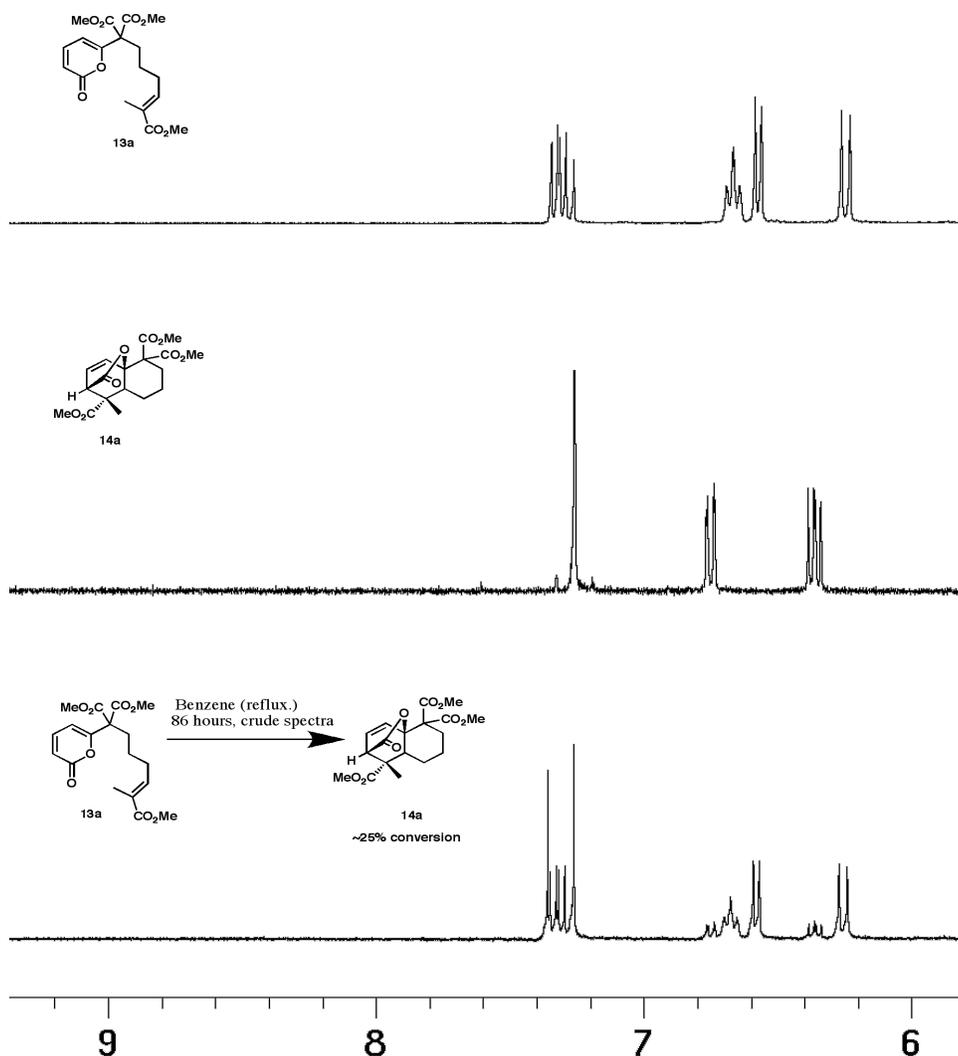


**Supporting Information for “Progress Toward the Synthesis of the Basiliolides and Transtaganolides: an Intramolecular Pyrone Diels-Alder Entry Into a Novel Class of Natural Products”**

Hosea M. Nelson and Brian M. Stoltz

*The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, USA***I. General Comments.****Figure 1.**

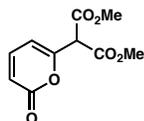
As stated in the text, heating of **13a** to reflux in benzene results in low conversion to **14a**. Shown below is a  $^1\text{H}$  NMR spectra taken after 86 hours. For comparison, the spectra of pure **14a** (prepared by radical dehalogenation of **14b**), and the spectra of **13a** are shown.



## II. Materials and Methods.

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. 6-Chloro-2*H*-pyran-2-one was purchased from Sigma-Aldrich Chemical Company and used as received. 1-Methoxycarbonylethylidetriphenylphosphorane was prepared using known methods<sup>1</sup>. Thin-layer chromatography (TLC), both preparatory and analytical, were performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, p-anisaldehyde, I<sub>2</sub>, or KMnO<sub>4</sub> staining. ICN Silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz) or on a Varian Unity Inova 500 (at 500 MHz). <sup>1</sup>H NMR spectra are reported relative to CDCl<sub>3</sub> (7.26 ppm). Data for <sup>1</sup>H NMR spectra are reported as follows: chemical shift, multiplicity, coupling constant (Hz), integration. Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept. = septet, m = multiplet, comp. m = complex multiplet, app. = apparent, bs = broad singlet. <sup>13</sup>C NMR were reported relative to CDCl<sub>3</sub> (77.0 ppm). FTIR spectra were recorded on a Perkin Elmer SpectrumBX spectrometer and are reported in frequency of absorption (cm<sup>-1</sup>). High resolution mass spectra were obtained from the Caltech Mass Spectral Facility. Crystallographic data were obtained from the Caltech X-ray Diffraction Facility.

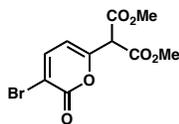
## III. Experimental Procedures



**Dimethyl 2-(2-oxo-2*H*-pyran-6-yl)propanedioate (21).** To a suspension of Sodium hydride (60% in mineral oil) (399 mg, 16.6 mmol, 1.9 equiv) in tetrahydrofuran (75 ml) at 0 °C was added dimethyl malonate (2 ml, 17.5 mmol, 2 equiv) over 5 minutes. The mixture was warmed to ambient temperature and stirred for 20 minutes. The solution was then cooled to 0 °C, and a solution of 6-chloro-2*H*-pyran-2-one (1.1 g, 8.8 mmol, 1 equiv) in tetrahydrofuran (5 ml) was added dropwise over 5 minutes. The reaction was allowed to come to ambient temperature, then stirred for an additional hour. The reaction mixture was acidified to pH 5 by the addition of 3N HCl(aq). Water was then added (50 mL), and the reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 200 ml). The combined organic extracts were dried over Na<sub>2</sub>SO<sub>4</sub>(anhydrous) and concentrated by rotary evaporation. The resulting residue was chromatographed (50%⇒100% diethyl ether in petroleum ether on SiO<sub>2</sub>) to yield 1.7 g of **21** as a yellow oil (84.5%). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.31 (dd, J = 9.5, 6.8 Hz, 1H), 6.34 (d, J = 6.6 Hz, 1H), 6.26 (d, J = 9.3 Hz, 1H), 4.52 (s, 1H), 3.78 (s, 6H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 165.5, 161.4, 155.6, 143.3, 116.0,

<sup>1</sup> Werkhoven, T. M.; van Nipsen, R.; Lugtenburg, *J. Eur. J. Org. Chem.* **1999**, 11, 2909-2914.

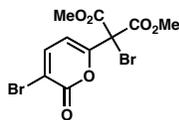
105.9, 56.2, 53.8; FTIR (Neat Film NaCl) 1740, 1640, 1559, 1437, 1277, 1241, 1201, 1155, 1099, 1027, 808  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calc'd for  $\text{C}_{10}\text{H}_{10}\text{O}_6$  [ $\text{M}^+$ ]: 226.0477, found 226.0479.



