Tetrahedron 66 (2010) 5607–5611

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Hydrogenation of *ortho*-nitrochalcones over Pd/C as a simple access to 2-substituted 1,2,3,4-tetrahydroquinolines

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ARTICLE INFO

Article history:
Received 2 March 2010
Received in revised form 30 April 2010
Accepted 24 May 2010
Available online 1 June 2010

ABSTRACT

The preparation of some 2-substituted-1,2,3,4-tetrahydroquinoline has been achieved by the one-pot reductive intramolecular cyclization of *ortho*-nitrochalcones with gaseous hydrogen in the presence of a Pd/C catalyst and the best selectivity was observed using CH_2Cl_2 as solvent. The method is operationally simple and versatile since *ortho*-nitrocalchones are easily accessible by Claisen–Schmidt condensation of 2-nitrobenzaldehydes and enolizable ketones. Selected examples on structurally different substrates have been considered and a novel tetrahydroquinoline and a benzo[*h*]tetrahydroquinoline were prepared and characterised.

1. Introduction

Quinolines and the related tetrahydroquinolines derivatives constitute a group of heterocycles largely occurring in plants and microorganism[1] whose main importance resides in their broad range of biological activities. They have been reported as antibacteric,[2] fungicide[3] or pesticide agents[4] and their inhibiting or antagonist properties towards specific enzymes or receptors involved in human diseases make them promising compounds in anticancer,[5] antidepressive,[6] antiinflammatory[7] and antidiabetes[8] therapies. Quinoline-based compounds, e.g., quinine or chloroquine, have been widely employed as effective and cheap antimalarial drugs, but a continuous effort is directed toward the development of related molecules in order to overcome chemoresistance problems.[9]

The 2-substituted 1,2,3,4-tetrahydroquinoline platform has been recently used in the design of selective estrogen receptor modulators[10] and inhibitors of the cholesteryl ester transfer protein,[11] whose activity can be potentially exploited for the treatment of estrogen responsive cancer and osteoporosis or in the therapeutical control of the blood level of cholesterol.

Among the different methods available for the synthesis of 1,2,3,4-tetrahydroquinolines (THQs),[12] the selective reduction of nitrogen ring in quinoline derivatives[13] has been applied and its enantioselective version represents the method of choice for the preparation of chiral THQs, thanks to the development of different phosphorous-based catalysts displaying excellent levels of asymmetric induction in metal-promoted or organocatalytic hydrogenations.[14]

The synthesis of different functionalised THQs has been also accomplished by multicomponent aza-Diels–Alder reaction in the presence of various Lewis acid catalysts[15] or by intramolecular cyclization of suitable designed amino-[16] or nitro-[17] aromatic compounds. In this context, we developed a simple and versatile method for the preparation of 2-substituted THQs starting from *ortho*-nitrochalcones and the obtained results are here reported.

2. Results and discussion

In a recent paper Barros et al.[18] have reported that *ortho*-nitrochalcones can be subjected to a reductive intramolecular coupling to afford mixtures of quinolines and quinolines *N*-oxides using ammonium formate as the hydrogen source and Pd/C as catalyst and the reaction course was found to be substrate-dependent, so that in some cases only the reduction of nitrogroup without further cyclization occurred. However, the same strategy could be useful to prepare THQs from *ortho*-nitrocalchones under one-pot hydrogenation conditions following the different routes depicted in Scheme 1. In both cases when the reduction of the ethylenic bond occurs as first reaction step (path A), or the hydrogenation of an intermediate aminocalchone proceeds at higher reaction rate with respect to its cyclization (path B_1) a saturated aminoketone as **5a** could be formed as suitable substrate for the subsequent formation of 3,4-dihydroquinoline, further hydrogenated to THQ. Since aromatic quinolines could be also produced (path B_2) as final products or as other reducible intermediates contributing to the formation of THQ, the competitive hydrogenation/cyclization routes should lead to different quinoline/THQ ratios. So, we decided to investigate the

