Nickel Boride Catalyzed Reductions of Nitro Compounds and Azides: Nanocellulose-Supported Catalysts in Tandem Reactions

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Abstract Nickel boride catalyst prepared in situ from NiCl₂ and sodium borohydride allowed, in the presence of an aqueous solution of TEMPO-oxidized nanocellulose (0.01 wt%), the reduction of a wide range of nitroarenes and aliphatic nitro compounds. Here we describe how the modified nanocellulose has a stabilizing effect on the catalyst that enables low loading of the nickel salt pre-catalyst. Ni-B prepared in situ from a methanolic solution was also used to develop a greener and facile reduction of organic azides, offering a substantially lowered catalyst loading with respect to reported methods in the literature. Both aromatic and aliphatic azides were reduced, and the protocol is compatible with a one-pot Boc-protection of the obtained amine yielding the corresponding carbamates. Finally, bacterial crystalline nanocellulose was chosen as a support for the Ni-B catalyst to allow an easy recovery step of the catalyst and its recyclability for new reduction cycles.

Key words Ni-B, nickel boride, nitro reduction, azide reduction, nickel boride catalyzed hydrogenation, TEMPO nanocellulose, crystalline nanocellulose

1 Introduction

Aromatic and heteroaromatic amines are important intermediates in the chemical and pharmaceutical industry.1 There are several different ways to produce these compounds and the most used synthetic routes are the hydrogenation4 of nitroarenes (Scheme 1) and metal-catalyzed C–N coupling chemistry. During recent years, nanostructured particles (NPs) have emerged as important in catalysis due to their high catalytic activity and high surface areas. Several NPs have been utilized for nitroarene reductions5 using both precious metals (gold,4 platinum,5,6 palladium5,7) and cheaper, more abundant metals (e.g., cobalt,8 nickel,9 iron10) (Scheme 1). There is a drive to develop routes for organic reactions in ‘green’ solvents, e.g., water. Recently, Lipshutz and co-workers developed a mild and ligand-free procedure with Fe/Pd nanoparticles that catalyzed the reduction of nitroarenes at room temperature in water using sodium borohydride in the presence of a designed PEG surfactant (Scheme 1).11 However, the green methodologies based on more abundant and cheaper transition metals, such as nickel, are challenging. In the early 1950s, Schlesinger et al. and Paul et al. reported that the reduction of nickel salts with sodium borohydride in aqueous or alcoholic solvents gave a finely divided black precipitate that contained both nickel and boron, i.e., nickel boride.12,13a,b
Biographical Sketches

Giampiero Proietti obtained his M.Sc. from ‘La Sapienza University of Rome’ in 2015 with a thesis work on the synthesis of a photo- and thermo-responsive polymer. He joined Peter Diner’s group at the Royal Institute of Technology in 2017 as Ph.D. student and his research revolves around organic azides, developing methodologies for their reduction or exploiting the unique reactivity of perfluorinated aromatic azides in a photo-promoted synthesis of optical active sulfonimidamides and their applications in materials.

Kaniraj Jeya Prathap obtained his Ph.D. in 2012 at the Central Salt and Marine Chemicals Research Institute (Bhavnagar, Gujarat, India) working mainly with asymmetric catalysis. After a short stay at the Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences (IOCB Prague, Czech Republic), he was awarded a post-doctoral grant (PBC & Lady Davis Post-doctoral Fellow) to join Prof. Maayan at Technion – Israel Institute of Technology to work with novel peptidomimetics. In 2016, he was awarded the Wenner-Gren postdoctoral fellowship to join Prof. Diner’s group at KTH – Royal Institute of Technology (Stockholm, Sweden) to work on nickel boride catalyzed reduction using nanocellulose. In 2019, Dr. Prathap joined Wageningen University & Research (Netherlands) as a senior post-doctoral fellow working on synthesis of therapeutic peptides. Currently, he works as a researcher at the University of Groningen.

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Richard T. Olsson is an Assoc. Prof. at KTH Royal Institute of Technology, Stockholm, Sweden, in the Department of Fibre and Polymer Technology. He received his Ph.D. from KTH in 2007 on processing of microwave absorbing nanocomposite materials. His postdoctoral studies were at the CSIC, Spain, with a focus on sustainable nanomaterials. He is editor of Scientific Reports, and his research focuses on nanocomposite materials and inorganic/polymeric interfaces for sustainable material engineering in novel applications.

Peter Dinér obtained his Ph.D. in 2005 at University of Gothenburg. In 2006, he joined Prof. K. A. Jørgensen at Center for Catalysis at Aarhus University working on enantioselective organocatalysis. He moved back to University of Gothenburg under the guidance of Prof. M. Grøtli working on medicinal chemistry. In 2010 he started his independent research group at Uppsala as an Assist. Prof. In 2013, he was granted a position as an Assoc. Prof. at the Royal Institute of Technology, Department of Chemistry, where his research centers around metal- and organocatalysis and since 2015 he acts as the Head of Division of Organic Chemistry.
nickel. The nickel boride material has mainly been used in organic synthesis as a stoichiometric reagent, particularly in the hydrogenation of alkenes and alkynes, reduction of N-heterocycles, reduction of nitroarenes, deoxygenation reactions, desulfurization reactions, dehalogenation reactions, etc. However, only a few catalytic applications have been reported.

The main reasons for the use of stoichiometric amounts of nickel boride are related to the inherent instability of the material in aqueous media under oxygen-containing atmosphere in which the nickel boride converts into nickel oxide and nickel metal. A potential solution to the instability of nickel nanoparticles is to use a support for the nickel boride nanoparticles. A support can stabilize the nanoparticles and enables easier recyclability of the nanoparticles, which is important due to the possible toxicity and sensitizing effects of nickel. In recent years, nanocellulose (NC) derivatives have been studied as potentially efficient, cheap, and renewable supports for catalysis. The use of nanocelluloses as supports for NP catalysts is appealing due to their high surface area (300–450 m²/gram). The natural functionality of the celluloses depends on the reactive hydroxyl groups present in the glucose repetitive units in the cellulose crystals. The primary hydroxyl groups on the surface of the nanocellulose can be chemically modified to carboxylic acids in a 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) mediated oxidation, which separates cellulose fibrils from their natural bundle configuration to nanocellulose fibers due to repulsion between the negatively charged carboxylic acids functionalities. Nanocellulose suspensions in water are stable over time with limited formation of aggregates. The unmodified nanocelluloses have a hydrophilic surface covered with hydroxyl groups, while chemically modified nanocellulose can also contain e.g. sulfuric acid derived sulfate. The highly dispersed nanocellulose fibers are arranged in a fine, fibrous cellulose network containing cavities that include both solvent molecules and the functional groups on the surface of the nanocellulose (Figure 1).

