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Note

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01930 • Publication Date (Web): 28 Sep 2017

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

One-Pot Synthesis of Quinoxalinones via Tandem Nitrosation/Cyclization of *N*-Aryl Cyanoacetamides

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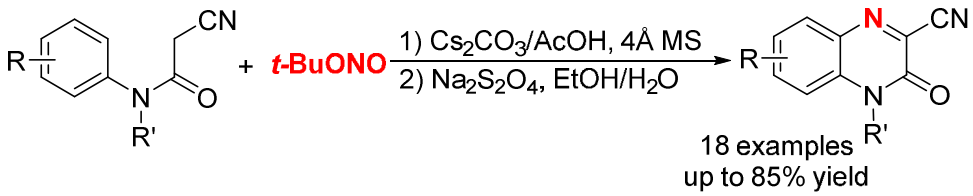
Abstract

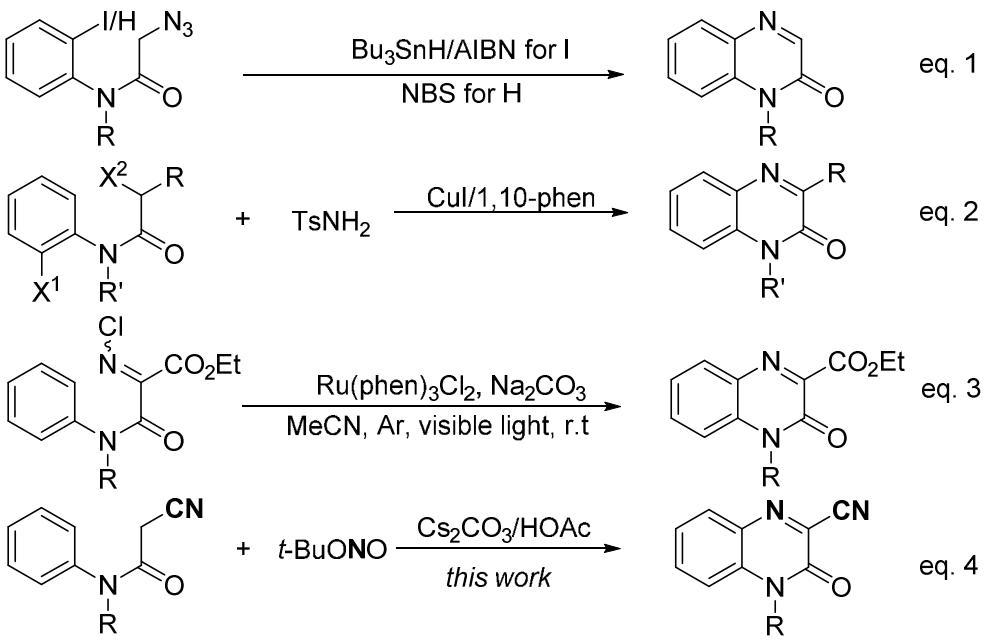


A new one-pot strategy for the synthesis of quinoxalin-2-ones from the tandem nitrosation/cyclization reaction of *N*-aryl cyanoacetamides with *tert*-butyl nitrite has been developed. The dehydrogenative *N*-incorporation is achieved through a sequence of nitrosation, tautomerization and cyclization, affording quinoxalin-2-ones in moderate to good yields with good functional group tolerance.

Quinoxalinones are important heterocyclic scaffolds which display a wide range of biological and medicinal properties including antithrombotic and antitumor activity,[1] and are also employed as kinases inhibitors, antimicrobial agents and benzodiazepine receptor agonist.[2] Accordingly, many versatile methods have been developed for the construction of quinoxalinones,[3] but most of them focus on the condensation of *o*-phenylenediamine with 1,2-dicarbonyls or their equivalents.[3g, 4] Recently, the radical cyclization of 2-azido-*N*-phenylacetamides has also been found to be an effective approach for their preparation (Scheme 1, eq 1).[5] In 2010, Bao reported a copper-catalyzed double amination of 2-halo-*N*-(2-halophenyl)-acetamides with $TsNH_2$ for the synthesis of quinoxalin-2-ones (eq 2).[6] In 2015, Yu group developed a strategy for the synthesis of quinoxalin-2-ones from visible light-induced radical

cyclization of *N*-chloroimines (eq 3).[7] Despite the significance of these methods, the general and efficient approach for constructing quinoxalinones is desirable, especially using a one-pot strategy from readily available materials. Herein, we wish to report a one-pot synthesis strategy of 3-cyano-quinoxalin-2-ones *via* sequential nitrosation/cyclization reaction of *N*-aryl cyanoacetamides using *tert*-butyl nitrite as nitrogen source (eq 4).

