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Synthesis of *trans*-perhydroisoquinolines by 6-*endo*-*trig* radical cyclization of amino-tethered vinyl bromides and cyclohexenes

Josefina Quirante,* Xavier Vila, Laura Paloma, Josep M. Guiu and Josep Bonjoch*

Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII s/n, 08028-Barcelona, Spain

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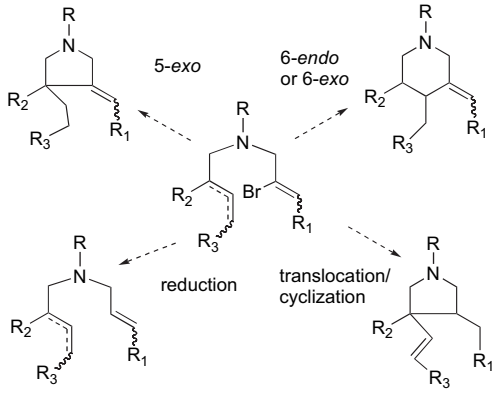
Abstract—Bu_3SnH-promoted cyclization of several *N*-(2-bromoprop-2-enyl)-*N*-[(4-oxocyclohex-1-enyl)methyl]alkylamines is reported. It has been found that the generated vinyl radicals evolve through a 6-*endo*-cyclization pathway giving rise to the corresponding 4,6-functionalized perhydroisoquinolines in a prevalent trans-relative configuration.

1. Introduction

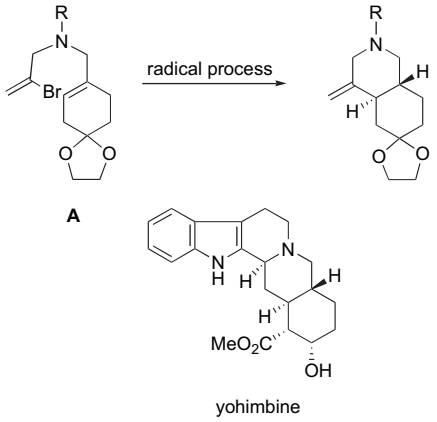
3-Azacarboradicals centered at a vinyl carbon have been little used for the synthesis of nitrogen-containing six-membered rings.[1,2] Since Padwa's pioneering studies in this field about the 5-*exo* versus 6-*endo* regioselectivity,[3] working with vinyl halides and Bu_3SnH, and Crich's reevaluation of this process,[4] few valuable syntheses have been reported involving either 6-*endo*[5] or 6-*exo* cyclizations.[6] Different competitive pathways encountered in attempts to form a six-membered ring through a radical process are depicted in Scheme 1. The aforementioned 5-*exo* versus 6-*endo* dichotomy appears when starting from 1-alkenyl-3-aza-5-hexenyl radicals, while 1-alkenyl-3-aza-6-heptenyl radicals sometimes result in a competition between a 1,5-hydrogen translocation followed by a five-membered cyclization[7] and the 6-*exo* cyclization process. Additionally, a problem in this type of radical cyclizations is that the high reactivity of the vinyl radical increases the rate of hydrogen abstraction from the stannane resulting in simple reduction.

In this work, we decided to explore the radical process originating in vinyl radicals coming from cyclohexene-tethered 2-bromopropenylamines of structure **A** in order to evaluate its regioselectivity and stereoselectivity (Scheme 2). The results reported in this paper introduce a new synthetic entry to *trans*-perhydroisoquinoline derivatives.[8,9] The *trans*-perhydroisoquinoline nucleus is part of the pentacyclic structure of the potent and selective α_2 adrenergic receptor antagonist



Scheme 1.

yohimbine[10,11] and related indole alkaloids,[12] and is found in some synthetic compounds that exhibit several pharmacological activities.[13]



Scheme 2.

Keywords: Vinyl radicals; Decahydroisoquinolines; Radical cyclization; Nitrogen heterocycles.
* Corresponding authors. Tel.: +34 934024540; fax: +34 934024539 (J.B.); e-mail: josep.bonjoch@ub.edu

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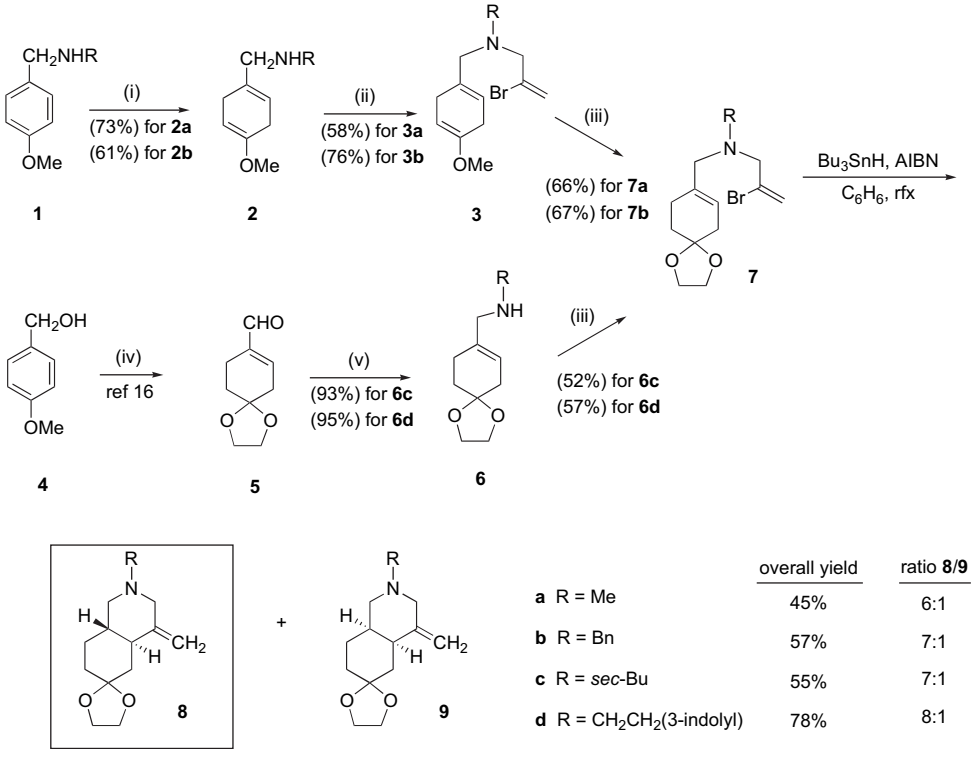
2. Results and discussion

Initially, we decided to prepare four vinyl halides (**7a–d**) to test the aforementioned radical process. The syntheses were carried out as outlined in Scheme 3. For the *N*-methyl substituted amine **7a**, the known benzylamine **1** (R=Me)[14] was subjected to Birch reduction to give the dihydroanisole **2a**, which after alkylation with 2,3-dibromopropene and treatment of the resulting enol ether **3a** with ethylene glycol in acid medium afforded the required amino alkene **7a**. For the *N*-benzyl derivative **7b**, the Birch reduction was carried out using the primary amine **1** (R=H), and the resulting dihydroanisole[15] was submitted to a reductive amination with benzaldehyde to give **2b**, which following the same synthetic sequence as from **2a** gave the tertiary amine **7b**. The syntheses of the amino derivatives **7c** and **7d** started from *p*-anisyl alcohol **4**, which was transformed to aldehyde **5**[16] in a three-step sequence using a described protocol: (i) Birch reduction, (ii) conversion of the generated enol ether into its ethylene acetal, and (iii) oxidation with PCC. Reductive amination of aldehyde **5** with *sec*-butylamine and tryptamine, using $NaBH(OAc)_3$ as a reducing agent, furnished secondary amines **6c** and **6d**, respectively, which in turn were alkylated with 2,3-dibromopropene to afford the required vinyl halides **7c** and **7d**.

