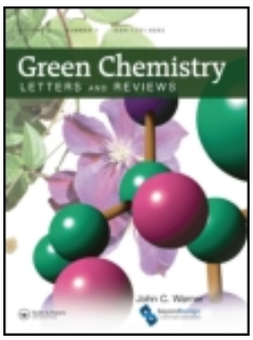

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A green chemical approach toward the synthesis of 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates catalyzed by *p*-toluenesulfonic acid under focused microwave irradiation

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RESEARCH LETTER

A green chemical approach toward the synthesis of 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates catalyzed by *p*-toluenesulfonic acid under focused microwave irradiation

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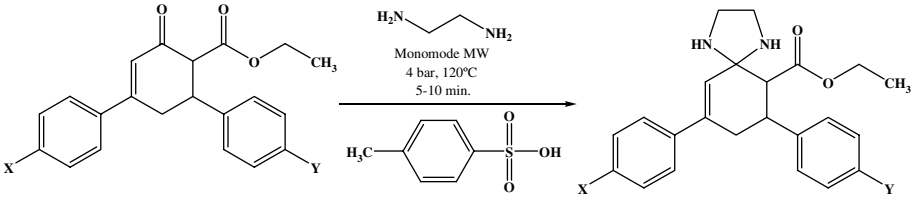
In the present work, a new series of novel 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates **11**–**20** was synthesized by the reaction of 6-carbethoxy-3,5-diarylcyclohex-2-enones **1**–**10** with ethylene diamine in the presence of *p*-toluenesulfonic acid (*p*-TSA) in solvent-free conditions under focused microwave irradiation (MWI) and were characterized by melting point, elemental analysis, MS, FT-IR, one-dimensional NMR (^{1}H, D_2O exchanged ^{1}H & ^{13}C), and two-dimensional Heteronuclear Multiple Quantum Coherence (HMQC) spectroscopic data.



Keywords: 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates; 6-carbethoxy-3,5-diarylcyclohex-2-enones; ethylene diamine; p-toluenesulfonic acid; focused microwave irradiation

Introduction

Imidazolidine is a nitrogen-containing heterocycle derived from imidazole. Generally, imidazolidines are synthesized by the treatment of aldehydes with ethylene diamine in high yields of crystalline solids (*1*). Condensation of cyclohexanone with ethylene diamine yields 1,4-diazaspiro[4.5]decane, a *N,N*'-unsubstituted imidazolidine (*2*). A convenient synthesis of unsymmetrical and optically active imidazolidines in good yields is reported via Mannich reaction (*3*). Recently, imidazolidine derivatives are synthesized by sono-synthetic method (*4*). Spiro imidazolidine–oxazolidine derivatives are used as an intermediate in the aziridination reaction (*5*).

In recent decades, the synthesis of imidazolidine derivatives has attracted considerable attention because these heterocycles exhibit a wide range of pharmacological activities (*6, 7*). In spite of the wide applications as drugs and drug-intermediates, derivatives of imidazolidine-2-thione, namely azolothiaiznes and benzimidazolidine-2-thiones play a potent role in medicinal chemistry (*8–10*). A novel series of five-membered imidazolidine-2,4-dione derivatives act as HIV protease inhibitors, and they exhibit potent activity against both wild-type virus and a mutant strain (A17) that is highly resistant to lopinavir (*11*).

The present study describes the use of 6-carbethoxy-3,5-diarylcyclohex-2-enones (*12*), an intermediate with three versatile functional groups, i.e. ketone, olefin, and ester for the synthesis of imidazolidine derivatives, since in recent years there has been a great deal of interest in exploiting more than one proximal functional groups for designing novel structures capable of performing a variety of functions. In continuation with our earlier work on the green synthesis of structurally diverse biologically active hybrid heterocyclic ring systems and as part of our ongoing research program (*13–23*), we planned to design imidazolidine derivatives bearing a cyclohexene substituent on the carbon between the nitrogen centers to give a new series of heterocycles, namely 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl