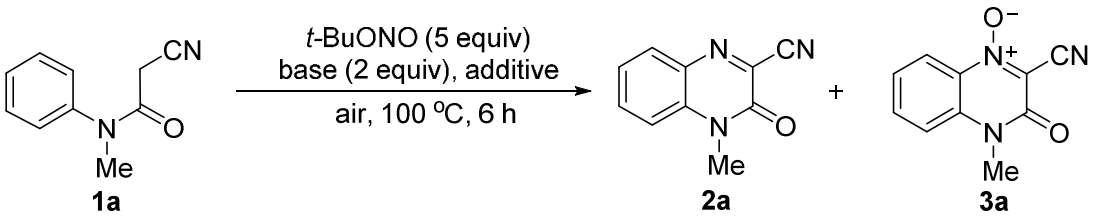
Scheme 1. Construction of Quinoxalinones



We began our studies by testing the reaction between 2-cyano-*N*-methyl-*N*-phenylacetamide (**1a**)[8] and TBN (the nitrogen source) to optimize the reaction conditions (Table 1). Firstly, substrate **1a** was reacted with 5 equiv of TBN and 2 equiv of Cs_2CO_3 in DMF at 100 ^oC for 6 h, giving the target product **2a** in 12% yield and its oxide **3a** in 19% yield (entry 1). To enhance the reaction yield, several solvents were examined, including dioxane, toluene and MeCN (entries 2-4). MeCN was found to give the best results. Subsequently, a variety of bases, such as Li_2CO_3, K_2CO_3, $NaHCO_3$, and CsOAc were investigated, but all were less effective than Cs_2CO_3 (entries 5-8). Inspired by some of our previous work,[9] 5 equiv of HOAc was added into the reaction, and we found that products **2a** and **3a** were isolated in 45% and 34% yield, respectively (entry 9). Only 14% yield was obtained when the reaction was conducted in 5 equiv of HOAc without Cs_2CO_3 (entry 10), which implied that the acidity of buffer solution Cs_2CO_3/AcOH played as a crucial role in the cyclization reaction. Consistent with this hypothesis, only trace amount of product was observed when a stronger acid (CF_3COOH) was used (entry 11). To inhibit the hydrolysis of amide, 100 mg 4 Å molecular sieve was added into the reaction. We were pleased to find that the product **2a** was isolated in 39% yield, accompanied by 52% of its oxide **3a** (entry 12). We supposed that product **3a** was produced from the oxidation of **2a** by excessive TBN, and could be converted back to product **2a** through a simple reduction process. As expected, without

further separation, the mixture of **2a** and oxide **3a** could be easily reduced by a solution of $Na_2S_2O_4$ in ethyl alcohol and water to afford quinoxalinone **2a** as a sole product in 85% yield (entry 13). Lower yield was observed when the reaction was carried out in the presence of 4 equiv of TBN or 4 equiv of HOAc (entries 14 and 15).

Table 1. Screening of Optimal Reaction Conditions[a]

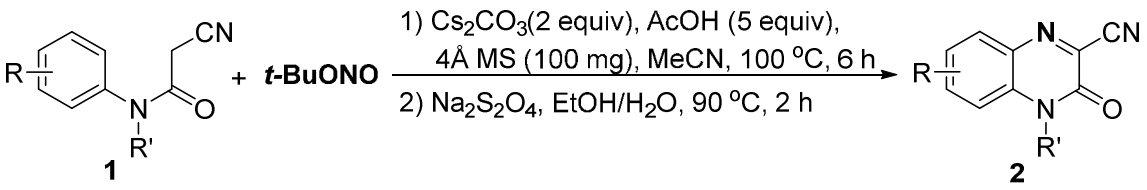


1a **2a** **3a**

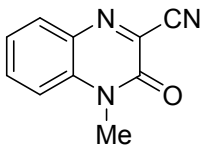
entry	base	additive	solvent	isolated yield (%) 2a	3a
1	Cs_2CO_3	-	DMF	12	19
2	Cs_2CO_3	-	dioxane	16	13
3	Cs_2CO_3		toluene	trace	16
4	Cs_2CO_3	-	MeCN	41	22
5	Li_2CO_3	-	MeCN	26	trace
6	K_2CO_3	-	MeCN	24	17
7	$NaHCO_3$	-	MeCN	23	17
8	CsOAc	-	MeCN	28	24
9	Cs_2CO_3	HOAc	MeCN	45	34
10	-	HOAc	MeCN	14	trace
11	Cs_2CO_3	CF_3CO_2H	MeCN	trace	0
12[b]	Cs_2CO_3	HOAc	MeCN	39	52
13[b,c]	Cs_2CO_3	HOAc	MeCN	85	0
14[b,c,d]	Cs_2CO_3	HOAc	MeCN	67	0
15[b,c,e]	Cs_2CO_3	HOAc	MeCN	78	0

[a]Reaction conditions: **1a** (0.2 mmol), *t*-BuONO (1.0 mmol), base (2.0 equiv) and additive (5.0 equiv) in solvent (1 mL) under air atmosphere at 100 °C for 6 h. [b]4 Å MS (100 mg) was added. [c]After reaction finished, a solution of $Na_2S_2O_4$ (0.7 mmol) in ethyl alcohol (2 mL) and water (4 mL) was added, then stirred at 90 °C for 2 h. [d]4.0 equiv *t*-BuONO. [e]4.0 equiv HOAc.

