

**Construction of Complex Bisether-Bridged  
Medium-Sized Cyclic Compounds from  
*o*-(1-(Acyloxy)propargyl)benzaldehydes under Base and  
Acid Catalysis**

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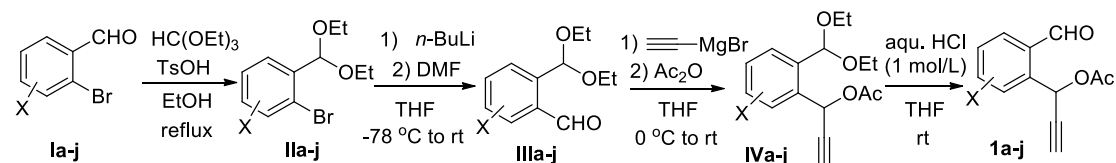
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## 1. Repreparation of reactants 1.

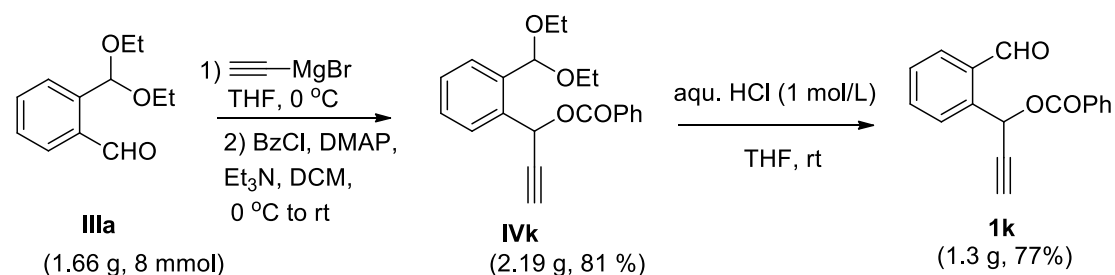
**Scheme S1.** Preparation of 2-(1-( acetyloxy)propargyl)benzaldehydes **1a-1j**.



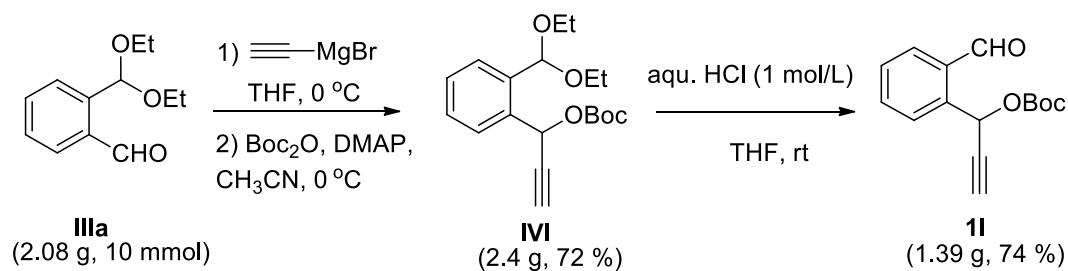
**Table S1.** The quantity of the reactant used and the chemical yield of each step in the preparation of **1a-1j**.

I, X (mmol)	Yield			
	II	III	IV	1
<b>Ia</b> , H (20)	<b>IIa</b> , 95%, 4.96 g	<b>IIIa</b> , 87%, 3.44 g (from 4.92 g of <b>IIa</b> )	<b>IV</b> , 91%, 2.51 g (from 2.06 g of <b>IIIa</b> )	<b>1a</b> , 86%, 1.57 g (from 2.49 g of <b>IVa</b> )
<b>Ib</b> , 4-OMe (14)	<b>IIb</b> , 93%, 3.76 g	<b>IIIb</b> , 84%, 2.14 g (from 3.09 g of <b>IIb</b> )	<b>IVb</b> , 89%, 2.45 g (from 2.14 g of <b>IIIb</b> )	<b>1b</b> , 85%, 1.58 g (from 2.45g of <b>IVb</b> )
<b>Ic</b> , 4-Me (25.1)	<b>IIc</b> , 99%, 6.79 g	<b>IIIc</b> , 95%, 3.17 g (from 4.1 g of <b>IIc</b> )	<b>IVc</b> , 89%, 3.36 g (from 2.89 g of <b>IIIc</b> )	<b>1c</b> , 83%, 1.88 g (from 3.05 g of <b>IVc</b> )
<b>Id</b> , 4-Cl (30)	<b>IIId</b> , 99%, 8.72 g	<b>IIId</b> , 85%, 6.13 g (from 8.72 g of <b>IIId</b> )	<b>IVd</b> , 81%, 3.65 g (from 3.52 g of <b>IIId</b> )	<b>1d</b> , 73%, 1.9 g (from 3.42 g of <b>IVd</b> )
<b>Ie</b> , 4-F (24.1)	<b>IIe</b> , 89%, 5.94 g	<b>IIIe</b> , 92%, 4.16 g (from 5.54 g of <b>IIe</b> )	<b>IVe</b> , 79%, 2.88 g (from 2.81 g of <b>IIIe</b> )	<b>1e</b> , 76%, 1.62 g (from 2.85 g of <b>IVe</b> )
<b>If</b> , 4-CF <sub>3</sub> (20)	<b>IIIf</b> , 91%, 5.95 g	<b>IIIIf</b> , 73%, 3.63 g (from 5.89 g of <b>IIIf</b> )	<b>IVf</b> , 94%, 4.21 g (from 3.59 g of <b>IIIIf</b> )	<b>1f</b> , 78%, 2 g (from 3.27 g of <b>IVf</b> )
<b>Ig</b> , 5-OMe (18.6)	<b>IIg</b> , 96%, 5.16 g	<b>IIIg</b> , 88%, 3.36 g (from 4.63 g of <b>IIg</b> )	<b>IVg</b> , 77%, 3.16 g (from 3.19 g of <b>IIIg</b> )	<b>1g</b> , 71%, 1.7 g (from 3.16 g of <b>IVg</b> )
<b>Ih</b> , 5-Me (25)	<b>IIh</b> , 95%, 6.49 g	<b>IIIh</b> , 78%, 3.38 g (from 5.33 g of <b>IIh</b> )	<b>IVh</b> , 83%, 3.49 g (from 3.22 g of <b>IIIh</b> )	<b>1h</b> , 71%, 1.84 g (from 3.48 g of <b>IVh</b> )
<b>Ii</b> , 5-Cl (11.2)	<b>IIi</b> , 91%, 2.99 g	<b>IIIi</b> , 90%, 2.16 g (from 2.91 g of <b>IIi</b> )	<b>IVi</b> , 85%, 2.17 g (from 1.99 g of <b>IIIi</b> )	<b>1i</b> , 74%, 1.21 g (from 2.14 g of <b>IVi</b> )
<b>Ij</b> , 5-F (28.8)	<b>IIj</b> , 98%, 7.82 g	<b>IIIj</b> , 91%, 5.81 g (from 7.82 g of <b>IIj</b> )	<b>IVj</b> , 94%, 4.4 g (from 3.6 g of <b>IIIj</b> )	<b>1j</b> , 83%, 2.67 g (from 4.3 g of <b>IVj</b> )

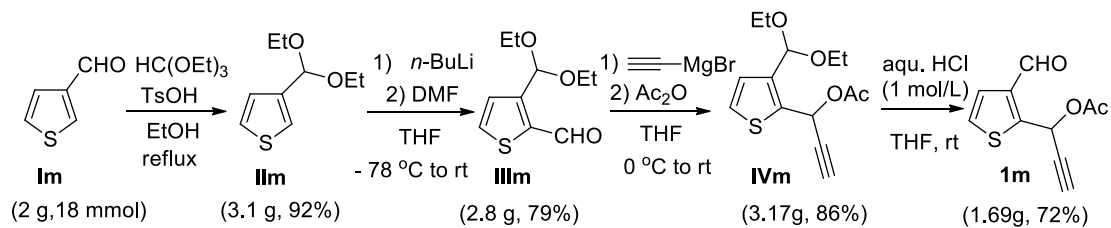
**Scheme S2.** Preparation of 2-(1-(benzoyloxy)propargyl)benzaldehyde **1k**.



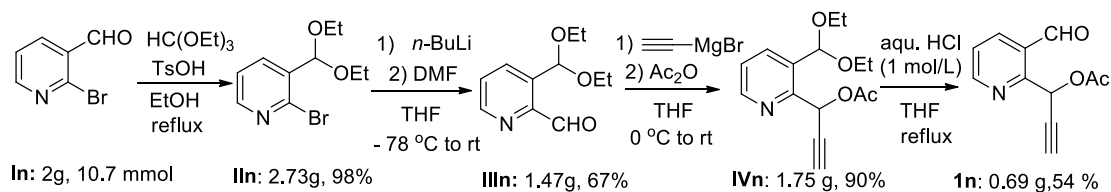
**Scheme S3.** Preparation of 2-(1-((*t*-butoxycarbonyl)oxy)propargyl)benzaldehyde **1l**.



**Scheme S4.** Preparation of 2-(1-(acetyloxy)propargyl)-thiophene-3-carbaldehyde **1m**.



**Scheme S5.** Preparation of 2-(1-(acetyloxy)propargyl)nicotinaldehyde **1n**.



## 2. Crystal data and structure refinements for products **3a**, **4a**, **7a**, **8a** and **9a**.

Crystals of compound **3a** were obtained by slow evaporation of a solution of **3a** in dichloromethane and *n*-hexane. Single crystal X-ray diffraction intensity data of compound **3a** was collected on a 'XtaLAB Synergy R, DW system, HyPix' diffractometer equipped with graphite monochromatized CuK $\alpha$  ( $\lambda = 1.54184$  Å) at 100 K. The structure was solved by the program ShelXL (Sheldrick, 2015) and refined with the program ShelXT (Sheldrick, 2015). The crystal data and structure refinement results for compound **3a** are listed in the Table S2.

**Table S2.** Crystal data and structure refinement for **3a** (CCDC 1919071).

Identification code	20190104a
Empirical formula	C <sub>24</sub> H <sub>20</sub> O <sub>6</sub>
Formula weight	404.40
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	Pbca
<i>a</i> /Å	20.3439(4)
<i>b</i> /Å	8.3230(2)
<i>c</i> /Å	22.9542(5)
$\alpha$ /°	90
$\beta$ /°	90
$\gamma$ /°	90
Volume/Å <sup>3</sup>	3886.66(15)
<i>Z</i>	8
$\rho_{\text{calc}}$ (g/cm <sup>3</sup> )	1.382
$\mu$ /mm <sup>-1</sup>	0.822
<i>F</i> (000)	1696.0
Crystal size/mm <sup>3</sup>	0.3 × 0.03 × 0.01
Radiation	CuK $\alpha$ ( $\lambda = 1.54184$ )
2 $\theta$ range for data collection/°	7.702 to 151.186
Index ranges	-25 ≤ <i>h</i> ≤ 25, -9 ≤ <i>k</i> ≤ 10, -25 ≤ <i>l</i> ≤ 28
Reflections collected	13714
Independent reflections	3887 [ <i>R</i> <sub>int</sub> = 0.0325, <i>R</i> <sub>sigma</sub> = 0.0320]
Data/restraints/parameters	3887/0/273
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.075
Final <i>R</i> indexes [ <i>I</i> ≥ 2σ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0378, <i>wR</i> <sub>2</sub> = 0.0940
Final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0434, <i>wR</i> <sub>2</sub> = 0.1000
Largest diff. peak/hole / e Å <sup>-3</sup>	0.24/-0.25

Crystals of compound **4a** were obtained by slow evaporation of a solution of **4a** in dichloromethane and *n*-hexane. Single crystal X-ray diffraction intensity data of compound **4a** was collected on a SuperNova (Dual, Cu at home/near, AtlasS2) diffractometer equipped with graphite monochromatized CuK $\alpha$  ( $\lambda = 1.54184$  Å) at 100 K. The structure was solved by the program ShelXL (Sheldrick, 2015) and refined with the program ShelXT (Sheldrick, 2015). The crystal data and structure refinement results for compound **4a** are listed in the Table S3.

**Table S3.** Crystal data and structure refinement for **4a** (CCDC 1919076).

Identification code	20181018a
Empirical formula	C <sub>24</sub> H <sub>20</sub> O <sub>6</sub>
Formula weight	404.40
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /c
<i>a</i> /Å	20.7497(5)
<i>b</i> /Å	9.0408(2)
<i>c</i> /Å	10.2972(3)
$\alpha$ /°	90
$\beta$ /°	99.140(3)
$\gamma$ /°	90
Volume/Å <sup>3</sup>	1907.17(9)
<i>Z</i>	4
$\rho_{\text{calc}}$ (g/cm <sup>3</sup> )	1.408
$\mu$ /mm <sup>-1</sup>	0.838
<i>F</i> (000)	848.0
Crystal size/mm <sup>3</sup>	0.2 × 0.2 × 0.15
Radiation	CuK $\alpha$ ( $\lambda = 1.54184$ )
2 $\theta$ range for data collection/°	8.632 to 143.812
Index ranges	-23 ≤ <i>h</i> ≤ 25, -10 ≤ <i>k</i> ≤ 10, -12 ≤ <i>l</i> ≤ 6
Reflections collected	12879
Independent reflections	3699 [ <i>R</i> <sub>int</sub> = 0.0341, <i>R</i> <sub>sigma</sub> = 0.0301]
Data/restraints/parameters	3699/0/273
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.027
Final <i>R</i> indexes [ <i>I</i> ≥ 2 $\sigma$ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0383, <i>wR</i> <sub>2</sub> = 0.0939
Final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0476, <i>wR</i> <sub>2</sub> = 0.1007
Largest diff. peak/hole / e Å <sup>-3</sup>	0.29/-0.29

Crystals of compound **7a** were obtained by slow evaporation of a solution of **7a** in dichloromethane and *n*-hexane. Single crystal X-ray diffraction intensity data of compound **7a** was collected on a 'XtaLAB Synergy R, DW system, HyPix' diffractometer equipped with graphite monochromatized CuK $\alpha$  ( $\lambda = 1.54184$  Å) at 100 K. The structure was solved by the program ShelXT (Sheldrick, 2015) and refined with the program ShelXL (Sheldrick, 2015). The crystal data and structure refinement results for compound **7a** are listed in the Table S4.

**Table S4.** Crystal data and structure refinement for **7a** (CCDC 1919079).

Identification code	20190305a
Empirical formula	C <sub>22</sub> H <sub>18</sub> O <sub>5</sub>
Formula weight	362.36
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /c
<i>a</i> /Å	16.8387(4)
<i>b</i> /Å	6.7800(2)
<i>c</i> /Å	15.4079(4)
$\alpha$ /°	90
$\beta$ /°	106.205(3)
$\gamma$ /°	90
Volume/Å <sup>3</sup>	1689.17(8)
<i>Z</i>	4
$\rho_{\text{calc}}$ (g/cm <sup>3</sup> )	1.425
$\mu$ /mm <sup>-1</sup>	0.831
<i>F</i> (000)	760.0
Crystal size/mm <sup>3</sup>	0.3 × 0.08 × 0.05
Radiation	CuK $\alpha$ ( $\lambda = 1.54184$ )
2 $\theta$ range for data collection/°	5.466 to 150.914
Index ranges	-21 ≤ <i>h</i> ≤ 21, -5 ≤ <i>k</i> ≤ 8, -19 ≤ <i>l</i> ≤ 17
Reflections collected	11399
Independent reflections	3382 [ <i>R</i> <sub>int</sub> = 0.0444, <i>R</i> <sub>sigma</sub> = 0.0435]
Data/restraints/parameters	3382/0/245
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.077
Final <i>R</i> indexes [ <i>I</i> ≥ 2 $\sigma$ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0460, <i>wR</i> <sub>2</sub> = 0.1211
Final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0557, <i>wR</i> <sub>2</sub> = 0.1291
Largest diff. peak/hole / e Å <sup>-3</sup>	0.26/-0.29

Crystals of compound **8a** were obtained by slow evaporation of a solution of **8a** in acetone and *n*-hexane. Single crystal X-ray diffraction intensity data of compound **8a** was collected on a 'XtaLAB Synergy R, DW system, HyPix' diffractometer equipped with graphite monochromatized CuK $\alpha$  ( $\lambda = 1.54184$  Å) at 100 K. The structure was solved by the program ShelXT (Sheldrick, 2015) and refined with the program ShelXL (Sheldrick, 2015). The crystal data and structure refinement results for compound **8a** are listed in the Table S5.

**Table S5.** Crystal data and structure refinement for **8a** (CCDC 1919096).

Identification code	20190520c
Empirical formula	C <sub>22</sub> H <sub>18</sub> O <sub>6</sub>
Formula weight	378.36
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	P2 <sub>1</sub> /c
<i>a</i> /Å	8.10270(10)
<i>b</i> /Å	27.9899(5)
<i>c</i> /Å	7.55070(10)
$\alpha$ /°	90
$\beta$ /°	101.480(2)
$\gamma$ /°	90
Volume/Å <sup>3</sup>	1678.19(4)
<i>Z</i>	4
$\rho_{\text{calc}}$ (g/cm <sup>3</sup> )	1.498
$\mu$ /mm <sup>-1</sup>	0.909
<i>F</i> (000)	792.0
Crystal size/mm <sup>3</sup>	0.12 × 0.1 × 0.08
Radiation	CuK $\alpha$ ( $\lambda = 1.54184$ )
2 $\theta$ range for data collection/°	6.316 to 151.45
Index ranges	-10 ≤ <i>h</i> ≤ 8, -28 ≤ <i>k</i> ≤ 34, -9 ≤ <i>l</i> ≤ 9
Reflections collected	10411
Independent reflections	3318 [ <i>R</i> <sub>int</sub> = 0.0312, <i>R</i> <sub>sigma</sub> = 0.0296]
Data/restraints/parameters	3318/0/255
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.074
Final <i>R</i> indexes [ <i>I</i> ≥ 2σ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0416, <i>wR</i> <sub>2</sub> = 0.0958
Final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0505, <i>wR</i> <sub>2</sub> = 0.1074
Largest diff. peak/hole / e Å <sup>-3</sup>	0.32/-0.32

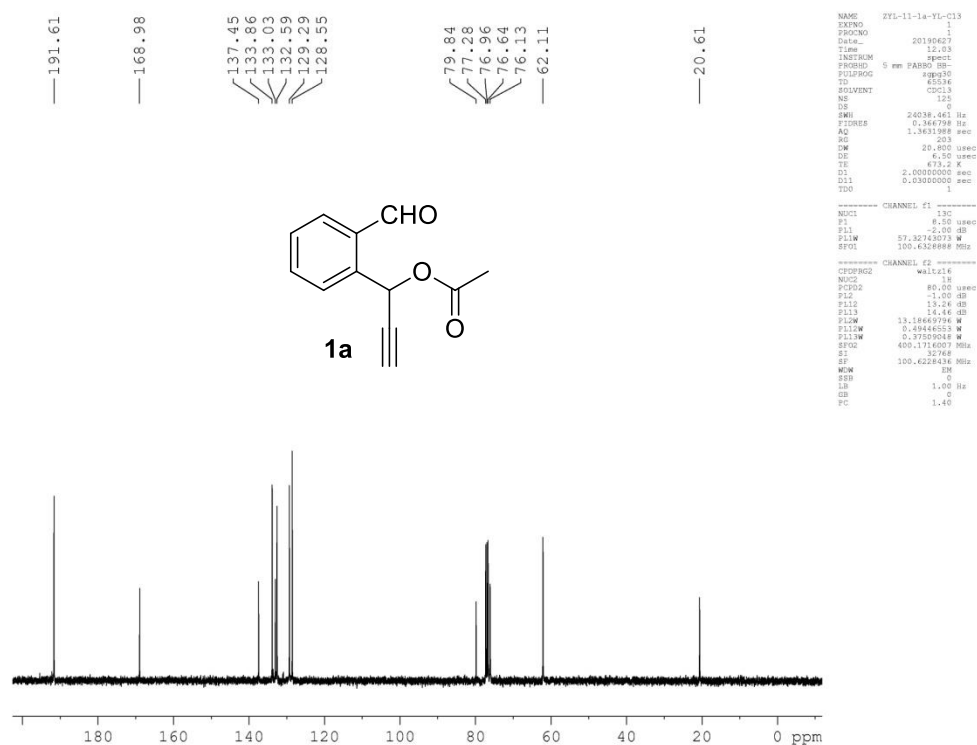
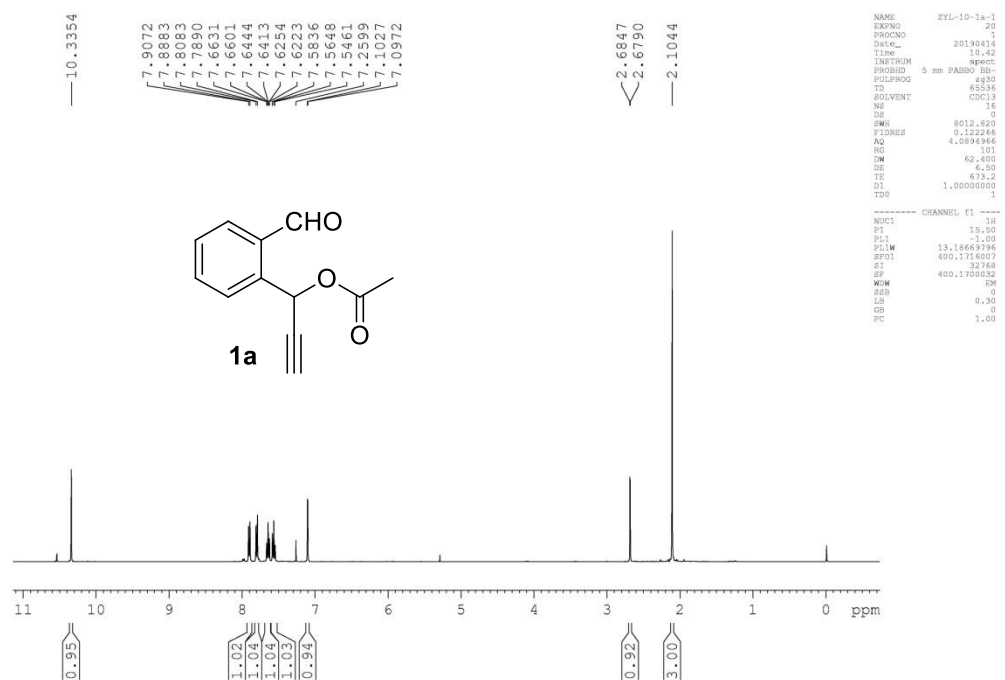
Crystals of compound **9a** were obtained by slow evaporation of a solution of **9a** in dichloromethane, chloroform and *n*-hexane. Single crystal X-ray diffraction intensity data of compound **9a** was collected on a 'XtaLAB Synergy R, DW system, HyPix' diffractometer equipped with graphite monochromatized CuK $\alpha$  ( $\lambda = 1.54184$  Å) at 100 K. The structure was solved by the program ShelXT (Sheldrick, 2015) and refined with the program ShelXL (Sheldrick, 2015). The crystal data and structure refinement results for compound **9a** are listed in the Table S6.

