

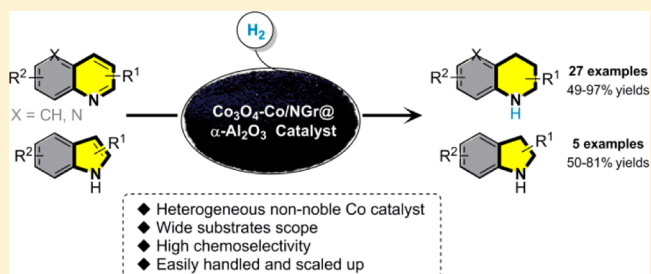
# Selective Catalytic Hydrogenation of Heteroarenes with *N*-Graphene-Modified Cobalt Nanoparticles ( $\text{Co}_3\text{O}_4\text{-Co/NGr}@ \alpha\text{-Al}_2\text{O}_3$ )

Feng Chen, Annette-Enrica Surkus, Lin He, Marga-Martina Pohl, Jörg Radnik, Christoph Topf, Kathrin Junge, and Matthias Beller\*

Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein Straße 29a, Rostock, 18059, Germany

**S** Supporting Information

**ABSTRACT:** Cobalt oxide/cobalt-based nanoparticles featuring a core-shell structure and nitrogen-doped graphene layers on alumina are obtained by pyrolysis of  $\text{Co}(\text{OAc})_2$ /phenanthroline. The resulting core-shell material ( $\text{Co}_3\text{O}_4\text{-Co/NGr}@ \alpha\text{-Al}_2\text{O}_3$ ) was successfully applied in the catalytic hydrogenation of a variety of *N*-heteroarenes including quinolines, acridines, benzo[*h*], and 1,5-naphthyridine as well as unprotected indoles. The peculiar structure of the novel heterogeneous catalyst enables activation of molecular hydrogen at comparably low temperature. Both high activity and selectivity were achieved in these hydrogenation processes, to give important building blocks for bioactive compounds as well as the pharmaceutical industry.



## INTRODUCTION

Reduction of arenes is of fundamental interest in organic synthesis and applied on large scale for the production of a variety of fine and bulk chemicals. In this context, hydrogen represents the most clean reductant.<sup>1</sup> Among the various arenes, selective hydrogenation of *N*-heteroarenes is a long-standing scientific and technological challenge due to the high resonance stability of these substrates and the potential poisoning of the catalysts by either substrates or their reduced products.<sup>2-4</sup> Despite the development of several molecularly defined homogeneous catalysts, e.g., Rh, Ru, Ir, and Os complexes,<sup>3,4</sup> in general harsh conditions and extra additives such as  $\text{I}_2$  are required for successful reductions. Notably, these precious catalysts always need to be specifically activated in advance and stored under an inert atmosphere. In addition, heterogeneous catalytic hydrogenations offer an alternative option.<sup>5</sup> Indeed, many classic heterogeneous catalysts, being largely dominated by platinum-group metals (PGM) and nickel, have been applied. These catalysts are usually highly active; hence, unselective hydrogenation of functionalized arenes with other reducible groups takes place, too. Thus, the search for advanced materials that enables the hydrogenation of *N*-heteroarenes with sufficient activity and high selectivity remains a challenging task.<sup>6</sup>

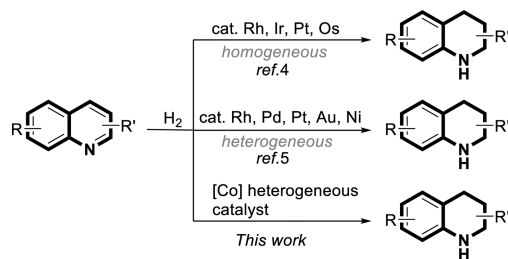
Recently, we developed novel nanoscaled cobalt and iron oxide on carbon support (Vulcan XC72R) which are modified by nitrogen-doped graphene layers (NGr). The peculiar structure of these core-shell catalysts is based on the pyrolysis of metal acetate complexes with nitrogen ligands, especially phenanthroline.<sup>7</sup> So far, these  $\text{Co}_3\text{O}_4/\text{NGr}@ \text{C}$  or  $\text{Fe}_2\text{O}_3/\text{NGr}@ \text{C}$  catalysts have been applied in the selective hydrogenation of nitroarenes, imines, and the selective

oxidation of alcohols to esters as well as nitriles.<sup>7</sup> Based on their performance in such redox transformations, we became interested in further exploitation of non-noble-metal-based systems for the more challenging reduction of *N*-heteroarenes.

1,2,3,4-Tetrahydroquinoline frameworks are ubiquitous in naturally occurring alkaloids and bioactive molecules, which have found broad applications in the synthesis of pharmaceuticals and agrochemicals.<sup>2e</sup> For instance, 1,2,3,4-tetrahydroquinoline derivatives are easily converted into important biologically active molecules such as a tubulin polymerization inhibitor,<sup>8</sup> flumequine<sup>9</sup> and ( $\pm$ )-galipinine.<sup>10</sup> Obviously, the hydrogenation of readily available quinolines offers a straightforward and convenient access to these compounds in terms of atom efficiency.<sup>2e,f</sup>

As shown in Scheme 1, different homogeneous<sup>4</sup> and heterogeneous<sup>5</sup> systems were developed for the hydrogenation

### Scheme 1. Hydrogenation of Quinolines to 1,2,3,4-Tetrahydroquinoline Derivatives



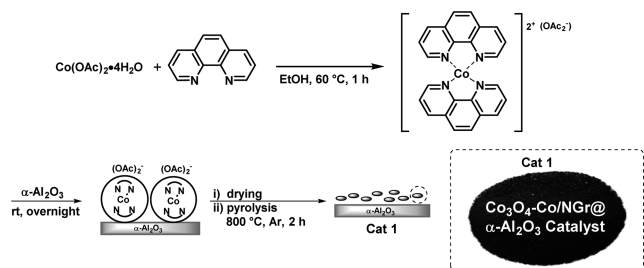
Received: June 23, 2015

Published: August 21, 2015

of quinolines. To further improve this transformation, we herein report the preparation and characterization of cobalt oxide/cobalt nanoparticles featuring nitrogen-doped graphene layers on alumina ( $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ ). This novel material constitutes the first heterogeneous cobalt-based catalyst, which is successfully applied in the hydrogenation of *N*-heteroarenes such as quinolines with high activity and selectivity. Meanwhile, we also report the hydrogenation of other heterocycles, e.g., unprotected indoles into indolines, which are also important scaffolds of numerous biologically active molecules.<sup>11</sup>

