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Aqua-mediated multicomponent synthesis of various 4*H*-pyran derivatives catalyzed by poly (4-vinylpyridine)-supported copper iodide nanoparticle catalyst

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Abstract A green and efficient approach for synthesis of some new 4*H*-pyran derivatives is reported, catalyzed by green recyclable poly(4-vinylpyridine)-supported copper iodide nanoparticle catalyst in water. This procedure has many advantages such as operational simplicity, short reaction time, clean procedure, and high product yield.

Keywords 4*H*-pyran derivatives · Malononitrile · Aldehyde · Poly (4-vinylpyridine)-supported copper iodide nanoparticles

Introduction

Pyran and chromene derivatives are an important class of oxygen-containing heterocycles, being the main components of many naturally occurring products and exhibiting a wide spectrum of biological activities [1, 2]. These compounds are widely employed as cosmetics, pigments, and potential biodegradable agrochemicals [3, 4]. Pyrans and chromenes can also serve as useful building blocks for production of a range of natural products showing molluscicidal, antibacterial, anticancer, anticoagulant, antiallergic, antibiotic, hypolipidemic, and immunomodulating activities [5, 6]. Because of these properties, pyran and chromene derivatives have received significant attention from many pharmaceutical scientists and chemists. Consequently, several catalysts have been reported for promoting synthesis of pyran and chromene derivatives [7–25].

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The multicomponent reaction approach has attracted attention from synthetic organic chemists for building up highly functionalized organic molecules and pharmacologically important heterocyclic compounds. These reactions present wide potential for efficient construction of highly complex molecules in a single procedural step, avoiding difficult purification operations and allowing savings of both solvents and reagents. Due to their atom economy, simplicity, high product yield, and time-saving nature, multicomponent reactions (MCRs) provide a simple and useful route for synthesis of various heterocyclic compounds [26, 27].

CuI, as a Lewis acid catalyst, promotes organic synthesis reactions effectively. However, it is a toxic compound and suffers from thermodynamic instability, nonrecyclability, and difficulty in separation of the products from the reaction mixture. Such drawbacks could be obviated by using polymer-supported CuI. The best supports are those which have nitrogen or oxygen binding sites and are chelated with copper catalysts. Nitrogen-based polymers have been shown to protect the metal center from oxidation and disproportionation, while enhancing the catalytic activity [28]. In previous research, we reported preparation and application of poly(4-vinylpyridine)-supported copper iodide nanoparticles (P_4VPy-CuI) in some organic reactions [29–33]. P_4VPy-CuI possesses increased advantages over CuI, being a safe, stable, easy to handle, and recyclable catalyst. It can be recovered simply by filtration and can be reused in subsequent runs without significant loss in catalytic activity. In continuation of our studies on synthesis of benzopyrans and chromene derivatives [34–37], we report herein synthesis of various 4*H*-pyran derivatives catalyzed by P_4VPy-CuI as an efficient recyclable catalyst in water.

Experimental

All known products were characterized by comparison of their spectroscopic [nuclear magnetic resonance (NMR) and infrared (IR)] data and physical properties with those reported in literature. The new compounds were identified by elemental analysis, physical properties, and IR and NMR spectra. IR spectra were recorded on a PerkinElmer 781 spectrophotometer. NMR spectra were recorded on a Bruker Advance 400 MHz. Yields refer to isolated pure products. P_4VPy-CuI was prepared according to the our previous articles [29, 30].

Determination of copper content in P_4VPy-CuI

P_4VPy-CuI (100 mg) was extracted with concentrated HCl (5 × 2 mL) in a screw-capped vessel, followed by treatment with concentrated nitric acid (2 mL) to digest the metal complex. The mixture was then transferred into a volumetric flask (100 mL), diluted 1:50 for a second time, and analyzed by inductively coupled plasma (ICP) analysis. The copper concentration was determined from atomic emission (324.754 nm) with reference to a linear ($R = 0.99$) calibration curve of (1–4 ppm) CuI prepared in a manner identical to the sample preparation. The loading of the supported catalyst was calculated to be 1.32 mmol CuI g^{-1} of prepared catalyst.

