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Metal-Free, Mild, Nonepimerizing, Chemo- and Enantio- or Diastereoselective N-Alkylation of Amines by Alcohols via Oxidation/Imine−Iminium Formation/Reductive Amination: A Pragmatic Synthesis of Octahydropyrazinopyridoindoles and Higher Ring Analogues

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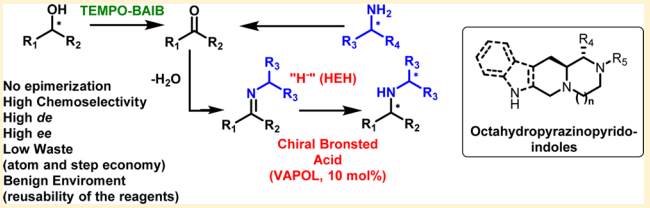
Supporting Information

ABSTRACT: A mild step and atom-economical nonepimerizing chemo- and enantioselective N-alkylating procedure has been developed via oxidation/imine−iminium formation/reduction cascade using TEMPO−BAIB−HEH−Brønsted acid catalysis in DMPU as solvent and a stoichiometric amount of amine. The optimized conditions were further extended for the nonenzymatic kinetic resolution of the chiral amine thus formed under nonenzymatic in situ hydrogen-transfer conditions using VAPOL-derived phosphoric acid (VAPOL-PA) as the Brønsted acid catalyst. The enantioselective cascade of the presented reaction was successfully utilized in the synthesis of octahydropyrazinopyridoindole and its higher ring analogues.



INTRODUCTION

The reductive amination reaction remains one of the most powerful and widely utilized transformations available to practitioners of chemical synthesis in the modern era.[1] Conventionally, the N-alkylation of amines is achieved either by their alkylation with the alkylating agents or by the addition of the nucleophiles or radicals on imines.[2] The most commonly used method for the preparation of secondary and tertiary amines is the substitution of alkyl halides by amines in the presence of a base.[3] However, in this process polyalkylation often occurs, which leads to a mixture of products along with undesired inorganic waste. Moreover, several alkyl halides are toxic and unnatural.

The use of accessible, reasonable, and less hazardous reagents such as alcohols instead of alkyl halides for N-alkylation of amines is considered as a better alternative approach with high atom-efficiency leading to the formation of water as a byproduct. The "borrowing hydrogen strategy (hydrogen autotransfer)", has allowed the direct use of alcohols as alkylating agents. This process has been applied to the formation of C−N bonds,[4] and the use of SiO_2[5] and Al_2O_3[6] as catalysts has been reported; however, under these conditions both the yields and the selectivities (monoalkylation versus bis-alkylation) are poor. The best known conditions involve transition-metal-based catalysts, including heterogeneous and homogeneous processes. When the reaction is performed with heterogeneous catalysts[3d] such as nickel,[7] copper,[8] platinum, ruthenium,[9] palladium,[10] gold,[11] silver,[12] or iron[13] the yields are good to excellent, but generally the main drawback is the need for harsh conditions such as high temperature which can be unfavorable for highly sensitive compounds. The landmark advancement in the field of understanding iminium activation through LUMO lowering activation phenomenon by MacMillan[1c−k] and more importantly Brønsted acid catalyzed imine activation concepts by Rueping[1l−t] added key reasons for major success in the reaction associated with fields like "highly regulated cascade".[1l]

Taylor et al. reported a mild one-pot oxidation/imine iminium formation/reduction sequence for the conversion of benzylic, allylic, or propargylic alcohols to amines using MnO_2 (as oxidant), a polymer-supported cyanoborohydride (as reductant), and acetic acid (as additive).[14] The homogeneous catalysts[3] such as ruthenium[15] or iridium[16] catalysts offered good yields of monoalkylated amines. However, the major drawbacks were the high temperature and a long reaction time except under microwave irradiation along with the epimerization of optically active alcohols that are involved in the N-alkylation of amines.[14b] Recently, N-alkylation of amines by direct nucleophilic substitution at the sp_3 carbon atom of alcohols was reported using iron and amino acid catalysts but again at elevated temperature with long reaction times.[17] Our recent research endeavors on developing effective methodologies for useful organic transformations[18] to construct

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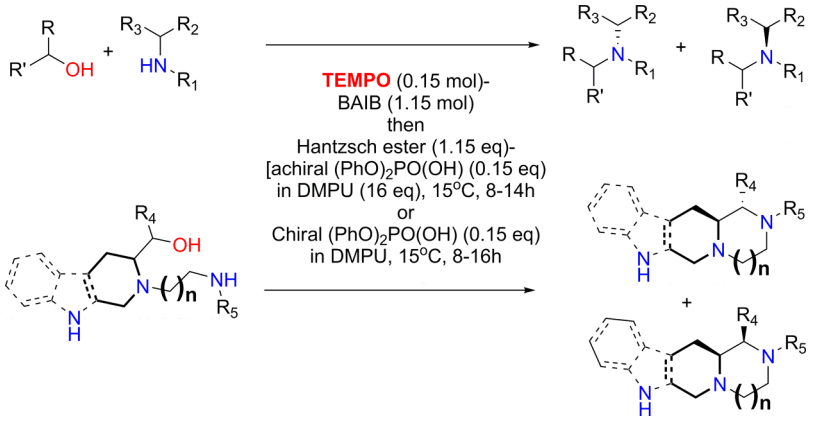
Scheme 1. General Representation of Oxidation/Imine−Iminium Formation Cascade in Both Possibilities of Intramolecular Coupling



octahydropyrazinopyridoindoles (*o*HPPs) and like molecules is of utmost interest. These *o*HPPs including the drug biriperone (centbutindole)[19] discovered by us have been associated with several pharmacological activities (Scheme 1).

CHEMISTRY

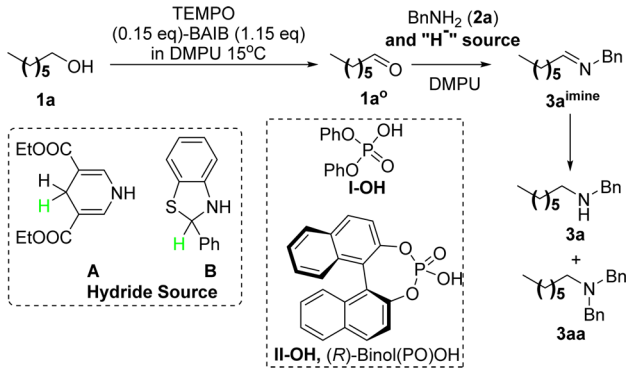
Herein, we report a one-pot oxidation/imine−iminium formation/reduction sequence under mild conditions (Scheme 1). This sequence allows the chemo- and enantioselective N-alkylation of amines with various nonactivated primary and secondary alcohols and prevents epimerization of optically active substrates (amines or alcohols) without metal involvement. This is of importance for medicinal chemists for preparing amines of biological interest because the metal in traces may lead to undesirable pathological conditions.[20] Thus, the method was further extended to the synthesis of the octahydropyrazinopyridoindoles and its higher ring analogues. These tetracyclic cores were synthesized from their respective aminols via intramolecular oxidation/imine−iminium formation/reduction cascade in high yield without such noted epimerization. Among the various conditions reported for the oxidation of alcohols, we selected the mild 4-hydroxy-2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO)−[bis(acetoxy)iodo]-benzene (BAIB) system which releases AcOH as an efficient additive for reductive aminations in the reaction medium.[21]

RESULTS AND DISCUSSION

First, the reaction sequence was standardized for the N-alkylation of benzylamine **2a** by heptanol **1a** for which the latter **1a** was oxidized by TEMPO (0.2 equiv) in the presence of BAIB (1.15 equiv) in DMPU as solvent at rt (25 °C). After 6 h, different reducing agents along with **2a** (3 equiv) were screened for the optimization of the reaction conditions (Table 1). Among different reducing agents, the use of $NaBH_4$ led to **3a** in almost quantitative yield with only traces of **3aa** (Table 1, entry 1c). The use of 1.0 equiv of benzylamine offered moderate yield (41−61%) of **3a** with a selectivity ratio **3a**/**3aa** = 71/28, 64/34 and 62/28 in the three solvents screened (Table 1, entries 1−3).

The use of excess amine (∼ 2.0 equiv) undoubtedly led to excellent yields in DCE as solvent. Since the use of excess amine is not possible in intramolecular cyclization via oxidation/imine−iminium formation/dehydration, we tried to avoid the use of excess amine in order to increase the selectivity for the monoalkylation. The use of commonly employed

Table 1. Standardization of Reaction Conditions



entry	solvent	"H" (hydride source)	2a	3a/3aa[a]	yield of 3a[b] (%)
1a	DMPU	$NaBH_4$	1.0	71/28	54
1b	DMF		1.0	64/34	41
1c	DCE		1.0	62/28	61
1d	DCE		2.0	94/6	84
1e	DCM		2.0	81/18	71
1f	MeOH		2.0	65/35	68
2a	DMPU	**A** (1.15 equiv) + **I-OH** (0.15 equiv)	1.0	97/3	quant
2b	DMF			95/5	quant
2c	DCE			97/3	75
2d	DCM			90/10	68
3	DMPU	$NaBH_3CN$	1.0	60/32	62
4		$NaBH(OAc)_3$		68/32	78
5		**B** (1.15 equiv) + AcOH (0.15 equiv)		95/5	67
6		**B** (1.15 equiv) + **I-OH** (0.15 equiv)		96/4	74
7		**A** (1.1 equiv) + **I-OH** (0.1 equiv)		97/3	84
8		**A** (1.15 equiv) + AcOH (0.15 equiv)		91/8	64
9		**A** (1.15 equiv) + **II-OH** (0.15 equiv)		97/3	95

[a]Determined through HPLC and ^{1}H NMR. [b]Isolated yield.

reagents viz. $NaBH_3CN$ and $NaBH(OAc)_3$ for reductive amination of aldehydes required longer reaction times and provided the mono-(**3a, major**) and di-(**3aa, minor**)-N-alkylated amines in low yield (Table 1, entries 3 and 4), whereas the alkylation of benzylamine (**2a**) with alcohol (**1a**) in stoichiometric amounts in the presence of HEH (**A**) as the

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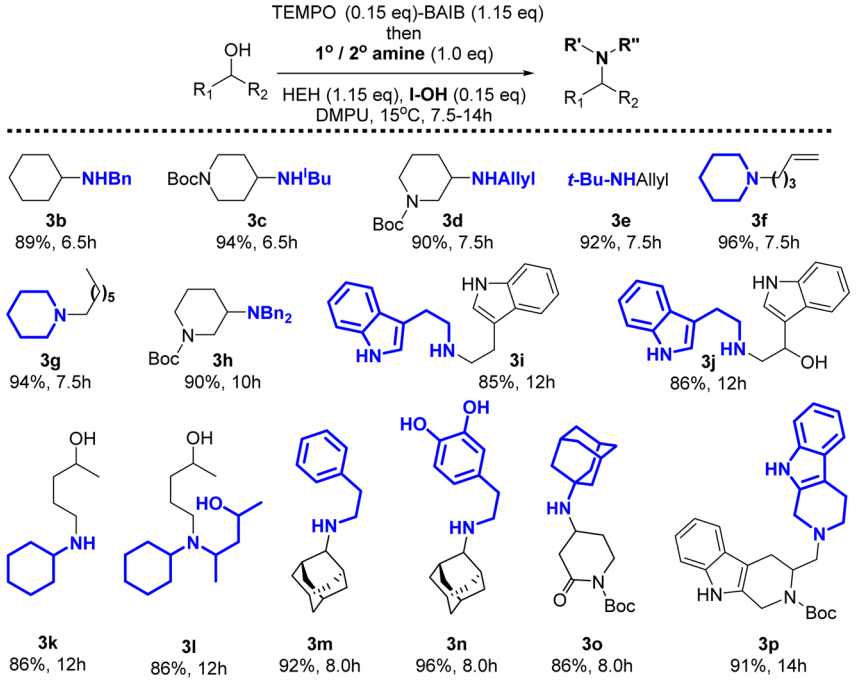

Figure 1. Mildness and chemoselective aspect of the reaction cascade.

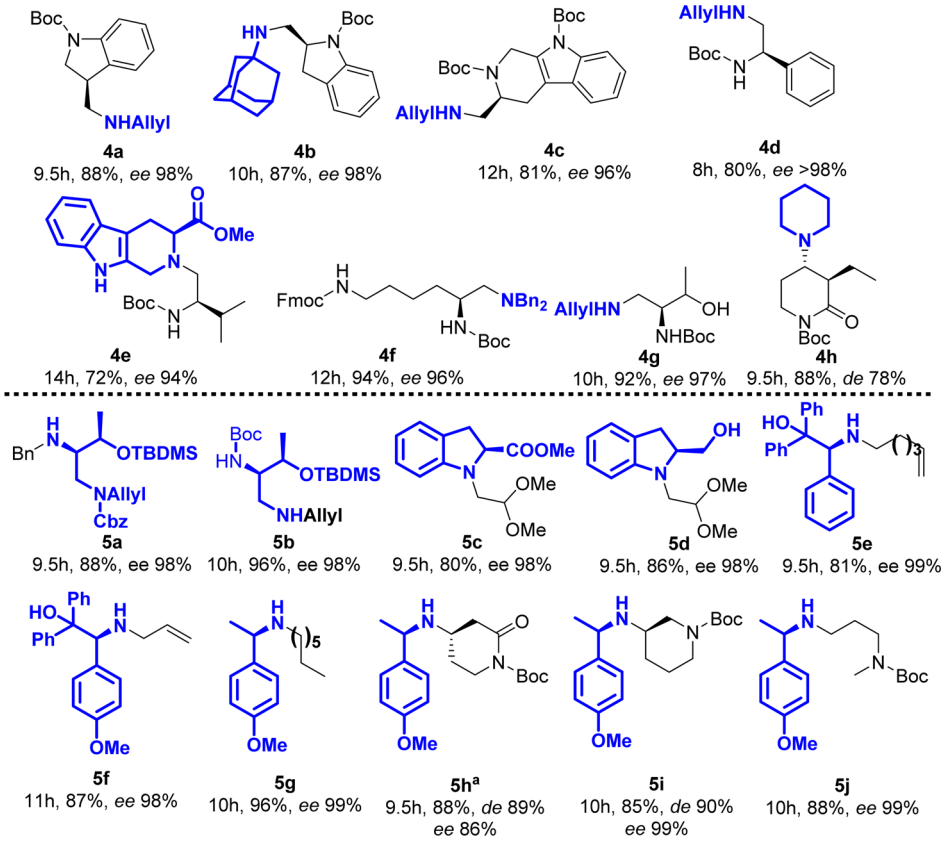

Figure 2. Nonepimerizing cases analyzed under the standardized reaction conditions.

