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Microwave-Assisted Efficient Synthesis of Spiropyridine Derivatives *via* Catalyst- and Solvent-Free One Pot Four Component Reaction

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A microwave-assisted, one-pot four-component reaction strategy has been developed for the synthesis of some novel spiropyridine derivatives from 1,3-dimethyl barbituric acid, chalcone, aromatic aldehyde and ammonium acetate under catalyst- and solvent-free conditions.

Keywords: Spiropyridine, 1,3-Dimethyl barbituric acid, Chalcone, Multi-component reaction.

INTRODUCTION

Pyridine moiety continues to attract attention from the synthetic chemists owing to their potent biological and diverse pharmacological activity such as antidepressants, antiviral, anticancer, anti-inflammatory, analgesic, antibacterial, anti-fungal, antitubercular, *etc*. [1-7]. The pyridine core is found in a number of alkaloids like nicotine, anabasine, coniine, piperine, quinine, morphine, ricinine, *etc*. In addition, they are also the important structural elements of vitamin B_3 and B_6. As a result, apart from various well known classical reactions such as Chichibabin pyridine synthesis [8], Ciamician-Dennstedt rearran-gement [9], Bönnemann cyclization [10], Hantzsch synthesis [11] and Gattermann-Skita synthesis [12], the last decade has witnessed significant advances towards the development of new and efficient synthetic protocols for assembling this important substructure [13-18]. Although literature enjoys a rich variety of attractive methodologies for the synthesis of the pyridine moiety [19-24] but simple, rapid and eco-friendly methods are significantly less and thus involves considerable synthetic challenges.

Over the years, the multi component reaction (MCR) strategy has become a powerful and widely used strategy for the construction of *N*-containing six-membered heterocyclic units as it ensures high atom economy and targeted synthesis in a single step. Numbers of synthetic groups have craftily employed the MCR reaction to construct substructures of biological and pharmaceutical significance [25-27]. More often than not, developing such synthetic strategy requires high energy requirements and the use of hazardous solvents. During the last few decades there have been significant developments in designing mild and 'green' protocol for the construction of a wide range of bio-active molecules in one step by using microwave as the source of energy. Microwave energy fulfills two basic criteria of organic synthesis *viz*. minimization of energy content and considerable reduction in reaction time [28-36]. Again, solvent-free processes have also brought organic synthesis under the umbrella of Green Chemistry by eliminating the need of hazardous organic solvents. Thus, MCR carried under microwave heating coupled with solvent less condition presents a powerful green alternative to conventional synthesis of annulated heterocycles [37-41] in general, and pyridine in particular. As such, new and improved methodologies, preferably employing catalyst- and solvent-free conditions are still desired for the synthesis of pyridine derivatives.

EXPERIMENTAL

All the commercially available reagents were used as such. Melting points were recorded in a Buchi M-560 melting point apparatus. FTIR spectra were recorded on a SHIMADZU FTIR-8400 instrument. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded on 300 MHz Advance DPX FT-NMR spectrometer by using tetramethylsilane (TMS) as an internal standard. ^{13}C NMR spectra were recorded on 75 MHz Advance DPX FT-NMR spectrometer and Chemical shifts (δ) are given

from $CDCl_3$ (77 ppm). Mass spectra were recorded on ESQUIRE 3000 Mass spectrometer. The progress of each and every reaction was monitored by thin layer chromatography (TLC). TLC was performed on a pre-coated silica gel plates (Merck). After elution, plate was visualized under UV illumination at 254 nm for UV active materials. Further visualization was achieved by spraying $KMnO_4$ and warming in a hot air oven. All MW reactions were carried out in a Synthos 3000 (Anton Paar) microwave reactor. The multitude microwave has a twin magnetron (2.45 GHz) with maximum output power of 1400 W.

General procedure: Chalcone (1 mmol), 1,3-dimethyl barbituric acid (**2**) (1 mmol), aromatic aldehyde (**3**) (1 mmol) and ammonium acetate (**4**) (1.2 mmol) were mixed and irradiated in a closed vessel in absence of any solvent in a Synthos 3000 microwave reactor at 700 W, 14 bar and 70 ºC for 5 min. The crude product mixture was recrystallized from methanol to get pure product **5**.

