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Hydrocyanation of 2-arylmethyleneindan-1,3-diones using potassium hexacyanoferrate(II) as a nontoxic cyanating agent

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Abstract: The hydrocyanation of 2-arylmethyleneindan-1,3-diones with potassium hexacyanoferrate(II) as a nontoxic cyanating agent to synthesize 2-(1,3-dioxoindan-2-yl)-2-arylacetonitriles in the presence of benzoyl chloride as a promoter and potassium carbonate as a base by a one-pot procedure is described. The use of nontoxic and inexpensive cyanide source, high yield and simple workup procedures are the advantages of this protocol.

Keywords: 2-arylmethyleneindan-1,3-dione; hydrocyanation; nontoxic cyanating agent; potassium hexacyanoferrate(II).

1 Introduction

The conjugate addition of various cyanating agents as nucleophiles to Michael acceptors is an important method for the formation of C-CN bonds in organic synthesis [1–5]. The produced β-cyano ketones can be widely used in organic synthesis [6–8], and cyano unit can be readily converted into different groups including amides, amines, carboxylic acids, tetrazoles and amidines [9, 10]. However, the reported reactions generally use various strong toxic or unstable chemicals, such as HCN [11], LiCN [12], NaCN [13], KCN [14, 15], diethylaluminum cyanide [16, 17], trimethylsilyl cyanide [18–31] and acetone cyanohydrin [32–34], as cyanating agents. Therefore, it is still necessary to explore a nontoxic cyanating agent for the cyanation reaction.

Potassium hexacyanoferrate(II), $K_4[Fe(CN)_6]$, as a nontoxic and abundant inorganic chemical has been used in the food industry. Recently, it has been used as a nontoxic cyanating agent to synthesize benzonitriles [35–53], aroyl cyanides [54], sulfonyl cyanides [55], benzyl cyanides [56, 57] and cinnamonitriles [58] by substitution reactions. Our research work currently focused on the addition reactions for unsaturated substances using $K_4[Fe(CN)_6]$ as a nontoxic cyanating agent [59–75].

Indan-1,3-dione scaffolds are essential in medicinal chemistry as they can be used as anticancer agents [76], and in material chemistry as they can be used as optoelectronic additives [77]. Therefore, the exploration for synthetic methods for diverse compounds bearing indan-1,3-dione moiety has potential benefits for the future.

In this work, we report the hydrocyanation of 2-arylmethyleneindan-1,3-diones using $K_4[Fe(CN)_6]$ as a nontoxic cyanating agent to synthesize a series of β-cyano ketones bearing indan-1,3-dione moiety.

2 Materials and methods

^{1}H nuclear magnetic resonance (NMR) and ^{13}C NMR spectra were obtained with the Mercury-400 MB or Mercury-600 MB instrument using $CDCl_3$ as solvent. Elemental analyses were conducted on a Vario El Elemental Analysis instrument. 2-Arylmethyleneindan-1,3-diones were synthesized using methods from the literature [78, 79].

2.1 The general procedure for the hydrocyanation of 2-arylmethyleneindan-1,3-diones

The mixture of potassium hexacyanoferrate(II) (0.2 mmol, 0.08 g) and benzoyl chloride (1.2 mmol, 0.17 g) was stirred at 160°C for 3 h. Then, the resulting mixture was cooled to room temperature, and 2-arylmethleneindan-1,3-dione (1 mmol, **1a**: 0.26 g, **1b**: 0.28 g, **1c**: 0.28 g, **1d**: 0.28 g, **1e**: 0.29 g, **1f**: 0.28 g, **1g**: 0.28 g, **1h**: 0.30 g, **1i**: 0.34 g, **1j**: 0.34 g, **1k**: 0.34 g, **1l**: 0.31 g, **1m**: 0.33 g, **1n**: 0.27 g, **1o**: 0.25 g, **1p**: 0.29 g, **1q**: 0.23 g), potassium carbonate (0.2 mmol, 0.03 g) and water (2 mmol, 0.04 g) in 5 ml of DMF were added, and the system was stirred at room temperature for another 4 h. After the completion of the reaction, the solids were removed by filtration. The solution was evaporated under reduced pressure, and the residue was separated by column chromatography using ethyl acetate and petroleum ether (1:2) as eluent to obtain pure product. The analytical data for products are shown below and for the NMR spectra see Supplementary material.