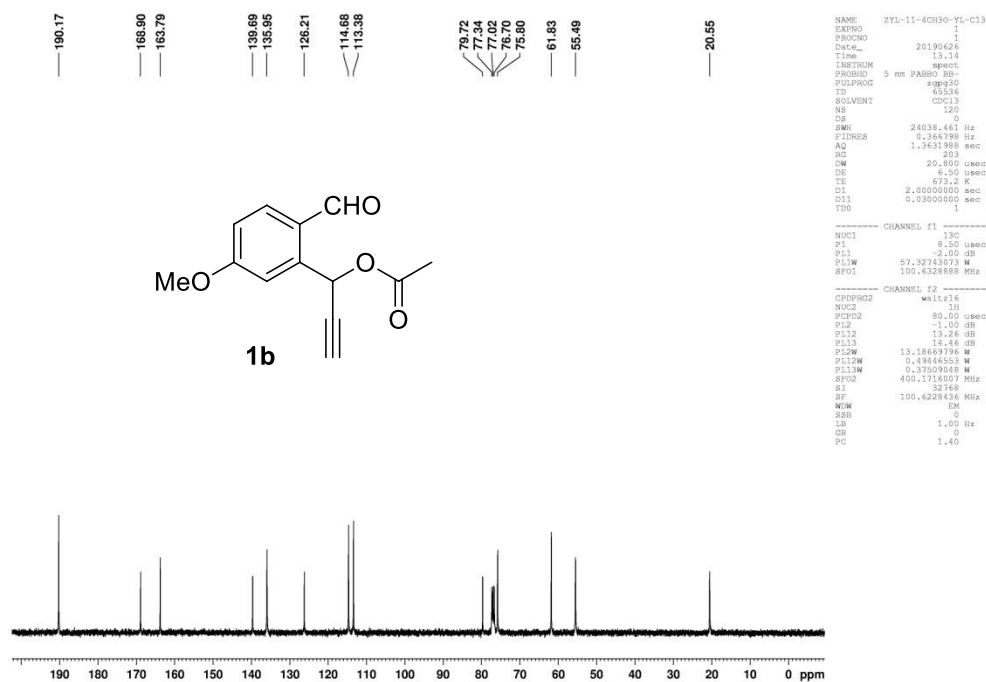
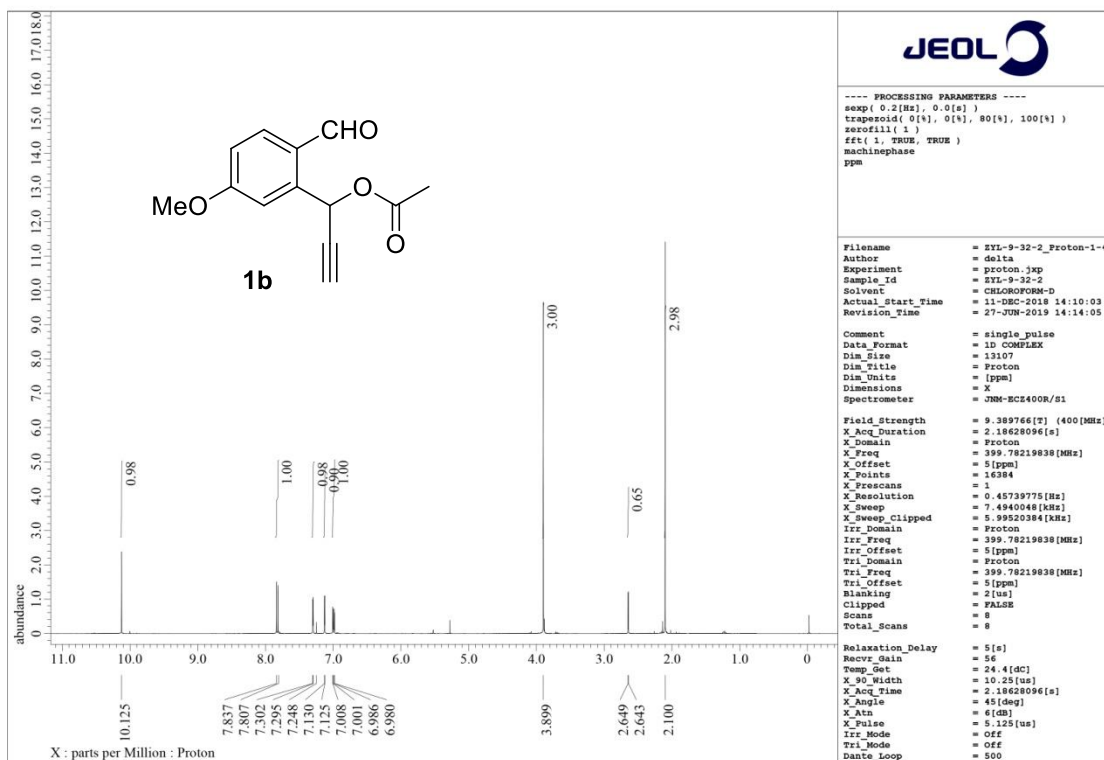
**Table S6.** Crystal data and structure refinement for **9a** (CCDC 1919100).

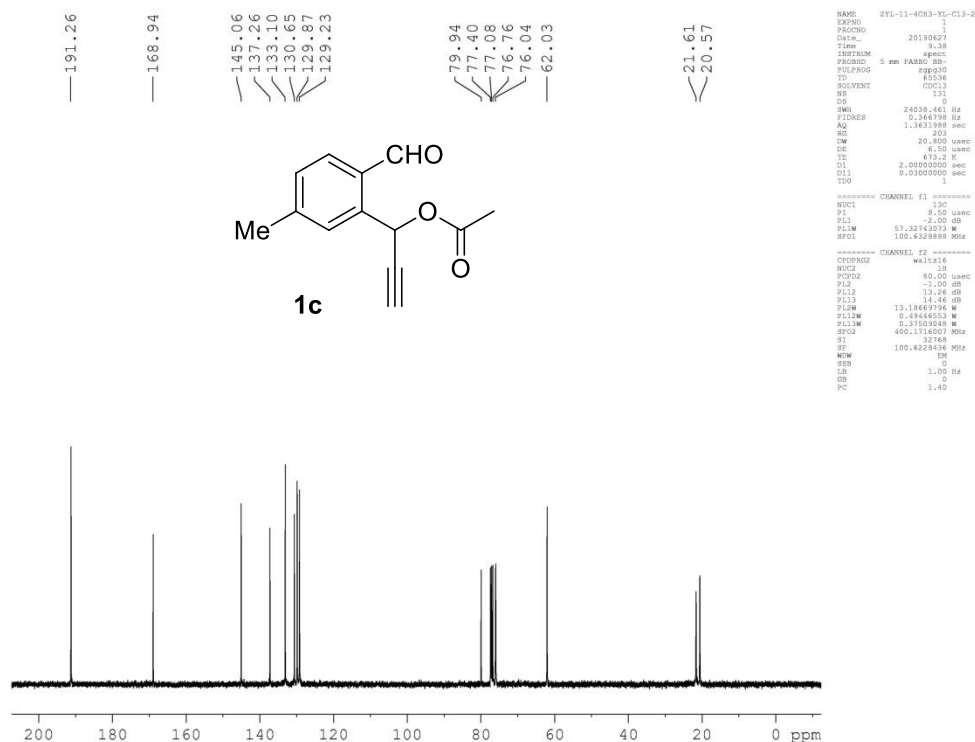
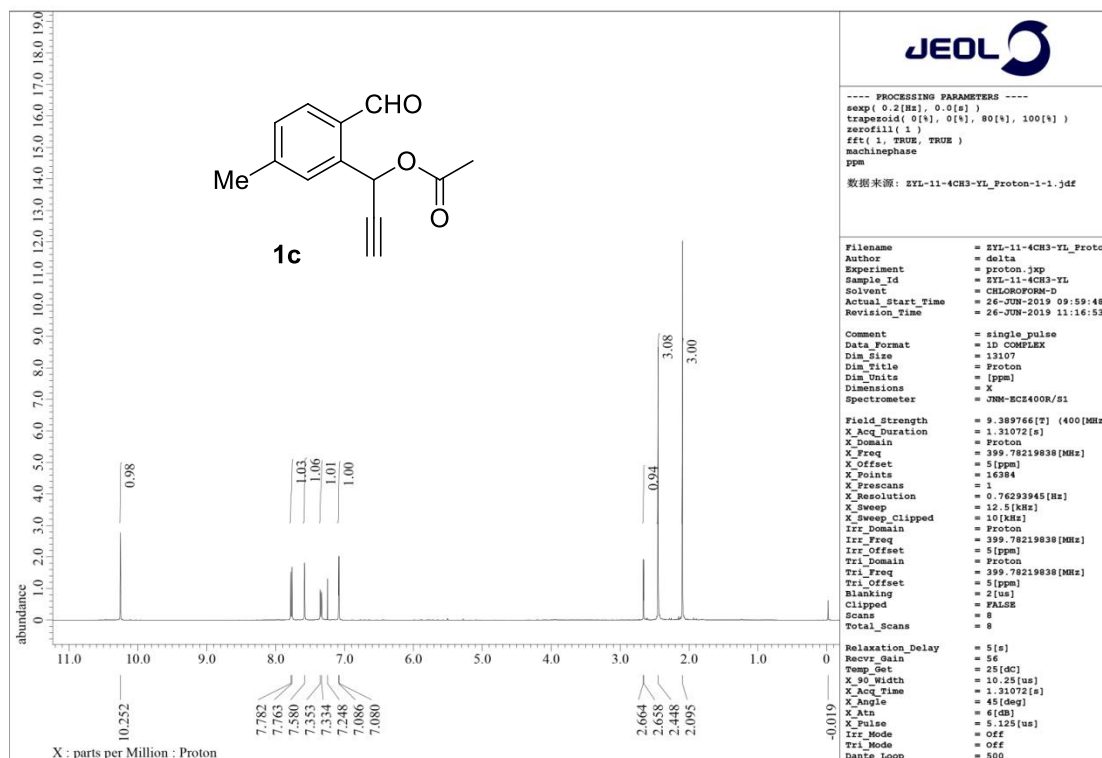
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Empirical formula	C <sub>24</sub> H <sub>22</sub> O <sub>7</sub>
Formula weight	422.41
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	Pca2 <sub>1</sub>
<i>a</i> /Å	14.0881(2)
<i>b</i> /Å	7.88590(10)
<i>c</i> /Å	35.7414(4)
$\alpha$ /°	90
$\beta$ /°	90
$\gamma$ /°	90
Volume/Å <sup>3</sup>	3970.78(9)
<i>Z</i>	8
$\rho_{\text{calc}}$ /cm <sup>3</sup>	1.413
$\mu$ /mm <sup>-1</sup>	0.866
<i>F</i> (000)	1776.0
Crystal size/mm <sup>3</sup>	0.3 × 0.2 × 0.1
Radiation	CuK $\alpha$ ( $\lambda = 1.54184$ )
2 $\theta$ range for data collection/°	4.944 to 151.126
Index ranges	-17 ≤ <i>h</i> ≤ 17, -9 ≤ <i>k</i> ≤ 9, -44 ≤ <i>l</i> ≤ 44
Reflections collected	27953
Independent reflections	7424 [ <i>R</i> <sub>int</sub> = 0.0279, <i>R</i> <sub>sigma</sub> = 0.0220]
Data/restraints/parameters	7424/1/567
Goodness-of-fit on <i>F</i> <sup>2</sup>	1.021
Final <i>R</i> indexes [ <i>I</i> ≥ 2σ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0303, <i>wR</i> <sub>2</sub> = 0.0770
Final <i>R</i> indexes [all data]	<i>R</i> <sub>1</sub> = 0.0315, <i>wR</i> <sub>2</sub> = 0.0786
Largest diff. peak/hole / e Å <sup>-3</sup>	0.23/-0.20

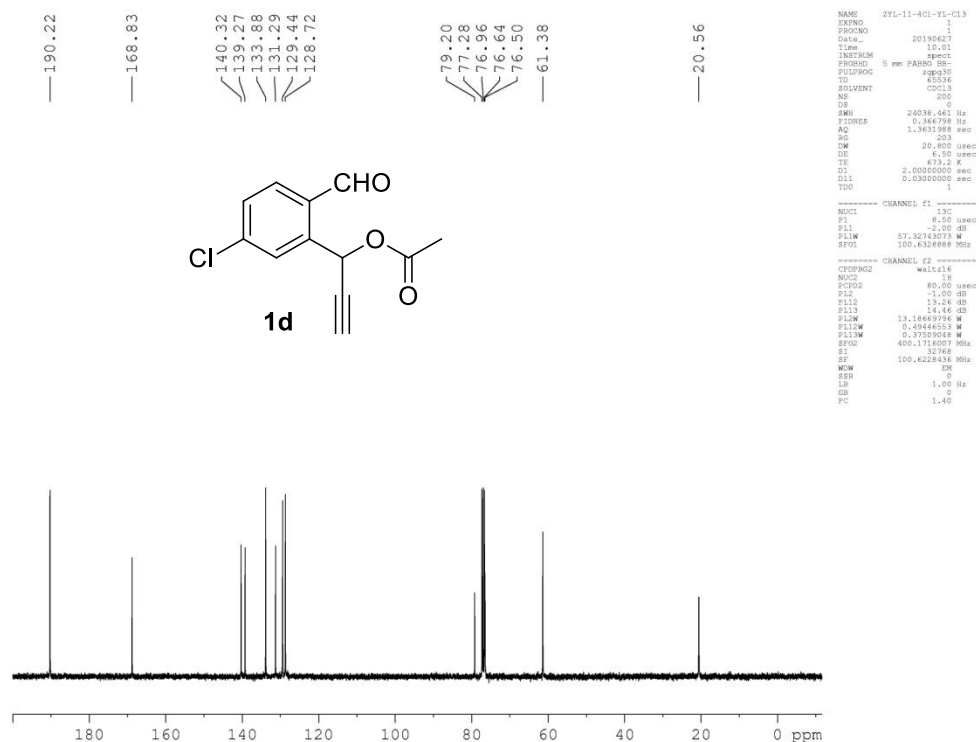
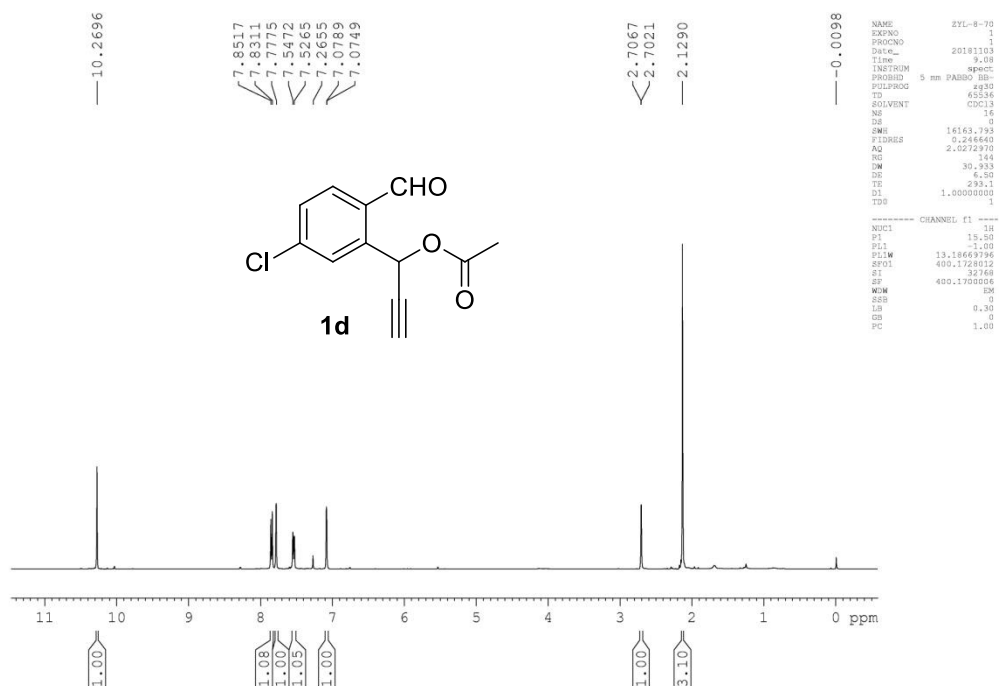


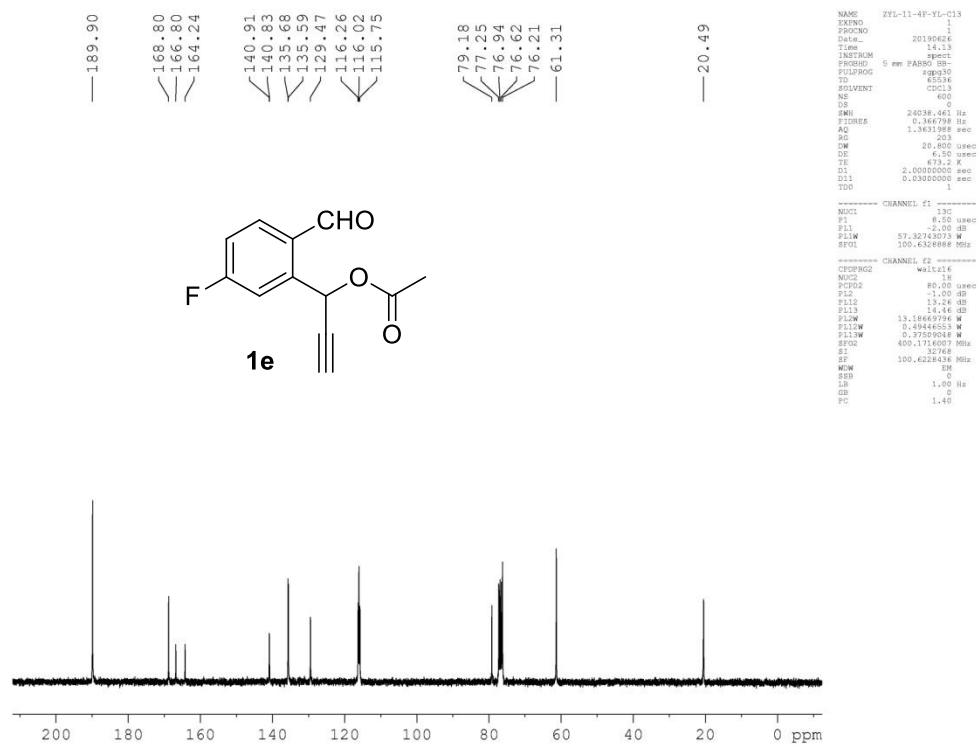
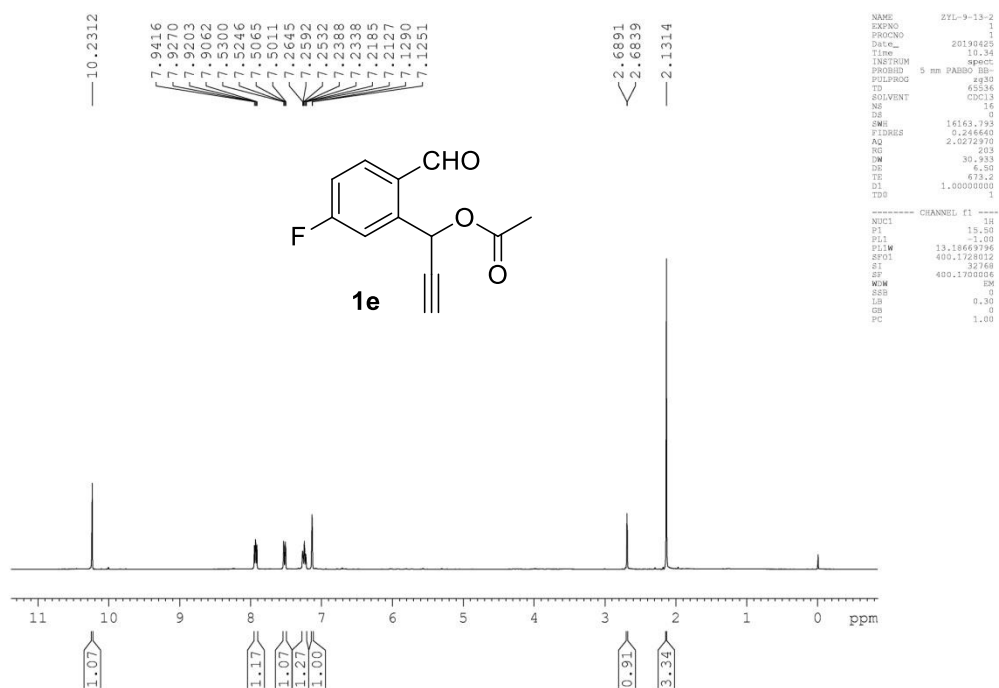
### 3. NMR spectra of reactants 1 and products 3-9.

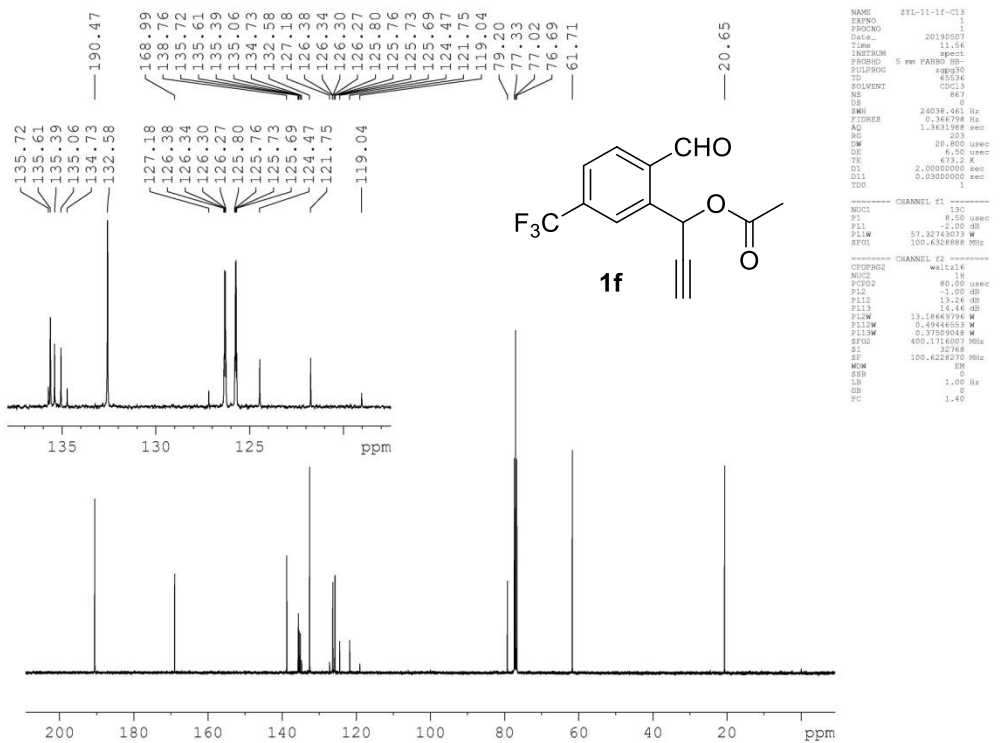
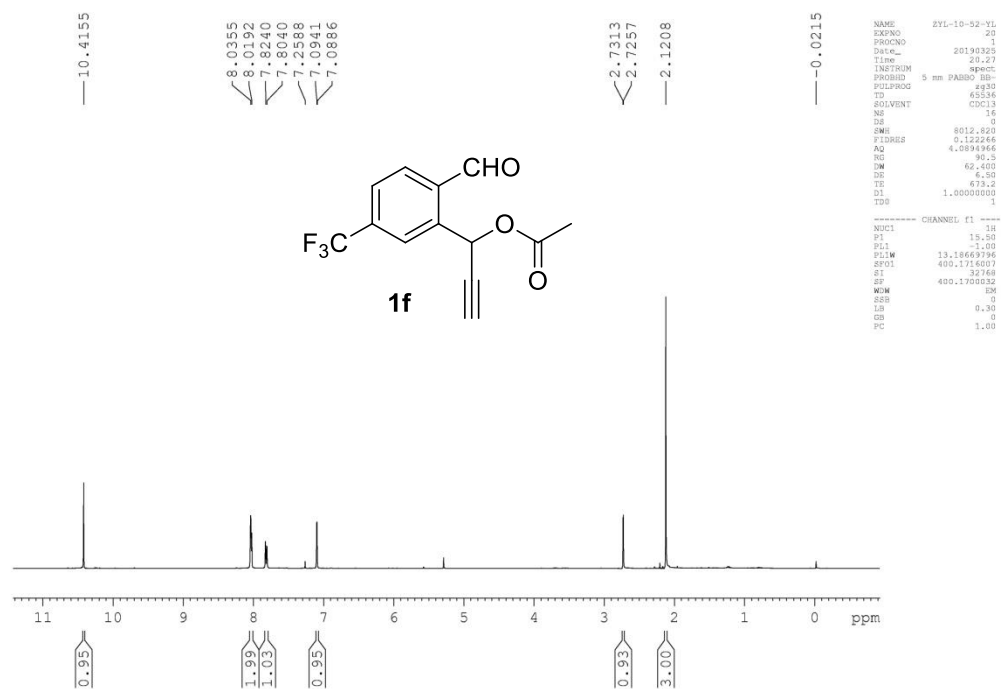


