Alumina-Supported Gold Nanoparticles as a Bifunctional Catalyst for the Synthesis of 2-Amino-3-arylimidazo[1,2-a]pyridines

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Supporting Information

ABSTRACT: The bifunctional catalytic efficacy of alumina-supported gold nanoparticles (Au/Al2O3) was investigated for the synthesis of a series of 2-amino-3-aryl-imidazopyridines through the chemoselective reduction of the corresponding 2-nitro-3-aryl-imidazo[1,2-a]pyridines in high isolated yields. This highly efficient protocol was initially applied for the synthesis of 2-nitro-3-aryl imidazo[1,2-a]pyridines via the reaction between 2-aminoypyridine and nitroalkenes catalyzed by the present catalytic system Au/Al2O3. Moreover, the heterogeneous surface γ-Al2O3 was also found to catalyze this pathway in a comparable manner. However, only Au/Al2O3 was further proved as the appropriate catalytic system for the selective transfer hydrogenation of the synthesized 2-nitro-imidazopyridine derivatives into the corresponding 2-amino-3-aryl imidazopyridines using NaBH4 as a hydrogen-donor molecule. In addition, the one-pot two-step reaction between nitroalkenes and aminopyridines in the presence of Au/Al2O3−NaBH4 provided directly the fast and facile synthesis of 2-amino-3-aryl imidazopyridines, highlighting a useful synthetic application of the catalytic protocol.

INTRODUCTION

The imidazo[1,2-a]pyridine core is one of the most important class of biologically active nitrogen-containing heterocyclic molecules that display a wide range of applications in drug synthesis, medicinal chemistry, and materials science. Therefore, significant synthetic strategies have been directed toward the preparation of imidazo[1,2-a]pyridine derivatives, such as condensation, multicomponent, intramolecular cyclization, tandem reactions, and oxidative couplings, using 2-amino pyridines as key precursors. Beyond the most common synthetic approaches starting with diketones or enones and 2-amino pyridine, the condensation between the latter and nitroalkenes have received significant attention in the last years. On the basis of this reaction, numerous synthetic procedures have been proposed for the synthesis of 3-nitro imidazo[1,2-a]pyridine derivatives; however, studies on the synthesis of the corresponding regioisomers 2-nitro imidazo[1,2-a]pyridines are limited. In specific, the Fe(NO3)3-catalyzed C–H amination under ambient air has been initially proposed (Scheme 1, i). Moreover, an alternative visible-light-assisted process using eosin Y as the photocatalyst under an open atmosphere has also been developed (Scheme 1, ii). Recently, metal–organic framework MIL68 has been proposed as the first heterogeneous catalyst for the synthesis of 2-nitro-3-arylimidazo[1,2-a]pyridines via the oxidative amination of 2-aminopyridines and nitroalkenes using air as oxidant; however, the presence of formic acid as a co-catalyst is required to accelerate this transformation (Scheme 1, iii).