General procedure

A mixture of aldehyde (1 mmol), malononitrile (1 mmol), resorcinol or 3-methyl-1-phenyl-2-pyrazolin-5-one (1 mmol) or 1,3-dicarbonyl compounds (1 mmol), and P_4VPy-CuI (0.07 g) in water (10 mL) was stirred at reflux conditions. After reaction completion as monitored by thin-layer chromatography (TLC), the reaction mixture was cooled to room temperature and filtered, and hot ethanol was added. Then, the catalyst was recovered for subsequent use by filtration. Evaporation of the solvent from the filtrate and recrystallization of the solid residue from hot ethanol afforded pure products in high yields. The spectral and analytical data for the new compounds are as follows:

Table 2, entry 13: White solid, m.p.: 196–198 °C; IR (KBr) ν_{max}/cm^{-1}: 3450, 3300, 3200, 2200, 1640, 1590, 1540, 1395, 1340, 1120, 1060, 1040, 1020, 750. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 1.82 (s, 3H, CH_3), 4.91 (s, 1H, CH), 7.31 (t, 1H, $J = 7.41$ Hz, Ar), 7.37 (s, 2H, NH_2), 7.48 (t, 2H, $J = 8.16$ Hz, Ar), 7.65 (d, 1H, $J = 8.32$ Hz, Ar), 7.78 (t, 3H, $J = 8.26$ Hz, Ar), 8.04 (s, 1H, Ar). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 12.5, 35.7, 56.7, 97.2, 119.7, 120.1, 123.3, 124.5, 126.2, 129.2, 131.7, 133.2, 137.4, 144.0, 144.9, 145.0, 147.8, 159.7, 159.7. Elem. Anal. Found: C, 58.99 %; H, 3.51 % N, 17.23 % (calculated for $C_{20}H_{14}N_5O_2Cl$: C, 58.90 %; H, 3.46 %; N, 17.17 %).

Table 2, entry 14: White solid, m.p.: 257–259 °C; IR (KBr) ν_{max}/cm^{-1}: 3500, 3400, 3200, 3100, 2200, 1650, 1600, 1540, 1510, 1410, 1320, 1240, 1080, 1040, 960, 840, 810. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 2.00 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.90 (s, 1H, CH), 7.16 (d, 2H, $J = 8.38$ Hz, Ar), 7.23 (t, 1H, $J = 7.29$ Hz, Ar), 7.41–7.46 (m, 6H, Ar, NH_2), 7.70 (d, 2H, $J = 8.08$ Hz, Ar), 9.85 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 11.6, 23.8, 32.6, 54.8, 95.6, 118.9, 119.0, 120.5, 125.5, 127.3, 128.8, 136.7, 137.1, 137.2, 146.2, 155.2, 167.9, 168.0. Elem. Anal. Found: C, 68.61 %; H, 5.02 % N, 18.23 % (calculated for $C_{21}H_{16}N_4$: C, 68.55 %; H, 4.96 %; N, 18.17 %).

Table 2, entry 15: Yellow solid, m.p.: 202–204 °C; IR (KBr) ν_{max}/cm^{-1}: 3466, 3340, 2191, 1641, 1587, 1505, 1459, 1406, 1344, 1309, 1247, 1155, 1111, 1056, 1012, 964. ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 2.10 (s, 3H, CH_3), 4.74 (s, 1H, CH), 4.98 (s, 2H, NH_2), 5.16 (s, 2H, CH_2), 6.83 (d, 2H, $J = 8.68$ Hz, Ar), 7.09–7.12 (m, 4H, Ar), 7.25–7.39 (m, 4H, Ar), 7.60 (d, 4H, $J = 7.91$ Hz, Ar). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 11.6, 32.3, 57.8, 69.1, 97.3, 114.3, 119.8, 120.4, 125.5, 127.5, 127.7, 128.1, 128.4, 128.9, 137.2, 146.2, 156.6, 157.1, 158.3, 158.4, 164.1. Elem. Anal. Found: C, 74.71 %; H, 5.17 % N, 13.07 % (calculated for $C_{27}H_{22}N_4O_2$: C, 74.63 %; H, 5.10 %; N, 12.98 %).

Table 4, entry 11: White solid, m.p.: 200–202 °C; IR (KBr) ν_{max}/cm^{-1}: 3425, 3312, 3186, 2961, 2183, 1655, 1381, 1251, 1215, 1161, 1043. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 1.03 (s, 6H, $2CH_3$), 1.66–1.71 (m, 1H), 1.83–1.88 (m, 1H), 2.12 (d, 1H, $J = 16$ Hz), 2.24 (d, 1H, $J = 16$ Hz), 2.33 (d, 1H, $J = 17.6$ Hz), 2.40 (d, 1H, $J = 18.4$ Hz), 2.43–2.49 (m, 1H), 3.29 (t, 1H, $J = 4.4$ Hz), 7.01 (s, 2H), 7.11–7.18 (t, 1H, $J = 7.6$, d, 2H, $J = 7.6$, Ar), 7.27 (t, 2H, $J = 7.6$, Ar). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 27.4, 28.7, 29.7, 31.1, 32.0, 36.5, 50.5, 55.5, 112.7, 120.6, 126.1, 128.5, 128.8, 142.1, 160.4, 160.5, 163.7, 196.7. Elem. Anal. Found: C,

74.57 %; H, 6.92 % N, 8.73 % (calculated for $C_{20}H_{22}N_2O_2$: C, 74.50 %; H, 6.88 %; N, 8.69 %).