2.1.1 2-(1,3-Dioxoindan-2-yl)-2-phenylacetonitrile (2a): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93–7.91 (m, 2H, ArH), 7.82–7.79 (m, 2H, ArH), 7.37–7.36 (d, J = 6.9 Hz, 2H, ArH), 7.28–7.21 (m, 3H, ArH),

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4.75–4.74 (d, J = 3.2 Hz, 1H, CH), 3.61–3.60 (d, J = 3.2 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.37 (CO), 195.26 (CO), 136.24 (Ar), 136.15 (Ar), 128.94 (Ar), 128.72 (Ar), 128.50 (Ar), 123.57 (Ar), 123.54 (Ar), 118.03 (CN), 55.89 (CH), 34.06 (CH). Anal. Calcd. for $C_{17}H_{11}NO_2$: C, 78.15; H, 4.24; N, 5.36. Found: C, 78.01; H, 4.26; N, 5.38.

2.1.2 2-(1,3-Dioxoindan-2-yl)-2-(*o*-tolyl)acetonitrile (2b): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06–8.02 (m, 1H, ArH), 7.98–7.97 (m, 1H, ArH), 7.90–7.86 (m, 2H, ArH), 7.68–7.67 (d, J = 7.0 Hz, 1H, ArH), 7.26–7.22 (m, 2H, ArH), 7.18–7.17 (d, J = 6.8 Hz, 1H, ArH), 4.89–4.88 (d, J = 3.2 Hz, 1H, CH), 3.44–3.43 (d, J = 3.2 Hz, 1H, CH), 2.43 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.98 (CO), 195.17 (CO), 142.32 (Ar), 141.80 (Ar), 136.42 (Ar), 136.25 (Ar), 135.05 (Ar), 131.01 (Ar), 130.91 (Ar), 129.28 (Ar), 128.86 (Ar), 126.74 (Ar), 123.73 (Ar), 123.70 (Ar), 117.69 (CN), 54.72 (CH), 31.14 (CH), 19.11 (CH_3). Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.64; H, 4.74; N, 5.06.

2.1.3 2-(1,3-Dioxoindan-2-yl)-2-(*m*-tolyl)acetonitrile (2c): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93–7.91 (m, 2H, ArH), 7.82–7.79 (m, 2H, ArH), 7.18 (s, 1H, ArH), 7.15–7.12 (m, 2H, ArH), 7.03–7.02 (d, J = 4.1 Hz, 1H, ArH), 4.71–4.70 (d, J = 3.3 Hz, 1H, CH), 3.59–3.57 (d, J = 3.2 Hz, 1H, CH), 2.27 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.39 (CO), 195.33 (CO), 142.22 (Ar), 142.06 (Ar), 138.80 (Ar), 136.19 (Ar), 136.13 (Ar), 131.30 (Ar), 129.45 (Ar), 129.10 (Ar), 128.78 (Ar), 125.49 (Ar), 123.54 (Ar), 123.51 (Ar), 118.10 (CN), 55.92 (CH), 34.01 (CH), 21.26 (CH_3). Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.48; H, 4.75; N, 5.11.

2.1.4 2-(1,3-Dioxoindan-2-yl)-2-(*p*-tolyl)acetonitrile (2d): Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.90 (m, 2H, ArH), 7.84–7.79 (m, 2H, ArH), 7.25–7.23 (d, J = 8.1 Hz, 2H, ArH), 7.07–7.04 (d, J = 8.3 Hz, 2H, ArH), 4.73–4.72 (d, J = 3.2 Hz, 1H, CH), 3.60–3.59 (d, J = 3.2 Hz, 1H, CH), 2.24 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.51 (CO), 195.41 (CO), 142.26 (Ar), 142.03 (Ar), 138.62 (Ar), 136.22 (Ar), 136.13 (Ar), 129.60 (Ar), 128.46 (Ar), 128.36 (Ar), 123.57 (Ar), 123.54 (Ar), 118.26 (CN), 55.95 (CH), 33.70 (CH), 20.99 (CH_3). Anal. Calcd. for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.53; H, 4.76; N, 5.09.

