

Experimental section

I. Chemistry

General methods and materials

THF was freshly distilled from LiAlH_4 before use. DMF was stored over 4Å molecular sieves. All the other solvents were used as received. Starting materials were commercially available. Reactions were performed under anhydrous conditions unless noted otherwise. Reactions were followed by TLC analysis on Merck TLC aluminum sheets Silicagel 60 F254. Flash column chromatography was performed on silicagel, 30-60 μm (J.T. Baker). Melting points were measured on an Electrothermal IA9200 apparatus or a Mettler FP-5 + FP-052 apparatus equipped with a microscope and are uncorrected. ^1H NMR spectra were recorded on a Bruker AC 200 (^1H NMR: δ 200.1 MHz). The ^1H NMR chemical shifts (δ) are expressed in ppm values relative to CDCl_3 (δ = 7.26 ppm). Abbreviations used in description of NMR spectra: s = singlet, d = doublet, t = triplet, q = quartet, dd = double doublet, dt = double triplet, m = multiplet and bs = broad singlet. All phthalazinones had an elemental analysis (C, H and N) within $\pm 0.4\%$ of the theoretical value.

General procedure for the N-alkylation of phthalazinones

Sodium hydride (60% dispersion in mineral oil, 1.1 equivalent) was added to a suspension of phthalazinone **2a** (5.0 to 25 mmol) in DMF (25 to 250 mL). After stirring the reaction mixture for 2 h, the selected alkyl halide (1.1 equivalent) was added and the resulting mixture was stirred for another 4 h. The reaction mixture was poured into water and the product was extracted with ethyl acetate. The combined organic layers were washed with water and brine and dried over MgSO_4 . Removal of the solvent under reduced pressure and crystallization or flash column chromatography followed by crystallization yielded the pure products. Experimental data for the separate compounds are listed below.

cis-4-(3,4-Dimethoxyphenyl)-2-methyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3a) -

Synthesized following the general procedure using iodomethane as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from petroleum ether (60-80). Yield 26%. Mp 110-112 °C. ^1H NMR (CDCl_3): δ 1.20-1.95 (m, 7H, H5, H6, H7, H8), 2.44-2.78 (m, 2H, H8a, H8'), 2.99-3.19 (m, 1H, H4a), 3.49 (s, 3H, NCH_3), 3.94 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.87 (d, 1H, 3J = 8.4 Hz, H5-arom), 7.22 (dd, 1H, 4J = 2.0 Hz, 3J = 8.4 Hz, H6-arom), 7.49 (d, 1H, 4J = 2.0 Hz, H2-arom). Anal. Calcd ($\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_3$) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-ethyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3b) -

Synthesized following the general procedure using bromoethane as the alkylating agent. Crystallized from methanol. Yield 32%. Mp 105-106 °C. ^1H NMR (CDCl_3): δ 1.22-1.96 (m, 10H, H5, H6, H7, H8, CH_2CH_3), 2.46-2.77 (m, 2H, H8a, H8'), 2.99-3.19 (m, 1H, H4a), 3.75-4.12 (m, 8H, CH_2CH_3 , OCH_3), 6.87 (d, 1H, 3J = 8.4 Hz, H5-arom), 7.23 (dd, 1H, 4J = 2.0 Hz, 3J = 8.4 Hz, H6-arom), 7.49 (d, 1H, 4J = 2.0 Hz, H2-arom). Anal. Calcd ($\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_3$) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-propyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3c) -

Synthesized following the general procedure using 1-bromopropane as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from petroleum ether (60-80). Yield 36%. Mp 95-96 °C. ^1H NMR (CDCl_3): δ 0.96 (t, 3H, 3J = 7.4 Hz, CH_2CH_3), 1.22-2.01 (m, 9H, H5, H6, H7, H8, CH_2CH_3), 2.46-2.78 (m, 2H, H8a, H8'), 2.98-3.18 (m, 1H, H4a), 3.60-3.80 (m, 1H, NCHH'), 3.83-4.09 (m, 7H, NCHH' , OCH_3), 6.87 (d, 1H, 3J = 8.4 Hz, H5-arom), 7.23 (dd, 1H, 4J = 2.0 Hz, 3J = 8.4 Hz, H6-arom), 7.48 (d, 1H, 4J = 2.0 Hz, H2-arom). Anal. Calcd ($\text{C}_{19}\text{H}_{26}\text{N}_2\text{O}_3$) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-isopropyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3d) -

Synthesized following the general procedure using 2-bromopropane as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether/petroleum ether (60-80). Yield 17%. Mp 79-81 °C. ^1H NMR (CDCl_3): δ 1.18-1.95 (m, 13H, H5, H6, H7, H8, CH_3 -i-Pr), 2.48-2.75 (m, 2H, H8a, H8'), 2.96-3.16 (m, 1H, H4a), 3.93 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.97-5.20 (m, 1H, NCH), 6.87 (d, 1H, 3J = 8.4 Hz, H5-arom), 7.25 (dd, 1H, 4J = 1.9 Hz, 3J = 8.4 Hz, H6-arom),

7.54 (d, 1H, $^4J = 1.9$ Hz, H2-arom). Anal. Calcd (C₁₉H₂₆N₂O₃) C, H, N.

cis-2-tert-Butyl-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3e) - A mixture of γ -keto acid **1a** (2.0 g, 6.85 mmol), *tert*-butylhydrazine hydrochloride (5.0 g, 40.1 mmol) and triethylamine (5.6 mL, 40.3 mmol) in toluene (50 mL) was heated for 20 h in a Dean-Stark apparatus. The reaction mixture was concentrated *in vacuo*, the residue dissolved in ethyl acetate and washed with 1N NaOH, 1N HCl and water. The organic layer was dried over MgSO₄ and the solvents were removed under reduced pressure. The residual oil was purified by flash column chromatography using dichloromethane and the title compound was crystallized from petroleum ether (60-80) at -20 °C. Yield 73%. Mp 99-101 °C. ¹H NMR (CDCl₃): δ 1.23-1.90 (m, 16H, H5, H6, H7, H8, CH₃-*tert*-Bu), 2.43-2.67 (m, 2H, H8a, H8'), 2.91-3.10 (m, 1H, H4a), 3.92 (s, 3H, OCH₃), 3.93 (s, 3H, OCH₃), 6.86 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.21 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.49 (d, 1H, $^4J = 2.0$ Hz, H2-arom). Anal. Calcd (C₂₀H₂₈N₂O₃) C, H, N.

