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One-Pot Synthesis of 2-Cyano-1,4-diketones: Applications to Synthesis of Cyanosubstituted Furans, Pyrroles, and Dihydropyridazines

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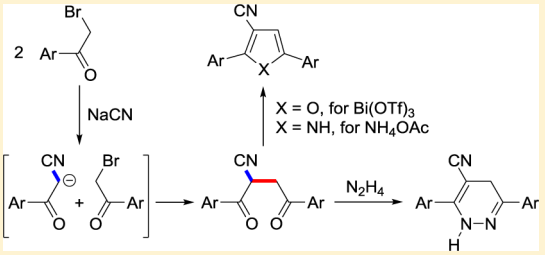
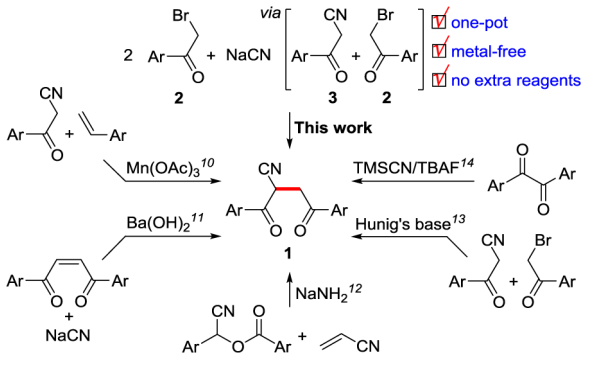
Supporting Information

ABSTRACT: A convenient synthetic route for the construction of functionalized 2-cyano-1,4-diketones has been established from the nucleophilic substitution of 2-bromoacetophenones with NaCN via the *in situ*-generated β-ketonitriles. This method was further applied to the synthesis of cyanosubstituted furans, pyrroles, or dihydropyridazines, which were obtained in good to excellent yields using $Bi(OTf)_3$, NH_4OAc, or N_2H_4. The key structures were confirmed by X-ray single crystal diffraction analysis.



The 1,4-Diketones are valuable synthetic building blocks for the preparation of heterocyclic compounds such as furans, pyrroles, thiophenes, selenophenes, and pyridazines.[1] A variety of synthetic routes have been developed for the construction of 1,4-diketones, including the one-carbon expansion of 1,3-dicarbonyl compounds,[2] oxidative coupling of enolates,[3] acylation of homoenolate synthons,[4] photolytic dimerization of β-ketosulfones,[5] nucleophilic substitution of enolates with α-haloketones,[6] and other methods.[7] A series of 2-cyano-1,4-diketones (**1**) are found in numerous bioactive molecules and functionalized materials.[8] Because of the versatile possible transformations of the cyano group, the introduction of a cyano substitutent is of significant interest.[9] As shown in Scheme 1, a number of reported methods for the formation of 2-cyano-1,4-diketones **1** have been studied, including the $Mn(OAc)_3$-facilitated oxidation of β-ketonitriles with styrene,[10] $Ba(OH)_2$-activated addition of 1,4-enediones with NaCN,[11] $NaNH_2$-promoted benzoylative decyanation of *O*-aroylmandelonitriles with acrylonitrile,[12] and additional approaches.[13] Accordingly, further synthetic application for **1** is a continuing need. Therefore, Alexakis and co-workers developed a NHC-catalyzed domino annulation of **1** with ynals to afford the vitamin B_1 analogues.[14]

Scheme 1. Synthesis of 2-Cyano-1,4-diketones 1



With the known synthetic routes, the extra addition of the reagent was the common point, including the reaction conditions of $Mn(OAc)_2$/AcOH,[10] $Ba(OH)_2$/EtOH,[11] $NaNH_2$/DMF,[12] Hunig's base/$MgCl_2$,[13] or TMSCN/TBAF.[14] Compared with the reports, our protocol for the synthesis of 2-cyano-1,4-diketones is performed as a one-pot and convenient route via treatment of substituted 2-bromoacetophenones **2** with NaCN in the cosolvent of dioxane and water. No extra reagents are needed.

Recently, we utilized β-ketosulfone as the building block to prepare diversified benzoannulated frameworks.[15] Following that success, further synthetic applications of β-ketonitriles **3** were attempted. We found that when the sulfonyl group was substituted with a cyano group, the NaCN-mediated double reaction with two equiv of 2-bromoacetophenones **2** was observed in addition to the predicted mononucleophilic substitution. To the best of our knowledge, **1** was isolated in combination with **3** using 1.5 equiv of NaCN in yields of 55% (for **1a**) and 40% (for **3a**), respectively. Therefore, we aimed to use sodium cyanide in the same reaction condition to prepare a series of functionalized 2-cyano-1,4-diketones **1**.

To examine the one-pot transformation from **2** to **1** and **3**, 2-bromoacetophenone (**2a**, Ar = Ph) was selected as the model substrate. As shown in Table 1, the nucleophilic substitution reactions of **2a** with the use of sodium cyanide (NaCN), potassium cyanide (KCN), and copper(I) cyanide (CuCN) were tested. Initially, the reaction of **2a** with 1.1 equiv of NaCN

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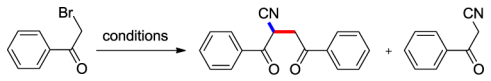
Table 1. Reaction Conditions for the Construction of 1a[a]



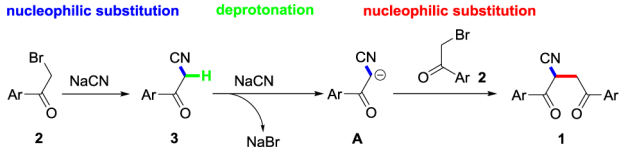
entry	cyanide (equiv)	solvent (v/v)	T (°C)	yield (%)[b] 1a	3a
1	NaCN (1.1)	dioxane/H_2O (9/1)	25	25	60[c]
2	NaCN (1.5)	dioxane/H_2O (9/1)	25	55	40
3	NaCN (2.2)	dioxane/H_2O (9/1)	25	80	*d*
4	NaCN (3.5)	dioxane/H_2O (9/1)	25	75	*d*
5	KCN (2.2)	dioxane/H_2O (9/1)	25	75	20
6	KCN (3.5)	dioxane/H_2O (9/1)	25	60	10
7	CuCN (1.5)	dioxane/H_2O (9/1)	25	*d*	17[c]
8	CuCN (2.2)	dioxane/H_2O (9/1)	25	*d*	12[c]
9	CuCN (3.5)	dioxane/H_2O (9/1)	25	*d*	10[c]
10	NaCN (2.2)	MeCN/H_2O (9/1)	25	58	10[c]
11	NaCN (2.2)	THF/H_2O (9/1)	25	62	15[c]
12	NaCN (2.2)	MeOH/H_2O (9/1)	25	60	18[c]
13	NaCN (2.2)	DMF/H_2O (9/1)	25	65	16[c]
14	NaCN (2.2)	dioxane/H_2O (9/1)	100	60	10[e]

[a]Conditions: **2a** (2.0 mmol), cosolvent (10 mL), 3 h. [b]Isolated yield. [c]**2a** was recovered (entry 1, 13%; entry 7, 70%; entry 8, 63%; entry 9, 50%; entries 10−13, trace amounts). [d]No observation. [e]10% of unknown products was isolated.

in the cosolvent of dioxane and water for 3 h at room temperature gave **1a** (25%) and **3a** (60%) with recovered **2a** in 13% yield (entry 1). When 1.5 equiv of NaCN was used, **1a** was increased to the yield of 55% and **3a** was decreased to 40% yield (entry 2). When the amount of NaCN was increased to 2.2 equiv, **1a** was obtained in the yield of 80% with trace amounts of **3a** (entry 3). A similar yield of **1a** was obtained in the reaction of **2a** with 3.5 equiv of NaCN (entry 4). Furthermore, reactions of **2a** with 2.2 or 3.5 equiv of KCN were attempted; **1a** was isolated in moderate yield (75%, 60%) with **3a** (20%, 10%) in entries 5−6. Different amounts of CuCN were also tested with **2a**, but only trace amounts of **3a** were obtained with recovered starting material **2a** (entries 7−9). Solvents were also screened for their effect on the reaction. When the reaction was performed in MeCN, THF, MeOH, or DMF, **1a** was isolated in a lower yield (58%, 62%, 60%, and 65%) with only a small amount of **3a** (10%, 15%, 18%, and 16%) and trace amount of recovered **2a** at room temperature (entries 10−13). Increasing the temperature to 100 °C gave the desired product **1a** in 60% yield with 10% yield of **3a**, but some unknown products were also isolated (entry 14). Notably, **2a** reacted with 2.2 equiv of NaCN effectively in a mixture of dioxane and water for 3 h at room temperature to give **1a** in 80% yield.

