

# A novel multicomponent Zr-catalyzed synthesis of functionalized pyrano[3,2-*b*]pyrrole derivatives

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**Abstract** A novel, efficient, and rapid procedure, one-pot condensation of 3-hydroxypyrrole, malononitrile, and aromatic aldehydes, with 10 mol % bis[*N*-(3,5-dicumylsalicylidene)anthracylaminato]zirconium(IV) dichloride as catalyst, in the presence of ultrasonic irradiation, has been developed for synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole derivatives.

**Keywords** Pyrano[3,2-*b*]pyrrole · One-pot · Organometal

## Introduction

Multicomponent reactions (MCRs) are very useful for rapid and efficient generation of complex and diverse molecules. The exploratory power of MCRs is very high and, because they are highly flexible and efficient, they can be regarded as among the most versatile classes of tandem reaction [1]. In recent years, MCRs have been important in synthetic organic chemistry because of their valued features, for example convergence, productivity, facile execution, and generally high yield of

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products [2–4]. Recently, we have reported several MCRs for synthesis of indenoquinolinones [5], pyranoidoles [6], and phenanthroimidazoles [7].

It is well known that pyrans are important core units in several natural products and photochromic materials [8]. Much research has been devoted to the synthesis of a variety of pyran derivatives, for example benzopyrans, naphthopyrans, and 4-substituted pyrans, to obtain more biologically potent heterocyclic systems [9, 10]. Compounds with pyran ring systems have many pharmacological properties and are important in biochemical processes [11, 12]. Recently, several methods have been reported for the synthesis of pyran derivatives via three-component condensation reactions [12–14].

The 4*H*-pyran derivatives are of the immense interest in the synthesis of drugs for example their varied pharmacological and biological activity, for example antimicrobial [14], mutagenicity [15], anti-proliferative [16], sex pheromone [17], antitumor, and central nervous system activity [18]. Accordingly, the synthesis of such compounds is an interesting challenge.

Use of organometallic compounds enable extensive exploration for new methods and techniques in organic synthesis. Our interest in organometallic compounds [19] prompted us to investigate use of these as catalysts. To the best of our knowledge, one-pot Zr-catalyzed synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrrole derivatives under ultrasonic irradiation conditions has not yet been reported. In continuation of our recent MCR synthesis [20–24], we report herein the details of this study.

## Experimental

### General procedure for synthesis of pyranopyrrole derivatives

A mixture of aldehyde (1 mmol), 3-hydroxypyrrole (1 mmol), malononitrile (1.1 mmol), and catalyst (0.1 mmol) in CH<sub>3</sub>CN (4 mmol) was stirred at 50 °C under ultrasonication in an ultrasonic cleaner with a frequency of 40 kHz and a nominal power 100 W for the appropriate time (TLC). On completion of the reaction, the mixture was extracted with AcOEt (2 × 10 ml) and washed with aq. NaHCO<sub>3</sub> solution (2 × 10 ml). The organic phase was then dried over MgSO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel. <sup>1</sup>H NMR, <sup>13</sup>C NMR, and DEPT <sup>13</sup>C NMR spectra were recorded on a Bruker 400-MHz spectrometer with chloroform as solvent and TMS as internal standard. IR spectra were recorded using KBr disks on a FT-IR Bruker Tensor spectrometer. The procedure for synthesis of the catalyst has been reported elsewhere [19].

### 5-Amino-1,7-dihydro-7-(4-hydroxyphenyl)pyrano[3,2-*b*]pyrrole-6-carbonitrile (5a)

Anal Calcd for C<sub>14</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub> (253.26): C, 66.40; H, 4.38; N, 16.59 %. Found C, 66.38; H, 4.37; N, 16.55 %. IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3,408 and 3,276 (asym. and sym. str. of –NH<sub>2</sub>), 3,402 (NH), 2,160 (–CN str.), 1,255 (asym. str. of cyclic ArC–O–C ether). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  (ppm): 5.48 (*s*, 1H, pyran H<sub>4</sub>), 6.15 (*d*, 1H, pyrrole H<sub>3</sub>), 6.59

