Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Supporting Information

Regio- and stereocontrolled synthesis of novel 3-sulfonamido-2,3,4,5-tetrahydro-1,5-benzothiazepines from 2-(bromomethyl)- or 2-(sulfonyloxymethyl)aziridines

Michinori Karikomi, Matthias D'hooghe, Guido Verniest and Norbert De Kimpe*

Synthesis of 3-aminobenzothiazepines 6, 7 and 8

As a representative example, the synthesis of 3-benzenesulfonamido-2,3,4,5-tetrahydro-1,5-benzothiazepine **6a** is described here. To an ice-cooled, stirred solution of 1-toluenesulphonyl-2-(bromomethyl)aziridine **2a** (2.76 g, 10 mmol) in dry THF (20 mL) was added 2-aminothiophenol (1.50 g, 12 mmol) and potassium carbonate (1.66 g, 12 mmol). The mixture was stirred for 1 hour at 0 °C and 2 hours at room temperature, and then refluxed for 5 hours. The reaction mixture was poured into water (40 mL) and extracted with dichloromethane (3 × 40 mL). Drying ($MgSO_4$), filtration of the drying agent, removal of the solvent in vacuo and recrystallization from toluene afforded 3-benzenesulfonamido-2,3,4,5-tetrahydro-1,5-benzothiazepine **6a** as 2:1 mixed crystals with toluene.

3-Benzenesulfonamido-2,3,4,5-tetrahydro-1,5-benzothiazepine 6a. ^{1}H NMR (270 MHz, $CDCl_3$): δ 2.60 (1H, d×d×d, J = 14.5, 4.9, 1.3 Hz); 2.75 (1H, d×d, J = 14.5, 2.6 Hz); 2.93 (1H, d×d, J = 13.9, 1.6 Hz); 3.31 (1H, m); 3.64 (1H, m); 3.91 (1H, m); 6.00 (1H, d, J = 10.2 Hz); 6.77 (1H, d×d, J = 7.9, 1.0 Hz); 6.85 (1H, t×d, J = 7.9, 1.0 Hz); 7.10 (1H, t×d, J = 7.9, 1.0 Hz); 7.36 (1H, d×d, J = 7.6, 1.3 Hz); 7.56 (3H, m); 7.96 (2H, m). ^{13}C NMR (68 MHz, $CDCl_3$): δ 37.0, 51.4, 52.0, 120.6, 122.1, 125.1, 126.9, 128.5, 129.3, 132.8, 132.9, 141.6, 151.3. IR (neat, cm^{-1}): ν = 3320, 1588, 1475, 1323. MS (70 eV): m/z (%): 310 (M^+, 5); 243 (39); 203 (100). Anal. Calcd for $C_{15}H_{16}N_2O_2S_2 \cdot 0.4C_7H_8$: C 59.84, H 5.42, N 7.84. Found: C 58.86, H 5.65, N 7.76.

3-(*N*-toluenesulfonamido)-2,3,4,5-tetrahydro-1,5-benzothiazepine 6b. ^{1}H NMR (270 MHz, $CDCl_3$): δ 2.44 (3H, s); 2.59 (1H, d×d, J = 13.5, 4.9 Hz); 2.74 (1H, d×d, J = 14.5, 2.7 Hz); 2.95 (1H, d×d, J = 13.5, 2.0 Hz); 3.30 (1H, m); 3.70 (1H, d, J = 4.6 Hz); 3.85 (1H, m); 6.00 (1H, d, J = 9.9 Hz); 6.76 (1H, d×d, J = 7.6, 1.3 Hz); 7.08 (1H, t×d, J = 7.6, 1.6 Hz); 7.33 (3H, m); 7.81 (2H, d, J = 8.2 Hz). ^{13}C NMR (68 MHz, $CDCl_3$): δ 21.6, 51.5, 51.8, 120.5, 121.9, 124.9, 127.0, 128.4, 129.8, 132.8, 138.6, 143.5, 151.3. IR (neat, cm^{-1}): ν = 3354, 3284, 1476, 1320. MS (70 eV): m/z (%): 334 (M^+, 0.7); 278 (30); 84 (100).

