Supporting Information
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Supporting Information for

The Highly Efficient 1,4-Addition of Me₃SiCN to Aromatic Enones Catalyzed by CsF with Water as the Additive

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General: ¹H NMR spectra are recorded on a Bruker AVIII 400 spectrometer, operating at 400 MHz for ¹H NMR, and 100 MHz for ¹³C NMR. Chemical shifts for ¹H NMR and ¹³C NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe₄ and relative to the signal of chloroform-d. The IR spectra are recorded on a PerkinElmer Spectrum One with KBr pellets. The elemental analyses are performed on an Elementar Vario MICRO CUBE instrument. All melting points are determined on a XT4A melting point apparatus and uncorrected. Analytical thin layer chromatography (TLC) is performed using F254 pre-coated silica gel plate. Subsequent to elution, plates are visualized using UV irradiation (254 nm). Column chromatography is performed with silica gel (200-300 mesh). Petroleum ether (PE) has a boiling point range of 60-90 °C.

All reactions are carried out under argon atmosphere using typical vacuum-line techniques unless otherwise noted. Me₃SiCN and CsF are purchased from Alfa Aesar and used directly. Dioxane and THF were dried and distilled from sodium/benzophenone under argon prior to use. Substrates (1a-j) are synthesized according to reported procedure¹.
Optimization of reaction conditions:

Table S-1. Optimization of Reaction Conditions

<table>
<thead>
<tr>
<th>entry</th>
<th>cat (mol%)</th>
<th>additive (equiv)</th>
<th>concn (M)</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
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<td>1</td>
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<tr>
<td>6</td>
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<td>CsF(20)</td>
<td>H₂O(4)</td>
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<tr>
<td>13</td>
<td>CsF(1)</td>
<td>H₂O(4)</td>
<td>0.3 reflux</td>
<td>4</td>
<td>99</td>
<td></td>
</tr>
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</table>

*a* Unless otherwise noted, all reactions are conducted with 0.15 mmol (0.1 M) or 0.3 mmol (0.3 M) of chalcone (1a) in dioxane under argon. *b* Quantity relative to 1a. *c* Isolated yield. *d* Performed in THF. *e* Performed in toluene. *f* Comparable results are obtained under open-to-air condition.

Optimization of reaction conditions are conducted with chalcone (1a) and Me₃SiCN (Table S-1). Initially, various fluorides as catalysts are examined in dioxane at reflux temperature. 41% yield is obtained with 20 mol% KF·2H₂O (entry 1). Bu₄NF gives 75% yield (entry 2). CsF make the reaction proceeding smoothly to afford the product 2a in 92% yield (entry 3). The product is obtained in 16% yield when CsCl is used as catalyst (entry 4). Subsequently, solvent and temperature are changed. The yield is sharply decreasing in THF or toluene (entries 5 and 6), or at lower temperature (entry 7). Decreasing CsF loading, yield also decreases (entries 8 and 9). Yield is obviously decreased at high concentration of 1a even for a long reaction time (entry 10). The excellent yield is obtained even at high concentration with only 1 mol% CsF and 4 equiv of H₂O (entries 11-13). The reactions proceed cleanly without any by-products.
Typical procedure for the 1,4-addition of Me₃SiCN to aromatic enones 1a-1j:

After CsF (0.5 mg, 0.003 mmol, 1 mol%), enones (1) (0.3 mmol), 1 mL dioxane are added into a dry Schlenk tube equipped with cold finger under argon, Me₃SiCN (84 μL, 0.66 mmol, 2.2 equiv), H₂O (22 μL, 1.2 mmol, 4 equiv) are added. The reaction mixture is stirred at reflux temperature until the reaction is completed (monitored by TLC). 1 M HCl (0.3 mL) is added to quench the reaction with additional 20 min stirring at room temperature. The resulting mixture is extracted with ethyl acetate (5 mL) (Caution! HCN generated in the reaction mixture is highly toxic. Those operations should be conducted in a well-ventilated hood). The extract is washed with water, brine, dried over anhydrous Na₂SO₄, and concentrated. The crude product is purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 20:1, v/v, unless otherwise noted) to afford pure products (2).

4-Oxo-2,4-diphenylbutanenitrile (2a): white solid, 99% yield; mp 120-122 °C (lit. 2 mp 122-125 °C); ¹H NMR (400 MHz, CDCl₃) δ: 3.52 (dd, J = 6.0, 18.0 Hz, 1H, NCCHCH₃H₃CO), 3.74 (dd, J = 8.0, 18.0 Hz, 1H, NCCHCH₃H₃CO), 4.57 (dd, J = 6.0, 8.0 Hz, 1H, NCCHCH₃H₃CO), 7.34-7.49 (m, 7H, ArH), 7.58-7.62 (m, 1H, ArH), 7.92-7.94 (m, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃) δ: 31.9, 44.5, 120.6, 127.5, 128.1, 128.4, 128.8, 129.3, 133.9, 135.3, 135.8, 194.6; IR (KBr, cm⁻¹): ν 1681, 2236.

