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# Tris(pentafluorophenyl)borane-Catalyzed Formal Cyanoalkylation of Indoles with Cyanohydrins

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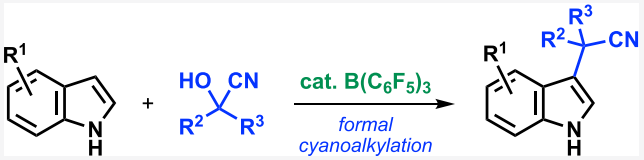
**ABSTRACT:** Despite the significant achievements related to the C3 functionalization of indoles, cyanoalkylation reactions continue to remain rather limited. We herein report on the formal C3 cyanoalkylation of indoles with cyanohydrins in the presence of a tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) catalyst. It is noteworthy that cyanohydrins are used as a cyanoalkylating reagent in the present reaction, even though they are usually used as only a HCN source. Mechanistic investigations revealed the unique reactivity of the $B(C_6F_5)_3$ catalyst in promoting the decomposition of a cyanohydrin by a Lewis acidic activation through the coordination of the cyano group to the boron center. In addition, a catalytic three-component reaction using indoles, aldehydes as a carbon unit, and acetone cyanohydrin that avoids the discrete preparation of each aldehyde-derived cyanohydrin is also reported. The developed methods provide straightforward, highly efficient, and atom-economic access to various types of synthetically useful indole-3-acetonitrile derivatives containing $\alpha$-tertiary or quaternary carbon centers.






## INTRODUCTION

Indole derivatives exhibit unique chemical and biological properties and find wide applications in the fields of organic, medicinal, and pharmaceutical chemistry.[1] Due to their great importance, significant efforts have been devoted to the development of new methodologies for the synthesis of these types of derivatives in the past decades.[2] As a result, two distinct synthetic strategies have emerged for constructing indole cores and for the functionalization of parent indoles. The vast majority of the latter strategy involves the C3 functionalization of indoles due to the nucleophilic reactivity of these molecules.[3]

Indole-3-acetonitriles comprise an important class of compounds that can be readily converted into valuable tryptamine derivatives, which are useful intermediates for the synthesis of pharmaceutically important indole alkaloids.[4−6] Despite the significant advancements that have been achieved in the C3 functionalization of indoles, methods that enable the straightforward C3 cyanoalkylation to provide indole-3-acetonitriles remain scarce. The classical approach is three-step synthesis, in which the Mannich reaction of indoles is followed by quaternization of the amine moiety and subsequent nucleophilic substitution by cyanide (Scheme 1a).[7] In 2019, the use of an iron porphyrin complex with diazoacetonitrile for direct cyanomethylation was reported (Scheme 1b).[8] However, the method involves the preparation of a hazardous diazoacetonitrile using a laborious flow system and poses some safety concerns. In addition, the above two approaches were only applied to the synthesis of simple indole-3-acetonitriles.[9] As a result, further transformations are required to access derivatives that have $\alpha$-tertiary and quaternary carbon centers.[7] Meanwhile, the indium-catalyzed three-component reaction of *N*-methylindole, a ketone (or an alkyne), and trimethylsilyl cyanide has been reported, which permits the synthesis of nitriles containing a quaternary $\alpha$-carbon center (Scheme 1c).[10] However, an excess of an indole substrate is required, and this is a significant drawback from a synthetic point of view. To develop a more efficient cyanoalkylation method, we focused on the use of readily available cyanohydrins as an ideal cyanoalkylating reagent, even though they are usually used only the HCN source.[11] The proposed reaction would involve not a direct dehydrative substitution[12] but a stepwise reaction, in which the indole first reacts with a carbonyl compound that is generated in situ from cyanohydrines, and the resulting alcohol intermediate then undergoes substitution by HCN (Scheme 1d).[13,14] Herein, we report that the use of a tris(pentafluorophenyl)borane ($B(C_6F_5)_3$) catalyst permits this formal C3 cyanoalkylation of indoles with cyanohydrins to proceed, thus providing various indole-3-acetonitrile derivatives. This unprecedented method is a highly efficient and atom-economic process, in which cyanohydrins function as a source of not only HCN but also carbonyl compounds, and only water is generated as the byproduct.

## RESULTS AND DISCUSSION

Our group recently developed several electrophilic cyanation reactions utilizing Lewis acidic boron compounds that can

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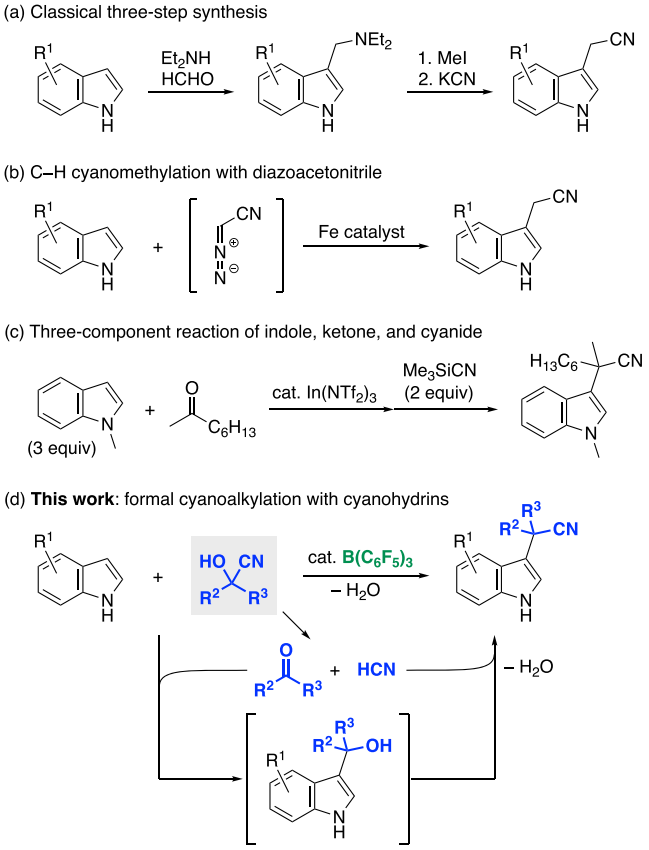
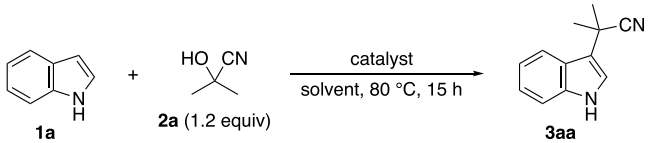
**Scheme 1. Synthetic Approaches to the Production of Indole-3-acetonitriles from Indoles**




activate a cyano group of the cyanating reagent.[15] In 2019, Oestreich et al. reported on an intriguing approach for transfer hydrocyanation using boron Lewis acids that enable isocyanide to be captured from cyclohexa-1,4-diene-based HCN surrogates.[16] Based on our previous studies and literature reports on reactions that proceed via the activation of a cyano group by a boron Lewis acid,[17] we began our investigation by screening a series of boron Lewis acid catalysts for the reaction of indole (**1a**), which was used as the limiting reagent, with acetone cyanohydrin (**2a**). The target reaction proceeded effectively when 5 mol % $B(C_6F_5)_3$ was added to the reaction mixture using MeCN as the solvent at 80 °C, affording the desired cyanoalkylated product **3aa** in nearly quantitative yield (Table 1, entry 1). Meanwhile, strong but moisture-sensitive boron Lewis acids such as $BF_3{\cdot}OEt_2$, $BCl_3$, and $BBr_3$ as well as weak Lewis acid $BPh_3$ failed to promote the reaction (entries 2–5). In the present reaction using **2a** as an alkylating reagent, the use of indium catalysts, $InCl_3$ and $In(NTf)_3$, resulted in low efficiency, even though $In(NTf)_3$ was successfully applied to a three-component reaction, as described in Scheme 1c (entries 6 and 7).[10] We also examined some commonly used Lewis acids, such as $Zn(OTf)_2$, $Cu(OTf)_2$, $Sc(OTf)_3$, and $Me_3SiOTf$, but they were ineffective for this reaction (entries 8–11). The product **3aa** was not obtained when Brønsted acids such as trifluoromethanesulfonic acid (TfOH) and *p*-toluenesulfonic acid (TsOH) were used as catalysts (entries 12 and 13).[18] No reaction was observed in the absence of a catalyst (entry 14). These results clearly demonstrate the unique and high catalytic activity of $B(C_6F_5)_3$ in this cyanoalkylation. In addition, screening a series of solvents revealed that $MeNO_2$ and 1,4-

**Table 1. Survey of Lewis Acid Catalysts and Solvents**[a]




| entry | catalyst (mol %) | solvent | yield (%)[b] |
|---|---|---|---|
| 1 | $B(C_6F_5)_3$ (5) | MeCN | >95 (85)[c] |
| 2 | $BF_3{\cdot}OEt_2$ (10) | MeCN | <5 |
| 3 | $BCl_3$ (10)[d] | MeCN | 6 |
| 4 | $BBr_3$ (10) | MeCN | <5 |
| 5 | $BPh_3$ (10) | MeCN | <5 |
| 6 | $InCl_3$ (10) | MeCN | 10 |
| 7 | $In(NTf_2)_3$ (10) | MeCN | 29 |
| 8 | $Zn(OTf)_2$ (10) | MeCN | 9 |
| 9 | $Cu(OTf)_2$ (10) | MeCN | <5 |
| 10 | $Sc(OTf)_3$ (10) | MeCN | <5 |
| 11 | $Me_3SiOTf$ (10) | MeCN | <5 |
| 12[e] | TfOH (5) | $MeNO_2$ | <5 |
| 13[e] | TsOH (5) | $MeNO_2$ | <5 |
| 14 | none | MeCN | 0 |
| 15[e] | $B(C_6F_5)_3$ (5) | $MeNO_2$ | >95 |
| 16[e] | $B(C_6F_5)_3$ (5) | 1,4-dioxane | >95 |
| 17[e] | $B(C_6F_5)_3$ (5) | toluene | 91 |
| 18[e] | $B(C_6F_5)_3$ (5) | 1,2-DCE | 75 |

[a]Reactions were performed on a 0.5 mmol scale. [b]Determined by $^1H$ NMR analysis of the crude product using 1,1,2,2-tetrachloroethane as an internal standard. [c]Isolated yield. [d]1.0 M in heptane. [e]**2a** (2 equiv) was used.

dioxane represented efficient alternatives to MeCN (entries 15 and 16), while the use of toluene and 1,2-dichloroethane (DCE) resulted in slightly lower efficiencies (entries 17 and 18).

