Facile synthesis of 2-benzoxepin-3(1*H*)-ones

A Project Report

Submitted to the Department of Chemistry

Indian Institute of Technology, Hyderabad

As part of the requirements for the degree of

Master of Science

By

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Indian Institute of Technology Hyderabad

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY, HYDERABAD

APRIL, 2014

Declaration

Declaration

I hereby declare that the matter embodied in this report is the result of investigation carried out by me in the Department of Chemistry, Indian Institute of Technology Hyderabad under the supervision of **Dr. G. Satyanarayana**.

In keeping with general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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Approval Sheet

Approval Sheet

This thesis entitled **"Facile synthesis of 2-benzoxepin-3(1*H*)-ones"** by Madhurima Hazra is approved for the degree of Master of Science from IIT Hyderabad.

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Co-Advisor

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Name and affiliation

Chairman

Acknowledgement

First and foremost, I offer my sincere, gratitude to my supervisor, *Dr. G. Satyanarayana*, who has supported me throughout the course with his patience and knowledge whilst allowing me the room to work in my own way. It has been a great privilege and honour to be associated with him. Particularly I am very much thankful to him for creating an intense interest on this field of research.

I sincerely thank, "Department of Chemistry of Indian Institute of Technology (IIT) Hyderabad", for providing basic infrastructure and extending all the necessary facilities. My special thanks to the Head of the Department *Prof. F.A. Khan*. I am grateful to all the faculty members of the department, for their timely assistance whenever it was required and also for their encouragement. I am also thankful to all my group members for their constant help and valuable suggestions during my stay in the lab.

In this context, I must acknowledge the wise counselling of J. Krishna. I am in short of words in expressing my heart full thanks to Niharika Pedireddi, Ravi Kumar D, A. Gopi Krishna Reddy, Suchand Basuli, L. Mahender and B. Venkatramulu. My acknowledgement will be incomplete without mentioning the encouragement and suggestion of my colleagues Amrita and Jyoti Nandi.

I wish to express my deep sense of gratitude to my parents for their infinite love and encouragement.

Finally, I thank Department of Chemistry, Indian Institute of Technology Hyderabad, for giving me the project opportunity.

Dedicated to

My Parents

Abstract

A new route for the synthesis of 2-benzoxepin-3(1*H*)-ones derivatives has been devised starting from Heck reaction, subsequent reduction followed by base mediated cyclization. The initial Heck coupling involve construction of C-C bond, whereas the final cyclization step follows intramolecular condensation.

Contents

Facile synthesis of 2-benzoxepin-3(1*H*)-ones

1.1 INTRODUCTION:

Natural products have been used to be a rich source of lead molecules in drug discovery. Natural products have played a major role in the invention of numerous medicines. The combination of synthetic organic chemistry and combinatorial chemistry strategies such as diversity-oriented synthesis (DOS) have enabled the synthesis and improved the desired of biological properties of natural products as well as the identification of novel compounds.[1]

Compounds having α,β-unsaturated lactones display a wide variety of biological activities. Many research groups have tested both natural and unnatural α,β-unsaturated lactones for as-yet undiscovered biological properties (Figure 1).[2]

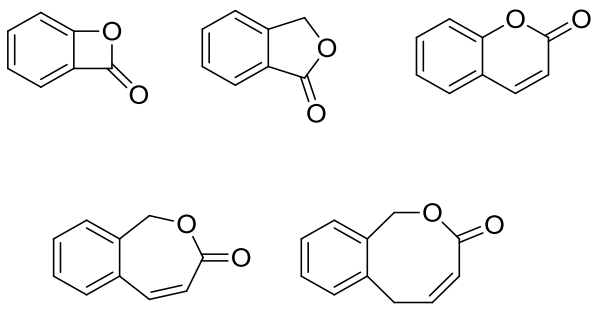


Figure 1. Various lactones reported in literature.

Among them, 7-membered ring lactones are ubiquitous framework of many natural products of interest but they are difficult to prepare by conventional methods.[3] Particularly, compounds with a benzoxepine moiety includes anti-inflammatory, analgesic, and various other types of biological activities.[4] This arises great interest towards the functionalization of benzoxepin skeleton.

1.2 Isolation from natural source:

Endophytes are rich sources of new secondary metabolite which are having astonishing chemical diversity.[5] The fermentation broth of cultured *Pestalotiopsis virgatula* isolated TC-320 from Terminalia chebula Retz. (Combretaceae) disclosed the presence of a simple but unprecedented low-molecular-weight metabolite, 9-hydroxybenzo[c]oxepin-3[1*H*]-one.[5] Also a new

benzoxepin derivative had been isolated from *Phomopsis strain*, KS-37-2, which was isolated from the stem of a cherry tree in Yamagata, Japan.[6]

1.3 Biological Activity:

The 2-benzoxepin-3(1*H*)-ones are not only present as basic core structure in antibiotics xylarinol (A) and xylarinol (B)[7] but also forms the part structure of new tyrosinekinase (p56lck) inhibitor ulocladol[8] and cytotoxic alterlactone.[9] Analogues of 2-benzoxepin-3(1*H*)-ones have also been reported to exhibit analgesic activities (Figure 2).

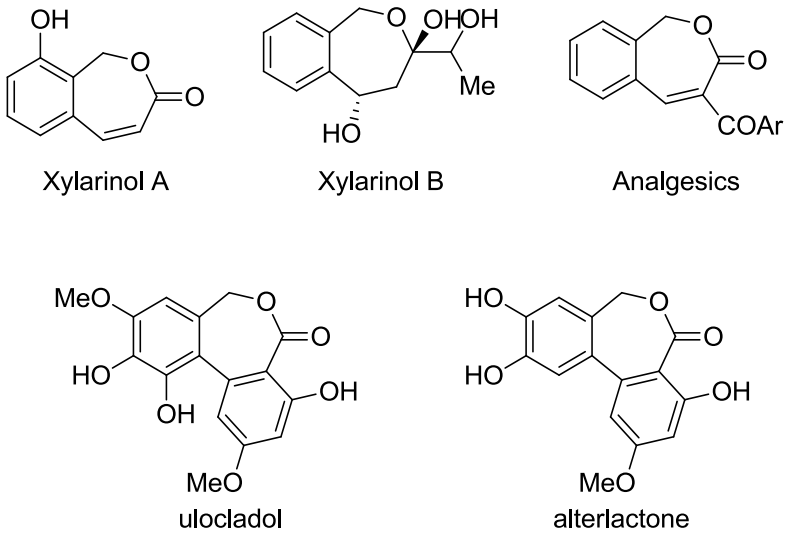
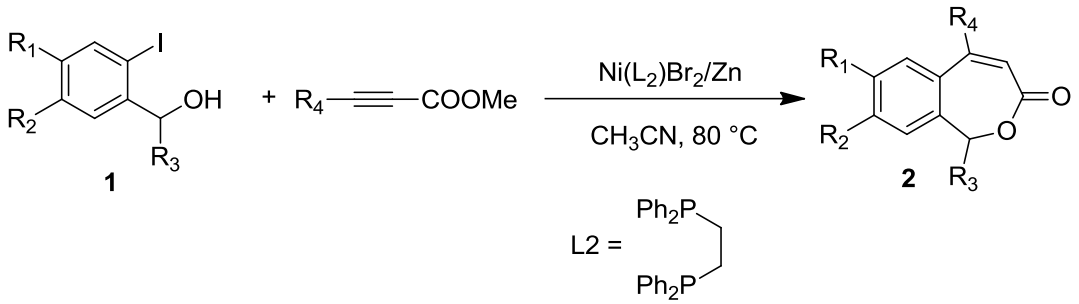


Figure 2. Representative examples of naturally occurring benzoxepin-3(1*H*)-one.

1.4 Background study:

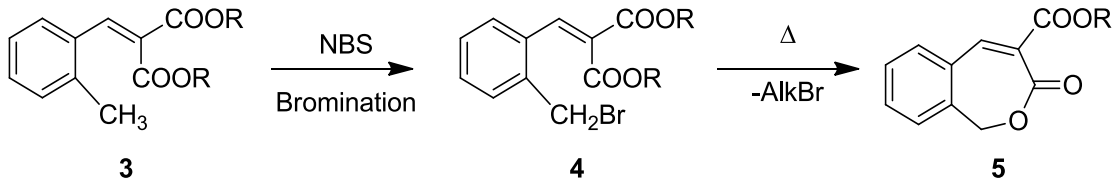
A number of methods have been reported in literature for the synthesis of various derivatives of 7-membered lactenones. Among them, few are discussed as:

Cheng designed a highly regio, stereo selective and novel method for the synthesis of 7-membered lactones. This method is bimetallic cyclization of 2-iodobenzyl alcohols with alkyl propiolates. This method involves the use of nickel and zinc halides as catalyst for cyclization (Scheme 1).[10]



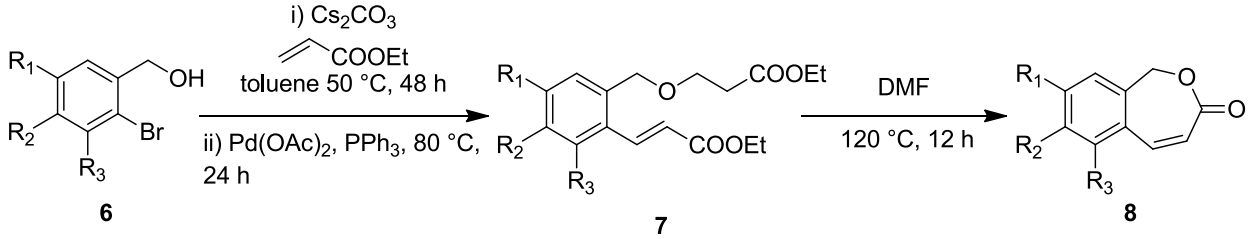
Scheme 1. Cheng approach for the Synthesis of Seven-membered Lactones

In 2008, Kirillov developed a new method for the synthesis of 7-membered α,β-unsaturated lactones, where alkyl-1,3-dihydro-3-oxobenzo[c]oxepine-4-carboxylates were obtained by bromination of dialkyl-2-(2-methylbenzylidene) malonates with N-bromosuccinimide (NBS) followed by the cyclization of dialkyl-2-(2-bromomethylbenzylidene) malonates by heating compound for 1 h at 190 °C led the liberation of bromomethane, and a cyclization occurred providing methyl 1,3-dihydro-3-oxobenzo-[c]oxepine-4-carboxylate.[11]



Scheme 2. Kirillov's method for the synthesis of 7-membered lactones

In continuation of our ongoing research interest on transition-metal catalysis and domino/sequential one-pot processes, we have recently reported a sequential one-pot intermolecular oxy-Michael addition, subsequent intermolecular Heck coupling with the Michael acceptor followed by intramolecular lactonization (Scheme 3).[12]

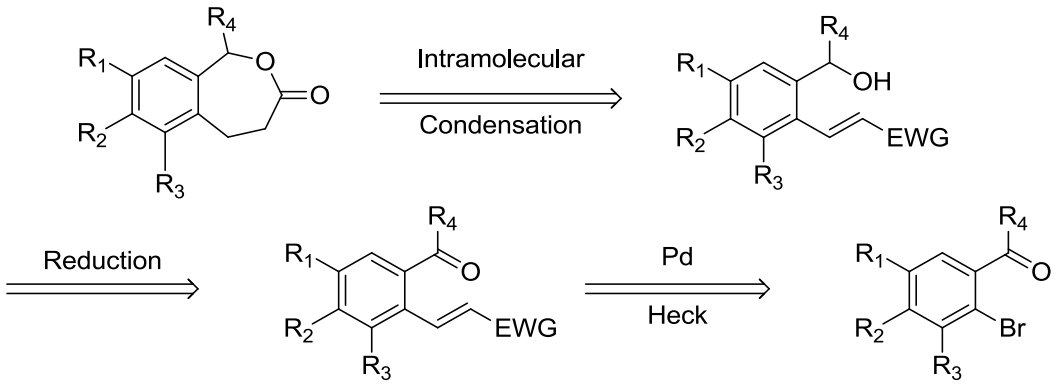


Scheme 3. Sequential one-pot process for the synthesis of benzoxepines.

With this background, we have outlined another synthetic strategic route for the synthesis of benzoxepin-3(1*H*)-ones. The ultimate aim of this strategy is to use the carbonyl ester for the synthesis of benzoxepines. Next step is the selective reduction of carbonyl group with mild reducing agent such as $NaBH_4$ followed by base mediated cyclization.

1.5 Result and Discussion:

The general strategy for the synthesis of 2-benzoxepin-3(1*H*)-ones is as shown in the retrosynthetic analysis (Scheme 4). Our approach involves the key intramolecular [Pd]-catalyzed C-O bond formation. The required procedure involves Pd-catalyzed Heck reaction on *ortho*-bromo benzaldehyde to obtain corresponding ester, subsequent reduction with $NaBH_4$ followed by base mediated intramolecular condensation to obtain cyclized product.

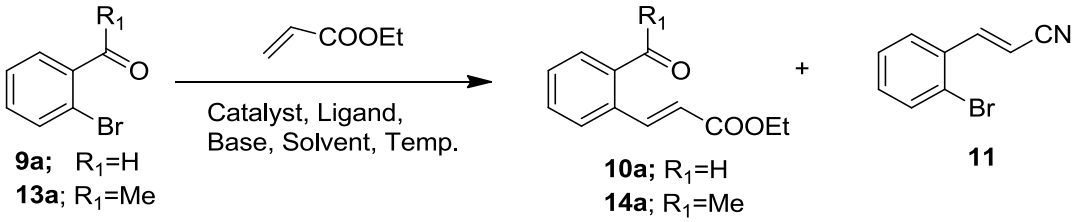


Scheme 4. Retrosynthetic Analysis of 2-Benzoxepin-3(1*H*)-ones.

In this strategy, step-1 follows the synthesis of carbonyl ester through Pd-catalyzed Heck reaction[13] on *ortho*-bromobenzaldehydes with ethyl acrylate. *ortho*-Bromobenzaldehydes are obtained through bromination[14] of commercially available aromatic aldehydes. Various attempts had been carried out using different solvents and bases using $Pd(OAc)_2$ (5 mol%) as catalyst and PPh_3 (10 mol%) as ligand. Interestingly, it was found that combination of strong base (such as Cs_2CO_3) and CH_3CN as solvent had given Aldol condensation product (Table 1, entry 1). While switching to milder conditions, such as using NEt_3 as base and CH_3CN as solvent, furnished desired product **10a** but with moderate yields (Table 1, entry 2). Various feasibilities were carried out and found that NEt_3 and toluene is the best condition for obtaining aldehyde esters with excellent yields (Table 1, entry 3). After the attainment of **10a**, to check the

extent and limitations of the present method, these optimized conditions were applied to the other systems of bromoaldehydes **9a-9h**. The structures of aldehyde ester products (**10a-10h**) were further confirmed by NMR data analysis. Presence of the molecular ion peak at m/z 317.1000 $(C_{15}H_{18}NaO_6)^+$ in the mass spectrum and from the ^{1}H NMR spectrum (Figure 3a), presence of one singlet at δ 10.13 (CH=O) and two doublets at δ 8.04 (ArC*H*=CHCOOEt) and δ 6.21 (ArCH=C*H*COOEt), established the structure of **10h**. The appearance of the one doublet at δ 189.9 (CH=O) and one singlet at δ 166.1 (O=COEt) in the ^{13}C NMR (Figure 3b), spectrum established the structure of **10h**.

Table 1. Attempts of Pd catalysed intermolecular C-C bond formation.[a]



9a; R_1=H
13a; R_1=Me

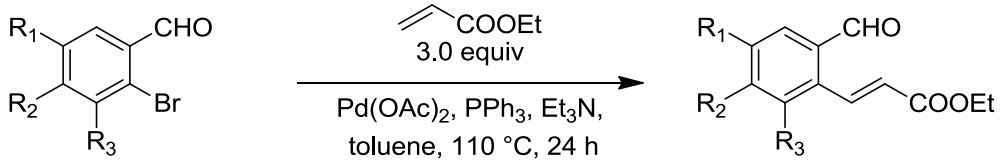
10a; R_1=H
14a; R_1=Me

11

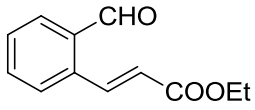
Entry	R_1	Catalyst [mol%]	Ligand [mol%]	Base [equiv]	Solvent [mL]	Temp. °C	Time h	Yield Of 10a [%]	Yield Of 14a [%]	Yield of 11 [%]
1	H	$Pd(OAc)_2$ (5)	PPh_3 (10)	CS_2CO_3 (1.5)	CH_3CN (6)	80	19	-	-	36
2	H	$Pd(OAc)_2$ (5)	PPh_3 (10)	Et_3N (1.0)	CH_3CN (2)	80	22	58	-	-
3	H	$Pd(OAc)_2$ (5)	PPh_3 (10)	Et_3N (3)	toluene (2)	110	24	90	-	-
4	Me	$Pd(OAc)_2$ (5)	PPh_3 (10)	Et_3N (3)	toluene (2)	110	24	-	33	-
5	Me	$Pd(OAc)_2$ (5)	PPh_3 (10)	Et_3N (3)	DMF (2)	150	24	-	60	-
6	Me	$Pd(OAc)_2$ (5)	PPh_3 (10)	DIPEA (3)	toluene (2)	110	24	-	84	-

[a] Isolated yields of the pure products.

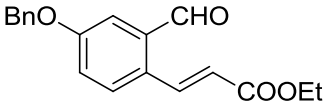
Table 2. Synthesis of aldehyde esters (**10a**-**10h**) from *ortho*-bromoaldehydes (**9a**-**9h**).[a]



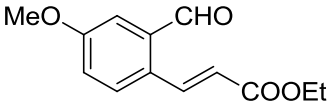
9a-9h **10a-10h**



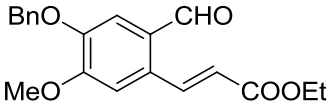
10a (90%)



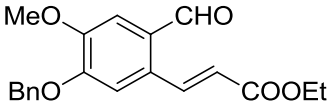
10b (75%)



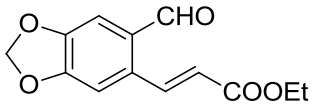
10c (90%)



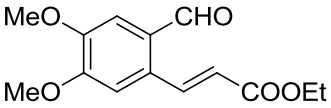
10d (93%)



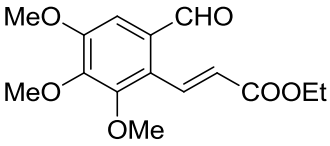
10e (94%)



10f (93%)



10g (93%)



10h (93%)

[a] Isolated yields of the pure products.

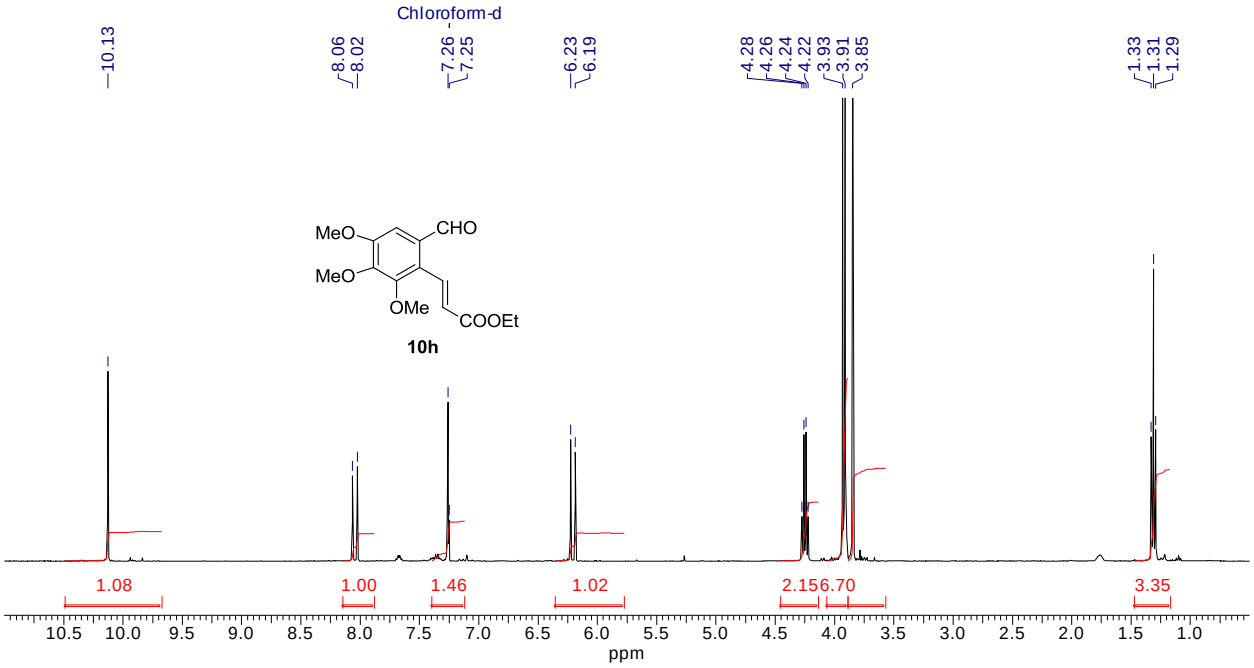


Figure 3a. ^{1}H NMR (400 MHz) spectrum of **10h** in $CDCl_3$

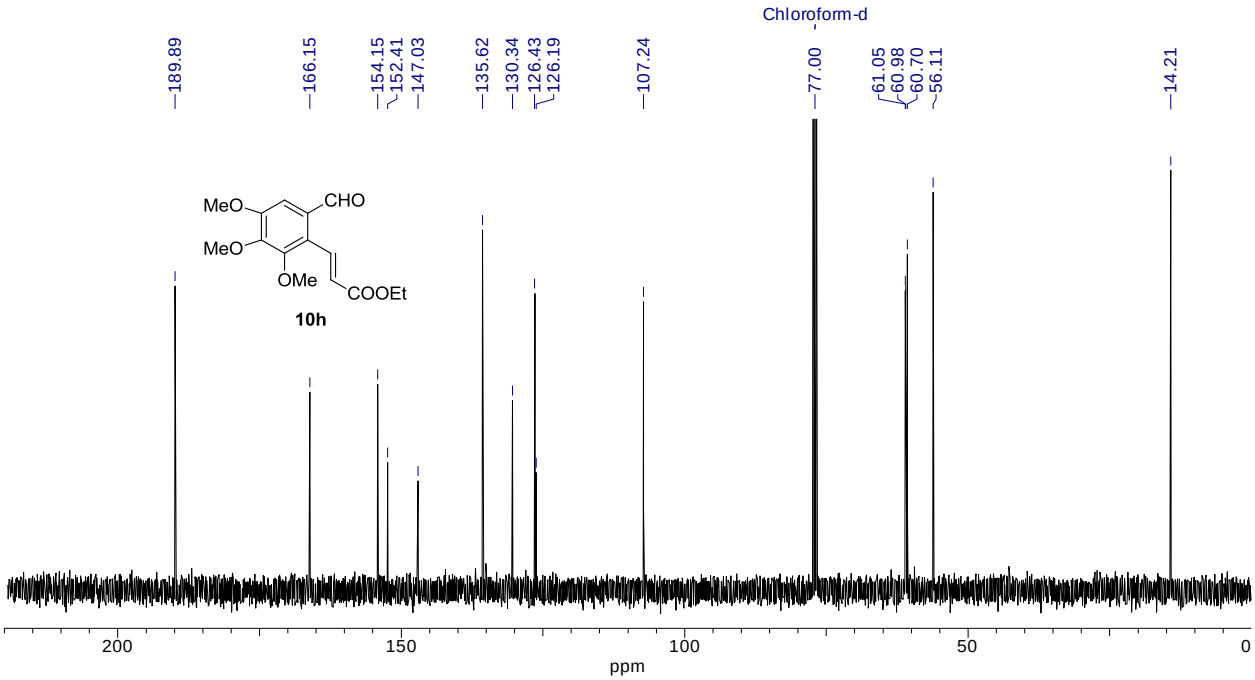
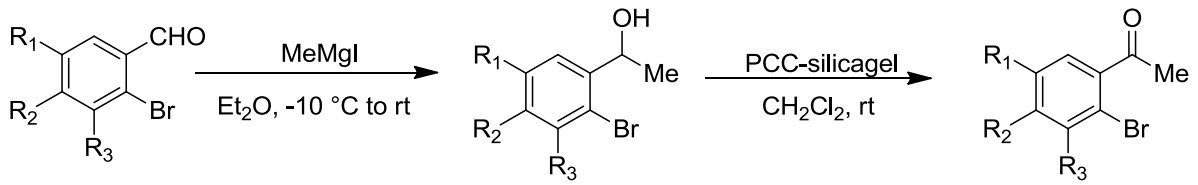


Figure 3b. ^{13}C NMR (100 MHz) spectrum of **10h** in $CDCl_3$

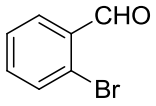
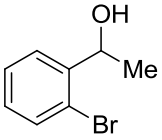
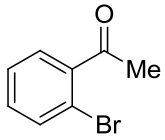
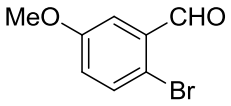
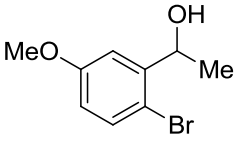
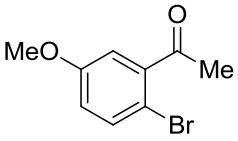
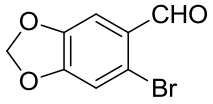
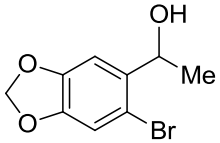
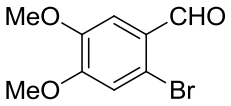
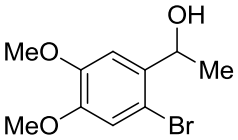
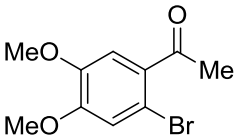
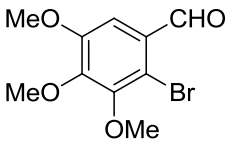
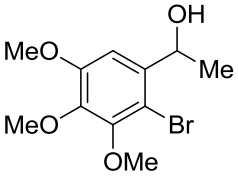
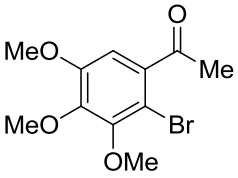
Further to obtain various analogues, methyl-Grignard reaction was carried out on *ortho*-bromoaldehydes which yielded secondary alcohols. The oxidation of these secondary alcohols

with PCC had given corresponding *ortho*-bromoketones and the details are summarised in Table 3.

Table 3. Synthesis of *ortho*-bromoacetophenones (**13a-13h**) from *ortho*-bromoaldehydes (**9a-9h**).[a]



9a-9h **12a-12h** **13a-13h**

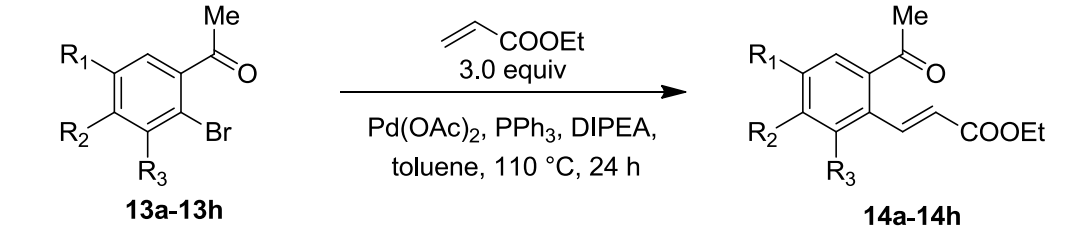
 **9a**	 **12a** (90%)	 **13a**(94%)
 **9c**	 **12c** (95%)	 **13c** (97%)
 **9f**	 **12f** (80%)	 **13f** (82%)
 9g	 **12g** (81%)	 **13g** (95%)
 9h	 **12h** (90%)	 **13h** (95)%)

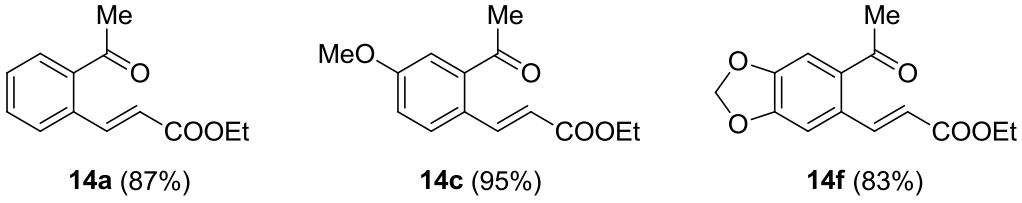
[a] Isolated yields of the pure products.

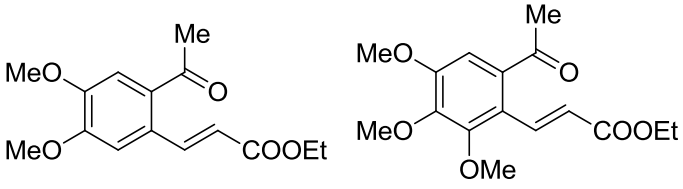
To this *ortho*-bromoketones Pd catalysed Heck reaction was carried out to obtain various acetophenone-esters. Similar conditions (i.e. NEt_3 as base and toluene as solvent) were applied on *ortho*-bromoacetophenones but we obtain desired product with low yield (Table 1, entry 4). Another attempt was carried out using DMF instead of toluene as solvent. We were successful in our desired target but with moderate yield (Table 2, entry 5). In order to explore different conditions we tried with Hunig's base and toluene, which results in corresponding acetophenone

esters in very good yields (Table 1, entry 6). Notably, it was found that NEt_3 is not a suitable base for bromo-acetophenones. The structures of acetophenone ester products (**14a-14h**) were further confirmed by NMR data analysis. Presence of the molecular ion peak at m/z 331.1151 $(C_{16}H_{20}NaO_6)^+$ in the mass spectrum and from the ^{1}H NMR spectrum (Figure 4a), absence of singlet for CH=O and presence of two doublets at δ7.78 (ArC*H*=CHCOOEt) and δ6.29 (ArCH=C*H*COOEt), established the structure of (**14h**). The appearance of the two singlets at δ202.3 (C=O) and δ166.8 (O=COEt) in the ^{13}C NMR (Figure 4b), spectrum established the structure of **14h**.

Table 4. Synthesis of acetophenone esters (**14a-14h**) from *ortho*-bromoacetophenones (**13a-13h**).[a]







[a] Isolated yields of the pure products.

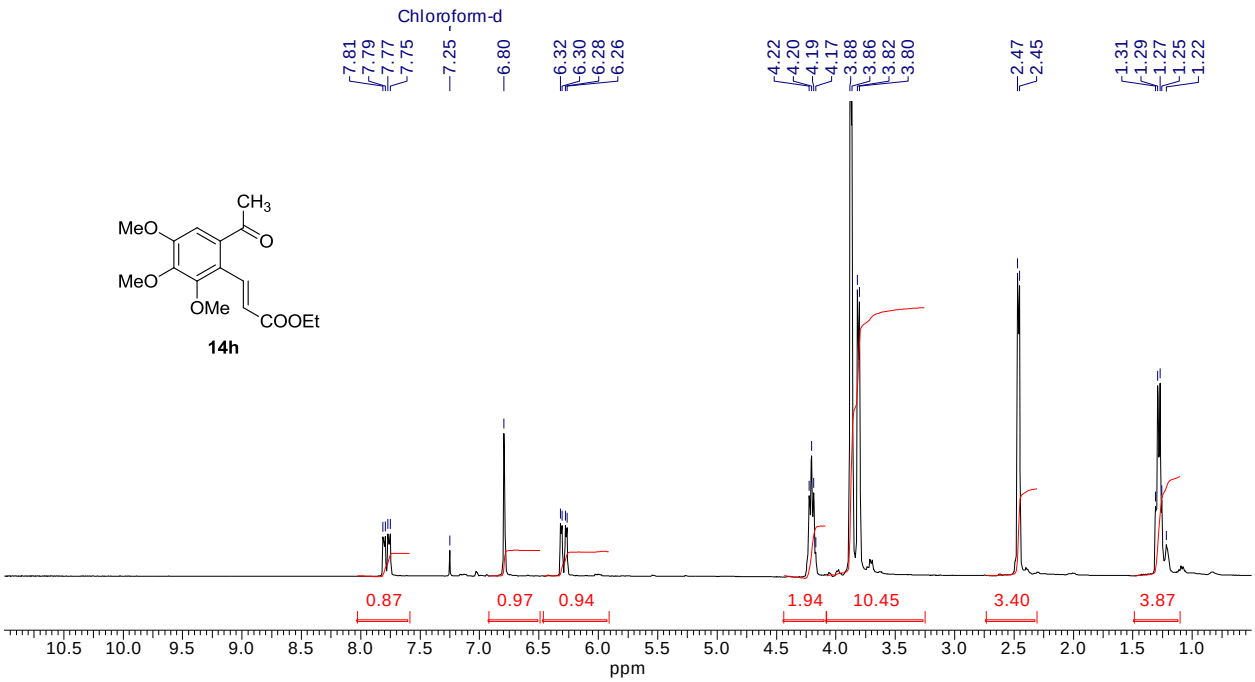


Figure 4a. ^{1}H NMR (400 MHz) spectrum of **14h** in $CDCl_3$

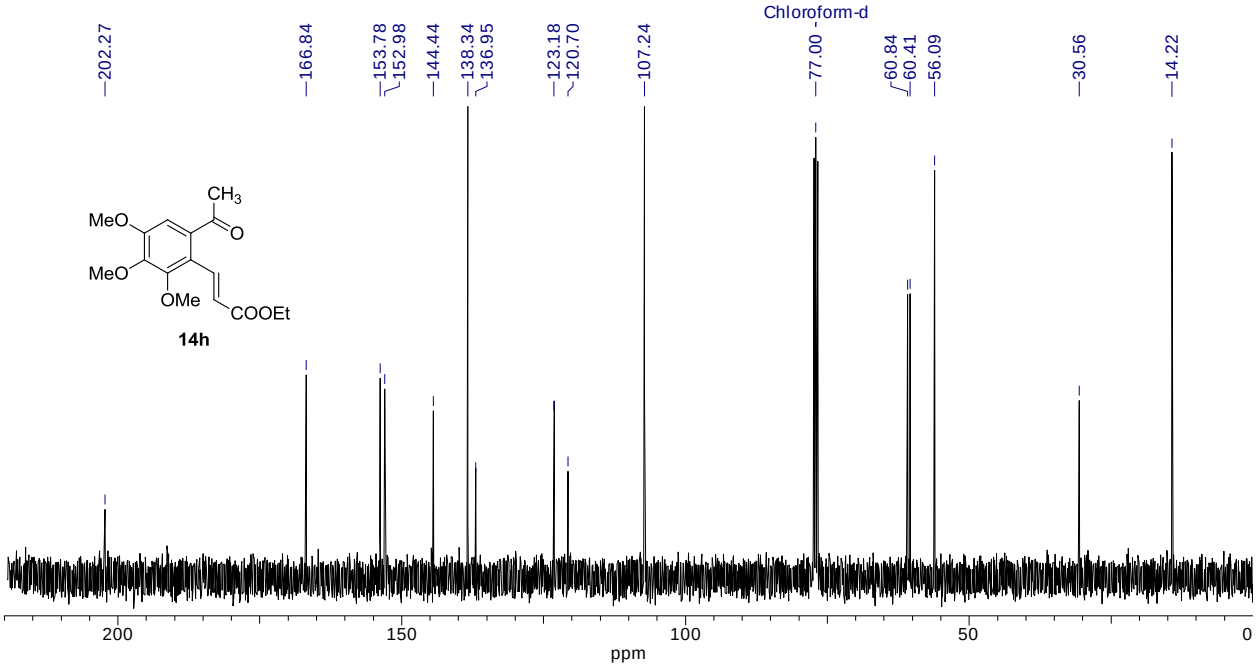
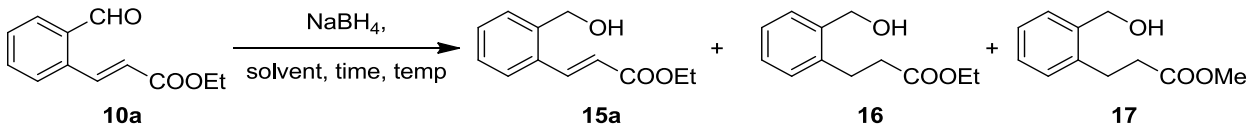


Figure 4b.^{13}C NMR (100 MHz) spectrum of **14h** in $CDCl_3$

Selective reduction had been carried out at carbonyl centre with mild reducing agent. As known from literature,[15] $NaBH_4$ has been used for selective reduction at carbonyl centre in presence of ester group. So, reduction was carried out with $NaBH_4$ in MeOH. Interestingly, it was observed

that not only carbonyl group but also double bond had also been reduced. It also results in trans-esterification products. Initially reduction was carried out with $NaBH_4$ in MeOH at -20 °C. We obtained mixture of products **15a** (6%) and **16** (30%) (Table 5, entry 1). We achieved our target product but with very low yield. Further studies had been carried out with decreasing the temperature to -40 °C. Here, also results are same but the yield of our desired product had increased to 24% (Table 5, entry 2). To check the feasibility various reactions were carried out at different temperatures and found that at 0 °C it results in trans-esterification product (Table 5, entry 3). In literature,[16] the combination of $NaBH_4$ and $CeCl_3.7H_2O$ has been used for selective reduction at carbonyl centre in presence of various other reactive functional groups. So, we used $CeCl_3.7H_2O$ along with $NaBH_4$ in MeOH. We succeeded in our attempt but results in moderate yields (Table 5, entry 5). Once, we had used $NaBH_4$ and CH_3COOH as solvent instead of MeOH. Here, not only we achieved our desired product but also we were successful in obtaining excellent yields (Table 5, Entry 6). The structures of primary alcohol ester products (**15a-15h**) were further confirmed by NMR data analysis. Presence of the molecular ion peak at m/z 319.1153 $(C_{15}H_{20}NaO_6)^+$ in the mass spectrum and from the ^1H NMR spectrum (Figure 5a), presence of two doublets at δ7.78 (ArC*H*=CHCOOEt) and δ6.55 (ArCH=C*H*COOEt) and one br. s, at δ2.69 (CH_2OH) established the structure of **15h**. The absence of signals for CH=O and appearance of the one singlet at δ168.0 (O=COEt) in the ^{13}C NMR (Figure 5b), spectrum established the structure of **15h**.

Table 5. Attempts of Reduction.[a]



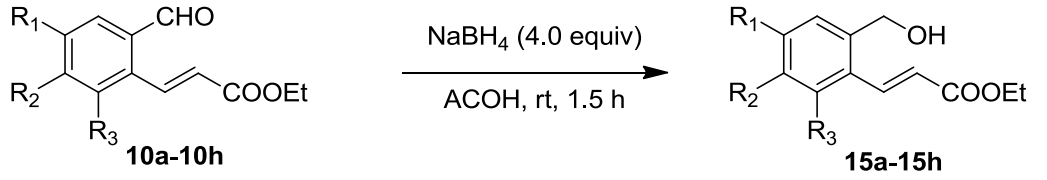
10a **15a** **16** **17**

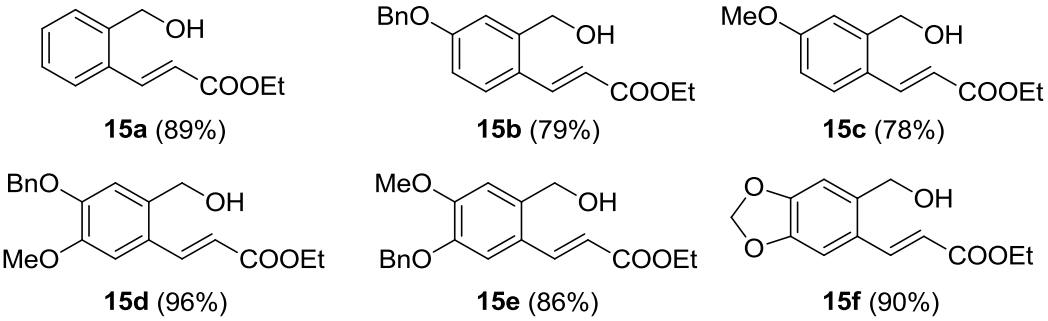
Entry	$NaBH_4$ [equiv]	$CeCl_3.7H_2O$ [equiv]	MeOH [mL]	AcOH [mL]	dry THF [mL]	Time h	Temp °C	Yield 15a [%]	Yield 16 [%]	Yield 17 [%]
1	2.0	-	4.0	-	-	1.5	– 20	6	30	-
2	2.0	-	4.0	-	-	2.0	– 40	24	12	

3	2.0	-	4.0	-	-	4.0	0	-	-	40
4	3.0	-	4.0	-	-	24	rt	-	83	-
5	2.0	1.0	4.0	-	-	6	– 20 to rt	68	-	-
6	4.0	-	-	1.5	-	1.5	rt	89	-	-
7	3.0	-	-	-	3.0	24	rt	-	-	-

[a] Isolated yields of the pure products.

Table 6. Synthesis of primary alcohol esters (**15a**-**15h**) from aldehyde esters (**10a**-**10h**). [a]





[a] Isolated yields of the pure products.

