

Synthesis of Alkaloids of *Galipea officinalis* by Alkylation of an α -Amino Nitrile

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Keywords: Alkaloids / Alkylation / Tetrahydroquinolines / α -Amino nitriles / Umpolung

A new synthetic approach directed towards the synthesis of naturally occurring 2-alkyl-tetrahydroquinolines is described. The C–C bonds in the α position relative to the nitrogen atom were formed by the reversal of the polarity of the C=N bond of α -amino nitrile **6**, which was prepared electrochemically from 1-(phenylethyl)-tetrahydroquinoline. A NaBH₄-mediated reductive decyanation process furnished benzylic amines **16a–d** as mixtures of diastereomers (50–

60 % de). The catalytic hydrogenolysis of these amines was performed in the presence of Pearlman's catalyst to give the tetrahydroquinolines **17a–d** in yields ranging from 70 % to 95 %. Methylation of the free nitrogen atom afforded the title compounds **1–4** in 70–90 % yields.

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Introduction

N-Methyl-2-propyl-tetrahydroquinoline (**1**), angustureine (**2**), cuspareine (**3**) and galipinine (**4**) are tetrahydroquinoline alkaloids isolated by Jacquemont-Collet from the bark of *Galipea officinalis* Hancock (Figure 1).^[1] This shrub is indigenous to the mountains of Venezuela and belongs to the genus *Galipea* Aublet, which consists of approximately 20 species that are found in northern South America. Preparations from *Galipea officinalis* have been used in folk medicine for the treatment of various disorders such as dysentery and fever.^[2] More recently, ethanolic extracts of the trunk bark of *Galipea officinalis* have shown antiplasmodial and cytotoxic activities that might further contribute to the efficacy of the folklore preparations.^[3]

These promising biological activities have incited chemists to elaborate new approaches directed towards the synthesis of tetrahydroquinolines **1–4**. Key steps in these previous methodologies have included enantioselective hydrogenation of quinolines,^[4] ring-closing metathesis,^[5] hydroamination of anilino-alkynes,^[6] Petasis-type condensa-

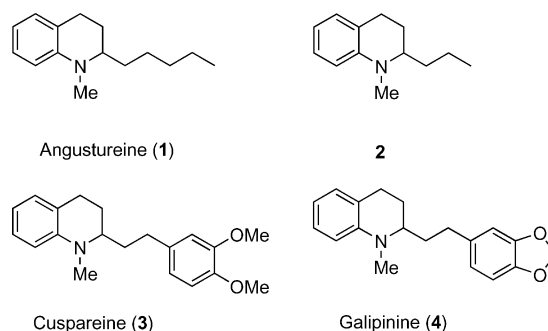


Figure 1. Structures of 2-substituted tetrahydroquinolines isolated from *Galipea officinalis*.

tion,^[7] CuI-catalysed coupling of iodobenzene with homo-chiral β -aminoesters^[8] and aza-xylylene Diels–Alder cycloaddition.^[9]

In the light of our previous experience in heterocyclic chemistry,^[10] and more particularly with nitrogen-based compounds, we envisaged a new route to tetrahydroquinolines **1–4**.^[11] To this end, the use of an α -amino nitrile seemed to us a promising possibility. These bifunctional derivatives have been shown to be interesting synthetic intermediates in the elaboration of numerous alkaloids through the use of the reversible Umpolung of the reactivity of the C=N bond.^[12] In other words, when the α -amino nitrile bears an α -hydrogen, it is possible to deprotonate it with a strong base to yield a nitrile-stabilised carbanion, which can then be condensed with a range of electrophiles.^[13] Our retrosynthetic plan is delineated in Scheme 1 and calls for the α -amino nitrile **6** to be elaborated. This α -amino nitrile moiety should ensure the formation of the new C–C bond, and we were also curious to investigate the influence of the

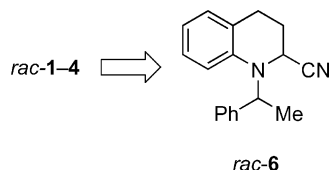
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asymmetric carbon on the stereochemical outcome of the chemical manipulations. In this study all compounds are racemic, and all the stereogenic centres are consequently represented in relative configuration.

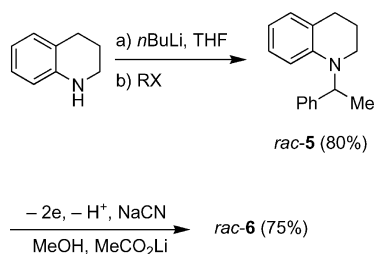


Scheme 1. Retrosynthesis of tetrahydroquinolines **1–4**.

Results and Discussion

Preparation and Alkylation of α -Amino Nitrile **6**

As outlined in Scheme 2, our synthesis began with the condensation of lithiated tetrahydroquinoline (*n*BuLi, THF) with (1-bromoethyl)benzene. The reaction was carried out at a temperature between $-80\text{ }^{\circ}\text{C}$ and $-20\text{ }^{\circ}\text{C}$ for 12 h. Under these conditions, 1-(1-phenylethyl)-tetrahydroquinoline (**5**) was obtained in 80% yield.



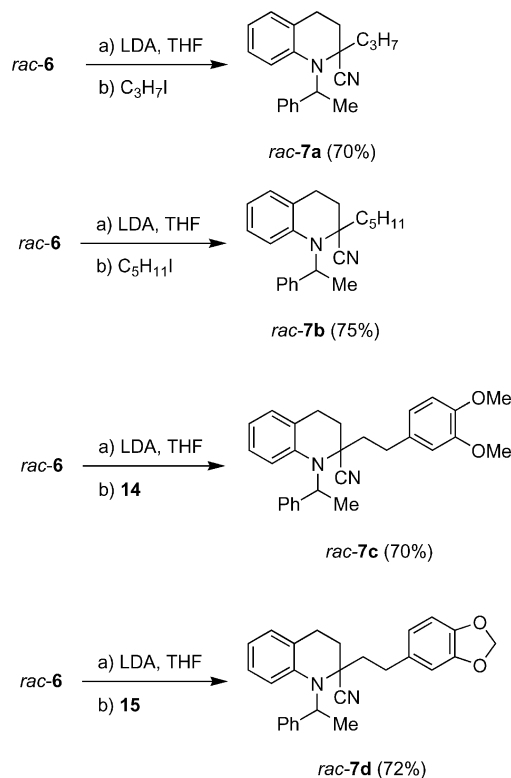
Scheme 2. Synthesis of α -amino nitrile **6**.

For the synthesis of α -amino nitrile **6**, several sets of reaction conditions were investigated. Prior to the macroscale electrolysis, an analytical study was carried out at a vitreous carbon electrode at a sweep rate of 50 mVs^{-1} . Amine **5** (20 mmol L^{-1}) was dissolved in methanol containing lithium acetate (20 g L^{-1}) as a supporting electrolyte and sodium cyanide (6 equiv. per mol of substrate) as a trapping agent. The voltammogram revealed the presence of two successive irreversible peaks at $E_{pA} = +0.95\text{ V/SCE}$ and $E_{pB} = +1.25\text{ V/SCE}$. These observations are consistent with previous results obtained in our laboratory and indicate that a selective bielectronic oxidation process could be performed at peak A. The controlled-potential oxidation of **5** was thus carried out at $+0.80\text{ V/SCE}$ on a 4 g scale in a divided cell fitted with a glassy carbon electrode as anode and a carbon rod as cathode. In our preliminary experiments, the current dropped rapidly from 150 mA to 20 mA, and electrolysis took place over a 24 h period. After the consumption of 2.2 Faradays per mol of substrate, the voltammogram showed the disappearance of the first oxidation peak at $+0.95\text{ V/SCE}$. Classical workup and chromatographic purification over a silica column afforded the α -amino nitrile **6** in 45%

yield and as a separable mixture (60:40) of diastereomers. We noticed the formation of intractable tars and passivation of the working electrode through polymer formation. To overcome these drawbacks, it was felt that the lifetime of the nitrogen-centred cation radical should be reduced through the rapid loss of an α -proton.^[14] To this end, six equivalents of sodium methoxide (formed in situ by the addition of Na) were added to the electrolysis medium. Under these more basic reaction conditions, passivation of the working electrode did not occur, and the α -amino nitrile **6** was obtained in a satisfactory 75% yield.^[15]

Preparation of α -Amino Nitriles **7a–d**

The condensation of the lithiated α -amino nitrile **6** with the requisite alkyl halides is the key step in our synthetic approach, as a new C–C bond is formed α to the nitrogen atom (Scheme 3). The lithiation procedures were carried out by dissolving α -amino nitrile **6** in THF at $-78\text{ }^{\circ}\text{C}$, followed by the slow addition of LDA (1.5 equiv., prepared from *n*-BuLi and diisopropylamine) at the same temperature. The resulting anion solutions were allowed to warm to $-20\text{ }^{\circ}\text{C}$ over a 2 h period, and the electrophiles were added at temperatures ranging from $-70\text{ }^{\circ}\text{C}$ to $-60\text{ }^{\circ}\text{C}$. Results are collected in Table 1 and deserve further comment.



Scheme 3. Synthesis of α -amino nitriles **7a–d**.

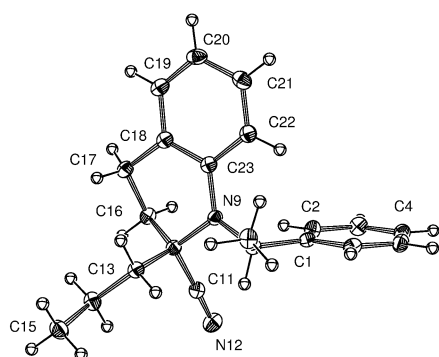
Addition of 1-iodopropane (Entry 1) at $-60\text{ }^{\circ}\text{C}$, followed by 3 h stirring at $-20\text{ }^{\circ}\text{C}$, led to the rapid formation of **7a** in a 70% isolated yield as a separable mixture (52:48) of diastereomers (Scheme 3). Upon chromatographic purifica-

Table 1. Synthesis of α -amino nitriles **7a–d**.