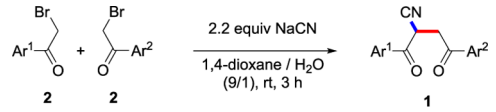
On the basis of these results, a reaction mechanism was proposed and is shown in Scheme 2. Initially, the S_N2 reaction of **2** with NaCN took place to form nitrile **3**. We believe the excess equiv of NaCN also acts as a base to conduct

Scheme 2. Possible Mechanism



deprotonation of **3** producing intermediate **A** and NaBr, followed by the S_N2 reaction of **A** with starting **2** to yield the desired product **1**. With the optimal reaction conditions in hand (Table 1, entry 3), we further investigated the substrate scope and limitation of this reaction. Various 2-bromoacetophenones **2** were subjected to the reaction under identical conditions, and the representative results and yields are shown in Table 2, entries 1−12. Substituted 2-bromoacetophenones **2**

Table 2. Scope of Substituted 2-Bromoacetophenones[a,b]



entry	2, Ar^1, Ar^2	1 (%)[b]
1	**2a**, Ph, Ph	**1a**, 80
2	**2b**, 4-FC_6H_4, 4-FC_6H_4	**1b**, 82
3	**2c**, 4-$MeOC_6H_4$, 4-$MeOC_6H_4$	**1c**, 87
4	**2d**, 4-MeC_6H_4, 4-MeC_6H_4	**1d**, 83
5	**2e**, 3-$MeOC_6H_4$, 3-$MeOC_6H_4$	**1e**, 85
6	**2f**, 2-naphthyl, 2-naphthyl	**1f**, 90
7	**2g**, 4-$CF_3C_6H_4$, 4-$CF_3C_6H_4$	**1g**, 83
8	**2h**, 4-PhC_6H_4, 4-PhC_6H_4	**1h**, 88
9	**2i**, 3,4,5-$(MeO)_3C_6H_2$, 3,4,5-$(MeO)_3C_6H_2$	**1i**, 86
10	**2j**, 3,4-$OCH_2OC_6H_3$, 3,4-$OCH_2OC_6H_3$	**1j**, 85
11	**2d**, 4-MeC_6H_4, **2k**, 2,4-$(MeO)_2C_6H_3$	**1k**, 55
12	**2b**, 4-FC_6H_4, **2c**, 4-$MeOC_6H_4$	**1l**, **1m** 62[c]

[a]Conditions: **2** (2.0 mmol), NaCN (4.4 mmol), 3 h, rt. [b]Isolated yields. [c]1:1 of ratio.

reacted readily with NaCN in dioxane and water at room temperature to afford functionalized 2-cyano-1,4-diketones **1** in good to excellent yields. The reaction demonstrated a wide tolerance toward a variety of substituted groups such as electron-withdrawing groups 4-fluorophenyl (**1b**, 82%) and 4-trifluoromethylphenyl (**1g**, 83%) and electron-donating groups, 4-methoxyphenyl (**1c**, 87%), 3-methoxyphenyl (**1e**, 85%), 3,4,5-trimethoxyphenyl (**1i**, 86%), 3,4-methylenedioxyphenyl (**1j**, 85%), 4-methylphenyl (**1d**, 83%), 2-naphthyl (**1f**, 90%), and biphenyl (**1h**, 88%). The structure of **1f** was also determined by single-crystal X-ray crystallography.[16] In this one-pot protocol, the preparation of pseudosymmetrical **1a**−**1j** was effective with good yields. To our delight, we further explored the unsymmetrical **1** through the reaction of **2d** (Ar = 4-MePh) and **2k** (Ar = 2,4-$(MeO)_2$Ph) under identical reaction conditions to give **1k** (55%). As expected, **2b** and **2c** reacted with NaCN to afford **1l** and **1m** (62%) at an approximate ratio of 1:1 (Figure 1). The configuration of the newly formed C−C

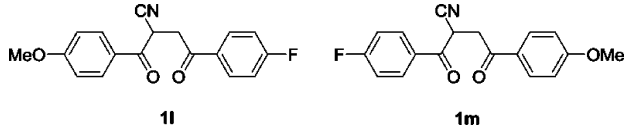


Figure 1. Structures of **1l** and **1m**.

bond in **1k** was assigned by NOE-cross correlation spectroscopic studies (Figure 2). According to the results of Table 2 and entry 11, **1k** was obtained in a sole isomer. We think that for the reaction selectivity of **2d** (Ar = 4-MeC_6H_4) and **2k** (Ar = 2,4-$(MeO)_2C_6H_3$), NaCN preferred to react with **2d** because **2k** with the 2-methoxy substituent had more steric

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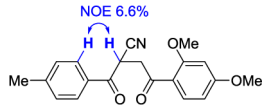


Figure 2. NOE correlation of **1k**.

hindrance. Subsequently, in situ generated β-ketonitrile reacted with **2k** to produce **1k**. From the results, no observation of two isomers occurred. With the results of Table 2 and entry 12, **1l** and **1m** were obtained in the inseparable mixture. We think that the reaction selectivity has not been performed in the NaCN-mediated one-pot reaction because no steric hindrance occurred between **2b** (Ar = 4-FC_6H_4) and **2c** (Ar = 4-$MeOC_6H_4$). From the result, the mixture of **1l** and **1m** with a ratio of 1:1 was observed. On the basis of the formation of the sole **1k** and the inseparable mixture of **1l** and **1m**, we envision that the 2-methoxy substituent on the aryl group with a steric hindrance is an important factor affecting the formation of unsymmetrical 2-cyano-1,4-diketone. Therefore, the reaction trend is attributed to the preparation of pseudosymmetrical 2-cyano-1,4-diketone.

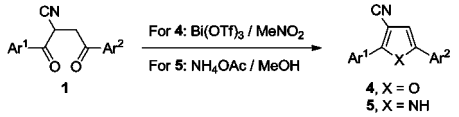
Because of the unique versatility of 1,4-diketone, we further explored the applications of **1** in the construction of heterocyclic five-membered ring moieties.[17] Within this structural family, furans and pyrroles are particularly meaningful molecules and commonly synthesized in organic chemistry.[18] Cyanosubstituted furans and pyrroles are widely used in medical chemistry and have been prepared by numerous research groups.[19]

Because of our previous work in the synthesis of substituted furans,[15b] we believed that $Bi(OTf)_3$ was an effective reagent to form the furan motif and thus chose it as the Lewis acid to react with **1** to afford furan skeletons. The treatment of $Bi(OTf)_3$ with **1** readily gave the desired furans **4** in entries 1−11 in good to excellent yields (65−92%). Because of the inseparable mixture of **1l** and **1m** (Table 1, entries 12−13), the mixture reacted with $Bi(OTf)_3$. Fortunately, in this step, **4l** and **4m** could be separated in 75% and 78% yields (entries 12−13), respectively. We also adopted our experience with NH_4OAc-mediated domino aminocyclization[15a] for the synthesis of 3-cyanosubstitutedpyrroles from **1**. Therefore, NH_4OAc (1.5 mmol) was added to a solution of **1a−e** in MeOH at reflux to give the desired pyrroles **5a−e** (entries 14−18). All yields are shown in Table 3, and the NOE-cross correlations of **4l** and **4m** are depicted in Figure 3.

