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Solvent-Free Enantioselective Friedländer Condensation with Wet 1,1′-Binaphthalene-2,2′-diamine-Derived Prolinamides as Organocatalysts

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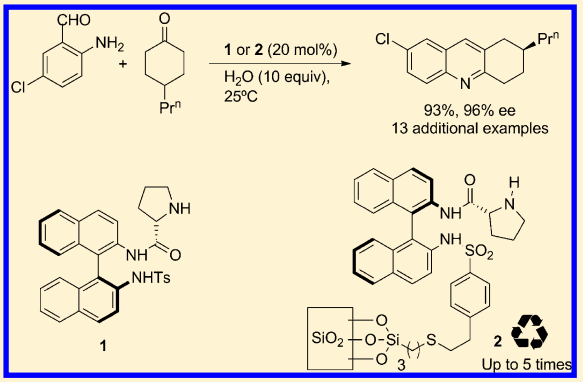
Supporting Information

ABSTRACT: Wet unsupported and supported 1,1′-binaphthalene-2,2′-diamine (BINAM) derived prolinamides are efficient organocatalysts under solvent-free conditions at room temperature to perform the synthesis of chiral tacrine analogues in good yields (up to 93%) and excellent enantioselectivies (up to 96%). The Friedländer reaction involved in this process takes place with several cyclohexanone derivatives and 2-aminoaromatic aldehydes, and it is compatible with the presence of either electron-withdrawing or electron-donating groups at the aromatic ring of the 2-aminoaryl aldehyde derivatives used as electrophiles. The reaction can be extended to cyclopentanone derivatives, affording a regioisomeric but separable mixture of products. The use of the wet silica gel supported organocatalyst, under solvent-free conditions, for this process led to the expected product (up to 87% enantiomeric excess), with its reuse being possible at least up to five times.



INTRODUCTION

The quinoline ring[1] is a very common structural motif found in a wide range of natural and synthetic products that exhibit interesting physiological and pharmaceutical properties, such as antimalarial, antiasthmatic, antihypertensive, and antibacterial activities. But most importantly, some of them have been found to be potent acetylcholinestarease inhibitors,[2] and they have been applied as drugs for the treatment of some neurodegenerative disorders such as Alzheimer's disease. In this context, tacrine ($R^1 = R^2 = H$, Figure 1),[3,4] sold under the name

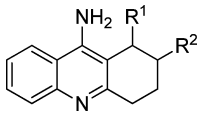


Figure 1. Tacrine and analogues.

of Cognex, was the first approved drug introduced in therapy, but its use has been limited by serious side effects such as hepatotoxicity. Tacrine showed other pharmacological activities such as the blockage of potassium channels and inhibition of the neuronal uptake of noradrenaline, dopamine, and serotonin.[5,6] Therefore, many efforts have been made for the synthesis of new tacrine anologues,[7−9] with only a few dealing with the synthesis of chiral derivatives of this type, although they showed important pharmacological activities.[10−12]

This type of analogues can be easily synthesized from their corresponding quinolines,[9] by applying the Friedländer reaction,[13,14] known 130 years ago. This reaction takes place by a base- or acid-promoted condensation of a carbonyl derivative, which contains a reactive α-methylene group with an aromatic 2-amino-substituted carbonyl compound, followed by cyclodehydration. However, use of the Friedländer synthesis for this type of compounds suffers other drawbacks such as low yields, long reaction times, hazardous and expensive catalysts, harsh reaction conditions, and tedious workup.[15] Only recently, catalytic asymmetric versions of this reaction, consisting of the condensation of 2-aminoaryl aldehydes with a carbonyl compound, were reported, using either enamine catalysis mediated by *trans*-4-hydroxyproline[16,17] or a chiral phosphoric acid derivative in combination with an achiral amine[18] as promoter, both leading to high levels of enantioselectivities. Although the organocatalyzed aldol reaction[19−25] has been deeply studied in the last 10 years, only a few reports dealing with the desymmetrization of the prochiral ketones[26−37] used as nucleophiles, which is one of the prerequisite for success of the synthesis of the chiral quinoline analogues, have been reported. Furthermore, the synthesis of the quinolines required the use of *o*-aminobenzaldehydes as electrophiles, which are less reactive than the generally activated aromatic aldehydes used in the enamine-catalyzed aldol reaction.

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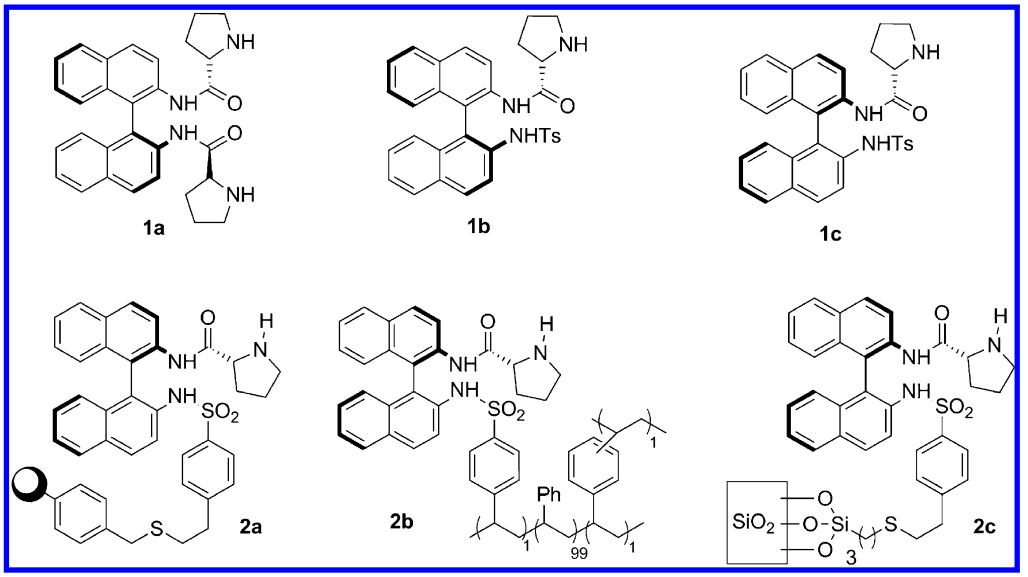

Figure 2. BINAM prolinamide derivatives used as organocatalyst under solvent-free conditions.

