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Stereoselective Synthesis of 2-(2-Aminoalkyl)- and 1,3-Disubstituted Tetrahydro-1*H*-pyrido[4,3-*b*]- Benzofuran and Indole Derivatives

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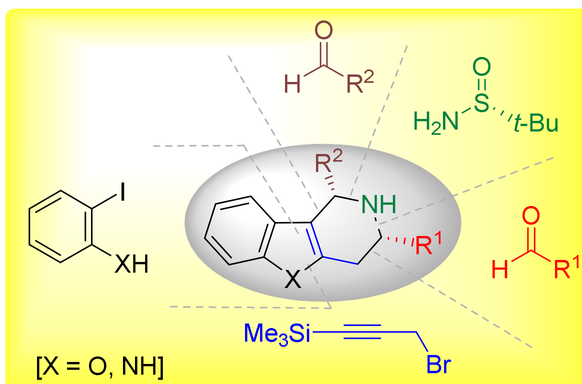


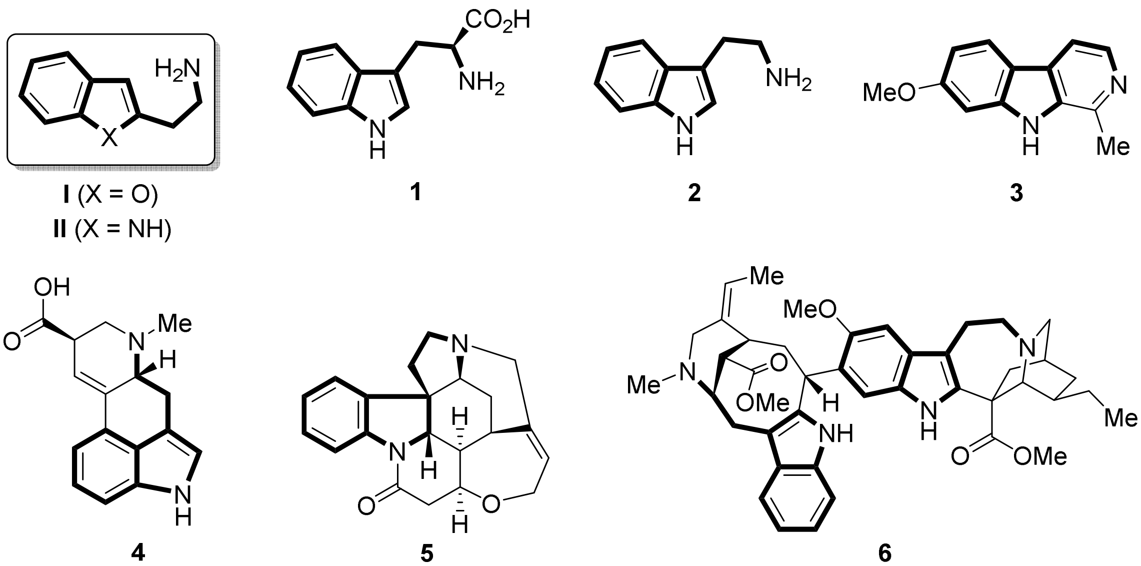
ABSTRACT. The addition of an allenyl indium intermediate to chiral *N*-*tert*-butanesulfinyl imines **7** proceeds with high levels of diastereocontrol. The resulting homopropargylic amine derivatives **10** were transformed into 2-(2-aminoalkyl)benzofuran and indole derivatives **13** and **19**, after Sonogashira-coupling with *o*-iodophenol or *o*-iodoaniline, followed by formation of the heteroaromatic ring through an intramolecular cyclization. Enantioenriched tetrahydropyrido-benzofuran and indole derivatives **16** and **21** were prepared through a Picted-Spengler condensation of the free amines derived from compounds **15** and **20**, involving the nucleophilic 3-position of the benzofuran or indole moiety.

KEYWORDS. Chiral sulfinyl imines, diastereoselective propargylation, tetrahydropyridobenzofurans, tetrahydropyridoindoles, Sonogashira-coupling, Picted-Spengler reaction.

INTRODUCTION

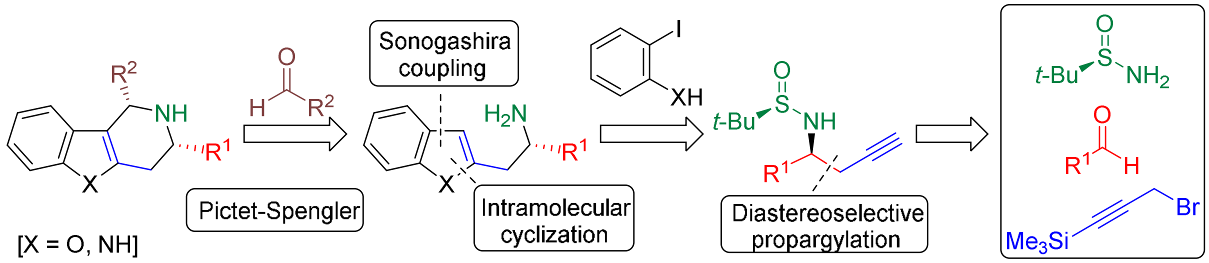
A large percentage of drugs and drug candidates contains the amine functionality,[1] which is also widespread among natural products, organocatalysts[2] and ligands of organometallic catalysts. Remarkably, in many of these compounds the nitrogen atom is bonded to a stereogenic center, so the development of general and versatile asymmetric methodologies for preparing enantioenriched chiral amines is of great importance in synthesis.[3] Compounds with the indole unit bearing a 2-aminoalkyl substituent at the 3-position are part of the family of these aminated compounds which have attracted the interest of chemists and pharmacologists mainly due to their possible physiological activities. Many indole alkaloids have been known for years and used in ancient cultures as psychotropic, stimulants and poisons. All these natural products derive from the amino acid tryptophan (**1**)[4] and show wide structural diversity, going from the simplest compound tryptamine (**2**), a non-selective serotonin receptor agonist and serotonin-norepinephrine-dopamine releasing agent,[5] to, for instance, harmine (**3**), a fluorescent harmala alkaloid which reversibly inhibits monoamine oxidase which shows also cytotoxicity against different cell lines,[6] and lysergic acid (**4**), a precursor of different ergoline alkaloids. Amide derivatives of **4** were used as psychedelic drugs. Other representative indole alkaloids with more complex structures are strychnine (**5**), a poison which produces muscular convulsions isolated from the seeds of the *Strychnos nux-vomica* tree,[7] and the bisindole derivative voacamine (**6**) found in *Voacanga Africana*[8] (Figure 1). Regioisomeric benzofurans and indoles with a 2-aminoalkyl substituent at the 2-position with general structures **I** and **II** (Figure 1) are less common compounds and have been synthesize in order to explore their biological actitivity. Thus, some benzofuran derivatives on type **I** were found to display a potent and selective enhancement of the impulse propagation mediated release of catecholamines and serotonin in the brain,[9] and also, histamine H_3 receptor antagonist activity,[10] meanwhile, some indole derivatives of type **II** have been found to inhibit intracellular Ca^{2+} release in human TT cells,[11] or act as serotonin-3 receptor antagonists.[12]

Figure 1. Representative Natural Products Bearing the 3-(2-Aminoalkyl)indole Moiety



On the other hand, over the past decade, *N*-*tert*-butanesulfinyl imines[13] have been extensively used as electrophiles in a wide range of synthetic applications due to easy access to both enantiomers from commercially available *tert*-butanesulfinamide at reasonable prices. Importantly, the *tert*-butanesulfinyl group can be removed under mild reaction conditions leading to free amines and, in addition, useful synthetic procedures have been developed in order to recycle the chiral *tert*-butanesulfinamide,[14] being this process at the end as a non-immolative removal procedure of the chiral auxiliary. Regarding our research in this area, we have described the stereoselective indium promoted coupling of *N*-*tert*-butanesulfinyl imines with allylic bromides[15] and also with trimethylsilyl propargyl bromide[16] to give the corresponding homoallyl and homopropargyl amine derivatives, respectively, which have been used as precursors in the synthesis of natural products[17] and other structurally diverse nitrogen-containing compounds.[18] Being aware of the potential interest of 2-aminoalkyl benzofurans and indoles of type **I** and **II** with regard to biological activity, we decided to explore new synthetic pathways to access to these compounds and other polyheterocyclic derivatives in an enantioenriched form, from *N*-*tert*-butanesulfinyl homopropargylamines and *ortho*-iodoaniline or *ortho*-iodophenol, through a tandem Sonogashira-cyclization reaction and final Pictet-Spengler type intramolecular electrophilic substitution (Scheme 1).

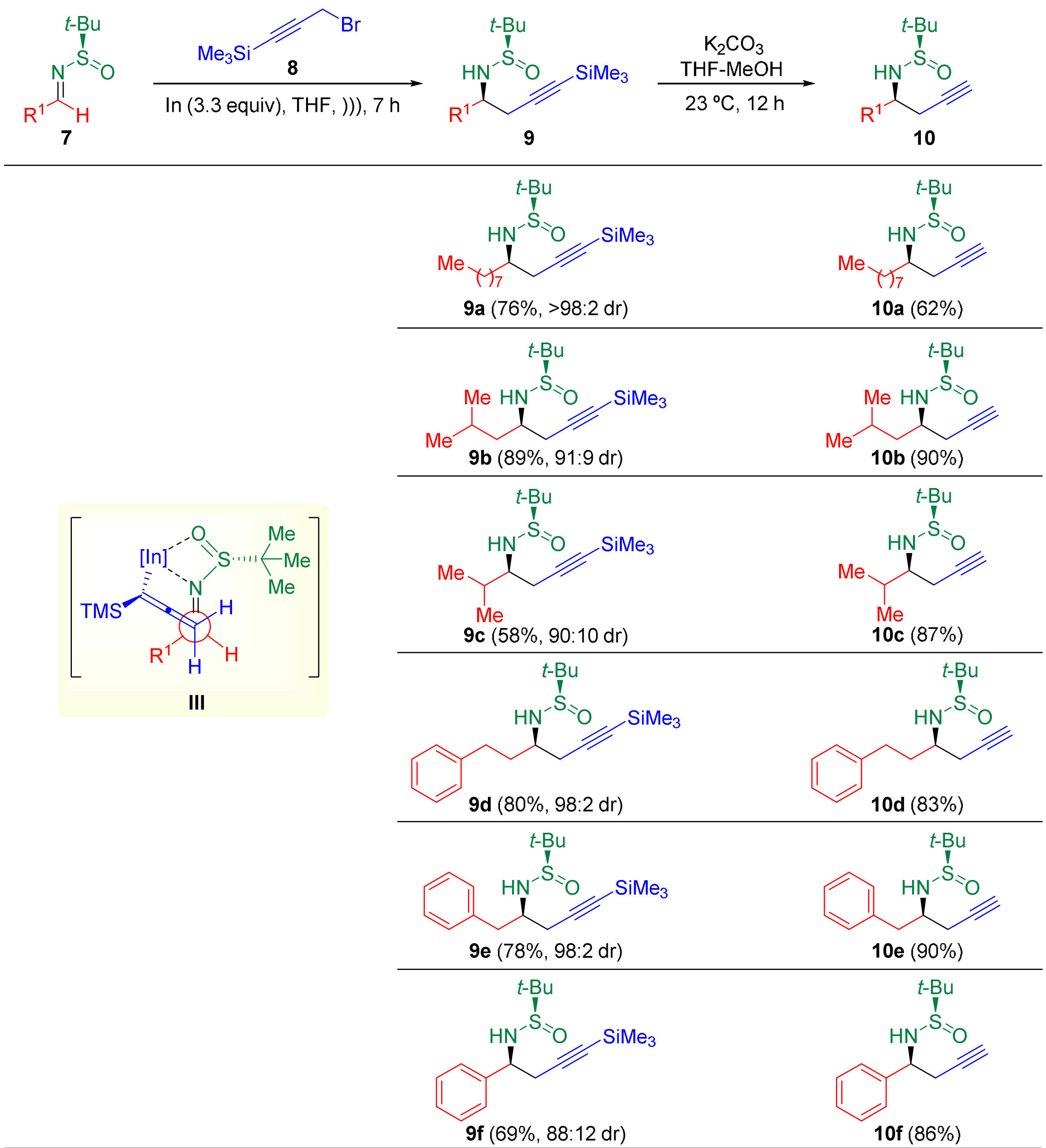
Scheme 1. Retrosynthetic analysis of synthesis of 2-aminoalkyl indoles, benzofurans and tetrahydropyridoindole and furan derivatives



RESULTS AND DISCUSSION

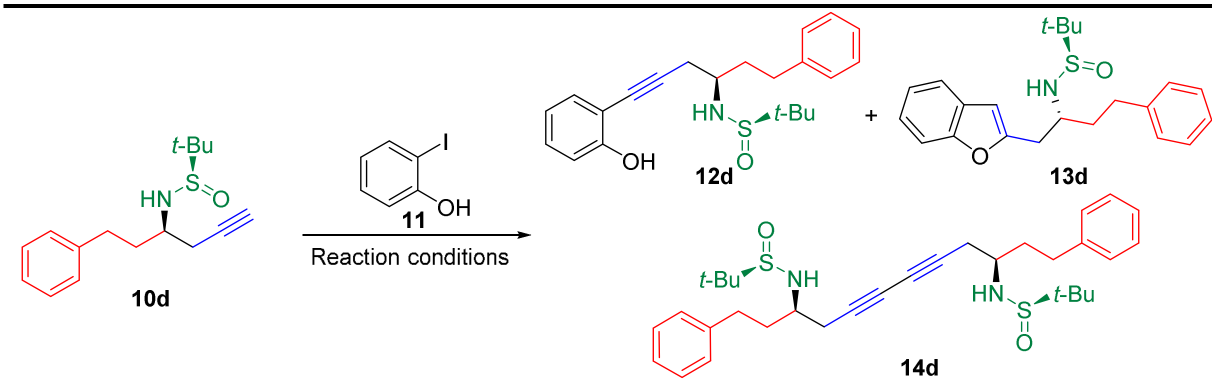
We have already reported that the reaction of 3.3 equivalents of trimethylsilylpropargyl bromide **8** with different chiral *N-tert*-butanesulfinyl aldimines **7** in the presence of 3.3 equivalents of indium metal under sonication for 7 hours led to the formation of the corresponding silylated homopropargyl amine derivatives **9** in variable yields, but always with excellent diastereomeric ratios. It is worth mentioning that enantiomerically pure compounds **9** were isolated after column chromatography purification in all cases (Scheme 2).[16] Addition of silicon-stabilized allenylindium intermediate took place predominantly to the *Si* face of imines with R_S configuration. In order to explain that, we proposed a six-membered ring transition state **III**, with the simultaneous coordination of the indium atom of the to both the nitrogen and oxygen atoms of the imine, so fixing a conformation in which nucleophilic attack proceeded at the less hindered *Si* face for these imines (Scheme 2). The silicon unit was selectively removed upon treatment of compounds **9** with potassium carbonate in THF/methanol at room temperature for 12 hours, leading to terminal alkynes **10** in high yields (Scheme 2). Under these mild reaction conditions the sulfinyl group remained unaltered. This is important in order not to perturb the desired further transformations.

