An Efficient Synthesis of a (−)-Physostigmine's Library for Identifying Potential Anti-*Alzheimer*'s Agents

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An efficient route for the synthesis of (−)-physostigmine analogs **1a**–**1g** and **2a**–**2k** is described. Analogs **1a**–**1g** were synthesized *via* copper(I)-catalyzed cycloaddition between the optically pure azide **10** and a variety of alkynes. Similarly, analogs **2a**–**2k** were prepared through 'three-component *Huisgen* cycloaddition' using various amines, propargyl bromine, and **10** in H_2O. Facile preparation of **10** *via MacMillan*'s organocatalysis has made it possible to generate a great diversity of natural product-like compounds that can be screened for anti-*Alzheimer*'s effects.

Introduction. – (−)-Physostigmine was first isolated from the African Calabar bean seed *Physostigma venenosum* (*Fig. 1*) [1]. Possessing a hexahydropyrrolo[2,3-*b*]indole ring system, (−)-physostigmine is one of the earliest compounds to be used as an inhibitor of acetylcholinesterase and a therapeutic agent against *Alzheimer*'s disease [2]. However, this drug has the major drawbacks of low bioavailability and a narrow therapeutic window by its rapid metabolism and inefficient passage across the blood–brain barrier [3]. (−)-Phenserine, a synthetic analog of (−)-physostigmine with improved bioavailability, is a more potent and selective inhibitor of acetylcholinesterase [4], and it can inhibit the formation of the β-amyloid precursor protein [5].

The five-membered 1,2,3-triazole moiety is a commonly used pharmacophore associated with anti-HIV [6], anti-allergic [7], antifungal [8], antimicrobial [9], and other biological activities. The 'click chemistry' [10] to synthesize 1,2,3-triazoles has been widely used as a powerful tool in generating diverse compound libraries.

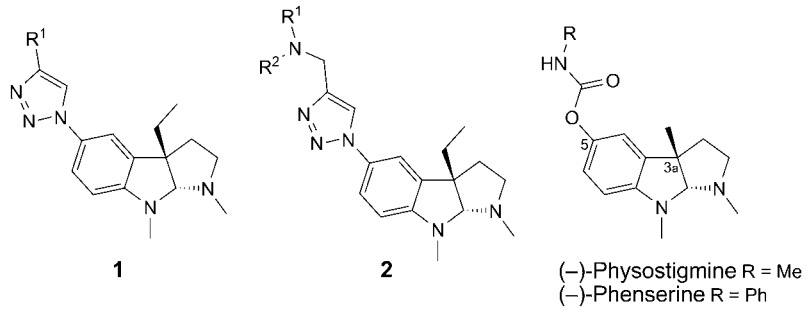
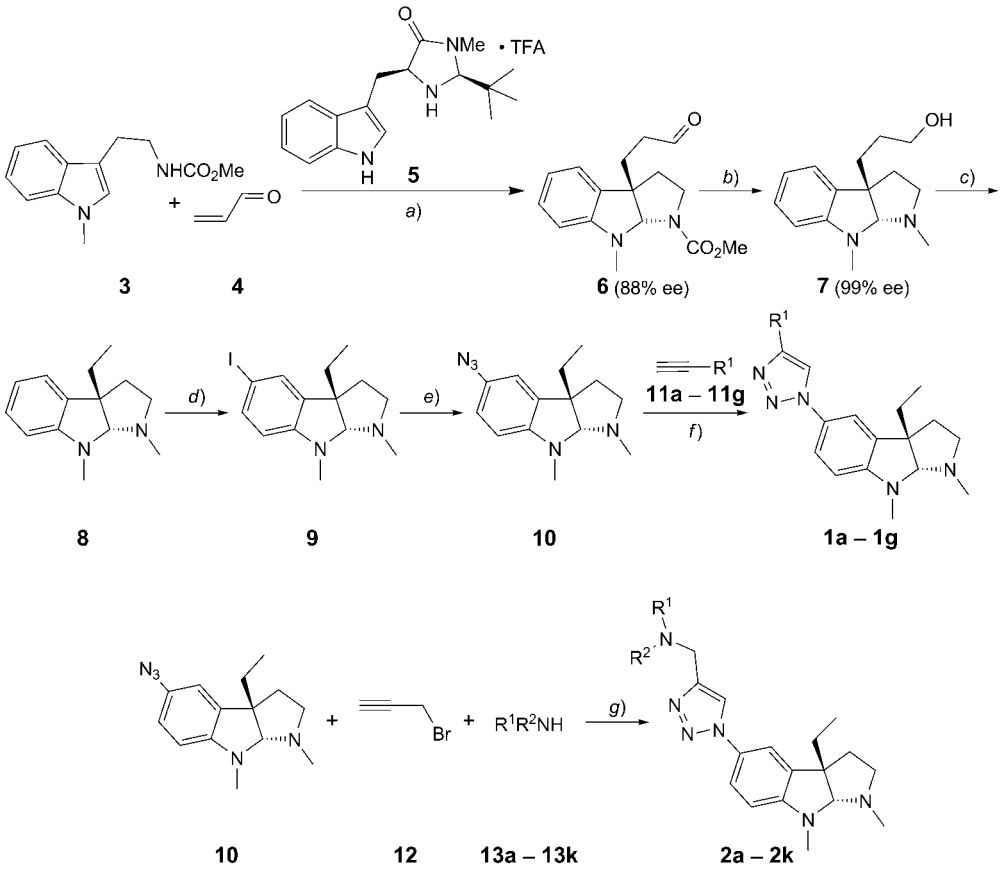


Fig. 1. *Structure of (−)-Physostigmine and Its Analogs (−)-Phenserine,* **1***, and* **2**

Given that several physostigmine-like natural alkaloids with different substituents at C(3a) show a variety of biological activities [11], and that replacing the methyl carbamate of (−)-physostigmine at C(5) with a different carbamate improves its pharmacological activity [12], in this article, we describe the design and synthesis a series of (−)-physostigmine analogues with variations at C(5) and C(3a) that can be screened for anti-*Alzheimer*'s activity.

Results and Discussion. – The synthetic strategy for the preparation of (−)-physostigmine analogues **1** and **2** is shown in the *Scheme*. Although the synthesis of chiral 3a-substituted hexahydropyrrolo[2,3-*b*]indoles has been intensively investigated over the past two decades because of the importance and richness of natural products with this skeleton [11], a catalytic and reliable procedure involving easy preparation of

Scheme. *Synthesis of (−)-Physostigmine Analogs* **1a**–**1g** *and* **2a**–**2k**



a) CH_2Cl_2/H_2O 85:15, −78°; 87%. *b*) $LiAlH_4$, THF, reflux; 86%. *c*) *Raney*-Ni, toluene, reflux; 60%. *d*) NIS, CH_2Cl_2, r.t.; 93%. *e*) NaN_3, CuI, *N*,*N*′-dimethylethane-1,2-diamine, sodium ascorbate, DMSO/H_2O 5:1, r.t.; 80%. *f*) CuI, sodium ascorbate, DMF; 50–91%. *g*) CuI, Et_3N, H_2O; 61–80%.

