J IRAN CHEM SOC
DOI 10.1007/s13738-014-0574-8

ORIGINAL PAPER

Expedient one-pot three-component catalyst-free access to 5,6-dihydropyrimidin-4(3*H*)-one derivatives

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Received: 25 August 2014 / Accepted: 8 December 2014
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Abstract The synthesis of novel 5,6-dihydropyrimidin-4(3*H*)-one derivatives was accomplished in good yields via one-pot three-component condensation of Meldrum's acid, aldehydes and benzamidine in EtOH. Short reaction time, mild reaction condition, use of simple experimental procedure and prompt isolation of the products are some advantages of this protocol.

Keywords 5,6-Dihydropyrimidin-4(3*H*)-one · Benzamidine · Meldrum's acid · Three-component reaction

Introduction

The so-called multicomponent reactions (MCRs) are one-pot processes in which at least three or more different simple substrates react for the preparation of target materials [1–7]. These reactions have gained much attention during the past years and frequently occur not through a single-step procedure, but rather by several sequential steps or multicomponent cascade or domino reactions [8–13]. Simplicity, greater efficiency and atom economy with generation of molecular complexity and diversity in one-pot transformation are some of the advantages of these reactions.

The six-membered pyrimidines, abundantly widespread among natural bases [14–16], are an important class of heterocycles to medicinal chemistry due to their biological activities. These compounds have been reported as antitumor [17–20], interferon inducer [21–23], antiviral [24], anti-hypertensive [25, 26], hypoglycemic [27], anticonvulsant [28], antinociceptive [29, 30], anti-amoebic [31] and anti-inflammatory [32] agents.

As an important subclass of pyrimidine, the dihydropyrimidine and their derivatives are known as calcium channel modulators [33], mitotic kinesine inhibitors [34], adrenergic receptor antagonists [35], antibacterial [36], and antiviral agents [37].

Pyrimidine or pyrimidinone derivatives have traditionally been synthesized via condensation of a Michael acceptor with a uronium-containing molecule such as urea [38], thiourea [39], amidines [40], guanidines [41] or their derivatives. Due to the rather slow rates, 1 to 2 days are needed for the reactions to be completed. Therefore, different catalysts including $BF_3.OEt_2$ [42], $LaCl_3.H_2O$ [43], $InBr_3$ [44], HY [45], amberlyst-15 or Nafion-H [46], montmorillonite-KSF [47], MCM-41-R-SO_3H [48], MCM-41 supported $FeCl_3$ [49] and amino-functionalized MCM-41 [50] have been used for these reactions. In addition, microwave radiation has also been used to accelerate reaction rates [40].

In continuation of our own interest in MCRs [51–54], herein we report an expedient one-pot three-component access to 5,6-dihydropyrimidin-4(3*H*)-one derivatives via condensation of Meldrum's acid, aldehydes and benzamidine in EtOH.

Experimental

General information

All commercially available chemicals and reagents were purchased from Merck Chemical Company and used without further purification. Melting points were determined with an Electrothermal model 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu

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Published online: 16 December 2014

4300 spectrophotometer, in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-500-AVANCE spectrometer at 300 (^1H) and 75 MHz (^{13}C) using $CDCl_3$ as solvent and with the residual solvent signal as internal reference ($CDCl_3$ 7.24 and 77.0 ppm). Mass spectra of the products were obtained with an HP (Agilent technologies) 5937 Mass Selective Detector. Elemental analyses were carried out by a CHN-Rapid Heraeus elemental analyzer (Wellesley, MA, USA).

*General procedure for the preparation of **2a–n***

A mixture containing benzamidine hydrochloride (0.210 g, 1.2 mmol), triethylamine (0.101 g, 1.0 mmol), aldehydes **1a–n** (1.0 mmol) and Meldrum's acid (0.144 g, 1.0 mmol) in EtOH (3 mL) was stirred at reflux for 1 h. After completion as indicated by TLC, the solid was filtered and washed with EtOH to afford **2a–n**.

