Heterogeneous Hydrogenation of Quinoline Derivatives Effected by a Granular Cobalt Catalyst

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- facile and glovebox-free system
- ligand-free approach
- non-precious-metal-based protocol
- inexpensive, non-hazardous reagents

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Abstract We communicate a convenient method for the pressure hydrogenation of quinolines in aqueous solution by using a particulate cobalt-based catalyst that is prepared in situ from simple Co(OAc)₂·4H₂O through reduction with abundant zinc powder. This catalytic protocol permits a brisk and atom-efficient access to a variety of 1,2,3,4-tetrahydroquinolines thereby relying solely on easy-to-handle reagents that are all readily obtained from commercial sources. Both the reaction set-up assembly and the autoclave charging procedure are conducted on the bench outside an inert-gas-operated containment system, thus rendering the overall synthesis time-saving and operationally very simple.

Key words heterogeneous catalysis, hydrogenation, cobalt, zinc, tetrahydroquinolines

1,2,3,4-Tetrahydroquinoline derivatives (THQs) are N-heterocyclic key motifs that are found in a vast array of interesting pharmacologically active compounds and, consequently, their cost-effective and rational syntheses are highly rewarding and sought-after.¹ In this context, the catalytic hydrogenation of the corresponding quinoline derivatives, by either homogeneous or heterogeneous strategies, represents a worthwhile approach for the preparation of the targeted THQ compounds by virtue of the unmitigated atom efficiency of H₂-driven reductions.²

Whereas noble-metal-based homogeneous hydrogenation protocols utilize Rh,³ Ir,⁴ Ru,⁵ Pd,⁶ or Os,⁷ base-metal-related approaches mainly deploy Mn,^{8,9} Fe,^{8,10} Mo,¹¹ or Co^{8,12} (vide infra) as catalytically active metal centers. Regarding cobalt, certain complexes thereof were also demon-

strated to function as transfer hydrogenation catalysts that enable the quinoline reduction by using either formic acid¹³ or the ammonia-borane adduct¹⁴ as hydrogen source. In a similar vein, simple Cu(ClO₄)₂ facilitates the reduction of the given N-heterocycles by employing the oxazaborolidine complex.¹⁵ By contrast, transfer hydrogenation strategies that rely on precious metals utilize Ru,¹⁶ Rh,¹⁷ or Ir¹⁸ coordination compounds as catalysts.

The heterogeneous hydrogenation of quinolines is carried out using again either precious or non-noble metals.¹⁹ With respect to the former, related protocols rely on the deployment of Pd,²⁰ Rh,^{20e,21} Ru,^{20e,22} Ir,^{20e,23} Pt,^{20e,24} or Au,²⁵ whereas non-noble-metal-based strategies are well centered around the implementation of Cu,²⁶ Fe,²⁷ Ni,²⁸ or Co²⁹ in MOF-derived or supported (composite) materials. The latter type of solid catalysts is frequently prepared through pyrolysis of well-defined metal complexes³⁰ that are grafted onto suitable carriers by wet-impregnation prior to thermal heat treatment under an inert gas atmosphere. In this respect, cobalt³¹ plays a dominant role in the manufacture of such nanocomposites by virtue of its good abundance and decent redox activity. Consequently, pyrolytically activated cobalt complexes have also been successfully applied in the related transfer hydrogenation of quinolines.³²

On the other hand, free cobalt nanoparticles³³ have also been shown to bring about the title transformation. However, most of the corresponding protocols entail the use of anhydrous CoX₂ (X = Cl or Br) in combination with moisture- and/or air-sensitive reductants such as LiBHET₃,³⁴ NaBH₄,³⁵ or lithium naphthalenide.³⁶

Interestingly, the popular RANEY® cobalt has not yet been reported to catalyze the reduction of quinolines with H₂ gas,³⁷ whereas the congeneric and significantly more reactive RANEY® nickel does bring about the given reduction, either with gaseous H₂³⁸ or with water as the sole hydrogen source.³⁹ It is worth mentioning here that the kindred

Urushibara-type nickel is a useful catalyst for the deoxygenation of both quinoline *N*-oxides and pyridine *N*-oxides to yield the corresponding untagged *N*-heterocycles.⁴⁰

Strikingly, it was also demonstrated that the non-noble main group metal Ba also efficiently catalyzes the heterogeneous hydrogenation of quinoline to 1,2,3,4-tetrahydroquinoline.⁴¹

Within a slightly different context, a granular catalyst prepared from CoBr₂ and pyrophoric NaBHET₃ was demonstrated to facilitate the heterogeneous hydrogenation of nitriles to afford primary amines.⁴² Quite recently, we reported on a solid cobalt catalyst which was generated in situ through reduction of simple hydrated Co(OAc)₂ with harmless zinc powder and that brought about the same catalytic transformation.⁴³ In order to expand upon the scope of our Co(II)/Zn(0) approach, we initially tested parent quinoline **1a** as substrate for the pertinent heterogeneous hydrogenation reaction.

On applying Co(OAc)₂·4H₂O (5 mol%) and fine Zn dust (50 mol%), we were delighted to promptly observe full conversion of the starting material, resulting in an excellent yield of the desired tetrahydroquinoline **2a** at 70 °C and under H₂ (40 bar) after overnight reaction (Table 1, entry 1). Moreover, GC-MS analyses of the quenched reaction mixture did not indicate the formation of any byproduct.

Encouraged by these initial positive results, we attempted to find milder reaction conditions, while at the same time maintaining decent catalytic activity of the heterogeneous in situ system. As a first step, we aimed to reduce the

Table 1 Optimization of the Reaction Conditions for the Cobalt-Catalyzed Hydrogenation of Quinoline^a

Entry	Co(OAc) ₂ ·4H ₂ O (mol%)	Zn (mol%)	Temp (°C)	H ₂ pressure (bar)	Conv. ^b (%)	Yield ^b (%)
1	5	50	70	40	>99	99
2	5	50	70	30	>99	99
3	5	50	60	30	>99	97
4	5	50	40	30	19	19
5	5	50	rt	30	17	13
6	2.5	25	70	30	>99	99
7	2	20	70	30	65	64
8	5	50	70	20	>99	97
9	2.5	25	70	20	98	95

^a Reaction conditions: **1a** (0.5 mmol), H₂O (1.5 mL).

^b Determined by GC-MS analysis using chlorobenzene as internal standard.

H₂ pressure from 40 bar to 30 bar, which was indeed achieved without any loss of either conversion or yield (Table 1, entry 2). Next, the reaction temperature was gradually decreased from 70 °C to room temperature (entries 2–5) and, rewardingly, the reaction still produced an excellent

Biographical Sketches

Daniel Timelthaler received his B.Sc. in Technical Chemistry at the Johannes Kepler University (JKU) in Linz, Austria in 2016 on synthetic organic chemistry in the group of M. Waser. He

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Christoph Topf studied Technical Chemistry at the Johannes Kepler University (JKU) in Linz, Austria, and received his Diploma (2009) for work with U. Monkowius on coinage metal-NHC complexes. Later, he earned his PhD (2012) under the guidance of G. Knör for the synthesis and characterization

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2016, he returned to Linz where he co-founded the Institute of Catalysis (INCA) at the JKU. Currently, Christoph finishes his habilitation under the mentorship of M. Hapke in the field of non-precious-metal-based redox catalysis.

yield of compound **2a** at a temperature of 60 °C. Further reduction to 40 °C or even to room temperature caused a steep decline of activity, thus rendering these conditions non-suitable for the target transformation.

Deterred by the high metal loadings of 5 mol% Co and 50 mol% Zn, respectively, we consequently performed the model reaction with lower amounts of the Co(II) precursor salt and the zinc additive whilst keeping the Co/Zn ratio constant. Strikingly, full conversion of the benchmark quinoline **1a** and almost quantitative yield of **2a** was also achieved at 70 °C and 30 bar H₂ with a halved amount of the given components, i.e. Co salt (2.5 mol%) and Zn (25 mol%) (entry 6). However, further attempts at reducing the catalyst loading and the H₂ pressure resulted in a significant loss in catalytic activity of our in situ system (entries 7–9).

