Organocatalytic Enantioselective (3+2) Cycloaddition using Stable Azomethine Ylides

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General Methods.¹ NMR spectra were acquired on a Bruker 300 spectrometer, running at 300 and 75 MHz for ¹H and ¹³C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CHCl₃, 7.26 ppm for ¹H NMR, CDCl₃, 77.0 ppm for ¹³C NMR). The following abbreviations are used to indicate the multiplicity in ¹H NMR spectra: s, singlet; d, doublet; t, triplet; m, multiplet; bs, broad singlet; a, apparent. ¹³C NMR spectra were acquired on a broad band decoupled mode. Infrared (IR) spectra were measured in a Perkin-Elmer 1600 apparatus and only characteristic bands are given. Mass spectra (HMRS/MS) were recorded on a Mass Espectrometer provided with a Time of Fight (TOF) (GCT de Micromass) coupled to a Gas Chromatograph (Agilent 6890N). Analytical thin layer chromatography (TLC) was performed using pre-coated aluminumbacked plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or Phosphomolybdic Acid dip.² Melting points (M.p.) were measured in a Büchi B-540 apparatus. Optical rotations were measured on a Perkin-Elmer 241 polarimeter and Jasco P-2000. The enantiomeric excess (e.e.) of the products were determined by chiral stationary phase HPLC in a Waters 2695 using photodiode array detector Waters 2998 and using Daicel Chiralpak (AS-H, AD-H) and Daicel Chiralcel (OD) columns.

Materials. Analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography silica gel (Silica gel 60, 230-400 mesh, Merck) was used.

¹SGIker technical support (MEC, GV/EJ and European Social Fund) is gratefully acknowledged (X-ray analysis).

² Stalh, E. *Thin Layer Chromatography*, Springer-Verlag; Berlin, 1969.

Experimental Procedures and Characterizations.

General Procedure for the Preparation of Ylides 1a-b. The corresponding nitrogen heterocycle (2.0 mmol) was added into a solution of tetracyanoethylene oxide $(TCENO)^3$ (1.0 mmol) in THF at 0 °C. The reaction was stirred at 4 °C during the necessary time and the formed solid was recrystalized or filtrated under vacuum.



Isoquinolinium-2-dicyanomethanide (1a). Following the general procedure 1a (6.26 g, 32.4 mmol) was synthesized by adding isoquinoline (2.77 g, 21.4 mmol) to a solution of TCNEO (6.00 g, 41.6 mmol) in THF (50 mL) at 0 °C The reaction was stirred at 4 °C during 20 h. Then, the solvent was evaporated

and the formed solid was recrystalized in EtOH. Yield: 78%. M.p.: 253-255 °C (Lit.⁴: 258-259 °C).



Phthalazinium-2-dicyanomethanide (1b). Following the general procedure **1b** (0.89 g, 4.16 mmol) was synthesized by adding phthalazine (1.89 g, 14.58 mmol) to a solution of TCNEO (0.70 g, 4.86 mmol) in THF (50 mL) at 0 °C. The reaction was stirred at this temperature during 2 h. Then, the formed solid

was filtrated and washed with cold THF (3 \times 25 mL). Yield: 95%. M.p.: 255-256 °C (Lit.⁵: 264-265 °C).

General Procedure for the Synthesis of Aldehydes 4a-l. (2S,5S)-(-)-5-Benzyl-2-tert-butyl-3methyl-4-imidazolidinone 3c (0.10 mmol) and trifluoroacetic acid (TFA) (0.10 mmol) were dissolved in the appropriate solvent (1 mL) and the excess of additive was evaporated under vacuum. After that, a solution of the α , β -unsaturated aldehyde 2a-f (1.04 mmol) in the adequate solvent (2 mL) was added and the mixture was stirred for 30 min at the indicated temperature before the ylide 1a-b (0.52 mmol) was added. The reaction was next stirred at that temperature until full conversion. Afterwards the solvent was evaporated under vacuum and directly charged onto silica gel and subjected to flash column chromatography. The enantiomeric excess of the compounds were determined after transformation of the aldehydes 4a-l to the corresponding alcohols 5a-l. Racemic samples were prepared using a racemic mixture of the catalyst 3c.

³ W. J. Linn, Organic Syntheses, 1969, **49**, 103.

⁴ K. Matsumoto, R. Ohta, T. Uchida, H. Nishioka, M. Yoshida, A. Kakehi, J. Heterocyclic Chem., 1997, 34, 203.

⁵ R. N. Butler, D. M. Farrell, C. S. Pyne, *J. Chem. Research* (S), 1996, 418.



(1*R*,2*R*,10b*R*)-1-Formyl-2-methyl-1,2-dihydropyrrolo[2,1-*a*]isoquinoline-3,3(10b*H*)-dicarbonitrile (*endo*-4a, major diastereoisomer). Following the general procedure, working at room temperature, starting from crotonaldehyde 2a (86 μ L, 1.04 mmol) and ylide 1a (0.10 g, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol),

using THF (2 mL) as solvent and after 10 min, the title compound **4a** (0.12 g, 0.45 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). d.r.: 88:12. Yield: 87%. ¹H NMR (δ, ppm): 1.53 (d, 3H, J = 6.4 Hz), 3.05-3.50 (m, 2H), 5.13 (d, 1H, J = 7.7 Hz), 6.04 (d, 1H, J = 7.4 Hz), 6.35 (d, 1H, J = 7.4 Hz), 6.99-7.01 (m, 1H), 7.10-7.12 (m, 1H), 7.20-7.33 (m, 2H), 9.90 (d, 1H, J = 2.2 Hz). ¹³C NMR (δ, ppm): 14.4, 45.4, 59.3, 60.4, 61.4, 111.7, 111.8, 112.7, 123.6, 125.2, 126.6, 128.2, 128.6, 128.9, 130.8, 197.1. MS (70 eV) m/z (%): 263 (4), 237 (56), 194 (100), 193 (60), 130 (81), 129 (45). HRMS: Calculated for [C₁₆H₁₃N₃O]: 263.1059; found: 263.1052. IR (Film): 1725 (C=O) cm⁻¹. [α]_D²⁰: +400.3 (c = 0.8, CH₂Cl₂).