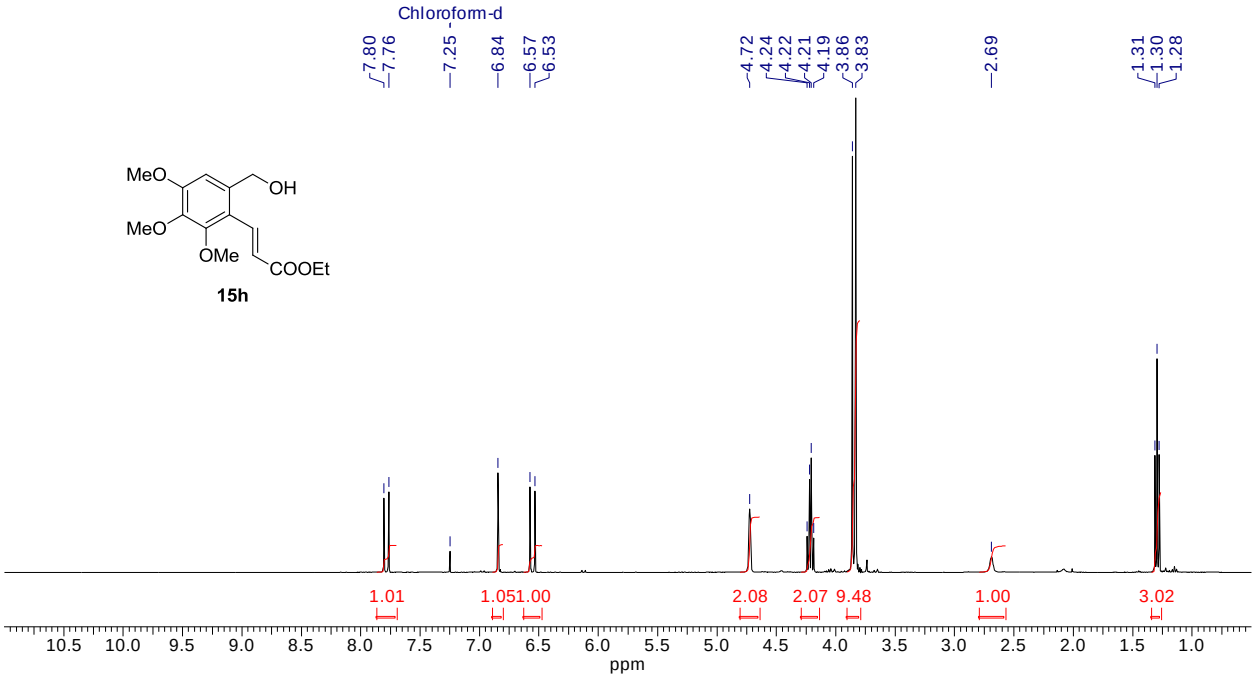


Figure 5a. ^{1}H NMR (400 MHz) spectrum of **15h** in $CDCl_3$

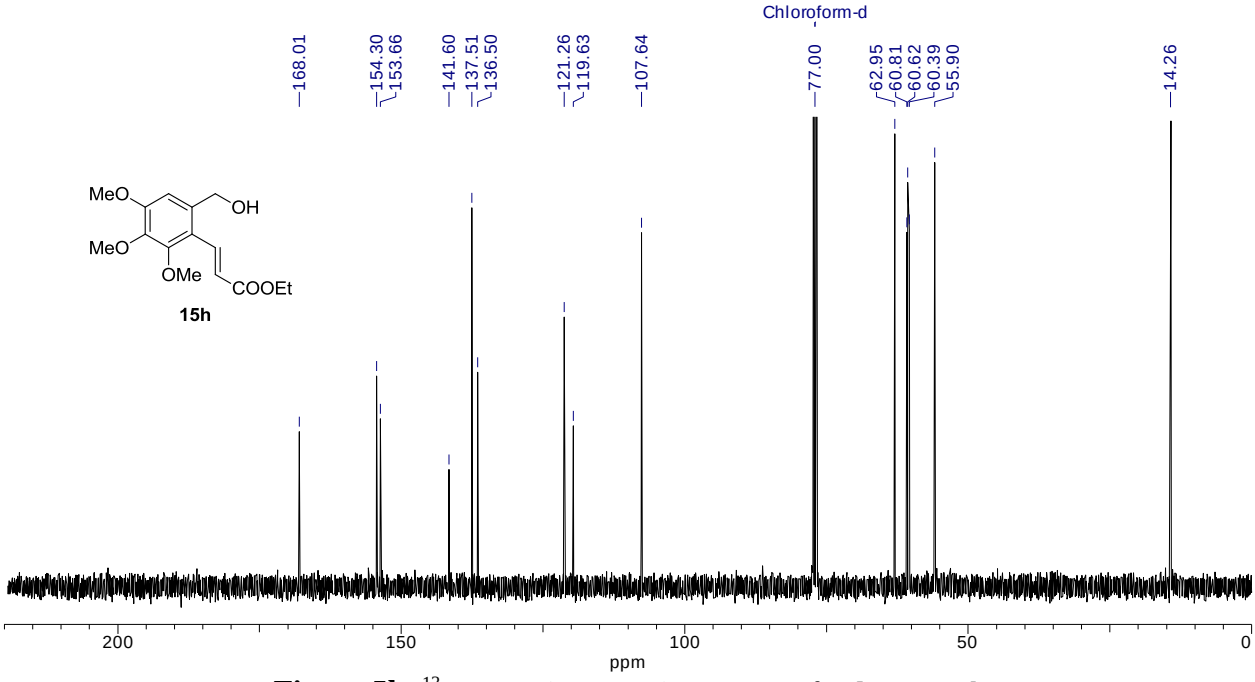
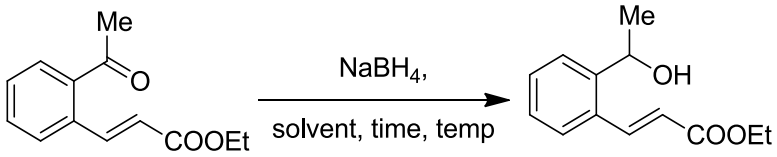


Figure 5b. ^{13}C NMR (100 MHz) spectrum of **15h** in $CDCl_3$

For reduction of acetophenone ester, we first thought to apply the same strategy (i.e. $NaBH_4$ in CH_3COOH) as described in case of aldehyde ester. However, this method is not successful in case of secondary alcohols as we recovered starting material (Table 7, entry 1). So, we switched

to previous strategy of reduction i.e. combination of $CeCl_3.7H_2O$ and $NaBH_4$ in MeOH for selective reduction at carbonyl centre. The optimization of the reaction is given below (Table 7). Presence of the molecular ion peak at m/z 303.1201 $(C_{15}H_{20}NaO_5)^+$ in the mass spectrum and from the ^{1}H NMR spectrum (Figure 6a), presence of two doublets at δ7.93 (ArC*H*=CHCOOEt) and δ6.21 (ArCH=C*H*COOEt) and one br. s, at δ2.49 (CH_2O*H*) established the structure of **18g**. The absence of signals for C=O and appearance of the one singlet at δ167.1 (O=COEt) in the ^{13}C NMR (Figure 6b) spectrum established the structure of **18g**.

Table 7. Optimization of reduction reaction.[a]

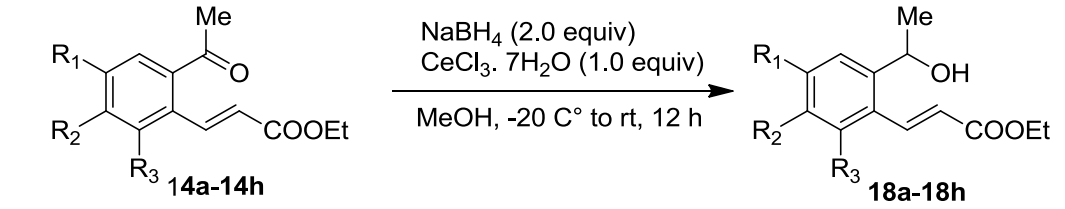


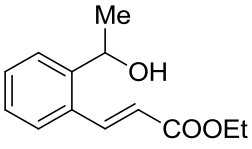
14a **18a**

Entry	$NaBH_4$ [equiv]	$CeCl_3.7H_2O$ [equiv]	MeOH [mL]	AcOH [mL]	Time h	Temp °C	Yield 18a [%]
1	2.0	-	-	1	2	rt	-
2	5.0	-	-	3	2.0	100	-
3	5.0	2.0	5.0	-	4.0	-20 to rt	37
4	2.0	1.0	3.0	-	12	-20 to rt	78

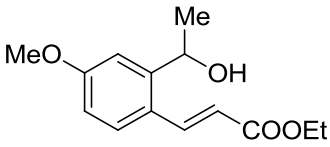
[a] Isolated yields of the pure products.

Table 8. Synthesis of secondary alcohol esters (**18a-18h**) from acetophenone esters (**14a-14h**).[a]

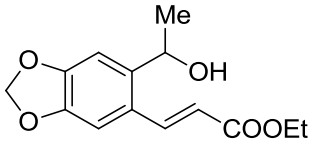




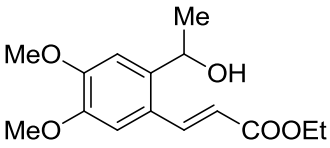
18a (78%)



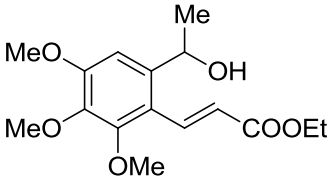
18c (89%)



18f (65%)



18g (77%)



18h (81%)

[a] Isolated yields of the pure products.

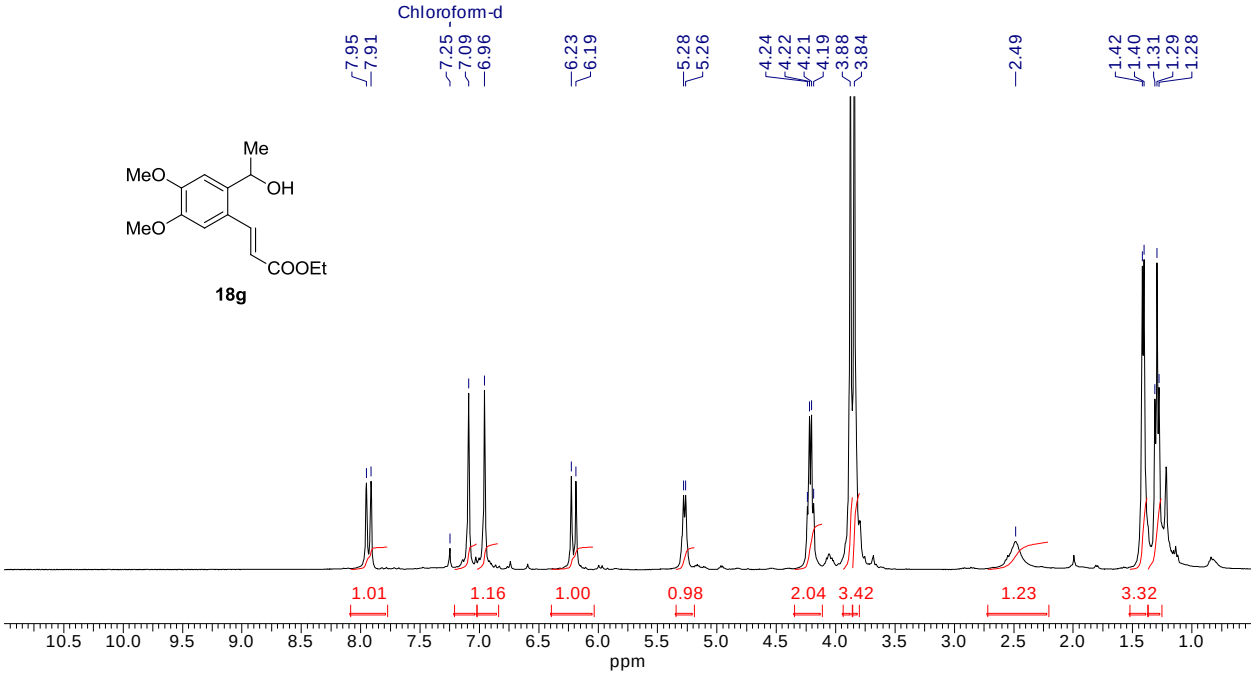


Figure 6a. ^{1}H NMR (400 MHz) spectrum of **18g** in $CDCl_3$

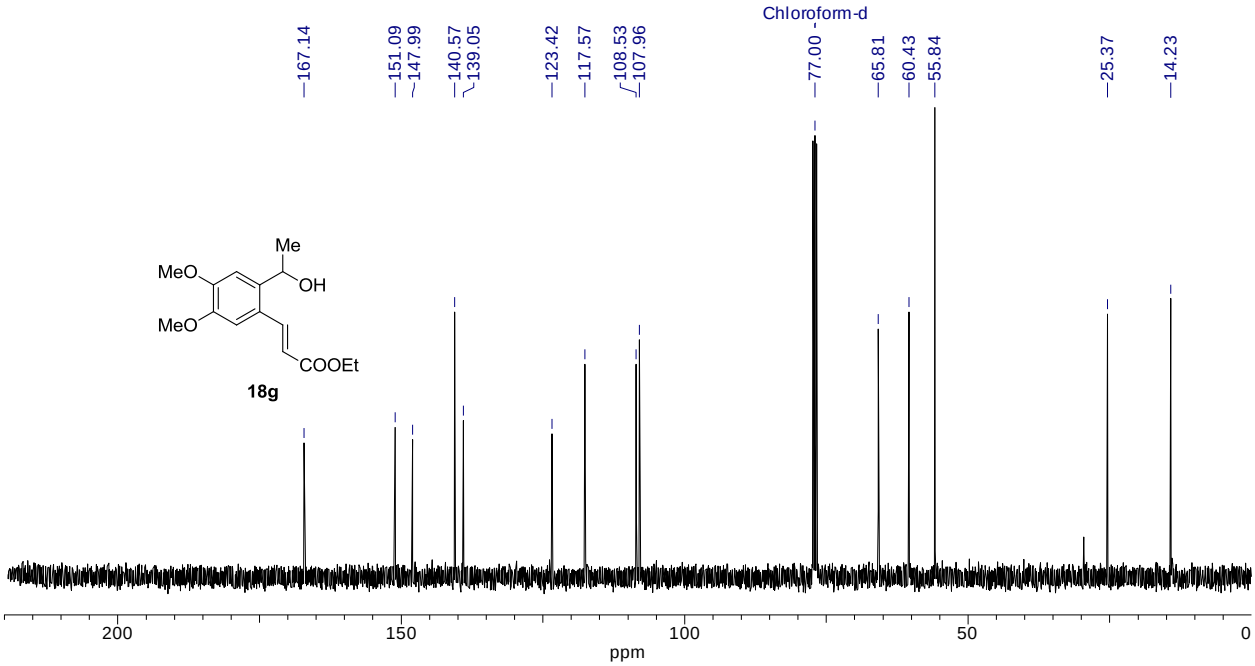
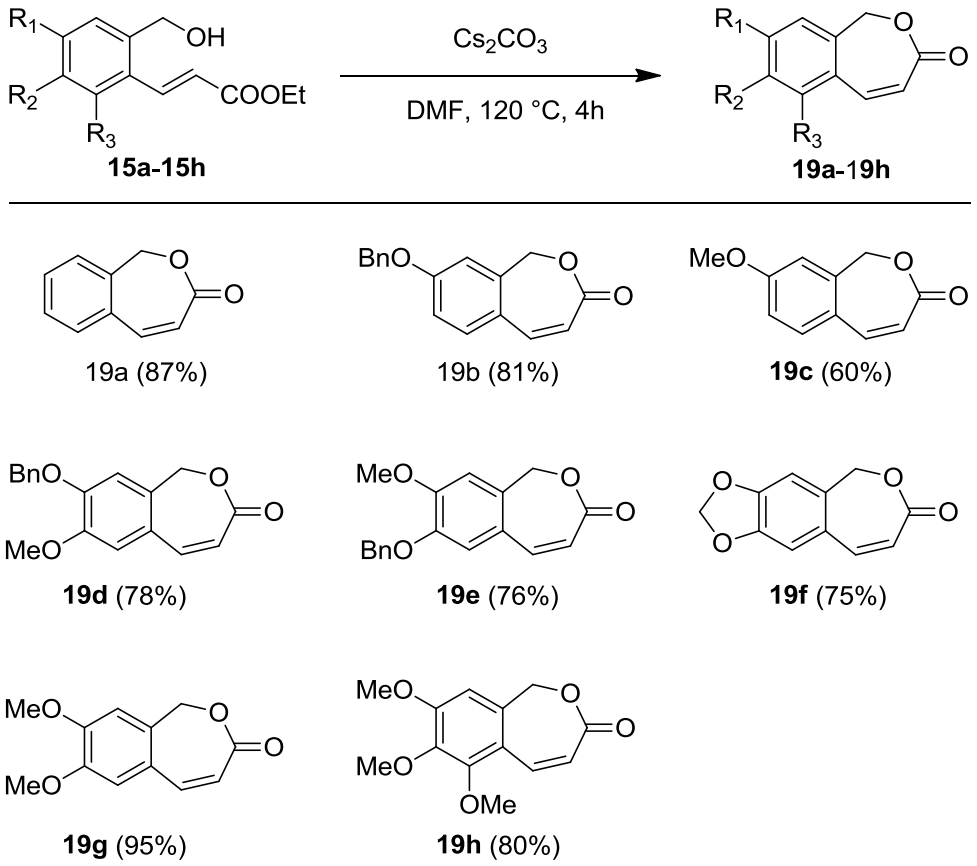


Figure 6b. ^{13}C NMR (100 MHz) spectrum of **18g** in $CDCl_3$

From our previous literature [12] we had found that intramolecular cyclization's were carried using Cs_2CO_3 as base and DMF as solvent. Hence, the final step i.e. base promoted intramolecular cyclization reaction was carried out at similar conditions and we got succeeded in obtaining desired product with good yields.

Table 9. Synthesis of lactenones (**19a-19h**) from primary alcohol esters (**15a-15h**).[a]



[a] Isolated yields of the pure products.

Presence of the molecular ion peak at m/z 251.0913 $(C_{13}H_{15}O_5)^+$ in the mass spectrum and from the ^{1}H NMR spectrum (Figure 7a), absence of quartet at δ4.21 (OCH_2CH_3), triplet at δ1.30 (OCH_2CH_3) and one br. s, at δ2.69 (CH_2OH) established the structure of **19h**. The absence of signals at δ60.4 (OCH_2CH_3) and δ14.2 (OCH_2CH_3) in the ^{13}C NMR (Figure 7b), spectrum established the structure of **19h**.

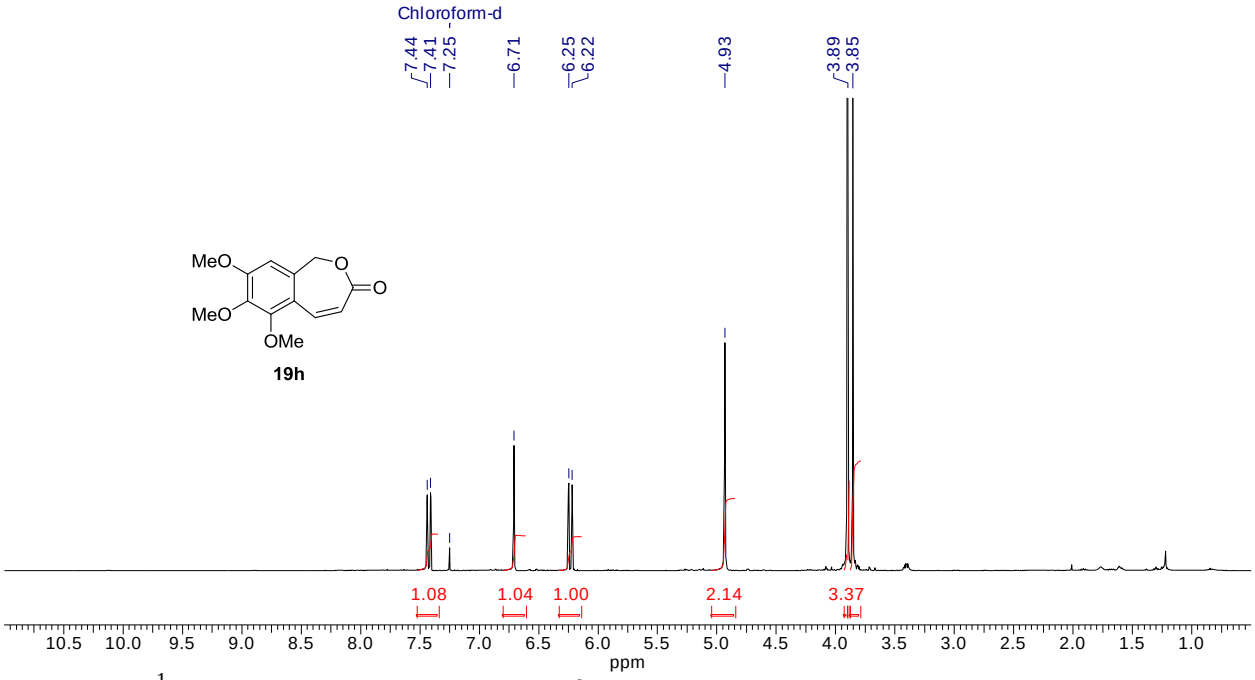


Figure 7a. ^{1}H NMR (400 MHz) spectrum of **19h** in $CDCl_3$.

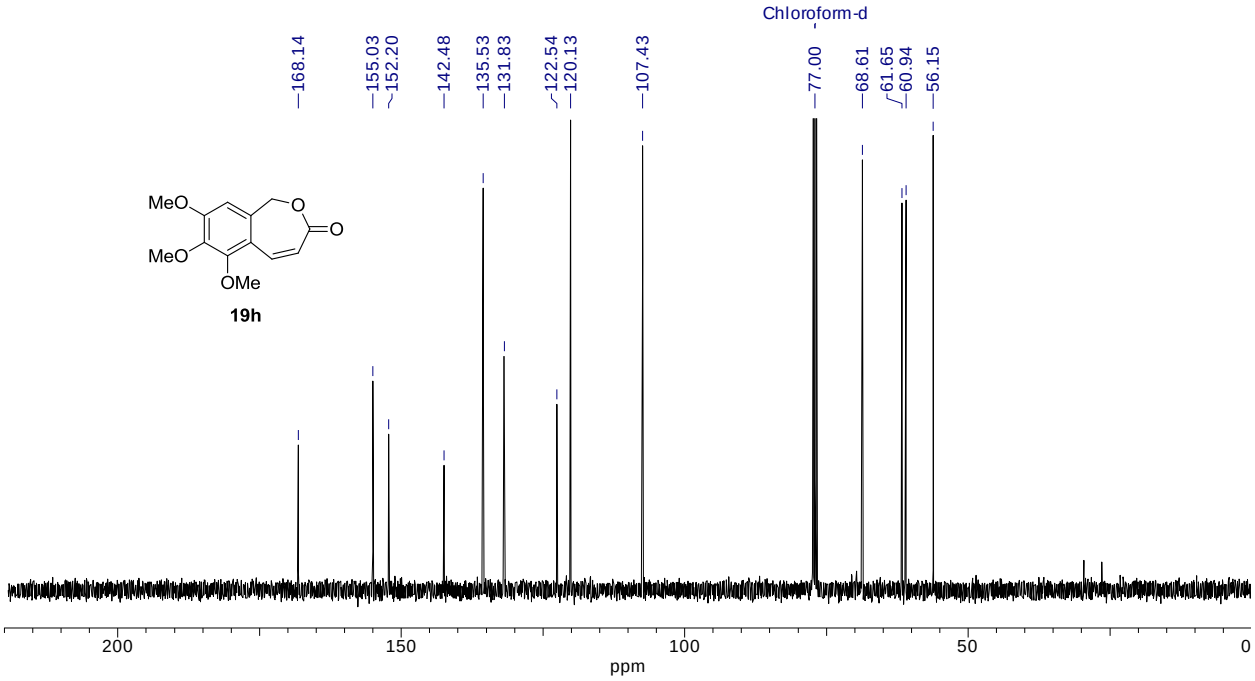
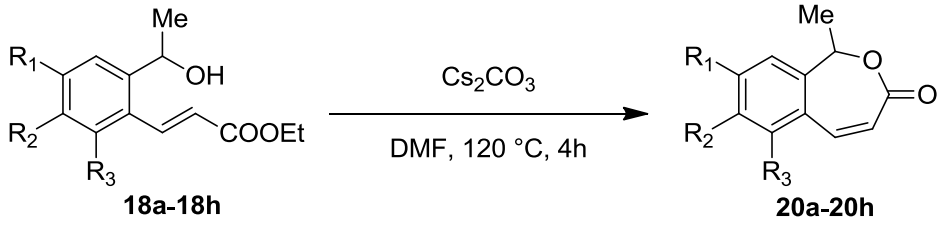


Figure 7b. ^{13}C NMR (100 MHz) spectrum of **19h** in $CDCl_3$.

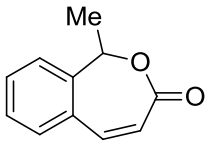
Table 10. Synthesis of lactenones (**20a-20h**) from secondary alcohol esters (**15a-15h**). [a]

[a] Isolated yields of the pure products.

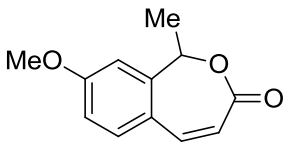
Presence of the molecular ion peak at m/z 287.0890 $(C_{14}H_{16}NaO_5)^+$ in the mass spectrum and from the ^{1}H NMR spectrum (Figure 8a), absence of quartet at δ4.22 (OCH_2CH_3), triplet at δ1.31 (OCH_2CH_3) and one br. s, at δ2.37 (CH_2OH) established the structure of **20h**. The absence of signals at δ60.4 (OCH_2CH_3) and δ14.2 (OCH_2CH_3) in the ^{13}C NMR (Figure 8b), spectrum established the structure of **20h**.



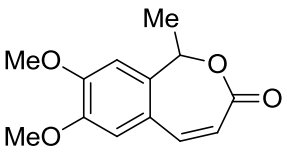
18a-18h **20a-20h**



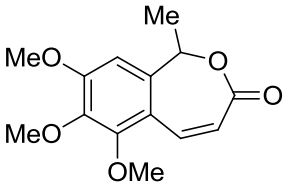
20a (67%)



20c (65%)



20g (71%)



20h (80%)

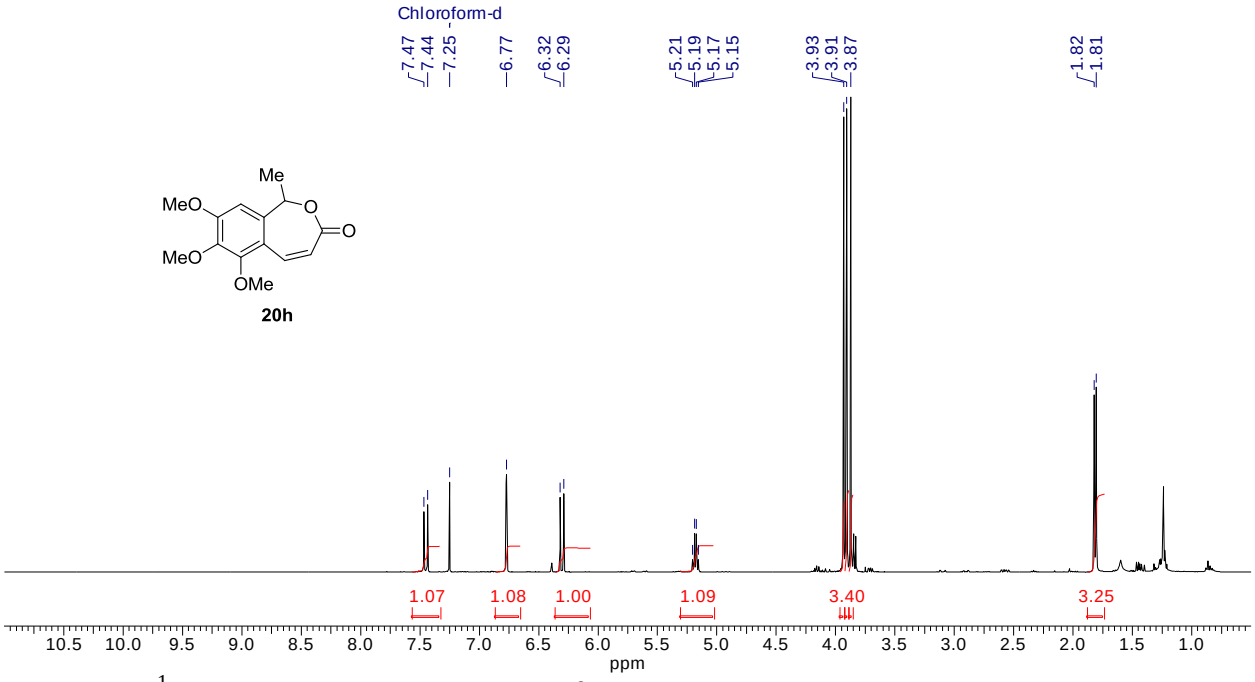


Figure 8a. ^{1}H NMR (400 MHz) spectrum of **20h** in $CDCl_3$

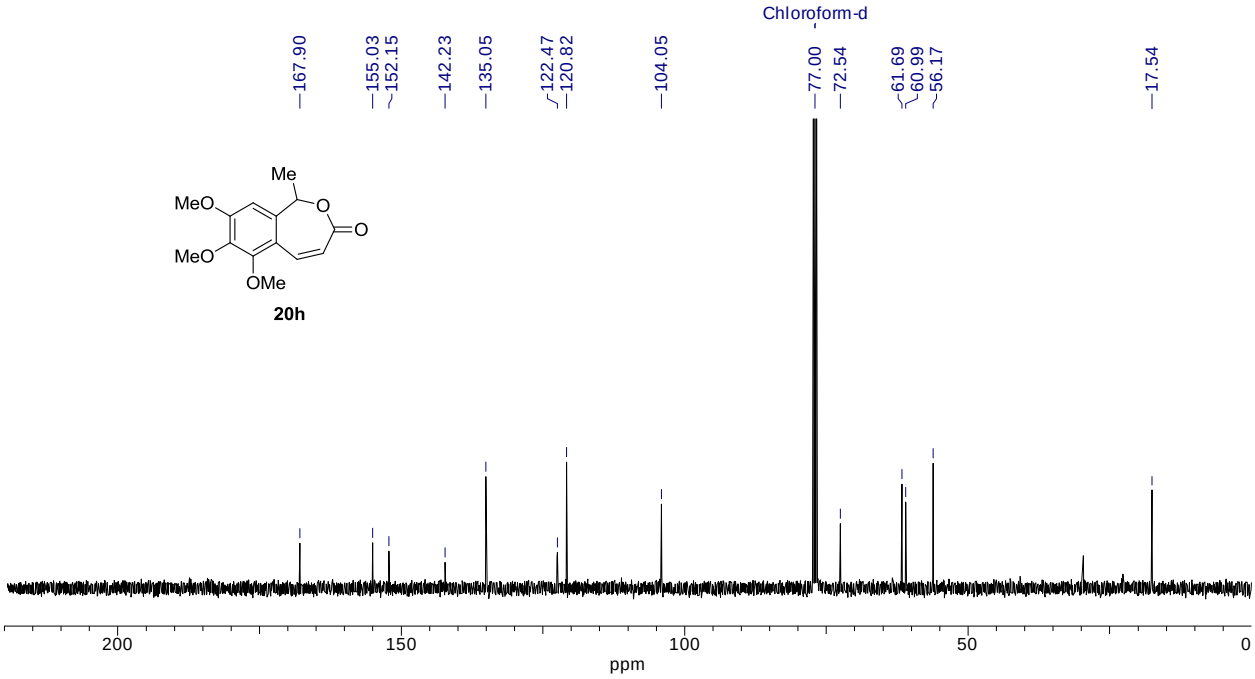
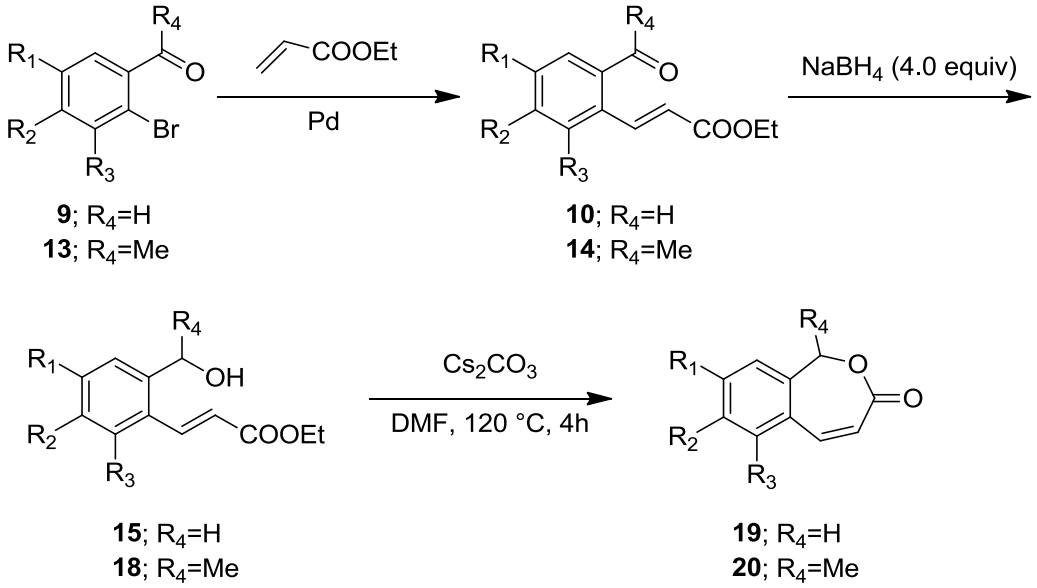


Figure 8b. ^{13}C NMR (100 MHz) spectrum of **20h** in $CDCl_3$

1.6 Conclusion:

We have developed a short and efficient strategy for the synthesis of functionalized 2-benzoxepin-3(1*H*)-ones using Pd-catalysed Heck coupling and reduction followed by intramolecular cyclization protocol. Significantly, these systems found in naturally occurring biologically active compounds. Initial step involves C-C bond formation whereas final cyclization step involves the formation of C-O bond through unprecedented condensation reaction path promoted by base.

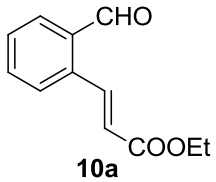


Scheme 8. Three-Step strategy for the synthesis of α,β-unsaturated lactones.

1.7 Experimental Section

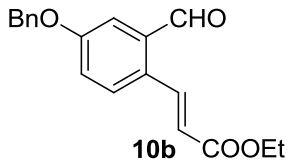
General: IR spectra were recorded on a Bruker Tensor 37 (FT-IR) spectrophotometer. ^{1}H NMR spectra were recorded on BrukerAvance 400 (400 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ in ppm) and coupling constants (J in Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H =0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C NMR spectra were recorded on BrukerAvance 400 (100 MHz) spectrometer at RT in $CDCl_3$; chemical shifts (δ in ppm) are reported relative to $CHCl_3$ [δ_C = 77.00 ppm (central line of triplet)]. In the ^{13}C NMR, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra, and is given in parentheses and noted as s = singlet (for C), d = doublet (for CH), t = triplet (for CH_2) and q = quartet (for CH_3). In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui =quintet, m = multiplet and br. s = broad singlet, septd = septet of doublets. The assignment of signals was confirmed by ^{1}H, ^{13}C CPD and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF using multimode source. All small scale dry reactions were carried out using standard syringe-septum technique. Reactions were monitored by TLC on silica gel using a mixture of petroleum ether and ethyl acetate as eluents. Reactions were generally run under an argon or nitrogen atmosphere. All Solvents were distilled prior use; petroleum ether with a boiling range of 60 to 80 °C, diethyl ether, dichloromethane (DCM), ethyl acetate, toluene, were used which are purchased from locally available commercial sources. All aromatic aldehydes, bromine, iodine, magnesium metal, methyliodide, 4 A Molecular sieves, sodium metal, silica gel (60–120 mesh), triethylamine (Et_3N) were used which are purchased from locally available commercial sources. Palladium(II)acetate, PPh_3 ethyl acrylate, diisopropylethylamine (DIPEA) were purchased from sigma-Aldrich which were used without further purification. Cs_2CO_3 dried at 150–170 $^{\circ}C$ over oil bath. DMF dried over CaH, diethyl ether and toluene were dried over benzophenone/sodium. Acme's silica gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

General Procedure-1 for Pd-mediated heck reaction on *ortho*-bromobenzaldehyde (9a-9h): To a stirred solution of an oven dried Schlenk tube under nitrogen atmosphere, were added *ortho*-bromobenzaldehyde **9a-9h** (2.0 mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), Et_3N (6.0 mmol), dry toluene (5 mL) and followed by addition of ethyl acrylate (6.0 mmol). The resulted reaction mixture was stirred at 110 °C for 24 h. The reaction mixture was quenched by addition of aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product **10a-10h** was purified by column chromatography on silica using petroleum ether/ethyl acetate as eluent.



10a

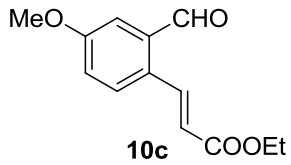
Ethyl (2E)-3-(2-formylphenyl)acrylate (**10a**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9a** (370 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9a**)=0.85, R_f(**10a**)=0.55 (petroleum ether/ethyl acetate 90:10, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 95:5 to 90:10) gave title compound **10a** (367 mg, 90%), yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2982, 2928, 1694, 1635, 1568, 1481, 1316, 1280, 1177, 1034, 976, 861, 765 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=10.28 (s, 1H, CHO), 8.50 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.86 (dd, 1H, *J*=7.3 and 1.0 Hz, Ar-H), 7.65–7.50 (m, 3H, Ar-H), 6.36 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.27 (q, 2H, *J*=7.3 Hz, OC$H_2$$CH_3$), 1.33 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=191.7 (d, CH=O), 166.2 (s, O=COEt), 140.9 (d, Ar-*C*H=CHCOOEt), 136.6 (d, Ar-CH), 133.9 (d, Ar-CH), 133.8 (s, Ar-C), 132.1 (d, Ar-CH), 129.8 (d, Ar-CH), 127.9 (d, Ar-CH), 123.2 (d, Ar-CH=*C*HCOOEt), 60.7 (t, O*C*$H_2$$CH_3$), 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{12}H_{12}NaO_3]^+$=$[M+Na]^+$: 227.0679; found: 227.0680.



10b

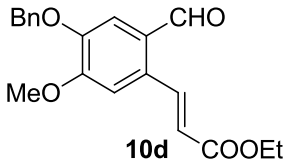
Ethyl (2E)-3-[4-(benzyloxy)-2-formylphenyl]acrylate (**10b**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9b** (452 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9b**)=0.80, R_f(**10b**)=0.60 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 80:20) gave title compound **10b** (465 mg, 75%), as yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 84–86 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1705, 1599, 1495, 1455, 1291, 1258, 1179, 1159, 1097, 1081, 1025, 737, 697 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=10.31 (s, 1H, CHO), 8.43 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.59 (d, 1H, *J*=8.8 Hz, Ar-H), 7.55–7.30 (m, 6H, Ar-H), 7.19 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.31 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.13 (s, 2H, $PhCH_2O$), 4.26 (q, 2H, *J*=7.3 Hz, OC$H_2$$CH_3$), 1.33 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=190.9 (d, CH=O), 166.4 (s, EtOC=O), 160.0 (s, Ar-C), 139.6 (d, Ar-*C*H=CHCOOEt), 135.8 (s, Ar-C), 135.0 (s, Ar-C), 129.5 (s, Ar-C), 129.4 (d, Ar-CH), 128.7 (d,

2C, Ar-CH), 128.3 (d, Ar-CH=*C*HCOOEt), 127.5 (d, 2C, Ar-CH), 121.4 (d, Ar-CH), 121.3 (d, Ar-CH), 115.6 (d, Ar-CH), 70.3 (t, $PhCH_2O$), 60.6 (t, OCH_2CH_3), 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{19}H_{18}NaO_4]^+$=[M+Na]$^+$: 333.1097; found: 333.1103.



10c

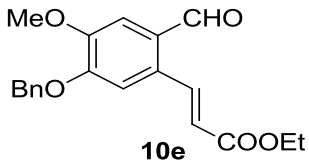
Ethyl (2*E*)-3-(2-formyl-4-methoxyphenyl)acrylate (**10c**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9c** (430 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9c**)=0.75, R_f(**10c**)=0.60 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 80:20) gave title compound **10c** (421 mg, 90%), as brown semi-solid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1709, 1601, 1497, 1464, 1292, 1263, 1180, 1161, 1098, 1033, 976, 834 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=10.33 (s, 1H, CHO), 8.42 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.59 (d, 1H, *J*=8.8 Hz, Ar-H), 7.36 (d, 1H, *J*=2.9 Hz, Ar-H), 7.13 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.30 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.26 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.88 (s, 3H, Ar-OCH_3), 1.33 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=190.9 (d, CH=O), 166.4 (s, EtOC=O), 160.9 (s, Ar-C), 139.6 (d, Ar-*C*H=CHCOOEt), 135.0 (s, Ar-C), 129.4 (d, Ar-CH), 129.3 (s, Ar-C), 121.2 (d, Ar-CH=*C*HCOOEt), 120.7 (d, Ar-CH), 114.4 (d, Ar-CH), 60.6 (t, OCH_2CH_3), 55.6 (q, OCH_3), 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{13}H_{14}NaO_4]^+$=[M+Na]$^+$: 257.0784; found: 257.0788.



10d

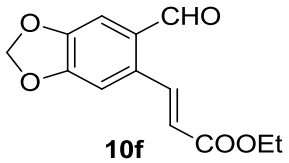
Ethyl (2*E*)-3-[4-(benzyloxy)-2-formyl-5-methoxyphenyl]acrylate (**10d**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9d (**642 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9d**)=0.60, R_f(**10d**)=0.50 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 80:20) gave title compound **10d** (632 mg, 93%), pale yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2923, 1710, 1683, 1590, 1513, 1277, 1173, 1113, 1029, 996, 743, 697, 541 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=10.24 (s, 1H, CHO), 8.43 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.43 (d, 2H, *J*=7.8 Hz, Ar-H), 7.42 (s, 1H,

Ar-H), 7.36 (dd, 2H, *J*=7.8 and 7.3 Hz, Ar-H), 7.30 (t, 1H, *J*=7.3 Hz, Ar-H), 7.05 (s, 1H, Ar-H), 6.33 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 5.19 (s, 2H, $PhCH_2O$), 4.27 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.95 (s, 3H, Ar-OCH_3), 1.33 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=189.1 (d, CH=O), 166.2 (s, EtOC=O), 154.1 (s, Ar-C), 149.6 (s, Ar-C), 139.4 (d, Ar-*C*H=CHCOOEt), 135.8 (s, Ar-C), 131.7 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.2 (d, Ar-CH), 127.5 (s, Ar-C), 127.4 (d, 2C, Ar-CH), 121.8 (d, Ar-CH=*C*HCOOEt), 113.2 (d, Ar-CH), 109.3 (d, Ar-CH), 70.9 (t, $PhCH_2O$), 60.7 (t, OCH_2CH_3), 56.1 (t, Ar-OCH_3) , 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{20}H_{20}NaO_5]^+$=$[M+Na]^+$: 363.1203; found: 363.1201.



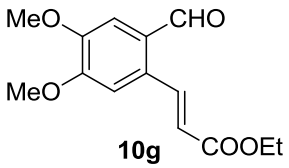
10e

Ethyl (2*E*)-3-[5-(benzyloxy)-2-formyl-4-methoxyphenyl]acrylate (**10e**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9e** (642 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9e**)=0.60, R_f(**10e**)=0.50 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 75:25) gave title compound **10e** (639 mg, 94%), as orange solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 124–126 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2922, 2852, 1709, 1680, 1589, 1513, 1356, 1275, 1174, 1109, 1028, 868, 742, 698 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=10.29 (s, 1H, CHO), 8.40 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.45–7.30 (m, 6H, Ar-H), 7.09 (s, 1H, Ar-H), 6.22 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 5.22 (s, 2H, $PhCH_2O$), 4.26 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.94 (s, 3H, Ar-OCH_3), 1.33 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=189.1 (d, CH=O), 166.2 (s, EtOC=O), 152.7 (s, Ar-C), 151.0 (s, Ar-C), 139.3 (d, Ar-*C*H=CH-COOEt), 135.6 (s, Ar-C), 131.3 (s, Ar-C), 128.7 (d, 2C, Ar-CH), 128.3 (d, Ar-CH), 127.8 (s, Ar-C), 127.3 (d, 2C, Ar-CH), 121.8 (d, Ar-CH=*C*HCOOEt), 111.4 (d, Ar-CH), 111.0 (d, Ar-CH), 70.9 (t, $PhCH_2O$), 60.7 (t, OCH_2CH_3), 56.1 (q, OCH_3) , 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{20}H_{20}NaO_5]^+$=$[M+Na]^+$: 363.1203; found: 363.1195.