cis-2-Cyclopentyl-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3f) - Synthesized following the general procedure using bromocyclopentane as the alkylating agent. Crystallized from methanol. Yield 61%. Mp 111-114 °C. ¹H NMR (CDCl₃): δ 1.17-2.08 (m, 15H, H5, H6, H7, H8, CH₂-cyclopentyl), 2.46-2.73 (m, 2H, H8a, H8'), 2.96-3.15 (m, 1H, H4a), 3.92 (s, 3H, OCH₃), 3.93 (s, 3H, OCH₃), 5.15-5.38 (m, 1H, NCH), 6.87 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.23 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.52 (d, 1H, $^4J = 2.0$ Hz, H2-arom). Anal. Calcd (C₂₁H₂₈N₂O₃) C, H, N.

cis-2-Cycloheptyl-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3g) - Synthesized following the general procedure using bromocycloheptane as the alkylating agent. Crystallized from methanol. Yield 60%. Mp 102-104 °C. ¹H NMR (CDCl₃): δ 1.20-2.12 (m, 19H, H5, H6, H7, H8, CH₂-cycloheptyl), 2.45-2.71 (m, 2H, H8a, H8'), 2.95-3.15 (m, 1H, H4a), 3.92 (s, 3H, OCH₃), 3.95 (s, 3H, OCH₃), 4.74-4.96 (m, 1H, NCH), 6.87 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.23 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.52 (d, 1H, $^4J = 2.0$ Hz, H2-arom). Anal. Calcd (C₂₃H₃₂N₂O₃) C, H, N.

cis-2-Allyl-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3h) - Synthesized following the general procedure using allyl chloride as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from petroleum ether (60-80). Yield 54%. Mp 99-101 °C. ¹H NMR (CDCl₃): δ 1.23-1.93 (m, 7H, H5, H6, H7, H8), 2.45-2.80 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.92 (s, 3H, OCH₃), 3.94 (s, 3H, OCH₃), 4.49 (AB, 2H, NCH₂), 5.12-5.36 (m, 2H, HC=CH₂), 5.86-6.09 (m, 1H, HC=CH₂), 6.86 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.22 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.48 (d, 1H, $^4J = 2.0$ Hz, H2-arom). Anal. Calcd (C₁₉H₂₄N₂O₃) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-prop-2-ynyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3i) - Synthesized following the general procedure using propargyl bromide as the alkylating agent, NaOEt was used instead of NaH. Purified by flash column chromatography using dichloromethane. Crystallized from methanol. Yield 32%. Mp 118-121 °C. ¹H NMR (CDCl₃): δ 1.23-1.96 (m, 7H, H5, H6, H7, H8), 2.23 (t, 1H, $^4J = 2.4$ Hz, CCH), 2.47-2.68 (m, 1H, H8a), 2.68-2.81 (m, 1H, H8'), 3.01-3.21 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.95 (s, 3H, OCH₃), 4.66 (AB, 2H, NCH₂), 5.60-5.89 (m, 2H, HC=CH), 6.87 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.24 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.51 (d, 1H, $^4J = 2.0$ Hz, H2-arom). Anal. Calcd (C₁₉H₂₂N₂O₃) C, H, N.

cis-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-yl]acetonitrile (3j) - Synthesized following the general procedure using 3-chloromethyl-1,2,4-oxadiazole as the alkylating agent. Crystallized from ethyl acetate. Yield 60%. Mp 160-163 °C. ¹H NMR (CDCl₃): δ 1.22-1.99 (m, 7H, H5, H6, H7, H8), 2.47-2.70 (m, 1H, H8a), 2.71-2.87 (m, 1H, H8'), 3.08-3.28 (m, 1H, H4a), 3.94 (s, 3H, OCH₃), 3.96 (s, 3H, OCH₃), 4.79 (AB, 2H, NCH₂), 6.88 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.25 (dd, 1H, $^4J = 1.9$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.48 (d, 1H, $^4J = 1.9$ Hz, H2-arom). Anal. Calcd (C₁₈H₂₁N₃O₃)

C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-(2-hydroxyethyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3k)** - A mixture of γ -keto acid **1a** (2.0 g, 6.8 mmol), 2-hydroxyethylhydrazine (2.0 g, 26 mmol) and triethylamine (5.0 mL, 36 mmol) in 1-propanol (100 mL) was refluxed for 18 hours. After the solvent was evaporated *in vacuo*, the remainder was dissolved in ethyl acetate and washed with 1N HCl and water. The title compound was crystallized from diethyl ether and recrystallized from methanol at -20 °C. Yield 71%. Mp 128-129 °C. ¹H NMR (CDCl₃): δ 1.29-1.95 (m, 7H, H5, H6, H7, H8), 2.44-2.68 (m, 1H, H8a), 2.71-3.00 (m, 2H, H8', OH), 3.02-3.22 (m, 1H, H4a), 3.84-4.25 (m, 10H, NCH₂, HOCH₂, OCH₃), 6.88 (d, 1H, ³J = 8.5 Hz, H5-arom), 7.23 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.5 Hz, H6-arom), 7.41 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₁₈H₂₄N₂O₄) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-(3-hydroxypropyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3l)** - Synthesized following the general procedure using 3-chloro-1-propanol as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether/petroleum ether (60-80). Yield 37%. Mp 94-97 °C. ¹H NMR (CDCl₃): δ 1.25-2.09 (m, 9H, H5, H6, H7, H8, CH₂-Pr), 2.43-2.68 (m, 1H, H8a), 2.70-2.83 (m, 1H, H8'), 3.01-3.24 (m, 2H, H4a, OH), 3.62 (t, 2H, ³J = 5.7 Hz, CH₂OH), 3.87-4.20 (m, 8H, NCH₂, OCH₃), 6.87 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.23 (dd, 1H, ⁴J = 2.1 Hz, ³J = 8.4 Hz, H6-arom), 7.45 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₁₉H₂₆N₂O₄) C, H, N.

***cis*-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-yl]acetic acid ethyl ester (3m)** - Synthesized following the general procedure using ethyl bromoacetate as the alkylating agent. Crystallized from ethanol at -20 °C. Yield 73%. Mp 97-99 °C. ¹H NMR (CDCl₃): δ 1.20-1.98 (m, 10H, H5, H6, H7, H8, CH₂CH₃), 2.42-2.68 (m, 1H, H8a), 2.71-2.89 (m, 1H, H8'), 3.03-3.23 (m, 1H, H4a), 3.92 (s, 3H, OCH₃), 3.93 (s, 3H, OCH₃), 4.22 (q, 2H, ³J = 7.1 Hz, CH₂CH₃), 4.63 (AB, 2H, NCH₂), 6.86 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.22 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.43 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₀H₂₆N₂O₅) C, H, N.