Entry	Electrophile	T [°C] / t [h]	Product, % yield ^[a]	% de ^[b]
1	$n\text{-C}_3\text{H}_7\text{I}$	$-60 \rightarrow -20$ / 3	7a , 70	5
2	$n\text{-C}_5\text{H}_{11}\text{I}$	$-60 \rightarrow -20$ / 3	7b , 75	10
3	12	$-60 \rightarrow -20$ / 12	7c , 35	15
4	12	$-60 \rightarrow 20$ / 24	7c , 35	15
5	14	$-60 \rightarrow -20$ / 12	7c , 70	15
6	15	$-60 \rightarrow -20$ / 12	7d , 72	5

[a] Yields are of isolated products after column chromatography through silica gel. [b] Determined by ^1H NMR spectroscopy.

tion over a silica column, the more polar diastereomer was collected as a white powder (m.p. 146–148 °C). Slow crystallisation of this powder from a biphasic system (dichloromethane/pentane) afforded a single crystal, X-ray diffraction study of which revealed a (R^* , S^*) relative configuration of the two stereogenic centres C-2 and C-2', as shown in Figure 2.

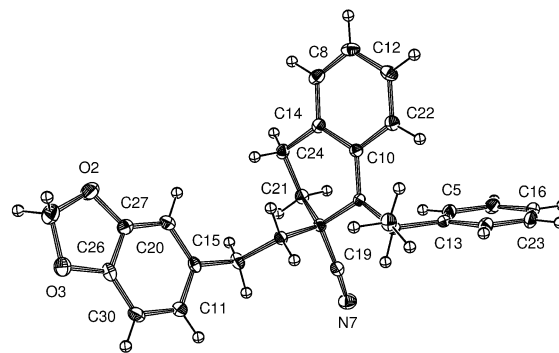
Figure 2. ORTEP drawing of α -amino nitrile (R^* , S^*)-**7a** (for details see Table 5).

Having successfully installed a propyl chain on α -amino nitrile **6**, we turned our efforts towards the synthesis of **7b**, a potential precursor of angustureine (Entry 2). The anion solution of **6** was allowed to react with 1-iodopentane at -20 °C for 12 h, providing adduct **7b** in 75% yield. The ^1H NMR spectrum of **7b** closely resembles that of **7a**, indicating that an inseparable mixture of diastereomers (55:45) was produced during the formation of **7b**.

To extend the scope of our methodology, we also decided to prepare new precursors of cuspareine (**3**) and galipinine (**4**). This involved the synthesis of alkyl halides **12–15** from the corresponding carboxylic acids as shown in Scheme 4.^[16,17]

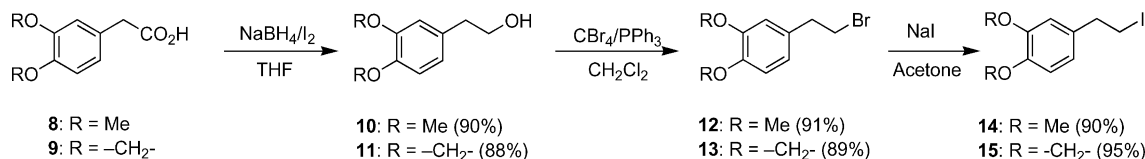
Treatment of the anion solution of **6** with bromide **12** at -60 °C (Entry 3) and continuous stirring at -20 °C for 12 h afforded the bifunctional α -amino nitrile **7c** in a modest

32% yield, along with a 20–25% yield of starting material. Prolonged stirring of the anion solution at room temperature (Entry 4) had little effect. Interestingly, close examination of the ^1H NMR spectrum of unreacted bromide **12** revealed the presence of 3,4-dimethoxy-1-vinylbenzene (35%), which showed two characteristic doublets at $\delta = 5.15$ ppm ($J = 11.0$ Hz) and 5.60 ppm ($J = 17.0$ Hz). This result indicates that an unavoidable elimination process took place between the lithiated α -amino nitrile **6** and the bromide **12**. This problem prompted us to investigate the condensation of **6** with the more reactive iodide **14** (Entry 5). The deprotonation step was carried out as above, and the reaction mixture was maintained at -20 °C overnight. Gratifyingly, the alkylation proceeded cleanly and reproducibly to yield **7c** (70%) as a mixture (57:43) of inseparable diastereomers. Likewise, the alkylation of **6** (Entry 6) with the iodide **15** afforded the adduct **7d** in a 72% yield, as a mixture (52:48) of inseparable diastereomers after column chromatography. The crude mixture was taken up in ethanol to yield a white powder that melted at 159–161 °C. We were pleased to find that spectroscopic data (^1H , ^{13}C NMR) revealed the presence of only one geometric isomer. Interestingly, single crystals could be obtained by a slow crystallisation in a biphasic system (dichloromethane/pentane). A subsequent X-ray diffraction study performed on one of these crystals revealed a (R^* , S^*) relative configuration of the two stereogenic centres C-2 and C-2' as shown in Figure 3.

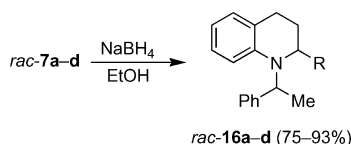
Figure 3. ORTEP drawing of α -amino nitrile (R^* , S^*)-**7d** (for details see Table 5).

Reductive Decyanation of α -Amino Nitriles **7a–d**

The reductive decyanation of α -amino nitriles consists of the neat replacement of the cyano group by a hydrogen atom (Scheme 5). The reaction proceeds through an ionic or a radical pathway according to the nature of the reducing

Scheme 4. Synthesis of alkyl halides **12–15**.

agent. In the first mode, the α -amino nitrile yields an intermediate iminium cation, which is reduced in situ by a hydride donor (NaBH_4 ,^[18] BH_3 ,^[19] $\text{AgBF}_4/\text{Zn}(\text{BH}_4)_2$ ^[20] or Dibal-H^[21]). In the second mode, the reduction proceeds by electron transfer in the presence of an alkali metal such as sodium, in a mixture of liquid ammonia and THF. An intermediary radical anion is formed and carries on to the decyanated product through the loss of CN^- .^[22] Recently, Husson reported the reductive decyanation of α -amino nitriles in the presence of Raney nickel under mild conditions.^[23] From a simple examination of these methods, it was clear that for technical convenience, NaBH_4 was the reactant of choice. Reduction of the α -amino nitrile **7a** was therefore performed in EtOH at 20 °C for 24 h in the presence of four equivalents of NaBH_4 . After treatment, amine **16a** was obtained in a low 25% yield, accompanied by unreacted starting material. In a second experiment, direct heating of **7a**, even at reflux, did not improve the yield significantly (30%). Apparently, it was difficult to obtain the intermediary iminium ion through the cleavage of the C–CN bond. This problem was solved when the α -amino nitrile **7a** was kept in solution with NaBH_4 in EtOH at 20 °C for a 12 h stirring period, with a subsequent 3 h at reflux. Under these reaction conditions, amine **16a** was obtained in a 93% isolated yield. Apparently, in this sequence, the initial step consist of the formation of a complex between the cyano group and borane. This complex favoured a “push–pull” mechanism to produce the intermediary iminium ion, which is attacked by a hydride anion. These results are in keeping with the observations of Ogura,^[19] who pointed out that both cyano groups of α,α' -dicyano amines could be removed with NaBH_4 in a moderate 47% yield. In our case, delocalisation of the nitrogen lone pair onto the aromatic ring decreases the $n\text{--}\sigma_{\text{C--CN}}^*$ interaction.^[24] The well resolved ^1H NMR spectrum of **16a** indicates the presence of a mixture (80:20) of diastereomers that could not be separated by column chromatography. When subjected to these optimised reaction conditions, α -amino nitriles **7b–d** underwent clean reduction processes to produce the expected amines **16b–d** in yields ranging between 75% and 89% (Table 2). It is worthy of note that the stereochemical out-

Scheme 5. Reductive decyanation of α -amino nitriles **7a–d**.Table 2. Reductive decyanation of α -amino nitrile **7a–d**.

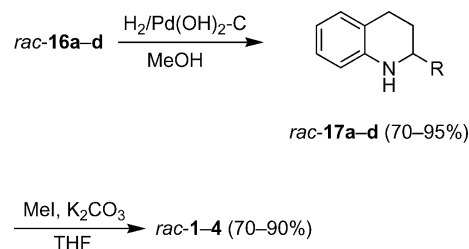
Entry	Product	% Yield ^[a]	% <i>de</i>
1	16a , R = C_3H_7	93	60 ^[b]
2	16b , R = C_5H_{11}	89	60 ^[b]
3	16c , R = 3,4-(MeO) ₂ Ph-(CH_2) ₂	75	56 ^[c]
4	16d , R = 3,4-(OCH_2O) ₂ Ph-(CH_2) ₂	78	51 ^[c]

[a] NaBH_4 (4 equiv.), EtOH, 12 h; then 3 h reflux. [b] Determined by VPC. [c] Determined by ^1H NMR spectroscopy.

comes of the reductive decyanation processes were quite insensitive to the lengths and the natures of the side chains (Table 2, Entries 1–4).

Synthesis of Tetrahydroquinoline Alkaloids 1–4

In the penultimate step, the *N*-benzyl bond in amines **16a–d** was cleaved by catalytic hydrogenolysis in the presence of $\text{Pd}(\text{OH})_2\text{--C}$ (20%) in a mixture (4:1) of methanol and ethyl acetate under hydrogen (2 atm; Scheme 6). After purification over silica, the free amines **17a–d** were obtained as colourless oils in yields ranging between 70% and 95% (Table 3).

Scheme 6. Synthesis of tetrahydroquinoline alkaloids **1–4**.Table 3. Hydrogenolysis of benzylic amines **16a–d**.