Treatment of vinyl halides **7** (1 equiv) with Bu_3SnH (2 equiv) in refluxing benzene (100 mL) at 0.01 M concentration, using AIBN (0.3 equiv) as the initiator, in all cases gave the corresponding *trans*-perhydroisoquinoline derivative **8**(**a–d**) as the main product through a 6-*endo* radical process. The corresponding cis isomers (**9a–d**) were also detected through NMR and GC–MS experiments but they could not be isolated in pure form. The yields of the ring closure varied from 45% from **7a** to 80% from **7d**, the ratio of trans/cis isomers (**8/9**) being around 7:1 in all the series.

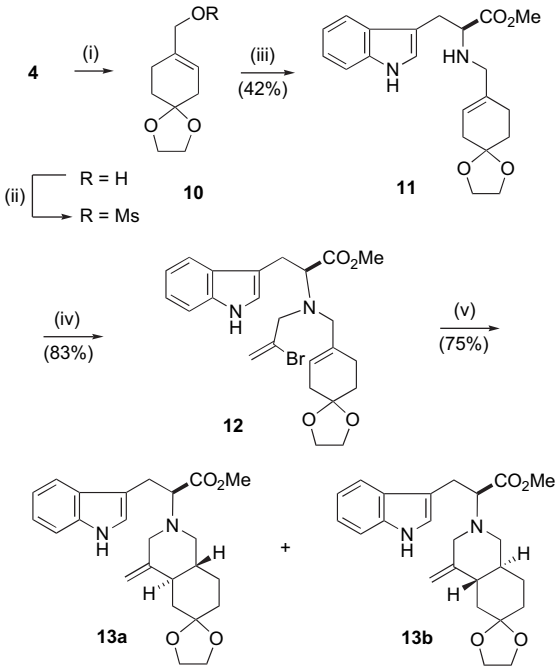
This regiochemical outcome is probably the result of a direct 6-*endo* cyclization of the initially formed vinyl radical that gives the fused radical adduct, since the amount of reducing agent used precluded the possibility of an initial 5-*exo* process and rearrangement of an homoallyl radical through a cyclopropylcarbinyl radical. In other words, as the *endo* product was formed in the presence of 2 equiv of hydride, we assumed that its formation reflected a kinetic control rather than the equilibration between radical intermediates through an intramolecular rearrangement.[17,18] The alkene substitution pattern present in the radicals derived from **7** retarded the usually favored 5-*exo* cyclization mode in benefit of the 6-*endo* mode.[19,20]

The stereochemistry of azabicyclic compounds synthesized was elucidated by 2D NMR spectra (COSY, HSQC). The key evidence for the relative configuration of *trans*-decahydroisoquinolines **8** was found in the ^{13}C NMR chemical shift of C-1 (δ 61.8 for **8a**), as well as that of the methine carbons at C-4a and C-8a (δ 42.4 and 41.2, respectively, for **8a**).[21] The ^{13}C NMR chemical shifts for these methine carbons of the minor *cis*-decahydroisoquinolines **9a–d** appear between 31.7–33.7 and 40.6–42.3.



Scheme 3. Synthesis of *cis*-decahydroquinolines. Reagents and conditions: (i) for series a: NH_3 liq, Li, EtOH, −78 °C. For series b: from **1** (R=H) after the Birch reduction, C_6H_5CHO, then $NaBH_4$; (ii) 2,3-dibromopropene, LiI, K_2CO_3, CH_3CN, rfx; (iii) $(CH_2OH)_2$, $BF_3\cdot Et_2O$, THF, rt, 24 h; (iv) NH_3 liq, Na, EtOH, −78 °C; $(CH_2OH)_2$, $BF_3\cdot Et_2O$, THF, rt, 24 h; PCC/Celite, CH_2Cl_2, rfx, 2.5 h; (v) *sec*-butylamine (series c) or tryptamine (series d), $NaBH(OAc)_3$, CH_2Cl_2, rt, 18 h.

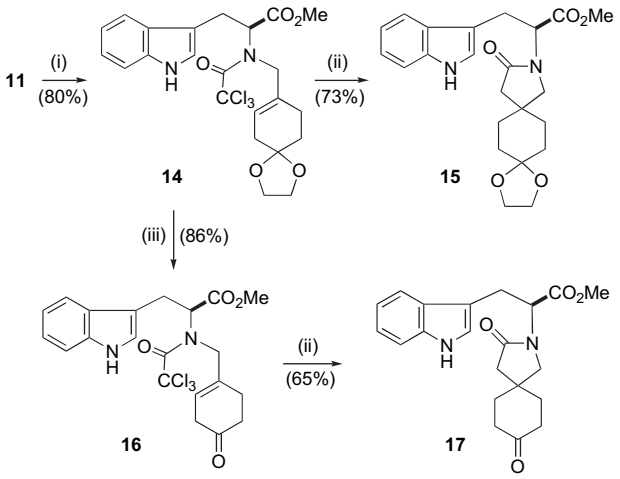
With the aim of extending the above regioselective 6-*endo* cyclizations to the preparation of enantiopure compounds, we next turned our attention to vinyl bromide **12** (Scheme 4). Allylic mesylate **10**, prepared from the corresponding alcohol previously used in the synthesis of aldehyde **5**, was treated with the methyl ester of tryptophan to give the enantiopure secondary amine **11**. Subsequent alkylation furnished the required proradical compound **12**, which under the aforementioned radical conditions efficiently gave the corresponding *trans*-perhydroisoquinoline ring in 75% yield. In contrast, from the diastereoselective point of view the result was disappointing, since ^{1}H NMR showed the crude cyclization product to be a nearly equimolecular mixture of the corresponding *trans*-perhydroisoquinolines **13a** and **13b**.



Scheme 4. Reagents and conditions: (i) mesyl chloride, TEA, THF, 0 °C, 45 min; (ii) tryptophane methyl ester, Na_2CO_3, CH_3CN, 40 °C, overnight; (iii) 2,3-dibromopropene, LiI, K_2CO_3, CH_3CN, rfx, 24 h; (iv) Bu_3SnH, AIBN, benzene, rfx, 3 h.

At this point, we decided to use another type of proradical to check if it was possible to increase the diastereoselectivity while maintaining the 6-*endo* regioselectivity. Thus, we prepared the trichloroacetamide **14** to test the radical cyclization.[22] In this new series, the regioselectivity changed, and azaspirane **15** being isolated as the only cyclized compound.[23] When the reaction was carried out with trichloroacetamide **16**, which might have a slightly different geometry, the synthetic result disappointingly was similar leading to azaspirane **17** (Scheme 5).[24]

In summary, a new synthetic entry to functionalized *trans*-decahydroisoquinolines has been reported. Since the observed stereoselectivity in the radical cyclization of *N*-alkyl-1-vinyl-3-aza-5-hexenyl radicals bearing a cyclohexenone ring gives access to yohimbine-type stereochemistries, decahydroisoquinolines **8d** and **13** could be applied to the synthesis of yohimban indole alkaloids.