***cis*-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-yl]acetic acid (3n)** - Ethyl ester **3m** (1.5 g, 4.0 mmol) was stirred for 3 h in a mixture of 2N NaOH (200 mL), THF (100 mL) and methanol (100 mL). The reaction mixture was concentrated to a volume of 150 mL and acidified with concentrated HCl. The product was extracted with ethyl acetate, the combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. Compound **3n** was crystallized from acetone/petroleum ether (60-80). Yield 63%. Mp 183-187 °C. ¹H NMR (CDCl₃): δ 1.19-1.98 (m, 7H, H5, H6, H7, H8), 2.42-2.67 (m, 1H, H8a), 2.71-2.88 (m, 1H, H8'), 3.03-3.23 (m, 1H, H4a), 3.92 (s, 3H, OCH₃), 3.94 (s, 3H, OCH₃), 4.68 (AB, 2H, NCH₂), 6.86 (d, 1H, ³J = 8.5 Hz, H5-arom), 7.22 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.5 Hz, H6-arom), 7.43 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₁₈H₂₂N₂O₅) C, H, N.

***cis*-6-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-yl]hexanoic acid, sodium salt (3o)** - Synthesized following the general procedure using 6-bromohexanoic acid as the alkylating agent and 2 equivalents of NaH. Workup was performed as described below. The DMF was evaporated under reduced pressure and the residue was dissolved in ethyl acetate. The product was extracted with 1N NaOH, the combined basic extracts were acidified with concentrated HCl and the product was extracted with ethyl acetate. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The remainder was purified by flash column chromatography using ethyl acetate. The title compound was dissolved in diethyl ether and a concentrated solution of NaOEt was added, the precipitate was filtered off and recrystallized from methanol/diethyl ether. Yield 18%. Mp 140-143 °C. ¹H NMR (CDCl₃/CD₃OD): δ 1.03-1.92 (m, 13H, H5, H6, H7, H8, CH₂-pentyl), 1.98-2.19 (m, 2H, CH₂COOH), 2.36-2.69 (m, 2H, H8a, H8'), 2.86-3.08 (m, 1H, H4a), 3.52-4.00 (m, 8H, OCH₃, NCH₂), 6.77 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.13 (dd, 1H, ⁴J = 1.9 Hz, ³J = 8.4 Hz, H6-arom), 7.34 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₂H₂₉N₂O₅Na) C, H, N.

cis-8-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-yl]octanoic acid (3p) - Prepared from phthalazinone **2a** and 8-bromooctanoic acid as described for **3o**. Purified by flash column chromatography using ethyl acetate. Crystallized from diethyl ether. Yield 29%. Mp 90-91 °C. ¹H NMR (CDCl₃): δ 1.18-1.92 (m, 17H, H5, H6, H7, H8, CH₂-heptyl), 2.34 (t, 2H, ³J = 7.5 Hz, CH₂COOH), 2.42-2.79 (m, 2H, H8a, H8'), 2.99-3.19 (m, 1H, H4a), 3.64-4.10 (m, 8H, OCH₃, NCH₂), 6.87 (d, 1H, ³J = 8.5 Hz, H5-arom), 7.23 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.5 Hz, H6-arom), 7.47 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₄H₃₄N₂O₅) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(2-dimethylaminoethyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one fumarate (3q) - Synthesized following the general procedure using 2-bromoethyl-N,N-dimethylamine hydrobromide as the alkylating agent and 2 equivalents of NaH. Purified by flash column chromatography using ethyl acetate. Crystallized as the fumarate from diethyl ether/fumaric acid. Yield 15%. Mp 74-76 °C. ¹H NMR (CDCl₃): δ 1.17-1.95 (m, 7H, H5, H6, H7, H8), 2.38-2.63 (m, 1H, H8a), 2.64-2.97 (m, 7H, NCH₃, H8'), 3.01-3.42 (m, 3H, NCH₂, H4a), 3.82-4.45 (m, 8H, NCH₂, OCH₃), 6.73 (s, 2H, HC=CH-fum), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.25 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.43 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₀H₂₉N₃O₃·C₄H₄O₄) C, H, N.

cis-2-(4-Bromobutyl)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (3.1r) - Synthesized following the general procedure using 1,4-dibromobutane (4 equivalents) as the alkylating agent. Purified by flash column chromatography using dichloromethane to yield the title compound as a colorless oil. Yield 75%. ¹H NMR (CDCl₃): δ 1.20-2.08 (m, 11H, H5, H6, H7, H8, CH₂-Bu), 2.43-2.80 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.49 (t, 2H, ³J = 6.2 Hz, CH₂Br), 3.73-4.14 (m, 8H, NCH₂, OCH₃), 6.87 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.22 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.47 (d, 1H, ⁴J = 2.0 Hz, H2-arom).

cis-4-(3,4-Dimethoxyphenyl)-2-(4-dimethylaminobutyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one fumarate (3r) - Bromide **3.1r** (2.0 g, 4.7 mmol) was added to a 30% solution of dimethylamine in ethanol (50 mL) and the whole was stirred overnight. The reaction mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography using ethyl acetate. The title compound was crystallized as the fumarate from diethyl ether/fumaric acid. Yield 60%. Mp 119-121 °C. ¹H NMR (CDCl₃): δ 1.20-1.97 (m, 11H, H5, H6, H7, H8, CH₂-Bu), 2.38-2.63 (m, 1H, H8a), 2.68-2.88 (m, 7H, NCH₃, H8'), 2.97-3.22 (m, 3H, NCH₂, H4a), 3.74-4.12 (m, 8H, NCH₂, OCH₃), 6.75 (s, 2H, HC=CH-fum), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.24 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.43 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₂H₃₃N₃O₃·C₄H₄O₄) C, H, N.