Entry	Product	% Yield ^[a]
1	17a , R = C_3H_7	70
2	17b , R = C_5H_{11}	93
3	17c , R = 3,4-(MeO) ₂ Ph-(CH_2) ₂	72
4	17d , R = 3,4-(OCH_2O) ₂ Ph-(CH_2) ₂	95

[a] 20% $\text{Pd}(\text{OH})_2\text{--C}$, H_2 (30 psi), MeOH/EtOAc (4:1), room temp. 48 h.

Methylation of the free nitrogen atom was carried out under the experimental conditions described by Nishida, by treatment of the tetrahydroquinolines **17a–d** in THF at reflux in the presence of MeI (6 equiv.) and powdered K_2CO_3 (Scheme 6).^[5] After workup, the expected tetrahydroquinolines **1–4** were obtained in yields ranging between 71% and 90% (Table 4). The high-field ^1H NMR spectra of compounds **1–4** confirm the molecular formulas, and the ^{13}C NMR spectra were consistent with the literature data.^[6,7]

Table 4. *N*-Methylation of tetrahydroquinolines **17a–d**.

Entry	Product	% Yield ^[a]
1	1	90
2	2	85
3	3	75
4	4	80

[a] MeI (6.0 equiv.), K_2CO_3 , THF, reflux, 12 h.

Conclusions

In summary, a new and reliable route to *Galipea officinalis* alkaloids from tetrahydroquinoline has been developed. In this process, the α -CH bond of the tetrahydroquinoline nucleus was activated electrochemically to produce an

α -amino nitrile. A reversal in polarity of the C=N bond ("umpolung") allows the formation of a nitrile-stabilised carbanion, which was condensed with a range of alkyl iodides. A stereoselective approach to these alkaloids based on the use of α -methylbenzylamine as a chiral auxiliary is currently under investigation in our laboratory.

Experimental Section

General: Purification by column chromatography was performed with 70–230 mesh silica gel (Merck). TLC analyses were carried out on alumina sheets precoated with silica gel (60 F254) and visualised with UV light; R_f values are given for guidance. NMR spectra were recorded with a Bruker Avance DRX 500 FT spectrometer [500 MHz (^1H) and 100 MHz (^{13}C)] or a Bruker AH 300 FT spectrometer [300 MHz (^1H) and 75 MHz (^{13}C)]. Chemical shifts are expressed in ppm downfield from TMS. Data are reported as follows: chemical shift [multiplicity (s: singlet, d: doublet, dd: double doublet, ddd: double double doublet, dm: double multiplet, dt: double triplet, t: triplet, td: triple doublet, tm: triple multiplet, tt: triple triplet, q: quartet, quint: quintuplet, m: multiplet, br: broad), coupling constants (J) in Hertz, integration]. The number of attached proton(s) in the ^{13}C NMR spectra were elucidated by use of DEPT 135 and non-decoupling mode and are described as: (p) primary, RCH_3 ; (s) secondary, R_2CH_2 ; (t) tertiary, R_3CH ; (q) quaternary, R_4C . High-resolution mass spectra were obtained with a Mat 311 double focussing instrument at the CRMPO "Centre de Mesures Physiques de l'Ouest" with a source temperature of 170 °C. An ion accelerating potential of 3 kV and ionising electrons of 70 eV were used. Elemental analyses were carried out on a Flash EA 1112 CHNS/O Thermo Electron instrument and are expressed as percentage values. Melting points were measured on a Kofler apparatus; the values are reported in °C and are uncorrected. For air-sensitive reactions, all glassware was oven-dried (120 °C) over a 24 h period and cooled under a stream of argon. All commercially available reagents were used as supplied. THF was distilled from sodium benzophenone ketyl and stored under argon. Diisopropylamine was distilled from potassium hydroxide. Air-sensitive reagents were transferred by syringe or with a double-ended needle. Yields refer to chromatographically and spectroscopically (^1H , ^{13}C) homogeneous material.

1-(1-Phenylethyl)-1,2,3,4-tetrahydroquinoline (5): *n*-BuLi (1.6 M in hexane 30.50 mL, 48.80 mmol) was added by syringe, under argon at –80 °C, to a stirred solution of 1,2,3,4-tetrahydroquinoline (5.0 g, 37.5 mmol) in THF (30 mL). The solution was allowed to warm to –20 °C and was stirred at that temperature for 3 h. The solution was cooled to –80 °C, and (1-bromoethyl)benzene (9.04 g, 6.67 mL, 48.84 mmol) was added by syringe. The mixture was allowed to warm to 20 °C over a 3 h period and was stirred at that temperature for 1 h. The reaction mixture was quenched with an excess of water, and THF was evaporated under reduced pressure. The resulting paste was taken up with water (100 mL) and was then extracted with diethyl ether (100 mL $\times$ 2). The combined organic layers were dried with MgSO_4 and concentrated in vacuo. The crude yellow oil was purified by column chromatography (diethyl ether/petroleum ether, 10:90) to afford **5** (7.12 g, 80%) as a viscous, colourless oil. R_f (diethyl ether/petroleum ether, 10:90) = 0.90. ^1H NMR (CDCl_3 , 500 MHz): δ = 1.55 (d, J = 6.9 Hz, 3 H), 1.81–1.87 (m, 2 H), 2.70–2.79 (m, 2 H), 3.00–3.03 (m, 1 H), 3.10–3.13 (m, 1 H), 5.10 (q, J = 6.9 Hz, 1 H), 6.55 (t, J = 7.3 Hz, 1 H), 6.68 (d, J = 8.3 Hz, 1 H), 6.95 (d, J = 7.4 Hz, 1 H), 7.01 (t, J = 8.5 Hz, 1 H), 7.21 (tm, J = 7.4 Hz, 1 H), 7.28–7.39 (m, 4 H) ppm. ^{13}C NMR (CDCl_3 ,

125 MHz): δ = 15.9 (p), 22.2 (s), 28.5 (s), 42.5 (s), 54.6 (t), 110.6 (t), 115.47 (t), 122.8 (q), 126.7 (t), 126.9 (t), 127.1 (t), 128.3 (t), 129.2 (t), 142.7 (q), 145.5 (q) ppm. HRMS ($\text{C}_{17}\text{H}_{19}\text{N}$, $[\text{M}]^+$): calcd. for 237.1517; found 237.1517. $\text{C}_{17}\text{H}_{19}\text{N}$ (237.34): calcd. C 86.03, H 8.07, N 5.90; found C 85.73, H 8.17, N 5.54.

Electrolysis of Tetrahydroquinoline 5: Compound **5** (1.0 g, 4.21 mmol) was dissolved in MeOH (150 mL) containing lithium acetate (1.5 g) and NaCN (1.0 g, 20.40 mmol). Sodium (0.40 g, 17.39 mmol) was then allowed to react with the resulting solution. The solution was placed in a divided electrolysis cell fitted with a planar vitreous carbon electrode (diameter: 100 mm) as anode and a carbon rod as cathode. The working potential was adjusted +0.65 vs. SCE, and after 2.2 F mol $^{-1}$ had been consumed, the solvent was evaporated under reduced pressure. The resulting paste was taken up with water (50 mL) and extracted with diethyl ether (100 mL $\times$ 2). The combined organic layers were dried with MgSO_4 and concentrated in vacuo. The residue was purified by column chromatography (diethyl ether/petroleum ether, 90:10) to afford α -amino nitrile **6** (0.83 g, 75%, orange paste) as a mixture of diastereomers (60:40), which could be separated by careful chromatography over a silica column. The (R^* , S^*) relative configuration of the major diastereomer has been determined previously by X-ray diffraction analysis.^[15]

(R^* , S^*)-1-(1-Phenylethyl)-1,2,3,4-tetrahydroquinoline-2-carbonitrile (6): Colourless plates, m.p. 96 °C (diethyl ether); R_f = 0.20 (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.75 (d, J = 7.0 Hz, 3 H), 1.84–1.95 (m, 1 H), 2.00–2.07 (m, 1 H), 2.80 (dd, J = 17.0, 5.3 Hz, 1 H), 3.17 (ddd, J = 17.0, 13.3, 6.3 Hz, 1 H), 4.06 (m, 1 H), 5.22 (q, J = 7.0 Hz, 1 H), 6.76 (td, J = 7.4, 1.0 Hz, 1 H), 6.88 (d, J = 8.3 Hz, 1 H), 7.06 (d, J = 7.4 Hz, 1 H), 7.13 (t, J = 7.8 Hz, 1 H), 7.26–7.40 (m, 5 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 14.8 (p), 24.3 (s), 25.4 (s), 42.9 (t), 55.0 (t), 112.1 (t), 118.3 (t), 120.3 (q), 121.4 (q), 127.3 (t), 127.5 (t), 127.7 (t), 128.8 (t), 128.89 (t), 140.5 (q), 142.2 (q) ppm. HRMS ($\text{C}_{18}\text{H}_{18}\text{N}_2$, $[\text{M}]^+$): calcd. for 262.1470; found 262.1469. $\text{C}_{18}\text{H}_{18}\text{N}_2$ (262.35): calcd. C 82.41, H 6.92, N 10.68; found C 82.10, H 7.10, N 10.60.

(R^* , R^*)-6: Colourless plates, m.p. 83 °C (diethyl ether/petroleum ether); R_f = 0.10 (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.62, (d, J = 6.9 Hz, 3 H), 2.02 (tt, J = 13.2, 4.7 Hz, 1 H), 2.20 (dm, J = 13.2 Hz, 1 H), 2.83 (dm, J = 16.6 Hz, 1 H), 3.16 (ddd, J = 16.6, 13.3, 5.7 Hz, 1 H), 4.37 (ddd, J = 4.4, 3.1, 1.5 Hz, 1 H), 5.13 (q, J = 6.9 Hz, 1 H), 6.73 (td, J = 7.4, 1.0 Hz, 1 H), 6.78 (d, J = 8.1 Hz, 1 H), 7.02–7.07 (m, 2 H), 7.27–7.46 (m, 5 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 16.0 (p), 24.5 (s), 25.7 (s), 46.3 (t), 57.7 (t), 114.2 (t), 118.3 (t), 119.3 (q), 122.1 (q), 127.1 (t), 127.2 (t), 127.6 (t), 128.8 (t), 129.6 (t), 140.7 (q), 141.7 (q) ppm. HRMS ($\text{C}_{18}\text{H}_{18}\text{N}_2$, $[\text{M}]^+$): calcd. for 262.1470; found 262.1469. $\text{C}_{18}\text{H}_{18}\text{N}_2$ (262.35): calcd. C 82.41, H 6.92, N 10.68; found C 82.30, H 6.95, N 10.10.

