1610, found 517.1611.



**(Z,Z)-Ester 12.** A solution of phosphonate **11** (1.00 g, 1.95 mmol) in THF (11 mL) was added to a flask containing 18-crown-6 ether (1.02 g, 3.89 mmol). The solution was cooled to 0 °C, and potassium hexamethyldisilazane (0.5 M solution in toluene, 3.70 mL, 1.85 mmol) was added dropwise to the mixture. After stirring for 30 min at 0 °C, (*Z*)-3-iodo-2-methyl-2-propenal (174 mg, 0.885 mmol) in THF (5 mL) was added dropwise via cannula at -78 °C. The mixture was allowed to stir at -78 °C for 3 h, and then was quenched with satd aq NH<sub>4</sub>Cl (2 mL). After warming to rt, the mixture was extracted with diethyl ether and the combined organic solution was washed with water and brine, dried over anh MgSO<sub>4</sub>, and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/10) to give 283 mg (71 %) of a pale yellow oil.

$R_f$ : 0.6 (EtOAc/hexanes, 1/5)  
 $^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  6.20 (s, 1H), 6.07 (t,  $J = 1.5$  Hz, 1H), 5.68 (m, 2H), 4.20 (q, 2H), 4.16 (m, 2H), 3.07 (m, 2H), 1.98 (s, 3H), 1.27 (t, 3H), 0.90 (s, 9H), 0.06 (s, 6H).  
 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  167.7, 143.5, 137.3, 132.3, 126.3, 78.1, 63.5, 60.7, 36.9, 25.9, 22.9, 18.4, 14.0, -5.16  
 IR: (neat)  
 $\nu$  2954, 2895, 1721, 1471, 1462, 1376  $\text{cm}^{-1}$   
 HRMS: (FAB-MS)  
 Calcd. for  $\text{C}_{18}\text{H}_{31}\text{IO}_3\text{Si}$   $[(\text{M} + \text{Na})]^+$  473.0985, found 473.1028.

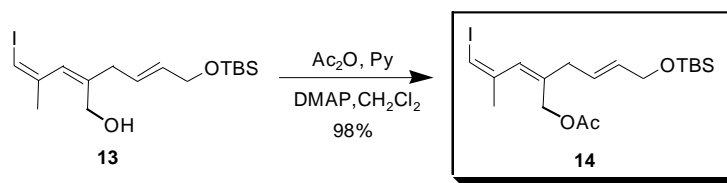
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**(Z,Z)-Alcohol 13.** To a stirred solution of ester **12** (46.7 mg, 0.103 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (3 mL) was added diisobutylaluminum hydride (1.0 M solution in Hexanes, 309  $\mu\text{L}$ , 0.300 mmol) at  $-78^\circ\text{C}$ . The reaction mixture was stirred for 45 min at  $-78^\circ\text{C}$ , and then quenched with methanol (150  $\mu\text{L}$ ). The resulting mixture was warmed to rt and stirred with Celite<sup>®</sup> for 2h. Then it was filtered through Celite and the Celite was washed with  $\text{CH}_2\text{Cl}_2$ . The combined filtrate was dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/5) to give 41 mg (99 %) of a colorless oil.

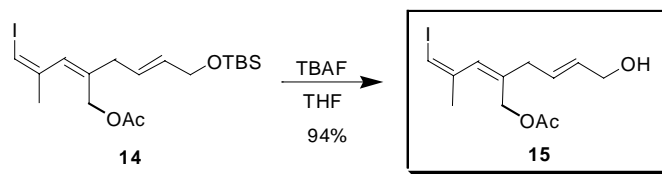
$R_f$ : 0.3 (EtOAc/hexanes, 1/5)  
 $^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  6.06 (t, 1H), 5.70 (m, 3H), 4.17 (m, 2H), 4.10 (m, 2H), 2.95 (m, 2H), 1.97 (s, 3H), 0.09 (s, 9H), 0.06 (s, 6H).  
 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  144.9, 140.4, 131.6, 129.5, 127.8, 77.5, 63.6, 61.3, 36.8, 25.9, 24.9, -5.16.  
 IR: (neat)  
 $\nu$  3427, 3378, 2929, 2407, 1470, 1264, 1122, 1045, 869  $\text{cm}^{-1}$   
 HRMS: (ESI-MS)  
 Calcd. for  $\text{C}_{16}\text{H}_{30}\text{IO}_2\text{Si}$   $[(\text{M} + \text{H})]^+$  409.1060, found 409.1067.

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**(Z,Z)-Acetate 14.** To a stirred solution of alcohol **13** (84.2 mg, 0.206 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (821  $\mu$ L) was added DMAP (8.40 mg, 0.0206 mmol) and pyridine (46.8  $\mu$ L, 0.574 mmol). After 10 min, acetic anhydride (21  $\mu$ L, 0.217 mmol) was added. After stirring for 40 min, the reaction mixture was quenched by addition of H<sub>2</sub>O, and the organic solution was washed with 10 % HCl, H<sub>2</sub>O, satd aq NaHCO<sub>3</sub>, and brine. The organic solution was dried over anh MgSO<sub>4</sub>, and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/5) to give 93 mg (98 %) of a colorless oil.

*R<sub>f</sub>*: 0.7 (EtOAc/hexanes, 1/5)  
<sup>1</sup>H NMR: (600 MHz, CDCl<sub>3</sub>)  
 $\delta$  6.08 (s, 1H), 5.80 (s, 1H), 5.67 (m, 2H), 4.54 (s, 2H), 4.16 (d, *J* = 2.9 Hz, 2H), 2.87 (d, *J* = 4.4 Hz, 2H), 2.04 (s, 3H), 1.95 (s, 3H), 0.08 (s, 9H), 0.06 (s, 6H).  
<sup>13</sup>C NMR: (100 MHz, CDCl<sub>3</sub>)  
 $\delta$  170.7, 144.3, 135.8, 132.4, 132.0, 126.7, 80.1, 63.5, 62.7, 37.4, 25.9, 24.4, 20.4, -5.2.  
 IR: (neat)  
 $\nu$  2953, 2856, 1742, 1369, 1226, 1045 cm<sup>-1</sup>  
 HRMS: (ESI-MS)  
 Calcd. for C<sub>18</sub>H<sub>32</sub>IO<sub>3</sub>Si [(M + H)]<sup>+</sup> 451.1165, found 451.1172.



**(Z,Z)-Allylic Alcohol 15.** To a solution of TBS ether **14** (93.0 mg, 0.206 mmol) in THF (1.20 mL) was added TBAF (1.0 M solution in THF, 474  $\mu$ L, 0.473 mmol) at 0 °C. After stirring for 1 hr at rt, the reaction mixture was quenched by addition of satd aq NH<sub>4</sub>Cl, and then extracted with diethyl ether. The combined organic solution was dried over anh MgSO<sub>4</sub>, and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/3) to give 62 mg (94 %) of a pale yellow oil.

*R<sub>f</sub>*: 0.4 (EtOAc/hexanes, 1/3)  
<sup>1</sup>H NMR: (600 MHz, CDCl<sub>3</sub>)  
 $\delta$  6.10 (s, 1H), 5.82 (s, 1H), 5.76 (m, 2H), 4.56 (s, 2H), 4.12 (d, *J* = 4.2 Hz, 2H), 2.90 (d, *J* = 5.4 Hz, 2H), 2.05 (s, 3H), 1.96 (s, 3H), 1.72 (bs, 1H).  
<sup>13</sup>C NMR: (100 MHz, CDCl<sub>3</sub>)  
 $\delta$  170.8, 144.1, 135.5, 131.9, 131.8, 128.8, 78.3, 63.3, 62.6, 37.1, 24.6,

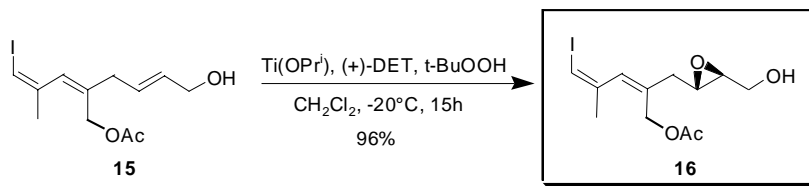


20.8.

IR: (neat)

 $\nu$  3501, 3442, 3306, 2963, 1734, 1369, 1265, 1026, 973  $\text{cm}^{-1}$ 

HRMS: (ESI-MS)

Calcd. for  $\text{C}_{12}\text{H}_{17}\text{IO}_3\text{Na}$   $[(\text{M} + \text{Na})]^+$  359.0120, found 359.0108.

**(Z,Z)-Epoxy Alcohol 16.** A flask containing 4Å molecular sieves (50 mg) and  $\text{CH}_2\text{Cl}_2$  (11 mL) was cooled to  $-20^\circ\text{C}$ , and (+)-DET (20.0  $\mu\text{L}$ , 0.115 mmol) and  $\text{Ti}(\text{OPr}^i)_4$  (24.0  $\mu\text{L}$ , 0.08 mmol) were added successively. After 20 min,  $t\text{-BuOOH}$  (5.0-6.0 M in decanes, 469  $\mu\text{L}$ , 2.35 mmol) was added dropwise via syringe at  $-20^\circ\text{C}$ . After 30 min, allylic alcohol **15** (394 mg, 1.17 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was added dropwise via cannula. The reaction mixture was allowed to stir for 11 h at  $-20^\circ\text{C}$  and then warmed to  $0^\circ\text{C}$ . To the reaction mixture was added dropwise satd aq  $\text{Na}_2\text{SO}_4$  via syringe and also diethyl ether. The reaction mixture was warmed to rt and vigorously stirred overnight. After the suspension was filtered through Celite®, the filtrate was dried over anhydrous  $\text{Na}_2\text{SO}_4$ , and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/1) to give 396 mg (92%) of a pale yellow oil (>99% ee as determined by Mosher ester analysis).  $[\alpha]_D^{21}$  (c 0.98,  $\text{CH}_2\text{Cl}_2$ ) =  $-9.18^\circ$

R<sub>f</sub>: 0.3 (EtOAc/hexanes, 1/1) $^1\text{H}$  NMR: (400 MHz,  $\text{CDCl}_3$ )

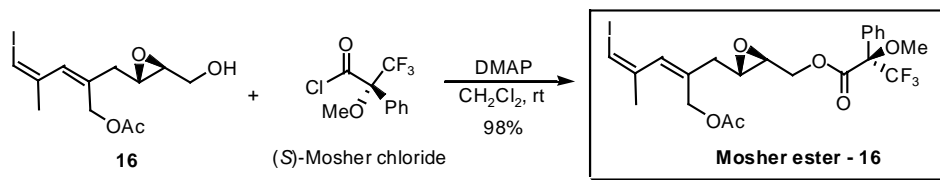
$\delta$  6.11 (s, 1H), 5.89 (s, 1H), 4.59 (s, 2H), 3.89 (d,  $J = 12.6$  Hz, 1H), 3.65 (m, 1H), 3.13 (dt,  $J = 5.4$  Hz,  $J = 2.2$  Hz, 1H), 3.01 (m, 1H), 2.45 (dd,  $J = 15$  Hz,  $J = 5.8$  Hz, 1H), 2.38 (dd,  $J = 15$  Hz,  $J = 5.8$  Hz, 1H), 2.06 (s, 3H), 1.97 (s, 3H).

 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ ) $\delta$  170.6, 143.9, 133.1, 133.0, 78.7, 63.0, 61.4, 58.2, 54.3, 36.5, 24.5, 20.8.

IR: (neat)

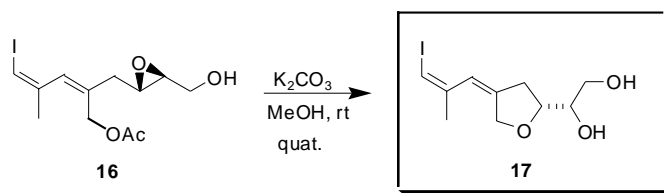
 $\nu$  3455, 2935, 1737, 1369, 1230, 1026, 970  $\text{cm}^{-1}$ 

HRMS: (FAB + ESI)

Calcd. for  $\text{C}_{12}\text{H}_{17}\text{IO}_4\text{Na}$   $[(\text{M} + \text{Na})]^+$  375.0069, found 375.0064.

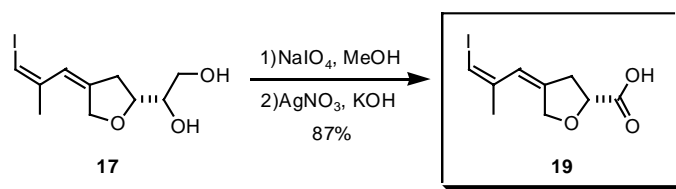
**Mosher ester of 16.** A methylene solution (5 mL) of epoxy alcohol 16 (17.3 mg, 0.0491 mmol), maintained at rt, was treated with DMAP (12.0 mg, 0.0982 mmol). Then (*S*)- $\alpha$ -methoxy- $\alpha$ -trifluoro-methylphenyl-acetyl chloride (18.5  $\mu$ L, 0.0982 mmol) was slowly added and the reaction mixture allowed to stir for 4 hr. The crude reaction mixture was filtered through a pad of silica gel and was washed extensively with methyl chloride in order to afford the product (26.7 mg, 98%).

$R_f$ : 0.7 (EtOAc/hexanes, 1/1)  
 $^1\text{H NMR}$ : (600 MHz,  $\text{CDCl}_3$ )  
 $\delta$  7.42 (m, 5H), 6.14 (s, 1H), 5.88 (s, 1H), 4.62 (dd,  $J = 12.5$  Hz,  $J = 3.5$  Hz, 1H), 4.58 (s, 2H), 4.25 (dd,  $J = 11.9$  Hz,  $J = 6.5$  Hz, 1H), 3.56 (s, 3H), 3.12 (m, 1H), 3.05 (dt,  $J = 5.5$  Hz,  $J = 3.5$  Hz, 1H), 2.41 (m, 2H), 2.05 (s, 3H), 1.97 (s, 3H).



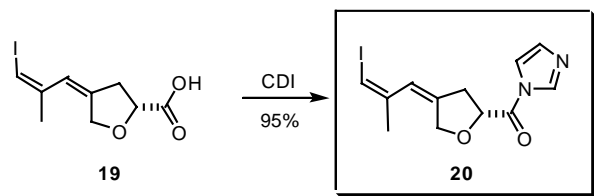
**(*Z,Z*)-Diol 17.** To a stirred solution of epoxy alcohol 16 (133 mg, 0.378 mmol) in MeOH (11 mL) was added finely ground  $\text{K}_2\text{CO}_3$  (157 mg, 1.13 mmol) in a single portion. The reaction mixture was stirred for 2 h and poured into  $\text{CH}_2\text{Cl}_2$  and half-satd aq  $\text{NH}_4\text{Cl}$ . The resulting mixture was extracted with  $\text{CH}_2\text{Cl}_2$  and the combined organic solution was dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The crude product was purified on silica gel with EtOAc/hexane (1/1) to give 117 mg (quantitative yield) of a pale yellow solid.

$R_f$ : 0.2 (EtOAc/hexanes, 1/1)  
 $^1\text{H NMR}$ : (400 MHz,  $\text{CDCl}_3$ )  
 $\delta$  6.27 (s, 1H), 6.02 (s, 1H), 4.64 (d,  $J = 14.1$  Hz, 1H), 4.45 (d,  $J = 14.1$  Hz, 1H), 3.93 (m, 2H), 3.75 (bs, OH), 3.75 (dd,  $J = 3.6$  Hz,  $J = 11.5$  Hz, 1H), 3.66 (dd,  $J = 11.2$  Hz,  $J = 5.99$  Hz, 1H), 2.72 (d,  $J = 7.2$  Hz, 2H), 1.98 (s, 3H).  
 $^{13}\text{C NMR}$ : (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  143.7, 141.8, 123.5, 78.9, 78.3, 72.2, 69.1, 63.7, 36.1, 23.0.  
 IR: (neat)  
 $\nu$  3720-3090 (br), 2930, 1455, 1240, 1135, 1040  $\text{cm}^{-1}$   
 HRMS: (FAB)  
 Calcd. for  $\text{C}_{10}\text{H}_{15}\text{IO}_3\text{Na}$   $[(\text{M} + \text{Na})]^+$  332.9964, found 332.9960.



**(Z,Z)-Carboxylic Acid 19.** To a stirred solution of the diol **17** (110 mg, 0.354 mmol) in MeOH (9.00 mL) was added dropwise a solution of NaIO<sub>4</sub> (90.8 mg, 0.424 mmol) in H<sub>2</sub>O (796  $\mu$ L) at 0 °C. After 2 h at 0 °C, the reaction mixture was filtered and the solid inorganic precipitate was washed with CH<sub>2</sub>Cl<sub>2</sub>. The filtrate was extracted with CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic solution was dried over anhydrous MgSO<sub>4</sub>, and concentrated to afford a pale yellow syrupy material. To a solution of AgNO<sub>3</sub> (163 mg, 0.959 mmol) in H<sub>2</sub>O (398  $\mu$ L) was added a solution of the above crude material in EtOH (478  $\mu$ L). This was followed by dropwise addition of a solution of KOH (141 mg, 2.51 mmol) in H<sub>2</sub>O (515  $\mu$ L) at 0 °C with vigorous stirring. The reaction mixture was stirred for an additional 15 h at rt. It was then filtered and the inorganic precipitate was washed with H<sub>2</sub>O. The washings were added to the filtrate and the combined aqueous solution was concentrated to remove ethanol. The residue was cooled to 0 °C and acidified with 2N HCl (pH = 2). The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic solution was washed with H<sub>2</sub>O, dried over anhydrous MgSO<sub>4</sub>, and concentrated to give 99.3 mg (87 %) of a clean pale yellow solid.

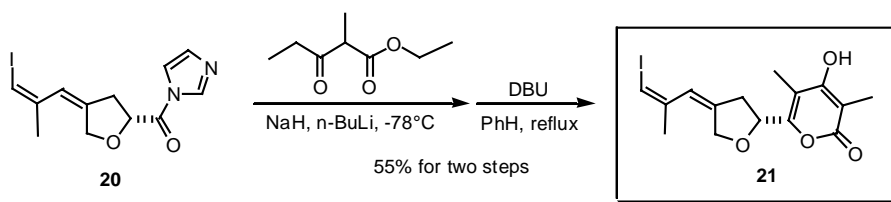
R<sub>f</sub>: 0.3 (2 % MeOH/ CH<sub>2</sub>Cl<sub>2</sub>)  
<sup>1</sup>H NMR: (500 MHz, CDCl<sub>3</sub>)  
 $\delta$  10.3 (br, 1H), 6.32 (s, 1H), 6.08 (s, 1H), 4.79 (d, *J* = 14.4 Hz, 1H), 4.66 (d, *J* = 14.4 Hz, 1H), 4.64 (t, *J* = 5.4 Hz, 1H), 3.14 (dd, *J* = 16.4 Hz, *J* = 8.4 Hz, 1H), 2.94 (dd, *J* = 16.4 Hz, *J* = 2.9 Hz, 1H), 2.00 (s, 3H).  
<sup>13</sup>C NMR: (100 MHz, CDCl<sub>3</sub>)  
 $\delta$  177.3, 141.7, 140.9, 124.4, 79.5, 75.7, 69.8, 38.5, 23.2.  
 IR: (neat)  
 $\nu$  3330, 2986, 1735, 1321, 1240, 1153, 1021 cm<sup>-1</sup>  
 HRMS: (ESI)  
 Calcd. for C<sub>9</sub>H<sub>11</sub>IO<sub>3</sub>Na [(M + Na)]<sup>+</sup> 316.9651, found 316.9654.



**(Z,Z)-Acyl imidazole 20.** To a stirred solution of carboxylic acid **19** (47.7 mg, 0.162 mmol) in THF (324  $\mu$ L) was added carbonyl diimidazole (31.3 mg, 0.192 mmol) at rt. After 1 h, the solvent was removed by reduced pressure on the rotary evaporator and the residue was partitioned between CH<sub>2</sub>Cl<sub>2</sub> and H<sub>2</sub>O. The combined organic solution was

dried over anhydrous  $\text{MgSO}_4$ , and concentrated, leaving 99.3 mg (95 %) of an unstable pale yellow solid.

$R_f$ : 0.3 (2 % MeOH/  $\text{CH}_2\text{Cl}_2$ )  
 $^1\text{H}$  NMR: (400 MHz,  $\text{CDCl}_3$ )  
 $\delta$  8.31 (s, 1H), 7.53 (s, 1H), 7.07 (s, 1H), 6.31 (s, 1H), 6.06 (s, 1H), 5.04 (dd,  $J = 7.6$  Hz,  $J = 5.2$  Hz, 1H), 4.68 (s, 2H), 3.17 (dd,  $J = 16.4$  Hz,  $J = 4.8$  Hz, 1H), 3.09 (dd,  $J = 16.4$  Hz,  $J = 8.0$  Hz, 1H), 1.95 (s, 3H).  
 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  168.2, 141.6, 140.2, 137.2, 131.0, 124.8, 116.6, 79.9, 76.6, 70.0, 37.8, 23.2.  
 IR: (neat)  
 $\nu$  3123, 2981, 1742, 1473, 1328, 1237, 1065  $\text{cm}^{-1}$

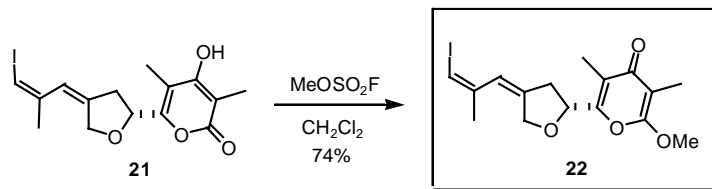


**(Z,Z)- $\alpha$ -Pyrone 21.** To a stirred suspension of NaH (60 % in mineral oil, 68.3 mg, 1.63 mmol) in THF (3 mL) was added dropwise 2-methyl-3-oxopentanoic acid ethyl ester (257 mg, 1.63 mmol) in THF (4 mL) at 0 °C. After 10 min, the reaction mixture was cooled to  $-78$  °C, and n-BuLi (1.6 M solution in hexane, 1.04 mL, 1.63 mmol) was added dropwise. After 15 min at  $-78$  °C, the reaction mixture was warmed to  $-10$  °C and allowed to stir for 10 min. Then it was cooled to  $-78$  °C, and a solution of acylimidazole **20** (280 mg, 0.813 mmol) in THF (3 mL) was added dropwise. After 2h, the reaction mixture was warmed to  $-23$  °C and stirred at that temperature for an additional 2h. The reaction was quenched by 5 % HCl (1 mL) at  $-23$  °C. After warming to rt, the reaction mixture was diluted with diethyl ether and water and extracted with ether. The combined organic solution was washed  $\text{H}_2\text{O}$  and brine, dried over anhydrous  $\text{MgSO}_4$ , and concentrated. Excess 2-methyl-3-oxopentanoic acid ethyl ester was removed on silica gel with EtOAc/hexane (1/5), allowing the recovery of a pale yellow solid suitable for use in the next step.