It is worth mentioning here that, in stark contrast to our previous work on nitrile hydrogenation with a similar catalytic system,⁴³ a tenfold molar excess of the reductant versus Co(II) is necessary to effect full substrate conversion. Corresponding experiments directed at reducing the Co/Zn molar ratio to 1:5 or 1:3 with respect to a Co(II) salt loading of 2.5 mol% resulted in a sharp drop in conversion to 58% and 13%, respectively (see Supporting Information, SI, Table S2, entries 5 and 6). The influence of the ratio of the Co(II) precursor salt and the Zn metal on the catalyst performance is further outlined in a conversion–time diagram (Figure 1). It clearly shows that the conversion of **1a** is brought to completion after a period of 15 hours if the initial Zn loading is doubled (gray trace vs red trace). Interestingly, applying twice the amount of the cobalt salt, whilst keeping the original Zn quantity fixed, does not further expedite the given catalytic transformation (green curve). On the other hand, doubling the Co(II) and the Zn(0) portion simultaneously gives rise to full conversion after a reaction time of only 6 hours (blue trace).

To illustrate the heterogeneous nature of the catalyst described here, we first performed a Hg-poisoning experiment. For this purpose, the pertinent catalytic transformation was conducted in the presence of a few drops of elemental mercury. We did not detect any tetrahydroquinoline **2a**, and it is noteworthy that the reaction solution adopted a pink turbid appearance, which indicated the formation of a Zn–Hg amalgam that effectively prohibited the vital reduction of Co(II) to active Co(0) particles. Furthermore, we conducted Maitlis's hot filtration test⁴⁴ under inert conditions so as to establish the particulate character of the activated catalyst. Accordingly, the hydrogenation of quinoline **1a** was allowed to proceed for 6 hours, whereupon the reaction solution was filtered through a PTFE membrane (0.2 µm pore size). The catalytic transformation was then re-enacted with the obtained clear filtrate and, as expected, the catalytic activity had completely ceased after

Figure 1 Conversion vs time diagram of the Co-catalyzed heterogeneous hydrogenation of quinoline (**1a**) to tetrahydroquinoline (**2a**), showing the influence of catalyst loading and the Co(II)/Zn(0) molar ratio (substrate conversion determined by GC analysis using chlorobenzene as internal standard)

this procedure. Since the active material was fully retained by the filter that was used, the catalyst particles fall outside the nanoscopic scale (1–100 nm).⁴⁵

Next, we decided to study the influence of the reaction medium on the performance of our in situ prepared heterogeneous cobalt catalyst. In this context, a recent report from the groups of Fischmeister and Beller³⁵ communicates the suitability of water as a green and benign solvent for the heterogeneous hydrogenation of quinoline derivatives. Inspired by this finding, we decided to use the same solvent in our initial catalytic experiments described herein. To assess the influence of the reaction medium, we performed the hydrogenation of model compound **1a** in various solvents at 70 °C under H₂ (30 bar) by using Co(OAc)₂·4H₂O (2 mol%) and Zn (20 mol%) (SI, Table S1). Strikingly, under these reaction conditions, the presence of water proved to be indispensable for the Co particles to develop catalytic activity. Neither polar protic solvents such as short-chain alcohols and acetonitrile nor nonpolar toluene enabled the formation of any product **2a**. Regrettably, the same negative result was found for the otherwise excellent solvent THF. For the sake of completeness, we also conducted the catalytic reaction in neat quinoline, but also in this case the amount of 1,2,3,4-tetrahydroquinoline was negligibly small in the reaction mixture (Table S1, entries 1–8).

Having identified water as the best solvent for this Co-based in situ system, we then investigated the influence of various additives on the catalytic activity. With the intention to activate quinoline **1a** through electrophilic interaction, the hydrogenation experiment was run in the presence of the Lewis acids $\text{Zn}(\text{OTf})_2$ or $\text{Al}(\text{OTf})_3$. Surprisingly, both triflates had a deleterious impact on product formation in that we were not able to detect any desired **2a** via GC-MS analysis (SI, Table S1, entries 9 and 10). Addition of a Brønsted acid or base turned out to be unsuitable for the reaction too. It is worth mentioning here that in our previous work on nitrile hydrogenation enabled by a similar catalyst system,⁴³ both ammonia and triflate-based Lewis acids were useful additives that increased the catalyst's activity and curbed the formation of detrimental side products. Regrettably, these positive effects were not reproduced within the cobalt-catalyzed quinoline hydrogenation described herein (entries 11–14).

Additionally, we anticipated that the use of surfactants as emulsifying agents⁴⁶ would expedite the catalytic transformation, since these compounds are supposed to increase the materials exchange between the gas phase and the liquid portion of the reaction mixture. In fact, however, our approaches employing sodium dodecyl sulfate (SDS), polyethylene glycol (PEG), and a commercial detergent failed to improve the catalyst activity (SI, Table S1, entries 15–17).

In light of the forgoing experimental results, we decided to elaborate the catalytic protocol without any further additives, thus rendering the synthetic procedure simple and time-saving.

Subsequently, we probed several Co(II) salts for their aptitude to function as precursors for the in situ generation of the granular metal catalyst. Simple $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ used from the very start provided the best results in terms of substrate conversion and product yield. In contrast, the congeneric $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ and $\text{Co}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}$ were both heavily outperformed by the acetate (SI, Table S2, entries 9 and 10). Anhydrous CoI_2 furnished particles of only minute activity, whereas the solid material derived from CoF_3 and $[\text{Co}(\text{acac})_2]$ did not enable the formation of any tetrahydroquinoline **2a** at all (entries 11–13). Lastly, we carried out blank tests without any Co(II) sources and, as expected, product formation was not observed by GC-MS (entries 19 and 21).

We continued testing different reducing agents for their ability to produce the active Co(0) particles from the respective acetate precursor. While previously reported systems rely on highly reactive but very air- and moisture sensitive reductants such as NaBH_4 ,³⁵ NaBHET_3 ,⁴² LiBHET_3 ,³⁴ LiAlH_4 ,⁴⁷ or lithium naphthalenide³⁶ for the (in situ) preparation of the Co-based catalyst material, we aimed to employ air-stable and easy-to-handle electropositive metals other than zinc. As summarized in the SI, Table S2, the hydrogenation experiments carried out with powdered manganese, magnesium, or iron did not yield any tetrahydro-

quinoline **2a**, although minor conversion of starting material **1a** was observed in all three cases (entries 14–16). It is noteworthy that when the popular reductant sodium dithionite was used, the catalytic activity fully collapsed, because Co(II) was not transformed into Co(0), since the color of the reaction solution remained pink (entry 18). Yet the addition of aluminum enabled the formation of some tetrahydroquinoline product, namely 8% yield, although this value still seriously lagged behind that of the Zn approach (entries 17 and 7).

After the systematic variation of the physical reaction parameters and the additives, we explored the scope and limitations of this heterogeneous Co-based hydrogenation protocol. As summarized in Scheme 1, selected structurally diverse quinolines **1** were neatly converted into the corresponding tetrahydroquinoline products **2** after reaction overnight at 70–150 °C and under H_2 (30 bar), whereby the reaction temperature and the catalyst loading were markedly substrate-dependent. It is worth mentioning here that the isolation of the products was considerably alleviated by the addition of anhydrous Na_2SO_4 to the quenched reaction mixture and subsequent filtration of the thus-obtained suspension over cotton wool, since this procedure removes the water and the catalyst particles in a single step.

