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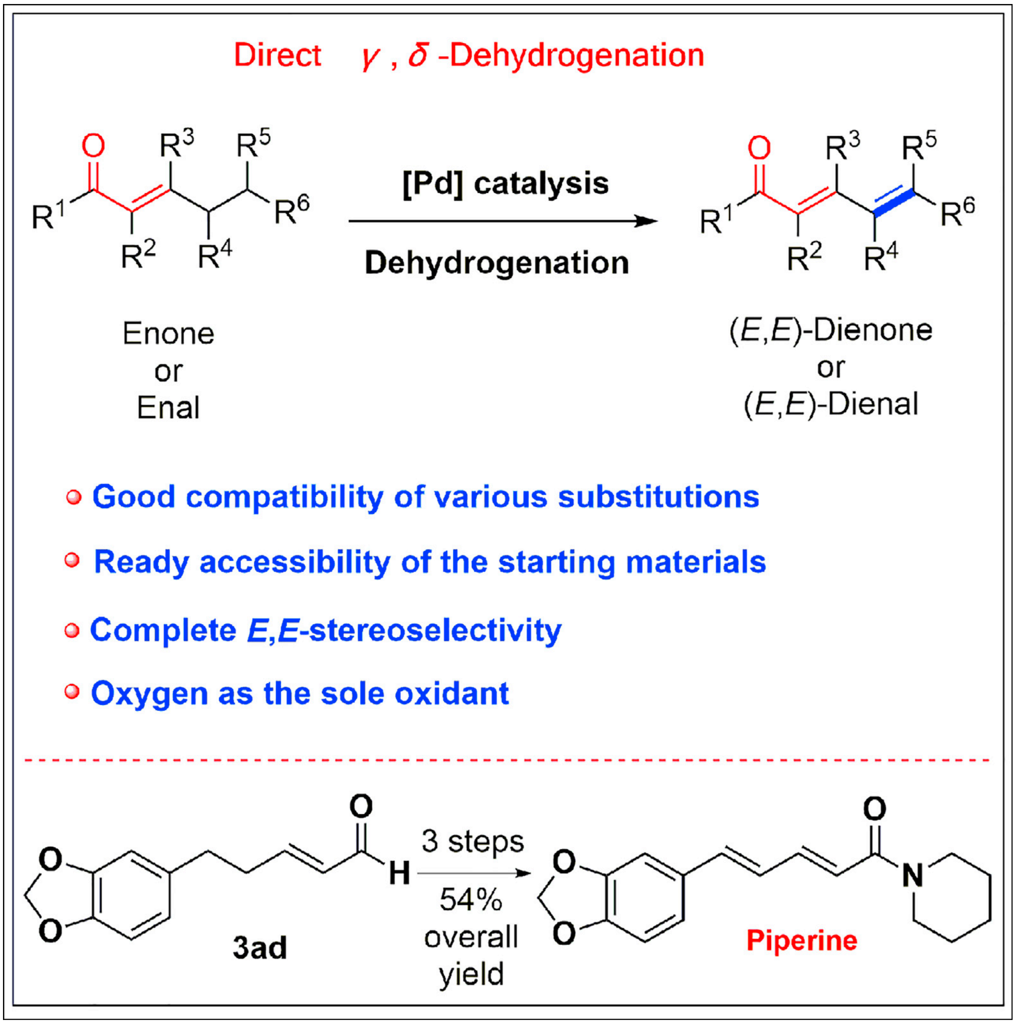

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HIGHLIGHTS

Good compatibility of various substitutions

Complete *E*,*E*-stereoselectivity

Ready accessibility of the starting materials

Oxygen as the sole oxidant

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Synthesis of (*E*,*E*)-Dienones and (*E*,*E*)-Dienals via Palladium-Catalyzed γ,δ-Dehydrogenation of Enones and Enals

Gao-Fei Pan,[1,2] Xing-Long Zhang,[1,2] Xue-Qing Zhu,[1] Rui-Li Guo,[1] and Yong-Qiang Wang[1,3,*]

SUMMARY

A new strategy for the synthesis of conjugated (*E*,*E*)-dienones and (*E*,*E*)-dienals via a palladium-catalyzed aerobic γ,δ-dehydrogenation of enones and enals has been developed. The method can be employed in the direct and efficient synthesis of various (*E*,*E*)-dienones and (*E*,*E*)-dienals, including non-substituted α-, β-, and γ- and/or δ-substituted (*E*,*E*)-dienones and (*E*,*E*)-dienals. The protocol is featured by the ready accessibility and elaboration of the starting materials, good functional group compatibility, and mild reaction conditions. Furthermore, the reaction is of complete *E*,*E*-stereoselectivity and uses molecular oxygen as the sole clean oxidant.

INTRODUCTION

(*E*,*E*)-α,β,γ,δ-unsaturated carbonyl structural motifs are prevalent in natural products, drug molecules, and functional organic materials (Harned and Volp, 2011; Woerly et al., 2014). Conjugated dienones and dienals are also versatile precursors for 1,2- (Zhang and Morken, 2009), 1,4- (Csákÿ et al., 2010; Amoah and Dieter, 2017), or 1,6-addition (Poulsen et al., 2015; den Hartog et al., 2015; Caruana et al., 2014; Shaw and White, 2015; Gu et al., 2015); Diels-Alder reaction (Xiong et al., 2012; Li et al., 2012; Tian et al., 2014); cycloaddition (Horie et al., 2011; Albrecht et al., 2012); and other transformations (Meisner et al., 2012; Bos et al., 2013). Traditionally, the approaches to access conjugated dienones or dienals involve Knoevenagel condensation (He et al., 2011), Wittig-Horner reaction (An et al., 2015; Poulsen et al., 2016), Claisen rearrangement (Cookson and Gopalan, 1978; Motika et al., 2015), and addition-elimination reaction (Crouch et al., 2011; Yuan and Han, 2012; Kim and Oh, 2015; Li et al., 2019). These methods usually require basic conditions, which might be incompatible with the existing functional groups and/or the original stereochemistry. Moreover, these methods are often multistep sequences and suffer from low yields. In 1988, Trost's group (Trost and Schmidt, 1988; Trost and Kazmaier, 1992; Trost and Rudd, 2002; Trost and Rudd, 2005; Trost and Biannic, 2015) and Lu's group (Guo and Lu, 1993; Inoue and Imaizumi, 1988; Kwong et al., 2008; Lu et al., 2001; Ma et al., 1988, 1989) independently and virtually simultaneously developed the isomerization of alkynones to the corresponding conjugated dienones (Scheme 1A, a). Recently, Li's group reported a palladium-catalyzed isomerization of 4-alkynals to conjugated dienals (Scheme 1A, b) (Hearne and Li, 2017). In spite of the alkyne isomerization protocol being a great advance in view of the relatively mild reaction conditions, the inherent structural feature of alkyne prevents the method from the direct preparation of multi-substituted dienones and dienals. More recently, Alexanian et al. reported an elegant cobalt-catalyzed carbonylative cross-coupling of alkyl tosylates and dienes to synthesize conjugated dienones (Scheme 1A, c) (Sargent and Alexanian, 2017). Also, Huang et al. reported a great direct aerobic α,β-dehydrogenation of γ,δ-unsaturated amides and acids to produce conjugated dienamides and dienoic acids by an iridium/copper relay catalysis process (Scheme 1A, d) (Wang et al., 2018). Although these remarkable progresses have been made, significant challenges remain unaddressed, for example, limited substrate scope and tedious preparation of starting material. Therefore, new strategies for facile and efficient synthesis of conjugated dienones and dienals are still highly desirable.

Our group has long sought catalytic conditions for aerobic dehydrogenation reactions. We thought if dienones or dienals could be prepared by the aerobic γ,δ-dehydrogenation of enones or enals (Scheme 1B). This strategy has two advantages: (1) the precursors, enones or enals, can be obtained readily (some of them are commercially available and they also can be easily synthesized by aldol-like condensations, α-substitution of carbonyl compounds and subsequent elimination, oxidative α,β-dehydrogenation of saturated ketones or aldehydes, and so on) (Wade, 2005; Smith and March 2001; Nicolaou et al., 2000; Nicolaou et al., 2002; Izawa et al., 2011; Diao and Stahl, 2011; Bigi and White, 2013; Huang and Dong, 2013; Deng et al.,

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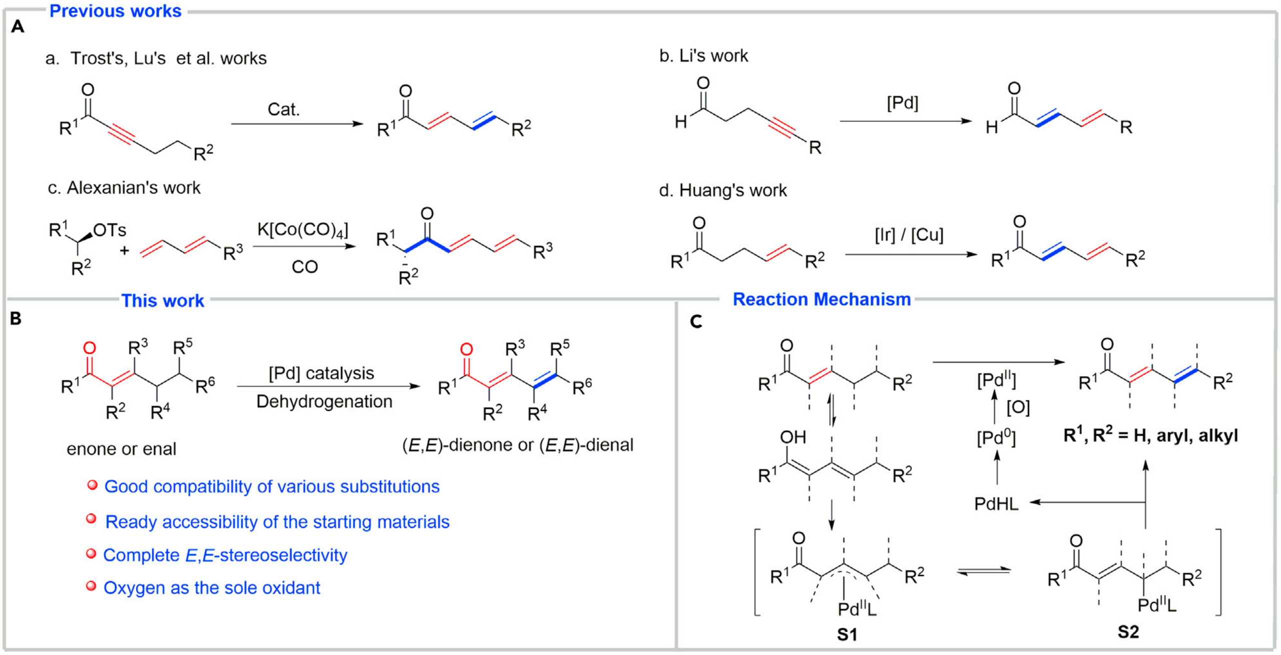


Scheme 1. Strategies for Synthesis of (*E*,*E*)-Dienones and (*E*,*E*)-Dienals

(A) Previous work for synthesis of (*E*,*E*)-dienones and (*E*,*E*)-dienals.

(B) Our work for synthesis of (*E*,*E*)-dienones and (*E*,*E*)-dienals.

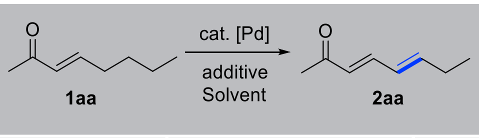
(C) Reaction mechanism for the palladium-catalyzed γ,δ-dehydrogenation of enones and enals.

2014; Huang et al., 2015; Jie et al., 2016; Yoshii et al., 2016; Chen et al., 2017) and (2) dienones and dienals bearing substituent groups in various positions could be produced directly. Despite these obvious benefits, to the best our knowledge, the efficient γ,δ-dehydrogenation of enones or enals to produce conjugated dienones or dienals has not been reported so far.

Mechanistically, we conceived that transition metal, especially palladium, could activate the allylic C–H bond to afford a π-allylpalladium intermediate (**S1**), which could generate a γ-palladation enone or enal (**S2**) (Patil and Yamamoto, 2006), which then underwent a sequence β-hydride elimination to give conjugated dienyl carbonyl product and Pd^{II}-hydride intermediate that underwent reductive elimination and oxidation to complete the catalytic cycle (Scheme 1C). In this protocol, there were two challenges: one is the avoiding the direct oxidation of alkene bond of starting material (e.g., Wacker-type oxidation) and the other is preventing the product from the deeper oxidation (e.g., to generate trienone). To address the challenges, an efficient but mild catalytic oxidative system should be developed.

RESULTS AND DISCUSSION

To test this proposal, we chose enone (**1aa**) as the model substrate to begin our investigation. Initially, various palladium catalysts were examined with DMSO as the solvent and molecular oxygen as the terminal oxidant (Table 1, entries 1–7). $Pd(TFA)_2$, $Pd(OAc)_2$, $Pd(PPh_3)_4$, and $Pd_2(dba)_3$ reaction systems afforded the desired product **2aa** in 38%, 23%, 25%, and 18% yields, respectively, whereas $PdCl_2$ and $Pd(PPh_3)_2Cl_2$ systems could not react and $Pd(OH)_2$ reaction system only provided trace **2aa**. Considering that trifluoroacetic acid (TFA) and $Pd(OAc)_2$ can generate more electropositive $[Pd(II)O_2CCF_3]^+$ species *in situ* (Lu et al., 1999; Jia et al., 2000), which is predictably easier to form π-allylpalladium intermediate (Scheme 1C, **S1**) and γ-palladation enone (Scheme 1C, **S2**), thereby facilitating the γ,δ-dehydrogenation reaction, 0.2 equiv. of TFA was introduced into $Pd(OAc)_2$-catalyzed reaction system. To our delight, the reaction gave (*E*,*E*)-dienone **2aa** in 63% yield with complete double bond (*E*,*E*)-stereoselectivity (Table 1, entry 8). Then, 0.2 equiv. TFA was added into other palladium-catalyzed reaction systems. Interestingly, the yields of most of the reactions were improved to a certain extent; nevertheless, the result of the combination of $Pd(OAc)_2$ and TFA was still the better (Table 1, entries 9–14). Next, the solvent was screened, and DMSO proved to be the best solvent (Table 1, entries 15–17). After careful investigation of the amount of TFA, 2.0 equiv. TFA provided



Entry	Pd source	TFA (equiv.)	Solvent	Yield[a] (%)
1	$Pd(TFA)_2$	–	DMSO	38
2	$Pd(OAc)_2$	–	DMSO	23
3	$Pd(PPh_3)_4$	–	DMSO	25
4	$Pd_2(dba)_3$	–	DMSO	18
5	$PdCl_2$	–	DMSO	NR
6	$Pd(PPh_3)_2Cl_2$	–	DMSO	NR
7	$Pd(OH)_2$	–	DMSO	Trace
8	$Pd(OAc)_2$	0.2	DMSO	63
9	$Pd(TFA)_2$	0.2	DMSO	51
10	$Pd(PPh_3)_4$	0.2	DMSO	48
11	$Pd_2(dba)_3$	0.2	DMSO	56
12	$PdCl_2$	0.2	DMSO	Trace
13	$Pd(PPh_3)_2Cl_2$	0.2	DMSO	NR
14	$Pd(OH)_2$	0.2	DMSO	59
15	$Pd(OAc)_2$	0.2	DMF	25
16	$Pd(OAc)_2$	0.2	CH_3CN	50
17	$Pd(OAc)_2$	0.2	THF	20
18[b]	$Pd(OAc)_2$	2.0	DMSO	73
19[c]	$Pd(OAc)_2$	2.0	DMSO	<13

Table 1. Optimization of the Reaction Conditions

Reaction conditions: Unless otherwise noted, the reaction was carried out with **1aa** (0.5 mmol), [Pd] (10 mol %) in solvent (2.5 mL) under O_2 (1 atm) atmosphere at 80°C for 12 h.

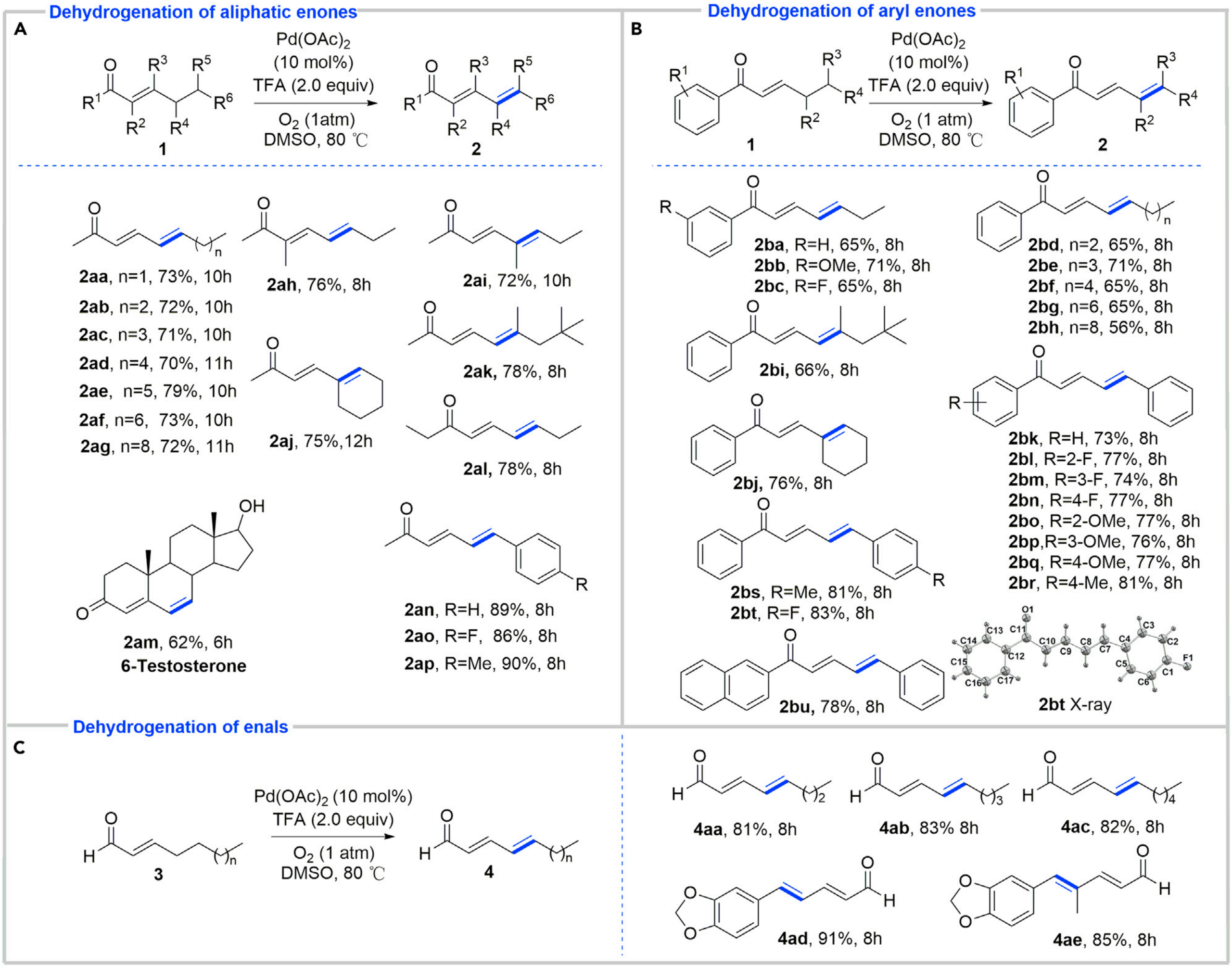
[a] Isolated yield.

[b] Amount of TFA: 0.1 equiv. (30%), 0.2 equiv. (63%), 0.5 equiv. (66%), 1.0 equiv. (68%), 1.5 equiv. (70%), 3.0 equiv. (68%).

[c] Other acid (1.0 mL): for hydrochloric acid and benzoic acid, no product; AcOH and TsOH, trace product; CF_3SO_3H, 12% yield.

the highest yield (Table 1, entry 18). Replacing TFA with other acids proved to be either less effective or totally ineffective (Table 1, entry 19). Thus the optimized reaction conditions for the γ,δ-dehydrogenation of **1aa** were identified as following: **1aa** (0.5 mmol), $Pd(OAc)_2$ (10 mol%), and TFA (2.0 equiv.) under oxygen atmosphere in DMSO at 80°C.

With the optimized reaction conditions in hand, we next surveyed the substrate scope (Scheme 2A). First, the length of carbon chain of enones was increased to check if further oxidation could happen. Delightedly, all of them only provided the desired (*E*,*E*)-dienones in 70%–79% yields and no further oxidative product (e.g., trienone) was observed (Scheme 2A, **2aa-2ag**). Substitutions at each position (i.e., α-, β-, γ-, or δ-positions or beyond), despite their increasing steric hindrance, were all well-tolerated (**2ah-2am**). Note that the γ,δ-dehydrogenation could occur not only on aliphatic chain but also on aliphatic cycles (**2aj**). Interestingly, a steroid compound **1am** also successfully underwent the γ,δ-dehydrogenation to give 6-testosterone (**2am**) in good yield. This case together with **2al** showed that the current catalytic reaction conditions preferred γ,δ-dehydrogenation to α,β-dehydrogenation, highlighting the advantage of the process for the synthesis of dienones. δ-Aryl-substituted enones could also be γ,δ-dehydrogenated in excellent yields



Scheme 2. Substrate Scope of the Palladium-Catalyzed γ,δ-Dehydrogenation of Enones and Enals

(A) Dehydrogenation of aliphatic enones.

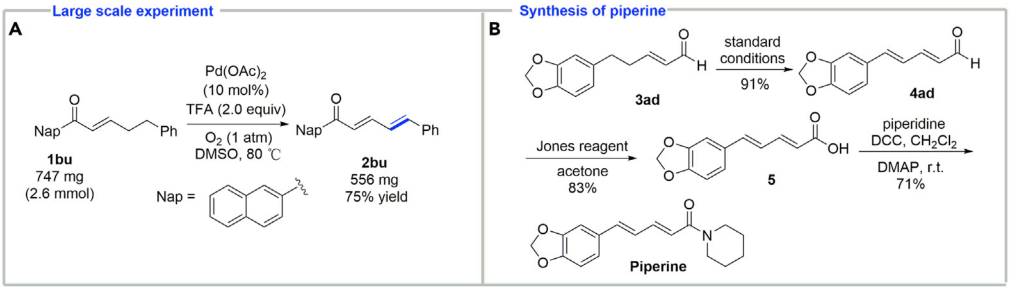
(B) Dehydrogenation of aryl enones.

(C) Dehydrogenation of enals.

(**2an**-**2ap**). It is noteworthy that, in all cases, only *E*,*E*-isomers were obtained, and no *Z*-isomers can be detected by analyzing the reaction mixtures.

Next, we investigated another kind of enones, aryl enones (Scheme 2B). 1-Arylhept-2-en-1-ones bearing either electron-donating or electron-withdrawing groups all reacted smoothly to provide the desired dienones in good yields (**2ba**-**2bc**). Increasing the length of the alkyl chain (**2bd**-**2bh**) or changing the straight chain to branched chain (**2bi**) or aliphatic cycle (**2bj**) was permitted. A series of substituted (*E*)-1,5-diphenylpent-2-en-1-ones (**1bk**-**1bt**) were also investigated. The results indicated that both the position (*o*-, *m*- or *p*-) and the electronic properties (electron-donating or electron-withdrawing property) of substitution groups did not affect the dehydrogenation and that they all afforded the corresponding (*E*,*E*)-dienones in 73%–81% yields. The other aromatic substrate, naphthyl enone, was also suitable for the reaction to give dienone **2bu** in good yields. Again, only *E*,*E*-isomers were obtained. The structure of **2bt** was confirmed by single-crystal X-ray diffraction (see Supplemental Information).

Then, we focused on the γ,δ-dehydrogenation of enals, which were challenging substrates due to the aldehyde's susceptibility toward oxidation under oxidative conditions (Padala and Jeganmohan, 2012; Liu et al., 2015; Santhoshkumar et al., 2015) and undesired metal insertion into an acyl C−H bond (Bosnich, 1998;



Scheme 3. The Practicality of the Palladium-Catalyzed γ,δ-Dehydrogenation of Enones and Enals
(A) Large-scale experiment.
(B) Synthesis of piperine.

Fristrup et al., 2008; Garralda, 2009; Jun et al., 2007; Leung and Krische, 2012; Modak et al., 2012; Murphy and Dong, 2014; Willis, 2010). Pleasingly, all enals worked well as enones to produce the desired (*E*,*E*)-dienals in good to excellent yields, and the susceptible aldehyde group remained intact, indicating that the oxidative dehydrogenation conditions were very mild (Scheme 2C). The reaction also only provided *E*,*E*-isomers, and no *Z*-isomers could be detected.

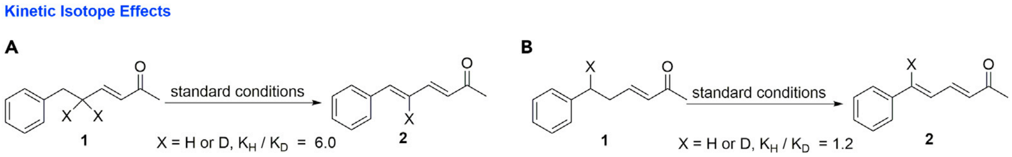
To test the practicality of the method, a large-scale experiment has been carried out. With the above-mentioned standard reaction conditions, **1bu** (747 mg, 2.6 mmol) was converted into the desired dienone **2bu** (556 mg) in 75% yield (Scheme 3A). Notably, when the catalyst loading was reduced to 6 mol %, the yield was not decreased, although more reaction time was required.

To highlight the synthetic utility of this methodology, we employed it as a key step to rapidly synthesize a natural product, piperine, an alkaloid responsible for the pungency of black pepper and long pepper. Recent investigations have shown that piperine has diverse bioactivities including chemopreventive, antioxidant, immunomodulatory, anticarcinogenic, stimulatory, hepatoprotective, anti-inflammatory, antimicrobial, and antiulcer activities (Doucette et al., 2013; Gorgani et al., 2017). Enal **3ad** was converted into (*E*,*E*)-dienal **4ad** under standard conditions, followed by oxidation with Jones reagent to acid and the condensation with piperidine to give piperine in three steps in 54% overall yield (Scheme 3B).

To gain insight into the reaction mechanism, we carried out a series of kinetic isotope effect (KIE) experiments (Scheme 4). The KIE value of two parallel competition reactions of **1an** and γ-deuterated [D$_2$]-**1an** was found to be 6.0 (Scheme 4A), and the intramolecular KIE value for the reaction of δ-deuterated [D]-**1an** was 1.2 (Scheme 4B). These results showed that the cleavage of the γ-C—H bond should be involved in the rate-determining step, whereas the elimination of δ-C—H bond was fast and not rate limiting. The complete *E*,*E*-stereoselectivity of dienones and dienals might be attributed to the formation of the thermodynamically more stable *E*-product at β-hydride elimination step in the current heating reaction conditions (80°C) and also to the probable presence of Pd-mediated isomerization of olefins under the current Pd-catalyzed reaction system (Bond and Hellier, 1965; Stang and White, 2011). In the reaction system, there were the nucleophilic TFA and H_2O, which could react with π-allylpalladium intermediate (Chen and White, 2004; Chen et al., 2005), but we could not detect any corresponding product, which probably could be ascribed to the fast β-hydride elimination of γ-palladation **S2**, or the fast elimination of TFA or H_2O of the corresponding –O_2CCF_3- or –OH-substituted products under the current acidic reaction conditions. In-depth studies are currently underway to fully elucidate the mechanistic details.

Conclusion

In summary, we have developed a new strategy for the synthesis of conjugated (*E*,*E*)-dienones and (*E*,*E*)-dienals via a palladium-catalyzed aerobic γ,δ-dehydrogenation of enones and enals. Compared with the previous methods, the biggest advantage of the method is the generality. The method can be employed in the direct and efficient synthesis of various (*E*,*E*)-dienones and (*E*,*E*)-dienals, including non-substituted and α-, β-, γ-, and/or δ-substituted (*E*,*E*)-dienones and (*E*,*E*)-dienals. Another advantage of the method is the ready accessibility and elaboration of the starting materials, enones and enals, some of which are commercially available, and they also can be easily obtained by conventional approaches. Furthermore, the reaction is of complete *E*,*E*-stereoselectivity and uses molecular oxygen as the sole clean oxidant.



Scheme 4. Kinetic Isotope Effect

(A) The KIE value of two parallel competition reactions of **1an** and γ-deuterated [D_2]-**1an**.

(B) The intramolecular KIE value for the reaction of δ-deuterated [D]-**1an**.

Owing to mild reaction conditions and good functional group compatibility, the approach should have broad applications in organic synthesis, medical, and material chemistry.

Limitations of the Study

α,β-Unsaturated amides, acids, and ester provided the γ,δ-dehydrogenated products in low yields under the current reaction conditions.

METHODS

All methods can be found in the accompanying Transparent Methods supplemental file.

DATA AND CODE AVAILABILITY

The structures of **2bt** reported in this article have been deposited in the Cambridge Crystallographic Data Center under accession numbers CCDC: 1892057.

SUPPLEMENTAL INFORMATION

Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.09.027.

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AUTHOR CONTRIBUTIONS

G.-F. P. and X.-L. Z. contributed equally to this work. G.-F. P. and Y.-Q. W. conceived the project and designed the experiments. G.-F. P., X.-L. Z., X.-Q. Z., and R.-L. G., performed and analyzed the experiments. G.-F. P. and Y.-Q. W. wrote the manuscript. All the authors discussed the results and commented on the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Supplemental Information

Synthesis of (*E*,*E*)-Dienones and (*E*,*E*)-Dienals via Palladium-Catalyzed γ,δ-Dehydrogenation of Enones and Enals

Gao-Fei Pan, Xing-Long Zhang, Xue-Qing Zhu, Rui-Li Guo, and Yong-Qiang Wang

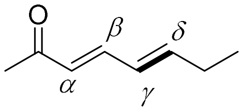
Transparent Methods

1. General information

All commercial reagents and solvents were used as received without further purification. Reactions were followed with TLC (0.254 mm silica gel 60-F plates). Visualization was accomplished with UV light. Flash chromatographies were carried out on silica gel 200-300 mesh. Optical rotations were reported as follows: $[\alpha]^{27}_{D}$ (c g/100 mL, in solvent). Melting points (m. p.) were measured on electrothermal digital melting point apparatus and were uncorrected. ^{1}HNMR and ^{13}CNMR spectra were recorded at 400 MHz using $CDCl_3$ as solvent. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, br. s = broad singlet. Infrared (IR) data were recorded as films on potassium bromide plates on a Bruker Tensor 27 FT-IR spectrometer. Absorbance frequencies are reported in reciprocal centimeters (cm^{-1}). High resolution mass spectra were acquired on a Bruker Daltonics MicroTof-Q II mass spectrometer. X-ray crystal structure analyses were measured on Bruker Smart APEXIICCD instrument using Mo-Kα radiation. The structures were solved and refined using the SHELXTL software package.

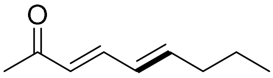
2. General Procedure for the Palladium-Catalyzed *γ,δ*-Dehydrogenation reaction

A seal tube containing enones or enals (0.5 mmol) and $Pd(OAc)_2$ (10 mol%), was evacuated and filled with dioxygen gas using an oxygen containing balloon. Then, DMSO (2.5 mL), trifluoroacetic acid (TFA) (1.0 mmol) were sequentially added to the system via syringe under an oxygen atmosphere. The reaction mixture was stirred at 80 ℃ until completion of the reaction (TLC). Then the reaction was cooled to room temperature and partitioned between water and ethyl acetate. The layers were separated and the organic layer was washed with water (3 × 5.0 mL) and washed with aqueous saturated brine solution (3 × 5.0 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by flash chromatography afforded the (*E*, *E*)-dienones or (*E*, *E*)-dienals.



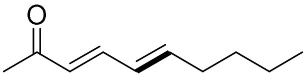
2aa

(*3E*, *5E*)-octa-3,5-dien-2-one (2aa) (Ma et al., 1989) Prepared according to general procedure to afford as pale yellow oil (73% yield). R_f= 0.56 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.11 (dd, J = 15.6, 9.6 Hz, 1H, β-H), 6.31 – 6.13 (m, 2H, γ-H and δ-H), 6.06 (d, J = 15.7 Hz, 1H, α-H), 2.26 (s, 3H, CH$_3$), 2.22 – 2.10 (m, 2H, CH$_2$), 1.06 (t, J = 7.4 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 198.6, 147.0, 144.0, 128.8, 127.9, 27.1, 26.1, 12.8. HRMS (ESI) for $C_8H_{13}O$ [M+H$^+$]: Calcd: 147.0780; Found: 147.0788. IR (KBr): 2925, 2854, 1722, 1670, 1459, 1257, 1054, 1012, 800, 617 cm^{-1}.



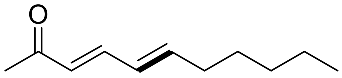
2ab

(*3E*, *5E*)-nona-3,5-dien-2-one (2ab) (Ma et al., 1989) Prepared according to general procedure to afford as pale yellow oil (72% yield). R_f= 0.50 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.19 – 7.02 (m, 1H, β-H), 6.21 – 6.14 (m, 2H, γ-H and δ-H), 6.06 (d, J = 15.6 Hz, 1H, α-H), 2.26 (s, 3H, CH$_3$), 2.21 – 2.13 (m, 2H, CH$_2$), 1.53 – 1.42 (m, 2H, CH$_2$), 0.93 (t, J = 7.4 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz , CDCl$_3$): δ = 198.9, 145.6, 144.1, 129.0, 128.8, 35.2, 27.2, 22.0, 13.7. HRMS (ESI) for $C_9H_{14}NaO$ [M+Na$^+$]: Calcd: 161.0937; Found: 161.0943. IR (KBr): 3448, 2965,1724, 1677, 1459, 1361, 1284, 1130, 981, 742 cm^{-1}.



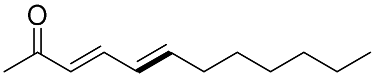
2ac

(*3E*, *5E*)-deca-3,5-dien-2-one (2ac) (Yoo et al., 2006) Prepared according to general procedure to afford as colorless oil (71% yield). R_f= 0.45 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.14 – 7.05 (m, 1H, β-H), 6.22 – 6.17 (m, 2H, γ-H and δ-H), 6.06 (d, J = 15.6 Hz, 1H, α-H), 2.19 (s, 3H, CH$_3$), 2.23 – 2.16 (m, 2H, CH$_2$), 1.47 – 1.37 (m, 2H, CH$_2$), 1.37 – 1.28 (m, 2H, CH$_2$), 0.89 (t, J = 7.2 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz , CDCl$_3$): δ = 198.9, 146.0, 144.2, 128.9, 128.8, 32.9, 30.9, 27.2, 22.4, 14.0. HRMS (ESI) for $C_{10}H_{16}NaO$ [M+Na$^+$]: Calcd: 175.1093; Found: 175.1086. IR (KBr): 2940, 2834, 1704, 1457, 1376, 1267, 1193, 1126, 1027 cm^{-1}.



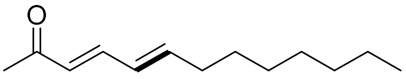
2ad

(*3E*, *5E*)-undeca-3,5-dien-2-one (2ad) (Ma et al., 1989) Prepared according to general procedure to afford as colorless oil (70% yield). R_f= 0.45 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 – 7.06 (m, 1H, β-H), 6.21 – 6.16 (m, 2H, γ-H and δ-H), 6.05 (d, J = 15.5 Hz, 1H, α-H), 2.26 (s, 3H, CH_3), 2.22 – 2.15 (m, 2H, CH_2), 1.48 – 1.40 (m, 2H, CH_2), 1.38 – 1.23 (m, 4H, 2CH_2), 0.90 (t, J = 6.9 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 145.9, 144.1, 128.8, 128.8, 33.1, 31.4, 28.4, 27.1, 22.5, 14.0. HRMS (ESI) for $C_{11}H_{18}NaO$ [M+Na$^+$]: Calcd: 189.1250; Found: 189.1238. IR (KBr): 2927, 2859, 1668, 1459, 1359, 1253, 1151, 998 cm^{-1}.



2ae

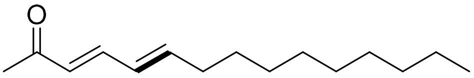
(*3E*, *5E*)-dodeca-3,5-dien-2-one (2ae) Prepared according to general procedure to afford as pale yellow (79% yield). R_f= 0.36 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 – 7.06 (m, 1H, β-H), 6.21 – 6.16 (m, 2H, γ-H and δ-H), 6.05 (d, J = 15.6 Hz, 1H, α-H), 2.26 (s, 3H, CH_3), 2.22 – 2.16 (m, 2H, CH_2), 1.46 – 1.39 (m, 2H, CH_2), 1.36 – 1.27 (m, 6H, 3CH_2), 0.89 (t, J = 6.7 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.8, 145.9, 144.1, 128.9, 128.8, 33.2, 31.7, 28.9, 28.7, 27.2, 22.6, 14.1. HRMS (ESI) for $C_{12}H_{21}O$ [M+H$^+$]: Calcd: 181.1587; Found: 181.1590. IR (KBr): 2958, 2922, 2854, 1658, 1584, 1450, 1263, 1096, 1025, 803 cm^{-1}.



2af

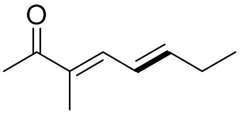
(*3E*, *5E*)-trideca-3,5-dien-2-one (2af) Prepared according to general procedure to afford as pale yellow oil (73% yield). R_f = 0.45 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 – 7.06 (m, 1H, β-H), 6.20 – 6.15 (m, 2H, γ-H and δ-H), 6.05 (d, J = 15.5 Hz, 1H, α-H), 2.26 (s, 3H, CH_3), 2.21 – 2.15 (m, 2H, CH_2), 1.47 –

1.41 (m, 2H, CH_2), 1.33 – 1.20 (m, 8H, $4CH_2$), 0.88 (t, *J* = 6.9 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 146.0, 144.2, 128.9, 128.8, 33.2, 31.9, 29.2, 29.2, 28.8, 27.2, 22.7, 14.2. HRMS (ESI) for $C_{13}H_{22}NaO$ [M+Na$^+$]: Calcd: 217.1563; Found: 217.1572. IR (KBr): 2925, 2854, 1675, 1458, 1257, 1187, 1124, 1027, 725 cm^{-1}.



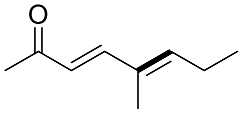
2ag

(*3E*, *5E*)-pentadeca-3,5-dien-2-one (2ag) Prepared according to general procedure to afford as pale yellow oil (72% yield). R_f= 0.56 (EtOAc / hexanes 1 : 30); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.14 – 7.06 (m, 1H, β-H), 6.21 – 6.15 (m, 2H, γ-H and δ-H), 6.05 (d, *J* = 15.5 Hz, 1H, α-H), 2.26 (s, 3H, CH_3), 2.21 – 2.14 (m, 2H, CH_2), 1.46 – 1.38 (m, 2H, CH_2), 1.32 – 1.24 (m, 12H, $6CH_2$), 0.88 (t, *J* = 6.9 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.9, 146.0, 144.2, 128.9, 128.9, 33.3, 32.0, 29.6, 29.5, 29.4, 29.3, 28.8, 27.2, 22.8, 14.2. HRMS (ESI) for $C_{15}H_{26}NaO$ [M+Na$^+$]: Calcd: 245.1876; Found: 245.1882. IR (KBr): 3411, 2927, 2856, 1671, 1459, 1363, 1257, 1189, 1156, 1027 cm^{-1}.



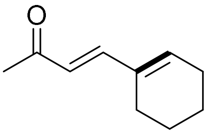
2ah

(*3E*, *5E*)-3-methylnona-3,5-dien-2-one (2ah) Prepared according to general procedure to afford as pale yellow oil (76% yield). R_f= 0.43 (EtOAc / hexanes 1 : 20). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.02 (d, *J* = 10.9 Hz, 1H, β-H), 6.50 – 6.38 (m, 1H, γ-H), 6.22 – 6.14 (m, 1H, δ-H), 2.33 (s, 3H, CH_3), 2.30 – 2.20 (m, 2H, CH_2), 1.87 (s, 3H, CH_3), 1.08 (t, *J* = 7.5 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.0, 145.5, 140.0, 134.8, 125.8, 26.6, 25.6, 13.3, 11.5. HRMS (ESI) for $C_{10}H_{16}NaO$ [M+Na$^+$]: Calcd: 175.1093; Found: 175.1086. IR (KBr): 2958, 2930, 2872, 1715, 1674, 1459, 1372, 1239, 1169, 976 cm^{-1}.



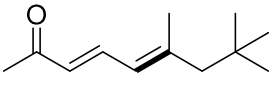
2ai

(*3E*, *5E*)-5-methylocta-3,5-dien-2-one (2ai) (Zou et al., 2008) Prepared according to general procedure to afford as pale yellow oil (72% yield). R_f= 0.53 (EtOAc / hexanes 1 : 20). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.15 (d, J = 16.0 Hz, 1H, β-H), 6.08 (d, J = 16.0 Hz, 1H, α-H), 5.94 (t, J = 7.3 Hz, 1H, δ-H), 2.29 (s, 3H, CH$_3$), 2.28 – 2.18 (m, 2H, CH$_2$), 1.78 (s, 3H, CH$_3$), 1.04 (t, J = 7.5 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 199.1, 148.9, 145.0, 132.7, 125.3, 27.3, 22.4, 13.6, 12.1. HRMS (ESI) for $C_9H_{14}NaO$ [M+Na$^+$]: Calcd: 161.0937; Found: 161.0950. IR (KBr): 2964, 1671, 1574, 1455, 1359, 1257, 1176, 1045, 977 cm^{-1}.



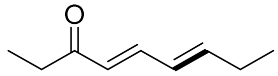
2aj

(*E*)-4-(cyclohex-1-en-1-yl)but-3-en-2-one (2aj) (Polaquini et al., 2017) Prepared according to general procedure to afford as yellow oil (75% yield). R_f = 0.43 (EtOAc / hexanes 1 : 20); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.12 (d, J = 16.1 Hz, 1H, β-H), 6.22 (t, J = 3.9 Hz, 1H, δ-H), 6.05 (d, J = 16.1 Hz, 1H, α-H), 2.28 (s, 3H, CH$_3$), 2.26 – 2.18 (m, 2H, CH$_2$), 2.17 – 2.12 (m, 2H, CH$_2$), 1.75 – 1.67 (m, 2H, CH$_2$), 1.67 – 1.60 (m, 2H, CH$_2$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 199.1, 147.2, 140.0, 135.3, 124.2, 27.2, 26.7, 24.2, 22.1, 22.0. HRMS (ESI) for $C_{10}H_{14}NaO$ [M+Na$^+$]: Calcd: 173.0937; Found: 173.0932. IR (KBr): 2935, 2863, 1671, 1621, 1428,1359, 1257, 1172, 1074 cm^{-1}.



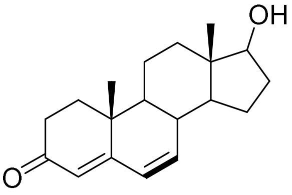
2ak

(*3E*, *5E*)-6,8,8-trimethylnona-3,5-dien-2-one (2ak) Prepared according to general procedure to afford as pale yellow oil (78% yield). R_f = 0.42 (EtOAc / hexanes 1 : 20); ^{1}H NMR (400 MHz, CDCl$_3$): 7.44 (dd, J = 15.3, 11.5 Hz, 1H, β-H), 6.09 (d, J = 15.3 Hz, 1H , α-H), 5.96 (d, J = 11.4 Hz, 1H, γ-H), 2.28 (s, 3H, CH$_3$), 2.07 (s, 2H, CH$_2$), 1.97 (s, 3H, CH$_3$), 0.94 (s, 9H, 3CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 199.0, 149.8, 139.5, 128.5, 127.1, 54.4, 32.7, 30.2 (3 C), 27.7, 20.4. HRMS (ESI) for $C_{12}H_{21}O$ [M+H^+]: Calcd: 181.1587; Found: 181.1585. IR (KBr): 2957, 2924, 2855, 1654, 1583, 1434, 1223, 1089, 1011, 812 cm^{-1}.



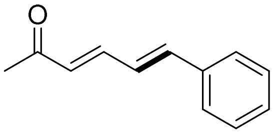
2al

(*4E*, *6E*)-nona-4,6-dien-3-one (2al) (Ma et al., 1989) Prepared according to general procedure to afford as colorless oil (78% yield). R_f= 0.40 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (dd, J = 15.5, 9.6 Hz, 1H, β-H), 6.30 – 6.15 (m, 2H , γ-H and δ-H), 6.10 (d, J = 15.6 Hz, 1H, α-H), 2.58 (q, J = 7.3 Hz, 2H, CH_3), 2.28 – 2.14 (m, 2H, CH_2), 1.11 (t, J = 7.4 Hz, 3H, CH_3), 1.06 (t, J = 7.4 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.6, 146.9, 143.0, 128.1, 127.8, 33.8, 26.3, 13.0, 8.5. HRMS (ESI) for $C_9H_{14}NaO$ [M+Na^+]: Calcd: 161.0937; Found: 161.0950. IR (KBr): 2960, 2924, 1957, 1261, 1091, 1023, 800 cm^{-1}.



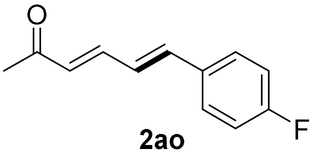
2am

(*10R*,*3S*)-17-hydroxy-10,13-dimethyl-1,2,8,9,10,11,12,13,14,15,16,17-dodecahydro-3H-cyclopenta[a]phenanthren-3-one (2am) (Peart et al., 2011) Prepared according to general procedure to afford as white solid (62% yield). R_f = 0.38 (EtOAc / hexanes 1 : 20). m. p. = 224 – 226 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.11 (s, 2H, γ-H and δ-H), 5.68 (s, 1H, α-H), 3.70 (t, J = 8.3 Hz, 1H, CH), 2.65 – 2.50 (m, 1H), 2.47 – 2.38 (m, 1H), 2.25 (t, J = 10.7 Hz, 1H, CH), 2.20 – 2.08 (m, 1H), 2.05 – 1.97 (m, 1H), 1.97 – 1.86 (m, 1H), 1.85 – 1.76 (m, 2H), 1.75 – 1.66 (m, 1H), 1.65 – 1.57 (m, 1H), 1.55 – 1.42 (m, 3H), 1.23 (br, 1H), 1.22 – 1.15 (m, 2H), 1.13 (s, 3H, CH_3), 0.85 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 199.8, 163.9, 140.6, 128.1, 123.8, 81.3, 50.9, 48.4, 44.0, 37.8, 36.4, 36.2, 34.03, 34.02, 30.5, 23.1, 20.4, 16.4, 11.1. HRMS (ESI) for $C_{19}H_{11}NaO_2$ [M+Na^+]: Calcd: 309.1825; Found: 309.1824. IR (KBr): 3335, 3025, 2964, 2928, 2859, 1657, 1614, 1583, 1061 cm^{-1}.



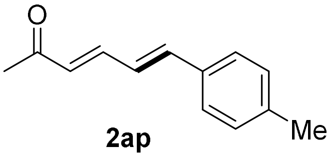
2an

(*3E*, *5E*)-6-phenylhexa-3,5-dien-2-one (2an) (Wu et al., 2016) Prepared according to general procedure to afford as yellow solid (89% yield). R_f= 0.46 (EtOAc / hexanes 1 : 20); m. p. = 37 – 38 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.45 (d, J = 7.4 Hz, 2H, Ar-H), 7.37 – 7.22 (m, 4H, Ar-H and β-H), 6.95 – 6.80 (m, 2H, γ-H and δ-H), 6.23 (d, J = 15.5 Hz, 1H, α-H), 2.29 (s, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 198.4, 143.5, 141.3, 136.0, 130.5, 129.2, 128.9, 127.3, 126.7, 27.4. HRMS (ESI) for $C_{12}H_{13}O$ [M+H$^+$]: Calcd: 173.0961; Found: 173.0950. IR (KBr): 3059, 3028, 3000, 1960, 1882, 1712, 1653, 1614, 1591, 1360, 1254, 995 cm^{-1}.