hydride source and a catalytic amount of $(PhO)_2(PO)OH$ (**I-OH**) as the Brønsted acid gave a quantitative yield of the desired monoalkylated amine (**3a**) without any formation of dialkylated amine (**3aa**, Table 1, entries 2 and 6−8). The use of 2-phenylbenzothiazoline (**B**) as hydride source resulted in lower yields (67% with **3a**/**3aa** ratio of 95/5) but was better than HEH (**A**). The former failed to perform better in the presence of **I-OH**, which could be explained on the basis of asymmetric counterion pair catalysis which is observed due to the formation of a chiral ion pair between imine and phosphoric acid. The use of BINOL-derived phosphoric acid

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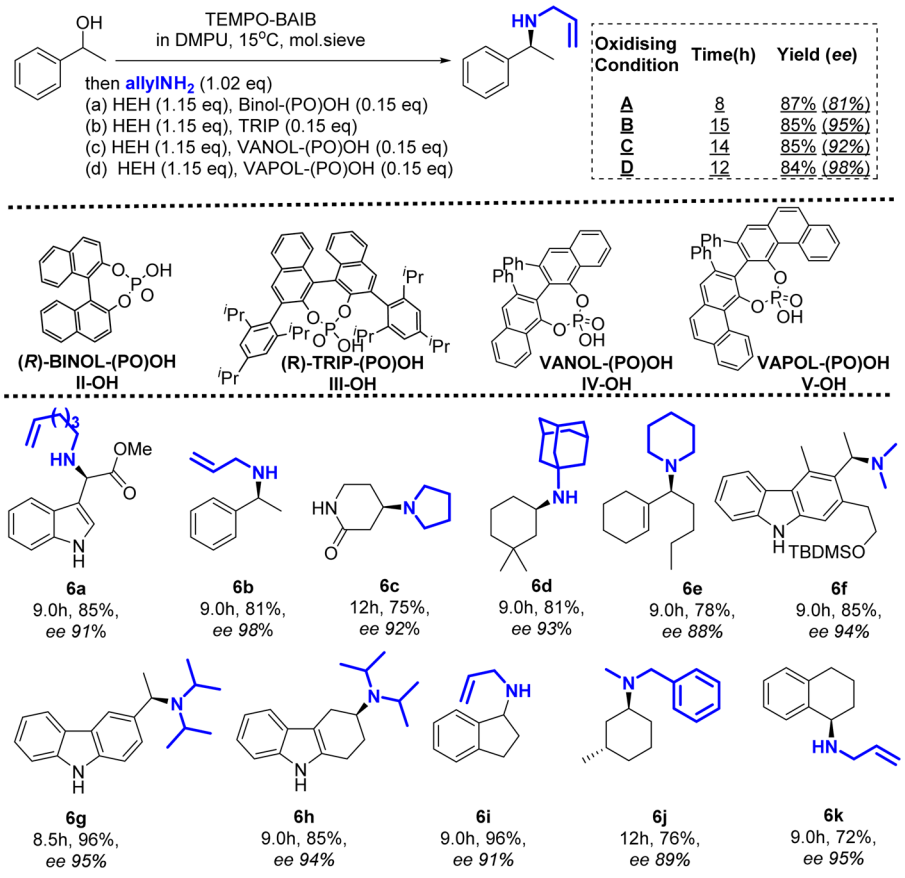

Figure 3. Enantioselective conversion of achiral or racemic alcohols to their respective chiral amines.

(**II-OH**) instead of **I-OH** was equally effective in affording **3a** selectively under similar reaction conditions (Table 1, entry 8).

The reaction is versatile and allows the monoalkylation of a wide range of amines including the hindered amines which are difficult for reductive alkylation. The results obtained with various amines and alcohols are reported in Figure 1. It is interesting to note that HEH (Hantszch ester) was a better substitute than $NaBHX_3$ as reducing agents. Different amines viz benzylamine, *tert*-butylamine, allylamine, piperidine, dibenzylamine, phenylethylamine, dopamine and admantamine resulted in the formation of products **3a**−**b**, **3c** and **3e**, **3d**, **3f**−**g**, **3h**, **3m**, **3n** and **3o**, respectively. It is also worth noting that *N*-Boc-3-hydroxypiperidine was quantitatively transformed to the corresponding N-alkylated Boc-3-aminopiperidine (**3d**, **h**, **o**) with the corresponding amines. Allylamine was N-alkylated in good yields by primary (**3e**) or secondary alcohols (**3c**) without any isomerization of the double bond (Figure 1). Furthermore, a sterically hindered amine such as *tert*-butylamine was also monoalkylated to form **3d** in good yields. Secondary amines were also N-alkylated by primary or secondary alcohols to the corresponding tertiary amines (**3f**−**h**, **l**, **p**, Figure 1). This one-pot process is chemoselective as it showed great selectivity potential of transforming diols (**1j**−**k**) to the respective amino alcohol **3j**−**k** in excellent yield without isolation of any intermediates (Figure 1).

When the N-alkylation of amines was carried out with optically active alcohols possessing a stereocenter at the β-position such as **4a**−**f**, even the use of the recently reported ruthenium catalyst led to the epimerization of the stereogenic center,[14b] while no epimerization of the stereogenic center occurred when the reaction was carried out using our aforementioned reaction conditions where **4a**−**f** were isolated in good yields with excellent enantiomeric excesses (Figure 2). Optically active amines may also be employed in this oxidation/imine−iminium formation/reduction sequence, without any racemization. Thus, when this sequence was applied to various achiral alcohols and optically active amine **5a**−**j** (having a stereogenic center at α position), these compounds were isolated in quantitative yield and with an excellent enantiomeric excess (ee > 96%, Figure 2). The compounds **5h** and **4h** were isolated in good yields and with diastereoisomeric ratios 89/11 and 78/22, respectively. In the case of *N*-Boc-3-hydroxypiperidine the corresponding product *N*-Boc-3-aminopiperidine (**5i**) was obtained with a diastereoisomeric ratio of 84/16 in favor of the (3*S*)-isomer when (*S*)-4-methoxylphenylethylamine was used (Figure 2).

After successful standardization of the reaction conditions, we further extended this methodology for the enantioselective reduction of the imine formed with 1-phenylethanol and allylamine. Thus, for this we screened various chiral Brønsted acids (oxidizing conditions A−D) for catalyzing the HEH-mediated reduction in one pot. The standardized conditions were used on various unsymmetrical alcohols (**6a**−**k**, Figure 3), and it was observed that binol derivatives possessing 3-aryl substituents (**III-OH**, TRIP-PA) and vaulted derivative (**V-OH**, VAPOL-PA) offered excellent enantioselectivity in the reaction. The employment of VAPOL-derived phosphoric acid as catalyst for the reductive amination offered excellent conversion to the chirally enhanced amines from achiral or racemic alcohols.

After optimization for the enantioselective amination of the alcohols, we moved toward the intramolecular conversion of

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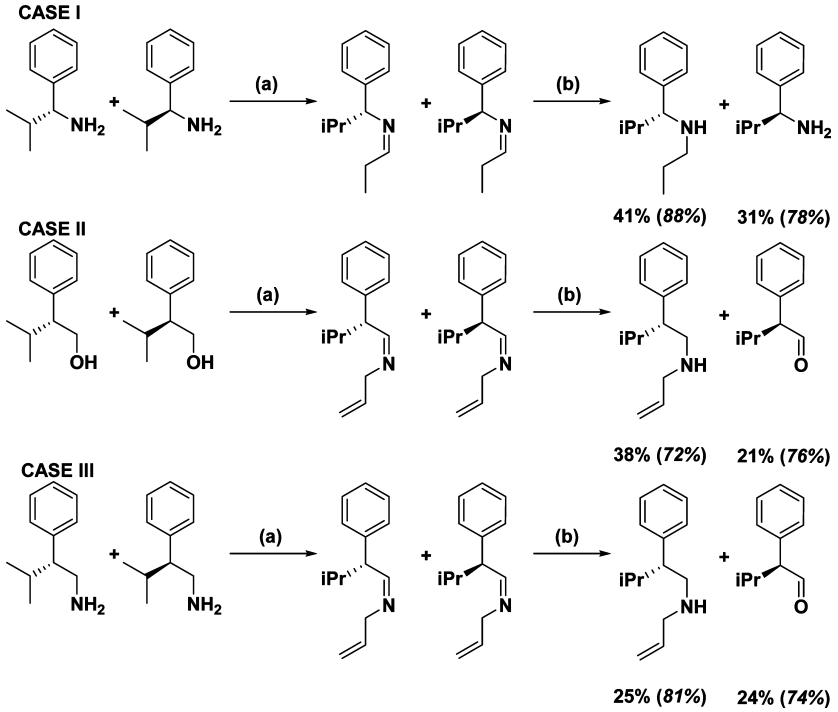
Scheme 2. Example of Dynamic Kinetic Resolution (DKR)[a]



[a]Reagents and conditions. Cases I and III: (a) alcohol (1.0 equiv), TEMPO (0.15 equiv), BAIB (1.15 equiv), molecular sieve (20% w/v) DMPU, 15 °C, 2−3 h; (b) HEH (0.8 equiv), VAPOL-PA (0.15 equiv), amine (0.8 equiv), DMPU, 15 °C, 6.5 h. Case II: (a) TEMPO (0.15 equiv), BAIB (1.15 equiv), molecular sieves (20% w/v) DMPU, 15 °C, 2−3 h; (b) amine (0.75 equiv), HEH (0.85 equiv), VAPOL-PA (0.8 equiv), DMPU, 15 °C, 6 h.

the aminols to their respective cyclized secondary or tertiary amines. Furthermore, we used this strategy for a general stereoselective synthesis of octahydropyrazinopyridoindole derivatives (oHPPs).[19] It was also observed that TEMPO−BAIB-catalyzed oxidation followed by (*S*)-VAPOL-PA−HE-mediated reductive amination methodology could effectively be utilized in the kinetic resolution of the amines possessing a chiral center at the α-center. The chirality at β-carbon center both in the case of amine amd alcohol were also found to impart a significant effect at the HEH-mediated and (*S*)-VAPOL-PA as chiral-catalyzed reductive amination. Therefore, kinetic resolution of racemic amines possessing chiral α and/or β carbon atoms and racemic alcohols bearing β-chiral carbon atoms was also analyzed for each case (Scheme 2). The obtained results showed good results in the case of α-substituted chiral amines (**case I**), whereas the results in the case of β-chiral substrates (i.e., amine and aldehyde **case II** and **III**) were moderate, although this dimension of the reaction is in too early a state in our laboratory to draw conclusions. Indeed, the initial findings have showed the potential of the reagent system toward a nonenzymatic kinetic isolation of racemic mixtures of amine and aldehyde.

In order to standardize the efficacious method of oxidation/imine−iminium formation/reductive amination protocol for the synthesis of the substrates bearing both the desired functionalities by coupling of tetrahydropyridoindoles (tHPs) with N-protected aminols of required carbon chain length as the model substrate (Figure 4), the tetracyclic scaffolds **7a−e** were obtained by using *N*-Boc and *N*-benzyl derivatives of aminopropanol,-butanol, -pentanol, and -hexanol in good to excellent yields with no observed epimerization using **I-OH** as catalyst. The precursors for the compounds **7a−e** were obtained in a three-step process comprising BINOL-PA-catalyzed intermolecular oxidation/imine−iminium formation/reductive amination followed by LAH-mediated ester reduction to the corresponding alcohol and then deprotection of *N*-Boc by using HCl−dioxane for generation of the desired aminols in good overall yields. The compounds **7f−h** were obtained with excellent diastereoselectivity (on the basis of NMR and HPLC) possessing chirality adjacent to the α-carbon atom (the precursor was derived from *l*-tryptophan, described in the Supporting Information) using VAPOL-derived phosphoric acid (**V-OH**) as catalyst at the reductive amination stage. The tetracyclic products bearing a chiral center at δ-carbon were also obtained with excellent results both in terms of stereoselectivities and yields. After the successful stereoselective construction of larger ring analogues of *o*HPP we have also succeeded in the synthesis of oxadiazacino analogues (**8e−f**) in good yields with excellent stereoselectivity (Figure 4) using the vaulted biphenanthrol phosphoric acid (VAPOL-PA) as catalyst. Furthermore, we also successfully synthesized compound **9a**, which does not carry a β-carboline skeleton, in good yield and conhydrine (**9b**) in moderate yield (52%) due to the equally effective formation of **9c** (36%). In both of these positional isomers we found excellent diastereoselection, which was further supported through HPLC and NMR studies using $Co(acac)_2$ as the paramagnetic reagent.