To a stirred solution of this material (230 mg, 0.529 mmol) in dry benzene (6 mL) was added DBU (0.950 mL, 0.635 mmol) at rt. The reaction mixture was stirred at reflux for 3h under Ar. The solvent was removed by concentration on the rotary evaporator and the crude product was purified on silica gel with 2 % MeOH/ $\text{CH}_2\text{Cl}_2$ , affording 170 mg (54 % for two step) of a pale yellow solid.  $[\alpha]_D^{22}(\text{c } 1.0, \text{CH}_2\text{Cl}_2) = -10.0^\circ$

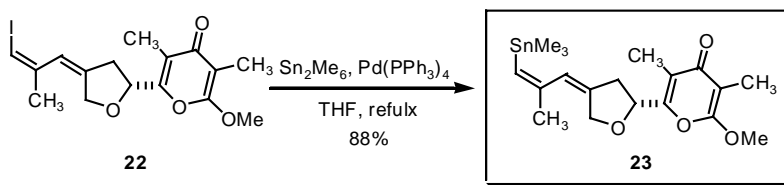
$R_f$ : 0.2 (2 % MeOH/  $\text{CH}_2\text{Cl}_2$ )  
 $^1\text{H}$  NMR: (500 MHz,  $\text{CDCl}_3$ )  
 $\delta$  6.29 (s, 1H), 6.05 (s, 1H), 4.97 (t,  $J = 7.5$  Hz, 1H), 4.80 (d,  $J = 14.0$  Hz, 1H), 4.56 (d,  $J = 14.0$  Hz, 1H), 3.09 (dd,  $J = 16.4$  Hz,  $J = 8.0$  Hz, 1H), 2.90 (dd,  $J = 16.4$  Hz,  $J = 6.4$  Hz, 1H), 2.06 (s, 3H), 2.01 (s, 3H), 1.99 (s, 1H).

$^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  165.8, 164.9, 153.4, 142.7, 141.6, 123.3, 110.2, 100.0, 78.4, 73.3, 69.4, 37.8, 22.8, 9.1, 8.5.  
 IR: (neat)  
 $\nu$  3158 (br), 2980, 1675, 1569, 1378, 1265, 1180, 1056  $\text{cm}^{-1}$   
 HRMS: (ESI)  
 Calcd. for  $\text{C}_{15}\text{H}_{18}\text{IO}_4$   $[(\text{M} + \text{H})]^+$  389.0250, found 389.0240.



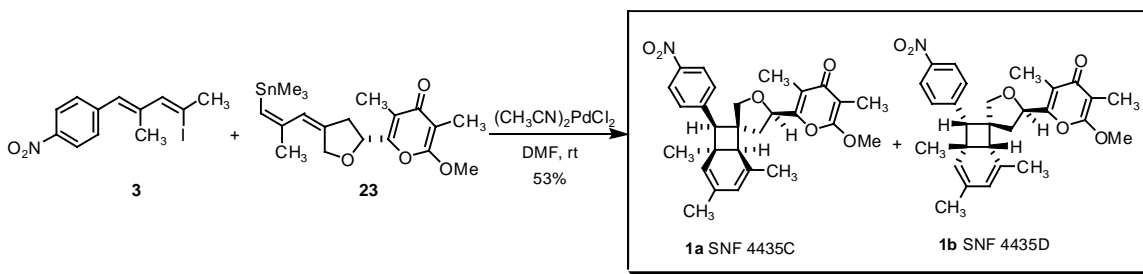
**(Z,Z)- $\gamma$ -Pyrone 22.** To a stirred solution of  $\alpha$ -pyrone **21** (167 mg, 0.429 mmol) in  $\text{CH}_2\text{Cl}_2$  (4 mL) was added methyl fluorosulfonate (0.342 mL, 4.29 mmol) at rt under Ar. After 3h, the reaction mixture was concentrated and the crude material was partitioned between with 4 mL of  $\text{CH}_2\text{Cl}_2$  and 4 mL of 1N NaOH. The aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  and the combined organic solution was dried over anhydrous  $\text{MgSO}_4$ , and concentrated. The residue was subjected to silica gel with EtOAc/hexane (1/1), affording 127 mg (74 %) of a pale yellow solid.  $[\alpha]_D^{22}$  (c 1.06,  $\text{CH}_2\text{Cl}_2$ ) =  $-34.9^\circ$

$R_f$ : 0.2 (EtOAc/hexanes, 1/1)  
 $^1\text{H}$  NMR: (400 MHz,  $\text{CDCl}_3$ )  
 $\delta$  6.36 (s, 1H), 6.08 (s, 1H), 5.14 (dd,  $J = 7.2$  Hz,  $J = 6.4$  Hz, 1H), 4.75 (d,  $J = 14.4$  Hz, 1H), 4.64 (d,  $J = 14.4$  Hz, 1H), 3.91 (s, 3H), 3.04 (dd,  $J = 16.4$  Hz,  $J = 7.6$  Hz, 1H), 2.94 (dd,  $J = 16.4$  Hz,  $J = 6.0$  Hz, 1H), 2.014 (s, 3H), 2.011 (s, 3H), 1.84 (s, 3H).  
 $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ )  
 $\delta$  180.5, 162.0, 154.5, 142.9, 141.3, 123.6, 120.2, 100.0, 79.2, 73.4, 69.6, 55.4, 38.1, 23.0, 9.4, 6.8.  
 IR: (neat)  
 $\nu$  2924, 1665, 1597, 1461, 1325, 1255, 1164, 1054  $\text{cm}^{-1}$   
 HRMS: (ESI)  
 Calcd. for  $\text{C}_{16}\text{H}_{20}\text{IO}_4$   $[(\text{M} + \text{H})]^+$  403.0406, found 403.0389.



**(Z,Z)-Vinyl stannane 23.** To a stirred solution of iodo- $\gamma$ -pyrone **22** (24.7 mg, 0.0614 mmol) in dry THF (500  $\mu$ L) was added hexamethylditin (24.1  $\mu$ L, 0.0737 mmol) and 5 mol% of tetrakis(triphenylphosphine)palladium (3.50 mg, 0.00307 mmol). The mixture was degassed with bubbling by an Ar stream for 10 min and then was heated to 80  $^{\circ}$ C for 6h. The mixture was cooled to rt, and stirred with KF on Celite<sup>®</sup> (50/50 wt). The resulting suspension was filtered through Celite<sup>®</sup> and the filtrate was concentrated. The residue was purified by chromatography on a short pad of basic alumina, eluted with Et<sub>2</sub>O/pentane (1/1). Concentration afforded a pale yellow oil 23.7 mg (88 %), sufficiently pure for use in the next step.

R<sub>f</sub>: 0.4 (EtOAc/hexanes, 1/1)  
<sup>1</sup>H NMR: (400 MHz, C<sub>6</sub>D<sub>6</sub>)  
 $\delta$  6.10 (s, 1H), 5.78 (s, 1H), 4.67 (t,  $J$  = 6.8 Hz, 1H), 4.64 (d,  $J$  = 14.1 Hz, 1H), 4.42 (d,  $J$  = 14.1 Hz, 1H), 3.22 (s, 3H), 2.39 (m, 2H), 2.11 (s, 3H), 2.05 (s, 3H), 1.83 (s, 3H), 0.19 (s, 9H).



**SNF 4435 C (1a) and D (1b).** To a solution of iododiene **3** (62.9 mg, 0.191 mmol) in dry DMF (1.30 mL) was added vinyl stannane **23** (56.0 mg, 0.127 mmol) and 10 mol%  $(\text{CH}_3\text{CN})_2\text{PdCl}_2$  catalyst (3.3 mg, 0.0127 mmol) at rt. The reaction flask was wrapped by aluminum foil. After 16 h at rt, catalyst (1.65 mg, 0.00635 mmol) was added again, and the reaction mixture was stirred for 6h at rt. To remove trimethyltin iodide, the reaction was stirred with KF on Celite<sup>®</sup> (50/50 wt) for 2 h and filtered through Celite<sup>®</sup>. The resulting solution was washed with aq NaHCO<sub>3</sub> and the aqueous layer was extracted with Et<sub>2</sub>O. The combined organic solution was washed with water and brine, dried over anhydrous MgSO<sub>4</sub>, and concentrated. The crude product was purified by column chromatography with Et<sub>2</sub>O/hexane (1/1) to give 32.3 mg (53 %) of a yellow solid. The <sup>1</sup>H nmr spectrum of the mixture was consistent with a cyclization product that was a 4:1 mixture of SNF 4435C and D.

HRMS: (ESI)  
 Calcd. for C<sub>28</sub>H<sub>32</sub>NO<sub>6</sub> [(M + H)]<sup>+</sup> 478.2230, found 478.2245.

SNF4435 C and D were separated by preparative TLC with Et<sub>2</sub>O/hexane (1/1) to give SNF4435 C [ $\alpha$ ]<sub>D</sub><sup>21</sup> (c 0.1, CH<sub>2</sub>Cl<sub>2</sub>) = − 72.6 $^{\circ}$  and SNF4435 D [ $\alpha$ ]<sub>D</sub><sup>21</sup> (c 0.09, CH<sub>2</sub>Cl<sub>2</sub>) = + 56.4 $^{\circ}$ .<sup>9</sup>

<sup>9</sup> Takahashi, K.; Tsuda, E.; Kurosawa, K. *J. Antibiot.* **2001**, *54*, 548.

SNF 4435C (**1a**) $R_f$ : 0.2 (EtOAc/hexanes, 1/1) $^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ ) $\delta$  8.19 (d,  $J = 8.4$  Hz, 2H), 7.54 (d,  $J = 8.4$  Hz, 2H), 5.58 (s, 1H), 4.94 (s, 1H), 4.77 (t,  $J = 7.8$  Hz, 1H), 4.32 (d,  $J = 10$  Hz, 1H), 3.97 (d,  $J = 10$  Hz, 1H), 3.95 (s, 3H), 3.63 (s, 1H), 2.84 (s, 1H), 2.42 (d,  $J = 7.8$  Hz, 2H), 1.88 (s, 3H), 1.82 (s, 3H), 1.73 (s, 3H), 1.71 (s, 3H), 1.29 (s, 3H) $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ ) $\delta$  180.5, 162.0, 155.0, 146.3, 145.0, 131.0, 130.4, 129.1, 123.7, 123.5, 122.0, 119.6, 110.2, 73.5, 70.5, 63.6, 55.5, 51.7, 51.1, 46.3, 42.9, 30.3, 22.9, 22.1, 9.3, 6.9.

IR: (neat)

 $\nu$  2951, 2856, 1666, 1599, 1518, 1462, 1377, 1346  $\text{cm}^{-1}$ SNF 4435D (**1b**) $R_f$ : 0.195 (EtOAc/hexanes, 1/1) $^1\text{H}$  NMR: (600 MHz,  $\text{CDCl}_3$ ) $\delta$  8.14 (d,  $J = 8.4$  Hz, 2H), 7.46 (d,  $J = 8.4$  Hz, 2H), 5.69 (s, 1H), 4.77 (t,  $J = 7.8$  Hz, 1H), 4.88 (s, 1H), 4.17 (d,  $J = 10$  Hz, 1H), 3.83 (d,  $J = 10$  Hz, 1H), 3.74 (s, 1H), 3.52 (s, 3H), 2.73 (s, 1H), 2.49 (dd,  $J = 7.8$  Hz, 2H), 1.88 (s, 3H), 1.82 (s, 3H), 1.73 (s, 3H), 1.71 (s, 3H), 1.29 (s, 3H) $^{13}\text{C}$  NMR: (100 MHz,  $\text{CDCl}_3$ ) $\delta$  178.8, 161.9, 155.2, 146.2, 144.0, 131.2, 130.4, 129.8, 124.3, 123.3, 123.1, 119.7, 110.0, 72.3, 70.6, 61.0, 55.2, 54.8, 51.1, 45.4, 42.9, 30.7, 22.4, 22.1, 9.2, 6.8.

IR: (neat)

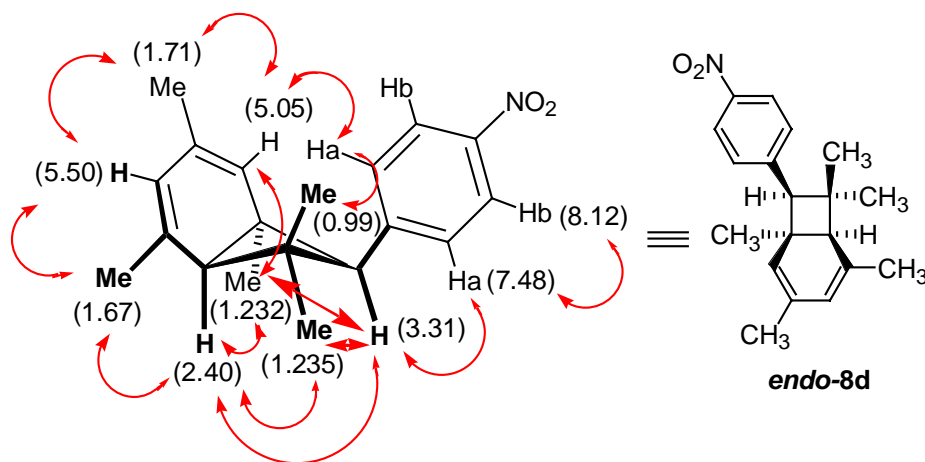
 $\nu$  2952, 2856, 1667, 1599, 1519, 1462, 1346  $\text{cm}^{-1}$ 

HRMS: (ESI)

Calcd. for  $\text{C}_{28}\text{H}_{32}\text{NO}_6$   $[(\text{M} + \text{H})]^+$  478.2230, found 478.2245.

- Difference NOE for **endo-8d**

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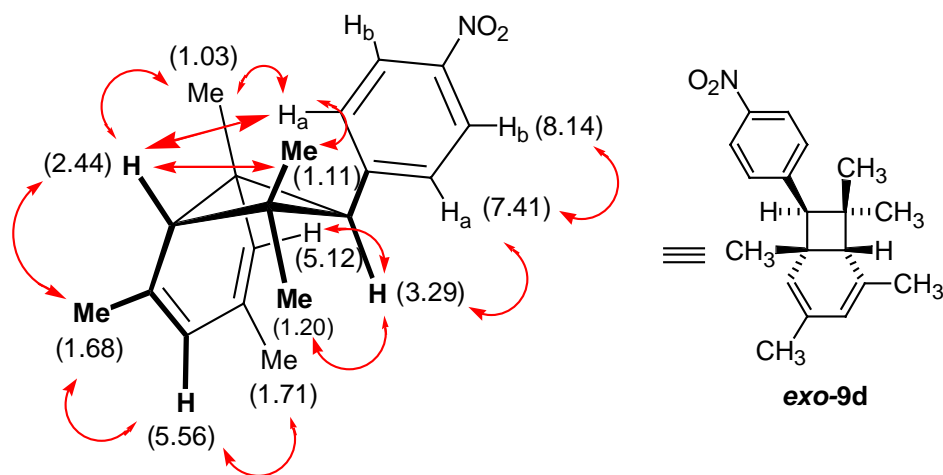
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Irradiated (saturated) peak	Enhanced peaks
5.50 ppm	1.71 ppm, 1.67 ppm
5.05 ppm	7.48 ppm, 1.71 ppm, 1.232 ppm
3.31 ppm	7.48 ppm, 2.40 ppm, 1.235 ppm, 1.232 ppm
2.40 ppm	3.31 ppm, 1.67 ppm, 1.235 ppm, 1.232 ppm
7.48 ppm	8.12 ppm, 5.05 ppm, 3.31 ppm, 0.99 ppm
8.12 ppm	7.48 ppm



- Difference NOE for **exo-9d**

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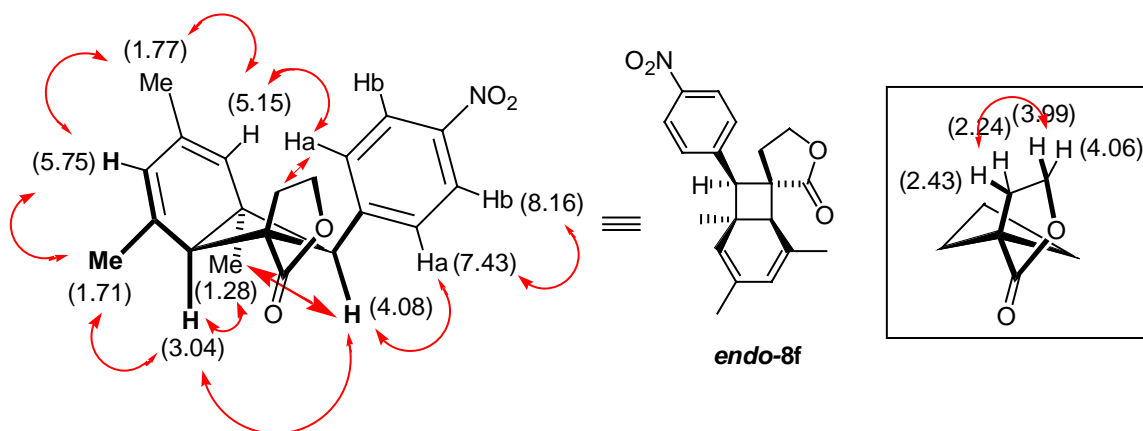


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Irradiated (saturated) peak	Enhanced peaks
5.56 ppm	1.71 ppm, 1.68 ppm
5.12 ppm	3.29 ppm, 1.71 ppm, 1.03 ppm
3.29 ppm	7.41 ppm, 5.12 ppm, 1.20 ppm
2.44 ppm	7.41 ppm, 1.68 ppm, 1.11 ppm, 1.03 ppm
7.41 ppm	8.14 ppm, 3.29 ppm, 1.11 ppm, 1.03 ppm

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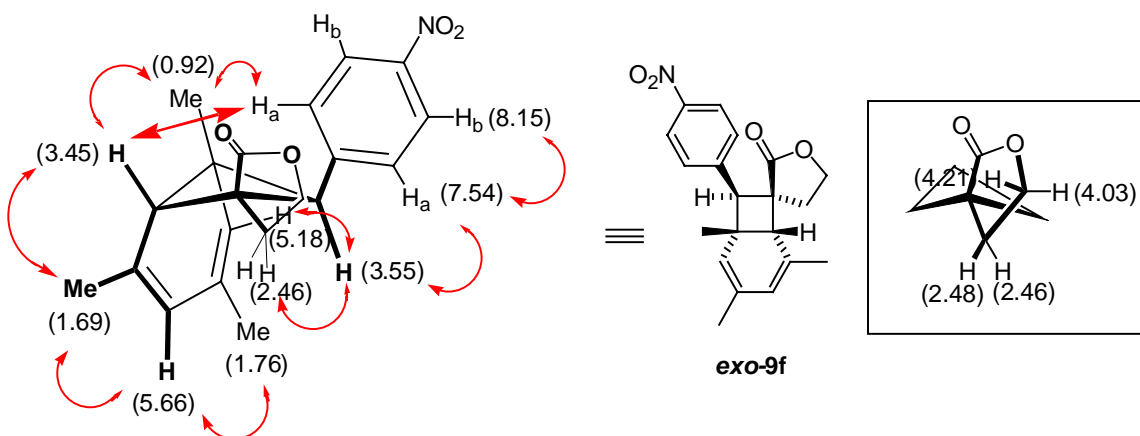


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Irradiated (saturated) peak	Enhanced peaks
5.75 ppm	1.77 ppm, 1.71 ppm
5.15 ppm	7.43 ppm, 1.77 ppm, 1.28 ppm
3.04 ppm	4.08 ppm, 1.71 ppm, 1.28 ppm
2.24 ppm	7.43 ppm, 4.06 ppm, 2.43 ppm
7.43 ppm	8.16 ppm, 5.15 ppm, 4.08 ppm, 2.24 ppm

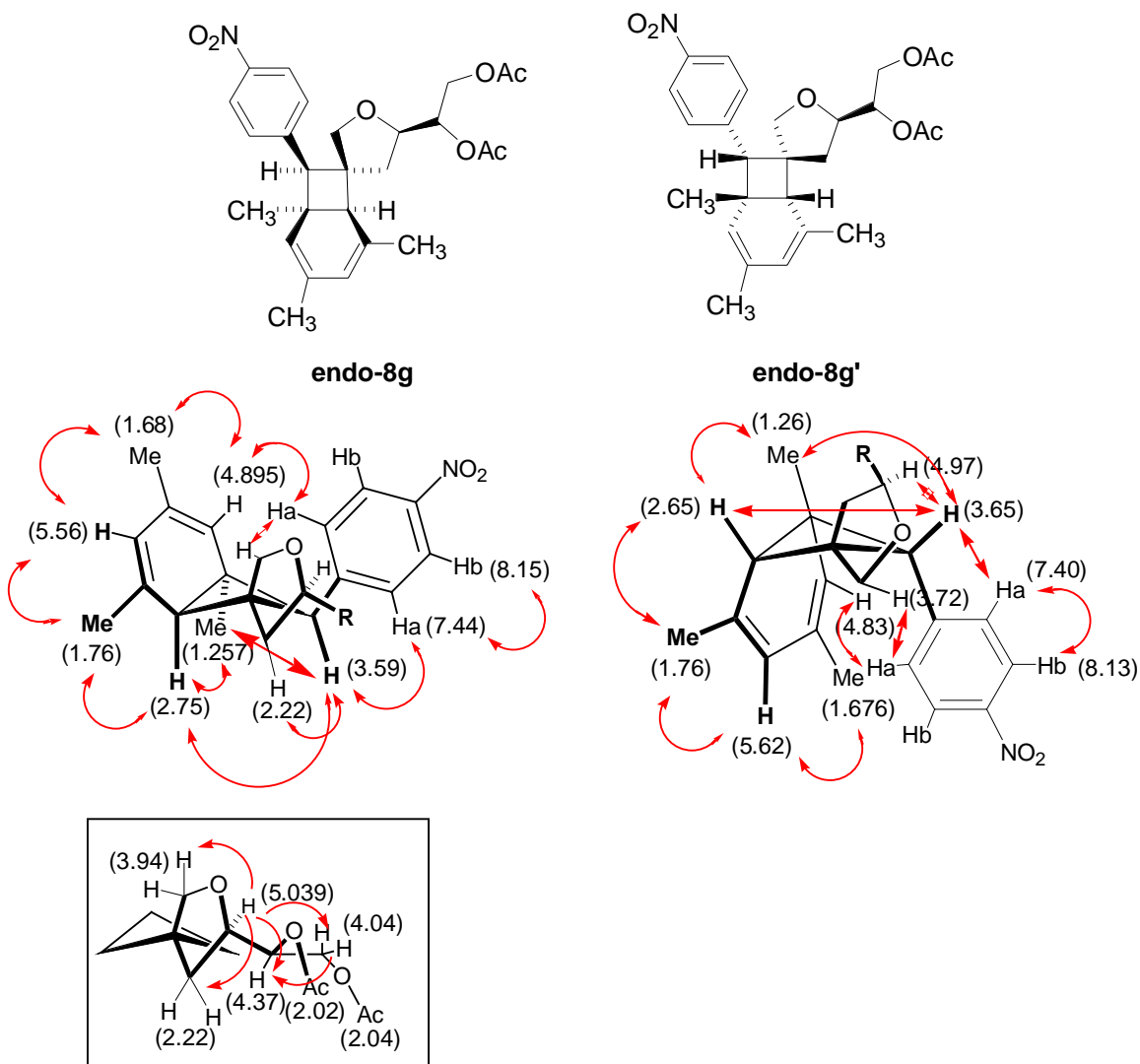
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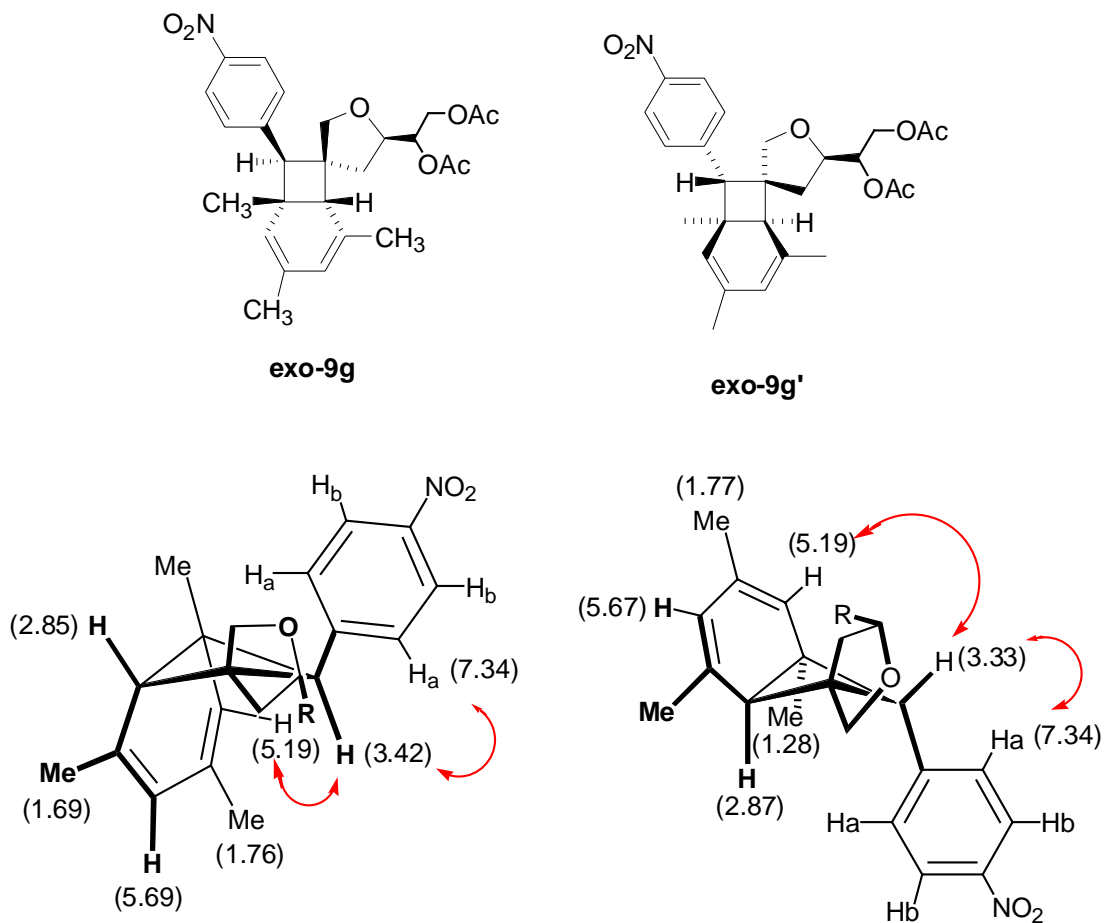
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Irradiated (saturated) peak	Enhanced peaks
5.66 ppm	1.76 ppm, 1.69 ppm
5.18 ppm	3.55 ppm, 1.76 ppm, 0.92 ppm
3.55 ppm	7.54 ppm, 5.18 ppm, 2.46 ppm
3.45 ppm	7.54 ppm, 1.69 ppm, 0.92 ppm
7.54 ppm	8.15 ppm, 3.55 ppm, 3.45 ppm, 0.92 ppm