1-(1-Phenylethyl)-2-propyl-1,2,3,4-tetrahydroquinoline-2-carbonitrile (7a): α -Amino nitrile **6** (1.5 g, 5.72 mmol, mixture of diastereomers, 60:40) was dissolved in THF (20 mL), and the system was cooled to –80 °C. A THF solution (5 mL) of LDA [prepared from 1.6 M *n*BuLi in hexane (5.36 mL, 8.57 mmol) and diisopropylamine (0.98 g, 1.38 mL, 9.68 mmol)] was added by syringe at the same temperature over a 10 min period. The orange solution was stirred at –20 °C for 3 h. The reaction mixture was cooled to –80 °C, and 1-iodopropane (0.83 mL, 1.44 g, 8.51 mmol) was added dropwise. The reaction mixture was allowed to warm to –20 °C until TLC indicated the absence of starting material. Water (15 mL) was then added, and the resulting solution was extracted with diethyl ether

(50 mL $\times$ 3). The combined extracts were dried with MgSO_4 , and the solvents were removed under reduced pressure. The crude product was purified by rapid filtration through a chromatography column (diethyl ether/petroleum ether, 20:80) to afford **7a** (1.22 g, 70%) as a mixture (52:48) of diastereomers. The more polar (R^* , S^*)-**7a** could be separated from (R^* , R^*)-**7a** by careful filtration through a silica column (diethyl ether/petroleum ether, 10:90) to afford a white powder. A further slow crystallisation (72 h) of this powder from a biphasic system (dichloromethane/pentane, 1:5) afforded colourless crystals, which were analysed by X-ray diffraction.

(R^* , S^*)-7a: White powder, m.p. 146–148 °C (petroleum ether); R_f = 0.60 (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): δ = 1.02 (t, J = 7.2 Hz, 3 H), 1.48–1.63 (m, 2 H), 1.84 (d, J = 6.9 Hz, 3 H), 1.85–1.92 (m, 1 H), 2.07 (ddd, J = 16.4, 10.5, 5.8 Hz, 1 H), 2.32–2.45 (m, 2 H), 2.77–2.81 (m, 2 H), 5.15 (q, J = 6.9 Hz, 1 H), 6.26 (d, J = 8.3 Hz, 1 H), 6.57 (t, J = 7.3 Hz, 1 H), 6.75 (t, J = 8.6 Hz, 1 H), 6.95 (d, J = 7.3 Hz, 1 H), 7.20 (t, J = 6.8 Hz, 1 H), 7.31 (t, J = 7.3 Hz, 2 H), 7.41 (d, J = 8.2 Hz, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ = 14.1 (p), 17.4 (p), 18.2 (s), 23.4 (s), 30.5 (s), 38.4 (s), 56.4 (t), 62.1 (q), 116.5 (t), 117.2 (t), 121.6 (q), 122.4 (q), 126.0 (t), 126.3 (t), 126.6 (t), 128.5 (t), 128.8 (t), 140.1 (q), 141.5 (q) ppm. HRMS ($\text{C}_{21}\text{H}_{24}\text{N}_2$, $[\text{M}]^+$): calcd. for 304.1939; found 304.1946. $\text{C}_{21}\text{H}_{24}\text{N}_2$ (304.43): calcd. C 82.85, H 7.95, N 9.20; found C 82.57, H 8.00, N 9.19.

(R^* , R^*)-1-(1-Phenylethyl)-2-propyl-1,2,3,4-tetrahydroquinoline-2-carbonitrile (7a): Viscous, pale yellow oil; R_f = 0.70 (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): δ = 0.90 (t, J = 7.2 Hz, 3 H), 1.48–1.62 (m, 2 H), 1.70–1.80 (m, 1 H), 1.74 (d, J = 6.9 Hz, 3 H), 1.97–2.10 (m, 2 H), 2.48 (dt, J = 13.5, 3.7 Hz, 1 H), 2.71 (dt, J = 16.0, 3.6 Hz, 1 H), 3.11 (ddd, J = 16.0, 13.5, 3.6 Hz, 1 H), 5.03 (q, J = 6.9 Hz, 1 H), 6.36 (d, J = 7.8 Hz, 1 H), 6.66 (t, J = 7.3 Hz, 1 H), 6.81 (t, J = 8.8 Hz, 1 H), 6.97 (d, J = 7.3 Hz, 1 H), 7.24 (t, J = 6.8 Hz, 1 H), 7.34 (m, 2 H), 7.40–7.42 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 14.0 (p), 16.7 (p), 18.3 (s), 25.1 (s), 32.8 (s), 41.8 (s), 56.8 (t), 61.8 (q), 118.3 (t), 118.6 (t), 121.2 (q), 124.9 (q), 126.1 (t), 126.1 (t), 126.5 (t), 128.4 (t), 128.5 (t), 141.0 (q), 143.6 (q) ppm.

2-Pentyl-1-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline-2-carbonitrile (7b): α -Amino nitrile **6** (1.5 g, 5.72 mmol, mixture of diastereomers, 60:40) was dissolved in THF (20 mL), and the system was cooled to –80 °C. A THF solution (5 mL) of LDA [prepared from 1.6 M $n\text{BuLi}$ in hexane (5.36 mL, 8.57 mmol) and diisopropylamine (1.38 mL, 0.98 g, 9.68 mmol)] was added by syringe at the same temperature over a 10 min period. The orange solution was stirred at –20 °C for 3 h and cooled to –80 °C. 1-Iodopentane (1.12 mL, 1.69 g, 8.58 mmol) was added dropwise. The reaction mixture was allowed to warm to –20 °C until TLC indicated the absence of starting material. Water (15 mL) was then added, and the resulting solution was extracted with diethyl ether (50 mL $\times$ 3). The combined extracts were dried with MgSO_4 and the solvents were removed under reduced pressure. The crude product was purified by rapid filtration through a chromatography column (diethyl ether/petroleum ether, 20:80) to afford **7b** (1.42 g, 75%) as an inseparable mixture (55:45) of diastereomers and as a pale yellow oil. R_f (diethyl ether/petroleum ether, 10:80) = 0.70. ^1H NMR (CDCl_3 , 300 MHz): δ = 0.84 (t, J = 7.0 Hz, 3 H), 0.90 (t, J = 7.0 Hz, 3 H), 1.20–1.60 (m, 10 H), 1.74 (d, J = 7.0 Hz, 3 H), 1.83 (d, J = 7.0 Hz, 3 H), 1.70–1.90 (m, 2 H), 1.97–2.12 (m, 3 H), 2.35–2.40 (m, 2 H), 2.47 (dt, J = 13.5, 3.7 Hz, 1 H), 2.66–2.80 (m, 3 H), 3.12 (ddd, J = 16.0, 13.0, 3.5 Hz, 1 H), 5.07 (q, J = 7.0 Hz, 1 H), 5.18 (q, J = 7.0 Hz, 1 H), 6.26 (d, J = 8.0 Hz, 1 H), 6.36 (d, J = 8.0 Hz, 1 H),

6.56 (t, J = 8.0 Hz, 1 H), 6.66 (t, J = 8.0 Hz, 1 H), 6.72–7.42 (m, 14 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 13.8 (p), 13.9 (p), 16.7 (p), 18.2 (p), 22.4 (s), 23.4 (s), 23.7 (s), 24.6 (s), 25.1 (s), 30.5 (s), 31.7 (s), 31.7 (s), 32.8 (s), 36.2 (s), 39.7 (s), 56.4 (t), 56.8 (t), 61.9 (q), 62.1 (q), 116.5 (t), 117.2 (t), 118.3 (t), 118.6 (t), 121.2 (q), 121.6 (q), 122.4 (t), 124.9 (t), 126.0 (t), 126.1 (t), 126.1 (t), 126.3 (t), 126.5 (t), 126.6 (t), 126.8 (t), 128.4 (t), 128.5 (t), 140.1 (q), 141.0 (q), 142.2 (q), 143.6 (q) ppm. HRMS ($\text{C}_{23}\text{H}_{28}\text{N}_2$, $[\text{M}]^+$): calcd. for 332.2252; found 332.2251. $\text{C}_{23}\text{H}_{28}\text{N}_2$ (332.48): calcd. C 83.09, H 8.49, N 8.43; found C 83.02, H 8.47, N 8.20.

4-(2-Bromoethyl)-1,2-dimethoxybenzene (12): (3,4-Dimethoxyphenyl)acetic acid (**8**, 8.0 g, 40.77 mmol) and NaBH_4 (4.0 g, 105.74 mmol) were dissolved in THF (100 mL), and the system was cooled to 0 °C. A THF solution (15.0 mL) of iodine (10.40 g, 40.97 mmol) was added dropwise over a 1 h period. The resulting colourless solution was heated at reflux for 24 h. Methanol was added until evolution of H_2 had ceased. The clear solution was stirred at 20 °C, and the solvents were evaporated under reduced pressure. The resulting paste was taken up with aqueous NaOH (5%, 50 mL) and extracted with dichloromethane (50 mL $\times$ 3). The combined organic layers were dried with MgSO_4 and concentrated in vacuo. The crude product was purified by column chromatography (diethyl ether/petroleum ether, 80:20) to afford 2-(3,4-dimethoxyphenyl)ethanol (**10**, 6.68 g, 90%) as a colourless, viscous oil. R_f (diethyl ether/petroleum ether, 80:20) = 0.40. ^1H NMR (CDCl_3 , 500 MHz): δ = 2.25 (br. s, 1 H), 2.78 (t, J = 6.6 Hz, 2 H), 3.79 (t, J = 6.6 Hz, 2 H), 3.83 (s, 3 H), 3.85 (s, 3 H), 6.74–6.75 (m, 2 H), 6.79 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR (CDCl_3 , 125 MHz): δ = 38.7 (s), 55.8 (p), 55.9 (p), 63.6 (s), 111.3 (t), 112.2 (t), 120.9 (t), 131.1 (q), 147.5 (q), 148.9 (q) ppm. HRMS ($\text{C}_{10}\text{H}_{14}\text{O}_3$, $[\text{M}]^+$): calcd. for 182.0943; found 182.0942. $\text{C}_{10}\text{H}_{14}\text{O}_3$ (182.22): calcd. C 65.91, H 7.74; found C 66.15, H 7.82.