CONCLUSIONS

In conclusion, we have shown that amines can be alkylated by nonactivated alcohols in a metal-free one-pot oxidation/imine−iminium formation/reduction sequence at rt. This sequence of reactions is easy to carry out and allows the formation of secondary and tertiary amines under mild conditions in good yields and with good functional group tolerance. Optically active amines and alcohols can be involved in this sequence

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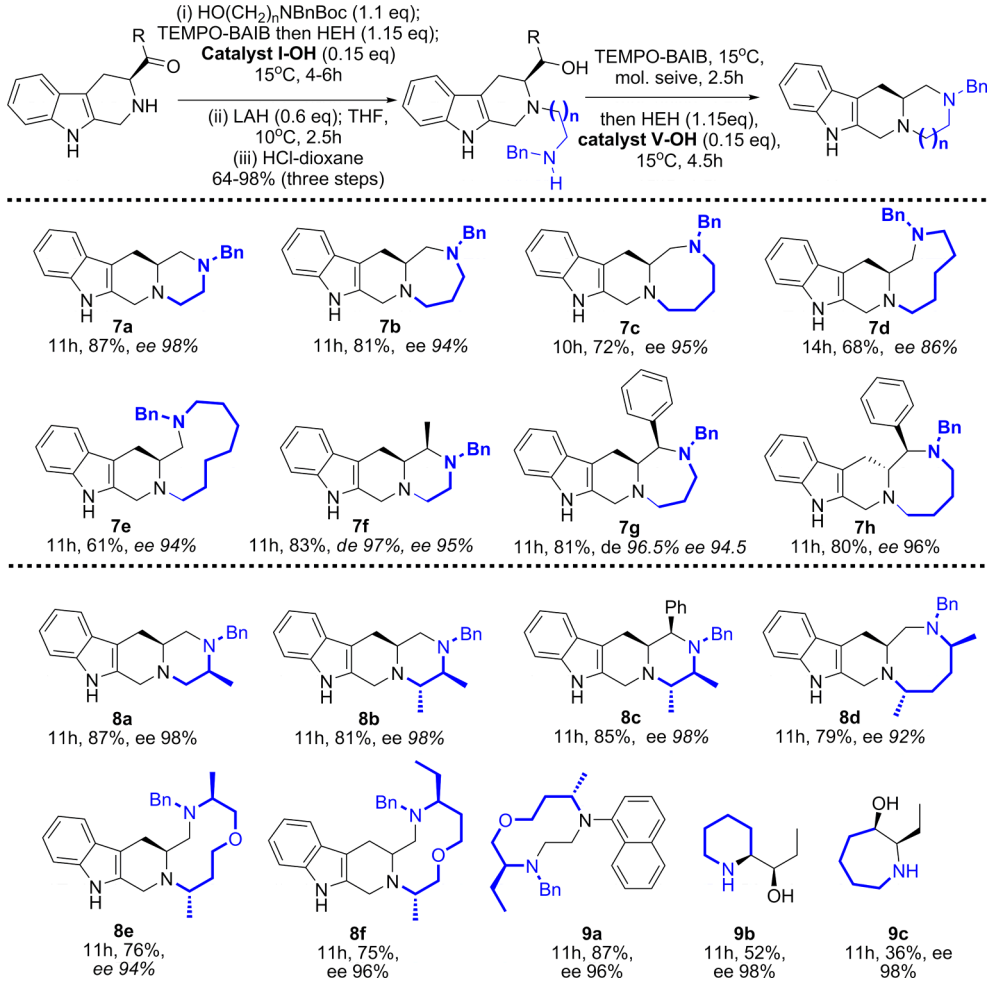

Figure 4. Preparation of octahydropyrazinopyridoindoles derivatives (*o*HPPs) and their higher ring analogues.

without epimerization. We are currently investigating this sequence of reactions in order to have access to biologically active amino compounds.

■ EXPERIMENTAL SECTION

General Information. All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with 300 and 400 MHz spectrometers for ^{1}H NMR and 75 MHz and 100 MHz for ^{13}C NMR. Chemical shifts δ are given in ppm relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$/DMSO-d_6 for ^{1}H and ^{13}C NMR. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quratet (q), multiplet (m). High-resolution mass spectra were taken with a mass spectrometer. Column chromatography was performed using silica gel (100−200 mesh) as the stationary phase. All reactions were monitored by thin-layer chromatography (TLC). The purity and characterization of these compounds were further established using ESI-MS and HRMS mass spectra recorded on a microTOF focus spectrometer. Analytical HPLC were performed on a reversed-phase C-18 column (250 mm × 4.6 mm). Retention times on HPLC (Chiralpak IA, IC normal phase and Chiradex and Chirasphere reversed-phase column; 150 × 4.6 mm; 5 μm) with UV detection at 220/254 nm. Melting points were measured on a capillary melting point apparatus and are uncorrected.

General Procedure. 2,2,6,6-Tetramethyl-1-piperidinyloxyl TEMPO (30 mg, 0.18 mmol, 0.18 equiv) and [bis(acetoxy)iodo]-benzene BAIB (370 mg, 1.15 mmol, 1.15 equiv) were added to a stirred solution of specified alcohol (1 mmol) in CH_2Cl_2 (4 mL), and the mixture was stirred at rt until complete conversion of alcohol (2−14 h) checked by TLC or GC/MS. When the oxidation completion was not reached after 16 h, additional BAIB (up to 240 mg, 0.75 mmol) was added to the reaction mixture. Then, the specified amine (2 mmol, 2 equiv), HEH (or similar reagent when specified) (414 mg, 1 mmol, 1 equiv), and chiral Brønsted acid (15 mol %) were added to the reaction mixture. After a few hours (2−10 h), the mixture was quenched carefully with aq $NaHCO_3$ (10 mol %, 10 mL) and extracted with Et_2O or EtOAc (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification was achieved by one of the following methods. Method A (chlorhydrate precipitation): The crude material was acidified with aq HCl (10%, 10 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2, and the amine chlorohydrate was precipitated by addition of diethyl ether (PE) (∼10 mL), recovered by filtration, basified with aq NaOH (10 mol %, 10 mL), and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford the product amine. Method B (acido-basic washing): The crude material was dissolved in Et_2O (20 mL), and the organic layer was extracted with aq HCl (10%, 3 × 15 mL). The acidic extracts were combined, basified with NaOH at 0 °C, and then extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford the product amine. Method C (chromatography): The crude material was purified by flash chromatography.

***N*-Benzylheptan-1-amine (3a):** yellow liquid; yield 204 mg (99.4%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H

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NMR (300 MHz, $CDCl_3$, ppm) δ 7.31 (s, 5H), 3.98−3.50 (m, 2H), 2.60 (q, J = 7.0 Hz, 2H), 1.70−1.46 (m, 2H), 1.20 (dq, J = 17.4, 7.1, 6.6 Hz, 8H), 0.87 (dd, J = 9.6, 3.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 142.5, 129.0, 128.7, 127.1, 53.7, 49.7, 32.2, 30.6, 30.2, 27.6, 23.1, 14.4; ES-MS (M + H^+, m/z) 205.2; HRMS calcd for $C_{14}H_{23}N$ 205.1830, found 205.1838.

***N*,*N*-Dibenzylheptan-1-amine (3aa):** deep yellow liquid; yield; IR (KBr, ν_{max}, cm^{-1}) 2136.2, 1425.6, 1235.6; ^{1}H NMR (300 MHz, $CDCl_3$, ppm); ^{1}H NMR (200 MHz,) δ 7.40 (t, J = 6.3 Hz, 4H), 7.36−7.07 (m, 6H), 3.59 (s, 4H), 2.34 (t, J = 7.3 Hz, 2H), 1.87−1.63 (m, 2H), 1.56 (dd, J = 14.1, 7.2 Hz, 2H), 1.35−1.03 (m, 6H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 140.2, 129.2, 128.5, 127.5, 59.6, 53.2, 32.0, 30.6, 27.3, 26.9, 22.7, 14.4; ES-MS (M + H^+, m/z) 296.3; HRMS calcd for $C_{21}H_{29}N$ 295.2300, found 295.2305. Anal. Calcd: C, 85.37; H, 9.89; N, 4.74. Found: C, 85.30; H, 9.82; N, 4.71.

***N*-Benzylcyclohexanamine (3b):** yellow liquid; yield 169.1 mg (89%); IR (KBr, ν_{max}, cm^{-1}) 3152.2, 2325.8, 1422.7, 935.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.69−6.93 (m, 5H), 4.05−3.46 (m, 2H), 2.70−2.25 (m, 1H, CH), 2.00−1.32 (m, 9H), 1.34−1.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 128.9, 128.3, 127.1, 52.1, 52.0, 30.6, 25.7, 24.4; ES-MS (M + H^+, m/z) 190.2. Anal. Calcd for $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.34; H, 10.01; N, 7.31.

(±)-*tert*-Butyl 4-(*tert*-butylamino)piperidine-1-carboxylate (3c): yellow liquid; yield 240 mg (94%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.75 (dd, J = 9.8, 6.5 Hz, 1H), 3.60−3.26 (m, 2H), 3.26−2.65 (m, 2H), 1.48 (s, 13H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 158.8, 77.7, 53.1, 45.6, 38.3, 29.8, 29.5, 28.8; ES-MS (M + H^+, m/z) 257.2, 157.2; HRMS calcd for $C_{14}H_{28}N_2O_2$ 256.2151, found 256.2147.

(±)-*tert*-Butyl 3-(allylamino)piperidine-1-carboxylate (3d): light yellow liquid; yield 216 mg (90%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 5.73 (ddd, J = 17.0, 5.8, 2.9 Hz, 1H), 5.10 (dd, J = 19.2, 14.5 Hz, 2H), 3.63 (d, J = 13.1 Hz, 1H), 3.41−2.79 (m, 7H), 1.93−1.62 (m, 2H), 1.63−1.29 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 155.5, 133.8, 115.9, 78.8, 52.6, 52.5, 44.4, 42.4, 30.0, 28.8, 17.1; ES-MS (M + H^+, m/z) 241.2, 141.2; HRMS calcd for $C_{13}H_{24}N_2O_2$ 240.1838, found 240.1841.

***N*-*tert*-Butylprop-2-en-1-amine (3e):** colorless liquid; yield 104 mg (92%); bp 112.5 °C; IR (KBr, ν_{max}, cm^{-1}) 3284.2; rest of the data matched the literature reported data.

1-Hex-5-en-1-ylpiperidine (3f): faint yellow liquid; yield 160 mg (96%); IR (KBr, ν_{max}, cm^{-1}) 3235.8, 2135.2, 1152.2; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.09−5.40 (m, 1H), 5.14−4.72 (m, 2H), 2.74−2.46 (m, 4H), 2.35 (t, J = 6.7 Hz, 2H), 1.87 (hept, J = 7.0, 6.1 Hz, 6H), 1.65−1.41 (m, 4H), 1.29 (dd, J = 10.8, 3.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 139.3, 115.3, 57.1, 56.1, 34.6, 27.8, 26.4, 26.2, 25.67; ES-MS (M + Na^+, m/z) 192.5, 168.2. Anal. Calcd for $C_{11}H_{21}N$: C, 78.97; H, 12.65; N, 8.37. Found: C, 78.85; H, 12.54; N, 8.29.

1-Heptylpiperidine (3g): deep yellow liquid; yield 172.2 mg (94%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.79−2.46 (m, 4H), 2.33 (s, 2H), 2.06−1.74 (m, 4H), 1.75−1.39 (m, 6H), 1.41−1.06 (m, 6H), 0.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 59.3, 57.0, 32.0, 30.1, 27.8, 27.1, 26.3, 25.7, 22.7, 14.4; ES-MS (M + Na^+, m/z) 208.4, 184.2. Anal. Calcd for $C_{12}H_{25}N$ C 78.62; H, 13.75; N, 7.64. Found: C 78.55; H, 13.64; N, 7.52.

(±)-*tert*-Butyl 3-(dibenzylamino)piperidine-1-carboxylate (3h): yellow gum; yield 204 mg (99.4%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.66−7.37 (m, 5H), 7.20 (s, 5H), 3.88 (d, J = 13.6 Hz, 2H), 3.73 (d, J = 13.7 Hz, 2H), 3.65−3.41 (m, 1H), 3.20−3.02 (m, 2H), 2.98−2.63 (m, 2H), 1.77−1.57 (m, 1H), 1.58−1.36 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 155.5, 140.4, 129.3, 128.6, 127.5, 78.8, 58.0, 57.3, 47.1, 42.4, 30.6, 28.8, 18.2; ES-MS (M + H^+, m/z) 381.5, 290.1, 281.4, 200.4; HRMS calcd for $C_{24}H_{32}N_2O_2$ 380.2464, found 380.2464.

Bis(2-(1*H*-indol-3-yl)ethyl)amine (3i): yellow solid; yield 257 mg (85%); mp 198 °C; IR (KBr, ν_{max}, cm^{-1}) 3264.3, 3125.8, 2437.8, 1458.2, 1315.5, 1314.2, 935.2; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.66−7.97 (m, 2H), 7.58 (d, J = 7.2 Hz, 2H), 7.37 (d, J = 7.4 Hz, 2H), 7.27−6.94 (m, 6H), 3.37−3.16 (m, 4H), 3.16−2.98 (m, 4H), 2.00−1.39 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 138.3, 127.9, 122.8, 122.6, 120.1, 118.9, 112.6, 111.0, 50.3, 23.3; ES-MS (M + H^+, m/z) 304.2; HRMS calcd for $C_{20}H_{21}N_3$ 303.1735, found 303.1732.

(±)-2-((2-(1*H*-Indol-3-yl)ethyl)amino)-1-(1*H*-indol-3-yl)ethan-1-ol (3j): dirty yellow solid; yield 274 mg (86%); mp 157 °C; IR (KBr, ν_{max}, cm^{-1}) 3321.5, 3248.7, 2487.2, 1548.2, 1007.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 9.77−9.02 (m, 1H), 8.82−8.09 (m, 1H), 7.85−7.67 (m, 1H), 7.58 (d, J = 7.3 Hz, 1H), 7.44−7.29 (m, 3H), 7.24 (s, 1H), 7.20−6.94 (m, 4H), 5.12−4.71 (m, 1H), 3.56−3.24 (m, 3H), 3.20−2.99 (m, 2H), 2.92−2.73 (m, 1H), 2.73−2.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 138.3, 137.9, 128.3, 127.6, 124.5, 123.0, 122.8, 122.7, 120.6, 120.2, 120.1, 118.9, 118.5, 112.7, 112.6, 110.1, 61.8, 56.2, 51.1, 23.5; ES-MS (M + H^+, m/z) 320.2, 302.5; HRMS calcd for $C_{20}H_{21}N_3O$ 319.1685, found 319.1688.

(±)-5-(Cyclohexylamino)pentan-2-ol (3k): yellow liquid; yield 159 mg (86%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.83−3.51 (m, 1H), 2.93−2.79 (brs, 1H), 2.67 (d, J = 7.2 Hz, 2H), 2.50−2.25 (m, 1H), 1.84−1.32 (m, 12H), 1.32−0.96 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 68.3, 51.5, 48.5, 35.7, 29.9, 25.7, 24.6, 23.65, 23.59; ES-MS (M + H^+, m/z) 186.5.

5-(Cyclohexyl(4-hydroxypentan-2-yl)amino)pentan-2-ol (3l): yellow liquid; yield 233 mg (86%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 4.29−3.91 (m, 1H), 3.69 (m, 1H), 3.05−2.70 (m, 3H), 2.67−2.25 (m, 3H), 1.88−1.39 (m, 15H), 1.36−0.77 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 66.9, 66.0, 57.4, 52.2, 46.6, 42.1, 36.3, 32.4, 25.9, 25.7, 23.7, 23.4, 22.8, 20.; ES-MS (M + H^+, m/z) 272.2.

***N*-Phenethyladamantan-2-amine (3m):** yellow liquid; yield 234 mg (92%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.13 (d, J = 36.3 Hz, 5H), 2.93−2.58 (m, 5H), 2.56−2.20 (brs, 1H), 1.94−1.30 (m, 10H), 1.25−0.72 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 139.9, 128.2, 127.9, 126.7, 59.5, 49.6, 36.7, 35.2, 34.5, 33.5, 32.5, 31.5, 30.5, 27.1; ES-MS (M + H^+, m/z) 256.8; HRMS calcd for $C_{18}H_{25}N$ 255.1987, found 255.1983.