Difference NOE for **endo-8g**<Difference NOE chart of compound **endo-8g** and **endo-8g'**>

Irradiated peak	Enhanced peaks	Irradiated peak	Enhanced peaks
7.44ppm	8.15, 4.895, 3.59, 3.94 ppm	7.40 ppm	8.13, 4.83, 3.72, 3.65 ppm
5.56 ppm	1.76, 1.68 ppm	5.62 ppm	1.76, 1.676 ppm
4.895 ppm	7.44, 1.68, 1.257 ppm	4.83 ppm	7.40, 1.676, 1.26 ppm
3.59 ppm	7.44, 2.75, 2.22, 1.257 ppm	3.65 ppm	7.40, 4.97, 2.65, 1.26 ppm
2.75 ppm	3.59, 1.76, 1.257 ppm	2.65 ppm	3.65, 1.76, 1.26 ppm
5.039 ppm	4.37, 4.04, 3.94, 2.22 ppm	4.97 ppm	3.65 ppm

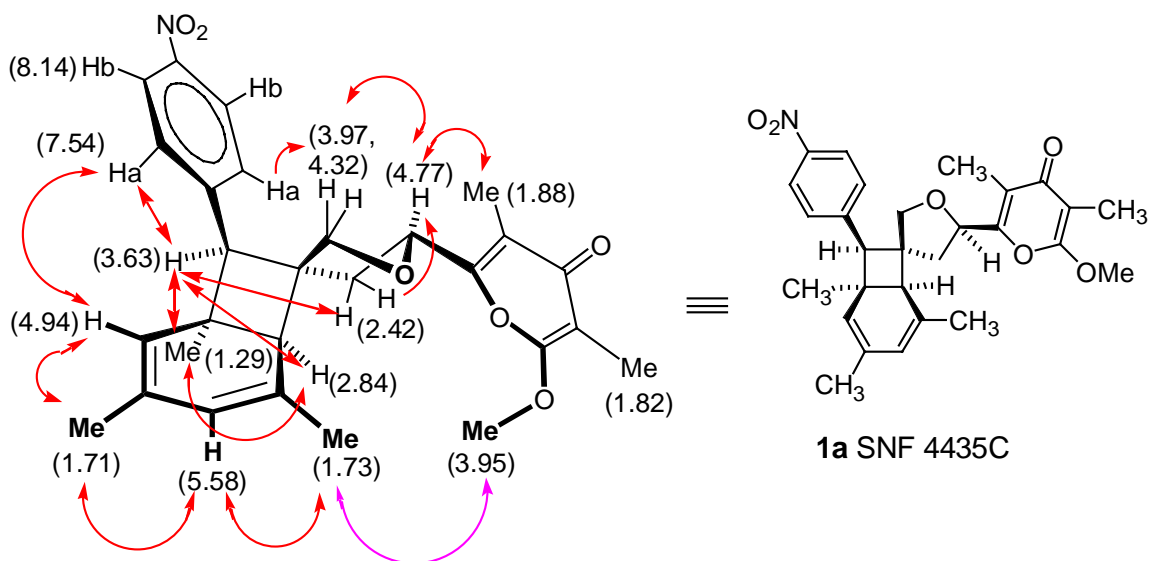
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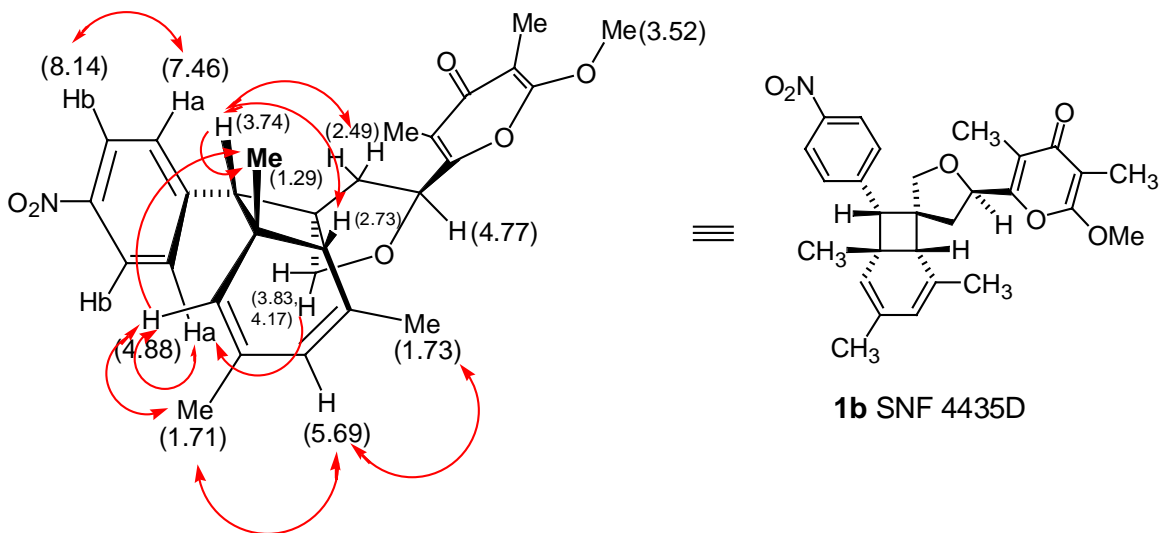
Irradiated peak	Enhanced peaks	Irradiated peak	Enhanced peaks
5.19 ppm	3.42, 1.76 ppm	5.19 ppm	3.33, 1.77 ppm
5.69 ppm	1.76, 1.69 ppm	5.67 ppm	1.77 ppm
3.42 ppm	7.34, 5.19 ppm	3.33 ppm	7.34, 5.19 ppm

- Difference NOE for **1a**

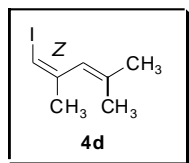
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Irradiated (saturated) peak	Enhanced peaks
5.58 ppm	1.73 ppm, 1.71 ppm
4.94 ppm	7.54 ppm, 1.71 ppm, 1.29 ppm
3.63 ppm	7.54 ppm, 2.84 ppm, 2.42 ppm, 1.29 ppm
2.84 ppm	3.63 ppm, 1.73 ppm, 1.29 ppm
3.95 ppm	1.73 ppm
4.77 ppm	4.32, 3.07 ppm, 2.42 ppm, 1.88 ppm
7.54 ppm	8.14 ppm, 4.94 ppm, 3.63 ppm, 4.32, 3.97 ppm

- Difference NOE for **1b**

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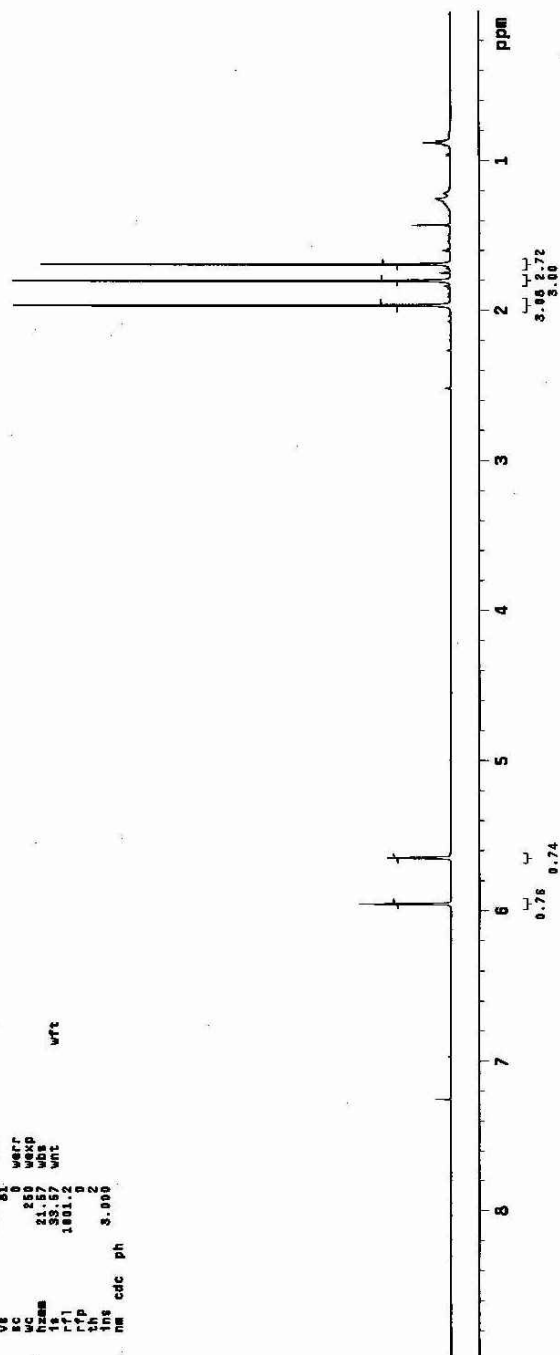
Irradiated (saturated) peak	Enhanced peaks
5.69 ppm	1.73 ppm, 1.71 ppm
4.88 ppm	7.46 ppm, 1.71 ppm, 1.29 ppm
3.74 ppm	7.46 ppm, 2.73 ppm, 2.49 ppm, 1.29 ppm
2.73 ppm	3.74 ppm, 1.73 ppm, 1.29 ppm
3.83 ppm	7.46 ppm, 4.17 ppm
7.46 ppm	8.14 ppm, 4.88 ppm, 3.74 ppm, 4.17, 3.83 ppm



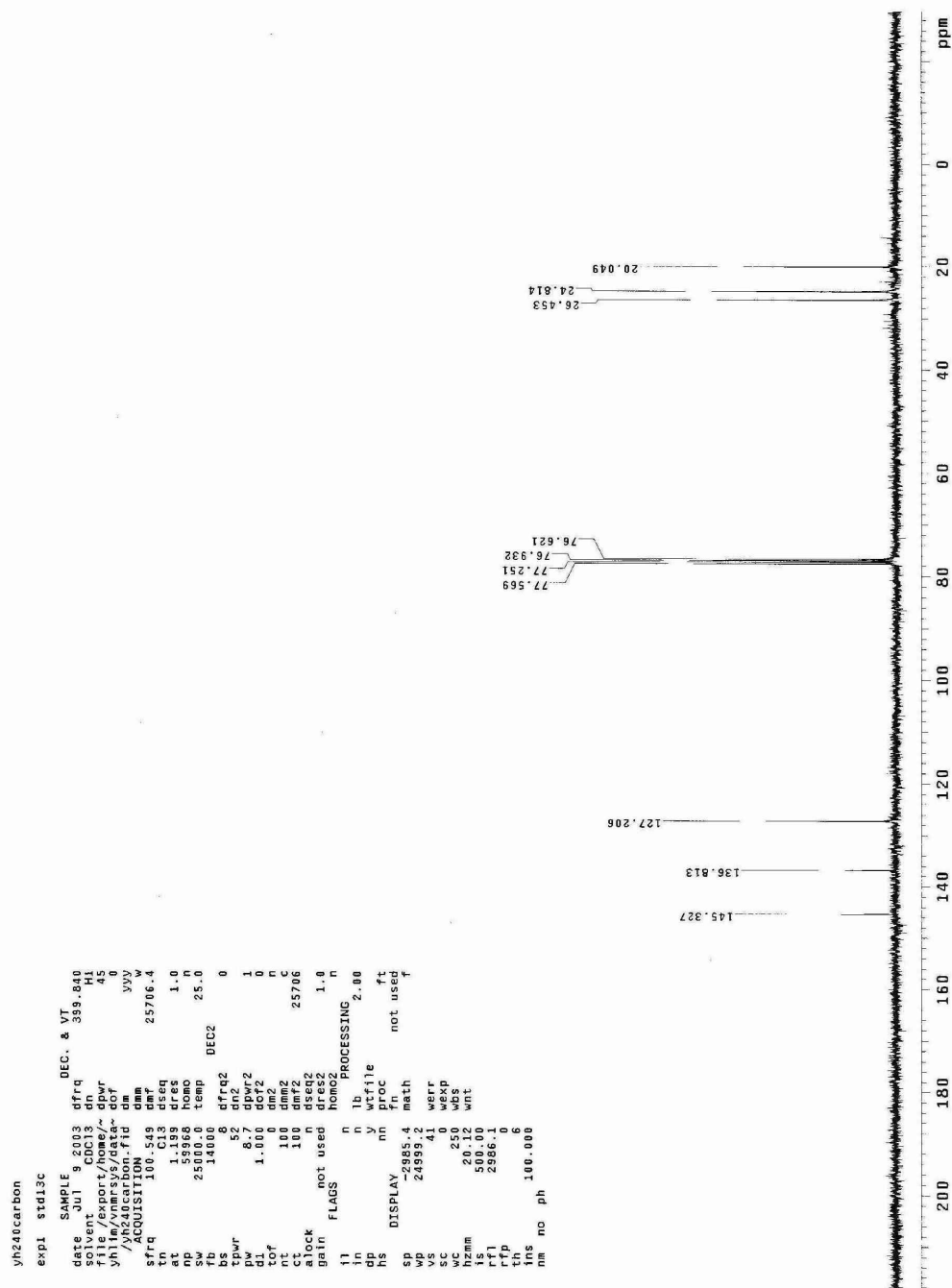
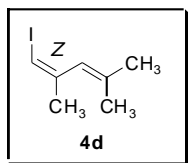
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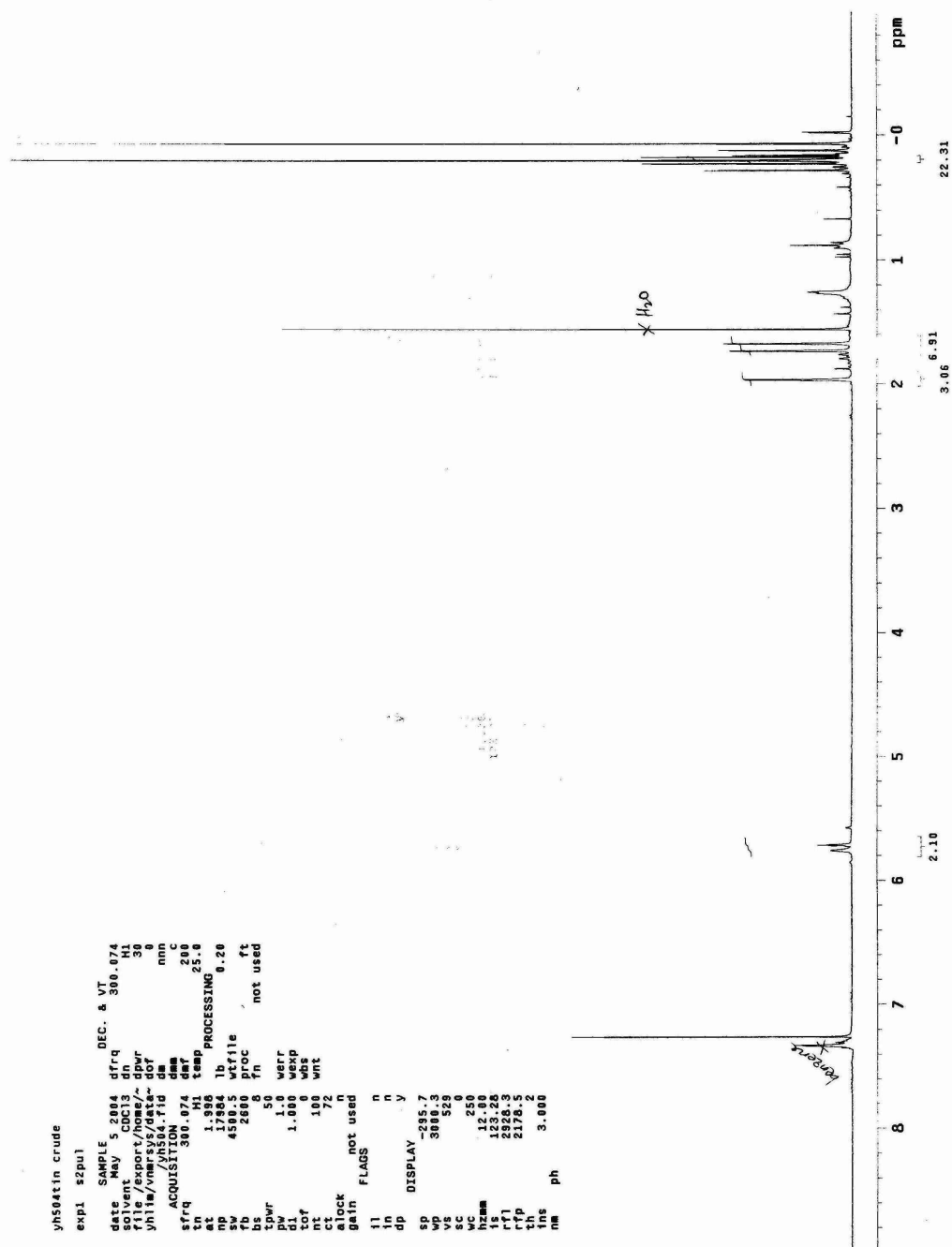
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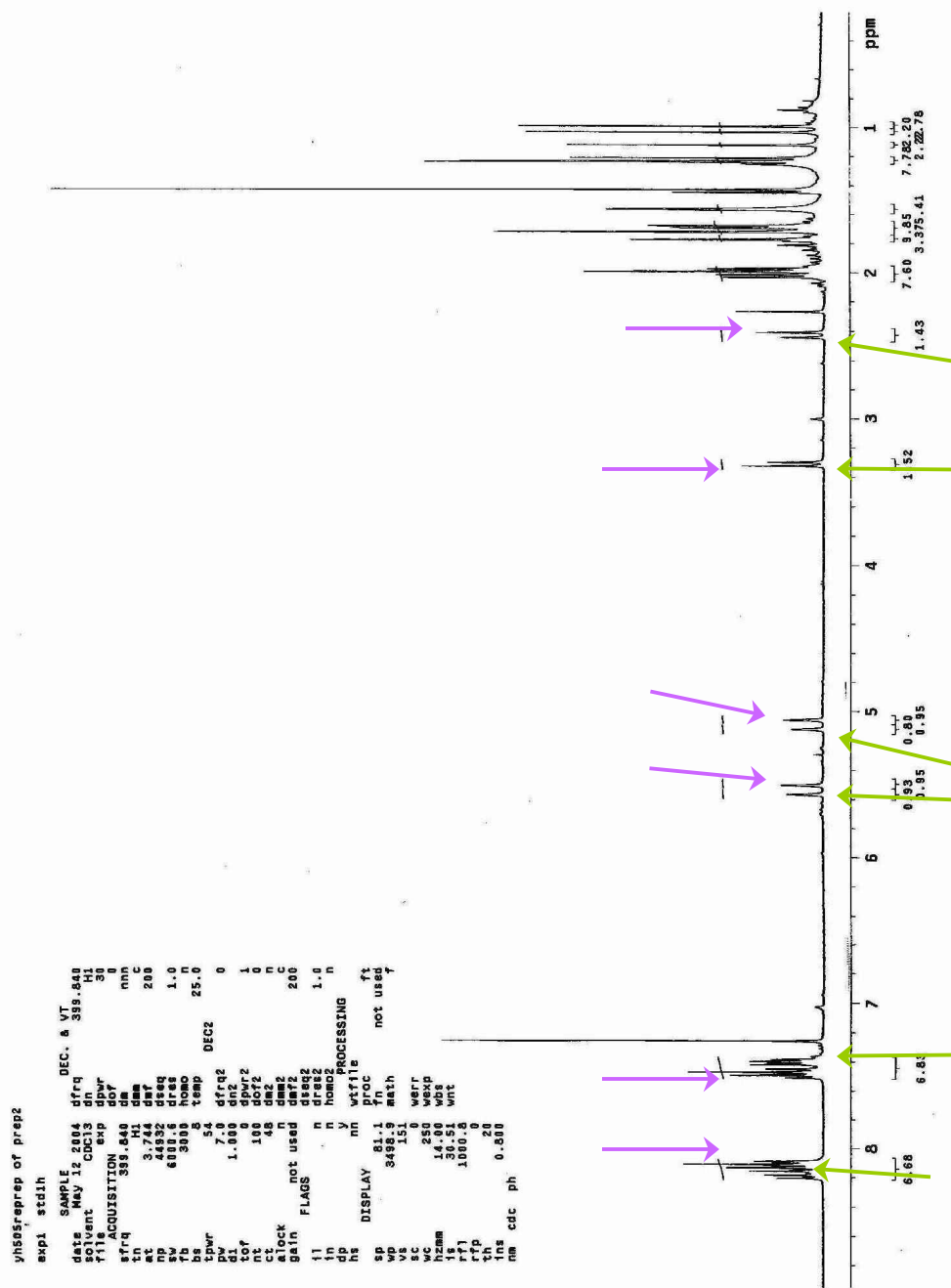
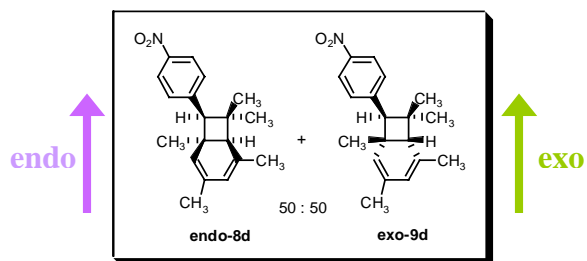
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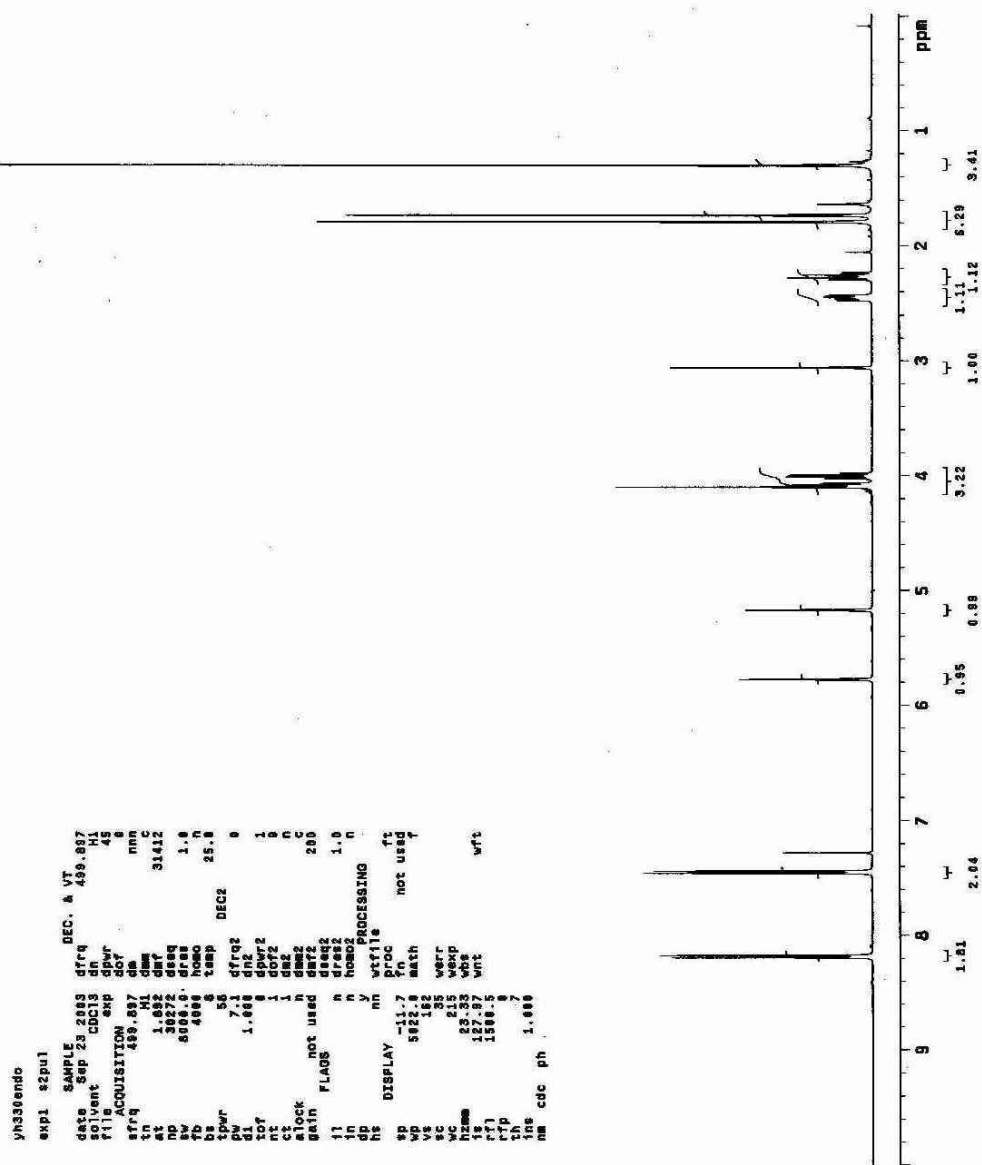
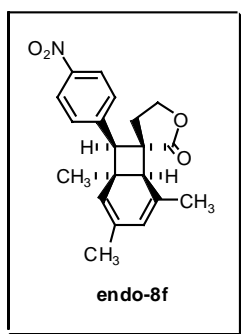




