Reduction of quinolines to 1,2,3,4-tetrahydroquinolines with hydrosilane/ethanol catalyzed by TiO_2-supported gold nanoparticles under solvent free conditions

Anastasia Louka, Charis Gryparis, and Manolis Stratakis*

Department of Chemistry, University of Crete, Voutes, 71003 Iraklion, Greece
E-mail: stratakis@chemistry.uoc.gr

Dedicated to Professor Michael Orfanopoulos on the occasion of his 67th birthday and retirement, and for his remarkable contribution in physical organic chemistry

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Abstract

Gold nanoparticles supported on TiO_2 (1 mol%) catalyze the reduction of a series of functionalized quinolines into 1,2,3,4-tetrahydroquinolines using hydrosilanes/ethanol (hydride/proton) as the reductant system. A typical reaction requires 4 molar equivalents of phenyldimethylsilane (reductant of choice), 4 molar equivalents of ethanol as a reagent and heating to 70 ^oC under solvent free conditions. The isolated yields are moderate to excellent and in certain cases the reaction rate is exceedingly fast. Mechanistic analysis revealed the stereoselective addition of two hydrides (from hydrosilane) on positions C2 and C4 of the quinoline ring and two protons (from ethanol) on positions C3 and the nitrogen atom.

Keywords: Catalysis, gold nanoparticles, reduction, quinolines, hydrosilanes

Introduction

Heterogeneous reductive processes catalyzed by supported gold nanoparticles (Au NPs)[1-5] and nanoporous gold[6] have received considerable attention especially over the past decade. The reductants employed are H_2 (direct hydrogenation) and CO/H_2, formates, alcohols, hydrosilanes or hydroborane (transfer hydrogenation). It is generally accepted that reduction takes place via the formation of gold hydride species. Owing to the relative instability and the difficulty for the formation of Au-hydrides, Au NPs-catalyzed reduction protocols are more controllable and selective relative to the analogous Pd or Pt-catalyzed processes; the facile accumulation of Pd or Pt-hydrides on the catalyst's surface often leads to side reactions (*e.g.*, dehalogenation or overeduction pathways).[7] While much effort has been devoted to Au-catalyzed reduction of

carbonyl and nitro compounds, there are only a few examples regarding the reduction of π systems. Cao and co-workers have shown that Au NPs supported on high surface area titania (HAS-TiO_2) catalyze the chemoselective reduction of quinolines into 1,2,3,4-tetrahydro-quinolines using H_2.[8] At the same time, Yamamoto's group reported a nanoporous gold catalyst which employs hydrosilane/H_2O to semireduce alkynes into *cis*-alkenes.[9] More recently, further progress has been achieved in the direct hydrogenation of terminal alkynes over supported Au NPs[10] or Au nanoclusters.[11]

The reports by Cao[8] and Yamamoto[9] urged us to examine the possible reduction of quinolines into 1,2,3,4-tetrahydroquinolines via supported Au NPs-catalyzed transfer hydrogenation using hydrosilanes, 1,2-disilanes or ammonia borane. These substances have been previously used in other Au NPs-catalyzed reductive applications.[12-18] The endeavours for this specific reduction arise from the fact that 1,2,3,4-tetrahydroquinones constitute a very important class of heterocyclic compounds, since they appear as the core skeleton in a variety of bioactive naturally occurring substances or pharmaceutical products. Thus, the interest of organic chemists for their synthesis is continuous[19] with a great body of publications focusing on the reduction of precursor quinolines. While our research efforts towards this goal using supported Au NPs were in progress and had reached a level of maturity, an efficient method for the reduction of quinolines by hydrosilanes catalyzed by an unsupported nanoporous gold catalyst was reported.[20]

Herein, we present our results which employ hydrosilanes/ethanol as the reducing system under solvent free conditions and Au nanoparticles supported on TiO_2 as the most suitable catalyst. In addition, a stepwise pathway was established with an initially fast 1,2-reduction mode to form 1,2-dihydroquinolines, while the new C2 and C4 hydrogen atoms on reduction products arise from the hydrosilane as supported via labelling experiments. Alternative approaches using 1,2-disilanes or ammonia borane as reductants provided inferior results.

