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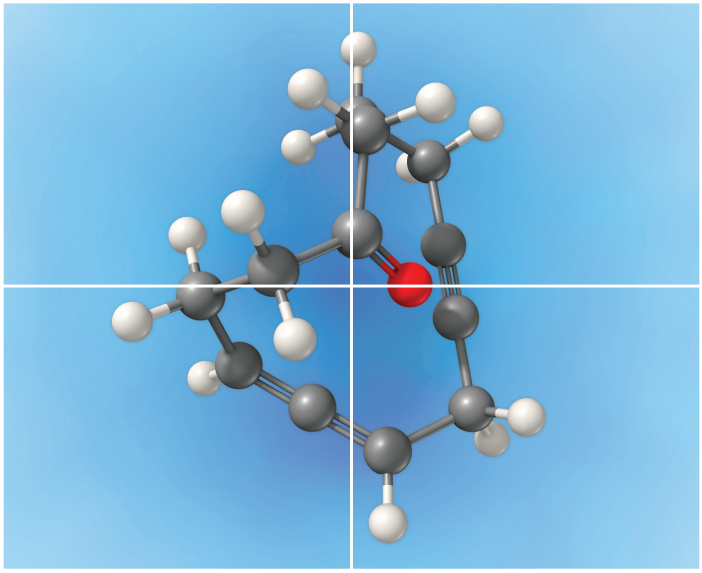

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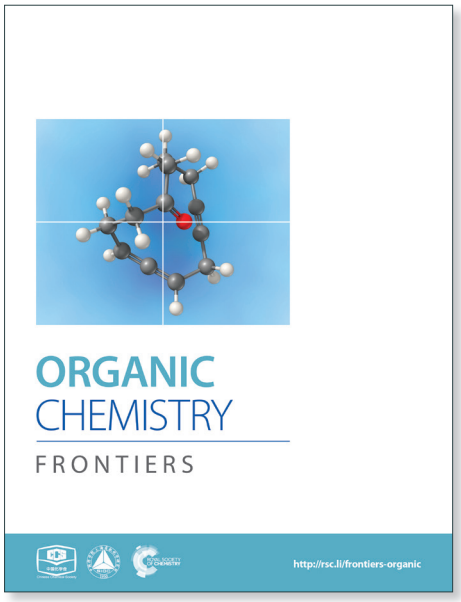

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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Acceptorless dehydrogenative condensation of *o*-aminobenzamides with aldehydes to quinazolinones in water catalyzed by a water-soluble iridium complex $[Cp^*Ir(H_2O)_3][OTf]_2$

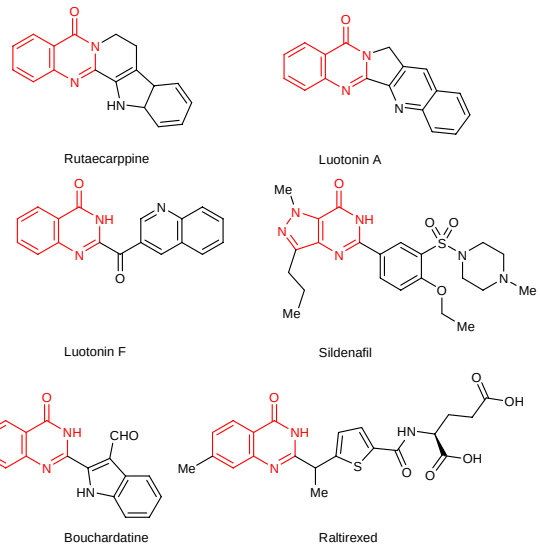
Feng Li,*[a,b] Lei Lu[a] and Juan Ma[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

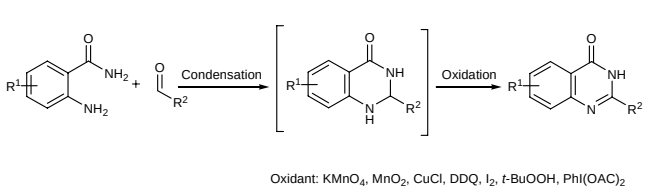
A general and efficient method for the synthesis of quinazolinones *via* acceptorless dehydrogenative condensation of *o*-aminobenzamides with aldehydes in water has been accomplished. In the presence of $[Cp^*Ir(H_2O)_3][OTf]_2$, a variety of desirable products were obtained in high yields with high atom economy under environmentally benign conditions. Notably, this research will facilitate the progress of acceptorless dehydrogenative reactions in water catalyzed by water-soluble organometallic complexes.

Introduction

Quinazolinones represent a class of privileged scaffolds that occur in approximately 150 naturally occuring alkaloids, such as Rutaecarppine, Luotonin A, Luotonin F, Sildenafil, Bouchardatine and Raltirexed (Scheme 1).[1] They exhibit also a wide range of biological and pharmacological activities, including antibacterial,[2] antifungal,[3] antiviral,[4] antiinflammatory,[5] anticonvulsant,[6] antimalarial[7] and anticancer properties.[8] Although numerous methods have been developed,[9] the most classical and general protocols for the synthesis of quinazolinones are still through the condensation between *o*-aminobenzamides and aldehydes followed by the oxidation of the resulting



Scheme 1 Selected examples of quinazolinones as scaffolds of naturally occuring alkaloids.



Scheme 2 Classical and general methods for the synthesis of quinazolinones.

aminal intermediates (Scheme 2).[10] However, these procedures suffer from the use of stoichiometric or excess amount of toxic and/or harardous oxidants, such as $KMnO_4$,[10a] MnO_2,[10b] CuCl,[10c] DDQ,[10d] I_2,[10e] *t*-BuOOH[10f] and $PhI(OAc)_2$,[10g] and the generation of a large amount of harmful byproducts. In 2012, Mulakayala, Oruganti and co-workers reported the synthesis of quinazolinones from *o*-aminobenzamides with aldehydes in the presence of $InCl_3$ (10 mol%) without additional oxidant and oxygen gas may work as the oxidant.[11] In addition, above procedures were generally performed in organic solvents, which might cause the environmental pollution.