In the confined space of the cavities in the nanocellulose network, the oxygen-containing surface moieties can function as effective metal center stabilizers via the formation of coordinative bonds (Figure 1B), which can be reduced with an external reducing agent (Figure 1C). Several hybrid metal nanoparticle/cellulose materials have been synthesized from transition metals, such as silver, gold, palladium, cadmium, and iron. However, the production of nickel-based nanoparticles supported on nanocellulose and their use in catalytic applications has been scarcer. In few cases, nickel-based nanoparticles on cellulose have been prepared via the reduction of nickel salts and a reducing agent in the presence of cellulose and show that cellulose can facilitate the formation of small nickel nanoparticles (5–60 nm) in a nanocellulose matrix. Recently, we generated nickel boride nanoparticles in a solution containing TEMPO-oxidized nanocellulose and the result shows that the nanocellulose facilitates the formation of smaller nanoparticles (15–60 nm) compared to similar conditions in water (see Figure 2). The pre-coordination of Ni²⁺ ions to the carboxyl groups was confirmed by UV-vis spectroscopy by the appearance of a new shoulder at 390–400 nm upon the addition of nickel chloride to a dispersion of TEMPO-NC (0.01 wt%), which correlates with the UV maximum at 395 nm for nickel acetate (Figure 2B). The nickel boride was then
generated via reduction of nickel chloride with sodium borohydride. The TEM analysis suggests that the nickel boride nanoparticles are embedded in the nanocellulose network, demonstrating its importance as a stabilizer in the formation of the nanoparticles, which in turn open for the use of the entire extensive surface area of the Ni nanoparticles (Figure 2C). Without the nanocellulose, the nickel boride material is formed as an aggregated black precipitate (Figure 2A), which stresses the importance of the nanocellulose in solution for the formation of smaller and more reactive nanoparticles (Figure 2). Further examples of the supportive nature of the nanocellulose matrix, i.e. to avoid particle aggregation that may limit the reactivity of the particles, can be found in cellulose both present as released/extracted more highly crystalline, individual fibers, or consolidated networks of fibers that can stabilize the nucleation and growth of the particle phase.\textsuperscript{30}

To confirm the increased reactivity, the nanocellulose-nickel boride nanoparticles were first evaluated in the reduction of nitroarenes (Figure 3).\textsuperscript{29} The in situ prepared fiber-associated nanoparticles showed the ability to reduce nitroarenes to anilines in merely 50 min in water solutions containing the nanocellulose. The low nickel loading (0.25 mol\% clearly contrasts previously reported nitroarene reductions promoted by stoichiometric amounts of nickel boride.\textsuperscript{16,18} The enhanced efficacy was verified in the reduction of three different nitro compounds that were reduced in the presence and absence of the TEMPO-NC. The results clearly demonstrate that higher isolated yields (84–95\%) are obtained from the reactions with nanocellulose than the reactions performed only in water (43–28\%) (Figure 3).

![Figure 3](image)

**Figure 3** Isolated yields for the reduction of nitro compounds with in situ prepared nickel boride with and without TEMPO-oxidized nanocellulose in water

Decreasing the amount of nickel chloride (0.1 mol\%) led to an even larger difference in turnover frequency and isolated yields (about 8 times) due to the stabilizing effect of the nanocellulose and that the hybrid nanocellulose-supported nickel boride nanoparticles function as efficient catalyst for the reduction of nitro compounds in water at very low nickel concentrations.

The reaction showed a large substrate scope and about 25 different aromatic and aliphatic nitro compounds were efficiently reduced (see selected examples in Scheme 2).

![Scheme 2](image)

**Scheme 2** Reduction of aromatic nitro compounds (reduced group in bold)

In order to increase the synthetic utility of the method, two efficient tandem protocols using the hybrid catalyst system were developed. In these protocols, the in situ

![Scheme 3](image)

**Scheme 3** Nitro group reduction in combination with in situ Boc protection or in situ epoxide ring-opening
formed amines were either Boc-protected to carbamates or further reacted with an epoxide to yield β-amino alcohols (Scheme 3).29

2 Azide Reduction – With and Without Nanocellulose Support

Due to the success of the nanocellulose-nickel boride catalytic system in reducing nitro compounds,29 the reactivity of the hybrid catalyst was investigated in the reduction of organic azides. The nickel boride catalytic system was investigated in three different systems; (1) dispersed together with TEMPO-oxidized nanocellulose; (2) embedded in a crystalline bacterial nanocellulose support, or (3) as low concentration nickel boride in methanol. Initially, the nickel boride catalyst was prepared in an aqueous solution containing TEMPO-oxidized nanocellulose29 and was evaluated in the reduction of benzyl azide. In contrast to the nanocellulose-nickel boride catalyzed reduction of nitro compounds, no rate enhancement was observed in the reduction of the benzyl azide compared to the reaction in deionized water without nanocellulose.

However, our initial investigations showed a high reactivity at low catalyst loading which led us to investigate the potential for the NiCl₂/NaBH₄ as a green method with a broad applicability for organic azides reduction (Table 1). The reaction was investigated in both aqueous and methanolic solvents using NiCl₂·6H₂O (0.5–1.5 mol%) together with NaBH₄ (2.5 equiv), where the sodium borohydride provided the stoichiometric reducing agent.

In our study on the reduction of aliphatic azides, the formation of a coupling side product was observed for n-octyl azide,31,32 which led to lower conversion into the desired amine. Therefore, the reaction with aliphatic azides was performed in the presence of Boc anhydride that traps the formed amine in situ in a tandem reduction-protection reaction to form the carbamate. The nickel boride catalyzed reduction of benzyl azide was active in aqueous solution at low catalyst loading (1.0 mol%), but at lower catalyst loadings (0.25–0.75 mol%) led only to a partial conversion. On the other hand, in methanol, which is also referred as a green solvent,33 the benzyl azide was completely reduced in 3 hours to the Boc-protected amine employing merely 0.5 mol% of the nickel catalyst (Table 1). These low catalyst loadings represent an important improvement with respect to previously reported transition-metal-catalyzed hydrogenations of azides.34–37 A series of organic azides were evaluated with the optimized reduction protocol, aliphatic azides showed high conversions and were isolated as the corresponding carbamate after subsequent in situ Boc-protection (Table 2). The reaction resulted also suitable for less accessible azides, and indeed, both secondary and tertiary azides were converted into their reduced products in good yields (Table 2, entries 4 and 5). The azido moiety has orthogonal reactivity and is therefore an attractive strategy to mask reactive amino groups in carbohydrate chemistry or in multistep synthesis.38 With this in mind, the benzyl-protected sugar-based azide 1f was evaluated with the optimized reduction conditions. The azide functionality was easily reduced yielding the Boc-protected product 2f in 74% yield (Table 2, entry 6). In this reaction, the benzyl groups were not affected by the reduction condition suggesting that this method can be a more convenient route to azide reduction than the standard hydrogenation using H₂/Pd/C. The more reactive aromatic azides39 were also successfully reduced under the reaction conditions (Scheme 4). Remarkably, reduction-sensitive functionalities as nitrile (2h), carboxylic group (2i), amide (2l), and ester (2o) were all well tolerated by the system. The azide was chemoselectively reduced even in the presence of the benzyl ether group, which is often cleaved-off via transition-metal-catalyzed hydrogenation.40

A modified protocol was developed in order to achieve chemoselectivity in aromatic compounds containing halogen substituents on the aromatic ring. 1-Azido-2-chlorobenzene (1p) was successfully reduced to the corresponding aniline when the reaction temperature was lowered to –20 °C, and under these conditions the dehalogenation side reaction was completely suppressed. Replacing the chloro with the iodo substituent, compound 1n, the chemoselectivity was decreased leading to increased formation of aniline. Depriving the system of the necessary reductant by lowering the equivalents of sodium borohydride (0.85 equiv) prevented the over-reduction of the 4-iodoaniline to aniline, leading to the formation of the product in 84% yield at –20 °C. Unfortunately, attempts to obtain similar chemoselectivity in the presence of a terminal olefin [1-azido-4-

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**Table 1 Optimization of Catalyst Loading and Solvent**

| Entry | NiCl₂ (mol%) | Time (h) | Solvent | Conversion (%) | Yield (%) |
|-------|--------------|----------|---------|---------------|-----------|
| 1     | 0.75         | 2        | H₂O     | 86⁺          |           |
| 2     | 0.25         | 6.5      | H₂O     | 36⁺          |           |
| 3     | 1.5          | 1.5      | H₂O     | 100⁺         |           |
| 4     | 1.0          | 3        | MeOH    | 100’ [96]⁺   |           |
| 5     | 0.5          | 16       | MeOH    | 100⁺         |           |
| 6     | 0.5          | 3        | MeOH    | 98⁺ [89]⁺    |           |
| 7     | 0.25         | 3        | MeOH    | 86’ [80]⁺    |           |

* Reaction conditions: 1a (0.3 mmol, 0.15 M), NiCl₂·6H₂O (x mol%), NaBH₄ (3.0 equiv), Boc₂O (1.5 equiv), degassed solvent, rt.
* Determined by ’H NMR spectroscopy.
* Determined by GC-FID using anisole as internal standard.
* Yield determined with GC-FID using anisole as internal standard.
(vinylxylo)benzene] resulted in a mixture of products mainly containing the target compound [4-(vinylxylo)aniline] together with the final aniline with the double bond reduced. In an effort to disclose the synthetic appeal of the reduction system, a tandem reaction was devised involving the synthesis of the azide (1a) starting from benzyl bromide, followed by the reduction and Boc-protection of the newly formed amine in a one-pot protocol leading to a satisfying 86% overall yield (Scheme 5).