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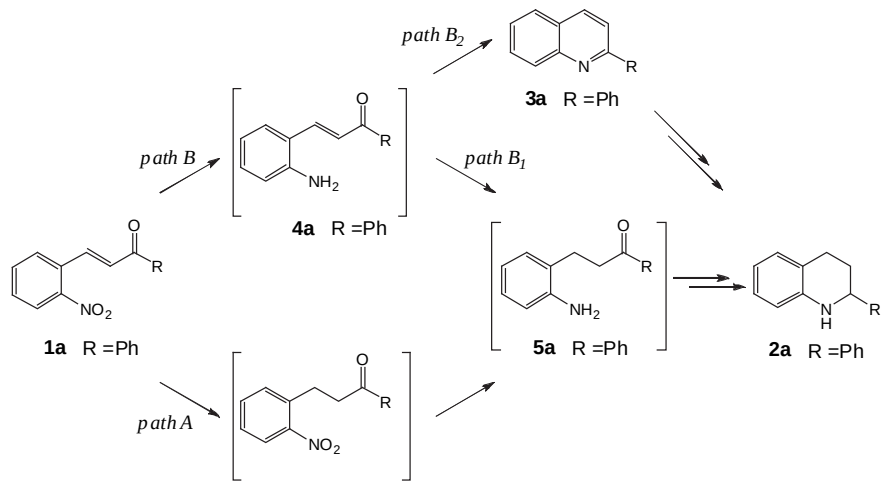
doi:10.1016/j.tet.2010.05.090



Scheme 1. Possible cyclization under hydrogenation conditions.

hydrogenation reaction of **1a** in search of the optimal conditions for the selective formation of **2a**.

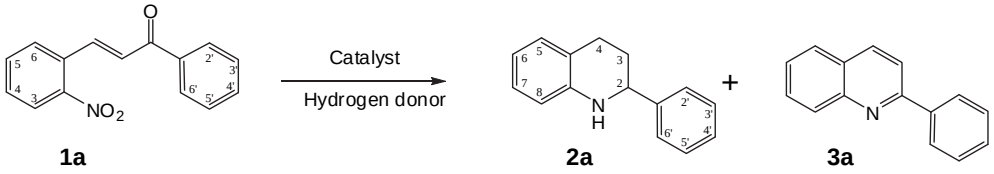
The synthesis of chalcones is usually accomplished by Claisen–Schmidt condensation of enolizable ketones and benzaldehydes in the presence of a base or a Lewis acid and solvent-free or microwave-assisted modified methods have been also reported.[19] Different procedures for the condensation of acetophenone and 2-nitrobenzaldehyde were tested and it was found that the reaction in the presence of 40% $ZrCl_4$ at 40 °C for 20 h afforded the best result giving nitrochalcone **1a** in 85% yield, easily obtained as pure compound by crystallization. When the $ZrCl_4$ percentage was decreased as reported in the original procedure,[19d] significant amount of the aldol product was isolated from the reaction mixture.

Compound **1a** was then subjected to hydrogenation in MeOH in the presence of different metal catalysts and the composition of the reaction mixtures was determined by ^1H NMR analysis (Table 1). With Pd/C catalyst (10% w/w) and gaseous H_2 (1.2 atm) the substrate was firstly converted in a mixture of different compounds that converged after 12 h to tetrahydroquinoline **2a** and quinoline **3a** in 1:1 ratio (entry 1), as the result of a similar reaction rates for both path B_1 and path B_2 shown in Scheme 1.

Using the same Pd/C catalyst and excess of ammonium formate as hydrogen source, **3a** was obtained as main product (entry 2) and no quinoline *N*-oxide was detected in the reaction mixture, contrary to the reported data.[18] The observed reaction outcome, that could be related with a strongly favoured cyclization rather than hydrogenation of **4a**, seems to be substrate-specific since in the same conditions the ethylenic bond of 1,3-diphenyl-2-propenone was reduced in quantitative yield.

In the presence of $Pd(OH)_2/C$ and H_2 **1a** gave a complex mixture of aromatic products, none of which was predominant, whereas Ni/Raney catalyst induced good selectivity affording a 9:1 mixture of **2a** and **3a** (entry 4) in acceptable chemical yield.

