Ugi MCR followed by an intramolecular nucleophilic substitution: convergent multicomponent synthesis of 1-sulfonyl 1,4-diazepan-5-ones and of their benzo-fused derivatives

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SUPPORTING INFORMATION

GENERAL EXPERIMENTAL METHODS

NMR spectra were taken, unless otherwise stated, in CDCl₃ at 300 MHz (¹H), and 75 MHz (¹³C), using TMS as internal standard for ¹H NMR and the central peak of CDCl₃ (at 77.02 ppm) for ¹³C NMR. When taken in DMSO-*d*₆, the central peak of DMSO (at 2.506 for ¹H and at 39.429 ppm for ¹³C) was taken as reference. Chemical shifts are reported in ppm (δ scale), coupling constants are reported in hertz. Peak assignments were made with the aid of DEPT, gCOSY and gHSQC experiments. In AB system, proton A is upfield. GC-MS were carried out using an HP-1 column (12.5 m long, 0.2 mm wide), electron impact at 70 eV, and a mass temperature of about 170°C. Only *m/z* > 33 were detected. All analyses were performed with a constant He flow of 0.9 ml/min with initial temp. of 55°C, init. time 2 min, rate 20°C/min, final temp. 250°C, inj. temp. 150°C, det. temp. 280°C. *R_t* are in min. IR spectra were measured as CHCl₃ solutions. Values of [α]_D were determined in CHCl₃ (containing 0.75-1% EtOH) solution. The d.r. of mixture **20a,b** was determined by HPLC on an instrument equipped with a DAD detector (at 220 nm) and a C₁₈ column (i.d. 4.6 mm, l 25 cm), using MeOH:H₂O 8:2 as eluent at 1 ml/min flow. *R_t* are in min. Melting points are uncorrected. TLC analyses were carried out on silica gel plates and developed at U.V. or by dipping into a solution of (NH₄)₄MoO₄·4 H₂O (21 g) and Ce(SO₄)₂·4 H₂O (1 g) in H₂SO₄ (31 ml) and H₂O (469 ml) and warming. *R_f* were measured after an elution of 7-9 cm. Chromatographies were carried out on 220-400 mesh silica gel using the “flash” methodology. Petroleum ether (40-60°C) is abbreviated as PE.

Synthesis and data of imines **5** - oxazolidines **6** from aliphatic aldehydes and ethanolamine.

Compounds 5b/6b: They were prepared from valeraldehyde as described in the general procedure. Yield: 49%. B.p. 90°C (40 mbar). ¹H NMR showed a 23.5:76.5 ratio between **5b** and **6b**. **5b**: δ 0.92 [3 H, t, CH₃, J 7.3]; 1.28-1.58 [4 H, m, CH₂CH₂]; 2.27 [2 H, dt, CH₂CH=N, J_t 7.2, J_d 5.1]; 3.51 (mc) [2 H, m, CH₂N]; 3.79 [2 H, t, CH₂OH, J 5.3]; 7.72 [1 H, tt, CHN, J 5.1, 1.5]. **6b**: δ 0.91 [3 H, t, CH₃, J 7.1]; 1.28-1.58 [4 H, m, CH₂CH₂]; 1.59-1.70 [2 H, m, CH₂CHN]; 3.01 [1 H, dt, CHHN, J_t 7.6, J_d 11.7]; 3.24 [1 H, dt, CHHN, J_t 5.9, J_d 11.7]; 3.70 [2 H, dd, CH₂O, J 6.3, 7.5]; 4.31 [1 H, t, CHN, J 5.6]. ¹³C-NMR: **5b**: δ 13.8 [CH₃]; 22.3 [CH₂]; 28.0 [CH₂]; 35.5 [CH₂C=N]; 62.0 [CH₂OH]; 63.0 [CH₂N]; 167.7 [CH=N]. **6b**: δ 13.9 [CH₃]; 22.6 [CH₂]; 27.6 [CH₂]; 33.8 [CH₂CHN]; 46.2 [CH₂N]; 64.7 [CH₂OH]; 92.4 [CHN]. GC-MS: *R_t* 4.09; *m/z* 129 (M⁺, 0.4); 128 (3.0); 100 (4.4); 98 (7.4); 87 (15.0); 72 (100.0); 70 (12.6); 69 (4.3); 56 (22.0); 45 (10.2); 44 (30.8); 43 (6.4); 42 (21.7); 41 (16.8); 39 (7.1).