Table 4, entry 12: Yellow solid, m.p.: 244–246 °C; IR (KBr) ν_{max}/cm^{-1}: 3453, 3334, 2961, 2193, 1681, 1657, 1353, 1247, 1211, 1145, 1038, 725. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 1.05 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.89 (d, 1H, $J = 16$ Hz), 2.13 (d, 1H, $J = 16$ Hz), 2.63 (t, 2H, $J = 18$ Hz), 6.01 (s, 1H, CH), 7.07 (s, 2H, NH_2), 7.43–7.49 (m, 2H, Ar), 7.52–7.60 (m, 2H Ar), 8.09 (d, 3H, $J = 8.1$ Hz, Ar), 8.54 (s, 1H), 8.66 (d, 1H, $J = 8.8$ Hz, Ar). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 27.2, 28.9, 29.8, 32.0, 50.4, 58.6, 114.3, 119.7, 123.6, 124.9, 125.1, 125.4, 125.5, 126.4, 127.8, 129.2, 129.3, 130.2, 131.2, 131.4, 132.0, 135.0, 158.4, 158.5, 162.4, 196.1. Elem. Anal. Found: C, 79.27 %; H, 5.71 % N, 7.19 % (calculated for $C_{26}H_{22}N_2O_2$: C, 79.16 %; H, 5.62 %; N, 7.10 %).

Table 4, entry 13: White solid, m.p.: 218–220 °C; IR (KBr) ν_{max}/cm^{-1}: 3456, 3387, 3317, 3254, 3208, 2958, 2898, 2191, 1686, 1658, 1601, 1507, 1461, 1367, 1241, 1140, 1030, 842, 747. ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 1.03 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 2.19 (d, 1H, $J = 16$ Hz), 2.23 (d, 1H, $J = 16$ Hz), 2.43 (s, 2H), 4.36 (s, 1H), 4.50 (s, 2H, NH_2), 5.01 (s, 2H), 6.88 (d, 2H, $J = 8.6$ Hz, Ar), 7.14–7.16 (d, 2H, $J = 8.6$ Hz, Ar), 7.31–7.42 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 26.8, 28.3, 31.7, 34.7, 50.0, 58.5, 69.2, 112.9, 114.4, 119.7, 127.6, 127.8, 128.2, 128.4, 137.1, 137.1, 157.1, 158.3, 158.4, 162.1, 195.6. Elem. Anal. Found: C, 75.07 %; H, 6.09 % N, 7.08 % (calculated for $C_{25}H_{24}N_2O_3$: C, 74.97 %; H, 6.04 %; N, 6.99 %).

Table 4, entry 14: White solid, m.p.: 199–201 °C; IR (KBr) ν_{max}/cm^{-1}: 3456, 3330, 3206, 2941, 2195, 1681, 1601, 1509, 1457, 1418, 1368, 1245, 1198, 1171, 1136, 1067, 1005, 835. ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 1.96–2.03 (m, 2H), 2.31–2.37 (m, 2H), 2.53–258 (m, 2H), 4.38 (s, 1H), 4.56 (s, 2H, NH_2), 5.00 (s, 2H), 6.88 (d, 2H, $J = 8.6$ Hz, Ar), 7.15 (d, 2H, $J = 8.6$ Hz, Ar), 7.31–7.41 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 19.8, 26.4, 34.6, 36.3, 58.4, 69.2, 114.5, 119.8, 127.6, 127.8, 128.2, 128.4, 137.1, 137.1, 157.1, 158.3, 158.4, 164.1, 195.8. Elem. Anal. Found: C, 74.26 %; H, 5.48 % N, 7.59 % (calculated for $C_{23}H_{20}N_2O_3$: C, 74.17 %; H, 5.41 %; N, 7.52 %).

Table 4, entry 17: White solid, m.p.: 128–130 °C; IR (KBr) ν_{max}/cm^{-1}: 3376, 3326, 3194, 2959, 2189, 1680, 1657, 1603, 1383, 1209, 1176, 1137, 1005, 743. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 1.63–1.70 (m, 1H), 1.75–192 (m, 3H), 2.25–2.29 (m, 2H), 2.38–2.49 (m, 3H), 3.28 (t, 1H, CH, $J = 4.4$ Hz), 6.99 (s, 2H, NH_2), 7.11–7.18 (m, 3H, 3H, Ar), 7.26 (t, 2H $J = 7.6$ Hz, Ar). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 20.2, 26.9, 29.7, 30.9, 36.3, 36.8, 55.4, 113.8, 120.6, 126.1, 128.5, 128.7, 142.2, 160.3, 160.4, 165.4, 196.9. Elem. Anal. Found: C, 73.53 %; H, 6.22 % N, 9.59 % (calculated for $C_{18}H_{18}N_2O_2$: C, 73.44 %; H, 6.16 %; N, 9.51 %).

