JOC The Journal of Organic Chemistry

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Copper-Catalyzed *N*-Cyanation of Sulfoximines by AIBN

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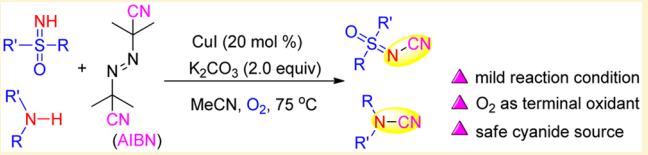
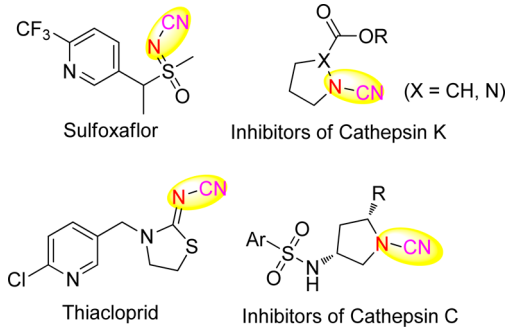
Supporting Information

ABSTRACT: The direct copper-catalyzed *N*-cyanation of sulfoximines was achieved by using AIBN as a safe cyanide source. It represents a simple and environmentally benign procedure for the construction of the N−CN bond. Furthermore, some *sec*-amines can also be tolerated well under this procedure.



The N−CN bonds are ubiquitous and frequently found in innumerable natural products, biologically active molecules, and medicinally relevant structures (Scheme 1).[1−5] For example, sulfoxaflor and thiacloprid play key roles in insecticide field.[6,7] Inhibitors of cathepsin K show efficiency on bone resorption,[1] while inhibitors of cathepsin C are utilized in neutrophil-dominated inflammatory diseases.[5] Meanwhile, cyanamides are not only employed as ligands in coordination chemistry[8−11] but also the key intermediates leading to guanidines[12−16] and heterocycles.[17−24] Moreover, as a safe cyanide source, cyanamides were widely applied in the cyanation reaction.[25−28]

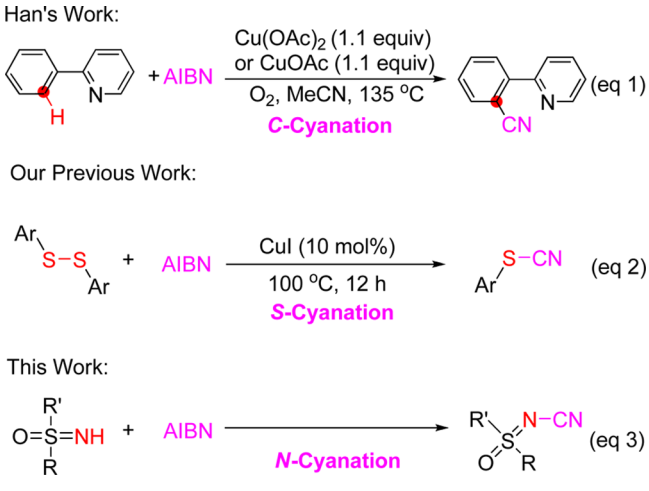
Scheme 1. Bioactive Compounds Containing N−CN Bonds



To date, several elegant approaches have been developed for C−CN bond formation by safe cyanide sources.[29−42] However, to the best of our knowledge, the construction of the N−CN bond was generally limited to the von Braun reaction, where XCN (X = halo) was highly toxic.[43−45] Very recently, we developed the formation of the N−CN bond via oxidative coupling using CuCN as cyanide source.[46] In view of the toxicity of CuCN, the development of safe cyanide source in N−CN bond formation is still highly promising.

AIBN is widely known as a radical initiator.[47,48] However, recently, Han pioneered the application of AIBN as a "CN" source in the formation of C−CN bonds (Scheme 2, eq 1).[49] Subsequently, we described an *S*-cyanation reaction by AIBN (Scheme 2, eq 2).[50] Herein, we report the employment of AIBN in *N*-cyanation of sulfoximines (Scheme 2, eq 3). Importantly, *N*-cyanosulfoximines have attracted significant attention in crop protection as promising pesticides.[6,7,51]

