ChemPubSoc Europe

DOI: 10.1002/cctc.201501385

CHEMCATCHEM Full Papers

Quinazolinones from *o*-Aminobenzonitriles by One-Pot Sequential Selective Hydration/Condensation/Acceptorless Dehydrogenation Catalyzed by an Iridium Complex

Wei Zhao,[a] Pengcheng Liu,[a] and Feng Li*[a, b]

A new strategy for the direct synthesis of quinazolinones from *o*-aminobenzonitriles was proposed and accomplished. In the presence of $[Cp^*IrCl_2]_2$ (Cp^* = pentamethylcyclopentadienyl), a variety of desirable products was obtained easily through the one-pot sequential selective hydration/condensation/acceptorless dehydrogenation. This protocol is highly attractive because it uses readily available starting materials, has a high atom efficiency, good to excellent yields, and minimal consumption of chemicals and energy. Notably, this research exhibited new potential for the development of transition-metal-catalyzed one-pot sequential reactions that involve acceptorless dehydrogenation.

Introduction

Quinazolinones are an important class of fused heterocyclic compounds that occur as key scaffolds in many natural alkaloids (Figure 1)[1] and exhibit a broad spectrum of biological properties, such as antibacterial,[2a] antiviral,[2b] and anticancer activities.[2c] Recently, quinazolinones have been utilized as potent inhibitors of nicotinamide phosphoribosyltransferase (Nampt),[3a] microsomal prostaglandin synthase 1 (mPGES 1),[3b] histone deacetylase-6,[3c] and ADP-Ribosyltransferase ARTD3/PARP3.[3d] Although a number of synthetic methods has been developed,[4] most classical and versatile routes to quinazolinones rely on the condensation between *o*-aminobenzamides and aldehydes followed by the oxidation of the resulting aminal intermediates (Scheme 1).[5] However, these procedures require the use of stoichiometric amounts or a large excess of environmentally harmful oxidants, such as $KMnO_4$,[5a] MnO_2,[5b] I_2,[5c] 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[5d] $PhI(OAc)_2$,[5e] and *t*BuOOH.[5f] Moreover, only a limited number of *o*-aminobenzamides is available commercially, and most of them are typically prepared by the hydration of *o*-aminobenzonitriles in the presence of a strong acid or base under harsh conditions.[6] From the standpoint of sustainable chemistry, the development of a new strategy for the synthesis of quinazolinones from easily available starting materials under environmentally benign conditions is highly desirable.

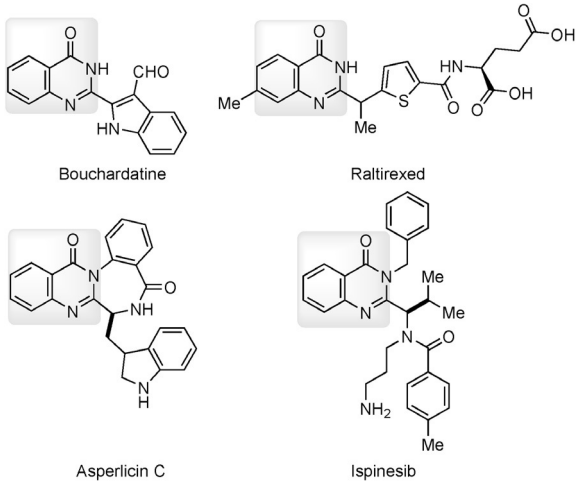
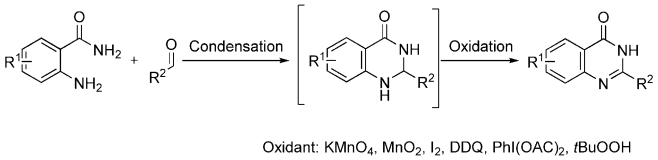


Figure 1. Selected examples of quinazolinones as key scaffolds of natural alkaloids.



Scheme 1. Classical and versatile routes for the synthesis of quinazolinones.

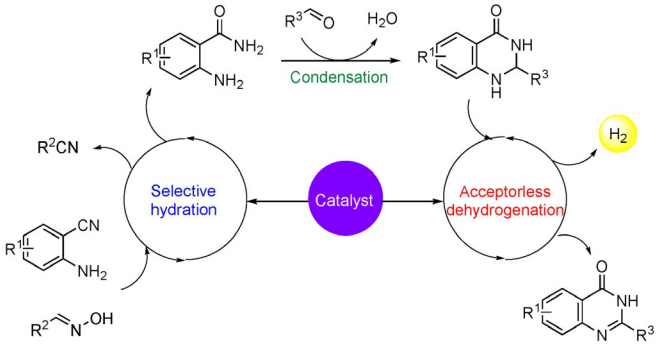
Recently, much attention has been paid to the development of acceptorless dehydrogenation reactions accompanied by the liberation of hydrogen gas without the use of any oxidants,[7] such as the acceptorless dehydrogenation of alcohols[8] and N-containing heterocycles.[9] Such methodologies provide the clearest and most atom-economical processes as alternatives to traditional oxidation reactions.

[a] *W. Zhao, P. Liu, Dr. F. Li*
School of Chemical Engineering
Nanjing University of Science & Technology
200 Xiaolingwei Street, Nanjing 210094 (P.R. China)
Fax: (+86) 25-84431939
E-mail: fengli@njust.edu.cn

[b] *Dr. F. Li*
State Key Laboratory of Fine Chemicals
Dalian University of Technology
2 Lingong Road, Dalian 116024 (P.R. China)

Supporting Information for this article can be found under http://dx.doi.org/10.1002/cctc.201501385.

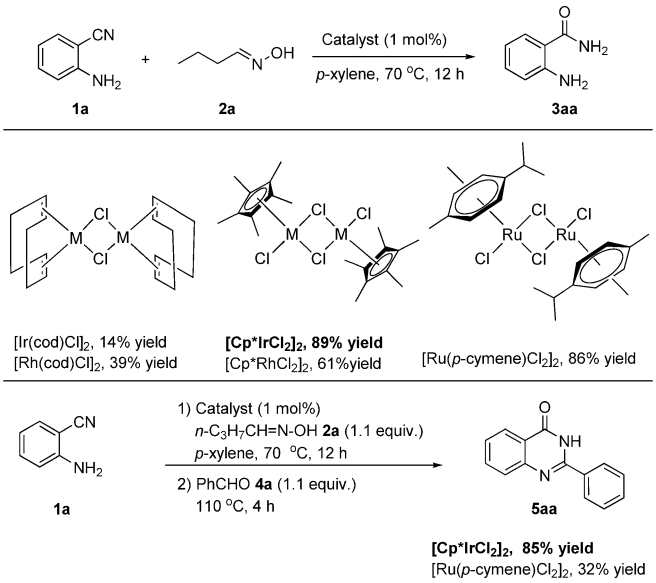
We have reported a series of environmentally friendly reactions based on "hydrogen autotransfer" or "dehydrogenation" catalyzed by Ir[10] and Rh complexes.[11] As part of our continuing effort in this field, we are interested in the exploration of the direct synthesis of quinazolinones from commercially available *o*-aminobenzonitriles by one-pot sequential selective hydration/condensation/acceptorless dehydrogenation (Scheme 2). In the presence of a single catalyst, *o*-aminobenzonitriles undergo selective hydration with aldoximes as water surrogates to form *o*-aminobenzamides, which undergo condensation with aldehydes to afford dihydroquinazolinones. These were further converted to quinazolinones through acceptorless dehydrogenation. Transition metal salts or complexes based on Rh,[12a] Pd,[12b] In,[12c] Cu,[12d–e] Ni,[12f] and Ir[10f] have been utilized as efficient catalysts for the hydration of nitriles with aldoximes to amides under neutral reaction conditions. However, these procedures generally required high catalyst loading (5–10 mol%) and/or an excess of aldoximes (2–5 equiv.). Moreover, only one example was presented for the hydration of *o*-aminobenzonitrile, and the desirable *o*-aminobenzamide was obtained in only 71% yield with 25% of an unidentified byproduct.[12d]



Scheme 2. Proposed strategy for the synthesis of quinazolinones from *o*-aminobenzonitriles.