## RESULTS AND DISCUSSION

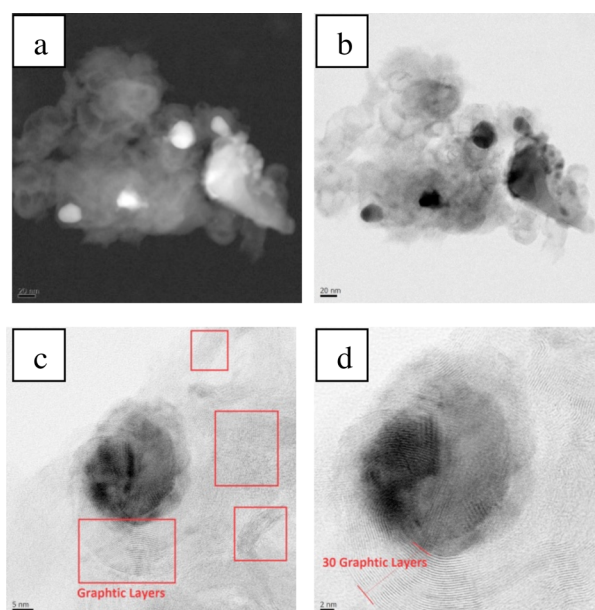
**Catalyst Preparation.** Initially, a series of novel materials using iron, cobalt, and nickel salts as metal precursors have been prepared by pyrolysis in the presence of 1,10-phenanthroline (L1), 2,2'-bipyridine (L2), and 2,2':6',2''-terpyridine (L3) as selected nitrogen ligands (conditions: 600–800 °C for 2 h under argon atmosphere). In contrast to our previous studies,<sup>7</sup> different inorganic supports, e.g., alumina, magnesium oxide, boron carbide, and silica, were applied in the pyrolysis process under various conditions. All these materials were tested for their catalytic activity for the benchmark hydrogenation of quinoline to tetrahydroquinoline at 120 °C and 2 MPa of hydrogen. Interestingly, our previously described known carbon-supported pyrolyzed materials showed interesting activity (see [Supporting Information](#)). However, the best catalyst was prepared using  $\text{Co}(\text{OAc})_2\cdot 4\text{H}_2\text{O}$  as metal precursor and 1,10-phenanthroline as nitrogen ligand on  $\alpha\text{-Al}_2\text{O}_3$  (Figure 1). Thermal analysis of the pyrolysis process



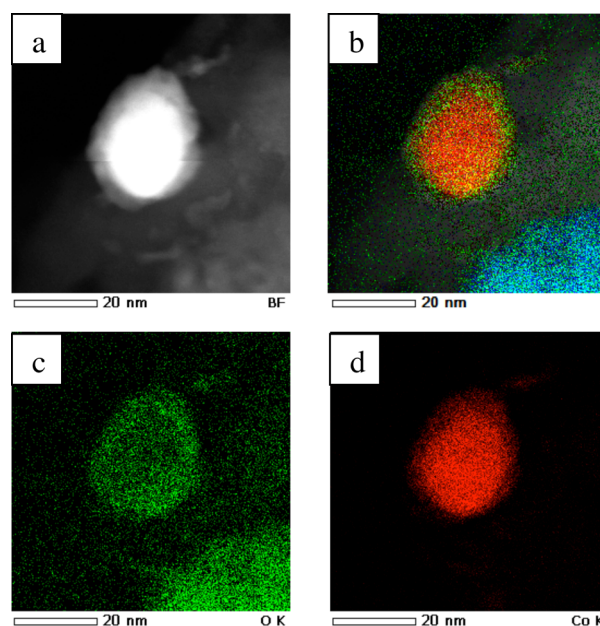
**Figure 1.** Synthesis of  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ .

disclosed that the ligand is mainly decomposed between 200 and 400 °C (see [Supporting Information](#)). Typically, all the catalyst materials were prepared batchwise on 1 g scale. Preparation on a 5 g scale gave similar results.

**Catalyst Characterization.** The Co content of the most active catalyst ( $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ ) is 2.923 wt %, which is determined by the elemental analysis. Meanwhile, the contents of C, N, and H are 14.240%, 0.541% and 0.060% respectively. High-angle annular dark field (HAADF) experiments using spherical aberration (Cs)-corrected transmission electron microscopy showed the complete size spectra of the nanocomposites of the catalyst (Figure 2a). Meanwhile, annular bright field (ABF) experiments revealed that the cobalt nanoparticles are surrounded by a large amount of graphitic layers (Figure 2b–d). Furthermore, the HAADF images show that the cobalt particles of this active catalyst have a core–shell structure with a  $\text{Co}_3\text{O}_4$  surface, which is displayed clearly via energy-dispersive X-ray spectroscopy (EDXS) (Figure 3a–d). However, the core of the material is composed of metallic cobalt.



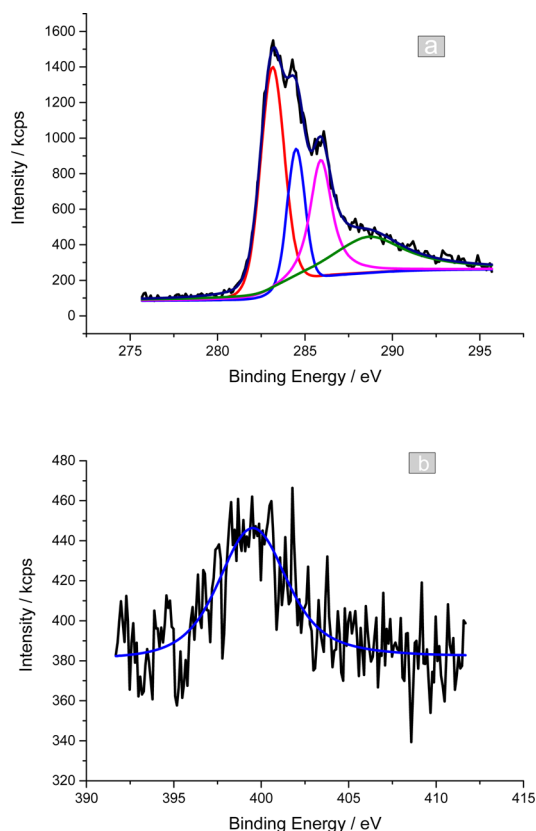
**Figure 2.** (a) HAADF TEM image of  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ , (b–d) ABF TEM images of  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ .



**Figure 3.** EDXS maps of  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ .

To obtain further insight into the chemical composition of this catalyst, the X-ray photoelectron spectroscopy (XPS) spectrum has been recorded. As shown in Figure 4, four peaks are observed in the C 1s spectra of  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$  with an electron-binding energy of 283.14 eV, 284.5 eV, 285.91 eV, and 288.64 eV and a peak in the N 1s spectra with an electron-binding energy of 399.5 eV. The results of XPS show that the graphitic layers contain different types of carbon as well as nitrogen atoms, the latter being in the form of pyridinic or pyrrolic species.<sup>12</sup>

This general composition is in agreement with the elemental analysis. The observed carbon layers might be generated from the metal precursor (acetate) and/or the ligand (1,10-phenanthroline), while carbonization of nitrogen-containing ligands should lead to nitrogen-doped graphene-type structures



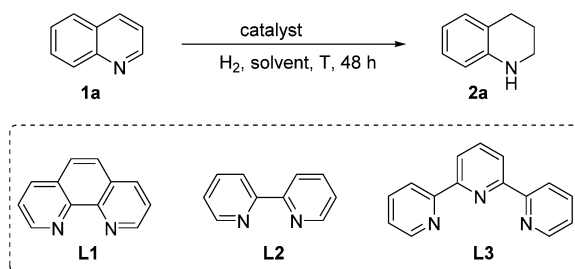
**Figure 4.** XPS spectrum of  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ : (a) C 1s XPS spectra; (b) N 1s XPS spectra.

(NGr).<sup>13</sup> The graphitic layers contain at least four different carbon species (C–C, C–O) as revealed by the XPS measurements. This result coincides with Raman spectroscopy where several signals of C atoms are detected in the disorder-band (D-band) (see [Supporting Information](#)).

To understand the composition of the cobalt nanoparticles (NPs) in the catalyst more accurately, X-ray diffraction (XRD) investigations have been carried out, too (see [Supporting Information](#)). Here, only metallic cobalt was identified. This result indicates that the main constituent of cobalt in the catalyst is metallic cobalt, which is in agreement with results of the HAADF images and EDXS maps. As shown in [Figure 3a–d](#), the thickness of the shell cobalt oxide is not more than 3 nm while the diameter of the whole metal particle is about 20 nm. Furthermore, the formed graphitic layers are assumed to be amorphous because no crystal carbon peak is detected in the XRD spectra.

**Catalysis.** Initial hydrogenation experiments were conducted with quinoline (**1a**) as model substrate (0.5 mmol scale). Using the  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$  NPs (Cat1) the desired product 1,2,3,4-tetrahydroquinoline (**2a**) is obtained in 90% yield under 1 MPa  $\text{H}_2$  at 120 °C for 48 h in toluene ([Table 1](#), entry 1). Variation of the catalyst loading showed that 4 mol % of Cat1 gave optimal results ([Table 1](#), entries 2 and 3). Under similar conditions, Cat2 and Cat3 made from 2,2'-bipyridine (L2) and 2,2':6',2''-terpyridine (L3) as ligands, respectively, showed significantly lower activity for this transformation ([Table 1](#), entries 4 and 5). As expected, applying a homogeneous catalyst mixture of  $\text{Co(OAc)}_2\cdot 4\text{H}_2\text{O}$  (4 mol %) with 1,10-phenanthroline (8 mol %) did not result in any desired 1,2,3,4-tetrahydroquinoline (**2a**) ([Table 1](#), entry 6).

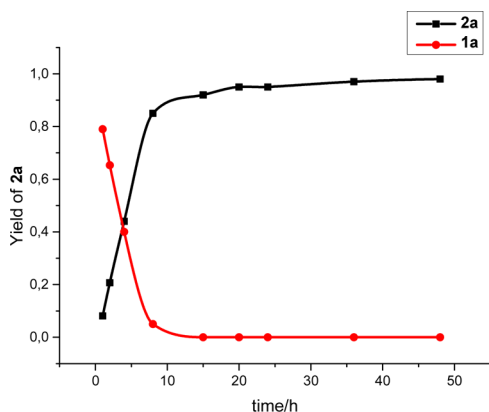
**Table 1. Catalytic Hydrogenation of Quinoline: Variation of Catalysts and Reaction Conditions<sup>a</sup>**



entry	catalyst (mol %)	$\text{H}_2$ (MPa)	solvent	T (°C)	yield <sup>b</sup> (%)
1	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	1	toluene	120	90 (88 <sup>c</sup> )
2	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (3)	1	toluene	120	94
3	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (2)	1	toluene	120	92
4	Co/L2/ $\alpha\text{-Al}_2\text{O}_3$ (4)	1	toluene	120	37
5	Co/L3/ $\alpha\text{-Al}_2\text{O}_3$ (4)	1	toluene	120	52
6 <sup>c</sup>	$\text{Co(OAc)}_2\cdot 4\text{H}_2\text{O}$ (4)	2	toluene	120	0
7 <sup>d</sup>	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	2	toluene	120	0
8	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	1	1,4-dioxane	120	83
9	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	1	THF	120	94
10	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	1	MeCN	120	0
11	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	2	toluene	120	98
12	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	0.5	toluene	120	50
13	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	0.3	toluene	120	24
14 <sup>f</sup>	Co/L1/ $\alpha\text{-Al}_2\text{O}_3$ (4)	2	toluene	120	90

<sup>a</sup>Reaction conditions: 0.5 mmol of **1a**, 4 mol %  $\text{Co}_3\text{O}_4\text{-Co/NGr@}\alpha\text{-Al}_2\text{O}_3$ , in 2 mL toluene under  $\text{H}_2$ . <sup>b</sup>GC yield using dodecane as an internal standard. <sup>c</sup>1,10-Phenanthroline (8 mol %) was used. <sup>d</sup>The catalyst was not pyrolyzed. <sup>e</sup>Isolated yield. <sup>f</sup>10 mmol scale reaction.

