

New Findings on the Cerium(IV) Ammonium Nitrate Catalyzed Povarov Reaction: Stereoselective Synthesis of 4-Alkoxy-2-aryl-1,2,3,4-tetrahydroquinoline Derivatives

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Abstract: Cerium(IV) ammonium nitrate catalyzes the three-component, imino Diels–Alder (Povarov) reaction between anilines, aromatic aldehydes, and acyclic vinyl ethers, giving *cis*-4-alkoxy-2-aryl-1,2,3,4-tetrahydroquinolines with almost complete diastereoselectivity. The corresponding reaction starting from cyclic vinyl ethers gave the two possible diastereomers, with the *endo*-compound as the major product. This stereochemical outcome is explained through a stepwise mechanism for the imino Diels–Alder reaction, and this mechanism was subsequently proved by trapping the putative oxonium intermediate in the presence of ethanol.

Key words: cycloadditions, multicomponent reactions, stereoselective synthesis, Lewis acids, quinolines

Several bioactive natural products, including the well-known marine alkaloids discorhabdin¹ and martinelline² and the antiviral agent virantmycin,³ contain a 1,2,3,4-tetrahydroquinoline structural fragment. Many other, simpler tetrahydroquinoline derivatives, including oxamniquine, a schistosomicide, and L-689,560, a very potent NMDA antagonist (Figure 1), exhibit a variety of other relevant pharmacological properties.⁴ Tetrahydroquinolines are also useful starting materials for the preparation of quinolines, which have a great pharmacological relevance as well.⁵

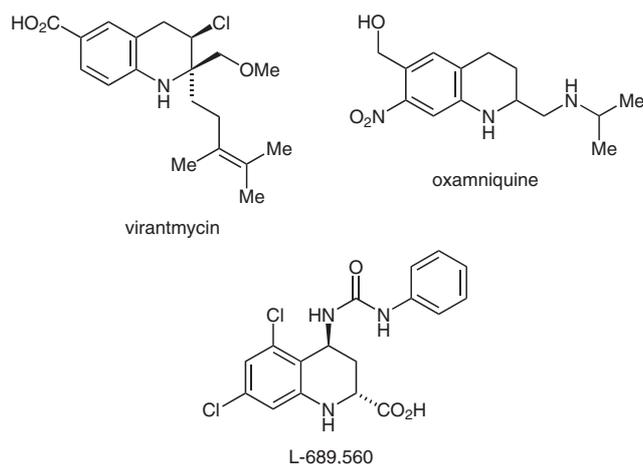


Figure 1 Some bioactive natural products and drugs containing 1,2,3,4-tetrahydroquinoline substructures

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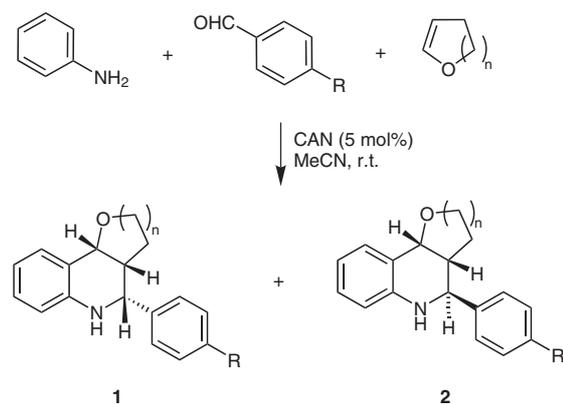
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One of the most direct methods allowing the synthesis of 1,2,3,4-tetrahydroquinolines is the Povarov reaction, an imino Diels–Alder reaction⁶ between aromatic imines and electron-rich alkenes that are normally vinyl ethers. Although this reaction was first described about 40 years ago,⁷ it received relatively little attention until the discovery of its efficient catalysis by lanthanide trifluoromethanesulfonates⁸ or chlorides⁹ acting as Lewis acids. The high cost of these catalysts and their sensitivity to moisture has prompted the study of the effects of a number of alternative catalysts, including lithium tetrafluoroborate,¹⁰ triphenylphosphonium perchlorate,¹¹ potassium hydrogen sulfate,¹² iodine,¹³ and zirconium(IV) chloride,¹⁴ on the Povarov reaction. In spite of the findings from these studies, there is still a need to identify catalysts for the Povarov reaction that are stable, easily handled, inexpensive, and commercially available. Cerium(IV) derivatives, and cerium(IV) ammonium nitrate (CAN) in particular, meet these requirements. Although CAN is normally employed as a one-electron stoichiometric oxidant in processes such as oxidative demethylation, its use in carbon–carbon and carbon–heteroatom bond-forming reactions has attracted much attention over the last decade.¹⁵ These studies are still in their early stages and, as stated in a 2003 review on the subject,^{15c} the current main goal in this area is the development of the use of CAN as a catalyst in organic synthesis.¹⁶