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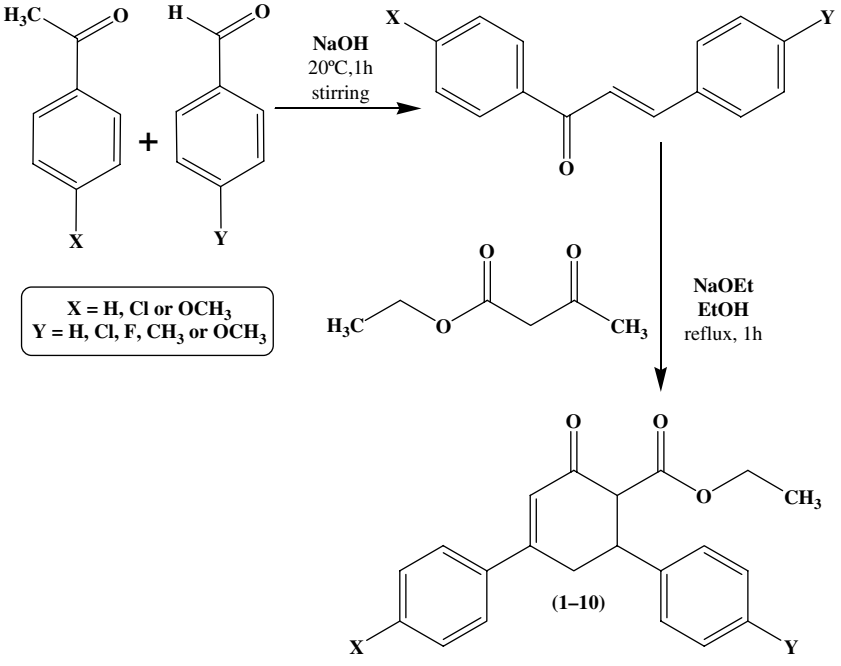
carboxylates **11–20** since imidazolidine derivatives are known pharmacophores in several structure-based drug design approaches (*24–28*).

Results and discussion

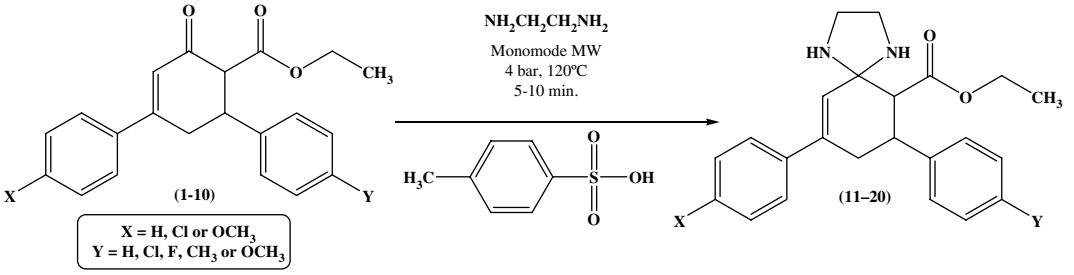
Condensation of appropriate acetophenone and appropriate benzaldehyde in the presence of sodium hydroxide yields the respective 1,3-diaryl-prop-2-en-1-ones which on treatment with ethyl acetoacetate in the presence of sodium ethoxide gives 6-carbethoxy-3,5-diarylcyclohex-2-enones **1–10** by Knoevenagel reaction (Scheme 1). Synthesis of novel 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates **11–20** was carried out by the reaction of 6-carbethoxy-3,5-diarylcyclohex-2-enones **1–10** with ethylene diamine in the presence of *p*-toluenesulfonic acid (*p*-TSA) in solvent-free conditions under focused microwave irradiation (MWI), since the applications of microwave technology to rapid synthesis of biologically significant heterocyclic molecules under solvent-free conditions are very promising and numerous and have recently been recognized as a useful tool for a drug-discovery program especially in combinatorial chemistry (*14–19*). The reactions were performed at 120°C and 4 bar pressure for 5 min. After completion of the reaction as indicated by the TLC, the reaction mixture was poured into ice water. The mixture was extracted with dichloromethane and washed with 10% sodium bicarbonate solution, finally washed with distilled water, concentrated in rotary evaporator and purified by flash column chromatography using toluene:ethyl acetate (8:2) as eluent.

The synthetic route for the formation of compounds **11–20** is given in Scheme 2. The physical and analytical data are given in Table 1. The structures of all the synthesized compounds **11–20** are discussed with the help of m.p.'s, elemental analysis, FT-IR, MS, one-dimensional ^{1}H NMR, D_2O exchanged ^{1}H NMR, ^{13}C NMR, and two-dimensional Heteronuclear Multiple Quantum Coherence (HMQC) spectra. In order to investigate the spectral assignments, 7,9-diphenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate **11** was chosen as a representative compound.