Together with the nitro derivatives, the amino-substituted imidazo[1,2-a]pyridines represent an important core of molecules with high biological and medicinal properties. In particular, imidazo[1,2-a]pyridine derivatives bearing amino groups in the 2-position of the imidazole ring exhibit potent anticancer and antiviral activities, as well as are valuable building blocks in drug discovery. Although several approaches provide access to the 3-amino substituted derivatives, synthetic pathways for 2-amino-imidazo[1,2-a]pyridines have been rarely reported in the literature. So far, Hamdouchi et al. described the synthesis of substituted 6-(2,6-difluorobenzoyl)imidazopyridines via the subsequent cyclization and N-alkylation of key cyanamide prepared from 2-chloropyridines with different bromo acetophenones under basic condition. Recently, Chang and co-workers reported an alternative synthetic approach via I2/KI-mediated oxidative cyclization of N-aryl amidines (Scheme 1). In addition, Hajra et al. developed an oxidative dianimation reaction of nitroalkenes with 2-aminopyridines to form 2-nitro-imidazo[1,2-a]pyridines catalyzed by Fe(NO3)3. In this paper, only the reduction of 2-nitro-3-phenylimidazopyridine to the corresponding 2-amino derivative was tested using Zn dust and NH4Cl in acetic acid at 80 °C (Scheme 1).
Given the importance of this type of transformation and in terms of sustainability, the use of more eco-friendly, inexpensive, and widely abundant catalyst for the synthesis of 2-amino-3-aryl imidazo[1,2-a]pyridine derivatives continues to be a long-standing goal of chemical research. In this respect, it is interesting that heterogeneous catalysis offers advantages associated with catalyst recovery and reusability, easy separation, and waste minimization. In light of our ongoing research on developing sustainable catalytic processes to construct N-heterocyclic organic molecules of high biological interest, and on the metal nanoparticle-catalyzed transfer hydrogenation processes of nitroarenes into amines, herein we elaborate the synthesis of 2-amino-3-arylimidazo[1,2-a]pyridines using Au/Al2O3 as a catalyst and NaBH4 as a reducing agent in ambient conditions (Scheme 1). Our protocol also provides access to a library of the corresponding 2-nitro-3-aryl-imidazo[1,2-a]pyridines with excellent isolated yields and selectivity. To the best of our knowledge, the use of Au/Al2O3 catalytic systems for the synthesis of both 2-nitro- and 2-amino-3-arylimidazo[1,2-a]pyridine derivatives has not been reported yet (Scheme 1).

■ RESULTS AND DISCUSSION

For the catalytic reductions, we employed commercially available supported gold nanoparticles Au/TiO2, Au/Al2O3, and Al/ZnO, as well as the oxides TiO2 (Degussa), ZnO, Al2O3, and SiO2. The commercial catalyst Au/TiO2, Au/Al2O3, and Au/ZnO feature a ca. 1 wt % Au loading and exhibit an average AuNPs size of about 2–3 nm. The commercially available copper (I), copper (II), silver (I), zinc (II), gold (I), and gold (III) salts were used without further purification. The used nitroalkenes were prepared according to the literature procedure starting with nitroalkane and the corresponding carbonyl compounds through a condensation reaction (for detail experimental, see the Supporting Information). To optimize the reaction conditions, 2-aminoypyridine 1 and (E)-1-methyl-4-(2-nitrovinyl) benzene 2 were selected as model substrates. The reaction was carried out in a sealed tube with 1,2-dichloroethane (DCE) as the solvent at 80 °C under air atmosphere for 24 h (Scheme 2). It is worth noting that a control experiment in the absence of catalyst shows the formation of the Michael adduct 3 as the major product accompanied by small amount of the corresponding 2-nitro-4-methylphenyl imidazo[1,2-a]pyridine 4 in 13% relative yield, as measured by 1H NMR of the crude reaction mixture (Table 1, entry 1). The structure of the adduct 4 was determined using two-dimensional homonuclear correlation spectroscopy 1H COSY (see the Supporting Information, Scheme S1). Furthermore, cyclization reaction of the adduct 3 in the presence of CuBr leads to the corresponding 3-nitro-4-methylphenyl-imidazo[1,2-a]pyridine 5 (Scheme 2), and its structure was determined by 1H NMR and further confirmed with that given in the literature (Scheme S2). Addition of small amount of D2O to the NMR tube solution results in the disappearance of the NH peak at 5.23 ppm, as well as the multiplicity change in the peak from quartet to triplet that corresponds to the benzylic proton H2 at 5.65 ppm (see Scheme S3). Moreover, we studied the model reaction in the presence of different copper salts, such as Cu(ClO4)2, Cu(OTf)2, CuBr2, Cu(NO3)2, Cu(OAc)2, and CuBr (Table S1, entries 1–6). In all the cases, mixtures of the corresponding adduct 3 and the regioisomer 5 were mainly observed by 1H NMR. On the other hand, using the corresponding Au(I) and Au(III) salts, AuCl3 and Ph3AuNTf2, low yields of 4 were obtained (Table S1, entries 7 and 8), whereas the reaction in the presence of AgOTf resulted in only traces of product 4 (Table S1, entry 9). Similarly, the reactions using the
Table 1. Catalytic Evaluation in the Reaction of 2-Aminopyridine (1) and (E)-1-Methyl-4-(2-nitrovinyl)benzene (2)

