Directed *Ortho* Lithiation of *N*-Alkylphenylaziridines

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Experimental Section

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General. Tetrahydrofuran (THF) was freshly distilled under a nitrogen atmosphere over sodium/benzophenone ketyl. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was distilled over finely powdered calcium hydride. Petroleum ether refers to the 40-60 °C boiling fraction. All other chemicals were of commercial grade and used without further purification. Aziridines **1f** and **1g** were commercially available. Commercial solution of *s*-BuLi (1.3 M solution in cyclohexane) was titrated by using *N*-pivaloyl-*o*-toluidine prior to use.¹ For the ¹H and ¹³C NMR spectra (¹H NMR 300, 500 MHz; ¹³C NMR 75.4, 125 MHz), CDCl₃ was used as the solvent. GC-MS spectrometry analyses were performed on a gas chromatograph HP 6890 (dimethylsilicon capillary column, 30 m, 0.25 mm i.d.) equipped with a mass selective detector operating at 70 eV (EI). MS-ESI analyses were performed on Agilent 1100 LC/MSD trap system VL. Melting points were uncorrected. Analytical thin-layer chromatography (TLC) was carried out on Merck precoated 0.25 mm thick plates of Kieselgel 60 F₂₅₄; visualization was accomplished by UV light (254 nm) or by spraying with a solution of 5 % (w/v) ammonium molybdate and 0.2 % (w/v) cerium(III) sulfate in 100 ml 17.6 % (w/v) aqueous sulphuric acid and heating to 200 °C for some time until blue spots appear. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware using syringe-septum cap technique.

¹ Suffert, J. *J. Org. Chem.* **1989**, *54*, 509-510.

General procedure for the preparation of *N*-alkyl phenylaziridines.

Aziridines **1a–e** were prepared using dimethyl- α -styrylsulphonium bromide as intermediate as reported² and an aqueous solution of the suitable amine. To a stirred solution of styrylsulphonium bromide (5 mmol) in 10 mL of H₂O at rt a solution of the amine in water was added dropwise (MeNH₂, commercially available 40 %, 100 mmol; EtNH₂, commercially available 70 %, 100 mmol; *n*-PrNH₂, 70 %, 25 mmol; *n*-BuNH₂, 70 %, 25 mmol; *i*-PrNH₂, 70 %, 25 mmol) and the resulting mixture stirred overnight. The mixture was poured into 20 mL of saturated brine, extracted with diethyl ether (3 $\times$ 10 mL), dried (Na₂SO₄), and the solvent evaporated under reduced pressure. Kugelrohr distillation furnished the desired aziridines with yields ranging from 85 to 95 %). Spectroscopic data for **1a**³, **1b**⁴, **1c**⁵, **1e**⁶ have been reported.

1-Butyl-2-phenylaziridine (1d): Colorless oil, >98 %. ¹H NMR (CDCl₃, 500 MHz) δ : 0.88 (t, J = 7.3 Hz, 3 H), 1.36 (sext, J = 7.3 Hz, 2 H), 1.56 (m, overlapping d at 1.60, 2 H), 1.60 (d, J = 6.1, 1 H), 1.84 (d, J = 3.7, 1 H), 2.25 (dd, J = 6.1, 3.7 Hz, 1 H), 2.23 – 2.31 (m, overlapping dd at 2.25, 1 H), 2.41 – 2.48 (m, 1 H), 7.15 – 7.26 (m, 5 H). ¹³C NMR (CDCl₃, 125 MHz) δ : 13.9, 20.4, 31.8, 37.6, 41.1, 61.4, 126.0, 126.5, 128.0, 140.4; GC-MS (70 eV) m/z (%) 175 (M⁺, 11), 174 (72), 132 (100), 118 (60), 104 (14), 98 (37), 91 (96), 77 (13). FT-IR (Film) cm⁻¹: 3038, 2958, 2930, 1606, 1496, 1456, 1206, 1085, 1030, 747, 698.

² Chow, Y. L.; Bakker, B. H.; Iwai, K. *J. Chem. Soc. Chem. Comm.* **1980**, 521–522.

³ Barsetti, P.; Crist, D. R. *J. Heterocyclic Chem.* **1975**, 12, 1287.

⁴ (a) Gaillot, J.-M.; Gelas-Mialhe, Y.; Vessiere, R. *Chem. Lett.* **1983**, 1137–1140. (b) Katritzky, A. R.; Jiang, J.; Urogdi, L. *Synthesis*, **1990**, 565–567.

⁵ Chamchaang, W.; Pinhas, A. R. *J. Org. Chem.* **1990**, 55, 2943–2950.

⁶ Piotti, M.; Alper, H. *J. Org. Chem.* **1996**, 118, 111–116.

