

## Sodium Bis(trimethylsilyl)amide in the "One-Flask" Transformation of Aromatic Esters to Nitriles

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**Abstract:** A new "one-flask" method was developed for the conversion of aromatic esters to the corresponding nitriles by use of sodium bis(trimethylsilyl)amide.

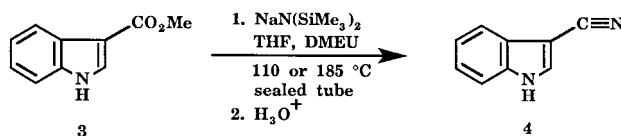
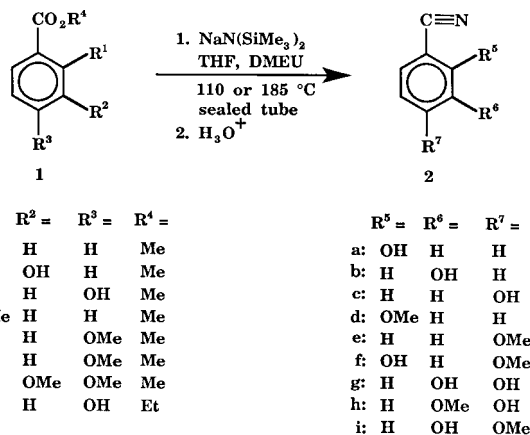
**Key words:** sodium bis(trimethylsilyl)amide, esters, nitriles, one-flask, 1,2-elimination

The hindered base, sodium bis(trimethylsilyl)amide [NaN(SiMe<sub>3</sub>)<sub>2</sub>], is frequently used in the deprotonation of organic compounds.<sup>1</sup> This commercially available reagent can also function as a nucleophile for the cleavage of alkyl aryl ethers.<sup>2</sup> It possesses the ability to monodemethylate dimethoxybenzene derivatives selectively.<sup>2</sup> The selectivity comes from the steric congestion and the  $\alpha$ -stabilizing effect of the silyl groups.

Organic nitriles are traditionally synthesized from the corresponding carboxylic acids by ultimate dehydration of the corresponding amide intermediates.<sup>3</sup> The transformations consist of two steps or more, and isolation of intermediates is required. Several "one-flask" methods have been reported for the conversion of carboxylic acids to nitriles.<sup>4-6</sup> Acyl chlorides can also be converted to nitriles by sulfonamide in a "one-flask" reaction.<sup>7</sup> To the best of our knowledge, only two methods have been documented for the direct conversion of esters to nitriles.<sup>8</sup> Firstly, Weinreb et al.<sup>9</sup> used freshly prepared dimethylaluminum amide for the transformation; the aluminum reagent is neither commercially available nor stable.<sup>9</sup> Secondly, Rao et al.<sup>10</sup> converted silyl esters to nitriles in 40–80% yields by using P<sub>2</sub>O<sub>5</sub> and HN(SiMe<sub>3</sub>)<sub>2</sub>. Herein we report our new findings on the application of the commercially available alkali amide NaN(SiMe<sub>3</sub>)<sub>2</sub> for a "one-flask" transformation of aromatic esters to nitriles (Scheme 1). The yields were good to excellent.

To search for the optimum conditions, we carried out reactions by varying the solvent, including toluene, 1,3-dimethylimidazolidin-2-one (DMEU), THF, and diethyl ether, and the reaction temperature between 100 and 200°C. A reliable procedure for the generation of nitriles involved treatment of an aromatic ester with 2.5 equivalents of NaN(SiMe<sub>3</sub>)<sub>2</sub> in a mixture of THF and DMEU in a sealed tube at 110 or 185 °C for 24 hours. The esters included methyl salicylate (**1a**), methyl 3-hydroxybenzoate (**1b**), methyl 4-hydroxybenzoate (**1c**), methyl 2-methoxybenzoate (**1d**), methyl 4-methoxybenzoate (**1e**), methyl 4-methoxysalicylate (**1f**), methyl 3,4-dimethoxybenzoate (**1g**), ethyl 4-hydroxybenzoate (**1h**), and methyl indole-3-carboxylate (**3**). The results are summarized in the Table.