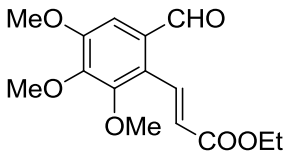
10f

Ethyl (2*E*)-3-(6-formyl-1,3-benzodioxol-5-yl)acrylate (**10f**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9f** (458 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9f**)=0.75, R_f(**10f**)=0.55 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20) gave title compound **10f** (461 mg, 93%), as yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 112–114 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2921, 2852, 1710, 1679, 1606, 1504, 1480, 1377, 1290, 1265, 1182, 1035, 973, 930, 510 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=10.23 (s, 1H, CHO), 8.39 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.31 (s, 1H, Ar-H), 7.03 (s, 1H, Ar-H), 6.28 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 6.08 (s, 2H, OCH_2O), 4.26 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 1.32 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=188.7 (d, CH=O), 166.2 (s, EtOC=O), 152.5 (s, Ar-C), 149.5 (s, Ar-C), 139.3 (d, Ar-*C*H=CHCOOEt), 133.8 (s, Ar-C), 129.5 (s, Ar-C), 122.3 (d, Ar-CH=*C*HCOOEt), 108.8 (d, Ar-CH), 106.7 (d, Ar-CH), 102.4 (t, OCH_2O), 60.8 (t, OCH_2CH_3), 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{13}H_{12}NaO_5]^+$=$[M+Na]^+$: 271.0577; found: 271.0571.



10g

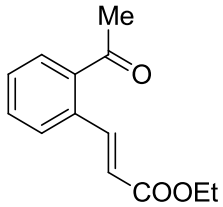
Ethyl (2*E*)-3-(2-formyl-4,5-dimethoxyphenyl)acrylate (**10g**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9g** (490 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9g**)=0.50, R_f(**10g**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20 to 70:30) gave title compound **10g** (483 mg, 93%), as orange solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 110–112 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2982, 1711, 1679, 1594, 1561, 1522, 1356, 1300, 1272, 1164, 1106, 988, 790 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=10.27 (s, 1H, CHO), 8.40 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.34 (s, 1H, Ar-H), 7.01 (s, 1H, Ar-H), 6.31(d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.24 (q, 2H, *J*=7.3, OCH_2CH_3), 3.94 (s, 3H, Ar-OCH_3), 3.92 (s, 3H, Ar-OCH_3), 1.30 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=189.0 (d, CH=O), 166.1 (s, EtOC=O), 153.5 (s, Ar-C), 150.5 (s, Ar-C), 139.2 (d, Ar-*C*H=CHCOOEt), 131.5 (s, Ar-C), 127.6 (s, Ar-C), 121.8 (d, Ar-CH=*C*HCOOEt), 111.0 (d, Ar-CH), 108.9 (d, Ar-CH), 60.7 (t, OCH_2CH_3), 56.1 (q, Ar-OCH_3), 56.0 (q, Ar-OCH_3), 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{14}H_{16}NaO_5]^+$=$[M+Na]^+$: 287.0890; found: 287.0892.



10h

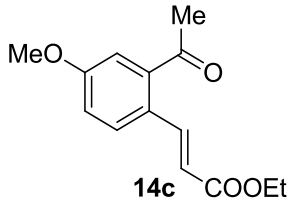
Ethyl (2*E*)-3-(6-formyl-2,3,4-trimethoxyphenyl)acrylate (**10h**): General procedure-**1** was carried out with *ortho*-bromobenzaldehyde **9h** (552 mg, 2.0 mmol), $Pd(OAc)_2$ (22.5 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), Et_3N (607 mg, 6.00 mmol), dry toluene (2 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**9h**)=0.40, R_f(**10h**)=0.30 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20 to 70:30) gave title compound **10h** (548 mg, 93%), as pink solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 72–74 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2923, 2852, 1714, 1687, 1583, 1488, 1461, 1330, 1301, 1175, 1127, 1029, 985, 925, 861 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=10.13 (s, 1H, CHO), 8.04 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.26 (s, 1H, Ar-H), 6.21 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.25 (q, 2H, *J*=7.3 Hz, OC$H_2$$CH_3$), 3.93 (s, 3H, Ar-$OCH_3$), 3.91(s, 3H, Ar-$OCH_3$), 3.85 (s, 3H, Ar-$OCH_3$), 1.31 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=189.9 (d, CH=O), 166.1 (s, EtOC=O), 154.1 (s, Ar-C), 152.4 (s, Ar-C), 147.0 (s, Ar-C), 135.6 (d, Ar-*C*H=CHCOOEt), 130.3 (s, Ar-C), 126.4 (d, Ar-CH=*C*HCOOEt), 126.2 (s, Ar-C), 107.2 (d, Ar-CH), 61.1 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 60.7 (t, O*C*$H_2$$CH_3$), 56.1 (q, Ar-$OCH_3$), 14.2 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{15}H_{18}NaO_6]^+$=$[M+Na]^+$: 317.0996; found: 317.1000.

General Procedure-2 for Pd-mediated heck reaction *ortho*-bromoacetophenone **(13a-13h):** To a stirred solution of an oven dried Schlenk tube under nitrogen atmosphere, were added *ortho*-bromoacetophenone **13a-13h** (2.0 mmol), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%) and DIPEA (6.0 mmol), dry toluene (5 mL) and followed by addition of ethyl acrylate (6.0 mmol). The resulted reaction mixture was stirred at 110 °C for 24 h. The reaction mixture was quenched by addition of aqueous NH_4Cl and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product **14a-14h** was purified by column chromatography on silica using petroleum ether/ethyl acetate as eluent.



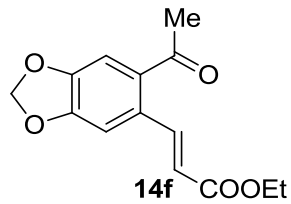
14a

Ethyl (2*E*)-3-(2-acetylphenyl)acrylate (**14a**): General procedure-**2** was carried out with *ortho*-bromoacetophenone **13a** (398 mg, 2.0 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), DIPEA (775.2 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**13a**)=0.50, R_f(**13h**)=0.35 (petroleum ether/ethyl acetate 90:10, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 95:5 to 90:10) gave title compound **13a** (379 mg, 87%), as orange semi-solid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2923, 2852, 1711, 1682, 1634, 1364, 1315, 1278, 1251, 1178, 1038, 975, 957, 768, 608 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.12 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.72 (dd, 1H, *J*=7.3 and 1.5 Hz, Ar-H), 7.56 (dd, 1H, *J*=7.8 and 1.5 Hz, Ar-H), 7.50 (ddd, 1H, *J*=7.8, 7.3 and 1.5 Hz, Ar-H), 7.43 (ddd, 1H, *J*=7.8, 7.3 and 1.5 Hz, Ar-H), 6.26 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.24 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 2.59 (s, 3H, $COCH_3$), 1.31 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 200.8 (s, C=O), 166.5 (s, O=COEt), 143.8 (d, Ar-*C*H=CHCOOEt), 138.2 (s, Ar-C), 134.8 (s, Ar-C), 131.9 (d, Ar-CH), 129.3 (d, Ar-CH), 129.1(d, Ar-CH=*C*HCOOEt), 128.3 (d, Ar-CH), 120.9 (d, Ar-CH), 60.5 (t, OCH_2CH_3), 29.2 (q, $COCH_3$), 14.2 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{13}H_{14}NaO_3]^+$=$[M+Na]^+$: 241.0835; found: 241.0830.

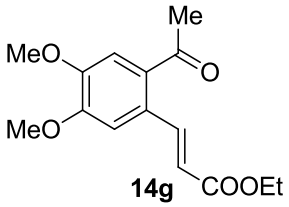


Ethyl (2*E*)-3-(2-acetyl-4-methoxyphenyl)acrylate (**14c**): General procedure-**2** was carried out with *ortho*-bromoacetophenone **13c** (458 mg, 2.0 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), DIPEA (775.2 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**13c**)=0.40, R_f(**14c**)=0.30 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 85:15) gave title compound **14c** (472 mg, 95%), as yellow liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2921, 2851, 1708, 1687, 1633, 1601, 1489, 1295, 1271, 1215,1172, 1038, 870, 830 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.01 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.56 (d, 1H, *J*=8.8 Ar-H), 7.16 (d, IH, *J*=2.9, Ar-H), 7.02 (dd, 1H, *J*=8.8 and 2.9, Ar-H), 6.22 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.24 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.86 (s, 3H, Ar-OCH_3), 2.58 (s, 3H, $COCH_3$), 1.32 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR

($CDCl_3$, 100 MHz): δ= 201.1 (s, C=O), 166.7 (s, O=COEt), 160.3 (s, Ar-C), 142.8 (d, Ar-*C*H=CHCOOEt), 140.3 (s, Ar-C), 129.6 (d, Ar-CH), 126.5 (s, Ar-C), 119.1 (d, Ar-CH=*C*HCOOEt), 116.8 (d, Ar-CH), 114.5 (d, Ar-CH), 60.4 (t, O*C*$H_2$$CH_3$), 55.6 (q, Ar-O*C*$H_3$), 29.6 (q, CO*C*$H_3$), 14.3 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{14}H_{16}KO_4]^+$=$[M+K]^+$: 287.0680; found: 287.0675.

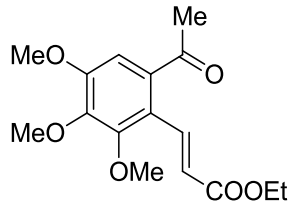


Ethyl (2*E*)-3-(6-acetyl-1,3-benzodioxol-5-yl)acrylate (**14f**): General procedure-**2** was carried out with *ortho*-bromoacetophenone **13f** (482 mg, 2.0 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), DIPEA (775.2 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**13f**)=0.45, R_f(**14f**)=0.30 (petroleum ether/ethyl acetate 90:10, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 85:15) gave title compound **14f** (430 mg, 83%), as yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2921, 2852, 1708, 1680, 1632, 1508, 1379, 1299, 1225, 1197, 1181, 1117, 1034, 972, 852 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.07 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.16 (s, IH, Ar-H), 7.00 (s, 1H, Ar-H), 6.16 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 6.05 (s, 2H, OCH_2O), 4.23 (q, 2H, *J*=7.3 Hz, OC*H*$_2$$CH_3$), 2.53 (s, 3H, $COCH_3$) 1.30 (t, 3H, *J*=7.3 Hz, OCH_2C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 199.0 (s, C=O), 166.6 (s, O=COEt), 150.5 (s, Ar-C), 148.5 (s, Ar-C), 143.6 (d, Ar-CH=CHCOOEt), 133.1 (s, Ar-C), 130.9 (s, Ar-C), 119.8 (d, Ar-CH=CHCOOEt), 109.1 (d, Ar-CH), 107.7 (d, Ar-CH), 102.3 (t, OCH_2O), 60.5, (t, O*C*$H_2$$CH_3$), 29.2 (q, CO*C*$H_3$), 14.3 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{14}H_{14}NaO_5]^+$=$[M+Na]^+$: 285.0733; found: 285.0738.



Ethyl (2*E*)-3-(2-acetyl-4,5-dimethoxyphenyl)acrylate (**14g**): General procedure-**2** was carried out with *ortho*-bromoacetophenone **13g** (518 mg, 2.0 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), DIPEA (775.2 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**13g**)=0.40, R_f(**14g**)=0.30 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 80:20) gave title compound **14g** (473 mg, 85%), as brown

viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 2924, 2852, 1705, 1674, 1631, 1596, 1513, 1361, 1270, 1172, 1149, 1060, 1034, 860 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 8.18 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.22 (s, 1H, Ar-H), 7.04 (s, IH, Ar-H), 6.24 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 4.27 (q, 2H, *J*=7.3 Hz, OC$H_2$$CH_3$), 3.96 (s, 6H, Ar-$OCH_3$), 2.60 (s, 3H, $COCH_3$) 1.34 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 199.2 (s, C=O), 166.6 (s, O=COEt), 151.6 (s, Ar-C), 149.4 (s, Ar-C), 143.8 (d, Ar-CH=C*H*COOEt), 131.3 (s, Ar-C), 128.9 (s, Ar-C), 119.6 (d, Ar-CH=CHCOOEt), 111.9 (d, Ar-CH), 110.1 (d, Ar-CH), 60.4 (t, OC$H_2$$CH_3$), 56.1 (q, Ar-O*C*$H_3$), 56.0 (q, Ar-O*C*$H_3$), 29.3 (q, CO*C*$H_3$), 14.2 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{15}H_{18}NaO_5]^+$=$[M+Na]^+$: 301.1046; found: 301.1046.

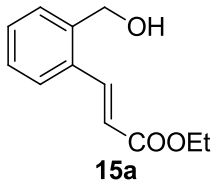


14h

Ethyl (2*E*)-3-(6-acetyl-2,3,4-trimethoxyphenyl)acrylate (**14h**): General procedure-**2** was carried out with *ortho*-bromoacetophenone **13h** (576 mg, 2.0 mmol), $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), PPh_3 (52.4 mg, 0.20 mmol), DIPEA (775.2 mg, 6.00 mmol), dry toluene (5 mL) and ethyl acrylate (0.65 mL, 6.0 mmol) at 110 °C for 24 h [TLC control R_f(**13h**)=0.40, R_f(**14h**)=0.25 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20 to 75:25) gave title compound **14h** (517 mg, 84%), as yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): $\nu_{max=}$ 2917, 2849, 1712, 1584, 1462, 1328, 1302, 1260, 1163, 1124, 1026, 719 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.78 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 6.80 (s, 1H, Ar-H), 6.29 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.20 (q, 2H, *J*=7.3 Hz, OC$H_2$$CH_3$), 3.88 (s, 3H, Ar-$OCH_3$), 3.86 (s, 3H, Ar-$OCH_3$), 3.81 (s, 3H, Ar-$OCH_3$), 2.46 (s, 3H, $COCH_3$), 1.28 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 202.3 (s, C=O), 166.8 (s, O=COEt), 153.8 (s, Ar-C), 153.0 (s, Ar-C), 144.4 (s, Ar-C), 138.3 (d, Ar-*C*H=CHCOOEt), 136.9 (s, Ar-C), 123.2 (d, Ar-CH), 120.7 (d, Ar-CH), 107.2 (d, Ar-CH=*C*HCOOEt), 60.9 (q, Ar-O*C*H_3), 60.8 (q, Ar-O*C*H_3), 60.4 (t, OC$H_2$$CH_3$), 56.1 (q, Ar-O*C*$H_3$), 30.6 (q, CO*C*$H_3$), 14.3 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{16}H_{20}NaO_6]^+$=$[M+Na]^+$: 331.1152; found: 331.1151.

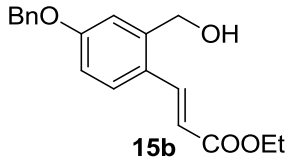
General Procedure-3 (For primary alcohols): To magnetically stirred solution of an aldehyde ester **10a-10h** (0.50 mmol) in AcOH (2 mL), was added sodium borohydride (2.0 mmol). Then the reaction mixture was stirred at rt for 1.5 h. The reaction mixture was quenched by addition of aqueous $NaHCO_3$ solution and extracted with ethyl acetate (3 × 15 mL). The organic layer was

washed with saturated NaCl solution, dried over Na_2SO_4. Evaporation of the organic layer under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished alcohol ester (**15a-15h**) (78–96%).



15a

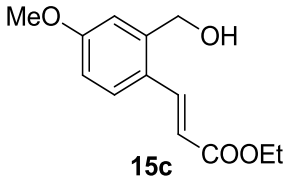
Ethyl (2*E*)-3-[2-(hydroxymethyl)phenyl)acrylate (**15a**): General procedure-**3** was carried with an aldehyde ester **10a** (102 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10a**)=0.85, R_f(**15a**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **15a** (92 mg, 89%), as brown viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3416, 2923, 2853, 1710, 1633, 1462, 1367, 1315, 1276, 1179, 1033, 978, 766 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=8.02 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.58 (d, 1H, *J*=7.3, Ar-H), 7.43 (d, 1H, *J*=7.3, Ar-H), 7.37 (dd, 1H, *J*=7.3 and 7.3 Hz, Ar-H), 7.31 (dd, 1H, *J*=7.3 and 7.3 Hz, Ar-H), 6.38 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.80 (s, 2H, CH_2OH), 4.25 (q, 2H, J=7.3, OCH_2CH$_3$), 2.59 (br. s, 1H, OH), 1.33 (t, 3H, *J*=7.3 Hz, OCH$_2$CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.0 (s, O=COEt), 141.4 (d, Ar-*C*H=CHCOOEt), 139.6 (s, Ar-C), 133.0 (s, Ar-C), 130.1 (d, Ar-CH), 128.7 (d, Ar-CH), 128.1 (d, Ar-CH), 126.7 (d, Ar-CH=*C*HCOOEt), 120.1 (d, Ar-CH), 62.7 (t, *C*H$_2$OH), 60.6 (t, OCH$_2$CH$_3$), 14.2 (q, OCH$_2$*C*H$_3$) ppm. HR-MS (ESI+) m/z calculated for $[C_{12}H_{14}NaO_3]^+$=$[M+Na]^+$: 229.0835; found: 229.0844.



15b

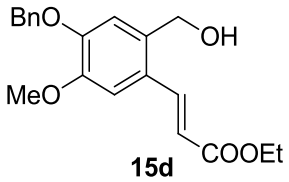
Ethyl (2*E*)-3-[4-(benzyloxy)-2-(hydroxymethyl)phenyl]acrylate (**15b**): General procedure-**3** was carried with an aldehyde ester **10b** (155 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10b**)=0.60, R_f(**15b**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **15b** (123 mg, 79%), as pale orange solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 94–96 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 3433, 2923, 2853, 1705, 1601, 1495, 1455, 1294, 1255, 1160, 1095, 1026, 977, 735, 696 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.91 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.54 (d, 1H, *J*=8.8 Hz, Ar-H) , 7.45–7.30 (m, 5H, Ar-H), 7.08 (d, 1H, *J*=2.9), 6.89 (d, 1H, *J*=8.8 Hz, Ar-H), 6.27 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.07 (s, 2H, PhCH$_2$O), 4.78 (s, 2H, CH_2OH), 4.23 (q, 2H, *J*=7.3 Hz, OCH_2CH$_3$), 2.03 (br. s, 1H, CH$_2$O*H*),

1.31 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.4 (s, EtOC=O), 160.4 (s, Ar-C), 141.7 (s, Ar-C), 140.7 (d, Ar-*C*H=CHCOOEt), 136.4 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.4 (d, Ar-CH), 128.1 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 125.3 (s, Ar-C), 117.6 (d, Ar-CH=*C*HCOOEt), 114.4 (d, Ar-CH), 114.3 (d, Ar-CH), 70.0 (t, $PhCH_2O$), 62.6 (t, CH_2OH), 60.5 (t, OCH_2CH_3), 14.3 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{19}H_{20}NaO_4]^+$=$[M+Na]^+$: 335.1254; found: 335.1257.



15c

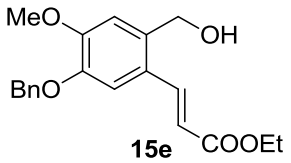
Ethyl (2*E*)-3-[2-(hydroxymethyl)-4-methoxyphenyl]acrylate (**15c**): General procedure-**3** was carried with an aldehyde ester **10c** (117 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10c**)=0.60, R_f(**15c**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **15c** (92 mg, 78%), as yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3433, 2924, 1704, 1630, 1601, 1496, 1464, 1296, 1256, 1179, 1158, 1095, 1031, 977, 860, 816 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.89 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.53 (d, 1H, *J*=8.8 Hz, Ar-H), 6.99 (d, 1H, *J*=2.9 Hz, Ar-H), 7.81 (dd, 1H, *J*=8.8 and 2.9 Hz, Ar-H), 6.25 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 4.78 (s, 2H, CH_2OH), 4.21 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.80 (s, 3H, Ar-OCH_3), 2.02 (br. s, 1H, CH_2OH), 1.30 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.4 (s, EtOC=O), 161.2 (s, Ar-C), 141.7 (s, Ar-C), 140.8 (d, Ar-*C*H=CHCOOEt), 128.3 (d, Ar-CH), 125.0 (s, Ar-C), 117.4 (d, Ar-CH=*C*HCOOEt), 113.6 (d, Ar-CH), 113.4 (d, Ar-CH), 62.5 (t, CH_2OH), 60.4 (t, OCH_2CH_3), 55.3 (q, Ar-OCH_3), 14.3 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{13}H_{16}NaO_4]^+$=$[M+Na]^+$: 259.0941; found: 259.0946.



15d

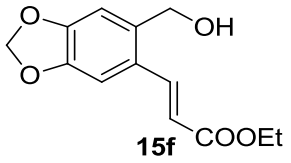
Ethyl (2*E*)-3-[4-(benzyloxy)-2-(hydroxymethyl)-5-methoxyphenyl]acrylate (**15d**): General procedure-**3** was carried with an aldehyde ester **10d** (170 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10d**)=0.50, R_f(**15d**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **15d** (164 mg, 96%), as yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 114–116 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2957, 2920, 2851, 1706, 1600, 1514, 1464, 1275, 1170, 1105, 1028, 863, 739 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.93 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.42

(d, 2H, *J*=6.8 Hz, Ar-H), 7.36 (dd, 2H, *J*=7.3 and 6.8 Hz, Ar-H), 7.31 (t, 1H, *J*=7.3 Hz, Ar-H), 7.09 (s, 1H, Ar-H), 6.98 (s, 1H, Ar-H) , 6.29 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 5.15 (s, 2H, $PhCH_2O$), 4.70 (s, 2H, CH_2OH), 4.24 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.88 (s, 3H, Ar-OCH_3), 2.36 (br. s, 1H, CH_2OH), 1.33 (t, 3H, *J*=7.3 Hz, OCH_2CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.2 (s, EtOC=O), 150.0 (s, Ar-C), 149.0 (s, Ar-C), 140.8 (d, Ar-*C*H=CH-COOEt), 136.4 (s, Ar-C), 133.5 (s, Ar-C), 128.5 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.3 (d, 2C, Ar-CH), 125.4 (s, Ar-C), 117.6 (d, Ar-CH=*C*HCOOEt), 113.7 (d, Ar-CH), 109.4 (d, Ar-CH), 70.7 (t, $PhCH_2O$), 62.1 (t, CH_2OH), 60.5 (t, OCH_2CH_3), 56.0 (q, Ar- OCH_3) , 14.3 (q, OCH_2CH_3) ppm HR-MS (ESI+) m/z calculated for $[C_{20}H_{22}NaO_5]^+$=$[M+Na]^+$: 365.1359; found: 365.1362.



15e

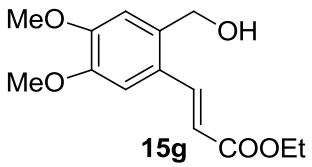
Ethyl (2*E*)-3-[5-(benzyloxy)-2-(hydroxymethyl)-4-methoxyphenyl]acrylate (**15e**): General procedure-**3** was carried with an aldehyde ester **10e** (170 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10e**)=0.50, R_f(**15e**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **15e** (147 mg, 86%), as pale yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 126–128 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2921, 2852, 1709,1600, 1513, 1463, 1272, 1175, 1103, 1029, 865, 722 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.90 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.43 (d, 2H, *J*=7.3 Hz, Ar-H), 7.36 (dd, 2H, *J*=7.3 and 7.3 Hz, Ar-H), 7.30 (t, 1H, *J*=7.3 Hz, Ar-H), 7.11 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 6.16 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 5.12 (s, 2H, $PhCH_2O$), 4.74 (s, 2H, CH_2OH), 4.22 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.88 (s, 3H, Ar-OCH_3), 2.55 (br. s, 1H, CH_2OH), 1.31 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.2 (s, EtOC=O), 151.5 (s, Ar-C), 147.6 (s, Ar-C), 140.7 (d, Ar-*C*H=CH-COOEt), 136.6 (s, Ar-C), 134.1 (s, Ar-C), 128.6 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 127.4 (d, 2C, Ar-CH), 125.0 (s, Ar-C), 117.5 (d, Ar-CH=*C*HCOOEt), 111.9 (d, Ar-CH), 111.8 (d, Ar-CH), 71.1 (t, $PhCH_2O$), 62.2 (t, CH_2OH), 60.5 (t, OCH_2CH_3), 55.9 (q, Ar- OCH_3) , 14.3 (q, OCH_2CH_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{20}H_{22}NaO_5]^+$=$[M+Na]^+$: 365.1359; found: 365.1359.



15f

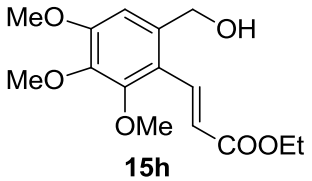
Ethyl (2*E*)-3-[6-(hydroxymethyl)-1,3-benzodioxol-5-yl]acrylate (**15f**) **:** General procedure-**3** was carried with an aldehyde ester **10f** (124 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10f**)=0.75, R_f(**15f**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20 to 70:30) gave title compound **15f** (113 mg, 90%), as yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 94–96 °C. IR (MIR-ATR, 4000–600

cm^{-1}): ν_{max}=2921, 2851, 1707, 1463, 1265, 1179, 909 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.89 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.03 (s, 1H, Ar-H), 6.89 (s, 1H, Ar-H), 6.16 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.96 (s, 2H, OCH_2O), 4.70 (s, 2H, CH_2OH), 4.21 (q, 2H, *J*=7.3 Hz, OC$H_2$$CH_3$), 2.59 (br. s, 1H, CH_2O*H*), 1.30 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.2 (s, EtOC=O), 149.4 (s, Ar-C), 147.6 (s, Ar-C), 140.6 (d, Ar-C*H*=CHCOOEt), 135.3 (s, Ar-C), 126.6 (s, Ar-C), 117.8 (d, Ar-CH=C*H*COOEt), 109.0 (d, Ar-CH), 105.9 (d, Ar-CH), 101.5 (t, OCH_2O), 62.3 (t, CH_2OH), 60.5 (t, O*C*$H_2$$CH_3$), 14.2 (q, *OCH$_2CH_3$*) ppm. HR-MS (ESI+) m/z calculated for $[C_{13}H_{14}NaO_5]^+$=$[M+Na]^+$: 273.0733; found: 273.0730.



15g

Ethyl (2*E*)-3-[2-(hydroxymethyl)-4,5-dimethoxyphenyl]acrylate (**15g**): General procedure-**3** was carried with an aldehyde ester **10g** (132 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10g**)=0.50, R_f(**15g**)=0.40 (petroleum ether/ethyl acetate 70:40, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 70:30 to 60:40) gave title compound **15g** (121 mg, 91%), as brown solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 72–74 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3482, 2923, 2853, 1702, 1629, 1600, 1513, 1464, 1269, 1170, 1103, 1034, 998, 859 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.93 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 7.05 (s, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 6.26 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.76 (t, 2H, CH_2OH), 4.22 (q, 2H, J=7.3, OC$H_2$$CH_3$), 3.88 (s, 3H, Ar-OMe), 3.87 (s, 3H, Ar-OMe), 2.46 (br. s, 1H, CH_2O*H*), 1.30 (t, 3H, *J*=7.3 Hz, OCH_2C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.2 (s, EtOC=O), 150.7 (s, Ar-C), 148.5 (s, Ar-C), 140.8 (d, Ar-C*H*=CHCOOEt), 133.6 (s, Ar-C), 125.0 (s, Ar-C), 117.5 (d, Ar-CH=C*H*COOEt), 111.5 (d, Ar-CH), 108.8 (d, Ar-CH), 62.2 (t, CH_2OH), 60.5 (t, O*C*$H_2$$CH_3$), 55.9 (q, 2C, Ar-$OCH_3$), 14.3 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{14}H_{18}NaO_5]^+$=$[M+Na]^+$: 289.1046; found: 289.1057.

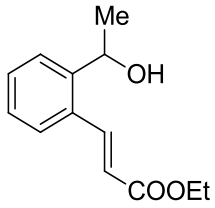


15h

Ethyl (2*E*)-3-[6-(hydroxymethyl)-2, 3, 4-trimethoxyphenyl]acrylate (**15h**): General procedure-**3** was carried with an aldehyde ester **10h** (148 mg, 0.50 mmol) and $NaBH_4$ (74.6 mg, 2.0 mmol) in AcOH (2 mL) for 1.5 h at rt, [TLC control R_f(**10h**)=0.50, R_f(**15h**)=0.30 (petroleum ether/ethyl acetate 50:50, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 60:40 to 50:50) gave title compound **15h** (134 mg, 90%), as yellow solid (recrystallized from a mixture of petroleum ether/dichloromethane). m.p.: 78–80 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3482, 2922, 2852, 1710, 1627, 1590, 1489, 1462, 1406, 1329, 1301, 1176, 1127, 1030, 982 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.78 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 6.84 (s, 1H, Ar-H), 6.55 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 4.72 (t, 2H,

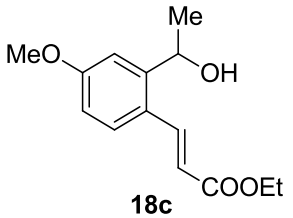
C*H*$_2$OH), 4.21 (q, 2H, *J*=7.3 Hz, OC*H*$_2$CH$_3$), 3.86 (s, 3H, Ar-OCH$_3$), 3.83 (s, 6H, Ar-OCH$_3$), 2.69 (br. s, 1H, CH$_2$O*H*), 1.30 (t, 3H, *J*=7.3 Hz, OCH$_2$C*H*$_3$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): *δ*=168.0 (s, EtOC=O), 154.3 (s, Ar-C), 153.7 (s, Ar-C), 141.6 (s, Ar-C), 137.5 (d, Ar-*C*H=CHCOOEt), 136.5 (s, Ar-C), 121.3 (d, Ar-CH=*C*HCOOEt), 119.6 (s, Ar-C), 107.6 (d, Ar-CH), 62.9 (t, O*C*H$_2$CH$_3$), 60.8 (q, Ar-OCH$_3$), 60.6 (q, Ar-OCH$_3$), 60.4 (t, CH$_2$OH), 55.9 (t, Ar-OCH$_3$) 14.3 (q, OCH$_2$*C*H$_3$) ppm. HR-MS (ESI+) m/z calculated for [C$_{15}$H$_{20}$NaO$_6$]$^+$=[M+Na]$^+$: 319.1152; found: 319.1153.

General Procedure-4 (For secondary alcohols): To a magnetically stirred solution of a acetophenone ester **14a-14h** (0.5 mmol) in methanol (4 mL), was added CeCl$_3$.7H$_2$O (0.5 mmol) at –20 °C followed by addition of sodium borohydride (1.0 mmol) after 10 mins at the same temperature. Then reaction mixture was stirred at rt for 12 h. Solvent was removed under reduced pressure, treated with aqueous 1 N HCl (10 mL) solution and extracted with DCM (3 × 15 mL). The organic layer was washed with saturated NaCl solution, dried (Na$_2$SO$_4$), and filtered. Evaporation of the filtrate under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished secondary alcohol ester **18a-18h** (65–89%).



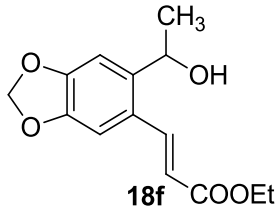
18a

Ethyl (2*E*)-3-[2-(1-hydroxyethyl)phenyl]acrylate (**18a**): General procedure-**4** was carried out with acetophenone ester **14a** (109 mg, 0.50 mmol) in methanol (4 mL), CeCl$_3$.7H$_2$O (186 mg, 0.50 mmol), NaBH$_4$ (37.3 mg, 1.0 mmol) at –20 °C, [TLC control R_f(**14a**)=0.55, R_f(**18a**)=0.50 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 80:20) gave title compound **18a** (86 mg, 78%), as yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2919, 2850, 1713, 1632, 1462, 1368, 1315, 1269, 1178, 1075, 1036, 898, 763 cm^{-1}. ^{1}H NMR (CDCl$_3$, 400 MHz): *δ*= 8.06 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.59 (d, 1H, *J*=7.8 Hz, Ar-H), 7.51 (d, 1H, *J*=7.8, Ar-H), 7.39 (dd, 1H, *J*=7.8 and 7.3 Hz, Ar-H), 7.26 (dd, 1H, *J*=7.8 and 7.3 Hz, Ar-H), 6.32 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.27 (q, 1H, *J*=6.4 Hz, C*H*CH$_3$), 4.24 (q, 2H, *J*=7.3 Hz, OC*H*$_2$CH$_3$), 2.62 (br. s, 1H, OH), 1.46 (d, 3H, *J*=6.4 Hz , CHC*H*$_3$), 1.33 (t, 3H, *J*=7.3 Hz, OCH$_2$C*H*$_3$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): *δ*=166.9 (s, O=COEt), 144.7 (s, Ar-C), 141.5 (d, Ar-*C*H=CHCOOEt), 131.7 (s, Ar-C), 130.2 (d, Ar-CH), 127.5 (d, Ar-CH), 126.7 (d, Ar-CH=*C*HCOOEt), 125.4 (d, Ar-CH), 120.3 (d, Ar-CH), 66.5 (d, C*H*CH$_3$), 60.6 (t, O*C*H$_2$CH$_3$), 24.9 (q, CH*C*H$_3$), 14.2 (q, OCH$_2$*C*H$_3$) ppm. HR-MS (ESI+) m/z calculated for [C$_{13}$H$_{16}$NaO$_3$]$^+$=[M+Na]$^+$: 243.0992; found: 243.0990.



18c

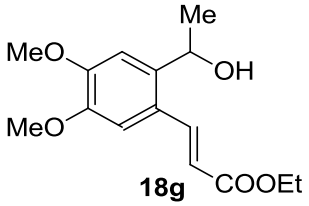
Ethyl (2*E*)-3-[2-(1-hydroxyethyl)-4-methoxyphenyl]acrylate (**18c**): General procedure-**4** was carried out with acetophenone ester **14c** (124 mg, 0.50 mmol) in methanol (4 mL), $CeCl_3.7H_2O$ (186 mg, 0.50 mmol), $NaBH_4$ (37.3 mg, 1.0 mmol) at –20 °C, [TLC control R_f(**14c**)=0.60, R_f(**18c**)=0.50 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **18c** (111 mg, 89%), as yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3417, 2922, 2852, 1708, 1604, 1484, 1261, 1181, 1039, 933, 869, 804 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ= 7.96 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.51 (d, 1H, *J*=8.8 Ar-H), 7.15 (d, IH, *J*=2.9, Ar-H), 6.81 (dd, 1H, *J*=8.8 and 2.9, Ar-H), 6.25 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.31 (q, 1H, *J*=6.4 Hz, C*H*CH_3), 4.25 (q, 2H, *J*=7.3 Hz, OCH_2CH_3), 3.84 (s, 3H, Ar-OCH_3), 1.88 (br. s, 1H, OH), 1.46 (d, 3H, *J*=6.4, CHCH_3), 1.32 (t, 3H, *J*=7.3 Hz, OCH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.3 (s, O=COEt), 161.4 (s, Ar-C), 147.1 (s, Ar-C), 140.7 (d, Ar-*C*H=CHCOOEt), 128.2 (d, Ar-CH), 123.9 (s, Ar-C), 117.6 (d, Ar-CH=*C*HCOOEt), 113.3 (d, Ar-CH), 110.2 (d, Ar-CH), 66.2 (d, C*H*CH_3), 60.4 (t, O*C*H_2CH_3), 55.2 (q, Ar-O*C*H_3), 25.1 (q, CH*C*H_3), 14.2 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{14}H_{18}NaO_4]^+$=$[M+Na]^+$: 273.1097; found: 273.1095.



18f

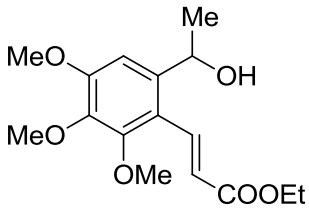
Ethyl (2*E*)-3-[6-(1-hydroxyethyl)-1, 3-benzodioxol-5-yl]acrylate (**18f**): General procedure-**4** was carried out with acetophenone ester **14f** (131 mg, 0.50 mmol) in methanol (4 mL), $CeCl_3.7H_2O$ (186 mg, 0.50 mmol), $NaBH_4$ (37.3 mg, 1.0 mmol) at –20 °C, [TLC control R_f(**14f**)=0.55, R_f(**18f**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **18f** (86 mg, 65%), as brown viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}= 3393, 2921, 2851, 1704, 1616, 1503, 1483, 1286, 1255, 1180, 1100, 1038, 934, 852 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ= 7.93 (d, 1H, *J*=15.6, Hz, ArC*H*=CHCOOEt), 7.09 (s, IH, Ar-H),

6.97 (s, 1H, Ar-H), 6.19 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.97 (d, 1H, *J*=12.2 Hz, OC*H*$_a$H$_b$O), 5.96 (d, 1H, *J*=12.2 Hz, OCH$_a$*H*$_b$O), 5.27 (q, 1H, *J*=6.4 Hz, C*H*CH$_3$), 4.23 (q, 2H, *J*=7.3 Hz, OC*H*$_2$CH$_3$), 2.11 (br. s, 1H, CHO*H*), 1.42 (d, 3H, *J*=6.4, CHC*H*$_3$), 1.31 (t, 3H, *J*=7.3 Hz, OCH$_2$C*H*$_3$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ=167.1 (s, O=COEt), 149.7 (s, Ar-C), 147.1 (s, Ar-C), 140.6 (s, Ar-C), 140.5 (d, Ar-*C*H=CHCOOEt), 125.1 (s, Ar-C), 118.2 (d, Ar-CH=*C*HCOOEt), 105.7 (d, Ar-CH), 105.6 (d, Ar-CH), 101.5 (t, OCH$_2$O), 66.0 (d, *C*HCH$_3$), 60.5, (t, O*C*H$_2$CH$_3$), 25.2 (q, CH*C*H$_3$), 14.3 (q, OCH$_2$*C*H$_3$) ppm. HR-MS (ESI+) m/z calculated for [C$_{14}$H$_{16}$NaO$_5$]$^+$=[M+Na]$^+$: 287.0890; found: 287.0888.



18g

Ethyl (2*E*)-3-[2-(1-hydroxyethyl)-4, 5-dimethoxyphenyl]acrylate (**18g**): General procedure-**4** was carried out with acetophenone ester **14g** (139 mg, 0.50 mmol) in methanol (4 mL), CeCl$_3$.7H$_2$O (186 mg, 0.50 mmol), NaBH$_4$ (37.3 mg, 1.0 mmol) at –20 °C, [TLC control R_f(**14g**)=0.50, R_f(**18g**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 75:25 to 65:35) gave title compound **18g** (108 mg, 77%), as pale yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): $\nu_{max=}$ 3467, 2922, 2851, 1706, 1602, 1510, 1463, 1286, 1266, 1173, 1120, 1021, 977, 866 cm^{-1}. ^{1}H NMR (CDCl$_3$, 400 MHz): δ= 7.93 (d, 1H, *J*=15.6 Hz, ArC*H*=CHCOOEt), 7.09 (s, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 6.21 (d, 1H, *J*=15.6 Hz, ArCH=C*H*COOEt), 5.27 (q, 1H, *J*=6.4 Hz, C*H*CH$_3$), 4.21 (q, 2H, *J*=7.3 Hz, OC*H*$_2$CH$_3$), 3.88 (s, 3H, Ar-OCH$_3$), 3.84 (s, 3H, Ar-OCH$_3$), 2.49 (br. s, 1H, CHO*H*), 1.41 (d, 3H, *J*=6.4 Hz, CHC*H*$_3$), 1.29 (t, 3H, *J*=7.3 Hz, OCH$_2$C*H*$_3$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ= 167.1 (s, O=COEt), 151.1 (s, Ar-C), 148.0 (s, Ar-C), 140.6 (d, Ar-*C*H=CHCOOEt), 139.1 (s, Ar-C), 123.4 (s, Ar-C), 117.6 (d, Ar-CH=*C*HCOOEt), 108.5 (d, Ar-CH), 108.0 (d, Ar-CH), 65.8 (d, *C*HCH$_3$), 60.4 (t, O*C*H$_2$CH$_3$), 55.8 (q, 2C, Ar-O*C*H$_3$), 25.4 (q, CH*C*H$_3$), 14.2 (q, OCH$_2$*C*H$_3$) ppm. HR-MS (ESI+) m/z calculated for [C$_{15}$H$_{20}$NaO$_5$]$^+$=[M+Na]$^+$: 303.1203; found: 303.1201.



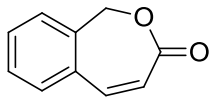
18h

Ethyl (2*E*)-3-[6-(1-hydroxyethyl)-2,3,4-trimethoxyphenyl]acrylate (**18h**): General procedure-**4** was carried out with acetophenone ester **14h** (154 mg, 0.50 mmol) in methanol (4 mL), CeCl$_3$.7H$_2$O (186 mg, 0.50 mmol), NaBH$_4$ (37.3 mg, 1.0 mmol) at –20 °C, [TLC control

R_f(**14h**)=0.55, R_f(**18h**)=0.45 (petroleum ether/ethyl acetate 60:40, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 70:30 to 60:40) gave title compound **18h** (126 mg, 81%), as pale yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): $\nu_{max=}$3430, 2919, 2850, 1711, 1590, 1487, 1462, 1326, 1297, 1241, 1175, 1129, 1040, 976 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.75 (d, 1H, *J*=16.1 Hz, ArC*H*=CHCOOEt), 6.99 (s, 1H, Ar-H), 6.50 (d, 1H, *J*=16.1 Hz, ArCH=C*H*COOEt), 5.24 (m, 1H, C*H*CH_3), 4.22 (m, 2H, OC*H*$_2$$CH_3$), 3.88 (s, 3H, Ar-$OCH_3$), 3.84 (s, 3H, Ar-$OCH_3$), 3.81 (s, 3H, Ar-$OCH_3$), 2.37 (br. s, 1H, CHO*H*), 1.43 (d, 3H, *J*=5.8 Hz, CHC*H*$_3$), 1.31 (t, 3H, *J*=7.3 Hz, OCH_2C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.8 (s, O=COEt), 154.5 (s, Ar-C), 153.0 (s, Ar-C), 141.9 (d, Ar-*C*H=CHCOOEt), 137.1 (s, Ar-C), 121.7 (s, Ar-C), 118.5 (d, Ar-CH=*C*HCOOEt), 104.3 (d, Ar-CH), 104.1 (d, Ar-CH), 66.2 (d, *C*HCH_3), 60.8 (q, Ar-O*C*H_3), 60.5 (q, Ar-O*C*H_3), 60.4 (t, O*C*$H_2$$CH_3$), 55.9 (q, Ar-O*C*$H_3$), 25.1 (q, CH*C*$H_3$), 14.3 (q, OCH_2*C*H_3) ppm. HR-MS (ESI+) m/z calculated for $[C_{16}H_{22}NaO_6]^+$=$[M+Na]^+$: 333.1309; found: 333.1315.

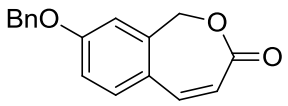
General Procedure-5 (For intramolecular cyclization):

In an oven dried Schlenk tube, were added alcohol ester **15a-15h and 18a-18h** (0.40 mmol), and Cs_2CO_3 (1.2 mmol) followed by the addition of DMF (4 mL) at rt under nitrogen atmosphere. The resulted reaction mixture was stirred at 120 °C in an oil bath for 4h. The reaction was quenched by the addition of aqueous NH_4Cl and extracted with ethylacetate (3 × 10 mL). The organic layer was washed with saturated NaCl solution, dried over Na_2SO_4, and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished lactenones **19a-19h** (60–95%) and **20a-20h** (35–80%)



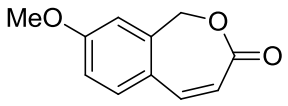
19a

2-Benzoxepin-3(1*H*)-one (**19a**): General procedure-**5** was carried with an alcohol ester **15a** (82.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15a**)=0.20, R_f(**19a**)=0.30 (petroleum ether/ethyl acetate 90:10, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 95:5 to 90:10) gave title compound **19a** (56 mg, 87%).