FT-IR spectrum of **11** shows characteristic absorption frequencies in the region of 3267–3528 cm^{-1}, suggesting the presence of NH stretching frequency. The absorption frequency at 1738 cm^{-1} is due to the presence of carbonyl stretching of ester group. Moreover, the absorption frequency at 1607 cm^{-1} is due to the presence of C = C stretching. The presence of band at 1445 cm^{-1} (C–N) is more evident for the formation of **11**. The observed NH stretching, C = C stretching, and C = 0 of ester functional group absorption bands, all support for the formation of compound **11**. The mass spectrum of **11** shows molecular ion peak at m/z 363($M^{+\bullet}+1$) which is consistent with the proposed structure of **11**. Elemental analysis [C_{cal} 76.21, C_{obs} 76.11; H_{cal} 7.23, H_{obs} 7.15; N_{cal} 7.73, N_{obs} 7.63] is consistent with the molecular formula [$C_{23}H_{26}N_2O_2$] of **11**. The assignments of signals in ^{1}H NMR spectrum have been done based on total widths, position, and spin



Scheme 1. Synthesis of ethyl 4,6-diaryl-2-oxocyclohex-3-enecarboxylates.



Scheme 2. Synthesis of novel 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates.

multiplicities. A singlet observed at 6.54 ppm is conveniently assigned to H-10 proton of cyclohexene moiety. Two multiplets that appeared in the region of 2.97–3.02 ppm is due to methylene protons H-8 of cyclohexene moiety. Another multiplet observed in the range 3.04–3.22 ppm is due to benzylic proton H-7. The methyl protons (CH_3) of ester group appeared as a triplet, centered at 0.90 ppm. The methylene protons (CH_2) of ester group observed as a quartet, centered at 3.90 ppm. A signal observed as multiplet between 3.51 and 3.67 ppm corresponding to one proton is unambiguously assigned to H-6 proton. The two NH protons of imidazolidine moiety were observed as broad singlet at 5.98 ppm corresponding to two protons. In addition, methylene protons (H-2, H-3) at C-2 and C-3 of imidazolidine moiety observed as a multiplet at around 4.02–4.13 ppm. The aromatic protons appeared as a multiplet in the range 7.10–7.79 ppm. The presence of labile –NH protons at positions 1 and 4 is confirmed by recording the ^{1}H NMR spectrum after adding D_2O. The peak at 5.98 ppm due to two NH protons at positions 1 and 4 have disappeared in the D_2O exchanged ^{1}H NMR spectrum.

In ^{13}C NMR spectrum, six resonances in the aliphatic region 13.7, 58.7, 49.3, 59.9, 35.2, and 43.8 ppm have been observed (with the help of HMQC the individual assignment could be carried out). The remaining ^{13}C resonances at 169.2, 137.3, and 141.4 ppm are due to quaternary carbons. The ^{13}C resonance at 121.9 ppm may be due to C-10 carbon.

Table 1. Physical and analytical data for the title compounds **11**–**20**.

					Elemental analysis (%)			
Compounds	X	Y	M.P. (°C)	Yield (%)	C Found (calculated)	H Found (calculated)	N Found (calculated)	m/z $(M+1)^{+\bullet}$ Molecular formula
11	H	H	77	95	76.11 (76.21)	7.15 (7.23)	7.63 (7.73)	363 $C_{23}H_{26}N_2O_2$
12	H	Cl	100	93	69.48 (69.60)	6.24 (6.35)	6.95 (7.06)	397, 399 $C_{23}H_{25}N_2O_2Cl$
13	H	F	65	92	72.52 (72.61)	6.57 (6.62)	7.23 (7.36)	381 $C_{23}H_{25}N_2O_2F$
14	H	CH_3	117	90	76.49 (76.56)	7.43 (7.50)	7.32 (7.44)	377 $C_{24}H_{28}N_2O_2$
15	H	OCH_3	112	93	73.33 (73.44)	7.10 (7.19)	7.01 (7.14)	393 $C_{24}H_{28}N_2O_3$
16	Cl	H	68	91	69.52 (69.60)	6.30 (6.35)	6.97 (7.06)	397, 399 $C_{23}H_{25}N_2O_2Cl$
17	OCH_3	H	65	92	73.32 (73.44)	7.11 (7.19)	7.03 (7.14)	393 $C_{24}H_{28}N_2O_3$
18	Cl	CH_3	73	93	70.04 (70.15)	6.53 (6.62)	6.78 (6.82)	411, 413 $C_{24}H_{27}N_2O_2Cl$
19	OCH_3	Cl	69	95	67.42 (67.52)	6.25 (6.37)	6.51 (6.56)	427, 429 $C_{24}H_{27}N_2O_3Cl$
20	Cl	OCH_3	99	93	67.44 (67.52)	6.29 (6.37)	6.48 (6.56)	427, 429 $C_{24}H_{27}N_2O_3Cl$