Scheme 2. Diastereoselective synthesis of homopropargyl amine derivatives **10**



All the attempts to perform a palladium(0)-catalyzed sila-Sonogashira coupling of compounds **9d** with *ortho*-iodophenol (**11**) in the presence of CuCl in DMF,[19] or on potassium fluoride doped alumina under microwave irradiation,[20] failed. Decomposition of the starting compound **9d** was always observed. However, better results were obtained working with desilylated compounds **10**. Homopropargylamine derivative **10d** was taken as a model compound for the optimization of tandem Sonogashira-cyclization process with *ortho*-iodophenol (**11**). The reaction of **10d** with **11** in the presence of catalytic amounts of $Pd(PPh_3)_4$ (2 mol%) and CuI (2 mol%), in Et_3N at room temperature for 14 hours led to the cross-coupling product **12d** as the major component of the reaction mixture, along with the desired tandem coupling-cyclization product **13d**, and compound **14d**, resulting from the homocoupling of the terminal alkyne **10d** (Table 1, entry 1). The formation of the homocoupling product **14d** is facilitated working at higher temperatures. Thus, **14d** became the major component of the reaction mixture at 40 ºC, meanwhile **12b** and **13d** were in an almost 1:1 ratio (Table 1, entry 2). At 60 ºC, compound **14d** was formed in a similar extension as at 40 ºC, but we observed that the initially formed Sonogashira-coupling product **12d** underwent intramolecular cyclization leading to **13d** (Table 1, entry 3).[21] Fortunately, formation of undesired compound **14d** was minimized working at 60 ºC under microwave irradiation, and the amount of the desired compound **13d** increased by increasing reaction time from 15 to 45 minutes (Table 1, entries 4 to 6). Longer reaction times under microwave irradiation led to significant decomposition of the 2-(2-aminoalkyl)furan derivative **13d**.

Table 1. Optimization of the tandem Sonogashira-cyclization reaction of terminal alkyne **10d** and *ortho*-iodophenol (**11**)

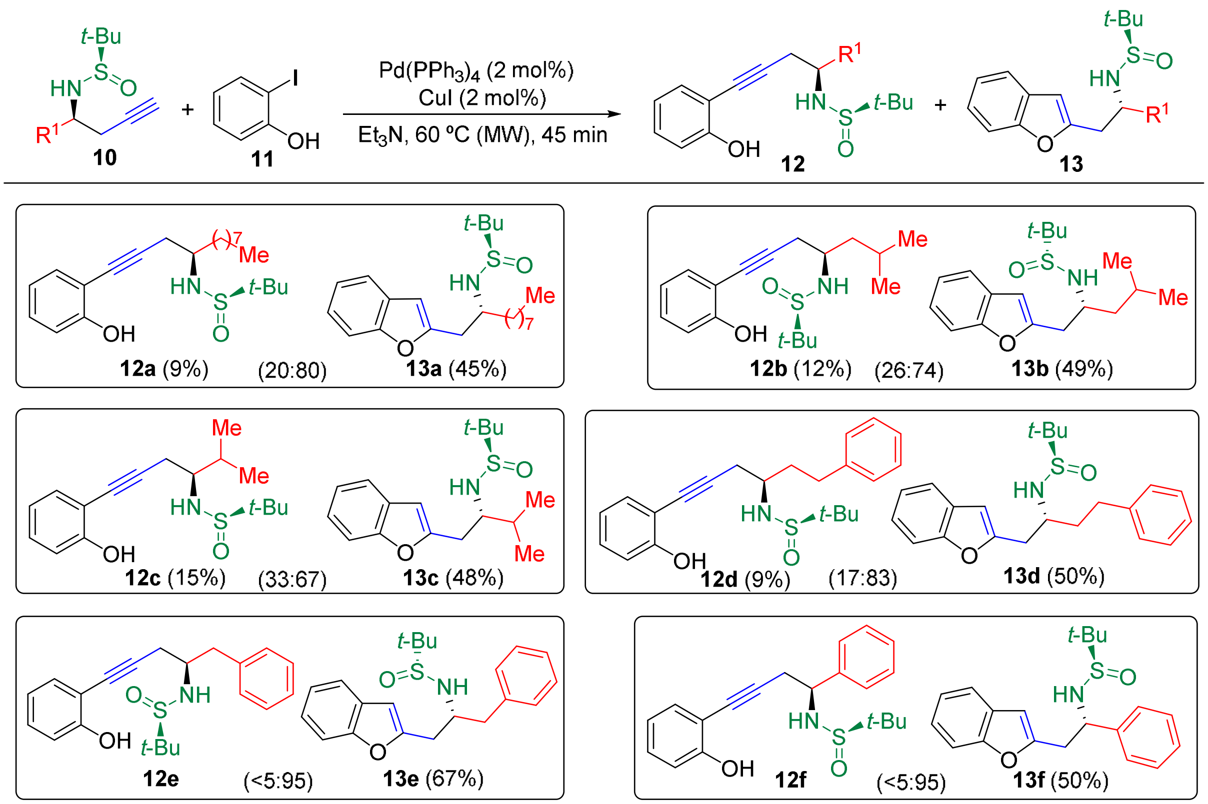


Entry	Reaction conditions	**12d**:**13d**:**14d** Ratio[a]
1	$Pd(PPh_3)_4$ (2 mol%), CuI (2 mol%), Et_3N, 23 °C, 14 h	51:23:26
2	$Pd(PPh_3)_4$ (2 mol%), CuI (2 mol%), Et_3N, 40 °C, 6 h	26:27:47
3	$Pd(PPh_3)_4$ (2 mol%), CuI (2 mol%), Et_3N, 60 °C, 14 h	4:49:47
4	$Pd(PPh_3)_4$ (2 mol%), CuI (2 mol%), Et_3N, 60 °C (MW), 15 min	39:52:9
5	$Pd(PPh_3)_4$ (2 mol%), CuI (2 mol%), Et_3N, 60 °C (MW), 30 min	28:64:8
6	$Pd(PPh_3)_4$ (2 mol%), CuI (2 mol%), Et_3N, 60 °C (MW), 45 min	16:81:3

[a] Ratio was determined from ^{1}H-NMR spectrum of the crude reaction mixture. In all cases total consumption of the starting compound **10d** was observed.

We studied next the scope of the reaction with different homopropargylamine derivatives **10**, by applying the optimized conditions depicted in Table 1, entry 6. In all cases, the corresponding benzofuran derivative **13** was obtained as the major reaction product, the Sonogashira-coupling product **12** being formed in a lesser extension. Importantly, for the homoproparglylamines **10e** and **10f** derived from aldehydes phenylacetaldehyde and benzaldehyde, compounds **12** were neither isolated nor detected. Anyway, products **12** and **13** were formed in ratios ranging from 26:74 to <5:95, and were purified very easily by column chromatography (Scheme 3).

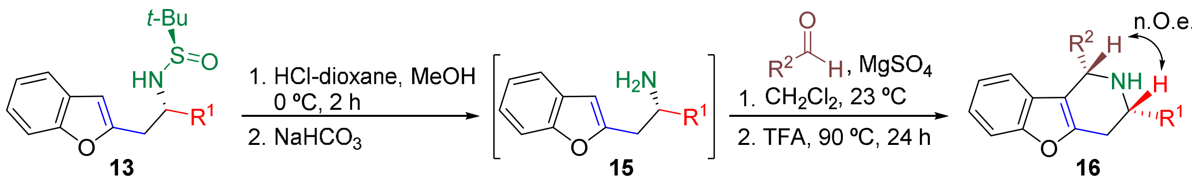
Scheme 3. Synthesis of 2-(2-aminoalkyl)furan derivatives **13** from terminal alkynes **10**

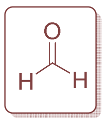
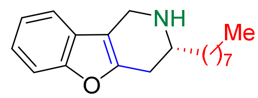
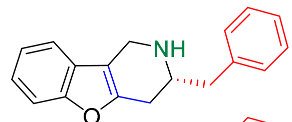
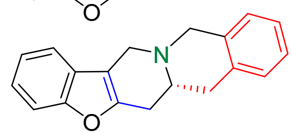
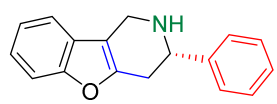
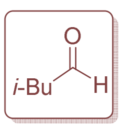
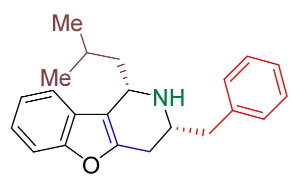
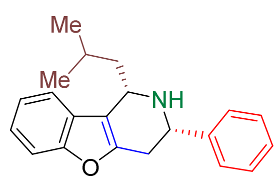
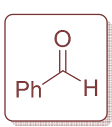
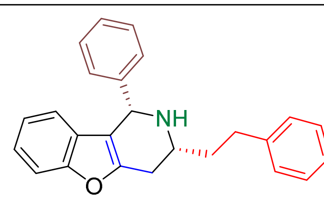
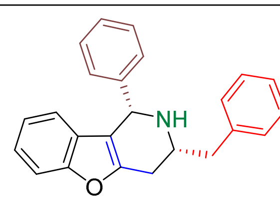


12:**13** Ratio is given in parenthesis and was determined from ^{1}H-NMR spectrum of the crude reaction mixture. Yield refers to isolated compounds after column chromatography purification.

The previously commented methodology allow us an easy access to *N*-*tert*-butanesulfinyl substituted 2-(2-aminoalkyl)furans **13**, which can be transformed into the free amines **15** by removal of the sulfinyl group upon treatment first of a methanolic solution of compounds **13** with hydrogen chloride 4.0 M in dioxane, and then, with a saturated sodium bicarbonate solution. After that, the crude amines **15** were treated with an aldehyde in dichloromethane at room temperature to form the corresponding imines. The progress of the reaction could be follow by gas chromatography and it took around 5 hours to go to completion. Once the intermediate imine was formed, anhydrous magnesium sulfate was added and after filtration of the solid and removal of the solvent, the resulting crude imine was treated with trifluoroacetic acid (TFA) in a high pressure tube and heated at 90 ºC for 24 hours, leading to the expected tetrahydropyridofuran derivatives **16** in variable yields, after intramolecular electrophilic aromatic substitution at the electron-rich 3-position of the indole system (Table 2). In the case of formaldehyde, 1.5 equivalents from a 37% aqueous solution of formaldehyde was used in this Pictet-Spengler type cyclization (Table 2, entries 1-3). Surprisingly, for the 2-(2-aminoalkyl)fenzofuran **13e**, derived from the imine of phenylacetaldehyde, along with the expected tetrahydropyridofuran **16ea**, the pentacyclic compound **16ea'**, resulting from a double aromatic electrophilic substitution involving also the phenyl group of the starting phenylacetaldehyde, was also formed in a significant amount (Table 2, entry 2). This double electrophilic substitution was not observed starting from compound **13f**, derived from the imine of benzaldehyde. In this case, the Pectet-Spengler cyclization involving the phenyl group leading to a five-membered ring did not take place under the essayed reaction conditions (Table 2, entry 3). Importantly, when other aldehydes, such as isobutyraldehyde and benzaldehyde, were used, the expected 1,3-disubstituted tetrahydropyridofurans **16** were obtained as a single diastereoisomer (Table 2, entries 4-7). The relative configuration was unambiguously determined to be *cis* by NOESY experiments in compounds **16**. Moreover, on the contrary to formaldehyde, **15e** did not undergo double electrophilic aromatic substitution when reacting with isobutyraldehyde and benzaldehyde (Table 2, entries 4 and 7).

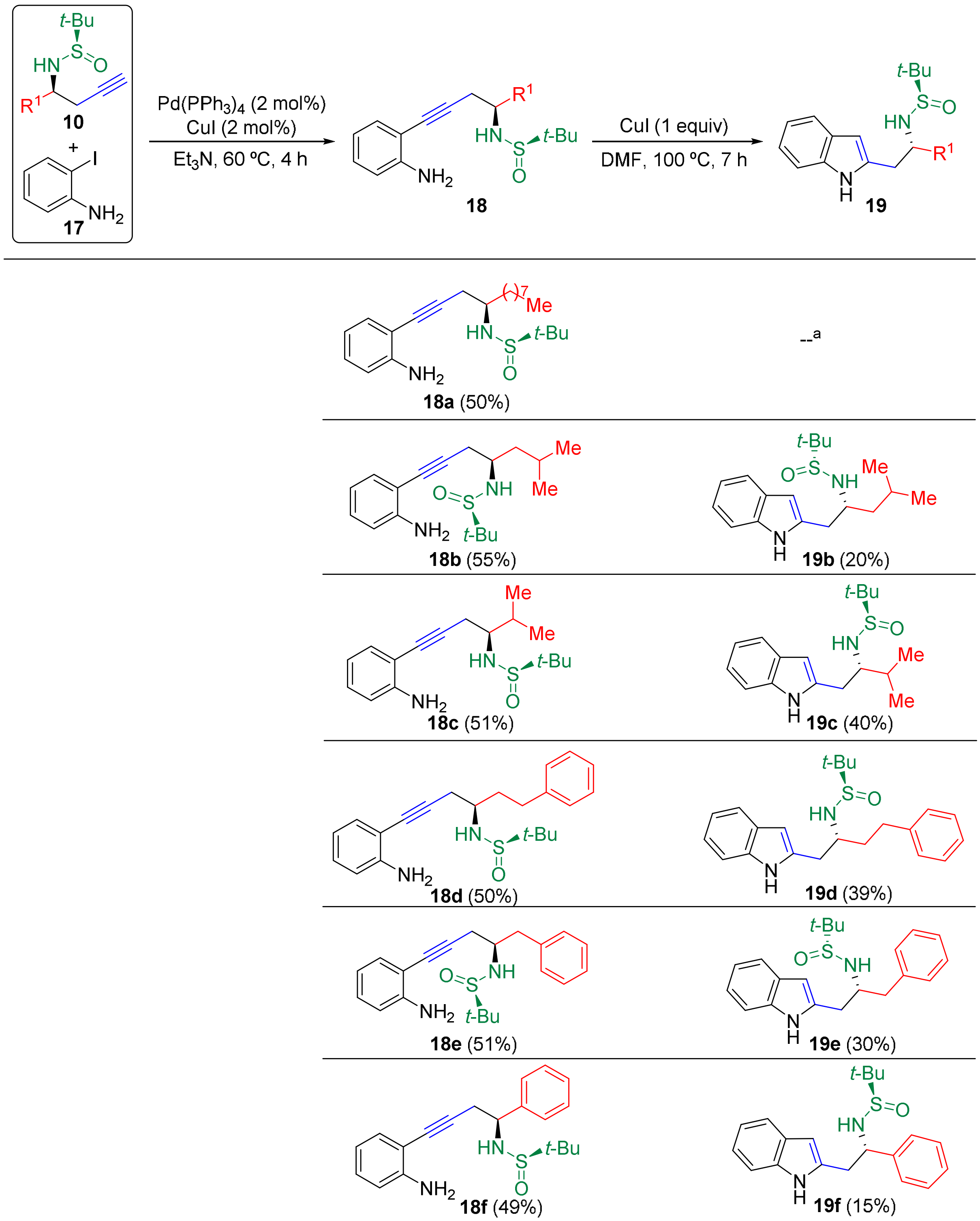
Table 2. Synthesis of tetrahydro-1*H*-pyrido[4,3-*b*]benzofurans **16**