In recent years, transition-metal-catalyzed acceptorless dehydrogenative oxidation with the liberation of hydrogen gas has attracted much attention because it represent a clean and atom ecomomical strategy instead of traditional oxidation reactions.[12] The liberated hydrogen gas is also regarded as one of the most promising energies in the future.[13] Significant advances include dehydrogenative oxidation of alcohols,[14] nitrogen-containing heterocycles,[15] amines to nitriles,[16] C−C single bonds adjacent to functional groups to form *α,β*-unsaturated compounds.[17] In the other hand, the development of organic synthesis in water is becoming increasingly important because water is cheap, safe and environmentally benign solvent compared with organic solvents.[18] Despite these advances, acceptorless dehydrogenative oxidation in water catalyzed by water-soluble organometallic

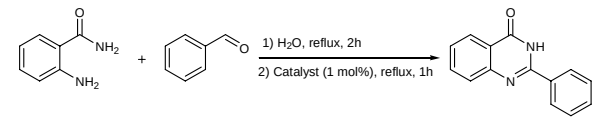
complexes remains less explored. Untill recently, Fujita, Yamaguchi and co-workers demonstrated the dehydrogenative oxidation of alcohols to carbonyl compounds and dehydrogenative lactonization of diols in water catalyzed by a water-soluble bifuncational iridium complex [Cp*Ir(6,6'-$(OH)_2$bpy)(H_2O)][OTf]$_2$ (Cp* = η^5-pentamethylcyclopentadienyl, bpy = 2,2'-bipyridine).[19] From both synthetic and environmental point of views, the development of efficient homogeneous catalytic system for the acceptorless dehydrogenative oxidation of nitrogen-containing heterocycles in water is apparently highly desirable.

We have reported a series of iridium-catalyzed C-N and C-C bond-forming reactions based on the activation of alcohols as electrophiles.[20] In 2014, we demonstrated the rearrangement of aldoximes to amides[21a] and the *N*-alkylation of sulfonamides with alcohols to *N*-alkylated sulfonamides[21b] in water catalyzed by water-soluble iridium complexes. As part of our continuing interest in the development of iridium-catalyzed reactions in water, we herein wish to report the acceptorless dehydrogenative condensation of *o*-aminobenzamides with aldehydes to quinazolinones in water catalyzed by a water-soluble iridium complex.

Results and discussion

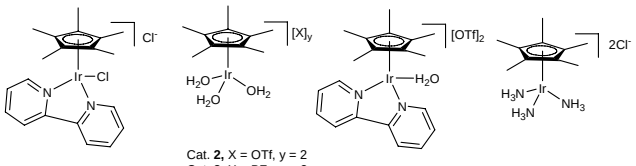
Our initial investigation focused on the reaction of *o*-aminobenzamide (**1a**) with benzaldehyde (**2a**) in water. As shown in Table 1, several different types of water-soluble Cp*Ir complexes were assayed for their catalytic ability to this model reaction. In a typical procedure, the reaction of **1a** and **2a** was refluxed in water for 2 h and the mixture of reaction continued to be refluxed for 1 h when a catalyst (1 mol%) was added. In the presence of a cationic iridium complex [Cp*Ir(bpy)Cl]Cl (bpy = 2,2'-bipyridine) (Cat. **1**), the reaction afforded the desired product **3aa** in 83% yield (Table 1, entry 1). When Cp*Ir complexes bearing more aqua ligands [Cp*Ir$(H_2O)_3$][OTf]$_2$ (Cat. **2**),

Table 1 Dehydrogenative condensation of *o*-aminobenzamide (**1a**) with benzaldehyde (**2a**) under various conditions. [a]



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

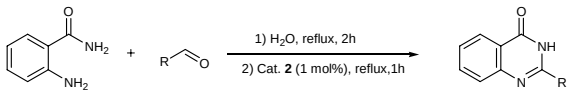
Entry	Catalyst	Yield (%)[b]
1	Cat.**1**	83
2	**Cat.2**	**89**
3	Cat.**3**	80
4	Cat.**4**	82
5	Cat.**5**	30
6	Cat.**6**	85



Cat. **1** Cat. **2,** X = OTf, y = 2; Cat. **3,** X = BF_4, y = 2; Cat. **4,** X = SO_4, y = 1 Cat. **5** Cat .**6**

[a] Reaction conditions: 1) **1a** (0.5 mmol), **2a** (0.5 mmol), H_2O (1 mL), reflux, 2 h; 2) Catalyst (1 mol%), reflux, 1 h. [b] Isolated yield.

Table 2 Dehydrogenative condensation of *o*-aminobenzamide (**1a**) with various aldehydes (**2**) in water.[a]