(*d*, 2H, Ar–H), 6.65 (*d*, 1H, pyrrole H<sub>2</sub>), 6.88 (*s*, 2H, D<sub>2</sub>O exch. NH<sub>2</sub>), 6.95 (*d*, 2H, Ar–H), 7.44 (*s*, 1H, pyrrole NH). <sup>13</sup>C NMR (250 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> (ppm): 27.9 (pyran C<sub>4</sub>), 58.5 (pyran C<sub>3</sub>), 104.1 (pyran C<sub>6</sub>), 104.8 (pyrrole C<sub>3</sub>), 120.3 (pyrrole C<sub>1</sub>), 124.2 (CN), 125.1 (pyran C<sub>5</sub>), 119.1, 128.3, 130.9, 153.8 (Ar–C), 170.49 (pyran C<sub>2</sub>).

#### 5-Amino-1,7-dihydro-7-(4-methoxyphenyl)pyrano[3,2-*b*]pyrrole-6-carbonitrile (**5b**)

Anal Calcd for C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub> (267.28): C, 67.40; H, 4.90; N, 15.72 %. Found C, 66.22; H, 4.78; N, 15.59 %. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>): 3,411 and 3,279 (asym. and sym. str. of –NH<sub>2</sub>), 3,400 (NH), 2,160 (–CN str.), 1,251 (asym. str. of cyclic ArC–O–C ether). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> (ppm): 3.37 (*s*, 3H, OCH<sub>3</sub>), 5.43 (*s*, 1H, pyran H<sub>4</sub>), 6.11 (*d*, 1H, pyrrole H<sub>3</sub>), 6.63 (*d*, 2H, Ar–H), 6.68 (*d*, 1H, pyrrole H<sub>2</sub>), 6.89 (*s*, 2H, D<sub>2</sub>O exch. NH<sub>2</sub>), 7.05 (*d*, 2H, Ar–H), 7.54 (*s*, 1H, pyrrole NH). <sup>13</sup>C NMR (250 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> (ppm): 28.6 (pyran C<sub>4</sub>), 55.23 (O–CH<sub>3</sub>), 59.5 (pyran C<sub>3</sub>), 101.5 (pyran C<sub>6</sub>), 104.9 (pyrrole C<sub>3</sub>), 119.3 (pyrrole C<sub>1</sub>), 122.0 (CN), 126.1 (pyran C<sub>5</sub>), 119.2, 127.4, 130.3, 154.6 (Ar–C), 171.4 (pyran C<sub>2</sub>).

#### 5-Amino-1,7-dihydro-7-phenylpyrano[3,2-*b*]pyrrole-6-carbonitrile (**5c**)

Anal Calcd for C<sub>14</sub>H<sub>11</sub>N<sub>3</sub>O (237.26): C, 70.87; H, 4.67; N, 17.71 %. Found C, 68.59; H, 4.62; N, 16.97 %. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>): 3,405 and 3,283 (asym. and sym. str. of –NH<sub>2</sub>), 3,405 (NH), 2,157 (–CN str.), 1,247 (asym. str. of cyclic ArC–O–C ether). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> (ppm): 5.51 (*s*, 1H, pyran H<sub>4</sub>), 6.25 (*d*, 1H, pyrrole H<sub>3</sub>), 6.73 (*d*, 1H, pyrrole H<sub>2</sub>), 6.75 (*s*, 2H, D<sub>2</sub>O exch. NH<sub>2</sub>), 7.09–7.15 (*m*, 5H, Ar–H), 7.50 (*s*, 1H, pyrrole NH). <sup>13</sup>C NMR (250 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> (ppm): 30.6 (pyran C<sub>4</sub>), 55.8 (pyran C<sub>3</sub>), 101.6 (pyran C<sub>6</sub>), 106.4 (pyrrole C<sub>3</sub>), 117.9 (pyrrole C<sub>1</sub>), 123.5 (CN), 129.7 (pyran C<sub>5</sub>), 122.8, 129.1, 127.9, 130.8 (Ar–C), 173.7 (pyran C<sub>2</sub>).