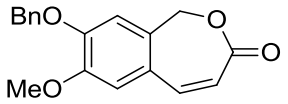
19b

8-(Benzyloxy)-2-benzoxepin-3(1*H*)-one (**19b**): General procedure-**5** was carried with an alcohol ester **15b** (125.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15b**)=0.30, R_f(**19b**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 85:15) gave title compound **19b** (86.0 mg, 81%).



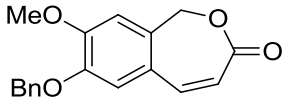
19c

8-Methoxy-2-benzoxepin-3(1*H*)-one (**19c**): General procedure-**5** was carried with an alcohol ester **15c** (94.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(15c)=0.40, R_f(**19c**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 80:20) gave title compound **19c** (46.0 mg, 60%).



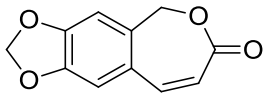
19d

8-(Benzyloxy)-7-methoxy-2-benzoxepin-3(1*H*)-one (**19d**): General procedure-**5** was carried with an alcohol ester **15d** (137.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15d**)=0.40, R_f(**19d**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 75:25) gave title compound **19d** (93.0 mg, 78%).



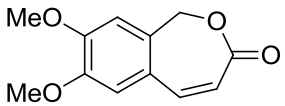
19e

7-(Benzyloxy)-8-methoxy-2-benzoxepin-3(1*H*)-one (**19e**): General procedure-**5** was carried with an alcohol ester **15e** (137.0mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15e**)=0.40, R_f(**19e**)=0.45 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20 to 75:25) gave title compound **19e** (90.0 mg, 76%).



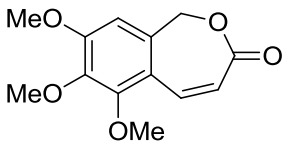
19f

[1,3]Dioxolo[4,5-*h*][2]benzoxepin-7(5*H*)-one (**19f**): General procedure-**5** was carried with an alcohol ester **15f** (100.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15f**)=0.30, R_f(**19f**)=0.40 (petroleum ether/ethyl acetate 70:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 80:20 to 75:25) gave title compound **19f** (61.0 mg, 75%).



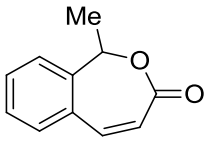
19g

7,8-Dimethoxy-2-benzoxepin-3(1*H*)-one (**19g**): General procedure-**5** was carried with an alcohol ester **15g** (106.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15g**)=0.20, R_f(**19g**)=0.30 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 75:25 to 70:30) gave title compound **19g** (84.0 mg, 95%).



19h

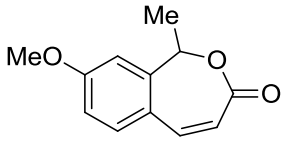
6,7,8-Trimethoxy-2-benzoxepin-3(1*H*)-one (**19h**): General procedure-**5** was carried with an alcohol ester **15h** (119.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**15h**)=0.30, R_f(**19h**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 75:25 to 70:30) gave title compound **19h** (80 mg, 80%).



20a

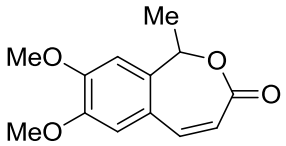
1-Methyl-2-benzoxepin-3(1*H*)-one (**20a**): General procedure-**5** was carried with an alcohol ester **18a** (88.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**18a**)=0.30, R_f(**20a**)=0.35 (petroleum ether/ethyl acetate 90:10, UV detection)].

Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 90:10 to 85:15) gave title compound **20a** (47.0 mg, 67%).



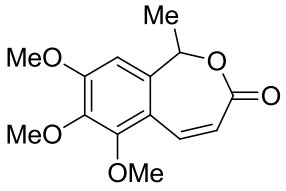
20c

8-Methoxy-1-methyl-2-benzoxepin-3(1*H*)-one (**20c**): General procedure-**5** was carried with an alcohol ester **18c** (100.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**18c**)=0.35, R_f(**20c**)=0.40 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 85:15 to 80:20) gave title compound **20c** (53.0 mg, 65%).



20g

7,8-Dimethoxy-1-methyl-2-benzoxepin-3(1*H*)-one (**20g**): General procedure-**5** was carried with an alcohol ester **18g** (112.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**18g**)=0.40, R_f(**20g**)=0.45 (petroleum ether/ethyl acetate 60:30, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 75:25 to 65:35) gave title compound **20g** (67.0 mg, 71%).

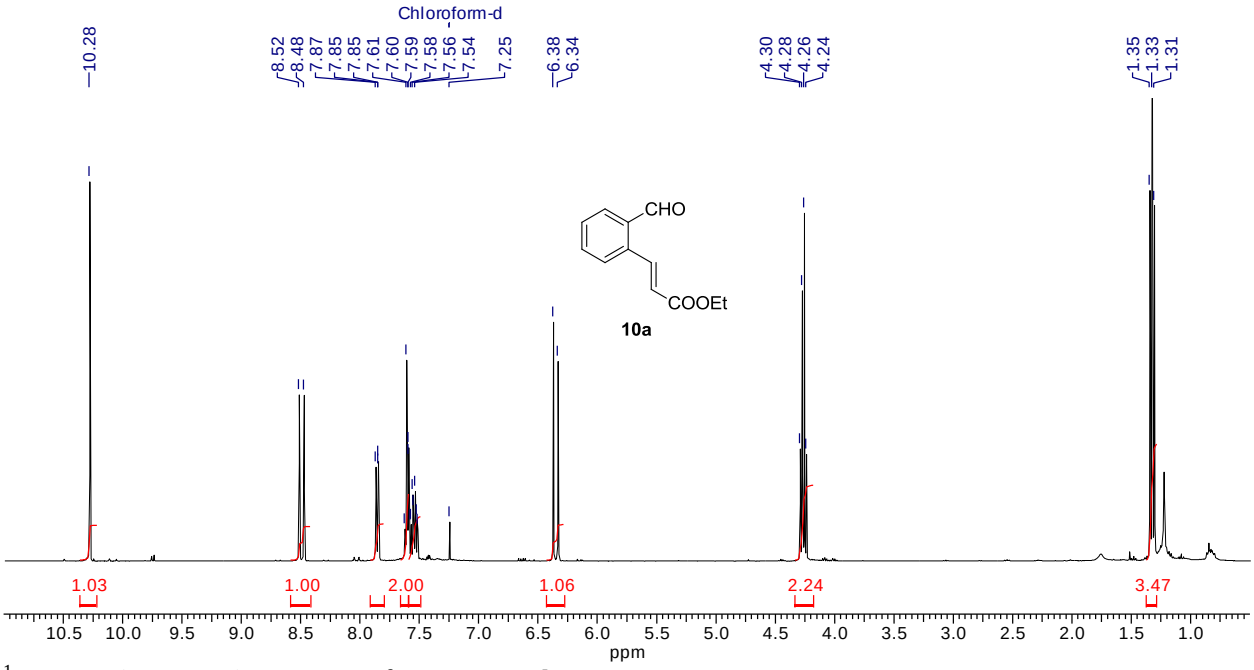


20h

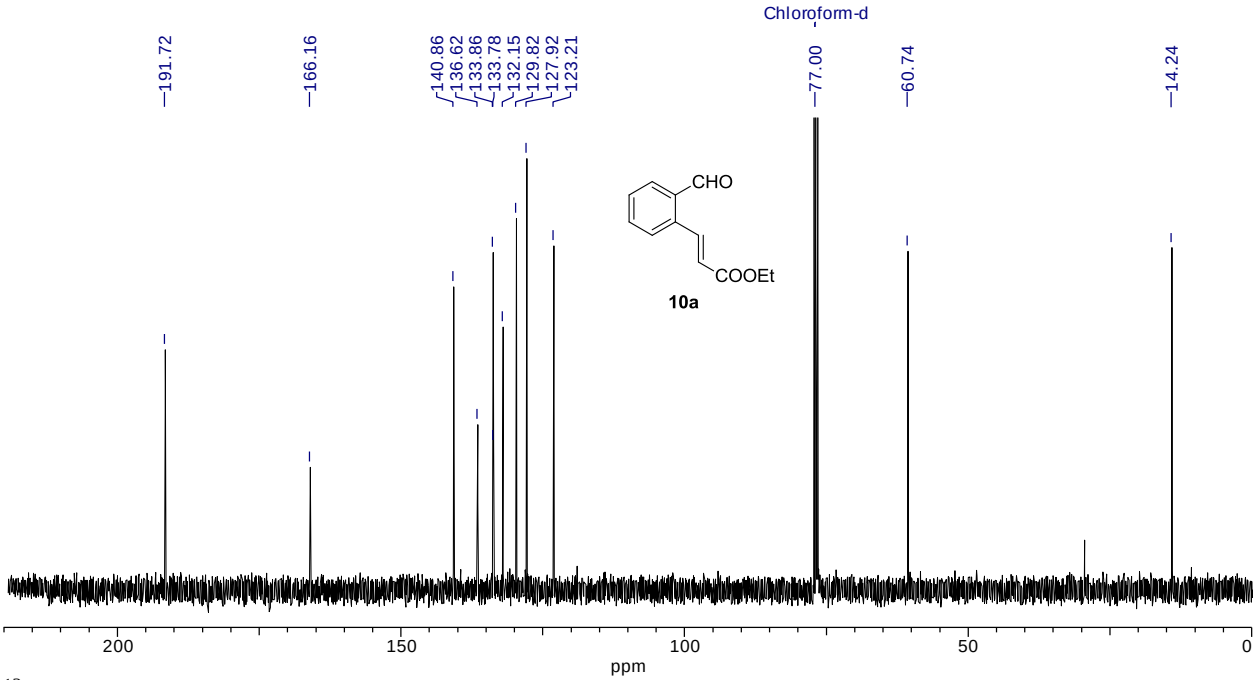
6,7,8-Trimethoxy-1-methyl-2-benzoxepin-3(1*H*)-one (**20h**): General procedure-**5** was carried with an alcohol ester **18h** (124.0 mg, 0.40 mmol) and Cs_2CO_3 (391.0 mg1.2 mmol) in DMF (4 mL) at 120 °C [TLC control R_f(**18h**)=0.25, R_f(**20h**)=0.30 (petroleum ether/ethyl acetate 80:20, UV detection)]. Silica gel column chromatography (20 g, petroleum ether/ethyl acetate 75:25 to 65:35) gave title compound **20h** (86 mg, 80%), as yellow viscous liquid. IR (MIR-ATR, 4000–600 cm^{-1}): $\nu_{max=}$2918, 2850, 1706, 1596, 1463, 1376, 1352, 1123, 1078, 1020, 749, 721 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ= 7.45 (d, 1H, *J*=12.2 Hz, ArC*H*=CHCOOEt), 6.77 (s, 1H, Ar-H), 6.26 (d, 1H, *J*=12.2 Hz, ArCH=C*H*COOEt), 5.18 (q, 1H, *J*=6.4 Hz, C*H*CH_3), 3.93 (s, 3H, Ar-OCH_3), 3.91 (s, 3H, Ar-OCH_3), 3.87 (s, 3H, Ar-OCH_3), 1.81 (d, 3H, *J*=6.4 Hz, CHC*H*$_3$) ppm.

^{13}C NMR ($CDCl_3$, 100 MHz): δ=167.9 (s, O=COEt), 155.0 (s, Ar-C), 152.1 (s, Ar-C), 142.2 (s, Ar-C), 135.1 (d, Ar-*C*H=CHCOOEt), 135.0 (s, Ar-C), 122.5 (s, Ar-C), 120.8 (d, Ar-CH=*C*HCOOEt), 104.0 (d, Ar-CH), 77.2 (d, *C*HCH$_3$), 61.7 (q, Ar-O*C*H$_3$), 61.0 (q, Ar-O*C*H$_3$), 56.1 (q, Ar-O*C*H$_3$), 17.5 (q, CH*C*H$_3$) ppm. HR-MS (ESI+) m/z calculated for $[C_{14}H_{16}NaO_5]^+$=$[M+Na]^+$: 287.0890; found: 287.0890.

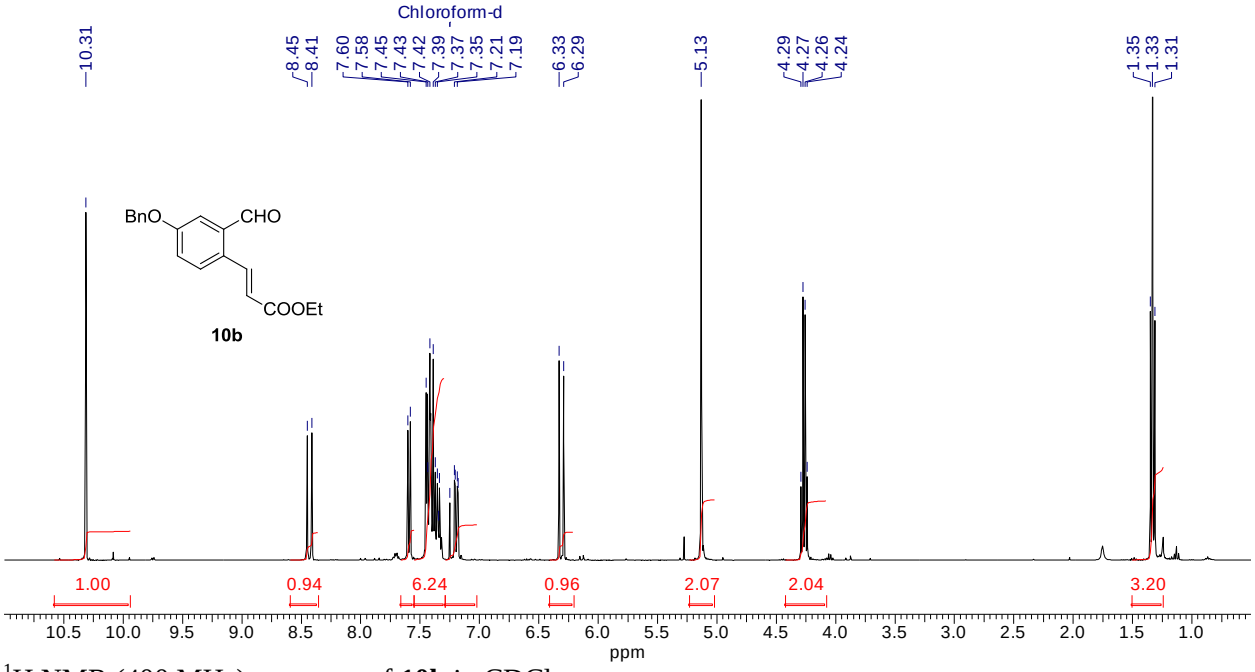
^{1}H and ^{13}C NMR Spectra for all compounds



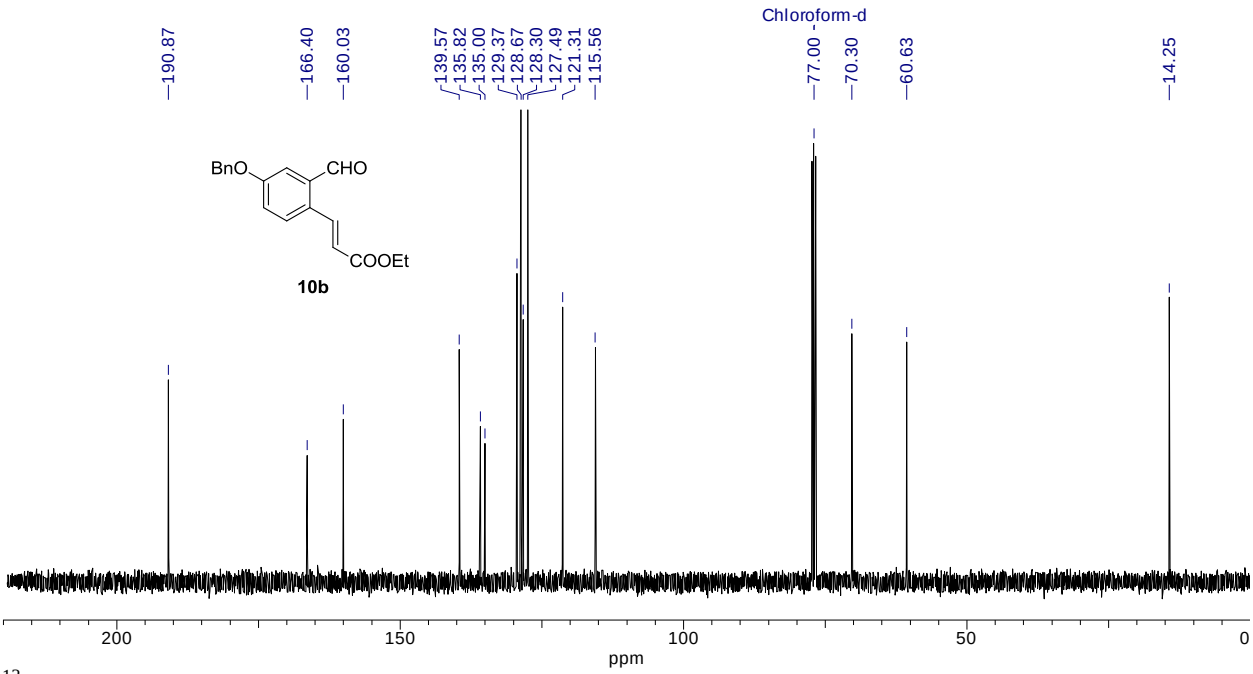
^{1}H NMR (400 MHz) spectrum of **10a** in $CDCl_3$



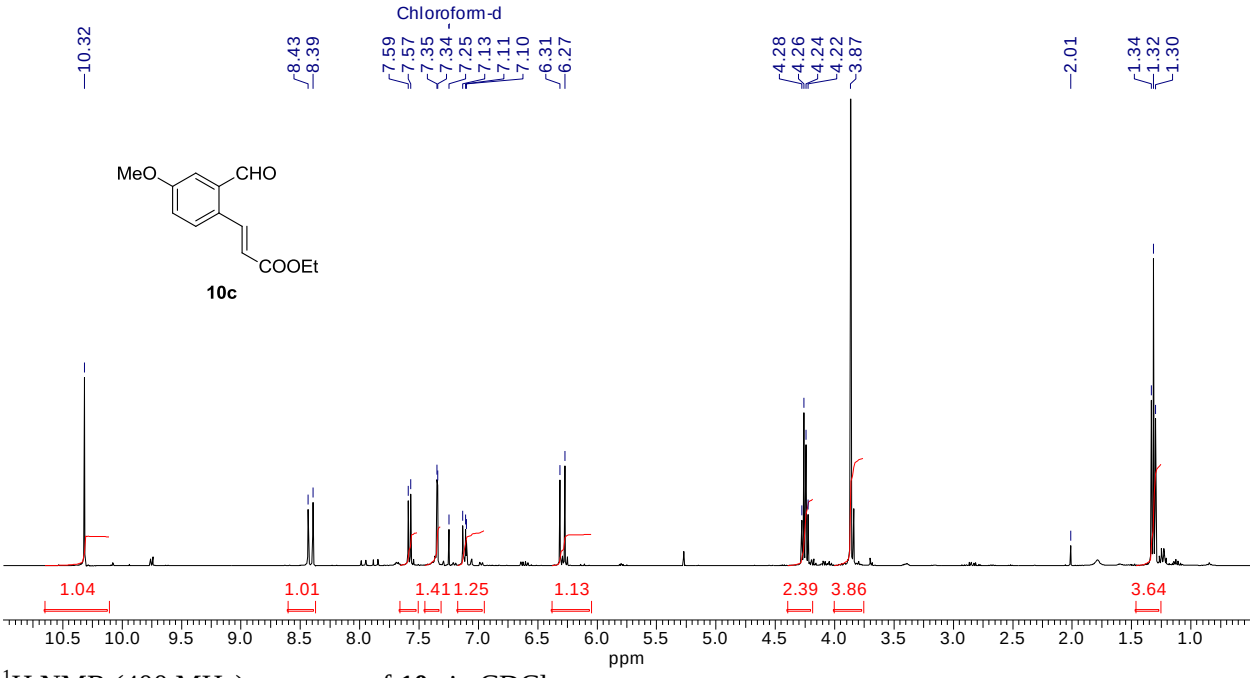
^{13}C NMR (100 MHz) spectrum of **10a** in $CDCl_3$



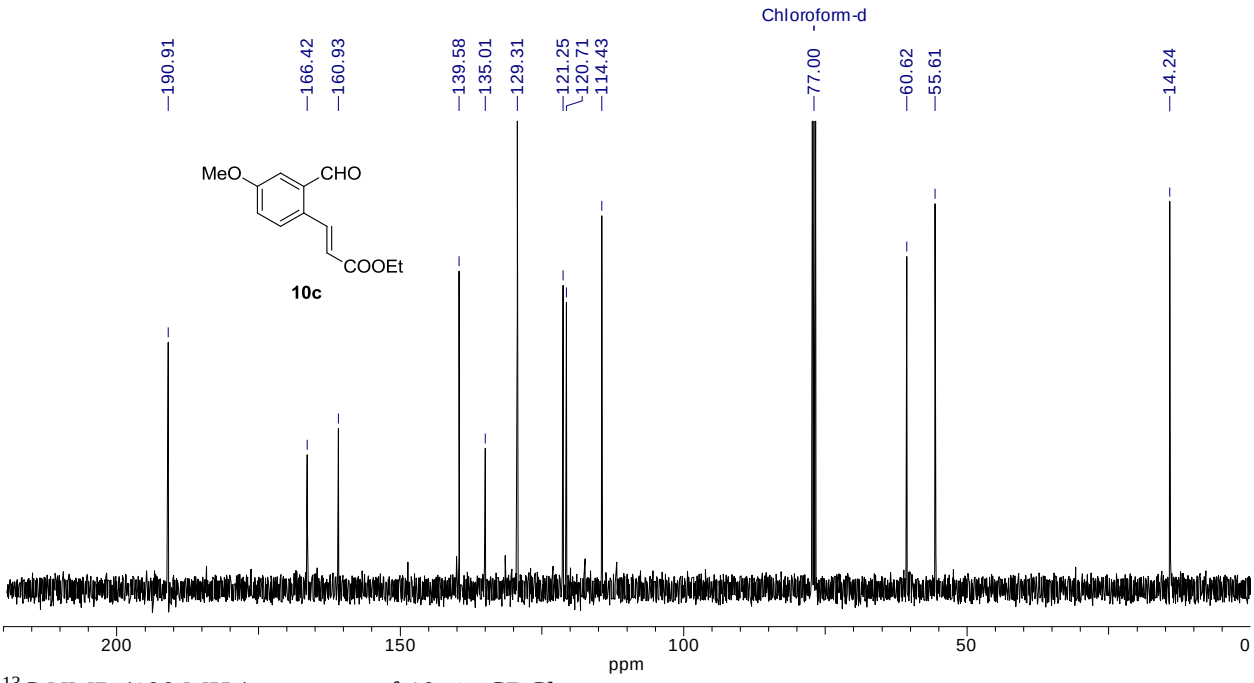
^{1}H NMR (400 MHz) spectrum of **10b** in $CDCl_3$



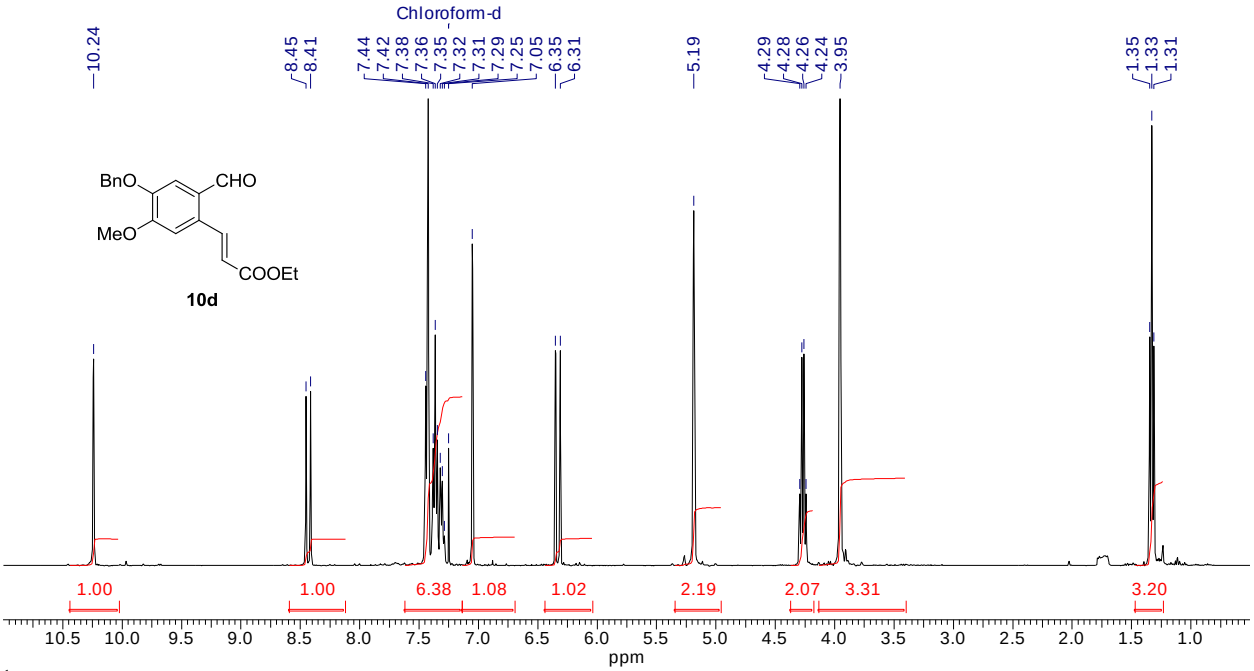
^{13}C NMR (100 MHz) spectrum of **10b** in $CDCl_3$



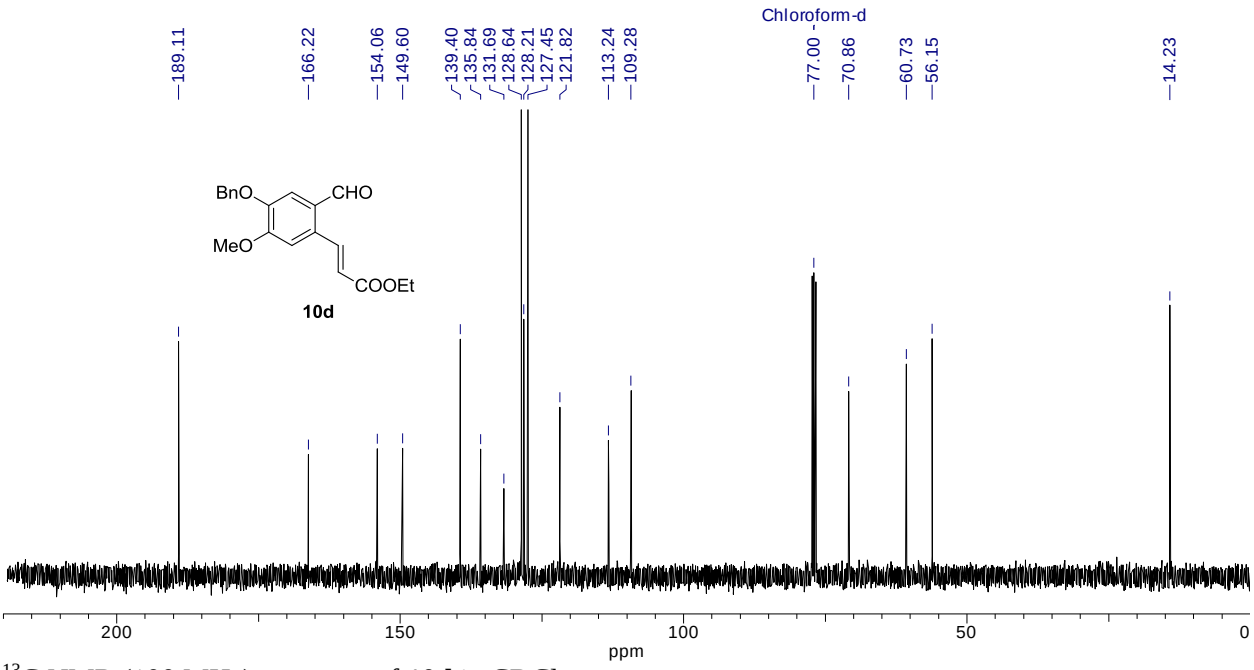
^{1}H NMR (400 MHz) spectrum of **10c** in $CDCl_3$



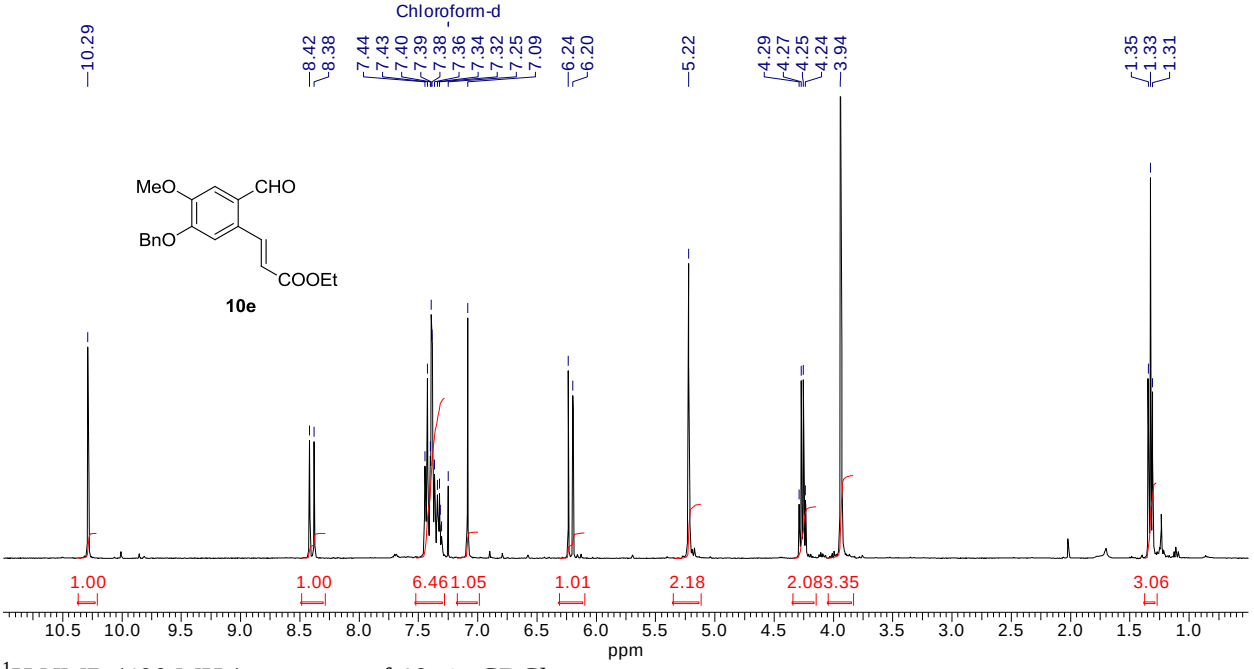
^{13}C NMR (100 MHz) spectrum of **10c** in $CDCl_3$



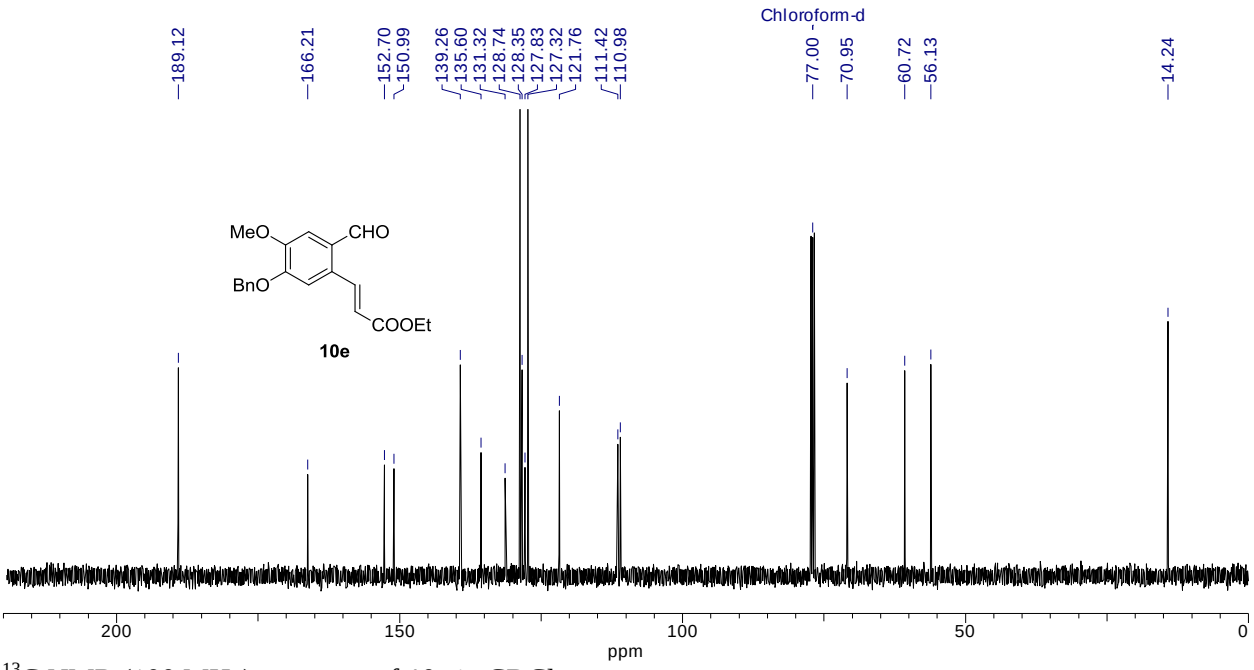
^{1}H NMR (400 MHz) spectrum of **10d** in $CDCl_3$



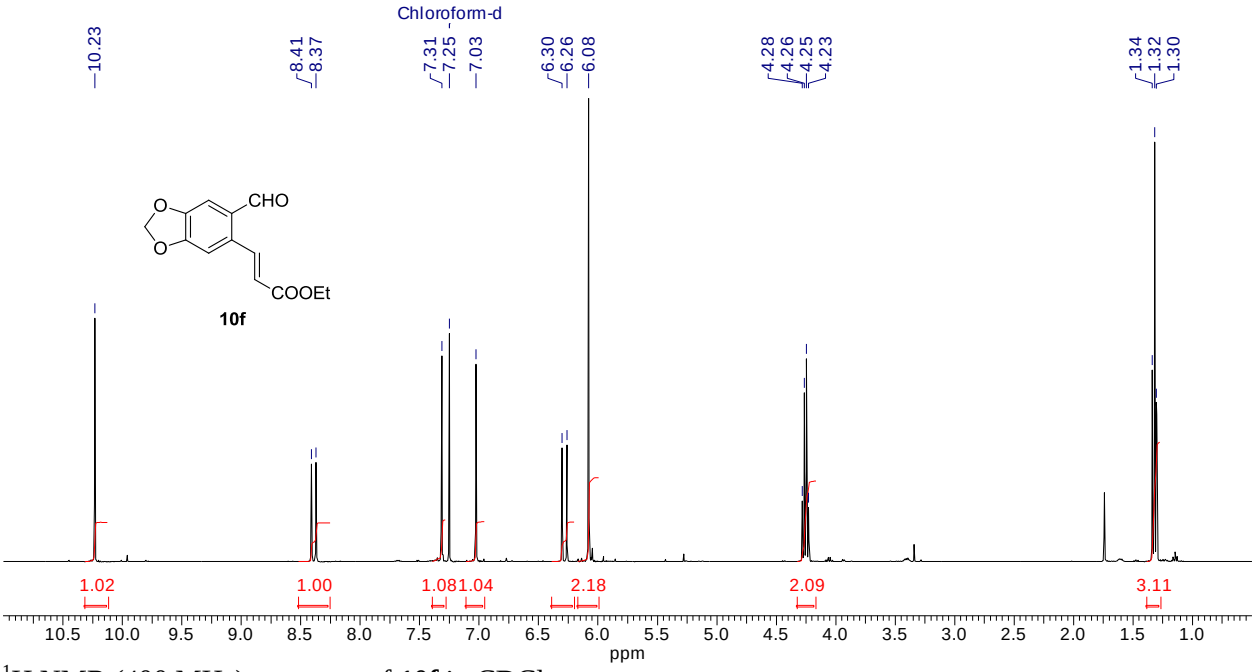
^{13}C NMR (100 MHz) spectrum of **10d** in $CDCl_3$



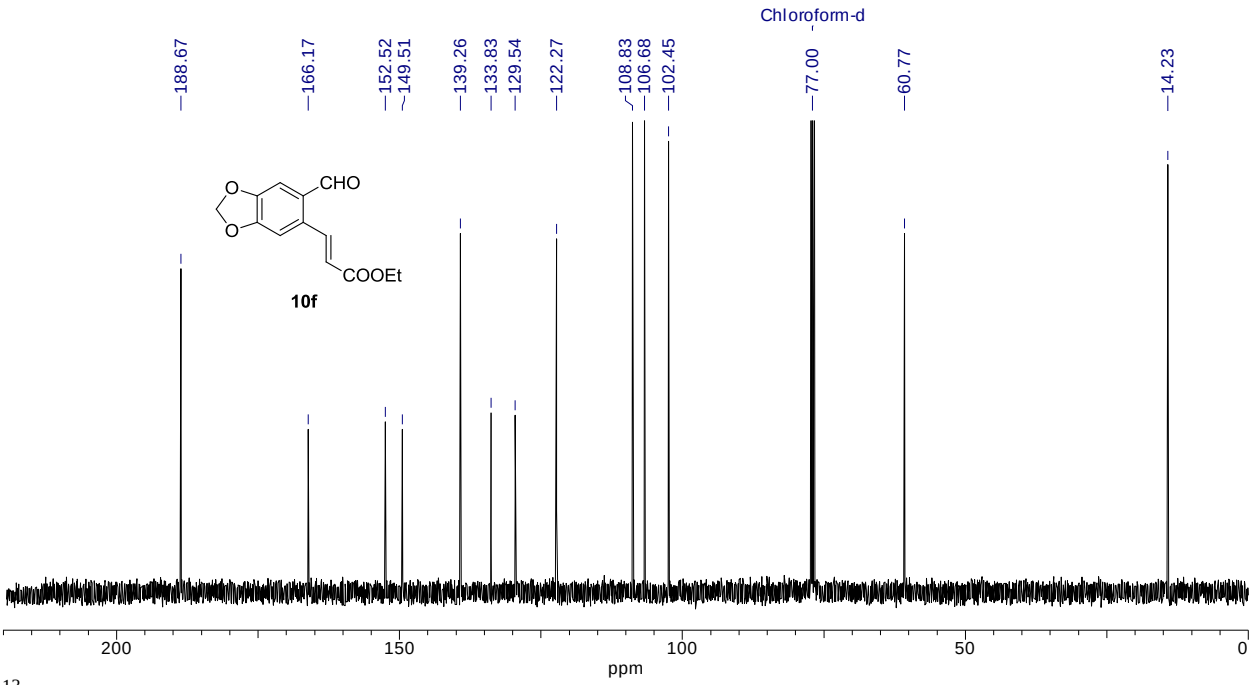
^{1}H NMR (400 MHz) spectrum of **10e** in $CDCl_3$



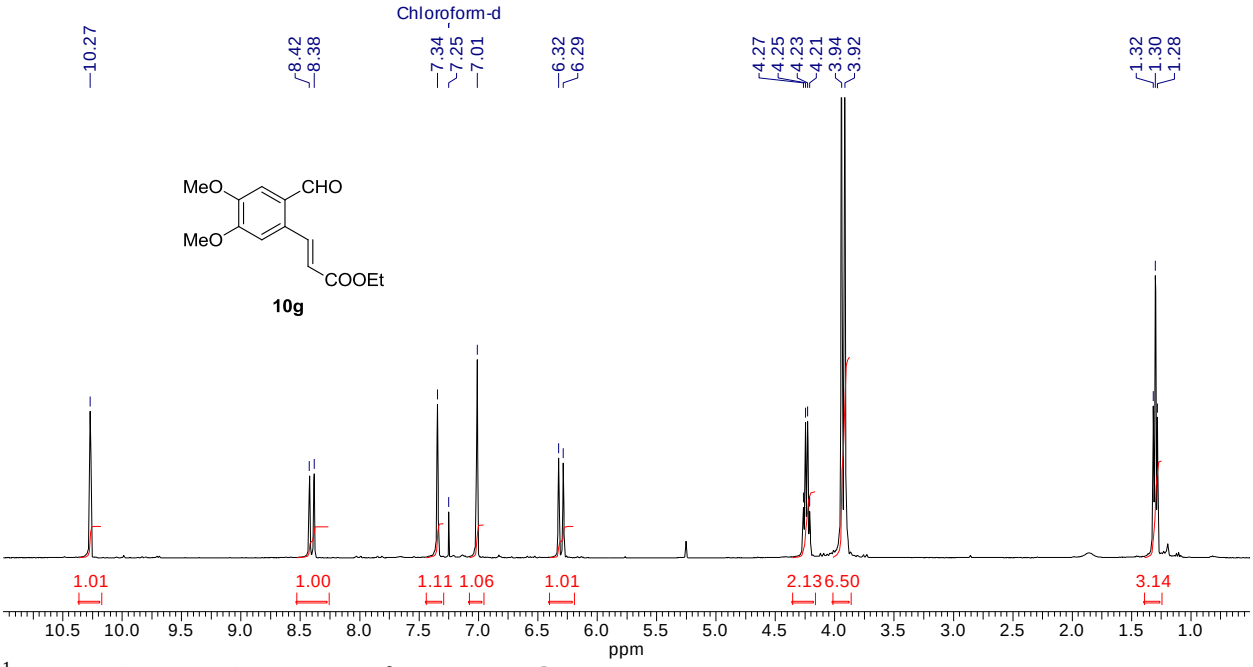
^{13}C NMR (100 MHz) spectrum of **10e** in $CDCl_3$



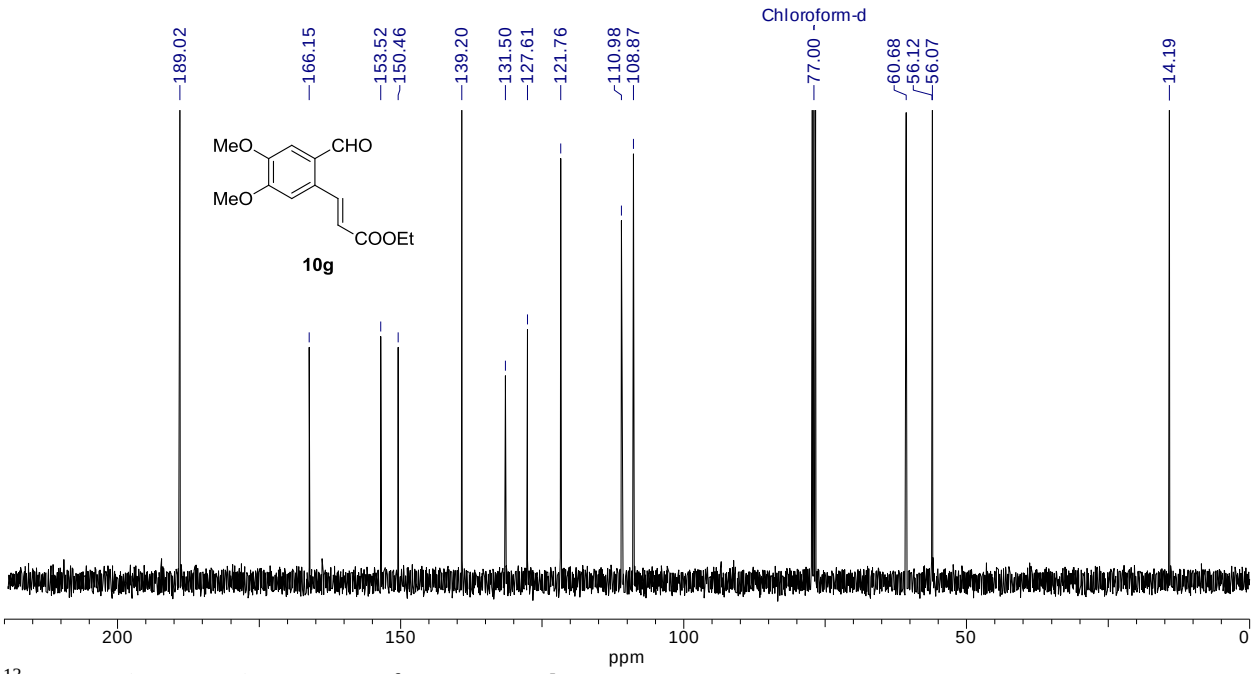
^{1}H NMR (400 MHz) spectrum of **10f** in $CDCl_3$