The use of an excess of NaN(SiMe<sub>3</sub>)<sub>2</sub> (5.0 equiv) at 185 °C to react with **1g** produced 3,4-dihydroxybenzonitrile (**2g**) and 4-hydroxy-3-methoxybenzonitrile (**2h**) in 86% over-



Scheme 1

all yields (**2g/2h** 2.7:1). Thus, *O*-demethylation of the ether components depends on the reaction temperature and the amount of NaN(SiMe<sub>3</sub>)<sub>2</sub> applied.

The synthetic strategy is applicable to aromatic esters that bear an electron-donating group, such as hydroxy and methoxy functionalities (i.e., **1a–h**, see the Table). It can also be extended to heteroaryl methyl esters, such as methyl indole-3-carboxylate (**3**). Nevertheless, under the same conditions, methyl benzoate without any substituent cannot be converted to the corresponding nitriles. The results indicate the essential role associated with the electron-donating substituents, such as OH and OMe groups, on the benzene ring.

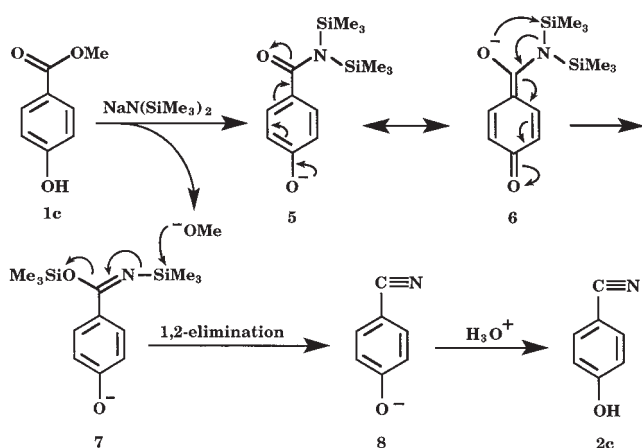
A plausible mechanism for the conversion of aromatic esters to nitriles is illustrated in Scheme 2 by use of **1c** as a representative example. During the amide formation, the hydroxy proton is removed by NaN(SiMe<sub>3</sub>)<sub>2</sub>. For related methoxy derivatives (such as **1d**, **1e**, and **1g**), demethylation by NaN(SiMe<sub>3</sub>)<sub>2</sub> can take place in situ.<sup>7</sup> The resultant amide phenoxide **5** has a canonical form **6**, in which an oxide center is close to the silicon atom. Thus silyl migration can proceed easily.<sup>11, 12</sup> Then a 1,2-elimination occurs to the silylimidate **7** to form product **2c** through protonation of the intermediate **8**.

In conclusion, an efficient way was developed for the conversion of aromatic esters to nitriles in good to excellent

**Table.** Conversion of Aromatic Esters to the Corresponding Nitriles with  $\text{NaN}(\text{SiMe}_3)_2$  (2.5 Equiv) in a Mixture of THF and DMEU at 110 or 185 °C

Aromatic Ester	Nitrile	Yield (%)	
		110 °C	185 °C
methyl salicylate ( <b>1a</b> )	2-hydroxybenzonitrile ( <b>2a</b> )	81	85
methyl 3-hydroxybenzoate ( <b>1b</b> )	3-hydroxybenzonitrile ( <b>2b</b> )	78	85
methyl 4-hydroxybenzoate ( <b>1c</b> )	4-hydroxybenzonitrile ( <b>2c</b> )	88	93
methyl 2-methoxybenzoate ( <b>1d</b> )	2-hydroxybenzonitrile ( <b>2a</b> ) + 2-methoxybenzonitrile ( <b>2d</b> )	60 22	83 0
	4-hydroxybenzonitrile ( <b>2c</b> ) + 4-methoxybenzonitrile ( <b>2e</b> )	59 26	86 0
methyl 4-methoxybenzoate ( <b>1e</b> )	2-hydroxybenzonitrile ( <b>2a</b> ) + 4-methoxybenzonitrile ( <b>2e</b> )	80 90	90 0
	3,4-dihydroxybenzonitrile ( <b>2g</b> ) + 4-hydroxy-3-methoxybenzonitrile ( <b>2h</b> ) + 3-hydroxy-4-methoxybenzonitrile ( <b>2i</b> )	0 55 18	63 23 0
ethyl 4-hydroxybenzoate ( <b>1h</b> )	4-hydroxybenzonitrile ( <b>2c</b> )	80	87
methyl indole-3-carboxylate ( <b>3</b> )	3-cyanoindole ( <b>4</b> )	75	81