Entry	R^2CHO	Benzofuran **13**	Tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran **16** No.	Structure	Yield (%)
1		**13a** [R^1 = $(CH_2)_7Me$]	**16aa**		45
2		**13e** [R^1 = CH_2Ph]	**16ea**		47
			16ea'		33
3		**13f** [R^1 = Ph]	**16fa**		49
4		**13e** [R^1 = CH_2Ph]	**16eb**		30
5		**13f** [R^1 = Ph]	**16fb**		46
6		**13d** [R^1 = $(CH_2)_2Ph$]	**16dc**		55
7		**13e** [R^1 = CH_2Ph]	**16ec**		50

Unfortunatelly, the reaction of homopropargylamine derivatives **10** with *ortho*-iodoaniline (**17**) under the palladium-catalyzed microwave irradiation conditions, which were found to be optimal for the Sonogashira-coupling and subsequent cyclization in the case of *ortho*-iodophenol (**11**) in Table 1, entry 6, led always to very low yields of the expected indole derivative **19**, taking place especially decomposition of the starting homopropargylamines **10**.[22] Since the formation of the 2-(2-aminoalkyl)indole derivatives **19** from compounds **10** and *ortho*-aniline (**17**) in a single synthetic operation failed, we planned to perform first the Sonogashira-coupling reaction exclusively under thermal conditions and after that, the intramolecular cyclization to produce the five-membered ring of the indole system. The palladium-catalyzed coupling of terminal alkynes **10** and *ortho*-iodoaniline (**17**) in Et_3N at 60 ºC produced compounds **18** in moderate yields. Further treatment of *orto*-alkynylaniles **18** with 1 equivalent of copper iodide in DMF at 100 ºC led to the expected 2-(2-aminoalkyl)indoles **19**.[23] Although TLC monitoring of this reaction reflected a clean transformation (a single spot corresponding to the reaction product was developed), compounds **19** were obtained in relatively low isolated yields after column chromatography purification. Even, for the aniline derivative **18a**, the expected indole **19** could not be isolated in a significant amount in order to be characterized (Scheme 4).

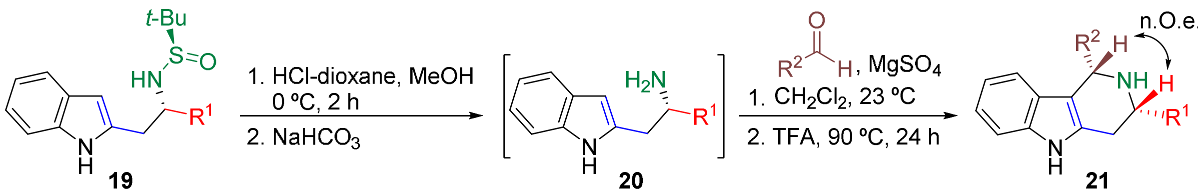
Scheme 4. Synthesis of 2-(2-aminoalkyl)indole derivatives **19** from terminal alkynes **10**.

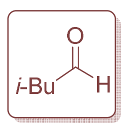
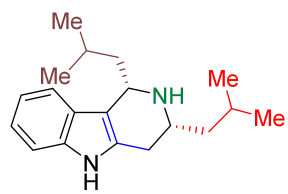
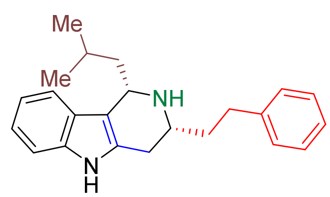
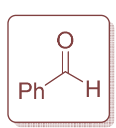
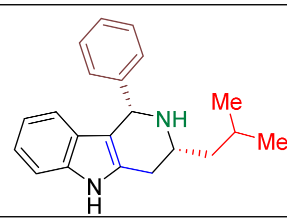
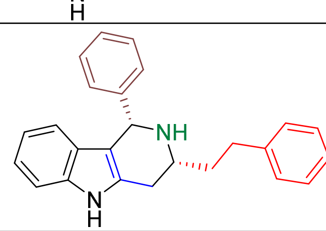


[a] Compound **19a** could not be isolated.

Finally, tetrahydropyridoindoles **21** were prepared from compounds **19**, following the same strategy depicted in Table 2: first removal of the *tert*-butanesulfinyl group under acidic conditions and then, reaction of the resulting free amine **20** with an aldehyde in trifluoroacetic acid (Table 3). Overall yields are similar to those obtained in the case of furan derivatives **16**. Tetrahydropyridoindoles **21** with substituents at 1- and 3-positions exhibited also *cis* relative configuration (Table 3).

Table 3. Synthesis of tetrahydro-1*H*-pyrido[4,3-*b*]indoles **21**



Entry	R^2CHO	Indole **19**	Tetrahydro-1*H*-pyrido[4,3-*b*]indole **21** No.	Structure	Yield (%)
1		**19b** [R^1 = CH_2*i*-Pr]	**21bb**		45
2		**19d** [R^1 = $(CH_2)_2Ph$]	**21db**		55
3		**19b** [R^1 = CH_2*i*-Pr]	**21bc**		52
4		**19d** [R^1 = $(CH_2)_2Ph$]	**21dc**		47

In summary, 1,3-disubstituted tetrahydro-1*H*-pyrido[4,3-*b*]-benzofuran and indole derivatives **16** and **21**, respectively, were prepared in a highly stereoselective fashion from *tert*-butanesulfinamide, trimethylsilylpropargyl bromide, two aldehydes and *ortho*-iodophenol or *ortho*-iodoaniline. The methodology presented here comprised as key steps a diastereoselective addition of an allenyl indium intermediate to the chiral sulfinyl imine **7**, a Sonogashira-coupling reaction of a terminal alkyne and *ortho*-iodophenol or aniline, and a final Pictet-Spengler condensation involving a five-membered heteroaromatic ring. Tetrahydropyridobenzofuran and indole derivatives **16** and **21** with substituents at 1- and 3-positions exhibit *cis*-relative configuration and since the addition of the allenyl indium intermediate to the sulfinyl imine is stereospecific, the stereochemistry of the reaction products is determined by the configuration of the *tert*-butanesulfinamide.

EXPERIMENTAL SECTION

General Remarks: (R_S)-*tert*-Butanesulfinamide was a gift of Medalchemy (> 99% ee by chiral HPLC on a Chiracel AS column, 90:10 n-hexane/*i*-PrOH, 1.2 mL/min, λ=222 nm). TLC was performed on silica gel 60 F_{254}, using aluminum plates and visualized with phosphomolybdic acid (PMA) stain. Flash chromatography was carried out on handpacked columns of silica gel 60 (230-400 mesh). Melting points are uncorrected. Optical rotations were measured using a polarimeter with a thermally jacketted 5 cm cell at approximately 20 ºC and concentrations (*c*) are given in g/100 mL. Infrared analyses were performed with a spectrophotometer equipped with an ATR component; wavenumbers are given in cm^{-1}. Low-resolution mass spectra (EI) were obtained at 70 eV; and fragment ions in *m/z* with relative intensities (%) in parentheses. High-resolution mass spectra (HRMS) were also carried out using the electron impact mode (EI) at 70 eV with a Q-TOF analyzer. ^{1}H NMR spectra were recorded at 300 or 400 MHz for ^{1}H NMR and 75 or 100 MHz for ^{13}C NMR, using $CDCl_3$ as the solvent and TMS as internal standard (0.00 ppm). The data are being reported as: s = singlet, d = doublet, t = triplet, q = quatriplet, h = heptet, m = multiplet or unresolved, br s = broad signal, coupling constant(s) in Hz, integration. ^{13}C NMR spectra were recorded with ^{1}H-decoupling at 100 MHz and referenced to $CDCl_3$ at 77.16 ppm. DEPT-135 experiments were performed to assign CH, CH_2 and CH_3. Microwave-assisted synthesis was performed using microwave oven CEM Discover Intellivent Explorer in sealed reaction vessels, and the temperature was monitored using a vertically focused IR temperature sensor. Compounds **7a**,[24] **7b**,[25] **7c**,[26] **7d**,[27] **7e**,[26] and **7f**[26] were prepared from the corresponding aldehyde and (R_S)-*tert*-butanesulfinamide in THF in the presence of two equivalents of titanium tetraethoxide.

General Procedure for the Propargylation of *N-tert*-Butanesulfinylimines 7. Synthesis of Homopropargylamine Derivatives 9: A mixture of *N-tert*-butanesulfinyl imine **7** (0.5 mmol), 3-bromo-1-trimethylsilyl-1-propyne (**8**; 313 mg, 0.275 mL, 1.65 mmol), and indium (189 mg, 1.65 mmol) was sonicated in dry THF (2 mL) for 7 h. Then the resulting mixture was hydrolyzed with H_2O (5 mL) and extracted with EtOAc (3 × 15 mL). The organic phase was washed with brine (3 × 10 mL), dried with anhydrous $MgSO_4$, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield products **9**. Yields, physical and spectroscopic data follow.

(4*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-(trimethylsilyl)dodec-1-yn-4-amine (9a):[16] The representative procedure was followed by using imine **7a** (122.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **9a** (134.8 mg, 0.38 mmol, 76%) as a colorless oil; $[\alpha]_D^{20}$ –11.4 (c = 1.16, CH_2Cl_2); R_f 0.65 (hexane/EtOAc, 1:1); IR ν (film) 3203, 2956, 2924, 2855, 2173, 1466,1363, 1249, 1052, 840, 759, 648 cm^{-1}; δ_H 3.58 (d, J = 7.7 Hz, 1H), 3.38–3.27 (m, 1H), 2.65 (dd, J = 16.8, 5.7 Hz, 1H), 2.48 (dd, J = 16.8, 5.0 Hz, 1H), 1.65–1.50 (m, 2H), 1.39–1.24 (m, 12H), 1.23 (s, 9H), 0.88 (t, J = 6.8 Hz, 3H), 0.15 (s, 9H); δ_C 102.8, 88.2, 55.9 (C), 54.4 (CH), 34.7, 31.8, 29.4, 29.3, 29.2, 27.9, 25.6 (CH_2), 22.7, 14.1, 0.04 (CH_3); LRMS (EI) m/z 301 (M^+–C_4H_8, 7%), 253 (29), 189 (26), 142 (12), 140 (25), 84 (13), 77 (11), 75 (16), 74 (10), 73 (100), 70 (24), 69 (13); HRMS (EI): Calculated for $C_{15}H_{31}NOSSi$ (M^+–C_4H_8) 301.1896; found 301.1897.

(4*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-6-methyl-1-(trimethylsilyl)hept-1-yn-4-amine (9b): The representative procedure was followed by using imine **7b** (283.5 mg, 1.50 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **9b** (401.3 mg, 1.30 mmol, 89%) as a yellow oil; $[\alpha]_D^{20}$ –5.2 (c = 1.72, CH_2Cl_2); R_f 0.52 (hexane/EtOAc, 1:1); IR ν (film) 3198, 2956, 2929, 2903, 2868, 2174, 1467, 1364, 1248, 1050, 838, 758 cm^{-1}; δ_H 3.57 (d, J = 8.7 Hz, 1H), 3.49-3.35 (m, CH, 1H), 2.68 (dd, J = 16.8, 5.8 Hz, 1H), 2.49 (dd, J = 16.8, 4.3 Hz, 1H), 1.83-1.64 (m, 1H), 1.62-1.47 (m, 1H), 1.48-1.29 (m, 1H), 1.23 (s, 9H), 0.96-0.87 (m, 6H), 0.16 (s, 9H); δ_C 102.8, 88.2 (C), 55.9 (CH), 52.9 (C), 44.2, 28.4 (CH_2), 24.5 (CH), 22.7, 22.6, 22.0, 0.03 (CH_3); LRMS (EI) m/z 301 (M^+, 0.5%), 197 (44), 149 (11), 140 (15), 133 (31), 86 (100), 73 (55), 57 (48), 43 (63); HRMS (EI): Calculated for $C_{11}H_{22}NSi$ (M^+–C_4H_9OS) 196.1522; found 196.1519.

(3*S*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-2-methyl-6-(trimethylsilyl)hex-5-yn-3-amine (9c):[16] The representative procedure was followed by using imine **7c** (87.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **9c** (83.4 mg, 0.29 mmol, 58%) as a white solid; mp 40–43 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –8.3 (c = 1.01, CH_2Cl_2); R_f 0.60 (hexane/EtOAc, 1:1); IR ν (film) 3449, 3263, 3123, 2959, 2929, 2898, 2870, 2174, 1473, 1466, 1429, 1366, 1248, 1008, 838, 758, 698, 646 cm^{-1}; δ_H 3.61 (d, J = 8.0 Hz, 1H), 3.17–3.06 (m, 1H), 2.65 (dd, J = 17.0, 5.8 Hz, 1H), 2.56 (dd, J = 17.0, 5.1 Hz, 1H), 2.06–1.94 (m, 1H), 1.24 (s, 9H), 0.94 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 0.15 (s, 9H); δ_C 102.9, 88.2 (C), 59.8 (CH), 56.1 (C), 31.2 (CH), 25.0 (CH_2), 22.8, 18.8, 18.4, 0.03 (CH_3); LRMS (EI) m/z 231 (M^+–C_4H_8, 7%), 188 (10), 184 (16), 183 (100), 140 (33), 120 (23), 119 (65), 102 (17), 83 (10), 75 (23), 73 (85), 72 (19), 59 (11), 57 (67), 56 (33), 55 (10); HRMS (ESI): Calculated for $C_{10}H_{21}NOSSi$ (M^+–C_4H_8) 231.1113, found 231.1124.

(3*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-phenyl-6-(trimethylsilyl)hex-5-yn-3-amine (9d):[16] The representative procedure was followed by using imine **7d** (118.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **9d** (139.4 mg, 0.40 mmol, 80%) as a white solid; mp 51–52 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –16.1 (c = 1.01, CH_2Cl_2); R_f 0.50 (hexane/EtOAc, 1:1); IR ν (film) 3271, 2959, 2928, 2175, 1250, 1032, 838, 759, 697 cm^{-1}; δ_H 7.33–7.14 (m, 5H), 3.65 (d, J = 8.1 Hz, 1H), 3.45–3.31 (m, 1H), 2.79–2.62 (m, 2H), 2.71 (dd, J = 16.9, 5.9 Hz, 1H), 2.53 (dd, J = 16.8, 4.6 Hz, 1H), 2.01–1.87 (m, 2H), 1.26 (s, 9H), 0.16 (s, 9H); δ_C 141.4 (C), 128.5, 128.3, 126.0 (CH), 102.4, 88.4, 56.0 (C), 53.9 (CH), 36.6, 31.8, 28.0 (CH_2), 22.7, 0.04 (CH_3); LRMS (EI) m/z 293 (M^+–C_4H_8, 5%), 246 (13), 245 (58), 140 (13), 91 (99), 75 (16), 73 (100).

