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Journal Name

ARTICLE

Infrared irradiation assisted both the synthesis of (*Z*)-(aminomethyl)(aryl)phenylhydrazones via the Mannich coupling reaction and its application to the palladium-catalyzed Heck reaction.

0Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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The Mannich coupling reaction between arylhidrazones, formaldehyde and a secondary amine to generate the (*Z*)-(aminomethyl)(aryl)phenylhydrazones **1a-h** assisted with infrared irradiation (IR) under solvent-free conditions is herein reported, and the catalytic potential of compounds **1a-h** in the palladium-catalyzed and IR-assisted Heck coupling reaction are also evaluated. Coupling products are obtained in high yields and short reaction times. We show the advantages of this new alternative to promote both Mannich and Heck coupling reactions.

Introduction

Since its early application, the Mannich reaction has become a powerful tool for the synthesis of various β-amino ketones and esters, which are versatile synthetic building blocks for the preparation of compounds containing nitrogen, and privileged structures useful in synthetic and medicinal chemistry.[1] In this context, the Mannich reaction of hydrazones has only shown moderate to good yields using formaldehyde.[2] This methodology was extended allows efficient coupling reactions between hydrazones, another aldehydes and secondary amines.[2b] The hydrazones and their derivatives are a versatile class of compound mainly useful in heterocycle synthesis,[3] as organocatalysts,[4] and as ligands in metallic complexes.[5] Aryl hydrazones are applied as efficient ligands in the palladium-catalyzed Heck reaction,[6] the coupling reaction of Suzuki,[7] the reaction of Hiyama,[8] and the coupling reaction of allyl acetate with boric acid.[9]

The Heck reaction is one of the most general and useful method for the formation of C-C bonds.[10] This coupling reaction has a wide variety of applications including total synthesis of natural products,[11] fine chemicals syntheses,[12] bioorganic chemistry,[13] material science[14] and industrial applications,[15] among others.

This reaction involves an appropriated chemical source of palladium, in combination with phosphine ligands, and a base under inert conditions.[10] Nevertheless, the high cost of phosphines and their sensitivity to air and moisture conditions have favored the development more robust new catalytic systems based on different ligands and/or phosphine-free catalytic systems. Among ligands with different donor groups, we can find extensive examples that include N-heterocyclic, [16] carbocyclic,[17] and anionic carbocyclic carbenes,[18] Schiff bases,[19] pyridines,[20] imidazoles,[21] pyrazoles,[22] oxazolines,[23] hydrazones,[24] selenides,[25] ureas,[26] thioureas,[27] among others. Extensive studies have shown the efficiency and robustness of palladacycles,[28] pincer-type complexes,[29] palladium nanoparticles,[30,31] Pd(II) species supported in mesoporous materials,[32] etc. in performing this coupling reaction

On the other hand, new experimental methodologies based on non-convectional energy sources for the activation of chemical reactions different to conventional heating, such as microwaves,[33] ultrasound,[34] mechanochemistry[35] and infrared,[36-39] have gained growing attention in recent years, as an important section of what is nowadays known as Green Chemistry.[40] In particular, microwave irradiation under controlled conditions is an invaluable technology that has enormous applications in different areas, including academic[41a] and industrial[41b] researches. However, the successful use of this methodology is limited to the access of specific and expensive equipment.[42] Infrared irradiation is an energy source hardly explored in comparison to other energy sources.[36-39]

Due to the high value of IR as an energy source for the activation of chemical reactions, and few precedent in the literature regarding to the use of infrared irradiation in both Mannich and Heck coupling reactions, recently we report to use of the IR in the Heck coupling reaction with very good results.[43] To continue with the use of IR as energy source for the activation of chemical reactions, we herein report a practical and efficient method for the system synthesis of type (*Z*)-(aminomethyl)(aryl)phenylhydrazones via Mannich

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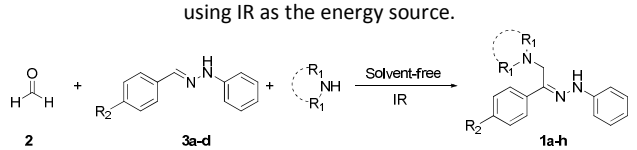
coupling and their application to the palladium-catalyzed Heck coupling reaction assisted by IR.

Results and discussion

The (*Z*)-(aminomethyl)(aryl)phenylhydrazones **1a-h** were prepared according to a procedure described in the literature[2c,d] via the Mannich reaction between formaldehyde (**2**), a phenylhidrazone **3a-d**, piperidine or diethylamine as base, under solventless conditions (chromatography was required for purification) and using infrared irradiation (IR) as the energy source. This method is clean and rapid and affords the corresponding (*Z*)-(aminomethyl)(aryl)phenylhydrazones **1a-h** with very good yields.

Table 1. Synthesis of (*Z*)-(aminomethyl)(aryl)phenylhydrazones **1a-h** using IR as the energy source.



2 3a-d 1a-h

Entry	R_1	R_2	Product	Time (min)	Yield [%]
1	$-(CH_2)_5-$	H	**1a**	120[a] (180)[b]	92[a] (90)[b]
2	$-(CH_2)_5-$	OCH_3	**1b**	120[a] (180)[b]	80[a](80)[b]
3	$-(CH_2)_5-$	Cl	**1c**	45[a] (120)[b]	90[a](87)[b]
4	$-(CH_2)_5-$	NO_2	**1d**	15[a] (45)[b]	99[a](97)[b]
5	C_2H_5	H	**1e**	120[a] (180)[b]	70[a](65)[b]
6	C_2H_5	OCH_3	**1f**	120[a] (180)[b]	85[a](80)[b]
7	C_2H_5	Cl	**1g**	60[a] (120)[b]	80[a](80)[b]
8	C_2H_5	NO_2	**1h**	30[a] (60)[b]	85[a](80)[b]

[a]Under infrared irradiation using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V). For controlling the temperature, a Digi-Sense variable-time power controller was used. [b]Under conventional heating

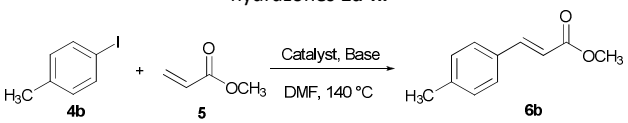
According with the results showed in Table 1, the use of IR allows the reduction of the reaction time compared with conventional heating, particularly, when electron-withdrawing groups are included in phenylhydrazone (**3**) (Table 1, entries 3, 4, and 8).

The compounds **1a-h** were fully characterized by conventional spectroscopic methods, FT-IR, ^{1}H-NMR, ^{13}C-NMR and mass spectra.