4-(2-((Adamantan-2-yl)amino)ethyl)benzene-1,2-diol (3n): yellow liquid; yield 204 mg (99.4%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.37 (brs, 1H), 6.72 (d, J = 7.3 Hz, 1H), 6.58 (s, 1H), 6.48 (d, J = 7.3 Hz, 1H), 5.43 (brs, 1H), 2.91−2.72 (m, 3H), 2.64 (d, J = 6.1 Hz, 2H), 2.55−2.27 (brs, 1H), 1.96−1.38 (m, 12H), 1.27−0.53 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 143.8, 142.6, 135.7, 120.4, 115.2, 114.3, 59.5, 49.9, 36.7, 36.0, 34.5, 33.5, 32.5, 31.5, 30.5, 27.1; ES-MS (M + H^+, m/z) 288.4; HRMS calcd for $C_{18}H_{25}NO_2$ 287.1885, found 287.1881.

***tert*-Butyl (*R*)-4-((adamantan-1-yl)amino)-2-oxopiperidine-1-carboxylate (3o):** yellow liquid; yield 299.6 mg (86%); IR (KBr, ν_{max}, cm^{-1}) 3258.2, 2457.2, 1745.2, 1687.3, 1654.2, 1615.2, 1462.2, 1012.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 4.01−3.64 (m, 2H), 3.57−3.05 (m, 2H), 2.67−2.29 (m, 2H, $COCH_2$), 1.99 (s, 3H), 1.96−1.74 (m, 7H), 1.75−1.03 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 174.4, 154.6, 81.5, 53.7, 44.7, 39.9, 38.9, 37.9, 37.6, 30.4, 28.5, 27.3; ES-MS (M + H^+, m/z) 349.6, 249.3; HRMS calcd for $C_{20}H_{32}N_2O_3$ 348.2413, found 348.2417.

(±)-*tert*-Butyl 3-((1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indol-2-yl)methyl)-1,3,4,9-tetrahydro-2*H*-pyrido [3,4-*b*]indole-2-carboxylate (3p): yellow liquid; yield 415 mg (91%); IR (KBr, ν_{max}, cm^{-1}) 3254.2, 2457.2, 1452.2, 1005.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.19 (brs, 1H) 7.86 (brs, 1H, NH), 7.73−7.55 (m, 1H), 7.55−7.35 (m, 2H), 7.33−7.17 (m, 2H), 7.17−7.06 (m, 2H), 7.06−6.89 (m, 2H), 4.68 (d, J = 16.4 Hz, 1H), 4.36 (d, J = 16.6 Hz, 1H), 4.20−3.96 (m, 1H), 3.49−3.03 (m, 7H), 3.03−2.77 (m, 4H), 2.77−2.42 (m, 2H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 155.5, 138.3, 134.7, 133.3, 132.3, 128.2, 125.7, 120.8, 120.5, 118.8, 118.5, 118.4, 117.5, 112.0, 111.6, 110.7, 110.6, 79.1, 54.2, 51.1, 44.1, 41.0, 39.2, 29.1, 25.1, 23.4; ES-MS (M + H^+, m/z) 457.2; HRMS calcd for $C_{28}H_{32}N_4O_2$ 456.2525, found 456.2529.

(+)-*tert*-Butyl 3-((allylamino)methyl)indoline-1-carboxylate (4a): yellow semisolid; yield 253.4 mg (88%); $[\alpha]^{22.1}_D$ +26.5 (*c*

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1.03, $CHCl_3$); HPLC using Chiralpak IC, at flow rate 0.6 mL/min, ACN/Hex (5:95, isocratic) 18.66 min (99%) and 19.8 min (1%); ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.07 (d, J = 7.4 Hz, 1H), 7.32 (s, 2H), 7.09 (dt, J = 4.8, 2.5 Hz, 1H), 6.14−5.76 (m, 1H), 5.15−4.95 (m, 2H), 4.95−4.81 (m, 1H), 3.97−3.83 (m, 1H), 3.41−3.15 (m, 1H), 3.14−2.96 (m, 2H), 2.96−2.81 (m, 1H), 2.81−2.53 (m, 1H), 1.57 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 153.0, 144.2, 134.9, 131.0, 129.0, 125.7, 123.7, 115.4, 114.4, 77.9, 55.6, 51.2, 49.9, 42.2, 28.5; ES-MS (M + H^+, m/z) 289.3. Anal. Calcd for $C_{17}H_{24}N_2O_2$: C, 70.80; H, 8.39; N, 9.71; O, 11.10. Found: C, 70.77; H, 8.25; N, 9.65.

***tert*-Butyl (*S*)-2-(((adamantan-1-yl)amino)methyl)indoline-1-carboxylate (4b):** yellow solid; yield 332 mg (87%); mp 136−138 °C; $[\alpha]^{21.6}_D$ +52.6 (c 1.05, $CHCl_3$); HPLC using Chiralpak IC at flow rate 0.6 mL/min, ACN/IPA/Hex (2:95:3) isocratic, 23.1 min (1%) and 24.73 min (99%); IR (KBr, ν_{max}, cm^{-1}) 3245.6, 2854.3, 1694.1, 1657.2, 1245.6, 1158.9, 985.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.79 (d, J = 7.5 Hz, 1H), 7.26 (t, J = 6.6 Hz, 1H), 7.19−7.04 (m, 1H), 6.94 (d, J = 6.6 Hz, 1H), 4.38−3.96 (m, 1H), 3.62−3.36 (brs, 1H), 3.15−2.95 (m, 2H), 2.34−2.06 (m, 1H), 1.91 (s, 3H), 1.72−1.30 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 150.5, 142.5, 131.6, 128.2, 126.7, 124.3, 119.9, 79.3, 57.7, 53.6, 48.2, 40.3, 36.9, 30.4, 29.8, 28.7; ES-MS (M + H^+, m/z) 383.4, 283.5; HRMS calcd for $C_{24}H_{34}N_2O_2$ 382.2620, found 382.2624.

Di-*tert*-butyl (*S*)-3-((allylamino)methyl)-3,4-dihydro-1*H*-pyrido[3,4-*b*]indole-2,9-dicarboxylate (4c): deep yellow liquid (gum); yield 35.8 mg (81%); $[\alpha]^{23.1}_D$ −41.5 (c 0.63, MeOH); HPLC using Chiralpak IA at Flow rate 0.6 mL/min, IPA/Hex:TEA (7:93:0.001), Rt 25.48 min (98%) and 26.7 min (2%); IR (KBr, ν_{max}, cm^{-1}) 3315.6, 2854.6, 2158.3, 1723.6, 1687.5, 1645.2, 1456.3, 1235.3, 1015.2; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.98 (d, J = 7.1 Hz, 1H), 7.64−7.40 (m, 1H), 7.25 (dq, J = 15.3, 7.6 Hz, 2H), 6.16−5.74 (m, 1H), 5.38−5.07 (m, 2H), 4.86 (d, J = 16.4 Hz, 1H), 4.57−4.15 (m, 2H), 3.46−3.08 (m, 5H), 3.08−2.79 (m, 2H), 2.75−2.55 (m, 1H), 1.65 (d, J = 5.3 Hz, 9H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 158.4, 153.9, 138.6, 138.3, 132.3, 128.5, 122.4, 121.1, 120.9, 116.3, 115.8, 111.8, 83.1, 79.2, 54.2, 51.1, 45.0, 39.7, 28.9, 28.5, 26.6; ES-MS (M + H^+, m/z) 442.6, 344.5, 244.4. Anal. Calcd for $C_{25}H_{35}N_3O_4$: C, 68.00; H, 7.99; N, 9.52. Found: C, 67.92; H, 7.92; N, 9.43.

***tert*-Butyl (*R*)-(2-(allylamino)-1-phenylethyl)carbamate (4d):** yellow liquid; yield 22.2 mg (80%); $[\alpha]^{19.3}_D$ +29.3 (c 0.1, MeOH); HPLC using Chiralpak IA at Flow rate 0.7 mL/min; ACN: Hex (8:92, isocratic), t_R 11.19 (98.04%) and 13.13 min (1.95%); IR (KBr, ν_{max}, cm^{-1}) 3325.6, 3154.8, 1736..5, 1714.3, 1685.3, 1624.3, 1215.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.37 (dt, J = 7.4, 3.7 Hz, 2H), 7.24−7.02 (m, 1H), 6.90 (d, J = 7.8 Hz, 2H), 6.26−5.85 (m, 1H), 5.83−5.50 (brs, 1H), 5.38 (d, J = 10.3 Hz, 1H), 5.15 (d, J = 17.3 Hz, 1H), 4.74 (d, J = 7.1 Hz, 1H), 3.50−2.75 (m, 6H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 155.1, 141.8, 135.3, 130.4, 127.7, 126.9, 115.0, 79.3, 54.7, 54.5, 52.7, 28.7; ES-MS (M + H^+, m/z) 277.5; HRMS calcd for $C_{16}H_{24}N_2O_2$ 276.1838, found 276.1831.

Methyl (*S*)-2-((*R*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate (4e): yellow liquid; yield 29.8 mg (72%); $[\alpha]^{19.5}_D$ −65.9 (c 0.1 $CHCl_3$); HPLC using Chiradex at flow rate 0.6 mL/min, MeOH/H_2O/ACN (20:70:10, isocratic), t_R 15.3 min (2.6%), 16.7 min (88.27%), 21.37 min (8.4%), 23.66 (0.66%); ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.16 (s, 1H), 7.47 (s, 1H), 7.30 (d, J = 7.7 Hz, 1H), 7.12 (dd, J = 10.8, 4.0 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 5.21−4.62 (brs, 1H), 3.98−3.62 (m, 5H), 3.44 (q, J = 15.1 Hz, 2H), 3.36−3.05 (m, 4H), 1.62 (dd, J = 9.8, 3.5 Hz, 1H), 1.42 (s, 9H), 0.92 (dd, J = 19.9, 6.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 174.1, 155.5, 135.2, 133.1, 126.4, 120.9, 119.1, 118.3, 110.7, 103.9, 79.2, 61.4, 53.5, 52.4, 51.7, 49.4, 32.8, 28.6, 20.0, 18.7, 18.3; ES-MS (M + H^+, M + Na^+, m/z) 416.5, 439.9; HRMS calcd for $C_{23}H_{33}N_3O_4$ 415.2471, found 415.2465.

(9*H*-Fluoren-9-yl)methyl *tert*-butyl (6-(dibenzylamino)hexane-1,5-diyl) (*S*)-dicarbamate (4f): yellow liquid; yield 59.5 mg (94%); $[\alpha]^{16.8}_D$ +22.6 (c 0.14 $CHCl_3$); HPLC using Chiradex at flow rate 0.5 mL/min, H_2O/TEA/MeCN/IPA (95:0.001:2.2:2.6 → 80:0.001:8:9.5, gradient over 50 min) t_R 40.1 (98%) and 44.0 (2%); ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.77 (d, J = 6.9 Hz, 2H), 7.62 (d, J = 7.4 Hz, 2H), 7.54−7.18 (m, 13H), 7.16−6.88 (m, 2H), 5.90−5.46 (brs, 1H), 5.45−4.86 (brs, 1H), 4.45 (d, J = 6.3 Hz, 2H), 4.40−4.07 (m, 2H), 3.72 (s, 4H), 3.12−2.83 (m, 2H), 2.75−2.36 (m, 2H), 1.41 (d, J = 20.3 Hz, 15H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 157.2, 156.2, 144.0, 140.6, 140.1, 128.9, 128.5, 127.9, 127.5, 127.0, 125.0, 119.8, 80.3, 66.1, 60.1, 56.9, 50.6, 47.2, 40.1, 35.4, 29.0, 28.8, 25.7; ES-MS (M + H^+, m/z) 634.4, 657.8; HRMS calcd for $C_{40}H_{47}N_3O_4$ 633.3567, found 633.3568.

***tert*-Butyl ((2*S*)-1-(allylamino)-3-hydroxybutan-2-yl)carbamate (4g):** yellow liquid; yield 22.4 mg (92%); $[\alpha]^{16.9}_D$ −62.3 (c 0.2 CH_2Cl_2); HPLC using Chiralpak IA, at flow rate 0.6 mL/min, IPA/Hex/TEA (5:95:0.001, isocratic) t_R 8.5 min (1.94%), 8.9 min (0.5%), 10.3 (0.94%) and 10.8 min (96.5%); ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 6.43−5.83 (m, 1H), 5.62−5.31 (m, 1H), 5.16 (d, J = 17.5 Hz, 1H), 3.91−3.48 (m, 2H), 3.23 (s, 4H), 2.95−2.63 (m, 2H), 1.42 (s, 9H), 1.17 (d, J = 5.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 156.3, 135.0, 115.4, 81.0, 70.8, 54.6, 53.9, 48.8, 28.8, 20.4; ES-MS (M + H^+, m/z) 245.2; HRMS calcd for $C_{12}H_{24}N_2O_3$ 244.1787, found 244.1780.

***tert*-Butyl (3′*R*,4′*S*)-3′-ethyl-2′-oxo[1,4′-bipiperidine]-1′-carboxylate (4h):** orange-yellow liquid; yield 27.2 mg (88%); $[\alpha]^{19.6}_D$ −13.9 (c 0.1 $CHCl_3$); HPLC using C18 at flow rate 0.7 mL/min, H_2O/IPA/TEA (85:5:0.01) t_R 26.5 min (11%) and 26.3 min (89%); IR (neat, ν_{max}, cm^{-1}) 1715.2, 1685.3, 1610.3, 1345.2, 1263.2; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 4.03−3.50 (m, 2H), 2.89−2.67 (m, 1H), 2.63−2.32 (m, 5H), 2.24−1.89 (m, 3H), 1.81−1.24 (m, 16H), 0.97 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 176.9, 154.6, 84.3, 63.8, 54.8, 49.9, 41.3, 27.9, 26.3, 26.1, 25.4, 23.1, 12.5; ES-MS (M + H^+, m/z) 311.2; HRMS calcd for $C_{17}H_{30}N_2O_3$ 310.2256, found 310.2257.