With the optimized reaction conditions (Table 1, entry 1), we next investigated the substrate scope of indoles in $B(C_6F_5)_3$-catalyzed cyanoalkylation with acetone cyanohydrin (**2a**) (Scheme 2). A number of indoles bearing electron-donating and -withdrawing groups at the 5-position were subjected to the reaction, and all of the reactions proceeded smoothly to afford high yields of the corresponding nitriles **3** bearing an $\alpha$-quaternary carbon center (**3aa**–**3ia**). The synthetic utility of this cyanoalkylation was demonstrated by a gram-scale reaction using **1a**, which resulted in the formation of **3aa** in excellent yield (1.64 g, 89%). Although highly electron-deficient substrates with ester, cyano, and nitro groups showed low reactivity, increasing the catalyst loading to 10 mol % and the amount of **2a** was effective in improving the product yield (**3ga**–**3ia**). It is noteworthy that this catalytic reaction was also compatible with various functional groups, which include halogens (**3da**–**3fa**), ester (**3ga**), cyano (**3ha**), and nitro (**3ia**) groups. The influence of the substitution pattern of the indoles was also investigated. Substituents at the 1-, 2-, 6-, and 7-positions had little effect on reactivity, affording the corresponding products in high yields (**3ja**–**3pa**). However, a 4-methyl substituent was found to have a significant influence on reactivity. Interestingly, 4-methyl-1*H*-indole preferentially underwent *N*-alkylation to give **3qa′**,[19] rather than 3-alkylation to give **3qa**, probably due to steric hindrance. We also tested the reactivity of 3-methyl-1*H*-indole for this cyanoalkylation and found that the *N*-alkylated product **3ra′** was produced preferentially along with the 2-alkylated product **3ra** being produced in a lower yield.[20,21] Unfortunately, the method could not be successfully applied to reactions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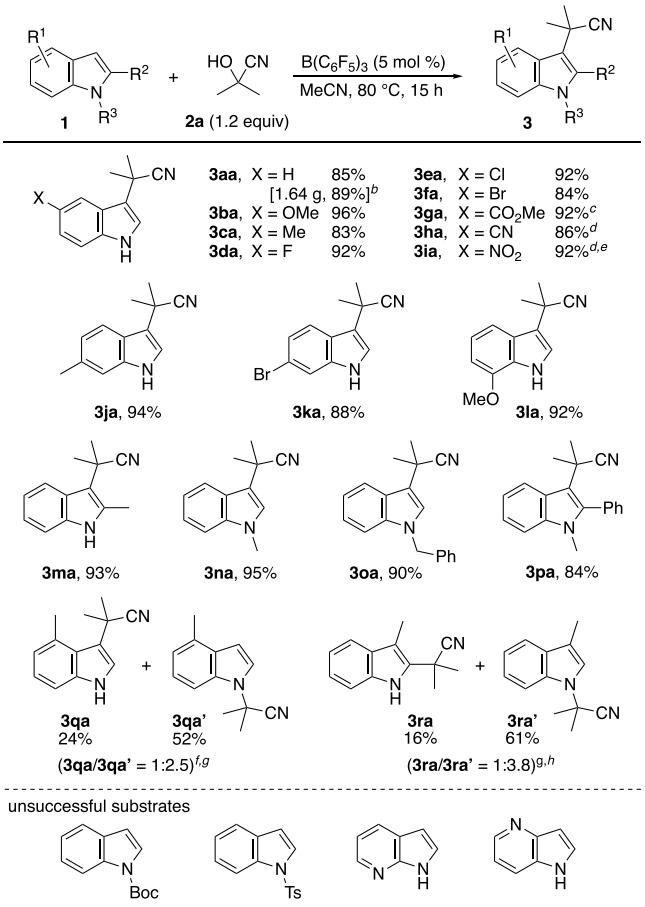
**Scheme 2. Scope and Limitation of Indoles**[a]



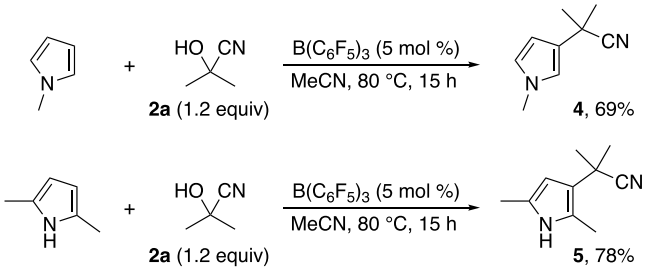

[a]Reactions were performed on a 0.5 mmol scale. Yields are isolated yields. [b]Reaction was performed on a 10 mmol scale. [c]$B(C_6F_5)_3$ (10 mol %) and **2a** (1.5 equiv) were used. The reaction was conducted for 20 h. [d]$B(C_6F_5)_3$ (10 mol %) and **2a** (2 equiv) were used. [e]$MeNO_2$ was used as a solvent. [f]$B(C_6F_5)_3$ (10 mol %) and **2a** (5 equiv) were used. [g]Determined by $^1H$ NMR analysis of the crude product. [h]**2a** (5 equiv) was used.

involving electron-deficient *N*-Boc- and *N*-Ts-protected indoles and azaindoles.

The reactivity of pyrroles toward the present cyanoalkylation was also investigated (Scheme 3). 1-Methylpyrrole and 2,5-dimethylpyrrole underwent selective C3 cyanoalkylation under the standard conditions to provide **4** and **5**, respectively, in good yields.[22] The synthesized pyrrole derivatives are potentially useful intermediates for the synthesis of pharmaceuticals.[23]

We next examined the scope of cyanohydrins for the cyanoalkylation of **1a** (Scheme 4). In addition to acetone

**Scheme 3. Cyanoalkylation of Pyrroles**




cyanohydrin (**2a**), various other types of ketone-derived cyanohydrins, such as cyclohexanone-, 1,3-diphenylacetone-, and acetophenone-derived reagents (**2b**–**2d**), were found to be applicable to the reaction, providing the corresponding cyanoalkylated products **3** in high yields. Mandelonitrile (**2e**) was also found to be efficiently coupled with **1a**, demonstrating that the method can be used to prepare $\alpha$-monosubstituted nitrile **3**. It is noteworthy that the present method allowed for the synthesis of derivatives bearing an aryl group at the $\alpha$-position (products from **2d** and **2e**) that would be difficult to access by $\alpha$-arylation of indole-3-acetonitriles. However, the use of electron-deficient 1,1,1-trifluoroacetone-derived cyanohydrin **2f**[24] as well as glycolonitrile (**2g**) resulted in almost no desired product.

We then performed several experiments to gain insights into the reaction mechanism (Scheme 5). Our hypothesis was that a cyanohydrin is decomposed in situ to form HCN and the corresponding carbonyl compounds in the initial step. To confirm this, the reaction mixture, which was prepared by mixing **2a** with 5 mol % of $B(C_6F_5)_3$ in MeCN-$d_3$ at 80 °C for 30 min, was monitored by $^1H$ NMR (Scheme 5a). In the $^1H$ NMR spectrum of the mixture, signals corresponding to acetone and HCN were observed with consumption of **2a**,[25] while most of **2a** remained in the absence of $B(C_6F_5)_3$. These results clearly demonstrate that $B(C_6F_5)_3$ promotes the decomposition of **2a**.[26] In addition, the decomposition of mandelonitrile (**2e**) to form benzaldehyde and HCN was also observed in the presence of the $B(C_6F_5)_3$ catalyst, even though the reaction rate was much slower than that of **2a**.[27] Interestingly, $B(C_6F_5)_3$ was found to accelerate the decomposition of a cyanohydrin but not the backward addition reaction.[28] This is further supported by the fact that mixing **2a** with benzaldehyde in the presence of the $B(C_6F_5)_3$ catalyst at 80 °C led to the formation of acetone and HCN with only trace amounts of **2e** being produced (Scheme 5b). The use of indole, **2a**, and acetone-$d_6$ provided almost equimolar amounts of **3aa** and the deuterated product **3aa-*d***(Scheme 5c), ruling out a mechanism involving the direct substitution of the hydroxy group of **2a** with **1a**. This result also indicates that the rate of decomposition of **2a** would be faster than that of the addition of **1a** to the existing acetone-$d_6$.

To obtain more detailed insights into the activation mode of a cyanohydrin with $B(C_6F_5)_3$, a mixture of **2e** and 1 equiv of $B(C_6F_5)_3$ in toluene was monitored by $^{13}C\{^1H\}$ NMR spectroscopy (Scheme 5d).[25] The addition of $B(C_6F_5)_3$ to **2e** led to an upfield shift in the signal corresponding to the cyano group ($\delta$ = 119.3 ppm for **2e** to 114.4 ppm for **2e**·$B(C_6F_5)_3$). This characteristic upfield shift strongly indicates that the cyano group of **2e** and not the hydroxyl group coordinates to $B(C_6F_5)_3$.[16,29] Additional support for the coordination came from the $^{11}B$ NMR ($\delta$ = 58.9 ppm for $B(C_6F_5)_3$ to −10.2 ppm for **2e**·$B(C_6F_5)_3$) and $^{19}F\{^1H\}$ NMR spectroscopy.[25] These NMR analyses indicate that the decomposition of a cyanohydrin is promoted by unprecedented Lewis acidic activation that occurs through the coordination of its cyano group to $B(C_6F_5)_3$.[16] Product analysis of the reaction of **1a** with **2a** for 1 h showed that, in addition to **3aa**, an alcohol intermediate is not generated from the addition of **1a** to acetone, but the formation of a small amount of bis(indoyl)methane **6a** was observed.[30] To examine its role as a potentially reactive intermediate, the reaction of **6a** with **2b** in the presence of $B(C_6F_5)_3$ was examined. This resulted in the formation of **3aa**, involving the release of one indole moiety that undergoes cyanoalkylation with **2b** to give **3ab** (Scheme 5e). This result suggests that bis(indoyl)methane **6** is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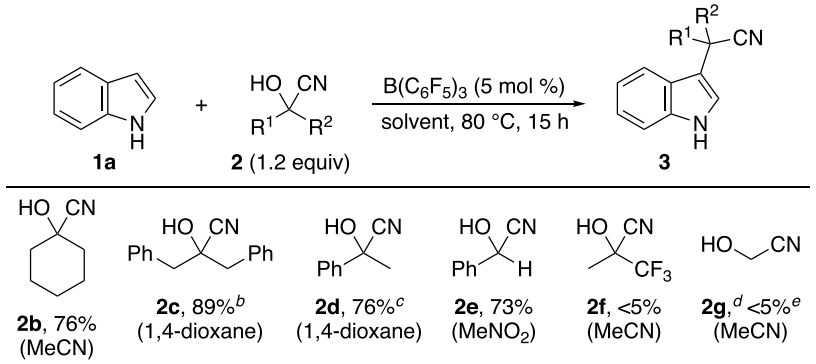
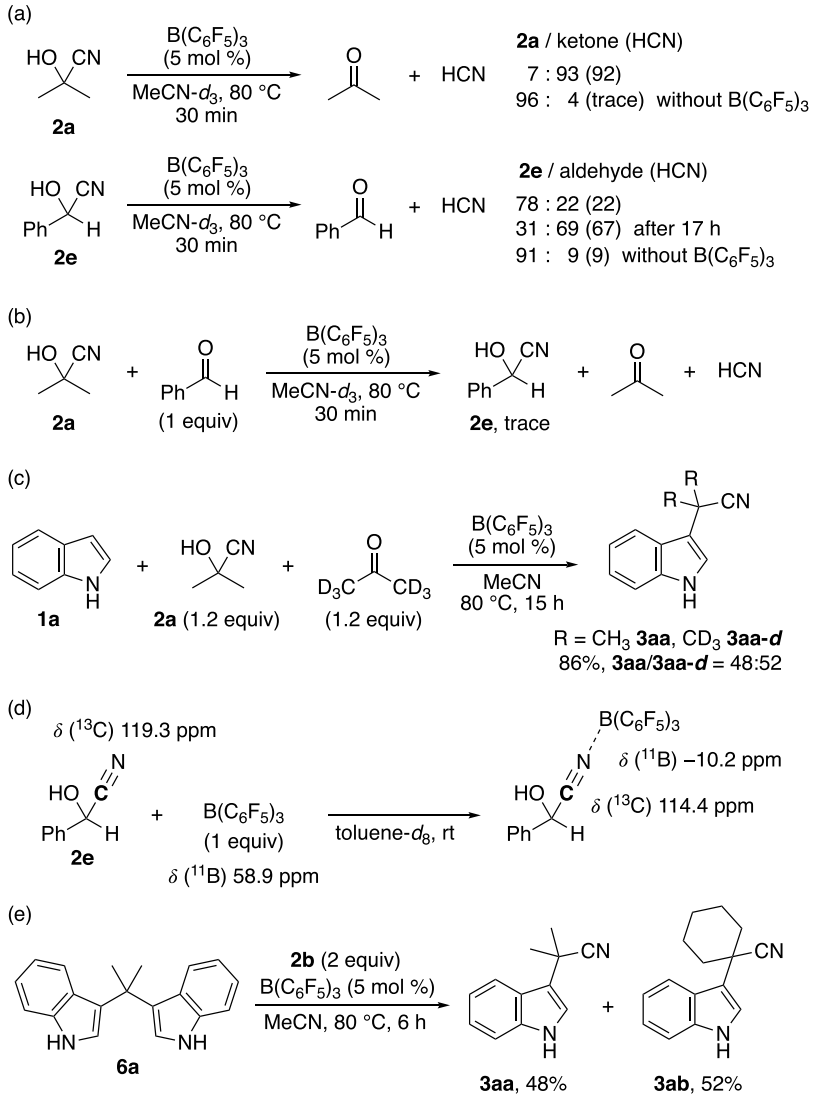
**Scheme 4. Scope and Limitation of Cyanohydrins**[a]




[a]Reactions were performed on a 0.5 mmol scale. Yields are isolated yields. [b]**2c** (2 equiv) was used. The reaction was conducted at 100 °C. [c]Reaction was conducted for 24 h. [d]**2g** (ca. 52% in water) was used. [e]Unreacted starting material **1a** was recovered (>90%).

