Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications


# Supporting Information

## Synthesis and antiplasmodial evaluation of aziridine-(iso)quinoline hybrids and their ring-opening products

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# Experimental procedures and spectral data

*Synthesis of {[2-(bromomethyl)aziridin-1-yl]methyl}quinolines **7a-c***

General procedure: In a microwave recipient of 80 mL, quinoline-3-carboxaldehyde **5** (2 mmol), triethylamine (2 mmol, 1 equiv), magnesium sulfate (3 mmol, 1.5 equiv) and 2,3-dibromopropylamine hydrobromide (2.2 mol, 1.1 equiv) were dissolved in dichloromethane (40 mL). After stirring for 15-20 min at 90 °C under microwave irradiation, the reaction mixture was poured into water (30 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic extracts were dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded the crude imine products **6a-c**. Because of their instability, these compounds were immediately used for the subsequent reaction step:

In a microwave recipient of 80 mL, imine **6** (2 mmol) was dissolved in methanol (40 mL), and sodium borohydride (3 mmol, 1.5 equiv) was added slowly to this solution. After stirring for 15-45 min at 65 °C under microwave irradiation, the reaction mixture was cooled down to room temperature, after which a second portion of sodium borohydride (3 mmol, 1.5 equiv) was added slowly. After stirring again for 15-45 min at 65 °C under microwave irradiation, the reaction mixture was poured into brine (30 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, and filtration of the drying agent and removal of the solvent in vacuo afforded {[2-(bromomethyl)aziridin-1-yl]methyl}quinolines **7a-c**.

*Synthesis of {[2-(1-methyl-3-trifluoromethyl-1H-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl}quinolines **11a-c***

General procedure: To a solution of {[2-(bromomethyl)aziridin-1-yl]methyl}quinoline **7** (6 mmol) in DMF (40 mL), sodium iodide (0.6 mmol, 0.1 equiv), 2-methyl-5-trifluoromethyl-2H-pyrazole-3-ol (6 mmol, 1 equiv) and sodium hydroxide (12 mmol, 2 equiv) were added. After stirring for 60 h at room temperature under nitrogen atmosphere, the reaction mixture was poured into brine (50 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic layers were washed with brine (10 × 20 mL) and dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded {[2-(1-methyl-3-triflormethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl} quinolines **11a-c**, which were purified by means of column chromatography on silica gel, preparative thin layer chromatography or recrystallization.

*Synthesis of 2-(quinolinylmethyl)amino-3-(1-methyl-3-trifluoromethyl-1H-pyrazole-5-yloxy)propan-1-ols **12a-b***

General procedure: To a solution of {[2-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl}quinoline **11** (2 mmol) in a tetrahydrofuran/water (1/1) solvent mixture (30 mL), *para*-toluenesulfonic acid (2 mmol, 1 equiv) was added. After stirring for 24 h at room temperature, the reaction mixture was poured into water (30 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic layers were subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and

removal of the solvent in vacuo afforded the crude products **12a-b**, which were purified by means of column chromatography on silica gel or recrystallization in ethanol.

*Synthesis of N-[(2-chloroquinolin-3-yl)methyl]-1-methoxy-3-(1-methyl-3-trifluoromethyl-1H-pyrazole-5-yloxy)propane-2-amine* ***12c***

General procedure: To a solution of 2-chloro-3-{[2-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl}quinoline **11b** (1 mmol) in methanol (20 mL) was added boron trifluoride etherate (0.5 mmol, 0.5 equiv). After stirring for 20 h at reflux temperature, the reaction mixture was poured into water (30 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic layers were subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded the crude product **12c**, which was purified by means of column chromatography on silica gel.

*Synthesis of N-[(2-chloroquinolin-3-yl)methyl]-1-methoxy-3-(1-methyl-3-trifluoromethyl-1H-pyrazole-5-yloxy)propane-2-amine* ***12d***

General procedure: To a solution of 2-chloro-3-{[2-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl}quinoline **11b** (1 mmol) in methanol (20 mL) was added boron trifluoride etherate (0.5 mmol, 0.5 equiv). After stirring for 1 h at 90 °C under microwave irradiation, the reaction mixture was poured into water (30 mL) and extracted with dichloromethane (3 × 15 mL). The combined organic layers were subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded products **12c** and **12d**, which were separated by means of column chromatography on silica gel.

*Synthesis of 1-[1-(quinolinylmethyl)aziridin-2-ylmethyl]-4-trifluoromethyl-1H-pyrimidin-3-ones* ***13a-b***

The procedure for the synthesis of compounds **11a-c** was applied for the preparation of 1-[1-(quinolinylmethyl)aziridin-2-ylmethyl]-4-trifluoromethyl-1H-pyrimidin-3-ones **13a-c**. The crude products **13a-b** were purified by column chromatography on silica gel.

*Synthesis of 4,5-dichloro-2-[1-(quinolinylmethyl)aziridin-2-ylmethyl]-2H-pyridazin-3-ones* ***14a-c***

The procedure for the synthesis of compounds **11a-c** was applied for the preparation of 4,5-dichloro-2-[1-(quinolinylmethyl)aziridin-2-ylmethyl]-2H-pyridazin-3-ones **14a-c**. The crude products **14a-c** were purified by column chromatography on silica gel or recrystallization from ethanol.

*Synthesis of 4,5-dichloro-2-{3-hydroxy-2-[(quinolinylmethyl)amino]propyl}-2H-pyridazin-3-ones* ***15a-c***

The procedure for the synthesis of compounds **12a-b** was also applied for the preparation of 4,5-dichloro-2-{3-hydroxy-2-[(quinolinylmethyl)amino]propyl}-2*H*-pyridazin-3-ones **15a-c**.

The crude products **15a-c** were purified by means of column chromatography on silica gel and preparative thin layer chromatography.

*Synthesis of 4,5-dichloro-2-{3-methoxy-2-[(quinolin-4-ylmethyl)amino]propyl}-2H-pyridazin-3-one* ***15d***

The procedure for the synthesis of compound **12c** was also applied for the preparation of 4,5-dichloro-2-{3-methoxy-2-[(quinoline-4-ylmethyl)amino]propyl}-2*H*-pyridazin-3-one **15d**. The crude product was purified by means of preparative thin layer chromatography on silica gel.

*Synthesis of 5-{[1-(arylmethyl)aziridin-2-yl]methoxy}isoquinolines* ***17a-h***

General procedure: To a solution of 1-aryl-2-(bromomethyl)aziridine (1 mmol) in dimethylformamide (20 mL) was added sodium hydroxide (1.5 mmol, 1.5 equiv). After stirring for 1 h at room temperature, 5-hydroxyquinoline **16** was added and the mixture was stirred again for 2-4 h at 100 °C. Subsequently, the reaction mixture was poured into brine (30 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (3 × 20 mL) and subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded the crude products **17a-h**, which were purified by means of column chromatography on silica gel or recrystallization.

*Synthesis of 2-arylmethylamino-3-(isoquinolin-5-yloxy)propane-1-ols* ***18a,b,f,g***

General procedure: To a solution of 5-[(1-arylmethylaziridin-2-yl)methoxy]isoquinoline **17** (1 mmol) in a THF/water (1/1) solvent mixture (25 mL), *para*-toluenesulfonic acid (1 mmol, 1 equiv) was added. After stirring for 3 h at reflux temperature, the reaction mixture was neutralized with sodium bicarbonate, poured into water (30 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic layers were washed with distilled water (3 × 20 mL) and subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded the crude products **18,a,b,f,g**, which were purified by means of column chromatography on silica gel.

*Synthesis of N-arylmethyl-1-(isoquinolin-5-yloxy)-3-methoxypropane-2-amines* ***19a,c-e,h***

General procedure: To a solution of 5-[(1-arylmethylaziridin-2-yl)methoxy]isoquinoline **17** (1 mmol) in methanol (4 mL) in a microwave recipient of 6 mL, boron trifluoride diethyl etherate (0.5 mmol, 0.5 equiv) was added slowly. After microwave irradiation for 30 min at 90 °C, the reaction mixture was neutralized with sodium hydroxide (pH = 7) and then poured into water (30 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with distilled water (3 × 20 mL) and subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded the crude products **19a,c-e,h**, which were purified by means of column chromatography on silica gel.

*Synthesis of $N^2$-arylmethyl-3-(isoquinolin-5-yloxy)-$N^1$-phenylpropane-1,2-diamines **20a-b***

General procedure: To a solution of 5-[(1-arylmethylaziridin-2-yl)methoxy]isoquinoline **17** (1 mmol) in dichloromethane (4 mL) in a microwave recipient of 6 mL, boron trifluoride diethyl etherate (0.5 mmol, 0.5 equiv) and aniline (1.1 mmol, 1.1 equiv) were slowly added. After microwave irradiation for 60 min at 65 °C, the product was observed as a precipitate in the recipient. After removal of the solvent in vacuo, the precipitate was dissolved in DMSO (5 mL), to which water (10 mL) was added, followed by extraction with diethyl ether (3 × 10 mL). The combined organic layers were washed with distilled water (3 × 10 mL) and subsequently dried over anhydrous magnesium sulfate. Filtration of the drying agent and removal of the solvent in vacuo afforded the crude products **20a-b**, which were purified by means of column chromatography on silica gel.