2-(2-Methoxyphenyl)-4-oxo-4-phenylbutanenitrile (2b): white solid, 99% yield; mp 84-86 °C; ¹H NMR (400 MHz, CDCl₃) δ: 3.50 (dd, J = 4.8, 18.0 Hz, 1H, NCCHCH₃H₃CO), 6.91-7.02 (m, 2H, ArH), 7.31-7.35 (m, 1H, ArH), 7.56-7.61 (m, 1H, ArH), 7.93-7.95 (m, 2H, ArH); ¹³C NMR (100 MHz, CDCl₃) δ: 27.5, 42.2, 55.6, 111.0, 120.5, 121.1, 123.2, 128.1, 128.7, 129.0, 129.8, 133.6, 136.0, 156.3, 195.3; IR (KBr, cm⁻¹): ν 1685, 2245.
2-(3-Methoxyphenyl)-4-oxo-4-phenylbutanenitrile (2c): white solid, 99% yield; mp 106-108 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 3.50 (dd, \(J = 6.0, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 3.72 (dd, \(J = 8.0, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 3.82 (s, 3H, OCH\(_3\)), 4.55 (dd, \(J = 6.0, 8.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 6.86-6.88 (m, 1H, ArH), 6.96-7.02 (m, 2H, ArH), 7.28-7.32 (m, 1H, ArH), 7.45-7.49 (m, 2H, ArH), 7.58-7.62 (m, 1H, ArH), 7.92-7.94 (m, 2H, ArH); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 31.9, 44.5, 55.4, 113.3, 113.8, 119.6, 120.5, 128.1, 128.8, 133.9, 135.8, 136.7, 160.2, 194.6; IR (KBr, cm\(^{-1}\)): \(\nu\) 1678, 2236.

2-(4-Methoxyphenyl)-4-oxo-4-phenylbutanenitrile (2d): white solid, 99% yield; mp 111-113 °C (lit.\(^2\) mp 113-114 °C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 3.50 (dd, \(J = 6.4, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 3.73 (dd, \(J = 7.6, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 3.80 (s, 3H, OCH\(_3\)), 4.53 (dd, \(J = 6.4, 7.6\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 6.89-6.92 (m, 2H, ArH), 7.33-7.36 (m, 2H, ArH), 7.45-7.49 (m, 2H, ArH), 7.57-7.61 (m, 1H, ArH), 7.91-7.93 (m, 2H, ArH); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 31.2, 44.6, 55.4, 114.6, 120.9, 127.2, 128.1, 128.7, 133.8, 135.8, 159.6, 194.7; IR (KBr, cm\(^{-1}\)): \(\nu\) 1677, 2234.

4-Oxo-4-phenyl-2-p-tolylbutanenitrile (2e): white solid, 99% yield; mp 129-131 °C (lit.\(^2\) mp 135-137 °C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 2.35 (s, 3H, CH\(_3\)), 3.49 (dd, \(J = 6.4, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 3.70 (dd, \(J = 8.0, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 4.53 (dd, \(J = 6.4, 8.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 7.19 (d, \(J = 8.0\) Hz, 2H, ArH), 7.31 (d, \(J = 8.0\) Hz, 2H, ArH), 7.45-7.48 (m, 2H, ArH), 7.57-7.61 (m, 1H, ArH), 7.91-7.93 (m, 2H, ArH); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 21.0, 31.5, 44.6, 55.4, 120.8, 127.4, 128.1, 128.8, 132.3, 133.8, 135.8, 138.3, 194.7; IR (KBr, cm\(^{-1}\)): \(\nu\) 1674, 2239.

2-(2-Chlorophenyl)-4-oxo-4-phenylbutanenitrile (2f): white solid, 99% yield; mp 100-102 °C (lit.\(^3\) mp 106-108 °C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 3.53 (dd, \(J = 4.8, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 3.68 (dd, \(J = 9.2, 18.0\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 4.93 (dd, \(J = 4.8, 9.2\) Hz, 1H, NCCHCH\(_3\)H\(_2\)CO), 7.29-7.38 (m, 2H, ArH), 7.42-7.50 (m, 3H, ArH), 7.58-7.62 (m, 1H, ArH), 7.67-7.69 (m, 1H, ArH), 7.94-7.96 (m, 2H, ArH);
$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 30.1, 42.4, 119.7, 127.8, 128.1, 128.8, 129.5, 129.9, 130.3, 132.7, 133.9, 135.6, 194.4; IR (KBr, cm$^{-1}$): $\nu$ 1686, 2247.