Table 4, entry 18: Yellow solid, m.p.: 248–250 °C; IR (KBr) ν_{max}/cm^{-1}: 3451, 3337, 2949, 2192, 1678, 1656, 1352, 1244, 1203, 1139, 997, 724. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 1.78–181 (m, 1H), 1.93–2.08 (m, 2H), 2.15–2.22 (m, 1H), 2.69–2.76 (m, 2H), 6.00 (s, 1H), 7.06 (s, 2H, NH_2), 7.46–7.48 (m, 2H, Ar), 7.52–7.60 (m, 2H, Ar), 8.08 (d, 3H, $J = 8.8$ Hz, Ar), 8.54 (s, 1H), 8.67 (d, 1H, $J = 8.8$ Hz, Ar). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 20.4, 27.1, 29.9, 36.8, 58.5, 115.2, 119.7, 123.4, 124.9, 125.1, 125.4, 125.5, 126.4, 127.8, 129.2, 129.3,

130.3, 131.2, 131.4, 132.0, 134.9, 158.3, 158.3, 164.2, 196.1. Elem. Anal. Found: C, 78.75 %; H, 5.02 % N, 7.71 % (calculated for $C_{24}H_{18}N_2O_2$: C, 78.67 %; H, 4.95 %; N, 7.64 %).

Table 6, entry 14: White solid, m.p.: 151–152 °C; IR (KBr) ν_{max}/cm^{-1}: 3444, 3337, 3217, 2193, 1645, 1587, 1408, 1156, 1114. ^{1}H NMR (DMSO-d_6, 400 MHz), δ (ppm): 4.69 (s, 1H), 6.43 (d, 1H, $J = 2.4$), 6.51–6.53 (dd, 1H, $J = 2.4$), 6.83 (d, 1H, $J = 8.4$), 6.98 (s, 2H, NH_2), 7.19 (d, 1H, $J = 7.6$), 7.29 (t, 1H, $J = 7.6$), 7.35–7.36 (m, 1H), 7.41–7.44 (m, 1H), 9.78 (s, 1H). ^{13}C NMR (DMSO-d_6, 100 MHz), δ (ppm): 38.3, 56.1, 102.7, 113.0, 113.4, 120.9, 122.3, 127.0, 130.0, 130.4, 130.4, 131.3, 149.3, 149.5, 157.7, 160.8. Elem. Anal. Found: C, 54.48 %; H, 3.41 % N, 8.53 % (calculated for $C_{15}H_{11}N_2O_2Br$: C, 54.40 %; H, 3.34 %; N, 8.45 %).

Results and discussion

P_4VPy-CuI was prepared by a coprecipitation method and characterized by Brunauer–Emmett–Teller (BET) surface area, Fourier-transform infrared (FT-IR) spectroscopy (Fig. 1), energy-dispersive x-ray spectroscopy (EDS), X-ray diffraction (XRD) analysis (Fig. 2), scanning electron microscopy (SEM) analysis (Fig. 3), and ICP analysis [29, 30]. SEM imaging of the prepared catalyst indicated that CuI nanoparticles were homogeneously immobilized on poly(4-vinylpyridine) surface. According to SEM images of P_4VPy-CuI, the average size of copper nanoparticles was estimated to be 75–100 nm. Sharp peaks were observed in the XRD pattern of

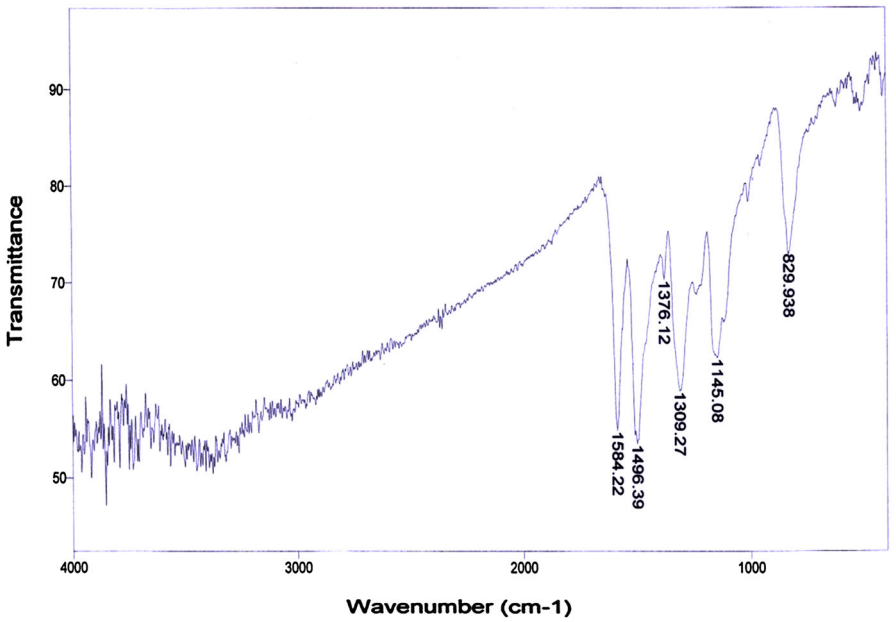


Fig. 1 FT-IR spectrum of poly(4-vinylpyridine)-supported copper iodide nanoparticles