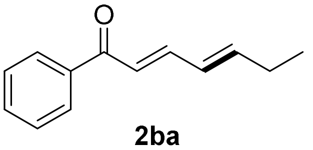
2ao

(*3E*, *5E*)-6-(4-fluorophenyl)hexa-3,5-dien-2-one (2ao) (Wu et al., 2016) Prepared according to general procedure to afford as yellow solid (86% yield). R_f = 0.55 (EtOAc / hexanes 1 : 20); m. p. = 40 – 41 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.45 (dd, J = 8.6, 5.5 Hz, 2H, Ar-H), 7.27 (dd, J = 15.5, 10.6 Hz, 1H, β-H), 7.07 – 7.03 (m, 2H, Ar-H), 6.94 – 6.75 (m, 2H, γ-H and δ-H), 6.25 (d, J = 15.5 Hz, 1H, α-H), 2.31 (s, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 198.6, 163.30 (d, J = 250.1 Hz), 143.4, 140.0, 132.3 (d, J = 3.4 Hz), 130.6, 129.1 (d, J = 8.3 Hz), 126.5 (d, J = 2.5 Hz), 116.1 (d, J = 21.9 Hz). 27.5. HRMS (ESI) for $C_{12}H_{12}FO$ [M+H$^+$]: Calcd: 191.0867; Found: 191.0877. IR (KBr): 2996, 2928, 2922, 1713, 1682, 1360, 1229, 1178, 978, 811 cm^{-1}.



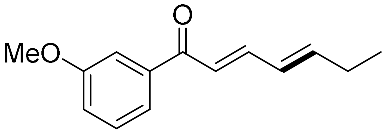
2ap

(*3E*, *5E*)-6-(p-tolyl)hexa-3,5-dien-2-one (2ap) (Wu et al., 2016) Prepared according to general procedure to afford as pale yellow solid (90% yield). R_f= 0.46 (EtOAc / hexanes 1 : 20); m. p. = 60 – 61 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.35 (d, J = 8.1 Hz, 2H, Ar-H), 7.27 (dd, J = 15.5, 10.3 Hz, 1H, β-H), 7.15 (d, J = 8.0 Hz, 2H, Ar-H), 6.93 – 6.77 (m, 2H, *γ*-H and *δ*-H), 6.21 (d, *J* = 15.5 Hz, 1H, *α*-H), 2.35 (s, 3H, CH_3), 2.29 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 198.4, 143.8, 141.4, 139.5, 133.3, 130.0, 129.6, 127.3, 125.7, 27.3, 21.4. HRMS (ESI) for $C_{13}H_{15}O$ [M+H$^+$]: Calcd: 187.1117; Found: 187.1115. IR (KBr): 3073, 2996, 2928, 1713, 1599, 1590, 1509, 1417, 1360, 1228, 1157, 977, 830 cm^{-1}.



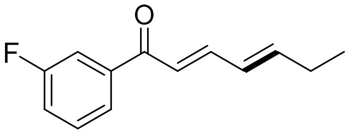
2ba

(*2E*, *4E*)-1-phenylhepta-2,4-dien-1-one (2ba) (Ma et al.,1989) Prepared according to general procedure to afford as yellow oil (65% yield). *R*$_f$= 0.39 (EtOAc / hexanes 1 : 30); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.99 – 7.90 (m, 2H, Ar-H), 7.58 – 7.52 (m, 1H, Ar-H), 7.51 – 7.45 (m, 2H, Ar-H), 7.43 – 7.35 (m, 1H, *β*-H), 6.89 (d, *J* = 15.0 Hz, 1H, *α*-H), 6.33 – 6.25 (m, 2H, *γ*-H and *δ*-H), 2.29 – 2.20 (m, 2H, CH_2), 1.08 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* = 191.1, 148.0, 145.7, 138.4, 132.7, 128.7, 128.5, 128.3, 123.7, 26.4, 13.0. HRMS (ESI) for $C_{13}H_{15}O$ [M+H$^+$]: Calcd: 187.1117; Found: 187.1115. IR (KBr): 3062, 2960, 2867, 1673, 1619, 1452, 1284, 1103, 1010, 798, 696 cm^{-1}.



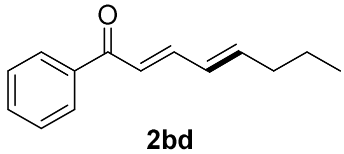
2bb

(*2E*, *4E*)-1-(3-methoxyphenyl)hepta-2,4-dien-1-one (2bb) Prepared according to general procedure to afford as yellow oil (71% yield). *R*$_f$= 0.47 (EtOAc / hexanes 1 : 10). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* = 7.56 – 7.47 (m, 2H, Ar-H), 7.47 – 7.33 (m, 2H, Ar-H and *β*-H), 7.10 (dd, *J* = 8.0, 2.4 Hz, 1H, Ar-H), 6.87 (d, *J* = 15.0 Hz, 1H, *α*-H), 6.34 – 6.29 (m, 2H, *γ*-H and *δ*-H), 3.87 (s, 3H, OCH_3), 2.29 – 2.19 (m, 2H , CH_2), 1.08 (t, *J* = 7.4 Hz, 3H , CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) *δ* = 190.7, 160.0, 148.1, 145.7, 139.8, 129.6, 128.3, 123.7, 121.0, 119.3, 112.8, 55.6, 26.4, 13.0. HRMS (ESI) for $C_{14}H_{17}O_2$ [M+H$^+$]: Calcd: 217.1223; Found: 217.1228. IR (KBr): 3075, 2959, 2931, 2035, 1720, 1680, 1590, 1487, 1459, 1430, 1265, 1041, 756 cm^{-1}.



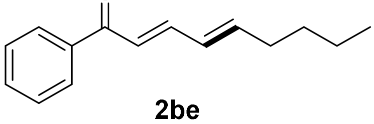
2bc

(2*E*, 4*E*)-1-(3-fluorophenyl)hepta-2,4-dien-1-one (2bc) Prepared according to general procedure to afford as yellow oil (65% yield). R_f= 0.54 (EtOAc / hexanes 1 : 10). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.71 (d, J = 7.8 Hz, 1H, Ar-H), 7.67 – 7.60 (m, 1H, Ar-H), 7.48 – 7.39 (m, 2H, Ar-H and β-H), 7.28 – 7.21 (m, 1H, Ar-H), 6.84 (d, J = 14.9 Hz, 1H, α-H), 6.36 – 6.30 (m, 2H, γ-H and δ-H), 2.30 – 2.19 (m, 2H, CH$_2$), 1.08 (t, J = 7.5 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 189.6, 163.0 (d, J = 247.7 Hz), 148.7, 146.4, 140.6 (d, J = 6.2 Hz), 130.3 (d, J = 7.7 Hz), 128.2, 124.1 (d, J = 2.9 Hz), 123.2, 119.6 (d, J = 21.5 Hz), 115.3 (d, J = 22.3 Hz). 26.4, 12.9. HRMS (ESI) for $C_{13}H_{14}O$ [M+Na$^+$]: Calcd: 227.0831; Found: 227.0833. IR (KBr): 2959, 2927, 2867, 1724, 1599, 1506, 1461, 1410, 1273, 1235, 1156, 1038, 844 cm^{-1}.



2bd

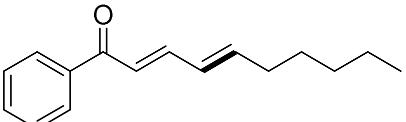
(2*E*, 4*E*)-1-phenylocta-2,4-dien-1-one (2bd) (Kim et al., 2015) Prepared according to general procedure to afford as yellow oil (65% yield). R_f= 0.55 (EtOAc / hexanes 1 : 10). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.96 – 7.91 (m, 2H, Ar-H), 7.58 – 7.51 (m, 1H, Ar-H), 7.50 – 7.36 (m, 2H, Ar-H), 7.41 (dd, J = 15.1, 10.4 Hz, 1H, β-H), 6.88 (d, J = 15.1, 1H, α-H), 6.38 – 6.20 (m, 2H, γ-H and δ-H), 2.25 – 2.17 (m, 2H, CH$_2$), 1.54 – 1.43 (m, 2H, CH$_2$), 0.94 (t, J = 7.4 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 191.1, 146.5, 145.6, 138.4, 132.6, 129.4, 128.5, 123.7, 35.4, 22.1, 13.8. HRMS (ESI) for $C_{14}H_{16}NaO$ [M+Na$^+$]: Calcd: 223.1093; Found: 223.1085. IR (KBr): 3015, 2961, 2860, 1660, 1591, 1452, 1351, 1268, 1090, 692 cm^{-1}.



2be

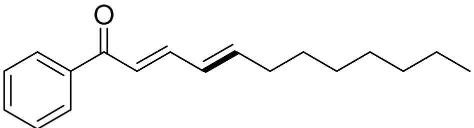
(2*E*, 4*E*)-1-phenylnona-2,4-dien-1-one (2be) (Armstrong et al., 2010) Prepared according to general procedure to afford as yellow oil (71% yield). R_f= 0.28 (EtOAc /

hexanes 1 : 20). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.96 – 7.91 (m, 2H, Ar-H), 7.58 – 7.51 (m, 1H, Ar-H), 7.50 – 7.43 (m, 2H, Ar-H), 7.41 (dd, J = 15.0, 10.0 Hz, 1H, β-H), 6.88 (d, J = 15.1 Hz, 1H, α-H), 6.37 – 6.20 (m, 2H, γ-H and δ-H), 2.27 – 2.15 (m, 2H, CH$_2$), 1.52 – 1.23 (m, 4H, 2CH$_2$), 0.92 (t, J = 7.2 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 191.1, 146.8, 145.6, 138.5, 132.6, 129.3, 128.7, 128.6, 128.5, 123.7, 33.0, 31.0, 22.4, 14.0. HRMS (ESI) for $C_{15}H_{18}NaO$ [M+Na$^+$]: Calcd: 237.1250; Found: 237.1245. IR (KBr): 3025, 2960, 2867, 1662, 1592, 1450, 1353, 1268, 1090, 696 cm^{-1}.



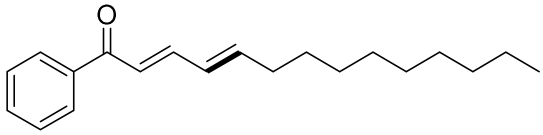
2bf

(*2E*, *4E*)-1-phenyldeca-2,4-dien-1-one (2bf) Prepared according to general procedure to afford as yellow oil (65% yield). R_f= 0.50 (EtOAc / hexanes 1 : 20). ^{1}H NMR (400 MHz, CDCl$_3$): δ= 7.97 – 7.90 (m, 2H, Ar-H), 7.57 – 7.52 (m, 1H, Ar-H), 7.50 – 7.44 (m, 2H, Ar-H), 7.40 (dd, J = 15.1, 10.0 Hz, 1H , β-H), 6.88 (d, J = 15.1 Hz, 1H, α-H), 6.39 – 6.20 (m, 2H, γ-H and δ-H), 2.27 – 2.15 (m, 2H, CH$_2$), 1.51 – 1.40 (m, 2H, CH$_2$), 1.38 – 1.24 (m, 4H, CH$_2$), 0.90 (t, J = 6.9 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) : δ = 191.1, 146.8, 145.6, 138.5, 132.6, 129.2, 128.7, 128.5, 123.7, 33.3, 31.5, 28.5, 22.6, 14.1. HRMS (ESI) for $C_{16}H_{21}O$ [M+H$^+$]: Calcd: 229.1587; Found: 229.1590. IR (KBr): 2917, 2863, 1664, 1592, 1452, 1263, 1008, 769, 696 cm^{-1}.



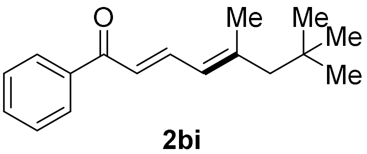
2bg

(*2E*, *4E*)-1-phenyldodeca-2,4-dien-1-one (2bg) Prepared according to general procedure to afford as yellow oil (65% yield). R_f= 0.56 (EtOAc / hexanes 1 : 20); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.98 – 7.90 (m, 2H, Ar-H), 7.59 – 7.51 (m, 1H, Ar-H), 7.50 – 7.43 (m, 2H, Ar-H), 7.41 (dd, J = 15.1, 10.0 Hz, 1H, β-H), 6.89 (d, J = 15.1 Hz, 1H, α-H), 6.39 – 6.19 (m, 2H, γ-H and δ-H), 2.28 – 2.15 (m, 2H, CH$_2$), 1.52 – 1.39 (m, 2H, CH$_2$), 1.33 – 1.27 (m, 8H, 4CH$_2$), 0.89 (t, J = 6.8 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 191.1, 146.9, 145.7, 138.4, 132.6, 129.2, 128.6, 128.5, 123.6, 33.4, 31.9, 29.3, 29.2, 28.8, 22.8, 14.2. HRMS (ESI) for $C_{18}H_5O$ [M+H$^+$]: Calcd: 257.1900; Found: 257.1891. IR (KBr): 2919, 2950, 1658, 1585, 1463, 1357, 1268, 1074, 1001, 692 cm^{-1}.



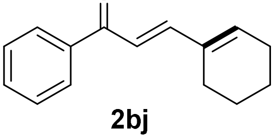
2bh

(*2E*, *4E*)-1-phenyltetradeca-2,4-dien-1-one (2bh) (Kim et al., 2015) Prepared according to general procedure to afford as yellow oil (56% yield). R_f= 0.43 (EtOAc / hexanes 1 : 20); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.96 – 7.91 (m, 2H, Ar-H), 7.59 – 7.52 (m, 1H, Ar-H), 7.51 – 7.44 (m, 2H, Ar-H), 7.43 (dd, J = 15.1, 10.0 Hz, 1H, β-H), 6.88 (d, J = 15.1 Hz, 1H, α-H), 6.38 – 6.20 (m, 2H, γ-H and δ-H), 2.28 – 2.15 (m, 2H, CH$_2$), 1.50 – 1.40 (m, 2H, CH$_2$), 1.35 – 1.21 (m, 12H, 6CH$_2$), 0.88 (t, J = 6.8 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 191.1, 146.9, 145.7, 138.5, 132.6, 129.2, 128.7, 128.5, 123.7, 33.4, 32.0, 29.7, 29.6, 29.5, 29.4, 28.8, 22.8, 14.3. HRMS (ESI) for $C_{20}H_{29}O$ [M+H$^+$]: Calcd: 285.2213; Found: 285.2217. IR (KBr): 2950, 2919, 1658, 1585, 1463, 1357, 1268, 1074, 1001, 692 cm^{-1}.



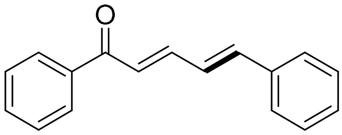
2bi

(*2E*, *4E*)-5,7,7-trimethyl-1-phenylocta-2,4-dien-1-one (2bi) Prepared according to general procedure to afford as yellow oil (66% yield). R_f= 0.43 (EtOAc / hexanes 1 : 20). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.98 – 7.95 (m, 2H, Ar-H), 7.77 (dd, J = 14.8, 11.8 Hz, 1H, β-H), 7.74 – 7.51 (m, 1H, Ar-H), 7.49-7.45 (m, 2H, Ar-H), 6.92 (d, J = 14.8 Hz, 1H, α-H), 6.11 (d, J = 11.8 Hz, 1H, γ-H), 2.10 (s, 2H, CH$_2$), 2.01 (s, 3H, CH$_3$), 0.95 (s, 9H, 3CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 191.1, 150.9, 141.2, 138.6, 132.6, 128.6, 128.4, 127.6, 123.3, 54.4, 32.8, 30.3, 20.6. HRMS (ESI) for $C_{17}H_{22}NaO$ [M+H$^+$]: Calcd: 265.1563; Found: 265.1579. IR (KBr): 3062, 3030, 2954, 2926, 2865, 1968, 1598, 1490, 1450, 1269, 1180, 1007, 694 cm^{-1}.



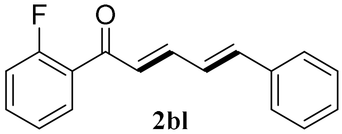
2bj

(*E*)-3-(cyclohex-1-en-1-yl)-1-phenylprop-2-en-1-one (2bj) (Kim et al., 2015) Prepared according to general procedure to afford as yellow oil (76% yield). R_f = 0.43 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.96 – 7.91 (m, 2H, Ar-H), 7.59 – 7.51 (m, 1H, Ar-H), 7.49 – 7.46 (m, 2H, Ar-H), 7.42 (d, J = 16.0 Hz, 1H, β-H), 6.85 (d, J = 15.4 Hz, 1H, α-H) , 6.29 (t, J = 12.0 Hz, 1H, δ-H), 2.34 – 2.19 (m, 4H, CH$_2$), 1.78 – 1.69 (m, 2H, CH$_2$), 1.69 – 1.60 (m, 2H, CH$_2$). ^{13}C NMR (100 MHz , CDCl$_3$): δ = 191.4, 148.6, 140.9, 138.7, 135.7, 132.5, 128.6, 128.5, 118.9, 26.8, 24.5, 22.2, 22.1. HRMS (ESI) for $C_{15}H_{16}NaO$ [M+Na$^+$]: Calcd: 235.1093; Found: 235.1100. IR (KBr): 2925, 2854, 1582, 1650, 1444, 1290, 1122, 970, 831, 682 cm^{-1}.



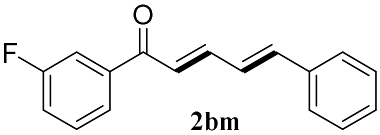
2bk

(*2E*, *4E*)-1,5-diphenylpenta-2,4-dien-1-one (2bk) (Armstrong et al., 2010) Prepared according to general procedure to afford as yellow solid (73% yield). R_f = 0.46 (EtOAc / hexanes 1 : 20); m. p. = 91 – 94 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.98 – 7.94 (m, 2H), 7.65 – 7.51 (m, 2H), 7.49 – 7.43 (m, 4H), 7.39 – 7.26 (m, 3H), 7.07 (d, J = 14.9 Hz, 1H), 7.01 – 6.93 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 190.5, 144.9, 142.0, 138.3, 136.1, 132.7, 129.3, 128.9, 128.6, 128.4, 127.4, 127.0, 125.5. HRMS (ESI) for $C_{17}H_{14}NaO$ [M+Na$^+$]: Calcd: 257.0937; Found: 257.0925. IR (KBr): 3060, 3029, 2958, 2928, 2597, 1963, 1903, 1717, 1682, 1657, 1578, 1284, 1253, 1010, 695 cm^{-1}.



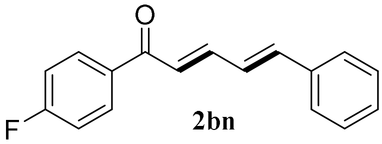
2bl

(2*E*, 4*E*)-1-(2-fluorophenyl)-5-phenylpenta-2,4-dien-1-one (2bl) Prepared according to general procedure to afford as yellow gum (77% yield). R_f = 0.42 (EtOAc / hexanes 1 : 20); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.81 (td, J = 7.5, 1.8 Hz, 1H), 7.60 – 7.49 (m, 4H), 7.43 – 7.32 (m, 3H), 7.27 (td, J = 7.5, 0.9 Hz, 1H), 7.17 (ddd, J = 10.7, 8.3, 0.7 Hz, 1H), 7.05 – 7.01 (m, 2H), 6.97 (dd, J = 15.0, 2.8 Hz, 1H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 189.2, 161.2 (d, J = 252.9 Hz), 145.1, 142.5, 136.1, 133.9 (d, J = 8.7 Hz), 131.0 (d, J = 8.0 Hz), 129.4, 129.1 (d, J = 6.5 Hz), 129.0, 127.5, 127.3 (d, J = 13.4 Hz), 127.0, 124.6 (d, J = 3.4 Hz), 116.6 (d, J = 23.2 Hz). HRMS (ESI) for $C_{17}H_{13}FNaO$ [M+Na^{+}]: Calcd: 275.0843; Found: 275.0836. IR (KBr): 3062, 3030, 2926, 1655, 1609, 1579, 1282, 1012, 798, 692 cm^{-1}.



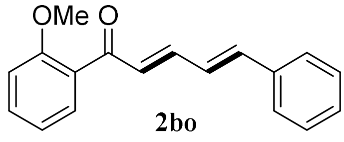
2bm

(2E, 4E)-1-(3-fluorophenyl)-5-phenylpenta-2,4-dien-1-one (2bm) Prepared according to general procedure to afford as yellow solid (74% yield). R_f = 0.36 (EtOAc / hexanes 1 : 20); m. p. = 52 – 56 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.74 (d, J = 7.7 Hz, 1H), 7.68 – 7.55 (m, 2H), 7.52 – 7.46 (m, 2H), 7.46 – 7.40 (m, 1H), 7.39 – 7.28 (m, 3H), 7.28 – 7.20 (m, 1H), 7.06 – 6.97 (m, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 189.0 (d, J = 2.0 Hz), 162.9 (d, J = 247.7 Hz), 145.6, 142.6, 140.4 (d, J = 6.3 Hz), 136.0, 130.3 (d, J = 7.7 Hz), 129.5, 129.0, 127.5, 126.8, 124.8 124.1 (d, J = 2.9 Hz), 119.7 (d, J = 21.5 Hz), 115.3 (d, J = 22.3 Hz). HRMS (ESI) for $C_{17}H_{14}FO$ [M+H^{+}]: Calcd: 253.1023; Found: 253.1026. IR (KBr): 3070, 3029, 2922, 1680, 1658, 1581, 1486, 1262, 1001, 790 cm^{-1}.



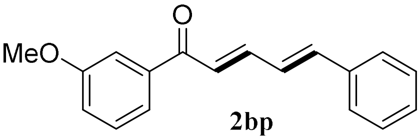
2bn

(2E, 4E)-1-(4-fluorophenyl)-5-phenylpenta-2,4-dien-1-one (2bn) (Polaquini et al., 2017) Prepared according to general procedure to afford as yellow solid (77% yield). R_f= 0.36 (EtOAc / hexanes 1 : 20); m. p. = 80 – 83 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.94 – 7.86 (m, 2H), 7.55 – 7.45 (m, 1H), 7.39 (d, J = 7.1 Hz, 2H), 7.31 – 7.18 (m, 3H), 7.08 – 7.02 (m, 2H), 6.96 (d, J = 14.9 Hz, 1H), 6.92 – 6.88 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 188.8, 165.6 (d, J = 254.2 Hz), 145.1, 142.3, 136.1, 134.6 (d, J = 3.0 Hz). 131.0 (d, J = 9.2 Hz), 129.4, 128.9, 127.4, 126.9, 124.9, 115.8 (d, J = 21.8 Hz). HRMS (ESI) for $C_{17}H_{13}FNaO$ [M+Na^{+}]: Calcd: 275.0843; Found: 275.0836. IR (KBr): 3067, 3024, 2959, 2924, 1652, 1602, 1502, 1250, 1002, 800, 619 cm^{-1}.



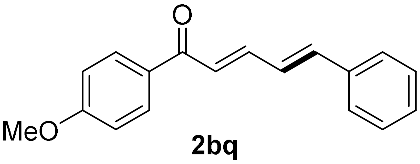
2bo

(2*E*, 4*E*)-1-(2-methoxyphenyl)-5-phenylpenta-2,4-dien-1-one (2bo) Prepared according to general procedure to afford as yellow gum (77% yield). R_f = 0.36 (EtOAc / hexanes 1 : 20); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (dd, J = 7.6, 1.7 Hz, 1H), 7.51 – 7.38 (m, 4H), 7.38 – 7.28 (m, 3H), 7.05 – 6.89 (m, 5H), 3.89 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 158.1, 143.7, 141.3, 136.4, 132.8, 130.6, 130.4, 129.4, 129.2, 128.9, 127.3, 120.8, 111.7, 55.8. HRMS (ESI) for $C_{18}H_{16}NaO_2$ [M+Na$^+$]: Calcd: 287.1043; Found: 287.1051. IR (KBr): 3026, 3024, 2939, 1648, 1598, 1483, 1462, 1288, 1245, 1020, 755 cm^{-1}.



2bp

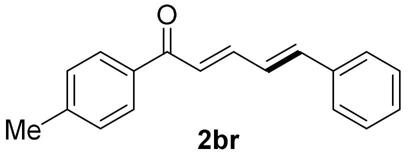
(2*E*, 4*E*)-1-(3-methoxyphenyl)-5-phenylpenta-2,4-dien-1-one (2bp) (Polaquini et al., 2017) Prepared according to general procedure to afford as yellow solid (76% yield). R_f= 0.46 (EtOAc / hexanes 1 : 10); m. p. = 71 – 75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 – 7.49 (m, 3H), 7.49 – 7.42 (m, 2H), 7.40 – 7.25 (m, 4H), 7.08 (ddd, J = 8.4, 2.6, 0.8 Hz, 1H), 7.04 (d, J = 14.9 Hz, 1H), 7.02–6.91 (m, 2H), 3.82 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.0, 159.9, 144.8, 141.9, 139.6, 136.1, 129.5, 129.2, 128.8, 127.3, 126.9, 125.4, 120.9, 119.2, 112.7, 55.4. HRMS (ESI) for $C_{18}H_{16}NaO_2$ [M+Na$^+$]: Calcd: 287.1043; Found: 287.1051. IR (KBr): 3003, 2958, 2928, 1724, 1647, 1649, 1595, 1508, 1253, 1170, 1023, 998, 846, 691 cm^{-1}.



2bq

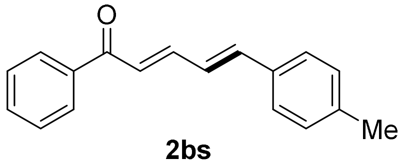
(2*E*, 4*E*)-1-(4-methoxyphenyl)-5-phenylpenta-2,4-dien-1-one (2bq) (Armstrong et al., 2010) Prepared according to general procedure to afford as pale yellow solid (77% yield). R_f= 0.55 (EtOAc / hexanes 1:10). m. p. = 55 – 58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.8 Hz, 2H), 7.59 (ddd, J = 14.8, 9.0, 1.1 Hz, 1H), 7.48 (d, J

= 6.8 Hz, 2H), 7.39 – 7.26 (m, 3H), 7.10 (d, *J* = 14.9 Hz, 1H), 7.02 – 6.91 (m, 4H), 3.85 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.7, 163.4, 144.1, 141.5, 136.3, 131.2, 130.8, 129.2, 128.9, 127.3, 127.1, 125.3, 113.9, 55.5. HRMS (ESI) for $C_{18}H_{16}NaO_2$ [M+Na$^+$]: Calcd: 287.1043; Found: 287.1047. IR (KBr): 3052, 3003, 2958, 2929, 1597, 1356, 1257, 1023, 999, 845, 737 cm^{-1}.



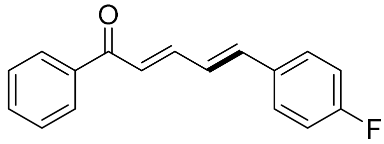
2br

(*2E*, *4E*)-5-phenyl-1-(p-tolyl)penta-2,4-dien-1-one (2br) (Polaquini et al., 2017) Prepared according to general procedure to afford as pale yellow solid (81% yield). *R*$_f$ = 0.46 (EtOAc / hexanes 1 : 10); m. p. = 78 – 82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.1 Hz, 2H), 7.58 (dd, *J* = 14.9, 9.5 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.39 – 7.28 (m, 3H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 14.9 Hz, 1H), 7.04 – 6.91 (m, 2H), 2.39 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.9, 144.4, 143.5, 141.7, 136.1, 135.6, 129.3, 129.2, 128.9, 128.6, 127.3, 127.0, 125.4, 21.7. HRMS (ESI) for $C_{18}H_{16}NaO$ [M+Na$^+$]: Calcd: 271.1093; Found: 271.1091. IR (KBr): 2921, 2856, 2732, 1673, 1444, 1251, 997, 802, 688 cm^{-1}.



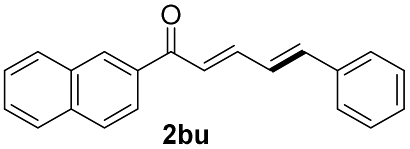
2bs

(*2E*, *4E*)-1-phenyl-5-(p-tolyl)penta-2,4-dien-1-one (2bs) (Armstrong et al., 2010) Prepared according to general procedure to afford as as yellow solid (81% yield). *R*$_f$= 0.47 (EtOAc / hexanes 1 : 20). m. p. = 62 – 65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.63 – 7.52 (m, 2H), 7.50 – 7.43 (m, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 14.9 Hz, 1H), 7.00 – 6.95 (m, 2H), 2.35 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.6, 145.3, 142.2, 139.6, 138.4, 133.5, 132.7, 130.0, 129.7, 128.7, 128.5, 127.4, 126.1, 125.0, 21.5. HRMS (ESI) for $C_{18}H_{17}O$ [M+ H$^+$]: Calcd: 249.1274; Found: 249.1282. IR (KBr): 3026, 2923, 2862, 2295, 1721, 1650, 1575, 1447, 1252, 1005, 842, 808, 692 cm^{-1}.



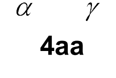
2bt

(*2E*, *4E*)-5-(4-fluorophenyl)-1-phenylpenta-2,4-dien-1-one (2bt) (Armstrong et al., 2010) Prepared according to general procedure to afford as as yellow solid (83% yield). R_f= 0.44 (EtOAc / hexanes 1 : 20). m. p. = 58 – 60 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.99 – 7.93 (m, 2H), 7.60 – 7.50 (m, 2H), 7.48 – 7.39 (m, 4H), 7.09 – 6.98 (m, 3H), 6.93 – 6.85 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 190.2, 163.2 (d, J = 250.0 Hz), 144.6, 140.5, 138.2, 132.7, 132.4 (d, J = 3.4 Hz), 129.0 (d, J = 8.2 Hz), 128.6, 128.4, 126.7 (d, J = 2.5 Hz), 125.4 (d, J = 0.9 Hz), 115.9 (d, J = 21.8 Hz). HRMS (ESI) for $C_{17}H_{14}FO$ [M+H$^+$]: Calcd: 253.1023; Found: 253.1013. IR (KBr): 3061, 2958, 2929, 2595, 1893, 1721, 1655, 1580, 1508, 1449, 1284, 1250, 1201, 1155, 1011, 1011, 844, 824, 694 cm^{-1}. Crystallographic data of **2bt** is available free of charge from the Cambridge Crystallographic Data Centre under accession number CCDC-1892057.



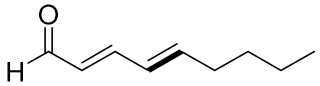
2bu

(*2E*, *4E*)-1-(naphthalen-2-yl)-5-phenylpenta-2,4-dien-1-one (2bu) (Polaquini et al., 2017) Prepared according to general procedure to afford as as yellow solid (78% yield). R_f= 0.45 (EtOAc / hexanes 1 : 20). m. p. = 104 – 106 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 8.50 (s, 1H), 8.07 (dd, J = 8.6, 1.7 Hz, 1H), 8.02 – 7.84 (m, 3H), 7.72 – 7.49 (m, 5H), 7.44 – 7.30 (m, 3H), 7.15 – 6.99 (m, 2H). ^{13}C NMR (100 MHz, CDCl$_3$) : δ = 190.4, 144.9, 142.1, 136.3, 135.7, 135.6, 132.7, 129.9, 129.7, 129.4, 129.0, 128.7, 128.5, 128.0, 127.5, 127.2, 126.9, 125.6, 124.6. HRMS (ESI) for $C_{21}H_{17}O$ [M+H$^+$]: Calcd: 285.1274; Found: 285.1261. IR (KBr): 3056, 3025, 2957, 2864, 1725, 1655, 1622, 1580, 1496, 1463, 1360, 1285,1149, 1000, 747, 693, cm^{-1}.



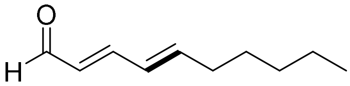
4aa

(*2E*, *4E*)-octa-2,4-dienal (4aa) Prepared according to general procedure to afford as colourless oil liquid (81% yield). R_f= 0.49 (EtOAc / hexanes 1 : 30); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.54 (d, J = 8.0 Hz, 1H, CHO), 7.09 (dd, J = 15.3, 9.7 Hz, 1H, β-H), 6.39 – 6.21 (m, 2H, γ-H and δ-H), 6.08 (dd, J = 15.4, 8.0 Hz, 1H, α-H), 2.25 – 2.15 (m, 2H, CH_2), 1.55 – 1.44 (m, 2H, CH_2), 0.95 (t, J = 7.4 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.2, 153.1, 147.3, 130.2, 128.9, 35.3, 21.9, 13.8. HRMS (ESI) for $C_8H_{12}NaO$ [M+Na$^+$]: Calcd: 147.0780; Found: 147.0789. IR (KBr): 2923, 2854, 1681, 1459, 1374, 1116, 792 cm^{-1}.



4ab

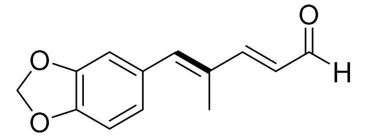
(*2E*, *4E*)-nona-2,4-dienal (2ab) (Kelly et al., 2015) Prepared according to general procedure to afford as colourless oil liquid (83% yield). R_f= 0.47 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (d, J = 8.0 Hz, 1H, CHO), 7.10 (dd, J = 15.2, 10.0 Hz, 1H, β-H), 6.36 – 6.24 (m, 2H, γ-H and δ-H), 6.08 (dd, J = 15.3, 8.0 Hz, 1H, α-H), 2.25 – 2.17 (m, 2H, CH_2), 1.50 – 1.40 (m, 2H, CH_2), 1.40 – 1.30 (m, 2H, CH_2), 0.92 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.1, 153.0, 147.5, 130.1, 128.8, 33.0, 30.8, 22.4, 14.0. HRMS (ESI) for $C_9H_{14}NaO$ [M+Na$^+$]: Calcd: 161.0937; Found: 161.0945. IR (KBr): 2929, 2865, 1687, 1637, 1164, 1118, 987, 734 cm^{-1}.



4ac

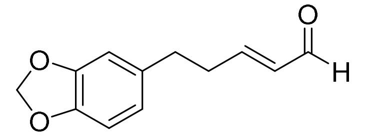
(*2E*, *4E*)-deca-2,4-dienal (4ac) (Holan et al., 2014) Prepared according to general procedure to afford as colorless oil (82% yield). R_f= 0.55 (EtOAc / hexanes 1 : 30). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.54 (d, J = 8.0 Hz, 1H, CHO), 7.09 (dd, J = 15.2, 9.6 Hz, 1H, β-H), 6.44 – 6.22 (m, 2H, γ-H and δ-H), 6.08 (dd, J = 15.3, 8.0 Hz, 1H, α-H), 2.24 – 2.16 (m, 2H, CH_2), 1.51 – 1.42 (m, 2H, CH_2), 1.39 – 1.18 (m, 4H, $2CH_2$), 0.90 (t, J = 7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.1, 153.1, 147.6, 130.2, 128.8, 33.3, 31.5, 28.4, 22.6, 14.1. HRMS (ESI) for $C_{10}H_{17}O$ [M+H$^+$]: Calcd:

153.1274; Found: 153.1280. IR (KBr): 2923, 2856, 1671, 1085, 624 cm^{-1}.



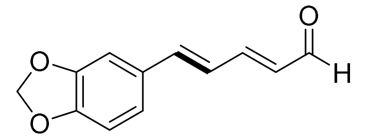
4ae

(*2E*, *4E*)-5-(benzo[d][1,3]dioxol-5-yl)-4-methylpenta-2,4-dienal (4ae) (Riveira et al., 2012) Prepared according to general procedure to afford as yellow solid (85% yield). R_f = 0.51 (EtOAc / hexanes 1 : 4). m. p. = 70 – 71 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 9.53 (d, J = 7.8 Hz, 1H, CHO), 7.17 (d, J = 15.5, 1H, β-H), 6.83 – 6.66 (m, 4H, Ar-H and δ-H), 6.15 (dd, J = 15.5, 7.8 Hz, 1H, α-H), 5.91 (s, 2H, CH$_2$), 1.99 (s, 3H, CH$_3$). ^{13}C NMR (100 MHz, CDCl$_3$) : δ = 194.0, 158.4, 147.8, 147.82, 140.78, 133.1, 130.4, 127.7, 124.7, 109.5, 108.5, 101.4, 14.0. HRMS (ESI) for $C_{13}H_{13}O_3$ [M+H$^+$]: Calcd: 217.0859; Found: 217.0862. IR (KBr): 2913, 1673,1599, 1495, 1444, 1359, 1296,1253, 1195,1154, 1035, 983, 798 cm^{-1}.



3ad

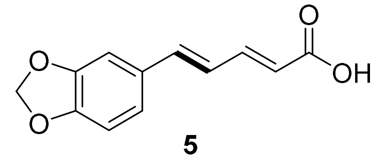
(*E*)-5-(benzo[d][1,3]dioxol-5-yl)pent-2-enal (3ad) R_f = 0.51 (EtOAc / hexanes 1 : 10); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 9.49 (d, J = 7.8 Hz, 1H, CHO), 6.90 – 6.78 (m, 1H), 6.77 – 6.59 (m, 3H), 6.12 (dd, J = 15.6, 7.8 Hz, 1H), 5.94 (s, 2H, OCH$_2$O), 2.85 – 2.70 (m, 2H, CH$_2$), 2.70 – 2.52 (m, 2H, CH$_2$). ^{13}C NMR (100 MHz, CDCl$_3$): δ = 194.1, 157.4, 147.9, 146.1, 134.1, 133.5, 121.3, 108.8, 108.4, 101.0, 34.6, 33.9. HRMS (ESI) for $C_{12}H_{12}O_3Na$ [M+Na$^+$]: Calcd: 227.0679; Found: 227.0683. IR KBr): 2362, 1681, 1488, 1239, 1117, 1032, 919, 804, 742 cm^{-1}.



4ad

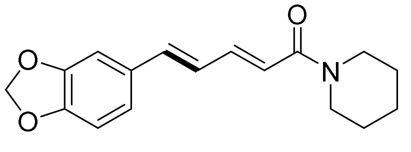
(*2E*,*4E*)-5-(benzo[d][1,3]dioxol-5-yl)penta-2,4-dienal (4ad) (Chandrasekhar et al., 2000) Prepared according to general procedure to afford as yellow solid (91% yield). R_f = 0.45 (EtOAc / hexanes 1 : 10). m. p. = 77 – 78 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ

= 9.59 (d, *J* = 8.0 Hz, 1H, CHO), 7.24 (dd, *J* = 14.9, 10.4 Hz, 1H, *β*-H), 7.08 – 6.75 (m, 5H, Ar-H and *γ*-H and *δ*-H), 6.23 (dd, *J* = 15.1, 8.0 Hz, 1H, *α*-H), 6.01 (s, 2H, OCH_2O). ^{13}C NMR (100 MHz, $CDCl_3$) : *δ* = 193.7, 152.5, 149.3, 148.5, 142.4, 131.0, 130.2, 124.6, 123.8, 108.8, 106.2, 101.7. HRMS (ESI) for $C_{12}H_{10}O_3Na$ [M+Na$^+$]: Calcd: 225.0522; Found: 225.0516. IR (KBr): 2914, 1675, 1599, 1495, 1444, 1359, 1296, 1253, 1195, 1154, 1035, 983, 797 cm^{-1}.



5

(*2E*,*4E*)-5-(benzo[d][1,3]dioxol-5-yl)penta-2,4-dienoic acid (5) Prepared according to previous literature's procedure (Chandrasekhar et al., 2000) to afford as yellow solid (83% yield). R_f= 0.40 (EtOAc / hexanes 1 : 4). m. p. = 194 – 195 °C. ^1H NMR (400 MHz, DMSO-d_6): *δ* = 12.29 (br, 1H, COOH), 7.31 (ddd, *J* = 15.2, 6.6, 3.7 Hz, 1H, *β*-H), 7.24 (d, *J* = 1.2 Hz, 1H, Ar-H), 7.05 – 6.88 (m, 4H, Ar-H and *γ*-H and *δ*-H), 6.06 (s, 2H, CH_2), 5.93 (d, *J* = 15.2 Hz, 1H, *α*-H). ^{13}C NMR (100 MHz, DMSO-d_6) : *δ* = 168.1, 148.6, 148.5, 145.1, 140.3, 131.0, 125.3, 123.6, 121.6, 109.0, 106.2, 101.8. HRMS (ESI) for $C_{12}H_{10}O_4Na$ [M+Na$^+$]: Calcd: 241.0471; Found: 241.0482. IR (KBr): 2921, 2544, 1679, 1601, 1459, 1449, 1368, 1309, 1257, 1193, 1148, 1104, 1035, 998, 930, 851, 797, 607 cm^{-1}.



Piperine

Piperine Prepared according to previous literature's procedure (Chandrasekhar et al., 2000) to afford as pale yellow solid (71% yield). R_f= 0.42 (EtOAc / hexanes 1 : 10). m. p. = 121 – 122 °C. ^1H NMR (400 MHz, $CDCl_3$): *δ* = 7.40 (ddd, *J* = 14.6, 7.3, 2.9 Hz, 1H, *β*-H), 6.97 (s, 1H, Ar-H), 6.88 (d, *J* = 8.0 Hz, 1H, Ar-H), 6.81 – 6.71 (m, 3H, Ar-H and *γ*-H and *δ*-H), 6.44 (d, *J* = 14.7 Hz, 1H, *α*-H), 5.96 (s, 2H, CH_2), 3.57 (d, *J* = 44.1 Hz, 4H, $2CH_2$), 1.62 (dd, *J* = 28.2, 4.5 Hz, 6H, $3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) : *δ* = 165.4, 148.2, 148.1, 142.5, 138.2, 131.0, 125.4, 122.5, 120.1, 108.5, 105.7, 101.3, 46.9, 43.3, 26.8, 25.7, 24.7. HRMS (ESI) for $C_{17}H_{20}NO_3$ [M+H$^+$]: Calcd: 286.1438; Found: 286.1447. IR (KBr): 3007, 2938, 1634, 1583, 1489, 1444, 1363, 1252, 1194, 1132, 1027, 926, 850 cm^{-1}.

3. General Procedure for the Mechanistic Experiments

3.1. Parallel experiments for k_H / k_D

Deuterated-substratep reparation: Synthesis of [5,5-*d*$_2$] (*E*)-6-phenylhex-3-en-2-one (**S1-*d*$_2$**)

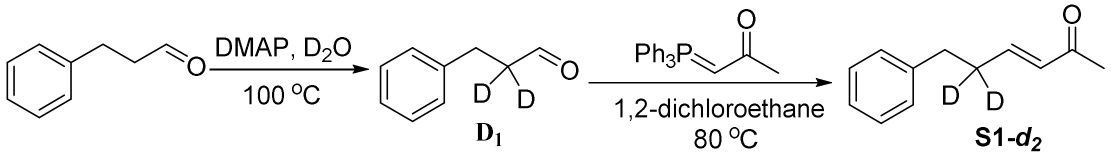


Figure S1 Synthesis of substrate **S1-*d*$_2$**, related to **Scheme 4**

[2,2-*d*$_2$]-3-phenylpropanal (D$_1$). (Ariza et al., 2010) Hydrocinnamaldehyde (1 mL) with D_2O (1 mL) was heated to 100 °C in the presence of 4-(N,N-dimethylamino)pyridine (4-DMAP, 13 mg) for 1 h in a septum-sealed flask. Thus, CH_2Cl_2 (4 mL) and 1M aq. HCl (1 mL) were added to the mixture at room temperature. The organic layer was then washed with aq. $NaHCO_3$ and brine.The organic layer was dried ($MgSO_4$) and the solvent was carefully removed. The crude product was shown to be 99 % deuterated material, and was distilled in vacuo to yield **D$_1$** (98% yield, 99% D) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.85 (s, 1H, CHO), 7.39 – 7.34 (m, 2H, Ar-H), 7.30 – 7.23 (m, 3H, Ar-H), 3.00 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 201.9, 140.4, 128.7, 128.4, 126.4, 45.1 – 44.4 (m), 28.0. HRMS (ESI) for $C_9H_9D_2NaO$ [M+Na$^+$]: Calcd: 159.0749; Found: 159.0755. IR (KBr): 3060, 3027, 2927, 2859, 2723, 1722, 1495, 1450, 745, 700 cm^{-1}.

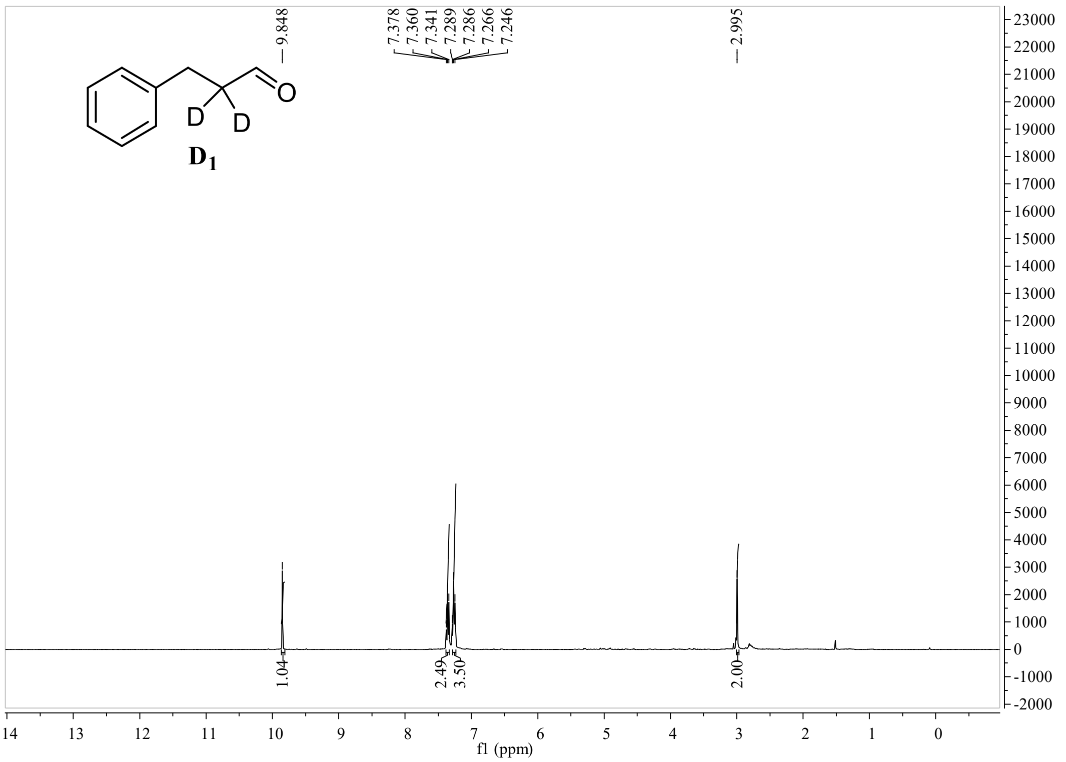


Figure S2 ^{1}H NMR spectrum of compound **D$_1$**, related to **Scheme 4**

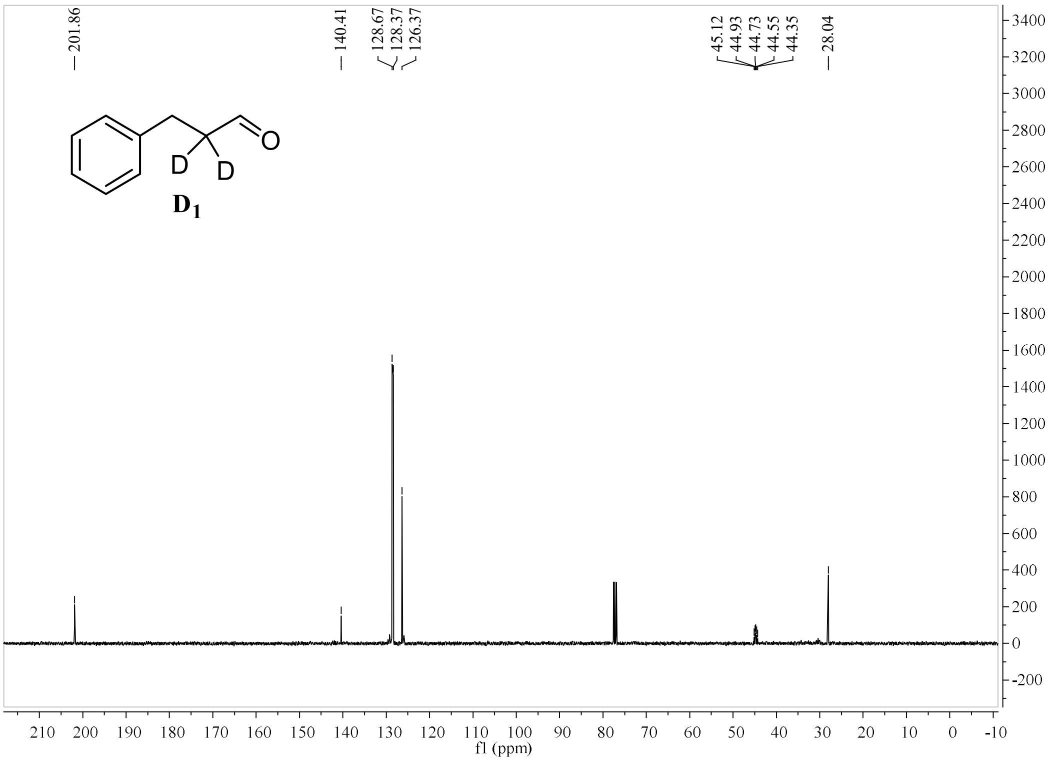


Figure S3 ^{13}C NMR spectrum of compound **D$_1$**, related to **Scheme 4**

[5,5-d$_2$]-(E)-6-phenylhex-3-en-2-one (S1-*d$_2$*). (Shih et al., 2015) A mixture of (acetylmethylene)Triphenylphosphorane (1 g, 318, 3.3 mmol) and **D1** (408 mg, 3.0

mmol) was heated at 80 °C in a two necked round bottom flask using 1,2-dichloroethane (10.0 mL) as solvent for 16 hour. The completion of the reaction was monitored by TLC. Then solvent was evaporated in rotary evaporator under reduced pressure to obtain the residue. The residue was purified by flash column chromatography on silica gel to isolate the product. The product was obtained colorless liquid. (83% yield, 99% D). ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.30 – 7.22 (m, 2H, Ar-H), 7.21 – 7.11 (m, 3H, Ar-H), 6.78 (d, J = 16.0 Hz, 1H, β-H), 6.06 (d, J = 16.0 Hz, 1H, α-H), 2.74 (s, 2H, CH_2), 2.19 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 198.4, 146.9, 140.5, 131.7, 128.4, 128.2, 126.1, 34.1, 34.0 – 33.1 (m), 26.7. HRMS (ESI) for $C_{12}H_{12}D_2NaO$ [M+Na$^+$]: Calcd: 199.1062; Found: 199.1057. IR (KBr): 3309, 3059, 3027, 2926, 2859, 1673, 1626, 1360, 1257, 988, 743, 701 cm^{-1}.