General procedure for the *ortho*-lithiation-deuteration sequence of *N*-alkyl-substituted phenylaziridines 1a-e. The case of 1a is described: A solution of the 1-alkyl-2-phenylaziridine **1a** (1.0 mmol) in 10 mL of dry THF at -78 °C under N₂ was reacted with *s*-BuLi (1.5 mmol, 1.2 M in cyclohexane). The resulting orange mixture was stirred for 2.0 h, (4h for **1b-d**) at -78 °C. Then, at this temperature, D₂O (2.0 mmol), was added dropwise. The resulting reaction mixture was allowed to warm-up to rt and finally quenched with sat. aq. NH₄Cl, poured into 20 mL of saturated brine, extracted with diethyl ether (3 × 10 mL), dried (Na₂SO₄), and evaporated under reduced pressure. The crude mixture was analyzed by NMR: no starting material or other byproduct could be observed in addition to the *ortho*-deuterated phenylaziridine **3a** which showed the following data:

1-Methyl-2-(*o*-deuteriophenyl)aziridine (3a): Colorless oil, > 98 %. > 98 % D. ¹H NMR (CDCl₃, 500 MHz) δ: 1.55 (d, *J* = 6.5 Hz, 1 H), 1.83 (d, *J* = 3.3 Hz, 1 H), 2.19 (dd, *J* = 6.5, 3.3 Hz, 1 H), 2.41 (s, 3 H), 7.10–7.25 (m, 4H). ¹³C NMR (CDCl₃, 125 MHz) δ: 39.2, 42.2, 48.0, 125.6 (t, ¹*J*_{C-D} = 24 Hz), 125.9, 126.7, 128.1, 128.2, 140.4. GC-MS (70 eV) *m/z* (%) 134 [*M*⁺] (14), 133 (100), 118 (14), 92 (48), 78 (6).

ortho-Deuterated aziridines **3n-p** obtained as above described, showed the following data:

1-Ethyl-2-(*o*-deuteriophenyl)aziridine (3n): Colorless oil, > 98 %. > 98 % D. ¹H NMR (CDCl₃, 500 MHz) δ: 1.25 (t, *J* = 7.3 Hz, 3 H), 1.66 (d, *J* = 6.6, 1H), 1.91 (d, *J* = 3.2 Hz, 1 H), 2.30 (dd, *J* = 6.6, 3.4 Hz, 1 H), 2.50 (q, *J* = 7.1 Hz, 2 H), 7.20–7.35 (m, 4 H); ¹³C NMR (CDCl₃, 125 MHz) δ: 14.3, 37.4, 41.0, 55.7, 125.7 (t, ¹*J*_{C-D} = 24 Hz), 126.0, 126.6, 128.0, 128.1, 140.2. GC-MS (70 eV) *m/z* (%) 148 [*M*⁺] (12), 147 (100), 119 (21), 92 (83), 78 (9). FT-IR (Film) cm⁻¹: 3038, 2973, 2869, 1377, 1120, 738, 698.

2-(*o*-Deuteriophenyl)-1-propylaziridine (3o): Colorless oil, >98 %. > 98 % D. ^1H NMR (CDCl_3 , 500 MHz) δ : 0.96 (t, $J = 7.5$ Hz, 3 H), 1.58–1.70 (m, 3 H), 1.88 (d, $J = 3.0$ Hz, 1 H), 2.28–2.33 (m, 2 H), 2.45–2.52 (m, 1 H), 7.21–7.32 (m, 4 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ : 11.9, 22.9, 37.6, 41.2, 63.5, 125.8 (t, $^1J_{\text{C D}} = 24$ Hz), 126.1, 126.7, 128.0, 128.2, 140.4; GC-MS (70 eV) m/z (%) 162 (M^+ , 11), 161 (81), 133 (21), 119 (46), 92 (76), 78 (12). FT-IR (Film, cm^{-1}) 3039, 2959, 2932, 2814, 1463, 1379, 1206, 1081, 774, 727, 698, 632.

1-Butyl-2-(*o*-deuteriophenyl)aziridine (3p): Colorless oil, > 98 %. > 98 % D. ^1H NMR (CDCl_3 , 500 MHz) δ : 0.93 (t, $J = 7.3$ Hz, 3 H), 1.41 (sext, $J = 7.3$ Hz, 2 H), 1.56 (m, overlapping d at 1.66, 2 H), 1.66 (d, $J = 6.7$, 1 H), 1.89 (d, $J = 3.0$, 1 H), 2.30 (dd, $J = 6.1$, 3.0 Hz, 1 H), 2.33–2.36 (m, overlapping dd at 2.3, 1 H), 2.47–2.53 (m, 1 H), 7.20–7.31 (m, 4 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ : 14.0, 20.5, 31.9, 37.7, 61.5, 125.8 (t, $^1J_{\text{C D}} = 24$ Hz), 126.1, 126.6, 128.0, 128.1, 140.4, 140.5; GC-MS (70 eV) m/z (%) 176 (M^+ , 7), 175 (51), 134 (23), 133 (86), 132 (100), 119 (47), 92 (79), 78 (16). FT-IR (Film, cm^{-1}) 3039, 2958, 2931, 2873, 2816, 1606, 1496, 1457, 1379, 1206, 1084, 1029, 775, 746, 698.