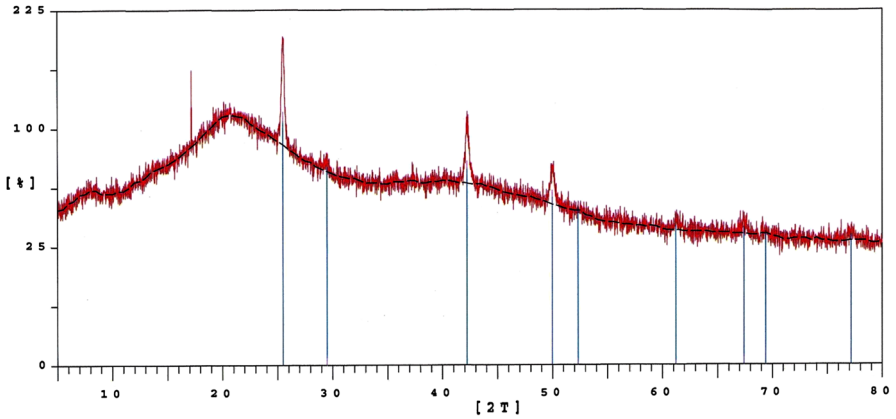


Fig. 2 XRD pattern of poly(4-vinylpyridine)-supported copper iodide nanoparticles

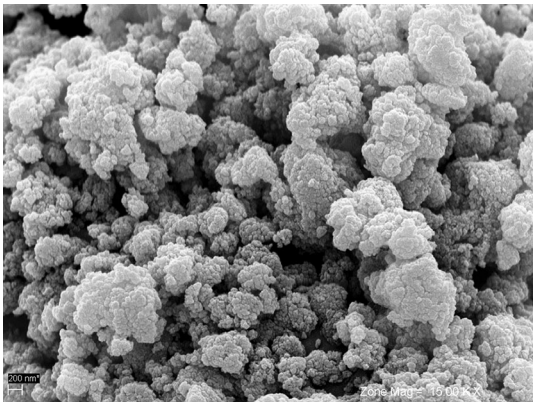
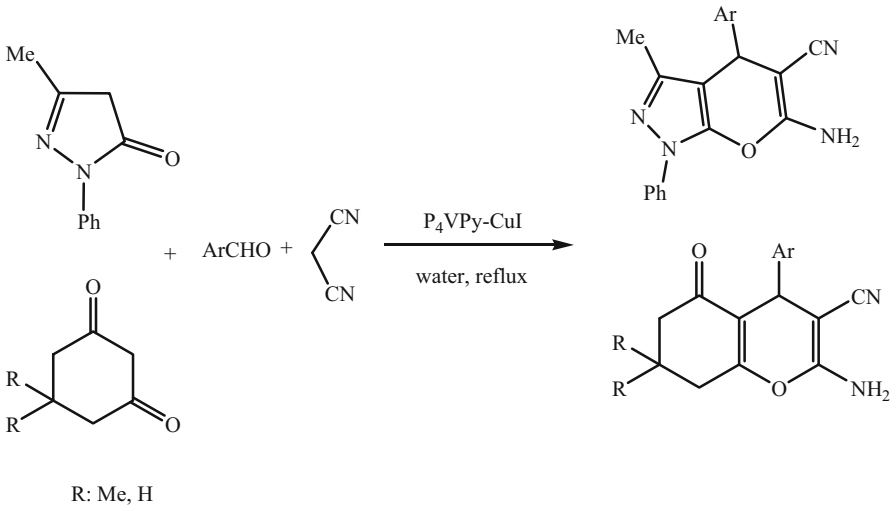


Fig. 3 SEM image of poly(4-vinylpyridine)-supported copper iodide nanoparticles

P_4VPy-CuI, and their positions were consistent with metallic copper and copper iodide nanocrystals. The size of copper nanoparticles was also determined from X-ray line broadening using the Debye–Scherrer formula (obtained size: 75 nm).