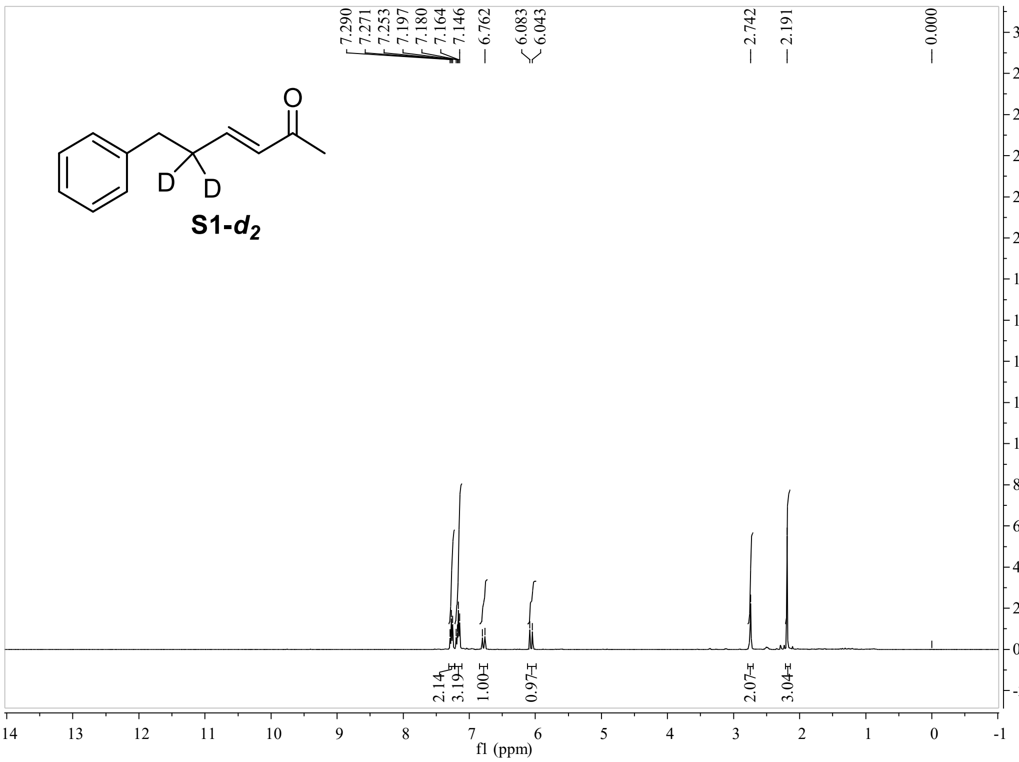


Figure S4 ^{1}H NMR spectrum of compound **S1-*d*$_2$**, related to **Scheme 4**

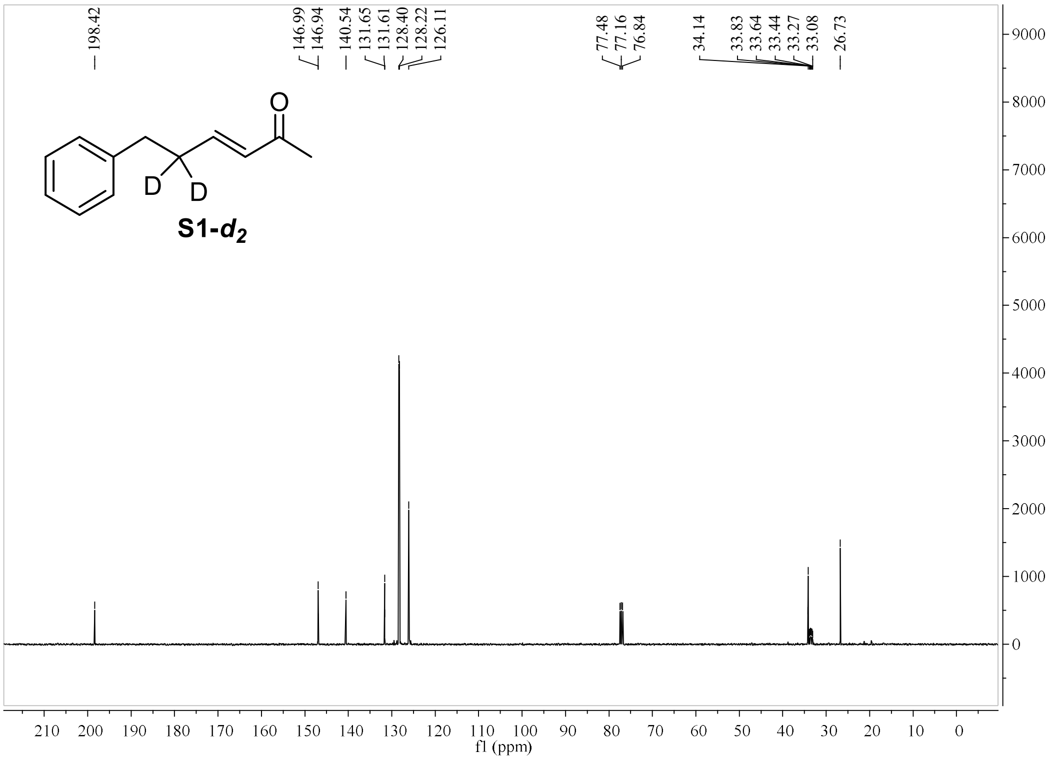
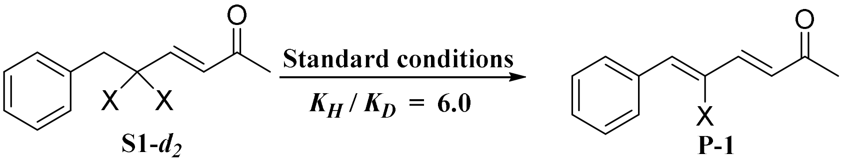


Figure S5 ^{1}H NMR spectrum of compound **S1-d_2**, related to **Scheme 4**

KIE experiment: We use **1an** and deuterated **S1-d_2** as starting materials and two parallel sets reactions at standard conditions. The conversion was measured by ^{1}H NMR analysis for five times (30 min, 60 min, 90 min, 120 min, 150 min) to compare the initial reaction rates.

Table S1. Conversion (%) of the reaction of **1an** (**α-H$_2$** and **α-D$_2$**), related to **Scheme 4**



reaction time (min)	H-Conversion (%)	D-Conversion (%)
30	12.8%	2.9%
60	18.9%	3.8%
90	26.2%	6.0%
120	35.8%	6.5%
150	40.2%	7.7%

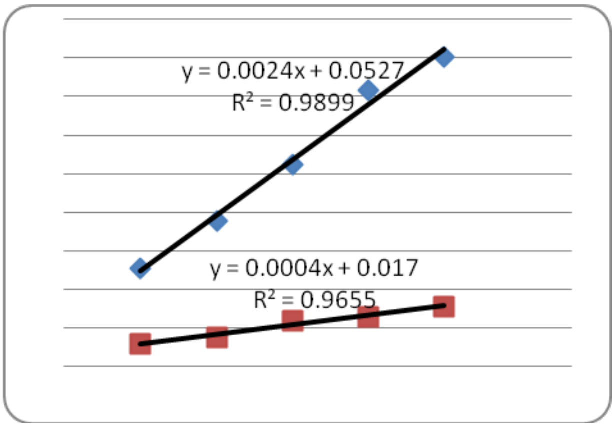


Figure S6. Conversion (%) versus Time (min), related to **Scheme 4**

3.2. Intramolecular competitive reaction for K_H / K_D

Deuterated-substrate preparation (Diao et al., 2012)**:** Synthesis of [6-d] (*E*)-6-phenylhex-3-en-2-one (**S2-*d₁***)

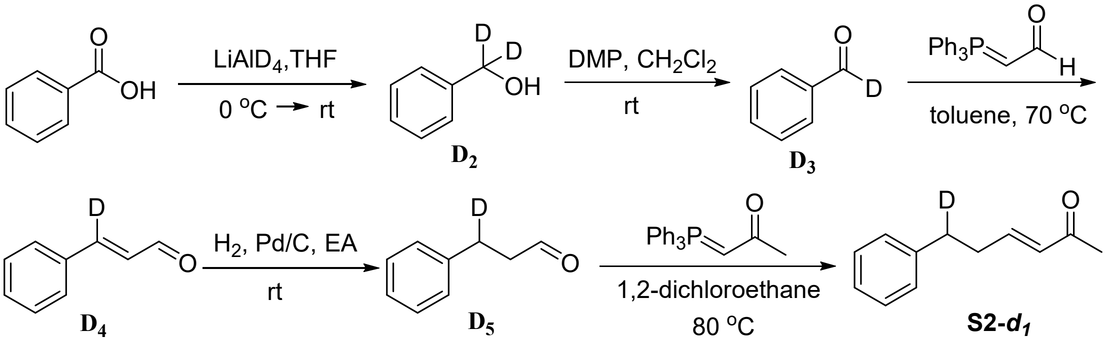


Figure S7. Synthesis of substrate **S2-*d₁***, related to **Scheme 4**

[1,1-*d₂*]-Benzyl alcohol (D_2). (Diao et al., 2012) An oven-dried 250 mL round bottom flask was equipped with a stir bar. After purging with N_2, the flask was charged with $LiAlD_4$ (513 mg, 13.5 mmol, 1.1 equiv) and 50 mL THF and stirred at 0 °C. A oven-dried 100 mL round bottom flask equipped with stir bar and septum was purged with N_2. A solution of benzoic acid (1.50 g, 12.3 mmol, 1 equiv) in 50 mL THF were added to the 100 mL flask and stirred at 0 °C. Above benzoic acid solution were added dropwise to the $LiAlD_4$ suspension at 0 °C using a cannula. The reaction mixture was slowly warmed to room temperature and allowed stirring for overnight. The mixture was diluted to 2 × its original volume with ethyl acetate and quenched by dropwise addition of water at 0 °C. The mixture was extracted with diethyl ether (3 × 50 mL), and the combined organic layers were washed with brine (2 × 50 mL), dried over Na_2SO_4, and concentrated by evaporation. Distillation in vacuo yielded **D_2** (45%, 99% D) as a colorless oil. ^{1}H NMR data match previously reported data. ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.41 – 7.16 (m, 5H, Ar-H), 3.74 (br, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 140.7, 128.6, 127.7, 127.1, 64.4-60.6 (m). HRMS (ESI) for $C_7H_6D_2NaO$ [M+Na$^+$]: Calcd: 133.0593; Found: 133.0600. IR (KBr): 3325, 3027, 2197, 2135, 2085, 1494, 1447, 1227, 1095, 1058, 1024, 965, 921, 716 cm^{-1}.

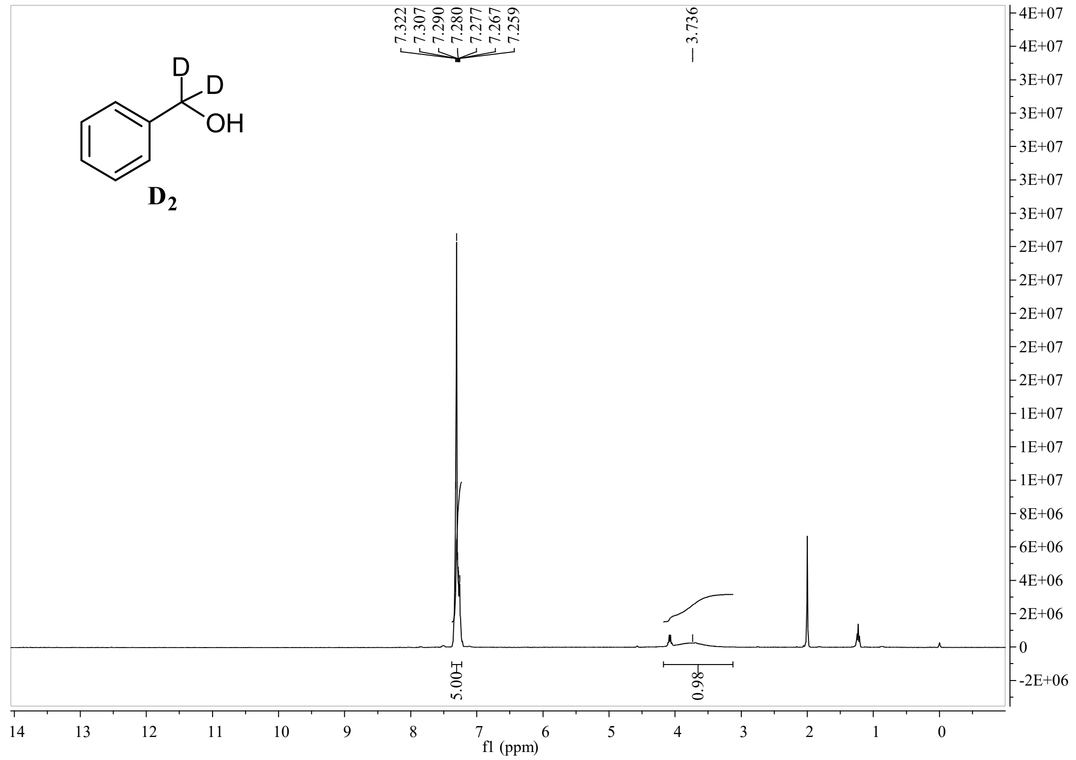


Figure S8 ^{1}H NMR spectrum of compound **D_2**, related to **Scheme 4**

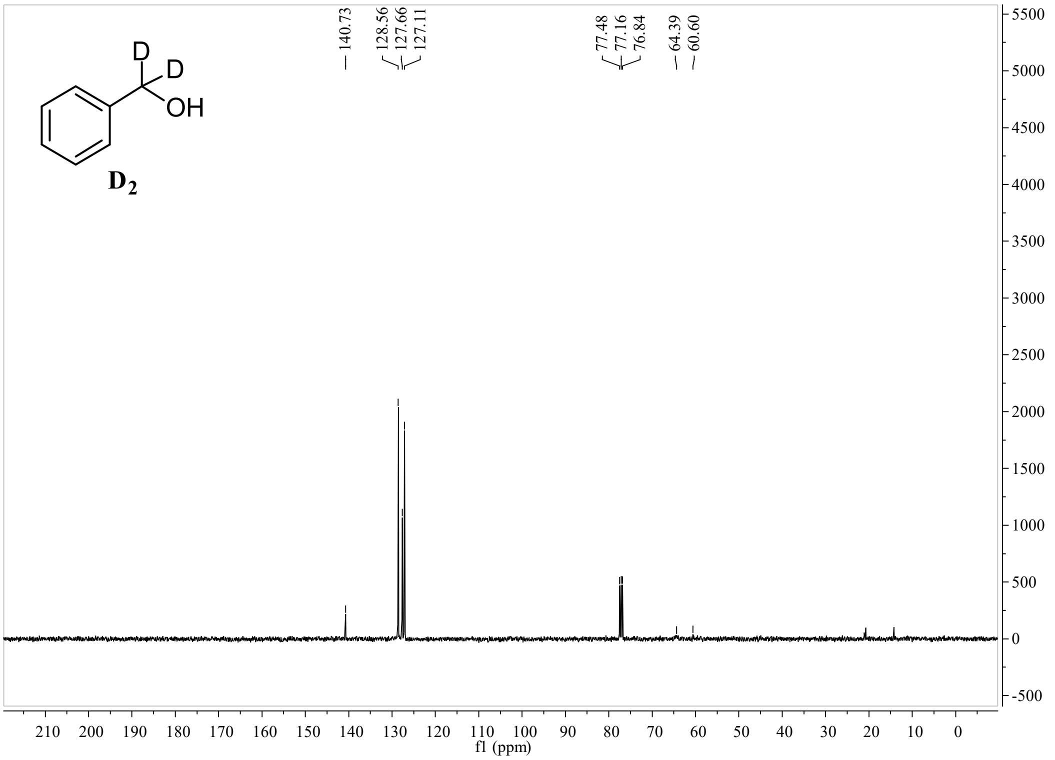


Figure S9 ^{13}C NMR spectrum of compound $\mathbf{D_2}$, related to **Scheme 4**

[1-d_1]-Benzaldhyde ($\mathbf{D_3}$) (Diao et al., 2012) A 100 mL round bottom flask equipped with a stir bar was charged with 20 mL CH_2Cl_2 and $\mathbf{D_2}$ (380 mg, 3.44 mmol). Then DMP (1,1,1-Triacetoxy-1,1-Dihydro-1,2-Benziodoxol-3(1H)-One (2.19 g, 5.16 mmol, 1.5 equiv.) were added with stirring. The solution was stirred at room temperature and consumption of starting material was monitored by TLC. Upon reaction completion, the reaction mixture was filtered through a plug of silica. Removal of solvent afforded $\mathbf{D_3}$ (90% yield, 99% D) as a colorless oil. ^{1}H NMR data match previously reported data. ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.89 (d, J = 8.1 Hz, 2H, Ar-H), 7.67 – 7.57 (m, 1H, Ar-H), 7.56 – 7.47 (m, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ =187.4 (t, J = 26 Hz), 131.5, 129.7, 125.0, 124.2. HRMS (ESI) for C_7H_6DO [M+H$^+$]: Calcd: 108.0554; Found: 108.0553. IR (KBr): 3061, 3030, 2989, 2937, 2827, 2595, 1687, 1450, 1266, 1113, 1083, 1031, 736, 697 cm^{-1}.

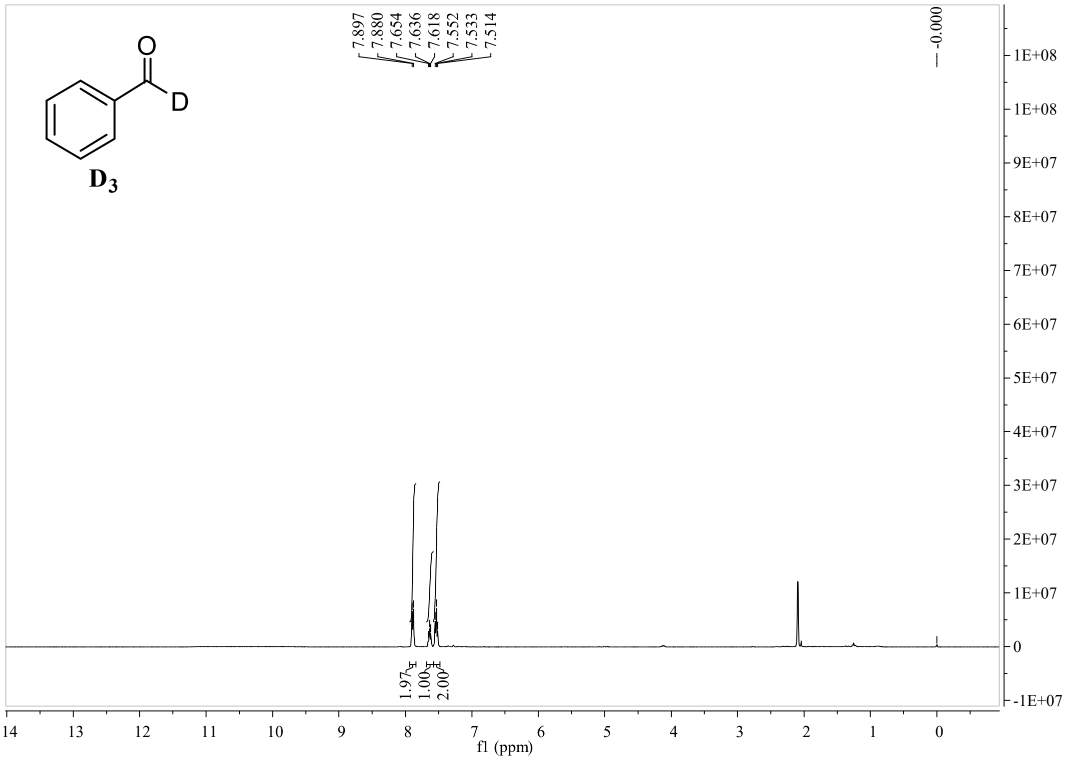


Figure S10 ^{1}H NMR spectrum of compound **D$_3$**, related to **Scheme 4**

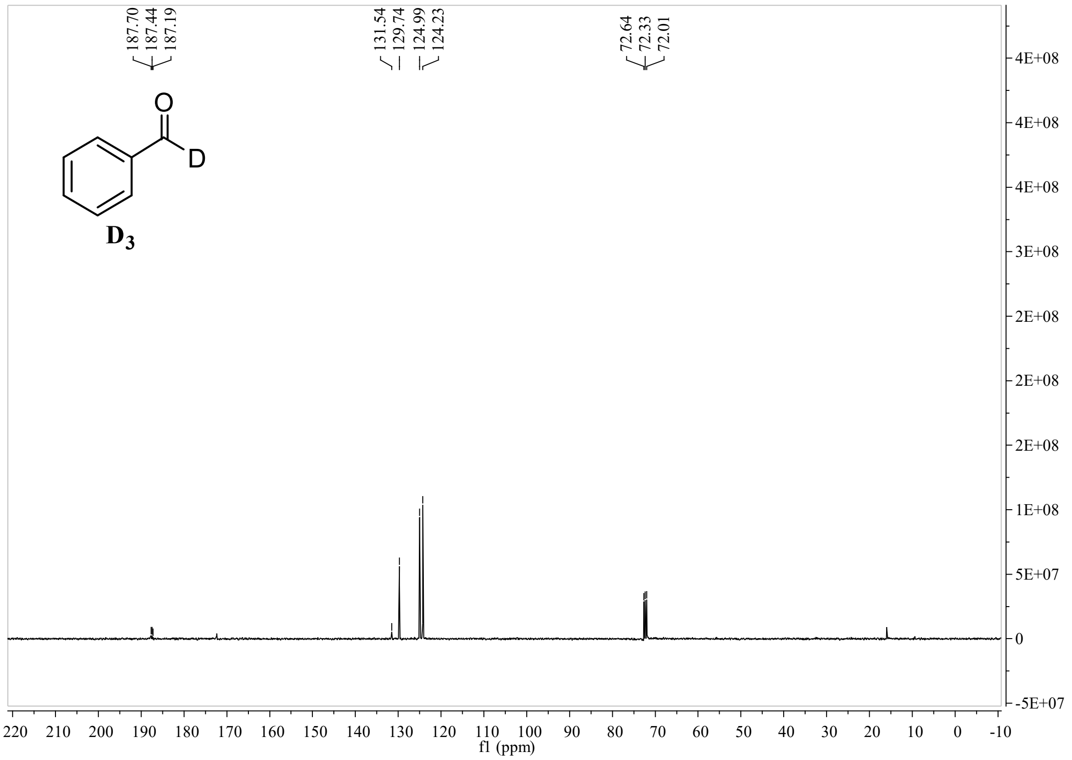


Figure S11 ^{13}C NMR spectrum of compound **D$_3$**, related to **Scheme 4**

[3-d_1]-cinnamaldehyde (D$_4$) (Diao et al., 2012) A mixture of (acetaldehyde)Triphenylphosphoranylidene (1 g, 3.3 mmol) and **D$_3$** (321 mg, 3.0

mmol) was heated at 80 °C in a two necked round bottom flask using 1,2-dichloroethane (10.0 mL) as solvent for 16 hour. The completion of the reaction was monitored by TLC. Then solvent was evaporated in rotary evaporator under reduced pressure to obtain the residue. The residue was purified by flash column chromatography on silica gel to isolate the product. The product was obtained colorless liquid (52% Yield, 99% D). ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.71 (d, J = 7.7 Hz, 1H, CHO), 7.60 – 7.54 (m, 2H, Ar-H), 7.47 – 7.41 (m, 3H, Ar-H), 6.78 – 6.68 (m, 1H, α-H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 193.8, 152.5 (t, J = 23.0 Hz), 134.0, 131.3, 129.1 (2C), 128.5 (3C). HRMS (ESI) for C_9H_7DNaO [M+Na$^+$]: Calcd: 156.0530; Found: 156.0535. IR (KBr): 3058, 3026, 2970, 2828, 2727, 2614, 1676, 1612, 1149, 891, 691 cm^{-1}.

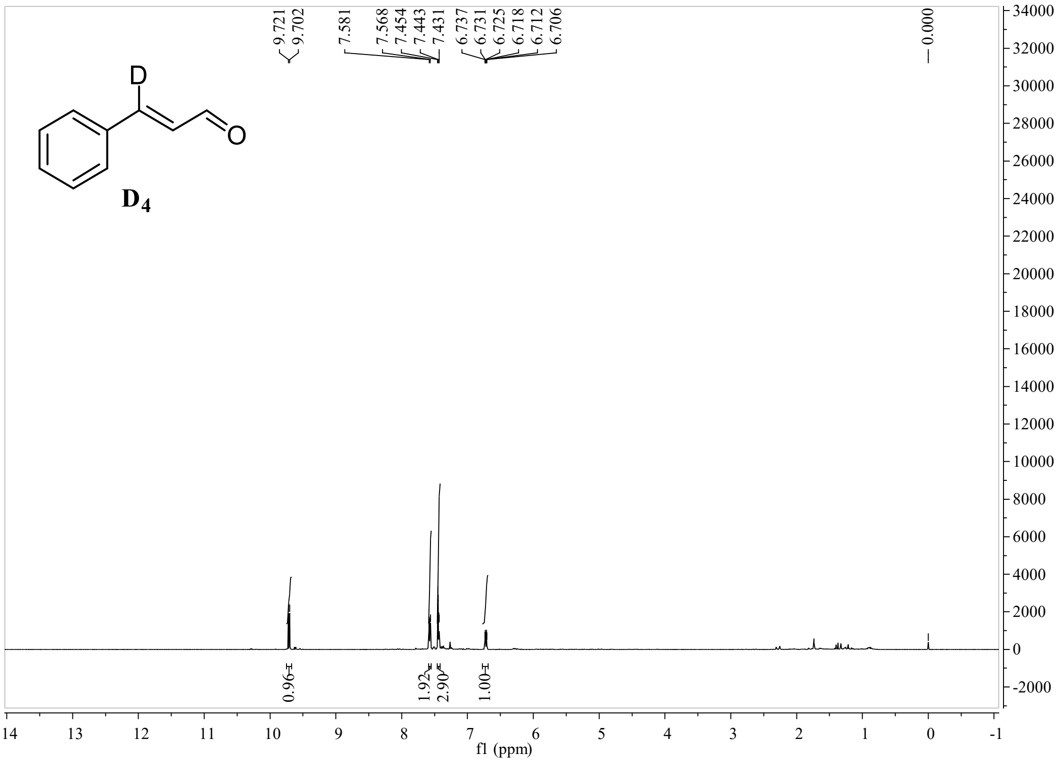


Figure S12 ^{1}H NMR spectrum of compound **D$_4$**, related to **Scheme 4**

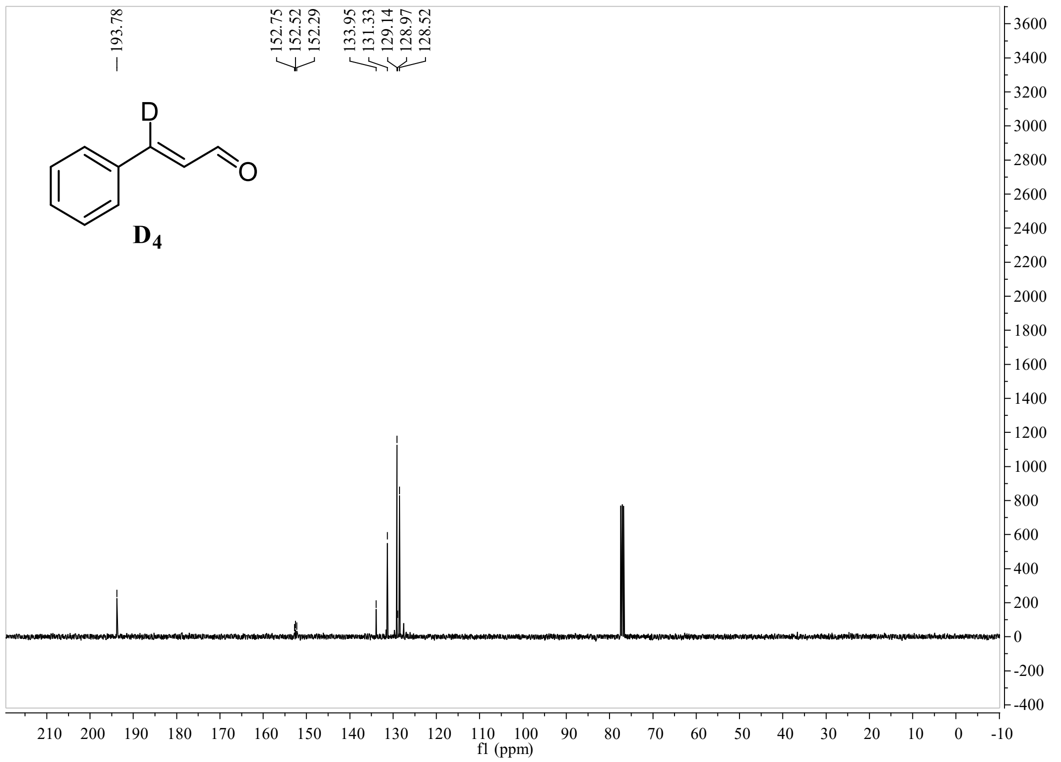


Figure S13 ^{13}C NMR spectrum of compound **D_4**, related to **Scheme 4**

[3-d_1]-3-phenylpropanal (D_5) (Diao et al., 2012) A 50 mL round bottom flask equipped with stir bar and septum was charged with EtOAc (10 mL), **D_4** (211.5 mg, 1.5 mmol), and 5% Pd/C (10 wt % of the substrate). A balloon was purged three times with H_2, and introduced into the reaction via a needle. The reaction was allowed to stir at room temperature under H_2 (1 atm) for 2 h. Filtration through a plug of celite and the solvent was removed in vacuo and the crude material was purified by column chromatography using a 10% EtOAc in hexane gradient to afford **D_5** as a colorless liquid (82% yield, 99% D). ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 9.79 (s, 1H, CHO), 7.32 – 7.24 (m, 2H, Ar-H), 7.23 – 7.17 (m, 3H, Ar-H), 2.92 (t, J = 7.4 Hz, 1H, β-H), 2.75 (d, J = 7.6 Hz, 2H, α-H). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 201.6, 140.4, 128.6, 128.3, 126.3, 45.2, 27.8 (t, J = 20.0 Hz). HRMS (ESI) for C_9H_9DNaO [M+Na$^+$]: Calcd: 158.0687; Found: 158.0683. IR (KBr): 3060, 3027, 2929, 2724, 1710, 1495, 1286, 792, 700 cm^{-1}.

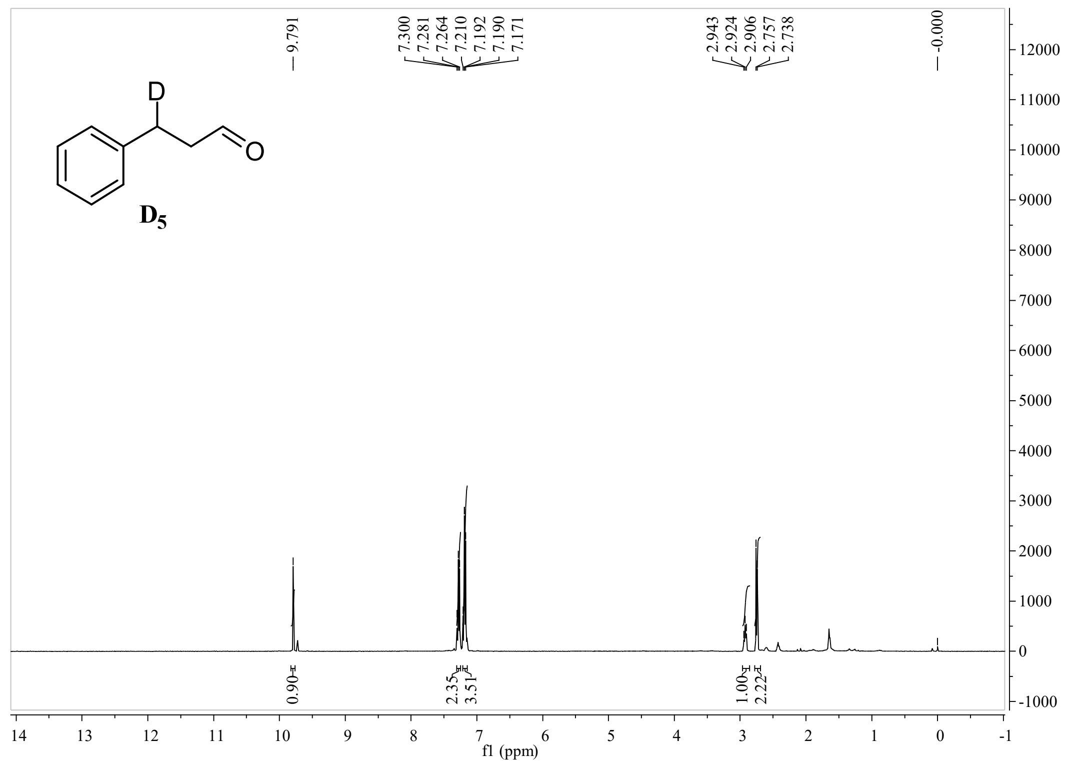


Figure S14 ^{1}H NMR spectrum of compound **D$_5$**, related to **Scheme 4**

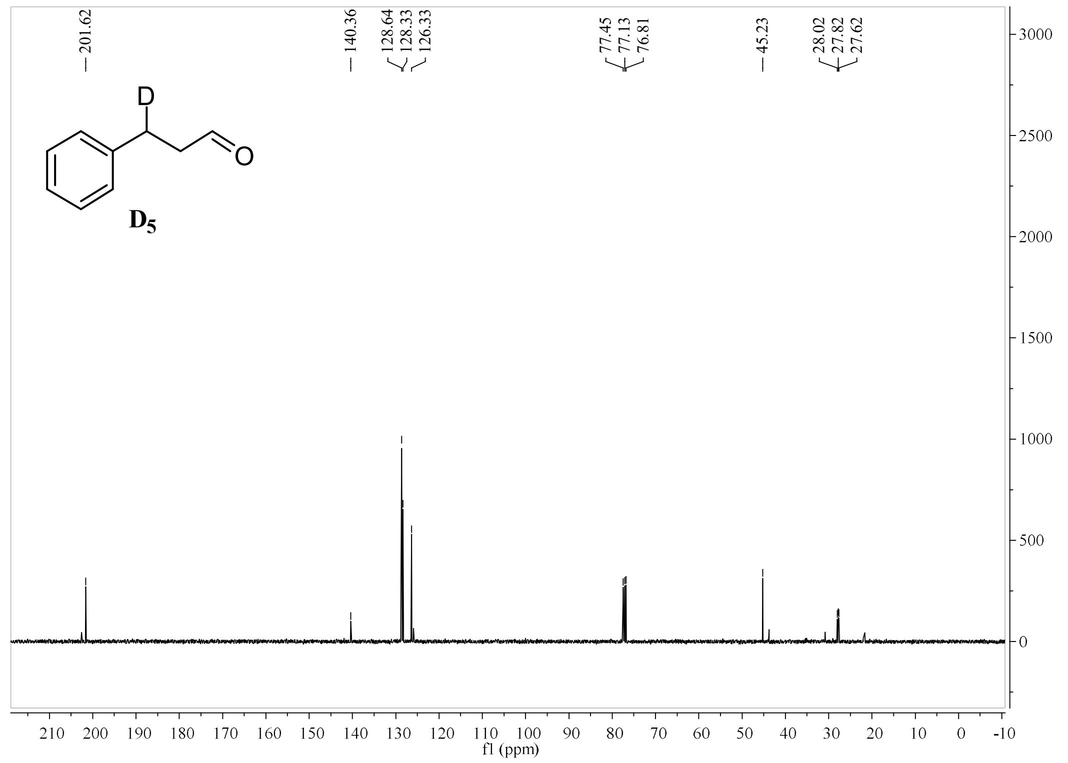


Figure S15 ^{1}H NMR spectrum of compound **D$_5$**, related to **Scheme 4**

[6-*d$_1$*]-(*E*)-6-phenylhex-3-en-2-one (S2-*d$_1$*) (Diao et al., 2012) A mixture of (acetylmethylene)Triphenylphosphorane (1 g, 3.3 mmol) and **D$_3$** (321 mg, 3.0 mmol) was heated at 80 °C in a two necked round bottom flask using 1,2-dichloroethane (10.0 mL) as solvent for 16 hour. The completion of the reaction was monitored by TLC. Then solvent was evaporated in rotary evaporator under reduced pressure to obtain the residue. The residue was purified by flash column chromatography on silica gel to isolate the product. The product was obtained colorless liquid. (92% Yield, 99% D). ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 7.33 – 7.24 (m, 2H, Ar-H), 7.23 – 7.12 (m, 3H, Ar-H), 6.81 (dt, J = 15.6, 6.8 Hz, 1H, β-H), 6.08 (d, J = 15.9 Hz, 1H, α-H), 2.75 (t, J = 7.4 Hz, 1H, CHD), 2.56 – 2.47 (m, 2H, CH_2), 2.21 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 198.6, 147.1, 140.6, 131.7, 128.5, 128.3, 126.2, 34.3 – 33.7 (m, 2C), 26.9. HRMS (ESI) for $C_{12}H_{13}DNaO$ [M+Na$^+$]: Calcd: 198.1000; Found: 198.0996. IR (KBr): 3313, 3058, 3026, 2926, 1673, 1628, 1360, 1255, 979, 741, 700 cm^{-1}.

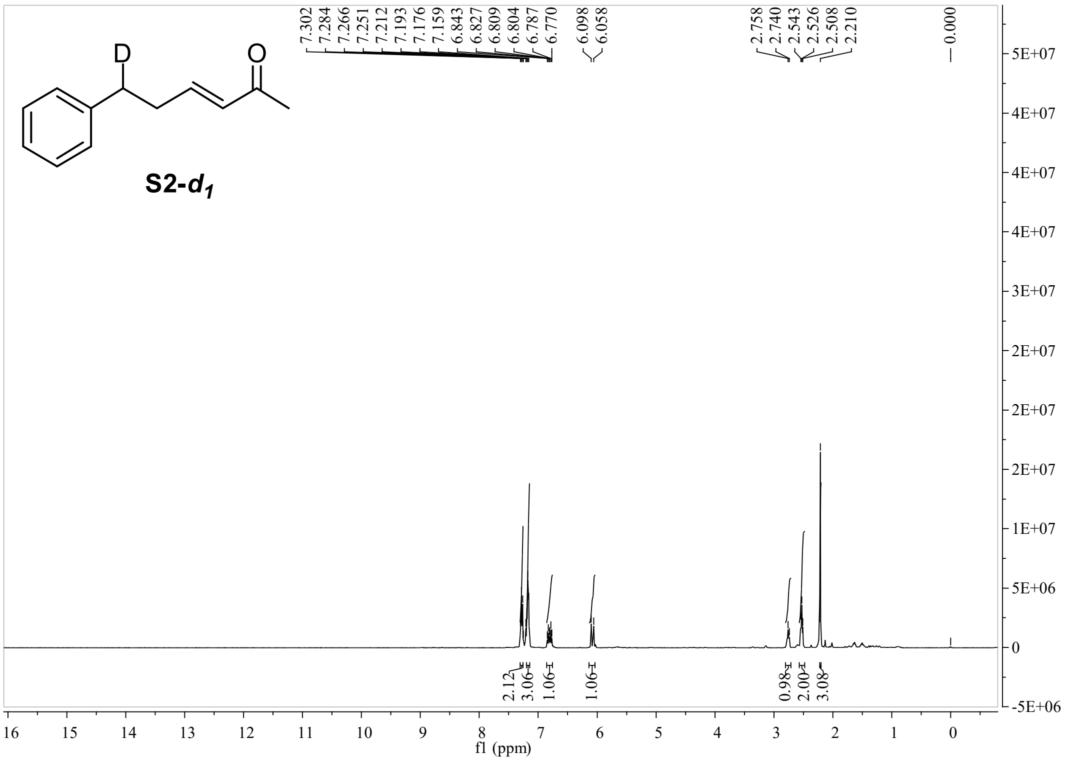


Figure S16 ^{1}H NMR spectrum of compound **S2-d_1**, related to **Scheme 4**

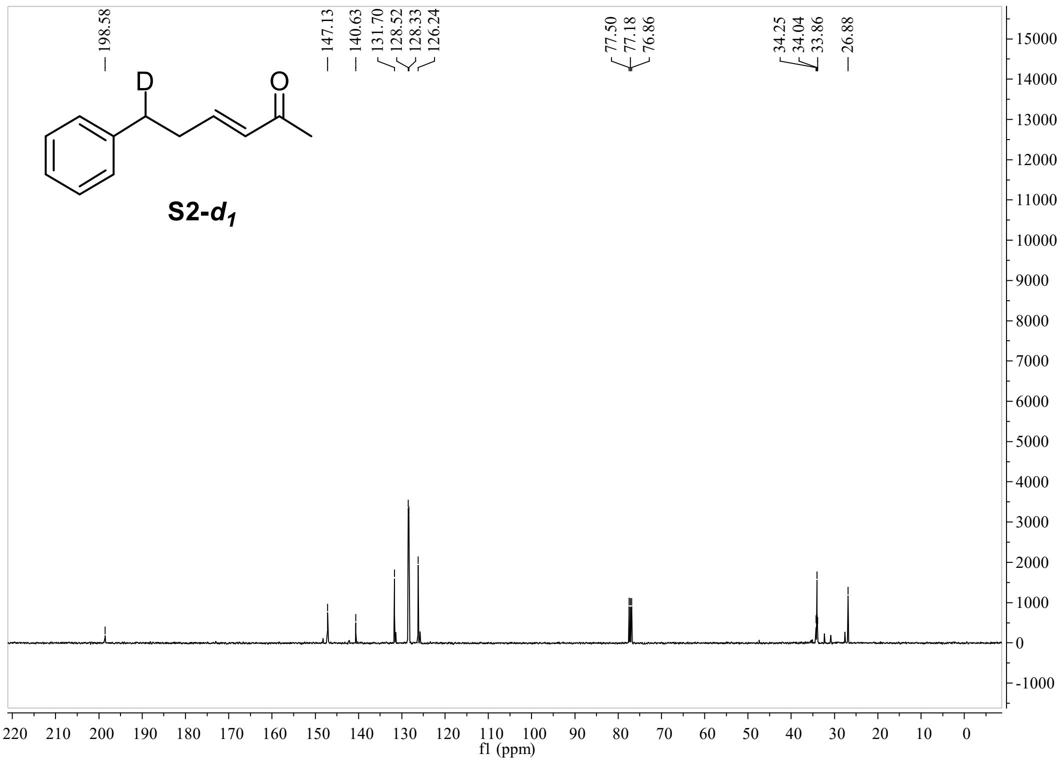


Figure S17 ^{13}C NMR spectrum of compound **S2-d_1**, related to **Scheme 4**

KIE experiment: We use deuterated S2-d_1 as starting materials to compare the initial reaction rates.

