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Article

Metal Halide Hydrates as Lewis Acid Catalysts for the Conjugated Friedel-Crafts Reactions of Indoles and Activated Olefins

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O uso de haletos metálicos hidratados, tais como, $SnCl_2 \cdot 2H_2O$, $MnCl_2 \cdot 4H_2O$, $SrCl_2 \cdot 6H_2O$, $CrCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ e $CeCl_3 \cdot 7H_2O$ como catalisadores ácidos de Lewis foi investigado nas reações conjugadas tipo Friedel-Crafts entre indóis e olefinas ativadas. A utilização de enonas alifáticas forneceu as respectivas β-indolilcetonas à temperatura ambiente em longos tempos de reação, enquanto que nas reações com chalconas foi necessário o uso de condições de refluxo em isopropanol. As reações dos indóis com nitroestirenos foram efetuadas tanto em fase líquida como em condições sem solvente. Em todos os casos estudados foram obtidos rendimentos de razoáveis a bons.

Metal halide hydrates such as $SnCl_2 \cdot 2H_2O$, $MnCl_2 \cdot 4H_2O$, $SrCl_2 \cdot 6H_2O$, $CrCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ e $CeCl_3 \cdot 7H_2O$ were investigated as mild Lewis acids catalysts for the conjugate Friedel-Crafts reaction between indoles and activated olefins. The reactions were carried out with aliphatic unsaturated ketones over a period of days at room temperature, while chalcones reacted only under reflux conditions. The reactions with nitrostyrenes were either performed in solvent or under solventless conditions. In all cases reasonable to good yields were obtained.

Keywords: Friedel-Crafts, indoles, activated olefins, metal halide hydrates, Lewis acids, Michael addition

Introduction

The investigation of synthetic methodologies for the preparation of 3-substituted indole derivatives has been a continuous challenge in the chemistry of heterocyclic compounds.[1-3]

The C_3 alkylation reaction of indoles through the conjugated Friedel-Crafts (CFC) reaction has received much attention in the last decade.[4-6] Not only they allow access to advanced building blocks in the synthesis of natural compounds, but also their diverse biological properties of derivatives have pharmaceutical applications.[7-11]

Over the past few years a range of methods for the preparation of β-indolylketones by CFC reaction of indoles with α,β-unsaturated ketones has appeared in the literature in which both Brønsted or Lewis acidic catalysts have successfully been employed. However, in the curse of Brønsted acid catalysis, many procedures involve strong acidic conditions, expensive reagents, longer reaction times, low yields, complex handling procedures and problematic side reactions, such as dimerization and polymerization.[12]

On the other hand, the employment of suitable metal halides such as $InCl_3$,[13] $InBr_3$,[14] SmI_3,[15] GaI_3,[16] $SbCl_3$,[17] $ScCl_3$,[18] $AlCl_3$,[19] $ZrCl_4$,[20] and $HfCl_4$[18] as Lewis acid catalysts have attracted attention due to their ability to efficiently activate the α,β-unsaturated carbonyl system for the CFC reaction. However, many of them are moisture sensitive needing a careful handling and the achievement of a substitute is welcome. Additionally, others environmentally-benign, oxygen and/or moisture tolerant Lewis acids such as $Yb(OTf)_3$,[7] $Sc(OTf)_3$,[21] $Bi(OTf)_3$,[22] $Hf(OTf)_4$,[21] and $Zr(OTf)_4$ [23] have been applied to this transformation, but they are expensive.

A few previous uses of metal salt hydrates such as: $NaAuCl_4 \cdot 2H_2O$,[24] $ZrOCl_2 \cdot 8H_2O$,[25] $RuCl_3 \cdot nH_2O$[26] and $Fe(BF_4)_2 \cdot 6H_2O$[27] have been reported.

As a part of our ongoing investigation searching for moisture compatible Lewis acids, including their use in protic solvents, for the synthesis of small molecules of biological interest,[28-36] we decide to investigate the

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metal halide hydrates as a potential catalysts for the CFC reaction. We have earlier demonstrated the successful use of $SnCl_2 \cdot 2H_2O$ as an alcoholic compatible Lewis acid catalyst for the multicomponent dihydropyrimidinone synthesis.[37] The Lewis acidity of $SnCl_2 \cdot 2H_2O$ has been reported by others in different reactions types.[38-40]

Although the hydrogen Brønsted acid catalysis has been suggested by Spencer as the main process when a metal halide is used as a Lewis catalyst in aqueous (or protic alcoholic) solvents,[41] other authors postulated the water-tolerance of many metal halides. Kobayashi suggests that the certain metal halides are able to complex with the electrophile before the hydrolysis occurs. These characteristics depends on the hydrolysis constant (K_h) within a certain range and a high water-exchange rate constant (WERC).[42] On the other hand, Fringuelli *et al.*[43] report the use of $AlCl_3$, $TiCl_4$, and $SnCl_4$ as the Lewis acids catalysts in aqueous solvent. Although the authors agree with the fast hydrolysis of metal salts, they affirm that the hydrated metal cation remains as the effective species as Lewis acid catalyst.

Recent studies of Lindstrom[44] show that the water tightly coordinated to the metal halide become more labile upon complexation of an organic ligand (electrophile), leading to a higher rate of exchange with substrate molecules and consequently to higher reaction rates.

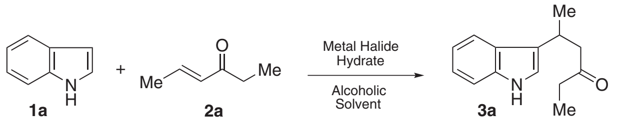
The $SnCl_2 \cdot 2H_2O$ was employed as a Lewis acid catalyst in the esterification of oleic acid. The authors proved the ethanol-compatibility of the catalyst as a Lewis acid through the recovery of $SnCl_2 \cdot 2H_2O$ and verified that the catalytic activity of the recovered $SnCl_2 \cdot 2H_2O$ remains unaltered in successive reactions with oleic acid.[45]

Based on these previous studies, we report in this paper, our efforts to apply a series of metal halide hydrates such as: $SnCl_2 \cdot 2H_2O$, $MnCl_2 \cdot 4H_2O$, $SrCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ and $CrCl_3 \cdot 6H_2O$ as Lewis acid catalysts for the CFC reaction of indoles and activated olefins, carried out in benign alcoholic solvents.

Results and Discussion

Reactions of indoles with alkylidene-alkylketones

In our first experiment, we investigated the use of various metal halide hydrates as Lewis acid catalysts in the reaction of indole (**1a**) and 4-hexen-3-one (**2a**) under different alcoholic solvents, temperatures and catalyst loading. In all experiments the desired β-indolylketone **3a** was obtained in good yield (Scheme 1).



Scheme 1. Synthesis of β-indolylketone **3a.**

As shown in Table 1, the yield of the product **3a** was quite good when the reaction was carried out in *i*-PrOH at room temperature. The reaction proceeded cleanly[46] as observed by comparative TLC and *i*-PrOH was chosen as the default solvent for the other reactions (c.f. entries 1-3).

Table 1. Synthesis of β-indolylketone **3a** under different conditions

entry	Lewis Acid (equiv.)		Solvent	Temperature	time (h)	Yield (%)
1	$SnCl_2 \cdot 2H_2O$	(0.1)	MeOH	r. t.	96	82
2	$SnCl_2 \cdot 2H_2O$	(0.1)	EtOH	r. t.	96	88
3	$SnCl_2 \cdot 2H_2O$	(0.1)	*i*-PrOH	r. t.	96	96
4	$SnCl_2 \cdot 2H_2O$	(0.2)	*i*-PrOH	r. t.	96	97
5	$SnCl_2 \cdot 2H_2O$	(0.5)	*i*-PrOH	r. t.	96	90
6	$MnCl_2 \cdot 4H_2O$	(0.1)	*i*-PrOH	r. t.	120	93
7	$SrCl_2 \cdot 6H_2O$	(0.1)	*i*-PrOH	r. t.	120	70
8	$CoCl_2 \cdot 6H_2O$	(0.1)	*i*-PrOH	r. t.	120	79
9	$SnCl_2 \cdot 2H_2O$	(0.1)	*i*-PrOH	reflux	3	98
10	$CoCl_2 \cdot 6H_2O$	(0.1)	*i*-PrOH	reflux	5	98
11	$CrCl_3 \cdot 6H_2O$	(0.1)	*i*-PrOH	reflux	5	98

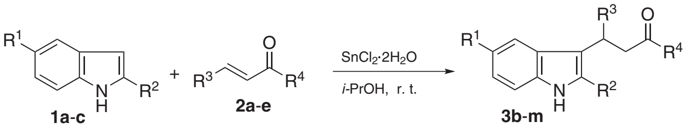
For the $SnCl_2 \cdot 2H_2O$, the increase of the catalyst loading did not improve the yields and the catalytic amount of 10 mol% was chosen as the default load of the catalyst (entries 3, 4 and 5, respectively).

Although long reaction times were required, in general, reasonable to good yields were observed when $MnCl_2 \cdot 4H_2O$, $SrCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ were used as catalysts in experiments carried out at room temperature (entries 6, 7 and 8). On the other hand, shorter reaction times of 3-5 h and refluxing conditions were enough to complete the consumption of the reagents when $SnCl_2 \cdot 2H_2O$, $CoCl_2 \cdot 6H_2O$ and $CrCl_2 \cdot 6H_2O$ were used (entries 9, 10 and 11, respectively).

Due to the easy availability, good stability and low cost, $SnCl_2 \cdot 2H_2O$ was chosen as the default catalyst. Its use as a Lewis acid catalyst in the reaction of indoles **1a-c** and ketones **2a-e** afforded the respective β-indolylketones **3b-m** in reasonable to good yields (Scheme 2). The results are summarized in the Table 2.

As can be observed, the yields of adducts **3** were high, except for the cases where cyclohexenone was used as the Michael acceptor in the reactions with indole **1a** (entries 4 and 9, respectively). In both cases, we were able to isolate variable amounts of two other side products, which showed a strong absorption in UV-light (254 nm).

Table 2. Synthesis β-Indolylketones **3b-m** under $SnCl_2 \cdot 2H_2O$ catalyst at room temperature



entry	Indole			α,β-Unsaturated ketone			time (h)	Product	Yield (%)
		R^1	R^2		R^3	R^4			
1	**1a**	H	H	**2a**	H	Et	48	**3b**	96
2	**1a**	H	H	**2b**	C_5H_{11}	Me	96	**3c**	96
3	**1a**	H	H	**2c**	cyclopentenone		78	**3d**	96
4	**1a**	H	H	**2d**	cyclohexenone		72	**3e**	40
5	**1b**	MeO	H	**2e**	Me	Et	96	**3f**	98
6	**1b**	MeO	H	**2a**	H	Et	96	**3g**	80
7	**1b**	MeO	H	**2b**	C_5H_{11}	Me	96	**3h**	90
8	**1b**	MeO	H	**2c**	cyclopentenone		72	**3i**	95
9	**1b**	MeO	H	**2d**	cyclohexenone		32	**3j**	41
10	**1c**	H	Me	**2e**	Me	Et	72	**3k**	88
11	**1c**	H	Me	**2a**	H	Et	48	**3l**	97
12	**1c**	H	Me	**2c**	cyclopentenone		48	**3m**	81

We believe that the side products are generated by a second attack of an indole molecule to the initial β-indolylketone formed. Alternatively, a third molecule of indole could be added to the *bis*-indolyl adduct **3n** and **3o** to form the *tris*-indolyl adduct **3p** and **3q**, respectively, as reported recently by Shi *et al.*[23] (Figure 1).

All of the yields refer to isolated products after purification by column chromatography and the ^1H NMR, ^{13}C NMR and IR spectral data were in accordance with the proposed structures.

Reactions of indoles with arylidene-phenylketones

Next, we investigated the conjugated Friedel-Crafts reaction of indoles **1a-c** with chalcones[47] **2f-i** in presence of $SnCl_2 \cdot 2H_2O$ as the catalyst and *i*-PrOH as the solvent (Scheme 2).

In contrast with alkylidene-alkylketones, the chalcone **2f** was not reactive with indole **1a** at room temperature over 144 h, even at 50 mol% catalyst loading (cf. entries 1-3, Table 3). On the other hand, the use of reflux conditions led to the formation of the desired adduct **3r** after 5 h in good yield (entry 4). Other catalysts such as $MnCl_2 \cdot 4H_2O$, $SrCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ and $CeCl_3 \cdot 7H_2O$ were also effective (entries 5 and 8).

The chalcones **2f-i** were reacted under the previous reaction conditions and the β-indolylchalcones **3r-z** were obtained in reasonable to good yields after purification by column chromatography (entries 9-15). The lower reactivity of chalcones may be attributed to their inferior electrophilicity as well as the increase of steric hindrance at the β-position of the ketone.

Reactions of indoles with nitrostyrenes

Due to the success of previous experiments we decided to investigate the CFC reactions of indoles **1a-c** with nitroolefins **4a-g**. The nitroolefins are recognized as excellent Michael aceptors[48,49] and their derivatives are important intermediates in organic synthesis

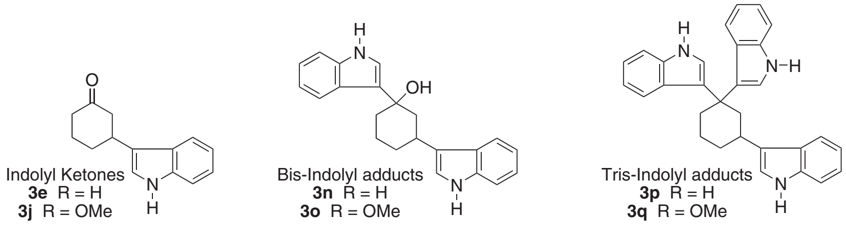
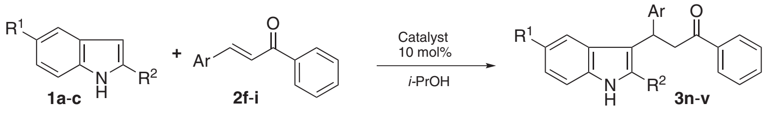


Figure 1. The possible structures of *bis*- and *tris*-indolyl adducts.



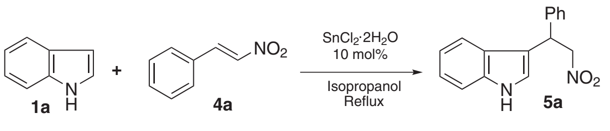
Scheme 2. Conjugated Friedel-Crafts reaction of indoles **1a-c** with chalcones **2f-i.**

Table 3. Synthesis of β-indolylketones **3r-z** via Scheme 2

entry	Indole		Olefin	Catalyst (equiv.)	Temperature	time (h)	**3** / Yield (%)
	R¹	R²	Ar				
1	H	H	Ph	$SnCl_2{\cdot}2H_2O$ (0.1)	r. t.	144	**3r** / -
2	H	H	Ph	$SnCl_2{\cdot}2H_2O$ (0.2)	r. t.	144	**3r** / -
3	H	H	Ph	$SnCl_2{\cdot}2H_2O$ (0.5)	r. t.	144	**3r** / -
4	H	H	Ph	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3r** / 96
5	H	H	Ph	$MnCl_2{\cdot}4H_2O$ (0.1)	reflux	8	**3r** / 60
6	H	H	Ph	$SrCl_2{\cdot}6H_2O$ (0.1)	reflux	5	**3r** / 60
7	H	H	Ph	$CoCl_2{\cdot}6H_2O$ (0.1)	reflux	5	**3r** / 85
8	H	H	Ph	$CeCl_3{\cdot}7H_2O$ (0.1)	reflux	5	**3r** / 98
9	H	H	1-naftyl	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3s** / 60
10	H	H	4-MeO-C_6H_4	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3t** / 80
11	H	H	2-thienyl	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3u** / 74
12	MeO	H	Ph	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3v** / 96
13	MeO	H	1-naftyl	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3w** / 70
14	MeO	H	4-MeO-C_6H_4	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3x** / 95
15	MeO	H	2-thienyl	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3y** / 92
16	H	Me	Ph	$SnCl_2{\cdot}2H_2O$ (0.1)	reflux	5	**3z** / 87

due to the synthetic versatility of the nitro-group as precursor of other organic functionalities.[50-52] First, we investigated the reaction of indole **1a** wiyh nitrostyrene **4a** carried out under the reactions conditions described above (*i*-PrOH, room temperature and 10 mol% of $SnCl_2{\cdot}2H_2O$). Unfortunately, no product was formed even after 6 days. A second experiment was carried out under reflux conditions over 5 h and total consumption of the starting materials was observed. The TLC analysis revealed the presence of very polar mixture of byproducts[53] which were not identified. After purification by chromatography, product **5a** was obtained in only 54% yield (Scheme 3).

With the aim of improving the chemo-selectivity of the reaction and the yields of the products, the catalyst was changed to $CoCl_2{\cdot}6H_2O$, which had been successfully applied previously (see Table 1 entry 10 and Table 3, entry 7, respectively).

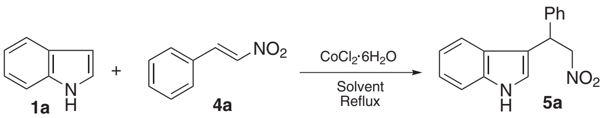


Scheme 3. Conjugated Friedel-Crafts reaction of indole with nitrostyrene **4a**.

The reaction was carried out in *i*-PrOH under reflux conditions for 2 h, when total consumption of the starting material was observed by TLC. After purification by chromatography, the nitro-adduct **5a** was isolated in 95% yield (Table 4, entry 1).

At this point we decided to investigate a set of different solvents. The experiments were carried out in polar protic

Table 4. Synthesis of adduct **5a** promoted by $CoCl_2{\cdot}6H_2O$ under different solvents



entry	Catalyst	Solvent	time (h)	Temperature	Yield (%)
1	$CoCl_2{\cdot}6H_2O$	*i*-PrOH	2	reflux	95
2	$CoCl_2{\cdot}6H_2O$	MeOH	2	reflux	72
3	$CoCl_2{\cdot}6H_2O$	EtOH	2	reflux	73
4	$CoCl_2{\cdot}6H_2O$	THF	2	reflux	58
5	$CoCl_2{\cdot}6H_2O$	CH_3CN	2	reflux	55
6	$CoCl_2{\cdot}6H_2O$	CH_2Cl_2	2	reflux	0
7	$CoCl_2{\cdot}6H_2O$	C_6H_6	2	reflux	71

solvents such as MeOH and EtOH; polar non protic solvents such as THF, CH_3CN and CH_2Cl_2 and in the non polar non protic solvent such as C_6H_6. The results are shown in Table 4.

As can be seen, the best result was achieved when the reaction was carried out under reflux of *i*-PrOH (Table 4, entry 1). On the other hand, the reaction did not proceed in CH_2Cl_2 (entry 6). It should be noted that the yield of product **5a** in the reaction performed in C_6H_6 was similar to those obtained in MeOH or EtOH (entries 7, 2 and 3, respectively).

Solventless CFC reactions of indoles with nitrostyrenes

Due to the constant search for environmentally-friendly protocols that avoid the collateral production of wastes in the synthetic organic chemistry, many efforts have been made to develop organic reactions in solventless conditions.[54-56]

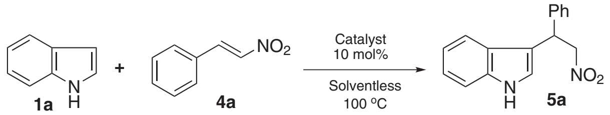
Therefore, we decided to investigate the viability of CFC reaction of indoles and nitrostyrenes catalyzed by metal halide hydrates under solventless conditions. The results are summarized in Table 5.

The best result was achieved when $CoCl_2{\cdot}6H_2O$ was employed over 15 min at 100 °C (entry 1). Good yields were also achieved with $CrCl_3{\cdot}6H_2O$ and $CeCl_3{\cdot}7H_2O$ with little increase of the reaction times (entries 2 and 3). The employment of $MnCl_2{\cdot}4H_2O$, $NiCl_2{\cdot}6H_2O$ or $SrCl_2{\cdot}6H_2O$ showed lower activity and an increase of the reaction time was needed to complete the consumption of the reagents (entries 4-6, respectively). In presence of $SnCl_2{\cdot}2H_2O$, even over prolonged time, poor yield was obtained (entry 7).

To explore the generality of the solventless conjugated Friedel-Crafts reaction, we synthesized a set of nitrostyrene derivatives through a methodology reported in the literature.[57] Reaction of nitromethane with various aromatic aldehydes in the presence of ammonium acetate under heating (Scheme 4) afforded the respective nitroolefins **4a-g** in 65-89% yields, after recrystallization (Figure 2).

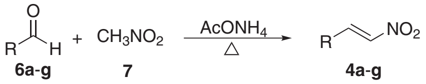
The solventless CFC reactions were carried out under the same conditions disclosed above and afforded the respective nitro adducts **5b-q**. The results are summarized in Table 6.

Table 5. Synthesis of adduct **5a** under different catalysts in solventless conditions



Entry	Catalyst	Condition	time (h)	Temp. (°C)	Yield (%)
1	$CoCl_2{\cdot}6H_2O$	solventless	0,25	100	97
2	$CrCl_3{\cdot}6H_2O$	solventless	0,50	100	81
3	$CeCl_3{\cdot}7H_2O$	solventless	0,50	100	93
4	$MnCl_2{\cdot}4H_2O$	solventless	2	100	95
5	$NiCl_2{\cdot}6H_2O$	solventless	8	100	95
6	$SrCl_2{\cdot}6H_2O$	solventless	12	100	96
7	$SnCl_2{\cdot}2H_2O$	solventless	120	100	57

In general, all reactions afforded the nitro-adducts in good yields. The reactivity of the nitroolefin **4d** was lower for both indoles **1a** and **1b** (entries 3 and 10, respectively). This may be due to the strong electron releasing effect of the *N*,*N*-dimethyl group attached at 4-position of the aromatic ring. Also, the steric hindrance caused by the bulky naphtyl group could be responsible for de increase of the reaction times with the indoles **1a** and **1c** and the nitroolefin **4f** (entry 5 and 15, respectively).



Scheme 4. Synthesis of nitroolefins **4a-g.**

Synthesis of β-carboline derivative via Pictet-Spengler reaction

To demonstrate the synthetic utility of the nitro adduct intermediate **5a** we performed the transformation of the nitro group into an amino group by reduction in the presence of NH_4OAc and catalytic amounts of Pd/C.[58] The triptamine derivative **8** was obtained in 90% yield as a crude product.

After the treatment of compound **8** with benzaldehyde under the Pictet-Spengler reaction conditions, the

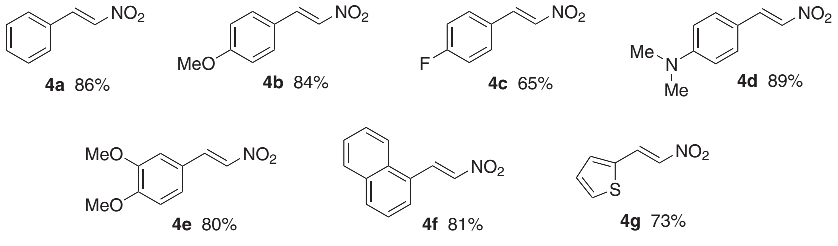
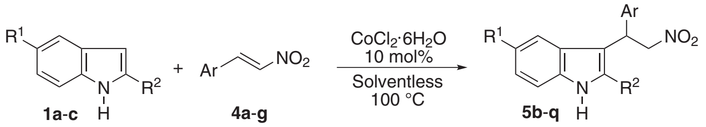


Figure 2. Structures of nitroolefins **4a-g**.

Table 6. Synthesis of adduct **5b**-**q** by CFC reaction under solventless conditions



entry		Indole			Nitroolefin	time (min)	Product	Yield (%)
		R^1	R^2		Ar			
1	**1a**	H	**H**	**4b**	4-MeO-C_6H_4	15	**5b**	92
2	**1a**	H	H	**4c**	4-F-C_6H_4	15	**5c**	97
3	**1a**	H	H	**4d**	4-*N*,*N*(Me)$_2$-C_6H_4	60	**5d**	98
4	**1a**	H	H	**4e**	3,4-(MeO)-C_6H_3	15	**5e**	90
5	**1a**	H	H	**4f**	1-naphtyl	30	**5f**	97
6	**1a**	H	H	**4g**	2-thienyl	15	**5g**	98
7	**1b**	MeO	H	**4a**	Ph	15	**5h**	95
8	**1b**	MeO	H	**4b**	4-MeO-C_6H_4	15	**5i**	86
9	**1b**	MeO	H	**4c**	4-F-C_6H_4	15	**5j**	96
10	**1b**	MeO	H	**4d**	4-*N*,*N*(Me)$_2$-C_6H_4	30	**5k**	87
11	**1b**	MeO	H	**4e**	3,4-(MeO)-C_6H_3	15	**5l**	98
12	**1b**	MeO	H	**4f**	1-naphtyl	15	**5m**	98
13	**1b**	MeO	H	**4g**	2-thienyl	15	**5n**	93
14	**1c**	H	Me	**4a**	Ph	15	**5o**	94
15	**1c**	H	Me	**4f**	1-naphtyl	30	**5p**	93
16	**1c**	H	Me	**4g**	2-thienyl	15	**5q**	98

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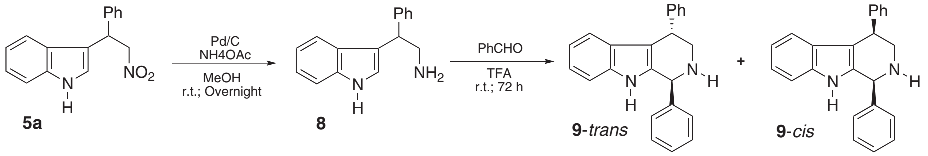

Scheme 5. Synthesis of 1,2,3,4-tetrahydro-β-carbolines.

β-Carboline derivative **9** was isolated as a diastereomeric mixture of 87:13 ratios. After purification by chromatography, the compound **9**-*trans* was isolated in 70% yield. The relative *trans* configuration of the major distereoisomer was inferred by comparison of the ^{1}H NMR data with the reported literature (Scheme 5).[59]

Conclusions

We have demonstrated that many metal halides hydrates are able to catalyze the conjugate Friedel-Crafts reaction of indoles and activated olefins in good to excellent yields. The alcoholic solvents were superior and *i*-PrOH was found to be the best choice.

For the reactions with aliphatic enones longer reaction times were needed for those reaction carried out at room temperature, whereas shorter times were observed under refluxing conditions. The metal halide hydrates $SnCl_2 \cdot 2H_2O$, $MnCl_2 \cdot 4H_2O$, $CrCl_2 \cdot 6H_2O$, $CoCl_2 \cdot 6H_2O$ were all effective.

Chalcones as Michael acceptors afforded the desired adducts only under refluxing conditions using $SnCl_2 \cdot 2H_2O$ as catalysts.

For the reaction with of nitroolefins, refluxing conditions are imperative under the liquid phase. Here, the alcoholic *i*-PrOH was superior. On the other hand, $SnCl_2 \cdot 2H_2O$ leads to the formation of several byproducts and therefore it was abandoned. The best results were achieved in the presence of $CoCl_2 \cdot 6H_2O$. These reactions were also investigated in the absence of solvents under 100 °C. The metal halide hydrates $CoCl_2 \cdot 6H_2O$, $CrCl_3 \cdot 6H_2O$, $CeCl_3 \cdot 7H_2O$, $MnCl_2 \cdot 4H_2O$, $NiCl_2 \cdot 6H_2O$ and $SrCl_2 \cdot 6H_2O$ were all effective in the reaction, but with different reaction times. The $CoCl_2 \cdot 6H_2O$, $CrCl_3 \cdot 6H_2O$ and $CeCl_3 \cdot 7H_2O$ were the most effective catalysts. In summary, we have demonstrated the use of cheaper and easy to handle metal halide hydrates as Lewis acids catalysts in the conjugated Friedel-Crafts reaction under enviromentally benign alcoholic solvents or under eco-friendly solventless protocols.

Experimental

All reactions were carried out under air. The chalcones[47] (**2f**-**i**) and the nitrostyrenes[57] (**4a**-**g**) were prepared according to the literature. All other reagents and solvents were purchased from commercial suppliers and used without further purification except hexane which was distilled prior to use. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian VNMRS spectrometer at 300 MHz and 75 MHz, respectively. The chemical shifts (δ) are reported in ppm relative to TMS (0.00 ppm) for ^{1}H NMR and to the central line of $CDCl_3$ (77.0 ppm) for ^{13}C NMR. Coupling constants *J* are reported in Hertz (Hz). IR spectra were recorded on a FTIR-Varian 640-IR spectrometer. Melting points were measured on an Olympus BX41 microscope equipped with a Mettler-Toledo FP82HT hot stage (Mettler-Toledo FP90 controller) and are uncorrected. Reactions were monitored using thin layer chromatography (TLC) carried out on Merck silica gel 60 F_{254} precoated aluminium plates. The visualization was achieved under UV light (254 nm) or staining with I_2. Chromatographic separations were achieved on silica gel columns (70-230 mesh, Aldrich) using gradient of hexanes/ethyl acetate as eluent.

General procedure for the synthesis of β-indolylketones ***3a-m***

In a 25 mL round-bottom flask, equipped with magnetic stirrer were added the indoles **1a**-**c** (1.0 mmol), the α,β-unsaturated ketones **2a**-**e** (1.1 mmol) and $SnCl_2\cdot 2H_2O$ (0.1 mmol) in *i*-PrOH (2 mL). The reaction mixture was stirred at room temperature for the appropriate time shown in the Table 2. After the completion of the reaction, monitored by TLC, the solvent was removed under vacuum and the crude products **3a-m** were purified by column chromatography using a gradient of hexanes/ethyl acetate as eluent.

5-(1H-Indol-3-yl)hexan-3-one (***3a***):[60] 96%, viscous brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (br s, 1H), 7.63 (m, 1H), 7.28 (m, 1H), 7.18-7.04 (m, 2H), 6.82 (s, 1H), 3.62 (m, 1H), 2.86 (dd, *J* 15.9 and 6.3 Hz, 1H), 2.64 (dd, *J* 15.9 and 8.1 Hz, 1H), 2.31 (q, *J* 7.2 Hz, 2H), 1.34 (d, *J* 6,9 Hz, 3H), 0.96 (t, *J* 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.8, 136.4, 126.0, 121.7, 120.5, 120.2, 118.9, 118.9, 111.3, 50.1, 36.3, 26.9, 21.1, 7,6; IR ν_{max}/cm^{-1} (neat, film) 3411 (NH), 2971, 1705 (C=O), 1458, 1375, 1354, 1341, 743.

1-(1H-Indol-3-yl)pentan-3-one (***3b***):[61] 96%, brown solid, mp 86-87 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (br s, 1H), 7.56 (d, *J* 7.8 Hz, 1H), 7.27 (d, *J* 8.1Hz, 1H), 7.20-7.05 (m, 2H), 6.89 (d, *J* 1.8 Hz, 1H), 3.03 (t, *J* 7.2 Hz, 2H), 2.77 (t, *J* 7.2 Hz, 2H), 2.26 (q, *J* 7.5 Hz, 2H), 1.01 (t, *J* 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.8, 136.2, 127.0, 121.8, 121.5, 119.0, 118.5, 114.9, 111.2, 42.7, 35.9, 19.3, 7.7; IR ν_{max}/cm^{-1} (KBr) 3323 (NH), 1704 (C=O), 1458, 736.

4-(1H-Indol-3-yl)nonan-2-one (***3c***):[60] 96%, viscous brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.64 (d, *J* 7.8 Hz, 1H), 7.31 (d, *J* 7.8 Hz, 1H), 7.21-7.05 (m, 2H), 6.91 (d, *J* 2.4 Hz, 1H), 3.43 (m, 1H), 2.88 (dd, *J* 15.9 and 7.5 Hz, 1H), 2.78 (dd, *J* 15.9 and 6.9 Hz, 1H), 2.00 (s, 3H), 1.62-1.82 (m, 2H), 1.23 (br s, 6H), 0.81 (br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 136.5, 126.5, 121.8, 121.2, 119.2, 119.1, 118.8, 111.3, 50.2, 35.8, 32.9, 31.8, 30.4, 27.2, 22.5, 14.0; IR ν_{max}/cm^{-1} (neat, film) 3412 (NH), 2956, 2928, 2856, 1707 (C=O), 1458, 1357, 742 .