*Synthesis of 2-benzyl-5-[(1-benzylaziridin-2-yl)methoxy]-2-isoquinolinium bromide **21***

To a solution of 5-[(1-benzylaziridin-2-yl)methoxy]isoquinoline **17** (1 mmol) in acetonitrile (25 mL) was added benzyl bromide (1 mmol, 1 equiv). After stirring for 5 h at reflux temperature, the solvent was removed in vacuo affording crude product **21**, which was purified by means of recrystallization from methanol.

*Synthesis of 2-benzyl-5-[2-bromo-3-(dibenzylamino)propyloxy]-2-isoquinolinium bromide **22***

To a solution of 2-benzyl-5-[(1-benzylaziridin-2-yl)methoxy]-2-isoquinolinium bromide **21** (1 mmol) in acetonitrile (25 mL) was added benzyl bromide (1 mmol, 1 equiv). After stirring for 5 h at reflux temperature, the solvent was removed in vacuo affording crude product **22**, which was purified by means of recrystallization from methanol.

## Spectral data

**3-{[2-(Bromomethyl)aziridin-1-yl]methyl}quinoline 7a** (96%)

Brown crystals. $R_f$ ($SiO_2$) = 0.11 (hexane/EtOAc 1/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.72 (1H, d, *J* = 6.1 Hz); 1.90 (1H, d, *J* = 3.3 Hz); 1.99-2.07 (1H, m); 3.27 (1H, dd, *J* = 10.2, 7.4 Hz); 3.39 (1H, dd, *J* = 10.2, 5.5 Hz); 3.63 (1H, d, *J* = 13.8 Hz); 3.71 (1H, d, *J* = 13.8 Hz); 7.52-7.57 (1H, m); 7.67-7.72 (1H, m); 7.80-7.84 (1H, m); 8.10 (1H, d, *J* = 8.3 Hz); 8.19 (1H, d, *J* = 1.1 Hz); 8.88 (1H, d, *J* = 2.2 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 35.2, 35.9, 40.6, 61.6, 126.7, 127.8, 127.9, 129.2, 131.5, 134.6, 147.5, 151.0. IR ($cm^{-1}$): $\nu_{max}$ = 3050, 2988, 2964, 2924, 2863, 1236, 743, 631. MS (70 eV): m/z (%): 277/279 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{13}H_{14}BrN_2$ 277.0335 $[M+H]^+$, found 277.0333. $T_m$ = 57 °C.

**3-{[2-(Bromomethyl)aziridin-1-yl]methyl]-2-chloroquinoline 7b** (98%)

Light yellow crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1,75 (1H, d, *J* = 6.6 Hz); 2.02 (1H, d, *J* = 3.3 Hz); 2.06-2.14 (1H, m); 3.35 (1H, dd, *J* = 10.5, 7.7 Hz); 3.53 (1H, dd, *J* = 10.5, 5.0 Hz); 3.68 (1H, d, *J* = 16.0 Hz); 3.80 (1H, d, *J* = 16.0 Hz); 7.54-7.60 (1H, m); 7.68-7.74 (1H, m); 7.88 (1H, dd, *J* = 8.3, 1.1 Hz); 8.02 (1H, d, *J* = 8.3 Hz); 8.55 (1H, s). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 35.1, 36.1, 41.0, 60.8, 127.2, 127.5, 127.7, 128.3, 130.2, 130.9, 137.3, 146.8, 149.7. IR ($cm^{-1}$): $\nu_{max}$ = 3059, 2979, 2963, 2929, 2856, 1323, 1234, 1030, 746. MS (70 eV): m/z (%) 311/313/315 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{13}H_{13}BrClN_2$ 310.9945 $[M+H]^+$, found 310.9941. $T_m$ = 136 °C.

**4-{[2-(Bromomethyl)aziridin-1-yl]methyl}quinoline 7c** (96%)

Brown viscous oil. $R_f$ ($SiO_2$) = 0.21 (hexane/EtOAc 1/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.71 (1H, d, *J* = 6.6 Hz); 1.97 (1H, d, *J* = 3.3 Hz); 2.02-2.10 (1H, m); 3.34 (1H, dd, *J* = 10.5, 7.7 Hz); 3.44 (1H, dd, *J* = 10.5, 5.5 Hz); 3.79 (1H, d, *J* = 14.9 Hz); 4.15 (1H, d, *J* = 14.9 Hz); 7.54-7.61 (2H, m); 7.69-7.75 (1H, m); 8.00 (1H, dd, *J* = 8.3, 1.1 Hz); 8.13 (1H, d, *J* = 7.7 Hz); 8.91 (1H, d, *J* = 4.4 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 35.0, 36.3, 40.8, 60.7, 119.9, 123.2, 126.69, 126.73, 129.3, 130.2, 144.2, 148.0, 150.5. IR ($cm^{-1}$): $\nu_{max}$ = 3034, 2986, 2918, 2842, 1594, 848, 754. MS (70 eV): m/z (%): 277/279 ($M^+$+1, 100).

**3-{[2-(1-Methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl}quinoline 11a** (10%)

Yellow oil. $R_f$ ($SiO_2$) = 0.12 (EtOAc 100%). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.64 (1H, d, *J* = 6.6 Hz); 1.93 (1H, d, *J* = 3.3 Hz); 2.06-2.13 (1H, m); 3.63 (1H, d, *J* = 14.0 Hz); 3.75 (1H, d, *J* = 14.0 Hz); 3.78 (3H, s); 4.01 (1H, dd, *J* = 11.0, 7.2 Hz); 4.27 (1H, dd, *J* = 11.0, 4.4 Hz); 5.91 (1H, s); 7.52-7.57 (1H, m); 7.67-7.72 (1H, m); 7.81 (1H, d, *J* = 7.7 Hz); 8.10 (1H, d, *J* = 8.3 Hz); 8.23 (1H, s); 8.87 (1H, d, *J* = 2.2 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 31.5, 37.3, 37.8, 61.3, 71.1, 92.3, 119.4 (q, *J* = 268.8 Hz), 126.4, 127.6, 127.8, 128.9, 129.0, 131.8, 132.1 (q, *J* = 38.5 Hz), 134.2, 147.3, 150.8, 160.7. $^{19}$F NMR (282 MHz, $CDCl_3$): δ -60,80 (3F, s). IR ($cm^{-1}$): $\nu_{max}$ = 2988, 2946, 2835, 1493, 1273, 1187, 1123, 1018, 752, 728. MS (70 eV): m/z (%): 363 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{18}F_3N_4O$ 363.1427 $[M+H]^+$, found 363.1434.

**2-Chloro-3-[2-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-ylmethyl]quinoline 11b** (28%)

Light yellow crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.70 (1H, d, *J* = 6.6 Hz); 2,03 (1H, d, *J* = 3.3 Hz); 2.09-2.16 (1H, m); 3.58 (1H, d, *J* = 16.2 Hz); 3.88 (1H, d, *J* = 16.2 Hz); 3.81 (3H, s); 4.04 (1H, dd, *J* = 11.0, 7.7 Hz); 4.43 (1H, dd, J = 11.0, 3.9 Hz); 5.96 (1H, s); 7.55-7.59 (1H, m); 7.69-7.74 (1H, m); 7.84 (1H, d, *J* = 8.3 Hz); 8.01 (1H, d, J = 8.3 Hz); 8.62 (1H, s). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 31.7, 37.6, 38.4, 60.5, 71.4, 92.5, 119.6 (q, *J* = 267.7 Hz), 127.1, 127.60, 127.64, 128.2, 130.0, 131.2, 132.7 (q, *J* = 39.2 Hz), 137.0, 146.7, 149.7, 161.0. $^{19}$F NMR (282 MHz, $CDCl_3$): δ -60.69 (3F, s). IR ($cm^{-1}$): $\nu_{max}$ = 2941, 2928, 1492, 1272, 1113, 1023. MS (70 eV): m/z (%): 397/399 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{17}ClF_3N_4O$ 397.1037 $[M+H]^+$, found 397.1040. $T_m$ = 87.7 °C. Recrystallization from ethanol.

