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COMMUNICATION

β-Cyclodextrin/IBX in water: Highly facile biomimetic one pot deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative cleavage of chalcone epoxides and oxidative dehydrogenation of alcohols

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Sumit Kumar* and Naseem Ahmed*

Abstract. A mild and efficient one-pot deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative cleavage of epoxides and oxidative dehydrogenation of alcohols to form β-hydroxy 1, 2 diketones, 1, 2, 3 triketones and conjugated aromatic carbonyl systems (chalcones) using β-Cyclodextrin/IBX in water has been developed. o-Iodoxybenzoic acid, a readily available hypervalent iodine (V) reagent, was found to be highly effective with β-Cyclodextrin in carrying out deprotection and sequel transformations under eco-friendly environment. The reaction gave moderate to excellent yields ranging from 50-99% at 60 °C in 40 min to 6 h.

Protection and deprotection of hydroxyl groups have fundamental importance and most frequently used strategies in the multi-steps organic syntheses. In particular, these two phenomena are extremely important because of their presence in a number of natural products, biological and synthetic compounds such as carbohydrates, peptides, macrolides, nucleotides, steroids and polyethers [1]. Among the various methods for protecting hydroxy group, the formation of tetrahydropyranyl ethers (THPEs) is one of the most commonly employed methods due to its easy formation and inertness to various reaction conditions like strong bases such as metal hydrides, organolithium compounds, Grignard reagents, catalytic hydrogenation and alkylating or acylating conditions [2]. Likewise, methoxymethyl chloride (MOMCl), acetyl chloride/acetic anhydride (CH_3COCl/Ac_2O) and tosyl chloride (TsCl) are also important reagents for the alcoholic and phenolic group protection. Various methods have been reported for the deprotection of THPEs that include protic acids [3a-d], BF_3–etherate [3e], LiBr [3f], LiOTf [3g], $LiBF_4$ [3h], $LiClO_4$ [3i], $In(OTf)_3$ [3j], $Sc(OTf)_3$, [3k], I_2 [3l], $InCl_3$ [3m], $ZrCl_3$ [3n], $CuCl_2$ [3o], NH_4Cl [3p] and other catalysts. Similarly, Many catalysts have been used to remove the MOM group under acidic conditions such as using protic acids [4a] Lewis acids [4b], Lewis acid-thiol, [4c], boron halides, [4d], $YbCl_3$ [4e] CBr_4-PPh_3 [4f] $ZnBr_2$ [4g] and silica-supported $NaHSO_4$ [4h] and TMSOTf (TESOTf)-2,2'-bipyridyl [4i]. Several catalysts have been reported for the deacetylation and detosylation of alcohols and phenols under acidic and basic conditions including NaOMe [5a], micelles [5b], Zn-MeOH [5c], enzymes [5d], metallo-enzyme [5e] metal complexes [5f] and antibodies [5g], montmorillonite K-10 [5h], I_2 [5i], $NaBO_3$ [5j] and TFA [5k]. Most of these methods however have one or other drawbacks such as low yields, long reaction time, reflux at high temperature, excess amounts of reagents and tedious workup procedures [6]. Hence, there is still scope to develop milder and efficient methods in the detetrahydropyranylation, demethoxymethylation, deacetylation and detosylation of hydroxyl groups.

In recent years much attention has been focused on oxidations involving hypervalent iodine reagents. These reagents are well-known for their selective, efficient, mild, and eco-friendly properties as oxidizing agents [7]. The utility of hypervalent iodine (V) compounds such as 2-iodoxybenzoic acid (IBX) has been sufficiently evidenced by several examples of their selectivity in oxidation reactions [8].

Cyclodextrins (CDs), which are cyclic oligosaccharides possessing hydrophobic cavities, exert microenvironmental effects leading to selective reactions. They catalyse reactions by supramolecular catalysis through non-covalent bonding forming reversible host-guest complexes just like in enzymes. We used β-Cyclodextrin as the catalyst because it is easily accessible and inexpensive among the CDs. The concept of green chemistry has attracted the attention of performing reactions in aqueous medium. However the fundamental problem in performing the organic reactions in water is that many organic substrates are hydrophobic and are insoluble in water. But this can be overcome by the use of cyclodextrins [9].

The upsurge in interest to develop new methodology in protection-deprotection chemistry [4e], herein, we report a simple and efficient one pot deprotection of MOM/THP/Ac/Ts ethers and concomitant oxidative cleavage of chalcone epoxides and oxidative dehydrogenation of alcohols to form β-hydroxy 1, 2 diketones, 1, 2, 3 triketones and α, β-unsaturated ketones employing a mild and environmentally friendly catalytic system β-CD/IBX in water as a novel reagent. These β-hydroxy 1, 2 diketones, 1, 2, 3 triketones and α, β-unsaturated ketones (chalcones) are widely used as synthetic intermediates of high significance in organic and medicinal chemistry.

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247 667, Uttarakhand, India.
**Corresponding author. Fax and Tel.: +91 1332 285745.*
E-mail address: sumitdcy@iitr.ac.in; nasemfcy@iitr.ac.in
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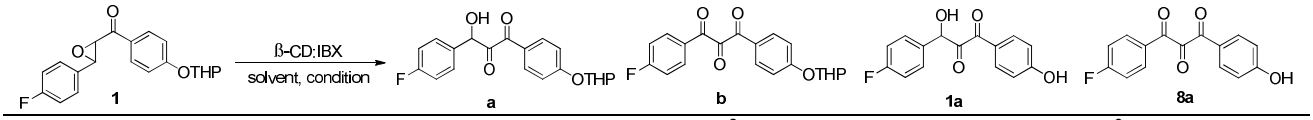
In our initial study toward the development of this methodology, a model reaction was conducted by treating substrate **1** with 1.1 mmol of IBX in acetone at room temperature and product **a** was obtained in moderate yield (45%, Table 1, entry 1). When IBX loading was increased to 2.2 mmol, the product **b** was attained in 46% yield (Table 1, entry 2). But introduction of 1 mmol of β-CD alongwith 1.1 mmol of IBX as a supramolecular host in this reaction, to our delight, detetrahydropyranylation took place with the sequel oxidative cleavage of epoxide to give product **1a** in 55% (Table 1, entry 3). The role of β-CD in this reaction may be that it complexes with the epoxide and OTHP and also it facilitates the solubility of IBX in water and conducts the reaction smoothly. During the exploratory studies conducted, this prototype reaction was attempted by increasing the IBX quantity as well as by increasing the reaction times and temperatures. For instance, on taking 1 : 2.2 of reagent ratio (β-CD : IBX), product **8a** was obtained in 57% yield (Table 1, entry 4). It led to conclude that the extra quantity of IBX added was utilised in further oxidation of β-hydroxy 1,2 diketone **1a** to 1, 2, 3 triketone **8a**. It is also remarkable that on increasing the β-CD : IBX ratio to 1:3 or more with prolonging reaction time did not bring about further oxidation of the triketone **8a**. Then we study the effect of temperature of same prototype reaction in acetone. It was observed that on increasing the temperature of the reaction system to 55 ^{o}C (reflux), the products yields (**a**, **b**, **1a**, **8a** respective to the β-CD : IBX ratio) were increased significantly (Table 1, entries 5-8).

Table 1. Optimization of reaction conditions for deprotection and concomitant oxidative cleavage of chalcone epoxide[c].



Entry	β-CD : IBX (mmol)	Solvent	Temp. (^{o}C)	Time (h)	Yield[e] (%)			
					a	b	1a	8a
1	0 : 1.1	Acetone	rt	14	45	-	-	-
2	0 : 2.2	Acetone	rt	14	-	46	-	-
3	1 : 1.1	Acetone	rt	14	-	-	55	-
4	1 : 2.2	Acetone	rt	18	-	-	-	57
5	0 : 1.1	Acetone	55	4	75	-	-	-
6	0 : 2.2	Acetone	55	4	-	74	-	-
7	1 : 1.1	Acetone	55	4	-	-	75	-
8	1 : 2.2	Acetone	55	4.5	-	-	-	73
9	1 : 2.2	$CHCl_3$	60	7	-	-	-	80
10	1 : 2.2	CH_3CN	80	2	-	-	-	89
11	1 : 2.2	Toluene	80	-	-	-	-	0[d]
12	1 : 2.2	THF	80	-	-	-	-	0[d]
13	0 : 1.1	H_2O	70	2	80	-	-	-
14	0 : 2.2	H_2O	70	2	-	82	-	-
15	1 : 1.1	H_2O	70	2	-	-	79	-
16	1 : 2.2	H_2O	70	3	-	-	-	80
17	0 : 1.1	H_2O : Acetone	60	40 min	90	-	-	-
18	0 : 2.2	H_2O : Acetone	60	40 min	-	91	-	-
19	**1 : 1.1**	**H_2O : Acetone**	**60**	**40 min**	**-**	**-**	**98**	**-**
20	**1 : 2.2**	**H_2O : Acetone**	**60**	**1**	**-**	**-**	**-**	**99**

[c]Reaction was carried out on 1 mmol scale; [d]Solvent oxidation observed; [e]Isolated yield.

After that the effect of the solvents like $CHCl_3$, CH_3CN, $PhCH_3$, THF, neat H_2O and mixed solvents (H_2O : acetone) on the reaction system was investigated (Table 1, entries 9-12, 15,16, 19, 20). The reaction proceeded smoothly in neat water at 70 ^{o}C furnishing the products in appreciable yields. But H_2O : acetone mixture was found to be the best solvent at 60 ^{o}C affording the products **1a** and **8a** in 98 and 99% yield in 40 min and 1h respectively (Table 1, entries 19, 20). This is because of the low or non-solubility of compounds in neat water but the addition of some drops of acetone improves the solubility of the compounds and hence product yields were enhanced. Solvents like $PhCH_3$ and THF did not provide the desired products at all (Table 1, entries 19, 20). So, it led to conclude that H_2O : acetone mixture at 60 ^{0}C temperature was the optimal condition for the reaction to get best yields of the products **1a** and **8a**. Recently, from the viewpoint of green chemistry, use of H_2O in organic transformations is highly demanded, so we carried out the reactions in H_2O as solvent. The use of aqueous medium as solvent also lessens the harmful effects of organic solvents. Finally, it can conclusively be substantiated that in the absence of β-CD, the reaction did not yield the detetrahydropyranylated products **1a** or **8a**.

After getting optimization conditions, various chalcone epoxides were examined for detetrahydropyranylation and demethoxymethylation and concomitant oxidative cleavage of epoxide ring. The results are summerized in Table 2.

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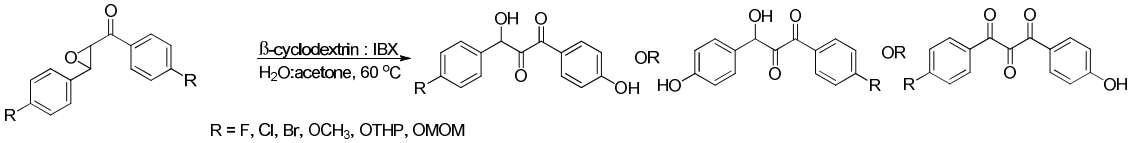
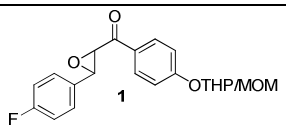
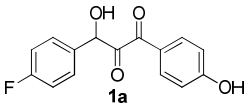
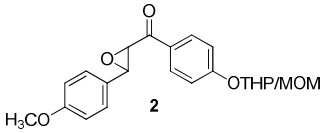
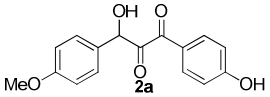
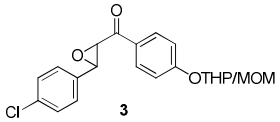
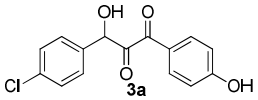
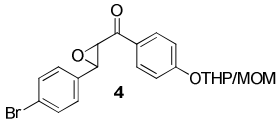
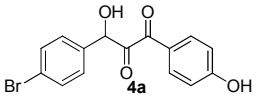
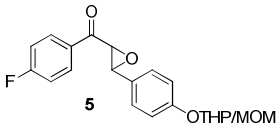
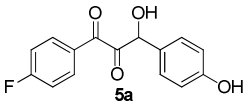
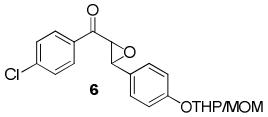
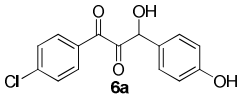
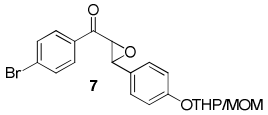
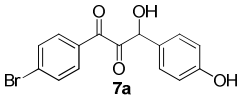
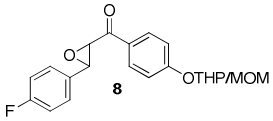
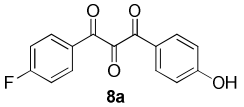
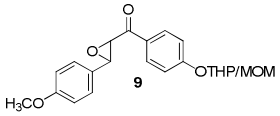
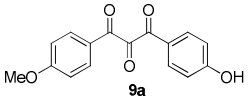
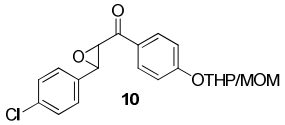
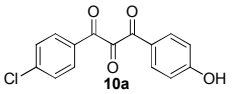
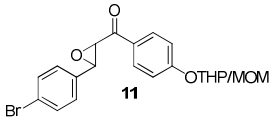
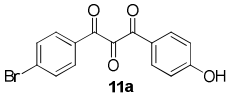
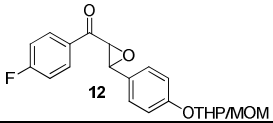
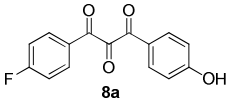
Table 2. β-CD/IBX mediated one pot deprotection and sequel oxidative cleavage of epoxide to form β-hydroxy 1,2 deketones and 1,2,3 triketones.



R = F, Cl, Br, OCH_3, OTHP, OMOM

Entry	Substrate	Product	Time (min)	Yields (%)	
				a	b
1[c]			40	98	97
2[c]			40	96	94
3[c]			40	99	98
4[c]			40	93	93
5[c]			40	95	95
6[c]			40	96	95
7[c]			40	93	96
8[d]			90	99	99
9[d]			90	97	95
10[d]			90	96	94
11[d]			90	95	96
12[d]			90	95	90

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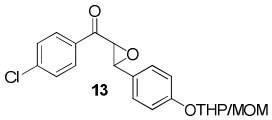
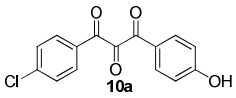
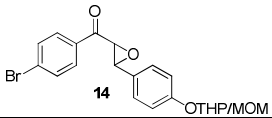
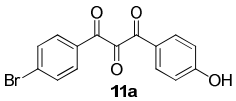
13[d]	 **13**	 **10a**	90	93	94
14[d]	 **14**	 **11a**	90	96	97

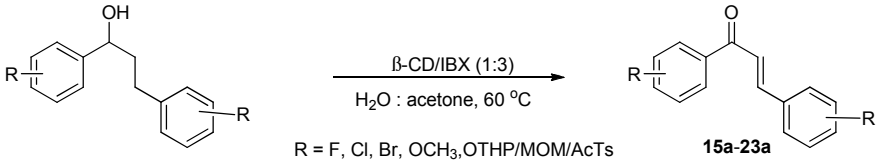
Reactions were carried out on 1 mmol scale at 60 °C; [c]β-CD : IBX (1:1.1 mmol) for entries 1-7; [d]β-CD : IBX (1:2.2 mmol) for the entries 8-14.
[a, b]Isolated yields of detetrahydropyranylation, demethoxymethylation.

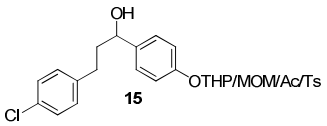
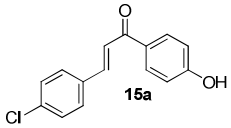
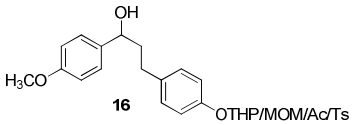
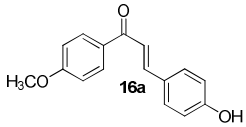
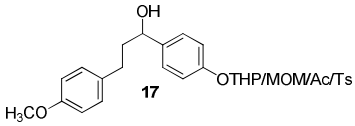
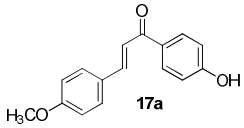
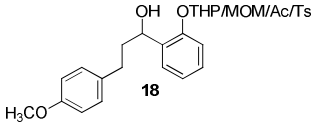
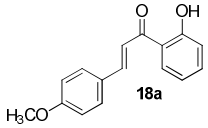
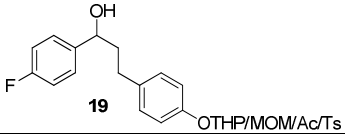
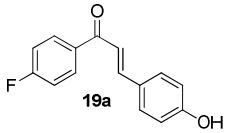
The products were confirmed on the basis of FTIR NMR and mass (ESI†). For instance, compound **2a**, the ^{1}H-NMR spectrum displayed the characteristic broad peaks at δ 4.81 and 2.52 ppm for phenolic and alcoholic hydroxyl group respectively. Disappearance of one doublet of -CH- and a broad peak at 3422 cm^{-1} for –OH groups, peaks of two >C=O groups at 1685 cm^{-1} and 1647 cm^{-1} in IR spectrum indicate the deprotection with oxidative cleavage of chalcone epoxide **2** and confirm the formation of compound **2a**.

The universality and utility of conjugated aromatic carbonyl systems in organic chemistry coupled with the complications that are often associated with their construction led us to explore the possibility of obtaining them using an iodine (V)-based reagent. Because IBX is well-known for the oxidation of alcohols, the anticipation of achieving multiple oxidative processes in one operation was particularly alluring. Encouraged by the above results, the scope of the present study (Deprotection and sequel oxidation) was extended to various phenolic OH protected diversely substituted substrates (**15**-**23**) toward this novel transformation and the results were tabulated in Table 3. It was resulted into the deprotection of THP/MOM/Ac/Ts ethers and sequel oxidative dehydrogenation to give conjugated aromatic carbonyl systems (chalcones **15a**-**23a**) in good to excellent yields.

Under optimized reaction conditions, using β-CD : IBX (1 : 3 for this transformation, 1.5 equiv. per alcohol or C-C bond to be oxidized), the reaction underwent deprotection and sequel oxidative dehydrogenation to α, β unsaturated ketones in excellent yields for detetrahydropyranylation, demethoxymethylation and deacetylation (91–98%) and moderate yield for detosylation (50–57%) within 6h at 60 °C (Table 3, entries 1–9). In case of detosylation, reaction was subjected for a longer time (8-10h), but no improvement in the yield was observed.

Table 3. β-CD/IBX mediated one pot deprotection and sequel oxidative dehydrogenation of alcohols to form chalcones.



Entry	Substrate	Product	Time (h)	Yields (%)			
				a	b	c	d
1	 **15**	 **15a**	6	92	95	98	55
2	 **16**	 **16a**	6	93	96	94	57
3	 **17**	 **17a**	6	94	96	94	55
4	 **18**	 **18a**	6	94	94	97	52
5	 **19**	 **19a**	6	91	92	95	50

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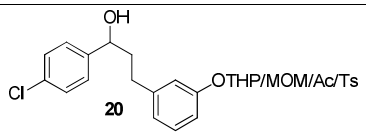
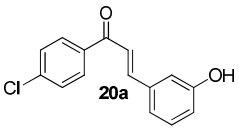
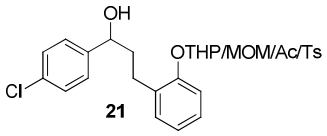
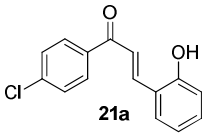
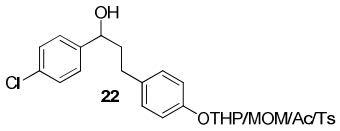
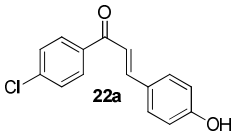
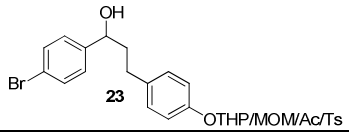
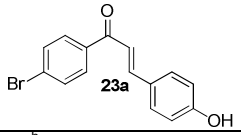
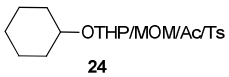
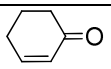
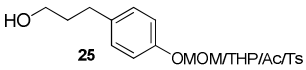
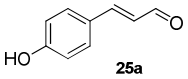
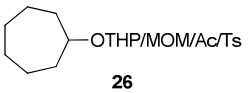
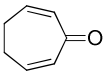
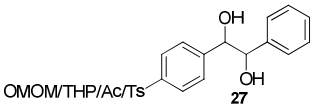
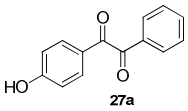
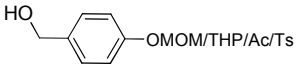
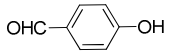
6	 **20**	 **20a**	6	95	94	96	52
7	 **21**	 **21a**	6	96	91	93	54
8	 **22**	 **22a**	6	93	97	94	55
9	 **23**	 **23a**	6	97	98	96	53

Reactions were carried out on 1 mmol scale at 60 °C, [b]β-CD:IBX (1:3 mmol); [a,b,c,d] Isolated yields of detetrahydropyranylation, demethoxymethylation, deacetylation, detosylation respectively.