11-(4-Fluorophenyl)-2,4-dimethyl-9-phenyl-7-p-tolyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5a): White solid m.p. 212-214ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99-7.95 (m, Ar, 2H), 7.44-6.92 (m, Ar, 11H), 5.58 (s, 1H), 3.87 (dd, 1H $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.46 (ddd, 1H ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J= 3. Hz), 3.15 (dd, 1H, ^2J = 18.3Hz, ^3J = 6.2 Hz), 3.04 (s, 3H), 2.80 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.2, 167.6, 166.1, 149.9, 138.5, 137.8, 135.8, 134.3, 134.3, 130.3, 129.9, 129.8, 129.0, 128.4, 127.2, 126.5, 115.9, 115.7, 70.1, 59.3, 44.2, 31.1, 28.4, 27.7, 21.1. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3025, 2955, 1743, 1689, 1447. MS (GC-MS) = *m/z* 483.2 $[M]^+$; Anal. calcd. (found) % for $C_{29}H_{26}N_3O_3F$: C, 72.03 (72.08); H, 5.42 (5.40); N, 8.69 (8.72).

7-(4-Bromophenyl)-2,4-dimethyl-9,11-diphenyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5b): White solid m.p 196-198 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99-7.94 (m, Ar, 2H), 7.46-7.03 (m, Ar, 12H) 5.70 (s, 1H) 4.04 (dd, 1H, $^3J_1$ = 11.6 Hz, $^3J_2$ = 6 Hz), 3.48 (ddd, 1H, ^2J = 17.6 Hz, $^3J_1$ = 11.6 Hz, ^5J = 2.8. Hz), 3.17 (dd, 1H, ^2J = 17.6 Hz, ^3J = 6Hz), 3.02 (s, 3H), 2.87 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.1, 167.2, 166.2, 149.7, 138.5, 138.4, 137.6, 131.4, 130.4, 129.4, 128.9, 128.6, 128.4, 128.1, 127.4, 122.0, 68.6, 59.0, 46.1, 30.4, 28.5, 27.7. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3028, 2955, 1744, 1682, 1444. MS (GC-MS) = *m/z* 529.1 $[M]^+$; Anal. calcd. (found) % for $C_{28}H_{24}N_3O_3Br$: C, 63.40 (63.46); H, 4.56 (4.50); N, 7.92 (7.98).

2,4-Dimethyl-9,11-diphenyl-7-(*p*-tolyl)-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5c): White solid m.p. 188-190 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14-7.02 (m, Ar, 14H), 5.93 (s, 1H), 3.87 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.44 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.18 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.01 (s, 3H), 2.72 (s, 3H), 2.12 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 167.9, 164.1, 149.8, 139.4, 137.5, 134.8, 134.7, 134.5, 134.3, 129.9, 129.6, 129.5, 128.4, 127.9, 126.5, 117.9, 115.2, 70.8, 59.8, 44.1, 31.4, 28.2, 27.6, 21.5. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3025, 2955, 1743, 1678, 1447. MS (GC-MS) = *m/z* 465.2 $[M]^+$; Anal. calcd. (found) % for $C_{29}H_{27}N_3O_3$: C, 74.82 (74.78); H, 5.85 (5.80); N, 9.03 (8.99).

11-(4-Fluorophenyl)-2,4-dimethyl-7-(4-nitrophenyl)-9-phenyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5d): Pale yellow solid, m.p. 172-173 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18-8.10 (m, Ar, 2H), 7.93-6.92 (m, Ar, 11H), 5.99 (s, 1H), 4.09 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.49 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.22 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.12 (s, 3H), 2.85 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8, 167.8, 165.1, 149.8, 140.5, 139.8, 137.8, 137.7, 137.6, 135.3, 134.9, 129.8, 129.6, 128.8, 127.6, 126.9, 115.9, 115.4, 70.6, 59.8, 44.9, 33.8, 29.4, 27.2, IR ($CHCl_3$, ν_{max}, cm^{-1}): 3028, 2959, 1738, 1688, 1449. MS (GC-MS) = *m/z* 514.2 $[M]^+$; Anal. calcd. (found) % for $C_{28}H_{23}N_4O_5F$: C, 63.36 (63.29); H, 4.51 (4.46); N, 10.89 (10.82).