**4-{[2-(1-Methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxymethyl)aziridin-1-yl]methyl}quinoline 11c** (12%)

Yellow oil. $R_f$ ($SiO_2$) = 0.15 (hexane/EtOAc 1/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.64 (1H, d, *J* = 6.6 Hz); 1.99 (1H, d, *J* = 3.3 Hz); 2.07-2.14 (1H, m); 3.80 (3H, s); 3.98 (2H, s); 4.08 (1H, dd, J = 11.0, 7.2 Hz); 4.31 (1H, dd, J = 11.0, 4.4 Hz); 5.98 (1H, s); 7.52-7.57 (1H, m); 7.68-7.74 (2H, m); 7.94 (1H, d, *J* = 7.7 Hz); 8.13 (1H, d, *J* = 8.8 Hz); 8.90 (1H, d, *J* = 4.4 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 32.0, 37.6, 38.3, 60.5, 71.3, 92.6, 119.57 (q, *J* = 270.0 Hz), 119.60, 123.0, 126.61, 126.63, 129.2, 130,2, 132,7 (q, J = 39,2 Hz), 144,6, 147,9, 150,5, 161.0. $^{19}$F NMR (282 MHz, $CDCl_3$): d -60.68 (3F, s). IR ($cm^{-1}$): $\nu_{max}$ = 2987, 2950, 1492, 1273, 1187, 1124, 1019, 755, 729. MS (70 eV): m/z (%): 363 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{18}F_3N_4O$ 363.1427 $[M+H]^+$, found 363.1432.

**2-(Quinolin-3-ylmethyl)amino-3-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxy)propan-1-ol 12a** (11%)

Viscous dark yellow oil. $R_f$ ($SiO_2$) = 0.12 (EtOAc/$Et_3N$ 97/3). $^1H$ NMR (300 MHz, $CDCl_3$): δ 3,14 (1H, quint, *J* = 5.5 Hz); 3.60-3.83 (2H, m); 3.79 (3H, s); 4.10 (2H, d, *J* = 2,2 Hz); 4.24 (1H, dd, *J* = 10.6, 5.5 Hz); 4.31 (1H, dd, *J* = 10.6, 5.2 Hz); 5.99 (1H, s); 7.52-7.57 (1H, m); 7.65-7.72 (1H, m); 7.79 (1H, d, *J* = 8.3 Hz); 8.10 (1H, d, *J* = 8.3 Hz); 8.91 (1H, d, *J* = 2.2 Hz). $^{13}C$ NMR (75 MHz, ref = $CDCl_3$): δ 37.3, 48.8, 57.8, 61.0, 69.1, 92.2, 119.4 (q, *J* = 268.8 Hz), 126.5, 127.5, 127.8, 128.7, 128.9, 132.3 (q, *J* = 39.2 Hz), 133.2, 134.5, 147.0, 151.2, 161.0. $^{19}F$ NMR (282 MHz, $CDCl_3$): δ -60,76 (3F, s). IR ($cm^{-1}$): $\nu_{NH, OH}$ = 3284, $\nu_{max}$ = 2932, 2878, 1493, 1459, 1273, 1187, 1122, 1078, 1038, 751. MS (70 eV): m/z (%): 381 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{20}F_3N_4O_2$ 381.1533 $[M+H]^+$, found 381.1542.

**2-(2-Chloroquinolin-3-ylmethyl)amino-3-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxy)propan-1-ol 12b** (24%)

White crystals. $^1H$ NMR (300 MHz, $CDCl_3$): δ 3.17 (1H, quint, *J* = 5.5 Hz); 3.65 (1H, dd, *J* = 11.1, 5.2 Hz); 3.81 (1H, dd, *J* = 11.1, 5.0 Hz); 3.77 (3H, s); 4.13 (2H, s); 4.26 (1H, dd, *J* = 10.9, 5.8 Hz); 4.32 (1H, dd, *J* = 10.9, 5.0 Hz); 5.99 (1H, s); 7.53-7.59 (1H, m); 7.69-7.75 (1H, m); 7.81 (1H, d, *J* = 7.7 Hz); 8.01 (1H, d, *J* = 8.8 Hz); 8.23 (1H, s). $^{13}C$ NMR (75 MHz, ref = $CDCl_3$): δ 37.7, 48.5, 57.8, 61.1, 68.9, 92.6, 119.5 (q, *J* = 268.8 Hz), 127.3, 127.41, 127.44, 128.3, 130.3, 131.7, 133,1 (q, *J* = 78.5 Hz), 137.5, 146.9, 150.6, 161.1. $^{19}F$ NMR (282 MHz, $CDCl_3$): δ -60.75 (3F, s). IR ($cm^{-1}$): $\nu_{NH, OH}$ = 3270, $\nu_{max}$ = 2954, 2830, 1482, 1270, 1163, 1154, 1114, 1033. MS (70 eV): m/z (%): 415/417 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{19}ClF_3N_4O_2$ 415.1143 $[M+H]^+$, found 415.1152. $T_m$ = 120,1 °C. Recrystallization from ethanol.

***N*-[(2-chloroquinolin-3-yl)methyl]-1-methoxy-3-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxy)propane-2-amine 12c** (12%)

Yellow oil. $R_f$ ($SiO_2$) = 0.23 (hexane/EtOAc 1/1). $^1H$ NMR (300 MHz, $CDCl_3$): δ 3.24 (1H, quint, *J* = 5.5 Hz); 3.38 (3H, s); 3.51-3.61 (2H, m); 3.77 (3H, s); 4.15 (2H, s); 4.23 (2H, d, *J* = 5.5 Hz); 6.01 (1H, s); 7.52-7.57 (1H, m); 7.67-7.73 (1H, m); 7.80 (1H, d, *J* = 8.3 Hz); 8.00 (1H, d, *J* = 8.3 Hz); 8.30 (1H, s). $^{13}C$ NMR (75 MHz, ref = $CDCl_3$): δ 37.6, 48.6, 56.2, 59.2, 69.2, 72.5, 92.4, 119.5 (q, *J* = 268.8 Hz); 127.0, 127.4, 127.6, 128.2, 130.0, 131.2, 132.6 (q, *J* = 39.2 Hz), 137.3, 146.7, 150.6, 161.1. $^{19}F$ NMR (282 MHz, $CDCl_3$): δ -60.70 (3F, s). IR ($cm^{-1}$): $\nu_{NH}$ = 3330, $\nu_{max}$ = 2929, 2896, 1493, 1458, 1274, 1188, 1129, 1038, 1029. MS (70 eV): m/z (%): 429/431 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{21}ClF_3N_4O_2$ 429.1300 $[M+H]^+$, found 429.1300.

***N*-[(2-methoxyquinolin-3-yl)methyl]-1-methoxy-3-(1-methyl-3-trifluoromethyl-1*H*-pyrazole-5-yloxy)propane-2-amine 12d** (38%)

Yellow oil. $R_f$ ($SiO_2$) = 0.14 (hexane/EtOAc 1/1). $^1H$ NMR (300 MHz, $CDCl_3$): δ 3.19 (1H, quint, *J* = 5.5 Hz); 3.35 (3H, s); 3.52 (2H, d, *J* = 5.5Hz); 3.76 (3H, s); 3.99 (2H, s); 4.09 (3H, s); 4.19 (2H, d, *J* = 5.5 Hz); 5.99 (1H, s); 7.33-7.38 (1H, m); 7.52-7.61 (1H, m); 7.67-7.70 (1H, m); 7.82 (1H, d, *J* = 8.3 Hz); 7.98 (1H, s. $^{13}C$ NMR (75 MHz, ref = $CDCl_3$): δ 37.6, 46.7, 53.5, 55.7, 59.1, 69.3, 72.5, 92.4, 119.6 (q, *J* = 268.8 Hz); 124.1, 124.4, 125.4, 126.9, 127.3, 129.0, 132.6 (q, *J* = 41.5 Hz), 136.5, 145.8, 160.8, 161.2. $^{19}F$ NMR (282 MHz, $CDCl_3$): δ -60.68 (3F, s). IR ($cm^{-1}$): $\nu_{NH}$ = 3333, $\nu_{max}$ = 2952, 2897, 1494, 1274, 1188, 1147, 1126. MS (70 eV): m/z (%): 425 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{24}F_3N_4O_3$ 425.1795 $[M+H]^+$, found 425.1795.