2.1.5 2-(1,3-Dioxoindan-2-yl)-2-(4-methoxyphenyl)acetonitrile (2e): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93–7.90 (m, 2H, ArH), 7.82–7.78 (m, 2H, ArH), 7.26–7.25 (d, J = 7.6 Hz, 2H, ArH), 6.76–6.74 (d, J = 7.5 Hz, 2H, ArH), 4.70–4.69 (d, J = 3.3 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 3.57–3.56 (d, J = 3.2 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.62 (CO), 195.47 (CO), 159.66 (Ar), 142.33 (Ar), 142.04 (Ar), 136.24 (Ar), 136.13 (Ar), 129.80 (Ar), 123.55 (Ar), 123.52 (Ar), 123.15 (Ar), 118.39 (CN), 114.25 (Ar), 56.00 (CH), 55.18 (OCH_3), 33.32 (CH). Anal. Calcd. for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81. Found: C, 74.09; H, 4.52; N, 4.85.

2.1.6 2-(1,3-Dioxoindan-2-yl)-2-(4-hydroxyphenyl)acetonitrile (2f): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92–7.90 (m, 2H, ArH), 7.82–7.80 (m, 2H, ArH), 7.20–7.18 (dd, J = 8.6, 2.2 Hz, 2H, ArH), 6.69–6.67 (dd, J = 8.6, 2.1 Hz, 2H, ArH), 5.42 (s, 1H, OH), 4.68–4.67 (d, J = 5.0 Hz, 1H, CH), 3.58–3.57 (d, J = 5.0 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.75 (CO), 195.63 (CO), 156.02 (Ar), 142.31 (Ar), 142.02 (Ar), 136.36 (Ar), 136.24 (Ar), 130.00 (Ar), 123.59 (Ar), 123.55 (Ar), 123.04 (Ar), 118.42 (CN), 115.83 (Ar), 55.97 (CH), 33.33 (CH). Anal. Calcd. for $C_{17}H_{11}NO_3$: C, 73.64; H, 4.00; N, 5.05. Found: C, 73.71; H, 3.99; N, 5.03.

2.1.7 2-(1,3-Dioxoindan-2-yl)-2-(2-fluorophenyl)acetonitrile (2g): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03–8.01 (m, 1H, ArH), 7.99–7.95 (m, 1H, ArH), 7.89–7.86 (m, 2H, ArH), 7.70–7.67 (td, J = 7.7, 1.6 Hz, 1H, ArH), 7.37–7.32 (m, 1H, ArH), 7.25–7.20 (t, J = 7.6 Hz, 1H, ArH), 7.09–7.04 (m, 1H, ArH), 5.02–5.01 (d, J = 3.7 Hz, 1H, CH), 3.58–3.57 (d, J = 3.7 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.24 (CO), 194.95 (CO), 160.29 (Ar), 158.64 (Ar), 142.00 (d, J = 64.9 Hz, Ar), 136.40 (d, J = 14.8 Hz, Ar), 133.69 (Ar), 130.81 (d, J = 8.1 Hz, Ar), 130.63 (d, J = 2.4 Hz, Ar), 130.15 (Ar), 128.46 (Ar), 124.71 (d, J = 3.9 Hz, Ar), 123.72 (d, J = 9.2 Hz, Ar), 119.48 (d, J = 13.5 Hz, CN), 116.69 (Ar), 115.68 (d, J = 20.8 Hz, Ar), 54.32 (CH), 28.45 (d, J = 4.0 Hz, CH). Anal. Calcd. for $C_{17}H_{10}FNO_2$: C, 73.11; H, 3.61; N, 6.80. Found: C, 73.03; H, 3.60; N, 6.84.

