Selective Reduction of Nitroarenes by a Hantzsch 1,4-Dihydropyridine: A Facile and Efficient Approach to Substituted Quinolines

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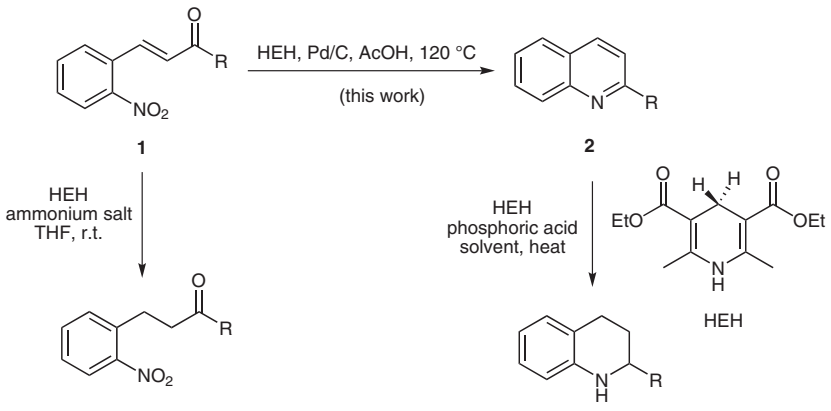
Abstract: An efficient reductive cyclization of *o*-nitrocinnamoyl compounds was achieved by employing a Hantzsch 1,4-dihydropyridine ester as a biomimetic reducing agent in the presence of catalytic palladium on carbon. This approach was successfully applied to the synthesis of substituted quinolines.

Key words: quinolines, reductive cyclization, Hantzsch ester, biomimetic reducing agent

The search for a more efficient chemoselective hydrogenation is one of the most intensely pursued challenges in modern chemistry. In this regard, the selective transformation of nitroarenes bearing reducible functional groups to functionalized anilines is an important research area because of the relevance of these compounds to the pharmaceutical and fine chemical industries. The functionalization of quinolines, thanks to the abundance of quinolines in biologically and medicinally active compounds,[1] has received much attention to date. The reduction of *o*-nitrocinnamoyl compounds with reducing agents, followed by cyclization to form quinolines, is one of the major routes to access functionalized quinolines; however, the process is somewhat difficult because of the lack of selectivity in the reduction of a nitro group in the presence of olefinic and carbonyl substituents. Reduction systems such as CO,[2] Sm–$TiCl_4$,[3] Zn–$TiCl_4$,[4] SmI_2,[5] In,[6] $SnCl_2$,[7] $HCOONH_4$–Pd/C,[7] Fe/AcOH[8] and baker's yeast[9] have been used for the selective reductive cyclization of 2-nitrochalcones; however, some of these methods suffer from relatively low yields, poor regioselectivity, tedious reaction procedures, relatively expensive reagents and/or rather lengthy synthetic sequences. Therefore, the development of new strategies for the efficient reductive cyclization of *o*-nitrocinnamoyl compounds is urgently needed.

Generally, the reduction of nitro compounds to amines is approached using one of three methods. First is the catalytic hydrogenation of the nitro compounds with molecular hydrogen by metal catalysts.[10] The second is the stoichiometric reduction of the corresponding aromatic nitro compounds by using iron,[11a] tin,[11b] zinc[11c] and so on. The third is the chemoselective hydrogenation of aromatic nitro compounds catalyzed by metals in the presence of organic reductants, such as silane/siloxane[12] and ammonium formate/copper nanoparticles.[13] In contrast to the chemical conversions described above, the biomimetic reduction of nitroarenes using nicotinamide adenine dinucleotide (NADH) models has seldom been reported.[14] The Hantzsch 1,4-dihydropyridine HEH (diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate, see Scheme 1), a model compound of coenzyme NAD(P)H, is one of the most widely investigated biomimetic reductants. Recent



Scheme 1

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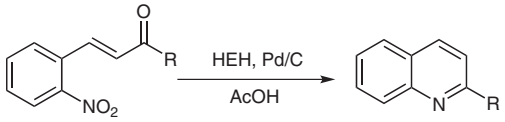
studies in our laboratory have shown that the reducibility of HEH is dramatically enhanced in the presence of palladium on carbon (Pd/C).[15] Moreover, high chemoselectivities have been observed by regulating reaction conditions, such as the amount of HEH, reaction temperatures and solvents. We have examined the selective reduction of a nitro group with HEH and Pd/C in the presence of epoxy, ester or amide substituents and have successfully accomplished the synthesis of 2*H*-1,4-benzoxazine,[15c] benzoxazole[15e] and benzimidazole[15e] derivatives. In this paper, we report that substituted quinolines can be efficiently synthesized by the highly chemoselective Pd/C-catalyzed reduction of *o*-nitrocinnamoyl compounds by HEH (Scheme 1).

