Chapter - 3

Introduction: One - Pot methodologies in Organic synthesis

Present Work

PART - I: Synthesis of Fluorinated Stilbenes using One - pot Wittig - Heck reaction

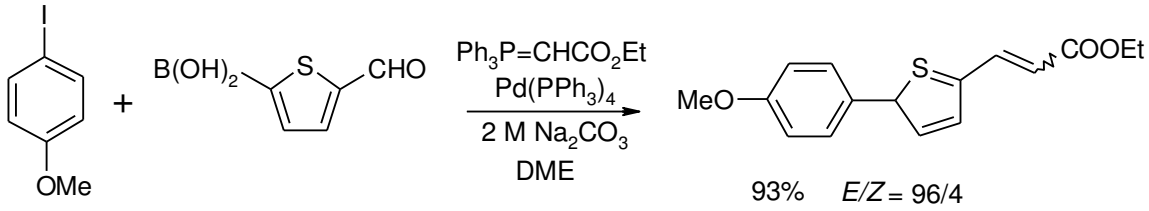
PART - II: One - pot Wittig olefination-Suzuki coupling reaction

INTRODUCTION

Synthetic protocols in which more than one steps are carried out simultaneously or as one-pot process, offer a number of advantages to the chemists. Mainly the combination of operations results in the lowering of the overall consumption of reagents for reaction/work up. Moreover there is reduction in the total reaction time, avoids purification of unstable, toxic or volatile intermediates and often fulfill some of the requirements of the alternative greener synthesis. In a way they can be referred as "Greener Synthetic Procedures." In recent decades several procedures are developed for making useful molecules and intermediates by adopting one-pot or domino or tandem synthetic Schemes[1] owing to their practical advantages. Due to their various applications in organic synthesis, in the present work we have developed two different one-pot methodologies for the synthesis of variety of stilbene derivatives.

Discussion will be divided into two parts, one will comprise of one-pot **Wittig - Heck olefination** reaction for preparation of fluorinated stilbene derivatives, while the second part will focus on one-pot **Wittig olefination - Suzuki coupling** reaction for the synthesis of styryl biphenyl derivatives.

One - pot **Wittig olefination - Suzuki** reaction developed by Thiemann et al.[2a] shows the compatibility of conjugated phosphoranes in Pd(0) catalyzed C-C bond forming reactions. They have synthesized biaryl/hetrarylacrylates, biaryl/hetarylenones and acrylonitrites with extended π-systems with formylboronic acids as central building blocks, in one step by a combined Suzuki cross-coupling-Wittig olefination reaction, where stabilized phosphoranes were used.

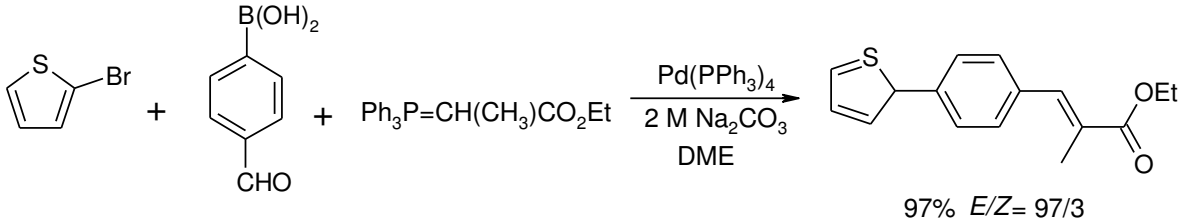


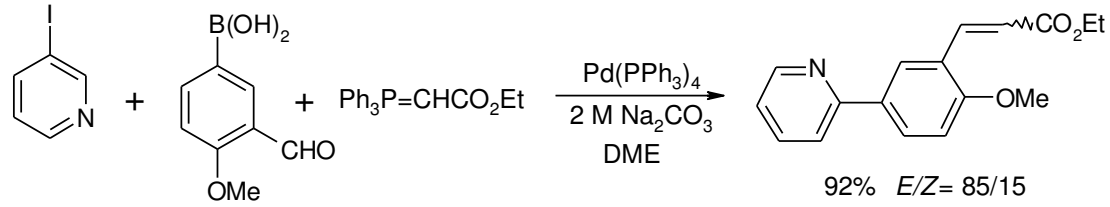
Scheme 1: One - pot Wittig olefination - Suzuki coupling reaction

The stability of the π - conjugated phosphoranes, while still reactive towards carbonyl groups, in a number of different reaction conditions provides the opportunity to combine the Wittig olefination reaction with a second transformation in a one - pot procedure. This reaction also has been performed under ultrasound at ambient

temperature in a biphasic system of aq. Na_2CO_3 and the organic phase consisting of hexane and ether, which can be removed easily at the end of the reaction.

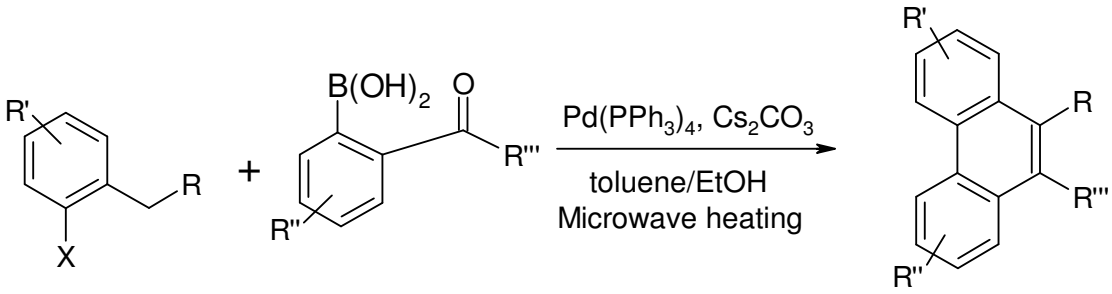
A variety of commercially available formylarylboronic acids and formylthienylboronic acids could be used in the reactions. In all the cases, *E* isomer of acrylates was the major isomer formed, as can be expected for a Wittig olefination with a stabilized phosphorane. The *E* : *Z* isomer ratios were >90%, except for the products where the methoxy substituent, present close to the formyl group, has a directing effect and the *E* : *Z* ratio was lower.





Scheme 2: One - pot Wittig olefination - Suzuki coupling reaction - variation of the phosphorane component

Heo et al. have developed an efficient cascade reaction, a **Suzuki - Miyaura coupling** followed by an **aldol condensation**, for the construction of phenanthrene derivatives using microwave irradiation.[3] Since phenanthrenes belong to an important skeleton of organic compounds due to their core structure in natural products[4a] and interesting biological activities such as antimalarial,[4b] anticancer,[4c] and emetic activity.[4d] They also serve as a common structural motif in materials science based on their photoconducting, photochemical and electroluminescent properties.[4e] For the last several decades, much attention has focused on the development of synthetic methods for the construction of phenanthrene derivatives. There is still demand for methods with improved yields and greater diversity of substituents for the synthesis of highly functionalized phenanthrene derivatives. Thus Heo have designed a two - step sequence, Suzuki - Miyaura coupling followed by intramolecular aldol - type condensation for the rapid access of phenanthrenes under microwave irradiation (**Scheme 3**).

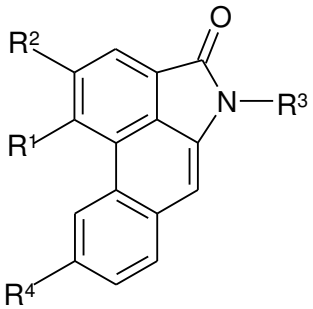


R = CN, CO_2Me, CONHMe, $COCH_3$, SO_2Ph, R' and R'' = substituents, R''' = H, Me, X = Br, Cl.

Scheme 3: One - pot synthesis of Phenanthrenes via Suzuki - Miyaura coupling/Aldol condensation cascade reaction

This one-pot method has also proved to be a robust and rapid route to construct a central ring of phenanthrenes from readily available *ortho* substituted aryl bromides and *o*-formyl- or *o*-acetyl-arylboronic acids. For example, the reaction of methyl 2-bromophenylacetamide with 2-formyl-phenylboronic acid in the presence of a Pd catalyst and a base provided a biaryl intermediate, which underwent *in situ* cyclization to afford the corresponding phenanthrene in high yield.

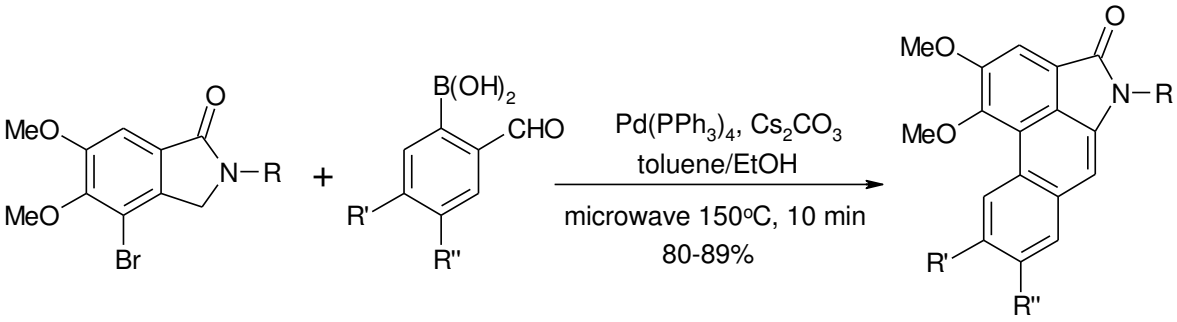
Later on they have reported the application of this one - pot synthesis of phenanthrenes that employs a **Suzuki - Miyaura coupling/aldol condensation cascade sequence** to the total synthesis of aristolactams and have synthesized several unnatural aristolactam analogues. Aristolactams belong to a large and important family of naturally occurring alkaloids that possess the phenanthrene lactam skeleton[5a] (fig-1). They possess an interesting array of biological properties including anticancer,[5b] anti-inflammatory,[5c] anitplatelet,[5d] and neuroprotective[5e] activities.



Aristolactam BII (**1**); $R^1 = R^2 = OMe$, $R^3 = R^4 = H$
Aristolactam BIII (**2**); $R^1 = R^2 = R^4 = OMe$, $R^3 = H$
Aristolactam FI (**3**); $R^1 = OH$, $R^2 = OMe$, $R^3 = R^4 = H$
N-Methyl piperolactam A (**4**); $R^1 = OH$, $R^2 = OMe$, $R^3 = Me$, $R^4 = H$
Sauristolactam (**5**); $R^1 = OMe$, $R^2 = OH$, $R^3 = Me$, $R^4 = H$

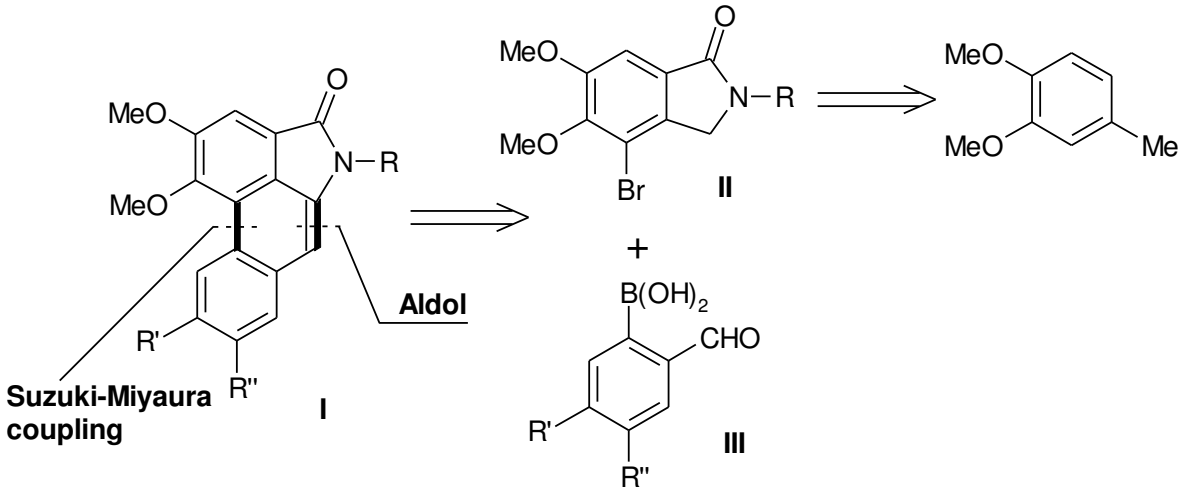
Figure 1: Aristolactam analogues

A direct one - pot synthesis of phenanthrene lactams, which employs a Suzuki - Miyaura coupling/aldol condensation cascade reaction of isoindolin-1-one with 2-formylphenylboronic acid, has been developed by Heo (**Scheme 4**).



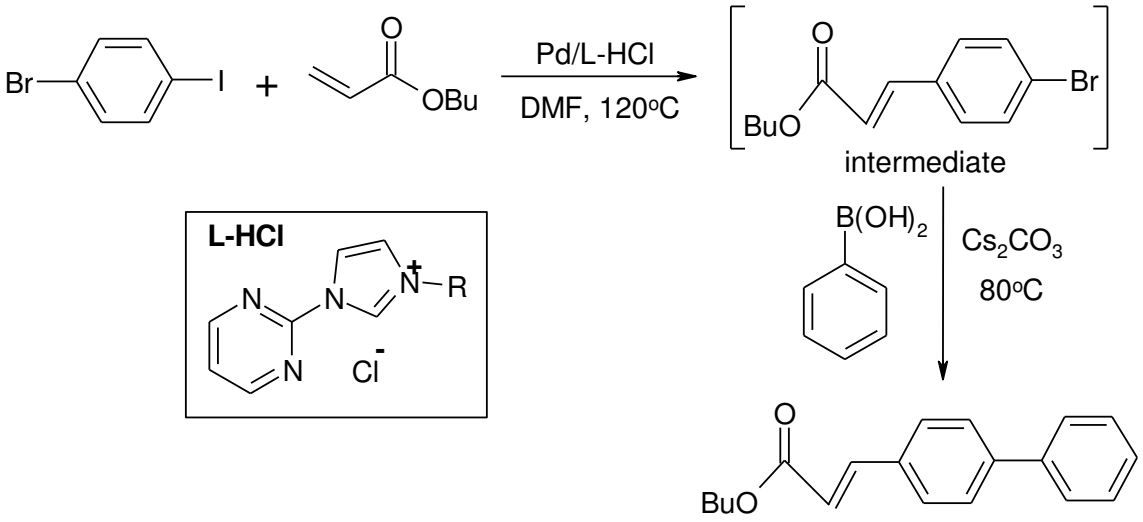
Scheme 4: Total synthesis of Aristolactams via One-pot Suzuki-Miyaura coupling/Aldol condensation cascade reaction

A crucial feature of this new synthetic strategy arises from the recognition that phenanthrene lactam (I) can be synthesized from the reaction of 4-bromoisoindolin-1-one (II) with 2-formylarylboronic acid (III) via a Suzuki - Miyaura coupling/aldol - type condensation cascade reaction (Scheme 5). Moreover, the key intermediate, 4-bromoisoindolin-1-one (II) derives from commercially available 3,4-dimethoxytoluene via several straightforward functional group transformations.



Scheme 5: Construction of Phenanthrene lactam via Suzuki-Miyaura coupling/Aldol condensation cascade reaction

Zhang et al. have described a simple method for one - pot sequential **Heck/Suzuki coupling** reactions of a range of substituted aryl dihalides.[6] The $Pd(OAc)_2$/imidazolium system catalyzed this double coupling reactions were proceeded without isolation of the intermediates giving unsymmetrically polysubstituted biphenyls in good to excellent yields (**Scheme 6**).



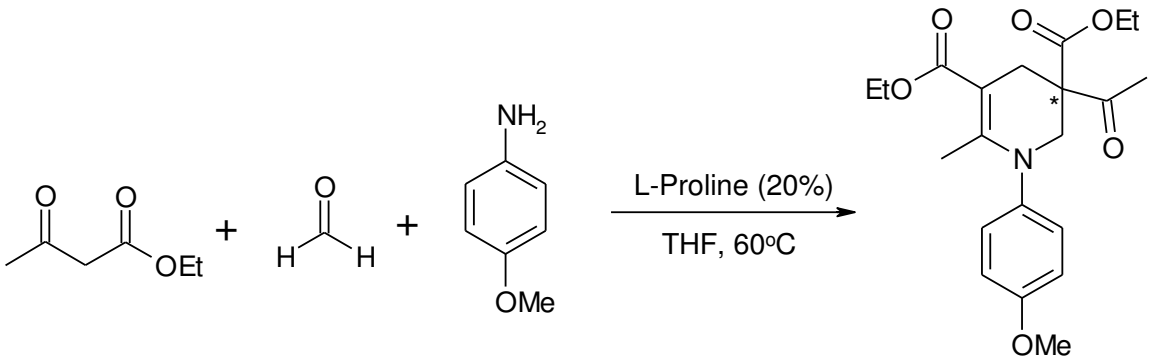
Scheme 6: Sequential Heck/Suzuki reactions

Two different carbon - carbon bond formation reactions could be achieved in one-pot by using a simple catalyst. Here pyrimidine group plays an important role in stabilizing the catalyst and preventing the formation of palladium black. This protocol is convenient and efficient for various combinations of dihaloarene, olefin and arylboronic acid. In addition, the biphenyl products bearing chloride could be further converted to polysubstituted terphenyls and aminobiphenyls via additional C-C and C-N coupling reactions with substituted arylboronic acids and amines respectively.

During the last few years, **organocatalytic enantioslective cascade reactions**[7] have emerged as powerful tools to construct complex molecules from simple and readily available starting materials in only one operation, thereby minimizing waste management as compared to a series of individual stepwise reactions. Therefore as a continuous interest in the development of new methodologies for the asymmetric synthesis of six-membered nitrogen-containing heterocycles, Yu et al. developed a more practical, simple to perform and single - operation cascade reaction, which employed commercially available materials directly. They described an L-proline catalyzed multi-component cascade reaction to afford tetrahydropyridines with an all carbon quaternary stereocentre, which is a big challenge to access in chemical synthesis. The functionalized piperidine ring systems are not only important starting materials for numerous biologically active compounds, but are also important structural building blocks of many natural products and pharmaceuticals.[8] This fact has stimulated a large number of investigations exploring new methodologies for asymmetric assembly of polysubstituted piperidines.[9]

Hence a novel organocatalytic asymmetric multicomponent cascade reaction to construct tetrahydropyridines with moderate yields and enantioselectivities have

been reported by Yu et. al[10] (**Scheme 7**). The merit of this cascade process is highlighted by its high efficiency of producing five new bonds, three C-C bonds and two C-N bonds, and an all-carbon quaternary stereocentre in one operation, which otherwise is a big challenge to access by traditional strategies. Despite unsatisfactory enantioselectivities, this strategy easily provides an access to structurally diverse tetrahydropyridines.



Scheme 7: Organocatalytic enantioselective multicomponent cascade reaction

FLUORINATED POLYAROMATIC HYDROCABONS (FPHCs)

Importance of FPHCs:

Fluorinated polyaromatic hydrocarbons (F-PHCs) play an important role in understanding the action and the mechanism of carcinogenesis of this class of compounds. Presence of fluorine at different positions of the PHC helps to narrow the possible active sites to bind with DNA[11] or in modulating the carcinogenicity from the remote sites[12] or understanding other conformational parameters.[13] The study has established that certain F-PHCs have lower biological activity due to the presence of fluorine at the crucial section of the molecular framework and hence are less tumorigenic than the parent PHCs.[11b,14] The derivatives of F-PHCs also have a significant role in the study of reactions of standard nucleophiles with radical cations.[15] Recently polyaromatic compounds such as hexabenzocoronenes with the presence of a number of fluorine substituents have shown novel metastable molecular conformations.[16] Besides these the F-PHCs have a wide range of applications in molecular recognition, Host-guest interactions, material chemistry, biologically important compounds,[17] medicinal chemistry,[18] liquid crystals[19] and crystal engineering.[20] The area of chemistry of fluorinated organic molecules has been a subject of immense research and several monograms and books are available for reference.[21]

Synthesis of F-PHCs:

Generally the fluorine atom is introduced by various special fluorinating methods on the substrate molecules.[22] This approach of accessing F-PHCs often has a drawback of formation of unwanted isomers.[22c,23] The other option is to select appropriately fluorinated starting molecule and build the structure of F-PHC and has been successfully demonstrated in some cases.[24]

Recently we have developed phosphine-free catalyst systems for efficient Mizoroki - Heck reaction[25a] as well as a one-pot Wittig - Heck reaction sequence.[25b] One of the useful methods of synthesis of phenanthrenes, benzo[c]phenanthrenes and helicenes is photocyclization of the corresponding stilbene derivatives.[25c] In this chapter, we present synthesis of a series of fluorinated styrylbenzene derivatives by the Mizoroki - Heck reaction using phosphine-free catalytic conditions or by adopting the one - pot Wittig - Heck reaction sequence. These fluorinated strylbenzene derivatives can be used as precursor for the synthesis of fluorinated phenanthrenes, benzo[c]phenanthrenes and helicenes by photocyclization.

Results and Discussion

PART - I Synthesis of Fluorinated Stilbenes

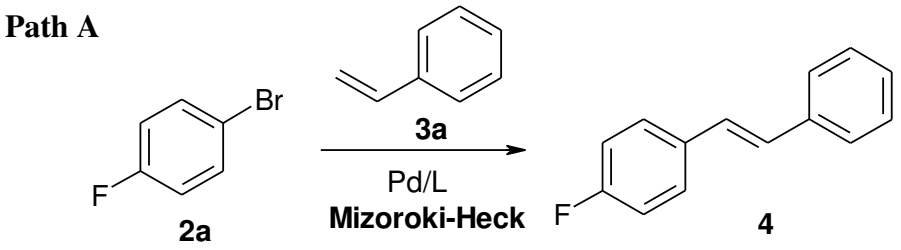
In this part of the chapter we present two different paths (Path A and Path B) to synthesize fluorinated stilbenes.

Path A: Synthesis of fluorinated stilbenes by Mizoroki - Heck reaction

Path B: Synthesis of fluorinated stilbenes by one-pot Wittig - Heck reaction

Path A: Synthesis of Fluorinated Stilbenes by Mizoroki - Heck reaction

Path A of **Scheme 8** describes the basic Mizoroki - Heck reaction to construct fluorinated styrylbenzene derivatives using our phosphine-free catalyst system [comprising of the *in situ* mixture of ligand 1-(α-aminobenzyl)-2-naphthols **1** and $Pd(OAc)_2$].



Scheme 8: Direct Mizoroki-Heck reaction

As discussed earlier, we continue to explore readily accessible aminobenzylnaphthols as phosphine-free ligands for Pd mediated cross-coupling reactions, we have chosen ligand **1c** for the present study (**Fig 2**). This catalyst was screened for standard Mizoroki-Heck reaction with fluorinated aromatic bromo compounds **2a**-**2c** with good conversions as shown in **Table 1.**

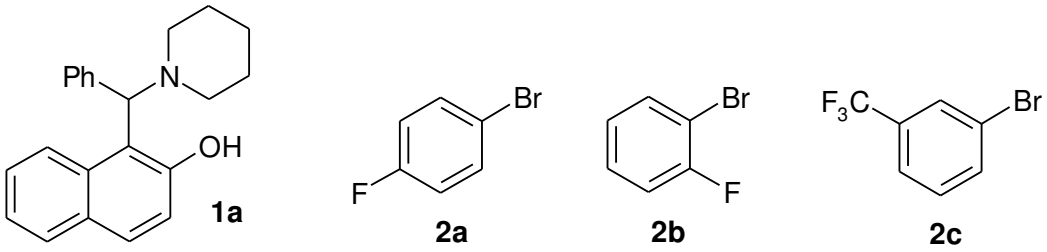
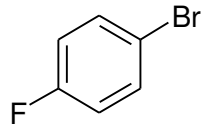
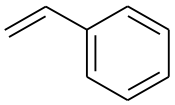
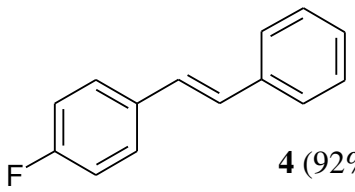
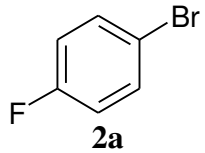
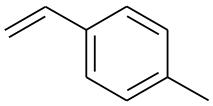
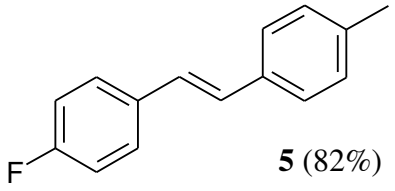
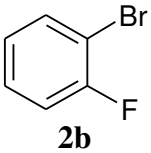
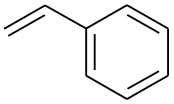
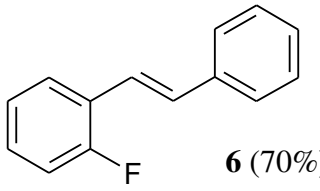
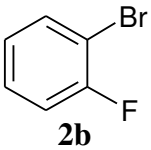
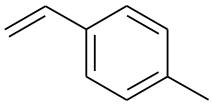
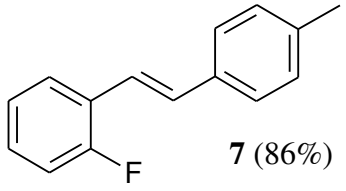
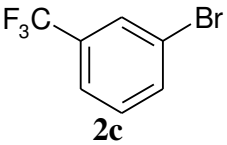
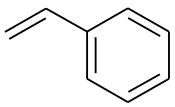
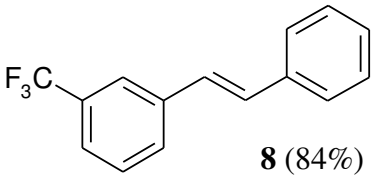
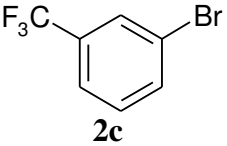
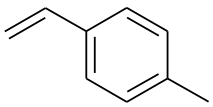
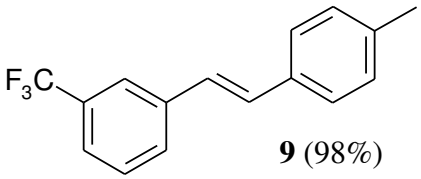


Figure 2: Ligand 1c, List of fluorinated aryl halides used for Mizoroki-Heck reaction

In order to demonstrate the generality of this approach to prepare variety of fluorinated stilbenes a series of fluorinated aryl bromides were used, which are listed in **Fig 2**.

Table 1. Synthesis of Fluorinated stilbene derivatives by Path A.

No	Aryl halide (1 eq)	Olefine (1.5 eq)	Product (% Yield)
1	 **2a**	 **3a**	 **4** (92%)
2	 **2a**	 **3b**	 **5** (82%)
3	 **2b**	 **3a**	 **6** (70%)
4	 **2b**	 **3b**	 **7** (86%)
5	 **2c**	 **3a**	 **8** (84%)
6	 **2c**	 **3b**	 **9** (98%)

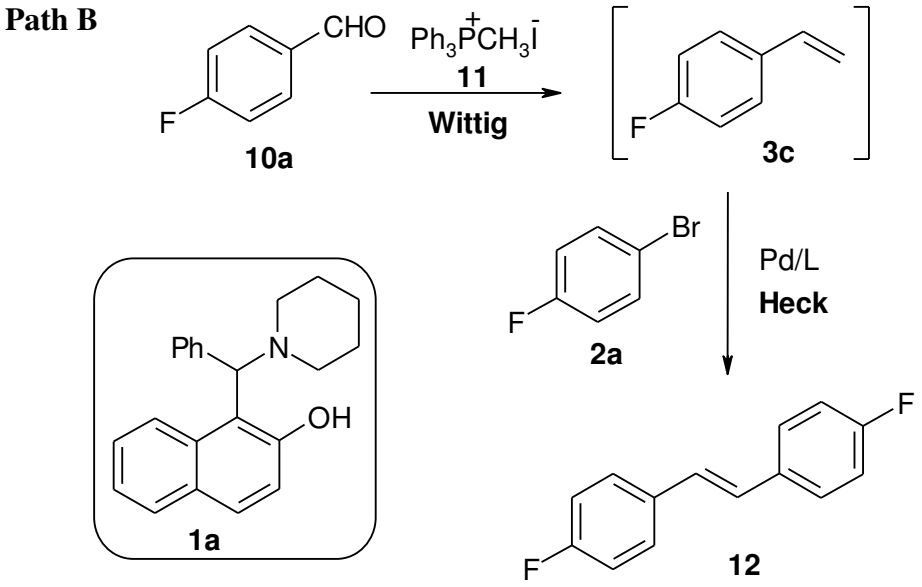
Mizoroki - Heck conditions: Ar-Br (1.0 eq.), styrene (1.5 eq.), $Pd(OAc)_2$ (0.5 mol %), **1a** (0.6 mol %), K_2CO_3 (2.5 eq.), TBAB (0.2 eq.), DMA, N_2 atm., 140^oC, 40 h.

The mixture of suitable fluorinated aryl halide, an excess of K_2CO_3, catalytic quantity of $Pd(OAc)_2$-ligand in dry DMA was heated at 140^oC under N_2 atmosphere. Careful thin layer chromatography analysis indicated the formation of corresponding fluorinated stilbenes, which were isolated and characterized. The results are presented

in **Table 1**. The stilbenes obtained are isolated in excellent yield under the experimental conditions.