Benzyl allyl((2*R*,3*R*)-2-(benzylamino)-3-((*tert*-butyldimethylsilyl)oxy)butyl)carbamate (5a): yellow liquid; yield 42.2 mg (88%); $[\alpha]^{19.5}_D$ +52.3 (c 0.1 MeOH); HPLC Chiralpak IA, at flow rate 0.6 mL/min IPA/Hex (5:95), t_R 11.5 (99.1%) and 15.6 min (0.8%); IR (KBr, ν_{max}, cm^{-1}) 3324.6, 3053.8, 1731..5, 1684.3, 1634.3, 1215.3, 1185.3, 995.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.42−7.00 (m, 10H), 6.04−5.34 (m, 1H), 5.10 (d, J = 12.3 Hz, 3H), 5.05−4.95 (m, 1H), 4.13−3.98 (m, 1H), 3.87 (dd, J = 9.1, 2.9 Hz, 2H), 3.85−3.70 (m, 2H), 3.07−2.65 (m, 2H), 2.51−2.17 (m, 1H), 1.98−1.48 (brs, 1H), 0.89 (m, 12H), −0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 157.3, 143.2, 138.2, 132.6, 129.1, 128.8, 128.7, 128.1, 127.8, 127.1, 116.6, 71.0, 67.4, 61.6, 52.9, 51.4, 47.7, 26.3, 21.9, 20.9, −4.7; ES-MS (M + H^+, m/z) 483.5; HRMS calcd for $C_{28}H_{42}N_2O_3Si$ 482.2965, found 482.2968.

***tert*-Butyl ((2*R*,3*R*)-1-(allylamino)-3-((*tert*-butyldimethylsilyl)oxy)butan-2-yl)carbamate (5b):** light yellow glassy solid; yield 34.3 mg (98%); mp 96−98 °C; $[\alpha]^{22.5}_D$ +12.5 (c 0.09 EtOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (5:95, isocratic), 25.2 min (0.9%) and 26.3 min (99.1%); ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 6.24−5.81 (m, 1H), 5.57−5.33 (m, 1H), 5.16 (d, J = 17.5 Hz, 1H), 5.09−4.86 (brs, 1H), 4.28−3.91 (m, 1H), 3.91−3.48 (m, 1H), 3.38−3.10 (m, 2H), 2.89−2.53 (m, 2H), 1.70−1.55 (brs, 1H), 1.42 (s, 9H), 1.25−1.03 (m, 3H), 0.85 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 156.5, 135.0, 115.4, 81.0, 72.1, 54.9, 54.8, 49.0, 28.8, 26.3, 21.6, 18.6, −4.9; ES-MS (M + H^+, m/z) 359.4; HRMS calcd for $C_{18}H_{38}N_2O_3Si$ 358.2652, found 358.2657.

Methyl (*S*)-1-(2,2-dimethoxyethyl)indoline-2-carboxylate (5c): yellow solid; yield 228.5 mg (80%); M. P. 96 °C; $[\alpha]^{23.8}_D$ +57.3 (c 1.0, $CHCl_3$); HPLC using Chiralpak IC at floe rate 0.7 mL/min, IPA/Hex (5:95, isocratic) t_R 11.4 min (99.1%) and 15.6 min (0.9%); IR (KBr, ν_{max}, cm^{-1}) 1754.2, 1434.7, 1256.3, 1005, 995.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.26−6.98 (m, 1H), 6.90 (d, J = 7.8 Hz, 1H), 6.83−6.54 (m, 2H), 4.44 (m, 1H), 4.16 (dd, J = 11.9, 4.1 Hz, 1H), 3.89−3.51 (m, 5H), 3.32 (s, 6H), 3.01 (dt, J = 16.7, 8.6 Hz, 1H), 2.87−2.51 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 171.5, 151.2, 130.6, 126.5, 124.8, 120.2, 118.0, 99.8, 65.1, 54.7, 53.8, 52.0, 29.5; ES-MS (M + H^+, m/z) 266.8. Anal. Calcd for $C_{14}H_{19}NO_4$ (265.1314): C, 63.38; H, 7.22; N, 5.28. Found: C, 63.31; H, 7.18; N, 5.24.

(*S*)-(1-(2,2-Dimethoxyethyl)indolin-2-yl)methanol (5d): yellow liquid; yield 20.5 mg (86%); $[\alpha]^{19.4}_D$ +32.6 (c 0.08, MeOH); HPLC using Chiralpak IC at flow rate 0.6 mL/min, IPA/Hex (5:95, isocratic),

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t_R 14.5 (99.1%) and 15.9 min (0.8%); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.98 (dt, J = 14.2, 7.2 Hz, 2H), 6.87−6.50 (m, 2H), 4.62 (m, 1H), 4.03−3.69 (m, 2H), 3.69−3.50 (m, 2H), 3.50−3.41 (m, 1H), 3.33 (s, 6H), 3.26−3.05 (m, 1H), 2.74−2.43 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 152.6, 131.8, 126.0, 124.9, 119.5, 116.4, 100.1, 65.1, 60.8, 55.0, 52.2, 29.8; ES-MS (M + H$^+$, m/z) 238.4. Anal. Calcd for $C_{13}H_{19}NO_3$ (237.1365): C, 65.80; H, 8.07; N, 5.90. Found: C, 65.72; H, 8.11; N, 6.19.

(*S*)-2-(Hex-5-en-1-ylamino)-1,1,2-triphenylethan-1-ol (5e): light yellow syrup; yield 330.2 mg (81%); $[\alpha]^{19.4}_D$ −86.6 (c 0.1, $CHCl_3$); HPLC using Chiralpak IA at flow rate 0.9 mL/min, IPA/Hex/*n*-pentane (8:62:30, isocratic) t_R 12.0 min (0.5%) and 13.2 min (99.5%); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.90−7.14 (m, 13H), 7.16−6.83 (m, 2H), 5.98−5.45 (m, 1H), 5.17−4.69 (m, 2H), 4.24 (brs, 1H), 4.12−3.70 (m, 1H), 2.74−2.39 (m, 2H), 2.37−2.08 (brs, 1H), 2.05−1.67 (m, 2H), 1.62−1.36 (m, 2H), 1.38−1.05 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 145.2, 144.9, 142.7, 139.5, 128.5, 128.43, 128.39, 127.7, 127.5, 125.9, 115.3, 79.5, 71.4, 47.7, 34.9, 29.3, 29.1; ES-MS (M + H$^+$, m/z) 372.4. Anal. Calcd for $C_{26}H_{29}NO$ (371.2249): C, 84.06; H, 7.87; N, 3.77. Found: C, 84.00; H, 7.81; N, 3.69.

(*S*)-2-(Allylamino)-2-(4-methoxyphenyl)-1,1-diphenylethan-1-ol (5f): colorless thick liquid; yield 31.2 mg (87%); $[\alpha]^{15.8}_D$ −81.3 (c 1.0 CH_2Cl_2); HPLC using Chiralpak IA at flow rate 0.7 mL/min, IPA/Hex (7:93, isocratic) t_R 7.43 min (99.1%) and 14.05 min (0.8%); IR (neat, ν_{max}, cm^{-1}) 3356.2, 3135.2, 1532.2, 1325.3, 1054.3, 996.3; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.99−7.19 (m, 10H), 7.12−6.42 (m, 4H), 6.19−5.67 (m, 1H), 5.15 (d, J = 10.2 Hz, 1H), 5.00 (d, J = 16.6 Hz), 4.24 (brs, 1H), 3.99 (d, J = 7.9 Hz, 1H), 3.77 (s, 3H), 2.20−1.84 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 159.8, 144.2, 143.9, 135.1, 134.6, 129.0, 128.5, 127.7, 125.9, 114.7, 114.4, 78.0, 72.1, 54.7, 51.4; ES-MS (M + H$^+$, m/z) 360.5. Anal. Calcd for $C_{24}H_{25}NO_2$ (359.1885): C, 80.19; H, 7.01; N, 3.90. Found: C, 80.10; H, 6.95; N, 3.84.

(*R*)-*N*-(1-(*p*-Tolyl)ethyl)heptan-1-amine (5g): colorless liquid; yield 23.9 mg (98%); $[\alpha]^{23.5}_D$ −96.3 (c 0.4, IPA); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex/TEA (97.3:6.5:0.01, isocratic) t_R 5.71 min (99.8%) and 8.6 min (0.8%); IR (neat, ν_{max}, cm^{-1}) 3368.3, 1562.3, 1356.2, 1236.8; 1056.9, 994.6; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.17 (d, J = 7.9 Hz, 2H), 6.83 (d, J = 7.9 Hz, 2H), 3.77 (s, 3H), 3.70−3.46 (m, 1H), 2.77−2.39 (m, 2H), 1.72−1.46 (m, 2H), 1.44−1.06 (m, 8H), 1.06−0.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 160.1, 138.7, 128.5, 114.8, 57.8, 54.7, 46.7, 46.3, 33.5, 31.8, 31.6, 30.4, 26.6, 24.1, 23.1, 14.4; ES-MS (M + H$^+$, m/z) 250.7. Anal. Calcd for $C_{16}H_{27}NO$ (249.2093): C, 77.06; H, 10.91; N, 5.62. Found: C, 77.00; H, 10.81; N, 5.60.

***tert*-Butyl 4-(((*R*)-1-(4-methoxyphenyl)ethyl)amino)-2-oxopiperidine-1-carboxylate (5h):** colorless liquid (thick); yield 30.6 mg (88%); $[\alpha]^{22.8}_D$ −15.4 (c 0.2, MeOH); HPLC using Chiralpak IC at flow rate 0.6 mL/min, IPA/MeCN/Hex (5:6:89, isocratic), t_R 22.98 min (87%), 26.11 min (6.4%), 31.86 (5.8%), 0.3%); IR (neat, ν_{max}, cm^{-1}) 3285.6, 2154.7, 1685.9, 1635.2, 1045.3, 995.8; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.34 (d, J = 7.7 Hz, 2H), 6.78 (d, J = 8.2 Hz, 2H), 4.15−3.91 (m, 1H), 3.91−3.53 (m, 5H), 2.41−2.15 (m, 2H), 1.57−1.17 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 175.0, 160.0, 154.1, 138.9, 128.1, 114.3, 83.9, 58.3, 54.7, 48.1, 46.3, 40.4, 39.0, 33.5, 27.9, 27.5, 23.5; ES-MS (M + H$^+$, m/z) 349.5; HRMS calcd for $C_{19}H_{28}N_2O_4$ 348.2049, found 348.2040.

***tert*-Butyl (*R*)-3-(((*R*)-1-(4-methoxyphenyl)ethyl)amino)-piperidine-1-carboxylate (5i):** colorless liquid; yield 28.4 mg (85%); $[\alpha]^{19.6}_D$ +32.8 (c 0.23, IPA); HPLC using Chiralpak IA at flow rate 0.7 mL/min, IPA/Hex/TEA (4.5:93.5:0.01, isocratic) t_R 8.8 min (0.093%), 9.5 min (94.26%), 10.3 min (4.7%) and 11.2 min (0.004%); IR (neat, ν_{max}, cm^{-1}) 3368.3, 1562.3, 1356.2, 1236.8; 1056.9, 994.6; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.17 (d, J = 8.0 Hz, 2H), 6.80 (d, J = 7.9 Hz, 2H), 4.08−3.57 (m, 4H), 3.46−3.08 (m, 2H), 3.07−2.58 (m, 3H), 1.79−1.39 (m, 13H), 1.29 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 160.1, 157.2, 138.1, 128.6, 114.9, 78.9, 57.5, 54.7, 51.1, 50.0, 46.3, 42.3, 33.5, 30.3, 28.2, 24.5, 16.8; ES-MS (M + Na$^+$, m/z) 334.8, 335.4; HRMS calcd for $C_{19}H_{30}N_2O_3$ 334.2256, found 334.2261.

***tert*-Butyl (*R*)-(3-((1-(4-methoxyphenyl)ethyl)amino)propyl)-(methyl)carbamate (5j):** colorless liquid; yield 28.3 mg (88%); $[\alpha]^{15.9}_D$ −21.5 (c 0.15, MeOH); HPLC using Chiralpak IA flow rate 0.5 mL/min, IPA/Hex/TEA (6.5:93.5:0.01, isocratic) t_R 14.2 (99.4%) and 19.2 min (0.6%); IR (neat, ν_{max}, cm^{-1}) 3362.3, 1685.3, 1602.3, 1582.3, 1286.8; 1026.9, 994.6; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.17 (d, J = 7.9 Hz, 2H), 6.83 (d, J = 7.9 Hz, 2H), 4.03−3.57 (m, 4H), 3.15 (dt, J = 12.4, 7.1 Hz, 5H), 2.87−2.51 (m, 3H), 2.01−1.62 (m, 2H), 1.39 (d, J = 24.6 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 160.1, 157.4, 138.8, 128.5, 114.8, 77.4, 57.8, 54.7, 46.3, 45.1, 35.8, 33.5, 28.9, 27.8, 24.1; ES-MS (M + H$^+$, m/z) 323.5; HRMS calcd for $C_{18}H_{30}N_2O_3$ 322.2256, found 322.2260.

Methyl (*R*)-2-(hex-5-en-1-ylamino)-2-(1*H*-indol-3-yl)acetate (6a): colorless liquid; yield 24.3 mg (85%); $[\alpha]^{21.5}_D$ −8.6 (c 0.2, CH_2Cl_2); HPLC using Chiralpak IC at flow rate 0.6 mL/min, IPA/Hex/TEA (6.5:93.5:0.01, isocratic) t_R 16.5 min (95.5%) and 19.7 min (4.5%); IR (neat, ν_{max}, cm^{-1}) 3367.3, 1764.3, 1368.2, 1286.7; 1054.9, 964.4; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 8.54−8.05 (brs, 1H), 8.00−7.74 (m, 1H), 7.71−7.40 (m, 2H), 7.33−6.98 (m, 2H), 6.10−5.45 (m, 1H), 5.19−4.84 (m, 2H), 4.75 (d, J = 6.2 Hz), 3.70 (s, 3H), 2.89−2.58 (m, 2H), 2.51−2.17 (brs, 1H), 2.01−1.65 (m, 2H), 1.65−1.44 (m, 2H), 1.41−1.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 171.9, 136.3, 134.4, 129.6, 124.2, 121.5, 120.7, 119.1, 115.3, 111.2, 111.1, 55.0, 51.6, 47.1, 35.0, 28.9, 28.8; ES-MS (M + H$^+$, m/z) 287.5; HRMS calcd for $C_{17}H_{22}N_2O_2$ 286.1681, found 286.1678.