Table 1
Hydrogenation of **1a** in different systems[a]



Entry	Catalyst	H_2 source	Solvent	Time (h)	**2a**/**3a**[b]	**2a**[c] (%)
1	Pd/C	H_2	MeOH	12	50/50	45
2	Pd/C	$HCOONH_4$	MeOH[d]	3	8/92	6
3	$Pd(OH)_2$	H_2	MeOH	20	—[e]	—
4	Ni Raney	H_2	MeOH	20	90/10	75
5	Pd/C	H_2	Toluene	20	85/15	78
6	Pd/C	H_2	THF[f]	20	95/5	85
7	Pd/C	H_2	EtOAc	20	95/5	85
8	Pd/C	H_2	CH_2Cl_2	4	93/7	84
9	Pd/C	H_2	CH_2Cl_2[g]	4	82/18	58
10	Pd/C	H_2[h]	CH_2Cl_2	2	95/5	86

[a] See Experimental section.
[b] Determined by ^1H NMR analysis of the reaction mixture.
[c] Isolated yield refers to substrate.
[d] Under reflux.
[e] Compound **2a** was not detected.
[f] Freshly distilled.
[g] Reaction at 40 °C.
[h] H_2 (2.5 atm).

The difficulty of achieving selective hydrogenation of substrates containing different reducible functions has been ascribed to the high activity of the metal catalysts and the use of additives or selected reaction solvents has been reported effective in suppressing reactivity or controlling chemoselectivity.[20] The hydrogenation of **1a** on Pd/C was then carried out in different solvents. In toluene a higher **2a**/**3a** ratio with respect to MeOH was measured (entry 5). More selective conversion of **1a** into the target **2a** was achieved in AcOEt or freshly distilled THF after 20 h (entries 6 and 7); however, CH_2Cl_2 proved to be the best solvent for the higher reaction rate and comparable selectivity (entry 8). Changing the operational temperature to 40 °C, the reaction in CH_2Cl_2 proceeded with a sensible decrease in the selectivity and some unidentified product other than **2a** and **3a** was also present in the final reaction mixture (entry 9); on the contrary, applying a doubled H_2 pressure high **2a**/**3a** ratio and concomitant twofold increase in the reaction rate were determined (entry 10).

When the hydrogenation of **1a** in CH_2Cl_2 at room temperature was terminated after 2 h, a 1:1 ratio of **2a** and aminochalcone **4a** was determined; the structure of **4a** was unequivocally determined after isolation on the basis of its NMR spectra, displaying the diagnostic doublets for two protons in a *trans* ethylenic system and a carbonyl resonance, and its spontaneous cyclization in CH_2Cl_2 solution to quinoline **3a**. Under the same reaction conditions **3a** did not react, so that the presence of **4a** as intermediate compound and the low amount of **3a** in the final reaction mixture support the preferential occurrence of path B_1 (Scheme 1) for the hydrogenation of **1a** in CH_2Cl_2.

The standard conditions (10% w/w Pd/C, CH_2Cl_2, 1.2 atm, rt) developed for **1a** were then applied to nitrochalcones **1b**–**g**, prepared varying the ketone or the 2-nitrobenzaldehyde component in the aldol condensation, and the corresponding THQs **2b**–**g** could be obtained as predominant products (Table 2) in all the cases. Although both substituted nitrocalchones **1b** and **1c** were reduced with comparable reaction rate, the hydrogenation of **1c** displayed lower selectivity affording about 30% of the aromatic heterocycle together with THQ **2c**. Conversion of **1d** into **2d** proceeded with high level of selectivity but lower reaction rate (entry 4), probably for the sterical hindrance of the naphtyl moiety in the cyclization step.

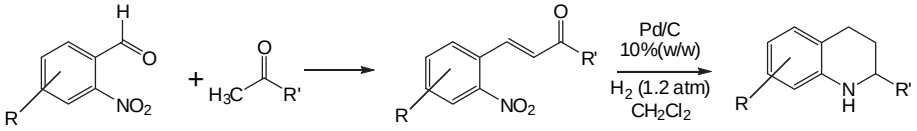
Substitution on the nitrophenyl ring led to a marked decrease in the reactivity and under the standard conditions **1e** and **1f** gave a mixture containing uncyclised intermediates in addition to both THQs and quinolines. However, upon doubling the amount of the catalyst the reaction profiles were comparable with those observed for the other nitrochalcones (entries 5 and 6). The hydrogenation/cyclization protocol could be also applied to the synthesis of 2-alkyl-1,2,3,4-tetrahydroquinoline, as evidenced in the case of **2g** (entry 7), but the lack of selective methods for the Claisen-Schmidt condensation of benzaldehydes and aliphatic ketones could represent a limit in the availability of the starting nitrocalchones.