Scheme 5. Reagents and conditions: (i) Cl_3CCOCl, CH_2Cl_2, Et_3N, rfx; (ii) Bu_3SnH, AIBN, benzene, rfx; (iii) 3 N HCl, rt.

3. Experimental

3.1. General

All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions. Analytical TLC was performed on SiO_2 (silica gel 60 F_{254}, Merck) or Al_2O_3 (ALOX N/UV_{254}, Polygram), and the spots were located with 1% aqueous $KMnO_4$. Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60, SDS, 230–240 mesh ASTM) or Al_2O_3 (aluminum oxide 90, Merck). Drying of organic extracts during workup of reactions was performed over anhydrous Na_2SO_4. Chemical shifts of ^{1}H and ^{13}C NMR spectra are reported in parts per million downfield (δ) from Me_4Si. In ^{13}C NMR analysis, always a DEPT experiment was included. Two-dimensional NMR experiments (gCOSY and gHSQC) were performed in a Varian Mercury 400 instrument.

3.1.1. *N*-[(4-Methoxy-2,5-dihydrophenyl)methyl]methylamine (2a). A solution of *N*-methyl-*p*-methoxybenzylamine[14] (**1a**, 2.94 g, 19.4 mmol) in EtOH (59 mL) was added to liquid ammonia (60 mL) at −78 °C. To this mixture was added portionwise Li (136 mg, 7 equiv) over 1 h. After quenching with NH_4Cl (4 g) in H_2O (15.6 mL), the solvents were removed, the aqueous suspension was extracted with CH_2Cl_2, and the organic extracts were dried and concentrated to give 2.25 g (73%) of **2a**, which was used without further purification. ^{1}H NMR (300 MHz) 2.40 (br s, 4H, H-3 and H-6), 2.77 (s, 3H, NCH_3), 2.31 (s, 2H, NCH_2), 3.56 (s, 3H, OCH_3), 4.67 (s, 1H, H-5), 5.37 (s, 1H, H-2); ^{13}C NMR (75 MHz) 27.9 and 28.9 (C-6 and C-9), 35.7 (NCH_3), 53.8 (OCH_3), 57.1 (NCH_2), 90.2 (C-5), 119.1 (C-2), 133.6 (C-1), 152.7 (C-4).

3.1.2. *N*-[(4-Methoxy-2,5-dihydrophenyl)methyl]benzylamine (2b). A mixture of benzaldehyde (1.31 g, 106 mmol) and dihydroanisole **2** (R=H,[15] 1.93 g, 13.9 mmol) in CH_2Cl_2 (12 mL) was stirred at rt for 3 h with activated 4 Å molecular sieves. The mixture was filtered through a short pad of Celite and concentrated. The resulting crude imine in MeOH (32 mL) was treated with $NaBH_4$ (0.93 g, 37.8 mmol), and

the reaction mixture was stirred for 4 h. After quenching with H_2O (30 mL), MeOH was evaporated, and the resulting aqueous suspension was extracted with CH_2Cl_2 and washed with brine. The organic extracts were dried, concentrated, and the residue was purified by chromatography (EtOAc/hexane 9:1) to afford 1.93 g (61%) of **2b**. ^{1}H NMR (200 MHz) 2.78 (br s, 4H, H-3 and H-6), 3.20 (s, 2H, NCH_2), 3.55 (s, 3H, OCH_3), 3.75 (s, 2H, CH_2Ph), 4.65 (m, $W_{1/2}$=8 Hz, 1H, H-5), 5.60 (m, $W_{1/2}$=8 Hz, 1H, H-2), 7.20–7.40 (m, 5H, ArH); ^{13}C NMR 28.0 and 28.9 (C-3 and C-6), 53.0 (CH_2Ph), 53.9 (OCH_3), 54.4 (NCH_2), 90.4 (C-5), 119.1 (C-2), 126.8, 128.1, 128.3 (C-*o*, C-*m*, C-*p*), 134.5 (C-1), 140.4 (C-*ipso*), 152.8 (C-4).

3.1.3. *N*-(2-Bromoprop-2-enyl)-*N*-[(4-methoxy-2,5-dihydrophenyl)methyl]methylamine (3a). To a solution of amine **2a** (0.5 g, 3.26 mmol) in acetonitrile (11 mL) were added 2,3-dibromopropene (1.01 mL, 9.8 mmol), LiI (568 mg, 4.84 mmol), and K_2CO_3 (1.03 g, 7.5 mmol), and the reaction mixture was heated at reflux temperature for 24 h. After filtration and concentration, the residue was partitioned between H_2O and CH_2Cl_2 and the aqueous layer was extracted with CH_2Cl_2. The dried organic extracts were concentrated and the residue was purified by chromatography to yield 0.52 g (58%) of **8a**: ^{1}H (400 MHz) 2.72–2.79 (m, 2H, H-6), 2.79–2.85 (m, 2H, H-3), 2.93 (s, 2H, NCH_2), 3.10 (s, 2H, CH_2CBr), 3.55 (s, 3H, OCH_3), 4.65 (m, $W_{1/2}$=8 Hz, 1H, H-5), 5.56 (s, 1H, =CH), 5.59 (m, $W_{1/2}$=8 Hz, 1H, H-2), 5.85 (d, J=1.2 Hz, 1H, =CH); ^{13}C NMR (100 MHz) 28.0 and 29.1 (C-3 and C-6), 41.9 (NCH_3), 53.9 (OCH_3), 63.5 (NCH_2), 65.0 (CH_2CBr), 90.8 (C-5), 118.1 (=CH_2), 121.0 (C-2), 124.8 (=CBr), 133.5 (C-1), 152.5 (C-4).

3.1.4. *N*-(2-Bromoprop-2-enyl)-*N*-[(4-methoxy-2,5-dihydrophenyl)methyl]benzylamine (3b). Operating as above, starting from **2b** (390 mg, 1.31 mmol) and after chromatography, tertiary amine **3b** (0.35 g, 76%) was isolated. ^{1}H NMR (200 MHz) 2.85–3.00 (m, 4H, H-3 and H-6), 2.97 (s, 2H, NCH_2), 3.20 (s, 2H, CH_2CBr), 3.55 (s, 3H, OCH_3), 3.56 (s, 2H, CH_2Ph), 4.63 (m, $W_{1/2}$=8 Hz, 1H, H-5), 5.58 (s, 1H, =CH), 5.60 (m, $W_{1/2}$=8 Hz, 1H, H-2), 5.93 (s, 1H, =CH), 7.20–7.40 (m, 5H, ArH).