**Scheme 5. Mechanistic Experiments**




one of the intermediates that is produced in this cyanoalkylation.[10]

On the basis of the experimental results, a plausible reaction pathway is depicted in Scheme 6. First, a cyanohydrin is decomposed into HCN and the corresponding carbonyl compound by Lewis acidic activation through the coordination of its cyano group to $B(C_6F_5)_3$. Indole **1** then attacks the resulting carbonyl compound to provide alcohol **7**, which is followed by dehydration, leading to the formation of iminium intermediate **8**. The cyanide generated through the dehydration step adds to **8** to afford cyanoalkylated product **3**. When **1** participates in the addition step instead of cyanide, bis(indoyl)-



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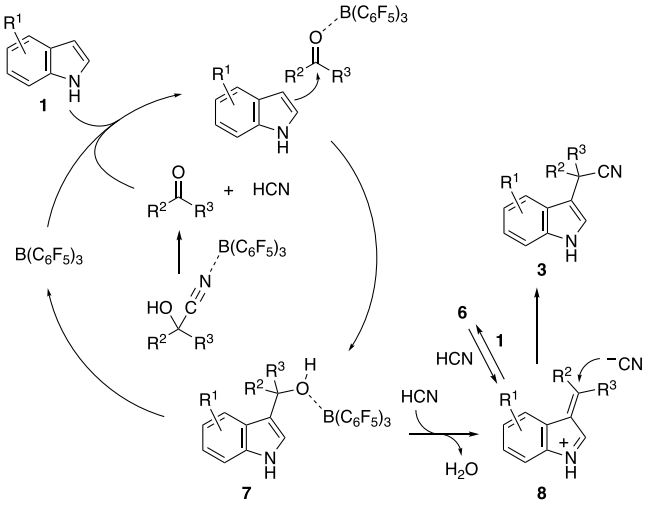
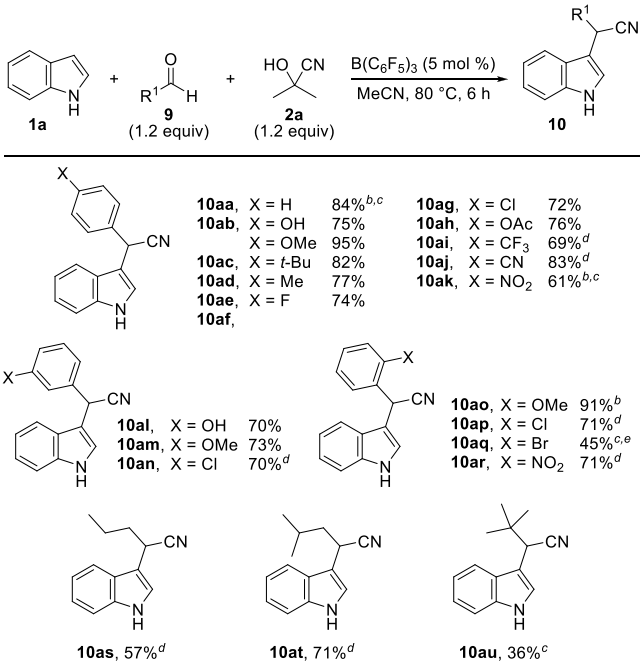
**Scheme 6. Plausible Reaction Pathway**



**Scheme 7. Cyanoalkylation of Indole Using Aldehydes as a Carbon Unit**[a]




[a]Reactions were performed on a 0.5 mmol scale. Yields are isolated yields. [b]1,4-Dioxane was used as a solvent. The reaction was conducted at 100 °C. [c]Reaction was conducted for 24 h. [d]$MeNO_2$ was used as a solvent. [e]**2b** was used instead of **2a**.

methane **6** is formed, but **6** can undergo a reverse reaction to **8** under the reaction conditions, leading to the formation of **3**. This reaction highlights the unique catalytic activity of $B(C_6F_5)_3$ that participates in the activation of cyanohydrins, carbonyl compounds, and alcohol intermediate **7**.[31]

An aldehyde-derived cyanohydrin was found to be suitable for use in this cyanoalkylation (Scheme 4, **2e**), but the preparation of cyanohydrins is somewhat laborious. We envisioned that a more practical process that would avoid the preparation of each cyanohydrin could be established by a three-component reaction using indoles, aldehydes as a carbon unit, and **2a**, in which indoles would react selectively with aldehydes over the acetone generated from **2a**. We then examined the reaction using **1a**, benzaldehyde, and with **2a** being added to a MeCN solution of the $B(C_6F_5)_3$ catalyst in succession and found that the desired **10aa** was selectively produced in 84% isolated yield, along with a small amount of **3aa** (<5%) (Scheme 7). A variety of aromatic aldehydes containing electron-donating and -withdrawing groups at the para, meta, and ortho positions were suitable substrates, affording the corresponding 2-(1*H*-indol-3-yl)-2-arylacetonitrile **5** in good to high yields (**10ab**−**10ar**). Moreover, this practical process could also be applied to aliphatic aldehydes. For example, butyraldehyde (**9s**) and 3-methylbutanal (**9t**) smoothly reacted to afford the desired products **10as** and **10at**, respectively. The use of the sterically hindered pivalaldehyde (**9u**) also provided **10au** albeit in a somewhat low yield due to the competitive side reaction that leads to the formation of **3aa**.

## CONCLUSIONS

In conclusion, we have developed the $B(C_6F_5)_3$-catalyzed formal C3 cyanoalkylation of indoles with cyanohydrins (and aldehydes). The key to the success of the reaction was the use of a $B(C_6F_5)_3$ catalyst that has the ability to promote the decomposition of a cyanohydrin through unique Lewis acidic activation, which was supported by mechanistic investigations including NMR spectroscopy analysis. This unprecedented method has a broad substrate scope with high functional group compatibility, thus offering a practical and general procedure for the synthesis of potentially valuable indole-3-acetonitrile derivatives.

## EXPERIMENTAL SECTION

**General Information.** New compounds were characterized by $^1H$ NMR, $^{13}C\{^1H\}$ NMR, $^{11}B$ NMR, $^{19}F\{^1H\}$ NMR, IR, mass spectrometry (MS), and high-resolution mass spectrometry (HRMS). $^1H$, $^{13}C\{^1H\}$, $^{11}B$, and $^{19}F\{^1H\}$ NMR spectra were recorded on a JEOL JMTC-400/54/SS spectrometer ($^1H$ NMR, 400 MHz; $^{13}C\{^1H\}$ NMR, 100 MHz; $^{11}B$ NMR, 128 MHz; $^{19}F\{^1H\}$ NMR, 377 MHz). $^1H$ NMR chemical shifts were determined relative to $Me_4Si$ (0.0 ppm) in $CDCl_3$, the signals of residual undeuterated acetonitrile (1.94 ppm) in $CD_3CN$, undeuterated toluene (2.08 ppm for the methyl group) in toluene-$d_8$, or undeuterated acetone (2.05 ppm) in acetone-$d_6$ as an internal standard. $^{13}C\{^1H\}$ NMR chemical shifts were determined relative to $CDCl_3$ (77.0 ppm), $CD_3CN$ (118.20 ppm), $CD_3C_6D_5$ (20.43 ppm), or $(CD_3)_2CO$ (29.84 ppm). $^{11}B$ NMR chemical shifts were determined relative to $BF_3{\cdot}OEt_2$ (0.0 ppm in toluene-$d_8$) as an external standard. $^{19}F\{^1H\}$ NMR chemical shifts were determined relative to $C_6F_6$ (−164.9 ppm in $CDCl_3$) as an external standard. Infrared spectra were recorded on a SHIMADZU IRAffinity-1 FT-IR spectrometer. Mass spectra were obtained on a SHIMADZU GCMS-QP2010 mass spectrometer. High-resolution mass spectra were obtained on a JEOL JMS-700 (magnetic sector type mass spectrometer). Melting points were determined on a Stanford Research Systems MPA100 OptiMelt Automated Melting Point System. All reactions were carried out under nitrogen. Products were purified by chromatography on silica gel BW-300 (Fuji Silysia Chemical Ltd.) or Chromatorex NH (Fuji Silysia Chemical Ltd.). Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel glass plates (Merck silica gel 60 $F_{254}$ and Fuji Silysia Chromatorex NH, 0.25 mm thickness). Compounds were visualized with a UV lamp or treatment with an ethanolic solution of phosphomolybdic acid followed by heating.

**Materials.** 2-Benzyl-2-hydroxy-3-phenylpropionitrile (**2c**) is a known compound and is prepared according to the reported procedure.[32] The $^1H$ NMR data for **2c** was in agreement with the reported data.[32] Dehydrated acetonitrile was used from a solvent purification system. Nitromethane was distilled over calcium sulfate



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before use. Indoles, cyanohydrins, aldehydes, and all other reagents and solvents were purchased and used as obtained.

*Typical Procedure for the Reaction of Indoles with Cyanohydrins (Typical Procedure A).* In a glovebox, an oven-dried reaction vial containing a magnetic stir bar was charged with $B(C_6F_5)_3$ (0.025 mmol, 5 mol %). The vial was capped and removed from the glovebox. Then, a solution of indoles (0.5 mmol, 1.0 equiv) in the indicated solvent (1 mL) and cyanohydrins (0.6 mmol, 1.2 equiv) were added to the vial, which was then sealed and placed in an aluminum block, which was preheated at 80 °C. After the mixture was stirred at 80 °C for 15 h, the reaction was quenched by sat. $NaHCO_3$ aq (10 mL), and the mixture was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were dried over $Na_2SO_4$. The solution was then concentrated under reduced pressure to give the crude product, which was analyzed by $^1H$ NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product.