3-(1H-Indol-3-yl)-cyclopentanone (***3d***):[61] 96%, viscous brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (br s, 1H), 7.60 (d, *J* 7.8 Hz, 1H), 7.32 (dd, *J* 7.8 and 0.9 Hz, 1H), 7.19 (dt, *J* 7.5 and 1.2 Hz, 1H), 7.12 (dt, *J* 7.5 and 1.2 Hz, 1H), 6.88 (d, *J* 1.8 Hz, 1H), 3.65 (m, 1H), 2.72 (dd, *J* 18.0 and 7.2 Hz, 1H), 2.65-2.17 (m, 4H), 2.17-1.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 220.0, 136.6, 126.5, 122.1, 120.0, 119.2, 118.9, 118.2, 111.3, 45.2, 38.1, 33.6, 29.7; IR ν_{max}/cm^{-1} (neat, film) 3410 (NH), 1734 (C=O), 1458, 1401, 1230, 1169, 744.

3-(1H-Indol-3-yl)-cyclohexenone (***3e***):[60] 40%, viscous brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (br s, 1H), 7.61 (d, *J* 7.8 Hz, 1H), 7.34 (d, *J* 8.1 Hz, 1H), 7.20 (t, *J* 7.5 Hz, 1H), 7.11 (t, *J* 7.5 Hz, 1H), 6.94 (d, *J* 1.5 Hz, 1H), 3.43 (m, 1H), 2.92-2.72 (m, 1H), 2.72-2.57 (m, 1H), 2.57-2.33 (m, 2H), 2.33-2.16 (m, 1H), 2.16-1.62 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.1, 136.4, 126.0, 122.1, 120.4, 119.5, 119.2, 118.9, 111.3, 48.0, 41.5, 35.9, 31.6, 24.8; IR ν_{max}/cm^{-1} (neat, film) 3411 (NH), 2971, 1705 (C=O), 1458, 1375, 1354, 1340, 743.

5-(5-Methoxy-1H-indol-3-yl)hexan-3-one (***3f***):[62] 98%, viscous brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (br s, 1H), 7.16 (d, *J* 8.7 Hz, 1H), 7.06 (d, *J* 2.1 Hz, 1H), 6.86 (d, *J* 2.1 Hz, 1H), 6.83 (dd, *J* 8.7 and 2.1 Hz, 1H), 3.84 (s, 3H), 3.59 (m, 1H), 2.86 (dd, *J* 15.9 and 6.0 Hz, 1H), 2.65 (dd, *J* 15.9 and 8.4 Hz, 1H), 2.32 (q, *J* 7.2 Hz, 2H), 1.34 (d, *J* 6.9 Hz, 3H), 0,98 (t, *J* 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.6; 153.5, 131.6, 126.4; 121.0; 120.4, 112.0, 111.7, 100.9, 55.8, 50.0, 36.3, 26.8, 21.1, 7.5; IR ν_{max}/cm^{-1} (neat, film) 3407 (NH), 3383, 2964, 1705 (C=O).

*1-(5-Methoxy-1H-indol-3-yl)-pentan-3-one (**3g**):* 80%, brown solid, mp 94-95 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.89 (br s, 1H), 7.24 (d, *J* 8.7 Hz, 1H), 7.02 (d, *J* 2.4 Hz, 1H), 6.96 (d, *J* 2.4 Hz, 1H), 6.85 (dd, *J* 8.7 and 2.4 Hz, 1H), 3.87 (s, 3H), 3.02 (t, *J* 7.5 Hz, 2H), 2.81 (t, *J* 7.5 Hz, 2H), 2.42 (q, *J* 7.2 Hz, 2H), 1.05 (t, *J* 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 211.5, 153.9, 131.4, 127.6, 122.2, 115.1, 112.2, 111.8, 100.6, 56.0, 42.6, 36.1, 19.4, 7.8; IR ν_{max}/cm^{-1} (KBr) 3340 (NH), 1704 (C=O), 1487, 1456, 1211, 1173, 806. HRMS(ESI$^+$, *m*/Na$^+$) Found: 254.11510. Calc. for C$_{14}$H$_{17}$O$_2$N/Na$^+$: 254.11515.

*4-(5-Methoxy-1H-indol-3-yl)-nonan-2-one (**3h**):*[60] 90%, viscous brown oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.35 (br s, 1H), 7.16 (d, *J* 8.7 Hz, 1H), 7.08 (d, *J* 2.4Hz, 1H), 6.87 (d, *J* 2.4Hz, 1H), 6.82 (dd, *J* 8.7 and 2.4 Hz, 1H), 3.85 (s, 3H), 3.42 (m, 1H), 2.85 (dd, *J* 15.9 and 7.5 Hz, 1H), 2.76 (dd, *J* 15.9 and 6.9 Hz, 1H), 2.00 (s, 3H), 1.60-1.80 (m, 2H), 1.38-1,07 (br s, 6H), 0.81 (br s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 209.3, 153.4, 131.7, 126.8, 122.0, 118.3, 111.9, 111.5, 101.2, 55.8, 50.0, 35.7, 32.6, 31.7, 30.3, 27.1, 22.4, 13.9; IR ν_{max}/cm^{-1} (neat, film) 3408 (NH), 2954, 2929, 1707 (C=O), 1484, 1457, 1215.

*3-(5-Methoxy-1H-indol-3-yl)-cyclopentanone (**3i**):* viscous brown oil, 95%; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.45 (br s, 1H), 7.21 (d, *J* 8.7 Hz, 1H), 7.05 (d, *J* 2.4 Hz, 1H), 6.88 (d, *J* 2.1 Hz, 1H), 6.87 (dd, *J* 8.7 and 2.1 Hz, 1H), 3.85 (s, 3H), 3.62 (m, 1H), 2.72 (dd, *J* 18.0 and 7.2 Hz, 1H), 2.55-2.22 (m, 4H), 2.15-1.98 (m, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 219.8, 153.5, 131.7, 126.8, 120.8, 117.7, 112.0, 111.9, 100.9, 55.8, 45.1, 37.9, 33.4, 29.5; IR ν_{max}/cm^{-1} (neat, film) 3408 (NH), 1736 (C=O), 1485, 1457, 1440, 1212, 1167.

*3-(5-Methoxy-1H-indol-3-yl)-cyclohexanone (**3j**):*[58] 41%, viscous brown oil,; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.11 (br s, 1H), 7.24 (d, *J* 8.7, 1H), 7.03 (d, *J* 2.4 Hz, 1H), 6.95 (d, *J* 2.1 Hz, 1H), 6.94 (dd, *J* 8.7 and 2.4 Hz, 1H), 3.84 (s, 3H), 3.39 (m, 1H), 2.86-2.73 (m, 1H), 2.63-2.51 (m, 1H), 2.51-2.33 (m, 2H), 2.33-2.20 (m, 1H), 2.13-1.73 (m, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 212.0, 153.8, 131.6, 126.4, 121.2, 119.2, 112.2, 112.0, 110.9, 56.0, 48.0, 41.5, 35.8, 31.5, 24.9; IR ν_{max}/cm^{-1} (neat, film) 3406 (NH), 2360, 1701 (C=O), 1484, 1456, 1216, 1171.

*5-(2-Methyl-1H-indol-3-yl)-hexan-3-one (**3k**):* 88%, viscous brown oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.96 (br. s, 1H), 7.59 (m, 1H), 7.17-7.10 (m, 1H), 7.09-6.98 (m, 2H), 3.55 (m, 1H), 2.97 (dd, *J* 15.6 and 7.8 Hz), 2.76 (dd, *J* 15.6 and 7.2 Hz), 2.32-2.21 (m, 5H), 1.39 (d, *J* 7.2 Hz, 3H), 0.87 (d, *J* 7.5 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 211.8, 135.4, 130.4, 126.8, 120.3, 118.7, 118.6, 114.6, 110.5, 49.1, 36.5, 27.1, 21.0, 11.6, 7.5; IR ν_{max}/cm^{-1} (neat, film) 3400 (NH), 2969, 2933, 1705 (C=O), 1461, 742. HRMS (ESI$^+$, *m*/Na$^+$) Found: 252.13575. Calc. for C$_{15}$H$_{19}$ON/Na$^+$: 252.13589.

*1-(2-Methyl-1H-indol-3-yl)pentan-3-one (**3l**):* 97%, viscous brown oil; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.91 (br s, 1H), 7.44 (m, 1H), 7.20-6.94 (m, 3H), 2.95 (t, *J* 7.2 Hz, 2H), 2.68 (t, *J* 7.2 Hz, 2H), 2.35-2.20 (m, 5H), 0.97 (t, *J* 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 211.9, 135.1, 131.1, 128.0, 120.6, 118.8, 117.5, 110.3, 110.0, 42.7, 36.1, 18.4, 11.2, 7.6; IR ν_{max}/cm^{-1} (neat, film) 3400 (NH), 2975, 2936, 2919, 1708 (C=O), 1462, 742. HRMS (ESI$^+$, *m*/Na$^+$) Found: 238.12015. Calc. for C$_{14}$H$_{17}$ON/Na$^+$: 238.12024.

*3-(2-Methyl-1H-indol-3-yl)-cyclopentanone (**3m**):*[46] 81%, yellow solid; mp 135-136 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.98 (br s, 1H), 7.53 (d, *J* 7.5 Hz, 1H), 7.28 (d, *J* 7.8 Hz, 1H), 7.23-7.00 (m, 2H), 3.59 (m, 1H), 2.87-2.20 (m, 10H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 219.8, 135.5, 130.9, 126.7, 120.9, 119.1, 118.6, 111.8, 110.7, 44.3, 39.4, 34.5, 29.7, 12.1; IR ν_{max}/cm^{-1} (KBr) 3342 (NH), 2961, 2897, 1729 (C=O), 1461, 1231, 1137, 743.

*General procedure for the synthesis of β-indolylchalcones **3r**-z*

In a 25 mL round-bottom flask, equipped with a reflux condenser and magnetic stirrer were added the indoles **1a**-**c** (1.0 mmol), the chalcones **2f**-**i** (1.1 mmol), and SnCl$_2$·2H$_2$O (0.1 mmol) in *i*-PrOH (2 mL). The reaction mixture was heated to reflux and stirred for the appropriate time showed in the Table 3. After the completion of the reaction, monitored by TLC, the solvent was removed under vaccum and the crude products **3r-z** were purified by column chromatography using hexanes/ethyl acetate as eluant.

*3-(1H-Indol-3-yl)-1,3-diphenylpropan-1-one (**3r**):*[64] 96%,brownish solid, mp 130-131 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.03 (br s, 1H), 7.91 (d, *J* 7.5 Hz, 2H), 7.51 (t, *J* 7.2 Hz, 1H), 7.46-7.06 (m, 10H), 6.99 (t, *J* 7.2 Hz, 1H), 6.90 (s, 1H), 5.05 (m, 1H), 3.80 (dd, *J* 16.8 and 6.9 Hz, 1H), 3.70 (dd, *J* 16.8 and 7.8 Hz, 1H); ^{13}C NMR (75 MHz, CDCl$_3$,) δ 198.7, 144.2, 137.0, 136.6, 133.0, 128.5, 128.4, 128.1, 127.8, 126.5, 126.2, 122.0, 121.4, 119.4, 119.3, 119.1, 111.1, 45.2, 38.2; IR ν_{max}/cm^{-1} (KBr) 3411 (NH), 1681 (C=O), 1456, 1448, 745, 700.

*3-(1H-Indol-3-yl)-3-(naphthalen-1-yl)-1-phenylpropan -1-one (**3s**)*: 60%, brownish solid, mp 97-98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (m, 1H), 7.96-7.80 (m, 4H), 7.68 (d, *J* 7.5 Hz, 1H), 7.54-7.17 (m, 9H), 7.09 (m, 1H), 6.96 (m, 1H), 6.70 (s, 1H), 5.92 (m, 1H), 3.94 (dd, *J* 17.4 and 7.8 Hz, 1H), 3.73 (dd, *J* 17.4 and 6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$,) δ 198.5, 139.9, 137.0, 136.6, 134.0, 133.1, 131.4, 128.8, 128.6, 128.0, 127.0, 126.6, 126.1, 125.5, 125.3, 124.4, 123.6, 122.2, 122.0, 119.4, 119.3, 118.9, 111.2, 44.6, 33.2; IR ν_{max}/cm^{-1} (KBr) 3412 (NH), 3055, 1681 (C=O), 1596, 1448, 1337, 1269, 780, 743; HRMS (ESI$^+$, *m*/Na$^+$) Found: 398.15161.Calc. for $C_{27}H_{21}ON/Na^+$: 398.15154.

*3-(1H-Indol-3-yl)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**3t**)*:[64] 80%, brownish solid, mp 114-115 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (br s, 1H), 7.92 (d, *J* 7.8 Hz, 2H), 7.53 (t, *J* 7.5 Hz, 1H), 7.47-7.36 (m, 3H), 7.29 (d, *J* 7.8 Hz, 1H), 7.25 (d, *J* 8.4 Hz, 2H), 7.13 (t, *J* 7.5 Hz, 1H), 7.00 (t, *J* 7.5, 1H), 6.95 (d, *J* 1.5 Hz, 1H), 6.78 (d, *J* 8.4 Hz, 2H), 5.01 (t, *J* 6.9 Hz, 1H), 3.83-3.63 (m, 5H); δ ^{13}C NMR (75 MHz, $CDCl_3$,) 198.8, 157.9, 137.1, 136.6, 136.3, 133.0, 128.7, 128.5, 128.1, 126.5, 122.0, 121.3, 119.5, 119.3, 113.7, 111.1, 55.1, 45.3, 37.4; IR ν_{max}/cm^{-1} (KBr) 3420 (NH), 1670 (C=O), 1510, 1249, 1177, 1031, 746.

*3-(1H-Indol-3-yl)-1-phenyl-3-(thiophen-2-yl)-propan-1-one (**3u**)*:[65] 74%, brown solid, mp 153-154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.93 (d, *J* 8.1 Hz, 2H), 7.53 (t, *J* 7.5 Hz, 2H), 7.42 (t, *J* 7.5 Hz, 2H), 7.31 (d, *J* 8.1 Hz, 1H), 7.20-7.00 (m, 4H), 6.95-6.83 (m, 2H), 5.36 (t, *J* 7.2 Hz, 1H), 3.83 (d, *J* 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$,) δ 198.1, 148.7, 137.0, 136.5, 133.1, 128.6, 128.1, 126.5, 126.2, 124.2, 123.4, 122.2, 121.6, 119.5, 119.4, 119.0, 111.2, 46.1, 33.5; IR ν_{max}/cm^{-1} (KBr) 3409 (NH), 3057, 1682 (C=O), 1268, 743, 689.

*3-(5-Methoxy-1H-indol-3-yl)-1,3-diphenylpropan-1-one (**3v**)*:[66] 96%, yellow solid, mp 136-137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.92 (d, *J* 7.2 Hz, 2H), 7.6-7.1 (m, 9H), 6.92 (d, *J* 1.5 Hz, 1H), 6.85-6.73 (m, 2H), 5.00 (m, 1H), 3.84-3.64 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 153.7, 144.1, 137.1, 133.0, 131.7, 128.5, 128.4, 128.1, 127.8, 127.0, 126.2, 122.2, 118.8, 112.1, 111.8, 101.4, 55.7, 45.1, 38.2; IR ν_{max}/cm^{-1} (KBr) 3366 (NH), 1679 (C=O), 1485, 1457, 1448, 1214, 1170, 723.

*3-(5-Methoxy-1H-indol-3-yl)-3-(naphthalen-1-yl)-1-phenylpropan-1-one (**3w**)*: 95%, pale brown solid, mp 156-157 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35-8.26 (m, 1H), 7.94 (d, *J* 7.8 Hz, 2H), 7.90-7.78 (m, 2H), 7.70 (d, *J* 6.9 Hz, 1H), 7.58-7.29 (m, 7H), 7.15 (d, *J* 9.0 Hz, 1H), 6.85 (d, *J* 2.1 Hz, 1H), 6.82-6.74 (m, 2H), 5.88 (m, 1H), 3.95 (dd, *J* 17.4 and 7.8 Hz, 1H), 3.79 (dd, *J* 17.4 and 6.3 Hz, 1H), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 153.8, 139.8, 137.1, 134.1, 133.1, 131.8, 131.5, 128.6, 128.5, 128.1, 127.1, 127.0, 126.1, 125.5, 125.3, 124.3, 123.6, 122.9, 118.8, 112.2, 111.8, 101.3; 55.8, 44.6, 33.2; IR ν_{max}/cm^{-1} (KBr) 3412 (NH), 1680 (C=O), 1484, 1212, 780; HRMS (ESI$^+$, *m*/Na$^+$) Found: 428.16208. Calc. for $C_{28}H_{23}O_2N/Na^+$: 428.16210.

*3-(5-Methoxy-1H-indol-3-yl)-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**3x**)*: 95%, brown solid, mp 70-71 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (br s, 1H), 7.91 (d, *J* 7.8Hz, 2H), 7.52 (t, *J* 7.8 Hz, 1H), 7.40 (t, *J* 7.5 Hz, 2H), 7.24 (d, *J* 8.7 Hz, 2H), 7.14 (d, *J* 8.7Hz, 1H), 6.90 (s, 1H), 6.83 (d, *J* 2.1 Hz, 1H), 6.77 (d, *J* 8.4 Hz, 3H), 4.95 (t, *J* 7.2 Hz, 1H), 3.81-3.61 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.9, 157.9, 153.6, 137.1, 136.2, 133.0, 131.7, 128.7, 128.5, 128.0, 126.9, 122.1, 119.1, 113.7, 112.0, 111.8, 101.4, 55.7, 55.1, 45.2, 37.4; IR ν_{max}/cm^{-1} (KBr) 3400 (NH), 2929, 1683 (C=O), 1509, 1485, 1247, 1212, 1175, 1033; HRMS (ESI$^+$, *m*/ Na$^+$) Found: 408.15689. Calc. for $C_{25}H_{23}O_3N/Na^+$: 408.15702.

*3-(5-Methoxy-1H-indol-3-yl)-1-phenyl-3-(thiophen-2-yl)propan-1-one (**3y**)*: 92%, pale yellow solid, mp 153-154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98-7.88 (m, 3H), 7.54 (m, 1H), 7.43 (m, 2H), 7.21 (d, *J* 8.7 Hz, 1H), 7.10 (m, 1H), 7.04 (d, *J* 2.4 Hz, 1H), 6.95 (d, *J* 2.4 Hz, 1H), 6.94-6.85 (m, 2H), 6.83 (dd, *J* 8.7 and 2.4 Hz, 1H), 5.32 (m, 1H), 3.82-3.75 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 153.9, 148.7, 137.0, 133.1, 131.6, 128.6, 128.1, 126.7, 126.5, 124.2, 123.5, 122.3, 118.8, 112.3, 111.9, 101.3, 55.9, 46.0, 33.4; IR ν_{max}/cm^{-1} (KBr) 3382 (NH), 1680 (C=O), 1485, 1438, 1213, 1171, 732; HRMS (ESI$^+$, *m*/Na$^+$) Found: 384.10283. Calc. for $C_{22}H_{19}O_2N/Na^+$: 384.10287.

*3-(2-Methyl-1H-indol-3-yl)-1,3-diphenylpropan-1-one (**3z**)*:[46] 96%, brownish solid, mp 130-131 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.91 (d, *J* 7.5 Hz, 2H), 7.51 (t, *J* 7.2 Hz, 1H), 7.46-7.06 (m, 10H), 6.99 (t, *J* 7.2 Hz, 1H), 6.90 (s, 1H), 5.05 (m, 1H), 3.80 (dd, *J* 16.8 and 6.9 Hz, 1H), 3.70 (dd, *J* 16.8 and 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 144.2, 137.0, 136.6, 133.0, 128.5, 128.4, 128.1, 127.8, 126.5, 126.2, 122.0, 121.4, 119.4, 119.3, 119.1, 111.1, 45.2, 38.2; IR ν_{max}/cm^{-1} (KBr) 3411 (NH), 1681 (C=O), 1456, 1448, 745, 700.

*Procedure for the synthesis of nitro-adducts **5a** in i-PrOH*

In a 25 mL round botton flask equipped with a reflux condenser, and magnetic stirrer was added the indole **1a** (1.0 mmol), the nitroolefin **4a** (1.1 mmol), and the $CoCl_2 \cdot 6H_2O$ (0.1 mmol) in *i*-PrOH (2 mL). The reaction mixture was heated to reflux temperature of *i*-PrOH and stirred for 2 h. After the completion of the reaction, monitored by TLC, the solvent was removed under vaccum and the crude product **5a** was purified by column chromatography using a mixture of hexanes/ethyl acetate 70:30 (v/v) as eluent.

*3-(2-Nitro-1-phenylethyl)-1H-indole (**5a**)*:[62] 97%, brownish solid, mp 99-100 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (br s, 1H), 7.37 (d, *J* 8.1 Hz, 1H), 7.25-7.05 (m, 7H), 7.00 (t, *J* 7.2 Hz, 1H), 6.72 (d, *J* 1.8 Hz, 1H), 5.08 (m, 1H), 4.87 (dd, *J* 12.3 and 7.5 Hz, 1H), 4.76 (dd, *J* 12.3 and 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 136.2, 128.7, 127.6, 127.3, 125.8, 122.3, 121.5, 119.6, 118.6, 113.7, 111.3, 79.3, 41.3; IR ν_{max}/cm^{-1} (KBr) 3401 (NH), 3052, 1536, 1455, 1424, 1377, 1097, 750, 704.

*General procedure for the synthesis of nitro-adducts **5b**-**q** under solventless conditions*

In a 25 mL round-botton flask equiped with a reflux condenser, and magnetic stirrer, were added the indoles **1a**-**c** (1.0 mmol), the nitroolefins **4b**-**g** (1.1 mmol) and $CoCl_2 \cdot 6H_2O$ (0.1 mmol). The reactional flask was placed in a 100 °C pre-heated silicone oil bath and was stirred for the appropriate time showed in the Table 6. After the completion of the reaction, monitored by TLC, the crude product **5b**-**q** were purified by column chromatography using a mixture of hexanes/ethyl acetate.

*3-(1-(4-Methoxyphenyl)-2-nitroethyl)-1H-indole (**5b**)*:[67] 92%, brownish solid, mp 146-147 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (br s, 1H), 7.43 (d, *J* 8.1 Hz, 1H), 7.35 (d, *J* 8.1 Hz, 1H), 7.24 (d, *J* 8.4 Hz, 2H), 7.19 (t, *J* 7.5 Hz, 1H), 7.07 (t, *J* 7.5 Hz, 1H), 7.01 (d, *J* 1.5 Hz, 1H), 6.84 (d, *J* 8.4 Hz, 2H), 5.14 (m, 1H), 5.04 (dd, *J* 12.3 and 7.5 Hz, 1H), 4.89 (dd, *J* 12.3 and 8.4 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 136.5, 131.2, 128.8, 126.1, 122.6, 121.4, 119.9, 119.0, 114.8, 114.3, 111.3, 79.7, 55.2, 40.8; IR ν_{max}/cm^{-1} (KBr) 3379 (NH), 1547, 1511, 1463, 1422, 1377, 1245, 1029, 750.

*3-(1-(4-Fluorophenyl)-2-nitroethyl)-1H-indole (**5c**)*:[67] 97%, orange solid, mp 77-78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (br s, 1H), 7.39 (d, *J* 7.8 Hz, 1H), 7.37-7.16 (m, 4H), 7.11-6.95 (m, 4H), 5.16 (m, 1H), 5.04 (dd, *J* 12.6 and 7.5 Hz, 1H), 4.89 (dd, *J* 12.6 and 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1 (d, *J* 245 Hz), 136.5, 134.9 (d, *J* 3 Hz), 129.3 (d, *J* 8 Hz), 125.9, 122.8, 121.4, 120.0, 118.8, 115.8 (d, *J* 21 Hz), 114.2, 111.4, 79.5, 40.8; IR ν_{max}/cm^{-1} (KBr) 3371 (NH), 1542, 1508, 1430, 1378, 1224, 748.

*4-(1-(1H-Indol-3-yl)-2-nitroethyl)-N,N-dimethylaniline (**5d**)*:[68] 98%, pink solid, mp 131-133 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (br s, 1H); 7.46 (d, *J* 8.1 Hz, 1H); 7.35 (d, *J* 8.1 Hz, 1H); 7.24-7.00 (m, 5H); 6.71 (d, *J* 8.4 Hz, 2H); 5.10 (m, 1H); 5.03 (dd, *J* 11.7 and 7.5 Hz, 1H); 4.88 (dd, *J* 11.7 and 8.4 Hz, 1H); 2.92 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.8; 136.5; 128.4; 126.7; 126.2; 122.5; 121.4; 119.8; 119.1; 115.1; 112.7; 111.3; 79.9; 40.8; 40.5; IR ν_{max}/cm^{-1} (KBr) 3434 (NH), 2916, 1611, 1519, 1379, 817, 743.

*3-(1-(3,4-Dimethoxyphenyl)-2-nitroethyl)-1H-indole (**5e**)*:[69] 90%, orange solid, mp 79-80 °C; ^{1}H NMR (300 MHz, CDCl3) δ 8.27 (br s, 1H), 7.43 (d, *J* 7.8 Hz, 1H), 7.28 (d, *J* 8.1 Hz, 1H), 7.16 (t, *J* 7.5 Hz, 1H), 7.05 (t, *J* 7.5 Hz, 1H), 6.93 (s, 1H), 6.87-6.80 (m, 2H), 6.76 (d, *J* 8.1 Hz, 1H), 5.11 (m, 1H), 5.00 (dd, *J* 12.3 and 7.5 Hz, 1H), 4.87 (dd, *J* 12.3 and 8.4 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 149.0, 148.2, 136.4, 131.7, 125.9, 122.4, 121.5, 119.7, 119.6, 118.7, 114.2, 111.4, 111.3, 111.1, 79.6, 55.7, 41.1; IR ν_{max}/cm^{-1} (KBr) 3405 (NH), 1549, 1515, 1262, 1141, 1023, 745.

*3-(1-(Naphthalen-1-yl)-2-nitroethyl)-1H-indole (**5f**)*:[67] 97%, redish solid, mp 140-142 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (d, *J* 8.4 Hz), 8.05 (br s, 1H, NH), 7.91-7.86 (m, 1H), 7.82-7.74 (m, 1H), 7.59-7.32 (m, 6H), 7.23-7.15 (m, 1H), 7.09-6.97 (m, 2H), 6.07 (m, 1H), 5.12 (dd, *J* 12.9 and 8.1 Hz, 1H), 5.07 (dd, *J* 12.9 and 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6, 134.6, 134.2, 131.1, 129.1, 128.3, 126.8, 126.1, 125.9, 125.3, 124.6, 122.7, 122.6, 120.0, 118.8, 114.3, 111.4, 78.5, 37.0; IR ν_{max}/cm^{-1} (KBr) 3420 (NH), 1545, 1509, 1458, 1381, 796, 777, 743.

*3-(2-Nitro-1-(thiophen-2-yl)ethyl)-1H-indole (**5g**)*:[69] 98%, brown solid, mp 86-87 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.49 (d, *J* 8.1 Hz, 1H), 7.29 (d, *J* 8.1 Hz, 1H), 7.22-7.05 (m, 3H), 6.98 (d, *J* 2.7 Hz, 1H), 6.96-6.87 (m, 2H), 5.42 (m, *J* 7.8 Hz, 1H), 4.99 (dd, *J* 12.3 and 8.1 Hz, 1H), 4.92 (dd, *J* 12.3 and 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 136.2, 126.9, 125.5, 125.1, 124.8, 122.5, 121.9, 119.9, 118.6, 113.6, 111.5, 79.8, 36.7; IR ν_{max}/cm^{-1} (KBr) 3416 (NH), 1550, 1455, 1433, 1418, 1377, 747, 720.

*5-Methoxy-3-(2-nitro-1-phenylethyl)-1H-indole (**5h**)*:[67] 95%, brownish solid, mp 130-131 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.02 (br s, 1H), 7.32-7.15 (m, 6H), 6.93 (s, 1H), 6.86-6.80 (m, 2H), 5.11 (m, 1H), 5.00 (dd, *J* 12.3 and 7.5 Hz, 1H), 4.89 (dd, *J* 12.3 and 8.4 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 154.0, 139.1, 131.5, 128.8, 127.7, 127.5, 126.5, 122.3, 113.9, 112.6, 112.1, 100.7, 79.4, 55.8, 41.4; IR ν_{max}/cm^{-1} (KBr) 3447 (NH), 1548, 1482, 1453, 1440, 1379, 1209, 1177.

*5-Methoxy-3-(1-(4-methoxyphenyl)-2-nitroethyl)-1H-indole (**5i**)*: 86%, pale yellow solid, mp 141-142 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.00 (br s, 1H), 7.28-7.21 (m, 3H), 6.99 (d, *J* 2.1 Hz, 1H), 6.88-6.82 (m, 4H), 5.09 (m, 1H), 5.02 (dd, *J* 11.7 and 7.2 Hz, 1H), 4.88 (dd, *J* 11.7 and 7.8 Hz, 1H), 3.77 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 158.9, 154.2, 131.6, 131.1, 128.8, 126.6, 122.1, 114.4, 114.3, 112.7, 112.1, 100.9, 79.7, 55.8, 55.2, 40.8; IR ν_{max}/cm^{-1} (KBr) 3434 (NH), 2959, 1545, 1513, 1480, 1456, 1247, 1208.

*3-(1-(4-Fluorophenyl)-2-nitroethyl)-5-methoxy-1H-indole (**5j**)*: 96%, brown solid, mp 102-103 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.11 (br s, 1H); 7.28-7.20 (m, 2H), 7.17 (d, *J* 8.7 Hz, 1H), 7.00-6.88 (m, 3H), 6.83 (dd, *J* 8.7 and 2.4 Hz, 1H), 6.78 (d, *J* 2.1 Hz, 1H), 5.08 (m, 1H), 4.97 (dd, *J* 12.3 and 7.5 Hz, 1H), 4.83 (dd, *J* 12.3 and 8.4 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 161.9 (d, *J* 2.4 Hz), 154.0, 134.8 (d, *J* 3 Hz), 131.5, 129.3 (d, *J* 8 Hz), 126.3, 122.1, 115.7 (d, *J* 21 Hz), 113.6, 112.6, 112.2, 100.7, 79.4, 55.7, 40.7; IR ν_{max}/cm^{-1} (KBr) 3434 (NH), 1551, 1509, 1482, 1454, 1439, 1377, 1226, 1207, 808.

*4-(1-(5-Methoxy-1H-indol-3-yl)-2-nitroethyl)-N,N-dimethylaniline (**5k**)*: 87%, pink solid, mp 134-135 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.99 (br s, 1H), 7.23 (d, *J* 8.1 Hz, 1H), 7.21-7.14 (m, 2H), 6.96 (d, *J* 2.4 Hz, 1H), 6.87 (d, *J* 2.4 Hz, 1H), 6.83 (dd, *J* 8.7 and 2.4 Hz, 1H), 6.68 (d, *J* 9 Hz, 2H), 5.07-4.95 (m, 2H), 4.92-4.80 (m, 1H), 3.77 (s, 3H), 2.90 (s, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 154.0, 149.7, 131.6, 128.4, 126.9, 126.6, 122.2, 114.7, 112.9, 112.5, 112.0, 101.0, 79.8, 55.8, 40.7, 40.6; IR ν_{max}/cm^{-1} (KBr) 3408 (NH), 1616, 1541, 1524, 1484, 1376, 1210, 1201. HRMS (ESI$^+$) Found: 340.16545. Calc. for $C_{19}H_{21}O_3N_3$: 340.16557.

*3-(1-(3,4-Dimethoxyphenyl)-2-nitroethyl)-5-methoxy-1H-indole (**5l**)*: 98%, brownish solid, mp 131-132 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.31 (br s, 1H), 7.15 (d, *J* 8.7 Hz, 1H), 6.94-6.74 (m, 6H), 5.06 (m, 1H), 4.98 (dd, *J* 11.7 and 7.2 Hz, 1H), 4.86 (dd, *J* 11.7 and 8.4 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 153.9, 149.0, 148.1, 131.6, 131.5, 126.4, 122.2, 119.6, 113.8, 112.3, 112.1, 111.2, 111.1, 100.7, 79.5, 55.7, 55.7, 55.6, 41.1; IR ν_{max}/cm^{-1} (KBr) 3436 (NH), 2955, 2931, 2830, 1544, 1510, 1259, 1020. HRMS (ESI$^+$, *m*/Na$^+$) Found: 379.12635. Calc. for $C_{19}H_{20}O_5N_2/Na^+$: 379.12644.