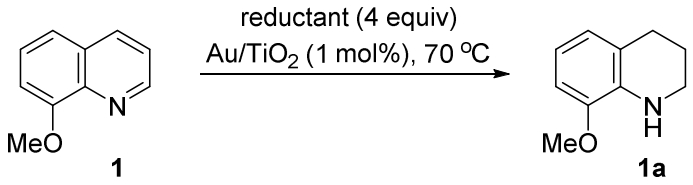
Results and Discussion

Optimization studies

As a model substrate we examined 8-methoxyquinoline (**1**), and in all experiments the loading of catalyst (Au/TiO_2, ~ 1 wt%) was kept at 1 mol% (Table 1). Although not shown, we have also tested other supported Au NPs catalysts (Au/Al_2O_3 and Au/ZnO) having identical gold content and size of nanoparticles (~2-3 nm on the average) to Au/TiO_2 but the results were inferior to those of Au/TiO_2. The first crucial observation in the reduction of the methoxyquinoline **1** was that apart from hydrosilane (hydride donor) a proton source was required (*e.g.*, ethanol) as also exemplified by labelling experiments presented in the accompanying mechanistic discussion. Thus, 8-methoxyquinoline is smoothly reduced into 8-methoxy-1,2,3,4-tetrahydroquinoline (**1a**) by hydrosilanes with the best results obtained using phenyldimethylsilane ($PhMe_2SiH$, 4 equiv) and equimolar amounts of ethanol as a proton source in the absence of any solvent and within a few minutes at 70 ^oC. Under these conditions, 100% consumption of the quinoline **1** was

observed, and the tetrahydroquinoline **1a** was isolated in 84% yield after column chromatography. It is important to stress that solvent free conditions in a given chemical process are highly desired. Triethylsilane exhibited inferior results, while 1,1,3,3-tetramethyldisiloxane (TMDS) which is an extremely reactive hydrosilane in other Au-catalyzed transformations[15,18,22] did not show better activity to $PhMe_2SiH$. Hexamethyldisilane (Me_3Si-$SiMe_3$) exhibited a moderate activity arising from transient *in situ* generated trimethylsilane during its Au/TiO_2-catalyzed ethanolysis.[16] Disappointingly, the use of ammonia borane (NH_3BH_3), a powerful and rapidly reductant of nitro compounds in the presence of Au/TiO_2,[17] provided only traces of the reduction product.

Table 1. Reduction of 8-methoxyquinoline (**1**) in the presence of various reducing agents catalyzed by Au/TiO_2.



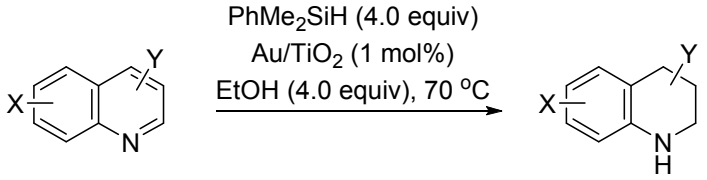
Reductant	solvent	Additive (equiv)	time	**1a** (%)[a]
$PhMe_2SiH$	DCE	EtOH (4)	1 h	65
$PhMe_2SiH$	THF	EtOH (4)	30 min	95
$PhMe_2SiH$	EtOAc	EtOH (4)	1 h	25
$PhMe_2SiH$	EtOH	-	1.5 h	65
$PhMe_2SiH$	-	EtOH (4)	5 min	65
$PhMe_2SiH$	-	EtOH (4)	15 min	100
$PhMe_2SiH$	-	H_2O (2)[b]	20 min	100
Et_3SiH	-	EtOH (4)	1 h	24
TMDS[c]	-	EtOH (4)	1 h	71
HMDS[d]	-	EtOH (4)	1 h	26
NH_3BH_3	EtOH	-	6 h	<5

[a] Conversion yields. [b] See ref. 21. [c] TMDS = 1,1,3,3-Tetramethyldisiloxane. [d] HMDS = Hexamethyl-1,2-disilane

Scope and limitations

Having identified the optimum experimental conditions for reducing the methoxyquinoline **1**, we then studied the scope and limitations of the reduction on a series of functionalized quinolines using 4 molar equivalents of the mixture $PhMe_2SiH$/EtOH and 1 mol% of catalyst (Au/TiO_2) under solvent free conditions (Table 2).

Table 2. Reduction of quinolines by $PhMe_2SiH$/EtOH catalyzed by Au/TiO_2 under solvent free conditions.