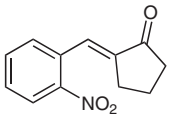
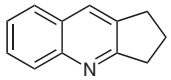
As a new direction in the research of enantioselective hydrogenation catalyzed by organocatalysts, considerable progress has been made over the past decade in the use of HEH to selectively reduce the electron-deficient carbon–carbon double bond of α,β-unsaturated carbonyl compounds.[16] The steady transfer hydrogenation of α,β-unsaturated carbonyl compounds[16a] **1** (Scheme 1 left) and quinolines[17] **2** (Scheme 1 right) has been reported to occur using HEH in the presence of organocatalysts. These two side reactions pose difficulties in obtaining the desired quinolines efficiently. Our preliminary studies focused on the reductive cyclization of 2-nitrochalcone (**1a**) with HEH (Table 1). No reaction occurred at room temperature using ethanol or acetic acid as a solvent (Table 1, entries 1 and 3). Initial success was obtained by refluxing an ethanolic solution of **1a** and HEH in the presence of Pd/C (Table 1, entry 2). To our delight, when the reaction was performed in refluxing acetic acid, quinoline **2a** was obtained in excellent yield (Table 1, entry 4). Importantly, no conversion was observed when the reaction was refluxed in acetic acid in the absence of Pd/C or HEH (Table 1, entries 5 and 6).

Under the optimized conditions, the scope of the reaction was explored with a variety of *o*-nitrocinnamoyl compounds. The results are summarized in Table 2. The reac-

Table 2 Synthesis of Quinolines[a]

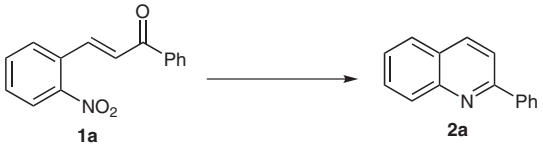


1 2

Entry	Substrate	Product[b]	Yield[c] (%)
1	**1a** R = Ph	**2a**	95
2	**1b** R = 4-MeC_6H_4	**2b**	85
3	**1c** R = 2-MeC_6H_4	**2c**	83
4	**1d** R = 4-MeOC_6H_4	**2d**	96
5	**1e** R = 3-MeOC_6H_4	**2e**	82
6	**1f** R = 2-MeOC_6H_4	**2f**	87
7	**1g** R = 4-ClC_6H_4	**2g**	72[d]
8	**1h** R = 4-BrC_6H_4	**2h**	70[d]
9	**1i** R = 4-F_3CC_6H_4	**2i**	80
10	**1j** R = 1-naphthyl	**2j**	78
11	**1k** R = 3-pyridyl	**2k**	86
12	**1l** R = Me	**2l**	79
13	 **1m**	 **2m**	82
14	**1n** R = H	**2n**	85[e]

[a] Reaction conditions: **1** (1.0 mmol), HEH (3.6 mmol), 10% Pd/C (2 wt% of HEH), AcOH (20 mL), 120 °C, 15 h.
[b] All products are known compounds and were characterized by EI-MS spectrometry, and IR, ^{1}H NMR and ^{13}C NMR spectroscopy.
[c] Isolated yields.
[d] HEH (3.2 mmol) was used.
[e] Analysis by GC-MS.

Table 1 Optimization of Reaction Conditions[a]



1a 2a

Entry	Conditions[a]	Yield (%)
1	10% Pd/C (2 wt% of HEH), HEH (3.6 equiv), EtOH, r.t., 15 h	0
2	10% Pd/C (2 wt% of HEH), HEH (3.6 equiv), EtOH, reflux, 15 h	49
3	10% Pd/C (2 wt% of HEH), HEH (3.6 equiv), AcOH, r.t., 15 h	0
4	10% Pd/C (2 wt% of HEH), HEH (3.6 equiv), AcOH, reflux, 15 h	95
5	HEH (3.6 equiv), AcOH, reflux, 15 h	0
6	10% Pd/C (18 mg), AcOH, reflux, 15 h	0

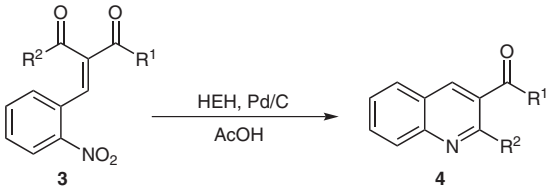
[a] Reactions were performed with **1a** (1.0 mmol) and solvent (0.05 M/[starting material]).