The benchmark quinoline **1a** gave rise to an almost quantitative yield of **2a** (96%), and this value was perfectly reproduced when a tenfold or twentyfold amount of starting material was used (Scheme 1). The methyl groups on the pyridine moiety of quinolines **1b–d** necessitated a doubling of the catalyst loading to achieve appreciable product formation. Moreover, the position of the methyl group had a strong impact on the required reaction temperature; the further away the methyl group was from the sp^2 nitrogen of the heterocycle, the more thermal energy had to be applied to maintain a decent product yield. It is important to note that compounds **2b** and **2d** are used as precursors for the manufacture of an antitrypanosomal compound⁴⁸ and a CNS depressant agent,⁴⁹ respectively (Scheme 2). However, it has to be stressed here that the hydrogenation of substrate **1d** afforded a substantial portion of the converse and non-desired 5,6,7,8-tetrahydroquinoline (Scheme 1).

When the methyl substituents were located on the benzene core, the corresponding tetrahydroquinolines **2e–g** were all obtained in excellent yields, all exceeding 95% (Scheme 1). However, twice the amount of catalyst had to be applied when the methyl motif was located at position 7 or 8 of the corresponding quinoline. Quite remarkably, the heterogeneous hydrogenation of ionic *N*-methylquinolinium iodide **1w**, which has the methyl group at position 1, produced significantly lower amounts of the product (23% yield) compared to its neutral congeners **1a–g** (56–97% yield).

Continuing with methoxy-functionalized substrates **1h–j** (Scheme 1), we found that these derivatives gave rise to excellent yields ($\geq 95\%$ throughout) of the corresponding

1,2,3,4-tetrahydroquinolines at 70 °C, which is of significant practical relevance given that compound **2j** is a sought-after precursor to a tubulin polymerization inhibitor (Scheme 2).⁵⁰ Notably, putting a methyl group in immediate spatial proximity to the N atom of the heterocycle diminished the reactivity of **1k** to such an extent that the temperature had to be increased to 130 °C so as to allow sound product formation (Scheme 1).

With respect to halogenated quinolines, the fluoro derivatives **1l–n** were cleanly transformed to the desired semi-hydrogenated N-heterocycles (91–98% yield), but we again observed the deleterious effect of a methyl motif adjacent to the sp² N atom as in the case of **1m** (100 °C for **1m** vs 70 °C for **1l** and **1n**) (Scheme 1). Importantly, the corresponding tetrahydroquinoline product **2m** is the starting material for the synthesis of the antibiotic drug flumequine (Scheme 2).⁵¹ Contrasting with these pleasing results ob-

tained for the fluoro compounds are the reaction outcomes observed for the kindred chloro- and bromo-substituted quinolines **1o–r** (Scheme 1). These derivatives proved to be significantly prone to hydrodehalogenation, which significantly lowered the yields of the products **2o–r** (51–79%). For the haloquinolines **1p**, **1q**, and **1r**, the extent of this detrimental side reaction was only mitigated through the reduction of the Zn loading from 50 mol% to 15 mol% versus the substrate in combination with an increase of the reaction temperature to compensate for the diminished catalyst activity (*vide supra*). At this point it must be emphasized that the given heterogeneous Co-catalyzed hydrogenation of substrates bearing a Cl substituent on any position of the pyridine moiety of the substrate molecule solely afforded pure, non-substituted tetrahydroquinoline **2a** as a result of full dehydrohalogenation.

Scheme 2 Overview of the syntheses of pharmaceutically relevant precursors that are accessible through this cobalt-catalyzed reaction

Aminoquinoline **2s**, with its exposed lone pair on the amine sp³ N atom, turned out to be a rather recalcitrant substrate for the given Co-based hydrogenation protocol (Scheme 1). This is presumably due to the fact that **2s** effectively poisons the catalyst through coordination of the NH₂ group onto the surface of the active particles. This unwanted catalyst deactivation process was, at least to some extent, curbed by the addition of aqueous HCl solution to the reaction mixture.

The presence of aryl groups, as in **1t** and **1u**, was well accommodated by our in situ system, although elevated reaction temperatures had to be applied for full conversion and satisfactory yields of tetrahydroquinolines **2t** and **2u**, whereby the pendent aromatics remained unaffected by the catalytic transformation (Scheme 1). Within a similar context, the hydrogenation of the mixed substrate **1v** demonstrated that the described catalyst system sharply discriminates between quinoline and the structurally very similar isoquinoline motif, whereby the latter remained untouched after hydrogenation.

We were further interested in testing the ability of the Co catalyst to reduce quinolinium *N*-oxide **1x** to the parent quinoline **1a** (Scheme 1), as the former is a common functional group that is encountered in a variety of ring-functionalization processes. Strikingly, the given catalyst selectively oxygenated **1x** to exclusively form quinoline **1a**, with no consecutive reaction leading to 1,2,3,4-tetrahydroquinoline **2a** observed as long as *N*-oxide was present in the reaction mixture. To our regret, this catalytic reaction was sluggish and forced reaction conditions (150 °C) were required for obtaining acceptable yields.

Apart from quinolines, the catalytic system also facilitated the heterogeneous hydrogenation of other N-, O-, and S-heterocycles (Table 2). Especially noteworthy is the hydrogenation of biomass-derived furfural **1ab**, since the reaction outcome was controlled by variation of the temperature, such that either alcohol **2ab** or the exhaustive hydrogenation product **2ab'** was obtained. As expected, the catalytic transformation of thiophene **1ac** to afford tetrahydrothiophene (THT) **2ac** was not successful, owing to the

intrinsic catalyst-poisoning-nature of the S atom; even with a catalyst loading as high as 8 mol% Co(II) no hydrogenation of the S-heterocycle was observed.

Table 2 Cobalt-Catalyzed Heterogeneous Hydrogenation of Selected N-, O-, and S-Heteroarenes other than Quinolines^a

Substrate	Temp (°C)	Product	Yield (%)
1y	150	2y	50
1z	100	2z	97
1aa	120 ^b	2aa	20
1ab	70 ^c	2ab	97
1ab	120 ^b	2ab'	52
1ac	150 ^d	2ac	0

^a Reaction conditions: **1** (0.5 mmol), Co(OAc)₂·4H₂O (5 mol%), Zn (50 mol%), H₂O (1.5 mL), temperature as indicated, H₂ (30 bar), 15 h; yields of isolated products shown.

^b The reaction time amounted to 40 h.

^c Co(OAc)₂·4H₂O (3 mol%) and Zn (30 mol%) were used.

^d Co(OAc)₂·4H₂O (8 mol%) and Zn (80 mol%) were used.

In conclusion, we introduced a user- and eco-friendly heterogeneous catalytic protocol for the hydrogenation of quinolines to yield the corresponding 1,2,3,4-tetrahydroquinolines, some of which are precursors to important biologically active compounds. The method dispenses with the need of any ligands and the selectivity of the given catalytic transformation is readily tuned by way of proper variation of the catalyst loadings and/or the physical reaction parameters. Apart from quinolines, selected N- and O-heterocycles, but not thiophene, are also amenable to hydrogenation mediated by the reported catalytic system.

All chemicals were purchased from Merck (including Sigma-Aldrich), Fluorochem, Acros Organics, Alfa Aesar, BLDPharm, VWR, Roth, TCI, or Chem Lab, whereby all compounds were used as received without further purification. The catalytic hydrogenation reactions were carried out in a 300 mL steel autoclave from Parr Instrument GmbH, while the employed hydrogen was purchased from Linde Gas GmbH with a purity of 5.0. Routine GC-MS analyses were carried out on a Shimadzu GC-MS QP-2020 instrument with helium (5.0 purity from Linde Gas GmbH) as carrier gas. HRMS measurements were performed on an Agilent QTOF 6520 instrument. IR spectroscopy was performed on a Bruker Alpha II spectrophotometer. Melting points were determined on a Büchi M-560 device. NMR measurements were performed on a Bruker Avance III 300 MHz (300 MHz for ¹H, 75.5 MHz for ¹³C) or 500 MHz (470.5 MHz for ¹⁹F) spectrometer. Chemical shifts δ in ppm were calibrated by using the residual nondeuterated solvents as reference for the ¹H and ¹³C NMR spectra.