(1R,2R,10bS)-1-Formyl-2-methyl-1,10b-dihydropyrrolo[2,1*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (*exo*-4a, minor diastereoisomer). Yield: 11%. ¹H NMR (δ , ppm): 1.56 (d, 3H, J = 7.2 Hz), 3.02-3.07 (m, 1H), 3.18-3.27 (m, 1H), 5.14 (d, 1H, J = 6.6 Hz), 5.84 (d, 1H, J = 7.7 Hz), 6.43 (d, 1H, J = 7.7 Hz), 7.03 (d, 1H, J = 7.5 Hz), 7.10 (d, 1H, J = 7.4 Hz), 7.17-7.24

(m, 1H), 7.26 (d, 1H, *J* = 7.5 Hz). 9.75 (d, 1H, *J* = 3.6 Hz).¹³C NMR (δ, ppm): 16.2, 44.8, 57.6, 59.3, 60.9, 109.1, 111.0, 112.6, 125.4, 125.9, 126.2, 127.6, 127.9, 128.9, 131.6, 198.2.



(1R,2R,10bR)-1-Formyl-2-propyl-1,10b-dihydropyrrolo[2,1*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (4b). Following the general procedure, working at room temperature, starting from (*E*)-2-hexenal 2b (120 μ L, 1.04 mmol) and ylide 1a (0.10 g, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol), using THF (2 mL) as

solvent and after 2 h, the title compound **4b** (77 mg, 0.26 mmol) was isolated by flash column chromatography (hexanes:EtOAc 9:1). d.r.: 65:35. Yield: 51%. ¹H NMR (δ , ppm): 1.03 (t, 3H, J = 7.2 Hz), 1.43-1.70 (m, 2H), 1.67-2.02 (m, 2H), 3.09-3.51 (m, 2H), 5.07 (d, 1H, J = 8.3 Hz), 6.04 (d, 1H, J = 7.4 Hz), 6.37 (d, 1H, J = 7.4 Hz), 6.90 (d, 1H, J = 6.6 Hz), 7.05 (d, 1H, J = 6.3 Hz), 7.12-7.36 (m, 2H), 9.93 (d, 1H, J = 2.7 Hz). ¹³C NMR (δ , ppm): 13.9, 20.8, 33.0, 50.1, 59.1, 59.5, 60.6,

111.6, 111.7, 113.2, 123.6, 125.1, 126.6, 128.1, 128.6, 128.9, 130.9, 197.5. MS (70 eV) m/z (%): 265 (100), 194 (43), 193 (44), 130 (66), 129 (26). HRMS: Calculated for $[C_{18}H_{18}N_{3}O (M+H)]^{+}$: 291.1450; found: 291.1443. IR (Film): 1724 (C=O) cm⁻¹. $[\alpha]_{D}^{20}$: +326.5 (c = 1.1, CH₂Cl₂).



(1*R*,2*R*,10*bR*)-1-Formyl-2-octyl-1,10b-dihydropyrrolo[2,1-*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (4c). Following the general procedure, working at room temperature, starting from (*E*)-2-undecenal 2c (206 μ L, 1.04 mmol) and ylide 1a (0.10g, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol), using toluene (2 mL) as solvent and

after 1 h, the title compound **4c** (85 mg, 0.23 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). d.r.: 63:37. Yield: 45%. ¹H NMR (δ , ppm): 0.88 (t, 3H, *J* = 6.8 Hz), 1.16-1.44 (m, 10H), 1.45-1.58 (m, 2H), 1.67-2.05 (m, 2H), 3.49-3.14 (m, 2H), 5.08 (d, 1H, *J* = 8.3 Hz), 6.04 (d, 1H, *J* = 7.4 Hz), 6.37 (d, 1H, *J* = 7.4 Hz), 6.90 (d, 1H, *J* = 6.7 Hz), 7.06 (d, 1H, *J* = 6.4 Hz), 7.12-7.33 (m, 2H), 9.94 (d, 1H, *J* = 2.7 Hz). ¹³C NMR (δ , ppm): 14.1, 22.6, 27.5, 29.1, 29.4, 30.9, 31.7, 50.4, 59.1, 59.5, 60.1, 111.6, 111.7, 113.2, 123.5, 125.1, 126.6, 128.1, 128.6, 128.9, 130.9, 197.5. MS (70 eV) *m*/*z* (%): 335 (16), 222 (16), 195 (15), 194 (100), 193 (52), 169(19), 130 (11). HRMS: Calculated for [C₂₃H₂₈N₃O (M+H)]⁺: 363.2232; found: 363.2242. IR (Film): 1650 (C=O) cm⁻¹. [α]_D²⁰: +252.2 (c = 1.0, CH₂Cl₂).



(1*R*,2*S*,10*bR*)-1-Formyl-2-phenyl-1,2-dihydropyrrolo[2,1-*a*]isoquinoline-3,3(10*bH*)-dicarbonitrile (4d). Following the general procedure, working at -30 °C, starting from (*E*)-cinnamaldehyde 2d (131 μ L, 1.04 mmol) and ylide 1a (0.10g, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol), using THF (2 mL) as solvent and after 5 days, the title

compound **4d** (0.12 g, 0.36 mmol) was isolated by flash column chromatography (hexanes:EtOAc 9:1). d.r.: 99:1. Yield: 70%. ¹H NMR (δ, ppm): 4.05-4.18 (m, 1H), 4.40 (d, 1H, *J* = 10.8 Hz), 5.24 (d, 1H, *J* = 8.5 Hz), 6.08 (d, 1H, *J* = 7.4 Hz), 6.39 (d, 1H, *J* = 7.4 Hz), 7.00 (d, 1H, *J* = 6.8 Hz), 7.12 (d, 1H, *J* = 7.1 Hz), 7.20-7.33 (m, 2H), 7.39-7.60 (m, 5H), 9.90 (d, 1H, *J* = 1.6 Hz). ¹³C NMR (δ, ppm): 55.4, 59.1, 59.2, 61.4, 111.7, 111.9, 112.7, 123.9, 125.4, 126.8, 128.3, 128.7, 128.8, 129.1, 129.7, 130.4, 131.1, 131.2, 196.8. MS (70 eV) *m*/*z* (%): 326 (2), 133 (100), 132 (31), 131 (33), 130 (52), 129 (33). HRMS: Calculated for $[C_{21}H_{16}N_3O (M+H)]^+$: 326.1293; found: 326.1299. IR (KBr): 1725 (C=O) cm⁻¹. $[\alpha]_D^{20}$: +402.2 (c = 1.0, CH₂Cl₂). M.p.: 115-120 °C (recrystalized in CH₂Cl₂).