Once efficiently prepared the compounds **1a-h**, we explored as catalytic precursors in the Heck cross-coupling reaction (Table 2). The effect of concentration of the catalytic system on the Heck reaction between methyl acrylate (**5**) and *p*-iodotoluene(**4**) under IR heating condition was evaluate. We chose the hydrazone **1a** and $Pd(AcO)_2$ as model precatalysts. The coupling reaction was stirred under reflux of DMF (5 mL), using different concentrations of the [$Pd(AcO)_2$/**1a**] system. Good yields were obtained within 30 minutes, when 0.01 and 0.05 % mol of [$Pd(AcO)_2$/**1a**] was used (Table 2, entries 1, 2). The base influence was also evaluated and employed different salts as K_3PO_4, Na_2CO_3, Na_3PO_4, K_2CO_3 and AcOK. We afforded **6b** with a good yield (Table 2, entry 2).

It is important to remark that all the compounds (**1a-h**) evaluated are effective for the Heck reaction (entries 10-16), where hydrazone **1a** provides a better yields in comparison to other compounds, with turn over numbers (TON) around ~10^3. Other sources of palladium were evaluated including $PdCl_2$, $Pd(PhCN)_2Cl_2$ and $Pd(PPh_3)_2Cl_2$ (Table 2, entries 7, 8, 9) but these salts obtained moderated yields in comparison with $Pd(OAc)_2$ (Table 2, entry 2).

Table 2. Optimization of the conditions of the Heck coupling reaction between *p*-iodotoluene (**4b**) and methyl acrylate (**5**), using hydrazones **1a-h.**[a]



4b 5 6b

Entry	Hidrazone (% mol)	Source of palladium	Time (min)[b]	Base	Yield (%)[c]	TON	TOF
1	**1a** (0.05)	$Pd(OAc)_2$	30	K_3PO_4	96	1920	3840
2	**1a (0.01)**	**$Pd(OAc)_2$**	**30**	**K_3PO_4**	**98**	**9800**	**19600**
3	**1a** (0.01)	$Pd(OAc)_2$	270	Li_3PO_4	50	5000	1111
4	**1a** (0.01)	$Pd(OAc)_2$	150	Na_3PO_4	60	6000	2400
5	**1a** (0.01)	$Pd(OAc)_2$	90	K_2CO_3	30	3000	2000
6	**1a** (0.01)	$Pd(OAc)_2$	60	AcOK	95	9500	9500
7	**1a** (0.01)	$PdCl_2$	30	K_3PO_4	86	8600	17200
8	**1a** (0.01)	$Pd(PhCN)_2Cl_2$	30	K_3PO_4	84	8400	16800
9	**1a** (0.01)	$Pd(PPh_3)_2Cl_2$	30	K_3PO_4	85	8500	17000
10	**1b** (0.01)	$Pd(OAc)_2$	30	K_3PO_4	85	8500	17000
11	**1c** (0.01)	$Pd(OAc)_2$	150	K_3PO_4	70	7000	2800
12	**1d** (0.01)	$Pd(OAc)_2$	150	K_3PO_4	76	7600	3040
13	**1e** (0.01)	$Pd(OAc)_2$	30	K_3PO_4	82	8200	16400
14	**1f** (0.01)	$Pd(OAc)_2$	30	K_3PO_4	75	7500	15000
15	**1g** (0.01)	$Pd(OAc)_2$	30	K_3PO_4	85	8500	1700
16	**1h** (0.01)	$Pd(OAc)_2$	120	K_3PO_4	74	7400	3700
17	None	$Pd(OAc)_2$	60	K_3PO_4	5	500	500
18	**1a**(0.01)	none	30	K_3PO_4	0	0	0
19[d]	**1a** (0.01)	$Pd(OAc)_2$	30	K_3PO_4	98	9800	19600
20[e]	**1a** (0.01)	$Pd(OAc)_2$	300	K_3PO_4	90	9000	1800

[a]All reactions were performed with *p*-iodotoluene (**4b**) (2 mmol), methyl acrylate (**5**) (3.3 mmol), DMF (5 mL), base (2.5 mmol). T = 140 °C under infrared irradiation using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V). For controlling the temperature, a Digi-Sense variable-time power controller was used.. [b]Time reaction based on total consumption of aryl iodide determined by TLC. [c]Isolated yields after extraction with hexane. [d]Preparing separately the [$Pd(AcO)_2$/**1a**] catalyst system. [e]Employing heating blanket.

With these results, we found the following optimized conditions: [$Pd(AcO)_2$/**1a**] system 0.01% mol, in DMF with K_3PO_4 at 140 °C for 30 minutes using infrared irradiation (IR) as an energy source.

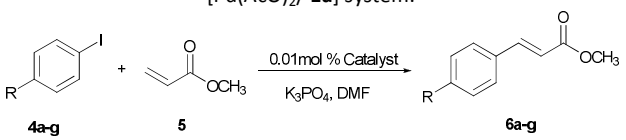
In order to know the molecular structure of the formed complex by the reaction between the hydrazone Ia and $Pd(OAc)_2$, we have conducted some experiments in different reaction conditions, observing in all cases the total consumption of the ligand, however , it was not possible to isolate these reaction product in neither case. In our experience, we believe that hydrazone behaves as [N,N] ligand, as in other structurally similar hydrazone ligands we have detected.[43,44] Thus, we conducted three additional experiments, the first one in absence of ligand, other one in absence of $Pd(OAc)_2$ and, as expected, only in the case of $Pd(OAc)_2$, we observe the formation of the coupling product but in low yield (Table 2, entries 17 and 18). In the last experiment, we carried out the preformation of the catalytic system and we observe a change of color and total consumption of the ligand. After that, we added the substrates and

base and the reaction was put in reflux under infrared irradiation. In this reaction condition, we obtained a similar yield of the coupling product (entry 19, Table 2), showing that the preformation of the palladium complex does not affect the C-C coupling reaction.

For to compare the energy sources, we made an experiment under the same reaction conditions described in Table 2, using conventional heating (entry 20), and this results showed a dramatic decreased time of reaction with the use of IR.

To evaluate the scope of [$Pd(AcO)_2$/**1a**] as a catalytic system in the Heck coupling reaction, a variety of activated and deactivated aryl iodides and methyl acrylate was examined using this catalytic system with the optimized condition reactions (Table 3). The results show that the [$Pd(AcO)_2$/**1a**] system is an active and efficient catalyst in the Heck coupling reaction producing good and moderate yields of the corresponding coupling product **6a-g**.