2.1.8 2-(4-Chlorophenyl)-2-(1,3-dioxoindan-2-yl)acetonitrile (2h): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (ddd, J = 4.6, 3.1, 1.6 Hz, 2H, ArH), 7.85–7.82 (m, 2H, ArH), 7.33–7.29 (m, 2H, ArH), 7.26–7.22 (m, 2H, ArH), 4.73–4.72 (d, J = 1.5 Hz, 1H, CH), 3.61–3.60 (dd, J = 3.0, 1.5 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.14 (CO), 194.95 (CO), 142.14 (Ar), 141.90 (Ar), 136.44 (Ar), 136.34 (Ar), 134.94 (Ar), 129.95 (Ar), 129.87 (Ar), 129.18 (Ar), 123.67 (Ar), 123.64 (Ar), 117.69 (CN), 55.81 (CH), 33.34 (CH). Anal. Calcd. for $C_{17}H_{10}ClNO_2$: C, 69.05; H, 3.41; N, 4.74. Found: C, 69.11; H, 3.40; N, 4.72.

2.1.9 2-(2-Bromophenyl)-2-(1,3-dioxoindan-2-yl)acetonitrile (2i): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08–8.04 (m, 1H, ArH), 8.01–7.98 (m, 1H, ArH), 7.92–7.88 (m, 2H, ArH), 7.63–7.61 (d, J = 7.9 Hz, 1H, ArH), 7.48–7.45 (q, J = 7.4 Hz, 2H, ArH), 7.29–7.27 (t, J = 7.7 Hz, 1H, ArH), 5.16–5.15 (d, J = 3.0 Hz, 1H, CH), 3.68–3.67 (dd, J = 3.4, 1.2 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.25 (CO), 195.20 (CO), 142.38 (Ar), 141.59 (Ar), 136.47 (Ar), 136.33 (Ar), 133.20 (Ar), 131.66 (Ar), 131.36 (Ar), 130.48 (Ar), 127.98 (Ar), 123.82 (Ar), 123.70 (Ar), 122.68 (Ar), 116.70 (CN), 53.81 (CH), 34.80 (CH). Anal. Calcd. for $C_{17}H_{10}BrNO_2$: C, 60.02; H, 2.96; N, 4.12. Found: C, 59.94; H, 2.98; N, 4.13.

2.1.10 2-(3-Bromophenyl)-2-(1,3-dioxoindan-2-yl)acetonitrile (2j): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97–7.93 (m, 2H, ArH), 7.86–7.82 (m, 2H, ArH), 7.54–7.53 (t, J = 1.9 Hz, 1H, ArH), 7.39–7.38 (d, J = 8.1 Hz, 1H, ArH), 7.35–7.34 (d, J = 8.0 Hz, 1H, ArH), 7.17–7.14 (t, J = 7.9 Hz, 1H, ArH), 4.71–4.70 (d, J = 3.2 Hz, 1H, CH), 3.61–3.60 (d, J = 3.2 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.97 (CO), 194.87 (CO), 142.03 (Ar), 141.91 (Ar), 136.46 (Ar), 136.40 (Ar), 133.60 (Ar), 132.05 (Ar), 131.51 (Ar), 130.48 (Ar), 127.24 (Ar), 123.73 (Ar), 123.71 (Ar), 122.91 (Ar), 117.39 (CN), 55.79 (CH), 33.45 (CH). Anal. Calcd. for $C_{17}H_{10}BrNO_2$: C, 60.02; H, 2.96; N, 4.12. Found: C, 60.08; H, 2.94; N, 4.15.

2.1.11 2-(4-Bromophenyl)-2-(1,3-dioxoindan-2-yl)acetonitrile (2k): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95–7.93 (m, 2H, ArH), 7.86–7.81 (m, 2H, ArH), 7.40–7.39 (d, J = 7.1 Hz, 2H, ArH), 7.27–7.24 (m, 2H, ArH), 4.71–4.70 (d, J = 2.8 Hz, 1H, CH), 3.62–3.61 (dd, J = 3.3, 1.3 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.15 (CO), 194.95 (CO), 142.12 (Ar), 141.87 (Ar), 136.48 (Ar), 136.38 (Ar), 132.15 (Ar), 130.25 (Ar), 130.17 (Ar), 128.46 (Ar), 123.71 (Ar), 123.66 (Ar), 117.65 (CN), 55.75 (CH), 33.39 (CH). Anal. Calcd. for $C_{17}H_{10}BrNO_2$: C, 60.02; H, 2.96; N, 4.12. Found: C, 60.06; H, 2.96; N, 4.10.