2-(3,4-Dimethoxyphenyl)ethanol (**10**, 2.0 g, 10.97 mmol) was dissolved in dichloromethane (25 mL) in the presence of carbon tetrabromide (4.37 g, 13.13 mmol). Triphenylphosphane (3.64 g, 13.88 mmol) was added in portions over a 30 min period, and the solution was stirred at ambient temperature over 12 h. The white precipitate was filtered off, and the resulting paste was taken up with diethyl ether (100 mL $\times$ 2). The combined organic layers were concentrated, and the excess of carbon tetrabromide was removed by vacuum sublimation (30–40 °C, 4×10^{-2} Torr). The resulting paste was purified by column chromatography (diethyl ether/petroleum ether, 90:10) to yield bromide **12** as a viscous oil (2.45 g, 91%), which solidified upon cooling. White powder; m.p. 57 °C; R_f = 0.50 (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): δ = 3.09 (t, J = 7.7 Hz, 2 H), 3.54 (t, J = 7.7 Hz, 2 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 6.72–6.74 (m, 2 H), 6.82 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): δ = 33.2 (s), 39.0 (s), 55.8 (p), 55.8 (p), 111.2 (t), 111.8 (t), 120.6 (t), 131.4 (q), 147.9 (q), 148.3 (q) ppm. HRMS ($\text{C}_{10}\text{H}_{13}\text{BrO}_2$, $[\text{M}]^+$): calcd. for 244.0099; found 244.0110. $\text{C}_{10}\text{H}_{13}\text{BrO}_2$ (245.11): calcd. C 49.00, H 5.35; found C 48.83, H 5.32.

4-(2-Iodoethyl)-1,2-dimethoxybenzene (14): Bromide **12** (1.83 g, 7.46 mmol) was dissolved in acetone (25 mL) in the presence of sodium iodide (3.38 g, 22.55 mmol). The solution was heated at reflux for 24 h, and excess sodium iodide was removed by filtration. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (diethyl ether/petroleum ether, 90:10) to yield iodide **14** (1.96 g, 90%) as a slightly yellow, viscous oil. R_f = 0.50 (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): δ = 3.10 (t, J = 7.9 Hz, 2 H), 3.32 (t, J = 7.9 Hz, 2 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 6.70–6.73 (m, 2

H), 6.81 (d, $J = 8.0$ Hz, 1 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 6.1$ (s), 39.9 (s), 55.8 (p, 2 C), 111.2 (t), 111.5 (t), 120.3 (t), 133.2 (q), 147.8 (q), 148.8 (q) ppm. HRMS ($\text{C}_{10}\text{H}_{13}\text{IO}_2$, $[\text{M}]^+$): calcd. for 291.9960; found 291.9941. $\text{C}_{10}\text{H}_{13}\text{IO}_2$ (292.11): calcd. C 41.12, H 4.49; found C 40.15, H 4.48.

5-(2-Bromoethyl)-1,3-benzodioxole (13): (3,4-Methylenedioxyphenyl)acetic acid (**9**, 4.0 g, 22.20 mmol) and NaBH_4 (2.0 g, 52.86 mmol) were dissolved in THF (100 mL), and the system was cooled to 0°C . A THF solution (15 mL) of iodine (5.60 g, 22.06 mmol) was added dropwise over a 1 h period, and the resulting colourless solution was heated at reflux for 24 h. Methanol was added until evolution of H_2 had ceased. The clear solution was stirred at 20°C , and the solvents were evaporated under reduced pressure. The resulting paste was taken up with aqueous NaOH (5%, 50 mL) and extracted with dichloromethane (50 mL $\times$ 3). The combined organic layers were dried with MgSO_4 and concentrated in vacuo. The crude material was purified by column chromatography (diethyl ether/petroleum ether, 70:30) to afford 2-(1,3-benzodioxol-5-yl)ethanol (**11**, 3.24 g, 88%) as a viscous, colourless oil. R_f (diethyl ether/petroleum ether, 70:30) = 0.50. ^1H NMR (CDCl_3 , 300 MHz): $\delta = 2.29$ (br. s, 1 H), 2.73 (t, $J = 6.6$ Hz, 2 H), 3.74 (t, $J = 6.6$ Hz, 2 H), 5.88 (s, 2 H), 6.63 (dd, $J = 7.8$, 1.5 Hz, 1 H), 6.69–6.74 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 38.8$ (s), 63.6 (s), 100.8 (s), 108.2 (t), 109.3 (t), 121.8 (t), 132.3 (q), 146.0 (q), 147.6 (q) ppm. HRMS ($\text{C}_9\text{H}_{10}\text{O}_3$, $[\text{M}]^+$): calcd. for 166.0630; found 166.0628. $\text{C}_9\text{H}_{10}\text{O}_3$ (166.17): calcd. C 65.05, H 6.07; found C 64.73, H 6.10.

2-(1,3-Benzodioxol-5-yl)ethanol (**11**, 2.0 g, 12.03 mmol) was dissolved in dichloromethane (25 mL) in the presence of carbon tetrabromide (4.80 g, 14.43 mmol). Triphenylphosphane (3.80 g, 14.48 mmol) was added in portions over a 30 min period, and the solution was stirred at ambient temperature for 12 h. The white precipitate was filtered off, and the resulting paste was taken up with diethyl ether (100 mL $\times$ 2). The combined organic layers were concentrated to afford a viscous oil, which was distilled under reduced pressure (80°C , $7.6 \cdot 10^{-2}$ Torr) to yield bromide **13** (2.48 g, 89%) as a viscous, colourless oil. R_f (diethyl ether/petroleum ether, 10:90) = 0.70. ^1H NMR (CDCl_3 , 300 MHz): $\delta = 3.05$ (t, $J = 7.6$ Hz, 2 H), 3.49 (t, $J = 7.6$ Hz, 2 H), 5.91 (s, 2 H), 6.64–6.67 (m, 2 H), 6.74 (d, $J = 7.8$ Hz, 1 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 33.2$ (s), 39.0 (s), 100.9 (s), 108.3 (t), 108.9 (t), 121.7 (t), 132.6 (q), 146.4 (q), 147.7 (q) ppm. HRMS ($\text{C}_9\text{H}_9\text{BrO}_2$, $[\text{M}]^+$): calcd. for 227.9786; found 227.9786. $\text{C}_9\text{H}_9\text{BrO}_2$ (229.07): calcd. C 47.19, H 3.96; found C 47.01, H 3.90.

5-(2-Iodoethyl)-1,3-benzodioxole (15): Bromide **13** (1.72 g, 7.50 mmol) was dissolved in acetone (25 mL) in the presence of sodium iodide (3.38 g, 22.55 mmol). The solution was heated at reflux for 24 h, and the excess of sodium iodide was removed by filtration. The solvent was evaporated under reduced pressure, and the residue was taken up with diethyl ether and concentrated. Purification by column chromatography (diethyl ether/petroleum ether, 90:10) yielded iodide **15** (1.97 g, 95%) as a slightly yellow, viscous oil. $R_f = 0.70$ (diethyl ether/petroleum ether, 10:90). ^1H NMR (CDCl_3 , 300 MHz): $\delta = 3.06$ (t, $J = 7.8$ Hz, 2 H), 3.28 (t, $J = 7.8$ Hz, 2 H), 5.93 (s, 2 H), 6.62–6.66 (m, 2 H), 6.74 (d, $J = 7.7$ Hz, 1 H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 6.10$ (s), 39.9 (s), 100.9 (s), 108.3 (t), 108.6 (t), 121.3 (t), 134.4 (q), 146.3 (q), 147.7 (q) ppm. HRMS ($\text{C}_9\text{H}_9\text{IO}_2$, $[\text{M}]^+$): calcd. for 275.9647; found 275.9654. $\text{C}_9\text{H}_9\text{IO}_2$ (276.07): calcd. C 39.16, H 3.29; found C 39.92, H 3.37.