Scheme 2. Employment of AIBN as "CN" Source

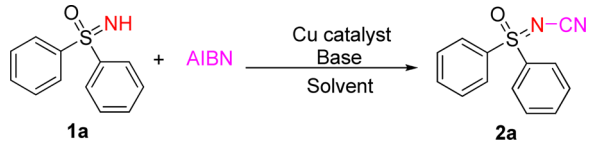


Initially, the reaction of sulfonimidoyldibenzene **1a** with AIBN (1.5 equiv) was tested in the presence of 2 equiv of K_2CO_3 and 0.2 equiv of $CuBr_2$ in MeCN at 75 °C under O_2. To our delight, the *N*-cyanation product **2a** was isolated in 65% yield (Table 1, entry 1). Among copper salts screened, such as $Cu(OAc)_2$, CuS, and CuI (Table 1, entries 2−4), CuI was the best, providing **2a** in 90% yield. The reaction became sluggish at 50 °C and could not proceed under N_2 (Table 1, entry 4). The blank reaction indicated that no cyanation product was detected at all in the absence of catalyst (Table 1, entry 5). Other common solvents, such as DCM, MeOH, and 1,4-

Received: November 16, 2014
Published: February 10, 2015

DOI: 10.1021/jo502607c
J. Org. Chem. 2015, 80, 2822−2826

Table 1. Optimization of the Reaction Conditions[a]



1a 2a

entry	catalyst	solvent	base	yield (%)
1	$CuBr_2$	MeCN	K_2CO_3	65
2	$Cu(OAc)_2$	MeCN	K_2CO_3	38
3	CuS	MeCN	K_2CO_3	18
4	CuI	MeCN	K_2CO_3	90 (20)[b] (<1)[c]
5		MeCN	K_2CO_3	<1
6	CuI	DCM	K_2CO_3	<1
7	CuI	1,4-dioxane	K_2CO_3	18
8	CuI	MeOH	K_2CO_3	<1
9	CuI	MeCN		<1
10	CuI	MeCN	$NaHCO_3$	58
11	CuI	MeCN	K_3PO_4	67
12	CuI	MeCN	TEA	80

[a]Reaction conditions: **1a** (0.2 mmol), AIBN (0.3 mmol), Cu catalyst (0.04 mmol), base (0.4 mmol), solvent (3.0 mL) at 75 °C for 24 h, under O_2. [b]50 °C. [c]Under N_2.

dioxane, were found to be less effective or ineffective for this transformation (Table 1, entries 6−8). Further investigation implied base played a crucial role in this reaction. No cyanation reaction took place in the absence of base (Table 1, entry 9). Other inorganic bases or organic base, such as $NaHCO_3$, K_3PO_4, or TEA, were inferior to K_2CO_3 (Table 1, entries 10−12).

With the optimal conditions established, the substrate scope of sulfoximines was tested. Both diaryl and aryl alkyl sulfoximines are tolerated well in this procedure (Figure 1), and most of the diaryl analogues provided target products in excellent yields (**2a−f**). In addition, aryl alkyl sulfoximines provided the desired products in moderate to good yields (**2g−l**). For example, 4-chloro(*S*-butylsulfonimidoyl)benzene (**1k**) generated the cyanation product in 73% yield (**2k**). Notably, substrates with halogen groups on the aromatic rings were tolerated well (**2c**, **2i**, **2k**, and **2l**), which makes further functionalization possible.

In addition, some cyclic *sec*-amines also ran smoothly under the standard procedure leading to the corresponding *N*-cyanation products in good to moderate yields (**4a−d**,**h**). For example, 1,2,3,4-tetrahydroisoqunoline could provide the desired product **4h** in 36% yield. However, noncyclic *sec*-amines were not tolerated well, and only trace amount of products were detected by GC−MS. Gratifyingly, this procedure could be applicable for *N*-cyclohexylaniline (**4f**). Importantly, the substrate scope was not limited to *sec*-amines; benzophenone imine also worked well under the standard procedure as well (**4e**). Although we made great efforts in order to improve the yields of **4e** and **4f**, the results were still unsatisfactory. Disappointedly, other secondary anilines such as *N*-methylaniline, diphenylamine, *N*-ethylaniline, and lactam derivatives could not proceed under standard conditions. To our delight, 1,1,3,3-tetramethylguanidine delivered the *N*-cyanation product in 72% yield (**4g**) (Figure 2).

To test the practicality of this procedure, a 2 mmol scale reaction was conducted, and **2a** was isolated in an excellent 84% yield.