The use of solvents is more than 80% of the mass of any pharmaceutical batch processes,[38] making the E-factor[39] in the pharmaceutical industry bigger than in other industry segments.[40] Therefore, the implementation of solvent-free methodologies[41] for the greener[42] synthesis of drugs is essential. In this context, the use of solvent-free methodologies to carry out the synthesis of heterocyclic compounds has rapidly increased in recent years,[43] including thermal solvent-free Friedländer reactions mediated by Lewis and organic acids.[44−47] Moreover, the use of solvent-free conditions for the organocatalyzed aldol processes[48] allows the normally used excess of nucleophile, required to shift the involved equilibrium, to be reduced to a minimum amount, which increases the global efficiency of the process.[49] However, the application of solvent-free conditions to the aldol reaction generally involves the use of ball-milling procedures in order to efficiently mix the reagents.[50]

In the last 5 years, we and others have developed several 1,1′-binaphthalene-2,2′-diamine (BINAM) prolinamide[51−61] derivatives **1** (Figure 2) as organocatalysts and applied them as catalysts in intermolecular and intramolecular aldol reactions. These catalysts have been used under solvent-free conditions, providing excellent results even with only conventional magnetic stirring.[56,58,59] Moreover, supported polymer[62,63] or silica-gel[64] BINAM prolinamide systems **2** have been synthesized and showed to be recyclable and efficient catalysts.

Here, we report the use of wet BINAM prolinamide derivatives, as well as the supported systems, as catalysts for the enantioselective synthesis of chiral tacrine analogues under solvent-free conditions.

RESULTS AND DISCUSSION

First, optimization of the reaction conditions was carried out, with the reaction between 2-aminobenzaldehyde (**3**) and 4-propylcyclohexanone (**4**) used as a reaction model. Several parameters such as the nature of the catalyst, reaction medium, catalyst loading, addition of water, addition of an acid as cocatalyst, amount of nucleophile, and temperature were studied. Initially, the best catalyst to perform the process was explored in dimethyl sulfoxide (DMSO) as solvent (Table 1, entries 1−3). While the best conversion was achieved with L-proline (30 mol %; Table 1, entry 3), the highest enantioselectivity was obtained with (S_a)-BINAM-sulfo-L-Pro (**1b**, 30 mol %, entry 2). In order to increase the conversion with the last catalyst, several reaction media, including solvent-free conditions, were tested (Table 1, entries 4−8). The best performance in terms of conversion and enantioselectivities (up to 92% ee) were achieved with pure water as solvent (Table 1, entry 7) or under solvent-free conditions (Table 1, entry 8); in both cases the amount of catalyst **1b** required was reduced to 20 mol %. Then, under solvent-free conditions and with catalyst **1b**, the reaction was carried out at 0 °C to establish the influence of temperature. As expected, the conversion decreased and a slight increase of the enantioselectivity was observed (Table 1, entry 9). At 25 °C, the influence of addition of a small amount of water and benzoic acid as cocatalysts in order to increase the reaction rate was studied. When 10 equiv of water was added to the reaction, the conversion was increased up to 90% without affecting the achieved enantioselectivities (Table 1, entry 10). Therefore, the reaction can be strictly considered neither as solvent-free nor as highly concentrated,[65] and is more appropriately considered as a solvent-free reaction catalyzed by wet[66] BINAM prolinamide derivatives. The addition of 5 mol % benzoic acid in the presence of 10 equiv of water gave a further increase of the conversion but a slight detrimental effect on the enantioselectivity was observed (Table 1, entry 11). In the absence of benzoic acid as cocatalyst, the addition of 5 or 25 equiv of water to the process led to a decrease in the conversion, maintaining the enantioselectivities (Table 1, entries 12 and 13). Thus, the influence of the catalyst loading was studied in the presence of 10 equiv of water (Table 1, entries 14 and 15), observing that worse results in terms of conversion were obtained when the catalyst amount was reduced to 10 or 5 mol %. Once the optimal amount of catalyst and cocatalyst was established, the amount of ketone used was decreased to 2 equiv and under these new reaction conditions the performance of the diastereomeric catalyst **1c**, catalyst **1a**, and L-Pro were evaluated (Table 1, entries 17−19). The results for catalyst **1c** were worse than those achieved by using its diasteroisomer **1b**, showing that the latter is the match-pair catalyst for this process (Table 1, entry 17). Also, worse results were achieved by using catalyst

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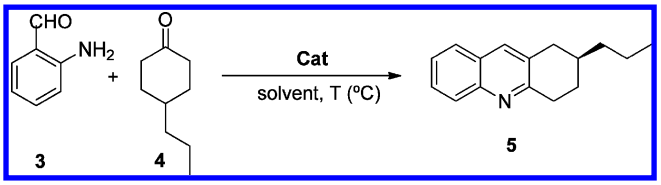
Table 1. Optimization of the Organocatalyzed Friedländer Reaction[a]



entry	solvent	cat.[b] (mol %)	T (°C)	H_2O (equiv)	t (days)	conversion[c] (%)	ee[d] (%)
1	DMSO	**1a** (30)	25		3	30	39
2	DMSO	**1b** (30)	25		3	50	85
3	DMSO	L-Pro (30)	25		3	100	71
4	THF	**1b** (30)	25		3	<20	88
5	AcOEt	**1b** (30)	25		3	<20	87
6	H_2O/DMF	**1b** (30)	25		3	<20	78
7	H_2O	**1b** (20)	25		1	66	91
8		**1b** (20)	25		1	73	92
9		**1b** (20)	0		3	33	95
10		**1b** (20)	25	10	1	90	93
11[e]		**1b** (20)	25	10	1	93	89
12		**1b** (20)	25	5	1	81	92
13		**1b** (20)	25	25	1	86	92
14		**1b** (10)	25	10	1	73	90
15		**1b** (5)	25	10	1	56	92
16[f]		**1b** (20)	25	10	1	93	93
17[f]		**1c** (20)	25	10	1	38	77
18[f]		**1a** (20)	25	10	1	60	55
19[f]		L-Pro (20)	25	10	1	0	
20[g]		**1b** (20)	25	10	3	89	92
21	**4**	**1b** (20)	25	10	1	86	89