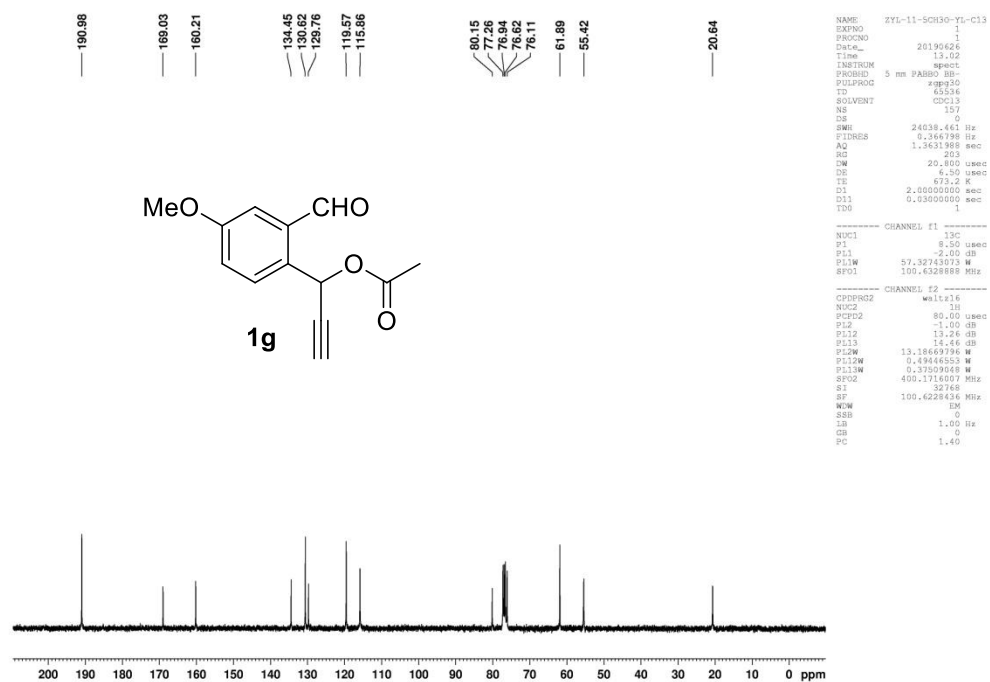
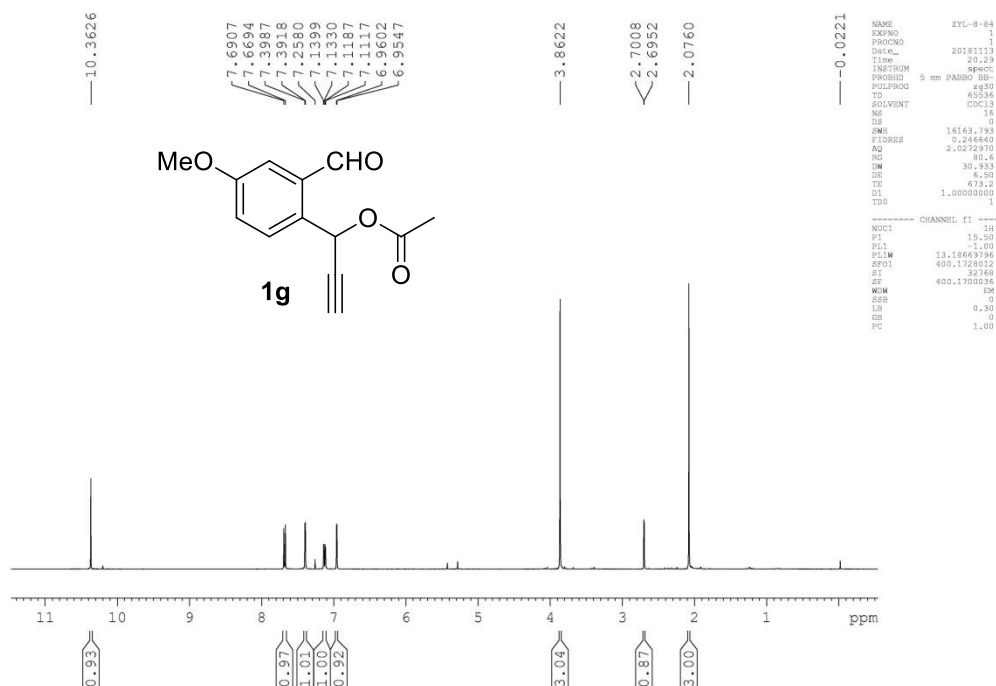


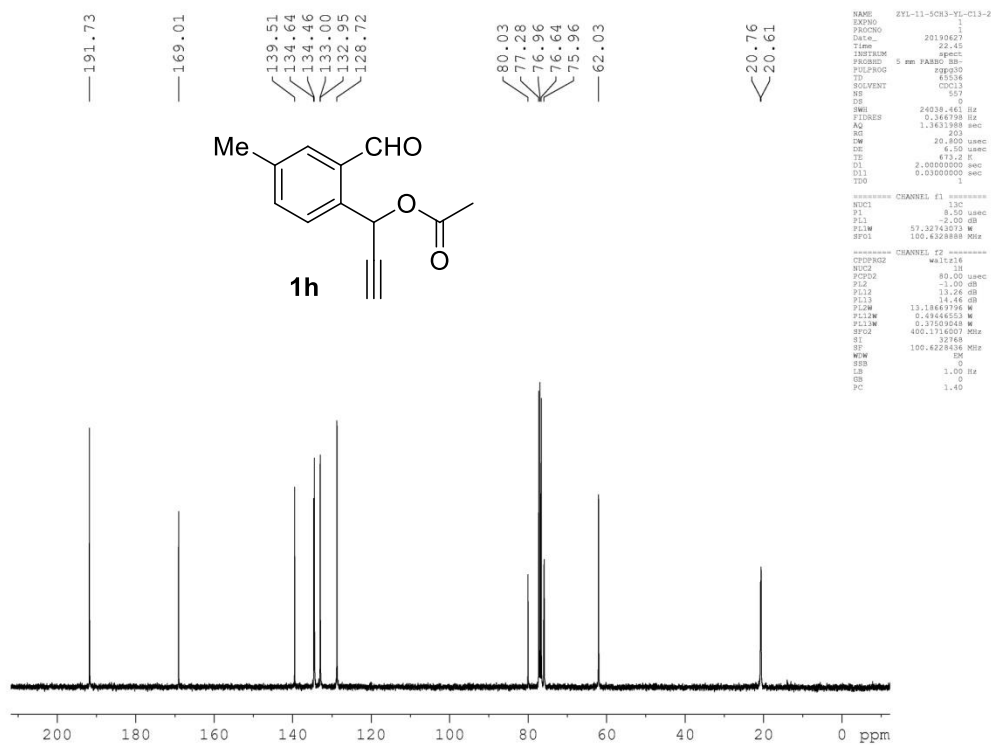
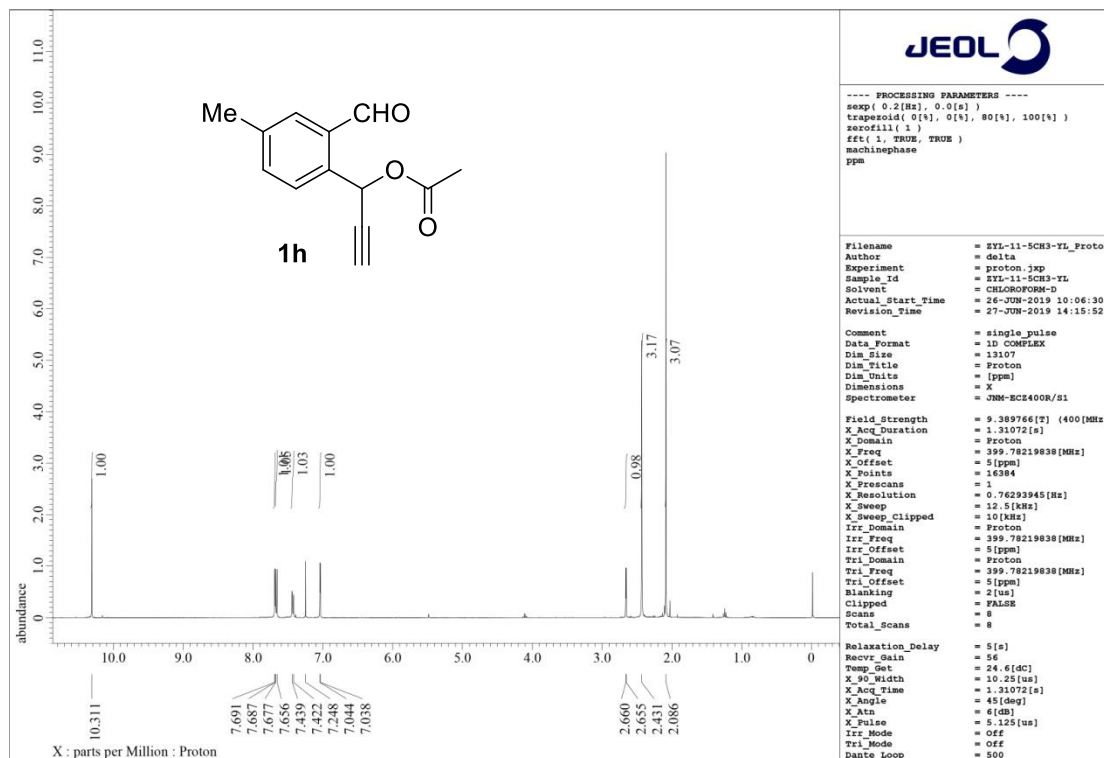




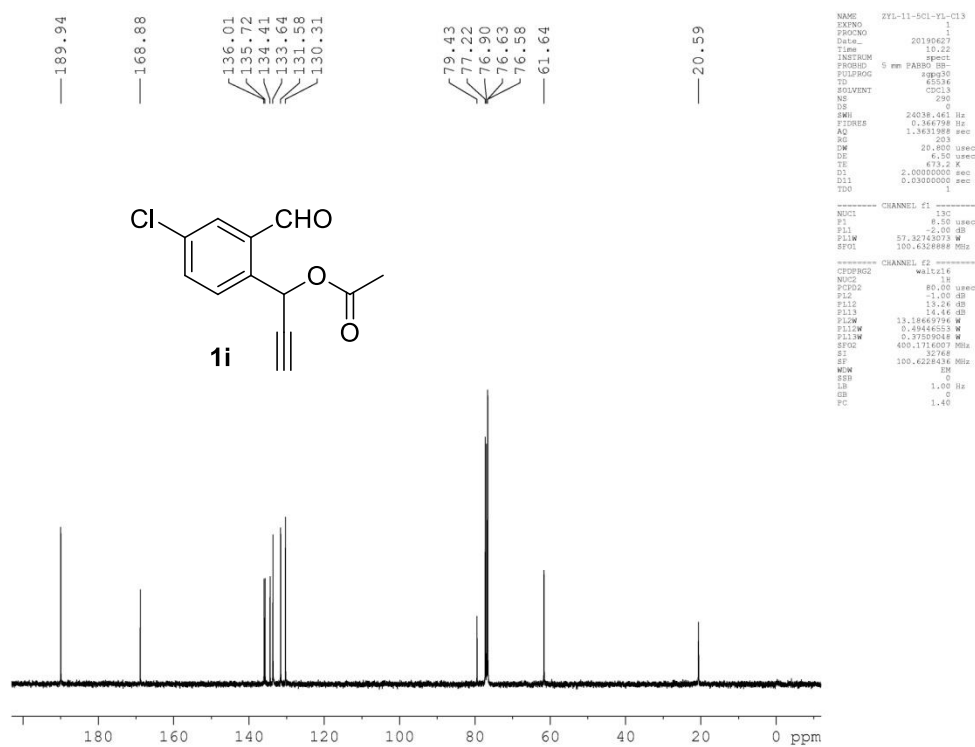
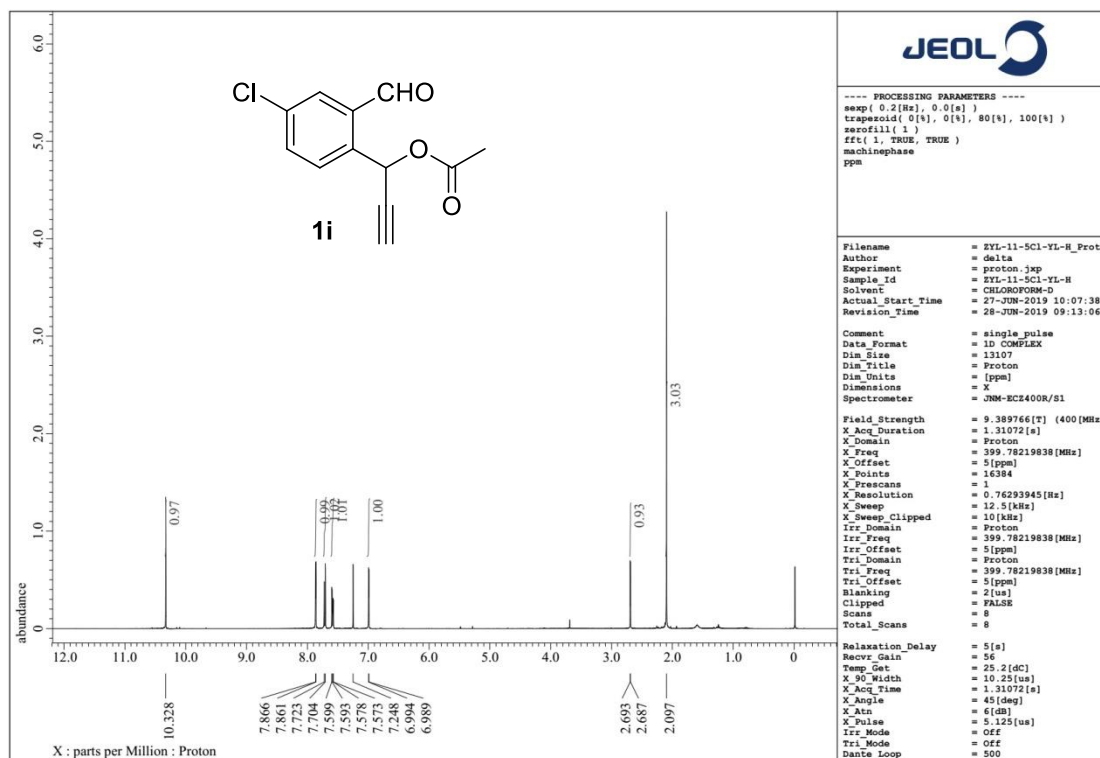


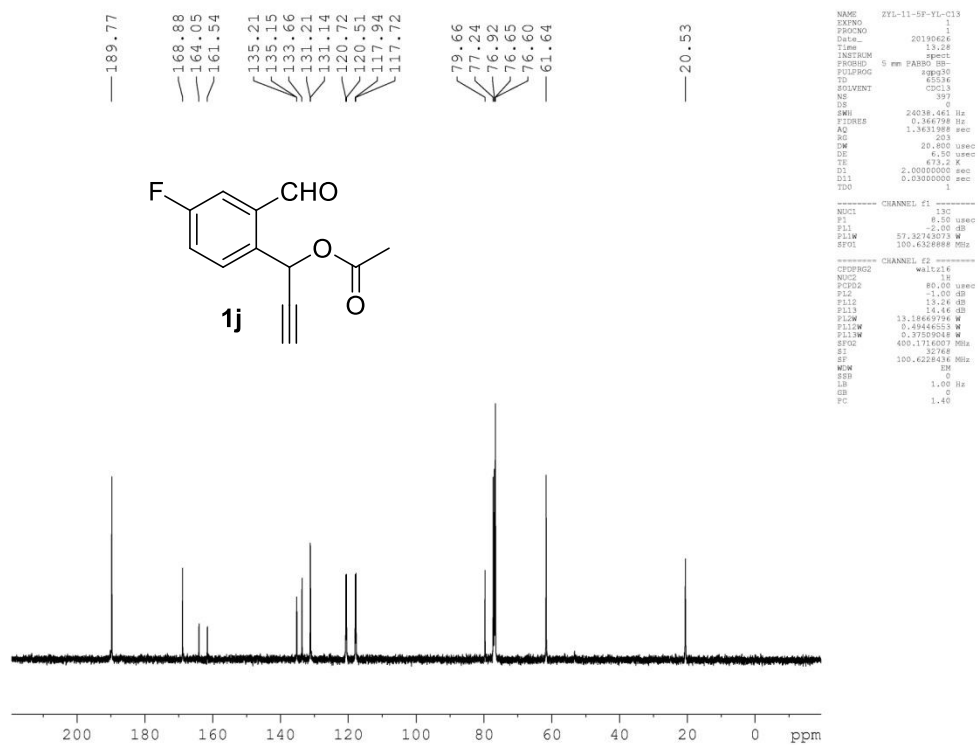
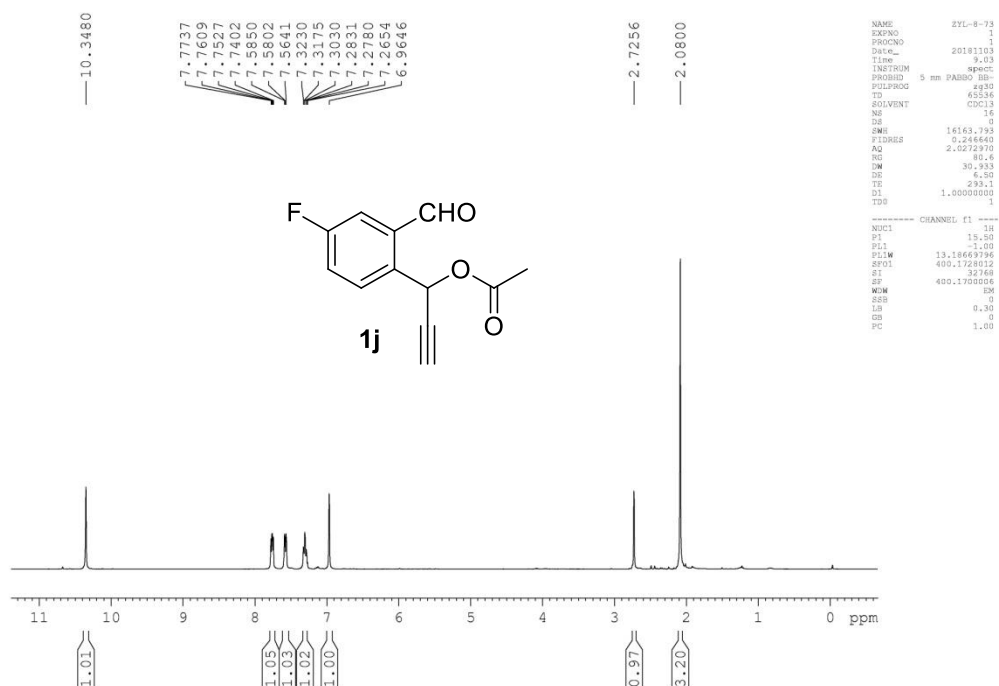


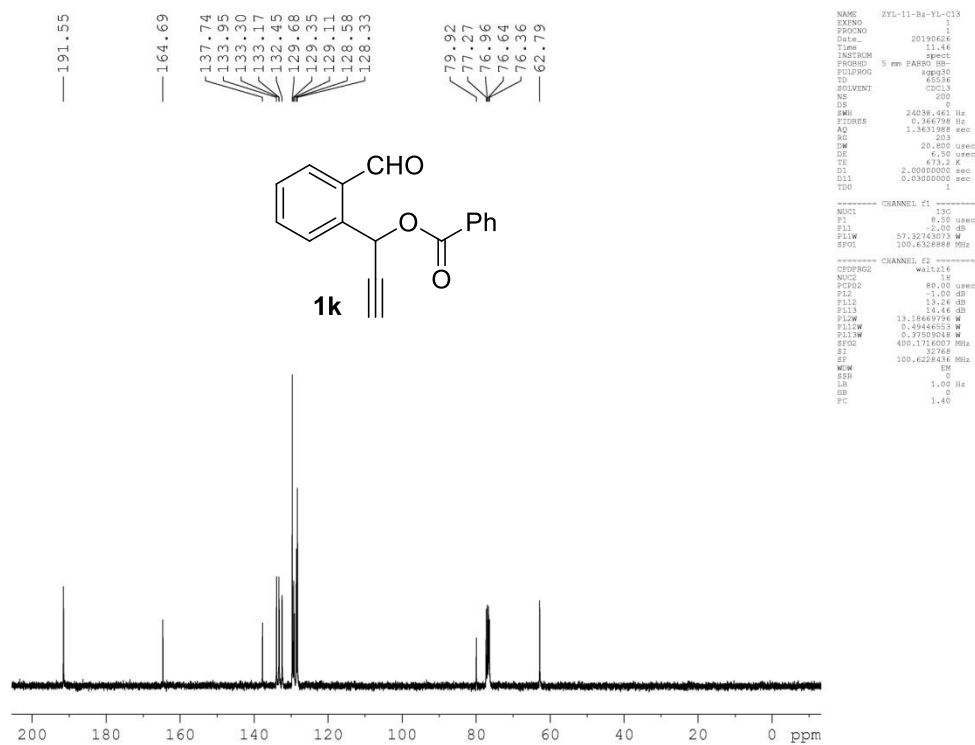
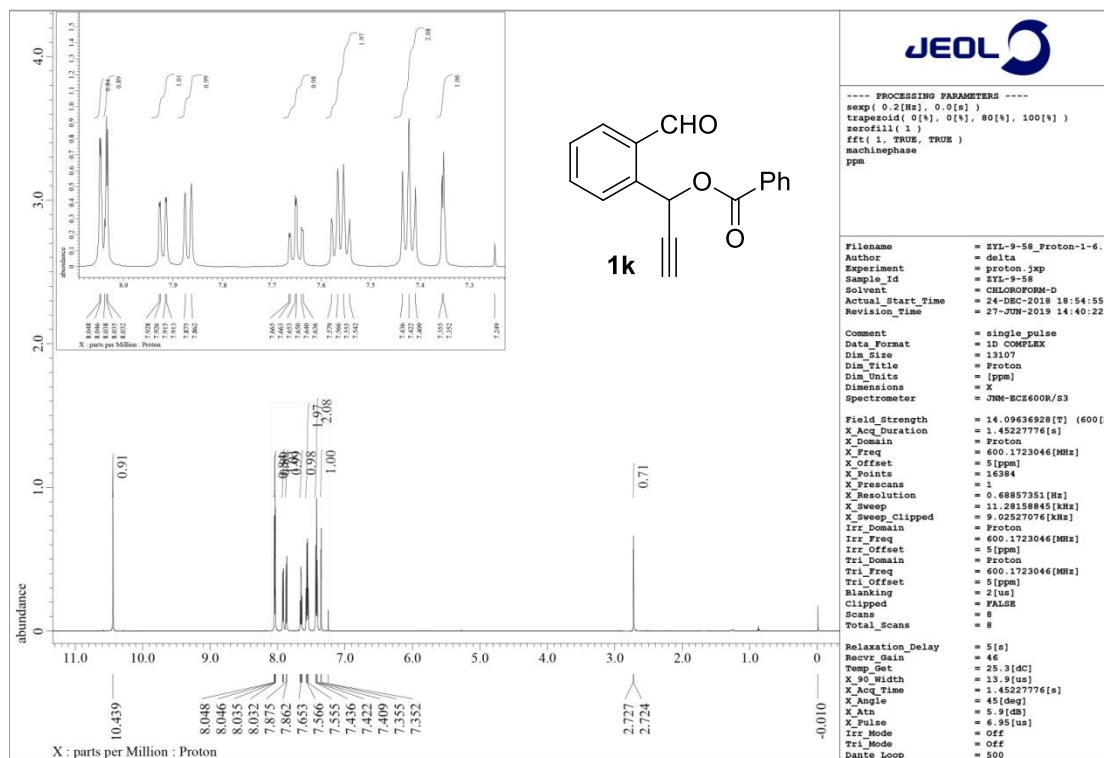