*5-Methoxy-3-(1-(naphthalen-1-yl)-2-nitroethyl)-1H-indole (**5m**)*: 98%, brown solid, mp 76-77 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.25 (d, *J* 8.1 Hz, 1H), 7.97 (br s, 1H), 7.92-7.74 (m, 2H), 7.58-7.17 (m, 5H), 6.95-6.81 (m, 3H), 6.00 (t, *J* 7.8 Hz, 1H), 5.08 (d, *J* 7.8 Hz, 2H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 154.2, 134.6, 134.2, 131.7, 131.2, 129.1, 128.3, 126.8, 126.6, 125.9, 125.3, 124.5, 123.3, 122.7, 114.0, 112.7, 112.1, 100.7, 78.5, 55.8, 37.0; IR ν_{max}/cm^{-1} (KBr) 3420 (NH), 1549, 1484, 1457, 1437, 1376, 1213, 800.

*5-Methoxy-3-(2-nitro-1-(thiophen-2-yl)ethyl)-1H-indole (**5n**)*: 93%, greenish brown solid, mp 83-85 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.15 (br s, 1H), 7.26-7.20 (m, 2H), 7.06-6.89 (m, 5H), 5.45 (m, 1H), 5.04 (dd, *J* 12.6 and 7.5 Hz, 1H), 4.99 (dd, *J* 12.6 and 8.1 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 154.1, 142.9, 131.4, 126.9, 126.1, 125.1, 124.8, 113.5, 112.6, 112.2, 100.6, 79.9, 55.8, 36.8; IR ν_{max}/cm^{-1} (KBr) 3336 (NH), 2929, 2829, 1551, 1489, 1436, 1376, 1214, 716; HRMS (ESI$^+$, *m*/ Na$^+$) Found: 325.06167. Calc. for $C_{15}H_{14}O_3N_2S/Na^+$: 325.06174.

*2-Methyl-3-(2-nitro-1-phenylethyl)-1H-indole (**5o**)*:[67] 94%, pale pink solid, mp 102-103 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.80 (br s, 1H), 7.35 (d, *J* 7.8 Hz, 1H), 7.32-7.16 (m, 6H), 7.08 (m, 1H), 7.00 (m, 1H), 5.23-5.04 (m, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 139.5, 135.3, 132.8, 128.7; 127.2, 127.0, 126.8, 121.2, 119.6, 118.5, 110.7, 108.7, 78.6, 40.4, 11.8; IR ν_{max}/cm^{-1} (KBr) 3403 (NH), 1550, 1459, 1428, 1377, 743, 700.

*2-Methyl-3-(1-(naphthalen-1-yl)-2-nitroethyl)-1H-indole (**5p**)*: 94%, pale yellow solid, mp 150-151 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.11 (m, 1H), 7.89-7.82 (m, 2H), 7.79 (d, *J* 8.1 Hz, 1H), 7.60 (d, *J* 7.2 Hz, 1H), 7.55 (d, *J* 7.2 Hz, 1H), 7.52-7.39 (m, 3H), 7.28-7.21 (m, 1H), 7.15-7.03 (m, 2H), 5.92 (m, 1H), 5.25 (dd, *J* 12.9 and 6.9 Hz, 1H), 5.19 (dd, *J* 12.9 and 8.7 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 135.3, 134.5, 134.1, 132.9, 131.3, 129.1, 128.3, 127.3, 126.6, 125.8, 125.1, 124.3, 123.0, 121.4, 119.8, 118.4, 110.7, 108.3, 78.0, 37.4, 12.3; IR ν_{max}/cm^{-1} (KBr) 3415, 3348, 2921, 2870, 1453, 903, 742; HRMS (ESI$^+$, *m*/Na$^+$) Found: 353.12611. Calc.for $C_{21}H_{18}O_2N_2/Na^+$: 353.12605.

*2-Methyl-3-(2-nitro-1-(thiophen-2-yl)ethyl)-1H-indole (**5q**)*: 98%, greenish brown solid, mp 89-91 °C ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (br s, 1H); 7.32 (d, *J* 7.8 Hz, 1H), 7.16-6.95 (m, 4H), 6.87-6.80 (m, 2H), 5.29 (dd, *J* 9.0 and 6.6 Hz, 1H), 5.10 (dd, *J* 12.3 and 6.6 Hz, 1H), 4.99 (dd, *J* 12.3 and 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 135.2, 133.0, 126.7, 126.1, 124.6, 124.2, 121.1, 119.5, 118.4, 110.7, 108.1, 78.7, 36.4, 11.4; IR ν_{max}/cm^{-1} (neat, film) 3404 (NH), 1551, 1460, 1427, 1378, 745, 702; HRMS (ESI$^+$, *m*/Na$^+$) Found: 309.06671. Calc. for $C_{15}H_{14}O_2N_2S$/Na$^+$: 309.06682.

*Preparation of the triptamine derivative **8***

To a stirred solution of compound **5a** (266.3 mg, 1 mmol) in CH_3OH (5 mL) were sequentially added Pd/C 10% (52mg) and $HCOONH_4$ (315.3 mg, 5 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was filtered on a celite pad, washed several times with CH_3OH and the solvent removed on a rotatory evaporator. To the white residue was added saturated Na_2CO_3(aq) until pH 8 was reached and then the aqueous mixture was extracted twice with EtOAc. The combined organic phases were dried over $MgSO_4$, filtered and the solvent removed under vacuum, affording compound **8**. The crude product was used in the next step without further purification.

*2-(1H-Indol-3-yl)-2-phenylethanamine (**8**):*[58] 90%, pale brown solid, mp 129-130 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (br s, 1H), 7.45 (d, *J* 7.8 Hz, 1H), 7.35-7.10 (m, 7H), 7.02 (t, *J* 7.5 Hz, 2H), 4.25 (m, 1H), 3.42 (dd, *J* 12.6 and 7.2 Hz, 1H), 3.27 (dd, *J* 12.6 and 7.8 Hz, 1H), 1.71 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 136.5, 128.5, 128.1, 127.0, 126.4, 122.1, 121.3, 119.4, 119.3, 117.4, 111.1, 47.1, 46.7; IR ν_{max}/cm^{-1} (KBr) 3415, 3348, 2921, 2870, 1453, 903, 742.

*Preparation of β-carboline derivative **9***

To a suspension of $MgSO_4$ (240 mg) and compound **8** (70.9 mg, 0.3 mmol) in CH_2Cl_2 (2 mL) was added benzaldehyde (37 µL, 0.36 mmol, 1.2 equiv.) at room temperature and the mixture was stirred at room temperature for 1 h. The suspension was cooled to 0 °C and TFA (45 µL 0.6 mmol, 2.0 equiv.) was slowly added. The reaction was stirred at room temperature for 72 h. The reaction was quenched by addition of sat. $NaHCO_3$ at 0 °C until pH 8 was reached. After filtration over celite, the filtrate was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and the solvent evaporated under vacuum. The ^{1}H NMR analysis of the crude product showed a mixture of two diastereoisomers in 87:13 ratio. The 1,4-*trans* relative configuration for the major isomer was assumed based on literature data. The crude product was purified by column chromatography using a mixture of hexanes/ethyl acetate 75:25 (v/v) as eluent. After purification only the major isomer was observed in the ^{1}H NMR spectra.

*trans-1,4-Diphenyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b] indole (**9**-trans):*[59] 70%, pale brown solid, mp 184-185 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (br s, 1H), 7.40-7.21 (m, 10 H), 7.18 (d, *J* 8.1 Hz, 1H), 7.06 (m, 1H), 6.90-6.78 (m, 2H), 5.25 (s, 1H), 4.37 (m, 1H), 3.53 (dd, *J* 12.6 and 5.1 Hz, 1H), 3.02 (dd, *J* 12.6 and 8.7 Hz, 1H), 1.91 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 141.4, 135.9, 135.8, 128.9, 128.6, 128.4, 128.3, 126.7, 126.5, 121.5, 119.8, 119.3, 112.5, 110.7, 58.2, 52.9, 41.7; IR ν_{max}/cm^{-1} (KBr) 3405, 3319, 3052, 3019, 2952, 2811, 1451, 1273, 750, 697.

Supplementary Information

The spectroscopic ^{1}H NMR, ^{13}C NMR, IR data as well as the HRMS of selected compounds are provided as supplementary information and available free of charge at http:// jbcs.sbq.org.br, as PDF file.

Acknowledgments

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Supplementary Information

Metal Halide Hydrates as Lewis Acid Catalysts for the Conjugated Friedel-Crafts Reactions of Indoles and Activated Olefins

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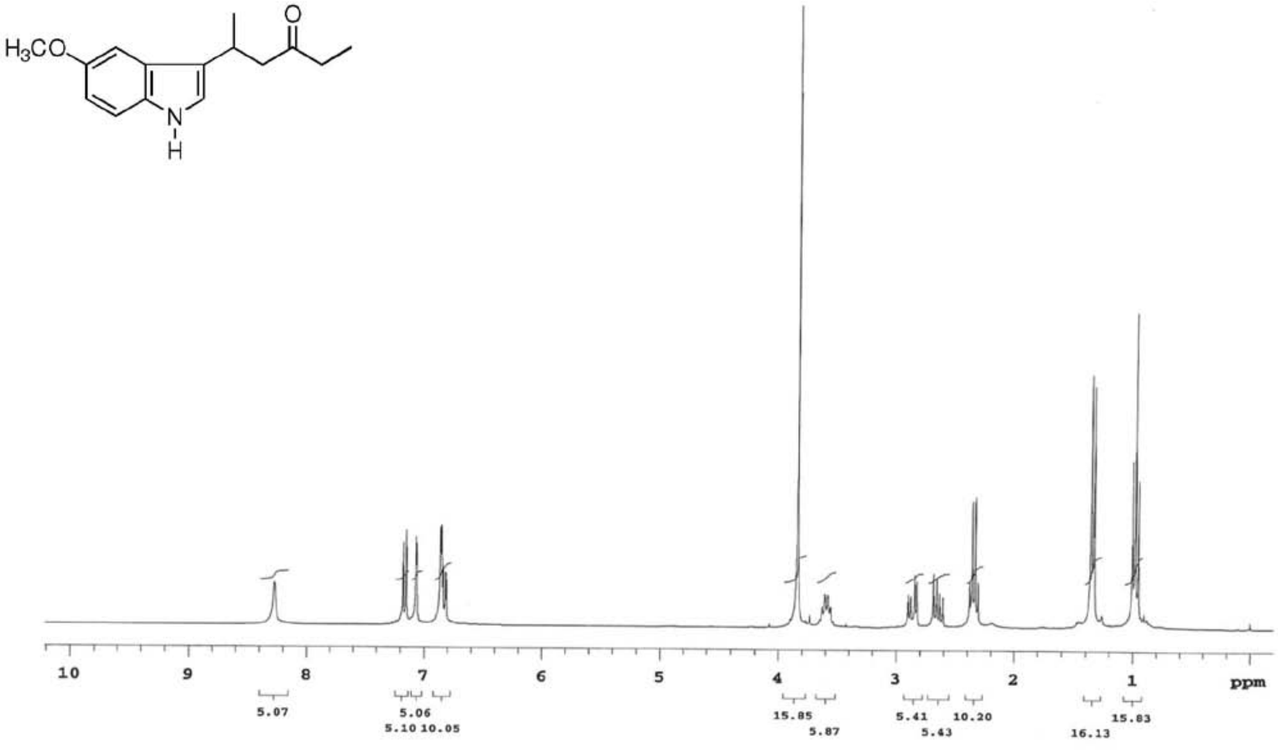

Figure S1. ^{1}H NMR ($CDCl_3$) of compound **3f.**

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*e-mail: dennis@iq.ufrgs.br

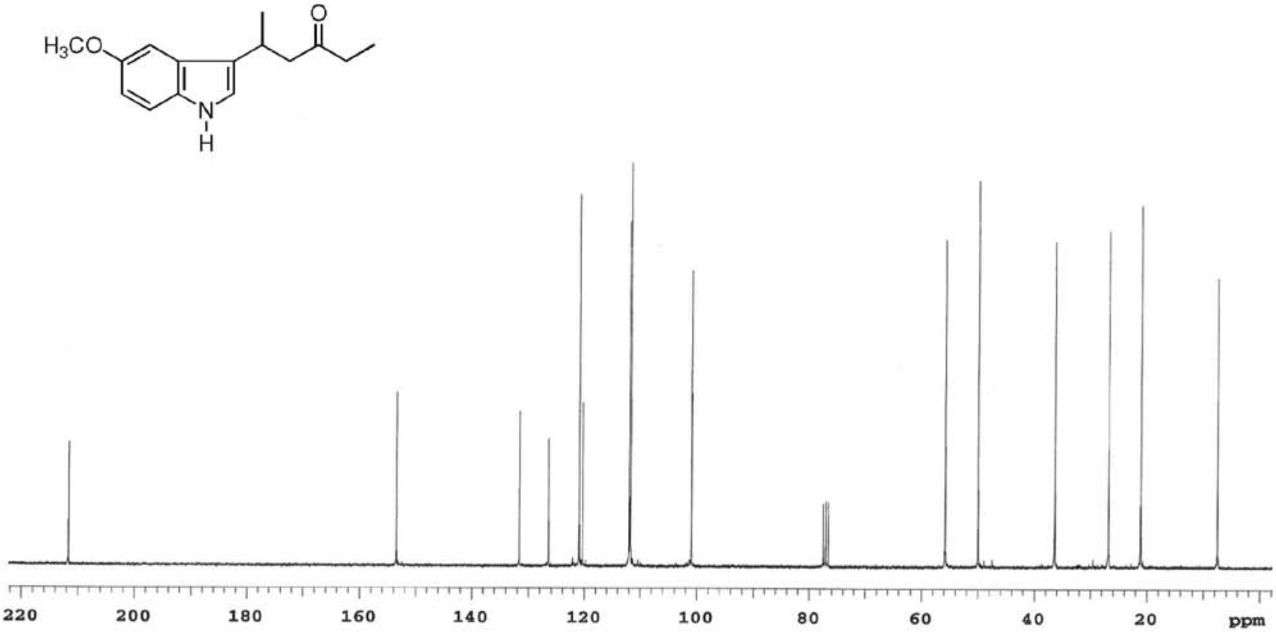

Figure S2. ^{13}C NMR (CDCl$_3$) of compound **3f.**

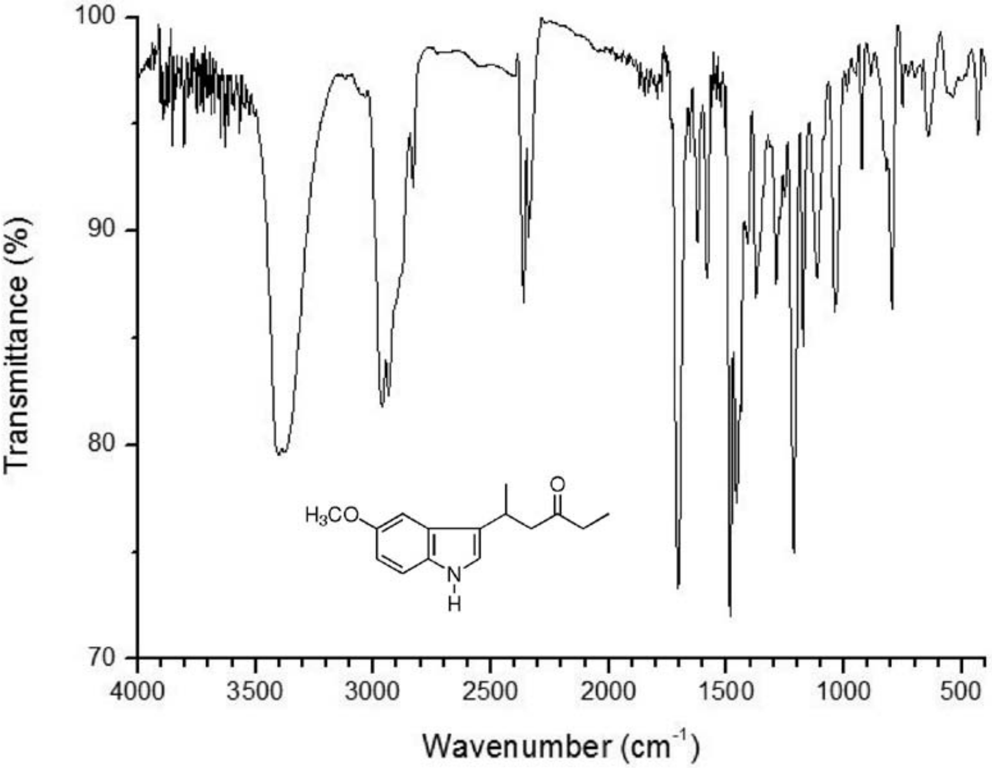

Figure S3. IR (neat) of compound **3f**.