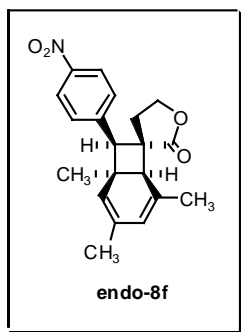
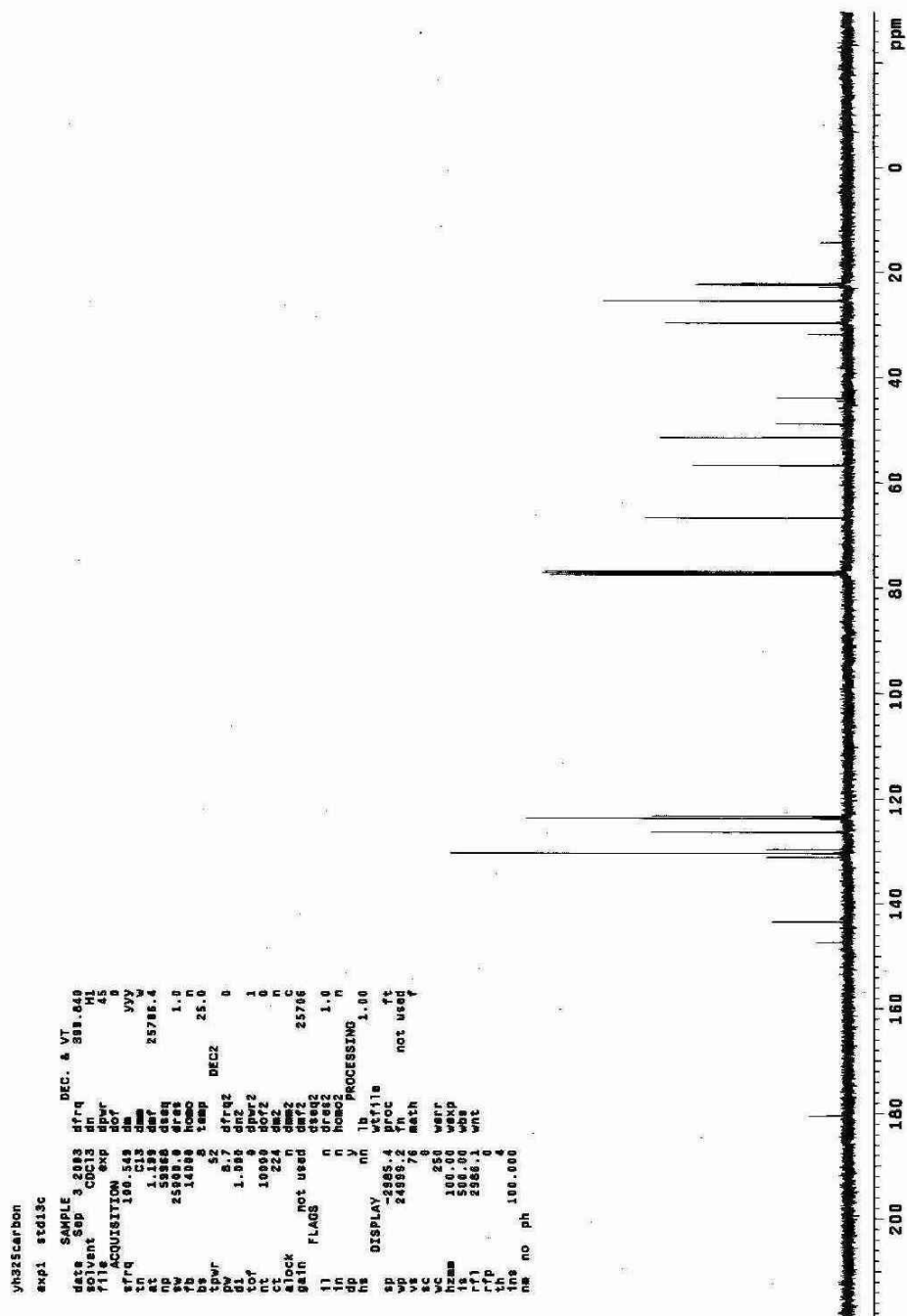


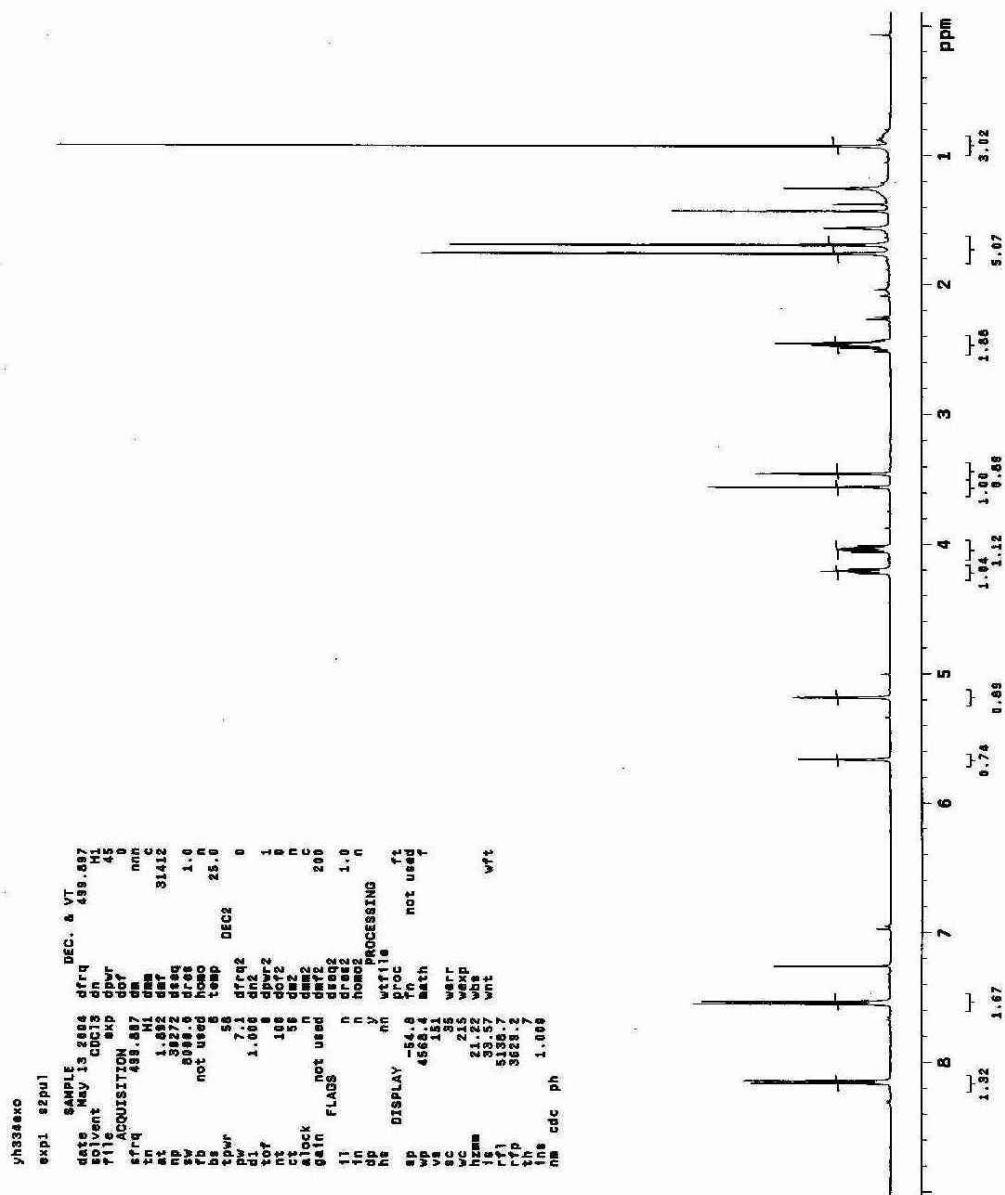
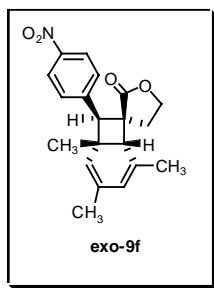






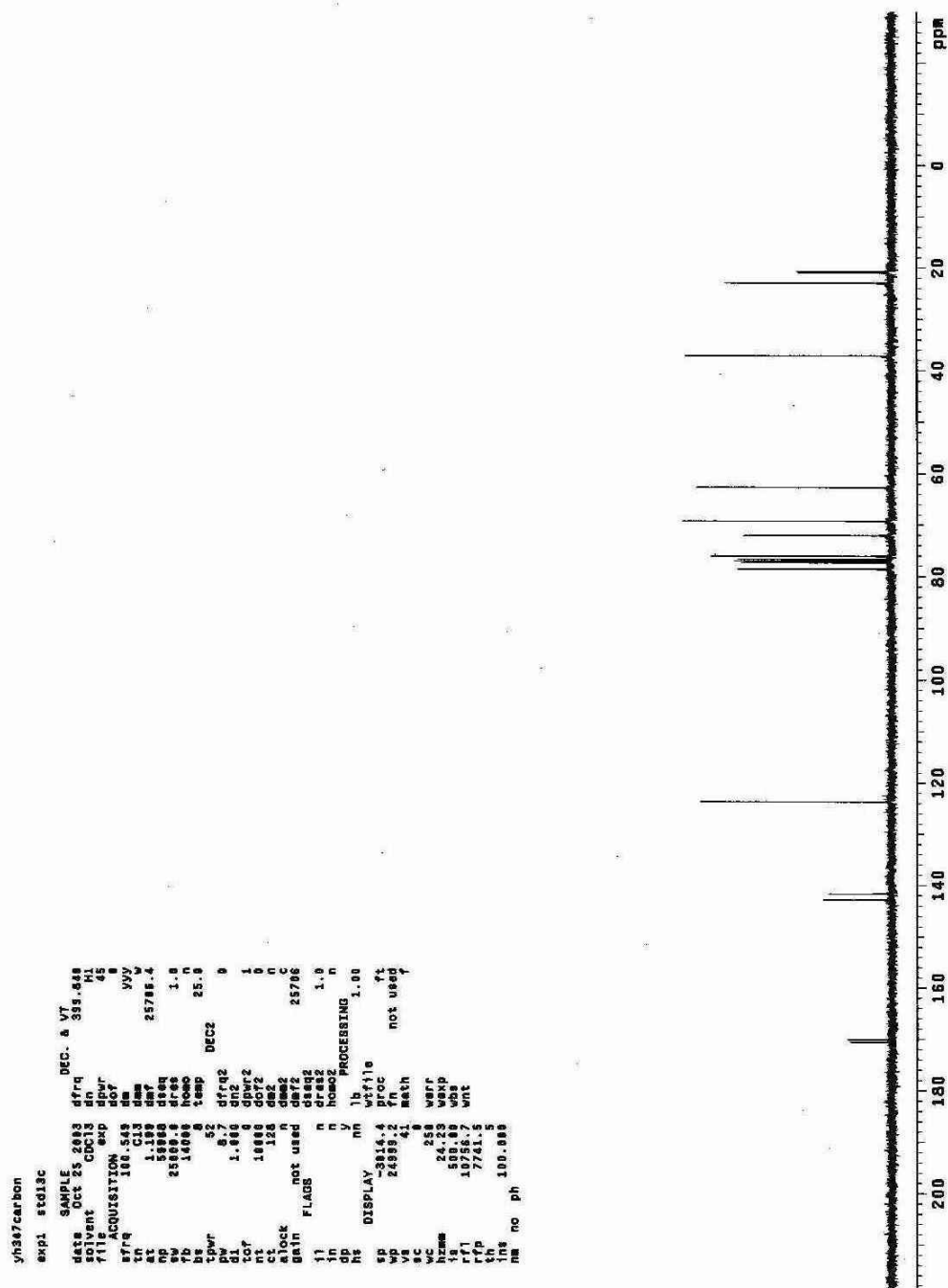
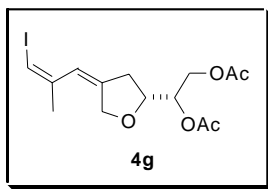


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endo

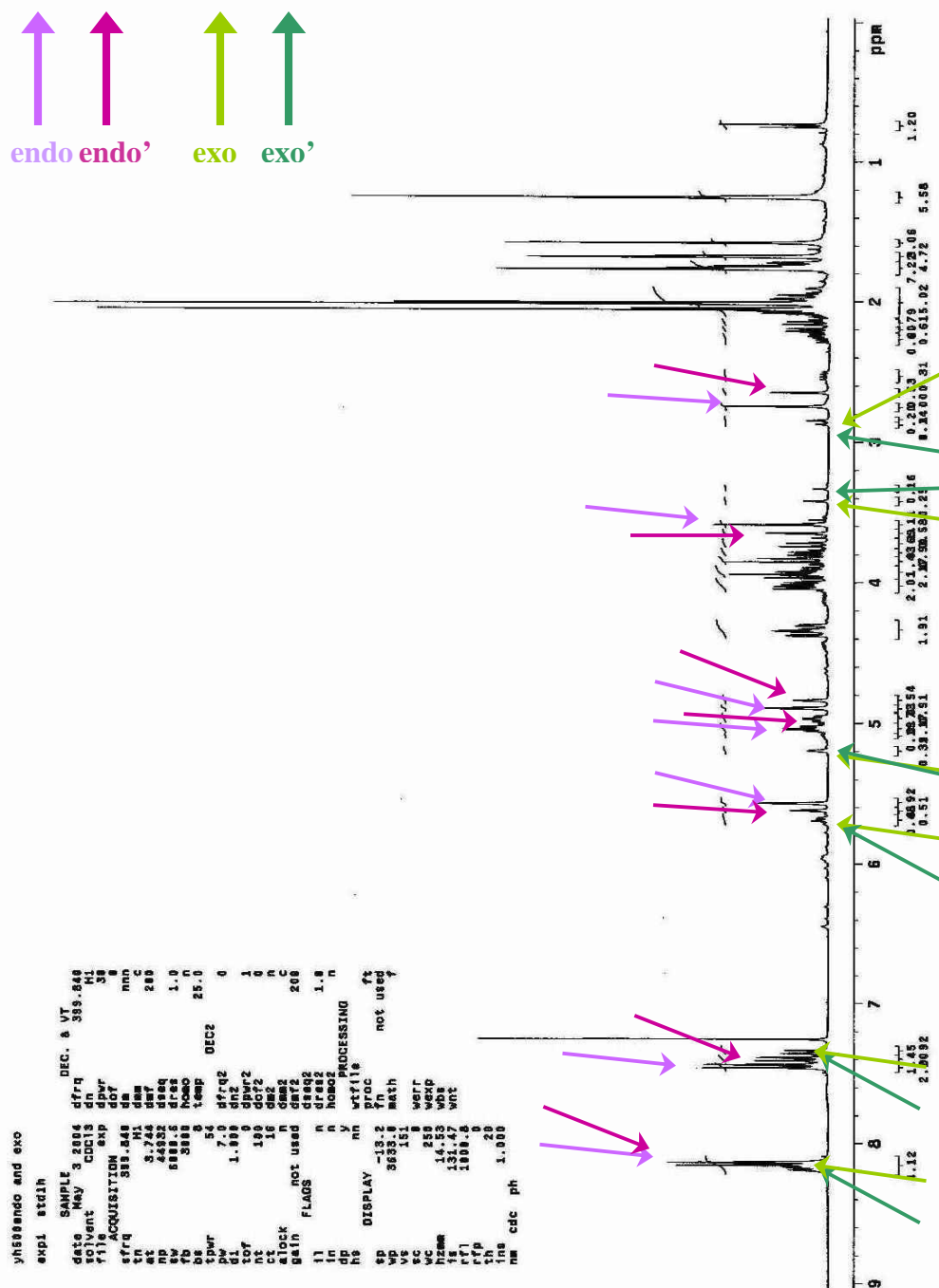
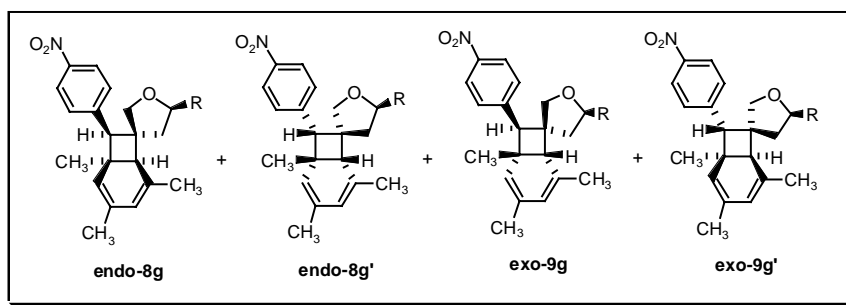


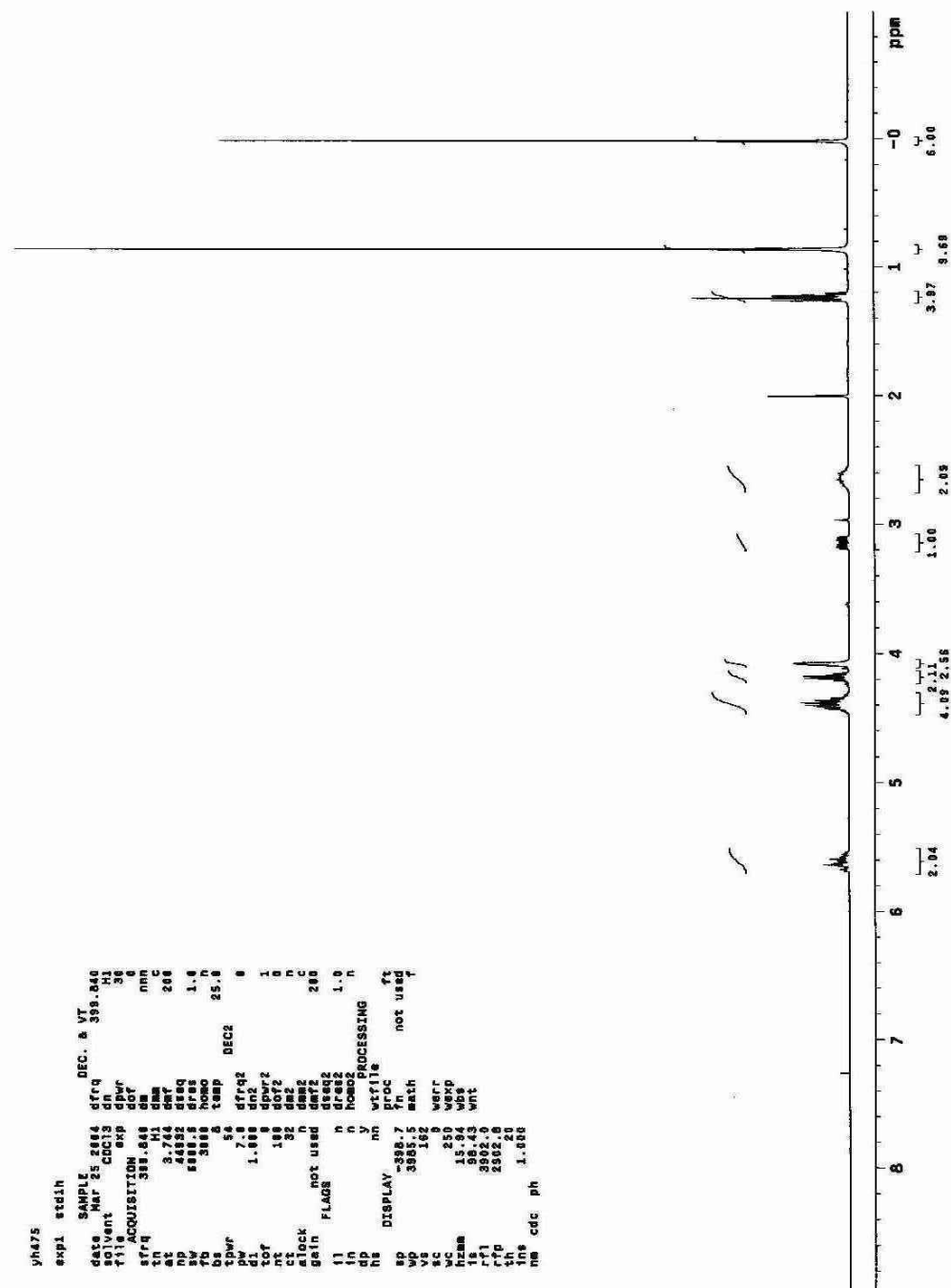
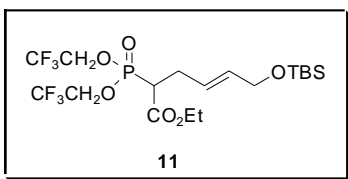