(1*R*,2*S*,10*bR*)-1-Formyl-2-(4-methoxyphenyl)-1,10b-

dihydropyrrolo[2,1-*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (4e). Following the general procedure, working at 4 °C, starting from (*E*)-4methoxycinnamaldehyde **2e** (0.180 g, 1.04 mmol) and ylide **1a** (0.10g, 0.52 mmol) in the presence of catalyst **3c** (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol), using THF (2 mL) as solvent and after 7 days, the

title compound **4e** (0.12 g, 0.32 mmol) was isolated by flash column chromatography (hexanes:EtOAc 7:3). d.r.: 99:1. Yield: 63%. ¹H NMR (δ , ppm): 3.83 (s, 3H), 4.07 (ddd, 1H, *J* = 10.9, 8.5, 2.1 Hz), 4.35 (d, 1H, *J* = 11.1 Hz), 5.24 (d, 1H, *J* = 8.4 Hz), 6.06 (d, 1H, *J* = 7.4 Hz), 6.37 (d, 1H, *J* = 7.4 Hz), 6.97-6.99 (m, 3H), 7.09-7.10 (m, 1H), 7.24-7.29 (m, 2H), 7.46 (d, 2H, *J* = 7.8 Hz), 9.87 (d, 1H, *J* = 2.1 Hz). ¹³C NMR (δ , ppm): 55.0, 55.4, 58.9, 59.3, 61.6, 111.7, 111.8, 112.7, 115.0, 122.5, 123.8, 125.3, 126.7, 128.2, 128.7, 129.0, 130.0, 131.0, 161.0, 196.9. HRMS: the compound is too unstable to undergo the conditions of the mass spectrometer. IR (Film): 1725 (C=O) cm⁻¹. [α]_D²⁰: +481.2 (c = 1.1, CH₂Cl₂).



(1R,2S,10bR)-1-Formyl-2-(4-nitrophenyl)-1,2-dihydropyrrolo[2,1*a*]isoquinoline-3,3(10bH)-dicarbonitrile (4f). Following the general procedure, working at 4 °C, starting from (*E*)-4-nitrocinnamaldehyde 2f (0.160 g, 1.04 mmol) and ylide 1a (0.10g, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 µL, 0.10 mmol), using THF (2 mL) as solvent and after 7 days, the title compound 4f (0.14 g, 0.37

mmol) was isolated by flash column chromatography (hexanes:EtOAc 7:3). d.r.: 99:1. Yield: 73%. ¹H NMR (δ, ppm): 4.06-4.13 (m, 1H), 4.57 (d, 1H, J = 9.7 Hz), 5.16 (d, 1H, J = 8.5 Hz), 6.13 (d, 1H, J = 7.4 Hz), 6.40 (d, 1H, J = 7.4 Hz), 7.06 (d, 1H, J = 6.0 Hz), 7.14 (d, 1H, J = 6.2 Hz), 7.30-7.32 (m, 2H), 7.70 (d, 2H, J = 8.7 Hz), 8.28 (d, 2H, J = 8.5 Hz), 9.95 (s, 1H). ¹³C NMR (δ, ppm): 54.1, 59.3, 59.4, 60.5, 111.2, 112.1, 112.5, 123.6, 124.6, 125.6, 126.6, 128.5, 128.7, 129.1, 129.9, 130.9, 139.2, 148.8, 195.8. HRMS: the compound is too unstable to undergo the conditions of the mass spectrometer. IR (Film): 1726 (C=O) cm⁻¹. [α]_D²⁰: +245.5 (c = 1.0, CH₂Cl₂).



(1R,2R,10bR)-1-Formyl-2-methyl-1,10b-dihydropyrrolo[2,1-

a]phthalazine-3,3(2*H*)-dicarbonitrile (4g). Following the general procedure, working at room temperature, starting from crotonaldehyde 2a (86 µL, 1.04

4g mmol) and ylide **1b** (99 mg, 0.52 mmol) in the presence of catalyst **3c** (25 mg, 0.10 mmol) and TFA (7.9 μL, 0.10 mmol), using toluene (2 mL) as solvent and after 10 min, the title compound **4g** (97 mg, 0.37 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). d.r.: 86:14. Yield: 71%. ¹H NMR (δ, ppm): 1.58 (d, 3H, J = 7.1 Hz), 3.11 (ddd, 1H, J = 9.2, 7.0, 2.0 Hz), 3.23-3.46 (m, 1H), 4.55 (d, 1H, J = 9.5 Hz), 7.10 (d, 1H, J = 7.2 Hz), 7.30-7.61 (m, 3H), 7.79 (s, 1H), 9.95 (d, 1H, J = 2.0 Hz). ¹³C NMR (δ, ppm): 19.1, 42.6, 56.6, 58.6, 60.6, 111.6, 113.0, 123.6, 125.0, 126.4, 129.2, 132.4, 132.5, 146.5, 196.6. MS (70 eV) *m*/*z* (%): 265 (12), 239 (15), 238 (100), 195 (43), 194 (24). HRMS: Calculated for [C₁₅H₁₃N₄O (M+H)]⁺: 265.1089; found: 265.1094. IR (Film): 1725 (C=O) cm⁻¹. [α]_D²⁰: -57.1 (c = 0.8, CH₂Cl₂).