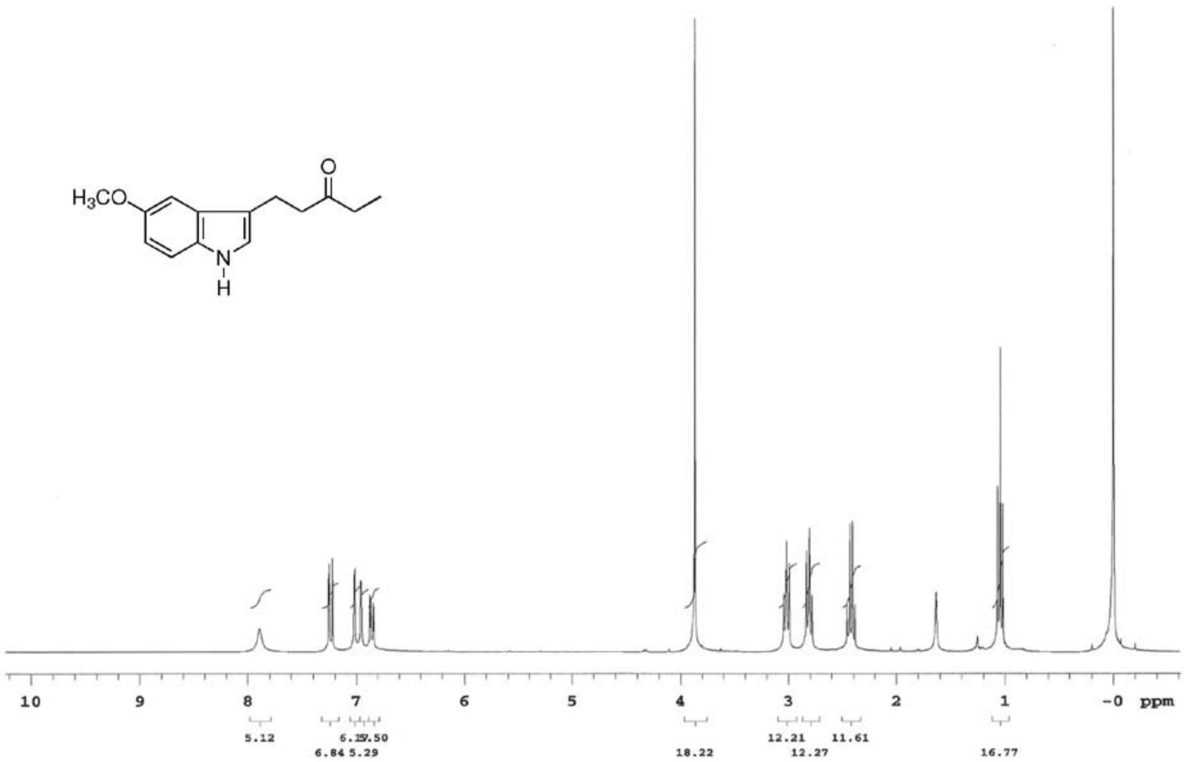

Figure S4. ^{1}H NMR ($CDCl_3$) of compound **3g**

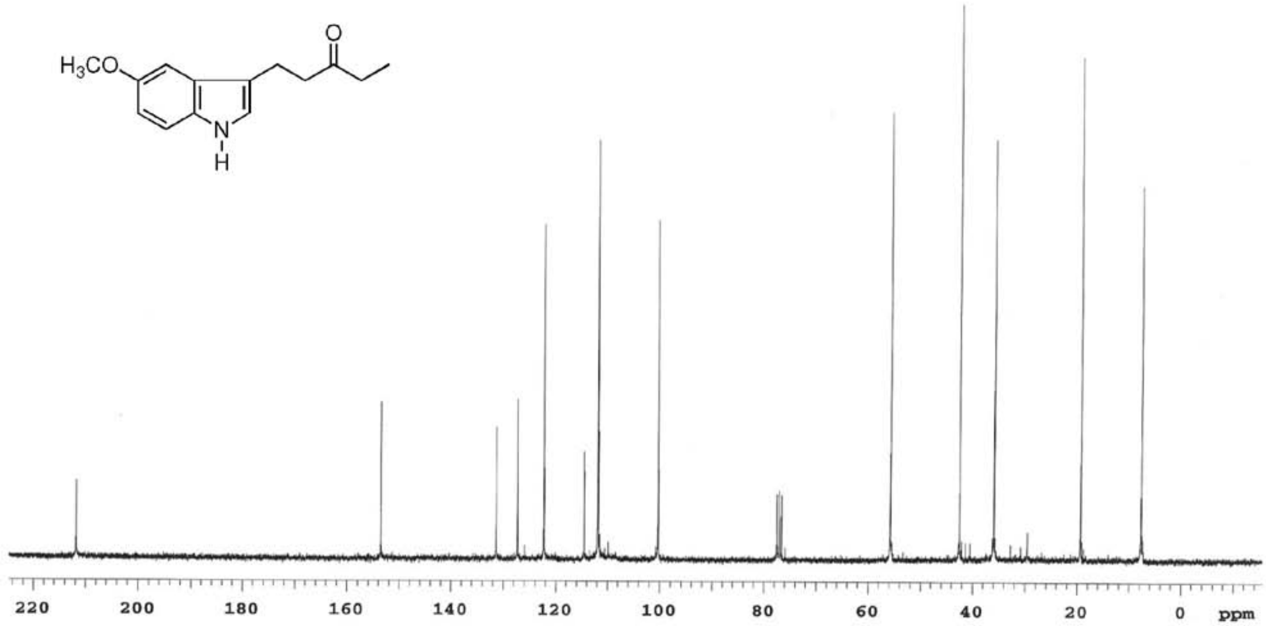

Figure S5. ^{13}C NMR ($CDCl_3$) of compound **3g**

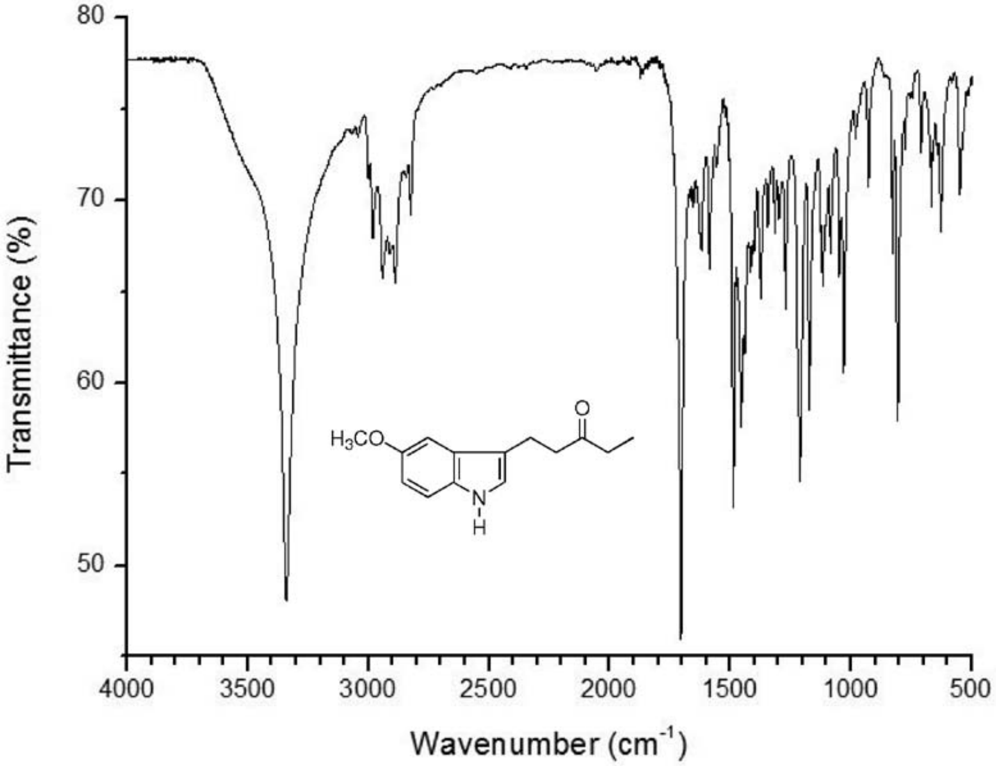

Figure S6. IR (KBr) of compound **3g.**

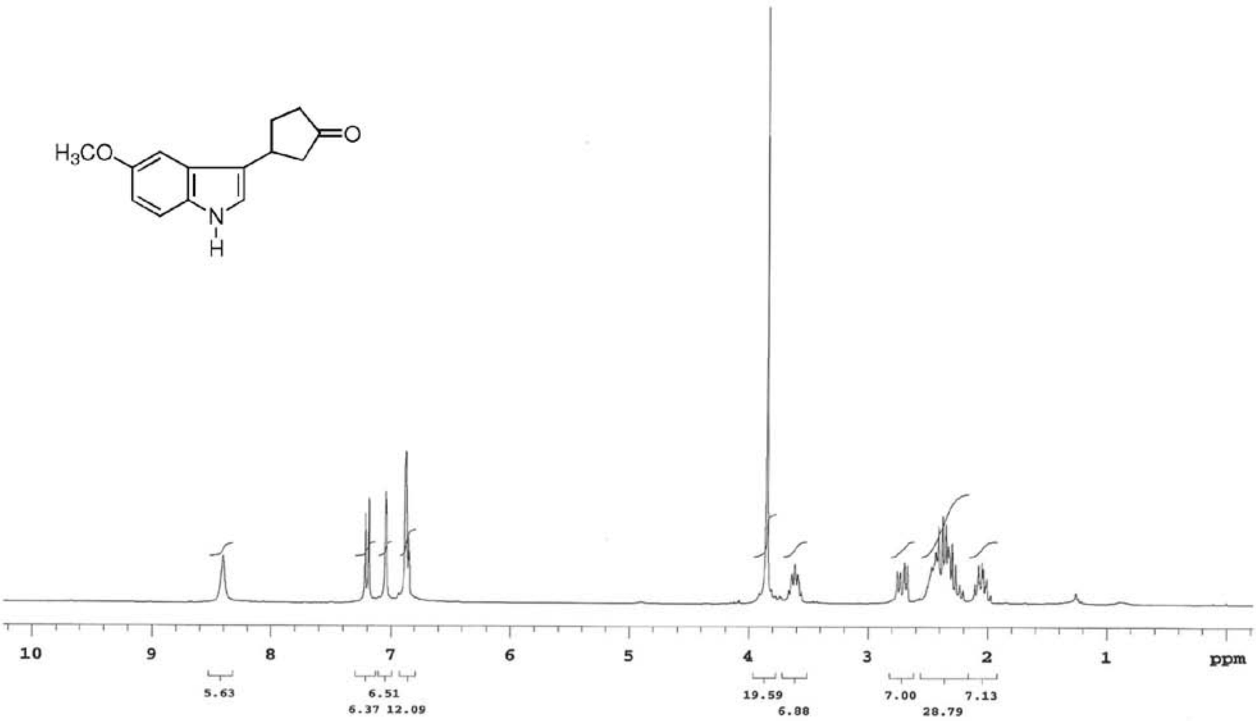

Figure S7. ^{1}H NMR (CDCl$_3$) of compound **3i.**

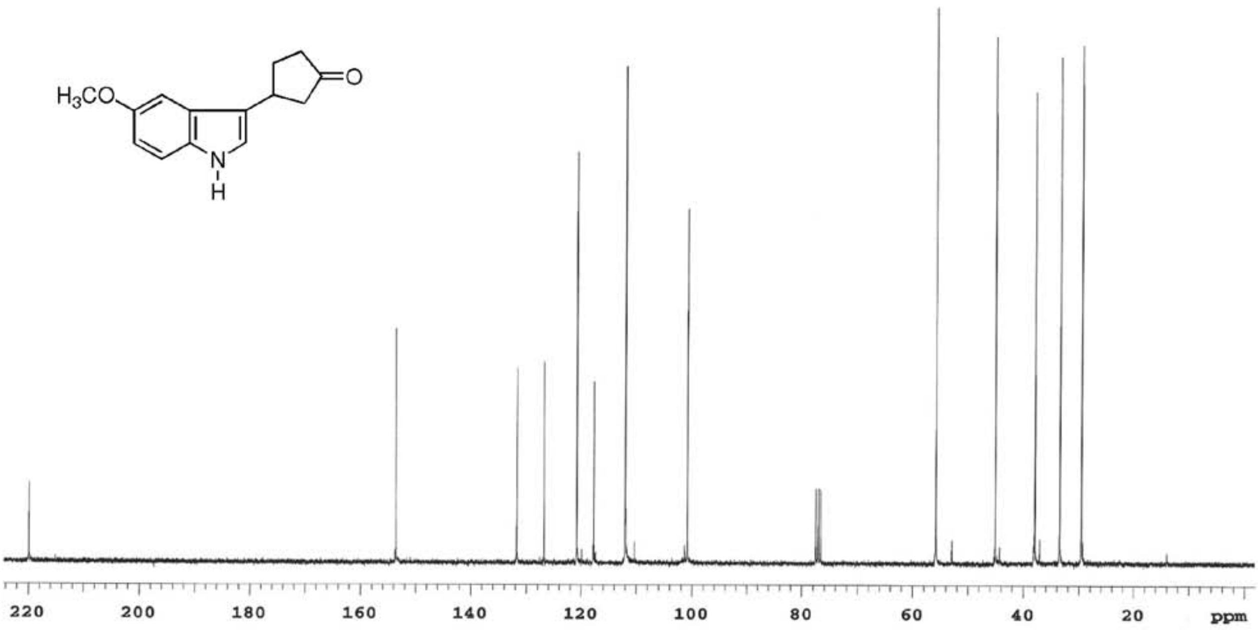

Figure S8. ^{13}C NMR (CDCl$_3$) of compound **3i**

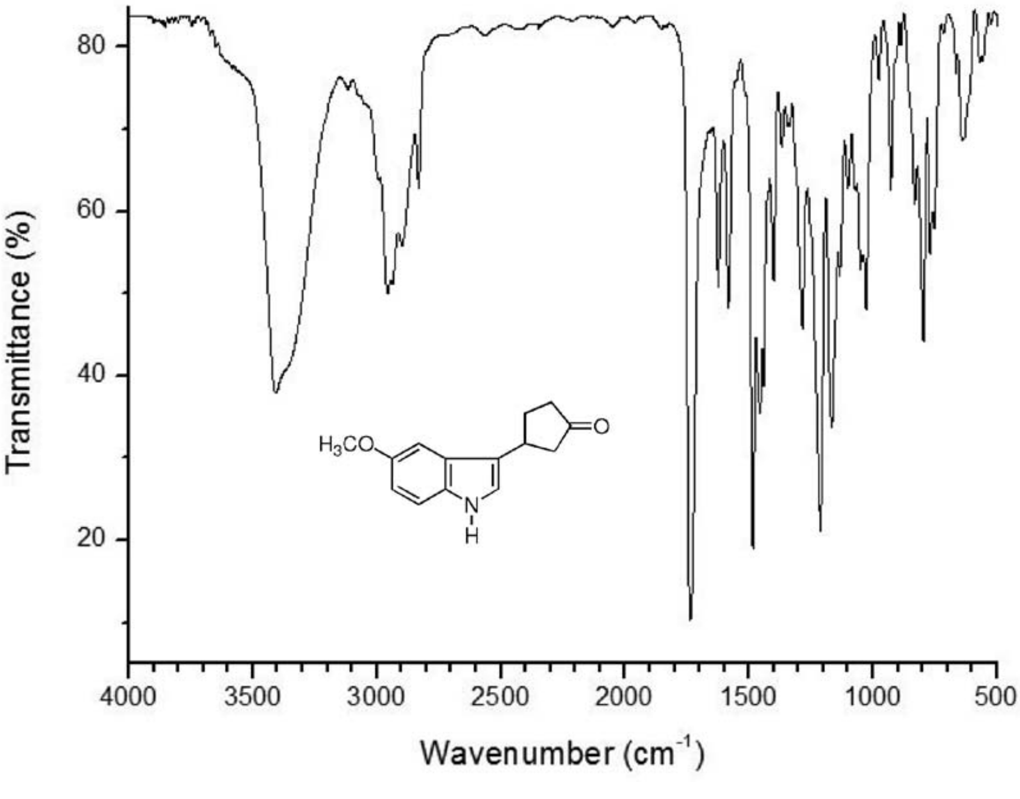

Figure S9. IR (neat) of compound **3i.**

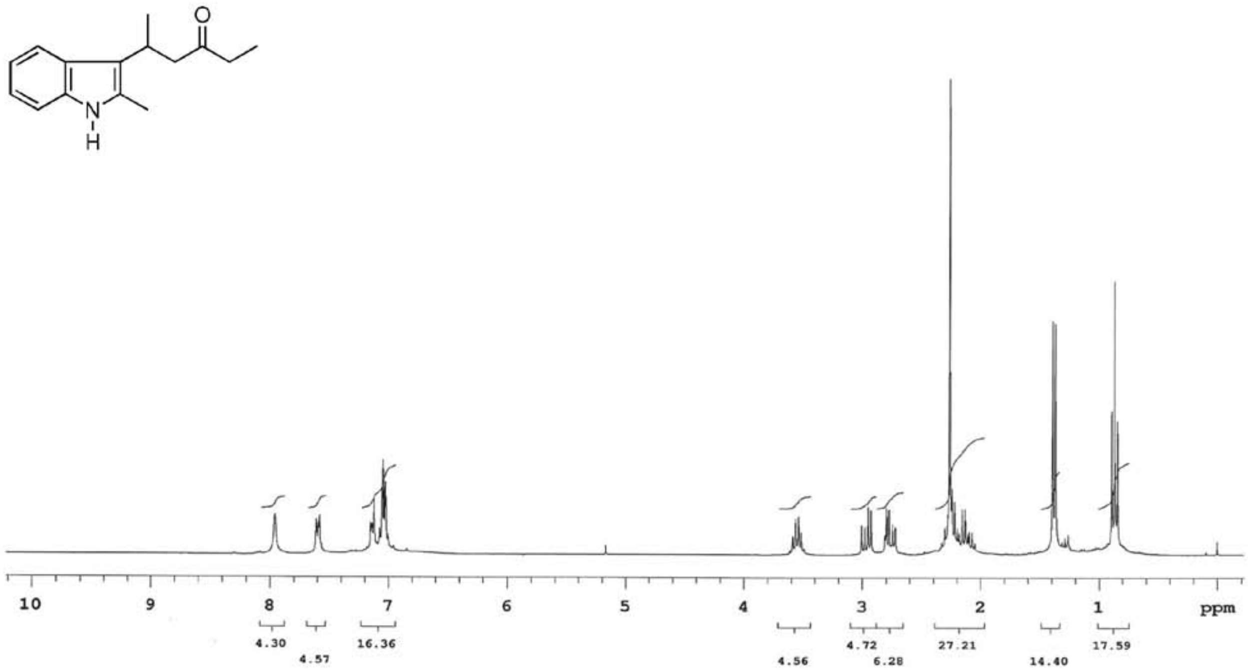

Figure S10. ^{1}H NMR ($CDCl_3$) of compound **3k.**

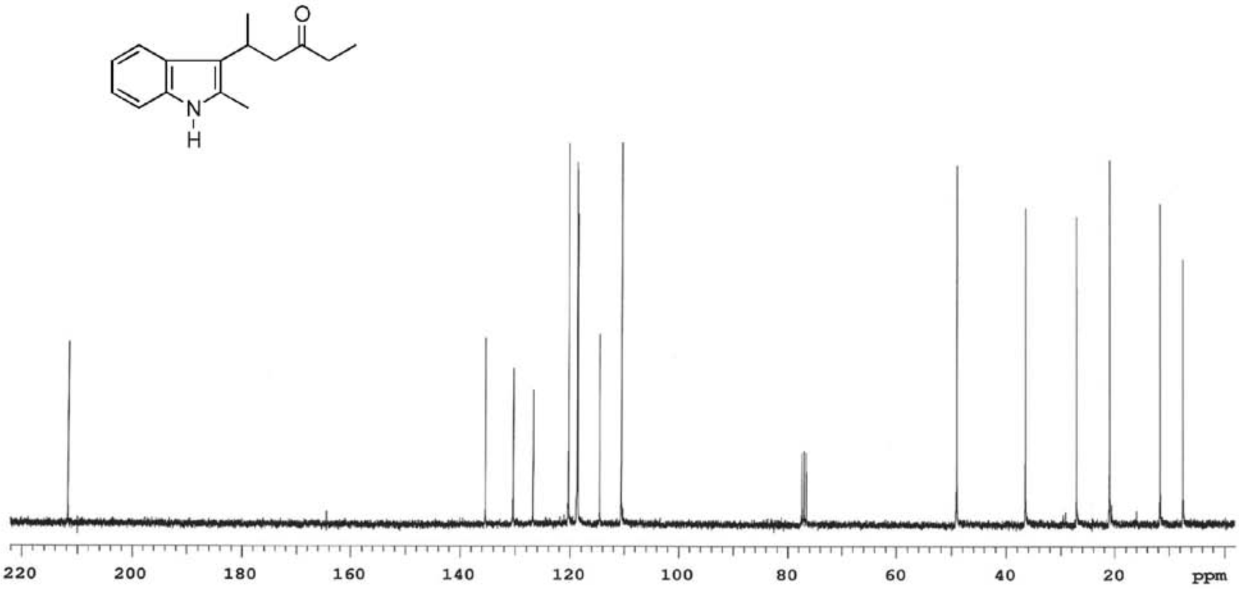

Figure S11. ^{13}C NMR ($CDCl_3$) of compound **3k.**

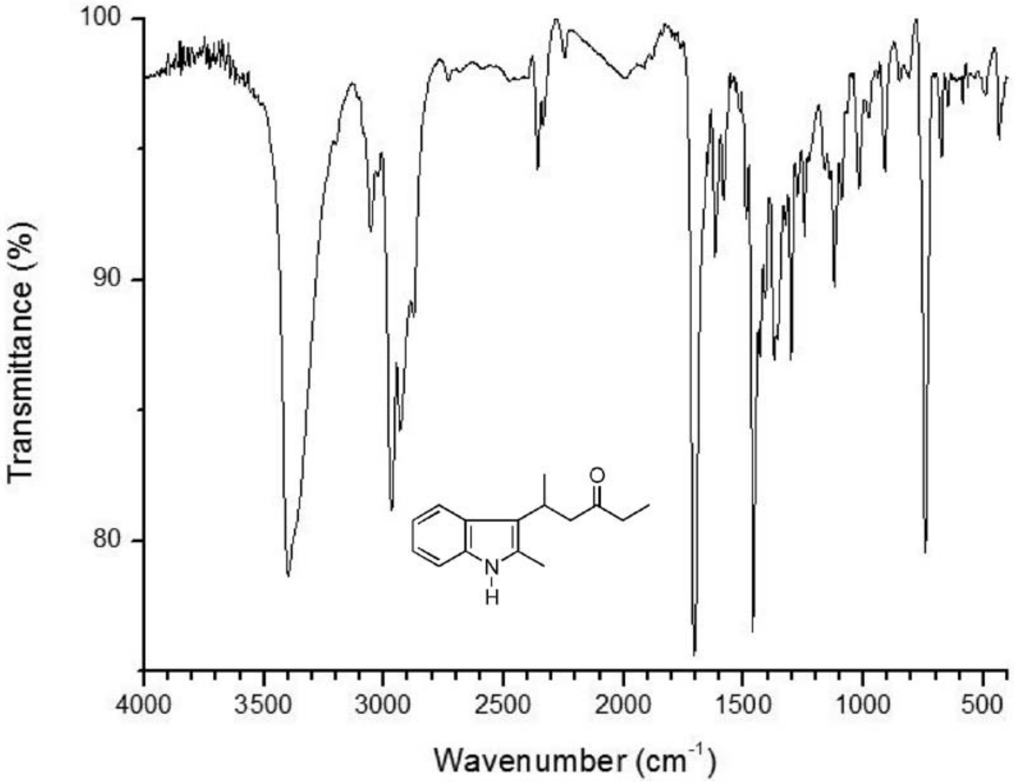

Figure S12. IR (neat) of compound **3k.**

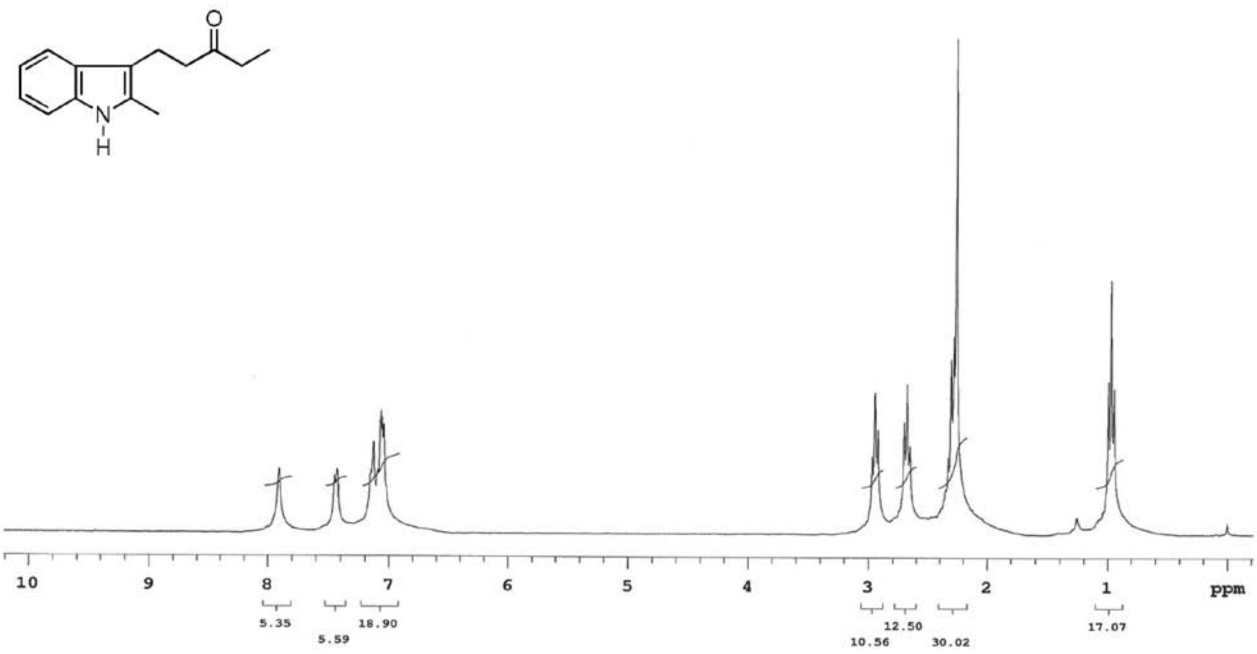

Figure S13. ^{1}H NMR ($CDCl_3$) of compound **3l.**

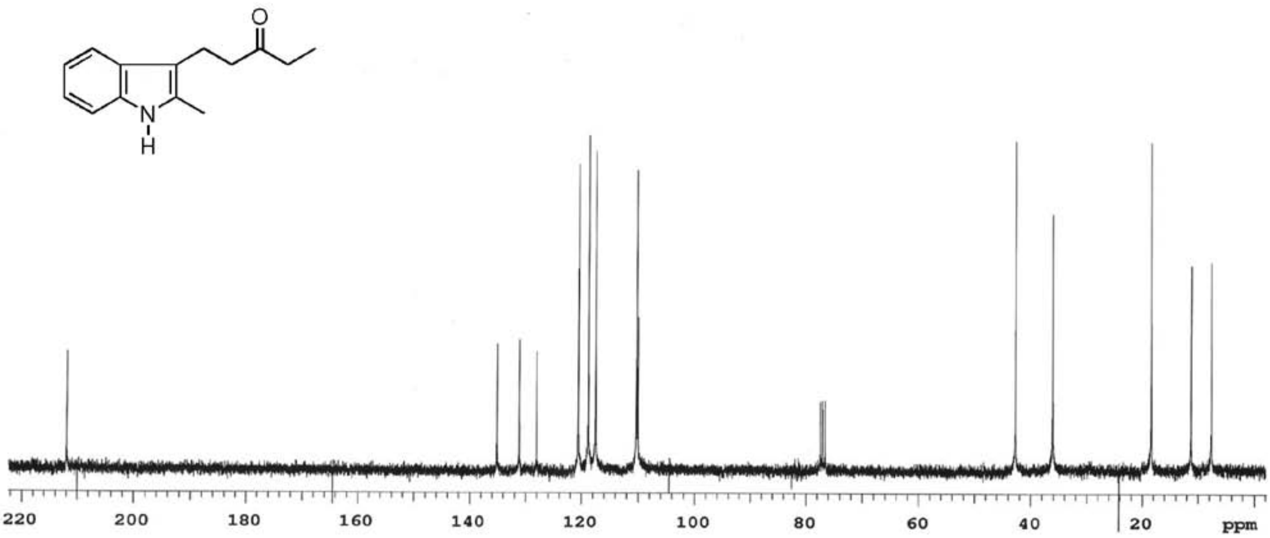

Figure S14. ^{13}C NMR (CDCl$_3$) of compound **3l.**

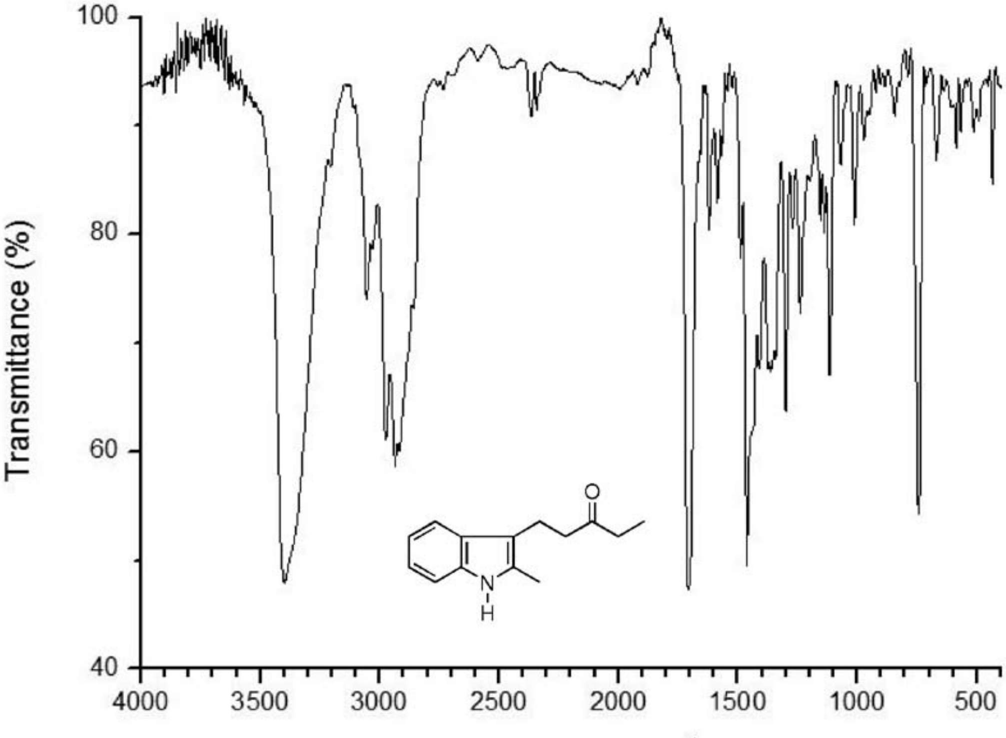

Figure S15. IR (neat) of compound **3l.**

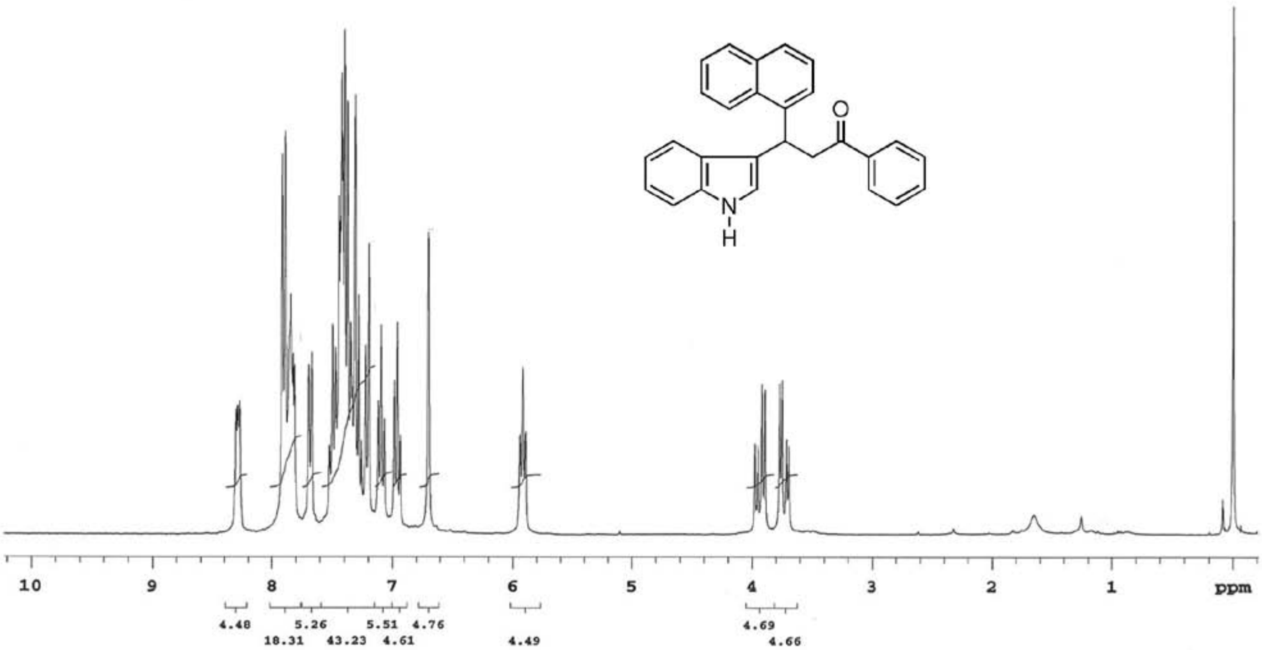

Figure S16. ^{1}H NMR ($CDCl_3$) of compound **3s.**

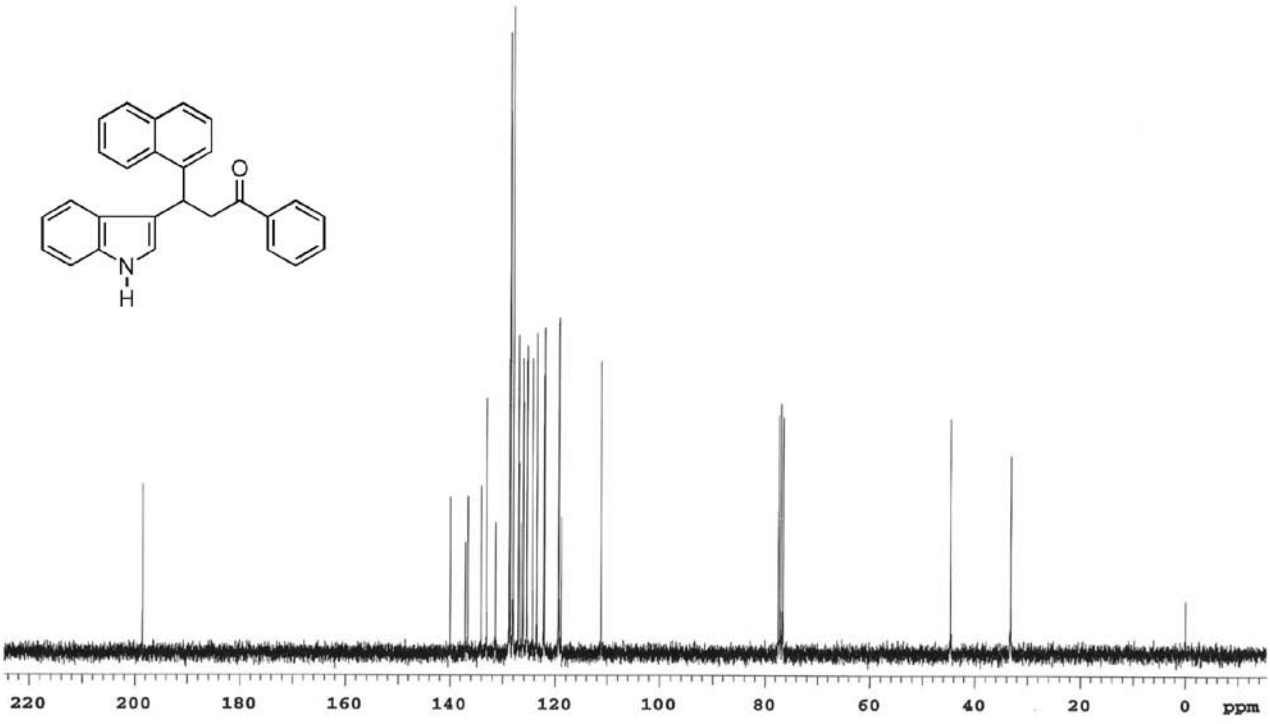