cis-2-(6-Bromohexyl)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydrophthalazin-1-one (3.1s) - Synthesized following the general procedure using 1,6-dibromohexane (4 equivalents) as the alkylating agent. Purified by flash column chromatography using ethyl acetate/petroleum ether (60-80) 1/2. Crystallized from petroleum ether (60-80). Yield 86%. Mp 74-75 °C. ¹H NMR (CDCl₃): δ 1.20-2.00 (m, 15H, H5, H6, H7, H8, CH₂-hexyl), 2.43-2.79 (m, 2H, H8a, H8'), 2.98-3.18 (m, 1H, H4a), 3.40 (t, 2H, ³J = 6.8 Hz, CH₂Br), 3.62-4.14 (m, 8H, NCH₂, OCH₃), 6.87 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.23 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.47 (d, 1H, ⁴J = 1.9 Hz, H2-arom).

cis-4-(3,4-Dimethoxyphenyl)-2-(6-dimethylaminoethyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one oxalate (3s) - Prepared from **3.1s** as described for **3r**. Crystallized from acetone/oxalic acid as the oxalate. Yield 65%. Mp 65-67 °C. ¹H NMR (CDCl₃): δ 1.22-1.98 (m, 15H, H5, H6, H7, H8, CH₂-hexyl), 2.43-2.78 (m, 2H, H8a, H8'), 2.82 (s, 6H, NCH₃), 2.92-3.20 (m, 3H, NCH₂, H4a), 3.68-4.10 (m, 8H, NCH₂, OCH₃), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.23 (dd, 1H, ⁴J = 1.9 Hz, ³J = 8.4 Hz, H6-arom), 7.45 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₄H₃₇N₃O₃·C₂H₂O₄) C, H, N.

cis-2-(6-Aminohexyl)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one fumarate (3t) - A solution of **3.1s** (5.0 g, 11 mmol) in a mixture of methanol (200 mL) and tetrahydrofuran (100 mL) was saturated with ammonia and stirred for 1 week. The reaction mixture was

concentrated under reduced pressure, the remainder was dissolved in ethyl acetate and washed with 1N NaOH and water. The organic layer was concentrated *in vacuo* and the title compound was crystallized as the fumarate from a mixture of methanol, ethyl acetate and fumaric acid. Yield 35%. Mp 127-129 °C. ¹H NMR (CDCl₃/D₂O): δ 1.11-1.90 (m, 15H, H5, H6, H7, H8, CH₂-hexyl), 2.31-2.71 (m, 2/4H, H8a, H8', NH₂), 2.80-3.11 (m, 3H, H4a, CH₂NH₂), 3.60-4.03 (m, 8H, NCH₂, OCH₃), 6.58 (s, 2H, HC=CH-fum), 6.83 (d, 1H, ³J = 8.5 Hz, H5-arom), 7.19 (dd, 1H, ⁴J = 1.8 Hz, ³J = 8.5 Hz, H6-arom), 7.40 (d, 1H, ⁴J = 1.8 Hz, H2-arom). Anal. Calcd (C₂₂H₃₃N₃O₃·C₄H₄O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-phenethyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6a) - Synthesized following the general procedure using (2-bromoethyl)benzene as the alkylating agent. Purified by flash column chromatography using ethyl acetate/petroleum ether (60-80) 1/3. Crystallized from methanol. Yield 59%. Mp 99-100 °C. ¹H NMR (CDCl₃): δ 1.01-1.83 (m, 7H, H5, H6, H7, H8), 2.41-2.73 (m, 2H, H8a, H8'), 2.92-3.17 (m, 3H, H4a, CH₂-Ph), 3.84-4.11 (m, 7H, NCHH', OCH₃), 4.22-4.44 (m, 1H, NCHH'), 6.86 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.11-7.34 (m, 6H, H6-arom, H-Ph), 7.42 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₄H₂₈N₂O₃) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(2-oxo-2-phenylethyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6b) - Synthesized following the general procedure using 2-bromoacetophenone as the alkylating agent. Purified by flash column chromatography using ethyl acetate/petroleum ether (60-80) 1/3. Crystallized from diethyl ether. Yield 31%. Mp 133-135 °C. ¹H NMR (CDCl₃): δ 1.20-2.02 (m, 7H, H5, H6, H7, H8), 2.46-2.69 (m, 1H, H8a), 2.81-2.96 (m, 1H, H8'), 3.08-3.27 (m, 1H, H4a), 3.89 (s, 3H, OCH₃), 3.91 (s, 3H, OCH₃), 5.33 (AB, 2H, NCH₂), 6.85 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.22 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.40 (d, 1H, ⁴J = 2.0 Hz, H2-arom), 7.43-7.70 (m, 3H, H-Ph), 7.95-8.09 (m, 2H, H-Ph). Anal. Calcd (C₂₄H₂₆N₂O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(3-phenoxypropyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6c) - Synthesized following the general procedure using 3-phenoxypropyl bromide as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from petroleum ether (60-80). Yield 64%. Mp 78-81 °C. ¹H NMR (CDCl₃): δ 1.24-1.93 (m, 7H, H5, H6, H7, H8), 2.12-2.34 (m, 2H, CH₂-Pr), 2.47-2.81 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.77-4.31 (m, 10H, NCH₂, OCH₂, OCH₃), 6.79-7.01 (m, 4H, H5-arom, H-Ph), 7.12-7.36 (m, 3H, H6-arom, H-Ph), 7.43 (d, 1H, ⁴J = 1.8 Hz, H2-arom). Anal. Calcd (C₂₅H₃₀N₂O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(3-phenylallyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6d) - Synthesized following the general procedure using trans-cinnamyl chloride as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether at -20 °C. Yield 42%. Mp 76-79 °C. ¹H NMR (CDCl₃): δ 1.20-1.94 (m, 7H, H5, H6, H7, H8), 2.46-2.81 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.89 (s, 3H, OCH₃), 3.92 (s, 3H, OCH₃), 4.64 (AB, 2H, NCH₂), 6.35 (dt, 1H, ³J_{1,2} = 6.4 Hz, ³J_{2,3} = 15.9 Hz, H2-allyl), 6.65 (d, 1H, ³J_{2,3} = 15.9 Hz, H3-allyl), 6.86 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.12-7.44 (m, 6H, H6-arom, H-Ph), 7.48 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₅H₂₈N₂O₃) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(2-methoxybenzyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6e) - Synthesized following the general procedure using 2-methoxybenzyl chloride as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether at -20 °C. Yield 50%. Mp 96-99 °C. ¹H NMR (CDCl₃): δ 1.20-1.90 (m, 7H, H5, H6, H7, H8), 2.50-2.84 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.84 (s, 3H, OCH₃), 3.85 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 5.11 (AB, 2H, NCH₂), 6.72-6.99 (m, 3H, H5-arom, H-Ph), 7.10-7.31 (m, 3H, H6-arom, H-Ph), 7.35 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₄H₂₈N₂O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(3-methoxybenzyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6f) - Synthesized following the general procedure using 3-methoxybenzyl chloride as the alkylating agent. Crystallized from methanol. Yield 85%. Mp 115 °C. ¹H NMR (CDCl₃): δ 1.17-1.93 (m, 7H, H5,