In addition to five-membered furans and pyrroles, the application of this reaction to the six-membered dihydropyridazine was our goal. Pyridazines are versatile in the synthesis of natural products, which are useful synthetic intermediates,[20] and are known to exhibit important pharmacological activities.[21] Among their derivatives, dihydropyridazines represent an important intermediate for aromatized pyridazines. Recently, we published a protocol for the synthesis of substituted pyridazines mediated by $In(OTf)_3$.[22] As shown in Table 4, compounds **1a−f** were subjected to this cyclocondensation with N_2H_4 **7a** in MeOH at reflux, and the corresponding products **6a−f** were obtained in high yields (entries 1−6). Encouraged by these results, phenylhydrazine was also tested in this conversion. Fortunately, the reaction of **1** with phenylhydrazine **7b** easily gave triphenylpyridazine **6g** in a yield of 90% (entry 7).

In summary, a convenient protocol for the synthesis of functionalized 2-cyano-1,4-diketones in good yields was developed. Further investigation regarding synthetic applications of 2-cyano-1,4-diketones including cyanosubstituted furans, pyrroles and dihydropyridazines, was conducted. The structure of some products were confirmed by X-ray crystallography.

Table 3. Synthesis of 3-Cyano Five-Membered Rings 4 and 5[a,b]



entry	1, Ar^1, Ar^2	4, 5 (%)[c]
1	**1a**, Ph, Ph	**4a**, 88
2	**1b**, 4-FC_6H_4, 4-FC_6H_4	**4b**, 86
3	**1c**, 4-$MeOC_6H_4$, 4-$MeOC_6H_4$	**4c**, 90
4	**1d**, 4-MeC_6H_4, 4-MeC_6H_4	**4d**, 89
5	**1e**, 3-$MeOC_6H_4$, 3-$MeOC_6H_4$	**4e**, 88
6	**1f**, 2-naphthyl, 2-naphthyl	**4f**, 92
7	**1g**, 4-$CF_3C_6H_4$, 4-$CF_3C_6H_4$	**4g**, 65
8	**1h**, 4-PhC_6H_4, 4-PhC_6H_4	**4h**, 87
9	**1i**, 3,4,5-$(MeO)_3C_6H_2$, 3,4,5-$(MeO)_3C_6H_2$	**4i**, 89
10	**1j**, 3,4-$OCH_2OC_6H_3$, 3,4-$OCH_2OC_6H_3$	**4j**, 88
11	**1k**, 4-MeC_6H_4, 2,4-$(MeO)_2C_6H_3$	**4k**, 89
12[d]	**1l**, 4-$MeOC_6H_4$, 4-FC_6H_4	**4l**, 75
13[d]	**1m**, 4-FC_6H_4, 4-$MeOC_6H_4$	**4m**, 78
14	**1a**, Ph, Ph	**5a**, 85
15	**1b**, 4-FC_6H_4, 4-FC_6H_4	**5b**, 83
16	**1c**, 4-$MeOC_6H_4$, 4-$MeOC_6H_4$	**5c**, 86
17	**1d**, 4-MeC_6H_4, 4-MeC_6H_4	**5d**, 87
18	**1e**, 3-$MeOC_6H_4$, 3-$MeOC_6H_4$	**5e**, 86

[a]Conditions: **1** (1.0 mmol), 2 h. [b]For **4**, $Bi(OTf)_3$ (13 mg, 2.0 mol %), rt; for **5**, NH_4OAc (160 mg, 2.1 mmol), reflux. [c]Isolated yield. [d]Inseparated mixture (**1l**/**1m** = 1:1).

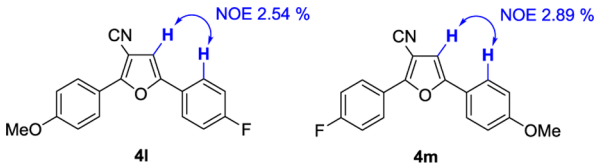
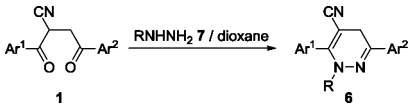


Figure 3. NOE correlation of **4l** and **4m**.

Table 4. Synthetic Route to 3-Cyano Dihydropyridazines 6[a,b]



entry	1, Ar^1, Ar^2	7, R	6 (%)[c]
1	**1a**, Ph, Ph	**7a**, H	**6a**, 95
2	**1b**, 4-FC_6H_4, 4-FC_6H_4	**7a**, H	**6b**, 96
3	**1c**, 4-$MeOC_6H_4$, 4-$MeOC_6H_4$	**7a**, H	**6c**, 94
4	**1d**, 4-MeC_6H_4, 4-MeC_6H_4	**7a**, H	**6d**, 95
5	**1e**, 3-$MeOC_6H_4$, 3-$MeOC_6H_4$	**7a**, H	**6e**, 93
6	**1f**, 2-naphthyl, 2-naphthyl	**7a**, H	**6f**, 90
7	**1a**, Ph, Ph	**7b**, Ph	**6g**, 90

[a]Conditions: **1** (1.0 mmol), 0.5 h, rt. [b]For **6a−6f**, N_2H_4 **7a** (1.0 mL); for **6g**, $PhNHNH_2$ **7b** (1.0 mmol). [c]Isolated yields.

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EXPERIMENTAL SECTION

General. All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Melting points were determined with a melting apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a spectrometer operating at 400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm), and the coupling constants (J) are given in Hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer microTOF-Q by ESI using a hybrid ion-trap. X-ray crystal structures were obtained with a diffractometer (CAD4, Kappa CCD). Infrared spectra were collected with neat material (oil or solid) on an FT-IR spectrometer, and ATR correction was performed on the spectra obtained.

General Synthetic Procedure for Synthesis of 1a−1l. NaCN (sodium cyanide, 216 mg, 4.4 mmol) was added to a solution of substituted 2-bromoacetophenones **2** (2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt. The reaction mixture was stirred at rt for 3 h, and the solvent was concentrated. The residue was diluted with water (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford the crude product. Purification on silica gel (hexanes/EtOAc = 10/1−4/1) afforded **1a−1m**.

2-Benzoyl-4-oxo-4-phenylbutanenitrile (1a).[14] According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2a** (398 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **1a** (80%, 421 mg; for Table 1 and entry 3). Colorless solid; mp = 64−65 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{17}H_{13}NO_2Na$ 286.0844, found 286.0840; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09−8.06 (m, 2H), 7.97−7.95 (m, 2H), 7.64 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 5.05 (dd, J = 4.4, 8.8 Hz, 1H), 4.05 (dd, J = 8.8, 18.4 Hz, 1H), 3.55 (dd, J = 4.4, 18.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.6, 188.9, 135.1, 134.5, 133.9, 133.8, 128.9 (2x), 128.8 (2x), 128.7 (2x), 128.0 (2x), 116.9, 37.4, 33.0. FT-IR (cm^{-1}): 2932, 2242, 1782, 1680, 1234, 740, 693. For **3a** (60%, 174 mg; Table 1 and entry 1).[23] Colorless solid; mp = 79−80 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for C_9H_7NONa 168.0425, found 168.0428; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.91 (m, 2H), 7.68−7.64 (m, 1H), 7.55−7.50 (m, 2H), 4.09 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1, 134.7, 134.3, 129.1 (2x), 128.4 (2x), 113.7, 29.3. FT-IR (cm^{-1}): 2922, 2263, 1696, 1597, 1217, 756, 688.