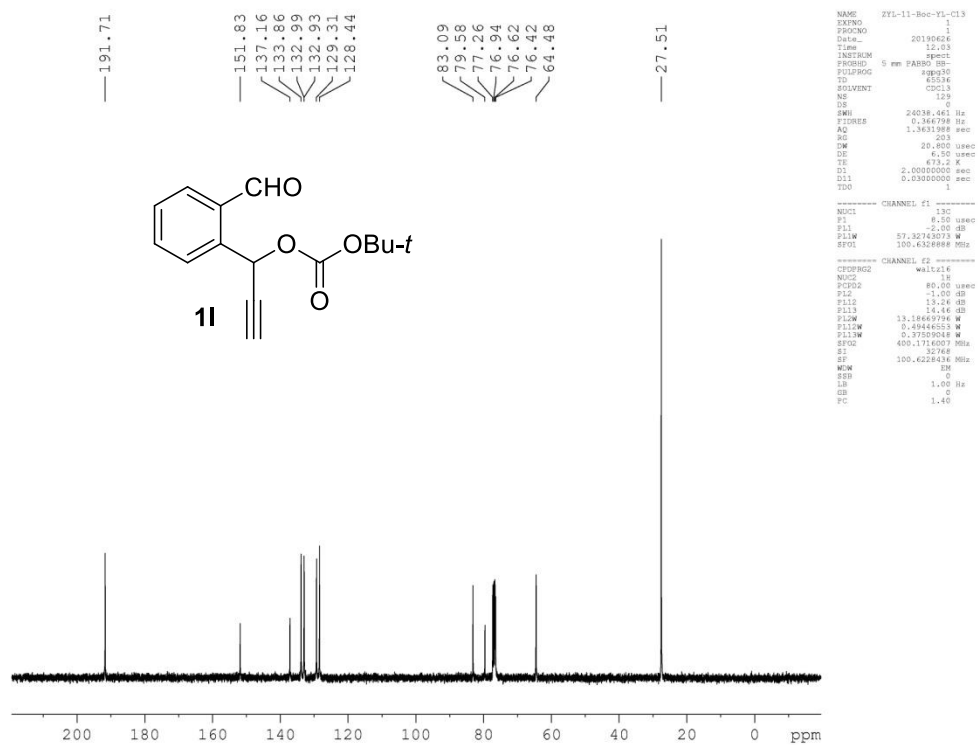
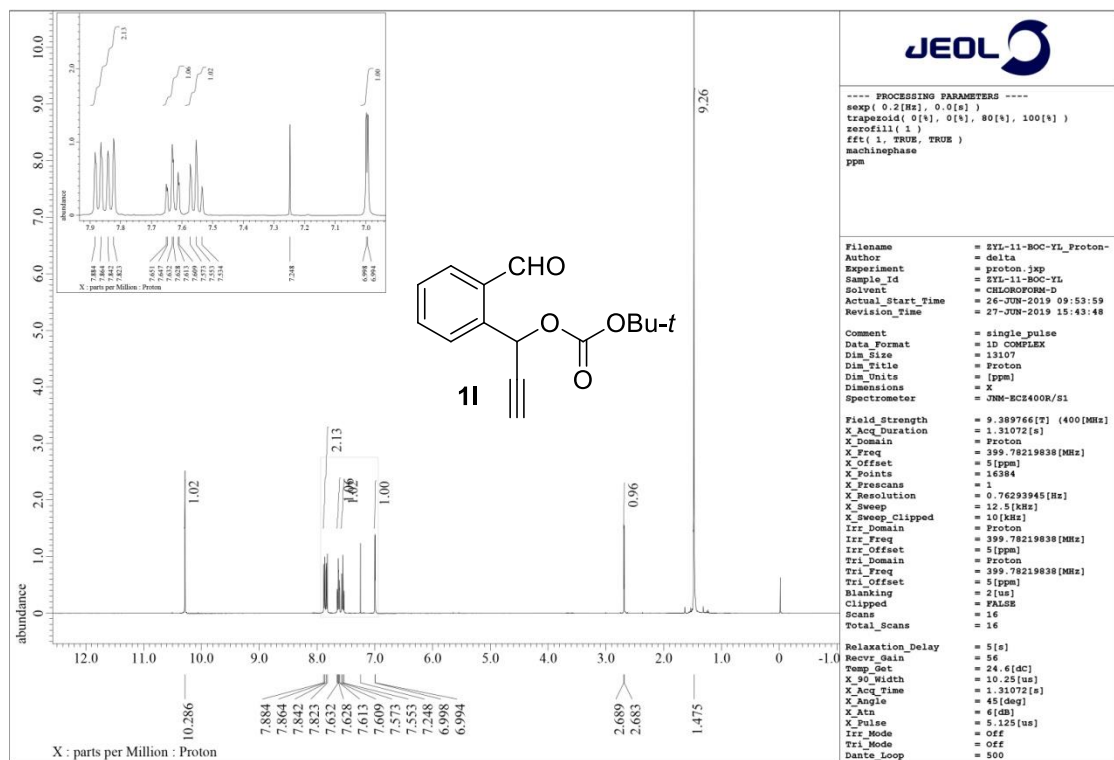


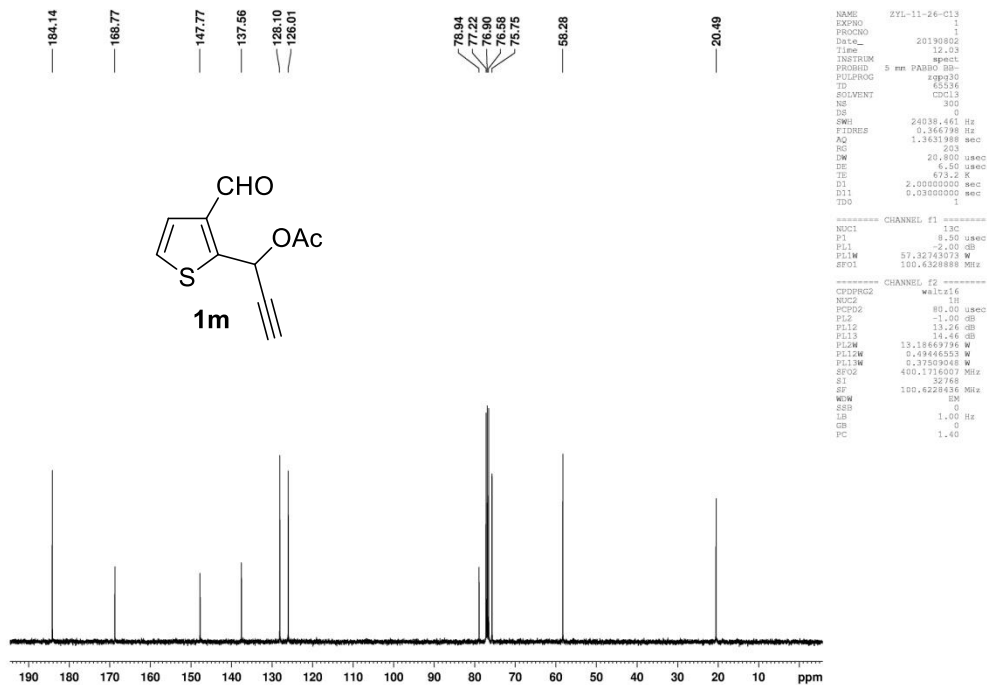
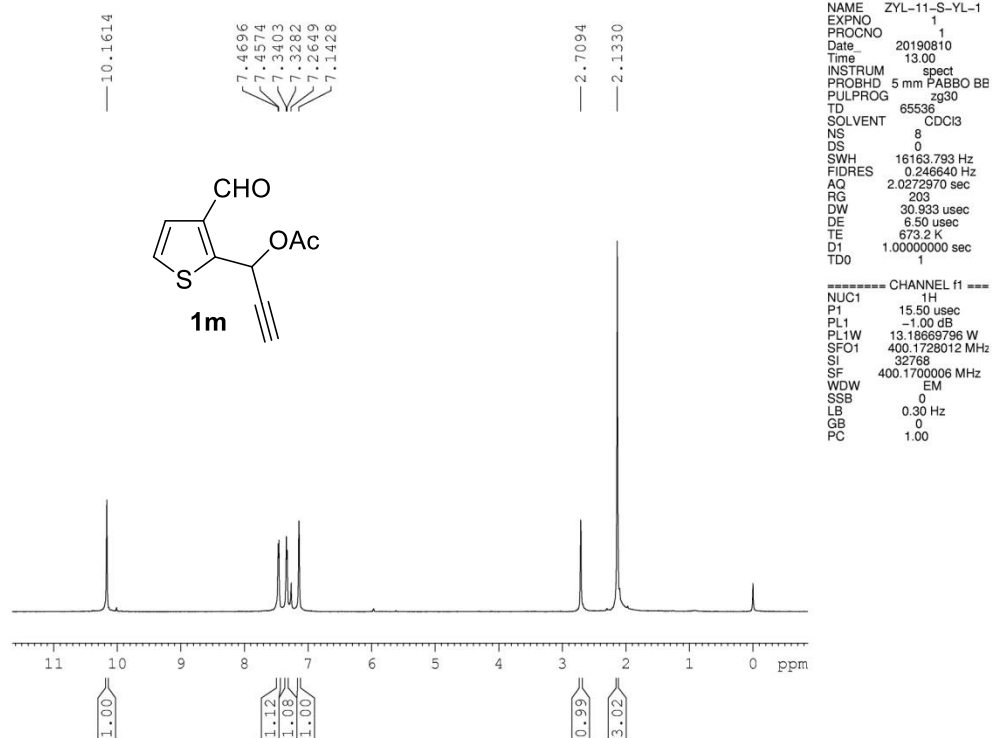


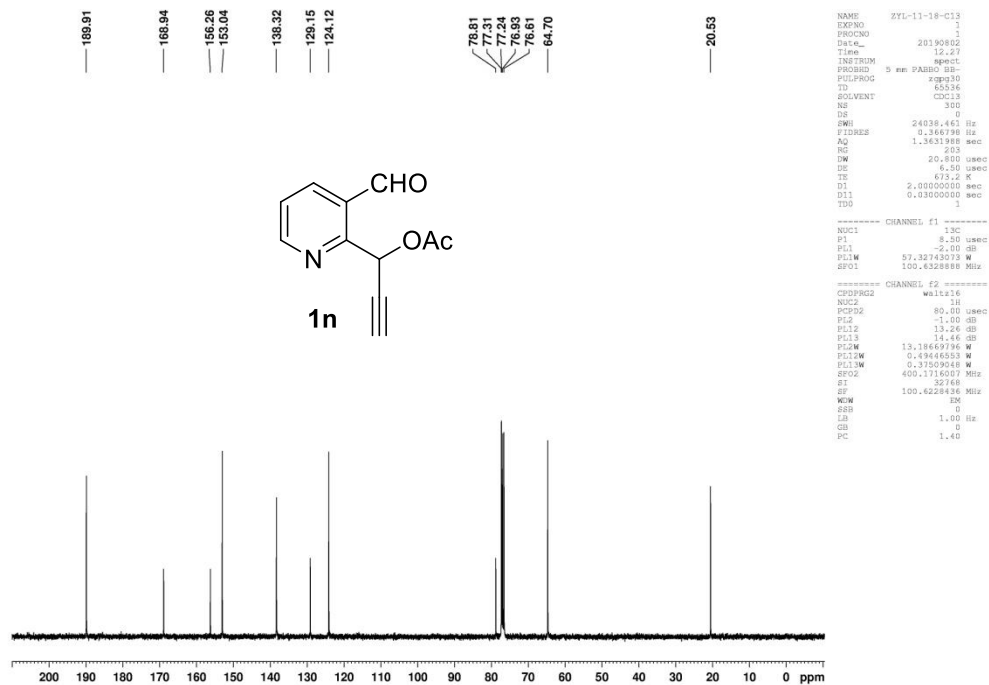
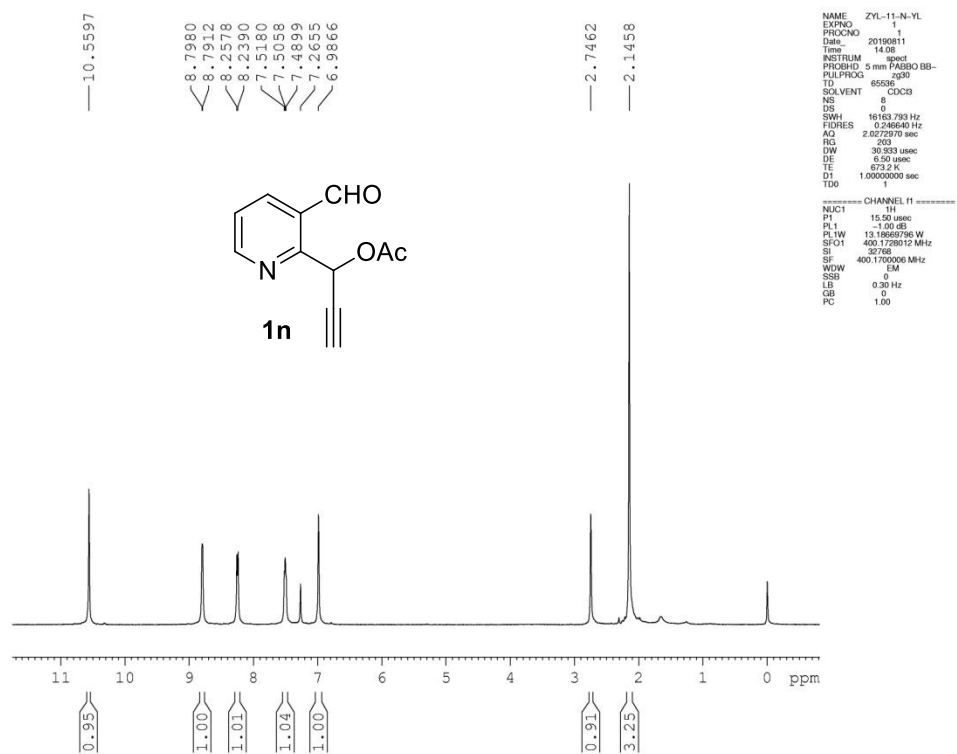


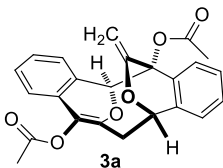
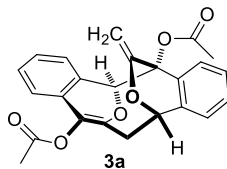


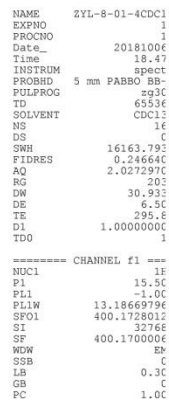




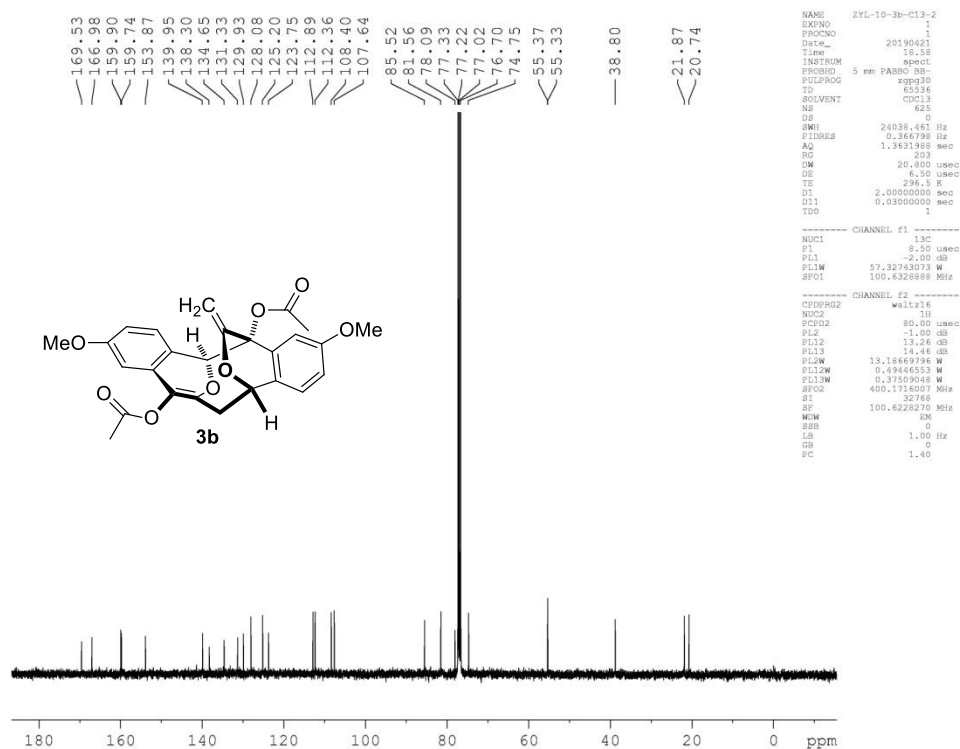
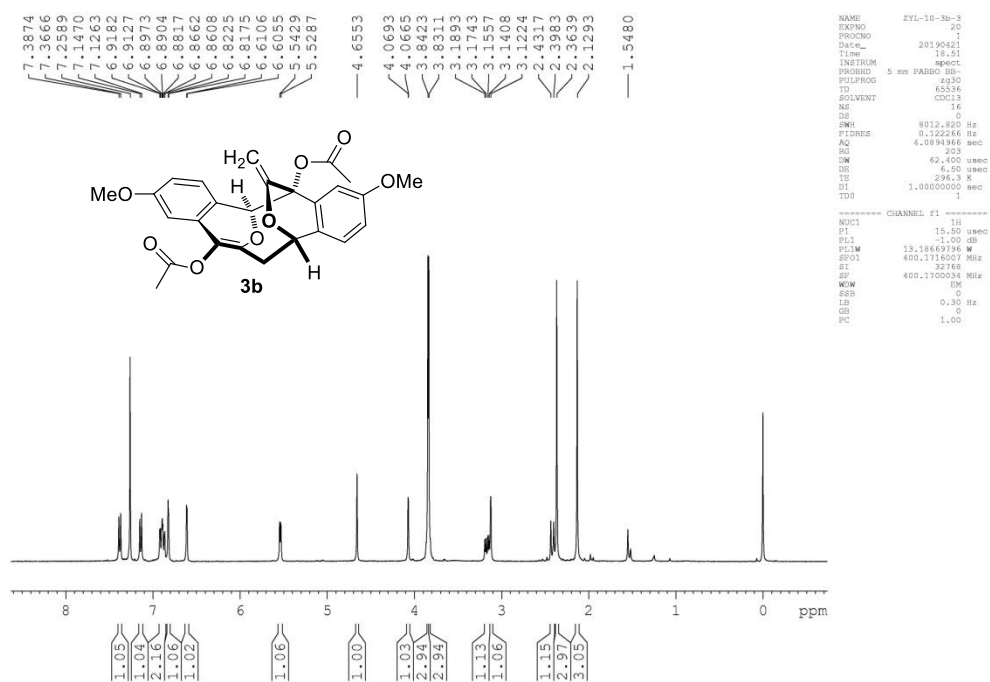


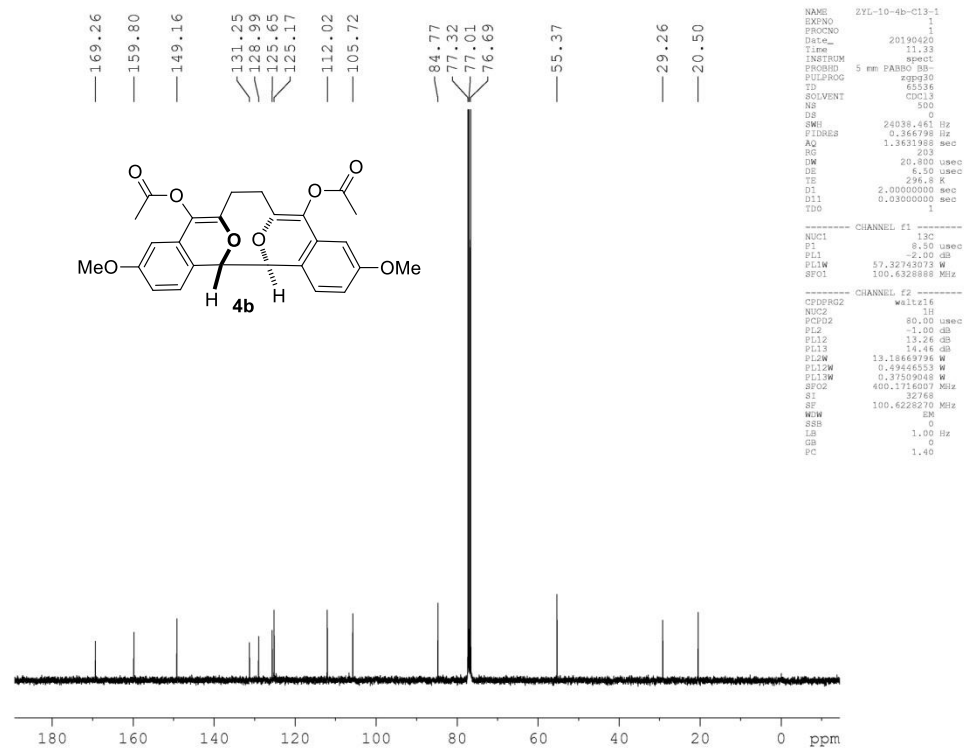
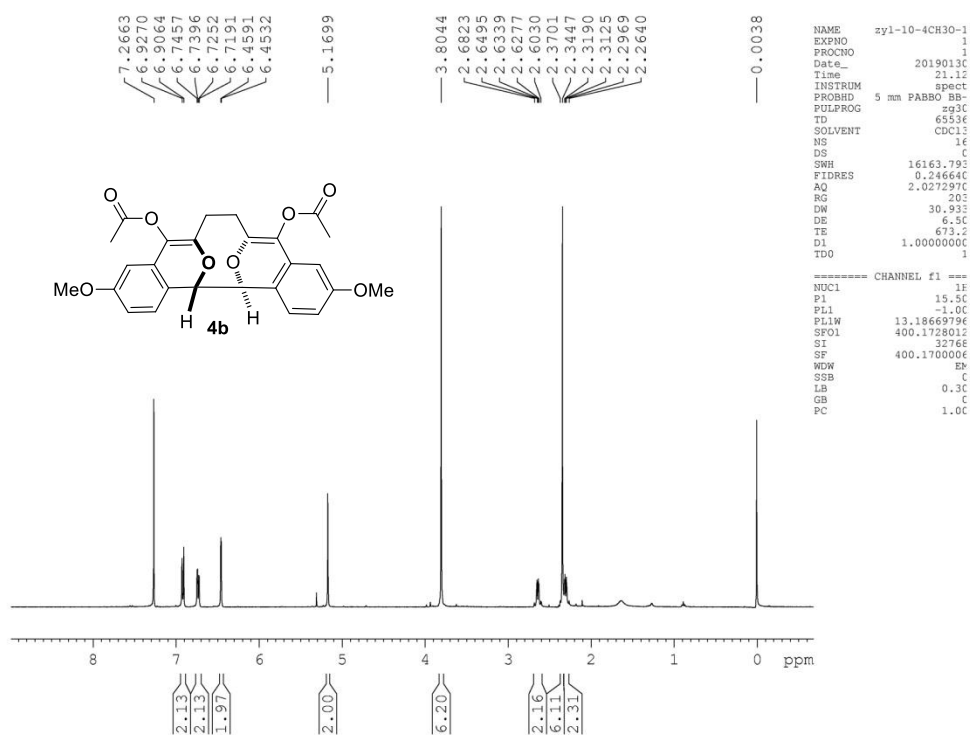








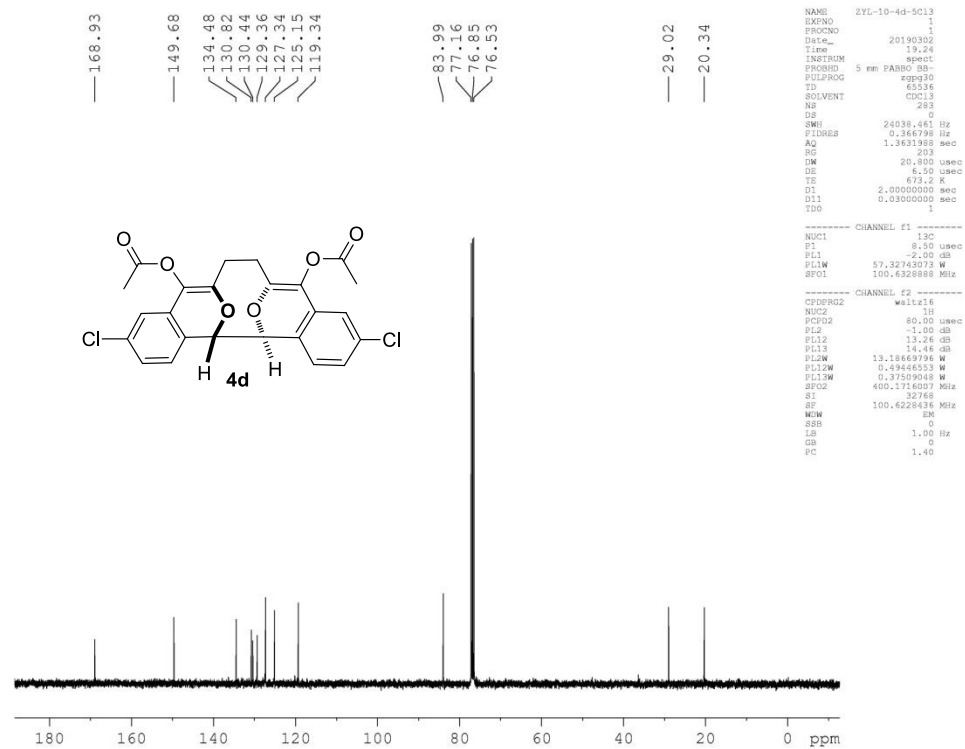
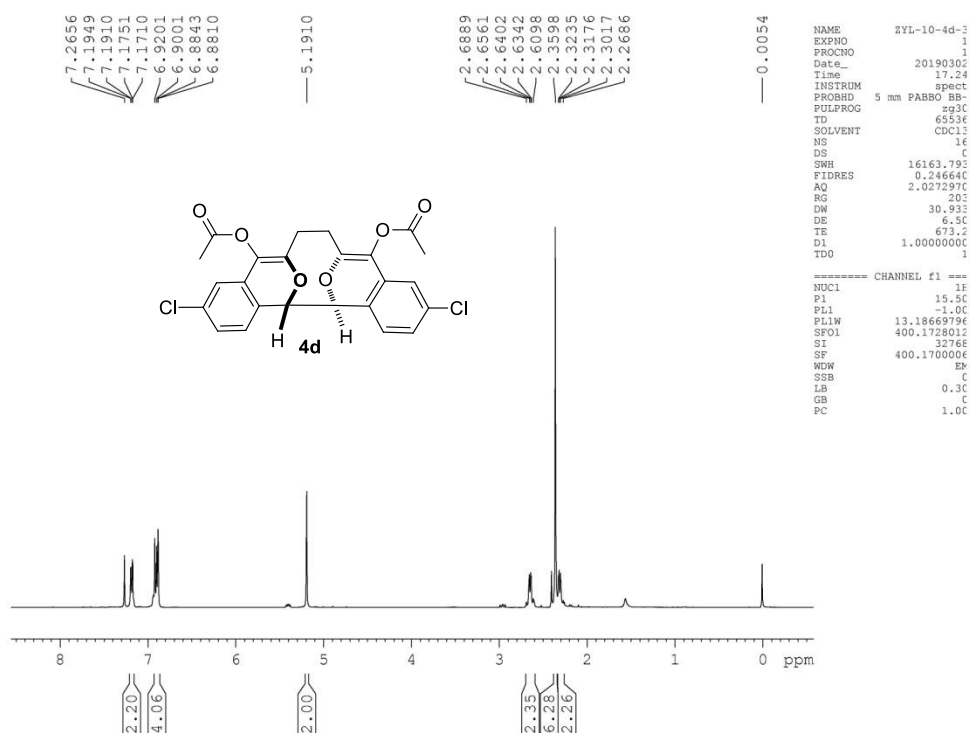