Results and Discussion

To explore the feasibility of the above proposal, some commercially available transition metal complexes, which include $[Ir(cod)Cl]_2$ (cod = 1,5-cyclooctadienyl), $[Cp^*IrCl_2]_2$ (Cp^* = pentamethylcyclopentadienyl), $[Rh(cod)Cl]_2$, $[Cp^*RhCl_2]_2$, and $[Ru(p\text{-cymene})Cl_2]_2$, were screened initially for their ability to catalyze the selective hydration of *o*-aminobenzonitrile with an aldoxime. In the presence of a catalyst (1 mol%), the reaction of *o*-aminobenzonitrile (**1a**) with *n*-butylaldoxime (**2a**) (1.1 equiv.) was performed in *p*-xylene at 70 °C for 12 h. $[Cp^*IrCl_2]_2$ and $[Ru(p\text{-cymene})Cl_2]_2$ exhibited high catalytic activities to afford 2-aminobenzamide (**3aa**) as the sole product in 89 and 86% yields, respectively (Scheme 3).[13] Furthermore, $[Cp^*IrCl_2]_2$ was selected as the catalyst for the one-pot sequential selective hydration/condensation/acceptorless dehydrogenation. After **1a** was converted completely to **3a**, benzylaldehyde (**4a**; 1.1 equiv.) was added, and the reaction proceeded at 110 °C for 4 h to give **5aa** in 85% yield. If we used $[Ru(p\text{-cymene})Cl_2]_2$ as an alternative catalyst for this one-pot sequential reaction, the product **5aa** was obtained in only 32% yield. Apparently, $[Cp^*IrCl_2]_2$ is better than $[Ru(p\text{-cymene})Cl_2]_2$ in the acceptorless dehydrogenation step.

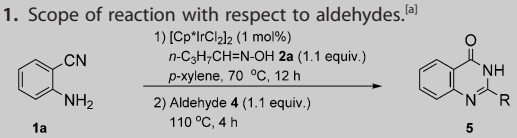


Scheme 3. Exploration of the feasibility of the model reaction.

With the established catalytic system in hand, we examined the scope of the reaction with respect to aldehydes, and the results are outlined in Table 1. Similar to the case of **4a**, halogenated benzaldehydes (**4b–4d**) were converted to the desired products **5ab–5ad** in 81–85% yield (Table 1, entries 1–3). The reactions of benzaldehydes that bear a stronger electron-withdrawing group, such as trifluoromethyl (**4e–4f**) and trifluoromethoxy (**4g**), afforded the corresponding products **5ae–5ag** in 78–84% yield (Table 1, entries 4–6). Benzaldehydes that bear one or two electron-donating groups, such as methyl (**4h–i**), isopropyl (**4j**), methoxy (**4k**), dimethyl (**4l**), and dimethoxy (**4m**), were tested, and the desired products **5ah–5am** were obtained in 76–87% yield (Table 1, entries 7–12). The catalytic system was also compatible with 2-thiophenaldehyde (**4n**) and 2-naphthaldehyde (**4o**) to afford the corresponding products **5an** and **5ao** in 83 and 87% yield, respectively (Table 2, entries 13–14). In addition to aromatic aldehydes, aliphatic ones, such as butyraldehyde (**4p**), cyclohexanecarbaldehyde (**4q**), and phenylpropyl aldehyde (**4r**), were suitable partners, and the desired products **5ap–5ar** were obtained in 77–85% yield (Table 1, entries 15–17).

The generality of the reaction with respect to *o*-aminobenzonitriles was then investigated. The transformations of *o*-aminobenzonitriles that bear one or two electron-withdrawing groups, such as fluorine (**1b–1c**) and chlorine (**1d–1e**), gave the corresponding products **5ba–5ea** in 75–91% yield (Table 2, entries 1–4). Furthermore, the reactions of *o*-aminobenzonitriles that bear a bromine on different positions (**1f–1i**) proceeded smoothly to afford the desired products **5fa–**

Table 1. Scope of reaction with respect to aldehydes.[a]



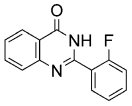
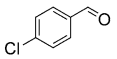
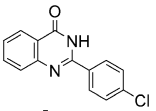
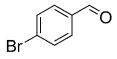
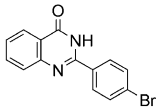
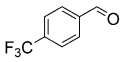
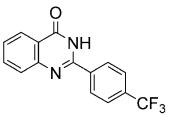
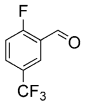
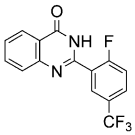
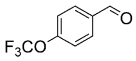
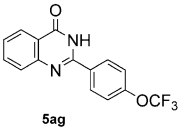
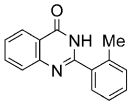
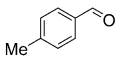
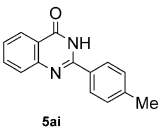
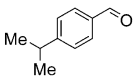
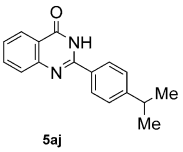
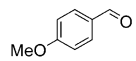
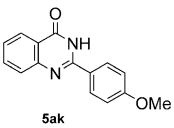
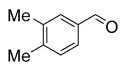
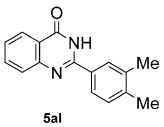
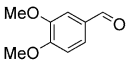
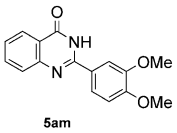
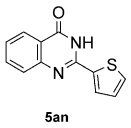
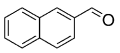
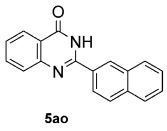
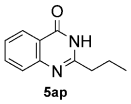
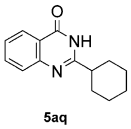
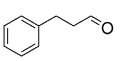
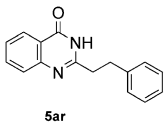
Entry	Aldehyde	Product	Yield [%][b]
1	 4b	 5ab	85
2	 4c	 5ac	81
3	 4d	 5ad	84
4	 4e	 5ae	82
5	 4f	 5af	84
6	 4g	 5ag	78
7	 4h	 5ah	84
8	 4i	 5ai	85
9	 4j	 5aj	76
10	 4k	 5ak	80
11	 4l	 5al	83

Table 1. (Continued)

Entry	Aldehyde	Product	Yield [%][b]
12	 4m	 5am	87
13	 4n	 5an	83
14	 4o	 5ao	87
15	 4p	 5ap	78[c]
16	 4q	 5aq	85
17	 4r	 5ar	77

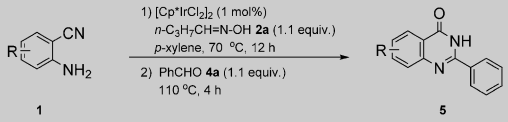
[a] Reaction conditions: 1) **1a** (1 mmol), **2a** (1.1 mmol), $[Cp^*IrCl_2]_2$ (1 mol%), *p*-xylene (2 mL), 70 °C, 12 h; 2) **4** (1.1 mmol), 110 °C, 4 h. [b] Isolated yield. [c] **4p** (2 mmol).