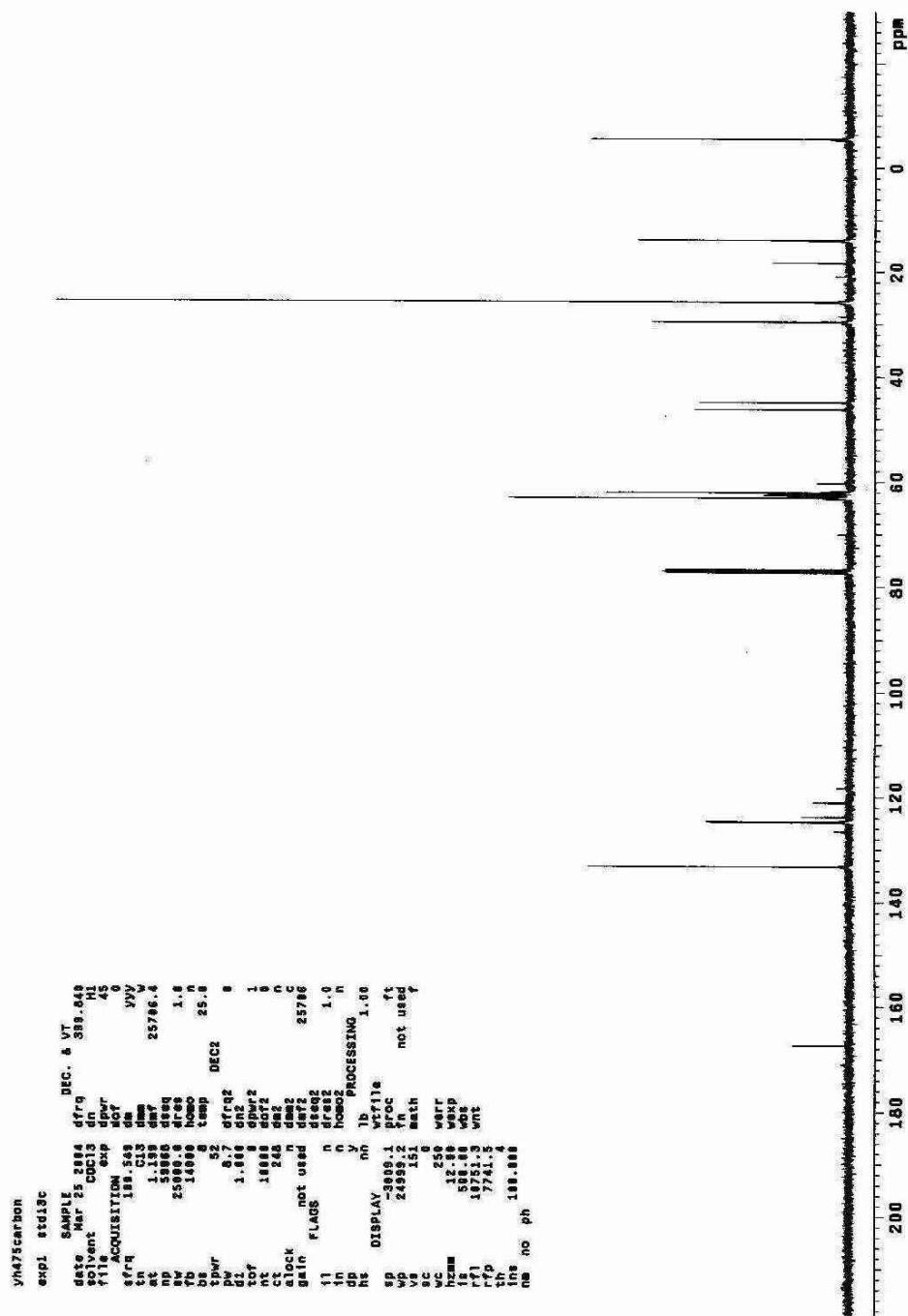
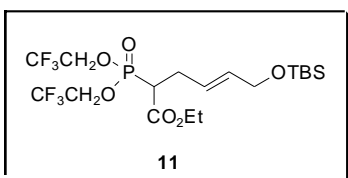


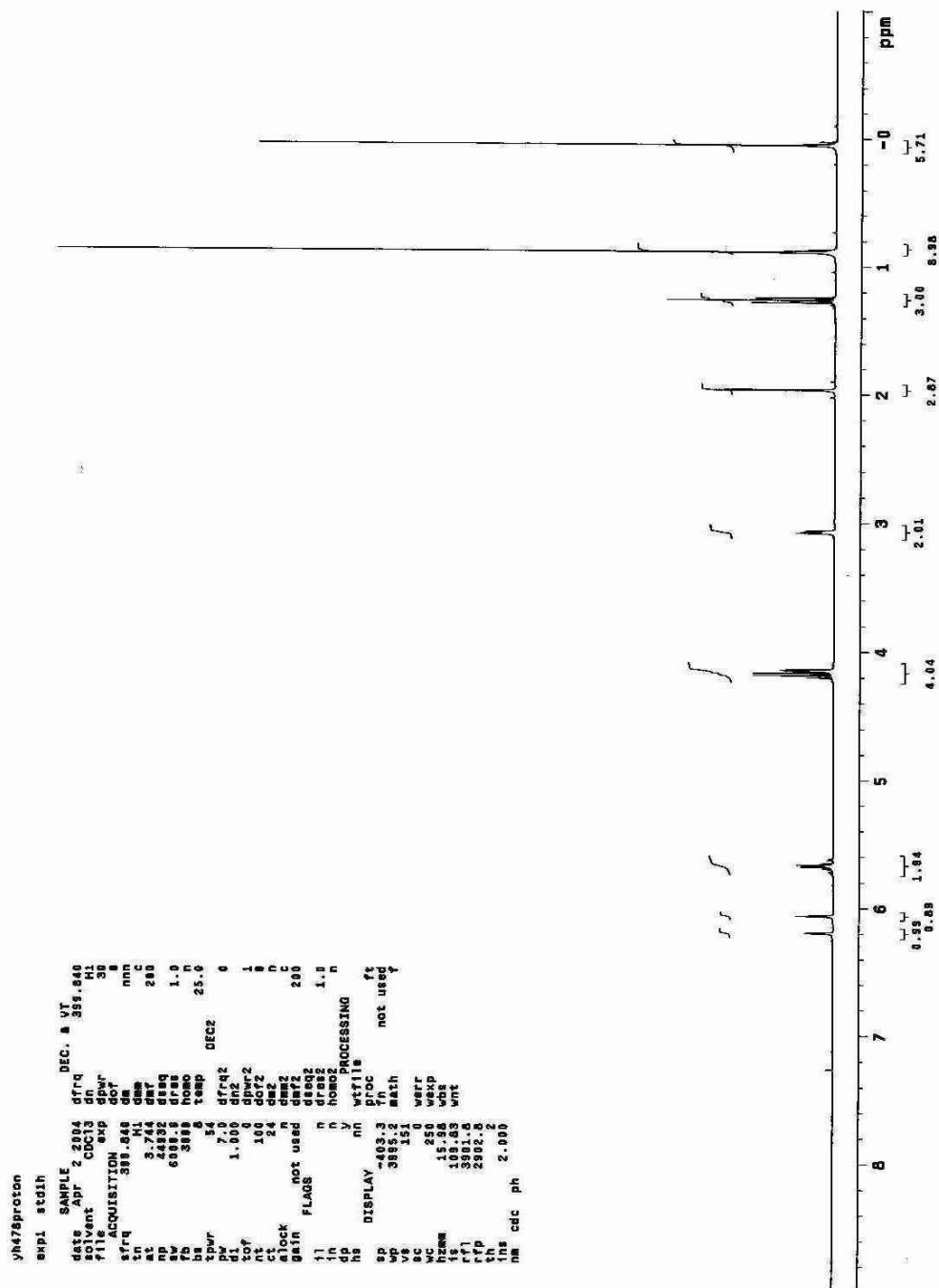
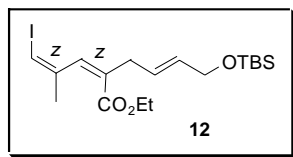


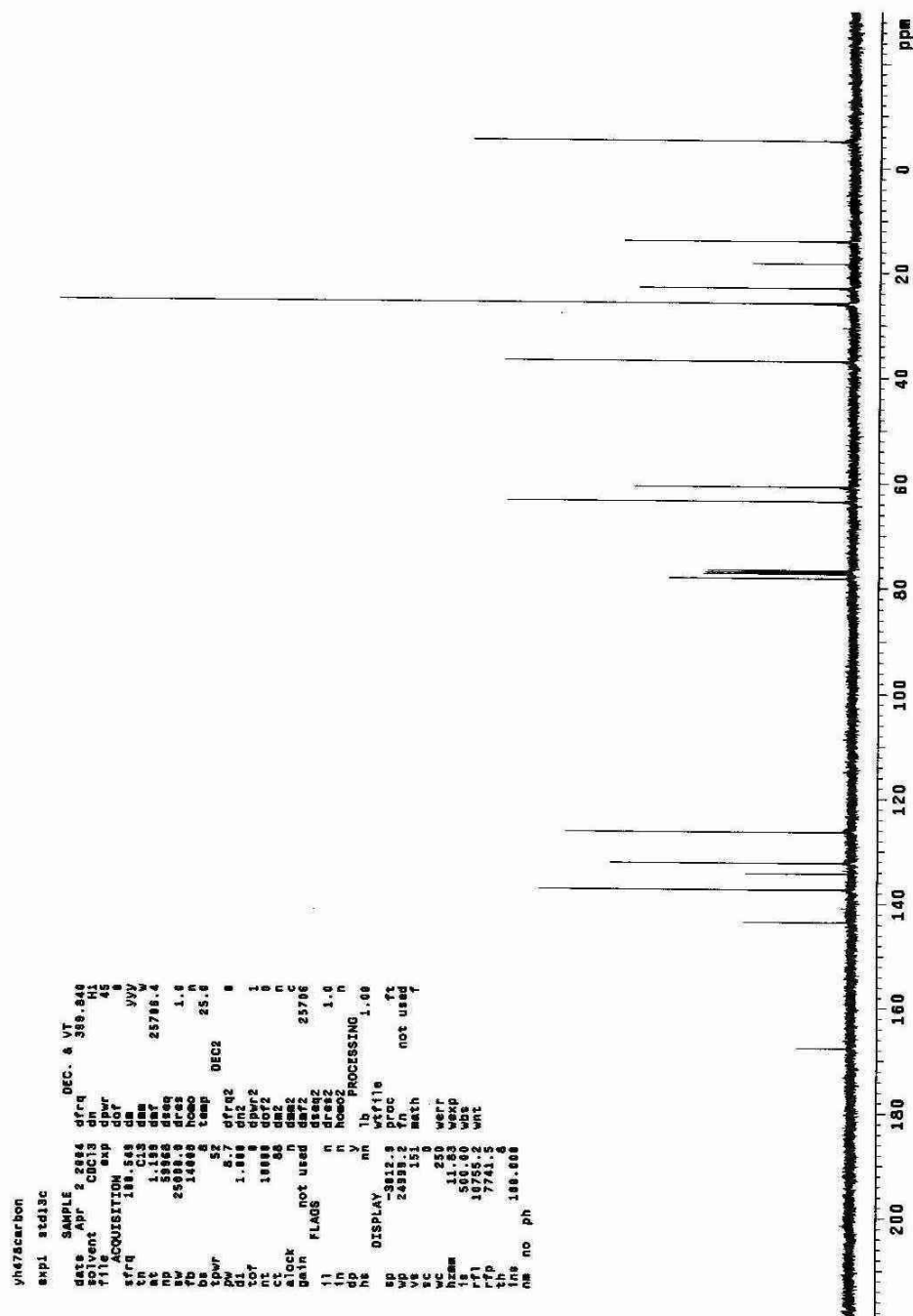
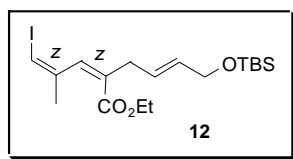


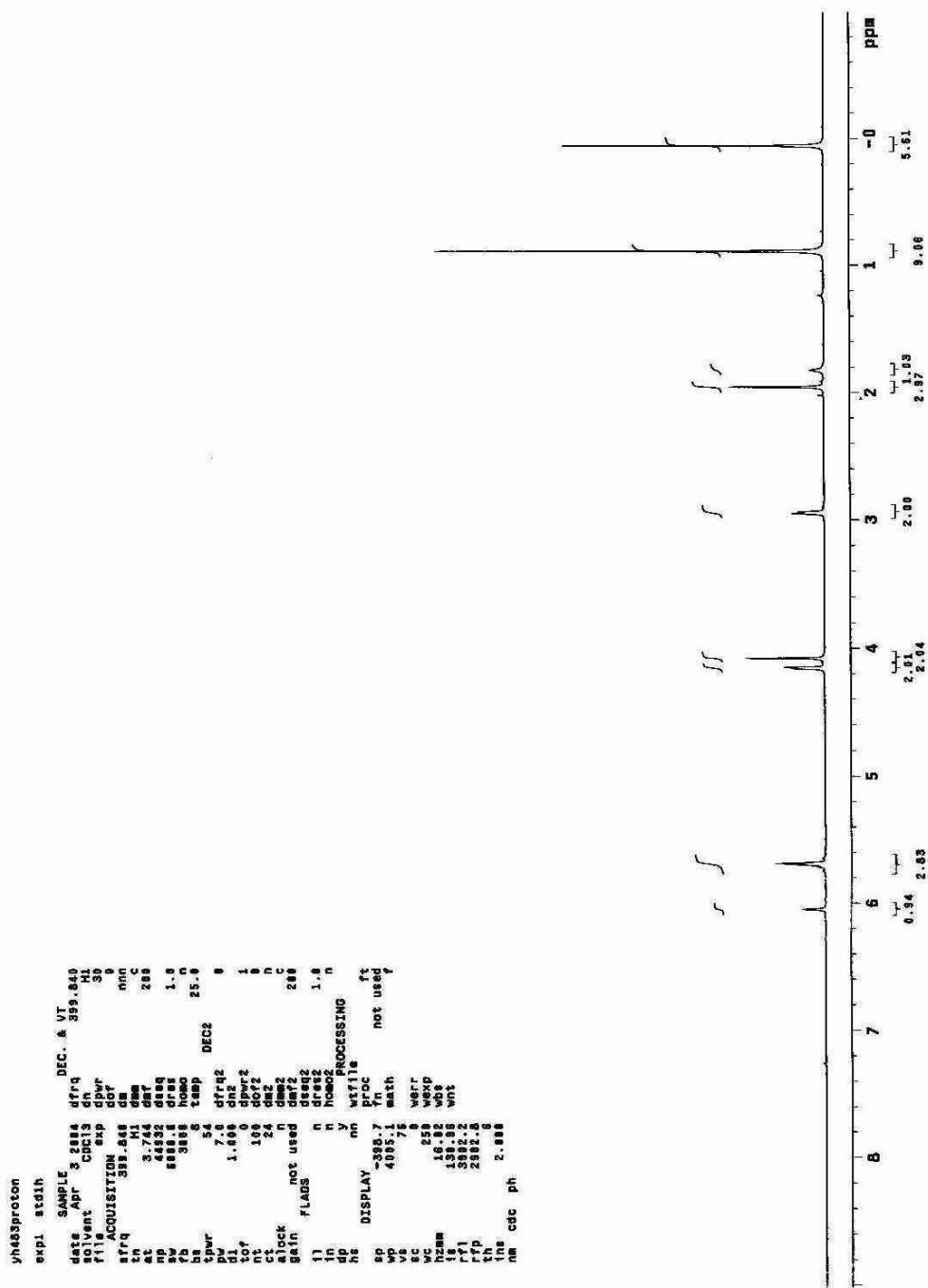
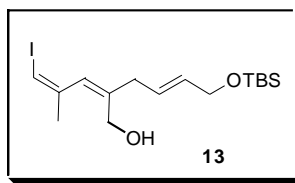


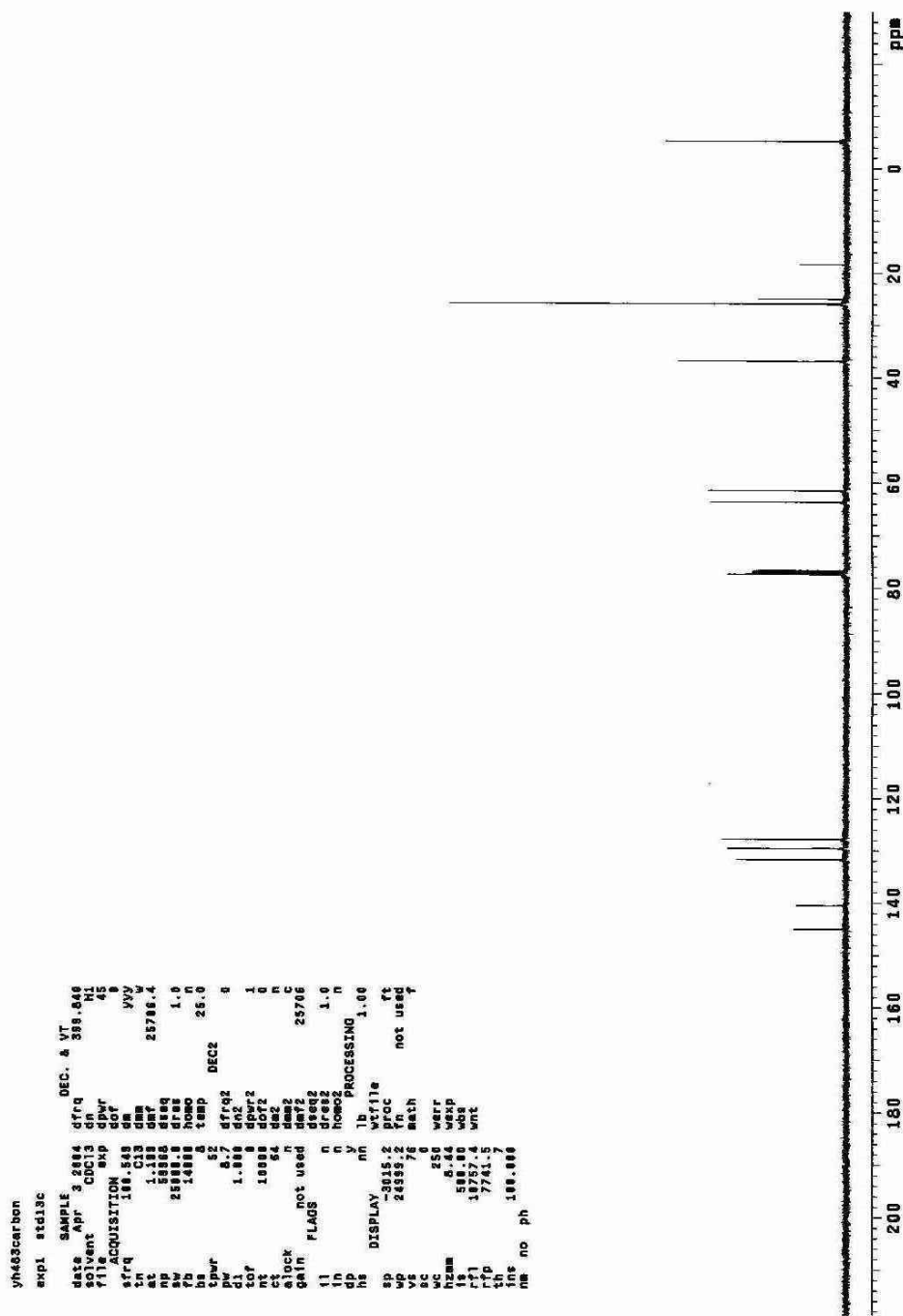
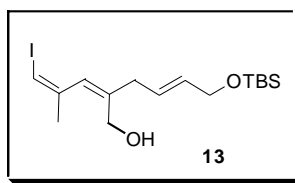