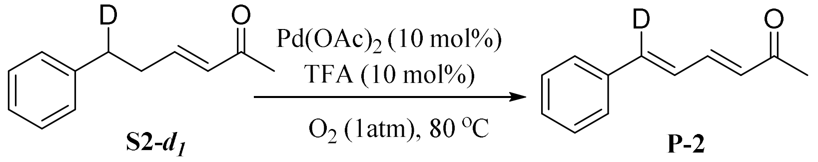


Figure S18 KIE experiment, related to **Scheme 4**

[6-*d*]-(3*E*,5*E*)-6-phenylhexa-3,5-dien-2-one. A seal tube containing **S2-d_1** (100%-D, 0.5 mmol) and Pd(OAc)$_2$ (10 mol%), was evacuated and filled with dioxygen gas using an oxygen containing balloon. Then, Dry DMSO (5 mL), trifluoroacetic acid (TFA) (1.0 mmol) were sequentially added to the system via syringe under an oxygen atmosphere. The reaction mixture was stirred at 80 °C until completion of the reaction (TLC). Then the reaction was cooled to RT and partitioned between water and ethyl acetate. The layers were separated and the organic layer was washed with aqueous saturated brine solution, dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. ^{1}H NMR specture was recorded without Further purification. (90% yield, 56% D). **k_H / k_D = 1.2 was also obtained by calculation of the ratio of two products.**

The ^{1}H NMR specture as follows:

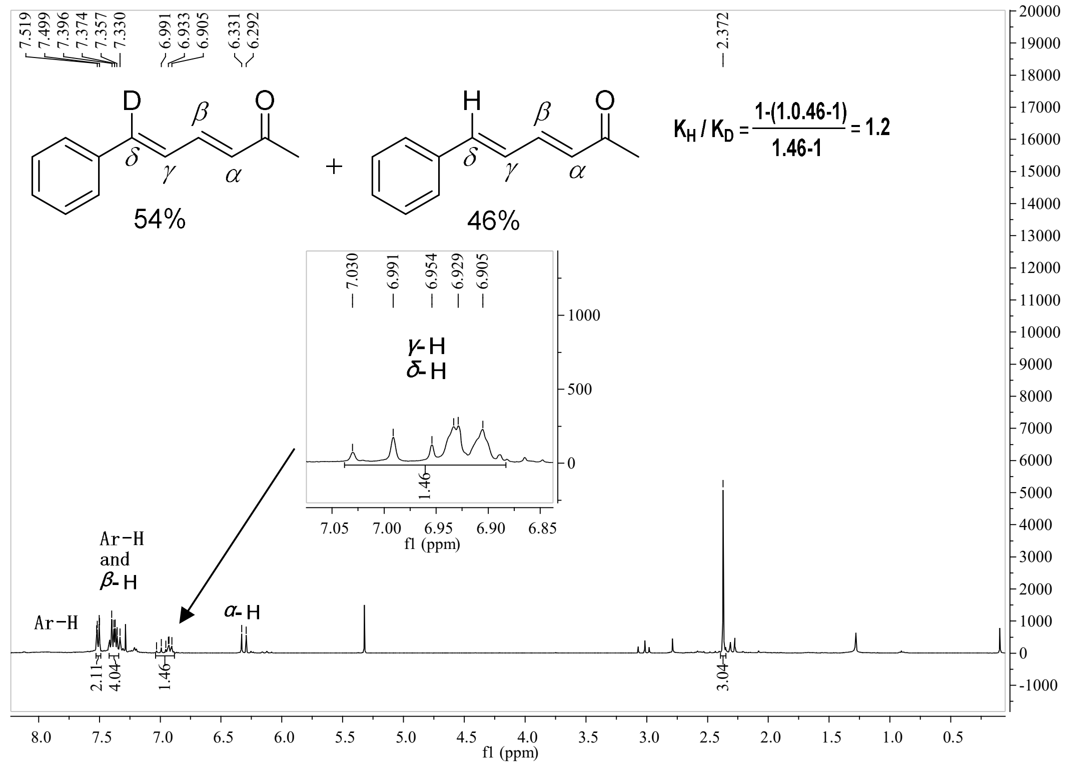


Figure S19 ^{1}H NMR spectrum for the KIE value, related to **Scheme 4**

4. Supplemental references

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5. Supplemental Figures for ^{1}H and ^{13}C NMR spectra