Immobilizing the metal nanoparticle on a solid support is an often-used strategy to stabilize or enhance the reactivity of the catalyst. Embedding the catalyst on a heterogeneous support can also enable an easy recovery step and thus the removal of the catalyst from the reaction mixture with the possibility to reuse it for a second cycle. To further simplify the reaction protocol, the active in situ generated catalyst was loaded onto a support that allowed the removal of the catalyst by filtration and, at the same time, provided a practical solution for recycling the catalyst. In line with recently published work of our group, the support of choice was bacterial crystalline nanocellulose (BNC), which represents a versatile support that offers high fibril uniformity and mechanical stability (Young's modulus > 100 GPa), high surface area (>200 m²/g), together with being a bio-sourced, biodegradable, and non-toxic material already used to stabilize different types of metal nanoparticles. In comparison with TEMPO-oxidized cellulose from natural forest material that require extensive oxidation to obtain the 3–5 nm fibrils, the BNC is acid extracted from the Acetobacter xylinum pellicle as 40–50 nm ribbons containing the tightly organized and highly crystalline Cellulose I crystals of typical length >2–3 μm. A sample of bacterial nanocellulose was dipped into an aqueous solution of the Ni(II) salt, the excess of water was removed and upon lyophilization the NiCl₂·6H₂O functionalized material was obtained.

Table 2  Tandem Reduction and Boc-Protection of Aliphatic Azides with Nickel Boride Catalyst

| Entry | Azide | Product | Yield (%) |
|-------|-------|---------|-----------|
| 1     | [N₃]  | [NH₃]   | 84        |
| 2     | [N₃]  | [NH₃]   | 82       |
| 3     | [N₃]  | [NH₃]   | 83        |
| 4     | [N₃]  | [NH₃]   | 76       |
| 5     | [N₃]  | [NH₃]   | 55       |
| 6     | [N₃]  | [NH₃]   | 73       |

* Reaction conditions: azide (0.3–0.6 mmol, 0.15 M), NiCl₂·6H₂O (0.5 mol%), NaN₃ (2.5 equiv), degassed MeOH, rt, 3 h.
* Isolated yield.
* 1.0 mol% catalyst loading used.
* 1.5 mol% catalyst loading used.

Scheme 4  Reduction of more reactive azides and halo-substituted azides. Reagents and conditions: azide (0.15–0.6 mmol, 0.15 M), NiCl₂·6H₂O (0.5 mol%), NaN₃ (2.5 equiv), NaBH₄ (2.5 equiv), degassed MeOH, rt, 3 h.

Scheme 5  Procedure for the one-pot synthesis, reduction, and Boc-protection of benzyl azide
Figure 4 SEM images of Ni-B nanoparticle supported on bacterial crystalline nanocellulose. (a) Overview of the functionalized support (scale bar 5.00 μm). Metal-NPs appears as bright spots on the nanocellulose material. (b) 30.0k magnification on NPs aggregates around nanocellulose fibrils (scale bar 1.00 μm). (c) Bacterial crystalline nanocellulose prior to functionalization (scale bar 5.00 μm).

The material was added to a solution of sodium borohydride in order to generate the active NiB-BNC catalyst. Scanning electron microscopy (SEM) analyses were carried out on the obtained functionalized solid support in order to investigate the interaction between the catalyst and its support. As anticipated, the in situ obtained Ni-B, formed spherical nanoparticles (NPs) associated to the nanofibrils of the cellulose. It was also visible that the nanoparticles vary in dimensions with the diameters of the NPs ranging between 10 and 100 nm, with a tendency to form larger aggregates (Figure 4).

The new NiB-BNC material was used in the reduction of the azide 1j under the usual reaction conditions, but with the Ni(II) salt loaded on the nanocellulose support, which upon addition of sodium borohydride is converted into the active catalyst Ni-B (see supporting information, Figure S1). After completion of the reaction, the catalyst was conveniently filtered off and reused for a further two cycles providing satisfying conversion. As noted elsewhere, the exposure of Ni-B catalyst to air lead to a drop of its catalytic performances and this observation was confirmed in our experiments (Figure 5).

Figure 5 Reduction of 1j using NiCl₂ loaded on nanocellulose. Reagents and conditions: azide (0.18 mmol, 0.18 M), NiCl₂·6H₂O (1.0 mol%), NaBH₄ (2.5 equiv), degassed MeOH, rt. At completion of the reaction, the mixture is filtered off and the catalyst support washed and reused for the next cycle. Reaction times are: 20 min, 25 min, and 33 min, 60 min, 120 min for cycles 1, 2, 3, 4 and 5, respectively.

In fact, the catalyst was recyclable only for a limited number of cycles (3) after which, the catalytic activity sharply decreased. Even when the reduction reaction was conducted in an oxygen free atmosphere, as in a glovebox, the conversion observed after repeated cycles were substantially lower. The mother liquors of the 1st and the 2nd cycle of a recycling experiment were collected and analyzed via ICP-OES to investigate the amount of leached nickel boride catalyst. The analyses showed that in the first cycle, 3.9% of the nickel catalyst was leached into the solution, whereas in the second cycle only 0.8% was leached. We hypothesize that the higher observed amount of nickel in the 1st cycle is due to a leaching of the NiCl₂ precatalyst during its formation which makes it more loosely bound to the cellulose support.

3 Conclusion

The developed procedure enlarges the portfolio of azide-reduction protocols providing organic chemists with a practically convenient method that is superior, or comple-
mentary, to already existing protocols present in the literature to perform the azide to amine conversion via hydroge-
nation. With the aim of designing a sustainable re-
action, the catalyst loading was successfully lowered to 0.5
mol%, representing a substantial improvement on respect
of already existing methodologies catalyzed by cheap and
abundant transition metal. The reaction system was
proved to be general for both aliphatic and aromatic azide
and a wide range of azides were tested in an attempt to
highlight the limits of the reaction system as well as its
functional group tolerability. The functionalization of the
solid support (i.e., crystalline nanocellulose) with the cata-
lyst’s precursor, further enhanced the operational simplic-
ty of the reaction system. In addition, a one-pot synthesis
of the Boc-protected benzylamine, starting from benzyl bro-
mide, was successfully carried out.