The synthesis of benzo[*h*]tetrahydroquinoline **2h** was then attempted using the same approach starting from 1-nitro-2-naphthylaldehyde and acetophenone (Scheme 2), but 50% Pd/C catalyst was required in order to achieve complete conversion of the reaction intermediates into **2h** and the corresponding aromatic derivative, isolated in 75% and 15% yield, respectively.

3. Conclusions

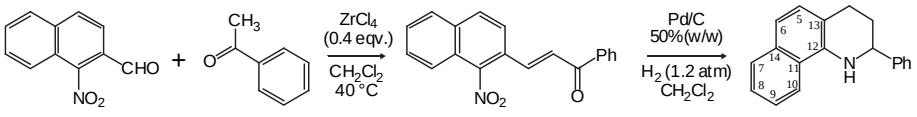
In summary, we have developed a simple route to the 2-substituted-1,2,3,4-tetrahydroquinoline skeleton based on a one pot hydrogenation/cyclization of 2-nitrochalcones in the presence of Pd/C catalyst and gaseous hydrogen. The solvent was found to be crucial on determining the reaction rate and selectivity and the best results were observed in CH_2Cl_2, a quite unusual solvent for this type of hydrogenation reaction. The advantages of the method reside in: (a) operationally simplicity, since the required hydrogen pressure is compatible with normal glassware; (b) good atom economy and atom efficiency;[21] (c) versatility, due to the easy access to a variety of the starting *ortho*-nitrochalcones by condensation of simple or substituted 2-nitrobenzaldehydes with enolizable ketones.

Table 2
Synthesis of tetrahydroquinolines from nitrocalchones



Entry	Substrate	R	R′	Time (h)	Product[a] (%)
1	**1a**	H	Ph	1.5	**2a** (88)
2	**1b**	H	(4-OMe)Ph	3	**2b** (87)
3	**1c**	H	(2-OMe)Ph	3	**2c** (65)
4	**1d**	H	2-Naphthyl	20	**2d** (82)
5	**1e**	4-NMe_2	Ph	20[b]	**2e** (77)
6	**1f**	5-OMe	Ph	15[b]	**2f** (82)
7	**1g**	H	CH_3	3	**2g** (90)

[a] Isolated yield; all the compound were characterised (^1H and ^{13}C NMR, ESI-MS) and their properties compared with literature data.
[b] Pd/C (20% w/w) catalyst.



1h
69% yield

2h
75% yield

Scheme 2. Synthesis of 2-phenyl-benzo[*h*]-1,2,3,4-tetrahydroquinoline.

4. Experimental section

4.1. General methods

All the reagents were from Aldrich and used as received. Column chromatography was performed on Si 60 (230–400 mesh) silica gel using the specified eluants. ^{1}H and ^{13}C NMR spectra were registered in $CDCl_3$, unless otherwise specified, at 400.13 and 100.69 MHz, respectively. 2D NMR spectra were performed using standard Bruker microprograms. Chemical shifts (δ) are given as parts per million relative to the residual solvent peak and coupling constants (J) are in hertz. Assignment of the resonances, when possible, was given following the chemical numeration showed in Table 1 or Scheme 2. Melting points are uncorrected. Elemental analyses were obtained from the Department of Pharmaceutical Sciences, University of Catania.

4.2. General procedure for the synthesis of nitrochalcones

*4.2.1. Chalcones **1a–f, 1h**.* To a mixture of 2-nitrobenzaldehyde (150 mg, 1.0 mmol) and ketone (1.0 mmol) in dry CH_2Cl_2 (1 mL), $ZrCl_4$ (93 mg, 0.4 mmol) was added and the suspension maintained at 40 °C under stirring for 20–48 h, until TLC analysis showed complete disappearance of the substrates. After addition of CH_2Cl_2 (2×30 mL) the mixture was extracted with water (30 mL) and the organic layer washed with brine (30 mL). The CH_2Cl_2 extract was dried over Na_2SO_4 and the taken to dryness. The crude solid was washed with hexane and then crystallized from hexane/ethyl acetate to give pure nitrochalcones in 70–85% yield.