*6-Butyl-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2a**)* White solid, mp: 105–107 °C, yield: 0.168 g (73 %). IR (KBr) (ν_{max}, cm^{-1}): 3,288 (NH), 1,692 (C = O), 1,642 (C = N); ^1H-NMR (300 MHZ, $CDCl_3$): δ_H = 0.95 (t, J = 7.0 Hz, 3H, $C\underline{H}_3CH_2$), 1.36–1.86 (m, 6H, $CH_2CH_2CH_2$), 2.31(dd, J = 16.4, 11.2 Hz, 1H, CHCO), 2.60 (dd, J = 16.4, 5.2 Hz, 1H, CHCO), 3.70–3.80 (m, 1H, CHN), 7.42–7.52 (m, 3H, Ar), 7.79 (d, J = 6.3 Hz, 2H, Ar), 8.67 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 14.0, 22.6, 28.1, 35.0, 35.5, 54.7, 126.5, 128.8, 131.1, 133.4, 151.5, 171.7 (C = O); EI-MS: *m/z* (%): 230 (21, M^+), 215 (1.5), 201 (4), 173 (100), 159 (9), 104 (59), 77 (28); Anal. Calcd for $C_{14}H_{18}N_2O$ (230.14): C 73.01, H 7.88, N 12.16 %. Found: C 72.59, H 8.20, N 11.77 %.

*6-Phenethyl-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2b**)* White solid, mp: 144–146 °C, yield: 0.222 g (80 %). IR (KBr) (ν_{max}, cm^{-1}): 3,253 (NH), 1,692 (C = O), 1,639 (C = N); ^1H-NMR (300 MHZ, $CDCl_3$): δ_H = 1.88–2.00 (m, 1H, C$\underline{H}$CHN), 2.04–2.16 (m, 1H, C$\underline{H}$CHN), 2.35(dd, J = 16.4, 11.8 Hz, 1H, CHCO), 2.60 (dd, J = 16.5, 5.1 Hz, 1H, CHCO), 2.85–3.02 (m, 2H, CH_2Ph), 3.71-3.81 (m, 1H, CHN), 7.19–7.34 (m, 5H, Ar), 7.44-7.55(m, 3H, Ar), 7.82 (d, J = 6.7 Hz, 2H, Ar), 8.55 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 32.2, 35.2, 37.4, 53.8, 125.9, 126.5, 128.4, 128.6, 128.9, 131.3, 133.3, 141.7, 150.5, 171.3 (CO); EI-MS: *m/z* (%): 278 (27, M^+), 249 (4), 174 (100), 145 (26), 104 (43), 91 (17), 77 (21); Anal. Calcd for $C_{18}H_{18}N_2O$ (278.14): C 77.67, H 6.52, N 10.06 %. Found: C 77.46, H 6.23, N 10.16 %.

*6-(2,4-Dichlorophenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2c**)* White solid, mp: 218–220 °C, yield: 0.217 g (68 %). IR (KBr) (ν_{max}, cm^{-1}): 3,246 (NH), 1,694 (C = O), 1,635 (C = N); ^1H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.36 (dd, J = 16.5, 13.6 Hz, 1H, CHCO), 3.01 (dd, J = 16.6, 5.0 Hz, 1H, CHCO), 5.28 (dd, J = 13.6, 5.0 Hz, 1H, CHN), 7.31 (dd, J = 8.4, 2.0 Hz, 1H, Ar), 7.42 (d, J = 2.0 Hz, 1H, Ar), 7.47–7.58 (m, 3H, Ar), 7.63 (d, J = 8.4 Hz, 1H, Ar), 7.87 (m, 2H, Ar), 8.80 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 35.8, 55.7, 126.5, 127.7, 129.0, 129.2, 131.7, 131.9, 132.9, 133.7, 138.7, 152.1, 170.2 (CO); EI-MS: *m/z* (%): 322(20, M^+, 2[^{37}Cl], 320 (77, M^+, [^{37}Cl], [^{35}Cl]), 318 (84, M^+, 2[^{35}Cl]), 291 (12), 283 (56), 267 (12), 226 (9), 173 (22), 104(100), 91(17), 77 (63 %); Anal. Calcd for $C_{16}H_{12}C_{l2}N_2O$: C, 60.21; H, 3.79; N, 8.78. Found: C, 59.93; H, 3.61; N, 8.81.