H6, H7, H8), 2.47-2.81 (m, 2H, H8a, H8'), 3.00-3.19 (m, 1H, H4a), 3.77 (s, 3H, OCH₃), 3.91 (s, 6H, OCH₃), 5.02 (AB, 2H, NCH₂), 6.74-6.90 (m, 2H, H5-arom, H-Ph), 6.92-7.06 (m, 2H, H-Ph), 7.14-7.27 (m, 2H, H6-arom, H-Ph), 7.44 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₄H₂₈N₂O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(4-methoxybenzyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6g) - Synthesized following the general procedure using 4-methoxybenzyl chloride as the alkylating agent. Crystallized from diethyl ether. Yield 34%. Mp 76-78 °C. ¹H NMR (CDCl₃): δ 1.20-1.93 (m, 7H, H5, H6, H7, H8), 2.48-2.79 (m, 2H, H8a, H8'), 2.98-3.17 (m, 1H, H4a), 3.78 (s, 3H, Bn-OCH₃), 3.91 (s, 3H, OCH₃), 3.93 (s, 3H, OCH₃), 4.97 (AB, 2H, NCH₂), 6.84 (d, 3H, ³J = 8.6 Hz, H5-arom, H-Ph), 7.19 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.5 Hz, H6-arom), 7.36 (d, 2H, ³J = 8.7 Hz, H-Ph), 7.44 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₄H₂₈N₂O₄) C, H, N.

cis-2-(3,5-Dimethoxybenzyl)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6h) - Synthesized following the general procedure using 3,5-dimethoxybenzyl chloride as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from methanol. Yield 39%. Mp 114-117 °C. ¹H NMR (CDCl₃): δ 1.21-1.90 (m, 7H, H5, H6, H7, H8), 2.48-2.82 (m, 2H, H8a, H8'), 2.99-3.19 (m, 1H, H4a), 3.76 (s, 6H, OCH₃), 3.91 (s, 6H, OCH₃), 4.98 (AB, 2H, NCH₂), 6.36 (t, 1H, ⁴J = 2.2 Hz, H-Ph), 6.57 (d, 2H, ⁴J = 2.2 Hz, H-Ph), 6.84 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.20 (dd, 1H, ⁴J = 1.9 Hz, ³J = 8.4 Hz, H6-arom), 7.44 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₅H₃₀N₂O₅) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(2-hydroxybenzyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6i) - Synthesized following the general procedure using 2-benzyloxybenzyl chloride as the alkylating agent. After workup the desired product (4.0 g, 8.3 mmol) was dissolved in ethanol (100 mL) and debenzylated at 50 °C using palladium on activated carbon (5% Pd, 0.5 g) and H₂-gas. After the reaction was complete (TLC), the mixture was filtered over celite and concentrated *in vacuo*. The title compound was crystallized from diethyl ether. Yield 53%. Mp 132-133 °C. ¹H NMR (CDCl₃): δ 1.18-1.98 (m, 7H, H5, H6, H7, H8), 2.45-2.80 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.99 (s, 3H, OCH₃), 4.99 (AB, 2H, NCH₂), 6.80-7.01 (m, 3H, H5-arom, H-Ph), 7.15-7.51 (m, 4H, H2-arom, H6-arom, H-Ph). Anal. Calcd (C₂₃H₂₆N₂O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(3-hydroxybenzyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6j) - Synthesized following the general procedure using 3-benzyloxybenzyl chloride as the alkylating agent. After workup the desired product was debenzylated as described for compound 6i. The title compound was purified by flash column chromatography using ethyl acetate/petroleum ether (60-80) 1/1, crystallized from diethyl ether and recrystallized from methanol. Yield 38%. Mp 165-167 °C. ¹H NMR (CDCl₃): δ 1.20-1.93 (m, 7H, H5, H6, H7, H8), 2.44-2.82 (m, 2H, H8a, H8'), 2.98-3.18 (m, 1H, H4a), 3.91 (s, 3H, OCH₃), 3.92 (s, 3H, OCH₃), 4.99 (AB, 2H, NCH₂), 6.69-6.80 (m, 1H, H-Ph), 6.84 (d, 1H, ³J = 8.4 Hz, H5-arom), 6.90-7.03 (m, 2H, H-Ph), 7.10-7.27 (m, 2H, H6-arom, H-Ph), 7.45 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₃H₂₆N₂O₄) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(4-hydroxybenzyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6k) - Synthesized following the general procedure using 4-benzyloxybenzyl chloride as the alkylating agent. After workup the desired product was purified by flash column chromatography using ethyl acetate/petroleum ether 1/2 and subsequently debenzylated as described for compound 6i. The title compound was crystallized from diethyl ether. Yield 39%. Mp 177-179 °C. ¹H NMR (CDCl₃): δ 1.13-1.94 (m, 7H, H5, H6, H7, H8), 2.46-2.80 (m, 2H, H8a, H8'), 2.98-3.17 (m, 1H, H4a), 3.91 (s, 3H, OCH₃), 3.92 (s, 3H, OCH₃), 4.95 (AB, 2H, NCH₂), 6.75 (d, 2H, ³J = 8.5 Hz, H-Ph), 6.85 (d, 1H, ³J = 8.5 Hz, H5-arom), 7.20 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.5 Hz, H6-arom), 7.28 (d, 2H, ³J = 8.5 Hz, H-Ph), 7.45 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₃H₂₆N₂O₄) C, H, N.

cis-3-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-ylmethyl]benzoic acid (6l) - Synthesized following the general procedure using 3-bromomethylbenzoic acid as the

alkylating agent and 2 equivalents of NaH. Purified by flash column chromatography using ethyl acetate. Crystallized from diethyl ether. Yield 40%. Mp 133-136 °C. ^1H NMR (CDCl_3): δ 1.20-1.93 (m, 7H, H5, H6, H7, H8), 2.48-2.83 (m, 2H, H8a, H8'), 3.00-3.21 (m, 1H, H4a), 3.91 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.11 (AB, 2H, NCH_2), 6.84 (d, 1H, $^3J = 8.5$ Hz, H5-arom), 7.19 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.35-7.52 (m, 2H, H2-arom, H-Ph), 7.68 (d, 1H, $^3J = 7.7$ Hz, H-Ph), 8.01 (d, 1H, $^3J = 7.7$ Hz, H-Ph), 8.20 (s, 1H, H-Ph). Anal. Calcd ($\text{C}_{24}\text{H}_{26}\text{N}_2\text{O}_5$) C, H, N.