Although the reaction between in situ generated imines and cyclic vinyl ethers using CAN as a catalyst has been reported in a preliminary communication,¹⁷ an intriguing discrepancy existed between the stereochemistry described for the major product of this reaction and the results obtained for the Povarov reaction using other catalysts.^{9–14} In addition, some key aspects of this transformation have remained unexplored, including the possibility of employing noncyclic vinyl ethers. Such ethers are less reactive than their cyclic counterparts, but their use would expand the scope of the reaction to include the synthesis of nonfused tetrahydroquinoline systems. The considerations summarized above prompted us to study these aspects of the CAN-catalyzed Povarov reaction.

Our first experiment re-examined the three-component reaction between anilines, aromatic aldehydes, and cyclic vinyl ethers in the presence of 5 mol% of CAN. As shown in Scheme 1 and Table 1, in our hands the reaction gave almost equimolar amounts of diastereomers **1** and **2**, but

compounds **2** were the major products, in contrast with the previous report. The use of a larger amount of catalyst (25 mol%), as previously described,¹⁷ did not lead to appreciable changes in the diastereomeric ratio.



Scheme 1

Table 1 Re-examination of the Stereochemical Outcome of Cerium(IV) Ammonium Nitrate Catalyzed Povarov Reactions of Cyclic Vinyl Ethers

Products 1 and 2	R	n	Time (min)	Yield (%)	Ratio (1/2)
a	H	1	30	93	46:54
b	Cl	1	30	92	43:57
c	H	2	90	81	42:58

The stereochemical assignment of compounds **1** and **2** was made using the coupling constants of the H-4a and H-5 protons, and was confirmed by nuclear Overhauser effect spectroscopy experiments (e.g., see Figure 2 for compounds **1c** and **2c**). The results are consistent with the coupling constant values described by previous authors that confirmed their assignment using X-ray diffraction.⁹

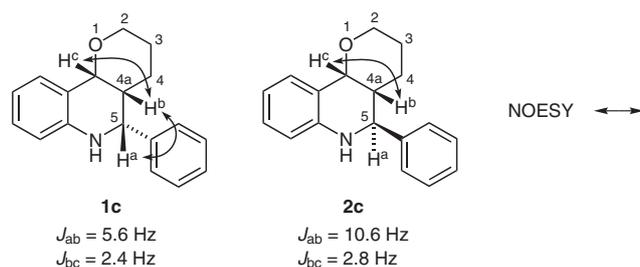
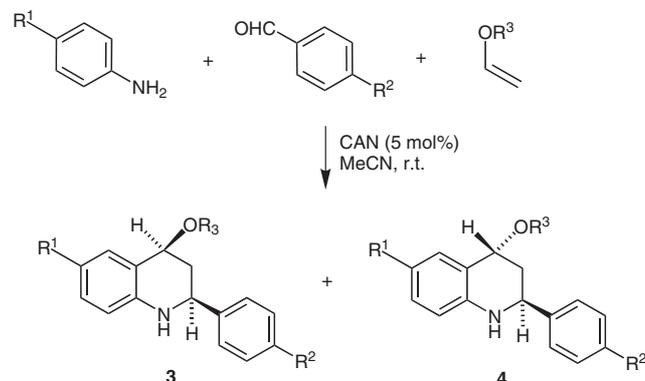


Figure 2

Although Povarov reactions involving acyclic vinyl ethers would provide ready access to nonfused 1,2,3,4-tetrahydroquinoline systems, which are of great chemical and biological relevance,¹⁸ such reactions have received very little attention in the literature, probably because of the lower reactivity of these alkenes compared with their

cyclic counterparts. This prompted us to examine the influence of CAN on these reactions. Our results, summarized in Scheme 2 and Table 2, show that the reactions proceed with almost complete diastereoselectivity to give the *cis*-tetrahydroquinoline derivatives **3** in good yields as the only isolated products.¹⁹