9-(4-Chlorophenyl)-2,4-dimethyl-7-(4-nitrophenyl)-11-phenyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5e): White solid, m.p. 195-197 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14-8.05 (m, Ar, 2H), 7.93-7.09 (m, Ar, 12H), 5.92 (s, 1H), 4.03 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.44 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.19 (dd, 1H, ^2J = 18.3Hz, ^3J = 6.2 Hz), 3.01 (s, 3H), 2.85 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.7, 169.1, 166.8, 142.9, 140.5, 139.8, 136.1, 130.1, 129.3, 128.9, 127.9, 127.6, 127.5, 127.4, 127.1, 126.8, 115.2, 115.1, 70.9, 69.5, 44.1, 30.1, 28.0, 27.4,. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3035, 2965, 1733, 1674, 1441. MS (GC-MS) = *m/z* 530.2 $[M]^+$; Anal. calcd. (found) % for $C_{28}H_{23}N_4O_5Cl$: C, 63.34 (63.28); H, 4.37 (4.36); N, 10.55 (10.52).

9-(4-Chlorophenyl)-2,4-dimethyl-7,11-diphenyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5f): White solid, m.p. 192-193 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99-7.90 (m, Ar, 2H), 7.42-7.02 (m, Ar, 12H), 5.70 (s, 1H), 4.10 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.54 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.20 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.03 (s, 3H), 2.82 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.2, 167.6, 166.1, 149.9, 138.5, 137.8, 135.8, 134.3, 134.3, 130.3, 129.9, 129.8, 129.0, 128.4, 127.2, 126.5, 115.9, 115.7, 70.1, 59.3, 44.2, 31.1, 28.4, 27.7, 21.1. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3029, 2975, 1749, 1680, 1444. MS (GC-MS) = *m/z* 485.2 $[M]^+$; Anal. calcd. (found) % for $C_{28}H_{24}N_3O_3Cl$: C, 69.20 (69.15); H, 4.98 (4.93); N, 8.65 (8.58).

7-(2-Chlorophenyl)-2,4-dimethyl-9,11-diphenyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5g): White solid, m.p. 202-204 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03-7.99 (m, Ar, 2H), 7.42-7.10 (m, Ar, 12H), 5.69 (s, 1H), 4.10 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.55 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.21 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.02 (s, 3H), 2.84 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.2, 167.2, 166.8, 149.1, 138.9, 138.8, 137.8, 137.3, 136.3, 135.3, 132.9, 131.8, 129.0, 127.4, 127.3, 126.8, 118.9, 117.7, 74.1, 58.3, 48.4, 31.9, 28.8, 27.7. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3026, 2945, 1723, 1674, 1457. MS (GC-MS) = *m/z* 485.2 $[M]^+$; Anal. calcd. (found) % for $C_{28}H_{24}N_3O_3Cl$: C, 69.20 (69.18); H, 4.98 (4.96); N, 8.65 (8.54).

11-(3-Bromophenyl)-2,4-dimethyl-7-phenyl-9-(*p*-tolyl)-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5h): White solid, m.p. 175-178 ºC, ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01-7.95 (m, Ar, 2H), 7.62-7.19 (m, Ar, 11H), 5.39 (s, 1H), 4.10 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.52 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.23 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.02 (s, 3H), 2.84 (s, 3H), 2.1 (s, 3H), ^{13}C NMR

(75 MHz, $CDCl_3$): δ 170.2, 167.2, 166.8, 149.1, 139.9, 139.8, 137.8, 137.3, 136.8, 133.3, 132.9, 131.9, 129.6, 127.8, 127.7, 126.1, 115.9, 115.7, 74.6, 58.5, 48.1, 31.9, 28.8, 27.2, 21.5. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3015, 2956, 1733, 1688, 1447. MS (GC-MS) = *m/z* 543.1 $[M]^+$; Anal. calcd. (found) % for $C_{29}H_{26}N_3O_3Br$: C, 63.98 (63.91); H, 4.81 (4.76); N, 7.72 (7.64).