**1-(1-Quinolin-3-ylmethylaziridin-2-ylmethyl)-4-trifluoromethyl-1*H*-pyrimidin-2-one 13a** (45%)

Dark yellow oil. $R_f$ ($SiO_2$) = 0.08 ($CH_2Cl_2$/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.82 (1H, d, *J* = 6.6 Hz); 1.98 (1H, d, *J* = 3.3 Hz); 2.33-2.56 (1H, m); 2.90 (1H, d, *J* = 12.7 Hz); 4.08 (1H, d, *J* = 12.7 Hz); 2.90 (1H, dd, *J* = 13.2, 8.8 Hz); 4.70 (1H, dd, *J* = 13.2, 2.8 Hz); 5.84 (1H, d, *J* = 6.6 Hz); 7.52-7.58 (2H, m); 7.70-7.81 (3H, m); 8.06 (1H, d, *J* = 8.3 Hz); 8.24 (1H, d, *J* = 1.1 Hz); 8.66 (1H, d, *J* = 5.0 Hz); 8.83 (1H, d, *J* = 2.2 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 33.2, 37.2, 54.8, 61.8, 98.6, 127.4, 127.5, 127.6, 129.1, 129.9, 131.3, 134.9, 147.4, 150.9, 151.5, 154.8. $^{19}$F NMR (282 MHz, $CDCl_3$): δ -71.41 (3F, s). IR ($cm^{-1}$): $\nu_{max}$ =3062, 2993, 1662, 1312, 1192, 1153. MS (70 eV): m/z (%): 361 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{16}F_3N_4O$ 361.1271 $[M+H]^+$, found 361.1276.

**1-[1-(2-Chloroquinolin-3-ylmethyl)aziridin-2-ylmethyl]-4-trifluoromethyl-1*H*-pyrimidin-2-one 13b** (12%)

Orange-brown oil. $R_f$ ($SiO_2$) = 0.02 ($CHCl_3$/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.78 (1H, d, *J* = 6.6 Hz); 2.03 (1H, d, *J* = 3.3 Hz); 2.31-2.37 (1H, m); 3.17 (1H, dd, *J* = 13.2, 7.7 Hz); 3.22 (1H, d, *J* = 13.8 Hz); 3.89 (1H, d, *J* = 13.8 Hz); 4.64 (1H, dd, *J* = 13.2, 3.3 Hz); 6.14 (1H, d, *J* = 6.6 Hz); 7.54 (1H, t, *J* = 7.7 Hz); 7.69-7.75 (2H, m); 7.88-8.02 (3H, m). $^{13}$C NMR (75 MHz, ref = acetone-d6): δ 32.8, 36.9, 53.9, 60.3, 98.7, 119.6 (q, *J* = 276.9 Hz), 127.3, 127.4, 127.8, 127.9, 130.3, 131.5, 137.9, 146.8, 150.1, 153.6, 154.6, 161.9 (q, *J* = 35.8 Hz). $^{19}$F NMR (282 MHz, $CDCl_3$): δ -71.35 (3F, s). IR ($cm^{-1}$): $\nu_{max}$ = 2923, 2854, 1671, 1320, 1902, 1154, 1140, 755, 733. MS (70 eV): m/z (%): 395/7 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{21}ClF_3N_4O_2$ 395.0881 $[M+H]^+$, found 395.0876.

**4,5-Dichloro-2-[1-(quinolin-3-ylmethyl)aziridin-2-ylmethyl]-2*H*-pyridazin-3-one 14a** (32%)

White crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.76 (1H, d, *J* = 6.1 Hz); 2.06 (1H, d, *J* = 3.3 Hz); 2.21-2.28 (1H, m); 2.87 (1H, d, *J* = 12.7 Hz); 4.17 (1H, d, *J* = 12.7 Hz); 3.61 (1H, dd, *J* = 13.2, 8.8 Hz); 4.52 (1H, dd, *J* = 13.2, 3.9 Hz); 7.34 (1H, s); 7.52-7.58 (1H, m); 7.68-7.77 (2H, m); 7.90 (1H, d, *J* = 2.2 Hz); 8.09 (1H, d, *J* = 8.3 Hz); 8.78 (1H, d, *J* = 2.2 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 33.9, 36.1, 56.4, 61.9, 127.1, 127.7, 129,3, 129,5, 131,5, 133,4, 134,9, 135.3, 136.4, 147.2, 151.5, 156.2. IR ($cm^{-1}$): $\nu_{max}$ = 3034, 2986, 1646, 748, 721. MS (70 eV): m/z (%): 361/363/365 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{17}H_{15}Cl_2N_4O$ 361.0617 $[M+H]^+$, found 361.0615. $T_m$ = 106 °C. Recrystallization from ethanol.

**4,5-Dichloro-2-[1-(2-chloroquinolin-3-ylmethyl)aziridin-2-ylmethyl]-2*H*-pyridazin-3-one 14b** (21%)

White crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.71 (1H, d, *J* = 6.6 Hz); 2.11 (1H, d, *J* = 3.3 Hz); 2.24-2.32 (1H, m); 3.33 (1H, d, *J* = 14.1 Hz); 3.93 (1H, d, *J* = 14.1 Hz); 3.95 (1H, dd, *J* = 13.2, 7.7 Hz); 4.50 (1H, dd, *J* = 13.2, 4.4 Hz); 7.54 (1H, s); 7.54-7.60 (1H, m); 7.70-7.75 (1H, m); 7.79-7.82 (1H, m); 8.01 (1H, d, *J* = 9.4 Hz); 8.22 (1H, s). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 33.4, 36.8, 55.9, 61.0, 127.3, 127.4, 127.5, 128.3, 130.4, 130.9, 133.9, 135.5, 136.6, 137.7, 146.8, 150.2, 156.5. IR ($cm^{-1}$): $\nu_{max}$ = 3044, 2923, 1646, 1047, 963, 753. MS (70 eV): m/z (%): 395/397/399/401 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{17}H_{14}Cl_3N_4O$ 395.0228 $[M+H]^+$, found 395.0222. $T_m$ = 129,9 °C. Recrystallization from ethanol.

**4,5-Dichloro-2-[1-(quinolin-4-ylmethyl)aziridin-2-ylmethyl]-2*H*-pyridazin-3-one 14c** (34%)

Yellow oil. $R_f$ ($SiO_2$) = 0.06 (hexane/EtOAc 1/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.78 (1H, d, *J* = 6.6 Hz); 2.11 (1H, d, *J* = 3.3 Hz); 2.21-2.27 (1H, m); 3.05 (1H, d, *J* = 12.9 Hz); 4.51 (1H, d, *J* = 12.9 Hz); 3.62 (1H,

dd, *J* = 13.2, 8.8 Hz); 4.47 (1H, dd, *J* = 13.2, 5.0 Hz); 6.93 (1H, s); 7.20 (1H, d, *J* = 4.4 Hz); 7.56-7.61 (1H, m); 7.69-7.74 (1H, m); 8.10 (1H, d, *J* = 8.3 Hz); 8.18 (1H, d, *J* = 8.3 Hz); 8.79 (1H, d, *J* = 4.4 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 34.4, 35.8, 55.9, 61.1, 120.9, 124.3, 126.4, 126.5, 129.0, 129.8, 133.1, 134.5, 136.0, 143.8, 147.6, 150.0, 155.7. IR ($cm^{-1}$): $\nu_{max}$ = 3062, 2984, 2950, 1650, 760, 750, 722. MS (70 eV): m/z (%): 361/363/365 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{17}H_{15}Cl_2N_4O$ 361.0617 $[M+H]^+$, found 361.0624.

**4,5-Dichloro-2-{3-hydroxy-2-[(quinolin-3-ylmethyl)amino]propyl}-2*H*-pyridazin-3-one 15a** (8%)

Yellow oil. $R_f$ ($SiO_2$) = 0.10 (EtOAc 100%). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.14-3.20 (1H, m); 3.51 (1H, dd, *J* = 11.8, 4.7 Hz); 3.69 (1H, dd, *J* = 11.8, 4.1 Hz); 4.02 (1H, d, *J* = 13.8 Hz); 4.09 (1H, d, *J* = 13.8 Hz); 4.31 (1H, dd, *J* = 13.2, 6.1 Hz); 4.39 (1H, dd, *J* = 13.2, 6.1 Hz); 7.52-7.57 (1H, m); 7.67-7.80 (3H, m); 8.05 (1H, d, *J* = 1.7 Hz); 8.09 (1H, d, *J* = 8.8 Hz); 8.85 (1H, d, *J* = 2.2 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 48.8, 53.3, 57.7, 61.3, 126.9, 127.7, 127.9, 129.1, 129.3, 132.8, 134.3, 134.8, 136.2, 136.9, 147.3, 151.4, 157.5. IR ($cm^{-1}$): $\nu_{NH, OH}$ = 3306, $\nu_{max}$ = 3059, 3008, 2937, 2856, 1654, 1579, 959, 748. MS (70 eV): m/z (%): 379/381/383 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{17}H_{17}Cl_2N_4O_2$ 379.0723 $[M+H]^+$, found 379.0725.