Quinolines 1u,v by Suzuki–Miyaura Cross-Coupling Reaction; General Procedure

The synthesis was performed in accordance with a published literature protocol.⁵² An oven-dried Schlenk tube was charged with the aryl halide (3.0 mmol) and the boronic acid (3.3 mmol), followed by addition of a 4 M solution of Na₂CO₃ in degassed H₂O (1.5 mL, 6 mmol). Thereafter, the mixture was taken up in degassed THF (6 mL) and Pd(PPh₃)₄ (103 mg, 0.089 mmol) was added before sealing the tube and stirring the solution at 80 °C for 15 h under an argon atmosphere. The mixture was then allowed to reach rt upon which it was diluted with H₂O (5 mL). The quenched solution was extracted thrice with EtOAc (3×), after which the combined organic layers were washed with brine and dried with Na₂SO₄. Subsequent removal of the volatiles under reduced pressure afforded the crude product, which was eventually purified by column chromatography.

6-(Naphthalen-1-yl)quinoline (1u)

6-Bromoquinoline (624 mg, 3.0 mmol) and 1-naphthalenylboronic acid (569 mg, 3.3 mmol) were used following the standard procedure. The crude product appeared as a brown oil and was purified by column chromatography (silica gel, heptane/EtOAc 1:1).

Yield: 601 mg (2.4 mmol, 78%); pale-yellow oil.

IR (KBr): 3043, 1589, 1495, 1394, 1371, 1121, 776 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 8.98 (dd, *J* = 4.2, 1.7 Hz, 1 H, Ar-H), 8.26–8.19 (m, 2 H, Ar-H), 7.98–7.85 (m, 5 H, Ar-H), 7.61–7.41 (m, 5 H, Ar-H).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 150.6, 147.6, 139.3, 139.2, 136.2, 133.8, 132.1, 131.6, 129.2, 128.5, 128.4, 128.3, 128.1, 127.4, 126.3, 126.0, 125.8, 125.4, 121.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₉H₁₄N: 256.11208; found: 256.11267.

3-(Isoquinolin-1-yl)quinoline (1v)

1-Chloroisquinoline (501 mg, 3.06 mmol) and 3-quinolinylboronic acid (571 mg, 3.30 mmol) were used, following the general procedure. The crude product appeared as a brown oil and was purified by column chromatography (silica gel, heptane/EtOAc 1:1).

Yield: 695 mg (2.7 mmol, 89%); white amorphous powder; mp 93–91 °C.

IR (KBr): 3055, 1618, 1533, 1492, 1389, 1313, 837, 747, 677 cm⁻¹.

^1H NMR (300 MHz, CDCl_3 , 20 °C): δ = 9.29 (d, J = 2.2 Hz, 1 H, Ar-H), 8.69 (d, J = 5.7 Hz, 1 H, Ar-H), 8.53 (d, J = 2.0 Hz, 1 H, Ar-H), 8.23 (d, J = 8.5 Hz, 1 H, Ar-H), 8.11 (d, J = 8.4 Hz, 1 H, Ar-H), 7.98–7.91 (m, 2 H, Ar-H), 7.85–7.70 (m, 3 H, Ar-H), 7.66–7.56 (m, 2 H, Ar-H).

^{13}C NMR (75.5 MHz, CDCl_3 , 20 °C): δ = 157.6, 151.4, 148.1, 142.7, 137.2, 137.1, 132.7, 130.5, 130.3, 129.6, 128.4, 128.0, 127.7, 127.4, 127.3, 127.1, 127.0, 120.7.

HRMS (ESI): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2$: 257.10732; found: 257.10771.

Tetrahydroquinolines 2 by Catalytic Hydrogenation; General Procedure

Without any protection from air, a 4 mL glass vial was initially charged with a magnetic stirring bar, the cobalt(II) salt (0.0125–0.04 mmol), and finely powdered Zn metal (0.075–0.4 mmol). After that, **1** (0.5 mmol) and the solvent (1.5 mL) were added. The vial was then sealed with a septum cap, which was subsequently penetrated with a steel cannula. The thus-prepared reaction vessel was then placed in a drilled Al-plate with a capacity to accommodate seven vials. Hereafter, this Al-inlay was transferred into the pressure tank which was then tightly sealed. The autoclave was then flushed with H_2 gas (3 $\times$ 30 bar) before being pressurized to the required value. After that, the autoclave was put on a stirring plate and heated to the required reaction temperature. On completion of the reaction, the autoclave was allowed to reach rt, upon which the H_2 pressure was released. Chlorobenzene (20 mg) served as a standard and was added to each of the reaction vials, followed by EtOH (2 mL) to ensure homogeneity of the reaction mixture. Thereafter, the solutions were degassed by gentle stirring in air for a period of 10 min, upon which an aliquot of 40 μL was taken from each vial; EtOH (0.5 mL) was added and the solutions were eventually analyzed by GC. In cases where the product was isolated, no standard was added in order not to compromise the purification process.

Procedure A: $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (3.1 mg, 0.0125 mmol, 2.5 mol%) and Zn (8.2, 0.125 mmol, 25 mol%) were used.

Procedure B: $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (6.2 mg, 0.025 mmol, 5 mol%) and Zn (16.3 mg, 0.25 mmol, 50 mol%) were used.

Procedure C: $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (6.2 mg, 0.025 mmol, 5 mol%) and Zn (4.9 mg, 0.075 mmol, 15 mol%) were used.

Isolation of the Hydrogenation Products 2; General Procedure

The aqueous-ethanolic product solution was transferred to a 25 mL round-bottomed flask whereupon EtOAc (5 mL) was added. The H_2O was removed from the mixture upon addition of solid anhydrous Na_2SO_4 . After that, the suspension was filtered over a plug of cotton to remove all solids from the mixture. Importantly, the finely dispersed catalyst particles were trapped within the Na_2SO_4 slurry and therefore the former were separated concurrently with the desiccation step. The volatiles were then removed under reduced pressure, leaving behind the product either as a solid or an oily substance. If incomplete conversion or side-product formation was observed, subsequent purification by column chromatography (silica gel) afforded the pure product.

Scale-up Experiment

A 100 mL baker was charged with a magnetic stirring bar, $\text{Co}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (0.25 mmol), and finely powdered Zn metal (2.5 mmol), after which quinoline (**1a**; 10 mmol) and H_2O (40 mL) were added. The baker was covered with Al foil, that was subsequently penetrated with three steel pins. The thus-prepared reaction vessel

was then transferred into the autoclave which was then tightly sealed. The autoclave was then flushed with H_2 gas (3 $\times$ 30 bar) before being pressurized to 30 bar H_2 . After that, the autoclave was placed on a stirring plate and heated to 70 °C. After 15 h, the autoclave was allowed to reach rt, at which the remaining H_2 gas was released. Thereafter, the reaction mixture was degassed by gently stirring in air for a period of 10 min. Then the two-phase mixture was transferred into a separating funnel, where the product was extracted with EtOAc (3 $\times$). The combined organic layers were dried over Na_2SO_4 and then the solvent was removed in vacuo, leaving behind product **2a** as a yellow oil; yield: 96%.

Safety Statement Concerning High-Pressure Hydrogenation

The H_2 pressure steel cylinder (200 bar, 50 L) was placed in a safety storage cabinet equipped with an installed tapping unit while the gas container was connected to a control panel that allowed for fine adjustment of the H_2 pressure used for the hydrogenation reactions. The autoclave charging procedure was performed in a fume hood that was equipped with a sensor that was wired to a magnetic valve. The latter instantaneously stops the gas supply in case of any H_2 leakage that might occur during the filling procedure. Furthermore, both optical and acoustic alarm signals are triggered whenever free flammable gas is detected inside the hood.