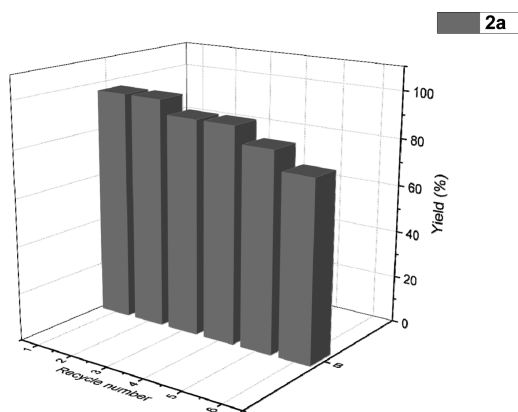
Similarly, the heterogenized catalyst without pyrolysis revealed no activation of hydrogen in the model reaction (Table 1, entry 7). In the presence of Cat1 different solvents such as 1,4-dioxane, THF, and MeCN were tested, but no improvement was observed (Table 1, entries 8–10). At lower hydrogen pressure (0.3–0.5 MPa) the reaction was retarded, whereas an enhanced product yield (98% of 1,2,3,4-tetrahydroquinoline 2a) was achieved under 2 MPa H<sub>2</sub> (Table 1, entries 11–13). As shown in Figure 5, the starting



**Figure 5.** Kinetic data of the hydrogenation of quinoline with Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs catalyst.

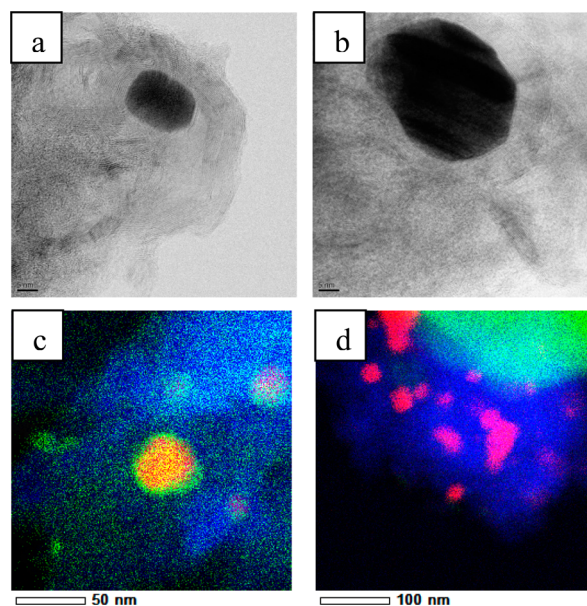
material is fully consumed after 15 h. Notably, no intermediates could be detected by gas chromatography during the whole reaction process. Under optimal conditions, hydrogenation of quinoline 1a on 10 mmol scale gave also 90% yield of the desired product (Table 1, entry 14).

The obvious advantage of heterogeneous catalysts compared to molecularly defined systems is their easy recycling. In order to demonstrate the stability and recyclability of the Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs, we reused the catalyst for the model system up to six times. As shown in Figure 6 the catalyst is



**Figure 6.** Hydrogenation of quinoline with Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs catalyst: recycling experiments.

stable under air atmosphere and showed only slight deactivation. After the sixth run the product yield was still 76% (Figure 6). No leaching occurred to the reaction media with this heterogeneous cobalt catalyst (see Supporting Information). The ABF TEM images and EDXS maps of the catalysts (Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub>) after the first run and the sixth run are shown in Figure 7. Even after the sixth run the

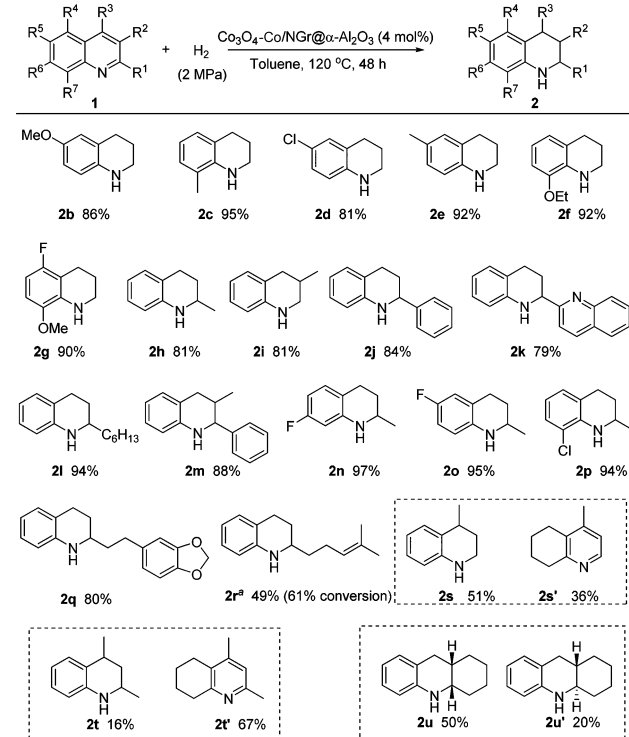


**Figure 7.** (a) ABF TEM image of Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> after the first run. (b) ABF TEM image of Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> after the sixth run. (c) EDXS map of Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> after the first run. (d) EDXS map of Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> after the sixth run.

nanoparticles stayed intact; however, the cobalt oxide shell structure disappeared according to the EDX map analysis. These results demonstrate that dispersed metallic cobalt nanoparticles are responsible for the catalytic properties.

Next, the substrate scope of the hydrogenation of different quinolines was explored under standard conditions (Scheme 2).

### Scheme 2. Co<sub>3</sub>O<sub>4</sub>–Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs Catalyzed Hydrogenation of Various Quinolines



Generally, quinolines with various functional groups are converted to the corresponding 1,2,3,4-tetrahydroquinolines in high yields and selectivities. Both substrates with electron-donating or electron-withdrawing groups were smoothly transformed to the desired products.