2-(2,4-Dichlorophenyl)-4-oxo-4-phenylbutanenitrile (2g): white solid, 99% yield; mp 90-91 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 3.52 (dd, $J = 4.8, 18.0$ Hz, 1H, NCCH$_3$H$_2$CO), 3.67 (dd, $J = 9.2, 18.0$ Hz, 1H, NCCH$_3$H$_2$CO), 4.88 (dd, $J = 4.8, 9.2$ Hz, 1H, NCCH$_3$H$_2$CO), 7.33-7.36 (m, 1H, ArH), 7.45-7.50 (m, 3H, ArH), 7.59-7.63 (m, 2H, ArH), 7.93-7.95 (m, 2H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 29.7, 42.2, 119.3, 128.08, 128.11, 128.9, 130.1, 130.5, 131.3, 133.5, 134.0, 135.3, 135.5, 194.1; IR (KBr, cm$^{-1}$): $\nu$ 1682, 2247; Anal. calcd for C$_{16}$H$_{11}$Cl$_2$NO: C, 63.18; H, 3.65; N, 4.60; found: C, 63.06; H, 3.73; N, 4.65.

2-(3-Nitrophenyl)-4-oxo-4-phenylbutanenitrile (2h): petroleum ether/ethyl acetate = 10:1, v/v. yellowish solid, 91% yield; mp 132-133 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 3.61 (dd, $J = 6.8, 18.0$ Hz, 1H, NCCH$_3$H$_2$CO), 3.80 (dd, $J = 6.8, 18.0$ Hz, 1H, NCCH$_3$H$_2$CO), 4.72 (dd, $J = 6.8, 6.8$ Hz, 1H, NCCH$_3$H$_2$CO), 7.47-7.51 (m, 2H, ArH), 7.59-7.64 (m, 2H, ArH), 7.83-7.85 (m, 1H, ArH), 7.92-7.94 (m, 2H, ArH), 8.20-8.23 (m, 1H, ArH), 8.33-8.34 (m, 1H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 31.6, 43.9, 119.5, 122.8, 123.6, 128.1, 129.0, 130.4, 133.9, 134.2, 135.3, 137.4, 148.7, 193.8; IR (KBr, cm$^{-1}$): $\nu$ 1680, 2245; Anal. calcd for C$_{16}$H$_{12}$N$_2$O$_3$: C, 68.56; H, 4.32; N, 9.99; found: C, 68.41; H, 4.45; N, 10.09.

2-(2-Chlorophenyl)-4-(4-nitrophenyl)-4-oxobutanenitrile (2i): petroleum ether/ethyl acetate = 10:1, v/v. white solid, 93% yield; mp 126-127 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 3.57 (dd, $J = 4.4, 18.0$ Hz, 1H, NCCH$_3$H$_2$CO), 3.71 (dd, $J = 9.6, 18.0$ Hz, 1H, NCCH$_3$H$_2$CO), 4.93 (dd, $J = 4.4, 9.6$ Hz, 1H, NCCH$_3$H$_2$CO), 7.33-7.40 (m, 2H, ArH), 7.44-7.46 (m, 1H, ArH), 7.69-7.71 (m, 1H, ArH), 8.10-8.13 (m, 2H, ArH), 8.32-8.35 (m, 2H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 30.0, 42.9, 119.2, 124.1, 127.9, 129.2, 129.5, 130.2, 130.4, 132.1, 132.6, 139.9, 150.8, 193.1; IR (KBr, cm$^{-1}$): $\nu$ 1691, 2252; Anal. calcd for C$_{16}$H$_{11}$ClN$_2$O$_3$: C, 61.06; H, 3.52; N, 8.90; found: C, 61.88; H, 3.84; N, 8.87.
2-Methyl-4-oxo-4-phenylbutanenitrile (2j): colorless oil, 97% yield; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 1.35 (d, $J = 6.8$ Hz, 3H, CH$_3$), 3.14 (dd, $J = 6.4$, 17.2 Hz, 1H, NCCHCH$_3$H$_2$CO), 3.27 (dd, $J = 6.4$, 13.2 Hz, 1H, NCCHCH$_3$H$_2$CO), 3.34 (m, 1H, NCCHCH$_3$H$_2$CO), 7.40-7.44 (m, 2H, ArH), 7.52-7.55 (m, 1H, ArH), 7.87-7.89 (m, 2H, ArH); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 17.9, 20.5, 42.2, 122.6, 128.0, 128.8, 133.8, 135.9, 195.1; IR (neat, cm$^{-1}$): $\nu$ 1686, 2236.

References:


$^1$H NMR and $^{13}$C NMR spectra of 2a-2j