**4,5-Dichloro-2-{3-hydroxy-2-[(2-chloroquinolin-3-ylmethyl)amino]propyl}-2*H*-pyridazin-3-one 15b** (9%)

Viscous yellow oil. $R_f$ ($SiO_2$) = 0.11 (hexane/EtOAc 2/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.16-3.22 (1H, m); 3.58 (1H, dd, *J* = 11.6, 4.4 Hz); 3.75 (1H, dd, *J* = 11.6, 3.9 Hz); 3.97 (1H, d, *J* = 15.1 Hz); 4.09 (1H, d, *J* = 15.1 Hz); 4.27 (1H, dd, *J* = 13.2, 6.6 Hz); 4.40 (1H, dd, *J* = 13.2, 6.1 Hz); 7.51-7.56 (1H, m); 7.66-7.72 (2H, m); 7.76 (1H, d, *J* = 7.7 Hz); 7.96 (1H, d, *J* = 8.3 Hz); 8.11 (1H, s). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 48.5, 53.5, 57.7, 61.5, 127.3, 127.5, 128.2, 130.3, 131.5, 134.3, 136.1, 136.8, 137.7, 146.8, 150.6, 157.4. IR ($cm^{-1}$): $\nu_{NH, OH}$ = 3329, $\nu_{max}$ = 3062, 2932, 2890, 2872, 1654, 1030, 959, 752, 730. MS (70 eV): m/z (%): 413/415/417/419 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{17}H_{16}Cl_3N_4O_2$ 413.0333 $[M+H]^+$, found 413.0339.

**4,5-Dichloro-2-{3-hydroxy-2-[(quinolin-4-ylmethyl)amino]propyl}-2*H*-pyridazin-3-one 15c** (11%)

Colorless oil. $R_f$ ($SiO_2$) = 0.11 (EtOAc 100%). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.20-3.23 (1H, m); 3.57 (1H, dd, *J* = 11.4, 4.1 Hz); 3.78 (1H, dd, *J* = 11.4, 3.3 Hz); 4.15-4.43 (4H, m); 7.33 (1H, d, *J* = 3.9 Hz); 7.50-7.55 (2H, m); 7.67-7.72 (1H, m); 8.00 (1H, d, *J* = 8.3 Hz); 8.09 (1H, d, *J* = 8.8 Hz); 8.79 (1H, d, *J* = 4.4 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 47.8, 53.4, 57.8, 61.2, 120.5, 123.4, 126.7, 126.8, 129.4, 130.2, 134.2, 135.9, 136.6, 145.2, 148.2, 150.2, 157.4. IR ($cm^{-1}$): $\nu_{NH, OH}$ = 3313, $\nu_{max}$ = 3088, 3060, 2916, 2862, 1651, 1579, 958, 751, 729. MS (70 eV): m/z (%): 379/381/383 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{17}H_{17}Cl_2N_4O_2$ 379.0723 $[M+H]^+$, found 379.0726.

**4,5-Dichloro-2-{3-methoxy-2-[(quinolin-4-ylmethyl)amino]propyl}-2*H*-pyridazin-3-one 15d** (10%)

Colorless oil. $R_f$ ($SiO_2$) = 0.50 (EtOAc 100%). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.24-3.33 (1H, m); 3.39 (3H, s); 3.46 (1H, dd, *J* = 9.9, 5.0 Hz); 3.61 (1H, dd, *J* = 9.9, 5.0 Hz); 4.04 (1H, dd, *J* = 13.2, 7.7 Hz); 4.39 (1H, dd, *J* = 13.2, 5.0 Hz); 4.14 (1H, d, *J* = 14.3 Hz); 4.40 (1H, d, *J* = 14.3 Hz); 7.31 (1H, d, *J* = 4.4 Hz); 7.40 (1H, s); 7.47-7.53 (1H, m); 7.66-7.72 (1H, m); 8.01 (1H, dd, J = 8.3, 1.1 Hz); 8.09 (1H, d, *J* = 8.3 Hz); 8.81 (1H, d, *J* = 4.4 Hz). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 48.2, 54.1, 55.9, 59.3, 72.5, 120.8, 123.7,

126.5, 126.9, 129.2, 130.2, 134.0, 135.2, 136.2, 145.4, 148.2, 150.2, 157.0. IR ($cm^{-1}$): $\nu_{NH}$ = 3327, $\nu_{max}$ = 1658, 1581, 1136, 1113, 960, 751. MS (70 eV): m/z (%): 393/395/397 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{18}H_{21}Cl_2N_4O_2$ 393.0880 $[M+H]^+$, found 393.0872.

**5-[(1-Benzylaziridin-2-yl)methoxy]isoquinoline 17a** (90%)

Dark brown viscous oil. $R_f$ ($SiO_2$) = 0.22 (hexane/EtOAc 1/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.66 (1H, d, *J* = 6.6 Hz); 1.93 (1H, d, *J* = 3.9 Hz); 2.07-2.14 (1H, m); 3.30 (1H, d, *J* = 13.2 Hz); 3.75 (1H, d, *J* = 13.2 Hz); 3.91 (1H, dd, *J* = 10.5, 7.7 Hz); 4.24 (1H, dd, *J* = 10.5, 4.4 Hz); 6.91 (1H, d, *J* = 7.2 Hz); 7.26-7.49 (6H, m); 7.45 (1H, d, *J* = 7.7 Hz); 7.75 (1H, d, *J* = 6.1 Hz); 8.46 (1H, d, *J* = 6.1 Hz); 9.16 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.8, 37.8, 64.5, 70.8, 108.5, 115.4, 119.4, 127.3, 127.4, 128.3, 128.5, 128.6, 129.5, 138.9, 142.6, 151.8, 153.5. IR ($cm^{-1}$): $\nu_{max}$ = 3027, 2985, 2924, 2833, 1583, 1277, 1249, 1109, 830, 735, 697. MS m/z (%): 291 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{19}N_2O$: 291.1497 $[M+H]^+$, found: 291.1491.

**5-{[1-(4-Chlorobenzyl)aziridin-2-yl]methoxy}isoquinoline 17b** (80%)

Orange crystals.$^1$H NMR (300 MHz, $CDCl_3$): δ 1.67 (1H, d, *J* = 6.6 Hz); 1.95 (1H, d, *J* = 3.3 Hz); 2.07-2.14 (1H, m); 3.24 (1H, d, *J* = 13.2 Hz); 3.76 (1H, d, *J* = 13.2 Hz); 3.89 (1H, dd, *J* = 10.5, 7.7 Hz); 4.27 (1H, dd, *J* = 10.5, 3.9 Hz); 6.92 (1H, d, *J* = 6.6 Hz); 7.28-7.52 (6H, m); 7.70 (1H, d, *J* = 6.6 Hz); 8.52 (1H, d, *J* = 6.6 Hz); 9.18 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.8, 37.8, 63.8, 70.7, 108.5, 115.2, 119.5, 127.3, 128.4, 128.7, 129.5, 129.7, 133.1, 137.4, 142.7, 151.9, 153.5. IR ($cm^{-1}$): $\nu_{max}$ = 3062, 2986, 2904, 2836, 1587, 1493, 1282, 1171, 1087, 818, 802, 756, 750. MS m/z (%): 325/7 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{18}ClN_2O$: 325.1108 $[M+H]^+$, found: 325.1100. $T_m$ = 80.4 °C. Recrystallization from ethanol.

**5-{[1-(4-Fluorobenzyl)aziridin-2-yl]methoxy}isoquinoline 17c** (75%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.20 (hexane/EtOAc 1/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.66 (1H, d, *J* = 6.6 Hz); 1.93 (1H, d, *J* = 3.3 Hz); 2.07-2.15 (1H, m); 3.28 (1H, d, *J* = 13.2 Hz); 3.71 (1H, d, *J* = 13.2 Hz); 3.90 (1H, dd, *J* = 10.2, 7.7 Hz); 4.26 (1H, dd, *J* = 10.2, 3.9 Hz); 6.93 (1H, d, *J* = 7.7 Hz); 6.99-7.05 (2H, m); 7.35-7.52 (4H, m); 7.74 (1H, d, *J* = 6.1 Hz); 8.50 (1H, d, *J* = 6.1 Hz); 9.18 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.8, 37.8, 63.8, 70.7, 108.5, 115.2, 115.4 (d, *J* = 20.8 Hz), 119.5, 127.4, 128.4, 129.5, 129.9 (d, *J* = 8.1 Hz), 134.7, 142.7, 151.9, 153.5, 162.2 (d, *J* = 244.6 Hz). $^{19}$F NMR (282 MHz, Ref = $CDCl_3$): -115.34 (1F, s); IR ($cm^{-1}$): $\nu_{max}$ = 3044, 2985, 2928, 2842, 1583, 1502, 1493, 1282, 1254, 1215, 1116, 1004, 867, 827, 816, 798, 780, 747. MS m/z (%): 309 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{18}FN_2O$: 309.1398 $[M+H]^+$, found: 309.1398.