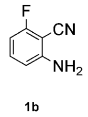
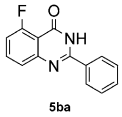
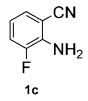
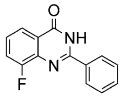
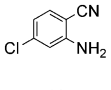
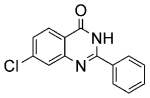
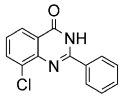
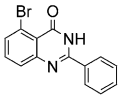
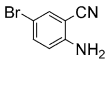
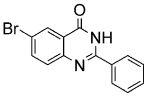
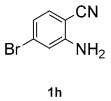
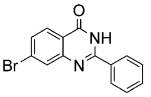
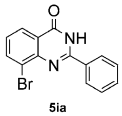
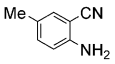
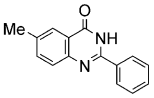
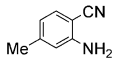
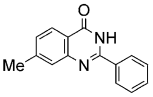
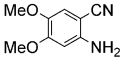
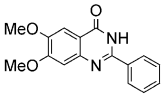
5ia in 77–87% yield (Table 2, entries 5–8). In the case of *o*-aminobenzonitriles that bear one or two electron-donating groups, such as methyl (**1j**–**1k**) and dimethoxy (**1l**), the corresponding products **5ja**–**5la** could be obtained in 83–88% yield (Table 2, entries 9–11).

A possible mechanism is proposed to account for the present one-pot sequential reaction (Scheme 4). In cycle I, the initial step involved the generation of iridium nitrile species **B**, which was subsequently attacked by aldoximes to give the five-membered cyclic species **C**. Accompanied by the decomposition of **C**, *o*-aminobenzamide was released and the catalytically active Ir species **A** was regenerated.[14] Furthermore, the condensation between *o*-aminobenzamides and aldehydes occurred to give dihydroquinazolinones. In cycle II, the β-hydrogen elimination of amido iridium species **D** and/or **E**, which were formed by the oxidative addition of the N–H bond of dihydroquinazolinones to coordinatively unsaturated Ir species, afforded quinazolinones as the desired products and iridium dihydride species **F**. Finally, catalytically active species **A** was regenerated with the liberation of hydrogen gas from iridium dihydride species **F**.

A series of mechanistic experiments was undertaken to support the proposed mechanism (Scheme 5). Initially, *n*-butyronitrile (**6**) was observed as a byproduct (85% yield) from ^{1}H NMR

Table 2. Scope of reaction with respect to *o*-aminobenzonitriles.[a]



Entry	*o*-Aminobenzonitrile	Product	Yield [%][b]
1	 1b	 5ba	80
2	 1c	 5ca	75
3	 1d	 5da	91
4	 1e	 5ea	83
5	 1f	 5fa	81
6	 1g	 5ga	87
7	 1h	 5ha	86
8	 1i	 5ia	77
9	 1j	 5ja	83
10	 1k	 5ka	86
11	 1l	 5la	88

[a] Reaction conditions: **1** (1 mmol), **2a** (1.1 mmol), $[Cp^*IrCl_2]_2$ (1 mol%), *p*-xylene (2 mL), 70 °C, 12 h; 2) **4a** (1.1 mmol), 110 °C, 4 h. [b] Isolated yield.

spectroscopy of the crude reaction mixture of the hydration of **1a** with **2a**. Furthermore, the condensation between **3aa** and **4a** proceeded for 1 h to give 2-phenyl-2,3-dihydroquinazolin-4(1*H*)-one (**7**) in 95% yield. In the presence of $[Cp^*IrCl_2]_2$ (1 mol%), the reaction of **7** afforded product **5aa** in 96% yield with an almost quantitative amount of hydrogen gas collected by water displacement. These experimental results support the proposed mechanism shown in Scheme 4.

Conclusions

We have established a new, efficient, and versatile strategy for the direct synthesis of quinazolinones from *o*-aminobenzonitriles. In the presence of $[Cp^*IrCl_2]_2$ (Cp^* = pentamethylcyclopentadienyl), a variety of desirable products was obtained easily through one-pot sequential selective hydration/condensation/acceptorless dehydrogenation. This protocol is highly attractive because of the readily available starting materials, high atom efficiency, good to excellent yields, and minimal consumption of chemicals and energy. Notably, this research exhibited new potential for the development of transition-metal-catalyzed one-pot sequential reactions that involve acceptorless dehydrogenation.

Experimental Section

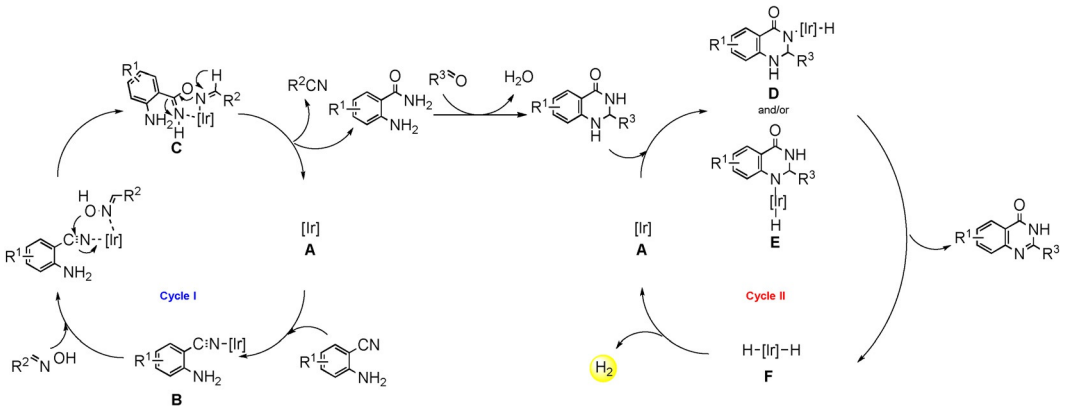
General details

HRMS was measured by using a HPLC-Q-Tof MS(Micro) spectrometer and are reported as *m/z* (relative intensity). Accurate masses are reported for the molecular ion $[M-H]^-$. ^{1}H NMR spectra were recorded at 500 MHz by using a Bruker Avance 500 spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane or relative to the center of the singlet at $\delta = 7.26$ ppm for $CDCl_3$ or $\delta = 2.50$ ppm for $[D_6]$DMSO. Coupling constants (*J*) are reported in Hertz (Hz), and the splitting patterns were designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; b, broad. ^{13}C NMR spectra were recorded at 125 MHz by using a Bruker Avance 500 spectrometer. Chemical shifts (δ) are reported relative to the center of the triplet at $\delta = 77.0$ ppm for $CDCl_3$ or $\delta = 39.5$ ppm for $[D_6]$DMSO. ^{13}C NMR spectra were performed routinely with broadband decoupling.