#### 5-Amino-1,7-dihydro-7-*p*-tolylpyrano[3,2-*b*]pyrrole-6-carbonitrile (**5d**)

Anal Calcd for C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O (251.28): C, 71.70; H, 5.21; N, 16.72 %. Found C, 70.93; H, 5.08; N, 16.14 %. IR (KBr, ν<sub>max</sub>, cm<sup>-1</sup>): 3,422 and 3,272 (asym. and sym. str. of –NH<sub>2</sub>), 3,419 (NH), 2,189 (–CN str.), 1,252 (asym. str. of cyclic ArC–O–C ether). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ<sub>H</sub> (ppm): 2.31 (*s*, 3H, Ar–CH<sub>3</sub>), 5.60 (*s*, 1H, pyran H<sub>4</sub>), 6.18 (*d*, 1H, pyrrole H<sub>3</sub>), 6.80 (*s*, 2H, D<sub>2</sub>O exch. NH<sub>2</sub>), 6.89 (*d*, 1H, pyrrole H<sub>2</sub>), 6.98–7.07 (*m*, 4H, Ar–H), 7.38 (*s*, 1H, pyrrole NH). <sup>13</sup>C NMR (250 MHz, CDCl<sub>3</sub>) δ<sub>C</sub> (ppm): 24.7 (–CH<sub>3</sub>), 29.21 (pyran C<sub>4</sub>), 54.6 (pyran C<sub>3</sub>), 100.1 (pyran C<sub>6</sub>), 107.3 (pyrrole C<sub>3</sub>), 115.7 (pyrrole C<sub>1</sub>), 126.5 (CN), 131.4 (pyran C<sub>5</sub>), 128.3, 129.1, 133.6, 137.9 (Ar–C), 169.1 (pyran C<sub>2</sub>).

#### 5-Amino-7-(4-bromophenyl)-1,7-dihydropyrano[3,2-*b*]pyrrole-6-carbonitrile (**5e**)

Anal Calcd for C<sub>14</sub>H<sub>10</sub>BrN<sub>3</sub>O (316.15): C, 53.19; H, 3.19; N, 13.29 %. Found C, 52.79; H, 3.14; N, 12.64 %. IR (KBr, ν, cm<sup>-1</sup>): 3,425 and 3,269 (asym. and sym. str.

of  $-\text{NH}_2$ ), 3,434 (NH), 2,201 ( $-\text{CN}$  str.), 1,242 (asym. str. of cyclic  $\text{ArC}-\text{O}-\text{C}$  ether).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  (ppm): 5.40 (*s*, 1H, pyran  $\text{H}_4$ ), 6.11 (*d*, 1H, pyrrole  $\text{H}_3$ ), 6.49 (*s*, 2H,  $\text{D}_2\text{O}$  exch.  $\text{NH}_2$ ), 7.06 (*d*, 2H,  $\text{Ar}-\text{H}$ ), 6.70 (*d*, 1H, pyrrole  $\text{H}_2$ ), 7.25 (*d*, 2H,  $\text{Ar}-\text{H}$ ), 7.39 (*s*, 1H, pyrrole NH).  $^{13}\text{C}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  (ppm): 31.4 (pyran  $\text{C}_4$ ), 64.9 (pyran  $\text{C}_3$ ), 100.5 (pyran  $\text{C}_6$ ), 109.5 (pyrrole  $\text{C}_3$ ), 117.3 (pyrrole,  $\text{C}_1$ ), 127.2 (CN), 130.3 (pyran  $\text{C}_5$ ), 123.6, 129.4, 130.9, 138.4 ( $\text{Ar}-\text{C}$ ), 179.7 (pyran  $\text{C}_2$ ).

