Ruthenium-Catalyzed Oxidant Free *ortho*-Alkenylation of Aromatic Amides with Alkenes at Room Temperature

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By

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Certificate

This is to certify that this dissertation entitled *"Ruthenium-Catalyzed Oxidant Free ortho-Alkenylation of Aromatic Amides with Alkenes at Room Temperature"* towards the partial fulfilment of the BS-MS dual degree program at the Indian Institute of Science Education and Research, Pune represents original research carried out by

M. Padmaja at IISER Pune under the supervision of "Dr. Masilamani Jeganmohan, Assistant Professor, IISER Pune Chemistry Department" during the academic year 2014-2015.
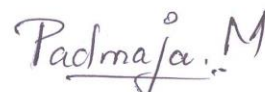
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Declaration

I hereby declare that the matter embodied in the report entitled *"Ruthenium-Catalyzed Oxidant Free ortho-Alkenylation of Aromatic Amides with Alkenes at Room Temperature"* are the results of the investigations carried out by me at the Department of Chemistry, Indian Institute of Science Education and Research (IISER), Pune, under the supervision of **Dr. Masilamani Jeganmohan** and the same has not been submitted elsewhere for any other degree.

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Contents

Ruthenium-Catalyzed Oxidant Free *ortho*-Alkenylation of Aromatic Amides with Acrylates at Room Temperature

1. Introduction

1.1 Abstract

Alkenylation is one of the important carbon-carbon bond formation reaction in organic synthesis. Because, alkene units are found in various natural products and biologically active molecules. Generally oxidant and higher temperature is required for palladium-catalyzed alkenylation reaction. Here we reported alkenylation of aromatic benzamides with alkenes in the presence of [{RuCl$_2$(p-cymene)}$_2$] , AgSbF$_6$ in 1,2 dichloroethane providing *ortho*-alkenylated amides in a highly regio- and stereoselective manner in the absence of oxidant at room temperature.

1.2 General aspects

Carbon-carbon bond formation is one of the central importances in synthetic organic chemistry. They provide the framework upon which many complex organic molecules are constructed. Such carbon-carbon or carbon-hetero atom bond formation can be done using coupling reactions like Stille coupling, Negishi coupling, Suzuki coupling, Heck reaction, Sonagashira coupling. In 2010, the Royal Swedish Academy of Sciences awards the Nobel Prize in Chemistry to Richard Heck, Ei-chi Negishi and Akira Suzuki for developing palladium-catalyzed carbon-carbon bond formation reactions. Among these heck reaction is quite important, because the variety of substituted alkenes are directly synthesized by using heck reaction. It is also known that the alkene structural units are present in various natural products and biologically active molecules.

1.3 Heck reaction

In the early 1970s, Heck and Mizoroki independently discovered this reaction. It is an efficient and powerful method for C–C bond formation where haloarenes and haloalkenes couple with alkenes in the presence of a palladium catalyst and a base to give the corresponding substituted alkenes (eq 1). Generally the reaction proceeds with high stereo- and regio selectivity.


$$(1)$$
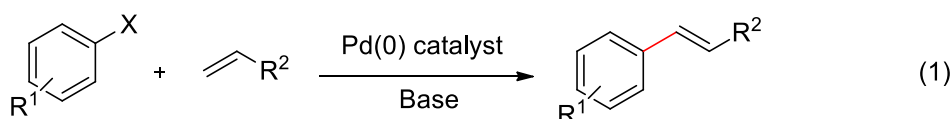
In 1971, Mizoroki *et al.* reported preliminary results on the PdCl$_2$-catalyzed coupling between iodobenzene and styrene in the presence of potassium acetate as base (eq 2). Methanol is used as solvent here.[1]

$$\text{0.1 equiv PdCl}_2$$
$$\text{1.2 equiv CH}_3\text{COOH}$$
$$\text{CH}_3\text{OH, 120 °C}$$

(2)
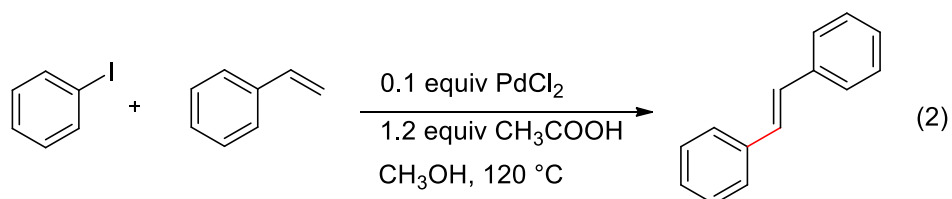
In 1972, Heck and Nolley improved the reaction by using Pd(OAc)$_2$ as catalyst And *n*-Bu$_3$N as base (eq 3). The reactions were performed without any solvent or in *N*-methylpyrrolidone (NMP) at 100°C.[2]

$$\text{Pd(OAc)}_2 \text{ (20 mol \%)}$$
$$\textit{n}\text{-Bu}_3\text{N} \quad \text{(1 equiv)}$$
$$\text{NMP,100 °C, 2 h}$$

(3)
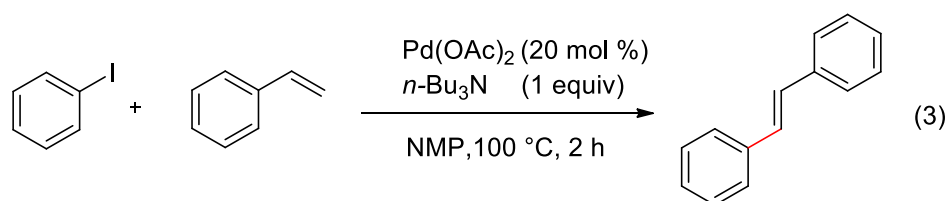
In 1974, Heck and Dieck developed the use of PPh$_3$ in association with Pd(OAc)$_2$. They also proposed the clear mechanism for reactions catalysed by Pd(OAc)$_2$ associated with monophosphine ligands which involve steps like reduction, oxidative insertion, syn insertion, internal C-C rotation, beta hydride elimination and reductive elimination (Scheme 1).[3]
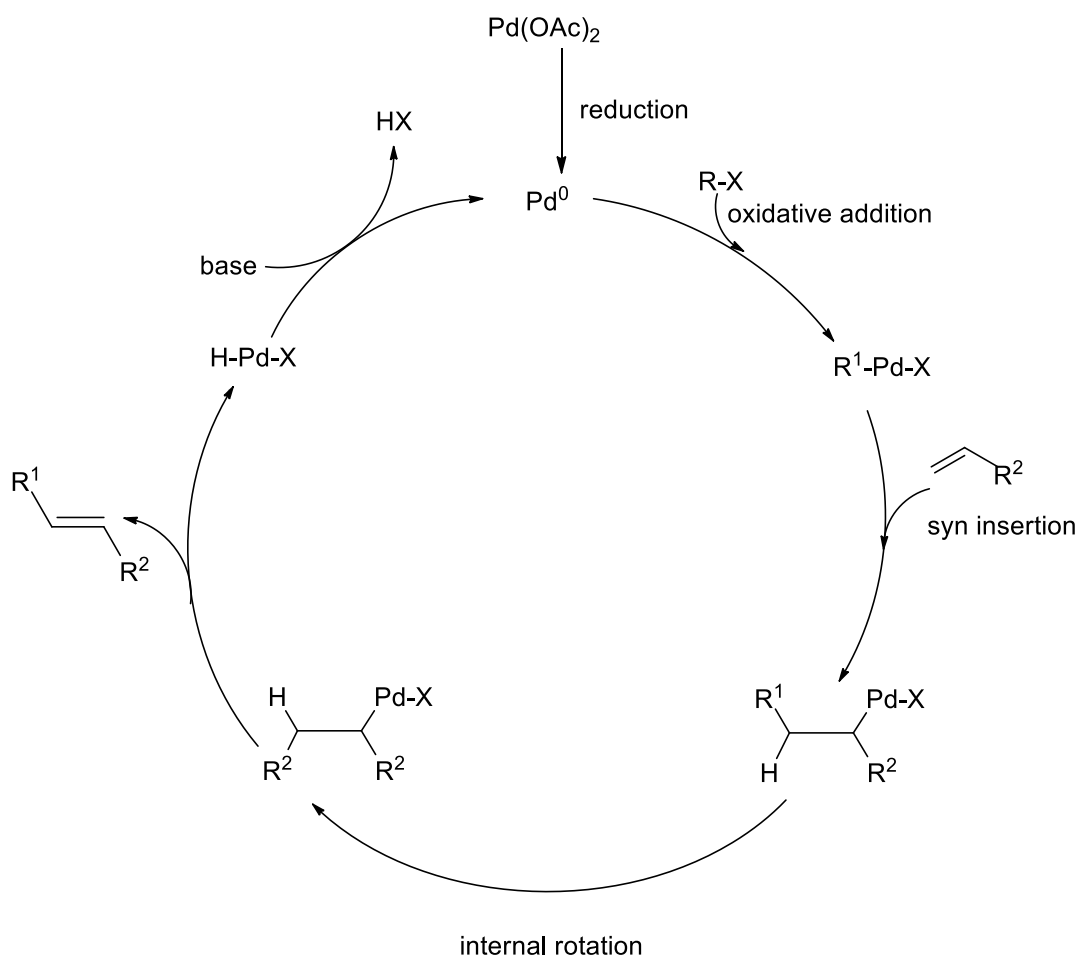
Scheme 1. Mechanism of heck reaction using palladium catalyst

Heck reaction benefited many communities especially the synthesis of pharmaceuticals and agro-chemicals. Alkene units are found in variety of natural products and biologically active molecules (Figure 1).[4]

Montelukast

Taxol
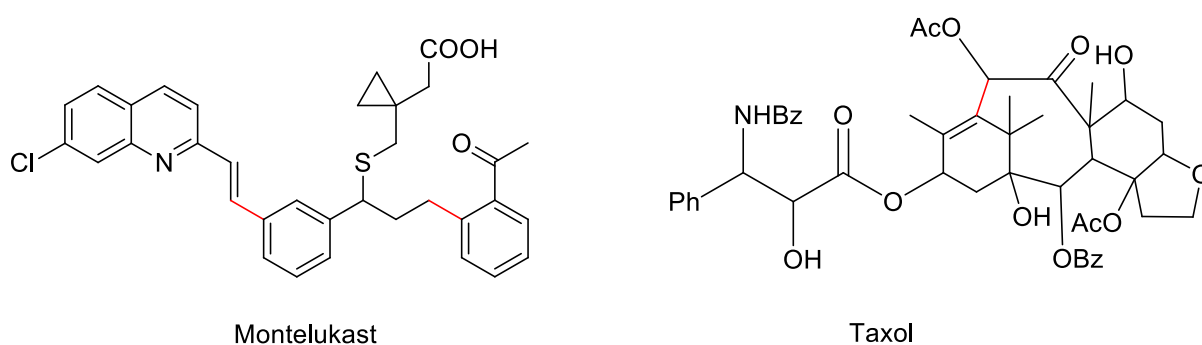
Figure 1. Natural products and biologically active molecules

The Heck reaction is applied industrially in the production of naproxen and the sunscreen component octylmethoxycinnamate. The synthesis of naproxen includes a coupling of a brominated naphthalene and ethylene (eq 4).[4]

(4)

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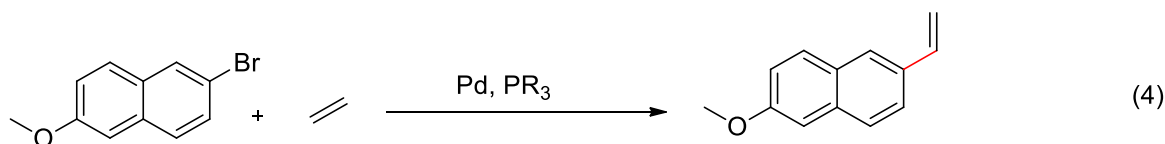
Lasiodiplodin, the anticancer macro cyclic natural product was synthesised in Fürstner's laboratory by using heck reaction to introduced the styrenyl moiety of an aryl triflate with ethylene gas (eq 5).[4]

(5)
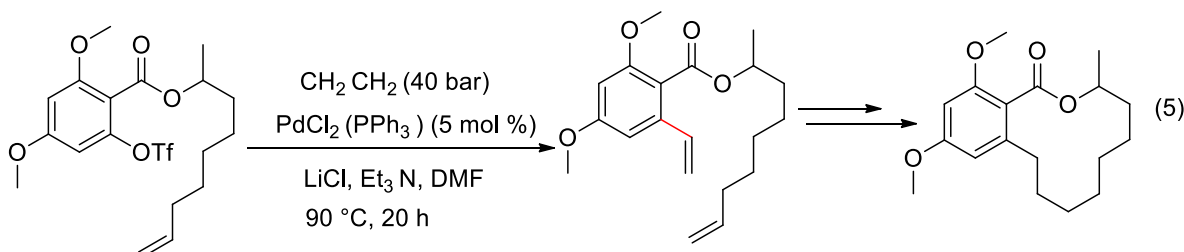
AstraZeneca in 2002, published a synthetic route to a key intermediate, through heck reaction by coupling of 3-bromopyridine and 3-butene-1, 2-diol in the presence of Pd-catalyst (eq 6). Even though the yield which they got was little low, there was a significant improvement than the previous method.[4]

(6)
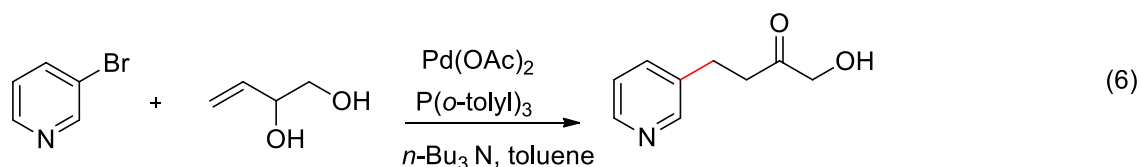
All these applications made Heck reaction an important transformation in organic synthesis.

1.4 Developments in Heck reaction:

The Mizoroki–Heck reaction is a highly valued synthetic method for the formation of C-C bonds. However, the pre-functionalized starting material (Ar-X; X=halogen, OTf) is required for this reaction. An attractive substitute was established by Moritani and Fujiwara. They developed oxidative Heck-type couplings, allowing the use of simple arenes as starting materials (eq 7).[5] In terms of atom economy and versatility this

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approach offers significant advantages over the traditional coupling. However, substituted arene gives regio isomeric mixture of products.

$$\text{(7)}$$
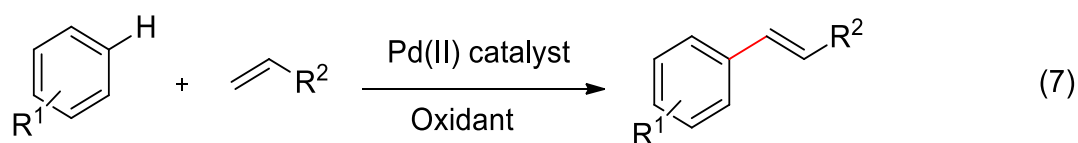
Recently, the metal-catalyzed directing group (DG)-assisted *ortho* C-H bond activation and oxidative alkene coupling became a powerful tool for the carbon-carbon bond formation. Directing group assisted alkenylation can be done by using various metal catalysts (eq 8). Among the metals palladium, rhodium and ruthenium are frequently used for such transformation.

$$\text{(8)}$$
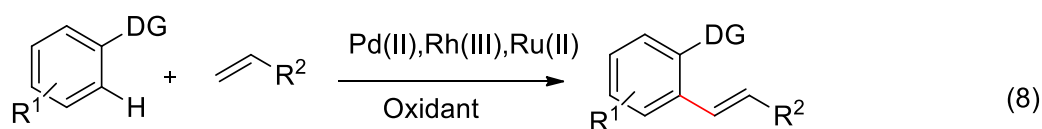
DG=NHCOR, CONHR, COR, C=N-OMe, COOH, CH(R)NH$_2$, Pyridyl etc