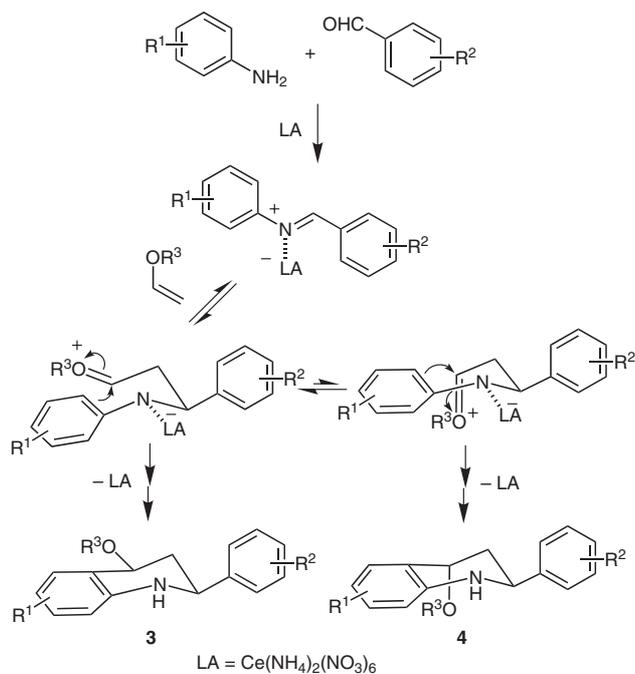


Scheme 2

Table 2 Diastereoselective Cerium(IV) Ammonium Nitrate Catalyzed Povarov Reactions of Alkyl Vinyl Ethers

Product 3	R ¹	R ²	R ³	Time (min)	Ratio (3/4)	Yield (%) of 3
a	H	H	Et	45	92:8	72
b	F	H	Et	45	97:3	70
c	OMe	H	Et	45	95:5	67
d	Me	H	Et	60	95:5	70
e	H	Me	Et	60	97:3	74
f	H	H	Bu	45	96:4	70
g	F	H	Bu	45	96:4	76
h	Me	H	Bu	60	95:5	74
i	H	Cl	Bu	60	97:3	77
j	Cl	H	Bu	60	96:4	71

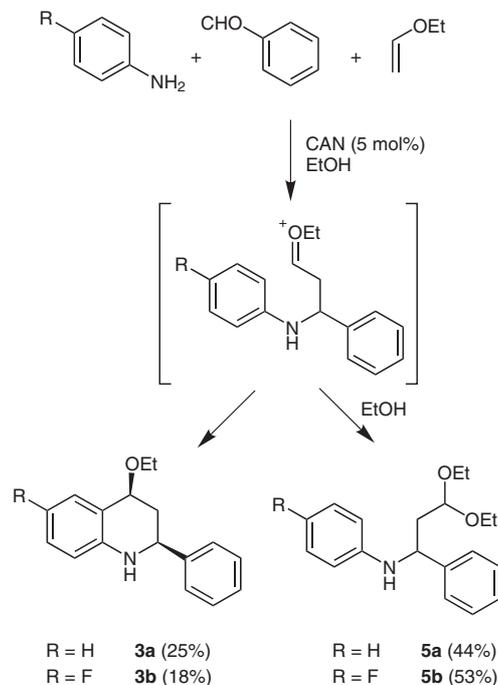
The *cis* diastereoselectivity can be explained by assuming that the reaction takes place through the three-step mechanism summarized in Scheme 3. This involves the initial formation of an imine from the starting aniline and aldehyde, followed by the addition of the vinyl ether to give an oxonium derivative. Finally, this intermediate undergoes intramolecular aromatic electrophilic substitution to give the observed products. A *cis* arrangement between the alkoxy and aryl groups leads to minimum interactions between these bulky substituents and the axial protons in the corresponding chair-like transition state of the cyclization step, which explains the observed preference for the formation of the *cis*-tetrahydroquinoline derivatives **3**.



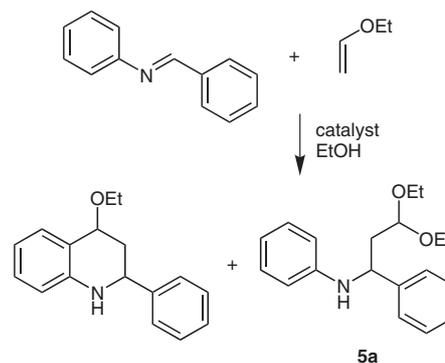
Scheme 3

To confirm this explanation, it was relevant to study whether our imino Diels–Alder reaction took place in a concerted or stepwise manner. Although the mechanism of the Povarov reaction is normally accepted to be stepwise,⁸ there is also evidence of concerted pathways in some cases.²⁰ For this reason, we wished to verify the generation of the putative intermediate oxonium species in the above-mentioned stepwise mechanism. In agreement with this hypothesis, when the reaction leading to compounds **3a** and **3b** was carried out in ethanol as a nucleophilic solvent, the major products were not the tetrahydroquinolines, but acetals **5** arising from a four-component process involving the trapping of the oxonium intermediate by a solvent molecule (Scheme 4). The accompanying tetrahydroquinoline derivatives **3a** and **3b** stem from the cyclization of the oxonium intermediate and not from the Lewis acid catalyzed cyclization of compounds **5**. This is shown by the fact that isolated acetal **5a** did not give **3a** under our reaction conditions, but remained unchanged instead.