General procedure for the *ortho*-lithiation of *N*-methylphenylaziridines **1a and reaction with electrophiles. The case of the methylation of **1a** is described:** A solution of the 1-methyl-2-phenylaziridine **1a** (1.0 mmol) in 10 mL of dry THF at -78 °C under N₂ was reacted with *s*-BuLi (1.5 mmol, 1.2 M in cyclohexane). The resulting orange mixture was stirred for 2.0 h at -78 °C. Then, the electrophile (1.1 mmol), neat if liquid or as solution in 2 mL of THF if solid, was added dropwise. The resulting reaction mixture was allowed to warm-up to rt and finally quenched with sat. aq. NH₄Cl, poured into 20 mL of saturated brine, extracted with AcOEt (3 × 10 mL), dried (Na₂SO₄), and evaporated under reduced pressure. The crude mixture was purified by distillation or flash-chromatography (silica gel; petroleum ether/AcOEt 6/4) to give the *ortho* substituted aziridine **3b**. Phthalans **5a**, **5f-h** were obtained directly.

1-Methyl-2-*o*-tolylaziridine (3b): Yellow oil, 85 %. ¹H NMR (CDCl₃, 500 MHz) δ: 1.60 (d, *J* = 6.1 Hz, 1 H), 1.84 (d, *J* = 3.0 Hz, 1 H), 2.34 (dd, *J* = 6.1, 3.0 Hz, 1 H), 2.42 (s, 3 H), 2.51 (s, 3 H), 7.10–7.30 (m, 4 H). ¹³C NMR (CDCl₃, 125 MHz) δ: 19.2, 37.6, 40.4, 48.0, 125.7, 125.9, 126.6, 129.5, 136.4, 138.0. GC-MS (70 eV) *m/z* (%) 147 (M⁺, 13), 146 (100), 132 (52), 131 (26), 117 (20), 105 (19), 91 (10), 77 (13); FT-IR (Film) cm⁻¹: 3047, 2967, 2849, 1491, 1459, 1383, 1191, 1013, 800, 753, 732.

Aziridines **3c-g**, **3i-m** and phthalans **5a**, **5f-h** showed the following data:

2-(2-Bromophenyl)-1-methylaziridine (3c): Yellow oil, 63 %. ¹H NMR (CDCl₃, 500 MHz) δ: 1.64 (d, *J* = 6.5 Hz, 1 H), 1.80 (d, *J* = 3.4 Hz, 1 H), 2.50 (s, 3 H), 2.56 (dd, *J* = 6.5, 3.3 Hz, 1 H), 7.02–7.05 (m, 1 H), 7.18–7.21 (m, 2 H), 7.47–7.48 (m, 1 H); ¹³C NMR (CDCl₃, 125 MHz) δ: 38.3, 42.2, 47.6, 123.8, 127.3, 127.5, 128.1, 132.0, 139.1; GC-MS (70 eV) *m/z* (%) 213 (M⁺ + 2, 10), 212 (100), 211 (M⁺, 7), 210 (94), 184 (14), 182 (20), 171 (37), 169 (36), 132 (61), 131 (73), 117 (34), 103 (33), 90 (33), 89 (32), 77 (24). FT-IR (Film) cm⁻¹: 3058, 2953, 2850, 1494, 1464, 1023, 752, 702, 667.

2-(2-Chlorophenyl)-1-methylaziridine (3d): Brown oil, 81 %. ^1H NMR (CDCl_3 , 500 MHz)

δ : 1.65 (d, $J = 6.5$ Hz, 1 H), 1.81 (d, $J = 3.3$ Hz, 1 H), 2.49 (s, 3 H), 2.61 (dd, $J = 6.5, 3.3$ Hz, 1 H), 7.11 (td, $J = 7.5, 1.8$ Hz, 1 H), 7.16 (td, $J = 7.3, 1.1$ Hz, 1 H), 7.20 (dd, $J = 7.5, 1.8$ Hz, 1 H), 7.30 (dd, $J = 7.8, 1.1$ Hz, 1 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 38.3, 39.7, 47.6, 126.7, 127.1, 127.7, 128.8, 133.8, 137.5. GC-MS (70 eV) m/z (%): 169 ($\text{M}^+ + 2$, 3), 168 (32), 167 (M^+ , 11), 166 (100), 132 (29), 131 (34), 125 (47), 117 (14), 89 (19). FT-IR (Film) cm^{-1} : 3060, 2947, 1477, 1442, 1382, 1071, 1052, 1034, 781, 751, 687.

2-(2-Iodophenyl)-1-methylaziridine (3e): Brown oil, 80 %. ^1H NMR (CDCl_3 , 500 MHz)

δ : 1.69 (d, $J = 6.7$ Hz, 1 H), 1.82 (d, $J = 3.0$ Hz, 1 H), 2.44 (dd, $J = 6.7, 3.0$ Hz, 1 H), 2.56 (s, 3 H), 6.93 (td, $J = 7.3, 1.2$ Hz, 1 H), 7.20 (dd, $J = 7.9, 1.8$ Hz, 1 H), 7.27 (t, $J = 7.3$ Hz, 1 H), 7.78 (dd, $J = 7.9$ Hz, 1 H). GC-MS (70 eV) m/z (%): 258 (M^+ , 100), 132 (57), 117 (43), 90 (25), 63 (12). FT-IR (Film) cm^{-1} : 3055, 2945, 1452, 1442, 1008, 748.