| entry | catalyst | conversion % | 3% | 4% |
|-------|----------|--------------|----|----|
| 1     | Au/TiO2  | 87           | 74 | 13 |
| 2     | Au/ZnO   | 51           | 34 | 17 |
| 3     | Au/Al2O3 | 47           | 37 | 10 |
| 4     | Au/Al2O3 (0.3 M HCl) | >99 | >99 |
| 5     | TiO2 (Degussa) | 52 | 34 | 18 |
| 6     | ZnO      | 52           | 48 | 4  |
| 7     | γ-Al2O3 | 91           | 4  | 87 |
| 8     | SiO2     | 48           | 20 | 28 |
| 9     | γ-Al2O3 (0.3 M HCl) | >99 | >99 |
| 10    | γ-Al2O3 (1 M HCl) | 93 | 77 |
| 11    | γ-Al2O3 (10% KOH) | 74 | 46 | 28 |
| 12    | HCl      |              |    |    |
| 13    | KOH      |              |    |    |
| 14    | CH3COOH  | 54           | 29 | 25 |

*aReaction conditions: pyridin-2-amine (0.35 mmol), (E)-1-methyl-4-(2-nitrovinyl)benzene (0.3 mmol), catalyst (% mol), and DCE (2 mL) at 80 °C for 24 h. Seventy milligrams of γ-alumina was used. bBased on the consumption of 2 determined from the crude 1H NMR mixture of the reaction. cRelative yields of 3 and 4 were determined by 1H NMR from the crude reaction mixture.

Experimental Section and the Scheme S4 in the Supporting Information. For the present heterogeneous conditions, Au/Al2O3 was initially used as the catalyst for testing this reaction. However, to support such a hypothesis, further kinetic studies on the structure limitation of the reaction process. Further, to support such a hypothesis, further kinetic studies on the reaction profile vs different sizes and wt % of the gold nanoparticles should be performed. On the contrary, using the rest of the supported gold catalysts, the product 4 was formed in only 10–17% relative yields, calculated by the 1H NMR of the crude reaction mixture (Table 1, entries 2 and 3). For comparison, a series of different supports including silica, TiO2 (Degussa), and ZnO were also examined to evaluate their catalytic activities; however, lower yields of 4 were obtained (Table 1, entries 5, 6, and 8).

Encouraged by these results, in the next set of experiments, we evaluated the acid–base surface properties of γ-Al2O3 on the model reaction. It is noteworthy that the treatment of γ-Al2O3 with aqueous hydrochloric acid (HCl 0.3 M) increases its catalytic activity, resulting in quantitative yield of 4, whereas the treatment of γ-Al2O3 with KOH resulted in considerable decrease in yield of 4 (Table 1, entries 9 and 11). Moreover, increase in the acidity of HCl solution resulted in a gradual drop in the yield of 4 (Table 1, entry 10). It is worth noting that the present reaction did not occur when HCl or KOH into the reaction was added to the solution in the absence of alumina (Table 1, entries 12 and 13). Finally, the presence of CH3COOH does not lead to a significant conversion or selectivity, as shown in Table 1, entry 14. The above results support the finding that γ-Al2O3 catalyzes the synthesis of 2-nitro-3-phenyl-imidazo[1,2-α]pyridine under the present heterogeneous conditions.