<sup>a</sup> Use of 5.0 equiv of  $\text{NaN}(\text{SiMe}_3)_2$



**Scheme 2**

yields (73–93%). It involves the use of commercially available sodium bis(trimethylsilyl)amide; the aromatic esters need to have a hydroxy or methoxy substituent. The extent of *O*-demethylation of the ether moieties in the substrate during the course of the reactions depends on the temperature and the amount of  $\text{NaN}(\text{SiMe}_3)_2$  applied.

EtOAc and hexanes were purchased from Mallinckrodt Chemical Co. EtOAc and hexanes were dried and distilled from  $\text{CaH}_2$ . 1,3-Dimethyl-2-imidazolidinone (DMEU) from Aldrich was dried and distilled from  $\text{CaH}_2$  under reduced pressure and stored in serum-capped bottles over molecular sieves 4A under argon. The following compounds were purchased from Aldrich Chemical Co.: ethyl 4-hydroxybenzoate, methyl 3,4-dimethoxybenzoate, methyl 3-hydroxybenzoate, methyl 4-hydroxybenzoate, methyl indole-3-carboxylate, methyl 2-methoxybenzoate, methyl 4-methoxybenzoate, methyl salicylate, methyl 4-methoxysalicylate, and  $\text{NaN}(\text{SiMe}_3)_2$ .

An explosion-proof oven from Blue M. Electric Co. and the Pyrex combustion tubes (8 × 10 × 200 mm) from Tung Kuang Glassware Industrial Corp. were used to carry out experiments that required high temperature (e.g., 185 °C). Mps were obtained by a Büchi 535 melting point apparatus. Analytical TLC was performed on precoated plates (silica gel 60 F-254), purchased from Merck Inc. Mixtures of EtOAc and hexanes were used as eluants. GC analyses were performed on a Hewlett-Packard 5890 Series II instrument equipped with a 25-m cross-linked methyl silicone gum capillary column (0.32 mm i.d.). Nitrogen was used as a carrier gas and the flow rate was kept constant at 14.0 mL/min. The retention time  $t_R$  was measured under the following conditions: injector temperature 260 °C, the initial temperature for column 70 °C, duration 2.00 min, increment rate 10 °C/min, and the final temperature for column 250 °C. GC and low resolution MS analyses were performed on a Hewlett-Packard 5890 Series II instrument equipped with a Hewlett-Packard 5971A Mass Selective Detector and a capillary HP-1 column. Purification by gravity column chromatography was carried out by use of Merck Reagents Silica Gel 60 (particle size 0.063–0.200 mm, 70–230 mesh ASTM).

IR spectra were measured on a Bomem Michelson Series FT-IR spectrometer. The wavenumbers reported are referenced to the polystyrene 1601  $\text{cm}^{-1}$  absorption. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; w, weak. Proton NMR spectra were obtained on a Varian Unity-400 (400 MHz) spectrometer or a Varian Gemini-300 (300 MHz) spectrometer by use of  $\text{CDCl}_3$  as solvent and TMS as internal standard.  $^{13}\text{C}$  NMR spectra were obtained on a Varian Unity-400 (100 MHz) spectrometer or a Varian Gemini-300 (75 MHz) spectrometer by use of  $\text{CDCl}_3$  as solvent.  $^{13}\text{C}$  chemical shifts are referenced to the center of the  $\text{CDCl}_3$  triplet ( $\delta = 77.0$ ). Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; *J*, coupling constant (Hz).

#### Standard Procedure for the Conversion of Aromatic Esters to Nitriles:

A solution containing an ester in DMEU was transferred into a Pyrex combustion tube under argon. 1.0 M  $\text{NaN}(\text{SiMe}_3)_2$  in THF was injected into the tube, which was then sealed by torch and heated in an oven at 110 or 185 °C for 24 h. The reaction mixture was then diluted with 10% HCl (6.0 mL), and extracted with  $\text{Et}_2\text{O}$  (3 × 15 mL). The combined ethereal solutions were washed with water (30 mL) and sat. brine (20 mL). The combined organic extracts were dried ( $\text{MgSO}_4$ ), filtered, and concentrated under reduced pressure. The residue was column chromatographed (silica gel, 2.2 cm × 16 cm column) to provide the desired product.