Furthermore, β-CD/IBX mediated deprotection and sequel oxidative dehydrogenation was tested on other substrates (**24**-**28**) also as given in Table 4.

Table 4. Some other examples of β-CD/IBX-mediated one pot deprotection and sequel oxidation.

Entry	Substrate	Product	Time (h)	Yields[d] (%)			
				a	b	c	d
1[a]	 **24**	 **24a**	10	93	89	92	55
2[a]	 **25**	 **25a**	8	94	95	98	50
3[b]	 **26**	 **26a**	14	91	85	89	49
4[b]	 **27**	 **27a**	15	90	88	92	51
5[c]	 **28**	 **28a**	8	93	92	98	91

Reactions were carried out on 1 mmol scale. [a]β-CD : IBX (1:3 mmol) for entries 1,2; [b]β-CD : IBX (1:4.5 mmol) for the entries 3, 4; [c]β-CD : IBX (1:1.5 mmol) for the entry 5.
[a,b,c,d] Isolated yields of detetrahydropyranylation, demethoxymethylation, deacetylation, detosylation respectively.

After having obtained success with deprotection of THP/MOM/Ac/Ts ethers of chalcone epoxides (**1a**-**11a**) and alcohols (**15a**-**28a**), we extended this protocol (β-CD alone in water) for other substrates (**29**-**38**) and delightfully on these scaffolds also it worked equally well as shown in Table 5.

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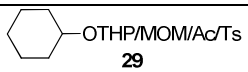
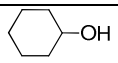
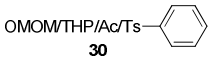
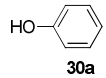
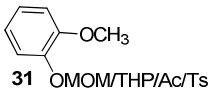
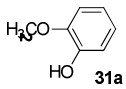
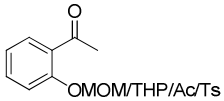
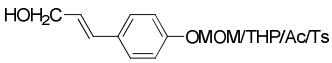
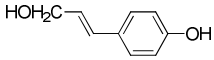
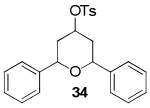
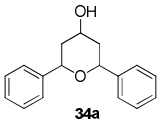
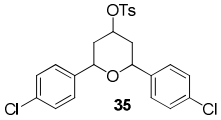
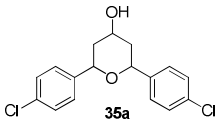
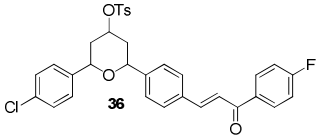
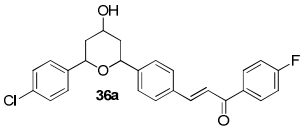
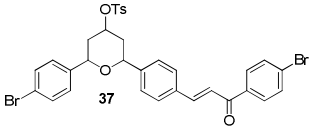
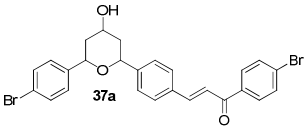
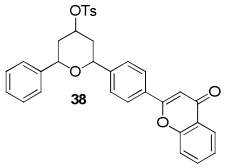
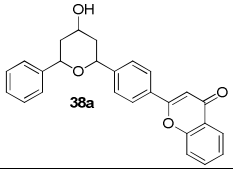
Table 5. Some examples of β-CD-mediated deprotection of alcoholic and phenolic hydroxyl group.

ROTHP/MOM/Ac/Ts —(ß-Cyclodextrin/water, 60 °C)→ ROH

Entry	Substrate	Product	Time (h)	Yields[d] (%)			
				a	b	c	d
1[a]	 **29**	 **29a**	7	90	89	91	51
2[b]	 **30**	 **30a**	5	91	88	92	57
3[c]	 **31**	 **31a**	5.5	98	95	99	57
4[a]	 **32**	 **32a**	5	95	90	93	60
5[a]	 **33**	 **33a**	6	93	87	95	59
6[c]	 **34**	 **34a**	8	-	-	-	55
7[a]	 **35**	 **35a**	8	-	-	-	56
8[b]	 **36**	 **36a**	8	-	-	-	51
9[c]	 **37**	 **37a**	8	-	-	-	55
10	 **38**	 **38a**	8	-	-	-	54

Reactions were carried out on a 0.5- to 1-mmol scale.
[a,b,c,d] Isolated yields of detetrahydropyranylation, demethoxymethylation, deacetylation, detosylation respectively.

All compounds were characterized by FTIR, NMR, mass (ESI†) and by comparison with the literature [5k, 10]. For example, product **16a**, the ^{1}H NMR spectra showed the characteristic olefinic peaks at δ ppm 7.74 (d, *J* = 15.5 Hz, 1H) and 7.51 (d, *J* = 16 Hz, 1H) for >CH=CH< and disappearance of 2 –CH_2, one –**CH**OH at 4.21 ppm and one –CH**OH** at 3.12 ppm and appearance of phenolic OH at 5.38 (s, 1H, D_2O exchangeable) peaks indicate deprotection and sequel oxidative dehydrogenation of compound **16**. In ^{13}C-NMR spectra, appearance of the characteristic peak of >C=O at δ 188.2 ppm and disappearance of peaks of –CH_2–CH_2– at 46.35 ppm and 30.51 ppm and of –**CH**OH at 74.1 ppm confirm the oxidative dehydrogenation. IR value at 3410, 1684 and 1599 cm^{-1} for –OH, >C=O and >C=C< bonds respectively indicate the said transformation.

A mechanistic description of this IBX-mediated demethoxymethylation is depicted in Fig. 1.

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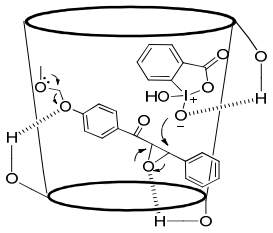
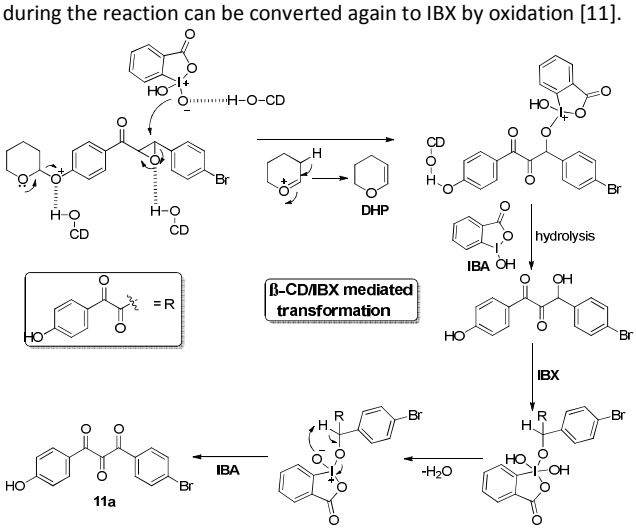


Fig. 1 Mechanistic Rationale of β-cyclodextrin/IBX induced deprotection of phenolic ether and concomitant oxidative cleavage of chalcone epoxide.

A plausible mechanism for detetrahdropyranylation and concomitant oxidative cleavage of chalcone epoxide is proposed in Scheme 1. The role of β-CD appears to be not only to activate the THP ether and epoxide by hydrogen bonding but also to promote highly regioselective ring opening due to inclusion complex formation and thereby facilitating the hydrolysis. Since the β-CD cavity is hydrophobic in nature it may also be forming reversible complexes with the THP ethers. In these reactions, Cyclodextrin can be recycled and reused, also the iodosobenzoic acid (IBA) obtained during the reaction can be converted again to IBX by oxidation [11].



Scheme 1. Plausible reaction mechanism of β-cyclodextrin/IBX induced deprotection of phenolic ether and concomitant oxidative cleavage of chalcone epoxide.

Conclusions

In summary, we have presented an elegant and simple methodology for one pot deprotection of MOM/THP/Ac/Ts ethers and concomitant oxidative cleavage of chalcone epoxides and oxidative dehydrogenation of alcohols employing a mild and eco-friendly oxidizing agent β-CD/IBX in water under supramolecular catalysis. Thus, we have demonstrated for the first time the synthesis of highly valuable synthons β-hydroxy 1, 2 diketones, 1, 2, 3 triketones and α, β-unsaturated ketones directly from the easily accessible chalcone epoxides and 1, 3 diphenyl alcohols in the presence of β-CD/IBX in water. β-CD was found indispensable for the deprotection reaction. To the best of our knowledge, this is the first report of deprotection with sequel transformations to form β-hydroxy 1, 2 diketones, 1, 2, 3 triketones and α, β-unsaturated ketones in aqueous medium and therefore represents a novel methodology. It is an economical and user-friendly protocol.

Experimental

General procedure for the deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative dehydrogenation of alcohols (15a-28a). To a solution of alcohol (**15**-**28**) in water (2 mL) and 3-4 drops of acetone was added to an aqueous solution of β-cyclodextrin (1 mmol in 10 mL of water) at 60 °C and allowed to cool to room temperature. Then, IBX (1.5 equiv. per alcohol or C-C bond to be oxidized) was added while stirring. The mixture was heated to 60 °C, and the reaction was constantly monitored by TLC until complete consumption of starting material was observed. The reaction mixture was cooled to room temperature and extracted with EtOAc (3 × 15 mL). The organic layer was washed with 5% aq. $NaHCO_3$ and dried over anhydrous Na_2SO_4 and concentrated in a vacuo. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (8:2) as an eluent if required otherwise compounds were pure enough for the spectral elucidation.

General procedure for the deprotection of THP/MOM/Ac/Ts ethers (29a-38a). β-cyclodextrin (0.1 mmol) was dissolved in water (25 ml) at 60 ^{o}C; THP/MOM/Ac/Ts ether (1 mmol) in water: acetone mixture (2 ml: 3-4 drops) was added slowly with stirring. The stirring was continued at 60 ^{o}C for the specified time (Table 5). Then the reaction mixture was cooled to room temperature and extracted with EtOAc (3 × 15 mL), dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (9:1) as eluent if required otherwise compounds were pure enough for the spectral elucidation.

Acknowledgements

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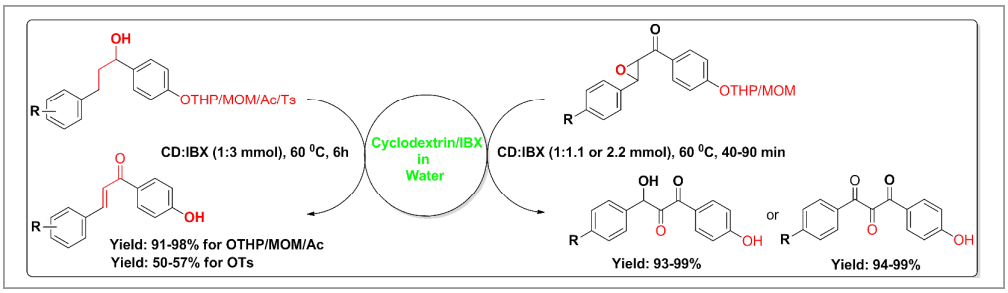

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Graphical Abstract

β-Cyclodextrin/IBX in water: Highly facile biomimetic one pot deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative cleavage of chalcone epoxides and oxidative dehydrogenation of alcohols

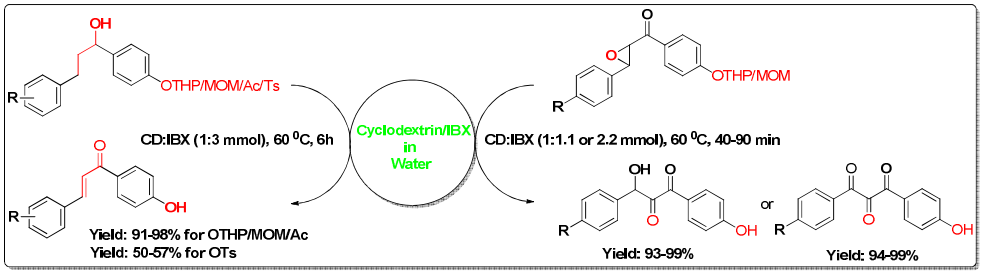
Sumit Kumar* and Naseem Ahmed*

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247 667, India

*Corresponding author. Fax and Tel.: +91 1332 285745.

E-mail address: sumitdcy@iitr.ac.in; nasemfcy@iitr.ac.in

Table of contents



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β-Cyclodextrin/IBX in water: Highly facile biomimetic one pot deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative cleavage of chalcone epoxides and oxidative dehydrogenation of alcohols

Sumit Kumar* and Naseem Ahmed*

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247 667, India

**Corresponding author. Fax and Tel.: +91 1332 285745.*

E-mail address: sumitdcy@iitr.ac.in; nasemfcy@iitr.ac.in

Table of contents

1. General methods

2. General procedure for the deprotection of THP, MOM, acetyl and tosyl ethers and concomitant oxidative cleavage of chalcone epoxides and oxidative dehydrogenation of alcohols

3. Characterization data for selected synthesized compounds

4. ^{1}H and ^{13}C NMR Spectra

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1. General methods

Unless otherwise noted, chemicals were purchased from commercial suppliers at the highest purity grade available and were used without further purification. Solvents were distilled by standard methods. Thin layer chromatography was performed on Merck precoated 0.25 mm silica gel plates (60F-254) using UV light as visualizing agent and/or iodine as developing agent. Silica gel (100-200 mesh) was used for column chromatography. IR spectra were recorded on FT-IR spectrometer and expressed as wave numbers (cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on a Brüker (500 MHz & 125 MHz) & Jeol (400 MHz & 100 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.23 ppm, the middle peak). Coupling constants are expressed in Hz. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet, br = broad. High-resolution mass spectra (HRMS) were obtained on a Brüker micrOTOF™-Q II mass spectrometer (ESIMS).

2. (a) General procedure for deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative cleavage of chalcone epoxides (1a-11a). The chalcone epoxides (1 mmol) dissolved in water (2 mL) and 3-4 drops of acetone was added to an aqueous solution of β-cyclodextrin (1 mmol in 10 mL of water) at 60 °C and allowed to cool to room temperature. Then, IBX (1.1 or 2.2 mmol depending on the desired product) was added while stirring and stirring was continued for 40-60 min at 60 °C. After completion of reaction, the mixture was cooled to room temperature and extracted with EtOAc (3 × 15 mL), dried, and concentrated in a vacuo. The crude product was purified by silica gel column chromatography using

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hexane/ethyl acetate (8:2) as an eluent if required otherwise compounds were pure enough for the spectral elucidation.

(b) General procedure for deprotection of THP/MOM/Ac/Ts ethers and concomitant oxidative dehydrogenation of alcohols (15a-28a). To a solution of alcohol (15-28) in water (2 mL) and 3-4 drops of acetone was added to an aqueous solution of β-cyclodextrin (1 mmol in 10 mL of water) at 60 °C and allowed to cool to room temperature. Then, IBX (1.5 equiv. per alcohol or C-C bond to be oxidized) was added while stirring. The mixture was heated to 60 °C, and the reaction was constantly monitored by TLC until complete consumption of starting material was observed. The reaction mixture was cooled to room temperature and extracted with EtOAc (3 × 15 mL). The organic layer was washed with 5% aq. $NaHCO_3$ and dried over anhydrous Na_2SO_4 and concentrated in a vacuo. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (8:2) as an eluent if required otherwise compounds were pure enough for the spectral elucidation.

(c) General procedure for deprotection of THP/MOM/Ac/Ts ethers (29a-38a). β-cyclodextrin (0.1 mmol) was dissolved in water (25 ml) at 60 ^{o}C; THP/MOM/Ac/Ts ether (1 mmol) in water: acetone mixture (2 ml: 3-4 drops) was added slowly with stirring. The stirring was continued at 60 ^{o}C for the specified time (Table 5). Then the reaction mixture was cooled to room temperature and extracted with EtOAc (3 × 15 mL), dried over anhydrous Na_2SO_4 and the solvent was removed in vacuo. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (9:1) as eluent if required otherwise compounds were pure enough for the spectral elucidation.

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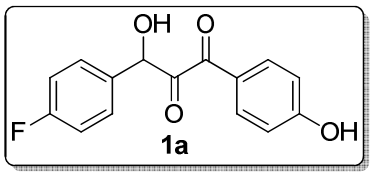
3. Characterization data for representative compounds

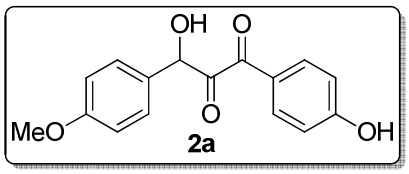
3-(4-fluorophenyl)-3-hydroxy-1-(4-hydroxyphenyl)propane-1,2-dione (1a)



1a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.95-7.90 (m, 2H), 7.74 (dd, *J* = 2, 10 Hz, 2H), 7.08-7.04 (m, 2H), 7.00 (dd, *J* = 2, 10 Hz, 2H), 5.37 (s, 1H), 4.55 (s, 1H, D_2O exchangeable), 2.54 (s, 1H, D_2O exchangeable). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 197.3, 191.5, 164.6, 163.1, 133.4, 132.5, 131.1, 129.0, 116.2, 115.8, 85.2. IR (KBr, cm^{-1}): 3420, 2945, 1687, 1649. HRMS (ESIMS) for $C_{15}H_{11}FNaO_4$ $(M+Na)^+$ Anal. calcd. 297.0533; found 297.0531.

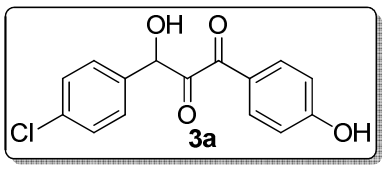
3-hydroxy-1-(4-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,2-dione (2a)



2a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.90 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.75 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.00 (dd, *J* = , 2.5, 8.5 Hz, 2H), 6.88 (dd, *J* = 2.5, 8.5 Hz, 2H), 5.28 (s, 1H), 4.81 (s, 1H, D_2O exchangeable), 3.80 (s, 3H), 2.52 (s, 1H, D_2O exchangeable). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 197.9, 191.4, 163.7, 163.2, 132.5, 130.8, 129.9, 129.0, 116.2, 113.7, 84.8, 55.5. IR (KBr, cm^{-1}): 3422, 2940, 1685, 1647. HRMS (ESIMS) for $C_{16}H_{14}NaO_5$ $(M+Na)^+$ Anal. calcd. 309.0733; found 309.0730.

3-(4-chlorophenyl)-3-hydroxy-1-(4-hydroxyphenyl)propane-1,2-dione (3a)



3a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.84 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.75 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.38 (dd *J* = 2.5, 8.5 Hz, 2H), 7.00 (dd, *J* = 2.5, 8.5 Hz, 2H), 5.32 (s, 1H), 4.81 (s, 1H, D_2O exchangeable), 2.55 (s, 1H, D_2O exchangeable). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 197.6, 191.4, 162.9, 139.7, 135.2, 132.5, 129.8, 129.1, 128.9, 116.2, 84.7. IR (KBr, cm^{-1}): 3423, 2947, 1684, 1645. HRMS (ESIMS) for $C_{15}H_{11}ClNaO_4$ $(M+Na)^+$ Anal. calcd. 313.0238; found 313.0232.

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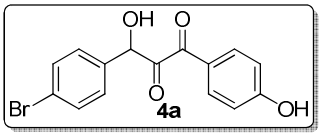
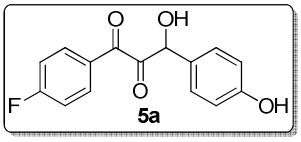
3-(4-bromophenyl)-3-hydroxy-1-(4-hydroxyphenyl)propane-1,2-dione (4a)



4a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.78-7.74 (m, 4H), 7.54 (dd, *J* = 2, 11 Hz, 2H), 6.99 (d, *J* = 11 Hz, 2H), 5.34 (s, 1H), 4.23 (s, 1H, D_2O exchangeable), 2.56 (s, 1H, D_2O exchangeable). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 197.8, 191.5, 162.9, 135.6, 132.6, 131.9, 129.9, 129.2, 128.5, 116.1, 83.7. IR (KBr, cm^{-1}): 3423, 2947, 1685, 1642. HRMS (ESIMS) for $C_{15}H_{11}BrNaO_4$ $(M+Na)^+$ Anal. calcd. 356.9732; found 356.9734.

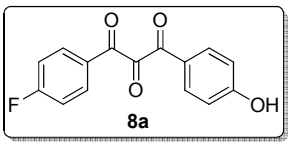
1-(4-fluorophenyl)-3-hydroxy-3-(4-hydroxyphenyl)propane-1,2-dione (5a)



5a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.98-7.93 (m, 2H), 7.76 (dd, *J* = 2, 10 Hz, 2H), 7.11-7.08 (m, 2H), 6.99 (dd, *J* = 2, 10 Hz, 2H), 5.35 (s, 1H), 4.54 (s, 1H, D_2O exchangeable), 2.55 (s, 1H, D_2O exchangeable). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 191.8, 191.2, 165.5, 162.8, 132.7, 132.6, 132.5, 125.8, 116.6, 116.4, 84.3. IR (KBr, cm^{-1}): 3420, 2946, 1686, 1647. HRMS (ESIMS) for $C_{15}H_{11}FNaO_4$ $(M+Na)^+$ Anal. calcd. 297.0533; found 297.0535.

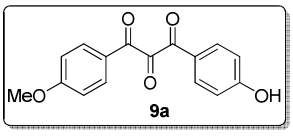
1-(4-fluorophenyl)-3-(4-hydroxyphenyl)propane-1,2,3-trione (8a)



8a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.92-7.89 (m, 2H), 7.71 (dd, *J* = 1.5, 11 Hz, 2H), 7.06-7.02 (m, 2H), 6.97 (dd, *J* = 1.5, 10.5 Hz, 2H), 2.71 (s, 1H, D_2O exchangeable). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 189.5, 166.9, 164.7, 133.4, 132.5, 131.0, 129.1, 116.1, 115.8. IR (KBr, cm^{-1}): 3425, 2948, 1640, 1599, 1582. HRMS (ESIMS) for $C_{15}H_9FNaO_4$ $(M+Na)^+$ Anal. calcd. 295.0377; found 295.0372.