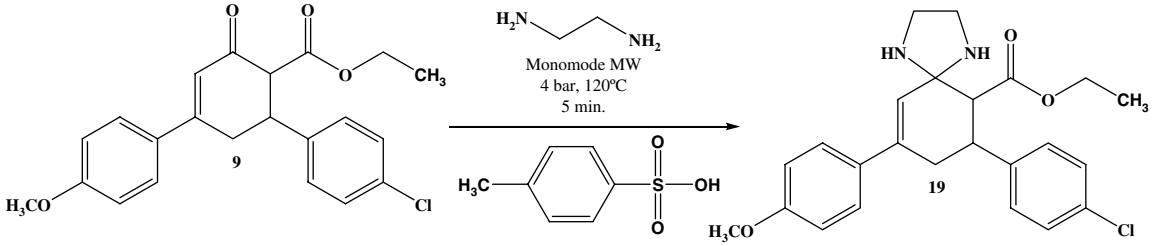
Aromatic carbons are observed in the range of 122.8–130.4 ppm. In the HMQC spectrum (Table 2), the one bond correlation (13.7/0.90 ppm) between methyl protons and methyl carbon of ester confirms that signal observed at 0.90 ppm must be due to methyl protons of ester and ^{13}C resonance at 13.7 ppm must be assigned to methyl carbon of ester. A multiplet observed in the region of 2.97–3.02 ppm is assigned to two methylene protons H-8. Since H-8 proton is assigned from HMQC spectrum, the cross peak (43.8/2.97–3.02 ppm) confirms that the ^{13}C resonance at 43.8ppm is due to C-8 carbon. In HMQC, the ^{13}C resonances at 35.2 ppm have correlations with benzylic proton H-7 (35.2/3.04–3.22 ppm); hence, C-7 resonates at 35.2 ppm and multiplet observed at around 3.04–3.22 ppm must be due to benzylic proton H-7. In HMQC the ^{13}C resonances at 58.7 ppm have correlations with the methylene protons of ester group (58.7/3.90 ppm) and hence methylene carbon of ester resonates at 58.7 ppm. The ^{13}C resonance at 121.9 ppm shows cross peak (121.9/6.54 ppm) with H-10 proton and hence that resonance has been assigned to C-10. The ^{13}C resonance at 59.9ppm has a cross peak (59.9/3.51–3.67 ppm) in HMQC with methine proton signal (H-6). Hence, the resonance at 59.9 ppm must be due to C-6 carbon. Moreover, the ^{13}C resonance at 49.3 ppm has correlation with a multiplet observed in range 4.02–4.13 ppm (49.3/4.02–4.13 ppm). The multiplet observed at around 4.02–4.13 ppm is unambiguously assigned to methylene protons at C-2 and C-3. The cross peaks (49.3/4.02–4.13ppm) confirm that ^{13}C resonances at 49.3 ppm must be due to methylene carbons at C-2 and C-3 of imidazole moiety. In HMQC, the ^{13}C resonances at 137.3, 141.4, 80.1 and 169.2 ppm have no correlations with protons. Among the carbon resonances, the ^{13}C resonances at 169.2 ppm must be due to carbonyl carbon of ester, and ^{13}C resonance at 80.1 ppm is due to spiro carbon (C-5). The ^{13}C resonances at 137.3 and 141.4 ppm are assigned to *ipso* carbons. The C-9 carbon resonance has merged with the aromatic region.

To achieve the best conditions for this reaction (Scheme 2), we examined the efficiency of different reaction media and amounts of catalyst for the condensation reactions of ethyl 6-(4-chlorophenyl)-4-(4-methoxyphenyl)-2-oxocyclohex-3-ene carboxylate and ethylene diamine as a model reaction (Table 3). Reactions at different conditions and various molar ratio of ethyl 6-(4-chlorophenyl)-4-(4-methoxyphenyl)-2-oxocyclohex-3-ene carboxylate/ethylene diamine/*p*-TSA under focused microwave-assisted and solvent-free conditions as a model reaction (Table 3).

Table 2. HMQC direct one-bond ^{1}H–^{13}C coupling correlations spectral data for **11**.