Table 3. Scope of the Heck cross-coupling using aril iodides and the [$Pd(AcO)_2$/ **1a**] system.[a]



4a-g **5** **6a-g**

Entry	R	Time (min)[b]	Product	Yield (%)[c]	TON	TOF
1	H	60	**4a**	95	9500	9500
2	CH_3	30	**4b**	98	9800	19600
3	OCH_3	60	**4c**	97	9700	9700
4	Br	90	**4d**	70	7000	4666
5	$COCH_3$	180	**4e**	50	5000	1666
6	$OCOCH_3$	120	**4f**	70	7000	3500
7	NO_2	120	**4g**	70	7000	3500

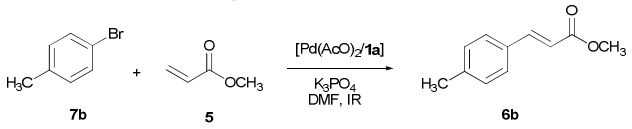
[a]All reactions were performed with aryl Iodides **4a-g** (2 mmol), methyl acrylate (**5**) (3.3 mmol), DMF (5 mL), K_3PO_4 (2.5 mmol), [$Pd(AcO)_2$/**1a**] = 0.01 % mol. T = 140 °C under infrared irradiation using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V). For controlling the temperature, a Digi-Sense variable-time power controller was used. [b]Time reaction based on total consumption of aryl iodide determined by TLC. [c]Isolated yields after extraction with hexane and SiO_2 column chromatography.

Under similar conditions, the cross-coupling reaction was carried out with *p*-bromotoluene **7b** and methyl acrylate (**5**), which provided methyl *trans*-cinnamate **6b**, unfortunately the reaction did not proceed (Table 4, entry 1). Consequently, we attempted to re-optimize the conditions for the coupling of *p*-bromotoluene (**7b**) and methyl acrylate (**5**) (Table 4).

When 0.1 % mol of the [$Pd(AcO)_2$/**1a**] system and 40% mol of TBAB were used, a small amount of the Heck reaction product was obtained (Table 4, entry 4). After increasing the concentration of the [$Pd(AcO)_2$/**1a**] system to 1 % mol and adding 50 % mol TBAB, the reaction produced good yields of **6b** in 1h. (Table 4, entry 7).

Finally, we studied the effect of several aryl bromides **7a-f** in the Heck reaction using methyl acrylate (**5**) (Table 5). Using *p*-substituted aryl bromides **7a-c** with electron-donor groups, we obtained good yields of **6a-c** (Table 5, entries 2, and 3). However, moderate yields were obtained using *p*-substituted aryl bromides **6d-f** with electron-withdrawing groups (Table 5, entries 4-7).

Table 4. Optimization of the reaction conditions on the Heck reaction of *p*-bromotoluene (**7a**) with **5**[a].

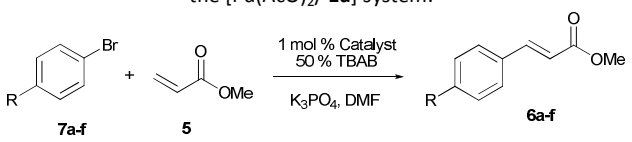


7b **5** **6b**

Entry	[$Pd(AcO)_2$/ 1a] (% mol)	TBAB	Time (min)[b]	Yield (%)[c]
1	0.01	0	420	N.R.
2	0.05	20	180	N.R
3	0.1	20	150	Traces
4	0.1	40	180	10
5	0.1	50	270	33
6	0.5	50	150	50
7	1	50	60	90

[a]All reactions were performed with *p*-bromotoulene **4a** (2 mmol), methyl acrylate (**5**) (3.3 mmol), DMF (5 mL), K_3PO_4 (2.5 mmol). T = 140 °C under infrared irradiation using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V). For controlling the temperature, a Digi-Sense variable-time power controller was used. [b]Time reaction based on total consumption of *p*-bromotoulene **7b** determined by TLC. [c]Isolated yields after extraction with hexane.

Table 5. Scope of Heck cross-coupling using aryl bromides **7a-f** and the [$Pd(AcO)_2$/ **1a**] system.[a]



7a-f **5** **6a-f**

Entry	R	Time (min)[b]	Product	Yield (%)[c]	TON	TOF
1	H	90	**6a**	70	7000	4666
2	CH_3	60	**6b**	85	8500	8500
3	OCH_3	180	**6c**	90	9000	3000
4	Cl	45	**6d**	80	8000	10666
5	$COCH_3$	60	**6e**	50	5000	5000
6	NO_2	30	**6f**	50	5000	10000

[a]All reactions were performed with *p*-iodotoulene **7a-f** (2 mmol), methyl acrylate (**5**) (3.3 mmol), DMF (5 mL), K_3PO_4 (2.5 mmol), [$Pd(AcO)_2$/**1a**] = 1 % mol, 50 % mol TBAB. T = 140 °C under infrared irradiation using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V). For controlling the temperature, a Digi-Sense variable-time power controller was used. [b]Time reaction based on total consumption of aryl iodide **7a-f** determined by TLC. [c]Isolated yields after purification by column chromatography with SiO_2 eluted with hexane.

In attempt to extend this methodology to aryl chlorides, we also conducted some experiments using *p*-chlorotoluene and *p*-nitrochlorobenzene in the optimized conditions for aryl bromides, but unfortunately, the corresponding coupling products were not detected.

Experimental

General

All operations were carried out in open atmosphere. Column chromatographies were performed using 70–230 mesh silicagel. All reagents and solvents were obtained from commercial suppliers and used without further purification. All compounds were characterized by IR spectra, recorded on a Perkin-Elmer 283B or 1420 spectrophotometer, by means of film and KBr techniques, and all data are expressed in wave numbers (cm^{-1}). Melting points were obtained on a Melt- Temp II apparatus and are uncorrected. NMR spectra were measured with a VARIAN +300 MHz, using $CDCl_3$ as solvent. Chemical shifts are in ppm (δ), relative to TMS. The MS-EI spectra were obtained on a JEOL SX 102A, the values of the signals are expressed in mass/charge units (*m/z*), followed by the relative intensity with reference to a 100% base peak.

IR equipment

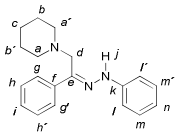
The equipment used for irradiation with IR energy was created by employing an empty cylindrical metal vessel in which an Osram lamp (bulb model Thera-Therm, 250 W, 125 V) was inserted.[27] This lamp is special short-wave IR lamp (IR-A) for use in body care and wellness applications, with a maximum radiation at a wavelength of 1100 nm. The lamp instantly emits a full thermal output as soon as it is switched on. For controlling the temperature, a Digi-Sense variable-time power controller was used. This time controller turned the output load on and off and then repeated the cycle. Although all the reactions were performed in open atmosphere, this arrangement also allows the use of inert conditions.