(1R,2R,10bR)-1-Formyl-2-propyl-1,10b-dihydropyrrolo[2,1-

a]**phthalazine-3,3**(*2H*)-**dicarbonitrile** (**4h**). Following the general procedure, working at room temperature, starting from (*E*)-2-hexenal **2b** (120 μ L, 1.04 mmol) and ylide **1b** (99 mg, 0.52 mmol) in the presence of catalyst **3c** (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol), using toluene (2 mL) as solvent

and after 16 h, the title compound **4h** (0.11 g, 0.37 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). d.r.: 83:17. Yield: 72%. ¹H NMR (δ , ppm): 1.02 (t, 3H, *J* = 7.3 Hz), 1.41-1.64 (m, 3H), 1.64-1.84 (m, 1H), 1.19-1.22 (m, 1H), 3.10-3.33 (m, 1H), 4.55 (d, 1H, *J* = 8.8 Hz), 7.12 (d, 1H, *J* = 7.2 Hz), 7.27-7.59 (m, 3H), 7.80 (d, 1H, *J* = 9.2 Hz), 9.93 (d, 1H, *J* = 2.1 Hz). ¹³C NMR (δ , ppm): 13.6, 20.1, 35.3, 47.5, 56.7, 56.9, 60.2, 111.6, 113.2, 123.6, 125.1, 126.4, 129.2, 132.3, 132.5, 146.4, 197.0. MS (70 eV) *m*/*z* (%): 293 (11), 267 (12), 266 (100), 195 (22), 194 (41), 131 (14). HRMS: Calculated for [C₁₇H₁₇N₄O (M+H)]⁺: 293.1402; found: 293.1491. IR (Film): 1725 (C=O) cm⁻¹. [α]_D²⁰: +277.0 (c = 0.9, CH₂Cl₂).



(1R,2R,10bR)-1-Formyl-2-octyl-1,10b-dihydropyrrolo[2,1-*a*]phthalazine-3,3(2*H*)-dicarbonitrile (4i). Following the general procedure, working at room temperature, starting from (*E*)-2-undecenal 2d (206 µL, 1.04 mmol) and ylide 1b (99 mg, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 μL, 0.10 mmol), using toluene (2 mL) as solvent and after 1 h, the title compound **4i** (0.12 g, 0.33 mmol) was isolated by flash column chromatography (hexanes:EtOAc 9:1). d.r.: 77:23. Yield: 64%. ¹H NMR (δ, ppm): 0.88 (t, 3H, J = 6.7 Hz), 1.11-1.55 (m, 12H), 1.66-1.83 (m, 1H), 1.98-2.14 (m, 1H), 3.11-3.24 (m, 2H), 4.54 (d, 1H, J = 8.7 Hz), 7.12 (d, 1H, J = 7.5 Hz), 7.29-7.58 (m, 3H), 7.78 (s, 1H), 9.93 (d, 1H, J = 1.8 Hz). ¹³C NMR (δ, ppm): 14.1, 22.6, 26.8, 29.1, 29.1, 29.2, 31.7, 33.3, 47.7, 56.7, 57.0, 60.2, 111.6, 113.2, 123.6, 125.1, 126.4, 129.2, 132.5, 132.6, 146.4, 197.1. MS (70 eV) m/z (%): 336 (63), 194 (37), 131 (100), 130 (49), 117 (43), 95 (59), 83 (28). HRMS: Calculated for [C₂₂H₂₇N₄O (M+H)]⁺: 363.2185; found: 363.2191. IR (Film): 1727 (C=O) cm⁻¹. [α]_D²⁰: -11.7 (c = 1.0, CH₂Cl₂).



(1R,2S,10bR)-1-Formyl-2-phenyl-1,10b-dihydropyrrolo[2,1*a*]phthalazine-3,3(2*H*)-dicarbonitrile (4j). Following the general procedure, working at room temperature, starting from (*E*)-cinnamanldehyde 2d (131 μ L, 1.04 mmol) and ylide 1b (0.100 g, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 μ L, 0.10 mmol), using toluene (2 mL)

as solvent and after 1 day, the title compound **4j** (0.13 g, 0.31 mmol) was isolated by flash column chromatography (hexanes:EtOAc 9:1). d.r.: 63:37. Yield: 61%. ¹H NMR (δ, ppm): 3.70-3.91 (m, 1H), 4.41 (d, 1H, J = 6.7 Hz), 4.63 (d, 1H, J = 9.3 Hz), 7.19 (d, 1H, J = 7.4 Hz), 7.32 (d, 1H, J = 2.8 Hz), 7.36-7.62 (m, 7H), 7.86 (s, 1H), 9.96 (s, 1H). ¹³C NMR (δ, ppm): 53.3, 56.8, 58.7, 61.9, 111.3, 112.8, 123.7, 125.3, 126.6, 128.6, 129.4, 129.5, 129.9, 132.5, 132.6, 135.9, 147.1, 196.1. MS (70 eV) m/z (%): 327 (15), 301 (22), 300 (100), 196 (14), 195 (65), 194 (38), 133 (39), 131 (22). HRMS: Calculated for [C₂₀H₁₅N₄O (M+H)]⁺: 327.1246; found: 327.1244. IR (Film): 1727 (C=O) cm⁻¹. [α]_D²⁰: + 402.2 (c = 1.0, CH₂Cl₂).



(1R,2S,10bS)-1-Formyl-2-(4-methoxyphenyl)-1,10b-dihydropyrrolo[2,1*a*]phthalazine-3,3(2*H*)-dicarbonitrile (4k). Following the general procedure, working at room temperature, starting from (*E*)-4methoxycinnamaldehyde 2e (0.180 g, 1.04 mmol) and ylide 1b (99 mg, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9

 μ L, 0.10 mmol), using toluene (2 mL) as solvent and after 1 day, the title compound **4k** (0.12 g, 0.32 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). d.r.: 71:29. Yield: 63 %. No spectroscopic data available due to the instability of the compound. See compound **5k**.