the starting material, high diastereo- and enatioselectivities, and high yield is still lacking. Recent advances in organocatalytic reactions [13], such as the highly efficient procedure of *MacMillan* and co-workers reported in 2008 [14], have provided easy access to chiral 3a-substituted hexahydropyrrolo[2,3-*b*]indoles. With slight modifications of *MacMillan*'s original conditions with a different starting material, a core structure of the chiral 3a-ethyl hexahydropyrrolo[2,3-*b*]indole was prepared from tryptamine derivative **3** and acrolein (**4**) in the presence 10 mol-% of imidazolidinone trifluoroacetic acid salt **5**, obtaining aldehyde **6** in 87% yield and with 88% ee. Attempts to improve the ee value of aldehyde **6** were unsuccessful, because **6** did not easily crystallize. Fortunately, after reduction of the methyl carbamate and aldehyde groups in **6** with $LiAlH_4$, the resulting alcohol **7** easily recrystallized from a mixture CH_2Cl_2/Et_2O 4:1 to form a white crystalline solid with 99% ee. The absolute configuration of **7** was determined by X-ray crystallographic analysis[1]) (*Fig. 2*). Compound **8** was obtained in 60% yield by heating **7** with *Raney*-Ni under reflux in toluene [15]. Reaction of **8** with *N*-iodosuccinimide (NIS) in anhydrous CH_2Cl_2 gave iodide **9** in 93% yield. Iodide replacement with azide [16] in **9** in the presence of the catalysts CuI and *N*,*N*′-dimethylethane-1,2-diamine in a mixture DMSO/H_2O 5:1 provided the key intermediate azide **10** in 80% yield.

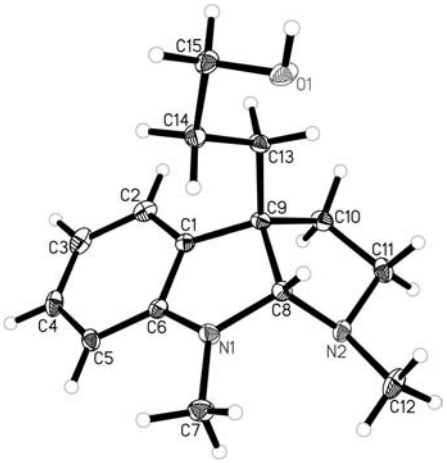


Fig. 2. *ORTEP Drawing of Compound* **7**

In the presence of CuI and sodium ascorbate, analogs **1a**–**1g** were synthesized in yields of 50–91% by reacting different terminal alkynes **11a**–**11g**, respectively, with azide **10** in DMF. The structures of the products **1a**–**1g** are shown in *Table 1*. Analogs **2a**–**2k** were prepared in 61–80% yield *via* a 'three-component *Huisgen* reaction' using

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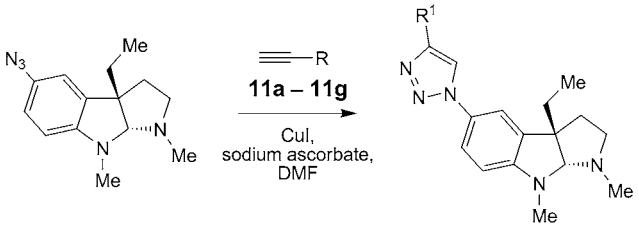
[1]) A colorless crystal of **7** ($C_{15}H_{22}N_2O$, m.p. 71–72°) for the X-ray-analysis was obtained by recrystallization from CH_2Cl_2 and Et_2O (4:1). CCDC-774697 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambride Crystallographic Data Centre*, *via* http://www.ccdc.cam.ac.uk/data_request.cif.

Table 1. *Copper(I)-Catalyzed Regioselective Cycloaddition of Azide* **10** *with Various Alkynes* **11a**–**11g**

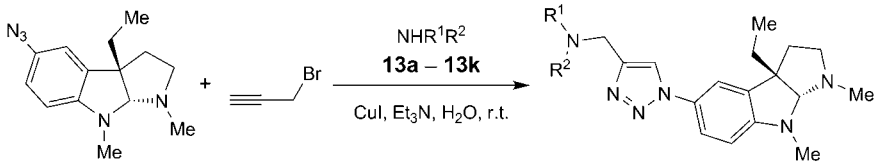


10 **1a – 1g**

Entry	**11**	R	**1**	R^1	Yield [%]
1	**11a**	Me_3Si	**1a**	H	50
2	**11b**	Ph	**1b**	Ph	80
3	**11c**	$HO–CH_2$	**1c**	$HO–CH_2$	61
4	**11d**	$HO–C(Me_2)$	**1d**	$HO–C(Me_2)$	91
5	**11e**	$HO–(CH_2)_2$	**1e**	$HO–(CH_2)_2$	85
6	**11f**	$HO–(CH_2)_4$	**1f**	$HO–(CH_2)_4$	84
7	**11g**	EtOOC	**1g**	EtOOC	62

commercially available amines **13a**–**13k**, respectively, propargyl bromide **12**, and the azide **10** in the presence of CuI and Et_3N in H_2O. The structures of the products **2a**–**2k** are shown in *Table 2*. We were pleased to find that the 1,3-dipolar cycloaddition reaction proceeded regioselectively, affording exclusively the 1,4-disubstituted 1,2,3-

Table 2. *Copper(I)-Catalyzed 'Three-Component* Huisgen *Reaction' Involving Amines* **13a**–**13j**, *Propargyl Bromine* **12**, *and Azide* **10**



10 **12** **2a – 2k**

Entry	**13**	R^1	R^2	**2**	Yield [%]
1	**13a**	Me	Me	**2a**	61
2	**13b**	Bu	Bu	**2b**	80
3	**13c**	Me	Ph	**2c**	64
4	**13d**	Cyclohexyl	Cyclohexyl	**2d**	70
5	**13e**	$–(CH_2)_4–$		**2e**	64
6	**13f**	$–(CH_2)_6–$		**2f**	68
7	**13g**	$–(CH_2)_2–O–(CH_2)_2–$		**2g**	74
8	**13h**	$–(CH_2)_2–N(Me)–(CH_2)_2–$		**2h**	70
9	**13i**	$–(CH_2)_2–N(Bn)–(CH_2)_2–$		**2i**	64
10	**13j**	$–(CH_2)_2–N(COPh)–(CH_2)_2–$		**2j**	61
11	**13k**	$–(CH_2)_2–N(CH_2Bn)–(CH_2)_2–$		**2k**	62

triazole derivatives [10e][10g]. Compounds **1a**–**1g** and **2a**–**2k** were fully characterized by IR, ^{1}H- and ^{13}C-NMR, and HR-MS.

Conclusions. – The (−)-physostigmine analogs **1a**–**1g** and **2a**–**2k**, containing a 3a-ethyl-5-(1*H*-1,2,3-triazol-1-yl)hexahydropyrrolo[2,3-*b*]indole skeleton, have been synthesized *via* a six-step route with an overall yield of 20–30%. Aldehyde **6** with the hexahydropyrrolo[2,3-*b*]indole skeleton was prepared in 87% yield and 88% ee through a highly efficient organocatalytic cascade reaction. The ee value of the core structure was greatly enhanced to 99% by a single recrystallization of alcohol **7**. Easy preparation of (−)-azide **10** under mild conditions allowed us to synthesize a diverse library focusing on the 1,2,3-triazole moiety using reliable 'click chemistry'. Evaluation of the synthesized library compounds **1a**–**1g** and **2a**–**2k** as potent inhibitors of acetylcholinesterase will be studied in due course.