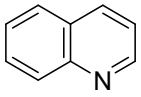
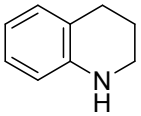
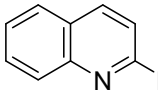
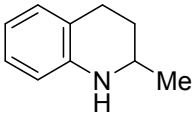
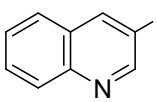
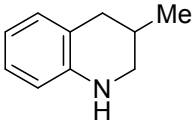
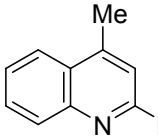
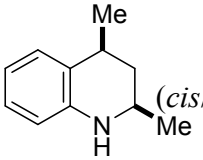
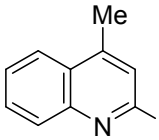
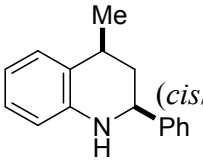
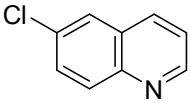
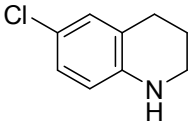
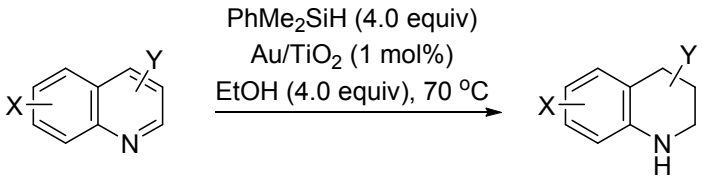
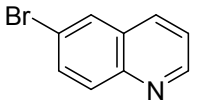
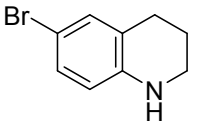
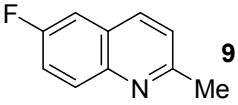
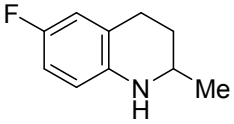
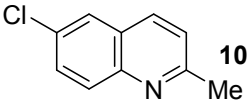
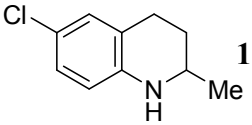
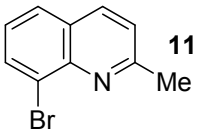
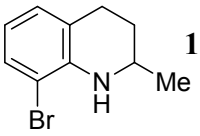
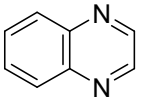
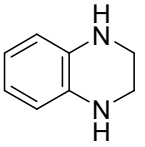
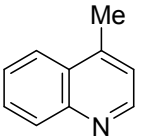
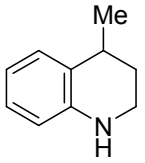
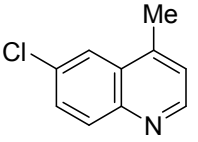
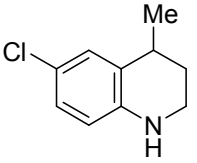
reactant		product		time	isolated yield (%)
	**2**		**2a**	5 h	33[a]
	**3**		**3a**	15 min	86
	**4**		**4a**	2 h	82
	**5**		**5a** (*cis*/*trans* 10:1)	3 h	75
	**6**		**6a** (*cis*/*trans* 10:1)	1 h	87
	**7**		**7a**	3 h	62[b]

Table 2 (continued)

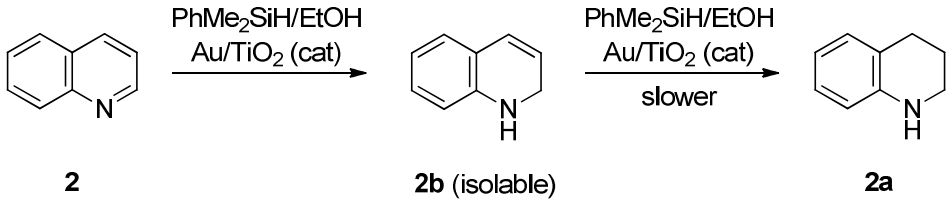


reactant		product		time	isolated yield (%)
	**8**		**8a**	3 h	84
	**9**		**9a**	20 min	82
	**10**		**10a**	1 h	84
	**11**		**11a**	1 h	81
	**12**		**12a**	3 h	5[c]
	**13**		**13a**	6 h	0
	**14**		**14a**	6 h	0

[a] With 10 equiv $PhMe_2SiH$/EtOH (12 h) the isolated yield increases to 56%. [b] With 6 equiv $PhMe_2SiH$/EtOH (3 h) the isolated yield increases to 79%. [c] Conversion yield. With 10 equiv $PhMe_2SiH$/EtOH (12 h) the conversion is 14%.

Quinolines substituted at C2 or C3 are smoothly reduced providing the corresponding 1,2,3,4-tetrahydroquinolines in very good yields. 2,4-Disubstituted quinolines **5** and **6** provided mainly the thermodynamically favourable *cis*-2,4-disubstituted tetrahydroquinolines (*cis*/*trans* ~ 10:1). Parent quinoline (**2**) was rather unreactive compared to the substituted analogues, and a large excess (>10 equiv) of reducing agents was required to achieve a decent conversion yield. The same poor reactivity was also observed with quinoxaline (**12**) that gave under standard reaction conditions 1,2,3,4-tetrahydroquinoxaline (**12a**) in very low yield (5%); this can be improved to 14% in the presence of 10 molar excess of hydrosilane/ethanol. On the other hand, the C4 methyl-substituted quinolines (lepidine **13** and 6-chlorolepidine **14**) were surprisingly completely unreactive, which was difficult to explain given that disubstituted **5** and **6** bearing a methyl group at C4 are readily reduced. Fortunately, the halide-substituted quinolines **7**-**11** did not suffer any protodehalogenation upon reduction, which is a typical, often undesireable side-reaction seen under Pd, Pt or Ru catalysis conditions.[8]