*Typical Procedure for the Three-Component Reaction Using Indole, Aldehydes, and Acetone Cyanohydrin (Typical Procedure B).* In a glovebox, an oven-dried reaction vial containing a magnetic stir bar was charged with $B(C_6F_5)_3$ (0.025 mmol, 5 mol %). The vial was capped and removed from the glovebox. Then, a solution of 1*H*-indole (0.50 mmol, 1.0 equiv) in the indicated solvent (1 mL), acetone cyanohydrin (0.6 mmol, 1.2 equiv), and aldehydes (0.60 mmol, 1.2 equiv) were added to the vial, which was then sealed and placed in an aluminum block, which was preheated at 80 °C. After the mixture was stirred at 80 °C for 6 h, The reaction was quenched by sat. $NaHCO_3$ aq (10 mL), and the mixture was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were dried over $Na_2SO_4$. The solution was then concentrated under reduced pressure to give the crude product, which was analyzed by $^1H$ NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. Purification by flash column chromatography on silica gel (hexane/EtOAc) gave the product.

*Experimental Procedure for $^1H$ NMR Monitoring of the Decomposition of Cyanohydrins.* Solutions of cyanohydrin (0.1 mmol, 1.0 equiv) in the presence and absence of $B(C_6F_5)_3$ (0.005 mmol, 5 mol %) in MeCN-$d_3$ (0.5 mL) were prepared and transferred to a sealed NMR tube. After subjection of them to indicated conditions, the resulting $^1H$ NMR spectra are shown in Figures S1 and S2. To confirm the generation of HCN, a 200 μL sample of the mixture was added to 500 μL of $CDCl_3$, and the resulting $^1H$ NMR spectrum was compared to the reported data.[33]

*Experimental Procedure for NMR Monitoring of a Mixture of Mandelonitrile (**2e**) and $B(C_6F_5)_3$.* A solution of mandelonitrile (**2e**) (0.1 mmol, 1.0 equiv) and $B(C_6F_5)_3$ (0.1 mmol, 1.0 equiv) in toluene-$d_8$ (0.5 mL) was prepared and transferred into a sealed NMR tube. The resulting $^1H$, $^{13}C\{^1H\}$, $^{11}B$, and $^{19}F\{^1H\}$ NMR spectra are shown in Figures S3−S6.[34]

*2-(1H-Indol-3-yl)-2-methylpropanenitrile (**3aa**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (78.2 mg, 85% yield). **Gram-scale synthesis of 3aa:** In a glovebox, an oven-dried vial containing a magnetic stir bar was charged with $B(C_6F_5)_3$ (256.0 mg, 0.5 mmol, 5 mol %). The vial was capped and removed from the glovebox. Then, the $B(C_6F_5)_3$, a solution of 1*H*-indole (1.17 g, 10.0 mmol, 1.0 equiv) in MeCN (10 mL), and acetone cyanohydrin (1.1 mL, 12.0 mmol, 1.2 equiv) were added to the sealed reaction tube. The mixture was stirred at 80 °C for 15 h. The reaction was quenched by sat. $NaHCO_3$ aq (60 mL), and the mixture was extracted with $Et_2O$ (3 × 20 mL). The combined organic layers were dried over $Na_2SO_4$. The solution was then concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (1.64 g, 89% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.11 (brs, 1H), 7.84 (d, $J$ = 8.0 Hz, 1H), 7.40 (d, $J$ = 8.0 Hz, 1H), 7.27−7.22 (m, 1H), 7.22−7.17 (m, 1H), 7.14 (d, $J$ = 2.4 Hz, 1H), 1.86 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.9, 124.6, 124.4, 122.5, 120.5, 120.0, 119.6, 116.9, 111.6, 31.3, 27.9; IR: (ATR) 3406, 3360, 3348, 3130, 3057, 2980, 2934, 2234, 1458, 766 $cm^{-1}$; MS (EI) $m/z$: 184 ($M^+$, 41), 169 (100), 142 (40), 115 (27); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{12}H_{12}N_2$ 184.1000; found 184.0998.

*2-(5-Methoxy-1H-indol-3-yl)-2-methylpropanenitrile (**3ba**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 5-methoxy-1*H*-indole (73.7 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (102.5 mg, 96% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.10 (brs, 1H), 7.30−7.21 (m, 2H), 7.06 (d, $J$ = 2.8 Hz, 1H), 6.90 (dd, $J$ = 8.8, 2.8 Hz, 1H), 3.88 (s, 3H), 1.83 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 154.1, 132.1, 124.9, 124.5, 121.1, 116.6, 112.7, 112.3, 101.7, 56.0, 31.2, 27.8; IR: (ATR) 3040, 3391, 3325, 2984, 2938, 2830, 2232, 1483, 1458, 1439, 1217, 1153, 1036, 831, 800 $cm^{-1}$; MS (EI) $m/z$: 214 ($M^+$, 54), 199 (100), 172 (40); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{14}N_2O$ 214.1106; found 214.1107.

*2-Methyl-2-(5-methyl-1H-indol-3-yl)propanenitrile (**3ca**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 5-methyl-1*H*-indole (65.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (82.7 mg, 83% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.05 (brs, 1H), 7.60 (s, 1H), 7.25 (d, $J$ = 8.4 Hz, 1H), 7.07−7.04 (m, 2H), 2.47 (s, 3H), 1.84 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 135.3, 129.3, 124.7, 124.6, 124.2, 120.5, 119.3, 116.5, 111.3, 31.3, 27.9, 21.6; IR: (ATR) 3408, 3399, 2980, 2924, 2870, 2232, 1483, 1458, 1438, 1419, 1340, 1146, 1107, 797, 760 $cm^{-1}$; MS (EI) $m/z$: 198 ($M^+$, 44), 183 (100), 156 (32); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1156.

*2-(5-Fluoro-1H-indol-3-yl)-2-methylpropanenitrile (**3da**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 5-fluoro-1*H*-indole (67.8 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (93.5 mg, 92% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.26 (brs, 1H), 7.47 (dd, $J$ = 2.4 Hz, $^3J_{H-F}$ = 9.6 Hz, 1H), 7.30 (dd, $J$ = 4.4 Hz, $^4J_{H-F}$ = 8.8 Hz, 1H), 7.15 (d, $J$ = 2.4 Hz, 1H), 6.98 (ddd, $J$ = 8.8, 2.4 Hz, $^3J_{H-F}$ = 8.8 Hz, 1H), 1.82 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 157.6 (d, $J_{C-F}$ = 233.9 Hz), 133.4, 124.6 (d, $J_{C-F}$ = 9.9 Hz), 124.4, 122.2, 116.7 (d, $J_{C-F}$ = 4.1 Hz), 112.4 (d, $J_{C-F}$ = 9.8 Hz), 110.9 (d, $J_{C-F}$ = 26.3 Hz), 104.5 (d, $J_{C-F}$ = 23.9 Hz), 31.0, 27.6; $^{19}F\{^1H\}$ NMR: (376 MHz, $CDCl_3$) $\delta$ −123.7; IR: (ATR) 3447, 3404, 3379, 3364, 3347, 2982, 2938, 2234, 1487, 1460, 1146, 797 $cm^{-1}$; MS (EI) $m/z$: 202 ($M^+$, 44), 187 (100), 160 (46), 133 (22); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{12}H_{11}FN_2$ 202.0906; found 202.0907.

*2-(5-Chloro-1H-indol-3-yl)-2-methylpropanenitrile (**3ea**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 5-chloro-1*H*-indole (76.1 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (100.8 mg, 92% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.25 (brs, 1H), 7.79 (d, $J$ = 1.6 Hz, 1H), 7.29 (d, $J$ = 8.8 Hz, 1H), 7.19−7.13 (m, 2H), 1.83 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 135.3, 125.7, 125.4, 124.3, 123.0, 121.9, 119.1, 116.8, 112.7, 31.1, 27.8; IR: (ATR) 3417, 3408, 3358, 3350, 2981, 2938, 2234 $cm^{-1}$; MS (EI) $m/z$: 220 ($[M+2]^+$, 14), 218 ($M^+$, 41), 205 (34), 203 (100), 176 (29); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{12}H_{11}ClN_2$ 218.0611; found 218.0613.

*2-(5-Bromo-1H-indol-3-yl)-2-methylpropanenitrile (**3fa**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 5-bromo-1*H*-indole (98.0 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (110.7 mg, 84% yield). $^1H$ NMR: (400 MHz, $CDCl_3$)


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$\delta$ 8.26 (brs 1H), 7.94 (d, $J$ = 2.0 Hz, 1H), 7.31 (dd, $J$ = 8.8, 2.0 Hz, 1H), 7.24 (d, $J$ = 8.8 Hz, 1H), 7.11 (d, $J$ = 3.2 Hz, 1H), 1.82 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 135.6, 126.1, 125.6, 124.3, 122.1, 121.7, 116.7, 113.3, 113.1, 31.1, 27.8; IR: (ATR) 3429, 3420, 3350, 3339, 2982, 2932, 2234, 1458, 1418, 1335, 1192, 1165, 1109, 1059, 885, 797, 752, 731 $cm^{-1}$; MS (EI) $m/z$: 264 ($[M + 2]^+$, 40), 262 ($M^+$, 40), 249 (98), 247 (100), 168 (77), 140 (29), 71 (18); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{12}H_{11}BrN_2$ 262.0106; found 262.0101.

*Methyl 3-(2-Cyanopropan-2-yl)-1H-indole-5-carboxylate (**3ga**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (25.6 mg, 0.05 mmol, 10 mol %), methyl 1*H*-indole-5-carboxylate (87.5 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (69 $\mu$L, 0.75 mmol, 1.5 equiv) was conducted at 80 °C for 20 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (111.8 mg, 92% yield). Mp: 122.5−123.4 °C; $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.57 (s, 1H), 8.41 (brs, 1H), 7.96 (dd, $J$ = 8.4, 1.4 Hz, 1H), 7.41 (d, $J$ = 8.4 Hz, 1H), 7.34 (d, $J$ = 2.4 Hz, 1H), 3.95 (s, 3H), 1.88 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 168.0, 139.6, 124.3, 123.98, 123.95, 122.4, 122.1, 122.0, 118.4, 111.5, 52.0, 31.3, 28.0; IR: (ATR) 3319, 3136, 2957, 2228, 1684, 1614, 1435, 1271, 1246, 1123, 982, 750 $cm^{-1}$; MS (EI) $m/z$: 242 ($M^+$, 46), 227 (100), 140 (24); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{14}H_{14}N_2O_2$ 242.1055; found 242.1052.

*3-(2-Cyanopropan-2-yl)-1H-indole-5-carbonitrile (**3ha**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (25.6 mg, 0.05 mmol, 10 mol %), 1*H*-indole-5-carbonitrile (71.1 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (92 $\mu$L, 1 mmol, 2.0 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (91.0 mg, 86% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.83 (brs, 1H), 8.79 (d, $J$ = 2.0 Hz, 1H), 8.14 (dd, $J$ = 9.2, 2.0 Hz, 1H), 7.46 (d, $J$ = 9.2 Hz, 1H), 7.34 (d, $J$ = 2.4 Hz, 1H), 1.89 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 138.6, 125.5, 125.3, 124.3, 123.9, 122.8, 120.3, 118.1, 112.6, 103.3, 31.1, 27.9; IR: (ATR) 3360, 2984, 2230, 2212, 1622, 1472, 1423, 1352, 1252, 1130, 1103, 876, 808, 760 $cm^{-1}$; MS (EI) $m/z$: 209 ($M^+$, 31), 194 (100), 167 (28), 140 (23); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{11}N_3$ 209.0953; found 209.0954.