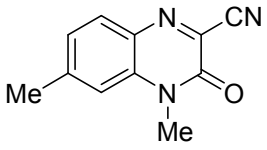
Scheme 2. Variation of *N*-aryl Cyanoacetamide[a]



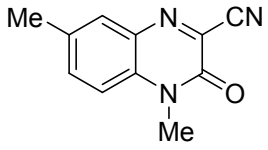
1 **2**



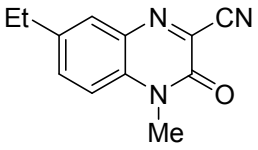
2a, 85%



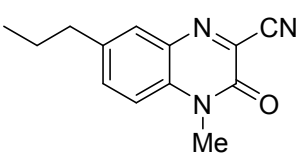
2b, 64%



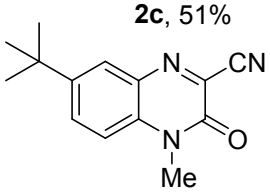
2c, 51%



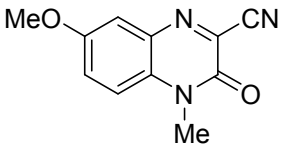
2d, 60%



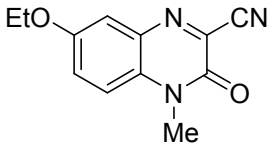
2e, 70%



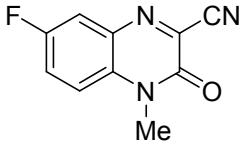
2f, 65%



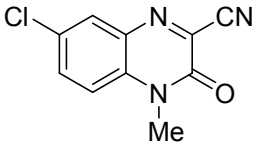
2g, 62%



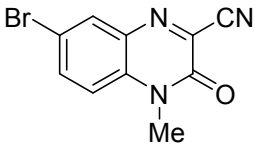
2h, 48%



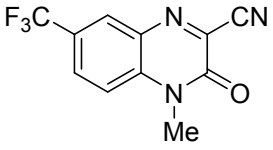
2i, 40%



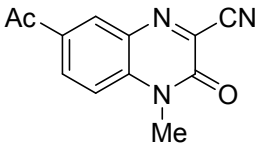
2j, 76%



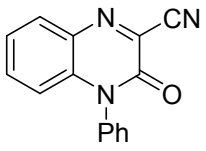
2k, 53%



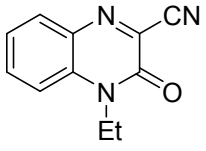
2l, 71%



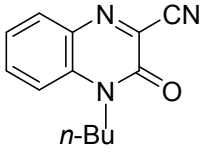
2m, 64%



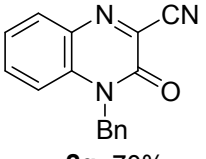
2n, 47%



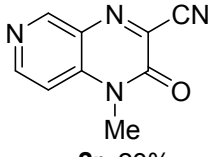
2o, 43%



2p, 51%



2q, 70%



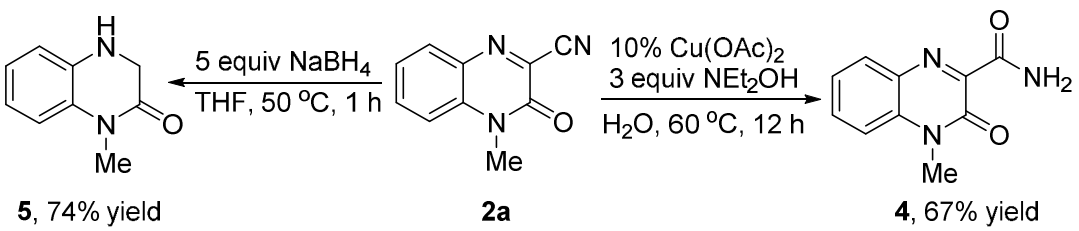
2r, 23%

[a]Reaction conditions: **1** (0.2 mmol), *t*-BuONO (1.0 mmol), Cs_2CO_3 (2.0 equiv), 100 mg 4 Å MS and HOAc (5.0 equiv) in MeCN (1 mL) under air atmosphere at 100 °C for 6 h. Then, a solution of $Na_2S_2O_4$ (0.7 mmol) in ethyl alcohol (2 mL) and water (4 mL) was added and stirred under air atmosphere at 90 °C for 2 h, isolated yield.

Having established the optimal conditions for this tandem reaction, we proceeded to explore the substrate scope by testing the reaction of a wide variety of *N*-aryl cyanoacetamides with TBN (Scheme 2). Firstly, the substitution effect on the aromatic ring was examined. The results disclosed that both electron-withdrawing group and electron-donating group in the *meta*- or *para*- position of aryl moiety were suitable and afforded the corresponding products in moderate to good yields. For example, *meta*-tolyl substituted acetamide **1b** provided the product **2b** in 64% yield, and *para*-tolyl substituted cyanoacetamide **1c** gave the product **2c** in 51% yield. *N*-Aryl cyanoacetamides bearing ethyl, propyl, *tert*-butyl, methoxy or ethoxy afforded products **2d**-**h** in 48-70% yields. In the case of halide substrates, fluorinated, chlorinated and brominated *N*-phenyl cyanoacetamides afforded the products **2i**-**k** in 40-76% yields. Moreover, the cyanoacetamides with strong electron-withdrawing group were also suitable substrates under standard reaction conditions. For example, trifluoromethyl and acetyl substituted phenyl cyanoacetamides provided **2l**, **m** in 71 and 64% yields, respectively. Subsequently, a number of substituents on the *N*-substituted moiety were examined. We were pleased to find that *N*-diphenyl, ethyl, *n*-butyl and benzyl substituted cyanoacetamides afforded corresponding products **2n**-**q** in moderate to good yields (43-70%). Interestingly, the reaction of nitrogen-containing heterocyclic compound **1r** proceeded smoothly to give pyrido[3,4-b]pyrazin-2-one **2r,** albeit in a low yield (23%).