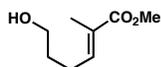
**Dimethyl 2-(3-bromo-2-oxo-2H-pyran-6-yl)propanedioate (23).** To a solution of **21** ( 283.0 mg, 1.2 mmol, 1.0 equiv ) in  $\text{CCl}_4$  ( 10 mL ) was added bromine ( 312 mg, 100  $\mu\text{L}$  , 1.9 mmol, 1.6 equiv ). The reaction mixture was stirred at ambient temperatures for 72 hours then quenched by the addition of 20 mL of 20%  $\text{Na}_2\text{SO}_4(\text{aq})$ . The solution was extracted with  $\text{CH}_2\text{Cl}_2$  ( 3 x 40 mL) and the combined organic layers were collected and dried over  $\text{Na}_2\text{SO}_4(\text{anhydrous})$ . After concentration by rotary evaporation, the crude residue was chromatographed ( 50% diethyl ether in petroleum ether on  $\text{SiO}_2$  ) to yield **23** as a white powder ( 181 mg, 48% ) and **24** as a yellow powder ( 152 mg, 32% ).

To a flame-dried flask charged with **24** ( 28.0 mg, 0.07 mmol, 1 equiv ), Zn dust ( 10 mg, 0.15, 2 equiv), and tetrahydrofuran ( 0.50 mL ) was added glacial acetic acid ( 0.25 mL ). The reaction was stirred at ambient temperatures for 30 minutes, filtered through Celite, and then extracted with  $\text{CH}_2\text{Cl}_2$  ( 2 x 1 mL ). The combined organic layers were washed with brine. After drying over  $\text{Na}_2\text{SO}_4(\text{anhydrous})$  and concentration by rotary evaporation, the crude residue was chromatographed ( 50% diethyl ether in petroleum ether on  $\text{SiO}_2$  ) to yield **23** (18 mg, 81%) as a white powder.

**24:**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.68 (d,  $J = 7.2$ , 1H), 6.30 (d,  $J = 7.2$  Hz, 1H), 4.55 (s, 1H), 3.79 (s, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  164.1, 157.9, 154.9, 144.4, 112.1, 106.6, 55.8, 53.9; FTIR (Neat Film NaCl) 1743, 1642, 1542, 1436, 1313, 1240, 1201, 1153, 1100, 1027, 978, 750  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calc'd for  $\text{C}_{10}\text{H}_9\text{BrO}_6$  [ $\text{M}^+$ ]:300.9582, found 303.9587.

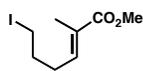


**Dimethyl 2-bromo-2-(3-bromo-2-oxo-2H-pyran-6-yl)propanedioate (24).** See preparation of **23** for experimental details.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (d,  $J = 7.2$ , 1H), 6.70 (d,  $J = 7.2$  Hz, 1H), 3.90 (s, 6H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  164.1, 156.8, 155.4, 143.8, 113.4, 106.4, 57.1, 55.2; FTIR (Neat Film NaCl) 1748, 1634, 1541, 1436, 1336, 1265, 1228, 1102, 1052, 1020, 979, 772, 748  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calc'd for  $\text{C}_{10}\text{H}_9\text{BrO}_6$  [ $\text{M}^+$ ]: 383.8667, found 383.8657.

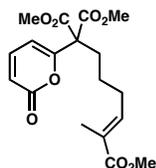


**(E)-Methyl 6-hydroxy-2-methylhex-2-enoate (17).** To a flame dried flask charged with  $\text{CH}_2\text{Cl}_2$  ( 60 mL ) was added  $\gamma$ -butyrolactone ( 1.1 g, 13.0 mmol, 1 equiv). The reaction was cooled to  $-78^\circ\text{C}$ , and a solution of Dibal-H ( 2.0 g, 14.3 mmol, 1.1 equiv ) in dry hexanes ( 11.5 ml ) was added over 15 minutes. The reaction was stirred for two hours then diluted with Ethyl

Acetate ( 50 mL ), and a saturated solution of sodium/potassium tartrate ( 50 mL ) was then added. After separation, the aqueous layer was further extracted with ethyl acetate ( 2 x 50 mL ). The combined organics were combined, dried over MgSO<sub>4</sub>(anhydrous), and concentrated by rotary evaporation. The crude oil was dissolved in benzene ( 50 mL ) and added to a flask charged with stabilized ylide **16**<sup>1</sup> ( 4.3 g, 12.3 mmol, 1.2 equiv ) and the reaction was heated to reflux and stirred for 12 hours. The reaction was cooled to ambient temperatures then diluted with diethyl ether ( 50 ml ) and saturated brine solution ( 50 mL). After separation the aqueous layers were further extracted with ether, and the combined organics were dried over MgSO<sub>4</sub>(anhydrous) and concentrated by rotary evaporation. The crude oil was chromatographed ( 0⇒100% ether in petroleum ether on SiO<sub>2</sub> ) to yield 1.4 g ( 68% ) of **17** as a clear colorless oil. <sup>1</sup>H NMR ( 300 MHz, CDCl<sub>3</sub> ) δ 6.70 ( t, J = 7.5, 1H ), 3.66 ( s, 3H ), 3.58 ( t, J = 6.3 Hz, 3H ), 2.64 ( br s, 1H ), 2.20 ( m, 2H ), 1.78( s, 3H ), 1.64 ( m, 2H ); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub> ) δ 169.0, 142.2, 128.1, 62.1, 51.9, 31.6, 25.2, 12.5; FTIR (Neat Film NaCl) 3404, 1714, 1649, 1438, 1268.81196, 1129, 1059, 747 cm<sup>-1</sup> ; HRMS (EI) m/z calc'd for C<sub>8</sub>H<sub>14</sub>O<sub>3</sub> [M<sup>+</sup>]: 158.0943, found 158.0943.

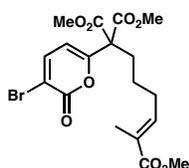


**(E)-Methyl 6-iodo-2-methylhex-2-enoate (18).** To a flame dried flask was added (*E*)-Methyl 6-hydroxy-2-methylhex-2-enoate (**17**) ( 700 mg, 4.4 mmol, 1 equiv ), iodine chips ( 2.0 g, 7.9 mmol, 1.8 equiv ), imidazole ( 897 mg, 13.2 mmol, 3 equiv ), triphenylphosphine ( 1.9 g, 7.0 mmol, 1.6 equiv ), and toluene ( 45 mL ). The reaction was stirred at room temperature for 2 hours then diluted with saturated NaHCO<sub>3</sub> (aq) ( 20 mL ) and saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>(aq)( 5 mL ). It was then extracted with Ethyl Acetate ( 3 x 20 mL ). The combined organic extracts were washed with brine, dried over anhydrous MgSO<sub>4</sub>, and concentrated by rotary evaporation. The crude oil was chromatographed ( hexanes in ethyl acetate 10:1 ⇒ 3:1 on SiO<sub>2</sub> ) to give iodide **18** as a yellow oil ( 873 mg, 74% ). <sup>1</sup>H NMR ( 300 MHz, CDCl<sub>3</sub> ) δ 6.65 ( t, J = 7.5, 1H ), 3.70 ( s, 3H ), 3.16 ( t, J = 6.7 Hz, 2H ), 2.26 ( m, 2H ), 1.92 ( m, 2H ), 1.84 ( s, 3H ); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub> ) δ 168.5, 140.1, 129.2, 52.0, 32.4, 29.5, 12.8, 6.2; FTIR ( Neat Film NaCl ) 1715, 1651, 1435, 1282, 1260, 1219, 1167, 1107 cm<sup>-1</sup> ; HRMS ( EI ) m/z calc'd for C<sub>8</sub>H<sub>13</sub>O<sub>2</sub>I [M<sup>+</sup>]: 267.9961, found 267.9967.