Figure S17. ^{13}C NMR ($CDCl_3$) of compound **3s.**

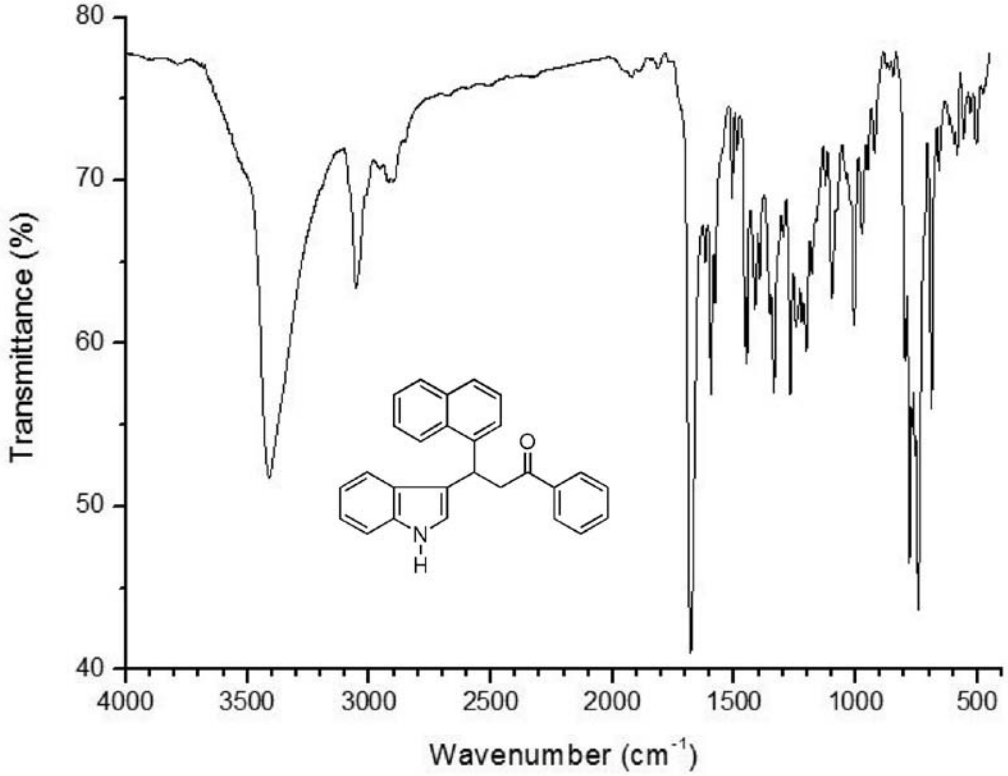

Figure S18. IR (KBr) of compound **3s.**

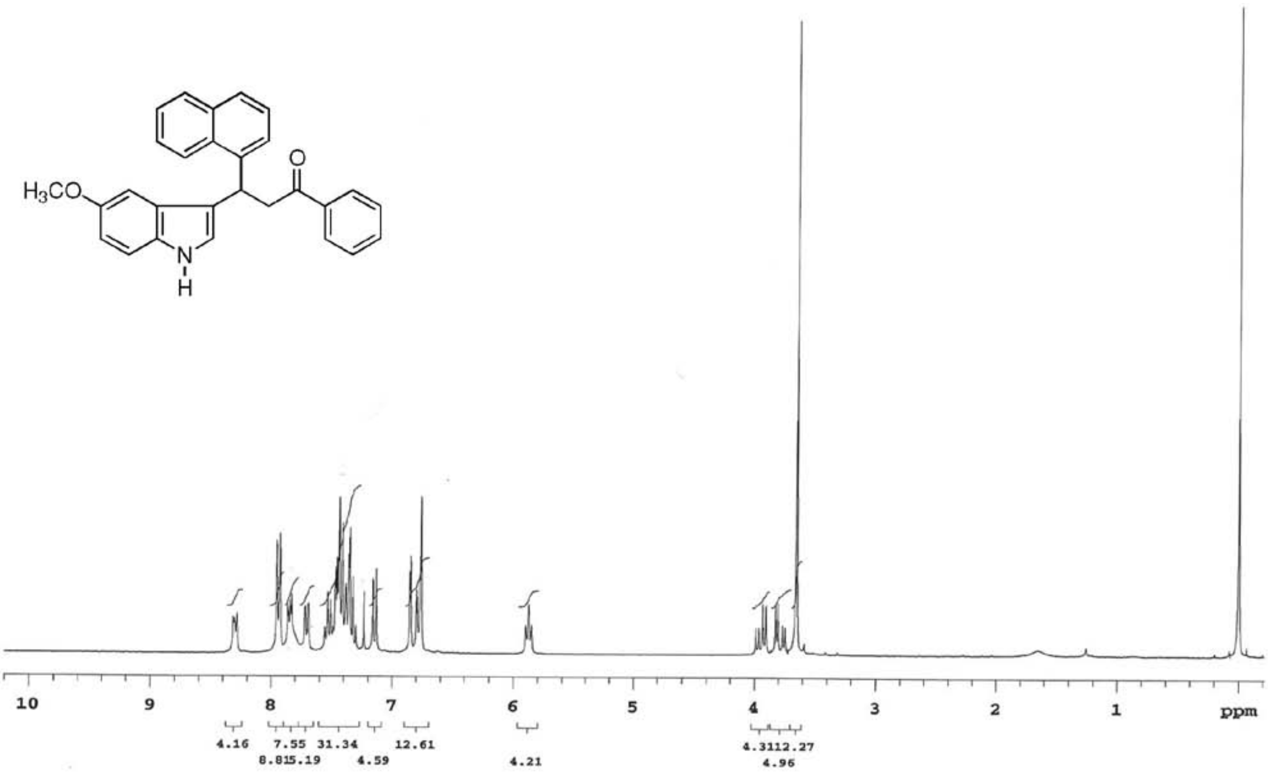

Figure S19. ^{1}H NMR (CDCl$_3$) of compound **3w.**

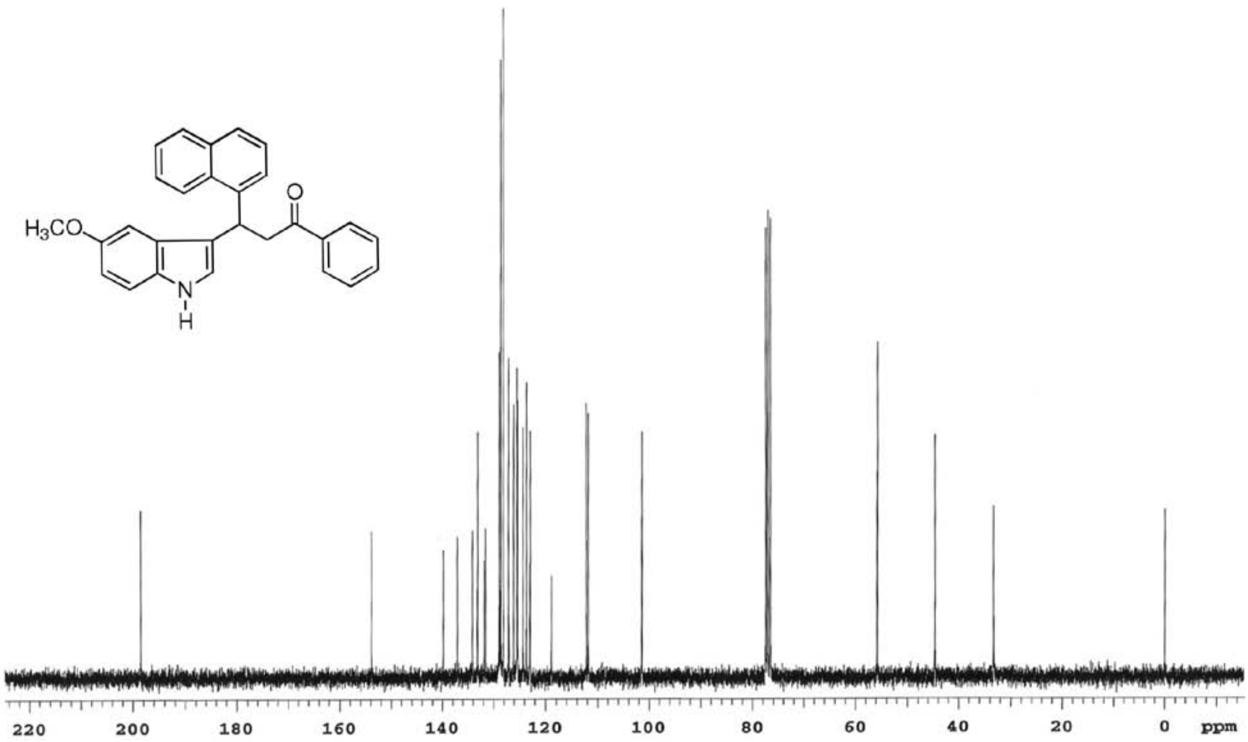

Figure S20. ^{13}C NMR ($CDCl_3$) of compound **3w.**

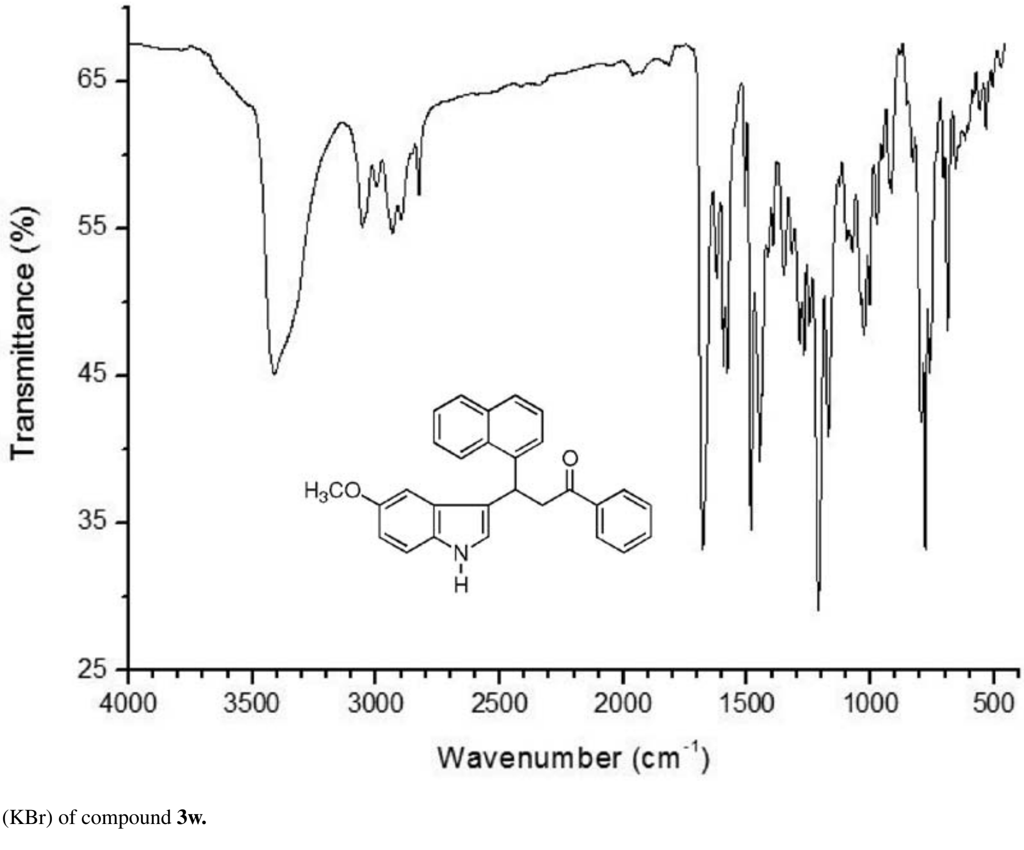

Figure S21. IR (KBr) of compound **3w.**

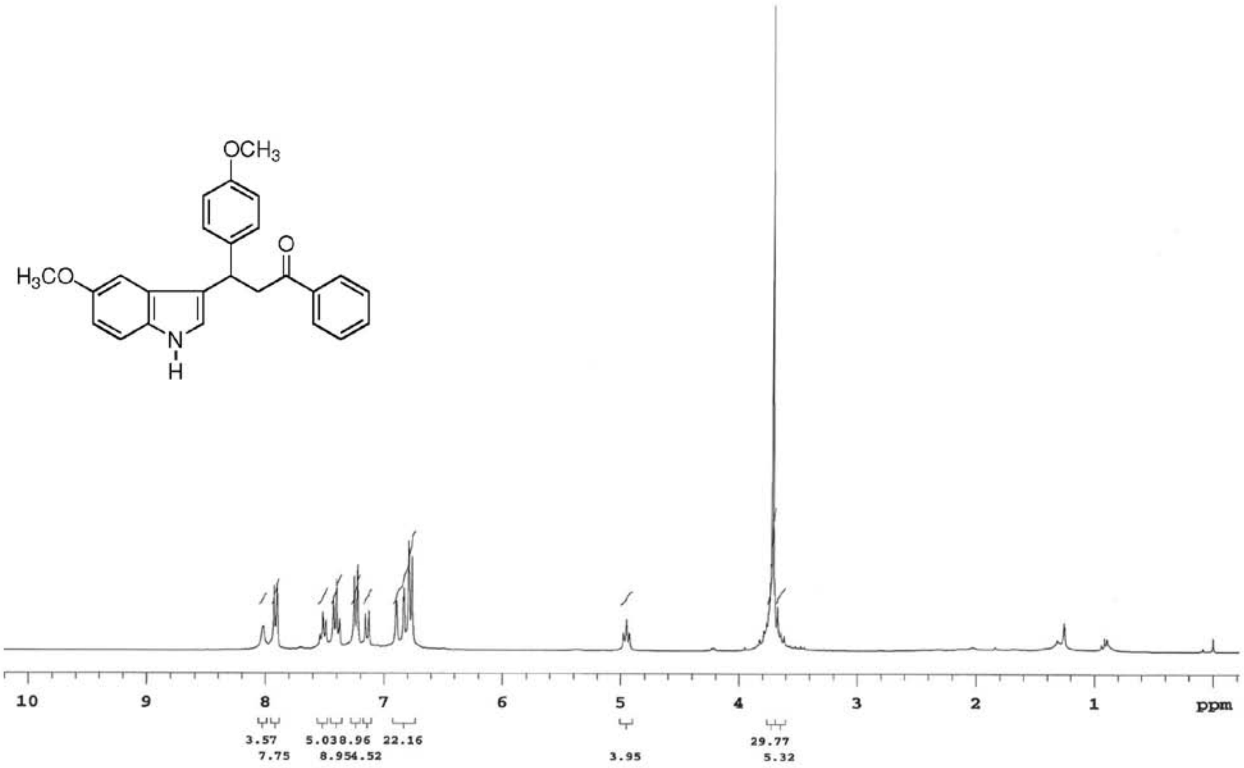

Figure S22. ^{1}H NMR (CDCl$_3$) of compound **3x.**

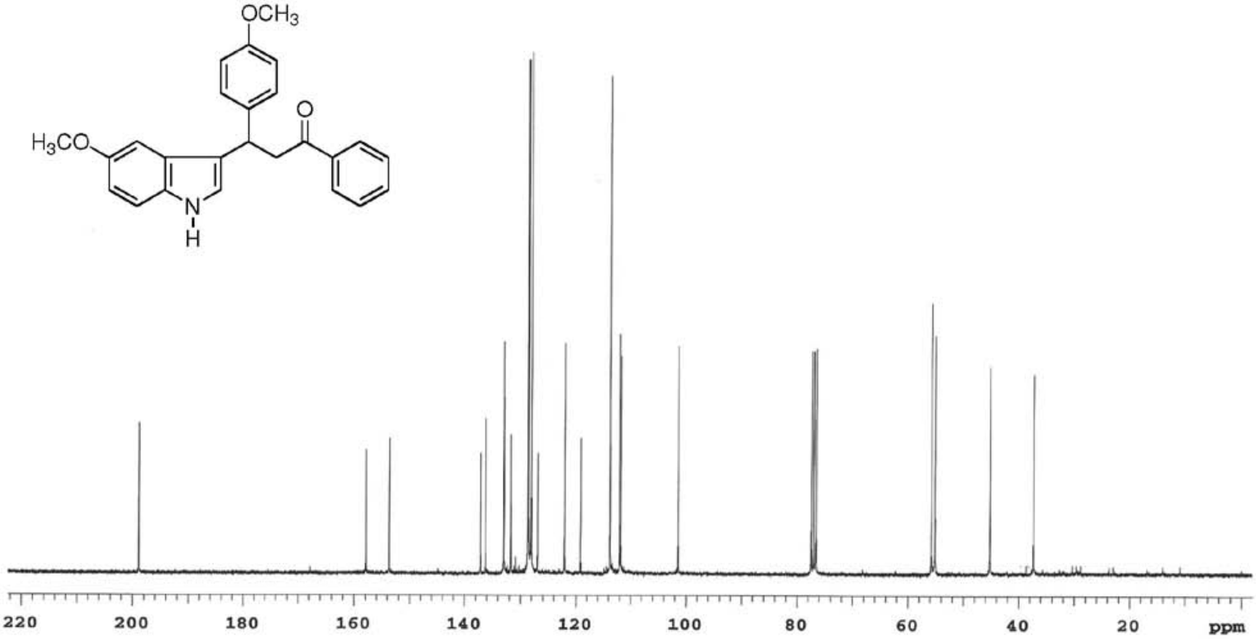

Figure S23. ^{13}C NMR (CDCl$_3$) of compound **3x.**

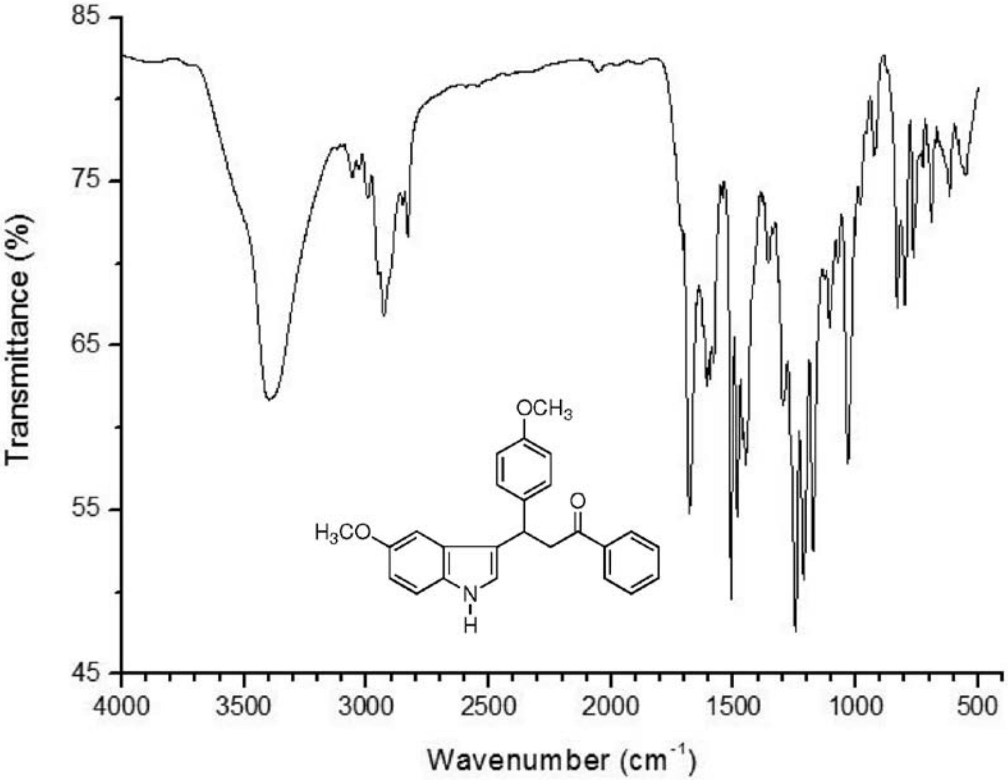

Figure S24. IR (KBr) of compound **3x.**

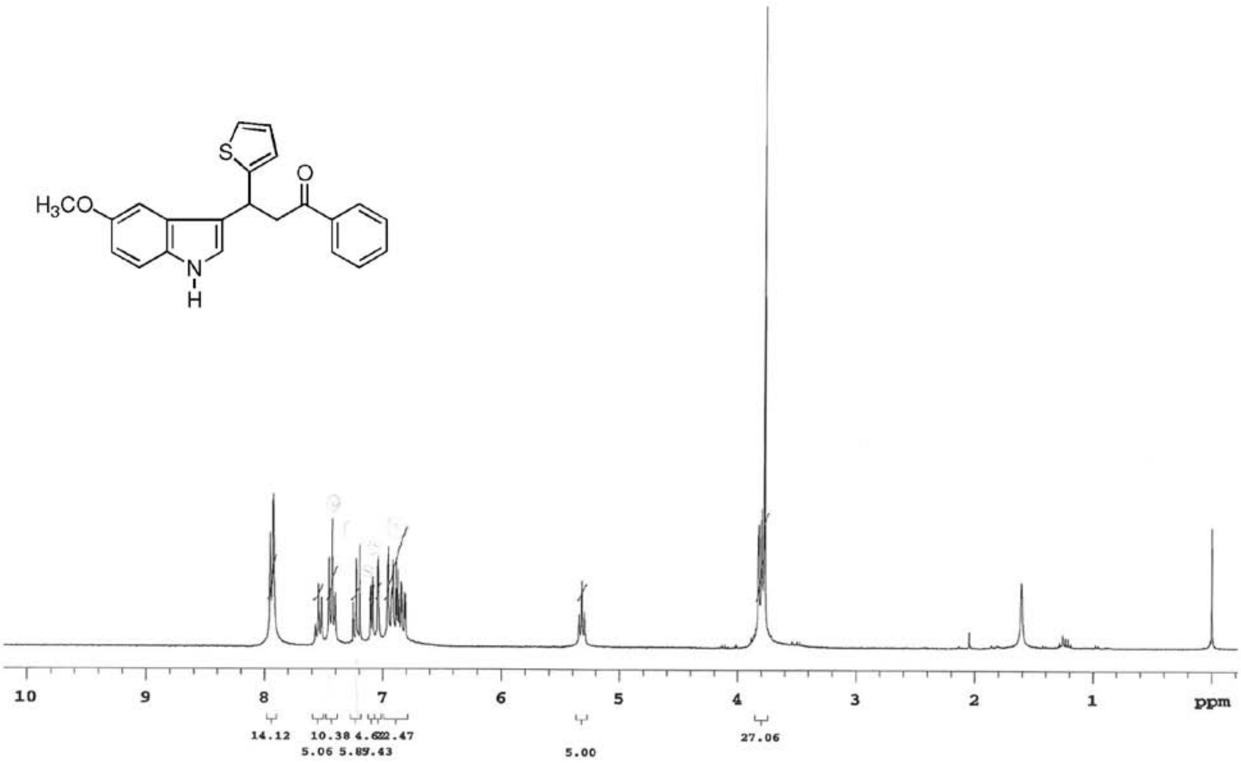

Figure S25. ^{1}H NMR (CDCl$_3$) of compound **3y.**

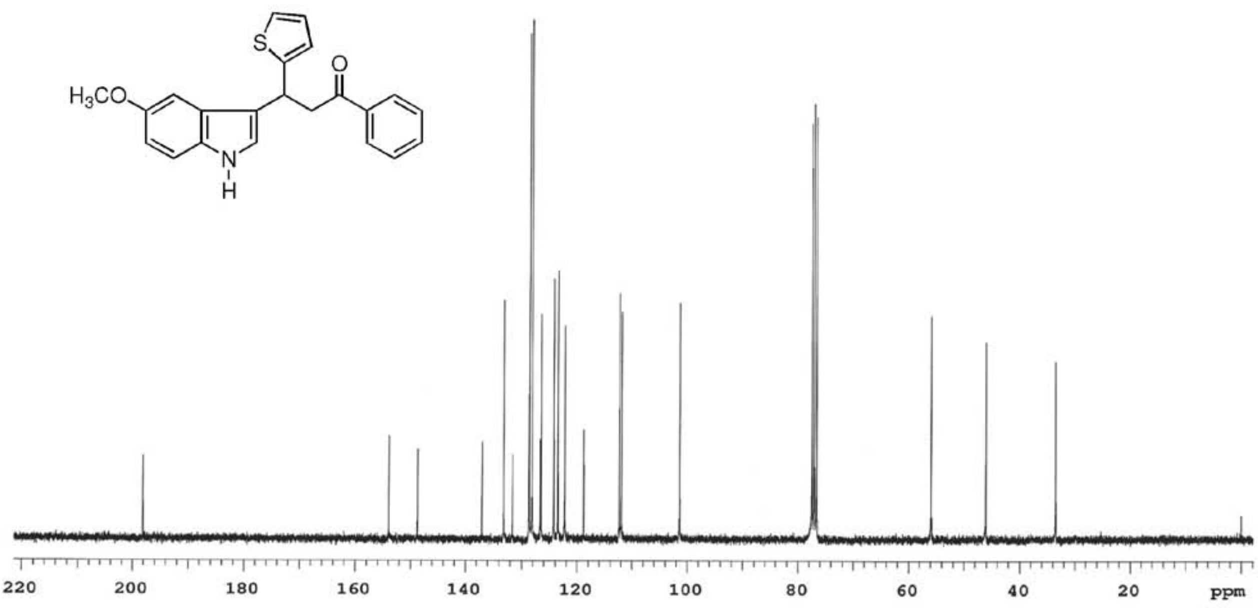

Figure S26. ^{13}C NMR ($CDCl_3$) of compound **3y.**

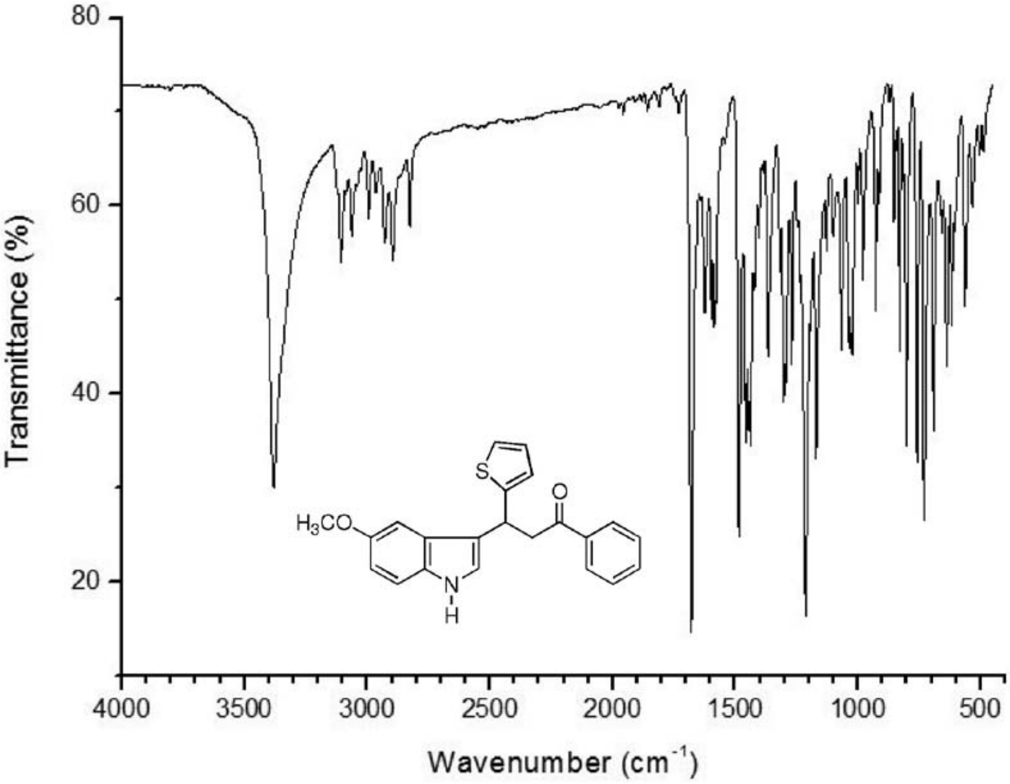

Figure S27. IR (KBr) of compound **3y.**

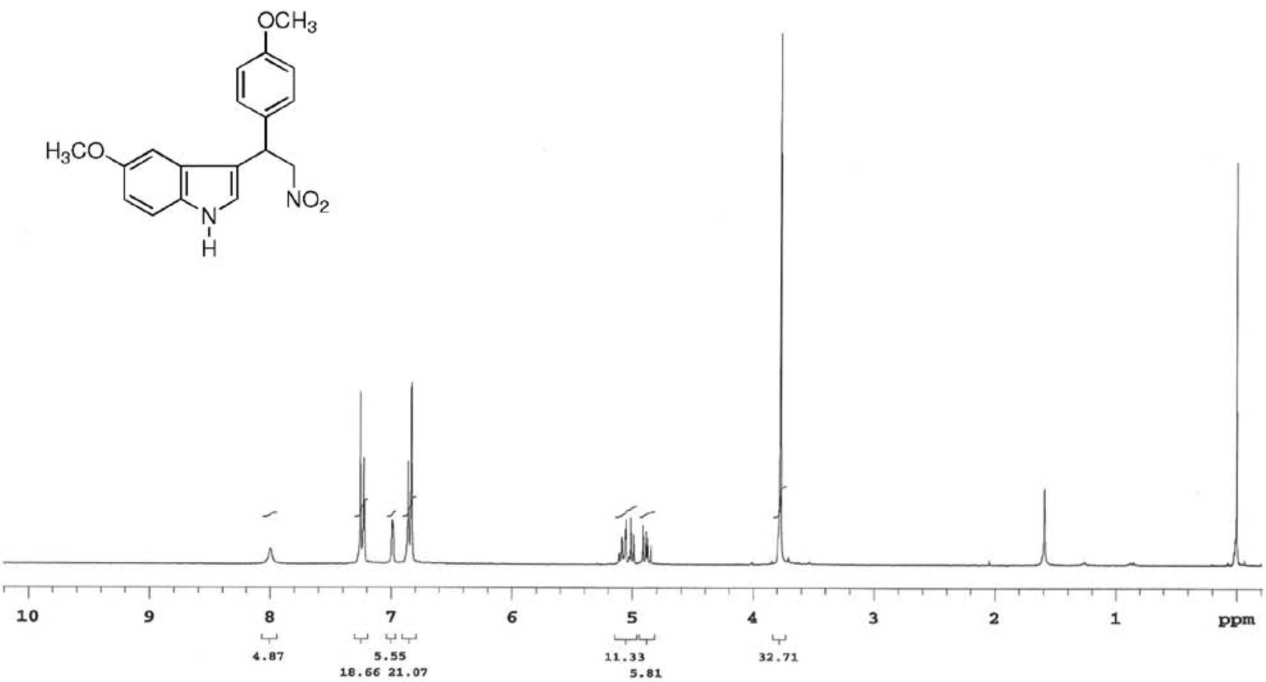

Figure S28. ^1H NMR ($CDCl_3$) of compound **5i.**

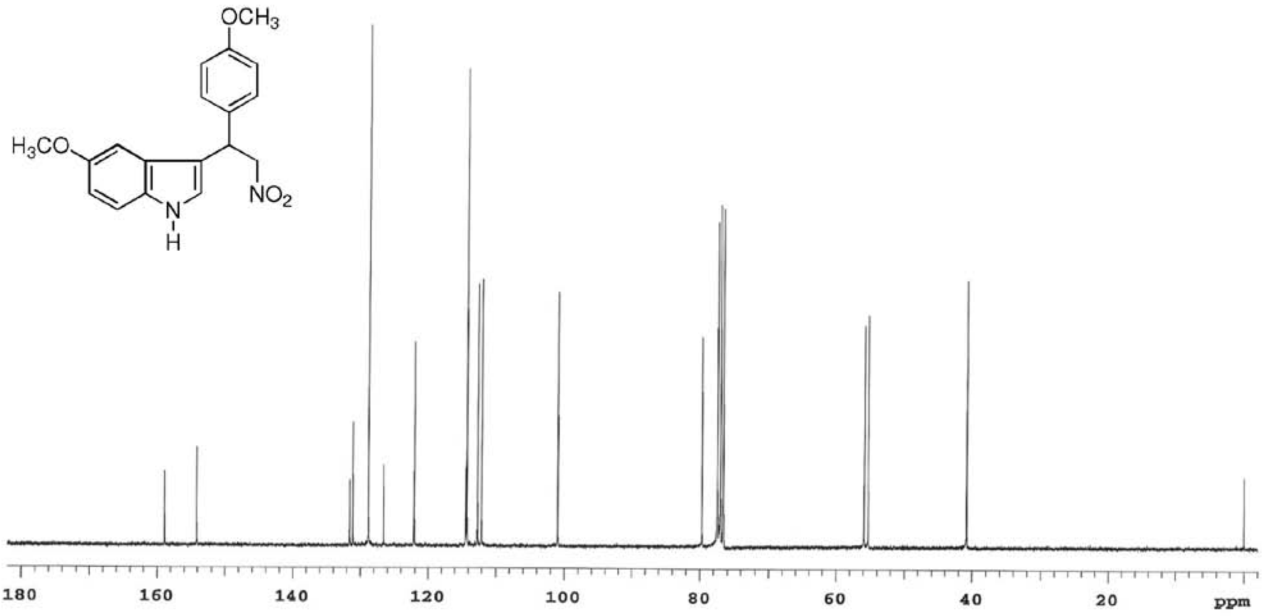

Figure S29. ^{13}C NMR ($CDCl_3$) of compound **5i.**

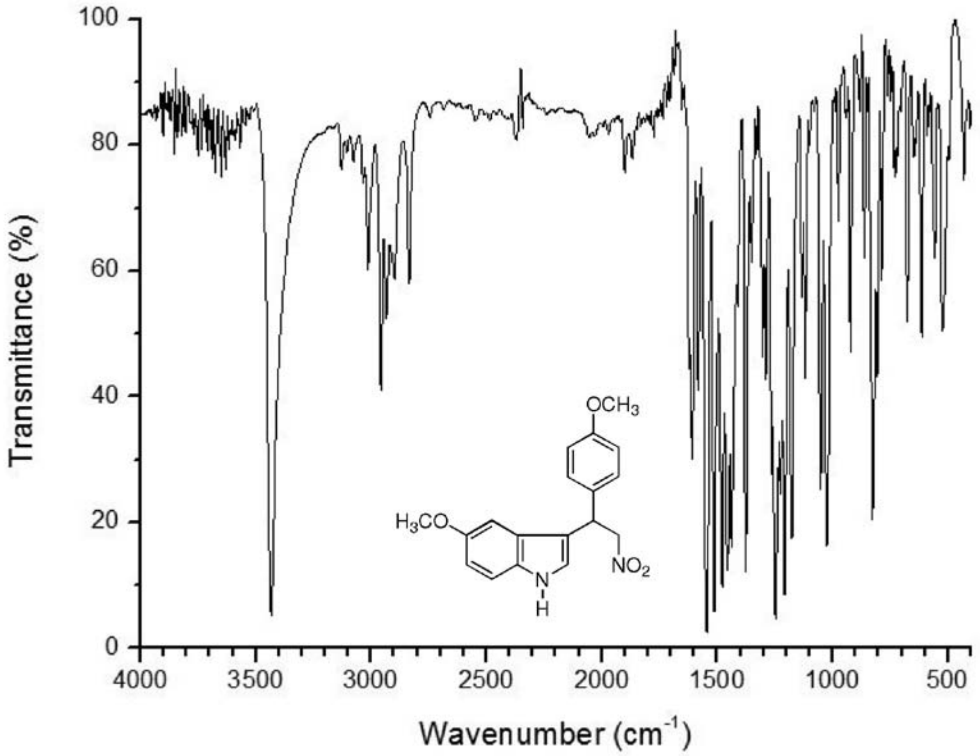