***cis*-4-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-ylmethyl]benzoic acid (6m)** - Synthesized following the general procedure using 4-chloromethylbenzoic acid as the alkylating agent and 2 equivalents of NaH. Purified by flash column chromatography using ethyl acetate. Crystallized from diethyl ether. Yield 44%. Mp 135-139 °C. ^1H NMR (CDCl_3): δ 1.10-1.95 (m, 7H, H5, H6, H7, H8), 2.45-2.83 (m, 2H, H8a, H8'), 3.01-3.21 (m, 1H, H4a), 3.91 (s, 6H, OCH_3), 5.11 (AB, 2H, NCH_2), 6.85 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.21 (dd, 1H, $^4J = 1.9$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.39 (d, 1H, $^4J = 1.9$ Hz, H2-arom), 7.49 (d, 2H, $^3J = 8.1$ Hz, H-Bn), 8.06 (d, 2H, $^3J = 8.1$ Hz, H-Bn). Anal. Calcd ($\text{C}_{24}\text{H}_{26}\text{N}_2\text{O}_5$) C, H, N.

***cis*-4-[4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,6,7,8,8a-hexahydro-1H-phthalazin-2-ylmethyl]benzoic acid methyl ester (6n)** - Thionyl chloride (3.0 mL, 41 mmol) was added slowly to a cooled (-20 °C) solution of benzoic acid **6m** (1.0 g, 2.4 mmol) in methanol (50 mL). After the addition was completed, the reaction mixture was allowed to reach room temperature and stirred for 6 h. The mixture was concentrated under reduced pressure and ester **6n** was crystallized from diethyl ether at -20 °C. Yield 86%. Mp 90-92 °C. ^1H NMR (CDCl_3): δ 1.18-1.91 (m, 7H, H5, H6, H7, H8), 2.48-2.70 (m, 1H, H8a), 2.70-2.83 (m, 1H, H8'), 3.00-3.20 (m, 1H, H4a), 3.90 (s, 6H, OCH_3), 3.91 (s, 3H, OCH_3), 5.09 (AB, 2H, NCH_2), 6.85 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.20 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.39 (d, 1H, $^4J = 2.0$ Hz, H2-arom), 7.46 (d, 2H, $^3J = 8.3$ Hz, H-Bn), 7.99 (d, 2H, $^3J = 8.3$ Hz, H-Bn). Anal. Calcd ($\text{C}_{25}\text{H}_{28}\text{N}_2\text{O}_5$) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-pyridin-2-ylmethyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6o)** - Synthesized following the general procedure using 2-picolyl chloride hydrochloride as the alkylating agent and 2 equivalents of NaH. Crystallized from diethyl ether. Yield 75%. Mp 181-182 °C. ^1H NMR (CDCl_3): δ 1.30-2.00 (m, 7H, H5, H6, H7, H8), 2.50-2.73 (m, 1H, H8a), 2.78-2.93 (m, 1H, H8'), 3.08-3.27 (m, 1H, H4a), 3.88 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 5.24 (AB, 2H, NCH_2), 6.84 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.11-7.33 (m, 3H, H6-arom, H-pyridyl), 7.39 (d, 1H, $^4J = 2.0$ Hz, H2-arom), 7.66 (dt, 1H, $^3J = 7.7$ Hz, $^4J = 1.7$ Hz, H-pyridyl), 8.56 (d, 1H, $^3J = 4.1$ Hz, H3-pyridyl). Anal. Calcd ($\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}_3$) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-pyridin-3-ylmethyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride (6p)** - Synthesized following the general procedure using 3-picolyl chloride hydrochloride as the alkylating agent and 2 equivalents of NaH. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether/HCl as the hydrochloride. Yield 72%. Mp 192-195 °C. ^1H NMR (CDCl_3): δ 1.15-1.98 (m, 7H, H5, H6, H7, H8), 2.40-2.61 (m, 1H, H8a), 2.68-2.82 (m, 1H, H8'), 3.07-3.27 (m, 1H, H4a), 3.93 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3), 5.20 (AB, 2H, NCH_2), 6.88 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.23 (dd, 1H, $^4J = 1.9$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.35 (d, 1H, $^4J = 1.9$ Hz, H2-arom), 7.87-8.02 (m, 1H, H-pyridyl), 8.52 (d, 2H, $^3J = 8.0$ Hz, H-pyridyl), 8.74 (d, 2H, $^3J = 5.2$ Hz, H-pyridyl), 8.84 (s, 1H, H-pyridyl). Anal. Calcd ($\text{C}_{22}\text{H}_{25}\text{N}_3\text{O}_3 \cdot \text{HCl}$) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-pyridin-4-ylmethyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (6q)** - Synthesized following the general procedure using 4-picolyl chloride hydrochloride as the alkylating agent and 2 equivalents of NaH. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether. Yield 71%. Mp 87-89 °C. ^1H NMR (CDCl_3): δ 1.20-1.97 (m, 7H, H5, H6, H7, H8), 2.44-2.71 (m, 1H, H8a), 2.71-2.86 (m, 1H, H8'), 3.03-3.23 (m, 1H, H4a), 3.90 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 5.07 (AB, 2H, NCH_2), 6.86 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.22

(dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.34 (d, 2H, $^3J = 6.0$ Hz, H-pyridyl), 7.38 (d, 1H, $^4J = 2.0$ Hz, H2-arom), 8.57 (d, 2H, $^3J = 5.9$ Hz, H-pyridyl). Anal. Calcd (C₂₂H₂₅N₃O₃) C, H, N.