(1R,2S,10bR)-1-Formyl-2-(4-nitrophenyl)-1,10b-dihydropyrrolo[2,1*a*]phthalazine-3,3(2*H*)-dicarbonitrile (4l). Following the general procedure, working at room temperature, starting from (*E*)-*p*nitrocinnamaldehyde 2f (0.160 g, 1.04 mmol) and ylide 1b (99 mg, 0.52 mmol) in the presence of catalyst 3c (25 mg, 0.10 mmol) and TFA (7.9 µL,

0.10 mmol), using toluene (2 mL) as solvent and after 16 h, the title compound **4l** (0.11 g, 0.31 mmol) was isolated by flash column chromatography (hexanes:EtOAc 7:3). d.r.: 67:40. Yield: 60%. ¹H NMR (δ , ppm): 3.76 (dd, 1H, *J* = 9.2, 5.9 Hz), 3.69-3.81 (m, 2H), 7.23 (d, 1H, *J* = 7.2 Hz), 7.32-7.66 (m, 5H), 7.90 (s, 1H), 8.21 (d, 2H, *J* = 8.6 Hz), 9.99 (s, 1H). ¹³C NMR (δ , ppm): 51.8, 56.9, 58.6, 61.3, 111.0, 112.1, 123.5, 124.6, 125.2, 126.9, 129.7, 129.9, 132.4, 132.8, 143.3, 147.9, 148.5, 195.1. HRMS: the compound is too unstable to undergo the conditions of the mass spectrometer. IR (Film): 1651 (C=O) cm⁻¹. [α]_D²⁰: +24.4 (c = 1.0, CH₂Cl₂).

General Procedure fot the Reduction of Aldehydes (4a-l) into the Corresponding Alcohols (5al). The aldehyde 4a-l (0.38 mmol) was dissolved in dry THF (15 mL) at -78 °C and LiBH₄ (0.38 mmol) was added. After stirring the mixture during the necessary time the reaction was quenched with aqueous NH₄Cl (sat., 5 ml) and CH₂Cl₂ was added. The reaction was stirred for 30 min and then the aqueous layer was extracted with CH₂Cl₂ (3×25 mL) and the solvent was evaporated under vacuum. The crude was charged onto silica gel and subjected to flash column chromatography to obtain the alcohols **5a-l**. Racemic samples were prepared reducing the racemic mixtures of the aldehydes **4a-l**.



(1*R*,2*R*,10*bR*)-1-Hydroxymethyl-2-methyl-1,10b-dihydropyrrolo[2,1*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (*endo*-5a, major diastereoisomer). Following the general procedure, aldehyde 4a (99 mg, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After

stirring the mixture for 15 min the title compound **5a** (72 mg, 0.27 mmol) was isolated by flash column chromatography (hexanes:EtOAc 7:3). Yield: 72%. ¹H NMR (δ , ppm): 1.47 (d, 3H, *J* = 6.9 Hz), 1.80 (bs, 1H), 2.52-2.70 (m, 1H), 2.97-3.12 (m, 1H), 3.96-4.15 (m, 2H), 4.68 (d, 1H, *J* = 8.0 Hz), 6.05 (d, 1H, *J* = 7.3 Hz), 6.37 (d, 1H, *J* = 7.3 Hz), 7.00-7.09 (m, 1H), 7.08-7.16 (m, 1H), 7.18-7.26 (m, 2H). ¹³C NMR (δ , ppm): 15.0, 46.3, 51.3, 59.8, 60.2, 62.0, 112.0, 112.4, 113.4, 123.1, 124.8, 127.4, 127.8, 128.0, 130.0, 131.3. MS (70 eV) *m*/*z* (%): 239 (100), 238 (26), 207 (12), 193

(28), 182 (14). HRMS: Calculated for $[C_{16}H_{16}N_3O (M+H)]^+$: 266.1293; found: 266.1304. IR (Film): 3425 (OH) cm⁻¹. $[\alpha]_D^{20}$: +425.8 (c = 0.9, CH₂Cl₂). e.e.: 88% (calculated by HPLC: Chiralcel OD column, 1 mL·min⁻¹, *n*-hexane: i PrOH 90:10. t_{major} = 13.22 min, t_{minor} = 26.07 min).



(1R,2R,10bS)-1-Hydroxymethyl-2-methyl-1,10b-dihydropyrrolo[2,1*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (*exo*-5a, minor diastereoisomer). Yield: 30%. ¹H NMR (δ , ppm): 1.51 (d, 3H, J = 7.3 Hz), 1.59 (s, 1H), 2.43-2.57 (m, 1H), 3.06-3.28 (m, 1H), 3.60-3.79 (m, 1H), 3.81-3.98 (m, 1H), 5.14 (d, 1H, J = 5.7 Hz), 5.64 (d, 1H, J = 7.6 Hz), 6.37 (d, 1H, J = 7.6 Hz), 6.99 (d, 2H, J = 7.3 Hz), 7.05-7.24 (m, 2H). ¹³C NMR (δ, ppm): 17.4, 45.9, 49.7, 59.3, 60.4, 61.3, 106.2, 112.0, 113.8, 125.5,

125.6, 126.8, 127.5, 128.2, 128.4, 131.7.



(1R,2R,10bR)-1-Hydroxymethyl-2-propyl-1,10b-dihydropyrrolo[2,1a]isoquinoline-3,3(2H)-dicarbonitrile (**5b**). Following the general procedure, aldehyde 4b (0.110 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for

15 min the title compound **5b** (63 mg, 0.21 mmol) was isolated by flash column chromatography (hexanes:EtOAc 7:3). Yield: 57%. ¹H NMR (δ , ppm): 1.03 (t, 3H, J = 7.2 Hz), 1.45-1.71 (m, 2H), 1.72-1.95 (m, 3H), 2.55-2.80 (m, 1H), 2.98 (dd, 1H, J = 15.6, 7.7 Hz), 3.87-4.21 (m, 2H), 4.64 (d, 1H, J = 7.8 Hz), 6.06 (d, 1H, J = 7.3 Hz), 6.41 (d, 1H, J = 7.3 Hz), 7.02-7.09 (m, 1H), 7.09-7.17 (m, 1H), 7.18-7.25 (m, 2H). ¹³C NMR (δ, ppm): 14.1, 20.7, 33.5, 50.1, 50.6, 59.0, 60.1, 62.3, 112.0, 112.4, 113.8, 123.2, 124.8, 127.5, 127.8, 128.0, 130.2, 131.5. MS (70 eV) m/z (%): 294 (54), 293 (39), 267 (100), 249 (68), 130 (72), 129 (38). HRMS: Calculated for $[C_{18}H_{20}N_3O (M+H)]^+$: 294.1606; found: 294.1608. IR (Film): 3548 (OH) cm⁻¹. $[\alpha]_D^{20}$: +260.1 (c = 1.1, CH₂Cl₂). e.e.: 84% (calculated by HPLC: Chiralpak AS-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH in gradient (lineal curve: min 0, 100:0; min 20, 95:5; min 30, 90:10). t_{major} = 43.07 min, t_{minor} = 29.46 min).