Figure S30. IR (KBr) of compound **5i.**

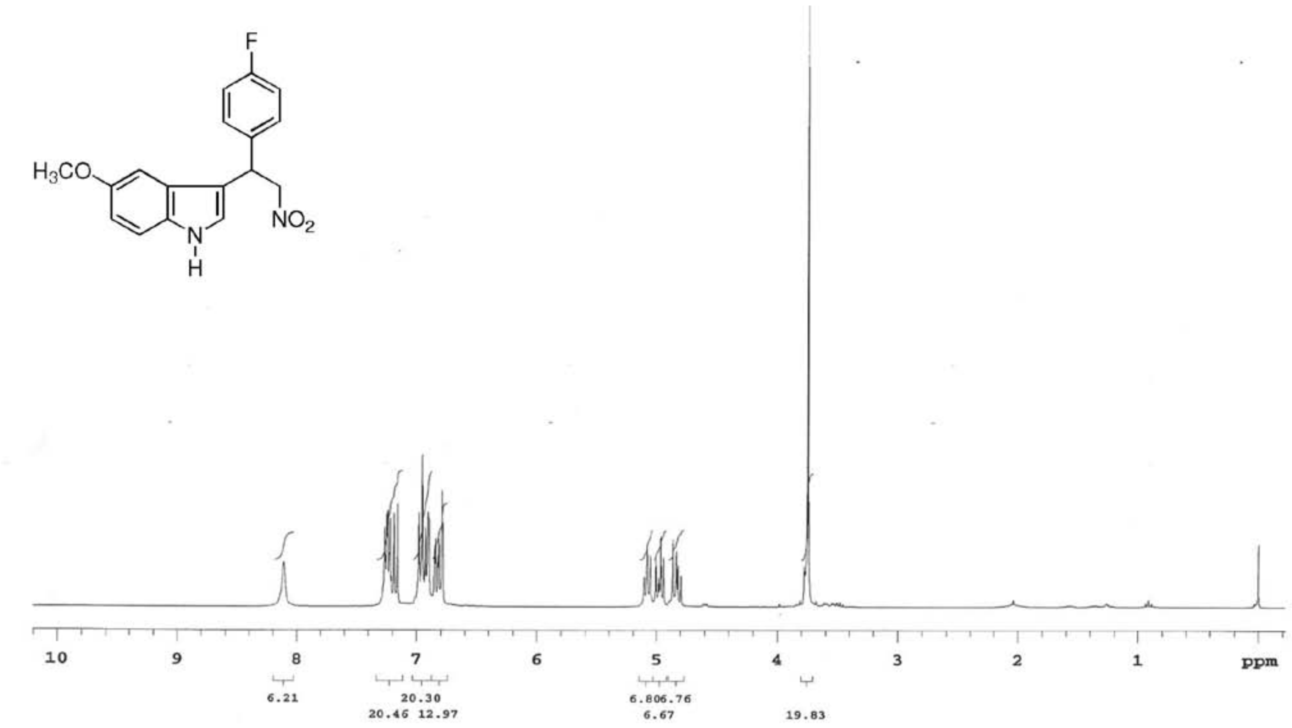

Figure S31. ^{1}H NMR ($CDCl_3$) of compound **5j.**

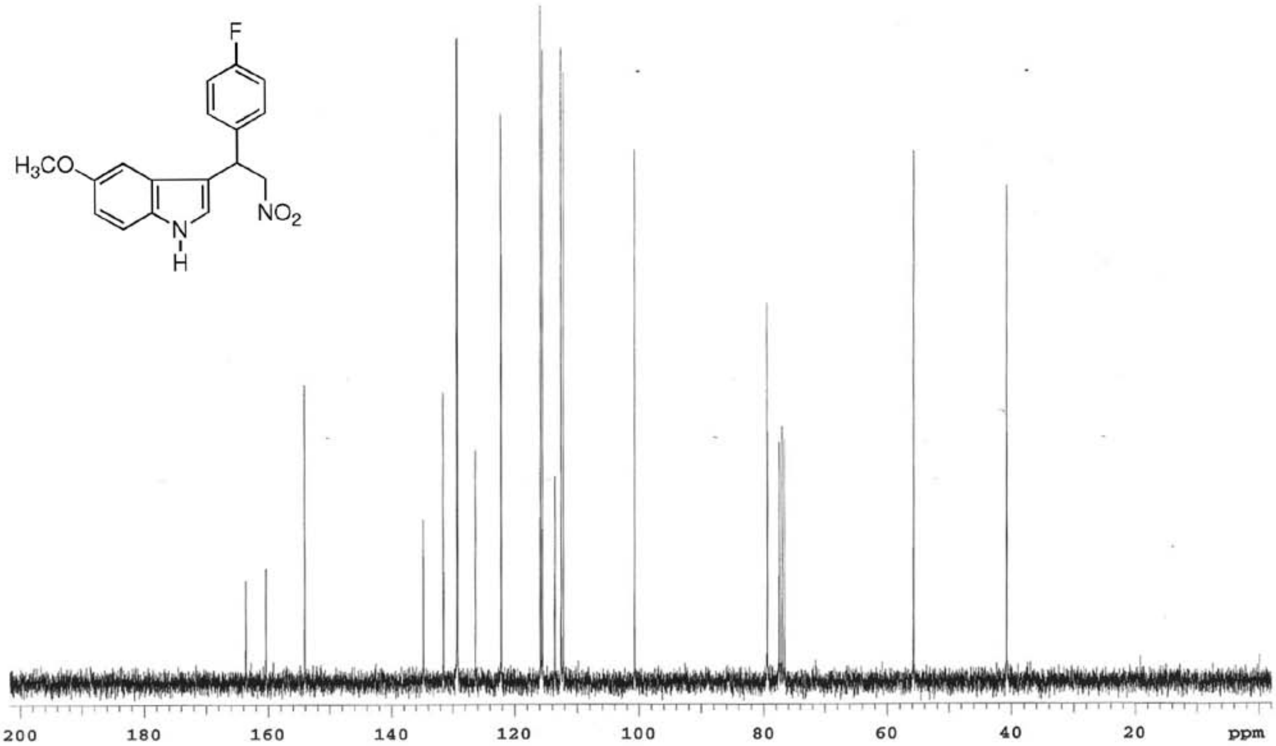

Figure S32. ^{13}C NMR ($CDCl_3$) of compound **5j.**

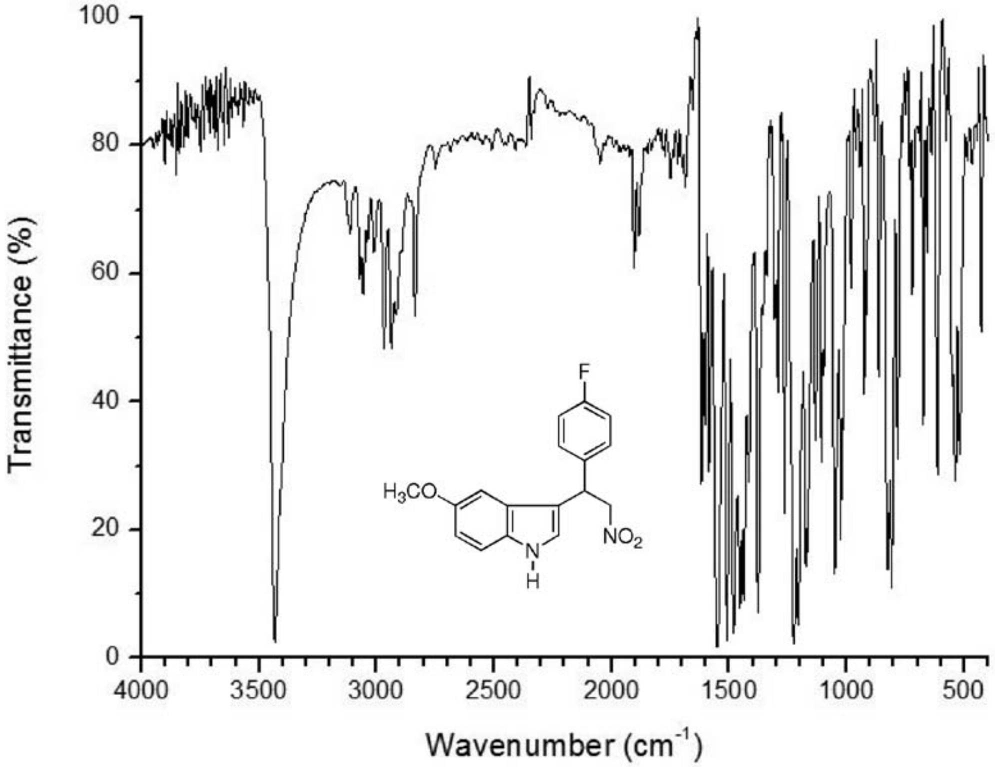

Figure S33. IR (KBr) of compound **5j.**

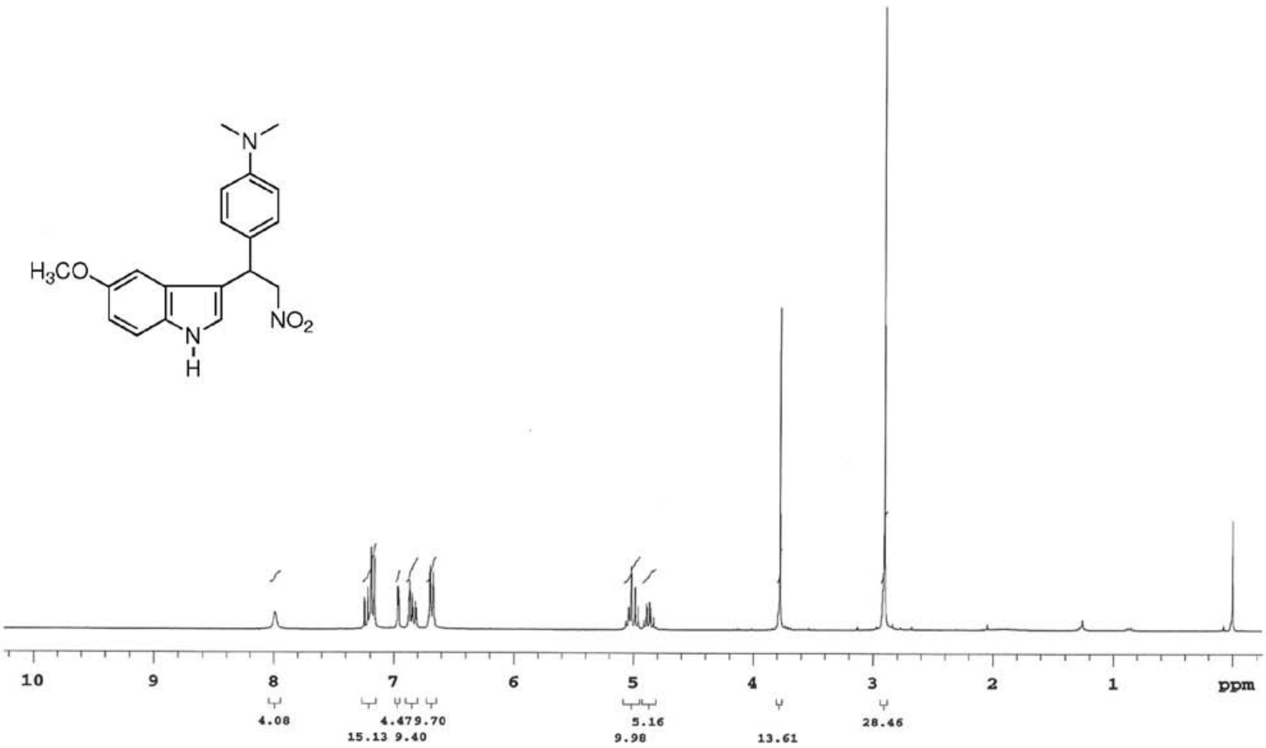

Figure S34. ^{1}H NMR ($CDCl_3$) of compound **5k.**

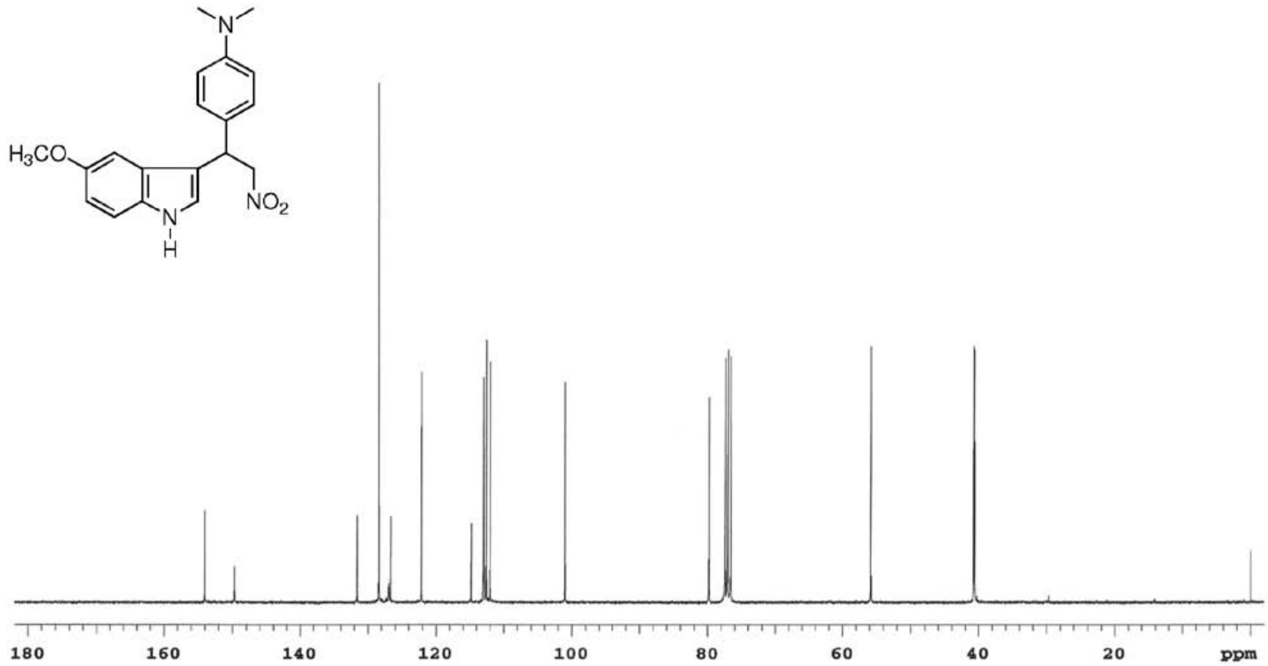

Figure S35. ^{13}C NMR ($CDCl_3$) of compound **5k.**

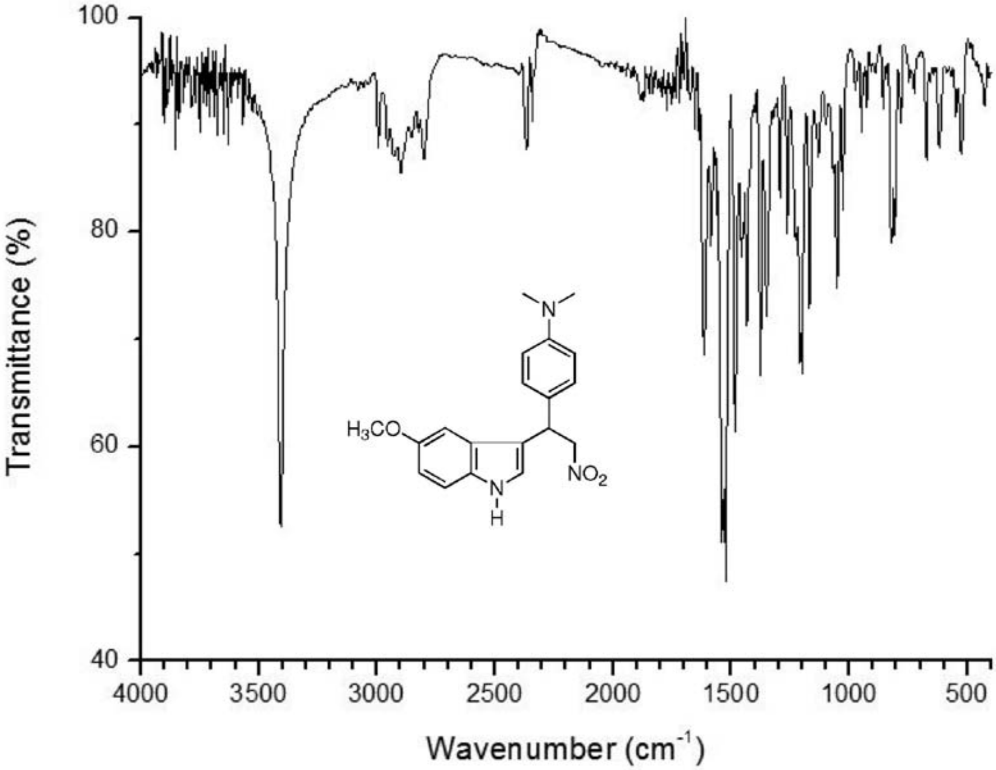

Figure S36. IR (KBr) of compound **5k.**

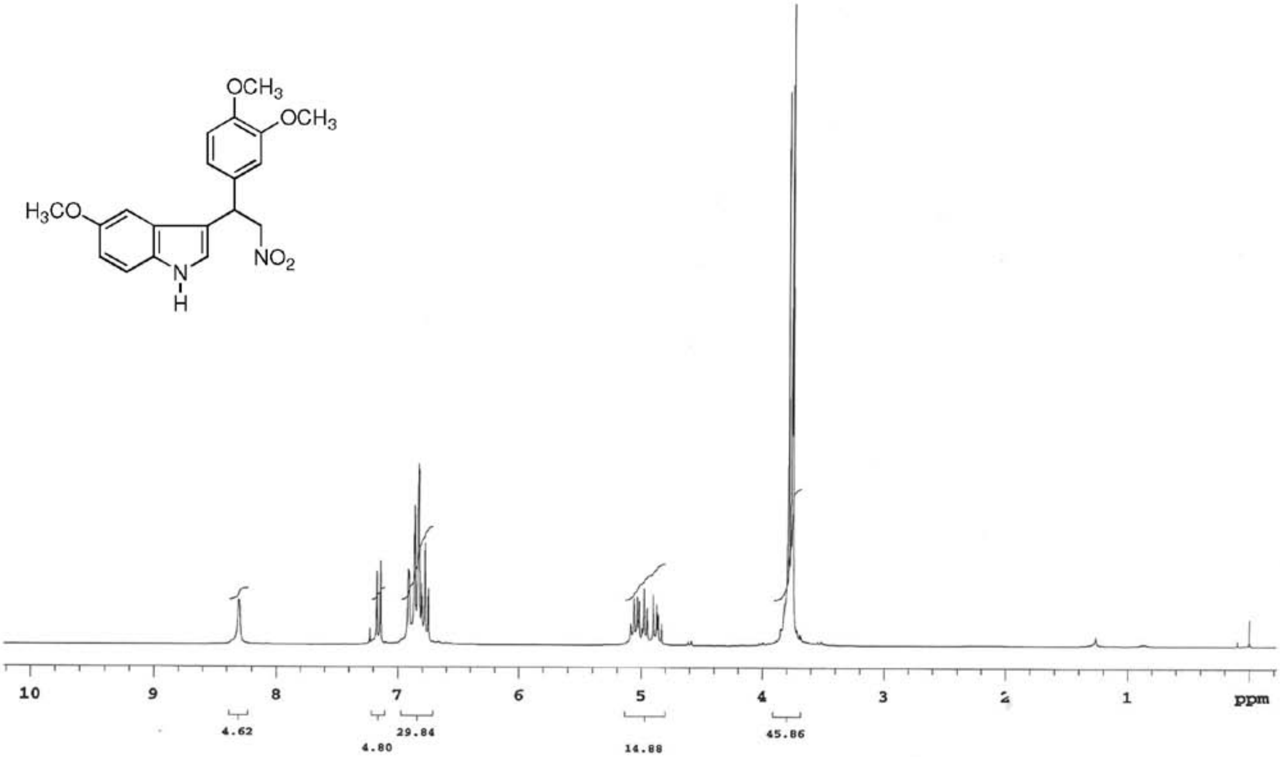

Figure S37. ^{1}H NMR (CDCl$_3$) of compound **5l.**

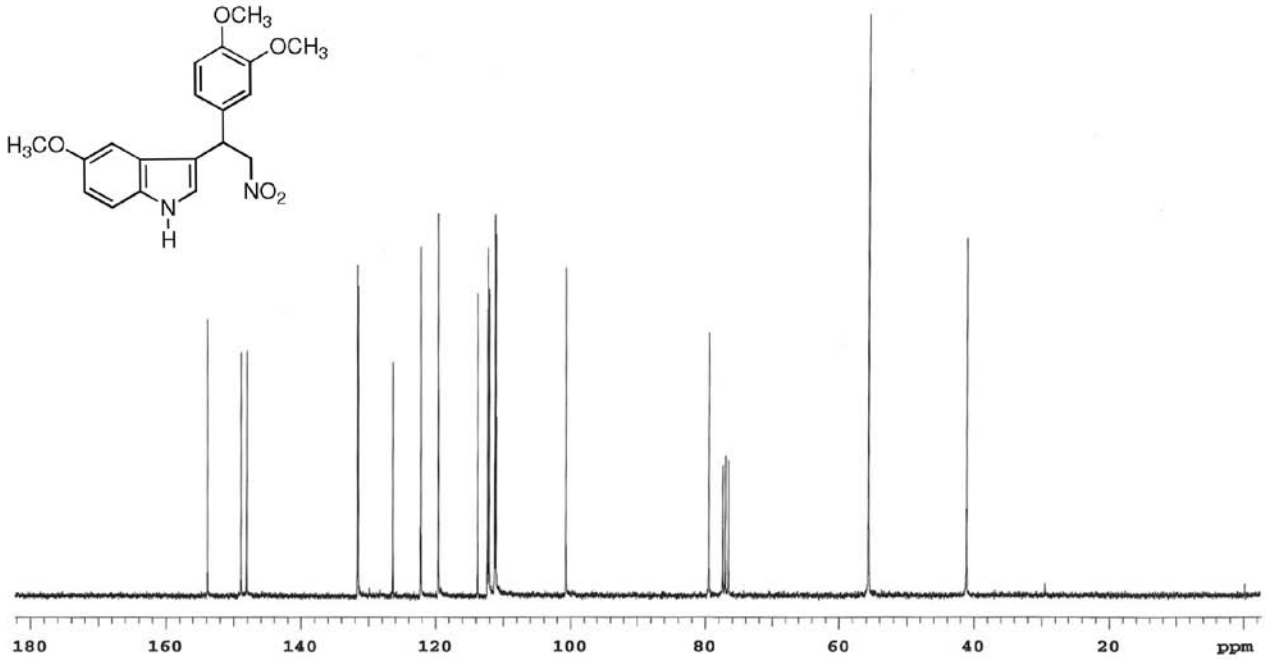

Figure S38. ^{13}C NMR (CDCl$_3$) of compound **5l.**

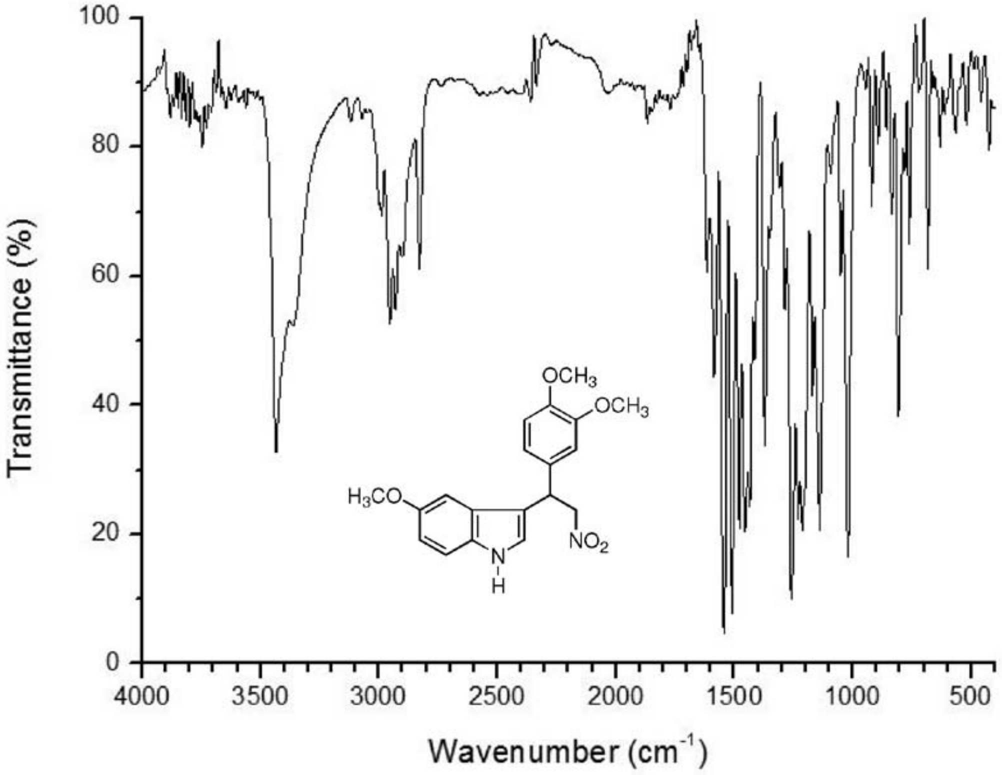

Figure S39. IR (KBr) of compound **5l.**

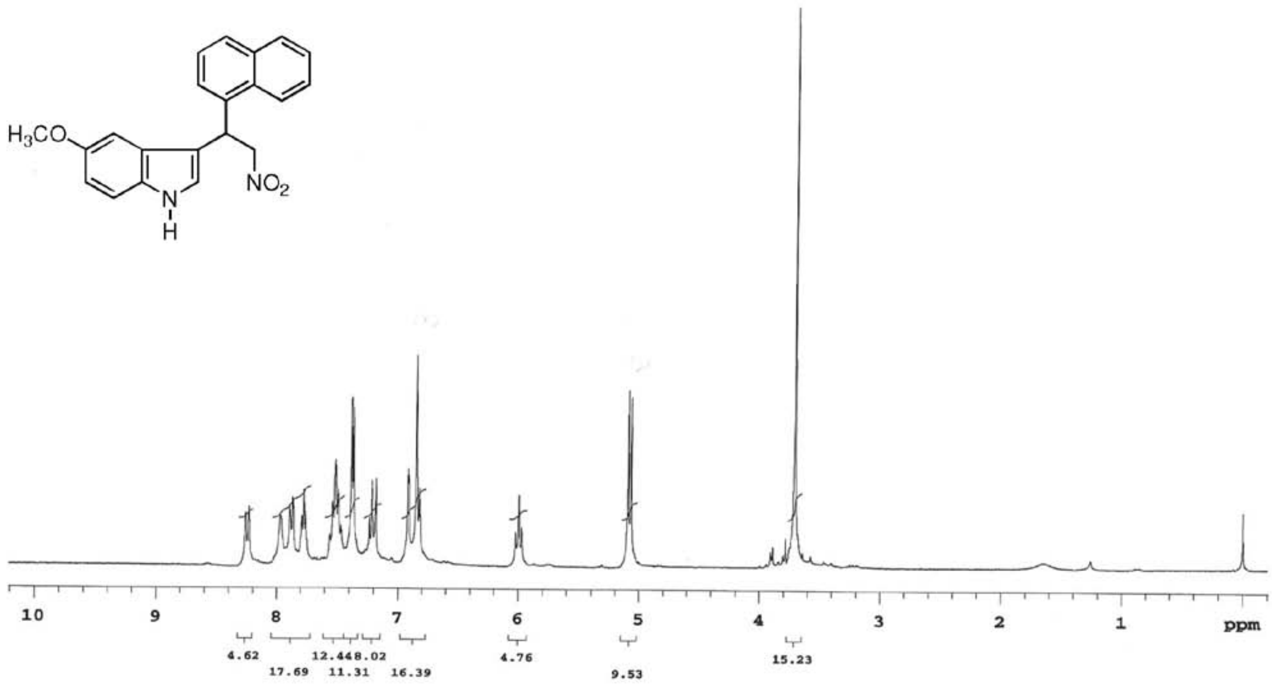

Figure S40. ^{1}H NMR ($CDCl_3$) of compound **5m.**

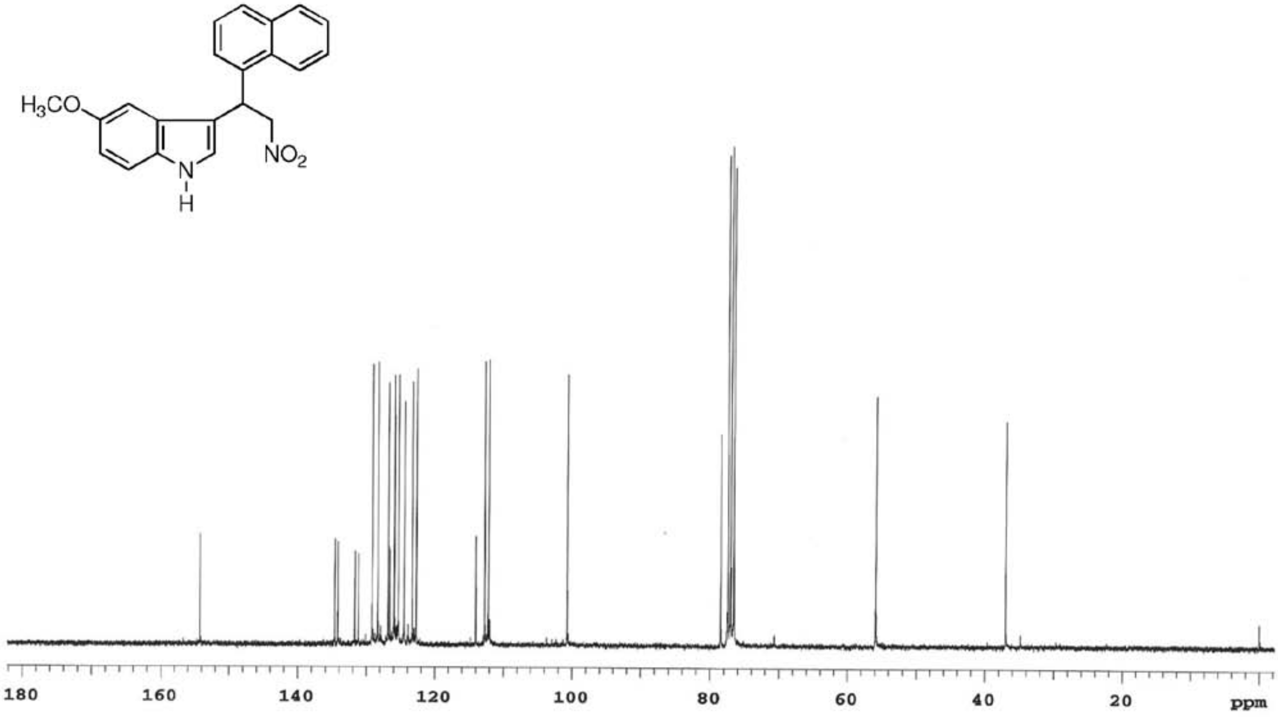

Figure S41. ^{13}C NMR ($CDCl_3$) of compound **5m.**

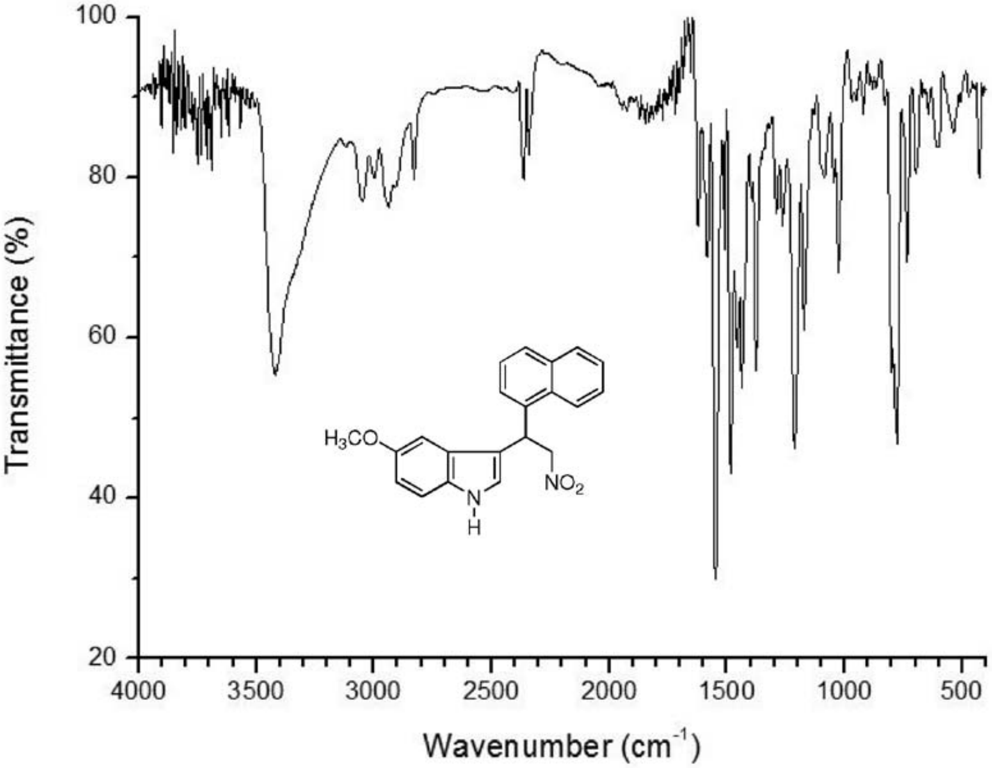

Figure S42. IR (KBr) of compound **5m.**

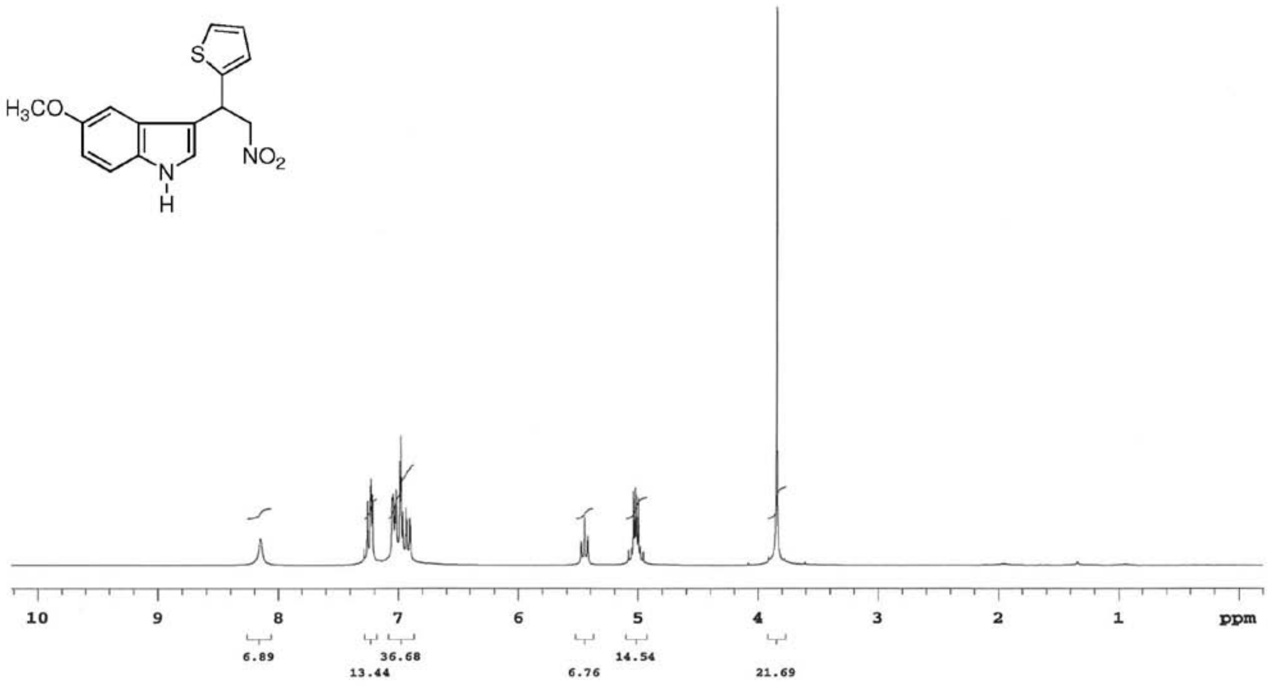

Figure S43. ^{1}H NMR (CDCl$_3$) of compound **5n.**