2-(4-Fluorobenzoyl)-4-(4-fluorophenyl)-4-oxobutanenitrile (1b).[14] According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2b** (434 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **1b** (82%, 491 mg). Colorless solid; mp = 68−69 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{17}H_{11}F_2NO_2Na$ 322.0656, found 322.0652. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14−8.11 (m, 2H), 8.03−8.00 (m, 2H), 7.24−7.15 (m, 4H), 4.99 (dd, J = 4.4, 9.2 Hz, 1H), 4.06 (dd, J = 9.2, 18.0 Hz, 1H), 3.51 (dd, J = 4.4, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 187.3, 166.6 (d, J = 256.2 Hz), 166.3 (d, J = 255.5 Hz), 131.8 (d, J = 9.8 Hz, 2x), 131.7 (d, J = 3.0 Hz), 131.0 (d, J = 9.1 Hz, 2x), 130.4 (d, J = 2.3 Hz), 116.7, 116.4 (d, J = 22.0 Hz, 2x), 116.1 (d, J = 22.0 Hz, 2x), 37.3, 33.0. FT-IR (cm^{-1}): 2931, 2244, 1723, 1686, 1232, 832, 745.

2-(4-Methoxybenzoyl)-4-(4-methoxyphenyl)-4-oxobutanenitrile (1c). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2c** (458 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **1c** (87%, 563 mg). Colorless solid; mp = 107−108 °C (recrystallized from hexanes and EtOAc). HRMS (ESI, M$^+$+Na) calcd for $C_{19}H_{17}NO_4Na$ 346.1055, found 346.1052. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 4.99 (dd, J = 4.8, 8.8 Hz, 1H), 3.98 (dd, J = 8.8, 18.0 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.46 (dd, J = 4.8, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 187.3, 164.6, 164.0, 131.3 (2x), 130.8, 130.5 (2x), 128.3, 126.8, 117.4, 114.2 (2x), 113.9, 55.5, 55.4, 37.1, 32.7. FT-IR (cm^{-1}): 2936, 2244, 1678, 1596, 1171, 843, 796.

2-(4-Methylbenzoyl)-4-oxo-4-(p-tolyl)butanenitrile (1d). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2d** (426 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **1d** (83%, 484 mg). Colorless solid; mp = 141−142 °C (recrystallized from hexanes and EtOAc). HRMS (ESI, M$^+$+Na) calcd for $C_{19}H_{17}NO_2Na$ 314.1157, found 314.1153. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 5.03 (dd, J = 4.4, 8.4 Hz, 1H), 4.06 (dd, J = 8.4, 17.6 Hz, 1H), 3.51 (dd, J = 4.4, 17.6 Hz, 1H), 2.45 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3, 188.5, 145.9, 145.0, 132.9, 131.6, 129.8 (2x), 129.5 (2x), 129.1 (2x), 128.4 (2x), 117.2, 37.5, 33.0, 21.8, 21.7. FT-IR (cm^{-1}): 2923, 2242, 1694, 1677, 1238, 820, 759.

2-(3-Methoxybenzoyl)-4-(3-methoxyphenyl)-4-oxobutanenitrile (1e). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2e** (458 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **1e** (85%, 550 mg). colorless oil; HRMS (ESI, M$^+$+Na) calcd for $C_{19}H_{17}NO_4Na$ 346.1055, found 346.1048. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.6 Hz, 1H), 7.57−7.54 (m, 2H), 7.47−7.37 (m, 3H), 7.19 (d, J = 7.6 Hz, 1H), 7.15 (d, J = 7.6 Hz, 1H), 5.01 (dd, J = 4.4, 8.8 Hz, 1H), 4.04 (dd, J = 8.8, 18.0 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.54 (dd, J = 4.4, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.5, 188.8, 160.0, 159.9, 136.5, 135.2, 130.0, 129.8, 121.4, 121.2, 120.8, 120.5, 116.9, 113.0, 112.3, 55.43, 55.37, 37.7, 33.3. FT-IR (cm^{-1}): 2940, 2246, 1723, 1685, 1262, 732, 684.

2-(2-Naphthoyl)-4-(naphthalen-2-yl)-4-oxobutanenitrile (1f). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2f** (498 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **1f** (90%, 654 mg). Colorless solid; mp = 145−146 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{25}H_{17}NO_2Na$ 386.1157, found 386.1154. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (s, 1H), 8.56 (s, 1H), 8.11−7.88 (m, 8H), 7.69−7.57 (m, 4H), 5.28 (dd, J = 4.4, 8.8 Hz, 1H), 4.30 (dd, J = 8.8, 17.6 Hz, 1H), 3.75 (dd, J = 4.4, 17.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.6, 188.9, 136.2, 135.9 (2x), 132.6, 132.4, 132.3, 131.4, 130.4, 129.9, 129.7, 129.4, 129.1, 129.0, 128.8, 127.84, 127.83, 127.2, 127.1, 123.9, 123.5, 117.2, 37.8, 33.3. FT-IR (cm^{-1}): 2926, 2245, 1678, 1626, 1189, 834, 753. Single-crystal X-ray diagram: crystal of **1f** was grown by slow diffusion of EtOAc into a solution of **1f** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group $P\bar{1}$, a = 7.9748(3) Å, b = 8.5090(4) Å, c = 13.9508(6) Å, V = 889.17(7) Å^3, Z = 2, d_{calcd} = 1.357 g/cm^3, $F(000)$ = 380, 2θ range 1.51−26.55°, R indices (all data) $R1$ = 0.0401, $wR2$ = 0.0959.

4-Oxo-2-(4-(trifluoromethyl)benzoyl)-4-(4-(trifluoromethyl)-phenyl)butanenitrile (1g).[14] According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2g** (534 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **1g** (83%, 663 mg). Colorless solid; mp = 96−97 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M$^+$+Na) calcd for $C_{19}H_{11}F_6NO_2Na$ 422.0592, found 422.0585. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 8.4 Hz, 2H), 5.02 (dd, J = 4.0, 9.2 Hz, 1H), 4.15 (dd, J = 9.2, 18.0 Hz, 1H), 3.60 (dd, J = 4.0, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.8, 188.1, 137.7, 136.6, 135.9 (q, J = 33.4 Hz), 135.5 (q, J = 32.6 Hz), 129.4 (2x),

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128.6 (2x), 126.2 (q, J = 3.8 Hz, 2x), 126.1 (q, J = 3.0 Hz, 2x), 123.4 (q, J = 271.4 Hz), 123.2 (q, J = 270.6 Hz), 116.1, 37.7, 33.5. FT-IR (cm^{-1}): 2926, 2255, 1718, 1687, 1323, 1131, 1067.

2-([1,1′-Biphenyl]-4-carbonyl)-4-([1,1′-biphenyl]-4-yl)-4-oxobutanenitrile (1h). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2h** (550 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **1h** (88%, 731 mg). Colorless solid; mp = 158−159 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{29}H_{21}NO_2Na$ 438.1470, found 438.1467. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.4 Hz, 2H), 8.08 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.67−7.63 (m, 4H), 7.52−7.48 (m, 4H), 7.46−7.41 (m, 2H), 5.11 (dd, J = 4.4, 8.8 Hz, 1H), 4.16 (dd, J = 8.8, 18.0 Hz, 1H), 3.60 (dd, J = 4.4, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.3, 188.4, 147.3, 146.7, 139.5, 139.3, 134.0, 132.6, 129.6 (2x), 129.01 (2x), 128.99 (2x), 128.8 (2x), 128.6, 128.4, 127.6 (2x), 127.4 (2x), 127.3 (2x), 127.2 (2x), 117.1, 37.6, 33.1. FT-IR (cm^{-1}): 2910, 2348, 1713, 1682, 1266, 763, 680.