#### 2-Hydroxybenzonitrile (**2a**):

The standard procedure was followed by use of methyl salicylate (**1a**; 123 mg, 0.809 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (2.0 mL, 2.0 mmol, 2.5 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel; 40% EtOAc/hexanes) to give pure **2a** (81.9 mg, 85%) as a colorless solid; <sup>13a</sup> mp 94–95 °C (MeOH) (lit.<sup>13b</sup> mp 92–95 °C); GC  $t_R$  8.82 min; TLC  $R_f$  0.36 (40% EtOAc/hexanes).

IR (neat):  $\nu = 3264, 2232, 1560, 1503, 1454 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.16$  (br s, 1 H, OH), 6.95–7.04 (m, 2 H, ArH-3 + ArH-5), 7.45–7.51 (m, 2 H, ArH-4 + ArH-6).

MS:  $m/z$  (%) = 119 ( $\text{M}^+$ , 100), 92 (10), 91 (79), 75 (3), 64 (27), 63 (20), 52 (9).

The same reaction was repeated at 110 °C and the results are listed in the Table.

### 3-Hydroxybenzoxonitrile (2b):

The standard procedure was followed by use of methyl 3-hydroxybenzoate (**1b**; 105 mg, 0.691 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (1.7 mL, 1.7 mmol, 2.5 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2b** (69.9 mg, 85%) as a colorless solid;<sup>13a</sup> mp 80–81 °C (MeOH) (lit.<sup>13b</sup> mp 79–81 °C); GC  $t_R$  12.56 min; TLC  $R_f$  0.40 (40% EtOAc/hexanes).

IR (neat):  $\nu = 3307, 2242, 1586, 1481, 1286 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 5.46$  (br s, 1 H, OH), 7.11–7.15 (m, 2 H, ArH-2 + ArH-4), 7.21 (d,  $J = 8.4$  Hz, 1 H, ArH-6), 7.33 (dd,  $J = 8.4, 8.4$  Hz, 1 H, ArH-5).

MS:  $m/z$  (%) = 119 ( $M^+$ , 100), 91 (22), 65 (12), 64 (17), 51 (10).

The same reaction was repeated at 110 °C and the results are listed in the Table.

### 4-Hydroxybenzoxonitrile (2c):

The standard procedure was followed by use of methyl 4-hydroxybenzoate (**1c**; 132 mg, 0.868 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (2.2 mL, 2.2 mmol, 2.5 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2c** (96.0 mg, 93%) as a colorless solid;<sup>13a</sup> mp 111–112 °C (MeOH) (lit.<sup>13b</sup> mp 110–113 °C); GC  $t_R$  11.43 min; TLC  $R_f$  0.35 (40% EtOAc/hexanes).

IR (neat):  $\nu = 3218, 2229, 1613, 1597, 1514, 1449, 1436, 1379, 1326 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.30$  (br s, 1 H, OH), 6.93 (d,  $J = 8.8$  Hz, 2 H, ArH-3 + ArH-5), 7.53 (d,  $J = 8.8$  Hz, 2 H, ArH-2 + ArH-6). MS:  $m/z$  (%) = 119 ( $M^+$ , 100), 91 (21), 64 (20), 63 (25), 61 (10), 51 (11).

The same reaction was repeated at 110 °C and the results are listed in the Table. In addition, the standard procedure was followed by use of ethyl 4-hydroxybenzoate (**1h**; 118 mg, 0.711 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (1.8 mL, 1.8 mmol, 2.5 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2c** (73.6 mg, 87%) as a colorless solid.

Furthermore, the same reaction was repeated at 110 °C and the results are listed in the Table.