(1R,2R,10bR)-1-Hydroxymethyl-2-octyl-1,10b-dihydropyrrolo[2,1-

a]isoquinoline-3,3(2*H*)-dicarbonitrile (5c). Following the general procedure, aldehyde 4c (0.137 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 45 min the

title compound 5c (47 mg, 0.13 mmol) was isolated by flash column chromatography

(hexanes:EtOAc 8:2). Yield: 34%. ¹H NMR (δ, ppm): 0.89 (t, 3H, J = 6.3 Hz), 1.18-1.46 (m, 10H), 1.48-1.71 (m, 2H), 1.69-1.95 (m, 3H), 2.56-2.74 (m, 1H), 2.96 (dd, 1H, J = 15.4, 7.8 Hz), 3.88-4.15 (m, 2H), 4.64 (d, 1H, J = 7.7 Hz), 6.06 (d, 1H, J = 7.3 Hz), 6.41 (d, 1H, J = 7.3 Hz), 7.01-7.09 (m, 1H), 7.10-7.17 (m, 1H), 7.17-7.25 (m, 2H). ¹³C NMR (δ, ppm): 14.1, 22.6, 27.4, 29.1, 29.2, 29.6, 31.4, 31.8, 50.1, 50.8, 59.1, 60.1, 62.4, 112.0, 112.3, 113.8, 123.1, 124.7, 127.5, 127.7, 127.9, 130.2, 131.5. MS (70 eV) m/z (%): 364 (36), 363 (30), 338 (26), 337 (100), 336 (50), 305 (35), 280 (28), 193 (40). HRMS: Calculated for [C₂₃H₃₀N₃O (M+H)]⁺: 364.2389; found: 364.2384. IR (Film): 3441 (OH) cm⁻¹. [α]_D²⁰: +115.2 (c = 0.9, CH₂Cl₂). e.e.: 84% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 95:5. t_{major} = 12.12 min, t_{minor} = 13.89 min).



(1R,2S,10bR)-1-Hydroxymethyl-2-phenyl-1,10b-dihydropyrrolo[2,1*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (5d). Following the general procedure, aldehyde 4d (0.123 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title compound 5d (99 mg, 0.30 mmol) was isolated by flash column

chromatography (hexanes:EtOAc 8:2). Yield: 80%. ¹H NMR (δ , ppm): 1.94 (bs, 1H), 3.25-3.45 (m, 1H), 3.80-3.95 (m, 1H), 4.00-4.12 (m, 1H), 4.15 (d, 1H, *J* = 9.9 Hz), 4.85 (d, 1H, *J* = 7.9 Hz), 6.08 (d, 1H, *J* = 7.3 Hz), 6.41 (d, 1H, *J* = 7.3 Hz), 7.05-7.16 (m, 1H), 7.20-7.35 (m, 3H), 7.38-7.55 (m, 5H). ¹³C NMR (δ , ppm): 49.7, 56.4, 59.5, 61.0, 61.4, 112.0, 112.3, 113.3, 123.3, 125.0, 127.5, 127.9, 128.2, 128.9, 129.3, 129.7, 130.2, 131.6, 133.2. MS (70 eV) *m*/*z* (%): 301 (51), 269 (100), 268 (83), 244 (52), 243 (75), 130 (40). HRMS: Calculated for [C₂₁H₁₈N₃O (M+H)]⁺: 328.1450; found: 328.1472. IR (Film): 3417 (OH) cm⁻¹. [α]_D²⁰: +60.4 (c = 1.0, CH₂Cl₂). e.e.: 94% (calculated by HPLC: Chiralcel OD column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 85:15. t_{major} = 20.56 min, t_{minor} = 12.41 min).



(1R,2S,10bR)-1-Hydroxymethyl-2-(4-methoxyphenyl)-1,10bdihydropyrrolo[2,1-*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (5e). Following the general procedure, aldehyde 4e (0.135 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title compound 5e (68 mg, 0.19 mmol) was

isolated by flash column chromatography (hexanes:EtOAc 6:4). Yield: 50%. ¹H NMR (δ, ppm): 1.87 (bs, 1H), 3.21-3.43 (m, 1H), 3.82 (s, 3H), 3.83-3.94 (m, 1H), 4.01-4.19 (m, 2H), 4.86 (d, 1H, J

= 8.0 Hz), 6.07 (d, 1H, *J* = 7.3 Hz), 6.40 (d, 1H, *J* = 7.3 Hz), 6.95 (d, 2H, *J* = 8.7 Hz), 7.02-7.15 (m, 1H), 7.20-7.30 (m, 3H), 7.41 (d, 2H, *J* = 8.7 Hz). ¹³C NMR (δ, ppm): 49.8, 55.4, 55.9, 59.4, 61.1, 61.5, 111.8, 112.4, 113.3, 114.7, 123.3, 124.7, 124.9, 127.5, 127.8, 128.1, 130.1, 131.6, 160.5. MS (70 eV) *m*/*z* (%): 331 (40), 299 (100), 298 (70), 274 (60), 273 (73). HRMS: Calculated for $[C_{22}H_{20}N_{3}O_{2} (M+H)]^{+}$: 358.1556; found: 358.1567. IR (Film): 3536 (OH) cm⁻¹. $[\alpha]_{D}^{20}$: -116.8 (c = 0.9, CH₂Cl₂). e.e.: 88% (calculated by HPLC: Chiralcel OD column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 80:20. t_{major} = 23.77 min, t_{minor} = 11.59 min).