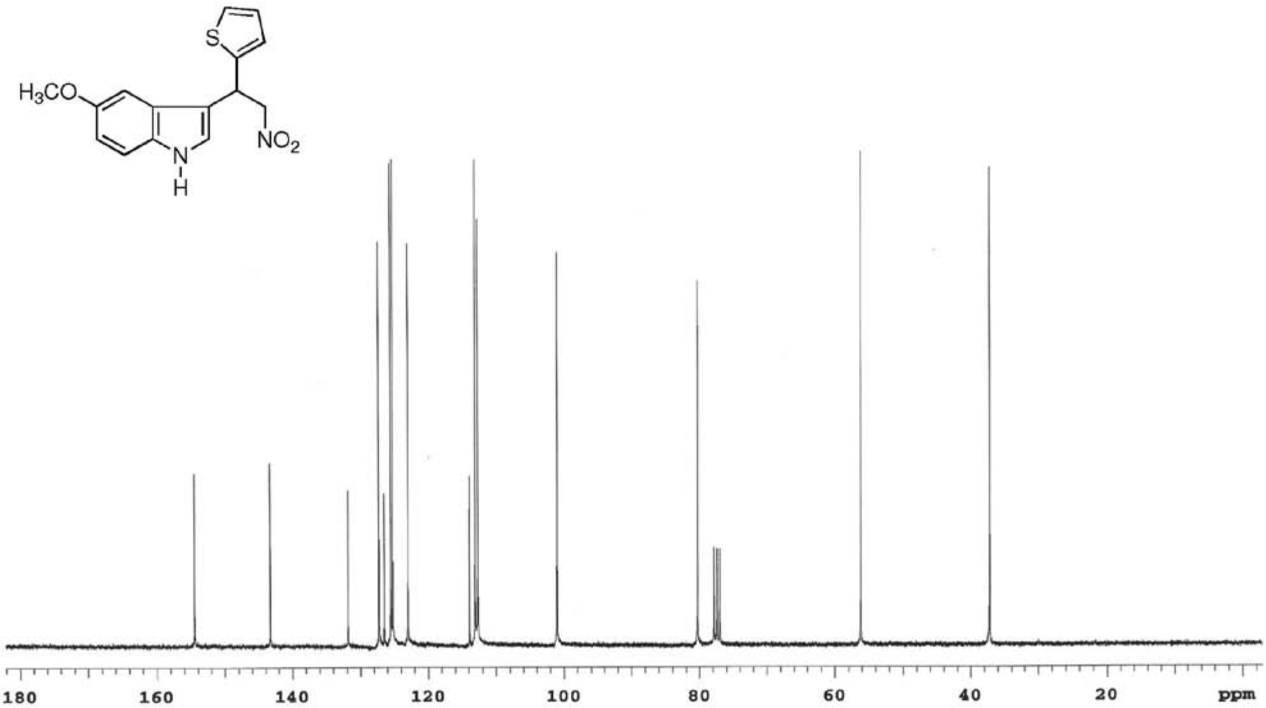

Figure S44. ^{13}C NMR (CDCl$_3$) of compound **5n.**

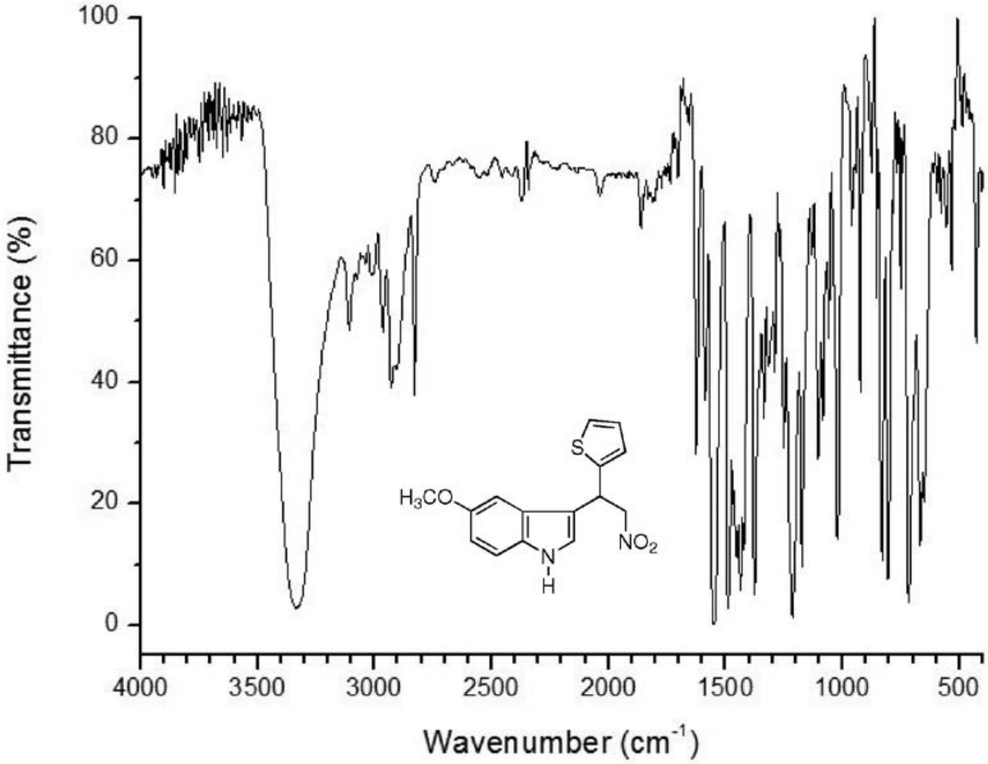

Figure S45. IR (KBr) of compound **5n.**

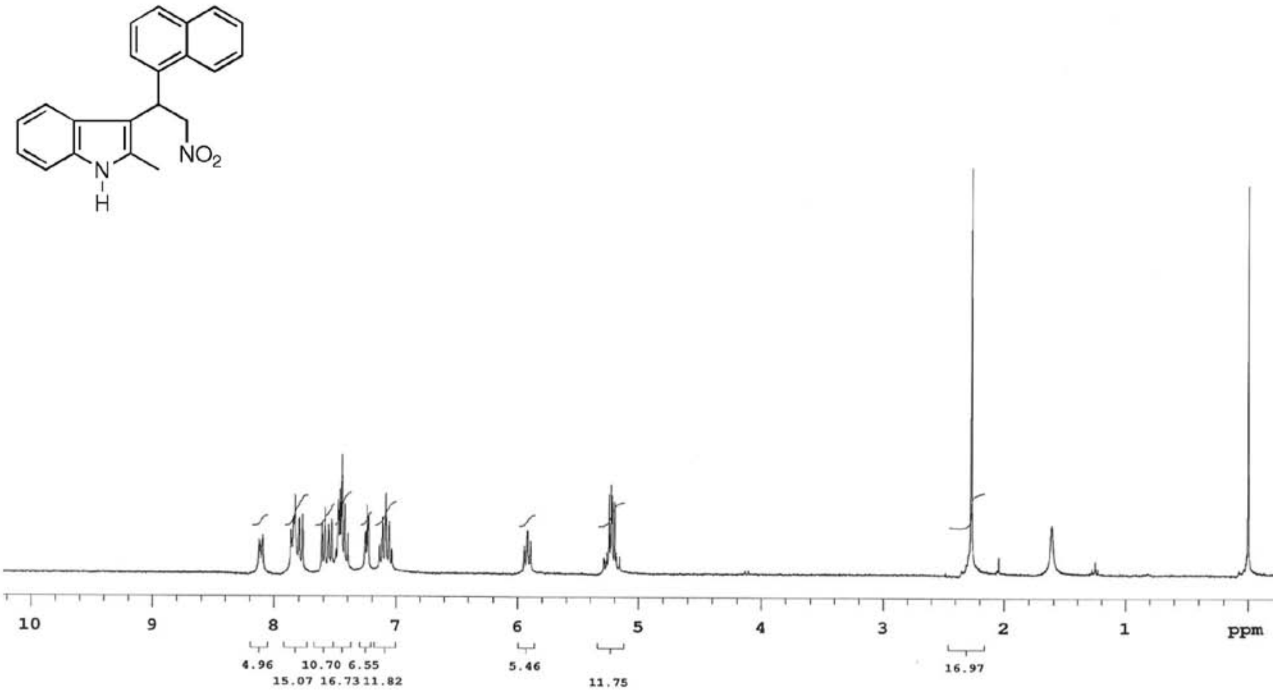

Figure S46. ^{1}H NMR ($CDCl_3$) of compound **5p.**

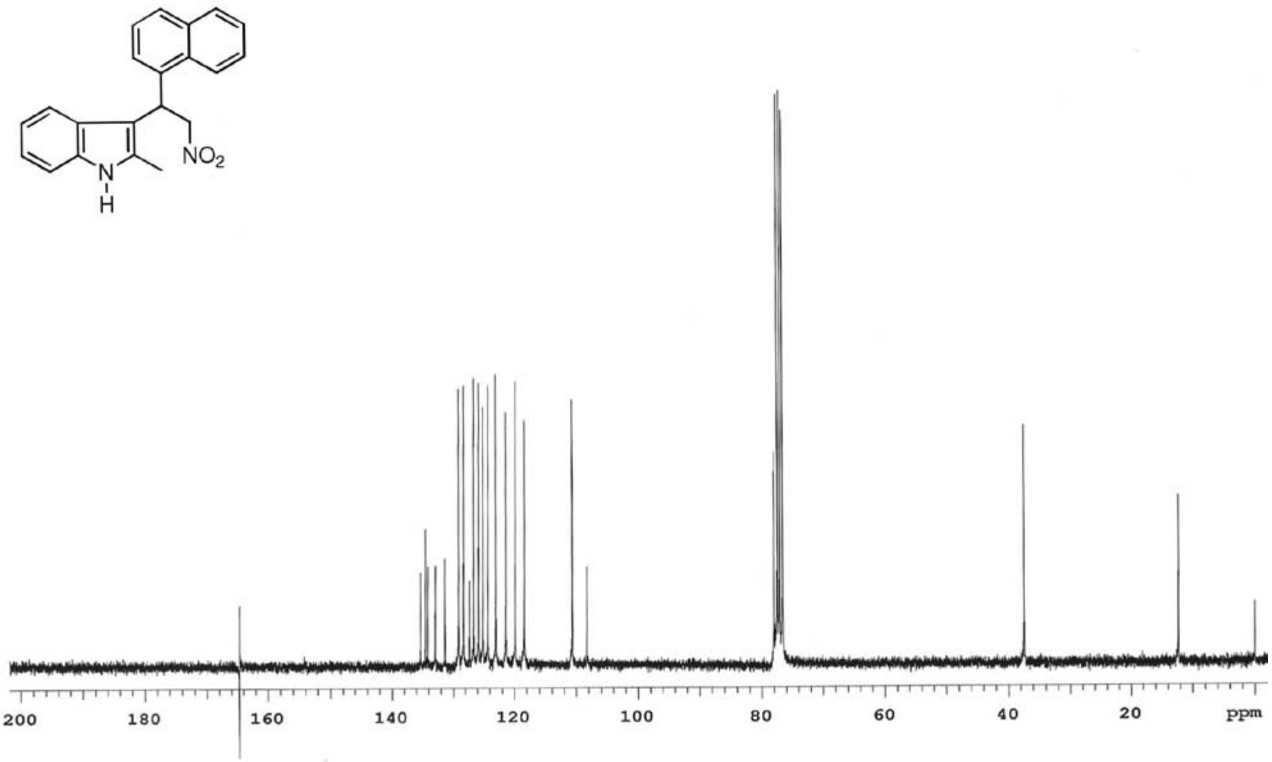

Figure S47. ^{13}C NMR ($CDCl_3$) of compound **5p.**

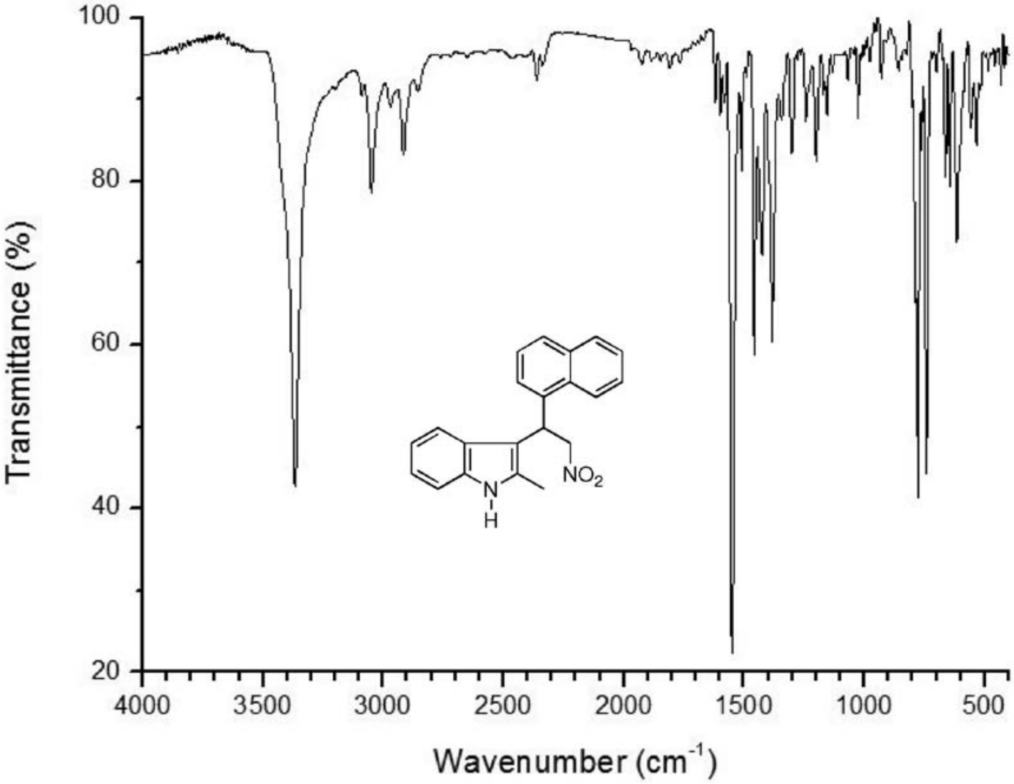

Figure S48. IR (KBr) of compound **5p.**

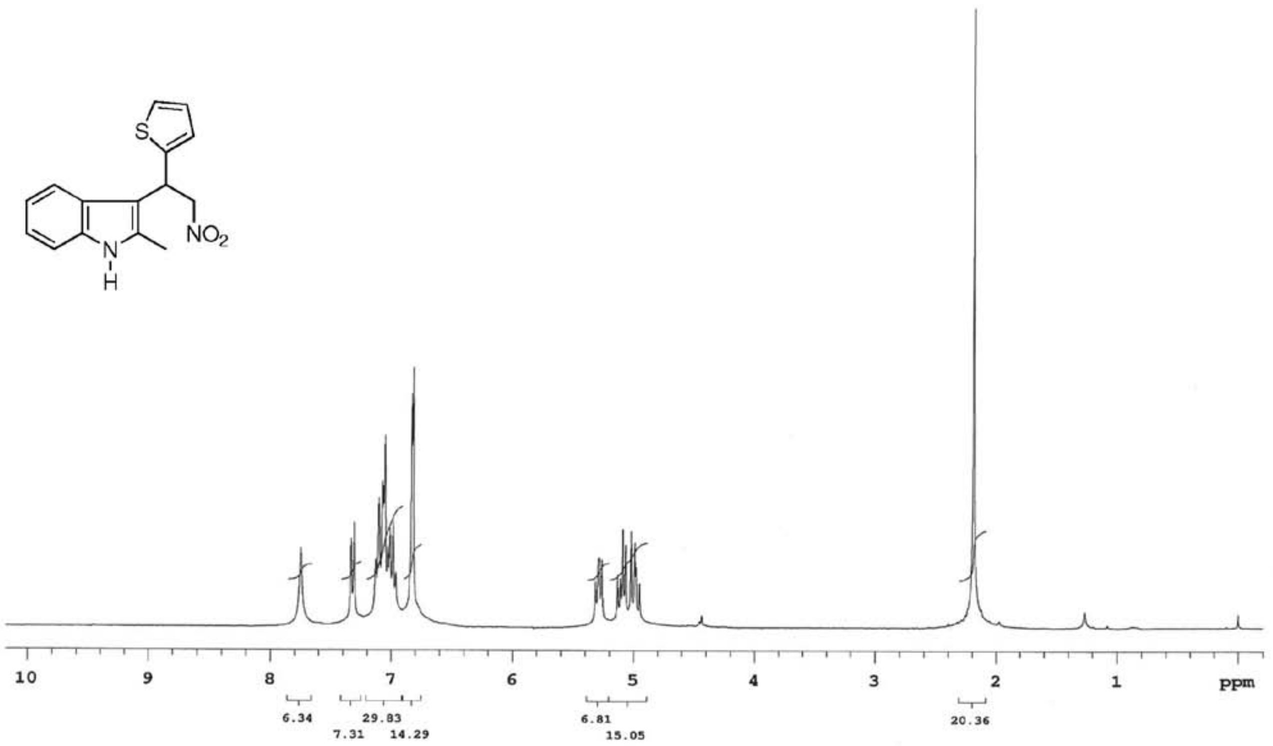

Figure S49. ^{1}H NMR (CDCl$_3$) of compound **5q.**

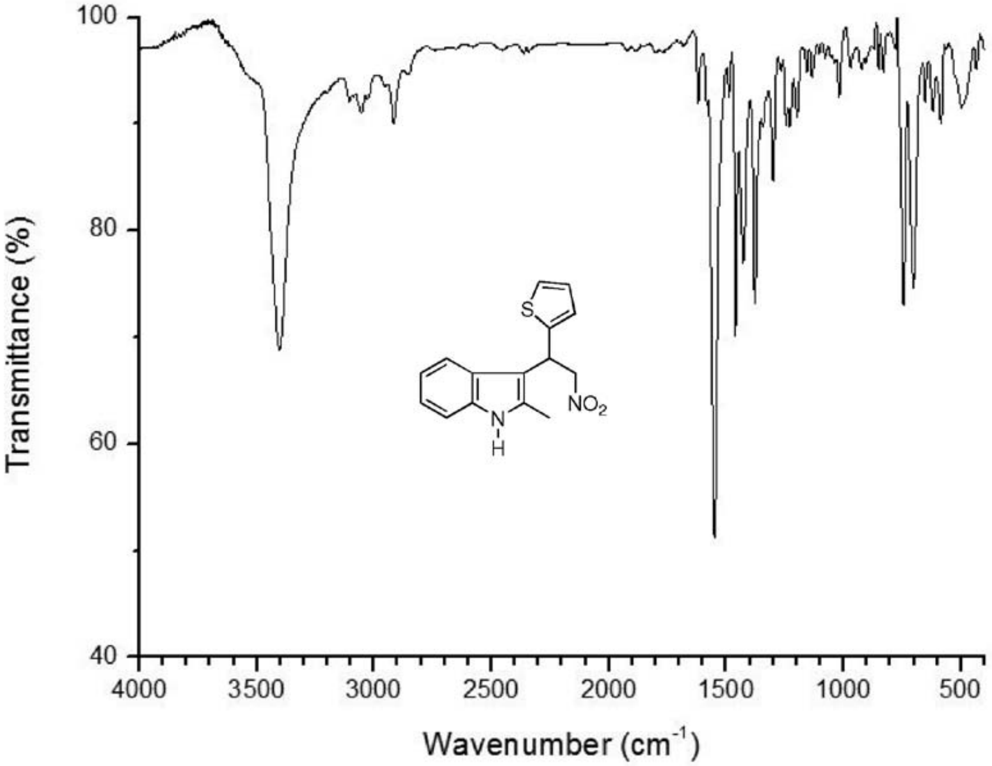

Figure S50. IR (KBr) of compound **5q.**

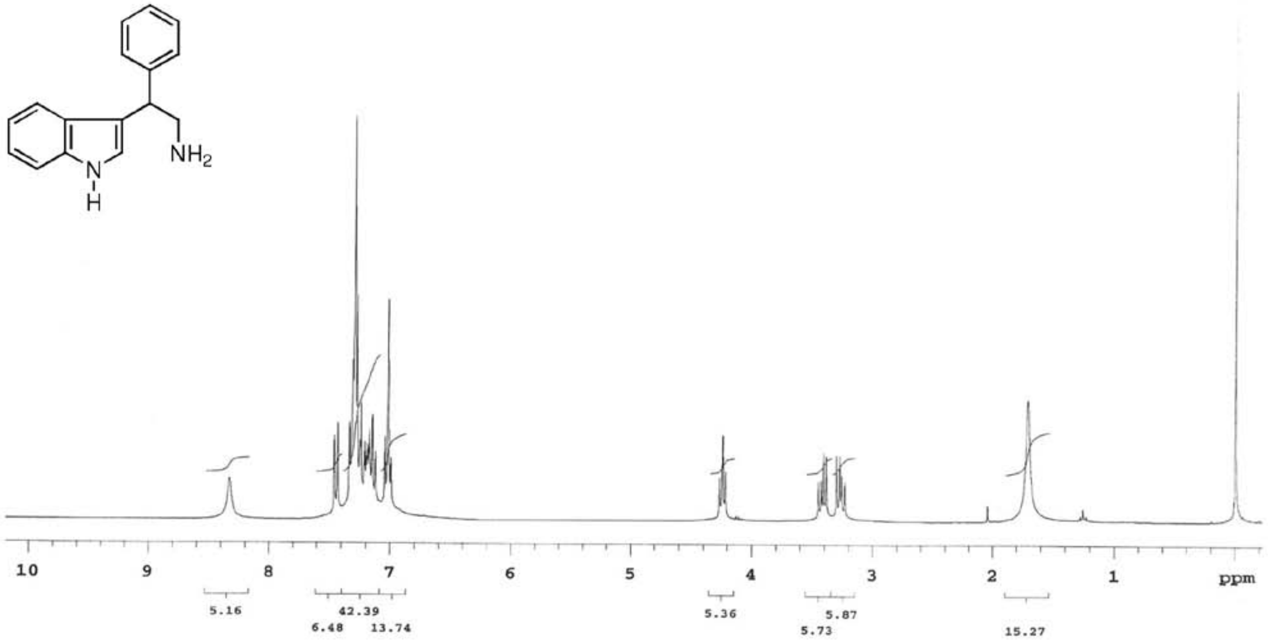

Figure S51. ^{1}H NMR (CDCl$_3$) of compound **8.**

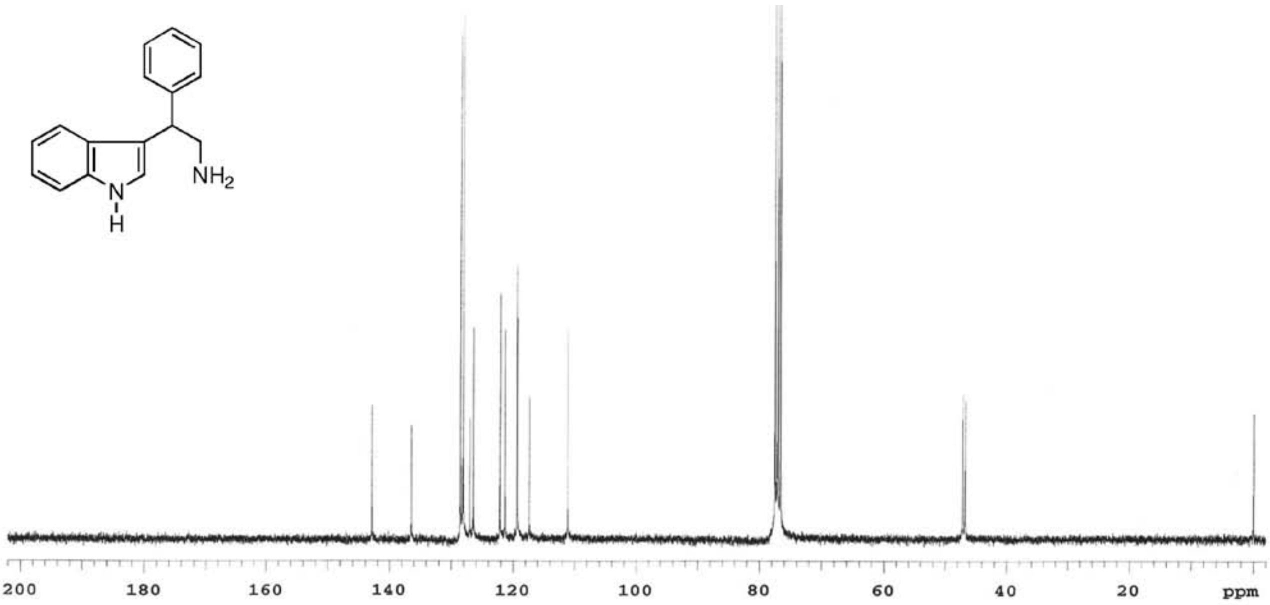

Figure S52. ^{13}C NMR (CDCl$_3$) of compound **8.**

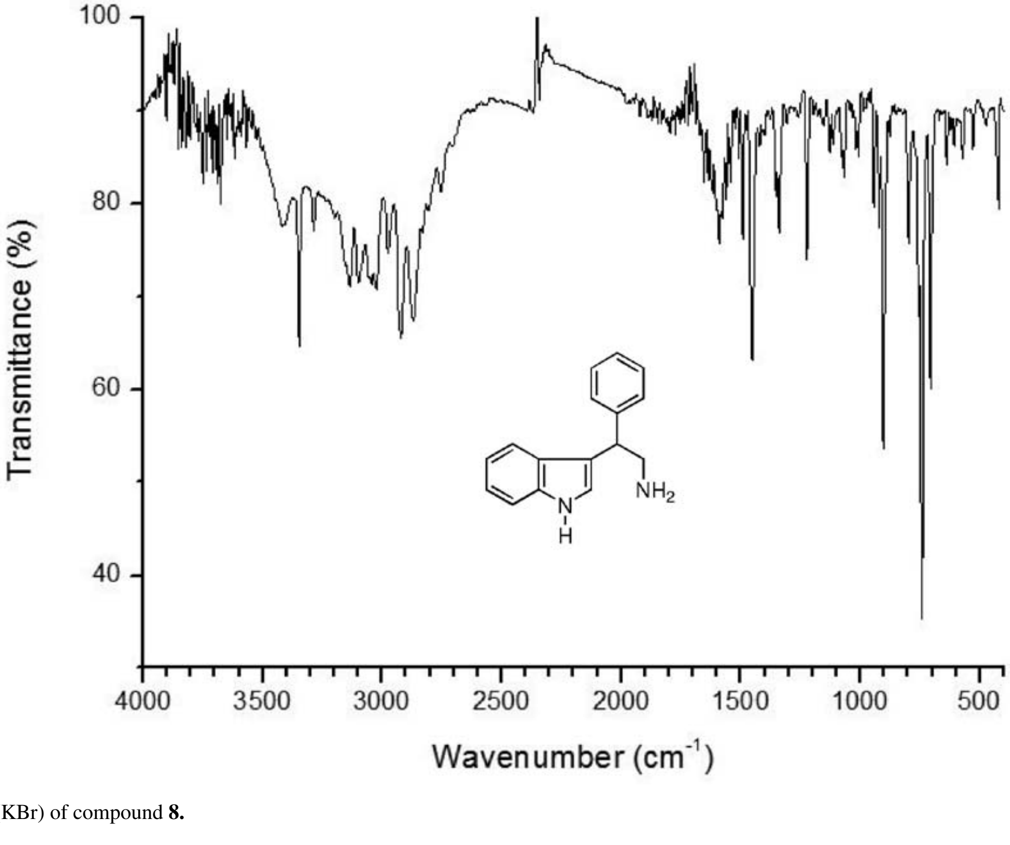

Figure S53. IR (KBr) of compound **8.**

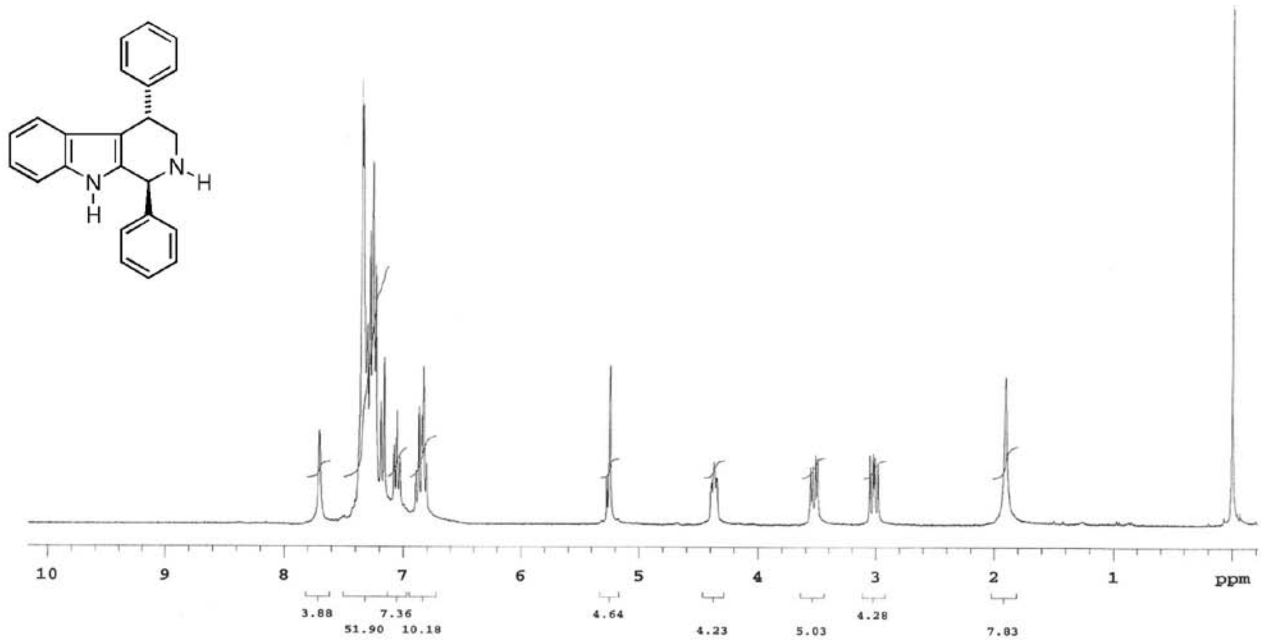

Figure S54. ^{1}H NMR ($CDCl_3$) of compound **9**-*trans.*

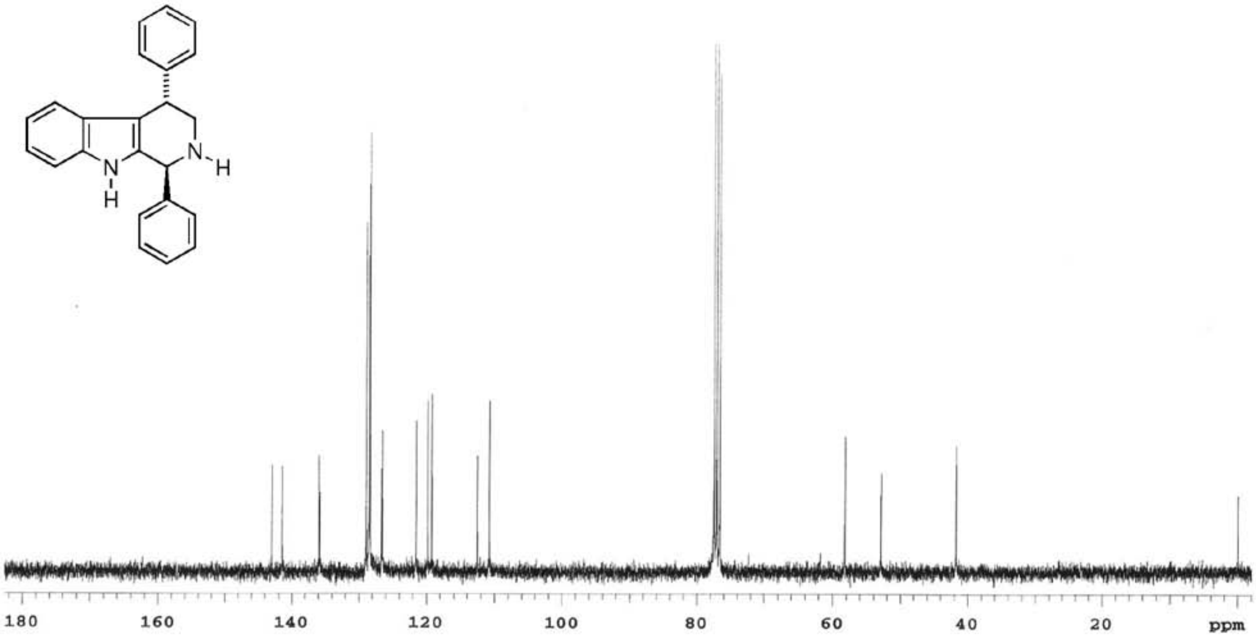

Figure S55. ^{13}C NMR ($CDCl_3$) of compound **9**-*trans***.**

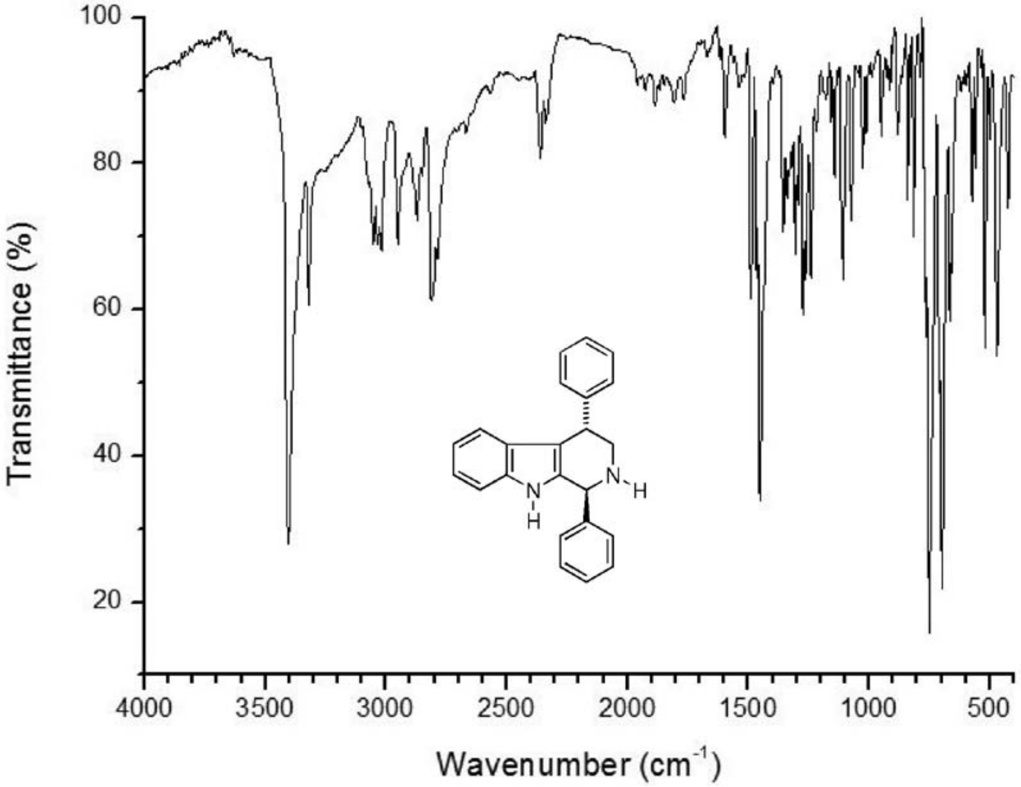

Figure S56. IR (KBr) of compound **9**-*trans*.