2-(1-Methylaziridin-2-yl)-benzaldehyde (3f): Brown oil, 98 %. ^1H NMR (CDCl_3 , 500

MHz) δ : 1.76 (d, $J = 6.6$ Hz, 1 H), 1.86 (d, $J = 3.0$ Hz, 1 H), 2.55 (s, 3 H), 3.19 (dd, $J = 6.6, 3.0$ Hz, 1 H), 7.38–7.42 (m, 1 H), 7.48–7.57 (m, 2 H), 7.78–7.80 (m, 1 H), 10.33 (s, 1 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 39.0, 39.2, 47.6, 127.0, 127.1, 132.3, 133.9, 134.2, 142.5, 192.8. GC-MS (70 eV) m/z (%): 161 (M^+ , 2), 160 (4), 132 (25), 118 (100), 103 (5), 90 (23), 77 (7). FT-IR (Film) cm^{-1} : 3050, 2948, 2780, 1688, 1600, 1572, 1453, 1380, 1194, 1013, 760, 656.

1-Methyl-2-(2-benzoylphenyl)aziridine (3g): Yellow oil, 50 %. ^1H NMR (CDCl_3 , 500 MHz) δ : 1.52 (d, $J = 6.5$ Hz, 1 H), 1.85 (d, $J = 3.0$ Hz, 1 H), 2.30 (s, 3 H), 2.49 (dd, $J = 6.5, 3.0$ Hz, 1 H), 7.24–7.40 (m, 3 H), 7.42–7.50 (m, 3 H), 7.55–7.65 (m, 1 H), 7.80–7.88 (m, 2 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 38.8, 40.0, 47.2, 125.9, 126.2, 128.2, 128.3, 130.0, 130.4, 133.0, 137.7, 138.3, 139.4, 197.9. MS-ESI m/z : 260 (100) [$\text{M} + \text{Na}$]; FT-IR (Film) cm^{-1} : 3058, 2946, 1664, 1597, 1449, 1269, 928, 764, 741, 702, 640.

(1R*,2'R*)/(1R*,2'S*)-[2-(1-Methylaziridin-2-yl)phenyl]ethanol (3i): Colourless oil ; 75 %, inseparable mixture of diastereoisomers, dr: 50/50. ^1H NMR (CDCl_3 , 300 MHz) δ : 1.57, (d, $J = 6.6$ Hz, 3 H), 1.58 (d, $J = 6.6$ Hz, 3 H), 1.64, (d, $J = 6.5$ Hz, 1 H), 1.67, (d, $J = 6.6$ Hz, 1 H), 1.90, (d, $J = 3.5$ Hz, 1 H), 1.92, (d, $J = 3.6$ Hz, 1 H), 2.52 (s, 6 H), 2.50 – 2.58 (m, 2 H), 4.00 – 4.50 (s, br, 1 H), 4.50 – 4.90 (s, br, 1 H), 5.07 (q, $J = 6.6$ Hz, 1 H), 5.20 (q, $J = 6.5$ Hz, 1 H), 7.15 – 7.55 (m, 8 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 21.6, 24.2, 36.1, 37.1, 39.0, 40.4, 47.0, 47.3, 65.5, 67.9, 124.6, 125.7, 125.9, 127.1, 127.2, 127.5, 127.7, 128.2, 135.9, 144.3, 144.6. GC-MS (70 eV) m/z (%): 177 (M^+ , 3), 133 (34), 105 (10), 77 (11), 44 (100). FT-IR (Film) cm^{-1} : 3377, 2971, 1682, 1452, 1382, 1191, 1079, 1012, 899, 761.

(1R*,2'R*)/(1R*,2'S*)-[2-(1-Methylaziridin-2-yl)phenyl]phenylmethanol (3j): White solid; 47 %, inseparable mixture of diastereoisomers dr: 60/40. ^1H NMR (CDCl_3 , 300 MHz) δ : 1.47 (d, $J = 6.6$ Hz, 1 H, minor), 1.54 (d, $J = 6.6$ Hz, 1 H, major), 1.78 – 1.81 (m, 2 H, major + minor), 1.98 (s, 3 H, minor), 2.25 (dd, $J = 6.7, 3.6$ Hz, 1 H, minor), 2.44 (s, 3 H, major), 2.51–2.57 (m, 1 H, major), 5.20–5.60 (s, br, 2 H, major + minor), 5.79 (s, 1 H, minor), 6.10 (s, 3 H, major), 7.16 – 7.39 (m, 9 H major + 9 H minor); ^{13}C NMR (CDCl_3 , 75 MHz) δ 36.7, 37.3, 41.3, 41.5, 46.8, 47.4, 72.7, 75.4,

127.1, 127.1₆, 127.2, 127.3, 127.4, 127.6, 127.7, 128.3, 128.4, 128.9, 129.4, 137.5, 142.3, 143.0, 144.0, 144.5. GC-MS (70 eV) m/z (%) 239 (M^+ , 3), 195 (30), 165 (27), 44 (100); FT-IR (KBr) cm^{-1} : 3300, 3157, 2946, 2904, 1451, 1383, 1038, 1027, 810, 796, 755. Anal. calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.38; H, 7.25; N, 5.92.