Path B: Synthesis of fluorinated stilbenes by one - pot Wittig - Heck reaction

However, the above approach is limited to the availability of the corresponding styrene derivatives. To overcome this limitation we had developed the one - pot approach of *in situ* synthesis of styrene from the aldehydes by the Wittig reaction and utilized it for the subsequent Mizoroki - Heck reaction. The prerequisite of planning the one-pot multi-step reaction is the compatibility of the reagent system and reaction conditions. In the present effort the second reaction, the Mizoroki - Heck reaction is carried out with Pd-catalyst and a suitable base. The required olefin is envisaged to be prepared by Wittig reaction of aldehyde with suitable phosphonium salt in the basic medium. The advantage of this reaction is the availability of a range of aldehydes with varied functional group and the elimination of need of purification of the styrene for the coupling reactions. This strategy utilizes two aromatic moieties (Ar_1CHO and Ar_2X), to construct the stilbene unit and offers a variety of two different fluorine containing substitutions as shown in Path B of **Scheme 9**.



Scheme 9: One - pot Wittig - Heck reaction

As an example, the reaction of 4-fluorobenzaldehyde **10a** with one carbon phosphorium salt ($Ph_3P^+CH_3I^-$) and base will produce 4-fluorostyrene **3c**, which will undergo *in situ* Mizoroki-Heck reaction with 1-bromo-4-fluorobenzene **2a** to form 4,4'-difluorostilbene **12** in moderate yield (**Scheme 9**). This one - pot procedure to generate styrene involves its *in situ* synthesis by the classical Wittig olefination. The

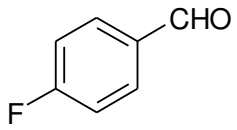
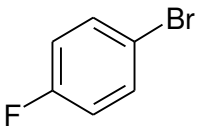
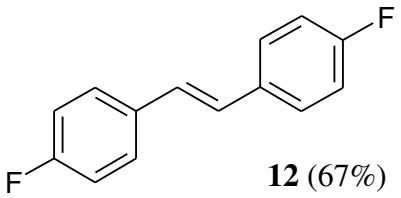
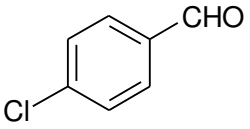
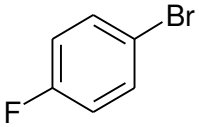
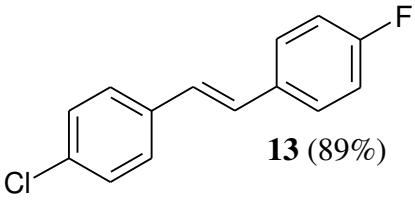
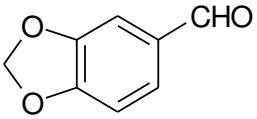
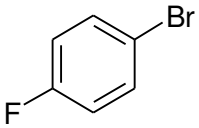
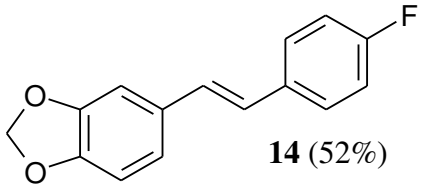
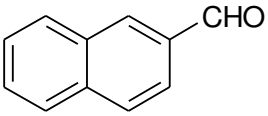
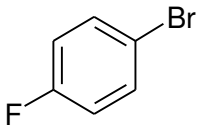
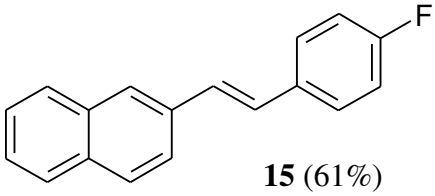
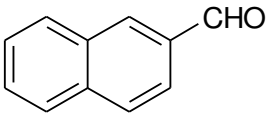
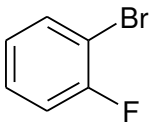
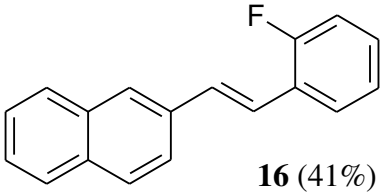
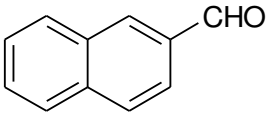
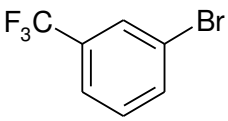
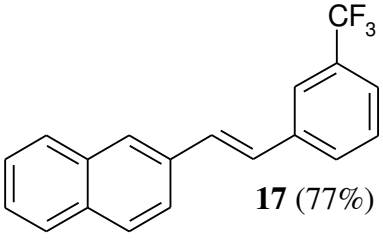
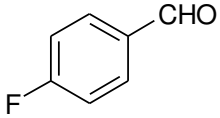
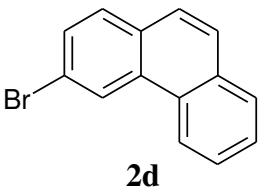
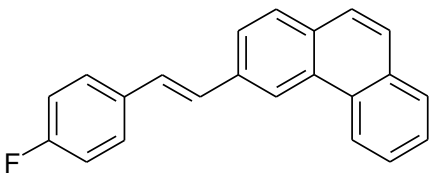
reaction of aromatic aldehyde with phosphonium salts undergo Wittig reaction even with weak base like K_2CO_3, which is available in the present Mizoroki - Heck conditions. Hence a concoction of equimolar amount of benzaldehyde, $Ph_3P^+CH_3I^-$, fluorinated aryl halide, excess of K_2CO_3, catalytic quantity of $Pd(OAc)_2$-Aminobenzylnaphthol ligand **1c**, TBAB as PTC was heated in DMA and fluorinated stilbene was isolated in good yield.

A series of fluorine containing styrylbenzenes were synthesized from corresponding aromatic aldehydes **10a-d** via their *in situ* conversion to styrenes and the subsequent Mizoroki-Heck reaction with suitable aryl halide as outlined in **Table 2**. This is a three component reaction and hence with the same number of variations available for the facile generation of F-substituted stilbenes.

Development of efficient synthesis of conjugated molecules is important for the preparation of several new materials capable of having unique properties due to the delocalization of electrons over several multiple bonds.[26] Among such entities the molecules with alternate double bonds and aromatic rings are prominent and have received some attention.[26] The present strategy of *in situ* generation of stilbene was further extended to synthesize distyryl benzenes from easily available stable starting materials.

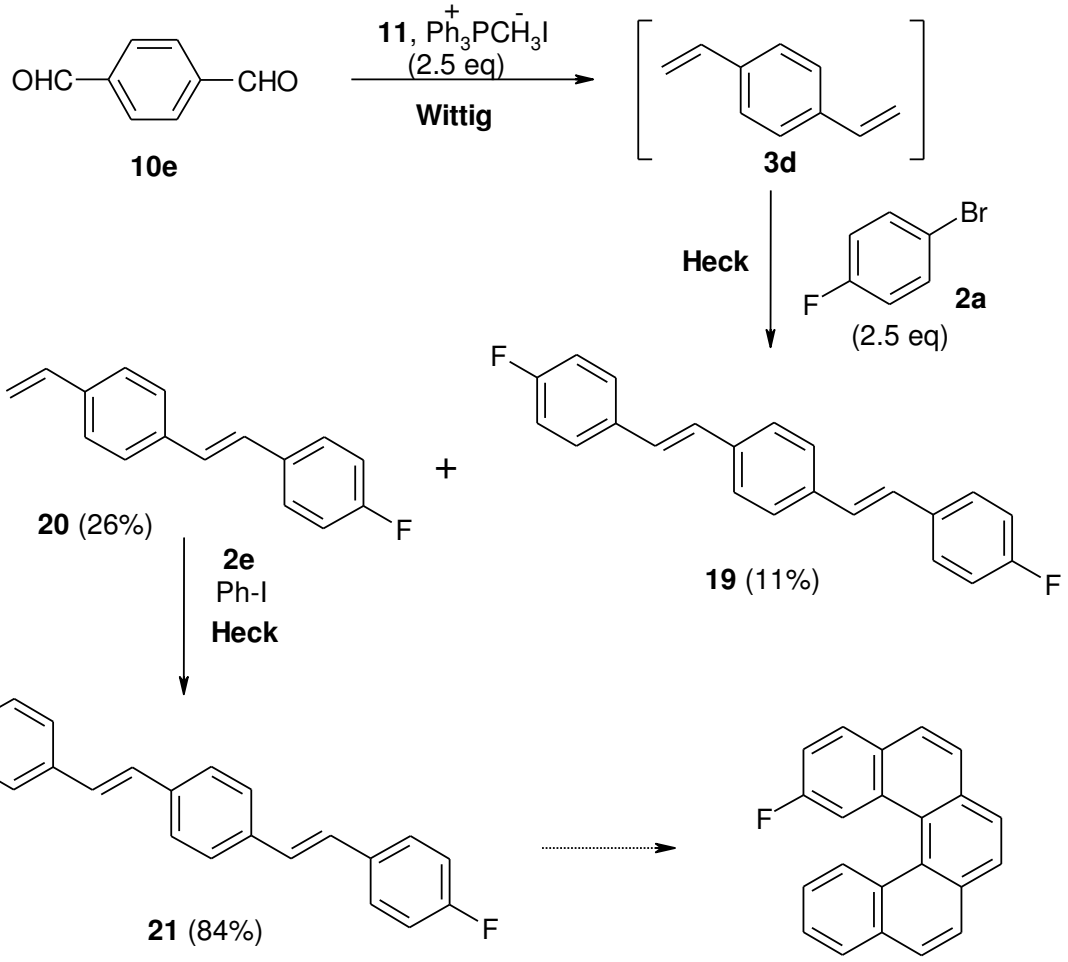
All the derivatives of Fluorinated styrylbenzene were purified by careful chromatography on silica gel and characterized by ^{1}H-NMR, IR and Mass analysis. In ^{1}H-NMR spectra of compound **14**, the -O-CH_2-O- protons give sharp singlet at 5.98 δ value. The mass spectra of compound **13** shows two peaks at 231 and 233 m/z having relative abundance in 3:1 ratio due to presence of -Cl.

Table 2: Synthesis of Fluorinated stilbene derivatives by Path B

No	Aldehyde (1 eq)	Aryl halide (1 eq)	Product (% Yield)
1	 **10a**	 **2a**	 **12** (67%)
2	 **10b**	 **2a**	 **13** (89%)
3	 **10c**	 **2a**	 **14** (52%)
4	 **10d**	 **2a**	 **15** (61%)
5	 **10d**	 **2b**	 **16** (41%)
6	 **10d**	 **2c**	 **17** (77%)
7	 **10a**	 **2d**	 **18** (70%)

One - pot Wittig - Heck conditions: Ar-CHO (1.5 eq.), CH_3PPh_3I **11** (1.5 eq.), Ar-Br (1.0 eq.), $Pd(OAc)_2$ (0.5 mol %), **1a** (0.6 mol %), K_2CO_3 (4.0 eq.), TBAB (0.2 eq.), DMA, N_2, 140°C, 40h.

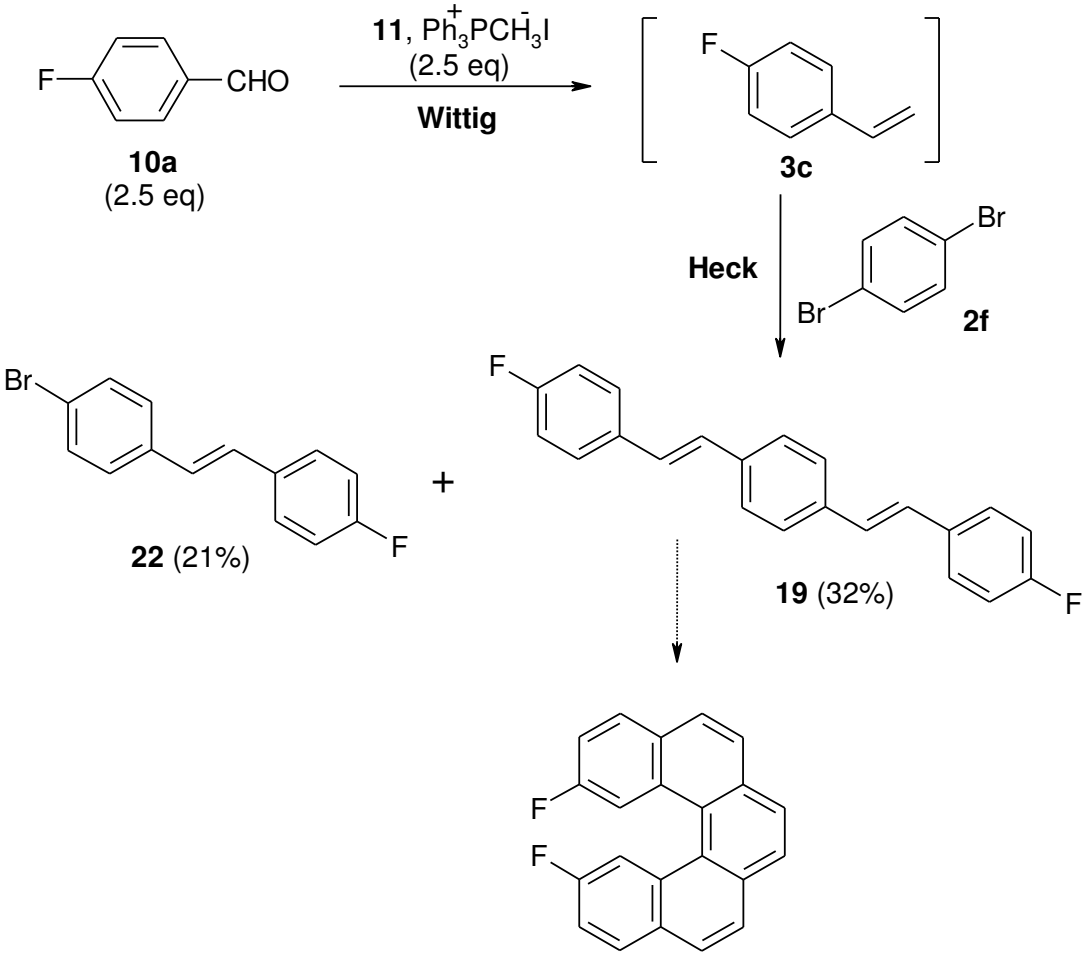
This approach involves simultaneous formation of two double bonds between three aromatic rings *via* a combination of Wittig and Mizoroki-Heck reaction between five reactant molecules in a single step process. This process involved *in situ* synthesis of divinylbenzene stating from terephthaldehyde **10e** and the Wittig salt $Ph_3P^+CH_3I^-$, which was trapped by the Mizoroki - Heck reaction with *p*-bromofluorobenzene **2a** (**Scheme 10**).



Scheme 10: One - pot Five component reaction for the synthesis of **21**

The reaction furnished a mixture of mono - Heck reaction product **20** and the expected double - Heck reaction product **19**, the former **20** was separated and further subjected to Mizoroki - Heck conditions[25a] with iodobenzene to prepare 1-(4-fluorostyryl)-4-styrylbenzene **21** in excellent yield.

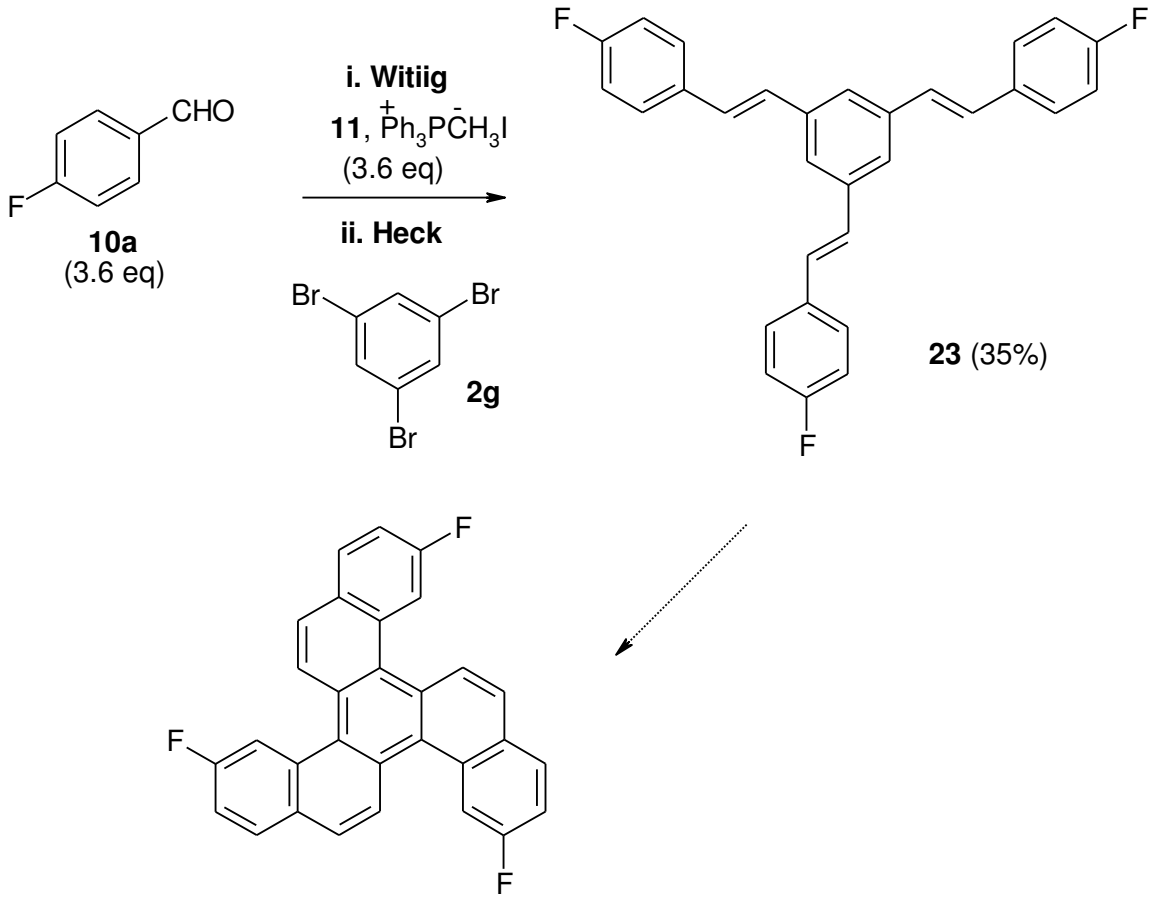
Synthesis of **19** by the above approach was less effective probably due to the polymerization and cross-linking of *in situ* formed divinylstyrene **3d**. Another approach for its synthesis was investigated where 4-fluorostyrene **3c** was *in situ* synthesized and subjected to a double Mizoroki - Heck reaction with 1,4-dibromobenzene **2f** (**Scheme 11**). This approach was a better option for accessing the desired 1,4-bis(4-fluostyryl)benzene **19**.



Scheme 11: Improved Synthesis of 1,4-bis(4-fluorostyryl)benzene **19**. *One - pot Five component Wittig - Heck condition*: $Ar(Br)_2$ **2f** (1.0 eq.), **10a** (2.5 eq.), CH_3PPh_3I (2.5 eq.), $Pd(OAc)_2$ (2.0 mol %), L (2.4 mol %), K_2CO_3 (8.0 eq.), TBAB (0.4 eq.), DMA, N_2 atm., 140°C, 40 h

In continuation with our efforts to construct highly conjugated fluorinated molecules a combination of Wittig - Heck reaction was performed. The one - pot seven component Wittig - Heck reaction was carried out on 4-fluorobenzaldehyde **10a** to make *in situ* 4-fluorostyrene **3c** which was trapped by the triple Heck reaction with 1,3,5-tribromobenzene **2g** to yield 1,3,5-tris(4-fluorostyrylbenzene) **23** (**Scheme 12**).

We refer this as a seven component reaction because seven reactant molecules are participating in the one - pot reaction.



Scheme 12: Synthesis of tri-styrylbenzene derivative. *One - pot Seven component Wittig - Heck condition*: $Ar(Br)_3$ **2g** (1.0 eq.), **10a** (3.6 eq.), CH_3PPh_3I (3.6 eq.), $Pd(OAc)_2$ (3.0 mol %), L (3.6 mol %), K_2CO_3 (12.0 eq.), TBAB (0.6 eq.), DMA, N_2 atm., 140^oC, 40 h

PART - II One - pot Wittig olefination - Suzuki coupling reaction

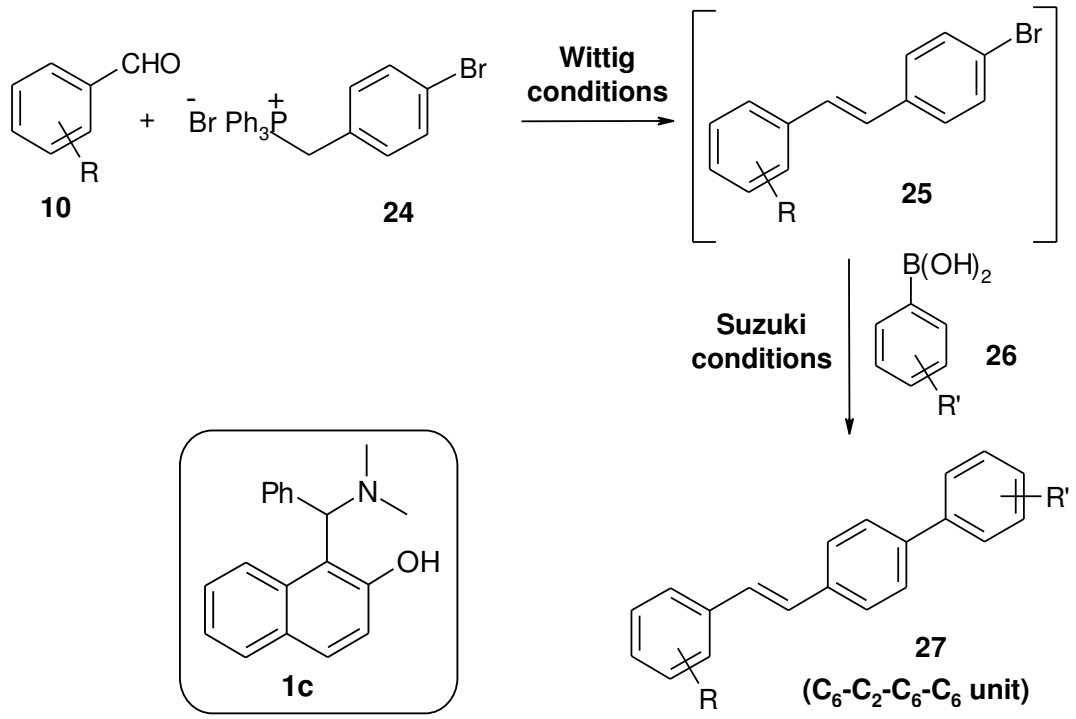
The strategy for cascade reactions involved carrying out a sequence of transformations in which the product of the first step serves as the substrate for the second step. The process involved a number of steps until finally a stable product was formed. The cascade reaction reduces the consumption of reagents, number of purifications and shortens reaction time, contributing to the better economy of chemical process. Many combinations of different bond making processes are combined for cascade reactions with reasonable success.[27]

Cascade reactions involving Suzuki reaction as one of the steps have been reported in the literature, although almost all involve phosphine-based catalyst systems.[28, 29]. A few examples of double Suzuki reactions have been reported in which excellent control for two different reagents was achieved.[30] In this chapter we present our efforts to apply phosphine-free Pd catalyst system for a one - pot combination of Wittig and Suzuki - Miyaura coupling reactions. Very few references are reported in the literature describing an organophosphine catalyzed one-pot Wittig - Suzuki reaction sequence with formylareneboronic acid[2] where the formyl group undergoes an olefination reaction. A case of one - pot Wittig - Suzuki reaction utilizing a phosphine-free catalyst system has not been reported.

The essential requirement of planning any one - pot multi-step reaction is the compatibility of the reagent system and reaction conditions. The stability of phosphonium salt, while still reactive towards carbonyl groups, under a number of different reaction conditions offers the opportunity to combine the Wittig olefination reaction with another transformation in a one - pot procedure.

In this one - pot method, phosphonium salt **24** was prepared from 4-bromobenzylbromide and triphenylphosphine as the Wittig component to react with –CHO. The intermediate bromo stilbene formed can undergo Suzuki coupling at its Ar-Br site. A separate aldehyde has been chosen to receive its carbonion/ylide for the olefination reaction. This approach is outlined in **Scheme 13**, considering the example of the *in situ* Wittig synthesis of stilbene and then the Suzuki reaction to form 4-styryl

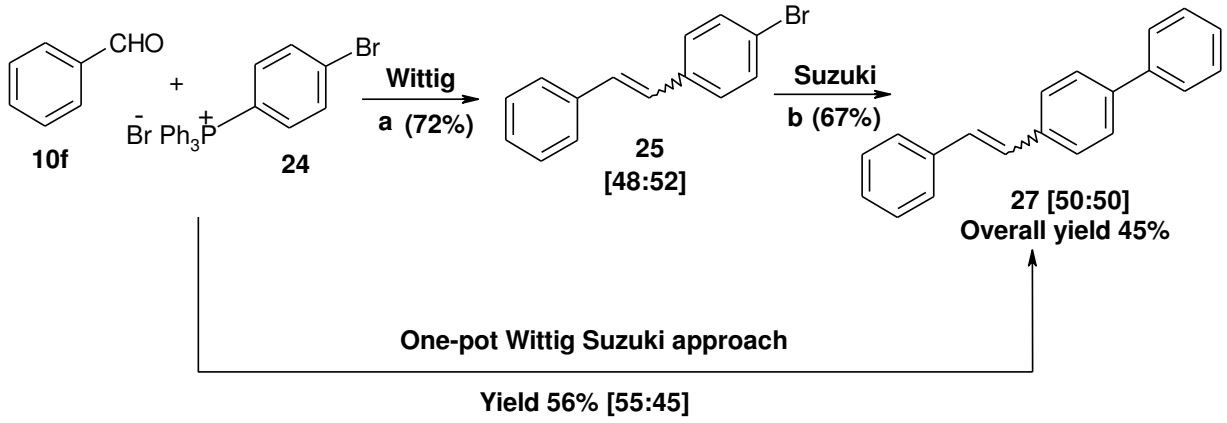
biphenyl. A similar class of molecule was synthesized by one - pot Heck - Suzuki sequence by Gruber et al.[31]



Scheme 13: One - pot three component approach for 4-styryl-biphenyl using Pd-**1c**

In order to effectively carry out our practical one-pot strategy, it was necessary to establish the efficacy of the solvent for both steps. It was also important to check whether the ratio of *Z* and *E* isomers was affected in the second step. To confirm this aspect an experiment was conducted in which the product 4-bromostilbene **25** was separated and characterized.

The ratio of *Z*:*E* isomer of **25** was established by ^{1}H-NMR analysis to be 48:52 and the isolated yield was 72%. The product **25** was then subjected to a separate step under Suzuki reaction conditions and the final product **27** was isolated in 67% yield, with a *Z* : *E* ratio of 50:50. Both steps were carried out in same solvent (anhydrous DMA) and the ratio of isomers was almost the same, indicating the compatibility of solvent and also establishing that negligible isomerization occurred in the second step of the one - pot sequence.