3.1.5. *N*-[(4-Oxocyclohex-1-enyl)methyl]*sec*-butylamine ethylene acetal (6c). To a solution of aldehyde **5**[16] (848 mg, 5.08 mmol) and *sec*-butylamine (0.51 mL, 5.08 mmol) in dichloroethane, $NaBH(OAc)_3$ (1.51 g, 7.11 mmol) was added and the mixture was stirred at rt for 18 h. The reaction mixture was quenched with aqueous saturated $NaHCO_3$ solution, and extracted with Et_2O. The ethereal extracts were dried and concentrated to give a residue, which was submitted to chromatography (SiO_2, EtOAc) yielding 1.06 g (93%) of **6c**. ^{1}H NMR (400 MHz) 0.90 (t, J=7 Hz, 3H, CH_3), 1.05 (d, J=7 Hz, 3H, CH_3), 1.35 and 1.55 (2m, 2H, CH_2-*sec* butyl), 1.80 (t, J=7 Hz, 2H, H-5), 2.20–2.30 (m, 4H, H-3 and H-6), 2.60 (m, 1H, CHN), 3.10 (m, 2H, NCH_2), 5.55 (m, $W_{1/2}$=8 Hz, 1H, H-2); ^{13}C NMR (100 MHz) 10.2 (CH_3), 20.0 (CH_3), 26.0 (C-5), 29.5 (CH_2-*sec*-butyl), 31.5 and 36.0 (C-3 and C-6), 52.0 (NCH_2), 54.0 (NCH), 108.0 (C-4), 120.0 (C-2), 136.0 (C-1).

3.1.6. *N*-[(4-Oxocyclohex-1-enyl)methyl]tryptamine ethylene acetal (6d). Operating as above, starting from aldehyde **5** (768 mg, 4.6 mmol) and tryptamine (737 mg, 4.60 mmol), and after workup, 1.37 g (95%) of **6d** was isolated, which was used without further purification. ^{1}H NMR (200 MHz) 1.65 (t, J=7 Hz, 2H, H-5), 2.24 (m, 4H, H-3 and H-6), 2.65 and 2.85 (2m AA′BB′ system, 4H, $InCH_2CH_2N$), 3.97 (s, 4H, OCH_2), 5.5 (m, $W_{1/2}$=8 Hz, 1H, H-2), 6.98 (d, J=2 Hz, 1H, H-2′), 7.00–7.22 (m, 2H, H-5′ and H-6′), 7.30 (d, J=7 Hz, 1H, H-7′), 7.60 (d, J=7 Hz, 1H, H-4′), 7.90 (br s, 1H, NH); ^{13}C NMR 23.0 (CH_2In), 26.0 (C-5), 31.0 and 35.7 (C-3 and C-6), 53.8 (NCH_2), 60.1 (CH_2CBr), 64.4 (OCH_2), 108.3 (C-4), 111.0 (C-7′), 114.5 (C-3′), 117.7 (=CH_2), 118.9 (C-5′), 119.1 (C-6′), 121.6 (C-2), 121.9 (C-2′), 127.5 (C-3a), 132.8 (BrC=), 135.8 (C-7a), 136.2 (C-1).

3.1.7. *N*-(2-Bromoprop-2-enyl)-*N*-[(4-oxocyclohex-1-enyl)methyl]methylamine ethylene acetal (7a). To a cooled solution (0 °C) of the enol ether **8a** (0.14 g, 0.52 mmol) in THF (0.9 mL) were added ethylene glycol (35 μL, 0.62 mmol) and $BF_3\cdot OEt_2$ (66 μL, 0.52 mmol). After stirring overnight, saturated aqueous $NaHCO_3$ was added, and the reaction mixture was extracted with EtOAc. The organic extracts were dried and concentrated to give 0.10 g (66%) of **7a**, which was used without further purification in the next step. ^{1}H NMR (400 MHz) 1.76 (t, J=6.4 Hz, 1H, H-5), 2.18 (s, 3H, CH_3), 2.04–2.07 (m, 4H, H-3 and H-6), 2.90 (s, 2H, NCH_2), 3.09 (s, 2H, CH_2CBr), 3.97 (s, 4H, OCH_2), 5.50 (br s, 1H, H-2), 5.54 (s, 1H, =CH), 5.83 (s, 1H, =CH); ^{13}C NMR (100 MHz) 25.8 (C-5), 31.0 (C-6), 35.7 (C-3), 41.9 (CH_3), 63.4 (CH_2CBr), 64.3 (CH_2O), 65.1 (CH_2N), 108.2 (C-4), 118.2 (=CH_2), 121.9 (C-2), 132.1 (C-1), 135.5 (=CBr).

3.1.8. *N*-(2-Bromoprop-2-enyl)-*N*-[(4-oxocyclohex-1-enyl)methyl]benzylamine ethylene acetal (7b). Operating as above, starting from enol ether **3b** (400 mg, 1.15 mmol) and after chromatography (EtOAc/hexane 9:1), 289 mg (67%) of acetal **7b** was isolated. ^{1}H NMR 1.67 (m, 2H, H-5), 2.30 (m, 4H, H-3 and H-6), 2.98 (s, 2H, NCH_2), 3.10 (s, 2H, CH_2CBr), 3.60 (s, 2H, CH_2Ph), 4.00 (s, 4H, OCH_2), 5.50 (br s, 1H, H-2), 6.00 (s, 1H, =CH), 5.90 (s, 1H, =CH), 7.20–7.40 (m, 5H, ArH); ^{13}C NMR 25.9 (C-5), 31.0 (C-6), 35.7 (C-3), 57.6 (NCH_2), 59.7 (CH_2CBr), 61.7 (CH_2Ph), 64.2 (OCH_2), 108.2 (C-4), 118.3 (=CH_2), 121.9 (C-2), 132.4 (C-1), 135.5 (=CBr), 139.2 (C-*ipso*). HRMS (ESI-TOF) calcd for $C_{19}H_{25}BrNO_2$ (M^++1) 378.1063, found 378.1076.

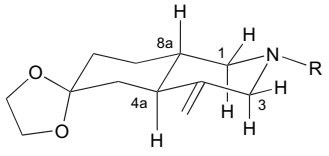
3.1.9. *N*-(2-Bromoprop-2-enyl)-*N*-[(4-oxocyclohex-1-enyl)methyl]*sec*-butylamine ethylene acetal (7c). To a solution of amine **6c** (583 mg, 4.37 mmol) in acetonitrile (65 mL) were added 2,3-dibromopropene (0.59 mL, 5.68 mmol), LiI (760 mg, 5.68 mmol), and K_2CO_3 (785 mg, 5.68 mmol), and the reaction mixture was heated at reflux temperature for 3 h. After filtration and concentration of the filtrate, the residue was partitioned between H_2O and CH_2Cl_2, and the aqueous layer was extracted with CH_2Cl_2. The dried organic extracts were concentrated and purified by chromatography to yield 0.79 g (52%) of amine **7c**. ^{1}H NMR 0.90 (t, J=6.3 Hz, 3H, CH_3), 0.93 (t, J=7.2 Hz, 3H, CH_3), 1.25 and 1.50 (2m, 2H, CH_2-*sec*-butyl), 2.10–2.52 (m, 4H, H-3 and H-6), 2.64 (q, J=6.6 Hz, 1H, CHN), 2.84 and 3.03 (2d, J=13.2 Hz, 2H, NCH_2), 3.04 and 3.26 (2d, J=15.6 Hz, 2H, CH_2CBr), 3.98 (s, 4H, OCH_2), 5.51 (m,

2H, H-2 and =CH), 5.90 (s, 1H, =CH); ^{13}C NMR 11.8 (CH_3), 13.2 (CH_3), 25.7 (C-5), 26.7 (CH_2-*sec*-butyl), 31.0 (C-6), 35.7 (C-3), 54.7 (CHN), 55.2 (NCH_2), 57.6 (CH_2CBr), 64.3 (CH_2O), 108.2 (C-4), 117.0 (=CH_2), 121.3 (C-2), 133.9 (=CBr), 136.0 (C-1). HRMS (ESI-TOF) calcd for $C_{16}H_{27}BrNO_2$ (M^++1) 344.1220, found 344.1209.