*2-Methyl-2-(5-nitro-1H-indol-3-yl)propanenitrile (**3ia**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (25.6 mg, 0.05 mmol, 10 mol %), 5-nitro-1*H*-indole (67.0 mg, 0.50 mmol, 1.0 equiv), $MeNO_2$ (1 mL), and acetone cyanohydrin (92 $\mu$L, 1 mmol, 2.0 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a yellow solid (105.7 mg, 92% yield). Mp: 135.0−136.1 °C; $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.80−8.70 (m, 2H), 8.14 (dd, $J$ = 8.8, 2.0 Hz, 1H), 7.45 (d, $J$ = 8.8 Hz, 1H), 7.34 (d, $J$ = 2.8 Hz, 1H), 1.90 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 141.8, 140.0, 124.0, 123.9, 123.8, 119.5, 118.2, 116.7, 111.9, 31.2, 28.0; IR: (ATR) 3381, 3132, 3105, 3080, 2990, 2924, 2852, 2235, 1512, 1469, 1458, 1327, 1290, 1103, 1082, 839, 810, 737 $cm^{-1}$; MS (EI) $m/z$: 229 ($M^+$, 35), 214 (100), 168 (40); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{12}H_{11}N_3O_2$ 229.0851; found 229.0852.

*2-Methyl-2-(6-methyl-1H-indol-3-yl)propanenitrile (**3ja**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 6-methyl-1*H*-indole (65.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 $\mu$L, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (93.4 mg, 94% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 7.99 (brs, 1H), 7.70 (d, $J$ = 8.4 Hz, 1H), 7.18 (s, 1H), 7.07−6.98 (m, 2H), 2.46 (s, 3H), 1.83 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 137.4, 132.5, 124.6, 122.3, 121.8, 119.8, 119.3, 116.9, 111.5, 31.3, 27.9, 21.6; IR: (ATR) 3360, 2984, 2938, 2862, 2232, 1653, 1628, 1549, 1456, 1387, 1366, 1341, 1109, 1032, 854, 827, 793 $cm^{-1}$; MS (EI) $m/z$: 198 ($M^+$, 47), 183 (100), 156 (29); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1159.

*2-(6-Bromo-1H-indol-3-yl)-2-methylpropanenitrile (**3ka**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 6-bromo-1*H*-indole (98.0 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 $\mu$L, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (115.2 mg, 88% yield). Mp: 167.1−168.0 °C; $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.19 (brs 1H), 7.70 (d, $J$ = 8.8 Hz, 1H), 7.55 (d, $J$ = 1.6 Hz, 1H), 7.29 (dd, $J$ = 8.8, 1.6 Hz, 1H), 7.09 (d, $J$ = 2.4 Hz, 1H), 1.83 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 137.7, 124.3, 123.4, 121.0, 120.8, 117.3, 116.2, 114.5, 31.1, 27.8 (one $sp^2$ signal was not observed because of overlapping); IR: (ATR) 3410, 3123, 2986, 2934, 2230, 1659, 1614, 1539, 1456, 1387, 1366, 1329, 1294, 1229, 1109, 1028, 1016, 893, 854, 829, 793, 781 $cm^{-1}$; MS (EI) $m/z$: 264 ($[M + 2]^+$, 40), 262 ($M^+$, 43), 249 (93), 247 (100), 168 (70), 141 (23), 140 (52), 114 (25), 71 (22), 63 (21); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{12}H_{11}BrN_2$ 262.0106; found 262.0109.

*2-(7-Methoxy-1H-indol-3-yl)-2-methylpropanenitrile (**3la**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 7-methoxy-1*H*-indole (73.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 $\mu$L, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (98.5 mg, 92% yield). Mp: 148.6−150.2 °C; $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 8.32 (brs, 1H), 7.42 (d, $J$ = 8.0 Hz, 1H), 7.15−7.06 (m, 2H), 6.68 (d, $J$ = 8.0 Hz, 1H), 3.95 (s, 3H), 1.84 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 146.3, 127.6, 125.7, 124.6, 120.5, 119.9, 117.6, 112.4, 102.3, 55.3, 31.4, 28.0; IR: (ATR) 3314, 3005, 2984, 2938, 2237, 1580, 1450, 1429, 1331, 1267, 1254, 1179, 1103, 1030, 1016, 781, 735, 700 $cm^{-1}$; MS (EI) $m/z$: 214 ($M^+$, 61), 199 (100), 172 (52); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{14}N_2O$ 214.1106; found 214.1109.

*2-Methyl-2-(2-methyl-1H-indol-3-yl)propanenitrile (**3ma**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 2-methyl-1*H*-indole (65.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 $\mu$L, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (92.0 mg, 93% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 7.92 (brs, 1H), 7.76 (d, $J$ = 8.0 Hz, 1H), 7.28 (d, $J$ = 8.4 Hz, 1H), 7.17−7.06 (m, 2H), 2.57 (s, 3H), 1.92 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 134.7, 130.6, 126.2, 125.3, 121.3, 119.7, 119.5, 110.6, 109.9, 32.4, 28.9, 14.0; IR: (ATR) 3391, 3356, 3339, 3321, 2980, 2932, 2232, 1460, 1425, 1194, 1078 $cm^{-1}$; MS (EI) $m/z$: 198 ($M^+$, 42), 183 (100), 156 (39); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1156.

*2-Methyl-2-(1-methyl-1H-indol-3-yl)propanenitrile (**3na**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1-methyl-1*H*-indole (66.1 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 $\mu$L, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (93.7 mg, 95% yield). $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 7.82 (d, $J$ = 7.6 Hz, 1H), 7.32−7.23 (m, 2H), 7.20−7.14 (m, 1H), 6.96 (s, 1H), 3.71 (s, 3H), 1.82 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 137.6, 125.1, 124.8, 124.6, 122.0, 119.7, 119.4, 115.2, 109.7, 32.6, 31.1, 27.9; IR: (ATR) 2980, 2934, 2232, 1464, 1331, 1229, 1107 $cm^{-1}$; MS (EI) $m/z$: 198 ($M^+$, 41), 183 (100), 156 (31); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1153.

*2-(1-Benzyl-1H-indol-3-yl)-2-methylpropanenitrile (**3oa**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1-benzyl-1*H*-indole (103.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 $\mu$L, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (124.1 mg, 90% yield). Mp: 130.0−130.9 °C; $^1H$ NMR: (400 MHz, $CDCl_3$) $\delta$ 7.85 (d, $J$ = 7.6 Hz, 1H), 7.37−7.27 (m, 4H), 7.25−7.15 (m, 2H), 7.12 (d, $J$ = 7.6 Hz, 2H), 7.07 (s, 1H), 5.30 (s, 2H), 1.85 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 137.3, 137.0, 128.8, 127.8, 126.8, 125.1, 124.6, 124.5, 122.3, 120.0, 119.8, 116.1, 110.2, 50.1, 31.3, 28.0; IR: (ATR) 2978, 2224, 1618, 1549, 1497, 1472, 1443, 1391, 1375, 1339, 1238, 1196, 1182, 1155, 1074, 1016, 970, 770, 733 $cm^{-1}$; MS (EI) $m/z$: 274 ($M^+$, 14), 259 (21), 91 (100); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{19}H_{18}N_2$ 274.1470; found 274.1468.



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*2-Methyl-2-(1-methyl-2-phenyl-1H-indol-3-yl)propanenitrile (**3pa**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1-methyl-2-phenyl-1*H*-indole (103.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless solid (115.1 mg, 84% yield). Mp: 145.2−146.6 °C; $^1$H NMR: (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.6 Hz, 1H), 7.53−7.43 (m, 3H), 7.37−7.27 (m, 4H), 7.25−7.20 (m, 1H), 3.37 (s, 3H), 1.65 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 136.8, 136.6, 132.9, 131.2, 129.2, 128.2, 125.3, 125.0, 122.2, 120.2, 119.9, 111.6, 109.6, 32.4, 30.1, 29.5; IR: (ATR) 3045, 2978, 2938, 2918, 2226, 1460, 1368 $cm^{-1}$; MS (EI) *m*/*z*: 274 ($M^+$, 45), 260 (22), 259 (100); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{19}H_{18}N_2$ 274.1470; found 274.1471.

*2-Methyl-2-(4-methyl-1H-indol-3-yl)propanenitrile (**3qa**), 2-Methyl-2-(4-methyl-1H-indol-1-yl)propanenitrile (**3qa′**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (25.6 mg, 0.05 mmol, 5 mol %), 4-methyl-1*H*-indole (66.8 mg, 0.51 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (227 μL, 2.5 mmol, 5.0 equiv) was conducted at 80 °C for 15 h, providing the mixture of **3qa** and **3qa′** in 1:2.5 ratio, as determined by $^1$H NMR analysis. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave **3qa** as a white solid (25.8 mg, 24% yield) and **3qa′** as a brown liquid (55.8 mg, 52% yield). **3qa**: mp: 146.5−147.7 °C; $^1$H NMR: (400 MHz, $CDCl_3$) δ 8.13 (brs, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.14 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.12 (d, *J* = 3.2 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 2.96 (s, 3H), 1.89 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 137.9, 130.2, 126.2, 124.2, 123.1, 122.8, 121.2, 118.2, 109.2, 30.9, 29.9, 23.2; IR: (ATR) 3337, 3130, 2974, 2932, 2868, 2236, 1433, 1406, 1389, 1327, 1148, 1026, 831, 779, 745 $cm^{-1}$; MS (EI) *m*/*z*: 198 ($M^+$, 49), 183 (100), 156 (29), 154 (22), 129 (28), 128 (21), 77 (20); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1156. **3qa′**: $^1$H NMR: (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.2 Hz, 1H), 7.21 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.18 (d, *J* = 4.0 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 4.0 Hz, 1H), 2.55 (s, 3H), 2.06 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 134.3, 130.9, 129.7, 122.5, 122.4, 120.7, 120.2, 109.3, 101.3, 51.3, 27.8, 18.6; IR: (ATR) 3146, 3109, 3080, 3049, 2994, 2940, 2859, 2239, 1487, 1319, 1279, 1238, 748, 710 $cm^{-1}$; MS (EI) *m*/*z*: 198 ($M^+$, 37), 183 (24), 131 (25), 130 (100), 103 (20), 77 (29); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1155.

*2-Methyl-2-(3-methyl-1H-indol-2-yl)propanenitrile (**3ra**), 2-Methyl-2-(3-methyl-1H-indol-1-yl)propanenitrile (**3ra′**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 3-methyl-1*H*-indole (65.7 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and acetone cyanohydrin (228 μL, 2.5 mmol, 5.0 equiv) was conducted at 80 °C for 15 h, providing the mixture of **3ra** and **3ra′** in 1:3.8 ratio, as determined by $^1$H NMR analysis. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave **3ra** as a colorless liquid (15.9 mg, 16% yield) and **3ra′** as a colorless liquid (60.2 mg, 61% yield). **3ra**: $^1$H NMR: (400 MHz, $CDCl_3$) δ 7.97 (brs, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.21 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.14 (dd, *J* = 7.6, 7.6 Hz, 1H), 2.44 (s, 3H), 1.86 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 134.2, 130.8, 129.8, 123.1, 122.5, 119.8, 118.5, 110.7, 108.1, 32.5, 27.3, 9.4; IR: (ATR) 3366, 3059, 2984, 2932, 2868, 2237, 1653, 1585, 1524, 1458, 1333, 1306, 1240, 1200, 1180, 1007, 741, 719 $cm^{-1}$; MS (EI) *m*/*z*: 198 ($M^+$, 21), 183 (100), 154 (28), 129 (21), 128 (35), 102 (21), 77 (22), 52 (22), 51 (30), 50 (25); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1160. **3ra′**: $^1$H NMR: (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.34−7.26 (m, 1H), 7.23−7.15 (m, 1H), 6.96 (s, 1H), 2.31 (s, 3H), 2.04 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 135.0, 130.4, 122.3, 120.7, 120.4, 119.9, 119.5, 112.0, 111.5, 51.1, 27.8, 9.5; IR: (ATR) 3051, 2992, 2918, 2864, 2248, 1611, 1456, 1371, 1342, 1310, 1238, 1211, 1184, 1088, 1020, 762, 739 $cm^{-1}$; MS (EI) *m*/*z*: 198 ($M^+$, 36), 183 (35), 130 (100), 77 (27); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1157.