In 1998, Miura co-workers reported oxidative coupling of sulfonamides and benzoic acids with alkenes in the presence of palladium as a catalyst and Cu(OAc)$_2$·H$_2$O as oxidant. Here, they observed alkenylation followed by cyclization product (eq 9).[6]

$$\text{(9)}$$
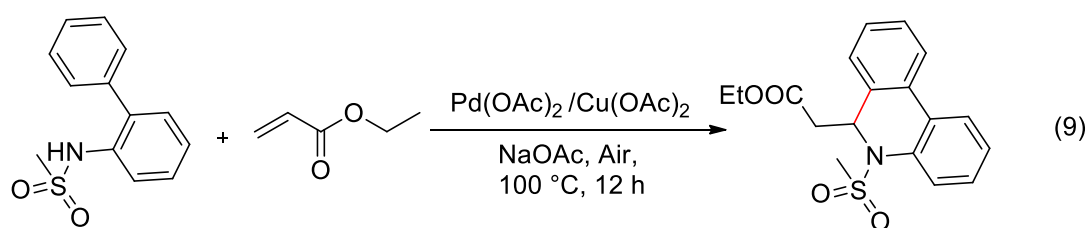
Later, in 2002, Johannes G. de Vries and Piet W. N. M. van Leeuwen reported oxidative coupling of anilides with olefins by activating C-H bond at room temperature (eq 10). Here, benzoquinone is used as oxidant. Acetic acid is used as the solvent.[7]

(10)
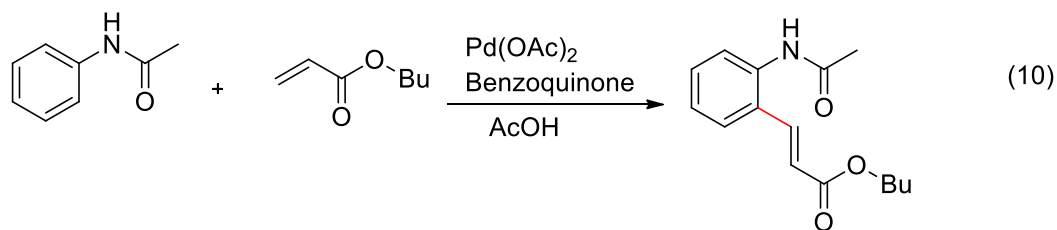
Recently in 2010, Jin-Quan Yu *et al.* published a palladium-catalyzed enantioselective C-H bond activated alkenylation of diphenylacetic acids in the presence of ligand and benzoquinone oxidant (eq 11). Solvent used here is *t*-AmOH. Reaction occurred at 90 $^{\circ}$C.[8]

(11)
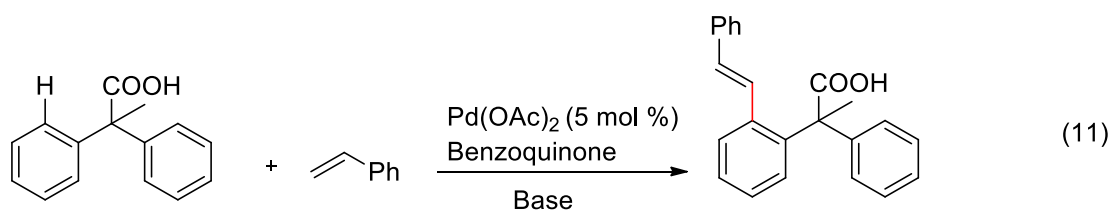
Thus, they succeeded in conducting the palladium-catalyzed oxidative coupling of many directing group assisted substrates with alkenes by using oxidant and base.
In addition, acids, metal salt additives and stabilizing ligands are frequently used; otherwise, decomposition of the palladium catalyst to inertmetallic palladium is a typical deactivation pathway of the catalyst. These issues have limited the practicability of palladium catalysis in the laboratory and in industry.

In the meantime, the rhodium-catalyzed oxidation of olefins was widely investigated because of its high efficiency, selectivity, and functional group tolerance. Actually, the last five years has witnessed drastic progress in this field of Rhodium(III) catalysts.

In the year 2009, Masahiro Miura co-workers reported a rhodium-catalyzed mono-divinylaton of 1-phenylpyrazoles with alkenes in the presence of $Cu(OAc)_2{\cdot}H_2O$ as oxidant (eq 12). DMF is used as solvent. In some cases, they observed both mono and di-alkenylated products.[9]

$$(12)$$
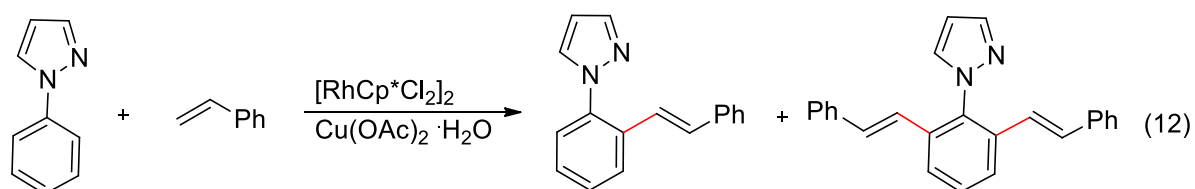
Later, in 2010, Frank Glorius reported a Rh-Catalyzed Olefination of Unactivated Acetanilides with alkenes (eq 13). Here, acetanilides is treated with styrene in the presence of oxidant and additives. The reaction mixture is heated up to 120 ^{o}C. Tertiary amylalcohol is used as solvent.[10]

$$(13)$$
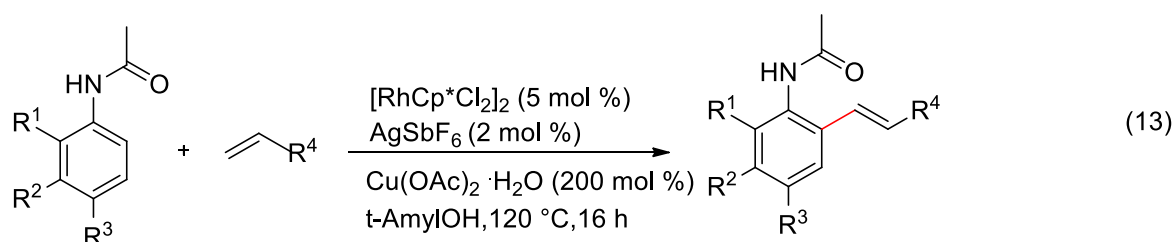
Then, in 2010, Robert G. Bergman and Jonathan A. Ellman reported a Rh(III)-catalyzed oxidative coupling of unactivated alkenes through C-H activation in the presence of Cu(OAc)$_2$·H$_2$O as oxidant, AgSbF$_6$ as additive and THF as solvent at 75 ^{o}C (eq 14).[11]

$$(14)$$
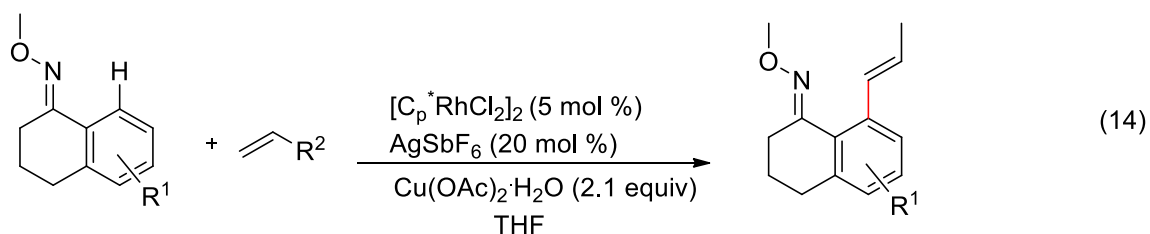
Recently, the use of easy-to-prepare and more stable ruthenium(II) catalysts has massively contributed to the discovery of cheaper and efficient catalytic systems, under the milder reaction conditions.[12]

In 1993, Murai co-workers reported alkylation of aromatic ketones with alkenes in the presence of Ru(0) catalyst (eq 15).[13]

$$(15)$$
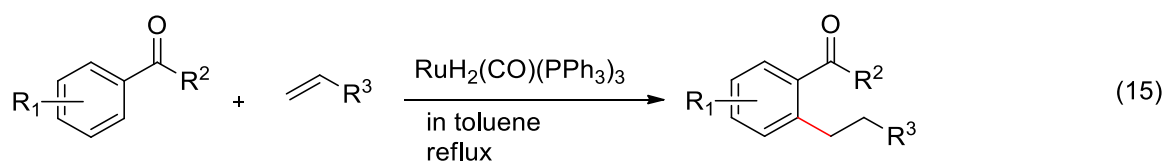
In 2012, we have reported a ruthenium-catalyzed alkenylation of weak directing groups containing aromatic aldehyde, ketone and esters with alkenes under an air atmosphere using 30 mol % of $Cu(OAc)_2 \cdot H_2O$ as oxidant in DCE at 100 $^{\circ}C$ for 12 h (eq 16).[14]

$$(16)$$

R_1= H, alkyl, OMe
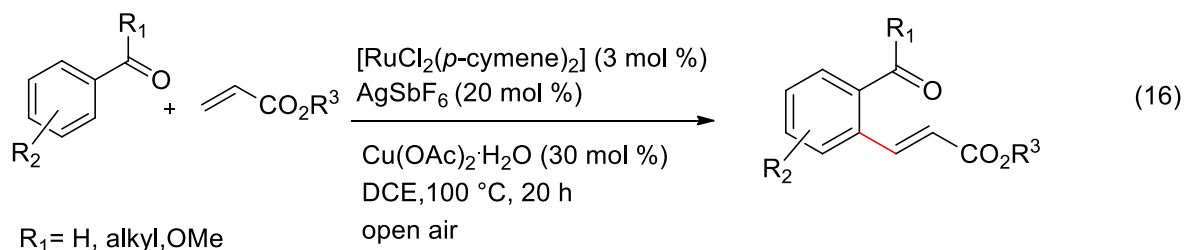
Subsequently, Miura's group reported an alkenylation of *N, N*-dimethyl benzamides with alkenes using Ru-catalyst in the presence of copper acetate as oxidant in tertiary amyl alcohol at 100°C (eq 17). In the reaction, $AgSbF_6$ additive was used.[15]

$$(17)$$
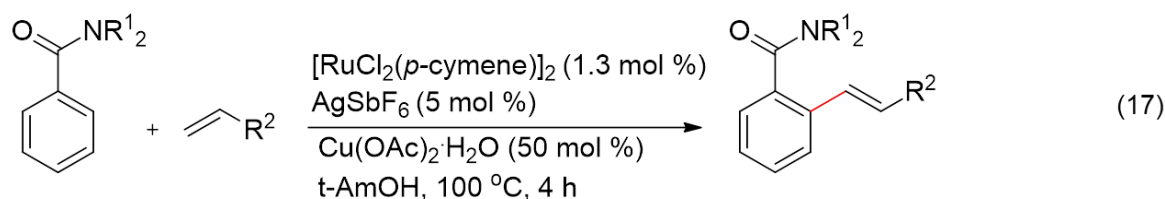
In the same year, Ackremann's group showed an alkenylation of anilides or benzamides with alkenes in the presence of Ru-catalyst, copper acetate oxidant and KPF_6 additive (eq 18). Water is the solvent here and the reaction mixture is heated to 120 °C for 20 h.[16]

$$(18)$$
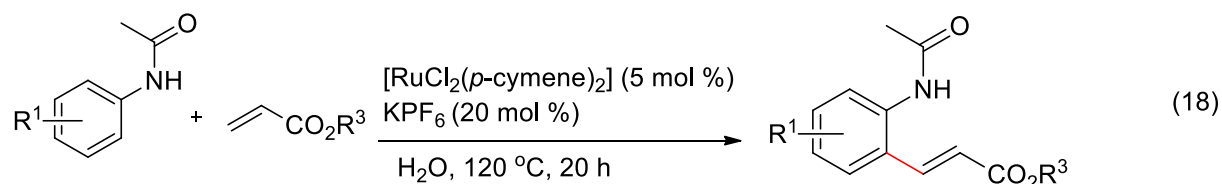
So far, many groups have reported directing group assisted C-H bond activation and alkenylation of arenes with alkenes using a variety of transistion metals such as palladium, rhodium and ruthenium catalysts. However, oxidant and higher temparature was required in most of the cases. Here, in my project, I tried

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alkenylation of aromatic amides with alkenes in the presence of ruthenium catalyst and AgSbF$_6$ as additive room temperature without any oxidant under the milder conditions. We used acetic acid as the acetate source instead of using metal acetates.

2. Results and Discussions:

Initially, we treated benzamide (**1a**) with methyl acrylate (**2a**) in the presence of [{RuCl$_2$(*p*-cymene)}$_2$] catalyst in 1,4-dioxane as solvent with acetic acid at 100 °C. Here, we didn't observe *ortho* alkenylated product. Interestingly, when we added AgSbF$_6$ as additive to the reaction mixture, we observed *ortho* alkenylated benzamide (**3aa**) in 40% yield. To increase the yield of the reaction, we further optimised the reaction condition by trying with different solvents (eq 19).

2.1 Solvent optimization:

We tried our reaction using various solvents such as THF, DME, DCE, methanol, toluene, acetonitrile, DMSO, DMF and water (Table 1). Methanol, toluene, acetonitrile, DMSO, DMF and water were ineffective for our reaction (entries 4-9). THF and DME were partially effective, yielding the product **3aa** in 52% and 54% yields, respectively (entries 1-2). In the case of DCE, we observed almost maximum conversion and giving alkenylated product **3aa** in 76% yield (entry 3).
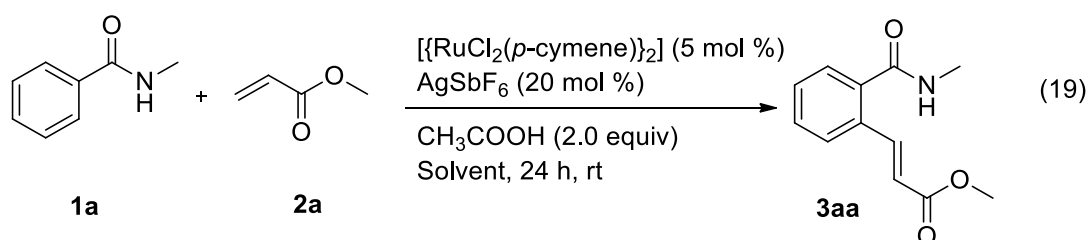
Table 1. Alkenylation of 1a with 2a in different Solvents to give 3aa.

S.no	Solvent (ml)	Yield of product 3aa (%)
1	THF	52
2	DME	54
3	DCE	76

4	Methanol	No reaction
5	Toluene	No reaction
6	Acetonitrile	No reaction
7	DMSO	No reaction
8	DMF	No reaction
9	Water	No reaction
10	1,4-dioxane	40

To further improvement of yield, we tried optimising the acrylate amount (Table 2). Initially, we added 1.5 equivalent of methyl acrylate to the reaction mixture and observed 76% yield of **3aa** (entry 1)**.** Surprisingly, when we used 2.0 equivalent of methyl acrylate (**2a**), we observed the alkenylated product **3aa** in yield of 86% (entry 2). There is no increment in yield by further increasing the amount of acrylate (entry 3).

Table 2. Alkenylation of 1a with different amounts of 2a to give 3aa.

S.no	Amount of acrylate (equiv)	Yield of product 3aa (%)
1	1.5	76
2	2	86
3	3	86

2.2 Optimization of additives and acids:

Next, we tried the reaction with different additives like $AgBF_4$, AgOTf, KPF_6 and $CuBF_4$ to increase the yield further (Table 3). There is no reaction with KPF_6 and $CuBF_4$ (entries 4-5). But, in case of $AgBF_4$ and AgOTf, we observed yield of 52% and 64% of alkenylated product **3aa** (entries 2-3).

Table 3. Alkenylation of 1a with 2a in different additives to give 3aa.

S.no	Additives (20 mol %)	Yield of product 3aa (%)
1	$AgSbF_6$	86
2	$AgBF_4$	52
3	AgOTf	64

4	KPF$_6$	No reaction
5	CuBF$_4$	No reaction

To make our reaction condition even better, we decided to optimize which acid could be more suitable for our reaction? We tried our reaction using different acids like pivalic acid (PivOH), mesitylinic acid, adamantane carboxylic acid, benzoic acid and acetic acid (Table 4). Unfortunately, in case of benzoic acid we observed very little conversion which yields 20% **3aa** (entry 4). But in PivOH, mesitylinic acid, adamantane carboxylic acid case, we got 69%, 64%, 61% yields of **3aa**, respectively (entries 1-3). But, in the case of acetic acid, we observed yield 86% of the alkenylated product **3aa** (entry 5).

Table 4. Alkenylation of 1a with 2a in different acids to give 3aa.