2,4-Dimethyl-7-(4-nitrophenyl)-9-phenyl-11-(*m*-tolyl)-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5i): Pale yellow solid, m.p. 186-188 ºC, ^1H NMR (300 MHz, $CDCl_3$): δ 8.11-8.08 (m, Ar, 2H), 7.62-7.10 (m, Ar, 11H), 5.64 (s, 1H), 4.12 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.55 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.20 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.01 (s, 3H), 2.84 (s, 3H), 2.1(s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 167.6, 166.1, 149.7, 138.4, 138.1, 137.8, 136.3, 136.1, 136.0, 132.9, 132.8, 129.7, 127.8, 127.3, 126.1, 118.9, 117.7, 74.1, 58.3, 48.9, 31.2, 28.2, 27.1, 21.3. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3025, 2985, 1740, 1681, 1447. MS (GC-MS) = *m/z* 510.2 $[M]^+$. Anal. calcd. (found) % for $C_{29}H_{26}N_4O_5$: C, 68.22 (68.18); H, 5.13 (5.11); N, 10.97 (10.94).

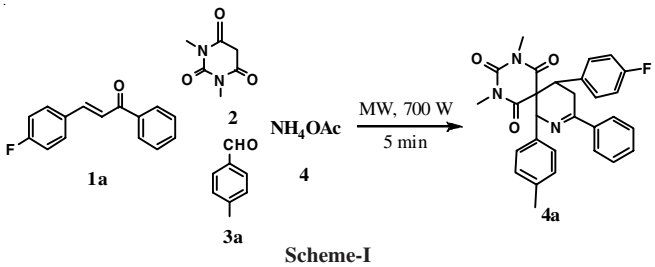
11-(4-Methoxyphenyl)-2,4-dimethyl-9-phenyl-7-(*p*-tolyl)-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5j): White solid, m.p. 196-198ºC, ^1H NMR (300 MHz, $CDCl_3$): δ 8.11-8.08 (m, Ar, 2H), 7.62-7.10 (m, Ar, 11H), 5.64 (s, 1H), 4.12 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.75 (s, 3H), 3.55 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3.0 Hz), 3.20 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.01 (s, 3H), 2.84 (s, 3H), 2.1 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 167.4, 166.1, 149.7, 138.4, 138.1, 137.8, 137.3, 137.1, 136.8, 132.9, 132.8, 129.7, 127.8, 127.3, 126.1, 118.9, 117.7, 74.1, 58.3, 55.2 48.9, 31.2, 28.2, 27.1, 21.3. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3020, 2965, 1723, 1698, 1442. MS (GC-MS) = *m/z* 495.2 $[M]^+$; Anal. calcd. (found) % for $C_{30}H_{29}N_3O_4$: C, 72.71 (72.68); H, 5.90 (5.86); N, 8.48 (8.42).

7-(3-Bromophenyl)-2,4-dimethyl-9,11-di-*p*-tolyl-2,4,8-triazaspiro[5.5]undec-8-ene-1,3,5-trione (5k): White solid, m.p. 188-190 ºC, ^1H NMR (300 MHz, $CDCl_3$): δ 8.01-7.08 (m, Ar, 12H), 5.64 (s, 1H), 4.12 (dd, 1H, $^3J_1$ = 12 Hz, $^3J_2$ = 6.2 Hz), 3.55 (ddd, 1H, ^2J = 18.3 Hz, $^3J_1$ = 12 Hz, ^5J = 3. Hz), 3.20 (dd, 1H, ^2J = 18.3 Hz, ^3J = 6.2 Hz), 3.01 (s, 3H), 2.84 (s, 3H), 2.2, (s, 3H), 2.1 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 168.6, 167.1, 149.7, 139.9, 138.1, 137.8, 137.3, 136.6, 136.4, 132.9, 131.7, 130.7, 128.8, 127.9, 126.1, 117.9, 116.7, 72.1, 62.3, 31.2, 28.2, 27.1, 23.1, 21.7. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3024, 2954, 1713, 1688, 1449. MS (GC-MS) = *m/z* 557.1 $[M]^+$; Anal. calcd. (found) % for $C_{30}H_{28}N_3O_3Br$: C, 64.52 (64.51); H, 5.05 (5.01); N, 7.52 (7.44).