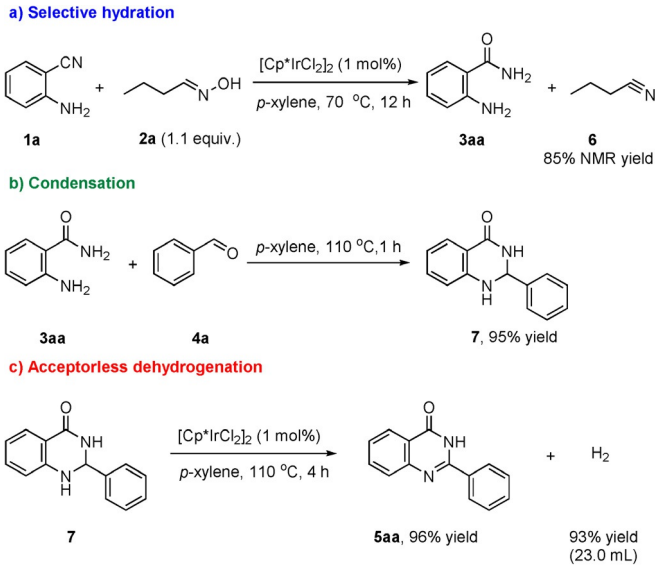
General procedure for the direct synthesis of quinazolinones from *o*-aminobenzonitriles by one-pot sequential selective hydration/condensation/acceptorless dehydrogenation

To an oven-dried, N_2-purged 25 mL Schlenk tube were added $[Cp^*IrCl_2]_2$ (0.01 mmol, 1 mol%), *o*-aminobenzonitrile (1 mmol), *n*-butylaldoxime (1.1 mmol, 1.1 equiv.) and *p*-xylene (2 mL), and the mixture was heated at 70 °C for 12 h. The reaction mixture was allowed to cool to RT, and aldehyde (1.1 mmol, 1.1 equiv.) was added. The Schlenk tube was flushed with nitrogen, and the mixture was heated at 110 °C for 4 h. The reaction mixture was cooled to RT, concentrated in vacuo, and purified by flash column chromatography with hexanes/ethyl acetate to afford the product.

2-Phenylquinazolin-4(3*H*)-one (5aa):[4i] White solid; 85% yield (189 mg); m.p. 237–238 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 11.56$ (br s, 1H), 8.34 (d, $J = 7.8$ Hz, 1H), 8.26 (dd, $J = 3.1$ Hz and 6.7 Hz, 2H), 7.80–7.86 (m, 2H), 7.59–7.60 (m, 3H), 7.51 ppm (t, $J = 7.3$ Hz, 1H); ^{13}C {1H} NMR (125 MHz, $CDCl_3$): $\delta = 163.9$, 151.8, 149.5, 134.9, 132.8, 131.6, 129.0, 128.0, 127.4, 126.7, 126.4, 120.9 ppm.



Scheme 4. Proposed reaction mechanism.



Scheme 5. Mechanistic experiments.

2-(2-Fluorophenyl)quinazolin-4(3*H*)-one (5ab):[15] White solid; 85% yield (204 mg); m.p. 162–163 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.58 (br s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.86 (t, J = 7.6 Hz, 1H), 7.78 (t, J = 7.5 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.60–7.65 (m, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.36–7.41 ppm (m, 2H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.4, 159.5 (d, J_{C-F} = 250.3 Hz), 149.9, 148.7, 134.6, 132.8 (J_{C-F} = 8.2 Hz), 131.0, 127.5, 127.0, 125.8, 124.6, 122.3 (d, J_{C-F} = 13.1 Hz), 121.1, 116.1 ppm (d, J_{C-F} = 21.3 Hz).

2-(4-Chlorophenyl)quinazolin-4(3*H*)-one (5ac):[4i] White solid; 81% yield (208 mg); m.p. 300–301 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.62 (br s, 1H), 8.20 (d, J = 8.6 Hz, 2H), 8.15 (d, J = 7.6 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.6 Hz, 2H), 7.54 ppm (t, J = 7.4 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): 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 ppm.

2-(4-Bromophenyl)quinazolin-4(3*H*)-one (5ad):[16] White solid; 84% yield (253 mg); m.p. 296–297 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.61 (br s, 1H), 8.15 (d, J = 8.0 Hz,1H), 8.13 (d, J = 8.6 Hz,2H), 7.84 (t, J = 7.6 Hz, 1H), 7.74–7.78 (m, 3H), 7.55 ppm (t, J = 7.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.1, 151.5, 148.6, 134.7, 131.9, 131.6, 129.8, 127.5, 126.7, 125.9, 125.2, 121.0 ppm.

2-[4-(Trifluoromethyl)phenyl]quinazolin-4(3*H*)-one (5ae):[4i] White solid; 82% yield (238 mg); m.p. 309–310 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.75 (br s, 1H), 8.38 (d, J = 8.2 Hz, 2H), 8.18 (dd, J = 1.2 Hz, J = 8.0 Hz, 1H), 7.93 (d, J = 8.3 Hz, 2H), 7.87 (t, J = 7.7 Hz, 1H), 7.79 (d, J = 7.7 Hz, 1H), 7.57 ppm (t, J = 7.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.0, 151.1, 148.4, 136.6, 134.7, 131.1 (q, J_{C-F} = 32.1 Hz), 128.7, 127.6, 127.1, 125.8, 125.4 (q, J_{C-F} = 3.0 Hz), 123.9 (q, J_{C-F} = 272.3 Hz), 121.2 ppm.

2-[2-Fluoro-5-(trifluoromethyl)phenyl]quinazolin-4(3*H*)-one (5af): White solid; 84% yield (259 mg); m.p. 235–237 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.73 (br s, 1H), 8.17–8.19 (m, 2H), 8.03 (s, br,1H), 7.87 (t, J = 7.3 Hz, 1H), 7.76 (d, J = 8.2 Hz, 1H), 7.66 (t, J = 9.1 Hz, 1H), 7.59 ppm (t, J = 7.4 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.4, 161.1 (d, J_{C-F} = 256.7 Hz), 148.5, 148.4, 134.6, 130.0 (d, J_{C-F} = 6.2 Hz), 128.6, 127.6, 127.3, 125.8, 125.5 (q, J_{C-F} = 33.5 Hz), 123.5 (q, J_{C-F} = 273.0 Hz), 123.2 (d, J_{C-F} = 15.0 Hz), 121.3, 117.7 ppm (d, J_{C-F} = 23.1 Hz); HRMS (EI, 70 eV) *m/z*: calcd for $C_{15}H_7F_4N_2O$: 307.0495 [M−H]$^-$; found 307.0489.