This catalyst is safe, easy to handle, and can be used as an efficient Lewis acid in synthesis of 4*H*-pyran derivatives. First, we examined the catalytic application of P_4VPy-CuI in synthesis of 4*H*-pyran derivatives via three-component reaction of aldehydes, malononitrile, and 3-methyl-1-phenyl-2-pyrazolin-5-one or 1,3-dicarbonyl compounds (Scheme 1). For optimization of reaction conditions, the reaction of benzaldehyde, malononitrile, and 3-methyl-1-phenyl-2-pyrazolin-5-one was investigated in a variety of conditions.

The effect of various factors such as catalyst loading, solvents, and temperature was investigated. The reaction was evaluated in the presence of different amounts of P_4VPy-CuI. It was observed that use of 0.07 g P_4VPy-CuI was sufficient for reaction completion after 22 min. Increase in the amount of catalyst (0.1 g) did not



Scheme 1 Synthesis of 4*H*-pyran derivatives catalyzed by P_4VPy–CuI

significantly affect reaction yield or time (Table 1). To study the solvent effect, the model reaction was carried out in various solvents. As shown in Table 1, the best results were obtained in water as solvent under reflux conditions. Finally, the best

Table 1 Optimization of reaction conditions in synthesis of 4*H*-pyran derivatives from aldehyde, 3-methyl-1-phenyl-2-pyrazolin-5-one, and malononitrile

Entry	Conditions[a]	Catalyst amount (g)	Time (min)	Yield (%)[b]
1	H_2O/reflux	–	180	–
2	EtOH/reflux	–	180	–
3	H_2O/r.t.	0.03	180	–
4	H_2O/r.t.	0.05	180	–
5	H_2O/reflux	0.03	45	75
6	H_2O/reflux	0.05	22	93
7	H_2O/reflux	0.07	20	93
8	EtOH/reflux	0.03	60	Trace
9	EtOH/reflux	0.05	60	60
10	CH_3OH/reflux	0.05	60	Trace
11	CH_3CN/reflux	0.05	60	Trace
12	Solvent free/80 °C	0.03	60	Trace
13	Solvent free/80 °C	0.05	60	65
14	Solvent free/100 °C	0.05	60	50

[a] Reaction conditions: aldehyde (1 mmol), 3-methyl-1-phenyl-2-pyrazolin-5-one (1 mmol), malononitrile (1 mmol)

[b] Yields refer to isolated pure products

results were obtained in presence of P_4VPy-CuI (0.07 g) in water under reflux conditions with relative ratio of benzaldehyde:malononitrile:3-methyl-1-phenyl-2-pyrazolin-5-one of 1:1:1.

Using these optimized conditions, the reactions of various aromatic aldehydes including electron-withdrawing groups such as nitro, nitrile, and aldehyde moieties and electron-donating groups such as methyl and methoxy moieties with malononitrile and 3-methyl-1-phenyl-2-pyrazolin-5-one were investigated (Table 2). It was observed that the desired products were obtained in short reaction times and high yields.

Moreover, synthesis of 4*H*-pyran derivatives via three-component reaction of aldehydes, malononitrile, and 1,3-dicarbonyl compounds (dimedone or 1,3-cyclohexandione) was investigated. To optimize the reaction conditions, the reaction of benzaldehyde, malononitrile, and dimedone was studied under a variety of conditions. The best result was achieved by running the reaction of each substrate (with 1 mmol) in the presence of 0.05 g P_4VPy-CuI (Table 3, entry 6).

After that, the reaction of various aromatic aldehydes was studied (Table 4). The evaluation showed that electron-withdrawing groups such as nitro on aromatic ring decreased the reaction time, whereas electron-releasing groups such as methoxy and methyl increased it. Furthermore, in the presence of P_4VPy-CuI, aliphatic aldehydes

Table 2 Synthesis of 4*H*-pyran derivatives from aldehyde, 3-methyl-1-phenyl-2-pyrazolin-5-one, and malononitrile catalyzed by CuO P_4VPy-CuI

Entry	Aldehyde	Time (min)	Yield (%)[a]	M.p. (°C)[b]
1	C_6H_5CHO	22	93	169–170
2	4-$O_2NC_6H_4CHO$	12	93	192–194
3	3-$O_2NC_6H_4CHO$	15	92	190–191
4	2,4-$Cl_2C_6H_4CHO$	12	91	183–185
5	4-ClC_6H_4CHO	16	91	175–177
6	2-ClC_6H_4CHO	16	93	145–146
7	3-ClC_6H_4CHO	14	92	157–159
8	4-$MeOC_6H_4CHO$	35	90	173–175
9	4-MeC_6H_4CHO	25	90	177–179
10	4-FC_6H_4CHO	20	92	168–169
11	4-HOC_6H_4CHO	40	90	209–211
12	4-CNC_6H_4CHO	15	89	217–219
13	4-Cl-3-$O_2NC_6H_3CHO$	12	92	196–198[c]
14	4-$MeCONHC_6H_4CHO$	20	89	257–259[c]
15	4-$C_6H_5CH_2OC_6H_4CHO$	35	90	202–204[c]