(1R,2S,10bR)-1-Hydroxymethyl-2-(4-nitrophenyl)-1,10b-



dihydropyrrolo[2,1-*a*]isoquinoline-3,3(2*H*)-dicarbonitrile (5f). Following the general procedure, aldehyde 4f (0.141 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title compound 5f (65 mg, 0.17 mmol) was

isolated by flash column chromatography (hexanes:EtOAc 6:4). Yield: 46%. ¹H NMR (δ , ppm): 2.16 (bs, 1H), 3.21-3.41 (m,1H), 3.87-4.00 (dd, 1H, J = 11.0, 4.2 Hz), 4.02-4.15 (dd, 1H, J = 11.0, 4.7 Hz), 4.29 (d, 1H, J = 8.7 Hz), 4.80 (d, 1H, J = 8.0 Hz), 6.12 (d, 1H, J = 7.4 Hz), 6.42 (d, 1H, J = 7.4 Hz), 7.05-7.33 (m, 4H), 7.65 (d, 2H, J = 8.7 Hz), 8.25 (d, 2H, J = 8.7 Hz). ¹³C NMR (δ , ppm): 50.4, 56.0, 59.7, 60.2, 61.6, 111.8, 112.5, 112.7, 123.1, 124.4, 125.2, 127.4, 128.1, 128.5, 129.9, 130.0, 131.4, 141.5, 148.5. HRMS: the compound is too unstable to undergo the conditions of the mass spectrometer. IR (Film): 3552 (OH) cm⁻¹. [α]_D²⁰: +58.9 (c = 1.0, CH₂Cl₂). e.e.: 84% (calculated by HPLC: Chiralcel OD column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 80:20. t_{major} = 21.38 min, t_{minor} = 15.04 min).



(1*R*,2*R*,10*bR*)-1-Hydroxymethyl-2-methyl-1,10b-dihydropyrrolo[2,1*a*]phthalazine-3,3(2*H*)-dicarbonitrile (5g). Following the general procedure, aldehyde 4g (0.100 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the

title compound **5g** (69 mg, 0.25 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). Yield: 68%. ¹H NMR (δ , ppm): 1.49 (d, *J* = 7.2 Hz, 3H), 1.95 (bs, 1H), 2.40-2.53 (m, 1H), 2.77-2.95 (m, 1H), 3.99 (ad, *J* = 5.8 Hz, 2H), 4.15 (d, *J* = 8.8 Hz, 1H), 7.27-7.54 (m, 4H), 7.77 (s, 1H). ¹³C NMR (δ , ppm): 19.8, 44.2, 48.8, 58.4, 60.7, 63.0, 112.3, 113.6, 123.4, 125.4, 126.0, 128.5, 132.0, 134.3, 146.6. MS (70 eV) *m/z* (%): 267 (13), 241 (17), 240 (100), 222 (14), 208

(13), 194 (13), 183 (12). HRMS: Calculated for $[C_{15}H_{15}N_4O (M+H)]^+$: 267.1246; found: 267.1259. IR (Film): 3521 (OH) cm⁻¹. $[\alpha]_D^{20}$: -29.6 (c = 1.1, CH₂Cl₂). e.e.: 76% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 95: 5. t_{major} = 43.89 min, t_{minor} = 45.44 min).



(1*R*,2*R*,10*bR*)-1-Hydroxymethyl-2-propyl-1,10b-dihydropyrrolo[2,1*a*]phthalazine-3,3(2*H*)-dicarbonitrile (5h). Following the general procedure, aldehyde 4h (0.111 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 40 min the

title compound **5h** (67 mg, 0.23 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). Yield: 60%. ¹H NMR (δ , ppm): 0.99 (t, 3H, J = 7.2 Hz), 1.38-1.76 (m, 2H), 1.80-2.03 (m, 1H), 2.13 (s, 1H), 1.78-2.13 (m, 1H), 2.48-2.61 (m, 1H), 2.62-2.81 (m, 1H), 3.76-4.03 (m, 2H), 4.14 (d, 1H, J = 8.5 Hz), 7.26-7.54 (m, 4H), 7.74 (s, 1H). ¹³C NMR (δ , ppm): 13.8, 19.9, 35.7, 46.4, 48.5, 58.6, 60.5, 63.2, 112.4, 113.7, 123.6, 125.4, 125.9, 128.5, 132.0, 134.5, 146.6. MS (70 eV) m/z (%): 295 (8), 269 (8), 268 (100), 267 (7), 211 (7), 194 (42). HRMS: Calculated for [C₁₇H₁₉N₄O (M+H)]⁺: 295.1559; found: 295.1555. IR (Film): 3537 (OH) cm⁻¹. [α]_D²⁰: +11.2 (c = 1.1, CH₂Cl₂). e.e.: 70% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH in gradient (lineal curve: min 0, 100:0; min 30, 95:5; min 60, 90:10). t_{major} = 44.38 min, t_{minor} = 50.61 min).



(1*R*,2*R*,10*bR*)-1-Hydroxymethyl-2-octyl-1,10b-dihydropyrrolo[2,1*a*]phthalazine-3,3(2*H*)-dicarbonitrile (5i). Following the general procedure, aldehyde 4i (99 mg, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title

compound **5i** (78 mg, 0.22 mmol) was isolated by flash column chromatography (hexanes:EtOAc 8:2). Yield: 57%. ¹H NMR (δ , ppm): 0.88 (t, J = 6.5 Hz, 3H), 1.15-1.40 (m, 11H), 1.53-1.77 (m, 2H), 1.83-2.20 (m, 2H), 2.50-2.62 (m, 1H), 2.62-2.74 (m, 1H), 3.79-4.05 (m, 2H), 4.15 (d, 1H, J = 8.3 Hz), 7.27-7.55 (m, 4H), 7.76 (s, 1H). ¹³C NMR (δ , ppm): 14.1, 22.6, 26.7, 29.2, 29.3, 29.4, 31.7, 33.7, 46.4, 48.8, 58.7, 60.6, 63.4, 112.3, 113.6, 123.6, 125.5, 125.9, 128.5, 131.9, 134.6, 146.5. MS (70 eV) m/z (%): 365 (9), 339 (18), 338 (100), 337 (13), 336 (9), 194 (48). HRMS: Calculated for [C₂₂H₂₉N₄O (M+H)]⁺: 365.2341; found: 365.2341. IR (Film): 3546 (OH) cm⁻¹. [α]_D²⁰: +6.8 (c = 0.7, CH₂Cl₂). e.e.: 95% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 90:10. t_{major} = 8.86 min, t_{minor} = 9.83 min).