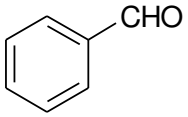
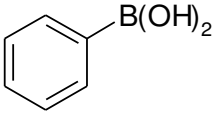
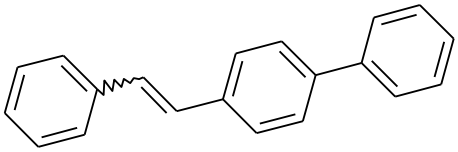
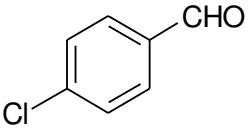
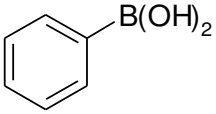
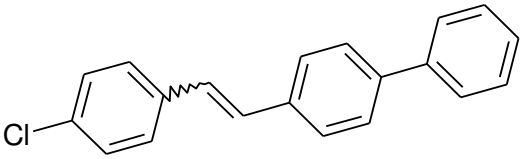
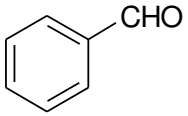
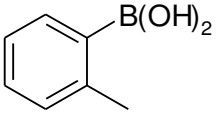
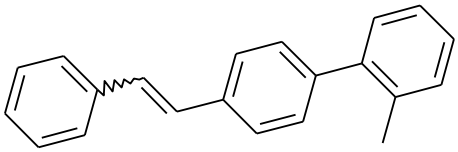
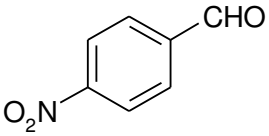
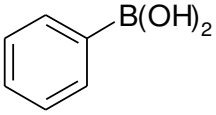
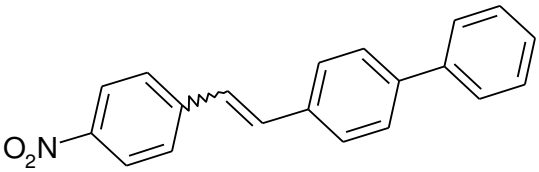
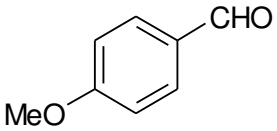
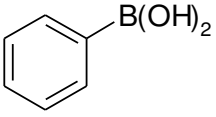
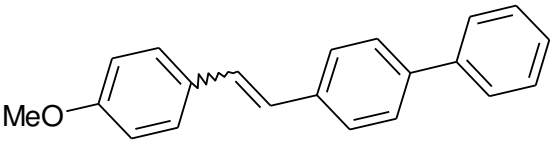
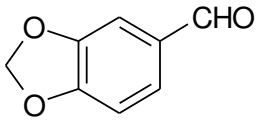
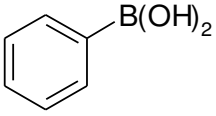
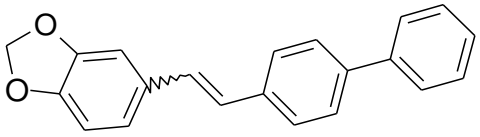
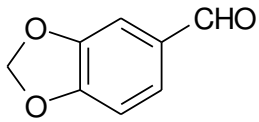
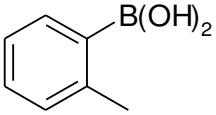
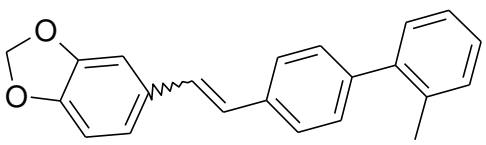
a : **Wittig conditions**: K_2CO_3 (3 eq.), DMA , 130°C, 6 h

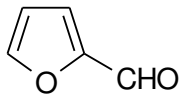
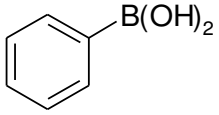
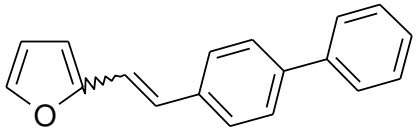
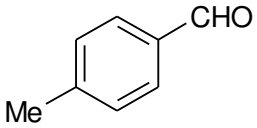
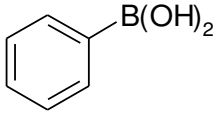
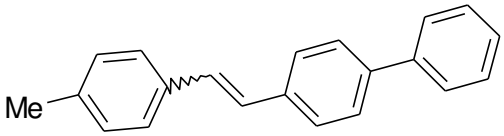
b : **Suzuki conditions**: Ph-$B(OH)_2$ (1.2 eq.), K_2CO_3 (2 eq.), TBAB (20%), $Pd(OAc)_2$ (1%), **1c** (1.2%), DMA, 130°C, 24 h

Scheme 14: Comparison study

We have also carried out comparison study of one-pot approach with the two-step reaction sequence (Wittig reaction and Suzuki reaction). From this study we concluded that one - pot approach gives high yield compared to two-step reaction sequence while *cis-trans* ratio of product is almost comparable in both cases. The overall reaction sequence involved three components or variables, although presently **24** has been used as the common element. By varying the other two components a series of styryl biphenyls were synthesized and the results are presented in **Table 3**.

Table 3: Examples of One - pot Wittig - Suzuki reaction

No	Aldehyde (1 eq)	Boronic acid (1.2 eq)	Product (% Yield) [*Z* : *E* ratio]
1	 **10f**	 **26a**	 **27** (56%) [55:45]
2	 **10b**	 **26a**	 **28** (80%) [57:43]
3	 **10f**	 **26b**	 **29** (63%) [59:41]
4	 **10g**	 **26a**	 **30** (77%) [9:91]
5	 **10h**	 **26a**	 **31** (64%) [55:45]
6	 **10c**	 **26a**	 **32** (73%) [55:45]
7	 **10c**	 **26b**	 **33** (67%) [56:44]

8	 **10i**	 **26a**	 **34** (55%) [33:62]
9	 **10j**	 **26a**	 **35** (77%) [55:45]

All reactions run with aldehyde (1 eq), 4-bromo benzyl triphenyl phosphonium bromide (1 eq), K_2CO_3 (3 eq), DMA (10 ml). After 6 h aryl boronic acid (1.2 eq), K_2CO_3 (2 eq), TBAB (20%), $Pd(OAc)_2$ (1%), **1c** (1.2%) in DMA (10 ml) were added.

The Wittig olefination reaction of aromatic aldehyde with phosphonium salt **24** took place even in the presence of a weak base like potassium carbonate (3 eq) in DMA under inert atmosphere (130^oC) initially to form **25**, an intermediate 4-bromostilbene. Boronic acid (1.2 eq), potassium carbonate (2 eq), a catalytic quantity of $Pd(OAc)_2$-ligand **1c**, and TBAB as phase transfer catalyst were added (after 6 h) and the reaction mixture was continued to completion. In all cases, the *Z* isomer of stilbene derivatives were obtained in excess in Wittig olefination.[32] The *Z* : *E* isomer ratios were close to ~55:45, except for product 4-nitrostyryl biphenyl **30**, where the nitro group controls the ratio in favour of the *E* isomer.

All the derivatives of styrylbiphenyl were obtained after careful column chromatography and characterized by ^{1}H-NMR, IR and Mass analysis. The *cis-trans* ratio was determined by ^{1}H-NMR. In the NMR spectra of derivative **28**, the *cis* - olefinic protons show two doublets at δ = 6.69 - 6.57 ppm (*J* = 12 Hz), while the *trans* - olefinic protons give singlet at 7.13 δ value. Whereas in case of derivative **29**, both *cis* and *trans* olefinic protons appear as singlet at δ = 6.65 and 7.18 respectively. The -O-CH_2-O- protons of derivative **32** and **33** show singlet around 6.0 δ value. In the mass spectra of derivative **28**, the ratio of relative abundance of [M]:[M+2] = 3:1, giving evidance for the presence of -Cl in compound.

Experimantal Part

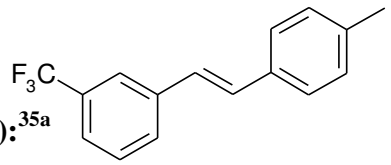
Reagents were purchased from Sigma-Aldrich Chemicals Limited, S. D. Fine, Sisco, Qualigens Limited etc. DMA was distilled and stored 24 h over molecular sieves (4 Å). Thin layer chromatography was performed on Merck 60 F254 Aluminium coated plates. The spots were visualized under UV light or with iodine vapour. All the compounds were purified by column chromatography using SRL made silica gel (60-120 mesh) unless mentioned otherwise. ^{1}H-NMR Spectra were recorded on Bruker Avance 200 or 400 and Inova-500 Spectrometers and were run in $CDCl_3$ unless otherwise stated. Mass spectra were recorded on Thermo-Fischer DSQ II GCMS instrument. IR spectra were recorded on a Perkin-Elmer FTIR RXI spectrometer as KBr pallets. Melting points were recorded in Thiele's tube using paraffin oil and are uncorrected.

PART - I Synthesis of Fluorinated Stilbenes

Path A: Synthesis of Fluorinated Stilbenes by Mizoroki - Heck reaction

General Procedure for the Mizoroki - Heck reaction:

1-((*E*)-4'-Methylstyryl)-3-trifluoromethyl-benzene (9):[35a]



Catalyst solution: A solution of palladium acetate (0.005 mg, 0.022 mmol) and ligand **1a** (0.0085 mg, 0.027 mmol) was made in dry dimethylacetamide (2 mL) under the nitrogen atmosphere. This was sonicated for 2-3 min to degas and to make the solution homogeneous.

In another two-necked flask, a mixture of 3-bromobenzotrifluoride (1.0 g, 4.44 mmol), dry potassium carbonate (1.547 g, 0.011 mmol), TBAB (0.287 g, 0.88 mmol) and dry dimethylacetamide (5 mL) was made and heated under a nitrogen atmosphere. When the temperature attained 60^{o}C, 4-methylstyrene (0.788 g, 6.67 mmol) was slowly introduced by syringe. The mixture was then heated to 100^{o}C and the previously prepared catalyst solution was added. The temperature was further raised to 140^{o}C and continued for another 40 h. The reaction mixture was quenched with water, neutralized using aqueous HCl (6N, 5 mL), and extracted with dichloromethane (3 x 25mL). The combined organic phase was washed with water and dried over anhydrous sodium sulfate. Solvent was removed in vacuum, and the

crude product was purified by column chromatography on silica gel to afford *trans*-1-fluoro-stilbene as white solid.

Yield: 98% (1.138 g), White crystalline solid.

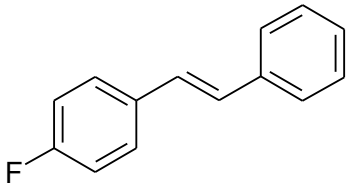
M.P. 90 - 92^{o}C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.74 (s, 1H), 7.66 - 7.64 (d, *J* = 7.2 Hz, 1H), 7.5 - 7.42 (m, 4H), 7.19 - 7.17 (d, *J* = 8 Hz, 2H), 7.17 - 7.04 (two d, *J* = 16 Hz, 2H), 2.37 (s, 3H).

IR (KBr): υ 3020, 1909, 1603, 1511, 1434, 1339, 1262, 1220, 1176, 1064, 968, 907, 892, 858, 810, 697, 662 cm^{-1}.

MS (EI): (*m/z*) 263 (M+1, 55), 262 (M^+, 80), 261 (100), 247 (50), 246 (49), 226 (20), 193 (23), 178 (66), 177 (20).

1-Fluoro-4-((*E*)-styryl)-benzene (4):



Compound **4** was prepared by same procedure as that of **9**.

Yield: 92% (0.26 g), White solid.

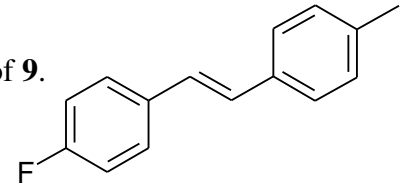
M.P. 120 - 122^{o}C (Lit.[33a] 118 - 119^{o}C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.5 - 7.44 (m, 4H), 7.37 - 7.32 (m, 2H), 7.28 - 7.23 (m, 1H), 7.08 - 6.98 (m, 4H).

IR (KBr): υ 3307, 2920, 2850, 1656, 1603, 1586, 1550, 1488, 1404, 1330, 1218, 1096, 1032, 1008, 983, 814, 792, 752 cm^{-1}.

MS (EI): (*m/z*) 199 (M+1, 14), 198 (M^+, 90), 197 (100), 196 (77), 182 (27), 178 (13), 177 (25), 83 (22), 77 (17).

1-Fluoro-4-((*E*)-4'-methylstyryl)-benzene (5):



Compound **5** was prepared by same procedure as that of **9**.

Yield: 82% (0.504 g), White crystalline solid.

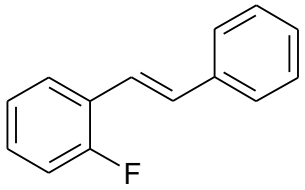
M.P. 124 - 126^{o}C (Lit.[33a] 125 - 126^{o}C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.51 - 7.42 (m, 4H), 7.21 - 7.19 (d, *J* = 8 Hz, 2H), 7.1 - 7.0 (m, 4H), 2.39 (s, 3H).

IR (KBr): υ 3020, 2916, 1895, 1653, 1596, 1510, 1417, 1232, 1097, 969, 830, 786, 718, 603 cm^{-1}.

MS (EI): (*m/z*) 213 (M+1, 10), 212 (M^+, 100), 211 (77), 197 (50), 196 (76), 195 (36), 177 (21), 91 (12), 81 (17), 69 (53).

1-Fluoro-2-((*E*)-styryl)-benzene (6):



Compound **6** was prepared by same procedure as that of **9**.

Yield: 70% (0.787 g), White solid.

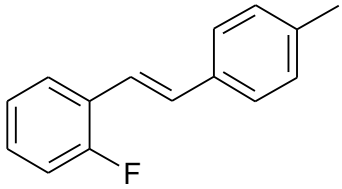
M.P. 98 - 100°C (Lit.[33b] 94 - 95°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.64 - 7.59 (dt, J_1 = 7.6, J_2 = 1.6 Hz, 1H), 7.55 - 7.53 (m, 2H), 7.39 - 7.35 (m, 2H), 7.31 - 7.2 (m, 4H), 7.16 - 7.0 (m, 2H).

IR (KBr): υ 3056, 3018, 1879, 1807, 1572, 1482, 1453, 1330, 1229, 1207, 1180, 1071, 965, 840, 782, 759, 713, 688 cm^{-1}.

MS (EI): (*m/z*) 198 (M^+, 77), 197 (100), 196 (63), 183 (47), 177 (33), 123 (35), 101 (27), 99 (55), 89 (52), 77 (31), 75 (72).

1-Fluoro-2-((*E*)-4'-Methylstyryl)-benzene (7):



Compound **7** was prepared by same procedure as that of **9**.

Yield: 86% (1.037 g), White solid.

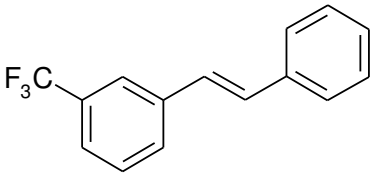
M.P. 130 - 132°C (Lit.[34a] 135 - 138°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.62 - 7.57 (dt, J_1 = 7.6, J_2 = 1.6 Hz, 1H), 7.44 - 7.42 (d, J = 8 Hz, 2H), 7.25 - 7.1 (m, 6H), 7.08 - 7.03 (m, 1H), 2.36 (s, 3H).

IR (KBr): υ 3058, 1906, 1789, 1684, 1572, 1485, 1451, 1365, 1234, 1180, 1038, 802, 724, 687 cm^{-1}.

MS (EI): (*m/z*) 212 (M^+, 94), 211 (88), 197 (40), 196 (81), 195 (32), 177 (23), 81 (77), 73 (35), 69 (100).

1-((*E*)-Styryl)-3-trifluoromethyl-benzene (8):



Compound **8** was prepared by same procedure as that of **9**.

Yield: 84% (0.929 g), White crystalline solid.

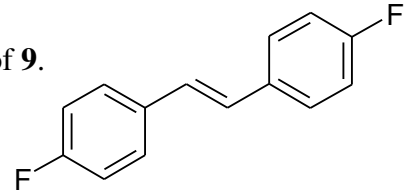
M.P. 68 - 70°C (Lit.[34b] 65 - 67°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.78 (s, 1H), 7.71 - 7.69 (d, J = 7.6 Hz, 1H), 7.57 - 7.48 (m, 4H), 7.43 - 7.37 (m, 2H), 7.35 - 7.3 (tt, J_1 = 7.2, J_2 = 1.2 Hz, 1H), 7.23 - 7.12 (dd, J_1 = 16.4, J_2 = 9.6 Hz, 2H).

IR (KBr): υ 3038, 1812, 1607, 1574, 1496, 1451, 1429, 1329, 1262, 1219, 1114, 990, 962, 908, 804, 752, 696, 666 cm^{-1}.

MS (EI): (*m/z*) 248 (M^+, 62), 247 (52), 233 (13), 179 (51), 178 (100), 176 (9), 81 (18), 71 (9), 69 (39).

1,2-Di-(4-fluorophenyl)ethene (12):



Compound **12** was prepared by same procedure as that of **9**.

Yield: 67% (0.415 g), white crystalline solid.

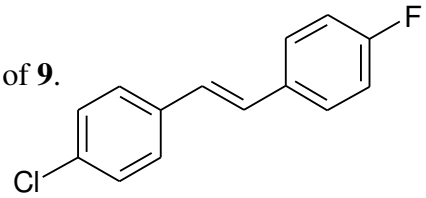
M.P. 128 - 130°C (Lit.[35b] 131 - 133°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.54 - 7.46 (m, 4H), 7.09 - 7.04 (m, 4H), 7.0 (s, 2H).

IR (KBr): υ 1895, 1597, 1500, 1414, 1330, 1295, 1234, 1108, 962, 836, 758, 691, 658 cm^{-1}.

MS (EI): (*m/z*) 216 (M^+, 82), 215 (100), 214 (41), 201 (17), 197 (14), 195 (26).

1-Chloro-4-((*E*)-4'-fluorostyryl)benzene (13):



Compound **13** was prepared by same procedure as that of **9**.

Yield: 89% (0.592 g), White crystalline solid.

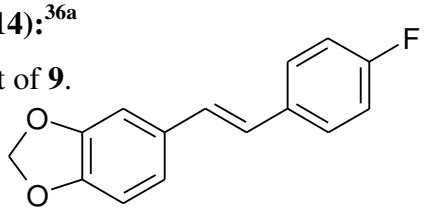
M.P. 134 - 136°C (Lit.[35c] 138 - 141°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.52 - 7.36 (m, 4H), 7.35 - 7.29 (m, 2H), 7.1 - 7.02 (m, 3H), 6.98 - 6.94 (d, *J* = 16 Hz, 1H).

IR (KBr): υ 3020, 1897, 1592, 1500, 1407, 1326, 1226, 1093, 1006, 965, 830, 680 cm^{-1}.

MS (EI): (*m/z*) 234 (16), 233 (M^+, 26), 232 (34), 231 (75), 197 (28), 196 (100), 194 (17), 177 (26), 176 (20), 98 (18), 85 (13), 75 (12).

5-[(*E*)-2-(4-Fluorophenyl)vinyl]benzo[1,3]dioxole (14):[36a]



Compound **14** was prepared by same procedure as that of **9**.

Yield: 50% (0.347 g), Off white solid.

M.P. 102 - 104°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.49 - 7.41 (m, 2H), 7.08 - 7.01 (m, 3H), 6.96 - 6.9 (m, 3H), 6.81 - 6.79 (d, *J* = 8 Hz, 1H), 5.98 (s, 2H).

IR (KBr): υ 3025, 2913, 1850, 1598, 1506, 1489, 1450, 1358, 1257, 1235, 1204, 1095, 1040, 966, 926, 829, 806, 766, 693 cm^{-1}.

MS (EI): (*m/z*) 243 (M+1, 21), 242 (M^+, 66), 241 (95), 224 (42), 223 (36), 184 (25), 183 (100), 182 (55), 164 (55), 91 (24).

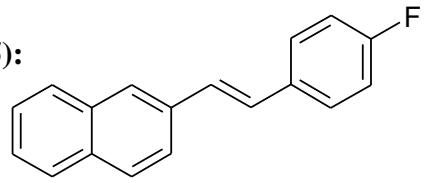
Path B: Synthesis of fluorinated stilbenes by one - pot Wittig - Heck reaction

General Procedure for the one - pot Wittig - Heck reaction:

trans-2-[2-(4-Fluorophenyl)vinyl]naphthalene (**15**):

In dry N_2 flushed two-necked r.b. flask a mixture of *p*-bromofluorobenzene (0.50 g, 2.857 mmol), 2-naphthaldehyde (0.67 g, 4.286 mmol), triphenylmethylphosphonium iodide (1.73 g, 4.286 mmol), palladium acetate (0.0032 g, 0.014 mmol) and **1a** (0.0055 mg, 0.017 mmol), TBAB (0.184 g, 0.571 mmol), and K_2CO_3 (1.591 g, 11.43 mmol) in dry N,N-dimethylacetamide (20 mL) was taken and kept under N_2 atmosphere. The reaction mixture heated to 140°C for 40h. The cooled mixture was then poured into water (25 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic layer was washed with water (2 x 20 mL), dried with anhydrous sodium sulfate, concentrated in vacuum and purified by column chromatography over silica gel and petroleum ether as eluent to give *trans*-2-[2-(4-fluorophenyl)vinyl]naphthalene **15** as white solid.

2-[(*E*)-2-(4-Fluoro-phenyl)-vinyl]-naphthalene (15):



Yield: 61% (0.428 g), White solid.

M.P. 148 - 150°C (Lit.[36b] 151 - 152°C).

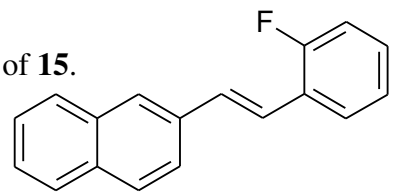
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.89 - 7.83 (m, 4H), 7.77 - 7.74 (dd, J_1 = 8.8, J_2 = 1.6 Hz, 1H), 7.6 - 7.46 (m, 4H), 7.22 (s, 2H), 7.12 - 7.07 (m, 2H).

IR (KBr): υ 3051, 3017, 2926, 2354, 1897, 1666, 1596, 1509, 1411, 1238, 1158, 1097, 966, 903, 855, 826, 740, 694, 641 cm^{-1}.

MS (EI): (*m/z*) 248 (M^+, 98), 247 (55), 246 (100), 245 (39), 229 (23).

2-[(*E*)-2-(2-Fluoro-phenyl)-vinyl]-naphthalene (16):

Compound **16** was prepared by same procedure as that of **15**.



Yield: 41% (0.29 g), White solid.

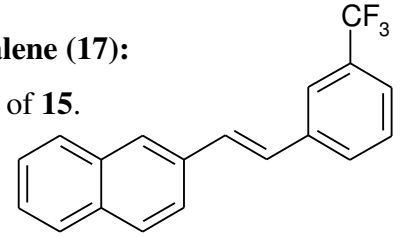
M.P. 138 - 140°C (Lit.[37a] 136 - 138°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.88 - 7.76 (m, which contains br s, doublet (J = 8 Hz) and doublet of triplet, J_1 = 8.8, J_2 = 1.6 Hz, 5H), 7.69 - 7.65 (dt, J_1 = 7.6, J_2 = 1.6 Hz, 1H), 7.49 - 7.44 (m, 2H), 7.39 - 7.36 (d, J = 12 Hz, 2H), 7.26 - 7.22 (m, 1H), 7.19 - 7.15 (dt, J_1 = 7.6, J_2 = 1.2 Hz, 1H), 7.12 - 7.07 (m, 1H).

IR (KBr): υ 3054, 2355, 1801, 1593, 1572, 1487, 1452, 1363, 1265, 1229, 1210, 1180, 1072, 1033, 965, 815, 750, 633 cm^{-1}.

MS (EI): (*m/z*) 248 (M^+, 95), 247 (58), 246 (100), 245 (35), 229 (26).

2-[(*E*)-2-(3-Trifluoromethyl-phenyl)-vinyl]-naphthalene (17):



Compound **17** was prepared by same procedure as that of **15**.

Yield: 77% (0.507 g), White crystalline solid.

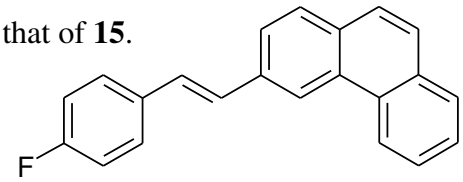
M.P. 116 - 118°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.91 - 7.88 (d, J = 12 Hz, 1H), 7.86 - 7.83 (m, 4H), 7.78 - 7.74 (m, 2H), 7.56 - 7.48 (m, 3H), 7.39 - 7.35 (d, J = 16 Hz, 1H), 7.29 - 7.25 (d, J = 16 Hz, 2H).

IR (KBr): υ 3048, 1815, 1607, 1574, 1486, 1451, 1429, 1339, 1262, 1219, 1114, 1075, 990, 962, 804, 752, 696, 665 cm^{-1}.

MS (EI): (*m/z*) 299 (M+1, 49), 298 (M^+, 72), 297 (100), 296 (33), 229 (46), 228 (69), 227 (43), 226 (23), 139 (18).

3-[(*E*)-2-(4-Fluoro-phenyl)-vinyl]-phenanthrene (18):



Compound **18** was prepared by same procedure as that of **15**.

Yield: 70% (0.506 g), White solid.

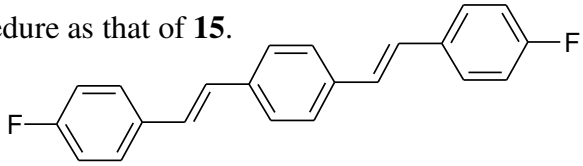
M.P. 130 - 132°C (Lit.[37b] 135 - 136°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.77 - 8.75 (d, J = 8 Hz, 1H), 8.74 (d, J = 0.8 Hz, 1H), 7.93 - 7.84 (m, which contains doublet, J = 8 Hz, 3H), 7.75 - 7.58 (m, 6H), 7.32 - 7.31 (d, J = 4 Hz, 2H), 7.15 - 7.11 (m, 2H).

MS (EI): (*m/z*) 299 (M+1, 18), 298 (M^+, 99), 297 (100), 296 (45), 294 (31), 282 (11), 276 (22), 148 (14), 97 (16), 71 (21).

1,4-Bis(4-fluorostyryl)benzene (19):[38a]

Compound **19** was prepared by same procedure as that of **15**.



Yield: 32% (0.215 g), Yellow solid.

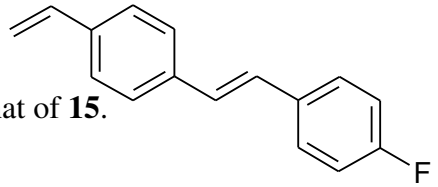
M.P. >250°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.5 (br s, 7H), 7.37 - 7.36 (m, 3H), 7.13 - 7.04 (m, 6H).

IR (KBr): υ 3055, 1897, 1594, 1498, 1414, 1335, 1291, 1234, 1108, 969, 856, 758, 691, 658 cm^{-1}.

MS (EI): (*m/z*) 319 (M+1, 15), 318 (M^+, 51), 317 (100), 300 (75), 299 (46), 282 (31), 220 (17), 202 (12), 196 (14), 178 (14).

(*E*)-1-(4-vinylstyryl)-4-fluorobenzene (20):[38b]



Compound **20** was prepared by same procedure as that of **15**.

Yield: 26% (0.22 g), White solid.

M.P. 162 - 164°C.

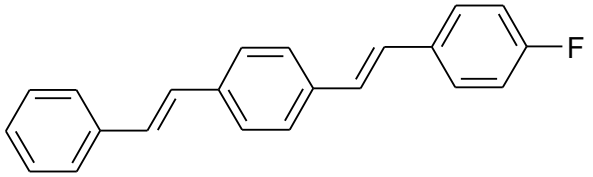
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.56 - 7.48 (m, 4H), 7.44 - 7.38 (m, 2H), 7.13 - 7.0 (m, which also contains doublet, J = 16.4 Hz, 4H), 6.78 - 6.71 (two d, J = 10.8 Hz, 1H), 5.82 - 5.77 (dd, J_1 = 17.6, J_2 = 0.8 Hz, 1H), 5.29 - 5.27 (dd, J_1 = 10.8, J_2 = 0.8 Hz, 1H).

IR (KBr): υ 3018, 1820, 1625, 1598, 1512, 1415, 1406, 1332, 1297, 1238, 1217, 1180, 1158, 1119, 1096, 993, 965, 907, 840, 785, 692 cm^{-1}.

MS (EI): (*m/z*) 225 (M+1, 13), 224 (M^+, 100), 223 (76), 206 (29), 196 (20), 195 (13), 178 (9).

1-((*E*)-4'-Fluorostyryl)-4-((*E*)-styryl)-benzene (21):[38c]

Compound **21** was prepared by same procedure as that of **15**.



Yield: 84% (0.138 g), Pale green solid.

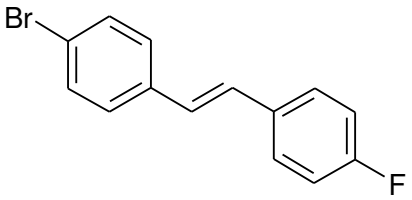
M.P. >250°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.74 - 7.67 (m, 8H), 7.47 - 7.43 (m, 2H), 7.38 - 7.26 (m, 7H).

IR (KBr): υ 3020, 2925, 2850, 1666, 1603, 1596, 1550, 1489, 1406, 1330, 1228, 1096, 1035, 985, 814, 795, 752 cm^{-1}.

MS (EI): (*m/z*) 301 (M+1, 19), 300 (M^+, 100), 299 (52), 282 (32), 281 (26), 202 (26), 178 (29), 77 (7).

1-Bromo-4-((*E*)-4'-fluorostyryl)-benzene (22):[38d]



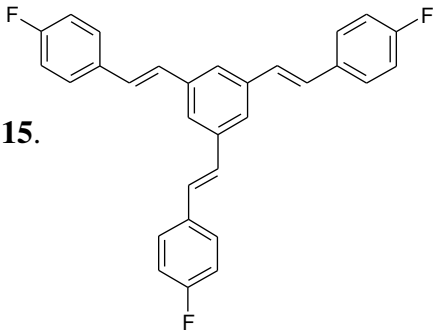
Yield: 21% (0.125 g), Pale yellow solid.

M.P. 118 - 120°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.88 - 7.85 (m, 4H), 7.75 (d, *J* = 8 Hz, 2H), 7.09 (d, *J* = 16 Hz, 1H), 7.08 (d, *J* = 8 Hz, 2H), 6.98 (d, *J* = 16 Hz, 1H).

MS (EI): (*m/z*) 278 (M+1, 24), 277 (M^+, 34), 276 (35), 197 (55), 196 (74), 177 (41), 176 (30), 135 (99), 71 (35).

1,3,5-Tris[(*E*)-2-(4-fluorophenyl)vinyl]-benzene (23):



Compound **23** was prepared by same procedure as that of **15**.

Yield: 35% (0.145 g), Yellow solid.

M.P. >250°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.59 - 7.52 (m, 9H), 7.22 - 7.16 (m, 3H), 7.13 - 7.06 (m, 9H).

IR (KBr): υ 3052, 1898, 1596, 1498, 1412, 1345, 1291, 1244, 1118, 969, 866, 758, 692 cm^{-1}.