At this point, we considered it to be of interest to verify experimentally the presence of the oxonium intermediate for those cases where other catalysts have been shown to be effective in promoting the Povarov reaction. To this end, we examined the reaction between isolated *N*-benzylideneaniline and ethyl vinyl ether in the presence of iodine, potassium hydrogen sulfate, triphenylphosphonium perchlorate, and ytterbium and dysprosium trifluoromethanesulfonate²¹ in ethanol. As shown in Scheme 5 and Table 3, compound **5a** was isolated in all cases, confirming the presence of the oxonium species postulated as an intermediate in Scheme 4.



Scheme 4



Scheme 5

Table 3 Povarov Reactions in Ethanol Using Five Alternative Catalysts

Entry	Catalyst	Quantity (mol%)	Time (h)	Yield (%) of the Povarov product	Yield (%) of 5a
1	I ₂	30	2	53	42
2	KHSO ₄	40	1	60	30
3	Ph ₃ P·HClO ₄	40	0.5	58	18
4	Yb(OTf) ₃	10	2	53	39
5	Dy(OTf) ₃	10	2	66	26

In conclusion, we have shown that CAN is an excellent catalyst for the synthesis of *cis*-2,4-disubstituted derivatives of the 1,2,3,4-tetrahydroquinoline system. A mechanistic study involving the trapping of the intermediate oxonium species has shown that the CAN-catalyzed reaction proceeds in a stepwise manner. This study also ex-

plains the observed diastereoselectivity relating to minimum interactions between the substituents in the 2- and 4-positions and the axial protons in the chair-like transition state of the cyclization step.

All reagents (Aldrich, Fluka, SDS, Probus) and solvents (SDS) were of commercial quality and were used as received. Reactions were monitored by TLC on aluminum plates coated with silica gel with fluorescent indicator (SDS CCM221254). Separations by flash chromatography were performed on silica gel (SDS 60 ACC 40–63 μm). Melting points were measured on a Reichert 723 hot stage microscope and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrophotometer with all compounds examined as thin films on NaCl disks. NMR spectra were obtained on a Bruker Avance 250 spectrometer operating at 250 and 63 MHz for ^1H and ^{13}C NMR spectra, respectively (CAI de Resonancia Magnética Nuclear, Universidad Complutense) with the signal of the residual non-deuterated solvent as an internal standard. Elemental analyses were determined by the CAI de Microanálisis Elemental, Universidad Complutense, using a Leco 932 CHNS combustion microanalyzer.

4-Alkoxy-2-aryl-1,2,3,4-tetrahydroquinolines 3a–j; General Procedure

To a stirred solution of the arylamine (2 mmol) and aromatic aldehyde (2 mmol) in MeCN (15 mL) were added the alkyl vinyl ether (3 mmol) and CAN (55 mg, 0.1 mmol). The mixture was stirred at r.t. for the corresponding time specified in Table 2. After completion of the reaction, as indicated by TLC, the mixture was extracted with CH_2Cl_2 (2×20 mL), and the extracts were washed with H_2O and brine and then dried (anhyd Na_2SO_4). The solvent was removed in vacuo to afford the crude product, which was purified by column chromatography (silica gel, petroleum ether–EtOAc, 95:5). Small amounts (3–8%) of the *trans*-products 4a–j were observed in the ^1H NMR spectra of the crude product mixtures (see Table 2); however, in spite of repeated attempts, they could not be isolated in pure form with the exception of compound 4a.

(\pm)-*cis*-4-Ethoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (3a)

Yield: 364 mg (72%); viscous liquid.