(IR,2S,10bR)-1-Hydroxymethyl-2-phenyl-1,10b-dihydropyrrolo[2,1a]phthalazine-3,3(2H)-dicarbonitrile (5j). Following the general procedure, aldehyde 4j (0.124 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title compound 5j (87 mg, 0.27 mmol) was isolated by flash column

chromatography (hexanes:EtOAc 8:2). Yield: 70%. ¹H NMR (δ , ppm): 2.23 (s, 1H), 3.00-3.15 (m, 1H), 3.94 (d, 1H, J = 5.6 Hz), 3.96-4.08 (m, 2H), 4.32 (d, 1H, J = 8.7 Hz), 7.29-7.58 (m, 9H), 7.80 (s, 1H). ¹³C NMR (δ , ppm): 49.7, 55.5, 58.4, 61.9, 62.5, 112.0, 113.4, 123.6, 125.6, 126.1, 128.7, 128.8, 129.2, 129.2, 132.2, 134.1, 137.9, 147.1. MS (70 eV) m/z (%):303 (22), 302 (100), 301 (29), 284 (34), 271 (28), 270 (47), 269 (16), 245 (36), 244 (29), 194 (22). HRMS: Calculated for $[C_{20}H_{17}N_4O (M+H)]^+$: 329.1402; found: 329.1391. IR (Film): 3433 (OH) cm⁻¹. $[\alpha]_D^{20}$: +147.5 (c = 0.9, CH₂Cl₂). e.e.: 97% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 90:10. t_{major} = 41.42 min, t_{minor} = 48.05 min).



(1R,2S,10bR)-1-Hydroxymethyl-2-(4-methoxyphenyl)-1,10bdihydropyrrolo[2,1-*a*]phthalazine-3,3(2*H*)-dicarbonitrile (5k). Following the general procedure, aldehyde 4k (0.138 g, 0.38 mmol) was dissolved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title compound 5k (98 mg, 0.27 mmol) was

isolated by flash column chromatography (hexanes:EtOAc 6:4). Yield: 72%. ¹H NMR (δ , ppm): 1.60 (bs, 1H), 2.97-3.23 (m, 1H), 3.68-3.90 (m, 2H), 3.82 (s, 3H), 4.05 (d, 1H, *J* = 5.9 Hz), 5.00 (d, 1H, *J* = 7.6 Hz), 6.96 (d, 2H, *J* = 8.5 Hz), 7.28-7.54 (m, 6H), 7.61 (s, 1H). ¹³C NMR (δ , ppm): 46.3, 55.4, 55.8, 58.8, 61.5, 64.6, 111.5, 113.3, 114.7, 125.0, 125.7, 125.9, 127.1, 129.1, 130.1, 131.1, 131.8, 144.7, 160.3. HRMS: the compound is too unstable to undergo the conditions of the mass spectrometer. IR (Film): 3425 (OH) cm⁻¹. [α]_D²⁰: -12.3 (c = 0.9, CH₂Cl₂). e.e.: 60% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH in gradient (lineal curve: min 0, 100:0; min 15, 80:20). t_{major} = 49.79 min, t_{minor} = 44.99 min).



(1*R*,2*S*,10*bR*)-1-Hydroxymethyl-2-(4-nitrophenyl)-1,10bdihydropyrrolo[2,1-*a*]phthalazine-3,3(2*H*)-dicarbonitrile (51).

Following the general procedure, aldehyde **41** (0.140 g, 0.38 mmol) was solved in dry THF (15 mL) and LiBH₄ (6 mg, 0.38 mmol) was added. After stirring the mixture for 30 min the title compound **51** (99 mg, 0.27 mmol)

was isolated by flash column chromatography (hexanes:EtOAc 6:4). Yield: 70%. ¹H NMR (δ, ppm): 2.27 (bs, 1H). 2.95-3.11 (m, 1H), 3.97-4.07 (m, 2H), 4.11 (d, J = 4.8 Hz, 1H), 4.33 (d, J = 8.6 Hz, 1H), 7.26-7.52 (m, 4H), 7.56 (d, J = 8.6 Hz, 2H), 7.86 (s, 1H), 8.19 (d, 2H, J = 8.6 Hz). ¹³C NMR (δ, ppm): 50.1, 54.8, 58.1, 61.3, 62.5, 111.7, 112.8, 123.2, 124.3, 125.5, 126.4, 129.0, 129.9, 132.5, 133.7, 145.3, 147.7, 148.1. HRMS: the compound is too unstable to undergo the conditions of the mass spectrometer. IR (Film): 3540 (OH) cm⁻¹. [α]_D²⁰: +23.4 (c = 1.0, CH₂Cl₂). e.e.: >99% (calculated by HPLC: Chiralpak AD-H column, 1 mL·min⁻¹, *n*-hexane:^{*i*}PrOH 80:20. t_{major} = 29.60 min, t_{minor} = 25.05 min).

Determination of the Absolute Configuration.

The absolute configuration of the aldehyde **4d** was determined by single-crystal X-ray analysis. The same stereochemistry was assumed for assigning the absolute configuration of the rest of the compounds.



Figure S1: X-ray determined crystal structure of (1R,2S,10bR)-1-Formyl-2-phenyl-1,2-dihydropyrrolo[2,1-*a*]isoquinoline-3,3(10b*H*)-dicarbonitrile (**4d**).

NMR spectra.









































HPLC Chromatograms.