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Experimental Part

General. All commercially available reagents were used without further purification. All solvents were dried and distilled before use. THF was distilled from Na/benzophenone; CH_2Cl_2 and DMF were distilled from CaH_2. Flash column chromatography (FC): silica gel (SiO_2; 200–300 mesh). IR Spectra: in KBr; *Nicolet 200SXY* FT-IR spectrophotometer. HPLC Analysis: *Varian ProStar*; column, *Chiral OD-H* (1.6 × 25 cm); wavelength 254 nm; flow rate, 1 ml/min; mobile phase: hexane/^{i}PrOH/Et_3N 90:10:0.3. ^{1}H- and ^{13}C-NMR Spectra: *Varian Unity INOVA 400/54* NMR spectrometer at 400 MHz and 100 MHz, in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. HR-FAB-MS: *Finnigan MAT 90* instrument.

*Methyl (3a*S*,8a*S*)-3,3a,8,8a-Tetrahydro-8-methyl-3a-(3-oxopropyl)pyrrolo[2,3-*b*]indole-1(2*H*)-carboxylate* (**6**). A round-bottom flask equipped with a magnetic stir bar, containing (2*S*,5*S*)-2-(*tert*-butyl)-5-(1*H*-indol-3-ylmethyl)-3-methylimidazolidin-4-one TFA salt (**5**; 1.50 g, 5.2 mmol) and methyl [2-(1-methyl-1*H*-indol-3-yl)ethyl]carbamate (**3**; 12.03 g, 51.7 mol) was charged with CH_2Cl_2 (85 ml) and H_2O (15 ml). The soln. was stirred for 5 min at −78° before acrolein (17.38 g, 310.3 mmol) was added. The resulting suspension was stirred at −78° until complete consumption of **5** was observed (TLC). Then, H_2O was added, the mixture was extracted with Et_2O, and the org. phase was concentrated in vacuum. The resulting residue was purified by FCC (in 20% AcOEt/petroleum ether (PE)) to afford **6** as colorless film (13.02 g, 87% yield). $[\alpha]_D^{20} = -330.6$ ($c = 2.5$, $CHCl_3$). IR: 2954, 2887, 2828, 1699, 1607, 1493, 1448, 1386, 1300, 1223, 1202, 1160, 1105, 1068, 1022, 999, 938, 880, 744. ^{1}H-NMR: 1.96–1.99 (*m*, 2 H); 2.13–2.16 (*m*, 2 H); 2.20–2.28 (*m*, 1 H); 2.40–2.44 (*m*, 1 H); 2.89 (*s*, 1 H); 2.98 (*s*, 3 H); 3.71 (*s*, 3 H); 3.70 (*s*, 1 H); 5.27 (*s*, 1 H); 6.38 (*d*, $J = 7.6$, 1 H); 6.68 (*t*, $J = 7.2$, 1 H); 6.97 (*d*, $J = 7.2$, 1 H); 7.12 (*t*, $J = 7.6$, 1 H); 9.64 (*s*, 1 H). ^{13}C-NMR: 30.2; 32.0; 38.0; 39.7; 45.4; 45.6; 52.2; 85.4; 105.6; 117.3; 122.2; 128.6; 130.4; 151.0; 155.9; 201.1. HR-FAB-MS: 343.1630 ($C_{17}H_{24}N_2NaO_4^+$, $[M + MeOH + Na]^+$; calc. 343.1628).

*3-[(3a*S*,8a*R*)-2,3,8,8a-Tetrahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-3a(1*H*)-yl]propan-1-ol* (**7**). To a soln. of **6** (10.23 g, 42 mmol) in THF (100 ml) at 0° was added $LiAlH_4$ (9.50 g, 250 mmol). The mixture was warmed to reflux temp. until complete consumption of **6** (determined by TLC), and quenched with sat. Na_2SO_4 soln. The mixture was extracted with AcOEt, filtered through a pad of *Celite*, and washed with AcOEt. The combined extracts were concentrated. The residue was purified by SiO_2 chromatography, eluted with 5–10% MeOH in CH_2Cl_2, to provide **7** as colorless solid (8.80 g, 86% yield with 88% ee). The ee value was determined by HPLC with *Chiral OD–H* (1.6 × 25 cm, wave length 254 nm; flow rate, 1 ml/min; mobile phase: hexane/^{i}PrOH/Et_3N 90:10:0.3). Compound **7** was recrystallized from a mixture CH_2Cl_2/Et_2O 4:1 to form a white crystalline solid (3.96 g, 45 % yield) with 99% ee. The ee value