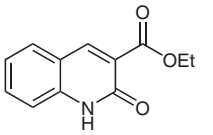
tion works well with an electron-donating group (R = 4-Tol, 2-Tol, 4-$MeOC_6H_4$, 3-$MeOC_6H_4$, 2-$MeOC_6H_4$; Table 2, entries 2–6) or an electron-withdrawing group (R = 4-$F_3CC_6H_4$; Table 2, entry 9) located on the benzoyl ring of the *o*-nitrocinnamoyl compounds. When the *para* position of the benzoyl ring was substituted by chlorine or bromine, a small amount of dehalogenated product was produced. To avoid overhydrogenation, the amount of HEH was decreased from 3.6 to 3.2 equivalents. The corresponding 2-(4-halophenyl)quinoline yields were 72% and 70%, respectively (Table 2, entries 7 and 8). Good results were obtained using 1-(naphthalen-1-yl)-3-(2-nitrophenyl)prop-2-en-1-one (**1j**; Table 2, entry 10) and 3-(2-nitrophenyl)-1-(pyridin-3-yl)prop-2-en-1-one (**1k**; Table 2, entry 11) as the starting materials. Aliphatic ketones were also suitable for the reductive cyclization procedure (Table 2, entries 12 and 13). In particular, 2-nitrocinnamaldehyde (**1n**) was converted into quinoline (Table 2, entry 14) in 85% yield, which indicates that this biomimetic reduction is tolerant to aldehydes and the present reductive cyclization is highly chemoselective.

To further broaden the scope of application, the synthesis of 2,3-disubstituted quinolines was carried out by employing a range of functionalized 2-(2-nitrobenzylidene)-1,3-dicarbonyl compounds **3** as reactants (Table 3). These starting materials have a highly electron-deficient double bond which can be easily reduced by HEH.[18] Again, good functional group tolerance was observed for the reductive cyclization reaction and the corresponding 2,3-disubstituted quinolines were obtained in moderate to excellent yields (Table 3, entries 1–5).

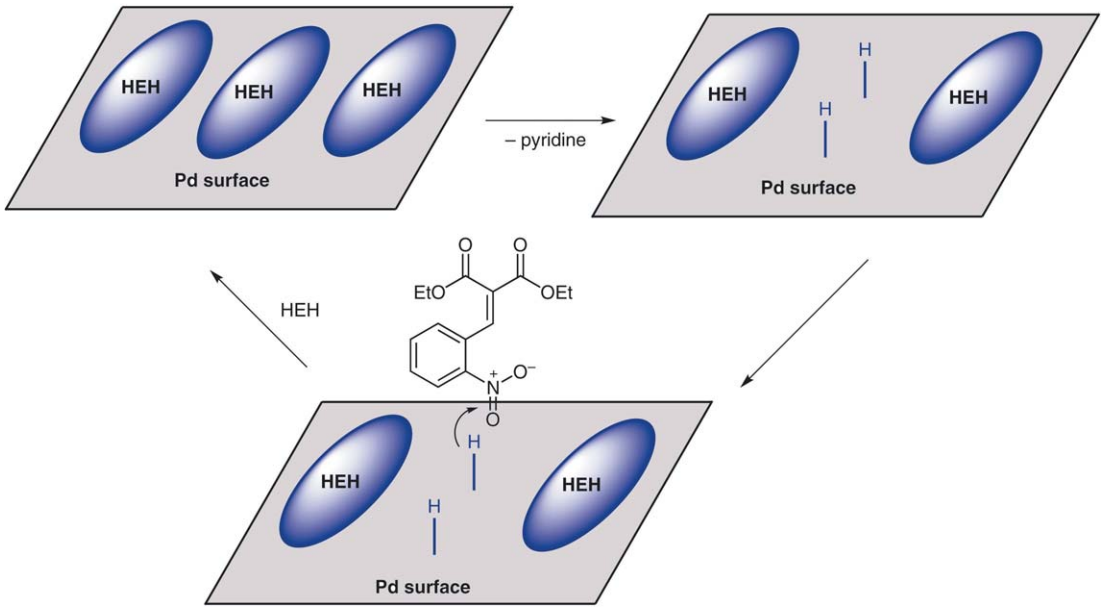
We also observed hydrogen gas evolution during refluxing in acetic acid containing HEH and catalytic Pd/C. The generation of hydrogen gas from HEH is supported by DFT calculations.[15e] These facts indicate that palladium hydride is generated during the aromatization of HEH catalyzed by Pd/C. As shown in Scheme 2, the high chemoselectivities of the hydrogenation may arise from the strong absorption of HEH on the palladium surface. Thus, HEH is not only the reductant of the reaction but also the modifier for the palladium surface. The preferential absorption of HEH hinders absorption and the selective hydrogenation of the less-reactive moiety, thereby leading to the predominant hydrogenation of the nitro group.