3.1.10. *N*-(2-Bromoprop-2-enyl)-*N*-[(4-oxocyclohex-1-enyl)methyl]tryptamine ethylene acetal (7d). Operating as above, starting from **6d** (1.37 g, 4.60 mmol) and after chromatography, amine **7d** (1.12 g, 57%) was isolated. ^{1}H NMR (200 MHz) 1.70 (t, *J*=6.5 Hz, 2H, H-5), 2.20–2.40 (m, 4H, H-3 and H-6), 2.80 and 2.90 (2m AA′BB′ system, 4H, $InCH_2CH_2N$), 3.08 (s, 2H, NCH_2), 3.31 (s, 2H, CH_2CBr), 3.97 (s, 4H, OCH_2), 5.54 (m, 2H, H-2 and =CH), 5.90 (s, 1H, =CH), 7.00–7.40 (m, 4H), 7.60 (d, *J*=7 Hz, 1H), 7.90 (br s, 1H, NH); ^{13}C NMR 23.0 (CH_2In), 26.0 (C-5), 31.0 and 35.7 (C-3 and C-6), 53.8 (NCH_2), 60.1 (CH_2CBr), 62.2 (NCH_2C=), 64.4 (OCH_2), 108.3 (C-4), 111.0 (C-7′), 114.5 (C-3′), 117.7 (=CH_2), 118.9 (C-5′), 119.1 (C-6′), 121.6 (C-2), 121.9 (C-2′), 127.5 (C-3′a), 132.8 (=CBr), 135.8 (C-7′a), 136.2 (C-1). HRMS (ESI-TOF) calcd for $C_{22}H_{28}BrN_2O_2$ (M^++1) 431.1329, found 431.1321.

3.2. General procedure for the synthesis of *trans*-perhydroisoquinolines (8a–d) by radical cyclization of the corresponding vinyl bromides (7a–d)

A solution of vinyl halide (1 equiv) and AIBN (0.3 equiv) in benzene (100 mL) was heated at reflux. Then, Bu_3SnH (2 equiv) was added dropwise and the reaction mixture was stirred at this temperature for 3 h. After removal of the solvent, the residue was dissolved in EtOAc and extracted with aqueous 1% HCl. The aqueous phase was basified with saturated Na_2CO_3 and extracted with CH_2Cl_2. Concentration of the dried organic extracts afforded a residue that was purified by chromatography.



8 (a-d)

3.2.1. 2-Methyl-4-methylene-*trans*-perhydroisoquinolin-6-one ethylene acetal (8a). Operating as above, starting from 100 mg (0.3 mmol) of **7a** and after chromatography (Al_2O_3, hexane/EtOAc 7:3), 30 mg (45%) of **8a**, containing a 15% of cis-isomer **9a**, was obtained. ^{1}H NMR (400 MHz, gCOSY) 1.32 (m, 1H, H-8a), 1.50–1.80 (m), 1.93 (dt, *J*=12.8, 2.8 Hz, 1H, H-7), 2.17 (s, 3H, NCH_3), 2.53 (d, *J*=11.6 Hz, 1H, H-3), 2.85 (d, *J*=10.4 Hz, 1H, H-1eq), 3.26 (dd, *J*=11.6, 1.6 Hz, 1H, H-3), 3.90–4.05 (m, 4H, OCH_2), 4.63 (s, 1H, =CH), 4.83 (d, *J*=1.2 Hz, 1H, =CH); ^{13}C NMR (100 MHz, gHSQC) 27.9 (C-8), 34.4 (C-5), 36.7 (C-7), 41.2 (C-8a), 42.4 (C-4a), 45.9 (NCH_3), 61.8 (C-1), 63.1 (C-3), 64.3 and 64.4 (OCH_2), 106.5 (=CH_2), 109.5 (C-6), 147.1 (C-4). HRMS (ESI-TOF) calcd for $C_{13}H_{22}NO_2$ (M^++1) 224.1645, found 224.1648.

3.2.2. 2-Benzyl-4-methylene-*trans*-perhydroisoquinolin-6-one ethylene acetal (8b). Operating as in the general procedure, starting from 87 mg (0.236 mmol) of **7b** and after chromatography (SiO_2, hexane/EtOAc 4:6), 39 mg (57%) of **8b**, containing a 15% of cis-isomer **9b**, was obtained. ^{1}H NMR (400 MHz, gCOSY) 1.20–2.00 (m, 6H), 1.25 (m, 1H, H-8a), 1.90 (m, 2H, H-1 and H-4a), 2.63 (d, *J*=12 Hz, 1H, H-3), 2.89 (d, *J*=11.4 Hz, 1H, H-1eq), 3.31 (dd, *J*=11.4, 1.8 Hz, 1H, H-3), 3.52 and 3.58 (2d, *J*=12 Hz, 2H, CH_2Ph), 3.90–4.00 (m, 4H, OCH_2), 4.63 (s, 1H, =CH), 4.78 (d, *J*=1.5 Hz, 1H, =CH), 7.20–7.40 (5H, ArH); ^{13}C NMR (100 MHz, gHSQC) 26.8 (C-8), 34.4 (C-5), 36.7 (C-7), 40.7 (C-8a), 42.9 (C-4a), 59.4 (C-1), 60.9 (C-3), 62.6 (CH_2Ph), 64.3 and 64.5 (OCH_2), 106.6 (=CH_2), 109.5 (C-6), 127.0, 128.2, 129.1 (C-*o*, C-*m*, C-*p*), 138.0 (*ipso*-C), 147.0 (C-4).