2-[4-(Trifluoromethoxy)phenyl]quinazolin-4(3*H*)-one (5ag):[5f] White solid; 78% yield (239 mg); m.p. 268–270 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.65 (br s, 1H), 8.30 (d, J = 8.7 Hz, 2H), 8.16 (d, J = 7.8 Hz, 1H), 7.84 (t, J = 7.4 Hz, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.52–7.56 ppm (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.1, 151.1, 150.4, 148.5, 134.6, 131.8, 130.1, 127.5, 126.8, 125.8, 121.0, 120.8, 120.0 ppm (d, J_{C-F} = 193.0 Hz).

2-(*o*-Tolyl)quinazolin-4(3*H*)-one (5ah):[4i] White solid; 84% yield (198 mg); m.p. 222–223 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.45 (br s, 1H), 8.17 (d, J = 7.7 Hz, 1H), 7.84 (t, J = 7.4 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.51 (d, J = 7.5 Hz, 1H),7.43 (t, J = 7.3 Hz, 1H), 7.31–7.36 (m, 2H), 2.38 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.7, 154.3, 148.7, 136.1, 134.4, 134.2, 130.5, 129.8, 129.1, 127.3, 126.6, 125.7, 125.6, 121.0, 19.5 ppm.

2-(*p*-Tolyl)quinazolin-4(3*H*)-one (5ai):[4i] white solid; 85% yield (200 mg); m.p. 242–243 °C; ^{1}H NMR (500 MHz, CDCl$_3$): δ = 12.45 (br s, 1H), 8.14 (d, J = 7.8 Hz, 1H), 8.09 (d, J = 8.1 Hz, 2H), 7.82 (t, J = 7.5 Hz, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 2.38 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, CDCl$_3$):

δ = 162.2, 152.2, 148.8, 141.4, 134.5, 130.0, 129.1, 127.6, 127.4, 126.3, 125.8, 120.9, 20.9 ppm.

2-(4-Isopropylphenyl)quinazolin-4(3*H*)-one (5 aj):[4i] White solid; 76% yield (200 mg); m.p. 210–212 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.48 (br s, 1H), 8.12–8.16 (m, 3H), 7.84 (t, *J* = 7.4 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 2.94–3.03 (m, 1H), 1.25 ppm (d, *J* = 6.7 Hz, 6H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.2, 152.2, 152.1, 148.8, 134.5, 130.3, 127.8, 127.4, 126.5, 126.4, 125.8, 120.9, 33.3, 23.6 ppm.

2-(4-Methoxyphenyl)quinazolin-4(3*H*)-one (5 ak):[4d] White solid; 80% yield (202 mg); m.p. 246–247 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.39 (br s, 1H), 8.19 (d, *J* = 8.7 Hz, 2H), 8.13 (d, *J* = 7.8 Hz, 1H), 7.80 (t, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 2H), 3.84 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.3, 161.8, 151.8, 148.9, 134.5, 129.4, 127.2, 126.1, 125.8, 124.8, 120.7, 114.0, 55.4 ppm.

2-(3,4-Dimethylphenyl)quinazolin-4(3*H*)-one (5 al):[4b] White solid; 83% yield (208 mg); m.p. 240–241 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.41 (br s, 1H), 8.14 (d, *J* = 7.7 Hz, 1H), 8.01 (s, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.82 (t, *J* = 7.4 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 2.31 (s, 3H), 2.29 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.2, 152.3, 148.8, 140.2, 136.6, 134.5, 130.1, 129.7, 128.6, 127.4, 126.3, 125.8, 125.1, 120.9, 19.4, 19.3 ppm.

2-(3,4-Dimethoxyphenyl)quinazolin-4(3*H*)-one (5 am):[17] White solid; 87% yield (245 mg); m.p. 242–243 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.43 (br s, 1H), 8.13 (d, *J* = 7.2 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.80–7.83 (m, 2H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 3.88 (s, 3H), 3.85 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): 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, 111.43, 110.7, 55.7 ppm (2C, overlap).

2-(Thiophen-2-yl)quinazolin-4(3*H*)-one (5 an):[4d] White solid; 83% yield (189 mg); m.p. 276–277 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.66 (br s, 1H), 8.23 (d, *J* = 3.2 Hz, 1H), 8.12 (d, *J* = 7.4 Hz, 1H), 7.87 (d, *J* = 4.7 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.23 ppm (t, *J* = 4.3 Hz 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.8, 148.6, 147.8, 137.3, 134.6, 132.1, 129.4, 128.5, 126.9, 126.3, 126.0, 120.9 ppm.

2-(Naphthalen-2-yl)quinazolin-4(3*H*)-one (5 ao):[4i] White solid; 87% yield (236 mg); m.p. 276–277 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): 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), 8.01 (d, *J* = 7.4 Hz, 1H), 7.86 (t, *J* = 7.3 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.61–7.66 (m, 2H), 7.54 ppm (t, *J* = 7.3 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 162.2, 152.2, 148.8, 134.6, 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 ppm.

2-Propylquinazolin-4(3*H*)-one (5 ap):[4a] White solid; 78% yield (147 mg); m.p. 198–199 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.15 (br s, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.76 (t, *J* = 7.7 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), 1.70–1.78 (m, 2H), 0.93 ppm (t, *J* = 7.4 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.8, 157.3, 148.9, 134.2, 126.8, 125.9, 125.6, 120.8, 36.3, 20.2, 13.4 ppm.

2-Cyclohexylquinazolin-4(3*H*)-one (5 aq):[4b] White solid; 85% yield (194 mg), m.p. 229–230 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.06 (br s, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 2.57 (tt, *J* = 11.8 Hz and *J* = 3.2 Hz, 1H, CH), 1.89 (d, *J* = 12.4 Hz, 2H), 1.78(d, *J* = 12.8 Hz, 1H), 1.67(d, *J* = 11.9 Hz, 1H), 1.54–1.61 (m, 2H), 1.20–1.33 ppm (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.9, 160.7, 148.9, 134.1, 126.9, 125.8, 125.6, 120.9, 42.8, 30.2, 25.5, 25.3 ppm.

2-Phenethylquinazolin-4(3*H*)-one (5 ar):[18] White solid; 77% yield (193 mg); m.p. 209–210 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.26 (br s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.78 (t, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.3 Hz, 1H), 7.27–7.30 (m, 3H), 7.17–7.21 (m, 1H), 3.05 (t, *J* = 8.0 Hz, 2H), 2.89 ppm (t, *J* = 8.0 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): 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 ppm.

5-Fluoro-2-phenylquinazolin-4(3*H*)-one (5 ba):[19] White solid; 80% yield (192 mg); m.p. 281–284 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.55 (br s, 1H), 8.17 (d, *J* = 7.2 Hz, 2H), 7.82–7.78 (m, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.57–7.54 (m, 3H), 7.28–7.24 ppm (m, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.6, 159.5 (d, J_{C-F} = 11.8 Hz), 153.3, 150.9, 135.1 (d, J_{C-F} = 10.4 Hz), 132.3, 131.7, 128.6, 127.9, 123.5, 112.9 (d, J_{C-F} = 20.5 Hz), 110.4 ppm (d, J_{C-F} = 6.0 Hz).