1,2,3,4-Tetrahydroquinoline (2a)

The title compound was synthesized according to procedure A from **1a** (63.6 mg, 0.49 mmol).

Yield: 63.0 mg (0.47 mmol, 96%); pale yellow oil, turns brown in air.

IR (KBr): 3403, 2925, 2839, 1605, 1495, 1309, 742 cm^{-1} .

^1H NMR (300 MHz, CDCl_3 , 20 °C): δ = 7.06–6.97 (m, 2 H, Ar-H), 6.67 (t, J = 7.3 Hz, 1 H, Ar-H), 6.52 (d, J = 7.9 Hz, 1 H, Ar-H), 3.85 (s, 1 H, N-H), 3.34 (t, J = 5.5 Hz, 2 H, CH_2), 2.82 (t, J = 6.4 Hz, 2 H, CH_2), 2.04–1.93 (m, 2 H, CH_2).

^{13}C NMR (75.5 MHz, CDCl_3 , 20 °C): δ = 144.8, 129.6, 126.8, 121.5, 117.0, 114.2, 42.0, 27.0, 22.2.

HRMS (ESI): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_9\text{H}_{12}\text{N}$: 134.09643; found: 134.09630.

2-Methyl-1,2,3,4-tetrahydroquinoline (2b)

The title compound was synthesized according to procedure A from **1b** (70.8 mg, 0.49 mmol).

Yield: 67.0 mg (0.46 mmol, 92%); yellow oil, turns brown in air.

IR (KBr): 3390, 2961, 2923, 2843, 1607, 1486, 1307, 742 cm^{-1} .

^1H NMR (300 MHz, CDCl_3 , 20 °C): δ = 7.07–6.99 (m, 2 H, Ar-H), 6.68 (td, J = 7.3, 0.8 Hz, 1 H, Ar-H), 6.56–6.50 (m, 1 H, Ar-H), 3.77 (s, 1 H, N-H), 3.52–3.39 (m, 1 H, CH), 2.99–2.74 (m, 2 H, CH_2), 2.05–1.93 (m, 1 H, CH_2), 1.73–1.58 (m, 1 H, CH_2), 1.27 (d, J = 6.3 Hz, 3 H, CH_3).

^{13}C NMR (75.5 MHz, CDCl_3 , 20 °C): δ = 144.8, 129.3, 126.7, 121.1, 117.0, 114.1, 47.2, 30.2, 26.6, 22.6.

HRMS (ESI): m/z [$\text{M} + \text{H}$] $^+$ calcd for $\text{C}_{10}\text{H}_{14}\text{N}$: 148.11208; found: 148.11219.

3-Methyl-1,2,3,4-tetrahydroquinoline (2c)

The title compound was synthesized according to procedure B from **1c** (78.1 mg, 0.55 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 20:1).

Yield: 65.2 mg (0.44 mmol, 81%); colorless oil, turns brown in air.

IR (KBr): 3407, 2952, 2912, 2831, 1606, 1493, 1281, 742 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.06–6.96 (m, 2 H, Ar-H), 6.66 (td, *J* = 7.3, 0.8 Hz, 1 H, Ar-H), 6.52 (d, *J* = 7.8 Hz, 1 H, Ar-H) 3.85 (s, 1 H, N-H), 3.36–3.24 (m, 1 H, CH₂), 2.99–2.88 (m, 1 H, CH₂), 2.88–2.77 (m, 1 H, CH₂), 2.55–2.71 (m, 1 H, CH₂), 2.20–2.01 (m, 1 H, CH), 1.10 (d, *J* = 6.6 Hz, 3 H, CH₃).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 144.4, 129.6, 126.8, 121.1, 116.9, 113.9, 48.0, 35.5, 27.2, 19.1.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11214.

4-Methyl-1,2,3,4-tetrahydroquinoline (2d)

The title compound was synthesized according to procedure B from **1d** (72.6 mg, 0.51 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 10:1, 2% triethylamine).

Yield: 41.6 mg (0.28 mmol, 56%); colorless oil, turns brown in air.

IR (KBr): 3405, 2955, 2923, 2852, 1605, 1497, 1313, 740 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.12–7.05 (m, 1 H, Ar-H), 7.03–6.95 (m, 1 H, Ar-H), 6.66 (td, *J* = 7.4, 1.2 Hz, 1 H, Ar-H), 6.50 (dd, *J* = 8.0, 1.1 Hz, 1 H, Ar-H), 3.86 (s, 1 H, N-H), 3.41–3.24 (m, 2 H, CH₂) 2.94 (sext, *J* = 6.3 Hz, 1 H, CH), 2.08–1.94 (m, 1 H, CH₂), 1.77–1.64 (m, 1 H, CH₂), 1.32 (d, *J* = 7.0 Hz, 3 H, CH₃).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 144.3, 128.5, 126.8, 126.7, 117.0, 114.2, 39.1, 30.3, 30.0, 22.7.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11204.

4-Methyl-5,6,7,8-tetrahydroquinoline (2d')

Synthesized according to procedure B from **1d** (72.6 mg, 0.507 mmol) and purified by column chromatography (silica gel, heptane/EtOAc 1:1, 2% triethylamine).

Yield: 17.8 mg (0.12 mmol, 24%); colorless oil, turns brown in air.

IR (KBr): 3379, 2930, 2858, 1587, 1435, 824 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 8.21 (d, *J* = 4.8 Hz, 1 H, Ar-H), 6.88 (d, *J* = 4.8 Hz, 1 H, Ar-H), 2.96–2.85 (m, 2 H, CH₂), 2.68–2.57 (m, 2 H, CH₂), 2.20 (s, 3 H, CH₃), 1.91–1.78 (m, 4 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 156.8, 146.3, 145.8, 131.2, 122.7, 33.1, 25.9, 23.0, 23.0, 19.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11204.

6-Methyl-1,2,3,4-tetrahydroquinoline (2e)

The title compound was prepared according to procedure A from **1e** (71.2 mg, 0.497 mmol).

Yield: 70.0 mg (0.48 mmol, 96%); yellow oil, turns brown in air.

IR (KBr): 3397, 2922, 2840, 1619, 1500, 1301, 806 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.88–6.77 (m, 2 H, Ar-H), 6.46 (d, *J* = 8.5 Hz, 1 H, Ar-H), 3.71 (s, 1 H, N-H), 3.31 (t, *J* = 5.3 Hz, 2 H, CH₂), 2.79 (t, *J* = 6.4 Hz, 2 H, CH₂), 2.27 (s, 3 H, CH₃), 1.98 (quint, *J* = 5.7 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 142.5, 130.1, 127.3, 126.3, 121.6, 114.5, 42.2, 27.0, 22.5, 20.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11225.

7-Methyl-1,2,3,4-tetrahydroquinoline (2f)

The title compound was synthesized according to procedure B from **1f** (70.5 mg, 0.49 mmol).

Yield: 69.3 mg (0.47 mmol, 96%); yellow oil, turns brown in air.

IR (KBr): 3399, 2922, 2840, 1618, 1489, 1309, 788 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.91 (d, *J* = 7.6 Hz, 1 H, Ar-H), 6.51 (d, *J* = 7.8 Hz, 1 H, Ar-H), 6.37 (s, 1 H, Ar-H), 3.75 (s, 1 H, N-H), 3.34 (t, *J* = 5.5 Hz, 2 H, CH₂) 2.80 (t, *J* = 6.4 Hz, 2 H, CH₂), 2.30 (s, 3 H, CH₃), 2.05–1.94 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 144.6, 136.4, 129.4, 118.6, 117.9, 114.8, 42.1, 26.7, 22.4, 21.2.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11241.

8-Methyl-1,2,3,4-tetrahydroquinoline (2g)

The title compound was prepared according to procedure B from **1g** (701.7 mg, 0.50 mmol).

Yield: 71.3 mg (0.48 mmol, 97%); yellow oil, turns brown in air.