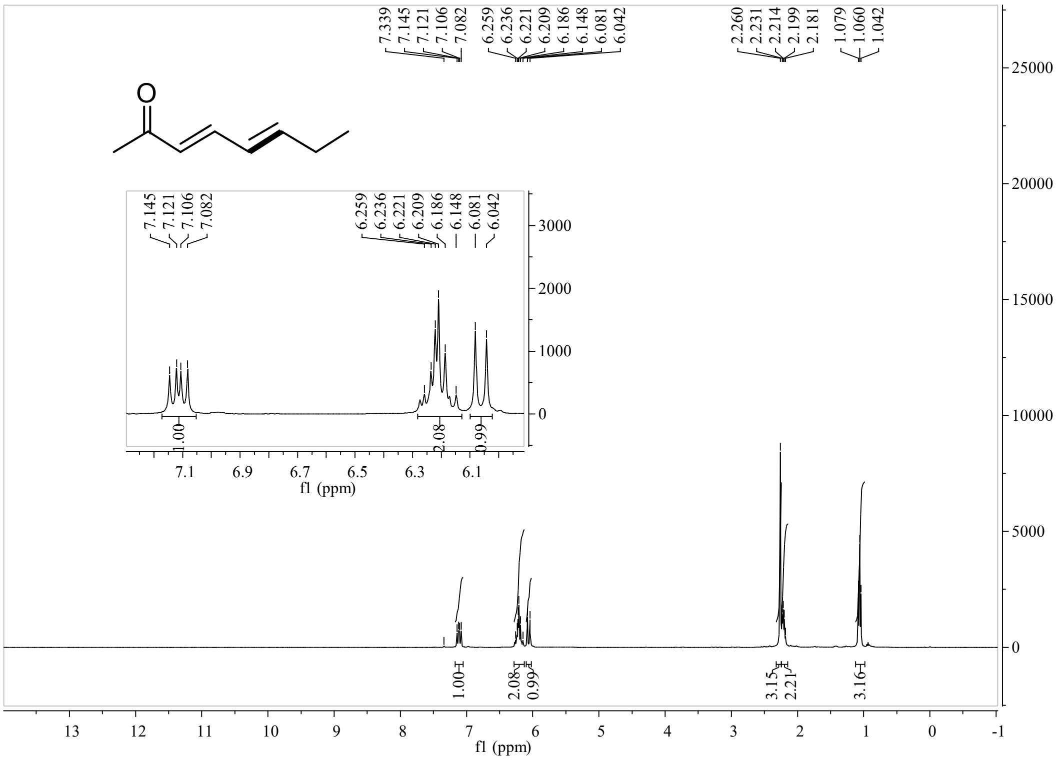

Figure S20 ^{1}H NMR spectrum of compound **2aa**, related to **Scheme 2**

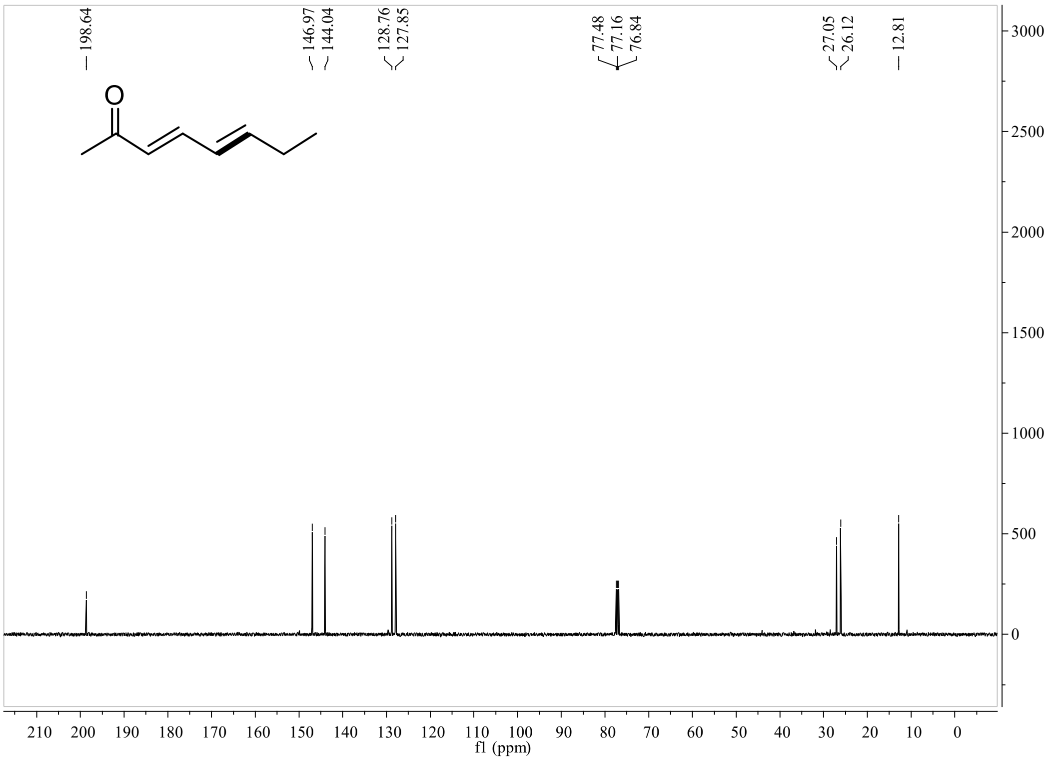

Figure S21 ^{13}C NMR spectrum of compound **2aa**, related to **Scheme 2**

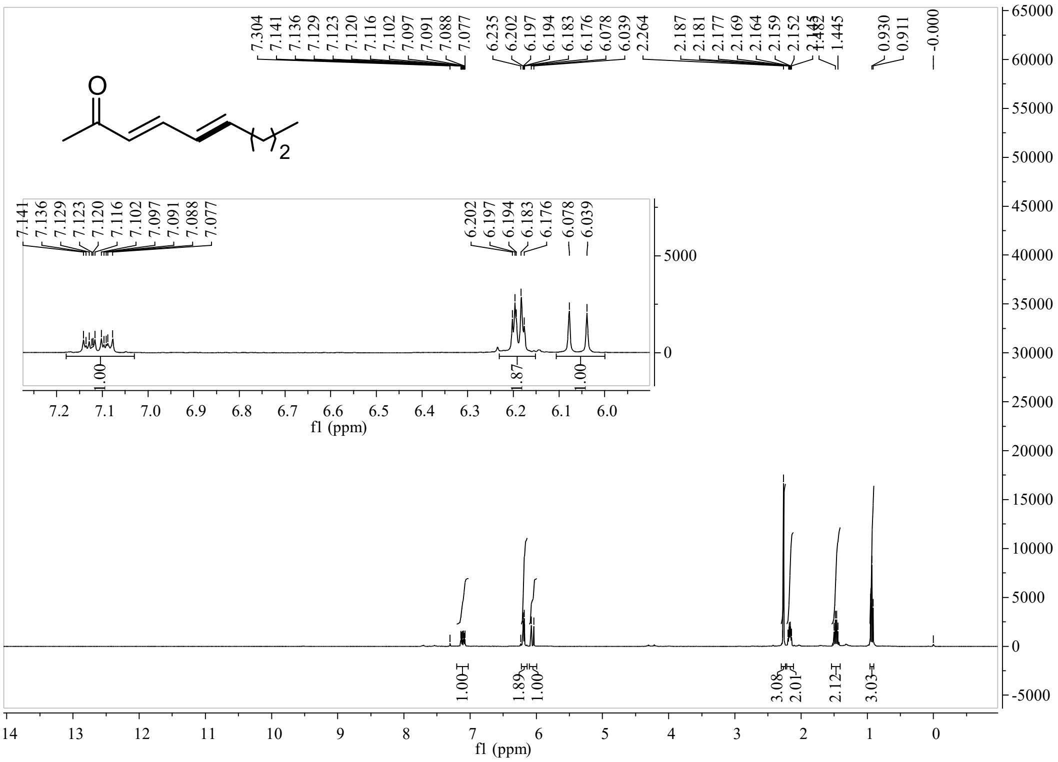

Figure S22 ^{1}H NMR spectrum of compound **2ab**, related to **Scheme 2**

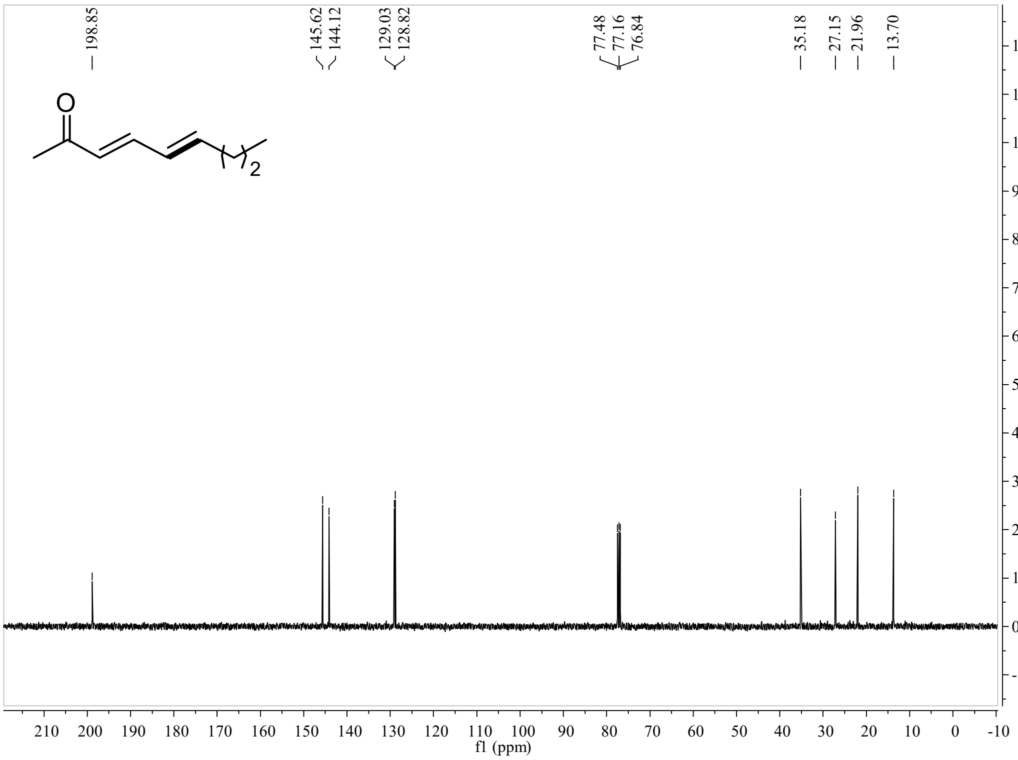

Figure S23 ^{13}C NMR spectrum of compound **2ab**, related to **Scheme 2**

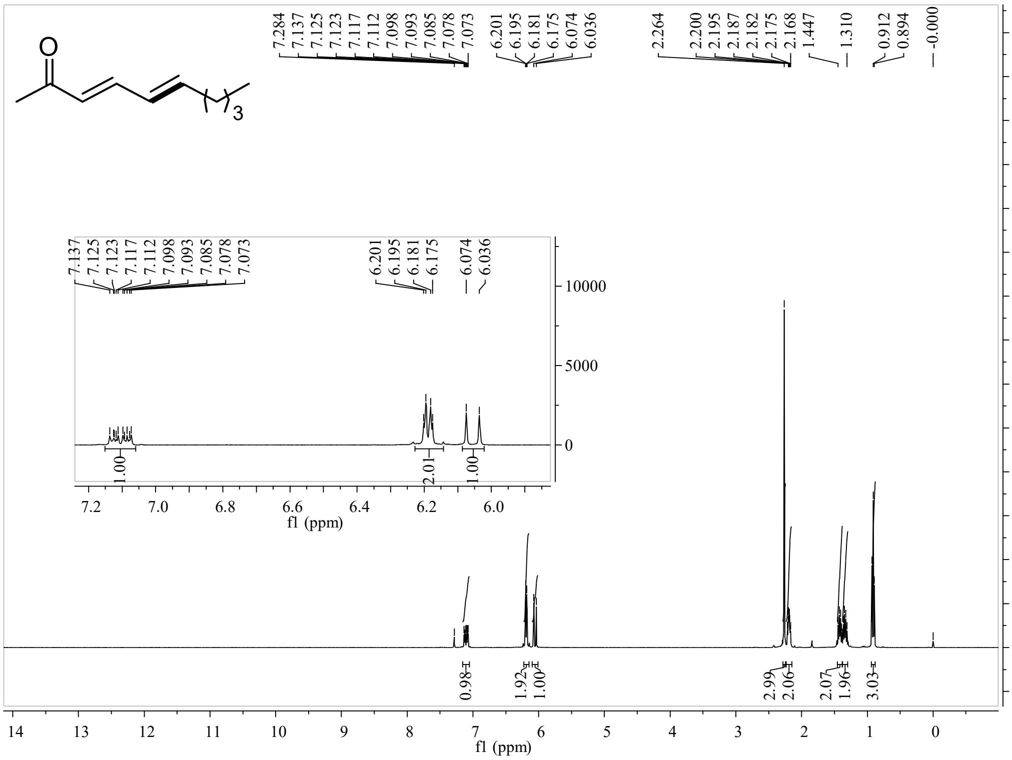

Figure S24 ^{1}H NMR spectrum of compound **2ac**, related to **Scheme 2**

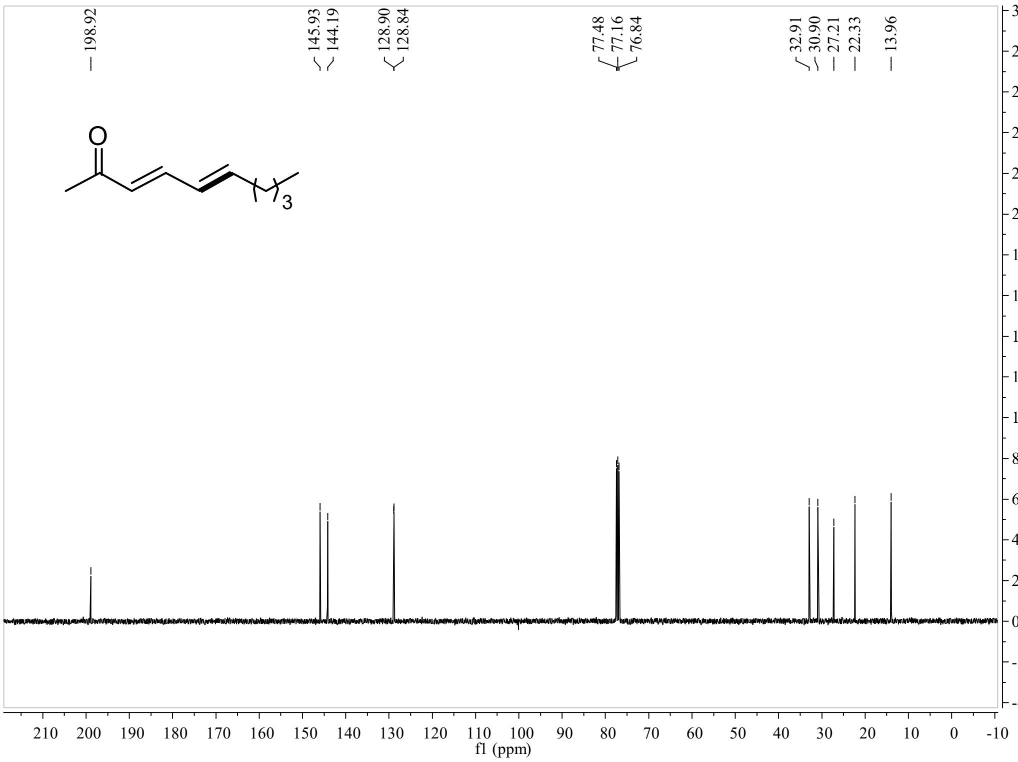

Figure S25 ^{13}C NMR spectrum of compound **2ac**, related to **Scheme 2**

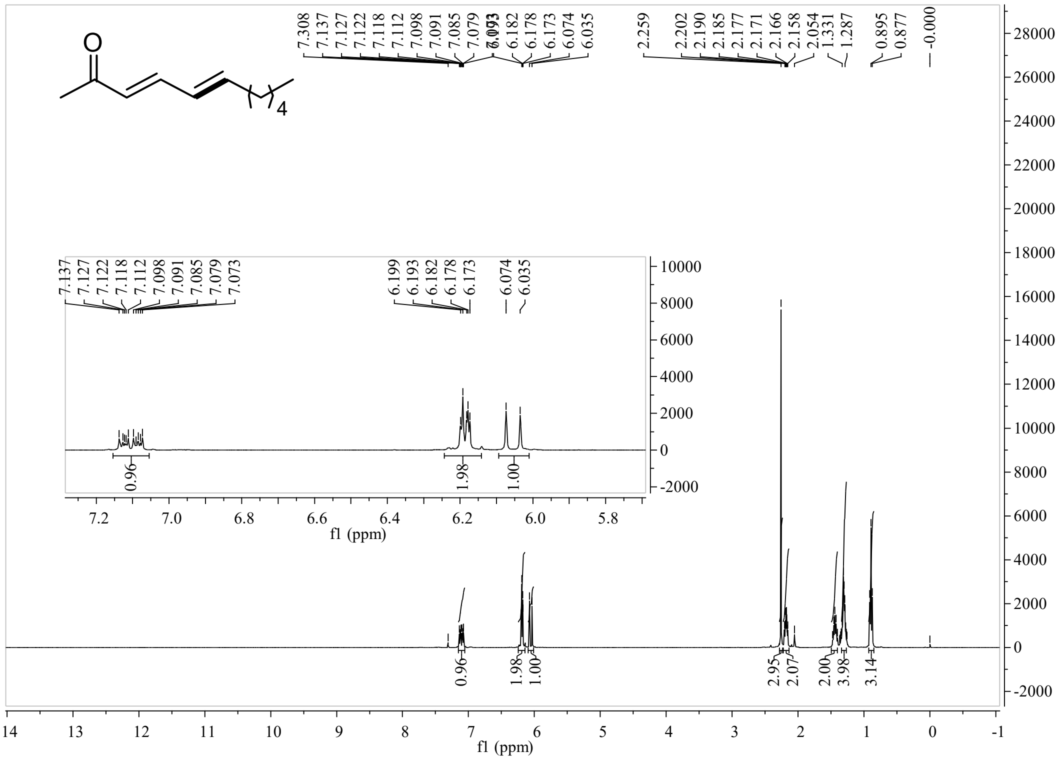

Figure S26 ^{1}H NMR spectrum of compound **2ad**, related to **Scheme 2**

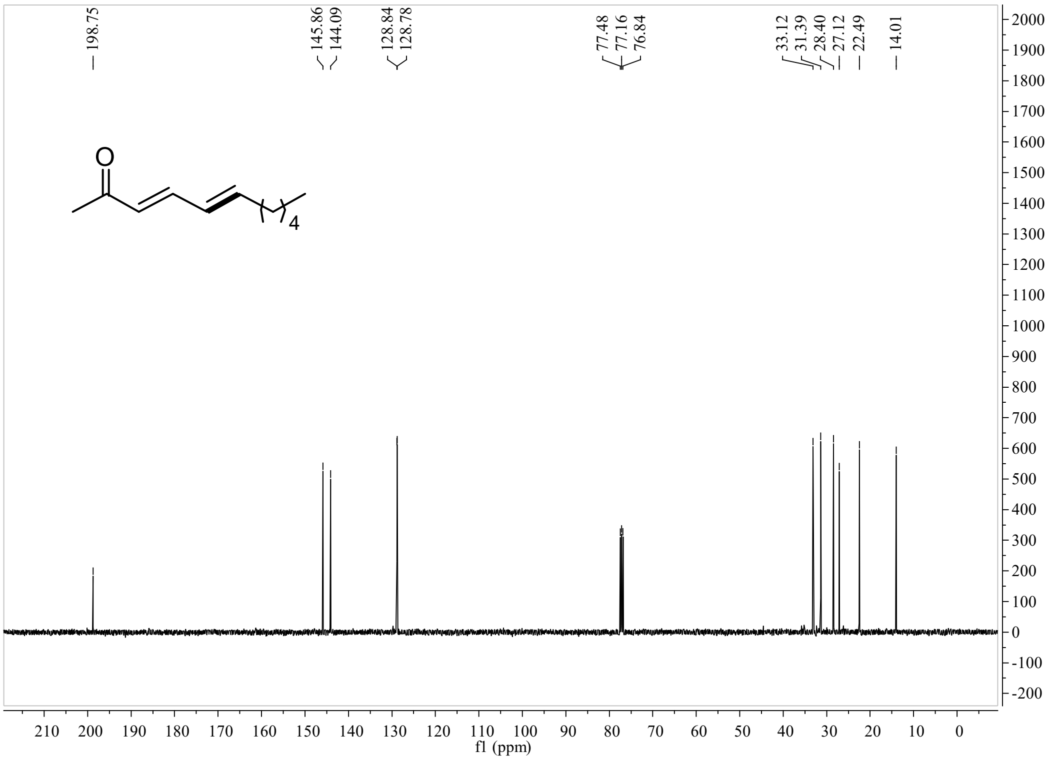

Figure S27 ^{13}C NMR spectrum of compound **2ad**, related to **Scheme 2**

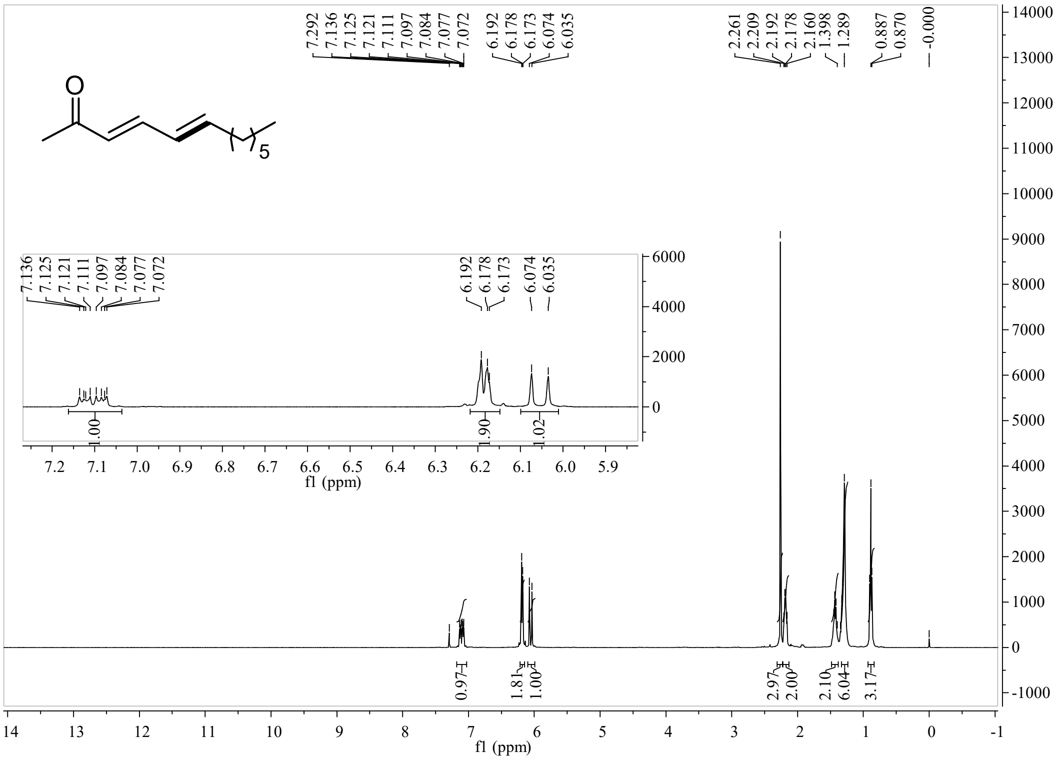

Figure S28 ^{1}H NMR spectrum of compound **2ae**, related to **Scheme 2**

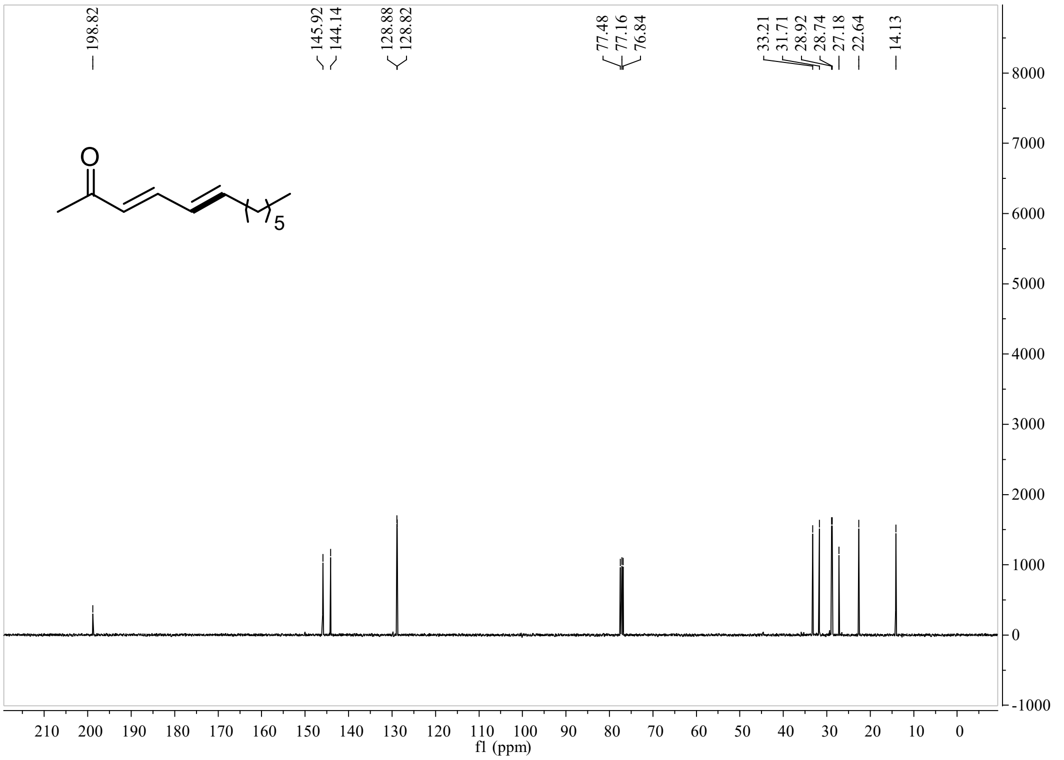

Figure S29 ^{13}C NMR spectrum of compound **2ae**, related to **Scheme 2**

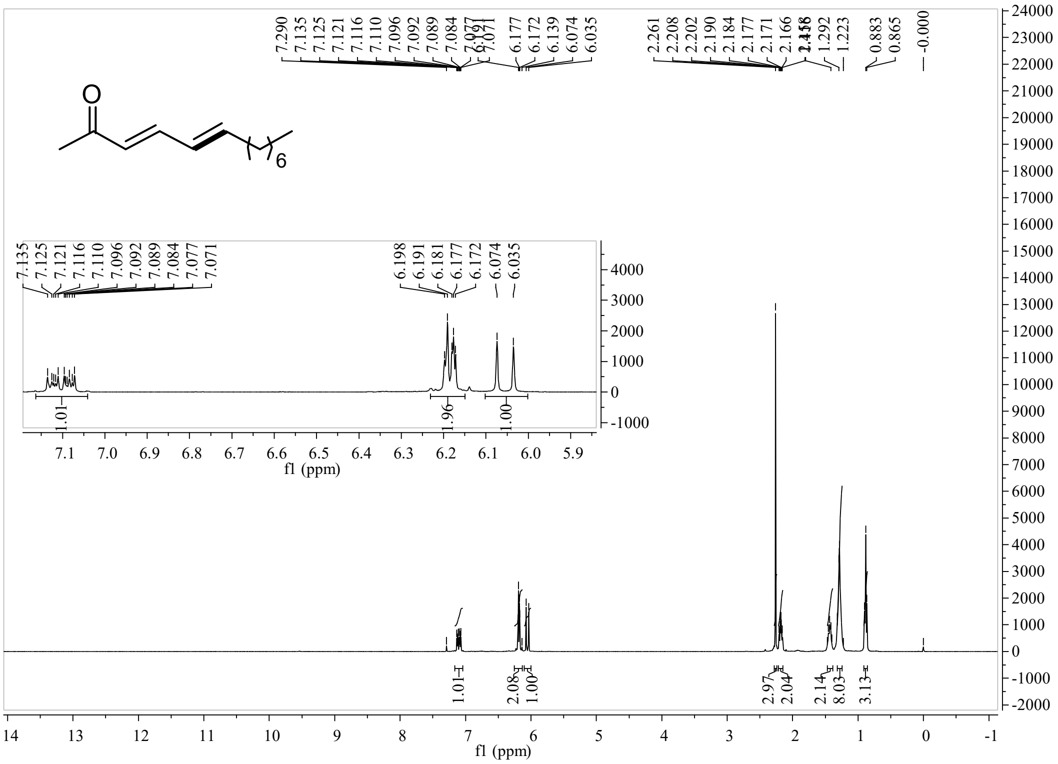

Figure S30 ^{1}H NMR spectrum of compound **2af**, related to **Scheme 2**

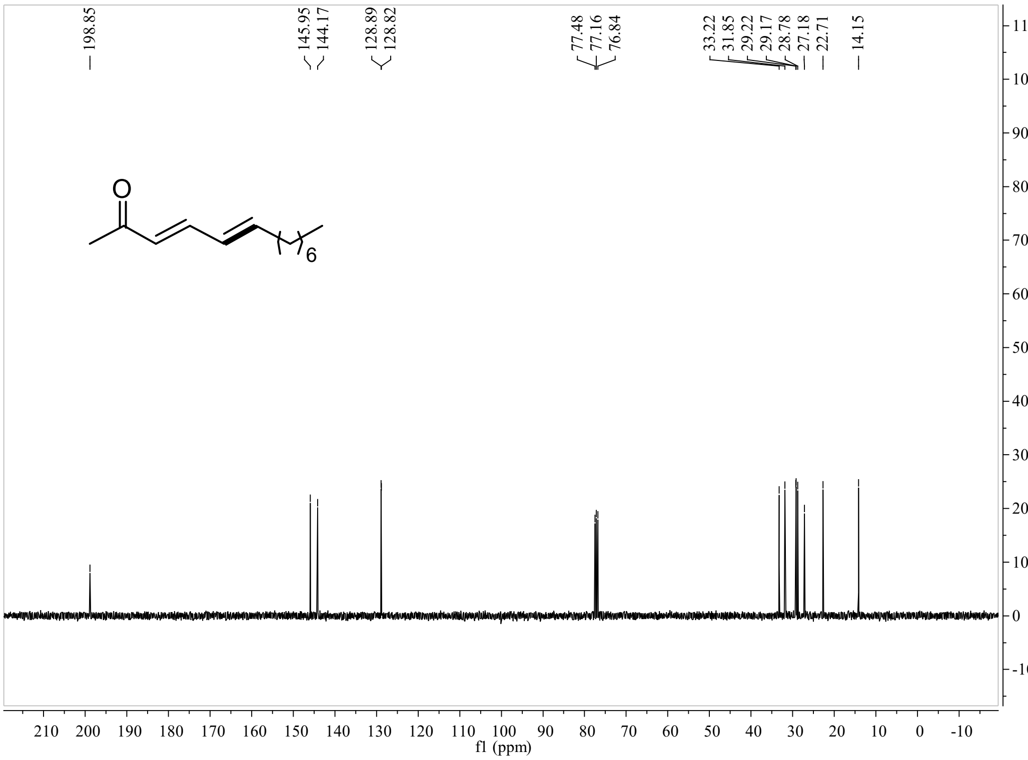

Figure S31 ^{13}C NMR spectrum of compound **2af**, related to **Scheme 2**

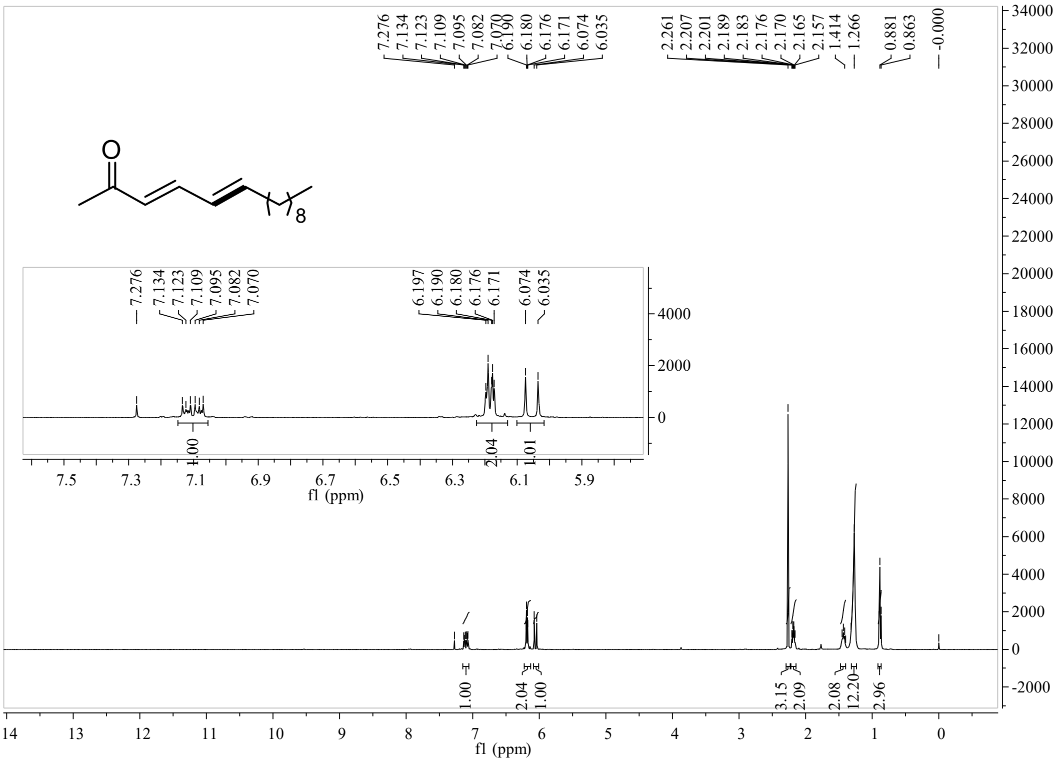

Figure S32 ^{1}H NMR spectrum of compound **2ag**, related to **Scheme 2**

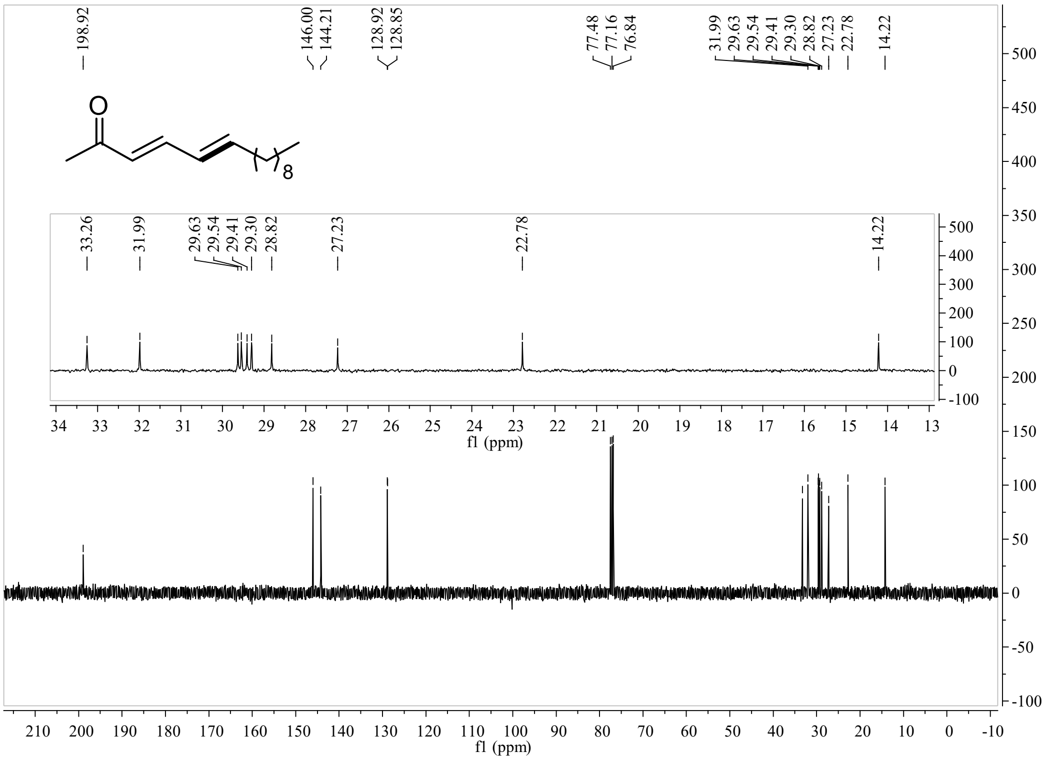

Figure S33 ^{13}C NMR spectrum of compound **2ag**, related to **Scheme 2**

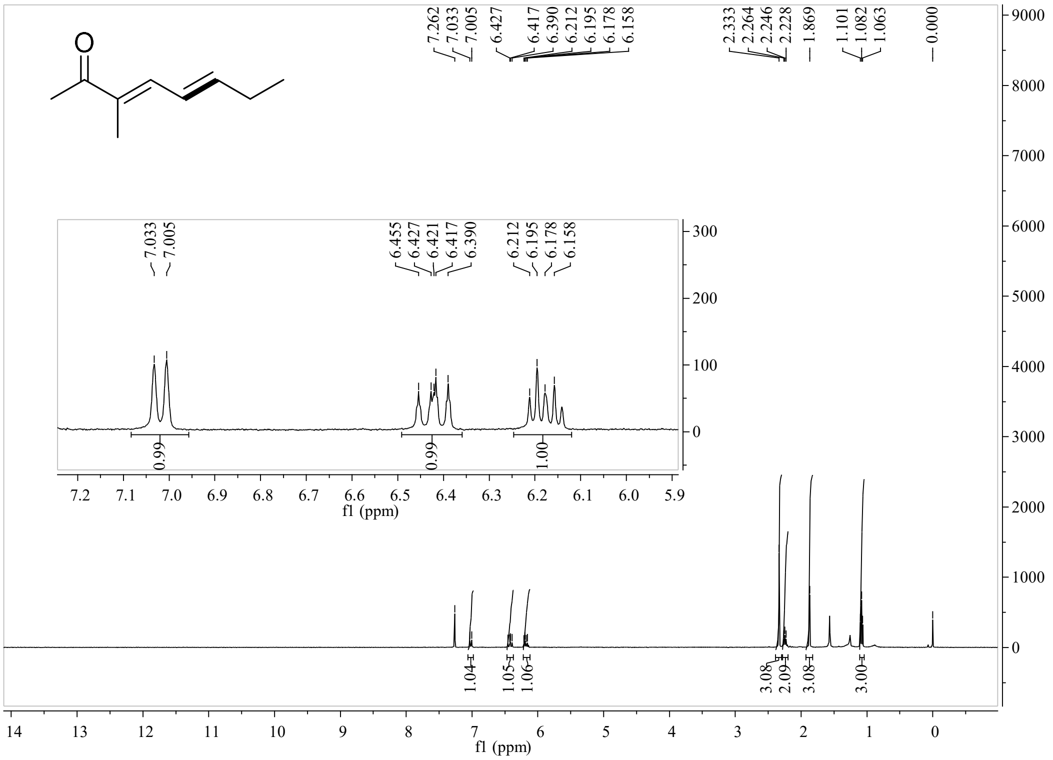

Figure S34 ^{1}H NMR spectrum of compound **2ah**, related to **Scheme 2**

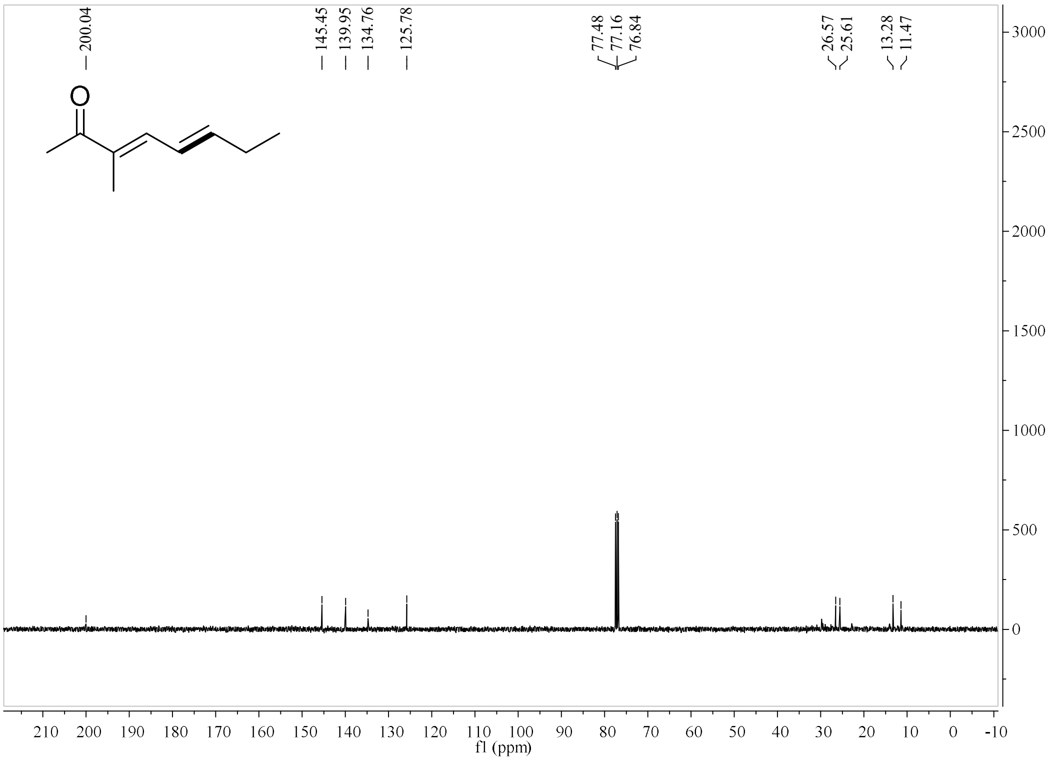

Figure S35 ^{13}C NMR spectrum of compound **2ah**, related to **Scheme 2**

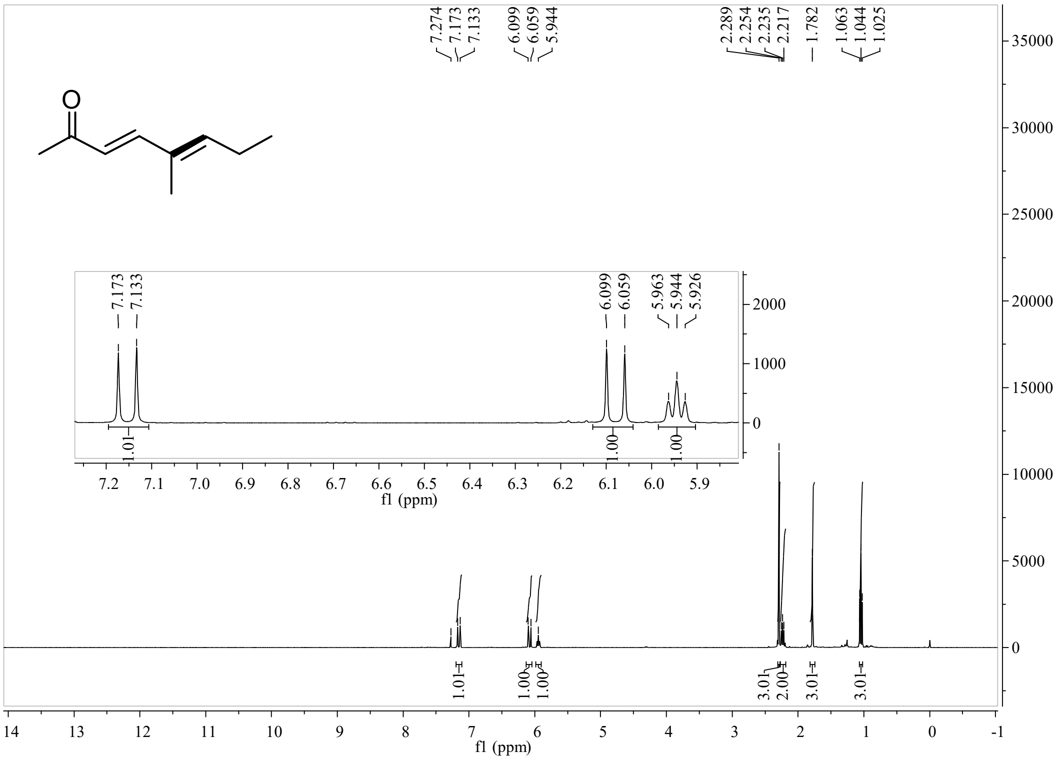

Figure S36 ^{1}H NMR spectrum of compound **2ai**, related to **Scheme 2**

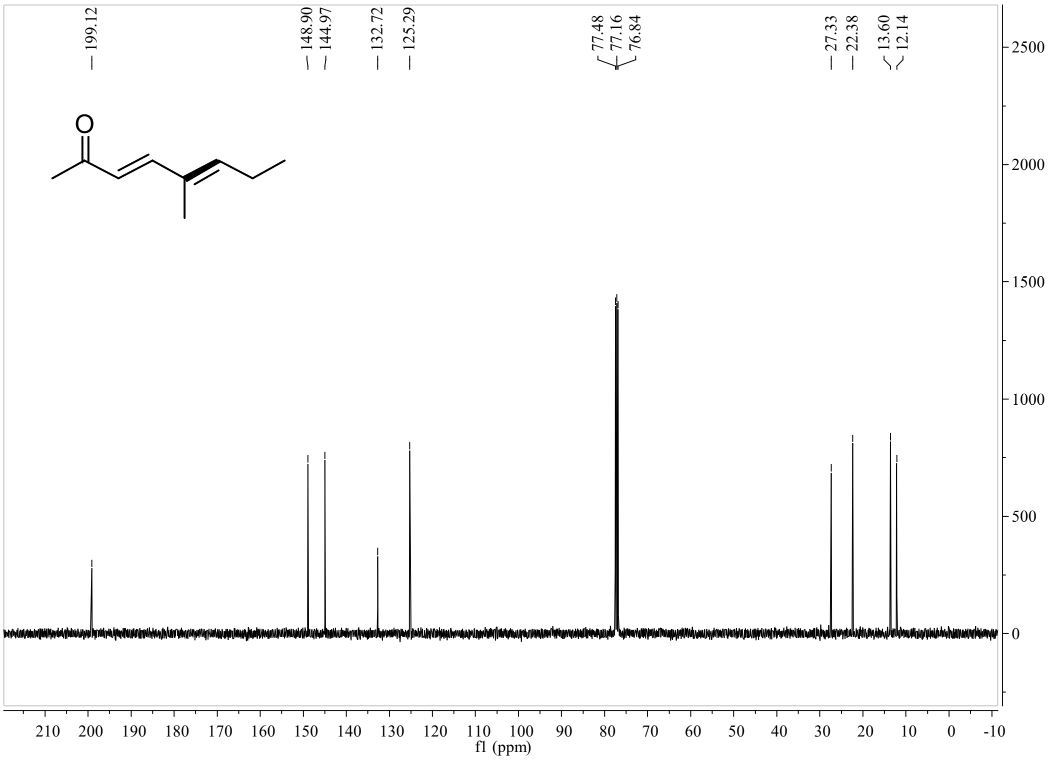

Figure S37 ^{13}C NMR spectrum of compound **2ai**, related to **Scheme 2**

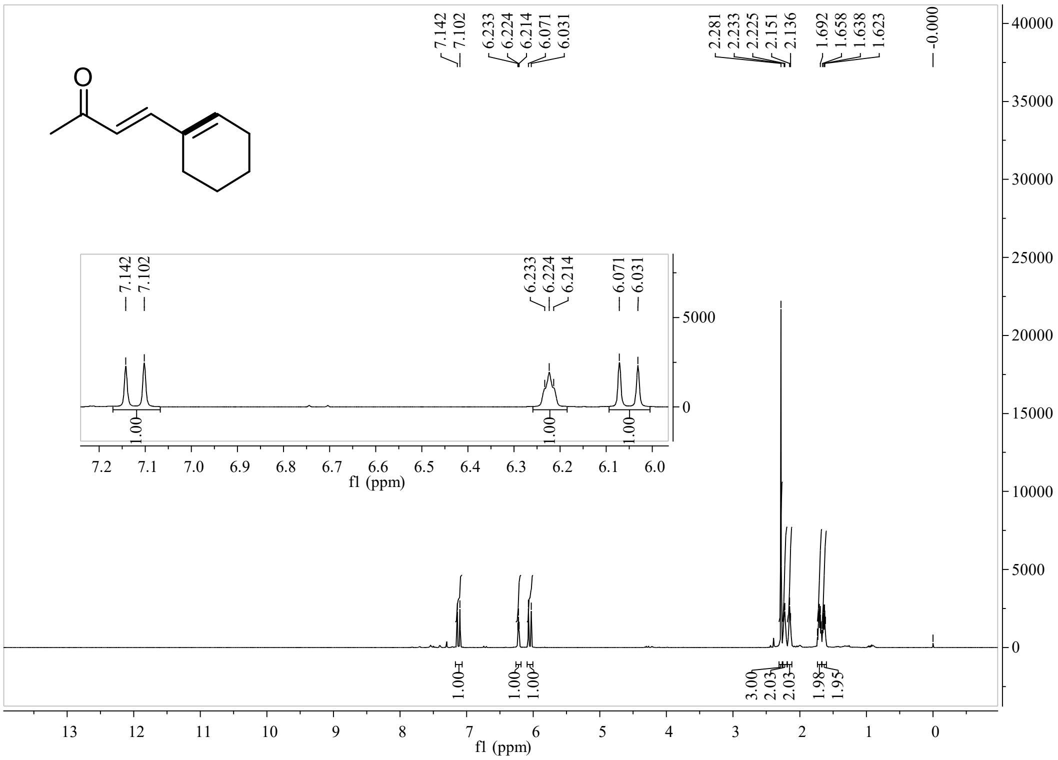

Figure S38 ^{1}H NMR spectrum of compound **2aj**, related to **Scheme 2**

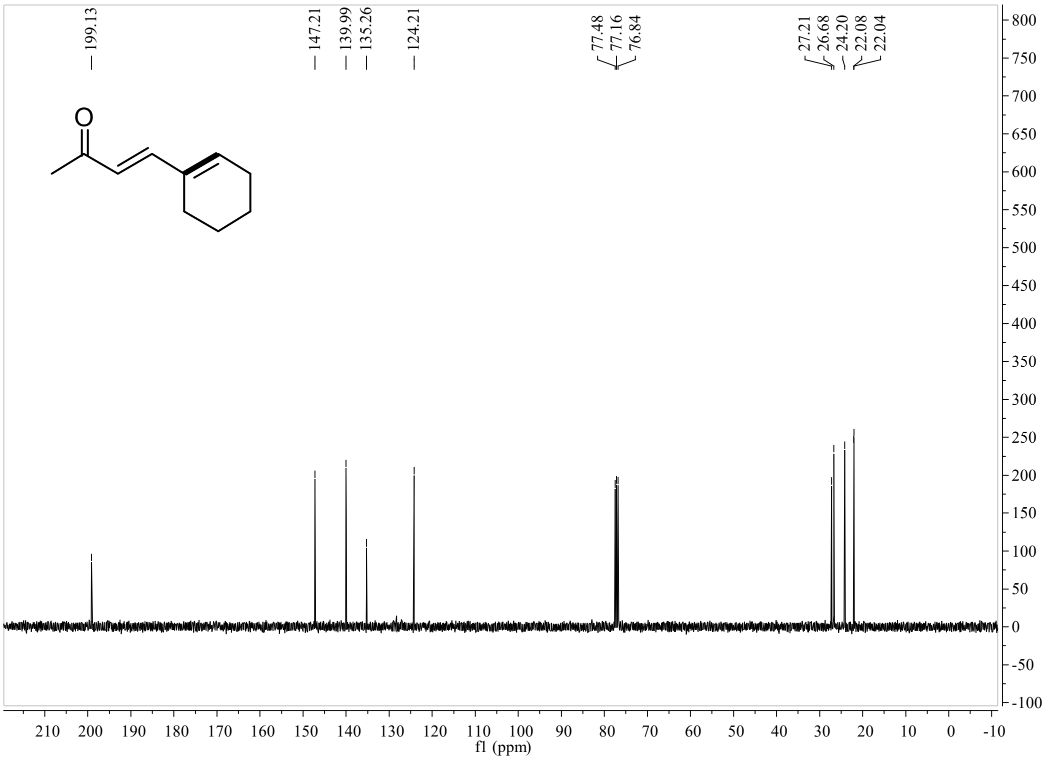

Figure S39 ^{13}C NMR spectrum of compound **2aj**, related to **Scheme 2**

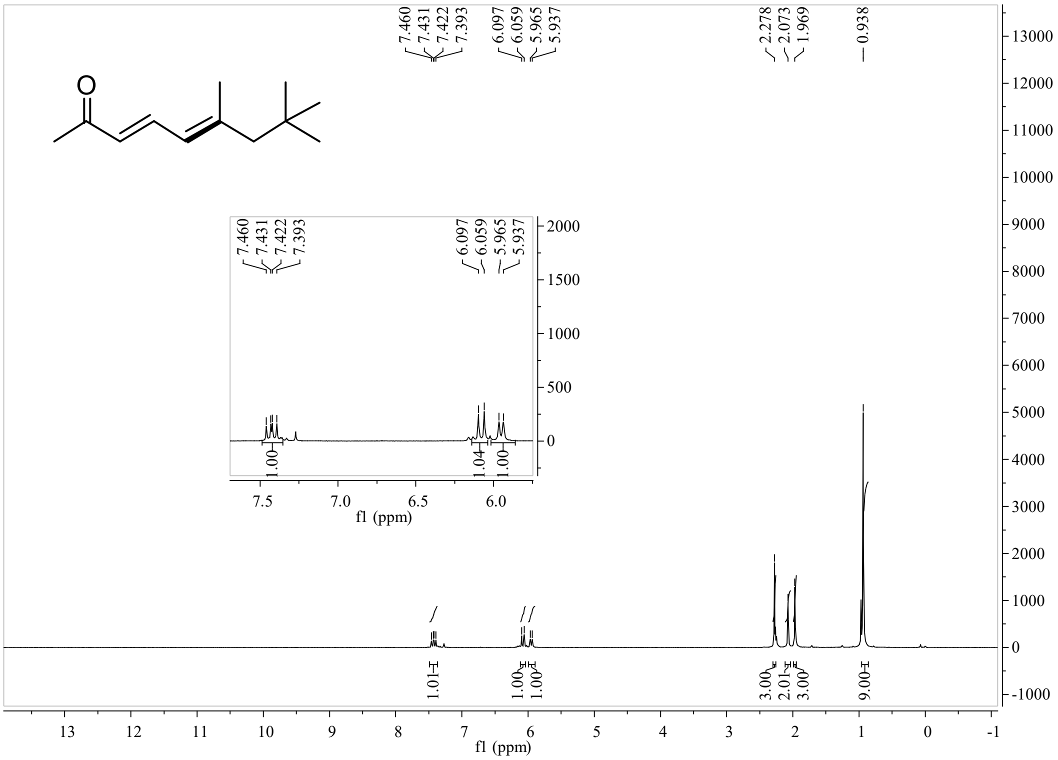

Figure S40 ^{1}H NMR spectrum of compound **2ak**, related to **Scheme 2**

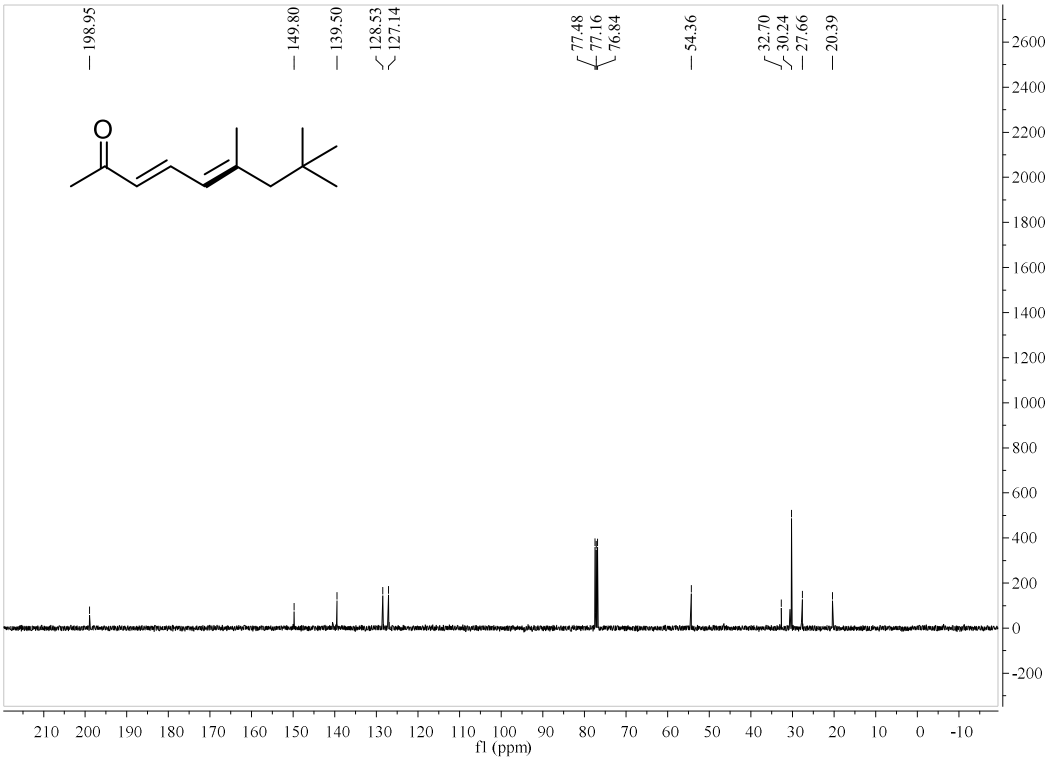

Figure S41 ^{13}C NMR spectrum of compound **2ak**, related to **Scheme 2**

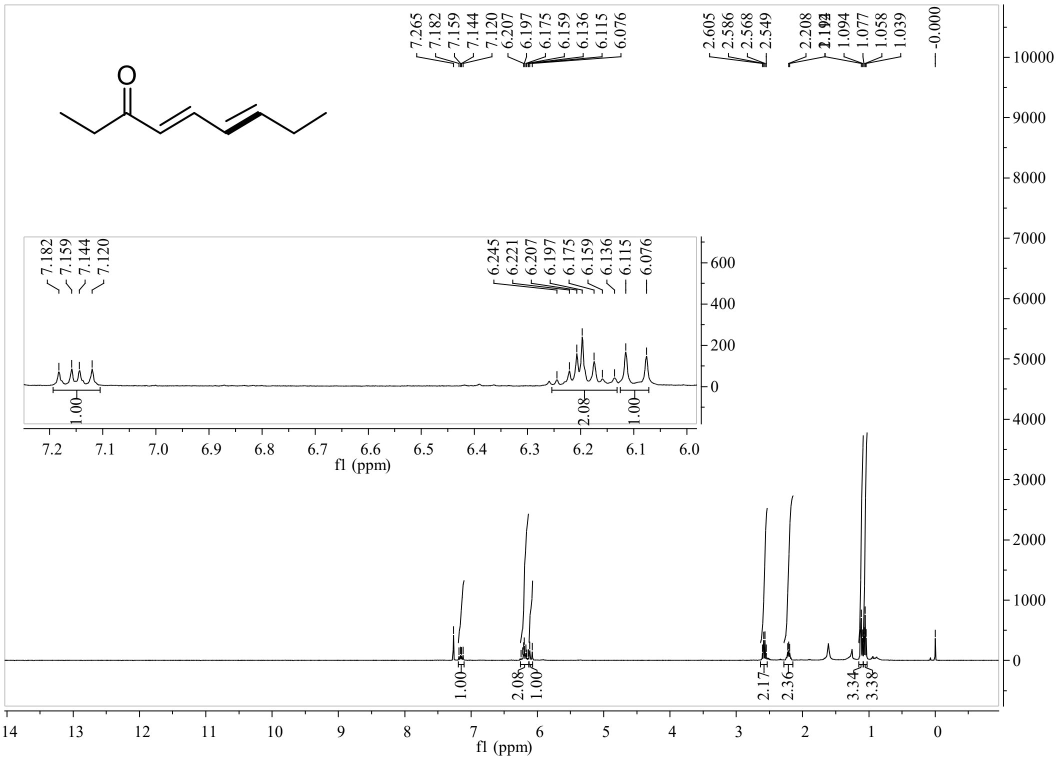

Figure S42 ^{1}H NMR spectrum of compound **2al**, related to **Scheme 2**