3.2.3. *2-sec*-Butyl-4-methylene-6,6-ethylenedioxy-*trans*-perhydroisoquinolin-6-one ethylene acetal (8c). Operating as in the general procedure, starting from 100 mg (0.29 mmol) of **7c** and after chromatography (SiO_2, CH_2Cl_2/MeOH 95:5), 48 mg (62%) of **8c**, containing a 15% of cis-isomer **9c**, was obtained. ^{1}H NMR (400 MHz, gCOSY) 0.91 (t, *J*=7.2 Hz, 3H, CH_3), 1.05 (d, *J*=6.8 Hz, 2H, CH_2-*sec*-butyl), 1.20–1.75 (m), 1.78 (dd, *J*=12.8, 1.6 Hz, 1H, H-5eq), 1.88 (t, *J*=10 Hz, H-4a), 1.91 (d, *J*=13 Hz, H-7eq), 2.05–2.25 (m, 1H, H-1), 2.57 (m, 1H, CH-*sec*-butyl), 2.80–3.00 (m, 2H, H-1 and H-3), 3.23–3.33 (m, 1H, H-3), 3.80–4.00 (m, 4H, OCH_2), 4.66 (s, 1H, =CH), 4.86 (s, 1H, =CH); ^{13}C NMR (100 MHz, gHSQC) 11.4 (CH_3), 13.5 (CH_3), 25.6 (CH_2), 28.0 (C-8), 34.3 (C-5), 36.7 (C-7), 40.9 (C-8a), 43.1 (C-4a), 53.4 and 55.1 (C-1), 55.8 and 57.5 (C-3), 60.9 (CH-*sec*-butyl), 64.3 and 64.4 (OCH_2), 107.1 (=CH_2), 109.4 (C-6), 146.5 (C-4). HRMS (ESI-TOF) calcd for $C_{16}H_{28}NO_2$ (M^++1) 266.2115, found 266.2112.

3.2.4. 2-[2-(3-Indolyl)ethyl]-4-methylene-*trans*-perhydroisoquinolin-6-one ethylene acetal (8d). Operating as in the general procedure, starting from 125 mg (0.29 mmol) of **7d** and after chromatography (Al_2O_3, CH_2Cl_2/MeOH 95:1), 80 mg (78%) of **8d**, containing a 15% of cis-isomer **9d**, was obtained. ^{1}H NMR (400 MHz, gCOSY) 0.9–1.9 (m), 1.98 (dd, *J*=12, 2 Hz, 1H, H-4a), 2.02–2.30 (m, 1H, H-1), 2.80–2.95 (m, 3H, H-3 and NCH_2), 3.16 (t, *J*=8.4 Hz, 2H, CH_2In), 3.23 (d, *J*=10.8 Hz, 1H, H-1eq), 3.66 (dd, *J*=11.6, 1.6 Hz, 1H, H-3), 4.06–4.20 (m, 4H, OCH_2), 4.84 (s, 1H, =CH), 5.04 (s, 1H, =CH), 7.16 (br s, 1H, H-2′), 7.27 (t, *J*=7.4 Hz, 1H, H-5′), 7.37 (t, *J*=7.4 Hz, 1H, H-6′), 7.49 (d, *J*=8 Hz, 1H, H-7), 7.77 (d, *J*=7.6 Hz, 1H, H-4′), 8.5 (br s, 1H, NH); ^{13}C NMR (100 MHz, gHSQC) 23.1 (CH_2In), 27.1 (C-8), 34.4 (C-5), 36.8 (C-7), 41.0 (C-8a), 43.0 (C-4a), 58.9 (NCH_2), 59.7 (C-1), 61.2 (C-3), 64.2 and 64.3 (OCH_2), 106.7 (=CH_2), 109.3 (C-6), 111.1 (C-7′), 114.2 (C-3′), 118.7 (C-4′), 119.1 (C-5′), 121.5 (C-6′), 121.8 (C-2′), 127.4 (C-3a), 136.3 (C-7a), 147.0 (C-4). HRMS (ESI-TOF) calcd for $C_{22}H_{29}N_2O_2$ (M^++1) 353.2224, found 353.2213.

3.2.5. (2*S*)-*N*-[(4-oxocyclohex-1-enyl)methyl]tryptophan ethylene acetal methyl ester (11). To a cooled solution (0 °C) of 4-hydroxymethylcyclohex-3-enone ethylene acetal[16] (1.08 g, 6.37 mmol) in THF (118 mL) were added

TEA (0.98 mL, 7.0 mmol) and mesyl chloride (0.5 mL, 6.37 mmol). After stirring for 1 h 30 min, the reaction mixture was filtered and concentrated to give crude mesylate **10**, which was used without further purification in the next step. To a mixture of tryptophan methyl ester (927 mg, 4.25 mmol) and Na_2CO_3 (675 mg, 6.37 mmol) in CH_3CN (100 mL) was added a solution of the crude mesylate **10** in CH_3CN (27 mL). The reaction mixture was heated at 45 °C overnight and then filtered and concentrated to give a residue, which was purified by chromatography (EtOAc) to give 876 mg (56%) of **11**. ^{1}H NMR 1.60 (m, 2H, H-5), 2.10 (m, 2H, H-6), 2.20 (s, 2H, H-3), 2.98–3.20 (m, 4H, CH_2In and CH_2N), 3.61 (dd, J=7.2, 6.1 Hz, 1H, CHN), 3.64 (s, 3H, OCH_3), 3.95 (s, 4H, OCH_2), 5.40 (m, $W_{1/2}$= 8 Hz, 1H, H-2), 7.07 (d, J=2.4 Hz, 1H, H-2), 7.12 (td, J=7.8, 0.9 Hz, 1H, H-5), 7.19 (td, J=7.8, 0.9 Hz, 1H, H-6), 7.35 (d, J=7.8, 1.3 Hz, 1H, H-7), 7.61 (dd, J=7.8, 1.3 Hz, 1H, H-4), 8.01 (br s, 1H, NH); ^{13}C NMR 25.8 (C-5), 29.3 (CH_2In), 30.8 and 35.4 (C-3 and C-6), 51.7 (OCH_3), 53.3 (NCH_2), 60.8 (CHN), 64.2 (OCH_2), 108.0 (C-4), 111.1 (C-7), 118.6 (C-3), 119.2 (C-4), 120.2 (C-5), 121.9 (C-2 and C-6), 122.8 (C-2′), 127.3 (C-3a), 135.2 (C-1′), 136.1 (C-7a), 175.3 (CO).

3.2.6. (2*S*)-*N*-(2-Bromoprop-2-enyl)-*N*-[(4-oxocyclohex-1-enyl)methyl]tryptophan ethylene acetal methyl ester (12). To a solution of amine **11** (140 mg, 0.57 mmol) in acetonitrile (1.7 mL) were added K_2CO_3 (181 mg, 1.31 mmol) and 2,3-dibromopropene (0.18 mL, 1.71 mmol). The reaction mixture was heated at 55 °C overnight and concentrated to dryness. The residue was taken up in water and extracted with CH_2Cl_2. Concentration of the dried organic extracts gave a residue, which was purified by chromatography to give 173 mg (83%) of **12**. IR 3409, 2950, 1730, 1210, 1166, 1114, 1011, 1059, 742; ^{1}H NMR 1.40–1.75 (m), 2.90–2.30 (m), 3.63 (s, 3H, OCH_3), 3.80 (m, 1H, CHN), 3.95 (s, 4H, OCH_2), 5.48 (m, $W_{1/2}$=8 Hz, 1H, H-2), 5.53 (s, 1H, =CH), 5.8 (d, J=0.6 Hz, 1H, =CH), 7.02 (d, J=2.4 Hz, 1H, H-2), 7.11 (td, J=7.5, 1.2 Hz, 1H, H-5), 7.18 (td, J=6.9, 1.2 Hz, 1H, H-6), 7.33 (dm, J=7.5 Hz, 1H, H-7), 7.60 (dm, J=7.2 Hz, 1H, H-4), 7.97 (br s, 1H, NH); ^{13}C NMR 26.7 (CH_2In), 25.9 (C-5), 30.8 and 35.6 (C-3 and C-6), 51.0 (OCH_3), 56.9 (NCH_2), 58.5 (CH_2CBr), 61.5 (CHN), 64.2 and 64.3 (OCH_2), 108.2 (C-7), 111.0 (C-4′), 111.9 (C-3), 118.2 (=CH_2), 118.6 (C-4), 119.2 (C-5), 121.8 (C-6), 122.8 (C-2′), 123.0 (C-2), 127.3 (C-3a), 132.5 (=CBr), 134.8 (C-1′), 136.1 (C-7a), 172.7 (CO). HRMS (ESI-TOF) calcd for $C_{24}H_{30}BrN_2O_4$ (M^++1) 489.1383, found 489.1379.