4-Oxo-2-(3,4,5-trimethoxybenzoyl)-4-(3,4,5-trimethoxyphenyl)butanenitrile (1i). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2i** (578 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **1i** (86%, 763 mg). Colorless solid; mp = 155−156 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{23}H_{25}NO_8Na$ 466.1478, found 466.1472. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (br s, 2H), 7.19 (br s, 2H), 5.00 (dd, J = 4.4, 8.8 Hz, 1H), 4.01 (dd, J = 8.8, 18.0 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 6H), 3.88 (s, 3H), 3.86 (s, 6H), 3.49 (dd, J = 4.4, 18.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.5, 187.7, 153.1 (2x), 153.0 (2x), 143.8, 143.2, 130.2, 128.8, 117.1, 106.4 (2x), 105.5 (2x), 60.84, 60.79, 56.2 (2x), 56.1 (2x), 37.4, 32.9. FT-IR (cm^{-1}): 2938, 2311, 1671, 1585, 1417, 1337, 1127.

4-(Benzo[*d*][1,3]dioxol-5-yl)-2-(benzo[*d*][1,3]dioxole-5-carbonyl)-4-oxobutanenitrile (1j). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol) and **2j** (486 mg, 2.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **1j** (85%, 597 mg). Colorless solid; mp = 131−132 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{13}NO_6Na$ 374.0641, found 374.0636. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (dd, J = 1.6, 8.4 Hz, 1H), 7.60 (dd, J = 1.6, 8.4 Hz, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.41 (d, J = 1.6 Hz, 1H), 6.90 (dd, J = 8.4, 18.8 Hz, 2H), 6.08 (s, 2H), 6.05 (s, 2H), 4.94 (dd, J = 4.4, 9.2 Hz, 1H), 3.98 (dd, J = 9.2, 17.6 Hz, 1H), 3.43 (dd, J = 4.4, 17.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.7, 186.9, 153.2, 152.5, 148.6, 148.3, 130.2, 128.7, 125.8, 124.8, 117.2, 108.5, 108.3, 108.1, 107.8, 102.2, 102.0, 37.4, 33.0. FT-IR (cm^{-1}): 2924, 2311, 1720, 1678, 1444, 1254, 1036.

4-(2,4-Dimethoxyphenyl)-2-(4-methylbenzoyl)-4-oxobutanenitrile (1k). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol), **2d** (213 mg, 1.0 mmol), and **2k** (259 mg, 1.0 mmol) in the cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **1k** (55%, 371 mg). Colorless solid; mp = 108−109 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{20}H_{19}NO_4Na$ 360.1212, found 360.1204. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.8 Hz, 1H), 7.33 (d, J = 8.4 Hz, 2H), 6.53 (dd, J = 2.4, 8.8 Hz, 1H), 6.47 (d, J = 2.4 Hz, 1H), 5.03 (dd, J = 4.4, 8.8 Hz, 1H), 4.00 (dd, J = 8.8, 18.8 Hz, 1H), 3.94 (s, 3H), 3.86 (s, 3H), 3.59 (dd, J = 4.4, 18.8 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.4, 189.2, 165.4, 161.6, 145.5, 133.2 (2x), 131.9, 129.7 (2x), 129.1 (2x), 118.8, 117.7, 105.6, 98.2, 55.6, 42.7, 33.2, 21.8. FT-IR (cm^{-1}): 2926, 2242, 1694, 1657, 1600, 1254, 1213.

2-(4-Fluorobenzoyl)-4-(4-methoxyphenyl)-4-oxobutanenitrile (1l) and 4-(4-Fluorophenyl)-2-(4-methoxybenzoyl)-4-oxobutanenitrile (1m). According to the general procedure, the reaction was performed in the presence of NaCN (216 mg, 4.4 mmol), **2b** (217 mg, 1.0 mmol), and **2c** (229 mg, 1.0 mmol) in cosolvent of 1,4-dioxane and water (10 mL, v/v = 9:1) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **1l** and **1m** (in Table 2, for entry 12, 62%, 193 mg; for entry 13, 62%, 193 mg). Two inseparable isomers, ratio = 1:1. Colorless solid; mp = 108−109 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{18}H_{14}FNO_3Na$ 334.0855, found 334.0852. ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.8 Hz, 1H), 8.12 (d, J = 8.8 Hz, 1H), 7.96 (d, J = 8.8 Hz, 2H), 7.25−7.21 (m, 2H), 6.97 (d, J = 8.8 Hz, 2H), 5.00 (dd, J = 4.4, 9.2 Hz, 1H), 4.06 (dd, J = 9.2, 17.6 Hz, 1H), 3.89 (s, 3H), 3.51 (dd, J = 4.4, 18.0 Hz, 1H).

General Synthetic Procedure for the Synthesis of Compounds 4a−4m. $Bi(OTf)_3$ (13 mg, 0.02 mmol) was added to a solvent of **1** (1.0 mmol) in dry $MeNO_2$ (5 mL) at rt. The reaction mixture was stirred at rt for 2 h, and the solvent was concentrated. The residue was diluted with water (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford the crude product. Purification on silica gel (hexanes/EtOAc = 10/1−5/1) afforded **4a−4m**.

2,5-Diphenylfuran-3-carbonitrile (4a).[19i] According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1a** (263 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **4a** (88%, 216 mg). Colorless solid; mp = 115−116 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_{11}NONa$ 268.0738, found 268.0735. ^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.8 Hz, 2H), 7.73 (d, J = 8.8 Hz, 2H), 7.54−7.36 (m, 6H), 6.87 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.7, 153.6, 130.1, 129.1 (2x), 129.0 (2x), 128.9, 128.7, 128.1, 125.3 (2x), 124.2 (2x), 114.9, 107.7, 93.4. FT-IR (cm^{-1}): 2924, 2229, 1727, 1486, 1242, 762, 684.

2,5-Bis(4-fluorophenyl)furan-3-carbonitrile (4b). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1b** (299 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **4b** (86%, 242 mg). Colorless solid; mp = 112−113 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_9F_2NONa$ 304.0550, found 304.0543. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05−8.02 (m, 2H), 7.70−7.67 (m, 2H), 7.22−7.13 (m, 4H), 6.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.6 (d, J = 250.2 Hz), 163.0 (d, J = 248.7 Hz), 157.9, 152.8, 127.5 (d, J = 9.1 Hz, 2x), 126.1 (d, J = 8.3 Hz, 2x), 125.0 (d, J = 3.8 Hz), 124.3 (d, J = 3.0 Hz), 116.5 (d, J = 22.0 Hz, 2x), 116.2 (d, J = 22.0 Hz, 2x), 114.7, 107.3, 93.2. FT-IR (cm^{-1}): 2920, 2229, 1599, 1496, 1234, 1160, 832.

2,5-Bis(4-methoxyphenyl)furan-3-carbonitrile (4c). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1c** (323 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4c** (90%, 275 mg). Colorless solid; mp = 106−107 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{15}NO_3Na$ 328.0950, found 328.0943. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.70 (s, 1H), 3.88 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 160.0, 158.6, 153.0, 127.0 (2x), 125.7 (2x), 121.9, 121.2, 114.5 (2x), 114.4 (2x), 114.3, 105.9, 91.6, 55.44, 55.40. FT-IR (cm^{-1}): 2925, 2225, 1614, 1508, 1252, 1177, 833.

2,5-Di-*p*-tolylfuran-3-carbonitrile (4d). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1d** (291 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4d** (89%, 243 mg). Colorless solid; mp = 134−135 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{15}NONa$ 296.1051, found 296.1045. ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 7.6 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 6.79 (s, 1H), 2.42 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 153.5, 140.4, 138.9, 129.8 (2x), 129.6 (2x), 126.2, 125.5, 125.3 (2x), 124.1 (2x),

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115.2, 106.9, 92.5, 21.5, 21.4; FT-IR (cm^{-1}): 2921, 2227, 1508, 1496, 818, 716, 495.