2,4-Dimethyl-7,9,11-triphenyl-2,4,8-triazaspiro[5.5]-undec-8-ene-1,3,5-trione (5l): White solid, m.p. 190-192 ºC, ^1H NMR (300 MHz, $CDCl_3$): δ 8.01-7.97 (m, Ar, 2H), 7.46-7.10 (m, Ar, 13H) 5.70 (s, 1H) 4.11 (dd, 1H, $^3J_1$ = 11.6 Hz, $^3J_2$ = 6 Hz), 3.55 (ddd, 1H, ^2J = 17.6 Hz, $^3J_1$ = 11.6 Hz, ^5J = 2.8 Hz), 3.21 (dd, 1H, ^2J = 17.6 Hz, ^3J = 6 Hz), 3.02 (s, 3H), 2.79 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8, 166.4, 166.1, 141.7, 138.8, 138.6, 137.4, 130.8, 130.1, 129.8, 127.6, 127.5, 127.2, 126.8, 125.3, 120.1, 68.4, 59.8, 44.1, 32.1, 29.8, 27.9. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3048, 2985, 1747, 1682, 1450. MS (GC-MS) = *m/z* 451.2 $[M]^+$; Anal. calcd. (found) % for $C_{28}H_{25}N_3O_3$: C, 74.48 (74.41); H, 5.58 (5.51); N, 9.31 (9.24).

RESULTS AND DISCUSSION

As a part of the continuous study towards the development of green methodology for the synthesis of heterocycles, a microwave assisted solvent- and catalyst-free four component synthesis of spiropyridine derivatives is developed from chalcone, 1,3-dimethyl barbituric acid, aldehyde and ammonium acetate. The method is simple and spiropyridine derivatives are obtained in uniformly excellent yields. In a typical procedure, chalcone (**1a**, 1 mmol), 1,3-dimethylbarbituric acid (**2**, 1 mmol), *p*-tolualdehyde (**3a**, 1 mmol) and ammonium acetate (**4**, 1.2 mmol) were mixed and irradiated inside a microwave reactor at 700 W for 5 min in absence of any catalyst and solvent to afford spiropyridine derivative **5a** in 85% yield (**Scheme-I**).



Scheme-I

Initially, the reaction was started in microwave by using 10 mL of ethanol as a solvent which gives about 15% yield. The progress of the reaction under the influence of organic solvents but surprisingly, it is observed that the reaction did not proceed efficiently (Table-1, entries 1-8) in organic solvents. Further, no product formation was observed when water was employed as the reaction medium (Table-1, entry 9). Thus, it can be concluded that 'no solvent' system is the 'best solvent' system for this transformation (Table-1, entry 10).

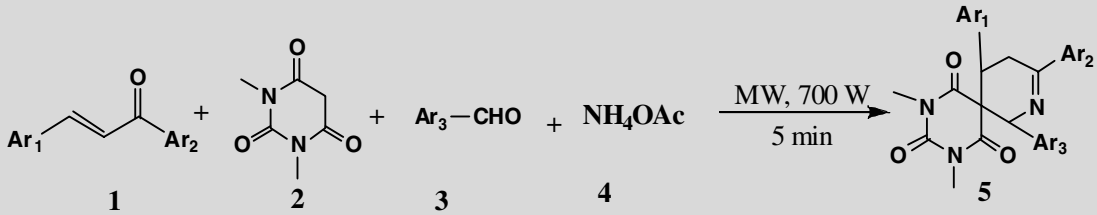
TABLE-1
OPTIMIZATION FOR THE SYNTHESIS OF COMPOUND **5a** UNDER MW IRRADIATIONS[a]

Entry	Solvent	Time (min)	Yield (%)[b]
1	Methanol	10	15
2	Ethanol	15	10
3	Acetonitrile	15	n.r
4	Chloroform	12	n.r
5	Toluene	12	n.r
6	Nitrobenzene	10	n.r
7	Tetrahydrofuran	8	n.r
8	Acetic acid	5	n.r
9	Water	10	n.r
10	No solvent	5	85