was determined by HPLC with *Chiral OD–H*; flow rate, 1 ml/min; mobile phase: hexane/^{i}PrOH/Et_3N 90:10:0.3). M.p. 71–72°. $[\alpha]_D^{20} = -96.5$ ($c = 0.63$, $CHCl_3$). IR: 3284, 3050, 2935, 2866, 2817, 1605, 1492, 1463, 1428, 1378, 1344, 1298, 1250, 1157, 1123, 1061, 1022, 937, 842, 793, 742. ^{1}H-NMR: 1.28–1.34 (*m*, 1 H); 1.44–1.50 (*m*, 1 H); 1.75 (*dd*, *J* = 12, 4.4, 1 H); 1.85 (*dd*, *J* = 12, 4.4, 1 H); 1.95–1.97 (*m*, 1 H); 2.02–2.05 (*m*, 1 H); 2.51 (*s*, 3 H); 2.53–2.57 (*m*, 1 H); 2.66–2.71 (*m*, 1 H); 2.94 (*s*, 3 H); 3.57 (*d*, *J* = 8.4, 2 H); 4.19 (*s*, 1 H); 6.41 (*d*, *J* = 8, 1 H); 6.67 (*t*, *J* = 7.6, 1 H); 6.96 (*d*, *J* = 6.4, 1 H); 7.08 (*t*, *J* = 7.6, 1 H). ^{13}C-NMR: 29.2; 36.3; 36.5; 37.7; 39.6; 52.4; 56.7; 62.5; 93.9; 106.6; 117.6; 122.6; 127.7; 134.5; 152.6. HR-FAB-MS: 247.1812 ($C_{15}H_{23}N_2O^+$, $[M+H]^+$; calc. 247.1805).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indole* (**8**). To a soln. of **7** (6.0 g, 24.4 mmol) in toluene (100 ml) was added 60 g of *Raney*-Ni slurry. The suspension was refluxed for 4–6 h with vigorous stirring to remove H_2O, and cooled to r.t. The mixture was filtered through a pad of *Celite*, and washed with AcOEt. The solvent was removed in vacuum to leave a pale residue, which was purified by chromatography eluted with 1–5% MeOH in CH_2Cl_2, to provide **8** as a colorless film (2.68 g, 51% yield). $[\alpha]_D^{20} = -71.0$ ($c = 1.2$, $CHCl_3$). IR: 3320, 3049, 2960, 2929, 2875, 2791, 1682, 1605, 1492, 1460, 1379, 1346, 1299, 1255, 1207, 1163, 1124, 1031, 968, 919, 786, 740, 635. ^{1}H-NMR: 0.75 (*t*, *J* = 7.2, 3 H); 1.70–1.73 (*m*, 1 H); 1.79–1.88 (*m*, 1 H); 1.89–1.94 (*m*, 1 H); 1.99–2.04 (*m*, 1 H); 2.52 (*s*, 3 H); 2.53–2.57 (*m*, 1 H); 2.66–2.71 (*m*, 1 H); 2.94 (*s*, 3 H); 4.16 (*s*, 1 H); 6.41 (*d*, *J* = 7.6, 1 H); 6.67 (*t*, *J* = 7.6, 1 H); 6.95 (*d*, *J* = 7.6, 1 H); 7.08 (*t*, *J* = 7.6, 1 H). ^{13}C-NMR: 10.0; 32.5; 36.4; 37.8; 39.3; 52.6; 57.5; 93.8; 106.5; 117.5; 122.7; 127.6; 134.6; 152.7. HR-FAB-MS: 217.1701 ($C_{14}H_{21}N_2^+$, $[M+H]^+$; calc. 217.1699).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-5-iodo-1,8-dimethylpyrrolo[2,3-*b*]indole* (**9**). To a soln. of **8** (2.68 g, 12.4 mmol) in dry CH_2Cl_2 (50 ml) at 0° was added a soln. of *N*-iodosuccinimide (NIS; 3.35 g, 14.9 mmol) in dry CH_2Cl_2. The mixture was allowed to warm to r.t., and then stirred for 4 h until complete consumption of **8** was observed by TLC. Then, sat. Na_2SO_3 soln. was added, and the mixture was extracted with CH_2Cl_2. The combined org. layers were dried ($NaSO_4$), filtered, and concentrated in vacuum. The residue was purified by CC (3% MeOH in CH_2Cl_2) to give **9** (3.94 g, 93% yield) as light yellow film. $[\alpha]_D^{20} = -77.1$ ($c = 0.41$, $CHCl_3$). IR: 2961, 2929, 2875, 2791, 1680, 1649, 1593, 1490, 1379, 1347, 1271, 1255, 1164, 1127, 1072, 1032, 969, 919, 877, 801, 644, 574. ^{1}H-NMR: 0.75 (*t*, *J* = 7.2, 3 H); 1.64–1.70 (*m*, 1 H); 1.75–1.84 (*m*, 1 H); 1.88–1.93 (*m*, 1 H); 1.99–2.02 (*m*, 1 H); 2.51 (*s*, 3 H); 2.56–2.58 (*m*, 1 H); 2.68–2.72 (*m*, 1 H); 2.91 (*s*, 3 H); 4.17 (*s*, 1 H); 6.18 (*d*, *J* = 8.4, 1 H); 7.18 (*d*, *J* = 1.2, 1 H); 7.33 (*dd*, *J* = 8.0, 1.6, 1 H). ^{13}C-NMR: 9.9; 32.3; 36.1; 37.5; 39.0; 52.4; 57.6; 78.1; 93.2; 108.7; 131.4; 136.4; 137.4; 152.3. HR-FAB-MS: 343.2261 ($C_{14}H_{20}IN_2^+$, $[M+H]^+$; calc. 343.2259).

*(3a*S*,8a*R*)-5-Azido-3a-ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indole* (**10**). Under N_2, **9** (296 mg, 0.87 mmol), NaN_3 (226 mg, 3.48 mmol), sodium ascorbate (17.2 mg, 0.087 mmol), *N*,*N*′-dimethylethane-1,2-diamine (29.2 mg, 0.348 mmol), and CuI (34.5 mg, 0.174 mmol) were dissolved in a degassed mixture of DMSO/H_2O 5:1 (50 ml). The mixture was stirred at r.t. for 24 h, then, brine was added. The mixture was extracted with AcOEt. The combined org. phases were washed with H_2O, dried with anh. $NaSO_4$, filtered, and concentrated in vacuum. The residue was purified by CC to give **10** (358 mg, 80% yield) as light green oil. $[\alpha]_D^{20} = -74.3$ ($c = 0.04$, MeOH). IR: 2961, 2927, 2876, 2852, 2792, 2101, 1613, 1593, 1498, 1448, 1380, 1347, 1292, 1253, 1164, 1135, 1111, 1033, 967, 928, 869, 802, 655. ^{1}H-NMR: 0.74 (*t*, *J* = 7.2, 3 H); 1.63–1.72 (*m*, 1 H), 1.78–1.86 (*m*, 1 H); 1.88–1.93 (*m*, 1 H); 1.97–2.03 (*m*, 1 H); 2.51 (*s*, 3 H); 2.56–2.59 (*m*, 1 H); 2.68–2.70 (*m*, 1 H); 2.92 (*s*, 3 H); 4.15 (*s*, 1 H); 6.36 (*d*, *J* = 8.4, 1 H); 6.63 (*d*, *J* = 2.0, 1 H); 6.75 (*dd*, *J* = 8.4, 2.4, 1 H). ^{13}C-NMR: 10.0; 32.4; 36.5; 38.0; 39.3; 52.6; 57.7; 94.2; 107.2; 114.0; 118.4; 136.3; 136.7; 150.5. HR-FAB-MS: 258.1725 ($C_{14}H_{20}N_5^+$, $[M+H]^+$; calc. 258.1713).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethyl-5-(1*H*-1,2,3-triazol-1-yl)pyrrolo[2,3-*b*]indole* (**1a**). To a soln. of **10** (25.7 mg, 0.10 mmol), CuI (3.8 mg, 0.02 mmol), and sodium ascorbate (4.0 mg, 0.02 mmol) in DMF (1 ml) was added *ethynyl(trimethyl)silane* (**11a**; 28 µl, 0.20 mmol) under N_2 at r.t. The mixture was stirred at 60° for 30 h. Then, brine was added, and the mixture was extracted with AcOEt. The combined org. phases were washed with H_2O, dried (Na_2SO_4), filtered, and concentrated in vacuum. The residue was purified by FCC to provide **1a** (14.2 mg, 50.0% yield) as a colorless film. $[\alpha]_D^{20} = -49.0$ ($c = 0.05$, $CHCl_3$). IR: 3744, 2960, 2919, 2851, 1694, 1511, 1462, 1260, 1093, 1026, 801. ^{1}H-NMR: 0.79 (*t*, *J* = 7.2, 3 H); 1.71–1.76 (*m*, 1 H); 1.85–1.90 (*m*, 1 H); 2.00–2.02 (*m*, 1 H); 2.05–2.07 (*m*, 1 H); 2.56 (*s*, 3 H); 2.61–2.63 (*m*, 1 H); 2.65–2.72 (*m*, 1 H); 3.01 (*s*, 3 H); 4.25 (*s*, 1 H); 6.42 (*d*, *J* = 9.2, 1 H);

7.32 (*d*, *J* = 7.6, 1 H); 7.33 (*s*, 1 H); 7.80 (*s*, 1 H); 7.85 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.3; 35.8; 38.1; 39.0; 52.7; 57.7; 93.9; 105.9; 116.6; 121.1; 121.9; 127.5; 134.0; 136.0; 152.7. HR-FAB-MS: 284.1877 ($C_{16}H_{22}N_5^+$, $[M+H]^+$; calc. 284.1870).