#### 5-amino-7-(4-fluorophenyl)-1,7-dihydropyrano[3,2-*b*]pyrrole-6-carbonitrile (**5f**)

Anal Calcd for  $\text{C}_{14}\text{H}_{10}\text{FN}_3\text{O}$  (255.25): C, 65.88; H, 3.95; N, 16.46 %. Found C, 65.81; H, 3.90; N, 16.43 %. IR (KBr,  $\nu$ ,  $\text{cm}^{-1}$ ): 3,422 and 3,267 (asym. and sym. str. of  $-\text{NH}_2$ ), 3,439 (NH), 2,211 ( $-\text{CN}$  str.), 1,240 (asym. str. of cyclic  $\text{ArC}-\text{O}-\text{C}$  ether).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  (ppm): 5.36 (*s*, 1H, pyran  $\text{H}_4$ ), 6.01 (*d*, 1H, pyrrole  $\text{H}_3$ ), 6.41 (*s*, 2H,  $\text{D}_2\text{O}$  exch.  $\text{NH}_2$ ), 7.01 (*d*, 2H,  $\text{Ar}-\text{H}$ ), 6.65 (*d*, 1H, pyrrole  $\text{H}_2$ ), 7.20 (*d*, 2H,  $\text{Ar}-\text{H}$ ), 7.33 (*s*, 1H, pyrrole NH).  $^{13}\text{C}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  (ppm): 31.0 (pyran  $\text{C}_4$ ), 62.7 (pyran  $\text{C}_3$ ), 100.9 (pyran  $\text{C}_6$ ), 108.9 (pyrrole  $\text{C}_3$ ), 116.7 (pyrrole,  $\text{C}_1$ ), 126.0 (CN), 130.0 (pyran  $\text{C}_5$ ), 122.6, 128.4, 133.7, 137.6 ( $\text{Ar}-\text{C}$ ), 177.5 (pyran  $\text{C}_2$ ).

#### 5-Amino-7-(2-bromophenyl)-1,7-dihydropyrano[3,2-*b*]pyrrole-6-carbonitrile (**5g**)

Anal Calcd for  $\text{C}_{14}\text{H}_{10}\text{BrN}_3\text{O}$  (316.15): C, 53.19; H, 3.19; N, 13.29 %. Found: C, 51.98; H, 3.16; N, 13.14 %. IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3415 and 3298 (asym. and sym. str. of  $-\text{NH}_2$ ), 3411 (NH), 2187 ( $-\text{CN}$  str.), 1257 (asym. str. of cyclic  $\text{ArC}-\text{O}-\text{C}$  ether).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  (ppm): 5.58 (*s*, 1H, pyran  $\text{H}_4$ ), 6.19 (*d*, 1H, pyrrole  $\text{H}_3$ ), 6.73 (*d*, 1H, pyrrole  $\text{H}_2$ ), 6.79 (*s*, 2H,  $\text{D}_2\text{O}$  exch.,  $\text{NH}_2$ ), 6.97-7.11 (*m*, 4H,  $\text{Ar}-\text{H}$ ), 7.58 (*s*, 1H, pyrrole NH).  $^{13}\text{C}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  (ppm): 28.3 (pyran  $\text{C}_4$ ), 57.5 (pyran  $\text{C}_3$ ), 108.6 (pyran  $\text{C}_6$ ), 108.9 (pyrrole  $\text{C}_3$ ), 121.6 (pyrrole,  $\text{C}_1$ ), 127.5 (CN), 131.5 (pyran  $\text{C}_5$ ), 122.8, 122.4, 128.9, 132.7, 133.0, 141.6 ( $\text{Ar}-\text{C}$ ), 179.0 (pyran  $\text{C}_2$ ).