All reagents were obtained from commercial sources and used with-
out further purification. All solvents were purified and dried accord-
ing to standard methods prior to use, unless stated otherwise. De-
gassed solvents were obtained by bubbling the solvent with inert gas
through a needle. TLC was performed using 60 mesh silica gel plates
visualized with short-wavelength UV light (254 nm). Silica gel 60
(200–300 mesh) was used for column chromatography. The surface
morphology of the catalyst loaded onto the support was analyzed us-
ing a Hitachi S-4800 field emission scanning electron microscope (FE-
SEM). A voltage of 3 kV and a current of 10 μA were used. The lyo-
philized materials were sputtered with a palladium/platinum (Pt/Pd)
target in an Agar High Resolution Sputter Coater (model 208RH). The
sputtering time for all samples was 45 s proving an estimated conduc-
tive layer of 1–2 nm. ICP-OES analyses were run with a Thermo Sci-
entific iCAP 6000 series instrument and standard Ni solutions were
prepared and measured prior to the real analyses to obtain the calibration
curve. A Bruker Ascend 400 spectrometer (400 MHz) or Bruker Avance
DMX 500 (500 MHz) spectrometer was used for the recording of 1H,
13C, and 19F NMR spectra. Proton chemical shifts are reported relative to
TMS with CDCl3 (δ = 7.26), DMSO-d6 (δ = 2.50), and methanol-d4 (δ = 3.31) as internal standards. 13C chemical shifts are reported relative to TMS with CDCl3 (δ = 77.16), DMSO-d6 (δ = 39.52), or methanol-d4 (δ = 49.0) as internal standards.

**Tandem Reduction and Boc-Protection of Aliphatic Azido Com-
ounds; General Procedure A (GPA)**

To a 5-mL sealed vial equipped with a magnetic stir bar, a solution
containing azido compound (1 equiv, 0.15 mM) in deoxygenated
MeOH, NiCl2·6H2O (0.5 mol%), and NaBH4 (2.5 equiv) were added. The
mixture was stirred at rt for 3 h protected from light. After comple-
tion of the reaction, the crude obtained upon solvent removal under
reduced pressure was purified via flash column chromatography (silica gel, petroleum ether/EtOAc) to afford the pure
product. All compounds synthesized herein are known in the litera-
ture. Proof of purity and identity was obtained by 1H, 13C, and 19F
NMR spectroscopy.

**Reduction of Aromatic Azido Compounds; General Procedure B
(GPB)**

To a 5-mL sealed vial equipped with a magnetic stir bar, a solution
containing azido compound (1 equiv, 0.15 mM) in deoxygenated
MeOH, NiCl2·6H2O (0.5 mol%), and NaBH4 (2.5 equiv) were added. The
mixture was stirred at rt for 3 h protected from light. After comple-
tion of the reaction, the crude obtained upon solvent removal under
reduced pressure, was re-dissolved in water and extracted with Et2O
or EtOAc, leaving the catalyst in the aqueous phase. The organic layer
was dried (Na2SO4), and the pure product was obtained upon in vacuo
solvent removal. All compounds were characterized by 1H and 13C
NMR spectroscopy.

**Synthesis of Substituted Aromatic Azido Compounds; General
Procedure C (GPC)**

To a methanolic solution of the boronic acid (1.0 equiv, 0.1 M) were
added NaN3 (1.5 equiv) and Cu(OAc)2 (0.05–0.1 equiv). The solution
was stirred for 24–48 h at 30 °C under air, protected from the light.
The solvent was then removed, and the crude was taken up with H2O
and extracted with Et2O. The organic layer was dried (Na2SO4), and
the pure product was either obtained at this stage or after a further
purification by flash column chromatography. All compounds were
characterized by 1H and 13C NMR spectroscopy.

**Catalyst Recycling Experiment; General Procedure D**

In a typical experiment, bacterial crystalline nanocellulose (ca. 3.5
mg), was soaked for 3 min in a 10 mM aq solution of NiCl2·6H2O. The
new material was then transferred into a vial and H2O removed via
lyophilization. The amount of the nickel salt loaded was obtained by
weighing the cellulose support after the functionalization [average
NiCl2·6H2O loading: 16.4 (±3.0) wt%]. The functionalized NiCl2-nano-
cellulose was subsequently transferred into a Biotage® 10-mL reactor
vial with PTFE frit equipped with stir bar and a rubber septum under
inert atmosphere. Compound 1j (1 equiv, 0.15 mM) in deoxygenated
MeOH and NaBH4 (2.5 equiv) were added. The mixture was stirred at
rt and upon completion of the reaction, the solution was worked up as in general procedure B, whilst the catalyst support was filtered-off,
flushed with MeOH and re-used in the next reaction cycle. The con-
version of the starting material was obtained via 1H NMR analysis.

**One-pot procedure for the synthesis of tert-butyl benzylcarba-
mate (2a)**

In a 5 mL sealed vial equipped with a magnetic stir bar, deoxygenated
methanol (3 mL), NaN3 (38 mg, 0.58 mmol, 2.2 equiv) and benzyl bro-
mide (45 mg, 0.26 mmol, 1 equiv) were added. The reaction mixture
was stirred at 55 °C for 3 hours protected from light until completion
of the substitution reaction as observed by TLC analysis. The reaction
mixture was let reach room temperature before adding a solution of NiCl2 in degassed methanol (0.0013 mmol, 32 μL, 42 mM). Boc anhy-
dride (69 mg, 0.30 mmol, 1.2 equiv) and NaBH4 (25 mg, 0.65 mmol, 2.5
equiv). The reaction was then stirred for further 3 hours at room
temperature. After completion of the reaction, the crude obtained
upon solvent removal under reduced pressure was purified via flash
column chromatography (silica gel, petroleum ether/EtOAc) to afford the pure product as a colorless oil in an overall 86% yield.

1H NMR (400 MHz, CDCl3): δ = 7.34–7.25 (br, 5 H), 4.88 (s, 1 H, NH),
4.30 (s, 2 H), 1.46 (s, 9 H). 

13C NMR (100 MHz, CDCl3): δ = 156.0, 139.1, 128.7, 127.6, 127.4, 79.6, 44.8, 28.5.

**tert-Butyl Benzylcarbamate (2a)**

The compound was obtained according to GPA using azido compound
1a (51 mg, 0.44 mmol, 1 equiv), NiCl2 (47 μL, 42 mM, 0.5 mol%), Boc2O
(95 mg, 0.44 mmol, 1.1 equiv), and NaBH4 (41 mg, 1.1 mmol, 2.8
Boc-Protected Methyl 6-Amino-2,3,4-tri-O-benzyl-6-deoxy-a-D-glucopyranoside (2f)

The compound was obtained according to GPA using azido compound 1f (143 mg, 0.3 mmol, 1 equiv), NiCl₂ (69 μL, 42 mM, 1.0 mol%), Boc₂O (79 mg, 0.36 mmol, 1.2 equiv), and NaBH₄ (28 mg, 0.74 mmol, 2.5 equiv). The pure product was obtained after flash column chromatography (silica gel, petroleum ether/CH₂Cl₂/EtOAc 8:11 → 4:1:1; Rf 0.44, petroleum ether/CH₂Cl₂/EtOAc 4:1:1) as colorless oil (120 mg, 73% yield).

1H NMR (CDCl₃, 400 MHz): δ = 7.34–7.42 (m, 15 H, Ar), 5.04 (d, J = 10.8 Hz, 1 H, CH₂Ar), 4.67–4.91 (m, 6 H, CH₂Ar + NH), 4.59 (d, J = 3.4 Hz, 1 H, H-1), 4.05 (t, J = 9.24 Hz, 1 H), 3.71–3.74 (m, 1 H), 3.52–3.56 (m, 2 H), 3.40 (s, 5 H, CH + OCH₃), 1.48 (s, 9 H, t-Bu).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 155.8, 138.7, 138.2, 138.1, 128.6, 128.51, 128.50, 128.4, 128.2, 128.1, 128.0, 127.9, 127.7, 98.0, 82.0, 80.1, 79.3, 78.6, 75.9, 75.2, 73.4, 69.4, 55.1, 41.0, 28.6.

Aniline (2g)

The compound was obtained according to GPB using azido compound 1g (65 μL, 0.66 mmol, 1 equiv), NiCl₂ (70 μL, 42 mM, 0.5 mol%), and NaBH₄ (64 mg, 1.7 mmol, 2.8 equiv) to give the product as colorless oil (45 mg, 81% yield).