IR (neat, NaCl): 3375.9, 3028.4, 2864.6, 1609.2, 1482.1, 1311.3, 1094.6 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.34 (t, J = 6.9 Hz, 3 H), 2.07–2.20 (m, 1 H), 2.48 (ddd, J = 12.3, 5.6, 2.6 Hz, 1 H), 3.57–3.79 (m, 2 H), 3.99 (br s, 1 H), 4.58 (dd, J = 11.6, 2.6 Hz, 1 H), 4.88 (dd, J = 10.5, 5.6 Hz, 1 H), 6.57 (dd, J = 8.0, 0.9 Hz, 1 H), 6.79 (td, J = 7.5, 1.0 Hz, 1 H), 7.11 (td, J = 7.5, 1.0 Hz, 1 H), 7.33–7.55 (m, 6 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 16.1, 37.5, 56.4, 63.9, 74.4, 114.5, 118.3, 123.0, 127.1, 127.7, 128.3, 128.7, 129.2, 144.1, 145.1.

Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{NO}$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.42; H, 7.32; N, 5.64.

(\pm)-*trans*-4-Ethoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (4a)

Yield: 25 mg (5%); viscous liquid.

IR (neat, NaCl): 3387.9, 3029.1, 2972.1, 2864.9, 1610.2, 1488.4, 1316.0, 1264.0, 1081.8 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.31 (t, J = 7.0 Hz, 3 H), 1.93 (ddd, J = 13.4, 12.4, 3.1 Hz, 1 H), 2.32 (dt, J = 13.6, 2.8 Hz, 1 H), 3.62–3.75 (m, 2 H), 4.22 (br s, 1 H), 4.39 (t, J = 2.9 Hz, 1 H), 4.65 (dd, J = 12.2, 2.8 Hz, 1 H), 6.63 (d, J = 8.1 Hz, 1 H), 6.74 (td, J = 7.5, 0.7 Hz, 1 H), 7.16 (td, J = 7.5, 1.2 Hz, 1 H), 7.23 (dd, J = 7.5, 1.2 Hz, 1 H), 7.35–7.54 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 16.2, 36.7, 52.1, 63.7, 73.2, 115.1, 117.2, 120.1, 127.4, 128.1, 129.0, 129.7, 131.4, 144.5, 145.2.

Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{NO}$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.31; H, 7.28; N, 5.21.

(\pm)-*cis*-4-Ethoxy-6-fluoro-2-phenyl-1,2,3,4-tetrahydroquinoline (3b)

Yield: 379 mg (70%); viscous liquid.

IR (neat, NaCl): 3375.5, 3031.4, 2867.3, 1603.3, 1498.2, 1305.8, 1252.4, 1094.4 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.32 (t, J = 7.0 Hz, 3 H), 2.00–2.14 (m, 1 H), 2.46 (ddd, J = 12.1, 5.6, 2.3 Hz, 1 H), 3.58–3.79 (m, 2 H), 3.89 (br s, 1 H), 4.53 (dd, J = 11.8, 2.3 Hz, 1 H), 4.82 (dd, J = 10.7, 5.8 Hz, 1 H), 6.48 (dd, J = 8.7, 4.7 Hz, 1 H), 6.82 (td, J = 8.6, 2.9 Hz, 1 H), 7.19 (dd, J = 9.6, 2.9 Hz, 1 H), 7.33–7.50 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 16.1, 37.3, 56.5, 64.2, 74.3, 114.0 (d, J = 22.9 Hz), 115.2 (d, J = 1.3 Hz), 115.5 (d, J = 13.9 Hz), 124.4 (d, J = 6.4 Hz), 127.1, 128.4, 129.2, 141.2 (d, J = 1.8 Hz), 143.8, 156.5 (d, J = 235.0 Hz).

Anal. Calcd for $\text{C}_{17}\text{H}_{18}\text{FNO}$: C, 75.25; H, 6.69; N, 5.16. Found: C, 75.55; H, 6.62; N, 5.26.

(\pm)-*cis*-4-Ethoxy-6-methoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (3c)

Yield: 379 mg (67%); viscous liquid.

IR (neat, NaCl): 3361.3, 3028.9, 2971.0, 2864.4, 1602.1, 1503.3, 1330.6, 1252.2, 1096.3 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.32 (t, J = 7.0 Hz, 3 H), 2.03–2.18 (m, 1 H), 2.45 (ddd, J = 12.3, 5.9, 2.5 Hz, 1 H), 3.58–3.78 (m, 2 H), 3.82 (s, 3 H), 3.91 (br s, 1 H), 4.50 (dd, J = 11.7, 2.5 Hz, 1 H), 4.87 (dd, J = 10.6, 5.9 Hz, 1 H), 6.53 (d, J = 8.7 Hz, 1 H), 6.73 (dd, J = 8.7, 2.9 Hz, 1 H), 7.07 (d, J = 2.9 Hz, 1 H), 7.32–7.53 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 16.2, 37.6, 56.3, 56.7, 63.8, 74.6, 112.6, 115.3, 115.8, 124.1, 127.1, 128.2, 129.1, 139.3, 144.2, 152.8.

Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.29; H, 7.38; N, 4.95.

(\pm)-*cis*-4-Ethoxy-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (3d)

Yield: 374 mg (70%); off-white solid; mp 96–97 °C.

IR (neat, NaCl): 3375.8, 2971.8, 2866.0, 1608.5, 1480.2, 1309.7, 1094.7 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.36 (t, J = 6.9 Hz, 3 H), 2.07–2.17 (m, 1 H), 2.33 (s, 3 H), 2.49 (ddd, J = 12.4, 5.8, 2.5 Hz, 1 H), 3.62–3.79 (m, 2 H), 3.91 (br s, 1 H), 4.55 (dd, J = 11.5, 2.5 Hz, 1 H), 4.88 (dd, J = 10.4, 5.8 Hz, 1 H), 6.53 (d, J = 8.1 Hz, 1 H), 6.96 (dd, J = 8.1, 2.1 Hz, 1 H), 7.29–7.66 (m, 6 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 16.2, 21.6, 37.6, 56.1, 63.9, 74.5, 114.5, 118.2, 123.0, 127.0, 127.7, 128.7, 129.8, 137.9, 141.1, 145.2.

Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.79; H, 7.77; N, 5.33.

(\pm)-*cis*-4-Ethoxy-2-(4-tolyl)-1,2,3,4-tetrahydroquinoline (3e)

Yield: 395 mg (74%); off-white solid; mp 88–89 °C.

IR (neat, NaCl): 3363.7, 3021.6, 2971.7, 2859.4, 1618.5, 1504.5, 1301.5, 1157.9, 1096.5 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.30 (t, J = 7.0 Hz, 3 H), 2.02–2.16 (m, 1 H), 2.29 (s, 3 H), 2.45 (ddd, J = 12.2, 5.2, 2.2 Hz, 1 H), 3.57–3.77 (m, 2 H), 3.87 (br s, 1 H), 4.52 (dd, J = 11.6, 2.2 Hz, 1 H), 4.83 (dd, J = 10.0, 5.2 Hz, 1 H), 6.49 (d, J = 8.2 Hz, 1 H), 6.91 (dd, J = 8.2, 1.6 Hz, 1 H), 7.25–7.49 (m, 6 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 16.1, 21.1, 37.7, 56.5, 63.9, 74.5, 114.7, 122.9, 127.1, 127.5, 128.1, 128.2, 129.1, 129.3, 142.7, 144.2.

Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}$: C, 80.86; H, 7.92; N, 5.24. Found: C, 81.00; H, 7.52; N, 5.45.

(\pm)-*cis*-4-Butoxy-2-phenyl-1,2,3,4-tetrahydroquinoline (3f)

Yield: 393 mg (70%); viscous liquid.

IR (neat, NaCl): 3385.6, 3028.3, 2957.1, 2869.6, 1609.3, 1481.7, 1310.7, 1095.0 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.00 (t, J = 7.2 Hz, 3 H), 1.45–1.57 (m, 2 H), 1.62–1.72 (m, 2 H), 2.04–2.13 (m, 1 H), 2.44–2.51 (m, 1 H), 3.52–3.75 (m, 2 H), 3.98 (br s, 1 H), 4.58 (dd, J = 11.7, 2.5 Hz, 1 H), 4.86 (dd, J = 10.6, 5.7 Hz, 1 H), 6.57 (dd, J = 8.1, 1.0 Hz, 1 H), 6.80 (td, J = 7.5, 1.0 Hz, 1 H), 7.11 (td, J = 7.5, 1.0 Hz, 1 H), 7.34–7.53 (m, 6 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 14.5, 19.9, 32.7, 37.5, 56.4, 68.5, 74.5, 114.5, 118.2, 123.1, 127.1, 127.7, 128.3, 128.7, 129.2, 144.1, 145.0.

Anal. Calcd for $\text{C}_{19}\text{H}_{23}\text{NO}$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.39; H, 7.98; N, 5.18.

(\pm)-*cis*-4-Butoxy-6-fluoro-2-phenyl-1,2,3,4-tetrahydroquinoline (3g)

Yield: 455 mg (76%); viscous liquid.