1-(4-hydroxyphenyl)-3-(4-methoxyphenyl)propane-1,2,3-trione (9a)



9a

^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 7.88 (dd, *J* = 2.5, 9 Hz, 2H), 7.73 (d, *J* = 11 Hz, 2H), 6.99 (d, *J* = 11 Hz, 2H), 6.86 (dd, *J* = 2.5, 11 Hz, 2H), 4.94 (s, 1H, D_2O exchangeable), 3.77 (s, 3H). ^{13}C

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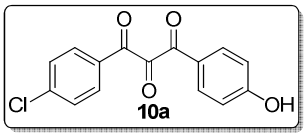
NMR (125 MHz, $CDCl_3$, ppm): δ 188.4, 163.7, 163.2, 132.5, 130.8, 129.9, 129.0, 116.2, 113.7, 55.4. IR (KBr, cm^{-1}): 3420, 2945, 1643, 1595, 1582. HRMS (ESIMS) for $C_{16}H_{12}NaO_4$ $(M+Na)^+$ Anal. calcd. 307.0576; found 307.0569.

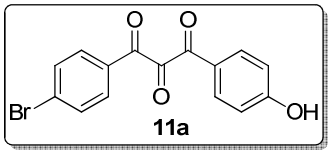
1-(4-chlorophenyl)-3-(4-hydroxyphenyl)propane-1,2,3-trione (10a)



10a

^1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.84 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.75 (dd, *J* = 2.5, 8.5 Hz, 2H), 7.38 (dd *J* = 2.5, 8.5 Hz, 2H), 7.00 (dd, *J* = 2.5, 8.5 Hz, 2H), 4.81 (s, 1H, D_2O exchangeable). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 189.7, 162.9, 139.7, 135.2, 132.5, 129.8, 129.2, 128.9, 116.1. IR (KBr, cm^{-1}): 3421, 2946, 1644, 1585. HRMS (ESIMS) for $C_{15}H_9ClNaO_4$ $(M+Na)^+$ Anal. calcd. 311.0081; found 311.0080.

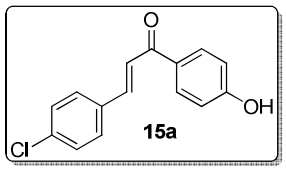
1-(4-bromophenyl)-3-(4-hydroxyphenyl)propane-1,2,3-trione (11a)



11a

^1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.83 (dd, *J* = 2.5, 10.5 Hz, 2H), 7.74 (dd, *J* = 2.5, 10.5 Hz, 2H), 7.37 (dd, *J* = 2.5, 10.5 Hz, 2H), 6.98 (d, *J* = 10.5 Hz, 2H), 4.94 (s, 1H, D_2O exchangeable). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 189.1, 162.8, 135.6, 132.6, 131.9, 129.9, 129.2, 128.5, 116.1. IR (KBr, cm^{-1}): 3421, 2946, 1644, 1585. HRMS (ESIMS) for $C_{15}H_9BrNaO_4$ $(M+Na)^+$ Anal. calcd. 354.9576; found 354.9571.

(E)-3-(4-chlorophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (15a)



15a

^1H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.99 (d, *J* = 8 Hz, 2H), 7.77 (d, *J* = 15.5 Hz, 1H), 7.63 (t, *J* = 8Hz, 2H), 7.46 (d, *J* = 15.5 Hz, 1H), 7.10 (t, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8 Hz, 2H), 5.38 (s, 1H, D_2O exchangeable). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 186.8, 162.0, 141.3, 131.4, 130.9, 130.8, 128.9, 121.8, 115.8, 115.2. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265, 1078, 862, 730. GC-MS (m/z): 302 [$M^{+\cdot}$, $C_{15}H_{11}BrO_2$], 304 [M+2].

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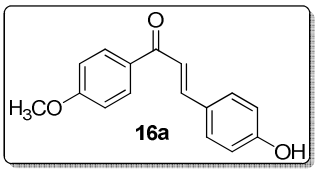
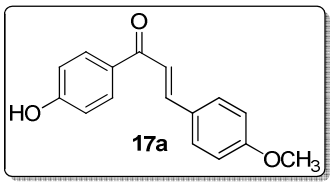
(E)-3-(4-hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (16a)



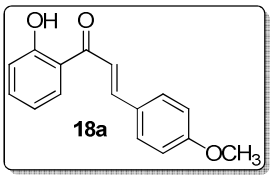
^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.03 (d, *J* = 8 Hz, 2H), 7.74 (d, *J* = 15.5 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 16 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 9 Hz, 2H), 5.48 (s, 1H, D_2O exchangeable), 3.89 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 188.2, 163.9, 142.7, 131.4, 131.3, 130.1, 121.5, 116.8, 116.6, 114.2, 55.1. IR (KBr, ν_{max} = cm^{-1}): 3410, 2928, 2880, 1684, 1599, 1265. GC-MS (m/z): 254 [M^+, $C_{16}H_{14}O_3$].

(E)-1-(4-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (17a)



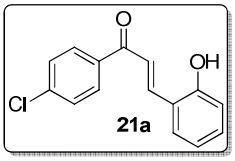
^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 8.03 (d, *J* = 8 Hz, 2H), 7.77 (d, *J* = 16 Hz, 1H), 7.55 (d, *J* = 8Hz, 2H), 7.42 (d, *J* = 15.5 Hz, 1H), 6.98 (d, *J* = 8 Hz, 2H), 6.89 (d, *J* = 8 Hz, 2H), 5.82 (s, 1H, D_2O exchangeable), 3.89 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 188.7, 163.6, 142.8, 131.2, 131.0, 130.4, 121.7, 116.3, 116.2, 114.0, 55.7. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265. GC-MS (m/z): 254 [M^+, $C_{16}H_{14}O_3$].

(E)-1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (18a)



^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.91-7.86 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 15.6 Hz, 1H), 7.49-7.45 (m, 2H), 7.00 (dd, *J* = 1.2, 8.8 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 2H), 3.84 (s, 3H), 1.68 (s, 1H, D_2O exchangeable). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 193.8, 163.7, 162.1, 145.5, 136.3, 130.7, 129.7, 127.4, 120.2, 118.9, 118.7, 117.7, 114.6, 55.6. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265. GC-MS (m/z): 254 [M^+, $C_{16}H_{14}O_3$].

(E)-1-(4-chlorophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (21a)



^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.92-7.84 (m, 2H), 7.64-7.58 (m, 3H), 7.53-7.49 (m, 1H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 2H), 4.84 (s, 1H, D_2O exchangeable). ^{13}C

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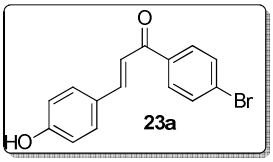
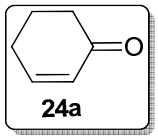
NMR ($CDCl_3$, 100 MHz, ppm) δ 193.6, 163.8, 144.1, 136.7, 133.2, 131.7, 130.0, 129.8, 129.5, 129.0, 120.7, 119.1, 118.9. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265. GC-MS (m/z): 258 [M^+, $C_{15}H_{11}ClO_2$], 260 $[M+2]^+$.

(E)-3-(4-bromophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (23a)



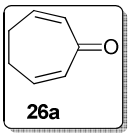
^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.99 (d, *J* = 8 Hz, 2H), 7.77 (d, *J* = 15.5 Hz, 1H), 7.63 (t, *J* = 8Hz, 2H), 7.46 (d, *J* = 15.5 Hz, 1H), 7.10 (t, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8 Hz, 2H), 5.48 (s, 1H, D_2O exchangeable). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 186.88, 162.05, 141.32, 131.41, 130.90, 130.83, 128.92, 121.85, 115.81, 115.21. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265, 1078, 862, 730. GC-MS (m/z): 302 [$M^{+\cdot}$, $C_{15}H_{11}BrO_2$], 304 [M+2].

Cyclohex-2-enone (24a)



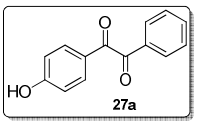
^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 6.71-6.69 (m, 1H), 5.90 (d, *J* = 10 Hz, 1H), 2.35 (t, *J* = 1 Hz, 2H), 1.91-1.89 (m, 2H), 1.72-1.66 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 198.1, 163.2, 127.1, 37.4, 24.5, 22.6. IR (KBr, ν_{max} = cm^{-1}): 1701, 1632. GC-MS (m/z): 96 [$M^{+\cdot}$, C_6H_8O].

Cyclohepta-2,6-dienone (26a)



^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 6.43 (d, *J* = 10.5 Hz, 2H), 6.31-6.29 (m, 2H), 2.34-2.26 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 194.8, 144.2, 135.1, 28.1. IR (KBr, ν_{max} = cm^{-1}): 1655, 1610, 1564, 1410. GC-MS (m/z): 108 [$M^{+\cdot}$, C_7H_8O].

1-(4-hydroxyphenyl)-2-phenylethane-1,2-dione (27a)



^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 7.99 (d, *J* = 7.5 Hz, 2H), 7.64-7.48 (m, 5H), 6.98 (d, *J* = 7.5 Hz, 2H), 5.48 (s, 1H, D_2O exchangeable). ^{13}C

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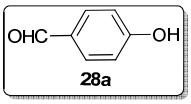
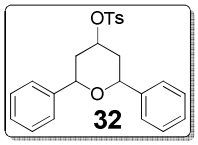
NMR ($CDCl_3$, 125 MHz, ppm) δ 191.7, 191.6, 162.6, 137.6, 134.7, 132.6, 130.7, 129.2, 124.7, 114.4. IR (KBr, ν_{max} = cm^{-1}): 3410, 1686, 1640. GC-MS (m/z): 226 [$M^{+\cdot}$, $C_{14}H_{10}O_3$].

4-hydroxybenzaldehyde (28a)



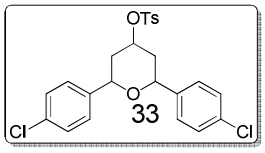
^{1}H NMR ($CDCl_3$, 500 MHz, ppm) δ 9.91 (s, 1H, D_2O exchangeable), 7.35 (d, *J* = 7.5 Hz, 2H), 6.94 (d, *J* = 8 Hz, 2H), 3.90 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz, ppm) δ 192.9, 163.0, 134.7, 130.2, 117.1. IR (KBr, ν_{max} = cm^{-1}): 3420, 2927, 2873, 1721. GC-MS (m/z): 122 [$M^{+\cdot}$, $C_7H_6O_2$].

2,6-diphenyltetrahydro-2H-pyran-4-yl 4-methylbenzenesulfonate (32)



^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 7.88 (d, *J* = 8Hz, 2H), 7.43-7.37 (m, 10H), 7.34-7.31 (m, 2H), 5.03 (tt, *J* = 4.5 and 11.5Hz, 1H), 4.59 (d, *J* = 11.5Hz, 2H), 2.48 (s, 3H), 2.34 (dd, *J* = 4.5, 12.5Hz, 2H), 1.88 (q, *J* = 12.5Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 144.7, 140.9, 134.2, 129.8, 128.3, 127.7, 127.5, 125.7, 78.1, 77.4, 61.2, 39.9, 21.5. IR (KBr, cm^{-1}): 3056, 3039, 2923, 2852, 2373, 1717, 1629, 1454, 1379, 1178, 1065, 945, 903, 757, 699.

2,6-bis(4-chlorophenyl)tetrahydro-2H-pyran-4-yl 4-methylbenzenesulfonate (33)



^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 7.80 (d, *J* = 8Hz, 2H), 7.35-7.27 (m, 10H), 4.93 (tt, *J* = 4.5, 11Hz, 1H), 4.50 (dd, *J* = 1.5, 11.5 Hz, 2H), 2.44 (s, 3H), 2.26 (dd, *J* = 4.5, 11.5Hz, 2H,), 1.75 (q, *J* = 11.5Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 145.0, 139.3, 134.2, 133.7, 130.0, 128.7, 127.6, 127.2, 77.6, 76.8, 39.9, 21.7.

(E)-2-(4-chlorophenyl)-6-(4-(3-(4-fluorophenyl)-3-oxoprop-1-en-1-yl)phenyl)tetrahydro-2H-pyran-4-yl 4-methylbenzenesulfonate (34)

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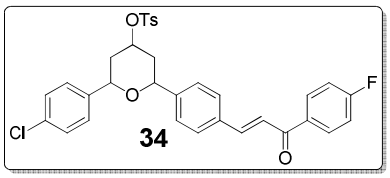
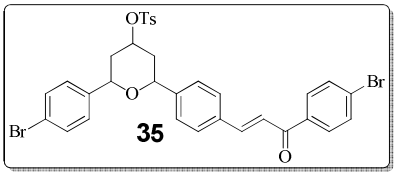


^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 8.02-8.05 (m, 4H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 5 Hz, 1H), 7.75 (d, *J* = 5 Hz, 1H), 7.60 (dd, *J* = 8, 2.5 Hz, 4H), 7.47 (d, *J* = 15.5 Hz, 2H), 7.39 (dd, *J* = 8.5, 3 Hz, 3H), 7.33 (d, *J* = 8 Hz, 2H), 4.96 (tt, *J* = 11, 4.5 Hz, 1H), 4.56-4.49 (m, 2H), 2.43 (s, 3H), 2.25-2.33 (m, 2H), 1.76-1.83 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 188.8, 164.6, 146.9, 144.8, 143.4, 139.3, 134.3, 134.1, 133.8, 133.6, 131.7, 131.1, 130.0, 128.6, 128.6, 127.6, 127.2, 126.4, 121.2, 77.6, 77.3, 76.9, 39.8, 39.8, 21.7. IR (KBr, cm^{-1}): 3000, 2945, 1678, 1614, 1350, 1200, 1121, 861. HRMS (ESIMS) for $C_{33}H_{28}ClFNaO_5S$ $(M+Na)^+$ Anal. calcd. 613.1228; found 613.1220.

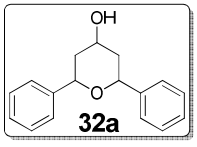
(E)-2-(4-bromophenyl)-6-(4-(3-(4-bromophenyl)-3-oxoprop-1-en-1yl)phenyl)tetrahydro-2H-pyran-4-yl 4-methylbenzenesulfonate (35)



^{1}H NMR (500MHz, $CDCl_3$, ppm): δ 7.86 (dd, *J* = 8.5, 2Hz, 4H), 7.60 (dd, *J* = 10.5, 8.5 Hz, 6H), 7.39-7.46 (m, 6H), 7.33 (d, *J* = 8 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 1H), 4.95 (tt, *J* = 6.5, 3Hz, 1H), 4.52 (dd, *J* = 28, 10 Hz, 2H), 2.43 (s, 3H), 2.29 (dd, *J* = 24, 12.5Hz, 2H), 1.77 (q, *J* = 11 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 189.18, 146.84, 143.35, 139.67, 136.75, 133.91, 133.67, 131.78, 131.46, 129.90, 128.50, 127.46, 127.42, 126.33, 121.03, 118.61, 77.43, 76.73, 72.70, 39.65, 21.55. IR (KBr, cm^{-1}): 3000, 2945, 1678, 1614, 1350, 1200, 1121, 861. HRMS (ESIMS) for $C_{33}H_{28}Br_2NaO_5S$ $(M+Na)^+$ Anal. calcd. 716.9922; found 716.9900.

(c) Spectral data of OTs deprotected product:

2,6-diphenyltetrahydro-2H-pyran-4-ol (32a)



^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 7.19-7.41 (m, 8H), 4.51-4.43 (m, 2H), 4.07 (tt, *J* = 4.5, 11.5 Hz, 1H), 2.28 (s, br, D_2O exchangeable, 1H, OH), 2.21 (dd, *J* = 4, 11.5Hz, 2H), 1.53 (q, *J* = 11.5 Hz, 2H). ^{13}C NMR (125

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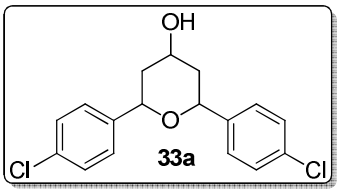
MHz, $CDCl_3$, ppm): δ 131.4, 128.3, 127.5, 125.8, 77.8, 68.6, 42.9. IR (KBr, cm^{-1}): 3433, 2965, 2921, 2852, 1634, 1452, 1382, 1265, 1156, 1065, 900, 760, 700. GC-MS (m/z): 410 [M^+, $C_{17}H_{18}O_2$].

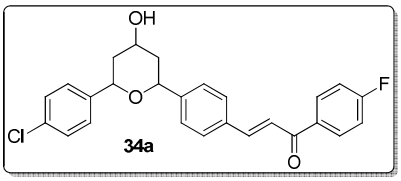
2,6-bis(4-chlorophenyl)tetrahydro-2H-pyran-4-ol (33a)



33a

^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 7.29-7.24 (m, 8H), 4.47 (d, *J* = 11.5 Hz, 2H), 4.06 (tt, *J* = 4.5, 11.5 Hz, 1H), 2.19 (dd, *J* = 4, 11.5 Hz, 2H), 1.48 (q, *J* = 11.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 139.2, 132.3, 127.5, 126.2, 77.8, 67.4, 41.9. IR (KBr, cm^{-1}): 3447, 2960, 2886, 1652, 1543, 1088, 804. GC-MS (m/z): 323 [M^+, $C_{17}H_{16}Cl_2O_2$].

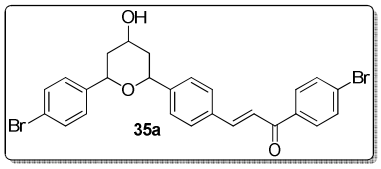
(E)-3-(4-(6-(4-chlorophenyl)-4-hydroxytetrahydro-2H-pyran-2-yl)phenyl)-1-(4-fluorophenyl)prop-2-en-1-one (34a)



34a

^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 8.18 (d, *J* = 8 Hz, 1H), 7.95 (d, *J* = 8 Hz, 2H), 7.59 (d, *J* = 9 Hz, 3H), 7.48 (d, *J* = 8 Hz, 2H), 7.41 (d, *J* = 9 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 9 Hz, 2H), 4.66 (t, *J* = 3 Hz, 2H), 4.14 (tt, *J* = 11, 3 Hz, 1H), 2.22-2.85 (m, 2H), 2.04 (s, br, D_2O exchangeable, 1H), 1.73-1.84 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 188.8, 166.7, 164.6, 144.6, 143.7, 140.8, 134.5, 134.3, 131.2, 130.0, 128.7, 127.7, 126.5, 125.9, 121.6, 115.9, 78.0, 77.7, 69.4, 40.0. IR (KBr, cm^{-1}): 3434, 3010, 2922, 2843, 1734, 1626, 1456, 1256, 1069, 808.8. HRMS (ESIMS): for $C_{26}H_{22}ClFNaO_3$ $(M+Na)^+$ Anal. calcd. 459.1139; found 459.1150.

(E)-1-(4-bromophenyl)-3-(4-(6-(4-bromophenyl)-4-hydroxytetrahydro-2H-pyran-2-yl)phenyl)prop-2-en-1-one (35a)



35a

^{1}H NMR (500 MHz, $CDCl_3$, ppm): δ 7.88 (d, *J* = 8 Hz, 2H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.78 (s, 1H), 7.61-7.66 (m, 4H), 7.47 (s, 1H), 7.35 (d, *J* = 8 Hz, 2H), 7.31-7.32 (m, 2H), 4.45

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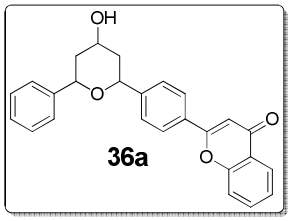
(d, J = 32, 11.5 Hz, 2H), 4.07 (tt, J = 10.5, 3 Hz, 1H), 2.30-2.35 (m, 2H), 2.20 (s, br, D_2O exchangeable, 1H), 1.77-1.86 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 189.8, 143.7, 140.7, 135.4, 134.4, 134.1, 129.8, 129.2, 128.5, 128.4, 127.8, 127.5, 126.2, 125.7, 122.0, 77.8, 77.4, 67.2, 39.8. IR (KBr, cm^{-1}): 3454, 2961, 2878, 1651, 1541, 1091, 801. HRMS (ESIMS): for $C_{26}H_{22}Br_2NaO_3$ $(M+Na)^+$ Anal. calcd. 562.9833; found 562.9853.

2-(4-(4-hydroxy-6-phenyltetrahydro-2H-pyran-2-yl)phenyl)-4H-chromen-4-one (36a)



36a

^1H NMR (500 MHz, $CDCl_3$, ppm): δ 7.74 (d, J = 8 Hz, 2H), 7.37 (dd, J = 6, 3 Hz, 2H), 7.27 (d, J = 8.5 Hz, 2H), 7.17-7.21 (m, 3H), 7.15 (d, J = 8.5 Hz, 2H), 6.92 (s, 1H), 6.79 (dd, J = 6.5, 3 Hz, 2H), 4.40 (t, J = 11.5 Hz, 2H), 3.90 (tt, J = 11, 3 Hz, 1H), 2.15-2.22 (m, 2H), 1.68-1.77 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm): δ 190.0, 163.0, 156.0, 139.8, 135.5, 134.1, 131.6, 129.9, 129.3, 128.6, 128.6, 127.6, 127.5, 126.3, 122.2, 121.8, 77.1, 76.9, 65.0, 39.8, 39.7. IR (KBr, cm^{-1}): 3446, 2971, 2880, 1652, 1513, 1208, 799. HRMS (ESIMS): for $C_{26}H_{21}NaO_4$ $(M+Na)^+$ Anal. calcd. 421.1416; found 421.1441.