1H NMR (CDCl₃, 400 MHz): δ = 7.12 (t, J = 7.56 Hz, 2 H), 6.73 (t, J = 7.10 Hz, 1 H), 6.64 (d, J = 8.28 Hz, 2 H), 3.5 (s, 2 H, NH).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 146.5, 129.4, 118.7, 115.2.

4-Aminobenzonitrile (2h)

The compound was obtained according to GPB using azido compound 1h (22 mg, 0.15 mmol, 1 equiv), NiCl₂ (25 μL, 42 mM, 0.5 mol%), and NaBH₄ (17 mg, 0.45 mmol, 2.9 equiv) to give the product as pale-yellow oil (15 mg, 83% yield).

1H NMR (CDCl₃, 400 MHz): δ = 7.41 (d, J = 8.66 Hz, 2 H), 6.64 (d, J = 8.66 Hz, 2 H), 4.15 (s, 2 H, NH).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 150.5, 133.9, 120.2, 114.6, 100.4.

4-Aminobenzoic Acid (2i)

To a 5-mL sealed vial equipped with a magnetic stir bar, a solution containing 4-azidobenzoic acid HCl (98 mg, 0.60 mmol, 1 equiv) in deoxygenated MeOH (4 mL), NiCl₂ (70 μL, 42 mM, 0.5 mol%), and NaBH₄ (56 mg, 1.5 mmol, 2.5 equiv) were added. The mixture was stirred at rt for 3 h protected from light. After completion of the reaction, the crude obtained upon solvent removal under reduced pressure was purified via flash column chromatography (silica gel, CH₂Cl₂/MeOH 95:5) as a white precipitate (50 mg, 61% yield).

1H NMR (CDCl₃, 400 MHz): δ = 7.76 (d, J = 7.83 Hz, 2 H), 6.65 (d, J = 7.83 Hz, 2 H), 4.93 (s, 2 H, NH).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 170.7, 154.6, 132.8, 119.1, 114.3.

4-(Benzylxoy)aniline (2j)

The compound was obtained according to GPB using azido compound 1j (130 mg, 0.6 mmol, 1 equiv), NiCl₂ (70 μL, 42 mM, 0.5 mol%), and NaBH₄ (65 mg, 1.7 mmol, 3.0 equiv) to give the product as a yellowish precipitate (114 mg, 99% yield).

1H NMR (CDCl₃, 400 MHz): δ = 7.34–7.25 (br, 5 H), 4.88 (s, 1 H, NH), 4.30 (s, 2 H, 1.46 (s, 9 H).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 156.0, 139.1, 128.7, 127.6, 127.4, 79.6, 44.8, 28.5.
4-Aminophenol (2k)
The compound was obtained according to GPB using azido compound 1k (80 mg, 0.6 mmol, 1 equiv), NiCl2 (70 µL, 42 mM, 0.5 mol%), and NaBH4 (38 mg, 1.5 mmol, 2.5 equiv) to give the product as a reddish precipitate (55 mg, 85% yield).

1H NMR (DMSO-d6, 400 MHz): δ = 7.86 (s, 1 H, OH), 6.48 (d, J = 8.62 Hz, 2 H), 6.14 (d, J = 8.62 Hz, 2 H), 3.43 (s, 2 H, NH).

13C{1H} NMR (DMSO-d6, 100 MHz): δ = 148.2, 140.6, 115.5, 115.2.

4-Methoxyaniline (2m)
The compound was obtained according to GPB using azido compound 1m (75 mg, 0.5 mmol, 1 equiv), NiCl2 (60 µL, 42 mM, 0.5 mol%), and NaBH4 (47 mg, 1.2 mmol, 2.5 equiv) to give the product as a colorless oil (55 mg, 89% yield).

1H NMR (CDCl3, 400 MHz): δ = 7.41 (d, J = 8.22 Hz, 2 H), 6.46 (d, J = 8.79 Hz, 2 H), 3.64 (br, 2 H, NH).

13C{1H} NMR (CDCl3, 100 MHz): δ = 152.8, 143.5, 130.5, 122.2, 114.3.

4-Iodoaniline (2n)
The compound was obtained according to GPB but using NaBH4 (0.85 equiv) dissolved in H2O/acetone (1:4; 50 mL), was added NaN3 (1.0 g, 15 mmol, 1.5 equiv). The mixture was stirred at rt for 48 h protected from light. Acetone was removed under reduced pressure and the crude extracted with CH2Cl2. The organic layer was dried (Na2SO4), and the pure product was obtained upon solvent removal under reduced pressure as a colorless oil (9.6 g, 72% yield).

1H NMR (CDCl3, 400 MHz): δ = 7.47–7.37 (m, 5 H), 4.37 (s, 2 H).

19F NMR (CDCl3, 376 MHz): δ = 22.8, 14.2.

Methyl 4-Amino-2,3,5,6-tetrafluorobenzoate (2q)
The compound was obtained according to GPB using azido compound 1q (149 mg, 0.6 mmol, 1 equiv), NiCl2 (75 µL, 42 mM, 0.5 mol%), and NaBH4 (56 mg, 1.5 mmol, 2.5 equiv) to give the product as an off-white precipitate (118 mg, 88% yield).

1H NMR (CDCl3, 400 MHz): δ = 4.43 (br, 2 H, NH), 3.90 (s, 3 H, COOCH3).

13C{1H} NMR (CDCl3, 100 MHz): δ = 135.5, 129.0, 128.4, 128.4, 54.9.

(Azidomethyl)benzene (1a)
To a single-neck 100-mL round-bottom flask equipped with a magnetic stir bar, containing benzyl bromide (1.2 mL, 10 mmol, 1 equiv) dissolved in H2O/acetone (1:4; 50 mL), was added NaN3 (1.0 g, 15 mmol, 1.5 equiv). The mixture was stirred at rt for 4 h protected from light. Acetone was removed under reduced pressure and the crude extracted with CH2Cl2. The organic layer was dried (Na2SO4), and the pure product was obtained upon solvent removal under reduced pressure as a colorless oil (9.6 g, 72% yield).

1H NMR (CDCl3, 400 MHz): δ = 7.47–7.37 (m, 5 H), 4.37 (s, 2 H).

13C{1H} NMR (CDCl3, 100 MHz): δ = 135.5, 129.0, 128.4, 128.4, 54.9.

1-Azidoctane (1b)
To a 100-mL round-bottom flask equipped with a magnetic stir bar, CHCl3 (40 mL) and octan-1-ol (40 mL, 1.0 mmol, 1 equiv) were added. The mixture was then cooled to 5 °C and pyridine (160 µL, 1.75 mmol, 3 equiv), together with p-toluenesulfonyl chloride (380 mg, 2.0 mmol, 2 equiv), added in small portions, were introduced. The reaction was stirred for 3 h until all the starting material was consumed as monitored by TLC analysis. The solvent was removed under reduced pressure and the crude dissolved in Et2O and washed with 2 M aq HCl, concd aq NaHCO3, and H2O. The ethereal phase was dried (Na2SO4) and concentrated in vacuo. The crude was dissolved in H2O/acetone (1:5; 20 mL) in a 50-mL round-bottom flask equipped with magnetic stir bar and a condenser. To the mixture was added NaN3 (440 mg, 2.4 mmol, 2.5 equiv) and then it was stirred at reflux for 24 h. Acetone was removed under reduced pressure and the crude extracted with Et2O. The organic layer was dried (Na2SO4), and the crude obtained upon solvent removal in vacuo was purified via flash column chromatography (silica gel, petroleum ether/Et2O 98:2, Rf = 0.15) to afford the pure product as a colorless oil (57 mg, 37% yield).