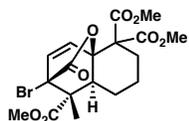


**(E)-Trimethyl 1-(2-oxo-2H-pyran-6-yl)hex-4-ene-1,1,5-tricarboxylate (13a).** To an ice cold mixture of acetonitrile ( 1 mL ) and Cs<sub>2</sub>CO<sub>3</sub> ( 132.0 mg, 0.4 mmol, 1.1 equiv ) was added a solution of **21** ( 100.0 mg, 0.442 mmol, 1.2 equiv ) in acetonitrile ( 0.5 mL ). The reaction was brought to ambient temperature and stirred for 10 minutes, then cooled to 0° C. A solution of **18** ( 99.0 mg, .4 mmol, 1 equiv ) in acetonitrile ( 0.5 mL ) was then added over 5 minutes. The reaction was allowed to warm to ambient temperature, then brought to reflux and stirred for 15

hours. The reaction was then cooled to room temperature and diluted with saturated  $\text{NH}_4\text{Cl}(\text{aq})$  ( 2 mL ) and extracted with ethyl acetate ( 3 x 2 mL ). The combined organics were dried over  $\text{Na}_2\text{SO}_4$  (anhydrous) and concentrated by rotary evaporation. The crude oil was chromatographed ( ethyl acetate in hexanes gradient 0 $\Rightarrow$ 100% on  $\text{SiO}_2$  ) to yield 111 mg ( 83% ) of yellow oil.  $^1\text{H}$  NMR ( 300 MHz,  $\text{CDCl}_3$  )  $\delta$  7.32 ( dd,  $J = 6.3, 6.9$  Hz, 1H ), 6.66 ( t,  $J = 7.4$  Hz, 1H ), 6.58 ( d,  $J = 6.6$  Hz, 1H ), 6.25 ( d,  $J = 6.3$  Hz, 1H ), 3.78 ( s, 6H ), 3.72 ( s, 3H ), 2.22 ( m, 4H ), 1.80 ( s, 3H ), 1.43 ( m, 3H );  $^{13}\text{C}$  NMR ( 75 MHz,  $\text{CDCl}_3$  )  $\delta$  168.7, 168.0, 161.3, 159.3, 143.3, 141.2, 128.6, 115.5, 105.5, 62.6, 53.6, 52.0, 34.0, 28.7, 24.1, 12.7; FTIR ( Neat Film NaCl ) 1741, 1636, 1556, 1436, 1240, 1093, 807  $\text{cm}^{-1}$ ; HRMS ( EI )  $m/z$  calc'd for  $\text{C}_8\text{H}_{13}\text{O}_2\text{I}$  [ $\text{M}^+$ ]: 366.1314, found 366.1330.



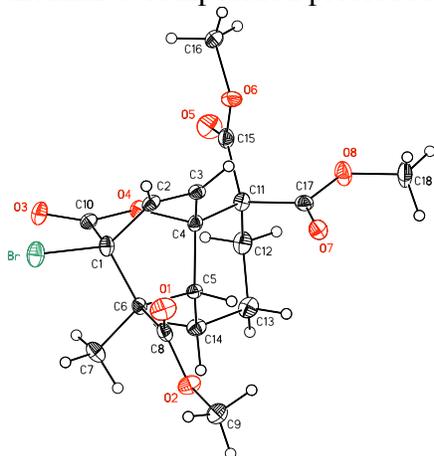
**(*E*)-Trimethyl 1-(3-bromo-2-oxo-2*H*-pyran-6-yl)hex-4-ene-1,1,5-tricarboxylate (13b).** To a mixture of dimethylformamide ( 3 mL ) and  $\text{K}_2\text{CO}_3$  ( 64.7 mg, 0.5 mmol, 1.1 equiv ) at 0° C was added a solution of **23** ( 130.2 mg, 0.4 mmol, 1.0 equiv ) in dimethylformamide ( 0.5 mL ) and **18** ( 342.10 mg, 1.28 mmol, 3.0 equiv ) in dimethylformamide ( 0.5 mL ). The reaction mix was brought to room temperature and stirred for 10 minutes, then heated to 50° C for 5 hours. The reaction was then cooled to room temperature and diluted with saturated aqueous  $\text{NH}_4\text{Cl}$  ( 20 mL ) and extracted with ethyl acetate ( 3 x 10 mL ). The combined organic extracts were washed with brine ( 6 x 10 mL ), dried over  $\text{Na}_2\text{SO}_4$ (anhydrous) and concentrated by rotary evaporation. The crude oil was chromatographed ( diethyl ether in petroleum ether gradient 50 $\Rightarrow$ 100% on  $\text{SiO}_2$  ) to yield 110 mg ( 58% ) of **13b** as a yellow powder. Furthermore, 170 mg of **18** was recovered as a clear oil.  $^1\text{H}$  NMR ( 300 MHz,  $\text{CDCl}_3$  )  $\delta$  7.66 ( d,  $J = 6.6$  Hz, 1H ), 6.66 ( t,  $J = 7.4$  Hz, 1H ), 6.54 ( d,  $J = 6.6$  Hz, 1H ), 3.79 ( s, 6H ), 3.72 ( s, 3H ), 2.22 ( m, 4H ), 1.81 ( s, 3H ), 1.4 ( m, 2H );  $^{13}\text{C}$  NMR ( 75 MHz,  $\text{CDCl}_3$  )  $\delta$  168.5, 167.6, 158.7, 157.6, 144.4, 141.0, 128.7, 111.2, 106.0, 62.3, 53.8, 52.0, 33.9, 28.6, 24.0, 12.7; FTIR ( Neat Film NaCl ) 1742, 1714, 1634, 1542, 1436, 1242, 1073, 974, 749  $\text{cm}^{-1}$ ; HRMS ( EI )  $m/z$  calc'd for  $\text{C}_{18}\text{H}_{21}\text{O}_8^{81}\text{Br}$  [ $\text{M}^+\text{H}$ ]: 447.0477, found 447.0461.



### 14b

A solution of **13b** ( 63.0 mg, 0.15 mmol, 1.0 equiv ) in benzene ( 10 mL ), was sealed in a scintillation vial and heated to reflux for 72 hours. The reaction mixture was cooled to room temperature, the solvent removed by rotary evaporation, and the crude residue chromatographed

(chloroform/diethyl ether/n-heptane, 1:1:1 on SiO<sub>2</sub>) to yield 14b as 48 mg (76%) of white powder. <sup>1</sup>H NMR (500 MHz), CDCl<sub>3</sub> δ 6.61 (d, J = 8.1 Hz, 1H), 6.59 (d, J=8.1 Hz, 1H), 3.77 (s, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 2.85 (dd, J= 15.0 Hz, 5.5 Hz, 1H), 2.23 (m, 2H), 1.8 (m, 2H), 1.4 (m, 1H), 1.38 (s, 3H), 1.2 (m, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 172.6, 169.3, 168.3, 166.7, 134.8, 133.3, 82.9, 66.0, 59.5, 53.1, 53.0, 52.8, 52.6, 46.1, 27.9, 24.8, 20.3, 19.1; FTIR (Neat Film NaCl) 1773, 1734, 1435, 1304, 1255, 1208, 1173, 1158, 1124, 1022, 945 cm<sup>-1</sup>; HRMS (EI) m/z calc'd for C<sub>18</sub>H<sub>21</sub>O<sub>8</sub>Br [M<sup>+</sup>]: 444.0420, found 444.0411. Crystals were grown from dichloromethane/Hexanes. MP: 156-170° C (at these temperatures decarboxylation is thought to occur, as the crystal and the resulting liquid were vigorously bubbling, thus it is unclear whether thermal decomposition precluded state change).



## HMN01

**Note:** The crystallographic data have been deposited in the Cambridge Database (CCDC). The deposition number is 656115.