(2*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-phenyl-5-(trimethylsilyl)pent-4-yn-2-amine (9e):[16] The representative procedure was followed by using imine **7e** (446.0 mg, 2.00 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **9e** (522.8 mg, 1.56 mmol, 78%) as a yellow oil; $[\alpha]_D^{20}$ –21.1 (c = 1.06, CH_2Cl_2); R_f 0.53 (hexane/EtOAc, 1:1); IR ν (film) 3444, 3118, 3020, 2959, 2177, 1473, 1456, 1426, 1364, 1249, 1081, 1052, 1026, 1003, 839, 743, 698 cm^{-1}; δ_H 7.36–7.14 (m, 5H), 3.70–3.57 (m, 2H), 2.99 (dd, J = 13.6, 6.1 Hz, 1H), 2.86 (dd, J = 13.6, 6.7 Hz, 1H), 2.58 (dd, J = 16.9, 5.7 Hz, 1H), 2.48 (dd, J = 16.9, 4.6 Hz, 1H), 1.15 (s, 9H), 0.19 (s, 9H); δ_C 137.6 (C), 129.5, 128.4, 126.6 (CH), 102.6, 88.7, 56.0 (C), 55.9 (CH), 40.9, 26.9 (CH_2), 22.5, 0.04 (CH_3); LRMS (EI) m/z 279 (M^+–C_4H_8, 1%), 231 (31), 188 (19), 167 (14), 140 (19), 104 (37), 98 (27), 91 (52), 75 (14), 73 (100), 71 (13); HRMS (ESI): Calculated for $C_{14}H_{21}NSi$ (M^+–C_4H_8OS) 231.1443, found 231.1437.

(1*S*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-phenyl-4-(trimethylsilyl)but-3-yn-1-amine (9f):[16] The representative procedure was followed by using imine **7f** (104.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **9f** (106.0 mg, 0.33 mmol, 69%) as a white solid; mp 80–82 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –133.1 (c = 1.00, CH_2Cl_2); R_f 0.52 (hexane/EtOAc, 1:1); IR ν (film) 3231, 3209, 2955, 2932, 2899, 2178, 1249, 1046, 1024, 837, 757, 697 cm^{-1}; δ_H 7.40–7.28 (m, 5H), 4.56 (m, 1H), 4.15 (br. s, 1H), 2.74 (dd, J = 16.9, 5.1 Hz, 1H), 2.64 (dd, J = 16.8, 8.3 Hz, 1H), 1.24 (s, 9H), 0.16 (s, 9H); δ_C 140.4 (C), 128.5, 128.0, 127.5 (CH), 102.2, 89.1 (C), 56.5 (CH), 55.7 (C), 30.3 (CH_2), 22.6, 0.1 (CH_3); LRMS (EI) m/z 217 (M^+–C_4H_8, 22%), 202 (14), 153 (74), 144 (10), 136 (20), 129 (20), 128 (20), 77 (14), 75 (16), 74 (10), 73 (100).

General Procedure for the Desilylation of Compounds 9. Synthesis of Terminal Alkynes 10: A suspension of K_2CO_3 (5 mg, 0.036 mmol) in methanol (4 mL) was added dropwise to a solution of the corresponding compound **9** (0.5 mmol) in THF (4 mL). The reaction mixture was stirred for 12 h at rt and then it was hydrolyzed with a 1 N NH_4Cl aqueous solution (8 mL) and extracted with methyl *tert*-butyl ether (3 × 15 mL). The organic phase was dried with anhydrous $MgSO_4$ and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc, 2:1) to yield products **10**. Yields, physical and spectroscopic data follow.

(4*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)dodec-1-yn-4-amine (10a): The representative procedure was followed by using compound **9a** (357.0 mg, 1.00 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **10a** (175.4 mg, 0.62 mmol, 62%) as a yellow oil; $[\alpha]_D^{20}$ –15.7 (c = 1.61, CH_2Cl_2); R_f 0.42 (hexane/EtOAc, 1:1); IR ν (film) 3222, 2954, 2923, 2855, 1465, 1363, 1051, 720, 625 cm^{-1}; δ_H 3.48 (d, J = 8.5 Hz, 1H), 3.44-3.26 (m, 1H), 2.66 (ddd, J = 16.7, 5.6, 2.6 Hz, 1H), 2.48 (ddd, J = 16.7, 4.5, 2.6 Hz, 1H), 2.06 (t, J = 2.6 Hz, 1H), 1.70-1.46 (m, 2H), 1.44-1.22 (m, 12H), 1.23 (s, 9H), 0.94-0.82 (m, 3H); δ_C 80.2 (C), 71.4 (CH), 56.0 (C), 54.8 (CH), 34.8, 31.8, 29.4, 29.3, 29.2, 26.6, 25.7 (CH_2), 22.7 (CH_3), 14.1 (CH_3); LRMS (EI) m/z 229 (M^+–C_4H_8, 1%), 213 (12), 140 (18), 126 (44), 116 (13), 113 (100), 100 (47), 67 (11), 56 (13); HRMS (EI): Calculated for $C_{12}H_{23}NOS$ (M^+–C_4H_8) 229.1500; found 229.1501.

(4*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-6-methylhept-1-yn-4-amine (10b): The representative procedure was followed by using compound **9b** (150.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **10b** (101.9 mg, 0.44 mmol, 90%) as a yellow oil; $[\alpha]_D^{20}$ –10.5 (c = 1.00, CH_2Cl_2); R_f 0.32 (hexane/EtOAc, 1:1); IR ν (film) 3217, 2955, 2929, 2868, 1468, 1388, 1364, 1050, 898, 632 cm^{-1}; δ_H 3.49-3.39 (m, 2H), 2.77-2.62 (m, 1H), 2.53-2.45 (m, 1H), 2.06 (t, J = 2.6 Hz, 1H), 1.80-1.65 (m, 1H), 1.61-1.50 (m, 1H), 1.41-1.31 (m, 1H), 1.23 (s, 9H), 0.92 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H); δ_C 80.2 (C), 71.5 (CH), 56.1 (C), 53.2 (CH), 44.1 (CH_2), 27.2 (CH_2), 24.5 (CH), 23.0 (CH_3), 22.7 (CH_3), 21.2 (CH_3); LRMS (EI) m/z 229 (M^+, 0.05%), 173 (18), 134 (38), 133 (100), 118 (13), 116 (41), 100 (13), 67 (16), 57 (79); HRMS (EI): Calculated for $C_5H_{12}NOS$ (M^+–C_7H_{11}) 134.0640; found 134.0630.

(3*S*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-2-methylhex-5-yn-3-amine (10c): The representative procedure was followed by using compound **9c** (106.2 mg, 0.37 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **10c** (69.4 mg, 0.32 mmol, 87%) as a yellow oil; $[\alpha]_D^{20}$ –23.5 (c = 1.33, CH_2Cl_2); R_f 0.35 (hexane/EtOAc, 1:1); IR ν (film) 3222, 2959, 2928, 2871, 1467, 1387, 1364, 1057, 889, 628 cm^{-1}; δ_H 3.46 (d, J = 8.8 Hz, 1H), 3.16-3.05 (m, 1H), 2.64 (ddd, J = 16.9, 5.8, 2.7 Hz, 1H), 2.58 (ddd, J = 16.9, 5.0, 2.6 Hz, 1H), 2.04 (t, J = 2.6 Hz, 1H), 2.03-1.96 (m, 1H), 1.24 (s, 9H), 0.95 (d, J = 5.8 Hz, 3H), 0.93 (d, J = 5.8 Hz, 3H); δ_C 80.3 (C), 71.4 (CH), 60.4 (CH), 56.2 (C), 31.2 (CH), 24.0 (CH_2), 22.8 (CH_3), 19.1, 18.3 (CH_3); LRMS (EI) m/z 215 (M^+, 0.6%), 197 (12), 159 (12), 149 (25), 133 (11), 120 (14), 119 (50), 116 (33), 83 (13), 73 (19), 70 (20), 57 (67), 43 (100), 41 (31); HRMS (ESI): Calculated for $C_7H_{13}NOS$ (M^+–C_4H_8) 159.0718, found 159.0723.

(3*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-phenylhex-5-yn-3-amine (10d):[16] The representative procedure was followed by using compound **9d** (174.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **10d** (115.2 mg, 0.41 mmol, 83%) as a yellow oil; $[\alpha]_D^{20}$ –23.5 (c = 0.86, CH_2Cl_2); R_f 0.20 (hexane/EtOAc, 1:1); IR ν (film) 3219, 3061, 3025, 2978, 2948, 2864, 2111, 1602, 1495, 1455, 1363, 1175, 1054, 699 cm^{-1}; δ_H 7.33-7.25 (m, 2H), 7.24-7.14 (m, 3H), 3.55 (d, J = 8.8 Hz, 1H), 3.47-3.32 (m, 1H), 2.82-2.61 m, CH_2, 3H), 2.56-2.44 (m, 1H), 2.07 (t, J = 2.6 Hz, 1H), 2.03-1.88 (m, 2H), 1.26 (s, 9H); δ_C 141.3 (C), 128.5 (CH), 128.3 (CH), 126.0 (CH), 79.9 (C), 71.7 (C), 56.1 (C), 54.3 (CH), 36.7 (CH_2), 32.0 (CH_2), 26.7 (CH_2), 22.6 (CH_3); LRMS (EI) m/z 221 (M^+–C_4H_8, 1%), 157 (11), 132 (53), 117 (51), 116 (28), 101 (16), 98 (16), 92 (10), 91 (100), 77 (16), 68 (32), 67 (28), 65 (19); HRMS (ESI): Calculated for $C_{12}H_{15}NOS$ (M^+–C_4H_8) 221.0874, found 221.0877.

(2*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-phenylpent-4-yn-2-amine (10e): The representative procedure was followed by using compound **9e** (167.5 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **10e** (120.6 mg, 0.46 mmol, 90%) as a yellow oil; $[\alpha]_D^{20}$ –16.5 (c = 1.16, CH_2Cl_2); R_f 0.25 (hexane/EtOAc, 1:1); IR ν (film) 3219, 2978, 2955, 2924, 2867, 1496, 1455, 1363, 1171, 1050, 902, 743, 700 cm^{-1}; δ_H 7.34-7.27 (m, 2H), 7.25-7.19 (m, 3H), 3.72-3.60 (m, 1H), 3.54 (d, J = 8.3 Hz, 1H), 2.98 (dd, J = 13.7, 6.7 Hz, 1H), 2.89 (dd, J = 13.7, 7.0 Hz, 1H), 2.59 (ddd, J = 16.8, 6.0, 2.6 Hz, 1H), 2.48 (ddd, J = 16.9, 4.6, 2.7 Hz, 1H), 2.14 (t, J = 2.6 Hz, 1H), 1.14 (s, 9H); δ_C 137.5 (C), 129.5, 128.5, 126.6 (CH), 80.0 (C), 71.9 (CH), 56.2 (C), 56.1 (CH), 40.9, 25.7 (CH_2), 22.5 (CH_3); LRMS (EI) m/z 263 (M^+–C_4H_8, 0.5%), 208 (13), 207 (59), 168 (15), 167 (60), 149 (24), 128 (16), 116 (100), 104 (20), 91 (98), 68 (20), 57 (82), 55 (17), 41 (34); HRMS (ESI): Calculated for $C_{11}H_{13}NOS$ (M^+–C_4H_8) 207.0718, found 207.0720.

(1*S*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-phenylbut-3-yn-1-amine (10f): The representative procedure was followed by using compound **9f** (96.3 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **10f** (64.2 mg, 0.26 mmol, 86%) as a white solid; mp 85–86 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –7.7 (c = 1.12, CH_2Cl_2); R_f 0.30 (hexane/EtOAc, 1:1); IR ν (film) 3210, 2958, 2937, 1454, 1428, 1348, 1202, 1049, 1050, 876, 776, 696, 638 cm^{-1}; δ_H 7.40-7.29 (m, 5H), 4.58 (ddd, J = 8.3, 5.2, 3.4 Hz, 1H), 4.04 (d, J = 3.3 Hz, 1H), 2.75 (ddd, J = 16.8, 5.2, 2.6 Hz, 1H), 2.67 (ddd, J = 16.8, 8.0, 2.6 Hz, 1H), 2.12 (t, J = 2.6 Hz, 1H), 1.23 (s, 9H); δ_C 140.3 (C), 128.5, 128.1, 127.4 (CH), 79.8 (C), 72.1 (CH), 56.8 (CH), 55.8 (C), 28.7 (CH_2), 22.6 (CH_3); LRMS (EI) m/z 249 (M^+, 0.3%), 193 (19), 154 (22), 153 (60), 129 (100), 128 (54), 104 (20), 57 (50), 43 (55); HRMS (ESI): Calculated for $C_{10}H_{11}NOS$ (M^+–C_4H_8) 193.0561, found 193.0553.

General Procedure for the Tandem Sonogashira-coupling Reaction and Cyclization of Terminal Alkynes 10 and *o*-Iodophenol 11. Isolation of compounds 12, 13 and 14: In a 10 mL vial containing a solution of the corresponding terminal alkyne **10** (0.3 mmol) in dry triethylamine (3 mL) was successively added *ortho*-iodophenol (**11**, 66 mg, 0.3 mmol), copper(I) iodide (1.1 mg, 0.006 mmol) and $Pd(PPh_3)_4$ (6.9 mg, 0.006 mmol). The mixture was irradiated for 45 min at 80 W power and 60 ºC. After that, the reaction mixture was cooled down to rt and filtered through a celite path with ethyl acetate (100 mL). The organic solution was washed with water (5 × 30 mL), dried with anhydrous $MgSO_4$, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield mainly products **12** and **13**. Yields, physical and spectroscopic data follow.

(4*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-(2-hydroxyphenyl)dodec-1-yn-4-amine (12a): The representative procedure was followed by using compound **10a** (85.5 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **12a** (9.8 mg, 0.02 mmol, 9%) as a yellow oil; $[\alpha]_D^{20}$ –39.1 (c = 0.98, CH_2Cl_2); R_f 0.45 (hexane/EtOAc, 2:1); IR ν (film) 3252, 2955, 2922, 2853, 1570, 1488, 1458, 1242, 1023, 1008, 749, 722 cm^{-1}; δ_H 8.47 (m, 1H), 7.29-7.24 (m, 1H), 7.21-7.15 (m, 1H), 6.92 (dd, J = 8.3, 0.9 Hz, 1H), 6.78 (td, J = 7.5, 1.1 Hz, 1H), 3.47-3.37 (m, 1H), 3.32 (d, J = 9.5 Hz, 1H), 2.95 (dd, J = 17.2, 3.8, 2.0 Hz, 1H), 2.54 (dd, J = 17.1, 7.3, 2.0 Hz, 1H), 1.61-1.48 (m, 2H), 1.37-1.15 (m, 21H), 0.88 (t, J = 6.8 Hz, 3H); δ_C 158.4 (C), 132.0, 129.8, 119.3, 116.2 (CH), 109.8, 91.5, 79.5 (C), 56.6 (CH), 56.5 (C), 36.7, 31.8, 29.4, 29.2, 28.2, 25.9 (CH_2), 22.6 (CH_3), 22.5 (CH_2), 14.1 (CH_3); LRMS (EI) m/z 377 (M^+, 7%), 304 (12), 274 (15), 273 (79), 216 (15), 190 (46), 175 (19), 174 (58), 162 (28), 161 (100), 160 (57), 142 (38), 131 (51), 77 (19), 57 (56), 43 (27; HRMS (EI): Calculated for $C_{18}H_{27}NO$ (M^+– C_4H_8OS) 273.2093; found 273.2082.