2,5-Bis(3-methoxyphenyl)furan-3-carbonitrile (4e). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1e** (323 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4e** (88%, 269 mg). Colorless solid; mp = 98−99 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{15}NO_3Na$ 328.0950, found 328.0943. ^1H NMR (400 MHz, $CDCl_3$): δ 7.65 (dq, J = 1.6, 8.0 Hz, 1H), 7.57 (dd, J = 1.6, 2.4 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.30 (dt, J = 1.6, 7.6 Hz, 1H), 7.24 (dd, J = 1.6, 2.4 Hz, 1H), 7.00 (ddd, J = 1.2, 2.8, 8.4 Hz, 1H), 6.92 (ddd, J = 1.2, 2.8, 8.4 Hz, 1H), 6.86 (s, 1H), 3.90 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.02, 160.00, 158.6, 153.5, 130.2, 130.1, 130.0, 129.2, 117.9, 116.8, 116.2, 114.8, 114.3, 110.4, 110.0, 108.0, 93.6, 55.43, 55.38. FT-IR (cm^{-1}): 2939, 2228, 1597, 1491, 1229, 1041, 706.

2,5-Di(naphthalen-2-yl)furan-3-carbonitrile (4f). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1f** (363 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **4f** (92%, 318 mg). Colorless solid; mp = 178−179 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{25}H_{15}NONa$ 368.1051, found 368.1048. ^1H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 1.2 Hz, 1H), 8.25 (d, J = 1.2 Hz, 1H), 8.19 (dd, J = 2.0, 8.8 Hz, 1H), 8.02−7.85 (m, 6H), 7.79 (dd, J = 2.0, 8.8 Hz, 1H), 7.59−7.51 (m, 4H), 7.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 153.9, 133.8, 133.31, 133.29, 133.1, 129.0, 128.9, 128.8, 128.3, 127.89, 127.87, 127.5, 127.04, 126.96, 126.8, 125.0, 125.4, 125.3, 123.3, 122.2, 121.9, 115.1, 108.4, 93.8. FT-IR (cm^{-1}): 2924, 2228, 1725, 1502, 858, 814, 472.

2,5-Bis(4-(trifluoromethyl)phenyl)furan-3-carbonitrile (4g). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1g** (399 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **4g** (65%, 248 mg). Colorless solid; mp = 159−160 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_9F_6NONa$ 404.0486, found 404.0483. ^1H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.05 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 153.1, 133.9, 133.4, 132.0 (q, J = 32.6 Hz), 131.3 (q, J = 27.2 Hz), 126.5 (q, J = 234.2 Hz), 126.3 (q, J = 236.5 Hz), 126.2 (q, J = 3.8 Hz, 2x), 126.0 (q, J = 3.7 Hz, 2x), 125.7 (2x), 124.6 (2x), 113.9, 109.8, 95.6. FT-IR (cm^{-1}): 2924, 2238, 1324, 1169, 1111, 1070, 841.

2,5-Di([1,1′-biphenyl]-4-yl)furan-3-carbonitrile (4h). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1h** (415 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **4h** (87%, 346 mg). Colorless solid; mp = 203−204 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++H) calcd for $C_{29}H_{20}NO$ 398.1545, found 398.1538. ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.51−7.46 (m, 4H), 7.43−7.37 (m, 2H), 6.93 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.6, 153.5, 142.8, 141.7, 140.1, 139.9, 129.0 (2x), 128.9 (2x), 128.0, 127.8, 127.71 (2x), 127.66 (2x), 127.6, 127.1 (2x), 127.0 (2x), 126.9, 125.8 (2x), 124.7 (2x), 115.0, 107.9, 93.5; FT-IR (cm^{-1}): 2923, 2229, 1484, 842, 768, 726, 694.

2,5-Bis(3,4,5-trimethoxyphenyl)furan-3-carbonitrile (4i). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1i** (443 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 6/1) afforded **4i** (89%, 379 mg). Colorless solid; mp = 146−147 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{23}H_{23}NO_7Na$ 448.1372, found 448.1366. ^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (s, 2H), 6.90 (s, 2H), 6.79 (s, 1H), 3.96 (s, 6H), 3.94 (s, 6H), 3.92 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 153.8, 153.7, 153.4, 140.0, 139.2, 124.3, 123.3, 115.1, 107.4, 102.9 (2x), 102.0 (2x), 93.1, 61.04, 61.02, 56.3 (6x). FT-IR (cm^{-1}): 2939, 2225, 1591, 1501, 1247, 1127, 1003.

2,5-Bis(benzo[*d*][1,3]dioxol-5-yl)furan-3-carbonitrile (4j). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1j** (351 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4j** (88%, 293 mg). Colorless solid; mp = 78−79 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{11}NO_5Na$ 356.0535, found 356.0530. ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, J = 1.6, 8.0 Hz, 1H), 7.48 (d, J = 2.0 Hz, 1H), 7.21 (dd, J = 1.6, 8.0 Hz, 1H), 7.14 (d, J = 2.0 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 6.68 (s, 1H), 6.05 (s, 2H), 6.02 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 152.9, 149.1, 148.3, 148.2, 124.0, 123.1, 122.3, 120.3, 118.5, 115.2, 108.9, 108.8, 106.4, 105.6, 104.7, 101.7, 101.5, 92.1; FT-IR (cm^{-1}): 2923, 2224, 1733, 1487, 1288, 1232, 1037.

5-(2,4-Dimethoxyphenyl)-2-(p-tolyl)furan-3-carbonitrile (4k). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1k** (337 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4k** (89%, 284 mg). Colorless solid; mp = 143−144 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{20}H_{17}NO_3Na$ 342.1106, found 342.1100. ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 8.0 Hz, 2H), 7.81 (d, J = 8.8 Hz, 1H), 7.29 (d, J = 8.0 Hz, 2H), 6.99 (s, 1H), 6.60 (dd, J = 2.4, 8.8 Hz, 1H), 6.55 (d, J = 2.4 Hz, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 157.4, 157.2, 149.9, 140.0, 129.7 (2x), 126.9, 125.8, 125.2 (2x), 115.6, 111.4, 110.4, 105.1, 98.7, 92.6, 55.50, 55.48, 21.5. FT-IR (cm^{-1}): 2924, 2228, 1725, 1606, 1459, 1213, 779.

5-(4-Fluorophenyl)-2-(4-methoxyphenyl)furan-3-carbonitrile (4l). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1l** (311 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4l** (37.5%, 110 mg). Colorless solid; mp = 146−147 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{18}H_{12}FNO_2Na$ 316.0750, found 316.0744. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 9.2 Hz, 2H), 7.70−7.66 (m, 2H), 7.17−7.11 (m, 2H), 7.02 (d, J = 9.2 Hz, 2H), 6.77 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6 (d, J = 250.4 Hz), 159.2, 152.0, 127.1 (2x), 126.0 (d, J = 8.4 Hz, 2x), 125.3 (d, J = 3.0 Hz), 120.9, 116.1 (d, J = 22.0 Hz, 2x), 115.2, 114.6 (2x), 107.20, 107.19, 91.7, 55.4. FT-IR (cm^{-1}): 2924, 2225, 1614, 1510, 1497, 1259, 825.

2-(4-Fluorophenyl)-5-(4-methoxyphenyl)furan-3-carbonitrile (4m). According to the general procedure, the reaction was performed in the presence of $Bi(OTf)_3$ (13 mg, 0.02 mmol) and **1l** (311 mg, 1.0 mmol) in dry $MeNO_2$ (5 mL) at rt for 2 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **4m** (39%, 114 mg). Colorless solid; mp = 111−112 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{18}H_{12}FNO_2Na$ 316.0750, found 316.0746. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05−8.02 (m, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.21−7.17 (m, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.72 (s, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4 (d, J = 250.1 Hz), 160.2, 153.9, 129.8 (d, J = 208.4 Hz), 127.3 (d, J = 8.4 Hz, 2x), 125.8 (2x), 124.6 (d, J = 3.8 Hz), 121.5, 116.3 (d, J = 22.8 Hz, 2x), 115.0, 114.5 (2x), 114.4, 106.0, 55.4; FT-IR (cm^{-1}): 2924, 2228, 1615, 1506, 1473, 1251, 835.