**Table 1. Crystal data and structure refinement for HMN01 (CCDC 656115).**

Empirical formula	C <sub>18</sub> H <sub>21</sub> O <sub>8</sub> Br
Formula weight	445.26
Crystallization Solvent	Dichloromethane/hexanes
Crystal Habit	Fragment
Crystal size	0.30 x 0.15 x 0.05 mm <sup>3</sup>
Crystal color	Colorless

## Data Collection

Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoKα
Data Collection Temperature	100(2) K
q range for 4422 reflections used in lattice determination	2.50 to 30.90°
Unit cell dimensions	a = 6.6117(3) Å b = 19.4403(16) Å c = 14.6195(13) Å
	b = 101.003(3)°

*Supporting Information for Nelson and Stoltz*

Volume	1844.6(2) Å <sup>3</sup>
Z	4
Crystal system	Monoclinic
Space group	P2 <sub>1</sub> /c
Density (calculated)	1.603 Mg/m <sup>3</sup>
F(000)	912
Data collection program	Bruker SMART v5.630
q range for data collection	1.76 to 33.90°
Completeness to q = 33.90°	89.1 %
Index ranges	-10 ≤ h ≤ 9, 0 ≤ k ≤ 29, 0 ≤ l ≤ 22
Data collection scan type	w scans at 5 f settings
Data reduction program	Bruker SAINT v6.45A
Reflections collected	11273
Independent reflections	11273 [R <sub>int</sub> = 0.0000]
Absorption coefficient	2.273 mm <sup>-1</sup>
Absorption correction	TWINABS
Max. and min. transmission	0.7466 and 0.5283

**Table 1 (cont.)****Structure solution and Refinement**

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on $F^2$
Data / restraints / parameters	11273 / 0 / 249
Treatment of hydrogen atoms	Riding
Goodness-of-fit on $F^2$	1.437
Final R indices [ $I > 2s(I)$ , 7706 reflections]	$R_1 = 0.0691$ , $wR_2 = 0.1161$
R indices (all data)	$R_1 = 0.1128$ , $wR_2 = 0.1245$
Type of weighting scheme used	Sigma
Weighting scheme used	$w = 1/s^2(F_o^2)$
Max shift/error	0.001
Average shift/error	0.000
Largest diff. peak and hole	1.261 and -0.700 e.Å <sup>-3</sup>

**Special Refinement Details**

The crystal is twinned. CELL\_NOW was used to establish the following relationship between domains. Domain 2 is rotated from first domain by 180.0 degrees about reciprocal axis -0.001 0.000 1.000 and real axis 0.425 -0.001 1.000. Of 999 reflections, 869 reflections within 0.250 of an integer index are assigned to domain 1 (130 reflections not yet assigned to a domain), 646 reflections within 0.250 of an integer index are assigned to domain 2, 121 of them exclusively.

The data were integrated with SAINT to give the following; ( $R_{int}$  all scans = 0.1057)

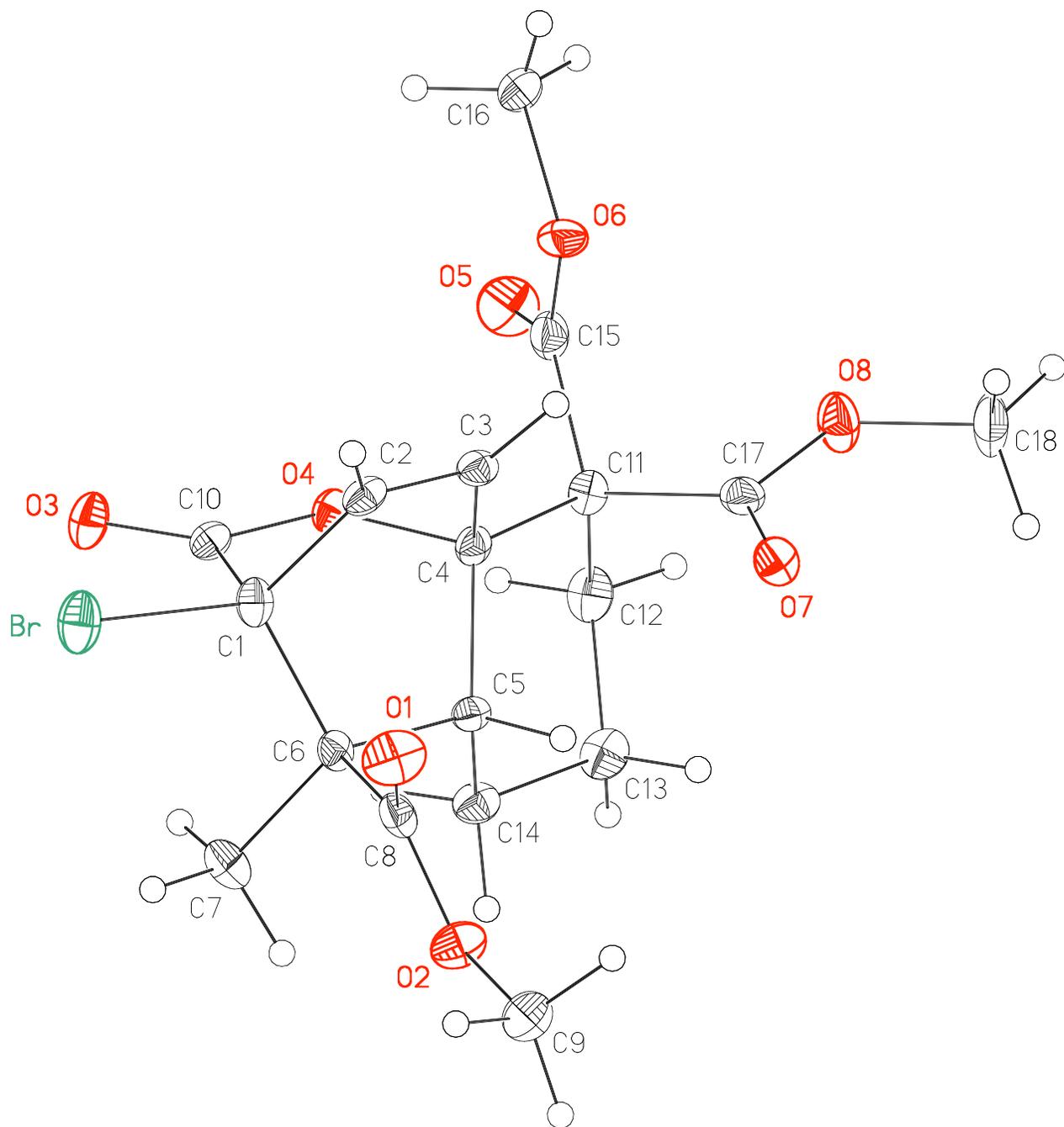
8959 data ( 2726 unique ) involve domain 1 only, mean  $I/\sigma$  4.1

8923 data ( 2744 unique ) involve domain 2 only, mean  $I/\sigma$  2.7

19687 data ( 6016 unique ) involve 2 domains, mean  $I/\sigma$  4.2

Refinement of  $F^2$  against ALL reflections. The weighted R-factor ( $wR$ ) and goodness of fit ( $S$ ) are based on  $F^2$ , conventional R-factors ( $R$ ) are based on  $F$ , with  $F$  set to zero for negative  $F^2$ . The threshold expression of  $F^2 > 2s(F^2)$  is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on  $F^2$  are statistically about twice as large as those based on  $F$ , and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.