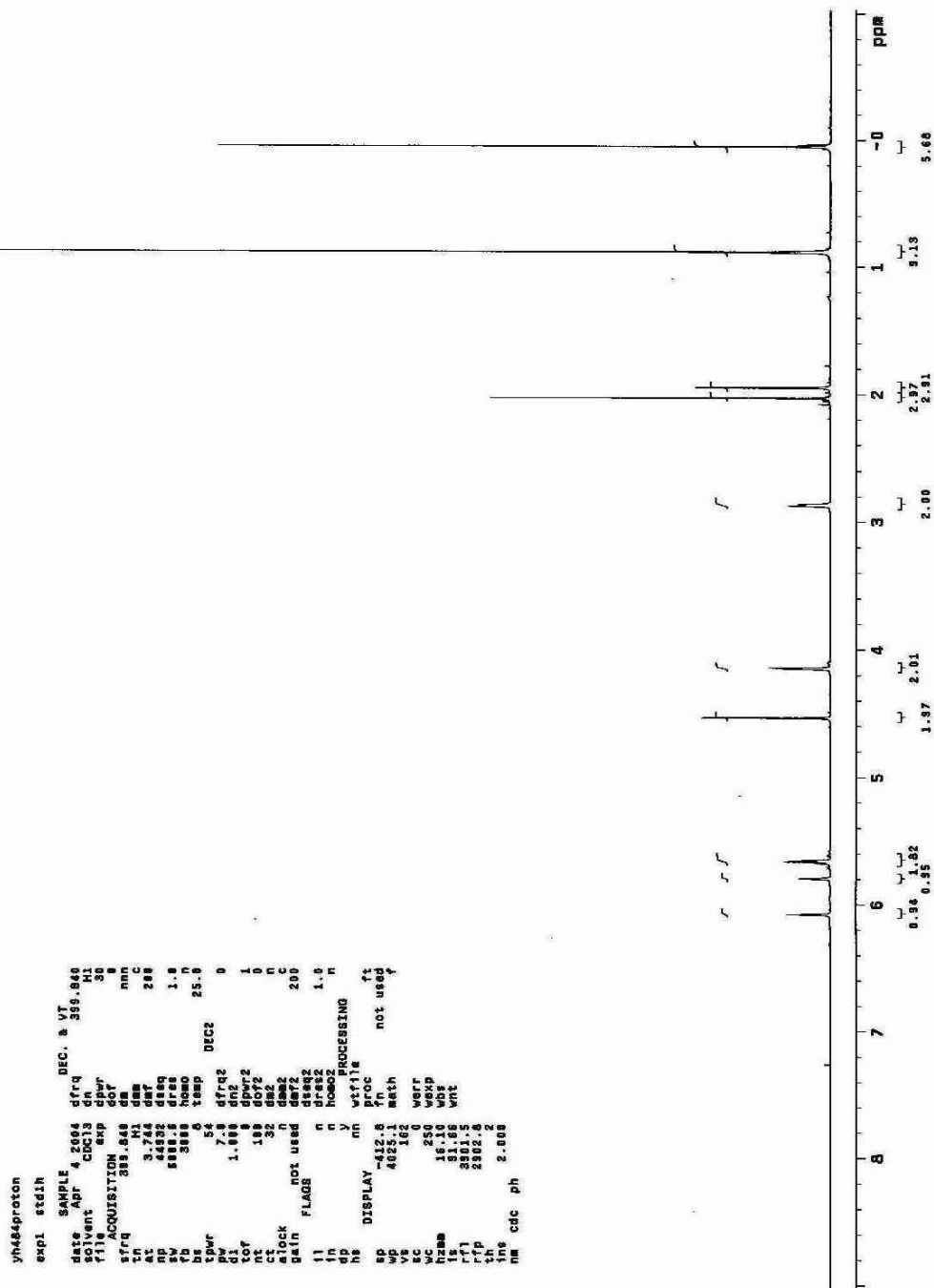
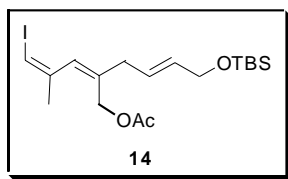


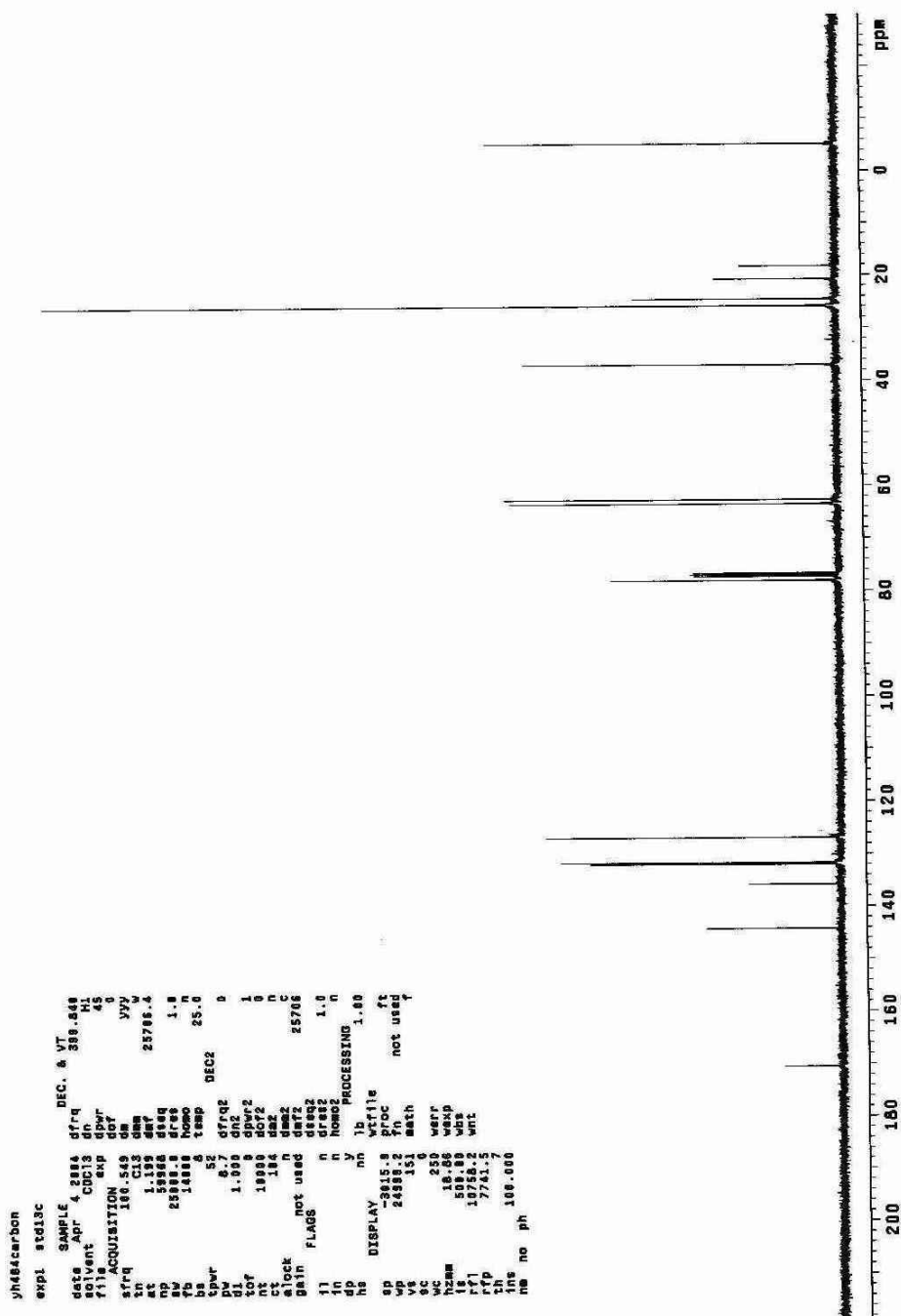
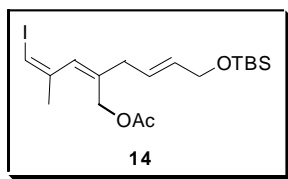


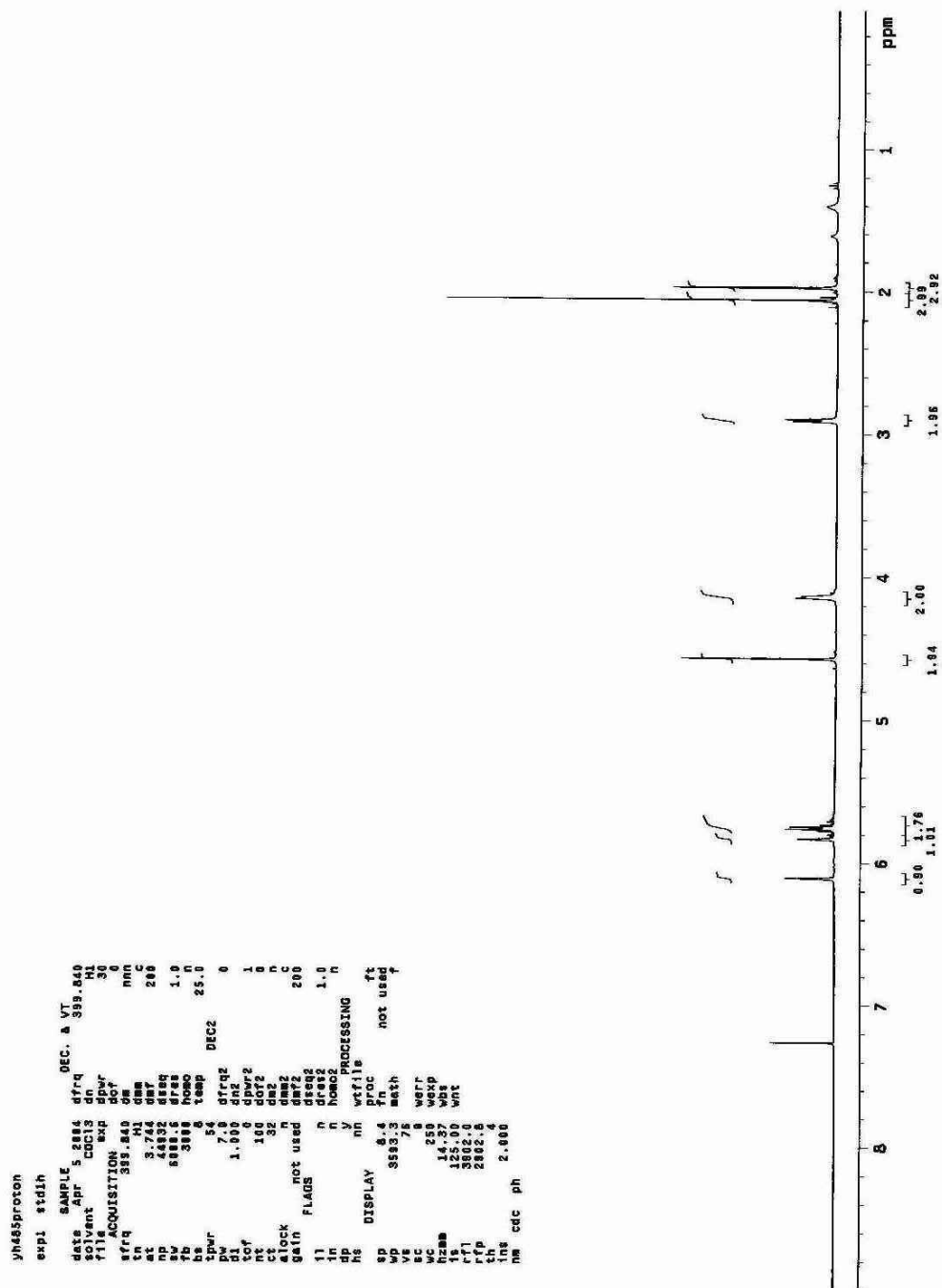




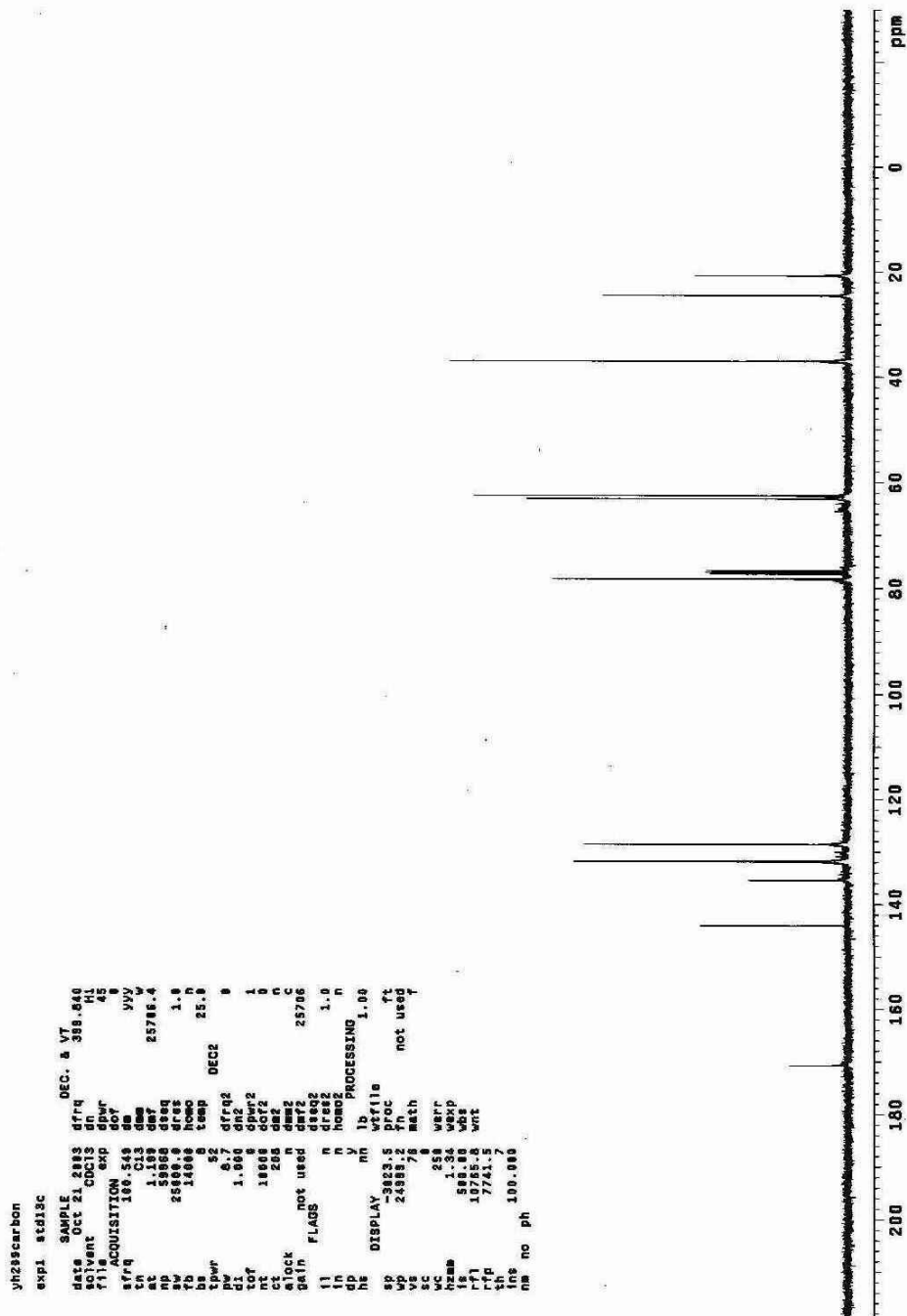
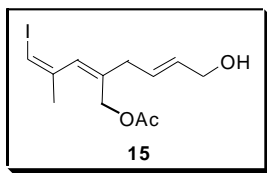


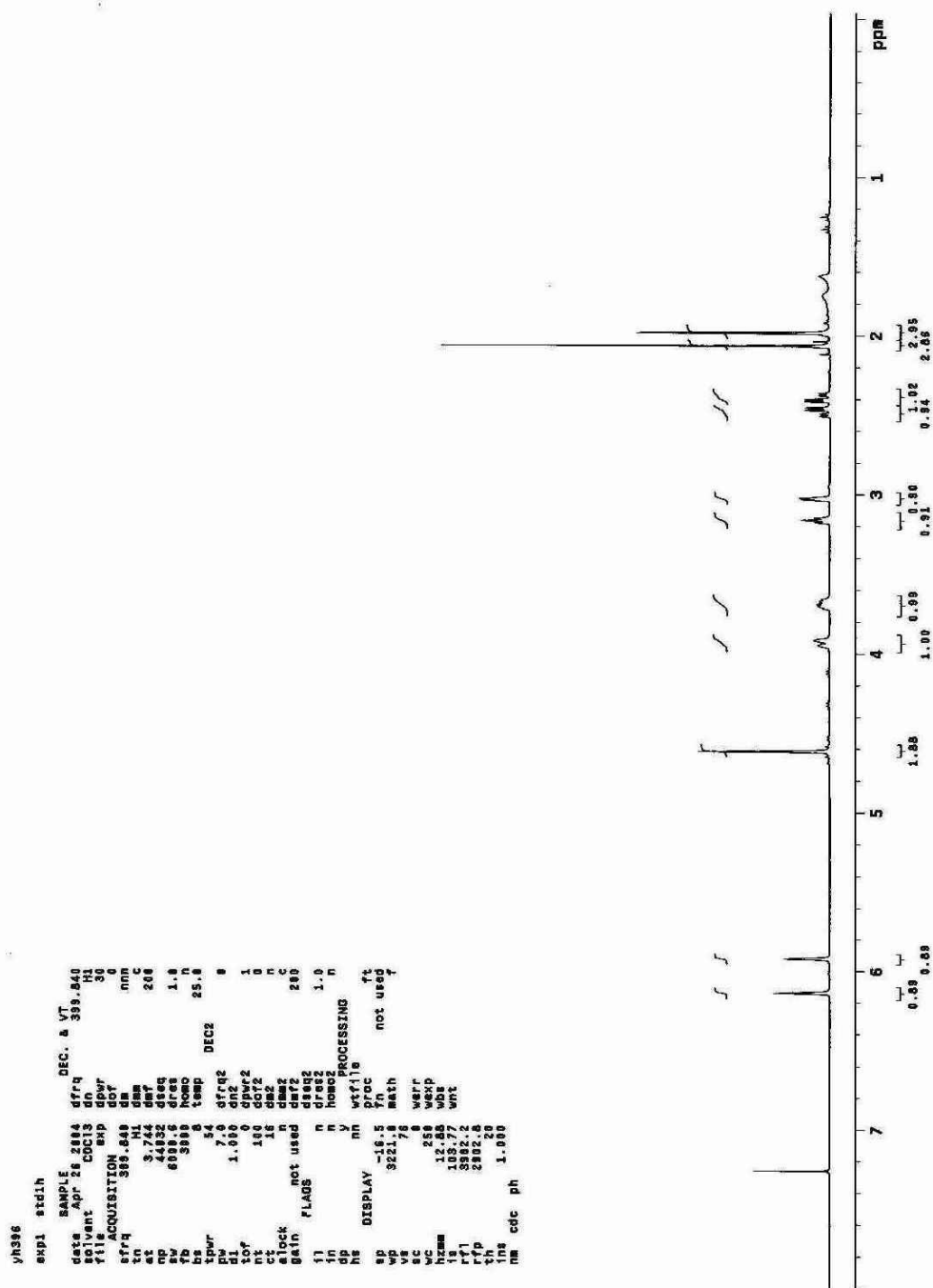
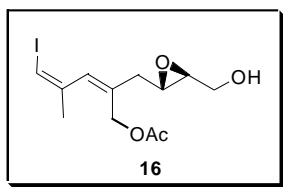


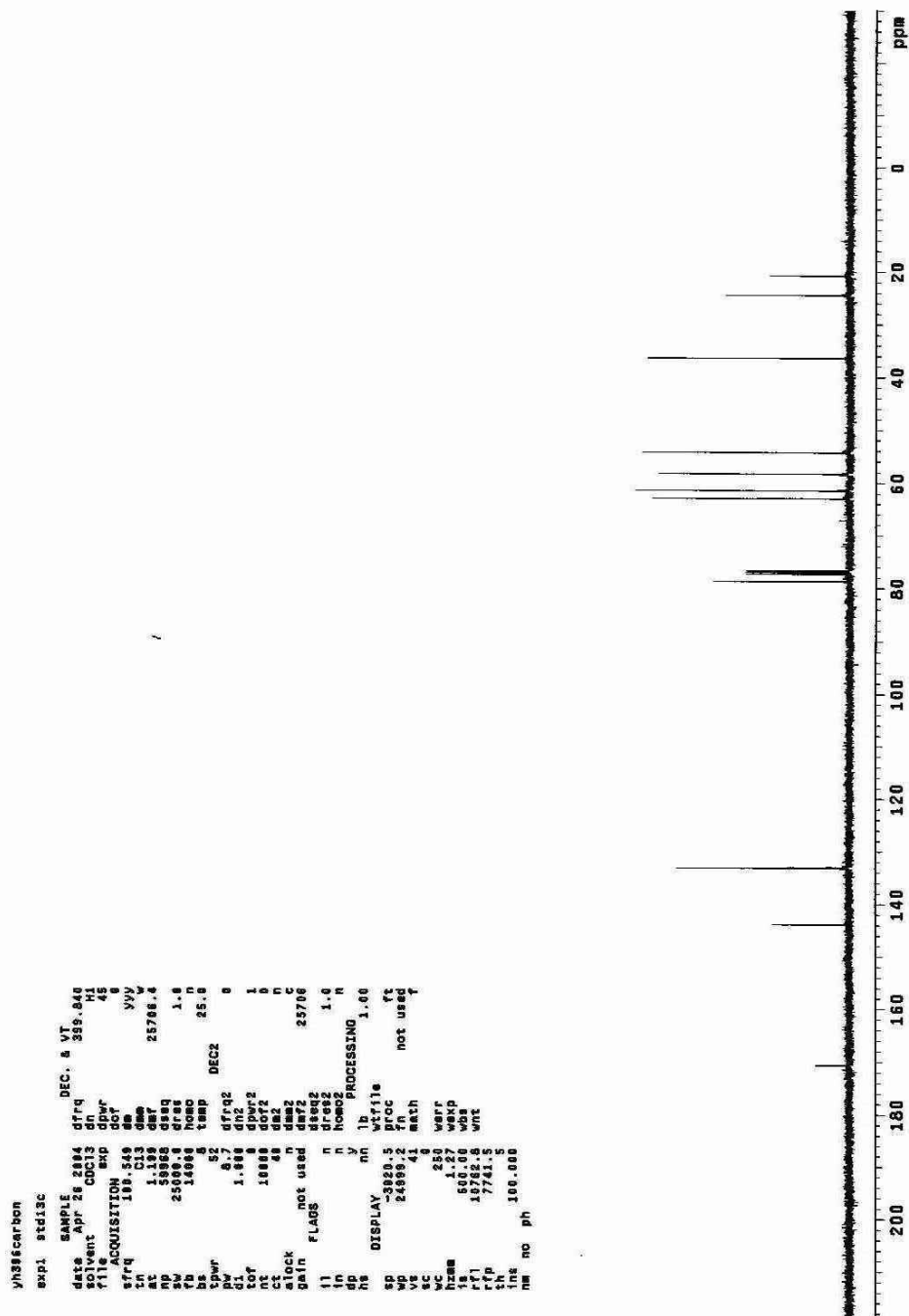
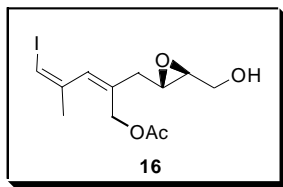