[a]General reaction conditions: the reaction was carried out with 2-aminobenzaldehyde (0.15 mmol) and 4-propylcyclohexanone (0.45 mmol, unless otherwise stated) in 0.15 mL of solvent (unless otherwise stated). [b]Catalysis amount in parentheses. [c]Conversion based on the amount of the unreacted aldehyde. [d]Determined by chiral-phase HPLC analysis. [e]Reaction was carried out in the presence of 5 mol % benzoic acid. [f]Two equivalents of ketone **4** were used. [g]One equivalent of ketone **4** was used.

1a, bearing two proline moieties (Table 1, entry 18), and wet L-proline was shown to be ineffective as promoter for this process under solvent-free conditions (Table 1, entry 19). Finally, increasing the amount of cyclohexanone to a huge excess, acting then both as solvent and reagent, or its reduction led to slightly lower results in terms of conversions and also enantioselectivities (Table 1, entries 20 and 21). The absolute configuration of the product **5a** was determined to be *S* by comparison with the optical rotation described value.[16]

Once the optimal reaction conditions were established (Table 1, entry 16), a study of the scope of the reaction was performed (Table 2). The reaction between several 4-substituted cyclohexanones and 2-aminobenzaldehyde gave the corresponding quinoline derivatives **5** in high yields and enantioselectivities (Table 2, entries 1−4). Both aliphatic and aromatic chains in the ketone were well tolerated, with longer reaction times being required when a bulkier substituent, as in 4-*tert*-butyl- or phenyl-substituted cyclohexanones (**4b** or **4c**) were used as nucleophiles (Table 2, entries 2 and 3). Then the influence of substitution at the aromatic ring in the aldehyde was explored (Table 2, entries 5−11). The presence of either electron-withdrawing groups, such as chloro, bromo, and trifluoromethyl, or electron-donating groups, such as naphthyl or methoxy groups, at the phenyl ring led to similar results in terms of enantioselectivities. Even the use of 1-amino-2-naphthaldehyde derivative (**4i**) as electrophile gave the corresponding quinoline derivative in good yield and enantioselectivity, although longer reaction time was required for the process (Table 2, entry 9). The introduction of an additional functional group in the final quinoline system, that may enlarge the synthesis of further quinoline derivatives through a simple functional-group derivatization, was studied by performing the reaction with 4-(trimethylsilyloxy)-cyclohexanone (**4l**) and ethyl 4-oxocyclohexanecarboxylate (**4m**). In both cases, longer reaction times were required, probably due to the bulkiness of the substituents, but compounds **5l** and **5m** were achieved in good results in terms of yields and enantioselectivies (Table 2, entries 12 and 13).

This Friedländer reaction process was extended to the use of 3-substituted cyclopentanones as nucleophiles under the same reaction conditions (Scheme 1). In this case, two different regioisomers, **7** and **8** were obtained. For the methyl derivative **6a**, products **7a** and **8a** were formed in a 1:4 diastereomeric ratio, while 1:3 regioselectivity was achieved for **7b** and **8b**. The reaction was faster (6 h) compared to the reaction of the cyclohexanone derivatives, as it happens in the intermolecular aldol reaction. Both regioisomers were achieved in high enantioselectivity and were easily separated by column chromatography.

Next, the possibility of using a supported BINAM prolinamide to catalyze the reaction and the study of recovery and reuse of catalyst was evaluated, with the results summarized in Table 3. The silica-supported catalyst **2c**[59] was chosen due to its advantages and higher reactivity compared to the polymer-supported systems **2a**[57] and **2b**.[58] The catalyst loading of the silica-supported derivative **2c** was found to be 0.32 mmol/g according to its elemental analysis. Under the optimized reaction conditions used with the homogeneous catalyst **1b**, catalyst **2c** was employed to give the quinoline system **5a** after 5 days of reaction, with only slightly inferior enantioselectivities (compare entry 16 in Table 1 with entry 1 in Table 3). The catalyst can be recovered by filtration and reused up to 5 times without changes in the achieved yields and enantioselectivities. To confirm the robustness of the supported catalyst, the silica gel containing the BINAM derivative coming from the last cycle (cycle 5) was resubmitted to elemental analysis, showing 0.27 mmol/g of catalyst loading. Although some catalyst was lost during the five cycles, the activity of the catalyst-supported material remained unchanged.

In summary, wet BINAM (S_a)-prolinesulfonamide derivative **1b** and silica-supported BINAM (S_a)-prolinesulfonamide **2c** are effective catalysts for the Friedländer reaction under solvent-free conditions with only conventional magnetic stirring and 2 equiv of ketone as nucleophiles. The corresponding tacrine analogues **5** were achieved in high yields (up to 93%) and enantioselectivities (up to 96% ee), independently of the nature of the cyclohexanone and 2-amino derivatives. These results are slightly better in terms of yields and very similar in terms of enantioselectivities than those previously reported for an *O*-protected hydroxyproline derivative[16] or achieved by use of a phosphoric acid derivative[18] as organocatalysts. Additionally, the use of wet BINAM prolinamide **1b** as organocatalyst does not required the use of organic solvent or amine additive to