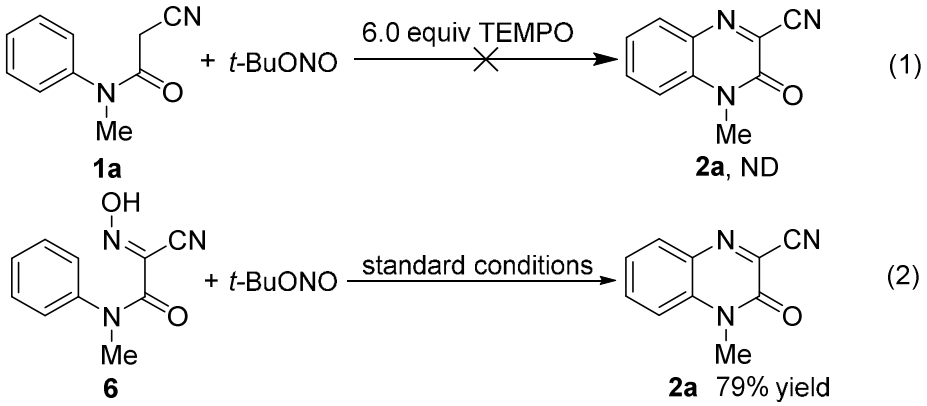
To illustrate the applicability of this reaction, further transformation of product **2a** was investigated as showed in Scheme 3. 1-Methyl-1,2-dihydroquinoxalin-2-one-3-carboxamide **4** was isolated in 67% yield when product **2a** was treated with 10 mol% $Cu(OAc)_2$ and 3 equiv NEt_2OH in H_2O at 60 °C for 12 h.[10] This result demonstrated that 3-cyano-quinoxalin-2-ones could be easily transformed to quinoxalinone-3-carboxamides, which exhibit a wide range of physicochemical properties, biological and medicinal properties including antibacterial and antiallergic activity.[11] Furthermore, in the presence of 5 equiv $NaBH_4$, product **2a** was reduced to 1-methyl-3,4-dihydroquinoxalin-2(1H)-one **5** in 74% yield, which has been reported to possess pharmaceutical and biological activity.[12]

Scheme 3. Synthetic Applications of **2a**

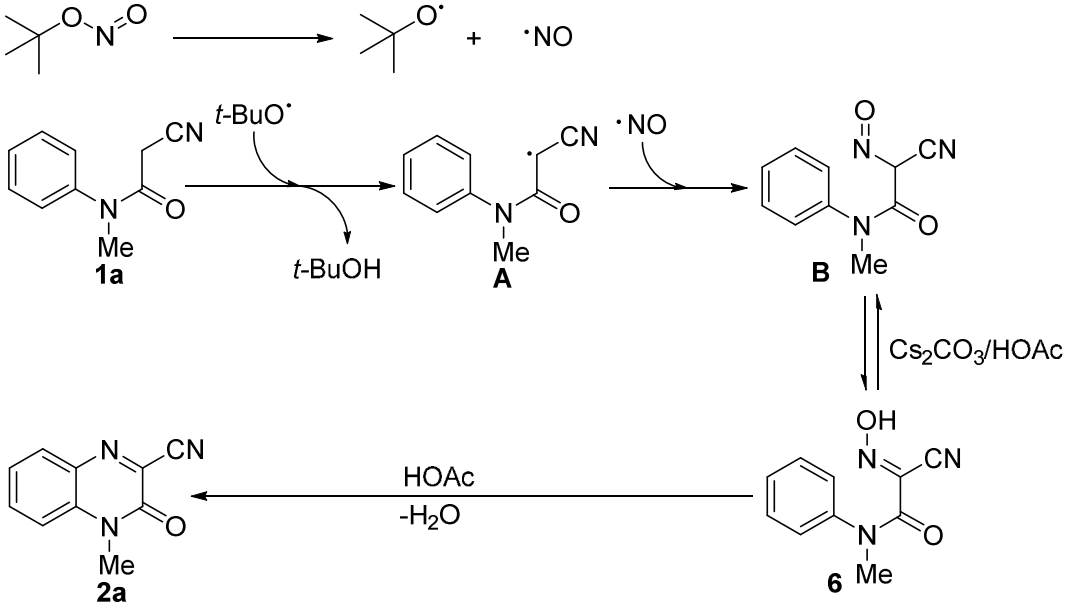


In order to probe the mechanism of this sequential nitrosation/cyclization, several control experiments were conducted as shown in Scheme 4. The reaction of substrate **1a** with TBN was performed under the standard conditions by adding 6.0 equiv of 2,2,6,6-tetramethylpiperidine oxide (TEMPO), a radical scavenger (Scheme 4, eq 1). The reaction were suppressed, neither the product **2a** nor its oxide **3a** could be detected. These results indicated that the reaction might be involved a free radical process. Furthermore, *N*-hydroxy-2-(methyl(phenyl)amino)-2-oxoacetimidoyl cyanide **6**[8] was performed with TBN under the optimal conditions. As expected, the desired product **2a** was isolated in 79% yield (eq 2), suggesting that oxime **6** might be a key intermediate for the cyclization in the tandem reaction.