2.1.12 2-(1,3-Dioxoindan-2-yl)-2-(3-nitrophenyl)acetonitrile (2l): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27–8.26 (t, J = 2.1 Hz, 1H, ArH), 8.17–8.15 (dd, J = 8.2, 2.2 Hz, 1H, ArH), 7.99–7.96 (m, 2H, ArH), 7.88–7.85 (m, 2H, ArH), 7.84–7.83 (d, J = 7.8 Hz, 1H, ArH), 7.56–7.53 (t, J = 8.0 Hz, 1H, ArH), 4.87–4.86 (d, J = 3.3 Hz, 1H, CH), 3.68–3.67 (d, J = 3.2 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.63 (CO), 194.48 (CO), 146.86 (Ar), 141.87 (Ar), 141.82 (Ar), 136.66 (Ar), 136.63

(Ar), 134.64 (Ar), 130.18 (Ar), 128.79 (Ar), 123.90 (Ar), 123.87 (Ar), 123.86 (Ar), 123.58 (Ar), 116.81 (CN), 55.73 (CH), 33.51 (CH). Anal. Calcd. for $C_{17}H_{10}N_2O_4$: C, 66.67; H, 3.29; N, 9.15. Found: C, 66.75; H, 3.28; N, 9.11.

2.1.13 2-(1,3-Dioxoindan-2-yl)-2-(4-(trifluoromethyl)phenyl) acetonitrile (2m): Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.93 (m, 2H, ArH), 7.88–7.83 (m, 2H, ArH), 7.5–7.53 (d, J = 1.7 Hz, 4H, ArH), 4.82–4.81 (d, J = 3.2 Hz, 1H, CH), 3.67–3.66 (d, J = 3.1 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.90 (CO), 194.73 (CO), 141.99 (Ar), 141.82 (Ar), 136.55 (Ar), 136.48 (Ar), 129.09 (Ar), 125.99 (q, J = 3.6 Hz, Ar), 123.77 (Ar), 123.73 (Ar), 117.33 (CN), 55.80 (CH), 33.61 (CH). Anal. Calcd. for $C_{18}H_{10}F_3NO_2$: C, 65.66; H, 3.06; N, 4.25. Found: C, 65.66; H, 3.06; N, 4.25.

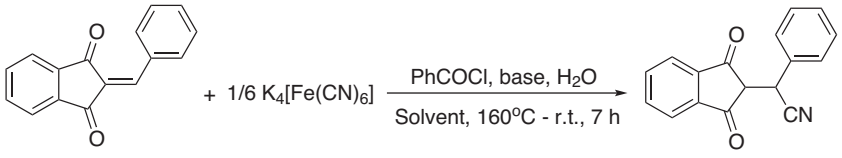
2.1.14 2-(1,3-Dioxoindan-2-yl)-2-(thiophen-2-yl)acetonitrile (2n): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98–7.95 (m, 2H, ArH), 7.85–7.83 (dd, J = 5.7, 3.0 Hz, 2H, ArH), 7.15–7.12 (m, 2H, ThH), 6.87–6.85 (dd, J = 5.1, 3.6 Hz, 1H, ThH), 5.00–4.99 (d, J = 3.2 Hz, 1H, CH), 3.63–3.62 (d, J = 3.2 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.03 (CO), 194.84 (CO), 142.35 (Ar), 142.05 (Ar), 136.35 (Ar), 136.25 (Ar), 132.17 (Th), 128.81 (Th), 127.10 (Th), 126.59 (Th), 123.68 (Ar), 123.66 (Ar), 117.29 (CN), 55.92 (CH), 29.25 (CH). Anal. Calcd. for $C_{15}H_9NO_2S$: C, 67.40; H, 3.39; N, 5.24. Found: C, 67.34; H,3.40; N, 5.27.