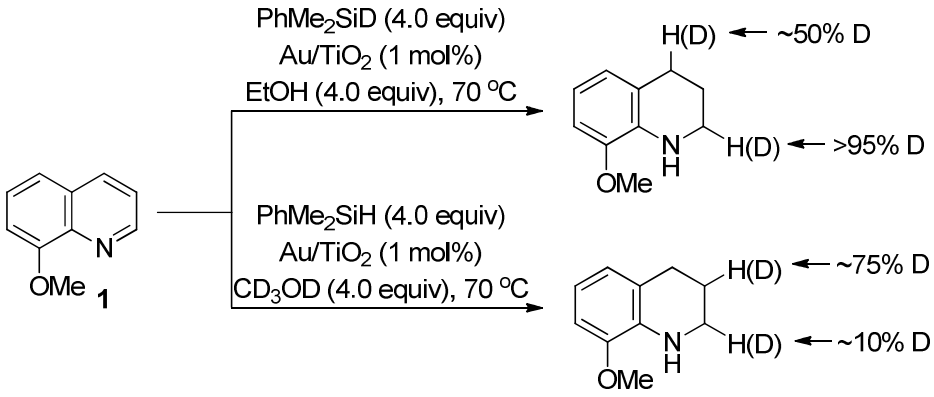
By studying the reduction of the slowly reacting parent quinoline (**2**) with ^{1}H NMR we found that initially the N-C double bond was reduced to form intermediate 1,2-dihydroquinoline (**2b**) which then slowly gave 1,2,3,4-tetrahydroquinoline (**2a**) (Scheme 1). We were able to isolate the dihydroquinoline **2b** by column chromatography as a mixture with final product **2a** (see Supporting Information). The intermediate 1,2-dihydroquinoline **2b** is known to gradually re-oxidized to quinoline **2** in atmospheric air.[23]



Scheme 1. Reaction profile in the Au-catalyzed reduction of quinoline (**2**) to 1,2,3,4-tetrahydroquinoline (**2a**) via intermediate formation of 1,2-dihydroquinoline (**2b**).

Mechanistic studies

To study the mechanism of reduction we prepared deuterium labelled $PhMe_2SiD$ (>98% D) by reaction of $PhMe_2SiCl$ with $LiAlD_4$ in THF. The smoothly reacting 8-methoxyquinoline (**1**) was chosen as a model substrate (Scheme 2). In the reaction of the methoxyquinoline **1** with $PhMe_2SiD$/EtOH we found >95% and ~50% D incorporation at C2 and C4, respectively (see ^{1}H NMR spectrum in Supporting Information), while with $PhMe_2SiH/CD_3OD$, ~75% D incorporation was seen at C3 and ~10% on C2 (see Supporting Information).



Scheme 2. Deuterium labelling experiments in the Au/TiO_2-catalyzed reduction of the methoxyquinoline **1** by hydrosilane/EtOH.

While it seems that the new C-H bonds on C2 and C4 arise from hydride Si-H functionality, and the new C-H bond on C3 from the proton of solvent (EtOH), the incomplete deuterium incorporation in both experiments on C3 and C4 was quite peculiar. To shed light on this, the reaction between the methoxyquinoline **1** and $PhMe_2SiD$/EtOH was monitored by GC-MS. To our surprise, during the initial stages of reaction, $PhMe_2SiD$ gradually underwent isotopic exchange to $PhMe_2SiH$ (Figure 1). This observation nicely explained the incomplete deuteration patterns appearing in Scheme 2. First, we consider that the quinolines were reduced quickly to intermediate 1,2-dihydroquinolines and then slowly to 1,2,3,4-tetrahydroquinolines (Scheme 1). Thus, $PhMe_2SiD$ quickly reduces the methoxyquinoline **1** to the corresponding 1,2-dihydroquinoline before undergoing significant deuterium depletion (>95% deuteration at C2). Since the second reduction step (1,2-dihydroquinolines to 1,2,3,4-tetrahydroquinolines) was slow, and $PhMe_2SiD$ had in the meantime undergone substantial D/H exchange, only 50% D incorporation was seen on C4. The same holds in the experiment using $PhMe_2SiH/CD_3OD$. Owing to isotopic scrabbling between the Si-H and O-D bonds, incomplete deuteration occurs on C3, while a small amount of deuterium appears on C2 which is attributed to the partial formation of $PhMe_2SiD$ under the reaction conditions. The depletion of deuterium in $PhMe_2SiD$ is not clearly understood and apparently is catalyzed by Au NPs. An analogous metal-catalyzed depletion of deuteride ($NaBD_4$) by a protic solvent (EtOH) is known in the literature.[24]