S.no	Acids (2 equiv)	Yield of product 3aa (%)
1	PivOH	69
2	Mesitylinic acid	64
3	Adamantane carboxylic acid	61
4	Benzoic acid	20
5	Acetic acid	86

2.3 Optimized condition:

Interestingly, when we reduced our reaction temperature to 80 °C, we observed product **3aa** in the same yield. So, finally we tried the same reaction at ambient temperature. Surprisingly, here also we got alkenylated product **3aa** in 86% isolated yield with an excellent regio- and stereoselectivity. Finally, we have decided benzamide (**1a**) (1.0 equiv) with methyl acrylate (**2a**) (2.0 equiv) in the presence of [{RuCl$_2$(*p*-cymene)}$_2$] (5.0 mol %), AgSbF$_6$ (20 mol %) and acetic acid (2.0 equiv) in DCE at RT for 24 h is the best condition for our reaction (eq 20).

(20)

1a **2a** **3aa**
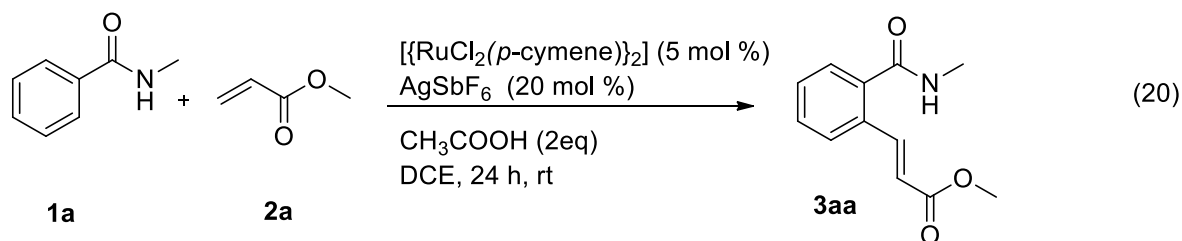
2.4 Substrate scope:

After finalising the optimised condition, we examined the alkenylation scope on several substituted amides Initially, we tried our reaction with various substituted aromatic amides like Me, OMe, F, Br, I, NO$_2$, in all the cases, we observed alkenylated product exclusively (Table 5) . Electron donating substituents like OMe and Me (**1b** and **1c**) were reacted with **2a** under the optimized condition gives the alkenylated product (**3ba** and **3ca**) in yield of 46% and 78%, respectively

(entries 1-2). Then, on reacting **2a** with halogen substituted amides like F, I and Br (**1d, 1e,** and **1f**), we got the corresponding alkenylated products of **3da, 3ea** and **3fa** with 71%, 55% and 61% yields respectively (entries 3-5).

But, in the case of less reactive electron withdrawing substituent NO$_2$ reacted with 2**a** gives very little conversion. So we tried increasing the amount of acrylate from 2.0 equiv to 3.0 equiv, we could find no improvement in the reaction. Then, we tried the reaction with different acids like pivalic acid, mesitylinic acid and adamantane carboxylic acid. However, no changes were observed. Then finally we tried the reaction by adding 4 equiv of acetic acid. Interestingly, we got the better conversion of **3ga** (eq 21) in 53% moderate yield (entry 6).

(21)

1g **2a** **3ga**
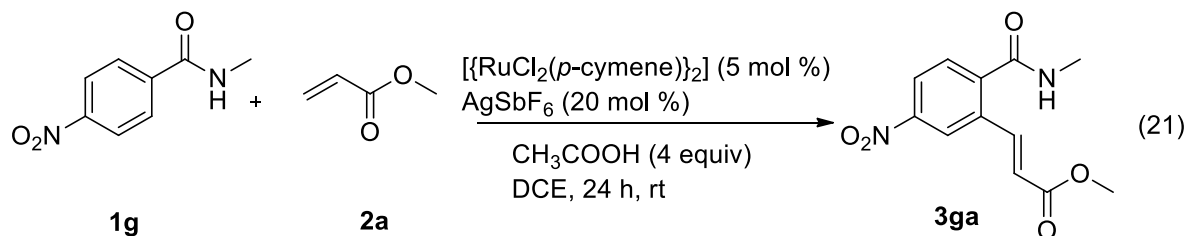
Sterically hindered *ortho* Methyl substituted amide also efficiently participated in the reaction yielding alkenylated product **3ha** in 70% yield (entry 7). Next, we tried our reaction with unsymmetrically substituted amides like *m*eta Chloro (**1i**) and 2-naphthyl amide (**1j**) reacted with **2a** effectively affording the alkenylated product **3ia**

and **3ja** (eq 22 and 23) in 68% and 83% yields, respectively (entries 8-9). In the reaction, alkenylation takes place at a less hindered C2 carbon.
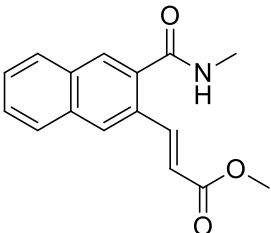

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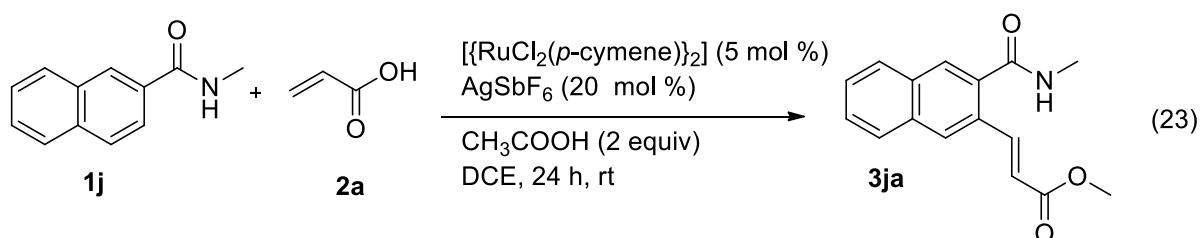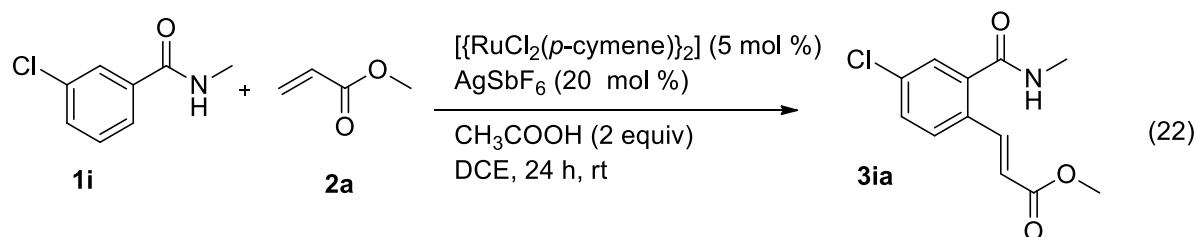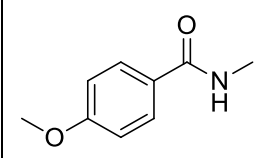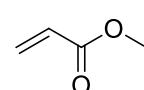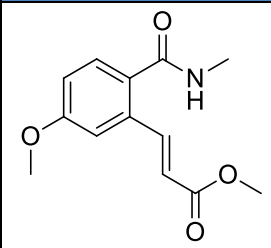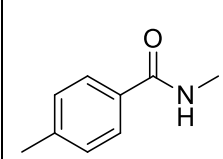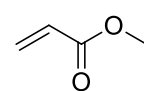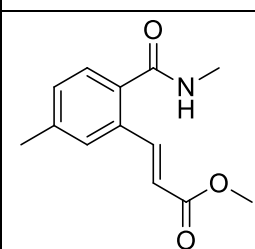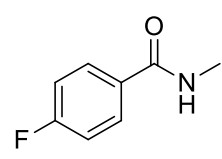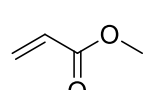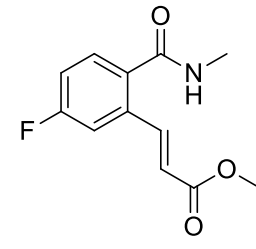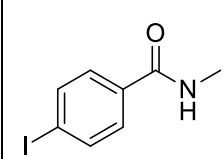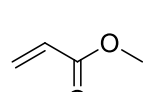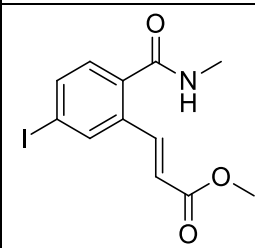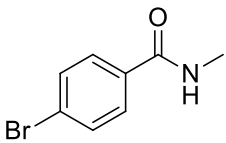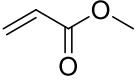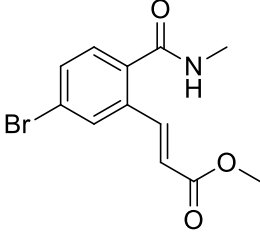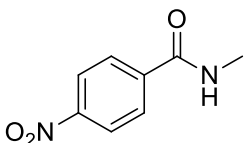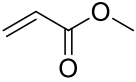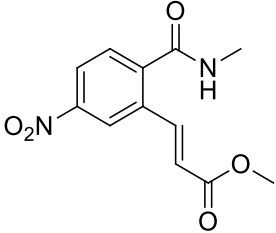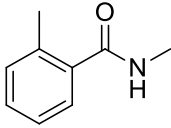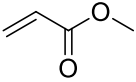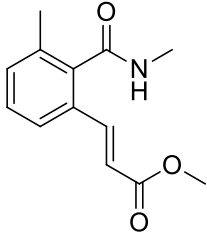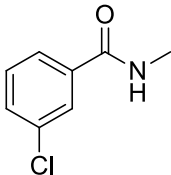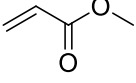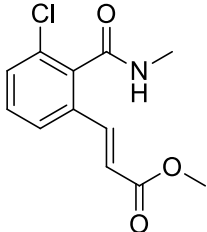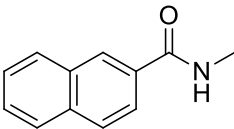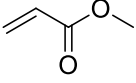
In contrast, when **2a** reacts with 3,4-(methylenedioxy) amide (**1k**) giving the product of **3ka** (eq 24) in 62% yield (entry 10). In the reaction, the alkenylation occurred at the sterically hindered carbon.
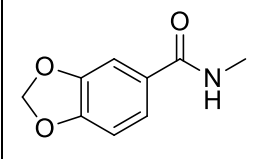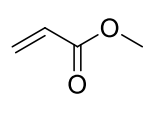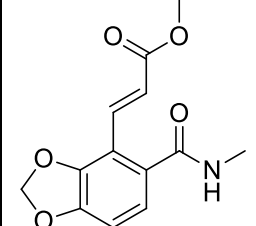

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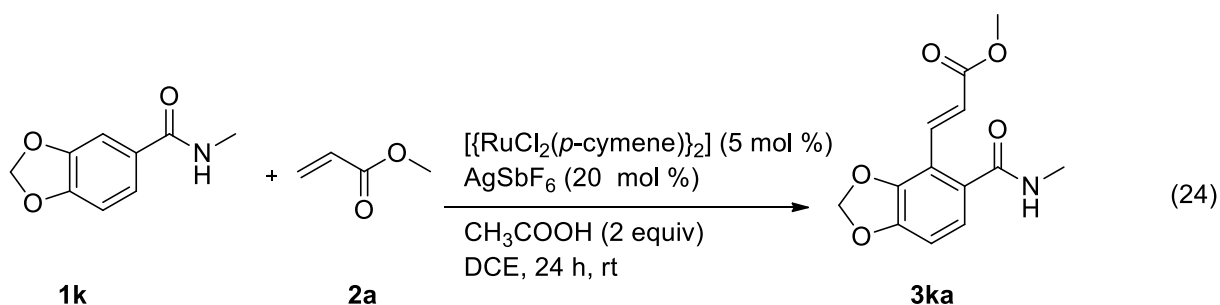
Finally, we are going to try the reaction of hetero aromatic thiophene substituted amide with **2a.**

Table 5. The alkenylation of Substituted amides (1b-l) with methyl acrylate (2a).

S.no	Substituted amides	Acrylate	Product	Yield (%)
1	1b	2a	3ba	46
2	1c	2a	3ca	78
3	1d	2a	3da	71
4	1e	2a	3ea	55

5	**1f**	**2a**	**3fa**	61
6	**1g**	**2a**	**3ga**	53
7	**1h**	**2a**	**3ha**	70
8	**1i**	**2a**	**3ia**	68
9	**1j**	**2a**	**3ja**	83

10	1k	2a	3ka	62

2.5 Alkene scope:

Further moving on to acrylate scope, we tried various acrylates like methyl, ethyl, phenyl, benzyl, cyclohexyl, *t*-butyl acrylates. We did reactions with unactivated alkene like styrene. We also tried $CH_2=CH-SO_2Ph$ (Table 6).

Amide **1a** reacts with ethyl (**2b**), phenyl (**2c**), benzyl (**2d**), cyclohexyl (**2e**) and *t*-butyl (**2f**) acrylates under the optimised conditions, giving the alkenylated products **3ab, 3ac, 3ad, 3ae** and **3af**, respectively (entries 1-5). Surprisingly phenylvinylsulphone ($CH_2=CH-SO_2Ph$) (**2g**) reacted efficiently with **1a,** providing **3ga** in yield of 59% (entry 6).

Unfortunately In the case of styrene (**2h**), we did not observe alkenylated product under the optimized reaction conditions. So, we further proceed this reaction by changing the acid source and by increasing the amount of acid source and acrylate. In all the above cases, we did not observe our desired product. So, further we screened same catalytic reaction with various solvents at room temperature, but no reaction observed. Finally, we tried the reaction with 1,4- dioxane as solvent and heated to 100 °C (eq 25). Surprisingly, we got the better conversion which affords the alkenylated product **3ah** in 43% yield (entry 7).
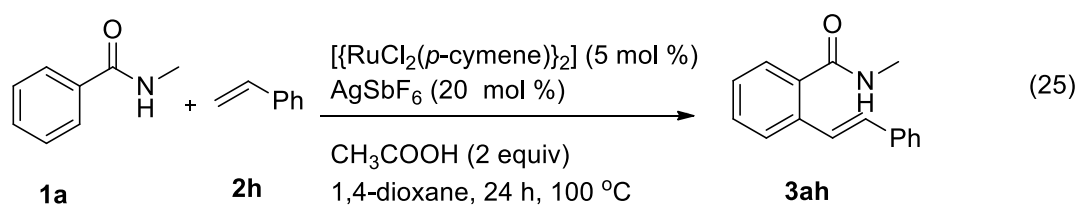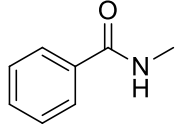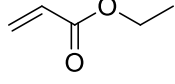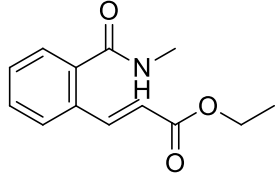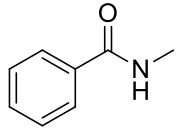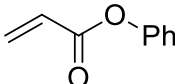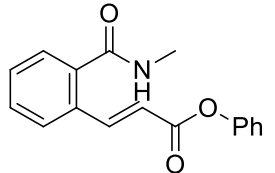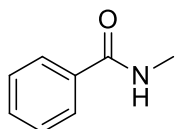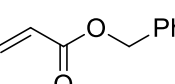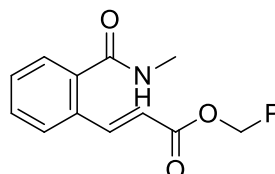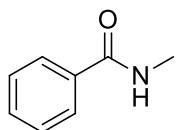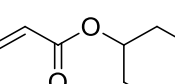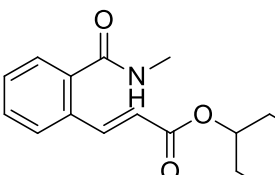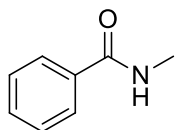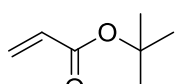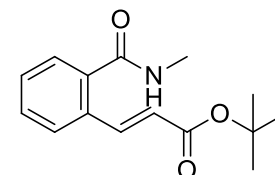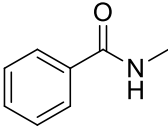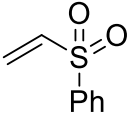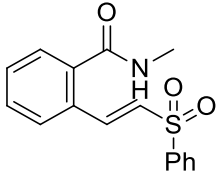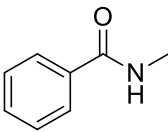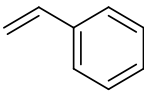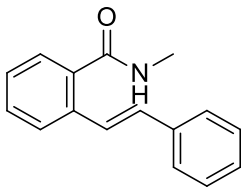
Table 6. The alkenylation of amide (1a) with different acrylates (2b-h).