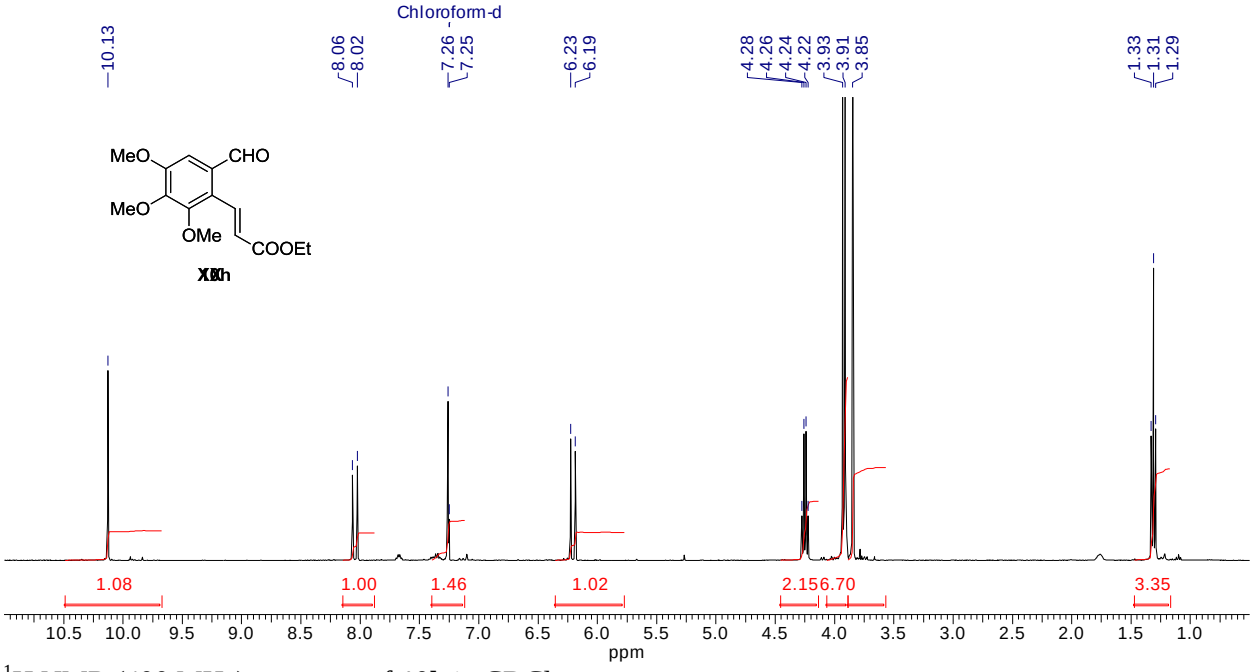
^{13}C NMR (100 MHz) spectrum of **10f** in $CDCl_3$



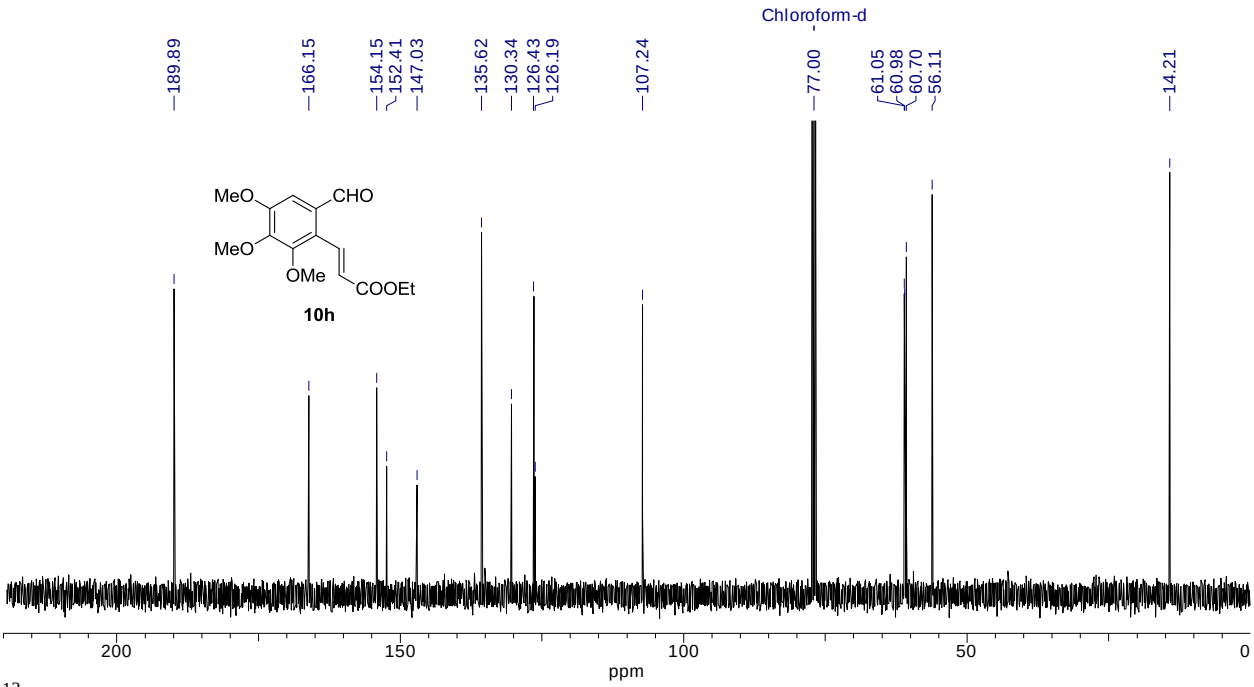
^{1}H NMR (400 MHz) spectrum of **10g** in $CDCl_3$



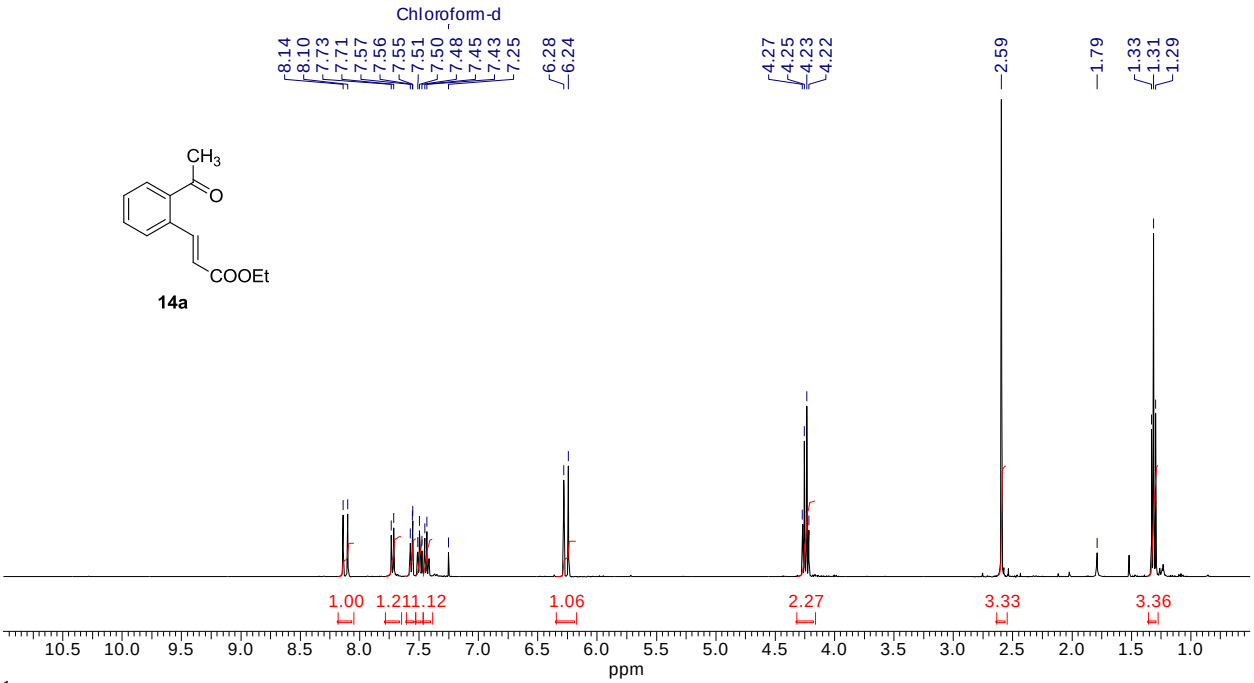
^{13}C NMR (100 MHz) spectrum of **10g** in $CDCl_3$



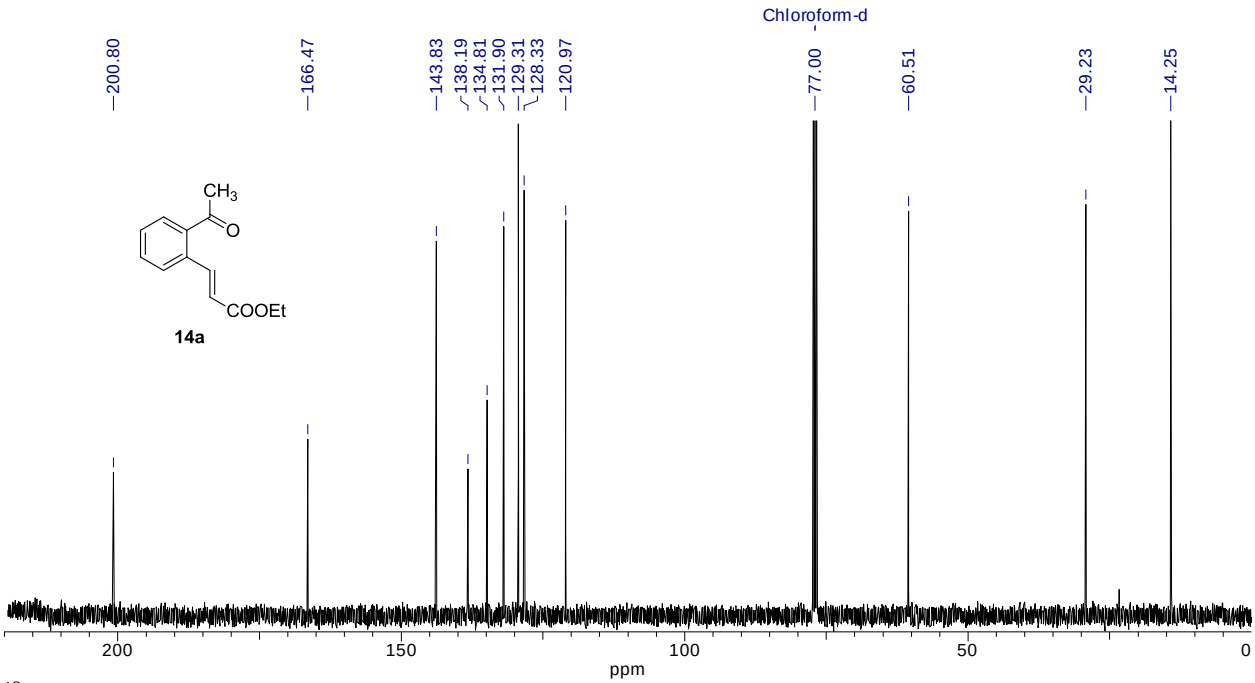
^{1}H NMR (400 MHz) spectrum of **10h** in $CDCl_3$



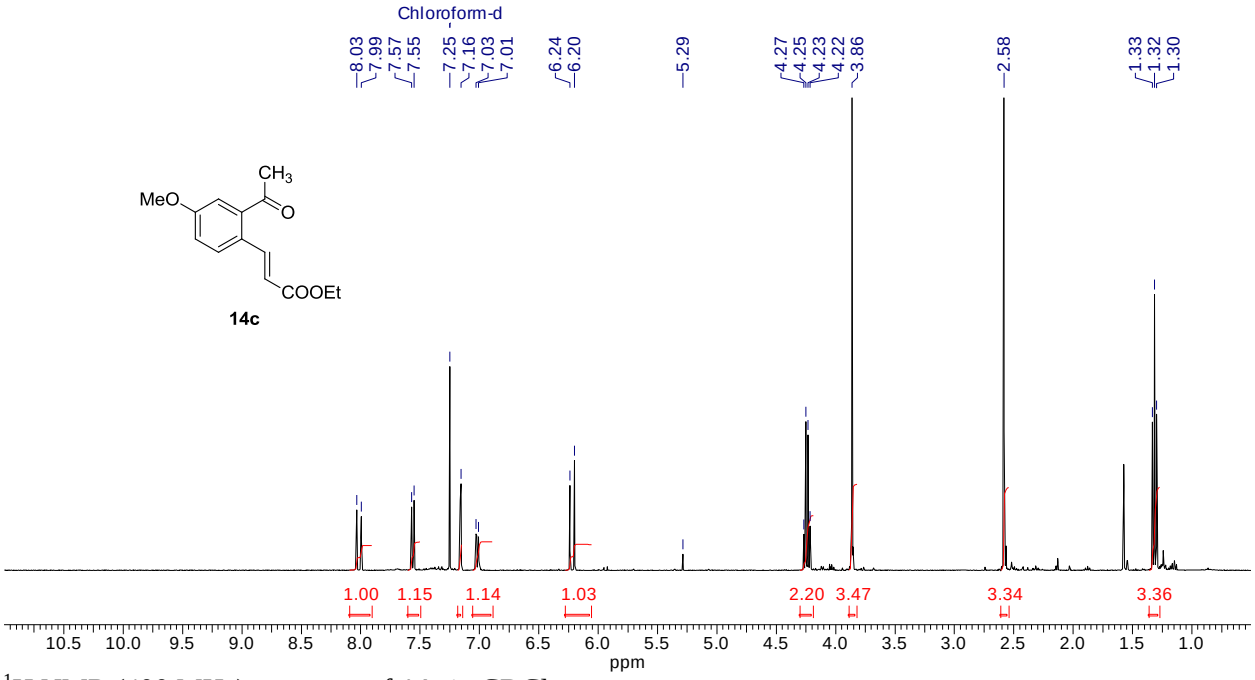
^{13}C NMR (100 MHz) spectrum of **10h** in $CDCl_3$



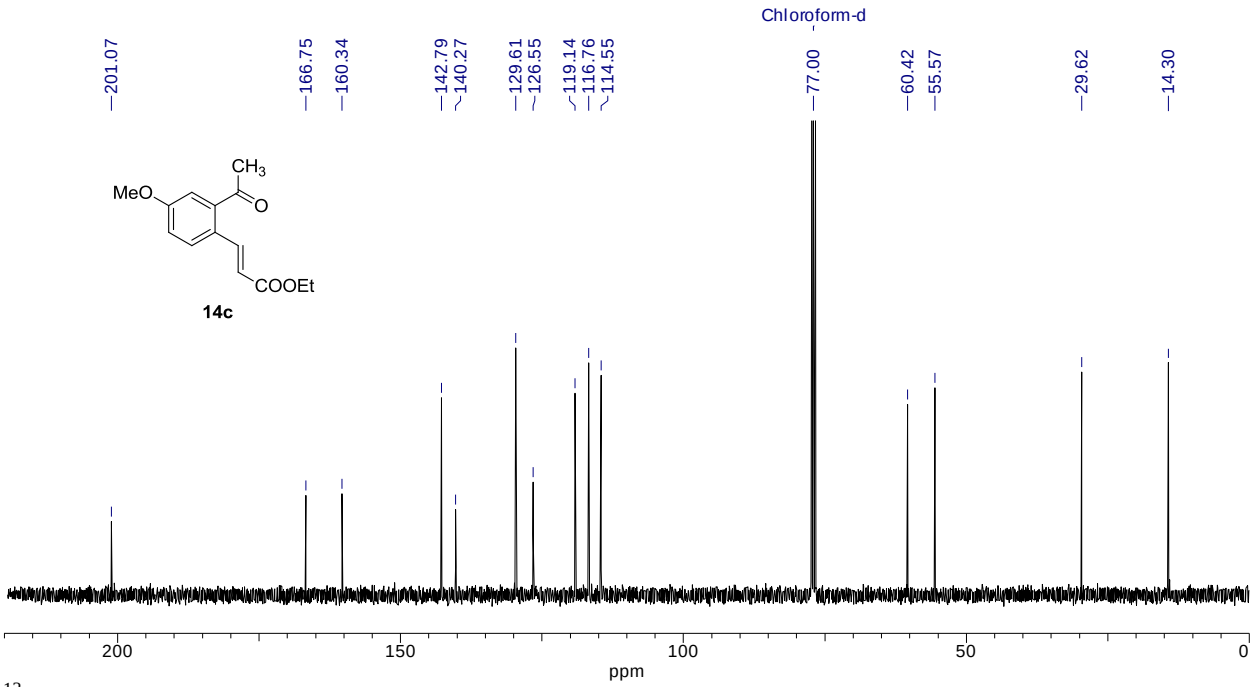
^{1}H NMR (400 MHz) spectrum of **14a** in $CDCl_3$



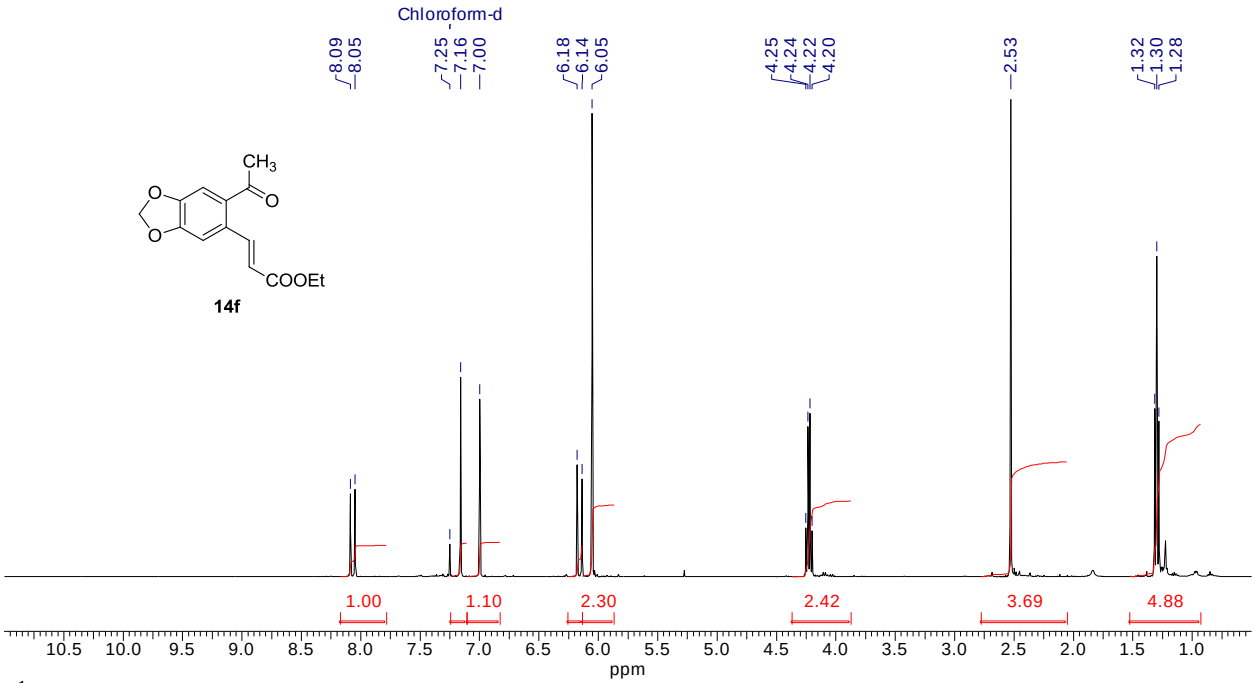
^{13}C NMR (100 MHz) spectrum of **14a** in $CDCl_3$



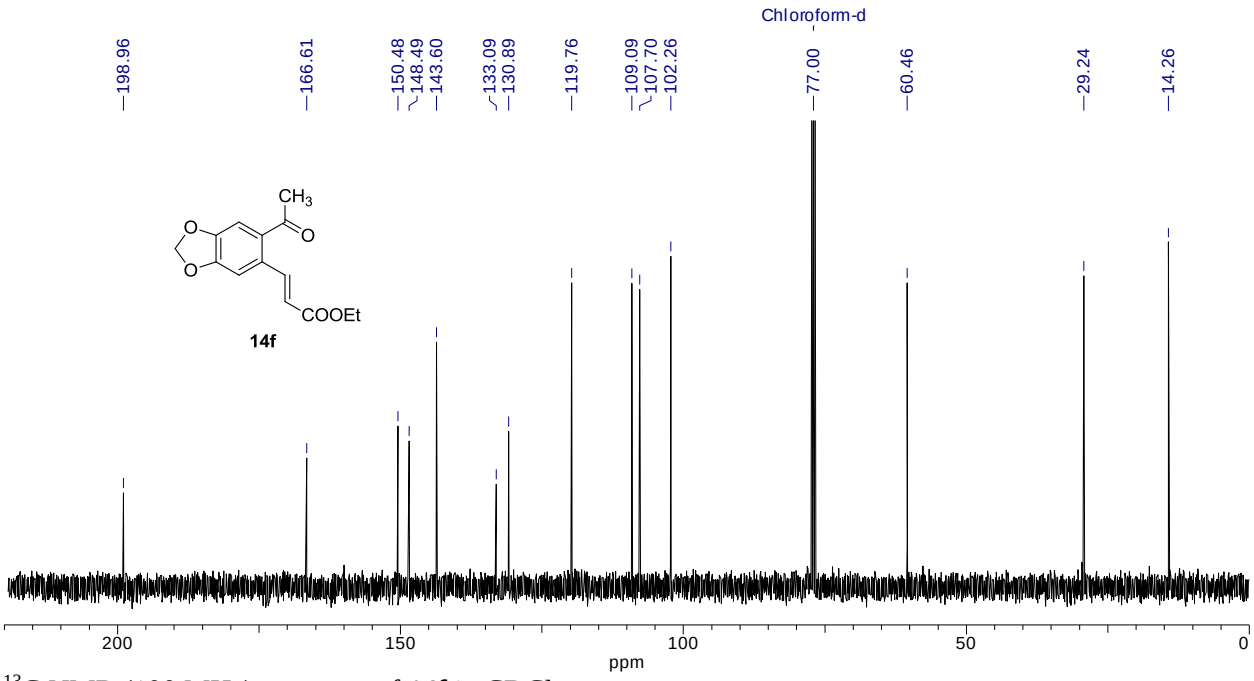
^{1}H NMR (400 MHz) spectrum of **14c** in $CDCl_3$



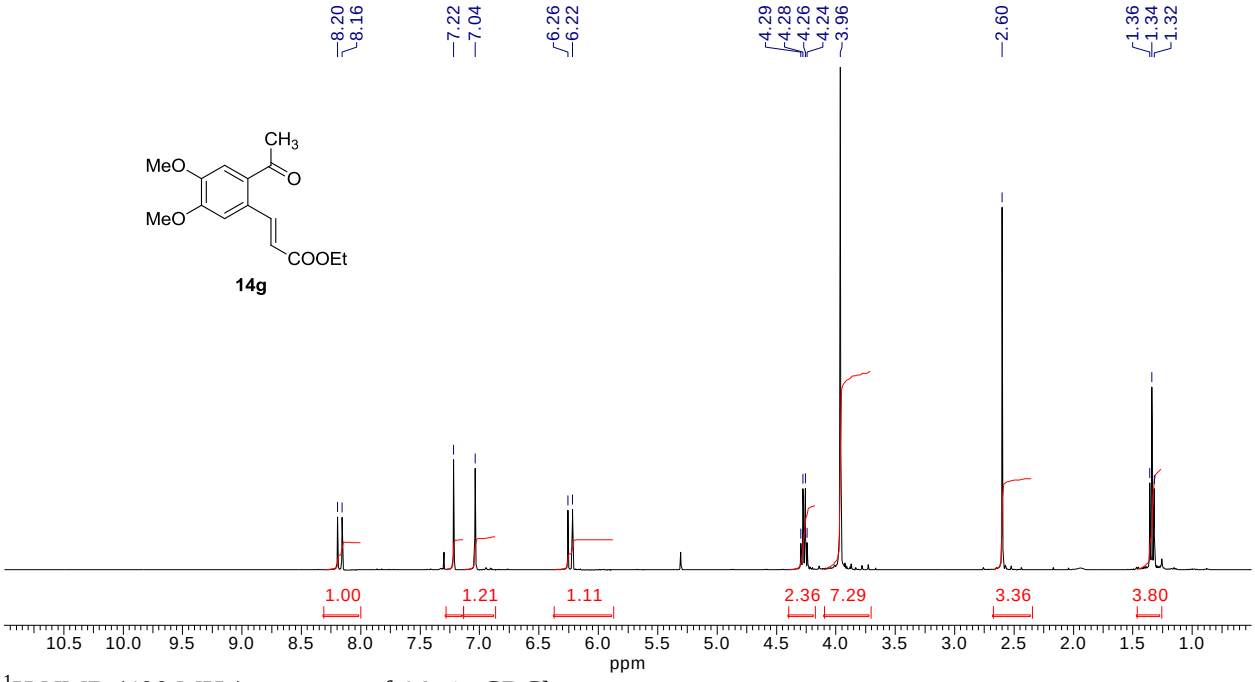
^{13}C NMR (100 MHz) spectrum of **14c** in $CDCl_3$



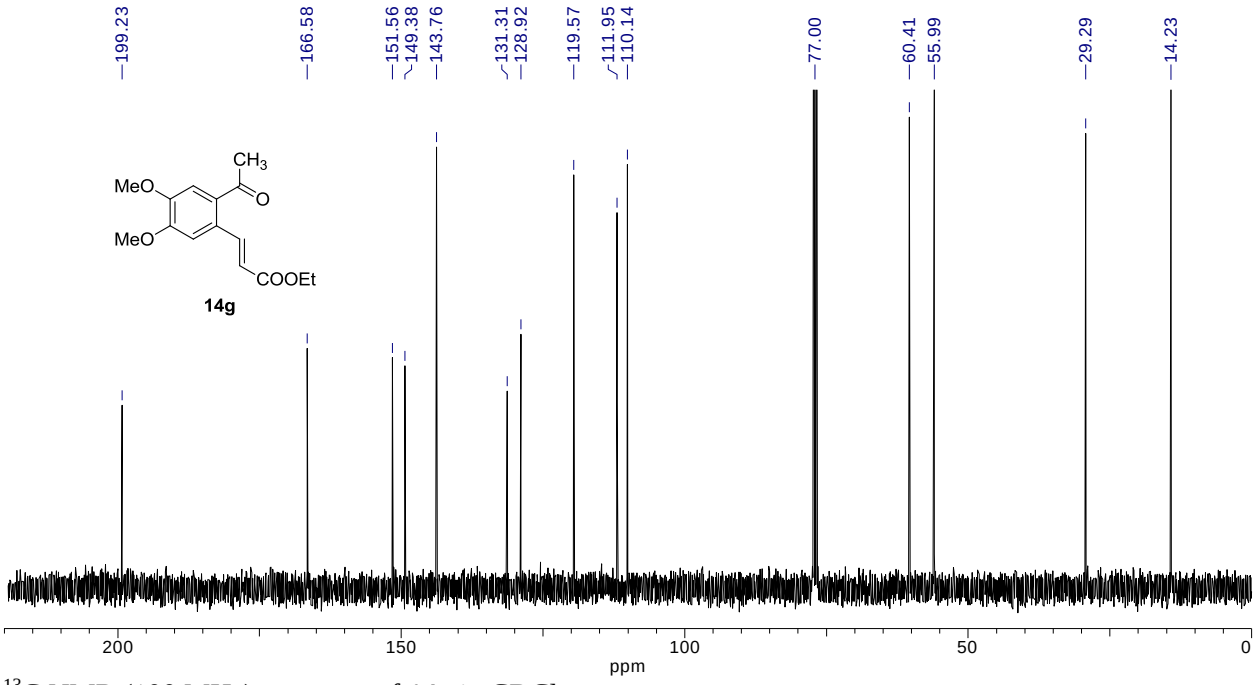
^{1}H NMR (400 MHz) spectrum of **14f** in $CDCl_3$



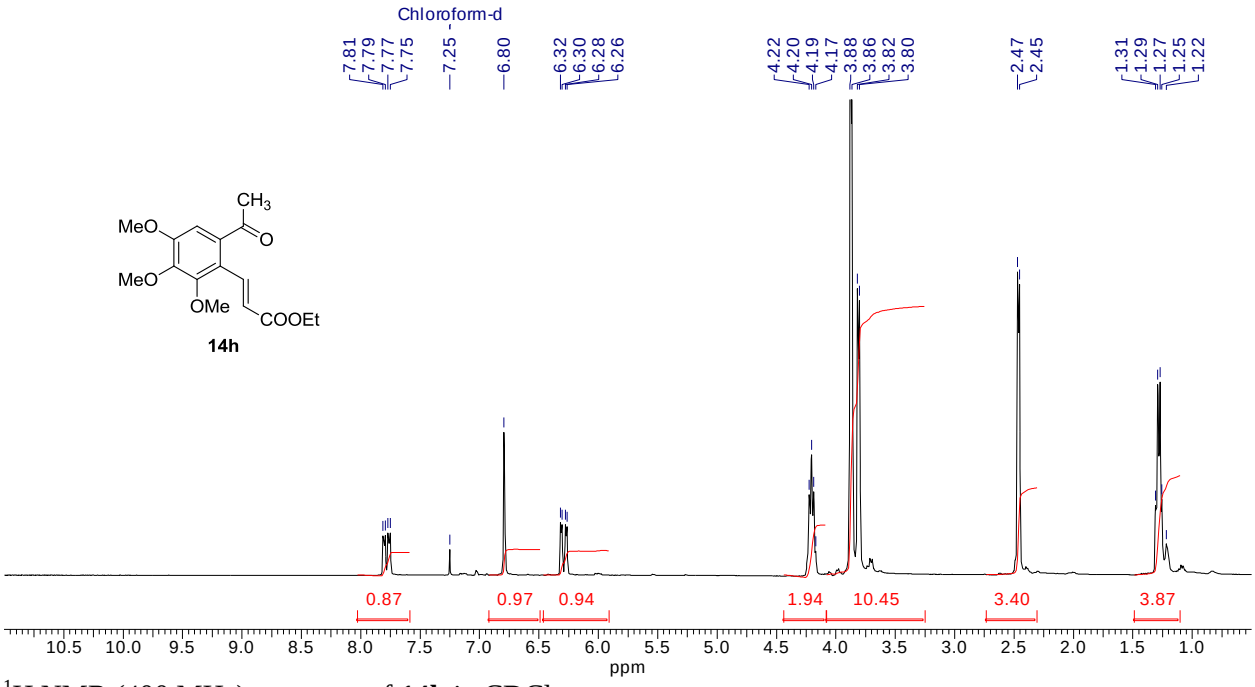
^{13}C NMR (100 MHz) spectrum of **14f** in $CDCl_3$



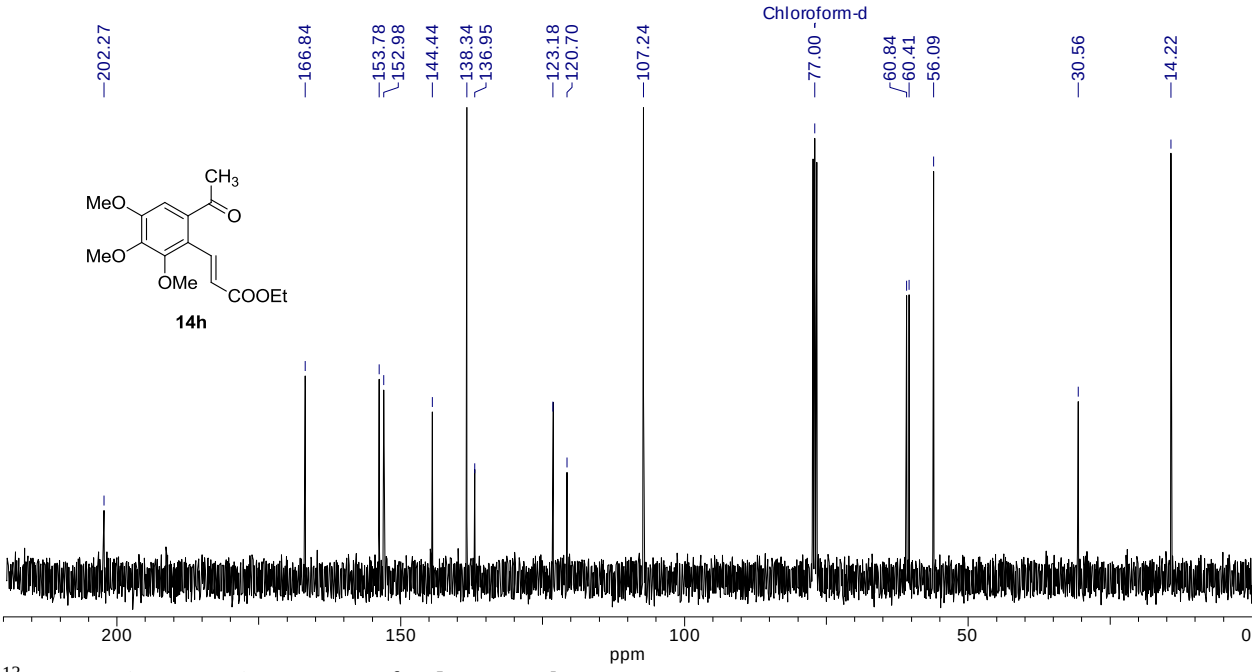
^{1}H NMR (400 MHz) spectrum of **14g** in $CDCl_3$



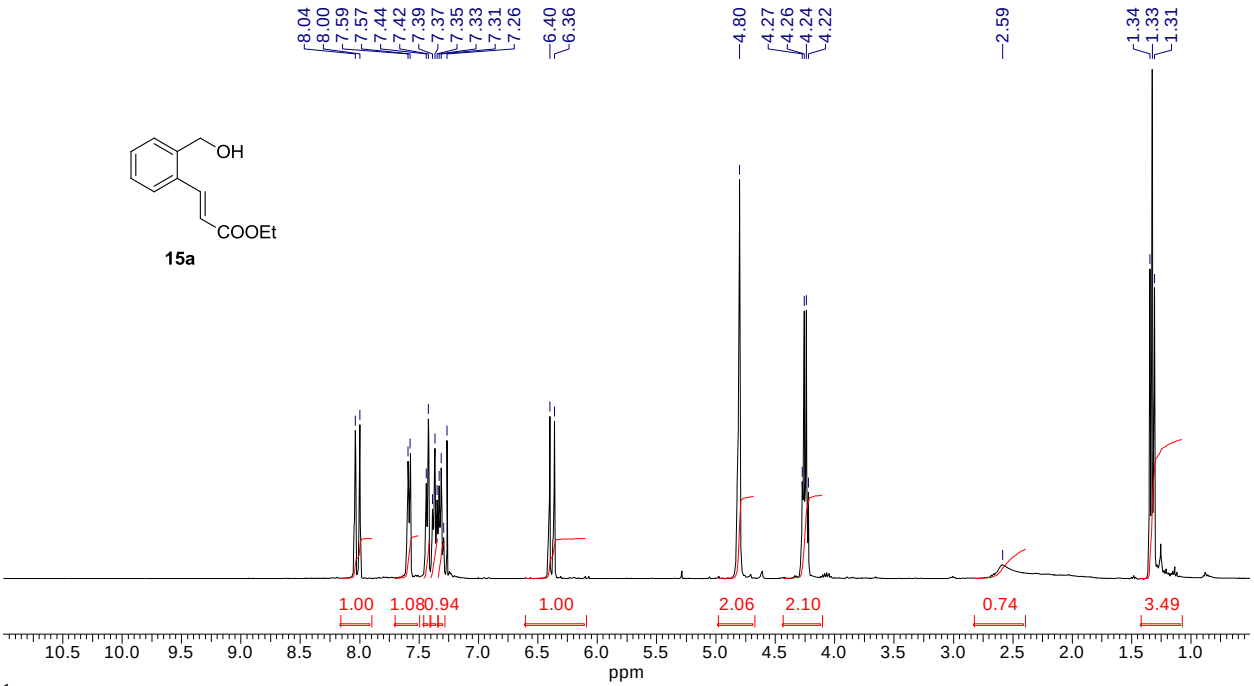
^{13}C NMR (100 MHz) spectrum of **14g** in $CDCl_3$



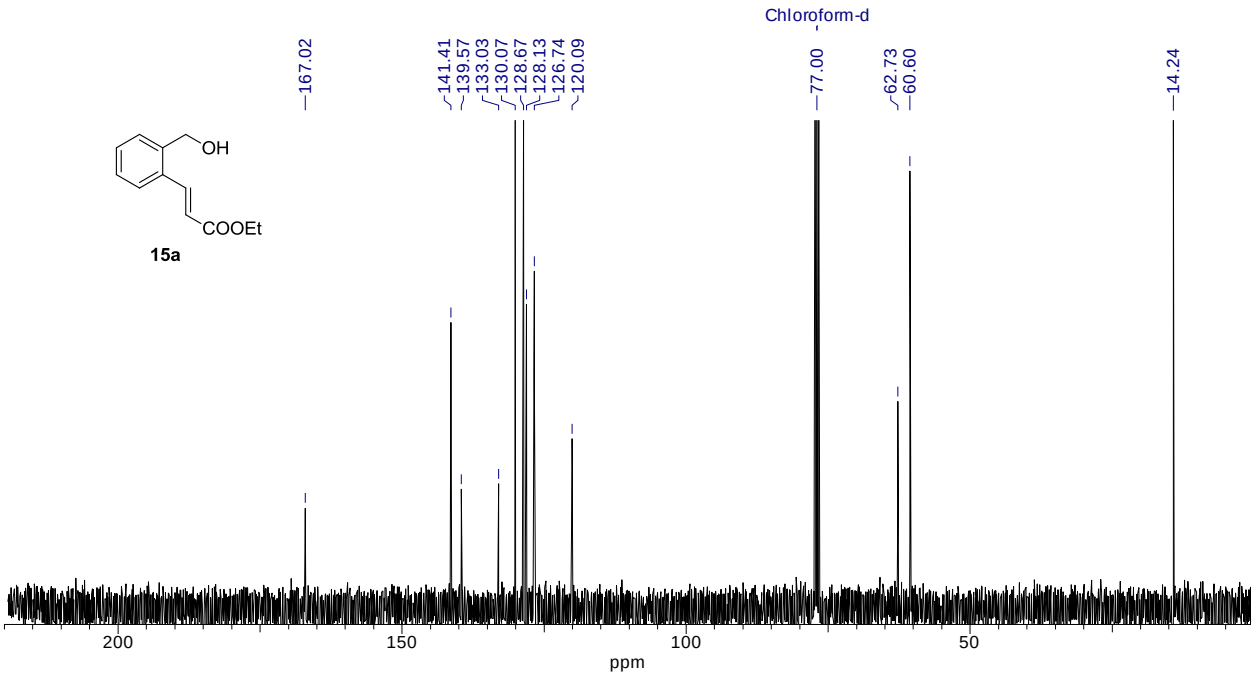
^{1}H NMR (400 MHz) spectrum of **14h** in $CDCl_3$



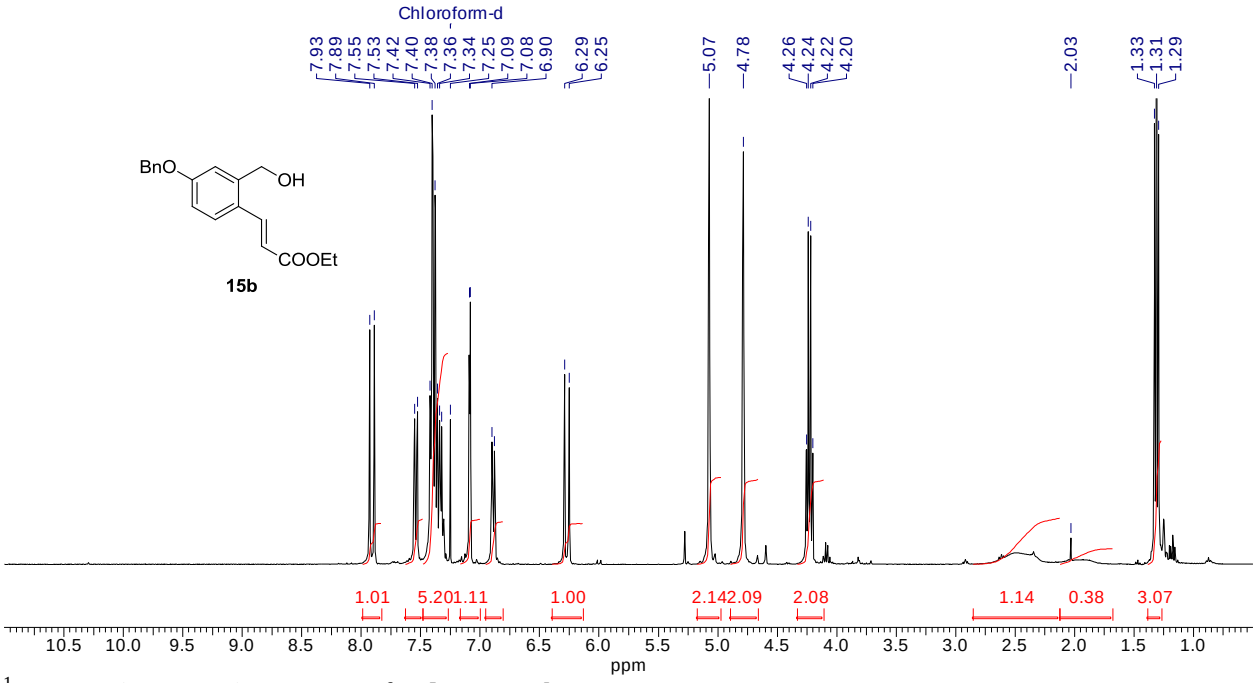
^{13}C NMR (100 MHz) spectrum of **14h** in $CDCl_3$