### 2-Methoxybenzoxonitrile (2d):

The standard procedure was followed by use of methyl 2-methoxybenzoate (**1d**; 116 mg, 0.699 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (1.7 mL, 1.7 mmol, 2.5 equiv), and DMEU (0.50 mL) at 110 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2a** (49.9 mg, 60%) as a colorless solid and **2d** (20.5 mg, 22%) as a colorless liquid.<sup>13b</sup>

**2d**: GC  $t_R$  9.96 min; TLC  $R_f$  0.43 (40% EtOAc/hexanes).

IR (neat):  $\nu = 3080, 3015, 2975, 2949, 2843, 2228, 1599, 1580, 1494, 1465, 1437 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.94$  (s, 3 H,  $\text{OCH}_3$ ), 6.97–7.03 (m, 2 H, ArH-3 + ArH-5), 7.53–7.57 (m, 2 H, ArH-4 + ArH-6).

MS:  $m/z$  (%) = 133 ( $M^+$ , 100), 105 (62), 104 (100), 90 (49), 76 (15), 75 (14), 63 (24).

The same reaction was repeated at 185 °C and the results are listed in the Table.

### 4-Methoxybenzoxonitrile (2e):

The standard procedure was followed by use of methyl 4-methoxybenzoate (**1e**; 134 mg, 0.807 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (2.0 mL, 2.0 mmol, 2.5 equiv), and DMEU (0.50 mL) at 110 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2c** (56.6 mg, 59%) as a colorless solid and **2e** (27.9 mg, 26%) as a yellow solid.<sup>13a</sup>

**2e**: mp 56–57 °C (MeOH) (lit.<sup>13b</sup> mp 57–59 °C); GC  $t_R$  7.85 min; TLC  $R_f$  0.41 (40% EtOAc/hexanes).

IR (neat):  $\nu = 2949, 2724, 2580, 2231, 1604, 1591, 1503, 1455 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.93$  (s, 3 H,  $\text{CH}_3$ ), 7.06 (d,  $J = 8.8$  Hz, 2 H, ArH-3 + ArH-5), 8.71 (d,  $J = 8.8$  Hz, 2 H, ArH-2 + ArH-6).

MS:  $m/z$  (%) = 133 ( $M^+$ , 68), 105 (62), 104 (100), 90 (55), 76 (14), 75 (12), 64 (19), 63 (19).

The same reaction was repeated at 185 °C and the results are listed in the Table.

### 2-Hydroxy-4-methoxybenzoxonitrile (2f):<sup>14</sup>

The standard procedure was followed by use of methyl 4-methoxysalicylate (**1f**; 142 mg, 0.780 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (2.0 mL, 2.0 mmol, 2.5 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2f** (105 mg, 90%) as a colorless solid; mp 111–112 °C (MeOH) (lit.<sup>14</sup> mp 111–113 °C); GC  $t_R$  11.65 min; TLC  $R_f$  0.36 (50% EtOAc/hexanes).

IR (neat):  $\nu = 3219, 2228, 1613, 1514, 1326, 1278, 1213 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.79$  (s, 3 H,  $\text{CH}_3$ ), 6.43 (d,  $J = 8.8$  Hz, 1 H, ArH-5), 6.52 (s, 1 H, ArH-3), 7.36 (d,  $J = 8.8$  Hz, 1 H, ArH-6).

MS:  $m/z$  (%) = 149 ( $M^+$ , 100), 134 (9), 106 (67), 92 (13), 91 (38), 79 (13), 63 (14), 52 (12), 51 (12).

The same reaction was repeated at 110 °C and the results are listed in the Table.

### 3,4-Dihydroxybenzoxonitrile (2g)<sup>15</sup> and 4-Hydroxy-3-methoxybenzoxonitrile (2h):

The standard procedure was followed by use of methyl 3,4-dimethoxybenzoate (**1g**; 113 mg, 0.577 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (2.8 mL, 2.8 mmol, 5.0 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel, 40% EtOAc/hexanes) to give pure **2g** (49.1 mg, 63%) as a yellow solid and **2h** (19.8 mg, 23%) as a yellow solid.

**2g**: mp 155–157 °C (MeOH) (lit.<sup>15</sup> mp 153–155 °C); TLC  $R_f$  0.30 (50% EtOAc/hexanes).

IR (neat):  $\nu = 3276, 2228, 1603, 1519, 1444, 1284, 1115 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 6.89$  (d,  $J = 8.8$  Hz, 1 H, ArH-5), 7.05 (d,  $J = 8.8$  Hz, 1 H, ArH-6), 7.13 (s, 1 H, ArH-2).