Compounds 5c/6c: They were prepared from *iso*-valeraldehyde as described in the general procedure. Yield: 47%. B.p. 85°C (38 mbar). ¹H NMR showed a 42:58 ratio between **5c** and **6c**. **5c**: δ 0.83 [6 H, d, CH₃, J 6.6]; 1.79 [1 H, nonuplet, CH(CH₃)₂, J 6.6]; 2.03 [2 H, t, CH₂C=N, J 6.0]; 3.38 [2 H, t, CH₂N, J 5.4]; 3.64 [2 H, t, CH₂OH, J 5.4]; 7.57 [1 H, t, CHN, J 5.3]. **6c**: δ 0.83 [6 H, d, CH₃, J

6.6]; 1.30-1.48 [2 H, m, $\text{CH}_2\text{CH}(\text{CH}_3)_2$]; 1.70 [1 H, nonuplet, $\text{CH}(\text{CH}_3)_2$, J 6.7]; 2.88 [1 H, dt, CHHN , J_t 7.8, J_d 11.7]; 3.11 [1 H, ddd, CHHN , J 5.1, 6.9, 11.7]; 3.52-3.60 [2 H, m, CH_2O]; 4.22 [1 H, t, CHN , J 6.0]. GC-MS: R_t 3.73; *m/z* 129 (M^+ , 0.3); 128 (2.1); 114 (7.0); 98 (3.8); 87 (20.8); 84 (7.6); 72 (100.0); 56 (39.4); 45 (19.1); 44 (38.6); 43 (14.0); 42 (35.8); 41 (18.2); 39 (7.4); 41 (3.9); 39 (1.7).

Compounds 5d/6d: They were prepared from cyclohexanecarboxyaldehyde as described in the general procedure. Yield: 66%. B.p. 99-101°C (12 mbar). ¹H NMR showed a 15:85 ratio between **5d** and **6d**. **5d**: δ 1.00-1.33 [4 H, m, CH_2 cyclohexyl]; 1.58-1.94 [6 H, m, CH_2 cyclohexyl]; 2.83 [1 H, t, CH cyclohexyl, J 5.0]; 3.48 [2 H, t, CH_2N , J 5.0]; 3.77 [2 H, t, CH_2OH , J 5.2]; **6d**: δ 1.00-1.33 [4 H, m, CH_2 cyclohexyl]; 1.45 (mc) [1 H, m, CH cyclohexyl]; 1.58-1.94 [6 H, m, CH_2 cyclohexyl]; 2.98 [1 H, dt, CHHN , J_t 7.7, J_d 11.7]; 3.21 [1 H, ddd, CHHN , J 4.7, 6.9, 11.6]; 3.56-3.72 [2 H, m, CH_2OH]; 4.05 [1 H, d, CHN , J 6.3]. ¹³C-NMR: **5d**: δ 25.4, 25.9, 29.6 [CH_2 cyclohexyl]; 43.6 [CH cyclohexyl]; 62.3, 63.0 [$\text{CH}_2\text{CH}_2\text{OH}$]; 171.5 [$\text{CH}=\text{N}$]. **6d**: 25.8, 25.9, 26.3, 28.7, 28.8 [CH_2 cyclohexyl]; 41.9 [CH cyclohexyl]; 46.3 [CH_2N]; 64.8 [CH_2O]; 96.2 [CHN]. GC-MS: R_t 6.13; *m/z* 155 (M^+ , 0.5); 154 (1.5); 124 (21.0); 100 (19.4); 96 (4.1); 95 (13.3); 87 (26.2); 72 (100.0); 67 (7.4); 55 (10.0); 45 (19.7); 44 (23.0); 42 (14.0); 41 (17.4); 39 (8.2).