Among the solvent studied herein, 1,2-dichloroethane (DCE) was found to promote the synthesis of 2-nitro-3-phenyl-imidazo[1,2-α]pyridine 4 in a higher yield (Table S2, entry 1). On the contrary, in the case of other aprotic and nonpolar solvents such as tetrahydrofuran, dimethyl carbonate, acetone, chloroform, and toluene, the Michael adduct 3 was formed as the major product (Table S2, entries 2–7). Exceptionally, acetonitrile (MeCN) was found to accelerate the synthesis of 4 as well, although in moderate yield of 65% (Table S2, entry 8). Interestingly, in the case of aprotic solvent such as methanol (MeOH) and ethanol (EtOH), the corresponding 2-alkoxy-imidazo[1,2-α]pyridine derivatives 6 and 7 were unexpectedly formed (Scheme 3 and Table S2, entries 9 and 10), and their structures were determined by 1H NMR. Further studies on the structure limitation of the synthesis procedure of 2-alkoxy-imidazo[1,2-α]pyridine derivatives under the present conditions are under investigation.

With these optimized conditions, we further explore the scope of this catalytic transformation by incorporating a wide range of nitroalkenes 2 and 8–18 to gain direct access to a library of 2-nitro-3-aryl imidazo[1,2-α]pyridines derivatives 19–33 in high isolated yields (Scheme 4). For the synthetic procedure of nitroalkenes and their structure, see the Experimental Section and the Scheme S4 in the Supporting Information. For the present heterogeneous conditions, Au/Al2O3 (70 mg) was initially used as the catalyst for testing this optimization, as shown in Scheme 4. The values not in
Scheme 3. Synthesis of 2-Alkoxy-imidazo[1,2-α]pyridine Products 6 and 7 via the Reaction between 1 and 2 Catalyzed by γ-Al2O3 in MeOH and EtOH, Respectively

Scheme 4. Regioselective Synthesis of 2-Nitro-3-aryl-imidazo[1,2-a]pyridines 19−33 Promoted by Au/Al2O3 and γ-Al2O3

Regardless of the electronic nature of the phenyl rings of the nitrostyrenes, bearing even electron-donating (Me, MeO) or electron-withdrawing (Cl, COOMe) groups, the desired 2-nitro-imidazopyridine derivatives were formed in good to high isolated yields and regioselectivity (Scheme 4). In addition, naphthyl and heterocyclic aromatic substituted nitroalkenes 17 and 18 give the corresponding product 29 and 30 in high yields of 91 and 90%, respectively. Moreover, the reaction between 3-methyl-2-amino pyridine (1′) and different nitrostyrenes was analyzed and the corresponding substituted imidazopyridines 31−33 were formed in good isolated yields (Scheme 4). These results indicate the broad generality of the present catalytic heterogeneous methodology toward the regioselective synthesis of 2-nitro-3-aryl-imidazo[1,2-α]-pyridines. The structures of the above synthesized imidazo[1,2-α]pyridines 19−33 were determined by 1H NMR, 13C NMR, and HR-MS. For comparison, the same catalytic reactions were accomplished using γ-Al2O3 as a catalyst (70 mg) in DCE at 70 °C within 24 h. In all cases, good to high isolated yields (Scheme 4, values in parentheses) further support the importance of the synthesis of the present heterogeneous catalytic system.
Scheme 5. Chemoselective Reduction of 2-Nitro-3-aryl-imidazo[1,2-a]pyridines 19−33 to the Corresponding 2-Amino-3-aryl-imidazo[1,2-a]pyridines 38−52 Catalyzed by Au/Al2O3−NaBH4

Table 2. Catalytic Reduction of 19 and 20 to the Corresponding Amines 38 and 39 Using Au/Al2O3

| entry | R   | reducing agent | conversion % | relative yields |
|-------|-----|----------------|--------------|-----------------|
| 1     | Me  | NaBH4          | 100          | 34, 35 (%)      |
| 2     | H   | NaBH4          | 100          | 36, 37 (%)      |
| 3     | Me  | NaBH4          | 100          | 38, 39 (%)      |
| 4     | H   | NaBH4          | 100          |                |
| 5     | Me  | TMDS           | 100          |                |
| 6     | H   | TMDS           | 100          |                |