General procedure for the synthesis of (*Z*)-(aminomethyl)(aryl)phenylhydrazones 1a-h.

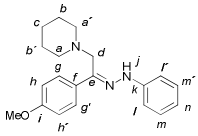
A mixture of 1 equivalent of phenylhydrazone (**3**), 2 equivalent of formaldehyde (in a 37 % aqueous solution), and 2 equivalent of secondary amine (piperydine or diethylamine) was irradiated using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V) at reflux and stirred for the time stated in table 1.

The reaction mixture was poured into water (15 mL) and extracted with ether (3 x 15 mL). The combined organic layers were washed with water (3 X 15 mL) and dried over anhydrous sodium sulfate. The crude product was finally purified by flash column chromatography on silica gel using hexane as an eluent to give the corresponding isolated products.

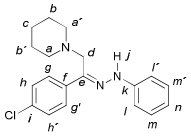
The starting phenylhydrazones (**1**) were prepared from phenylhydrazine with various commercially available benzaldehydes in methanol.[45]



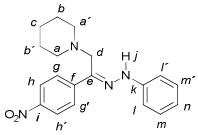
(*Z*)-1-(2-Phenyl-2-(phenylhydrazono)ethyl)piperidine 1a. This compound was obtained in a pure way in 92 % yield as a yellow solid. Mp.: 90-91 °C. MS-IE+ *m/z* (rel. intensity %): 293 $[M^+]$ (55), 201$[C_{13}H_{17}N_2]^+$ (60), 98$[C_6H_{12}N]^+$ (100). Select IR ν_{max}/cm^{-1} (KBr): 1597 (C=N), 1515 (C_{Ar}=C_{Ar}). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.50-1.64 (m, 6H, H-b, H-b´ y H-c), 2.5 (m, 4H, H-a, H-a´), 3.69 (s, 2H, H-d), 6.84 (d, 1H, H-n, J_{HnHm} = 6.9 Hz), 7.15 (d, 2H, H-l, H-l´ J_{HlHm} = 7.5 Hz), 7.25 (dd, 1H, H-m, J_{HmHn} = 6.9 Hz, J_{HmHl} = 7.5Hz), 7.30-7.37 (m, 4H, H-h, H-h´ and H-i), 7.77 (d, 2H, H-g, H-g´) y 11.45 (s, 1H, H-j). δ_C(75 MHz; $CDCl_3$;Me_4Si) 24.0 (C-c), 26.3 (C-b, C-b´), 53.7 (C-a, C-a´), 53.7 (C-d), 112.7 (C-l, C-l´), 119.5 (C-n), 125.5 (C-g, C-g´), 127.4 (C-i), 128.2 (C-h, C-h´), 129.1 (C-m, C-m´), 139.0 (C-f), 139.5 (C-k) y 145.7 (C-e).



(*Z*)-1-(2-(*p*-Metoxyphenyl)-2-(phenylhydrazono)ethyl)piperidine. 1b. Yellow solid in 80%. Yield. Mp.: 68-70 °C. MS-IE+ *m/z* (rel. intensity %): 323 $[M]^+$ (28), 231 $[C_{14}H_{19}N_2O]^+$ (27), 133$[C_8H_9N_2]^+$ (60), 98 $[C_6H_{12}N]^+$ (100). Select IR ν_{max}/cm^{-1} (KBr): 1601.25 (C=N), 1504.57 (C_{Ar}=C_{Ar}). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.57-1.61 (m, 6H, H-b, H-b´ y H-c), 2.46 (m, 4H, H-a, H-a´), 3.62 (s, 2H, H-d), 3.79 (s, 3H, OCH_3), 6.87 and 7.69 (2d, 4H, H-g, H-g´ and H-h, H-h´, J_{HgHh} = 9 Hz), 7.10-7.12 (m, 3H, H-l, H-l´ and H-n), 7.22-7.27 (m, 2H, H-m, H-m´), 11.27 (s, 1H, H-j). δ_C(75 MHz; $CDCl_3$;Me_4Si) 24.0 (C-c), 26.2 (C-b, C-b´), 53.7 (C-a, C-a´), 55.2 (C-OCH3), 57.2 (C-d), 112.6 (C-l, C-l´), 113.6 (C-g, C-g´), 119.2 (C-n), 126.8 (C-h, C-h´), 129.0 (C-m, C-m´), 131.9 (C-f), 139.6 (C-k), 145.9 (C-e) y 159.2 (C-i).

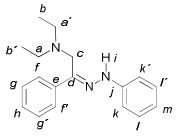


(*Z*)-1-(2-(*p*-Chlorophenyl)-2-(phenylhydrazono)ethyl)piperidine. 1c. This compound was obtained in a pure way in 90 % yield as a yellow solid. Mp: 72-74. MS-IE+ *m/z* (rel. intensity %): 327 $[M]^+$ (10), 235 $[C_{13}H_{16}N_2Cl]^+$ (20), 98 $[C_6H_{12}N]^+$ (100), 84$[C_5H_{10}N]^+$ (32). Select IR ν_{max}/cm^{-1} (KBr): 1600 (C=N), 1491 (C_{Ar}=C_{Ar}). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.53-1.63 (m, 5H, H-b, H-b´ y H-c), 2.63 (m, 4H, H-a, H-a´), 3.65 (s, 2H, H-d), 6.85 (d, 1H, H-n), 7.14 and 7.69 (2d, 4H, H-g, H-g´, H-h, H-h´, J_{HgHh} = 8.7 Hz), 7.25-7.32 (m, 4H, H-l, H-l´, H-m, H-m´), 11.43 (s, 1H, H-j). δ_C(75 MHz; $CDCl_3$;Me_4Si) 23.9 (C-c), 25.8 (C-b, C-b´), 53.7 (C-a, C-a´), 57.1 (C-d), 112.8 (C-l, C-l´), 119.7 (C-n), 126.6 (C-h, C-h´), 128.3 (C-g, C-g´), 129.1 (C-m, C-m´), 133.2 (C-k), 137.5 (C-i), 138.1 (C-f) y 145.4 (C-e).