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

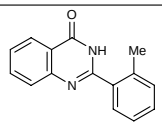
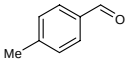
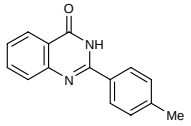
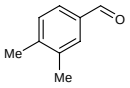
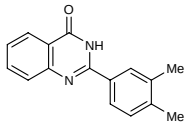
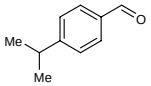
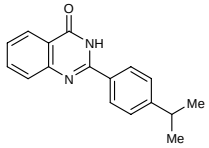
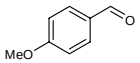
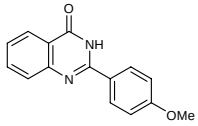
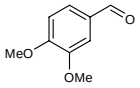
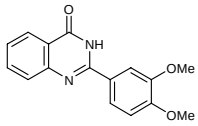
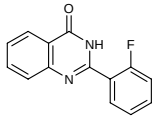
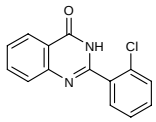
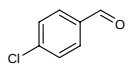
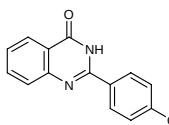
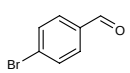
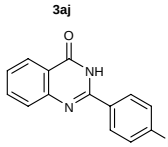
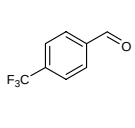
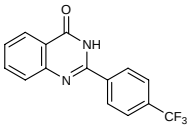
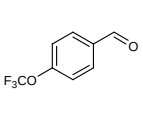
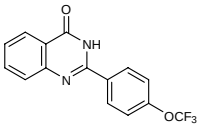
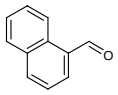
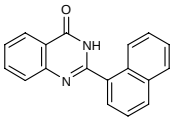
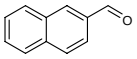
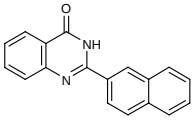
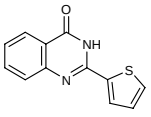
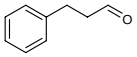
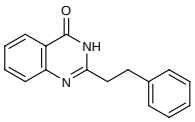
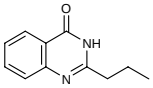
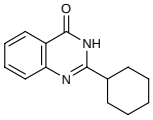
Entry	Aldehyde	Product	Yield (%)[b]
1	 **2b**	 **3ab**	87
2	 **2c**	 **3ac**	85
3	 **2d**	 **3ad**	86
4	 **2e**	 **3ae**	82
5	 **2f**	 **3af**	91
6	 **2g**	 **3ag**	86
7	 **2h**	 **3ah**	78
8	 **2i**	 **3ai**	82
9	 **2j**	 **3aj**	87
10	 **2k**	 **3ak**	78

Table 2 (Continued)

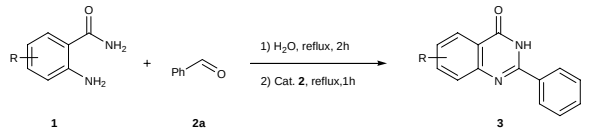
Entry	Aldehyde	Product	Yield (%)[b]
11	 **2l**	 **3al**	81
12	 **2m**	 **3am**	78
13	 **2n**	 **3an**	85
14	 **2o**	 **3ao**	81
15	 **2p**	 **3ap**	77
16	 **2q**	 **3aq**	84
17	 **2r**	 **3ar**	81
18	 **2s**	 **3as**	81

[a] Reaction conditions: 1) **1a** (0.5 mmol), **2** (0.5 mmol), H_2O (1 mL), reflux, 2h; 2) Cat. **2** (1 mol%), reflux, 1 h. [b] Isolated yield.

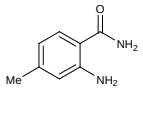
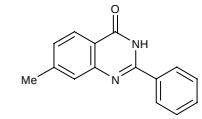
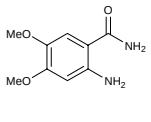
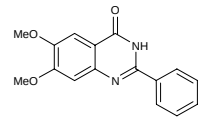
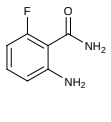
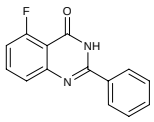
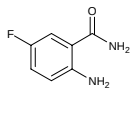
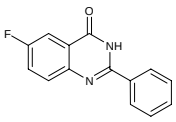
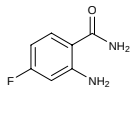
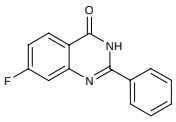
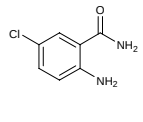
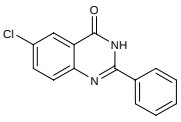
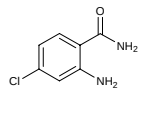
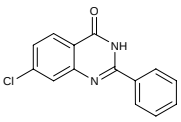
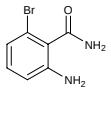
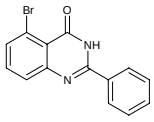
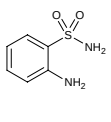
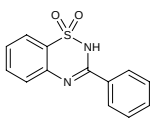
$[Cp^*Ir(H_2O)_3][BF_4]_2$ (Cat. **3**) and $[Cp^*Ir(H_2O)_3][SO_4]$ (Cat. **4**), were used as a catalyst, the product **3aa** was obtained in 80-89% yields (Table 1, entries 2-4). Using $[Cp^*Ir(bpy)(H_2O)][OTf]_2$ (Cat. **5**) as an alternative catalyst, this reaction gave the product **3aa** in only 30% yields (Table 1, entry 5). The Cp*Ir complex bearing three ammonia ligands $[Cp^*Ir(NH_3)_3][Cl]_2$ (Cat. **6**) was also screened, and the desired product **3aa** could be obtained in 85% yield (Table 1, entry 6). Apparently, apart from Cat. **5**, other tested catalysts exhibited highly catalytic activities. Among them, $[Cp^*Ir(H_2O)_3][OTf]_2$ is the most effective for this transformation.