*4.2.2. Chalcone **1g**.* To a solution of 2-nitrobenzaldehyde (150 mg, 1.0 mmol) in acetone (3 mL), Cs_2CO_3 (325 mg, 1.0 mmol) was added and the suspension stirred overnight at 40 °C. The mixture was then concentrated and partitioned between water (30 mL) and CH_2Cl_2 (2×30 mL). The organic extract was dried over Na_2SO_4 and taken to dryness to give a residue that was purified on Si gel column (*n*-hexane/AcOEt/CH_2Cl_2 3:1:1) to afford **1g** (88 mg, 46% yield) and the corresponding aldol in 1:1 ratio.

The above procedures afforded exclusively *trans*-chalcones, that were mainly characterised by NMR spectroscopy, and known compounds were identified by comparison of their properties with those reported in the literature.[18]

*4.2.3. 1-(2-Methoxyphenyl)-3-(2-nitrophenyl)-2-propen-1-one, **1c**.* Pale yellow solid (240 mg, 85% yield), mp 105–106 °C; IR (KBr) 1646, 1588, 1507, 1340, 1010 cm^{-1}; ^{1}H NMR: δ 3.92 (s, 3H, OMe), 7.01 (d, 1H, J=8.4, H-3′), 7.05 (t, 1H, J=7.6, H-5′), 7.24 (d, 1H, J=16.0, CH=), 7.50 (t, 1H, J=8.4, H-4′), 7.54 (t, 1H, J=7.6, H-4), 7.66 (m, 2H, H-5 and H-6′), 7.70 (d, 1H, J=7.6, H-6), 7.96 (d, 1H, J=16.0, CH=), 8.03 (d, 1H, J=7.6, H-3); ^{13}C NMR: δ 55.7 (OMe), 111.5 (C-3′), 120.8 (C-5′), 124.8 (C-3), 128.3 (C-1′), 129.2 (C-6), 130.0 (C-4), 130.5 (C-5), 131.3 (C-1), 131.6 (CH=), 133.3 (C-4′ and C-6′), 138.2 (CH=), 148.6 (C-2), 158.2 (C-2′), 192.5 (CO). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.79; H, 4.59; N, 4.90.

*4.2.4. 1-(2-Naphthyl)-3-(2-nitrophenyl)-2-propen-1-one, **1d**[22].* Brown solid (250 mg, 82% yield), mp 118–119 °C; IR (KBr) 1659, 1595, 1504, 1332, 1170 cm^{-1}; ^{1}H NMR: δ 7.46 (d, 1H, J=15.6, CH=), 7.60 (m, 2H, H-7′ and H-4), 7.63 (m, 1H, H-6′), 7.71 (t, 1H, J=7.6, H-5), 7.80 (d, 1H, J=7.6, H-6), 7.91 (d, 1H, J=7.9, H-5′), 7.95 (d, 1H, J=8.6, H-4′), 8.01 (d, 1H, J=7.9, H-8′), 8.09 (br d, 2H, H-3 and H-3′), 8.20 (d, 1H, J=15.6, CH=), 8.57 (s, 1H, H-1′); ^{13}C NMR: δ 124.5 (C-3′), 125.0 (C-3), 126.9 (C-7′), 127.5 (CH=), 127.8 (C-5′), 128.6 (C-6′), 128.7 (C-4′), 129.3 (C-6), 129.6 (C-8′), 130.3 (C-4), 130.6 (C-1′), 131.4 (C-1), 132.5 (C-9′), 133.5 (C-5), 134.7 (C-2′), 135.6 (C-10′), 140.1 (CH=), 148.6 (C-2), 190.3 (CO). Anal. Calcd for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 75.12; H, 4.29; N, 4.59.