MS (EI): (*m/z*) 439 (M+1, 17), 438 (M^+, 100), 437 (93), 436 (76), 314 (11), 313 (8), 220 (10), 109 (13).

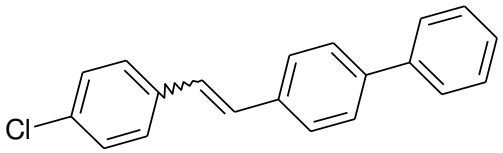
PART - II One - pot Wittig olefination - Suzuki coupling reaction

Representative procedure for the One - pot Wittig - Suzuki reaction:

In a dry N_2 – flushed two-necked round-bottom flask a mixture of 4-Chlorobenzaldehyde (0.2 g, 1.42 mmol), (4-bromobenzyl)triphenylphosphonium bromide **24** (0.729 g, 1.42 mmol) and dry potassium carbonate (0.59 g, 4.27 mmol) in dry N,N-dimethylacetamide (5 mL) was placed and kept under N_2 atmosphere. The reaction was heated to 130°C for 6 h and then phenylboronic acid (0.208 g, 1.71

mmol), potassium carbonate (0.393 g, 2.84 mmol), TBAB (0.092 g, 0.28 mmol), palladium acetate (3.19 mg, 0.014 mmol) and **1c** (4.71 mg, 0.017mmol) were added and again heated to 130°C for 24 h. The reaction mixture was added to 20 mL of water and extracted with ethyl acetate (3 x 25mL). The combined organic layer was washed with water (2 x 20mL), dried with anhydrous sodium sulfate and concentrated under vacuum. The residue was purified by flash chromatography on silica gel to give the desired product 4-(chlorostyryl)biphenyl (**28**) [39a]
(0.33 g, 80%).

White crystalline solid, *Z* : *E* = 57 : 43.



M.P. 100 - 102°C (*Z* isomer),

M.P. 242 - 244°C (*E* isomer).

^{1}H-NMR of *cis* isomer ($CDCl_3$, 400 MHz): δ 7.63 - 7.6 (m, 2H), 7.53 - 7.44 (m, 4H), 7.39 - 7.32 (m, 3H), 7.27 - 7.22 (m, 4H), 6.69 - 6.66 (d, 1H, *J* = 12 Hz, olefinic proton), 6.6 - 6.57 (d, 1H, *J* = 12.4 Hz, olefinic proton).

^{1}H-NMR of *trans* isomer ($CDCl_3$, 400 MHz): δ 7.66 - 7.59 (m, 6H), 7.49 - 7.46 (m, 4H), 7.4 - 7.35 (m, 3H), 7.13 (s, 2H, olefinic protons).

^{13}C-NMR of *trans* isomer ($CDCl_3$, 100 MHz): δ 140.6, 140.0, 135.8, 135.7, 132.8, 130.5, 130.3, 129.3, 129.1, 128.8, 128.5, 127.4, 126.9, 126.9.

IR (KBr): υ 3080, 3017, 2924, 1745, 1635, 1601, 1580, 1555, 1523, 1489, 1449, 1408, 1343, 1092, 966, 835, 761, 730, 722, 687 cm^{-1}.

MS (EI): (*m/z*) 292 (32), 291 (22), 290 (M^+, 100), 255 (16), 254 (25), 178 (13), 152 (5), 126 (9).

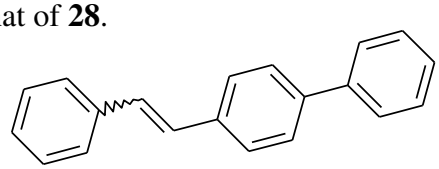
Anal. Calcd. For $C_{20}H_{15}Cl$: C, 81.35; H, 5.12. Found: C, 81.29; H, 4.62%.

4-Styryl-biphenyl (27):

Compound **27** was prepared by same procedure as that of **28**.

Yield: 56% (0.34 g), White crystalline solid.

Z : *E* = 55 : 45.



M.P. 64 - 66°C (*Z* isomer), 216 - 218°C (*E* isomer) (Lit.[39b] 209°C).

^{1}H-NMR of *cis* isomer ($CDCl_3$, 400 MHz): δ 7.63 - 7.61 (m, 2H), 7.51 - 7.44 (m, 4H), 7.38 - 7.33 (m, 5H), 7.31 - 7.24 (m, 3H), 6.66 (s, 2H, olefinic protons).

^{1}H-NMR of *trans* isomer ($CDCl_3$, 400 MHz): δ 7.66 - 7.63 (m, 6H), 7.58 - 7.56 (m, 2H), 7.49 - 7.46 (m, 2H), 7.42 - 7.35 (m, 3H), 7.32 - 7.29 (m, 1H), 7.18 (s, 2H, olefinic protons).

IR (KBr): υ 3078, 2934, 1748, 1645, 1607, 1588, 1529, 1489, 1444, 1418, 1349, 1092, 968, 835, 766, 740, 726, 6997 cm^{-1}.

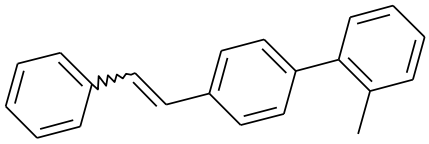
MS (EI): (*m/z*) 257 (M+1, 22), 256 (M^+, 100), 255 (25), 239 (53), 178 (28), 165 (12), 152 (6), 98 (11).

2-Methyl-4'-styryl-biphenyl (29):

Compound **29** was prepared by same procedure as that of **28**.

Yield: 63% (0.42 g), White solid.

Z : *E* = 59 : 41, **M.P.** 74 - 76°C.



^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.62 - 7.57 (m, 4H), 7.43 - 7.36 (m, 4H), 7.32 - 7.28 (m, 5H), 7.2 (s, 2H), 2.35 (s, 3H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 141.6, 141.5, 141.4, 140.8, 137.4, 135.9, 135.7, 135.4, 135.3, 130.5, 130.4, 130.3, 130.0, 129.8, 129.6, 129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 127.7, 127.4, 127.3, 127.2, 126.6, 126.3, 125.9, 125.8, 20.6, 20.6 (for mixture of *cis* and *trans* isomer).

IR (KBr): υ 3054, 3020, 2951, 2922, 1950, 1915, 1598, 1574, 1510, 1481, 1447, 1409, 1379, 1326, 1305, 966, 762, 729, 692 cm^{-1}.

MS (EI): (*m/z*) 271 (M+1, 21), 270 (M+, 100), 255 (12), 179 (12), 178 (14), 152 (3), 91 (3).

Anal. Calcd. For $C_{21}H_{18}$: C, 93.29; H, 6.73. Found: C, 93.39; H, 6.79%.

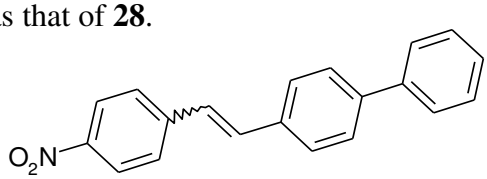
4-[2-(4-Nitrophenyl)vinyl]biphenyl (30):

Compound **30** was prepared by same procedure as that of **28**.

Yield: 77% (0.307 g),Yellow solid.

Z : *E* = 9 : 91.

M.P. 212 - 214°C (Lit.[40a] 216 - 218°C).



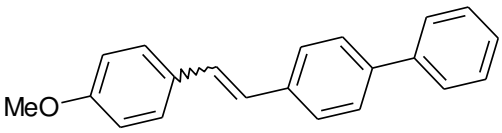
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 8.27 - 8.12 (m, 2H), 7.69 - 7.38 (m, 11H), 7.36 - 6.65 (four d, *J* = 16.4 Hz - *trans* olefinic proton, *J* = 12.4 Hz - *cis* olefinic proton, 2H).

MS (EI): (*m/z*) 302 (M+1, 21), 301 (M^+, 100), 254 (17), 253 (19), 252 (25), 239 (26), 226 (6), 178 (11), 152 (7).

4-[2-(4-Methoxyphenyl)vinyl]biphenyl (31):

Compound **31** was prepared by same procedure as that of **28**.

Yield: 64% (0.3 g), White crystalline solid.



Z : *E* = 55 : 45.

M.P. 234 - 236°C (Lit.[40b] 236 - 236.5°C).

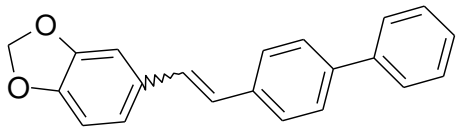
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.64 - 7.27 (m, 11H which contains olefinic proton of *trans* isomer), 6.82 - 6.68 (m, 2H), 6.61 - 6.58 (d, *J* = 12.4 Hz, olefinic proton of *cis* isomer, 1H), 6.57 - 6.54 (d, *J* = 12 Hz, olefinic proton of *cis* isomer, 1H), 3.82 - 3.81 (two s, -OMe of *cis* and *trans* isomer, 3H).

MS (EI): (*m/z*) 287 (M+1, 22), 286 (M^+, 42), 285 (100), 255 (9), 252 (16), 240 (10), 239 (28), 215 (11), 164 (12).

5-(2-Biphenyl-4-yl-vinyl)benzo[1,3]dioxole (32):

Compound **32** was prepared by same procedure as that of **28**.

Yield: 73% (0.29 g), White solid.



Z : *E* = 55 : 45.

M.P. 176 - 178°C (Lit.[41a] 188 - 189°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.66 - 7.35 (m, 9H), 7.12 - 6.75 (m, 4H, which contains olefinic protons of *trans* isomer), 6.55 (s, 1H, olefinic protons of *cis* isomer), 6.01 - 5.95 (two s, -CH_2- of *cis* & *trans* isomer, 2H).

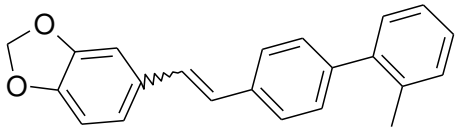
IR (KBr): υ 3028, 2962, 1929, 1630, 1605, 1513, 1488, 1444, 1359, 1311, 1265, 1108, 1041, 968, 944, 857, 735 cm^{-1}.

MS (EI): (*m/z*) 301 (M+1, 22), 300 (M^+, 100), 299 (10), 241 (23), 239 (22), 165 (11), 152 (3).

5-[2-(2'-Methylbiphenyl-4-yl)vinyl]benzo[1,3]dioxole (33):

Compound **33** was prepared by same procedure as that of **28**.

Yield: 67% (0.28 g), White crystalline solid.



Z : *E* = 56 : 44, **M.P.** 94 - 96°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.63 - 6.98 (m, 10H), 6.85 - 6.69 (m, 1H), 6.56 and 6.55 (two d, *J* = 12.4 Hz, 2H), 6.01 and 5.96 (two s, 2H, -CH_2- of *cis* and *trans* isomer), 2.33 and 2.32 (two s, 3H, -CH_3 of *cis* and *trans* isomer).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 148.2, 147.4, 147.3, 146.7, 141.6, 141.5, 141.0, 140.7, 135.9, 135.7, 135.4, 135.3, 131.9, 131.3, 130.4, 130.4, 129.9, 129.8, 129.7, 129.6, 129.5, 129.1, 128.9, 128.6, 128.5, 128.4, 127.3, 127.2, 126.7, 126.3, 126.0, 125.9, 125.8, 122.9, 121.5, 108.9, 108.5, 108.3, 105.6, 101.2, 100.9, 29.8, 20.6 (for mixture of *cis* and *trans* isomer).

IR (KBr): υ 3018, 2952, 1926, 1630, 1600, 1503, 1487, 1444, 1356, 1313, 1260, 1100, 1042, 968, 941, 851, 735, 612 cm^{-1}.

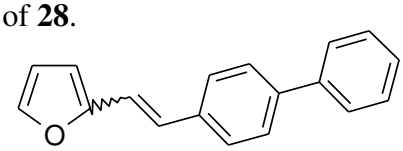
MS (EI): (*m/z*) 315 (M+1, 24), 314 (M^+, 100), 239 (15), 165 (12).

Anal. Calcd. For $C_{22}H_{18}O_2 \cdot 1/4H_2O$: C, 82.86; H, 5.69. Found: C, 83.02; H, 5.3%.

2-(2-Biphenyl-4-ylvinyl)furan (34):

Compound **34** was prepared by same procedure as that of **28**.

Yield: 55% (0.28 g), White solid.



M.P. 134 - 136°C.

Z : *E* = 38 : 62 (tentatively established by ^{1}H-NMR compound was unstable).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.67 - 7.36 (m, 10H), 7.10 and 6.97 (two d, *J* = 16 Hz, 2H), 6.54 - 6.36 (m, 2H).

^{13}C-NMR ($CDCl_3$, 100 MHz): δ 153.3, 142.2, 140.7, 140.3, 136.1, 129.2, 128.8, 127.4, 127.3, 127.0, 126.9, 126.8, 126.6, 116.6, 111.7, 108.8 (for mixture of *cis* and *trans* isomer).

IR (KBr): υ 3028, 2922, 1951, 1776, 1749, 1698, 1599, 1556, 1485, 1408, 1326, 1257, 963, 735, 693 cm^{-1}.

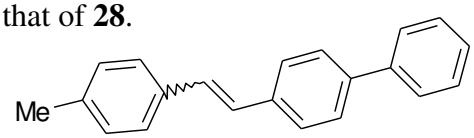
MS (EI): (*m/z*) 247 (M+1, 19), 246 (M^+, 100), 245 (16), 217 (30), 202 (22), 169 (4), 152 (3).

Anal. Calcd. For $C_{18}H_{14}O \cdot 1/4H_2O$: C, 86.2; H, 5.63. Found: C, 86.3; H, 4.95%.

4-[2-(4-Methylphenyl)vinyl]biphenyl (35):

Compound **35** was prepared by same procedure as that of **28**.

Yield: 77% (0.52 g), White crystalline solid.



Z : *E* = 55 : 45, **M.P.** 214 - 216°C (Lit.[41b] 219°C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.68 - 7.62 (m, 6H), 7.48 - 7.36 (m, 5H), 7.22 - 6.58 (two d, *J* = 12.4 Hz, merged with multiplet, which contains olefinic proton of *trans* isomer, 4H), 2.4 - 2.36 (two s, 3H, -CH_3 of *cis* & *trans* isomer).

IR (KBr): υ 3064, 3025, 2959, 2921, 1957, 1925, 1591, 1578, 1504, 1482, 1449, 1411, 1383, 1326, 1309, 967, 762, 724, 692 cm^{-1}.

MS (EI): (*m/z*) 271 (M+1, 7), 270 (M^+, 100), 255 (10), 254 (12), 253 (10), 239 (11), 178 (9).

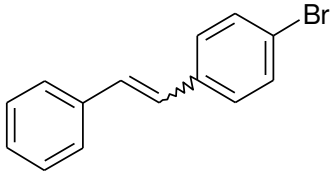
1-Bromo-4-styryl-benzene (25):

To an oven-dried two-necked round-bottom flask, equipped with a stirrer bar and nitrogen balloon was charged benzaldehyde (0.2 g, 1.88 mmol), potassium carbonate (0.787 g, 5.65 mmol) and (4-bromobenzyl)triphenylphosphonium bromide (0.965 g, 1.88 mmol) in DMA (10 mL). The reaction mixture was heated at 130^{o}C for 6 h. Then the reaction mixture was quenched with water and extracted with ethyl acetate (3 x 25 mL). The combined organic phase was washed with water and dried over anhydrous sodium sulfate. Solvent was removed under vacuum and the crude product was purified by column chromatography on silica gel to yield 4-bromostilbene **25**.

Yield: 72% (0.352 g), White crystalline solid,

Z : *E* = 48 : 52.

M.P. 132 - 134^{o}C (Lit.[41c] 139^{o}C).



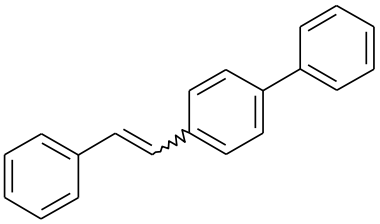
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.55 - 7.49 (m, 2H), 7.4 - 7.23 (m, 6H), 7.15 - 7.04 (m, 2H, which contains doublet of *trans* olefinic proton, *J* = 16.4 Hz), 6.67 - 6.52 (d, *J* = 12 Hz, 1H, cis olefinic proton).

IR (KBr): υ 3080, 3020, 1579, 1491, 1447, 1398, 1328, 1300, 1215, 1184, 1073, 1005, 967, 863, 813, 753, 690 cm^{-1}.

4-Styryl-biphenyl (36):

To an oven-dried two-necked round-bottom flask, equipped with a stirrer bar and nitrogen balloon was charged 4-bromostilbene (0.33 g, 1.27 mmol), potassium carbonate (0.352 g, 2.55 mmol), palladium acetate (2.86 mg, 0.0127 mmol), **1c** (4.24 mg, 0.0153 mmol) and TBAB (0.082 g, 0.255 mmol) in DMA (10 mL). To this reaction mixture phenyl boronic acid (0.186 g, 1.53 mmol) was added. The reaction mixture was heated at 130^{o}C for 24 h. Then the reaction mixture was quenched with

water and extracted with ethyl acetate (3 x 25 mL). The combined organic phase was washed with water and dried over anhydrous sodium sulfate. Solvent was removed under vacuum and the crude product was purified by column chromatography on silica gel to afford 4-styryl biphenyl **36**.



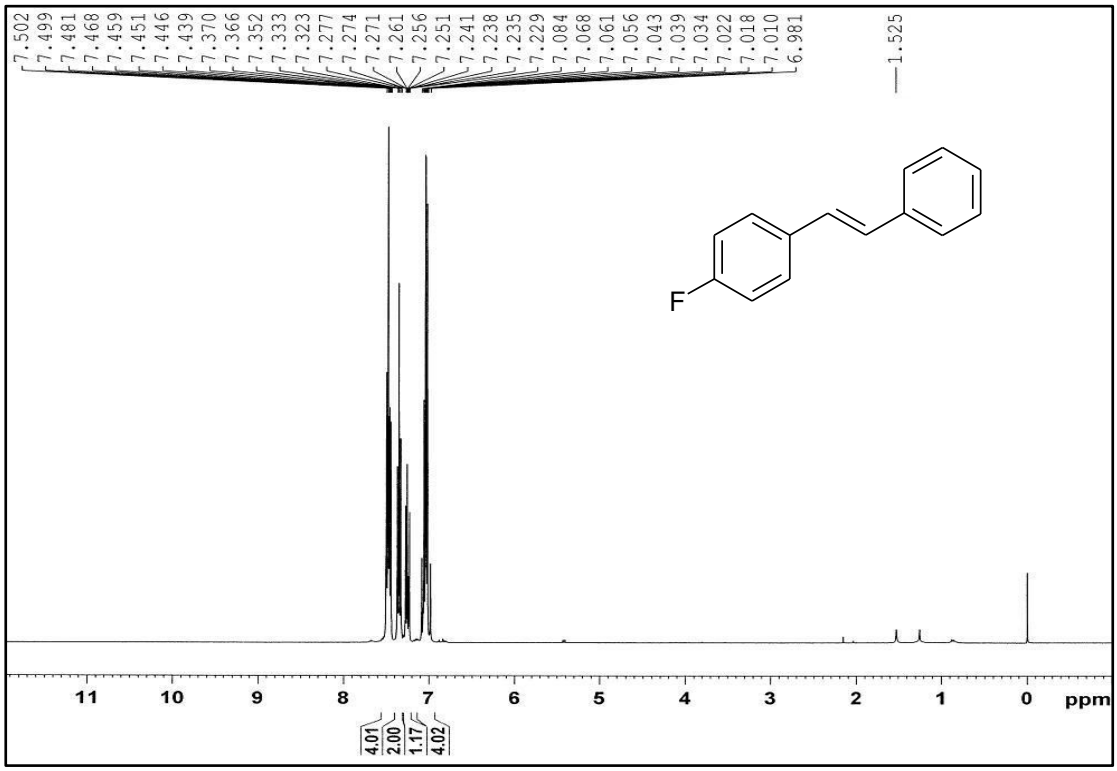
Yield: 67% (0.217 g), White crystalline solid,

Z : *E* = 50 : 50.

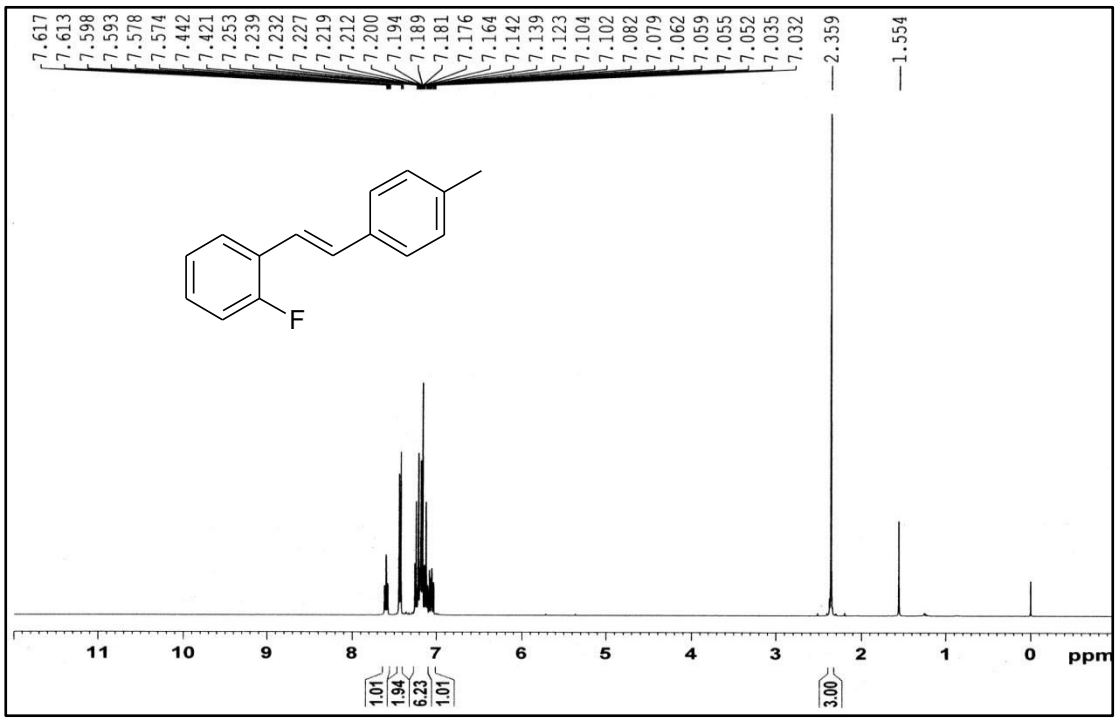
M.P. 198 - 200^{o}C (Lit.[39b] 209^{o}C).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.68 - 7.57 (m, 5H), 7.52 - 7.27 (m, 9H), 7.2 and 6.67 (two s, olefinic protons of *cis* and *trans* isomer, 2H).

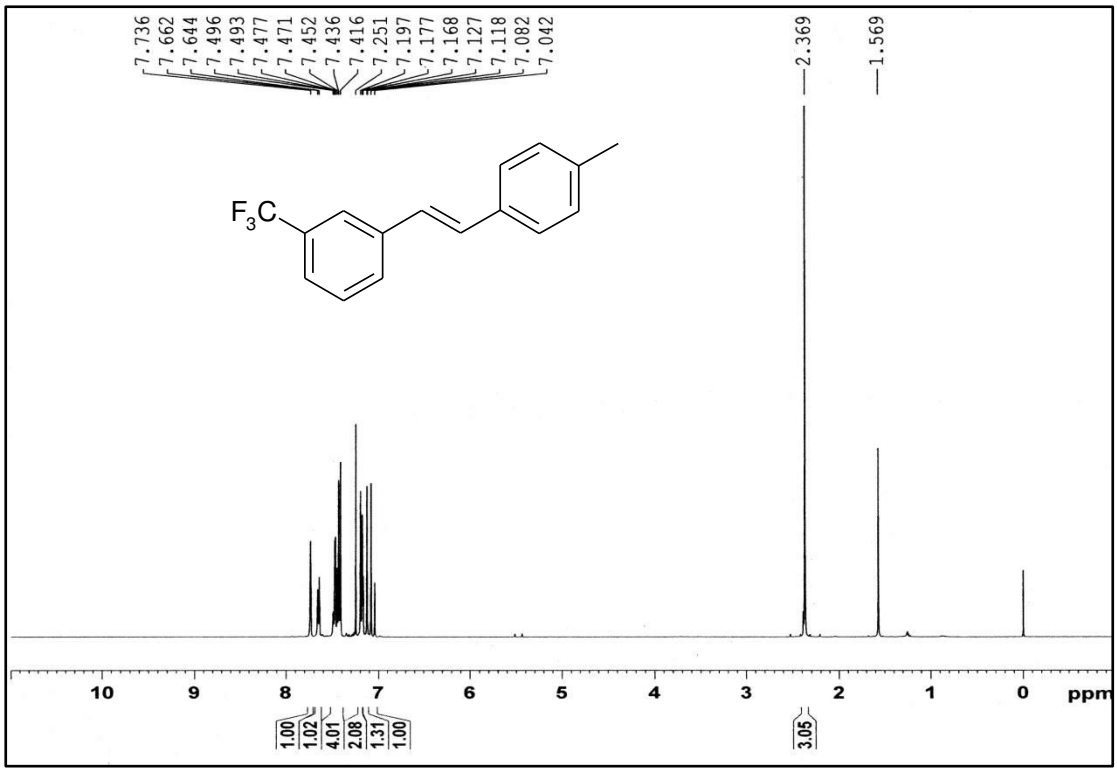
Spectral Data



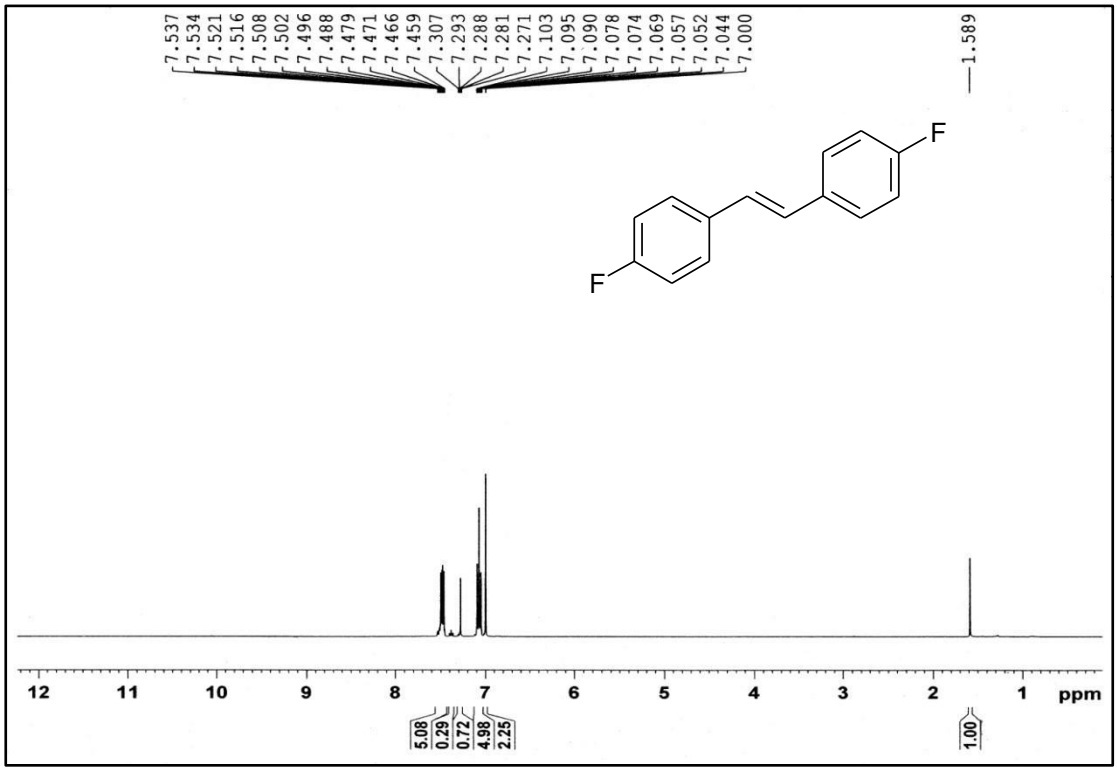
^{1}H-NMR Spectra of Compound 4 (400 MHz, $CDCl_3$)