(*S*)-*N*-(1-phenylethyl)prop-2-en-1-amine (6b): colorless liquid; yield 13.2 mg (86%); $[\alpha]^{21.5}_D$ −12.8 (c 0.4, EtOH); HPLC using Chiradex at flow rate 0.6 mL/min, H_2O/IPA/TEA (6.5:93.5:0.005, isocratic) t_R 26.5 min (99.2%) and 29.7 min (0.8%); IR (neat, ν_{max}, cm^{-1}) 3354.2, 1326.3, 1226.4; 1032.9, 984.6; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.25 (m, 4H), 7.19−6.91 (m, 1H), 6.14−5.61 (m, 1H), 5.43−4.90 (m, 2H), 4.03−3.65 (m, 1H), 3.53−3.03 (m, 2H), 2.17−1.86 (m, 1H), 1.39 (d, J = 5.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 144.8, 133.5, 128.5, 127.4, 126.6, 115.0, 52.1, 50.6, 22.8; ES-MS (M + H$^+$, m/z) 162.5; HRMS calcd for $C_{11}H_{15}N$ 161.1204, found 161.1208.

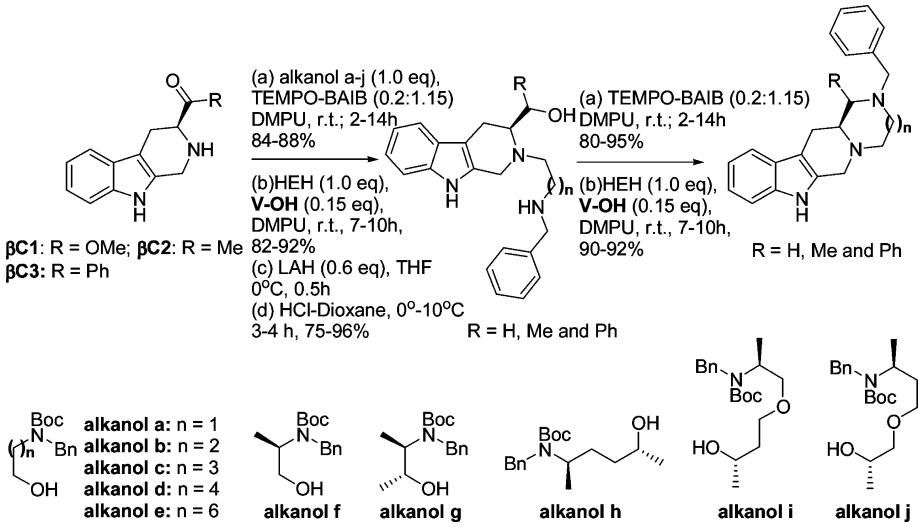
(*R*)-4-(Pyrrolidin-1-yl)piperidin-2-one (6c): colorless liquid; yield 12.6 mg (75%); $[\alpha]^{18.7}_D$ −73.9 (c 1.0 MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (6.5:93.5, isocratic) t_R 10.3 (96) and 8.7 min (4%); IR (neat, ν_{max}, cm^{-1}) 3368.3, 1675.2, 1545.3, 1338.2, 1126.8; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.19−5.62 (m, 1H), 3.70−3.33 (m, 2H), 2.91−2.80 (m, 1H), 2.81−2.53 (m, 4H), 2.44−2.12 (m, 2H), 2.03−1.65 (m, 5H), 1.62−1.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 174.2, 56.8, 50.8, 40.2, 38.2, 30.3, 23.9; ES-MS (M + H$^+$, m/z) 169.5; HRMS calcd for $C_9H_{16}N_2O$ 168.1263, found 168.1265.

***N*-((*R*)-3,3-Dimethylcyclohexyl)adamantan-1-amine (6d):** colorless liquid; yield 21.1 mg (81%); $[\alpha]^{19.5_D}$ +52.6 (c 0.5, IPA); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (6.5:93.5, isocratic) t_R 16.8 min (96) and 24.7 min (3.5%); IR (neat, ν_{max}, cm^{-1}) 3356.3, 2856.3; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.48 (m, 1H), 2.00 (s, 3H), 1.82−1.41 (m, 19H), 1.41−1.18 (m, 3H), 0.93 (d, J = 23.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 53.4, 46.8, 43.3, 39.8, 39.2, 38.0, 36.1, 32.4, 32.0, 30.5, 26.8, 22.2; ES-MS (M + H$^+$, m/z) 262.2. Anal. Calcd for $C_{18}H_{31}N$ (261.2457): C, 82.69; H, 11.95; N, 5.36. Found: C, 82.64; H, 11.90; N, 5.32.

(*S*)-1-(1-(Cyclohex-1-en-1-yl)pentyl)piperidine (6e): colorless liquid; yield 18.3 mg (78%); $[\alpha]^{16.5}_D$ +19.8 (c 0.2, EtOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min IPA/Hex (1:99 → 6.8:93.2, gradient) t_R 15.3 (6%) and 18.7 min (94.1%); IR (neat, ν_{max}, cm^{-1}) 3248.9, 2856.9, 1562.3, 1258.9; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 5.43 (t, J = 6.7 Hz, 1H), 2.89−2.67 (m, 4H), 2.67−2.46 (m, 1H), 2.32−1.81 (m, 4H), 1.81−1.50 (m, 10H), 1.50−1.29 (m, 4H), 1.29−1.03 (m, 2H), 1.03−0.60 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 139.8, 119.9, 68.7, 55.4, 32.4, 31.2, 28.2, 26.8, 26.16, 26.10, 25.8, 23.4, 21.6, 13.7; ES-MS (M + H$^+$, m/z) 236.5; HRMS calcd for $C_{16}H_{29}N$ 235.2300, found 235.2305.

(*R*)-1-(2-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-4-methyl-9*H*-carbazol-3-yl)-*N*,*N*-dimethylethan-1-amine (6f): colorless solid; yield 34.8 mg (85%); mp 154 °C; $[\alpha]^{22.8}_D$ +21.5 (c 0.2, MeOH);

Scheme 3. Representative Scheme Used for the Synthesis of Compounds 7a−h and 8a−f



HPLC using Chiralpak IC flow rate 0.6 mL/min, IPA/Hex:TEA (6.5:93.5:0.005, isocratic) t_R 10.5 min (97) and 8.7 min (3%); IR (neat, ν_{max}, cm^{-1}) 3154.8, 2857.9, 1502.6, 1254.7, 1128.9, 1084.6, 995.7; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.17 (t, J = 11.8 Hz, 2H), 7.42−7.19 (m, 3H), 7.14 (s, 1H), 4.16 (d, J = 6.6 Hz, 1H), 4.01−3.67 (m, 2H), 2.89−2.74 (m, 2H), 2.66 (s, 3H), 2.20 (s, 6H), 1.45 (d, J = 6.5 Hz, 3H), 0.98 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 140.7, 135.1, 131.8, 128.2, 127.4, 126.2, 122.2, 121.0, 120.8, 116.8, 111.8, 103.4, 63.2, 59.9, 41.5, 33.6, 26.5, 21.6, 18.9, 15.7, −5.7; ES-MS (E + H^+, m/z) 411.5; HRMS calcd for $C_{25}H_{38}N_2OSi$ 410.2753, found 410.2751.

(*R*)-*N*-(1-(9*H*-Carbazol-3-yl)ethyl)-*N*-isopropylpropan-2-amine (6g): yellow solid; yield 34.8 mg (85%); mp 169−170 °C; $[\alpha]_D^{18.8}$ +52.5 (*c* 0.55, EtOH); HPLC using Chiralpak IC flow rate 0.6 mL/min, IPA/Hex (7:93, isocratic) t_R 25.27 min (97.5) and 26.5 min (2.5%); ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 8.51 (brs, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.61−7.22 (m, 5H), 7.11 (td, J = 7.0, 3.2 Hz, 1H), 4.20 (d, J = 6.4 Hz, 1H), 2.99 (dd, J = 12.9, 6.6 Hz, 2H), 1.43 (d, J = 6.2 Hz, 3H), 1.09 (d, J = 5.6 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 141.7, 140.6, 138.4, 125.5, 125.2, 122.3, 121.9, 120.6, 117.7, 117.2, 112.4, 107.3, 56.3, 52.3, 46.3, 33.4, 24.8, 22.9, 22.5; ES-MS (M + H^+, m/z) 295.3. Anal. Calcd for $C_{20}H_{26}N_2$ (294.2096): C, 81.58; H, 8.90; N, 9.51. Found: C, 81.52; H, 8.85; N, 9.42.

(*S*)-*N*,*N*-Diisopropyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-amine (6h): colorless liquid; yield 23.0 mg (85%); $[\alpha]^{18.2}_D$ −28.7 (*c* 0.12, $CHCl_3$); HPLC using Chiralpak IA at flow rate 0.7 mL/min, IPA/Hex (6.5:93.5, isocratic) t_R 19.4 min (96%) and 21.8 min (4%); IR (neat, ν_{max}, cm^{-1}) 3162.5, 2658.4, 1468.3, 1279.6, 1284.5, 1156.2; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.80 (brs, 1H), 7.47 (s, 1H), 7.34−6.83 (m, 3H), 3.44−3.06 (m, 3H), 2.92−2.68 (m, 3H), 2.61−2.32 (m, 1H), 2.01−1.58 (m, 1H), 1.58−1.14 (m, 1H), 0.79 (d, J = 5.8 Hz, 14H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 136.2, 132.0, 129.7, 121.3, 120.1, 118.0, 110.8, 107.7, 51.9, 49.2, 28.7, 23.2, 22.5, 22.2; ES-MS (M + H^+, m/z) 271.5. Anal. Calcd for $C_{18}H_{26}N_2$ (270.2096): C, 79.85; H, 9.69; N, 10.36. Found: C, 79.81; H 9.65; N, 10.30.

(*S*)-*N*-Allyl-2,3-dihydro-1*H*-inden-1-amine (6i): colorless liquid; yield 16.6 mg (98%); $[\alpha]^{13.7}_D$ −22.5 (*c* 0.08, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (1:99 → 6.5:93.5, gradient over 30 min) t_R 8.7 min (4.7%) and 14.5 min (95.3%); IR (neat, ν_{max}, cm^{-1}) 3456.2, 2587.6, 1524.3, 1256.3, 1152.3, 991.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.41−7.27 (m, 1H), 7.24−6.86 (m, 3H), 5.86 (dt, J = 10.0, 5.1 Hz, 1H), 5.21 (d, J = 10.2 Hz, 1H), 5.03 (d, J = 16.6 Hz, 1H), 4.22 (d, J = 7.7 Hz, 1H), 3.47−3.06 (m, 4H), 3.04−2.86 (m, 1H), 2.84−2.61 (m, 1H), 2.31−2.01 (m, 1H), 2.02−1.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 142.2, 139.7, 134.0, 128.3, 128.2, 127.0, 125.2, 115.2, 61.2, 51.4, 31.8, 24.4; ES-MS (M + H^+, m/z) 174.2. Anal. Calcd for $C_{12}H_{15}N$ (173.1204): C, 83.19; H, 8.73; N, 8.08. Found: C, 83.12; H, 8.70; N, 8.67.

(1*R*)-*N*-Benzyl-N,3-dimethylcyclohexan-1-amine (6j): colorless liquid; yield 15.4 mg (76%); $[\alpha]^{18.8}_D$ −38.5 (*c* 0.21, $CHCl_3$); HPLC using Chiralpak IA at flow rate 0.8 mL/min, IPA/Hex/DIPEA (6.0:93.5:0.003, isocratic) t_R 18.3 min (94.5%) and 16.7 min (5.5%); IR (neat, ν_{max}, cm^{-1}) 2586.3, 1514.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.61−7.34 (m, 3H), 7.34−6.99 (m, 2H), 3.45 (q, J = 13.9 Hz, 2H), 3.19−3.04 (m, 1H), 2.27 (s, 3H), 2.13−1.89 (m, 1H), 1.89−1.53 (m, 4H), 1.53−1.28 (m, 3H), 1.19−0.74 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 136.2, 132.0, 129.7, 121.3, 120.1, 118.0, 110.8, 107.7, 51.9, 49.2, 28.7, 23.2, 22.5, 22.2; ES-MS (M + H^+, m/z) 204.2; HRMS calcd for $C_{14}H_{21}N$ 203.1674, found 203.1672.

(*R*)-*N*-Allyl-1,2,3,4-tetrahydronaphthalen-1-amine (6k): colorless liquid; yield 13.5 mg (72%); $[\alpha]^{17.5}_D$ +8.5 (*c* 0.095, EtOH); HPLC using Chiralpak IA at flow rate 0.5 mL/min, IPA/Hex (5:96.5) t_R 11.3 min (97.5%) and 16.3 min (2.5%); IR (neat, ν_{max}, cm^{-1}) 3312.5, 3456.2, 2857.4, 1562.3, 1254.6, 1156.3, 1005.3; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.39−6.61 (m, 4H, ArH), 6.06−5.68 (m, 1H), 5.21 (d, J = 9.5 Hz, 1H), 5.03 (d, J = 16.8 Hz, 1H), 3.94 (d, J = 8.8 Hz, 1H), 3.14−3.01 (m, 2H), 2.92−2.61 (m, 2H), 2.43−2.09 (m, 3H), 2.07−1.88 (brs, 1H), 1.68−1.28 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 137.3, 136.2, 134.2, 129.6, 127.8, 126.7, 125.9, 115.2, 51.2, 51.1, 31.3, 29.5, 21.8; ES-MS (M + H^+) 188.4. Anal. Calcd for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.30; H, 9.05; N, 7.46.

General Procedure for the Synthesis of Compounds 7a−h and 8a−f Using the Intramolecular Oxidation/Imine−Iminium Formation/Reductive Amination Cascade. *Step I.* 2,2,6,6-Tetramethyl-1-piperidinyloxyl TEMPO (30 mg, 0.2 mmol, 0.2 equiv) and [bis(acetoxy)iodo]benzene BAIB (370 mg, 1.15 mmol, 1.15 equiv) were added to a stirred solution of specified alkanols (alkanol **a−j**, 1 mmol) in CH_2Cl_2 (4 mL), and the mixture was stirred at rt until complete conversion of alcohol (2−10 h) checked by TLC or GC/MS. Then, the specified amine (**βC1−3**; 1 mmol, 1 equiv), HEH (or similar reagent when specified) (414 mg, 1 mmol, 1 equiv), and chiral Brønsted acid (15 mol %) were added to the reaction mixture. After a few hours (2−10 h), the mixture was quenched carefully with aq $NaHCO_3$ (10 mol %, 10 mL) and extracted with Et_2O or EtOAc (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification was achieved by using one of the methods (method A−C) mentioned above in the intramolecular oxidation/imine−iminium formation/reductive amination procedure to obtain **SMa−j**.

