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Efficient One-Pot Synthesis of 4-Aryl-3-cyano-2,5-dihydro-1*H*-indeno[1,2-*b*] pyridin-2-one and 4-Aryl-3-cyano-1,2,5,6-tetrahydrobenzo[*h*]quinolin-2-one Derivatives Under Solvent-Free Conditions

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Abstract: 4-Aryl-3-cyano-2,5-dihydro-1*H*-indeno[1,2-*b*]pyridin-2-one and 4-aryl-3-cyano-1,2,5,6-tetrahydrobenzo[*h*]quinolin-2-one have been prepared from indan-1-one or 3,4-dihydronaphthalen-1(2*H*)-one, aromatic aldehydes, 2-cyanoacetamide, in the presence of sodium hydroxide under solvent-free conditions. The rapid and facile method produced products in high yields.

Keywords: 2-Cyanoacetamide, 3-cyano-2-pyridones, one-pot reactions, solvent free, synthesis

There has been a gradual change from classical reaction conditions to more environmentally friendly routes.[1] This growth of green chemistry holds significant potential for reduction of the by-products, waste production and lowering of energy costs. As one of efficient synthetic methods of green chemistry, solvent-free synthesis is now used in a lot of chemical transformations for the synthesis of various compounds.[2]

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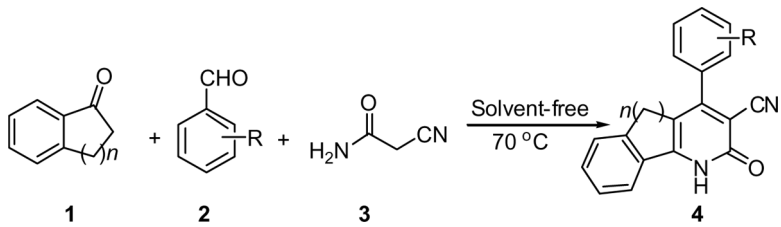
The most evident improvements are reduced reaction times and cleaner reactions because of fewer side products.

By virtue of the convergence of productivity, facile execution, and generally high yield of products, one-pot multicomponent reactions (MCRs) have attracted considerable attention from the point of view of ideal synthesis.[3] However, if the one-pot MCRs could be carried out under solvent-free conditions, it would be the most efficient synthetic methods of organic synthesis. As part of our continued interest[4] in the development of facile methods for the synthesis of organic compounds, herein we report a very simple and highly efficient method for the synthesis of 4-aryl-3-cyano-2,5-dihydro-1*H*-indeno[1,2-*b*]pyridin-2-one and 4-aryl-3-cyano-1,2,5,6-tetrahydro-benzo[*h*]quinolin-2-one derivatives via a three-component cyclocondensation reaction under solvent-free conditions.

Substituted 3-cyano-2-pyridones derivatives are important intermediates in the pharmaceutical, dye, and photo industries. Synthesis of these compounds have been widely studied using conventional heating in the presence of various catalysts and usually in polar solvents.[5–7] However, in reported literature, the organic solvent was necessary. In our recent research, we found these compounds also could be synthesized under solvent-free conditions. In the typical experimental procedure, indan-1-one, aromatic aldehydes, and 2-cyanoacetamide were mixed thoroughly with 0.2 g sodium hydroxide. The reaction mixture was heated at 70 °C for about 10–15 min and the 4-aryl-3-cyano-2,5-dihydro-1*H*-indeno[1,2-*b*] pyridin-2-one was afforded in excellent yields. To expand this reaction, 3,4-dihydronaphthalen-1(2*H*)-one was chosen to react with aromatic aldehydes and 2-cyanoacetamide under similar conditions. The reactions also could be carried out smoothly, and 4-aryl-3-cyano-1,2,5,6-tetrahydrobenzo[*h*]quinolin-2-one could be obtained with high yields (Scheme 1).

All structures of the compounds were confirmed from IR, ^{1}H NMR, and elemental analyses. The x-ray diffraction analysis of crystal **4 h**[8]



Scheme 1. The reaction of indan-1-one or 3,4-dihydronaphthalen-1(2*H*)-one, aromatic aldehydes, and 2-cyano-acetamide.

Table 1. The reaction results for compounds **4**

Entry	R	*n*	Product	Yields
1	4-Br	1	**4a**	85
2	4-F	1	**4b**	90
3	2-Cl	1	**4c**	89
4	4-Cl	1	**4d**	90
5	2,4-Cl_2	1	**4e**	92
6	3,4-Cl_2	1	**4f**	88
7	4-CH_3O	1	**4g**	86
8	4-F	2	**4h**	95
9	4-Br	2	**4i**	84
10	2-Cl	2	**4j**	85
11	4-Cl	2	**4k**	90
12	3,4-Cl_2	2	**4l**	89
13	4-CH_3	2	**4m**	82
14	4-CH_3O	2	**4n**	88

further confirmed the structures (Fig. 1). Our observations are recorded in Table 1.