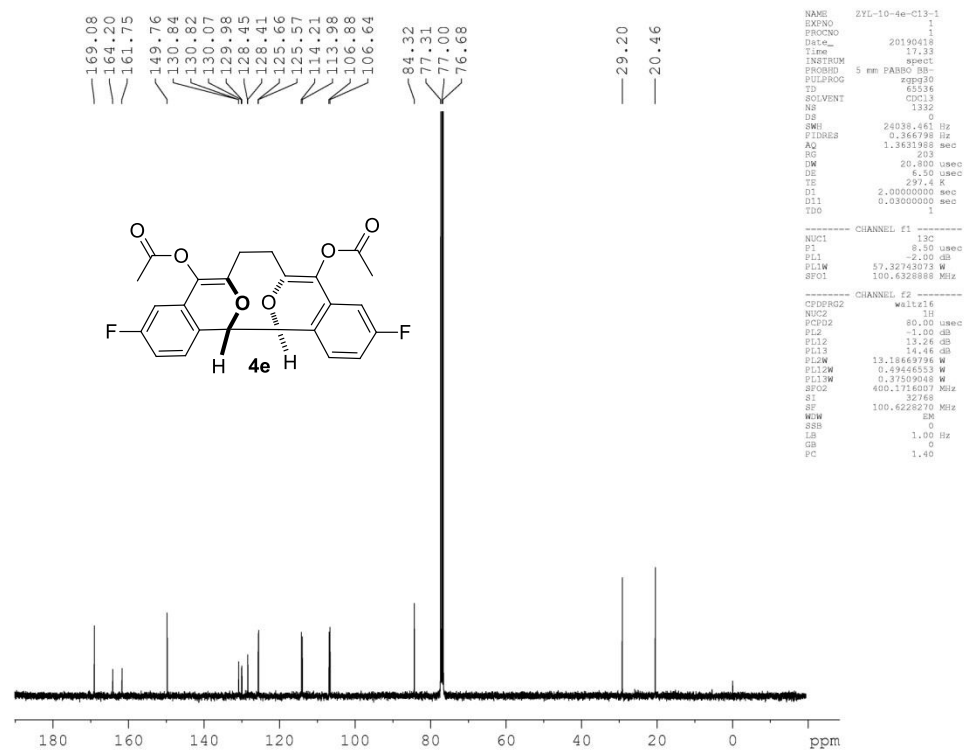
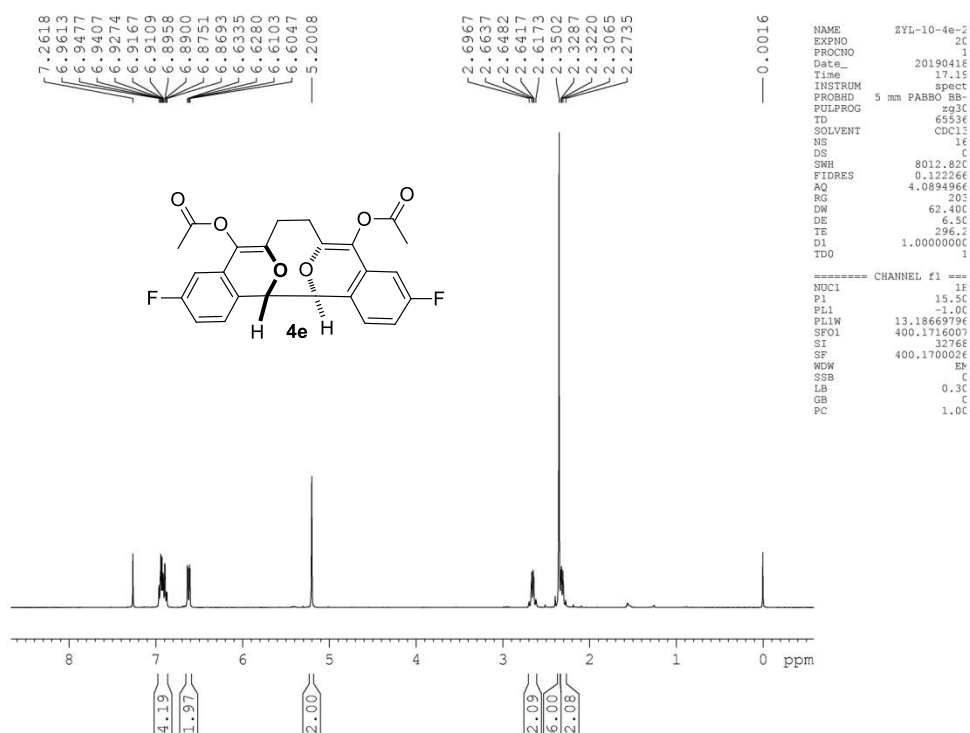




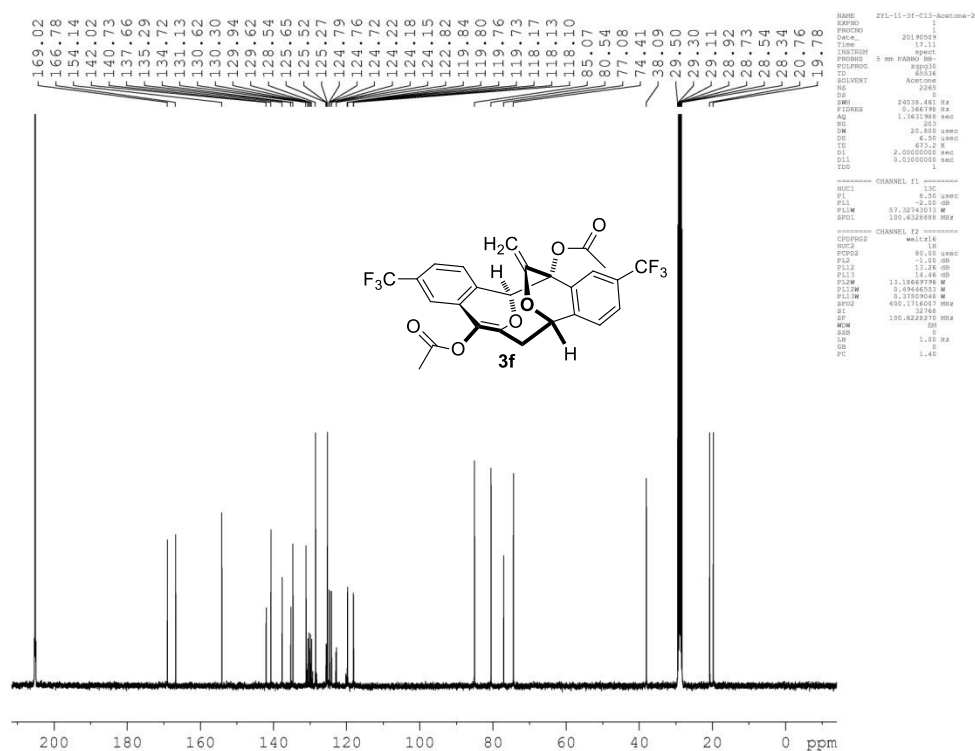
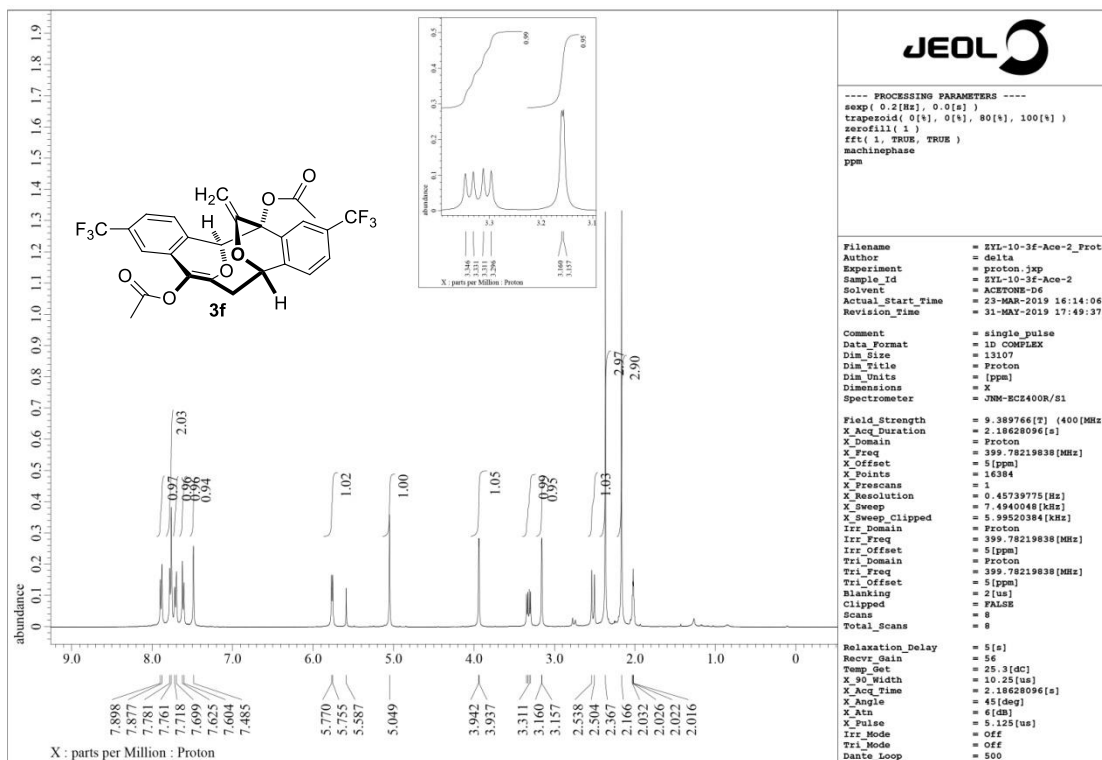


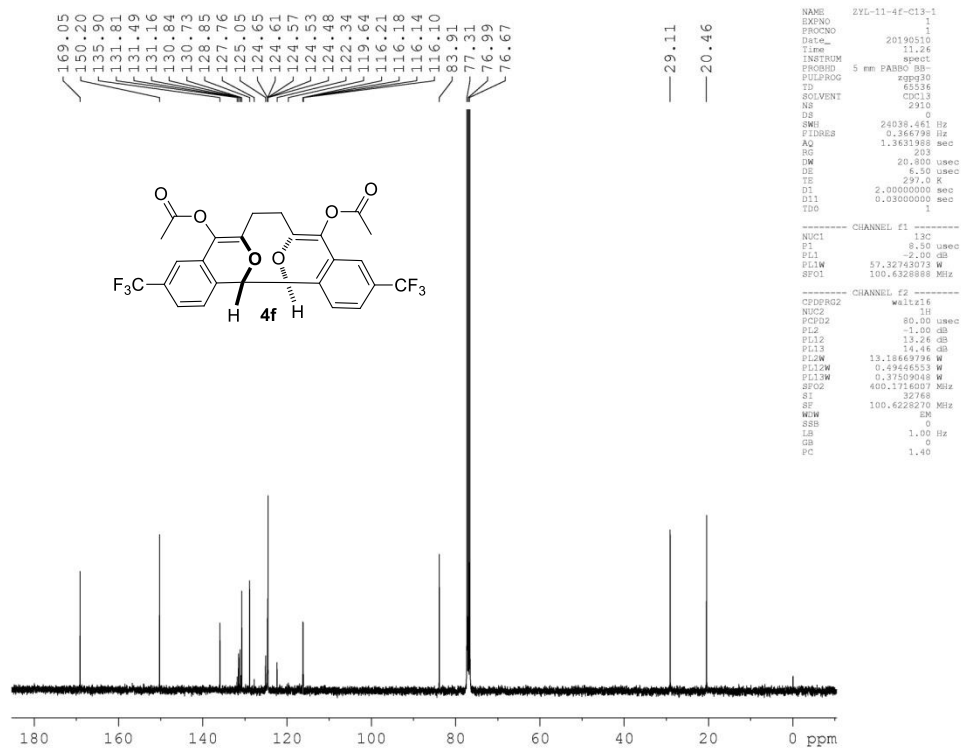
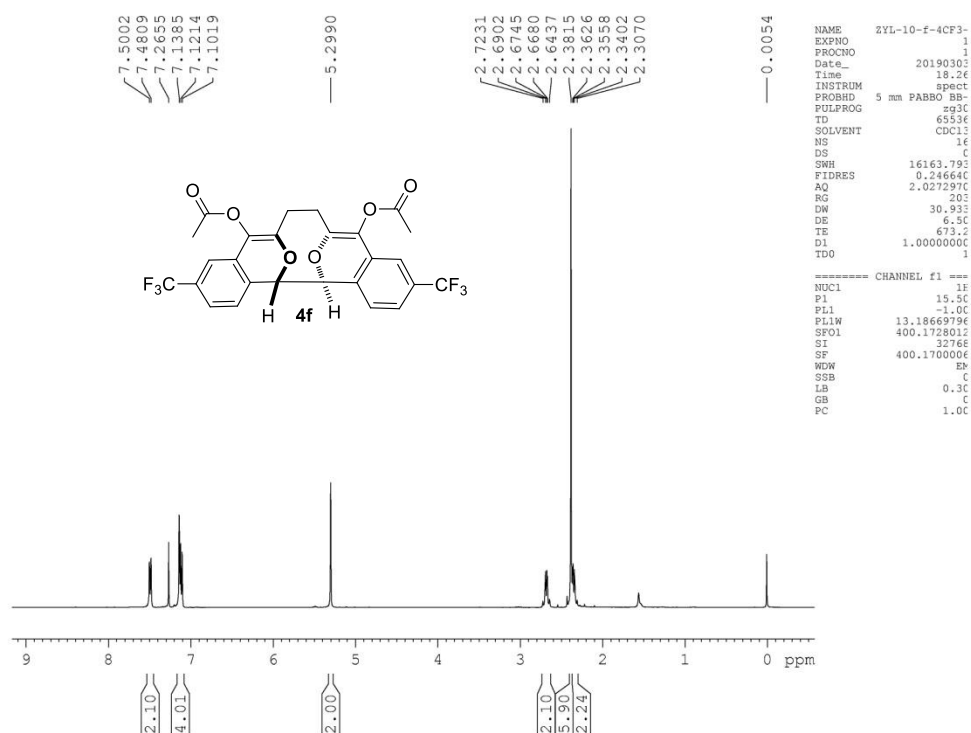


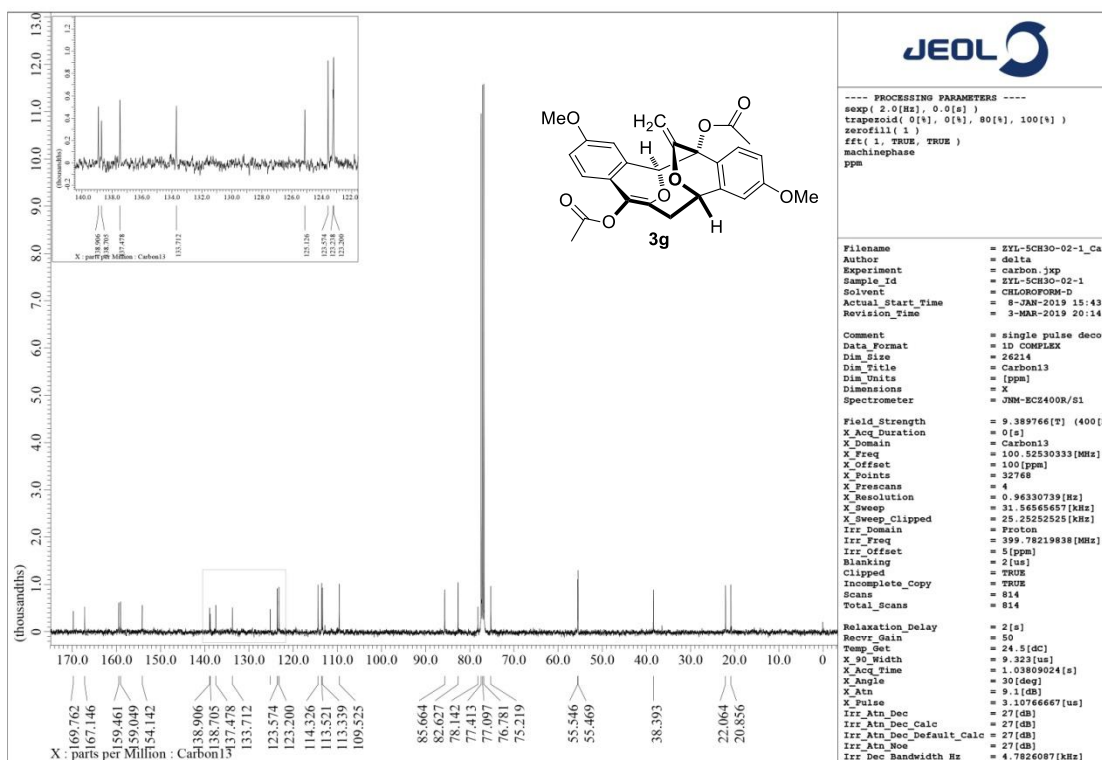
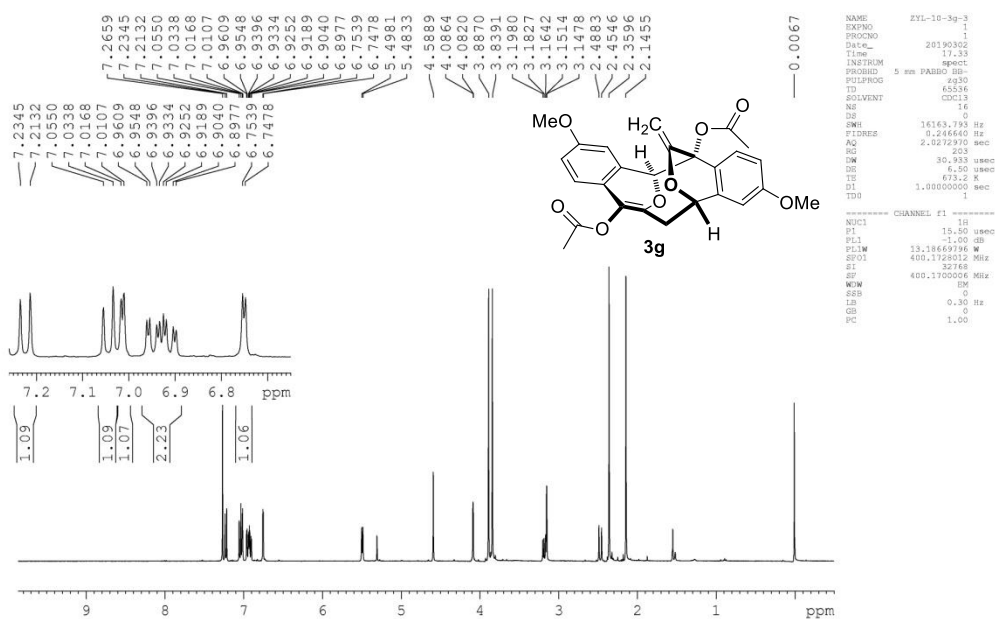


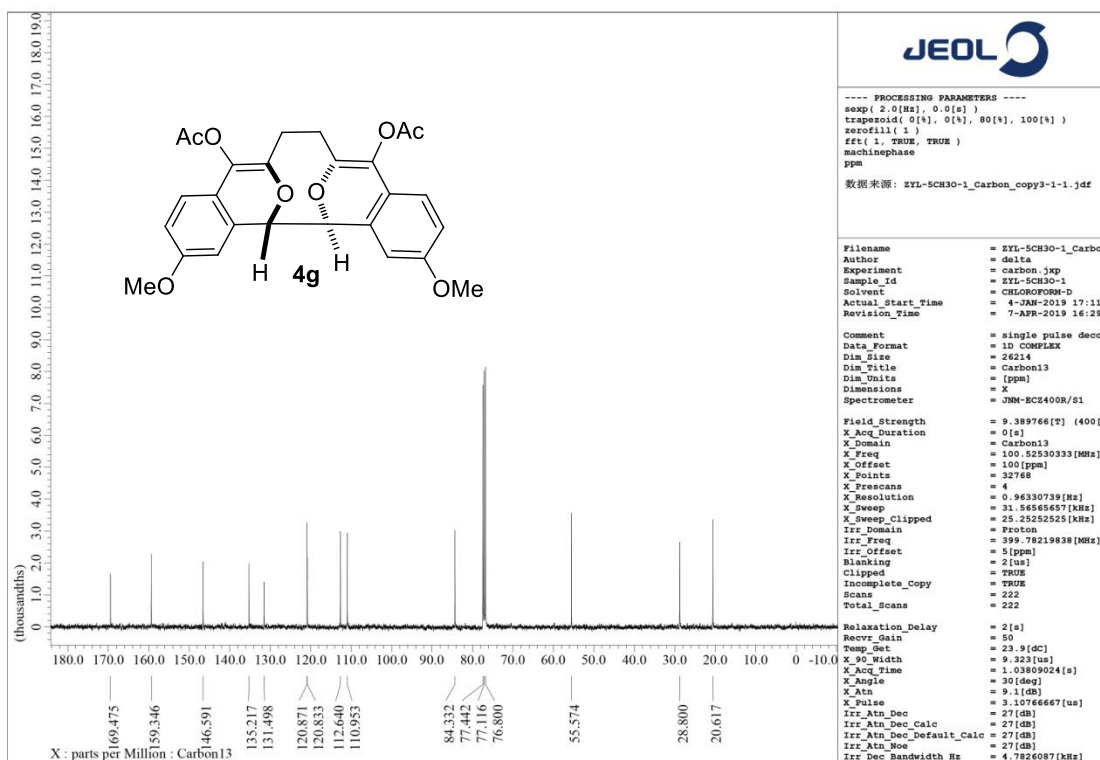
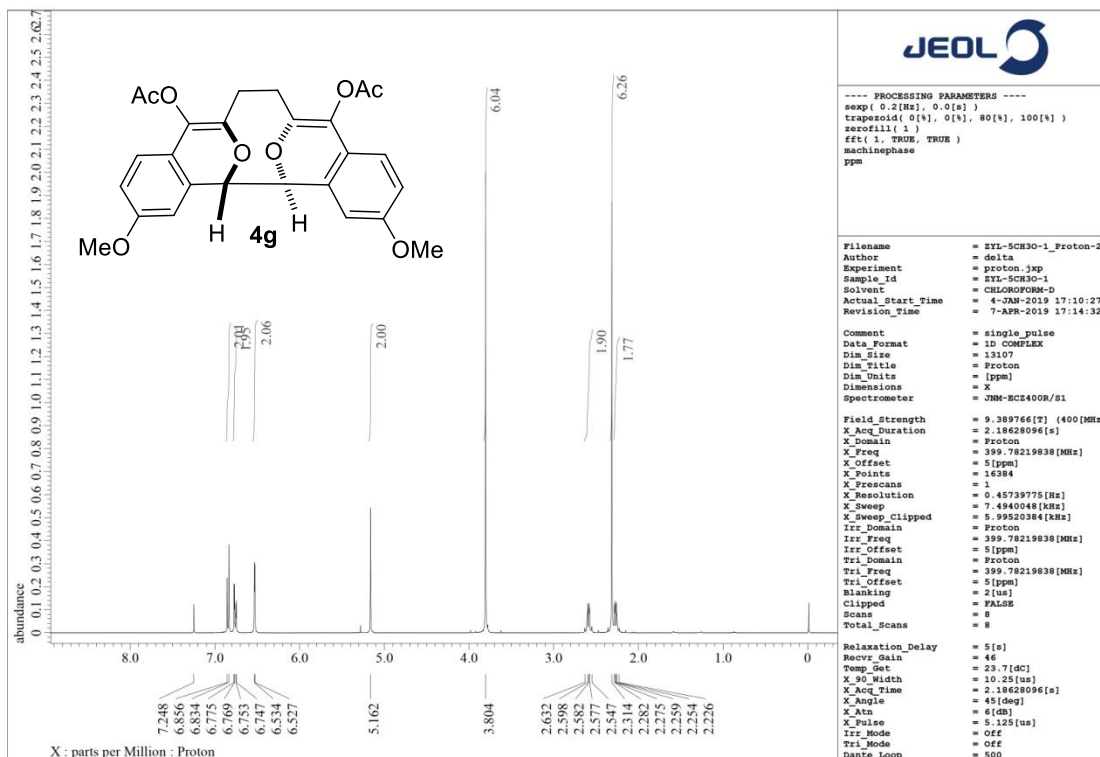