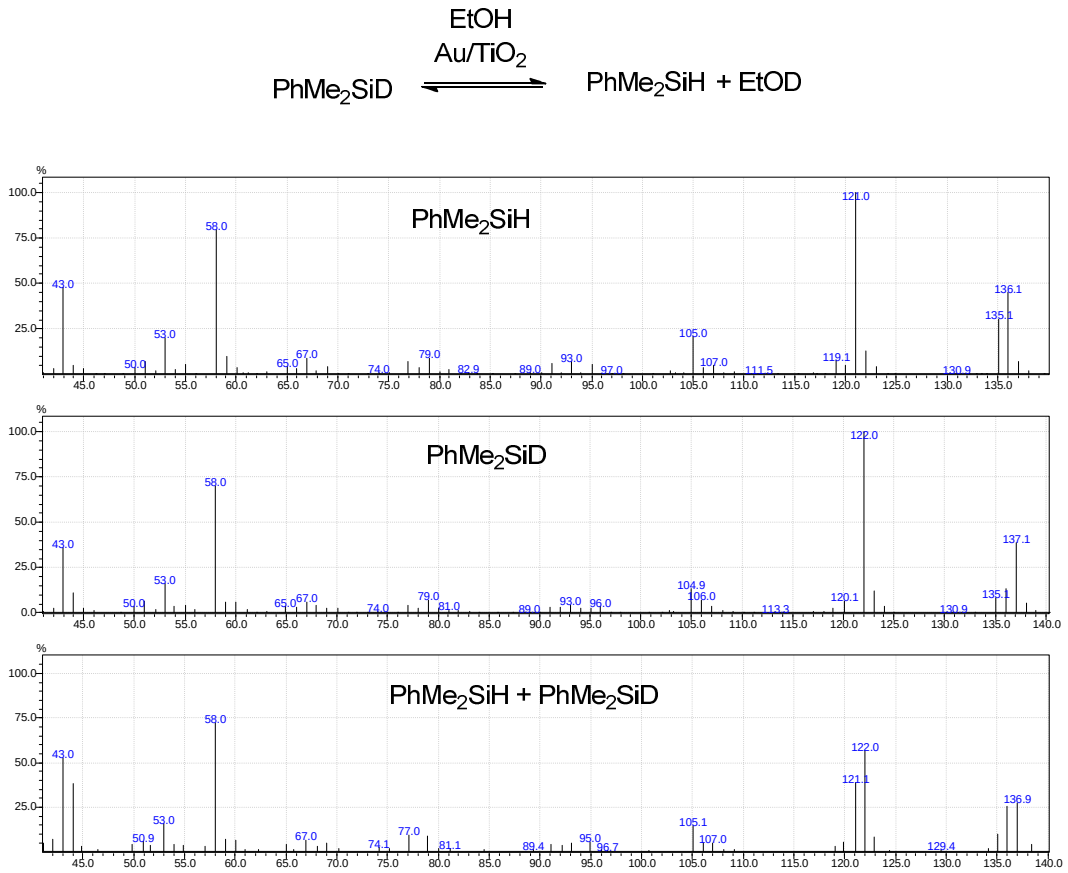
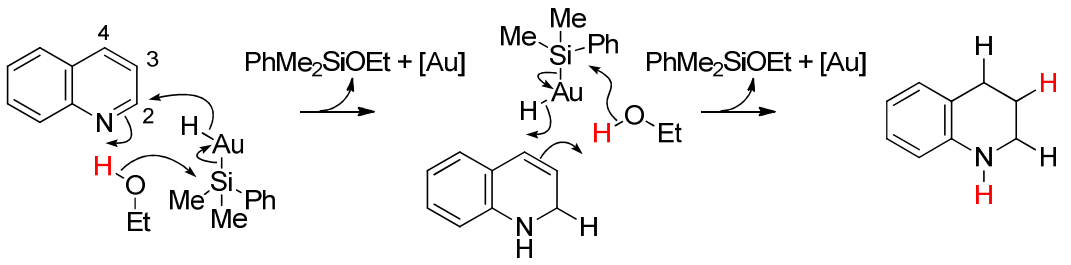


Figure 1. MS spectra of $PhMe_2SiH$ (MW = 136; top), $PhMe_2SiD$ (MW = 137; middle), and the mixture of $PhMe_2SiD$/$PhMe_2SiH$ (bottom) by the gradual depletion of $PhMe_2SiD$ from EtOH during the progress of reaction.