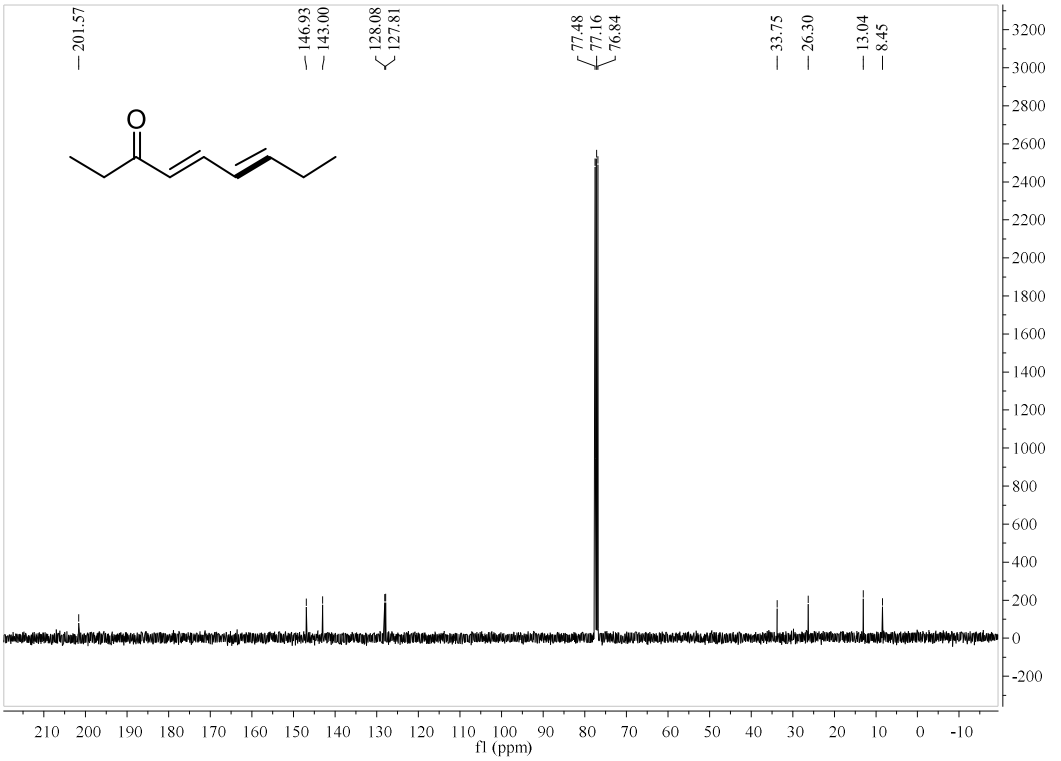

Figure S43 ^{13}C NMR spectrum of compound **2al**, related to **Scheme 2**

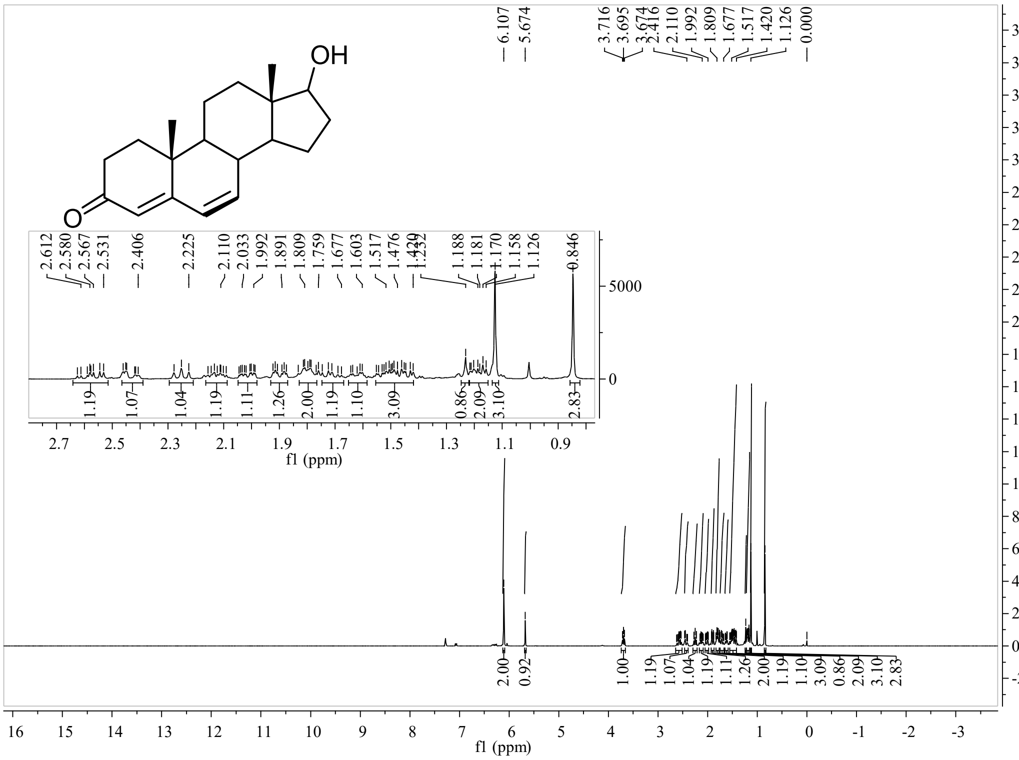

Figure S44 ^{1}H NMR spectrum of compound **2am**, related to **Scheme 2**

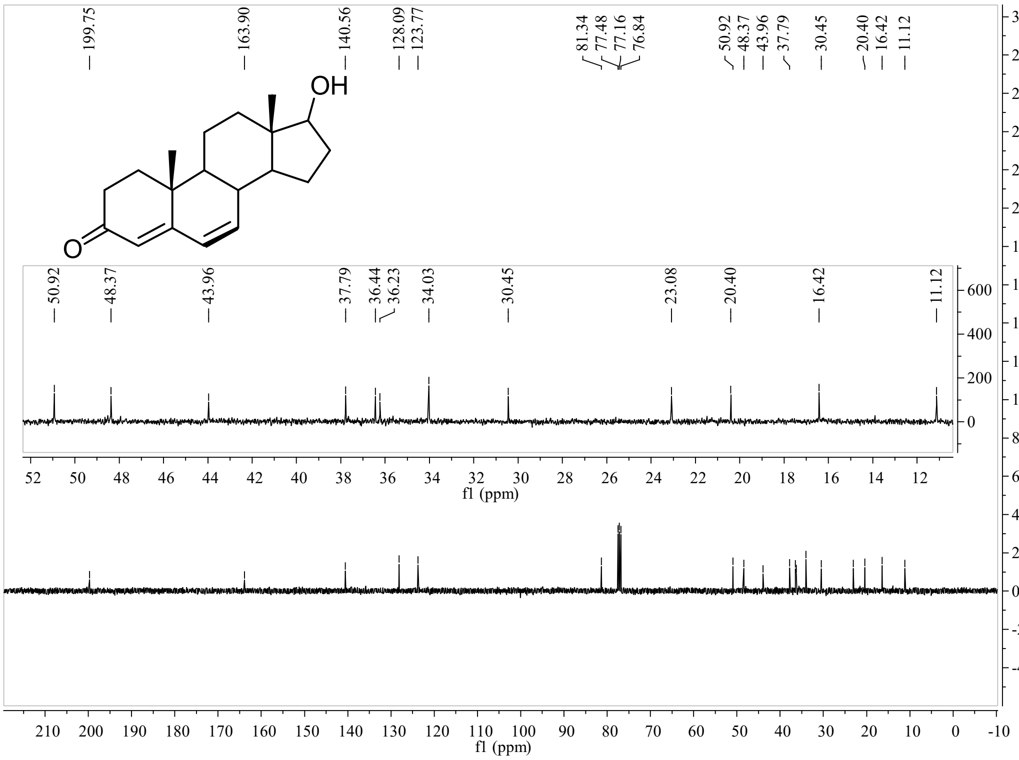

Figure S45 ^{13}C NMR spectrum of compound **2am**, related to **Scheme 2**

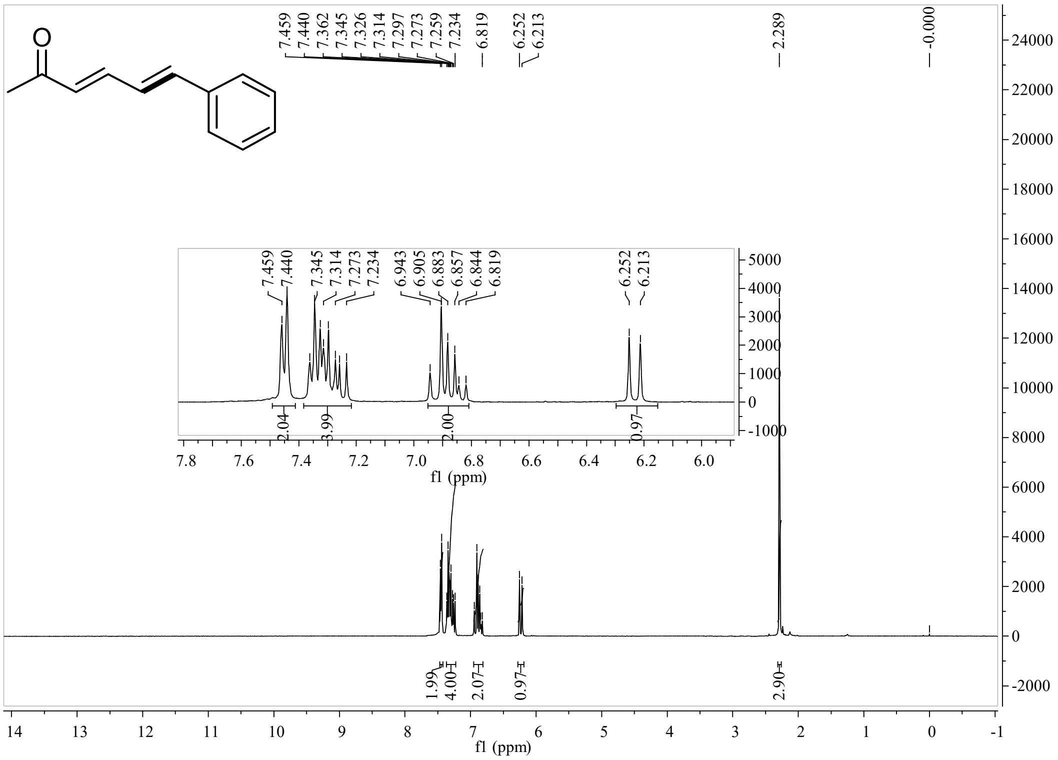

Figure S46 ^{1}H NMR spectrum of compound **2an**, related to **Scheme 2**

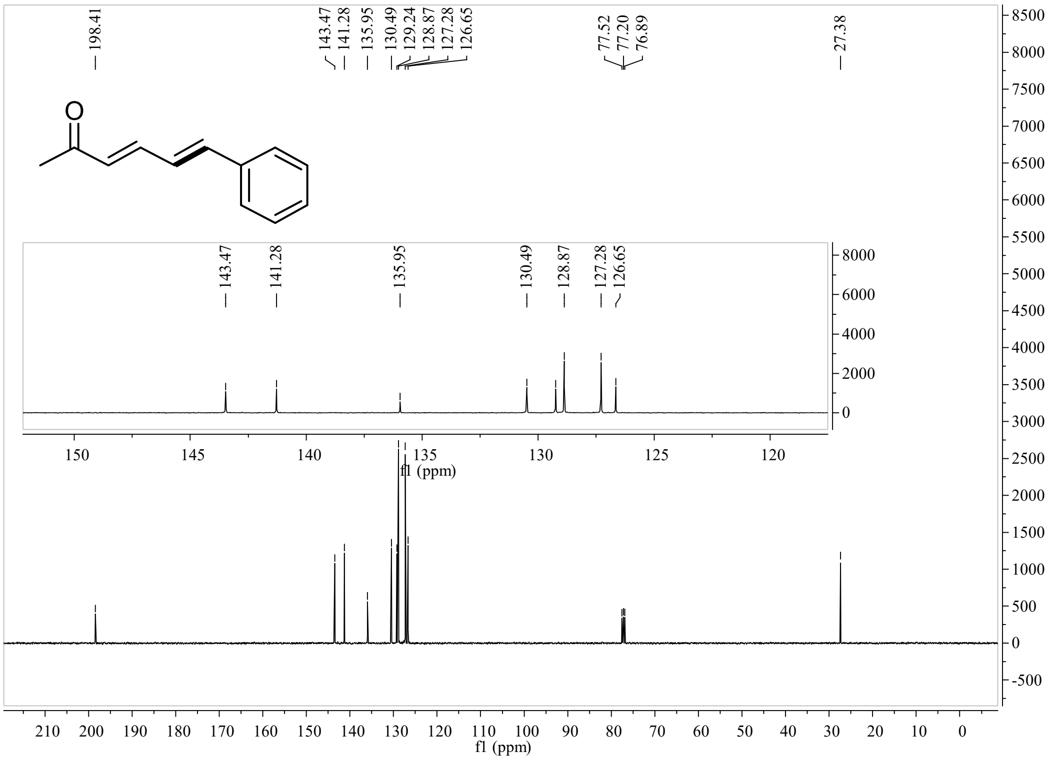

Figure S47 ^{13}C NMR spectrum of compound **2an**, related to **Scheme 2**

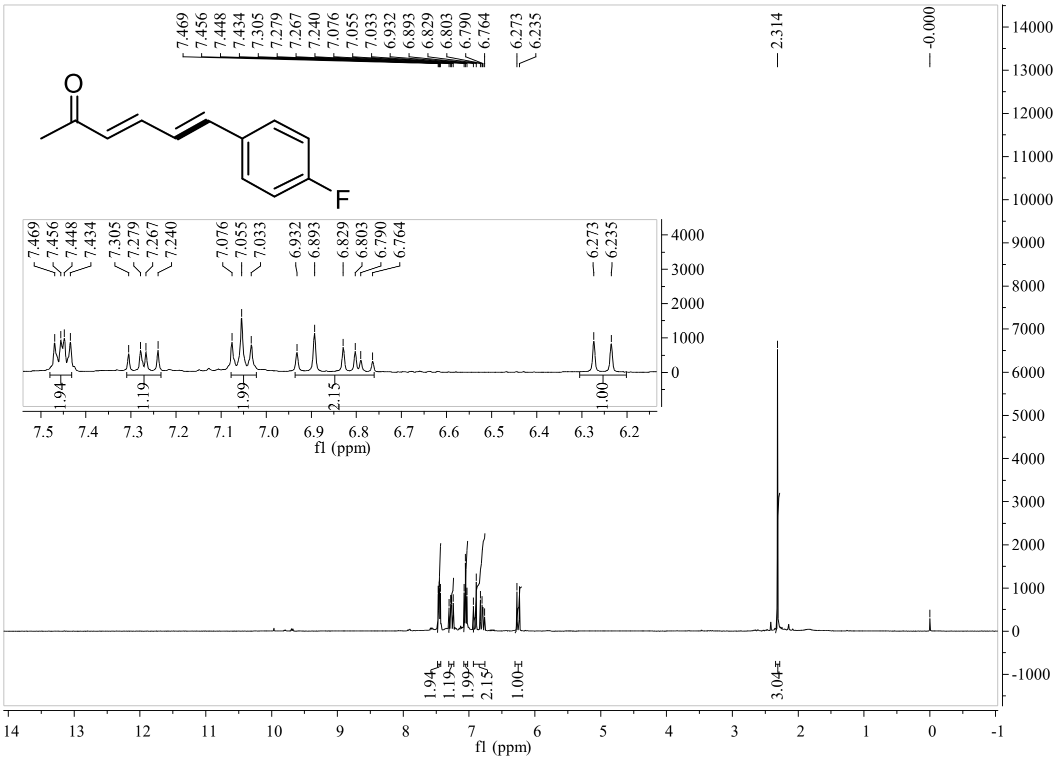

Figure S48 ^{1}H NMR spectrum of compound **2ao**, related to **Scheme 2**

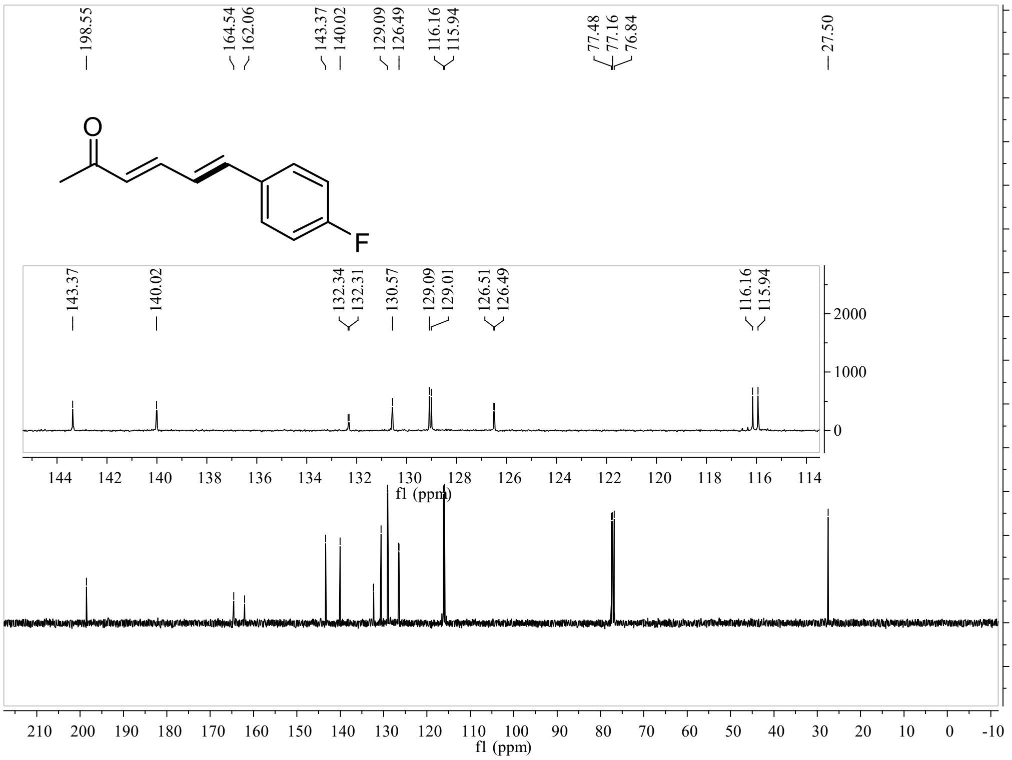

Figure S49 ^{13}C NMR spectrum of compound **2ao**, related to **Scheme 2**

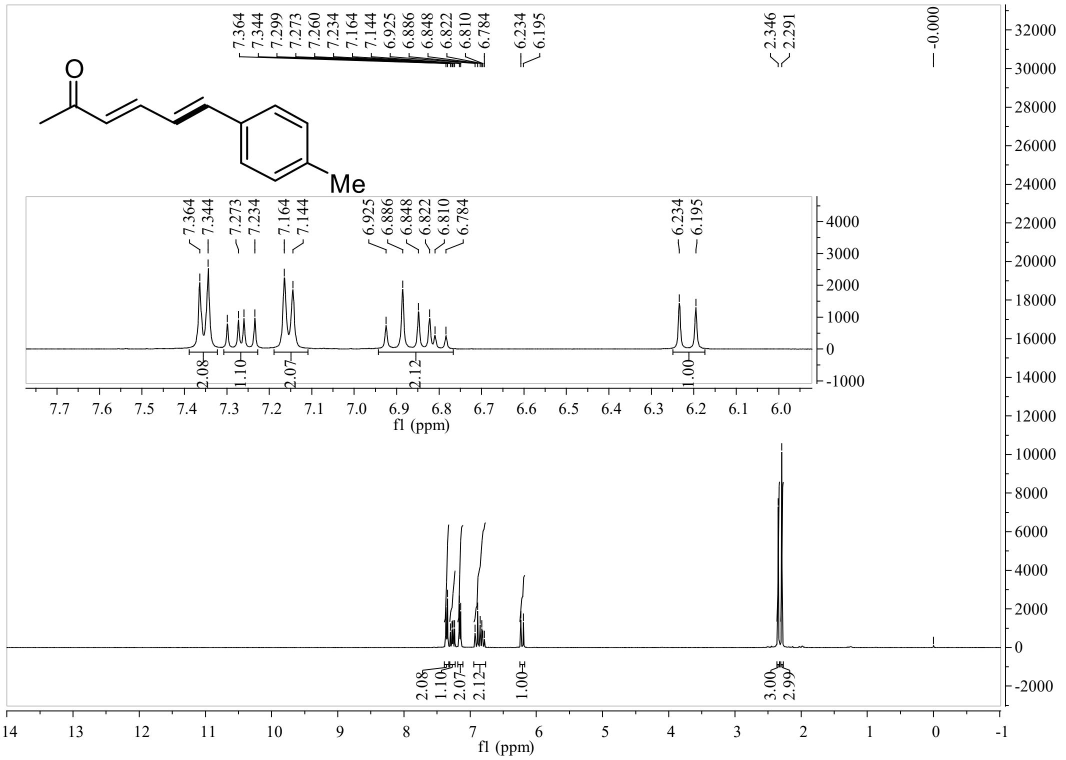

Figure S50 ^{1}H NMR spectrum of compound **2ap**, related to **Scheme 2**

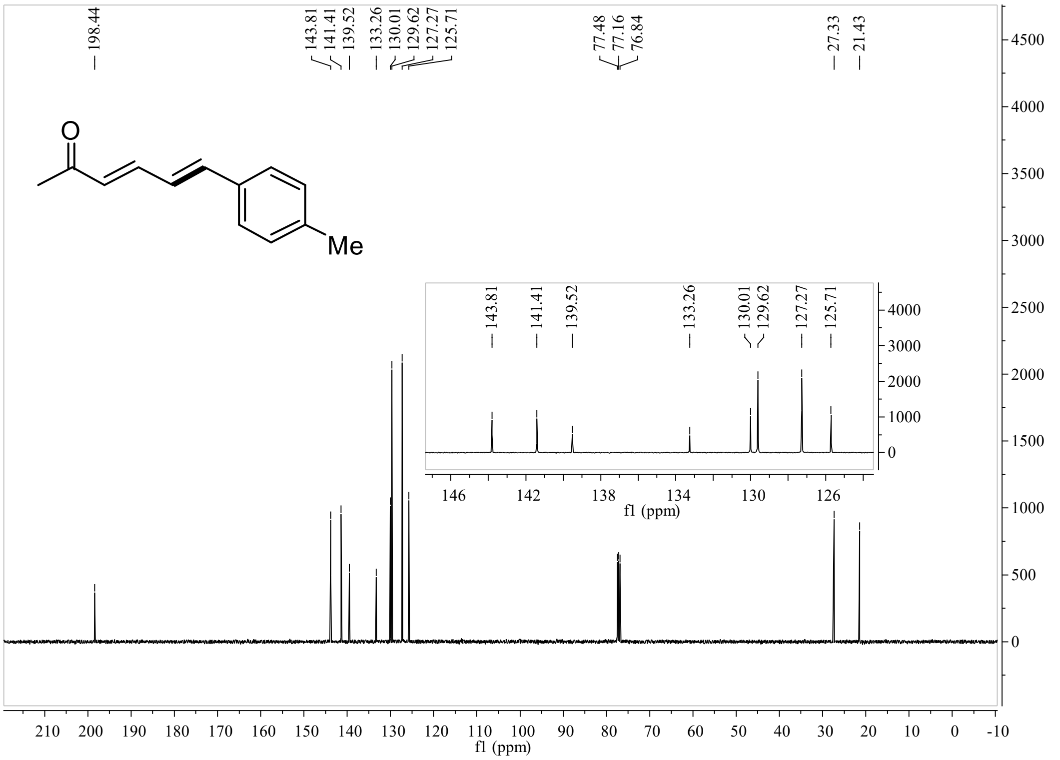

Figure S51 ^{13}C NMR spectrum of compound **2ap**, related to **Scheme 2**

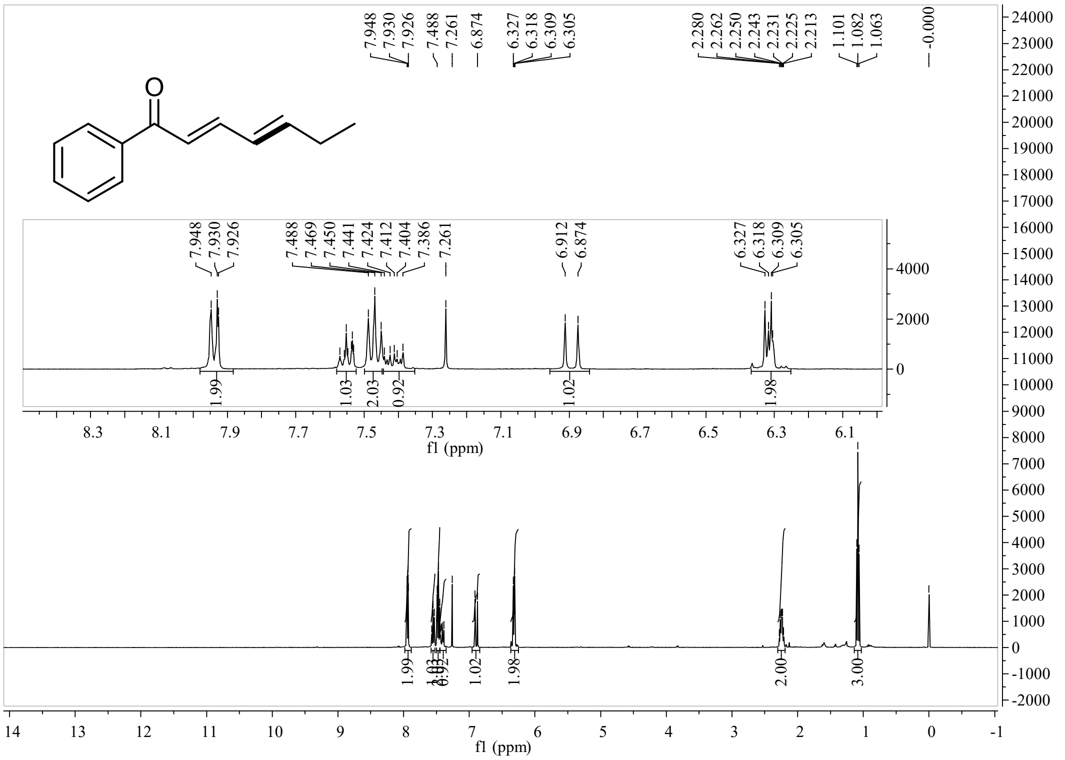

Figure S52 ^{1}H NMR spectrum of compound **2ba**, related to **Scheme 2**

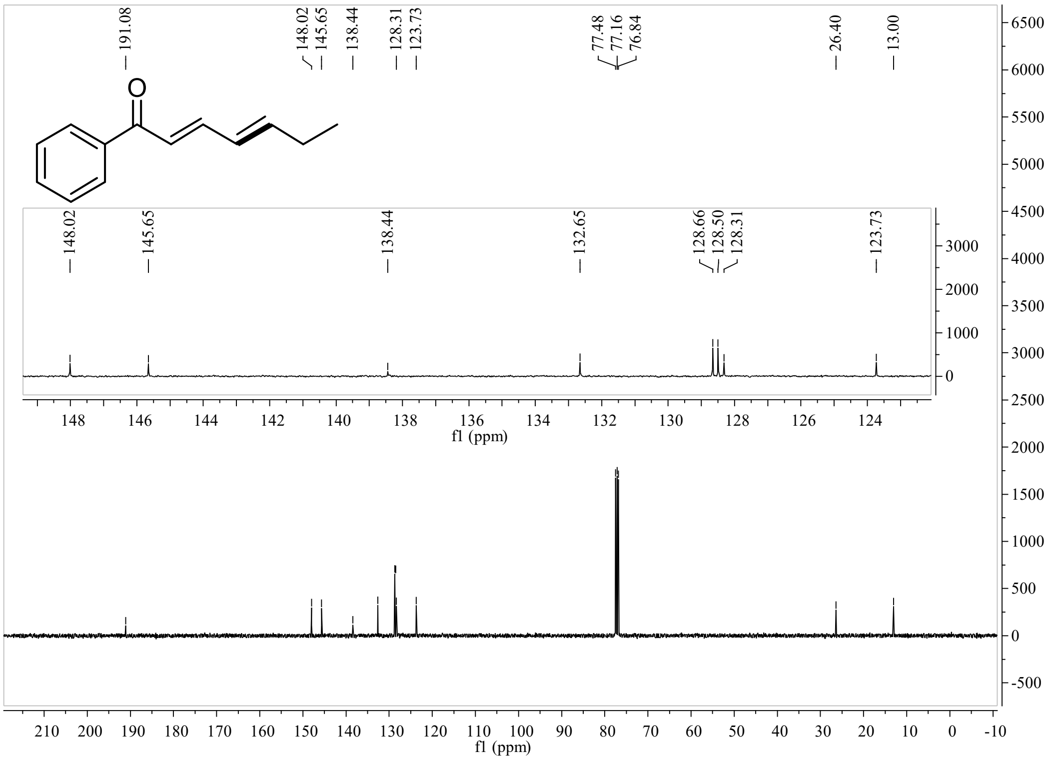

Figure S53 ^{13}C NMR spectrum of compound **2ba**, related to **Scheme 2**

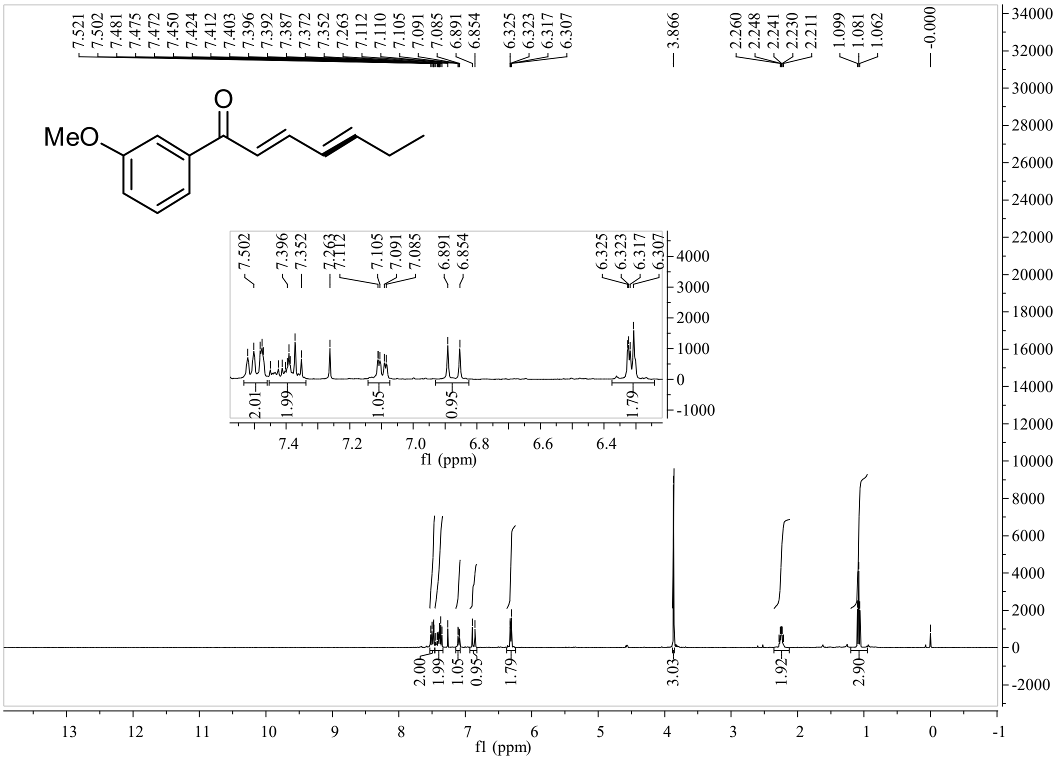

Figure S54 ^{1}H NMR spectrum of compound **2bb**, related to **Scheme 2**

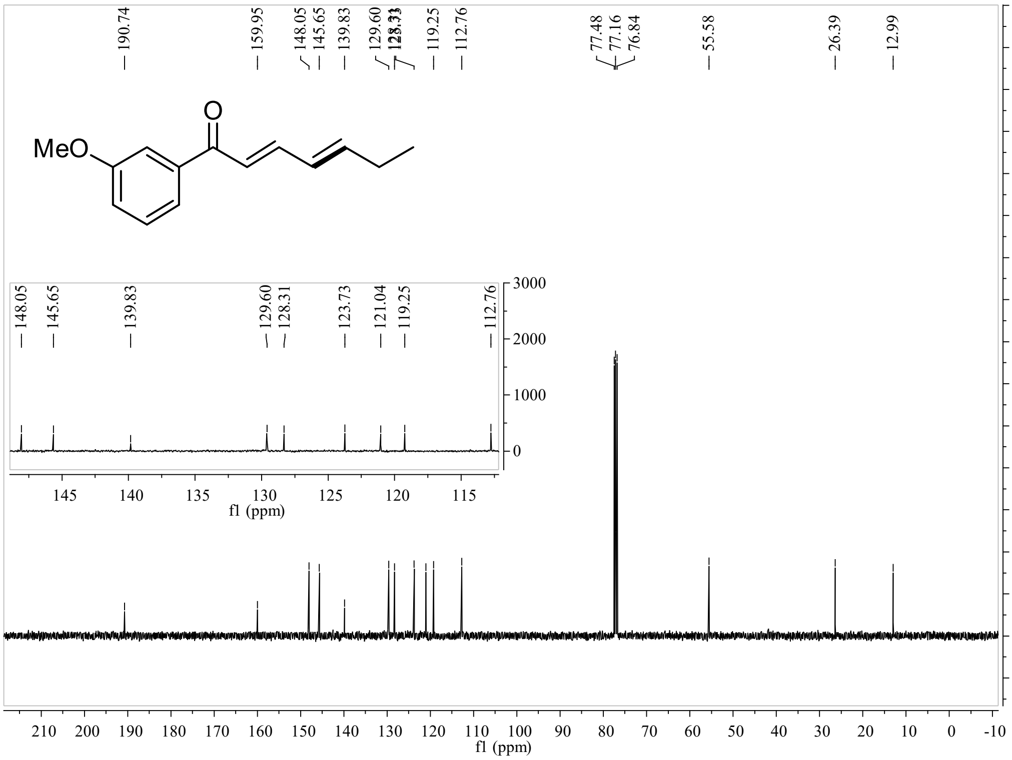

Figure S55 ^{13}C NMR spectrum of compound **2bb**, related to **Scheme 2**

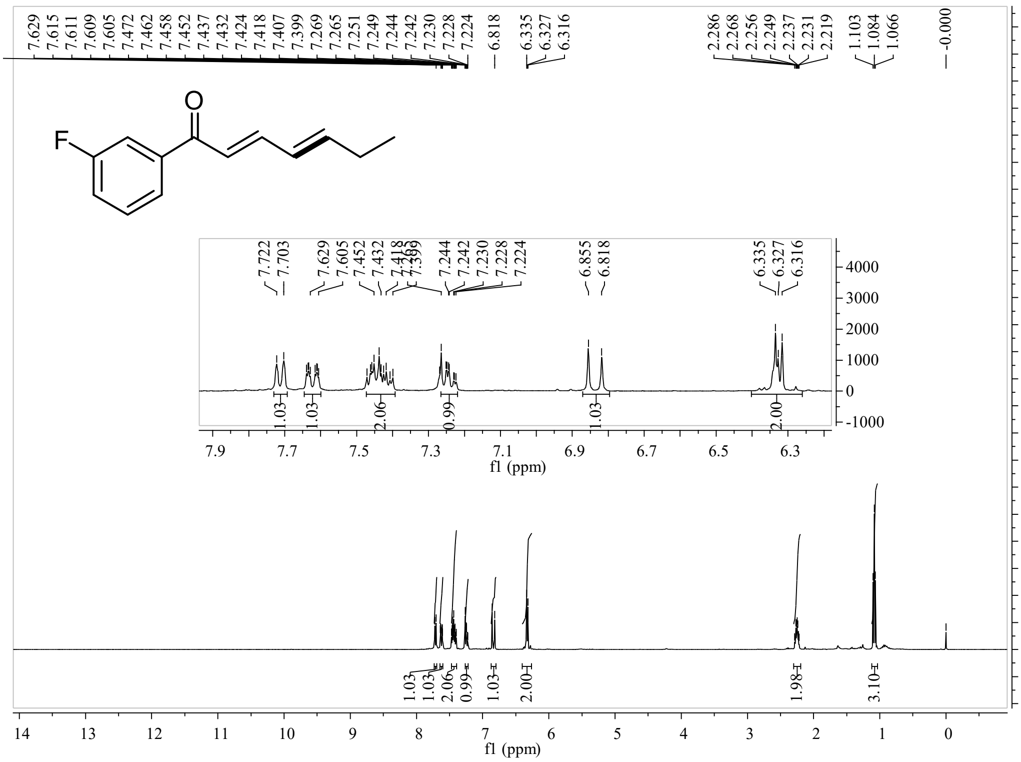

Figure S56 ^{1}H NMR spectrum of compound **2bc**, related to **Scheme 2**

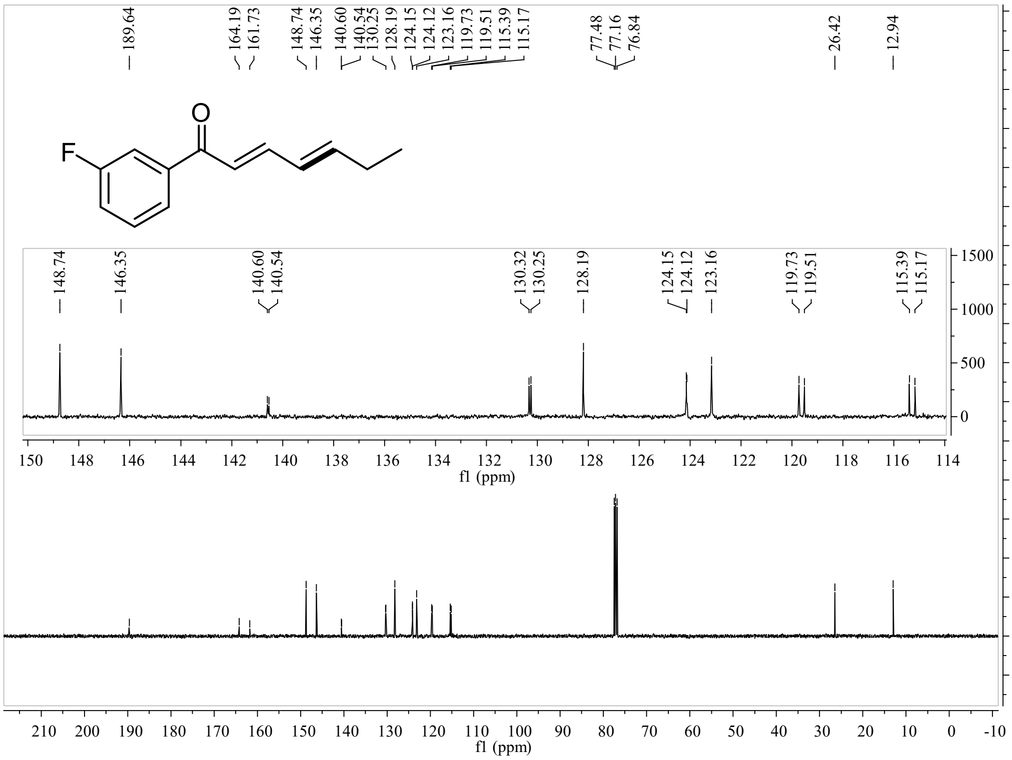

Figure S57 ^{13}C NMR spectrum of compound **2bc**, related to **Scheme 2**

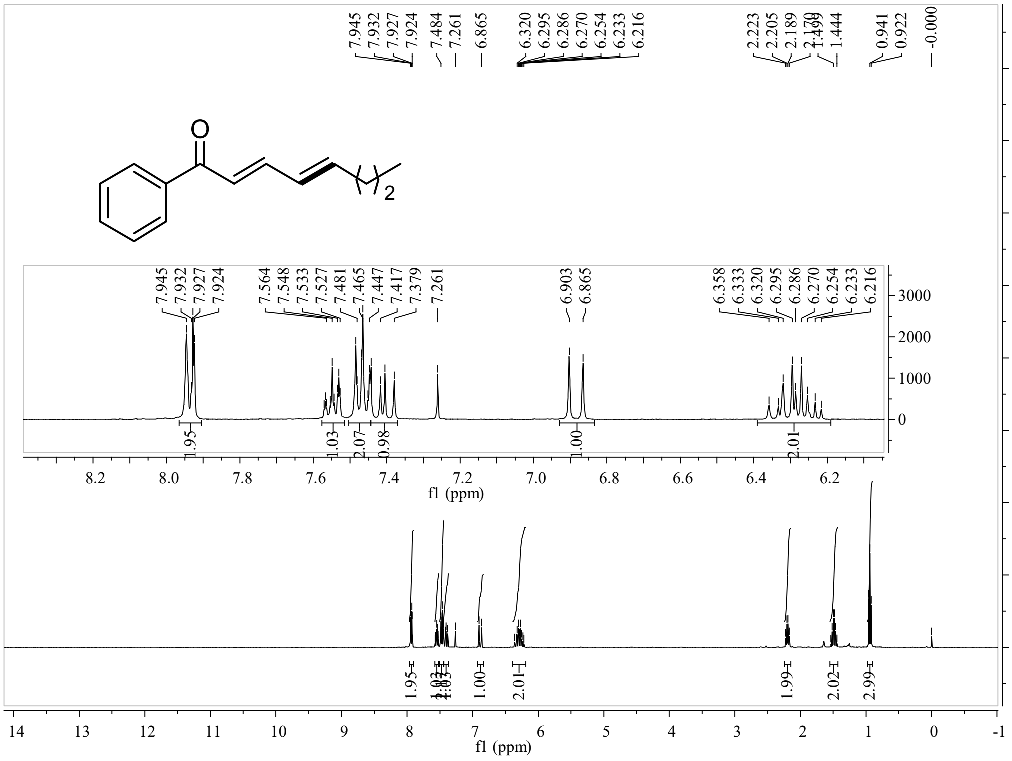

Figure S58 ^{1}H NMR spectrum of compound **2bd**, related to **Scheme 2**

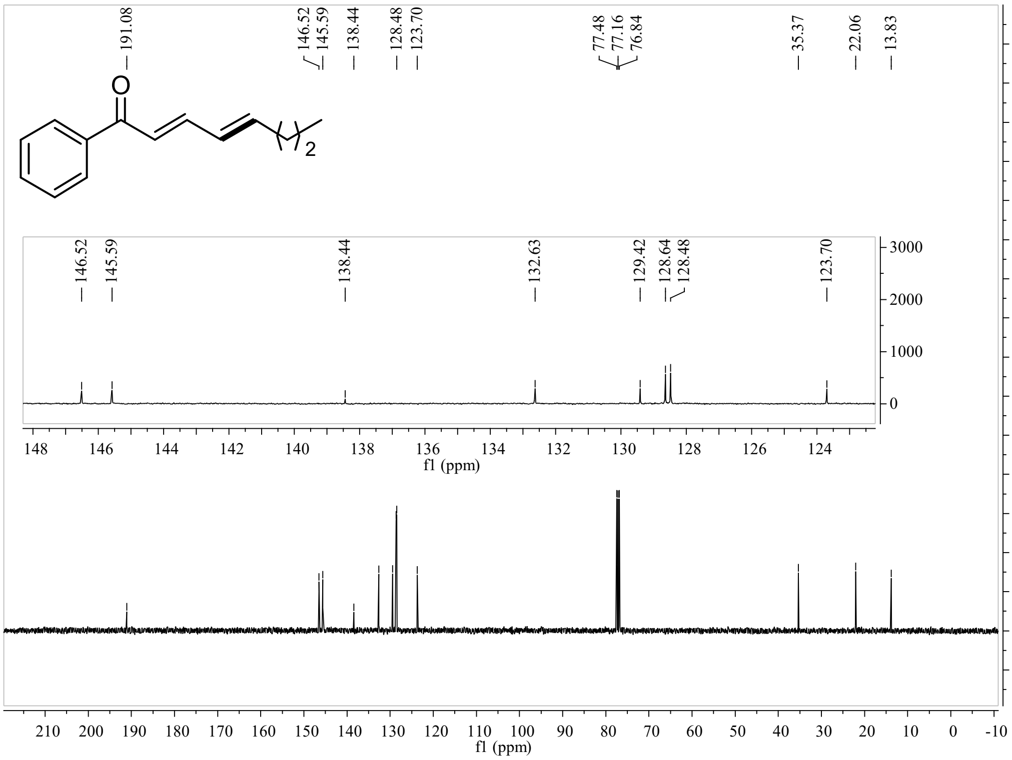

Figure S59 ^{13}C NMR spectrum of compound **2bd**, related to **Scheme 2**

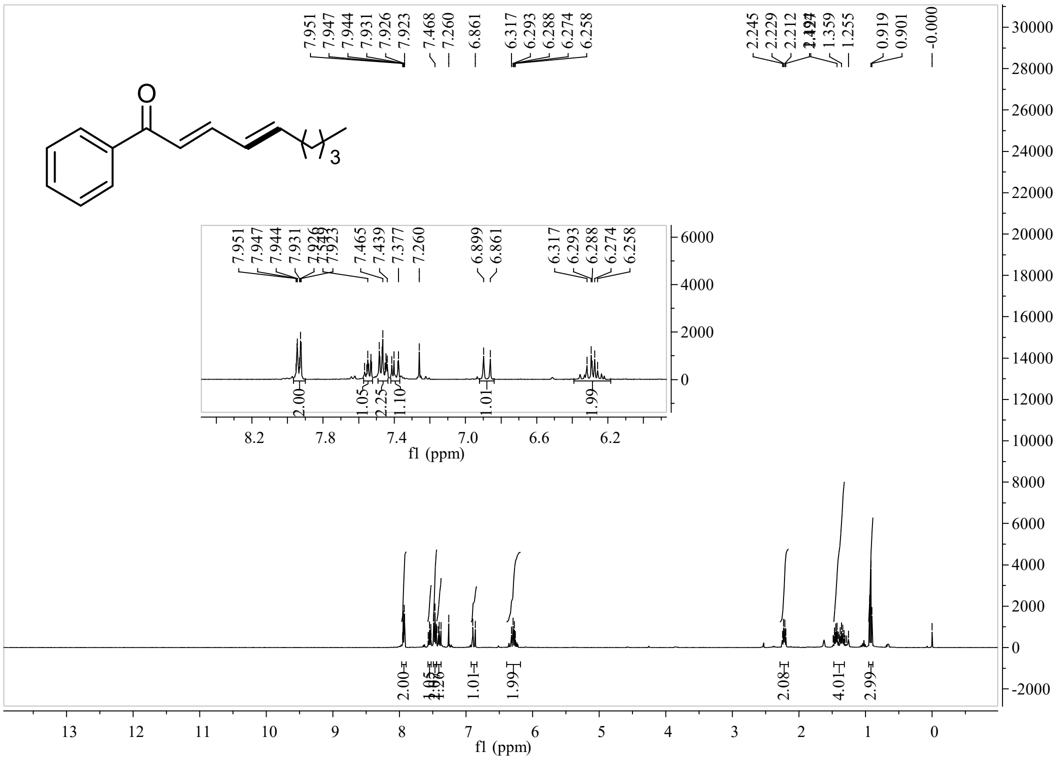

Figure S60 ^{1}H NMR spectrum of compound **2be**, related to **Scheme 2**

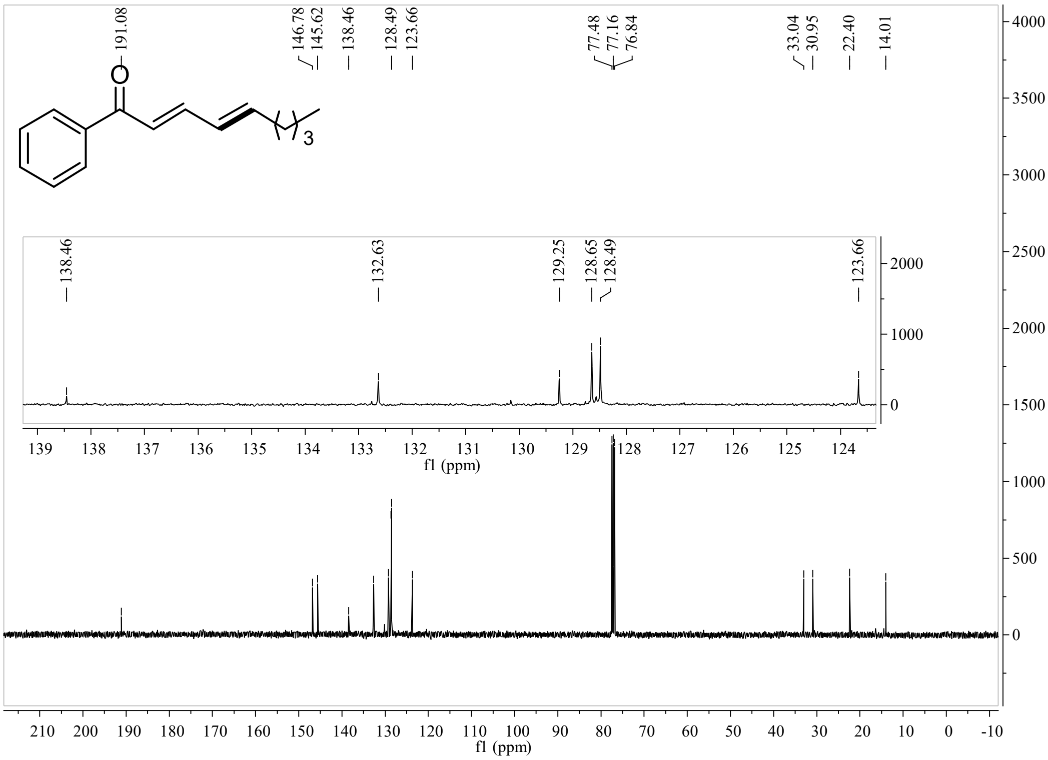

Figure S61 ^{13}C NMR spectrum of compound **2be**, related to **Scheme 2**

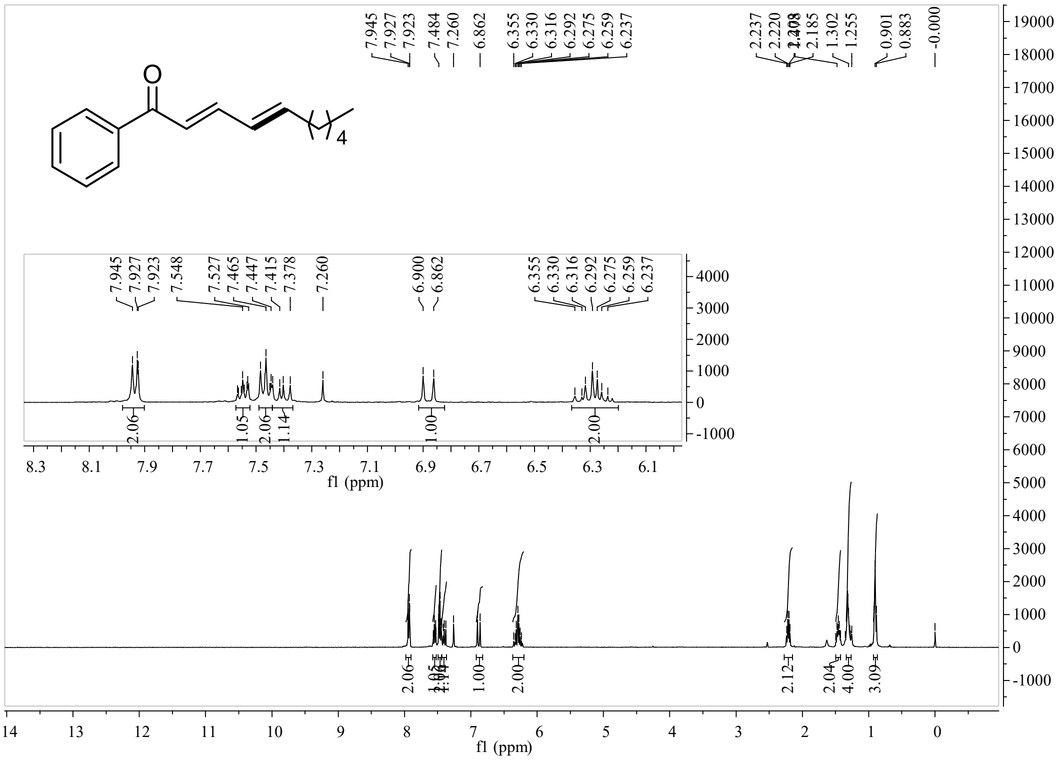

Figure S62 ^{1}H NMR spectrum of compound **2bf**, related to **Scheme 2**

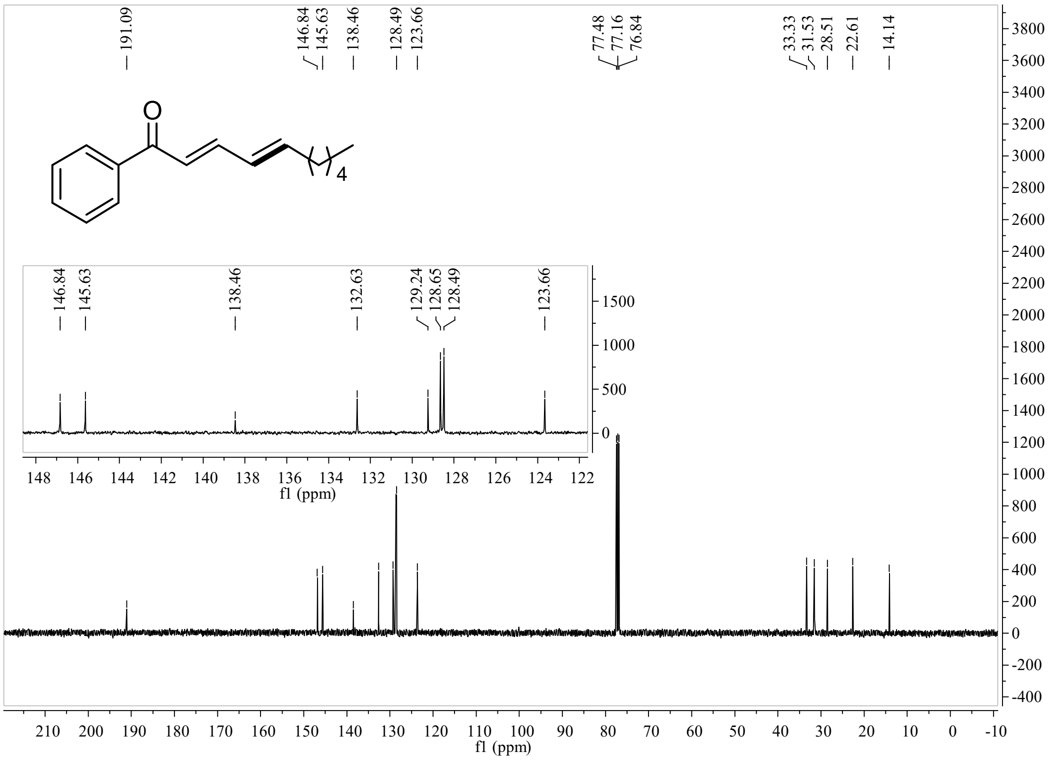

Figure S63 ^{13}C NMR spectrum of compound **2bf**, related to **Scheme 2**

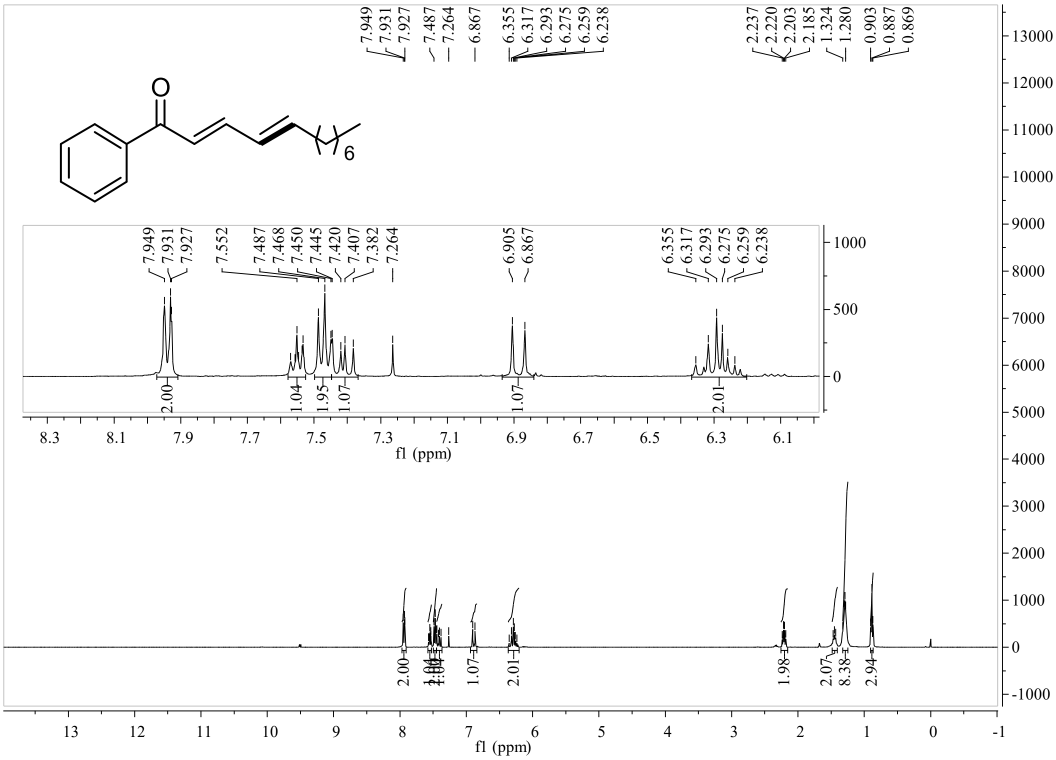

Figure S64 ^{1}H NMR spectrum of compound **2bg**, related to **Scheme 2**

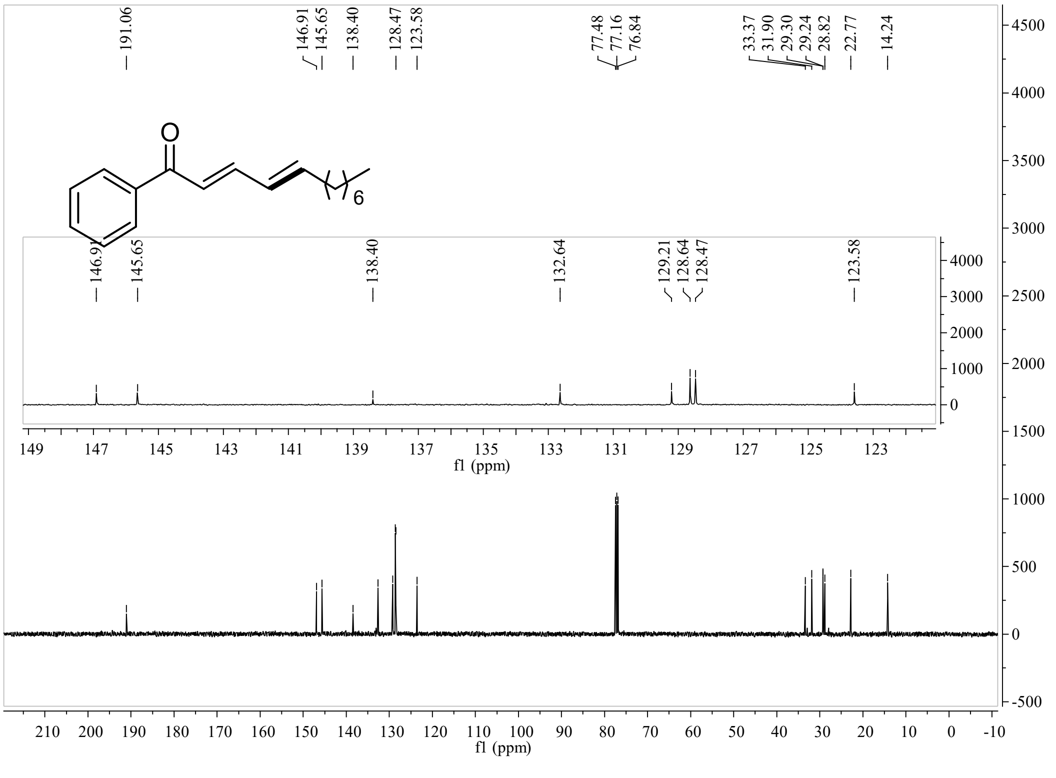

Figure S65 ^{13}C NMR spectrum of compound **2bg**, related to **Scheme 2**