*2,6-Diphenyl-5,6-dihydropyrimidin-4(3H)-one (**2d**)* White solid, mp: 185–187 °C, yield: 0.175 g (70 %). IR (KBr) (ν_{max}, cm^{-1}): 3,239 (NH), 1,691 (C = O), 1,637 (C = N); ^1H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.61 (dd, J = 16.5, 12.4 Hz, 1H, CHCO), 2.88 (dd, J = 16.5, 5.4 Hz, 1H, CHCO), 4.98 (dd, J = 12.4, 5.3 Hz, 1H, CHN), 7.29-7.34 (m, 1H, Ar), 7.39 (t, J = 7.4 Hz, 2H, Ar), 7.46-7.56 (m, 5H, Ar), 7.90 (d, J = 6.8 Hz, 2H, Ar), 9.13 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.5, 58.3, 126.6, 126.7, 127.4, 128.7, 128.8, 131.4, 133.2, 142.1, 151.4, 171.2 (CO); EI-MS: *m/z* (%): 250 (100, M^+), 221(22), 193 (9), 173 (5), 147 (1.6), 104 (61), 77 (16); Anal. Calcd for $C_{16}H_{14}N_2O$ (250.11): C 76.78, H 5.64, N 11.19 %. Found: C 76.36, H 5.23, N, 11.14 %.

*6-(4-Bromophenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2e**)* White solid, mp: 210–212 °C, yield: 0.171 g (52 %). IR (KBr) (ν_{max}, cm^{-1}): 3,250 (NH), 1,694 (C = O), 1,633 (C = N); ^1H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.56 (dd, J = 16.5, 12.8 Hz, 1H, CHCO), 2.86 (dd, J = 16.5, 5.2 Hz, 1H, CHCO), 4.93 (dd, J = 12.8, 5.2 Hz, 1H, CHN), 7.35 (d, J = 8.4 Hz, 2H, Ar), 7.46–7.57 (m, 5H, Ar), 7.85(d, J = 7.2 Hz, 2H, Ar), 8.47 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.4, 57.8, 121.3, 126.5, 128.3, 128.9, 131.6, 131.8, 133.0, 141.2, 151.5, 170.2 (CO); EI-MS: *m/z* (%): 330 (70, M^+ [^{81}Br]), 328 (49, M^+ [^{79}Br]), 299 (12), 273 (4), 249 (29), 104 (100), 77 (51); Anal. Calcd for $C_{16}H_{13}BrN_2O$ (328.02): C 58.38, H 3.98, N 8.51 %. Found: C 58.46, H 3.93, N 8.59 %.

*6-(4-Chlorophenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2f**)* White solid, mp: 195–197 °C, yield: 0.25 g (88 %). IR (KBr) (ν_{max}, cm^{-1}): 3,230 (NH), 1,696 (C = O), 1,633 (C = N); ^1H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.56 (dd, J = 16.5, 12.8 Hz, 1H, CHCO), 2.86 (dd, J = 16.5, 5.2 Hz, 1H, CHCO), 4.95 (dd, J = 12.7, 5.2 Hz, 1H, CHN), 7.35-7.43 (m, 4H, Ar), 7.46-7.56 (m, 3H, Ar), 7.85(d, J = 6.8 Hz, 2H, Ar), 8.47 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.4, 57.8, 126.5, 128.0, 128.8,

128.9, 131.6, 133.0, 133.2, 140.7, 151.5, 170.2 (CO); EI-MS: *m/z* (%): 286 (47, M^+ [^{37}Cl]), 284 (100, M^+ [^{35}Cl]), 255 (22), 227 (7), 138 (21), 104 (80), 77 (34); Anal. Calcd for $C_{16}H_{13}ClN_2O$ (284.07): C 67.49, H 4.60, N 9.84 %. Found: C 67.48, H 4.49, N 9.94 %.