(4*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-1-(2-hydroxyphenyl)-6-methylhept-1-yn-4-amine (12b): The representative procedure was followed by using compound **10b** (68.7 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **12b** (12.1 mg, 0.04 mmol, 12%) as a white solid; mp 143–145 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –38.5 (c = 0.99, CH_2Cl_2); R_f 0.38 (hexane/EtOAc, 2:1); IR ν (film) 3247, 2956, 2936, 2863, 1603, 1453, 1413, 1364, 1270, 1008, 934, 749, 644 cm^{-1}; δ_H 8.50 (br s, 1H), 7.30-7.23 (m, 1H), 7.22-7.14 (m, 1H), 6.92 (dd, J = 8.3, 0.9 Hz, 1H), 6.78 (td, J = 7.5, 1.1 Hz, 1H), 3.59-3.45 (m, 1H), 3.29 (d, J = 9.9 Hz, 1H), 2.97 (dd, J = 17.1, 3.9 Hz, 1H), 2.51 (dd, J = 17.1, 6.9 Hz, 1H), 1.82-1.65 (m, 1H), 1.61-1.47 (m, 1H), 1.37-1.28 (m, 1H), 1.25 (s, 9H), 0.93 (d, J = 8.1 Hz, 3H), 0.91 (d, J = 7.9 Hz, 3H); δ_C 158.5 (C), 131.9, 129.8, 119.3, 116.2 (CH), 109.8, 91.5, 79.6, 56.6 (C), 54.7 (CH), 45.7, 28.7 (CH_2), 24.6 (CH), 23.0, 22.7, 21.6 (CH_3); LRMS (EI) m/z 321 (M^+, 5%), 162 (20), 161 (100), 160 (29), 134 (19), 131 (16), 77 (11), 57 (27); HRMS (ESI): Calculated for $C_{18}H_{27}NO_2S$ (M^+) 321.1762, found 321.1764.

(3*S*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-6-(2-hydroxyphenyl)-2-methylhex-5-yn-3-amine (12c): The representative procedure was followed by using compound **10c** (64.5 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **12c** (14.6 mg, 0.05 mmol, 15%) as a white solid; mp 146–148 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –75.7 (c = 1.21, CH_2Cl_2); R_f 0.40 (hexane/EtOAc, 2:1); IR ν (film) 3271, 2957, 2927, 2868, 1484, 1363, 1244, 1030, 1011, 913, 756 cm^{-1}; δ_H 8.64 (br s, 1H), 7.26 (dd, J = 7.7, 1.7 Hz, 1H), 7.18 (ddd, J = 8.3, 7.4, 1.7 Hz, 1H), 6.91 (dd, J = 8.3, 0.9 Hz, 1H), 6.78 (td, J = 7.5, 1.2 Hz, 1H), 3.39-3.23 (m, 2H), 2.92-2.80 (m, 1H), 2.65-2.55 (m, 1H), 1.89-1.75 (m, 1H), 1.27 (s, 9H), 0.99-0.93 (m, 6H); δ_C 158.3 (C), 132.1, 129.7, 119.3, 116.4 (CH), 109.9, 91.4, 79.5 (C), 61.8 (CH), 56.7 (C), 33.6 (CH), 25.4 (CH_2), 22.8, 19.2, 17.9 (CH_3); LRMS (EI) m/z 307 (M^+, 5%), 203 (29), 160 (100), 131 (19), 120 (13), 57 (26); HRMS (ESI): Calculated for $C_{13}H_{17}NO_2S$ (M^+–C_4H_8) 251.0980, found 251.0982.

(3*R*,*R*$_S$)-*N*-(*tert*-Butanesulfinyl)-6-(2-hydroxyphenyl)-1-phenylhex-5-yn-3-amine (12d): The representative procedure was followed by using compound **10d** (83.1 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **12d** (10.0 mg, 0.027 mmol, 9%) as a colorless wax; $[\alpha]_D^{20}$ -28.7 (c = 1.48, CH_2Cl_2); R_f 0.28 (hexane/EtOAc, 2:1); IR ν (film) 3187, 2971, 2962, 1487, 1292, 1264, 1241, 1031, 734 cm^{-1}; δ_H 7.38-7.12 (m, 7H), 6.92 (dd, J = 8.3, 1.1 Hz, 1H), 6.78 (td, J = 7.5, 1.2 Hz, 1H), 3.54-3.43 (m, 2H), 3.07-2.91 (m, 1H), 2.82-2.53 (m, 3H), 1.97-1.82 (m, 2H), 1.28 (s, 9H); δ_C 158.4, 141.0 (C), 132.0, 130.0, 128.6, 128.3, 126.2, 119.4, 116.1 (CH), 109.8, 91.2, 79.7, 56.7 (C), 56.0 (CH), 38.4, 32.2, 28.2 (CH_2), 22.8 (CH_3); LRMS (EI) m/z 369 (M^+, 3%), 162 (19), 161 (100), 160 (21), 131 (17), 117 (28), 91 (43), 57 (23); HRMS (EI): Calculated for $C_{18}H_{19}NO$ (M^+–C_4H_8OS) 265.1467; found 265.1459.

(2*R*,*R*$_S$)-2-(2-Aminodecyl)-*N*-(*tert*-butanesulfinyl)benzofuran (13a): The representative procedure was followed by using compound **10a** (85.5 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **13a** (49.2 mg, 0.13 mmol, 45%) as a yellow oil; $[\alpha]_D^{20}$ –5.1 (c = 1.00, CH_2Cl_2); R_f 0.28 (hexane/EtOAc, 2:1); IR ν (film) 3208, 2953, 2923, 2854, 1598, 1589, 1454, 1251, 1172, 1050, 750, 722 cm^{-1}; δ_H 7.52-7.49 (m, 1H), 7.44-7.39 (m, 1H), 7.26-7.15 (m, 2H), 6.56 (s, 1H), 3.67-3.58 (m, 1H), 3.49 (d, J = 7.9 Hz, 1H), 3.17 (dd, J = 14.9, 5.8 Hz, 1H), 3.09 (dd, J = 14.9, 5.2 Hz, 1H), 1.60-1.34 (m, 4H), 1.33-1.23 (m, 10H), 1.22 (s, 9H), 0.87 (t, J = 6.8 Hz, 3H); δ_C 155.2, 154.8, 128.6 (C), 123.5, 122.6, 120.5, 110.9, 105.1 (CH), 55.9 (C), 55.4 (CH), 35.4, 35.1, 31.8, 29.5, 29.3, 29.2, 25.7 (CH_2), 22.7, 14.1 (CH_3); LRMS (EI) m/z 377 (M^+, 0.4%), 321 (18), 246 (18), 190 (100), 189 (39), 142 (43), 131 (55), 57 (28); HRMS (EI): Calculated for $C_{18}H_{27}NO_2S$ (M^+–C_4H_8) 321.1762; found 321.1759.

(2*R*,*R*$_S$)-2-(2-Amino-4-methylpentyl)-*N*-(*tert*-butanesulfinyl)benzofuran (13b): The representative procedure was followed by using compound **10b** (68.7 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **13b** (47.2 mg, 0.15 mmol, 49%) as a yellow oil; $[\alpha]_D^{20}$ +10.6 (c = 1.09, CH_2Cl_2); R_f 0.21 (hexane/EtOAc, 2:1); IR ν (film) 3212, 2954, 2926, 2868, 1598, 1454, 1364, 1251, 1049, 795, 750 cm^{-1}; δ_H 7.53-7.50 (m, 1H), 7.45-7.14 (m, 1H), 7.26-7.14 (m, 2H), 6.56 (d, J = 0.9 Hz, 1H), 3.79-3.62 (m, 1H), 3.46 (d, J = 9.1 Hz, 1H), 3.21 (dd, J = 14.9, 6.1 Hz, 1H), 3.10 (dd, J = 14.6, 4.5 Hz, 1H), 1.83-1.71 (m, 1H), 1.45-1.37 (m, 1H), 1.34-1.25 (m, 1H), 1.22 (s, 9H), 0.89 (d, J = 6.7 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H); δ_C 155.2, 154.8, 128.6 (C), 123.5, 122.6, 120.5, 110.9, 105.1 (CH), 55.9 (C), 55.4 (CH), 35.4, 35.1, 31.8, 29.5, 29.3, 29.2, 25.7 (CH_2), 22.7, 14.1 (CH_3); LRMS (EI) m/z 321 (M^+, 0.5%), 265 (20), 190 (19), 134 (100), 133 (62), 131 (55), 86 (22), 57 (31); HRMS (EI): Calculated for $C_{14}H_{19}NO_2S$ (M^+–C_4H_8) 265.1136; found 265.1132.

(2*R*,*R*$_S$)-2-(2-Amino-3-methylbutyl)-*N*-(*tert*-butanesulfinyl)benzofuran (13c): The representative procedure was followed by using compound **10c** (64.5 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **13c** (44.3 mg, 0.14 mmol, 48%) as a yellow oil; $[\alpha]_D^{20}$ -31.0 (c = 0.91, CH_2Cl_2); R_f 0.22 (hexane/EtOAc, 2:1); IR ν (film) 3163, 2957, 2926, 2868, 1589, 1455, 1364, 1252, 1060, 1004, 750 cm^{-1}; δ_H 7.53-7.48 (m, 1H), 7.43-7.39 (m, 1H), 7.25-7.16 (m, 1H), 6.57 (d, J = 0.7 Hz, 1H), 3.53-3.40 (m, 2H), 3.18-3.12 (m, 2H), 1.86-1.74 (m, 1H), 1.24 (s, 9H), 0.99 (d, J = 6.7 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H); δ_C 155.4, 154.8, 128.5 (C), 123.5, 122.6, 120.5, 110.8, 104.9 (CH), 60.7 (CH), 56.1 (C), 32.4 (CH_2), 31.1 (CH), 22.7, 19.1, 18.0 (CH_3); LRMS (EI) m/z 307 (M^+, 0.7%), 251 (33), 176 (18), 133 (23), 131 (87), 120 (100), 119 (64), 72 (38), 57 (43); HRMS (EI): Calculated for $C_{13}H_{17}NO_2S$ (M^+–C_4H_8) 251.0980; found 251.0980.

(2*R*,*R*$_S$)-2-(2-Amino-4-phenylbutyl)-*N*-(*tert*-butanesulfinyl)benzofuran (13d): The representative procedure was followed by using compound **10d** (83.1 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **13d** (54.9 mg, 0.15 mmol, 50%) as a yellow oil; $[\alpha]_D^{20}$ -4.2 (c = 1.01, CH_2Cl_2); R_f 0.19 (hexane/EtOAc, 2:1); IR ν (film) 3208, 3060, 3020, 2951, 2922, 2864, 1603, 1454, 1251, 1050, 943, 742, 698 cm^{-1}; δ_H 7.53-7.48 (m, 1H), 7.44-7.39 (m, 1H), 7.30-7.26 (m, 1H), 7.25-7.23 (m, 1H), 7.22-7.13 (m, 5H), 6.55 (d, J = 0.9 Hz, 1H), 3.73-3.61 (m, 1H), 3.58 (d, J = 8.3 Hz, 1H), 3.24 (ddd, J = 14.9, 8.0, 0.8 Hz, 1H), 3.13 (ddd, J = 14.9, 4.8, 0.7 Hz, 1H), 2.84-2.73 (m, 1H), 2.73-2.63 (m, 1H), 1.97-1.85 (m, 1H), 1.85-1.73 (m, 1H), 1.25 (s, 9H); δ_C 154.8, 141.4, 128,6 (C), 128.5, 128.4, 126.0, 123.6, 122.7, 120.6, 110.9, 105.3 (CH), 56.1 (C), 55.0 (CH), 37.1, 35.4, 32.1 (CH_2), 22.7 (CH_3); LRMS (EI) m/z 369 (M^+, 0.3%), 313 (31), 238 (20), 182 (22), 164 (43), 134 (37), 131 (60), 117 (100), 91 (60), 77 (11), 57 (27); HRMS (EI): Calculated for $C_{18}H_{19}NO_2S$ (M^+–C_4H_8) 313.1136; found 313.1134.

(2*R*,*R*$_S$)-2-(2-Amino-3-phenylpropanyl)-*N*-(*tert*-butanesulfinyl)benzofuran (13e): The representative procedure was followed by using compound **10e** (78.9 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **13e** (71.4 mg, 0.20 mmol, 67%) as a yellow oil; $[\alpha]_D^{20}$ +0.9 (c = 1.19, CH_2Cl_2); R_f 0.15 (hexane/EtOAc, 2:1); IR ν (film) 3218, 3060, 3030, 2951, 2922, 2863, 1603, 1584, 1454, 1251, 1048, 740, 699 cm^{-1}; δ_H 7.56-7.50 (m , 1H), 7.48-7.41 (m, 1H), 7.35-7.27 (m, 2H), 7.26-7.27 (m, 5H), 6.59 (d, J = 0.9 Hz, 1H), 3.99-3.90 (m, 1H), 3.59 (d, J = 7.4 Hz, 1H), 3.18 (dd, J = 14.7, 5.7 Hz, 1H), 3.13 (dd, J = 14.7, 5.3 Hz, 1H), 2.88-2.83 (m, 2H), 1.10 (s, 9H); δ_C 154.9, 137.9 (C), 129.6 (CH), 128.5 (C), 128.4, 126.5, 123.7, 122.7, 120.6, 110.9, 105.3, 56.7 (CH), 56.0 (C), 41.5, 34.6 (CH_2), 22.4 (CH_3); LRMS (EI) m/z 355 (M^+–C_4H_8, 0.5%), 300 (12), 299 (59), 224 (17), 168 (100), 167 (55), 150 (17), 132 (23), 131 (95), 120 (74), 104 (26), 91 (42), 77 (17), 57 (44); HRMS (EI): Calculated for $C_{17}H_{17}NO_2S$ (M^+–C_4H_8) 299.0980; found 299.0979.