*aReaction conditions: 2-nitro-pyridine derivatives 19 and 20 (0.1 mmol), 20 mg catalyst (1% mol), 0.4 mmol NaBH4 or 0.3 mmol of TMDS, and MeOH (1 mL) at room temperature (rt) for 1 h. *Based on the consumption of 19 and 20 determined from the crude 1H NMR mixture of the reaction. *Relative yields of the products were determined by 1H NMR from the crude reaction mixture. *In the absence of Au/Al2O3. A significant amount of unidentified products were measured from the 1H NMR of the crude mixture.
Furthermore, we explore the scope of this catalytic transformation by studying the selective reduction of the synthesized 2-nitro-derivatives (19–33) to the corresponding 2-amino-3-aryl-imidazo[1,2-α]pyridines (38–52) through a gold-catalyzed transfer hydrogenation process (Scheme 5). For this reason, the reduction of 19 and 20 was initially studied in the presence of NaBH₄ as the reducing agent and in the absence of catalyst. In both cases, the corresponding N-hydroxylamines 34 and 35 were formed as major products, accompanied by unidentified products as observed from the ¹H NMR of the crude reaction mixture (Table 2, entries 1 and 2). Incorporation of the Au/Al₂O₃ catalytic system led to the formation of the corresponding amines 38 and 39 in quantitative yields of up to 99% (Table 2, entries 3 and 4). For comparison, using Au/Al₂O₃ in the presence of 1,1,3,3-tetramethyldisiloxane (TMDS) as the reducing agent, under ambient conditions, the corresponding nitroso-compounds (34 and 35) and N-hydroxylamine derivatives (36 and 37) accompanied by a mixture of unidentified products were observed (Table 2, entries 5 and 6). Noteworthy, the 2-nitroso-3-aryl-imidazo[1,2-α]pyridines 34 and 35 have not been detected in the literature yet. However, different methodologies for the synthesis of 3-nitroso-2-aryl-imidazo[1,2-α]pyridines have been reported.⁵⁹–⁶¹ Based on these encouraging results, the Au/Al₂O₃–NaBH₄ heterogeneous catalytic system was used for the in situ reduction of the initially synthesized 2-nitro imidazopyridine derivatives (19–33) under ambient conditions and short reaction time (1 h).

As shown in Scheme 4, the corresponding 2-amino-3-aryl imidazo[1,2-α]pyridines (38–52) were formed in good to high isolated yields in the range of 80–98%. From the synthetic point of view, this two-step process for the synthesis of a series of 2-amino-3-aryl[1,2-α]imidazopyridines 38–52, starting from 2-aminopyridine and nitrostyrene in the presence of Au/Al₂O₃ and NaBH₄, has not been reported in the literature so far (Scheme 5). All the structures of the 2-amino-imidazo[1,2-α]pyridines were determined by ¹H NMR, ¹³C NMR, and HR-MS.

As mentioned in the introduction section, the approaches to synthesize 2-amino-imidazopyridine derivatives include different retrosynthetic scenarios,⁵⁸–⁶¹ however, only one example has been reported in previous study, which referred to the reduction of 20 to the corresponding 2-amino derivative 39, using Zn dust and NH₄Cl in acetic acid, at 80 °C (as shown in Scheme 1). The main aim of that study was to synthesize the 2-nitro-aryl derivatives using Fe(NO₃)₃ as a catalyst.⁶⁸ Herein, to further support the present proposed synthetic methodology, a one-pot two-step laboratory-scale procedure was performed for the direct synthesis of 39 starting from 2.5 mmol of 2-aminopyridine (1) and 2 mmol of nitrostyrene (2), without the isolation of the initially formed 2-nitroimidazopyridine 20 (Scheme 6). Thus, after the formation of 20 (monitored by thin-layer chromatography (TLC)), the solvent DCE was evaporated and MeOH was added to the appropriate amount of NaBH₄ for the reduction process. After the completion of the reaction (monitored by TLC), the mixture was filtered over a short path of silica to hold the catalyst, the solvent was evaporated, and the produced amine 38 was purified with column chromatography and isolated in good total yield of 79% (see Experimental Section). This one-pot process supports undoubtedly the synthetic importance of the present catalytic methodology. Importantly, no byproducts were observed during the catalytic procedure.