Having established the optimal reaction conditions (Table 1, entry 2), the scope of reaction with respect to aldehydes was

Table 3 Dehydrogenative condensation of a series of *o*-aminobenzamides (**1**) with benzaldehyde (**2a**) in water.[a]



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

Entry	*o*-Aminobenzamides	Product	Yield (%)[b]
1	 **1b**	 **3ba**	81
2	 **1c**	 **3ca**	78
3	 **1d**	 **3da**	84
4	 **1e**	 **3ea**	81
5	 **1f**	 **3fa**	75
6	 **1g**	 **3ga**	84
7	 **1h**	 **3ha**	85
8	 **1i**	 **3ia**	75
9	 **1j**	 **3ja**	26[c]

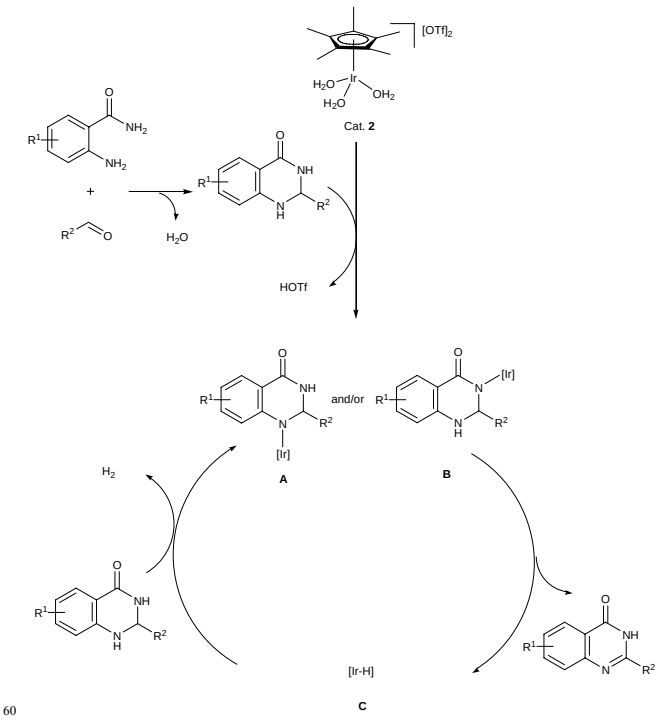
[a] Reaction conditions: 1) **1** (0.5 mmol), **2a** (0.5 mmol), H_2O (1 mL), reflux, 2h; 2) Cat. **2** (1 mol%), reflux, 1 h. [b] Isolated yield. [c] NMR yield

investigated and these results are shown in Table 2. Reactions with benzaldehyde bearing one or two electron-donating groups, such as methyl (**2b-c**), dimethyl (**2d**), isopropyl (**2e**), methoxy (**2f**) and dimethoxy **(2g**), gave the corresponding products **3ab-3ag** in 82-91% yields (Table 2, entries 1-6). Similarly, benzaldehydes bearing a halogen atom, such as fluoro (**2h**), chloro (**2i-j**) and bromo (**2k**), were converted to the desired products **3ah-3ak** in 78-87% yield (Table 2, entries 7-10). Benzaldehydes bearing a strong electron-withdrawing group, such as trifluoromethyl (**2l)** and trifluoromethoxy (**2m**), were also proven to be suitable substrates and the desired products **3al** and **3am** could be obtained in 81% and 78% yields, respectively (Table 2, entries 11-12). Furthermore, highly catalytic activities were found in transformations of 1-naphthaldehyde (**2n**), 2-naphthaldehyde (**2o**) and 2-thiophenaldehyde (**2p**) to the corresponding products **3an-3ap** (Table 2, entries 13-15). In the case of aliphatic aldehydes, such as phenylpropyl aldehyde (**2q**), butyraldehyde (**2r**) and cyclohexanecarbaldehyde (**2s**), the desired products **3aq-3as** could be obtained in 81-84% yields as well (Table 2, entries 16-18).

To further expand the scope of reaction, transformations with respect to *o*-aminobenzamides was then examined. Reactions of *o*-aminobenzamides bearing one or two electron-donating groups, such as methyl (**1b**) and dimethoxy (**1c**), gave the corresponding products **3ba** and **3ca** in 81% and 78% yields, respectively (Table 3, entries 1-2). When *o*-aminobenzamides bearing an electron-withdrawing group, such as fluoro (**1d-f**), chloro (**1g-h**) and bromo (**1i**), were used as substrates, the desired products **3da-3ia** were obtained in 75%-85% yields (Table 3, entries 3-8). The catalytic system was also applied to *o*-aminobenzenesulfonamide (**1j**), giving the corresponding product **3ja** in only 26% NMR yield (Table 3, entry 9).

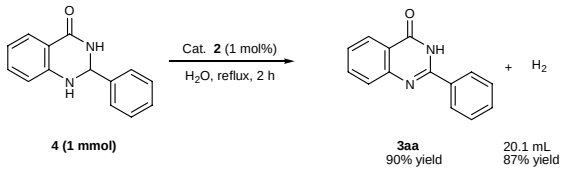
A possible mechanism was proposed to account for the acceptorless dehydrogenative condensation of *o*-aminobenzamides with aldehydes to quinazolinones in water (Scheme 3). The initial step of the reaction involved the formation of 2,3-dihydroquinazolinones *via* the condensation between *o*-aminobenzamides and aldehydes. Furthermore, the reaction of the resulting 2,3-dihydroquinazolinones with Cat. **2** afforded an amido iridium species **A** and/or **B**. Accompanied by the *ß*-hydrogen elimination of species **A** and/or **B**, the hydrido iridium species **C** were generated and quinazolinones were released as products.[22] Finally, hydrogen gas was liberated and catalytic active species **A** and/or **B** were regenerated through the reaction of iridium hydride species **C** and 2,3-dihydroquinazolinones.

To support the proposed mechanism, the confirmation of the liberation of hydrgogen gas in the process of the acceptorless dehydrogenative oxidation of 2-phenyl-2,3-dihydroquinazolin-4(*1H*)-one (**4**), which is synthesized *via* the condensation between **1a** and **2a**, was first undertaken (Scheme 4). In the presence of Cat. **2** (1 mo%), the reaction was carried out for 2 h in water to give the product **3aa** in 90% yield accompined by the generation of 20.1 mL of gas by water displacement. The collected gas was confirmed to be hydrogen gas by GC analysis and the yield of gas is calculated to be 87%. In addition, a peak (δ -15.6) was observed from ^{1}H NMR spectrum of the substoichiometric reaction of Cat. **2** with **4** (4 equiv) in $CDCl_3$ at ambient



Scheme 3 Proposed reaction mechanism.

temperature. It was speculated to be a characteristic signal of [Ir-H] (species **C**)[23] (see: ESI). These experimental results supported the proposed mechanism shown in Scheme 3.