2-Phenyl-6-(p-tolyl)-5,6-dihydropyrimidin-4(3H)-one ***(2g)*** White solid, mp: 179–18 °C, yield: 0.14 g (53 %). IR (KBr) (ν_{max} cm^{-1}): 3,255 (NH), 1,692 (CO), 1,642 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.36 (s, 3H, Me), 2.61 (dd, *J* = 16.5, 12.2 Hz, 1H, CHCO), 2.86 (dd, *J* = 16.5, 5.4 Hz, 1H, CHCO), 4.96 (dd, *J* = 12.1, 5.4 Hz, 1H, CHN), 7.19 (d, *J* = 7.9 Hz, 2H, Ar), 7.34 (d, *J* = 7.9 Hz, 2H, Ar), 7.45-7.53 (m, 3H, Ar), 7.87(d, *J* = 7.5 Hz, 2H, Ar), 8.69 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 21.1, 37.5, 58.1, 126.4, 126.6, 128.8, 129.4, 131.4, 133.2, 137.0, 139.1, 151.1, 170.9 (CO); EI-MS: *m/z* (%): 264 (100, M^+), 235 (27), 173 (4), 145 (16), 119 (27), 104 (35), 77 (20); Anal. Calcd for $C_{17}H_{16}N_2O$ (264.13): C 77.25, H 6.10, N 10.60 %. Found: C 76.81, H 6.04, N 10.60 %.

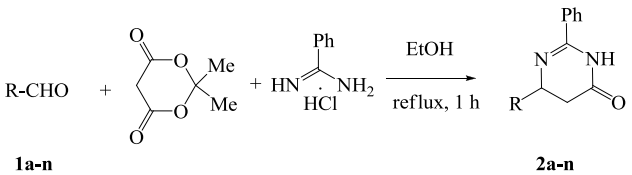
6-([1,1′-Biphenyl]-4-yl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one ***(2h)*** White solid, mp: 252–254 °C, yield: 0.231 g (71 %). IR (KBr) (ν_{max}, cm^{-1}): 3,257 (NH), 1,690 (C = O), 1,638 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.67 (dd, *J* = 16.5, 12.4 Hz, 1H, CHCO), 2.93 (dd, *J* = 16.5, 5.4 Hz, 1H, CHCO), 5.04 (dd, *J* = 12.4, 5.3 Hz, 1H, CHN), 7.33-7.38 (m, 1H, Ar), 7.42–7.64 (m, 11H, Ar), 7.88 (dd, *J* = 6.6, 1.6 Hz, 2H, Ar), 8.41 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.1, 57.2, 126.3, 126.6, 126.7, 126.8, 126.9, 127.8, 128.4, 130.4, 133.1, 139.1, 140.0, 141.5, 152.2, 170.3 (CO); EI-MS: *m/z* (%): 326 (35, M^+), 297 (16), 180 (43), 165 (15), 152 (78), 104 (100), 77 (80); Anal. Calcd for $C_{22}H_{18}N_2O$ (326.14): C 80.96, H 5.56, N 8.58 %. Found: C 80.92, H 5.30, N 8.64 %.

6-(4-Methoxyphenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one ***(2i)*** White solid, mp: 157–159 °C, yield: 0.205 g (73 %). IR (KBr) (ν_{max}, cm^{-1}): 3,200 (NH), 1,704 (C = O), 1,653 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.45 (dd, *J* = 16.5, 12.2 Hz, 1H, CHCO), 2.98 (dd, *J* = 16.5, 5.9 Hz, 1H, CHCO), 3.87 (s, 3H, Me), 5.32 (dd, *J* = 12.1, 5.4 Hz, 1H, CHN), 6.92 (d, *J* = 8.2 Hz, 1H, Ar), 7.01 (t, *J* = 7.6, 1H, Ar), 7.25–7.32 (m, 1H, Ar), 7.45-7.58 (m, 4H, Ar), 7.93 (d, *J* = 5.7 Hz, 2H, Ar), 9.31 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 35.9, 53.2, 55.3, 110.3, 126.7, 128.4, 128.8, 130.5, 131.2, 133.4, 151.6, 156.3, 171.9; EI-MS: *m/z* (%): 280 (100, M^+), 265 (34), 251 (24), 173 (12), 134 (19), 104 (75), 77 (40); Anal. Calcd for $C_{17}H_{16}N_2O_2$ (280.12): C 72.84, H 5.75, N 9.99 %. Found: C 73.08, H 5.67, N 10.15 %.