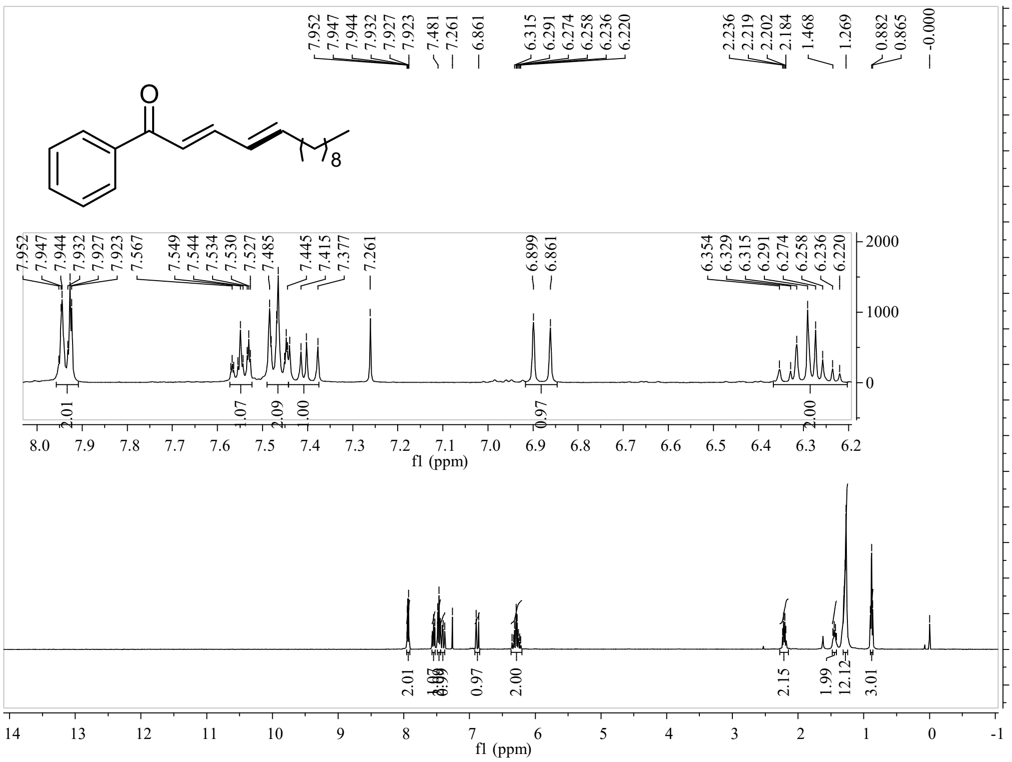

Figure S66 ^{1}H NMR spectrum of compound **2bh**, related to **Scheme 2**

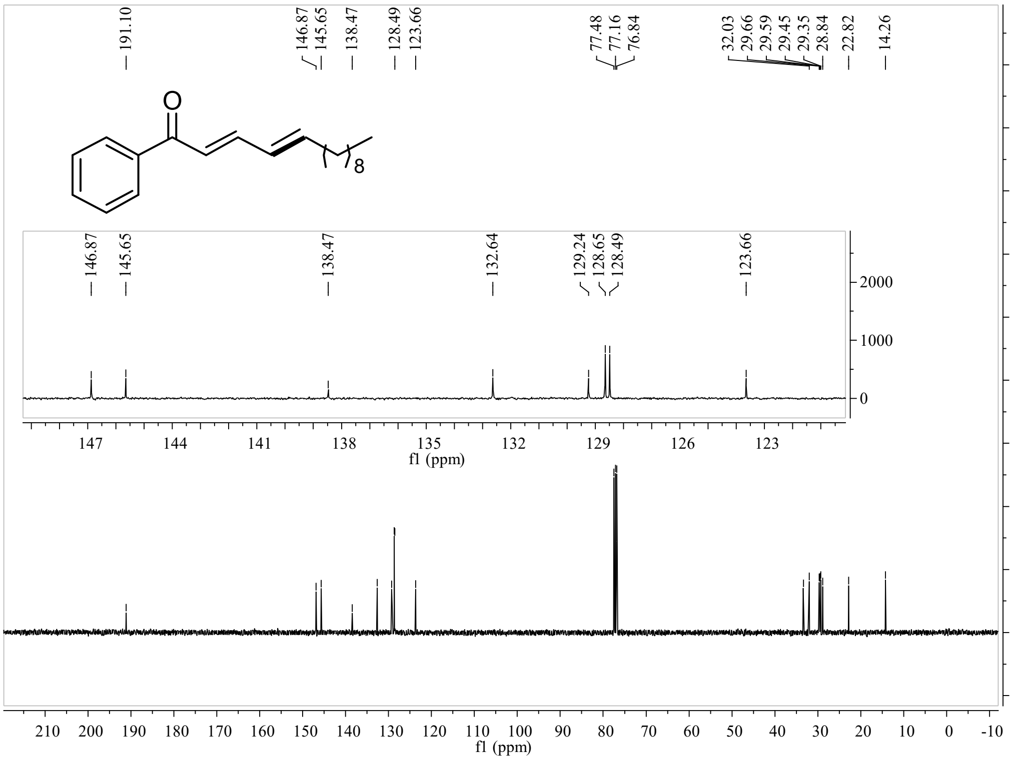

Figure S67 ^{13}C NMR spectrum of compound **2bh**, related to **Scheme 2**

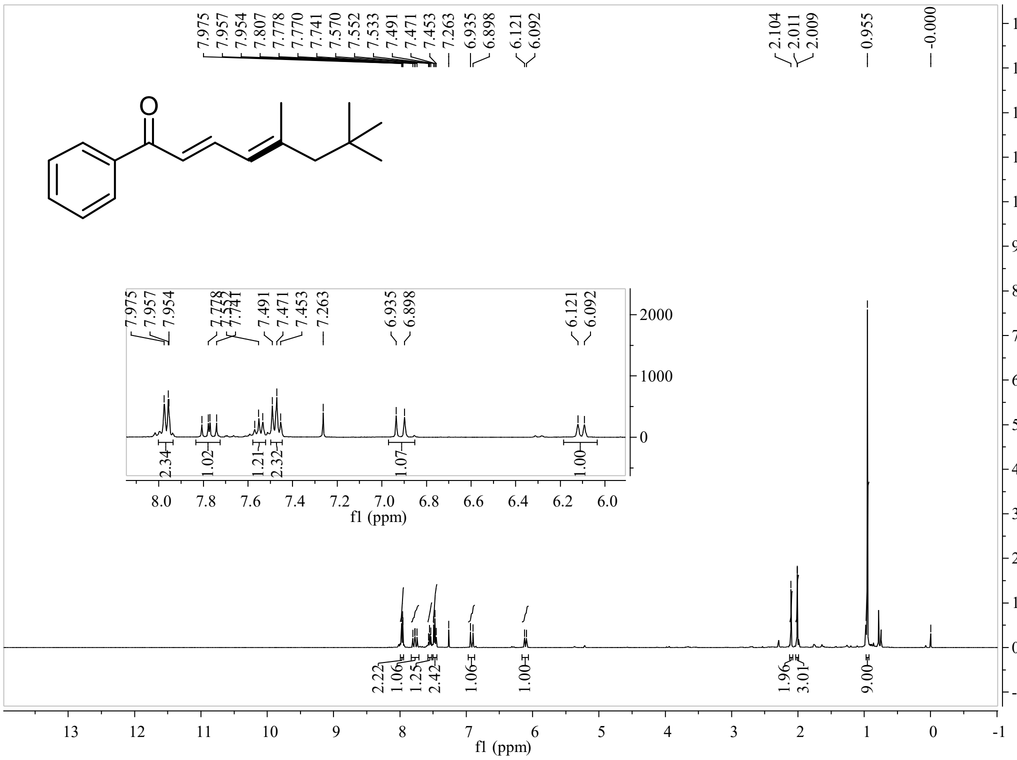

Figure S68 ^{1}H NMR spectrum of compound **2bi**, related to **Scheme 2**

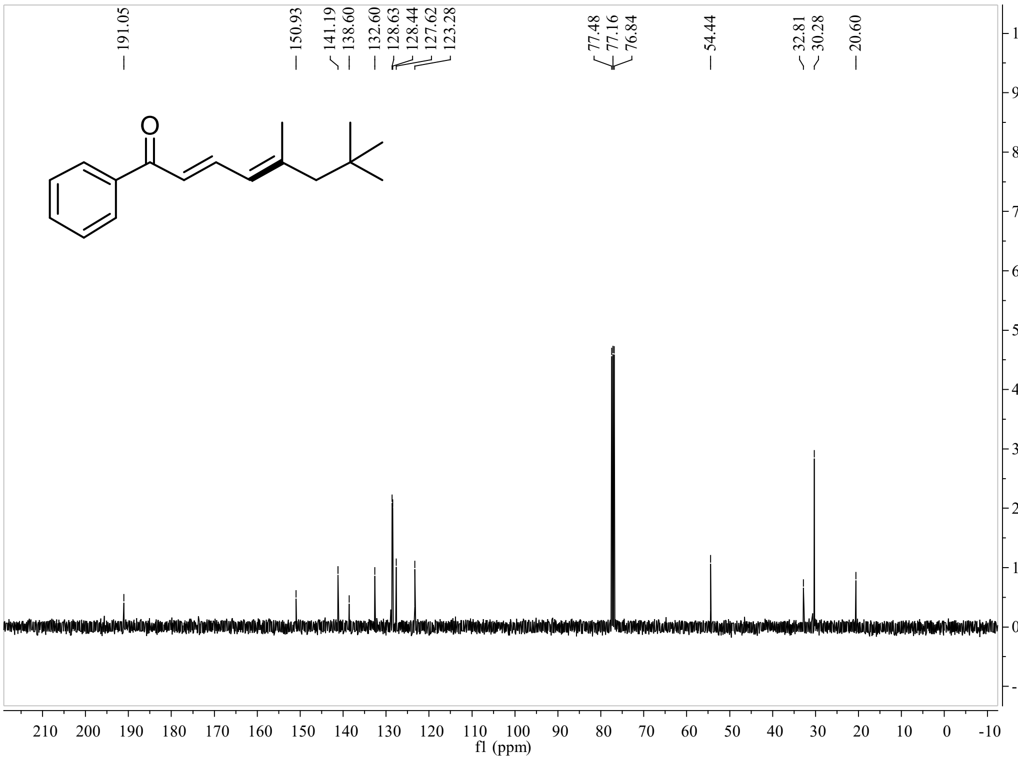

Figure S69 ^{13}C NMR spectrum of compound **2bi**, related to **Scheme 2**

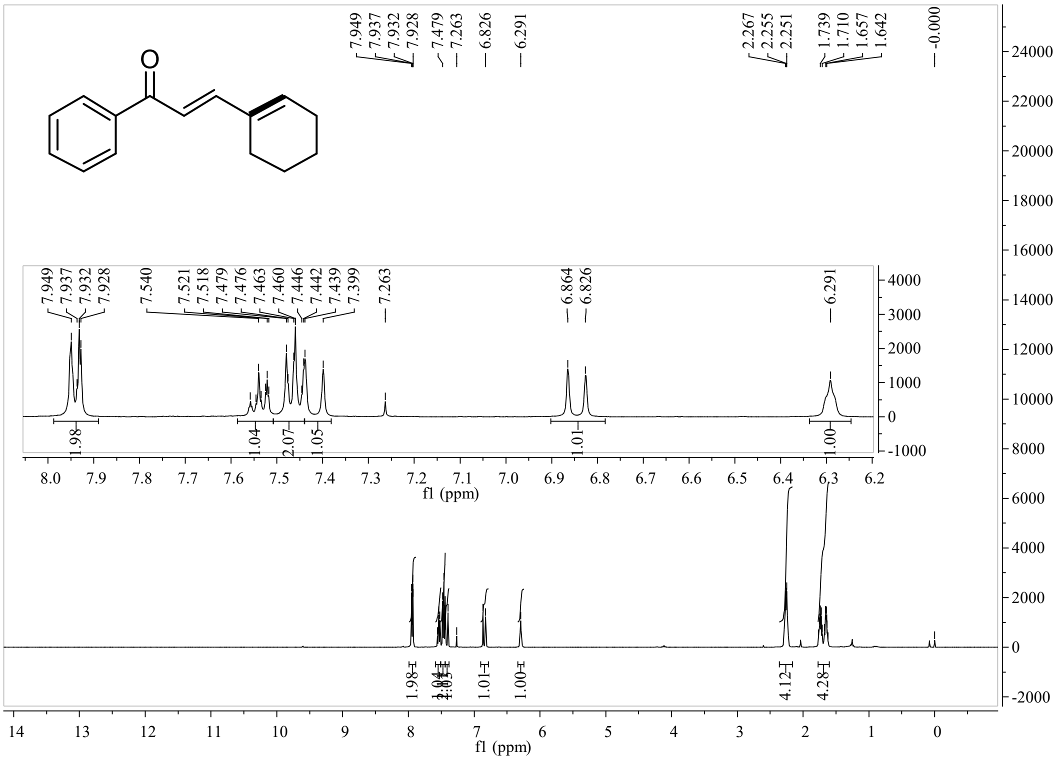

Figure S70 ^{1}H NMR spectrum of compound **2bj**, related to **Scheme 2**

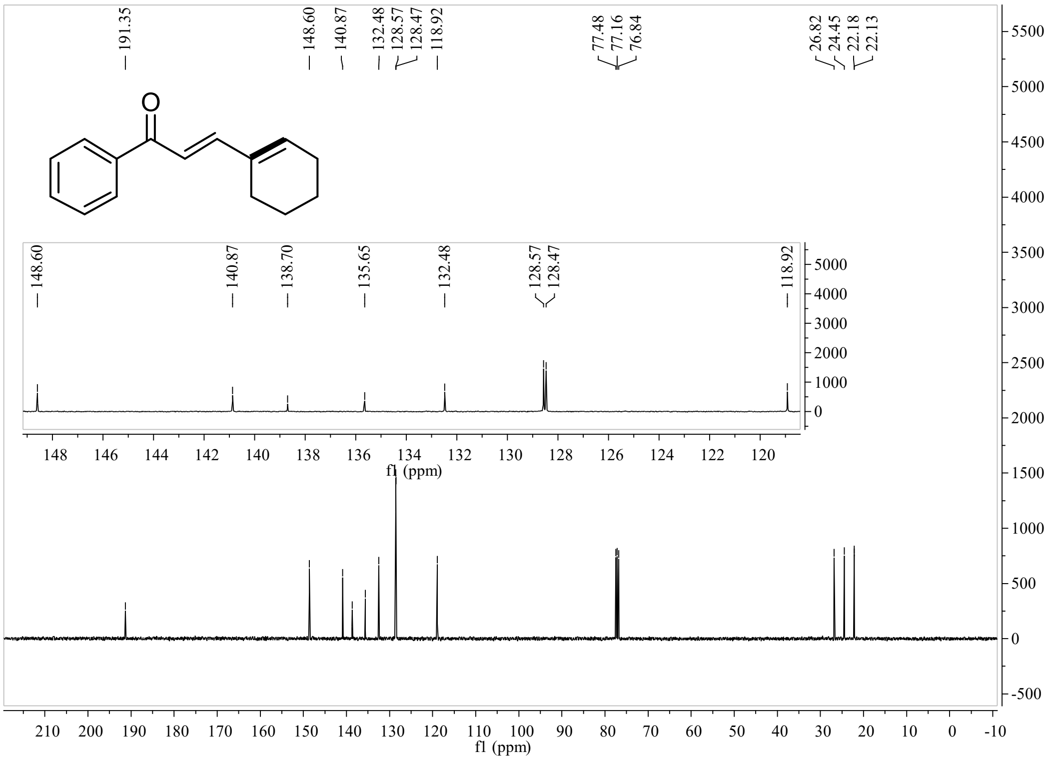

Figure S71 ^{13}C NMR spectrum of compound **2bj**, related to **Scheme 2**

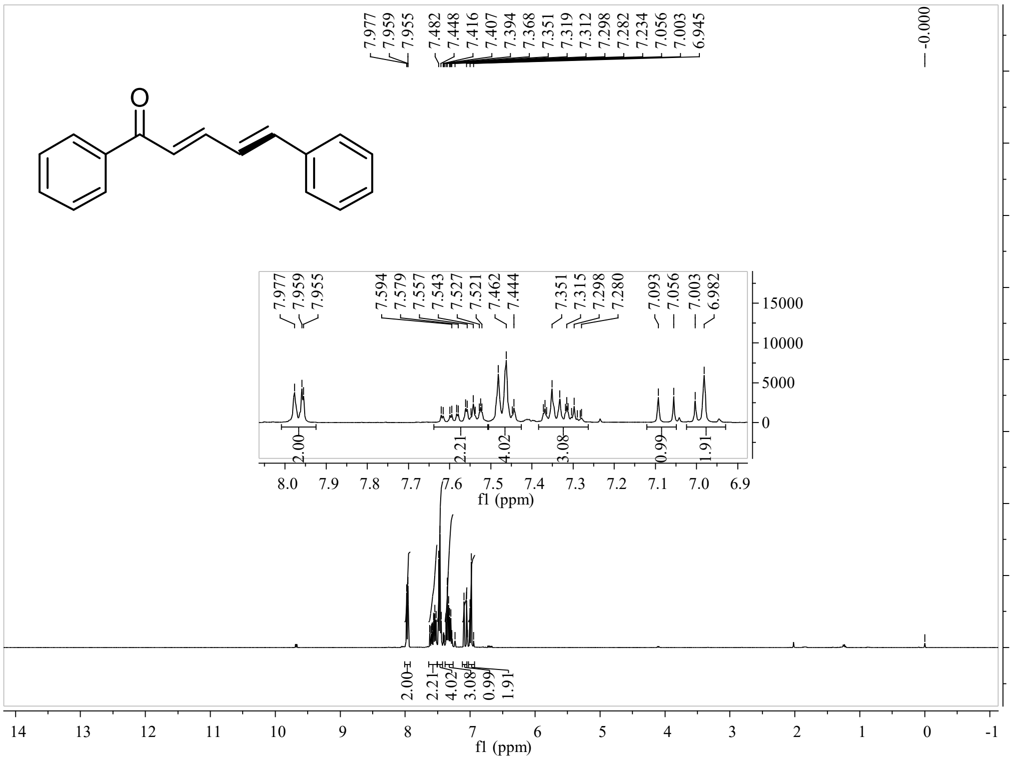

Figure S72 ^{1}H NMR spectrum of compound **2bk**, related to **Scheme 2**

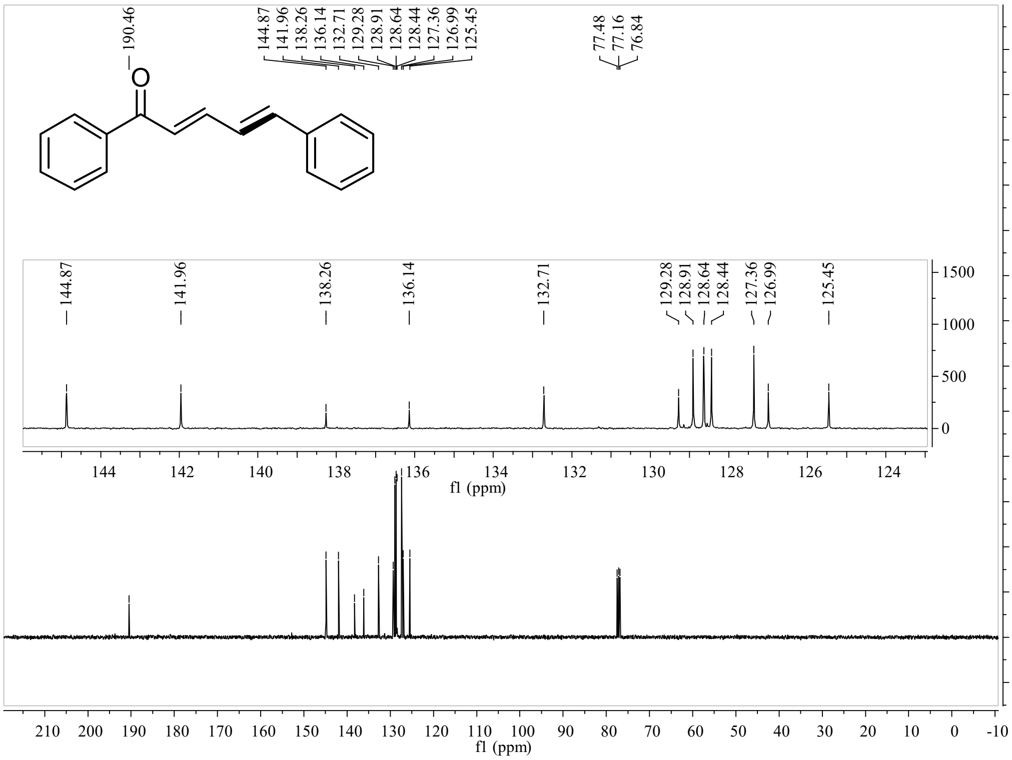

Figure S73 ^{13}C NMR spectrum of compound **2bk**, related to **Scheme 2**

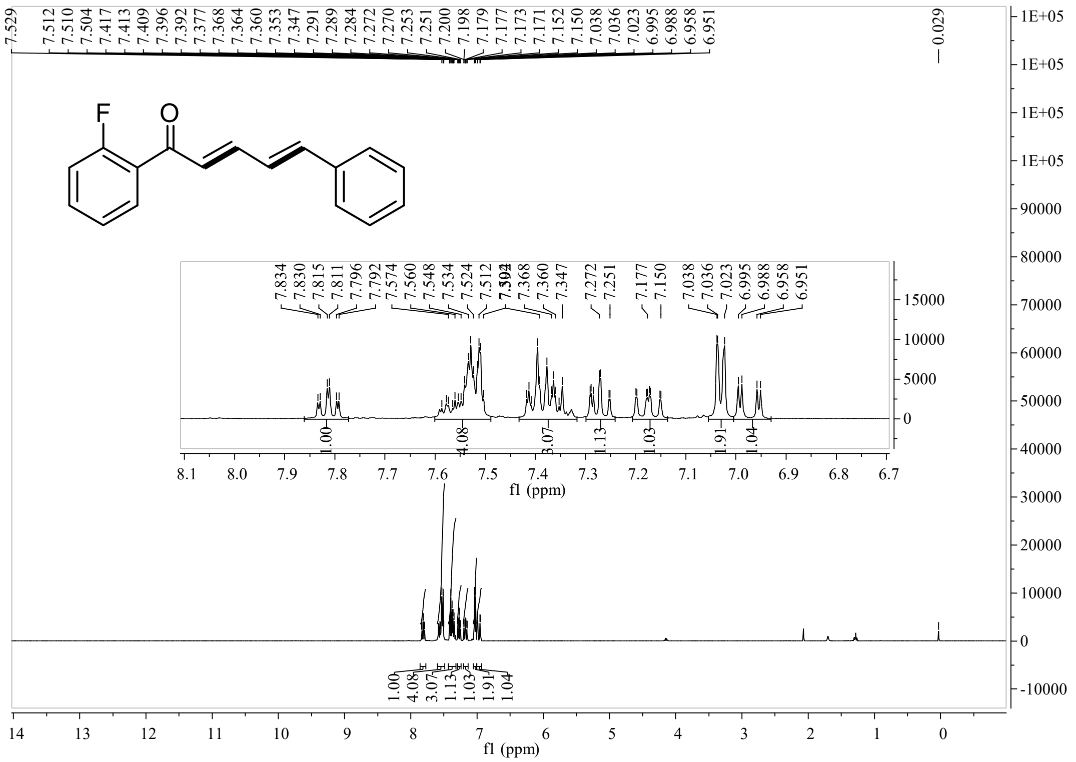

Figure S74 ^{1}H NMR spectrum of compound **2bl**, related to **Scheme 2**

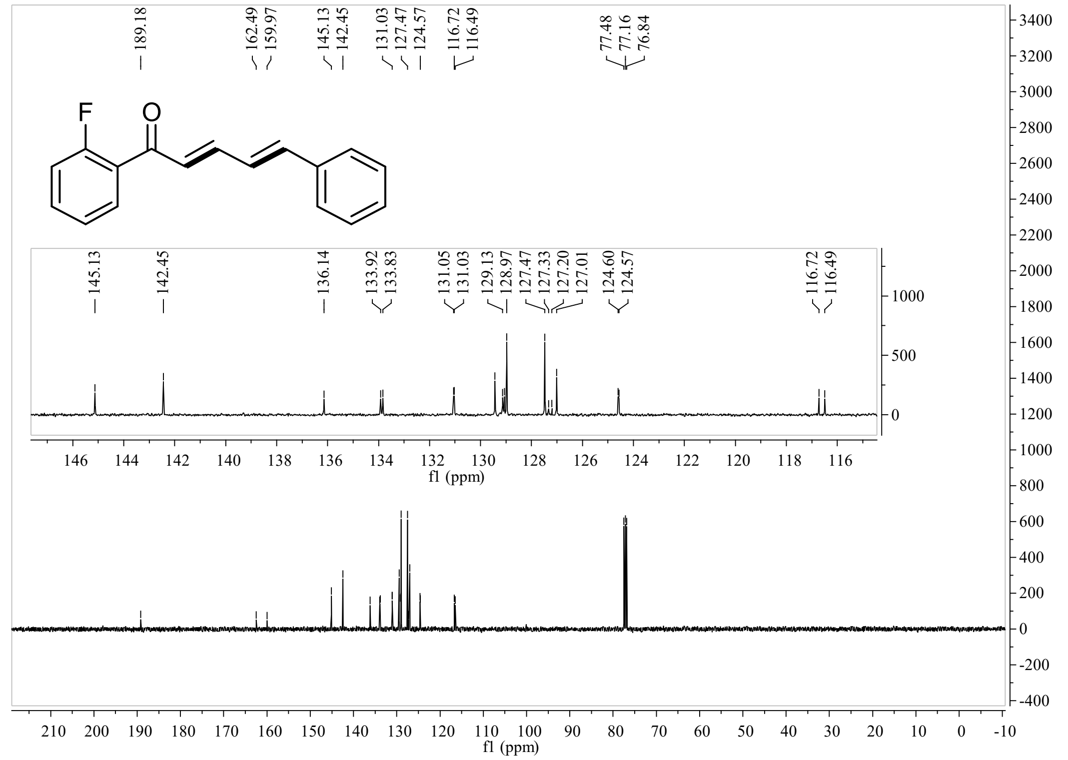

Figure S75 ^{13}C NMR spectrum of compound **2bl**, related to **Scheme 2**

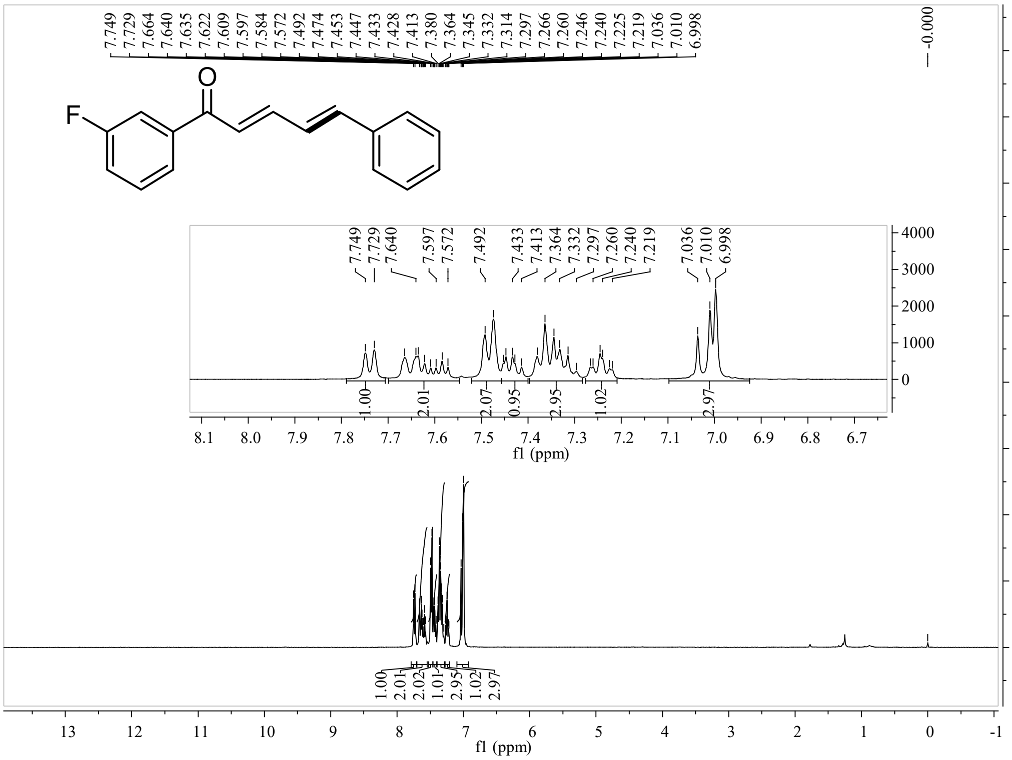

Figure S76 ^{1}H NMR spectrum of compound **2bm**, related to **Scheme 2**

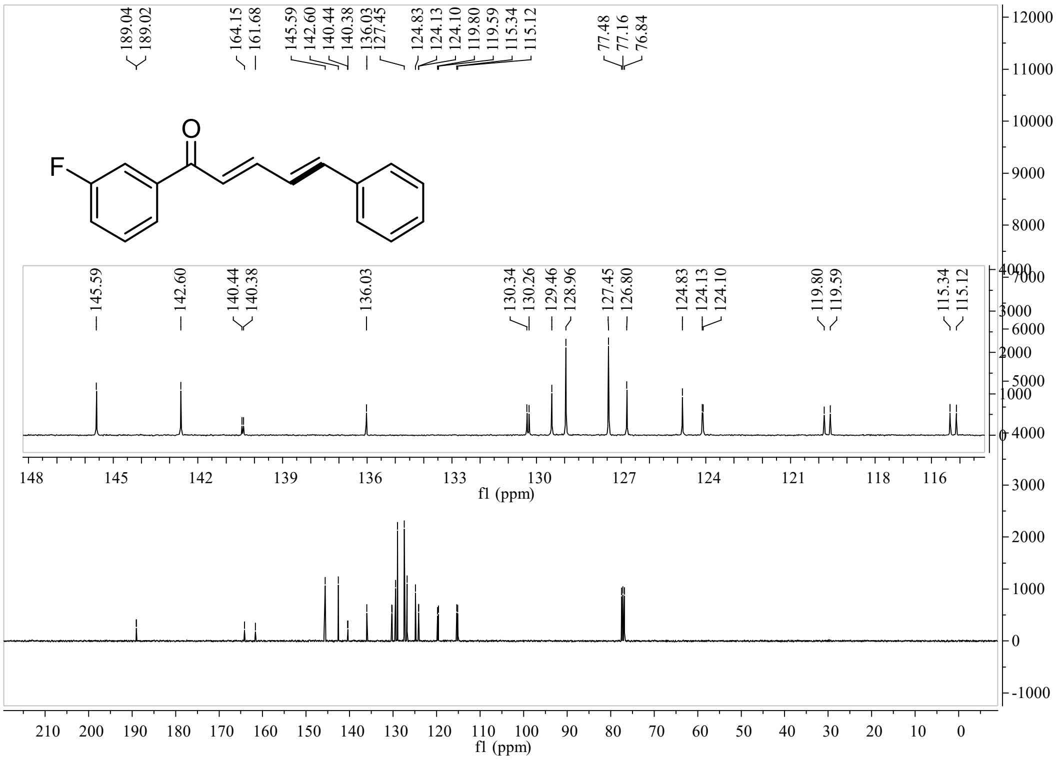

Figure S77 ^{13}C NMR spectrum of compound **2bm**, related to **Scheme 2**

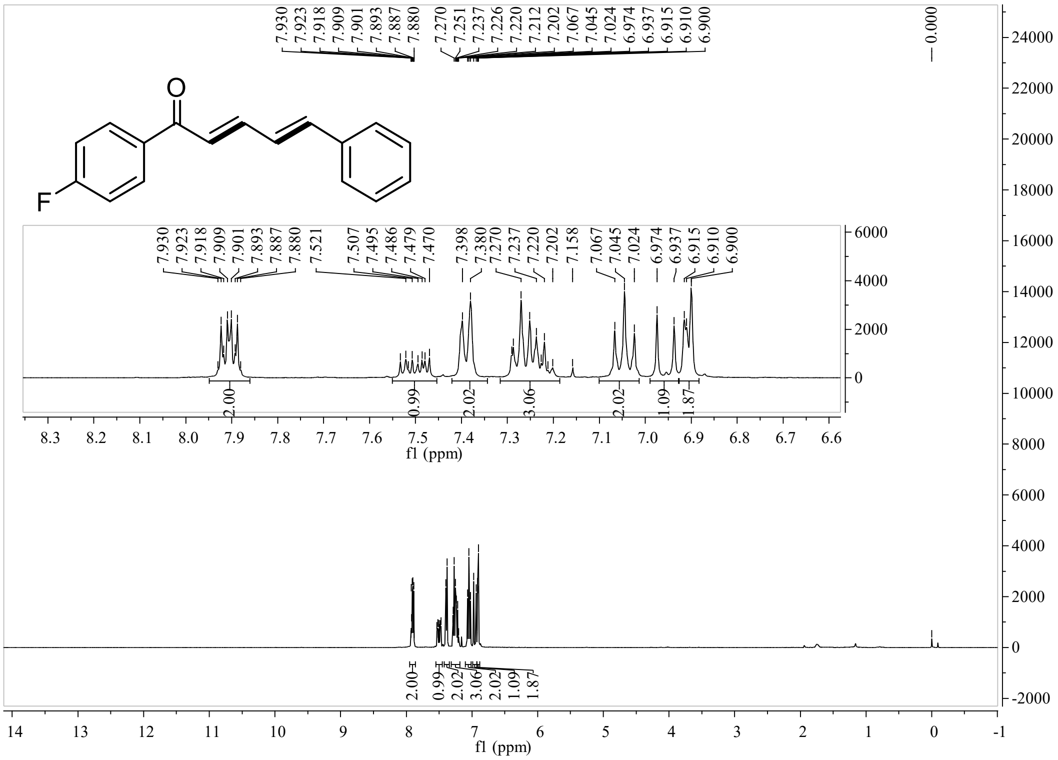

Figure S78 ^{1}H NMR spectrum of compound **2bm**, related to **Scheme 2**

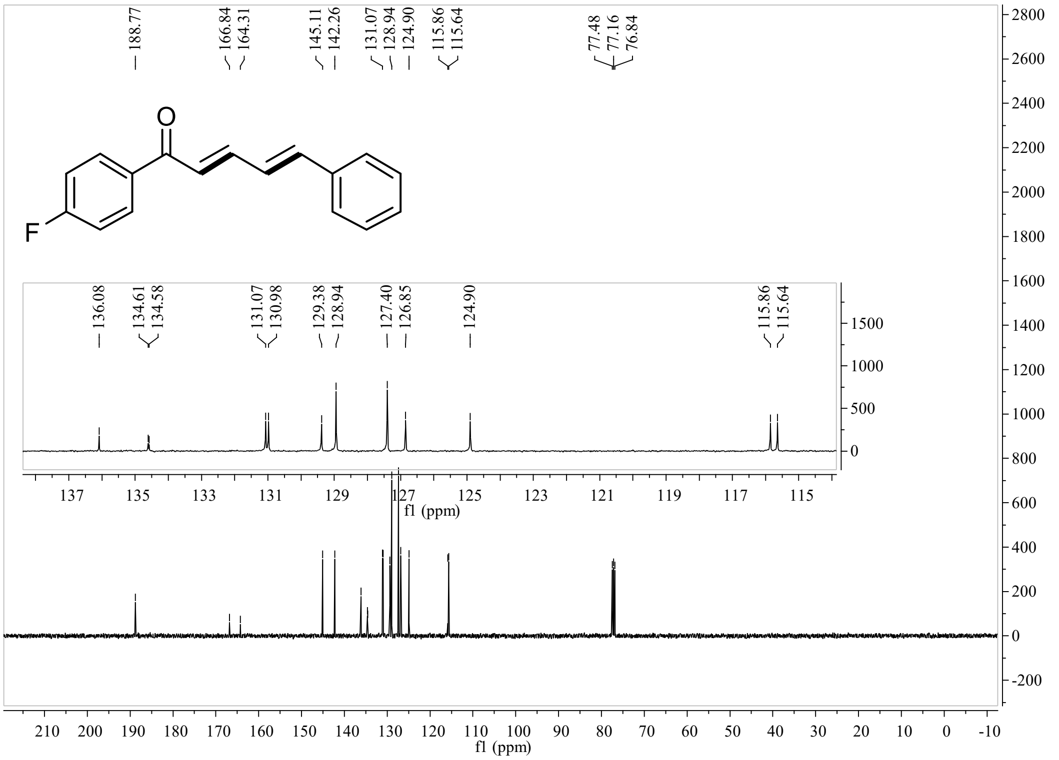

Figure S79 ^{13}C NMR spectrum of compound **2bm**, related to **Scheme 2**

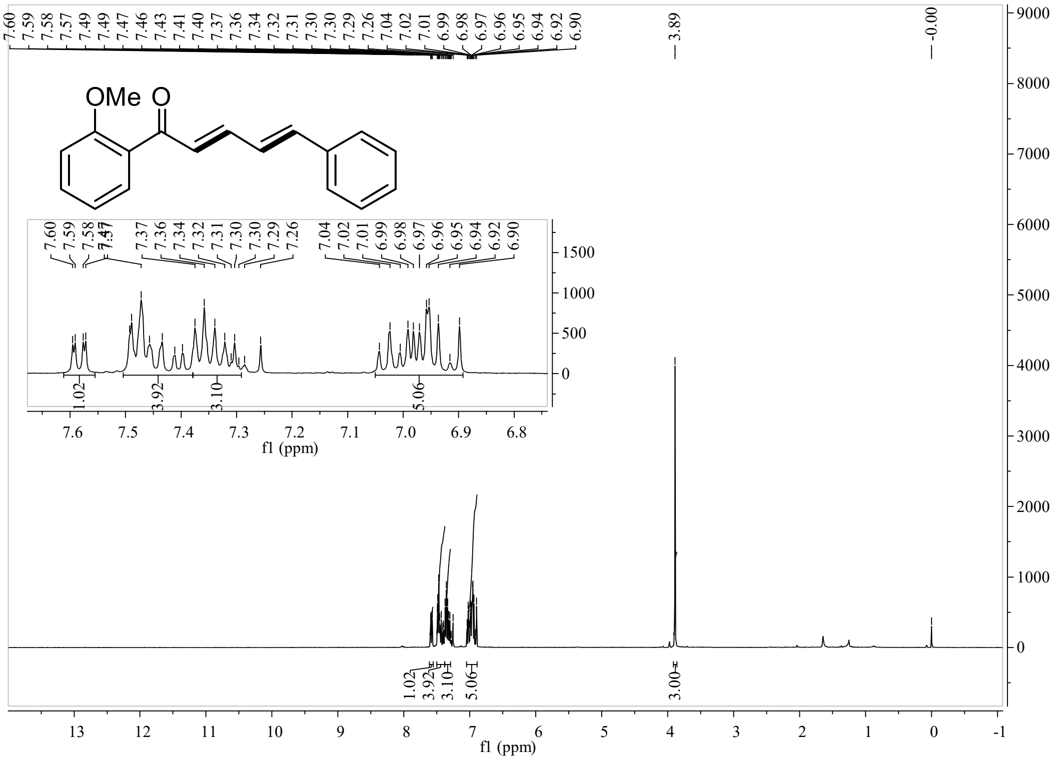

Figure S80 ^{1}H NMR spectrum of compound **2bo**, related to **Scheme 2**

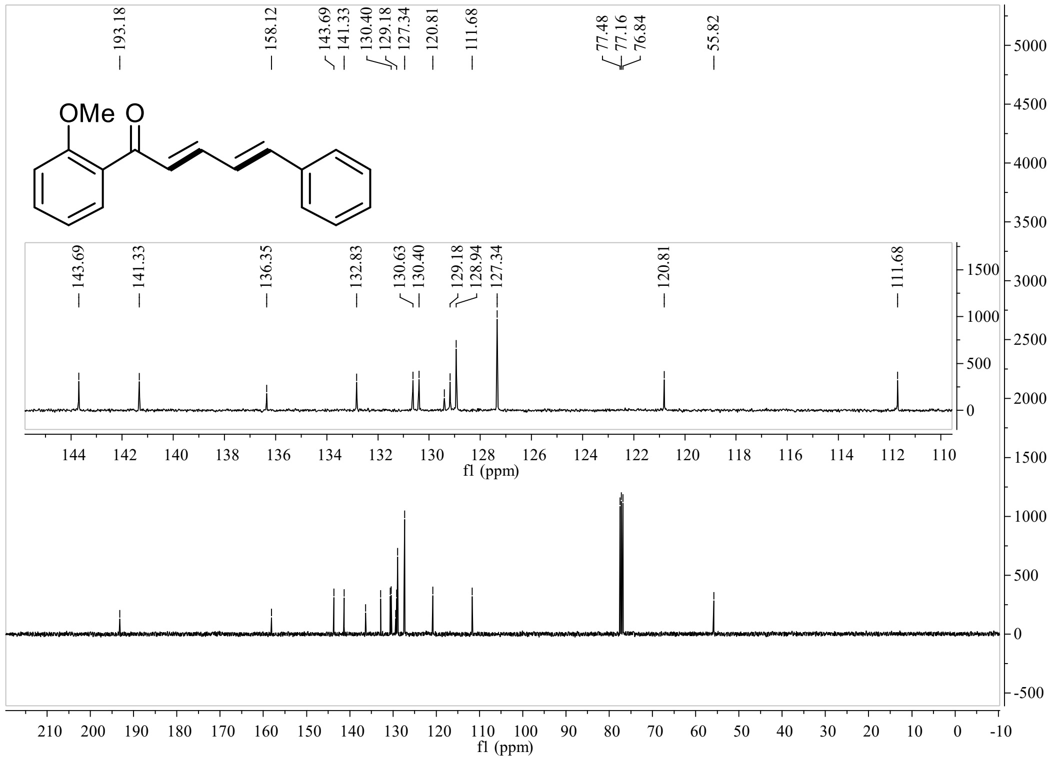

Figure S81 ^{13}C NMR spectrum of compound **2bo**, related to **Scheme 2**

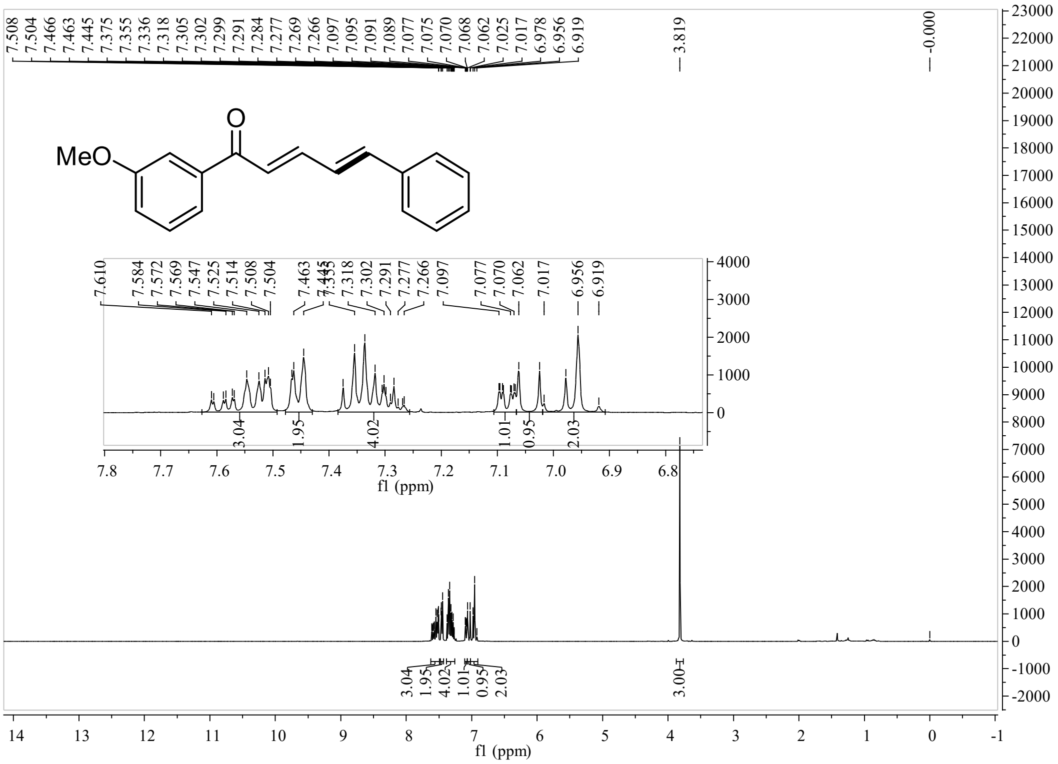

Figure S82 ^{1}H NMR spectrum of compound **2bp**, related to **Scheme 2**

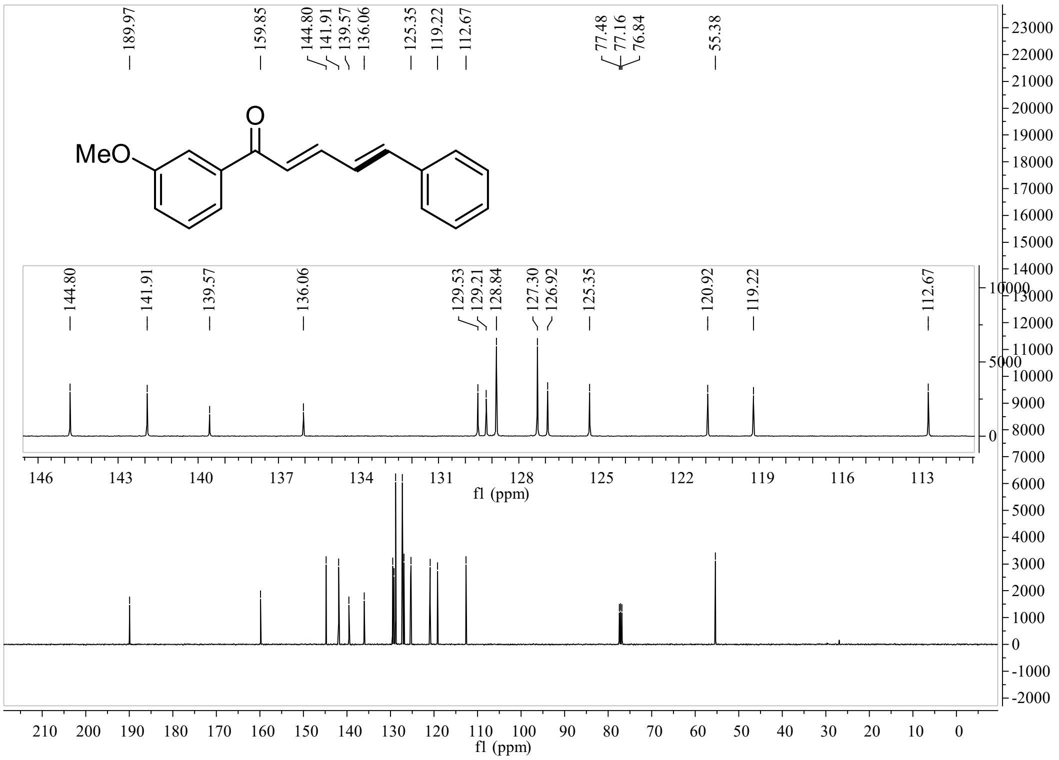

Figure S83 ^{13}C NMR spectrum of compound **2bp**, related to **Scheme 2**

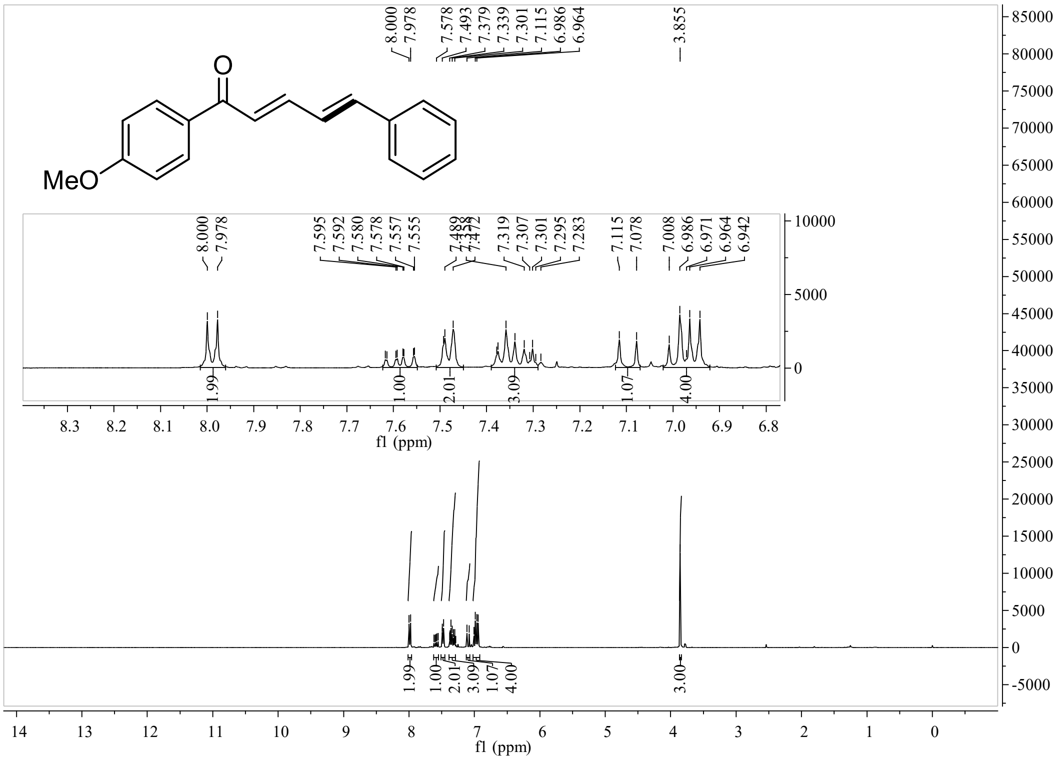

Figure S84 ^{1}H NMR spectrum of compound **2bq**, related to **Scheme 2**

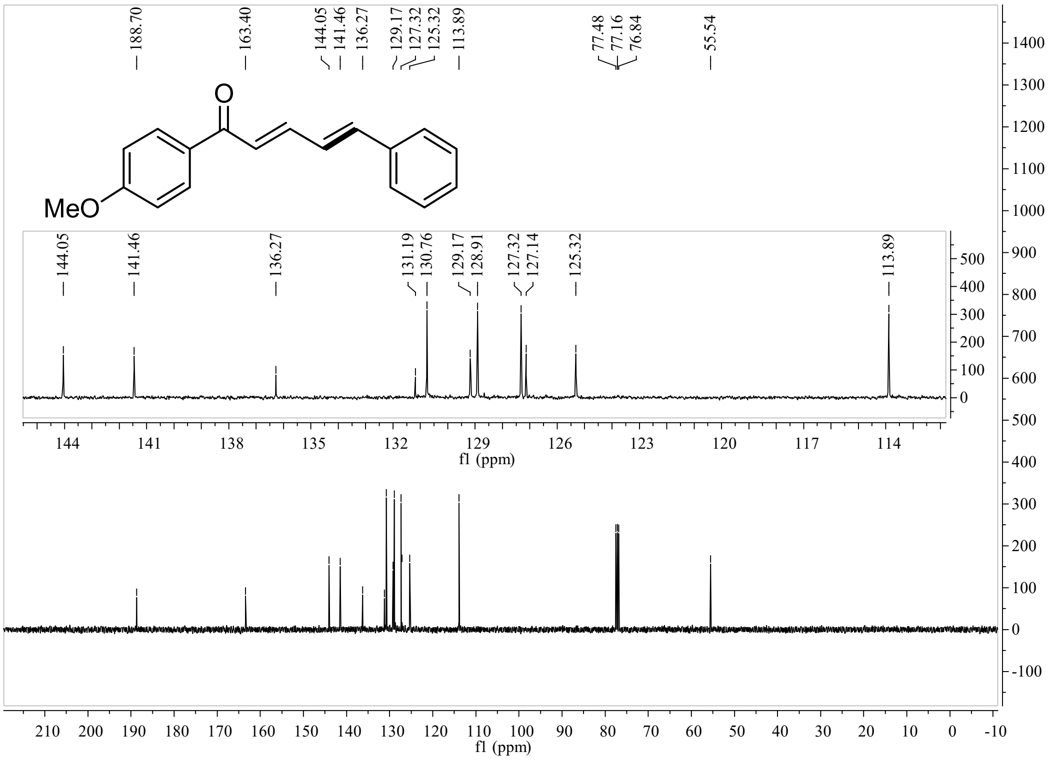

Figure S85 ^{13}C NMR spectrum of compound **2bq**, related to **Scheme 2**

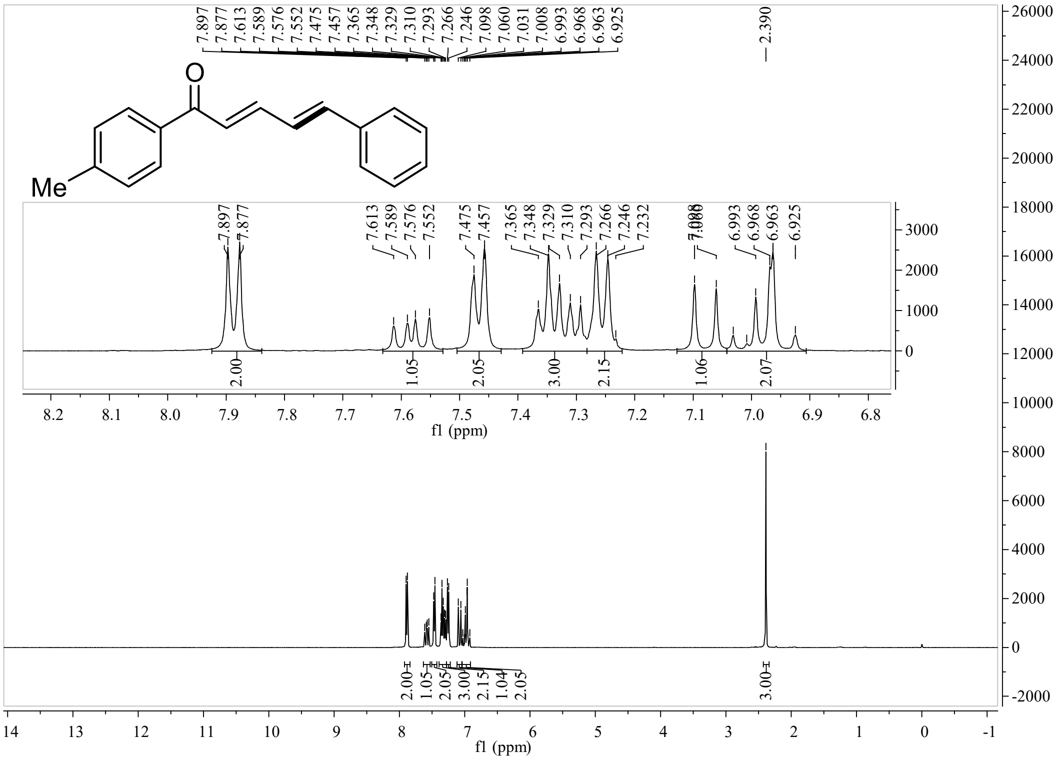

Figure S86^{1}H NMR spectrum of compound **2br**, related to **Scheme 2**

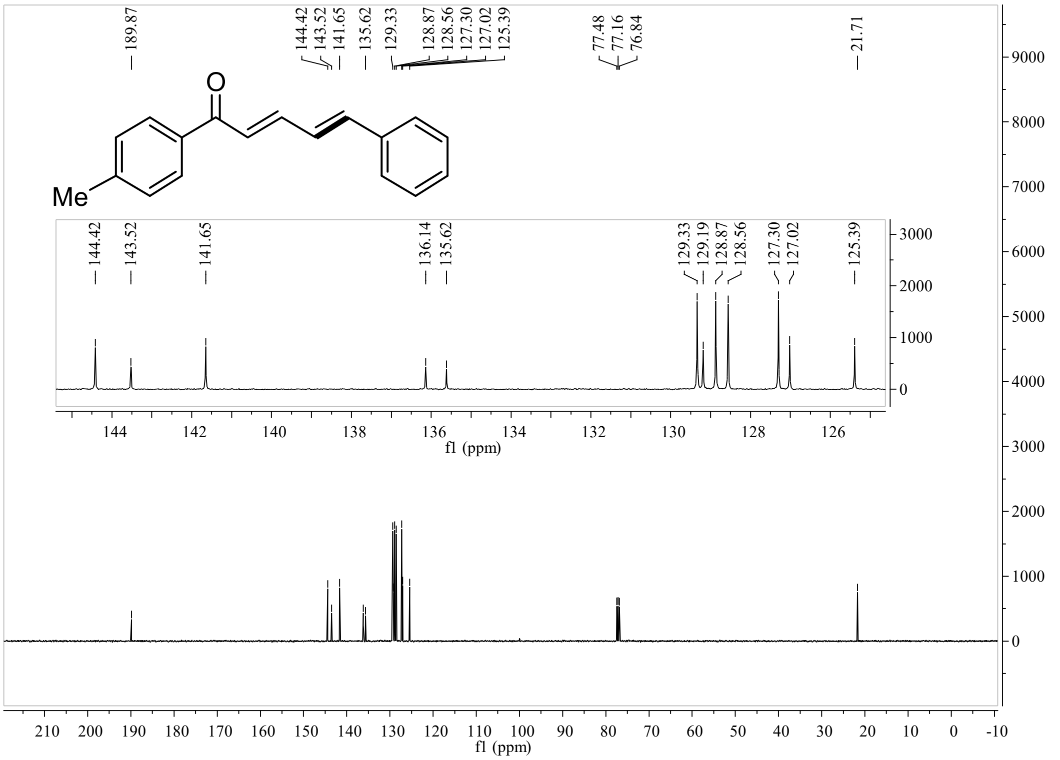

Figure S87 ^{13}C NMR spectrum of compound **2br**, related to **Scheme 2**

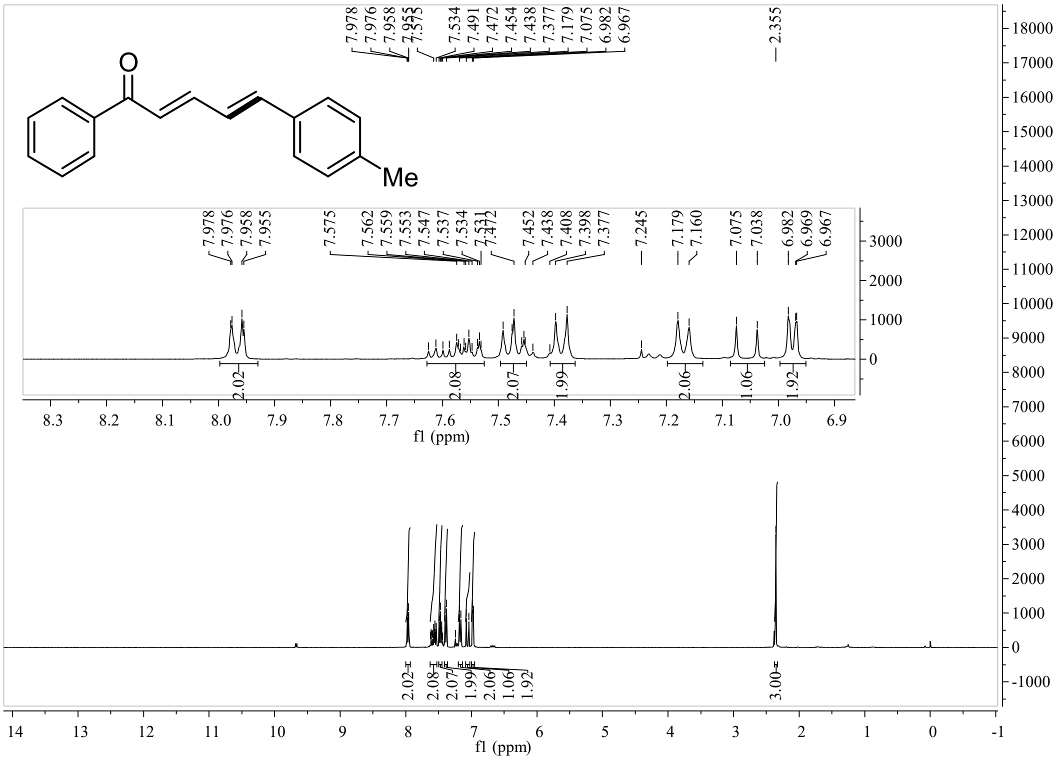