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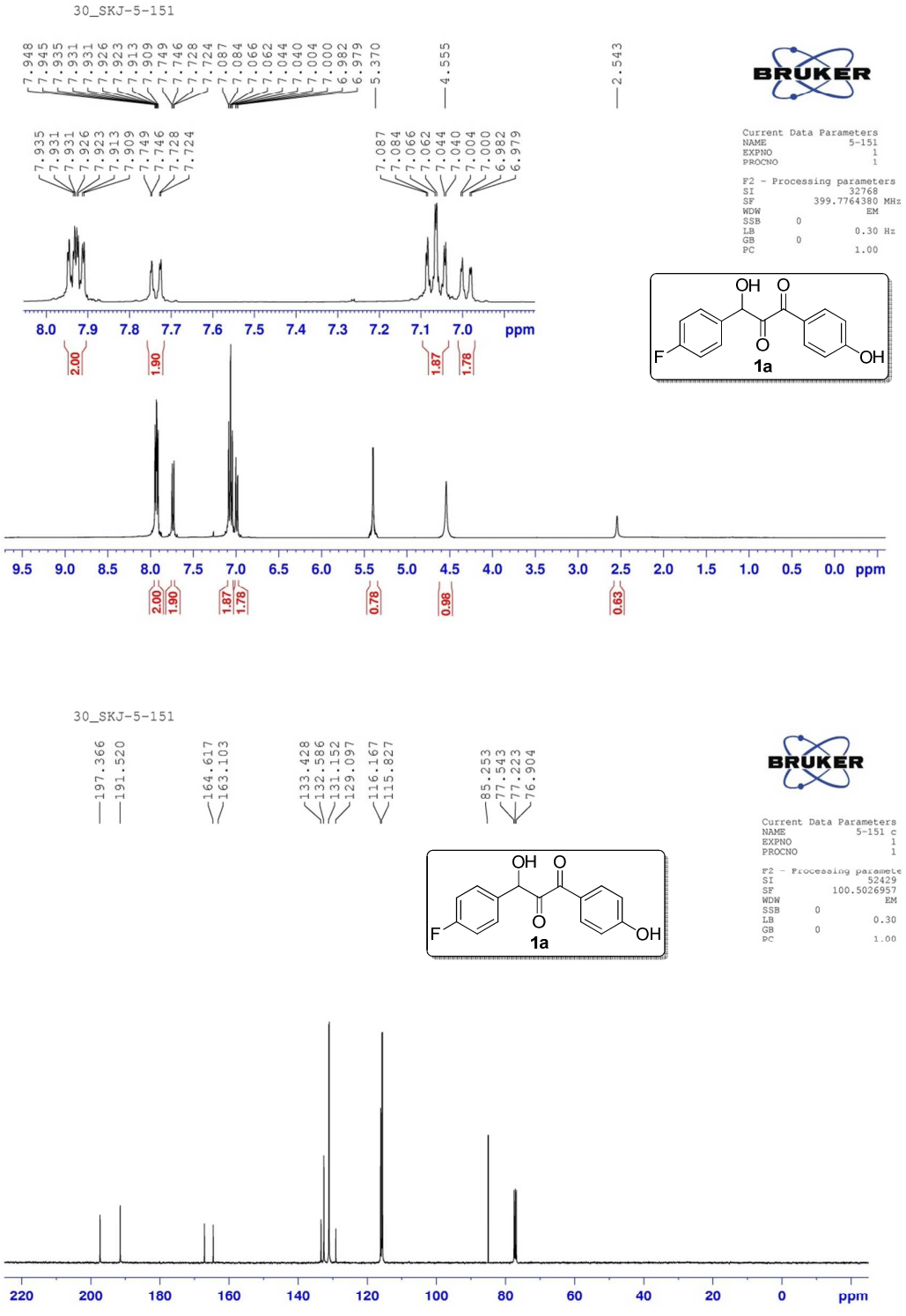
4. ^{1}H and ^{13}C NMR Spectra of representative compounds.



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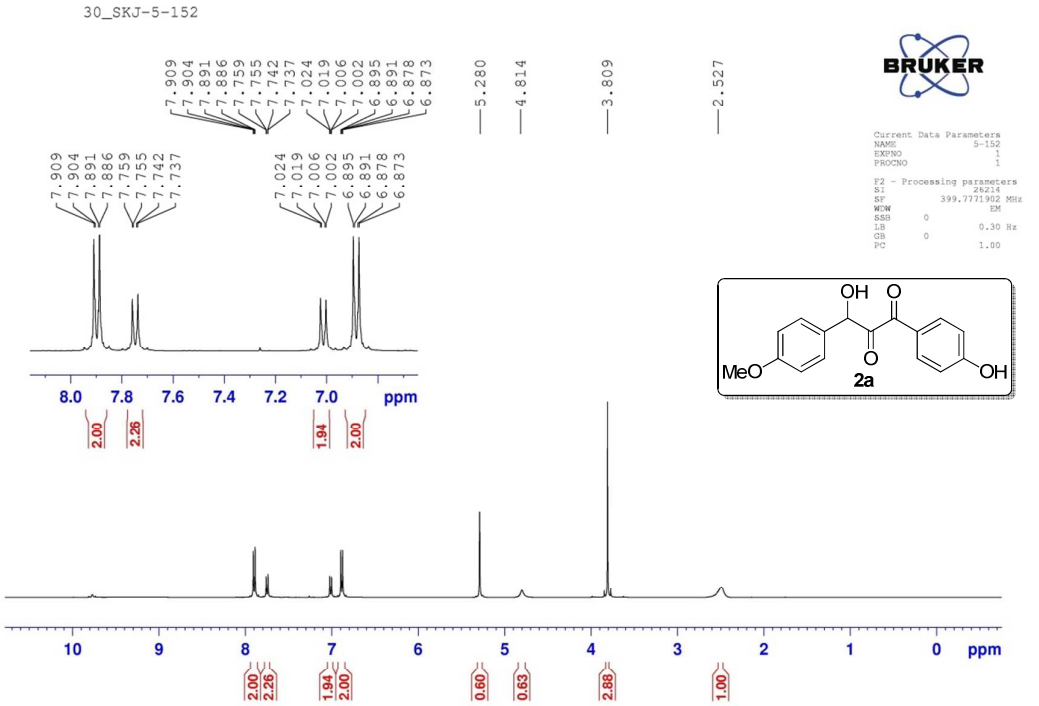

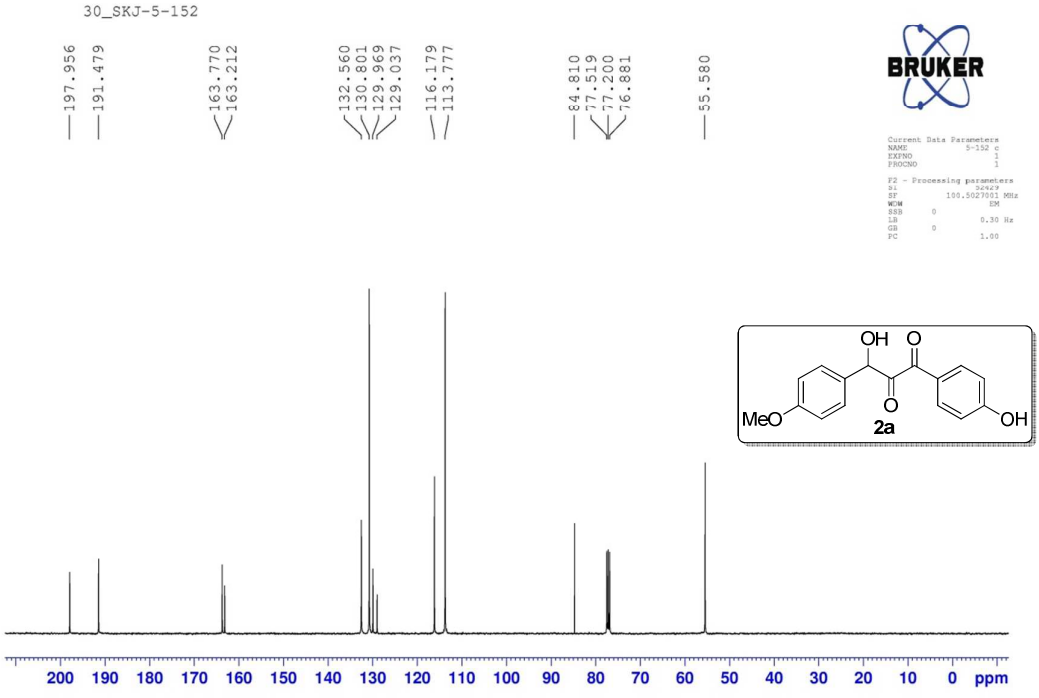

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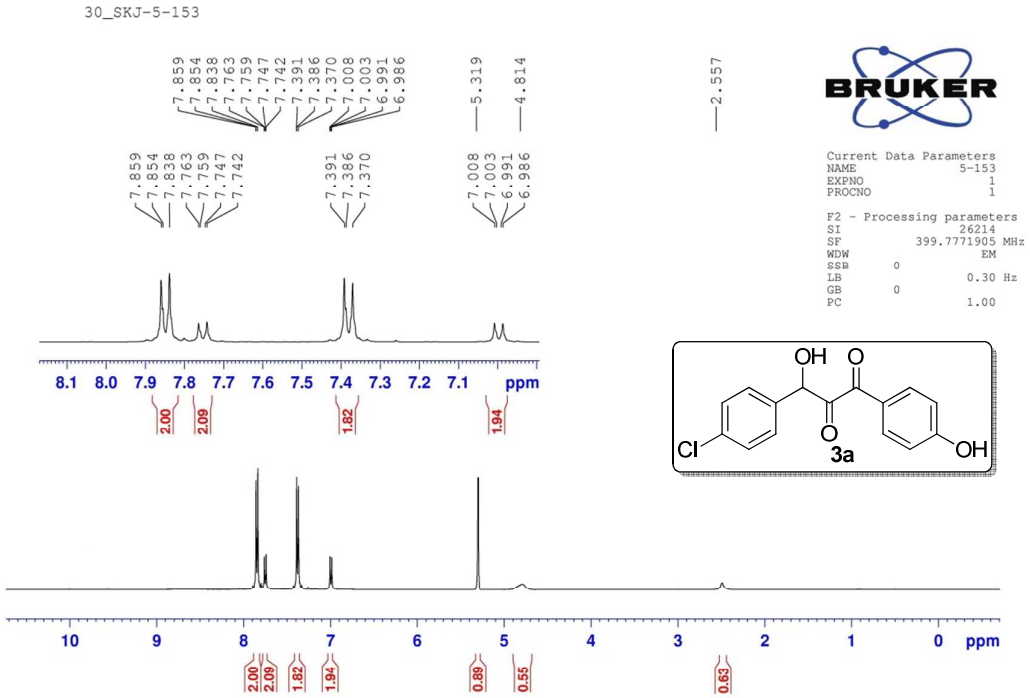

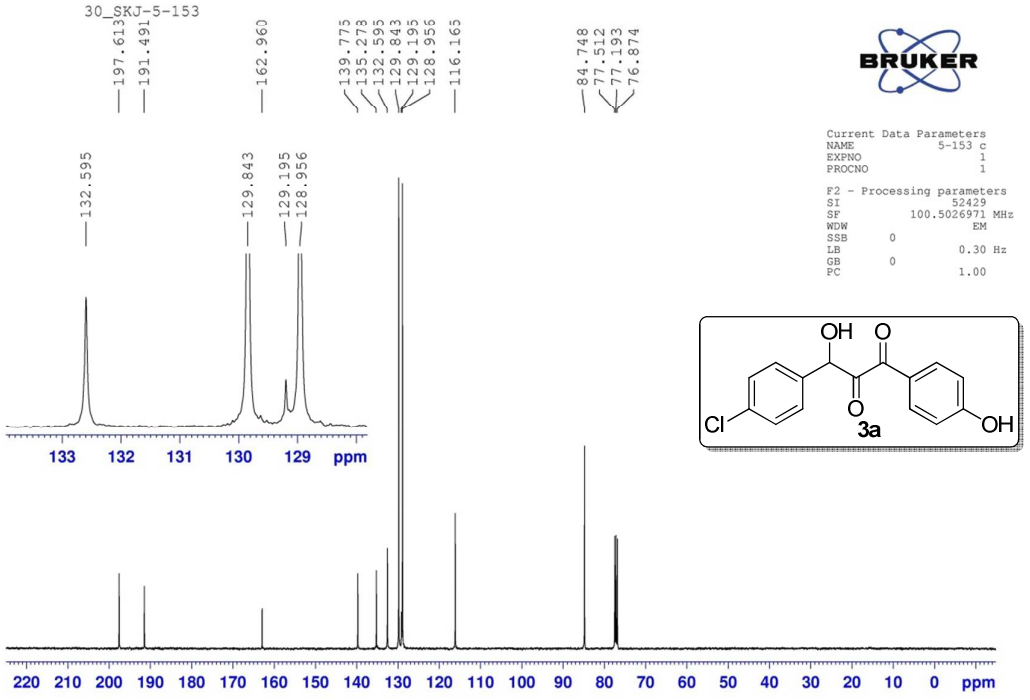

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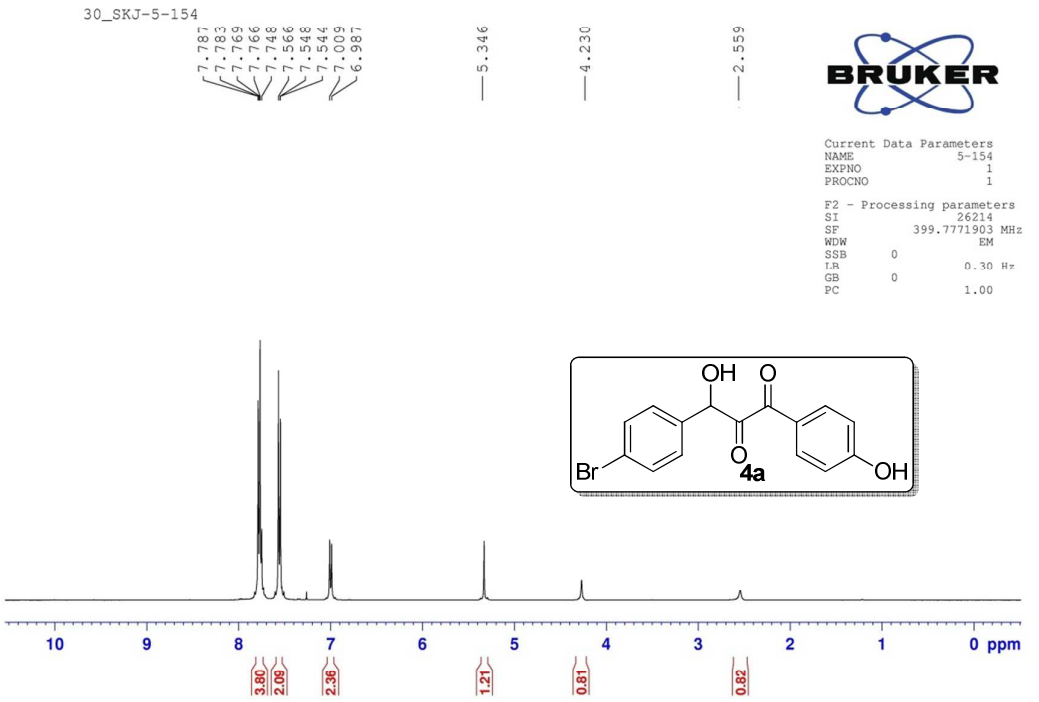

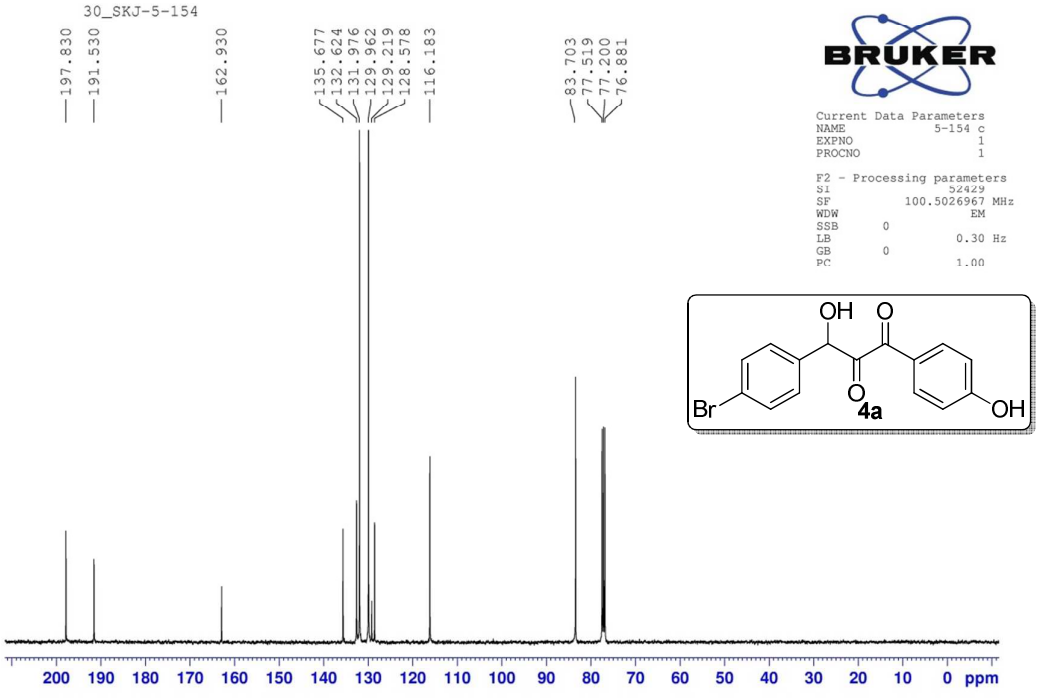

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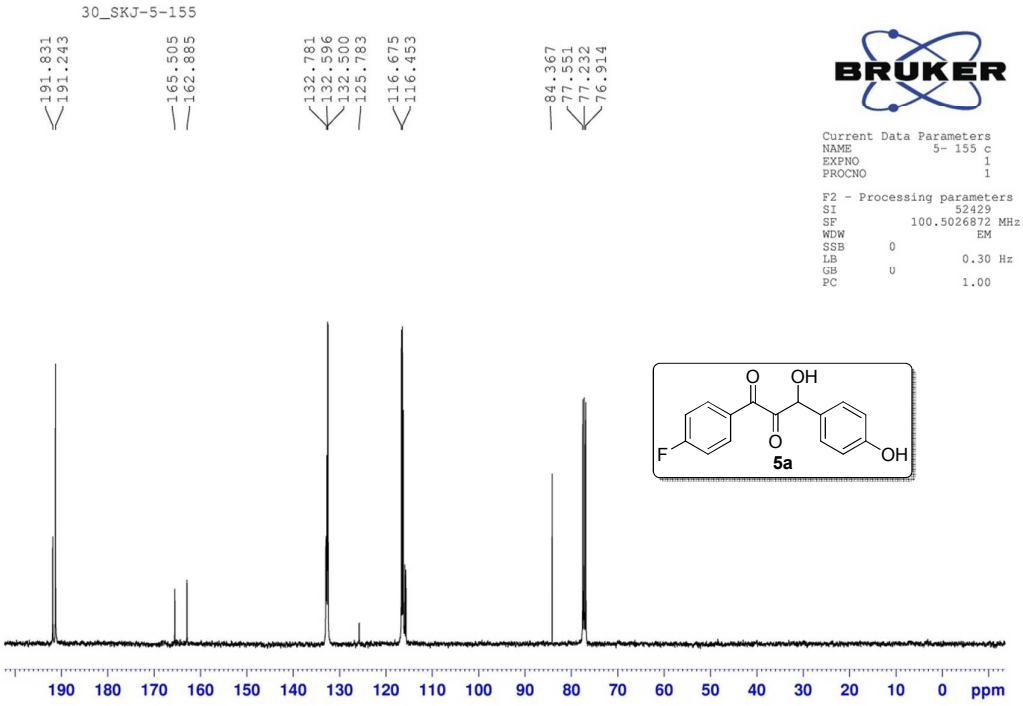