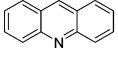
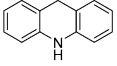
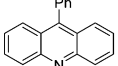
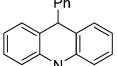
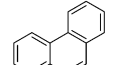
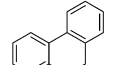
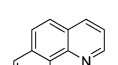
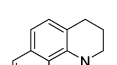
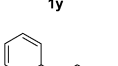
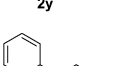
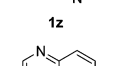
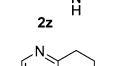
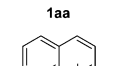
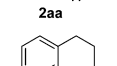
Interestingly, substrates bearing fluorine and chlorine atoms at the 5-, 6-, 7-, or 8-position are smoothly hydrogenated and no dehalogenation products were detected in this process. Surprisingly, 2,2'-biquinoline reacted in a selective manner to give 1,2,3,4-tetrahydro-2,2'-biquinoline (**2k**) with only one pyridyl ring hydrogenated. In the case of 2-(4-methylpent-3-en-1-yl)quinoline (**1r**) bearing a sensitive carbon-carbon double bond, no hydrogenation of the olefin was observed, the desired product (**2r**) is obtained in 49% yield, and 39% starting material was recovered. However, substrates with monosubstituted olefin moiety are not compatible under the same conditions (see [Supporting Information](#)). Interestingly, 4-methylquinoline is hydrogenated to give two products: 4-methyl-1,2,3,4-tetrahydroquinoline (**2s**) and 4-methyl-5,6,7,8-tetrahydroquinoline (**2s'**), respectively. Similarly, 2,4-dimethylquinoline led to 2,4-dimethyl-1,2,3,4-tetrahydroquinoline (**2t**) and 2,4-dimethyl-5,6,7,8-tetrahydroquinoline (**2t'**). These results show that hydrogenation of the phenyl ring of the substrates is possible, too. Apparently, hydrogenation of the heterocycle is very susceptible toward substitution at the 4-position of the quinoline ring. Thus, reduction of the heterocycle becomes more difficult in these cases. In agreement with this observation the reduction of **4,7** did not react. On the other hand, 1,2,3,4-tetrahydroacridine (**1u**) was converted into the (4*aS*,9*aS*)-1,2,3,4,4*a*,9,9*a*,10-octahydroacridine (**2u**) and (4*aR*,9*aS*)-1,2,3,4,4*a*,9,9*a*,10-octahydroacridine (**2u'**) with 50% and 20% yield, respectively.

Other *N*-heteroarenes such as acridine (**1v**), 9-phenylacridine (**1w**), phenanthridine (**1x**), benzo[*h*]quinoline (**1y**), and 3-methylbenzo[*f*]quinoline (**1z**) were hydrogenated selectively with the present catalytic system, and in most cases the corresponding products were obtained in good to excellent yields ([Table 2](#)). For example, 1,2,3,4-tetrahydro-1,5-naphthyridine (**2aa**) is obtained as a sole product in 86% yield. Notably, quinoline 1-oxide gave 1,2,3,4-tetrahydroquinoline (**2a**) in high yield under the standard conditions.

Given the usefulness of 1,2,3,4-tetrahydroquinolines in medicinal chemistry, the importance of this novel hydrogenation system was showcased in the synthesis of three different pharmacologically active compounds. For instance, the reduced 6-methoxy-1,2,3,4-tetrahydroquinoline (**2b**) was reacted with 3,4,5-trimethoxybenzoyl chloride to give the tubulin polymerization inhibitor (6-methoxy-3,4-dihydroquinolin-1(2*H*)-yl)(3,4,5-trimethoxyphenyl)methanone (**6**) in 92% yield. ([Scheme 3a](#)). Moreover, 6-fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (**2o**) was converted into flumequine in three steps in 78% total yield. ([Scheme 3b](#)). Finally, (±)-galipinine was synthesized from 2-(2-(benzo[*d*][1,3]-dioxol-5-yl)ethyl)-1,2,3,4-tetrahydroquinoline (**2q**) in 91% yield easily ([Scheme 3c](#)).

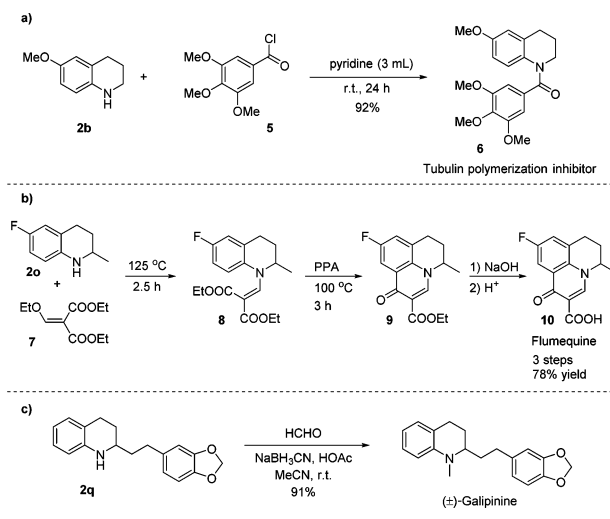
Encouraged by these results, we became interested in the hydrogenation of a series of unprotected indoles. The resulting indolines are useful building blocks for many biologically active natural and non-natural products. So far, for this transformation catalysts mainly based on noble metals (homogeneous, Rh, Ru, Ir;<sup>14</sup> heterogeneous, Rh, Pd, Pt, Ni-Al) have been developed. In general, *N*-protected indoles have to be applied as substrates.<sup>15</sup> To avoid tedious protection/deprotection steps,

**Table 2.** Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs Catalyzed Hydrogenation of Other *N*-Heteroarenes<sup>a</sup>

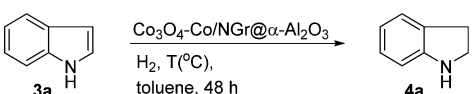
entry	substrate	H <sub>2</sub> (MPa)	T (°C)	t (h)	product	yield (%) <sup>b</sup>
1		2	120	48		86
2		3	120	48		70
3		2	120	48		73
4		3	140	60		92
5		3	140	60		93
6		2	120	48		73
7 <sup>c</sup>		2	120	48		90

<sup>a</sup>Reaction conditions: 0.5 mmol of substrate, 4 mol % Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub>, in 2 mL of toluene under H<sub>2</sub>. <sup>b</sup>Isolated yield. <sup>c</sup>GC yield using dodecane as an internal standard.