Proton	Carbon (ppm)	CH_3 of $COOCH_2CH_3$	CH_2 of $COOCH_2CH_3$	C = O of $COOCH_2CH_3$	C_2 &C_3	C-5	C-6	C-7	C-8	C-10	Aromatic carbons
		13.7	58.7	169.2	49.3	80.1	59.9	35.2	43.8	121.9	122.8–130.4
CH_3 of $COOCH_2CH_3$	0.90	Bonded									
CH_2 of $COOCH_2CH_3$	3.90		Bonded								
2[CH_2] at C-2 & C-3	4.02–4.13				Bonded						
H-6	3.51–3.67						Bonded				
H-7	3.04–3.22							Bonded			
H-8	2.97–3.02								Bonded		
H-10	6.54									Bonded	
Aromatic protons	7.10–7.79										Bonded
NH	5.98										

Table 3. Comparison of the reaction of ethyl 6-(4-chlorophenyl)-4-(4-methoxyphenyl)-2-oxocyclohex-3-ene carboxylate and ethylene diamine under various *p*-TSA loadings and reaction conditions.



Entry[a]	*p*-TSA Catalyst (mol%)	Reaction conditions	Time (min)	Conversion (%)[b]
1	30	Solvent-free, 90°C	45	25
2	20	Solvent-free, 90°C	45	20
3	10	Solvent-free, 90°C	45	20
4	0	Microwave, 4 bar pressure, 120°C	10	45
5	30	Microwave, DMF, 4 bar pressure, 120°C	5	30
6	20	Microwave, DMF, 4 bar pressure, 120°C	5	25
7	10	Microwave, DMF, 4 bar pressure, 120°C	5	20
8	30	Microwave, solvent-free, 2 bar pressure, 120°C	5	35
9	20	Microwave, solvent-free, 2 bar pressure, 120°C	5	60
10	10	Microwave, solvent-free, 2 bar pressure, 120°C	5	70
11	30	Microwave, solvent-free, 4 bar pressure, 120°C	5	40
12	20	Microwave, solvent-free, 4 bar pressure, 120°C	5	90
13	10	Microwave, solvent-free, 4 bar pressure, 120°C	5	95

[a]All reactions were run using 0.01 mol of ethyl 6-(4-chlorophenyl)-4-(4-methoxyphenyl) -2-oxocyclo hex-3-ene carboxylate and 0.01 mol of ethylene diamine.
[b]Isolated yield.

Experimental

Chemistry

General remarks

We used TLC (eluent: toluene–ethylacetate 8:2) to assess the reactions and the purity of the products. All the reported melting points were taken in open capillaries and are uncorrected. IR spectra were recorded in KBr (pellet forms) on a Thermo Nicolet-Avatar–330 FT-IR spectrophotometer and noteworthy absorption values (cm^{-1}) alone were listed. One-dimensional ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively, on Bruker AMX 400 NMR spectrometer using DMSO-*d* as solvent and tetramethylsilane (TMS) as internal standard. Two-dimensional HMQC spectrum was recorded at 500 MHz on Bruker DRX 500 NMR spectrometer using DMSO-d_6 as solvent and TMS as internal standard. The electron spray impact (ESI) positive (+ve) mass (MS) spectra were recorded on a Bruker Daltonics LC–MS spectrometer. Satisfactory microanalysis was obtained on a Carlo Erba 1106 CHN analyzer. Gyan Easiflash Flash column chromatography system, Italy, was used for flash column chromatography. BIOTAGE Initiator microwave synthesizer, Sweden, a scientific microwave oven, was used for the irradiation. By adopting the literature procedure, 6-carbethoxy-3,5-diarylcyclohex-2-enone **1–10** (*8*) were prepared.

General procedure for the synthesis of 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates ***11–20***

In a 10 mL pyrex glass tube was placed respective 6-carbethoxy-3,5-diarylcyclohex-2-enones (0.01 mol), ethylene diamine (0.01 mol), and catalytic amount of *p*-TSA (0.172 g, 0.001 mol). The top of glass tube was closed with teflon cover and it was placed in a teflon outer jacket and then the reaction tube was placed into the holder in the microwave cavity. The sample was irradiated under focused monomode irradiation at 120°C for 5 min. at 4 bar pressure. After allowing the mixture to cool to room temperature, the reaction vessel was opened and the contents were poured into ice cold water. The organic material was extracted with ethylacetate. The organic layer was washed with 10% sodium hydrogen carbonate, brine solution and then excess of water and dried over anhydrous sodium sulfate. After

evaporation of the ethylacetate under vacuum, solid mass obtained was subjected to flash column chromatography using toluene–ethylacetate as eluent.