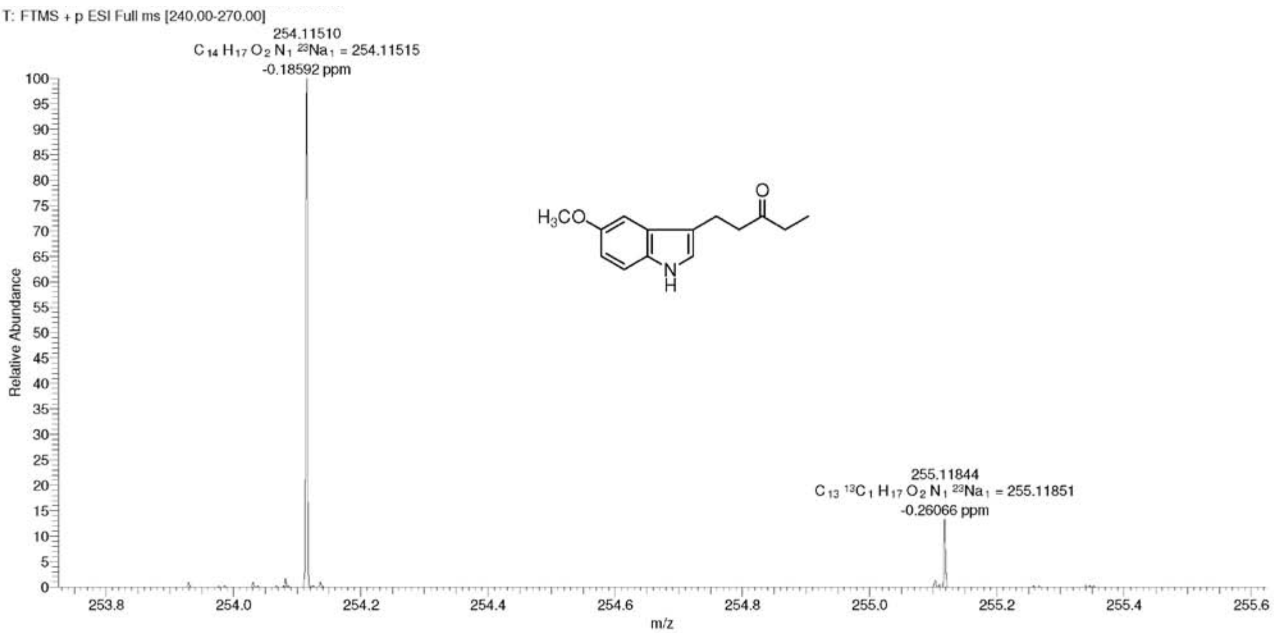

Figure S57. HRMS of compound **3g.**

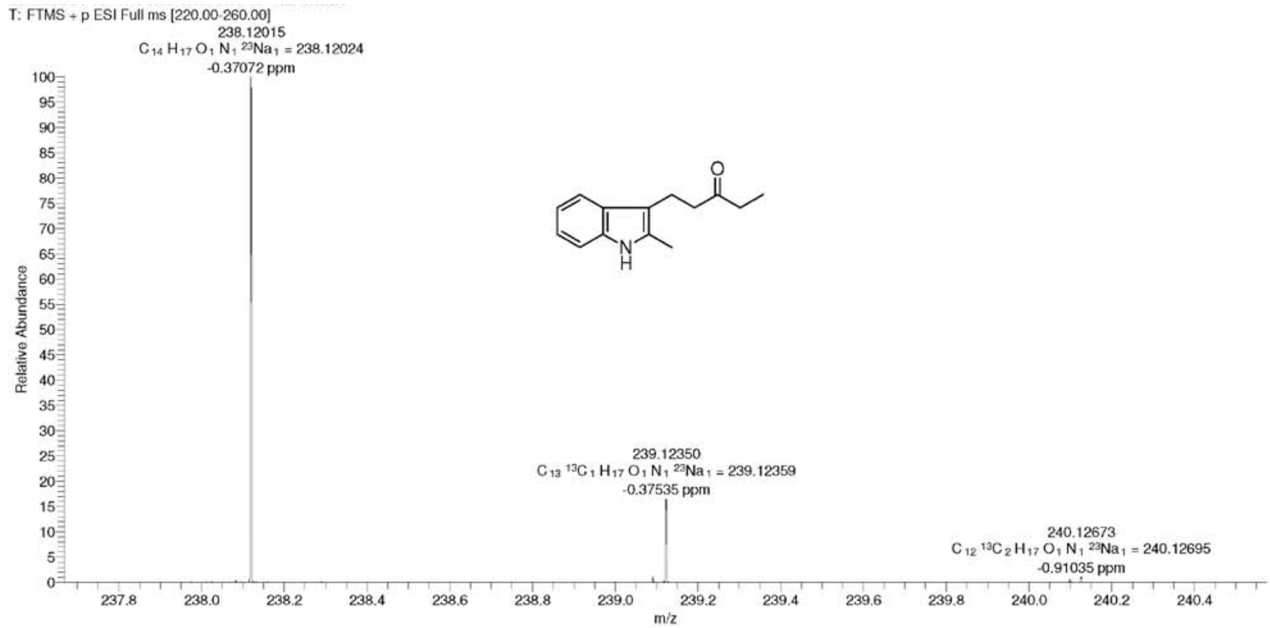

Figure S58. HRMS of compound **3l.**

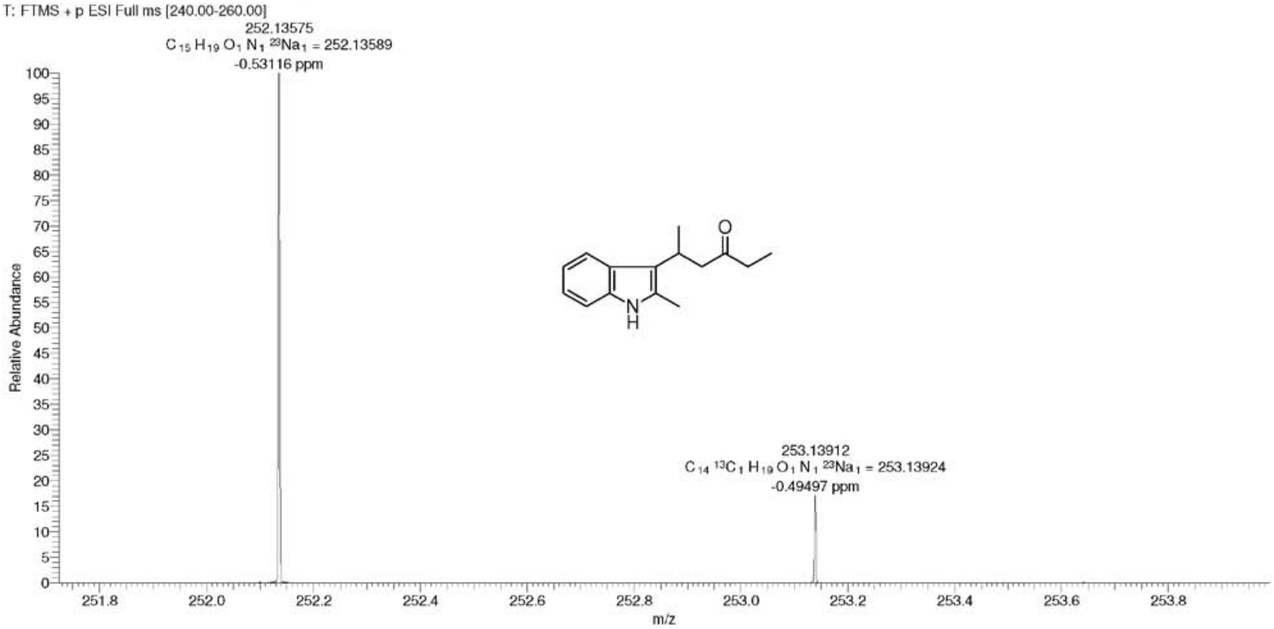

Figure S59. HRMS of compound **3k.**

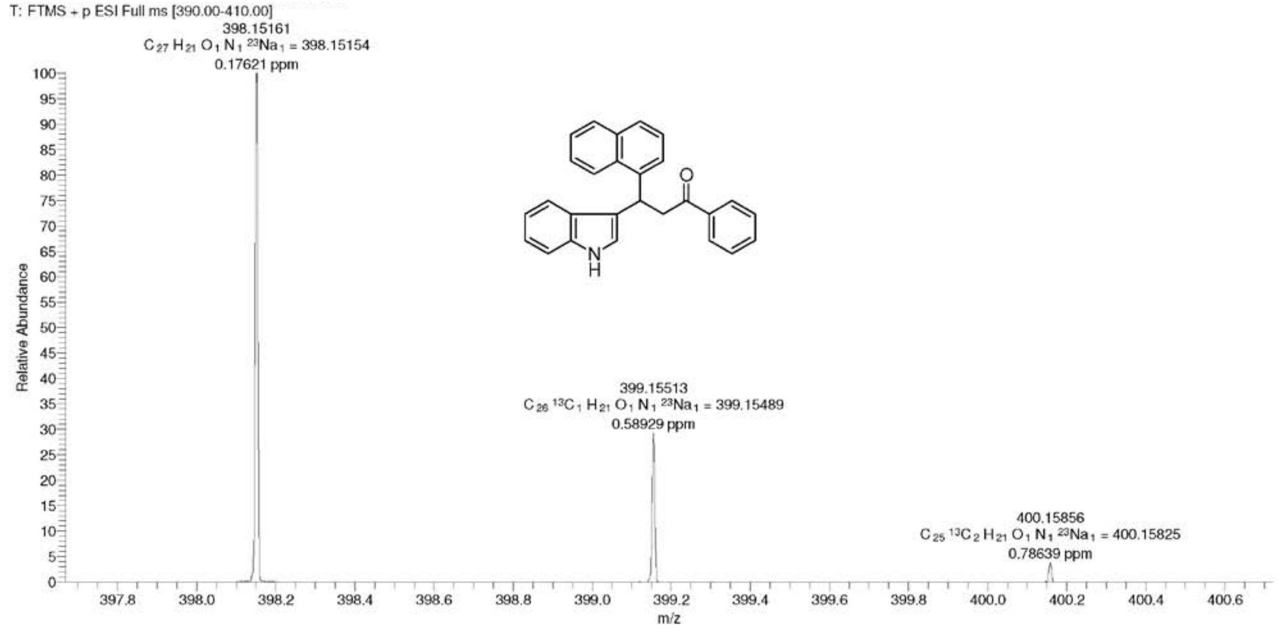

Figure S60. HRMS of compound **3s.**

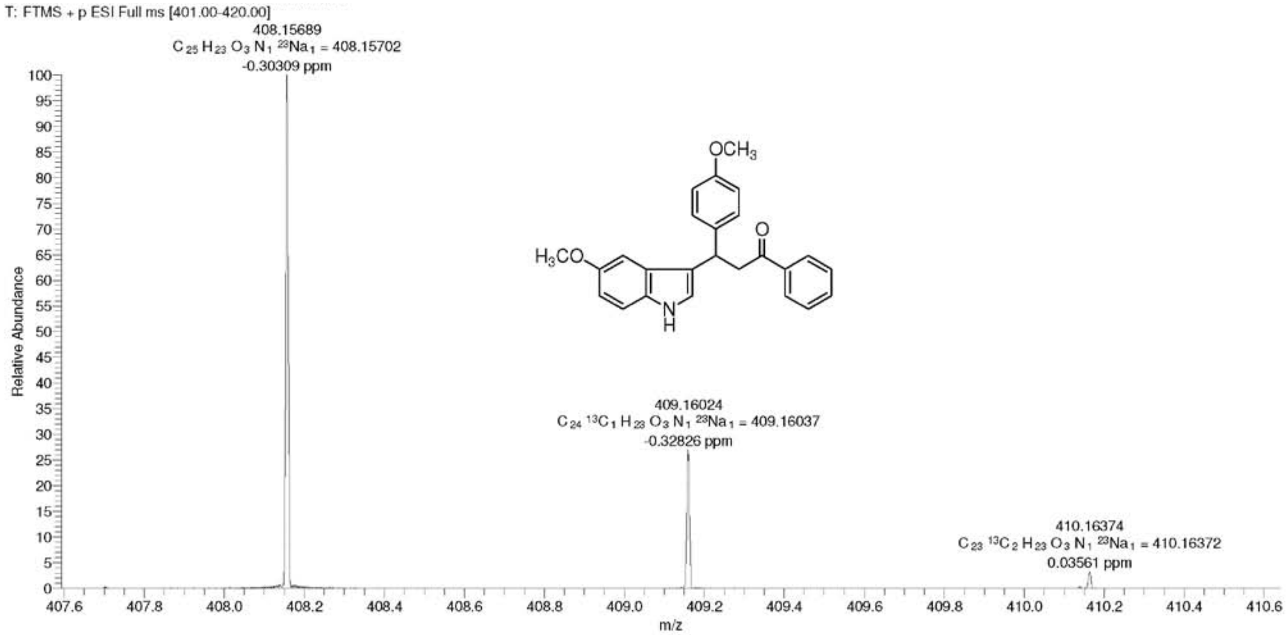

Figure S61. HRMS of compound **3x.**

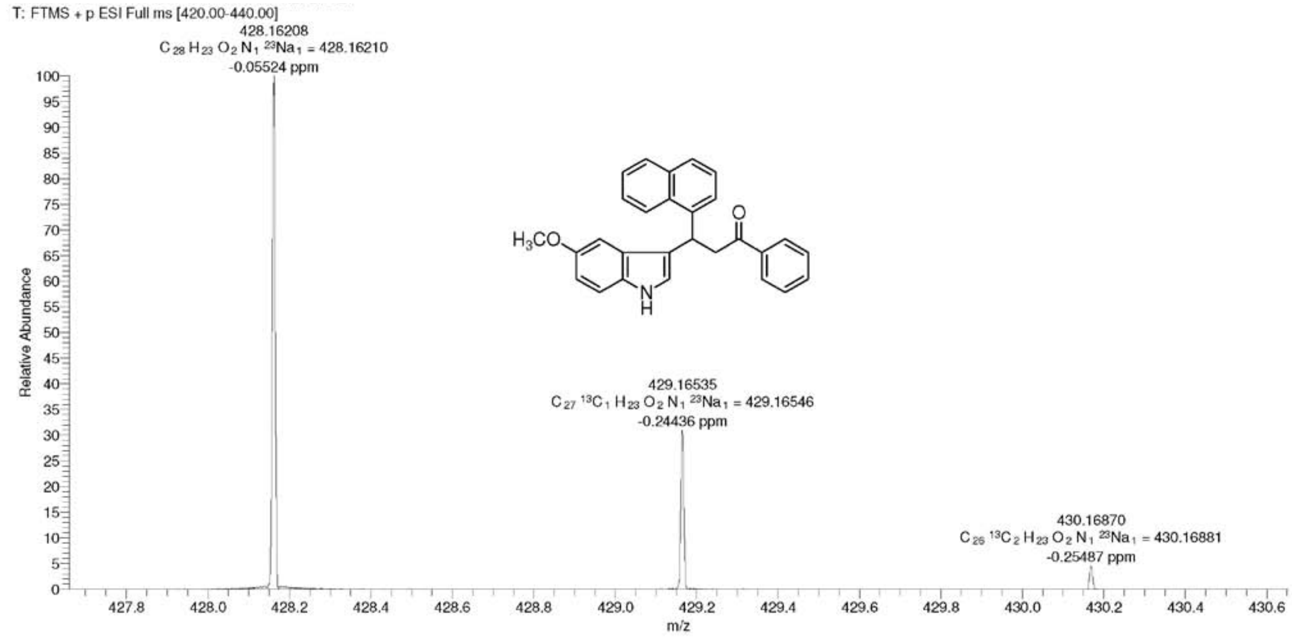

Figure S62. HRMS of compound **3w.**

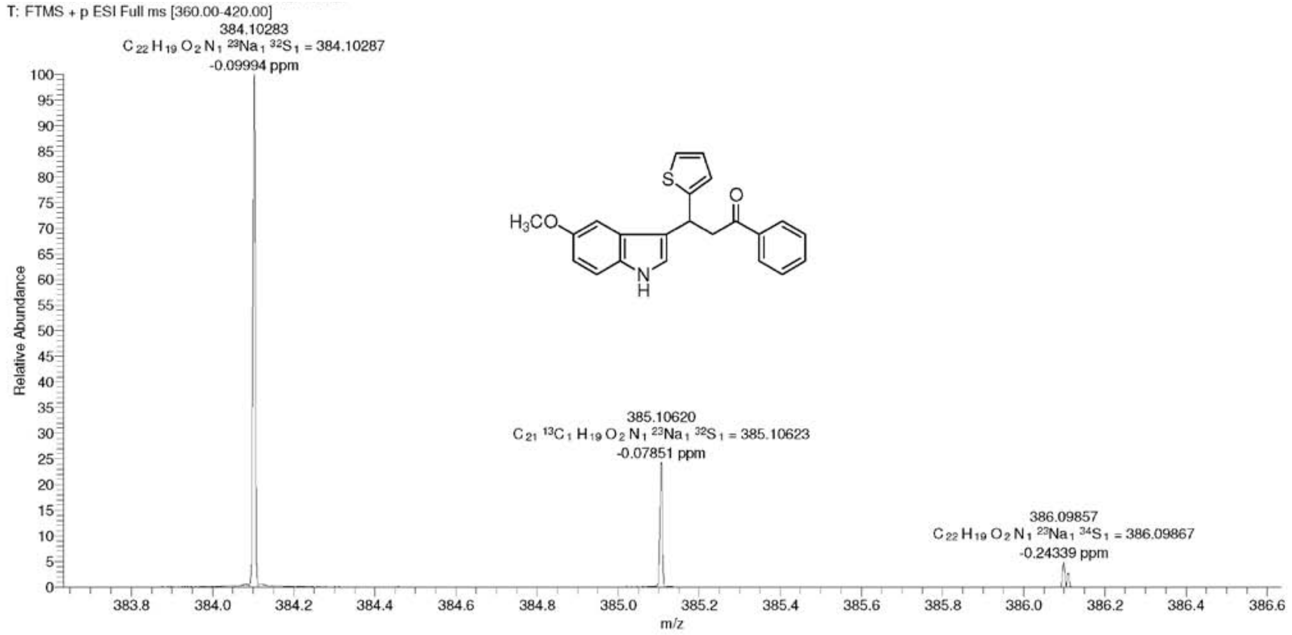

Figure S63. HRMS of compound **3y.**

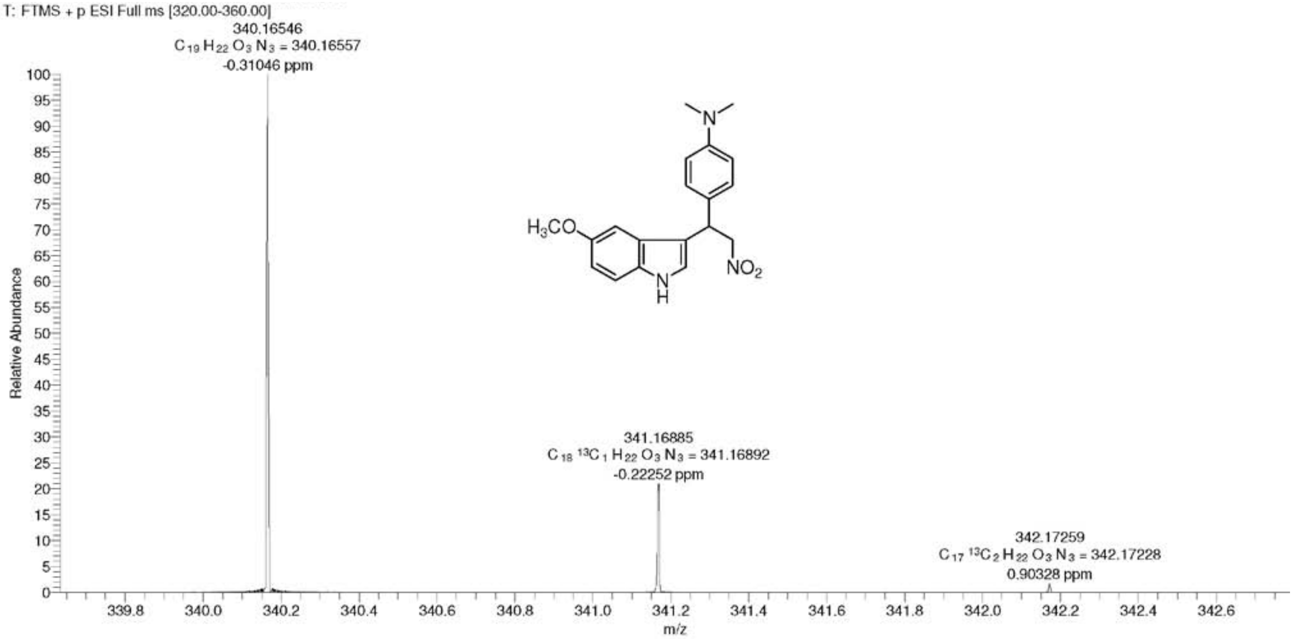

Figure S64. HRMS of compound **5k.**

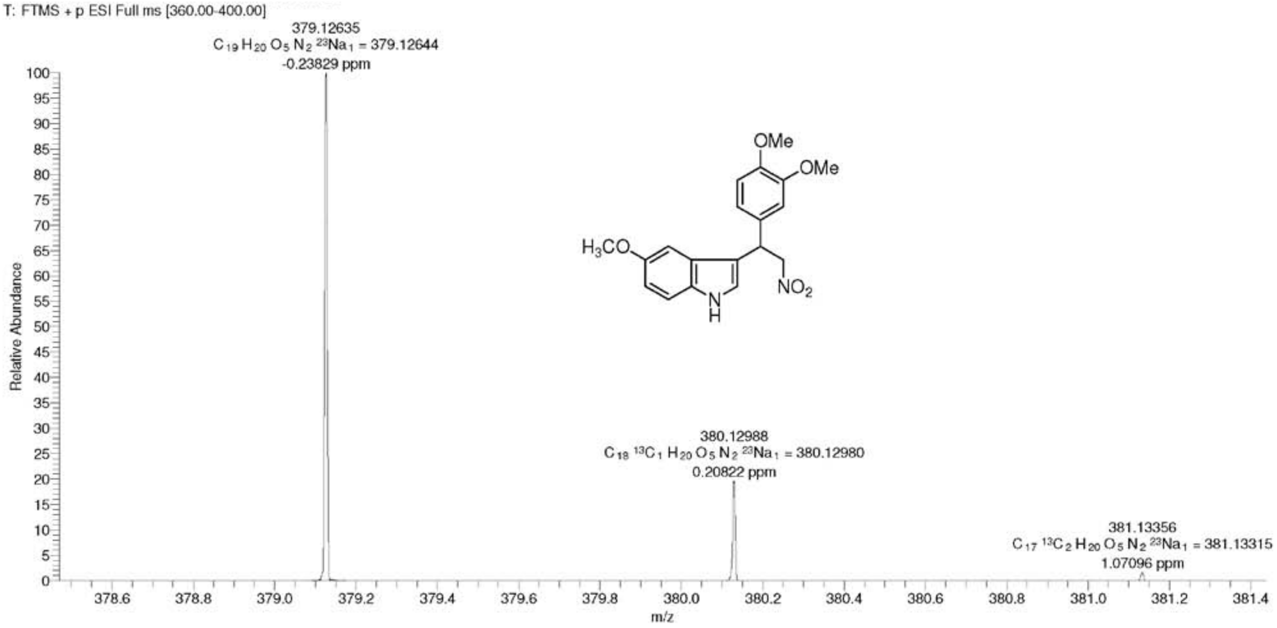

Figure S65. HRMS of compound **5l.**

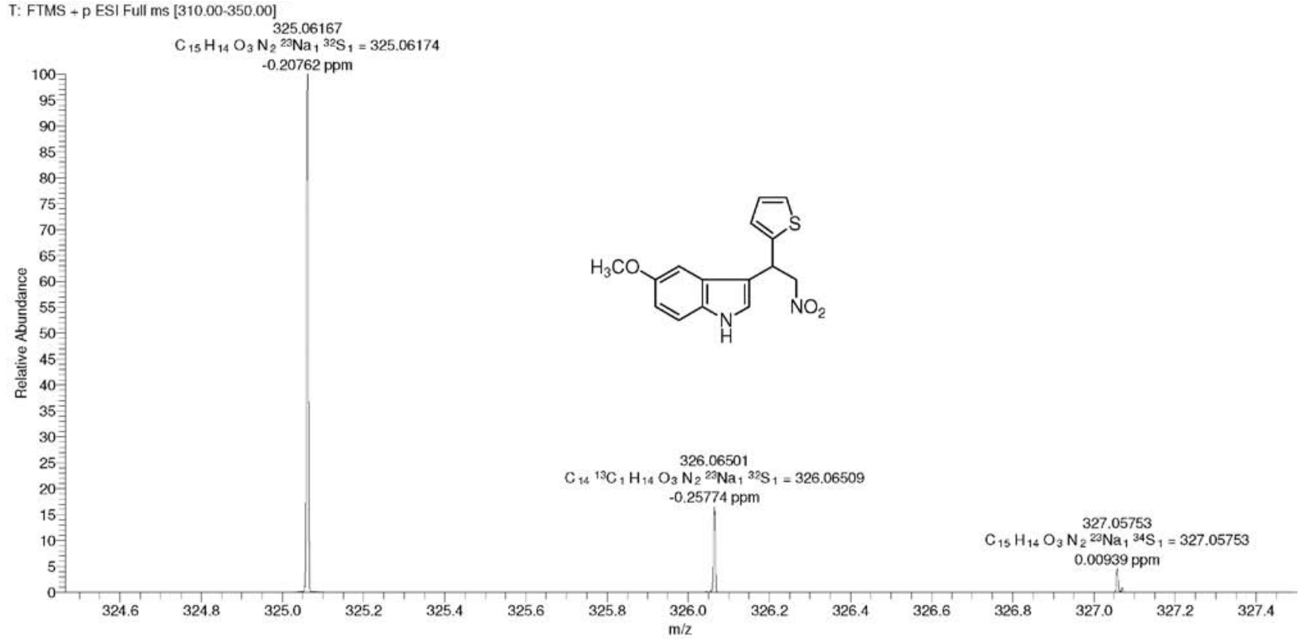

Figure S66. HRMS of compound **5n.**

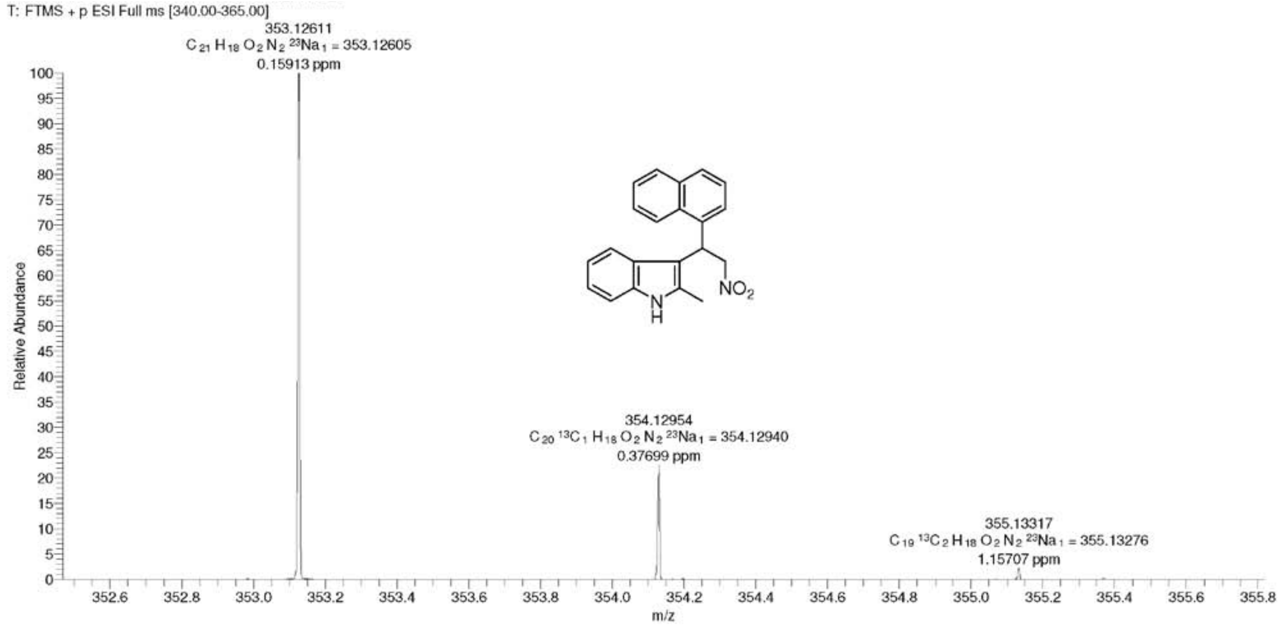

Figure S67. HRMS of compound **5p.**

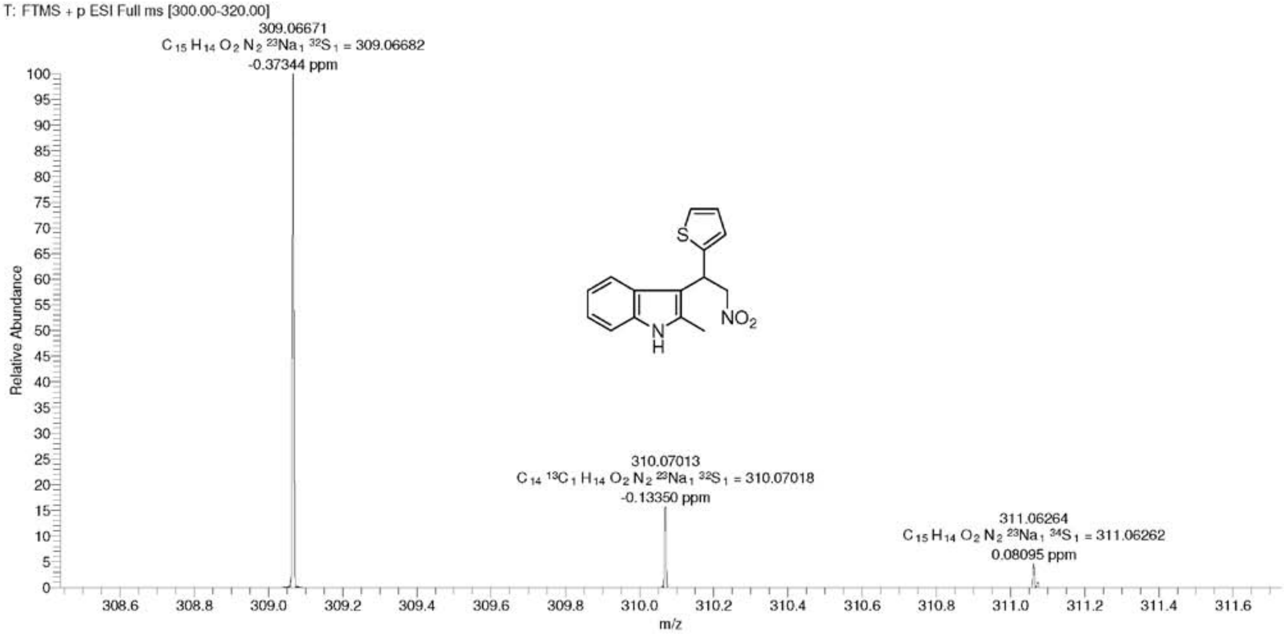

Figure S68. HRMS of compound **5q.**