2.1.15 2-(1,3-Dioxoindan-2-yl)-2-(furan-2-yl)acetonitrile (2o): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01–7.99 (m, 2H, ArH), 7.88–7.86 (dd, J = 5.7, 3.0 Hz, 2H, ArH), 7.20–7.19 (d, J = 1.8 Hz, 1H, FuH), 6.44–6.43 (d, J = 4.2 Hz, 1H, FuH), 6.28–6.27 (dd, J = 3.4, 1.9 Hz, 1H, FuH), 4.85–4.84 (d, J = 3.4 Hz, 1H, CH), 3.65–3.64 (d, J = 3.3 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.72 (CO), 194.57 (CO), 143.26 (Fu), 142.01 (Ar), 141.89 (Ar), 136.27 (Ar), 136.25 (Ar), 130.11 (Ar), 128.44 (Ar), 123.70 (Fu), 115.82 (CN), 110.91 (Fu) 109.85 (Fu), 53.47 (CH), 28.19 (CH). Anal. Calcd. for $C_{15}H_9NO_3$: C, 71.71; H, 3.61; N, 5.58. Found: C, 71.63; H, 3.63; N, 5.60.

2.1.16 (*E*)-2-(1,3-Dioxoindan-2-yl)-4-phenylbut-3-enenitrile (2p): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12–8.10 (m, 1H, ArH), 8.04–7.99 (m, 2H, ArH), 7.89–7.87 (m, 2H, ArH), 7.31–7.26 (m, 4H, ArH), 6.81–6.78 (dd, J = 15.7, 1.1 Hz, 1H, =CH), 6.11–6.07 (dd, J = 15.7, 7.4 Hz, 1H, =CH), 4.31–4.29 (ddd, J = 7.4, 3.5, 1.2 Hz, 1H, CH), 3.48–3.47 (d, J = 3.5 Hz, 1H, CH). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.48 (CO), 195.36 (CO), 142.25 (Ar), 142.12 (Ar), 136.49 (Ar), 136.43 (Ar), 136.36 (Ar), 135.02 (Ar), 133.70 (Ar), 130.16 (Ar), 128.65 (Ar), 128.63 (Ar), 128.46 (=CH), 126.79 (=CH), 123.76 (Ar), 123.71 (Ar), 118.15 (CN), 54.59 (CH), 31.73 (CH). Anal. Calcd. for $C_{19}H_{13}NO_2$: C, 79.43; H, 4.56; N, 4.88. Found: C, 79.51; H, 4.53; N, 4.85.

2.1.17 2-(1,3-Dioxoindan-2-yl)-3-methylbutanenitrile (2q): Yellow liquid; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04–8.00 (m, 2H, ArH), 7.91–7.87 (m, 2H, ArH), 3.31–3.30 (d, J = 3.8 Hz, 1H, CH), 3.07–3.04 (dd, J = 9.3, 3.8 Hz, 1H, CH), 2.53–2.47 (m, 1H, CH), 1.21–1.19 (d, J = 6.7 Hz, 3H, CH_3), 1.08–1.07 (d, J = 6.7 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.89 (CO), 196.19 (CO), 142.09 (Ar), 141.83 (Ar), 136.35 (Ar), 136.22 (Ar), 123.71 (Ar), 123.64 (Ar), 118.22 (CN), 51.77 (CH), 37.03 (CH), 28.49 (CH), 21.09 (CH_3), 20.54 (CH_3). Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.07; H, 5.75; N, 6.19.

Table 1: Condition optimization for reaction of **1a** with $K_4[Fe(CN)_6]$[a].