Scheme 4 Confirmation of the liberation of hydrogen gas.

Conclusion

We have demonstrated a general and efficient method for the synthesis of quinazolinones *via* the acceptorless dehyderogenative condensation of *o*-aminobenzamides with aldehydes in water. In the presence of $[Cp^*Ir(H_2O)_3][OTf]_2$, a variety of desirable products were obtained in high yields with high atom economy under environmentally benign conditions Notably, this research will facilitate the progress of acceptorless dehydrogenative reactions in water catalyzed by water-soluble organometallic complexes.

Experimental Section

Experimental Details. High-resolution mass spectra (HRMS) were obtained on a HPLC-Q-Tof MS(Micro) spectrometer and are reported as m/z (relative intensity). Accurate masses are reported for the deprotonated molecular ion $[M-H]^-$. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 500 MHz using a 500 spectrometer. Chemical shifts are reported

in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane or ppm relative to the center of the singlet at 7.26 ppm for $CDCl_3$ and 2.50 ppm for DMSO-d_6. Coupling constants J values are reported in Hertz (Hz), and the splitting patterns were designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; b, broad. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 125 MHz using a 500 spectrometer. Chemical shifts are reported in delta (δ) units, ppm relative to the center of the triplet at 77.0 ppm for $CDCl_3$ and 39.5 ppm for DMSO-d_6. ^{13}C NMR spectra were routinely run with broadband decoupling.

[Cp*Ir(bpy)Cl]Cl (Cat. **1**),[24] $[Cp^*Ir(H_2O)_3][OTf]_2$ (Cat. **2**),[25] $[Cp^*Ir(H_2O)_3][BF_4]_2$ (Cat. **3**),[25] $[Cp^*Ir(H_2O)][SO_4]$ (Cat. **4**),[25] $[Cp^*Ir(bpy)(H_2O)][OTf]_2$ (Cat. **5**)[26] and $[Cp^*Ir(NH_3)_3][Cl]_2$ (Cat. **6**)[27] were synthesized according to previous reports.

General procedure for acceptorless dehydrogenative condensation of *o*-aminobenzamides with aldehydes to quinazolinones in water catalyzed by a water-soluble iridium complex $[Cp^*Ir(H_2O)_3][OTf]_2$. In a round-bottomed flask with a condenser tube, *2*-aminobenzamide **1** (0.5 mmol), aldehyde **2** (0.5 mmol) and water (1 mL) were placed under an air atmosphere, and the reaction mixture was heated under reflux in an oil bath for 2 h. The reaction mixture was further heated under reflux for 1 h when Cat. **2** (0.005 mmol, 1 mol%) was added and the mixture was then cooled to ambient temperature, concentrated in *vacuo* and purified by flash column chromatography with hexanes/ethyl acetate to afford the corresponding products.

2-Phenylquinazolin-4(3*H*)-one (3aa).[9i] White solid, 90% yield (100 mg); mp 237-238 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 11.58 (br s, 1H), 8.34 (d, J = 7.8 Hz, 1H), 8.26 (dd, J = 3.1 Hz and 6.7 Hz, 2H), 7.80-7.85 (m, 2H), 7.59-7.60 (m, 3H), 7.51(t, J = 7.3 Hz, 1H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 163.9, 151.8, 149.5, 134.9, 132.8, 131.6, 129.0, 128.0, 127.4, 126.7, 126.3, 120.9.

2-(*o*-Tolyl)quinazolin-4(3*H*)-one (3ab).[9i] White solid, 87% yield (102 mg); mp 222-224 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.44 (br s), 8.16 (d, J = 5.9 Hz), 7.84 (s, 1H), 7.69 (d, J = 6.2 Hz, 1H), 7.50-7.54 (m, 2H), 7.43 (s, 1H), 7.34 (s, 2H), 2.38 (s, 3H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 161.8, 154.3, 148.7, 136.1, 134.4, 134.2, 130.5, 129.8, 129.1, 127.3, 126.6, 125.8, 125.7, 121.0, 19.5.

2-(*p*-Tolyl)quinazolin-4(3*H*)-one (3ac).[9i] white solid, 85% yield (100 mg); mp 242-244 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 11.48 (br s, 1H), 8.33 (d, J = 7.8 Hz, 1H), 8.15 (d, J = 7.8 Hz, 2H), 7.78-7.83 (m, 2H), 7.49 (t, J = 7.0 Hz, 1H), 7.38 (d, J = 7.8 Hz, 2H), 2.46 (s, 3H); ^{13}C {^1H} NMR (125 MHz, $CDCl_3$) δ 164.0, 151.8, 149.6, 142.1, 134.8, 130.0, 129.7, 127.9, 127.4, 126.5, 126.3, 120.8, 21.5.

2-(3,4-dimethylphenyl)quinazolin-4(3*H*)-one (3ad).[9b] White solid, 86% yield (108 mg); mp 239-242 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.40 (br s, 1H), 8.14 (d, J = 7.5 Hz, 1H), 8.01 (s, 1H), 7.92 (d, J = 7.2 Hz, 1H), 7.82 (t, J = 6.9 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.50 (t, J = 7.0 Hz, 1H), 7.30 (d, J = 7.4 Hz, 1H), 2.31 (s, 3H), 2.30 (s, 3H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 162.2, 152.3, 148.8, 140.2, 136.6, 134.5, 130.1, 129.6, 128.6, 127.3, 126.3, 125.8, 125.1, 120.8, 19.4, 19.3.