S.no	Amide	Substituted acrylates	Alkenylated products	Yield (%)
1	1a	2b	3ab	82
2	1a	2c	3ac	71
3	1a	2d	3ad	76
4	1a	2e	3ae	68
5	1a	2f	3af	67

6	**1a**	**2g**	**3ag**	59
7	**1a**	**2h**	**3ah**	43

3. Experimental section:

<u>General Procedure for the alkenylation of benzamides (**1**) with acrylates (**2**) Catalyzed by Ruthenium Catalyst</u>:

A 15-mL pressure tube with septum containing [{RuCl$_2$(*p*-cymene)}$_2$] (5.0 mol %) and AgSbF$_6$ (20 mol %) was evacuated and purged with nitrogen gas three times (AgSbF$_6$ was taken inside the glove box). To the tube were then added benzamide **1** (100 mg), acrylate **2** (2 equiv), and 1,2 dichloro ethane (3.0 mL) via syringes and again the reaction mixture was evacuated and purged with nitrogen gas three times. After that, the septum was taken out and immediately a screw cap was used to cover the tube under the nitrogen atmosphere. Then, the reaction mixture was allowed to stir at room temperature for 24 hours.

After 24 hours, the reaction mixture was diluted with CH$_2$Cl$_2$, filtered through Celite and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure alkenylated product **3**.

<u>General Procedure for the alkenylation of benzamides (**1**) with styrene (**2h**) Catalyzed by Ruthenium Catalyst</u>:

A 15-mL pressure tube with septum containing [{RuCl$_2$(*p*-cymene)}$_2$] (5.0 mol %) and AgSbF$_6$ (20 mol %) was evacuated and purged with nitrogen gas three times (AgSbF$_6$ was taken inside the glove box). To the tube were then added benzamide **1** (100 mg), styrene (**2h**) (2 equiv), and 1, 4-dioxane (3.0 mL) via syringes and again the reaction mixture was evacuated and purged with nitrogen gas three times. After that, the septum was taken out and immediately a screw cap was used to cover the tube under the nitrogen atmosphere. Then, the reaction mixture was allowed to stir at 100 ^{o}C for 24 hours.

After 24 hours, the reaction mixture was cooled to ambient temperature, diluted with CH$_2$Cl$_2$, filtered through Celite and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure alkenylated product **3ah**.

The isolated product is confirmed using ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry.

4. Future plan:

Alkenylated moieties are found in variety of natural products. Successful alkenylation mostly requires higher temperature and oxidant. But, here we showed that alkenylation can also be done at room temperature depending on the directing group of the substrate, using ruthenium catalyst. Further I would like to explore alkenylation reaction on different directing groups applying the same reaction condition.

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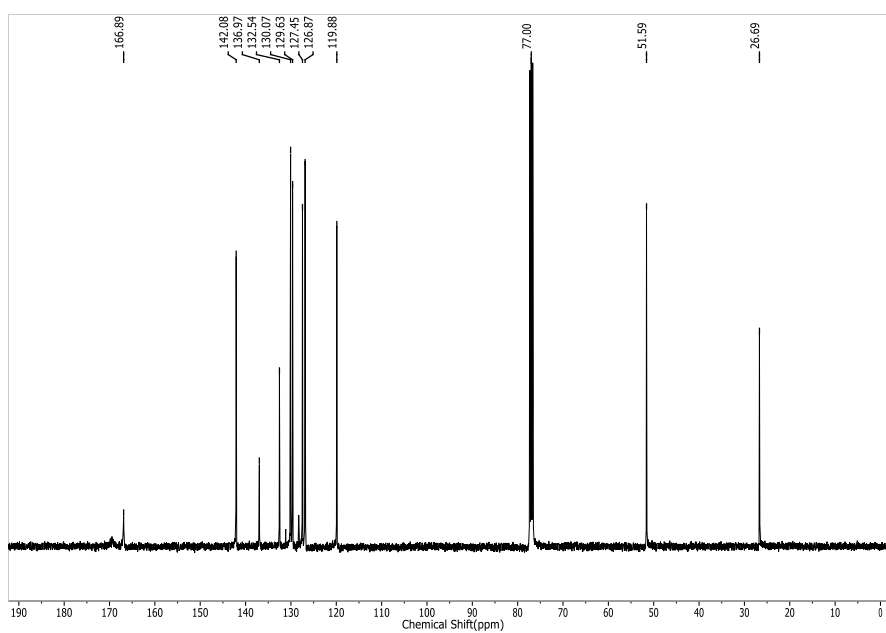15. Ueyama, T.; Mochida, S.; Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2011,** 13, 706.

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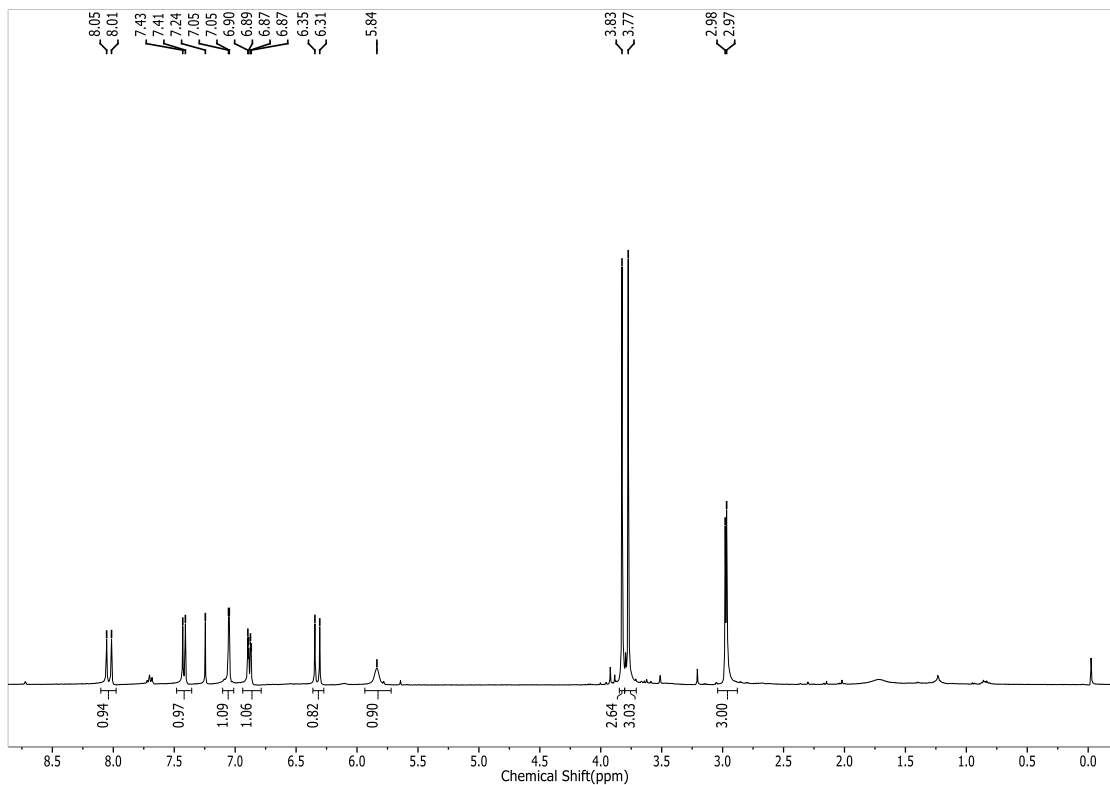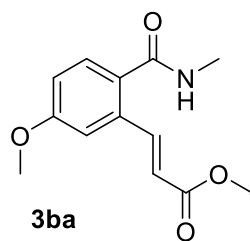## 6. Appendix:

^{1}H and ^{13}C NMR spectra of compound **3aa**

3aa
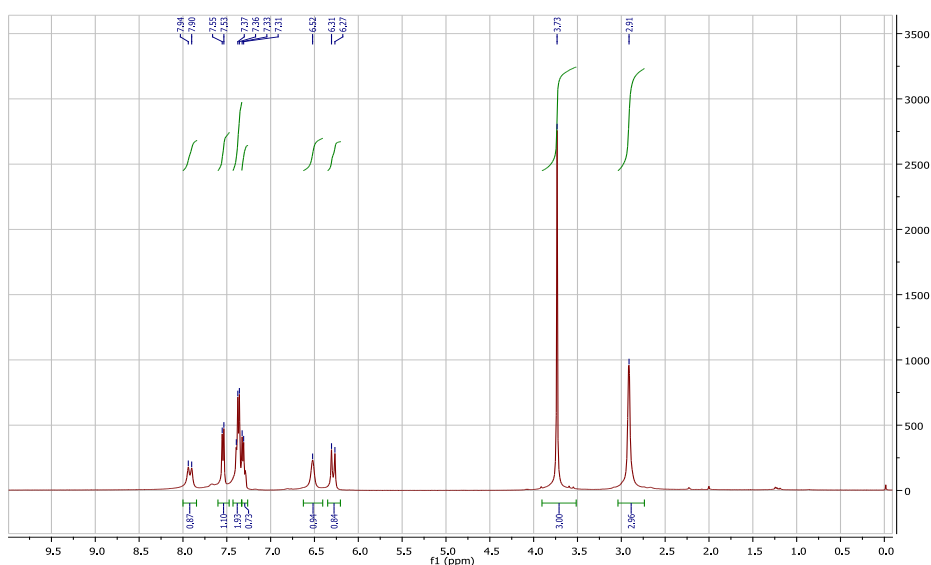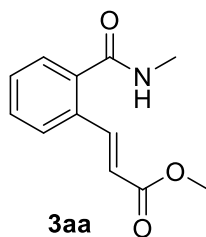
^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.92 (d, J = 16.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.32 (d, J = 8.0 Hz, 1H), 6.52 (s, 1H), 6.29 (d, J = 16.0 Hz, 1H), 3.73 (s, 3H), 2.91 (s, 3H).

^{13}C NMR (100 MHz, CDCl$_3$); δ 166.9, 142.1, 136.9, 132.5, 130.1, 129.7, 127.4, 126.9, 119.9, 51.6, 26.7.

¹H and ¹³C NMR spectra of compound **3ba**.

3ba

¹H NMR (CDCl_{3,} 400 MHz,) δ 8.03 (d, *J* = 16.0 Hz, 1H), 7.42 (d, *J* = 8.0Hz, 1H), 7.05 (d, *J* = 4.0 Hz, 1H), 6.88 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.33 (d, *J* = 16.0.Hz, 1H), 5.84 (s, 1H), 3.83 (s, 3H), 3.77 (s, 3H), 2.97 (d, *J* = 4.0 Hz, 3H).
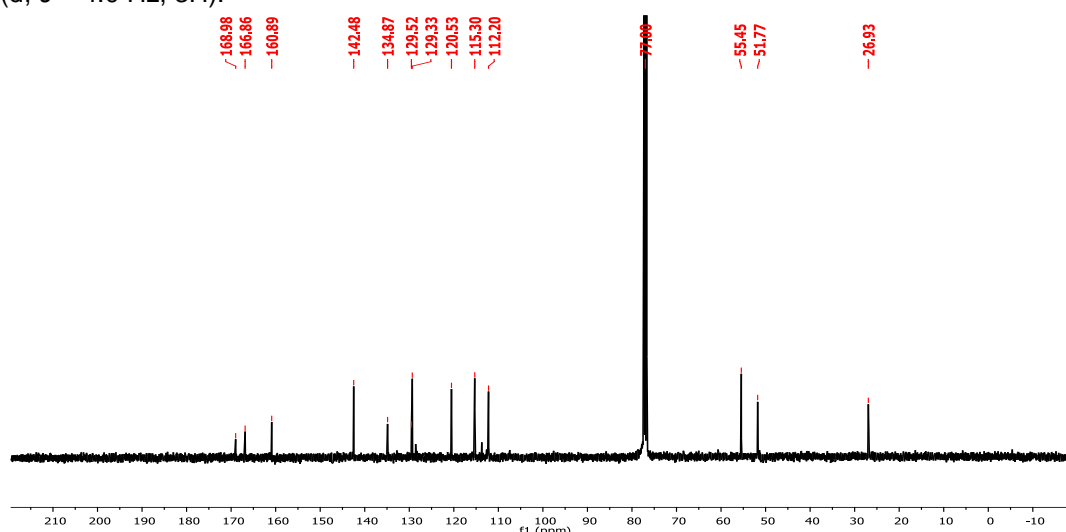

¹³C NMR (100 MHz, CDCl₃); δ 168.9, 166.8, 160.9, 142.5, 134.9, 129.5, 129.3, 120.5, 115.3, 112.2, 55.4, 51.7, 26.9.

¹H and ¹³C NMR spectra of compound **3ca.**
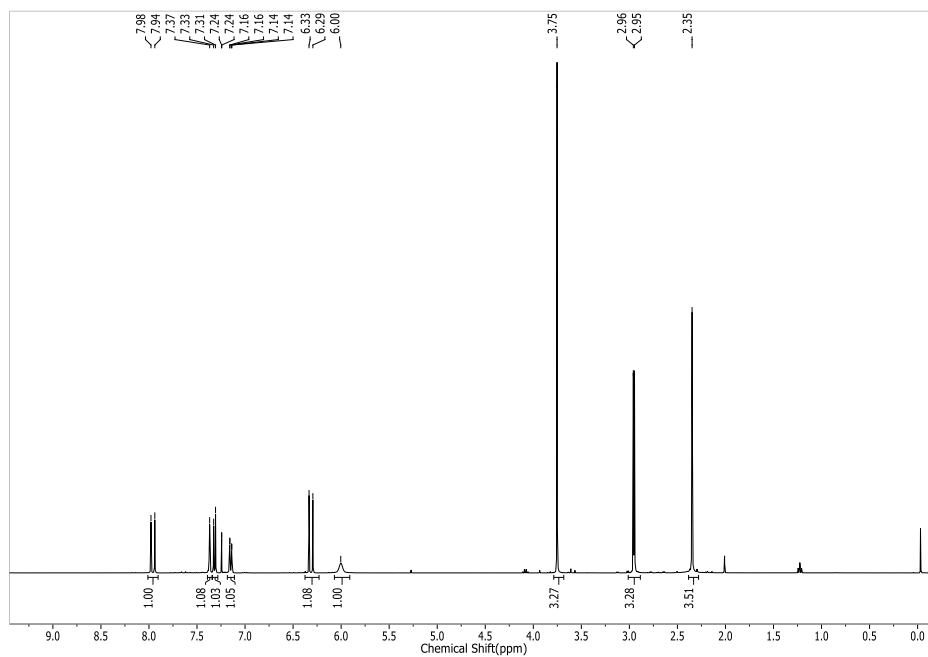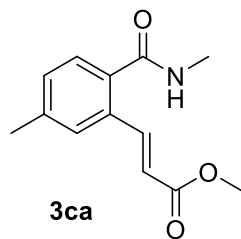
3ca

¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, *J* = 16.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 4.0 Hz, 1H), 6.88 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.33 (d, *J* = 16.0 Hz, 1H), 5.84 (s, 1H), 3.83 (s, 3H), 2.97 (d, *J* = 4.0 Hz, 3H), 2.34 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 169.4, 166.9, 142.3, 140.5, 134.2, 132.8, 130.49, 127.7, 127.6, 120.0, 51.7, 26.9, 21.3.