*1-(1H-Indol-3-yl)cyclohexane-1-carbonitrile (**3ab**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), and 1-hydroxycyclohexane-1-carbonitrile (75.1 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (84.9 mg, 76% yield). $^1$H NMR: (400 MHz, $CDCl_3$) δ 8.14 (brs, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.25−7.20 (m, 1H), 7.20−7.13 (m, 1H), 7.12 (d, *J* = 2.4 Hz, 1H), 2.53−2.31 (m, 2H), 2.00−1.72 (m, 7H), 1.42−1.21 (m, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 136.9, 124.5, 122.9, 122.5, 120.5, 119.93, 119.87, 117.2, 111.6, 38.2, 36.3, 25.3, 23.3; IR: (ATR) 3348, 2930, 2860, 2232, 1630, 1547, 1493, 1450, 1433, 1260, 1242, 1113, 1096, 1028, 1013, 995, 903, 816, 799, 760, 735 $cm^{-1}$; MS (EI) *m*/*z*: 224 ($M^+$, 82), 182 (22), 181 (100), 168 (79), 155 (31), 154 (32), 141 (26), 140 (37), 130 (27), 127 (21), 117 (33), 115 (31), 114 (24); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{16}N_2$ 224.1313; found 224.1309.

*2-Benzyl-2-(1H-indol-3-yl)-3-phenylpropanenitrile (**3ac**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in 1,4-dioxane (1 mL), and 2-benzyl-2-hydroxy-3-phenylpropanenitrile (237.2 mg, 1.0 mmol, 2.0 equiv) was conducted at 100 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (149.9 mg, 89% yield). Mp: 194.0−195.3 °C; $^1$H NMR: (400 MHz, $CDCl_3$) δ 7.95−7.87 (m, 2H), 7.43−7.36 (m, 1H), 7.33−7.22 (m, 2H), 7.19−7.09 (m, 6H), 7.01−6.94 (m, 4H), 6.79 (d, *J* = 2.4 Hz, 1H), 3.63 (d, *J* = 13.2 Hz, 2H), 3.39 (d, *J* = 13.2 Hz, 2H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 137.2, 135.6, 130.2, 127.9, 127.1, 124.4, 124.0, 122.4, 121.7, 120.1, 119.9, 112.2, 112.1, 46.7, 44.2; IR: (ATR) 3325, 3053, 3030, 2934, 2245, 1668, 1601, 1551, 1495, 1437, 1331, 1254, 1227, 1134, 1113, 1096, 1061, 1032, 1015, 970, 839, 760, 741, 702 $cm^{-1}$; MS (EI) *m*/*z*: 336 ($M^+$, 6), 245 (100), 91 (35); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{24}H_{20}N_2$ 336.1626; found 336.1623.

*2-(1H-Indol-3-yl)-2-phenylpropanenitrile (**3ad**).* According to the typical procedure A, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), 1,4-dioxane (1 mL), and 2-hydroxy-2-phenylpropanenitrile (80 μL, 0.6 mmol, 1.2 equiv) was conducted at 80 °C for 24 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (93.4 mg, 76% yield). Mp: 162.5−163.6 °C; $^1$H NMR: (400 MHz, $CDCl_3$) δ 8.22 (brs, 1H), 7.49−7.43 (m, 2H), 7.39−7.23 (m, 5H), 7.21−7.15 (m, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 2.14 (s, 3H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 140.9, 136.9, 128.8, 127.7, 126.1, 124.7, 123.1, 122.7, 122.3, 120.1, 120.0, 116.1, 111.4, 40.5, 28.5; IR: (ATR) 3348, 2940, 2932, 2862, 2234, 1632, 1547, 1493, 1450, 1433, 1341, 1260, 1242, 1134, 1113, 1096, 1030, 1013, 997, 903, 816, 795, 760, 735, 706 $cm^{-1}$; MS (EI) *m*/*z*: 246 ($M^+$, 40), 231 (100), 204 (21), 115 (27); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{17}H_{14}N_2$ 246.1157; found 246.1155.

*2-Methyl-2-(1-methyl-1H-pyrrol-3-yl)propanenitrile (**4**).* In a glovebox, an oven-dried reaction vial containing a magnetic stir bar was charged with $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %). The vial was capped, removed from the glovebox. Then, a solution of 1-methyl-1*H*-pyrrole (40.3 mg, 0.50 mmol, 1.0 equiv) in MeCN (1 mL) and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) were added to the vial. The mixture was stirred at 80 °C for 15 h. The reaction was quenched by sat. $NaHCO_3$ aq (10 mL), and the mixture was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were dried over $Na_2SO_4$. The solution was then under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (51.0 mg, 69% yield). $^1$H NMR: (400 MHz, $CDCl_3$) δ 6.65−6.59 (m, 1H), 6.59−6.53 (m, 1H), 6.15−6.08 (m, 1H), 3.63 (s, 3H), 1.65 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) δ 125.9, 125.4, 122.4, 118.1, 105.6, 36.2, 31.2, 29.1; IR: (ATR) 2980, 2938, 2232, 1551, 1508, 1466, 1458, 1422, 1387, 1366, 1346, 1207, 1190, 1119, 1086, 964, 777, 700 $cm^{-1}$; MS (EI) *m*/*z*: 148 ($M^+$, 21), 133 (100), 106 (29); HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_9H_{12}N_2$ 148.1000; found 148.1001.

*2-(2,5-Dimethyl-1H-pyrrol-3-yl)-2-methylpropanenitrile (**5**).* In a glovebox, an oven-dried reaction vial containing a magnetic stir bar was charged with $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %). The vial was capped, removed from the glovebox. Then, a solution of 2,5-dimethyl-


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1*H*-pyrrole (47.4 mg, 0.50 mmol, 1.0 equiv) in MeCN (1 mL) and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) were added to the vial. The mixture was stirred at 80 °C for 15 h. The reaction was quenched by sat. $NaHCO_3$ aq (10 mL), and the mixture was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were dried over $Na_2SO_4$. The solution was then concentrated under reduced pressure to give the crude product. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (63.3 mg, 78% yield). Mp: 74.9−76.3 °C; $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 7.71 (brs, 1H), 5.71 (d, $J$ = 2.8 Hz, 1H), 2.35 (s, 3H), 2.20 (s, 3H), 1.64 (s, 6H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 125.1, 124.7, 122.1, 119.0, 103.6, 30.4, 28.6, 12.7, 12.3; IR: (ATR) 3372, 2980, 2934, 2874, 2230, 1599, 1464, 1437, 1404, 1383, 1364, 1198, 1157, 775, 725 $cm^{-1}$; MS (EI) $m/z$: 162 ($M^+$, 29), 147 (100), 132 (37), 120 (27); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{10}H_{14}N_2$ 162.1157; found 162.1159.

*2-(1H-Indol-3-yl)-2-phenylacetonitrile (**3ae, 10aa**).* According to the typical procedure A, the reaction usign $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in $MeNO_2$ (1 mL), and 2-hydroxy-2-phenylacetonitrile (79.3 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 15 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (84.5 mg, 73% yield). According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in 1,4-dioxane (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol), and benzaldehyde (63.2 mg, 0.60 mmol, 1.2 equiv) was conducted at 100 °C for 24 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (97.6 mg, 84% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.20 (brs, 1H), 7.48−7.41 (m, 3H), 7.41−7.28 (m, 4H), 7.25−7.19 (m, 1H), 7.16 (d, $J$ = 2.0 Hz, 1H), 7.13−7.07 (m, 1H), 5.39 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.5, 135.3, 129.0, 128.2, 127.7, 125.2, 123.2, 122.9, 120.3, 119.8, 118.8, 111.5, 111.0, 34.4; IR: (ATR) 3366, 3354, 3057, 2886, 2247, 1491, 1458, 1341, 1217, 1105, 789, 741, 702 $cm^{-1}$; MS (EI) $m/z$: 232 ($M^+$, 98), 231 (35), 204 (31), 155 (100), 102 (29), 101 (21); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{12}N_2$ 232.1000; found 232.0998.

*2-(4-Hydroxyphenyl)-2-(1H-indol-3-yl)acetonitrile (**10ab**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-hydroxybenzaldehyde (73.3 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a pink solid (93.7 mg, 75% yield). Mp: 162.8−164.3 °C; $^1$H NMR: (400 MHz, acetone-$d_6$) $\delta$ 8.48 (brs, 1H), 7.55−7.40 (m, 2H), 7.40−7.25 (m, 3H), 7.20−7.10 (m, 1H), 7.10−6.95 (m, 1H), 6.90−6.80 (m, 2H), 5.64 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, acetone-$d_6$) $\delta$ 157.9, 138.0, 129.7, 128.3, 126.3, 124.5, 122.9, 121.2, 120.2, 119.5, 116.5, 112.6, 111.9, 33.9; IR: (ATR) 3397, 3067, 3032, 2963, 2878, 2241, 1614, 1603, 1514, 1258, 1096, 1065, 1020, 1009, 820, 799, 783 $cm^{-1}$; HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{12}N_2O$ 248.0950; found 248.0953.

*2-(1H-Indol-3-yl)-2-(4-methoxyphenyl)acetonitrile (**10ac**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-methoxybenzaldehyde (81.6 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a red liqud (125.0 mg, 95% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.20 (brs, 1H), 7.45−7.31 (m, 4H), 7.26−7.16 (m, 2H), 7.10 (dd, $J$ = 8.8, 8.8 Hz, 1H), 6.88 (d, $J$ = 8.8 Hz, 2H), 5.35 (s, 1H), 3.80 (s, 3H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 159.3, 136.6, 128.8, 127.4, 125.2, 123.1, 122.9, 120.2, 120.0, 118.8, 114.3, 111.5, 111.3, 55.3, 33.7; IR: (ATR) 3408, 2963, 2837, 2359, 2243, 1611, 1508, 1258, 1096, 1069, 1026, 795, 779, 741 $cm^{-1}$; MS (EI) $m/z$: 262 ($M^+$, 100), 261 (27), 231 (20), 155 (57), 154 (20); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{17}H_{14}N_2O$ 262.1106; found 262.1106.

*2-(4-(tert-Butyl)phenyl)-2-(1H-indol-3-yl)acetonitrile (**10ad**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-(*tert*-butyl)benzaldehyde (97.6 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (118.0 mg, 82% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.20 (brs, 1H), 7.50 (d, $J$ = 8.0 Hz, 1H), 7.41−7.34 (m, 5H), 7.22 (dd, $J$ = 8.0, 8.0 Hz, 1H), 7.16 (d, $J$ = 1.6 Hz, 1H), 7.11 (dd, $J$ = 8.0, 8.0 Hz, 1H), 5.36 (s, 1H), 1.30 (s, 9H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 151.1, 136.5, 132.3, 127.3, 125.9, 125.3, 123.2, 122.8, 120.2, 120.0, 118.8, 111.5, 111.1, 34.5, 34.0, 31.2; IR: (ATR) 3402, 3061, 3034, 2959, 2901, 2884, 2868, 2237, 1620, 1553, 1508, 1458, 1418, 1094, 1011, 853, 818, 789, 766, 737 $cm^{-1}$; MS (EI) $m/z$: 288 ($M^+$, 90), 273 (100), 231 (21), 208 (23), 207 (99), 156 (33), 155 (83), 128 (27), 122 (24), 117 (21); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{20}H_{20}N_2$ 288.1626; found 288.1628.