3.2.7. 2-[2-(3-Indolyl)-1(*S*)-methoxycarbonylethyl]-4-methylene-*trans*-perhydroisoquinolin-6-one ethylene acetal (13). A solution of **12** (123 mg, 0.25 mmol) and AIBN (8 mg, 0.05 mmol) in benzene (25 mL) was heated at reflux. Bu_3SnH (90 μL, 0.34 mmol) was added dropwise and the reaction mixture was stirred at this temperature for 3 h. After evaporation of the solvent, the residue was partitioned between CH_3CN and hexane, and extracted several times with CH_3CN. Concentration of the dried organic extracts afforded a residue that was purified by chromatography (SiO_2, hexane/EtOAc 98:2) to give isoquinoline **13** (75 mg, 75%) as a mixture of two diastereomers. IR 3290, 2952, 1728, 1249, 853, 744, 691, 611; ^{1}H NMR (400 MHz) 1.20–1.92 (m, 6H), 1.27 (m, 1H, H-8a), 1.86 (m, 1H, H-4a), 2.10 (t, J=10 Hz, 0.5H, H-1, diastereomer B), 2.20 (t, J=10 Hz, 0.5H, H-1, diastereomer A), 2.85 (d, J=10 Hz, 0.5H, H-3, diastereomer A), 2.86 (t, J=10 Hz, 0.5H, H-1, diastereomer A), 2.92 (d, J=10 Hz, 0.5H, H-3, diastereomer B), 3.00–3.10 (m, 1.5H, CH_2-In and H-1, diastereomer B), 3.20–3.30 (m, 1H, CH_2-In), 3.48 and 3.49 (2s, 3H, OCH_3), 3.50–3.60 (m, 1H, CHN), 3.84–3.94 (m, 4H, OCH_2), 4.59 (br s, 1H, =CH), 4.78 and 4.80 (2s, 1H, =CH), 6.95 (br s, 1H, H-2), 7.03 (t, J=7 Hz, 1H, H-5), 7.10 (t, J=7 Hz, 1H, H-6), 7.25 (d, J=8 Hz, 1H, H-7), 7.54 (dd, J=7.6, 2.4 Hz, 1H, H-4′), 7.99 (br s, 1H, NH); ^{13}C NMR (100 MHz) diastereomer A 25.5 (CH_2In), 28.1 (C-8), 34.7 (C-5), 37.0 (C-7), 41.8 (C-8a), 43.3 (C-4a), 51.2 (OCH_3), 58.9 (C-1), 60.5 (C-3), 64.7 (CH_2O), 68.7 (CHN), 106.9 (CH_2=), 109.3 (C-acetal), 111.4 (C-7), 112.2 (C-3), 119.0 (C-4), 119.6 (C-5), 122.2 (C-6), 123.0 (C-2), 127.7 (C-3a), 136.3 (C-7a), 147.0 (C=), 172.2 (CO); diastereomer B 25.8 (CH_2In), 28.2 (C-8), 34.7 (C-5), 37.0 (C-7), 41.7 (C-8a), 43.3 (C-4a), 51.3 (OCH_3), 53.9 (C-1), 55.7 (C-3), 64.6 (CH_2O), 68.6 (CHCOO), 106.9 (=CH_2), 109.3 (C-acetal), 111.4 (C-7), 112.2 (C-3), 119.0 (C-4), 119.6 (C-5), 122.2 (C-6), 122.9 (C-2), 127.7 (C-3a), 136.3 (C-7a), 147.4 (=C), 172.2 (CO). HRMS (ESI-TOF) calcd for $C_{24}H_{31}N_2O_4$ (M^++1) 411.2278, found 411.2271.

3.2.8. Methyl (*S*)-*N*-[(4-oxocyclohex-1-enyl)methyl]-*N*-(trichloroacetyl)tryptophan ethylene acetal (14). To a solution of amine **11** (267 mg, 0.72 mmol) in CH_2Cl_2 (1 mL) was added triethylamine (0.11 mL, 0.79 mmol). To this cooled solution (0 °C) was added dropwise trichloroacetyl chloride (0.121 mL, 1.08 mmol) and the reaction mixture was heated at reflux for 15 h. After cooling, CH_2Cl_2 was added and the organic solution was washed with saturated aqueous K_2CO_3, dried, and concentrated. The resulting residue was purified by chromatography (hexane/EtOAc 3:7) to give trichloroacetamide **14** (297 mg, 80%) as a yellow solid. IR (NaCl) 3374, 1742, 1666; ^{1}H NMR (300 MHz) 1.50–2.50 (m, 6H), 2.94 (d, J=14.4 Hz, 1H, CHN), 3.60 (d, J=7.2 Hz, 2H, CH_2In), 3.79 (s, 3H, OCH_3), 3.86–3.96 (m, 4H, OCH_2), 4.32 (dd, J=6.6 Hz, 1H, CH), 4.37 (d, J=14.4 Hz, 1H, CHN), 4.88 (m, $W_{1/2}$=10 Hz, 1H, H-3′), 7.04 (d, J=2.1 Hz, 1H, H-2), 7.13 (td, J=7.4, 1.1 Hz, 1H, H-5), 7.20 (td, J=7.4, 1.1 Hz, 1H, H-6), 7.38 (d, J=7.8 Hz, 1H, H-7), 7.58 (d, J=7.8 Hz, 1H, H-4), 8.03 (br s, 1H, NH); ^{13}C NMR (75 MHz) 23.7 (CH_2In), 25.1 (C-6′), 30.5 (C-5′), 35.6 (C-2′), 52.4 (OCH_3), 57.6 (CH_2N), 59.8 (CH), 64.2 and 64.3 (OCH_2), 92.9 (CCl_3), 107.4 (C-1), 111.0 (C-3), 111.4 (C-7), 118.4 (C-4), 119.4 (C-5), 122.2 (C-6), 123.7 (C-2), 127.0 (C-3 and C-3a), 131.7 (C-4), 136.2 (C-7a), 160.2 (CON), 170.0 (COO). Anal. Calcd for $C_{23}H_{25}Cl_3N_2O_5$: C, 53.55; H, 4.85; N, 5.43. Found: C, 53.23; H, 4.98; N, 5.36.