### Scheme 3. Applications of Synthesized 1,2,3,4-Tetrahydroquinoline Derivatives



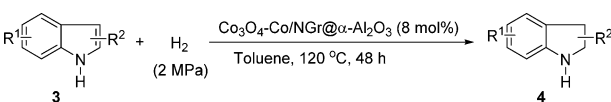
we studied the hydrogenation of unprotected indole **3a** as a model substrate. To our delight the Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs are suitable for the hydrogenation of **3a** under standard conditions, and indoline **4a** was obtained in 51% yield. Performing few optimization experiments gave the product **4a** in 83% yield ([Table 3](#)).

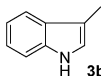
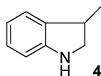
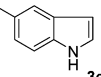
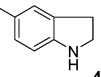
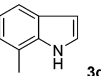
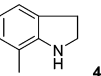
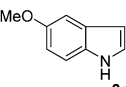
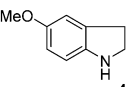
**Table 3. Catalytic Hydrogenation of Indole: Variation of Catalysts and Reaction Conditions<sup>a</sup>**


entry	catalyst (mol %)	H <sub>2</sub> (MPa)	T (°C)	yield <sup>b</sup> (%)
1	4	2	120	51
2	4	3	130	51
3	6	3	130	72
4	8	2	120	83

<sup>a</sup>3a (0.5 mmol), Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub>, toluene (2 mL). <sup>b</sup>GC yield using dodecane as an internal standard.

As shown in Table 4, methyl- and methoxy-substituted indoles led to the corresponding indolines in moderate yields.

**Table 4. Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> NPs Catalyzed Hydrogenation of Unprotected Indoles<sup>a</sup>**


entry	substrate	product	conversion(%)	yield (%) <sup>b</sup>
1			65	50
2			75	68
3			74	69
4			66	50

<sup>a</sup>3 (0.5 mmol), Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> (80 mg), toluene (2 mL). <sup>b</sup>Isolated yields.

It should be noted that in most cases part of the starting materials were recovered even after 48 h.

## CONCLUSION

Cobalt oxide/cobalt nanoparticles modified by nitrogen-doped graphene layers on alumina are obtained by pyrolysis of Co(OAc)<sub>2</sub>/phenanthroline on alumina. The resulting material (Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub>) constitutes an active catalyst for hydrogenation of a variety of *N*-heteroarenes including quinolines, acridines, benzo[*h*], and 1,5-naphthyridine as well as unprotected indoles. The peculiar structure of the novel heterogeneous catalyst enables activation of molecular hydrogen at comparably low temperature (120 °C). Good activity and high selectivity were achieved in hydrogenation processes to give important building blocks for bioactive compounds as well as the pharmaceutical industry. Further applications of these Co-containing NPs on various supports are currently under way in our laboratory.

## EXPERIMENTAL SECTION

**Preparation of the Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub>.** Co(OAc)<sub>2</sub>·4H<sub>2</sub>O (0.5 mmol) and 1,10-phenanthroline (1.0 mmol) were stirred in

ethanol (20 mL) for 15 min at room temperature. Then, the whole mixture was stirred at 60 °C for 1 h. The support α-Al<sub>2</sub>O<sub>3</sub> was added, and the mixture was stirred at room temperature overnight. Then, the ethanol was removed in vacuo and a pale brown sample was obtained. This solid was grinded to a fine powder, which was transferred into a ceramic crucible and placed in the oven. The oven was evacuated (5 mbar) and then flushed with argon for three times. The oven was heated to 800 °C at the rate of 25 °C per minute, and held at 800 °C for 2 h under argon atmosphere. After the heating was switched off, the oven was cooled to room temperature.

**General Procedure for Hydrogenation.** In a reaction vial (5 mL), quinoline 1 (0.5 mmol) and Co<sub>3</sub>O<sub>4</sub>-Co/NGr@α-Al<sub>2</sub>O<sub>3</sub> (40 mg) were mixed with 2 mL of toluene. The closed vials were placed into a 300 mL autoclave via a metal plate. The autoclave was flushed with hydrogen twice and pressurized with hydrogen. Then, the autoclave was placed into an aluminum block and the reaction was performed at 120 °C. After the reaction was complete, the autoclave was cooled to room temperature and the hydrogen was released. The crude reaction mixture was purified by flash chromatography on silica (eluent: hexane/ethyl acetate = 20:1 to 3:1) to afford 1,2,3,4-tetrahydroquinoline 2.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b06496.

Additional experimental results and procedures and characterization data (PDF)

## AUTHOR INFORMATION

### Corresponding Author

\*Matthias.Beller@catalysis.de

### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

The Federal Ministry of Education and Research (BMBF) and the State of Mecklenburg-Vorpommern are gratefully acknowledged for their general support. We thank the analytical department of Leibniz-Institute for Catalysis, Rostock, for their excellent analytical service.

## REFERENCES

- (1) (a) Rylander, P. N. *Catalytic Hydrogenation in Organic Syntheses*; Academic Press: New York, 1979. (b) De Vries, J. G.; Elsevier, C. J. *Handbook of Homogeneous Hydrogenation*; Wiley-VCH: Weinheim, Germany, 2007. (c) Andersson, P. G.; Munslow, I. J. *Modern Reduction Methods*; Wiley: New York, 2008. (d) Denmark, S. E. *Organic Reactions*, Vol. 71; Wiley: New York, 2008.
- (2) (a) Baliyah, V.; Jeyaraman, R.; Chandrasekaran, L. *Chem. Rev.* **1983**, *83*, 379–423. (b) Alvanipour, A.; Kispert, L. D. *J. Mol. Catal.* **1988**, *48*, 277–283. (c) Bird, C. W. *Tetrahedron* **1992**, *48*, 335–340. (d) Bentley, K. W. *Nat. Prod. Rep.* **2006**, *23*, 444–463. (e) Källström, S.; Leino, R. *Bioorg. Med. Chem.* **2008**, *16*, 601–635. (f) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *Tetrahedron* **1996**, *52*, 15031–15070. (g) Sridharan, V.; Suryavanshi, P. A.; Menéndez, J. C. *Chem. Rev.* **2011**, *111*, 7157–7259.
- (3) For reviews see: (a) Glorius, F. *Org. Biomol. Chem.* **2005**, *3*, 4171–4175. (b) Kuwano, R. *Heterocycles* **2008**, *76*, 909–922. (c) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. *Chem. Rev.* **2012**, *112*, 2557–2590. (d) Zhou, Y.-G. *Acc. Chem. Res.* **2007**, *40*, 1357–1366. For some examples see: (e) Jardine, I.; McQuillin, F. J. *J. Chem. Soc. D* **1970**, 626a–626a. (f) Laine, R. M. *New J. Chem.* **1987**, *11*, 543–547. (g) Sanchez-Delgado, R. A.; Gonzalez, E. *Polyhedron* **1989**, *8*, 1431–1436. (h) Baralt, E.; Smith, S. J.; Hurwitz, J.; Horvath, I. T.; Fish, R. H. *J. Am. Chem. Soc.* **1992**, *114*, 5187–5196. (i) Rosales,