Because of the heterogeneity of the present catalytic system, Au/Al₂O₃ can be easily separated from the reaction mixture by simple filtration and can be reused for the next catalytic reaction. To that end, the recyclability and stability of the catalyst were examined. First, the synthesis of 2-nitro-3-aryl-imidazo[1,2-α]pyridine 4 was tested in the above-described conditions and the catalyst could be used twice without any significant loss of its catalytic activity. However, in the third run, 64 and 36% relative yields of 4 and intermediate 3 (Figure 1A) were observed, respectively, whereas 3 was formed as the major product in the fourth run. It is noteworthy that 3 does not yield the imidazopyridine regiosomer 5 in the presence of Au/Al₂O₃, although it yields the desired product 4, as shown in Scheme S5. On the basis of these results, we can hypothesize that 3 was formed through a noncatalytic reaction between 1 and 2 due to the possible gradual deactivation of the catalyst, as also described above (Scheme 2). Consequently, the reduction of 4 to the corresponding amine 38 was studied using Au/Al₂O₃ as a catalyst and NaBH₄ and methanol as solvents at rt. Under the present reductive conditions, the catalyst was found to be active even after five recycle runs, as shown in Figure 1B (yields >95%). Herein, after each catalytic cycle, the reaction mixture was centrifuged and the catalyst was washed with methanol, dried for 2 h at 100 °C, and used for the next reduction process. These results enhance the synthetic approach of the present catalytic protocol for the regioselective synthesis of 2-amino-3-aryl-imidazo[1,2-α]-pyridines.

On the basis of our experimental results, further experiments were carried out for structure limitation propose and mechanistic studies.

(a) The use of aliphatic nitroalkene (E)-3-methyl-1-nitrobut-1-ene (53) in place of nitrostyrenes did not yield the desired imidazopyridine derivative (Scheme 7).

(b) In addition, the use of α-ethyl-substituted nitrostyrene 54, instead of nitrostyrene 2, did not promote the transformation (Scheme 7). These observations exclude the use of aliphatic and α-substituted nitro alkenes, although they support the necessity of a phenyl-substituted nitrostyrene in the convenient synthesis of 2-nitro-3-aryl-imidazo[1,2-α]pyridine derivatives.

(c) The use of methyl propiolate 55 yields a mixture of unidentified products; however, the use of other conjugated compounds, such as trans-cinnamic methyl ester 56 in place of nitrostyrene 2, showed no reactivity under the present conditions (Scheme 7). These results indicate the necessity of the conjugated nitroalkenes in the synthesis of imidazo[1,2-α]pyridine.

Thus, a plausible mechanistic pathways for the synthesis of 2-nitro-3-aryl-imidazo[1,2-α]pyridines is proposed. Initially, the surface of Au/Al₂O₃ adsorbs the 2-aminopyridine and nitroalkene substrates via the amino and nitro groups, respectively. This adsorption is probably enhanced by the nature of Al₂O₃ as the Lewis acid, as well as by a gold
electronic complexation with the nitro group. In the first part of the mechanism, a hydrogen atom transfer and/or an electron transfer mechanism can occur, leading to the generation of anionic intermediate I, as shown in Scheme 8. After that, I was transformed into the cyclized reduced form II, which, after protonation from the surface presumably, is oxidized to the desired imidazopyridines product (Scheme 8). In the second part of the mechanism, a transfer hydrogenation process occurs for the selective reduction of the produced 2-nitroderivative to the corresponding 2-amino imidazopyridine derivative (Scheme 8). The latter pathway also found support in our previous mechanistic studies on the reduction of nitroarenes to anilines, in which a proposed Au−H species are responsible for this selective reduction transformation.46

Scheme 7. Structure Limitation Studies for the Synthesis of 2-Nitro-imidazopyridine Derivatives