IR (neat, NaCl): 3381.9, 3031.0, 2957.9, 2868.8, 1604.0, 1498.2, 1330.4, 1253.1, 1147.6, 1093.8 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 0.99 (t, J = 6.9 Hz, 3 H), 1.41–1.62 (m, 2 H), 1.65–1.74 (m, 2 H), 2.02–2.12 (m, 1 H), 2.43–2.51 (m, 1 H), 3.50–3.75 (m, 2 H), 3.98 (br s, 1 H), 4.53 (dd, J = 11.8, 2.3 Hz, 1 H), 4.80 (dd, J = 10.4, 5.4 Hz, 1 H), 6.48 (dd, J = 8.7, 4.7 Hz, 1 H), 6.81 (td, J = 8.7, 2.9 Hz, 1 H), 7.18 (dd, J = 9.6, 2.5 Hz, 1 H), 7.33–7.50 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 14.4, 19.9, 32.7, 37.3, 56.5, 68.7, 74.4, 114.0 (d, J = 22.9 Hz), 115.2 (d, J = 1.7 Hz), 115.4 (d, J = 13.7 Hz), 124.5 (d, J = 6.4 Hz), 127.1, 128.4, 129.2, 141.2 (d, J = 1.8 Hz), 143.9, 156.5 (d, J = 234.9 Hz).

Anal. Calcd for $\text{C}_{19}\text{H}_{22}\text{FNO}$: C, 76.22; H, 7.41; N, 4.68. Found: C, 76.24; H, 7.36; N, 4.88.

(\pm)-*cis*-4-Butoxy-6-methyl-2-phenyl-1,2,3,4-tetrahydroquinoline (3h)

Yield: 437 mg (74%); viscous liquid.

IR (neat, NaCl): 3365.8, 3025.8, 2956.5, 2864.8, 1619.0, 1505.0, 1454.0, 1301.9, 1157.9, 1096.0 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.04 (t, J = 7.2 Hz, 3 H), 1.46–1.59 (m, 2 H), 1.67–1.76 (m, 2 H), 2.05–2.19 (m, 1 H), 2.35 (s, 3 H), 2.45–2.53 (m, 1 H), 3.55–3.77 (m, 2 H), 3.89 (br s, 1 H), 4.55 (dd, J = 11.7, 2.4 Hz, 1 H), 4.86 (dd, J = 10.5, 5.7 Hz, 1 H), 6.52 (d, J = 8.0 Hz, 1 H), 6.95 (dd, J = 8.0, 1.5 Hz, 1 H), 7.31 (d, J = 1.5 Hz, 1 H), 7.38–7.55 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 14.5, 19.9, 21.2, 32.8, 37.8, 56.6, 68.5, 74.7, 114.8, 123.1, 127.1, 127.5, 128.1, 128.2, 129.2, 129.4, 142.8, 144.3.

Anal. Calcd for $\text{C}_{20}\text{H}_{25}\text{NO}$: C, 81.31; H, 8.53; N, 4.74. Found: C, 81.30; H, 8.36; N, 4.92.

(\pm)-*cis*-4-Butoxy-2-(4-chlorophenyl)-1,2,3,4-tetrahydroquinoline (3i)

Yield: 487 mg (77%); viscous liquid.

IR (neat, NaCl): 3383.8, 2956.8, 2868.0, 1609.1, 1483.3, 1310.2, 1089.1, 1013.7 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.02 (t, J = 7.3 Hz, 3 H), 1.43–1.54 (m, 2 H), 1.62–1.74 (m, 2 H), 2.01–2.14 (m, 1 H), 2.40–2.47 (m, 1 H), 3.52–3.72 (m, 2 H), 3.98 (br s, 1 H), 4.55 (dd, J = 11.3, 2.6 Hz, 1 H), 4.83 (dd, J = 10.3, 5.5 Hz, 1 H), 6.58 (dd, J = 8.0, 0.9 Hz, 1 H), 6.82 (td, J = 7.5, 0.9 Hz, 1 H), 7.13 (td, J = 7.5, 0.9 Hz, 1 H), 7.37–7.48 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 14.5, 19.9, 32.7, 37.5, 55.7, 68.6, 74.4, 114.7, 118.5, 123.1, 127.9, 128.5, 128.8, 129.3, 133.7, 142.8, 144.8.

Anal. Calcd for $\text{C}_{19}\text{H}_{22}\text{ClNO}$: C, 72.25; H, 7.02; N, 4.43. Found: C, 72.23; H, 6.86; N, 4.53.

(\pm)-*cis*-4-Butoxy-6-chloro-2-phenyl-1,2,3,4-tetrahydroquinoline (3j)

Yield: 447 mg (71%); viscous liquid.