#### 5-Amino-7-(4-chlorophenyl)-1,7-dihydropyrano[3,2-*b*]pyrrole-6-carbonitrile (**5h**)

Anal Calcd for  $\text{C}_{14}\text{H}_{10}\text{ClN}_3\text{O}$  (271.7): C, 61.89; H, 3.71; N, 15.47 %. Found C, 61.34; H, 3.69; N, 15.43 %. IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3,414 and 3,259 (asym. and sym. str. of  $-\text{NH}_2$ ), 3,415 (NH), 2,156 ( $-\text{CN}$  str.), 1,256 (asym. str. of cyclic  $\text{ArC}-\text{O}-\text{C}$  ether).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{H}}$  (ppm): 5.48 (*s*, 1H, pyran  $\text{H}_4$ ), 6.16 (*d*, 1H, pyrrole  $\text{H}_3$ ), 6.42 (*s*, 2H,  $\text{D}_2\text{O}$  exch.  $\text{NH}_2$ ), 6.64 (*d*, 1H, pyrrole  $\text{H}_2$ ), 7.06 (*d*, 2H,  $\text{Ar}-\text{H}$ ), 7.21 (*d*, 2H,  $\text{Ar}-\text{H}$ ), 7.29 (*s*, 1H, pyrrole NH).  $^{13}\text{C}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta_{\text{C}}$  (ppm): 30.7 (pyran  $\text{C}_4$ ), 60.23 (pyran  $\text{C}_3$ ), 106.5 (pyran  $\text{C}_6$ ), 108.4 (pyrrole  $\text{C}_3$ ), 119.0 (pyrrole,  $\text{C}_1$ ), 124.8 (CN), 136.1 (pyran  $\text{C}_5$ ), 129.5, 129.4, 130.5, 132.8 ( $\text{Ar}-\text{C}$ ), 179.7 (pyran  $\text{C}_2$ ).

**5-Amino-7-(2-chlorophenyl)-1,7-dihydropyrano[3,2-*b*]pyrrole-6-carbonitrile (5i)**

Anal Calcd for C<sub>14</sub>H<sub>10</sub>ClN<sub>3</sub>O (271.7): C, 61.89; H, 3.71; N, 15.47 %. Found C, 61.23; H, 3.66; N, 15.18 %. IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3,458 and 3,256 (asym. and sym. str. of -NH<sub>2</sub>), 3397 (NH), 2167 (-CN str.), 1248 (asym. str. of cyclic ArC-O-C ether). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  (ppm): 5.51 (*s*, 1H, pyran H<sub>4</sub>), 6.28 (*d*, 1H, pyrrole H<sub>3</sub>), 6.64 (*d*, 1H, pyrrole H<sub>2</sub>), 6.84 (*s*, 2H, D<sub>2</sub>O exch. NH<sub>2</sub>), 7.09–7.19 (*m*, 4H, Ar-H), 7.43 (*s*, 1H, pyrrole NH). <sup>13</sup>C NMR (250 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  (ppm): 26.2 (pyran C<sub>4</sub>), 55.6 (pyran C<sub>3</sub>), 113.9 (pyran C<sub>6</sub>), 114.2 (pyrrole C<sub>3</sub>), 118.6 (pyrrole, C<sub>1</sub>), 129.1 (CN), 137.2 (pyran C<sub>5</sub>), 125.4, 127.3, 128.9, 132.7, 133.0, 139.6 (Ar-C), 173.7 (pyran C<sub>2</sub>).

**5-Amino-7-(4-cyanophenyl)-1,7-dihydropyrano[3,2-*b*]pyrrole-6-carbonitrile (5j)**

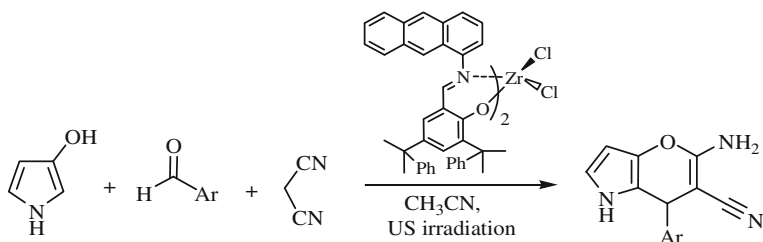
Anal Calcd for C<sub>15</sub>H<sub>10</sub>N<sub>4</sub>O (262.09): C, 68.69; H, 3.84; N, 21.36 %. Found C, 67.84; H, 3.75; N, 20.90 %. IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3,401 and 3,248 (asym. and sym. str. of -NH<sub>2</sub>), 3,418 (NH), 2,210 (-CN str.), 2,181 (-CN str.), 1,257 (asym. str. of cyclic ArC-O-C ether). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta_{\text{H}}$  (ppm): 5.51 (*s*, 1H, pyran H<sub>4</sub>), 6.10 (*d*, 1H, pyrrole H<sub>3</sub>), 6.48 (*s*, 2H, D<sub>2</sub>O exch. NH<sub>2</sub>), 6.60 (*d*, 1H, pyrrole H<sub>2</sub>), 7.24 (*s*, 1H, pyrrole NH), 7.26 (*d*, 2H, Ar-H), 7.38 (*d*, 2H, Ar-H). <sup>13</sup>C NMR (250 MHz, CDCl<sub>3</sub>)  $\delta_{\text{C}}$  (ppm): 34.6 (pyran C<sub>4</sub>), 62.78 (pyran C<sub>3</sub>), 111.7 (pyran C<sub>6</sub>), 114.5 (pyrrole C<sub>3</sub>), 122.4 (pyrrole, C<sub>1</sub>), 124.8 (CN), 126.5 (CN), 139.4 (pyran C<sub>5</sub>), 114.8, 129.9, 133.5, 139.5 (Ar-C), 176.3 (pyran C<sub>2</sub>).