(2*R*,*R*$_S$)-2-(2-Amino-2-phenylethyl)-*N*-(*tert*-butanesulfinyl)benzofuran (13f): The representative procedure was followed by using compound **10f** (74.7 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **13f** (50.9 mg, 0.15 mmol, 50%) as a white solid; mp 157–160 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –56.9 (c = 1.04, CH_2Cl_2); R_f 0.18 (hexane/EtOAc, 1:1); IR ν (film) 3281, 3025, 2957, 2918, 2873, 1603, 1584, 1454, 1250, 1163, 1060 744, 697 cm^{-1}; δ_H 7.50-7.46 (m, 1H), 7.44-7.39 (m, 1H), 7.38-7.33 (m, 4H), 7.33-7.29 (m, 1H), 7.25-7.17 (m, 2H), 6.46 (d, J = 0.9 Hz, 1H), 4.85 (ddd, J = 8.2, 5.9, 2.4 Hz, 1H), 4.01 (d, J = 2.5 Hz, 1H), 3.30-3.21 (m, 2H), 1.19 (s, 9H); δ_C 154.8, 154.3, 140.8 (C), 128.6 (CH), 128.3 (C), 128.0, 127.5, 123.9, 122.7, 120.7, 110.9, 104.8, 57.1 (CH), 55.6 (C), 37.9 (CH_2), 22.6 (CH_3); LRMS (EI) m/z 341 (M^+–C_4H_8, 0.1%), 221 (22), 210 (38), 154 (100), 153 (31), 131 (25), 77 (11), 57 (20); HRMS (ESI): Calculated for $C_{16}H_{13}NO$ (M^+–$C_4H_{10}SO$) 235.0997, found 235.0997.

(3*R*,10*R*,3*R*$_S$,10*R*$_S$)-*N*,*N'*-Di-(*tert*-butanesulfinyl)-1,12-diphenyldodeca-5,7-diyne-3,10-diamine (14d): The representative procedure was modified, performing the reaction at 40 ºC for 4 h without microway irradiation. Starting from compound **10d** (83.1 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 1:1) yielded **14d** (38.9 mg, 0.07 mmol, 47%) as a yellow oil; $[\alpha]_D^{20}$ -3.1 (c = 1.07, CH_2Cl_2); R_f 0.05 (hexane/EtOAc, 2:1); IR ν (film) 3321, 2947, 2927, 2868, 1454, 1438, 1363, 1178, 1038, 724, 698 cm^{-1}; δ_H 7.3-7.04 (m, 10H), 3.47 (d, J = 9.2 Hz, 2H), 3.44-3.31 (m, 2H), 2.85-2.70 (m, 4H), 2.69-2.50 (m, 4H), 2.01-1.82 (m, 4H), 1.25 (s, 18H); δ_C 141.2 (C), 128.5, 128.3, 126.0 (CH), 73.5, 68.1, 56.2 (C), 54.7 (CH), 36.8, 32.0, 27.7 (CH_2), 22.7 (CH_3); LRMS (EI) m/z 497 (M^+— C_4H_8, 1%), 495 (11), 243 (12), 238 (10), 223 (12), 222 (66), 212 (11), 211 (62), 166 (17), 164 (11), 134 (64), 132 (14), 117 (53), 91 (100), 71 (10), 57 (72), 44 (16). It was not possible to get HRMS (ESI) for this compound.

General Procedure for the Sonogashira-coupling Reaction and of Terminal Alkynes 10 and *o*-Iodoaniline 17. Isolation of Compounds 18: To a solution of the corresponding terminal alkyne **10**

(0.3 mmol) in dry triethylamine (3 mL) was successively added *ortho*-iodoaniline (**17**, 66 mg, 0.3 mmol), copper(I) iodide (1.1 mg, 0.006 mmol) and $Pd(PPh_3)_4$ (6.9 mg, 0.006 mmol). The mixture was stirred and 60 ºC for 4 h. After that, the reaction mixture was cooled down to rt and filtered through a celite path with ethyl acetate (100 mL). The organic solution was washed with water (5 × 30 mL), dried with anhydrous $MgSO_4$, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield products **18**. The yields are given in Scheme 4, the physical and spectroscopic data follow.

(4*R*,*R*$_S$)-1-(2-Aminophenyl)-*N*-(*tert*-butanesulfinyl)dodec-1-yn-4-amine (18a): The representative procedure was followed by using compound **10a** (59.3 mg, 0.21 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **18a** (38.6 mg, 0.10 mmol, 50%) as a yellow oil; $[\alpha]_D^{20}$ -2.0 (c = 0.78, CH_2Cl_2); R_f 0.33 (hexane/EtOAc, 1:1); IR ν (film) 3330, 3212, 2954, 2924, 2854, 1618, 1493, 1456, 1314, 1050, 745 cm^{-1}; δ_H 7.24 (dd, J = 7.6, 1.6 Hz, 1H), 7.09 (ddd, J = 8.1, 7.3, 1.6 Hz, 1H), 6.73-6.62 (m, 2H), 3.62 (d, J = 8.5 Hz, 1H), 3.49-3.38 (m, 1H), 2.97 (dd, J = 16.8, 5.2 Hz, 1H), 2.70 (dd, J = 16.8, 4.9 Hz, 1H), 1.69-1.55 (m, 2H), 1.47-1.24 (m, 12H), 1.23 (s, 9H), 0.92-0.83 (m, 3H); δ_C 148.0 (C), 132.0, 129.2, 117.8, 114.5 (CH), 108.3, 90.9, 80.5, 56.1 (C), 55.4 (CH), 35.5, 31.8, 29.5, 29.3, 29.2, 27.8, 25.8 (CH_2), 22.7 (CH_3), 22.6 (CH_2), 14.1 (CH_3); LRMS (EI) m/z 376 (M^+, 21%), 320 (10), 319 (15), 272 (45), 215 (15), 190 (28), 174 (14), 173 (42), 162 (17), 161 (23), 160 (80), 159 (46), 143 (12), 142 (61), 131 (26), 129 (100), 77 (14), 57 (40); HRMS (EI): Calculated for $C_{18}H_{26}N_2OS$ (M^+–C_4H_{10}) 318.1766; found 318.1765.

(4*R*,*R*$_S$)-1-(2-Aminophenyl)-*N*-(*tert*-butanesulfinyl)-6-methylhept-1-yn-4-amine (18b): The representative procedure was followed by using compound **10b** (68.7 mg, 0.30 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **18b** (52.7 mg, 0.16 mmol, 55%) as a yellow oil; $[\alpha]_D^{20}$ +13.1 (c = 0.88, CH_2Cl_2); R_f 0.26 (hexane/EtOAc, 1:1); IR ν (film) 3341, 3210, 2955, 2928, 2868, 1617, 1492, 1455, 1364, 1314, 1049, 910, 745, 646 cm^{-1}; δ_H 7.26-7.21 (m, 1H), 7.13-7.05 (m, 1H), 6.73-6.62 (m, 2H), 3.58 (d, J = 9.4 Hz, 1H), 3.55-3.44 (m, 1H), 3.02 (dd, J = 16.8, 5.1 Hz, 1H), 2.68 (dd, J = 16.8, 4.1 Hz, 1H), 1.82-1.68 (m, 1H), 1.67-1.55 (m, 1H), 1.46-1.32 (m, 1H), 1.23 (s, 9H), 0.93 (d, J = 6.6 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H); δ_C 148.1 (C), 132.0, 129.2, 117.7, 114.4 (CH), 108.2, 90.8, 80.6, 56.2 (C), 53.7 (CH), 44.7, 28.3 (CH_2), 24.5 (CH_3), 23.0 (CH), 22.7, 21.8 (CH_3); LRMS (EI) m/z 320 (M^+, 14%), 162 (10), 161 (17), 160 (100), 159 (30), 134 (18), 131 (13), 130 (53), 86 (21), 77 (12), 57 (26); HRMS (EI): Calculated for $C_{18}H_{28}N_2OS$ (M^+) 320.1922; found 320.1921.

(3*S*,*R*S)-6-(2-Aminophenyl)-*N*-(*tert*-butanesulfinyl)-2-methylhex-5-yn-3-amine (18c): The representative procedure was followed by using compound **10c** (68.2 mg, 0.32 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **18c** (46.5 mg, 0.16 mmol, 51%) as a yellow oil; $[\alpha]_D^{20}$ -7.2 (c = 1.96, CH_2Cl_2); R_f 0.32 (hexane/EtOAc, 1:1); IR ν (film) 3341, 3222, 2959, 2926, 1618, 1493, 1456, 1386, 1314, 1052, 893, 745 cm^{-1}; δ_H 7.23 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.08 (ddd, *J* = 8.1, 7.3, 1.6 Hz, 1H), 6.69 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.65 (td, *J* = 7.5, 1.1 Hz, 1H), 3.60 (d, *J* = 8.3 Hz, 1H), 3.27-3.16 (m, 1H), 2.92 (dd, *J* = 17.0, 5.2 Hz, 1H), 2.79 (dd, *J* = 17.0, 5.8 Hz, 1H), 2.04-1.91 (m, 1H), 1.24 (s, 9H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H); δ_C 148.1 (C), 132.0, 129.2, 117.7, 114.5 (CH), 108.2, 90.9, 80.4 (C), 60.9 (CH), 56.3 (C), 32.1 (CH), 24.9 (CH_2), 22.8, 19.0, 18.4 (CH_3); LRMS (EI) *m*/*z* 306 (M^+, 16%), 202 (16), 160 (19), 159 (100), 131 (13), 130 (51), 120 (13), 77 (10), 72 (18), 57 (22); HRMS (EI): Calculated for $C_{17}H_{26}N_2OS$ (M^+) 306.1766; found 306.1763.

(3*R*,*R*$_S$)-6-(2-Aminophenyl)-*N*-(*tert*-butanesulfinyl)-1-phenylhex-5-yn-3-amine (18d): The representative procedure was followed by using compound **10d** (82.5 mg, 0.29 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **18d** (51.0 mg, 0.14 mmol, 50%) as a yellow oil; $[\alpha]_D^{20}$ -19.3 (*c* = 0.45, CH_2Cl_2); R_f 0.24 (hexane/EtOAc, 1:1); IR ν (film) 3208, 3030, 2924, 2853, 1616, 1492, 1455, 1313, 1157, 1052, 908, 730, 699 cm^{-1}; δ_H 7.32-7.26 (m, 2H), 7.25-7.17 (m, 4H), 7.09 (ddd, *J* = 8.2, 7.3, 1.6 Hz, 1H), 6.71 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.66 (td, *J* = 7.5, 1.1 Hz, 1H), 3.71 (d, *J* = 8.7 Hz, 1H), 3.52-3.43 (m, 1H), 3.01 (dd, *J* = 16.9, 5.4 Hz, 1H), 2.84-2.62 (m, C*H*H, 3H), 2.03-1.92 (m, 2H), 1.26 (s, 9H); δ_C 147.8, 141.3 (C), 132.0, 129.3, 128.5, 128.3, 126.0, 117.9, 114.6 (CH), 108.2, 90.6, 80.6, 56.3 (C), 54.9 (CH), 37.3, 32.1, 27.9 (CH_2), 22.7 (CH_3); LRMS (EI) *m*/*z* 368 (M^+, 8%), 311 (11), 161 (16), 160 (100), 159 (18), 134 (21), 131 (11), 130 (43), 117 (19), 91 (33), 57 (18); HRMS (EI): Calculated for $C_{22}H_{28}N_2OS$ (M^+) 368.1922; found 368.1921.

(2*R*,*R*$_S$)-5-(2-Aminophenyl)-*N*-(*tert*-butanesulfinyl)-1-phenylpent-4-yn-2-amine (18e): The representative procedure was followed by using compound **10e** (52.6 mg, 0.20 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **18e** (35.0 mg, 0.10 mmol, 51%) as a yellow oil; $[\alpha]_D^{20}$ -11.1 (*c* = 0.80, CH_2Cl_2); R_f 0.20 (hexane/EtOAc, 1:1); IR ν (film) 3203, 3026, 2951, 2908, 2859, 1615, 1493, 1455, 1045, 932, 743, 700 cm^{-1}; δ_H 7.36-7.19 (m, 6H), 7.12 (ddd, *J* = 8.1, 7.4, 1.6 Hz, 1H), 6.83 (d, *J* = 8.1 Hz, 1H), 6.73 (td, *J* = 7.5, 1.1 Hz, 1H), 3.86 (d, *J* = 8.2 Hz, 1H), 3.81-3.65 (m, 1H), 3.07-2.82 (m, 3H), 2.73 (dd, *J* = 16.9, 5.5 Hz, 1H), 1.13 (s, 9H); δ_C 146.9, 137.7 (C), 132.0, 129.5, 129.3, 128.5, 126.6, 118.6, 115.2 (CH), 108.9, 91.1, 80.6 (C), 57.0 (CH), 56.2 (C), 41.8, 26.9 (CH_2), 22.6 (CH_3); LRMS (EI) *m*/*z* 354 (M^+, 8%), 160 (11), 159 (100), 130 (38), 120 (21), 91 (15), 57 (15); HRMS (EI): Calculated for $C_{21}H_{26}N_2OS$ (M^+) 354.1766; found 354.1772.

(1*S*,*R*$_S$)-4-(2-Aminophenyl)-*N*-(*tert*-butanesulfinyl)-1-phenylbut-3-yn-1-amine (18f): The representative procedure was followed by using compound **10f** (69.0 mg, 0.27 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **18f** (43.0 mg, 0.13 mmol, 49%) as a white solid; mp 112–114 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ -84.1 (*c* = 0.63, CH_2Cl_2); R_f 0.25 (hexane/EtOAc, 1:1); IR ν (film) 3311, 3065, 3035, 2981, 2951, 2922, 2853, 1623, 1494, 1456, 1316, 1030, 868, 746, 701 cm^{-1}; δ_H 7.43-7.30 (m, 5H), 7.21 (dd, J = 7.7, 1.6 Hz, 1H), 7.09 (ddd, J = 8.1, 7.3, 1.6 Hz, 1H), 6.70 (d, J = 8.2 Hz, 1H), 6.66 (td, J = 7.5, 1.1 Hz, 1H), 4.73-4.65 (m, 1H), 4.20 (d, J = 4.0 Hz, 1H), 3.05 (dd, J = 16.9, 5.4 Hz, 1H), 2.97 (dd, J = 16.9, 7.8 Hz, 1H), 1.23 (s, 9H); δ_C 147.6, 141.0 (C), 132.1, 129.4, 128.6, 128.0, 127.2, 118.1, 114.7 (CH), 108.0, 90.5, 80.8 (C), 57.9 (CH), 55.9 (C), 30.0 (CH_2), 22.6 (CH_3); LRMS (EI) *m*/*z* 340 (M^+, 24%), 284 (14), 283 (18), 237 (17), 236 (100), 235 (33), 221 (20), 220 (57), 219 (25), 218 (25), 217 (15), 210 (43), 205 (15), 204 (19), 202 (13), 154 (92), 136 (37), 132 (19), 131 (32), 130 (83), 106 (43), 104 (25), 77 (33), 57 (55), 43 (20); HRMS (EI): Calculated for $C_{16}H_{16}N_2$ (M^+─C_4H_8OS) 236.1313; found 236.1311.