**5-{[1-(2-Chlorobenzyl)aziridin-2-yl]methoxy}isoquinoline 17d** (74%)

Brown viscous oil. $R_f$ ($SiO_2$) = 0.19 (hexane/EtOAc 1/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.72 (1H, d, *J* = 6.6 Hz); 1.99 (1H, d, *J* = 3.3 Hz); 2.16-2.23 (1H, m); 3.48 (1H, d, *J* = 14.9 Hz); 3.84 (1H, d, *J* = 14.9 Hz); 3.98 (1H, dd, *J* = 10.5, 7.7 Hz); 4.32 (1H, dd, *J* = 10.5, 3.9 Hz); 6.98 (1H, dd, *J* = 7.7, 1.1 Hz); 7.21-7.27 (2H, m); 7.34-7.37 (1H, m); 7.43-7.53 (2H, m); 7.73-7.76 (1H, m); 7.87 (1H, d, *J* = 6.1 Hz); 8.49 (1H, d, *J* = 6.1 Hz); 9.19 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.7, 38.1, 61.2, 70.9, 108.6, 115.3, 119.5, 127.0, 127.4, 128.3, 128.5, 129.3, 129.5, 129.6, 133.1, 136.7, 142.7, 151.9, 153.5. IR ($cm^{-1}$): $\nu_{max}$ = 3059, 2984, 2922, 2855, 1583, 1277, 1248, 1109, 829, 747. MS m/z (%): 325/7 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{18}ClN_2O$: 325.1108 $[M+H]^+$, found: 325.1101.

**5-{[1-(4-Methoxybenzyl)aziridin-2-yl]methoxy}isoquinoline 17e** (77%)

Orange viscous oil. $R_f$ ($SiO_2$) = 0.21 (hexane/EtOAc 1/3). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.67 (1H, d, *J* = 6.6 Hz); 1.92 (1H, d, *J* = 3.3 Hz); 2.08-2.15 (1H, m); 3.22 (1H, d, *J* = 13.2 Hz); 3.74 (1H, d, *J* = 13.2 Hz); 3.81 (3H, s); 3.91 (1H, dd, *J* = 10.5, 7.7 Hz); 4.26 (1H, dd, *J* = 10.5, 4.4 Hz); 6.85-6.91 (2H, m); 6.93 (1H, dd, *J* = 7.7, 1.1 Hz); 7.30-7.35 (2H, m); 7.41-7.52 (2H, m); 7.73 (1H, d, *J* = 6.1 Hz); 8.47 (1H, d, *J* = 6.1 Hz); 9.18 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.8, 37.6, 55.3, 64.0, 70.8, 108.5, 113.9, 115.4, 119.4, 127.4, 128.5, 129.5, 129.6, 131.0, 142.6, 151.8, 153.6, 159.0. IR ($cm^{-1}$): $\nu_{max}$ = 3048, 3000, 2984, 2934, 2840, 1581, 1509, 1278, 1252, 1242, 1110, 1030, 989, 825, 818, 802, 756, 745. MS m/z (%): 321 ($M^+$+1, 100). HRMS calcd for $C_{20}H_{21}N_2O_2$: 321.1598 $[M+H]^+$, found: 321.1598.

**5-{[1-(2,4-Dichlorobenzyl)aziridin-2-yl]methoxy}isoquinoline 17f** (82%)

White crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.72 (1H, d, *J* = 6.6 Hz); 2.01 (1H, d, *J* = 3.3 Hz); 2.15-2.20 (1H, m); 3.42 (1H, d, *J* = 14.9 Hz); 3.80 (1H, d, *J* = 14.9 Hz); 3.96 (1H, dd, *J* = 10.5, 7.7 Hz); 4.34 (1H, dd, *J* = 10.5, 3.3 Hz); 6.98 (1H, d, *J* = 8.3 Hz); 7.21 (1H, dd, *J* = 8.3, 1.7 Hz); 7.38 (1H, d, *J* = 1.7 Hz); 7.44-7.55 (2H, m); 7.69 (1H, d, *J* = 8.3 Hz); 7.84 (1H, d, *J* = 5.5 Hz); 8.53 (1H, d, *J* = 5.5 Hz); 9.21 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.7, 38.1, 60.6, 70.7, 108.6, 115.1, 119.6, 127.3, 127.4, 128.4, 129.0, 129.5, 130.5, 133.5, 133.7, 135.4, 142.8, 152.0, 153.4. IR ($cm^{-1}$): $\nu_{max}$ = 3020, 2982, 2945, 2831, 1586, 1393, 1279, 1252, 1113, 992, 836, 824, 806, 797, 751, 744. MS m/z (%): 359/361/363 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{17}Cl_2N_2O$: 359.0718 $[M+H]^+$, found: 359.0716. $T_m$ = 107.1 °C. Recrystallization from ethanol.

**5-{[1-(4-(Trifluoromethyl)benzyl)aziridin-2-yl]methoxy}isoquinoline 17g** (84%)

Orange crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.69 (1H, d, *J* = 6.6 Hz); 1.99 (1H, d, *J* = 3.3 Hz); 2.10-2.18 (1H, m); 3.40 (1H, d, *J* = 13.8 Hz); 3.81 (1H, d, *J* = 13.8 Hz); 3.95 (1H, dd, *J* = 10.5, 7.7 Hz); 4.29 (1H, dd, *J* = 10.5, 3.9 Hz); 6.95 (1H, dd, *J* = 7.7, 1.1 Hz); 7.42-7.61 (6H, m); 7.77 (1H, d, *J* = 5.5 Hz); 8.47 (1H, d, *J* = 5.5 Hz); 9.19 (1H, s); $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.8, 38.1, 63.9, 70.7, 108.6, 115.1, 119.6, 124.3 (q, *J* = 273.8 Hz), 125.5 (q, *J* = 3.5 Hz), 127.4, 128.4, 129.5, 142.7, 142.9, 151.9, 153.4. $^{19}$F NMR (282 MHz, Ref = $CDCl_3$): -62.24 (3F, s). IR ($cm^{-1}$): $\nu_{max}$ = 3062, 2906, 1322, 1162, 1121, 1108, 1064, 828. MS m/z (%): 359 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{18}F_3N_2O$: 359.1371 $[M+H]^+$, found: 359.1369. $T_m$ = 96.8 °C. Recrystallization from ethanol.

**5-[1-(2-Methoxybenzyl)aziridin-2-ylmethoxy]isoquinoline 17h** (65%)

Brown oil. $R_f$ ($SiO_2$) = 0.26; $CH_2Cl_2$/MeOH (95/5). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.70 (1H, d, *J* = 6.6 Hz); 1.94 (1H, d, *J* = 3.3 Hz); 2.12-2.21 (1H, m); 3.37 (1H, d, *J* = 13.2 Hz); 3.78 (1H, d, *J* = 13.2 Hz); 3.81 (3H, s); 3.98 (1H, dd, *J* = 10.5, 7.7 Hz); 4.28 (1H, dd, *J* = 10.5, 4.4 Hz); 6.86 (1H, d, *J* = 8.3 Hz); 6.93-6.98 (2H, m); 7.25-7.31 (1H, m); 7.41-7.58 (3H, m); 7.84 (1H, d, *J* = 6.1 Hz); 8.48 (1H, d, *J* = 6.1 Hz); 9.18 (1H, s). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 31.8, 37.8, 55.4, 58.6, 70.9, 108.6, 110.2, 115.4, 119.3, 120.7, 127.3, 127.4, 128.3, 129.5, 142.6, 151.8, 153.6, 157.1, 162.6. IR ($cm^{-1}$): $\nu_{max}$ = 2933, 2836, 1672, 1584, 1492, 1277,1241, 1108, 1028, 752. MS (70 eV): m/z (%): 321 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{21}N_2O_2$ 321.1598 $[M+H]^+$, found 321.1601.

**2-Benzylamino-3-(isoquinolin-5-yloxy)propan-1-ol 18a** (94%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.21 (EtOAc/MeOH 95/5). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.27 (1H, quint, *J* = 5.5 Hz); 3.76 (1H, dd, *J* = 11.0, 5.0 Hz); 3.89 (1H, dd, *J* = 11.0, 4.4 Hz); 3.95 (2H, s); 4.18 (2H, dd, *J* = 5.5, 1.7 Hz); 6.94 (1H, t, *J* = 4.4 Hz); 7.25-7.44 (7H, m); 7.80 (1H, d, *J* = 6.1 Hz); 8.41 (1H, d, *J* = 6.1 Hz); 9.08 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 51.6, 57.6, 61.1, 68.1, 108.7, 115.0, 119.7, 127.3, 127.5, 128.2, 128.3, 128.7, 129.4, 140.1, 142.4, 151.8, 153.3. IR ($cm^{-1}$): $\nu_{NH,OH}$ = 3227, $\nu_{max}$ = 1584, 1392, 1276, 1249, 1110, 828, 732, 698. MS m/z (%): 309 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{21}N_2O_2$: 309.1603 $[M+H]^+$, found: 309.1604.