The fast depletion of Si-D functionality under the reaction conditions did not allow the conclusive study of other slowly reacting quinolines such as the parent **2**. For example, reduction of the slightly less reactive (compared to **1**) fluoroquinoline **9** with $PhMe_2SiD$, led to 60% D incorporation on C2, ~20% on C4 and ~10% on one of the two distereotopic protons of C3 (see Supporting Information). The minor deuteration on C3 can be attributed to the *in situ* formation of EtOD under the reaction conditions.

On the basis of the labelling experiments, we propose a reasonable stepwise mechanism that involves the regioselective addition of *in situ* formed silylgold hydride species[25,26] on C2 and C4 carbon atoms, accompanied by protonation with ethanol on C3 and nitrogen atoms, respectively (Scheme 3). Gold hydride $PhMe_2SiAuH$ has been postulated to be formed by insertion of Au NP on the Si-H bond.[27] The side product of reaction ($PhMe_2SiOEt$) was isolated and characterized (see Supporting Information).



Scheme 3. Proposed mechanism for the reduction of quinolines to 1,2,3,4-tetrahydroquinolines by $PhMe_2SiH$/EtOH catalyzed by Au/TiO_2.

Conclusions

We have demonstrated a solvent-free reduction of quinolines to 1,2,3,4-tetrahydroquinolines using $PhMe_2SiH$/EtOH as the reductant system, and as catalyst gold nanoparticles supported on TiO_2. This method complements a recently presented reduction protocol that uses a nanoporous gold catalyst.[20] The hydrogen atoms in the reduction products arise from hydrosilane (2 C-H bonds on C2 and C4) and from EtOH (C-H bond at C3 and N-H bond). Furthermore, an unexpected exchange of Si-H hydride by protons from solvent can occur under the reaction conditions. The current reduction protocol expands the potential of supported Au nanoparticles in catalysis.[1-6]

Experimental Section

General. Nuclear magnetic resonance spectra were recorded on 300 and 500 MHz spectrometers in $CDCl_3$. Isomeric purities were determined by ^{1}H NMR spectroscopy, by analytical gas chromatography and by GC-MS. 8-Methoxyquinoline (**1**)[28] was synthesized by treatment of commercially available 8-hydroxyquinoline with K_2CO_3 and CH_3I in DMF. Quinolines **5**[29] and **6**[30] were prepared by Friedlander condensation of 2'-aminoacetophenone with acetone or acetophenone, respectively, based on a literature procedure.[31] 8-Bromo-2-methylquinoline (**11**)[32] was synthesized via a Doebner–Miller condensation protocol[33] between 2-bromoaniline and crotonaldehyde. The rest of quinolines are commercially available substances.

Spectroscopic data of synthesized quinolines

8-Methoxyquinoline (1).[28] ^{1}H NMR (300 MHz, $CDCl_3$) 8.94-8.92 (m, 1H), 8.13 (dd, 1H, *J* 8.0, 1.5 Hz), 7.49-7.37 (m, 3H), 7.05 (dd, 1H, *J* 7.5, 1.5 Hz), 4.09 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 155.3, 149.1, 140.0, 136.0, 129.4, 126.7, 121.6, 119.5, 107.6, 56.0.

2,4-Dimethylquinoline (5).[29] ^{1}H NMR (300 MHz, $CDCl_3$): 8.05 (d, 1H, *J* 8.5 Hz), 7.94 (dd, 1H, *J* 8.5, 1.5 Hz), 7.67 (dt, 1H, *J* 8.5, 1.5 Hz), 7.50 (dt, 1H, *J* 8.5, 1.5 Hz), 7.14 (d, 1H, *J* 1.0 Hz),

2.71 (s, 3H), 2.66 (d, 3H, *J* 1.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 158.5, 147.4, 144.5, 129.2, 128.9, 126.5, 125.5, 123.6, 122.7, 25.0, 18.6.

4-Methyl-2-phenylquinoline (6).[30] ^{1}H NMR (300 MHz, $CDCl_3$) 8.22-8.15 (m, 3H), 8.02 (d, 1H, *J* 8.0 Hz), 7.75-7.69 (m, 2H), 7.58-7.43 (m, 4H), 2.78 (d, 3H, *J* 1.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 157.0, 148.1, 144.8, 139.8, 130.3, 129.3, 129.2, 128.8, 127.5, 127.2, 126.0, 123.6, 119.7, 19.0.

8-Bromo-2-methylquinoline (11).[32] ^{1}H NMR (300 MHz, $CDCl_3$) 8.04-7.98 (m, 2H), 7.72 (t, 1H, *J* 8.0 Hz), 7.35-7.26 (m, 2H), 2.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) 160.4, 144.8, 136.5, 133.0, 127.9, 127.4, 126.0, 124.1, 122.8, 25.7.