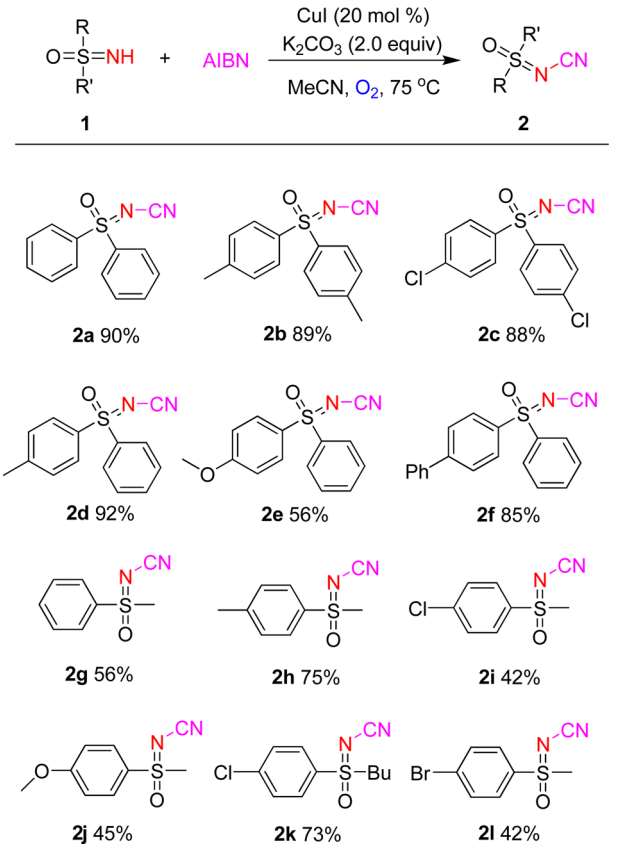


Figure 1. Substrate scope of sulfoximines. Reaction conditions: sulfoximine **1** (0.2 mmol), AIBN (0.3 mmol), CuI (0.04 mmol), K_2CO_3 (0.4 mmol), MeCN (3.0 mL) at 75 °C for 24 h, under O_2.

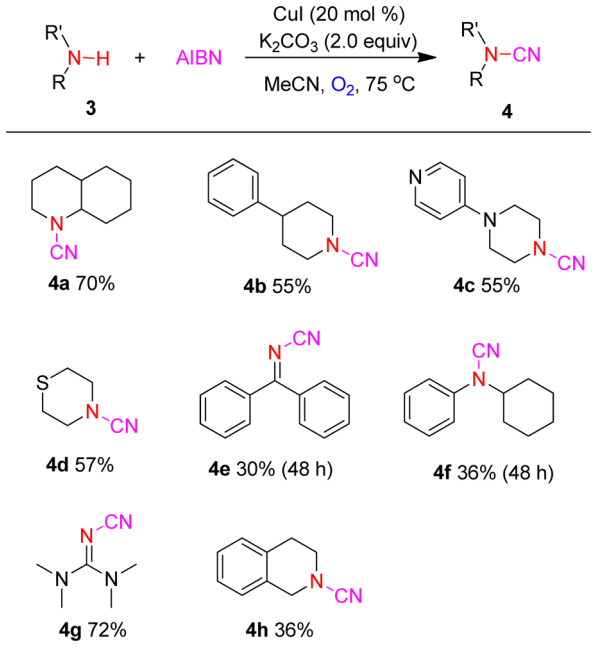


Figure 2. Substrate scope of *sec*-amines, imine, and guanidine. Reaction conditions: *sec*-amine (0.2 mmol), AIBN (0.3 mmol), CuI (0.04 mmol), K_2CO_3 (0.4 mmol), MeCN (3.0 mL) at 75 °C for 12 h, under O_2.

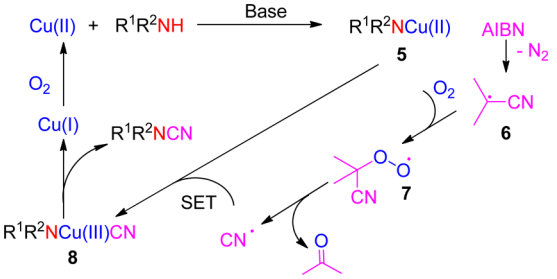
Further experiments were carried out to gain insight into the mechanism. First, after addition of 4.0 equiv TEMPO, the

DOI: 10.1021/jo502607c
J. Org. Chem. 2015, 80, 2822−2826

cyanation process of **3a** was completely inhibited, which implied this procedure might contain a radical pathway. As the byproduct, acetone was detected in this process by GC−MS (for details, see the Supporting Information). Moreover, the cyanide anion was detected by indicating paper even in the absence of MeCN (for details, see the Supporting Information).[52]

On the basis of the aforementioned experimental results, the proposed mechanism is outlined in Scheme 3.

Scheme 3. Plausible Mechanism



Initially, under O_2, the catalyst Cu(I) is oxidized to Cu(II). In the presence of base, the reaction between *sec*-amine and Cu(II) produces Cu(II) species **5**. Meanwhile, **6** is formed by homolytic cleavage of the C−N bond of AIBN by liberating 1 equiv of N_2. Then, in the presence of O_2, intermediate **7** produces cyanide radical and extrudes 1 equiv of acetone.[53] Subsequently, single-electron transfer between Cu(II) intermediate **5** and the cyanide radical takes place, and Cu(III) species **8** is formed. Finally, reduction elimination of **8** provides the desired products and regenerates Cu(I).