IR (KBr): 3423, 2925, 2841, 1598, 1481, 1307, 754, 732 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.97 (t, *J* = 7.5 Hz, 2 H, Ar-H), 6.67 (t, *J* = 7.4 Hz, 1 H, Ar-H), 3.69 (s, 1 H, N-H), 3.47 (t, *J* = 5.4 Hz, 2 H, CH₂), 2.90 (t, *J* = 6.3 Hz, 2 H, CH₂), 2.18 (s, 3 H, CH₃), 2.05 (quint, *J* = 6.0 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 142.7, 127.9, 127.4, 121.2, 120.9, 116.4, 42.4, 27.3, 22.2, 17.2.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11234.

3-Methoxy-1,2,3,4-tetrahydroquinoline (2h)

The title compound was synthesized following procedure B from **1h** (80.0 mg, 0.503 mmol).

Yield: 79.3 mg (0.49 mmol, 97%); yellow oil, turns brown in air.

IR (KBr): 3423, 2925, 2841, 1598, 1481, 1307, 754, 732 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.07–6.96 (m, 2 H, Ar-H), 6.68 (t, *J* = 7.3 Hz, 1 H, Ar-H), 6.53 (d, *J* = 8.0 Hz, 1 H, Ar-H), 3.93–3.72 (m, 2 H, N-H, CH), 3.53–3.40 (m, 4 H, CH₃, CH₂), 3.23 (dd, *J* = 11.0, 7.2 Hz, 1 H, CH₂), 3.06 (dd, *J* = 16.0, 4.0 Hz, 1 H, CH₂), 2.84 (dd, *J* = 16.0, 7.0 Hz, 1 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 143.9, 130.0, 127.0, 118.9, 117.5, 114.0, 72.7, 56.2, 45.2, 32.7.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄NO: 164.10699; found: 164.10667.

5-Methoxy-1,2,3,4-tetrahydroquinoline (2i)

The title compound was prepared following procedure B from **1i** (79.2 mg, 0.50 mmol).

Yield: 77.3 mg (0.474 mmol, 95%); pale-yellow oil, turns brown in air.

IR (KBr): 3401, 2937, 2835, 1589, 1492, 1346, 1239, 1120, 761, 707 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.98 (t, *J* = 8.1 Hz, 1 H, Ar-H), 6.23 (dd, *J* = 19.9, 8.1 Hz, 2 H, Ar-H), 3.84 (s, 4 H, N-H, CH₃), 3.28 (t, *J* = 5.3 Hz, 2 H, CH₂), 2.71 (t, *J* = 6.5 Hz, 2 H, CH₂), 1.97 (quint, *J* = 5.9 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 158.0, 145.9, 126.7, 109.8, 107.7, 99.2, 55.3, 41.6, 22.0, 20.6.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₀H₁₄NO: 164.10699; found: 164.10665.

6-Methoxy-1,2,3,4-tetrahydroquinoline (2j)

The title compound was synthesized according to procedure B from **1j** (80.0 mg, 0.503 mmol).

Yield: 81.0 mg (0.50 mmol, 99%); pale-yellow oil, turns brown in air.

IR (KBr): 3387, 2928, 2831, 1503, 1251, 1230, 1037, 804 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.66–6.57 (m, 2 H, Ar-H), 6.47 (d, J = 8.4 Hz, 1 H, Ar-H), 3.75 (s, 3 H, CH₃), 3.70 (s, 1 H, N-H), 3.26 (t, J = 5.5 Hz, 2 H, CH₂), 2.78 (t, J = 6.5 Hz, 2 H, CH₂), 2.00–1.90 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 151.8, 138.9, 122.9, 115.6, 114.9, 112.9, 55.8, 42.3, 27.2, 22.4.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₀H₁₄NO: 164.10699; found: 164.10678.

6-Methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (2k)

The title compound was synthesized following procedure B from **1k** (85.9 mg, 0.496 mmol).

Yield: 84.8 mg (0.478 mmol, 96%); pale-yellow oil, turns brown in air.

IR (KBr): 3374, 2928, 2831, 1499, 1236, 1151, 1037, 804 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.65–6.57 (m, 2 H, Ar-H), 6.47 (d, J = 8.2 Hz, 1 H, Ar-H), 3.75 (s, 3 H, CH₃), 3.58 (s, 1 H, N-H), 3.42–3.27 (m, 1 H, CH), 3.95–3.79 (m, 1 H, CH₂), 3.79–3.66 (m, 1 H, CH₂), 2.00–1.87 (m, 1 H, CH₂), 1.69–1.51 (m, 1 H, CH₂), 1.21 (d, J = 6.3 Hz, 3 H, CH₃).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 151.9, 138.9, 122.5, 115.4, 114.7, 112.9, 55.8, 47.5, 30.3, 26.9, 22.6.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₁H₁₆NO: 178.12264; found: 178.12263.

6-Fluoro-1,2,3,4-tetrahydroquinoline (2l)

The title compound was synthesized according to procedure B from **1l** (73.7 mg, 0.50 mmol).

Yield: 74.1 mg (0.49 mmol, 98%); pale-yellow oil, turns brown in air.

IR (KBr): 3399, 2929, 2844, 1501, 1247, 1221, 1190, 1140, 804 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.75–6.63 (m, 2 H, Ar-H), 6.40 (q, J = 4.5 Hz, 1 H, Ar-H), 3.70 (s, 1 H, N-H), 3.27 (t, J = 5.3 Hz, 2 H, CH₂), 2.75 (t, J = 6.2 Hz, 2 H, CH₂), 1.93 (q, J = 5.8 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 155.4 (d, J = 234.5 Hz, 1C), 141.0 (d, J = 1.8 Hz, 1C), 122.8 (d, J = 6.7 Hz, 1C), 115.6 (d, J = 21.5 Hz, 1C), 115.0 (d, J = 7.6 Hz, 1C), 113.2 (d, J = 22.4 Hz, 1C), 42.1, 27.1 (d, J = 0.9 Hz, 1C), 22.0.

¹⁹F NMR (470.5 MHz, CDCl₃, 20 °C): δ = –128.4.

HRMS (ESI): m/z [M + H]⁺ calcd for C₉H₁₁FN: 152.08700; found: 152.08753.

6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (2m)

The title compound was prepared following procedure B from **1m** (80.5 mg, 0.50 mmol).

Yield: 75.3 mg (0.46 mmol, 91%); pale-yellow oil, turns brown in air.

IR (KBr): 3397, 2963, 2926, 2847, 1407, 1230, 1141, 803 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.74–6.64 (m, 2 H, Ar-H), 6.44–6.37 (m, 1 H, Ar-H), 3.59 (s, 1 H, N-H), 3.42–3.29 (m, 1 H, CH), 2.91–2.77 (m, 1 H, CH₂), 2.77–2.65 (m, 1 H, CH₂), 1.98–1.86 (m, 1 H, CH₂), 1.65–1.47 (m, 1 H, CH₂), 1.21 (d, J = 6.2 Hz, 3 H, CH₃).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 155.6 (d, J = 234.4 Hz, 1C), 141.1 (d, J = 1.6 Hz, 1C), 122.6 (d, J = 6.7 Hz, 1C), 115.5 (d, J = 21.6 Hz, 1C), 114.8 (d, J = 7.5 Hz, 1C), 113.3 (d, J = 22.4 Hz, 1C), 47.4, 30.0, 26.8 (d, J = 1.1 Hz, 1C), 22.6.

¹⁹F NMR (470.5 MHz, CDCl₃, 20 °C): δ = –128.3.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₀H₁₃FN: 166.10265; found: 166.10268.

8-Fluoro-1,2,3,4-tetrahydroquinoline (2n)

The title compound was synthesized according to procedure A from **1n** (75.8 mg, 0.52 mmol).

Yield: 70.9 mg (0.469 mmol, 91%); pale-yellow oil, turns brown in air.