2-(4-isopropylphenyl)quinazolin-4(3*H*)-one (3ae).[9i] White solid, 82% yield (108 mg); mp 210-212 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.48 (br s, 1H), 8.12-8.15 (m, 3H), 7.83 (t, J = 7.5 Hz, 1H), 7.73 (d, J = 7.7 Hz, 1H), 7.51 (t, J = 7.0 Hz, 1H), 7.42 (d, J = 7.3 Hz, 2H), 2.96-2.99 (m, 1H), 1.24 (d, J = 6.0 Hz, 6H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 162.3, 152.2, 152.1, 148.8, 134.5, 130.3, 127.8, 127.4, 126.5, 126.4, 125.8, 120.9, 33.4, 23.6.

2-(4-methoxyphenyl)quinazolin-4(3*H*)-one (3af).[9d] White solid, 91% yield (115 mg); mp 246-248 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.41 (br s, 1H), 8.19 (d, J = 8.4 Hz, 2H), 8.13 (d, J = 7.6 Hz, 1H), 7.81 (t, J = 7.3 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.3 Hz, 1H), 7.09 (d, J = 8.3 Hz, 2H), 3.85 (s, 3H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 162.3, 161.8, 151.8, 148.9, 134.5, 129.4, 127.3, 126.1, 125.8, 124.8, 120.7, 113.9, 55.4.

2-(3,4-dimethoxyphenyl)quinazolin-4(3*H*)-one (3ag).[28] White solid, 86% yield (121 mg); mp 242-243 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.44 (br s, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.81-7.83 (m, 2H), 7.72 (d, J = 8.1 Hz, 1H), 7.49 (t, J = 7.4 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 162.3, 151.8, 151.6, 148.9, 148.5, 134.5, 127.3, 126.1, 125.8, 124.7, 121.1, 120.7, 111.3, 110.7, 55.7 (2C, overlap).

2-(2-fluorophenyl)quinazolin-4(3*H*)-one (3ah).[29] White solid, 78% yield (94 mg); mp 162-164 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.58 (br s, 1H), 8.17 (d, J = 7.8 Hz, 1H), 7.86 (t, J = 7.4 Hz, 1H), 7.79 (t, J = 7.1 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.63 (q, J = 6.6 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.36-7.41 (m, 2H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 161.5, 159.6 (d, $J_{C\text{-}F}$ = 249.1 Hz), 149.9, 148.7, 134.6, 132.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 131.0, 127.5, 127.0, 125.8, 124.6, 122.3 (d, $J_{C\text{-}F}$ = 12.7 Hz), 121.1, 116.1 (d, $J_{C\text{-}F}$ = 21.0 Hz).

2-(2-chlorophenyl)quinazolin-4(3*H*)-one (3ai).[9k] White solid, 82% yield (105 mg); mp 185-186 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.63 (br s, 1H), 8.18 (d, J = 7.4 Hz, 1H), 7.86 (t, J = 6.9 Hz, 1H), 7.71 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 6.9 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.58 (t, J = 7.4 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 161.4, 152.2, 148.5, 134.5, 133.8, 131.6, 131.5, 130.8, 129.6, 127.4, 127.2, 127.0, 125.8, 121.2.

2-(4-chlorophenyl)quinazolin-4(3*H*)-one (3aj).[9i] White solid, 87% yield (112 mg); mp 300-302 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.59 (br s, 1H), 8.20 (d, J = 7.6 Hz, 2H), 8.15 (d, J = 7.1 Hz, 1H), 7.84 (t, J = 6.4 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 6.6 Hz, 1H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 162.1, 151.3, 148.5, 136.3, 134.6, 131.5, 129.6, 128.6, 127.5, 126.7, 125.8, 121.0.

2-(4-bromophenyl)quinazolin-4(3*H*)-one (3ak).[30] White solid, 78% yield (118 mg); mp 296-298 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 12.60 (s, br, 1H), 8.12-8.16 (m, 3H), 7.84 (t, J = 7.1 Hz, 1H), 7.74-7.77 (m, 3H), 7.53 (t, J = 7.1 Hz, 1H); ^{13}C {^1H} NMR (125 MHz, DMSO-d_6) δ 162.1, 151.5, 148.5, 134.6, 131.9, 131.6, 129.8, 127.5, 126.7, 125.8, 125.2, 121.0.

2-(4-(trifluoromethyl)phenyl)quinazolin-4(3*H*)-one (3al).[9i] White solid, 81% yield (117 mg); mp 308-310 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.75 (br s, 1H), 8.37 (d, J = 7.8 Hz, 2H), 8.18 (d, J = 7.5 Hz, 1H), 7.93 (d, J = 7.8 Hz, 2H), 7.87 (t, J = 7.4 Hz, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 162.1, 151.1, 148.4, 136.6, 134.7, 131.1 (q, $J_{C\text{-}F}$ = 31.9 Hz), 128.7, 127.6, 127.0, 125.8, 125.4 (q, $J_{C\text{-}F}$ = 3.0 Hz), 123.9 (q, $J_{C\text{-}F}$ = 270.9 Hz).

2-(4-(trifluoromethoxy)phenyl)quinazolin-4(3*H*)-one (3am).[10f] White solid, 76% yield (120 mg); mp 268-271 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.65 (br s, 1H), 8.30 (d, J = 8.7 Hz, 2H), 8.16 (d, J = 7.8 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.53-7.56 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 162.1, 151.1, 148.4, 136.6, 134.6, 131.1 (q, $J_{C\text{-}F}$ = 31.9 Hz), 128.7, 127.6, 127.0, 125.8, 125.4, 123.9 (d, $J_{C\text{-}F}$ = 255.8 Hz), 121.1;

2-(naphthalen-1-yl)quinazolin-4(3*H*)-one (3an).[9d] White solid, 85% yield (102 mg); mp 287-288 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.67 (br s, 1H), 8.22 (d, J = 7.7 Hz, 1H), 8.17 (d, J = 7.6 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 7.3 Hz, 1H), 7.87 (t, J = 7.2 Hz, 1H), 7.80 (d, J = 6.7 Hz, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.57-7.62 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.8, 153.6, 148.7, 134.5, 133.1, 131.7, 130.3, 130.2, 128.3, 127.6, 127.4, 127.0, 126.7, 126.3, 125.8, 125.2, 125.0, 121.2.