**Table 2. Atomic coordinates (  $\times 10^4$ ) and equivalent isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for HMN01 (CCDC 656115).  $U_{eq}$  is defined as the trace of the orthogonalized  $U_{ij}$  tensor.**

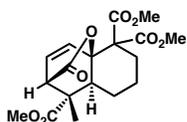
	x	y	z	$U_{eq}$
Br	2249(1)	6847(1)	71(1)	23(1)
O(1)	184(3)	6893(1)	1925(1)	25(1)
O(2)	2607(3)	6719(1)	3196(1)	20(1)
O(3)	5675(3)	7904(1)	152(1)	20(1)
O(4)	5019(3)	8586(1)	1275(1)	13(1)
O(5)	5955(3)	10171(1)	1567(2)	28(1)
O(6)	2525(3)	10033(1)	1213(2)	20(1)
O(7)	1630(3)	9172(1)	3348(1)	17(1)
O(8)	3101(3)	10212(1)	3340(2)	23(1)
C(1)	2879(4)	7589(1)	969(2)	15(1)
C(2)	1050(4)	8065(1)	944(2)	14(1)
C(3)	1473(4)	8608(1)	1471(2)	13(1)
C(4)	3680(4)	8651(1)	1978(2)	13(1)
C(5)	4156(4)	8012(1)	2618(2)	12(1)
C(6)	3644(4)	7343(1)	1997(2)	13(1)
C(7)	5477(4)	6843(2)	2057(2)	19(1)
C(8)	1915(4)	6963(1)	2347(2)	15(1)
C(9)	1088(4)	6368(2)	3626(2)	22(1)
C(10)	4658(4)	8021(1)	728(2)	14(1)
C(11)	4347(4)	9350(1)	2453(2)	13(1)
C(12)	6527(4)	9303(2)	3073(2)	20(1)
C(13)	6723(4)	8703(1)	3736(2)	19(1)
C(14)	6345(4)	8030(1)	3211(2)	16(1)
C(15)	4393(5)	9904(1)	1703(2)	18(1)
C(16)	2494(5)	10525(2)	463(2)	29(1)
C(17)	2832(4)	9553(1)	3078(2)	16(1)
C(18)	1813(5)	10453(2)	3980(2)	27(1)

**Table 3. Bond lengths [Å] and angles [°] for HMN01 (CCDC 656115).**

Br-C(1)	1.940(3)	C(8)-C(6)-C(7)	107.8(2)
O(1)-C(8)	1.200(3)	C(8)-C(6)-C(1)	110.1(2)
O(2)-C(8)	1.325(3)	C(7)-C(6)-C(1)	110.7(2)
O(2)-C(9)	1.453(3)	C(8)-C(6)-C(5)	107.2(2)
O(3)-C(10)	1.196(3)	C(7)-C(6)-C(5)	113.9(2)
O(4)-C(10)	1.352(3)	C(1)-C(6)-C(5)	107.2(2)
O(4)-C(4)	1.484(3)	O(1)-C(8)-O(2)	124.4(2)
O(5)-C(15)	1.206(3)	O(1)-C(8)-C(6)	125.7(3)
O(6)-C(15)	1.328(3)	O(2)-C(8)-C(6)	109.9(2)
O(6)-C(16)	1.451(3)	O(3)-C(10)-O(4)	120.8(2)
O(7)-C(17)	1.206(3)	O(3)-C(10)-C(1)	127.9(2)
O(8)-C(17)	1.339(3)	O(4)-C(10)-C(1)	111.3(2)
O(8)-C(18)	1.457(3)	C(17)-C(11)-C(15)	110.3(2)
C(1)-C(2)	1.517(4)	C(17)-C(11)-C(12)	107.9(2)
C(1)-C(10)	1.541(4)	C(15)-C(11)-C(12)	108.3(2)
C(1)-C(6)	1.565(4)	C(17)-C(11)-C(4)	109.3(2)
C(2)-C(3)	1.307(4)	C(15)-C(11)-C(4)	109.7(2)
C(3)-C(4)	1.508(4)	C(12)-C(11)-C(4)	111.3(2)
C(4)-C(5)	1.551(4)	C(13)-C(12)-C(11)	112.2(2)
C(4)-C(11)	1.551(4)	C(12)-C(13)-C(14)	111.0(2)
C(5)-C(14)	1.539(4)	C(13)-C(14)-C(5)	110.6(2)
C(5)-C(6)	1.584(4)	O(5)-C(15)-O(6)	124.6(3)
(6)-C(8)	1.529(4)	O(5)-C(15)-C(11)	123.5(3)
C(6)-C(7)	1.543(4)	O(6)-C(15)-C(11)	111.9(2)
C(11)-C(17)	1.531(4)	O(7)-C(17)-O(8)	123.6(3)
C(11)-C(15)	1.542(4)	O(7)-C(17)-C(11)	125.7(2)
C(11)-C(12)	1.553(4)	O(8)-C(17)-C(11)	110.6(2)
C(12)-C(13)	1.506(4)		
C(13)-C(14)	1.514(4)		
C(8)-O(2)-C(9)	115.5(2)		
C(10)-O(4)-C(4)	114.65(19)		
C(15)-O(6)-C(16)	114.2(2)		
C(17)-O(8)-C(18)	115.4(2)		
C(2)-C(1)-C(10)	107.5(2)		
C(2)-C(1)-C(6)	108.6(2)		
C(10)-C(1)-C(6)	105.4(2)		
C(2)-C(1)-Br	111.65(18)		
C(10)-C(1)-Br	108.98(18)		
C(6)-C(1)-Br	114.29(17)		
C(3)-C(2)-C(1)	113.5(2)		
C(2)-C(3)-C(4)	114.3(2)		
O(4)-C(4)-C(3)	107.7(2)		
O(4)-C(4)-C(5)	105.71(19)		
C(3)-C(4)-C(5)	108.6(2)		
O(4)-C(4)-C(11)	103.18(19)		
C(3)-C(4)-C(11)	115.7(2)		
C(5)-C(4)-C(11)	115.1(2)		
C(14)-C(5)-C(4)	112.5(2)		
C(14)-C(5)-C(6)	114.6(2)		
C(4)-C(5)-C(6)	108.3(2)		

**Table 4.** Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^4$ ) for HMN01 (CCDC 656115). The anisotropic displacement factor exponent takes the form:  $-2p^2 [h^2 a^{*2}U^{11} + \dots + 2hk a^* b^* U^{12}]$

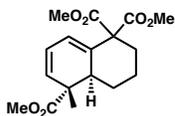
	U <sup>11</sup>	U <sup>22</sup>	U <sup>33</sup>	U <sup>23</sup>	U <sup>13</sup>	U <sup>12</sup>
Br	227(2)	246(1)	214(2)	-91(1)	69(1)	-62(1)
O(1)	142(10)	318(12)	278(12)	49(10)	22(9)	-55(10)
O(2)	184(11)	222(11)	209(12)	53(8)	57(9)	-57(8)
O(3)	211(11)	248(11)	174(11)	-37(8)	99(9)	-33(8)
O(4)	111(10)	171(9)	116(10)	-7(8)	47(8)	-12(7)
O(5)	227(13)	270(11)	388(14)	65(10)	169(10)	-56(9)
O(6)	258(12)	163(10)	205(12)	73(8)	79(10)	34(8)
O(7)	153(10)	159(10)	229(12)	3(8)	86(9)	-23(8)
O(8)	309(13)	156(10)	277(13)	-61(9)	155(10)	-50(9)
C(1)	131(15)	166(13)	164(15)	-44(11)	50(12)	-27(11)
C(2)	98(13)	209(14)	112(14)	30(11)	11(11)	-4(11)
C(3)	106(13)	164(13)	134(15)	32(11)	25(11)	20(11)
C(4)	129(14)	139(12)	123(14)	3(10)	52(12)	-9(11)
C(5)	116(14)	133(13)	114(14)	18(10)	18(11)	4(10)
C(6)	105(13)	133(12)	152(15)	3(10)	61(12)	3(10)
C(7)	161(14)	153(12)	270(16)	-18(13)	57(12)	18(12)
C(8)	147(15)	116(14)	208(16)	-11(11)	86(12)	4(11)
C(9)	236(17)	225(15)	245(18)	57(13)	142(14)	-24(13)
C(10)	133(13)	166(14)	98(14)	-6(10)	-22(11)	3(11)
C(11)	110(13)	148(13)	143(15)	-20(11)	31(12)	-40(11)
C(12)	180(16)	219(14)	200(16)	-51(12)	37(13)	-52(12)
C(13)	129(14)	255(15)	170(16)	-21(12)	-10(13)	-29(12)
C(14)	116(13)	208(15)	160(15)	27(11)	9(12)	10(11)
C(15)	226(16)	162(14)	189(17)	-12(12)	106(14)	-1(12)
C(16)	470(20)	234(16)	214(17)	93(13)	207(16)	111(14)
C(17)	195(15)	140(13)	142(16)	3(11)	-10(12)	16(11)
C(18)	384(19)	211(15)	260(18)	-82(13)	205(16)	-32(14)