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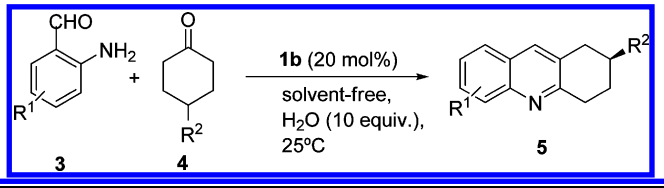
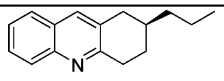
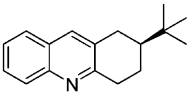
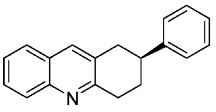
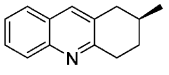
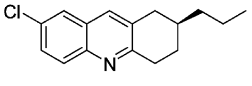
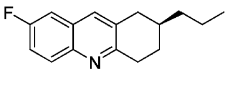
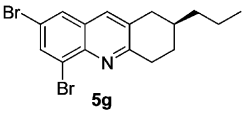
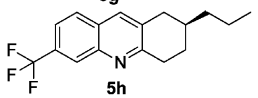
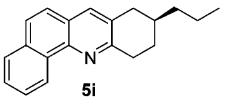
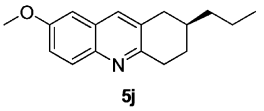
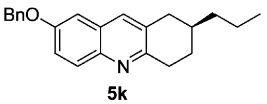
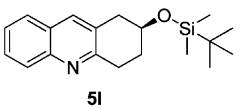
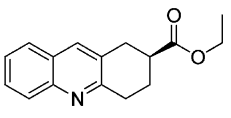
Table 2. Solvent-Free Friedländer Reaction Catalyzed by Wet 1b[a]



entry	Product	t (d)	yield (%)[b]	ee (%)[c]
1	 **5a**	1	89	93
2	 **5b**	3	85	85
3	 **5c**	3	88	89
4	 **5d**	1	89	93
5	 **5e**	1	93	96
6	 **5f**	1	90	93
7	 **5g**	1	92	83
8	 **5h**	1	91	86
9	 **5i**	3	80	82
10	 **5j**	1	83	93
11	 **5k**	1	78	92
12	 **5l**	4	75	91
13	 **5m**	2	82	85

[a]Reaction conditions: the reaction was carried out with 0.15 mmol of **3**, 0.30 mmol of **4**, 20 mol % of catalyst **1b**, and 10 equiv of water at 25 °C. [b]After purification by column chromatography. [c]Determined by chiral-phase HPLC analysis.

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Scheme 1. Solvent-Free Friedländer Reaction with 3-Substituted Cyclopentanones Catalyzed by Wet 1b

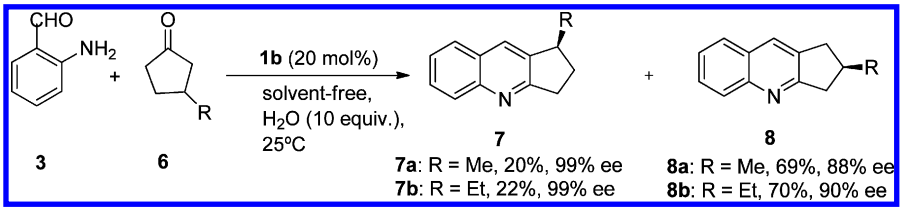
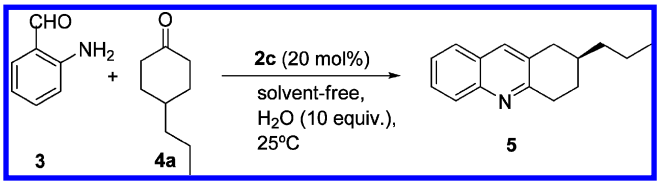


Table 3. Recycling Studies of Catalyst 2c[a]



cycle	yield[b] (%)	ee[c] (%)
1	84	87
2	85	89
3	87	87
4	82	86
5	84	88

[a]Reaction conditions: **3** (0.15 mmol), **4a** (0.3 mmol), H_2O (10 equiv) and catalyst **2c** (20 mol %). [b]After purification by column chromatography. [c]Determined by chiral-phase HPLC analysis.

perform the reaction. Furthermore, the reaction can be extended to 3-substituted cyclopentanones as nucleophiles, achieving a mixture of the two possible regioisomers. The encountered results by using the silica-supported catalyst **2c** are mostly similar to those obtained under homogeneous conditions, with the recyclability of the catalyst being possible at least up to five cycles without detrimental results. The application of these type of catalysts to other similar desymmetrization processes under solvent-free conditions is currently under study.

EXPERIMENTAL SECTION

All reactions for catalyst preparation were carried out under argon. Dry *N*,*N*-dimtheylformamide (DMF), dry toluene, dry CH_2Cl_2, dry tetrahydrofuran (THF), pyridine, and triethylamine and all others reagents were commercially available and used without further purification. Only the structurally most important peaks of the IR spectra are listed. ^{1}H NMR (300 or 400 MHz) and ^{13}C NMR (75 or 100 MHz) spectra were obtained at 25 °C with $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard, unless otherwise stated. Optical rotations were measured on a polarimeter. HPLC analyses were performed with a chiral column (detailed for each compound below), with mixtures of *n*-hexane/isopropyl alcohol as mobile phase, at 25 °C. Analytical thin-layer chromatography (TLC) was performed on silica gel plates and the spots were visualized under UV light (λ = 254 nm). For flash chromatography we employed silica gel 60 (0.063−0.2 mm). High-resolution mass spectrometry (HRMS) was carried out by electronic impact (EI) on a spectrometer of double magnetic sector. Syntheses of **1a**, **1b**, and **2c** were done as described.[53,57,61] NMR and HLPC spectra are given in the Supporting Information.

Elemental Analysis of Silica-Supported Catalyst 2c. Catalyst load: 0.32 mmol/g (calculated on the percentage of nitrogen found in the elemental analysis). Nitrogen percentage calcd for 100% incorporation, 1.52 (0.36 mmol/g); found, 1.36 (corresponds to 89.5% incorporation). Nitrogen percentage found after 5 reaction cycles: 1.16 (corresponds to 76.3% incorporation or 0.27 mmol/g loading).