2-[2-(3,4-Dimethoxyphenyl)ethyl]-1-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline-2-carbonitrile (7c): α -Amino nitrile **6** (1.0 g, 3.81 mmol, mixture of diastereomers, 60:40) was dissolved in THF

(20 mL), and the system was cooled to -80°C . A THF solution (5 mL) of LDA [prepared from 1.6 M $n\text{BuLi}$ in hexane (3.57 mL, 5.71 mmol) and diisopropylamine (0.90 mL, 0.64 g, 6.32 mmol)] was added by syringe at the same temperature over a 10 min period. The orange solution was allowed to warm to -20°C over 2 h and the reaction mixture was then cooled to -80°C . A THF solution (5 mL) of iodide **14** (1.66 g, 5.68 mmol) was added dropwise to the anion solution. The reaction mixture was allowed to warm to -20°C for 12 h, until TLC indicated the absence of starting material. Water (15 mL) was then added, and the resulting solution was extracted with diethyl ether (50 mL $\times$ 3). The combined extracts were dried with MgSO_4 , and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (diethyl ether/petroleum ether, 30:70) to afford **7c** (1.14 g, 70%) as a mixture (57:43) of diastereomers. $R_f = 0.20$ (diethyl ether/petroleum ether, 30:70). ^1H NMR (CDCl_3 , 500 MHz): $\delta = 1.75$ (d, $J = 6.9$ Hz, 3 H), 1.80 (d, $J = 6.9$ Hz, 3 H), 2.09–2.53 (m, 8 H), 2.69–2.87 (m, 7 H), 3.16 (ddd, $J = 16.2$, 17.2, 3.4 Hz, 1 H), 3.74 (s, 3 H), 3.79 (s, 3 H), 3.84 (s, 3 H), 3.88 (s, 3 H), 5.09 (q, $J = 6.9$ Hz, 1 H), 5.18 (q, $J = 6.9$ Hz, 1 H), 6.30 (d, $J = 8.3$ Hz, 1 H), 6.44 (d, $J = 8.2$ Hz, 1 H), 6.50 (d, $J = 2.0$ Hz, 1 H), 6.58–6.60 (m, 2 H), 6.68–6.85 (m, 7 H), 6.97–7.00 (m, 2 H), 7.19–7.24 (m, 2 H), 7.29–7.34 (m, 4 H), 7.40–7.43 (m, 4 H) ppm. ^{13}C NMR (CDCl_3 , 125 MHz): $\delta = 16.9$ (p), 18.3 (p), 23.4 (s), 25.1 (s), 30.1 (s), 30.5 (s), 30.6 (s), 32.8 (s), 38.3 (s), 41.6 (s), 55.7 (p), 55.8 (p), 55.8 (p), 56.6 (t), 57.1 (t), 61.7 (q), 62.0 (q), 111.3 (t), 111.4 (t), 111.6 (t), 116.7 (t), 117.5 (t), 118.6 (t), 118.8 (t), 120.0 (t), 120.1 (t), 121.0 (q), 121.3 (q), 122.4 (q), 124.9 (q), 126.0 (t), 126.2 (t), 126.4 (t), 126.5 (t), 126.6 (t), 128.5 (t), 128.5 (t), 128.6 (t), 128.9 (t), 132.6 (q), 139.9 (q), 141.0 (q), 141.4 (q), 143.5 (q), 147.4 (q), 147.6 (q), 148.9 (q), 149.0 (q) ppm. HRMS ($\text{C}_{28}\text{H}_{30}\text{N}_2\text{O}_2$, $[\text{M}]^+$): calcd. for 399.2210; found 399.2210 ($\text{C}_{27}\text{H}_{29}\text{NO}_2$, $[\text{M} - \text{HCN}]^+$). $\text{C}_{28}\text{H}_{30}\text{N}_2\text{O}_2$ (426.55): calcd. C 78.84, H 7.09, N 6.57; found C 78.36, H 7.07, N 6.44.

2-[2-(1,3-Benzodioxol-5-yl)ethyl]-1-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline-2-carbonitrile (7d): α -Amino nitrile **6** (1.0 g, 3.81 mmol, mixture of diastereomers, 60:40) was dissolved in THF (20 mL), and the system was cooled to -80°C . A THF solution (5 mL) of LDA [prepared from 1.6 M $n\text{BuLi}$ in hexane (3.57 mL, 5.71 mmol) and diisopropylamine (0.90 mL, 0.64 g, 6.46 mmol)] was added by syringe at that temperature over a 10 min period. The orange solution was allowed to warm to -20°C for 2 h, and the reaction mixture was cooled to -80°C . A THF solution (5 mL) of iodide **15** (1.57 g, 5.68 mmol) was added dropwise to the anion solution. The reaction mixture was allowed to warm to -20°C for 12 h, until TLC indicated the absence of starting material. Water (15 mL) was then added, and the resulting solution was extracted with diethyl ether (50 mL $\times$ 3). The combined extracts were dried with MgSO_4 , and the solvents were removed under reduced pressure. The crude product was purified by column chromatography (diethyl ether/petroleum ether, 30:70) to afford **7d** (1.12 g, 72%) as a mixture (52:48) of diastereomers. The mixture was taken up in ethanol to yield (R^* , S^*)-**7d** (0.35 g) as a white powder. A further slow crystallisation (72 h) of this powder from a biphasic system (dichloromethane/pentane, 1:5) afforded colourless crystals, which were analysed by X-ray diffraction.

Isomer (R^* , S^*)-7d: White powder, m.p. 159 – 161°C (petroleum ether); $R_f = 0.20$ (diethyl ether/petroleum ether, 20:80). ^1H NMR (CDCl_3 , 300 MHz): $\delta = 1.81$ (d, $J = 6.9$ Hz, 3 H), 2.09–2.20 (m, 1 H), 2.29–2.41 (m, 1 H), 2.44–2.53 (m, 2 H), 2.68–2.88 (m, 4 H), 5.17 (q, $J = 6.9$ Hz, 1 H), 5.92 (s, 2 H), 6.29 (d, $J = 8.3$ Hz, 1 H), 6.57–6.80 (m, 5 H), 6.98 (d, $J = 7.2$ Hz, 1 H), 7.21 (t, $J = 6.6$ Hz, 1 H), 7.32 (m, 2 H), 7.39–7.42 (m, 2 H) ppm. ^{13}C NMR (CDCl_3 ,

75 MHz): δ = 18.3 (p), 23.3 (s), 30.3 (s), 30.5 (s), 38.4 (s), 56.7 (t), 61.9 (q), 100.9 (s), 108.4 (t), 108.7 (t), 116.8 (t), 117.5 (t), 121.1 (t), 121.3 (q), 122.3 (q), 126.0 (t), 126.4 (t), 126.7 (t), 128.5 (t), 128.9 (t), 133.8 (q), 139.9 (q), 141.4 (q), 146.1 (q), 147.8 (q) ppm. HRMS ($C_{27}H_{26}N_2O_2$, $[M]^+$): calcd. for 410.1994; found 433.1870 ($C_{27}H_{26}N_2O_2Na$, $[M + Na]^+$). $C_{27}H_{26}N_2O_2$ (410.50): calcd. C 79.00, H 6.38, N 6.82; found C 78.88, H 6.42, N 6.76.

Isomer (*R,*R**)-7d:** ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 16.8 (p), 25.1 (s), 30.9 (s), 32.8 (s), 41.8 (s), 57.1 (t), 61.6 (q), 100.8 (s), 108.2 (t), 108.6 (t), 118.6 (t), 118.8 (t), 120.9 (q), 121.0 (t), 124.9 (q), 126.1 (t), 126.2 (t), 126.5 (t), 128.5 (t), 133.8 (q), 140.7 (q), 141.4 (q), 140.7 (q), 143.4 (q), 145.9 (q), 147.6 (q) ppm.

General Procedure for the Reductive Decyanation of α -Aminonitriles 7a–d: $NaBH_4$ (4 equiv.) was added in portions to an ethanolic solution (25 mL) of an α -aminonitrile 7a–d. After complete dissolution (approximately 15 min) the solution was stirred at room temperature for 12 h. The solution was then heated at reflux for 3 h until TLC indicated the absence of starting material. The solvent was removed under reduced pressure, and the crude material was taken up with ammonia solution (15%, 50 mL) and extracted with dichloromethane (50 mL $\times$ 3). The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. The crude mixtures of amines 16a–d were purified by column chromatography.

1-(1-Phenylethyl)-2-propyl-1,2,3,4-tetrahydroquinoline (16a): Colourless oil, 1.23 g, 93%. R_f = 0.80 (diethyl ether/petroleum ether, 5:95). 1H NMR ($CDCl_3$, 300 MHz): δ = 0.86 (t, J = 7.3 Hz, 3 H), 1.20–1.50 (m, 6 H), 1.64 (d, J = 7.0 Hz, 3 H), 2.54–2.60 (m, 1 H), 2.72–2.76 (m, 1 H), 3.14–3.21 (m, 1 H), 5.02 (q, J = 7.0 Hz, 1 H), 6.57 (t, J = 7.3 Hz, 1 H), 6.70 (d, J = 8.0 Hz, 1 H), 6.95–7.00 (m, 2 H), 7.17–7.31 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.2 (p), 17.8 (p), 19.2 (s), 22.8 (s), 23.1 (s), 35.2 (s), 51.3 (t), 57.5 (t), 113.9 (t), 115.6 (t), 122.4 (q), 126.6 (t), 126.7 (t), 126.8 (t), 128.2 (t), 129.4 (t), 142.7 (q), 144.6 (q) ppm. HRMS ($C_{20}H_{25}N$, $[M]^+$): calcd. for 279.1987; found 279.1984. $C_{20}H_{25}N$ (279.42): calcd. C 85.97, H 9.02, N 5.01; found C 85.64, H 9.14, N 4.82.

2-Pentyl-1-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline (16b): Colourless oil, 1.5 g, 89%. R_f = 0.90 (diethyl ether/petroleum ether, 5:95). 1H NMR ($CDCl_3$, 500 MHz): δ = 0.85 (t, J = 6.8 Hz, 3 H), 1.00–1.52 (m, 9 H), 1.64 (d, J = 7.0 Hz, 3 H), 1.65–1.68 (m, 1 H), 2.56–2.60 (m, 1 H), 2.71–2.78 (m, 1 H), 3.14–3.18 (m, 1 H), 5.03 (q, J = 7.0 Hz, 1 H), 6.57 (td, J = 7.3, 1.0 Hz, 1 H), 6.70 (d, J = 8.2 Hz, 1 H), 6.96–7.00 (m, 2 H), 7.20–7.35 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.0 (p), 17.8 (p), 22.6 (s), 22.8 (s), 23.1 (s), 25.6 (s), 31.9 (s), 32.9 (s), 51.6 (t), 57.4 (t), 113.7 (t), 115.5 (t), 122.4 (q), 126.6 (t), 126.7 (t), 126.8 (t), 128.2 (t), 129.4 (t), 142.7 (q), 144.6 (q) ppm. HRMS ($C_{22}H_{29}N$, $[M]^+$): calcd. for 307.2300; found 307.2307. $C_{22}H_{29}N$ (307.47): calcd. C 85.94, H 9.51, N 4.56; found C 85.85, H 9.43, N 4.60.