### CONCLUSIONS

In conclusion, Au/Al2O3 represents an efficient bifunctional catalyst for the regioselective synthesis of 2-amino-3-aryl-imidazo[1,2-α]-pyridines. First, the corresponding 2-nitro-3-aryl-imidazo[1,2-α] pyridine derivatives were formed through a stepwise reaction between 2-amino pyridine and appropriate nitroalkene. The catalyst could be used twice without any significant loss of its activity. Importantly, γ-Al2O3 as a heterogeneous surface can also catalyze the above process. Second, the chemoselective reduction of the synthesized 2-nitro derivatives was performed using Au/Al2O3 in the presence of NaBH4 in ambient conditions. The second catalytic pathway was found to be more efficient, and the catalyst can be used at least five times without significant decrease in its activity. Thus, a series of substituted 2-amino-3-arylimidazo[1,2-α]pyridines were prepared—for the first time—under mild conditions using the present catalytic methodology in excellent yields through a fast and clean process.

### EXPERIMENTAL SECTION

**General.** All the reagents and solvents were purchased from Sigma-Aldrich, Fluorochem, and Acros and used without further purification. Thin-layer chromatography was performed on Millipore precoated silica gel plates (0.20 mm thick, particle size 25 μm). Nuclear magnetic resonance spectra were recorded on an Agilent 500 {1H NMR (500 MHz), 13C NMR (126 MHz)}. Chemical shifts for 1H NMR were reported as δ values and coupling constants were measured in hertz (Hz). The following abbreviations were used for spin multiplicity: s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, qin = quintet, dd = double of doublet, ddd = double doublet of doublets, and m = multiplet. Mass spectra (HRMS) were determined on an electrospray ionization mass spectrometry (ESI-MS) by using a Thermo-Fisher Scientific (Bremen, Germany) model LTQ Orbitrap Discovery MS at a flow rate of 10 μL/min using a syringe pump. The infusion experiments were run using a standard ESI source operating in a positive ionization mode. Source operating conditions were a 3.7 kV spray voltage and a 300 °C heated capillary temperature.

**General Synthesis of Nitroalkenes 2 and 8–18.** All the nitroalkenes were synthesized according to the literature...
Gold catalyst Au/Al₂O₃ (1 mol % Au) was placed in a 5 mL chromatography (TLC) and the slurry was filtered under pressure through a short pad of silica with the aid of DCM and EtOAc. The filtrate was evaporated under vacuum to afford the corresponding products in pure form.

Synthesis of 2-Nitro-3-aryl-imidazopyridines from β-Nitrostyrenes and 2-Aminopyridines. To a sealed tube, which contains 2 β-nitrostyrene and 0.35 mmol of 2-aminopyridine (79% yield), 10 mL of DCE as a solvent and 250 mg of Au/Al₂O₃ as a catalyst. The reaction mixture was stirred at 80 °C for 24 h. The reaction was monitored by thin-layer chromatography (TLC) under stirring for appropriate time; after the completion of the reaction, the slurry was filtered under pressure through a short pad of silica to withhold the catalyst with the aid of methanol (~5 mL). The filtrate was evaporated under vacuum and the residue was used for the corresponding products in good to high isolated yields. All the spectroscopic data were compared to those in the literature.

Synthesis of 3-Nitro-2-aryl-imidazopyridines from β-Nitrostyrenes and 2-Aminopyridines. To a sealed tube, which contains 0.3 mmol of β-nitrostyrene and 0.35 mmol of 2-aminopyridine, were added 1 mL of DCE as a solvent and 70 mg Au/Al₂O₃ as a catalyst. The reaction mixture was stirred at 80 °C for 24 h. The reaction was monitored by thin-layer chromatography (TLC); after the completion of the reaction, the slurry was filtered under pressure through a short pad of silica to withhold the catalyst with the aid of methanol (~5 mL). The filtrate was evaporated under vacuum to afford the corresponding products in pure form.

ASSOCIATED CONTENT
Supporting Information
The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b03047.

Optimization, catalytic results, copies of ¹H, ¹³C, and NOESY-1D NMR spectra of the products (PDF)

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Notes
The authors declare no competing financial interest.
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