Scheme 4. Control Experiments



Scheme 5. Possible Mechanism



On the basis of the present results and related precedents,[9b, 13] a plausible mechanism for the nitrosation/cyclization of *N*-aryl cyanoacetamide is presented in Scheme 5. Initially, ·NO radical and

tert-butoxy radical is generated from the decomposition of *tert*-butyl nitrite. Then, the hydrogen abstraction of *tert*-butoxy radical with cyanoacetamide **1a** affords alkyl radical intermediate **A**.[13c] Subsequently, intermediate **A** reacts with the ·NO radical to give intermediate **B**, which is further converted to oxime **6** *via* tautomerization in Cs_2CO_3/AcOH buffer solution. Finally, the acidic dehydration of key intermediate oxime **6** in the presence of HOAc leads to the desired product **2a**.[9a]

In summary, we have developed a convenient and efficient method for the synthesis of quinoxalin-2-ones *via* one-pot tandem nitrosation/cyclization of *N*-aryl cyanoacetamides. A variety of *N*-aryl cyanoacetamides underwent the nitrosation/cyclization reaction with *tert*-butyl nitrite successfully to afford the corresponding quinoxalin-2-ones in moderate to good yields. Compared to traditional nitrosation with $NaNO_2$ and strong acid, this reaction applied TBN as the nitroso group source in the absence of strong acid, which provided a new route for the nitrosation of some acid-sensitive substrates.

Experimental Section

General Information:

Chemicals were either purchased or purified by standard techniques. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C), using DMSO-d_6 as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given in δ relative to TMS, and the coupling constants J are given in hertz. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. All reactions under air atmosphere were conducted using standard Schlenk techniques. Melting points were measured on an X4 melting point apparatus and were uncorrected. Column chromatography was performed using EM silica gel 60 (300-400 mesh).

General Procedure for the Synthesis of Cyanoacetanilides 1:

To a stirred suspension of cyanoacetic acid (550 mg, 6.5 mmol) in dichloromethane (25 mL) was added oxalyl chloride (0.52 mL, 6 mmol) followed by three drops of DMF at 0 °C. The reaction mixture was stirred at rt for 3 h. To this solution was added a solution of anilines (5 mmol) in dichloromethane (20 mL) followed by triethylamine (1.74 mL, 12.5 mmol) at 0 °C. The reaction mixture was stirred for

12-24 h and then washed with water (10 mL) and 1 N HCl (10 mL). The organic layer was dried over Na_2SO_4 and evaporated to afford a crude solid, which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, v/v) to afford pure Cyanoacetanilides **1**.[8]

General Procedure for the Synthesis of Quinoxalin-2-ones 2:

Cyanoacetanilides **1** (0.2 mmol), TBN (103 mg, 1.0 mmol), Cs_2CO_3 (130.4 mg, 0.4 mmol), HOAc (60 mg, 1.0 mmol), and 4 Å MS (100 mg) in MeCN (1 mL) was added to a flame-dried Schlenk tube with a magnetic stirring bar. The reaction mixture was stirred at 100 °C for 6 h. Then, $Na_2S_2O_4$ (120 mg, 0.7 mmol) in ethyl alcohol (2 mL) and water (4 mL) was added to this solution. The reaction mixture was stirred at 90 °C for a further 2 h under air atmosphere. After the reaction equilibrium, the reaction mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 x 10 mL) and brine (1 x 10 mL). After the aqueous layer was extracted with ethyl acetate, the organic layer was collected, dried over anhydrous $MgSO_4$, and evaporated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, v/v) to afford the desired products.

Procedure for the Synthesis of 1-Methyl-1, 2-dihydroquinoxalin-2-one-3-carboxamide 4:

To a flame-dried Schlenk tube with a magnetic stirring bar were charged 3-Cyano-1-methyl-1,2-dihydroquinoxalin-2-one **2a** (37 mg, 0.2 mmol), $Cu(OAc)_2$ (3.62 mg, 10 mol%), NEt_2OH (53.4 mg, 3 equiv**)** in H_2O (2 mL). The reaction mixture was stirred at 60 °C for 12 h. After the reaction equilibrium, the mixture was poured into ethyl acetate, which was washed with brine (2 x 10 mL). After the combined organic layer was extracted with ethyl acetate, dried over anhydrous $MgSO_4$ and evaporated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether /ethyl acetate, v/v) to afford the desired product **4** in 67% yield.

Procedure for the Synthesis of *1-Methyl-3,4-dihydroquinoxalin-2(1H)-one* 5:

$NaBH_4$ (38 mg, 5 equiv) was added to a solution of **2a** (37mg, 0.2 mmol) in dry THF (1 mL) at room temperature. The reaction mixture was stirred at 50 °C for 1 hour. After the removal of solvent, the

product was purified by column chromatography on silica gel (petroleum ether /ethyl acetate, v/v) to afford the desired product **5** in 74% yield.