Figure S88 ^{1}H NMR spectrum of compound **2bs**, related to **Scheme 2**

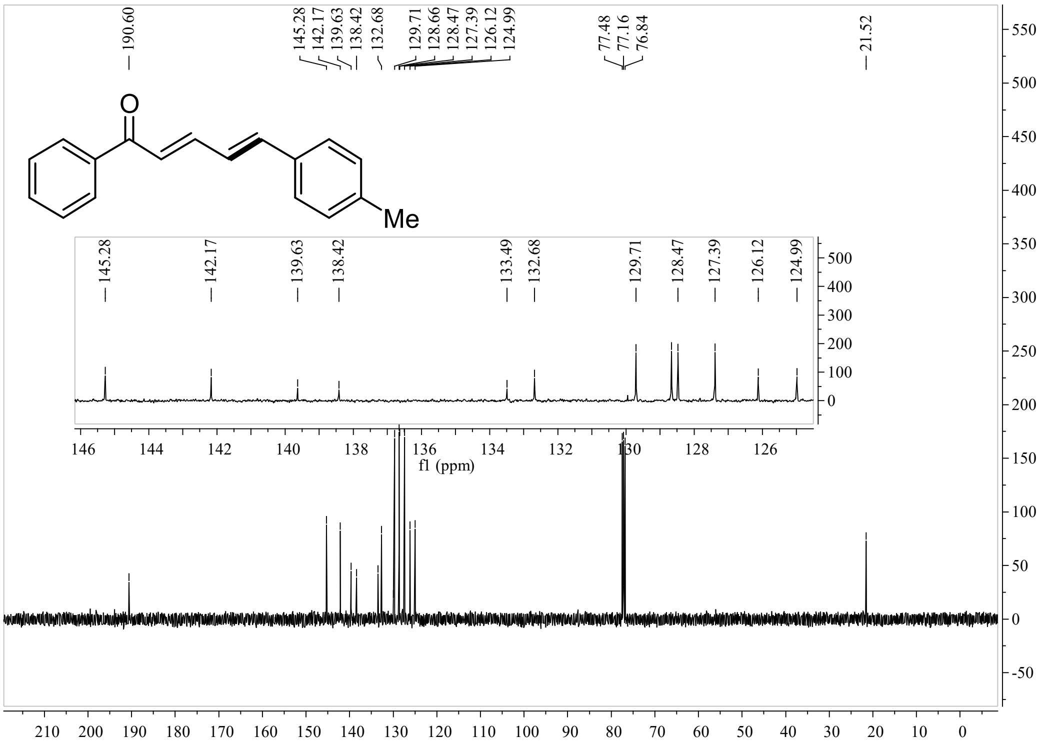

Figure S89 ^{13}C NMR spectrum of compound **2bs**, related to **Scheme 2**

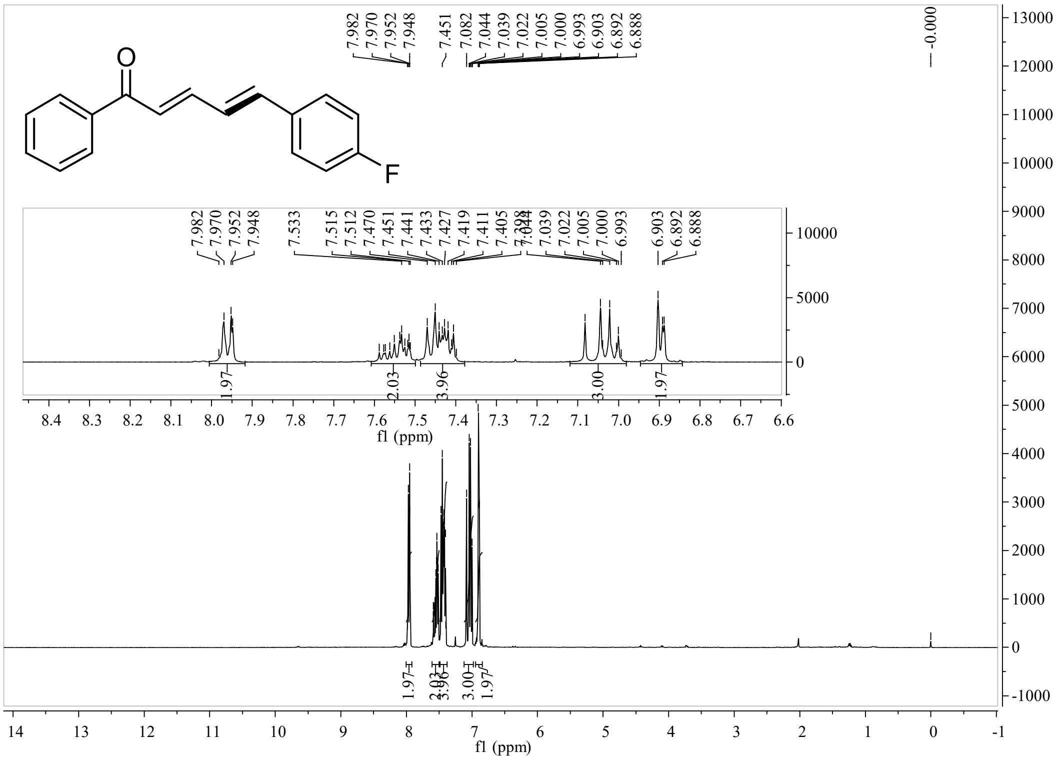

Figure S90 ^{1}H NMR spectrum of compound **2bt**, related to **Scheme 2**

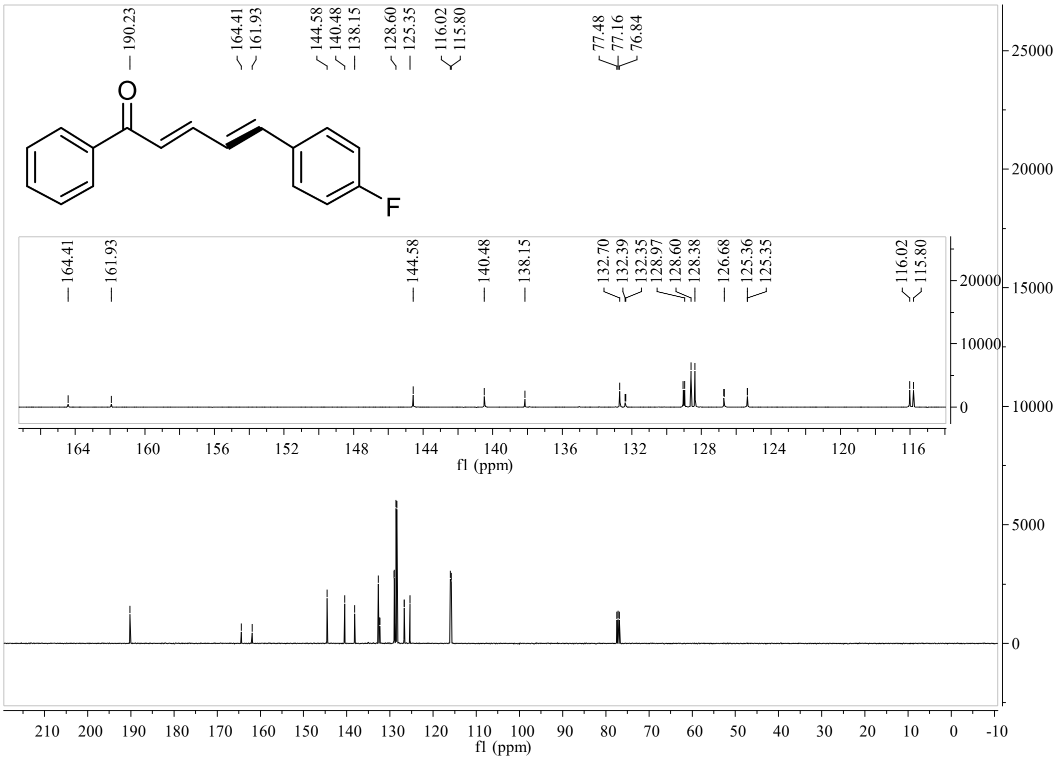

Figure S91 ^{13}C NMR spectrum of compound **2bt**, related to **Scheme 2**

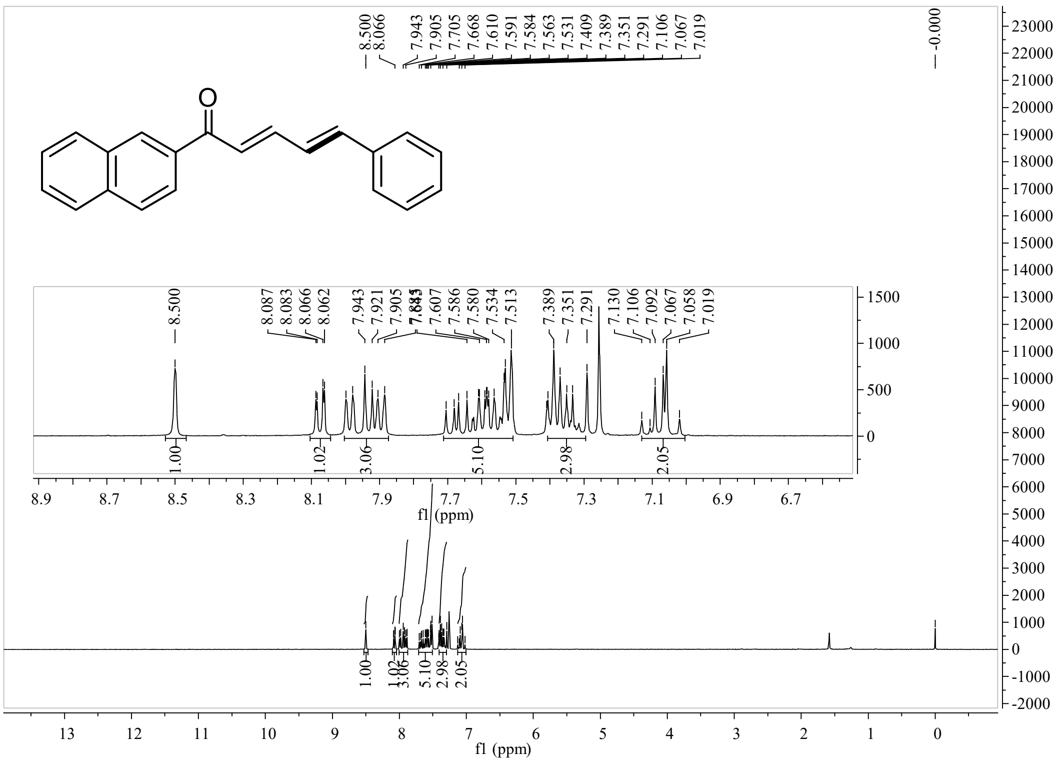

Figure S92 ^{1}H NMR spectrum of compound **2bu**, related to **Scheme 2**

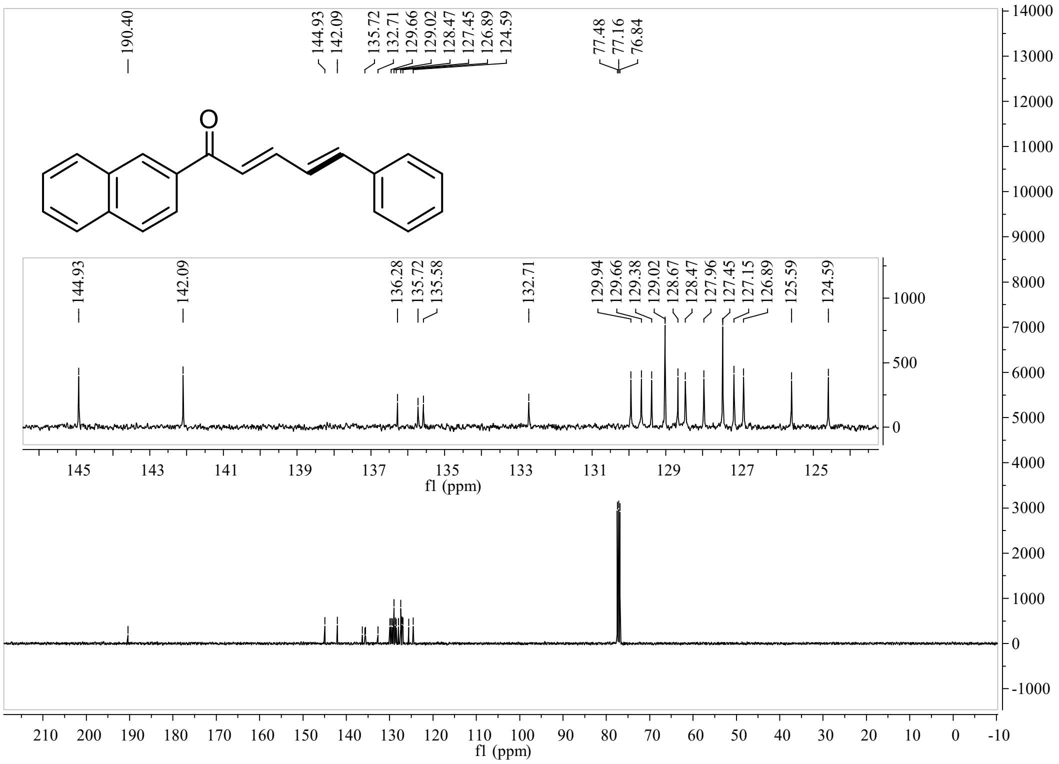

Figure S93 ^{13}C NMR spectrum of compound **2bu**, related to **Scheme 2**

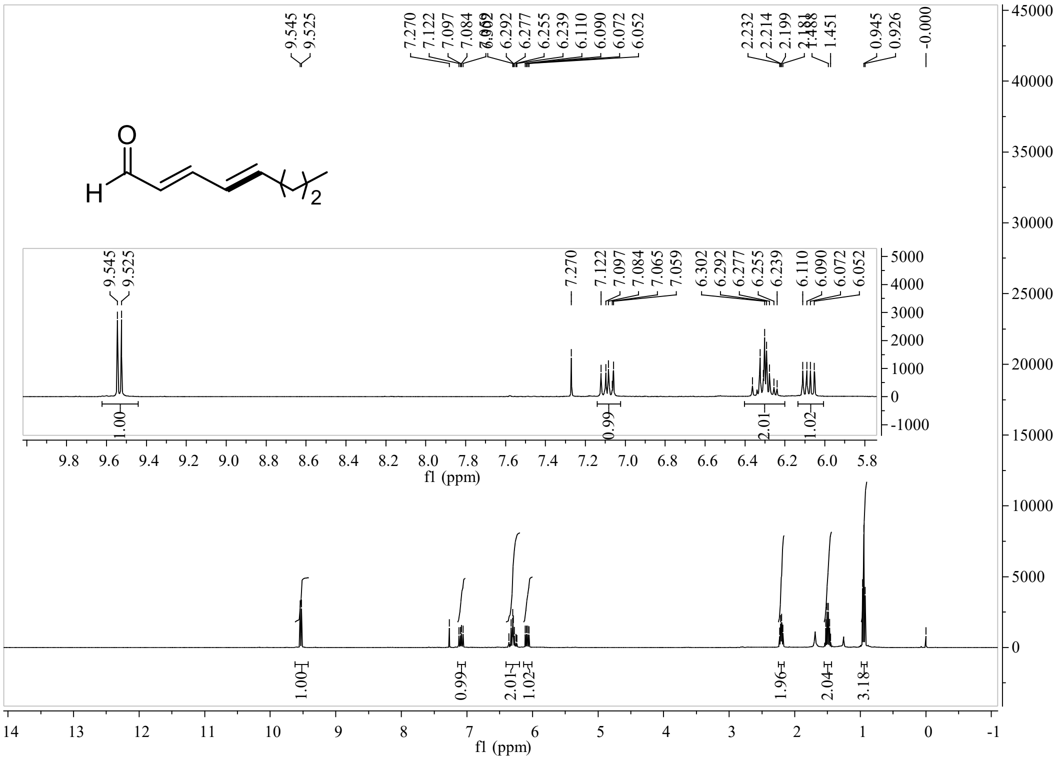

Figure S94 ^{1}H NMR spectrum of compound **4aa**, related to **Scheme 2**

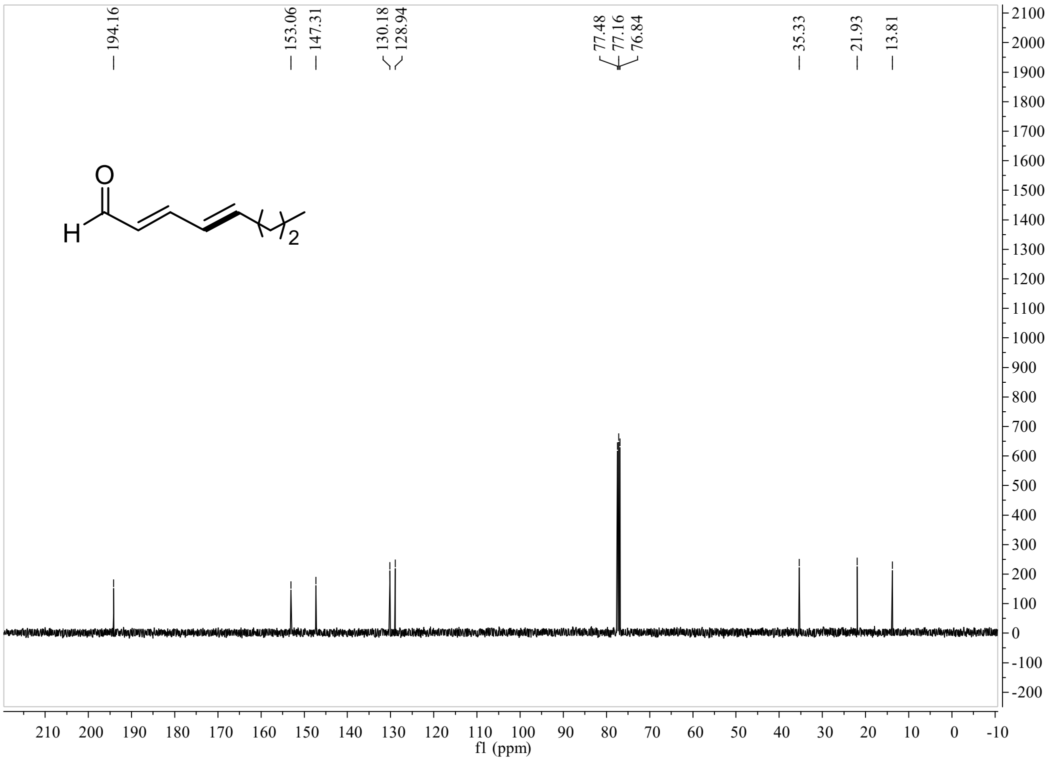

Figure S95 ^{13}C NMR spectrum of compound **4aa**, related to **Scheme 2**

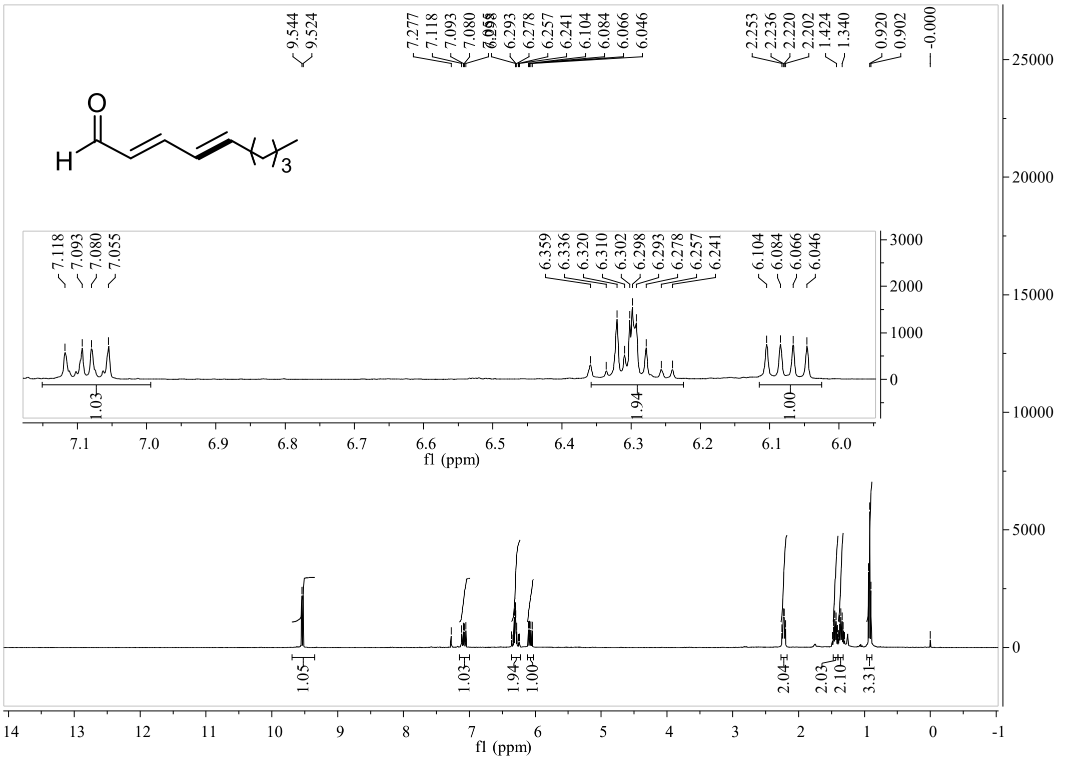

Figure S96 ^{1}H NMR spectrum of compound **4ab**, related to **Scheme 2**

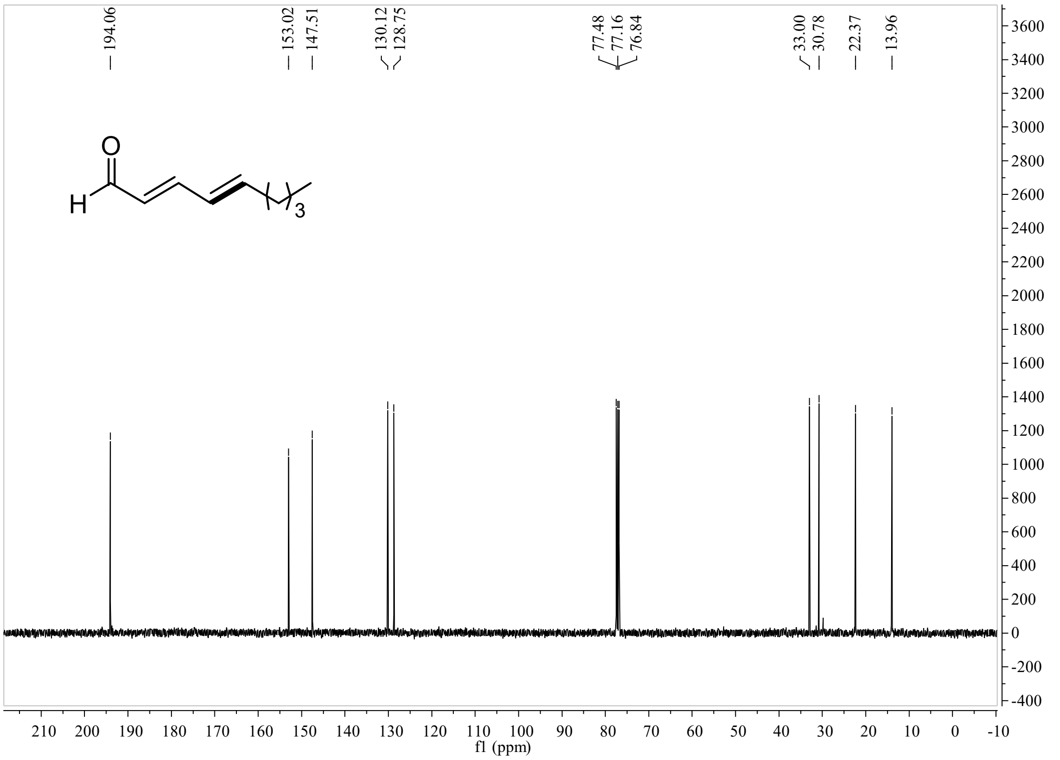

Figure S97 ^{13}C NMR spectrum of compound **4ab**, related to **Scheme 2**

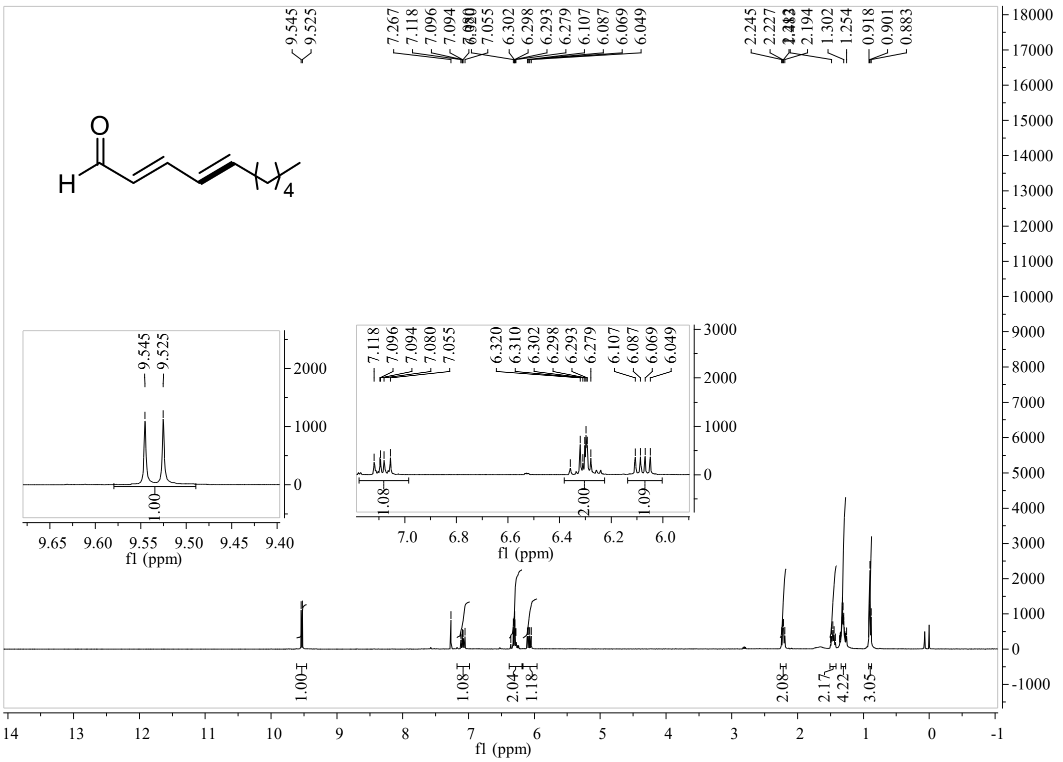

Figure S98 ^{1}H NMR spectrum of compound **4ac**, related to **Scheme 2**

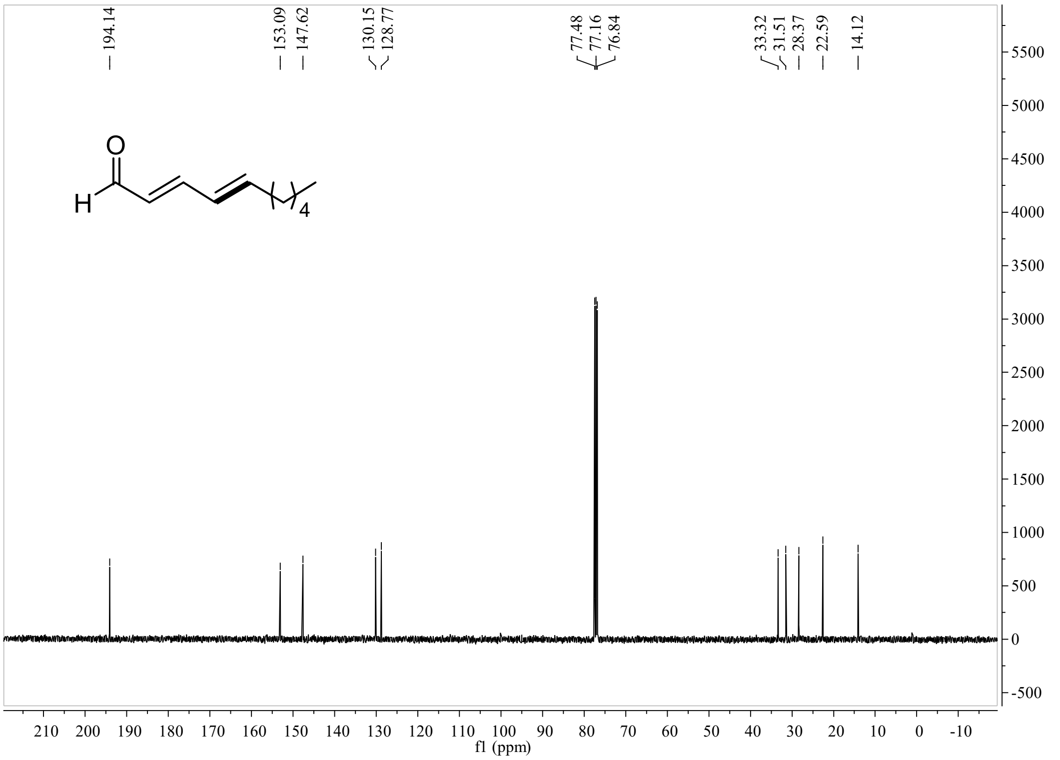

Figure S99 ^{13}C NMR spectrum of compound **4ac**, related to **Scheme 2**

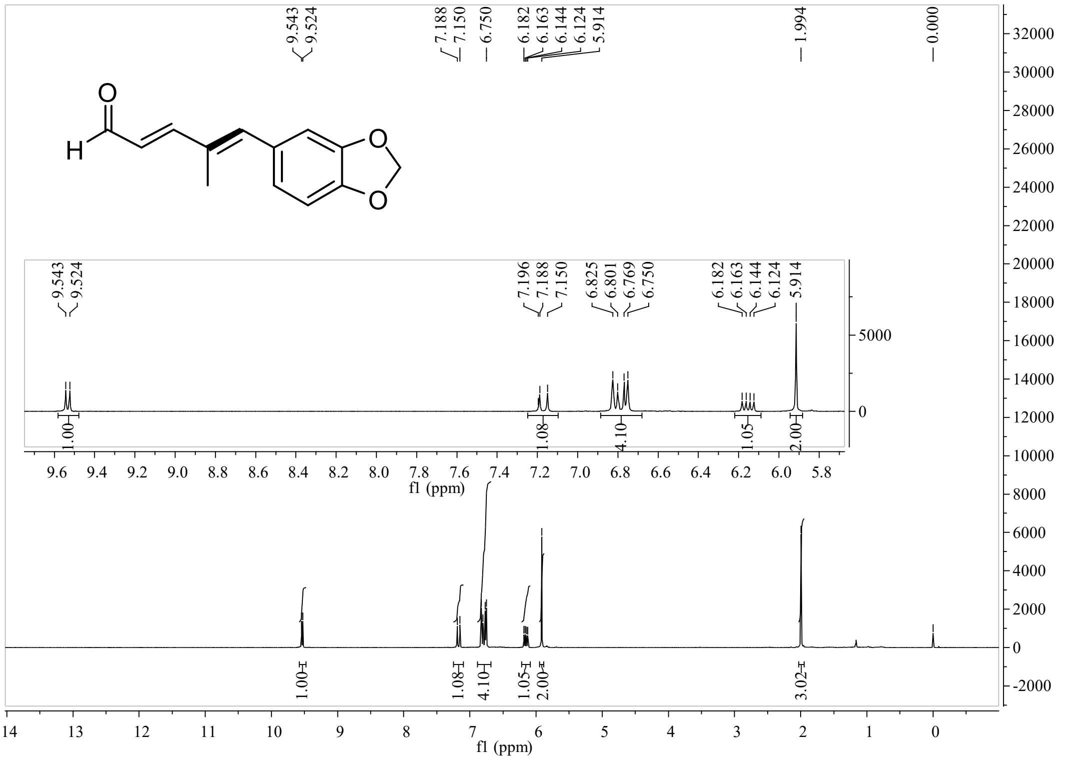

Figure S100 ^{1}H NMR spectrum of compound **4ae**, related to **Scheme 2**

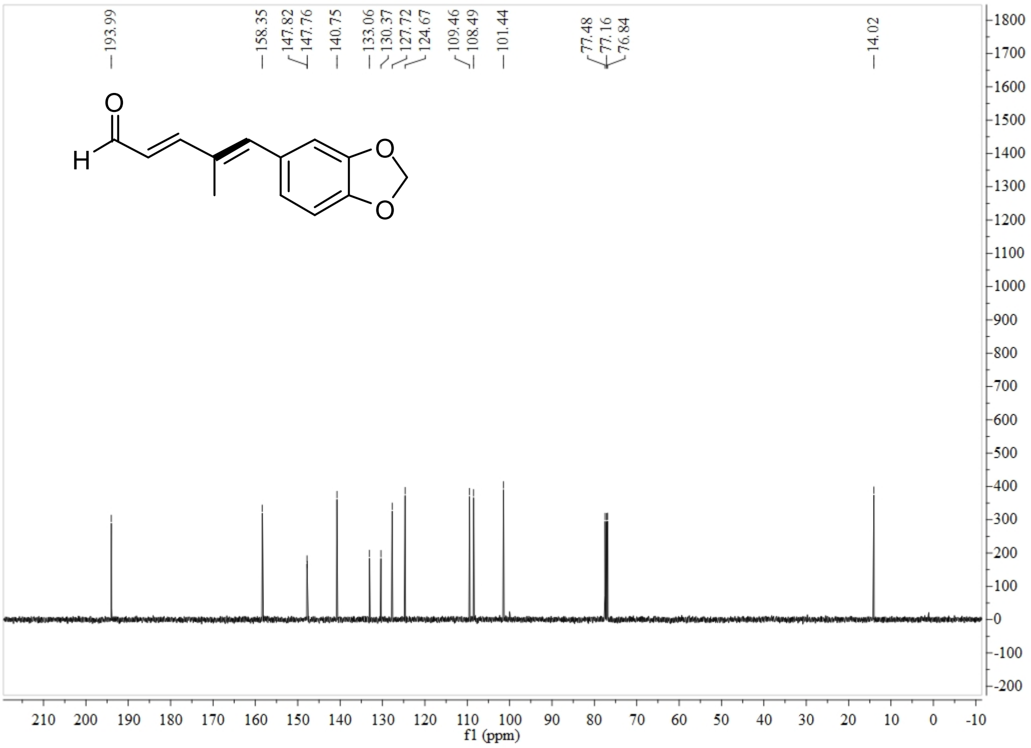

Figure S101 ^{13}C NMR spectrum of compound **4ae**, related to **Scheme 2**

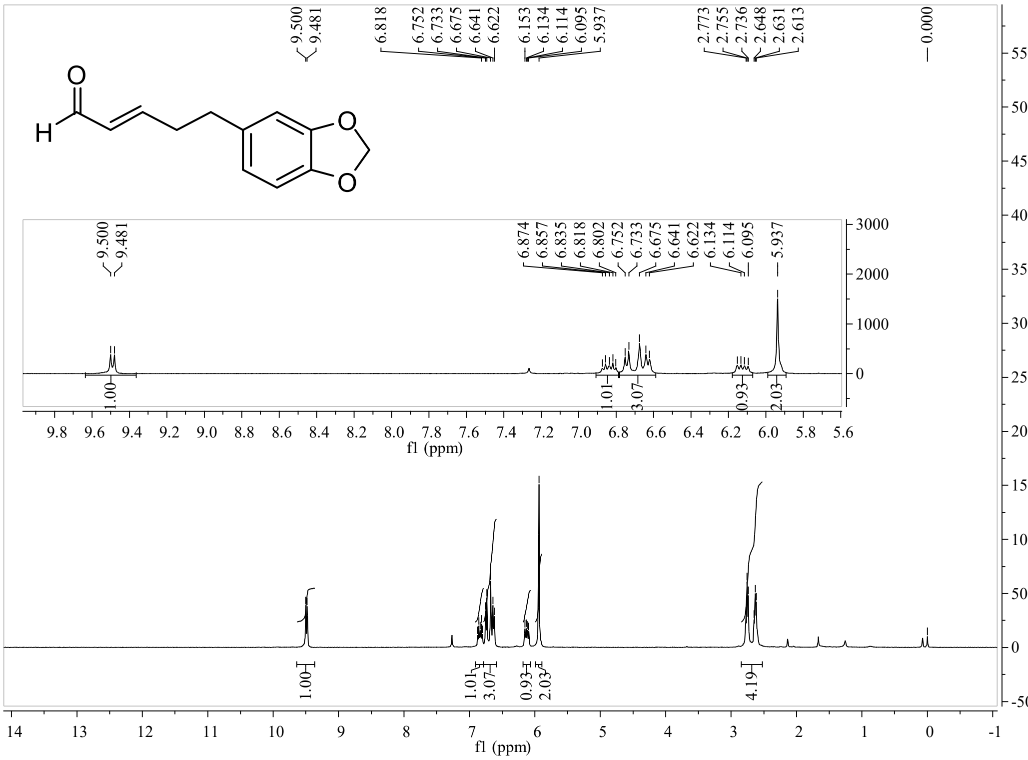

Figure S102 ^{1}H NMR spectrum of compound **3ad**, related to **Scheme 3**

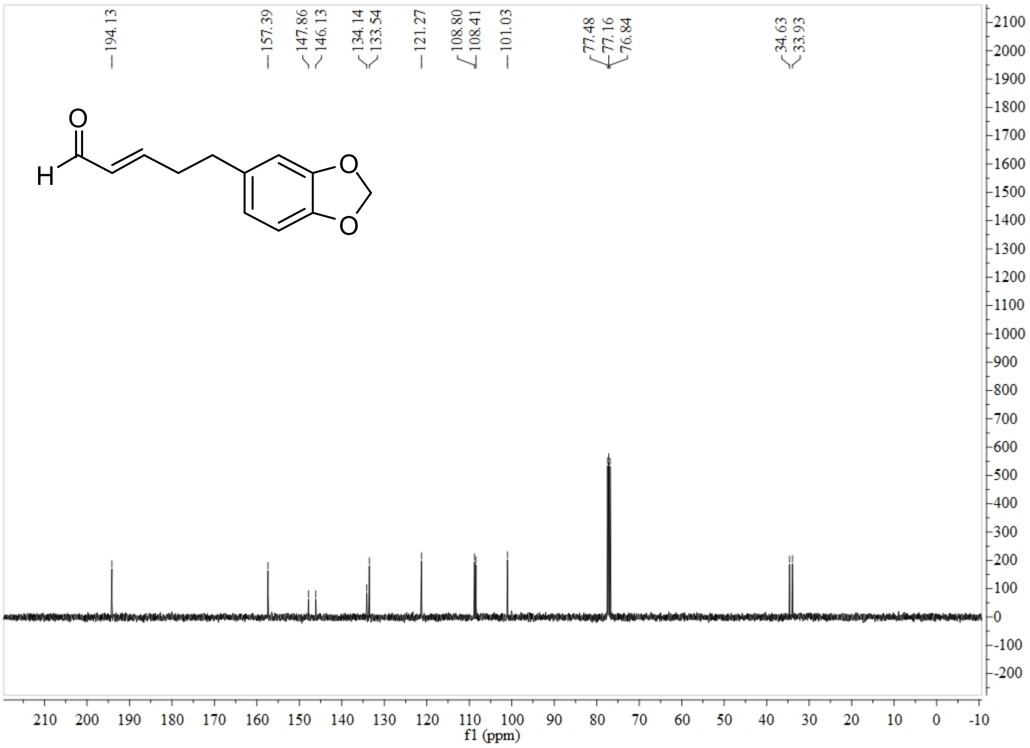

Figure S103 ^{13}C NMR spectrum of compound **3ad**, related to **Scheme 3**

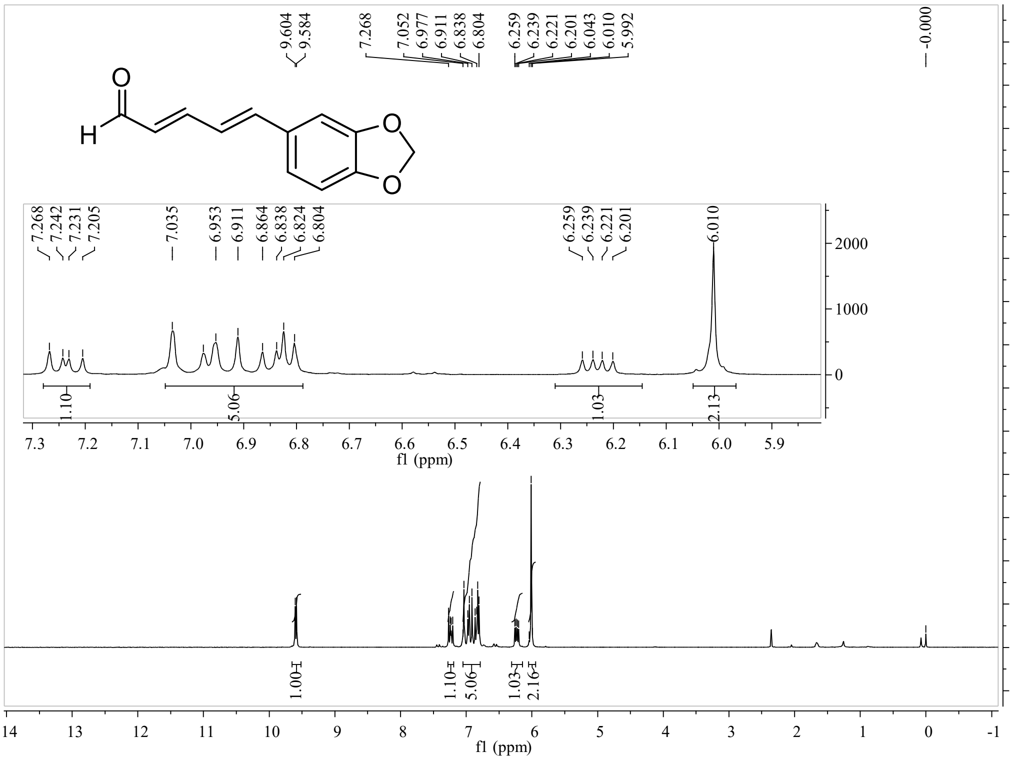

Figure S104 ^{1}H NMR spectrum of compound **4ad**, related to **Scheme 3**

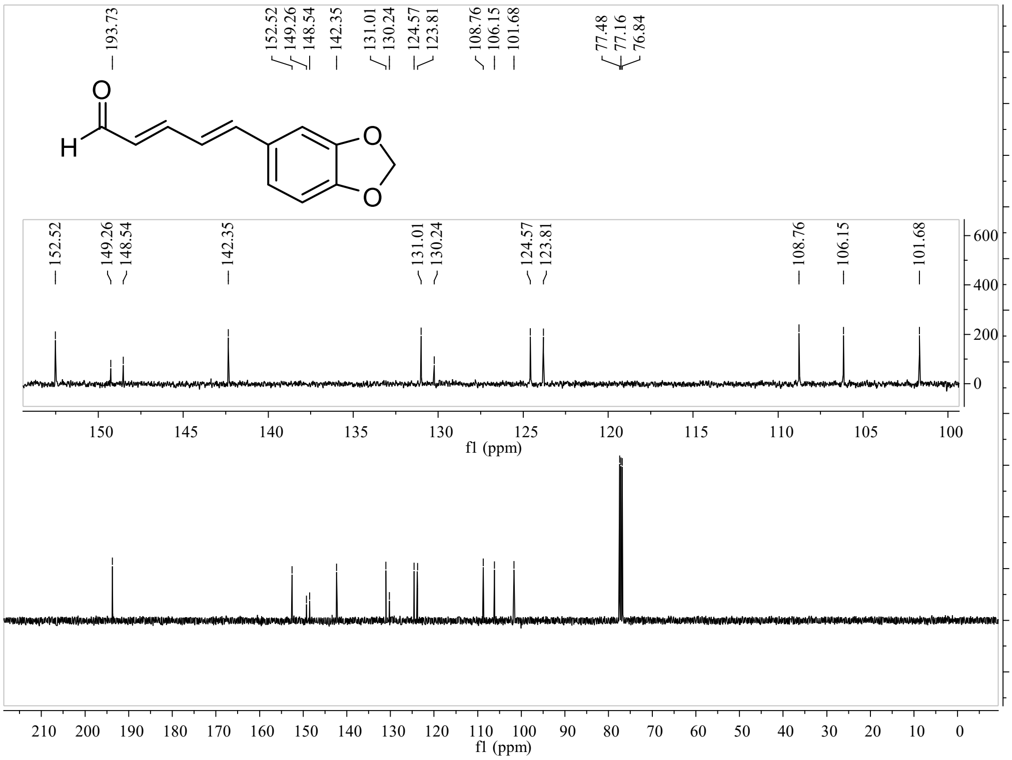

Figure S105 ^{13}C NMR spectrum of compound **4ad**, related to **Scheme 3**

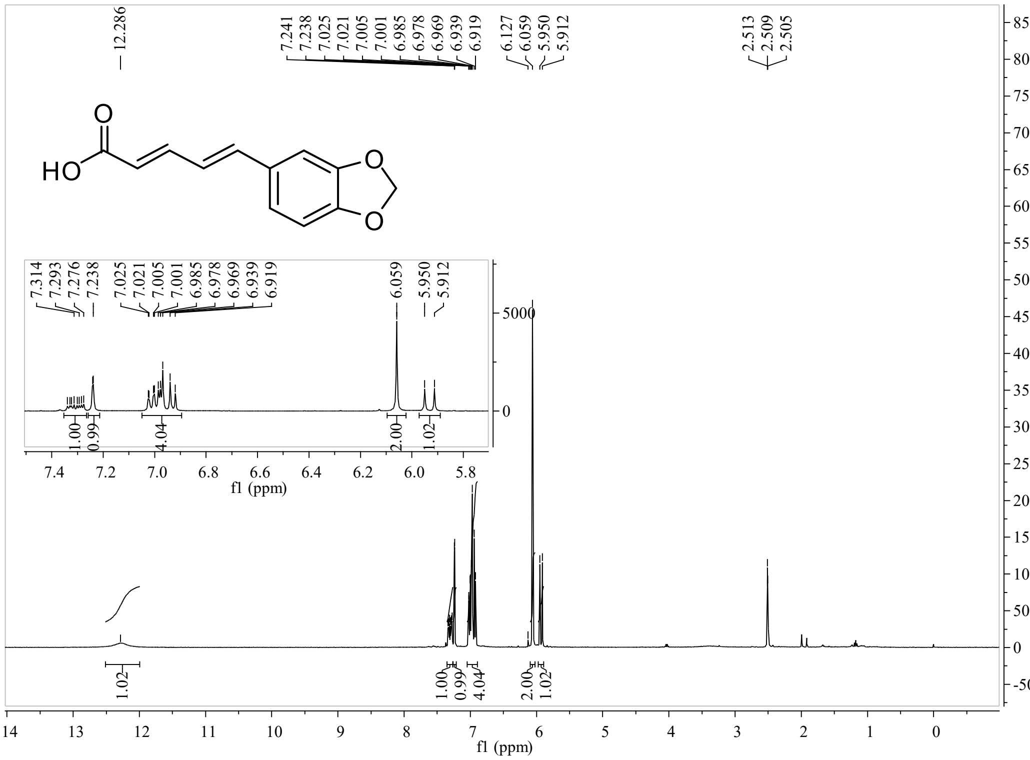

Figure S106 ^{1}H NMR spectrum of compound **5**, related to **Scheme 3**

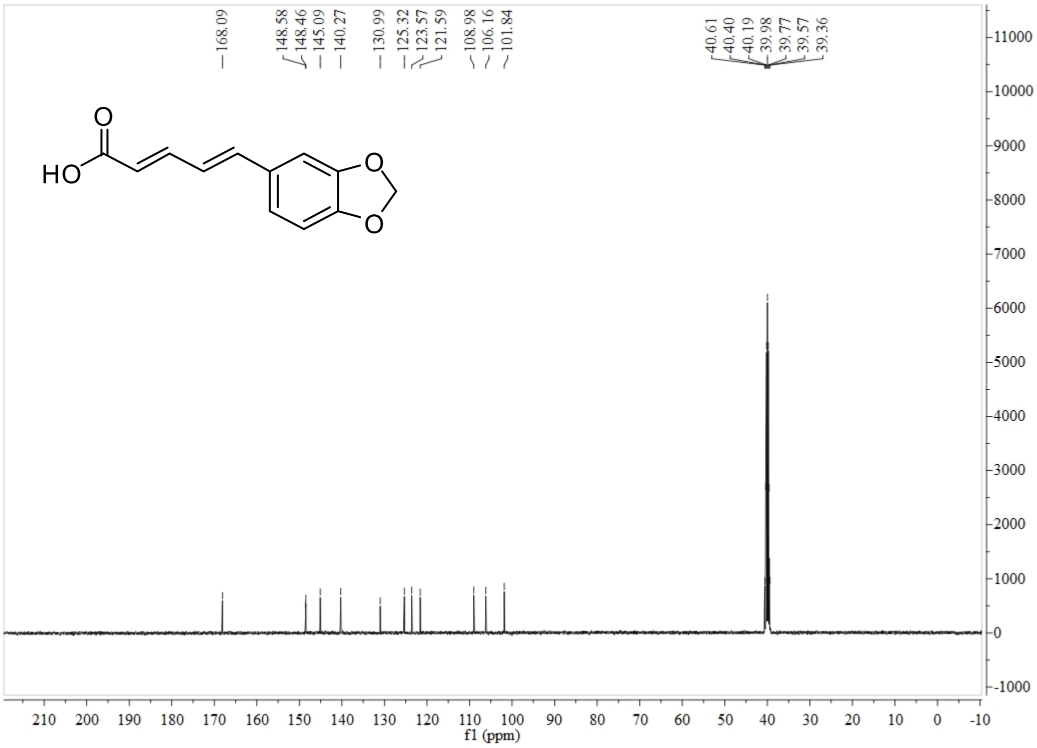

Figure S107 ^{13}C NMR spectrum of compound **5**, related to **Scheme 3**

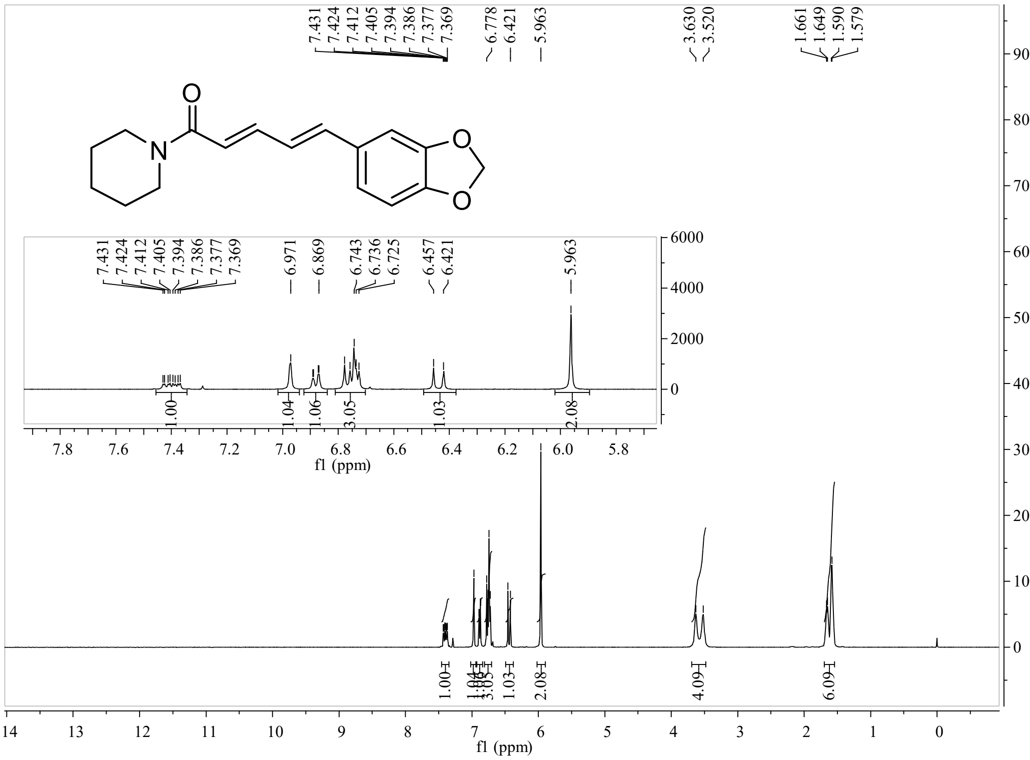

Figure S108 ^{1}H NMR spectrum of **Piperine**, related to **Scheme 3**

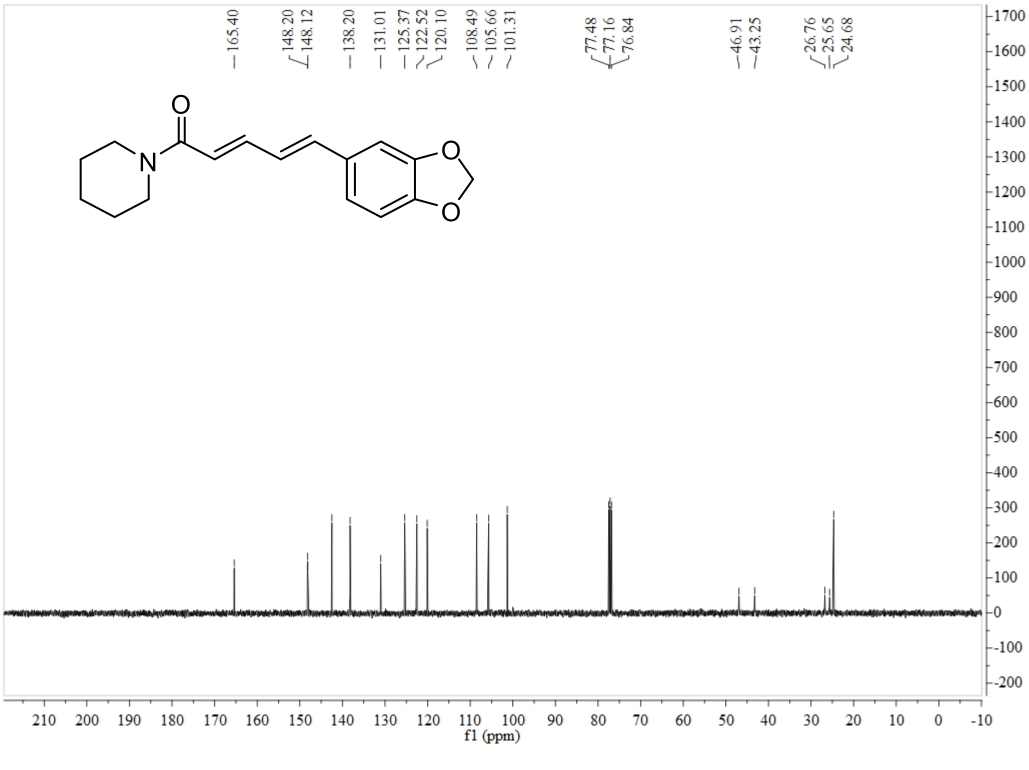

Figure S109 ^{13}C NMR spectrum of **Piperine**, related to **Scheme 3**

6. X-ray Crystal Structure of Compounds 2bt

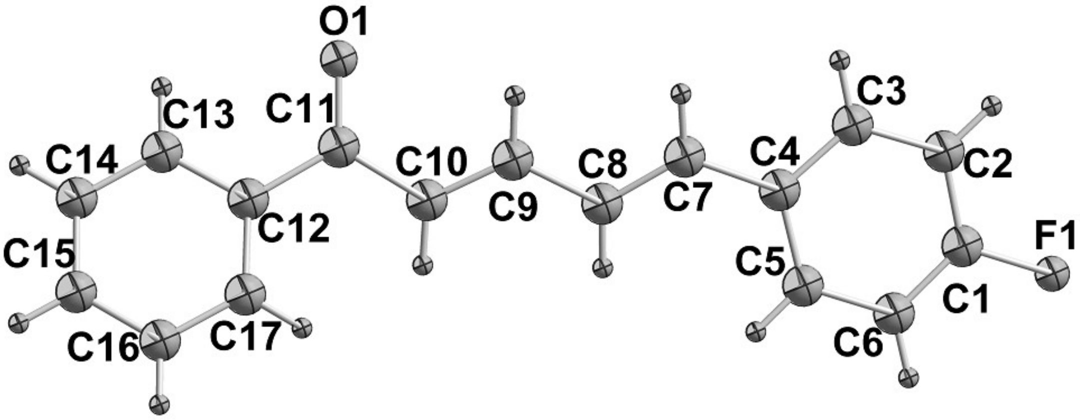

Figure S110 X-ray Crystal Structure of compound **2bt**, related to **Scheme 2**