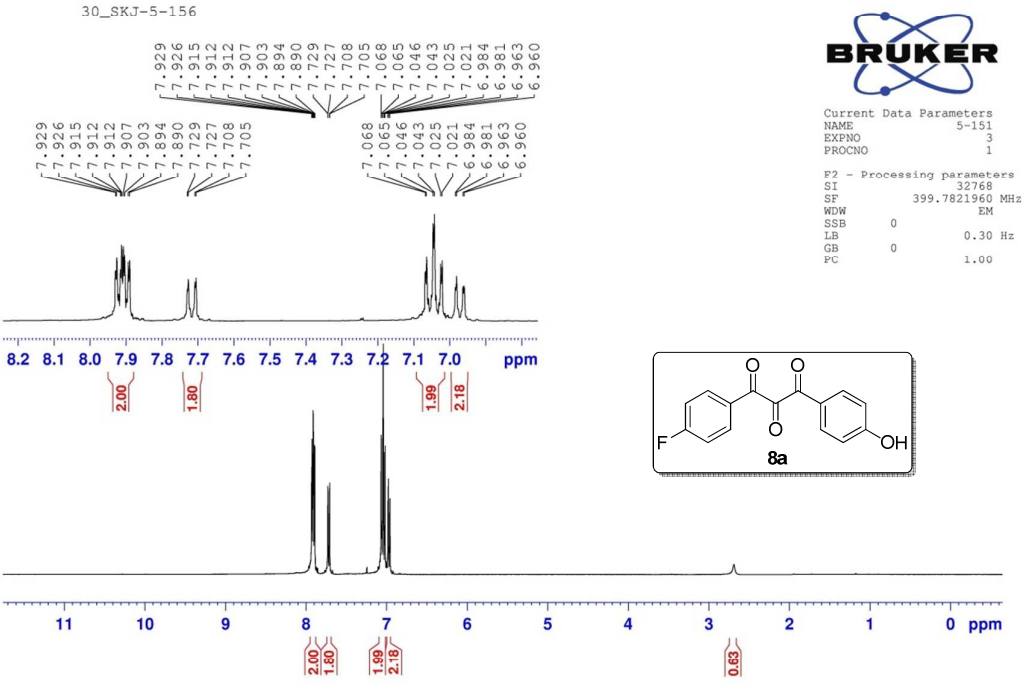

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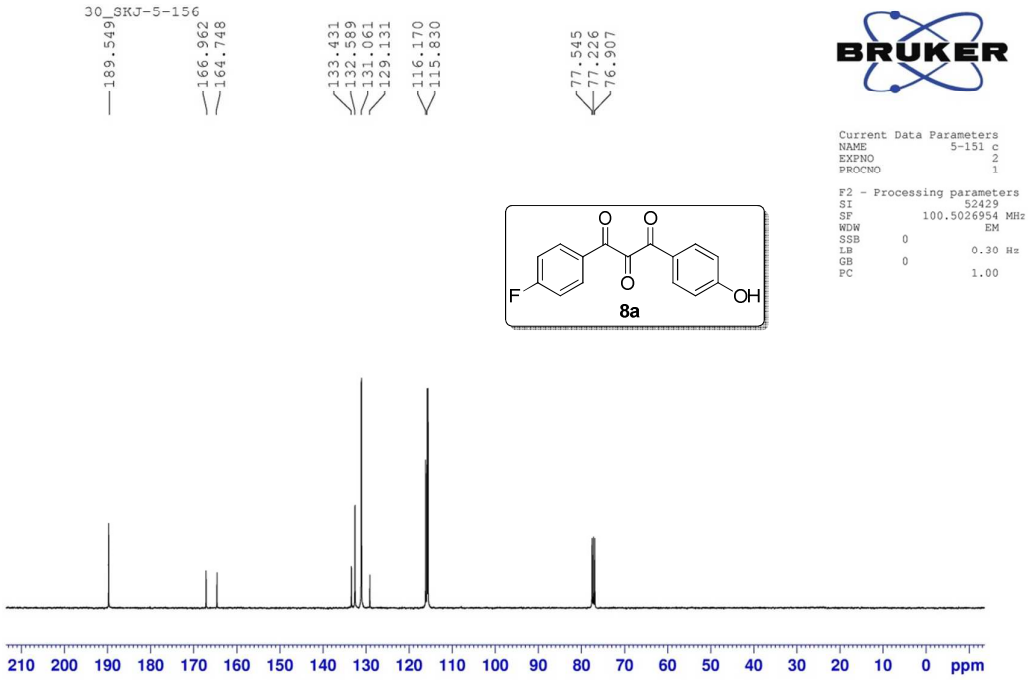

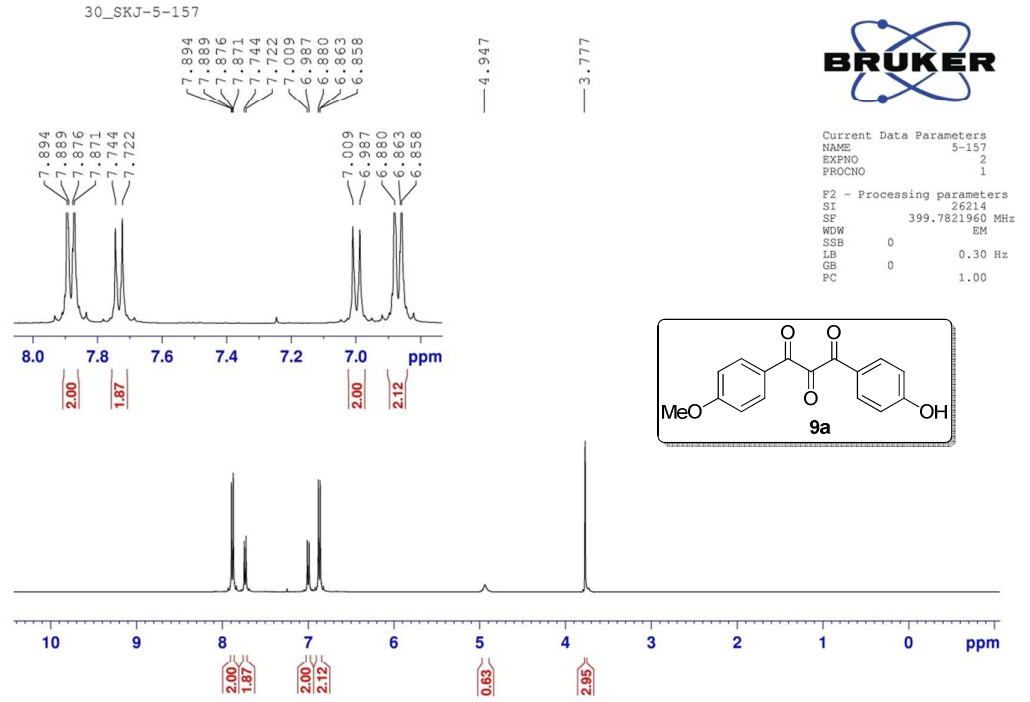

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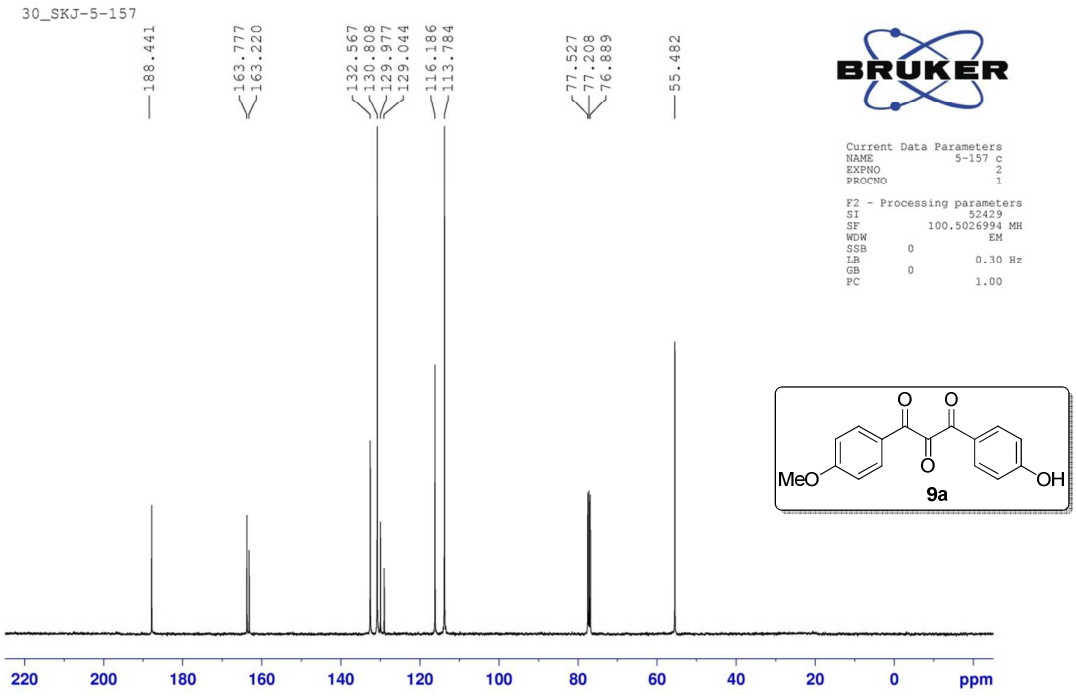

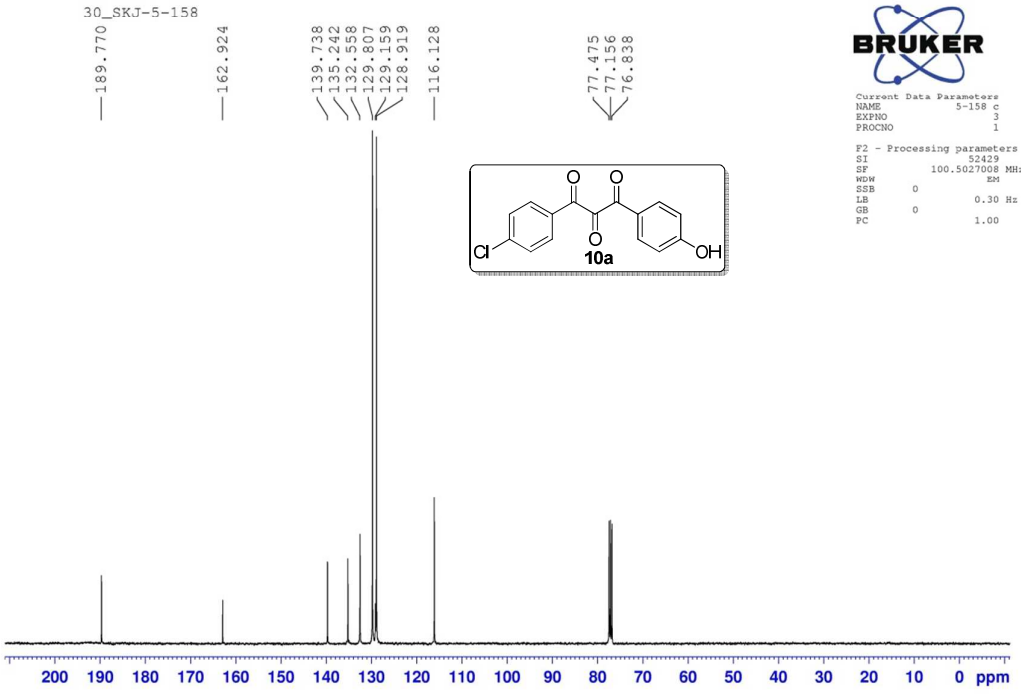

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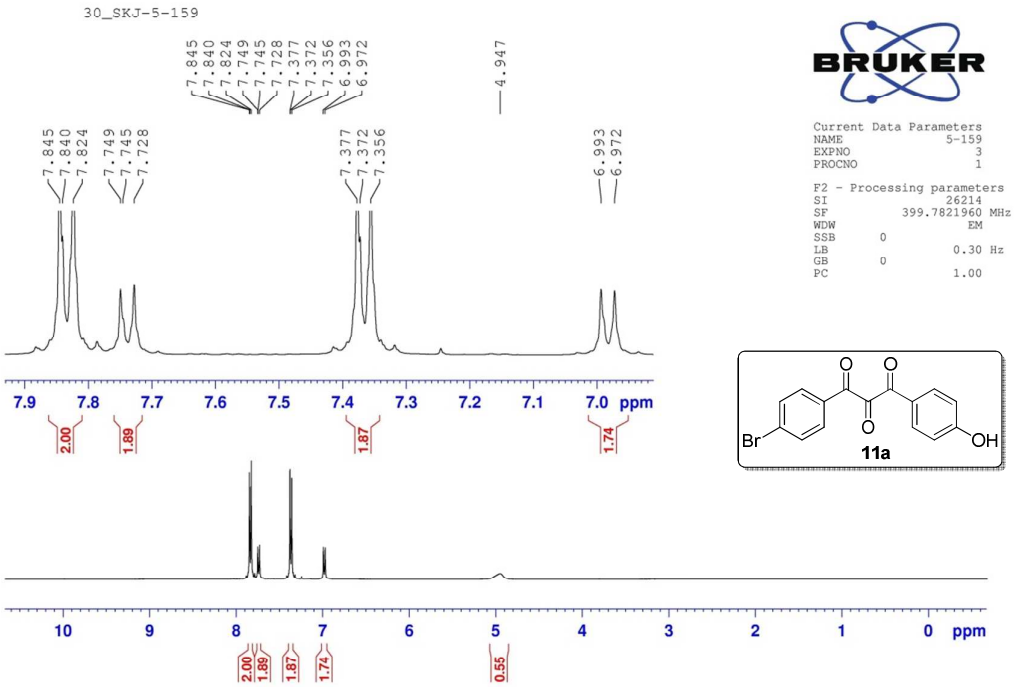

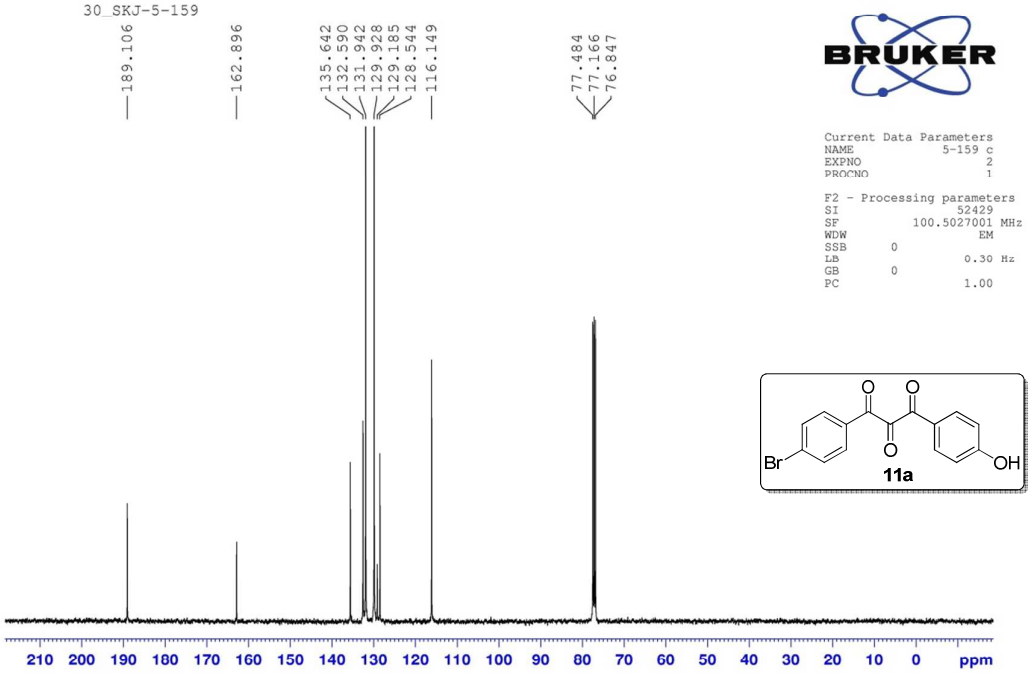

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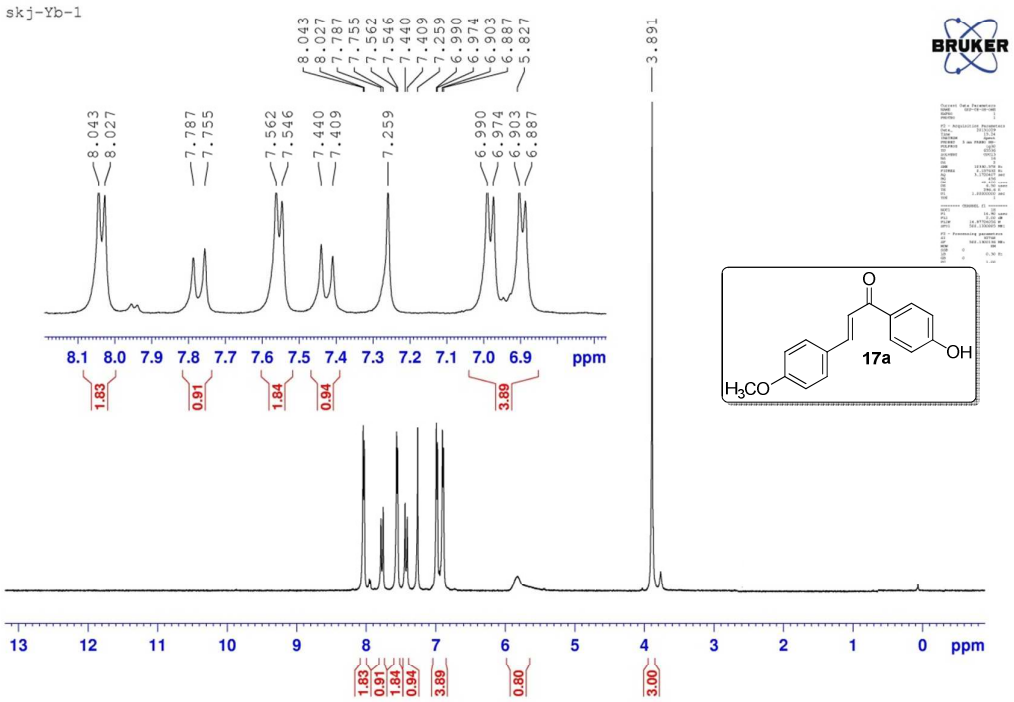

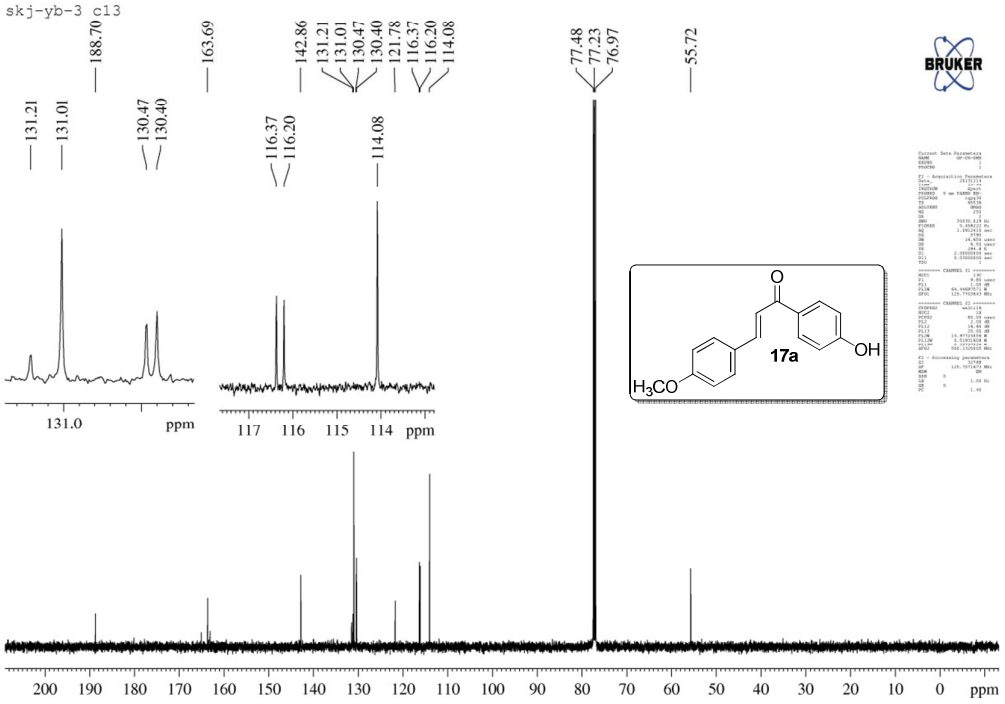

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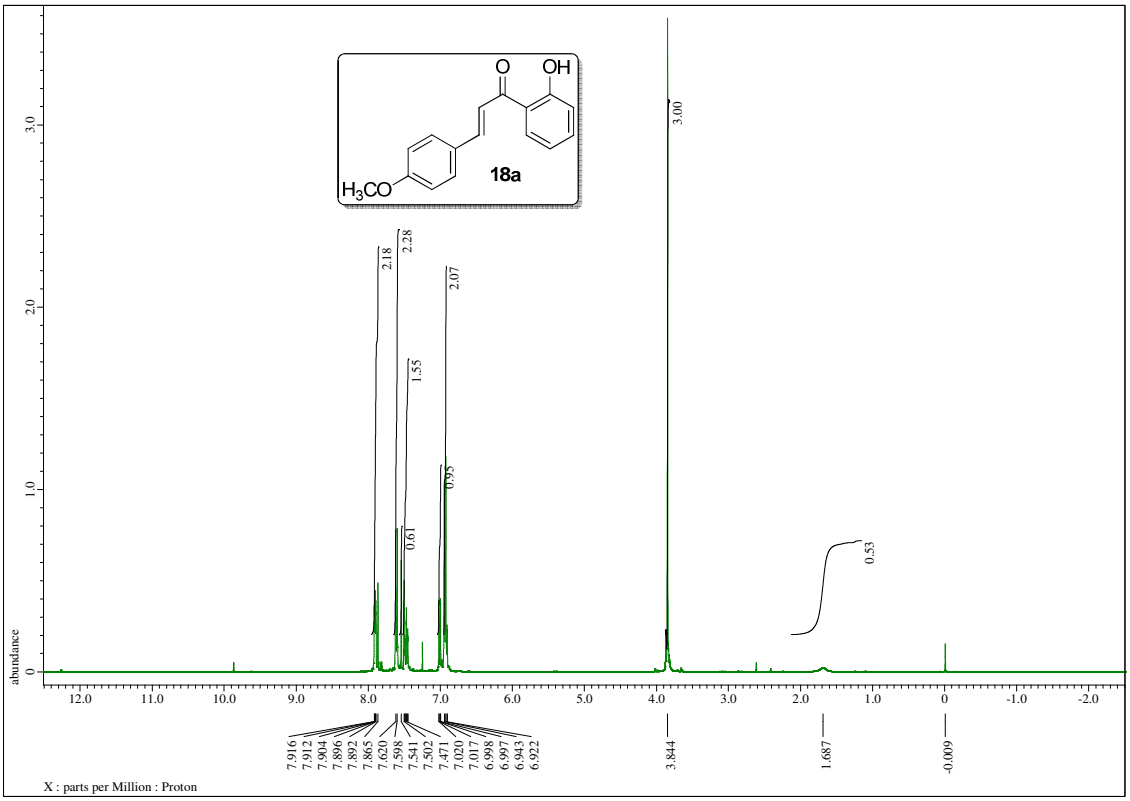