In conclusion, we have developed a facile approach leading to *N*-cyanation compounds by AIBN as a safe cyanide source. Sulfoximines, some *sec*-amines, as well as 1,1,3,3-tetramethylguanidine are compatible with this procedure as well. In addition, the transformation employs O_2 as the clean terminal oxidant under mild conditions. Thus, it represents important and practical progress to *N*-cyanation reaction.

EXPERIMENTAL SECTION

General Information. All chemicals were used as received without further purification unless stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a 300 or 400 MHz spectrometer (75 or 100 MHz for ^{13}C). NMR experiments are reported in δ units, parts per million (ppm), and were referenced to $CDCl_3$ (δ 7.26 or 77.0 ppm) as the internal standard. The coupling constants J are given in hertz. Column chromatography was performed using EM silica gel 60 (300−400 mesh) or neutral aluminum oxide (200−300 mesh).

General Procedure for 0.2 mmol Scale. Under O_2, a 20 mL Schlenk tube equipped with a stir bar was charged with sulfoximine or *sec*-amine (0.2 mmol), AIBN (0.3 mmol, 49.3 mg), CuI (0.04 mmol, 7.6 mg), K_2CO_3 (0.4 mmol, 55.3 mg), and CH_3CN (3 mL) and sealed with a Teflon-lined cap. The reaction mixture was stirred at 75 °C for 24 or 12 h in oil bath. After the completion of the reaction (monitored by TLC), the solvent was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel or Al_2O_3 with petroleum ether−ethyl acetate as the eluent to give the desired product.

General Procedure for 2 mmol Scale. A 100 mL round-bottom flask equipped with a stir bar was charged with sulfonimidoyldibenzene **1a** (2 mmol, 434.6 mg), AIBN (3 mmol, 492.6 mg), CuI (0.4 mmol, 76 mg), K_2CO_3 (4 mmol, 552.8 mg), and CH_3CN (30 mL). A balloon filled with oxygen gas was installed on the reaction flask. The reaction mixture was stirred at 75 °C for 24 h in an oil bath. After completion of the reaction (monitored by TLC), the solvent was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel with petroleum ether−ethyl acetate as the eluent to give **2a** in 84% yield.

***N*-Cyanodiphenylsulfoximine (2a).**[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:6) gave the product (44.0 mg, 90% yield) as a white solid: mp 104−106 °C (lit.[46] mp 108−110 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.56−7.60 (m, 4H), 7.65−7.69 (m, 2H), 7.97−7.99 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 111.9, 127.7, 129.9, 134.7, 137.1.

***N*-Cyano-4,4′-dimethyldiphenylsulfoximine (2b).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:6) gave the product (48.2 mg, 89% yield) as a yellowish solid: mp 103−105 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.41 (s, 6H), 7.35−7.37 (m, 4H), 7.83−7.85 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 112.2, 127.7, 130.5, 134.4, 146.0; MS (EI) 270 (M^+); HRMS (ESI) m/z calcd for $C_{15}H_{15}N_2OS$ $(M + H)^+$ 271.0900, found 271.0893; IR (KBr) 3086, 3065, 3038, 2982, 2924, 2197, 1591, 1491.

***N*-Cyano-4,4′-dichlorodiphenylsulfoximine (2c).**[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:6) gave the product (54.6 mg, 88% yield) as a white solid: mp 131−134 °C (lit.[46] mp 137−139 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58 (d, J = 8.8 Hz, 4H), 7.92 (d, J = 8.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 111.2, 129.3, 130.5, 135.3, 142.2.

***N*-Cyano-4-methyldiphenylsulfoximine (2d).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) gave the product (47.1 mg, 92% yield) as a yellowish liquid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.42 (s, 3H), 7.37−7.39 (m, 2H), 7.55−7.59 (m, 2H), 7.64−7.68 (m, 1H), 7.85−7.87 (m, 2H), 7.95−7.98 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.6, 112.1, 127.6, 127.9, 129.9, 130.6, 134.0, 134.5, 137.6, 146.2; MS (EI) 256 (M^+); HRMS (ESI) m/z calcd for $C_{14}H_{13}N_2OS$ $(M + H)^+$ 257.0743, found 257.0746; IR (KBr) 3088, 3063, 2922, 2850, 2197, 1593, 1475, 1446.