1a **2a**

Entry	Base	Solvent	Yield (%)[b]
1	–	DMF	0
2	KOH	DMF	71
3	K_2CO_3	DMF	87
4	Cs_2CO_3	DMF	84
5	$NaHCO_3$	DMF	78
6	DBU	DMF	30
7	DABCO	DMF	47
8	Et_3N	DMF	38
9	*t*-BuOK	DMF	57
10	K_2CO_3	CH_2Cl_2	0
11	K_2CO_3	PhMe	0
12	K_2CO_3	1,4-Dioxane	0
13	K_2CO_3	DMSO	70
14	K_2CO_3	EtOH	47
15	K_2CO_3	MeCN	23

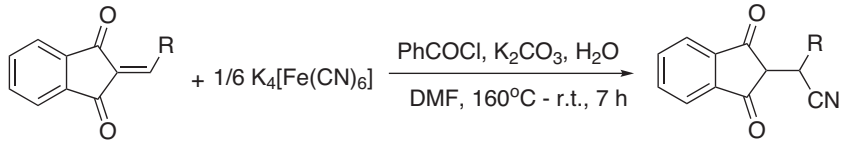
[a]Reaction conditions: $K_4[Fe(CN)_6]$ (0.2 mmol) and benzoyl chloride (1.2 mmol) were stirred at 160°C for 3 h, then **1a** (1 mmol), base (0.2 mmol) and H_2O (2 mmol) in 5 ml of solvent were added, and the mixture was stirred at room temperature for 4 h. [b]Isolated yields.

3 Results and discussion

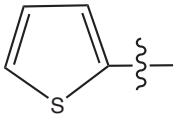
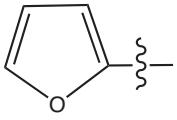
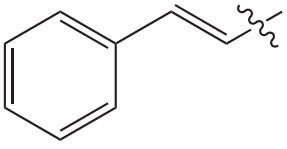
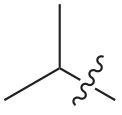
Initially, 2-benzylideneindan-1,3-dione (**1a**) was used as a substrate to examine hydrocyanation by using $K_4[Fe(CN)_6]$ as a nontoxic cyanating agent. In our previous work on the hydrocyanation of α,β-unsaturated ketones, benzoyl chloride was used to promote the reaction through the formation of an intermediate, benzoyl cyanide [80]. In this reaction, benzoyl chloride was also used as a promoter. It was found that the hydrocyanation of **1a** could take place in the presence of an appropriate base to give 2-(1,3-dioxoindan-2-yl)-2-phenylacetonitrile (**2a**). Meanwhile, for 1 equiv. of **1a**, 0.2 equiv. of $K_4[Fe(CN)_6]$ was required. That implied six CN^- of $K_4[Fe(CN)_6]$ could be fully used for this reaction.

In order to optimize the reaction conditions, we took the bases and solvents into consideration (Table 1). It was found that the reaction could not be conducted in the absence of a base (Table 1, entry 1). Inorganic bases, such as

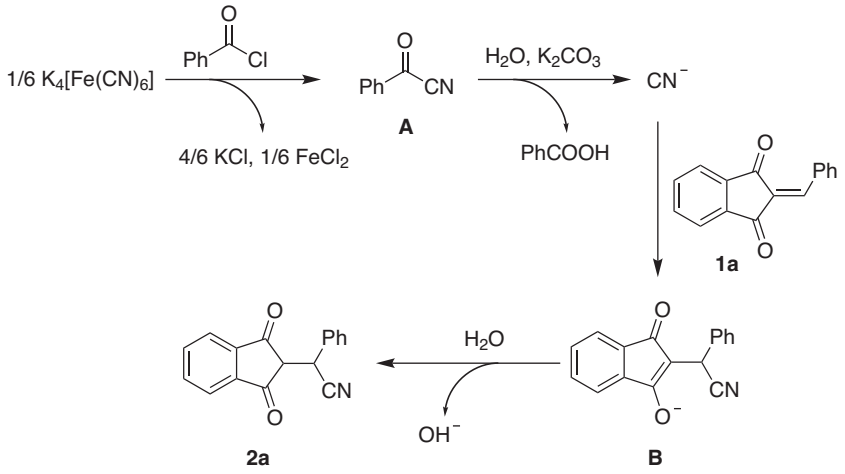
Table 2: The scope of 2-arylmethyleneindan-1,3-diones for the hydrocyanation.[a]