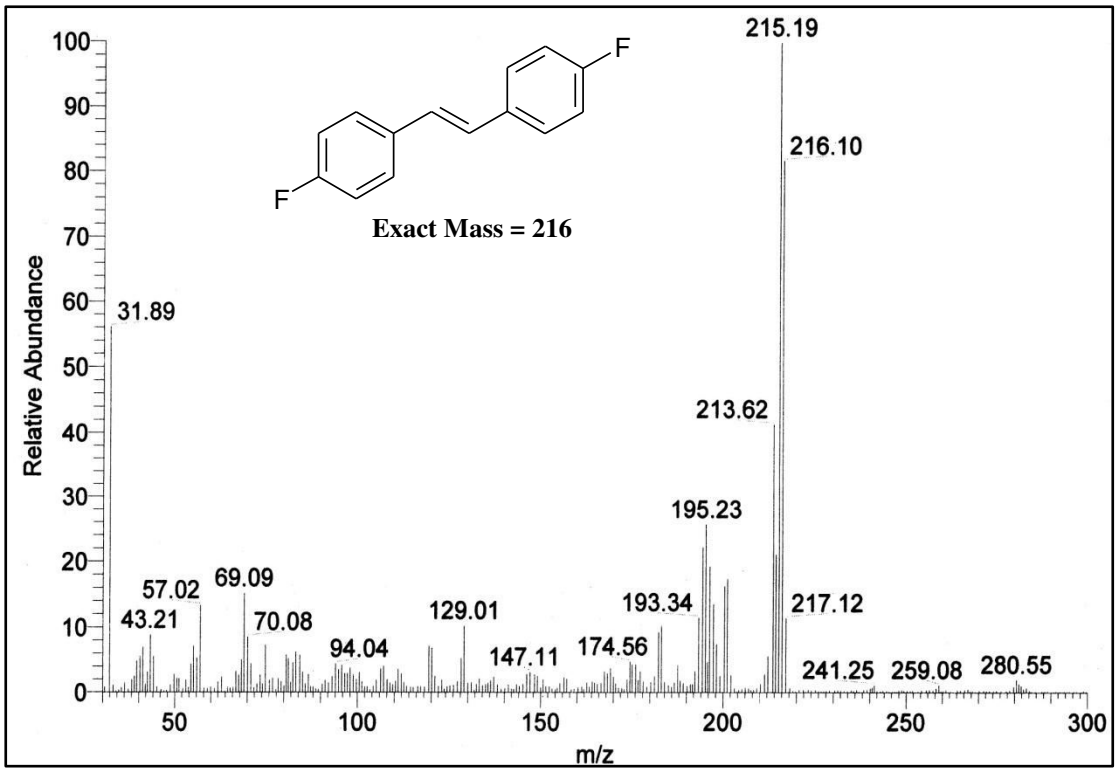
^{1}H-NMR Spectra of Compound 7 (400 MHz, $CDCl_3$)



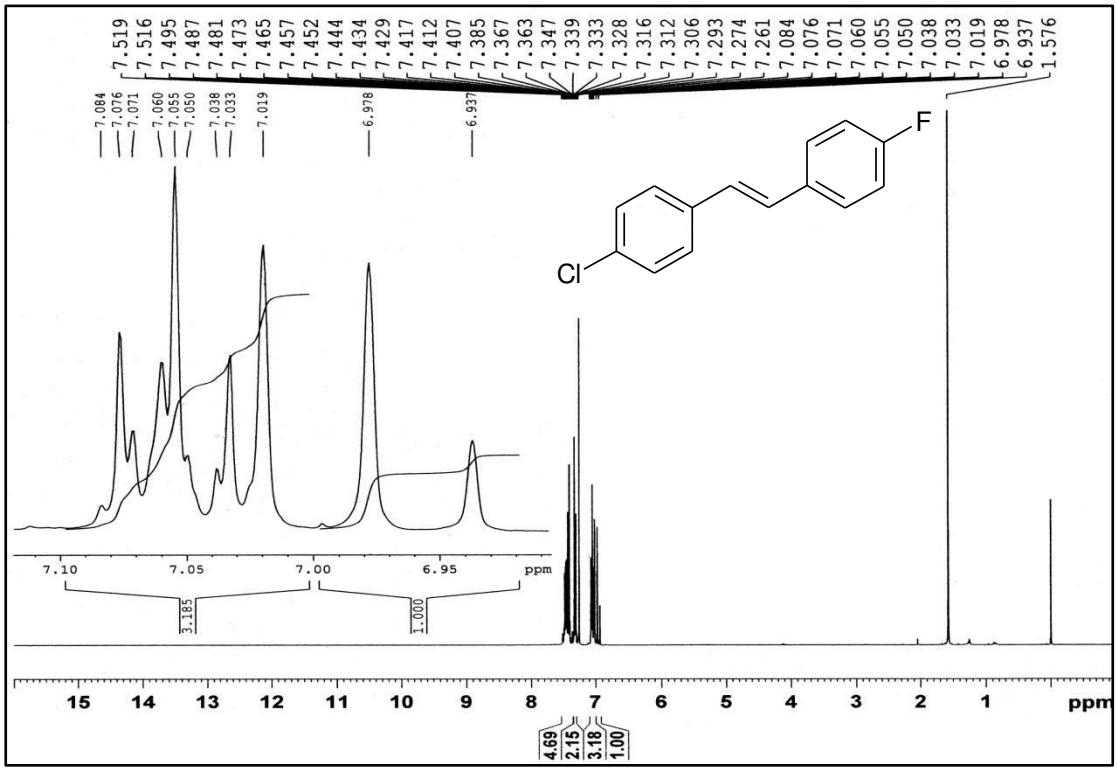
^{1}H-NMR Spectra of Compound 9 (400 MHz, $CDCl_3$)



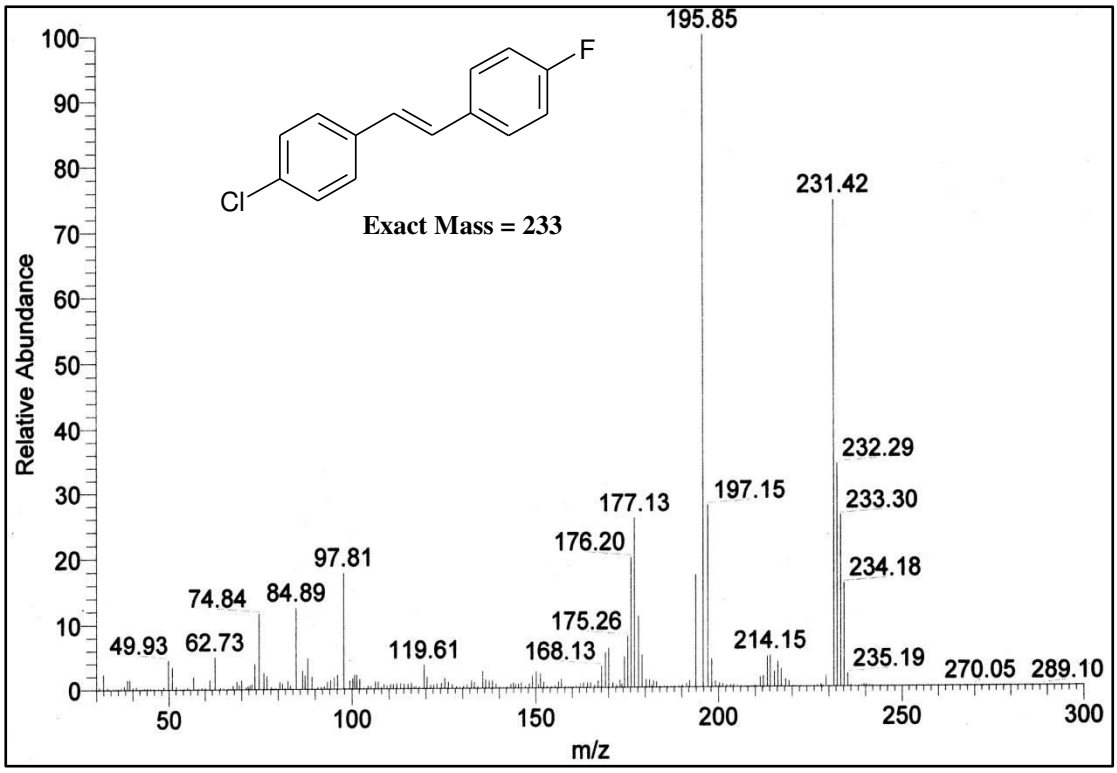
^{1}H-NMR Spectra of Compound 12 (400 MHz, $CDCl_3$)



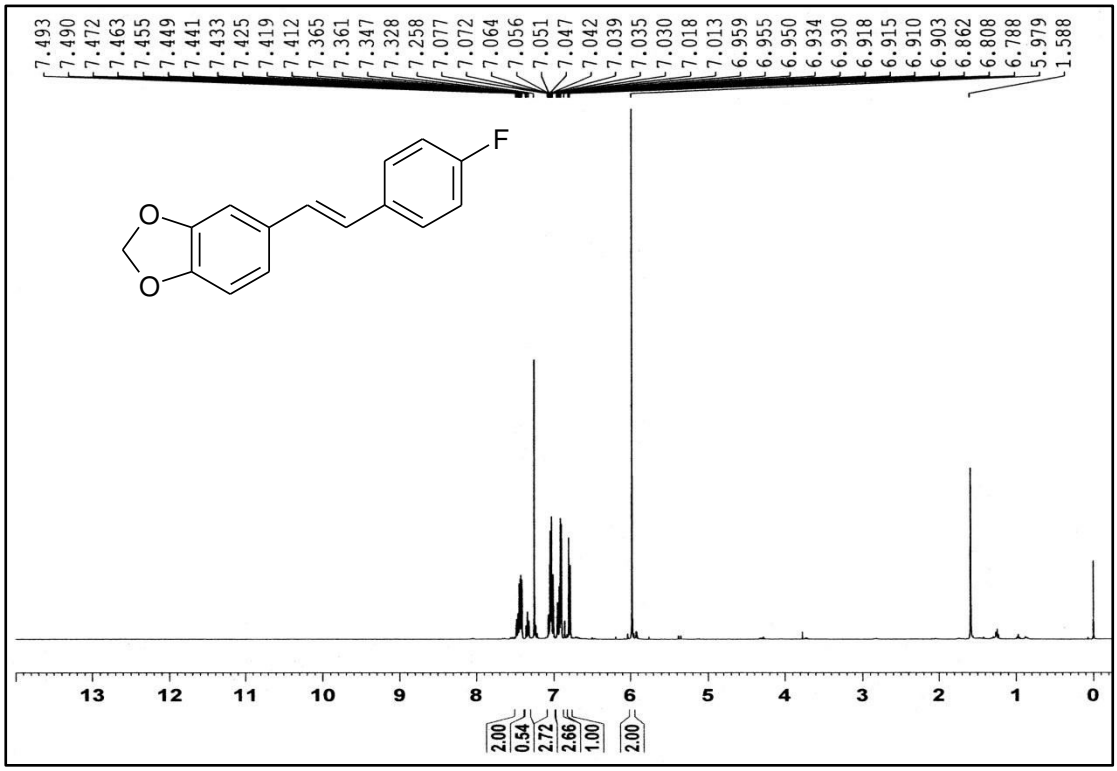
EI-Mass Spectra of Compound 12



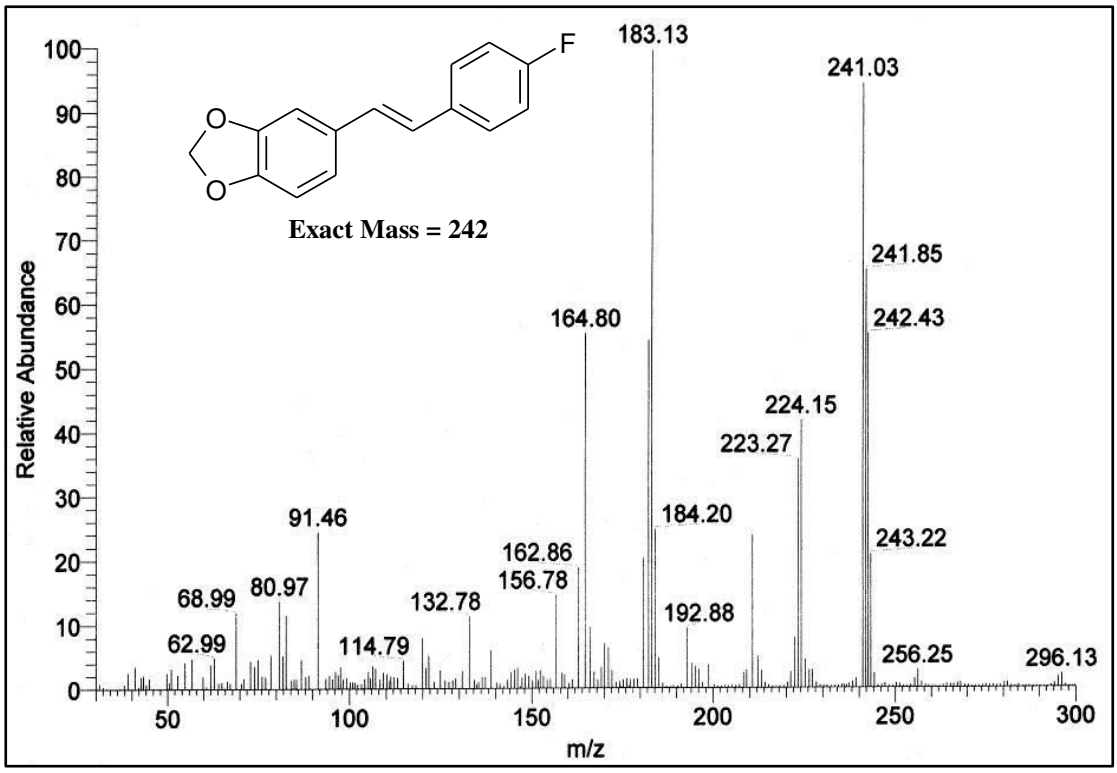
^{1}H-NMR Spectra of Compound 13 (400 MHz, $CDCl_3$)



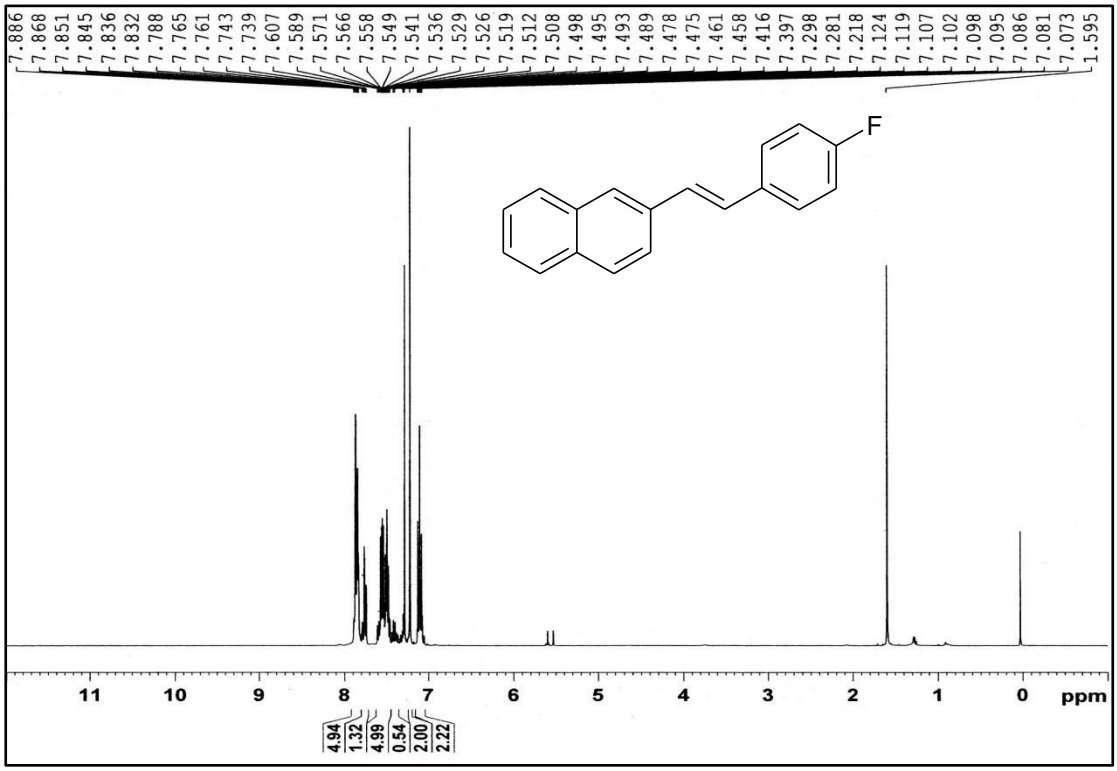
EI-Mass Spectra of Compound 13



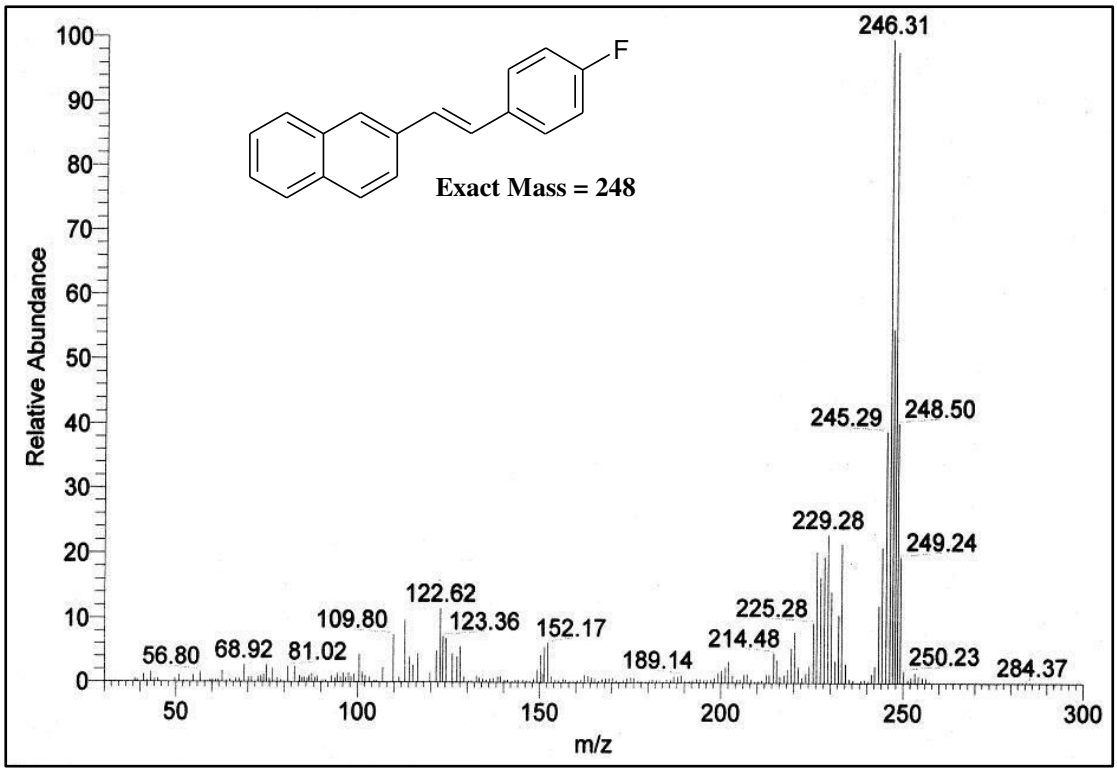
^{1}H-NMR Spectra of Compound 14 (400 MHz, $CDCl_3$)



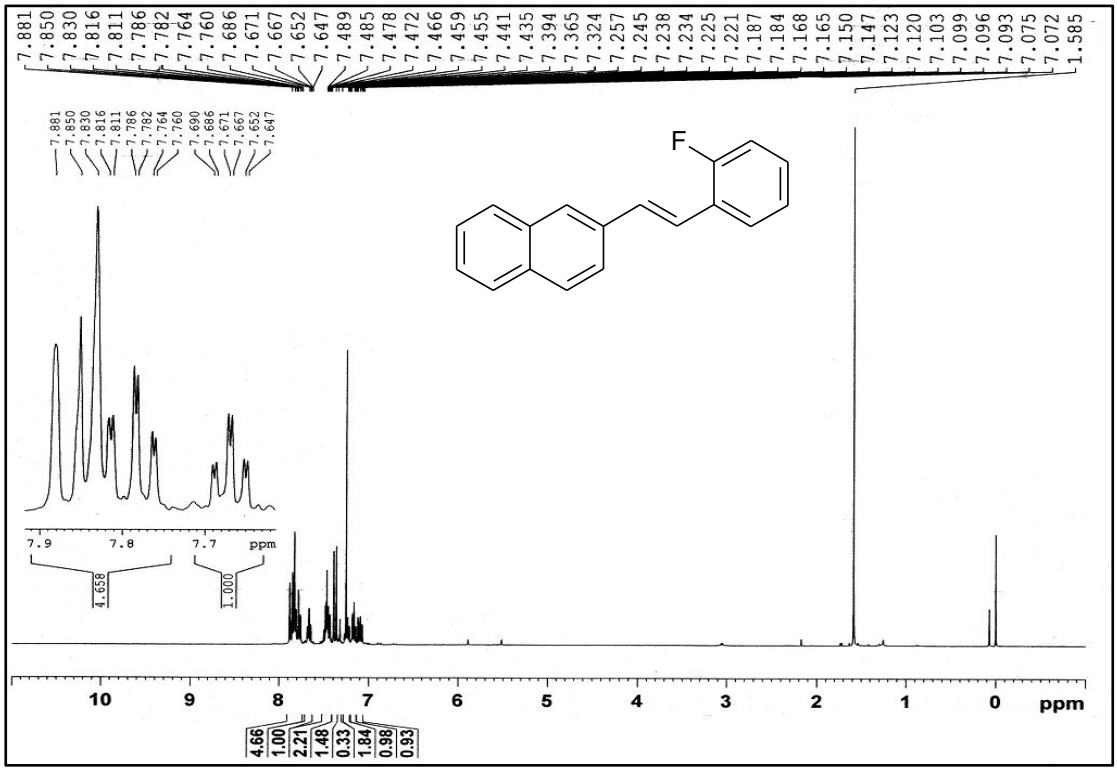
EI-Mass Spectra of Compound 14



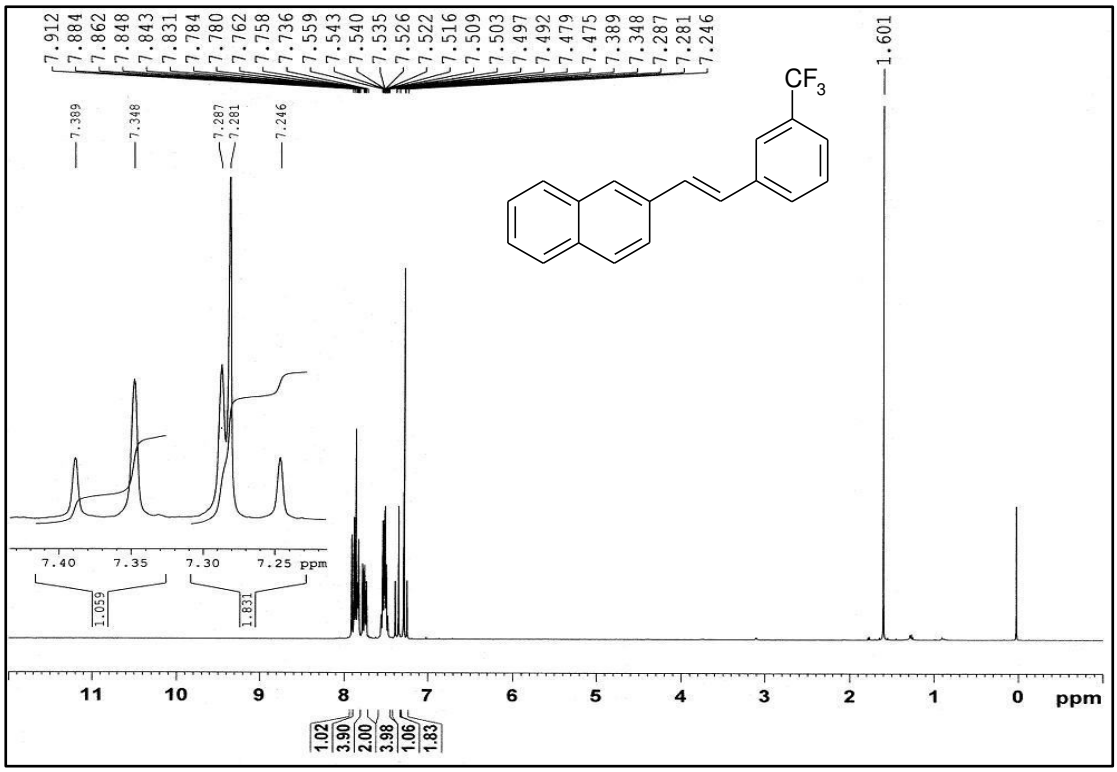
^{1}H-NMR Spectra of Compound 15 (400 MHz, $CDCl_3$)



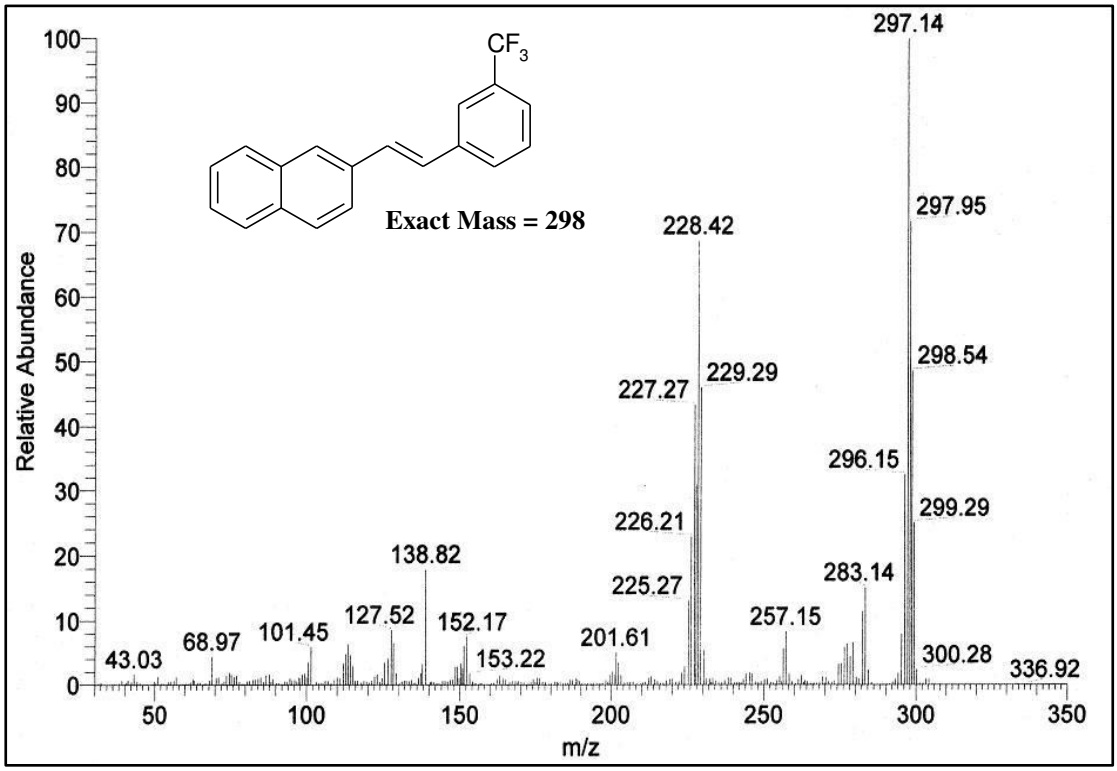
EI-Mass Spectra of Compound 15



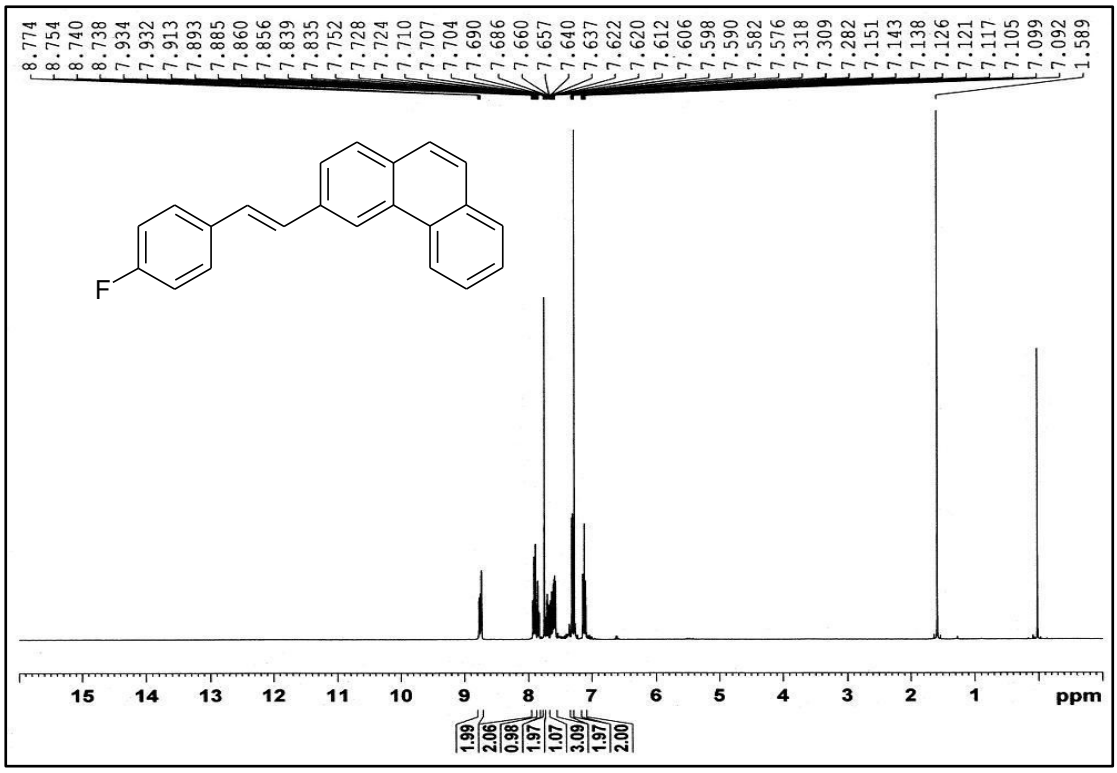
^{1}H-NMR Spectra of Compound 16 (400 MHz, $CDCl_3$)