General Synthetic Procedure for the Synthesis of Compounds 5a−5e. NH_4OAc (160 mg, 2.1 mmol) was added to a solvent of **1** (1.0 mmol) in MeOH (5 mL) at rt. The reaction mixture was refluxed for 2 h. The reaction mixture was cooled to rt, concentrated and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 8/1−3/1) afforded **5a−5e**.

2,5-Diphenyl-1*H*-pyrrole-3-carbonitrile (5a).[19h] According to the general procedure, the reaction was performed in the presence of NH_4OAc (160 mg, 2.1 mmol) and **1a** (263 mg, 1.0 mmol) in MeOH (5 mL) at reflux for 2 h. Purification on silica gel (hexanes/EtOAc =

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4/1) afforded **5a** (85%, 208 mg). Colorless solid; mp = 223−224 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_{12}N_2Na$ 267.0898, found 267.0892. ^1H NMR (400 MHz, $CDCl_3$): δ 11.51 (br s, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.16−7.02 (m, 5H), 6.96−6.92 (m, 1H), 6.42 (d, J = 2.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 133.2, 130.3, 129.4, 128.0 (2x), 127.9 (2x), 127.6, 126.5, 126.0 (2x), 124.2 (2x), 117.2, 109.1, 89.9. FT-IR (cm^{-1}): 3424, 2256, 1649, 1026, 1000, 766, 632.

2,5-Bis(4-fluorophenyl)-1*H*-pyrrole-3-carbonitrile (5b). According to the general procedure, the reaction was performed in the presence of NH_4OAc (160 mg, 2.1 mmol) and **1b** (299 mg, 1.0 mmol) in MeOH (5 mL) at reflux for 2 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **5b** (83%, 233 mg). Colorless solid; mp = 83−84 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_{10}F_2N_2Na$ 303.0710, found 303.0712. ^1H NMR (400 MHz, $CDCl_3$): δ 11.45 (br s, 1H), 7.71−7.66 (m, 2H), 7.52−7.47 (m, 2H), 7.02−6.95 (m, 2H), 6.95−6.89 (m, 2H), 6.50 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1 (d, J = 247.2 Hz), 161.6 (d, J = 245.6 Hz), 138.7, 132.7, 128.2 (d, J = 7.6 Hz, 2x), 127.1 (d, J = 3.0 Hz), 126.4 (d, J = 7.6 Hz, 2x), 126.1 (d, J = 3.1 Hz), 117.4, 115.4 (d, J = 21.9 Hz, 2x), 115.2 (d, J = 21.3 Hz, 2x), 109.3, 90.3. FT-IR (cm^{-1}): 3422, 2218, 1505, 1221, 1025, 999, 774.

2,5-Bis(4-methoxyphenyl)-1*H*-pyrrole-3-carbonitrile (5c). According to the general procedure, the reaction was performed in the presence of NH_4OAc (160 mg, 2.1 mmol) and **1c** (323 mg, 1.0 mmol) in MeOH (5 mL) at reflux for 2 h. Purification on silica gel (hexanes/EtOAc = 3/1) afforded **5c** (86%, 262 mg). Colorless solid; mp = 97−98 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{16}N_2O_2Na$ 327.1110, found 327.1108. ^1H NMR (400 MHz, $CDCl_3$+d^6DMSO): δ 11.15 (br s, 1H), 7.65 (d, J = 8.8 Hz, 2H), 7.45 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.45 (d, J = 2.8 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 158.5, 139.4, 133.0, 127.6 (2x), 126.0 (2x), 123.9, 122.7, 118.1, 113.8 (2x), 113.8 (2x), 108.2, 89.3, 55.00, 54.96. FT-IR (cm^{-1}): 3498, 2224, 1645, 1025, 1000, 828, 769.

2,5-Di-*p*-tolyl-1*H*-pyrrole-3-carbonitrile (5d). According to the general procedure, the reaction was performed in the presence of NH_4OAc (160 mg, 2.1 mmol) and **1d** (291 mg, 1.0 mmol) in MeOH (5 mL) at reflux for 2 h. Purification on silica gel (hexanes/EtOAc = 4/1) afforded **5d** (87%, 237 mg). Colorless solid; mp = 183−184 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{16}N_2Na$ 295.1211, found 295.1204. ^1H NMR (400 MHz, $CDCl_3$): δ 8.84 (br s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 2.8 Hz, 1H), 2.40 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.4, 138.9, 137.7, 133.1, 129.9 (2x), 129.8 (2x), 127.9, 126.9, 125.6 (2x), 124.3 (2x), 117.6, 109.7, 91.1, 21.3, 21.2. FT-IR (cm^{-1}): 3242, 2922, 2224, 1508, 1460, 820, 792.

2,5-Bis(3-methoxyphenyl)-1*H*-pyrrole-3-carbonitrile (5e). According to the general procedure, the reaction was performed in the presence of NH_4OAc (160 mg, 2.1 mmol) and **1e** (323 mg, 1.0 mmol) in MeOH (5 mL) at reflux for 2 h. Purification on silica gel (hexanes/EtOAc = 3/1) afforded **5e** (86%, 262 mg); Colorless solid; mp = 129−130 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{16}N_2O_2Na$ 327.1110, found 327.1104. ^1H NMR (400 MHz, $CDCl_3$): δ 11.42 (br s, 1H), 7.37−7.31 (m, 2H), 7.24−7.16 (m, 4H), 6.78 (ddd, J = 0.8, 2.4, 8.0 Hz, 1H), 6.70 (ddd, J = 1.2, 3.6, 8.0 Hz, 1H), 6.62 (d, J = 2.8 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.6, 159.5, 139.5, 133.5, 131.0, 129.5, 129.5, 118.7, 117.7, 117.2, 113.9, 112.4, 111.6, 110.7, 110.4, 110.0, 90.6, 55.1, 55.0. FT-IR (cm^{-1}): 3418, 2218, 1592, 1491, 1234, 1026, 784.

General synthetic procedure for synthesis of compounds 6a-6f is as follows. N_2H_4 (80%, 1.0 mL) was added to a solvent of **1** (1.0 mmol) in 1,4-dioxane (5 mL) at rt. The reaction mixture was stirred at rt for 3 h, and the solvent was concentrated. The residue was diluted with water (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc = 10/1−5/1) afforded **6a−6f**.

3,6-Diphenyl-2,5-dihydropyridazine-4-carbonitrile (6a).[20a] According to the general procedure, the reaction was performed in the presence of N_2H_4 (80%, 1.0 mL) and **1a** (263 mg, 1.0 mmol) in 1,4-dioxane (5 mL) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **6a** (95%, 246 mg). Colorless solid; mp = 177−178 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_{13}N_3Na$ 282.1007, found 282.1003. ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 (br s, 1H), 7.77−7.74 (m, 2H), 7.63−7.61 (m, 2H), 7.53−7.47 (m, 3H), 7.46−7.42 (m, 3H), 3.54 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 142.2, 135.0, 131.5, 131.0, 130.0, 129.2 (2x), 128.6 (2x), 127.6 (2x), 125.9 (2x), 120.2, 71.8, 24.8. FT-IR (cm^{-1}): 3302, 2195, 1627, 1472, 1339, 772, 693. Single-crystal X-ray diagram: crystal of **6a** was grown by slow diffusion of EtOAc into a solution of **6a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P21/c$, a = 26.157(2) Å, b = 7.4363(5) Å, c = 6.8127(5) Å, V = 1315.79(17) Å^3, Z = 4, d_{calcd} = 1.309 g/cm^3, $F(000)$ = 544, 2θ range 0.78−26.44°, R indices (all data) $R1$ = 0.0715, $wR2$ = 0.0457.