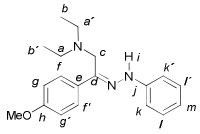


(*Z*)-1-(2-(*p*-Nitrophenyl)-2-(phenylhydrazono)ethyl)piperidine. 1d. This compound was obtained in a pure way in 99 % yield as an orange solid. Mp: 140-141 °C. MS-IE+ *m/z* (rel. intensity %): 338

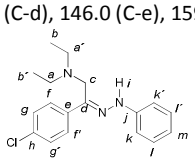
$[M]^+$ (47), 246 $[C_{13}H_{16}N_3O_2]^+$ (38), 105$[C_6H_5N_2]^+$ (30), 98 $[C_6H_{12}N]^+$(100), 84 $[C_6H_{10}N]^+$ (58), 77 $[C_6H_5]^+$ (56). Select IR ν_{max}/cm^{-1} (KBr): 1595 (C=N), 1514 (C_{Ar}=C_{Ar}), 1542, 1337 (N=O). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.48-1.52 (m, 5H, H-b, H-b´ y H-c), 2.46 (m, 4H, H-a, H-a´), 3.67 (s, 2H, H-d), 6.87 (d, 1H, H-n, J_{HnHm} = 4.5 Hz), 7.13 (dd, 2H, H-m, H-m´, J_{HmHn} = 4.5 Hz, J_{HmHl} = 5.1 Hz), 7.27 (d, 2H, H-l, H-l´, J_{HlHm} = 5.1 Hz), 7.85 and 8.14 (2d, 4H, H-g, H-g´, H-h, H-h´ J_{HgHh} = 7.2 Hz), 11.75 (s, 1H, H-j). δ_C(75 MHz; $CDCl_3$;Me_4Si) 23.9 (C-c), 25.8 (C-b, C-b´), 53.0 (C-a, C-a´), 56.8 (C-d), 113.1 (C-l, C-l´), 120.7 (C-n), 123.6 (C-h, C-h´), 125.4 (C-g, C-g´), 129.2 (C-m, C-m´), 136.1 (C-k), 144.7 (C-e), 145.0 (C-f) y 146.4 (C-i).



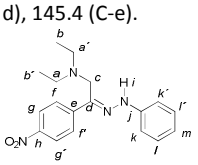
(*Z*)-*N,N*-Diethyl-2-phenyl-2-(2-phenylhydrazono)ethanamine. 1e. Yellow oil in 70 % yield. MS-IE+ *m/z* (rel. intensity %): 281 $[M]^{+\cdot}$.(60), 209 $[C_{14}H_{13}N_2]^+$ (20), 189 $[C_{12}H_{17}N_2]^+$ (60), 86$[C_5H_{12}N]^+$ (100). Select IR ν_{max}/cm^{-1} (KBr): 2817, 2932, 2968 (H-Csp^3), 3023, 3056, (H-Csp^2), 1599 (C=N), 1556, 1491, (C_{Ar}=C_{Ar}), 1443 (CH_2), 1384 (CH_3). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.11 (t, 6H, H-a, H-a' J_{HaHb} = 6.9 Hz), 2.6 (q, 4H, H-b, H-b', J_{HbHa} = 6.9 Hz), 3.77 (s, 2H, H-c), 6.83 (d, 1H, H-m, *J* = 7.8 Hz), 7.14 (d, 2H, H-k, H-k', *J* = 8.1 Hz), 7.24-7.37 (m, 5H, H-l, H-l', H-g, H-g', H-h), 7.77 (d 2H, H-f, H-f', *J* = 8.1 Hz). δ_C(75 MHz; $CDCl_3$;Me_4Si) 12.0 (C-a, C-a'), 46.9 (C-b, C-b'), 52.5 (C-c), 112.7 (C-k, C-k'), 119.4 (C-m), 125.4 (C-f, C-f'), 127.4 (C-h), 128.2 (C-l, C-l'), 129.1 (C-g, C-g'), 139.0 (C-d), 140.0 (C-j), 145.6 (C-e).



(*Z*)-*N,N*-Diethyl-2-(*p*-metoxiphenyl)-2-(2-phenylhydrazono)ethanamine. 1f. Yellow oil in 80 % yield. MS-IE+ *m/z* (rel. intensity %): 311 $[M]^+$ (80), 281 $[C_{18}H_{23}N_3]^+$ (25), 239 $[C_{15}H_{15}N_2O]^+$ (20), 133 $[C_9H_9O]^+$ (100), 86 $[C_5H_{12}N]^+$ (90). Select IR ν_{max}/cm^{-1} (KBr): 2835 (H-Csp^3), 2932, 2966, (H-Csp^2), 1599 (C=N), 1503, 1463, (C_{Ar}=C_{Ar}), 1440 (CH_2), 1384 (CH_3). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.11 (t, 6H, H-a, H-a', J_{HaHb} = 7.2 Hz), 2.59 (q, 4H, H-b, H-b', J_{HbHa} = 7.2 Hz), 3.74 (s, 2H, H-c), 6.81 (d, 1H, H-m, J_{HmHl} = 8.1 Hz), 6.89 (d, 2H, H-k, H-k', J_{HkHl} = 8.7 Hz), 7.27 (dd, 2H, H-l, H-l', J_{HlHm} = 8.1 Hz, J_{HlHk} = 8.7 Hz), 7.11 and 7.70 (2d, 4H, H-g, H-g' and H-f, Hf' *J* = 9 Hz), 11.31 (s, 1H, H-i). δ_C(75 MHz; $CDCl_3$;Me_4Si) 12.2 (C-a, C-a'), 47.0 (C-b, C-b'), 52.6 (C-c), 112.7 (C-g, C-g'), 113.8 (C-k, C-k'), 119.3 (C-m), 126.9 (C-f, C-f'), 129.2 (C-l, Cl'), 132.0 (C-d), 140.4 (C-j), 139.0 (C-d), 146.0 (C-e), 159.4 (C-h).



(*Z*)-*N,N*-Diethyl-2-(*p*-chlorophenyl)-2-(2-phenylhydrazono)ethanamine. 1g. Yellow oil in 80% yield. MS-IE+ *m/z* (rel. intensity %): 315 $[M]^+$ (60), 223 $[C_{12}H_{16}ClN_2]^+$ (45), 137 $[C_8H_6Cl]^+$ (63), 105 $[C_6H_5N_2]^+$ (65), 86 $[C_5H_{12}N]^+$ (100), 77 $[C_6H_5]$ (50). Select IR ν_{max}/cm^{-1} (KBr): 2819, 2932, 2968 (H-Csp^3,H-Csp^2), 1599 (C=N), 1574, 1548, 1488, (C_{Ar}=C_{Ar}), 1400 (CH_2), 1384 (CH_3). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.07 (t, 6H, H-a, H-a', J_{HaHb} = 6.9 Hz), 2.54 (q, 4H, H-b, H-b' J_{HbHa} = 6.9 Hz), 3.69 (s, 2H, H-c), 6.80 (d, 1H, H-m, J_{HmHl} = 8.4 Hz), 7.06 (d, 2H, H-k, J_{HkHl} = 6.6 Hz), 7.22 (dd, 2H, H-l, J_{HlHm} = 8.4, J_{HlHk} = 6.6 Hz), 7.27 and 7.64 (2d, 4H, H-g, Hg' and H-f, Hf', *J* = 9.0 Hz), 11.42 (s, 1H, H-i). δ_C(75 MHz; $CDCl_3$;Me_4Si) 12.0 (C-a, C-a'), 46.9 (C-b, C-b'), 52.3 (C-c), 112.7 (C-k, C-k'), 119.7 (C-m), 126.5 (C-f, C-f'), 128.3 (C-l, C-l'), 129.1 (C-g, C-g'), 133.8 (C-h), 137.4 (C-j), 138.7 (C-d), 145.4 (C-e).