Step II. The compounds (**SMa−j**) thus obtained were dissolved in 3 mL of THF (dry) under nitrogen atmosphere, and the thus obtained solution was then added dropwise to a suspension of LAH (0.6 equiv)

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under nitrogen atmosphere at 0 °C after the completion of the reduction the reduced crude product obtained by the aqueous work. The isolated crude product was purified through column chromatography. The purified product was then dissolved in HCl−dioxane to obtain the starting material for the intramolecular cyclization mediated through oxidation/imine−iminium formation/reductive amination following the general procedure mentioned above (Scheme 3).

(*S*)-2-Benzyl-1,2,3,4,6,7,12,12a-octahydropyrazino[1′,2′:1,6]-pyrido[3,4-*b*]indole (7a): colorless solid; yield 27.5 mg (87%); mp 124−128 °C; $[\alpha]^{21.6}_{D}$ −58.6 (*c* 0.3, $CHCl_3$); HPLC using Chiralpak IA t_R at flow rate 0.6 mL/min, IPA/Hex/DIPEA (6.5:93.5:0.01, gradient) 21.3 min (99%) and 26.7 min (1%); IR (neat, ν_{max}, cm^{-1}) 3154.6, 2568.6, 1502.3, 1463.2, 1256.3, 1102.3, 996.3; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H), 7.53 (d, *J* = 7.4 Hz, 1H), 7.38 (d, *J* = 7.1 Hz, 2H), 7.24−7.05 (m, 5H), 6.96 (q, *J* = 7.4 Hz, 1H), 3.55 (dd, *J* = 29.3, 15.2 Hz, 2H), 3.48 (s, 2H), 3.29 (dd, *J* = 11.6, 4.3 Hz, 1H), 2.94 (dd, *J* = 15.9, 7.2 Hz, 1H), 2.76 (dd, *J* = 11.3, 8.2 Hz, 1H), 2.71−2.39 (m, 5H), 2.03 (dd, *J* = 11.2, 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 139.7, 136.5, 131.9, 129.3, 128.2, 127.1, 125.8, 120.9, 118.8, 118.3, 110.6, 108.4, 63.3, 62.0, 58.0, 51.3, 51.0, 26.0; ES-MS (M + H^+, *m*/*z*) 318.3. Anal. Calcd for $C_{21}H_{23}N_3$ (317.1892): C, 79.46; H, 7.30; N, 13.24. Found: C, 79.40; H, 7.26; N, 13.18.

(*S*)-2-Benzyl-2,3,4,5,7,8,13,13a-octahydro-1*H*-[1,4]diazepino-[1′,2′:1,6]pyrido[3,4-*b*]indole (7b): colorless sticky semisolid; yield 26.8 mg (81%); $[\alpha]^{21.6}_{D}$ −42.8 (*c* 0.25, $CHCl_3$); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (6.5:93.5, isocratic), t_R 14.3 min (97%) and 12.3 min (3%); IR (neat, ν_{max}, cm^{-1}) 3185.6, 3105.2, 2154.6, 1358.6, 1204.2, 1152.3, 985.3; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.27 (dt, *J* = 13.1, 5.7 Hz, 2H), 7.23−7.15 (m, 4H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.65 (s, 2H), 3.39 (q, *J* = 15.0 Hz, 2H), 3.17 (tt, *J* = 11.1, 5.6 Hz, 1H), 3.03 (dt, *J* = 12.7, 6.0 Hz, 1H), 2.93−2.60 (m, 6H), 2.59−2.42 (m, 2H), 1.65 (p, *J* = 5.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.8, 136.5, 133.8, 129.2, 128.2, 127.6, 127.5, 120.9, 118.8, 117.8, 111.0, 110.6, 63.3, 58.0, 56.5, 52.0, 50.2, 48.0, 27.9, 25.4; ES-MS (M + Na^+, M + H^+, *m*/*z*) 354.2, 332.5. Anal. Calcd for $C_{22}H_{25}N_3$ (331.2048): C, 79.72; H, 7.60; N, 12.68. Found: C, 79.65; H, 7.54; N, 12.60.

(*S*)-2-Benzyl-1,2,3,4,5,6,8,9,14,14a-decahydro[1,4]diazocino-[1′,2′:1,6]pyrido[3,4-*b*]indole (7c): colorless solid; yield 24.8 mg (72%); mp 167−169 °C; $[\alpha]_{D}^{18.5}$ −28.4 (*c* 0.18, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (6.5:93.5), t_R 16.3 (97%) and 18.7 min (2.5%); IR (KBr, ν_{max}, cm^{-1}) 3125.6, 2845.7, 1563.2, 1236.3, 1185.6, 1054.6, 986.3; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.38−7.28 (m, 2H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.20−7.15 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.64 (s, 2H), 3.38 (q, *J* = 15.0 Hz, 2H), 3.12 (dd, *J* = 8.5, 5.3 Hz, 1H), 2.86−2.76 (m, 1H), 2.71 (t, *J* = 4.7 Hz, 2H), 2.58 (d, *J* = 4.7 Hz, 2H), 2.47 (dt, *J* = 9.6, 5.2 Hz, 3H), 1.57−1.47 (m, 2H, CH_2), 1.46−1.36 (m, 2H, CH_2); ^{13}C NMR (100 MHz,$CDCl_3$, ppm) δ 140.8, 136.5, 133.8, 129.2, 128.2, 127.6, 127.5, 120.92, 118.8, 117.8, 111.0, 110.6, 63.3, 58.0, 56.5, 52.0, 50.2, 48.0, 27.9, 25.4; ES-MS (M + H^+, *m*/*z*) 346.5. Anal. Calcd for $C_{23}H_{27}N_3$ (345.2205): C, 79.96; H, 7.88; N, 12.16. Found: C, 79.90; H, 7.84; N, 12.10.

(*S*)-2-Benzyl-2,3,4,5,6,7,9,10,15,15a-decahydro-1*H*-[1,4]-diazonino[1′,2′:1,6]pyrido[3,4-*b*] indole (7d): colorless solid; yield 24.4 mg (68%); mp 142 °C; $[\alpha]^{19.5}_{D}$ −38.9 (*c* 0.36, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min IPA/Hex (6.5:93.5, isocratic), t_R 17.3 min (93%) and 18.7 min (6.8%); IR (KBr, ν_{max}, cm^{-1}) 3256.6, 2157.6, 1569.3, 1426.3, 1205.3, 995.3; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.30 (dt, *J* = 10.3, 4.7 Hz, 2H), 7.23 (t, *J* = 5.5 Hz, 1H, ArH), 7.17 (dd, *J* = 3.0, 0.7 Hz, 3H), 7.14−7.05 (m, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.70 (s, 2H), 3.26 (q, *J* = 15.0 Hz, 2H), 3.17−3.04 (m, 1H), 2.95−2.83 (m, 1H), 2.70 (t, *J* = 4.8 Hz, 2H), 2.55 (dd, *J* = 14.2, 5.3 Hz, 3H,), 2.49 (t, *J* = 4.7 Hz, 2H), 1.57−1.45 (m, 2H), 1.45−1.31 (m, 2H), 0.98 (dq, *J* = 13.4, 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 141.3, 136.3, 136.0, 128.8, 128.2, 127.5, 127.4, 120.9, 118.8, 118.1, 112.4, 110.9, 63.1, 56.7, 54.8, 54.1, 52.3, 51.7, 29.4, 28.6, 26.2, 22.3; ES-MS (M + H^+, *m*/*z*) 360.2; HRMS calcd for $C_{24}H_{29}N_3$ 359.2361, found 359.2354.

(*S*)-2-Benzyl-2,3,4,5,6,7,8,9,11,12,17,17a-dodecahydro-1*H*-[1,4]-diazacycloundecino[1′,2′:1,6]pyrido-[3,4-*b*]indole (7e): yellow solid; yield 23.6 mg (61%); mp 157−159 °C; $[\alpha]^{19.5}_{D}$ −31.8 (*c* 0.24, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min, IPA/Hex (6.5:93.5, isocratic) t_R 14.3 min (96%) and 17.3 min (4%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.39−7.28 (m, 2H), 7.23 (t, *J* = 5.5 Hz, 1H), 7.20−7.15 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.68 (s, 2H), 3.26 (q, *J* = 15.0 Hz, 2H), 3.11−2.98 (m, 1H), 2.96−2.76 (m, 1H), 2.66 (dd, *J* = 12.2, 4.8 Hz, 4H), 2.54 (dd, *J* = 16.0, 5.4 Hz, 1H), 2.45 (t, *J* = 4.8 Hz, 2H), 1.67−1.48 (m, 2H), 1.47−1.34 (m, 2H), 1.28 (td, *J* = 4.9, 0.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.9, 136.3, 135.3, 128.8, 128.2, 127.5, 120.9, 118.8, 118.1, 111.7, 110.9, 63.49, 59.41, 55.36, 53.7, 53.2, 51.4, 30.0, 29.5, 26.8, 25.95 25.0, 24.5; ES-MS (M + H^+, *m*/*z*) 388.8; HRMS calcd for $C_{26}H_{33}N_3$ 387.2674, found 387.2668.

(1*R*,12a*S*)-2-Benzyl-1-methyl-1,2,3,4,6,7,12,12a-octahydro-pyrazino[1′,2′:1,6]pyrido[3,4-*b*]indole (7f): deep yellow solid; yield 27.4 mg (81%); mp 148 °C; $[\alpha]^{16.8}_{D}$ +14.9 (*c* 0.39, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min IPA/Hex:DIPEA (5:95:0.002, isocratic) t_R 10.5 (2.46%), 11.3 min (96.03%), 13.8 min (1.46%%), 14.6 min (0.03%); IR (neat, ν_{max}, cm^{-1}) 3325.3, 2856.6, 1547.7, 1254.8, 1105.6, 968.3; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H, NH), 7.57−7.42 (m, 3H), 7.36−7.23 (m, 3H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.90 (d, *J* = 13.2 Hz, 1H, BenzylC*H*H), 3.67−3.32 (m, 3H, benzylCH*H*, 2-indoleCH_2), 3.13−2.94 (m, 2H, 3-indoleCH*H*, α-CH), 2.94−2.77 (m, 1H, CH), 2.76−2.62 (m, 3H, 3-indoleC*H*H, NC*H*HC*H*HN), 2.61−2.46 (m, 2H), 1.26 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 139.1, 137.0, 131.7, 129.1, 128.4, 127.3, 125.6, 120.9, 118.8, 118.3, 110.6, 109.3, 63.9, 62.9, 59.4, 51.4, 51.1, 50.9, 24.9, 11.7; ES-MS(M + H^+, *m*/*z*) 332.6; HRMS calcd for $C_{22}H_{25}N_3$ 331.2048, found 331.2051.

(1*R*,13a*S*)-2-Benzyl-1-phenyl-2,3,4,5,7,8,13,13a-octahydro-1*H*-[1,4]diazepino[1′,2′:1,6]pyrido[3,4-*b*]indole (7g): colorless semi-solid; yield 32.1 mg (81%); $[\alpha]^{22.4}_{D}$ +19.4 (*c* 0.15, MeOH; HPLC using Chiralpak IA at flow rate 0.6 mL/min IPA/Hex/DIPEA (5:95:0.05, isocratic) t_R 8.2 min (0.2%); 8.7 min (0.09%); 9.7 min (2.7%) and 9.9 min (96%); IR (neat, ν_{max}, cm^{-1}) 3354.6, 2865.3, 1563.2, 1228.6, 1004.3; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (brs, 1H, NH), 7.54 (d, *J* = 7.8 Hz, 1H), 7.23 (dtdd, *J* = 32.6, 25.2, 11.0, 7.1 Hz, 13H), 6.96 (t, *J* = 7.6 Hz, 1H), 4.21 (d, *J* = 4.9 Hz, 1H, PhCH), 3.98−3.69 (m, 2H, benzylC*H*H), 3.47 (q, *J* = 15.0 Hz, 2H, 2-indoleCH_2), 3.28 (ddd, *J* = 12.4, 10.2, 9.5 Hz, 2H), 3.17−2.94 (m, 3H), 2.88 (d, *J* = 8.1 Hz, 2H), 2.86−2.69 (m, 3H), 2.64 (dd, *J* = 15.6, 5.7 Hz, 1H), 1.84−1.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.8, 139.5, 136.3, 133.7, 129.2, 128.2, 128.1, 127.6, 127.4, 127.0, 126.2, 120.9, 118.8, 117.6, 110.6, 108.7, 62.7, 59.4, 51.0, 50.8, 50.0, 46.3, 33.4, 27.7, 24.6, 22.5; ES-MS (M + H^+, *m*/*z*) 408.5. Anal. Calcd for $C_{28}H_{29}N_3$ (407.2361): C, 82.52; H, 7.17; N, 10.31. Found: C, 82.40; H, 7.10; N, 10.28.

(1*R*,14a*S*)-2-Benzyl-1-phenyl-1,2,3,4,5,6,8,9,14,14a-decahydro-[1,4]diazocino[1′,2′:1,6]pyrido[3,4-b]indole (7h): yellow glassy liquid, yield 33.6 mg (75%); $[\alpha]^{22.4}_{D}$ +19.4 (*c* 0.15, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min IPA/Hex:DIPEA (6.5:93.5:0.005, isocratic) t_R 8.3 (97.5%) and 7.7 min (2.5); IR (neat, ν_{max}, cm^{-1}) 3321.4, 2562.3, 1425.3, 1263.5, 1002.3; ^{1}H NMR (400 MHz, CDCl3, ppm) δ 8.01 (brs, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.40−7.34 (m, 2H), 7.33−7.21 (m, 6H), 7.20−7.14 (m, 3H), 7.12 (dd, *J* = 13.3, 5.9 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 4.21 (d, *J* = 4.9 Hz, 1H, PhCH), 3.80 (d, *J* = 13.4 Hz, 1H, benzylC*H*H), 3.46 (q, *J* = 15.0 Hz, 2H, benzylC*H*H, α−CH), 3.31 (d, *J* = 13.5 Hz, 1H), 3.25−3.13 (m, 1H), 2.97 (dd, *J* = 15.4, 8.6 Hz, 1H), 2.83 (ddd, *J* = 14.4, 7.9, 4.7 Hz, 4H), 2.61 (dd, *J* = 15.6, 5.7 Hz, 1H), 1.57 (ddd, *J* = 6.3, 4.3, 2.5 Hz, 2H), 1.44 (dd, *J* = 7.9, 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 128.7, 128.2, 127.6, 126.7, 126.2, 120.9, 118.8, 117.9, 110.9, 77.4, 77.0, 76.6, 73.3, 62.2, 59.0, 54.4, 53.5, 49.9, 46.2, 33.4, 31.4, 27.3, 24.2; ES-MS (M + H^+, *m*/*z*) 422.4. Anal. Calcd for $C_{29}H_{31}N_3$ (421.2518): C, 82.62; H, 7.14; N, 9.97. Found: C, 82.58; H, 7.11; N, 9.92.