6-(3-Hydroxy-4-methoxyphenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one ***(2j)*** White solid, mp: 178–180 °C, yield: 0.186 g (63 %). IR (KBr) (ν_{max}, cm^{-1}): 3,439 (OH), 3,259 (NH), 1,695 (C = O), 1,640 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.59 (dd, *J* = 16.5, 12.1 Hz, 1H, CHCO), 2.84 (dd, *J* = 16.5, 5.4 Hz, 1H, CHCO), 3.89 (s, 3H, Me), 4.90 (dd, *J* = 12.0, 5.4 Hz, 1H, CHN), 5.72 (s, 1H, OH), 6.84 (d, *J* = 8.3 Hz, 1H, Ph), 6.91 (dd, *J* = 8.3, 1.8 Hz, 1H, Ph), 7.03 (d, *J* = 1.8 Hz, 1H, Ph), 7.44–7.55 (m, 3H, Ph), 7.86 (d, *J* = 6.8 Hz, 2H, Ph), 8.60 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.5, 56.0, 57.8, 110.8, 113.0, 118.0, 126.6, 128.8, 131.4, 133.1, 135.4, 145.8, 145.9, 151.1, 170.8 (CO); EI-MS: *m/z* (%): 296 (100, M^+), 267 (22), 240 (4) 177 (15), 150 (16), 104 (39), 77 (20); Anal. Calcd for $C_{17}H_{16}N_2O_3$ (296.12): C 68.91, H 5.44, N 9.45 %. Found: C 69.19, H 5.04; N 9.10 %.

2-Phenyl-6-(3,4,5-trimethoxyphenyl)-5,6-dihydropyrimidin-4(3H)-one ***(2k)*** Pale yellow solid, mp: 157–158 °C, yield: 0.16 g (47 %). IR (KBr) (ν_{max}, cm^{-1}): 3,265 (NH), 1,690 (C = O), 1,647 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.62 (dd, *J* = 16.4, 13.2 Hz, 1H, CHCO), 2.86 (dd, *J* = 16.5, 5.1 Hz, 1H, CHCO), 3.85 (s, 3H, Me), 3.88 (s, 6H, Me), 4.88 (dd, *J* = 13.1, 5.0 Hz, 1H, CHN), 6.69 (s, 2H, Ar), 7.46–7.57 (m, 3H, Ar), 7.87 (d, *J* = 8.0 Hz, 2H, Ph), 8.69 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.7, 56.2, 58.6, 60.8, 103.6, 126.6, 128.9, 131.5, 133.1, 137.2, 138.0, 151.3, 153.45, 170.8 (CO); EI-MS: *m/z* (%): 340 (100, M^+), 325 (41), 311 (14), 297 (9), 221(14), 194 (12), 104 (57), 77 (21); Anal. Calcd for $C_{19}H_{20}N_2O_4$ (340.14): C 67.05, H 5.92, N 8.23 %. Found: C 66.85, H 5.65, N 8.48 %.

6-(2-Nitrophenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one ***(2l)*** Pale yellow solid, mp: 182–184 °C, yield: 0.163 g (55 %). IR (KBr) (ν_{max}, cm^{-1}): 3,362 (NH), 1,699 (C = O), 1,654 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.52 (dd, *J* = 16.2, 14.3 Hz, 1H, CHCO), 3.12 (dd, *J* = 16.5, 4.8 Hz, 1H, CHCO), 5.52 (dd, *J* = 13.9, 4.8 Hz, 1H, CHN), 7.45–7.55 (m, 4H, Ar), 7.67 (t, *J* = 7.6 Hz, 1H, Ar), 7.84 (d, *J* = 7.8 Hz, 1H, Ar), 7.89 (d, *J* = 7.7 Hz, 2H, Ar), 7.98 (d, *J* = 8.1 Hz, 1H, Ar), 9.65 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 36.8, 55.3, 124.6, 126.7,