(*Z*)-*N,N*-Diethyl-2-(*p*-nitrophenyl)-2-(2-phenylhydrazono)ethanamine. 1f. Orange oil in 85 % yield. MS-IE+ *m/z* (rel. intensity %): 326 $[M]^{+\cdot}$ (35), 281 $[C_{18}H_{23}N_3O]^+$ (50), 234 $[C_{12}H_{16}N_3O_2]^+$ (30), 105 $[C_6H_5N_2]^+$ (85), 86 $[C_5H_{12}N]^+$ (100), 77 $[C_6H_5]$ (95). Select IR ν_{max}/cm^{-1} (KBr): 2931, 2968 (H-Csp^3, H-Csp^2), 1593 (C=N), 1544, (C_{Ar}=C_{Ar}), 1490, 1331 (N=O), 1407 (CH_2), 1384 (CH_3). δ_H(300 MHz; $CDCl_3$;Me_4Si) 1.06 (t, 6H, H-a, H-a', J_{HaHb} = 6.9 Hz), 2.53 (q, 4H, H-b, H-b', J_{HbHa} = 6.9 Hz), 3.74 (s, 2H, H-c), 6.83 (d, 1H, H-m, J_{HmHl} = 6.6 Hz), 7.06 (d, 2H, H-k, H-k', J_{HkHl} = 8.4 Hz), 7.22 (dd, 2H, H-l, H-l', J_{HlHm} = 6.6 Hz, J_{HlHk} = 8.4 Hz), 7.83 and 8.12 (2d, 4H, H-g, H-g' and H-f, H-f', *J* = 9.3 Hz), 11.79 (s, 1H, H-i). δ_C(75 MHz; $CDCl_3$;Me_4Si) 11.9 (C-a, C-a'), 46.8 (C-b, C-b'), 52.0 (C-c), 1131 (C-k, C-k'), 120.6 (C-m), 123.7 (C-g, C-g'), 125.3 (C-f, C-f'), 129.2 (C-l, C-l'), 136.6 (C-j), 144.6 (C-d), 145.0 (C-e), 146.3 (C-h).

General procedure for Mizoroki–Heck coupling reactions

In a 50-mL round-bottomed flask, a mixture of aryl halide (2 mmol), methyl acrylate (3.3 mmol), and the corresponding base (2.5 mmol), was placed in 5 mL of DMF, then the source of palladium and the corresponding hydrazone **1** were added (see Tables 2-5). The reaction mixture was irradiated using an Osram lamp (bulb model Thera-Therm, 250 W, 125 V) for the time stated in tables 2-5 at 140 °C. The reaction mixture was poured into water (10 mL) and extracted with ether or hexane (3 X 10 mL). The combined organic layers were dried over anhydrous sodium sulfate.

The crude product was finally purified by flash column chromatography on silica-gel to give the isolated products in yields stated in the tables 2-5. The purified product was identified by means of determination of mp and by ^1H and ^{13}C NMR, the data obtained are consistent with literature.[46]

Note: The entire round flasks used in each coupling reaction were meticulously cleaned with aqua regia to avoid the presence of unseen palladium catalyst.

Conclusions

We describe the synthesis of new (*Z*)-(aminomethyl)(aryl)phenylhydrazones (**1a-h**) with good yields via the Mannich coupling reaction using IR as a source energy and solvent-free conditions. These new hydrazones **1a-h** are promising for the catalysis of Heck coupling reactions using IR and $Pd(AcO)_2$. Particularly, the [$Pd(AcO)_2$/**1a**] system showed to be a good

catalyst in this reaction, being more active when electron-rich aryl halide are used as substrates.

As we have described, the use of infrared as energy source favors the Mannich and Heck coupling reactions to obtain the corresponding products in an efficient manner. The reaction times decrease in all the cases, in comparison to experiments conducted in conductive heating. Thus, infrared irradiation effectively penetrates the reaction vessel and causes a sudden increase in temperature, which allows to easily reach the activation energy to transform substrates into products.

Therefore, we evidence that infrared irradiation (IR) is an efficient, economical and accessible alternative source of energy to assist both, the synthesis of (*Z*)-(aminomethyl)(aryl)phenylhydrazones, and Heck coupling reactions.

Acknowledgements

The authors would like to acknowledge the technical assistance provided by Luis Velasco and Javier Pérez. The authors also thank CONACYT 153059 and Facultad de Estudios Superiores Cuautitlán PIAPIC14 projects.