**Results and discussion**

In a preliminary experiment we found that the three-component condensation reaction of 3-hydroxypyrrole, malononitrile, and benzaldehyde in CH<sub>3</sub>CN using 10 mol % Zr catalyst as promoter in the presence of ultrasonic irradiation worked very well and the corresponding pyrano[3,2-*b*]pyrrole was obtained in good yield. In this paper, therefore, an efficient and rapid procedure for one-pot synthesis of pyrano[3,2-*b*]pyrrole derivatives by using a Zr catalyst in the presence of ultrasonic waves is described (Scheme 1).

When toluene and benzene, as apolar media, were used for the model reaction, chemical yields and reaction times were poor compared with those achieved by use of acetonitrile as polar solvent.

The generality of this process was demonstrated by the wide range of substituted aromatic aldehydes used to synthesize a series of functionalized pyrano[3,2-*b*]pyrrole derivatives (Table 1, entries 1–8). It was found that the electronic nature of substituents on the aromatic aldehyde could affect the reactions in terms of reaction times and chemical yields. Yield of the reactions were increased by changing the substituent groups on the benzaldehyde from hydroxyl and methoxy to Br and F.



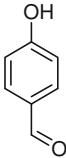
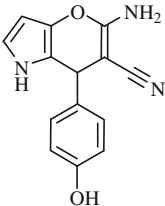
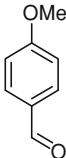
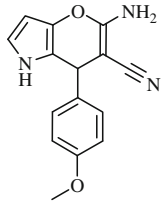
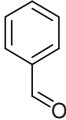
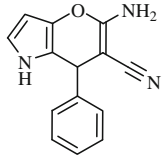
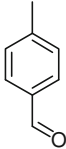
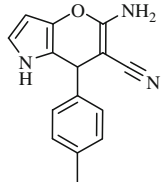
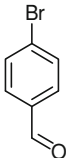
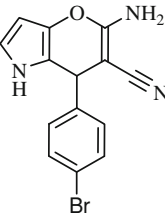
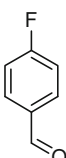
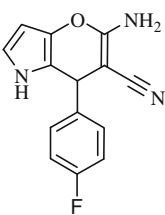
**Scheme 1** Zr-catalyzed synthesis of functionalized pyrano[3,2-*b*]pyrrole derivatives

As illustrated in Scheme 2, the catalyst could be coordinated with carbonyl oxygen increasing the reactivity of the carbonyl compound. Moreover, the catalyst is capable of binding with the nitrogen atom to facilitate heterocyclization to afford the corresponding pyrano[3,2-*b*]pyrrole product.

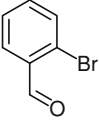
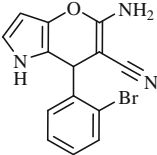
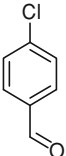
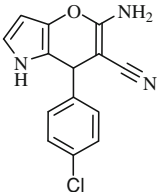
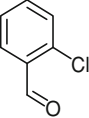
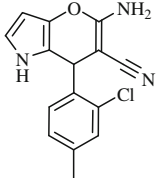
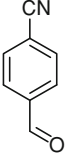
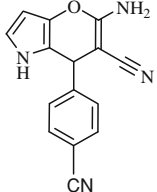
On the basis of recent reports which have proposed *ortho*-quinone methides (*o*QMs) as in-situ intermediates in one-pot three-component synthesis of naphthopyran derivatives [16], we envisaged a mechanism with a similar intermediate (**A**; Scheme 2). Michael-type addition of malononitrile to **A** is followed by attack of a hydroxyl group on one of two nitrile groups to afford the final product.