1,1-Diphenyl-1-[2-(1-methylaziridin-2-yl)phenyl]methanol (3k): White solid, m.p.

137-139 °C (hexane), 52 %. 1H NMR ($CDCl_3$, 500 MHz) δ : 1.55 (d, J = 6.8 Hz, 1 H), 1.63 (s, 3 H), 1.93 (d, J = 3.6 Hz, 1 H), 2.21 (dd, J = 6.7, 3.6 Hz, 1 H), 6.53 (d, J = 7.9 Hz, 1 H), 7.01–7.04 (m, 1 H), 7.19–7.40 (m, 13 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ : 37.1, 43.5, 45.5, 81.6, 126.5, 126.7, 126.7₃, 127.2, 127.6, 127.8, 128.1, 128.2, 129.9, 131.0, 137.8, 146.8, 147.1, 148.5; GC-MS (70 eV) m/z (%): 272 [M^+ – 44] (22), 254 (7), 193 (18), 165 (21), 44 (100); FT-IR (KBr) cm^{-1} : 3058, 2788, 1597, 1489, 1447, 1401, 1188, 1022, 898, 813, 758, 737, 637. Anal. calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.60; H, 6.78; N, 4.27.

In the reaction with butyrophenone, the two diastereoisomers could be separated as follows. Washing the crude reaction mixture with hexane the (**1R*,2'R***)-**3l** isomer precipitates as a white solid. The organic phase was evaporated and the crude purified by chromatography (ethyl acetate/petroleum ether 6/4) to give the (**1R*,2'S***)-**3l** isomer (R_f 0.4). Further elution with AcOEt/MeOH 90/10 gave the phthalan (**1R*,3R***)-**5e** (R_f 0.1) as a single diastereoisomer.

(1R*,2'R*)-[1-(1-Methylaziridin-2-yl)phenyl]-1-phenylbutanol (3l): White solid,

m.p. 125-127 °C (hexane), 27 %. 1H NMR ($CDCl_3$, 500 MHz) δ : 0.91 (t, J = 7.3 Hz, 3 H), 1.15 – 1.27 (m, 1 H), 1.38 (d, J = 6.7 Hz, 1 H), 1.42 – 1.54 (m, 1 H), 1.65, (d, J = 3.4 Hz, 1 H), 2.07, (s, 3 H), 2.10 – 2.34, (m, 2 H), 2.44 (dd, J = 6.7, 3 Hz, 1 H), 4.20 (s, br, 1 H), 7.15 – 7.44 (m, 9 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ : 14.4, 17.2, 39.0, 41.1, 45.2, 46.9, 78.5, 126.0, 126.2, 126.4, 126.6, 127.5, 127.7, 127.8, 138.5, 145.0, 147.3. GC-MS (70 eV) m/z (%): 281 (M^+ , 1), 237 (21), 219 (10), 195 (21), 178 (8), 165 (20), 91 (10), 44 (100). FT-IR (KBr) cm^{-1} : 3173, 2952, 1601, 1450, 1196, 748, 732, 717. Anal. calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.40; H, 8.28; N, 5.16.

(1R*,2'S*)-[1-(1-Methylaziridin-2-yl)phenyl]-1-phenylbutanol (3l): White waxy solid, m.p. 71-74 °C, 12 %. ¹H NMR (CDCl₃, 500 MHz) δ: 0.90 (t, *J* = 7.3 Hz, 3 H), 1.23 – 1.33 (m, 2 H), 1.37 (d, *J* = 6.8 Hz, 1 H), 1.76, (d, *J* = 3.6 Hz, 1 H), 1.88, (s, 3 H), 2.03, (dd, *J* = 6.7, 3.6 Hz, 1 H), 2.14 – 2.19 (m, 2 H), 6.8 (s, br, 1 H), 7.15 – 7.36 (m, 8 H), 7.59 – 7.62 (d, *J* = 7.8 Hz, 1 H). ¹³C NMR (CDCl₃, 125 MHz) δ: 14.5, 17.7, 37.2, 42.8, 45.7, 46.2, 78.0, 126.2, 126.8, 126.8_i, 127.1, 127.5, 127.8, 130.7, 138.3, 145.4, 148.0. GC-MS (70 eV) *m/z* (%): 281 (M⁺, 1), 237 (21), 219 (10), 195 (21), 178 (8), 165 (20), 91 (10), 44 (100). FT-IR (KBr) cm⁻¹: 3431, 2951, 1598, 1451, 1056, 764, 750, 709. Anal. calcd for C₁₉H₂₃NO: C, 81.10; H, 8.24; N, 4.98,. Found: C, 81.38; H, 8.13; N, 5.05.