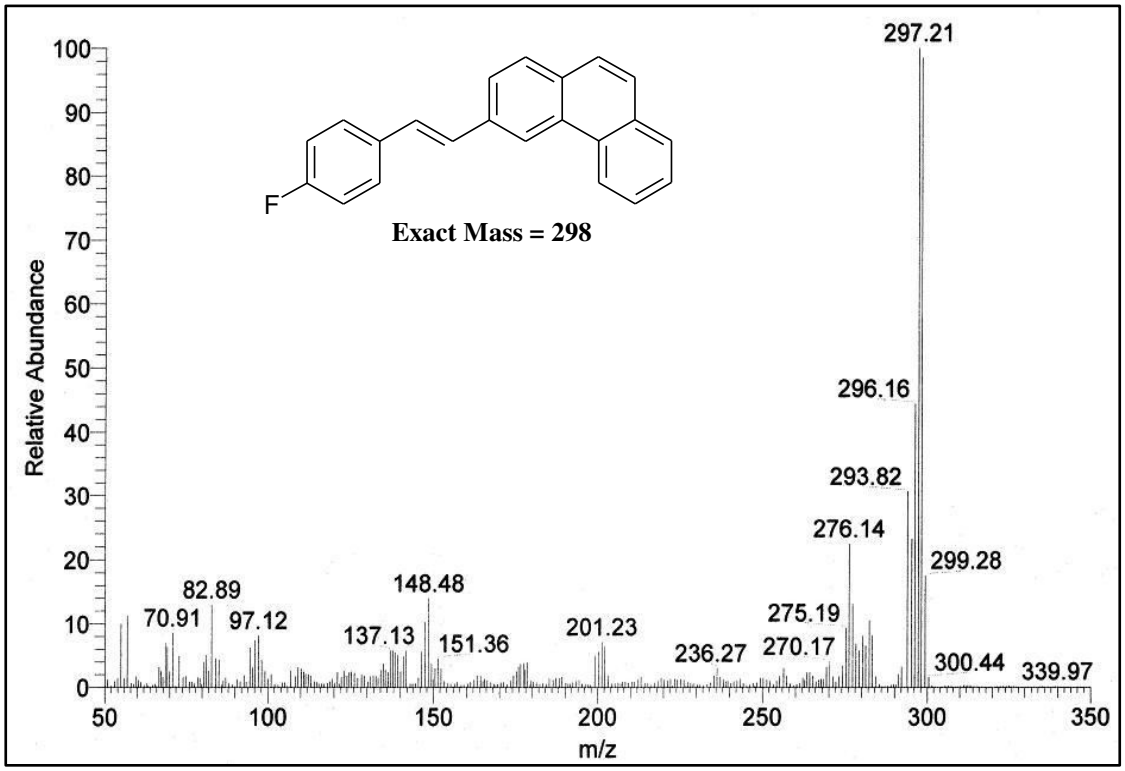
^{1}H-NMR Spectra of Compound 17 (400 MHz, $CDCl_3$)



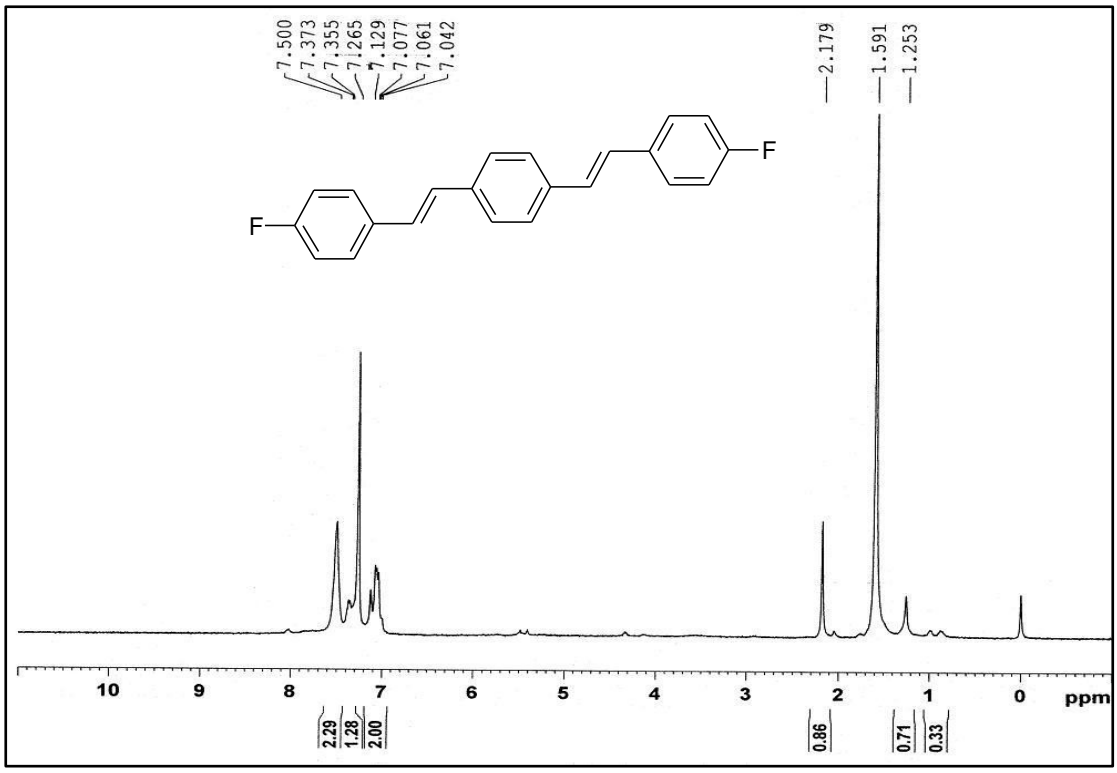
EI-Mass Spectra of Compound 17



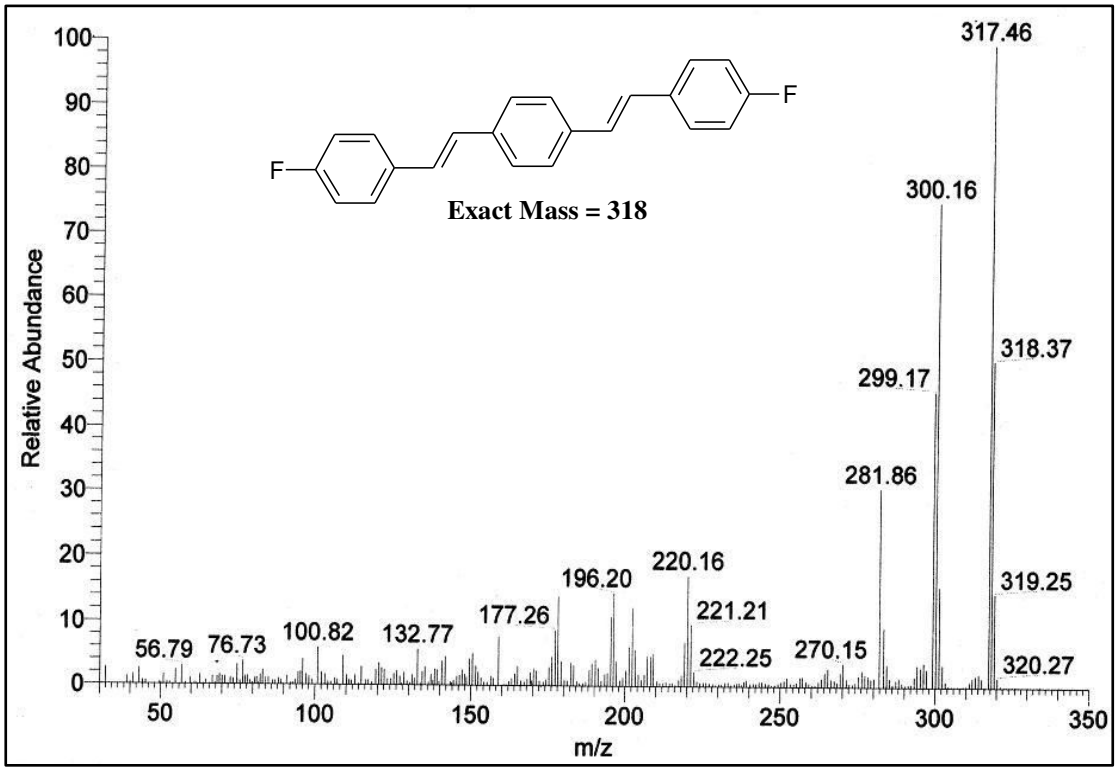
^{1}H-NMR Spectra of Compound 18 (400 MHz, $CDCl_3$)



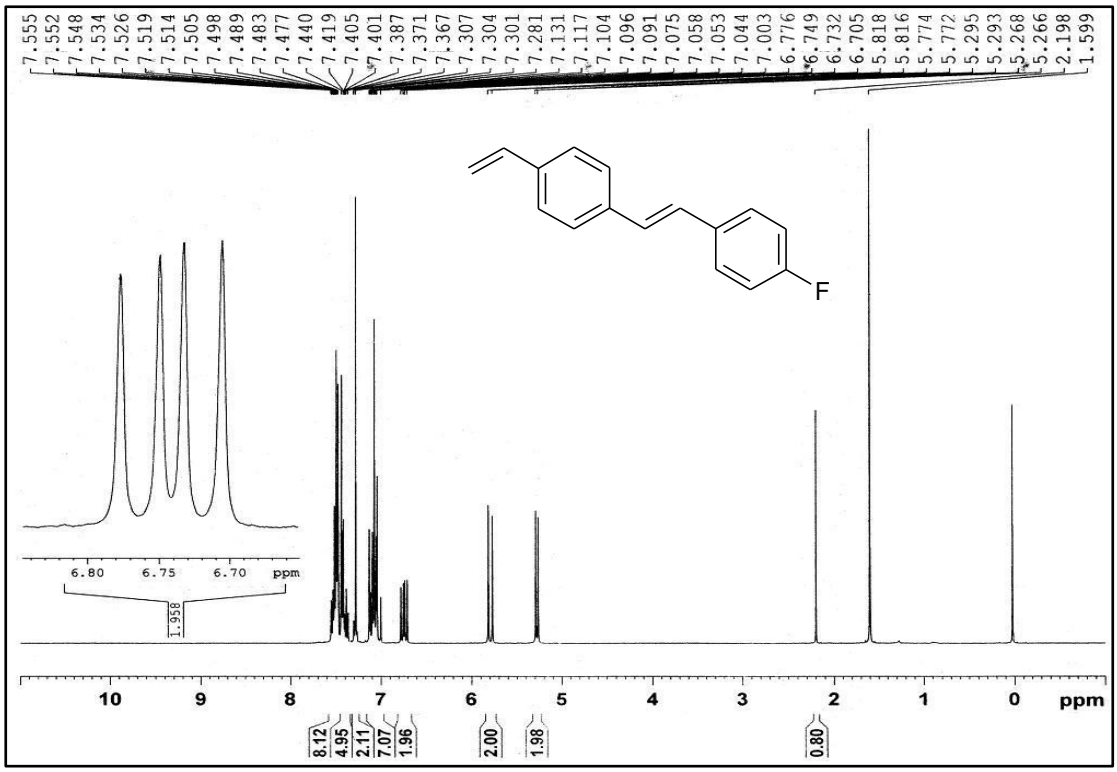
EI-Mass Spectra of Compound 18



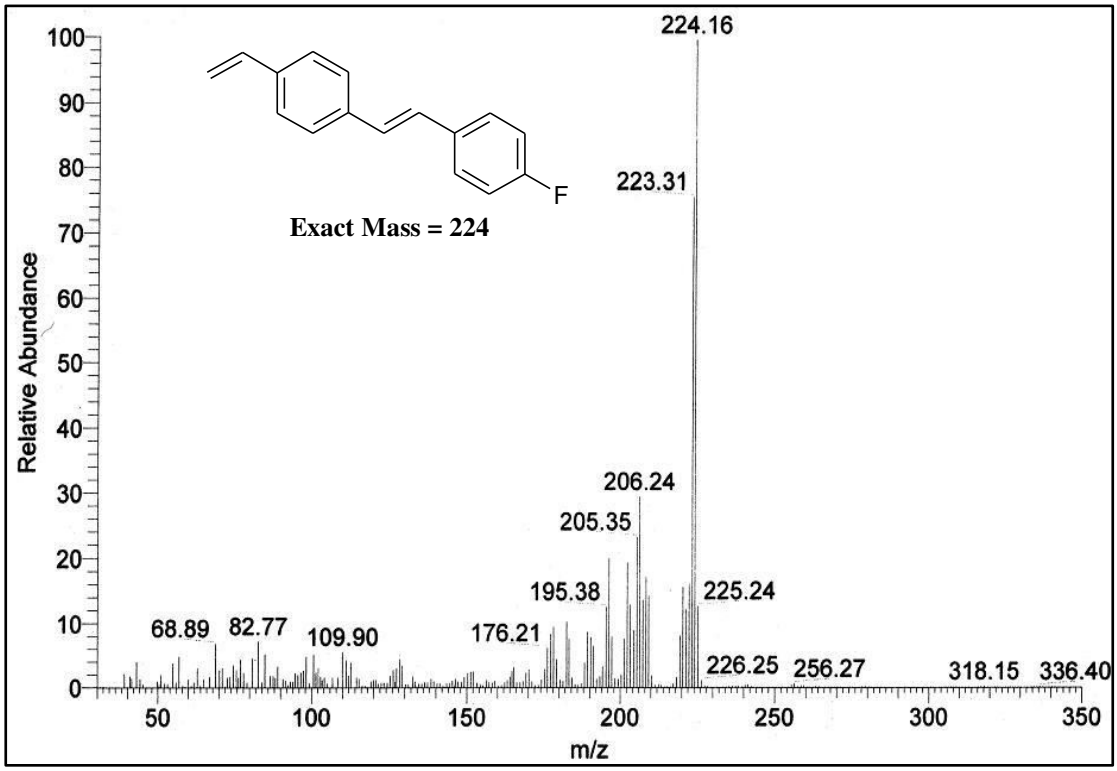
^{1}H-NMR Spectra of Compound 19 (400 MHz, $CDCl_3$)



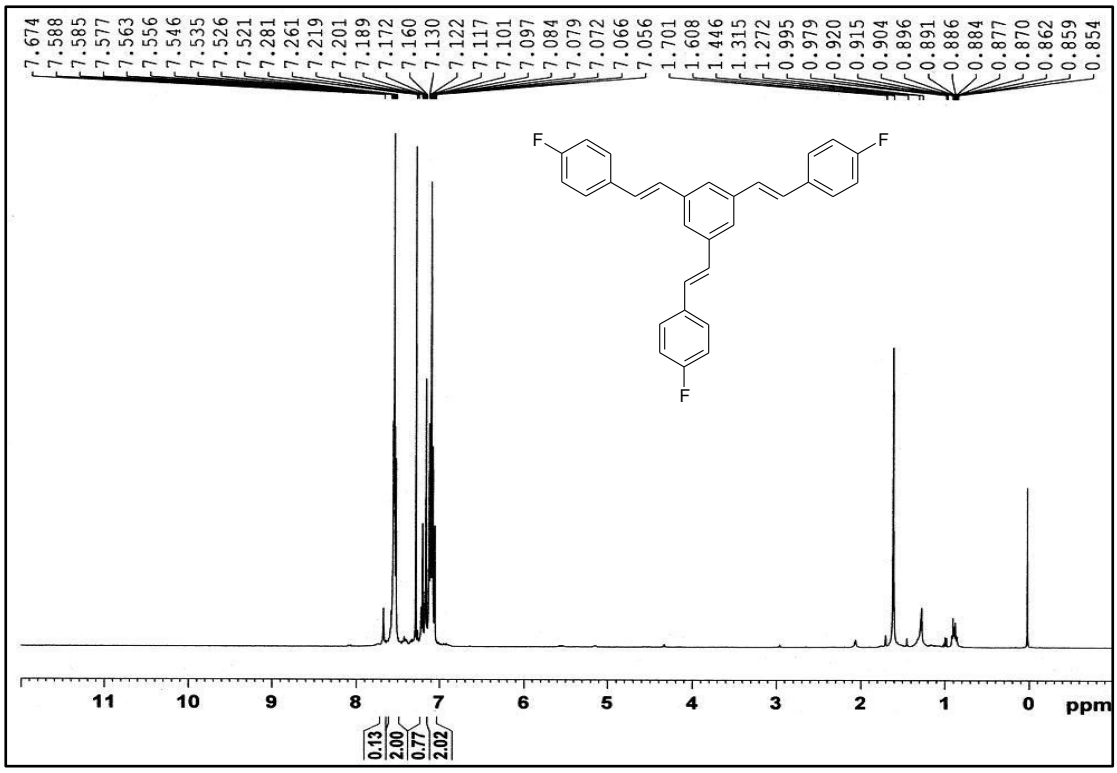
EI-Mass Spectra of Compound 19



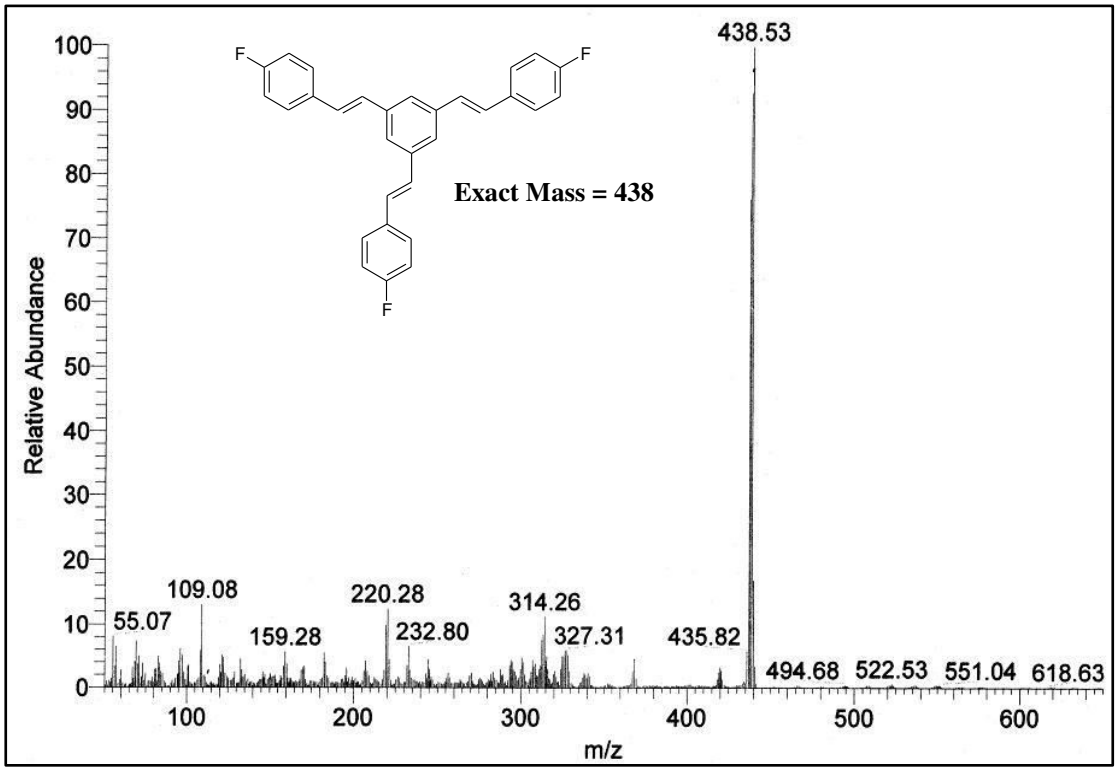
^{1}H-NMR Spectra of Compound 20 (400 MHz, $CDCl_3$)



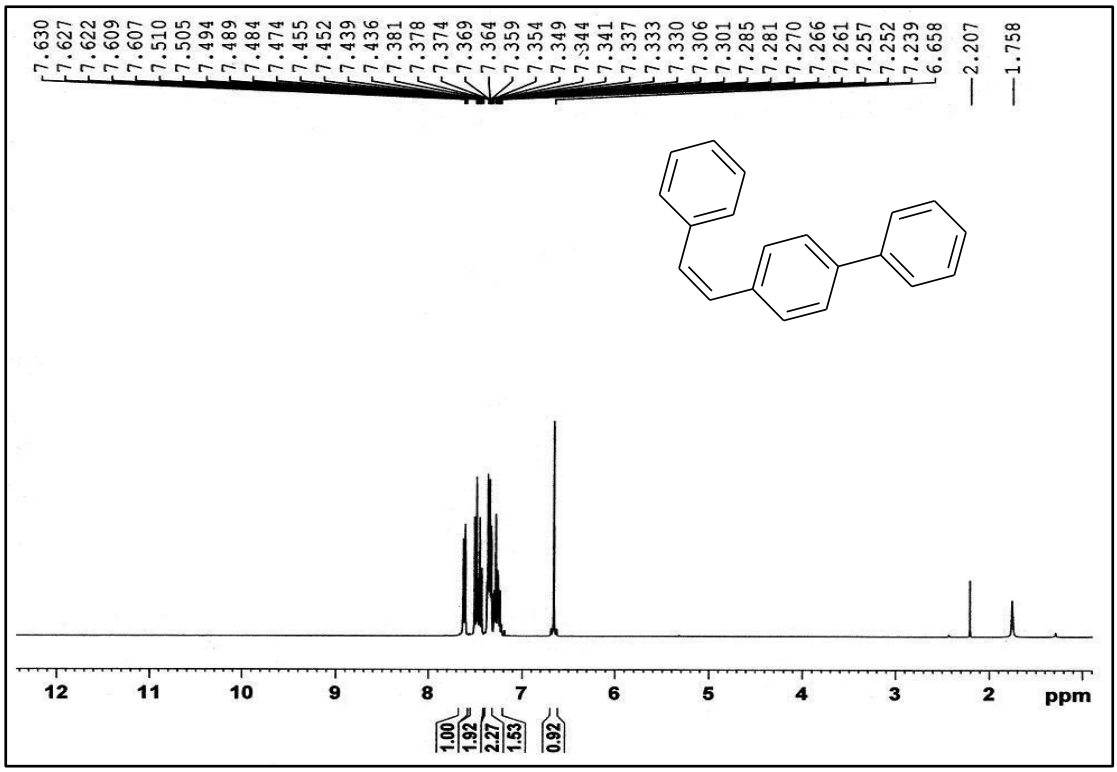
EI-Mass Spectra of Compound 20



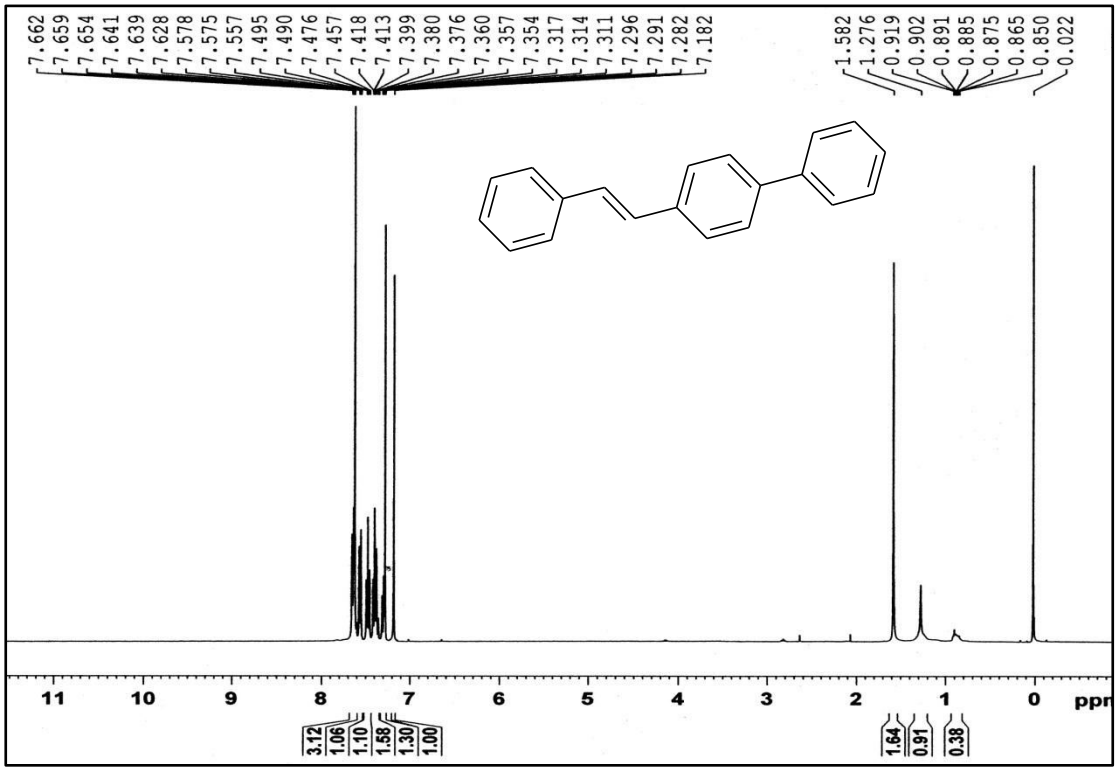
^{1}H-NMR Spectra of Compound 23 (400 MHz, $CDCl_3$)



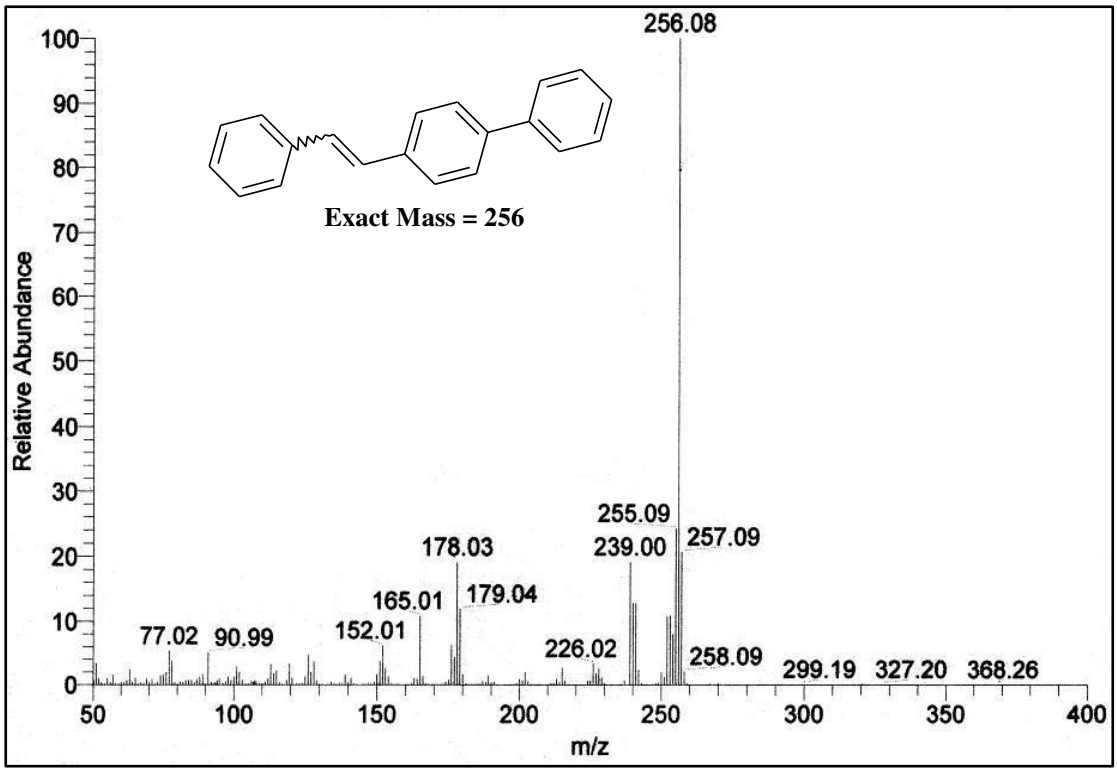
EI-Mass Spectra of Compound 23



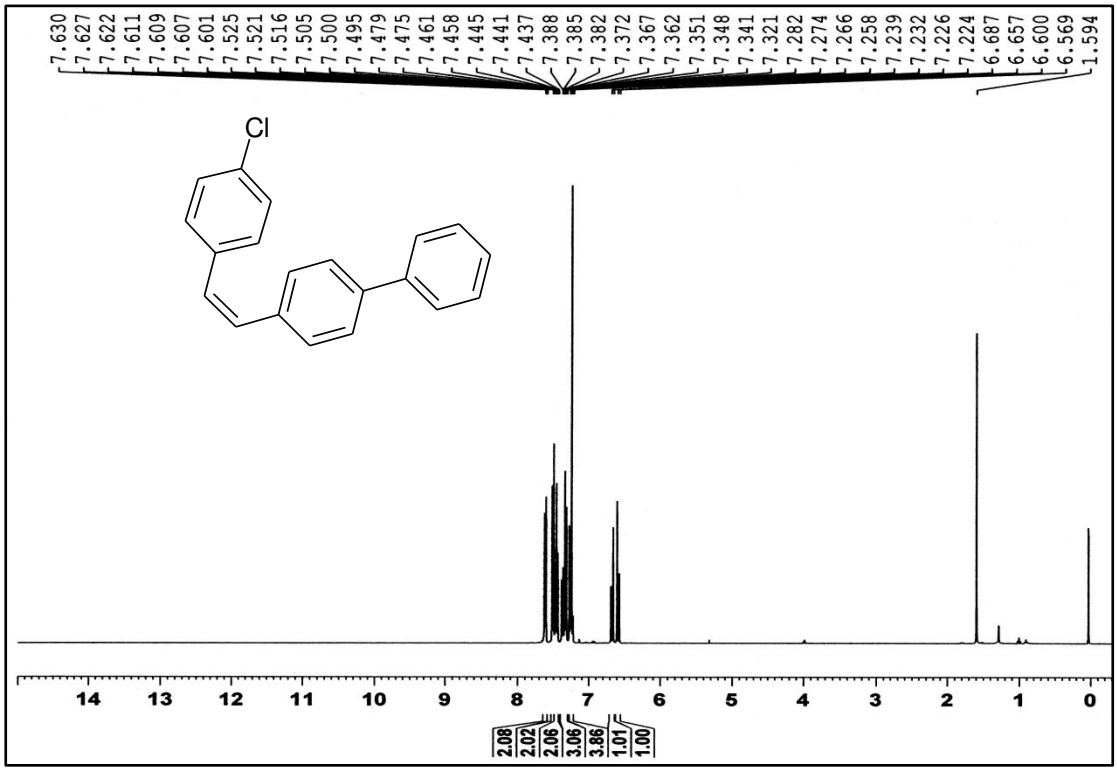
^{1}H-NMR Spectra of Compound 27 (Pure *cis* isomer) (400 MHz, $CDCl_3$)