In the  $^1\text{H}$  NMR spectrum of compound **2** the aromatic hydrogens give rise to multiplet signals in the aromatic region of the spectrum ( $\delta_{\text{H}} = 6.11\text{--}7.05$  ppm) and two broad singlet peaks are seen at 6.75 and 7.50 ppm that disappear at the presence of  $\text{D}_2\text{O}$ . On the basis of their integration, they are attributed to  $\text{NH}_2$  and  $\text{NH}$  groups, respectively. The proton next to the nitrogen atom of the pyrrole ring appears as a doublet peak at  $\delta_{\text{H}} = 6.68$  ppm. Conjugation with the N atom of pyrrole results in lower chemical shifts of the  $\text{H}_2$  and  $\text{H}_3$  hydrogens compared with five hydrogens of phenyl ring, being present at approximately 7.1 ppm.  $\text{H}_4$  of the pyran ring is substantially down-field, because of conjugation with the phenyl and pyrroles ring, and it is present at approximately 5.51 ppm. Two doublets are present at 6.25 and 6.73 ppm that split each other by the same coupling constant; these are ascribed to  $\text{H}_2$  and  $\text{H}_3$  of pyrrole. Also, sharp singlets at  $\delta_{\text{H}} = 3.37$  and  $\delta_{\text{H}} = 5.43$  ppm are assigned to the methoxy group and CH of the pyran ring, respectively. Resonance of the aromatic protons of the substituted aromatic ring on the pyran moiety possessing a methoxy group are observed at  $\delta_{\text{H}} = 6.63$  and 7.05 ppm. In addition, the  $^{13}\text{C}$  NMR spectrum of compound **1** contained 13 distinct resonances, in agreement with the proposed structure. Five signals ( $\delta_{\text{C}} = 28.6, 59.5, 101.5, 126.1,$  and  $171.4$  ppm) are assigned to the pyran carbon atoms. Two signals assigned to the pyrrole ring can be observed at  $\delta_{\text{C}} = 104.9$  and  $119.3$  ppm. Resonance of aromatic carbons of the substituted aromatic ring on the pyran moiety possessing methoxy group ( $\text{Ar-C}$ ), are observed at  $\delta_{\text{C}} = 119.2, 127.4, 130.3,$  and  $154.6$  ppm. Also, the resonance of the functional nitrile and methoxy groups could be carefully assigned in the range  $\delta_{\text{C}} = 55.23$  and  $122$  ppm.

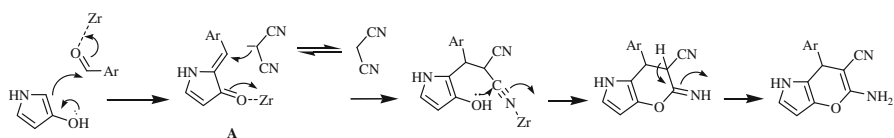
**Table 1** One-pot, three-component synthesis of 5-amino-7-aryl-6-cyano-4*H*-pyrano[3,2-*b*]pyrroles

Entry	Aldehyde	Product	Time (min)	Yield (%)
1			58	75
2			55	77
3			52	85
4			50	76
5			45	82
6			45	88

**Table 1** continued

Entry	Aldehyde	Product	Time (min)	Yield (%)
7			50	82
8			48	85
9			55	80
10			50	72

Reaction conditions: 1.0 equiv. 3-hydroxypyrrole, 1.0 equiv. aldehyde, 1.0 equiv. malononitrile, 10 mol % Zr catalyst, 4 ml CH<sub>3</sub>CN as solvent, 50 °C

**Scheme 2** The suggested mechanism for the one-pot synthesis of pyrano[3,2-*b*]indoles

## Conclusion

In conclusion, we have described a novel and efficient method for synthesis of pyrano[3,2-*b*]pyrrole derivatives by use of bis[*N*-(3,5-dicumylsalicylidene)-anthracylaminato]zirconium(IV) dichloride as catalyst with the aid of ultrasonic irradiation. The method has several advantages including good to high yields, short



reaction times, and broad applicability of substrates. Hence, it is a useful addition to the existing methods.