1H NMR (CDCl3, 400 MHz): δ = 3.25 (t, J = 6.96 Hz, 2 H, CH2N3), 1.60 (m, 2 H), 1.36–1.28 (m, 10 H), 0.88 (t, J = 6.72 Hz, 3 H, CH2CH3).

13C{1H} NMR (CDCl3, 100 MHz): δ = 51.7, 31.9, 29.3, 29.3, 29.0, 26.9, 22.8, 14.2.

2-[2-(Azidoethoxy)ethoxy]ethan-1-ol (1c)
To a 25-mL round-bottom flask equipped with a magnetic stir bar, containing 2-[2-(chloroethoxy)ethoxy]ethanol (1.0 mL, 6.9 mmol, 1 equiv) dissolved in H2O (10 mL), were added NaI (207 mg, 1.4 mmol, 2 equiv), added in small portions, were introduced. The reaction was cooled to 5 °C and pyridine (160 µL, 1.75 mmol, 3 equiv), together with p-toluenesulfonyl chloride (380 mg, 2.0 mmol, 2 equiv), added in small portions, were introduced. The reaction was stirred for 3 h until all the starting material was consumed as monitored by TLC analysis. The solvent was removed under reduced pressure and the crude extracted with CH2Cl2. The organic layer was dried (Na2SO4), and the crude obtained upon solvent removal in vacuo was purified via flash column chromatography (silica gel, petroleum ether/Et2O 98:2, Rf = 0.15) to afford the pure product as a colorless oil (57 mg, 37% yield).

1H NMR (CDCl3, 400 MHz): δ = 3.25 (t, J = 6.96 Hz, 2 H, CH2N3), 1.60 (m, 2 H), 1.36–1.28 (m, 10 H), 0.88 (t, J = 6.72 Hz, 3 H, CH2CH3).

13C{1H} NMR (CDCl3, 100 MHz): δ = 51.7, 31.9, 29.3, 29.3, 29.0, 26.9, 22.8, 14.2.

Feature
ganic layer was dried (Na$_2$SO$_4$), and the pure product was obtained upon solvent removal under reduced pressure as a pale yellow oil (1.039 g, 86% yield).

$^{1}$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 3.74 (m, 2 H), 3.69 (m, 6 H), 3.62 (m, 2 H), 3.40 (t, $J$ = 4.87 Hz, 2 H), 1.80 (br, 1 H).

$^{13}$C{1H} NMR (CDCl$_3$, 100 MHz): $\delta$ = 72.6, 70.8, 70.6, 70.2, 62.0, 50.8.

Azidocyclohexane (1d)$^{49}$

To a 250-mL round-bottom flask equipped with a magnetic stir bar, flame dried, were introduced under inert atmosphere, bromocyclohexene (1.25 mL, 10.2 mmol, 1 equiv) dissolved in dry DMF (60 mL). The reaction was stirred for 17 h at 80 °C protected from light. The product was extracted with Et$_2$O (4 × 50 mL) and washed with brine (6 × 30 mL). The organic layer was dried (Na$_2$SO$_4$), and the pure product was obtained upon solvent removal under reduced pressure as a colorless oil (0.766 g, 60% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 7.76–7.78 (m, 2 H, Ar), 7.26–7.40 (m, 15 H, Ar), 7.15–7.17 (m, 2 H, Ar), 4.98 (d, $J$ = 10.9 Hz, 1 H, CH$_2$Ph), 4.76–4.85 (m, 3 H, CH$_2$Ph), 4.64 (d, $J$ = 12.1 Hz, 1 H, CH$_2$Ph), 4.53 (d, $J$ = 3.4 Hz, 1 H, H-1), 4.44 (dd, $J$ = 10.7 Hz, 1 H, CH$_2$Ph), 4.19–4.21 (m, 2 H), 3.96 (t, $J$ = 9.23 Hz, 1 H), 3.77 (m, 1 H), 3.43–3.50 (m, 2 H), 3.32 (s, 3 H, OCH$_3$), 2.39 (s, 3 H, Ts-CH$_3$).

$^{13}$C{1H} NMR (CDCl$_3$, 100 MHz): $\delta$ = 144.9, 138.7, 138.1, 137.9, 133.0, 129.9, 128.6, 128.51, 128.50, 128.2, 128.0, 127.98, 127.94, 127.78, 128.0, 79.8, 77.0, 75.8, 75.1, 73.5, 68.7, 68.6, 55.4, 21.7.

Methyl 6-Azido-2,3,4-tri-O-benzoyl-6-deoxy-a-D-glucopyranoside (10)$^{33}$

To a 25-mL round-bottom flask equipped with a magnetic stir bar, flame dried, were introduced under inert atmosphere, NaN$_3$ (410 mg, 6.3 mmol, 1.5 equiv) and methyl 6-Azido-2,3,4-tri-O-benzoyl-6-deoxy-a-glucopyranoside (234 mg, 0.38 mmol, 1 equiv) dissolved in anhyd DMF (10 mL). The reaction was stirred for 4 h at 85 °C under inert atmosphere protected from light. The product was extracted from H$_2$O (15 mL) with Et$_2$O (4 × 15 mL) and washed with brine (5 × 20 mL). The organic layer was dried (Na$_2$SO$_4$), and the pure product was obtained after flash column chromatography (silica gel petroleum ether/CH$_2$Cl$_2$/EtOAc 10:1:1 → 6:1:1, $R_f$ = 0.38) as a colorless oil (143 mg, 77% yield).

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ = 7.25–7.37 (m, 15 H, Ar), 5.00 (d, $J$ = 10.9 Hz, 1 H, CH$_2$Ph), 4.90 (d, $J$ = 11.1 Hz, 1 H, CH$_2$Ph), 4.80 (m, 2 H, CH$_2$Ph), 4.67 (d, $J$ = 12.1 Hz, 1 H, CH$_2$Ph), 4.62 (d, $J$ = 3.6 Hz, 1 H, H-1), 4.58 (d, $J$ = 11.1 Hz, 1 H, CH$_2$Ph), 3.99 (t, $J$ = 9.3 Hz, 1 H), 3.78 (m, 1 H), 3.54 (dd, $J$ = 9.6, 3.6 Hz, 1 H), 3.44 (m, 2 H), 3.40 (s, 3 H, OCH$_3$), 3.33 (dd, $J$ = 13.0, 5.7 Hz, 1 H).

$^{13}$C{1H} NMR (CDCl$_3$, 125 MHz): $\delta$ = 138.7, 138.1, 138.0, 128.6, 128.59, 128.53, 128.19, 128.07, 128.06, 128.03, 127.88, 127.83, 81.9, 79.8, 77.0, 75.8, 75.1, 73.5, 68.7, 68.6, 55.4, 51.5.

Azido benzene (1g)

The compound was obtained according GPC using boronic acid (536 mg, 4.3 mmol, 1 equiv), Cu(OAc)$_2$ (40 mg, 0.22 mmol, 0.05 equiv). After 24 h of reaction the crude was worked up and the pure product was obtained after flash column chromatography (silica gel, petroleum ether/EtOAc 98:2, $R_f$ = 0.85) as a colorless oil (297 mg, 58% yield).

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 7.36 (t, $J$ = 7.6 Hz, 2 H), 7.15 (t, $J$ = 7.6 Hz, 1 H), 7.04 (d, $J$ = 8.4 Hz, 2 H).

$^{13}$C{1H} NMR (CDCl$_3$, 100 MHz): $\delta$ = 140.2, 129.9, 125.0, 119.2.

4-Azido benzonitrile (1h)

The compound was obtained according GPC using boronic acid (146 mg, 1.0 mmol, 1 equiv), Cu(OAc)$_2$ (18 mg, 0.1 mmol, 0.1 equiv). After 19 h of reaction the crude was worked up and the pure product was obtained after flash column chromatography (silica gel, petroleum ether/EtOAc 90:10) as a white crystalline precipitate (92 mg, 64% yield).