#### 14a

**14b** ( 18 mg, 0.04 mmol, 1.0 equiv ),  $\text{Bu}_3\text{SnH}$  ( 18 mg, 0.06 mmol, 1.5 equiv ), AIBN ( 1.5 mg, 0.009 mmol, 0.2 equiv ) and benzene ( 0.40 mL ) were combined in a 1 dm vial, and stirred at reflux for 3 hours. The reaction was cooled to ambient temperature, concentrated by rotary evaporation, diluted with wet diethyl ether ( 1 mL ), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) ( 10.5 mg, .07 mmol, 1.7 equiv ) was added. The resulting white suspension was stirred for 15 minutes, then filtered through Celite. The solvent was removed under vacuum, and the crude residue was purified by preparatory thin layer chromatography (chloroform/diethyl ether/n-heptane, 1:1:1 ) to yield 7.5 mg (

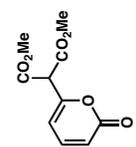
50%) of **14a** as a white residue.  $^1\text{H}$  NMR ( 500 MHz  $\text{CDCl}_3$ )  $\delta$  6.75 ( d,  $J = 8.0$  Hz, 1H ), 6.36 ( dd,  $J = 8.0, 6.0$  Hz, 1H ), 3.77 ( s, 1H ), 3.73 ( s, 3H ), 3.70 ( s, 3H ), 3.56 ( d,  $J = 6.0$  Hz, 1H ), 3.01 ( dd,  $J = 13$  HZ, 6 HZ, 1H ), 2.3 ( m, 2H ), 1.8 ( m, 2H ), 1.36 ( m, 2H ), 1.27 ( s, 3H );  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  175.4, 171.5, 169.5, 168.8, 136.2, 128.304, 83.5, 59.4, 53.0, 52.9, 52.7, 49.3, 48.0, 42.2, 28.1, 24.0, 21.4, 20.6; FTIR (Neat Film NaCl) 1761, 1734, 1626, 1542, 1434, 1255, 1203, 1160, 1108, 1019, 689  $\text{cm}^{-1}$  ; HRMS (EI)  $m/z$  calc'd for  $\text{C}_{18}\text{H}_{22}\text{O}_8$   $[\text{M}+\text{H}]^+$ : 367.1393, found 367.1392.