cis-2-(2-Bromoethyl)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydrophthalazin-1-one (6.1r) - A solution of bromine (4.00 g, 25.0 mmol) in dichloromethane (10 mL) was added dropwise to an ice cooled solution of triphenylphosphine (6.56 g, 25.0 mmol) in dichloromethane (50 mL) under a nitrogen atmosphere. Subsequently, a solution of compound **3k** (8.30 g, 25.0 mmol) in dichloromethane (25 mL) was added to the reaction mixture while keeping the temperature at 0 °C. After the last addition the mixture was allowed to reach room temperature and stirred for another 2 h. Aqueous sodium bicarbonate was then added to the reaction mixture. The organic layer was dried over MgSO₄ and concentrated under reduced pressure. The title compound was crystallized from the residue as a white solid using methanol. Yield 65%. Mp 134-136 °C. ¹H NMR (CDCl₃): δ 1.21-2.00 (m, 7H, H5, H6, H7, H8), 2.44-2.83 (m, 2H, H8a, H8'), 3.00-3.21 (m, 1H, H4a), 3.66 (t, 2H, $^3J = 6.7$ Hz, CH₂Br), 3.88-4.59 (m, 8H, NCH₂, OCH₃), 6.87 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.23 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.46 (d, 1H, $^4J = 2.0$ Hz, H2-arom).

cis-4-(3,4-Dimethoxyphenyl)-2-(2-imidazol-1-ylethyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride (6r) - A solution of **6.1r** (2.0 g, 5.1 mmol) and imidazole (3.0 g, 44 mmol) in methanol (50 mL) was stirred for 18 h. After removal of the solvent, the remainder was dissolved in ethyl acetate and washed with water. The organic layer was dried over MgSO₄ and filtered over silica. The title compound crystallized as the hydrochloride from tetrahydrofuran/HCl. Yield 67%. Mp 198-199 °C. ¹H NMR (CDCl₃): δ 0.98-1.92 (m, 7H, H5, H6, H7, H8), 2.34-2.73 (m, 2H, H8a, H8'), 3.00-3.20 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.97 (s, 3H, OCH₃), 4.23-4.58 (m, 2H, NCH₂), 4.63-4.83 (m, 2H, CH₂-imidazole), 6.88 (d, 1H, $^3J = 8.5$ Hz, H5-arom), 7.12-7.30 (m, 3H, H6-arom, HC=CH-imidazole), 7.36 (d, 1H, $^4J = 1.9$ Hz, H2-arom), 9.33 (s, 1H, H-imidazole). Anal. Calcd (C₂₁H₂₆N₄O₃·HCl) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-(4-imidazol-1-ylbutyl)-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride (6s) - Prepared from bromide **3.1r** and imidazole as described for **6r**. Purified by flash column chromatography using ethyl acetate. Crystallized as the hydrochloride from tetrahydrofuran/HCl. Yield 45%. Mp 210-212 °C. ¹H NMR (CDCl₃): δ 1.19-2.10 (m, 11H, H5, H6, H7, H8, CH₂-Bu), 2.42-2.82 (m, 2H, H8a, H8'), 3.00-3.21 (m, 1H, H4a), 3.81-4.13 (m, 8H, NCH₂, OCH₃), 4.44 (t, 2H, $^3J = 7.1$ Hz, NCH₂), 6.88 (d, 1H, $^3J = 8.5$ Hz, H5-arom), 7.15-7.40 (m, 3H, H6-arom, HC=CH-imidazole), 7.43 (d, 1H, $^4J = 2.0$ Hz, H2-arom), 9.47 (s, 1H, H-imidazole), 15.23 (bs, 1H, HCl). Anal. Calcd (C₂₃H₃₀N₄O₃·HCl) C, H, N.

cis-2-Cyclopropylmethyl-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7a) - Synthesized following the general procedure except using phthalazinone **2b** and (chloromethyl)cyclopropane as the alkylating agent. Crystallized from diethyl ether and recrystallized from methanol. Yield 40%. Mp 142-145 °C. ¹H NMR (CDCl₃): δ 0.30-0.62 (m, 4H, CH₂-cyclopropyl), 1.10-1.34 (m, 1H, CH-cyclopropyl), 2.09-2.38 (m, 3H, H5, H8), 2.81 (t, 1H, $^3J = 5.5$ Hz, H8a), 2.91-3.12 (m, 1H, H8'), 3.25-3.45 (m, 1H, H4a), 3.60 (dd, 1H, $^3J = 7.0$ Hz, $^2J = 13.7$ Hz, NCHH'), 3.81-4.05 (m, 7H, NCHH', OCH₃), 5.62-5.90 (m, 2H, HC=CH), 6.88 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.27 (dd, 1H, $^4J = 2.0$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.51 (d, 1H, $^4J = 2.0$ Hz, H2-arom). Anal. Calcd (C₂₀H₂₄N₂O₃) C, H, N.

cis-4-(3,4-Dimethoxyphenyl)-2-isopropyl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7b) - Synthesized following the general procedure except using phthalazinone **2b** and 2-bromopropane as the alkylating agent. Crystallized and recrystallized from methanol. Yield 78%. Mp 146-149 °C. ¹H NMR (CDCl₃): δ 1.22 (d, 3H, $^3J = 6.7$ Hz, CH₃-i-Pr), 1.34 (d, 3H, $^3J = 6.6$ Hz, CH₃-i-Pr), 1.91-2.36 (m, 3H, H5, H8), 2.69-2.82 (m, 1H, H8a), 2.92-3.13 (m, 1H, H8'), 3.24-3.41 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.95 (s, 3H, OCH₃), 4.94-5.19 (m, 1H, NCH), 5.61-5.88 (m, 2H, HC=CH), 6.88 (d, 1H, $^3J = 8.4$ Hz, H5-arom), 7.28 (dd, 1H, $^4J = 1.9$ Hz, $^3J = 8.4$ Hz, H6-arom), 7.54 (d, 1H, $^4J = 1.8$ Hz, H2-arom). Anal. Calcd (C₁₉H₂₄N₂O₃) C, H, N.

***cis*-2-Cyclopentyl-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7c)**

Synthesized following the general procedure except using phthalazinone **2b** and bromocyclopentane as the alkylating agent. Purified by flash column chromatography using dichloromethane. Crystallized from diethyl ether. Yield 83%. Mp 131-133 °C. ¹H NMR (CDCl₃): δ 1.50-2.32 (m, 11H, CH₂-cyclopentyl, H5, H8), 2.70-2.82 (m, 1H, H8a), 2.92-3.13 (m, 1H, H8'), 3.22-3.41 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.94 (s, 3H, OCH₃), 5.15-5.34 (m, 1H, NCH), 5.61-5.89 (m, 2H, HC=CH), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.27 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.52 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₁H₂₆N₂O₃) C, H, N.