^{1}H and ^{13}C NMR spectra of compound **3ca.**

3ca

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.03 (d, *J* = 16.0 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 4.0 Hz, 1H), 6.88 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.33 (d, *J* = 16.0 Hz, 1H), 5.84 (s, 1H), 3.83 (s, 3H), 2.97 (d, *J* = 4.0 Hz, 3H), 2.34 (s, 3H).
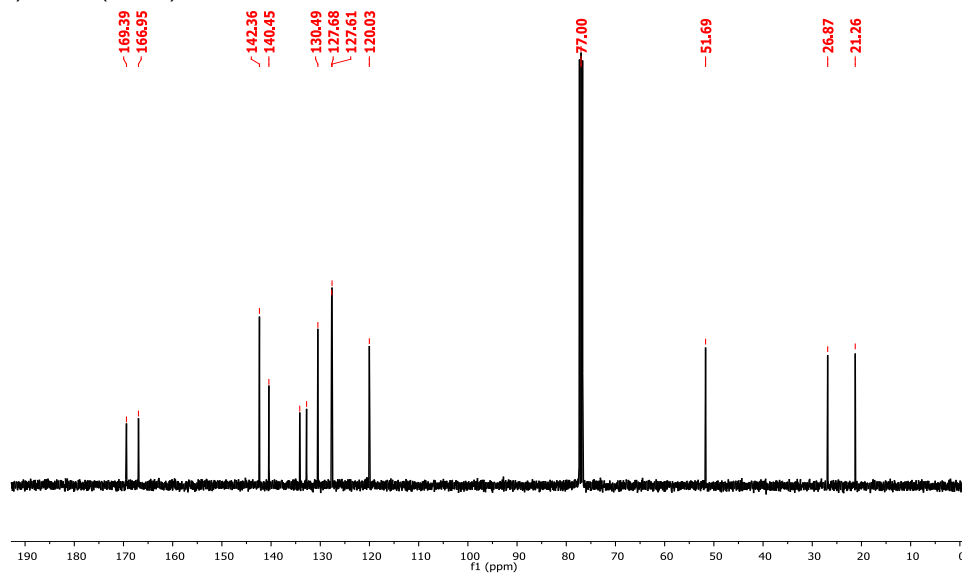
^{13}C NMR (100 MHz, CDCl$_3$) δ 169.4, 166.9, 142.3, 140.5, 134.2, 132.8, 130.49, 127.7, 127.6, 120.0, 51.7, 26.9, 21.3.

^{1}H and ^{13}C NMR spectra of compound **3da.**
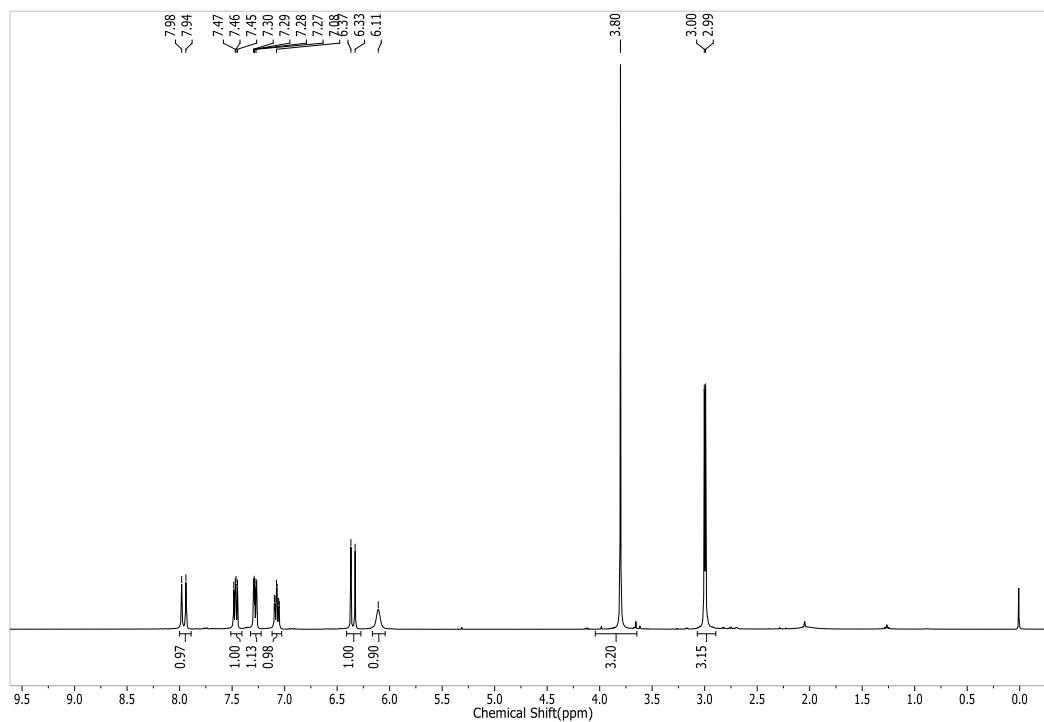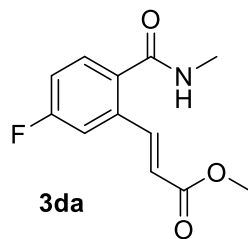
^{1}H NMR (400 MHz, CDCl$_3$): δ 7.96 (d, *J* = 16.0 Hz, 1H), 7.47 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.32 – 7.22 (m, 1H), 7.07 (td, *J* = 8.0, 4.0 Hz, 1H), 6.35 (d, *J* = 16.0 Hz, 1H), 6.11 (s, 1H), 3.80 (s, 3H), 3.0 (d, *J* = 4.0 Hz, 3H).
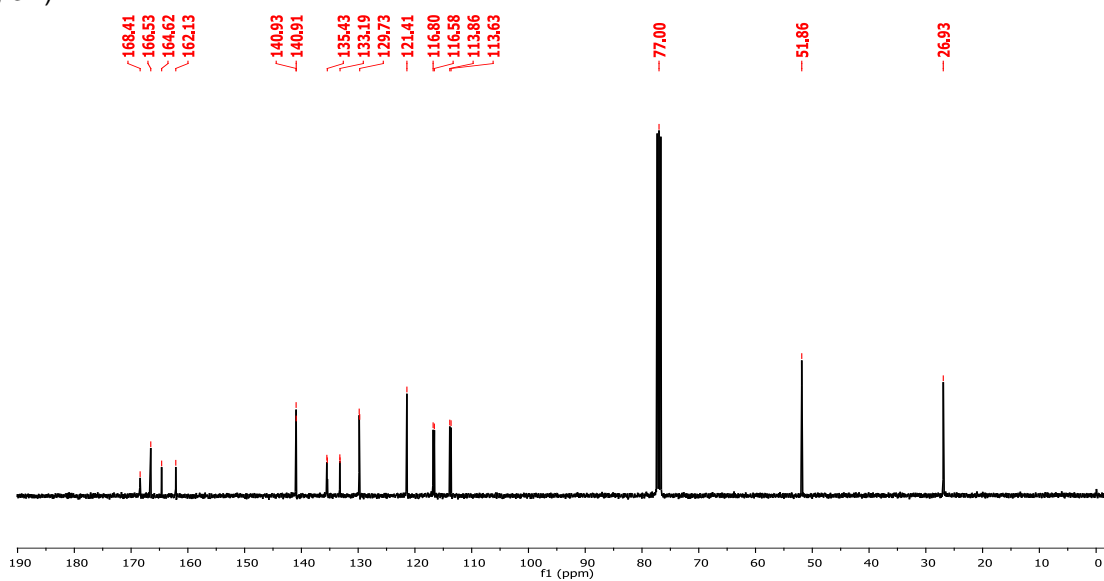
^{13}C NMR (100 MHz, CDCl$_3$) δ 168.4, 166.5, 164.6, 162.1, 141.0, 140.9 (F- coupling), 135.4, 133.2, 129.7, 121.4, 116.8, 116.6(F- coupling), 113.9, 113.6(F- coupling), 51.9, 26.9.

3ea
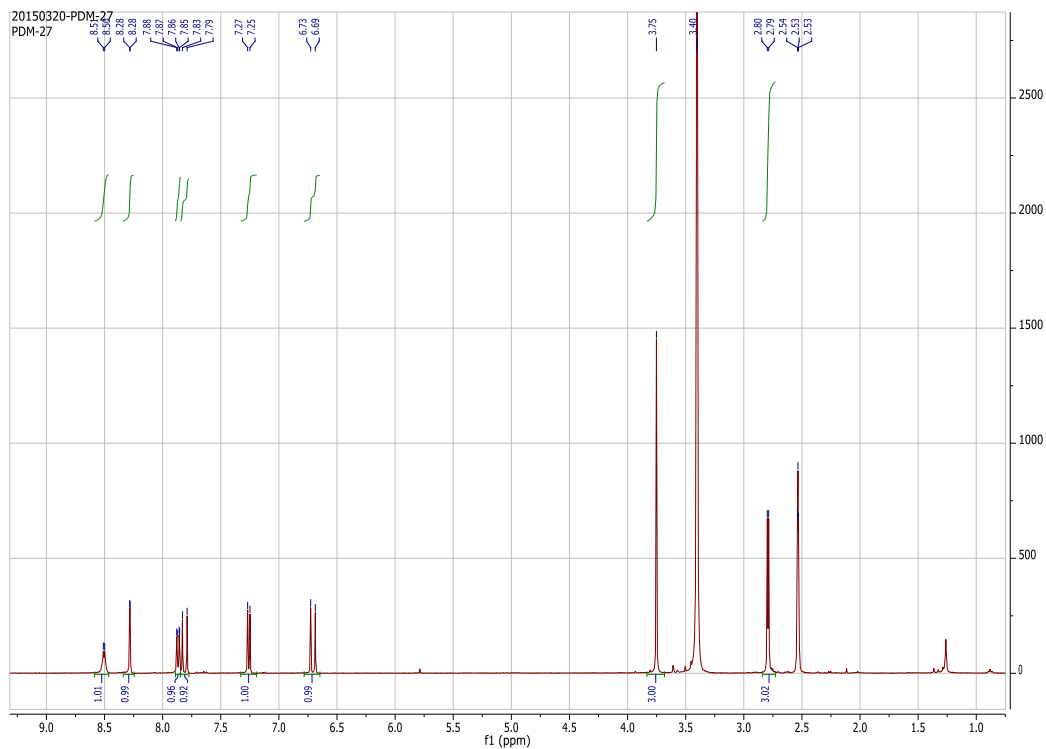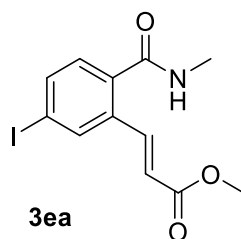
^{1}H NMR (400 MHz, DMSO d$_6$) δ 8.50 (d, J = 4.0 Hz, 1H), 8.28 (d, J = 4.0 Hz, 1H), 7.87 (dd, J = 8.0, 4.0 Hz, 1H), 7.81 (d, J = 16.0 Hz, 1H), 7.26 (d, J = 8.0Hz, 1H), 6.71 (d, J = 16.0 Hz, 1H), 3.75 (s, 3H), 2.79 (d, J = 4.0 Hz, 3H).
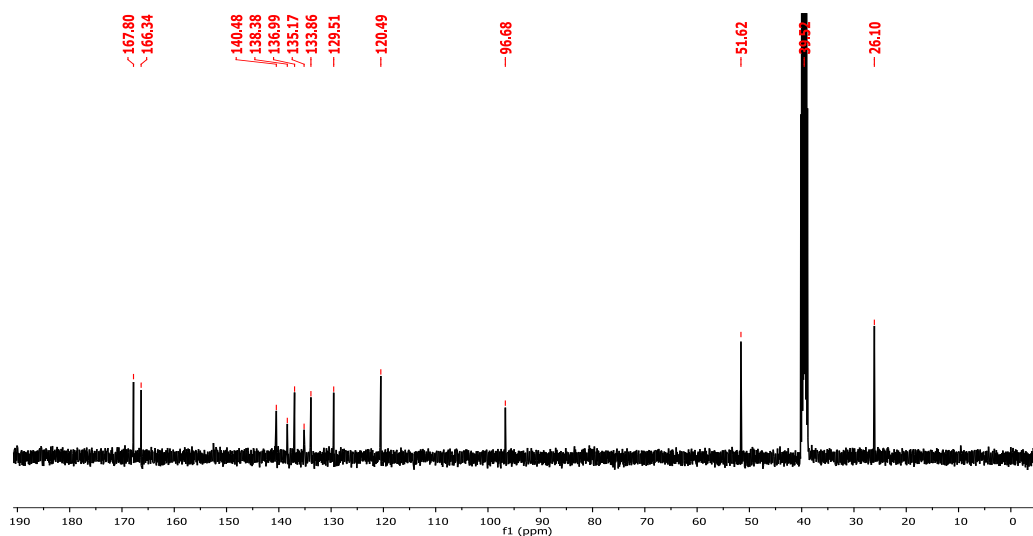
^{13}C NMR (101 MHz, CDCl$_3$) δ 167.8, 166.3, 140.5, 140.91, 138.4, 136.9, 35.2, 133.9, 129.5, 120.5, 96.7, 51.6, 26.1.

¹H and ¹³C NMR spectra of compound **3fa**.

3fa
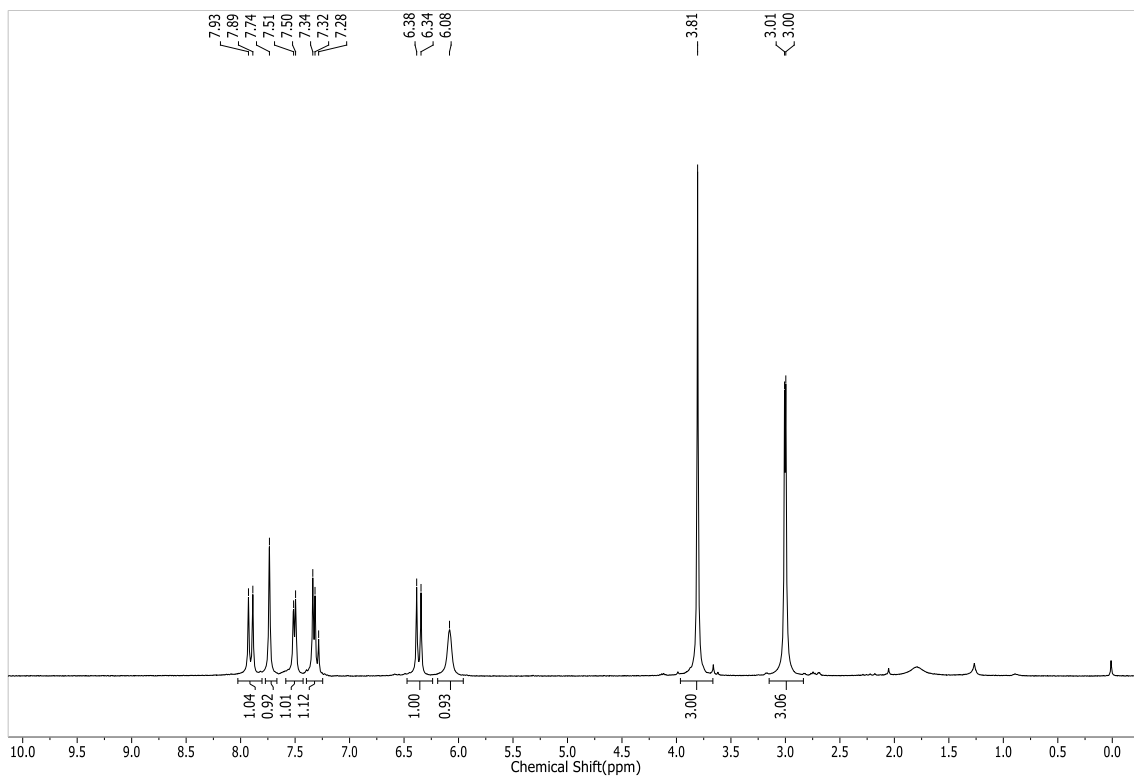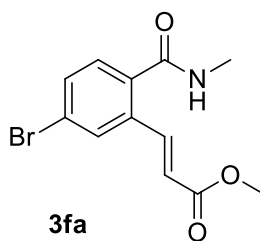
¹H NMR (400 MHz, CDCl$_3$) δ 7.91 (d, J = 16.0 Hz, 1H), 7.74 (s, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.40 – 7.25 (m, 1H), 6.36 (d, J = 16.0 Hz, 1H), 6.08 (s, 1H), 3.81 (s, 3H), 3.00 (d, J = 6.0 Hz, 3H).
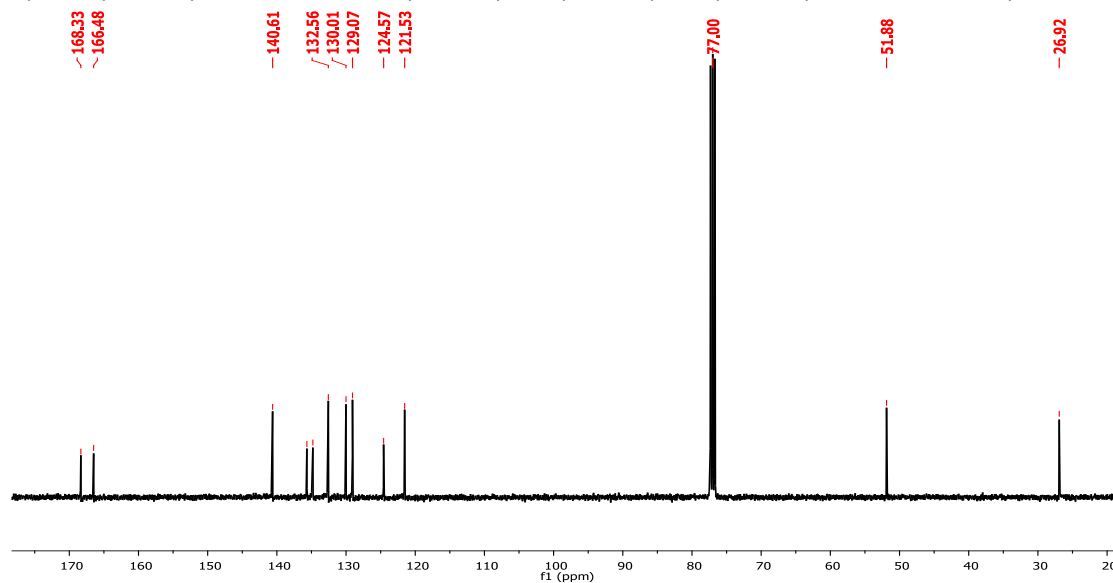
¹³C NMR (101 MHz, CDCl$_3$) δ 168.3, 166.5, 140.6, 135.6, 134.8, 132.6, 130.0, 129.1, 124.6, 121.5, 51.9, 26.9.