2-[2-(3,4-Dimethoxyphenyl)ethyl]-1-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline (16c): Slightly yellow oil, 0.63 g, 75%. R_f = 0.60 (diethyl ether/petroleum ether, 40:60). 1H NMR ($CDCl_3$, 300 MHz): δ = 1.25–1.44 (m, 1 H), 1.59 (d, J = 7.0 Hz, 3 H), 1.65–1.89 (m, 3 H), 2.39–2.49 (m, 1 H), 2.54–2.65 (m, 2 H), 2.70–2.86 (m, 1 H), 3.19–3.22 (m, 1 H), 3.81 (s, 3 H), 3.83 (s, 3 H), 5.01 (q, J = 7.0 Hz, 1 H), 6.57–6.72 (m, 3 H), 6.73–6.76 (m, 2 H), 6.97–7.02 (m, 2 H), 7.18–7.29 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.8 (p), 22.7 (s), 23.1 (s), 31.9 (s), 34.6 (s), 50.9 (t), 55.8 (p), 55.9 (p), 57.7 (t), 111.2 (t), 111.5 (t), 114.1 (t), 115.8 (t), 120.0 (t), 122.3 (q), 126.6 (t), 126.7 (t), 126.8 (t), 128.1 (t), 129.4 (t), 134.6 (q), 142.4 (q), 144.6 (q), 147.1 (q), 148.7 (q) ppm. HRMS ($C_{27}H_{31}NO_2$, $[M]^+$): calcd.

for 401.2355; found 401.2365. $C_{27}H_{31}NO_2$ (401.54): calcd. C 80.76, H 7.78, N 3.49; found C 81.20, H 7.80, N 3.50.

2-[2-(1,3-Benzodioxol-5-yl)ethyl]-1-(1-phenylethyl)-1,2,3,4-tetrahydroquinoline (16d): Slightly yellow oil, 0.55 g, 78%. R_f = 0.85 (diethyl ether/petroleum ether, 40:60). 1H NMR ($CDCl_3$, 300 MHz): δ = 1.25–1.40 (m, 1 H), 1.60 (d, J = 7.0 Hz, 3 H), 1.67–1.84 (m, 3 H), 2.36–2.84 (m, 4 H), 3.15–3.24 (m, 1 H), 5.01 (q, J = 7.0 Hz, 1 H), 5.87 (s, 2 H), 6.53–6.60 (m, 3 H), 6.67 (d, J = 8.0 Hz, 1 H), 6.72 (d, J = 7.0 Hz, 1 H), 6.97–7.04 (m, 2 H), 7.17–7.25 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 17.8 (p), 22.7 (s), 23.0 (s), 32.0 (s), 34.8 (s), 50.8 (t), 57.6 (t), 100.7 (s), 108.0 (t), 108.7 (t), 114.1 (t), 115.8 (t), 120.9 (t), 122.3 (q), 126.6 (t), 126.8 (t), 126.8 (t), 128.1 (t), 129.4 (t), 135.8 (q), 142.4 (q), 144.5 (q), 145.5 (q), 147.5 (q) ppm. HRMS ($C_{26}H_{27}NO_2$, $[M]^+$): calcd. for 385.2042; found 385.2049. $C_{26}H_{27}NO_2$ (385.50): calcd. C 81.01, H 7.06, N 3.63; found C 80.80, H 7.12, N 3.66.

General Procedure for the Hydrogenolysis of Tetrahydroquinolines 16a–d: Pearlman's catalyst [20% $Pd(OH)_2 \cdot C$, 20% in weight] was placed in a low-pressure hydrogenator in the presence of tetrahydroquinolines 16a–d dissolved in a mixture (4:1) of methanol and ethyl acetate. The desired hydrogen pressure (7.35×10^2 Torr, 1 bar) was applied, and the solution was stirred for 48 h. The catalyst was removed by filtration through a Celite bed and washed with ethanol. The solvents were evaporated under reduced pressure, and the crude mixture was purified by column chromatography to yield tetrahydroquinolines 17a–d.

2-Propyl-1,2,3,4-tetrahydroquinoline (17a): Colourless oil, 0.64 g, 70%. R_f = 0.80 (diethyl ether/petroleum ether, 10:90). 1H NMR ($CDCl_3$, 500 MHz): δ = 0.94 (t, J = 7.2 Hz, 3 H), 1.37–1.47 (m, 4 H), 1.54–1.61 (m, 1 H), 1.90–1.94 (m, 1 H), 2.73 (dt, J = 16.4, 4.9 Hz, 1 H), 2.79 (ddd, J = 16.4, 11.0, 5.6 Hz, 1 H), 3.19–3.24 (m, 1 H), 3.50–3.65 (br. s, 1 H), 6.44 (d, J = 7.6 Hz, 1 H), 6.57 (td, J = 7.3, 1.1 Hz, 1 H), 6.92–6.95 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.1 (p), 18.8 (s), 26.4 (s), 28.0 (s), 38.8 (s), 51.2 (t), 114.0 (t), 116.8 (t), 121.3 (q), 126.6 (t), 129.2 (t), 144.6 (q) ppm. HRMS ($C_{12}H_{17}N$, $[M]^+$): calcd. for 175.1361; found 175.1358. $C_{12}H_{17}N$ (175.27): calcd. C 82.23, H 9.78, N 7.99; found C 82.36, H 9.82, N 7.73.

2-Pentyl-1,2,3,4-tetrahydroquinoline (17b): Colourless oil, 1.00 g, 93%. R_f = 0.80 (diethyl ether/petroleum ether, 5:95). 1H NMR ($CDCl_3$, 500 MHz): δ = 0.90 (t, J = 6.9 Hz, 3 H), 1.25–1.37 (m, 6 H), 1.44–1.47 (m, 2 H), 1.52–1.61 (m, 1 H), 1.89–1.94 (m, 1 H), 2.68 (dt, J = 16.3, 4.6 Hz, 1 H), 2.78 (ddd, J = 16.3, 11.1, 5.5 Hz, 1 H), 3.16–3.21 (m, 1 H), 3.50–3.80 (br. s, 1 H), 6.43 (d, J = 7.6 Hz, 1 H), 6.57 (td, J = 7.4, 1.1 Hz, 1 H), 6.91–6.94 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.0 (p), 22.6 (s), 25.3 (s), 26.4 (s), 28.0 (s), 31.9 (s), 36.6 (s), 51.5 (t), 114.0 (t), 116.8 (t), 121.2 (q), 126.6 (t), 129.2 (t), 144.7 (q) ppm. HRMS ($C_{14}H_{21}N$, $[M]^+$): calcd. for 203.1674; found 203.1670. $C_{14}H_{21}N$ (203.32): calcd. C 82.70, H 10.41, N 6.89; found C 82.51, H 10.30, N 6.70.

2-[2-(3,4-Dimethoxyphenyl)ethyl]-1,2,3,4-tetrahydroquinoline (17c): Slightly yellow oil, 0.63 g, 72%. R_f = 0.40 (diethyl ether/petroleum ether, 40:60). 1H NMR ($CDCl_3$, 500 MHz): δ = 1.63–1.67 (m, 1 H), 1.76–1.82 (m, 2 H), 1.95–2.00 (m, 1 H), 2.67 (t, J = 8.0 Hz, 2 H), 2.70–2.82 (m, 2 H), 3.25–3.30 (m, 1 H), 3.73 (s, 3 H), 3.40–3.70 (br. s, 1 H), 3.87 (s, 3 H), 6.34 (d, J = 7.5 Hz, 1 H), 6.59 (t, J = 7.4 Hz, 1 H), 6.71–6.74 (m, 2 H), 6.78 (d, J = 8.0 Hz, 1 H), 6.92–6.94 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 26.1 (s), 27.9 (s), 31.7 (s), 38.3 (s), 51.1 (t), 55.8 (p), 55.9 (p), 111.2 (t), 111.5 (t), 114.1 (t), 116.9 (t), 120.0 (t), 121.2 (q), 126.6 (t), 129.2 (t), 134.4 (q), 144.4 (q), 147.2 (q), 148.8 (q) ppm. HRMS ($C_{19}H_{23}NO_2$, $[M]^+$): calcd.

for 297.1729; found 297.1721. $C_{19}H_{23}NO_2$ (297.39): calcd. C 76.73, H 7.80, N 4.71; found C 77.50, H 7.97, N 4.78.

2-[2-(1,3-Benzodioxol-5-yl)ethyl]-1,2,3,4-tetrahydroquinoline (17d): Slightly yellow oil, 0.30 g, 95%. $R_f = 0.40$ (diethyl ether/petroleum ether, 10:10). 1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.55$ – 1.81 (m, 3 H), 1.93 – 2.01 (m, 1 H), 2.62 – 2.86 (m, 4 H), 3.23 – 3.31 (m, 1 H), 3.50 – 4.20 (br. s, 1 H), 5.91 (s, 2 H), 6.45 (d, $J = 8.2$ Hz, 1 H), 6.58 (t, $J = 7.3$ Hz, 1 H), 6.62 – 6.74 (m, 3 H), 6.92 – 6.97 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.2$ (s), 27.9 (s), 31.8 (s), 38.4 (s), 50.9 (t), 100.8 (s), 108.2 (t), 108.7 (t), 114.1 (t), 117.0 (t), 121.01 (t), 121.2 (q), 126.7 (t), 129.2 (t), 135.6 (q), 144.4 (q), 145.7 (q), 147.6 (q) ppm. HRMS ($C_{18}H_{19}NO_2$, $[M]^+$): calcd. for 281.1416; found 281.1435.