2-(naphthalen-2-yl)quinazolin-4(3*H*)-one (3ao).[9i] White solid, 81% yield (110 mg); mp 276-278 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.67 (br s, 1H), 8.82 (s, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 7.6 Hz, 1H), 8.07 (t, J = 7.1 Hz, 1H), 8.02 (d, J = 7.2 Hz, 1H), 7.86 (t, J = 7.2 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.61-7.67 (m, 2H), 7.55 (t, J = 7.2 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 162.2, 152.2, 148.8, 134.59, 134.1, 132.3, 129.9, 128.9, 128.1, 128.1, 127.9, 127.6, 127.5, 126.9, 126.6, 125.9, 124.5, 121.0.

2-(thiophen-2-yl)quinazolin-4(3*H*)-one (3ap).[9d] White solid, 77% yield (88 mg); mp 276-277 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.66 (br s, 1H), 8.82 (s, 1H), 8.12 (d, J = 7.1 Hz, 1H), 7.87 (d, J = 3.2 Hz, 1H), 7.80 (t, J = 7.3 Hz, 1H), 7.65 (d, J = 7.3 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 7.24 (s, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.8, 148.6, 147.8, 137.4, 134.6, 132.1, 129.4, 128.5, 126.9, 126.3, 126.0, 120.9.

2-phenethylquinazolin-4(3*H*)-one (3aq).[31] White solid, 84% yield (105 mg); mp 209-211 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.26 (br s, 1H), 8.08 (d, J = 7.1 Hz, 1H), 7.78 (t, J = 6.9 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.1 Hz, 1H), 7.28 (s, 4H), 7.19 (s, 1H), 3.05 (t, J = 7.5 Hz, 2H), 2.89 (t, J = 7.6 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.7, 156.5, 148.8, 140.7, 134.3, 128.3, 126.8, 126.0, 126.0, 125. 7, 120.8, 36.3, 32.4.

2-propylquinazolin-4(3*H*)-one (3ar).[9a] White solid, 81% yield (76 mg); mp 198-199 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.16 (br s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.76 (t, J = 7.4 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 2.57 (t, J = 7.5 Hz, 2H), 1.71-1.78 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.8, 157.3, 148.9, 134.2, 126.8, 125.9, 125.6, 120.8, 36.3, 20.2, 13.4.

2-cyclohexylquinazolin-4(3*H*)-one (3as).[9b] White solid, 81% yield (92 mg), mp 229-230 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.08 (br s, 1H), 8.07 (d, J = 7.9 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.59 (d, J = 8.2 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 2.57 (tt, J = 11.8 Hz and J = 3.3 Hz, 1H, CH), 1.78-1.91 (m, 4H), 1.54-1.69 (m, 3H), 1.18-1.34 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.9, 160.7, 148.9, 134.2, 126.9, 125.8, 125.6, 120.9, 42.8, 30.2, 25.5, 25.3.

7-methyl-2-phenylquinazolin-4(3*H*)-one (3ba).[32] White solid, 81% yield (96 mg), mp 239-240 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.45 (br s, 1H), 8.17 (d, J = 7.3 Hz, 2H), 8.04 (d, J = 8.0 Hz, 1H), 7.53-7.60 (m, 4H), 7.34 (d, J = 8.0 Hz, 1H), 2.47 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 162.1, 152.3, 148.8, 145.0, 132.8, 131.3, 128.5, 128.0, 127.7, 127.0, 125.7, 118.6, 21.3.

6,7-dimethoxy-2-phenylquinazolin-4(3*H*)-one (3ca).[32] White solid, 78% yield (111 mg); mp 281-284 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.40 (br s, 1H), 8.16 (d, J = 7.3 Hz, 2H), 7.48-7.55 (m, 4H), 7.21 (s, 1H), 3.93 (s, 3H), 3.89 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.5, 154.7, 150.8, 148.6, 144.8, 132.8, 131.0, 128.5, 127.4, 114.0, 108.2, 105.0, 55.9, 55.7.

5-fluoro-2-phenylquinazolin-4(3*H*)-one (3da).[32] ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.55 (s, br, 1H), 8.17 (d, J = 6.8 Hz, 2H), 7.82-7.78 (m, 1H), 7.62-7.55 (m, 4H), 7.26 (d, J = 9.1 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.6, 159.5 (d, $J_{C\text{-}F}$ = 9.1 Hz), 153.3, 150.8, 135.1 (d, $J_{C\text{-}F}$ = 9.1 Hz), 132.2, 131.6, 128.6, 127.8, 123.5, 112.9 (d, $J_{C\text{-}F}$ = 20.2 Hz), 110.4.

6-fluoro-2-phenylquinazolin-4(3*H*)-one (3ea).[33] Gray solid, 81% yield (97 mg); mp 277-278 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.69 (s, br, 1H), 8.25-8.23 (m, 2H), 7.76-7.69 (m, 2H), 7.58 (dt, J = 8.7 Hz and 2.8 Hz, 1H), 7.50-7.47 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 165.0, 159.2 (d, $J_{C\text{-}F}$ = 241.9 Hz), 155.2, 146.7, 135.5, 130.3, 129.5 (d, $J_{C\text{-}F}$ = 7.7 Hz), 128.2, 127.7, 122.3 (d, $J_{C\text{-}F}$ = 7.5 Hz), 121.6, 121.4

7-fluoro-2-phenylquinazolin-4(3*H*)-one (3fa).[9i] Gray solid, 75% yield (113 mg); mp 252-253 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.60 (s, br, 1H), 8.21-8.14 (m, 3H), 8.15 (d, J = 7.30 Hz, 2H), 7.60 (t, J = 6.85 Hz, 1H), 7.55 (t, J = 7.13 Hz, 2H), 7.49 (d, J = 9.60 Hz, 1H), 7.37 (t, J = 8.03 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 165.9 (d, $J_{C\text{-}F}$ = 250.0 Hz), 161.7, 153.9, 151.0 (d, $J_{C\text{-}F}$ = 12.5 Hz), 132.5, 131.7, 129.0 (d, $J_{C\text{-}F}$ = 10.0 Hz), 128.7, 128.0, 118.0, 115.2 (d, $J_{C\text{-}F}$ = 23.8 Hz), 112.4 (d, $J_{C\text{-}F}$ = 21.2 Hz).