***N*-Cyano-4-methoxydiphenylsulfoximine (2e).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (30.5 mg, 56% yield) as a yellowish liquid: mp 99−101 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.86 (s, 3H), 7.03−7.05 (m, 2H), 7.55−7.59 (m, 2H), 7.63−7.67 (m, 1H), 7.90−7.96 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.9, 112.2, 115.3, 127.5, 127.7, 129.9, 130.3, 134.4, 138.1, 164.6; MS (EI) 272 (M^+); HRMS (ESI) m/z calcd for $C_{14}H_{13}N_2O_2S$ $(M + H)^+$ 273.0692, found 273.0693; IR (KBr) 3096, 3065, 2943, 2843, 2197, 1591, 1494.

***N*-Cyano-4-phenyldiphenylsulfoximine (2f).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:5) gave the product (54.1 mg, 85% yield) as a yellowish solid: mp 132−135 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.50 (m, 3H), 7.56−7.57 (m, 2H), 7.60−7.63 (m, 2H), 7.68−7.71 (m, 1H), 7.77−7.79 (m, 2H), 8.03−8.06 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 112.0, 127.3, 127.8, 128.4, 128.5, 129.0, 129.1, 130.0, 134.7, 135.5, 137.4, 138.4, 147.8. MS (EI) 318 (M^+); HRMS (ESI) m/z calcd for $C_{19}H_{15}N_2OS$ $(M + H)^+$ 319.0900, found 319.0901; IR (KBr) 3088, 3059, 3001, 2959, 2201, 1593, 1446.

***N*-Cyanomethylphenylsulfoximine (2g).**[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2.5) gave the product (20.1 mg, 56% yield) as a white solid: mp 66−69 °C (lit.[46] mp 68−70 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.34 (s, 3H), 7.66−7.70 (m, 2H), 7.76−7.80 (m, 1H), 7.98−8.00 (m 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.7, 111.8, 127.8, 130.2, 135.4, 135.9.

***N*-Cyanomethyl-4-methylphenylsulfoximine (2h).**[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (29.0 mg, 75% yield) as a white solid: mp 78−81 °C (lit.[46] mp 84−86 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.48 (s, 3H), 3.31 (s, 3H), 7.46 (d, J = 8.2 Hz, 2H), 7.85 (d, J = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7, 44.8, 112.0, 127.8, 130.8, 132.7, 146.9.

***N*-Cyanomethyl-4-chlorophenylsulfoximine (2i).**[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (18.0 mg, 42% yield) as a white solid: mp 99−102 °C (lit.[46] mp 108−110 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.35 (s, 3H),

DOI: 10.1021/jo502607c
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7.66 (d, J = 8.7 Hz, 2H), 7.94 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.8, 111.4, 129.4, 130.6, 134.4, 142.6.

***N*-Cyanomethyl-4-methoxyphenylsulfoximine (2j).**[51] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (19.0 mg, 45% yield) as a yellow solid: mp 97−99 °C (lit.[51] mp 102−103 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.31 (s, 3H), 3.91 (s, 3H), 7.11 (d, J = 8.9 Hz, 2H), 7.90 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.2, 56.0, 112.1, 115.5, 126.6, 130.2, 165.1.

***N*-Cyanobutyl-4-chlorophenylsulfoximine (2k).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:3) gave the product (37.3 mg, 73% yield) as a yellow solid: mp 89−91 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88−0.92 (m, 3H), 1.36−1.46 (m, 2H), 1.63−1.78 (m, 2H), 3.27−3.45 (m, 2H), 7.64 (d, J = 8.5 Hz, 2H), 7.88 (d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.3, 21.1, 24.1, 56.5, 111.7, 129.9, 130.5, 133.0, 142.4; MS (EI) 256 (M^+); HRMS (ESI) m/z calcd for $C_{11}H_{14}ClN_2OS$ $(M + H)^+$ 257.0510, found 257.0509; IR (KBr) 3096, 2964, 2941, 2901, 2189. 1574, 1470, 1456.

***N*-Cyanomethyl 4-bromophenylsulfoximine (2l).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) gave the product (21.7 mg, 42% yield) as a yellow solid: mp 102−105 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.34 (s, 3H) 7.81−7.87 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.7, 111.4, 129.4, 131.3, 133.6, 135.0. MS (EI) 257 (M^+); HRMS (ESI) m/z calcd for $C_8H_8BrN_2OS$ $(M + H)^+$ 258.9535, found 258.9534; IR (KBr) 3086, 3022, 2999, 2916, 2195. 1570, 1466.

Octahydroquinoline-1(2*H*)-carbonitrile (4a).[46] Flash column chromatography on Al_2O_3 (ethyl acetate/petroleum ether, 1:10) gave the product (23.1 mg, 70% yield) as a yellowish liquid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90−1.10 (m, 2H), 1.18−1.42 (m, 4H), 1.65−1.68 (m, 5H), 1.83−1.88 (m, 1H), 2.04−2.08 (m, 1H), 2.39−2.46 (m, 1H), 2.96−3.06 (m, 1H), 3.41−3.46 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.7, 25.0, 25.3, 30.0, 31.0, 32.0, 40.9, 51.2, 62.3, 116.8.