In conclusion, we have demonstrated a novel, one-pot, three-component reaction under solvent-free conditions that offers a facile and efficient route for the synthesis of 4-aryl-3-cyano-2,5-dihydro-1*H*-indeno[1,2-*b*]pyridin-2-one and 4-aryl-3-cyano-1,2,5,6-tetrahydrobenzo[*h*]quinolin-2-one derivatives. This method has some advantages,

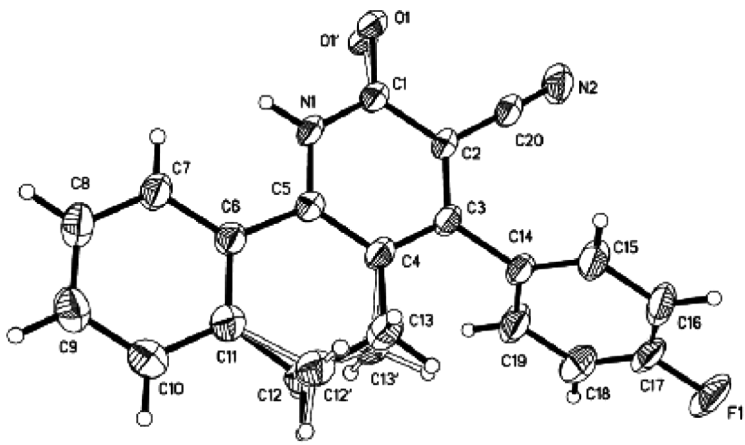


Figure 1. Structure of compound **4h**.

such as shorter reaction times, milder conditions, simplicity of the reaction, and good product yields.

EXPERIMENTAL

Melting points were uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr. ^{1}H NMR spectra were obtained in DMSO-d_6 solution with Me_4Si as internal standard using a Bruker-400 spectrometer. Elemental analyses were carried out using Perkin-Elmer 240 II analyzer. X-ray diffraction was measured on a Siemens P4 diffractometer.

General Procedure for the Syntheses of 4-Aryl-3-cyano-2,5-dihydro-1*H*-indeno[1,2-*b*]pyridin-2-one and 4-Aryl-3-cyano-1,2,5,6-tetrahydro-benzo[*h*]quinolin-2-one

The general procedure is represented as follows: indan-1-one (or 3,4-dihydronaphthalen-1(2*H*)-one) **1** (2 mmol), aromatic aldehyde **2** (2 mmol), 2-cyanoacetamide **3** (2 mmol), and NaOH (5 mmol) were added to a flask at 70 °C. The reaction could be completed within 10–15 min, and the reaction mixture was poured into water. The product was filtered, dried, and recrystallized from 25–30 mL 95% ethanol.

Data

Compound **4a**

Mp > 300 °C; IR (KBr) *v*: 3241 (NH), 2222 (CN), 1636 (CO) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.66 (2H, s, CH_2), 7.50–7.53 (2H, m, ArH), 7.63 (3H, t, $J = 7.8$, 8.4 Hz, ArH), 7.70 (2H, d, $J = 7.8$ Hz, Hz, ArH), 8.17 (1H, d, $J = 2.0$ Hz, ArH), 13.65 (1H, s, NH). Anal. calcd. for $C_{19}H_{11}BrN_2O$: C, 62.83; H, 3.05; N, 7.71. Found: C, 62.62; H, 3.10; N, 7.87.

Compound **4b**

Mp > 300 °C; IR (KBr) *v*: 3287 (NH), 2221 (CN), 1636 (CO) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.67 (2H, s, CH_2), 7.50 (2H, t, $J = 3.6$, 3.6 Hz, ArH), 7.63 (1H, d, $J = 6.0$ Hz, ArH), 7.67 (4H, t, $J = 8.4$, 8.4 Hz, ArH), 7.17 (1H, d, $J = 6.0$ Hz, ArH), 13.64 (1H, s, NH). Anal. calcd. for $C_{19}H_{11}FN_2O$: C, 75.49; H, 3.67; N, 9.27. Found: C, 75.60; H, 3.57; N, 9.34.