- M.; Alvarado, Y.; Boves, M.; Rubio, R.; Soscun, H.; Sanchez-Delgado, R. A. *Transition Met. Chem. (Dordrecht, Neth.)* **1995**, *20*, 246–251. (j) Glorius, F.; Spielkamp, N.; Holle, S.; Goddard, R.; Lehmann, C. W. *Angew. Chem., Int. Ed.* **2004**, *43*, 2850–2852. (k) Legault, C. Y.; Charette, A. B. *J. Am. Chem. Soc.* **2005**, *127*, 8966–8967. (l) Rosales, M.; Vallejo, R.; Soto, J.; Chacon, G.; Gonzalez, A.; Gonzalez, B. *Catal. Lett.* **2006**, *106*, 101–105. (m) Lu, S.-M.; Han, X.-W.; Zhou, Y.-G. *J. Organomet. Chem.* **2007**, *692*, 3065–3069. (n) Fish, R. H.; Thormodsen, A. D.; Cremer, G. A. *J. Am. Chem. Soc.* **1982**, *104*, 5234–5237. (o) Sanchez-Delgado, R. A.; Rondon, D.; Andriollo, A.; Herrera, V.; Martin, G.; Chaudret, B. *Organometallics* **1993**, *12*, 4291–4296.
- (4) (a) Wang, W.-B.; Lu, S.-M.; Yang, P.-Y.; Han, X.-W.; Zhou, Y.-G. *J. Am. Chem. Soc.* **2003**, *125*, 10536–10537. (b) Yamaguchi, R.; Ikeda, C.; Takahashi, Y.; Fujita, K.-I. *J. Am. Chem. Soc.* **2009**, *131*, 8410–8412. (c) Dobereiner, G. E.; Nova, A.; Schley, N. D.; Hazari, N.; Miller, S. J.; Eisenstein, O.; Crabtree, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 7547–7562. (d) Lu, S.-M.; Bolm, C. *Adv. Synth. Catal.* **2008**, *350*, 1101–1105. (e) Zhou, H.; Li, Z.; Wang, Z.; Wang, T.; Xu, L.; He, Y.; Fan, Q.-H.; Pan, J.; Gu, L.; Chan, A. S. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 8464–8467. (f) Wang, C.; Li, C.; Wu, X.; Pettman, A.; Xiao, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6524–6528. (g) Eggenstein, M.; Thomas, A.; Theuerkauf, J.; Franciò, G.; Leitner, W. *Adv. Synth. Catal.* **2009**, *351*, 725–731. (h) Li, Z.-W.; Wang, T.-L.; He, Y.-M.; Wang, Z.-J.; Fan, Q.-H.; Pan, J.; Xu, L.-J. *Org. Lett.* **2008**, *10*, 5265–5268. (i) Gou, F.-R.; Li, W.; Zhang, X.; Liang, Y.-M. *Adv. Synth. Catal.* **2010**, *352*, 2441–2444. (j) Yamagata, T.; Tadaoka, H.; Nagata, M.; Hirao, T.; Kataoka, Y.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Mashima, K. *Organometallics* **2006**, *25*, 2505–2513. (k) Tadaoka, H.; Cartigny, D.; Nagano, T.; Gosavi, T.; Ayad, T.; Genet, J.-P.; Ohshima, T.; Ratovelomanana-Vidal, V.; Mashima, K. *Chem. - Eur. J.* **2009**, *15*, 9990–9994. (l) Reetz, M. T.; Li, X. *Chem. Commun.* **2006**, 2159–2160. (m) Mrcic, N.; Lefort, L.; Boogers, J. A. F.; Minnaard, A. J.; Feringa, B. L.; de Vries, J. G. *Adv. Synth. Catal.* **2008**, *350*, 1081–1089. (n) Deport, C.; Buchotte, M.; Abecassis, K.; Tadaoka, H.; Ayad, T.; Ohshima, T.; Genet, J.-P.; Mashima, K.; Ratovelomanana-Vidal, V. *Synlett* **2007**, *2007*, 2743–2747. (o) Núñez-Rico, J. L.; Fernández-Pérez, H.; Benet-Buchholz, J.; Vidal-Ferran, A. *Organometallics* **2010**, *29*, 6627–6631. (p) Wang, D.-W.; Wang, X.-B.; Wang, D.-S.; Lu, S.-M.; Zhou, Y.-G.; Li, Y.-X. *J. Org. Chem.* **2009**, *74*, 2780–2787. (q) Qiu, L.; Kwong, F. Y.; Wu, J.; Lam, W. H.; Chan, S.; Yu, W. Y.; Li, Y. M.; Guo, R.; Zhou, Z.; Chan, A. S. C. *J. Am. Chem. Soc.* **2006**, *128*, 5955–5965.
- (5) (a) Nishimura, S. *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*, Wiley: New York, 2001. (b) Blaser, H. U.; Siegrist, U.; Steiner, H.; Studer, M. In *Fine Chemicals through Heterogeneous Catalysis*; Sheldon, R. A., van Bekkum, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001. (c) Shaw, J. E.; Stapp, P. R. *J. Heterocycl. Chem.* **1987**, *24*, 1477–1483. (d) Mevellec, V.; Roucoux, A. *Inorg. Chim. Acta* **2004**, *357*, 3099–3103. (e) Sanchez-Delgado, R. A.; Machalaba, N.; Ng-A-Qui, N. *Catal. Commun.* **2007**, *8*, 2115–2118. (f) Nador, F.; Moglie, Y.; Vitale, C.; Yus, M.; Alonso, F.; Radivoy, G. *Tetrahedron* **2010**, *66*, 4318–4325. (g) Beckers, N. A.; Huynh, S.; Zhang, X.; Lubber, E. J.; Buriak, J. M. *ACS Catal.* **2012**, *2*, 1524–1534. (h) Fang, M.; Machalaba, N.; Sanchez-Delgado, R. A. *Dalton Trans.* **2011**, *40*, 10621–10632. (i) Mao, H.; Chen, C.; Liao, X.; Shi, B. *J. Mol. Catal. A: Chem.* **2011**, *341*, 51–56. (j) Fang, M.; Sánchez-Delgado, R. A. *J. Catal.* **2014**, *311*, 357–368.