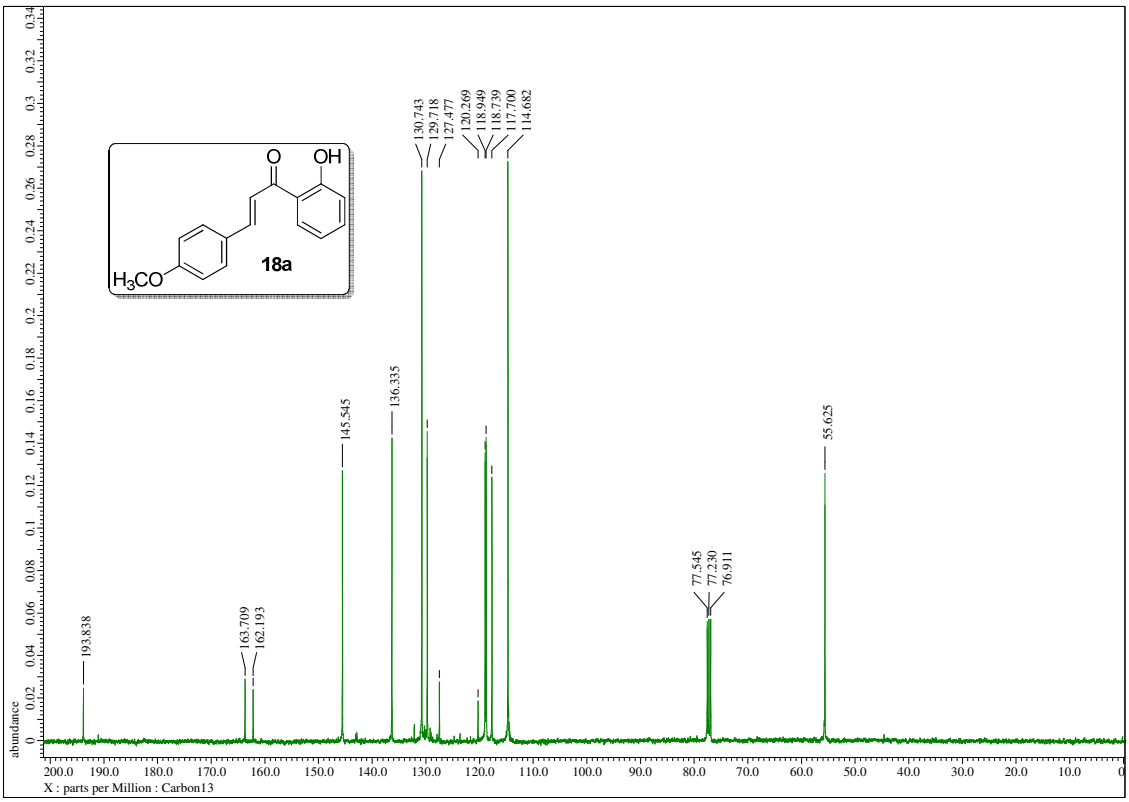

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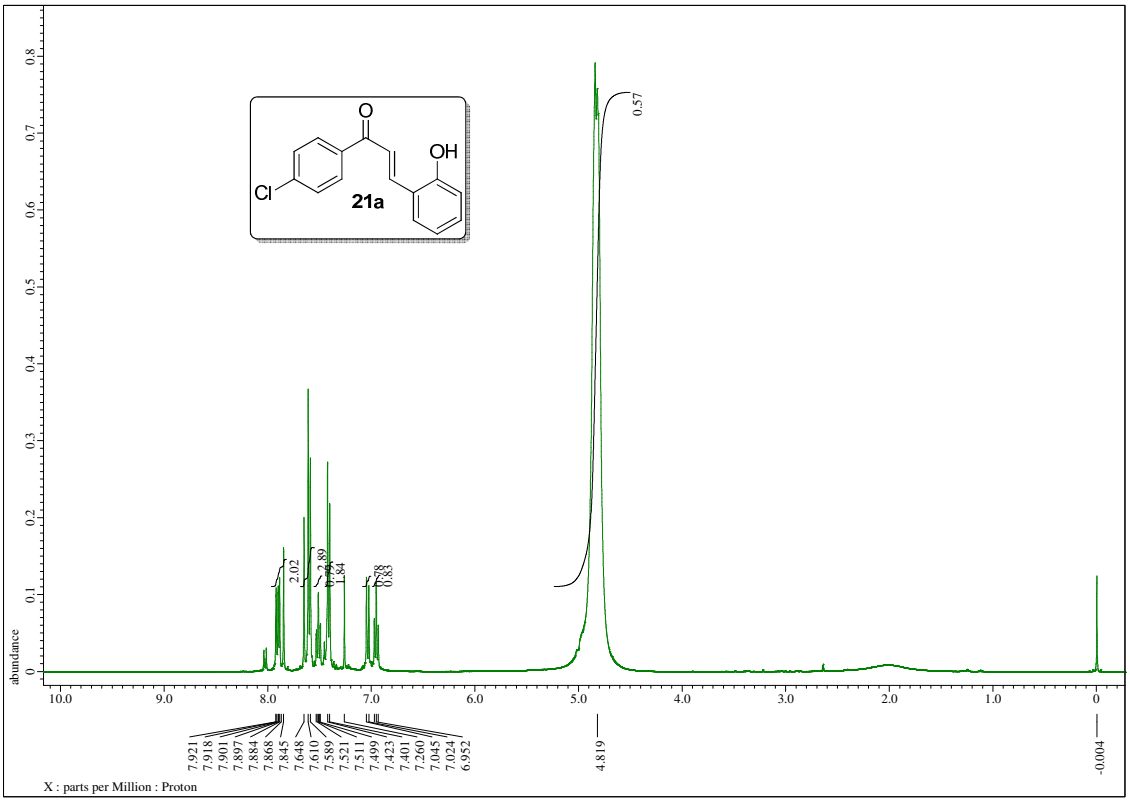

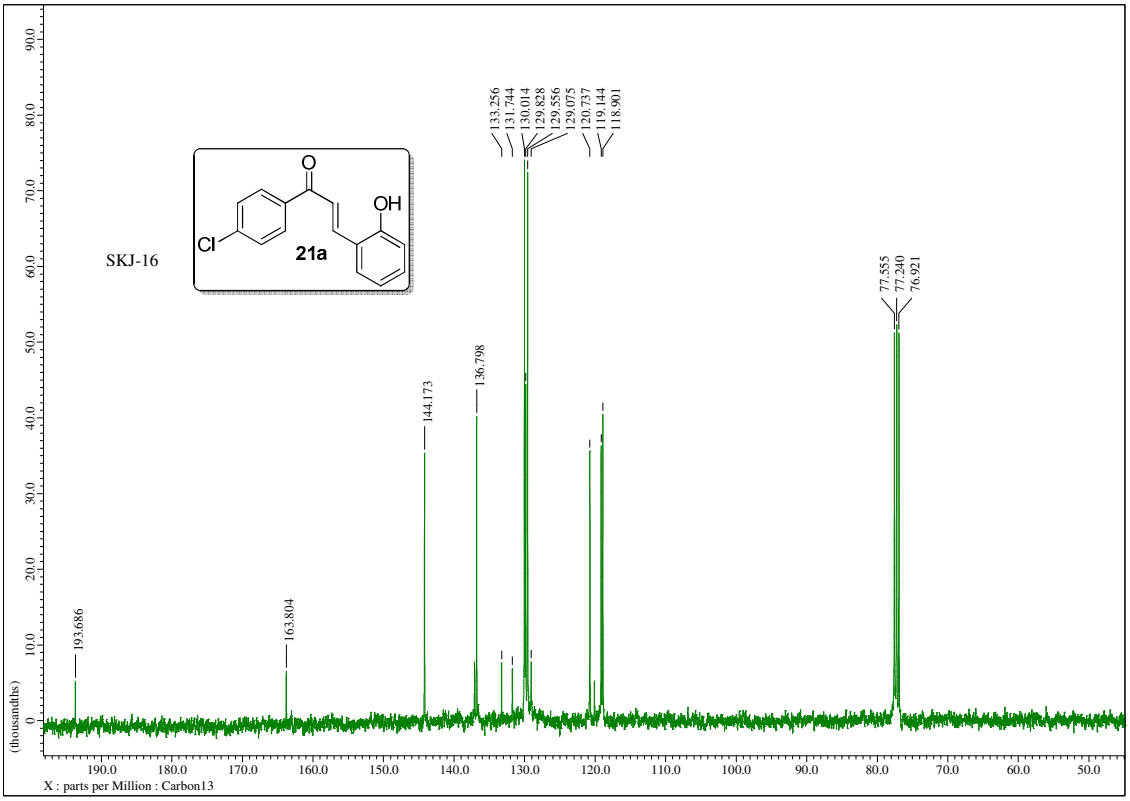

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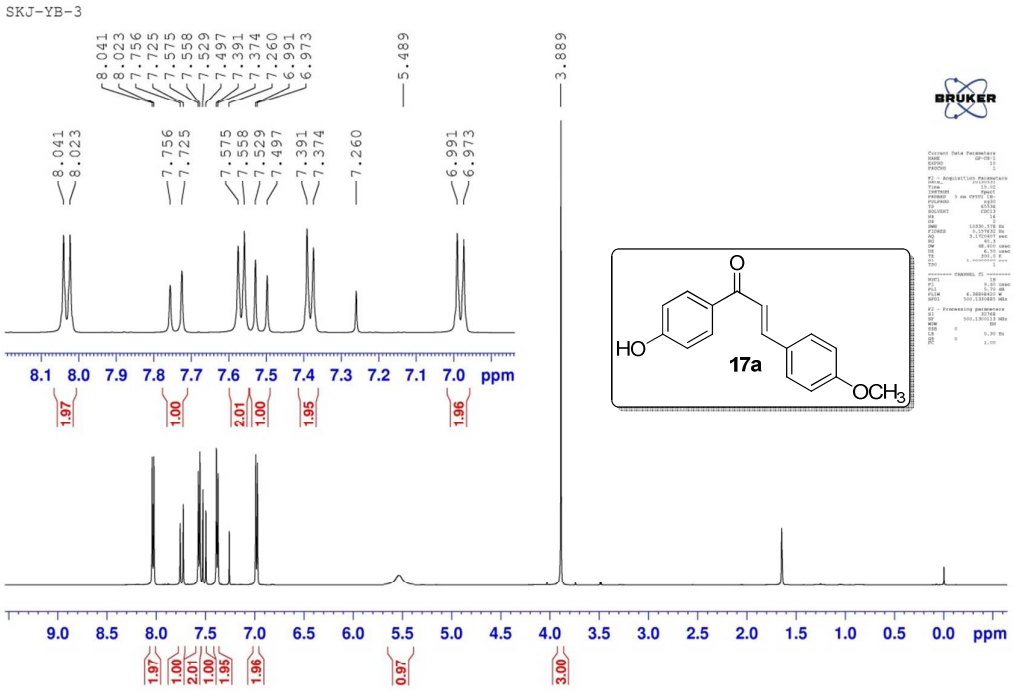

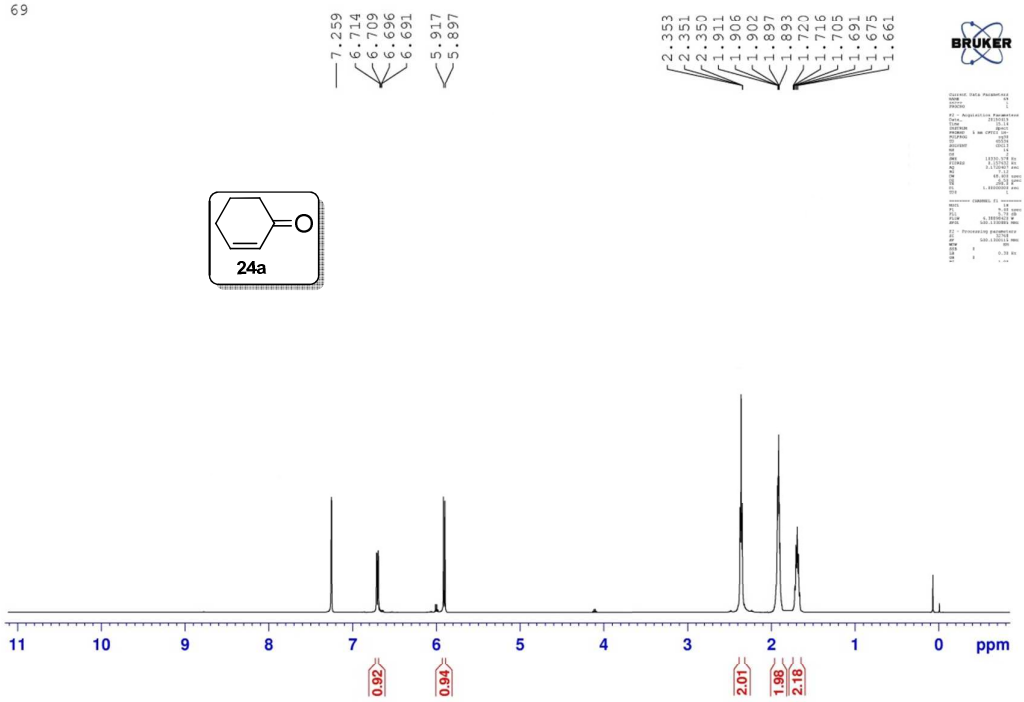

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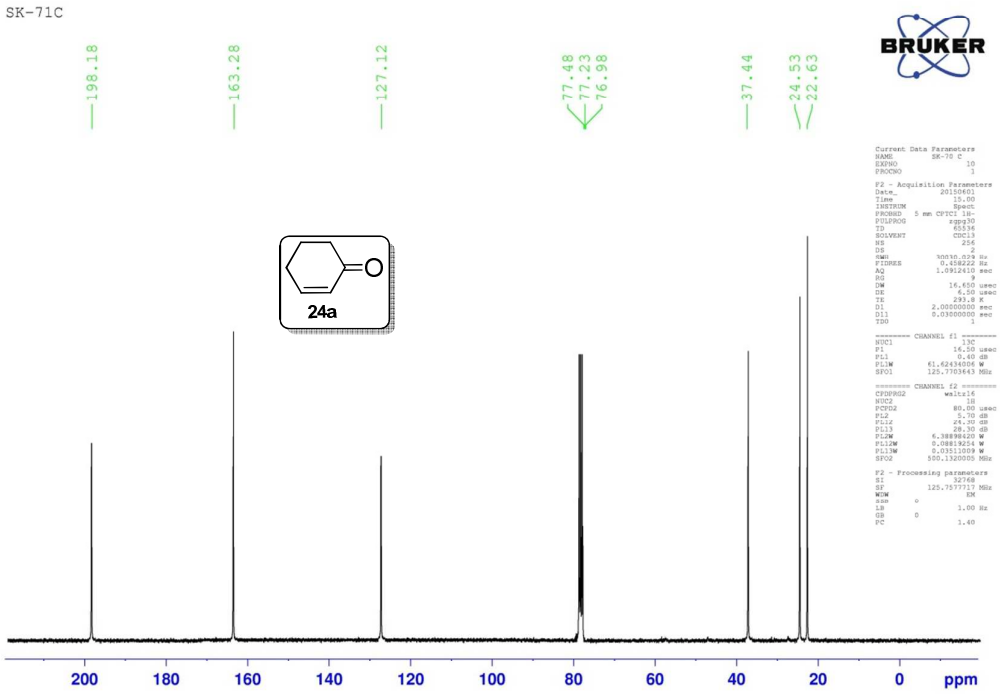

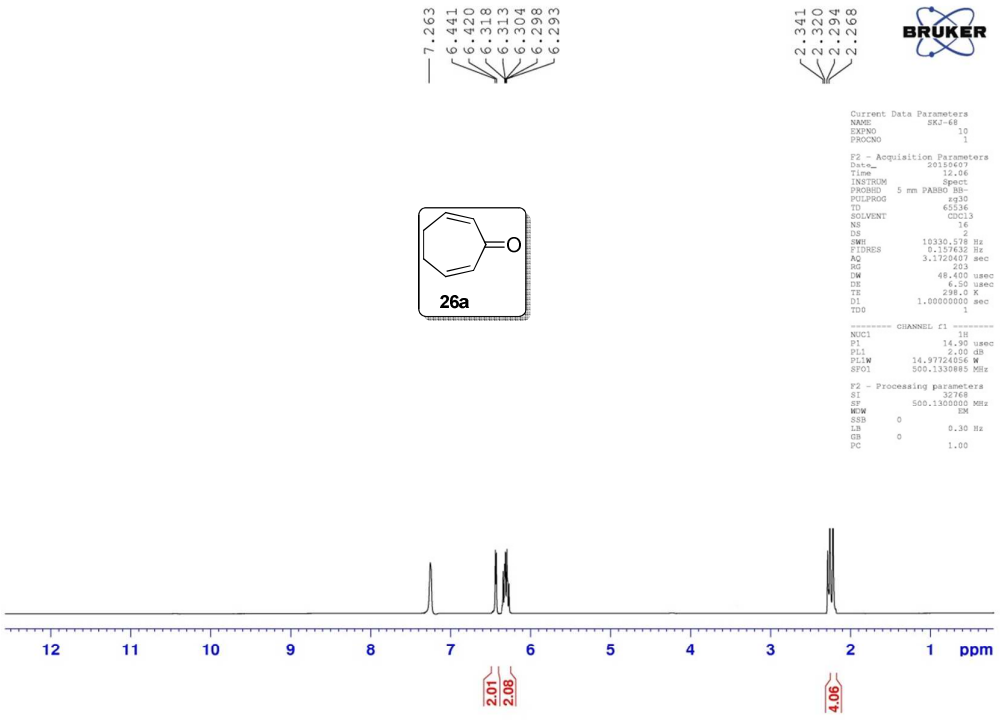

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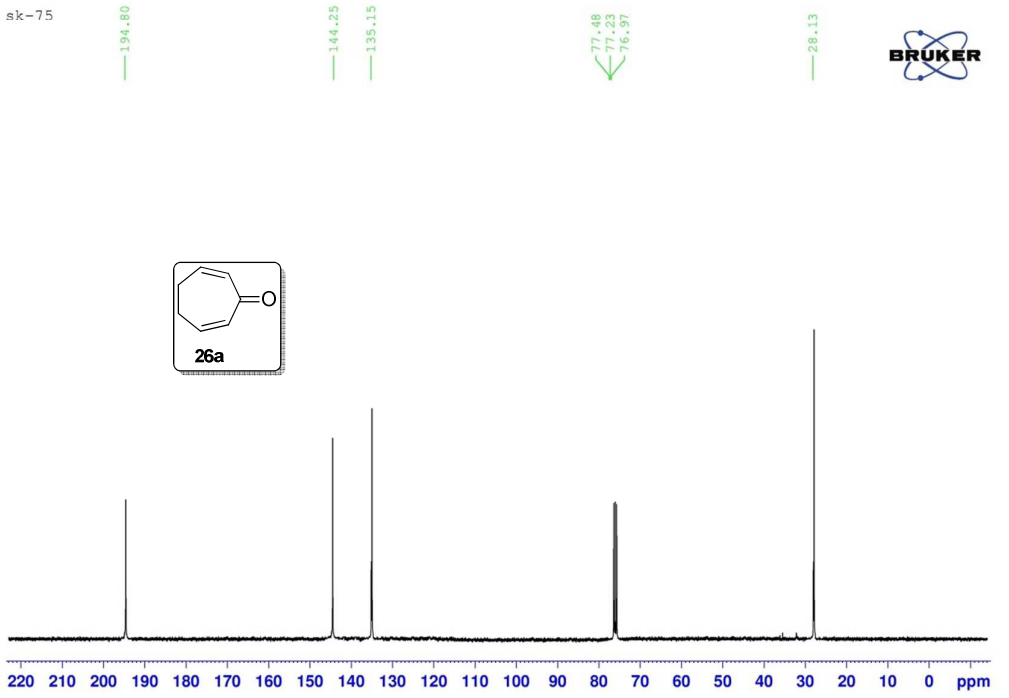