2-(1-Methylaziridin-2-yl)-benzoic acid ethyl ester (3m): Yellow oil, 20 %. ¹H NMR (CDCl₃, 500 MHz) δ 1.38 (t, *J* = 6.9 Hz, 3 H), 1.67 (d, *J* = 6.7 Hz, 1 H), 1.80 (d, *J* = 2.9 Hz, 1 H), 2.50 (s, 3 H), 3.11 (dd, *J* = 6.6, 3.3 Hz, 1 H), 4.34–4.38 (m, 2 H), 7.20–7.5 (m, 4 H). ¹³C NMR (CDCl₃, 125 MHz) δ: 14.3, 38.9, 40.8, 47.4, 60.8, 126.4, 126.9, 129.8, 130.1, 132.2, 141.9, 167.4; GC-MS (70 eV) *m/z* (%): 205 (M⁺, 10), 204 (63), 176 (17), 162 (33), 146 (28), 133 (100), 117 (10), 105 (21), 91 (17), 77 (25); FT-IR (Film) cm⁻¹: 2977, 2851, 1716, 1451, 1295, 1080, 746.

1,1-Dimethyl-3-methylaminomethyl-1-3-dihydroisobenzofuran (5a): Yellow oil, >95 %. ¹H NMR (CDCl₃, 500 MHz) δ: 1.46 (s, 3H), 1.55 (s, 3H), 2.49 (s, 3 H), 2.50 – 2.70 (s, br, 1 H), 2.80 (dd, *J* = 12, 7 Hz 1 H), 3.00 (dd, dd, *J* = 12, 3 Hz 1 H), 5.31 (dd, *J* = 7, 3 Hz 1 H), 7.10–7.40 (m, 4 H), 7.48–7.53 (m, 1 H). ¹³C NMR (CDCl₃, 125 MHz) δ: 28.8, 28.9, 36.4, 57.5, 80.5, 85.2, 120.5, 121.0, 127.2, 127.7, 139.4, 147.2. GC-MS (70 eV) *m/z* (%): 191 (M⁺, 1), 147 (37), 129 (32), 91 (10), 44 (100). MS-ESI *m/z* (%): 214 (42) [M+Na]⁺ 192 (100) [M+H]⁺ FT-IR (Film) cm⁻¹: 3329, 2927, 1455, 1361, 1154, 1032, 760.

3-Methylaminomethyl-3H-isobenzofuran-1-one (5f): Yellow oil, 73 %. ^1H NMR (CDCl_3 , 500 MHz) δ : 2.32 (s, br, 1 H), 2.46 (s, 3 H), 2.85 (dd, $J = 13$, 7.9 Hz, 1 H), 3.14 (dd, $J = 13.0$, 3.5 Hz, 1 H), 5.57 (dd, $J = 7.9$, 3.5 Hz, 1 H), 7.45–7.52 (m, 2 H), 7.61–7.68 (m, 1 H), 7.84–7.90 (m, 1 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 36.3, 55.3, 80.5, 121.8, 125.7, 129.3, 134.0, 148.0, 170.2; GC-MS (70 eV) m/z (%): 177 (M^+ , 1), 146 (2), 133 (4), 105 (7), 51 (6), 44 (100); ESI-MS m/z (%): 377 [$\text{M}_2 + \text{Na}$] $^+$ (60), 355 [$\text{M}_2 + \text{H}$] $^+$ (100), 200 [$\text{M} + \text{Na}$] $^+$ (45), 178 [$\text{M} + \text{H}$] $^+$ (31). FT-IR (Film) cm^{-1} : 3319, 3057, 2959, 1766, 1467, 1351, 1285, 1209, 1069, 1010, 743, 697.

(1*R,3*R**)/(1*R**,3*S**)-1-Chloro-1-ethoxy-3-(*N*-methyl-*N*-ethoxycarbonylaminomethyl)-1-3-dihydroisobenzofuran (5g):** Yellow oil, 25 %.

Inseparable mixture of diastereoisomers, dr: 1/1. ^1H NMR (CDCl_3 , 500 MHz) δ : 1.17 (t, $J = 6.7$ Hz, 3 H), 1.21 (t, $J = 6.7$ Hz, 3 H), 1.36 (t, $J = 7.3$ Hz, 6 H), 2.88 (s, 6 H), 3.50–3.60 (m, 2 H), 3.92–4.12 (m, 6 H), 4.30–4.36 (m, 4 H), 6.22–6.28 (m, 2 H), 7.32–7.35 (m, 2 H), 7.51–7.55 (m, 2 H), 7.76–7.86 (m, 4 H); ^{13}C NMR (CDCl_3 , 125 MHz) δ : 14.1, 14.5, 34.2, 35.0, 55.8, 56.0, 61.3, 128.0, 129.1, 130.1, 132.2, 132.3, 140.2, 140.4, 156.3, 156.7, 166.6, 166.8; GC-MS (70 eV) m/z (%) 278 [$\text{M} - \text{Cl}$] $^+$ (3), 277 (10), 160 (10), 116 (100), 44 (31); FT-IR (Film, cm^{-1}) 2981, 2930, 1705, 1602, 1486, 1266, 1215, 1145, 1079, 913, 737.