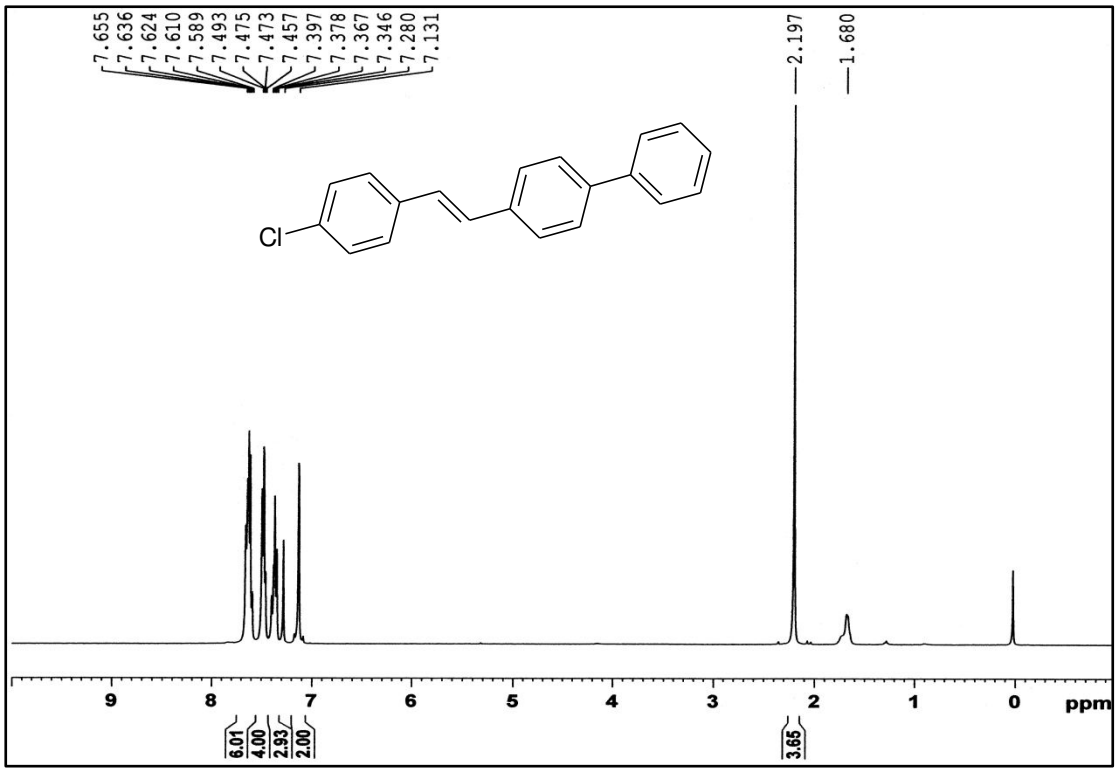
^{1}H-NMR Spectra of Compound 27 (Pure *trans* isomer) (400 MHz, $CDCl_3$)



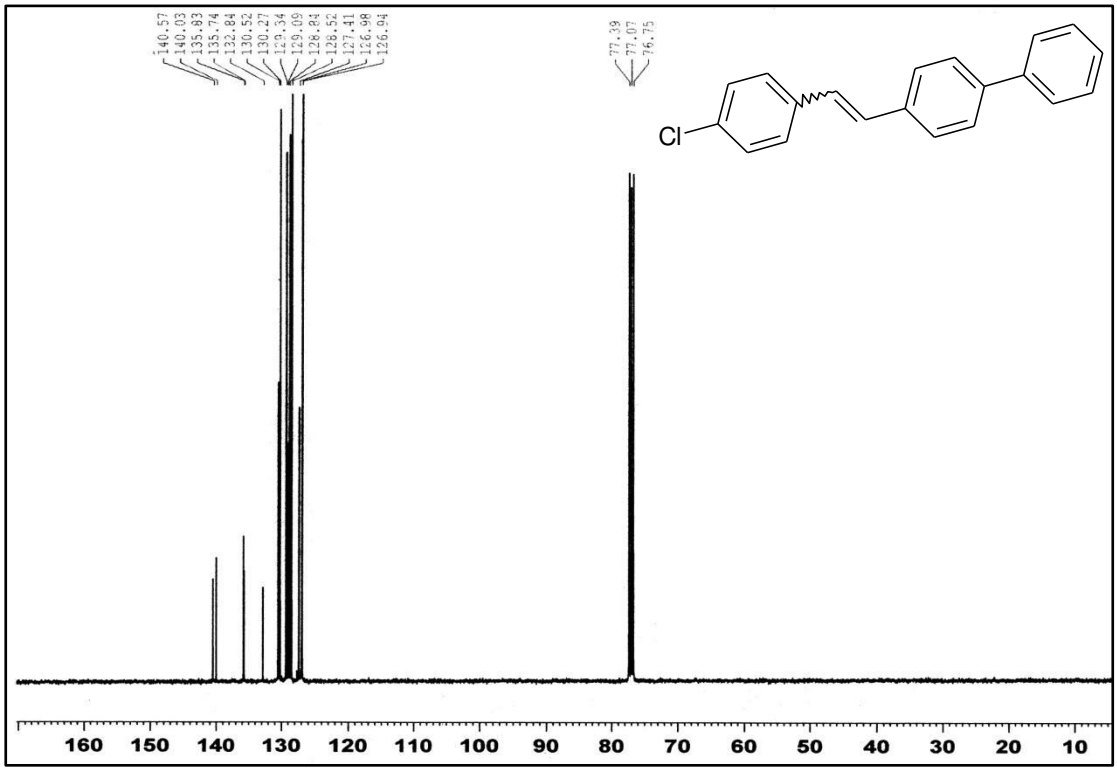
EI-Mass Spectra of Compound 27



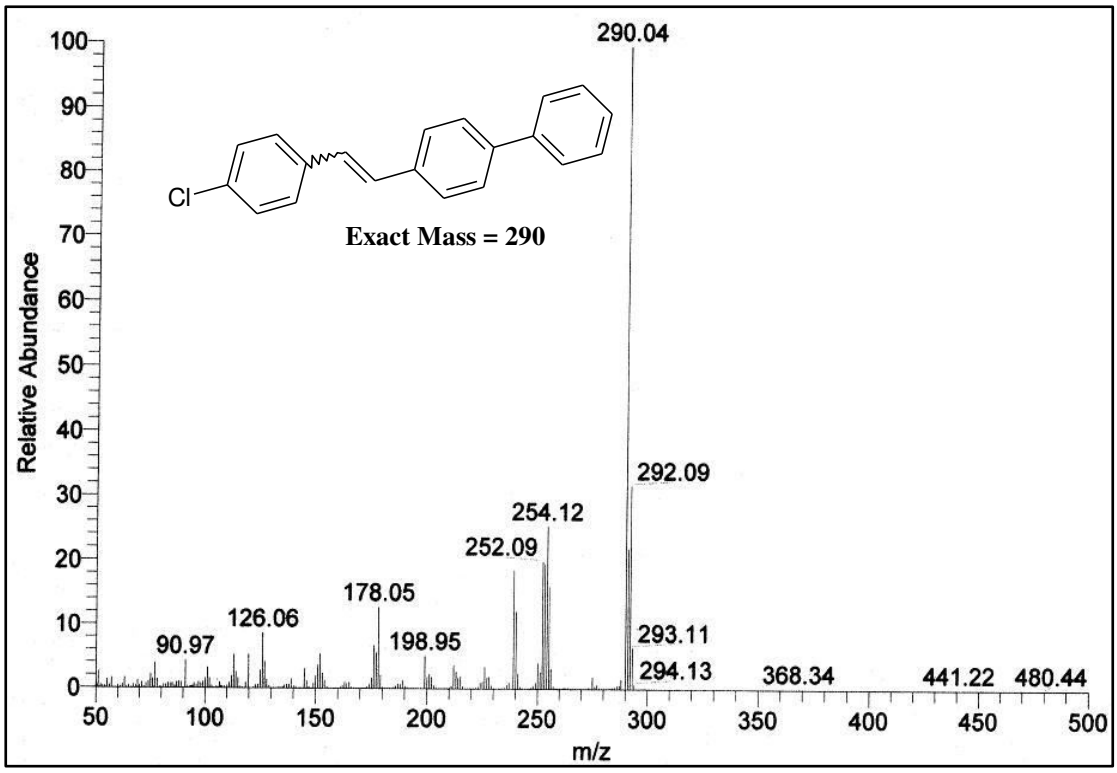
^{1}H-NMR Spectra of Compound 28 (Pure *cis* isomer) (400 MHz, $CDCl_3$)



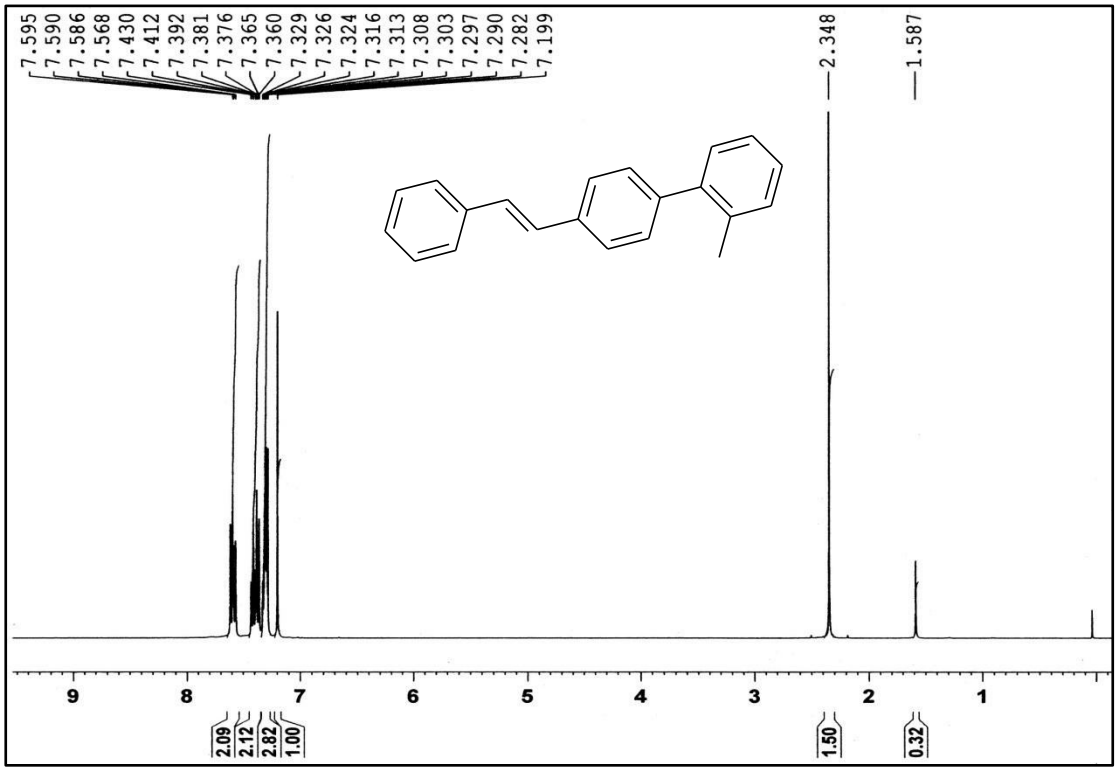
^{1}H-NMR Spectra of Compound 28 (Pure *trans* isomer) (400 MHz, $CDCl_3$)



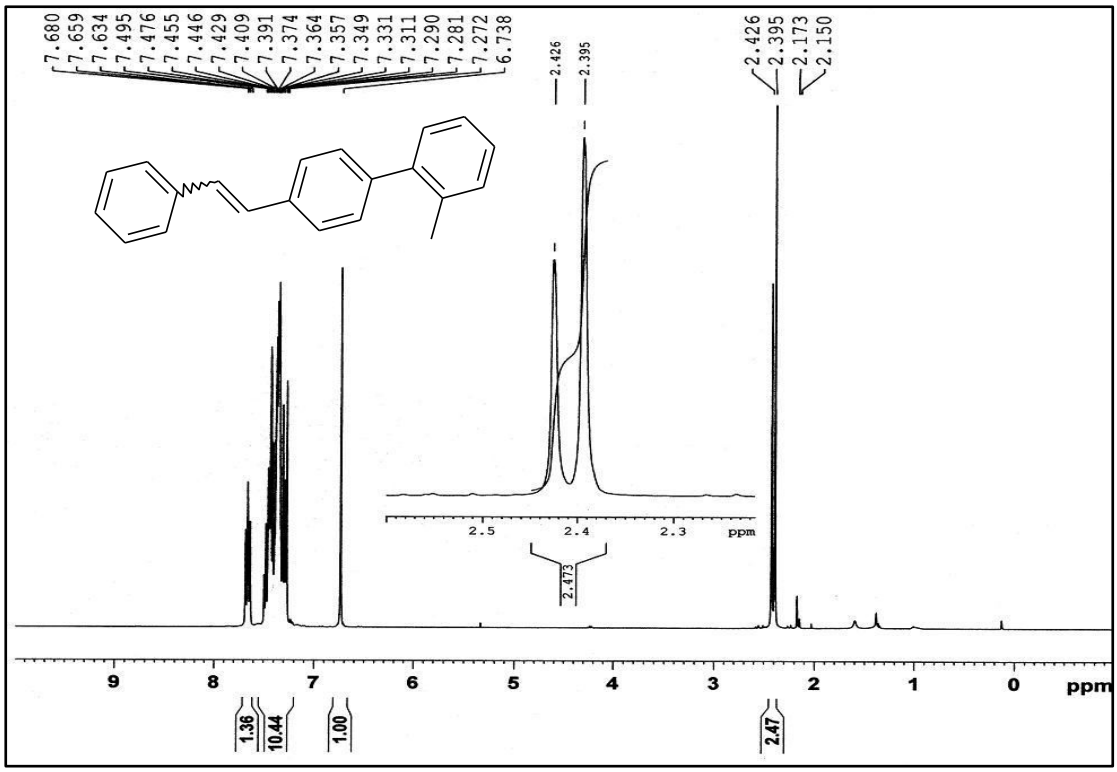
^{13}C-NMR Spectra of Compound 28 (100 MHz, $CDCl_3$)



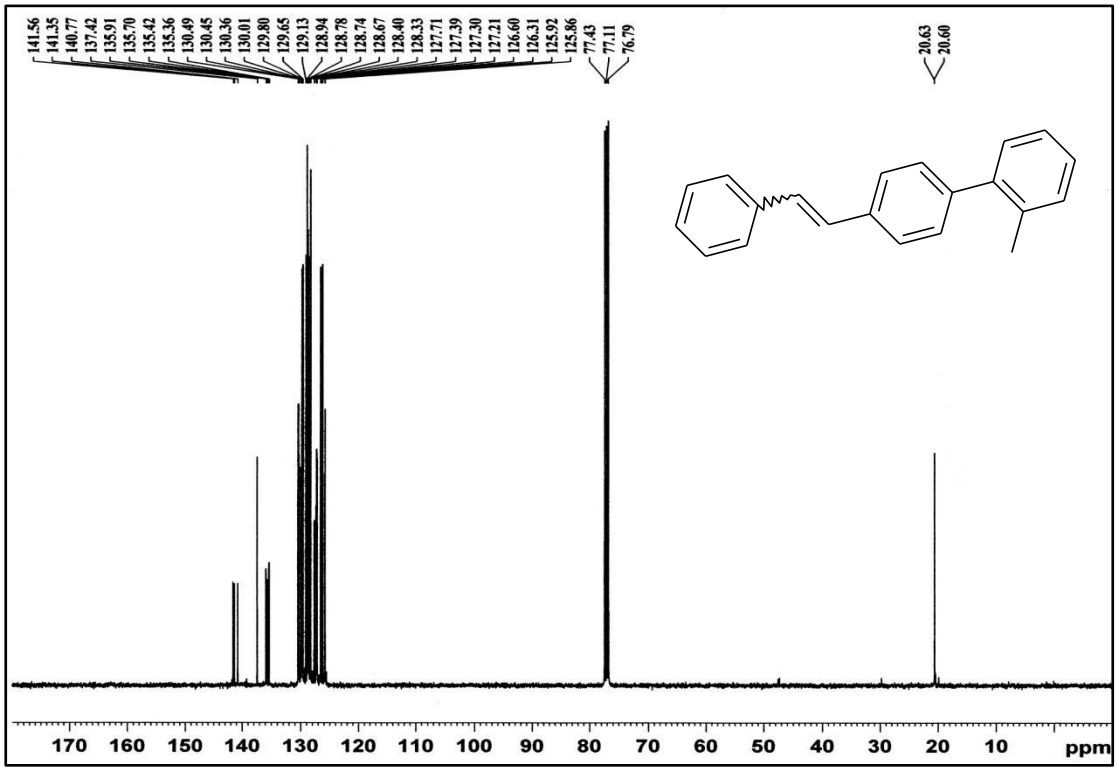
EI-Mass Spectra of Compound 28



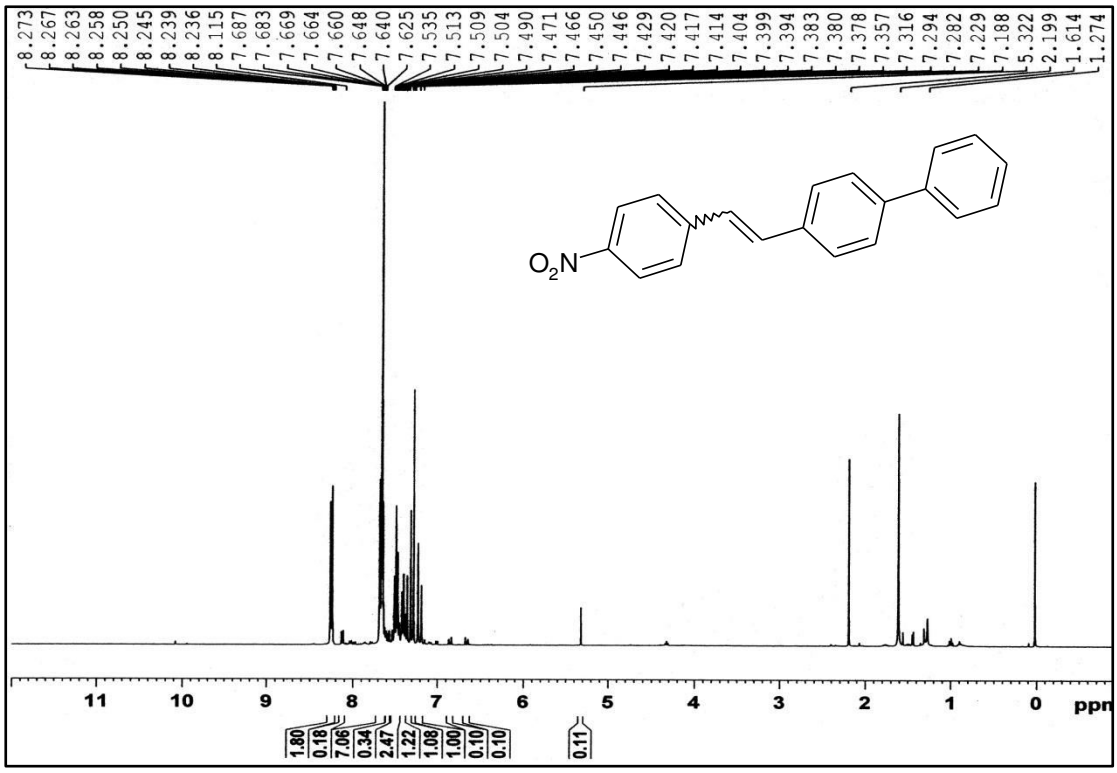
^{1}H-NMR Spectra of Compound 29 (Pure *trans* isomer) (400 MHz, $CDCl_3$)



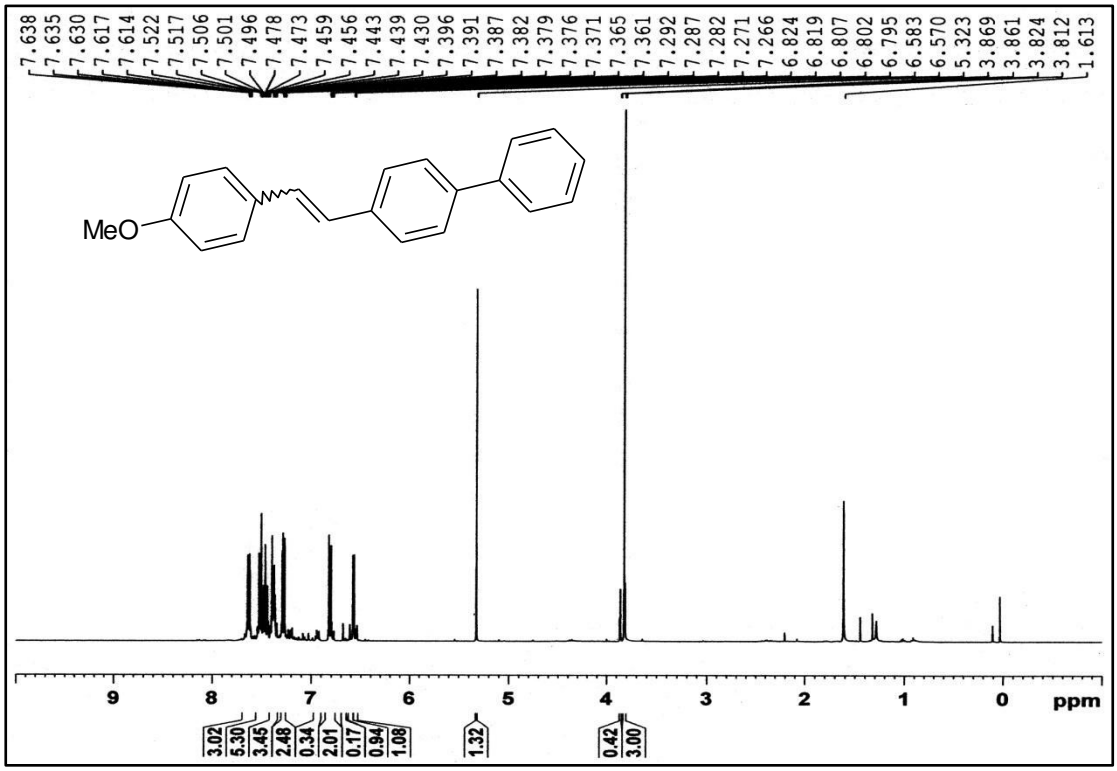
^{1}H-NMR Spectra of Compound 29 (*Z : E = 59 : 41*) (400 MHz, $CDCl_3$)



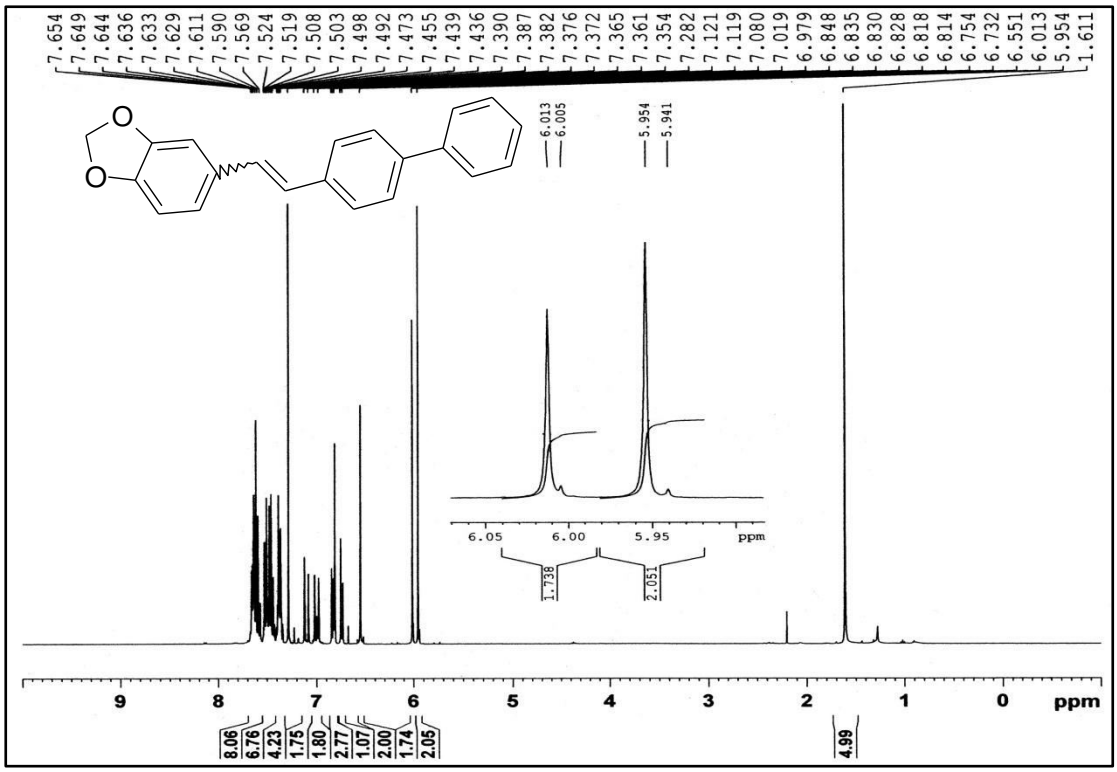
^{13}C-NMR Spectra of Compound 29 (100 MHz, $CDCl_3$)



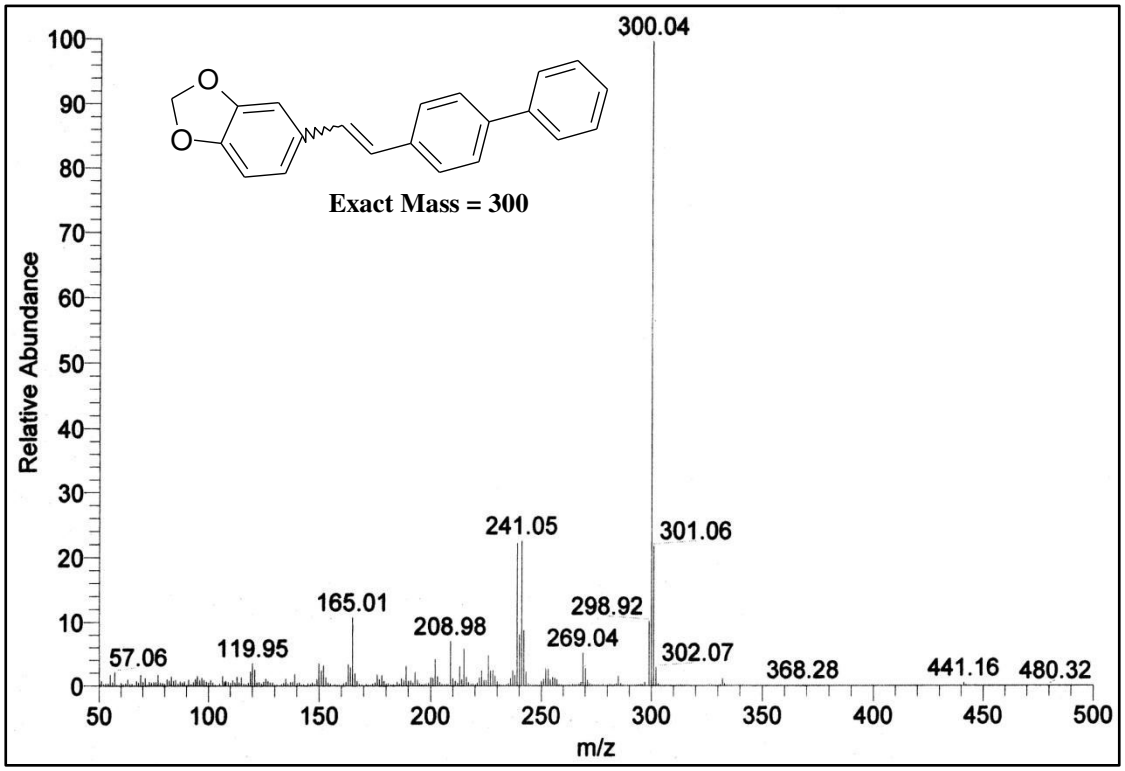
^{1}H-NMR Spectra of Compound 30 (*Z : E = 9 : 91*) (400 MHz, $CDCl_3$)