General Procedure for the Friedländer Reaction. To a mixture of the corresponding 2-aminobenzaldehyde (0.15 mmol), catalyst **1b** (0.03 mmol, 16 mg), and H_2O (1.5 mmol, 27 μL) at 25 °C was added the corresponding ketone (0.3 mmol). The reaction was stirred until the 2-aminobenzaldehyde was consumed (monitored by TLC). Then, the residue was purified by flash chromatography (with 25−30 mL of hexanes/EtOAc) to yield the pure product.

General Procedure for the Friedländer Reaction with the Silica-Supported Catalyst. To a mixture of the corresponding 2-aminobenzaldehyde (0.15 mmol), catalyst **2c** (0.03 mmol, 100 mg), and H_2O (1.5 mmol, 27 μL) at 25 °C was added the corresponding ketone (0.3 mmol). The reaction was stirred until the 2-aminobenzaldehyde was consumed (monitored by TLC). Then the mixture was filtered and washed with EtOAc (10−15 mL). The solvents were removed under reduced pressure and the residue was purified by flash chromatography (with 25−30 mL of hexanes/EtOAc) to yield the pure product. After filtration, the catalyst was dried under vacuum and reused for the next reaction cycle under the same reaction conditions with the same amount of reagents and catalysts in each cycle.

*(S)-2-Propyl-1,2,3,4-tetrahydroacridine (**5a**).*[16] General procedure described above was followed to afford compound **5a** as a yellow oil in 89% (30.0 mg) yield. R_f = 0.25 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −85.3 (*c* 1.0, $CHCl_3$, 93% ee); IR 2953, 2923, 2869, 1716, 1490, 1456, 1431, 1415, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.5 Hz, 1H), 7.80 (s, 1H), 7.70 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.60 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.43 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 3.23 (ddd, *J* = 17.9, 5.7, 3.8 Hz, 1H), 3.08 (ddd, *J* = 17.5, 11.1, 6.0 Hz, 2H), 2.60 (dd, *J* = 16.5, 10.6 Hz, 1H), 2.16−2.06 (m, 1H), 1.91−1.76 (m, 1H), 1.67−1.52 (m, 1H), 1.51−1.35 (m, 4H), 0.96 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 146.6, 135.0, 130.6, 128.5, 128.2, 127.1, 126.9, 125.5, 38.4, 35.9, 33.7, 33.0, 29.3, 20.1, 14.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{19}N$ 225.1517, found 225.1492; HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH 95/05, 1.0 mL/min, 280 nm) t_R = 8.2 min (major) and t_R = 9.4 min (minor).

*(S)-2-(tert-Butyl)-1,2,3,4-tetrahydroacridine (**5b**).* General procedure described above was followed to afford compound **5b** as a yellow oil in 85% (30.7 mg) yield. R_f = 0.35 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −97.2 (*c* 1.0, $CHCl_3$, 85% ee); IR 3056, 2954, 2897, 2866, 1493, 1415, 1366, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.5 Hz, 1H), 7.76 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 3.30−3.19 (m, 1H), 3.02 (m, 2H), 2.68 (dd, *J* = 16.0, 11.2 Hz, 1H), 2.18−2.10 (m, 1H), 1.61−1.45 (m, 2H), 0.98 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 146.5, 135.1, 131.1, 128.3, 128.2, 127.0, 126.7, 125.3, 44.5, 34.3, 32.4, 30.7, 27.2, 24.5. HRMS (*m*/*z*) $[M]^+$ calcd for $C_{17}H_{21}N$ 239.1674, found 239.1671; HPLC (Chiralpak AD, *n*-hexane/*i*-PrOH 90/10, 1.0 mL/min, 280 nm) t_R = 8.7 min (minor) and t_R = 12.3 min (major).

*(S)-2-Phenyl-1,2,3,4-tetrahydroacridine (**5c**).*[16] General procedure described above was followed to afford compound **5c** as a pale yellow oil in 88% (34.0 mg) yield. R_f = 0.20 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −43.1 (*c* 1.0, $CHCl_3$, 89% ee); IR: 3021, 2954, 2916, 1712, 1598, 1493, 1406, 1145, 752 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.5 Hz, 1H), 7.78 (s, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 7.61 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.43 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.39−7.20 (m, 5H), 3.42−2.99 (m, 5H), 2.37−2.23 (m, 1H), 2.20−2.00 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 146.6, 145.5, 135.0, 130.2, 128.6, 128.5, 128.2, 127.0, 126.9, 126.7, 126.4, 125.6, 40.3, 37.2, 33.5, 30.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{19}H_{17}N$ 259.1361, found 259.1372; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, 1.0 mL/min, 280 nm) t_R = 12.9 min (major) and t_R = 14.1 min (minor).

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*(S)-2-Methyl-1,2,3,4-tetrahydroacridine (**5d**).*[67] General procedure described above was followed to afford compound **5d** as a white solid in 89% (26.3 mg) yield. Mp = 64.6 °C (EtOAc; 63−65 °C);[60] R_f = 0.30 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −57.3 (*c* 1.0, $CHCl_3$, 93% ee); IR 3045, 2997, 2950, 2920, 2863, 1621, 1602, 1488, 1459, 1411, 752 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.79 (s, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.60 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.48−7.38 (m, 1H), 3.29−2.97 (m, 3H), 2.60 (dd, *J* = 16.5, 10.7 Hz, 1H), 2.13−1.94 (m, 2H), 1.71−1.52 (m, 1H), 1.13 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 146.6, 134.9, 130.6, 128.5, 128.2, 127.1, 126.8, 125.5, 37.8, 33.1, 31.4, 29.1, 21.65; HRMS (*m*/*z*): $[M]^+$ calcd for $C_{14}H_{15}N$ 197.1204, found 197.1182; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, 1.0 mL/min, 280 nm) t_R = 5.8 min (major) and t_R = 7.0 min (minor).