(1*R,3*R**)/(1*R**,3*S**)-1-Chloro-1-methoxy-3-(*N*-methyl-*N*-**

methoxycarbonylaminoethyl)-1,3-dihydroisobenzofuran (5h): Yellow oil, 55 %. Inseparable mixture of diastereoisomers, dr: 1/1. ^1H NMR (CDCl_3 , 500 MHz) δ : 2.84 (s, 3 H), 2.87 (s, 3 H), 3.51 (dd, $J = 14.6, 6.1$ Hz, 2 H), 3.58 (s, 3 H), 3.66 (s, 3 H), 3.86 (s, 3 H), 3.87 (s, 3 H), 3.92 (dd, $J = 14.0, 7.9$ Hz, 1 H), 4.01 (dd, $J = 14.0, 9.1$ Hz, 1 H), 6.20 – 6.25 (m, 2 H), 7.30–7.34 (m, 2 H), 7.50 – 7.55 (m, 2 H), 7.77 – 7.84 (m, 4 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ 34.3, 35.2, 52.3, 52.3₅, 52.5, 52.7, 55.7, 56.1, 56.3, 128.1, 128.7, 129.1, 129.2, 130.1, 132.4, 132.5, 140.2, 140.4, 156.7, 157.1, 167.0, 167.2; GC-MS (70 eV) m/z (%): 250 $[\text{M} - \text{Cl}]^+$ (3), 249 (8), 102 (100), 58 (14). MS-ESI m/z (%): 310 (21) $[\text{M} + 2 + \text{Na}]^+$, 308 (62) $[\text{M} + \text{Na}]^+$, 250 (100) $[\text{M} - \text{NaCl}]^+$. (FT-IR (Film) cm^{-1} : 2954, 1708, 1601, 1577, 1478, 1395, 1267, 1149, 1081, 913, 736, 460.

General procedure for the preparation of aminomethylphthalanes 5c-e: To a solution of the *ortho*-hydroxyalkylated phenylaziridine **3j-l** (1.0 mmol) in 10 mL of dry THF at rt, a catalytic amount of trifluoroacetic acid (10 % mol) was added and the resulting mixture stirred until the substrate disappeared (TLC monitoring, AcOEt/petroleum ether, 8/2). The resulting reaction mixture was poured into 20 mL of saturated brine, extracted with AcOEt (3 × 10 mL), dried (Na₂SO₄), and evaporated under reduced pressure. The crude mixture was purified by distillation or flash-chromatography (silica gel; CH₂Cl₂/MeOH, 9/1) to give the corresponding phthalans showing the following data:

(1*R,3*R**)/(1*R**,3*S**)-1-Methylaminomethyl-3-phenyl-1,3-dihydroisobenzofuran (5c):**

Yellow oil; 95 %, inseparable mixture of diastereoisomers, dr (1*R**,3*S**)/(1*R**,3*R**) : 60/40. ¹H NMR (CDCl₃, 500 MHz) δ: 2.48 (s, 3 H, minor), 2.49 (s, 3 H, major), 2.87 (dd, *J* = 12, 7.8 Hz, 1 H, major), 2.93 (dd, *J* = 12, 7.9 Hz, 1 H, minor), 2.98 (dd, *J* = 12, 3 Hz, 1 H, major), 3.14 (dd, *J* = 12.4, 3 Hz, 1 H, minor), 5.41 – 5.42 (m, 1 H, minor), 5.60 – 5.62 (m, 1 H, major), 6.10 (s, 1 H, minor), 6.20 (s, 1 H, major), 6.95 (d, *J* = 7.8, 1 H, minor), 7.02 (d, *J* = 7.9, 1 H, major), 7.22 – 7.36 (m, 8 H, major + 8 H minor). ¹³C NMR (CDCl₃, 125 MHz) δ: 36.3, 36.4, 57.0, 57.1, 82.3, 82.9, 85.4, 85.6, 120.8, 121.1, 122.4, 126.8, 127.6, 127.5, 127.9, 128.0, 128.2, 128.5, 139.8, 141.6, 142.1, 142.2, 142.5. GC-MS (70 eV) *m/z* (%): 239 (M⁺, 3), 195 (34), 165 (31), 44 (100). FT-IR (Film) cm⁻¹: 3319, 2058, 3029, 2928, 2851, 2797, 1689, 1477, 1457, 1200, 1024, 753, 699.

1,1-Diphenyl-3-methylaminomethyl-1,3-dihydroisobenzofuran (5d): Yellow oil, >95

%. ¹H NMR (CDCl₃, 500 MHz) δ: 2.00 (s, br, 1 H), 2.45 (s, 3 H), 2.88 (dd, *J* = 12, 7.8 Hz, 1 H), 3.03 (dd, *J* = 12, 3 Hz, 1 H), 5.40 (dd, *J* = 7.8, 3 Hz, 1 H), 7.12–7.37 (m, 14 H). ¹³C NMR (CDCl₃, 125 MHz) δ: 36.6, 56.6, 81.4, 92.3, 121.1, 124.0, 127.1, 127.2, 127.4, 127.6, 127.7, 127.8, 127.9, 132.5, 140.6, 144.5, 145.6. GC-MS (70 eV) *m/z* (%) 315 (M⁺, 1), 272 (34), 254 (10), 239 (12), 193 (24), 165 (28), 44 (100); FT-IR (Film) cm⁻¹: 3340, 3059, 3027, 2963, 2929, 2797, 1491, 1474, 1446, 1261, 1023, 799, 757, 699.