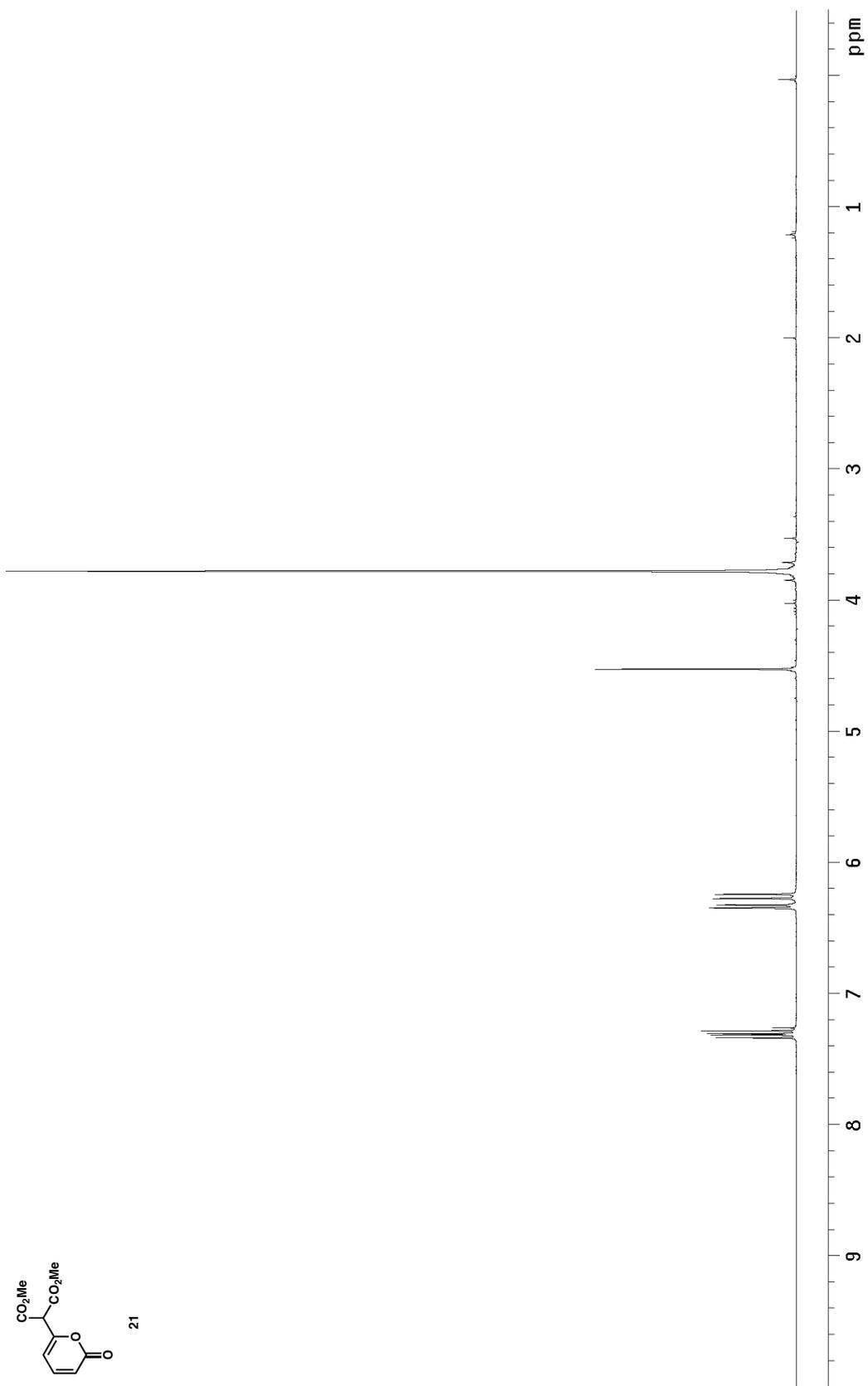
## 22

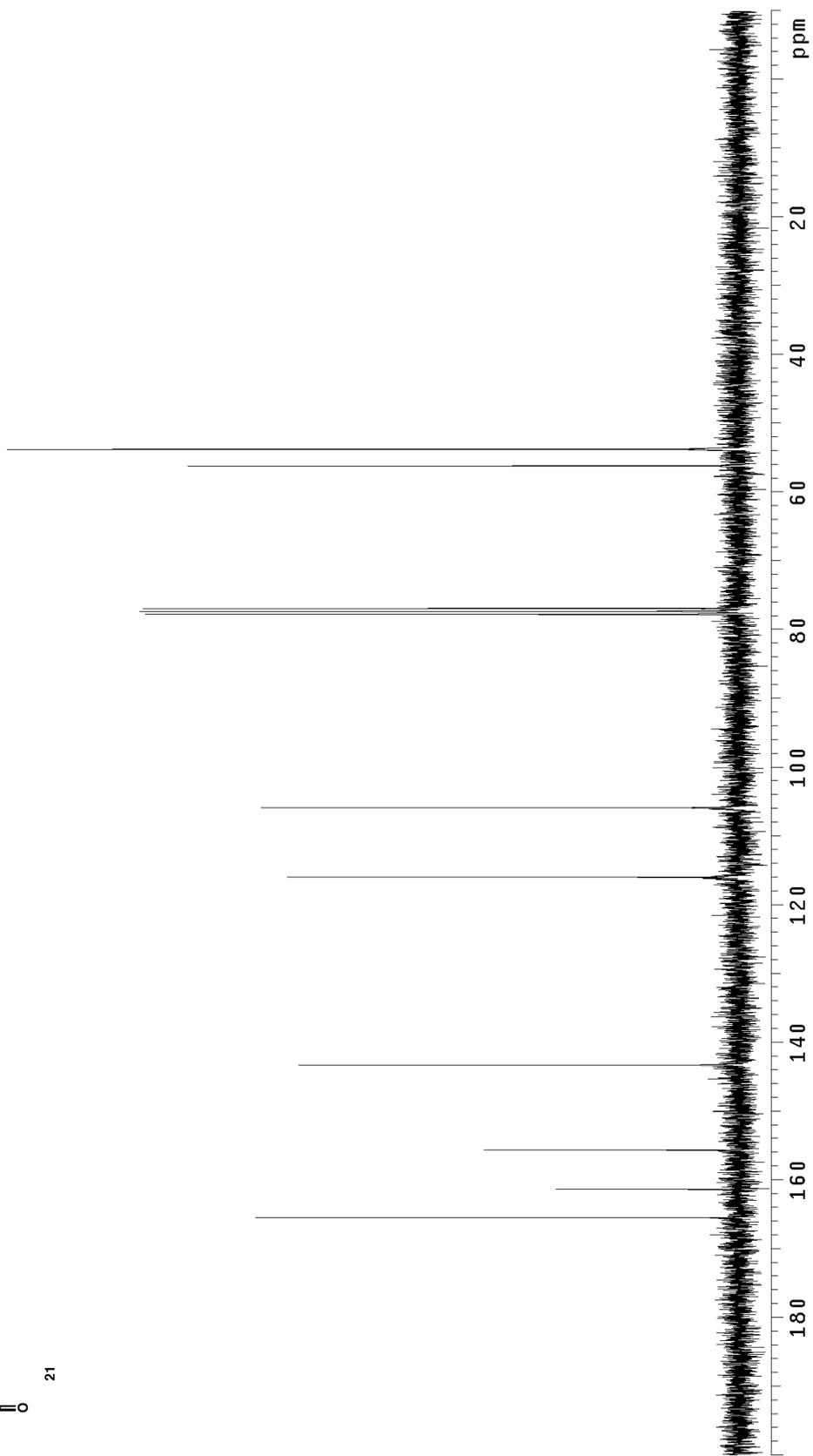
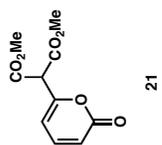
A solution of **13b** ( 63.0 mg, 0.15 mmol, 1.0 equiv ) in toluene ( 10 mL ) was sealed in a scintillation vial and heated to reflux for 72 hours. The reaction mixture was cooled to room temperature, the solvent removed by rotary evaporation, and the crude residue was purified by preparatory thin layer chromatography (30% ethyl acetate in hexanes) to yield **22** as 6.8 mg (62%) of white residue.  $^1\text{H}$  NMR (500 MHz),  $\text{CDCl}_3$   $\delta$  5.91 (dd,  $J = 9.0, 5.5$  Hz, 1H), 5.67 (d,  $J = 5.5$  Hz, 1H), 5.61 (d,  $J = 9.0$  Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.71 (s, 3H), 3.00 (dd,  $J = 6.0$  Hz, 1H), 3.01 (dd,  $J = 13, 4.5$  Hz, 1H), 2.44 (d,  $J = 13.5$  Hz 1H), 1.82 (m, 1H), 1.62 (m, 1H), 1.38 (m, 2H), 1.26 (s, 1H), 1.19, (s, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  177.2, 171.2, 170.9, 136.6, 129.7, 122.5, 119.5, 62.3, 52.8, 52.7, 52.4, 46.7, 41.1, 33.3, 29.7, 25.3, 21.6, 18.5; FTIR (Neat Film NaCl) 1731, 1435, 1255, 1139, 801  $\text{cm}^{-1}$  ; HRMS (EI)  $m/z$  calc'd for  $\text{C}_{17}\text{H}_{22}\text{O}_7$   $[\text{M}+\text{H}]^+$ : 323.1495, found 323.1485.