[a] Yields refer to isolated pure products

[b] Products characterized by comparison of their spectroscopic (NMR and IR) data and melting points with those reported in literature [8, 24, 25]

[c] New compounds

Table 3 Optimization of reaction conditions in synthesis of 4*H*-pyran derivatives from aldehyde, 1,3-dicarbonyl compounds, and malononitrile

Entry	Conditions[a]	Catalyst amount (g)	Time (min)	Yield (%)[b]
1	H_2O/reflux	–	180	–
2	EtOH/reflux	–	180	–
3	H_2O/r.t.	0.03	180	–
4	H_2O/r.t.	0.05	180	–
5	H_2O/reflux	0.03	30	60
6	H_2O/reflux	0.05	15	92
7	H_2O/reflux	0.07	15	92
8	EtOH/reflux	0.03	60	Trace
9	EtOH/reflux	0.05	60	50
10	CH_3OH/reflux	0.05	60	Trace
11	CH_3CN/reflux	0.05	60	Trace
12	Solvent free/80 °C	0.03	30	50
13	Solvent free/80 °C	0.05	30	70
14	Solvent free/100 °C	0.05	30	75

[a] Reaction conditions: aldehyde (1 mmol), dimedone (1 mmol), malononitrile (1 mmol)

[b] Yields refer to isolated pure products

such as 3-propianaldehyde were also converted to benzopyran derivatives in high yields (Table 4).

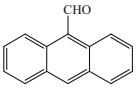
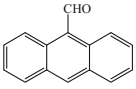
Similarly, 2-amino-4*H*-chromenes were obtained by condensation of aromatic aldehydes, malononitrile, and resorcinol under reflux conditions in water (Scheme 2).

To optimize these reaction conditions, the reaction of benzaldehyde, malononitrile, and resorcinol was investigated. It was observed that the best result was obtained by reaction of substrates (with 1:1:1 mol ratio) in the presence of 0.07 g P_4VPy-CuI under reflux conditions in water (Table 5).

Various aromatic aldehydes were investigated using the optimized conditions. From Table 6, it is clear that different aromatic aldehydes with either electron-donating or electron-withdrawing groups efficiently reacted to afford the desired products in good to high yields. We also observed that aliphatic aldehydes remained intact under the reaction conditions. Therefore, this method could be useful for chemoselective synthesis of 2-amino-4*H*-chromenes from aromatic aldehydes in the presence of aliphatic ones.

The activity of the recovered catalyst was also examined in three reactions under optimized conditions. In the synthesis of 4*H*-pyrans from 3-methyl-1-phenyl-2-pyrazolin-5-one or 1,3-dicarbonyl compounds, it was found that the catalyst could be recycled up to five times with desired products obtained in high yields after each run (Table 7). To explore this property, reaction of benzaldehyde, malononitrile, and 3-methyl-1-phenyl-2-pyrazolin-5-one or dimedone was again studied under

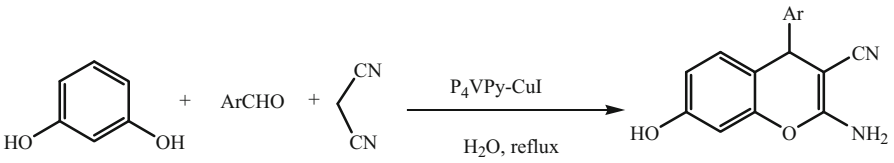
Table 4 Synthesis of 4*H*-pyran derivatives from aldehyde, 1,3-dicarbonyl compounds, and malononitrile catalyzed by P_4VPy-CuI

Entry	Aldehyde	R	Time (min)	Yield (%)[a]	M.p. (°C)[b]
1	C_6H_5CHO	Me	15	92	230–232
2	3-$O_2NC_6H_4CHO$	Me	12	94	209–210
3	4-$O_2NC_6H_4CHO$	Me	10	92	180–182
4	4-ClC_6H_4CHO	Me	12	92	207–208
5	3-ClC_6H_4CHO	Me	12	93	228–230
6	4-$MeOC_6H_4CHO$	Me	30	91	205–207
7	4-MeC_6H_3CHO	Me	20	91	212–214
8	4-HOC_6H_4CHO	Me	45	90	213–215
9	CH_3CH_2	Me	60	88	192–194
10	$C_6H_4CH{=}CHCHO$	Me	45	88	207–209
11	$C_6H_4CH_2CH_2CHO$	Me	35	90	200–202[c]
12		Me	22	90	244–246[c]
13	4-$C_6H_5CH_2OC_6H_4CHO$	Me	35	89	218–220[c]
14	4-$C_6H_5CH_2OC_6H_4CHO$	H	42	89	199–201[c]
15	4-ClC_6H_4CHO	H	15	91	227–229
16	4-$MeOC_6H_4CHO$	H	30	90	196–198
17	$C_6H_4CH_2CH_2CHO$	H	35	90	128–130[c]
18		H	25	90	248–250[c]

[a] Yields refer to isolated pure products

[b] Products characterized by comparison of their spectroscopic (NMR and IR) data and melting points with those reported in literature [12]

[c] New compounds



Scheme 2 Synthesis of 2-amino-4*H*-chromenes catalyzed by P_4VPy–CuI

optimized conditions (Table 7). After reaction completion, the catalyst was filtered, washed with hot ethanol, and after dryness reused in the next similar process.