3-(*N*-methanesulfonamido)-2,3,4,5-tetrahydro-1,5-benzothiazepine 6c. ^{1}H NMR (270 MHz, $CDCl_3$): δ 2.90 – 3.20 (6H, m); 2.52 (1H, m); 3.80 (1H, br s); 4.02 (1H, m); 5.75 (1H, d, J = 9.6 Hz); 6.81 (1H, d×d, J = 7.9, 1.0 Hz); 6.87 (1H, m); 7.13 (1H, t×d, J = 7.3, 1.3 Hz); 7.42 (1H, d×d, J = 7.6, 1.3 Hz). ^{13}C NMR (68 MHz, $CDCl_3$): δ 37.7, 42.7, 51.6, 52.4, 120.6, 122.1, 124.9, 128.5, 133.0, 151.3. IR (neat, cm^{-1}): ν = 3360, 3330, 1478, 1320. MS (70 eV): m/z (%): 217 (4); 138 (12); 84 (100).

***trans*-4-Phenyl-3-*p*-toluenesulfonamido-2,3,4,5-tetrahydro-1,5-benzothiazepine 7a**. ^{1}H NMR (270 MHz, $CDCl_3$): δ 2.38 (3H, s); 3.02 (1H, d×d, J = 14.8, 2.6 Hz); 3.37 (1H, s(br)); 3.90 (1H, m); 4.11 (1H, d×d, J = 14.8, 3.3 Hz); 4.75 (1H, d, J = 9.6 Hz); 4.85 (1H, d, J = 8.6 Hz); 6.40 (1H, d×d, J = 7.9, 1.3 Hz); 6.74 (1H, t×d, J = 7.9, 1.3 Hz); 6.92 (1H, t×d, J = 7.2, 1.6 Hz); 7.00-7.40 (10H, m). ^{13}C NMR (68 MHz, $CDCl_3$): δ 21.5, 36.8, 57.9, 64.1, 119.0, 120.7, 126.8, 127.4, 128.3, 129.1, 129.5, 131.0, 138.2, 139.5, 142.6, 146.6. IR (neat, cm^{-1}): ν = 3364, 3279, 3025, 1588, 1471. MS (70 eV): m/z (%): 410 (M^+, 0.4); 85 (100).

***trans*-4-Propyl-3-(*N*-toluenesulfonamido)-2,3,4,5-tetrahydro-1,5-benzothiazepine 7b**. ^{1}H NMR (270 MHz, $CDCl_3$): δ 0.78 (3H, t, J = 6.9 Hz); 1.2 – 1.5 (4H, m); 2.27 (1H, d×d, J = 14.8, 3.6 Hz); 2.44 (3H, s); 3.24 (1H, d×d, J = 14.8, 2.0 Hz); 3.32 (1H, br s); 3.55 (1H, br s); 3.64 (1H, d×d×d×d, J = 9.9, 5.9, 3.3, 2.7 Hz); 5.81 (1H, d, J = 9.9 Hz); 6.66 (1H, t×d, J = 7.6, 1.3 Hz); 6.80 (1H, t×d, J = 7.6, 1.3 Hz), 7.04 (1H, d×d, J = 7.6, 1.7 Hz), 7.24 (1H, d×d, J = 7.6, 1.7 Hz); 7.32 (2H, d, J = 8.2 Hz); 7.80 (2H, d, J = 8.2 Hz). ^{13}C NMR (68 MHz, $CDCl_3$): δ 14.7, 20.5, 22.6, 34.1, 34.5, 56.0, 60.0, 122.0, 122.6, 124.7, 127.8, 128.8, 130.8, 132.7, 139.6, 144.4, 148.6. IR (neat, cm^{-1}): ν = 3363, 3279, 1588, 1471. MS (70 eV): m/z (%): 377 (M^++1, 0.64); 362 (100); 84 (87).

***trans*-3-Methanesulfonamido-2-phenyl-2,3,4,5-tetrahydro-1,5-benzothiazepine 8**. ^{1}H NMR (270 MHz, $CDCl_3$): δ 2.39 (3H, s); 3.35 (1H, d×d, J = 14.2, 2.6 Hz); 3.84 (2H, m); 4.30 (1H, d, J = 9.2 Hz); 4.39 (1H, d×d, J = 14.2, 2.0 Hz); 5.03 (1H, d, J = 8.2 Hz); 6.64 (1H, d×d, J = 7.2, 1.0 Hz); 6.90-7.30 (5H, m); 7.39 (2H, d, J = 8.2 Hz). ^{13}C NMR (68 MHz, $CDCl_3$): δ 21.5, 49.2, 52.5, 59.3, 118.6, 120.4, 121.1, 127.0, 127.58, 127.64, 128.9, 129.5, 132.0, 136.7, 138.0, 143.2, 148.6. IR (neat, cm^{-1}): ν = 3386, 3298, 1600, 1498. MS (70 eV): m/z (%): 410 (M^+, 0.5); 125 (100).