Typical procedure for the reduction of quinolines

To a dry vial containing 8-methoxyquinoline, **1** (0.048 g, 0.3 mmol), Me_2PhSiH (185 μL, 1.2 mmol) and ethanol (70 μL, 1.2 mmol), Au/TiO_2 (60 mg, 1.0 mol%) was added. The Au content in catalyst was ~1 wt%. The mixture was heated to 70 ^{o}C and the progress of reaction was monitored by TLC and GC. After 15 min (100% conversion), ethanol (1 mL) was added and the resulting slurry was filtered under reduced pressure through a short pad of silica gel with the aid of ethanol (2-3 mL) to withhold the supported catalyst. The filtrate was evaporated under vacuum and the residue was chromatographed (*n*-hexane/ethyl acetate, 10:1) to afford 8-methoxy-1,2,3,4-tetrahydroquinoline (**1a**) (41 mg, 84% yield).

Spectroscopic data of reduction products

8-Methoxy-1,2,3,4-tetrahydroquinoline (1a).[28] ^{1}H NMR (300 MHz, $CDCl_3$) 6.65-6.55 (m, 3H), 3.83 (s, 3H), 3.36-3.32 (m, 2H), 2.78 (t, 2H, *J* 6.5 Hz), 2.00-1.92 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 146.4, 134.3, 121.7, 121.6, 115.9, 107.4, 55.4, 41.5, 26.6, 22.0.

1,2,3,4-Tetrahydroquinoline (2a). ^{1}H NMR (300 MHz, $CDCl_3$) 7.01-6.95 (m, 2H), 6.63 (t, 1H, *J* 8.0 Hz), 6.49 (d, 1H, *J* 8.0 Hz), 3.33-3.29 (m, 2H), 2.78 (t, 1H, *J* 6.5 Hz), 2.00-1.92 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 144.6, 129.5, 126.7, 121.5, 117.0, 114.2, 42.0, 26.9, 22.1.

2-Methyl-1,2,3,4-tetrahydroquinoline (3a).[34] ^{1}H NMR (300 MHz, $CDCl_3$) 7.01-6.95 (m, 2H), 6.62 (t, 1H, *J* 7.5 Hz), 6.49 (d, 1H, *J* 7.5 Hz), 3.47-3.36 (m, 1H), 2.91-2.69 (m, 2H), 1.98-1.90 (m, 1H), 1.67-1.54 (m, 1H), 1.22 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 144.2, 129.3, 126.7, 121.4, 117.4, 114.4, 47.3, 30.0, 26.5, 22.4.

3-Methyl-1,2,3,4-tetrahydroquinoline (4a).[34] ^{1}H NMR (300 MHz, $CDCl_3$) 7.02-6.95 (m, 2H), 6.65 (t, 1H, *J* 8.0 Hz), 6.55 (d, 1H, *J* 8.0 Hz), 3.29 (dd, 1H, *J* 11.0, 3.5 Hz), 2.90 (dd, 1H, *J* 11.0, 10.0 Hz), 2.79 (dd, 1H, *J* 16.0, 4.0 Hz), 2.44 (dd, 1H, *J* 16.0, 10.5 Hz), 2.18-2.02 (m, 1H), 1.07 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 144.0, 129.5, 126.7, 121.2, 117.1, 114.0, 48.8, 35.4, 27.1, 19.0.

***cis*-2,4-Dimethyl-1,2,3,4-tetrahydroquinoline (5a-*cis*)**.[35] ^{1}H NMR (300 MHz, $CDCl_3$) 7.14 (d, 1H, *J* 7.5 Hz), 6.97 (t, 1H, *J* 7.5 Hz), 6.68 (t, 1H, *J* 7.5 Hz), 6.48 (d, 1H, *J* 7.5 Hz), 3.53-3.42 (m, 1H), 3.04-2.91 (m, 1H), 1.98-1.91 (m, 1H), 1.42-1.23 (m, 1H), 1.33 (d, 3H, *J* 6.5 Hz), 1.20 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 144.7, 126.8, 126.7, 126.3, 117.3, 113.9, 47.4, 40.6, 30.8, 22.7, 20.3.

***trans*-2,4-Dimethyl-1,2,3,4-tetrahydroquinoline (5a-*trans*)**.[35] ^{1}H NMR (300 MHz, $CDCl_3$) 7.14 (d, 1H, *J* 7.5 Hz), 7.00 (t, 1H, *J* 7.5 Hz), 6.66 (t, 1H, *J* 7.5 Hz), 6.49 (d, 1H, *J* 7.5 Hz), 3.53-3.42 (m, 1H), 3.05-2.92 (m, 1H), 1.70-1.63 (m, 1H), 1.42-1.23 (m, 1H), 1.28 (d, 3H, *J* 6.5 Hz), 1.21 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 144.1, 129.1, 126.7, 126.3, 116.9, 114.0, 42.4, 37.1, 30.1, 24.7, 22.6.