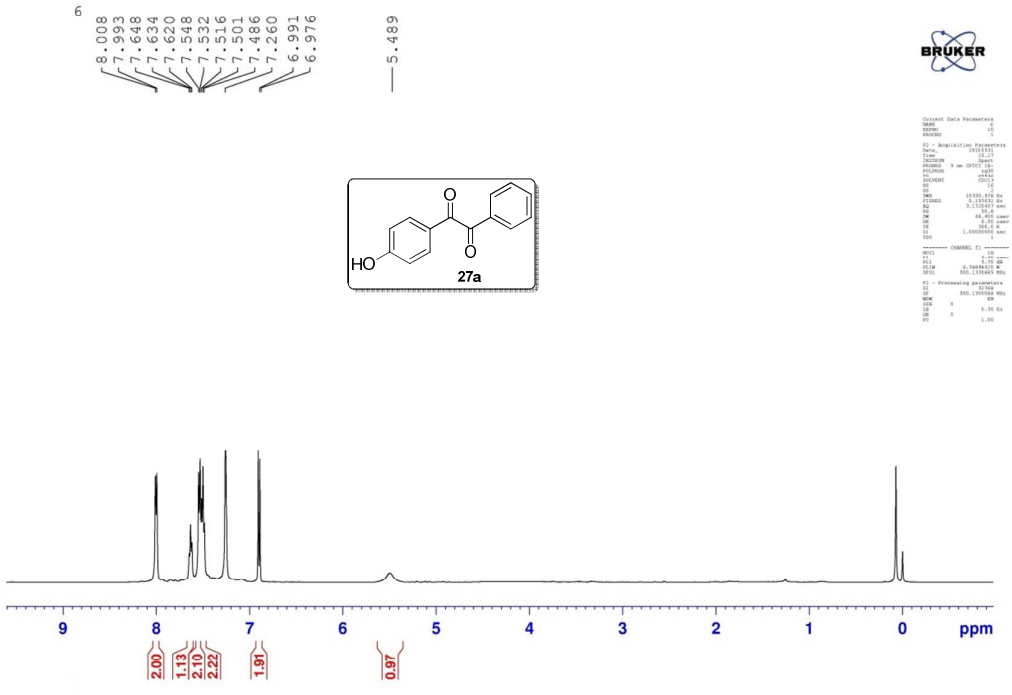

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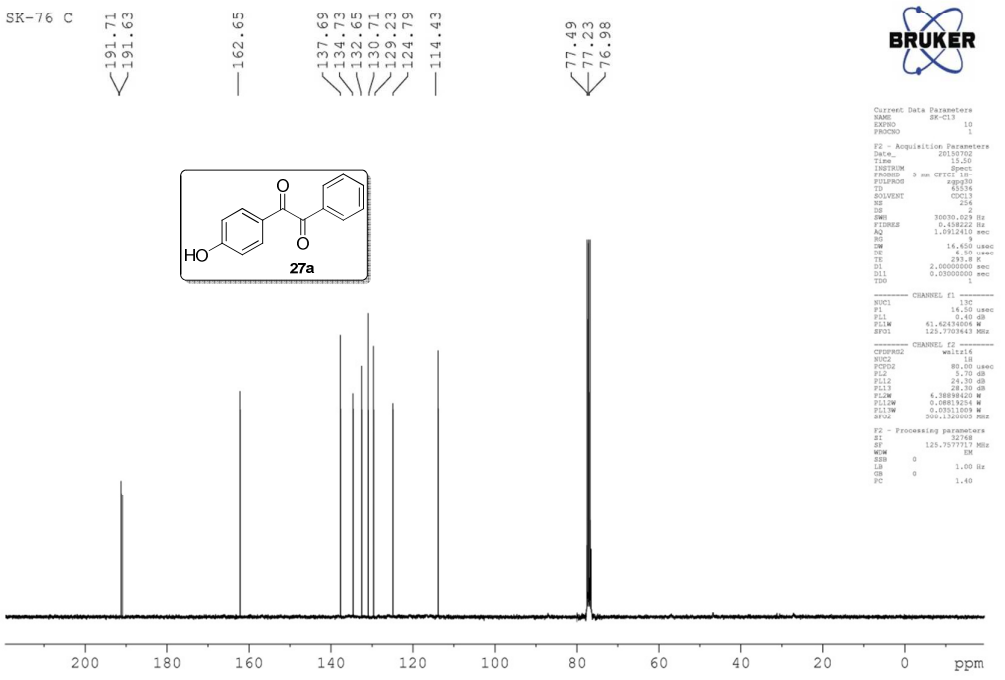

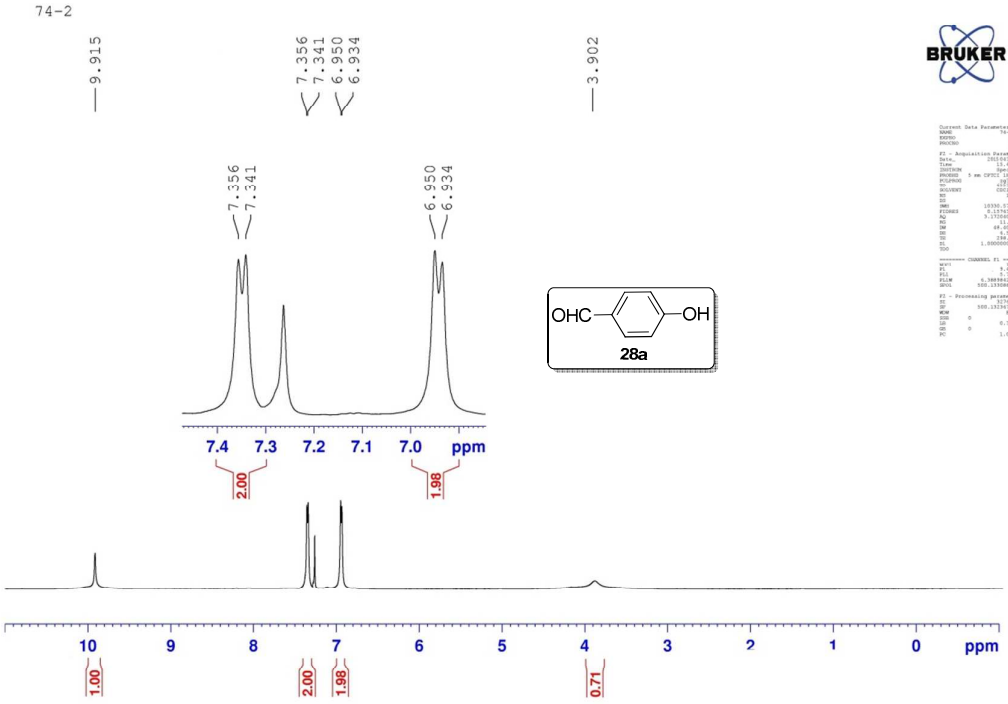

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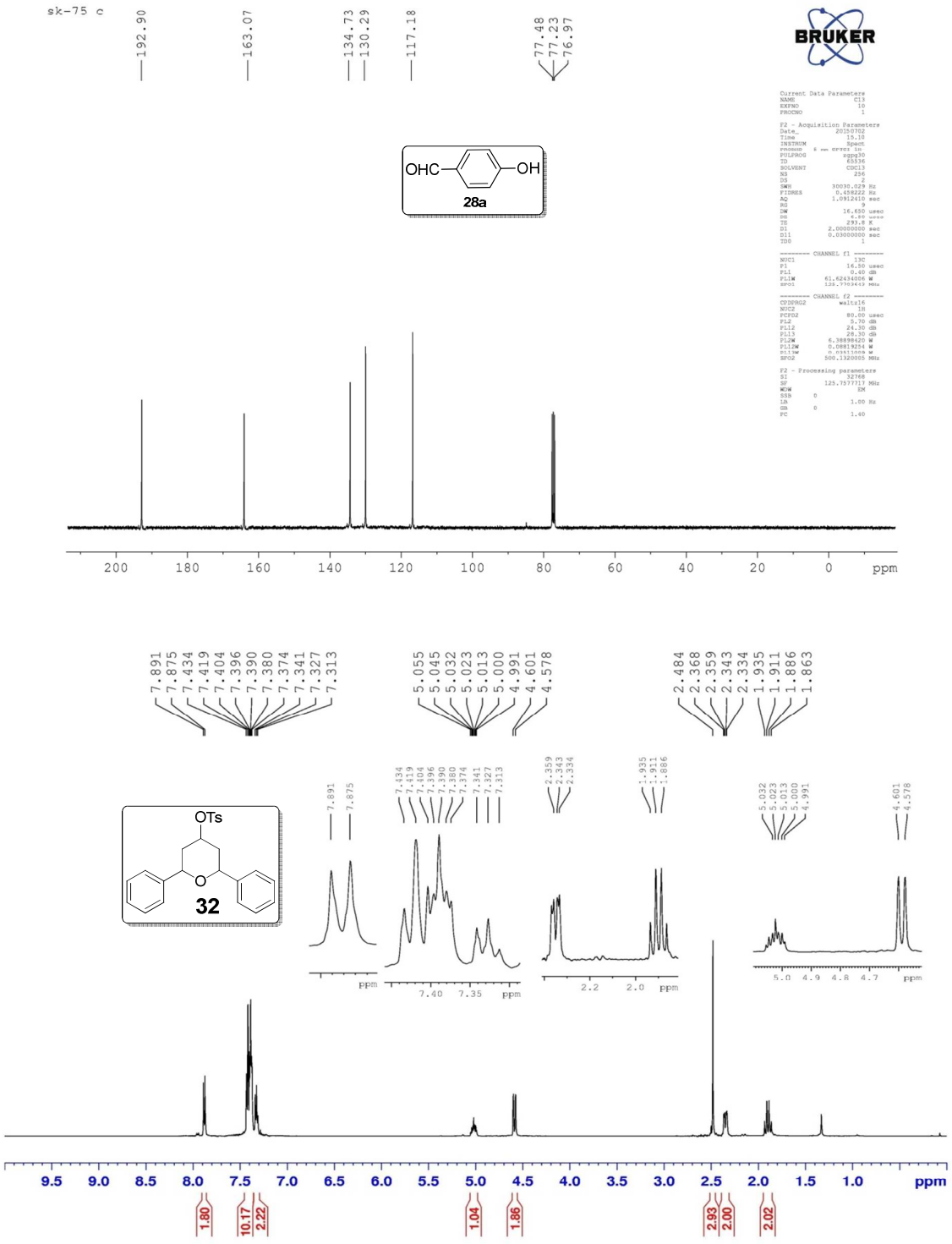

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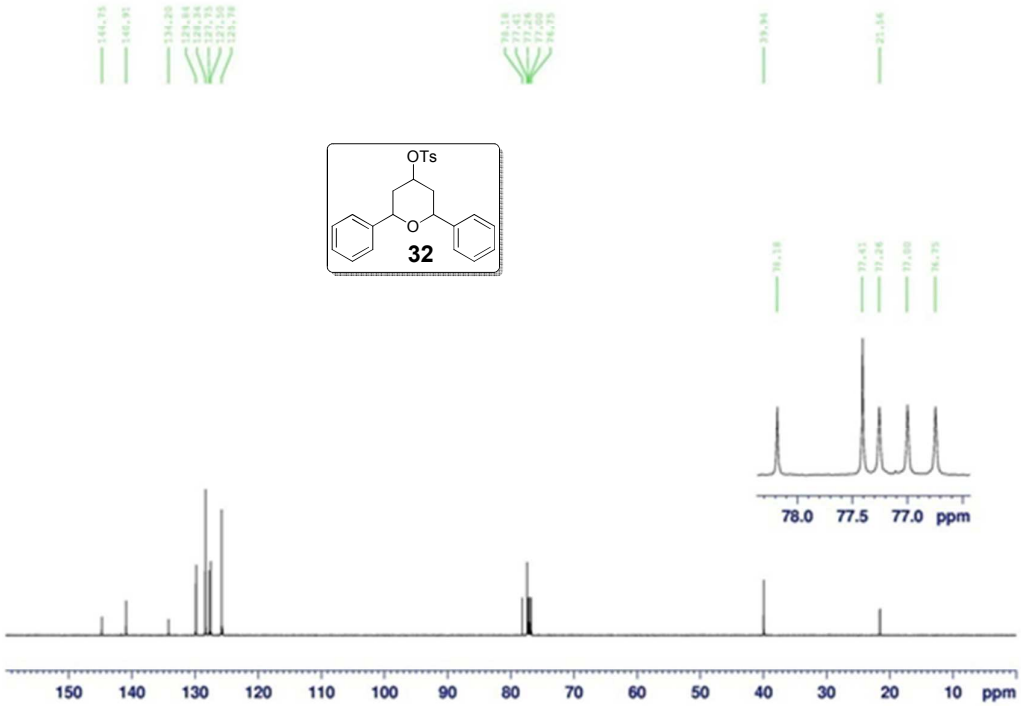

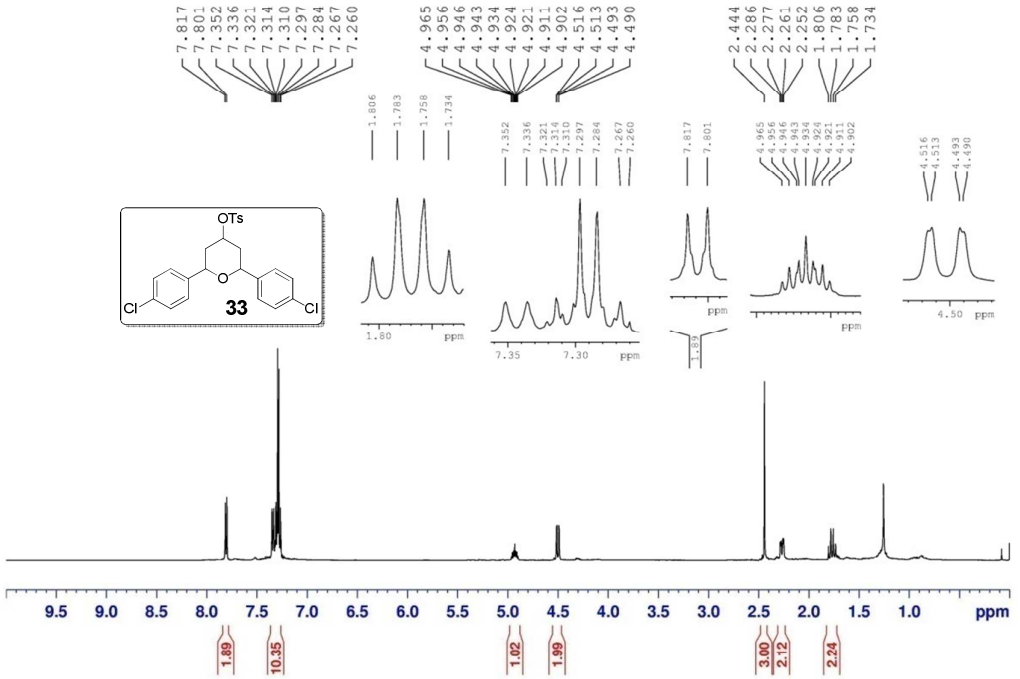

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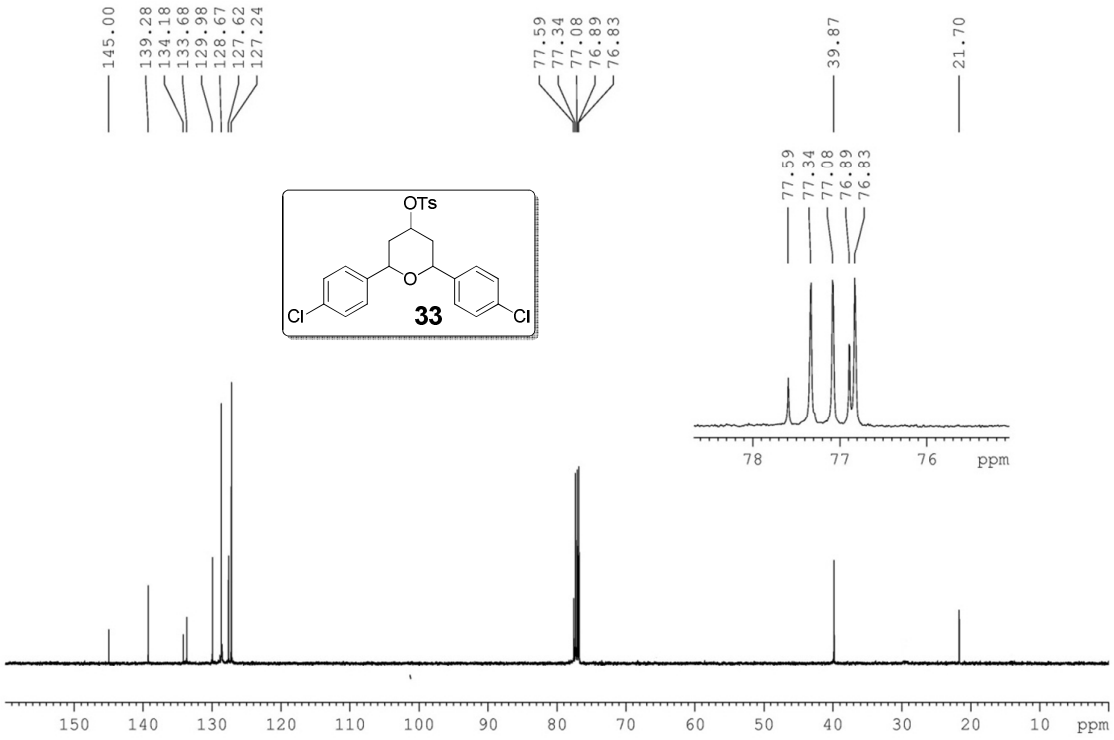

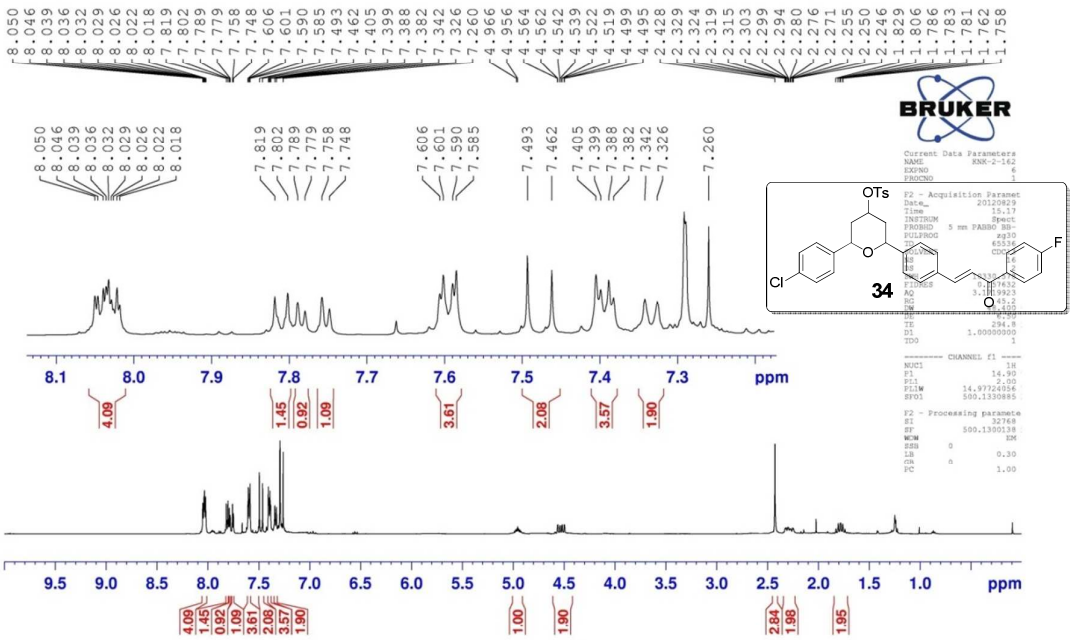

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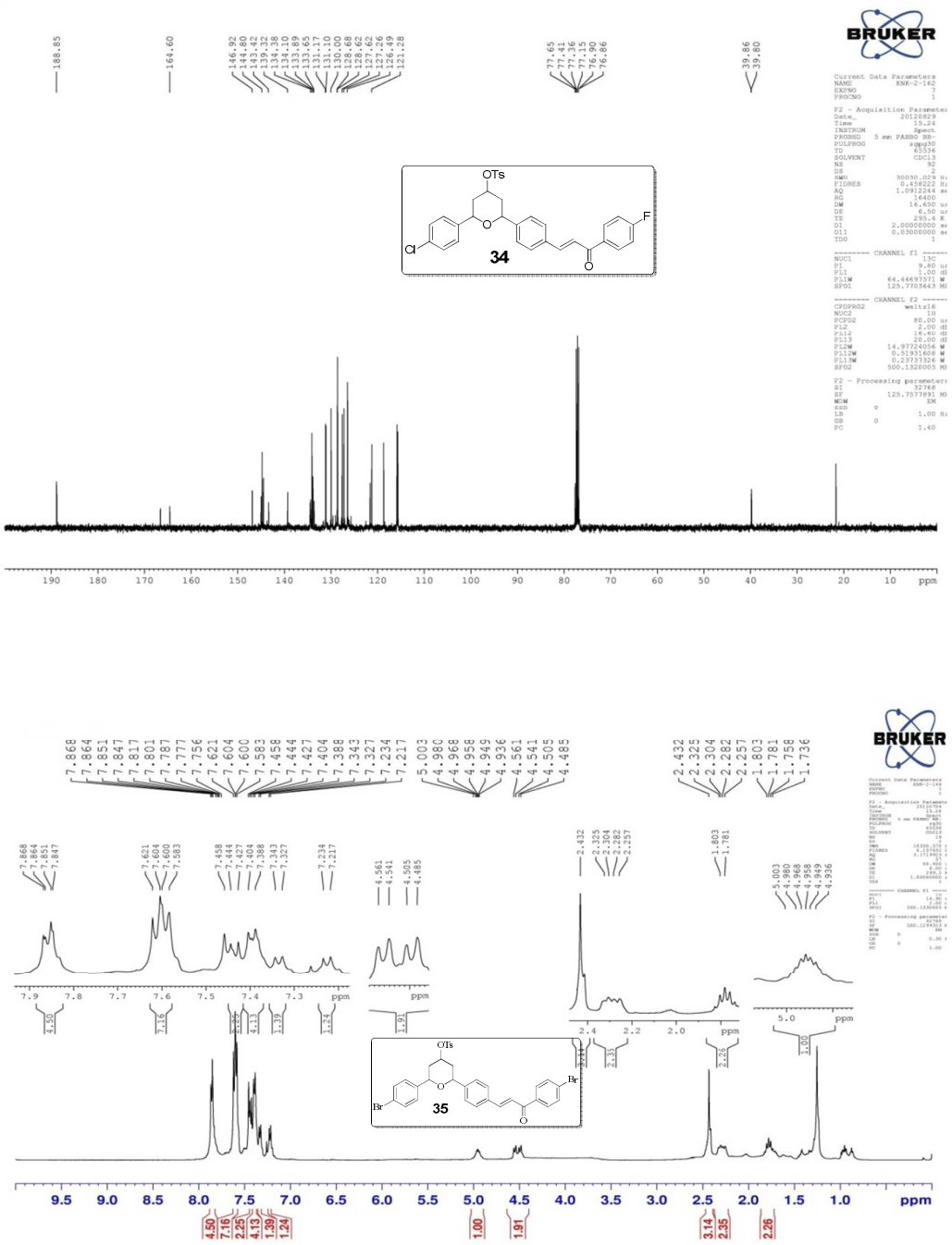