1a–q **2a–q**

Compound	R	Yield (%)[b]
2a	C_6H_5	87
2b	2-$CH_3C_6H_4$	89
2c	3-$CH_3C_6H_4$	93
2d	4-$CH_3C_6H_4$	95
2e	4-$CH_3OC_6H_4$	86
2f	4-OHC_6H_4	68
2g	2-FC_6H_4	57
2h	4-ClC_6H_4	73
2i	2-BrC_6H_4	76
2j	3-BrC_6H_4	84
2k	4-BrC_6H_4	80
2l	3-$O_2NC_6H_4$	49
2m	4-$CF_3C_6H_4$	89
2n		76
2o		87
2p		61
2q		66

[a]Reaction conditions: $K_4[Fe(CN)_6]$ (0.2 mmol) and benzoyl chloride (1.2 mmol) were stirred at 160°C for 3 h, then substrate **1a–q** (1 mmol), K_2CO_3 (0.2 mmol) and H_2O (2 mmol) in 5 ml of DMF were added, and the mixture was stirred at room temperature for 4 h. [b]Isolated yields.



Scheme 1: The mechanism for the hydrocyanation of **1a** with $K_4[Fe(CN)_6]$.

KOH, K_2CO_3, Cs_2CO_3 and $NaHCO_3$, could be efficiently advantageous to the formation of product **2a** (Table 1, entries 2–5), with K_2CO_3 affording the best yield (Table 1, entry 3). In contrast, organic bases, such as DBU, DABCO, Et_3N and *t*-BuOK, exhibited a poor effect on the reaction, and only a mediate yield of **2a** was afforded (Table 1, entries 6–9).

The solvent also had a significant effect on the reaction. Reaction in CH_2Cl_2, PhMe and 1,4-dioxane could not give any product (Table 1, entries 10–12). In contrast, reaction in DMSO, EtOH and MeCN could produce the corresponding product in medium to high yield (Table 1, entries 13–15). However, DMF exhibited the best effect on the reaction, giving **2a** in 87% of yield (Table 1, entry 3).

With the optimal conditions on hand, we turned our focus to unearth the generality of the method to access hydrocyanation of 2-arylmethyleneindan-1,3-diones with $K_4[Fe(CN)_6]$ using benzoyl chloride as a promoter and potassium carbonate as a base in DMF, and the results are shown in Table 2. It was found that the reactions could tolerate a wide range of functional groups including electron-donating and electron-withdrawing groups on aromatic rings. 2-Arylmethyleneindan-1,3-diones bearing electron-donating groups (Me, MeO and OH) on aromatic rings afforded the corresponding products in higher yield (Table 2, **2b**–**2f**). In contrast, 2-arylmethyleneindan-1,3-diones bearing electron-withdrawing groups (F, Cl, Br, NO_2 and CF_3) on aromatic rings afforded a slightly lower yield (Table 2, **2g**–**2m**). Gratifyingly, substrates containing heteroaryl, such as thienyl and furyl, were also transformed into the desired products in high yield (Table 2, **2n**, **2o**). In addition, the substrates including conjugate diene bonds could regioselectively conduct 1,4-addition to give the corresponding product in good yield (Table 2, **2p**). The reaction could also extend to the substrate bearing aliphatic moiety to give the corresponding product in good yield (Table 2, **2q**).

A plausible mechanism for the hydrocyanation of **1a** using $K_4[Fe(CN)_6]$ as a nontoxic cyanating agent is shown in Scheme 1. First, $K_4[Fe(CN)_6]$ reacts with benzoyl chloride to produce benzoyl cyanide (**A**) as an intermediate, which can be isolated and characterized [80]. Then, **A** is attacked by water under the condition of potassium carbonate as a base to afford cyanide ion *in situ*, which further reacts with **1a** by Michael addition to form intermediate **B**. The protonation of **B** by water yields the final product **2a**.

4 Conclusions

In conclusion, an efficient method for the hydrocyanation of 2-arylmethyleneindan-1,3-diones using $K_4[Fe(CN)_6]$ as a nontoxic cyanating agent by a one-pot procedure has been developed. The use of nontoxic and inexpensive cyanating agent, high yield and simple workup procedures are the features of this protocol. The products synthesized because of the inclusion of cyano groups, and indan-1,3-dione scaffolds will find potential applications in important organic synthesis and medicinal and material chemistry.

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