Table 3 Synthesis of 2,3-Disubstituted Quinolines[a]



Entry	Substrate	R^1	R^2	Product[b]	Yield[c] (%)
1	**3a**	Me	Me	**4a**	82
2	**3b**	Ph	Me	**4b**	74
3	**3c**	Ph	Ph	**4c**	77
4	**3d**	EtO	Me	**4d**	98
5	**3e**	EtO	EtO	 **4e**	74

[a] Reaction conditions: **3** (1.0 mmol), HEH (3.6 mmol), 10% Pd/C (2 wt% of HEH), AcOH (20 mL), 120 °C, 15 h.
[b] All products are known compounds and were characterized by EI-MS spectrometry, and IR, ^{1}H NMR and ^{13}C NMR spectroscopy.
[c] Isolated yields.



Scheme 2

In summary, we have demonstrated that the Hantzsch 1,4-dihydropyridine HEH, a model compound of coenzyme NAD(P)H, is a mild and efficient reductant for the reductive cyclization of *o*-nitrocinnamoyl compounds. The high chemoselectivities and good yields make this a promising method for the synthesis of substituted quinolines from simple and readily available nitroarenes. The chemical behavior of HEH in the presence of Pd/C is different from that reported in homogeneous systems. In comparison to the boom of research for HEH in homogeneous catalytic systems during the past few decades, more elegant applications of HEH in heterogeneous catalytic systems are expected.

^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury Plus instrument (at 400 MHz and 100 MHz, respectively) and internally referenced to the tetramethylsilane signal or residual protic solvent signals. ^{1}H NMR data are given as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet or unresolved), coupling constant(s) in Hz, integration. ^{13}C NMR data are reported in terms of chemical shift (δ, ppm). Mass spectra were recorded by EI methods on a TRACE DSQ mass spectrometer. IR spectra were recorded on a Nicolet NEXUS 670 FT-IR spectrometer. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on silica gel F_{254} plates. Silica gel (200–300 mesh) was used for column chromatography. The employed solvents were dried using standard procedures. Commercially obtained reagents were used without further purification.

o-Nitrocinnamoyl Compounds 1a–k; General Procedure[6b]

Starting materials **1a–k** were easily obtained via a modified Claisen–Schmidt reaction using *o*-nitrobenzaldehyde (5 mmol), the appropriate ketone (5 mmol), K_2CO_3 (3.5 g) and NaOH (200 mg); these compounds were placed into a triturator and ground for about 10 min. After completion of the reaction, the mixture was extracted with EtOAc (3 × 25 mL) and the extracts were washed with H_2O (3 × 25 mL) and concentrated. The product **1a–k** was purified using column chromatography (PE–acetone).

2-(2-Nitrobenzylidene)cyclopentanone (1m)[19]

A soln of cyclopentanone (100 mmol) and morpholine (9 mL, 100 mmol) in toluene (100 mL) was heated under reflux in a Dean–Stark apparatus until no further H_2O was collected. *o*-Nitrobenzaldehyde (100 mmol) was then added to the cooled solution and the mixture was heated under reflux until no further H_2O was collected. A 1:1 mixture of H_2O and concd HCl (50 mL) was added dropwise to the stirred, cooled solution which was left for a further hour. The solution was then washed with 10% aq Na_2CO_3 (100 mL), dried ($MgSO_4$), filtered and concentrated; the product was purified using column chromatography (PE–acetone, 10:1).

2-(2-Nitrobenzylidene)-1,3-dicarbonyl Compounds 3a–e; General Procedure[20]

A soln of *o*-nitrobenzaldehyde (1.0 mmol), the appropriate 1,3-dicarbonyl compound (1.1 mmol), piperidine (0.1 mmol) and glacial AcOH (0.5 mmol) in reagent grade benzene (0.2 M) was heated to reflux using a Dean–Stark apparatus for 5 h or until the reaction went to completion. The reaction mixture was cooled to r.t. and diluted with EtOAc (80 mL). This mixture was washed with 1 M aq HCl (2 × 15 mL), 1 M aq NaOH (2 × 15 mL) and brine (2 × 15 mL). The organic layer was dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (PE–acetone) to afford the product **3a–e**.