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1H NMR (CDCl₃, 400 MHz): δ = 7.53 (d, J = 8.0 Hz, 2 H), 7.09 (d, J = 8.0 Hz, 2 H).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 144.9, 133.8, 119.7, 118.4, 108.3.

4-Azidobenzoic Acid (1i)
The compound was obtained according GPC using boronic acid (500 mg, 3.0 mmol, 1 equiv), Na₂O₃ (250 mg, 3.8 mmol, 1.3 equiv), and Cu(OAc)₂ (50 mg, 0.3 mmol, 0.1 equiv). After 24 h of reaction the crude was dissolved in 1 M aq HCl and the product extracted with EtOAc, washed with brine, and the organic layer dried (Na₂SO₄). The compound was obtained according GPC using boronic acid (380 mg, 2.0 mmol, 1 equiv), Na₂O₃ (190 mg, 3.0 mmol, 1.5 equiv), and Cu(OAc)₂ (36 mg, 0.2 mmol, 0.1 equiv). After 24 h of reaction, the crude was worked up without further purification, affording a pale-yellow oil (215 mg, 72% yield).

1H NMR (CD₃OD, 400 MHz): δ = 6.99–6.93 (m, 4 H), 3.78 (s, 3 H, OCH₃).

13C{1H} NMR (CD₃OD, 100 MHz): δ = 158.7, 133.6, 121.0, 116.3, 56.0.

Ethyl 2-Azidobenzoate (1o)
The compound was obtained according GPC, employing EIOH as the solvent, using boronic acid (380 mg, 2.0 mmol, 1 equiv), NaN₃ (190 mg, 3.0 mmol, 1.5 equiv), and Cu(OAc)₂ (36 mg, 0.2 mmol, 0.1 equiv). After 24 h of reaction, the crude was worked up and the pure product was obtained after flash column chromatography (silica gel, petroleum ether/EtOAc 20:1) as a colorless oil (134 mg, 35% yield).

1H NMR (CDCl₃, 400 MHz): δ = 7.85 (d, J = 7.8 Hz, 1 H), 7.50 (m, 1 H), 7.23–7.15 (m, 2 H). 4.37 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.39 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 165.2, 139.9, 133.0, 131.64, 124.4, 123.0, 119.8, 61.3, 14.2.

Methyl 4-Azido-2,3,5,6-tetrafluorobenzoate (1q)⁵⁵
Methyl pentafluorobenzoate (9.5 g, 40 mmol) was dissolved in aceton/H₂O (2:1; 90 mL), NaN₃ (3.40 g, 52 mmol, 1.3 equiv) was added to the flask and the mixture was refluxed at 85 °C for 6 h. The mixture was subsequently cooled to rt, diluted with water (150 mL), and extracted with EtOAc (3 × 150 mL). The combined organic extracts were dried (MgSO₄) and the solvent removed under reduced pressure. The product was obtained after flash column chromatography (silica gel, hexane/EtOAc 40:1) as white crystals (9.467 g, 95% yield).

1H NMR (CDCl₃, 400 MHz): δ = 3.97 (s, 3 H, OCH₃).

13C{1H} NMR (CDCl₃, 100 MHz): δ = 158.7, 133.6, 121.0, 116.3, 56.0.

Conflict of Interest
The authors declare no conflict of interest.