General Procedure for the Synthesis of 2-(2-Aminoalkyl)indoles 19 from Compounds 18: To a solution of the corresponding aminoalkyne **18** (0.1 mmol) in dry DMF (2 mL) was added copper(I) iodide (10.3 mg, 0.1 mmol). The reaction mixture was degassed and stirred at 100 ºC for 7 h, and after that, it was cooled down to rt, hydrolyzed with water (20 mL) and extracted with EtOAc (3 × 15 mL). The combined organic phases were washed first with brine (3 × 10 mL), dried with anhydrous $MgSO_4$ and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield products **19**. The yields are given in Scheme 4, the physical and spectroscopic data follow.

(2*R*,*R*$_S$)-2-(2-Amino-4-methylpentyl)-*N*-(*tert*-butanesulfinyl)indole (19b): The representative procedure was followed by using compound **18b** (46.3 mg, 0.14 mmol). Purification by column chromatography (hexane/AcOEt, 5:1) yielded **19b** (6.4 mg, 0.02 mmol, 20%) as a colorless wax; $[\alpha]_D^{20}$ +89.3 (c = 0.30, CH_2Cl_2); R_f 0.23 (hexane/EtOAc, 4:1); IR ν (film) 3257, 2954, 2926, 2864, 1457, 1364, 1289, 1040, 919, 786, 734 cm^{-1}; δ_H 9.97 (br s, 1H), 7.60-7.53 (m, 1H), 7.42-7.34 (m, 1H), 7.18-7.01 (m, 2H), 6.25 (s, 1H), 3.71-3.53 (m, 1H), 3.46 (dd, J = 14.3, 5.4 Hz, 1H), 3.03 (d, J = 11.4 Hz, 1H), 2.87 (dd, J = 14.3, 1.9 Hz, 1H), 1.72-1.59 (m, 2H), 1.50-1.35 (m, 1H), 1.22 (s, 9H), 0.90 (d, J = 6.9 Hz, 3H), 0.87 (d, J = 7.0 Hz, 3H); δ_C 136.1, 133.5, 128.4 (C), 121.0, 119.6, 119.3, 110.9, 102.4 (CH), 56.4 (C), 54.6 (CH), 43.4, 35.0 (CH_2), 24.5 (CH), 23.0, 22.5, 21.4 (CH_3); LRMS (EI) *m*/*z* 320 (M^+, 21%), 199 (14), 190 (22), 134 (51), 132 (27), 131 (57), 130 (100), 86 (19), 57 (23), 43 (15); HRMS (ESI): Calculated for $C_{18}H_{28}N_2OS$ (M^+) 320.1922, found 320.1923.

(2*R*,*R*$_S$)-2-(2-Amino-3-methylbutyl)-*N*-(*tert*-butanesulfinyl)indole (19c): The representative procedure was followed by using compound **18c** (43.7 mg, 0.14 mmol). Purification by column chromatography (hexane/AcOEt, 6:1) yielded **19c** (17.1 mg, 0.05 mmol, 40%) as a colorless wax; $[\alpha]_D^{20}$ -7.3 (c = 1.50, CH_2Cl_2); R_f 0.20 (hexane/EtOAc, 4:1); IR ν (film) 3247, 2959, 2922, 2873, 1457, 1364, 1289, 1170, 1043, 1004, 885, 786, 734 cm^{-1}; δ_H 9.93 (br s, 1H), 7.54 (d, J = 7.6 Hz, 1H), 7.38 (dd, J = 8.0, 1.0 Hz, 1H), 7.20-7.00 (m, 2H), 6.28 (d, J = 2.4 Hz, 1H), 3.40-3.07 (m, 4H), 1.72-1.55 (m, 1H), 1.23 (s, 9H), 1.09 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 3H); δ_C 136.0, 133.8, 128.4 (C), 121.0, 119.6, 119.3, 110.9, 101.8, 63.1 (CH), 56.6 (C), 32.0 (CH_2), 31.3 (CH), 22.6, 20.2, 19.8 (CH_3); LRMS (EI) *m/z* 306 (M^+, 22%), 185 (17), 176 (19), 132 (23), 131 (54), 130 (100), 120 (34), 72 (21), 57 (25), 43 (20); HRMS (ESI): Calculated for $C_{17}H_{26}N_2OS$ (M^+) 306.1766, found 306.1768.

(2*R*,*R*$_S$)-2-(2-Amino-4-phenylbutyl)-*N*-(*tert*-butanesulfinyl)indole (19d): The representative procedure was followed by using compound **18d** (43.1 mg, 0.12 mmol). Purification by column chromatography (hexane/AcOEt, 4:1) yielded **19d** (20.3 mg, 0.045 mmol, 39%) as a colorless wax; $[\alpha]_D^{20}$ -15.3 (*c* = 0.80, CH_2Cl_2); R_f 0.14 (hexane/EtOAc, 4:1); IR ν (film) 3247, 2952, 2922, 2853, 1455, 1363, 1287, 1179, 1030, 788, 734, 699 cm^{-1}; δ_H 9.89 (br s, 1H), 7.54 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.38 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.31-7.26 (m, 2H), 7.22-7.04 (m, 5H), 6.28-6.25 (m, 1H), 3.62-3.51 (m, 1H), 3.46 (dd, *J* = 14.4, 5.4 Hz, 1H), 3.15 (d, *J* = 11.2 Hz, 1H), 2.93 (dd, *J* = 14.4, 1.9 Hz, 1H), 2.77-2.61 (m, 2H), 1.85-1.72 (m, 2H), 1.25 (s, 9H); δ_C 141.3, 136.1, 133.2 (C), 128.5 (CH), 128.4 (C), 128.3, 126.1, 121.1, 119.7, 119.3, 110.9, 102.4 (CH), 56.5 (C), 56.1 (CH), 36.6, 34.9, 32.6 (CH_2), 22.6 (CH_3); LRMS (EI) *m/z* 368 (M^+, 16%), 247 (11), 238 (32), 164 (24), 156 (12), 134 (32), 132 (27), 131 (53), 130 (100), 117 (41), 91 (33), 57 (20); HRMS (ESI): Calculated for $C_{22}H_{28}N_2OS$ (M^+) 368.1922, found 368.1923.

(2*R*,*R*$_S$)-2-(2-Amino-3-phenylpropanyl)-*N*-(*tert*-butanesulfinyl)indole (19e): The representative procedure was followed by using compound **18e** (29.0 mg, 0.08 mmol). Purification by column chromatography (hexane/AcOEt, 4:1) yielded **19e** (7.9 mg, 0.024 mmol, 30%) as a colorless wax; $[\alpha]_D^{20}$ -23.1 (*c* = 0.70, CH_2Cl_2); R_f 0.13 (hexane/EtOAc, 4:1); IR ν (film) 3238, 2953, 2922, 2853, 1455, 1289, 1182, 1032, 1012, 789, 738, 700 cm^{-1}; δ_H 9.94 (br s, 1H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.41 (d, *J* = 7.2 Hz, 1H), 7.32-7.26 (m, 2H), 7.24-7.05 (m, 5H), 6.35 (d, *J* = 2.3 Hz, 1H), 3.92-3.78 (m, 1H), 3.43 (dd, *J* = 14.5, 5.5 Hz, 1H), 3.18 (d, *J* = 11.1 Hz, 1H), 3.00 (dd, *J* = 14.5, 2.1 Hz, 1H), 2.84 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.68 (dd, *J* = 14.0, 8.7 Hz, 1H), 1.06 (s, 9H); δ_C 138.3, 136.2, 133.1 (C), 129.2, 128.4, 126.5, 121.1, 119.7, 119.4, 111.0, 102.7, 58.2 (CH), 56.4 (C), 40.8, 34.1 (CH_2), 22.3 (CH_3); LRMS (EI) *m/z* 354 (M^+, 20%), 298 (12), 233 (18), 224 (23), 168 (31), 132 (21), 131 (54), 130 (100), 120 (39), 91 (15), 57 (24); HRMS (ESI): Calculated for $C_{21}H_{26}N_2OS$ (M^+) 354.1766, found 354.1757.

(2*R*,*R*$_S$)-2-(2-Amino-2-phenylethyl)-*N*-(*tert*-butanesulfinyl)indole (19f): The representative procedure was followed by using compound **18f** (39.5 mg, 0.12 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **19f** (5.3 mg, 0.015 mmol, 15%) as a colorless wax; $[\alpha]_D^{20}$ -78.3 (*c* = 0.15, CH_2Cl_2); R_f 0.14 (hexane/EtOAc, 2:1); IR ν (film) 3222, 2957, 2918, 2859, 1456, 1264, 1151, 1027, 734, 699 cm^{-1}; δ_H 9.10 (br s, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.37-7.29 (m, 4H), 7.26-7.23 (m, 2H), 7.11 (ddd, J = 8.2, 7.1, 1.3 Hz, 1H), 7.09-7.00 (m, 1H), 6.11 (s, 1H), 4.86-4.78 (m, 1H), 3.83 (d, J = 6.9 Hz, 1H), 3.49 (dd, J = 14.7, 5.6 Hz, 1H), 3.30 (dd, J = 14.7, 5.4 Hz, 1H), 1.19 (s, 9H); δ_C 141.3, 136.5, 133.4 (C), 128.7 (CH), 128.5 (C), 127.8, 127.0, 121.5, 120.1, 119.6, 111.0, 102.9, 58.7 (CH), 56.3 (C), 37.4 (CH_2), 22.7 (CH_3); LRMS (EI) m/z 340 (M^+, 8%), 220 (14), 219 (14), 218 (12), 210 (60), 154 (100), 153 (11), 136 (22), 132 (15), 131 (39), 130 (83), 106 (20), 103 (12), 77 (13), 57 (31), 43 (26); HRMS (ESI): Calculated for $C_{11}H_{16}NOS$ (M^+−C_9H_8N) 210.0953, found 210.0958.

General Procedure for the Synthesis of Tetrahydro-1*H*-pyrido[4,3-*b*]- Benzofuran and Indole Derivatives 16 and 21: To a solution of the corresponding 2-(2-aminoalkyl)benzofuran or indole derivative, **13** or **19** (0.1 mmol), respectively, in MeOH (1 mL) was added under argon a 4 M HCl dioxane solution (0.3 mL) at 0 ºC. After 2 h of stirring at the same temperature, the solvent was evaporated (15 Torr) and a saturated sodium bicarbonate aqueous solution (10 mL) was added to the resulting residue. Then, it was extracted with EtOAc (3 × 15 mL), washed with brine (2 × 10 mL), dried with anhydrous $MgSO_4$ and the solvent evaporated (15 Torr). The resulting free amine **15** or **20** was dissolved in dry dichloromethane (1 mL) and then the corresponding aldehyde (0.13 mmol) was added. The reaction was stirred at rt for 5 h (until no starting material **15** or **20** was observed by GC). Then, anhydrous magnesium sulfate (0.5 g) was added, after 10 minutes filtered off, and the solvent was evaporated (15 Torr). A solution of the resulting residue in trifluoroacetic acid (0.6 mL) was placed in a high pressure tube and heated at 90 ºC for 24 h. Then, the reaction mixture was cooled down and the solvent evaporated (15 Torr). A saturated sodium bicarbonate aqueous solution (10 mL) was added to the resulting residue. Then, it was extracted with EtOAc (3 × 15 mL), dried with anhydrous $MgSO_4$ and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield products **16** and **21**. The yields are given in Tables 2 and 3, the physical and spectroscopic data follow.

(*R*)-3-Octyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16aa): The representative procedure was followed by using compound **13a** (31.0 mg, 0.08 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **16aa** (9.2 mg, 0.03 mmol, 45%) as a yellow oil; $[\alpha]_D^{20}$ -48.1 (c = 0.74, CH_2Cl_2); R_f 0.32 (hexane/EtOAc, 1:1); IR ν (film) 2953, 2923, 1642, 1451, 1184, 742, 722 cm^{-1}; δ_H 7.45-7.35 (m, 2H), 7.25-7.16 (m, 2H), 4.11-4.03 (m, 2H), 4.03-3.94 (m, 1H), 3.10-2.98 (m, 1H), 2.90-2.79 (m, 1H), 2.59-2.45 (m, 1H), 1.75-1.55 (m, 2H), 1.53-1.41 (m, 2H), 1.39-1.19 (m, 11H), 0.93-0.84 (m, 3H); δ_C 154.4, 152.6, 126.8 (C), 123.3, 122.4, 118.3 (CH), 112.1 (C), 111.0, 54.0 (CH), 41.2, 36.1, 31.9, 30.6, 29.7, 29.5, 29.3, 26.1, 22.7 (CH_2), 14.1 (CH_3); LRMS (EI) m/z 353 (M^+, 8%), 349 (16), 348 (15), 221 (18), 220 (100), 219 (46); HRMS (EI): Calculated for $C_{19}H_{27}NO$ (M^+) 285.2093; found 285.2094.

(*R*)-3-Benzyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16ea): The representative procedure was followed by using compound **13e** (45.0 mg, 0.13 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **16ea** (15.5 mg, 0.06 mmol, 47%) as a colorless oil; $[\alpha]_D^{20}$ -41.8 (c = 1.20, CH_2Cl_2); R_f 0.26 (hexane/EtOAc, 1:1); IR ν (film) 3060, 3023, 2923, 2848, 1644, 1602, 1450, 1185, 742, 699 cm^{-1}; δ_H 7.43-7.38 (m, 1H), 7.37-7.32 (m, 3H), 7.29-7.25 (m, 3H), 7.24-7.13 (m, 2H), 4.10-4.00 (m, 1H), 3.99-3.89 (m, 1H), 3.39-3.27 (m, 1H), 2.99-2.92 (m, 2H), 2.85-2.73 (m, 1H), 2.71-2.57 (m, 1H), 2.30 (br s, 1H); δ_C 154.5, 152.2, 138.1 (C), 129.3, 128.7 (CH), 126.7 (C), 126.6, 123.3, 122.4, 118.3 (CH), 111.9 (C), 111.0, 55.0 (CH), 42.3, 41.2, 30.4 (CH_2); LRMS (EI) m/z 263 (M^+, 1%), 173 (12), 172 (100), 170 (10), 145 (33), 144 (44), 115 (20), 91 (11); HRMS (EI): Calculated for $C_{11}H_{10}NO$ (M^+—C_7H_7) 172.0762; found 172.0766.

(*R*)-6,6a,7,14-Tetrahydro-12*H*-benzofuro[2',3':4,5]pyrido[1,2-*b*]isoquinoline (16ea'): The representative procedure was followed by using compound **13e** (45.0 mg, 0.13 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **16ea'** (11.1 mg, 0.04 mmol, 33%) as a white solid; mp 148–150 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –48.2 (c = 0.73, CH_2Cl_2); R_f 0.68 (hexane/EtOAc, 1:1); IR ν (film) 3025, 2955, 2853, 2765, 1662, 1451, 1211, 1191, 1076, 1020, 745, 736 cm^{-1}; δ_H 7.46-7.34 (m, 2H), 7.25-7.15 (m, 4H), 7.14-7.03 (m, 2H), 4.14-4.05 (m, 2H), 4.06-3.95 (m, 2H), 3.73-3.58 (m, 1H), 3.18-3.00 (m, 2H), 2.92 (dd, J = 16.8, 7.6 Hz, 1H), 2.78 (ddt, J = 17.0, 7.2, 2.1 Hz, 1H); δ_C 149.8, 145.6, 128.0, 127.5 (C), 123.9 (CH), 122.0 (C), 121.6, 121.5, 121.2, 118.5, 117.5, 113.3, 106.1 (CH), 104.7 (C), 48.5 (CH_2), 48.0 (CH), 42.3, 27.2, 22.5 (CH_2); LRMS (EI) m/z 275 (M^+, 25%), 145 (14), 144 (100); HRMS (ESI): Calculated for $C_{19}H_{17}NO$ (M^+) 275.1310, found 275.1303.