Quinolines 2 and 4; General Procedure

To a soln of the *o*-nitrocinnamoyl compound **1** or **3** (1.0 mmol) in AcOH (20 mL) were added HEH (3.6 mmol) and 10% Pd/C (2 wt% of HEH), and the mixture was refluxed under stirring and argon atmosphere for 15 h. After completion of the reaction, as monitored by TLC, the mixture was filtered and the filtrate was concentrated under reduced pressure. The corresponding quinoline **2** or **4** was isolated by silica gel column chromatography (PE–acetone) and identified by comparing its EI-MS and ^{1}H NMR, ^{13}C NMR and IR spectroscopic data with those reported in the literature.

2-Phenylquinoline (2a)

Yield: 195 mg (95%); white solid; mp 83–85 °C.

IR (KBr): 3421, 3053, 1596, 1553, 1447, 1318, 1074, 829, 766 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.57 (m, 4 H), 7.74 (dt, *J* = 7.4, 1.2 Hz, 1 H), 7.82 (d, *J* = 8.0 Hz, 1 H), 7.87 (d, *J* = 8.8 Hz, 1 H), 8.19–8.23 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.9, 126.2, 127.1, 127.4, 127.5, 128.8, 129.3, 129.6, 129.7, 136.7, 139.6, 148.3, 157.3.

EI-MS: *m*/*z* (%) = 205 (100.0) [M$^+$], 176 (8.4), 102 (21.5), 88 (7.5), 76 (5.4), 51 (2.4).

2-(4-Tolyl)quinoline (2b)

Yield: 186 mg (85%); white solid; mp 79–81 °C.

IR (KBr): 3420, 3058, 1927, 1702, 1595, 1575, 1498, 815, 788 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.50 (t, *J* = 7.2 Hz, 1 H), 7.71 (dt, *J* = 7.2, 1.2 Hz, 1 H), 7.79 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.85 (d, *J* = 8.8 Hz, 1 H), 8.07 (d, *J* = 8.0 Hz, 2 H), 8.17 (t, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 118.9, 126.1, 126.9, 127.1, 127.5, 129.2, 129.6, 129.7, 136.7, 136.9, 139.4, 148.3, 157.3.

EI-MS: *m*/*z* (%) = 219 (100.0) [M$^+$], 204 (23.6), 128 (3.7), 109 (13.8), 95 (6.1), 84 (4.7).

2-(2-Tolyl)quinoline (2c)

Yield: 182 mg (83%); white solid; mp 70–71 °C.

IR (KBr): 3423, 3057, 2958, 1952, 1726, 1598, 1456, 837, 760 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 7.29–7.36 (m, 3 H), 7.49–7.58 (m, 3 H), 7.74 (dt, *J* = 8.4, 1.2 Hz, 1 H), 7.85 (d, *J* = 7.6 Hz, 1 H), 8.18 (d, *J* = 8.8 Hz, 1 H), 8.20 (d, *J* = 8.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3, 122.3, 126.0, 126.4, 126.7, 127.5, 128.5, 129.5, 129.6, 129.7, 130.8, 136.0, 136.1, 140.6, 147.8, 160.2.

EI-MS: *m*/*z* (%) = 219 (38.1) [M$^+$], 218 (100) [M – 1]$^+$, 109 (33.0), 75 (11.4), 63 (15.5), 51 (17.4), 39 (23.1).

2-(4-Methoxyphenyl)quinoline (2d)

Yield: 226 mg (96%); white solid; mp 123–125 °C.

IR (KBr): 3412, 2960, 1718, 1598, 1498, 1430, 1251, 818, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (s, 3 H), 7.04 (d, *J* = 8.8 Hz, 2 H), 7.49 (dt, *J* = 7.6, 0.8 Hz, 1 H), 7.70 (dt, *J* = 7.8, 1.2 Hz, 1 H), 7.78–7.83 (m, 2 H), 8.12–8.17 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 114.2, 118.5, 125.9, 126.9, 127.4, 128.9, 129.5, 129.6, 132.2, 136.6, 148.2, 156.9, 160.8.

EI-MS: *m*/*z* (%) = 235 (100.0) [M$^+$], 220 (39.6), 192 (37.6), 149 (18.0), 95 (7.0), 44 (6.1).

2-(3-Methoxyphenyl)quinoline (2e)
Yield: 193 mg (82%); colorless oil.

IR (KBr): 3059, 2929, 1724, 1599, 1557, 1289, 1041, 830, 781 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.92 (s, 3 H), 7.01 (dd, *J* = 8.2, 2.4 Hz, 1 H), 7.42 (t, *J* = 8.0 Hz, 1 H), 7.51 (t, *J* = 8.0 Hz, 1 H), 7.69–7.73 (m, 2 H), 7.77–7.85 (m, 3 H), 8.18 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 112.7, 115.4, 119.0, 120.0, 126.3, 127.2, 127.4, 129.6, 129.7, 129.8, 136.7, 141.1, 148.2, 157.1, 160.1.