General Procedure for the Methylation of Tetrahydroquinolines 17a–d: Iodomethane (6 equiv.) was added to a THF (15 mL) solution of a tetrahydroquinoline **17a–d** in the presence of powdered K_2CO_3 (1 equiv.). The reaction mixture was heated at reflux for 12 h. The solvent was removed under reduced pressure, and the resulting paste was taken up with ammonia solution (10%). The aqueous layer was extracted with diethyl ether (50 mL $\times$ 3), and the combined organic layers were dried with $MgSO_4$. The solvent was removed under reduced pressure and the residues were purified by column chromatography to yield compounds **1–4**.

1-Methyl-2-propyl-1,2,3,4-tetrahydroquinoline (1): Colourless oil, 0.25 g, 90%. $R_f = 0.80$ (diethyl ether/petroleum ether, 5:95). 1H NMR ($CDCl_3$, 500 MHz): $\delta = 0.91$ (t, $J = 7.2$ Hz, 3 H), 1.23 – 1.30 (m, 1 H), 1.33 – 1.41 (m, 2 H), 1.52 – 1.58 (m, 1 H), 1.84 – 1.86 (m, 2 H), 2.62 (dt, $J = 16.2$, 4.1 Hz, 1 H), 2.74 – 2.81 (m, 1 H), 2.89 (s, 3 H), 3.19 – 3.24 (m, 1 H), 6.49 (d, $J = 8.2$ Hz, 1 H), 6.56 (td, $J = 7.3$, 1.0 Hz, 1 H), 6.94 (d, $J = 7.3$ Hz, 1 H), 7.05 (t, $J = 7.4$ Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 14.2$ (p), 19.3 (s), 23.5 (s), 24.4 (s), 33.5 (s), 37.9 (p), 58.6 (t), 110.3 (t), 115.1 (t), 121.7 (q), 127.0 (t), 128.6 (t), 145.3 (q) ppm. HRMS ($C_{13}H_{19}N$, $[M]^+$): calcd. for 189.1517; found 189.1514. $C_{13}H_{19}N$ (189.30): calcd. C 82.48, H 10.12, N 7.40; found C 82.43, H 10.22, N 7.27.

1-Methyl-2-pentyl-1,2,3,4-tetrahydroquinoline (2): Colourless oil, 0.30 g, 85%. $R_f = 0.85$ (diethyl ether/petroleum ether, 5:95). 1H NMR ($CDCl_3$, 500 MHz): $\delta = 1.00$ (t, $J = 6.9$ Hz, 3 H), 1.31 – 1.54 (m, 8 H), 1.65 – 1.72 (m, 1 H), 1.93 – 2.00 (m, 2 H), 2.74 (dt, $J = 16.2$, 4.1 Hz, 1 H), 2.86 – 2.93 (m, 1 H), 3.01 (s, 3 H), 3.29 – 3.34 (m, 1 H), 6.61 (d, $J = 8.2$ Hz, 1 H), 6.67 (td, $J = 7.3$, 1.0 Hz, 1 H), 7.06 (d, $J = 7.3$ Hz, 1 H), 7.17 (t, $J = 7.0$ Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 14.0$ (p), 22.6 (s), 23.5 (s), 24.4 (s), 25.7 (s), 31.1 (s), 32.0 (s), 37.9 (p), 58.9 (t), 110.3 (t), 115.1 (t), 121.7 (q), 127.0 (t), 128.6 (t), 145.3 (q) ppm. HRMS ($C_{15}H_{23}N$, $[M]^+$): calcd. for 217.1830; found 217.1830. $C_{15}H_{23}N$ (217.35): calcd. C 82.89, H 10.67, N 6.44; found C 82.13, H 10.48, N 6.40.

2-[2-(3,4-Dimethoxyphenyl)ethyl]-1-methyl-1,2,3,4-tetrahydroquinoline (3): Slightly yellow oil, 0.66 g, 75%. $R_f = 0.45$ (diethyl ether/petroleum ether, 40:60). 1H NMR ($CDCl_3$, 500 MHz): $\delta = 1.65$ – 1.73 (m, 1 H), 1.84 – 1.93 (m, 3 H), 2.48 (ddd, $J = 16.5$, 10.1 , 6.4 Hz, 1 H), 2.59 – 2.66 (m, 2 H), 2.81 (ddd, $J = 17.5$, 12.2 , 6.0 Hz, 1 H), 2.86 (s, 3 H), 3.21 – 3.25 (m, 1 H), 3.78 (s, 3 H), 3.81 (s, 3 H), 6.49 (d, $J = 8.1$ Hz, 1 H), 6.56 (td, $J = 7.3$, 1.0 Hz, 1 H), 6.67 – 6.69 (m, 2 H), 6.73 (d, $J = 8.3$ Hz, 1 H), 6.94 (d, $J = 7.2$ Hz, 1 H), 7.04 (t, $J = 8.3$ Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 23.5$ (s), 24.3 (s), 31.8 (s), 32.9 (s), 37.9 (p), 55.7 (p), 55.7 (p), 58.2 (t), 110.5 (t), 111.2 (t), 111.5 (t), 115.3 (t), 120.0 (t), 121.5 (q), 127.0 (t), 128.6 (t), 134.5 (q), 145.2 (q), 147.1 (q), 148.8 (q) ppm. HRMS ($C_{20}H_{25}NO_2$, $[M]^+$): calcd. for 311.1885; found 311.1906. $C_{20}H_{25}NO_2$ (311.42): calcd. C 77.14, H 8.09, N 4.50; found C 77.10, H 8.11, N 4.53.

2-[2-(1,3-Benzodioxol-5-yl)ethyl]-1-methyl-1,2,3,4-tetrahydroquinoline (4): Slightly yellow oil, 0.15 g, 80%. $R_f = 0.50$ (diethyl ether/petroleum ether, 10:90). 1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.58$ – 1.73 (m, 1 H), 1.80 – 1.95 (m, 3 H), 2.46 (ddd, $J = 16.4$, 10.0 , 6.6 Hz, 1 H), 2.56 – 2.70 (m, 2 H), 2.76 – 2.85 (m, 1 H), 2.87 (s, 3 H), 3.20 – 3.27 (m, 1 H), 5.87 (s, 2 H), 6.50 (d, $J = 8.2$ Hz, 1 H), 6.55 – 6.62 (m, 2 H), 6.66 (d, $J = 1.4$ Hz, 1 H), 6.70 (d, $J = 7.9$ Hz, 1 H), 6.95 (d, $J = 7.3$ Hz, 1 H), 7.06 (t, $J = 8.4$ Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 23.5$ (s), 24.3 (s), 31.9 (s), 33.0 (s), 38.0 (p), 58.1 (t), 100.7 (s), 108.1 (t), 108.6 (t), 110.5 (t), 115.4 (t), 120.9 (t), 121.6 (q), 127.0 (t), 128.6 (t), 135.7 (q), 145.2 (q), 145.5 (q), 147.5 (q) ppm. HRMS ($C_{19}H_{21}NO_2$, $[M]^+$): calcd. for 295.1572; found 295.1563. $C_{19}H_{21}NO_2$ (295.38): calcd. C 77.26, H 7.17, N 4.74; found C 77.10, H 7.11, N 4.63.

X-ray Crystallographic Study: Crystallographic data were collected with an APEX-II, Bruker-AXS diffractometer with use of graphite-monochromated Mo- K_α radiation. Details are given in Table 5. The structures were solved by direct methods with SIR-97,^[25] which revealed the non-hydrogen atoms of the molecules. Refinement was performed by full-matrix, least-squares techniques based on F^2 with SHELXL-97,^[26] with the aid of the WINGX^[27] program. All non-hydrogen atoms were refined with anisotropic thermal parameters. H atoms were finally included in their calculated positions. Figures were drawn with ORTEP-3 for Windows.^[28]

Table 5. X-ray crystallographic data for (R^* , S^*)-**7a** and (R^* , S^*)-**7d**.

	(R^* , S^*)- 7a	(R^* , S^*)- 7d
Formula	$C_{21}H_{24}N_2$	$C_{27}H_{26}N_2O_2$
Molecular mass	304.42	410.50
Crystal system	triclinic	triclinic
Space group	$P\bar{1}$	$P\bar{1}$
D_x [Mgm^{-3}]	1.183	1.301
a [$\text{\AA}$]	8.2420(11)	10.3357(12)
b [$\text{\AA}$]	8.5349(14)	10.4684(12)
c [$\text{\AA}$]	12.174(2)	10.9313(13)
α [$^\circ$]	89.041(6)	107.871(6)
β [$^\circ$]	86.935(5)	109.627(6)
γ [$^\circ$]	88.260(5)	91.988(7)
V [$\text{\AA}^3$]	854.7(2)	1047.7(2)
Z	2	2
$F(000)$	328	436
μ [cm^{-1}]	0.69	0.82
λ (Mo- K_α) [$\text{\AA}$]	0.71073	0.71073
T [K]	100(2)	100(2)
Crystal size [mm]	$0.60 \times 0.40 \times 0.26$	$0.63 \times 0.48 \times 0.32$
Radiation	Mo- K_α	Mo- K_α
Maximum θ [$^\circ$]	27.48	27.48
Range of hkl	$-10 \rightarrow 6$, $-11 \rightarrow 11$, $-15 \rightarrow 15$	$-13 \rightarrow 13$, $-13 \rightarrow 13$, $-14 \rightarrow 14$
Reflections measured	3880	4797
Reflections observed	3100	4143
$[I > 2.0\sigma(I)]$		
Final R_1	0.0467	0.0428
wR_2	0.1142	0.1144

CCDC-687864 [for (R^* , S^*)-**7a**] and -687865 [for (R^* , S^*)-**7d**] contain the supplementary crystallographic data. These data can be obtained from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments

J. M. is grateful to the Région Bretagne for a three-year doctoral fellowship, and F. L. is grateful to the Programme Franco-Algérien

de Formation Supérieure en France (PROFAS) for a doctoral fellowship. We are grateful for the financial support (Projet Theraquine) from the Région Bretagne.

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Received: May 27, 2008

Published Online: August 19, 2008