*(S)-7-Chloro-2-propyl-1,2,3,4-tetrahydroacridine (**5e**).* General procedure described above was followed to afford compound **5e** as a pale yellow solid in 93% (36.1 mg) yield. Mp = 63.8 °C (EtOAc); R_f = 0.25 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −112.3 (*c* 1.0, $CHCl_3$, 96% ee); IR 2955, 2912, 2867, 1588, 1473, 1072, 920, 796 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 9.0 Hz, 1H), 7.65 (s, 1H), 7.63 (d, *J* = 2.3 Hz, 1H), 7.51 (dd, *J* = 9.0, 2.3 Hz, 1H), 3.19 (ddd, *J* = 18.0, 5.7, 3.7 Hz, 1H), 3.04 (m, 2H), 2.55 (dd, *J* = 16.6, 10.6 Hz, 1H), 2.17 − 2.04 (m, 1H), 1.91−1.73 (m, 1H), 1.64−1.50 (m, 1H), 1.49−1.33 (m, 4H), 0.95 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 144.9, 133.9, 131.6, 130.9, 129.9, 129.3, 127.6, 125.4, 38.3, 35.8, 33.5, 33.0, 29.2, 20.0, 14.2; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{18}ClN$ 259.1128, found 259.1140; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/05, 1.0 mL/min, 280 nm) t_R = 5.7 min (major) and t_R = 10.7 min (minor).

*(S)-7-Fluoro-2-propyl-1,2,3,4-tetrahydroacridine (**5f**).* General procedure described above was followed to afford compound **5f** as a pale brown oil in 90% (32.8 mg) yield. R_f = 0.20 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −115.3 (*c* 1.0, $CHCl_3$, 93% ee); IR 2954, 2925, 2868, 1698, 1626, 1610, 1493, 1206, 829, 748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 9.2, 5.3 Hz, 1H), 7.76 (s, 1H), 7.42−7.28 (m, 2H), 3.23 (ddd, *J* = 17.9, 5.6, 3.9 Hz, 1H), 3.15−3.00 (m, 2H), 2.60 (dd, *J* = 16.5, 10.6 Hz, 1H), 2.17−2.07 (m, 1H), 1.92−1.77 (m, 1H), 1.66−1.55 (m, 1H), 1.52−1.35 (m, 4H), 0.96 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.6, 158.6, 143.4, 134.7, 131.6, 130.5, 127.7, 118.6, 109.9, 38.3, 35.8, 33.6, 32.7, 29.2, 20.1, 14.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{18}NF$ 243.1423, found 243.1421; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, 1.0 mL/min, 280 nm) t_R = 4.4 min (major) and t_R = 5.1 min (minor).

*(S)-5,7-Dibromo-2-propyl-1,2,3,4-tetrahydroacridine (**5g**).*[16] General procedure described above was followed to afford compound **5g** as a yellow oil in 92% (52.6 mg) yield. R_f = 0.55 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −37.2 (*c* 1.0, $CHCl_3$, 83% ee); IR 2953, 2924, 1583, 1459, 1392, 945, 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 2.1 Hz, 1H), 7.80 (d, *J* = 2.1 Hz, 1H), 7.67 (s, 1H), 3.29 (ddd, *J* = 18.2, 5.5, 3.8 Hz, 1H), 3.16−3.00 (m, 2H), 2.59 (dd, *J* = 16.7, 10.5 Hz, 1H), 2.18−2.05 (m, 1H), 1.95−1.75 (m, 1H), 1.65−1.53 (m, 1H), 1.51−1.33 (m, 4H), 0.95 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4, 142.4, 134.6, 134.3, 132.7, 128.9, 128.8, 124.9, 118.3, 38.3, 35.6, 33.5, 33.2, 29.1, 20.1, 14.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{17}Br_2N$ 380.9728, found 380.9760; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99/01, 1.0 mL/min, 280 nm) t_R = 5.9 min (major) and t_R = 8.7 min (minor).

*(S)-2-Propyl-6-(trifluoromethyl)-1,2,3,4-tetrahydroacridine (**5h**).*[16] General procedure described above was followed to afford compound **5h** as a white solid in 91% (40.0 mg) yield. Mp = 51.0 °C (EtOAc, 48−49 °C);[16] R_f = 0.50 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −50.8 (*c* 1.0, $CHCl_3$, 86% ee); IR 2919, 1435, 1322, 1164, 1112, 1057, 902, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.75 (s, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 3.21 (ddd, *J* = 18.0, 5.5, 3.7 Hz, 1H), 3.12−2.98 (m, 2H), 2.56 (dd, *J* = 16.6, 10.8 Hz, 1H), 2.15−2.06 (m, 1H), 1.89−1.75 (m, 1H), 1.61−1.51 (m, 1H), 1.48−1.35 (m, 4H), 0.95 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 145.3, 134.5, 132.8, 130.0 (q, *J* = 32.4 Hz), 128.4, 128.1−120.0 (q, *J* = 272.2 Hz), 127.9, 126.1 (d, *J* = 4.1 Hz), 120.9 (d, *J* = 2.5 Hz), 38.2, 35.8, 33.4, 33.0, 29.0, 20.0, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.55; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{17}H_{18}F_3N$ 293.1391, found 293.1388; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99.7/00.3, 0.7 mL/min, 280 nm) t_R = 15.2 min (major) and t_R = 22.5 min (minor).