EI-MS: *m*/*z* (%) = 235 (83.5) [M^+], 204 (100.0), 130 (97.1), 102 (53.5), 75 (38.1), 39 (49.0).

2-(2-Methoxyphenyl)quinoline (2f)
Yield: 204 mg (87%); colorless oil.

IR (KBr): 3059, 2933, 1714, 1599, 1497, 1253, 1023, 833, 757 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.87 (s, 3 H), 7.04 (d, *J* = 8.4 Hz, 1 H), 7.13 (dt, *J* = 7.6, 0.8 Hz, 1 H), 7.42 (dt, *J* = 8.4, 2.0 Hz, 1 H), 7.53 (dt, *J* = 8.0, 1.2 Hz, 1 H), 7.70 (dt, *J* = 6.8, 1.6 Hz, 1 H), 7.82–7.90 (m, 3 H), 8.14 (d, *J* = 8.4 Hz, 1 H), 8.17 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 111.3, 121.1, 123.3, 126.0, 126.9, 127.3, 129.0, 129.5, 129.6, 130.2, 131.4, 134.9, 148.2, 157.0, 157.1.

EI-MS: *m*/*z* (%) = 235 (84.8) [M^+], 204 (100.0), 191 (13.3), 130 (98.8), 102 (53.4), 89 (20.5), 75 (37.4), 63 (41.8), 51 (43.6), 39 (47.8).

2-(4-Chlorophenyl)quinoline (2g)
Yield: 172 mg (72%); light yellow crystals; mp 108–110 °C.

IR (KBr): 3394, 3061, 1938, 1710, 1594, 1428, 1286, 816, 786 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.55 (m, 3 H), 7.73 (t, *J* = 8.0 Hz, 1 H), 7.82 (d, *J* = 8.4 Hz, 2 H), 8.10–8.22 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.5, 126.5, 127.2, 127.5, 128.8, 129.0, 129.7, 129.8, 135.5, 137.0, 138.0, 148.2, 156.0.

EI-MS: *m*/*z* (%) = 239 (86.4) [M^+], 204 (100.0), 176 (11.3), 102 (17.4), 88 (11.3), 75 (8.1), 40 (5.2).

2-(4-Bromophenyl)quinoline (2h)
Yield: 198 mg (70%); white solid; mp 119–121 °C.

IR (KBr): 3417, 3059, 1712, 1596, 1552, 1362, 1221, 818, 768 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.54 (dt, *J* = 7.4, 1.2 Hz, 1 H), 7.65 (dd, *J* = 6.8, 2.0 Hz, 2 H), 7.73 (dt, *J* = 6.8, 1.2 Hz, 1 H), 7.83 (dd, *J* = 7.6, 1.2 Hz, 2 H), 8.05 (dd, *J* = 6.8, 2.0 Hz, 2 H), 8.16 (d, *J* = 8.4 Hz, 1 H), 8.22 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.5, 123.9, 126.5, 127.2, 127.5, 129.1, 129.7, 129.9, 132.0, 137.0, 138.5, 148.2, 156.0.

EI-MS: *m*/*z* (%) = 283 (64.9) [M^+], 204 (100.0), 176 (20.0), 149 (57.4), 102 (72.4), 75 (45.3), 50 (43.0).

2-[4-(Trifluoromethyl)phenyl]quinoline (2i)
Yield: 218 mg (80%); white solid; mp 141–142 °C.

IR (KBr): 3393, 2923, 1720, 1592, 1324, 1119, 1071, 816, 789 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.57 (t, *J* = 8.0 Hz, 1 H), 7.74–7.79 (m, 3 H), 7.84–7.90 (m, 2 H), 8.18 (d, *J* = 8.4 Hz, 1 H), 8.25–8.29 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.6, 124.2 (q, *J* = 271.0 Hz), 125.6 (q, *J* = 4.0 Hz), 126.8, 127.4, 127.5, 127.7, 129.8, 129.9, 131.0 (q, *J* = 30.0 Hz), 137.0, 142.8, 148.2, 155.5.

EI-MS: *m*/*z* (%) = 273 (100.0) [M^+], 204 (60.0), 101 (17.5), 76 (22.2), 69 (27.6), 50 (29.1).

2-(Naphthalen-1-yl)quinoline (2j)
Yield: 199 mg (78%); white solid; mp 95–97 °C.