3,6-Bis(4-fluorophenyl)-2,5-dihydropyridazine-4-carbonitrile (6b). According to the general procedure, the reaction was performed in the presence of N_2H_4 (80%, 1.0 mL) and **1b** (299 mg, 1.0 mmol) in 1,4-dioxane (5 mL) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 5/1) afforded **6b** (96%, 283 mg). Colorless solid; mp = 204−205 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{17}H_{11}F_2N_3Na$ 318.0819, found 318.0815. ^1H NMR (400 MHz, $CDCl_3$): δ 10.34 (br s, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.11 (t, J = 8.8 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 3.42 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3 (d, J = 249.4 Hz), 162.9 (d, J = 247.8 Hz), 148.4 (2x), 139.3, 131.3 (d, J = 3.1 Hz), 130.0 (d, J = 8.3 Hz, 2x), 127.3 (d, J = 8.3 Hz, 2x), 120.3 (d, J = 3.1 Hz), 115.2 (d, J = 22.0 Hz, 2x), 114.8 (d, J = 21.3 Hz, 2x), 68.9, 24.0. FT-IR (cm^{-1}): 3419, 2200, 1648, 1511, 1244, 1026, 999. Single-crystal X-ray diagram: crystal of **6b** was grown by slow diffusion of EtOAc into a solution of **6b** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P21/c$, a = 27.100(4) Å, b = 7.4176(12) Å, c = 6.8847(11) Å, V = 1372.8(4) Å^3, Z = 4, d_{calcd} = 1.429 g/cm^3, $F(000)$ = 608, 2θ range 0.76−26.47°, R indices (all data) $R1$ = 0.1825, $wR2$ = 0.4718.

3,6-Bis(4-methoxyphenyl)-2,5-dihydropyridazine-4-carbonitrile (6c). According to the general procedure, the reaction was performed in the presence of N_2H_4 (80%, 1.0 mL) and **1c** (323 mg, 1.0 mmol) in 1,4-dioxane (5 mL) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 3/1) afforded **6c** (94%, 300 mg). Colorless solid; mp = 143−144 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{19}H_{17}N_3O_2Na$ 342.1219, found 342.1215. ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (br s, 1H), 7.67 (d, J = 9.2 Hz, 2H), 7.55 (d, J = 8.8 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 9.2 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.48 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 149.6, 142.0, 130.5, 129.1 (2x), 127.7, 127.4 (2x), 123.7, 120.8, 114.5 (2x), 113.9 (2x), 70.0, 55.4, 55.3, 24.8. FT-IR (cm^{-1}): 3357, 2192, 1607, 1394, 1256, 1178, 835.

3,6-Di-*p*-tolyl-2,5-dihydropyridazine-4-carbonitrile (6d). According to the general procedure, the reaction was performed in the presence of N_2H_4 (80%, 1.0 mL) and **1d** (291 mg, 1.0 mmol) in 1,4-dioxane (5 mL) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 3/1) afforded **6d** (95%, 273 mg). Colorless solid; mp = 181−182 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++H) calcd for $C_{19}H_{18}N_3$ 288.1501, found 288.1493. ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (br s, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 3.49 (s, 2H), 2.40 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 142.2, 141.3, 140.1, 132.2, 129.8 (2x), 129.2 (2x), 128.6, 127.4 (2x), 125.8 (2x), 120.6, 70.8, 24.8, 21.4, 21.3. FT-IR (cm^{-1}): 3316, 2193, 1609, 1471, 1338, 1185, 819.

3,6-Bis(3-methoxyphenyl)-2,5-dihydropyridazine-4-carbonitrile (6e). According to the general procedure, the reaction was performed in the presence of N_2H_4 (80%, 1.0 mL) and **1e** (323 mg,

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1.0 mmol) in 1,4-dioxane (5 mL) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 3/1) afforded **6e** (93%, 297 mg). Colorless solid; mp = 130−131 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++H) calcd for $C_{19}H_{18}N_3O_2$ 320.1399, found 320.1393. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (br s, 1H), 7.39−7.25 (m, 4H), 7.17−7.11 (m, 2H), 7.02 (dd, J = 2.4, 8.4 Hz, 1H), 6.97 (dd, J = 2.4, 8.4 Hz, 1H), 3.83 (s, 6H), 3.50 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 159.7, 149.5, 141.9, 136.4, 132.6, 130.3, 129.5, 120.1, 119.7, 118.4, 116.9, 116.0, 112.9, 110.9, 71.7, 55.4, 55.3, 24.8. FT-IR (cm^{-1}): 3329, 2195, 1580, 1491, 1337, 1234, 785.

3,6-Di(naphthalen-2-yl)-2,5-dihydropyridazine-4-carbonitrile (6f). According to the general procedure, the reaction was performed in the presence of N_2H_4 (80%, 1.0 mL) and **1f** (363 mg, 1.0 mmol) in 1,4-dioxane (5 mL) at rt for 3 h. Purification on silica gel (hexanes/EtOAc = 3/1) afforded **6f** (90%, 323 mg). Colorless solid; mp = 202−203 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++H) calcd for $C_{25}H_{18}N_3$ 360.1501, found 360.1497. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 8.08 (d, J = 9.2 Hz, 2H), 8.04 (s, 1H), 7.97 (d, J = 8.4 Hz, 2H), 7.94−7.90 (m, 2H), 7.89−7.84 (m, 2H), 7.70 (dd, J = 2.0, 8.4 Hz, 1H), 7.59−7.52 (m, 4H), 3.72 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.6, 142.0, 134.3, 134.0, 133.0, 132.9, 132.5, 129.3, 128.8, 128.6, 128.6, 128.3, 127.9, 127.8, 127.7, 127.15, 127.08, 126.6, 126.0, 124.2, 123.6, 122.9, 120.4, 72.5, 24.7. FT-IR (cm^{-1}): 3300, 2193, 1623, 1472, 1400, 820, 731.

2,3,6-Triphenyl-2,5-dihydropyridazine-4-carbonitrile (6g). Phenylhydrazine (227 mg, 2.1 mmol) was added to a solvent of **1a** (263 mg, 1.0 mmol) in 1,4-dioxane (5 mL) at rt. The reaction mixture was stirred at rt for 3 h, and the solvent was concentrated. The residue was diluted with water (10 mL), and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford the crude product. Purification on silica gel (hexanes/EtOAc = 10/1−5/1) afforded **7** (90%, 302 mg). Colorless solid; mp = 120−121 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++Na) calcd for $C_{23}H_{17}N_3Na$ 358.1320, found 358.1317. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.90 (m, 2H), 7.50−7.46 (m, 3H), 7.33−7.27 (m, 5H), 7.23−7.15 (m, 4H), 7.05−7.01 (m, 1H), 3.60 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 143.5, 143.0, 134.5, 131.7, 130.2, 129.8 (2x), 128.6 (2x), 128.39 (2x), 128.37 (2x), 126.5 (2x), 125.0 (2x), 123.4 (2x), 120.2, 77.0, 26.0. FT-IR (cm^{-1}): 3061, 2195, 1593, 1493, 1337, 759, 695. Single-crystal X-ray diagram: crystal of **7** was grown by slow diffusion of EtOAc into a solution of **7** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group $P\bar{1}$, a = 9.9929(2) Å, b = 13.6834(3) Å, c = 14.2187(4) Å, V = 1814.91(8) Å^3, Z = 4, d_{calcd} = 1.227 g/cm^3, $F(000)$ = 704, 2θ range 1.47−26.39°, R indices (all data) $R1$ = 0.0651, $wR2$ = 0.1484.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01672.

X-ray analysis data for **1f** (CIF)

X-ray analysis data for **6a** (CIF)

X-ray analysis data for **6b** (CIF)

X-ray analysis data for **6g** (CIF)

Spectroscopic data for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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(16) CCDC 1400625 (**1f**), 1061524 (**6a**), 1405922 (**6b**), and 1409627 (**6g**) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax, 44-1223-336033; e-mail, deposit@-ccdc.cam.ac.uk).
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