Spectroscopic data

7,9-Diphenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 11

IR (KBr) (cm^{-1}): 3448, 3388, 3175, 3054, 3022, 2972, 2931, 2837, 1738, 1599, 1447, 1027, 827, 758, 698; ^{1}H NMR (δ ppm): 0.89–0.90 (*t*, 3H, ester CH_3); 2.97–3.02 (*m*, 2H, H_8), 3.04–3.22 (*m*, 1H, H_7), 3.51–3.67 (*m*, 1H, H_6), 3.87–3.92 (*q*, 2H, ester CH_2), 4.02–4.13 (*m*, 4H, imidazolidine $2CH_2$), 5.98 (*s*, 2H, imidazolidine 2NH), 6.54 (*s*, 1H, H_{10}), 7.10–7.79 (*m*, 10H, Ar–H's); in the D_2O exchanged ^{1}H NMR spectrum, singlet at 5.98 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 35.2 C-7, 43.8 C-8, 49.3 C-2 & C-3, 80.1 C-5, 58.7 ester CH_2, 59.9 C-6, 121.9 C-10, 122.88–130.4 Ar–C's, 137.3, 141.4 *ipso*-C, 169.2 C = O.

7-(4-Chlorophenyl)-9-phenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 12

IR (KBr) (cm^{-1}): 3535, 3437, 3382, 3295, 3065, 2978, 2924, 2847, 1735, 1601, 1445, 1018, 824, 758, 693; ^{1}H NMR (δ ppm): 0.92–0.93 (*t*, 3H, ester CH_3); 2.97–3.07 (*m*, 2H, H_8), 3.10–3.14 (*m*, 1H, H_7), 3.57–3.76 (*m*, 1H, H_6), 3.89–3.94 (*q*, 2H, ester CH_2), 4.02–4.15 (*m*, 4H, imidazolidine $2CH_2$), 6.12 (*s*, 2H, imidazolidine 2NH), 6.55 (*s*, 1H, H_{10}), 7.13–7.79 (*m*, 9H, Ar–H's); in the D_2O exchanged ^{1}H NMR spectrum, singlet at 6.12 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 34.9 C-7, 43.1 C-8, 48.4 C-2 & C-3, 80.2 C-5, 58.5 ester CH_2, 60.0 C-6, 121.9 C-10, 122.88–140.4 Ar–C's, 159.1, 160.4 *ipso*-C, 169.0 C = O.

7-(4-Fluorophenyl)-9-phenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 13

IR (KBr) (cm^{-1}): 3519, 3388, 3262, 3186, 3058, 2977, 2930, 2863, 1739, 1604, 1443, 1023, 832, 758, 694; ^{1}H NMR (δ ppm): 0.88–0.90 (*t*, 3H, ester CH_3); 2.74–2.94 (*m*, 2H, H_8), 2.98–3.13 (*m*, 1H, H_7), 3.56–3.88 (*m*, 1H, H_6), 3.87–3.92 (*q*, 2H, ester CH_2), 3.95–4.13 (*m*, 4H, imidazolidine $2CH_2$), 6.02 (*s*, 2H, imidazolidine 2NH), 6.57 (*s*, 1H, H_{10}), 6.83–7.94 (*m*, 9H, Ar–H's); in the D_2O exchanged ^{1}H NMR spectrum, singlet at 6.02 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 35.2 C-7, 42.9 C-8, 48.4 C-2 & C-3, 80.2 C-5, 59.8 ester CH_2, 61.0 C-6, 122.3 C-10, 113.1–136.1 Ar–C's, 157.8, 158.2 *ipso*-C, 169.1 C = O.

7-(4-Methylphenyl)-9-phenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 14

IR (KBr) (cm^{-1}): 3454, 3399, 3267, 3054, 3038, 2981, 2921, 2863, 1739, 1604, 1023, 832, 758, 694; ^{1}H NMR (δ ppm): 0.92–0.96 (*t*, 3H, ester CH_3); 2.26 (*s*, 3H, CH_3 of phenyl ring), 2.72–2.93 (*m*, 2H, H_8), 2.97–3.12 (*m*, 1H, H_7), 3.56–3.76 (*m*, 1H, H_6), 3.87–3.93 (*q*, 2H, ester CH_2), 4.00–4.09 (*m*, 4H, imidazolidine $2CH_2$), 5.94 (*s*, 2H, imidazolidine 2NH), 6.53 (*s*, 1H, H_{10}), 6.88–7.91 (*m*, 9H, Ar–H's); in the D_2O exchanged ^{1}H NMR spectrum, singlet at 5.94 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 20.5 CH_3 of phenyl ring, 35.3 C-7, 43.3 C-8, 48.9 C-2 & C-3, 80.2 C-5, 59.8 ester CH_2, 60.9 C-6, 121.9 C-10, 122.8–138.4 Ar–C's, 159.2, 160.0 *ipso*-C, 169.1 C = O.