Scheme 1 Preparation of dihydropyrimidin-4(3*H*)-one derivatives **2a–n**

Table 1 Isolated yields obtained for **2a–n**

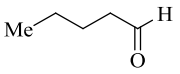
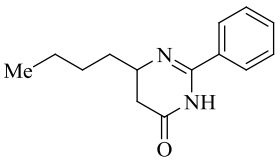
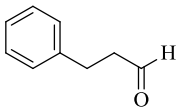
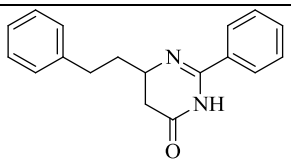
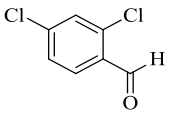
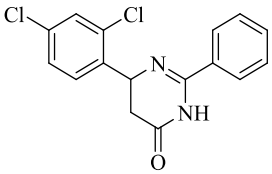
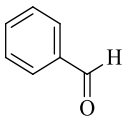
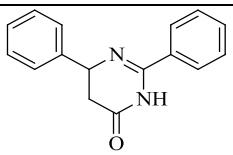
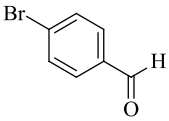
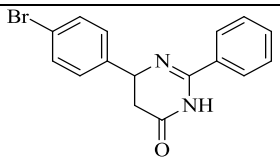
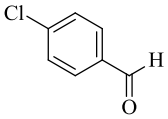
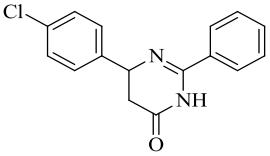
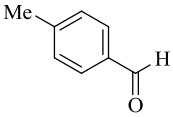
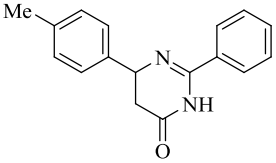
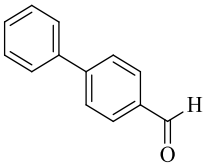
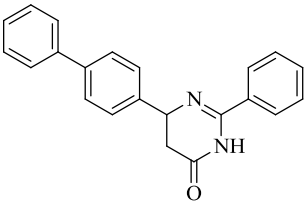
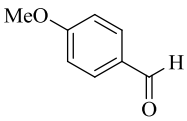
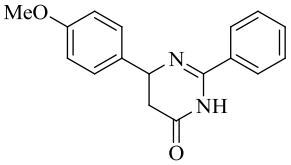
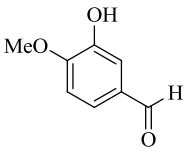
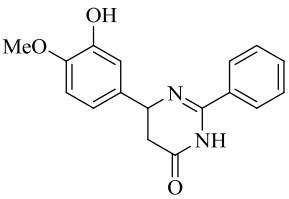
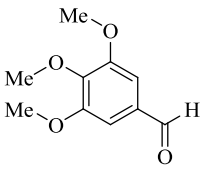
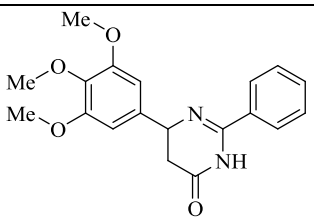
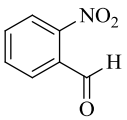
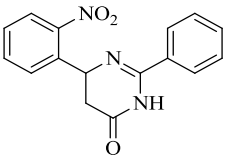
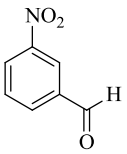
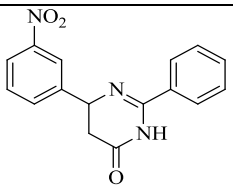
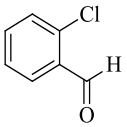
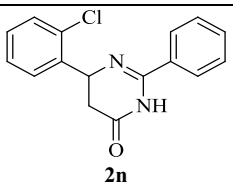
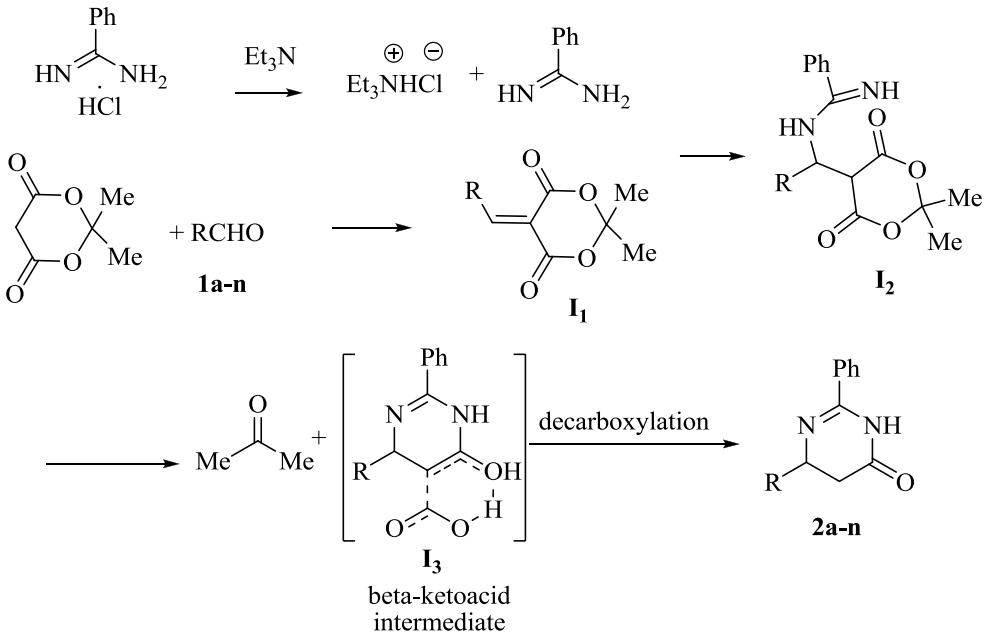
Entry	Aldehyde	product	Yield (%)
1	 **1a**	 **2a**	73
2	 **1b**	 **2b**	80
3	 **1c**	 **2c**	40
4	 **1d**	 **2d**	70
5	 **1e**	 **2e**	52
6	 **1f**	 **2f**	88
7	 **1g**	 **2g**	53