3.2.9. 2-[(1*S*)-2-(1*H*-Indol-3-yl)-1-(methoxycarbonyl)-ethyl]-2-azaspiro[4.5]decan-3,8-dione ethylene acetal (15). To a boiling solution of **14** (96 mg, 0.19 mmol) and AIBN (9 mg, 0.06 mmol) in benzene (1.60 mL) was added Bu_3SnH (0.175 mL, 0.65 mmol), and the mixture was heated under reflux for 3 h. After the solvent had been evaporated, the residue was purified by chromatography (EtOAc) to give **15** (55 mg, 73%) as a yellow oil. IR (NaCl) 3400, 1741,

1674; ^{1}H NMR (300 MHz) 1.16–1.46 (m, 8H), 2.12–2.27 (2d, J=16.7 Hz, 1H each, CH_2CO), 3.07–3.24 (2d, J=9.6 Hz, 1H each, NCH_2), 3.21 (m, 1H, CHIn), 3.43 (ddd, J=15.5, 4.8, 1 Hz, 1H, CHIn), 3.74 (s, 3H, OCH_3), 3.87 and 3.88 (2s, OCH_2), 5.26 (dd, J=11.5, 5.4 Hz, 1H, CHCO), 7.00 (d, J=1.8 Hz, 1H, H-2), 7.11 (td, J=11.1, 1.2 Hz, 1H, H-5), 7.15 (td, J=8, 1.1 Hz, 1H, H-6), 7.33 (dd, J=8.1, 0.9 Hz, 1H, H-7), 7.50 (d, J=7.5 Hz, 1H, H-4), 8.54 (br s, 1H, NH); ^{13}C NMR (75 MHz) 24.7 (CH_2In), 31.4, 33.3, 33.4, 35.7 (C-2′, C-3′, C-5′, C-6′), 43.0 (CH_2CO), 52.3 (OCH_3), 53.3 (CHCO), 54.0 (NCH_2), 64.1 (OCH_2), 107.9 (C), 110.3 (C-3), 111.2 (C-7), 118.1 (C-4), 119.4 (C-5), 121.8 (C-6), 122.0 (C-2), 127.1 (C-3a), 136.0 (C-7a), 171.2 (CON), 174.4 (CO). Anal. Calcd for $C_{23}H_{28}N_2O_5$: C, 67.65; H, 6.86; N, 5.88. Found: C, 67.38; H, 6.96; N, 5.76.

3.2.10. Methyl (*S*)-*N*-[(4-oxocyclohex-1-enyl)methyl]-*N*-(trichloroacetyl)tryptophan (16). A solution of acetal **14** (300 mg, 0.68 mmol) in 3 N HCl (30 mL) was stirred overnight at rt. The reaction mixture was basified and extracted with CH_2Cl_2. The organic extracts were dried and concentrated to give ketone **16** (190 mg, 86%) as a yellow oil. An analytical sample was obtained by chromatography (hexane/EtOAc 75:25). IR (NaCl) 3400, 1740, 1673; ^{1}H NMR (300 MHz, gCOSY) 2.16–2.34 (m, 2H, H-5′), 2.54–2.80 (m, 4H, H-3 and H-6), 2.96 (d, J=15 Hz, 1H, CHN), 3.56–3.68 (d, J=7.7 Hz, 2H, CH_2In), 3.81 (s, 3H, OCH_3), 4.31 (dd, J=8.4, 6.6 Hz, 1H, CH), 4.42 (d, J=15 Hz, 1H, CHN), 5.03 (m, $W_{1/2}$=9 Hz, 1H, H-2′), 7.04 (d, J=2.4 Hz, 1H, H-2), 7.13 (ddd, J=7.8, 7, 1.1 Hz, 1H, H-5), 7.21 (td, J=7.5, 1.1 Hz, 1H, H-6), 7.39 (d, J=8.1 Hz, 1H, H-7), 8.22 (br s, 1H, NH); ^{13}C NMR (75 MHz, gHSQC) 23.7 (CH_2In), 25.8 (C-6′), 38.0 (C-5′), 39.3 (C-2′), 52.6 (OCH_3), 57.1 (NCH_2), 60.2 (CH), 92.7 (CCl_3), 111.1 (C-3), 111.6 (C-7), 118.3 (C-4), 119.6 (C-5), 122.4 (C-6), 123.7 (C-2), 126.1 (C-3), 126.9 (C-3a), 132.8 (C-4), 136.2 (C-7a), 160.1 (CON), 169.7 (CO_2Me), 209.2 (CO). Anal. Calcd for $C_{21}H_{21}Cl_3N_2O_4$: C, 53.47; H, 4.49; N, 5.94. Found: C, 53.40; H, 4.67; N, 5.54.

3.2.11. 2-[(1*S*)-2-(1*H*-Indol-3-yl)-1-(methoxycarbonyl)-ethyl]-2-azaspiro[4.5]decan-3,8-dione (17). To a boiling solution of **16** (73 mg, 0.16 mmol) and AIBN (8 mg, 0.05 mmol) in benzene (1.3 mL) was added Bu_3SnH (0.145 mL, 0.54 mmol), and the mixture was heated under reflux for 3 h. After the solvent had been evaporated, the residue was purified by chromatography (EtOAc) to give **17** (42 mg, 65%) as a yellow oil. IR (NaCl) 3304, 1740, 1682; ^{1}H NMR (400 MHz) 1.35 (ddd, J=13.7, 7.9, 5.7 Hz, 1H, H-3′ or H-5′), 1.49 (ddd, J=13.7, 8.1, 5.7 Hz, 1H, H-3′ or H-5′), 1.85 (t, J=6.8 Hz, 2H, H-2′ or H-6′), 1.96 (ddd, J=14.2, 8.6 Hz, 1H, H-3′ or H-5′), 2.05 (ddd, J=14.8, 7.2, 6 Hz, 1H, H-3′ or H-5′), 2.24–2.31 (m, 2H, H-2′ or H-6′), 2.19 and 2.39 (2d, J=16.6 Hz, 2H, CH_2CO), 3.19 and 3.40 (2d, J=9.4 Hz, 2H, NCH_2), 3.28 (dd, J=15.6, 12 Hz, 1H, CHIn), 3.45 (ddd, J=15.6, 6, 1.2 Hz, 1H, CHIn), 5.29 (dd, J=11.4, 5 Hz, 1H, CHCO), 7.06 (d, J=2.4 Hz, 1H, H-2), 7.13 (td, J=7.5, 0.9 Hz, 1H, H-5), 7.20 (td, J=7.6, 0.9 Hz, 1H, H-6), 7.35 (d, J=8 Hz, 1H, H-7), 7.58 (d, J=8 Hz, 1H, H-7), 8.20 (br s, 1H, NH); ^{13}C NMR (100 MHz) 24.7 (CH_2In), 35.5 (C-3′ or C-5′), 35.7 (C-2′ or C-6′), 36.0 (C-4′), 37.5 (C-3′ or C-5′), 37.8 (C-2′ or C-6′), 42.6 (CH_2CO), 52.4 (OCH_3), 53.3 (CHCO), 53.4 (CH_2N), 110.5 (C-3), 111.3 (C-7), 118.1 (C-4), 119.7 (C-5), 121.8 (C-6), 122.4 (C-2), 127.2 (C-3a), 136.0 (C-7a), 171.3 (CON), 173.8 (CO_2Me), 209.9 (CO).

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