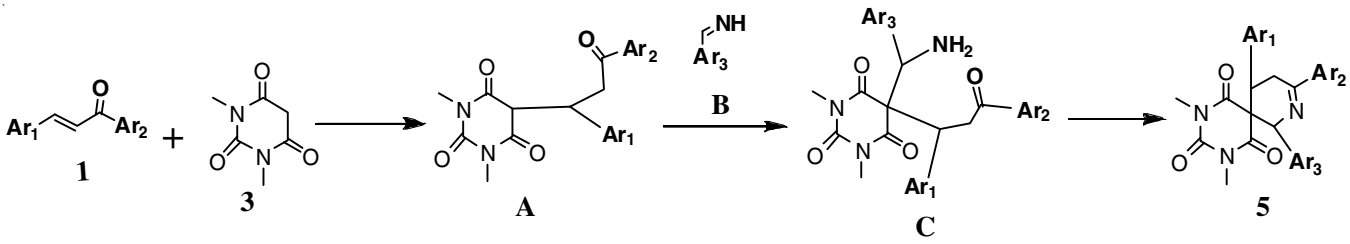
[a]Reaction conditions: Chalcone (**1a**) (1 mmol), 1,3-dimethylbarbituric acid (**2**) (1 mmol), *p*-tolyldehyde (**3a**) (1 mmol), and ammonium acetate (**4**) (1.2 mmol) were irradiated at 700 Watt in absence of any catalyst in a microwave reactor. [b]Isolated yield.

Structure of compound **5a** was ascertained from spectroscopic data and elemental analyses. The ^1H NMR spectra of the compound showed the presence of one *tert*-CH proton at δ 5.45 ppm and signals of the proton in the ABX system of CH_2-CH fragment appears at δ 3.2, 3.58 and δ 3.86 as dd, ddd and dd, respectively. The IR spectra showed the presence of the two carbonyl groups at 1689 and 1743 cm^{-1}.

TABLE-2
SYNTHESIS OF SPIROPYRIDINE DERIVATIVES (**5a-l**) UNDER MICROWAVE IRRADIATION



Entry	Ar_1	Ar_2	Ar_3	Product	Yield (%)
1	4-F-C_6H_4-	C_6H_5-	4-CH_3-C_6H_4-	**5a**	85
2	C_6H_5-	C_6H_5-	4-Br-C_6H_4-	**5b**	86
3	C_6H_5-	C_6H_5-	4-CH_3-C_6H_4-	**5c**	85
4	4-F-C_6H_4-	C_6H_5-	4-NO_2-C_6H_4-	**5d**	82
5	C_6H_5-	4-Cl-C_6H_4-	4-NO_2-C_6H_4-	**5e**	83
6	C_6H_5-	4-Cl-C_6H_4-	C_6H_5-	**5f**	87
7	C_6H_5-	C_6H_5-	2-Cl-C_6H_4-	**5g**	85
8	3-Br-C_6H_4-	4-CH_3-C_6H_4-	C_6H_5-	**5h**	86
9	3-CH_3-C_6H_4-	C_6H_5-	4-NO_2-C_6H_4-	**5i**	77
10	4-OCH_3-C_6H_4-	4-CH_3-C_6H_4-	C_6H_5-	**5j**	84
11	4-CH_3-C_6H_4-	4-CH_3-C_6H_4-	3-Br-C_6H_4-	**5k**	85
12	C_6H_5-	C_6H_5-	C_6H_5-	**5l**	84



Scheme-II: Synthetic route of spiropyridine Derivatives

The generality of the reaction was established by synthesizing a series of compounds **5b-l** (Table-2). It was observed that aromatic aldehydes having both electron donating and withdrawing substituents participated in the reaction to give the desired spiro-substituted pyridine derivative in excellent yield. Further, it was encouraging to note that substantial steric hindrance was tolerated on the aromatic aldehyde and no undesired side reaction was detected resulting spiro-substituted pyridine as the only product. However, when heterocyclic aldehydes such as furfural and thiophen-2-carbaldehyde were employed, the yield of the reaction became somewhat low and with aliphatic aldehydes the reaction did not proceed.

All the products obtained were characterized by IR, NMR and mass spectrometric analyses. Increase in the reaction time or the microwave power did not result in improvement in yield of the reaction, rather, decomposition of the product occurred.

Though detailed mechanism of the reaction is not studied, it is possible that chalcone (**1**) and barbituric acid (**3**) may undergo Michael type addition to form intermediate A which reacts with the imine B generated from aldehyde and ammonium acetate to form intermediate C. Finally, C undergoes cyclocondensation to form the final product **5** (**Scheme-II**).

Conclusion

In summary, an efficient microwave assisted four component strategy has been developed for the generation of some complex spiropyridine derivatives under catalyst- and solvent-free conditions. Overall, current procedure is simple, clean, and a green protocol for obtaining spiropyridines in excellent yields within a short period of time.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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