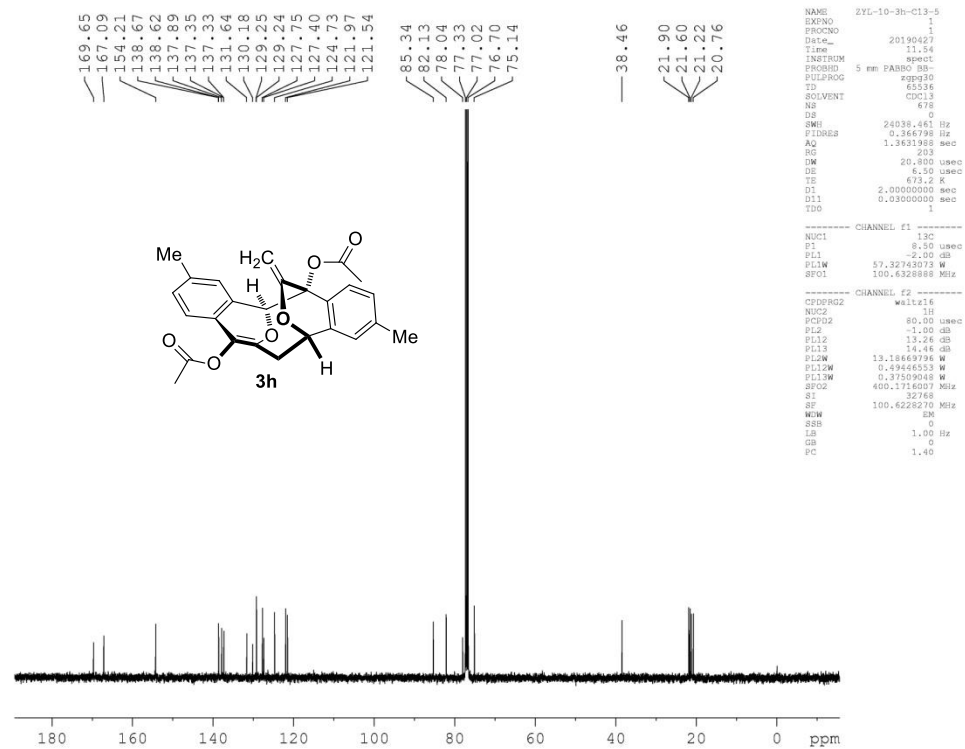
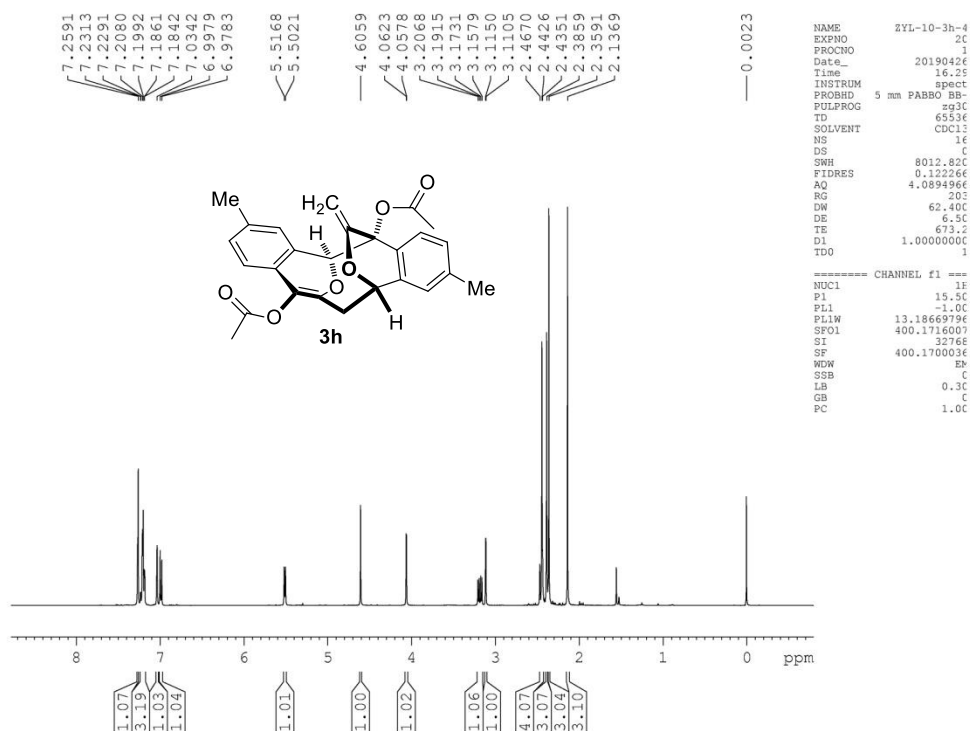


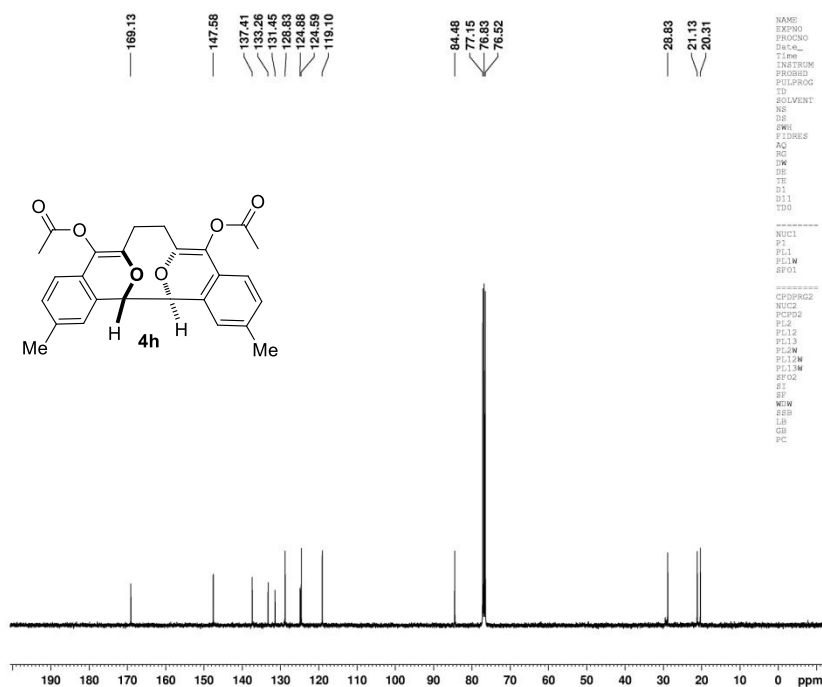
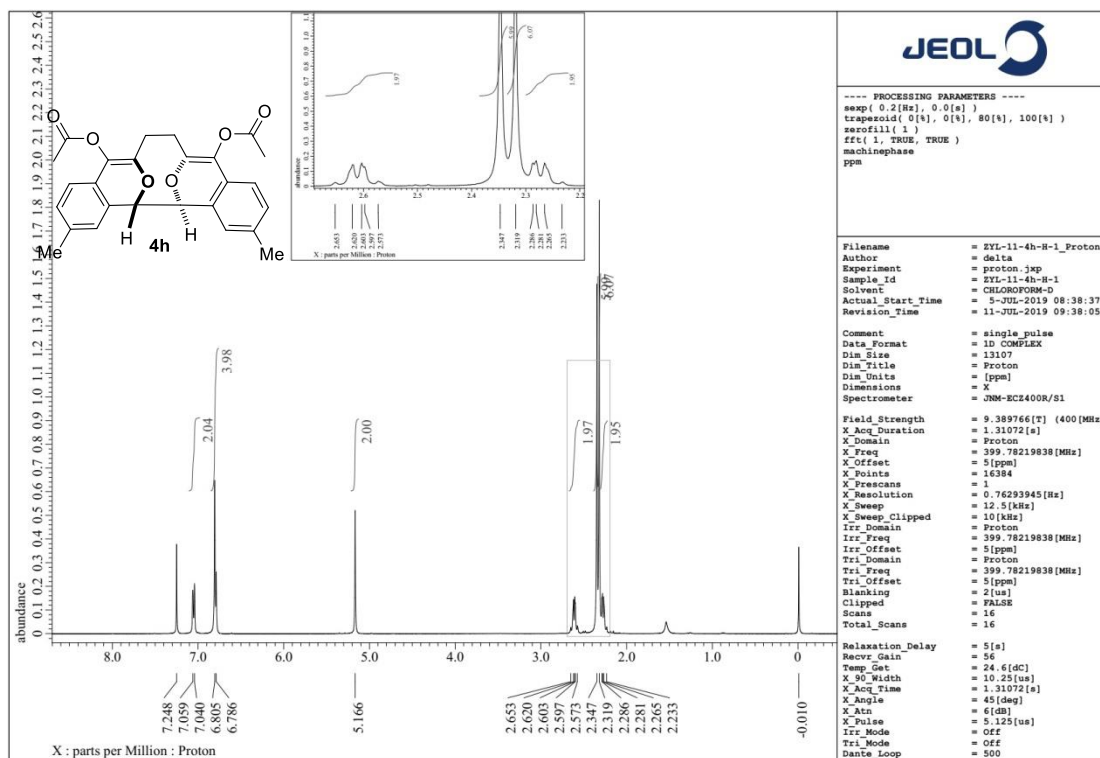


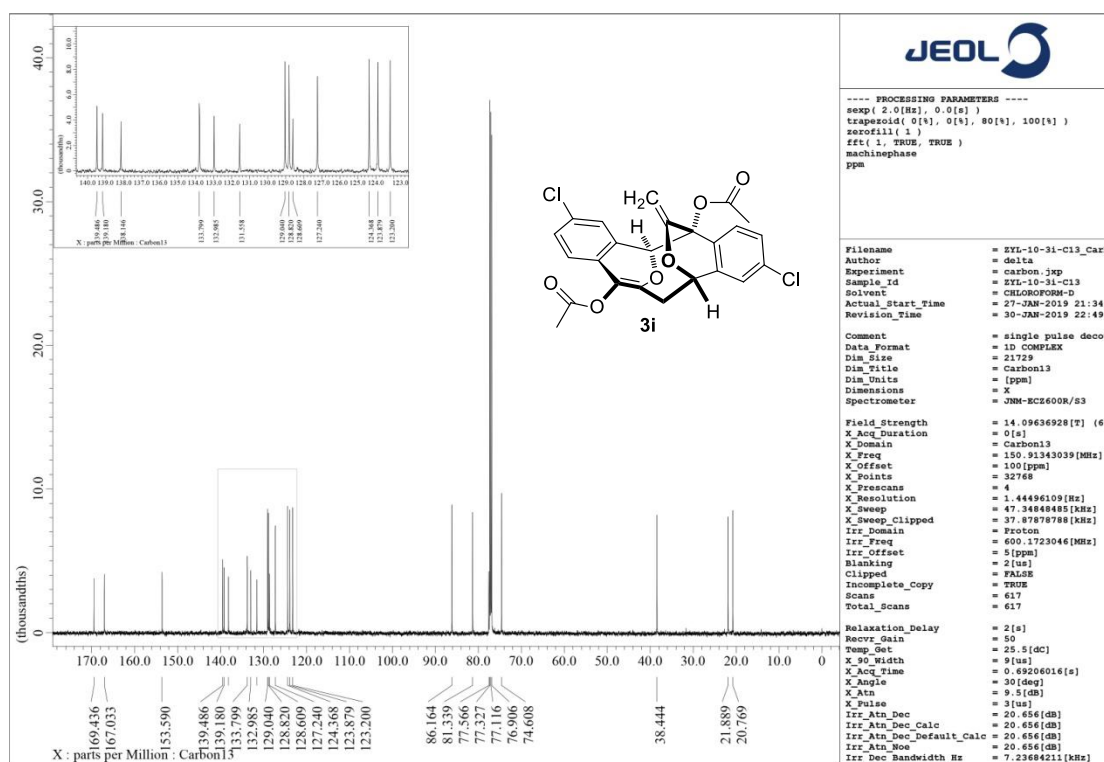
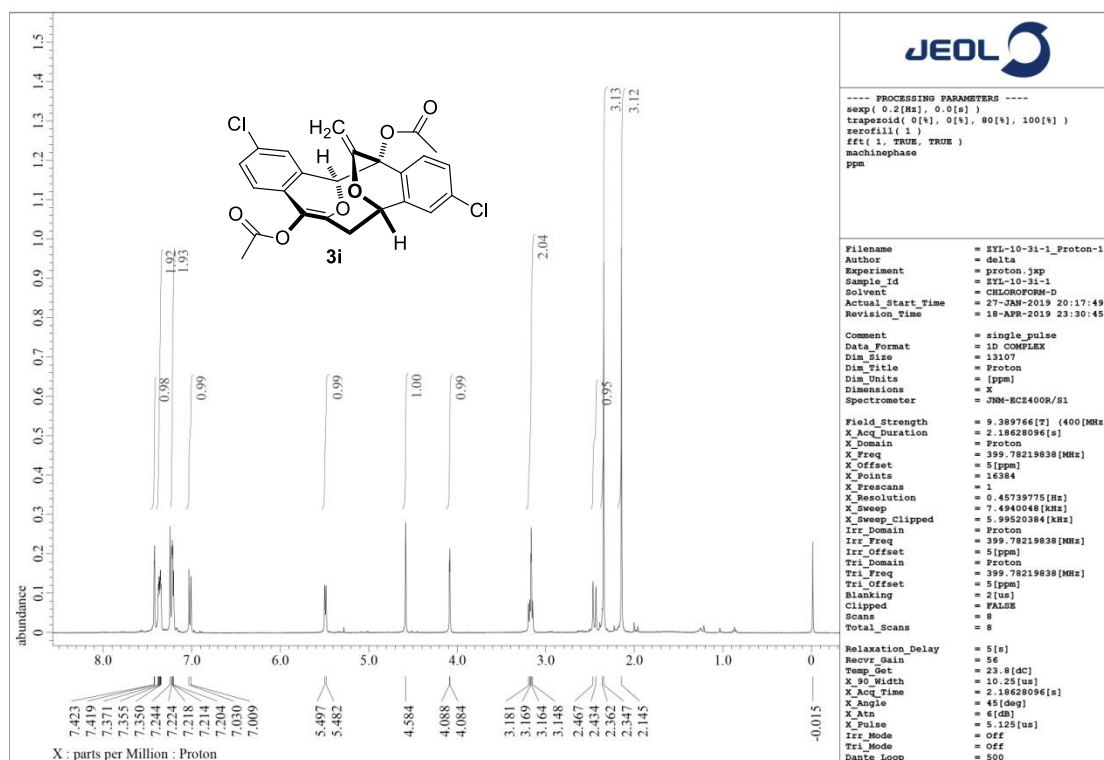


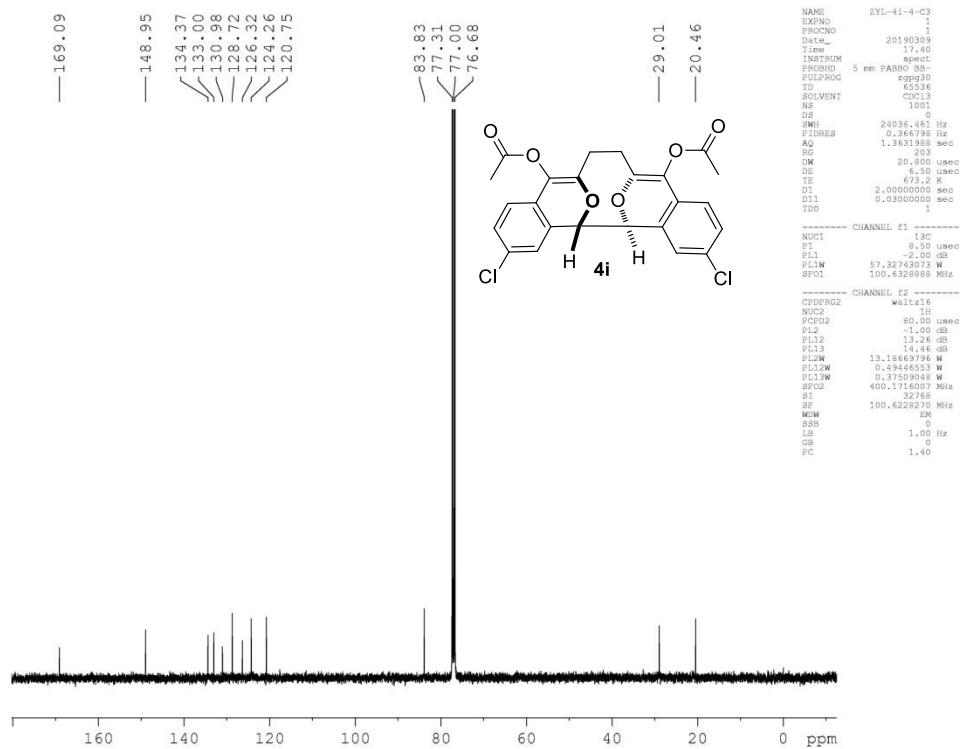
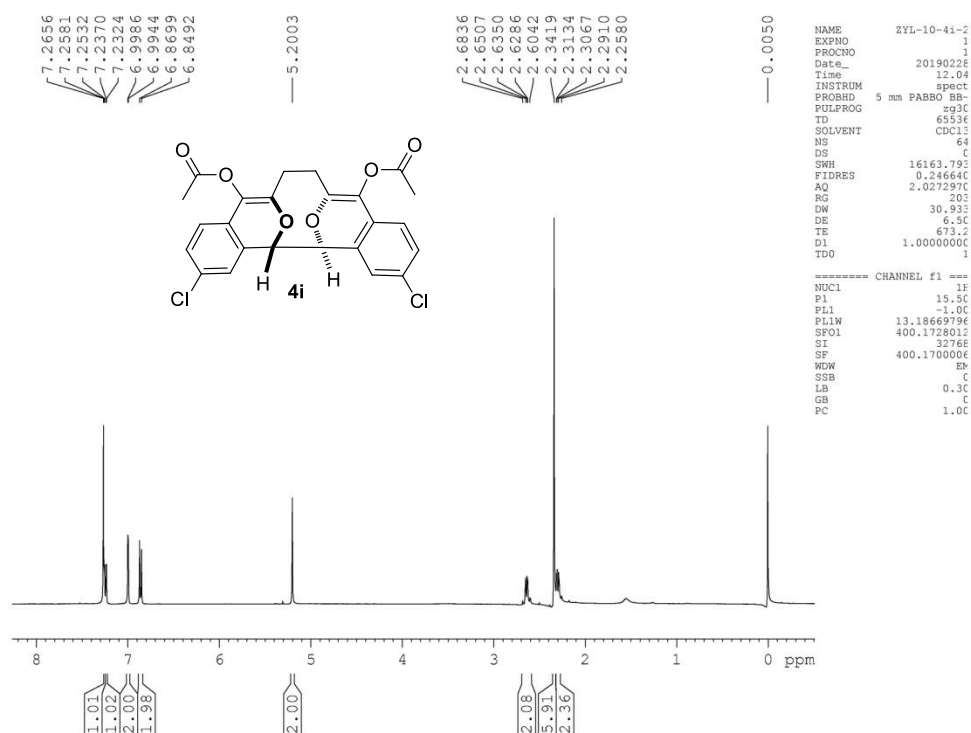




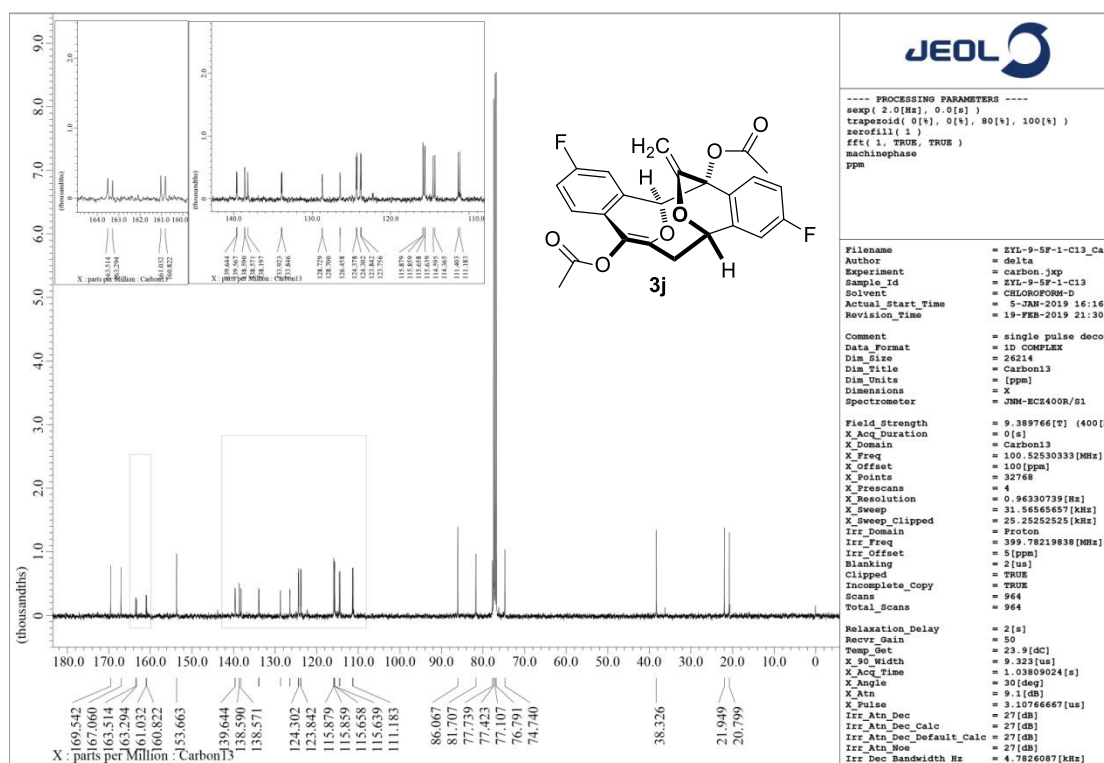
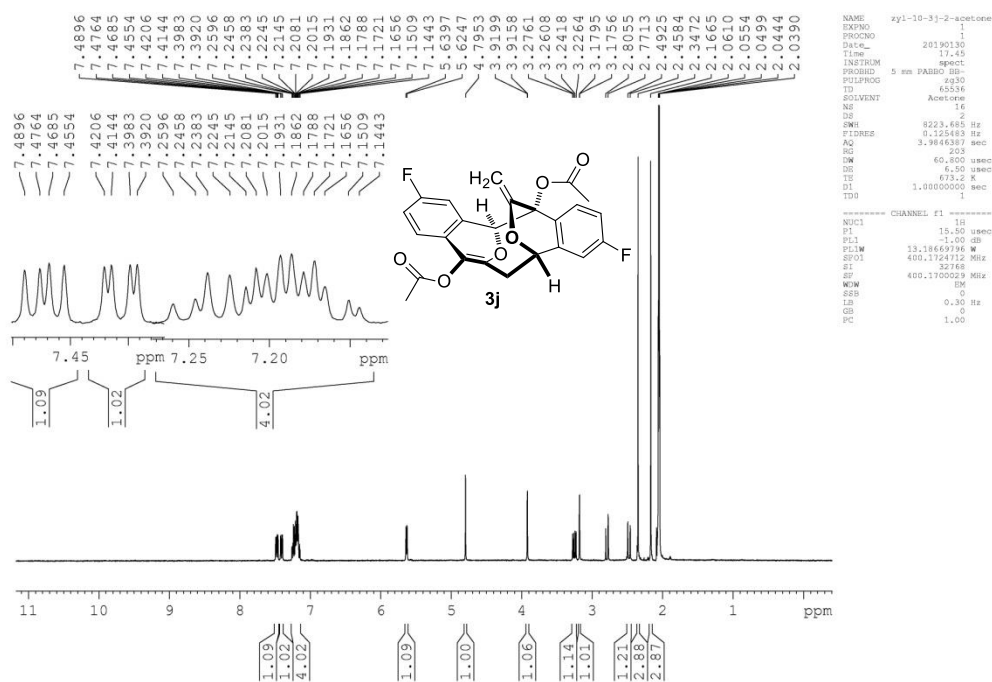