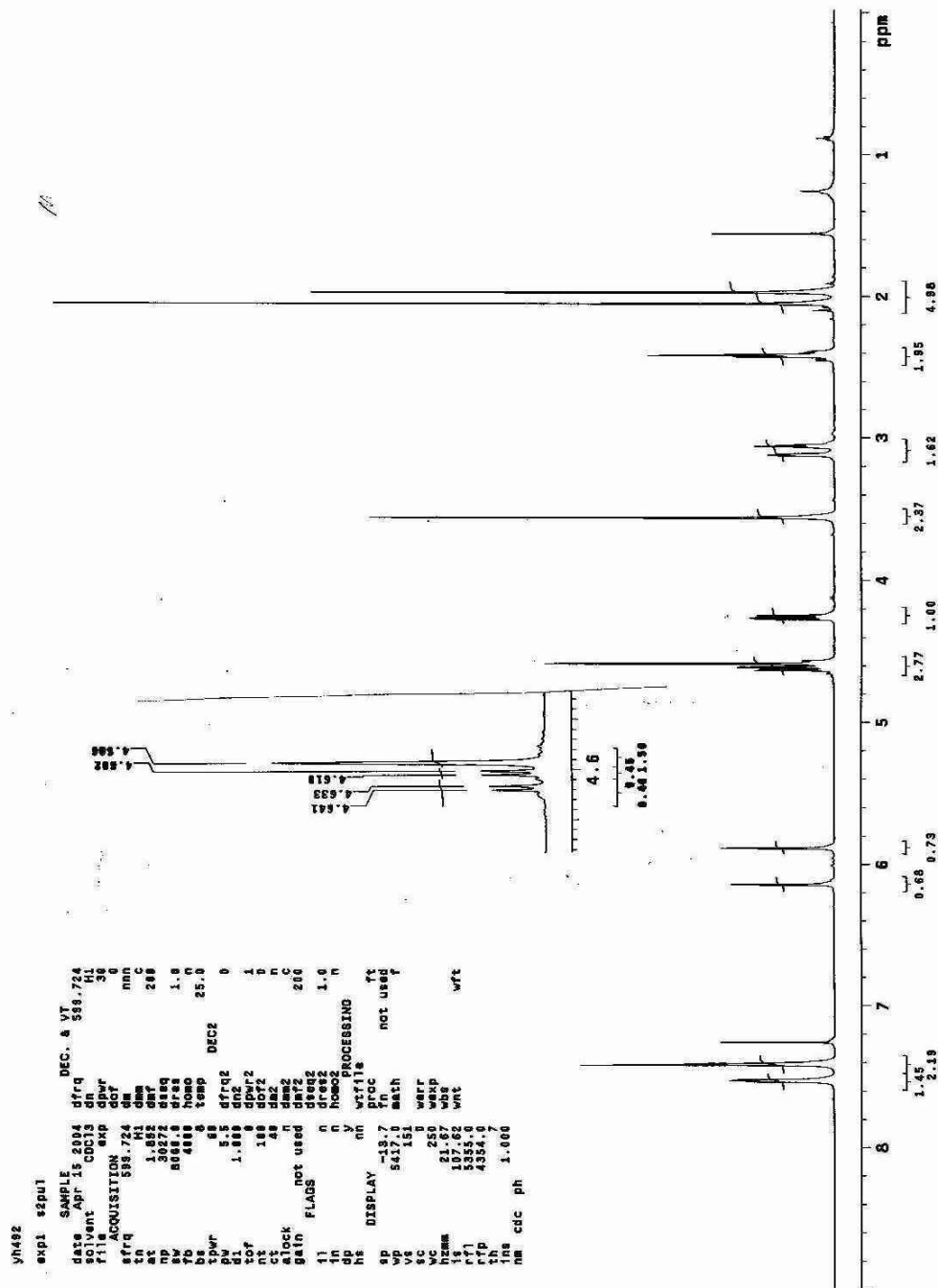
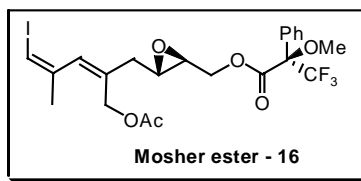


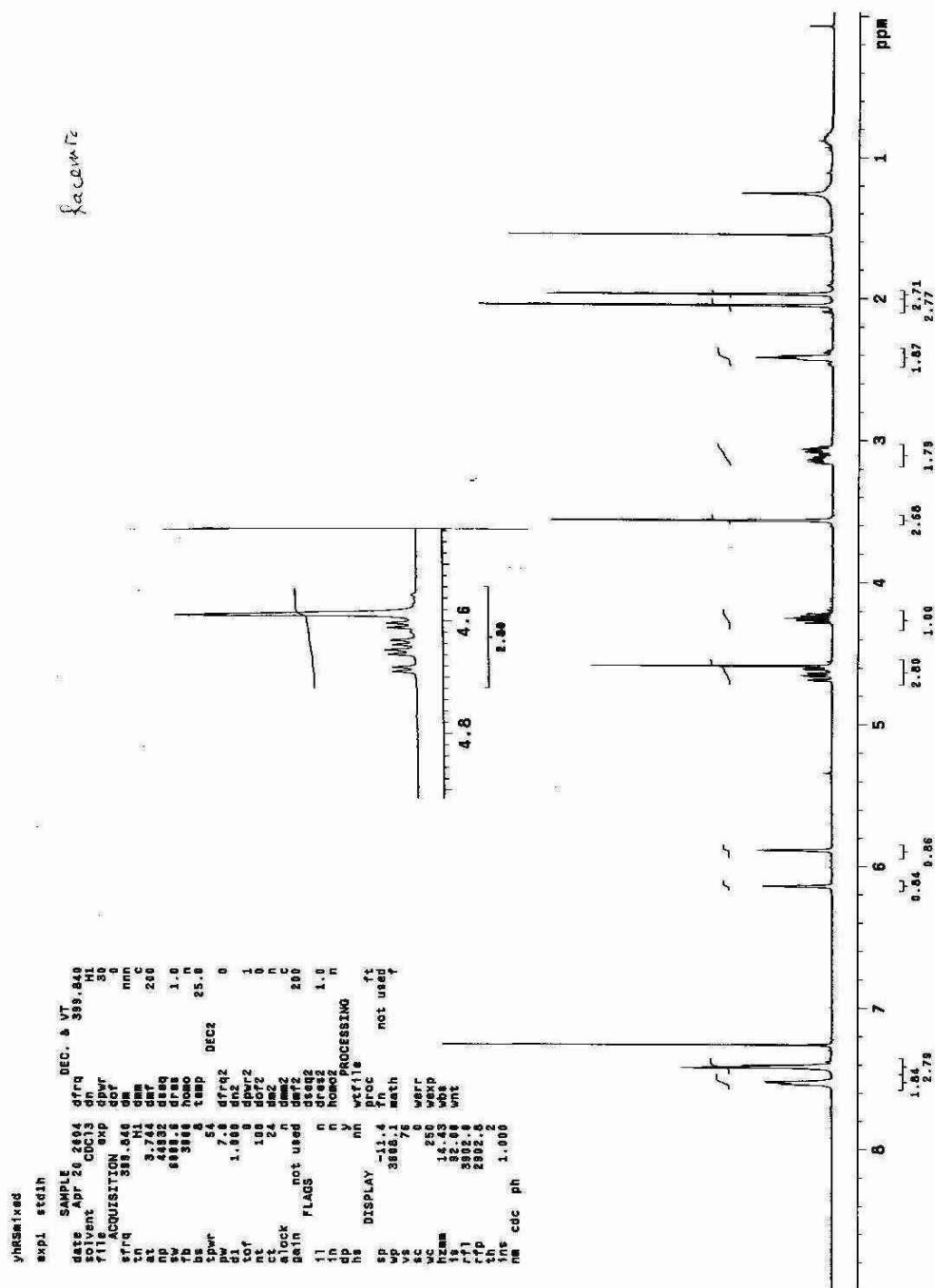
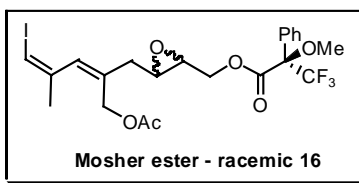






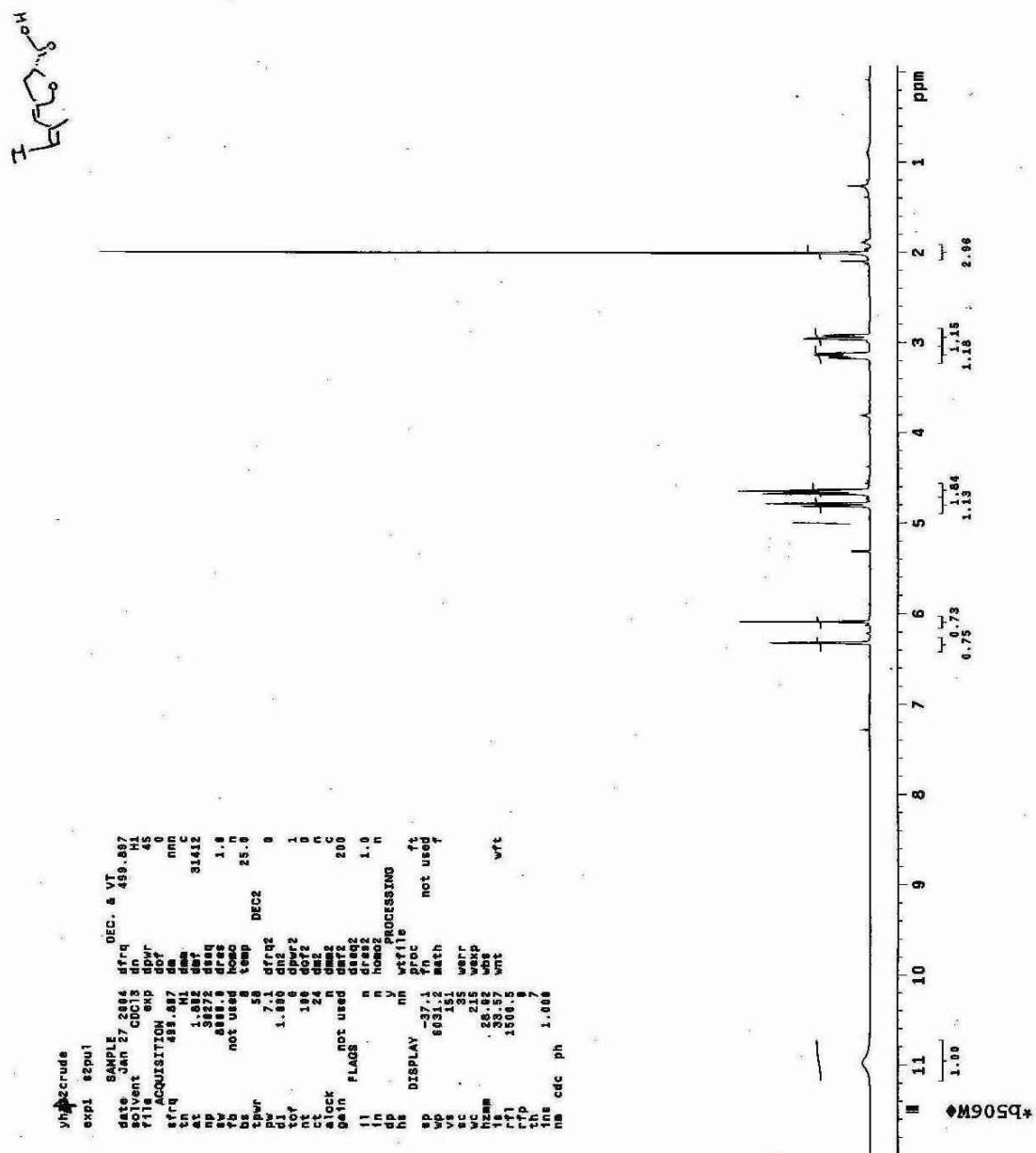
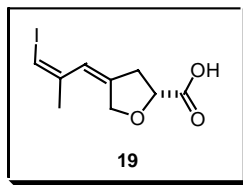








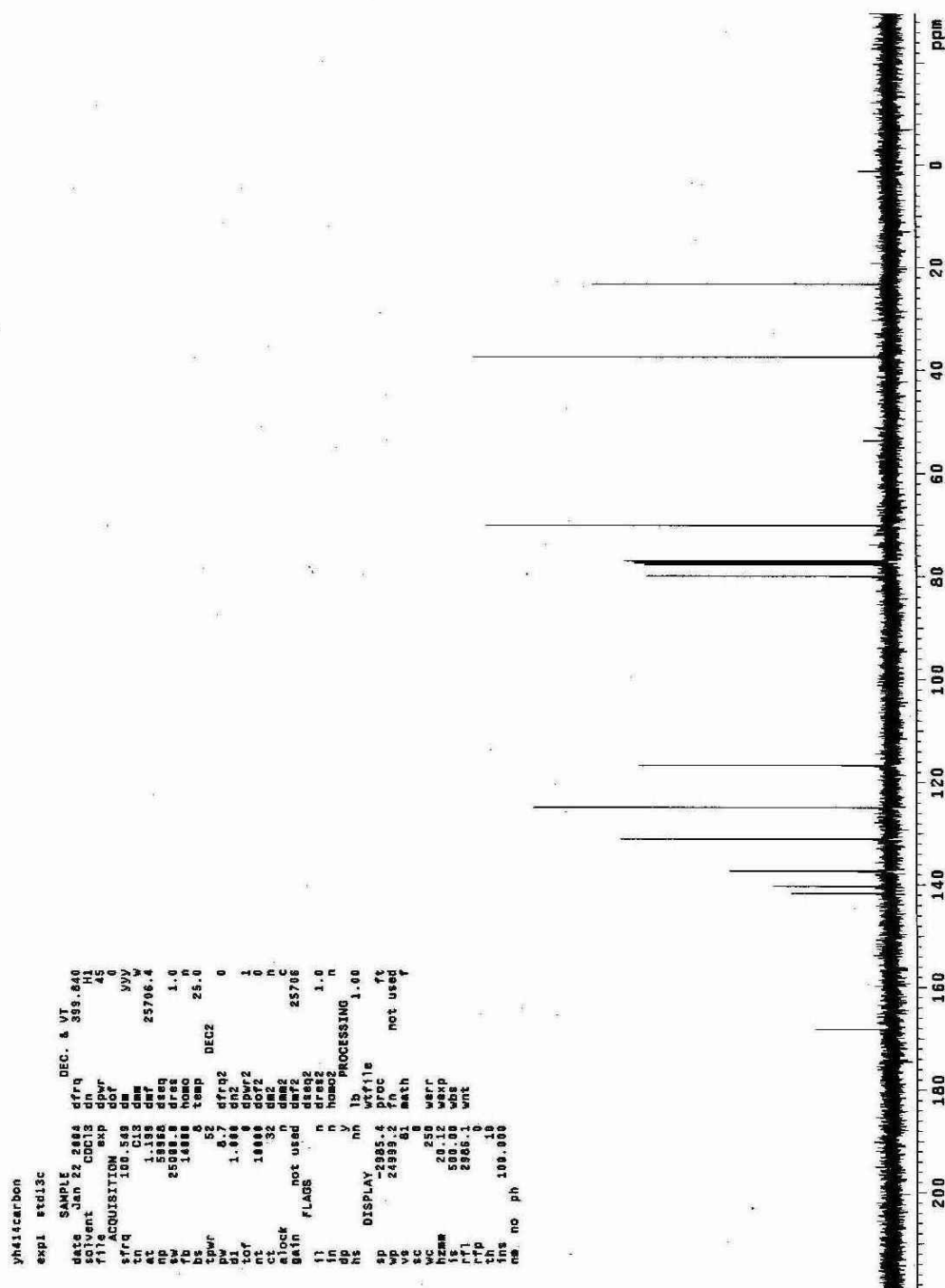
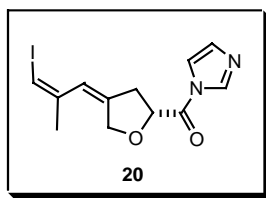


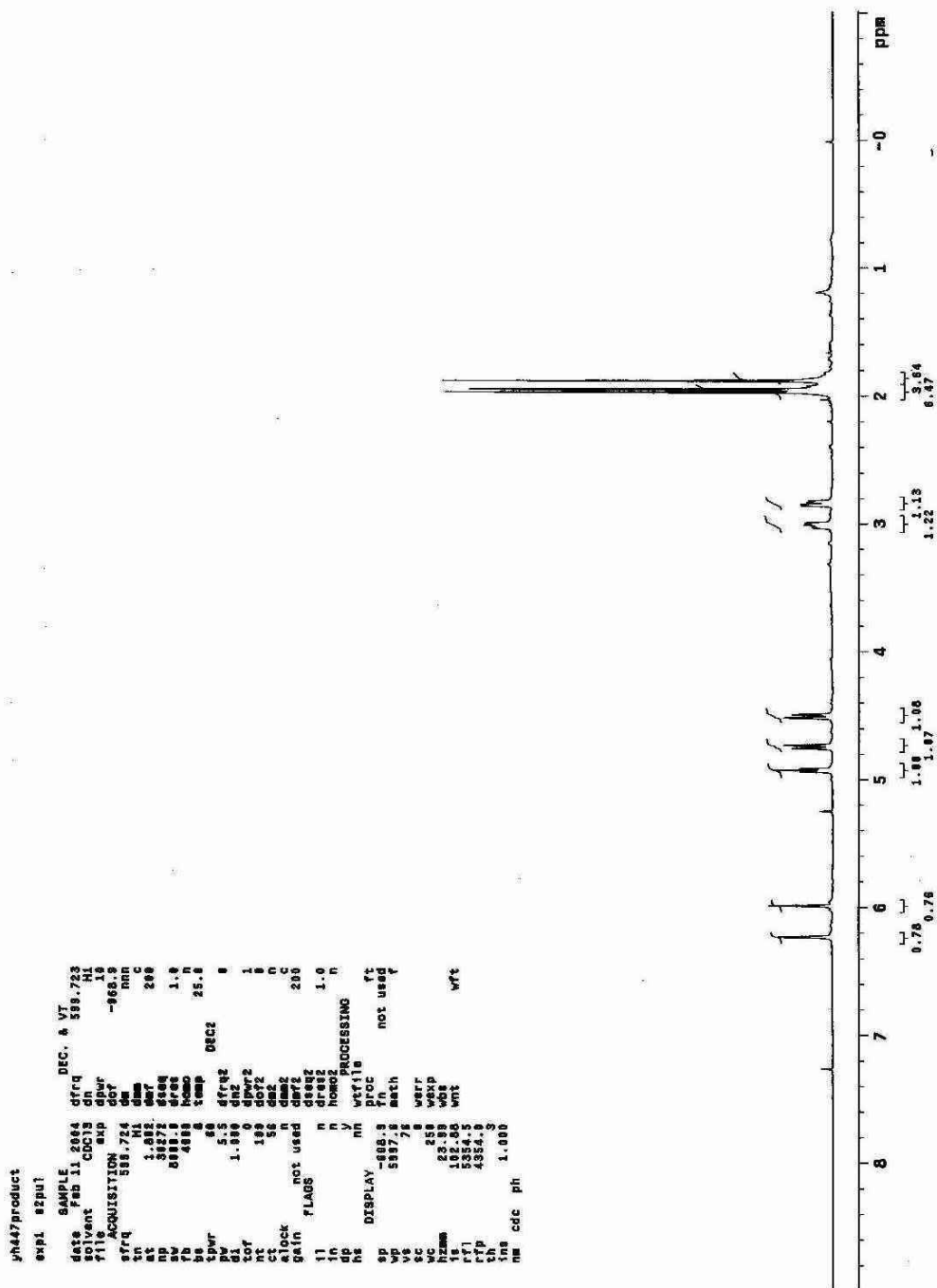
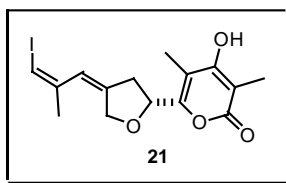




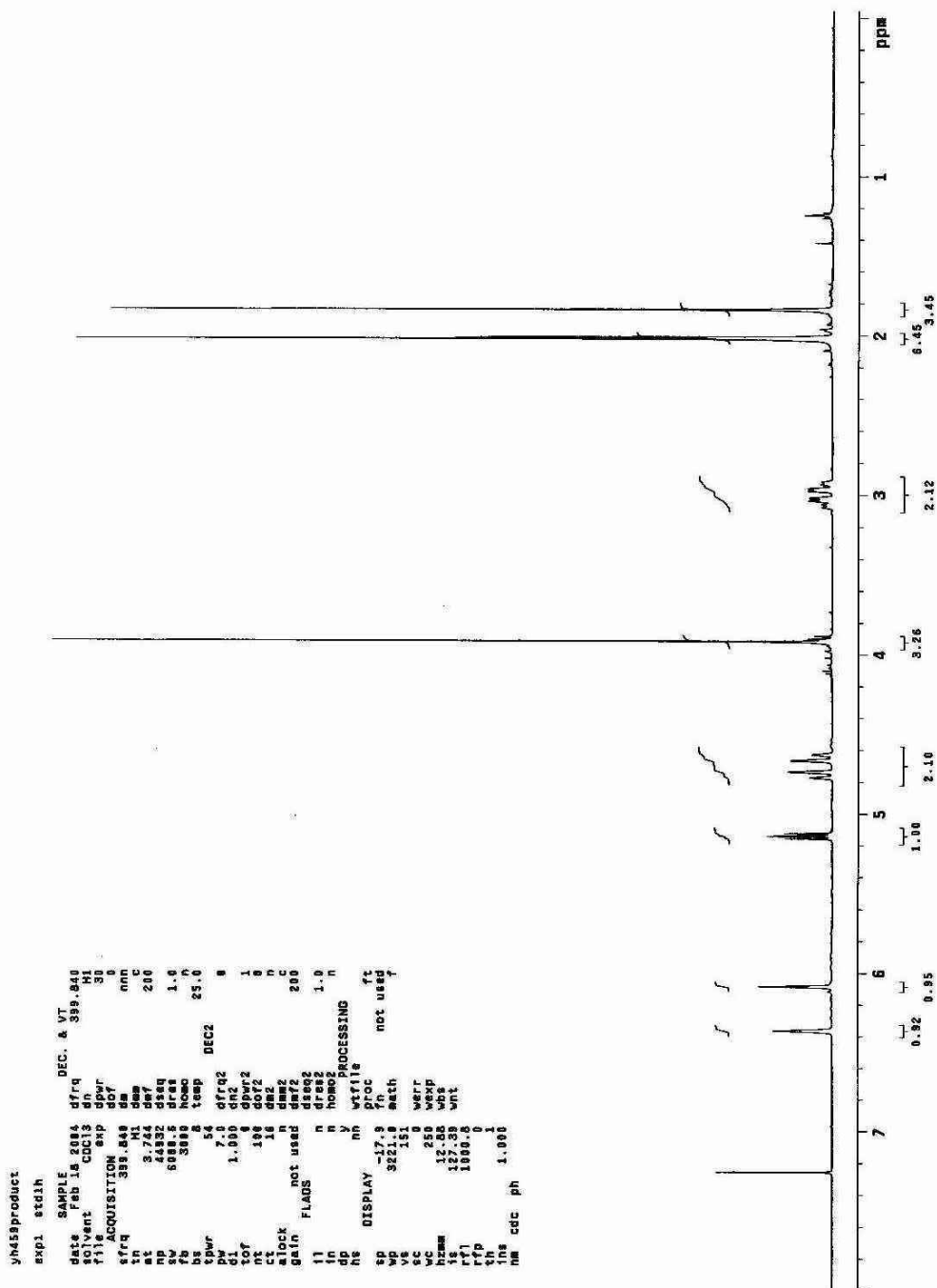
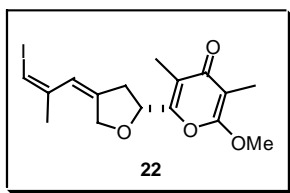