Compound **4c**

Mp > 300 °C; IR (KBr) *v*: 3337 (NH), 2222 (CN), 1698 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.50 (2H, dd, $J = 22.4$ Hz, $J = 22.4$ Hz, CH_2), 7.54 (2H, t, $J = 3.6$. 3.6 Hz, ArH), 7.58 (2H, br, ArH), 7.62 (2H, t, $J = 4.0$, 4.0 Hz, ArH), 7.72 (1H, d, $J = 7.2$ Hz, ArH), 8.20 (1H, d, $J = 4.0$ Hz, ArH), 13.68 (1H, s, NH). Anal. calcd. for $C_{19}H_{11}ClN_2O$: C, 71.59; H, 3.48; N, 8.79. Found: C, 71.39; H, 3.56; N, 8.84.

Compound **4d**

Mp > 300 °C; IR (KBr) *v*: 3296 (NH), 2219 (CN), 1637 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.68 (2H, s, CH_2), 7.53 (2H, t, $J = 5.6$. 5.6 Hz, ArH), 7.64 (1H, d, $J = 5.6$ Hz, ArH), 7.70 (4H, dd, $J = 8.4$ Hz, $J = 8.4$ Hz, ArH), 8.19 (1H, d, $J = 5.6$ Hz, ArH), 13.68 (1H, s, NH). Anal. calcd. for $C_{19}H_{11}ClN_2O$: C, 71.59; H, 3.48; N, 8.79. Found: C, 71.36; H, 3.58; N, 8.86.

Compound **4e**

Mp > 300 °C; IR (KBr) *v*: 3291 (NH), 2223 (CN), 1635 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 4.13 (2H, s, CH_2), 7.50–7.54 (1H, m, ArH), 7.52 (2H, t, $J = 6.4$, 6.4 Hz, ArH), 7.84 (2H, t, $J = 6.4$, 6.4 Hz, ArH), 7.89 (1H, d, $J = 6.8$ Hz, ArH), 8.00 (1H, s, ArH), 13.85 (1H, s, NH). Anal. calcd. for $C_{19}H_{10}Cl_2N_2O$: C, 64.61; H, 2.85; N, 7.93. Found: C, 64.91; H, 2.75; N, 7.83.

Compound **4f**

Mp > 300 °C; IR (KBr) *v*: 3339 (NH), 2219 (CN), 1658 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.71 (2H, s, CH_2), 7.54 (2H, t, $J = 6.0$ Hz, $J = 7.2$ Hz, ArH), 7.66 (1H, d, $J = 7.2$ Hz, ArH), 7.69 (1H, d, $J = 8.4$ Hz, ArH), 7.89 (1H, d $J = 8.0$ Hz, ArH), 8.04 (1H, d, $J = 7.6$ Hz, Hz, ArH), 8.19–8.21 (1H, br, ArH), 13.76 (1H, s, NH). Anal. calcd. for $C_{19}H_{10}Cl_2N_2O$: C, 64.61; H, 2.85; N, 7.93. Found: C, 64.47; H, 2.91; N, 7.86.

Compound **4g**

Mp > 300 °C; IR (KBr) *v*: 3292 (NH), 2219 (CN), 1637 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 3.72 (2H, s, CH_2), 3.87 (3H,

s, OCH3), 7.14 (2H, t, $J = 8.8$, 8.8 Hz, ArH), 7.52 (2H, t, $J = 3.6$, 3.6 Hz, ArH), 7.66 (1H, m, ArH), 7.89 (2H, d, $J = 8.8$ Hz, ArH), 8.17 (1H, br, ArH), 13.59 (1H, s, NH). Anal. calcd. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.62; H, 4.41; N, 8.80.

Compound **4h**

Mp > 300 °C; IR (KBr) *v*: 3131 (NH), 2220 (CN), 1634 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.33 (2H, br, CH_2), 2.74 (2H, t, $J = 7.2$, 7.2 Hz, CH_2), 7.35 (1H, d, $J = 6.4$ Hz, ArH), 7.39–7.46 (4H, m, ArH), 7.52 (2H, dd, $J = 5.2$ Hz, $J = 5.6$ Hz, ArH), 8.07 (1H, br, ArH), 12.77 (1H, s; NH). Anal. calcd. for $C_{20}H_{13}FN_2O$: C, 75.94; H, 4.14; N, 6.01. Found: C, 75.63; H, 4.07; N, 6.12.