^{1}H and ^{13}C NMR spectra of compound **3ga.**

3ga
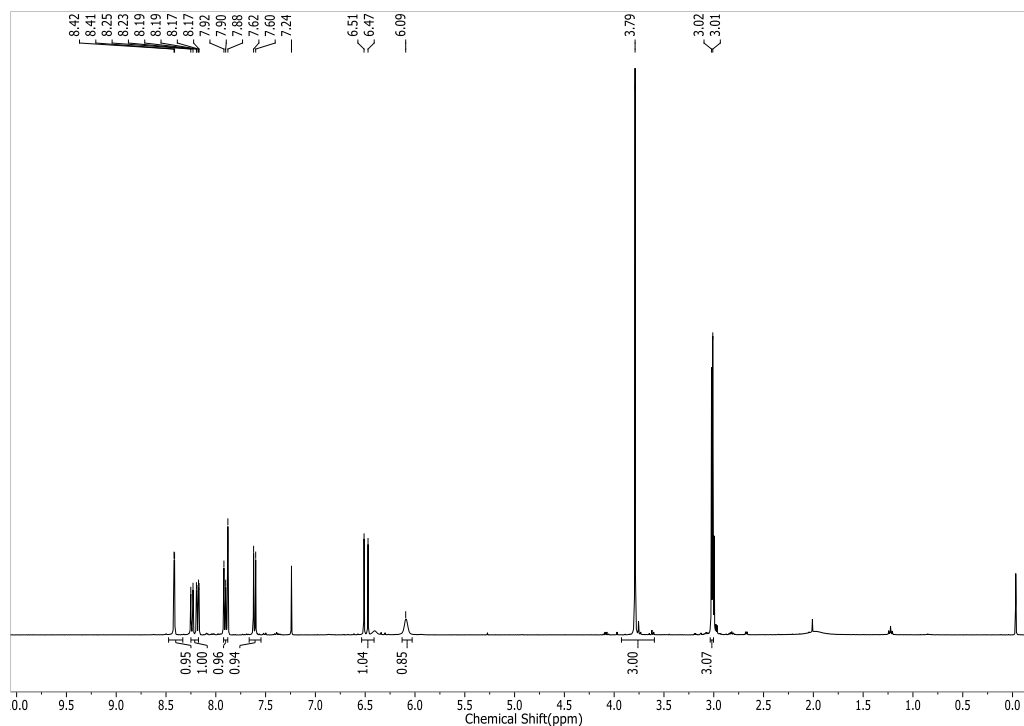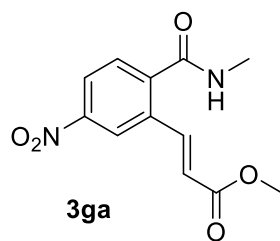
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.42 (d, J = 4.0 Hz, 1H), 8.25 – 8.17 (m, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 6.49 (d, J = 16.0 Hz, 1H), 6.09 (s, 1H), 3.79 (s, 3H), 3.02 (d, J = 4.0 Hz, 3H).
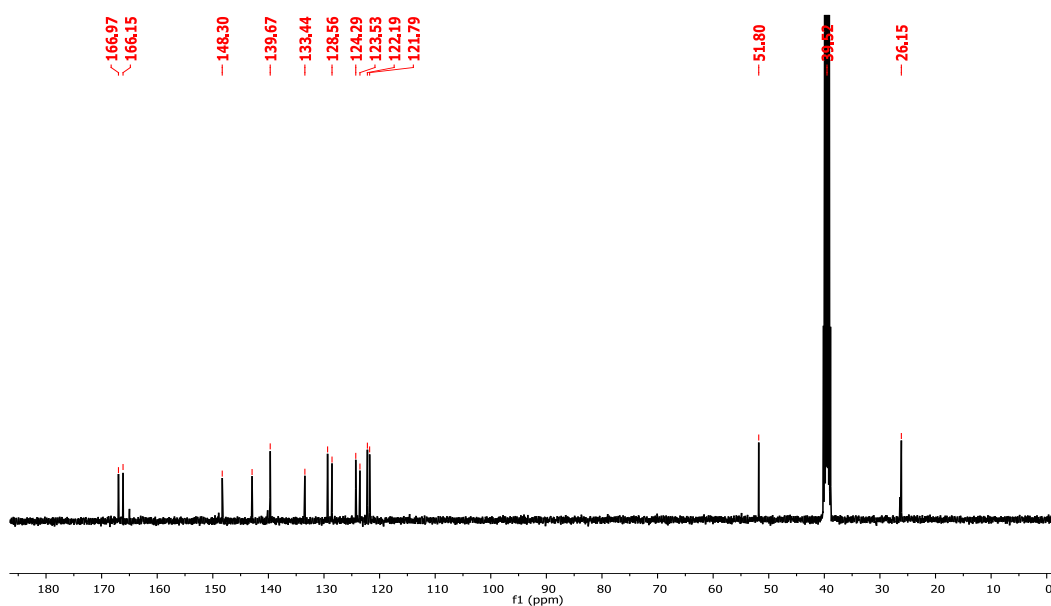
^{13}C NMR (100 MHz, DMSO-d$_6$) δ 166.9, 166.1, 148.3, 142.9, 139.7, 133.4, 129.3, 128.6, 124.3, 123.5, 122.2, 121.8, 51.8, 39.5, 26.1
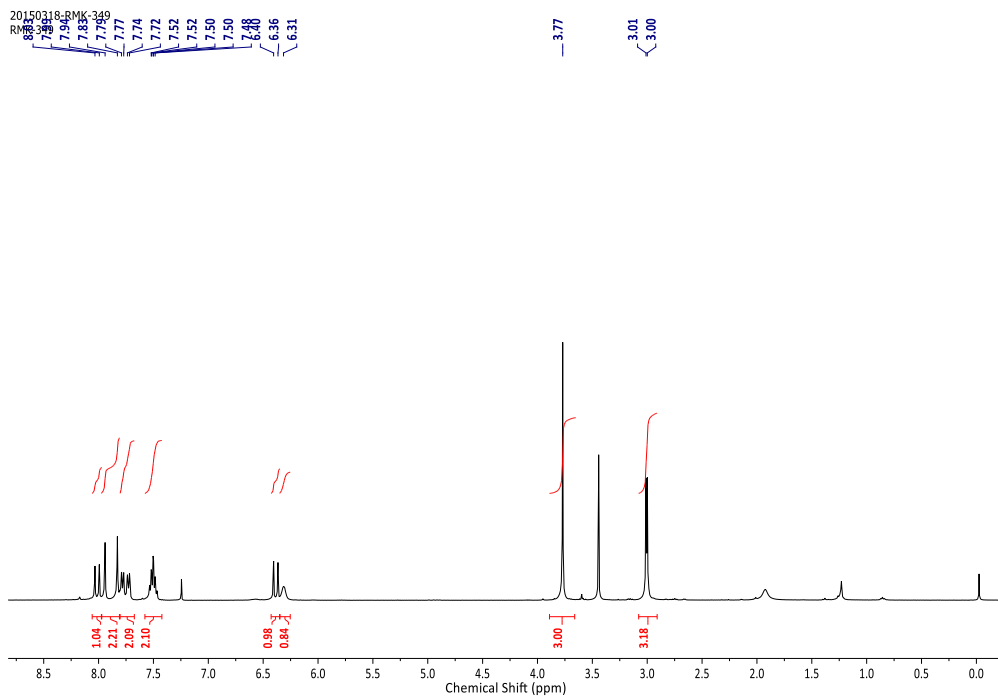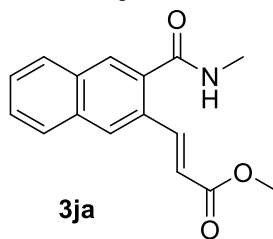
^{1}H and ^{13}C NMR spectra of compound **3ia.**
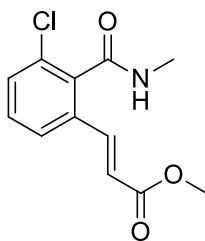
3ia
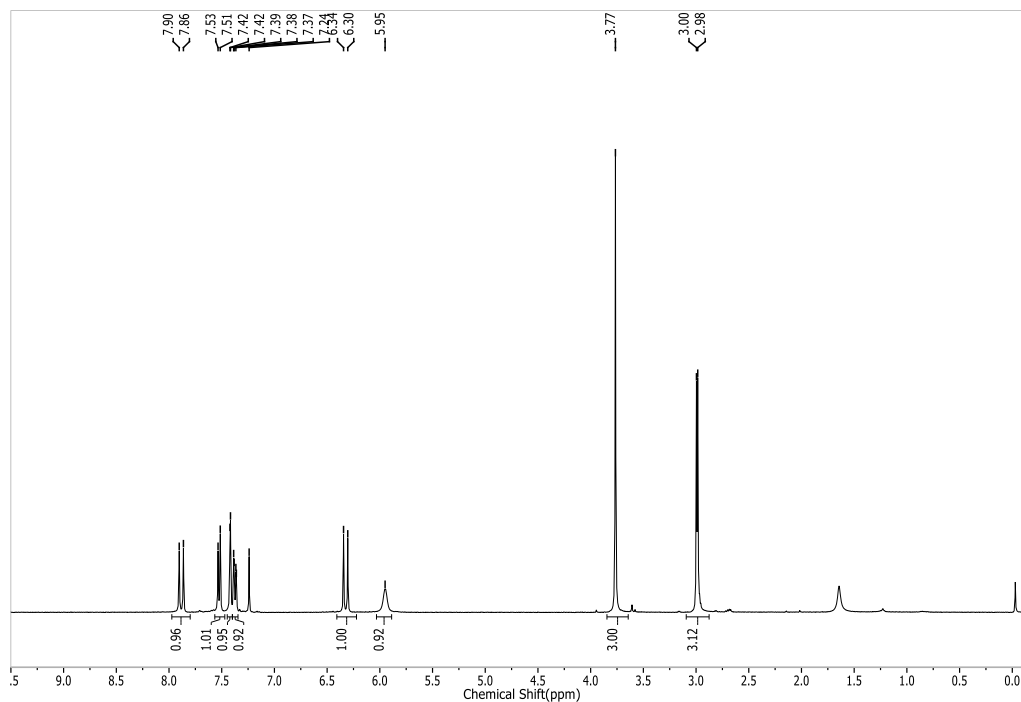
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.88 (d, J = 16.0 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 4.0 Hz, 1H), 7.37 (dd, J = 8.0, 4.0 Hz, 1H), 6.32 (d, J = 16.0 Hz, 1H), 5.95 (s, 1H), 3.77 (s, 3H), 2.99 (d, J = 4.0 Hz, 3H).
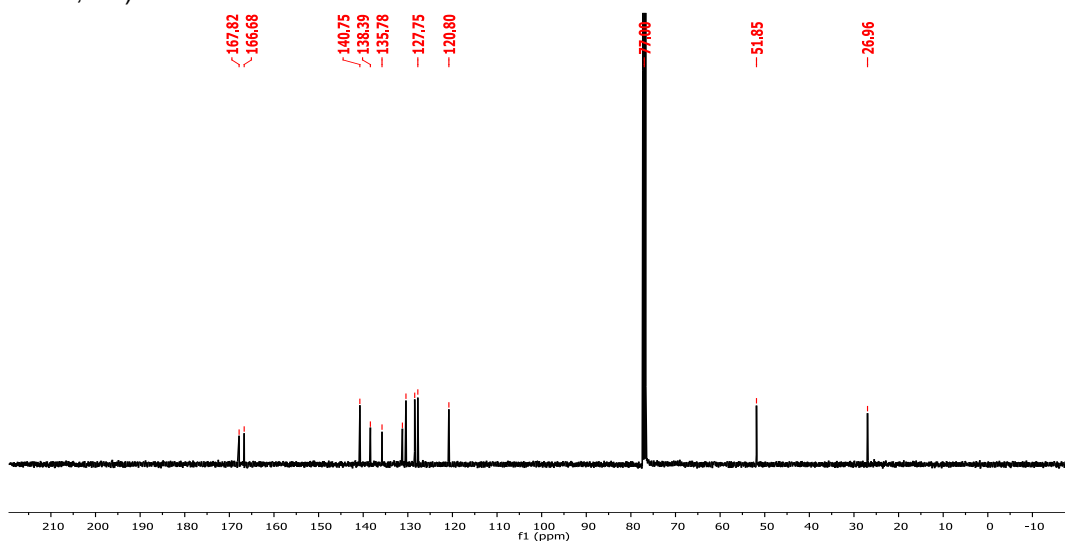
^{13}C NMR (101 MHz, CDCl$_3$) δ 167.8, 166.6, 140.7, 138.4, 135.8, 131.2, 130.4, 128.4, 127.7, 120.8, 51.8, 26.9.
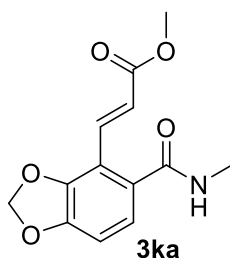
¹H and ¹³C NMR spectra of compound **3ja.**