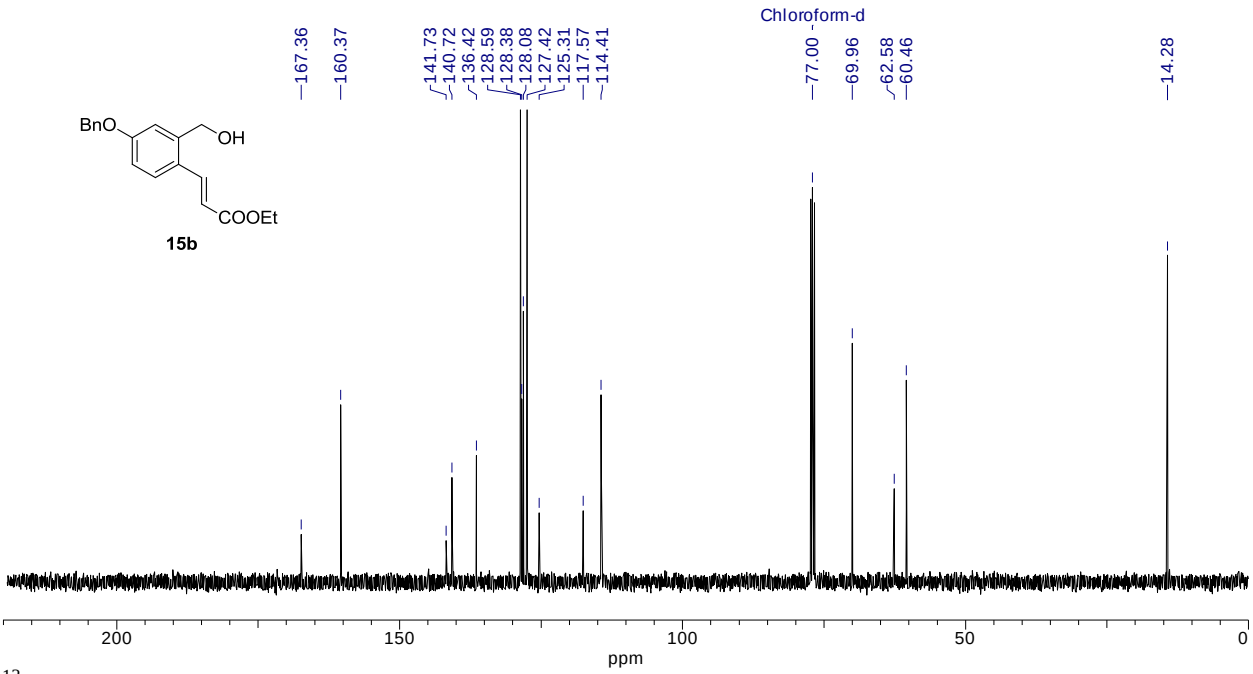
^{1}H NMR (400 MHz) spectrum of **15a** in $CDCl_3$



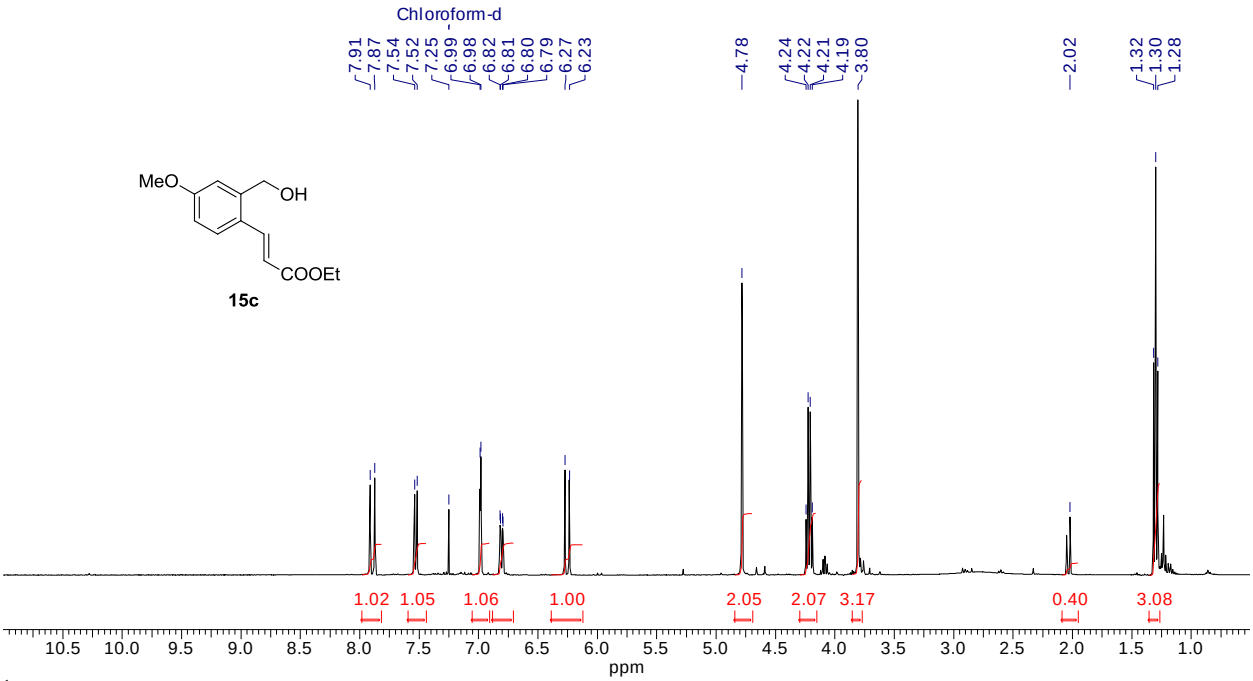
^{13}C NMR (100 MHz) spectrum of **15a** in $CDCl_3$



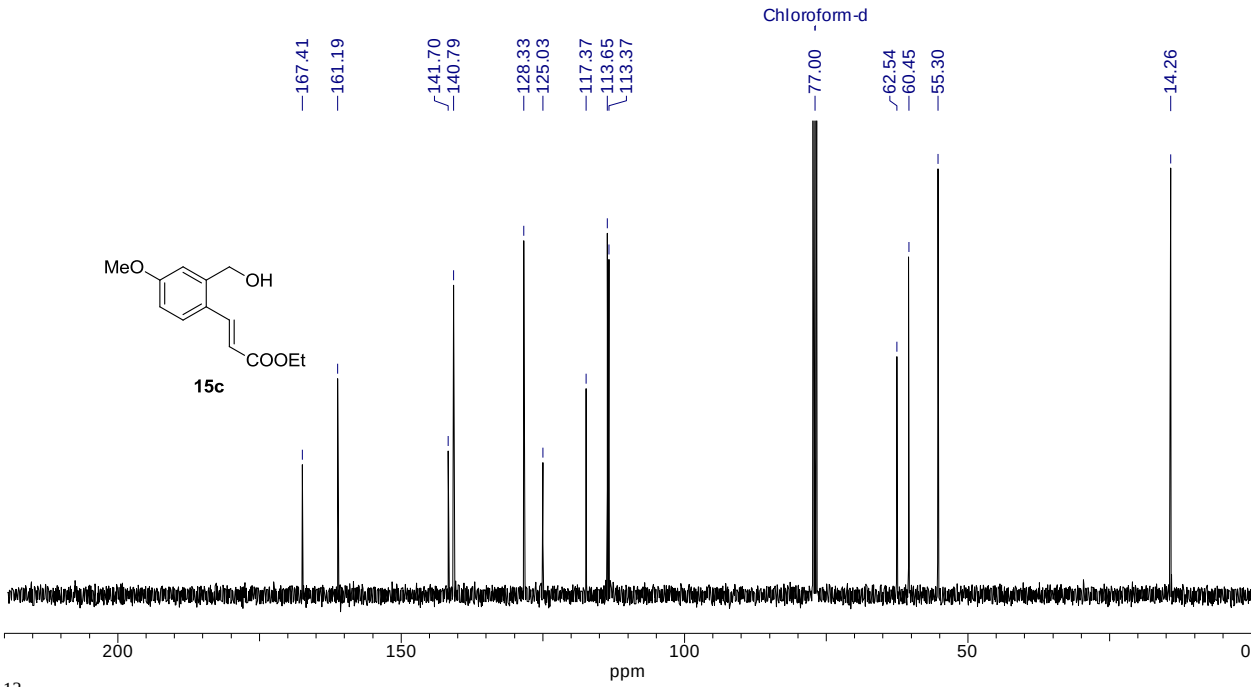
^{1}H NMR (400 MHz) spectrum of **15b** in $CDCl_3$



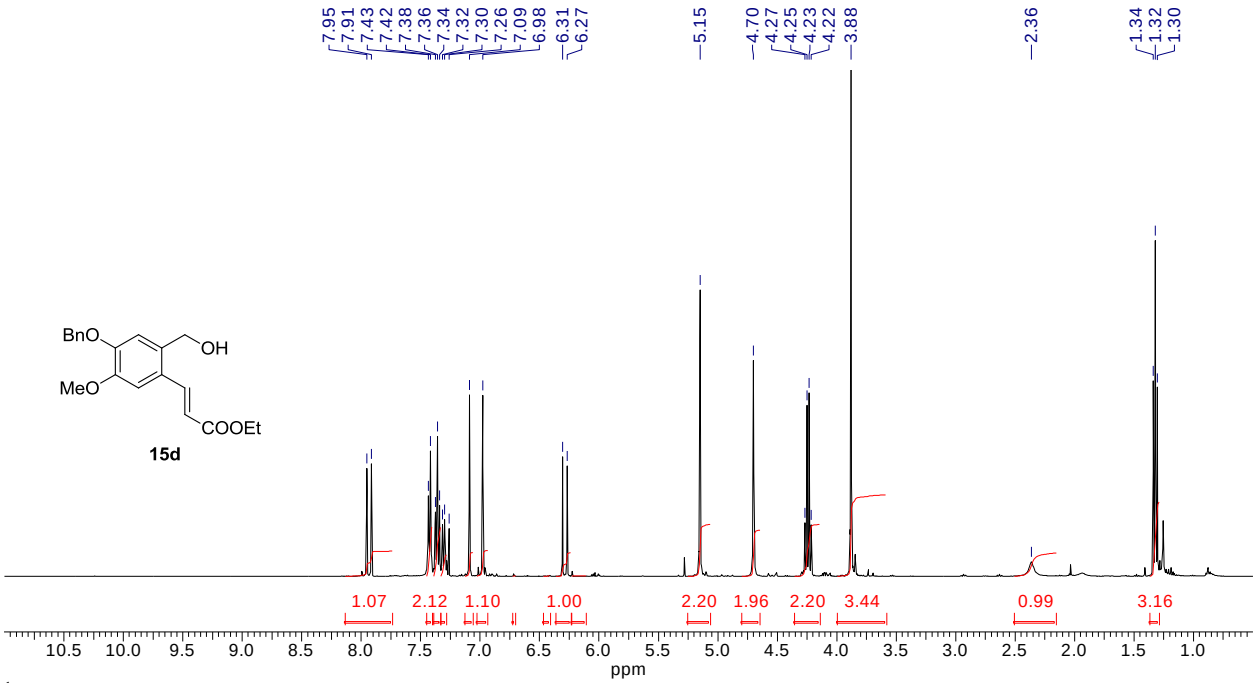
^{13}C NMR (100 MHz) spectrum of **15b** in $CDCl_3$



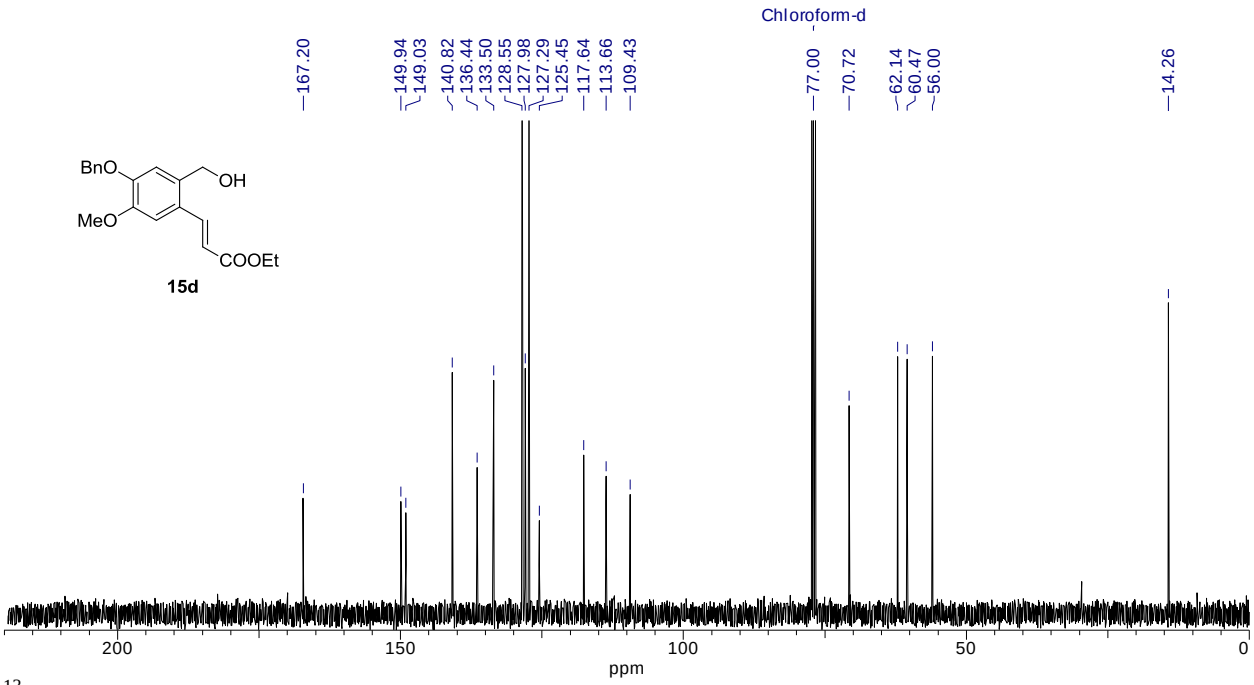
^{1}H NMR (400 MHz) spectrum of **15c** in $CDCl_3$



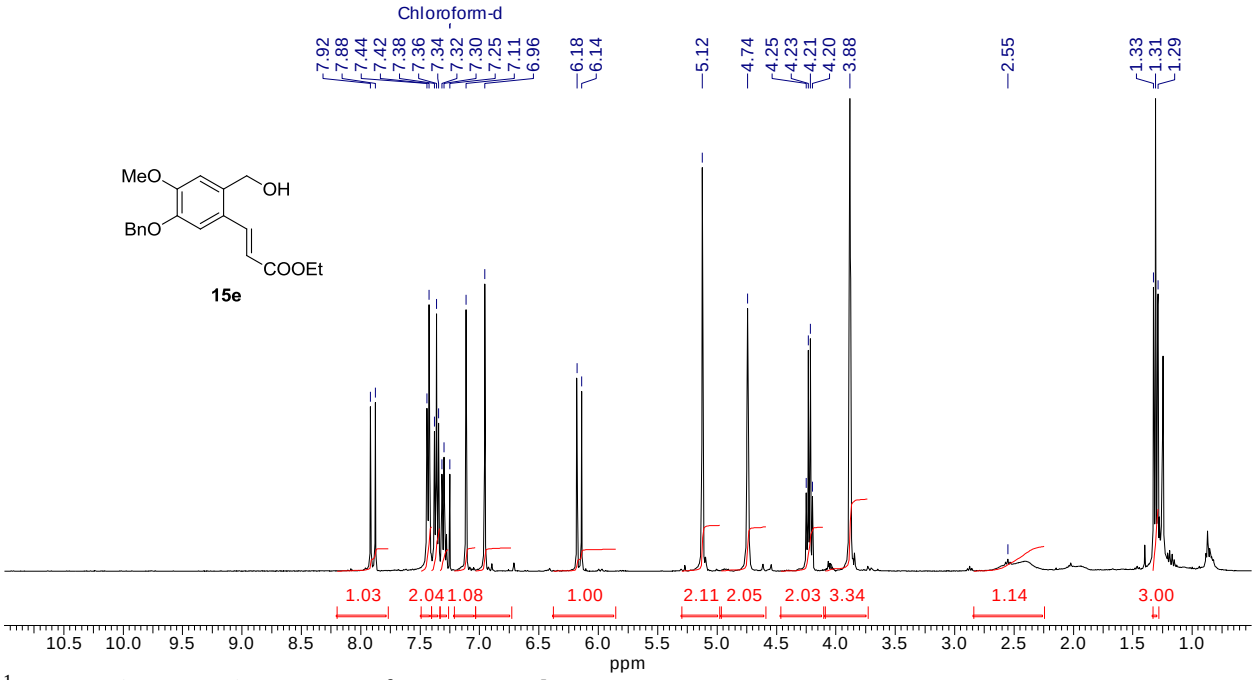
^{13}C NMR (100 MHz) spectrum of **15c** in $CDCl_3$



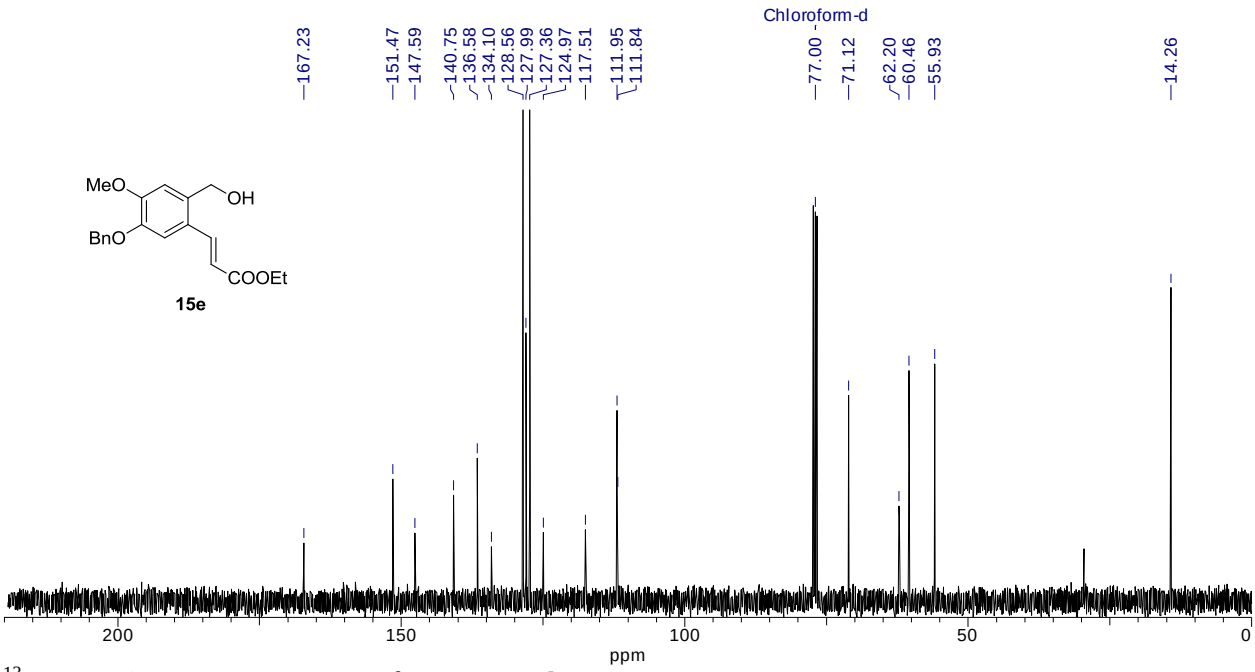
^{1}H NMR (400 MHz) spectrum of **15d** in $CDCl_3$



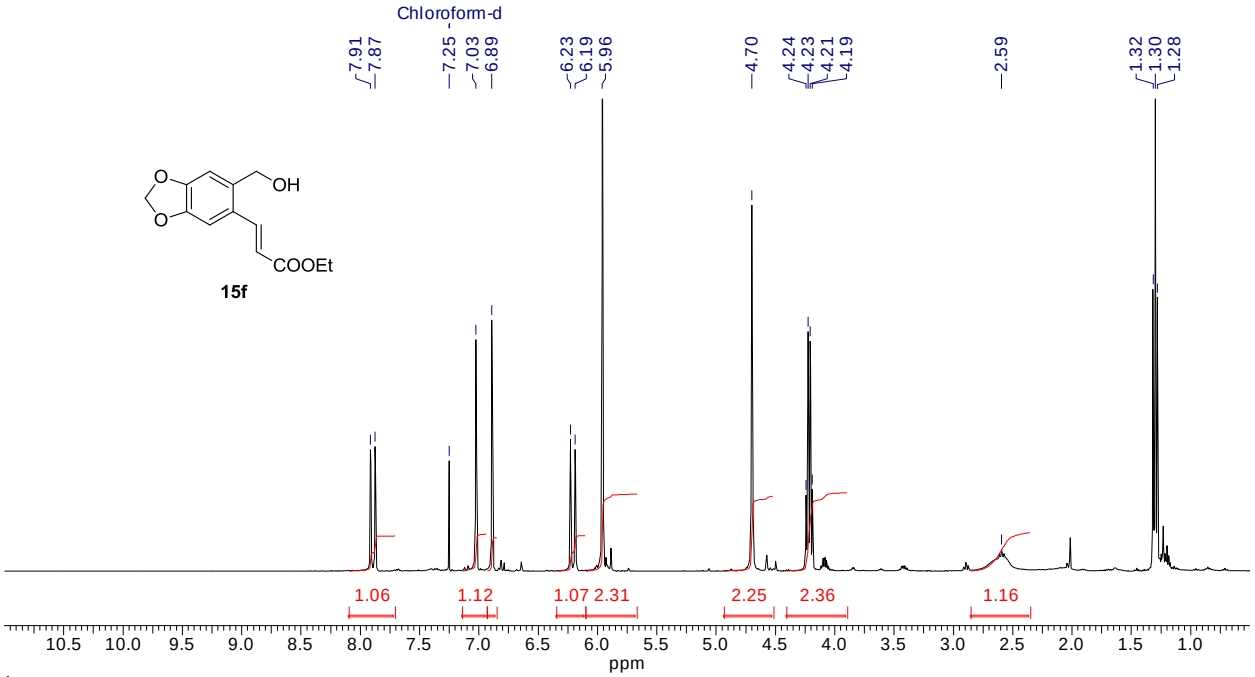
^{13}C NMR (100 MHz) spectrum of **15d** in $CDCl_3$



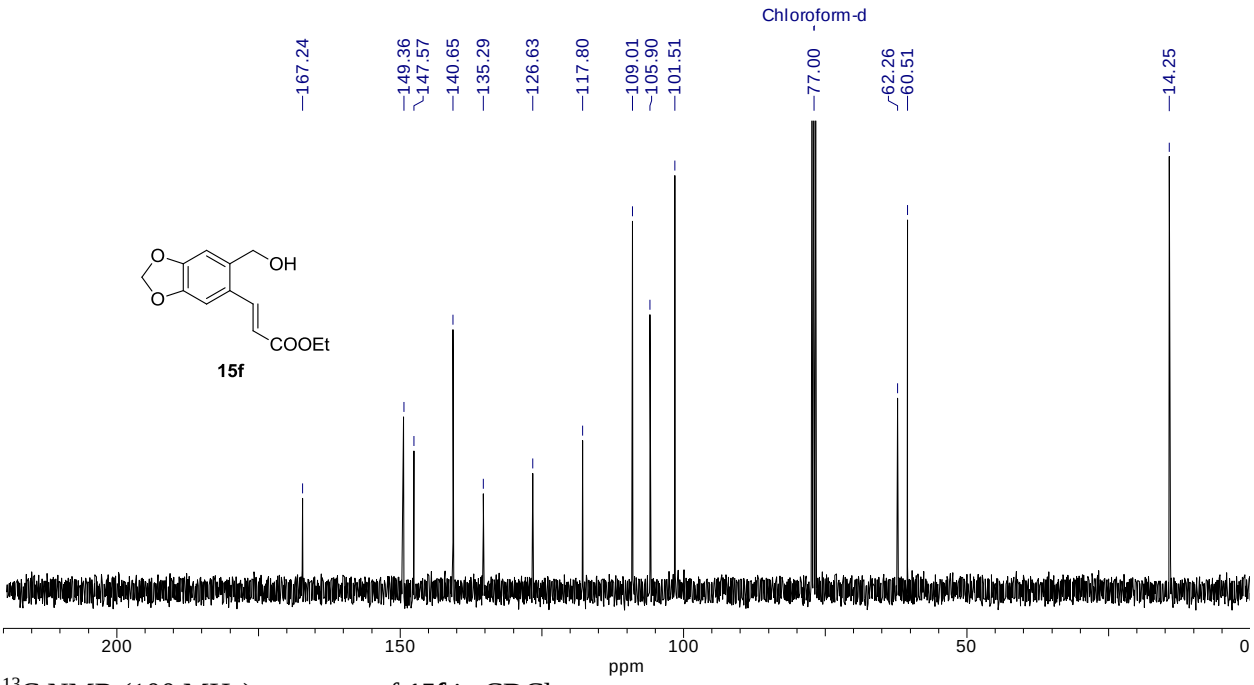
^{1}H NMR (400 MHz) spectrum of **15e** in $CDCl_3$



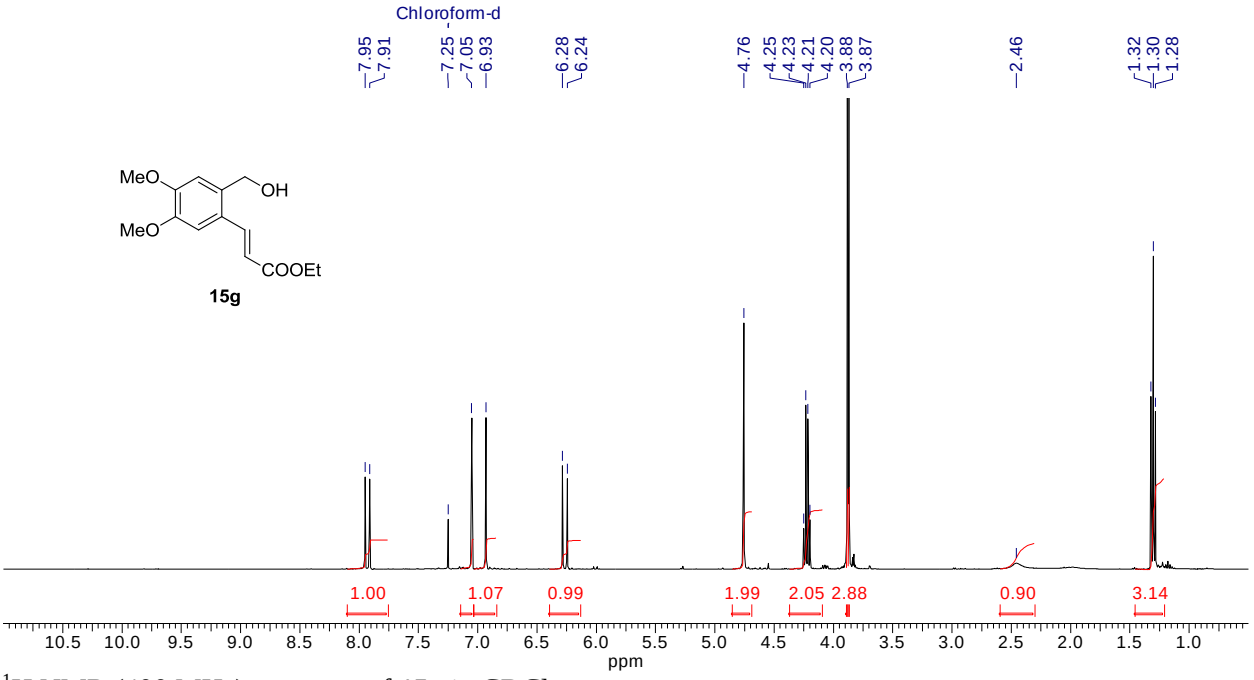
^{13}C NMR (100 MHz) spectrum of **15e** in $CDCl_3$



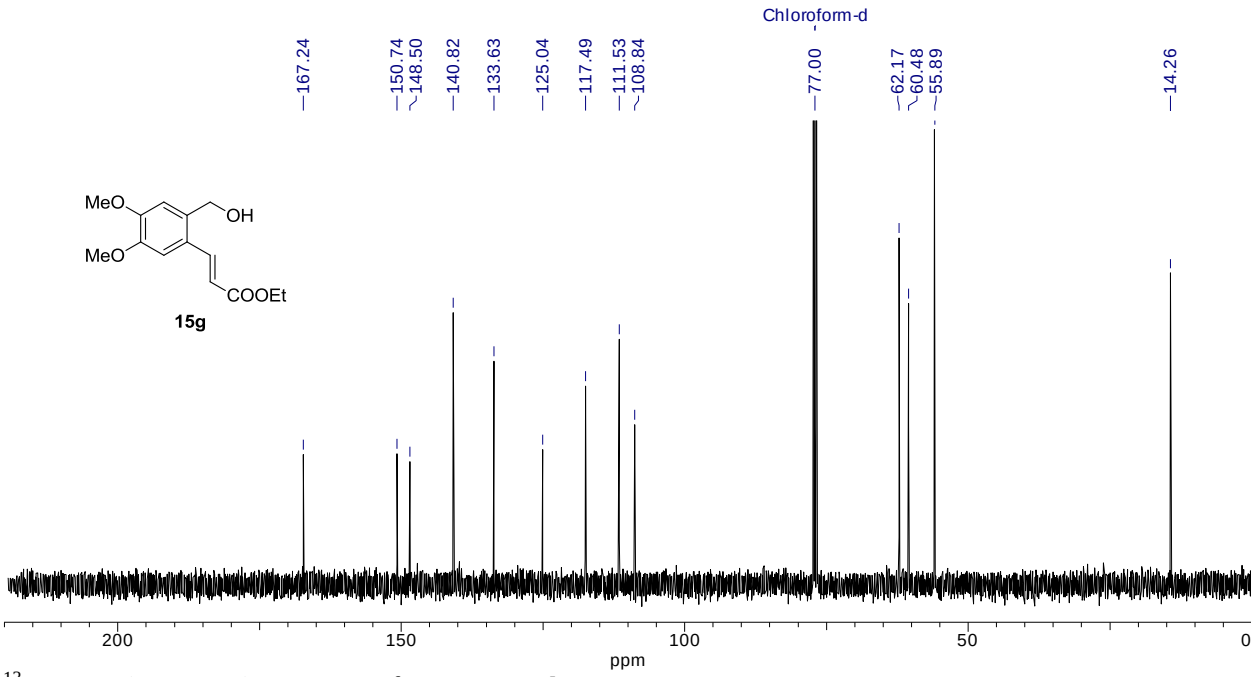
^{1}H NMR (400 MHz) spectrum of **15f** in $CDCl_3$



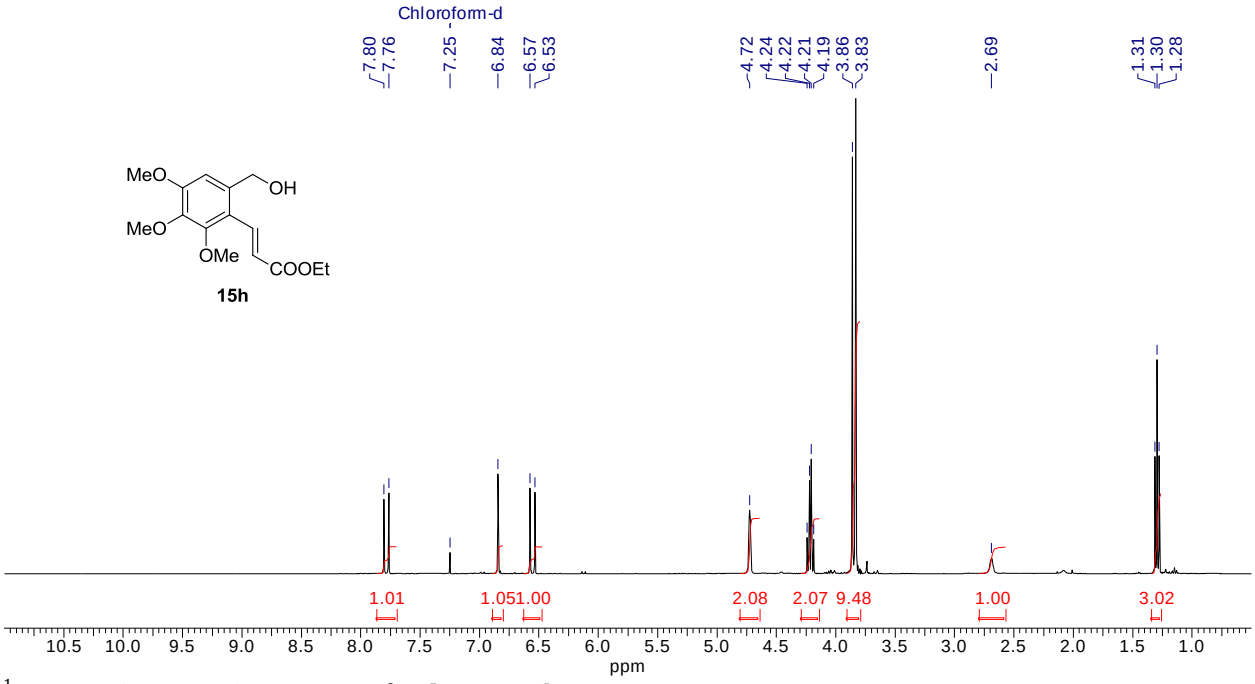
^{13}C NMR (100 MHz) spectrum of **15f** in $CDCl_3$



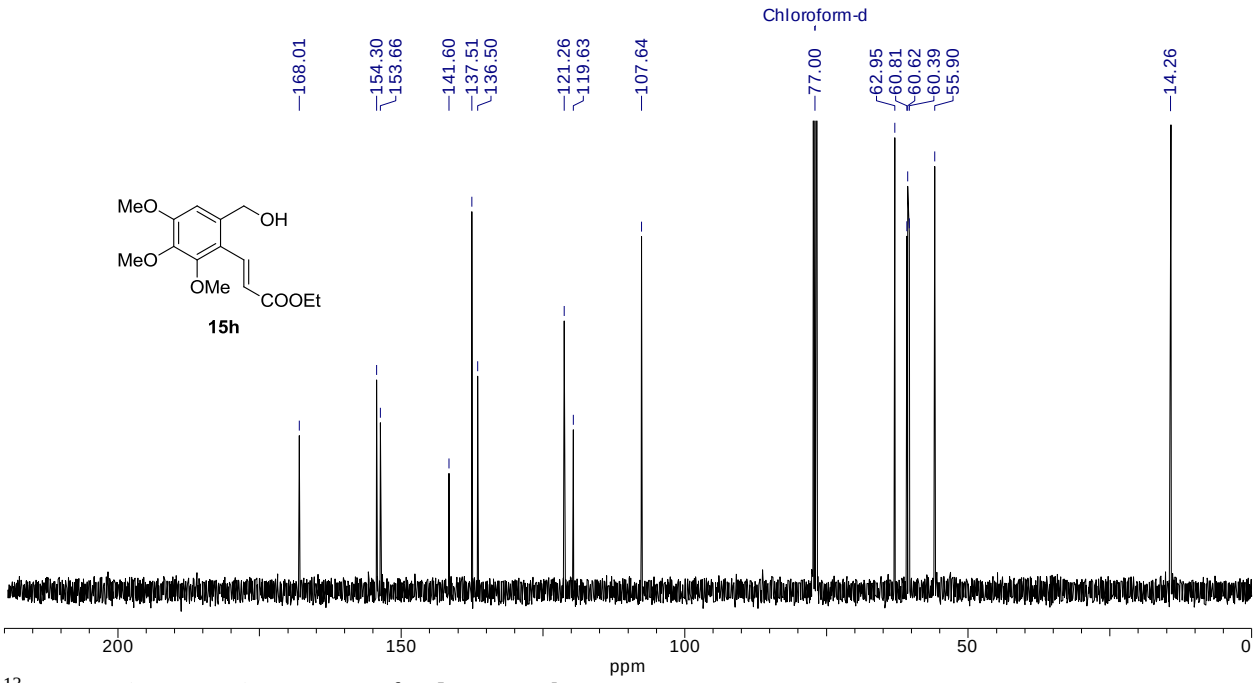
^{1}H NMR (400 MHz) spectrum of **15g** in $CDCl_3$



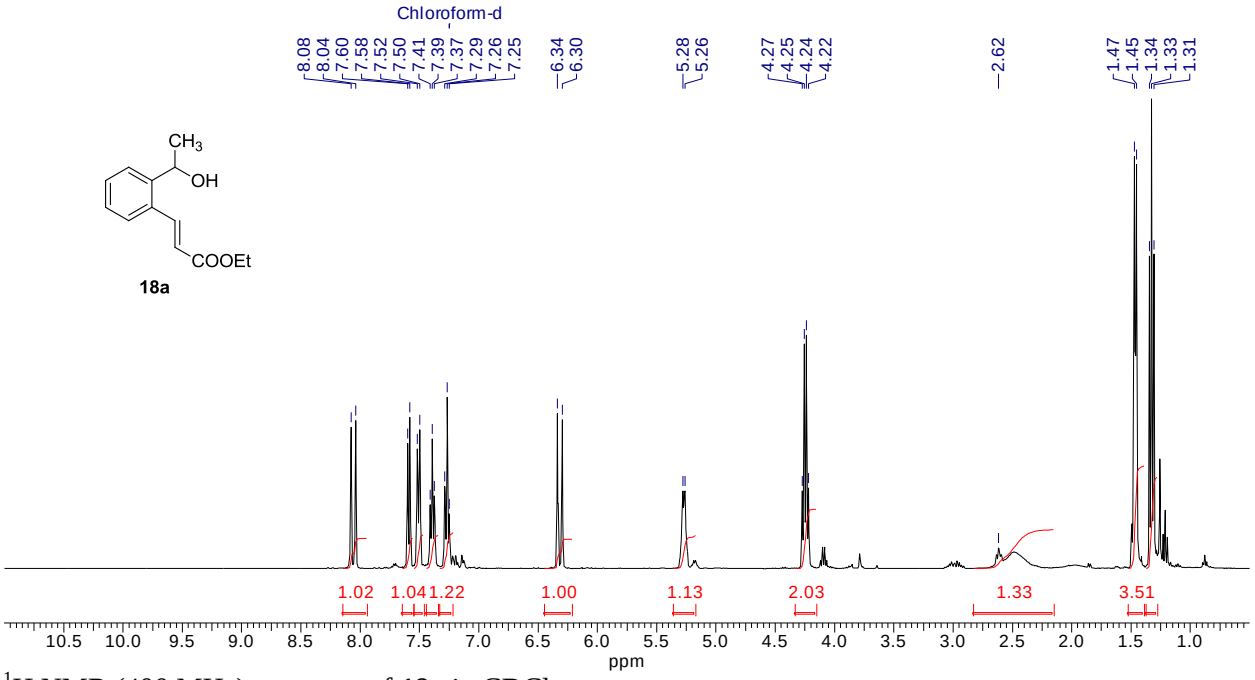
^{13}C NMR (100 MHz) spectrum of **15g** in $CDCl_3$



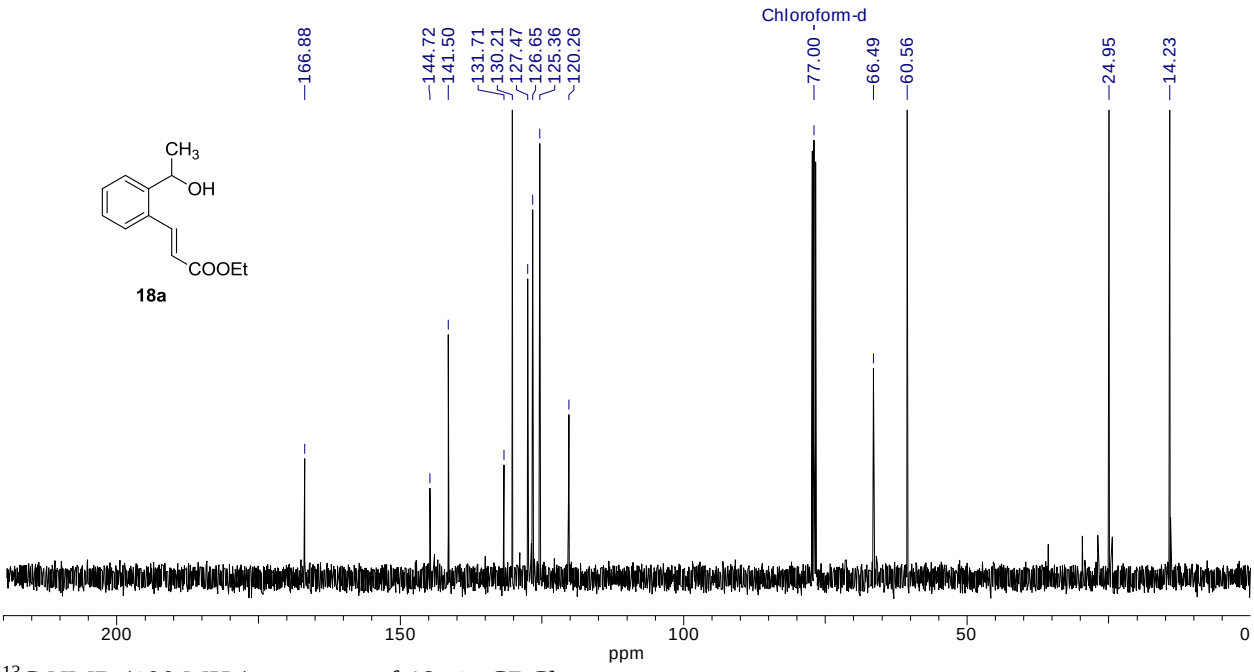
^{1}H NMR (400 MHz) spectrum of **15h** in $CDCl_3$



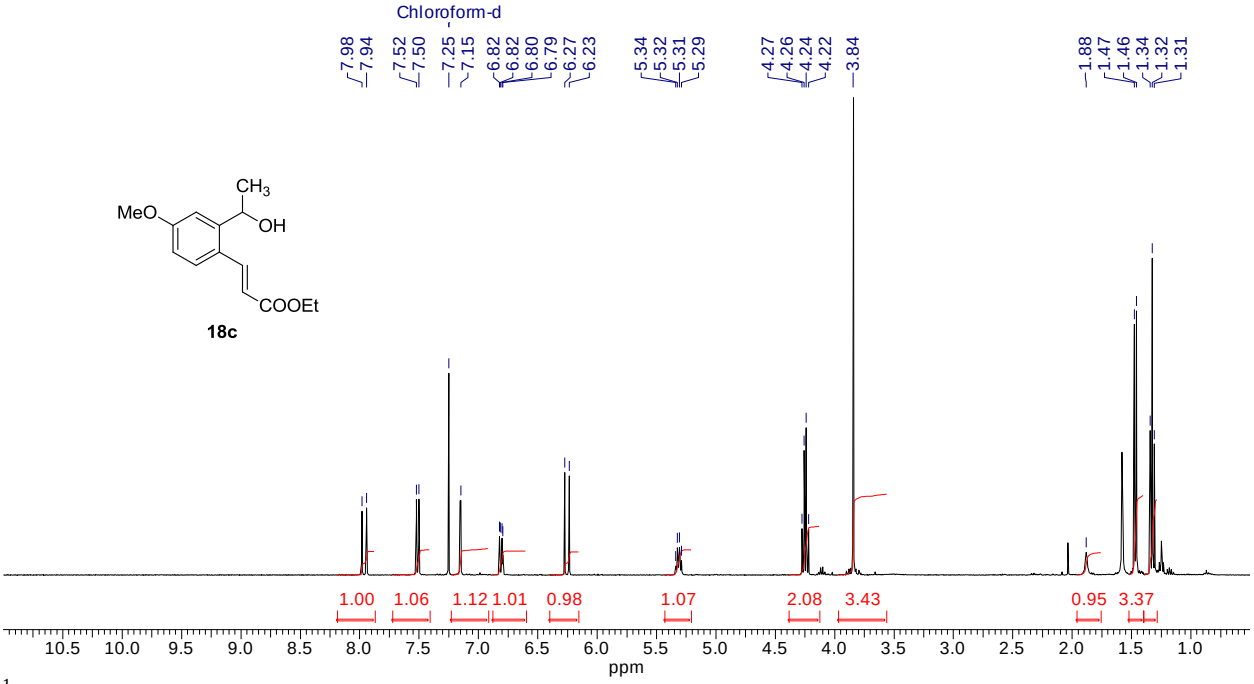
^{13}C NMR (100 MHz) spectrum of **15h** in $CDCl_3$