4-Phenylpiperidine-1-carbonitrile (4b).[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:15) gave the product (20.4 mg, 55% yield) as a white solid: mp 69−71 °C (lit.[46] mp 68−71 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.82−1.89 (m, 4H), 2.58−2.63 (m, 1H), 3.10−3.20 (m, 2H), 3.51−3.57 (m, 2H), 7.18−7.26 (m, 3H), 7.31−7.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 32.0, 41.2, 50.0, 118.3, 126.6, 126.7, 128.7, 144.5.

1-(Pyridin-4-yl)piperazine-1-carbonitrile (4c). Flash column chromatography on silica gel (ethyl acetate/petroleum ether/triethylamine, 20:10:1) gave the product (20.6 mg, 55% yield) as a yellowish solid: mp 64−67 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.34−3.44 (m, 8H), 6.66 (q, J = 2.2 Hz, 2H), 8.31 (q, J = 2.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 45.3, 48.3, 108.9, 116.8, 150.4, 154.4; MS (EI) 188 (M^+); HRMS (ESI) m/z calcd for $C_{10}H_{13}N_4$ $(M + H)^+$ 189.1135, found 189.1130; IR (KBr) 3049, 3009, 2976, 2868, 2214, 1603, 1516.

Thiomorpholine-4-carbonitrile (4d).[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gave the product (14.6 mg, 57% yield) as a white solid: mp 41−43 °C (lit.[46] mp 42−44 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.70 (t, J = 5.1 Hz, 4H), 3.46 (t, J = 5.1 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.1, 50.8, 117.3.

***N*-(Diphenylmethylene)cyanamide (4e).** Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:20) gave the product (12.4 mg, 30% yield) as a yellowish solid: mp 76−78 °C (lit.[54] mp 78−79 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45−7.49 (m, 2H), 7.56−7.57 (m, 4H), 7.63−7.67 (m, 2H), 7.80−7.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 114.6, 128.7, 131.2, 132.2, 134.4, 189.5; MS (EI) 206 (M^+); HRMS (ESI) m/z calcd for $C_{14}H_{11}N_2$ $(M + H)^+$ 207.0917, found 207.0903; IR (KBr) 3085, 2920, 2856, 2176, 1595, 1581, 1549, 1446.

Cyclohexanecarbamonitrile (4f). Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:80) gave the product (14.5 mg, 36% yield) as a yellowish liquid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.17−1.28 (m, 2H), 1.32−1.42 (m, 2H), 1.64−1.72 (m, 2H), 1.89−1.93 (m, 2H), 2.07−2.10 (m, 2H), 3.52−3.60 (m, 1H), 7.07−7.11 (m, 1H), 7.14−7.16 (m, 2H), 7.34−7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.0, 25.3, 31.0, 57.6, 112.5, 117.1, 123.7, 129.6, 140.0; MS (EI) 200 (M^+); HRMS (ESI) m/z calcd for $C_{13}H_{17}N_2$ $(M + H)^+$ 201.1386, found 201.1382; IR (KBr) 3083, 3008, 2933, 2856, 2212, 1597, 1495.

2-Cyano-1,1,3,3-tetramethylguanidine (4g):[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether: triethylamine, 20:10:1) gave the product (20.3 mg, 72% yield) as a yellow liquid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.91 (s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.8, 117.6, 166.0.

3,4-Dihydro-2(1*H*)-isoquinolinecarbonitrile (4h).[46] Flash column chromatography on silica gel (ethyl acetate/petroleum ether, 1:10) gave the product (11.4 mg, 36% yield) as a white solid: mp 63−65 °C (lit.[46] mp 68−70 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.96 (t, J = 5.9 Hz, 2H), 3.48 (t, J = 5.9 Hz, 2H), 4.41 (s, 2H), 7.03−7.05 (m, 1H), 7.13−7.15 (m, 1H), 7.19−7.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 27.5, 46.7, 49.9, 117.9, 125.9,126.6, 127.1, 129.1, 130.6, 132.5.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details on the mechanism study, along with copies of ^{1}H and ^{13}C NMR spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (nos. 21272028 and 21202013), "Innovation & Entrepreneurship Talents" Introduction Plan of Jiangsu Province, Jiangsu Key Laboratory of Advanced Catalytic Materials &Technology (BM2012110), Jiangsu Province Key Laboratory of Fine Petrochemical Engineering, and the Priority Academic Program Development of Jiangsu Higher Education Institutions and Open Research Fund of Top Key Discipline of Chemistry in Zhejiang Provincial Colleges for financial support.