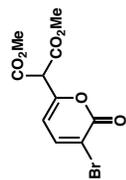
## IV. Spectra



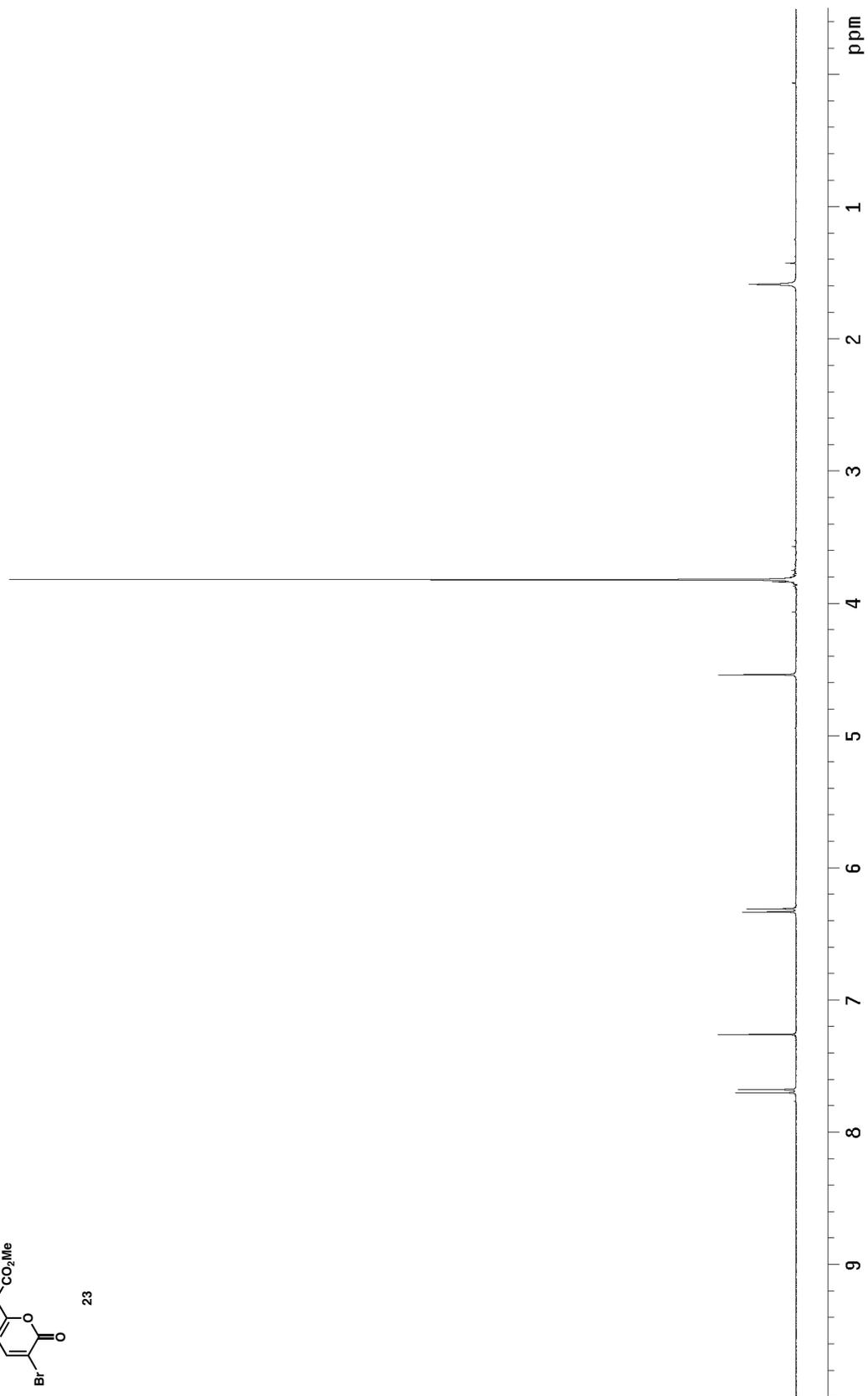
21

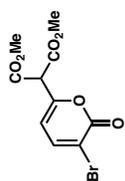




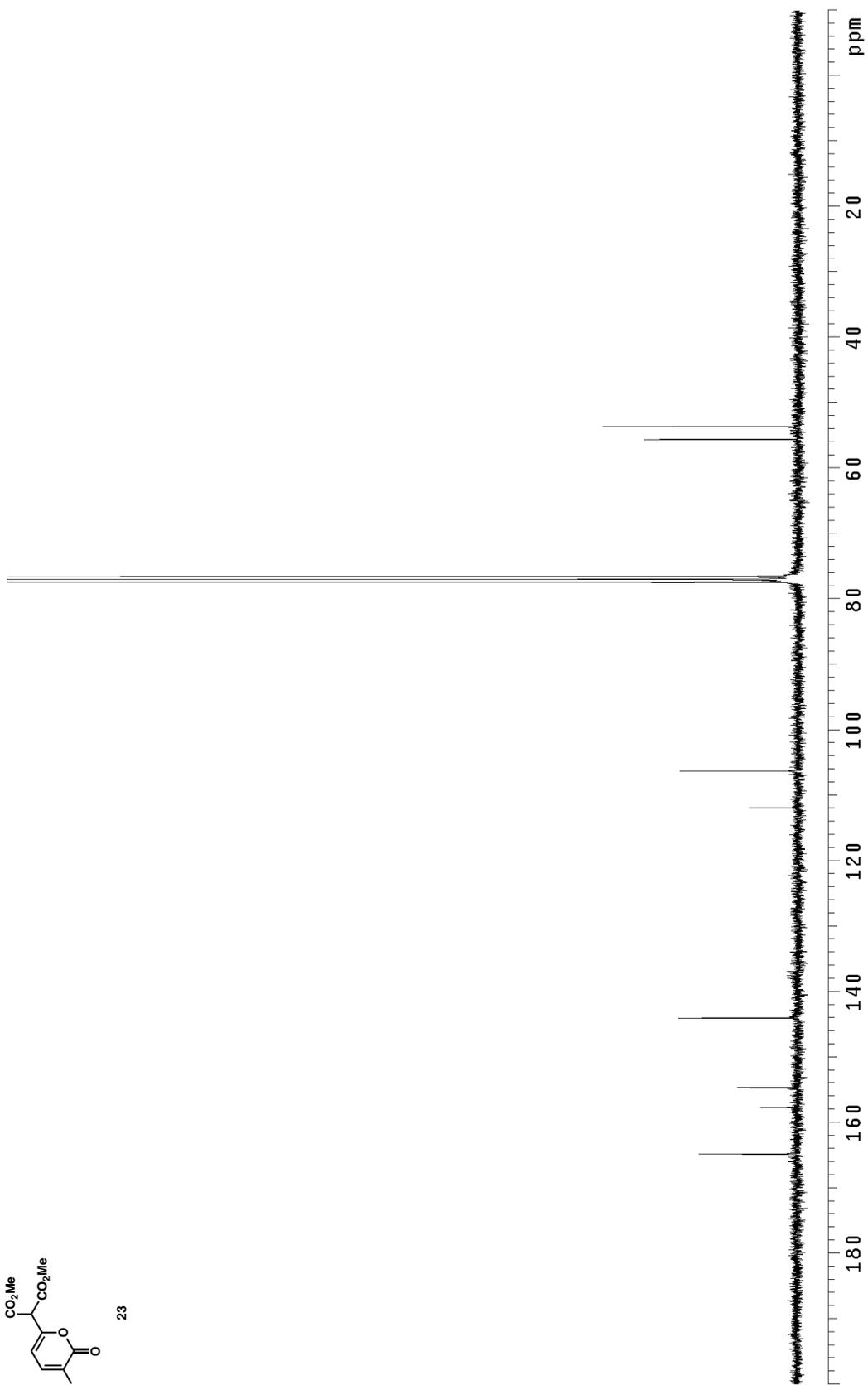


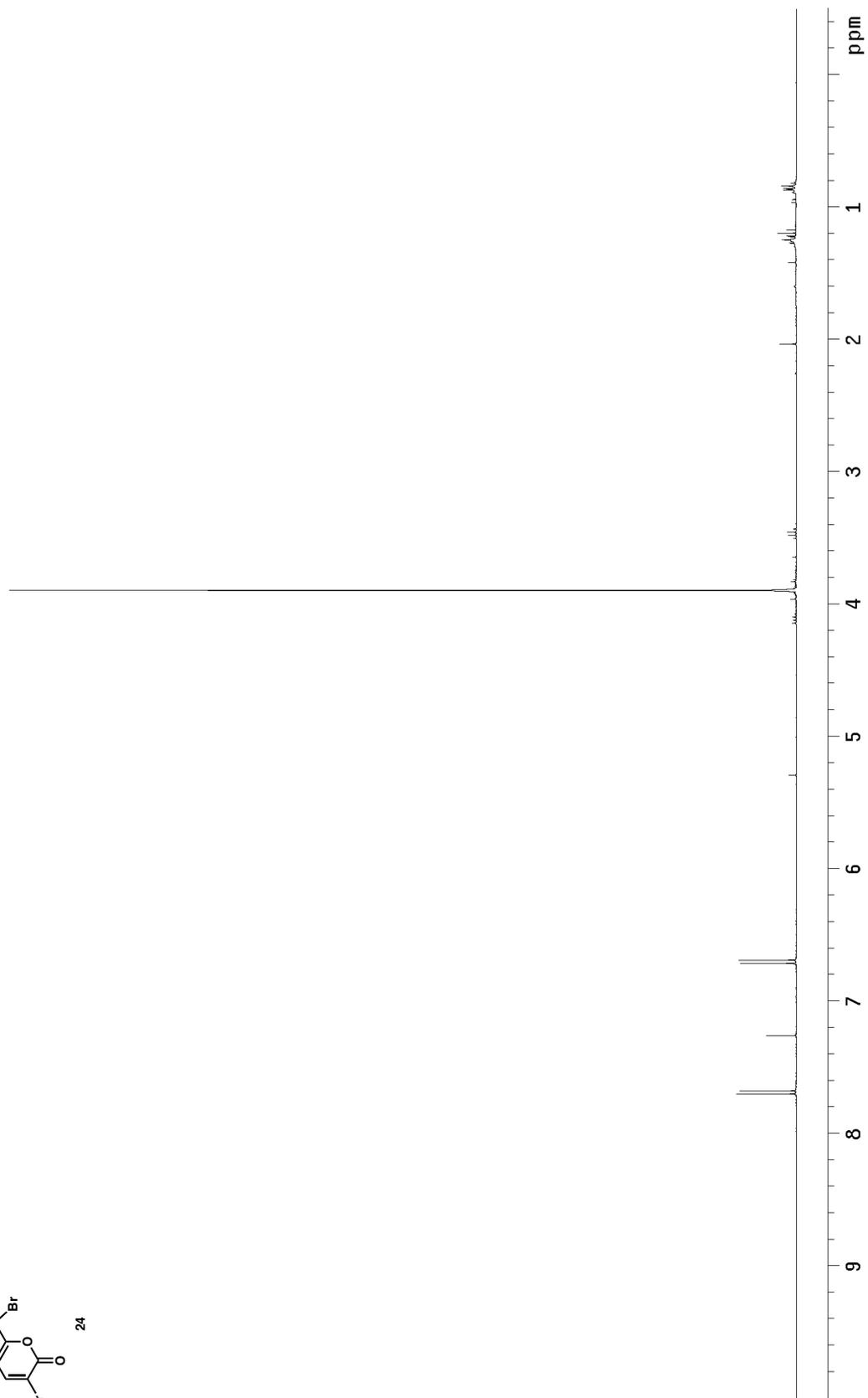
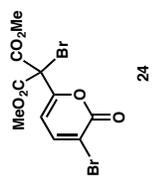
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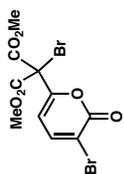




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