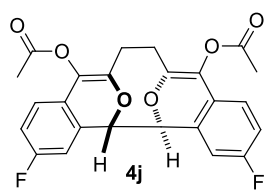
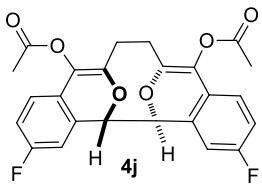


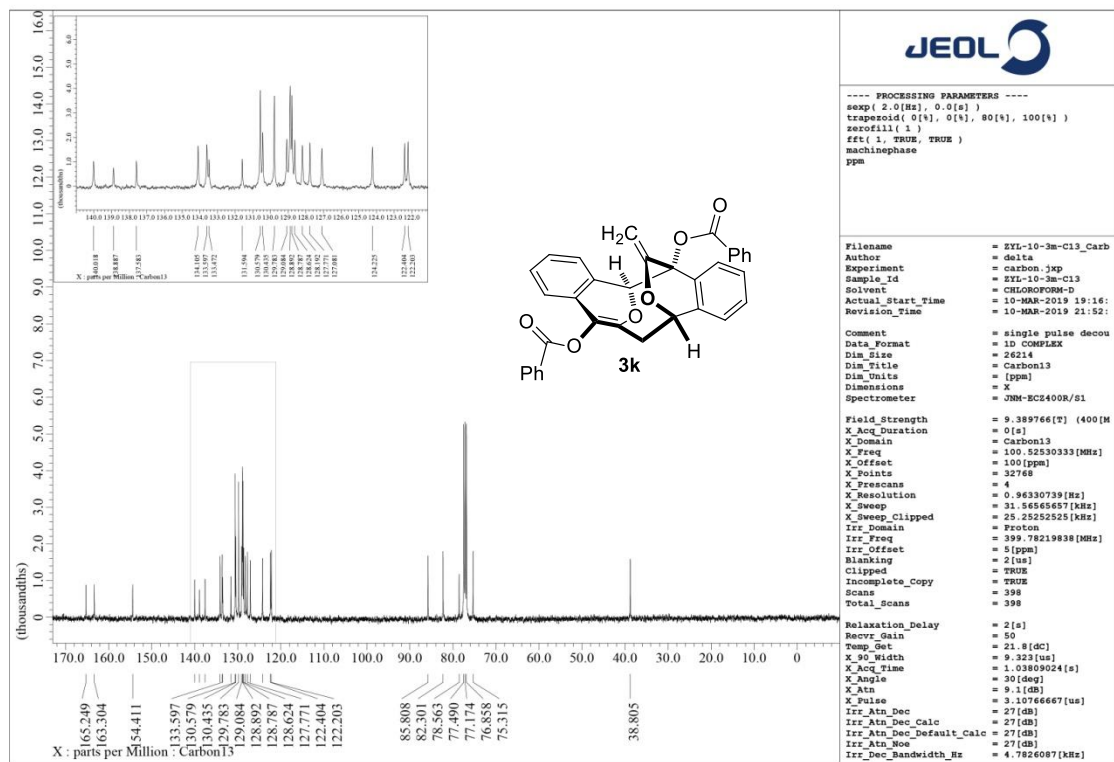
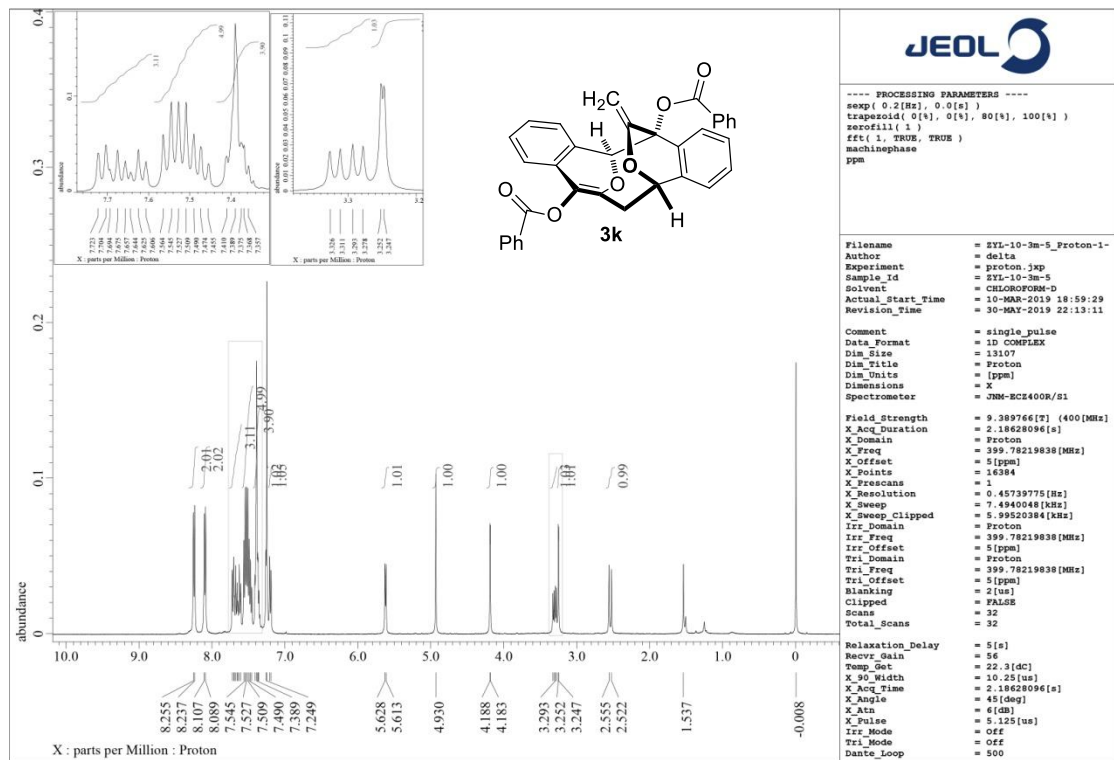


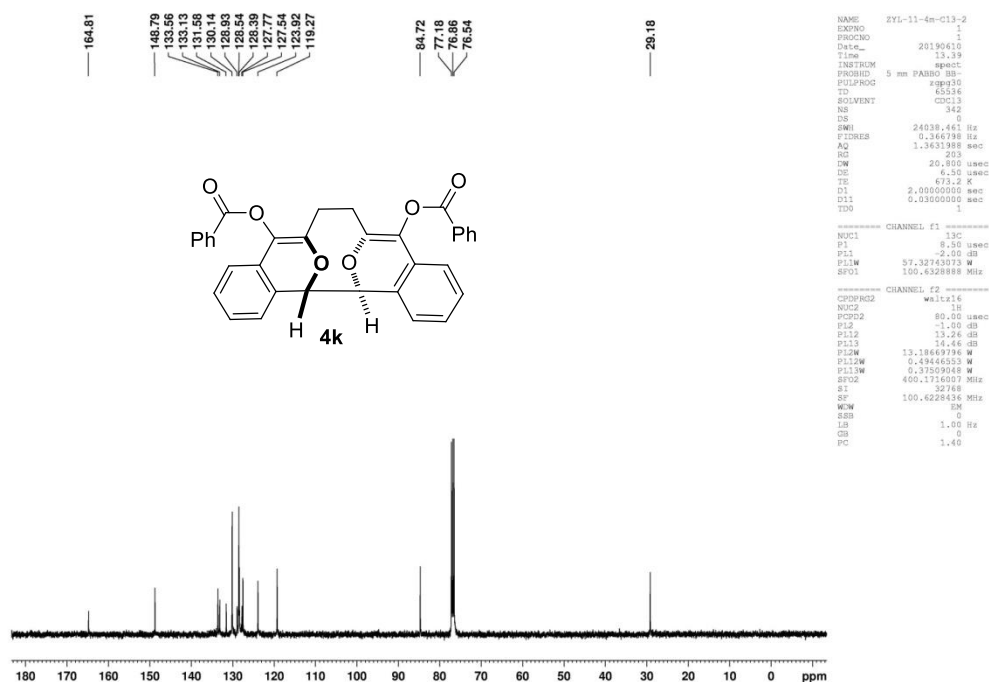
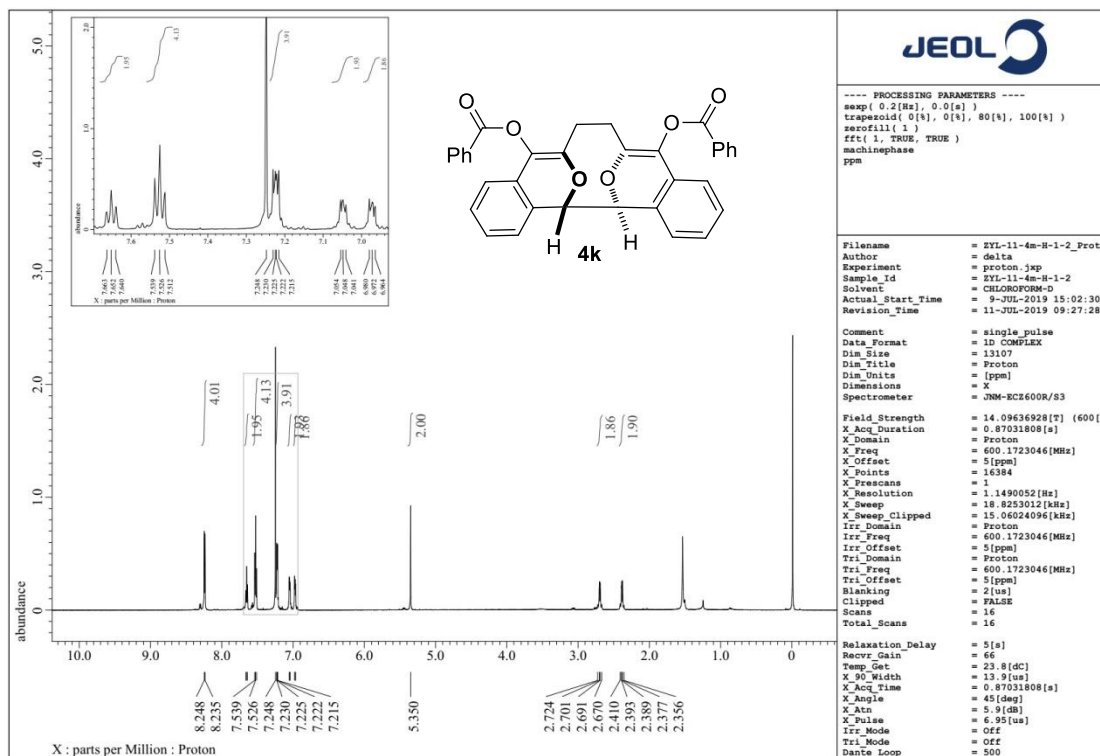


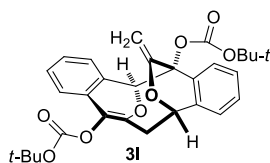
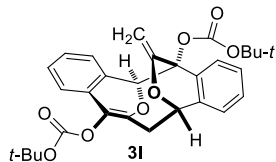


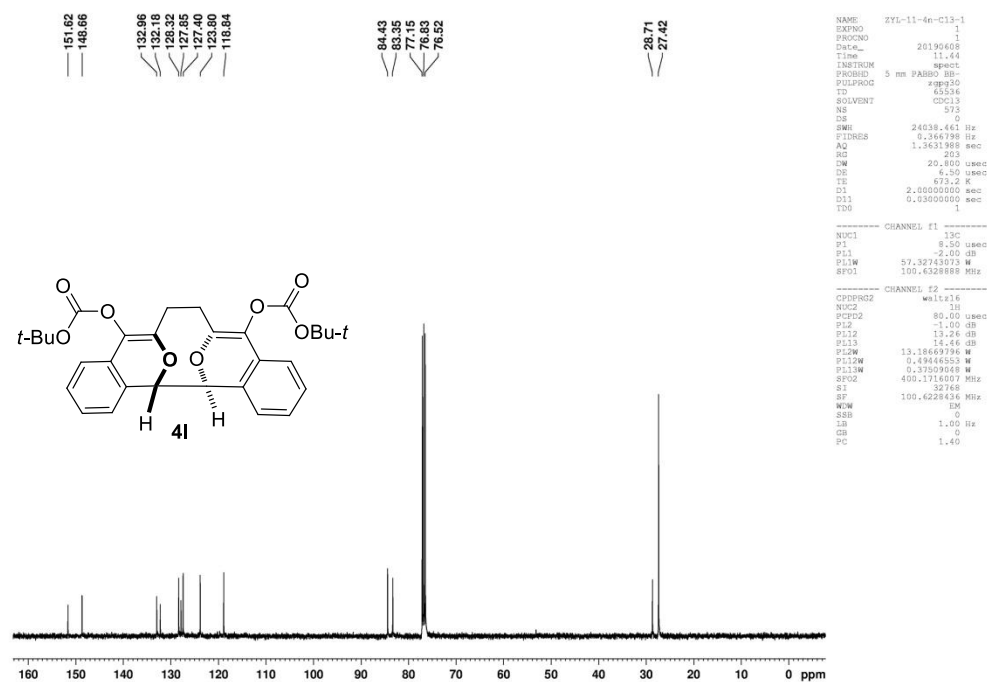
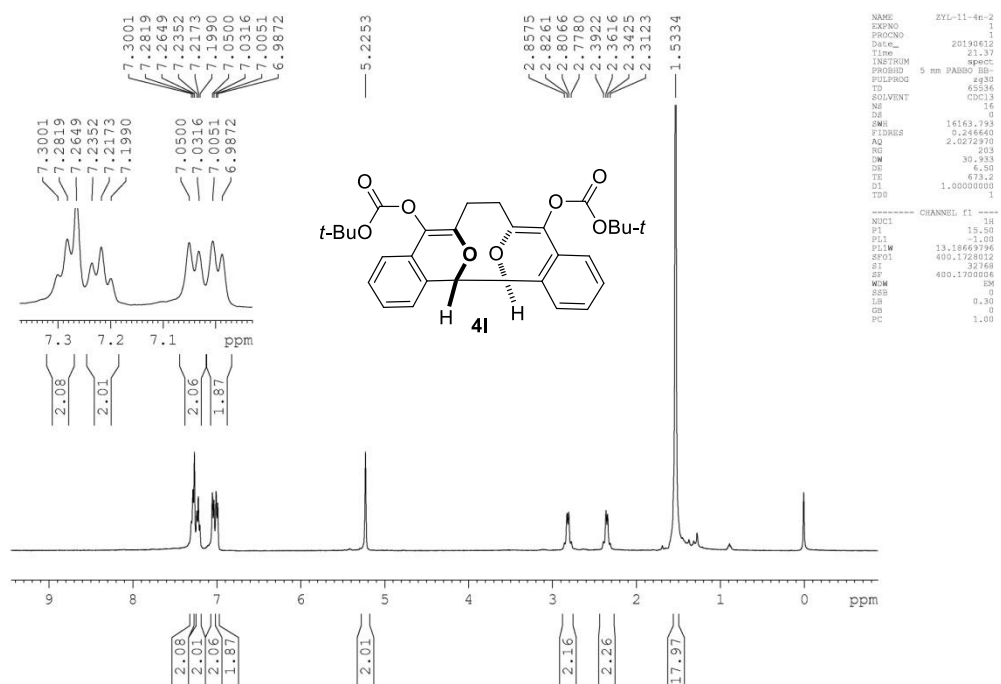


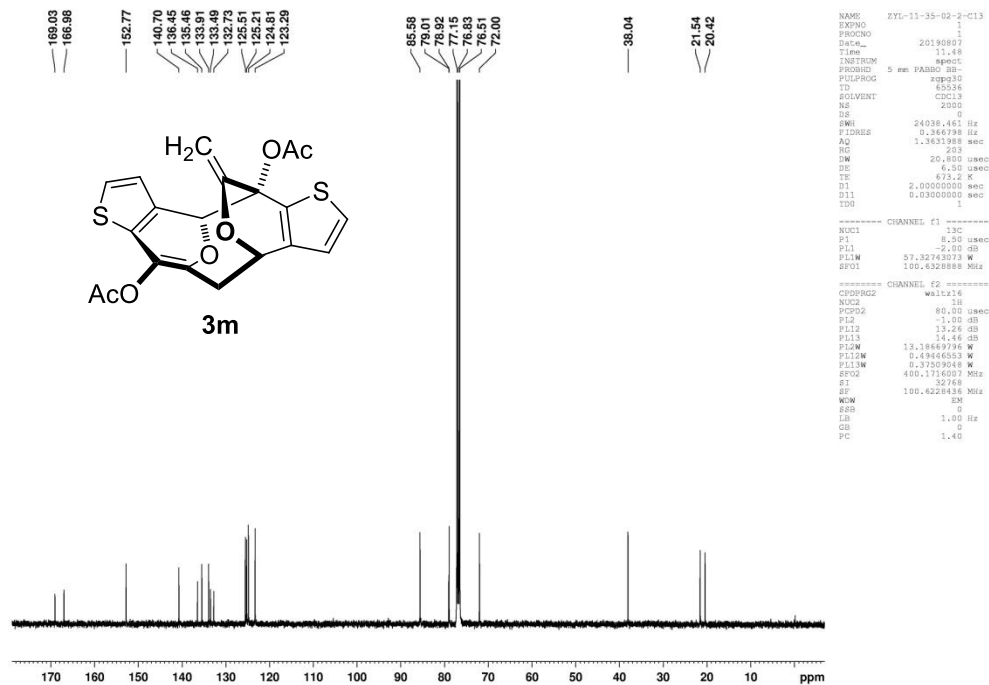
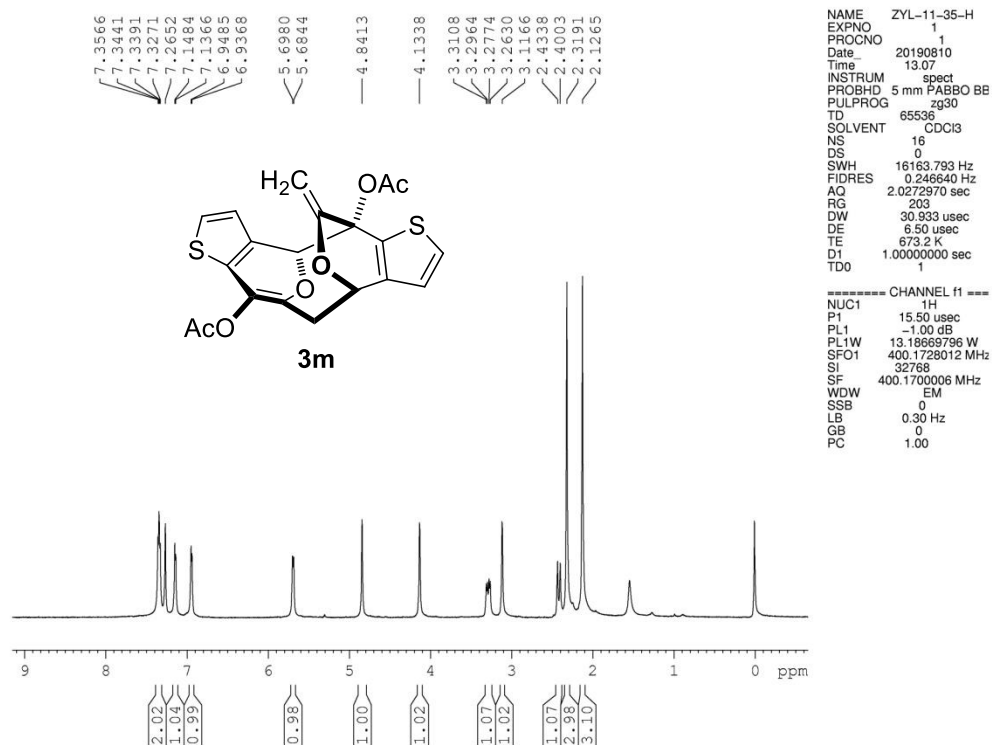


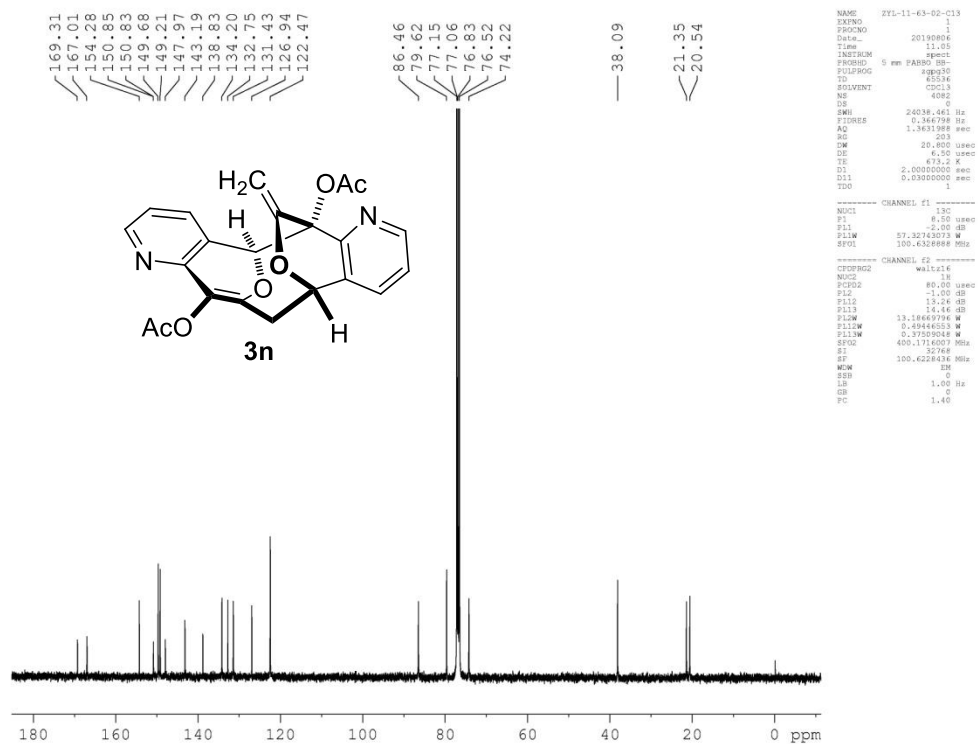
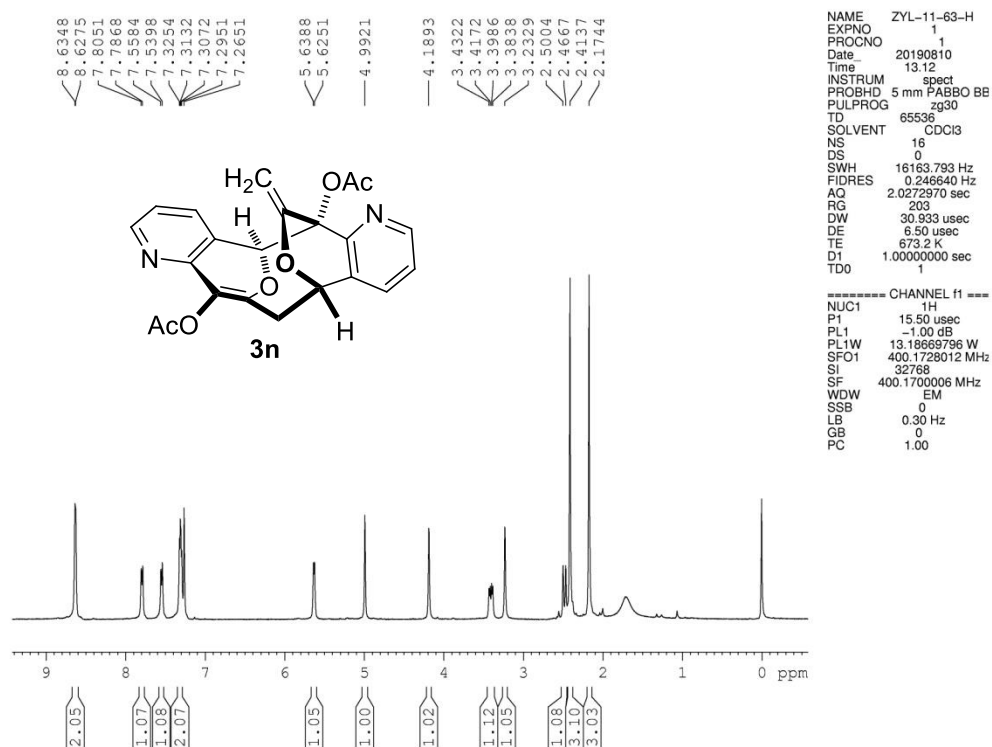