**2-(4-Chlorobenzyl)amino-3-(isoquinolin-5-yloxy)propan-1-ol 18b** (85%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.20 (EtOAc/MeOH 95/5). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.25 (1H, quint, *J* = 5.5 Hz); 3.76 (1H, dd, *J* = 11.0, 5.5 Hz); 3.89 (1H, dd, *J* = 11.0, 5.0 Hz); 3.92 (2H, s); 4.19 (2H, dd, *J* = 5.5, 2.8 Hz); 6.99 (1H, dd, *J* = 5.5, 3.3 Hz); 7.25-7.32 (4H, m); 7.44-7.48 (2H, m); 7.80 (1H, d, *J* = 6.1 Hz); 8.44 (1H, d, *J* = 6.1 Hz); 9.10 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 50.8, 57.5, 61.2, 68.0, 108.7, 114.9, 119.8, 127.5, 128.3, 128.8, 129.4, 129.5, 133.0, 138.6, 142.5, 151.9, 153.3. IR ($cm^{-1}$): $\nu_{NH,OH}$ = 3222, $\nu_{max}$ = 1492, 1276, 1249, 1110, 1088, 828, 800, 748, 734. MS m/z (%): 343/5 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{19}ClN_2O_2$: 343.1213 $[M+H]^+$, found: 343.1215.

**2-(2,4-Dichlorobenzyl)amino-3-(isoquinolin-5-yloxy)propan-1-ol 18f** (89%)

Yellow viscous oil. Rf ($SiO_2$) = 0.19 (EtOAc/MeOH 95/5). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.28 (1H, quint, *J* = 5.5 Hz); 3.73 (1H, dd, *J* = 11.0, 4.4 Hz); 3.92 (1H, dd, *J* = 11.0, 5.0 Hz); 4.01 (2H, s); 4.19 (1H, dd, *J* = 9.9, 6.1 Hz); 4.24 (1H, dd, *J* = 9.9, 5.0 Hz); 6.98 (1H, dd, *J* = 7.7, 1.1 Hz); 7.21 (1H, dd, *J* = 8.3, 1.7 Hz); 7.36-7.38 (2H, m); 7.45-7.56 (2H, m); 7.88 (1H, d, *J* = 6.1 Hz); 8.52 (1H, d, *J* = 6.1 Hz); 9.20 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 48.5, 57.8, 61.1, 68.1, 108.7, 115.1, 119.7, 127.2, 127.5, 128.2, 129.3, 129.4, 130.9, 133.5, 134.4, 136.2, 142.1, 151.6, 153.2. IR ($cm^{-1}$): $\nu_{NH,OH}$ = 3215, $\nu_{max}$ = 1585, 1391, 1276, 1249, 1110, 1046, 827, 800, 748. MS m/z (%): 377/379/381 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{19}Cl_2N_2O_2$: 377.0824 $[M+H]^+$, found: 377.0826.

**3-(Isoquinolin-5-yloxy)-2-{[4-(trifluoromethyl)benzyl]amino}propan-1-ol 18g** (93%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.20 (EtOAc/MeOH 95/5). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.28 (1H, quint, *J* = 5.5 Hz); 3.77 (1H, dd, *J* = 11.0, 5.5 Hz); 3.91 (1H, dd, *J* = 11.0, 5.0 Hz); 4.03 (2H, s); 4.17-4.27 (2H, m); 6.99 (1H, dd, *J* = 7.2, 1.1 Hz); 7.44-7.59 (6H, m); 7.84 (1H, d, *J* = 6.1 Hz); 8.48 (1H, d, *J* = 6.1 Hz); 9.15 (1H, d, *J* = 1.1 Hz). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 51.0, 57.6, 61.3, 68.0, 108.7, 114.8, 119.9, 124.2 (q, *J* = 272.3 Hz), 125.5, 125.6, 127.5, 128.31, 128.35, 129.4, 142.7, 144.2, 152.0, 153.2. $^{19}$F NMR (282 MHz, Ref = $CDCl_3$): -62.30 (3F, s); IR ($cm^{-1}$): $\nu_{NH,OH}$ = 3242, $\nu_{max}$ = 1323, 1277, 1160, 1110, 1065, 828, 749. MS m/z (%): 377 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{20}F_3N_2O_2$: 377.1477 $[M+H]^+$ , found: 377.1481.

***N*-Benzyl-1-(isoquinolin-5-yloxy)-3-methoxypropane-2-amine 19a** (91%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.23 (EtOAc/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.95 (1H, br s); 3.29-3.40 (1H, m); 3.39 (3H, s); 3.60 (1H, dd, *J* = 9.4, 5.5 Hz); 3.67 (1H, dd, *J* = 9.4, 5.5 Hz); 3.97 (2H, s); 4.19 (2H, d, *J* = 5.5 Hz); 7.00 (1H, dd, 7.2, 1.1 Hz); 7.23-7.40 (5H, m); 7.46-7.56 (2H, m); 7.94 (1H, d, *J* =

5.5 Hz); 8.53 (1H, d, *J* = 5.5 Hz); 9.21 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 51.9, 56.1, 59.3, 68.5, 72.4, 108.7, 115.0, 119.6, 127.2, 127.5, 128.2, 128.5, 128.6, 129.5, 140.4, 142.8, 152.0, 153.6. IR ($cm^{-1}$): $\nu_{max}$ = 1583, 1433, 1391, 1276, 1249, 1108, 1068, 828, 732, 698. MS m/z (%): 323 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{23}N_2O_2$: 323.1759 $[M+H]^+$, found: 323.1761.

***N*-(4-Fluorobenzyl)-1-(isoquinolin-5-yloxy)-3-methoxypropane-2-amine 19c** (79%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.22 (EtOAc/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.90 (1H, br s); 3.23 (1H, quint, *J* = 5.5 Hz); 3.29 (3H, s); 3.50 (1H, dd, *J* = 9.4, 5.5 Hz); 3.57 (1H, dd, *J* = 9.4, 5.5 Hz); 3.84 (2H, s); 4.08 (2H, d, *J* = 5.5 Hz); 6.88-6.94 (3H, m); 7.22-7.26 (2H, m); 7.36-7.46 (2H, m); 7.85 (1H, d, *J* = 5.5 Hz); 8.44 (1H, d, *J* = 5.5 Hz); 9.11 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 51.2, 56.1, 59.3, 68.4, 72.4, 108.7, 115.0 (d, *J* = 19.6 Hz), 115.5, 119.6, 127.5, 128.5, 129.5, 129.7 (d, *J* = 8.1 Hz), 136.2, 142.8, 152.0, 153.5, 162.0 (d, *J* = 244.6 Hz,). $^{19}$F NMR (282 MHz, Ref = $CDCl_3$): -115.67 (1F, s); IR ($cm^{-1}$): $\nu_{max}$ = 1583, 1508, 1276, 1248, 1218, 1108, 827, 802, 748. MS m/z (%): 341 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{22}FN_2O_2$: 341.1665 $[M+H]^+$, found: 341.1670.

***N*-(2-Chlorobenzyl)-1-(isoquinolin-5-yloxy)-3-methoxypropane-2-amine 19d** (82%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.22 (EtOAc/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 2.17 (1H, br s); 3.35 (1H, m); 3.39 (3H, s); 3.62 (1H, dd, *J* = 9.4, 5.5 Hz); 3.66 (1H, dd, *J* = 9.4, 5.5 Hz); 4.06 (2H, d, *J* = 1.7 Hz); 4.20 (2H, d, *J* = 5.5 Hz); 7.00 (1H, d, *J* = 7.7 Hz); 7.16-7.26 (2H, m); 7.34-7.37 (1H, m); 7.45-7.55 (3H, m); 7.95 (1H, d, *J* = 6.1 Hz); 8.52 (1H, d, *J* = 6.1 Hz); 9.20 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 49.5, 56.1, 59.3, 68.6, 72.5, 108.7, 115.0, 119.6, 127.0, 127.5, 128.5, 128.6, 129.5, 129.7, 130.2, 133.8, 137.7, 142.8, 152.0, 153.5. IR ($cm^{-1}$): $\nu_{max}$ = 1584, 1434, 1276, 1249, 1108, 828, 748. MS m/z (%): 357/9 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{20}H_{21}ClN_2O_2$: 357.1370 $[M+H]^+$, found: 357.1375.