General Procedure for the Synthesis of Analogs **1b**–**1g**. To a soln. of azide (0.10 mmol), CuI (0.02 mmol), and sodium ascorbate (0.02 mmol) in DMF (1 ml) was added the respective alkyne (0.15 mmol) under N_2 at r.t. The mixture was stirred at r.t. for 4 h, then brine was added, and the mixture was extracted with AcOEt. The combined org. phases were washed with H_2O, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by FCC to give **1b**–**1g**.

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyrrolo[2,3-*b*]indole* (**1b**). Colorless film, 80% yield. $[\alpha]_D^{20} = -68.9$ ($c = 0.38$, $CHCl_3$). IR: 3415, 2923, 2854, 1615, 1509, 1444, 1383, 1296, 1226, 1036, 810, 760, 702. ^{1}H-NMR: 0.80 (*t*, *J* = 7.2, 3 H); 1.73–1.79 (*m*, 1 H); 1.85–1.92 (*m*, 1 H); 2.03–2.04 (*m*, 1 H); 2.08–2.10 (*m*, 1 H); 2.57 (*s*, 3 H); 2.62–2.66 (*m*, 1 H); 2.75–2.77 (*m*, 1 H); 3.02 (*s*, 3 H); 4.30 (*s*, 1 H); 6.45 (*d*, *J* = 8.0, 1 H); 7.34–7.41 (*m*, 3 H); 7.45 (*t*, *J* = 7.6, 2 H); 7.90 (*d*, *J* = 7.2, 2 H); 8.06 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.3; 35.8; 38.1; 39.0; 52.7; 57.7; 94.0; 105.9; 116.5; 118.0; 121.1; 125.8 × 2; 128.2 × 2; 128.9 × 2; 130.6; 136.0; 147.9; 152.8. HR-FAB-MS: 360.2205 ($C_{22}H_{26}N_5^+$, $[M+H]^+$; calc. 360.2183).

*{1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}methanol* (**1c**). Colorless film, 61% yield. $[\alpha]_D^{20} = -49.8$ ($c = 0.21$, $CHCl_3$). IR: 3394, 2959, 2920, 2851, 1650, 1615, 1508, 1459, 1379, 1260, 1219, 1034, 805, 705. ^{1}H-NMR: 0.78 (*t*, *J* = 7.6, 3 H); 1.71–1.77 (*m*, 1 H); 1.83–1.90 (*m*, 1 H); 1.98–2.02 (*m*, 1 H); 2.03–2.12 (*m*, 1 H); 2.56 (*s*, 3 H); 2.60–2.65 (*m*, 1 H); 2.76–2.78 (*m*, 1 H); 3.01 (*s*, 3 H); 4.29 (*s*, 1 H); 4.87 (*s*, 2 H); 6.43 (*d*, *J* = 8.8, 1 H); 7.31 (*s*, 1 H); 7.32 (*d*, *J* = 8.8, 1 H); 7.84 (*s*, 1 H). ^{13}C-NMR: 9.7; 31.6; 31.9; 37.3; 41.8; 48.1; 52.6; 56.6; 96.8; 106.2; 116.5; 119.3; 120.2; 121.9; 128.6; 130.9; 136.2. HR-FAB-MS: 314.1985 ($C_{17}H_{24}N_5O^+$, $[M+H]^+$; calc. 314.1975).

*2-{1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}propan-2-ol* (**1d**). White amorphous solid, 91% yield. $[\alpha]_D^{20} = -65.8$ ($c = 0.31$, $CHCl_3$). IR: 3743, 3384, 3079, 2967, 2923, 2854, 1614, 1508, 1442, 1378, 1287, 1226, 1169, 1039, 806, 754, 705. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.74–1.77 (*m*, 1 H); 1.82–1.90 (*m*, 1 H); 1.96–2.02 (*m*, 1 H); 2.04–2.09 (*m*, 1 H); 2.55 (*s*, 3 H); 2.58–2.64 (*m*, 1 H); 2.67–2.74 (*m*, 1 H); 3.00 (*s*, 3 H); 4.24 (*s*, 1 H); 6.43 (*d*, *J* = 8.4, 1 H); 7.29 (*s*, 1 H); 7.32 (*d*, *J* = 8.4, 1 H); 7.74 (*s*, 1 H). ^{13}C-NMR: 9.9; 30.5 × 2; 32.2; 35.8; 38.0; 38.9; 52.7; 57.7; 68.5; 93.9; 105.9; 116.5 × 2; 117.8; 121.1; 128.4; 135.8; 152.6. HR-FAB-MS: 342.2290 ($C_{19}H_{28}N_5O^+$, $[M+H]^+$; calc. 342.2288).

*2-{1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}ethanol* (**1e**). Colorless film, 85% yield. $[\alpha]_D^{20} = -82.9$ ($c = 0.14$, $CHCl_3$). IR: 3744, 3359, 3079, 2962, 2926, 2856, 1612, 1586, 1507, 1440, 1383, 1346, 1261, 1218, 1120, 1037, 804, 755, 704. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.70–1.77 (*m*, 1 H); 1.84–1.91 (*m*, 1 H); 1.96–2.01 (*m*, 1 H); 2.04–2.09 (*m*, 1 H); 2.55 (*s*, 3 H); 2.58–2.64 (*m*, 1 H); 2.69–2.74 (*m*, 1 H); 3.00 (*s*, 3 H); 3.02 (*t*, *J* = 5.6, 2 H); 4.00 (*t*, *J* = 6, 2 H); 4.24 (*s*, 1 H); 6.41 (*d*, *J* = 8.4, 1 H); 7.30 (*s*, 1 H); 7.31 (*d*, *J* = 8.4, 1 H); 7.70 (*s*, 1 H). ^{13}C-NMR: 9.8; 28.7; 32.1; 35.7; 37.8; 38.7; 52.6; 57.6; 61.5; 93.8; 106.0; 116.3 × 2; 120.2; 121.0; 128.4; 135.7; 152.4. HR-FAB-MS: 328.2155 ($C_{18}H_{26}N_5O^+$, $[M+H]^+$; calc. 328.2132).