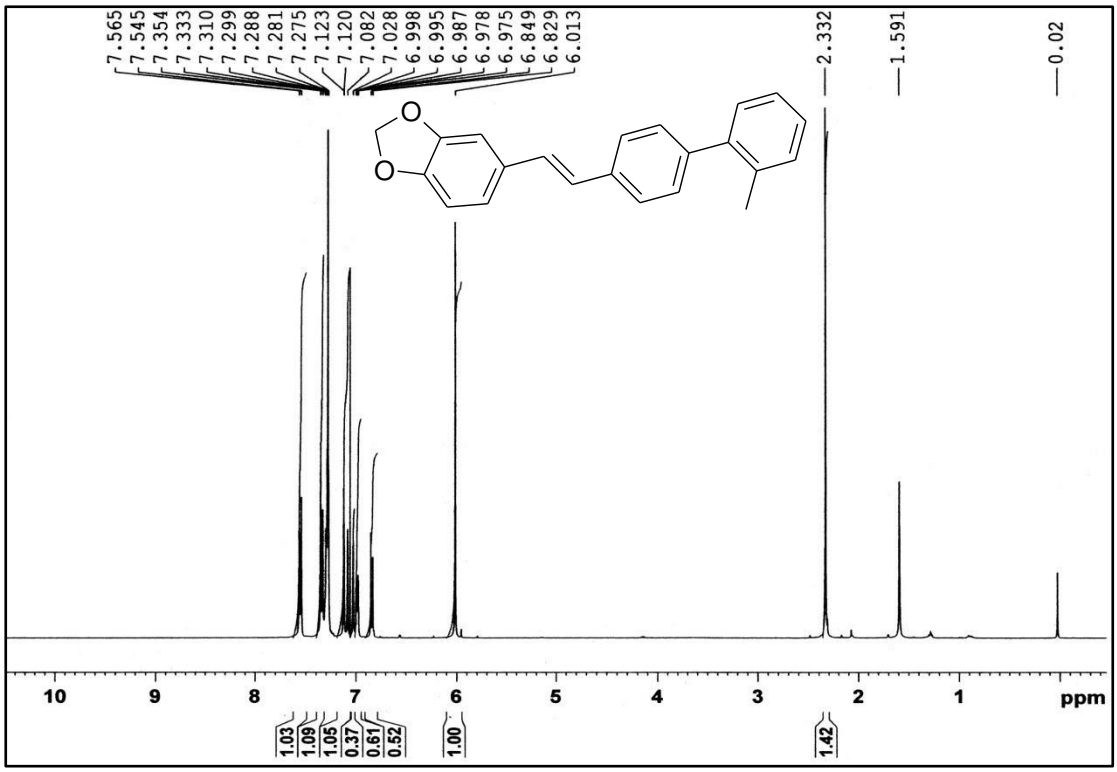
^{1}H-NMR Spectra of Compound 31 (*cis-trans mixture*) (400 MHz, $CDCl_3$)



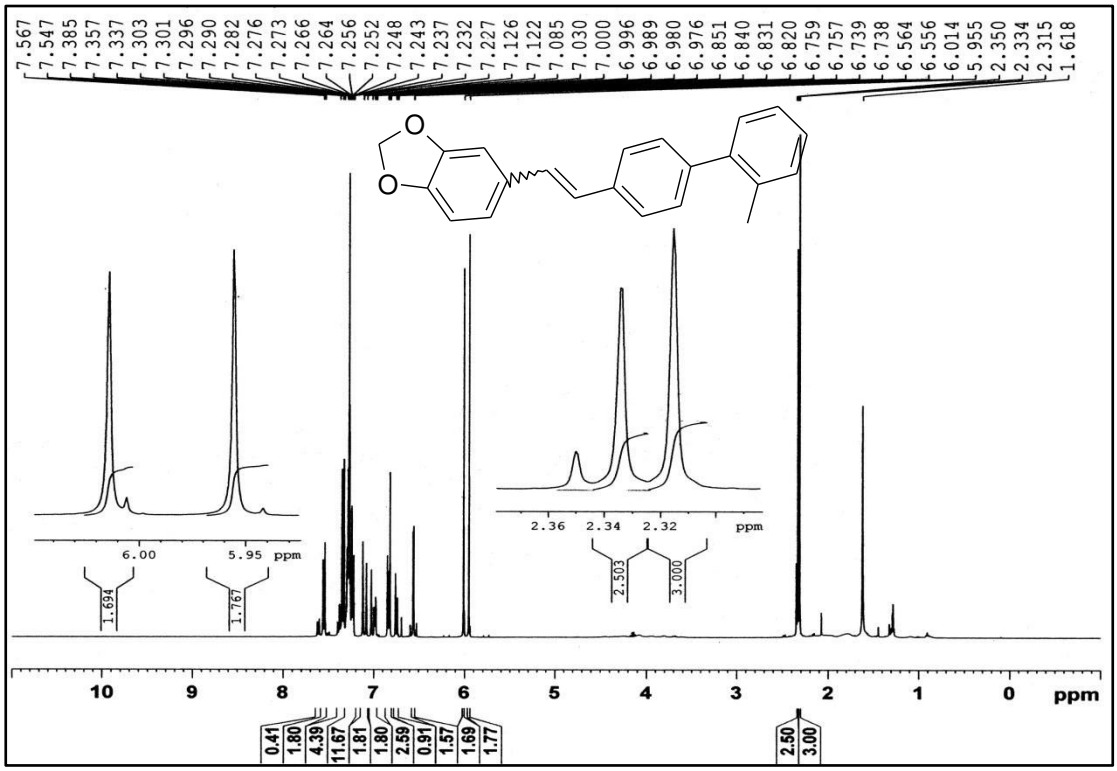
^{1}H-NMR Spectra of Compound 32 (*Z : E = 55 : 45*) (400 MHz, $CDCl_3$)



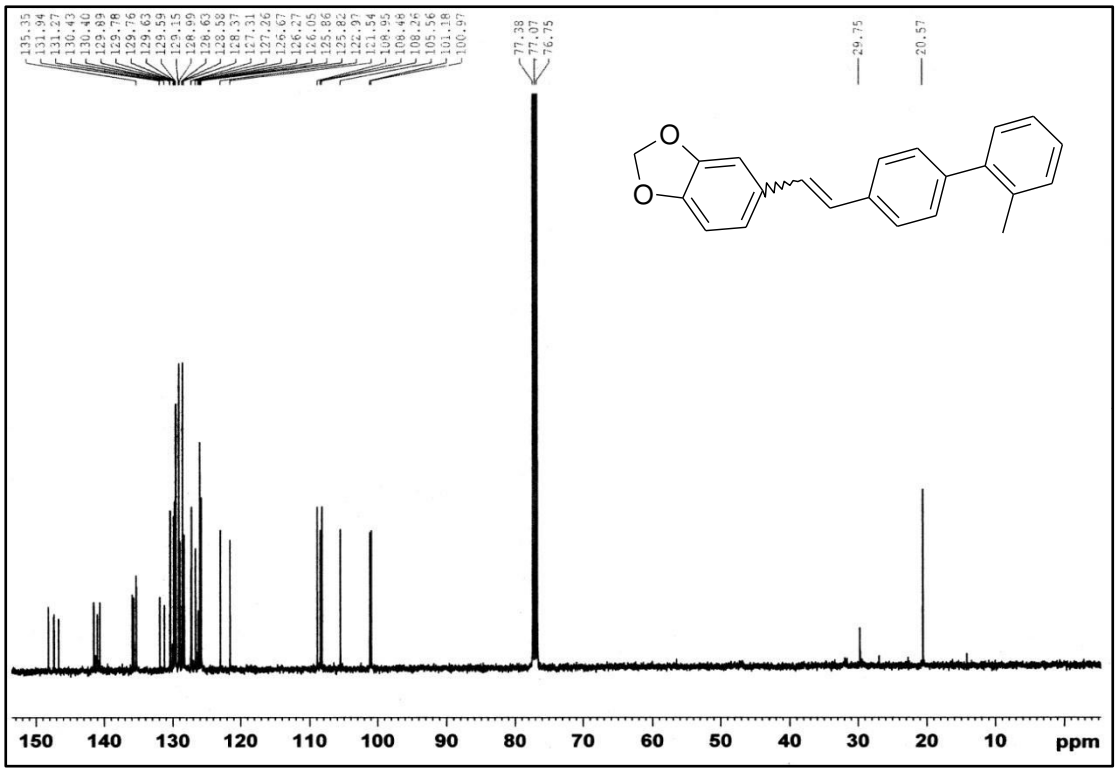
EI-Mass Spectra of Compound 32



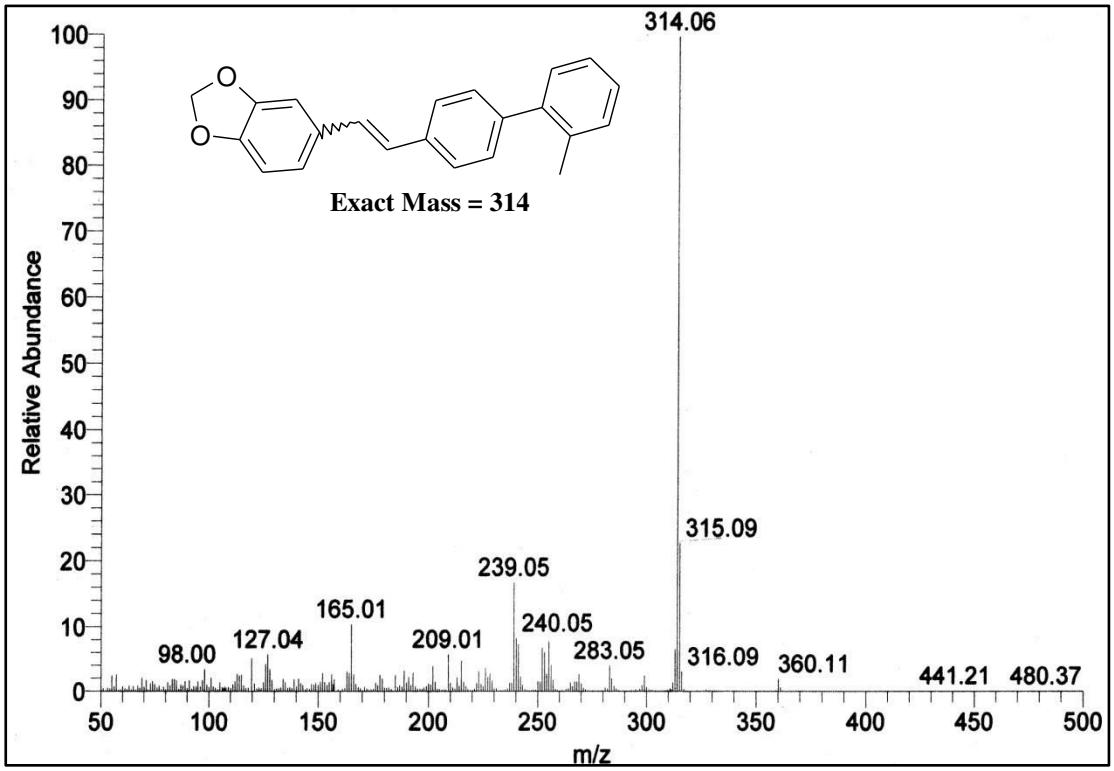
^{1}H-NMR Spectra of Compound 33 (Pure *trans* isomer) (400 MHz, $CDCl_3$)



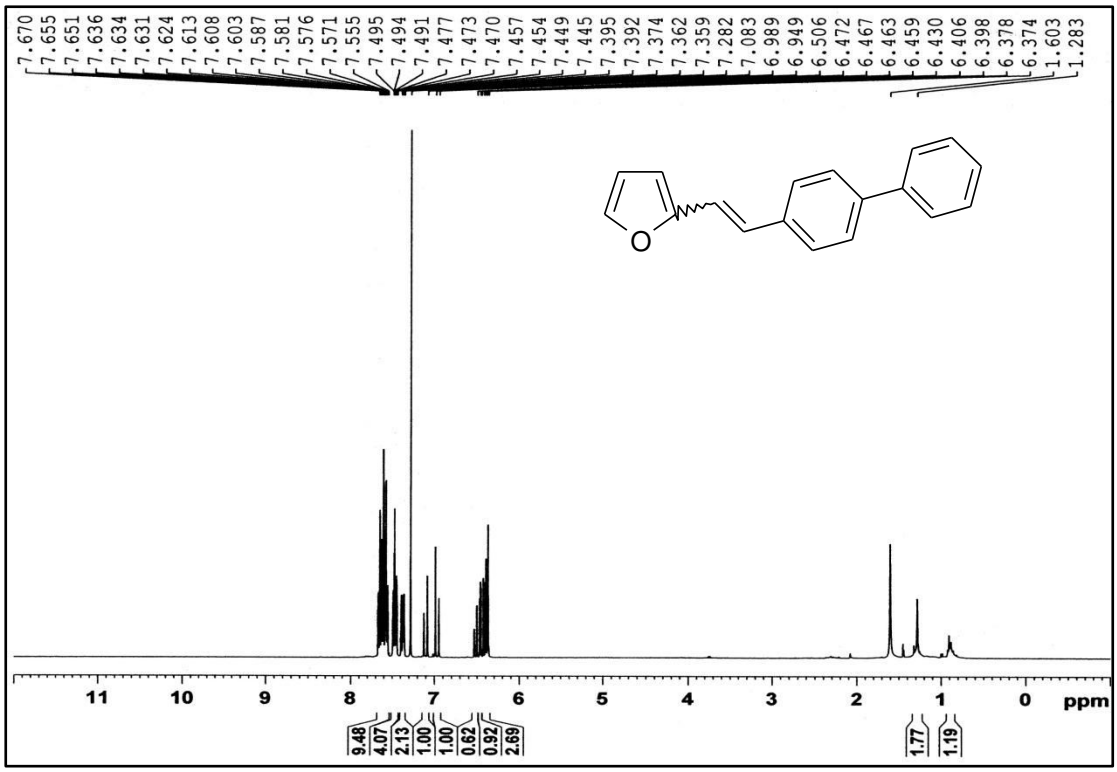
^{1}H-NMR Spectra of Compound 33 (*cis-trans mixture*) (400 MHz, $CDCl_3$)



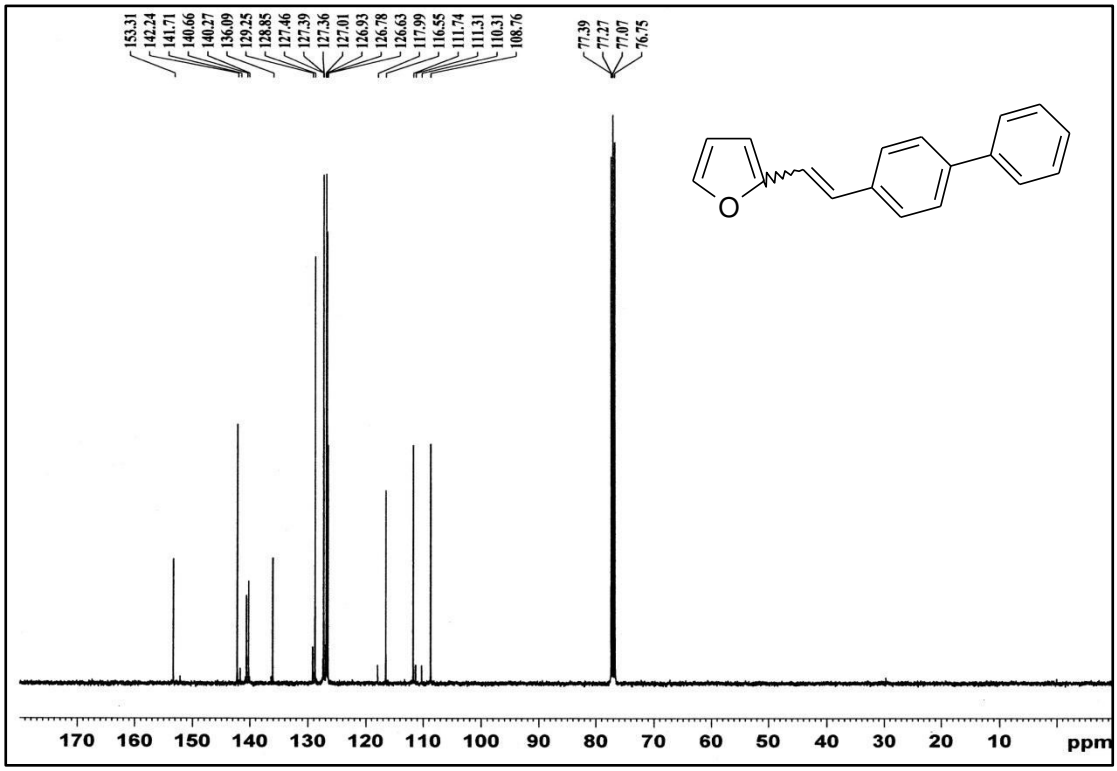
^{13}C-NMR Spectra of Compound 33 (100 MHz, $CDCl_3$)



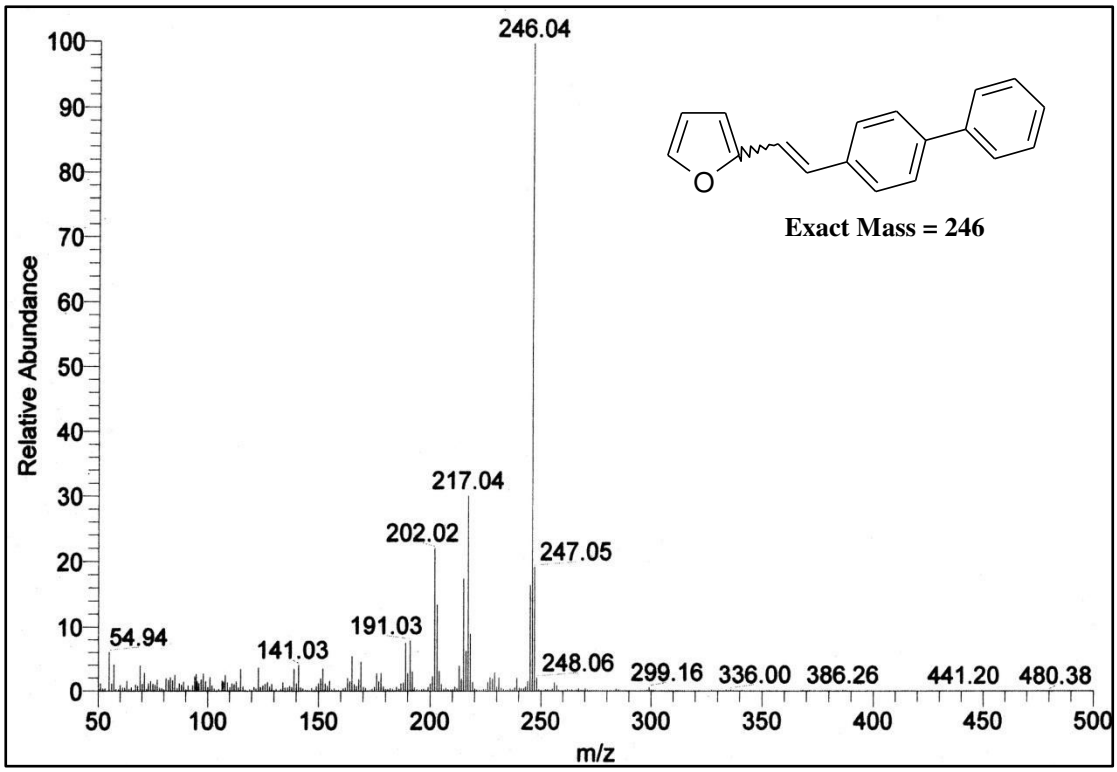
EI-Mass Spectra of Compound 33



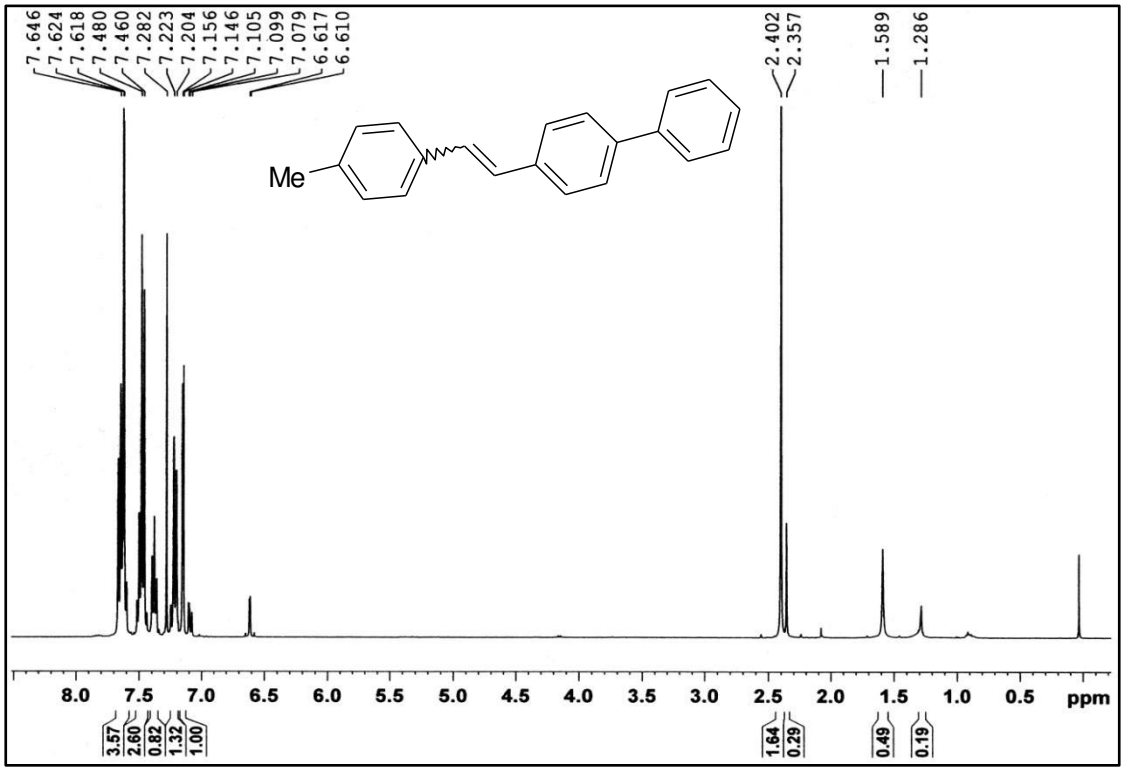
^{1}H-NMR Spectra of Compound 34 (*cis-trans mixture*) (400 MHz, $CDCl_3$)



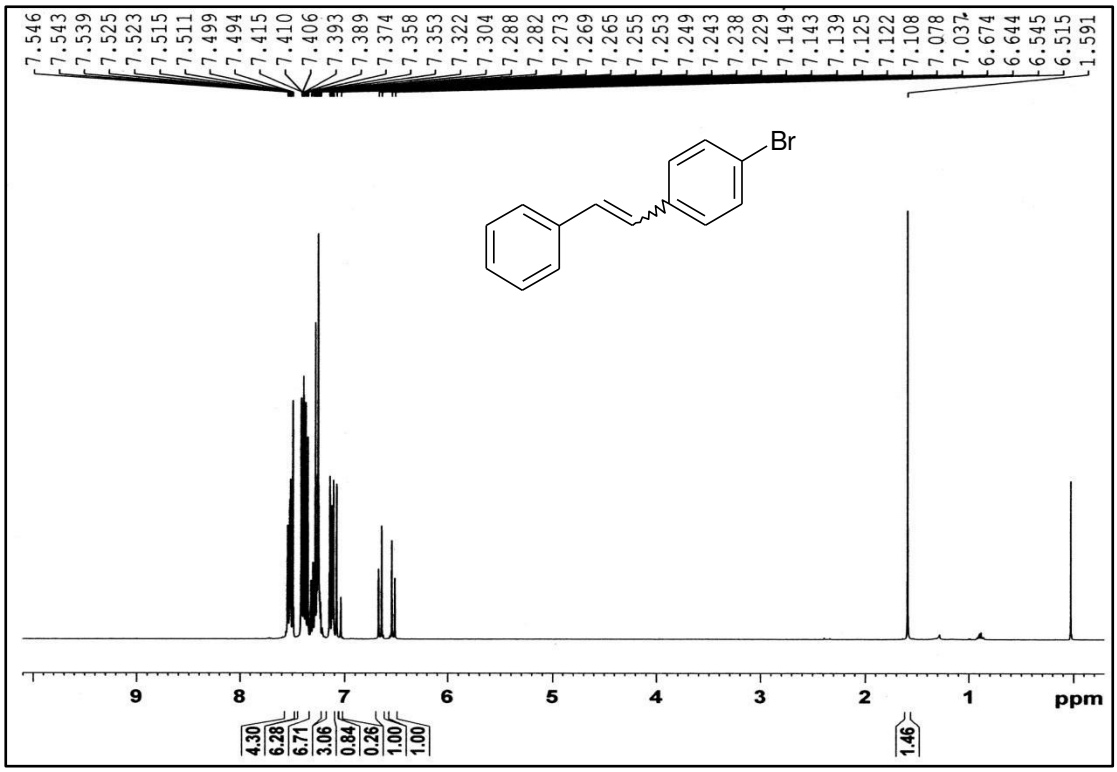
^{13}C-NMR Spectra of Compound 34 (100 MHz, $CDCl_3$)



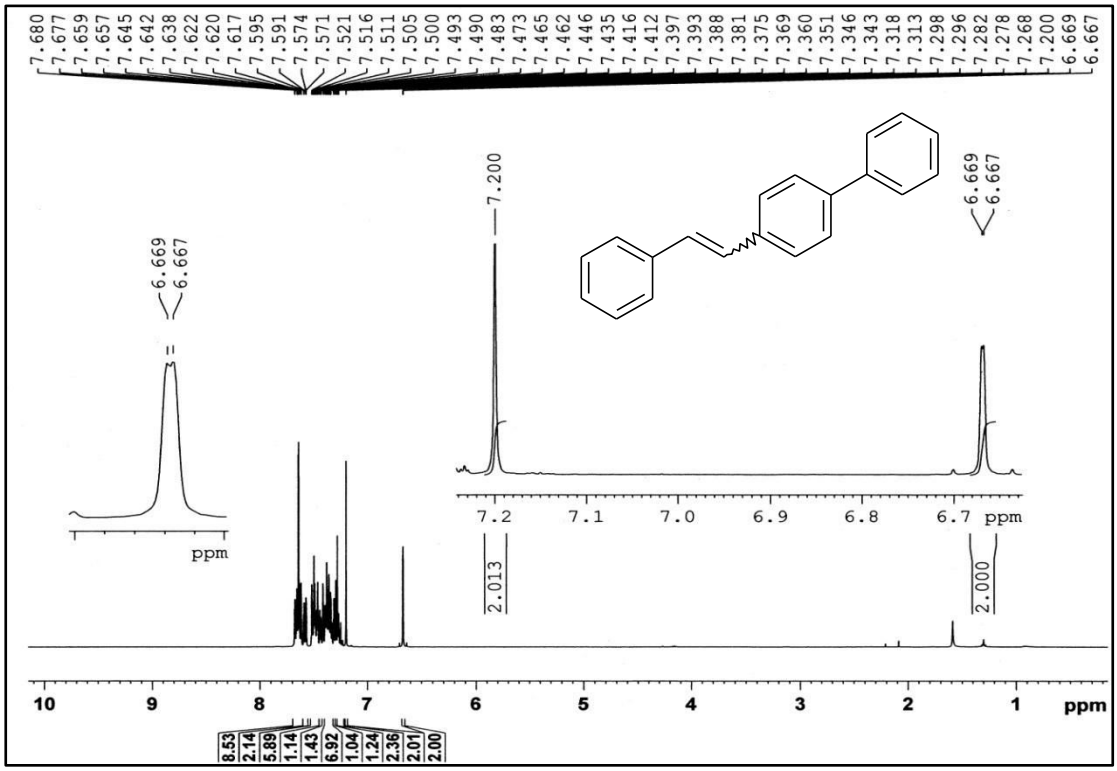
EI-Mass Spectra of Compound 34



^{1}H-NMR Spectra of Compound 35 (*cis-trans mixture*) (400 MHz, $CDCl_3$)



^{1}H-NMR Spectra of Compound 25 (*Z : E = 48 : 52*) (400 MHz, $CDCl_3$)



^{1}H-NMR Spectra of Compound 36 (*Z : E = 50 : 50*) (400 MHz, $CDCl_3$)

CONCLUSION

A series of fluorinated stilbene derivatives were synthesized by Mizoroki - Heck reaction using phosphine-free catalytic conditions or by adopting one - pot Wittig - Heck reaction sequence, which can be advantageous when unstable styrenes are one of the reactants for reaction.

Moreover, derivatives of 4-styryl biphenyl (C_6-C_2-C_6-C_6-unit) have been prepared with this catalyst system using the one-pot Wittig - Suzuki reaction with many possible substitution options. Such reactions carried out in one-pot or under cascade conditions reduce consumption of reagents such as solvent, save energy and offer many advantages which can make this a greener process.

References

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