■ REFERENCES

(1) Deaton, D. N.; Hassell, A. M.; McFayden, R. B.; Miller, A. B.; Miller, L. R.; Shewchuk, L. M.; Tavares, F. X.; Willard, D. H., Jr.; Wright, L. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1815.

(2) Carta, F.; Akdemir, A.; Scozzafava, A.; Masini, E.; Supuran, C. T. *J. Med. Chem.* **2013**, *56*, 4691.

(3) Kumar, R.; Rai, D.; Sharma, S. K.; Saffran, H. A.; Blush, R.; Tyrrell, D. L. J. *J. Med. Chem.* **2001**, *44*, 3531.

(4) Guay, D.; Beaulieu, C.; Percival, M. D. *Curr. Top. Med. Chem.* **2010**, *10*, 708.

(5) Lainé, D.; Palovich, M.; McCleland, B.; Petitjean, E.; Delhom, I.; Xie, H.; Deng, J.; Lin, G.; Davis, R.; Jolit, A.; Nevins, N.; Zhao, B.; Villa, J.; Schneck, J.; McDevitt, P.; Midgett, R.; Kmett, C.; Umbrecht, S.; Peck, B.; Davis, A. B.; Bettoun, D. *ACS Med. Chem. Lett.* **2011**, *2*, 142.

(6) Sparks, T. C.; Watson, G. B.; Loso, M. R.; Geng, C.; Babcock, J. M.; Thomas, J. D. *Pestic. Biochem. Physiol.* **2013**, *107*, 1.

(7) Park, S. J.; Baars, H.; Mersmann, S.; Buschmann, H.; Baron, J. M.; Amann, P. M.; Czaja, K.; Hollert, H.; Bluhm, K.; Redelstein, R.; Bolm, C. *ChemMedChem* **2013**, *8*, 217.

(8) Harb, C.; Kravtsov, P.; Choudhuri, M.; Sirianni, E. R.; Yap, G. P. A.; Lever, A. B. P.; Crutchley, R. J. *Inorg. Chem.* **2013**, *52*, 1621.

(9) Xiang, J.; Man, W.-L.; Yiu, S.-M; Peng, S.-M.; Lau, T.-C. *Chem.—Eur. J.* **2011**, *17*, 13044.

(10) Lindsey, C. C.; O'Boyle, B. M.; Mercede, S. J.; Pettus, T. R. R.; Crutchley, R. J. *Coord. Chem. Rev.* **2001**, *219*, 125.