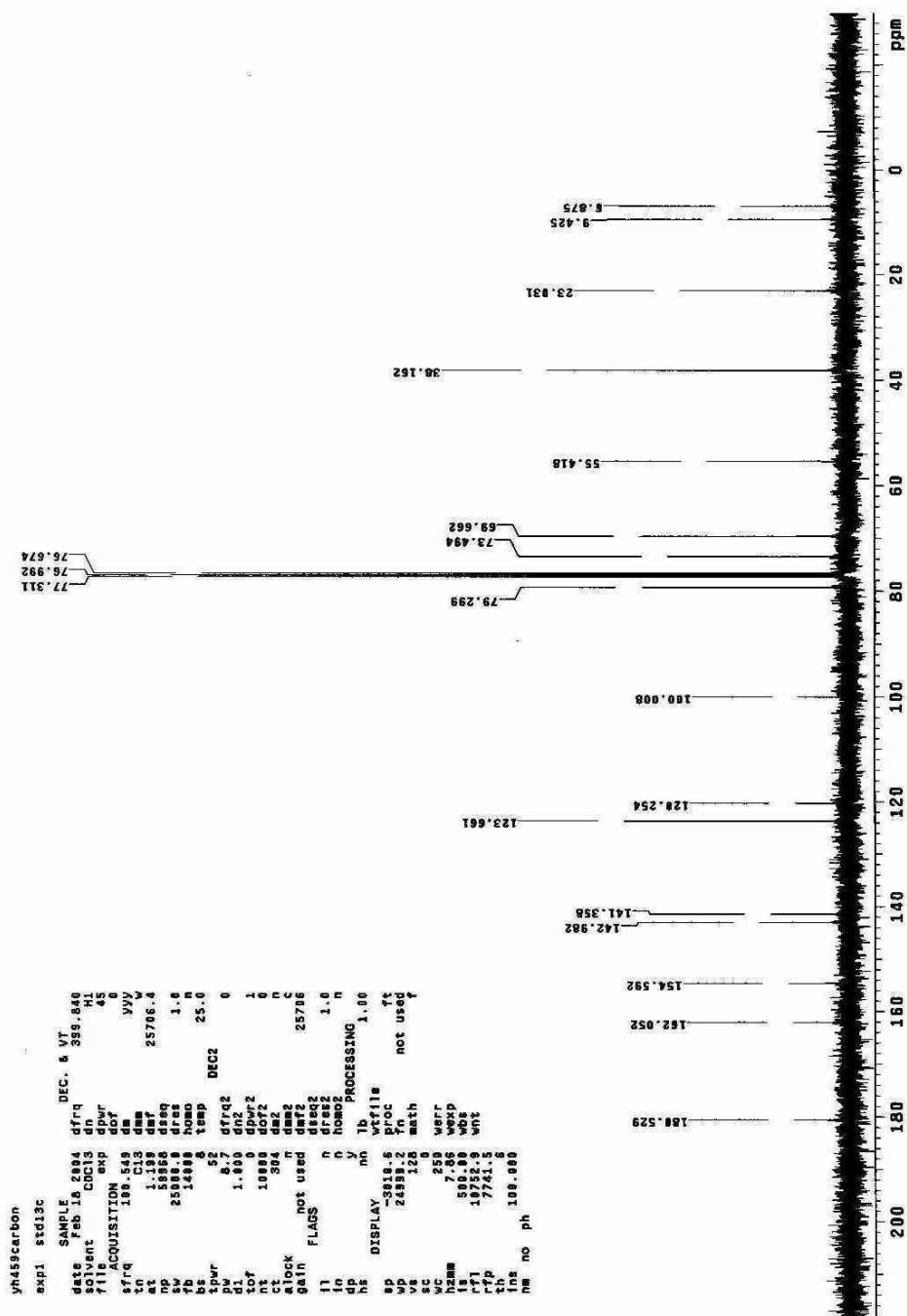
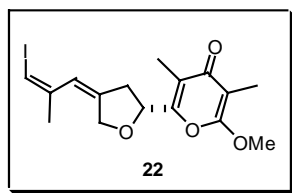


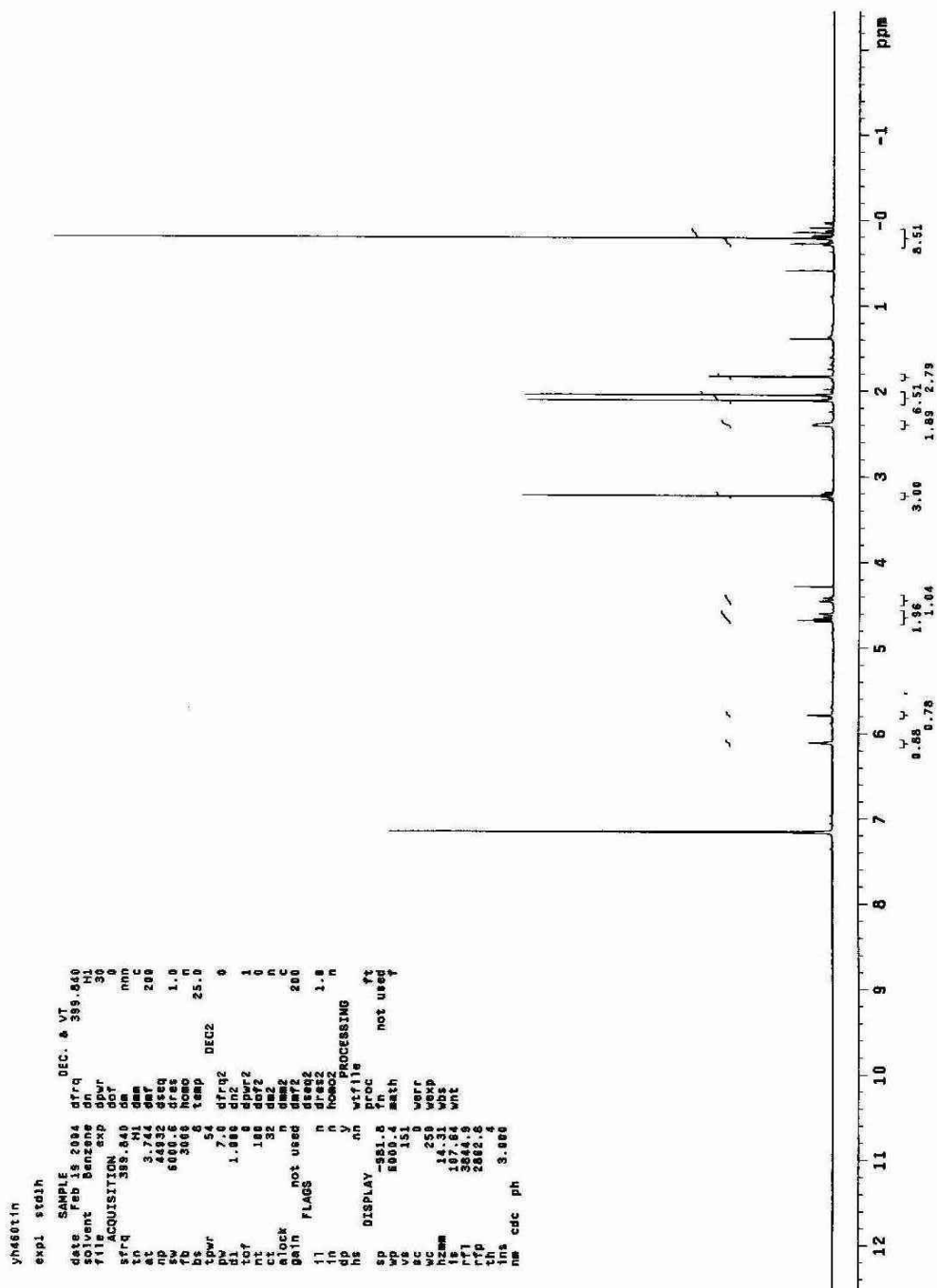
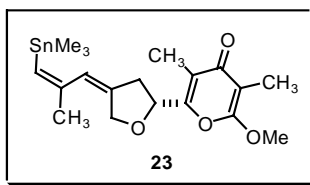




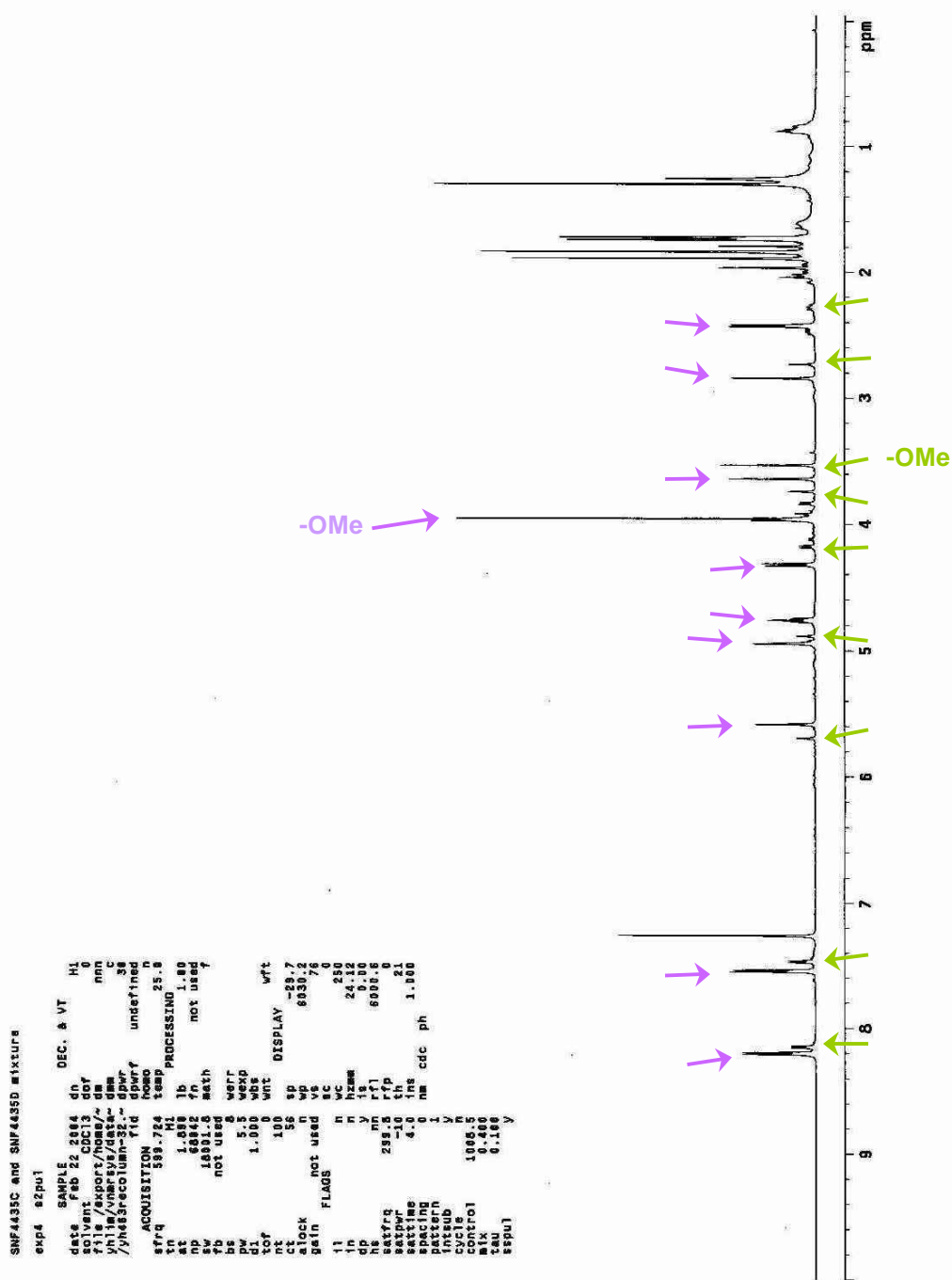


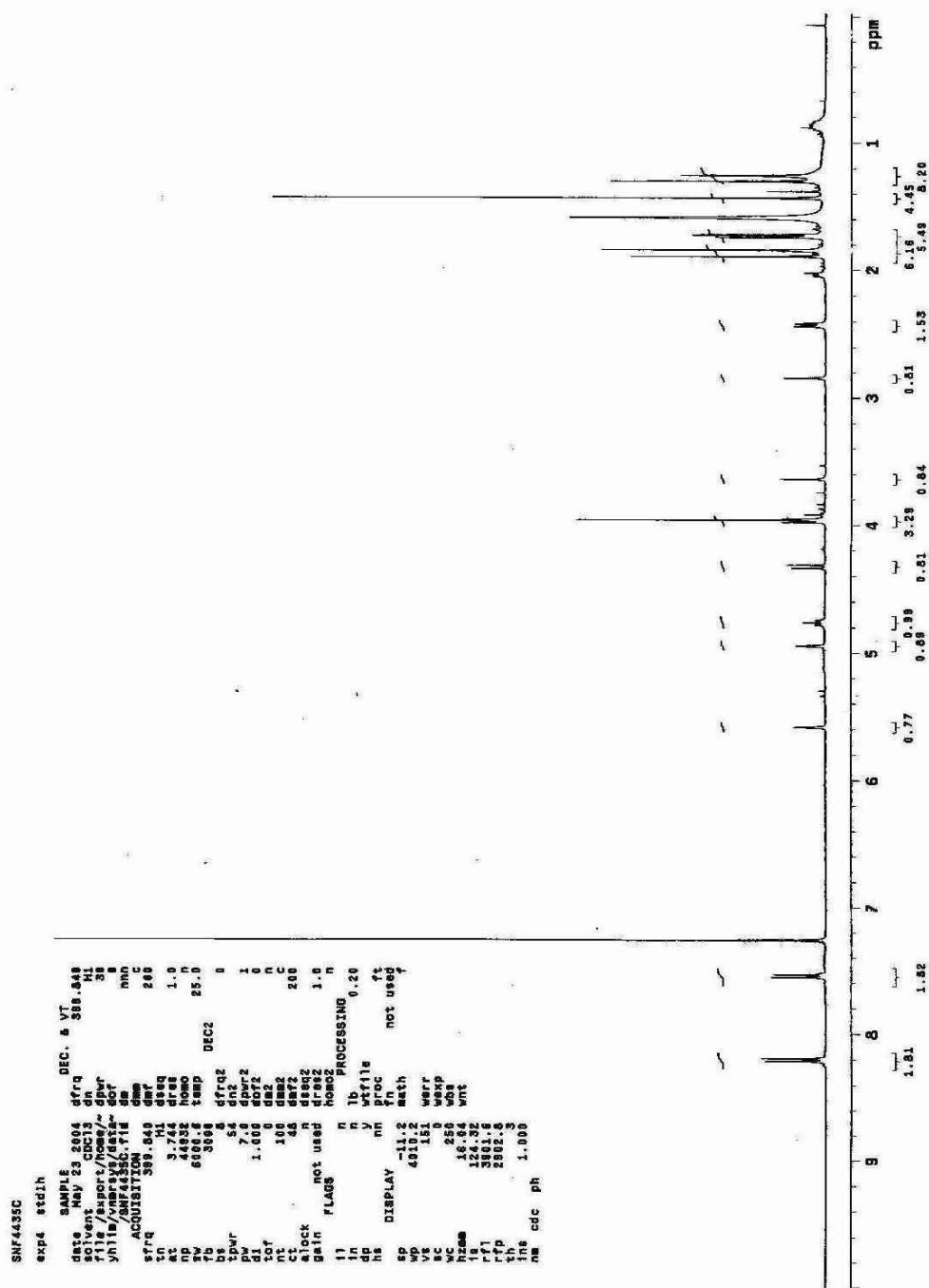
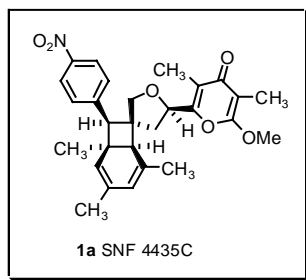


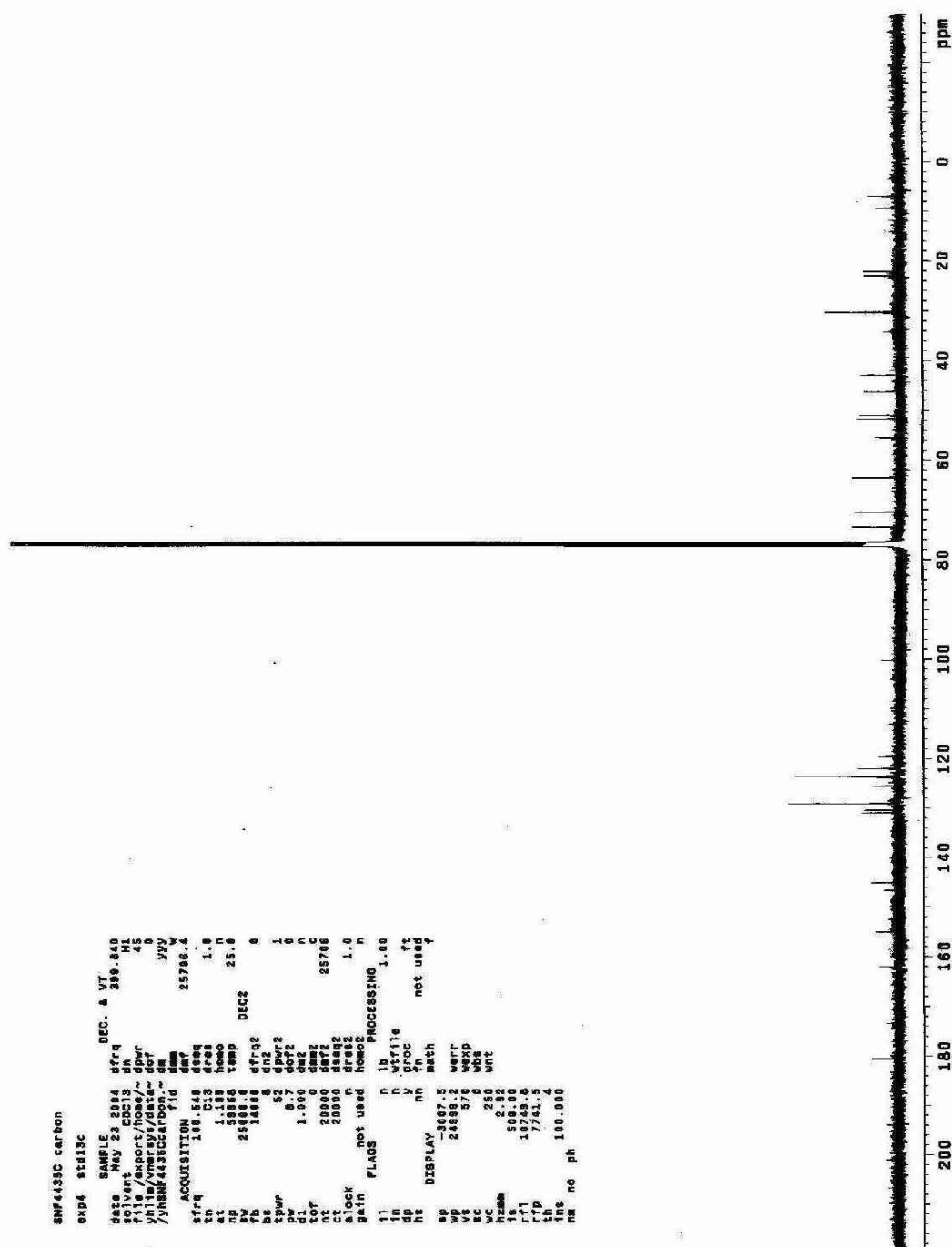
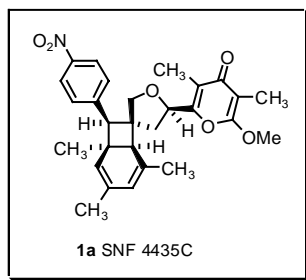


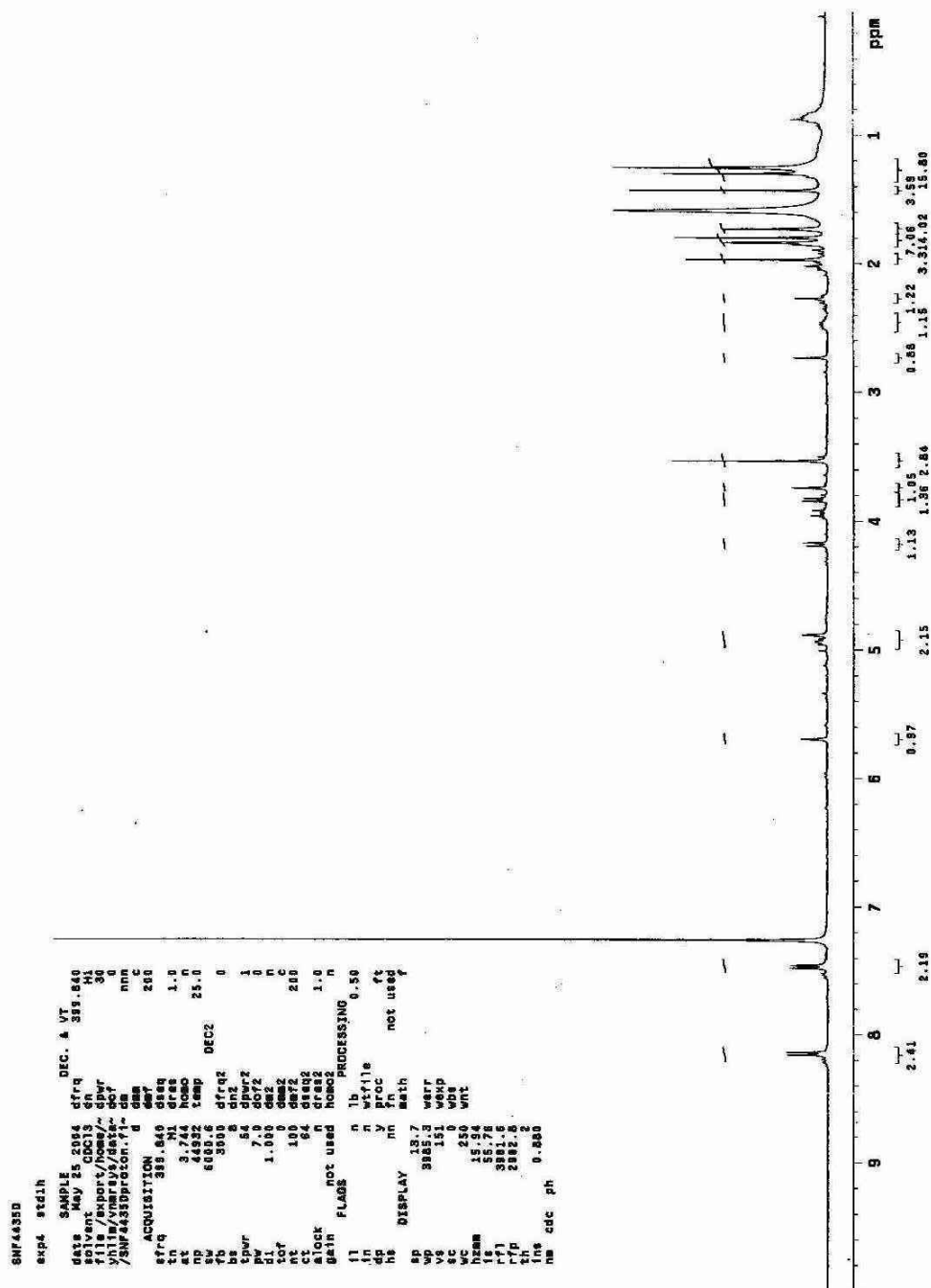


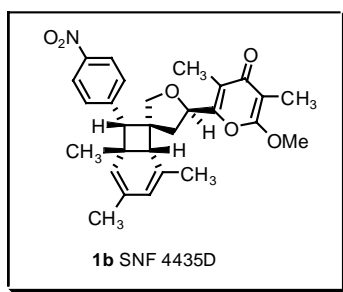












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ns 1013
fb 25000.0
bs 14000
dvr 57
d1 1.000
tof 20000
nt 20000
atock 1841n
gain not used
flags 11 n
dn 1 n
hs 1 n
DISPLAY nn
sp -3007.5
vp 24915.1
vc 1004
wc 250
hzmh 31.78
st 10245.8
rft 7741.5
th 100.000
na no ph
DEC. & VT
sfrq 399.500
dvr 45
dot 0
yvy 25708.4
dm 1.0
dres 1.0
temp 25.0
DEC2
d1 1.000
dvr2 1
dot2 0
dres2 1
dm2 1
dmf2 25705
dse2 1.0
dres2 1.0
nmr PROCESSING
1b 1.00
wtfile
proc not used
meth
warr
wexp
wss
wnt

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