References

1. (a) E. F. Kleinman, *In Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Eds., Pergamon, Oxford, 1991; Vol. 2, pp 893–895; (b) N. Risch, M. Arend and B. Westermann, *Angew. Chem. Ind. Ed*., 1998, **37**, 1044–1070; (c) W. N. Speckamp and M. J. Moolenaar, *Tetrahedron,* 2000, **56**, 3817–3856.
2. (a) G. Keil and W. Ried, *Liebigs Ann. Chem*., 1957, **605**, 167-179; (b) V. Atlan, H. Bienaymé, L. El Kaïm and A. Majee, *Chem. Commun*., 2000, 1585–1586; (c) L. El Kaïm,a L. Gautier,a L. Grimaud,a L. M. Harwoodb and V. Michauta, *Green Chem*., 2003, **5**, 477–479; (d) V. Atlan, L. El Kaïm, L. Grimaud, N. K. Jana and A. Majee, *Synlett*, 2002, 352–354.
3. K. Inamoto, M. Katsuno, T. Yoshino, Y. Arai, K. Hiroya and T. Sakamoto, *Tetrahedron*, 2007, **63**, 2695-2711.
4. N. Ghavtadze, R. Frohlich and E.-U. Wurthwein, *Eur. J. Org. Chem*., 2008, 3656-3667.
5. (a) P.Barbazan, R. Carballo, B. Covelo, C. Lodeiro, J. C. Lima and E. M. Vázquez-López, *Eur. J. Inorg. Chem*., 2008, 2713-2720; (b) S. Banerjee, S. Mondal, W. Chakraborty, S. Sen, R. Gachhui, R. J. Butcher, A. M. Z. Slawin, C. Mandal and S. Mitra, *Polyhedron*, 2009, **28**, 2785-2793.
6. (a) T. Mino, Y. Shirae, Y. Sasai, M. Sakamoto and T. Fujita, *J. Org. Chem*., 2006, **71**, 6834-6839; (b) T. Mino, H. Shindo, T. Kaneda, T. Koizumi, Y. Kasashima, M. Sakamoto and T. Fujita, *Tetrahedron Lett*., 2009, **50**, 5358-5360.
7. (a) T. Mino, Y. Shirae, M. Sakamoto and T. Fujita, *Synlett,* 2003, 882-884; (b) T. Mino, Y. Shirae, M. Sakamoto and T. Fujita, *J. Org. Chem*., 2005, **70**, 2191-2194.
8. T. Mino, Y. Shirae, T. Saito, M. Sakamoto and T. Fujita, *J. Org. Chem*. 2006, **71**, 9499-9502
9. T. Mino, K. Kajiwara, Y. Shirae, M. Sakamoto and T. Fujita, *Synlett*, 2008, 2711-2715.
10. For some representative reviews, see: (a) W. A. Herrmann, V.P.W. Böhm and C.-P. Reisinger, *J. Organomet. Chem*., 1999, **576**, 23-41; (b) I. P. Beletskaya and A. V Cheprakov, *Chem. Rev*., 2000, **100**, 3009-3066; (c) G. D. Daves and A. Hallberg, *Chem. Rev*., 1989, **89**, 1433-1445; (d) H. Li, C. C. Johansson-Seechurn and T. J. Colacot, *ACS Catal*., 2012, **2**, 1147-1164; (e) N. T. S. Phan, M. C. Van Der Sluys and W. Jones, *Adv. Synth. Catal*., 2006, **348**, 609-679.
11. K.-S. Masters and B. L Flynn, *Org. Biomol. Chem.,* 2010, **8**, 1290-1292.
12. (a) *Metal-Catalyzed Cross-Coupling Reactions*, ed. A. de Meijer and F. Diederich, Wiley-VCH, Weinheim, 2004; (b) A. Zapf and M.Beller, *Top. Catal.,* 2002, **19**, 101-109; (c) C.E. Tucker and J. G. de Vries, *Top. Catal.,* 2002, **19**, 111-118.
13. (a) K. Temburnikar, K. Brace and K. L. Seley-Radtke, *J. Org. Chem.,* 2013, **78**, 7305-7311. (b) A. C Häberli, and J. Leumann, *Org. Lett.,* 2001, **3**, 489-492.
14. Z. Feng, Q.-Q. Min, H.-Y. Zhao, J.-W. Gu, and X. Zhang, *Angew. Chem. Int. Ed.*, 2014, **53**, 1–6.
15. (a) B. Marudai, *Palladium in Heterocyclic Chemistry in Tetrahedron Organic Chemistry Series*, ed. J. Jack Li and G. W. Gribble, Elsevier, Netherlands, 2th edition, 2007, vol 26, Chapter 14, 587-620. (b) H.-U. Blaser, A. Indolese, F. Naud, U. Nettekoven and A. Schnyder, *Adv. Synth. Catal*., 2004, **346**, 1583-1598.
16. (a) M. Hoyos, D. Guest, O. Navarro in *N-Heterocyclic Carbenes*, S. P. Nolan Ed. Wiley-VCH, Weinheim, 2014 Ch.4, pp 85-109. (b)N. Marion and S. P. Nolan, *Acc. Chem. Res*., 2008, **41**, 1440-1449.
17. W. A. Herrmann, K. Ofele, S.K. Schneider, E. Herdtweck and Hoffmann, S. D. *Angew. Chem., Int. Ed.,* 2006, **45**, 3859-3862.
18. Q. Yao, M. Zabawa, J. Woo and Zheng, C. *J. Am. Chem. Soc*., 2007, **129**, 3088-3089.
19. (a) K.-M. Wu, C.-A. Huang, K.-F. Peng and C.-T. Chen, *Tetrahedron,* 2005, **61**, 9679-9687. (b) K. Mustafa, K. Hülya, E. Duygu Melis, *Appl. Organomet. Chem*. 2015, **29**, 543-548.
20. C. Najera, J. Gil-Moito, S. Karlstrum, and L.R. Falvello, *Org. Lett.,* 2003, **5**, 1451-1454. S.M. Sarkar, M. L. Rahman, M. M. Yusof. *RSC Adv*., 2015, **5**, 19630–19637
21. K. Kawamura, S. Haneda, Z. Gan, K. Eda and M. Hayashi, *Organometallics*, 2008, **27**, 3748-3752.
22. (a) V. Montoya, J. Pons, V. Branchadell, J. Garcia-Antón, X. Solans, M. Font-Bardía, and J. Ros, *Organometallics*, 2008, **27**, 1084-1091; (b) F. Li and T. S. A. Hor, *Adv. Synth. Catal*., 2008, **350**, 2391-2400.
23. S. Lee, *J. Organomet. Chem*., 2006, **691**, 1347-1355.
24. (a) T. Mino, M. Shibuya, S. Suzuki, K. Hirai, M. Sakamoto, T. Fujita. *Tetrahedron* 2012, **68**, 429-432. (b) T. Mino, H. Shindo, T. Kaneda, T. Koizumi, Y. Kasashima, M. Sakamoto, T. Fujita. *Tetrahedron Lett*., 2009, **50**, 5358–5360. (c) T. Mino, Y. Shirae, M. Sakamoto and T. Fujita, *J. Org. Chem*., 2006, **71**, 6834-6839
25. (a) Q. Yao, E.P. Kinney, and C. Zheng, *Org. Lett*. 2004, **6**, 2997-2999. (b) T. Chakraborty, K. Srivastava, H. B. Singh, R. J. Butcher. *J. Organomet. Chem*.2011, **696**, 2559-2564
26. X. Cui, Y. Zhou, N. Wang, L. Liu, and Q.-X. Guo, *Tetrahedron Lett.,* 2007, **48**, 163-167.
27. W. Chen, R. Li, B. Han, B.J. Li, Y.C. Chen, Y. Wu, L.S. Ding, and D. Yang, *Eur. J. Org. Chem*. 2006, 1177-1184.
28. (a) J. Dupont, C. S. Consorti and J. Spencer, *Chem. Rev*. 2005, **105**, 2527-2572. (b) Zapf, M. Beller. *Chem. Commun*., 2005, 431–440. (c) I. P. Beletskaya, A. V. Cheprakov. *J. Organomet. Chem.* 2004, **689**, 4055–4082
29. (a) C.M. Frech in *Pincer and Pincer-type complexes*, K. J. Szabó, O.F. Wendt Ed. Wiley-VCH, Weinheim, 2014 Ch.10, pp 249-280 (b) M. Hirotsu, Y. Tsukahara and I. Kinoshita, *Bull. Chem. Soc. Jpn*. 2010, **83**, 1058-1066. (c) Q.-L. Luo, J.-P. Tan, Z.-F Li, Y. Qin, L. Ma and D.-R. Xiao, *Dalton Trans*., 2011, **40**, 3601-3609.
30. A. Balanta, C. Godard, and C. Claver, *Chem. Soc. Rev*. 2011, **40**, 4973-4985.