Procedure for the Synthesis of *N*-Hydroxy-2-(methyl(phenyl)amino)-2-oxoacetimidoyl Cyanide 6:

To solution of cyanoacetanilide **1a** (348 mg, 2.0 mmol) in THF (7.0 mL) was added sodium hydride (96 mg, 60% dispersion in mineral oil, 2.4 mmol). The reaction mixture was stirred at 35 °C for 1 h. Then TBN (515 mg, 5.0 mmol) was added dropwise and the reaction mixture was stirred at 60 °C until complete consumption of the starting material as detected by TLC or GC-MS analysis Then, after the removal of solvent, the product was purified by column chromatography on silica gel (petroleum ether /ethyl acetate, v/v) to afford the desired product **6** in 34% yield.[8]

3-Cyano-1-methyl-1,2-dihydroquinoxalin-2-one (**2a**)[5c]: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a yellow solid (31.5 mg, 85% yield), mp 153-155 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.89 (d, J = 8.0 Hz, 1H), 7.83-7.80 (m, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.49-7.46 (m, 1H), 3.63 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.0, 134.6, 134.3, 133.7, 132.4, 130.8, 124.6, 115.5, 115.0, 29.6; LRMS (EI, 70 eV) m/z (%): 185 (M^+, 100), 156 (72), 130 (47); HRMS (ESI) calcd for $C_{10}H_7N_3ONa^+$ ([M + Na]$^+$) 208.0481, found 208.0471.

3-Cyano-1,7-dimethyl-1,2-dihydroquinoxalin-2-one (**2b**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a yellow solid (25.5 mg, 64% yield), mp 178-180 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.75 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.28 (d, J = 8.0 Hz, 1H), 3.58 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.2, 146.2, 134.4, 132.0, 130.9, 130.5, 126.1, 115.4, 115.2, 29.6, 22.0; LRMS (EI, 70 eV) m/z (%): 199 (M^+, 100), 170 (78), 156 (27); HRMS (ESI) calcd for $C_{11}H_9N_3ONa^+$ ([M + Na]$^+$) 222.0638, found 222.0642.

3-Cyano-1,6-dimethyl-1,2-dihydroquinoxalin-2-one (**2c**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a yellow solid (20.3 mg, 51% yield), mp 174-176 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.69 (s, 1H), 7.65 (d, J = 8.5 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 3.60 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.9, 135.9, 134.3, 133.4, 132.4, 132.3, 130.0, 115.3, 115.1, 29.6, 20.0; LRMS (EI, 70 eV) m/z (%):

199 (M^+, 100), 170 (70), 156 (27); HRMS (ESI) calcd for $C_{11}H_9N_3ONa^+$ ($[M + Na]^+$) 222.0638, found 222.0644.

3-Cyano-6-ethyl-1-methyl-1,2-dihydroquinoxalin-2-one (**2d**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (25.6 mg, 60% yield), mp 166-168 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.66 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 1H), 3.58 (s, 3H), 2.68 (q, J = 7.5 Hz, 2H), 1.18 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.9, 140.5, 134.9, 133.3, 132.45, 132.41, 128.8, 115.4, 115.0, 29.6, 27.0, 15.3; LRMS (EI, 70 eV) m/z (%): 213 (M^+, 51), 198 (100); HRMS (ESI) calcd for $C_{12}H_{11}N_3ONa^+$ ($[M + Na]^+$) 236.0794, found 236.0791.

3-Cyano-1-methyl-6-propyl-1,2-dihydroquinoxalin-2-one (**2e**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (31.8 mg, 70% yield), mp 141-143 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.62 (d, J = 9.0 Hz, 2H), 7.53 (d, J = 9.0 Hz, 1H), 3.56 (s, 3H), 2.61 (t, J = 7.5 Hz, 2H), 1.61-1.53 (m, 2H), 0.84 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.9, 138.9, 135.3, 133.3, 132.5, 132.4, 129.5, 115.3, 115.0, 35.9, 29.5, 23.8, 13.4; LRMS (EI, 70 eV) m/z (%): 227 (M^+, 63), 201 (100), 171 (40); HRMS (ESI) calcd for $C_{13}H_{14}N_3O^+$ ($[M + H]^+$) 228.1131, found 228.1137.

3-Cyano-1-methyl-6-(tert-butyl)-1,2-dihydroquinoxalin-2-one (**2f**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (31.4 mg, 65% yield), mp 182-184 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.87 (d, J = 9.0 Hz, 1H), 7.77 (s, 1H), 7.56 (d, J = 9.0 Hz, 1H), 3.58 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.9, 147.4, 133.3, 132.6, 132.22, 132.16, 126.4, 115.3, 115.0, 34.2, 30.8, 29.6; LRMS (EI, 70 eV) m/z (%): 241 (M^+, 17), 226 (100), 198 (18); HRMS (ESI) calcd for $C_{14}H_{15}N_3ONa^+$ ($[M + Na]^+$) 264.1107, found 264.1116.

3-Cyano-1-methyl-6-methoxy-1,2-dihydroquinoxalin-2-one (**2g**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a yellow solid (26.7 mg, 62% yield), mp 171-173 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (d, J = 9.0 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.30 (s, 1H), 3.75 (s, 3H), 3.53(s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.1, 152.7, 133.6, 133.2, 129.0, 124.2, 116.7, 115.1, 111.4, 56.0, 29.9; LRMS (EI, 70 eV) m/z (%): 215 (M^+, 100), 200 (44), 172 (52); HRMS (ESI) calcd for $C_{11}H_9N_3O_2Na^+$ ($[M + Na]^+$) 238.0587, found 238.0593.