IR (KBr): 3424, 2929, 2841, 1624, 1499, 1316, 1232, 758, 719 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.89–6.73 (m, 2 H, Ar-H), 6.59–6.47 (m, 1 H, Ar-H), 4.00 (s, 1 H, N-H), 3.36 (t, J = 5.5 Hz, 2 H, CH₂), 2.81 (t, J = 6.4 Hz, 2 H, CH₂), 2.04–1.93 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 160.0 (d, J = 237.7 Hz, 1C), 133.3 (d, J = 12.2 Hz, 1C), 124.6 (d, J = 2.9 Hz, 1C), 123.7 (d, J = 3.8 Hz, 1C), 115.6 (d, J = 7.5 Hz, 1C), 112.2 (d, J = 18.2 Hz, 1C), 41.3, 26.6 (d, J = 3.1 Hz, 1C), 21.9.

¹⁹F NMR (470.5 MHz, CDCl₃, 20 °C): δ = –139.0.

HRMS (ESI): m/z [M + H]⁺ calcd for C₉H₁₁FN: 152.08700; found: 152.08810.

5-Chloro-1,2,3,4-tetrahydroquinoline (2o)

The title compound was synthesized according to procedure B from **1o** (80.7 mg, 0.49 mmol) and then purified by column chromatography (silica gel, heptane/DCM, 10:1).

Yield: 41.8 mg (0.25 mmol, 51%); colorless oil, turns brown in air.

IR (KBr): 3414, 2947, 2928, 2856, 2840, 1596, 1487, 1303, 761 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.87 (t, J = 7.9 Hz, 1 H, Ar-H), 6.67 (dd, J = 7.9, 1.0 Hz, 1 H, Ar-H), 6.36 (dd, J = 8.0, 1.0 Hz, 1 H, Ar-H), 3.94 (s, 1 H, N-H), 3.26 (t, J = 5.5 Hz, 2 H, CH₂), 2.78 (t, J = 6.6 Hz, 2 H, CH₂), 2.02–1.90 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 146.5, 135.0, 127.2, 119.4, 117.6, 112.6, 41.5, 24.8, 22.0.

HRMS (ESI): m/z [M + H]⁺ calcd for C₉H₁₁ClN: 168.05745; found: 168.05775.

6-Chloro-1,2,3,4-tetrahydroquinoline (2p)

The title compound was synthesized according to procedure C from **1p** (81.5 mg, 0.498 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 10:1, 5% triethylamine).

Yield: 65.1 mg (0.39 mmol, 78%); colorless oil, turns brown in air.

IR (KBr): 3414, 2927, 2840, 1600, 1493, 1298, 804 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 6.92–6.86 (m, 2 H, Ar-H), 6.41–6.39 (m, 1 H, Ar-H), 3.85 (s, 1 H, N-H), 3.28 (t, J = 5.5 Hz, 2 H, CH₂), 2.72 (t, J = 6.4 Hz, 2 H, CH₂), 1.96–1.86 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 143.3, 129.2, 126.6, 123.1, 121.4, 115.3, 42.0, 27.0, 21.8.

HRMS (ESI): m/z [M + H]⁺ calcd for C₉H₁₁ClN: 168.05745; found: 168.05724.

8-Chloro-1,2,3,4-tetrahydroquinoline (2q)

The title compound was prepared according to procedure C from **1q** (81.5 mg, 0.498 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 20:1, 2% triethylamine).

Yield: 65.9 mg (0.39 mmol, 79%); colorless oil, turns brown in air.

IR (KBr): 3423, 2929, 2839, 1601, 1498, 1298, 754, 720 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.07 (t, *J* = 7.9 Hz, 1 H, Ar-H), 6.86 (d, *J* = 7.4 Hz, 1 H, Ar-H), 6.52 (t, *J* = 7.7 Hz, 1 H, Ar-H), 4.42 (s, 1 H, N-H), 3.44–3.35 (m, 2 H, CH₂), 2.79 (t, *J* = 6.4 Hz, 2 H, CH₂), 2.00–1.89 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 140.8, 127.8, 126.9, 122.7, 118.2, 116.4, 41.9, 27.3, 21.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₉H₁₁ClN: 168.05745; found: 168.05772.

6-Bromo-1,2,3,4-tetrahydroquinoline (2r)

The title compound was synthesized according to procedure C from **1r** (103.5 mg, 0.50 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 10:1).

Yield: 60.7 mg (0.29 mmol, 58%); colorless oil, turns brown in air.

IR (KBr): 3415, 2926, 2839, 1597, 1491, 1296, 802 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.08–6.99 (m, 2 H, Ar-H), 6.33 (d, *J* = 8.2 Hz, 1 H, Ar-H), 3.85 (s, 1 H, N-H), 3.28 (t, *J* = 5.5 Hz, 2 H, CH₂), 2.72 (t, *J* = 6.4 Hz, 2 H, CH₂), 1.96–1.86 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 143.7, 132.0, 129.4, 123.6, 115.7, 108.0, 41.9, 26.9, 21.8.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₉H₁₁BrN: 212.00694; found: 212.00690.

2-Phenyl-1,2,3,4-tetrahydroquinoline (2t)

The title compound was synthesized according to procedure B from **1t** (100.0 mg, 0.49 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 100:1).

Yield: 72.7 mg (0.35 mmol, 71%); colorless oil, turns brown in air.

IR (KBr): 3400, 3025, 2922, 2841, 1606, 1479, 1309, 743, 698 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.45–7.27 (m, 5 H, Ar-H), 7.08–6.98 (m, 2 H, Ar-H), 6.67 (t, *J* = 7.4 Hz, 1 H, Ar-H), 6.56 (d, *J* = 7.9 Hz, 1 H, Ar-H), 4.46 (dd, *J* = 9.2, 3.3 Hz, 1 H, CH), 4.05 (s, 1 H, N-H), 3.02–2.87 (m, 1 H, CH₂), 2.82–2.69 (m, 1 H, CH₂), 2.20–2.09 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 144.9, 144.8, 129.4, 128.7, 127.6, 127.0, 126.7, 121.0, 117.3, 114.1, 56.4, 31.1, 26.5.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₅H₁₆N: 210.12773; found: 210.12762.

6-(Naphthalen-1-yl)-1,2,3,4-tetrahydroquinoline (2u)

The title compound was synthesized according to procedure B from **1u** (113.1 mg, 0.44 mmol).

Yield: 113.5 mg (0.44 mmol, 99%); yellow oil, turns brown in air.

IR (KBr): 3405, 3042, 2925, 2838, 1732, 1611, 1503, 1352, 1301, 776 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 8.09 (d, *J* = 8.2 Hz, 1 H, Ar-H), 7.92 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.84 (d, *J* = 8.1 Hz, 1 H, Ar-H), 7.57–7.41 (m, 4 H, Ar-H), 7.21–7.14 (m, 2 H, Ar-H), 6.69 (d, *J* = 8.3 Hz, 1 H, Ar-H), 4.14 (s, 1 H, N-H), 4.11 (t, *J* = 5.5 Hz, 2 H, CH₂), 2.88 (t, *J* = 6.3 Hz, 2 H, CH₂), 2.05 (quint, *J* = 6.0 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 143.5, 140.7, 134.0, 132.0, 131.3, 130.0, 128.6, 128.3, 126.9, 126.8, 126.5, 125.8, 125.7, 125.6, 121.8, 114.6, 42.3, 27.0, 22.2.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₉H₁₈N: 260.14338; found: 260.14355.

3-(Isoquinolin-1-yl)-1,2,3,4-tetrahydroquinoline (2v)

The title compound was synthesized according to procedure B from **1v** (126.8 mg, 0.495 mmol).

Yield: 63.9 mg (0.25 mmol, 50%); white amorphous powder; mp 107–109 °C.