DOI: 10.1021/jo502607c
J. Org. Chem. 2015, 80, 2822−2826

(11) Kang, L.-C.; Chen, X.; Wang, X.-S.; Li, Y.-Z.; Song, Y.; Zuo, J.-L.; You, X.-Z. *Dalton Trans.* **2011**, *40*, 5200.
(12) Maestri, G.; Larraufie, M.-H.; Ollivier, C.; Malacria, M.; Fensterbank, L.; Lacôte, E. *Org. Lett.* **2012**, *14*, 5538.
(13) Larraufie, M.-H.; Ollivier, C.; Fensterbank, L.; Malacria, M.; Lacôte, E. *Angew. Chem., Int. Ed.* **2010**, *49*, 2178.
(14) Larraufie, M.-H.; Maestri, G.; Malacria, M.; Ollivier, C.; Fensterbank, L.; Lacôte, E. *Synthesis* **2012**, *44*, 1279.
(15) Nekrasov, D. D. *Russ. J. Org. Chem.* **2004**, *40*, 1387.
(16) Nekrasov, D. D. *Chem. Heterocycl. Compd.* **2004**, *40*, 1107.
(17) Boñaga, L. V. R.; Zhang, H.-C.; Maryanoff, B. E. *Chem. Commun.* **2004**, 2394.
(18) Lane, T. K.; Nguyen, M. H.; D'Souza, B. R.; Spahn, N. A.; Louie, J. *Chem. Commun.* **2013**, *49*, 7735.
(19) Habibi, D.; Nasrollahzadeh, M.; Sahebekhtiari, H.; Sajadi, S. M. *Synlett* **2012**, *23*, 2795.
(20) Stolley, R. M.; Maczka, M. T.; Louie, J. *Eur. J. Org. Chem.* **2011**, 3815.
(21) Wang, C.; Wang, D.; Xu, F.; Pan, B.; Wan, B. *J. Org. Chem.* **2013**, *78*, 3065.
(22) Lane, T. K.; D'Souza, B. R.; Louie, J. *J. Org. Chem.* **2012**, *77*, 7555.
(23) Wong, B.; Stumpf, A.; Carrera, D.; Gu, C.; Zhang, H. *Synthesis* **2013**, *45*, 1083.
(24) Katla, V. R.; Syed, R.; Kuruva, C. S.; Kuntrapakam, H. K.; Chamarthi, N. R. *Chem. Pharm. Bull.* **2013**, *61*, 25.
(25) Wang, R.; Falck, J. R. *Chem. Commun.* **2013**, *49*, 6516.
(26) Gong, T.-J.; Xiao, B.; Cheng, W.-M.; Su, W.; Xu, J.; Liu, Z.-J.; Liu, L.; Fu, Y. *J. Am. Chem. Soc.* **2013**, *135*, 10630.
(27) Chaitanya, M.; Yadagiri, D.; Anbarasan, P. *Org. Lett.* **2013**, *15*, 4960.
(28) Han, J.; Pan, C.; Jia, X.; Zhu, C. *Org. Biomol. Chem.* **2014**, *12*, 8603.
(29) Zhang, G.; Ren, X.; Chen, J.; Hu, M.; Cheng, J. *Org. Lett.* **2011**, *13*, 5004.
(30) Liu, B.; Wang, J.; Zhang, B.; Sun, Y.; Wang, L.; Chen, J.; Cheng, J. *Chem. Commun.* **2014**, *50*, 2315.
(31) Jin, J.; Wen, Q.; Lu, P.; Wang, Y. *Chem. Commun.* **2012**, *48*, 9933.
(32) Ding, S.; Jiao, N. *J. Am. Chem. Soc.* **2011**, *133*, 12374.
(33) Ren, X.; Chen, J.; Chen, F.; Cheng, J. *Chem. Commun.* **2011**, *47*, 6725.
(34) Kim, J.; Chang, S. *J. Am. Chem. Soc.* **2010**, *132*, 10272.
(35) Zhang, G.; Chen, S.; Fei, H.; Cheng, J.; Chen, F. *Synlett* **2012**, 2247.
(36) Kou, X.; Zhao, M.; Qiao, X.; Zhu, Y.; Tong, X.; Shen, Z. *Chem.—Eur. J.* **2013**, *19*, 16880.
(37) Wen, Q.; Jin, J.; Mei, Y.; Lu, P.; Wang, Y. *Eur. J. Org. Chem.* **2013**, 4032.
(38) Zhang, L.; Wen, Q.; Jin, J.; Wang, C.; Lu, P.; Wang, Y. *Tetrahedron* **2013**, *69*, 4236.
(39) Pan, C.; Jin, H.; Xu, P.; Liu, X.; Cheng, Y.; Zhu, C. *J. Org. Chem.* **2013**, *78*, 9494.
(40) Song, R.-J.; Wu, J.-C.; Liu, Y.; Deng, G.-B.; Wu, C.-Y.; Wei, W.-T.; Li, J.-H. *Synlett* **2012**, 2491.
(41) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790.
(42) Hong, X.; Wang, H.; Qian, G.; Tan, Q.; Xu, B. *J. Org. Chem.* **2014**, *79*, 3228.
(43) von Braun, J. *Ber.* **1907**, *40*, 3914.
(44) Hageman, H. A. *Org. React.* **1953**, *7*, 198.
(45) Fodor, G.; Nagubandi, S. *Tetrahedron* **1980**, *36*, 1279.
(46) Teng, F.; Yu, J.-T.; Jiang, Y.; Yang, H.; Cheng, J. *Chem. Commun.* **2014**, *50*, 8412.
(47) Oba, T.; Tateno, Y.; Ihara, M.; Fukusumi, T.; Takei, N.; Ito, S. *Tetrahedron Lett.* **2014**, *55*, 725.
(48) Schröder, K.; Konkolewicz, D.; Poli, R.; Matyjaszewski, K. *Organometallics* **2012**, *31*, 7994.
(49) Xu, H.; Liu, P.-T.; Li, Y.-H.; Han, F.-S. *Org. Lett.* **2013**, *15*, 3354.
(50) Teng, F.; Yu, J.-T.; Jiang, Y.; Yang, H.; Cheng, J. *Chem. Commun.* **2014**, *50*, 12139.
(51) Mancheño, O. G.; Bistri, O.; Bolm, C. *Org. Lett.* **2007**, *9*, 3809.
(52) For the cyanation reaction using MeCN as cyanide source, see refs 36, 39, and 40.
(53) Janzen, E. G.; Krygsman, P. H.; Lindsay, D. A.; Haire, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 8279.
(54) Jochims, J. C.; Rahman, M. A. *Chem. Ber.* **1984**, *117*, 502.

DOI: 10.1021/jo502607c
J. Org. Chem. 2015, 80, 2822−2826