*4-{1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}butan-1-ol* (**1f**). Colorless film, 84 % yield. $[\alpha]_D^{20} = -62.5$ ($c = 0.12$, $CHCl_3$). IR: 3368, 2964, 2926, 2798, 1614, 1508, 1459, 1378, 1288, 1228, 1169, 1042, 962, 807, 754, 706. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.66–1.76 (*m*, 3 H); 1.80–1.90 (*m*, 3 H); 1.98–2.02 (*m*, 1 H); 2.05–2.07 (*m*, 1 H); 2.53 (*s*, 3 H); 2.58–2.64 (*m*, 1 H); 2.72–2.74 (*m*, 1 H); 2.83 (*t*, *J* = 7.2, 2 H); 2.94 (*s*, 3 H); 3.71 (*t*, *J* = 5.4, 2 H); 4.25 (*s*, 1 H); 6.41 (*d*, *J* = 8.8, 1 H); 7.30 (*s*, 1 H); 7.31 (*d*, *J* = 7.2, 1 H); 7.60 (*s*, 1 H). ^{13}C-NMR: 9.9; 25.3; 25.6; 30.5; 32.3; 35.8; 39.0; 50.7; 52.7; 57.7; 62.4; 93.9; 105.9; 116.4; 116.5 × 2; 120.9; 121.1; 135.9; 152.7. HR-FAB-MS: 356.2424 ($C_{20}H_{30}N_5O^+$, $[M+H]^+$; calc. 356.2445).

*Ethyl 1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazole-4-carboxylate* (**1g**). Compound **1g** was prepared at $-20°$ as described for **1b**. Colorless film, 62 % yield. $[\alpha]_D^{20} = -65.9$ ($c = 0.085$, $CHCl_3$). IR: 3419, 2961, 2919, 2851, 1733, 1613, 1509, 1460, 1440, 1376, 1259, 1149, 1038, 804, 753, 705. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.43 (*t*, *J* = 7.2, 3 H); 1.68–1.77 (*m*, 1 H); 1.82–1.91 (*m*, 1 H); 1.95–2.02 (*m*, 1 H); 2.04–2.09 (*m*, 1 H); 2.55 (*s*, 3 H); 2.58–2.64 (*m*, 1 H); 2.68–2.73 (*m*, 1 H); 2.83 (*t*, *J* = 7.2, 2 H); 3.00 (*s*, 3 H); 4.24 (*s*, 1 H); 4.45 (*q*, *J* = 7.2, 2 H); 6.41 (*d*, *J* = 8.4,

1 H); 7.31 (*s*, 1 H); 7.34 (*d*, *J* = 8.4, 1 H); 8.35 (*s*, 1 H). ^{13}C-NMR: 9.8; 14.4; 32.2; 35.6; 38.0; 38.8; 52.7; 57.7; 61.3; 93.8; 105.9; 116.5; 121.3; 125.5; 136.0; 140.3; 153.0; 160.9; 186.3. HR-FAB-MS: 356.2092 ($C_{19}H_{26}N_5O_2^+$, $[M+H]^+$; calc. 356.2081).

General Procedure for the Synthesis of Analogs **2a**–**2k**. To a mixture of amine **13** (2 mmol), propargyl bromide **12** (2 mmol), and Et_3N (3.3 mmol) in H_2O (2 ml) was added azide **10** (1.0 mmol) and CuI (0.2 mmol). The mixture was stirred vigorously for 2 h at r.t. and then was added brine. The mixture was extracted with AcOEt. The combined org. phases were washed with brine, dried over anh. Na_2SO_4, filtered, and concentrated. The residue was purified by FCC to give the desired analog **2**.

*1-{1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}-*N,N*-dimethylmethanamine* (**2a**). Colorless film, 61% yield. $[\alpha]_D^{20} = -26.4$ ($c = 0.125$, $CHCl_3$). IR: 3413, 2957, 2920, 2851, 1726, 1662, 1613, 1509, 1465, 1381, 1259, 1123, 1030, 807. ^{1}H-NMR: 0.77 (*t*, *J* = 7.6, 3 H); 1.69–1.74 (*m*, 1 H); 1.83–1.89 (*m*, 1 H); 1.96–1.99 (*m*, 1 H); 2.00–2.02 (*m*, 1 H); 2.36 (*s*, 6 H); 2.54 (*s*, 3 H); 2.60–2.63 (*m*, 1 H); 2.69–2.73 (*m*, 1 H); 2.99 (*s*, 3 H); 3.73 (*s*, 2 H); 4.24 (*s*, 1 H); 6.40 (*d*, *J* = 8.4, 1 H); 7.30 (*s*, 1 H); 7.31 (*d*, *J* = 7.2, 1 H); 7.82 (*s*, 1 H). ^{13}C-NMR: 9.8; 32.3; 35.6; 38.4; 39.1; 45.0 × 2; 52.6; 54.3; 57.5; 94.0; 105.6; 116.3; 120.7; 120.8; 128.8; 136.1; 145.0; 152.7. HR-FAB-MS: 341.2440 ($C_{19}H_{29}N_6^+$, $[M+H]^+$; calc. 341.2448).

N-*Butyl*-N-*({1-[(3a*S*,8a*R*)-3a-ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}methyl)butan-1-amine* (**2b**). White amorphous solid, 80% yield. $[\alpha]_D^{20} = -42.5$ ($c = 0.36$, $CHCl_3$). IR: 3396, 2958, 2928, 2871, 1614, 1507, 1460, 1380, 1297, 1258, 1162, 1124, 1044, 969, 923, 887, 807. ^{1}H-NMR: 0.78 (*t*, *J* = 7.6, 3 H); 0.90 (*t*, *J* = 7.2, 6 H); 1.25–1.36 (*m*, 4 H); 1.47–1.54 (*m*, 4 H); 1.69–1.77 (*m*, 1 H); 1.82–1.86 (*m*, 1 H); 1.95–2.01 (*m*, 1 H); 2.03–2.06 (*m*, 1 H); 2.49 (*t*, *J* = 7.2, 4 H); 2.54 (*s*, 3 H); 2.57–2.63 (*m*, 1 H); 2.67–2.71 (*m*, 1 H); 2.99 (*s*, 3 H); 3.84 (*s*, 2 H); 4.23 (*s*, 1 H); 6.40 (*d*, *J* = 9.2, 1 H); 7.31 (*s*, 1 H); 7.32 (*d*, *J* = 6.8, 1 H); 7.77 (*s*, 1 H). ^{13}C-NMR: 9.9; 13.9 × 2; 20.5 × 2; 28.1; 32.3; 35.7; 38.4; 39.1; 48.7; 52.7; 53.0 × 2; 53.3; 57.6; 94.0; 105.7; 116.3 × 2; 120.7; 121.8; 128.1; 136.1; 152.8. HR-FAB-MS: 425.3378 ($C_{25}H_{41}N_6^+$, $[M+H]^+$; calc. 425.3387).

N-*({1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}methyl)-*N*-methylaniline* (**2c**). Colorless film, 64% yield. $[\alpha]_D^{20} = -20.0$ ($c = 0.06$, $CHCl_3$). IR: 3395, 2959, 2924, 2856, 1730, 1604, 1503, 1460, 1379, 1262, 1081, 1024, 801, 699. ^{1}H-NMR: 0.75 (*t*, *J* = 7.2, 3 H); 1.68–1.82 (*m*, 1 H); 1.86–1.91 (*m*, 1 H); 1.98–2.04 (*m*, 1 H); 2.08–2.12 (*m*, 1 H); 2.56 (*s*, 3 H); 2.59–2.62 (*m*, 1 H); 2.76–2.82 (*m*, 1 H); 3.00 (*s*, 3 H); 3.05 (*s*, 3 H); 4.35 (*s*, 1 H); 4.70 (*s*, 2 H); 6.41 (*d*, *J* = 8.4, 1 H); 6.75 (*t*, *J* = 7.2, 1 H); 6.83 (*d*, *J* = 8.0, 2 H); 7.23–7.29 (*m*, 4 H); 7.58 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.2; 35.2; 38.7; 40.0; 48.8 × 2; 52.6; 59.5; 93.7; 112.8 × 2; 116.3; 117.1; 119.8; 120.5; 121.1; 129.3 × 2; 131.3; 143.2; 147.9; 152.8; 165.6. HR-FAB-MS: 403.2617 ($C_{24}H_{31}N_6^+$, $[M+H]^+$; calc. 403.2605).