6-chloro-2-phenylquinazolin-4(3*H*)-one (3ga).[9a] White solid, 84% yield (107 mg); mp 287-289 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.71 (br s, 1H), 8.17 (d, J = 7.1 Hz, 2H), 8.09 (s, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.6 Hz, 1H), 7.54-7.62 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.3, 152.8, 147.4, 134.6, 132.4, 131.5, 130.7, 129.7, 128.6, 127.8, 124.8, 122.2.

7-chloro-2-phenylquinazolin-4(3*H*)-one (3ha).[9i] White solid, 85% yield (109 mg); mp 276-288 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.67 (br s, 1H), 8.17 (d, J = 7.5 Hz, 2H), 8.14 (d, J = 8.5 Hz, 1H), 7.79 (m, 1H), 7.61 (t, J = 7.1 Hz, 1H), 7.54-7.57 (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 161.3, 152.8,

147.4, 134.6, 132.4, 131.5, 130.7, 129.7, 128.6, 127.8, 124.8, 122.2.

5-bromo-2-phenylquinazolin-4(*3H*)-one (3ia). White Solid, 75% Yield (113 mg); mp 283-284 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.56 (s, br, 1H), 8.18-8.16 (m, 2H), 7.73 (m, 1H), 7.71 (dd, J = 3.5 Hz and 1.2 Hz, 1H), 7.66-7.59 (m, 2H), 7.55 (tt, J = 7.5 Hz and 1.5 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 160.5, 152.7, 151.1, 134.6, 132.6, 132.1, 131.6, 128.5, 127.8, 127.7, 120.1, 118.8. HRMS-EI (70 eV) m/z cacld for $C_{14}H_8BrN_2O$ [M-H]$^-$ 298.9820, found 298.9827.

3-phenyl-2*H*-benzo[*e*][1,2,4]thiadiazine 1,1−dioxide (3ja).[34] White solid, 26% yield (NMR); mp > 300 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.18 (s, br, 1H), 8.05 (d, J = 7.9 Hz, 2H), 7.86 (d, J = 8.0 Hz, 1H), 7.76-7.69 (m, 2H), 7.65-7.62 (m, 3H), 7.51 (t, J = 7.6 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 154.8, 135.5, 133.1, 132.8, 131.8, 128.8, 128.2, 126.7, 123.3, 121.5, 118.4.

Procedure for the hydrogen evolution experiment (Scheme 4).[35] **4** (1 mmol), Cat. **2** (1 mol %) and H_2O (1 mL) were added to a 5 ml thick walled glass vessel fitted with a side arm and a rubber septum. The vessel was previously degassed three times and placed under a N_2 atmosphere. The vessel was connected to the gas collection apparatus (standard water displacement apparatus, using a graduated cylinder to determine volume), and the entire system was flushed with N_2 for 5 min and allowed to equilibrate for 5 min. The reaction was stirred vigorously at a constant temperature until gas evolution ceased (2 h). The presence of hydrogen in the collected gas was confirmed by GC analysis.

The GC analysis was performed on a gas chromatograph with TCD detector. Injector temprature = 100 °C, column temprature = 50 °C, detector temperature (TCD) = 80 °C, carrier gas = N_2, column flow = 20 mL/min, t = 0.558 min.

The volume of 1 mol of H_2 at 283.15 K, 101810 Pa was calculated according to the van der Waals equation as shown below

$$(p+\frac{n^2a}{V^2})\ (V-nb) = nRT$$

where R = 8.3145 m^3 Pa·mol^{-1}·K^{-1}; T = 283.15 K; p = 101 810 Pa; a = 0.002476 m^6·Pa·mol^{-1}; b = 0.02661 × 10^{-3} m^3·mol^{-1}; thus, V (H_2, 283.15 K, 101 810 Pa) = 23.15 L·mol^{-1}.

The collected volume of gas in this experiment above was 20.1 mL, which corresponds to 0.87 mmol of H_2.

Procedure for the substoichiometric reaction of [Cp*Ir(H_2O)$_3$][OTf]$_2$ with 2-phenyl-2,3-dihydroquinazolin-4(*1H*)-one. Under an atmosphere of nitrogen, Cat. **2** (6.8 mg, 0.01 mmol), **4** (8.9 mg, 0.04 mmol) and $CDCl_3$ (1.0 mL) were placed in a NMR tube. The NMR tube was put into the NMR probe. After 30 min, ^{1}H NMR analysis was performed. The result is shown in Electronic Supplementary Information (ESI).

Acknowledgements

Financial support by National Natural Science Foundation of China (21272115) and the State Key Laboratory of Fine Chemicals (KF1401) is greatly appreciated.

Notes and references

[a] *School of Chemical Engineering, Nanjing University of Science & Technology, Nanjing 210094, P. R. China. Fax: +86-25-84431939; Tel: +86-25-84317316; E-mail: fengli@njust.edu.cn*
[b] *State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116024, P. R. China*

† Electronic Supplementary Information (ESI) available: Copies of the ^{1}H NMR and ^{13}C NMR spectra for all products. See DOI: 10.1039/b000000x/

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