(*S*)-3-Phenyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16fa): The representative procedure was followed by using compound **13f** (34.1 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 4:1) yielded **16fa** (12.1 mg, 0.048 mmol, 49%) as a white wax; $[\alpha]_D^{20}$ –31.3 (c = 0.48, CH_2Cl_2); R_f 0.42 (hexane/EtOAc, 1:1); IR ν (film) 3025, 2955, 2853, 2765, 1662, 1451, 1211, 1191, 1076, 1020, 745, 736 cm^{-1}; δ_H 7.55-7.33 (m, 9H), 7.25-7.19 (m, 1H), 4.24 (t, J = 7.1 Hz, 1H), 4.20-4.11 (m, 2H), 3.16-3.08 (m, 2H); δ_C 154.6, 151.7 (C), 128.9, 128.2, 127.1 (CH), 126.5 (C), 123.7, 122.6, 118.4, 111.2 (CH), 111.0 (C), 58.1 (CH), 41.3, 31.5 (CH_2); LRMS (EI) m/z 249 (M^+, 16%), 145 (13), 144 (100), 115 (22); HRMS (ESI): Calculated for $C_{17}H_{15}NO$ (M^+) 249.1154, found 249.1153.

(1*S*,3*R*)-3-Benzyl-1-isobutyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16eb): The representative procedure was followed by using compound **13e** (35.5 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 9:1) yielded **16eb** (9.9 mg, 0.03 mmol, 30%) as a yellow wax; $[\alpha]_D^{20}$ –60.5 (c = 0.44, CH_2Cl_2); R_f 0.42 (hexane/EtOAc, 1:1); IR ν (film) 3060, 3030, 2954, 2925, 2864, 1718, 1450, 1178, 742, 699 cm^{-1}; δ_H 7.49-7.26 (m, 8H), 7.21-7.16 (m, 2H), 4.14 (d, *J* = 10.3 Hz, 1H), 3.36-3.19 (m, 1H), 3.06-2.87 (m, 1H), 2.76-2.66 (m, 2H), 2.07-1.89 (m, 2H), 1.71-1.57 (m, 1H), 0.95 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.3 Hz, 3H); δ_C 154.73, 152.3, 138.1 (C), 129.1, 128.7, 126.7 (CH), 126.5 (C), 123.0, 122.2, 119.4, 111.2, 55.2, 51.1 (CH), 43.9, 42.2, 39.2 (CH_2), 24.4 (CH), 24.1, 21.3 (CH_3); LRMS (EI) *m*/*z* 319 (M^+, 1%), 273 (32), 263 (20), 262 (100), 229 (11), 228 (68), 200 (17), 185 (13), 183 (17), 170 (30), 157 (18), 91 (15); HRMS (ESI): Calculated for $C_{18}H_{16}NO$ (M^+—C_4H_9) 262.1232, found 262.1236.

(1*S*,3*S*)-1-Isobutyl-3-phenyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16fb): The representative procedure was followed by using compound **13f** (34.1 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 20:1) yielded **16fb** (13.9 mg, 0.045 mmol, 46%) as a yellow oil; $[\alpha]_D^{20}$ –87.0 (*c* = 0.95, CH_2Cl_2); R_f 0.62 (hexane/EtOAc, 9:1); IR ν (film) 2951, 2925, 2868, 1450, 1265, 1216, 1116, 1012, 844, 742, 698 cm^{-1}; δ_H 7.57-7.49 (m, 3H), 7.48-7.30 (ArH, 5H), 7.25-7.19 (m, 2H), 4.38 (d, *J* = 10.3 Hz, 1H), 4.13 (t, *J* = 7.1 Hz, 1H), 3.01 (br s, 2H), 2.07-1.89 (m, 2H), 1.76-1.57 (m, 1H), 1.07 (d, *J* = 6.2 Hz, 3H), 0.97 (d, *J* = 6.2 Hz, 3H); δ_C 154.7, 128.7 (C), 127.8, 127.0 (CH), 126.5 (C), 123.1, 122.3, 119.5, 111.2, 58.1, 51.4 (CH), 44.0, 29.7 (CH_2), 24.3 (CH_3), 24.2 (CH), 21.5 (CH_3); LRMS (EI) *m*/*z* 305 (M^+, 4%), 259 (27), 249 (19), 248 (100), 200 (41), 185 (18), 157 (33), 144 (14), 128 (12); HRMS (ESI): Calculated for $C_{21}H_{23}NO$ (M^+) 305.1780, found 305.1772.

(1*S*,3*R*)-3-Phenethyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16dc): The representative procedure was followed by using compound **13d** (40.1 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 9:1) yielded **16dc** (19.2 mg, 0.054 mmol, 55%) as a white solid; mp 69–70 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –26.2 (*c* = 1.69, CH_2Cl_2); R_f 0.33 (hexane/EtOAc, 9:1); IR ν (film) 3050, 3020, 2922, 2853, 1494, 1450, 1174, 1030, 819, 742, 698 cm^{-1}; δ_H 7.45-7.16 (m, 12H, NH), 7.20-7.07 (m, 1H), 6.94 (td, *J* = 7.6, 1.0 Hz, 1H), 6.59 (dt, *J* = 7.7, 1.0 Hz, 1H), 5.14-5.03 (m, 1H), 3.27-3.11 (m, 1H), 2.90 (ddd, *J* = 16.2, 4.0, 2.2 Hz, 1H), 2.84.2.65 (m, 3H), 2.08-1.87 (m, 2H); δ_C 154.5, 153.6, 141.5 (C), 128.6, 128.5, 128.4, 128.3, 128.0 (CH), 126.5 (C), 126.0, 123.0, 122.2, 119.6, 110.9, 58.3, 54.1 (CH), 32.3, 31.0, 29.7 (CH_2); LRMS (EI) *m*/*z* 353 (M^+, 8%), 349 (16), 348 (15), 221 (18), 220 (100), 219 (46); HRMS (ESI): Calculated for $C_{25}H_{23}NO$ (M^+) 353.1780, found 353.1776.

(1*S*,3*R*)-3-Benzyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]benzofuran (16ec): The representative procedure was followed by using compound **13e** (35.5 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 9:1) yielded **16ec** (16.2 mg, 0.05 mmol, 50%) as a white solid; mp 118–120 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ +6.6 (*c* = 1.28, CH_2Cl_2); R_f 0.32 (hexane/EtOAc, 9:1); IR ν (film) 3055, 3025, 2918, 2878, 2848, 1638, 1449, 1302, 1178, 1011, 835, 747, 700, 615 cm^{-1}; δ_H 7.41-7.21 (m, 12H), 7.16-7.07 (m, 1H), 6.98-6.88 (m, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 5.07 (br s, 1H), 3.53-3.40 (m, 1H), 3.03-2.85 (m, 2H), 2.83-2.70 (m, 2H); δ_C 154.6, 153.3, 138.1 (C), 129.2, 128.6, 128.5, 128.1, 126.6 (CH), 126.5 (C), 123.0, 122.2, 119.5, 110.9, 58.4, 56.0 (CH), 42.5, 31.0 (CH_2); LRMS (EI) *m*/*z* 339 (M^+, 1%), 334 (22), 249 (19), 248 (100), 246 (11), 221 (11), 220 (41), 191 (11), 91 (13); HRMS (ESI): Calculated for $C_{18}H_{16}NO$ (M^+–C_6H_5) 262.1232, found 262.1230.

(1*S*,3*R*)-1,3-Diisobutyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (21bb): The representative procedure was followed by using compound **19b** (32.0 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 1:1) yielded **21bb** (12.9 mg, 0.045 mmol, 45%) as a yellow solid; mp 88–90 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ -129.4 (c = 0.18, CH_2Cl_2); R_f 0.28 (hexane/EtOAc, 1:2); IR ν (film) 3400, 2952, 2927, 2868, 1461, 1366, 1316, 1126, 1018, 736 cm^{-1}; δ_H 7.77 (s, 1H), 7.58-7.53 (m, 1H), 7.31-7.27 (m, 1H), 7.14-7.03 (m, 2H), 4.27 (dd, *J* = 10.5, 2.4 Hz, 1H), 3.08-2.94 (m, 1H), 2.67 (ddd, *J* = 15.3, 3.7, 1.8 Hz, 1H), 2.56-2.42 (m, 1H), 2.22-2.11 (m, 1H), 2.01-1.91 (m, 1H), 1.87-1.77 (m, 1H), 1.60-1.39 (m, 3H), 1.09 (d, *J* = 6.5 Hz, 3H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.96 (d, *J* = 6.6 Hz, 6H); δ_C 135.9, 133.2, 125.6 (C), 120.8, 119.1, 119.1 (CH), 113.3 (C), 110.7, 51.6, 51.5 (CH), 45.8, 45.2, 31.3 (CH_2), 24.8, 24.5, 24.3, 22.8, 21.4 (CH_3, CH); LRMS (EI) *m*/*z* 284 (M^+, 2%), 228 (17), 227 (100), 184 (11), 169 (11), 43 (24); HRMS (ESI): Calculated for $C_{19}H_{28}N_2$ (M^+) 284.2252, found 284.2245.

(1*S*,3*S*)-1-Isobutyl-3-phenethyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (21db): The representative procedure was followed by using compound **19d** (36.8 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 1:1) yielded **21db** (18.2 mg, 0.055 mmol, 45%) as a yellow solid; mp 104–105 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ -73.6 (c = 0.15, CH_2Cl_2); R_f 0.37 (hexane/EtOAc, 1:2); IR ν (film) 3400, 3056, 3026, 2950, 2924, 2865, 1608, 1453, 1319, 1239, 1128, 1018, 738, 698 cm^{-1}; δ_H 7.82 (s, 1H), 7.54 (dd, *J* = 7.2, 1.7 Hz, 1H), 7.35-7.16 (m, 6H), 7.14-7.02 (m, 2H), 4.22 (dd, *J* = 10.6, 2.3 Hz, 1H), 3.03-2.88 (m, 1H), 2.87-2.75 (m, 2H), 2.75-2.49 (m, 2H), 2.14 (ddd, *J* = 13.6, 10.7, 2.6 Hz, 1H), 2.02-1.82 (m, 4H), 1.53 (ddd, *J* = 13.9, 10.6, 3.4 Hz, 1H), 1.08 (d, *J* = 6.5 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H); δ_C 141.8, 135.9, 132.9 (C), 128.4, 128.3, 125.9 (CH), 125.5 (C), 120.8, 119.1, 119.0 (CH), 113.2 (C), 110.7, 53.2, 51.5 (CH), 45.2, 38.0, 32.6, 31.0 (CH_2), 24.4, 24.3 (CH_3), 21.5 (CH); LRMS (EI) *m*/*z* 141.8, 135.9, 132.9 (C), 128.4, 128.3, 125.9 (CH), 125.5 (C), 120.8, 119.1, 119.0 (CH), 113.2 (C), 110.7, 53.2, 51.5 (CH), 45.2, 38.0, 32.6, 31.0 (CH_2), 24.4, 24.3 (CH_3), 21.5 (CH); HRMS (ESI): Calculated for $C_{23}H_{28}N_2$ (M^+) 332.2252, found 332.2231.

(1*S*,3*R*)-3-Isobutyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (21bc): The representative procedure was followed by using compound **19b** (32.0 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **21bc** (15.8 mg, 0.052 mmol, 52%) as a yellow solid; mp 84–85 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ -40.2 (c = 0.11, CH_2Cl_2); R_f 0.37 (hexane/EtOAc, 1:2); IR ν (film) 3395, 3060, 2953, 2922, 1455, 1316, 1239, 737, 699 cm^{-1}; δ_H 7.88 (s, 1H), 7.44-7.23 (m, 6H), 7.03 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 6.81 (td, J = 7.5, 1.0 Hz, 1H), 6.62 (d, J = 7.9 Hz, 1H), 5.19 (s, 1H), 3.34-3.16 (m, 1H), 2.81-2.57 (m, 2H), 1.91-1.75 (m, 1H), 1.72 (s, 1H), 1.63-1.38 (m, 2H), 0.97 (d, J = 6.6 Hz, 3H), 0.95 (d, J = 6.5 Hz, 3H); δ_C 143.4, 135.8, 134.1 (C), 128.6, 128.5, 127.5 (CH), 125.7 (C), 120.9, 119.2, 119.1 (CH), 112.2 (C), 110.4, 59.4, 52.5 (CH), 45.9, 31.0 (CH_2), 24.6 (CH), 22.9, 22.7 (CH_3); LRMS (EI) m/z 304 (M^+, 10%), 220 (18), 219 (95), 218 (100), 217 (23); HRMS (ESI): Calculated for $C_{21}H_{24}N_2$ (M^+) 304.1939, found 304.1932.

(1*S*,3*R*)-3-Phenethyl-1-phenyl-2,3,4,5-tetrahydro-1*H*-pyrido[4,3-*b*]indole (21dc): The representative procedure was followed by using compound **19d** (36.8 mg, 0.10 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **21dc** (16.4 mg, 0.047 mmol, 47%) as a yellow solid; mp 80–82 °C (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ -45.1 (c = 0.30, CH_2Cl_2); R_f 0.42 (hexane/EtOAc, 1:2); IR ν (film) 3193, 3025, 2927, 2838, 1494, 1453, 1317, 1238, 1028, 858, 839, 739, 698 cm^{-1}; δ_H 7.87 (m, 1H), 7.41-7.15 (m, 11H), 7.04 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 6.81 (ddd, J = 8.1, 7.1, 1.0 Hz, 1H), 6.62 (dd, J = 7.9, 1.0 Hz, 1H), 5.19-5.13 (m, 1H), 3.24-3.11 (m, 1H), 2.85-2.75 (m, 3H), 2.71 (ddd, J = 15.5, 10.3, 2.6 Hz, 1H), 2.03-1.89 (m, 2H); δ_C 143.3, 141.8, 135.7, 133.9 (C), 128.6, 128.5, 128.4, 128.3, 127.6, 125.9 (CH), 125.7 (C), 121.0, 119.2, 119.1 (CH), 112.2 (C), 110.4, 59.2, 54.1 (CH), 38.2, 32.4, 30.7 (CH_2); LRMS (EI) m/z 352 (M^+, 11%), 220 (20), 219 (100), 218 (86), 217 (21); HRMS (ESI): Calculated for $C_{25}H_{24}N_2$ (M^+) 352.1939, found 352.1943.

ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H, ^{13}C NMR and DEPT spectra for all the reported compounds and NOESY spectra for compounds **16fb**, **16dc**, **16ec**, **21bb**, **21db**, **21bc** and **21dc**.

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