***cis*-4-Methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (6a-*cis*)**.[36] ^{1}H NMR (500 MHz, $CDCl_3$) 7.47-7.29 (m, 5H), 7.20 (d, 1H, *J* 7.5 Hz), 7.02 (t, 1H, *J* 7.5 Hz), 6.73 (t, 1H, *J* 7.5 Hz), 6.54 (d, 1H, *J* 7.5 Hz), 4.49 (dd, 1H, *J* 11.5, 2.5 Hz), 3.18-3.11 (m, 1H), 2.14-2.09 (m, 1H), 1.81-1.73 (m, 1H), 1.39 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) 144.7, 144.5, 128.6, 127.6, 126.9, 126.8, 126.6, 126.0, 117.5, 114.1, 57.0, 41.6, 31.3, 20.1.

***trans*-4-Methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (6a-*trans*)**.[37] ^{1}H NMR (500 MHz, $CDCl_3$) 7.41-7.28 (m, 5H), 7.10 (d, 1H, *J* 7.5 Hz), 7.03 (t, 1H, *J* 7.5 Hz), 6.70 (t, 1H, *J* 7.5 Hz), 6.57 (d, 1H, *J* 7.5 Hz), 4.48 (dd, 1H, *J* 11.5, 2.5 Hz), 2.97-2.91 (m, 1H), 2.08-2.02 (m, 1H), 1.89-1.83 (m, 1H), 1.38 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) 144.8, 144.0, 128.8, 128.6, 127.4, 126.9, 126.6, 126.0, 117.1, 114.1, 52.1, 38.2, 29.9, 24.1.

6-Chloro-1,2,3,4-tetrahydroquinoline (7a).[8] ^{1}H NMR (300 MHz, $CDCl_3$) 6.92-6.88 (m, 2H), 6.41 (d, 1H, *J* 8.0 Hz), 3.31-3.27 (m, 2H), 2.73 (t, 1H, *J* 6.5 Hz), 1.96-1.88 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 142.8, 129.1, 126.5, 123.2, 121.6, 115.4, 41.9, 26.8, 21.7.

6-Bromo-1,2,3,4-tetrahydroquinoline (8a).[38] ^{1}H NMR (300 MHz, $CDCl_3$) 7.05-7.01 (m, 2H), 6.34 (d, 1H, *J* 8.0 Hz), 3.30-3.26 (m, 2H), 2.73 (t, 2H, *J* 6.5 Hz), 1.95-1.87 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) 143.1, 131.9, 129.4, 123.8, 115.9, 108.8, 41.8, 26.7, 21.6.

6-Fluoro-2-methyl-1,2,3,4-tetrahydroquinoline (9a).[34] ^{1}H NMR (300 MHz, $CDCl_3$) 6.71-6.65 (m, 2H), 6.44-6.39 (m, 1H), 3.39-3.33 (m, 1H), 2.89-2.66 (m, 2H), 1.97-1.88 (m, 1H), 1.64-1.51 (m, 1H), 1.21 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 155.6 (d, J_{CF} 233.5 Hz), 140.7 (d, J_{CF} 2.0 Hz), 122.6 (d, J_{CF} 6.5 Hz), 115.4 (d, J_{CF} 21.5 Hz), 114.9 (d, J_{CF} 7.5 Hz), 113.2 (d, J_{CF} 22.0 Hz), 47.4, 29.8, 26.6 (d, J_{CF} 1.5 Hz), 22.4.

6-Chloro-2-methyl-1,2,3,4-tetrahydroquinoline (10a).[34] ^{1}H NMR (300 MHz, $CDCl_3$) 6.93-6.88 (m, 2H), 6.39 (d, 1H, *J* 8.5 Hz), 3.44-3.33 (m, 1H), 2.86-2.65 (m, 2H), 1.96-1.89 (m, 1H), 1.62-1.49 (m, 1H), 1.21 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 143.2, 128.8, 126.5, 122.6, 121.3, 115.0, 47.2, 29.7, 26.4, 22.4.

8-Bromo-2-methyl-1,2,3,4-tetrahydroquinoline (11a). ^{1}H NMR (300 MHz, $CDCl_3$) 7.23 (d, 1H, *J* 8.0 Hz), 6.91 (d, 1H, *J* 8.0 Hz), 6.46 (t, 1H, *J* 8.0 Hz), 3.53-3.43 (m, 1H), 2.91-2.70 (m, 2H), 1.98-1.90 (m, 1H), 1.65-1.52 (m, 1H), 1.29 (d, 3H, *J* 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 141.7, 129.9, 128.1, 122.6, 116.9, 108.5, 47.4, 29.6, 26.9, 22.5. HRMS (ESI-Orbit trap) *m/z*: $[M+H]^+$ calcd for $C_{10}H_{12}BrN+H$, 226.0231; found 226.0227.

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