IR (KBr): 3422, 3055, 1709, 1596, 1503, 1423, 1301, 837, 782 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.53 (m, 2 H), 7.60 (t, *J* = 7.6 Hz, 2 H), 7.70–7.73 (m, 2 H), 7.78 (t, *J* = 7.2 Hz, 1 H), 7.90–7.96 (m, 3 H), 8.12 (d, *J* = 8.0 Hz, 1 H), 8.23 (d, *J* = 8.4 Hz, 1 H), 8.28 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 123.3, 125.4, 125.7, 126.0, 126.6, 126.6, 127.0, 127.6, 127.8, 128.3, 129.1, 129.7, 129.8, 131.3, 134.0, 136.3, 138.7, 148.1, 159.4.

EI-MS: *m*/*z* (%) = 255 (47.9) [M^+], 254 (100.0) [M – 1]$^+$, 127 (36.0), 113 (10.7), 75 (13.0), 63 (10.4), 51 (14.4), 39 (10.6).

2-(Pyridin-3-yl)quinoline (2k)
Yield: 177 mg (86%); yellow solid; mp 69–72 °C.

IR (KBr): 3499, 3004, 1710, 1598, 1507, 1362, 1224, 839, 788 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.46 (ddd, *J* = 8.0, 4.8, 0.4 Hz, 1 H), 7.57 (td, *J* = 8.0, 1.2 Hz, 1 H), 7.76 (dt, *J* = 6.8, 1.6 Hz, 1 H), 7.85 (d, *J* = 8.4 Hz, 1 H), 7.89 (d, *J* = 8.4 Hz, 1 H), 8.18 (d, *J* = 8.4 Hz, 1 H), 8.27 (d, *J* = 8.4 Hz, 1 H), 8.50 (td, *J* = 8.0, 2.0 Hz, 1 H), 8.70 (dd, *J* = 4.8, 1.6 Hz, 1 H), 9.36 (d, *J* = 2.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.5, 123.7, 126.8, 127.4, 127.5, 129.7, 130.0, 135.0, 135.2, 137.2, 148.4, 148.7, 150.1, 154.6.

EI-MS: *m*/*z* (%) = 206 (100.0) [M^+], 180 (35.5), 154 (10.5), 128 (31.2), 101 (16.8), 89 (24.5), 76 (33.2), 63 (21.9), 51 (62.1), 39 (21.0).

2-Methylquinoline (2l)
Yield: 113 mg (79%); colorless oil.

IR (KBr): 3390, 3055, 1716, 1658, 1602, 1504, 1425, 821, 783 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.74 (s, 3 H), 7.25 (d, *J* = 8.4 Hz, 1 H), 7.46 (t, *J* = 7.4 Hz, 1 H), 7.67 (t, *J* = 7.2 Hz, 1 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 8.00–8.04 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.3, 121.9, 125.6, 126.4, 127.4, 128.5, 129.3, 136.1, 147.7, 158.9.

EI-MS: *m*/*z* (%) = 143 (100.0) [M^+], 128 (17.6), 115 (25.7), 101 (10.1), 89 (11.1), 75 (16.5), 63 (16.2), 51 (21.7).

2,3-Dihydro-1*H*-cyclopenta[*b*]quinoline (2m)
Yield: 139 mg (82%); white solid; mp 59–60 °C.

IR (KBr): 3393, 3056, 1724, 1702, 1621, 1497, 1404, 862, 782 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.20 (quint, *J* = 7.6 Hz, 2 H), 3.08 (dt, *J* = 7.6, 1.2 Hz, 2 H), 3.16 (t, *J* = 7.6 Hz, 2 H), 7.45 (dt, *J* = 7.6, 0.8 Hz, 1 H), 7.61 (dt, *J* = 8.4, 1.2 Hz, 1 H), 7.72 (d, *J* = 7.6 Hz, 1 H), 7.87 (s, 1 H), 8.02 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.6, 30.5, 34.5, 125.5, 127.4, 127.4, 128.3, 128.5, 130.4, 135.6, 147.4, 167.9.

EI-MS: *m*/*z* (%) = 168 (100.0) [M – 1]$^+$, 140 (11.2), 115 (13.4), 89 (11.0), 84 (28.2), 63 (26.2), 51 (20.3), 39 (32.3).

1-(2-Methylquinolin-3-yl)ethanone (4a)
Yield: 152 mg (82%); yellow solid; mp 72–74 °C.

IR (KBr): 3057, 2965, 1708, 1679, 1562, 1420, 1196, 812, 780 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.72 (s, 3 H), 2.92 (s, 3 H), 7.56 (dt, *J* = 7.4, 1.2 Hz, 1 H), 7.79 (dt, *J* = 8.0, 1.2 Hz, 1 H), 7.86 (d, *J* = 8.0 Hz, 1 H), 8.04 (d, *J* = 8.8 Hz, 1 H), 8.48 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.6, 29.2, 125.6, 126.6, 128.3, 128.6, 131.1, 131.7, 138.1, 148.3, 157.6, 199.9.