31. J. Mondal, A. Modak, and A. Bhaumik. *J. Mol. Catal. A: Chemical*, 2011, **350**, 40–48.
32. A. Modak, J. Mondal, V. K. Aswal, and A. Bhaumik. *J. Mater. Chem*., 2010, **20**, 8099–8106.
33. (a) C. O. Kappe, D. Dallinger and S. S. Murphree, *Practical Microwave Synthesis for Organic Chemists Strategies, Instruments and Protocols*, Wiley-VCH, Weinheim, 2009; (b) A. Loupy, *Microwaves in Organic Synthesis*, Wiley-VCH, Weinheim, 2006. (c) M. Larhed and K. Olofsson, *Microwave Methods in Organic Synthesis*, Springer, Berlin, 2006; (d) M. Larhed, C. Moberg and A. Hallberg, *Acc. Chem. Res*., 2002, **35**, 717-727.
34. (a) G. Cravotto and P. Cintas, *Chem. Soc. Rev*., 2006, **35**, 180–196; (b) F. M. Nowak, *Sonochemistry: Theory, Reactions, Syntheses, and Applications;* Nova Science Publishers, New York, 2011; (c) T.J. Mason, *Chem. Soc. Rev*., 1997, **26**, 443-451.
35. (a) I.R. Baxendale, L. Brocken, C. J. Mallia, *Green Process Synth*., 2013, **2**, 211-230; (b) R. Wladimir, *Microreactors in Preparative Chemistry: Practical Aspects in Bioprocessing, Nanotechnology, Catalysis and More*, Wiley-VCH, Weinheim, 2013.
36. (a) M.A. Vázquez, M. Landa, L. Reyes, R. Miranda, J. Tamariz and F. Delgado, *Synth. Commun*., 2004, **34**, 2705-2718; (b) G. Alcerreca, R. Sanabria, R. Miranda, G. Arroyo, J. Tamariz and F. Delgado, *Synth. Commun*., 2000, **30**, 1295-1301; (c) M. Salmón, R. Osnaya, L. Gómez, G. Arroyo, F. Delgado, R. Miranda, *Rev. Soc. Quim. Mex*., 2001, **45**, 206-207.
37. J. E. Valdez-Rojas, H. Ríos-Guerra, A. Ramírez-Sánchez, G. García-González, C. Álvarez-Toledano, J. G. López-Cortés, R.A. Toscano and J. G. Penieres-Carrillo, *Can. J. Chem*., 2012, **90**, 567-573.
38. (a) G. Penieres-Carrillo, J.G. García-Estrada, J.L. Gutiérrez-Ramírez and C. Álvarez-Toledano, *Green. Chem*., 2003, **5**, 337-339; (b) G. Penieres, J.M. Aceves, A. Flores, G. Mendoza, O. García and C. Álvarez, *Heterocycl. Comm*., 1997, **3**, 507-508.
39. M.I. Flores-Conde, L. Reyes, R. Herrera, H. Ríos, M. A. Vázquez, R. Miranda, J. Tamariz and F. Delgado, *Int. J. Mol. Sci*., 2012, **13**, 2590-2617.
40. (a) P. Anastas and J. Warner, *Green Chemistry: Theory and Practice*, University Press, Oxford, 1998; (b) J.M. DeSimone, *Science*, 2002, **297**, 799-803; (c) R.A. Gross and B. Kalra, *Science*, 2002, **297**, 803-807; (d) M. Poliakoff, J.M. Fitzpatrick, T.R. Farren and P.T. Anastas, *Science*, 2002, **297**, 807-810.
41. (a) C. O. Kappe, *Angew. Chem., Int. Ed*. 2004, **43**, 6250-6282; (b) J. Thuery, *Microwaves: Industrial, Scientific and Medical Applications*, Artech House, Boston, 1992.
42. D. E. Bergbreiter and S. Furyk, *Green Chem,* 2004, **6**, 280-285.
43. F. Ortega-Jiménez, F.X. Domínguez-Villa, A. Rosas-Sánchez, G Penieres-Carrillo, J.G. López-Cortés, M. C. Ortega-Alfaro. *Appl. Organomet. Chem*. 2015, **29**, 556-560.
44. (a) F. Ortega-Jiménez, E. Gómez, P. Sharma, M.C. Ortega-Alfaro, R.A. Toscano, C. Alvarez-Toledano, C. *Z. Anorg. All. Chem*. 2002, **628**, 2104-2108. (b) F. Ortega-Jiménez, J.G. López-Cortés, M.C. Ortega-Alfaro, A. Toscano, G. Penieres, R. Quijada, C. Alvarez, *J. Organomet. Chem*. **2005**, *690*, 454-462.
45. J, Buckingham. *Q. Rev. Chem. Soc.***,** 1969, **23**, 37-56.
46. For NMR data of methyl 4-R-cinnamates, see: (a) R = MeO, Me, H*:* C. Diebold, S. Schweizer, J.-M. Becht and C. Le Drian, *Org. Biomol. Chem.,* 2010, **8**, 4834-4836; (b) R = Br, $COOCH_3$: F. FranÅois-Xavier, M. Karinne, S. Jean-Marc, F. Eric, I. Oier and L. Julia, *Chem. Eur. J*., 2010, **16**, 5191–5204; (c) R = NO_2: R. Bernini, S. Cacchi, G. Fabrizi, G. Forte, S. Niembro, F. Petrucci, R. Pleixats, A.Prastaro, R.M. Sebastia, R. Soler, M. Tristany and A. Vallribera, *Org. Lett*., 2008, **4**, 561–564; (d) R = Ac: M. Paul, F.B. John, K.C. David, K.G. Ewan, S.P. Jeremy and B.S. Joseph, *Org. Process Res. Dev.,* 2013, **17**, 397−405.