*4.2.5. 1-Phenyl-3-(2-nitro-4-dimethylaminophenyl)-2-propen-1-one, **1e**.* Orange solid (207 mg, 70% yield), mp 155–156 °C; IR (KBr) 1650, 1578, 1515, 1343, 1012 cm^{-1}; ^{1}H NMR: δ 3.11 (s, 6H, NMe_2), 6.89 (dd, 1H, J=2.8 and 8.8, H-5), 7.17 (d, 1H, J=2.8, H-3), 7.26 (d, 1H, J=15.6, CH=), 7.51 (t, 2H, J=7.6, H-3′ and H-5′), 7.58 (t, 1H, J=7.6, H-4′), 7.68 (d, 1H, J=8.8, H-6), 7.80 (d, 2H, J=7.6, H-2′ and H-6′), 8.04 (d, 1H, J=15.6, CH=); ^{13}C NMR: δ 40.0 (NMe_2), 106.5 (C-3), 115.4 (C-5), 116.2 (C-1), 122.2 (CH=), 128.5 (C-2′,C-3′, C-5′ and C-6′), 129.3 (C-6), 132.5 (C-4′), 138.0 (C-1′), 139.8 (CH=), 150.6 (C-2), 151.2 (C-4), 190.5 (CO). Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45. Found: C, 68.82; H, 5.40; N, 9.39.

*4.2.6. 1-Phenyl-3-(2-nitro-5-methoxyphenyl)-2-propen-1-one, **1f**.* Yellow solid (240 mg, 85% yield), mp 98–99 °C; IR (KBr) 1656, 1592, 1504, 1332, 1285, 1077 cm^{-1}; ^{1}H NMR: δ 3.95 (s, 3H, OMe), 7.00 (dd, 1H, J=2.4 and 8.8, H-4), 7.09 (d, 1H, J=2.4, H-6), 7.22 (d, 1H, J=15.6, CH=), 7.51 (t, 2H, J=7.6, H-3′ and H-5′), 7.60 (t, 1H, J=7.6, H-4′), 8.02 (d, 2H, J=7.6, H-2′ and H-6′), 8.16 (d, 1H, J=8.8, H-3), 8.20 (d, 1H, J=15.6, CH=); ^{13}C NMR: δ 56.0 (OMe), 114.3 (C-6), 114.7 (C-4), 127.3 (CH=), 127.7 (C-3), 128.6 (C-3′ and C-5′), 128.8 (C-2′ and C-6′), 133.1 (C-4′), 134.4 (C-1), 137.3 (C-1′), 141.2 (C-2), 141.5 (CH=), 163.4 (C-5), 190.8 (CO). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.75; H, 4.67; N, 4.99.

*4.2.7. 1-Phenyl-3-(1-nitro-2-naphthyl)-2-propen-1-one, **1h**.* Brown solid (210 mg, 69% yield), mp 198–199 °C; IR (KBr) 1655, 1582, 1514, 1343, 1012 cm^{-1}; ^{1}H NMR (CD_3COCD_3): δ 7.60 (t, 2H, J=7.6, H-3′ and H-5′), 7.70 (t, 1H, J=7.6, H-4′), 7.77–7.80 (m, 4H), 8.16 (d, 1H, J=7.6), 8.18–8.22 (m, 3H), 8.26 (d, 1H, J=8.8, H-3), 8.33 (d, 1H, J=8.8, H-4); ^{13}C NMR (CD_3COCD_3): δ 121.7, 123.0, 124.0, 127.4, 128.43, 128.6, 128.8, 129.5, 131.1, 133.4, 134.5, 134.8, 137.5 (C-1′), 148.8 (C-1), 188.3 (CO). Anal. Calcd for $C_{19}H_{13}NO_3$: C, 75.24; H, 4.32; N, 4.62. Found: C, 75.32; H, 4.29; N, 4.57.

4.3. General procedure for the hydrogenation reactions

4.3.1. With gaseous H_2. To a solution of **1a** (30 mg, 0.12 mmol) in the appropriate solvent (3 mL), the required catalyst (3 mg) was added. After the flask was evacuated and filled with H_2 the mixture was maintained under stirring at room temperature until TLC analysis showed complete disappearance of **1a**. The suspension was then filtered through a short plug of Celite and the solution evaporated to give a residue that was analysed by ^{1}H NMR in order to determine **2a**/**3a** ratio and then purified on Si gel column.

4.3.2. With NH_4COOH. In a sealed tube, to a solution of **1a** (50 mg, 0.20 mmol) in MeOH (5 mL), solid NH_4COOH (126 mg, 2.0 mmol) and Pd/C (5 mg) were added and the suspension was stirred at 65 °C for 3 h. The reaction mixture was then filtered through a short plug of Celite and the solution evaporated. The residue was analysed by ^{1}H NMR and then purified by column chromatography.