7-(4-methoxyphenyl)-9-phenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 15

IR (KBr) (cm^{-1}): 3524, 3424, 3267, 3054, 2989, 2929, 2830, 1739, 1445, 1607, 1033, 832, 760, 694; ^{1}H NMR (δ ppm): 0.92–0.94 (*t*, 3H, ester CH_3); 2.69–2.93 (*m*, 2H, H_8), 2.97–3.12 (*m*, 1H, H_7), 3.58–3.64 (*m*, 1H, H_6), 3.72 (*s*, 3H, OCH_3 of phenyl ring), 3.88–3.93 (*q*, 2H, ester CH_2), 3.96–4.36 (*m*, 4H, imidazolidine $2CH_2$), 5.94 (*s*, 2H, imidazolidine 2NH), 6.61 (*s*, 1H, H_{10}), 6.85–7.78 (*m*, 9H, Ar–H's); in the D_2O exchanged ^{1}H NMR spectrum, singlet at 5.94 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 35.4 C-7, 43.0 C-8, 48.5 C-2 & C-3, 80.3 C-5, 54.9 OCH_3 of phenyl ring, 59.8 ester CH_2, 60.9 C-6, 121.9 C-10, 113.1–158.2 Ar–C's, 159.3, 160.6 *ipso*-C, 169.2 C = O.

9-(4-chlorophenyl)-7-phenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 16

IR (KBr) (cm^{-1}): 3524, 3386, 3175, 3059, 3029, 2978, 2927, 2858, 1738, 1448, 1584, 1013, 824, 762, 699; ^{1}H NMR (δ ppm): 0.90–0.91 (*t*, 3H, ester CH_3); 2.71–2.97 (*m*, 2H, H_8), 3.00–3.15 (*m*, 1H, H_7), 3.60–3.78 (*m*, 1H, H_6), 3.88–3.93 (*q*, 2H, ester CH_2), 3.97–4.13 (*m*, 4H, imidazolidine $2CH_2$), 6.08 (*s*, 2H, imidazolidine 2NH), 6.59 (*s*, 1H, H_{10}), 6.88–7.79 (*m*, 9H, Ar–H's); in the D_2O exchanged ^{1}H NMR spectrum, singlet at 6.08 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 14.2 ester CH_3, 35.1 C-7, 43.0 C-8,

48.3 C-2 & C-3, 80.2 C-5, 59.9 ester CH_2, 61.0 C-6, 122.8 C-10, 114.3–137.6 Ar–C's, 141.4, 159.2 *ipso*-C, 168.9 C = O.

9-(4-methoxyphenyl)-7-phenyl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 17

IR (KBr) (cm^{-1}): 3450, 3444, 3065, 3033, 2924, 2852, 1736, 1605, 1447, 1037, 757, 695; ^1H NMR (δ ppm): 0.90–0.92 (*t*, 3H, ester CH_3); 2.72–2.98 (*m*, 2H, H_8), 3.01–3.16 (*m*, 1H, H_7), 3.59–3.71 (*m*, 1H, H_6), 3.73 (*s*, 3H, OCH_3 of phenyl ring), 3.88–3.93 (*q*, 2H, ester CH_2), 3.96–4.08 (*m*, 4H, imidazolidine $2CH_2$), 5.93 (*s*, 2H, imidazolidine 2NH), 6.51 (*s*, 1H, H_{10}), 6.83–7.81 (*m*, 9H, Ar–H's); In the D_2O exchanged ^1H NMR spectrum, singlet at 5.93 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 36.0 C-7, 43.7 C-8, 49.2 C-2 & C-3, 80.2 C-5, 54.3 OCH_3 of phenyl ring, 59.9 ester CH_2, 61.0 C-6, 122.3 C-10, 116.2–141.4 Ar–C's, 157.8, 159.2 *ipso*-C, 169.0 C = O.