Table 1 continued

8	 **1h**	 **2h**	71
9	 **1i**	 **2i**	73
10	 **1j**	 **2j**	63
11	 **1k**	 **2k**	47
12	 **1l**	 **2l**	55
13	 **1m**	 **2m**	57
14	 **1n**	 **2n**	54

128.3, 128.9, 129.9, 131.6, 132.8, 133.8, 138.1, 148.2, 152.2, 170.9; EI-MS: *m/z* (%): 296 (4, M^++1), 278 (12), 247 (43), 220 (24), 147 (100), 104 (94), 77 (51); Anal. Calcd for $C_{16}H_{13}N_3O_3$ (295.10): C 65.08, H 4.44, N 14.23 %. Found: C 64.75, H 4.20, N 14.24 %.



Scheme 2 Mechanistic rationalization for the formation of compound **2a–n**

*6-(3-Nitrophenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2m**)* Pale yellow solid, mp: 196–198 °C, yield: 0.170 g (57 %). IR (KBr) (ν_{max}, cm^{-1}): 3,215 (NH), 1,691 (C = O), 1,641 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.59 (dd, J = 16.2, 13.8 Hz, 1H, CHCO), 2.93 (dd, J = 16.5, 5.1 Hz, 1H, CHCO), 5.06 (dd, J = 13.8, 5.1 Hz, 1H, CHN), 7.48–7.61 (m, 4H, Ar), 7.83 (d, J = 7.5 Hz, 1H, Ar), 7.91 (d, J = 7.2 Hz, 2H, Ar), 8.19 (d, J = 8.1 Hz, 1H, Ar), 8.41 (s, 1H, Ar), 8.98 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.3, 57.7, 121.9, 122.5, 126.6, 129.0, 129.7, 131.8, 132.7, 132.8, 144.5, 148.6, 152.2, 170.2 (CO); EI-MS: *m/z* (%): 296 (76, M^++1), 278 (4), 248 (4), 220 (2), 173 (10), 104 (100), 77 (38); Anal. Calcd for $C_{16}H_{13}N_3O_3$ (295.10): C 65.08, H 4.44, N 14.23 %. Found: C 64.92, H 4.28, N 14.23 %.