(1*R,3*R**)-1-Methylaminomethyl-3-phenyl-3-propyl-1,3-dihydroisobenzofuran**

(5e): Yellow oil, 27.5 % ^1H NMR (CDCl_3 , 500 MHz) δ : 0.86 (t, $J = 7.3$ Hz, 3 H), 1.05 – 1.18 (m, 1 H), 1.26 – 1.40 (m, 1 H), 2.00 – 2.11 (m, 1 H), 2.12 – 2.20 (m, 1 H), 2.49 (s, 3 H), 2.74 (dd, $J = 12, 8.8$ Hz, 1 H), 2.95 (dd, $J = 12, 3$ Hz, 1 H), 3.52 (s, br, 1 H), 5.45 (dd, $J = 8.8, 3$ Hz, 1 H), 7.15 – 7.41 (m, 7 H), 7.50 – 7.60 (m, 2 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 14.2, 17.4, 36.1, 44.8, 57.2, 81.8, 91.2, 121.2, 122.5, 125.2, 126.8, 127.5, 127.8, 128.1, 140.1, 144.3, 146.2. GC-MS (70 eV) m/z (%): 281 (M^+ , 1), 237 (21), 219 (10), 195 (21), 178 (8), 165 (20), 91 (10), 44 (100). FT-IR (KBr) cm^{-1} : 3328, 2952, 1599, 1457, 1052, 1036, 754, 700. Anal. calcd for $\text{C}_{19}\text{H}_{23}\text{NO}$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.25; H, 8.26; N, 5.06.

(1*R,3*S**)-1-Methylaminomethyl-3-phenyl-3-propyl-1,3-dihydroisobenzofuran**

(5e): White solid, m.p. 128–129 °C, 27.5 % ^1H NMR (CDCl_3 , 500 MHz) δ : 0.89 (t, $J = 7.4$ Hz, 3 H), 1.10 – 1.40 (m, 2 H), 2.00 – 2.30 (m, 2 H), 2.59 (s, 3 H), 2.75 (s, br, 1 H), 2.93 (dd, $J = 12, 8.2$ Hz, 1 H), 3.16 (dd, $J = 12, 3$ Hz, 1 H), 5.38 (dd, $J = 8.2, 3$ Hz, 1 H), 7.10 – 7.60 (m, 9 H). ^{13}C NMR (CDCl_3 , 125 MHz) δ : 14.3, 17.6, 36.7, 44.4, 56.9, 80.7, 90.7, 121.0, 121.9, 125.0, 126.7, 127.5, 127.7, 128.1, 140.4, 145.0, 145.6. GC-MS (70 eV) m/z (%): 281 (M^+ , 1), 237 (21), 219 (10), 195 (21), 178 (8), 165 (20), 91 (10), 44 (100). FT-IR (KBr) cm^{-1} : 3338, 2956, 1599, 1474, 1446, 1130, 1061, 1035, 770, 700. Anal. calcd for $\text{C}_{19}\text{H}_{23}\text{NO}$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.08; H, 8.12; N, 5.00.

Lithiation of the *N*-Boc-2-phenylaziridine⁷ **1h:** A solution of the *N*-Boc-2-phenylaziridine **1h** (1.0 mmol) in 10 mL of dry THF at -98 °C under N₂ was reacted with *s*-BuLi (1.5 mmol, 1.2 M in cyclohexane). The resulting orange mixture was stirred for 5 min at -98 °C and finally quenched with D₂O, poured into 20 mL of saturated brine, extracted with AcOEt (3 × 10 mL), dried (Na₂SO₄), and evaporated under reduced pressure. The crude mixture was purified by distillation to give aziridines **6** as the sole product.

2-*tert*-Butoxycarbonyl-2-phenyl-1-*H*-aziridine (6**):** Colorless oil; 90 %, ¹H NMR (CDCl₃, 500 MHz) δ: 1.40 (s, 9 H), 1.90 (s, br, 1 H), 2.39 (s, br, 1 H), 7.02 – 7.52 (m, 5 H). ¹³C NMR (CDCl₃, 100.5 MHz) δ: 28.0, 28.2, 35.0, 82.6, 127.6, 128.0, 129.2, 137.0, 171.9. GC-MS (70 eV) *m/z* (%): 163 (M⁺ - 56, 38), 117 (100), 104 (22), 91 (24), 57 (14). FT-IR (Film) cm⁻¹: 3288, 2976, 1714, 1456, 1368, 1160, 842, 755, 700.

⁷ Wessig, P.; Schwarz, J. *Synlett* **1997**, 893 – 894.

Mixture of diastereomers
dr 90:10
major isomer (1*R**,3*R**)-5e

Mixture of diastomers
dr 90:10
major isomer (1*R**,3*S**)-**5e**

Mixture of diastereomers
dr 90:10
major isomer (1*R**,3*S**)-5e