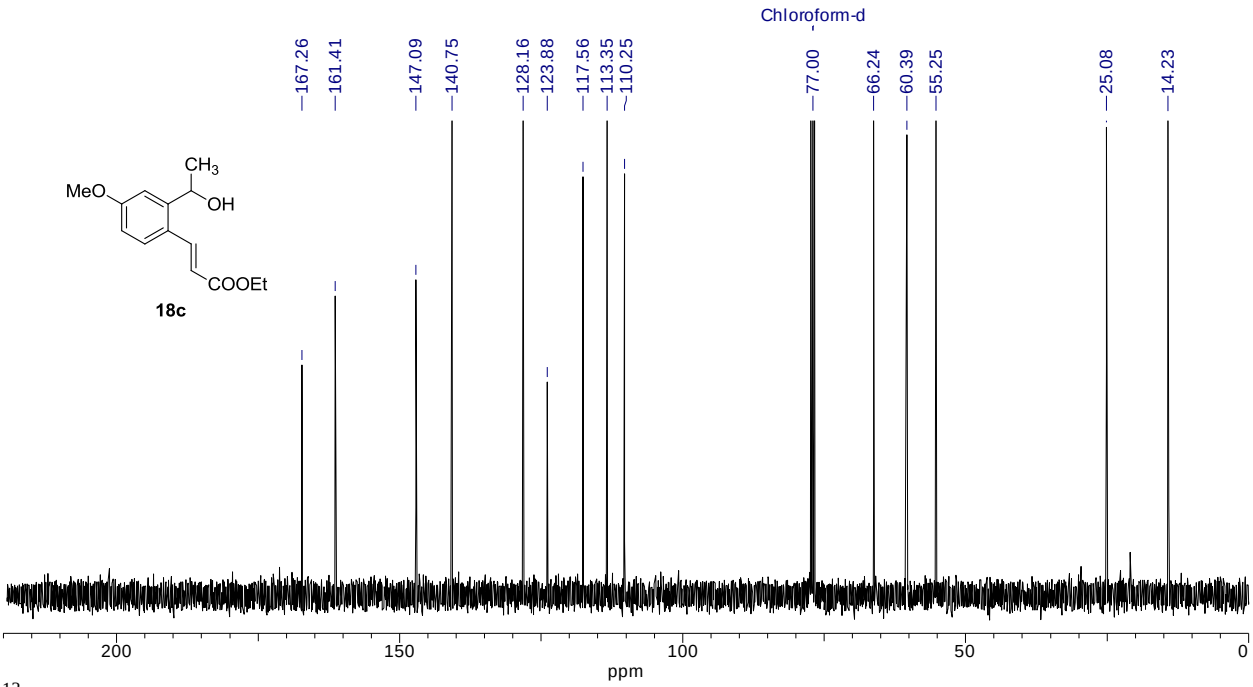
^{1}H NMR (400 MHz) spectrum of **18a** in $CDCl_3$



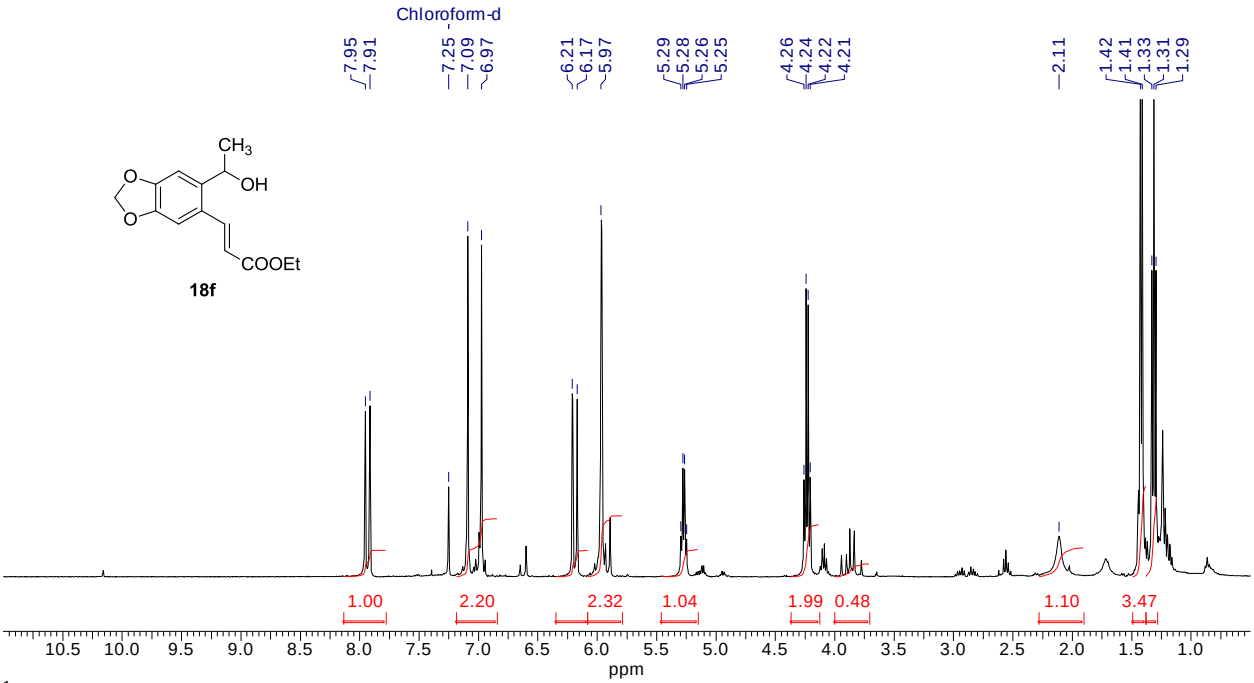
^{13}C NMR (100 MHz) spectrum of **18a** in $CDCl_3$



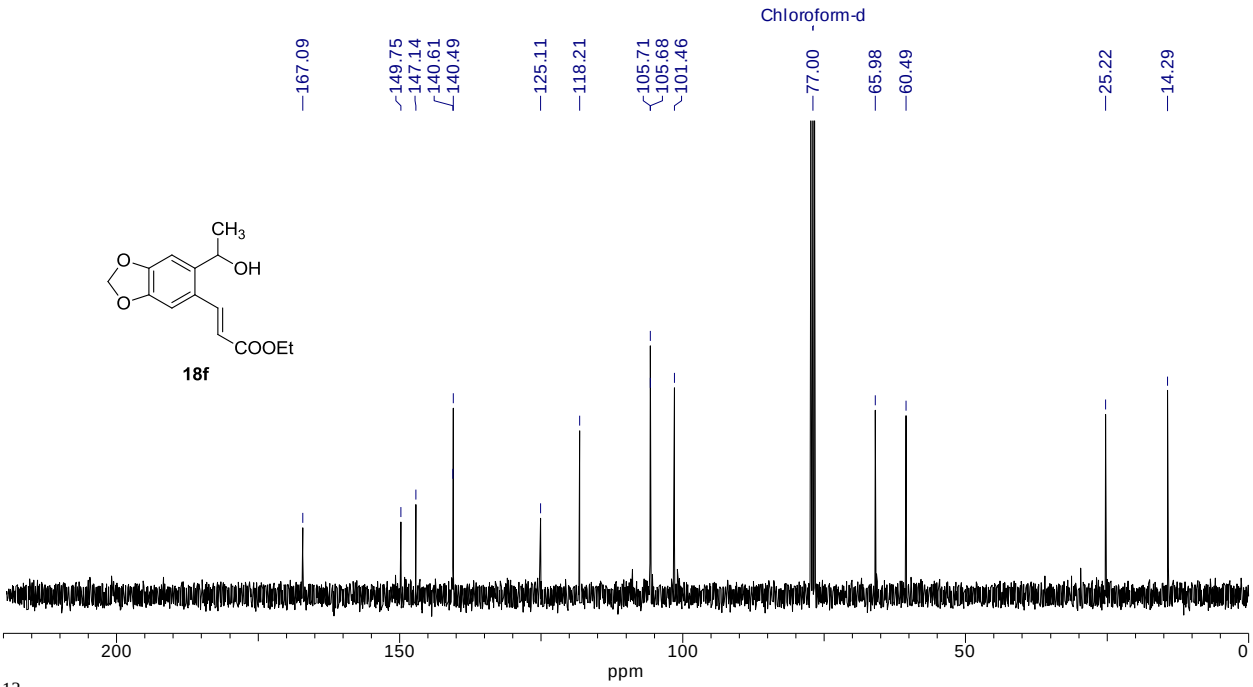
^{1}H NMR (400 MHz) spectrum of **18c** in $CDCl_3$



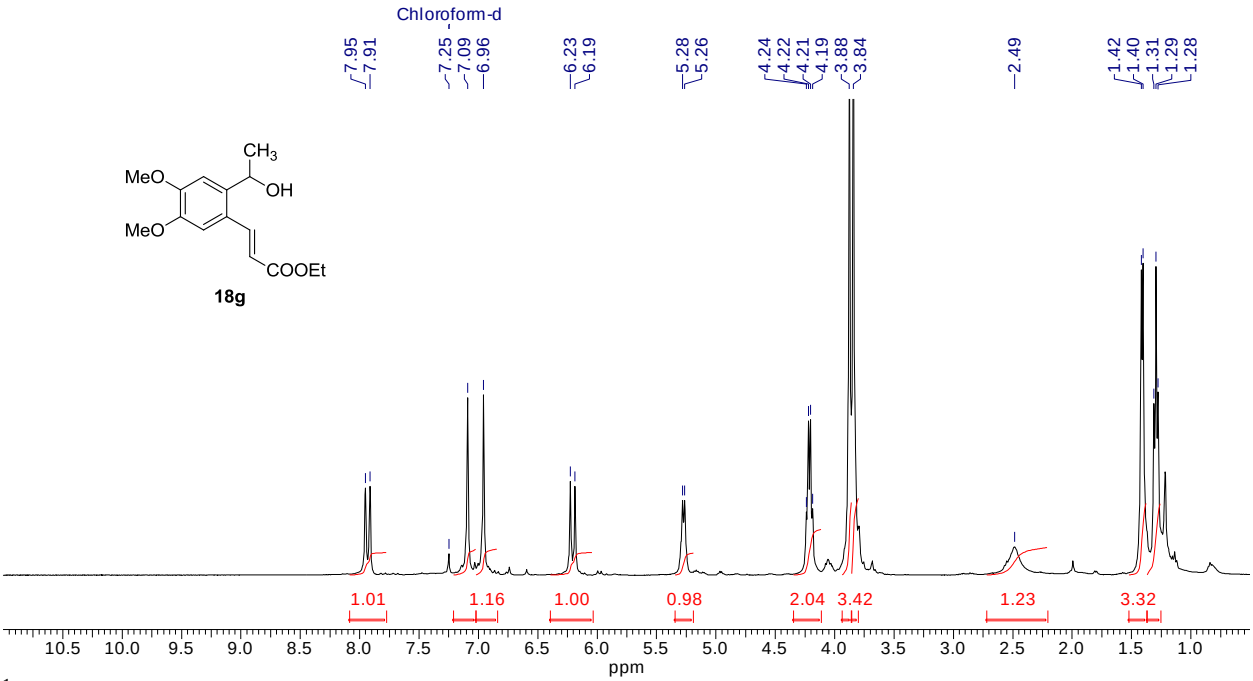
^{13}C NMR (100 MHz) spectrum of **18c** in $CDCl_3$



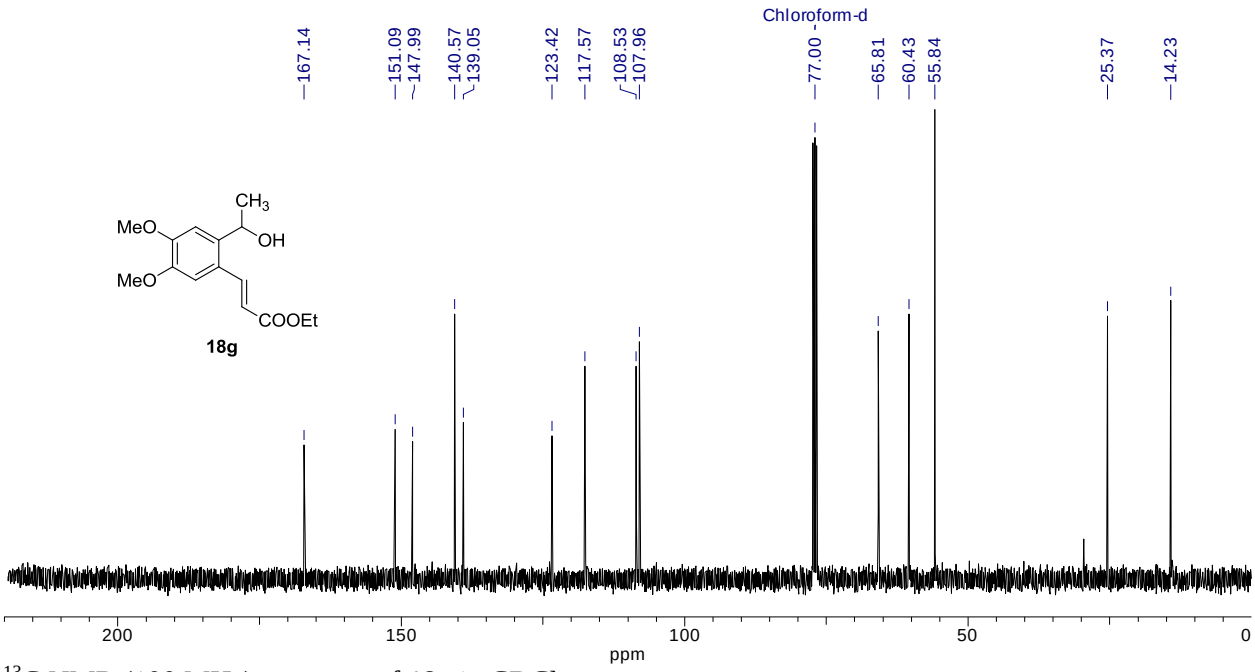
^{1}H NMR (400 MHz) spectrum of **18f** in $CDCl_3$



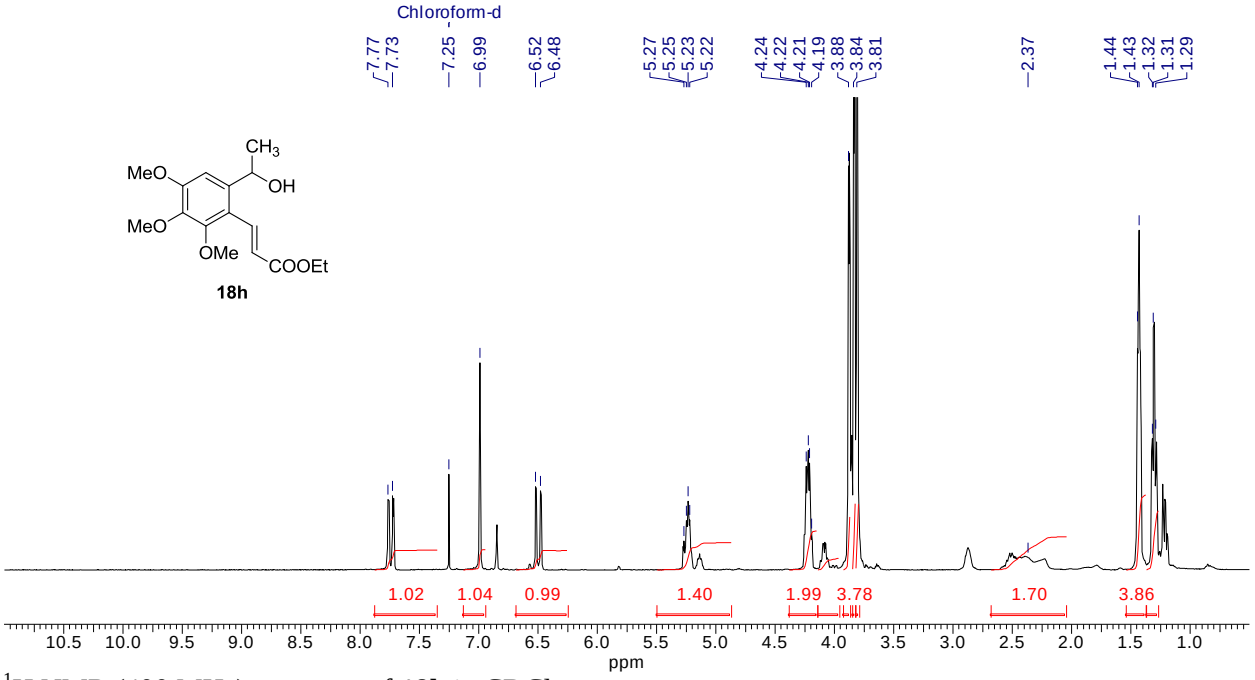
^{13}C NMR (100 MHz) spectrum of **18f** in $CDCl_3$



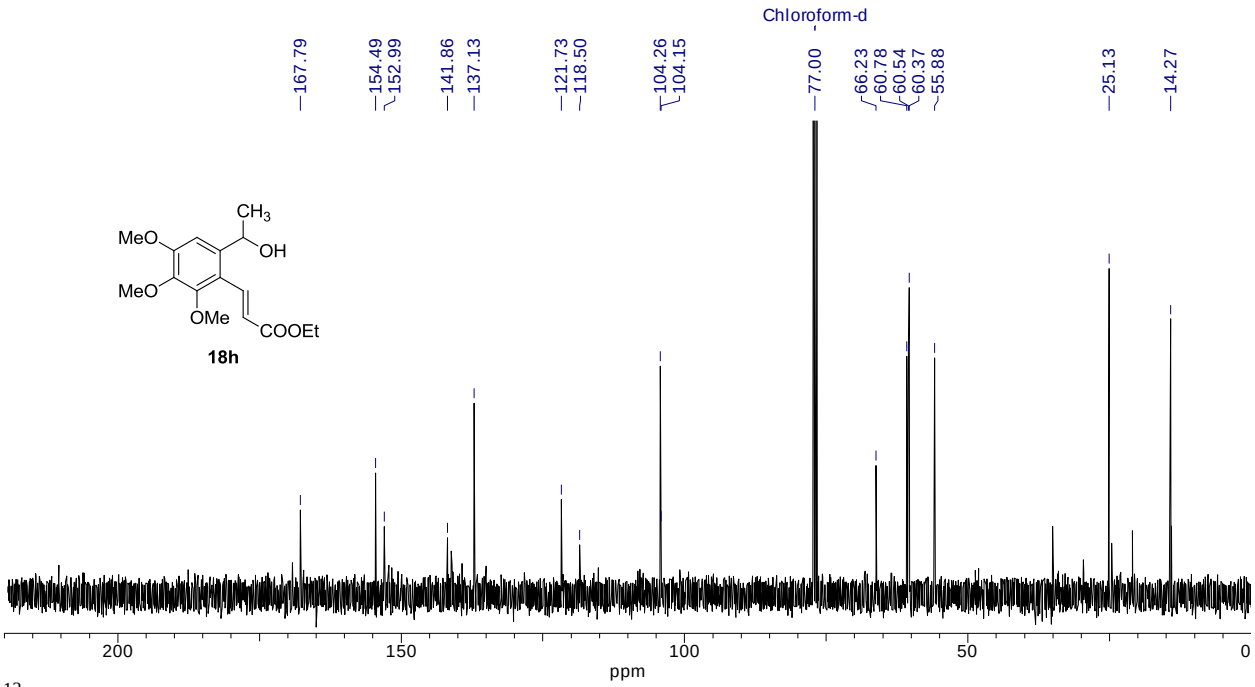
^{1}H NMR (400 MHz) spectrum of **18g** in $CDCl_3$



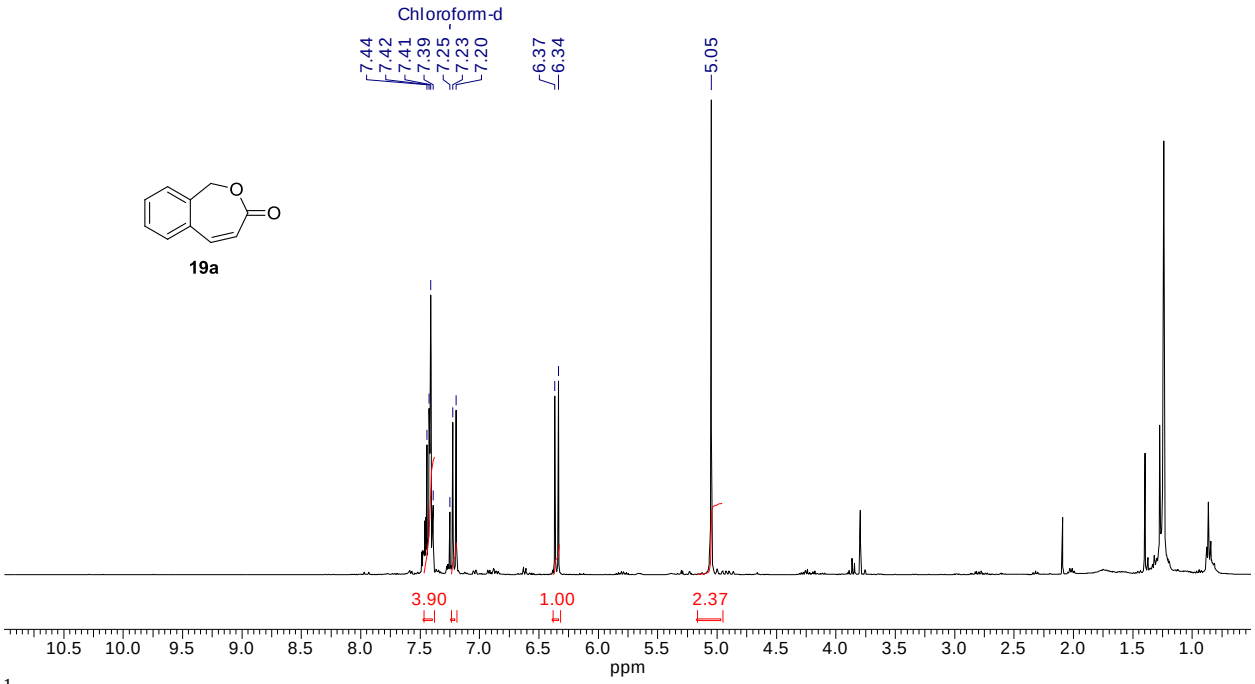
^{13}C NMR (100 MHz) spectrum of **18g** in $CDCl_3$



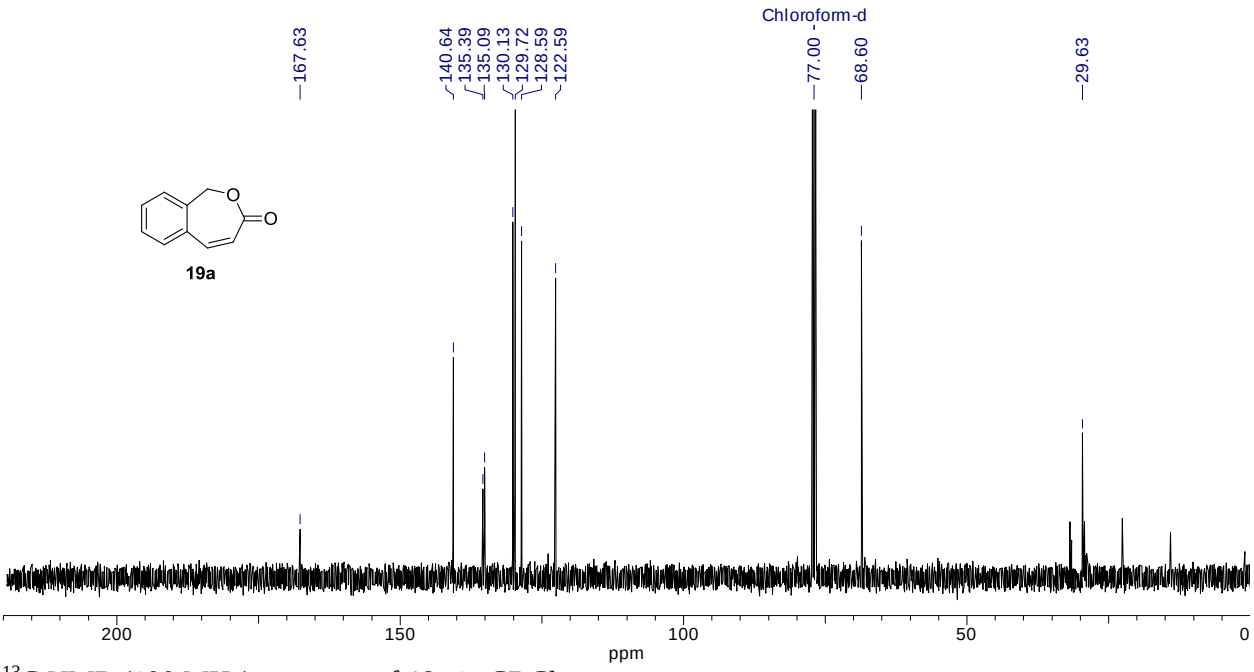
^{1}H NMR (400 MHz) spectrum of **18h** in $CDCl_3$



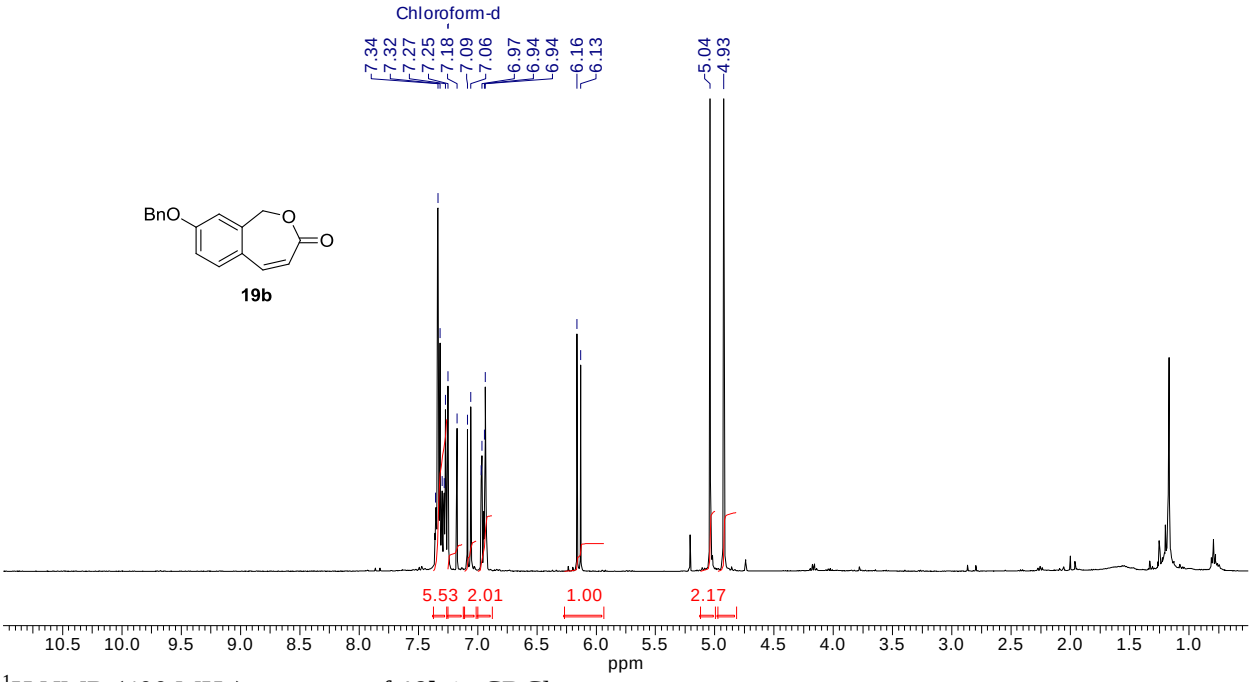
^{13}C NMR (100 MHz) spectrum of **18h** in $CDCl_3$



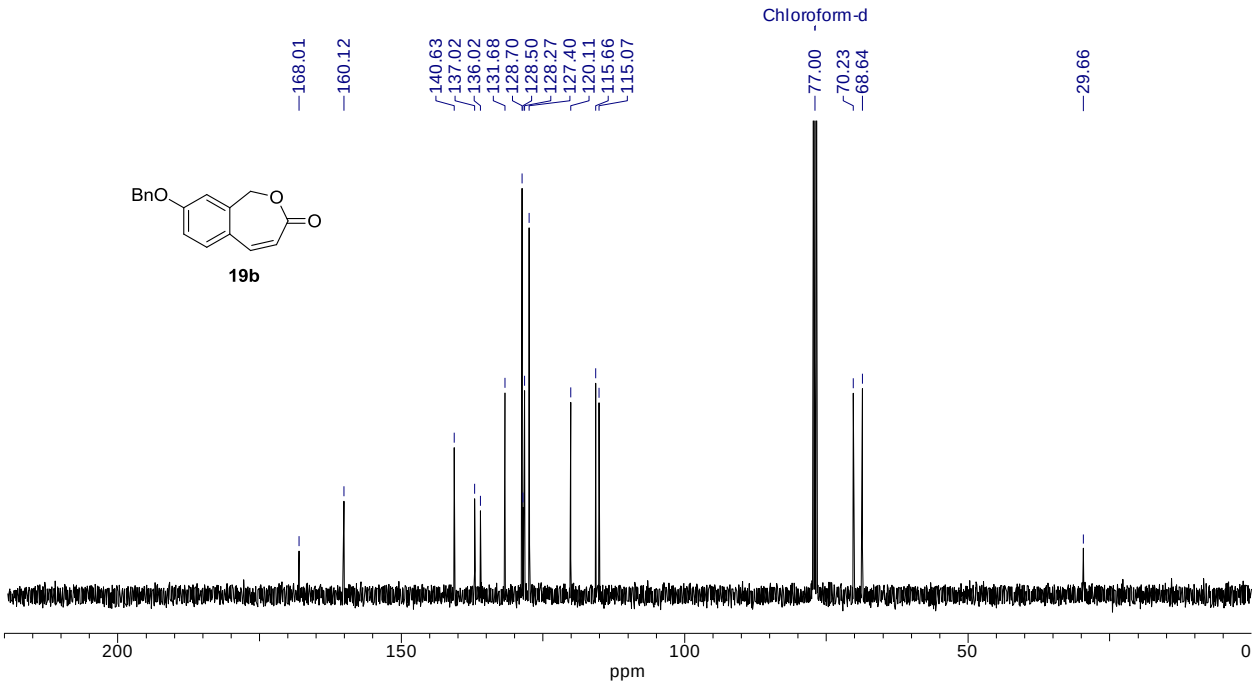
^{1}H NMR (400 MHz) spectrum of **19a** in $CDCl_3$



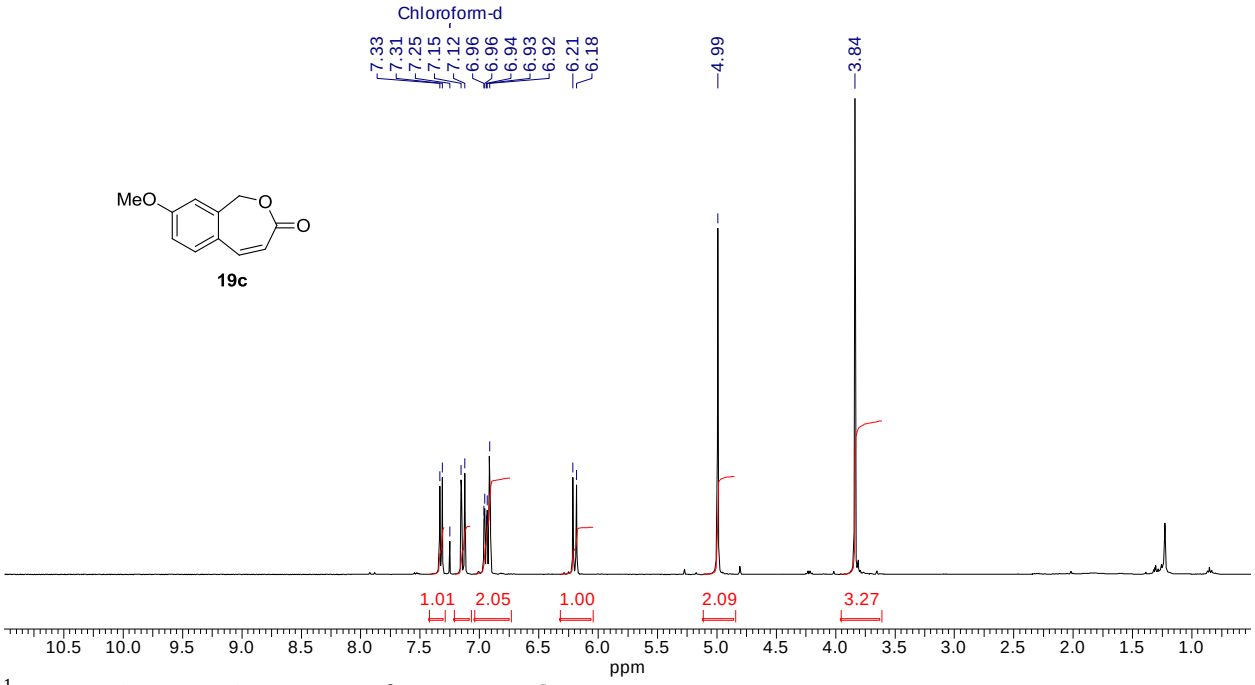
^{13}C NMR (100 MHz) spectrum of **19a** in $CDCl_3$



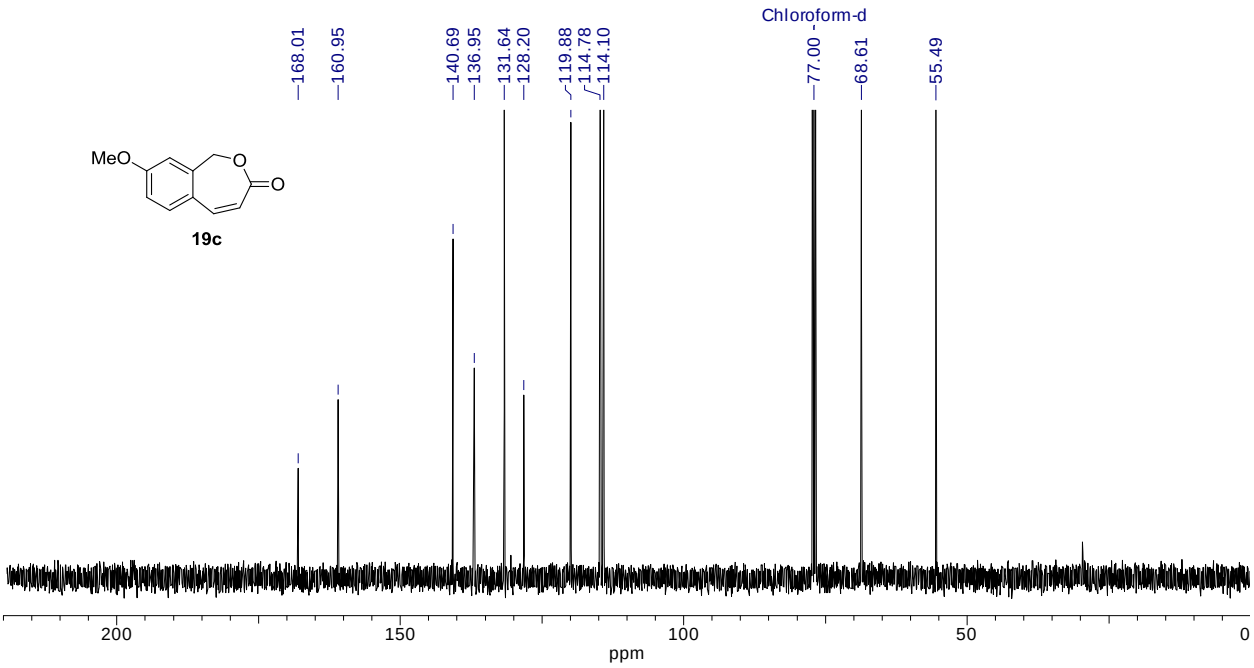
^{1}H NMR (400 MHz) spectrum of **19b** in $CDCl_3$



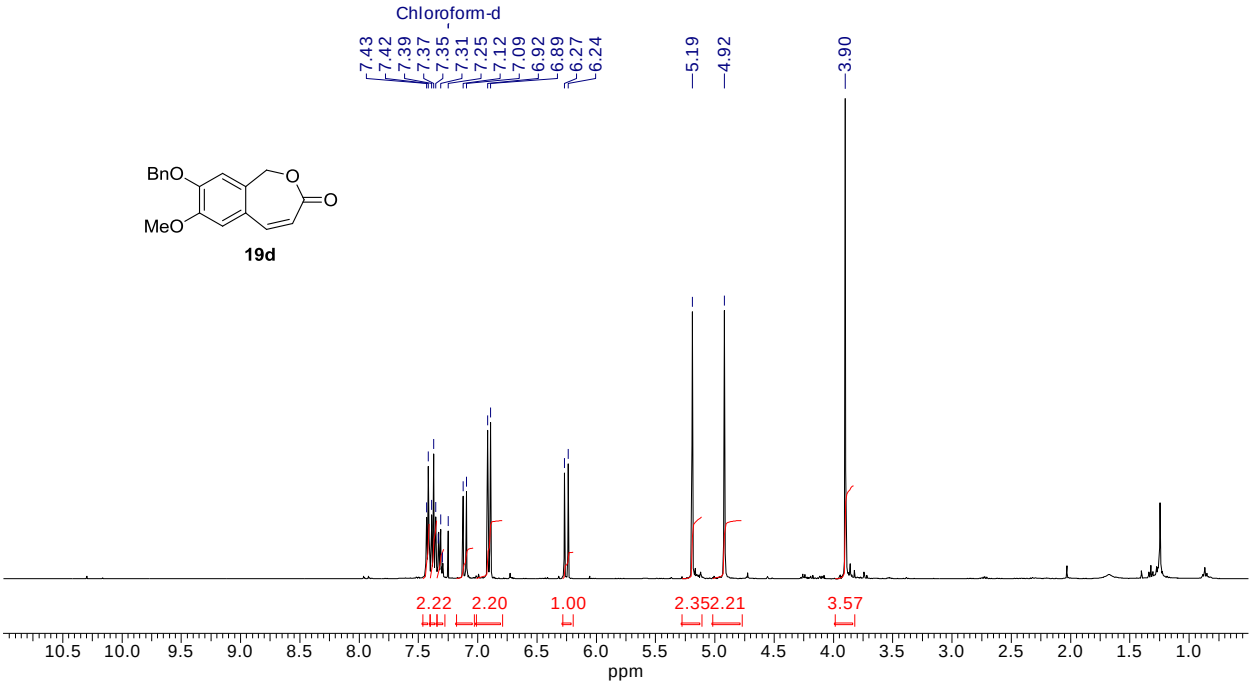
^{13}C NMR (100 MHz) spectrum of **19b** in $CDCl_3$



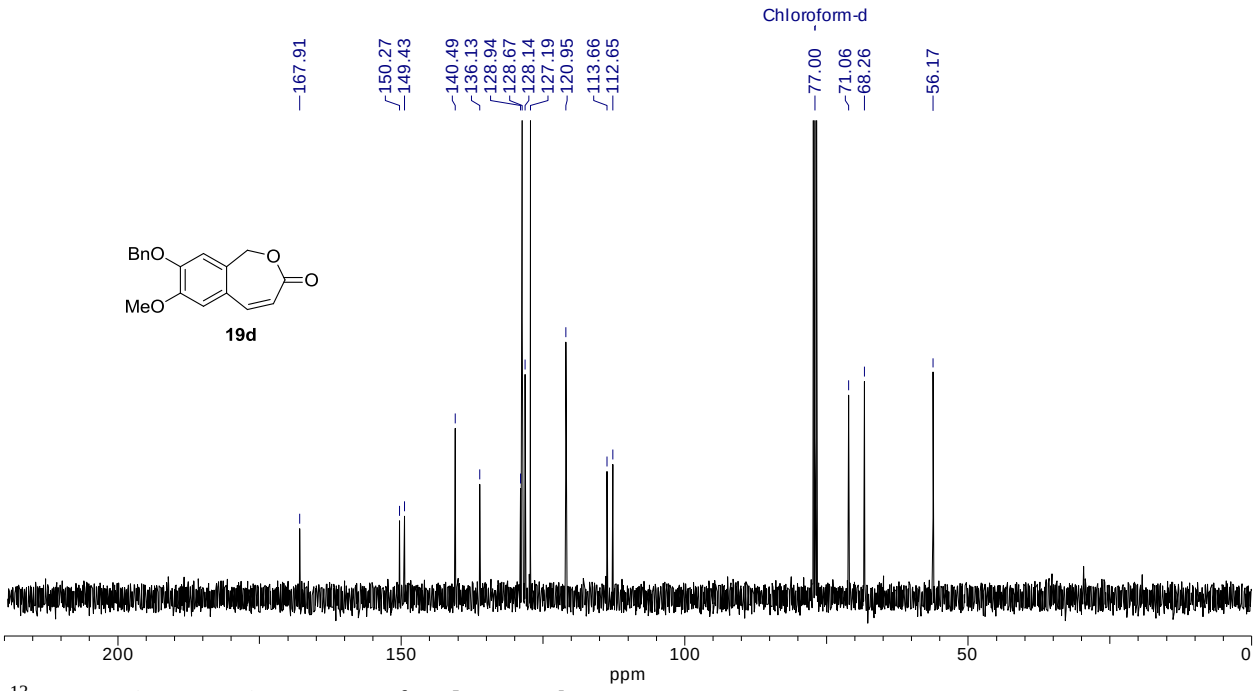
^{1}H NMR (400 MHz) spectrum of **19c** in $CDCl_3$