N-*Cyclohexyl*-N-*({1-[(3a*S*,8a*R*)-3a-ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}methyl)cyclohexanamine* (**2d**). Colorless film, 70% yield. $[\alpha]_D^{20} = -33.3$ ($c = 0.18$, $CHCl_3$). IR: 3380, 3080, 2930, 2854, 1584, 1507, 1439, 1381, 1349, 1216, 1123, 1069, 1032, 994, 924, 891, 757, 703, 666, 605. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.05–1.10 (*m*, 4 H); 1.47–1.49 (*m*, 2 H); 1.57–1.68 (*m*, 4 H); 1.72–1.87 (*m*, 10 H); 1.98–2.06 (*m*, 4 H); 2.50 (*s*, 3 H); 2.54–2.63 (*m*, 3 H); 2.88–2.90 (*m*, 1 H); 2.99 (*s*, 3 H); 3.92 (*s*, 2 H); 4.23 (*s*, 1 H); 6.40 (*d*, *J* = 8.0, 1 H); 7.32 (*d*, *J* = 7.2, 1 H); 7.33 (*s*, 1 H); 7.72 (*s*, 1 H). ^{13}C-NMR: 9.9; 24.7; 25.5 × 2; 25.8 × 4; 32.2 × 2; 35.8; 38.0; 39.0; 42.6 × 2; 52.7 × 2; 53.5; 53.8; 57.8; 93.9; 105.9; 116.2 × 2; 121.1; 127.9; 128.8; 135.9; 152.8. HR-FAB-MS: 477.3707 ($C_{29}H_{45}N_6^+$, $[M+H]^+$; calc. 477.3700).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethyl-5-[4-(pyrrolidin-1-ylmethyl)-1*H*-1,2,3-triazol-1-yl]pyrrolo[2,3-*b*]indole* (**2e**). Colorless film, 64% yield. $[\alpha]_D^{20} = -34.2$ ($c = 0.18$, $CHCl_3$). IR: 3397, 2959, 2918, 2850, 1613, 1583, 1508, 1460, 1439, 1380, 1348, 1259, 1216, 1122, 1070, 1031, 922, 806, 752, 704, 664, 605. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.69–1.75 (*m*, 1 H); 1.84–1.89 (*m*, 5 H); 1.96–1.99 (*m*, 1 H); 2.01–2.04 (*m*, 1 H); 2.52 (*s*, 3 H); 2.68–2.71 (*m*, 5 H); 3.00 (*s*, 3 H); 3.92 (*s*, 2 H); 4.23 (*s*, 1 H); 6.40 (*d*, *J* = 8.0, 1 H); 7.30 (*s*, 1 H); 7.33 (*d*, *J* = 6.4, 1 H); 7.89 (*s*, 1 H). ^{13}C-NMR: 9.9; 23.4 × 2; 32.3; 35.6; 38.4; 39.1; 50.3; 52.7; 53.6 × 2; 57.6; 94.0; 105.7; 116.3; 120.9; 121.7; 128.0; 130.9; 136.1; 152.9. HR-FAB-MS: 367.2613 ($C_{21}H_{31}N_6^+$, $[M+H]^+$; calc. 367.2605).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethyl-5-[4-(piperidin-1-ylmethyl)-1*H*-1,2,3-triazol-1-yl]pyrrolo[2,3-*b*]indole* (**2f**). Colorless film, 68% yield. $[\alpha]_D^{20} = -48.0$ ($c = 0.215$, $CHCl_3$). IR: 3395, 2922, 2852, 1612, 1584, 1508, 1440, 1382, 1344, 1257, 1220, 1112, 1035, 922, 806, 754, 704, 665, 606.

^{1}H-NMR: 0.78 (*t*, *J* = 7.6, 3 H); 1.46–1.47 (*m*, 2 H); 1.60–1.66 (*m*, 4 H); 1.70–1.75 (*m*, 1 H); 1.84–1.90 (*m*, 1 H); 1.98–2.03 (*m*, 1 H); 2.04–2.05 (*m*, 1 H); 2.55 (*s*, 3 H); 2.55–2.60 (*m*, 4 H); 2.59–2.64 (*m*, 1 H); 2.68–2.72 (*m*, 1 H); 3.00 (*s*, 3 H); 3.76 (*s*, 2 H); 4.23 (*s*, 1 H); 6.41 (*d*, *J* = 8.0, 1 H); 7.31 (*s*, 1 H); 7.33 (*d*, *J* = 8.4, 1 H); 7.85 (*s*, 1 H). ^{13}C-NMR: 9.8; 23.7; 25.2 × 2; 32.3; 35.6; 38.3; 39.1; 52.6; 53.6; 54.0 × 2; 57.5; 93.9; 105.6; 116.2; 120.8; 121.6; 128.0; 136.0; 143.6; 152.7. HR-FAB-MS: ($C_{22}H_{33}N_6^{+\cdot}$, $[M+H]^+$; calc. 381.2761) 381.2762.