EI-MS: *m*/*z* (%) = 185 (62.2) [M$^+$], 170 (91.7), 142 (100), 115 (31.8), 101 (13.1), 75 (10.2), 43 (11.2).

(2-Methylquinolin-3-yl)(phenyl)methanone (4b)
Yield: 183 mg (74%); white solid; mp 60–62 °C.

IR (KBr): 3421, 3059, 1718, 1617, 1591, 1553, 1222, 865, 771 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.16 (s, 3 H), 7.50–7.52 (m, 3 H), 7.60 (m, 1 H), 7.67–7.70 (m, 2 H), 7.79–7.81 (m, 1 H), 7.92 (d, *J* = 8.1 Hz, 1 H), 8.19 (d, *J* = 8.4 Hz, 1 H), 8.38 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4, 126.1, 127.2, 128.4, 128.8, 129.1, 129.3, 129.5, 134.8, 140.2, 140.9, 148.3, 156.8, 203.0.

EI-MS: *m*/*z* (%) = 247 (57.9) [M$^+$], 232 (100.0), 204 (35.8), 176 (17.6), 101 (17.2), 88 (12.0), 75 (37.6), 51 (44.0), 43 (79.3).

Phenyl(2-phenylquinolin-3-yl)methanone (4c)
Yield: 238 mg (77%); white solid; mp 134–136 °C.

IR (KBr): 3408, 3059, 1718, 1664, 1593, 1554, 1234, 871, 770 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.34 (m, 5 H), 7.47 (t, *J* = 7.4 Hz, 1 H), 7.60–7.64 (m, 3 H), 7.71 (dd, *J* = 8.4, 1.2 Hz, 2 H), 7.84 (dt, *J* = 7.2, 1.2 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 1 H), 8.25 (d, *J* = 8.8 Hz, 1 H), 8.34 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 125.8, 127.3, 128.1, 128.4, 128.4, 128.8, 129.3, 129.6, 130.0, 131.2, 132.8, 133.3, 137.0, 137.6, 139.6, 148.3, 157.4, 196.9.

EI-MS: *m*/*z* (%) = 309 (12.3) [M$^+$], 280 (32.1), 232 (17.4), 105 (32.5), 77 (100), 51 (59.7).

Ethyl 2-Methylquinoline-3-carboxylate (4d)
Yield: 211 mg (98%); brown solid; mp 65–66 °C.

IR (KBr): 3407, 3050, 1718, 1620, 1560, 1278, 1064, 870, 782 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (t, *J* = 7.2 Hz, 3 H), 3.00 (s, 3 H), 4.44 (q, *J* = 7.2 Hz, 2 H), 7.53 (t, *J* = 7.6 Hz, 1 H), 7.77 (t, *J* = 7.6 Hz, 1 H), 7.85 (d, *J* = 8.0 Hz, 1 H), 8.04 (d, *J* = 8.4 Hz, 1 H), 8.72 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 25.6, 61.3, 123.9, 125.7, 126.4, 128.4, 128.5, 131.6, 139.8, 148.5, 158.4, 166.5.

EI-MS: *m*/*z* (%) = 215 (95.9) [M$^+$], 187 (16.4), 169 (100.0), 142 (65.3), 115 (29.4), 101 (15.6), 75 (11.0).

Ethyl 2-Oxo-1,2-dihydroquinoline-3-carboxylate (4e)
Yield: 161 mg (74%); yellow solid; mp 162–164 °C.

IR (KBr): 3446, 3009, 1729, 1620, 1565, 1483, 1210, 874, 797 cm^{-1}.

^{1}H NMR (400 MHz, DMSO): δ = 1.29 (t, *J* = 6.8 Hz, 3 H), 4.26 (q, *J* = 6.8 Hz, 2 H), 7.21 (dt, *J* = 8.0, 1.2 Hz, 1 H), 7.31 (d, *J* = 8.4 Hz, 1 H), 7.59 (dt, *J* = 8.0, 1.2 Hz, 1 H), 7.80 (dd, *J* = 8.0, 0.8 Hz, 1 H), 8.47 (s, 1 H), 12.02 (s, 1 H).

^{13}C NMR (100 MHz, DMSO): δ = 14.1, 60.7, 115.0, 117.7, 122.2, 123.4, 129.4, 132.6, 140.1, 143.5, 158.5, 164.4.

EI-MS: *m*/*z* (%) = 217 (37) [M$^+$], 172 (36.7), 145 (100.0), 116 (24.2), 89 (23.0), 44 (27.8), 40 (63.9).

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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