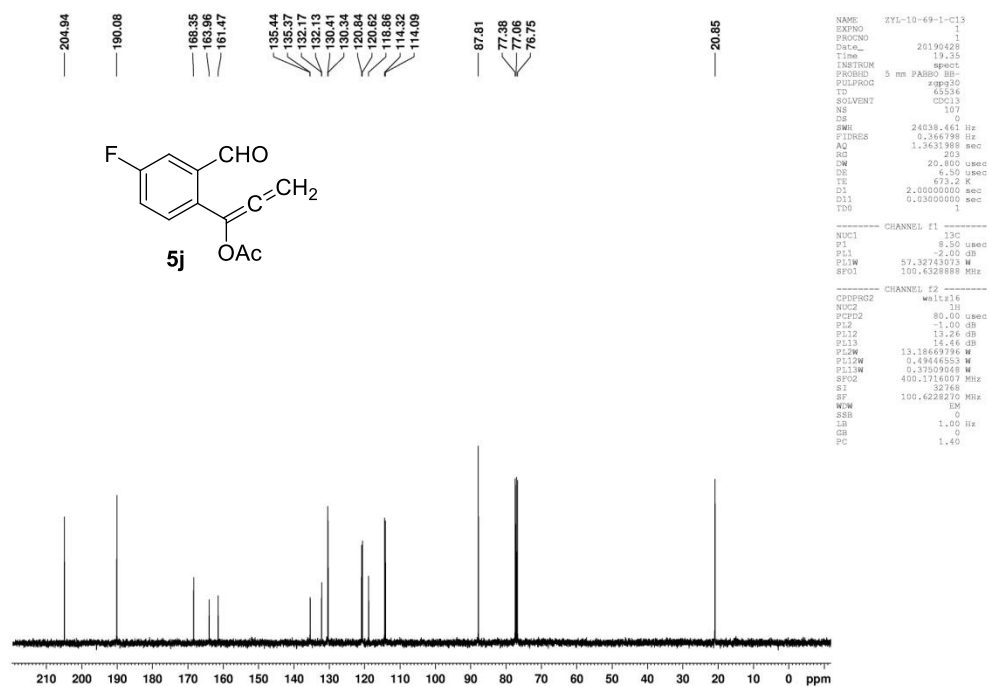
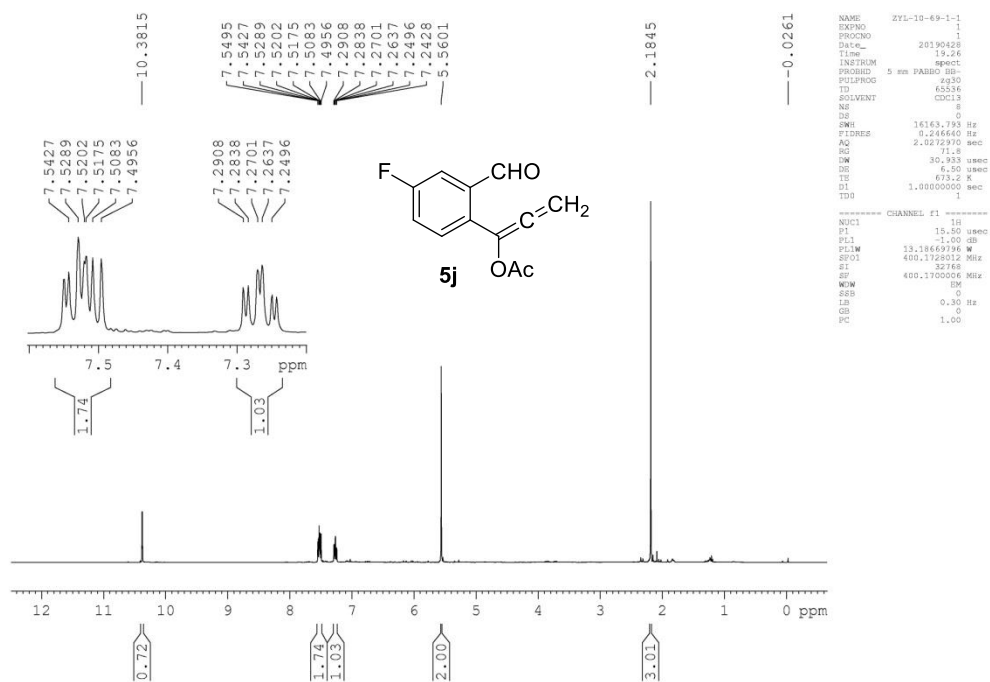


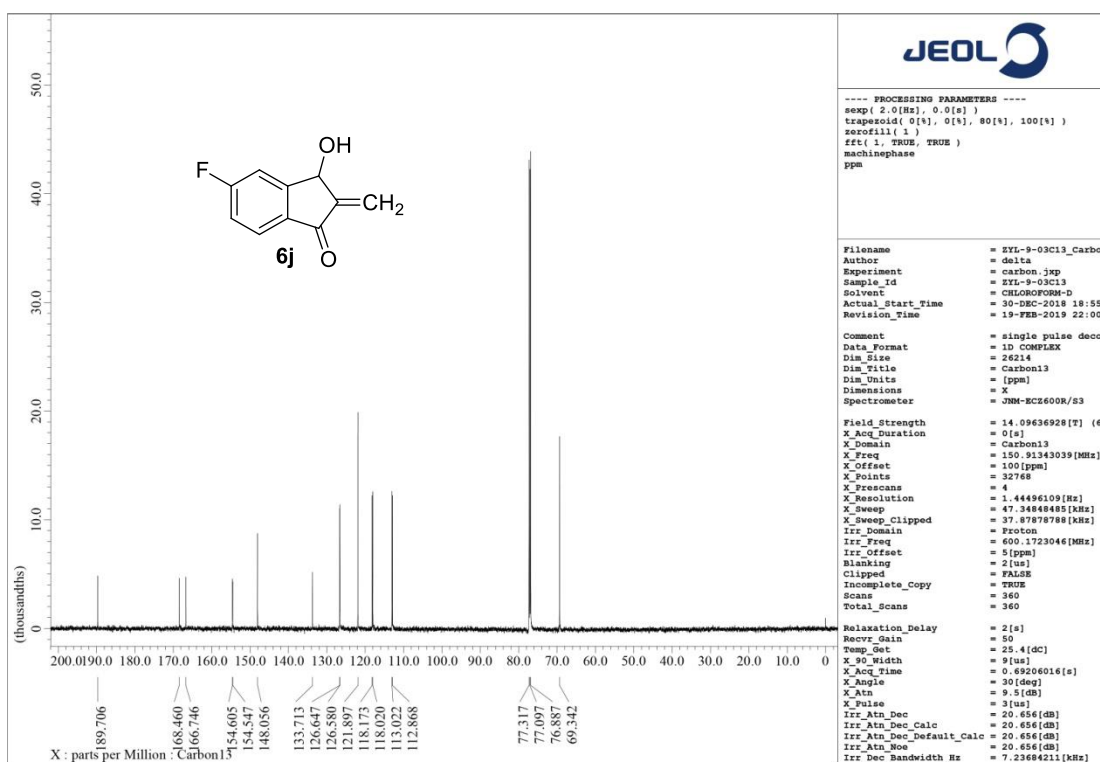
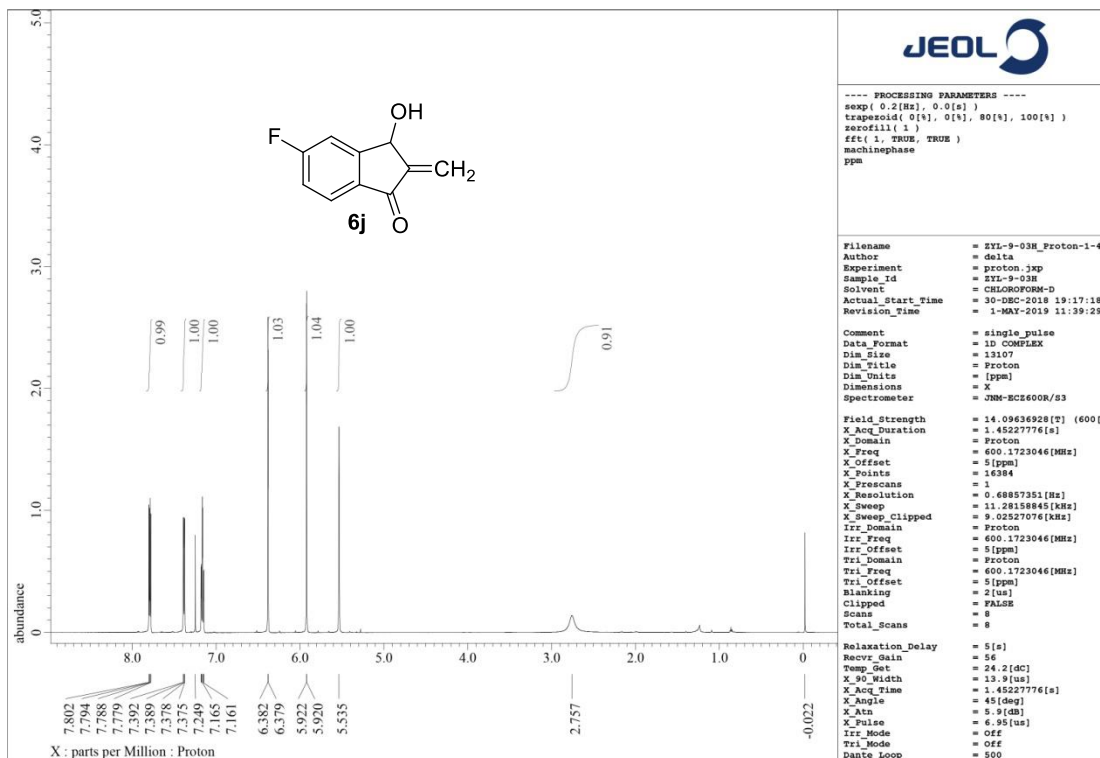


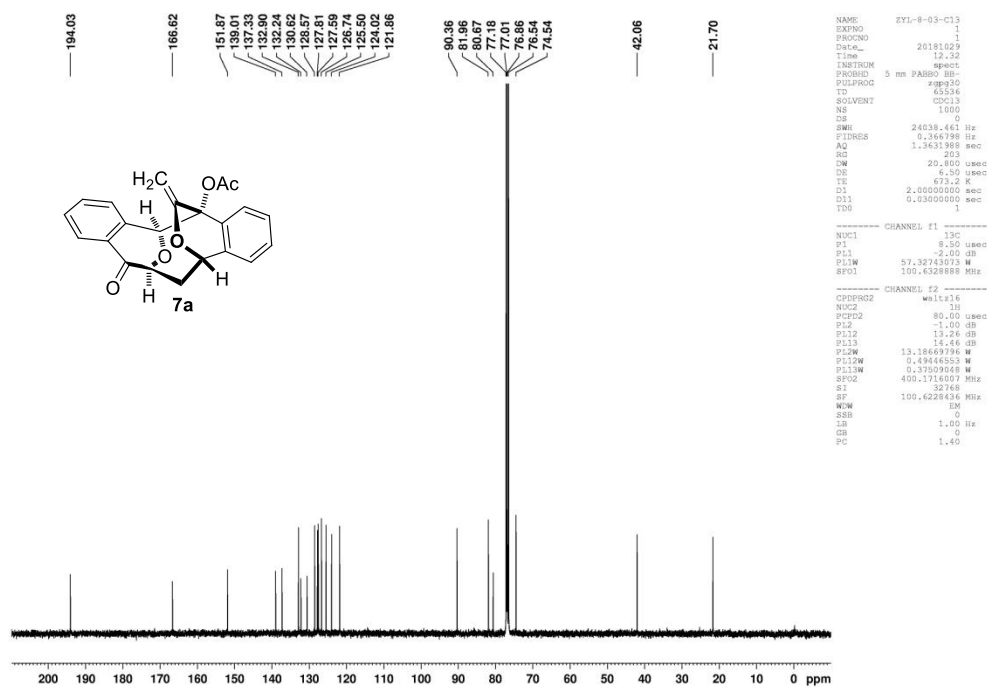
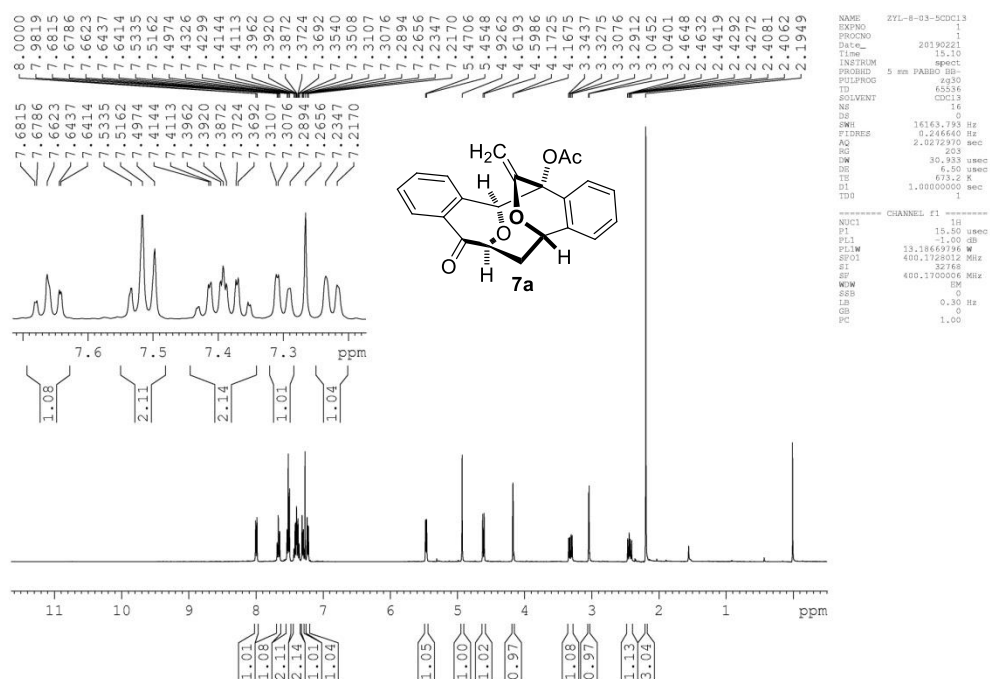


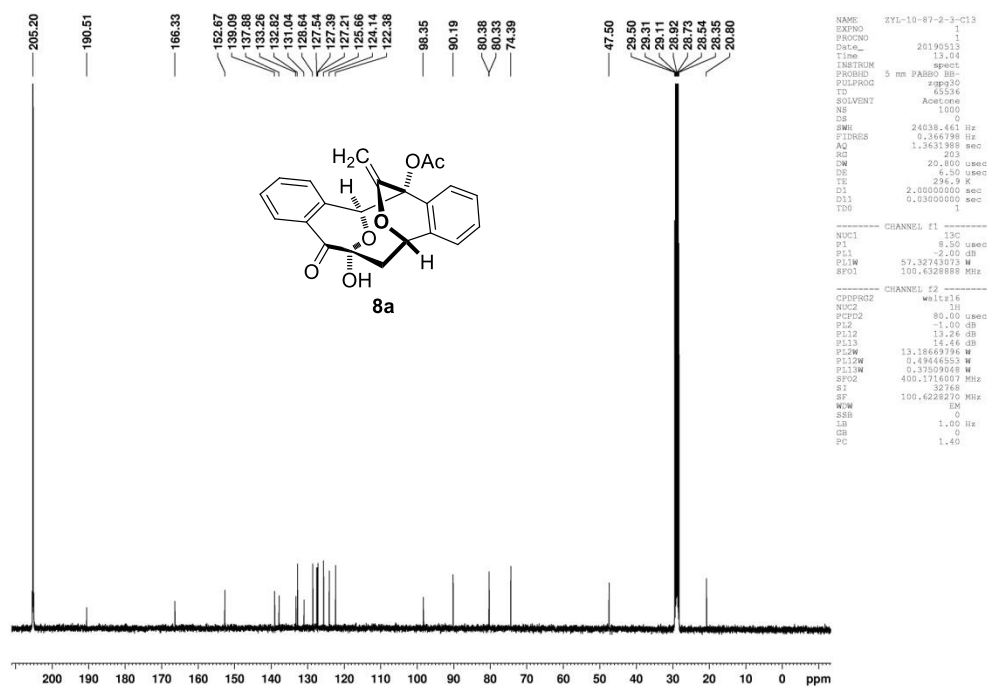
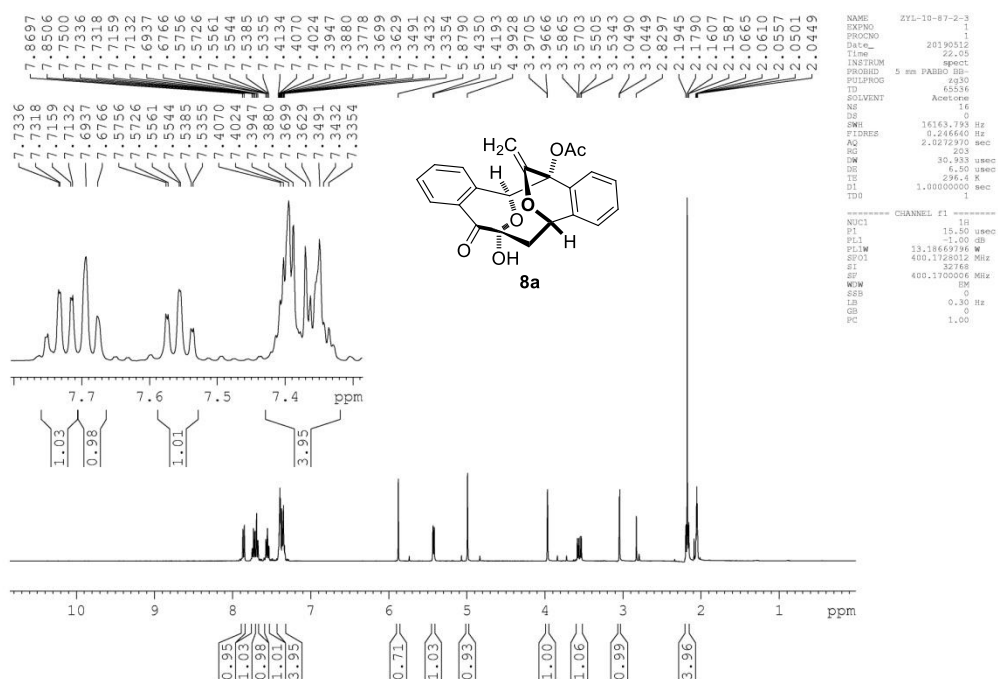


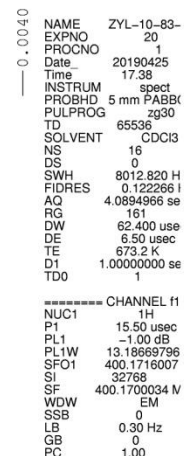


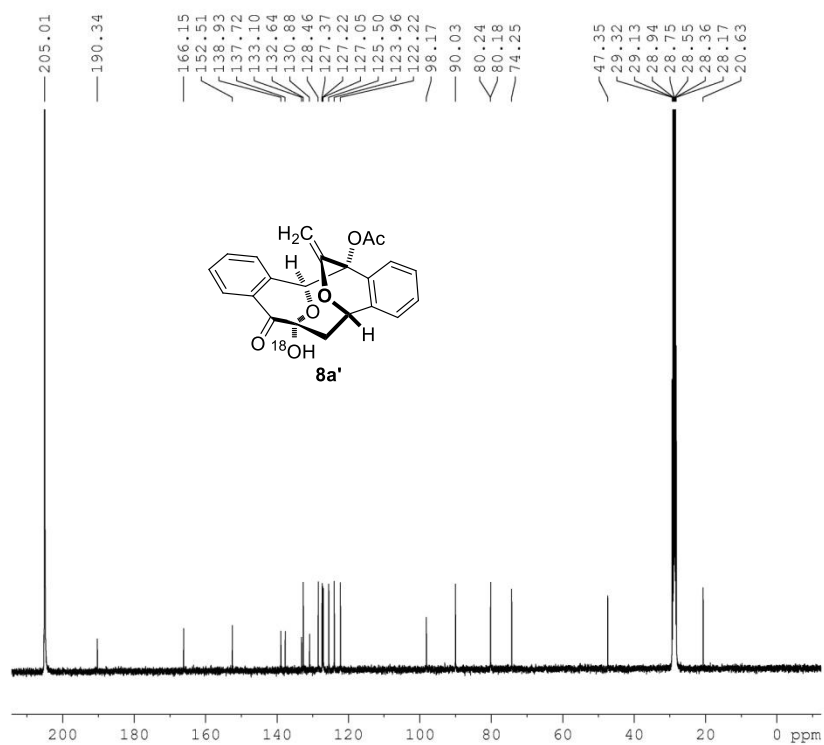
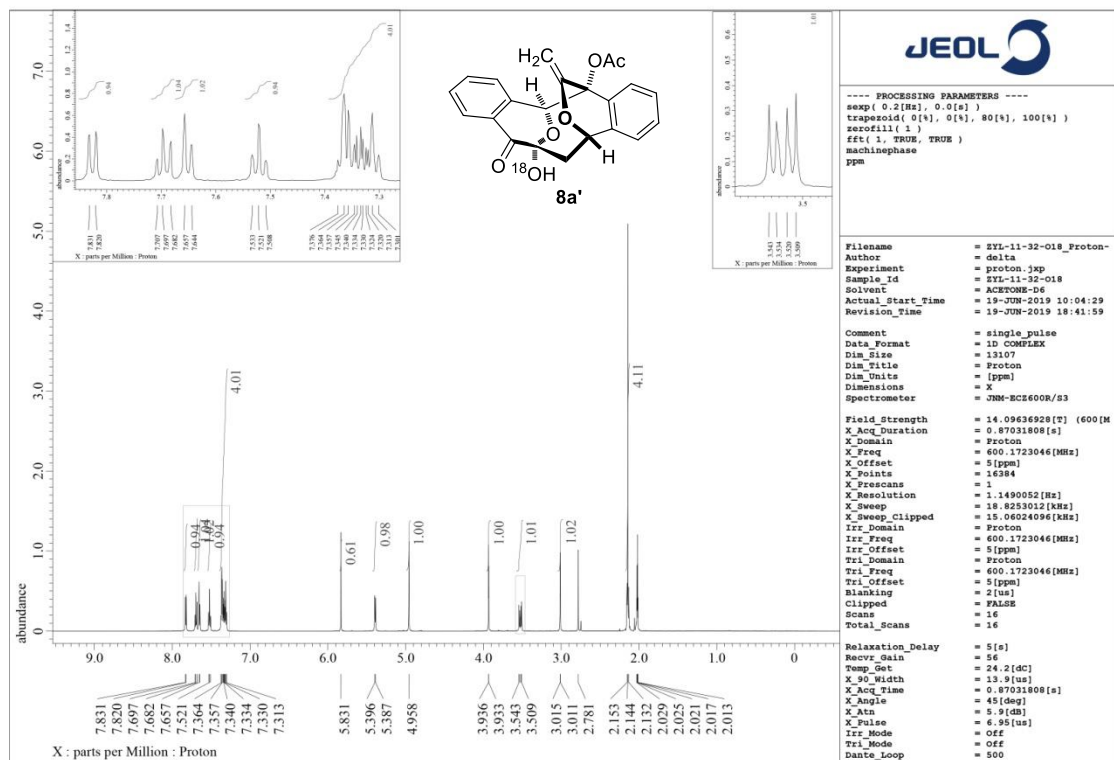












#### 4. HRMS spectra of O<sup>18</sup>-labelled product 8a.