IR (KBr): 3394, 3010, 2922, 2818, 1579, 1494, 1310, 1250, 834, 753, 431 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 8.53 (d, *J* = 5.7 Hz, 1 H, Ar-H), 8.28 (d, *J* = 8.4 Hz, 1 H, Ar-H), 7.86 (d, *J* = 7.8 Hz, 1 H, Ar-H), 7.73–7.66 (m, 1 H, Ar-H), 7.65–7.52 (m, 2 H, Ar-H), 7.12–7.00 (m, 2 H, Ar-H), 6.74–6.60 (m, 2 H, Ar-H), 4.25–4.03 (m, 2 H, CH, N-H), 3.74 (t, *J* = 10.9 Hz, 1 H, CH₂), 3.66–3.57 (m, 1 H, CH₂), 3.52–3.37 (m, 1 H, CH₂), 3.06 (dq, *J* = 16.1, 2.1 Hz, 1 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 162.3, 144.3, 142.2, 136.4, 129.9, 129.7, 127.7, 127.4, 127.1, 126.8, 124.6, 121.8, 119.6, 117.2, 114.3, 47.1, 36.0, 33.9.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₈H₁₇N₂: 261.13862; found: 261.13887.

1-Methyl-1,2,3,4-tetrahydroquinoline (2w)

The title compound was synthesized according to procedure B from **1w** (134.2 mg, 0.50 mmol) in a mixture of H₂O/MeOH (1:1); the product was obtained by subsequent extraction with heptane.

Yield: 16.5 mg (0.112 mmol, 23%); pale-yellow oil.

IR (KBr): 2926, 1601, 1498, 1320, 1207, 741 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.12–7.04 (m, 1 H, Ar-H), 7.00–6.93 (m, 1 H, Ar-H), 6.66–6.57 (m, 2 H, Ar-H), 3.23 (t, *J* = 5.6 Hz, 2 H, CH₂), 2.89 (s, 3 H, CH₃), 2.78 (t, *J* = 6.5 Hz, 2 H, CH₂), 2.04–1.93 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 146.9, 128.9, 127.2, 123.0, 116.3, 111.1, 51.4, 39.3, 27.9, 22.6.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₀H₁₄N: 148.11208; found: 148.11203.

Quinoline (1a)

The title compound was synthesized according to procedure B from **1x** (66.6 mg, 0.46 mmol).

Yield: 26.4 mg (0.20 mmol, 45%); yellow oil.

IR (KBr): 3396, 3057, 3037, 1500, 1314, 1118, 802, 784 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 8.91 (dd, *J* = 4.2, 1.4 Hz, 1 H, Ar-H), 8.17–8.07 (m, 2 H, Ar-H), 7.80 (dd, *J* = 8.1, 1.2 Hz, 1 H, Ar-H), 7.74–7.67 (m, 1 H, Ar-H), 7.57–7.49 (m, 1 H, Ar-H), 7.38 (dd, *J* = 4.2, 4.2 Hz, 1 H, Ar-H).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 150.5, 148.4, 136.2, 129.6, 129.5, 128.4, 127.9, 126.6, 121.2.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₉H₈N: 130.06513; found: 130.06520.

Indoline (2y)

The title compound was prepared according to procedure B from **1y** (57.3 mg, 0.49 mmol) and then purified by column chromatography (silica gel, heptane/EtOAc 5:1).

Yield: 28.9 mg (0.24 mmol, 50%); yellow oil, turns brown in air.

IR (KBr): 3408, 3052, 2925, 2851, 1606, 1485, 1455, 740 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.13 (d, *J* = 7.3 Hz, 1 H, Ar-H), 7.07–6.98 (m, 1 H, Ar-H), 6.75–6.63 (m, 2 H, Ar-H), 3.56 (t, *J* = 8.4 Hz, 2 H, CH₂), 3.04 (t, *J* = 8.4 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 151.7, 129.4, 127.3, 124.7, 118.8, 109.6, 47.4, 30.0.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₈H₁₀N: 120.08078; found: 120.08121.

1,2,3,4-Tetrahydro-1,5-naphthyridine (2z)

The title compound was prepared according to procedure A from **1z** (65.9 mg, 0.51 mmol).

Yield: 66.2 mg (0.49 mmol, 97%); white-yellow powder; mp 112–114 °C.

IR (KBr): 3225, 2949, 2931, 2833, 1579, 1454, 1297, 1268, 791, 731 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.77 (dd, *J* = 4.7, 1.2 Hz, 1 H, Ar-H), 6.80 (dd, *J* = 8.1, 4.7 Hz, 1 H, Ar-H), 6.64 (dd, *J* = 8.1, 1.3 Hz, 1 H, Ar-H), 4.36 (s, 1 H, N-H), 3.21 (t, *J* = 5.5 Hz, 2 H, CH₂), 2.85 (t, *J* = 6.5 Hz, 2 H, CH₂), 1.99–1.88 (m, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 142.5, 141.0, 137.5, 121.9, 120.2, 41.4, 30.2, 21.6.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₈H₁₁N₂: 135.09167; found: 135.09183.

2,3-Dihydrobenzofuran (2aa)

The title compound was synthesized according to procedure B from **1aa** (58.9 mg, 0.50 mmol) and then purified by column chromatography (silica gel, pentane/DCM 1:1).

Yield: 12.2 mg (0.10 mmol, 20%); colorless oil.

IR (KBr): 2923, 2853, 1597, 1483, 1461, 1227, 983, 746 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.23–7.17 (m, 1 H, Ar-H), 7.15–7.07 (m, 1 H, Ar-H), 6.88–6.75 (m, 2 H, Ar-H), 4.56 (t, *J* = 8.6 Hz, 2 H, CH₂), 3.21 (t, *J* = 8.7 Hz, 2 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 160.1, 128.1, 127.0, 125.0, 120.5, 109.5, 71.1, 29.9.

HRMS (ESI): product not detected; MS (EI): *m/z* = 120, 91, 65, 63, 51, 39.

Furan-2-ylmethanol (2ab)

The title compound was prepared from **1ab** (47.8 mg, 0.50 mmol) and Co(OAc)₂·4H₂O (3 mol%) and Zn (30 mol%).

Yield: 47.5 mg (0.48 mmol, 97%); pale-yellow liquid.

IR (KBr): 3327, 2929, 2873, 1504, 1147, 1008, 913, 791 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 7.37 (dd, *J* = 1.8, 0.7 Hz, 1 H, Ar-H), 6.34–6.28 (m, 1 H, Ar-H), 6.28–6.22 (m, 1 H, Ar-H), 4.54 (s, 2 H, CH₂), 2.78 (s, 1 H, O-H).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 154.2, 142.6, 110.4, 107.8, 57.3.

HRMS (ESI): product not detected; MS (EI): *m/z* = 98, 81, 69, 53, 41, 39, 29.

(Tetrahydrofuran-2-yl)methanol (2ab')

The title compound was synthesized according to procedure B from **1ab** (48.3 mg, 0.503 mmol) and then purified by column chromatography (silica gel, DCM/MeOH 50:1).

Yield: 26.6 mg (0.26 mmol, 52%); colorless oil.

IR (KBr): 3390, 2927, 2872, 1710, 1460, 1056, 773 cm⁻¹.

¹H NMR (300 MHz, CDCl₃, 20 °C): δ = 4.05–3.95 (m, 1 H, CH₂), 3.90–3.72 (m, 2 H, CH), 3.65 (dd, *J* = 11.6, 3.2 Hz, 1 H, CH₂), 3.48 (dd, *J* = 11.6, 6.2 Hz, 1 H, CH₂), 2.31 (s, 1 H, O-H), 1.97–1.83 (m, 3 H, CH₂), 1.69–1.56 (m, 1 H, CH₂).

¹³C NMR (75.5 MHz, CDCl₃, 20 °C): δ = 79.6, 68.4, 65.0, 27.2, 26.1.

HRMS (ESI): product not detected; MS (EI): *m/z* = 71, 43, 41, 31, 29, 27.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

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