4.4. General procedure for the synthesis of 2-substituted 1,2,3,4-tetrahydroquinolines

The required 2-nitrochalcone (50 mg) was dissolved in CH_2Cl_2 (5 mL) in a 100 ml flask equipped with a Teflon stopcock and Pd/C catalyst (10% Pd on activated carbon, 5 mg) was added. After the flask was evacuated and then refilled with H_2 (1.2 atm), the reaction mixture was stirred at room temperature. At the end of the reaction, the suspension was filtered through a short plug of Celite and the solution evaporated. The residue was purified by column chromatography (Si gel, *n*-hexane/Et_2O 95:5 or *n*-hexane/CH_2Cl_2/AcOEt

8:1:1) to afford pure tetrahydroquinolines as clear oils. Known compounds **2a**–**d**,[14b,c] **2f**[23] and **2g**[14d] were identified by comparison of their properties with those reported in the literature.

4.4.1. 2-Phenyl-7-dimethylamino-1,2,3,4-tetrahydroquinoline ***2e***. Yield 77% (33 mg); IR (liquid film) 3370, 2972, 1612, 1470, 1246 cm^{-1}; ^1H NMR: δ 1.99 (m, 1H, H-3a), 2.10 (m, 1H, H-3b), 2.67 (dt, 1H, J=4.8, 4.8 and 15.6, H-4a), 2.86 (ddd, 1H, J=5.2, 10.4 and 15.6, H-4b), 2.90 (s, 6H, NMe_2), 4.03 (br s, 1H, NH), 4.42 (dd, 1H, J=3.2 and 9.2, H-2), 5.98 (d, 1H, J=2.4, H-8), 6.19 (dd, 1H, J=2.4 and 8.4, H-6), 6.90 (d, 1H, J=8.4, H-5), 7.29 (t, 1H, J=7.2, H-4′), 7.36 (t, 2H, J=7.2, H-3′ and H-5′), 7.41 (d, 2H, J=7.2, H-2′ and H-6′); ^{13}C NMR: δ 25.5 (C-4), 31.6 (C-3), 41.0 (NMe_2), 56.4 (C-2), 98.6 (C-8), 103.5 (C-6), 110.3 (C-10), 126.6 (C-2′ and C-6′), 127.3 (C-4′), 128.5 (C-3′ and C-5′), 129.7 (C-5), 145.0 (C-1′), 145.2 (C-9) 150.4 (C-7). Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.82; H, 8.01; N, 11.15.

4.4.2. 2-Phenyl-benzo[h]-1,2,3,4-tetrahydroquinoline ***2h***. Yield 75% (32 mg); IR (liquid film) 3365, 2995, 2864, 1483, 1244 cm^{-1}; ^1H NMR: δ 2.15 (m, 1H, H-3a), 2.25 (m, 1H, H-3b), 2.88 (dt, 1H, J=4.8, 4.8 and 16.4, H-4a), 3.12 (ddd, 1H, J=5.6, 10.0 and 16.4, H-4b), 4.61 (dd, 1H, J=3.2 and 9.2, H-2), 4.68 (br s, 1H, NH), 7.19 (d, 1H, J=8.4, H-5), 7.24 (d, 1H, J=8.4, H-6), 7.34 (t, 1H, J=7.2, H-4′) 7.39–7.43 (m, 4H, H-3′, H-5′, H-8 and H-9), 7.48 (d, 2H, J=7.2, H-2′ and H-6′), 7.73 (m, 1H, H-7), 7.79 (m, 1H, H-10); ^{13}C NMR: δ 26.8 (C-4), 30.7 (C-3), 56.5 (C-2), 115.1, 117.0 (C-5), 119.4 (C-7), 122.7 (C-13), 124.8, 125.0, 126.6 (C-2′ and C-6′), 127.5, 128.3 (C-10), 128.6 (C-3′ and C-5′), 133.1 (C-11), 138.9 (C-12), 144.8 (C-1′). Anal. Calcd for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found: C, 87.86; H, 6.57; N, 5.44.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.05.090.

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