8-Fluoro-2-phenylquinazolin-4(3*H*)-one (5 ca):[20] White solid; 75% yield (180 mg); m.p. 272–274 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.73 (br s, 1H), 8.21 (d, *J* = 7.4 Hz, 2H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.72 (t, *J* = 9.2 Hz, 1H), 7.56–7.64 (m, 3H), 7.49–7.53 ppm (m, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.4, 156.7 (d, J_{C-F} = 253.8 Hz), 152.9, 153.9, 138.0 (d, J_{C-F} = 11.3 Hz), 132.5, 131.6, 128.6, 127.9, 126.7 (d, J_{C-F} = 7.5 Hz), 123.0, 121.6 (d, J_{C-F} = 3.3 Hz), 119.9 ppm (d, J_{C-F} = 18.8 Hz).

7-Chloro-2-phenylquinazolin-4(3*H*)-one (5 da):[4i] White solid; 91% yield (233 mg); m.p. 276–278 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.68 (br s, 1H), 8.17 (d, *J* = 7.5 Hz, 2H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.79 (d, *J* = 2.0 Hz, 1H), 7.61 (t, *J* = 7.2 Hz, 1H), 7.54–7.57 ppm (m, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.6, 153.7, 149.8, 139.1, 132.4, 131.6, 130.7, 128.6, 127.9, 127.9, 126.7, 126.5, 119.8 ppm.

8-Chloro-2-phenylquinazolin-4(3*H*)-one (5 ea):[4l] White solid; 83% yield (214 mg); m.p. 286–288 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.77 (br s, 1H), 8.24 (d, *J* = 7.1 Hz, 2H), 8.11 (dd, *J* = 8.0 Hz and 1.3 Hz, 1H), 7.99 (dd, *J* = 7.8 Hz and 1.3 Hz, 1H), 7.64–7.56 (m, 3H), 7.49 ppm (t, *J* = 7.8 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.8, 152.9, 145.2, 134.6, 132.4, 131.8, 131.0, 128.7, 128.0, 126.8, 125.0, 122.8 ppm.

5-Bromo-2-phenylquinazolin-4(3*H*)-one (5 fa):[10j] White Solid; 81% yield (244 mg); m.p. 283–284 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.56 (br s, 1H), 8.18 (d, *J* = 7.2 Hz, 2H), 7.71–7.74 (m, 2H), 7.67–7.63 (m, 1H), 7.61(t, *J* = 7.2 Hz, 1H), 7.56 ppm (t, *J* = 7.5 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 160.5, 152.7, 151.1, 134.6, 132.6, 132.1, 131.6, 128.6, 127.8, 127.7, 120.1, 118.8 ppm.

6-Bromo-2-phenylquinazolin-4(3*H*)-one (5 ga):[21] White solid; 87% yield (262 mg); m.p. 285–286 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.71 (br s, 1H), 8.22 (d, *J* = 2.1 Hz, 1H), 8.17 (d, *J* = 7.5 Hz, 2H), 7.98 (dd, *J* = 8.7 Hz and 2.0 Hz, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.60 (t, *J* = 7.1 Hz, 1H), 7.55 ppm (t, *J* = 7.4 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ = 161.2, 153.0, 147.7, 137.4, 132.5, 131.6, 129.8, 128.6, 128.0, 127.9, 122.6, 118.9 ppm.

7-Bromo-2-phenylquinazolin-4(3*H*)-one (5 ha): White solid; 86% yield (259 mg); m.p. 269–271 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 12.67 (br s, 1H), 8.16 (d, *J* = 7.3 Hz, 2H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.94 (d, *J* = 1.8 Hz, 1H), 7.68 (dd, *J* = 8.4 Hz and 1.8 Hz, 1H), 7.61 (t,

J=7.2 Hz, 1H), 7.56 ppm (t, J=7.4 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ=161.8, 153.7, 149.9, 132.4, 131.7, 129.6, 129.5, 128.6, 128.1, 127.9 (2C, overlap), 120.1 ppm; HRMS (EI, 70 eV) m/z: calcd for $C_{14}H_8BrN_2O$: 298.9820 [M−H]$^-$; found 298.9829.

8-Bromo-2-phenylquinazolin-4(3*H*)-one (5ia): White solid; 77% yield (232 mg); m.p. 281–283 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ= 12.78 (br s, 1H), 8.28 (d, J=7.2 Hz, 2H), 8.16 (d, J=7.8 Hz, 2H), 7.65–7.58 (m, 3H), 7.42 ppm (t, J=7.8 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ=161.9, 152.9, 146.1, 137.9, 132.4, 131.8, 128.6, 127.9, 127.3, 125.7, 122.6, 122.2 ppm; HRMS (EI, 70 eV) m/z: calcd for $C_{14}H_8BrN_2O$: 298.9820 [M−H]$^-$; found 298.9827.

6-Methyl-2-phenylquinazolin-4(3*H*)-one (5ja):[4b] White solid; 83% yield (196 mg), m.p. 238–240 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ= 12.46 (br s, 1H), 8.17 (d, J=6.9 Hz, 2H), 7.95 (s, 1H), 7.68–7.64 (m, 2H), 7.60–7.52 (m, 3H), 2.46 ppm (s, 3H); ^{13}C {1H} NMR (125 MHz, [D$_6$]DMSO): δ=162.1, 152.5, 146.7, 136.3, 135.9, 132.8, 131.2, 128.6, 127.6, 127.4, 125.2, 120.7, 20.8 ppm.

7-Methyl-2-phenylquinazolin-4(3*H*)-one (5ka):[19] White solid; 86% yield (203 mg), m.p. 239–240 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ=12.45 (br s, 1H), 8.17 (d, J=5.5 Hz, 2H), 8.03 (d, J= 7.0 Hz, 1H), 7.55 (s, 4H), 7.33 (d, J=6.8 Hz, 1H), 2.47 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ=162.1, 152.3, 148.8, 145.0, 132.8, 131.3, 128.5, 128.0, 127.7, 127.1, 125.7, 118.6, 21.3 ppm.

6,7-Dimethoxy-2-phenylquinazolin-4(3*H*)-one (5la):[19] White solid; 88% yield (248 mg); m.p. 281–284 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ=12.40 (br s, 1H), 8.16 (d, J=7.0 Hz, 2H), 7.57–7.52 (m, 3H), 7.49 (s, 1H), 7.22 (s, 1H), 3.93 (s, 3H), 3.89 ppm (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, [D$_6$]DMSO): δ=161.6, 154.8, 150.8, 148.6, 144.8, 132.9, 131.0, 128.6, 127.4, 114.0, 108.3, 105.0, 56.0, 55.7 ppm.

Procedure for the condensation between *o*-aminobenzonitrile and benzaldehyde

To an oven-dried, N_2-purged 25 mL Schlenk tube were added **3aa** (1 mmol), **4a** (1 mmol), and *p*-xylene (2 mL), and the mixture was heated at 110 °C for 1 h, at which point the reaction mixture was allowed to cool to RT. The mixture was concentrated in vacuo, and purified by flash column chromatography with hexane/ethyl acetate to give the product.