9-(4-chlorophenyl)-7-(4-methylphenyl)-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 18

IR (KBr) (cm^{-1}): 3459, 3386, 3273, 3169, 3049, 2983, 2923, 2856, 1739, 1612, 1447, 1013, 817, 744, 711; ^1H NMR (δ ppm): 0.92–0.94 (*t*, 3H, ester CH_3); 2.27 (*s*, 3H, CH_3 of phenyl ring), 2.75–2.98 (*m*, 2H, H_8), 2.98–3.15 (*m*, 1H, H_7), 3.57–3.77 (*m*, 1H, H_6), 3.87–3.93 (*q*, 2H, ester CH_2), 4.00–4.10 (*m*, 4H, imidazolidine $2CH_2$), 6.00 (*s*, 2H, imidazolidine 2NH), 6.55 (*s*, 1H, H_{10}), 6.89–7.98 (*m*, 8H, Ar–H's); in the D_2O exchanged ^1H NMR spectrum, singlet at 6.00 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 14.2 ester CH_3, 20.5 CH_3 of phenyl ring, 35.5 C-7, 43.2 C-8, 48.8 C-2 & C-3, 80.2 C-5, 59.8 ester CH_2, 61.0 C-6, 122.2 C-10, 123.2–154.5 Ar–C's, 157.8, 159.2 *ipso*-C, 169.0 C = O.

7-(4-chlorophenyl)-9-(4-methoxyphenyl)-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 19

IR (KBr) (cm^{-1}): 3442, 3393, 3284, 3065, 2962, 2923, 2850, 1738, 1598, 1457, 1140, 826, 718; ^1H NMR (δ ppm): 0.92–0.94 (*t*, 3H, ester CH_3); 2.77–2.98 (*m*, 2H, H_8), 2.77–2.98 (*m*, 1H, H_7), 3.48–3.75 (*m*, 1H, H_6), 3.77 (*s*, 3H, OCH_3 of phenyl ring), 3.88–3.93 (*q*, 2H, ester CH_2), 4.01–4.06 (*m*, 4H, imidazolidine $2CH_2$), 5.96 (*s*, 2H, imidazolidine 2NH), 6.55 (*s*, 1H, H_{10}), 6.96–7.82 (*m*, 8H, Ar–H's); in the D_2O exchanged ^1H NMR spectrum, singlet at 5.96 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 13.7 ester CH_3, 36.0 C-7, 43.7 C-8, 49.2 C-2 & C-3, 80.2 C-5, 55.2 OCH_3 of phenyl ring, 59.8 ester CH_2, 60.9 C-6, 119.9 C-10, 120.9–158.5 Ar–C's, 159.6, 161.2 *ipso*-C, 169.2 C = O.

9-(4-chlorophenyl)-7-(4-methoxyphenyl)-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylate 20

IR (KBr) (cm^{-1}): 3453, 3393, 3262, 3065, 2951, 2927, 2830, 1738, 1608, 1456, 1032, 824, 749, 711; ^1H NMR (δ ppm): 0.92–0.94 (*t*, 3H, ester CH_3); 2.87–3.09 (*m*, 2H, H_8), 3.12–3.19 (*m*, 1H, H_7), 3.59–3.70 (*m*, 1H, H_6), 3.71 (*s*, 3H, OCH_3 of phenyl ring), 3.87–3.92 (*q*, 2H, ester CH_2), 4.05–4.20 (*m*, 4H, imidazolidine $2CH_2$), 5.96 (*s*, 2H, imidazolidine 2NH), 6.55 (*s*, 1H, H_{10}), 7.24–7.91 (*m*, 8H, Ar–H's); in the D_2O exchanged ^1H NMR spectrum, singlet at 5.96 ppm which resonates due to 2NH's of imidazolidine moiety disappeared; ^{13}C NMR (δ ppm): 14.3 ester CH_3, 35.6 C-7, 43.1 C-8, 48.4 C-2 & C-3, 79.9 C-5, 55.2 OCH_3 of phenyl ring, 59.9 ester CH_2, 61.0 C-6, 119.9 C-10, 120.9–158.4 Ar–C's, 159.7, 161.2 *ipso*-C, 169.1 C = O.

Conclusion

To conclude, we have proposed an efficient method for the synthesis of novel 7,9-diaryl-1,4-diazaspiro[4.5]-deca-9-ene-6-ethyl carboxylates **11**–**20** by the reaction of 6-carbethoxy-3,5-diarylcyclohex-2-enones **1**–**10** with ethylene diamine in the presence of *p*-TSA in solvent-free conditions under focused MWI, and their structures were characterized by their spectral and analytical data. The advantages of the present reaction procedure include short reaction times for product formation, easy workup, clean reaction profiles, high yields, etc.

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