*6-(2-Chlorophenyl)-2-phenyl-5,6-dihydropyrimidin-4(3H)-one (**2n**)* White solid, mp: 176–178 °C, yield: 0.154 (54 %). IR (KBr) (ν_{max}, cm^{-1}): 3,268 (NH), 1,695 (C = O), 1,638 (C = N); ^{1}H-NMR (300 MHZ, $CDCl_3$): δ_H = 2.56 (dd, J = 16.5, 13.1 Hz, 1H, CHCO), 2.85 (dd, J = 16.5, 5.2 Hz, 1H, CHCO), 4.92 (dd, J = 13.1, 5.2 Hz, 1H, CHN), 7.27–7.34 (m, 3H, Ar), 7.45–7.57 (m, 4H, Ar), 7.90 (d, J = 6.7 Hz, 2H, Ar), 9.27 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 37.4, 57.8, 124.8, 126.7, 126.9, 127.6, 128.9, 130.0, 131.6, 132.9, 134.6, 144.3, 151.9, 171.0 (CO); EI-MS: *m/z* (%): 286 (5, M^+ [^{37}Cl]), 284 (100, M^+, [^{35}Cl]), 255 (20), 249 (12), 227 (9), 138 (19), 104 (96), 77 (43); Anal. Calcd for $C_{16}H_{13}ClN_2O$ (284.07): C 67.49, H 4.60, N 9.84 %. Found: C 67.37, H 4.30, N 9.85 %.

Results and discussion

Reaction of Meldrum's acid with benzamidine hydrochloride and benzaldehyde **1a-n** in EtOH in the presence of Et_3N at reflux over 1 h afforded **2a-n** (Scheme 1; Table 1). The structures of products were deduced by elemental analysis, MS, IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. For example, the mass spectra of **2f** displayed the molecular ion peak at 284 for M^+ ([^{35}Cl]) and 286 for M^+ ([^{37}Cl]) consistent with the molecular structure. The IR spectrum of **2a** displayed characteristic absorption bands at 3,220 and 1,696 cm^{-1} due to N–H and C = O stretching vibrations, respectively. The ^{1}H NMR spectrum of **2a** showed three doublet of doublets at δ 2.56 (J = 16.5, 12.8 Hz, 1H), 2.86 (J = 16.5, 5.2 Hz, 1H), 4.95 (J = 12.8, 5.2 Hz, 1H) and one singlet at δ 8.47 (1H) due to the CHC = O, CHC = O, CHN and NH protons, respectively. Moreover, the ^{13}C NMR spectrum of **2a** displayed 12 distinct signals including one appearing at δ 170.2 for C = O carbon, consistent with molecular structure.

As illustrated in Table 1, aliphatic or a range of electron-donating or electron-withdrawing substituted aromatic aldehydes are tolerated in these one-pot three-component reactions.

Although the precise mechanism is not known, a mechanistic postulate as shown in Scheme 2 may be invoked to rationalize the formation of **2a-n**. It is conceivable that the in situ generated Knoevenagel adducts $\mathbf{I_1}$ undergoes Michael addition by the liberated free benzamidine, affording the intermediate $\mathbf{I_2}$. The β-ketoacid $\mathbf{I_3}$ intermediate is subsequently generated via attack of the second

benzamidine NH group to C = O of the $\mathbf{I_2}$ with concomitant losing acetone. Upon thermal decarboxylation, it finally affords the products **2a-n**.

Conclusion

In conclusion, we have described a convenient route to novel 5,6-dihydropyrimidin-4(3*H*)-one derivatives from Meldrum's acid, aldehydes and benzamidine in EtOH. The 5,6-dihydropyrimidin-4(3*H*)-ones reported in this work broaden the scaffolds that are accessible through MCRs and seem to be of potential interest for drug discovery. The advantages of the present procedure are short reaction time, mild reaction condition, use of simple experimental procedure and prompt isolation of the products with generation of interesting heterocycles in one-pot transformation.

Acknowledgments The authors acknowledge the University of Tehran for financial support of this research.

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