## References

1. S. Damavandi, *Multicomponent Synthesis of Heterocyclic Compounds* (LAMBERT Academic Publishing, Germany, 2012)
2. M. Lei, L. Ma, L. Hu, *Monatsh. Chem.* **141**, 1005 (2010)
3. J.N. Tan, M. Lia, Y. Gu, *Green. Chem.* **12**, 908 (2010)
4. M. Lei, L. Ma, L. Hu, *Tetrahedron Lett.* **51**, 4746 (2010)
5. S. Damavandi, R. Sandaroos, *Heterocycl. Commun.* **17**, 121 (2011)
6. S. Damavandi, R. Sandaroos, *Heterocycl. Commun.* **17**, 125 (2011)
7. S. Damavandi, *Synth. React. Inorg. Met. Org. Nano. Met. Chem.* **41**, 1274 (2011)
8. S. Kumar, D. Hernandez, B. Hoa, Y. Lee, J.S. Yang, A. McCurdy, *Org. Lett.* **10**, 3761 (2008)
9. N.J. Thumar, M.P. Patel, *Arkivoc* **13**, 363 (2009)
10. V.T. Hong Nguyen, P. Langer, *Tetrahedron Lett.* **46**, 815 (2005)
11. C.P. Dell, C.W. Smith, *Eur. Pat. Appl.* **537**, 949 (1993)
12. N.V.T. Hong, P. Langer, *Tetrahedron Lett.* **46**(5), 815 (2005)
13. M.M. Khafagy, A.H.F. Abd El-Wahab, F. Eid, A.M. El-Agrody, *Farmaco* **57**, 715 (2002)
14. A. Martínez-Grau, J.L. Marco, *Bioorg. Med. Chem. Lett.* **7**(24), 3165 (1997)
15. P.W. Smith, S.L. Sollis, P.D. Howes, P.C. Cherry, I.D. Starkey, K.N. Cobley, H. Weston, J. Scicinski, A. Merritt, A. Whittington, P. Wyatt, N. Taylor, D. Green, R. Bethell, S. Madar, R.J. Fenton, P.J. Morley, T. Pateman, A. Beresford, *J. Med. Chem.* **41**(6), 787 (1998)
16. K. Hiramoto, A. Nasuhara, K. Michikoshi, T. Kato, K. Kikugawa, *Mutat. Res.* **395**(1), 47 (1997)
17. C.P. Dell, C.W. Smith, *Eur. Pat. Appl.* **537**, 949 (1993)
18. F. Eiden, F. Denk, *Arch. Pharm.* **324**(6), 353 (1991)
19. S. Damavandi, G.B. Galland, G.H. Zohuri, R. Sandaroos, *J. Pol. Res.* **18**, 1059 (2011)
20. S. Damavandi, R. Sandaroos, M. Pashirzad, *Res. Chem. Intermed.* **38**, 1969 (2012)
21. S. Damavandi, R. Sandaroos, *J. Chem. Sci.* **124**, 483 (2012)
22. S. Damavandi, R. Sandaroos, *Res. Chem. Intermed.* (2012). doi:[10.1007/s11164-012-0681-z](https://doi.org/10.1007/s11164-012-0681-z)
23. G. H. Zohuri, S. Damavandi, R. Sandaroos, *Res. Chem. Intermed.* (2012). doi:[10.1007/s11164-012-0743-2](https://doi.org/10.1007/s11164-012-0743-2)
24. R. Sandaroos, S. Damavandi, M. Salimi, A. Mohammadi, A. Karimian, M. Hasanpour, *Mol. Divers.* **16**, 269 (2012)