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References

(1) Downing, R.; Kunkele, P.; Van Bekkum, H. Catal. Today 1997, 37, 121.
(2) (a) Ono, N. The Nitro Group in Organic Synthesis; John Wiley & Sons: New York, 2001.
(b) Nishimura, S. Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis; John Wiley & Sons: New York, 2001.
(3) (a) Aditya, T.; Pal, A.; Pal, T. Chem. Commun. 2015, 51, 9410.
(b) Campelo, J. M.; Luna, D.; Luque, R.; Marinás, J. M.; Romero, A. ChemSusChem 2009, 2, 18.
(4) (a) Boronat, M.; Concepción, P.; Corma, A.; González, S.; Illas, F.; Serna, P. J. Am. Chem. Soc. 2007, 129, 16230. (b) Adhihari, B.; Biswas, A.; Banerjee, A. ACS Appl. Mater. Interfaces 2012, 4, 5472.
(5) Takasaki, M.; Motoyama, Y.; Higashi, K.; Yoon, S.-H.; Mochida, I.; Nagashima, H. Org. Lett. 2010, 10, 1601.
(6) Nie, R.; Wang, J.; Wang, L.; Qin, Y.; Chen, P.; Hou, Z. Carbon 2012, 50, 586.
(7) (a) Tuteja, J.; Nishimura, S.; Ebitani, K. RSC Adv. 2014, 4, 38241. (b) Wang, P.; Liu, H.; Niu, J.; Li, R.; Ma, J. Catal. Sci. Technol. 2014, 4, 1333. (c) Yamada, Y. M.; Yuyama, Y.; Sato, T.; Fujikawa, S.; Uozumi, Y. Angew. Chem. Int. Ed. 2014, 53, 127. (d) Guo, Y.; Li, J.; Zhao, F.; Lan, C.; Li, L.; Liu, Y.; Si, Y.; Jiang, Y.; Yang, B.; Yang, R. RSC Adv. 2016, 6, 7950.
(8) Zhao, Z.; Yang, H.; Li, Y.; Guo, Z. Chem. Commun. 2014, 16, 1274.
(9) (a) Rathore, P. S.; Patidar, R.; Shripathi, T.; Thakore, S. Catal. Sci. Technol. 2015, 5, 286. (b) Kalbasi, R. J.; Zamani, F. RSC Adv. 2014, 4, 7444. (c) Zamani, F.; Kianpour, S. Catal. Commun. 2014, 45, 1.
(10) (a) Gao, G.; Tao, Y.; Jiang, J. Green Chem. 2008, 10, 439. (b) Dey, R.; Mukherjee, N.; Ahammed, S.; Ranu, B. C. ChemSusChem 2019, 12, 35.
(11) (a) Nose, A.; Kudo, T. Chem. Pharm. Bull. 1984, 32, 2421.
(b) Nose, A.; Kudo, T. Chem. Pharm. Bull. 1988, 36, 1529.
(b) Schreiner, C.; Figi, R.; Zhang, Q.; Nyström, G. Nanoscale 2020, 12, 7383.
(12) (a) Khurana, J. M.; Gogia, A. Org. Prep. Proced. Int. 1997, 29, 1.
(b) Glavee, G. N.; Klabunde, K. J.; Sorensen, C. M.; Hadjipanayis, G. C. Langmuir 1994, 10, 4726. (b) Legrand, J.; Taleb, A.; Gota, S.; Guittet, M.-J.; Petit, C. Langmuir 2002, 18, 4131.
(13) (a) Sahiner, N.; Ozay, H.; Ozay, O. Aktas, N. Appl. Catal. A, 2010, 385, 201. (b) Wen, H.; Yao, K.; Zhang, Y.; Zhou, Z.; Kirschning, A. Catal. Commun. 2009, 10, 1207. (c) Rahman, A.; Jonnalagadda, S. Catal. Lett. 2008, 123, 264. (d) Wu, Z.; Zhang, M.; Li, W.; Mu, S.; Tao, K. J. Mol. Catal. A: Chem. 2007, 273, 277.
(14) Liu, D.; Wu, Q.; Andersson, R. L.; Hedenqvist, M. S.; Farris, S.; Olsson, R. T. J. Mater. Chem. A 2013, 1, 15745.
(15) Wu, T.; Zeng, Z.; Siqueira, G.; De France, K.; Sivaraman, D.; Schreiner, C.; Figi, R.; Zhang, Q.; Nyström, G. Nanoscale 2020, 12, 7383.
(16) (c) Eyley, S.; Thielemans, W. Nanoscale 2014, 6, 7764. (b) Sassi, J.-F.; Tekely, P.; Chanzy, H. Cellulose 2000, 7, 119.
(17) (d) Khurana, J. M.; Gogia, A. Catal. Sci. Technol. 2012, 2, 288. (c) Rezayat, M.; Blundell, R. K.; Camp, J. E.; Walsh, D. A.; Thielemans, W. ACS Sustainable Chem. Eng. 2014, 2, 1241.
(18) (c) Khurana, J. M.; Kandpal, B. M.; Kukreja, G.; Hoekstra, H. R.; Hyde, E. K. J. Am. Chem. Soc. 1955, 77, 215.
(19) Liu, D.; Wu, Q.; Andersson, R. L.; Hedenqvist, M. S.; Farris, S.; Olsson, R. T. J. Mater. Chem. A 2013, 1, 15745.
(20) Wu, T.; Zeng, Z.; Siqueira, G.; De France, K.; Sivaraman, D.; Schreiner, C.; Figi, R.; Zhang, Q.; Nyström, G. Nanoscale 2020, 12, 7383.
(21) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(22) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(23) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(24) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(25) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(26) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(27) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(28) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(29) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(30) (c) He, Y.; Qiao, M.; Hu, H.; Pei, Y.; Li, H.; Gregurec, D.; Iriogoyen, J.; Moya, S.; Ruiz, J.; Astruc, D. Angew. Chem. Int. Ed. 2016, 55, 3091.
(31) (a) Hayashi, H.; Ohno, A.; Oka, S. Bull. Chem. Soc. Jpn. 1976, 49, 506. (b) Martinez-Sarti, L.; Diez-González, S. ChemCatChem 2013, 5, 1722.
(32) Arai, N.; Onodera, N.; Ohkuma, T. Tetrahedron Lett. 2016, 57, 4183.
(33) Capello, C.; Fischer, U.; Hungerbühler, K. Green Chem. 2007, 9, 927.
(34) (a) Corey, E. J.; Nicolaou, K. C.; Balanson, R. D.; Machida, Y. Synthesis 1975, 590. (b) Gartiser, T.; Selve, C.; Delpuech, J.-J. Tetrahedron Lett. 1983, 24, 1609. (c) Kotsuki, H.; Ohishi, T.; Araki, T. Tetrahedron Lett. 1997, 38, 2129. (d) Jung, Y. J.; Chang, Y. M.; Lee, J. H.; Yoon, C. M. Tetrahedron Lett. 2002, 43, 8735.
(35) Udumula, V.; Nazari, S. H.; Burt, S. R.; Alfindee, M. N.; Michaelis, D. J. ACS Catal. 2016, 6, 4423.
(36) (a) Prakash Rao, H. S.; Reddy, K. S.; Turnbull, K.; Borchers, V. Synth. Commun. 1992, 22, 1339. (b) Prakash Rao, H. S.; Siva, P. Synth. Commun. 1994, 24, 549. (c) Yoon, N. M.; Choi, J.; Shon, Y. S. Synth. Commun. 1993, 23, 3047. (d) Maddani, M. R.; Moorthy, S. K.; Prabhu, K. R. Tetrahedron 2010, 66, 329.
(37) (a) Fringueuilli, F.; Pizzo, F.; Vaccaro, L. Synthesis 2000, 646. (b) Ahamed, S.; Saha, A.; Ranu, B. C. J. Org. Chem. 2011, 76, 7235.
(38) (a) Scriven, E. F.; Turnbull, K. Chem. Rev. 1988, 88, 297. (b) McDonald, F. E.; Danishefsky, S. J. J. Org. Chem. 1992, 57, 7001. (c) Cheng, J. M.; Chee, S. H.; Dölen, Y.; Verdoes, M.; Timmer, M. S.; Stocker, B. L. Carbohydr. Res. 2019, 486, 107840. (d) Nyffeler, P. T.; Liang, C.-H.; Koeller, K. M.; Wong, C.-H. J. Am. Chem. Soc. 2002, 124, 10773. (e) Sahoo, L.; Singhamahapatra, A.; Paul, K. J.; Loganathan, D. Tetrahedron Lett. 2013, 54, 5361.
(39) Rolla, F. J. Org. Chem. 1982, 47, 4327.
(40) Wuts, P. G.; Greene, T. W. Greene’s Protective Groups in Organic Synthesis, 4th ed; John Wiley & Sons: Hoboken, 2006.
(41) Ashour, R. M.; Abdel-Majied, A. F.; Wu, Q.; Oisson, R. T.; Forsberg, K. Polymers 2020, 12, 1104.
(42) (a) Jozala, A. F.; de Lencastre-Novaes, L. C.; Lopes, A. M.; de Carvalho Santos-Ebinuma, V.; Mazzola, P. G.; Pessoa, A. Jr.; Grotto, D.; Gerenucci, M.; Chaud, M. V. Appl. Microbiol. Biotechnol. 2016, 100, 2063. (b) Jeremic, S.; Djokic, L.; Ajdačić, V.; Božinović, N.; Pavlović, V.; Manojlović, D. D.; Babu, R.; Senthamaarikannan, R.; Rojas, O.; Opsenica, I. Int. J. Biol. Macromol. 2019, 129, 351. (c) Zhang, Q.; Zhang, L.; Wu, W.; Xiao, H. Carbohydr. Polym. 2020, 229, 115454.
(43) Saibo, T.; Kimura, S.; Nishiyama, Y.; Isogai, A. Biomacromolecules 2007, 8, 2485.
(44) Iguchi, M.; Yamanaka, S.; Budhionio, A. J. Mater. Sci. 2000, 35, 261.
(45) (a) Cantillo, D.; Moghaddam, M. M.; Cappe, C. O. J. Org. Chem. 2013, 78, 4530. (b) Kantam, M. L.; Reddy, R. S.; Srinivas, K.; Chakravarti, R.; Seedar, B.; Fijugras, F.; Reddy, C. V. J. Mol. Catal. A: Chem. 2012, 355, 96.
(46) Grimes, K. D.; Gupta, A.; Aldrich, C. C. Synthesis 2010, 1441.
(47) Gann, A. W.; Amoroso, J. W.; Einck, V. J.; Rice, W. P.; Chambers, J. J.; Schnarr, N. A. Org. Lett. 2014, 16, 2003.
(48) Salvagnini, C.; Gharbi, S.; Boxus, T.; Marchand-Brynaert, J. Eur. J. Med. Chem. 2007, 42, 37.
(49) Maury, J.; Feray, L.; Bertrand, M. P.; Kapat, A.; Renaud, P. Tetrahedron 2012, 68, 9606.
(50) Dryzhakov, M.; Hellal, M.; Wolf, E. N.; Falk, F. C.; Moran, J. J. Am. Chem. Soc. 2015, 137, 9555.
(51) Morrison, Z. A.; Nitz, M. Org. Lett. 2020, 22, 1453.
(52) Menuel, S. P.; Doumert, B.; Saitz, S. B.; Ponchel, A.; Delevoye, L.; Monflier, E.; Hapiot, F. D. R. Angew. Chem. Int. Ed. 2014, 53, 9629.
(53) Burland, P. A.; Osborn, H. M.; Turkson, A. Bioorg. Med. Chem. 2011, 19, 5679.
(54) Ryu, B.-Y.; Emrick, T. Angew. Chem. Int. Ed. 2010, 49, 9644.
(55) Xie, S.; Lopez, S. A.; Ramström, O.; Yan, M.; Houk, K. J. Am. Chem. Soc. 2015, 137, 2958.