2-Phenyl-2,3-dihydroquinazolin-4(1*H*)-one (7):[22] White solid; 95% yield (213 mg); m.p. 216–218 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.95 (d, J=7.7 Hz, 1H), 7.61–7.59 (m, 2H), 7.46–7.45 (m, 3H), 7.34 (t, J=7.7 Hz, 1H), 6.91 (t, J=7.5 Hz, 1H), 6.67 (d, J=8.1 Hz, 1H), 5.91 (s, 1H), 5.76 (br s, 1H), 4.39 ppm (br s, 1H); ^{13}C {1H} NMR (125 MHz, $CDCl_3$): δ=164.7, 147.2, 138.6, 134.0, 130.2, 129.1, 1328.7, 127.4, 119.7, 115.7, 114.6, 69.1 ppm.

Procedure for the hydrogen evolution experiment[9e]

Compound 7 (1 mmol), $[Cp^*IrCl_2]_2$ (1 mol%), and *p*-xylene (2 mL) were added to a 10 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 with 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 110 °C until gas evolution ceased (4 h). The presence of hydrogen in the collected gas was confirmed by GC analysis.

GC analysis was performed by using a gas chromatograph with a thermal conductivity detector (TCD). Injector temperature= 100 °C, column temperature=70 °C, detector temperature (TCD)= 100 °C, carrier gas=N_2, t=0.965 min.

The volume of 1.0 mol of H_2 at 296.15 K, 99920 Pa was calculated according to the van der Waals equation [Eq. (1)]:

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

in which R=8.3145 m^3 Pa mol^{-1} K^{-1}; T=296.15 K; p=99920 Pa; a= 0.02476 m^6 Pa mol^{-1}; and b=0.02661×10^{-3} m^3 mol^{-1}; thus, V (H_2, 296.15 K, 99920 Pa)=24.7 L mol^{-1}.

The collected volume of gas in this experiment above was 23.0 mL, which corresponds to 0.93 mmol of H_2.

Acknowledgements

Financial support by the National Natural Science Foundation of China (No.21272115) and the State Key Laboratory of Fine Chemicals (KF1401) is greatly appreciated.

Keywords: dehydrogenation · heterocycles · homogeneous catalysis · iridium · synthesis design

[1] For selected reviews, see: a) S. B. Mhaske, N. P. Argade, *Tetrahedron* **2006**, *62*, 9787–9826; b) I. Khan, A. Ibrar, N. Abbas, A. Saeed, *Eur. J. Med. Chem.* **2014**, *76*, 193–194.

[2] a) P. P. Kung, M. D. Casper, K. L. Cook, L. Wilson-Lingard, L. M. Risen, T. A. Vickers, R. Ranken, L. B. Blyn, R. Wyatt, P. D. Cook, D. Ecker, *J. Med. Chem.* **1999**, *42*, 4705–4713; b) Z. Wang, M. Wang, X. Yao, Y. Li, J. Tan, L. Wang, W. Qiao, Y. Geng, Y. Liu, Q. Wang, *Eur. J. Med. Chem.* **2012**, *53*, 275–282; c) S. Cao, Y. Feng, Y. Jiang, S. Liu, G. Ding, R. Li, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1915–1917.

[3] a) J. W. Lockman, B. R. Murphy, D. F. Zigar, W. R. Judd, P. M. Slattum, Z. Gao, K. Ostanin, J. Green, R. McKinnon, R. T. Terry-Lorenzo, T. C. Fleischer, J. J. Boniface, M. Shenderovich, J. A. Willardsen, *J. Med. Chem.* **2010**, *53*, 8734–8746; b) F. Rörsch, E. Buscato, K. Deckmann, G. Schneider, M. Schubert-Zsilavecz, G. Geisslinger, E. Proschak, S. Grosch, *J. Med. Chem.* **2012**, *55*, 3792–3803; c) C. Yu, P. Chang, L. Hsin, J. Chern, *J. Med. Chem.* **2013**, *56*, 6775–6791; d) A. E. G. Lindgren, T. Karlberg, T. Ekblad, S. Spjut, A. Thorsell, C. D. Andersson, T. T. Nhan, V. Hellsten, J. Weigelt, A. Linusson, *J. Med. Chem.* **2013**, *56*, 9556–9568.

[4] For selected examples, see: a) X. Liu, H. Fu, Y. Jiang, Y. Zhao, *Angew. Chem. Int. Ed.* **2009**, *48*, 348–351; *Angew. Chem.* **2009**, *121*, 354–357; b) B. Ma, Y. Wang, J. Peng, Q. Zhu, *J. Org. Chem.* **2011**, *76*, 6362–6366; c) W. Xu, H. Fu, *J. Org. Chem.* **2011**, *76*, 3846–3852; d) W. Xu, Y. Jin, H. Liu, H. Jiang, H. Fu, *Org. Lett.* **2011**, *13*, 1274–1277; e) L. Xu, Y. Jiang, D. Ma, *Org. Lett.* **2012**, *14*, 1150–1154; f) J. E. R. Sadig, R. Foster, F. Wakenhut, M. C. Willis, *J. Org. Chem.* **2012**, *77*, 9473–9486; g) Y. Wang, F. Zhang, S. Chiba, *Org. Lett.* **2013**, *15*, 2842–2845; h) X. Wu, L. He, H. Neumann, M. Beller, *Chem. Eur. J.* **2013**, *19*, 12635–12638; i) X. Jiang, T. Tang, J. Wang, Z. Chen, Y. Zhu, S. Ji, *J. Org. Chem.* **2014**, *79*, 5082–5087; j) T. B. Nguyen, J. L. Bescont, L. Ermolenko, A. Al-Mourabit, *Org. Lett.* **2013**, *15*, 6218–6221; k) X. Yang, G. Cheng, J. Shen, C. Kuai, X. Cui, *Org. Chem. Front.* **2015**, *2*, 366–368.

[5] a) T. Hisano, M. Ichikawa, A. Nakagawa, M. Tsuji, *Chem. Pharm. Bull.* **1975**, *23*, 1910–1916; b) C. Balakumar, P. Lamba, D. P. Kishore, B. L. Narayana, K. V. Rao, K. Rajwinder, A. R. Rao, B. Shireesha, B. Narsaiah, *Eur. J. Med. Chem.* **2010**, *45*, 4904–4913; c) K. Juvale, M. Wiese, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6766–6769; d) R. J. Abdel-Jalil, W. Voelter, M. Saeed, *Tetrahedron Lett.* **2004**, *45*, 3475–3476; e) R. Cheng, T. Guo, D. Zhang-Negrerie, Y. Du, K. Zhao, *Synthesis* **2013**, *45*, 2998–3006; f) M. Sharif, J. Opalach, P. Langer, M. Beller, X. Wu, *RSC Adv.* **2014**, *4*, 8–17.

[6] a) P. D. Bailey, T. J. Mills, R. Pettecrew, R. A. Price in *Comprehensive Organic Functional Group Transformations II, Vol. 5* (Eds.: A. R. Katritzky, R. J. K. Taylor), Elsevier, Oxford, **2005**, pp. 201 – 294; b) A. D. Roy, A. Subramanian, R. Roy, *J. Org. Chem.* **2006**, *71*, 382 – 385.

[7] For a review about acceptorless dehydrogenation and related transformations in chemical synthesis, see: B. Gnanaprakasam, D. Milstein, *Science* **2013**, *341*, 1229712.