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(3*S*,12a*S*)-2-Benzyl-3-methyl-1,2,3,4,6,7,12,12a-octahydropyrazino[1′,2′:1,6]pyrido[3,4-*b*]indole (8a): yellow solid; yield 28.7 mg (87%); mp 163−165 °C; $[\alpha]^{20.2}_{D}$ +29.9 (*c* 0.09, MeOH); HPLC using Chiralpak IA at flow rate 0.7 mL/min, IPA/Hex (6.5:93.5, isocratic) t_R 10.2 (99%) and 9.5 min (1%);^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.01 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.34−7.15 (m, 6H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 4.00−3.84 (m, 1H), 3.53−3.30 (m, 3H), 3.30−3.07 (m, 1H), 3.04−2.85 (m, 2H), 2.79 (ddd, *J* = 18.1, 7.7, 4.1 Hz, 2H), 2.64 (dd, *J* = 16.8, 7.8 Hz, 1H), 2.18−1.93 (m, 2H), 1.18 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.8, 136.4, 134.0, 128.9, 128.2, 127.4, 125.6, 120.9, 118.7, 118.6, 110.9, 109.7, 59.2, 58.4, 56.0, 55.8, 53.1, 50.5, 26.4, 16.0; ES-MS (M + H$^+$, *m*/*z*) 332.5; HRMS calcd for $C_{22}H_{25}N_3$ 331.2048, found 331.2035.

(3*S*,4*S*,12a*S*)-2-Benzyl-3,4-dimethyl-1,2,3,4,6,7,12,12a-octahydropyrazino[1′,2′:1,6]pyrido[3,4-*b*]indole (8b): colorless gum; yield 27.9 mg (81%); $[\alpha]^{22.9}_{D}$ +19.6 (*c* 0.21, MeOH); HPLC Chiralpak using Chiralpak IA flow rate 0.6 mL/min, IPA/Hex/DIPEA (4:95.5:0.001, isocratic) t_R 15.8 min (1%) anf 19.3 min (99%); IR (neat, ν_{max}, cm^{-1}) 3354.2, 1524.3, 1236.5, 995.6; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.36−7.19 (m, 6H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.81 (dt, *J* = 27.6, 14.3 Hz, 3H), 3.44 (d, *J* = 13.8 Hz, 1H), 3.36−3.16 (m, 1H), 2.86−2.62 (m, 4H), 2.54 (dd, *J* = 16.8, 7.8 Hz, 1H), 2.02 (dd, *J* = 11.6, 8.2 Hz, 1H), 1.06 (d, *J* = 5.9 Hz, 3H), 1.01 (d, *J* = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.4, 136.8, 133.6, 129.0, 128.4, 127.6, 126.0, 120.9, 118.8, 118.6, 110.9, 109.6, 60.9, 60.8, 59.7, 56.2, 52.1, 50.6, 26.2, 13.5, 12.4; ES-MS (M + H$^+$, *m*/*z*) 346.5; HRMS calcd for $C_{23}H_{27}N_3$ 345.2205, found 345.2201.

(1*R*,3*S*,4*S*,12a*S*)-2-Benzyl-3,4-dimethyl-1-phenyl-1,2,3,4,6,7,12,12a-octahydropyrazino[1′,2′:1,6]pyrido[3,4-*b*]indole (8c): light pink solid; yield 35.7 mg (81%); mp 144−146 °C; $[\alpha]^{18.4}_{D}$ −6.3 (*c* 0.2 MeOH); HPLC using a Chiradex flow rate 0.6 mL/min H_2O/IPA (86.5:14.4, gradient over 25 min), t_R 10.3 min (99.01%) and 12.36 min (0.98%); IR (neat, ν_{max}, cm^{-1}) 3524.2, 2785.4, 1524.3, 1324.8, 1185.6, 996.1; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00 (brs, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.37−7.29 (m, 4H), 7.29−7.21 (m, 4H), 7.21−7.14 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.93 (d, *J* = 13.5 Hz, 1H), 3.82 (dt, *J* = 27.3, 9.5 Hz, 2H), 3.61 (d, *J* = 13.5 Hz, 1H), 3.38 (s, 1H), 3.14−3.04 (m, 1H), 2.96 (dd, *J* = 16.8, 5.7 Hz, 1H), 2.92−2.73 (m, 3H), 2.67 (dd, *J* = 16.8, 11.7 Hz, 1H), 1.12 (d, *J* = 6.1 Hz, 3H), 0.97 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.1, 139.5, 136.7, 133.4, 131.9, 129.0, 128.3, 127.6, 127.0, 126.6, 125.8, 120.9, 118.7, 118.4, 110.9, 107.5, 63.6, 62.0, 60.7, 56.2, 50.6, 25.4, 13.3, 11.4; ES-MS (M + H$^+$, *m*/*z*) 422.3; HRMS calcd for $C_{29}H_{31}N_3$ 421.2518, found 421.2514.

(3*S*,6*S*,14a*S*)-2-Benzyl-3,6-dimethyl-1,2,3,4,5,6,8,9,14,14a-decahydro[1,4]diazocino[1′,2′:1,6]pyrido[3,4-*b*]indole (8d): colorless gum; yield 29.4 mg (79%); $[\alpha]^{21.8}_{D}$ −11.9 (*c* 0.32, MeOH); HPLC using Chiralpak IA flow rate 0.6 mL/min IPA/Hex/*n*-butanol (5:94:1, isocratic) t_R 17.3 (96.0%) and 24.7 min (3.99%); IR (neat, ν_{max}, cm^{-1}) 3125, 1563.4, 1436.2, 1165.3, 1036.2, 991.2; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00 (brs, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.35−7.18 (m, 6H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.94 (d, *J* = 13.5 Hz, 1H), 3.64−3.28 (m, 3H), 3.23−3.01 (m, 1H), 2.98−2.66 (m, 4H), 2.57 (d, *J* = 5.6 Hz, 2H), 2.44 (dd, *J* = 16.8, 6.9 Hz, 1H), 1.95−1.72 (m, 2H), 1.63 (dd, *J* = 12.4, 5.8 Hz, 2H), 1.09 (d, *J* = 6.3 Hz, 3H), 1.00 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 139.8, 136.8, 135.3, 129.1, 128.4, 127.9, 127.6, 120.9, 118.7, 118.1, 112.5, 110.9, 65.9, 61.3, 59.4, 55.2, 54.6, 51.5, 34.4, 33.6, 27.9, 18.0, 17.5; ES-MS (M + H$^+$, *m*/*z*) 374.5; HRMS calcd for $C_{25}H_{31}N_3$ 373.2518, found 373.2510.

(3*S*,8*S*,16a*S*)-2-Benzyl-3,8-dimethyl-1,2,3,4,7,8,10,11,16,16a-decahydro-6*H*-[1,4,7]oxadiazecino[7′,6′:1,6]pyrido[3,4-*b*]indole (8e): yellow liquid; yield 30.6 mg (76%); $[\alpha]^{21.9}_{D}$ −33.4 (*c* 0.42, MeOH); HPLC using Chiralpak IA at flow rate 0.6 mL/min IPA/Hex (8:93.5, isocratic) t_R 15.7 min (96.99%) and 18.0 min (3.04%); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00 (s, 1H), 7.61 (d, *J* = 7.6 Hz, 1H), 7.36−7.21 (m, 4H), 7.20−7.15 (m, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.87 (t, *J* = 10.3 Hz, 1H), 3.59 (q, *J* = 15.0 Hz, 2H), 3.42 (d, *J* = 13.8 Hz, 1H), 3.32 (t, *J* = 5.0 Hz, 2H), 3.19−3.08 (m, 1H), 3.04−2.93 (m, 3H), 2.85−2.64 (m, 4H), 2.48 (dd, *J* = 16.8, 6.9 Hz, 1H), 1.40 (dd, *J* = 11.5, 5.3 Hz, 2H), 1.10 (d, *J* = 6.3 Hz, 3H), 0.87 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 140.9, 136.8, 135.1, 128.4, 128.2, 127.8, 127.4, 120.9, 118.7, 118.2, 112.8, 110.9, 69.5, 62.9, 62.8, 58.8, 58.3, 55.8, 52.5, 49.8, 33.6, 27.5, 18.4, 15.7; ES-MS (M + H$^+$, *m*/*z*) 404.2; HRMS calcd for $C_{26}H_{33}N_3O$ 403.2624, found 403.2629.

(3*S*,8*S*)-2-Benzyl-3-ethyl-8-methyl-2,3,4,5,7,8,10,11,16,16a-decahydro-1*H*-[1,4,7]oxadiazecino[4′,5′:1,6]pyrido[3,4-*b*]indole (8f): colorless liquid; yield 31.2 mg (75%); $[\alpha]^{21.4}_{D}$ +19.2 (*c* 0.23, MeOH); HPLC using Chiralpak IC at flow rate 0.6 mL/min IPA/Hex (6.5:93.5, gradient) t_R 11.3 min (98%) and 12.7 min (1.99%); IR (neat, ν_{max}, cm^{-1}) 3251.2, 2685.4, 1524.3, 1263.7, 1002.6, 996.8; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.00 (s, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.36−7.28 (m, 1H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 3.96−3.76 (m, 1H), 3.60 (q, *J* = 15.0 Hz, 2H), 3.44 (dd, *J* = 13.4, 9.0 Hz, 3H), 3.26−3.05 (m, 1H), 2.95 (ddd, *J* = 10.1, 6.7, 3.6 Hz, 1H), 2.87−2.68 (m, 4H), 2.50 (dd, *J* = 15.9, 6.9 Hz, 1H), 2.44 (d, *J* = 5.7 Hz, 2H), 2.38 (ddd, *J* = 13.1, 11.7, 6.6 Hz, 1H), 1.76 (ddd, *J* = 12.4, 6.7, 5.2 Hz, 1H), 1.62 (dd, *J* = 11.4, 5.2 Hz, 2H), 1.38−1.16 (m, 1H), 0.96 (d, *J* = 6.6 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 139.8, 137.2, 135.2, 128.7, 128.2, 128.0, 127.6, 120.9, 118.8, 117.9, 112.1, 110.7, 67.9, 64.1, 62.5, 59.7, 58.9, 58.1, 53.6, 49.8, 33.5, 28.1, 24.9, 17.5, 9.6; ES-MS (M + H$^+$, *m*/*z*) 418.6; HRMS calcd for $C_{27}H_{35}N_3O$ 417.2780, found 417.2776.

(3*S*,8*S*)-4-Benzyl-3-ethyl-8-methyl-7-(naphthalen-1-yl)-1,4,7-oxadiazecane (9a): colorless liquid; yield 12.6 mg (75%); $[\alpha]^{19.4}_{D}$ +22.5 (*c* 0.32, MeOH); HPLC using Chirasphere flow rate 0.6 mL/min H_2O/IPA/L-proline (4%) (40:30:10, isocratic) t_R 18.1 min (2.0%) and 22.3 (97.9%); IR (neat, ν_{max}, cm^{-1}) 1524.3, 1363.2, 1285.6, 1163.7, 1085, 997.5; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.08 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.52−7.40 (m, 3H), 7.35 (t, *J* = 7.3 Hz, 2H), 7.32−7.18 (m, 5H), 3.98 (t, *J* = 5.6 Hz, 2H), 3.92−3.78 (m, 1H), 3.65 (t, *J* = 5.0 Hz, 2H), 3.39 (d, *J* = 13.5 Hz, 1H), 3.29 (dd, *J* = 12.3, 6.8 Hz, 3H), 3.25−3.12 (m, 1H), 3.05 (d, *J* = 2.9 Hz, 2H), 2.01 (dd, *J* = 11.5, 5.3 Hz, 2H), 1.57 (ddd, *J* = 12.7, 6.7, 5.9 Hz, 1H), 1.44−1.26 (m, 1H), 1.16 (d, *J* = 6.2 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 149.0, 138.7, 130.9, 129.4, 129.3, 128.8, 128.5, 127.3, 125.3, 125.0, 124.0, 117.6, 115.2, 72.5, 67.3, 66.2, 56.1, 55.5, 49.2, 44.2, 34.1, 21.6, 19.6, 10.0; ES-MS (M + H$^+$. *m*/*z*) 403.5; HRMS calcd for $C_{27}H_{34}N_2O$ 402.2671, found 402.2666.

(*R*)-1-((*S*)-Piperidin-2-yl)propan-1-ol (9b): colorless solid; yield 74.6 mg (52%); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.71−3.39 (m, 1H), 3.38−3.04 (m, 3H), 2.89−2.51 (m, 2H), 2.41−2.14 (m, 1H), 2.11−1.93 (m, 2H), 1.86−1.63 (m, 2H), 1.61−1.34 (m, 2H), 1.33−1.08 (m, 2H), 0.99 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 75.4, 56.8, 48.2, 31.9, 28.0, 25.6, 23.5, 10.9; ES-MS (M + H$^+$, *m*/*z*) 144.3. Anal. Calcd for $C_8H_{17}NO$ (143.1310): C, 67.09; H, 11.96; N, 9.78. Found: C, 67.01; H, 11.90; H, 9.71. The rest of the data were obtained in a manner similar to that for the literature reported data.

(2*R*,3*R*)-2-ethylazepan-3-ol (9c): Light yellow color liquid separated using general procedure C, 51.4 mg (36%); $[\alpha]^{19.3}_{D}$ −36.3 (*c* 0.1, MeOH); Yield ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 4.11−3.75 (m, 1H), 3.32−3.10 (m, 1H), 3.08−2.87 (m, 2H), 2.85−2.61 (m, 1H), 2.44 (dd, *J* = 2.7, 1.6 Hz, 1H), 2.03−1.84 (m, 1H), 1.78−1.26 (m, 8H), 0.98 (dd, *J* = 10.2, 4.5 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$, ppm) δ 75.08, 69.38, 48.91, 34.84, 30.89, 24.72, 21.8, 9.3; HRMS calcd for $C_8H_{17}NO$ 143.1310, found 143.1316.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, ^{1}H and ^{13}C NMR spectra of compounds **3a−p**, **4a−h**, **5a−j**, **6a−k**, **7a−h**, **8a−f**, and **9a−c** and HPLC details of compounds **4a−h**, **5a−j**, **6a−k**, **7a−h**, **8a−f**, and **9a**. 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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