*2-(1H-Indol-3-yl)-2-(p-tolyl)acetonitrile (**10ae**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-methylbenzaldehyde (72.5 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (95.3 mg, 77% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.20 (brs, 1H), 7.44 (d, $J$ = 8.0 Hz, 1H), 7.36 (d, $J$ = 8.0 Hz, 1H), 7.31 (d, $J$ = 8.0 Hz, 2H), 7.24−7.18 (m, 1H), 7.15 (d, $J$ = 8.0 Hz, 2H), 7.13 (d, $J$ = 2.8 Hz, 1H), 7.11−7.06 (m, 1H), 5.33 (s, 1H), 2.33 (s, 3H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 137.9, 136.5, 132.3, 129.7, 127.5, 125.2, 123.2, 122.8, 120.2, 120.0, 118.8, 111.5, 111.0, 34.1, 21.0; IR: (ATR) 3408, 3053, 2961, 2920, 2872, 2243, 1620, 1549, 1512, 1456, 1418, 1339, 1098, 1011, 812, 772, 739 $cm^{-1}$; MS (EI) $m/z$: 246 ($M^+$, 100), 245 (33), 231 (30), 207 (23), 155 (82), 128 (23), 102 (20), 77 (20); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{17}H_{14}N_2$ 246.1157; found 246.1159.

*2-(4-Fluorophenyl)-2-(1H-indol-3-yl)acetonitrile (**10af**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-fluorobenzaldehyde (74.2 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a orange liquid (92.9 mg, 74% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.22 (brs, 1H), 7.44−7.36 (m, 4H), 7.27−7.22 (m, 1H), 7.20 (d, $J$ = 2.4 Hz, 1H), 7.14−7.08 (m, 1H), 7.08−7.02 (m, 2H), 5.38 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 162.4 (d, $J_{C-F}$ = 246.2 Hz), 136.5, 131.1 (d, $J_{C-F}$ = 3.3 Hz), 129.3 (d, $J_{C-F}$ = 8.2 Hz), 125.0, 123.3, 122.9, 120.3, 119.7, 118.6, 116.0 (d, $J_{C-F}$ = 22.3 Hz), 111.6, 110.4, 33.7; $^{19}F\{^1H\}$ NMR: (376 MHz, $CDCl_3$) $\delta$ −116.3; IR: (ATR) 3402, 2963, 2903, 2369, 2239, 1508, 1260, 1092, 1018, 793, 737 $cm^{-1}$; MS (EI) $m/z$: 250 ($M^+$, 92), 249 (31), 222 (34), 155 (100), 128 (26), 101 (28), 77 (23), 75 (35); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{11}FN_2$ 250.0906; found 250.0910.

*2-(4-Chlorophenyl)-2-(1H-indol-3-yl)acetonitrile (**10ag**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-chlorobenzaldehyde (84.6 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (95.8 mg, 72% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.24 (brs, 1H), 7.42−7.29 (m, 6H), 7.26−7.20 (m, 1H), 7.13−7.08 (m, 1H), 7.13−7.08 (m, 1H), 5.36 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.5, 134.1, 133.9, 129.2, 129.0, 125.0, 123.3, 123.0, 120.4, 119.4, 118.6, 111.6, 110.4, 33.9; IR: (ATR) 3410, 3059, 2905, 2245, 1896, 1724, 1711, 1618, 1595, 1578, 1547, 1489, 1092, 1015, 814, 775, 741 $cm^{-1}$; MS (EI) $m/z$: 268 ($[M+2]^+$, 31), 266 ($M^+$, 82), 231 (29), 207 (51), 204 (26), 155 (100), 128 (22), 102 (31), 101 (34), 89 (22), 88 (28), 77 (23), 75 (40); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{11}ClN_2$ 266.0611; found 266.0609.

*4-(Cyano(1H-indol-3-yl)methyl)phenyl Acetate (**10ah**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025



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mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-formylphenyl acetate (98.7 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (110.5 mg, 76% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.27 (brs, 1H), 7.47−7.41 (m, 3H), 7.38 (d, $J$ = 8.4 Hz, 1H), 7.26−7.20 (m, 1H), 7.13−7.06 (m, 4H), 5.38 (s, 1H), 2.30 (s, 3H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 169.4, 150.3, 136.5, 132.9, 128.8, 125.1, 123.3, 122.9, 122.2, 120.3, 119.6, 118.7, 111.6, 110.5, 33.8, 21.1; IR: (ATR) 3397, 2963, 2359, 2243, 1748, 1605, 1504, 1260, 1194, 1165, 1094, 1016, 858, 794, 741 cm$^{-1}$; MS (EI) $m/z$: 290 ($M^+$, 52), 249 (20), 248 (100), 247 (32), 207 (49), 155 (63); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{18}H_{14}N_2O_2$ 290.1055; found 290.1050.

*2-(1H-Indol-3-yl)-2-(4-(trifluoromethyl)phenyl)acetonitrile (**10ai**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-(trifluoromethyl)-benzaldehyde (104.9 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a white solid (103.2 mg, 69% yield). Mp: 121.9−123.1 °C; $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.28 (brs, 1H), 7.62 (d, $J$ = 8.4 Hz, 2H), 7.56 (d, $J$ = 8.4 Hz, 2H), 7.45−7.36 (m, 2H), 7.28−7.21 (m, 1H), 7.20 (d, $J$ = 2.0 Hz, 1H), 7.15−7.07 (m, 1H), 5.44 (s, 1H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 139.2, 136.5, 130.4 (q, $J_{C-F}$ = 32.4 Hz), 128.1, 126.0 (br), 124.9, 123.8 (q, $J_{C-F}$ = 270.8 Hz), 123.4, 123.1, 120.5, 119.1, 118.5, 111.7, 109.8, 34.2; $^{19}$F{$^1$H} NMR: (376 MHz, $CDCl_3$) $\delta$ −65.2; IR: (ATR) 3333, 2255, 1620, 1458, 1422, 1323, 1260, 1219, 1153, 1132, 1105, 1067, 1018, 1011, 964, 862, 824, 791, 766, 745 cm$^{-1}$; MS (EI) $m/z$: 300 ($M^+$, 83), 155 (100); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{17}H_{11}F_3N_2$ 300.0874; found 300.0872.

*4-(Cyano(1H-indol-3-yl)methyl)benzonitrile (**10aj**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-formylbenzonitrile (78.7 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (106.8 mg, 83% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.29 (brs, 1H), 7.70−7.62 (m, 2H), 7.62−7.52 (m, 2H), 7.42 (d, $J$ = 8.4 Hz, 1H), 7.36 (d, $J$ = 8.4 Hz, 1H), 7.29−7.22 (m, 2H), 7.16−7.08 (m, 1H), 5.45 (s, 1H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 140.6, 136.6, 132.8, 128.4, 124.8, 123.5, 123.2, 120.6, 118.7, 118.3, 118.2, 112.2, 111.8, 109.3, 34.4; IR: (ATR) 3404, 3057, 2924, 2849, 2228, 1724, 1707, 1607, 1551, 1501, 1458, 1414, 1339, 1244, 824, 777, 766, 743 cm$^{-1}$; MS (EI) $m/z$: 257 ($M^+$, 75), 256 (20), 229 (22), 155 (100), 128 (20), 101 (25); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{17}H_{11}N_3$ 257.0953; found 257.0951.

*2-(1H-Indol-3-yl)-2-(4-nitrophenyl)acetonitrile (**10ak**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), 1,4-dioxane (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 4-nitrobenzaldehyde (90.7 mg, 0.60 mmol, 1.2 equiv) was conducted at 100 °C for 24 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a orange liquid (85.2 mg, 61% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.30 (brs, 1H), 8.25−8.20 (m, 2H), 7.63−7.60 (m, 2H), 7.43 (d, $J$ = 8.4 Hz, 1H), 7.37 (d, $J$ = 8.4 Hz, 1H), 7.31−7.20 (m, 2H), 7.15−7.05 (m, 1H), 5.50 (s, 1H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 147.7, 142.5, 136.6, 128.6, 124.8, 124.2, 123.5, 123.3, 120.7, 118.6, 118.3, 111.8, 109.3, 34.2; IR: (ATR) 3401, 3111, 3078, 2963, 2924, 2853, 2245, 1705, 1597, 1516, 1458, 1420, 1342, 1260, 1098, 1015, 856, 845, 818, 795, 785, 743, 725, 716 cm$^{-1}$; HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{11}N_3O_2$ 277.0851; found 277.0846.

*2-(3-Hydroxyphenyl)-2-(1H-indol-3-yl)acetonitrile (**10al**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in MeCN (1 mL) and acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv) and 3-hydroxybenzaldehyde (73.3 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a red liquid (86.5 mg, 70% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.18 (brs, 1H), 7.44 (d, $J$ = 8.4 Hz, 1H), 7.35 (d, $J$ = 8.4 Hz, 1H), 7.24−7.15 (m, 2H), 7.14−7.04 (m, 2H), 6.96 (d, $J$ = 8.4 Hz, 1H), 6.88 (s, 1H), 6.77 (dd, $J$ = 8.4, 1.4 Hz, 1H), 5.61 (brs, 1H), 5.30 (s, 1H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 156.2, 136.7, 136.4, 130.3, 125.1, 123.3, 122.9, 120.3, 120.0, 119.7, 118.7, 115.3, 114.6, 111.6, 110.4, 34.2; IR: (ATR) 3401, 3345, 2245, 1701, 1591, 1487, 1456, 1420, 1354, 1339, 1244, 1148, 1098, 1042, 770, 739 cm$^{-1}$; HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{12}N_2O$ 248.0950; found 248.0952.

*2-(1H-Indol-3-yl)-2-(3-methoxyphenyl)acetonitrile (**10am**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 3-methoxybenzaldehyde (81.9 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a yellow liquid (96.1 mg, 73% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.21 (brs, 1H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.38 (d, $J$ = 8.0 Hz, 1H), 7.28 (dd, $J$ = 8.0, 8.0 Hz, 1H), 7.22 (dd, $J$ = 8.0, 8.0 Hz, 1H), 7.18 (d, $J$ = 2.4 Hz, 1H), 7.11 (dd, $J$ = 8.0, 8.0 Hz, 1H), 7.03 (d, $J$ = 8.0 Hz, 1H), 7.00−6.95 (m, 1H), 6.85 (dd, $J$ = 8.0, 2.4 Hz, 1H), 5.36 (s, 1H), 3.77 (s, 3H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 160.0, 136.8, 136.5, 130.0, 125.2, 123.2, 122.9, 120.3, 120.0, 119.7, 118.8, 113.6, 113.4, 111.5, 110.8, 55.3, 34.4; IR: (ATR) 3402, 2963, 2835, 2243, 1599, 1585, 1487, 1456, 1433, 1260, 1096, 1036, 1013, 795, 741 cm$^{-1}$; HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{17}H_{14}N_2O$ 262.1106; found 262.1111.