IR (neat, NaCl): 3393.8, 3028.5, 2957.4, 2868.1, 1604.0, 1488.6, 1299.5, 1099.2 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 0.98 (t, J = 7.2 Hz, 3 H), 1.42–1.61 (m, 2 H), 1.64–1.70 (m, 2 H), 1.96–2.10 (m, 1 H), 2.43–2.49 (m, 1 H), 3.50–3.73 (m, 2 H), 3.99 (br s, 1 H), 4.54 (dd, J = 11.7, 2.5 Hz, 1 H), 4.75 (dd, J = 10.7, 5.6 Hz, 1 H), 6.46 (d, J = 8.5 Hz, 1 H), 7.02 (dd, J = 8.5, 2.4 Hz, 1 H), 7.35–7.48 (m, 6 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 14.4, 19.9, 32.7, 37.1, 56.3, 68.9, 74.2, 115.6, 122.8, 124.6, 127.0, 127.3, 127.4, 128.4, 128.5, 143.4, 143.7.

Anal. Calcd for $\text{C}_{19}\text{H}_{22}\text{ClNO}$: C, 72.25; H, 7.02; N, 4.43. Found: C, 72.30; H, 7.12; N, 4.35.

Cerium(IV) Ammonium Nitrate Catalyzed, Four-Component Reaction between Arylamines, Benzaldehyde, and Ethyl Vinyl Ether in Ethanol; General Procedure

To a stirred solution of the aniline (2 mmol) and benzaldehyde (212 mg, 2 mmol) in EtOH (15 mL) were added ethyl vinyl ether (216 mg, 3 mmol) and CAN (55 mg, 0.1 mmol). The mixture was stirred at r.t. for 1 h. After completion of the reaction, as indicated by TLC, the mixture was extracted with CH_2Cl_2 (2×20 mL), and the extracts were washed with H_2O and brine and then dried (anhyd. Na_2SO_4). The solvent was removed in vacuo to afford the crude product, which was purified by column chromatography (silica gel, petroleum ether–EtOAc, 95:5) to give compounds **3a** and **3b** together with **5a** and **5b**, respectively.

(\pm)-*N*-(3,3-Diethoxy-1-phenylpropyl)aniline (5a)

Yield: 263 mg (44%); viscous oil.

IR (neat, NaCl): 3388.5, 3024.6, 2974.4, 2872.0, 1602.4, 1507.9, 1317.7, 1120.2, 1058.9 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.29–1.37 (m, 6 H), 2.19–2.24 (m, 2 H), 3.54–3.82 (m, 4 H), 4.59 (t, J = 6.6 Hz, 1 H), 4.65 (t, J = 5.3 Hz, 1 H), 5.10 (br s, 1 H), 6.58 (dd, J = 8.5, 0.9 Hz, 2 H), 6.72 (tt, J = 7.4, 0.9 Hz, 1 H), 7.17 (t, J = 7.4 Hz, 2 H), 7.28–7.49 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): δ = 15.9, 42.8, 56.1, 61.6, 62.4, 101.9, 113.8, 117.5, 126.7, 127.5, 129.2, 129.6, 144.2, 148.0.

Anal. Calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.44; H, 8.45; N, 4.82.

(\pm)-*N*-(3,3-Diethoxy-1-phenylpropyl)-4-fluoroaniline (5b)

Yield: 336 mg (53%); viscous oil.

IR (neat, NaCl): 3386.0, 2974.8, 2880.1, 1613.6, 1510.7, 1452.3, 1221.6, 1120.2, 1058.0 cm^{-1} .

^1H NMR (250 MHz, CDCl_3): δ = 1.22–1.33 (m, 6 H), 2.14–2.20 (m, 2 H), 3.52–3.79 (m, 4 H), 4.49 (t, J = 7.2 Hz, 1 H), 4.62 (t, J = 5.4 Hz, 1 H), 4.98 (br s, 1 H), 6.46 (dd, J = 8.9, 4.4 Hz, 2 H), 6.84 (t, J = 8.7 Hz, 2 H), 7.29–7.45 (m, 5 H).

^{13}C NMR (63 MHz, CDCl_3): $\delta = 15.9, 42.7, 56.6, 61.7, 62.4, 101.9, 114.5$ (d, $J = 7.3$ Hz), 115.9 (d, $J = 22.2$ Hz), $126.7, 127.5, 129.2, 144.1, 144.4$ (d, $J = 1.7$ Hz), 156.0 (d, $J = 234.4$ Hz).

Anal. Calcd for $\text{C}_{19}\text{H}_{24}\text{FNO}_2$: C, 71.90; H, 7.62; N, 4.41. Found: C, 72.16; H, 7.65; N, 4.64.

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