3ja

¹H NMR (400 MHz, CDCl₃) δ 8.01 (d, *J* = 16.0 Hz, 1H), 7.89 (d, *J* = 4.0 Hz, 2H), 7.76 (dd, *J* = 8.0, 4.0 Hz, 2H), 7.50 (tt, *J* =16.0, 8.0 Hz, 2H), 6.39 (d, *J* = 16.0 Hz, 1H), 6.32 (s, 1H), 3.77 (s, 3H), 3.01 (d, *J* = 8.0 Hz, 3H).
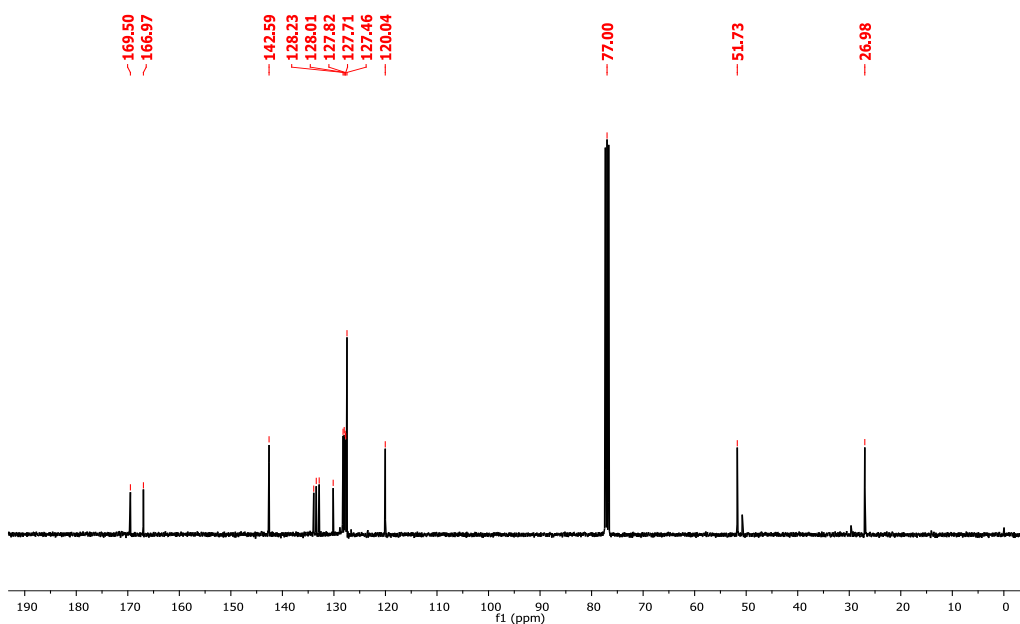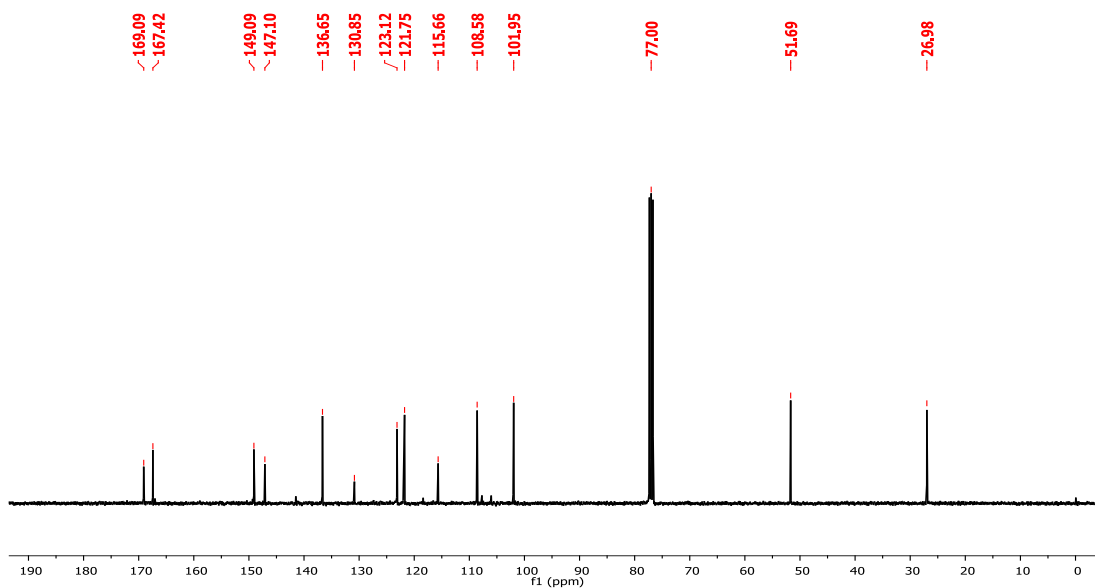

¹³C NMR (101 MHz, CDCl₃) δ 169.5, 166.9, 142.6, 133.9, 133.4, 132.9, 130.2, 128.2, 128.0, 127.8, 127.7, 127.5, 120.0, 51.7, 26.9
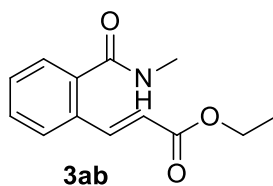
¹H and ¹³C NMR spectra of compound **3ka.**

3ka
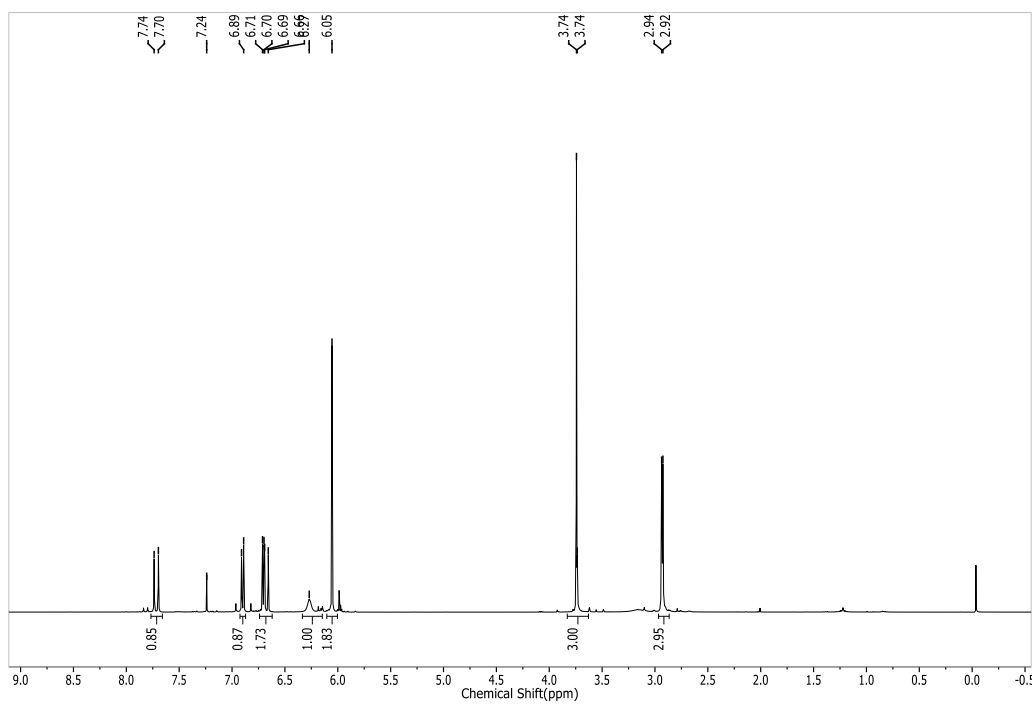
¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 16.0 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.74 – 6.62 (m, 2H), 6.27 (s, 1H), 6.05 (s, 2H), 3.74 (d, *J* = 4.0 Hz, 3H), 2.93 (d, *J* = 4.0 Hz, 3H).
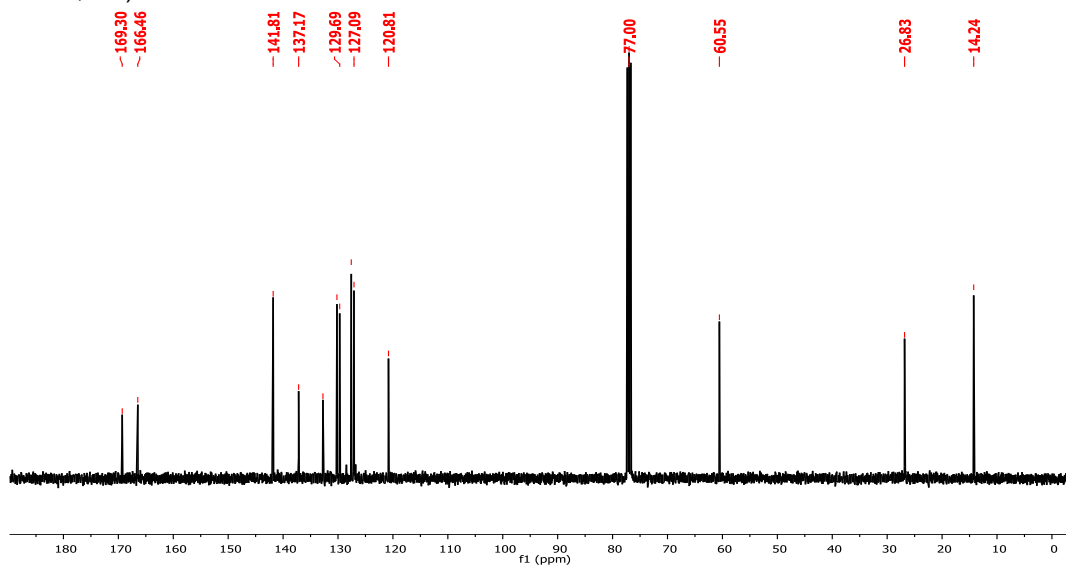

¹³C NMR (100 MHz, CDCl₃) δ 169.1, 167.4, 149.1, 147.1, 136.6, 130.8, 123.1, 121.7, 115.7, 108.6, 101.9, 51.7, 26.9.

Acrylate Scope:

^{1}H and ^{13}C NMR spectra of compound **3ab.**
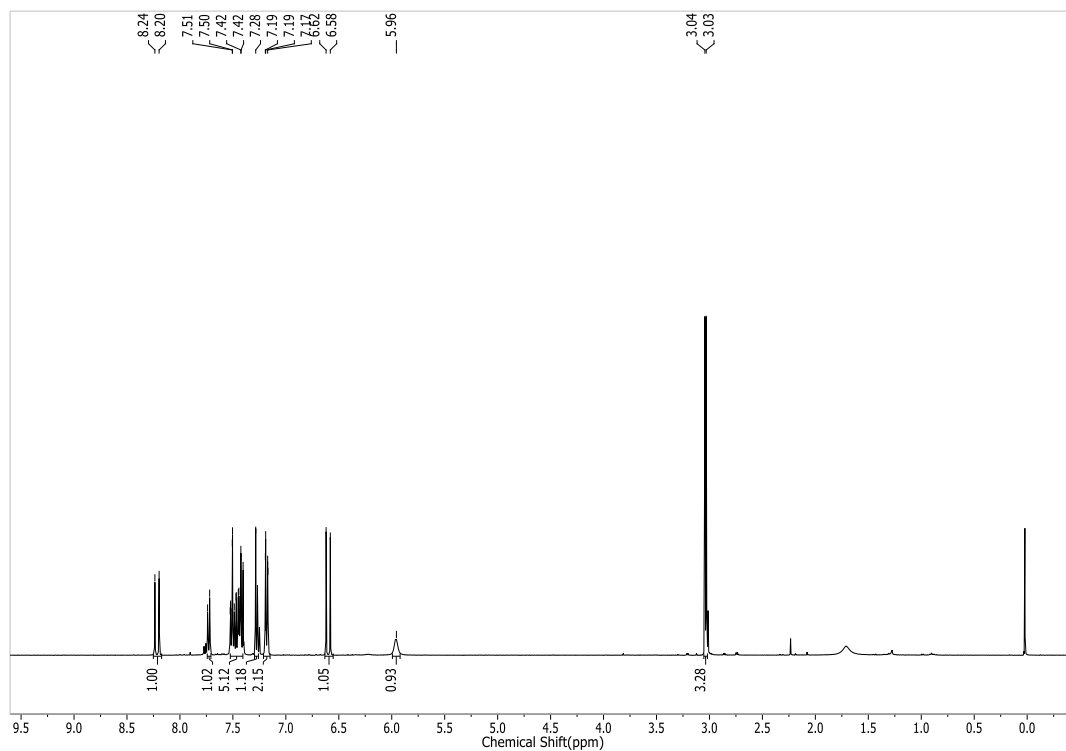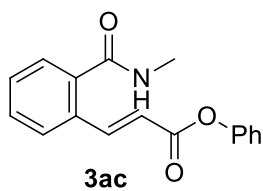

3ab
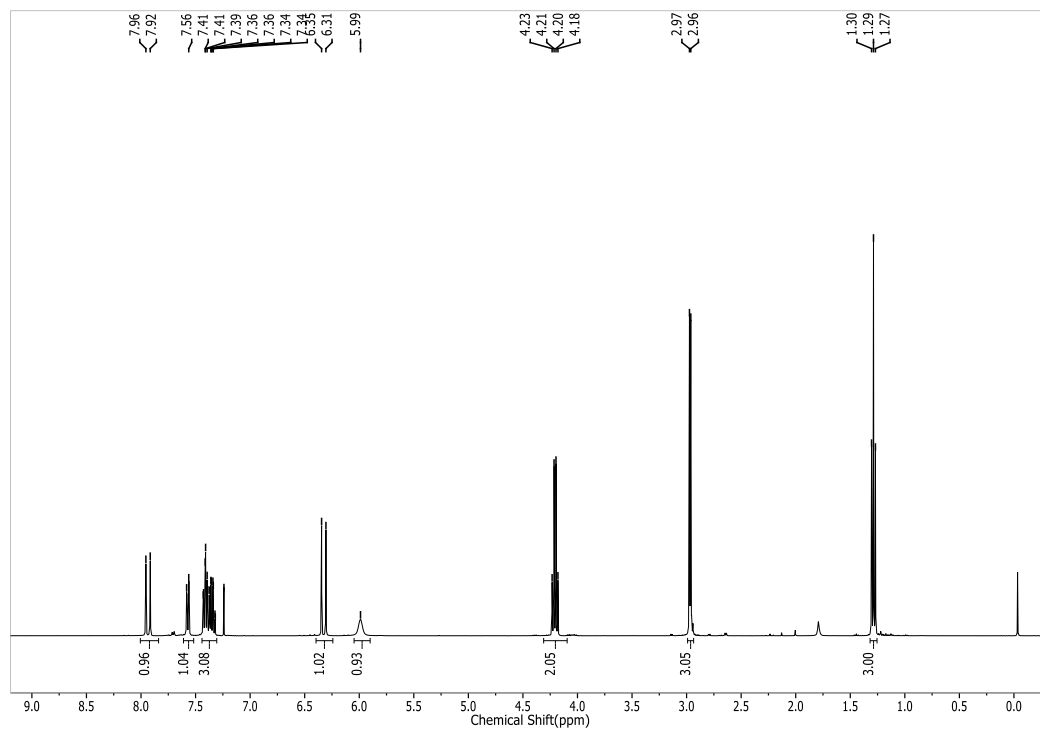
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (d, J = 16.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.44 – 7.31 (m, 3H), 6.33 (d, J = 16.0 Hz, 1H), 5.99 (s, 1H), 4.21 (q, J = 8.0 Hz, 2H), 2.97 (d, J = 4.0 Hz, 3H), 1.29 (t, J = 8.0 Hz, 3H).
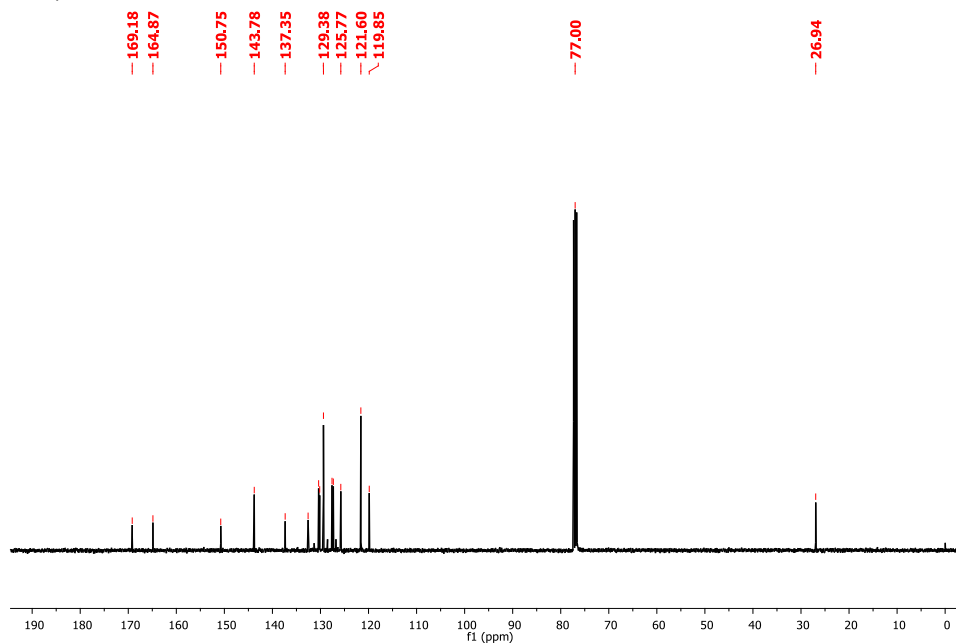

^{13}C NMR (101 MHz, CDCl$_3$) δ 169.3, 166.5, 141.8, 137.2, 132.7, 130.2, 129.7, 127.6, 127.1, 120.8, 60.5, 26.8, 14.2.