Moreover, in the synthesis reaction of 2-amino-4*H*-chromenes, the recyclability of the catalyst in the reaction of benzaldehyde, malononitrile, and resorcinol was

Table 5 Optimization of reaction conditions in synthesis of 2-amino-4*H*-chromenes from aldehyde, resorcinol and malononitrile

Entry	Conditions[a]	Catalyst amount (g)	Time (min)	Yield (%)[b]
1	H_2O/reflux	–	180	–
2	EtOH/reflux	–	180	–
3	H_2O/r.t.	0.03	180	Trace
4	H_2O/r.t.	0.05	180	Trace
5	H_2O/reflux	0.03	30	70
6	H_2O/reflux	0.05	20	92
7	EtOH/reflux	0.03	60	Trace
8	EtOH/reflux	0.05	60	70
9	CH_3OH/reflux	0.05	60	50
10	CH_3CN/reflux	0.05	60	Trace
11	Solvent free/80 °C	0.03	60	50
12	Solvent free/80 °C	0.05	60	70
13	Solvent free/100 °C	0.05	60	80

[a] Reaction conditions: aldehyde (1 mmol), resorcinol (1 mmol), malononitrile (1 mmol)

[b] Yields refer to isolated pure products

Table 6 Synthesis of 2-amino-4*H*-chromenes from aldehyde, resorcinol, and malononitrile catalyzed by P_4VPy-CuI

Entry	Aldehyde	Time (min)	Yield (%)[a]	M.p. (°C)[b]
1	C_6H_5CHO	15	94	232–234
2	2-ClC_6H_4CHO	17	92	189–191
3	3-ClC_6H_4CHO	15	91	103–105
4	4-ClC_6H_4CHO	12	92	162–163
5	2,4-ClC_6H_3CHO	8	93	257–259
6	2-$NO_2C_6H_4CHO$	15	91	163–165
7	3-$NO_2C_6H_4CHO$	16	91	170–172
8	4-BrC_6H_4CHO	20	92	224–226
9	4-FC_6H_4CHO	20	92	188–190
10	4-MeC_6H_4CHO	18	91	184–186
11	4-$MeOC_6H_4CHO$	25	90	111–113
12	4-HOC_6H_4CHO	32	90	250–252
13	3,4,5-$(MeO)_3C_6H_2CHO$	45	92	208–209
14	3-BrC_6H_4CHO	20	92	151–152[c]

[a] Yields refer to isolated pure products

[b] Products characterized by comparison of their spectroscopic (NMR and IR) data and melting points with those reported in literature [13, 16, 36]

[c] New compound

Table 7 Recyclability study of P_4VPy-CuI in synthesis of 2-amino-4*H*-chromenes from resorcinol (A), 4*H*-pyran derivatives from 3-methyl-1-phenyl-2-pyrazolin-5-one (B) or dimedone (C) with benzaldehyde, and malononitrile

Product	Run											
	1		2		3		4		5		6	
	Time (min)	Yield (%)[a]	Time (min)	Yield (%)[a]	Time (min)	Yield (%)[a]	Time (min)	Yield (%)[a]	Time (min)	Yield (%)[a]	Time (min)	Yield (%)[a]
A	15	94	15	94	20	93	22	90	25	90	32	87
B	22	93	25	92	25	90	30	90	40	88	–	–
C	15	92	15	92	18	90	25	88	30	87	–	–

Reaction conditions: benzaldehyde (1 mmol), 3-methyl-1-phenyl-2-pyrazolin-5-one, dimedone or resorcinol (1 mmol), malononitrile (1 mmol), in water at reflux conditions

[a] Yields refer to isolated pure products

investigated. It was observed that the catalyst could be recycled up to six times with consistent activity (Table 7).

Conclusions

A mild, efficient, and green procedure for synthesis of various 4*H*-pyran derivatives in the presence of recyclable P_4VPy-CuI at reflux conditions in water is reported. Moreover, high product yield, short reaction time, easy workup, and clean procedure are the most important advantages of this method, making this procedure a useful addition to available methods. We are exploring further applications of P_4VPy-CuI for other types of organic reactions in our laboratory.

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