***cis*-2-Cyclohexyl-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7d)** - Prepared from γ-keto acid **1b** and cyclohexylhydrazine hydrochloride as described for **3k**. The title compound was crystallized from methanol. Yield 46%. Mp 148-149 °C. ¹H NMR (CDCl₃): δ 0.96-2.26 (m, 13H, H5, H8, CH₂-cyclohexyl), 2.61-2.77 (m, 1H, H8a), 2.84-3.06 (m, 1H, H8'), 3.14-3.33 (m, 1H, H4a), 3.86 (s, 3H, OCH₃), 3.89 (s, 3H, OCH₃), 4.44-4.66 (m, 1H, NCH), 5.50-5.80 (m, 2H, HC=CH), 6.81 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.21 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.43 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₂H₂₈N₂O₃) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-(tetrahydropyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7e)**

- Prepared from γ-keto acid **1b** and 4-hydrazinotetrahydropyran hydrochloride as described for **3k**. The title compound was crystallized from methanol. Yield 49%. Mp 175-177 °C. ¹H NMR (CDCl₃): δ 1.50-1.82 (m, 2H, CH₂-THP), 1.90-2.42 (m, 5H, H5, H8, CH₂-THP), 2.77 (t, 1H, ³J = 5.7 Hz, H8a), 2.90-3.12 (m, 1H, H8'), 3.23-3.43 (m, 1H, H4a), 3.43-3.68 (m, 2H, OCH₂-THP), 3.83-4.20 (m, 8H, OCH₂-THP, OCH₃), 4.80-5.01 (m, 1H, NCH), 5.60-5.90 (m, 2H, HC=CH), 6.88 (d, 1H, ³J = 8.5 Hz, H5-arom), 7.29 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.51 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₁H₂₆N₂O₄) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7f)**

- Prepared from γ-keto acid **1b** and 4-hydrazinotetrahydrothiopyran hydrochloride as described for **3k**. The title compound was crystallized from methanol. Yield 22%. Mp 140-141 °C. ¹H NMR (CDCl₃): δ 1.90-2.47 (m, 7H, H5, H8, CH₂-THTP), 2.61-3.15 (m, 6H, H8a, H8', CH₂-THTP), 3.25-3.45 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.97 (s, 3H, OCH₃), 4.55-4.75 (m, 1H, NCH), 5.60-5.90 (m, 2H, HC=CH), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.30 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.49 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₁H₂₆N₂O₃S) C, H, N.

***cis*-2-Cyclooctyl-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7g)**

- Prepared from γ-keto acid **1b** and cyclooctylhydrazine hydrochloride as described for **3k**. Purified by flash column chromatography using dichloromethane. The title compound was crystallized from petroleum ether (60-80). Yield 45%. Mp 75-77 °C. ¹H NMR (CDCl₃): δ 1.42-2.35 (m, 17H, H5, H8, CH₂-cyclooctyl), 2.66-2.81 (m, 1H, H8a), 2.91-3.12 (m, 1H, H8'), 3.21-3.41 (m, 1H, H4a), 3.93 (s, 3H, OCH₃), 3.95 (s, 3H, OCH₃), 4.82-5.02 (m, 2H, NCH), 5.60-5.90 (m, 2H, HC=CH), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.26 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.52 (d, 1H, ⁴J = 1.9 Hz, H2-arom). Anal. Calcd (C₂₄H₃₂N₂O₃) C, H, N.

***cis*-2-Adamantan-2-yl-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7h)**

- Prepared from γ-keto acid **1b** and adamantylhydrazine hydrochloride as described for **3k**. Crystallized from methanol. Yield 57%. Mp 157-159 °C. ¹H NMR (CDCl₃): δ 1.50-2.45 (m, 16H, H5, H8, CH/CH₂-adamantanyl), 2.55-2.82 (m, 2H, H8a, CH/CH₂-adamantanyl), 2.90-3.12 (m, 1H, H8'), 3.22-3.42 (m, 1H, H4a), 3.91 (s, 3H, OCH₃), 3.93 (s, 3H, OCH₃), 4.67 (s, 1H, NCH), 5.61-5.90 (m, 2H, HC=CH), 6.88 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.25 (dd, 1H, ⁴J = 2.0 Hz, ³J = 8.4 Hz, H6-arom), 7.56 (d, 1H, ⁴J = 2.0 Hz, H2-arom). Anal. Calcd (C₂₆H₃₂N₂O₃) C, H, N.

***cis*-4-(3,4-Dimethoxyphenyl)-2-indan-2-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (7i)**

- Prepared from γ-keto acid **1b** and 2-indanylhiazine hydrochloride as described for **3k**. Crystallized from

methanol. Yield 60%. Mp 163-164 °C. ¹H NMR (CDCl₃): δ 1.92-2.39 (m, 3H, H5, H8), 2.72-2.87 (m, 1H, H8a), 2.95-3.18 (m, 3H, H8', CH₂-indanyl), 3.20-3.47 (m, 3H, H4a, CH₂-indanyl), 3.60 (s, 3H, OCH₃), 3.88 (s, 3H, OCH₃), 5.62-5.92 (m, 3H, NCH, HC=CH), 6.79 (d, 1H, ³J = 8.4 Hz, H5-arom), 7.05 (d, 1H, ⁴J = 2.0 Hz, H2-arom), 7.09-7.33 (m, 5H, H6-arom, H-indanyl). Anal. Calcd (C₂₅H₂₆N₂O₃) C, H, N.

***cis*-2-Cycloheptyl-4-{spiro[cyclopentane-1',2(3H)-7-methoxybenzofurane]-4-yl}-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (9)** - Synthesized following the general procedure except using phthalazinone **2c** and bromocycloheptane as the alkylating agent. Purification by flash column chromatography using petroleum ether (60-80)/ethyl acetate 3/1 and crystallized from petroleum ether (60-80) at -20 °C to give the title compound as a white solid. Yield 79%. Mp 118-120 °C. ¹H NMR (CDCl₃): δ 1.20-2.33 (m, 23H, CH₂-cycloheptyl, H5, H6, H7, H8, CH₂-cyclopentane), 2.42-2.71 (m, 2H, H8', H8a), 2.93-3.13 (m, 1H, H4a), 3.50 (s, 2H, CH₂Ph), 3.90 (s, 3H, OCH₃), 4.73-4.95 (m, 1H, NCH), 6.77 (d, 1H, ³J = 8.6 Hz, H5-arom), 7.00 (d, 1H, ³J = 8.7 Hz, H6-arom). Anal. Calcd (C₂₈H₃₈N₂O₃) C, H, N.