- (6) Ren, D.; He, L.; Yu, L.; Ding, R.-S.; Liu, Y.-M.; Cao, Y.; He, H.-Y.; Fan, K.-N. *J. Am. Chem. Soc.* **2012**, *134*, 17592–17598.
- (7) (a) Jagadeesh, R. V.; Surkus, A. E.; Junge, H.; Pohl, M.-M.; Radnik, J.; Rabeah, J.; Huan, H.; Schunemann, V.; Brückner, A.; Beller, M. *Science* **2013**, *342*, 1073–1076. (b) Westerhaus, F. A.; Jagadeesh, R. V.; Wienhöfer, G.; Pohl, M.-M.; Radnik, J.; Surkus, A.-E.; Rabeah, J.; Junge, K.; Junge, H.; Nielsen, M.; Brückner, A.; Beller, M. *Nat. Chem.* **2013**, *5*, 537–543. (c) Jagadeesh, R. V.; Junge, H.; Pohl, M.-M.; Radnik, J.; Brückner, A.; Beller, M. *J. Am. Chem. Soc.* **2013**, *135*, 10776–10782. (d) Banerjee, D.; Jagadeesh, R. V.; Junge, K.; Pohl, M.-M.; Radnik, J.; Brückner, A.; Beller, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 4359–4363. (e) Jagadeesh, R. V.; Wienhöfer, G.; Westerhaus, F. A.; Surkus, A. E.; Pohl, M.-M.; Junge, H.; Junge, K.; Beller, M. *Chem. Commun.* **2011**, *47*, 10972–10974. (f) Jagadeesh, R. V.; Junge, H.; Beller, M. *Nat. Commun.* **2014**, *5*, 4123. (g) Stemmler, T.; Surkus, A.-E.; Pohl, M.-M.; Junge, K.; Beller, M. *ChemSusChem* **2014**, *7*, 3012–3016. (h) Pisiewicz, S.; Stemmler, T.; Surkus, A.-E.; Junge, K.; Beller, M. *ChemCatChem* **2015**, *7*, 62–64.
- (8) Liou, J.-P.; Wu, Z.-Y.; Kuo, C.-C.; Chang, C.-Y.; Lu, P.-Y.; Chen, C.-M.; Hsieh, H.-P.; Chang, J.-Y. *J. Med. Chem.* **2008**, *51*, 4351–4355.
- (9) Bálint, J.; Egri, G.; Fogassy, E.; Böcskei, Z.; Simon, K.; Gajary, A.; Friesz, A. *Tetrahedron: Asymmetry* **1999**, *10*, 1079–1087.
- (10) (a) Rakotoson, J. H.; Fabre, N.; Jacquemond-Collet, I.; Hannedouche, S.; Fouraste, I.; Moulis, C. *Planta Med.* **1998**, *64*, 762–763. (b) Houghton, P. J.; Woldemariam, T. Z.; Watanabe, Y.; Yates, M. *Planta Med.* **1999**, *65*, 250–254.
- (11) (a) Ontoria, J. M.; Di Marco, S.; Conte, I.; Di Francesco, M. E.; Gardelli, C.; Koch, U.; Matassa, V. G.; Poma, M.; Steinkuhler, C.; Volpari, C.; Harper, S. *J. Med. Chem.* **2004**, *47*, 6443–6446. (b) Horton, D. A.; Bourne, G. T.; Smythe, M. L. *Chem. Rev.* **2003**, *103*, 893–930. (c) Boger, D. L.; Boyce, C. W.; Garbaccio, R. M.; Goldberg, J. A. *Chem. Rev.* **1997**, *97*, 787–828. (d) Bermudez, J.; Dabbs, S.; Joiner, K. A.; King, F. D. *J. Med. Chem.* **1990**, *33*, 1929–1932. (e) Glennon, R. A. *J. Med. Chem.* **1987**, *30*, 1–12.
- (12) (a) Casanovas, J.; Ricart, J. M.; Rubio, J.; Illas, E.; Jiménez-Mateos, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 8071–8076.
- (13) Pels, J. R.; Kapteijn, F.; Moulijn, J. A.; Zhu, Q.; Thomas, K. M. *Carbon* **1995**, *33*, 1641–1653.
- (14) (a) Kuwano, R.; Sato, K.; Kurokawa, T.; Karube, D.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 7614–7615. (b) Kuwano, R.; Kaneda, K.; Ito, T.; Sato, K.; Kurokawa, T.; Ito, T. *Org. Lett.* **2004**, *6*, 2213–2215. (c) Kuwano, R.; Kashiwabara, M. *Org. Lett.* **2006**, *8*, 2653–2655. (d) Baeza, A.; Pfaltz, A. *Chem. - Eur. J.* **2010**, *16*, 2036–2039.
- (15) (a) Coulton, S.; Gilchrist, T. L.; Keith, G. *Tetrahedron* **1997**, *53*, 791–798. (b) Kulkarni, A.; Zhou, W.; Török, B. *Org. Lett.* **2011**, *13*, 5124–5127. (c) Clarisse, D.; Fenet, B.; Fache, F. *Org. Biomol. Chem.* **2012**, *10*, 6587–6594. (d) Cho, H.; Török, F.; Török, B. *Org. Biomol. Chem.* **2013**, *11*, 1209–1215. (e) Bernas, H.; Kumar, N.; Aho, A.; Leino, R.; Murzin, D. Yu. *Catal. Commun.* **2014**, *56*, 41–44.