*(3a*S*,8a*R*)-3a-Ethyl-1,8-dimethyl-5-[4-(morpholin-4-ylmethyl)-1*H*-1,2,3-triazol-1-yl]-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole* (**2g**). Colorless film, 74% yield. $[\alpha]_D^{20} = -63.8$ (*c* = 0.66, $CHCl_3$). IR: 3421, 2959, 2920, 2852, 1613, 1509, 1456, 1381, 1346, 1288, 1261, 1221, 1116, 1046, 1032, 1005, 918, 864, 807, 753, 705. ^{1}H-NMR: 0.77 (*t*, *J* = 7.2, 3 H); 1.73–1.75 (*m*, 1 H); 1.82–1.90 (*m*, 1 H); 1.97–2.01 (*m*, 1 H); 2.04–2.09 (*m*, 1 H); 2.51 (*s*, 3 H); 2.55–2.63 (*m*, 5 H); 2.65–2.75 (*m*, 1 H); 3.00 (*s*, 3 H); 3.66–3.73 (*m*, 4 H); 3.73 (*s*, 2 H); 4.24 (*s*, 1 H); 6.41 (*d*, *J* = 8.0, 1 H); 7.31 (*s*, 1 H); 7.32 (*d*, *J* = 9.2, 1 H); 7.80 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.3; 35.7; 38.3; 39.1; 52.7; 53.4 × 2; 53.7; 57.6; 66.7 × 2; 94.0; 105.7; 116.4; 120.9; 121.1; 128.1; 136.1; 144.1; 152.8. HR-FAB-MS: 383.2561 ($C_{21}H_{31}N_6O^+$, $[M+H]^+$; calc. 383.2554).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethyl-5-[4-[(4-methylpiperazin-1-yl)methyl]-1*H*-1,2,3-triazol-1-yl]pyrrolo[2,3-*b*]indole* (**2h**). Colorless film, 70% yield. $[\alpha]_D^{20} = -57.1$ (*c* = 0.07, $CHCl_3$). IR: 3408, 2958, 2918, 2850, 1613, 1585, 1508, 1460, 1439, 1380, 1346, 1286, 1217, 1163, 1146, 1124, 1046, 1031, 922, 809, 752, 705, 664, 605. ^{1}H-NMR: 0.77 (*t*, *J* = 7.2, 3 H); 1.70–1.76 (*m*, 1 H); 1.84–1.89 (*m*, 1 H); 1.98–2.02 (*m*, 1 H); 2.04–2.08 (*m*, 1 H); 2.38 (*s*, 3 H); 2.55 (*s*, 3 H); 2.57–2.64 (*m*, 5 H); 2.72–2.74 (*m*, 5 H); 3.00 (*s*, 3 H); 3.79 (*s*, 2 H); 4.27 (*s*, 1 H); 6.41 (*d*, *J* = 8.4, 1 H); 7.30 (*s*, 1 H); 7.32 (*d*, *J* = 8.4, 1 H); 7.82 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.3; 35.7; 38.3; 39.1; 45.5; 52.1 × 2; 52.7; 53.0; 54.5 × 2; 57.7; 94.0; 105.8; 114.4; 116.4; 121.0; 121.3; 128.2; 143.7; 152.7. HR-FAB-MS: 396.2877 ($C_{22}H_{34}N_7^+$, $[M+H]^+$; calc. 396.2870).

*(3a*S*,8a*R*)-5-{4-[(4-Benzylpiperazin-1-yl)methyl]-1*H*-1,2,3-triazol-1-yl}-3a-ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indole* (**2i**). Colorless film, 64% yield. $[\alpha]_D^{20} = -50.2$ (*c* = 0.285, $CHCl_3$). IR: 3396, 2920, 2850, 1613, 1508, 1457, 1379, 1345, 1291, 1216, 1127, 1030, 1008, 922, 808, 748, 702. ^{1}H-NMR: 0.77 (*t*, *J* = 7.2, 3 H); 1.69–1.78 (*m*, 1 H); 1.82–1.90 (*m*, 1 H); 2.00–2.03 (*m*, 1 H); 2.04–2.09 (*m*, 1 H); 2.55 (*s*, 3 H); 2.57–2.62 (*m*, 5 H); 2.65–2.71 (*m*, 4 H); 2.73–2.78 (*m*, 1 H); 3.00 (*s*, 3 H); 3.55 (*s*, 2 H); 3.81 (*s*, 2 H); 4.29 (*s*, 1 H); 6.41 (*d*, *J* = 7.6, 1 H); 7.27–7.34 (*m*, 7 H); 7.85 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.3; 35.8; 38.1; 39.0; 52.4 × 2; 52.5 × 2; 52.6; 53.0; 57.7; 62.7; 93.8; 105.8; 116.3; 120.9; 121.4; 127.2; 128.3 × 3; 129.3 × 2; 135.9; 137.3; 143.6; 152.7. HR-FAB-MS: 472.3186 ($C_{28}H_{38}N_7^+$, $[M+H]^+$; calc. 472.3183).

*[4-({1-[(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indol-5-yl]-1*H*-1,2,3-triazol-4-yl}methyl)piperazin-1-yl](phenyl)methanone* (**2j**). Colorless film, 61% yield. $[\alpha]_D^{20} = -53.8$ (*c* = 0.24, $CHCl_3$). IR: 3434, 2960, 2918, 2850, 1620, 1577, 1508, 1436, 1380, 1345, 1279, 1260, 1227, 1161, 1125, 1045, 1023, 999, 923, 886, 807, 752, 710, 664. ^{1}H-NMR: 0.77 (*t*, *J* = 7.2, 3 H); 1.73–1.77 (*m*, 1 H); 1.85–1.88 (*m*, 1 H); 2.01–2.03 (*m*, 1 H); 2.05–2.09 (*m*, 1 H); 2.50–2.53 (*m*, 2 H); 2.56 (*s*, 3 H); 2.60–2.64 (*m*, 3 H); 2.76–2.77 (*m*, 1 H); 3.01 (*s*, 3 H); 3.45 (br. *s*, 2 H); 3.73 (*s*, 2 H); 3.78 (br. *s*, 2 H); 4.32 (*s*, 1 H); 6.43 (*d*, *J* = 8.0, 1 H); 7.32 (*s*, 1 H); 7.34 (*d*, *J* = 8.4, 1 H); 7.40 (*s*, 5 H); 7.79 (*s*, 1 H). ^{13}C-NMR: 9.9; 29.3; 32.3; 35.7; 38.1; 38.9; 52.7 × 2; 53.1 × 3; 57.7; 93.9; 105.9; 116.4; 120.9; 121.1; 127.0 × 2; 128.5 × 2; 129.7; 135.7; 143.9 × 2; 150.3; 152.5; 170.3. HR-FAB-MS: 486.2976 ($C_{28}H_{36}N_7O^+$, $[M+H]^+$; calc. 486.2976).

*(3a*S*,8a*R*)-3a-Ethyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethyl-5-(4-{[4-(2-phenylethyl)piperazin-1-yl]-methyl}-1*H*-1,2,3-triazol-1-yl)pyrrolo[2,3-*b*]indole* (**2k**). Colorless film, 62% yield. $[\alpha]_D^{20} = -40.0$ (*c* = 0.18, $CHCl_3$). IR: 2919, 2850, 1583, 1508, 1459, 1439, 1377, 1260, 1217, 1030, 804, 752, 703. ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 1.73–1.77 (*m*, 1 H); 1.84–1.90 (*m*, 1 H); 1.99–2.06 (*m*, 2 H); 2.51 (*s*, 3 H); 2.55–2.74 (*m*, 10 H); 2.79–2.83 (*m*, 2 H); 3.00 (*s*, 3 H); 3.79 (*s*, 2 H); 4.25 (*s*, 1 H); 6.41 (*d*, *J* = 8.4, 1 H); 7.20 (*d*, *J* = 6.0, 2 H); 7.21 (*s*, 1 H); 7.28–7.34 (*m*, 3 H); 7.42 (br. *s*, 1 H); 7.82 (*s*, 1 H). ^{13}C-NMR: 9.9; 32.4; 33.6; 35.7; 38.4; 39.2; 52.7; 52.8 × 2; 53.0 × 2; 53.3; 57.6; 60.5; 94.0; 105.7; 116.4; 120.9; 121.1; 126.1; 128.1; 128.4 × 2; 128.7 × 2; 136.2; 140.2; 144.2; 152.8. HR-FAB-MS: 486.3343 ($C_{29}H_{40}N_7^+$, $[M+H]^+$; calc. 486.3340).

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