[8] a) K. Fujita, N. Tanino, R. Yamaguchi, *Org. Lett.* **2007**, *9*, 109 – 111; b) K. Fujita, T. Yoshida, Y. Imori, R. Yamaguchi, *Org. Lett.* **2011**, *13*, 2278 – 2281; c) J. Zhang, E. Balaraman, G. Leitus, D. Milstein, *Organometallics* **2011**, *30*, 5716 – 5724; d) S. Musa, I. Shaposhnikov, S. Cohen, D. Gelman, *Angew. Chem. Int. Ed.* **2011**, *50*, 3533 – 3537; *Angew. Chem.* **2011**, *123*, 3595 – 3599; e) R. Kawahara, K. Fujita, R. Yamaguchi, *J. Am. Chem. Soc.* **2012**, *134*, 3643 – 3646; f) R. Kawahara, K. Fujita, R. Yamaguchi, *Angew. Chem. Int. Ed.* **2012**, *51*, 12790 – 12794; *Angew. Chem.* **2012**, *124*, 12962 – 12966; g) G. Zhang, S. K. Hanson, *Org. Lett.* **2013**, *15*, 650 – 653; h) K. T. Tseng, J. W. Kampf, N. K. Szymczak, *Organometallics* **2013**, *32*, 2046 – 2049; i) G. Zeng, S. Sakaki, K. Fujita, H. Sano, R. Yamaguchi, *ACS Catal.* **2014**, *4*, 1010 – 1020; j) H. Song, B. Kang, S. Hong, *ACS Catal.* **2014**, *4*, 2889 – 2895; k) S. Chakraborty, P. O. Lagaditis, M. Förster, E. A. Bielinski, N. Hazari, M. C. Holthausen, W. D. Jones, S. Schneide, *ACS Catal.* **2014**, *4*, 3994 – 4003; l) S. Chakraborty, P. E. Piszel, W. W. Brennessel, W. D. Jones, *Organometallics* **2015**, *34*, 5203 – 5206.

[9] a) R. Yamaguchi, C. Ikeda, T. Takahashi, K. Fujita, *J. Am. Chem. Soc.* **2009**, *131*, 8410 – 8412; b) J. Zhou, J. Fang, *J. Org. Chem.* **2011**, *76*, 7730 – 7736; c) K. Fujita, Y. Tanaka, M. Kobayashi, R. Yamaguchi, *J. Am. Chem. Soc.* **2014**, *136*, 4829 – 4832; d) S. Chakraborty, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2014**, *136*, 8564 – 8567; e) J. Wu, D. Talwar, S. Johnston, M. Yan, J. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 6983 – 6987; *Angew. Chem.* **2013**, *125*, 7121 – 7125; f) D. Talwar, A. Gonzalez-de-Castro, H. Li, J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 5223 – 5227; *Angew. Chem.* **2015**, *127*, 5312 – 5316.

[10] a) F. Li, H. Shan, L. Chen, Q. Kang, P. Zou, *Chem. Commun.* **2012**, *48*, 603 – 605; b) F. Li, C. Sun, H. Shan, X. Zou, J. Xie, *ChemCatChem* **2013**, *5*, 1543 – 1552; c) F. Li, P. Qu, J. Ma, X. Zou, C. Sun, *ChemCatChem* **2013**, *5*, 2178 – 2182; d) C. Sun, X. Zou, F. Li, *Chem. Eur. J.* **2013**, *19*, 14030 – 14033; e) P. Qu, C. Sun, J. Ma, F. Li, *Adv. Synth. Catal.* **2014**, *356*, 447 – 459; f) N. Wang, X. Zou, J. Ma, F. Li, *Chem. Commun.* **2014**, *50*, 8303 – 8305; g) F. Li, C. Sun, N. Wang, *J. Org. Chem.* **2014**, *79*, 8031 – 8039; h) F. Li, J. Ma, N. Wang, *J. Org. Chem.* **2014**, *79*, 10447 – 10455; i) L. Lu, J. Ma, P. Qu, F. Li, *Org. Lett.* **2015**, *17*, 2350 – 2353; j) F. Li, L. Lu, J. Ma, *Org. Chem. Front.* **2015**, *2*, 1589 – 1597; k) R. Wang, J. Ma, F. Li, *J. Org. Chem.* **2015**, *80*, 10769 – 10776.

[11] F. Li, X. Zou, N. Wang, *Adv. Synth. Catal.* **2015**, *357*, 1405 – 1415.

[12] a) J. Lee, M. Kim, S. Chang, H. Y. Lee, *Org. Lett.* **2009**, *11*, 5598 – 5601; b) E. S. Kim, H. S. Kim, J. N. Kim, *Tetrahedron Lett.* **2009**, *50*, 2973 – 2975; c) E. S. Kim, H. S. Lee, S. H. Kim, J. N. Kim, *Tetrahedron Lett.* **2010**, *51*, 1589 – 1591; d) A. Kiss, Z. Hell, *Tetrahedron Lett.* **2011**, *52*, 6021 – 6023; e) X. Ma, Y. He, Y. Hu, M. Lu, *Tetrahedron Lett.* **2012**, *53*, 449 – 452; f) X. Ma, Y. He, P. Wang, M. Lu, *Appl. Organomet. Chem.* **2012**, *26*, 377 – 382.

[13] In the presence of $[Cp^*IrCl_2]_2$, the reaction of **1a** with acetaldoxime (**2b**) as an alternative water source was performed to give the product **3aa** in 80% yield.

[14] Chang and co-workers proposed a similar mechanism for the hydration of nitriles with aldoximes to amides catalyzed by a Rh complex, see: M. Kim, J. Lee, H. Y. Lee, S. Chang, *Adv. Synth. Catal.* **2009**, *351*, 1807 – 1812 and Ref. [12a].

[15] A. Couture, H. Cornet, P. Grandclaudon, *Synthesis* **1991**, *11*, 1009 – 1010.

[16] X. Chen, T. Chen, F. Ji, Y. Zhou, S. Yin, *Catal. Sci. Technol.* **2015**, *5*, 2197 – 2202.

[17] M. Hour, L. Huang, S. Kuo, Y. Xia, K. Bastow, Y. Nakanishi, E. Hamel, K. Lee, *J. Med. Chem.* **2000**, *43*, 4479 – 4487.

[18] Y. Zhang, M. R. Sheets, E. K. Raja, K. N. Boblak, D. A. Klumpp, *J. Am. Chem. Soc.* **2011**, *133*, 8467 – 8469.

[19] X. Zhang, D. Ye, H. Sun, D. Guo, J. Wang, H. Huang, X. Zhang, H. Jiang, H. Liu, *Green Chem.* **2009**, *11*, 1881 – 1888.

[20] J. Chen, K. Natte, H. Neumann, X. Wu, *Chem. Eur. J.* **2014**, *20*, 16107 – 16110.

[21] Y. Feng, Y. Li, G. Cheng, L. Wang, X. Cui, *J. Org. Chem.* **2015**, *80*, 7099 – 7107.

[22] R. Sharma, A. K. Pandey, P. M. S. Chauhan, *Synlett* **2012**, *23*, 2209 – 2214.

Received: December 19, 2015
Published online on March 16, 2016