3-Cyano-6-ethoxy-1-methyl-1,2-dihydroquinoxalin-2-one (**2h**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a yellow solid (22.0 mg, 48% yield), mp 162-164 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.53 (d, J = 9.5 Hz, 1H), 7.38 (d, J = 9.5 Hz, 1H), 7.30 (s, 1H), 4.06 (q, J = 7.0 Hz, 2H), 3.57 (s, 3H), 1.32 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.2, 152.5, 133.4, 133.1, 128.7, 124.3, 116.4, 114.9, 111.9, 64.0, 29.7, 14.4; LRMS (EI, 70 eV) m/z (%): 229 (M^+, 100), 214 (37), 186 (40); HRMS (ESI) calcd for $C_{12}H_{11}N_3O_2Na^+$ ([M + Na]$^+$) 252.0743, found 252.0751.

3-Cyano-6-fluoro-1-methyl-1,2-dihydroquinoxalin-2-one (**2i**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a yellow solid (16.3 mg, 40% yield), mp 177-179 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.75-7.73 (m, 1H), 7.70-7.64 (m, 2H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.3 (d, J_{C-F} = 241.8 Hz), 152.7, 135.1, 132.7, 131.4, 122.4 (d, J_{C-F} = 24.1 Hz), 117.4, 115.4 (d, J_{C-F} = 22.6 Hz), 114.7, 29.9; LRMS (EI, 70 eV) m/z (%): 203 (M^+, 100), 174 (78), 148 (21); HRMS (ESI) calcd for $C_{10}H_7FN_3O^+$ ([M + H]$^+$) 204.0568, found 204.0571.

3-Cyano-6-chloro-1-methyl-1,2-dihydroquinoxalin-2-one (**2j**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a yellow solid (33.3 mg, 76% yield), mp 171-181 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (s, 1H), 7.81 (d, J = 9.0 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.8, 135.2, 134.0, 133.4, 132.8, 129.3, 128.6, 117.4, 114.7, 29.9; LRMS (EI, 70 eV) m/z (%): 219 (M^+, 100), 190 (53), 164 (18); HRMS (ESI) calcd for $C_{10}H_6ClN_3ONa^+$ ([M + Na]$^+$) 242.0092, found 242.0088.

6-Bromo-3-cyano-1-methyl-1,2-dihydroquinoxalin-2-one (**2k**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a yellow solid (27.9 mg, 53% yield), mp 184-186 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (s, 1H), 7.93 (d, J = 9.0 Hz, 1H), 7.59 (d, J = 9.0 Hz, 1H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.7, 142.1, 136.6, 133.8, 133.1, 132.3, 117.6, 116.2, 114.6, 29.8; LRMS (EI, 70 eV) m/z (%): 262 (M^+, 100), 234 (33), 155 (29); HRMS (ESI) calcd for $C_{10}H_7BrN_3O^+$ ([M + H]$^+$) 263.9767, found 263.9783.

3-Cyano-1-methyl-6-(trifluoromethyl)-1,2-dihydroquinoxalin-2-one (**2l**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (35.9 mg, 71% yield), mp 195-197 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.24 (s, 1H), 8.70 (d, J = 9.0 Hz, 1H), 7.81 (d, J = 9.0 Hz, 1H), 3.61 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.0, 137.0, 135.9, 131.6, 130.1, 127.9, 124.6 (q, J_{C-F} = 33.0 Hz), 123.6 (q, J_{C-F} = 271.0

Hz), 117.1, 114.6, 30.0; LRMS (EI, 70 eV) m/z (%): 253 (M^+, 100), 227 (55), 198 (25); HRMS (ESI) calcd for $C_{11}H_6F_3N_3ONa^+$ ($[M + Na]^+$) 276.0355, found 276.0372.

6-Acetyl-3-cyano-1-methyl-1,2-dihydroquinoxalin-2-one (**2m**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a yellow solid (29.1 mg, 64% yield), mp 189-191 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (s, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 7.73 (d, *J* = 9.0 Hz, 1H), 3.63 (s, 3H), 2.63 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 196.2, 153.0, 137.4, 134.9, 132.8, 132.7, 131.7, 131.3, 116.0, 114.6, 29.9, 26.7; LRMS (EI, 70 eV) m/z (%): 227 (M^+, 37), 212 (100); HRMS (ESI) calcd for $C_{12}H_{10}N_3O_2^+$ ($[M + H]^+$) 228.0768, found 228.0769.

3-Cyano-1-phenyl-1,2-dihydroquinoxalin-2-one (**2n**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (23.2 mg, 47% yield), mp 198-200 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.63-7.56 (m, 4H), 7.42-7.36 (m, 3H), 6.58 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.7, 135.2, 134.9, 134.8, 134.3, 132.4, 130.6, 130.3, 129.9, 128.2, 124.6, 115.8, 114.9; LRMS (EI, 70 eV) m/z (%): 247 (M^+, 100), 77 (54); HRMS (ESI) calcd for $C_{15}H_9N_3ONa^+$ ($[M + Na]^+$) 270.0638, found 270.0636.

1-Ethyl-3-cyano-1,2-dihydroquinoxalin-2-one (**2o**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (17.1 mg, 43% yield), mp 166-168 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.74 (d, *J* = 8.0 Hz, 1H), 7.68-7.65 (m, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.33-7.30 (m, 1H), 4.10 (q, *J* = 7.0 Hz, 2H), 1.08 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.6, 134.8, 133.7, 133.3, 132.7, 131.1, 124.6, 115.3, 115.0, 37.8, 12.2; LRMS (EI, 70 eV) m/z (%): 199 (M^+, 85), 187 (82), 143 (100); HRMS (ESI) calcd for $C_{11}H_9N_3ONa^+$ ($[M + Na]^+$) 222.0638, found 222.0641.