*2-(3-Chlorophenyl)-2-(1H-indol-3-yl)acetonitrile (**10an**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 3-chlorobenzaldehyde (84.5 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (93.1 mg, 70% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.24 (brs, 1H), 7.45−7.38 (m, 3H), 7.37−7.28 (m, 3H), 7.28−7.20 (m, 2H), 7.12 (dd, $J$ = 7.4, 7.4 Hz, 1H), 5.37 (s, 1H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 137.3, 136.5, 134.9, 130.3, 128.5, 127.9, 125.9, 125.0, 123.3, 123.1, 120.5. 119.2, 118.6, 111.6, 110.2, 34.1; IR: (ATR) 3406, 3059, 2982, 2903, 2245, 1724, 1595, 1474, 1458, 1423, 1354, 1339, 1244, 1098, 1080, 1043, 1011, 739, 716, 702 cm$^{-1}$; MS (EI) $m/z$: 268 ($[M+2]^+$, 22), 266 ($M^+$, 66), 231 (25), 155 (100), 128 (21), 102 (24), 101 (34), 88 (21), 75 (30); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{16}H_{11}ClN_2$ 266.0611; found 266.0615.

*2-(1H-Indol-3-yl)-2-(2-methoxyphenyl)acetonitrile (**10ao**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), 1,4-dioxane (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 2-methoxybenzaldehyde (81.8 mg, 0.60 mmol, 1.2 equiv) was conducted at 100 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a orange liquid (118.7 mg, 91% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.20 (brs, 1H), 7.47 (d, $J$ = 7.6 Hz, 1H), 7.36 (d, $J$ = 7.6 Hz, 1H), 7.32−7.16 (m, 4H), 7.11−7.06 (m, 1H), 6.98−6.86 (m, 2H), 5.77 (s, 1H), 3.90 (s, 3H); $^{13}$C{$^1$H} NMR: (100 MHz, $CDCl_3$) $\delta$ 156.3, 136.5, 129.5, 128.9, 125.5, 123.9, 123.3, 122.7, 120.9, 120.2, 120.1, 118.9, 111.4, 110.8, 110.5, 55.6, 27.9; IR: (ATR) 3404, 3057, 2965, 2938, 2837, 2243, 1489, 1456, 1437, 1246, 1101, 1047, 1024, 739 cm$^{-1}$; MS (EI) $m/z$: 262 ($M^+$, 76), 247 (22), 155 (25), 131 (59), 130 (100); HRMS (EI) $m/z$: $[M]^+$ calcd for $C_{17}H_{14}N_2O$ 262.1106; found 262.1110.

*2-(2-Chlorophenyl)-2-(1H-indol-3-yl)acetonitrile (**10ap**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 2-chlorobenzaldehyde (84.3 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product


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as a brown liquid (82.2 mg, 71% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.23 (brs, 1H), 7.50−7.42 (m, 3H), 7.39 (d, $J$ = 8.4 Hz, 1H), 7.32−7.18 (m, 4H), 7.11 (dd, $J$ = 8.4, 8.4 Hz, 1H), 5.83 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.6, 133.3, 133.1, 130.0, 129.74, 129.71, 127.6, 125.2, 123.6, 123.0, 120.4, 119.0, 118.7, 111.6, 109.7, 31.7; IR: (ATR) 3329, 3063, 2907, 2253, 1620, 1476, 1460, 1437, 1103, 1051, 1036, 1011, 945, 791, 735, 708 cm$^{-1}$; MS (EI) $m/z$: 268 ([M + 2]$^+$, 16), 266 (M$^+$, 50), 230 (23), 229 (22), 204 (51), 155 (100), 128 (32), 102 (40), 101 (50), 89 (27), 88 (36), 87 (21), 77 (38), 76 (25), 75 (70), 74 (26), 63 (32), 51 (35), 50 (33); HRMS (EI) $m/z$: [M]$^+$ calcd for $C_{16}H_{11}ClN_2$ 266.0611; found 266.0607.

*2-(2-Bromophenyl)-2-(1H-indol-3-yl)acetonitrile (**10aq**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in MeCN (1 mL), 1-hydroxycyclohexane-1-carbonitrile (75.7 mg, 0.60 mmol, 1.2 equiv), and 2-bromobenzaldehyde (111.5 mg, 0.60 mmol, 1.2 equiv) was copnducted at 80 °C for 24 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (69.1 mg, 45% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.23 (brs, 1H), 7.64 (dd, $J$ = 7.6, 1.6 Hz, 1H), 7.50−7.44 (m, 2H), 7.42−7.37 (m, 1H), 7.30 (ddd, $J$ = 7.6, 7.6, 1.6 Hz, 1H), 7.25−7.18 (m, 3H), 7.15−7.09 (m, 1H), 5.84 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.5, 134.7, 133.3, 129.94, 129.85, 128.2, 125.1, 123.7, 123.6, 122.9, 120.3, 119.1, 118.8, 111.6, 109.7, 34.5; IR: (ATR) 3426, 2922, 2251, 1620, 1570, 1549, 1476, 1458, 1443, 1416, 1339, 1254, 1217, 1188, 1123, 1094, 1038, 1028, 1011, 970, 827, 799, 741 cm$^{-1}$; MS (EI) $m/z$: 312 ([M + 2]$^+$, 39), 310 (M$^+$, 40), 231 (35), 230 (21), 229 (44), 204 (100), 203 (27), 176 (25), 155 (89), 128 (28), 127 (21), 102 (53), 101 (49), 89 (25), 88 (42), 77 (36), 76 (40), 75 (53), 74 (24), 63 (34), 51 (34), 50 (39); HRMS (EI) $m/z$: [M]$^+$ calcd for $C_{16}H_{11}BrN_2$ 310.0106; found 310.0113.

*2-(1H-Indol-3-yl)-2-(2-nitrophenyl)acetonitrile (**10ar**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv), $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 2-nitrobenzaldehyde (90.7 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a brown liquid (97.9 mg, 71% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.23 (brs, 1H), 8.06 (dd, $J$ = 8.2, 1.4 Hz, 1H), 7.80 (dd, $J$ = 8.2, 1.4 Hz, 1H), 7.64 (ddd, $J$ = 8.2, 8.2, 1.4 Hz, 1H), 7.52 (ddd, $J$ = 8.2, 8.2, 1.4 Hz, 1H), 7.44−7.35 (m, 2H), 7.31−7.18 (m, 2H), 7.13−7.08 (m, 1H), 6.37 (s, 1H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 147.8, 136.4, 134.0, 130.5, 130.3, 129.5, 125.7, 124.9, 123.9, 123.1, 120.6, 118.5, 111.7, 108.8, 30.9 (one $sp^2$ signal was not observed because of overlapping); IR: (ATR) 3401, 2963, 2247, 2214, 1520, 1341, 1258, 1096, 1080, 1013, 785, 764, 741, 700 cm$^{-1}$; HRMS (EI) $m/z$: [M]$^+$ calcd for $C_{16}H_{11}N_3O_2$ 277.0851; found 277.0849.

*2-(1H-Indol-3-yl)pentanenitrile (**10as**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %),1*H*-indole (58.8 mg, 0.50 mmol, 1.0 equiv), $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and butyraldehyde (43.7 mg, 0.61 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (56.2 mg, 57% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.16 (brs, 1H), 7.64 (d, $J$ = 8.4 Hz, 1H), 7.41 (d, $J$ = 8.4 Hz, 1H), 7.28−7.25 (m, 1H), 7.23 (d, $J$ = 2.4 Hz, 1H), 7.22−7.14 (m, 1H), 4.10 (dd, $J$ = 7.2, 7.2 Hz, 1H), 2.13−1.92 (m, 2H), 1.70−1.48 (m, 2H), 0.98 (t, $J$ = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.4, 125.2, 122.7, 122.2, 121.2, 120.0, 118.4, 111.6, 110.8, 35.9, 28.6, 20.4, 13.4; IR: (ATR) 3408, 3366, 2959, 2932, 2872, 2239, 1620, 1551, 1491, 1458, 1422, 1354, 1339, 1244, 1098, 1011, 822, 739 cm$^{-1}$; MS (EI) $m/z$: 198 (M$^+$, 12), 155 (100), 128 (24), 101 (30); HRMS (EI) $m/z$: [M]$^+$ calcd for $C_{13}H_{14}N_2$ 198.1157; found 198.1161.

*2-(1H-Indol-3-yl)-4-methylpentanenitrile (**10at**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in $MeNO_2$ (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and 3-methylbutanal (51.7 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 6 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (75.4 mg, 71% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.24 (brs, 1H), 7.64 (d, $J$ = 7.6 Hz, 1H), 7.36 (d, $J$ = 7.6 Hz, 1H), 7.26−7.20 (m, 1H), 7.19−7.14 (m, 1H), 7.12 (d, $J$ = 2.4 Hz, 1H), 4.09 (dd, $J$ = 9.6, 5.6 Hz, 1H), 2.11−1.79 (m, 3H), 1.01 (d, $J$ = 6.4 Hz, 3H), 0.98 (d, $J$ = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 136.3, 125.1, 122.6, 122.0, 121.4, 119.9, 118.3, 111.6, 110.6, 42.8, 26.8, 26.0, 22.5, 21.6; IR: (ATR) 3410, 3059, 2957, 2932, 2870, 2239, 1620, 1553, 1458, 1422, 1354, 1339, 1246, 1098, 1011, 816, 739 cm$^{-1}$; MS (EI) $m/z$: 212 (M$^+$, 26), 156 (38), 155 (100); HRMS (EI) $m/z$: [M]$^+$ calcd for $C_{14}H_{16}N_2$ 212.1313; found 212.1316.

*2-(1H-Indol-3-yl)-3,3-dimethylbutanenitrile (**10au**).* According to the typical procedure B, the reaction using $B(C_6F_5)_3$ (12.8 mg, 0.025 mmol, 5 mol %), a solution of 1*H*-indole (58.6 mg, 0.50 mmol, 1.0 equiv) in MeCN (1 mL), acetone cyanohydrin (55 μL, 0.6 mmol, 1.2 equiv), and pivalaldehyde (51.9 mg, 0.60 mmol, 1.2 equiv) was conducted at 80 °C for 24 h. Purification by flash column chromatography on silica gel (hexane/EtOAc = 8:2) gave the product as a colorless liquid (37.7 mg, 36% yield). $^1$H NMR: (400 MHz, $CDCl_3$) $\delta$ 8.31 (brs, 1H), 7.62 (d, $J$ = 7.6 Hz, 1H), 7.39 (d, $J$ = 7.6 Hz, 1H), 7.26−7.19 (m, 2H), 7.19−7.12 (m, 1H), 3.89 (s, 1H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR: (100 MHz, $CDCl_3$) $\delta$ 135.7, 126.7, 124.1, 122.4, 121.0, 120.1, 119.0, 111.4, 108.8, 40.7, 35.7, 27.5; IR: (ATR) 3406, 3366, 2963, 2936, 2907, 2891, 2870, 2236, 1620, 1543, 1458, 1422, 1368, 1354, 1339, 1219, 1099, 1013, 772, 739 cm$^{-1}$; MS (EI) $m/z$: 212 (M$^+$, 16), 156 (100), 155 (71), 130 (21), 128 (25), 101 (26), 57 (50); HRMS (EI) $m/z$: [M]$^+$ calcd for $C_{14}H_{16}N_2$ 212.1313; found 212.1316.

## ■ ASSOCIATED CONTENT

### Supporting Information

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Experimental procedures and copies of NMR spectra (PDF)

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### Notes

The authors declare no competing financial interest.

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