Synthesis and Stereochemical Assignment of *Exo*- and *Endo* - 7- Methyl-7-azabicyclo[2.2.1]heptan-2-ol

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Supporting Information

General procedure for preparation of *endo* / *exo*-7-methyl-7-azabicyclo-[2.2.1]heptan-2-ol (2 and 3). A solution of the alcohol (**8** or **9**, 250 mg, 1.26 mmol) in dry THF (2 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (185 mg, 5.03 mmol) in dry THF (10 mL) and refluxed for 4 h. The reaction mixture was cooled and quenched with four drops of water. Four drops of 15% NaOH, followed by an additional twelve drops of water were added and the reaction mixture was extracted with ether (3 × 20 mL). The residue was purified by column chromatography (methanol:NH_4OH, 100: 3) to give the corresponding N-methyl analogue (**2** or **3**) in 70-74% yield.

***exo*-7-Methyl-7-azabicyclo[2.2.1]heptan-2-ol (2):** white solid (117 mg, 74%); mp 46-47 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62 (dd, J = 2.1, 7.2 Hz, 1H), 3.21 (brs, OH), 3.19 (d, J = 2.7 Hz, 1H), 3.10 (d, J = 3 Hz, 1H), 2.25 (s, 3H), 1.71 (m, 3H), 1.55 (m, 1H), 1.16 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 74.0, 68.3, 60.0, 43.4, 34.2, 24.3, 21.2. FTIR (NaCl, thin film) 3392, 2934, 1638, 1462, 1101 cm^{-1}. Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10. 30; N, 11.01. Found: C, 66.05; H, 10. 17; N, 11.19.

***endo*-7-Methyl-7-azabicyclo[2.2.1]heptan-2-ol (3):** colorless thick oil, (111 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (t, J= 5.2 Hz, 1H), 3.25 (t, J = 4.4 Hz, 1H), 3.19 (t, J = 4.81 Hz, 1H), 2.99 (br s, OH), 2.28 (s, 3H), 2.13 (m, 2H), 1.88 (m, 1H), 1.67 (m, 1H), 1.47 (m, 1H), 0.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.3, 66.3, 62.7, 39.7, 34.6, 26.5, 17.5. FTIR (NaCl, thin film) 3381, 2967, 1627, 1461, 1364, 1318, 1263 cm^{-1}. Anal. Calcd for $C_7H_{13}NO$: C, 66.11; H, 10. 30; N, 11.01. Found: C, 66.12; H, 10. 25; N, 11.18.

***Cis*-1,2-Epoxy-4-[N-(methylamino)]cyclohexane (12):** To a solution of **11** (6.0 g, 27 mmol) in methanol (17 mL) was added dropwise a solution of potasium carbonate (4.7 g, 34 mmol) in water (17 mL). After stirring at room temperature for 5 h most of the methanol was removed on a rotary evaporator. The residue was extracted with ether (6 × 20 mL) and dried over potasium carbonate, filtered, and the solvent was removed under reduced pressure to afford **12** (2.2 g, 65%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 (d, J = 2 Hz, 2H), 2.38 (s, 3H), 2.20 (m, 3H), 1.80 (br m, 1H), 1.62 (m, 1H), 1.52 (m, 1H), 1.32(m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.8, 52.0, 51.2, 33.2, 30.8, 24.0, 23.7. FTIR (NaCl, thin film) 3295, 2925, 1660, 1413, 1369, 1268 cm^{-1}.

***Cis*/*trans*-1,2-Epoxy-4-[*N*-(methylamino)]cyclohexane (12/15):** To a solution of the trifluoroacetamide **7** (0.80 g, 3.6 mmol) and KOH (0.60 g, 11 mmol) in methanol (24 mL) and water (12 mL) was stirred at room temperature for 3 h. Most of the methanol was removed on a rotary evaporator and the residue was extracted with ether (6 × 15 mL). The

extract was dried over potasium carbonate, filtered, and , and the solvent was removed under reduced pressure to afford the mixture of isomers **12**/**15** (3:1, 266 mg, 58%) as a colorless oil. Diagnostic signals for the minor isomer **15**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.16 (d, J = 3.6 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 52.1, 51.4, 51.1, 33.3, 30.9, 25.3, 21.5.

***exo*-7-Methyl-7-azabicyclo[2.2.1]heptan-2-ol (2).** A solution of **12** (2.20 g, 17.3 mmol) and K_2CO_3 (69 mg, 0.50 mmol) in dry *N*-methylpyrrolidone (30 mL), was heated under N_2 atmosphere at 160 °C in oil bath for 72 h. The dark mixture was subjected to distillation under reduced pressure and the distillate was made slightly acidic with conc. hydrochloric acid. The solvent was distilled and the residue was washed with hot ether to furnish **2**•HCl. The salt **2**•HCl was dissolved in aqueous sodium carbonate followed by continuous extraction with dichloromethane (24 h). The solvent was then carefully removed under reduced pressure and the residue was purified by column chromatography (SiO_2, CH_2Cl_2: CH_3OH:NH_4OH, 100:10:1) to afford **2** as a solid. This was further purified by bulb-to-bulb distillation at 70 °C (0.3 mm Hg) to furnish **2** (1.3 g, 61%) as a white solid: mp 46-47 °C.