*(S)-9-Propyl-8,9,10,11-tetrahydrobenzo[c]acridine (**5i**).* General procedure described above was followed to afford compound **5i** as a pale yellow solid in 80% (33.0 mg) yield. Mp = 85 °C (EtOAc); R_f = 0.40 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −42.1 (*c* 1.0, $CHCl_3$, 82% ee); IR 3056, 2949, 2925, 2866, 1596, 1490, 1441, 1402, 763 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.26 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.71 − 7.55 (m, 4H), 7.50 (d, *J* = 8.8 Hz, 1H), 3.29 (ddd, *J* = 17.8, 5.5, 3.7 Hz, 1H), 3.21−3.04 (m, 1H), 2.97 (dd, *J* = 16.5, 3.9 Hz, 1H), 2.52 (dd, *J* = 16.4, 10.5 Hz, 1H), 2.14−2.02 (m, 1H), 1.87−1.73 (m, 1H), 1.64−1.50 (m, 1H), 1.47−1.30 (m, 4H), 0.94 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 144.3, 135.1, 133.2, 131.3, 130.8, 127.6, 127.4, 126.6, 126.4, 125.0, 124.7, 124.1, 38.4, 35.6, 33.7, 33.1, 29.4, 20.1, 14.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{20}H_{21}N$ 275.1674, found 275.1682; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99/01, 1.0 mL/min, 280 nm) t_R = 5.9 min (major) and t_R = 7.6 min (minor).

*(S)-7-Methoxy-2-propyl-1,2,3,4-tetrahydroacridine (**5j**).* General procedure described above was followed to afford compound **5j** as a yellow solid in 83% (31.8 mg) yield. Mp = 75.4 °C (EtOAc); R_f = 0.40 (hexane/EtOAc 4:1 v/v); $[\alpha]_D^{20}$ −75.3 (*c* 1.0, $CHCl_3$, 93% ee); IR 2954, 2926, 1624, 1603, 1494, 1220, 829 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 9.2 Hz, 1H), 7.69 (s, 1H), 7.26 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.96 (d, *J* = 2.8 Hz, 1H), 3.90 (s, 3H), 3.18 (ddd, *J* = 17.7, 5.8, 3.8 Hz, 1H), 3.11−2.97 (m, 2H), 2.58 (dd, *J* = 16.5, 10.6 Hz, 1H), 2.16−2.06 (m, 1H), 1.91−1.75 (m, 1H), 1.65−1.52 (m, 1H), 1.50−1.34 (m, 4H), 0.95 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.0, 156.6, 142.7, 134.0, 130.9, 129.7, 127.9, 121.1, 104.4, 55.4, 38.4, 35.9, 33.7, 32.7, 29.4, 20.1, 14.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{17}H_{21}NO$ 255.1653, found 255.1635; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99/01, 1.0 mL/min, 280 nm) t_R = 6.7 min (major) and t_R = 15.1 min (minor).

*(S)-7-(Benzyloxy)-2-propyl-1,2,3,4-tetrahydroacridine (**5k**).* General procedure described above was followed to afford compound **5k** as a pale yellow solid in 78% (38.7 mg) yield. Mp = 90.2 °C (EtOAc); R_f = 0.50 (hexane/EtOAc 4:1 v/v); $[\alpha]_D^{20}$ −62.0 (*c* 1.0, $CHCl_3$, 92% ee); IR: 3064, 3026, 2952, 2926, 2869, 1623, 1494, 1220, 1025, 737 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 9.2 Hz, 1H), 7.69 (s, 1H), 7.50−7.33 (m, 6H), 7.05 (d, *J* = 2.8 Hz, 1H), 5.16 (s, 2H), 3.19 (ddd, *J* = 17.8, 5.7, 3.8 Hz, 1H), 3.12−2.95 (m, 2H), 2.57 (dd, *J* = 16.4, 10.6 Hz, 1H), 2.18−2.02 (m, 1H), 1.90−1.75 (m, 1H), 1.66−1.51 (m, 1H), 1.51−1.33 (m, 4H), 0.95 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7, 156.2, 142.7, 136.7, 134.2, 130.9, 129.7, 128.6, 128.0, 127.9, 127.5, 121.6, 105.9, 70.2, 38.4, 35.9, 33.7, 32.7, 29.4, 20.1, 14.3; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{23}H_{25}NO$ 331.1936, found 331.1954; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 90/10, 1.0 mL/min, 280 nm) t_R = 7.9 min (major) and t_R = 9.4 min (minor).

*(S)-2-[(tert-Butyldimethylsilyl)oxy]-1,2,3,4-tetrahydroacridine (**5l**).* General procedure described above was followed to afford compound **5l** as a white solid in 75% (35.2 mg) yield. Mp = 73.5 °C (EtOAc); R_f = 0.30 (hexane/EtOAc 4:1 v/v); $[\alpha]_D^{20}$ −87.0 (*c* 1.0, $CHCl_3$, 91% ee); IR: 2951, 2928, 2855, 1492, 1253, 1092, 833, 773, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 1H), 7.78 (s, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.60 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.42 (*J* = 8.0, 7.0, 1.0 Hz, 1H), 4.32−4.20 (m, 1H), 3.34 (dt, *J* = 17.7, 6.5 Hz, 1H), 3.18−3.05 (m, 2H), 2.96 (dd, *J* = 16.4, 7.0 Hz, 1H), 2.15−1.98 (m, 2H), 0.88 (s, 9H), 0.11 (d, *J* = 5.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 146.6, 135.5, 128.7, 128.6, 128.3, 127.0, 126.8, 125.5, 66.8, 38.5, 31.6, 30.4, 25.8, 18.1, −4.7, −4.8; HRMS (*m*/*z*) $[M]^+$ calcd for $C_{19}H_{27}NOSi$ 313.1862, found 313.1850; HPLC (Chiralpak AD-H, *n*-hexane/*i*-PrOH 95/05, 1.0 mL/min, 280 nm) t_R = 8.5 min (major) and t_R = 9.9 min (minor).