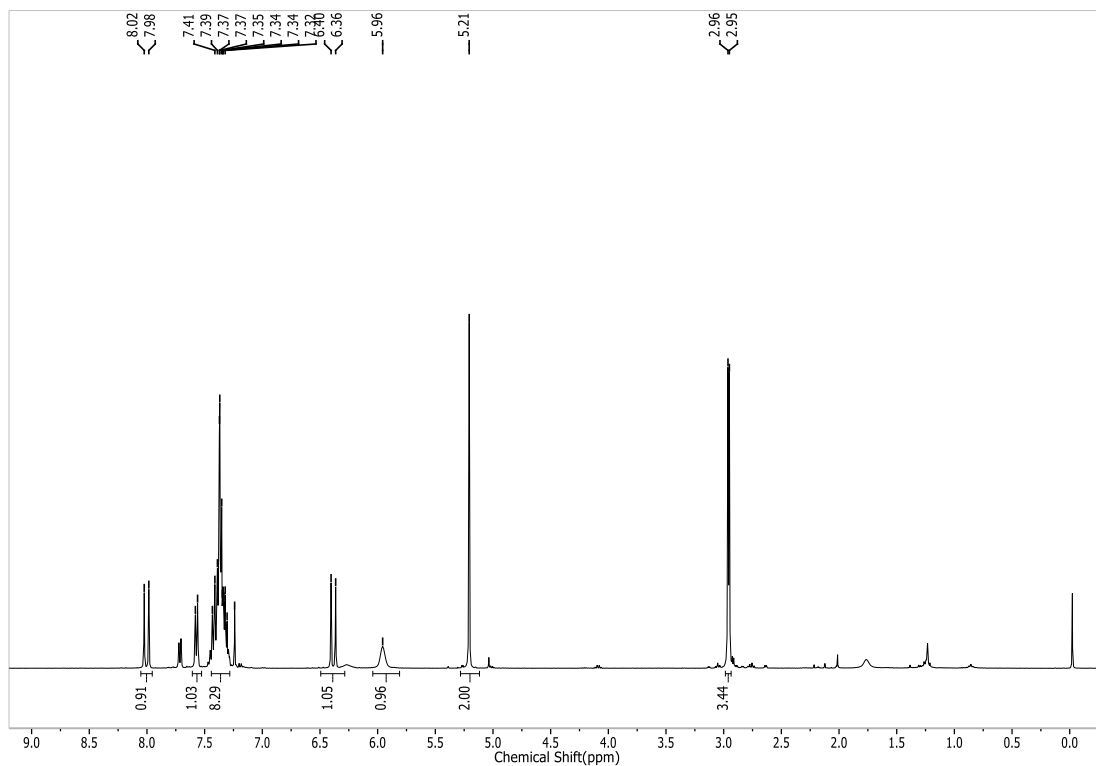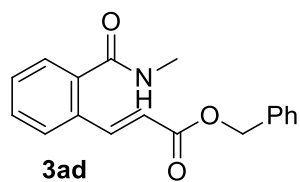¹H and ¹³C NMR spectra of compound **3ac.**

3ac

¹H NMR (400 MHz, CDCl₃) δ 8.22 (d, *J* = 16.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.52 – 7.41 (m, 5H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 8.0, 4.0 Hz, 2H), 6.60 (d, *J* = 16.0 Hz, 1H), 5.96 (s, 1H), 3.04 (d, *J* = 4.0 Hz, 3H).
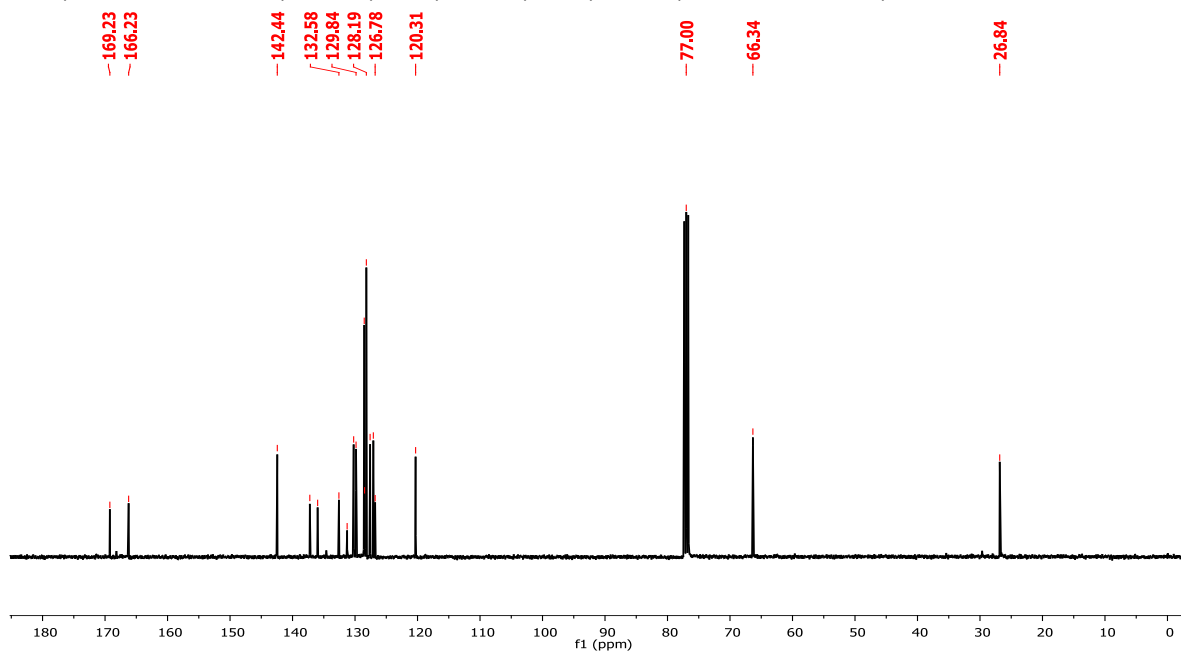

¹³C NMR (101 MHz, CDCl₃) δ 169.2, 164.9, 150.7, 143.8, 137.3, 132.6, 130.4, 130.2, 129.4, 127.6, 127.3, 125.7, 121.6, 119.8, 26.9.

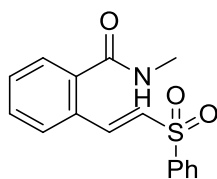## ^{1}H and ^{13}C NMR spectra of compound **3ad.**

3ad

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00 (d, *J* = 16.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.44 7.28 (m, 8H), 6.38 (d, *J* = 16.0 Hz, 2H), 5.96 (s, 2H), 5.21 (s, 2H), 2.96 (d, *J* = 4.0 Hz, 3H).
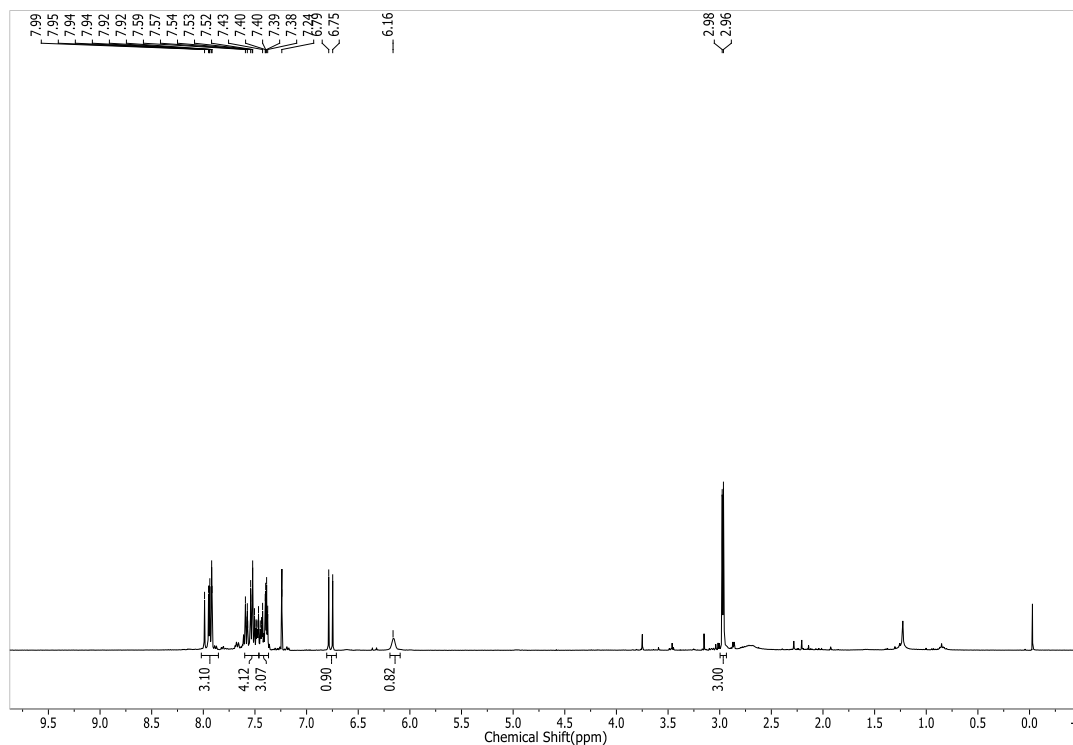

^{13}C NMR (101 MHz, CDCl$_3$) δ 169.2, 166.2, 142.4, 137.2, 135.9, 132.6, 131.3, 130.2, 129.8, 128.5, 128.5, 128.2, 127.6, 127.1, 126.8, 120.3, 66.3, 26.8.
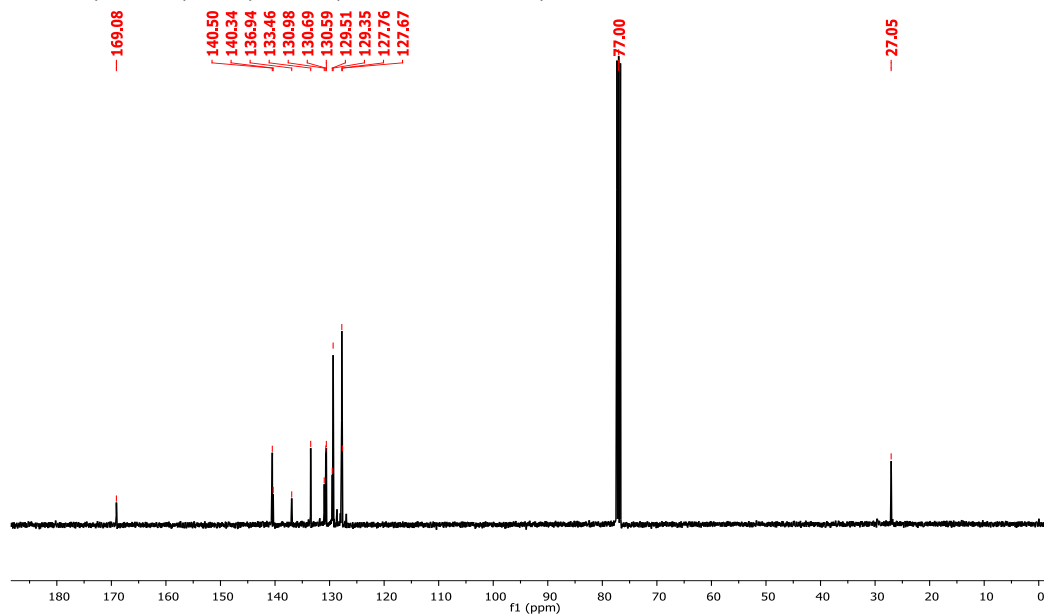
¹H and ¹³C NMR spectra of compound **3ag.**
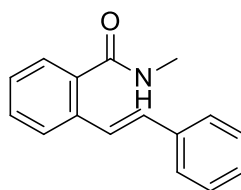

3ag

¹H NMR (400 MHz, CDCl₃) δ 8.02 – 7.90 (m, 3H), 7.61 – 7.50 (m, 4H), 7.46 – 7.37 (m, 3H), 6.77 (d, *J* = 16.0 Hz, 1H), 6.16 (s, 1H), 2.97 (d, *J* = 4.0 Hz, 3H).
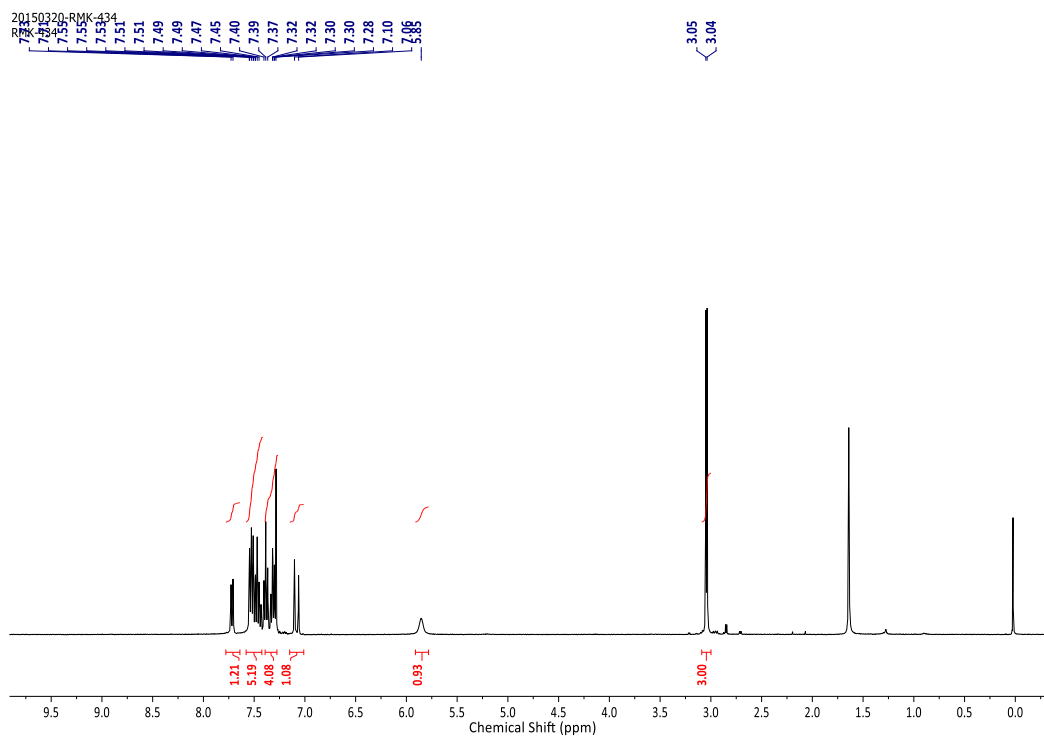

¹³C NMR (101 MHz, CDCl₃) δ 169.1, 140.5, 140.3, 136.9, 133.5, 130.9, 130.7, 130.6, 129.5, 129.3, 127.8, 127.7, 27.1.
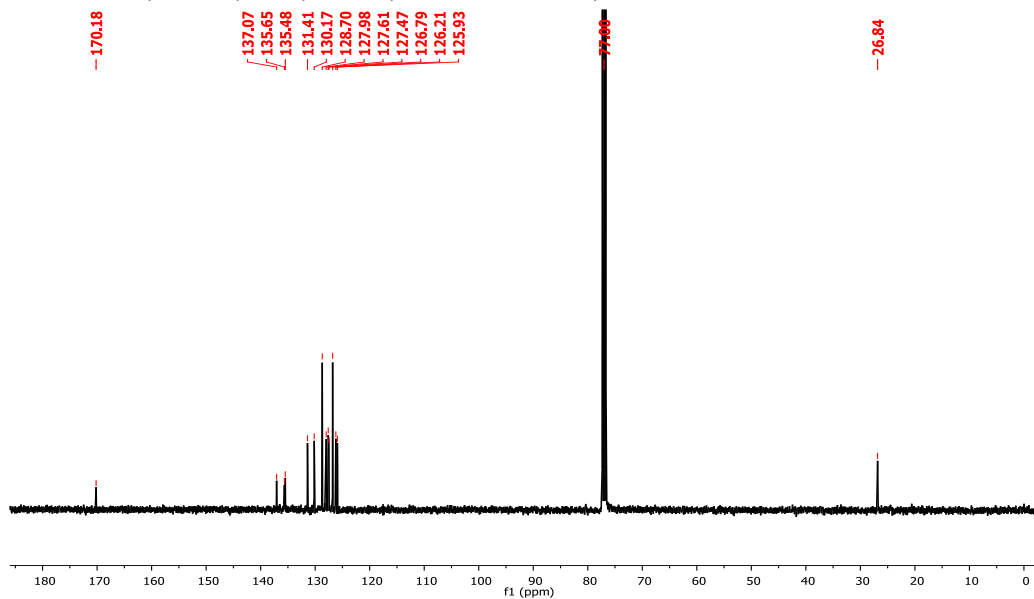
¹H and ¹³C NMR spectra of compound **3ah**

3ah

¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 7.5 Hz, 1H), 7.59 – 7.52 (m, 5H), 7.47 – 7.39 (m, 4H), 7.08 (d, *J* = 16.0 Hz, 2H), 5.85 (s, 1H), 3.04 (d, *J* = 4.0 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 170.2, 137.1, 135.6, 135.5, 131.4, 130.2, 128.7, 127.9, 127.6, 127.5, 126.8, 126.2, 125.9, 26.8.