Compound **4i**

Mp > 300 °C; IR (KBr) *v*: 3124 (NH), 2221 (CN), 1638 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.36 (2H, t, $J = 6.0$, 6.0 Hz, CH_2), 2.76 (2H, t, $J = 6.8$, 6.8 Hz, CH_2), 7.35 (1H, d, $J = 6.8$ Hz, ArH), 7.43 (4H, dd, $J = 8.4$ Hz, $J = 8.4$ Hz, ArH), 7.78 (2H, d, $J = 8.8$ Hz, ArH), 8.07 (1H, d, $J = 7.6$ Hz, ArH), 12.62 (1H, s, NH). Anal. calcd. for $C_{20}H_{13}BrN_2O$: C, 63.68; H, 3.47; N, 7.43. Found: C, 63.40; H, 3.51; N, 7.54.

Compound **4j**

Mp > 300 °C; IR (KBr) *v*: 3132 (NH), 2221 (CN), 1638 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.37 (2H, br, CH_2), 2.76 (2H, t, $J = 6.8$, 6.8 Hz, CH_2), 7.35 (1H, d, $J = 7.2$ Hz, ArH), 7.44 (4H, dd, $J = 8.0$ Hz, $J = 8.0$ Hz, ArH), 7.78 (2H, d, $J = 8.4$ Hz, ArH), 8.07 (1H, d, $J = 7.6$ Hz, ArH), 12.66 (1H, s, NH). Anal. calcd. for $C_{20}H_{13}ClN_2O$: C, 72.18; H, 3.94; N, 8.42. Found: C, 72.40; H, 3.92; N, 8.52.

Compound **4k**

Mp > 300 °C; IR (KBr) *v*: 3130 (NH), 2223 (CN), 1637 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.37 (2H, br, CH_2), 2.76 (2H, t, $J = 6.8$, 6.8 Hz, CH_2), 7.35 (1H, d, $J = 7.2$ Hz, ArH), 7.43 (2H, dd, $J = 7.2$ Hz, $J = 7.2$ Hz, ArH), 7.49 (2H, d, $J = 8.0$ Hz, ArH), 7.64 (2H, d, $J = 8.4$ Hz, ArH), 8.07 (1H, d, $J = 7.6$ Hz, ArH), 12.62 (1H, s, NH). Anal. calcd. for $C_{20}H_{13}ClN_2O$: C, 72.18; H, 3.94; N, 8.42. Found: C, 72.40; H, 3.85; N, 8.55.

Compound **4l**

Mp 287–289 °C; IR (KBr) *v*: 3123 (NH), 2218 (CN), 1635 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.28 (1H, t, $J = 7.2$, 6.8 Hz, CH_2), 2.38 (1H, t, $J = 6.8$, 7.2 Hz, CH_2),2.75 (2H, t, $J = 6.8$ Hz, $J = 8.0$ Hz, CH_2), 7.23–7.30 (1H, m, ArH), 7.35–7.48 (3H, m, ArH), 7.69–7.85 (2H, m, ArH), 8.03–8.09 (1H, m, ArH), 12.54 (1H, s, NH). Anal. calcd. for $C_{20}H_{12}Cl_2N_2O$: C, 65.41; H, 3.29; N, 7.63. Found: C, 65.66; H, 3.22; N, 7.51.

Compound **4m**

Mp > 300 °C; IR (KBr) *v*: 3128 (NH), 2221 (CN), 1634 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.37 (2H, br, CH_2), 2.40 (3H, s, CH_3), 2.76 (2H, t, $J = 7.2$, 7.2 Hz, CH_2), 7.31 (2H, d, $J = 8.4$ Hz, ArH), 7.36 (3H, d, $J = 8.4$ Hz, ArH), 7.43 (2H, t, $J = 6.4$ Hz, $J = 7.2$ Hz, ArH), 8.07 (1H, d, $J = 8.4$ Hz, ArH), 12.65 (1H, s, NH). Anal. calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.36; H, 5.21; N, 8.87.

Compound **4n**

Mp > 300 °C; IR (KBr) *v*: 3120 (NH), 2219 (CN), 1636 (CO) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) (δ, ppm): 2.41 (2H, t, $J = 6.0$, 7.2 Hz, CH_2), 2.75 (2H, t, $J = 6.0$, 7.2 Hz, CH_2), 3.84 (3H, s, CH_3O), 7.11 (2H, d, $J = 8.8$ Hz, ArH), 7.34 (1H, d, $J = 6.8$ Hz, ArH), 7.38 (3H, d, $J = 8.8$ Hz, ArH), 7.43 (1H, t, $J = 7.2$, 7.2 Hz, ArH), 8.06 (1H, d, $J = 7.2$ Hz, ArH), 12.58 (1H, s, NH). Anal. calcd. for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.55; H, 4.86; N, 8.62.

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