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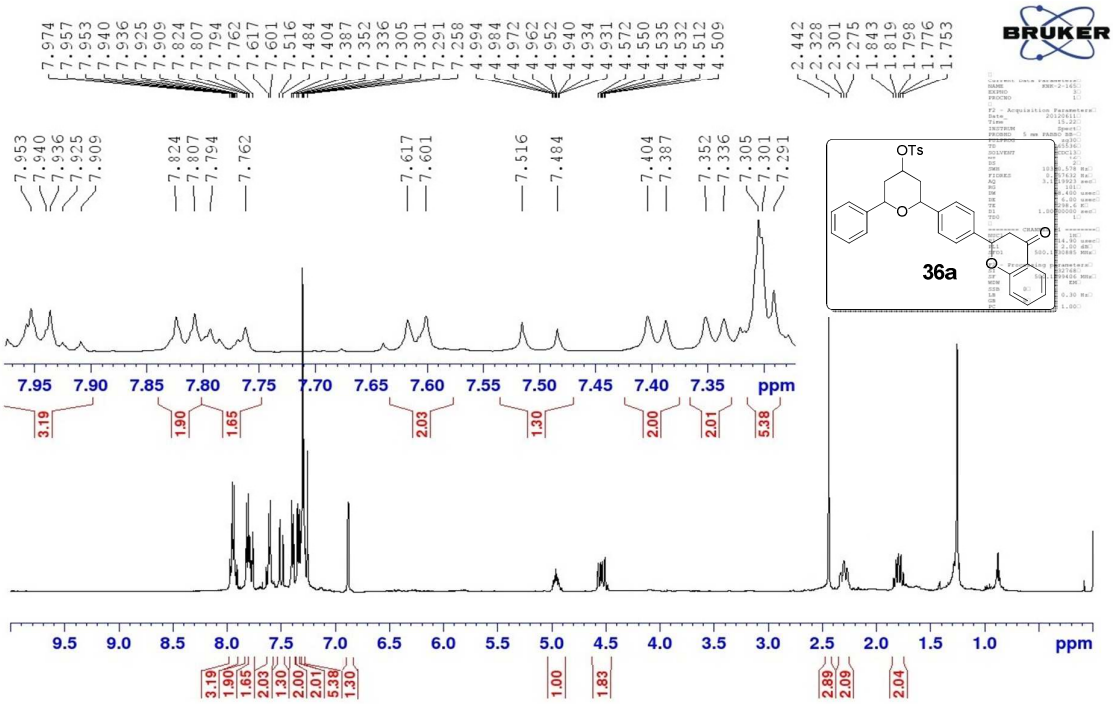

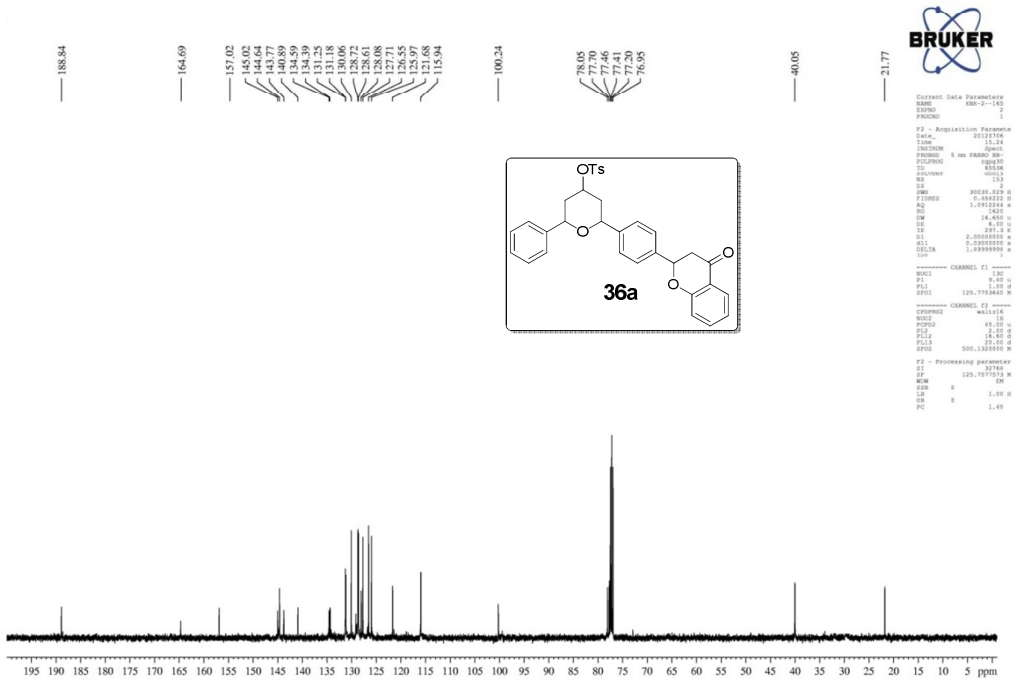

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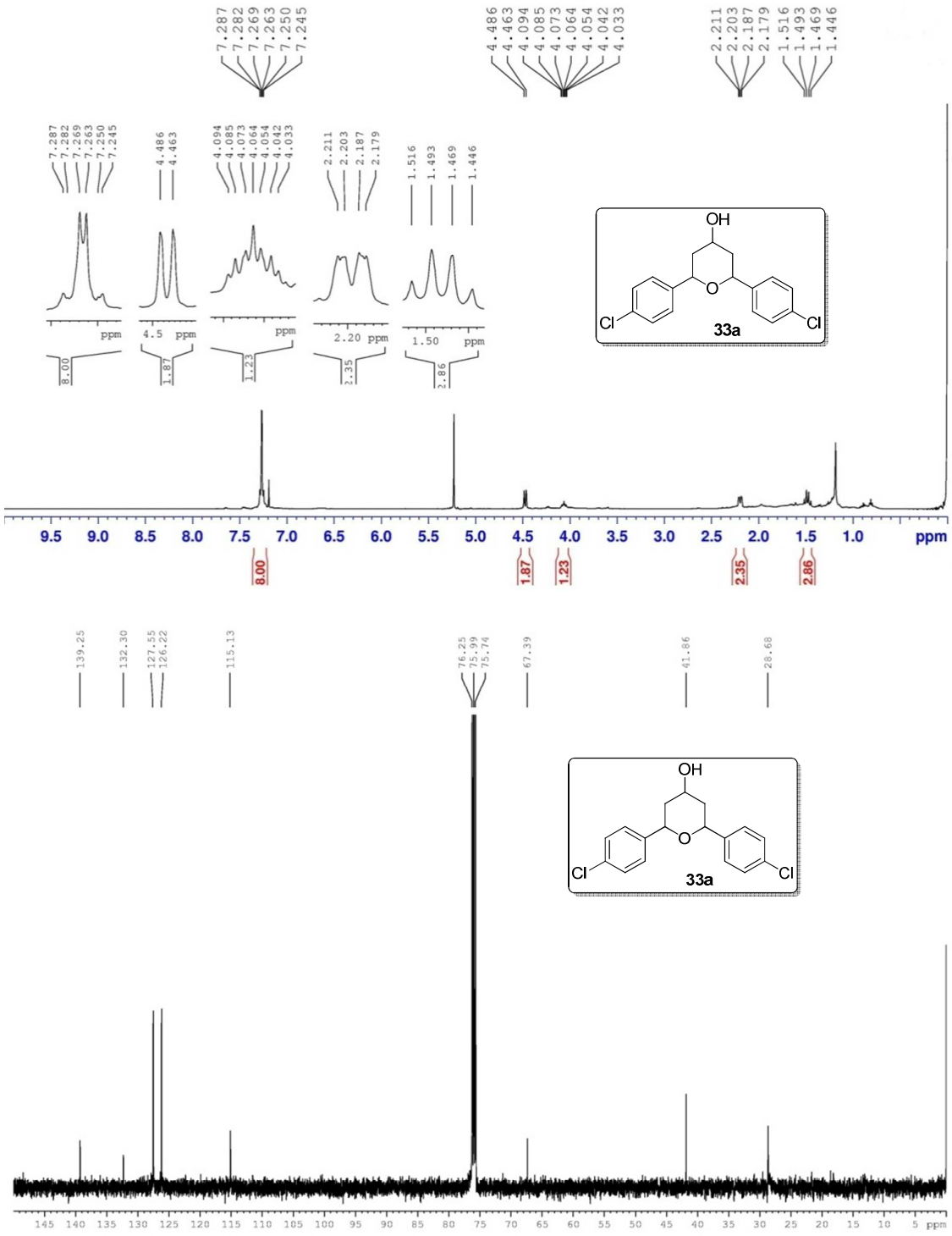

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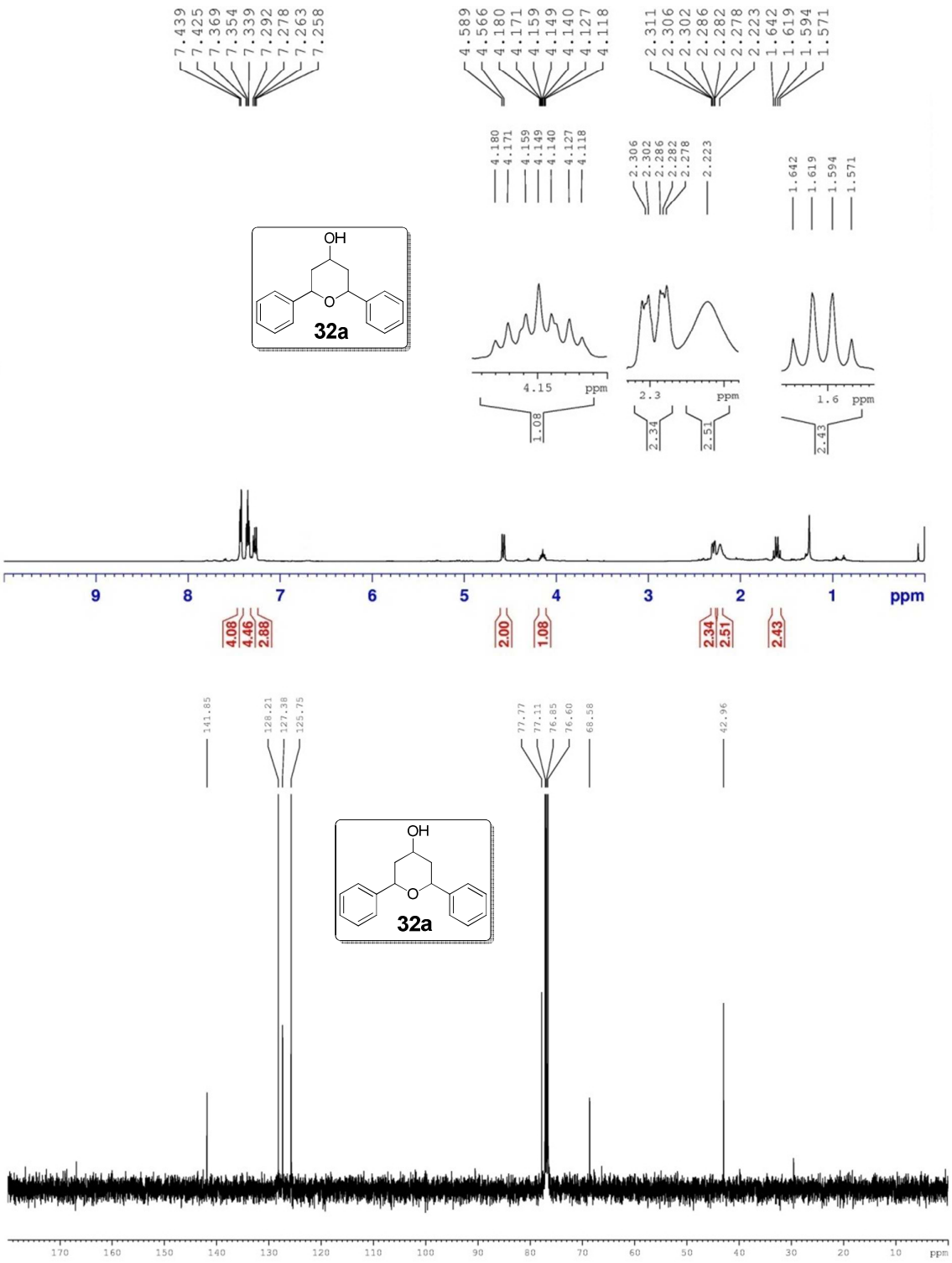

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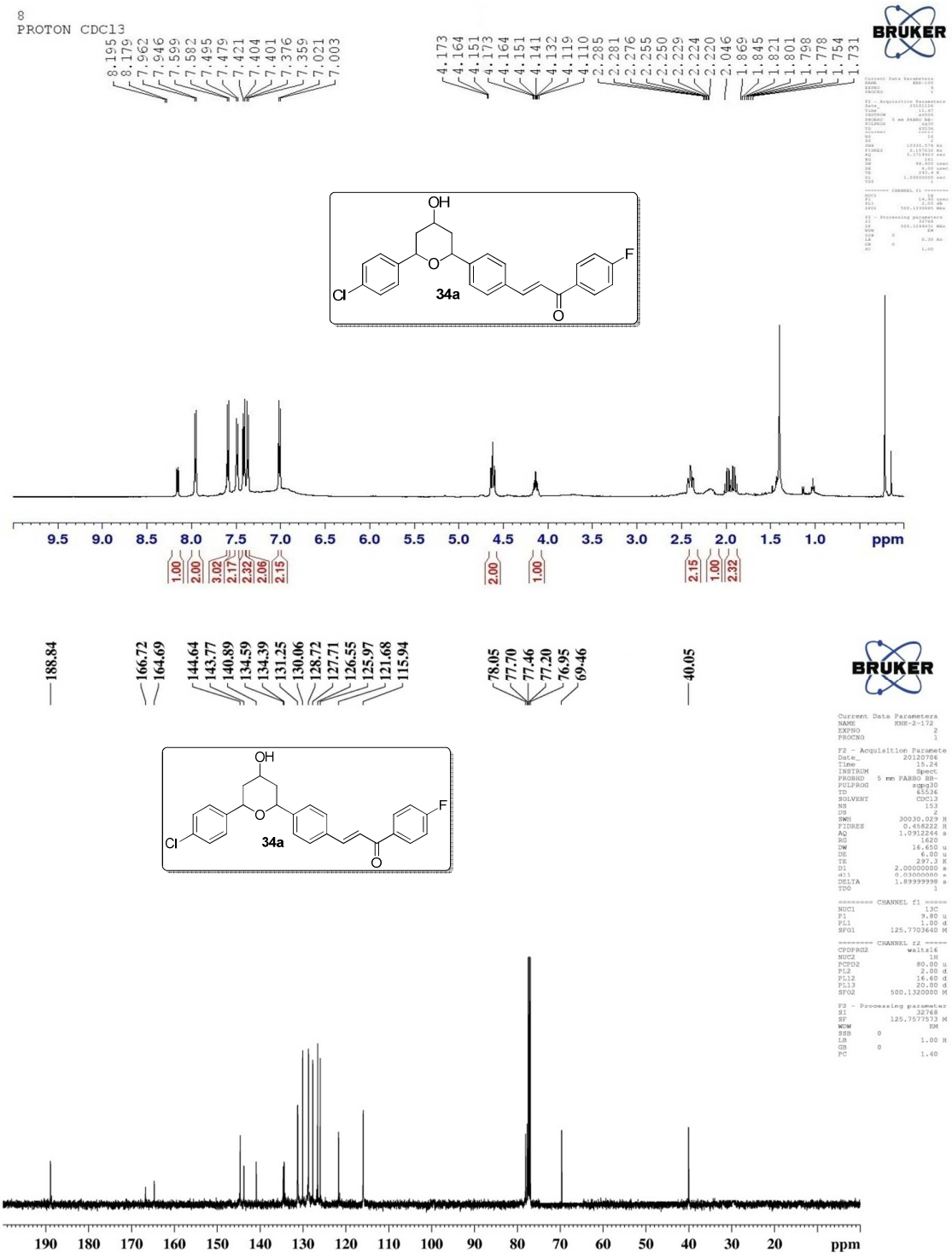

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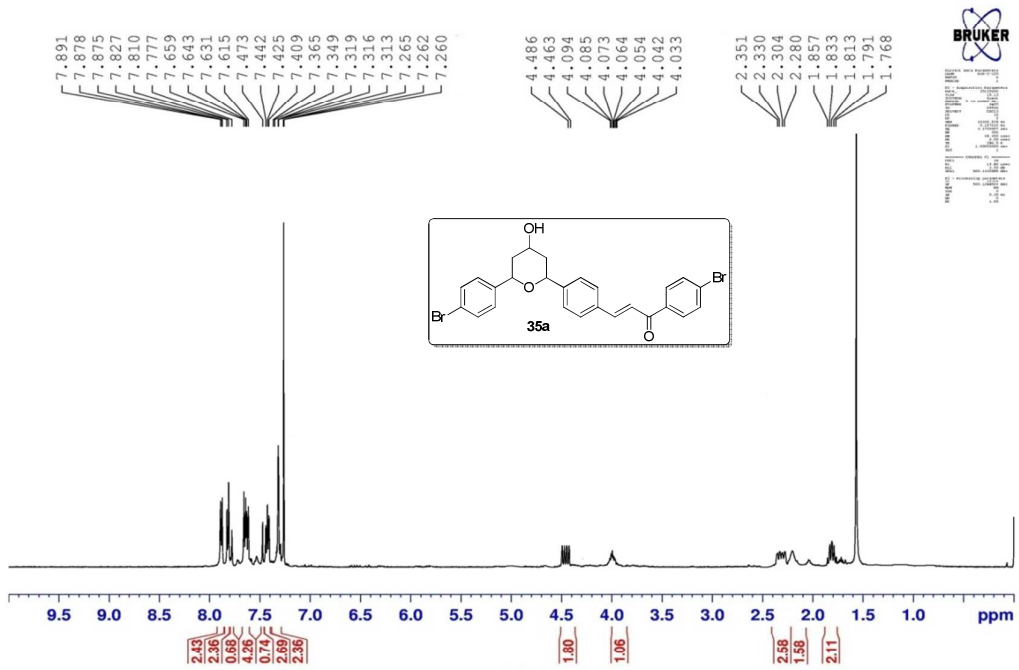

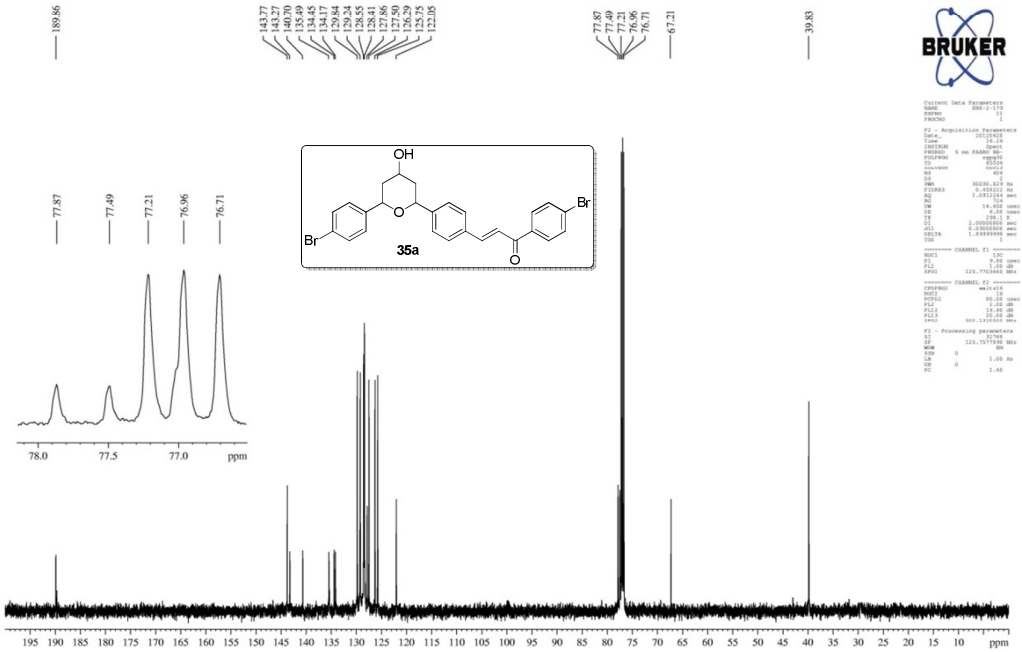

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