*(S)-Ethyl 1,2,3,4-Tetrahydroacridine-2-carboxylate (**5m**).* General procedure described above was followed to afford compound **5m** as a pale yellow solid in 82% (31.4 mg) yield. Mp = 77.1 °C (EtOAc); R_f = 0.20 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −103.7 (*c* 1.0, $CHCl_3$, 85% ee); IR: 2977, 2947, 1728, 1491, 1175, 1030, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.5 Hz, 1H), 7.82 (s, 1H), 7.69 (d, *J* = 8.2

dx.doi.org/10.1021/jo400522m | *J. Org. Chem.* XXXX, XXX, XXX−XXX

Hz, 1H), 7.61 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.43 (ddd, J = 8.0, 7.0, 1.0 Hz, 1H), 4.20 (qd, J = 7.1, 1.0 Hz, 2H), 3.31−3.07 (m, 4H), 2.84 (dtd, J = 11.1, 7.9, 3.4 Hz, 1H), 2.37 (dtd, J = 7.5, 5.9, 4.0 Hz, 1H), 2.15−2.04 (m, 1H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 157.6, 146.6, 135.1, 128.7, 128.6, 128.2, 127.0, 126.8, 125.6, 60.6, 39.4, 32.2, 31.2, 25.8, 14.1; HRMS (m/z) $[M]^+$ calcd for $C_{16}H_{17}NO_2$ 255.1259, found 255.1282; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 95/05, 1.0 mL/min, 280 nm) t_R = 11.1 min (major) and t_R = 14.9 min (minor).

*(S)-1-Methyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**7a**).* General procedure described above was followed to afford compound **7a** as a pale yellow oil in 20% (5.5 mg) yield. R_f = 0.50 (hexane/EtOAc 7:3 v/v); $[\alpha]_D^{20}$ −85.0 (c 1.0, $CHCl_3$, 99% ee); IR 3048, 2952, 2868, 1635, 1497, 1214, 920, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.5 Hz, 1H), 7.87 (s, 1H), 7.77 (d, J = 8.9 Hz, 1H), 7.68−7.60 (m, 1H), 7.52−7.43 (m, 1H), 3.45−3.30 (m, 1H), 3.27−3.09 (m, 2H), 2.50−2.40 (m, 1H), 1.82−1.70 (m, 1H), 1.42 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 140.6, 129.7, 128.6, 128.4, 128.3, 127.6, 127.5, 125.7, 37.3, 33.4, 33.0, 19.7; HRMS (m/z) $[M]^+$ calcd for $C_{13}H_{13}N$ 183.1048, found 183.1042; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99/01, 1.0 mL/min, 280 nm) t_R = 9.8 min (major) and t_R = 15.3 min (minor).

*(R)-2-Methyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**8a**).*[68] General procedure described above was followed to afford compound **7b** as a pale yellow oil in 69% (18.9 mg) yield. R_f = 0.20 (hexane/EtOAc 9:1 v/v); $[\alpha]_D^{20}$ −54.5 (c 1.0, $CHCl_3$, 92% ee); IR 3045, 2951, 2860, 1632, 1492, 1214, 920, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 1H), 7.84 (s, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.65 − 7.56 (m, 1H), 7.44 (m, 1H), 3.35−3.15 (m, 2H), 2.80 (dd, J = 16.6, 7.3 Hz, 1H), 2.75−2.60 (m, 2H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 147.5, 135.5, 130.4, 128.5, 128.2, 127.5, 127.4, 125.4, 42.8, 38.8, 32.8, 20.7; HRMS (m/z) $[M]^+$ calcd for $C_{13}H_{13}N$ 183.1048, found 183.1060; HPLC (Chiralcel OD-H, *n*-hexane/*i*-PrOH 99/01, 1.0 mL/min, 280 nm) t_R = 22.4 min (major) and t_R = 24.1 min (minor).

*(S)-1-Ethyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**7b**).* General procedure described above was followed to afford compound **7b** as a pale yellow oil in 22% (6.5 mg) yield. R_f = 0.45 (hexane/EtOAc 8:2 v/v); $[\alpha]_D^{20}$ −27.0 (c 1.0, $CHCl_3$, 99% ee); IR 3050, 2952, 2922, 2870, 1635, 1491, 1214, 758 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 1H), 7.82 (s, 1H), 7.74 (d, J = 8.1 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 3.28−2.94 (m, 3H), 2.39 (dtd, J = 12.9, 7.9, 5.2 Hz, 1H), 2.03−1.88 (m, 1H), 1.79 (dq, J = 12.6, 8.2 Hz, 1H), 1.65−1.46 (m, 1H), 1.05 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 147.6, 139.2, 129.7, 128.5, 128.3, 127.5, 127.3, 125.4, 44.1, 33.4, 29.8, 27.5, 11.6.; MS (m/z) M^+ 197. Elemental analysis calcd for $C_{14}H_{15}N$: C 85.24, H 7.66, N 7.10. Found: C 86.55, H 7.85, N 7.15. Chiral GC (Cyclosil-B, 160 °C, 14.3 Psi) t_R = 55.6 min (minor) and t_R = 60.2 min (major).

*(R)-2-Ethyl-2,3-dihydro-1H-cyclopenta[b]quinoline (**8b**).* General procedure described above was followed to afford compound **8b** as a pale yellow solid in 70% (20.7 mg) yield. Mp = 51.3 °C; R_f = 0.55 (hexane/EtOAc 8:2 v/v); $[\alpha]_D^{20}$ −37.8 (c 1.0, $CHCl_3$, 90% ee); IR 3055, 2957, 2927, 2878, 1619, 1500, 1412, 1215, 920, 742 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 1H), 7.81 (s, 1H), 7.70 (dd, J = 8.1, 1.2 Hz, 1H), 7.60 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.43 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 3.33−3.10 (m, 2H), 2.82 (dd, J = 16.9, 8.3 Hz, 1H), 2.69 (ddd, J = 16.2, 8.0, 1.5 Hz, 1H), 2.43 (dt, J = 15.3, 7.5 Hz, 1H), 1.66−1.49 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 147.4, 135.4, 130.1, 128.5, 128.1, 127.4, 127.3, 125.3, 40.8, 40.0, 36.6, 28.5, 12.4.; MS (m/z) M^+ 197. Elemental analysis calcd for $C_{14}H_{15}N$: C 85.24, H 7.66, N 7.10. Found: C 86.86, H 7.97, N 7.20; Chiral GC (Cyclosil-B, 160 °C, 14.3 Psi) t_R = 66.7 min (major) and t_R = 67.9 min (minor).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C NMR, and HPLC spectra of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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