**1-(Isoquinolin-5-yloxy)-3-methoxy-*N*-(4-methoxybenzyl)propane-2-amine 19e** (85%)

Yellow viscous oil. $R_f$ ($SiO_2$) = 0.20 (EtOAc/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 2.03 (1H, br s); 3.34 (1H, quint, *J* = 5.5 Hz); 3.38 (3H, s); 3.59 (1H, dd, *J* = 9.4, 5.5 Hz); 3.66 (1H, dd, *J* = 9.4, 5.5 Hz); 3.79 (3H, s); 3.90 (2H, s); 4.17 (2H, d, *J* = 5.5 Hz); 6.86 (2H, d, *J* = 8.8 Hz); 6.99 (1H, d, *J* = 7.7 Hz); 7.27-7.31 (2H, m); 7.45-7.55 (2H, m); 7.94 (1H, d, *J* = 6.1 Hz); 8.52 (1H, d, *J* = 6.1 Hz); 9.20 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 51.4, 55.4, 56.0, 59.3, 68.5, 72.5, 108.7, 114.0, 115.0, 119.5, 127.5, 128.5, 129.4, 129.5, 132.5, 142.8, 152.0, 153.6, 158.8. IR ($cm^{-1}$): $\nu_{NH}$ = 3323, $\nu_{max}$ = 1583, 1511, 1276, 1245, 1173, 1108, 1033, 828, 802, 749. MS m/z (%): 353 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{21}H_{25}N_2O_3$: 353.1865 $[M+H]^+$, found: 353.1870.

**[2-(Isoquinolin-5-yloxy)-1-methoxymethylethyl]-(2-methoxybenzyl)amine 19h** (75%)

Orange oil. $R_f$ ($SiO_2$) = 0.25 ($CH_2Cl_2$/MeOH 95/5). $^1$H NMR (300 MHz, $CDCl_3$): δ 2.67 (1H, br s); 3.33 (1H, quint, *J* = 5.5 Hz); 3.37 (3H, s); 3.62 (2H, d, *J* = 5.5 Hz); 3.75 (3H, s); 3.96 (2H, d, *J* = 3.9 Hz); 4.18 (2H, d, *J* = 5.5 Hz); 6.82-6.99 (3H, m); 7.21-7.31 (2H, m); 7.43-7.52 (2H, m); 7.93 (1H, d, *J* = 5.5 Hz); 8.52 (1H, d, *J* = 5.5 Hz); 9.19 (1H, s). $^{13}$C NMR (75 MHz, ref = $CDCl_3$): δ 47.5, 55.3, 55.8, 59.2, 68.5, 72.6, 108.6, 110.4, 115.1, 119.4, 120.6, 127.5, 128.2, 128.49, 128.54, 129.5, 129.9, 142.6, 152.0, 153.6, 157.7. IR ($cm^{-1}$): $\nu_{max}$ = 1584, 1492, 1276, 1241, 1110, 908, 829, 750, 726. MS (70 eV): m/z (%): 353 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{19}H_{21}ClF_3N_4O_2$ 353.1860 $[M+H]^+$, found 353.1864.

***N*$^2$-Benzyl-3-(isoquinolin-5-yloxy)-*N*$^1$-phenylpropane-1,2-diamine 20a** (92%)

Brown viscous oil. $R_f$ ($SiO_2$) = 0.31 (EtOAc/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 3.29-3.36 (1H, m); 3.45-3.50 (2H, m); 3.95 (2H, s); 4.25 (2H, d, *J* = 4.4 Hz); 6.64-6.75 (3H, m); 6.98 (1H, d, *J* = 7.2 Hz); 7.15-7.38 (7H, m); 7.45-7.55 (2H, m); 7.94 (1H, d, *J* = 5.5 Hz); 8.53 (1H, d, *J* = 5.5 Hz); 9.20 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 44.9, 51.4, 55.4, 69.1, 108.7, 113.2, 114.9, 117.8, 119.9, 127.4, 127.5, 128.2, 128.4, 128.7, 129.4, 129.5, 140.0, 142.9, 148.4, 152.1, 153.4. IR (cm$^{-1}$): $\nu_{NH}$ = 3327, $\nu_{max}$ = 1493, 1276, 1248, 746, 730, 695. MS m/z (%): 384 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{25}H_{26}N_3O$: 384.2075 $[M+H]^+$, found: 384.2078.

***N*$^2$-(4-Chlorobenzyl)-3-(isoquinolin-5-yloxy)-*N*$^1$-phenylpropane-1,2-diamine 20b** (91%)

Orange viscous oil. $R_f$ ($SiO_2$) = 0.30 (EtOAc/MeOH 9/1). $^1$H NMR (300 MHz, $CDCl_3$): δ 1.98 (1H, br s); 3.29-3.34 (1H, m); 3.39-3.49 (2H, m); 3.91 (2H, d, *J* = 2.2 Hz); 4.24 (2H, d, *J* = 5.0 Hz); 6.65 (2H, dd, *J* = 8.8, 1.1 Hz); 6.71-6.75 (1H, m); 6.98 (1H, d, *J* = 6.1 Hz); 7.15-7.30 (6H, m); 7.45-7.56 (2H, m); 7.92 (1H, d, *J* = 5.5 Hz); 8.54 (1H, d, *J* = 5.5 Hz); 9.21 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 45.0, 50.7, 55.4, 69.0, 108.7, 113.2, 114.8, 117.9, 120.0, 127.5, 128.4, 128.8, 129.47, 129.50, 129.50, 133.0, 138.7, 142.9, 148.4, 152.1, 153.3. IR (cm$^{-1}$): $\nu_{NH}$ = 3320, $\nu_{max}$ = 1602, 1584, 1492, 1276, 1248, 828, 801, 748, 729, 693. MS m/z (%): 418 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{25}H_{25}ClN_3O$: 418.1686 $[M+H]^+$, found: 418.1687.

**2-Benzyl-5-[(1-benzylaziridin-2-yl)methoxy]isoquinolinium bromide 21** (97%)

Brown crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 1.71 (1H, d, *J* = 6.6 Hz); 1.94 (1H, d, *J* = 3.3 Hz); 2.06-2.19 (1H, m); 3.17 (1H, d, *J* = 13.2 Hz); 3.78 (1H, d, *J* = 13.2 Hz); 3.85 (1H, dd, *J* = 10.5, 8.3Hz); 4.37 (1H, dd, *J* = 10.5, 3.9 Hz); 6.34 (2H, s); 7.21-7.38 (10H, m); 7.68-7.74 (2H, m); 7.97 (1H, d, *J* = 7.7 Hz); 8.12 (1H, d, *J* = 7.7 Hz); 8.62 (1H, dd, *J* = 7.7, 1.1 Hz); 11.05 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 31.8, 37.1, 63.8, 64.5, 71.6, 115.2, 121.5, 122.4, 127.5, 128.3, 128.4, 128.6, 129.5, 129.57, 129.62, 129.8, 132.2, 133.2, 133.4, 138.6, 149.5, 153.3. IR (cm$^{-1}$): $\nu_{max}$ = 3026, 2999, 1401, 1290, 747, 718, 699. MS m/z (%): 381/3 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{26}H_{26}N_2O$: 381.1961 $[M+H]^+$, found: 381.1963. $T_m$ = 62.3 °C. Recrystallization from methanol.

**2-Benzyl-5-[2-bromo-3-(dibenzylamino)propoxy]isoquinolinium bromide 22** (98%)

Brown crystals. $^1$H NMR (300 MHz, $CDCl_3$): δ 2.94 (1H, dd, *J* = 13.2, 5.0 Hz); 3.15 (1H, dd, *J* = 13.2, 9.9 Hz); 3.47 (1H, d, *J* = 13.2 Hz); 3.77 (1H, d, *J* = 13.2 Hz); 4.21 (1H, quint, *J* = 4.4 Hz); 4.32 (2H, m); 6.34 (1H, d, *J* = 13.8 Hz); 6.42 (1H, d, *J* = 13.8 Hz); 6.91 (2H, t, *J* = 7.7 Hz); 7.05 (3H, t, *J* = 7.7 Hz); 7.12 (1H, d, *J* = 7.7 Hz); 7.23 (3H, d, *J* = 7.7 Hz); 7.29-7.42 (5H, m); 7.75-7.83 (3H, m); 8.04 (1H, d, *J* = 7.2 Hz); 8.24 (1H, d, *J* = 7.7 Hz); 8.55 (1H, d, *J* = 7.2 Hz); 11.34 (1H, s). $^{13}$C NMR (75 MHz, Ref = $CDCl_3$): δ 33.7, 47.4, 57.1, 59.9, 63.9, 69.6, 114.7, 121.3, 122.8, 127.2, 128.4, 128.5, 128.7, 128.9, 129.0, 129.1, 129.5, 129.7, 130.0, 132.1, 133.1, 133.4, 138.7, 149.8, 152.9. IR (cm$^{-1}$): $\nu_{max}$ = 1604, 1452, 1400, 1290, 1262, 1104, 748, 718, 698. MS m/z (%): 551/3/5 ($M^+$+1, 100). HRMS (ESI) calcd for $C_{33}H_{33}BrN_2O$: 551.1698 $[M+H]^+$, found: 551.1692. $T_m$ = 54.1 °C. Recrystallization from methanol.