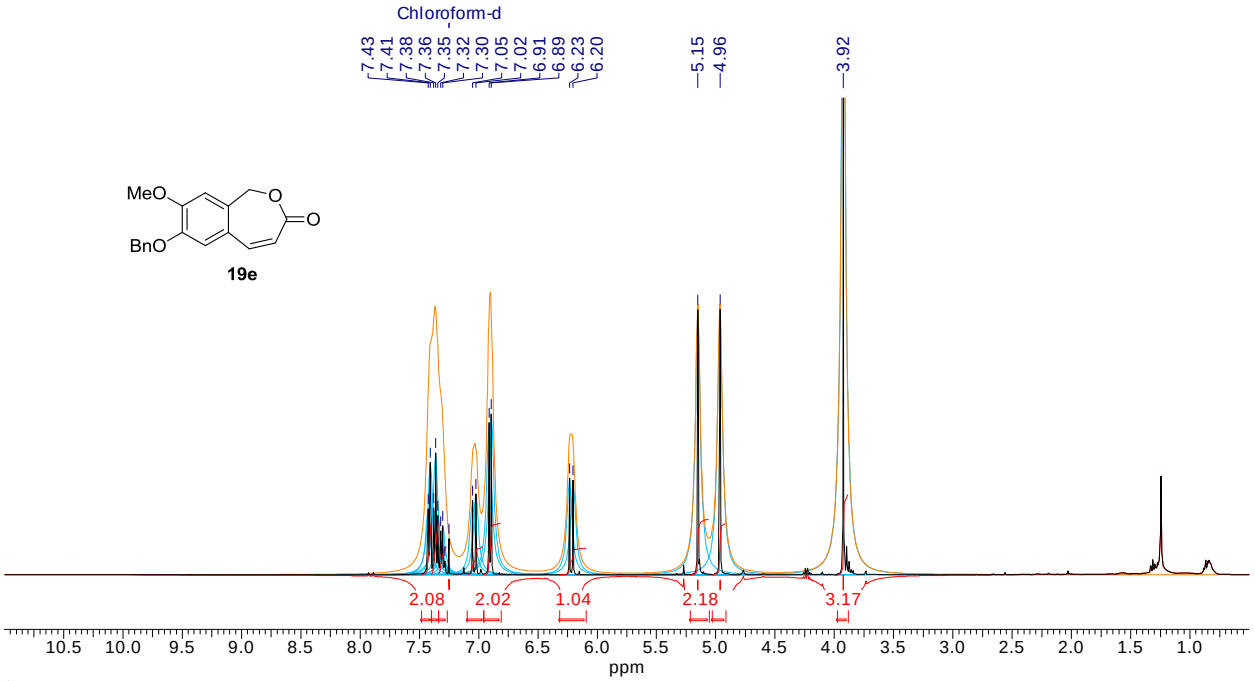
^{13}C NMR (100 MHz) spectrum of **19c** in $CDCl_3$



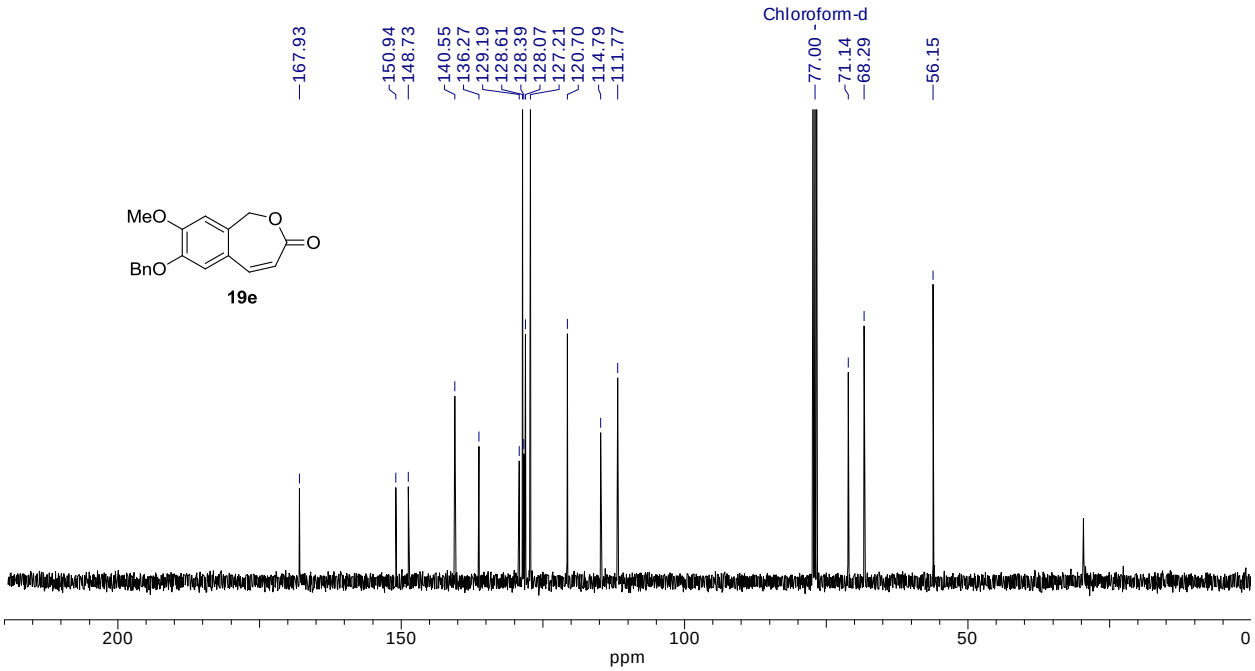
^{1}H NMR (400 MHz) spectrum of **19d** in $CDCl_3$



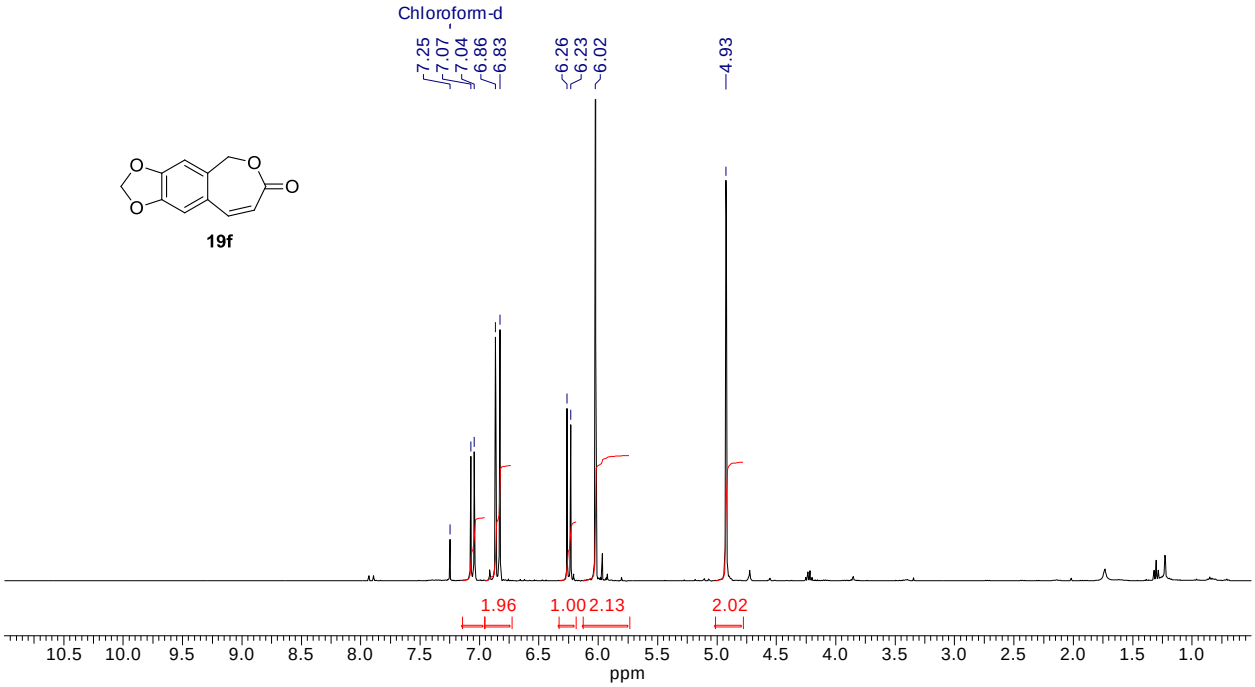
^{13}C NMR (100 MHz) spectrum of **19d** in $CDCl_3$



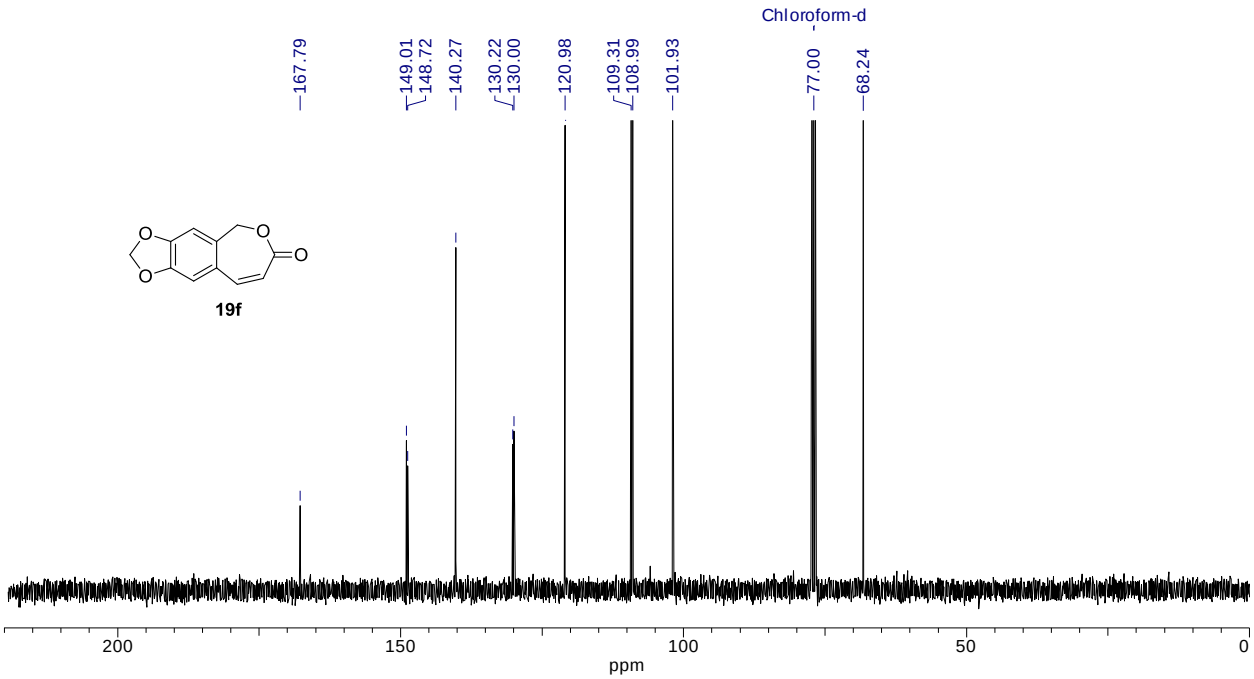
^{1}H NMR (400 MHz) spectrum of **19e** in $CDCl_3$



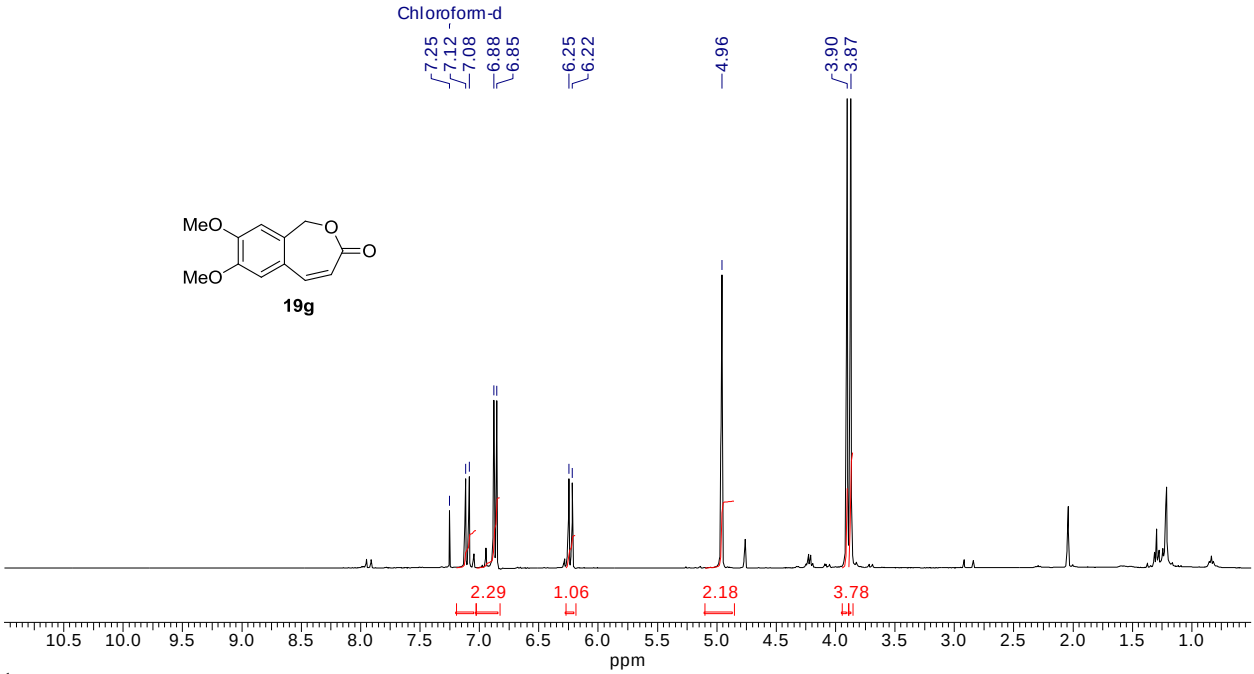
^{13}C NMR (100 MHz) spectrum of **19e** in $CDCl_3$



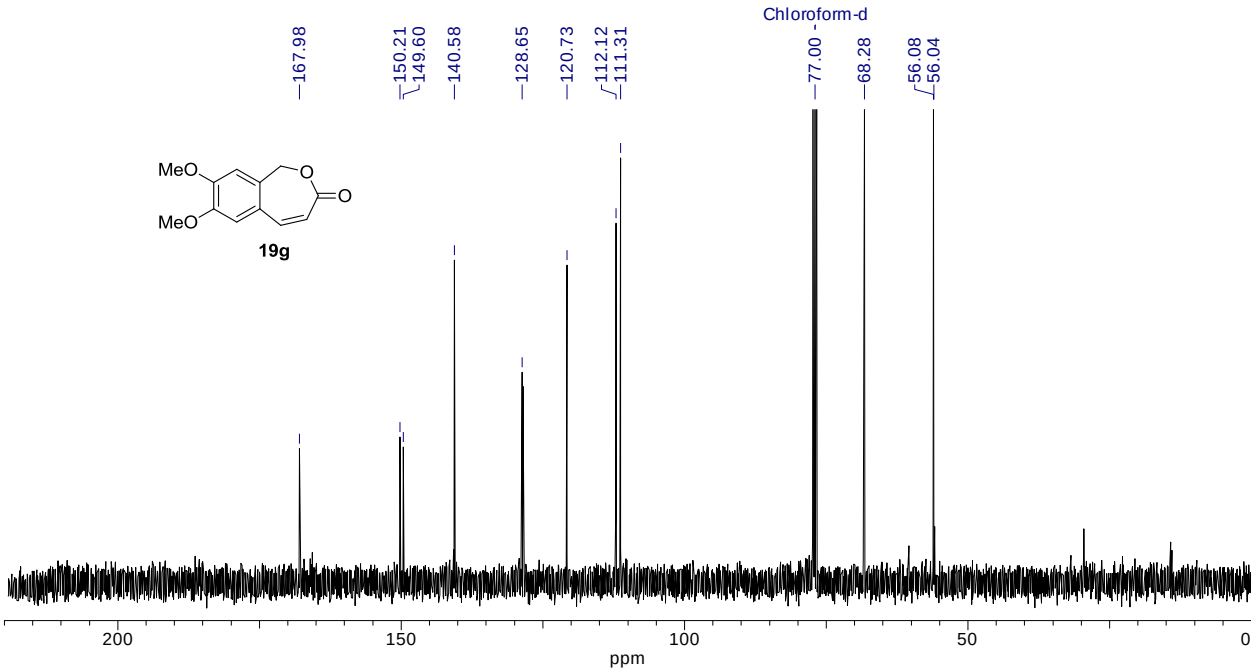
^{1}H NMR (400 MHz) spectrum of **19f** in $CDCl_3$



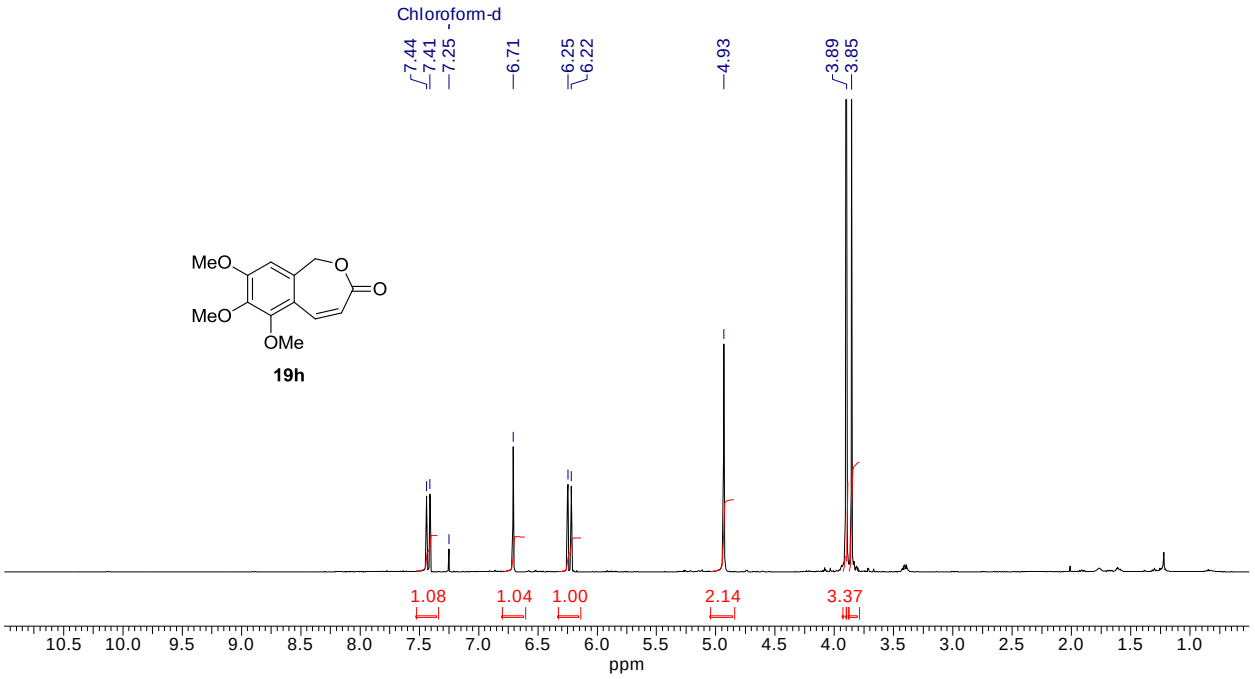
^{13}C NMR (100 MHz) spectrum of **19f** in $CDCl_3$



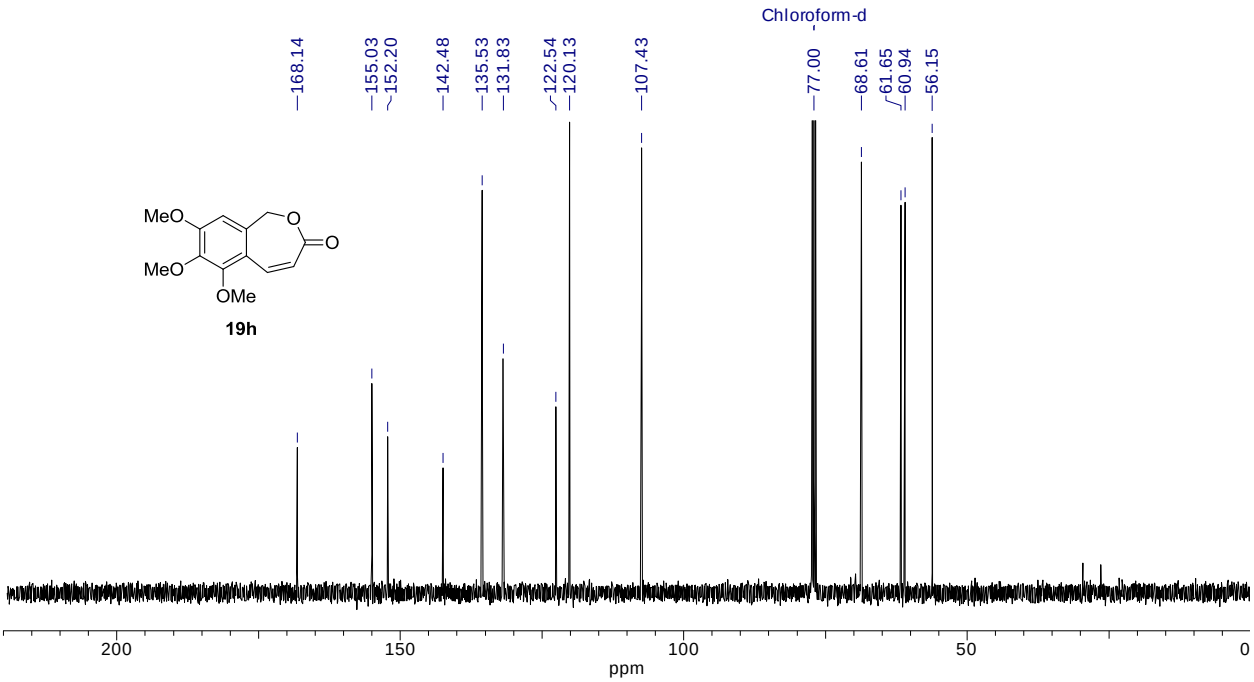
^{1}H NMR (400 MHz) spectrum of **19g** in $CDCl_3$



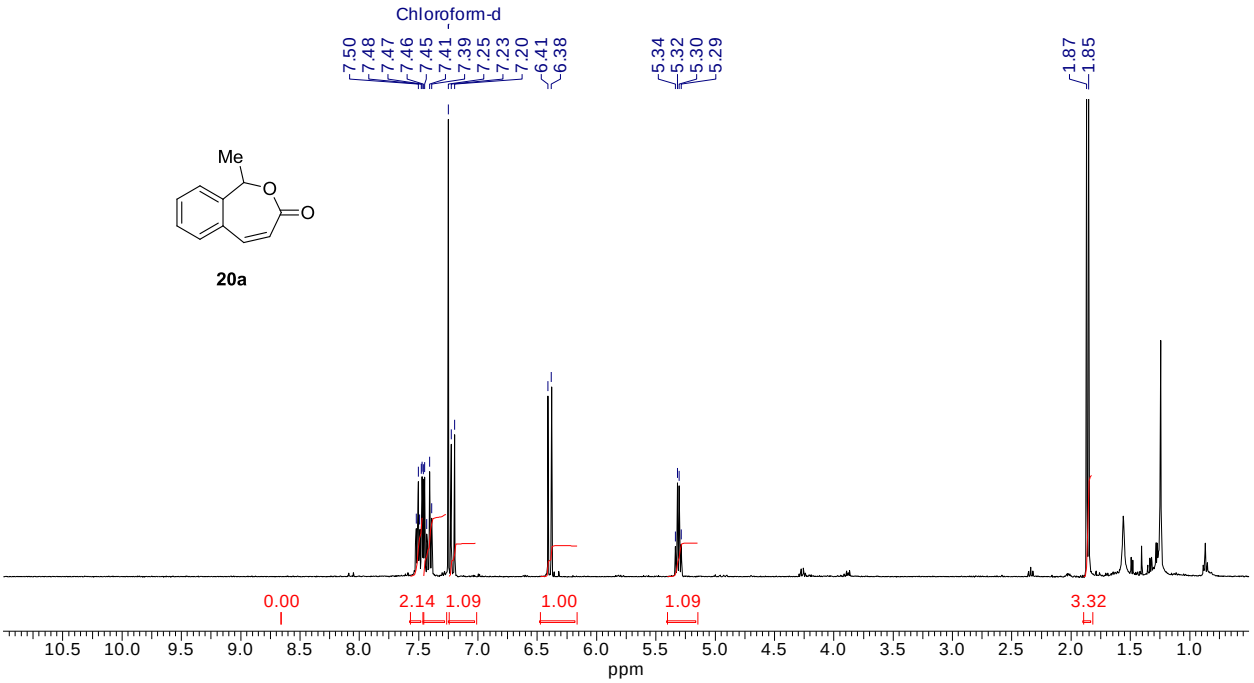
^{13}C NMR (100 MHz) spectrum of **19g** in $CDCl_3$



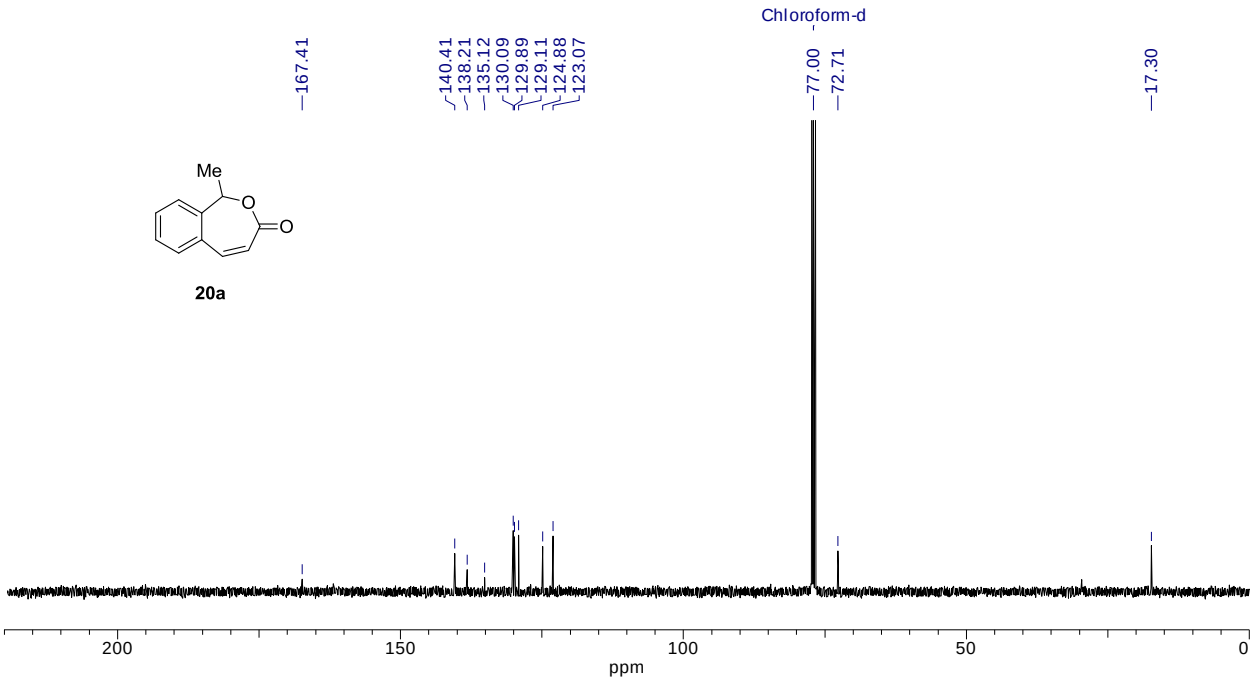
^{1}H NMR (400 MHz) spectrum of **19h** in $CDCl_3$



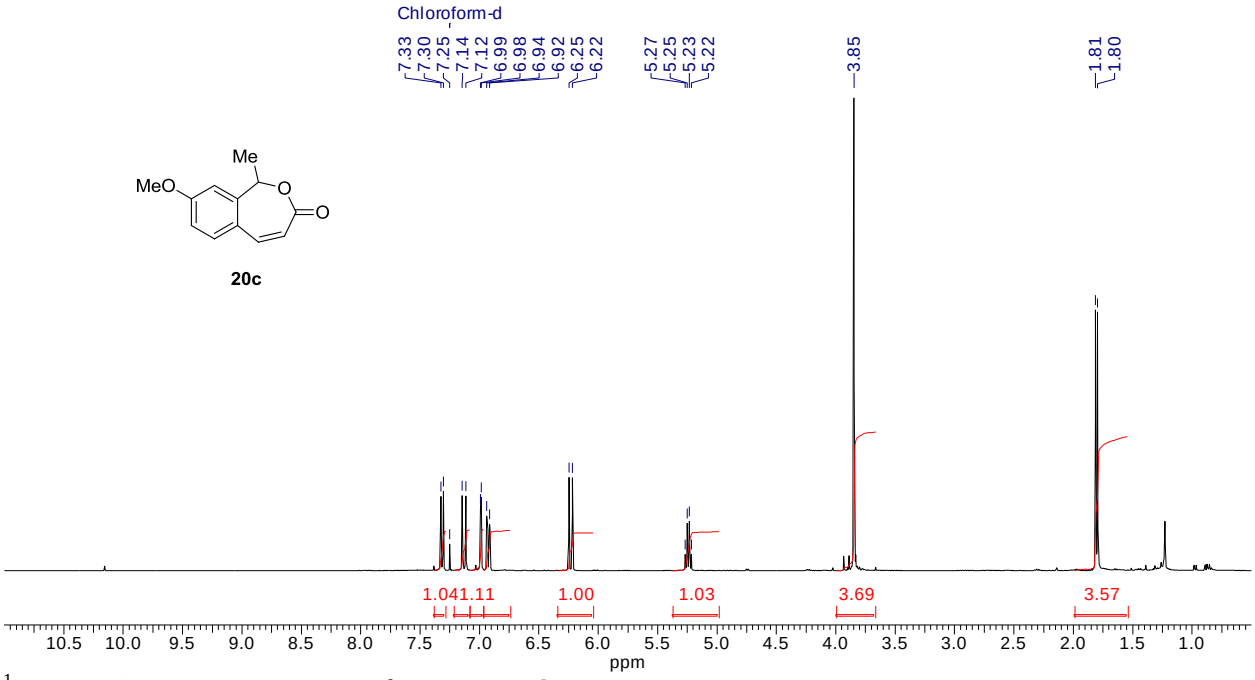
^{13}C NMR (100 MHz) spectrum of **19h** in $CDCl_3$



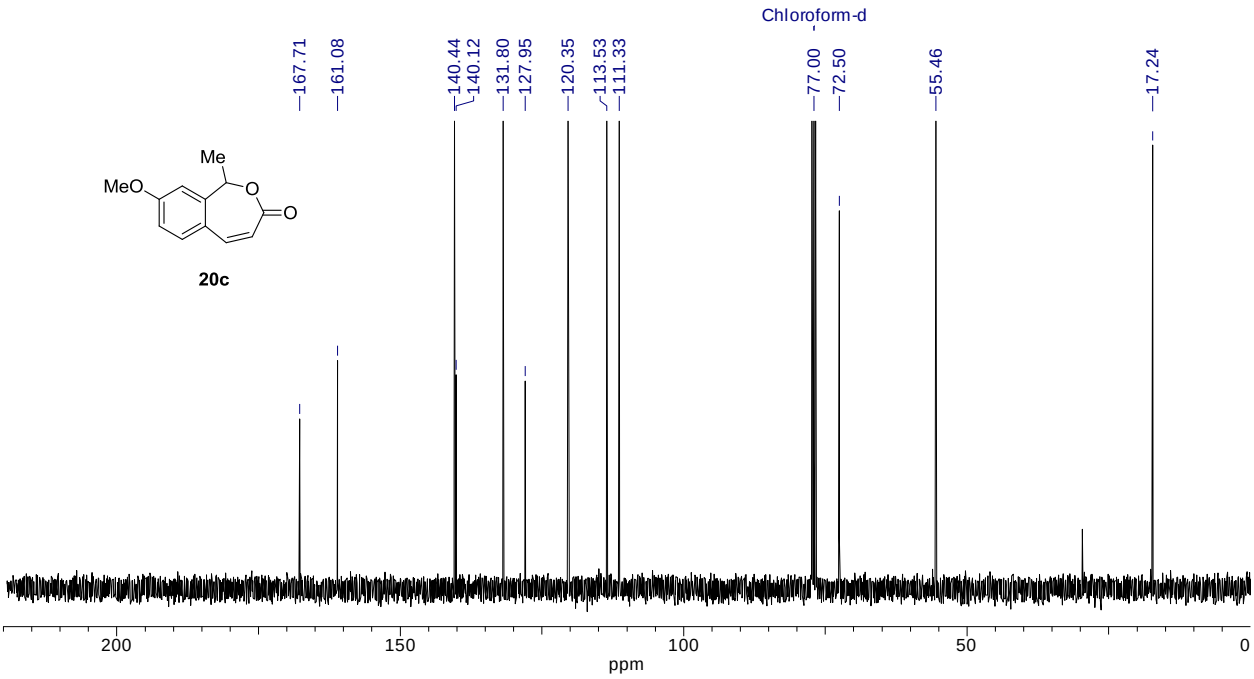
^{1}H NMR (400 MHz) spectrum of **20a** in $CDCl_3$



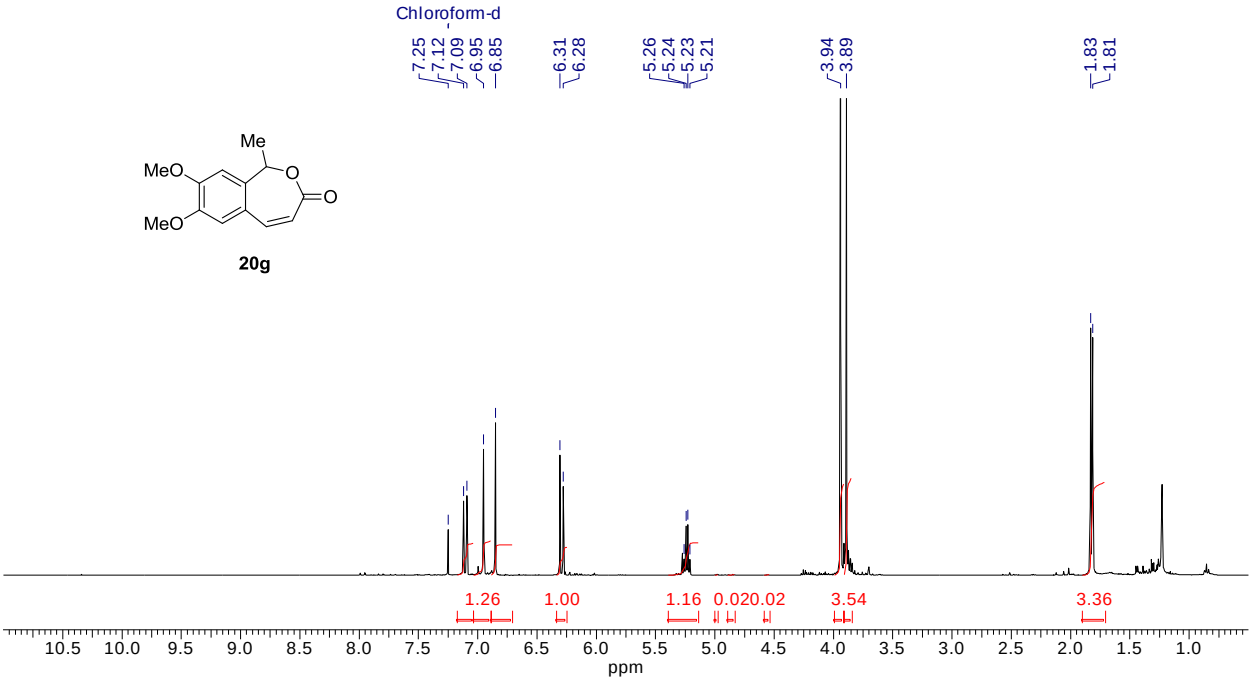
^{13}C NMR (100 MHz) spectrum of **20a** in $CDCl_3$



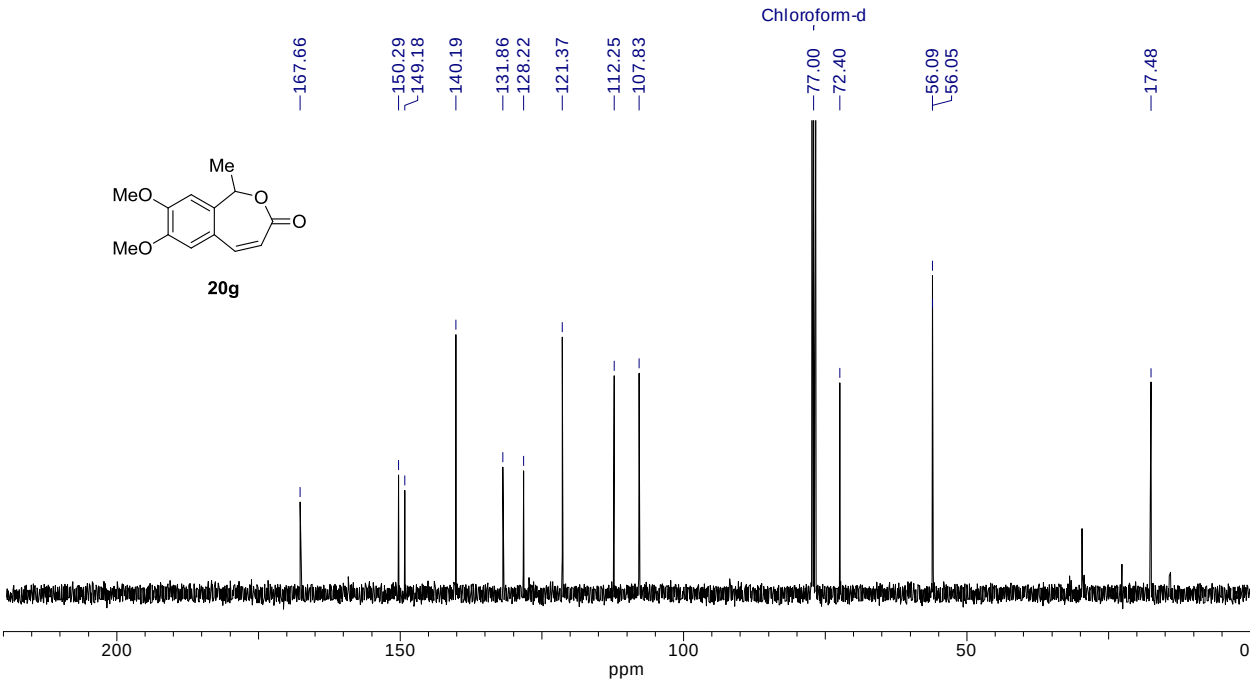
^{1}H NMR (400 MHz) spectrum of **20c** in $CDCl_3$



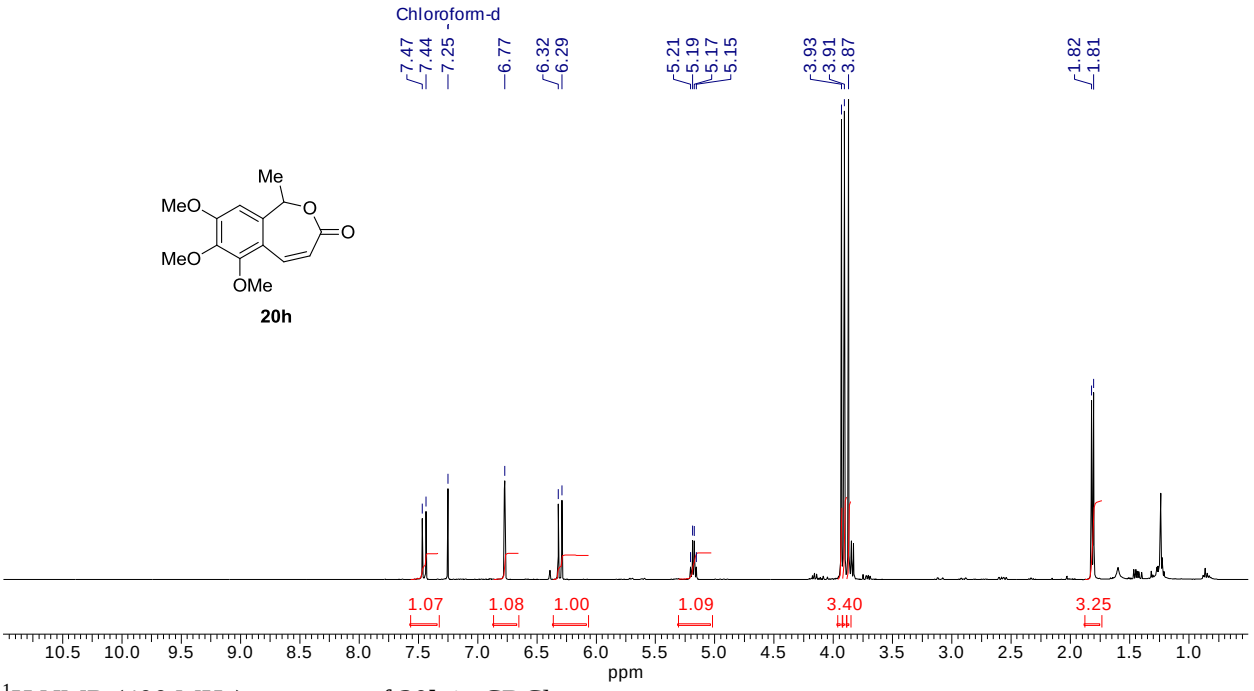
^{13}C NMR (100 MHz) spectrum of **20c** in $CDCl_3$



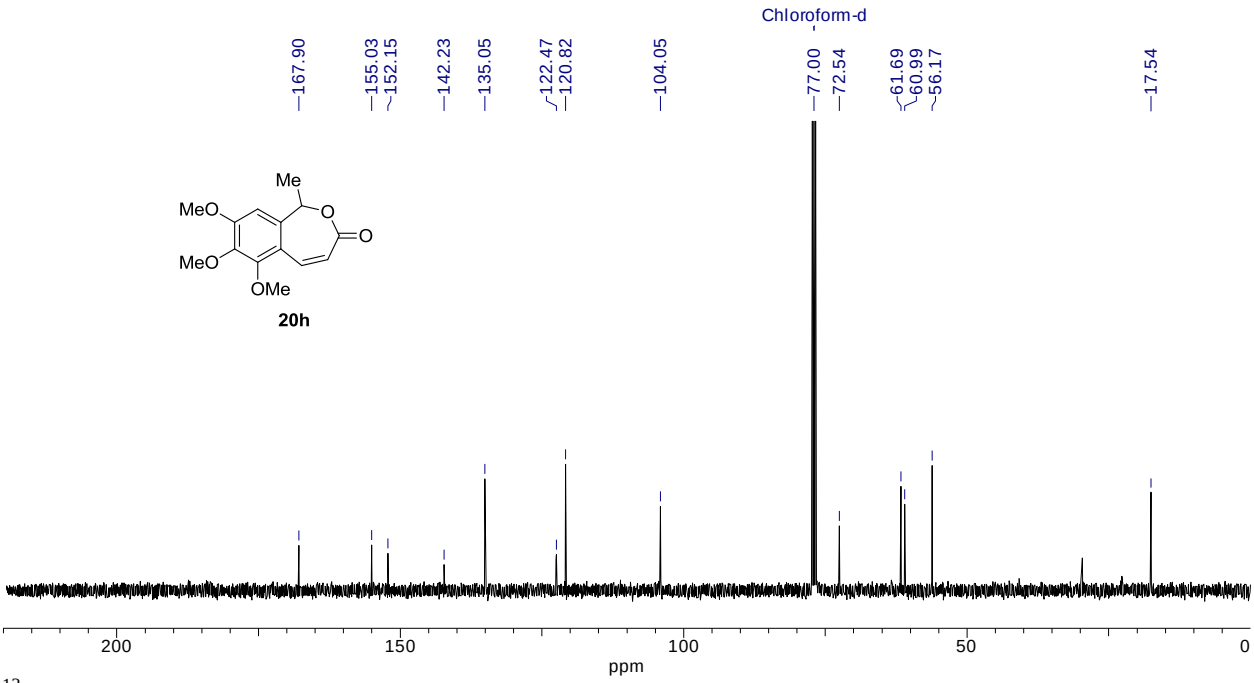
^{1}H NMR (400 MHz) spectrum of **20g** in $CDCl_3$



^{13}C NMR (100 MHz) spectrum of **20g** in $CDCl_3$



^{1}H NMR (400 MHz) spectrum of **20h** in $CDCl_3$



^{13}C NMR (100 MHz) spectrum of **20h** in $CDCl_3$

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