1-Butyl-3-cyano-3,4-dihydroquinoxalin-2-one (**2p**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (23.2 mg, 51% yield), mp 183-185 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.82-7.78 (m, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.47-7.44 (m, 1H), 4.20 (t, *J* = 8.0 Hz, 2H), 1.63-1.57 (m, 2H), 1.40-1.35 (m, 2H), 0.89 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.7, 134.6, 133.7, 133.5, 132.6, 131.0, 124.5, 115.4, 114.9, 42.2, 28.8, 19.5, 13.6; LRMS (EI, 70 eV) m/z (%): 227 (M^+, 100), 185 (92), 171 (94); HRMS (ESI) calcd for $C_{13}H_{14}N_3O^+$ ($[M + H]^+$) 228.1131, found 228.1136.

1-Benzyl-3-cyano-1,2-dihydroquinoxalin-2-one (**2q**)[5c]: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a yellow solid (36.6 mg, 70% yield), mp 169-171 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 (d, J = 8.0 Hz, 1H), 7.67-7.64 (m, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.40-7.37 (m, 1H), 7.29-7.24 (m, 4H), 7.21-7.18 (m, 1H), 5.45 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.2, 134.9, 134.4, 134.3, 133.5, 132.6, 130.9, 128.7, 127.5, 126.9, 124.7, 115.7, 114.9, 45.6; LRMS (EI, 70 eV) m/z (%): 261 (M^+, 24), 91 (100), 65 (13); HRMS (ESI) calcd for $C_{16}H_{11}N_3ONa^+$ ([M + Na]$^+$) 284.0794, found 284.0797.

3-Cyano-1-methyl-1,2-dihydropyrido[3,4-b]pyrazine-2-one (**2r**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 5:1, v/v) affords the title compound as a yellow solid (8.6 mg, 23% yield), mp 151-153 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.05 (s, 1H), 8.73 (d, J = 6.0 Hz, 1H), 7.65 (d, J = 6.0 Hz, 1H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.2, 152.3, 151.9, 139.5, 135.6, 128.7, 114.5, 109.7, 29.4; HRMS (ESI) calcd for $C_9H_7N_4O^+$ ([M + H]$^+$) 187.0614, found 187.0625.

3-Cyano-1-methyl-1,2-dihydroquinoxalin-2-one 4-Oxide (**3a**)[8]: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a yellow solid (20.9 mg, 52% yield), mp 213-215 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.14 (d, J = 8.0 Hz, 1H), 7.87-7.84 (m, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.46-7.43 (m, 1H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.4, 136.3, 134.9, 131.5, 125.4, 120.6, 117.5, 117.1, 112.2, 30.2; LRMS (EI, 70 eV) m/z (%): 201 (M^+, 100).

1-Methyl-1,2-dihydroquinoxalin-2-one-3-carboxamide (**4**)[14]: Purification by column chromatography on silica gel (ethyl acetate) affords the title compound as a pale yellow solid (27.2 mg, 67% yield), mp 172-174 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (s, 1H), 7.82 (d, J = 7.5 Hz, 1H), 7.79 (s, 1H), 7.69-7.65 (m, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.40-7.37 (m, 1H), 3.60 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.1, 152.9, 151.6, 133.7, 131.8, 131.5, 129.9, 124.0, 115.0, 29.1; HRMS (ESI) calcd for $C_{10}H_{10}N_3O_2^+$ ([M + H]$^+$) 204.0768, found 204.0768.

1-Methyl-3,4-dihydroquinoxalin-2(1H)-one (**5**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a pale yellow oil (23.8 mg, 74% yield); ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.87 (d, J = 8.0 Hz, 1H), 6.79-6.76 (m, 1H), 6.67-6.63 (m, 2H), 5.95 (s, 1H), 3.70 (s, 2H), 3.16 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3, 136.7, 128.6, 123.1, 118.2, 114.7, 113.6, 46.8, 28.1; LRMS (EI, 70 eV) m/z (%): 162 (M^+, 64), 133 (100), 92 (17); HRMS (ESI) calcd for $C_9H_{10}N_2ONa^+$ ([M + Na]$^+$) 185.0685, found 185.0684.

N-Hydroxy-2-(methyl(phenyl)amino)-2-oxoacetimidoyl Cyanide (**6**)[8]: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a white solid (138.0 mg, 34% yield), mp 154-156 °C (uncorrected); ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.14 (s, 1H), 7.45-7.42 (m, 2H), 7.35-7.34 (m, 3H), 3.36 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.5, 142.7, 129.6, 127.69, 127.65, 126.9, 108.8, 38.1; HRMS (ESI) calcd for $C_{10}H_9N_3O_2Na^+$ ([M + Na]$^+$) 226.0587, found 226.0590.

Acknowledgment. We thank the National Natural Science Foundation of China (No. 21272177) and Natural Science Foundation of Zhejiang Province (No. LR15B020002) for financial support.

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for product **2a-2r**, **3a, 4, 5** and **6**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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