MS:  $m/z$  (%) = 135 ( $M^+$ , 100), 117 (12), 106 (11), 89 (38), 79 (10), 62 (28), 52 (25), 51 (22).

**2h**: mp 87–88 °C (MeOH) (lit.<sup>13b</sup> mp 85–87 °C); GC  $t_R$  11.67 min; TLC  $R_f$  0.45 (50% EtOAc/hexanes).

IR (neat):  $\nu = 3364, 2955, 2225, 1599, 1515, 1458, 1423, 1271 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.93$  (s, 3 H,  $\text{CH}_3$ ), 6.98 (d,  $J = 8.0$  Hz, 1 H, ArH-5), 7.09 (s, 1 H, ArH-2), 7.23 (d,  $J = 8.0$  Hz, 1 H, ArH-6).

MS:  $m/z$  (%) = 149 ( $M^+$ , 91), 134 (100), 106 (80), 77 (8), 63 (9), 51 (16).

### 3-Hydroxy-4-methoxybenzoxonitrile (2i):<sup>16</sup>

The standard procedure was followed by use of methyl 3,4-dimethoxybenzoate (**1g**; 102 mg, 0.520 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (2.6 mL, 2.6 mmol, 5.0 equiv), and DMEU (0.50 mL) at 110 °C. The reaction products were purified by column chromatography (silica gel, 50% EtOAc/hexanes) to give pure **2h** (42.7 mg, 55%) as a yellow solid<sup>13a</sup> and **2i** (13.9 mg, 18%) as a yellow solid.

**2i**: mp 129–130 °C (MeOH) (lit.<sup>16</sup> mp 130–132 °C); GC  $t_R$  12.03 min; TLC  $R_f$  0.42 (50% EtOAc/hexanes).

IR (neat):  $\nu = 3385, 3078, 3027, 2984, 2950, 2227, 1732, 1605, 1591, 1515, 1458, 1447, 1421, 1378 \text{ cm}^{-1}$ .

<sup>1</sup>H NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta = 3.97$  (s, 3 H,  $\text{CH}_3$ ), 5.74 (bs, 1 H, OH), 6.89 (d,  $J = 8.8$  Hz, 1 H, ArH-5), 7.17 (s, 1 H, ArH-2), 7.19 (d,  $J = 8.8$  Hz, 1 H, ArH-6).

MS:  $m/z$  (%) = 149 ( $M^+$ , 100), 134 (10), 119 (23), 107 (17), 106 (73), 92 (16), 91 (44), 78 (14), 77 (10), 63 (16), 51 (10).

### 3-Cyanoindole (4):

The standard procedure was followed by use of methyl indole-3-carboxylate (**3**; 115 mg, 0.657 mmol, 1.0 equiv),  $\text{NaN}(\text{SiMe}_3)_2$  (1.6 mL, 1.6 mmol, 2.5 equiv), and DMEU (0.50 mL) at 185 °C. The reaction products were purified by column chromatography (silica gel, 40%

EtOAc/hexanes) to give pure **4** (75.6 mg, 81%) as a white solid;<sup>13a</sup> mp 178–179 °C (MeOH) (lit.<sup>13b</sup> mp 179–182 °C); GC  $t_R$  16.32 min; TLC  $R_f$  0.35 (40% EtOAc/hexanes).

IR (neat):  $\nu$  = 3260, 2995, 2223, 1769, 1758, 1523, 1432, 1241  $\text{cm}^{-1}$ . <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$  + CDCl<sub>3</sub>):  $\delta$  = 7.24–7.31 (m, 2 H, ArH-5 + ArH-6), 7.49 (d,  $J$  = 7.2 Hz, 1 H, ArH-4), 7.73 (s, 1 H, ArH-2), 7.74 (d,  $J$  = 8.0 Hz, 1 H, ArH-7), 11.06 (br s, 1 H, NH).

MS:  $m/z$  (%) = 142 ( $M^+$ , 100), 115 (51), 114 (40), 88 (31), 87 (22), 76 (14), 75 (12), 63 (23), 62 (22), 52(21), 51 (16).

The same reaction was repeated at 110 °C and the results are listed in the Table.

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