Characterization data of benzodiazepinones 1

1b: White solid. M.p.: 172.3-173.5°C. R_f: 0.59 (PE/acetone 75:25). Found: C, 57.5; H, 5.2; N, 7.1. $\text{C}_{28}\text{H}_{30}\text{BrN}_3\text{O}_4\text{S}$ requires C, 57.53; H, 5.17; N, 7.19. ¹H-NMR: δ 0.91 [3 H, t, CH_3 , J 7.2]; 1.26-1.38 [2 H, m, CH_2CH_3]; 1.42-1.54 [2 H, m, $\text{CH}_2\text{CH}_2\text{CH}_3$]; 2.43 [3 H, s, CH_3]; 3.12-3.50 [5 H, m, CHHN]; 3.78-3.93 [1 H, broad m, CHHN]; 5.96 [1 H, broad t, NH]; 6.01 [1 H, s, ArCHN]; 7.07 [1 H, d, H para to Br, J 7.8]; 7.19 [1 H, d, H meta to Br, J 7.8]; 7.25 [1 H, t, H meta to Br, J 7.2]; 7.26 [2 H, d, H meta to SO_2 , J 8.1]; 7.38 [1 H, dt, H para to $\text{C}=\text{O}$, J_d 1.5, J_t 7.8]; 7.41 [1 H, t, H ortho to Br and to alkyl, J 1.8]; 7.42 [1 H, dt, H para to N, J_d 1.5, J_t 7.5]; 7.46-7.53 [2 H, m, H ortho to Br and H ortho to N]; 7.50 [2 H, d, H ortho to SO_2 , J 8.1]; 7.70 [1 H, dd, H ortho to $\text{C}=\text{O}$, J 1.8, 7.5]. ¹³C-NMR: δ 13.7 [CH_3CH_2]; 20.1 [CH_2CH_3]; 21.7 [CH_3Ar]; 31.4 [$\text{CH}_2\text{CH}_2\text{CH}_3$]; 39.6, 43.1, 52.8 [CH_2N]; 59.5 [ArCHN]; 123.0 [C-Br]; 127.6 [CH ortho to SO_2]; 127.9 [CH para to Br]; 128.8 [CH para to N]; 129.6 [CH meta to SO_2]; 130.6 [CH meta to Br]; 130.7 [CH para to $\text{C}=\text{O}$]; 130.7 [CH ortho to $\text{C}=\text{O}$]; 132.0, 132.1, 132.2 [CH ortho to Br + CH ortho to N]; 134.5, 134.5, 136.8, 137.1, 143.6 [aromatic quat.]; 168.4, 169.7 [$\text{C}=\text{O}$]. I.R.: ν_{max} 3427 (broad), 3017, 3002, 2931, 2870, 1680, 1642, 1595, 1567, 1459, 1400, 1348, 1258, 1154, 1118, 1051 cm^{-1} .

1c: White solid. M.p.: 75.8-79.1°C R_f: 0.45 (PE/AcOEt 7:3). Found: C, 68.00; H, 6.55; N, 7.70. $\text{C}_{31}\text{H}_{35}\text{N}_3\text{O}_4\text{S}$ requires C, 68.23; H, 6.46; N, 7.70. ¹H-NMR: δ 0.85-1.46 [6H, m, CH_2 cyclohexyl]; 1.60-1.78 [4H, m, CH_2 cyclohexyl]; 1.86-2.02 [1H, m, CH cyclohexyl]; 2.34 [3 H, s, CH_3]; 3.28-3.42 [1 H, m, CHHN]; 3.61-3.74 [1 H, m, 2 CHHN]; 4.17-4.30 [1 H, m, 1 CHHN]; 4.23 [1 H, dd, CHHPh , J 4.4, 14.8]; 4.68 [1 H, dd, CHHPh , J 6.9, 14.8]; 4.73 [1 H, d, CHN]; 7.16 [2 H, d, H ortho to CH_3 , J 8.1]; 7.24-7.34 [6 H, m, aromatics]; 7.38 [1 H, dt, H para to N, J 1.5, 7.5]; 7.44 [1 H, dt, H para to $\text{C}=\text{O}$, J 1.8, 7.5]; 7.52 [2 H, d, H ortho to SO_2 , J 8.1]; 7.58 [1 H, dd, H ortho to $\text{C}=\text{O}$, J 1.7, 7.5]. ¹³C-NMR: δ 21.5 [CH_3Ar]; 25.6, 25.7, 26.1, 28.8, 29.8 [CH_2 cyclohexyl]; 36.8 [CH cyclohexyl]; 41.5 [CH_2N]; 43.7 [CH_2NH]; 52.4 [CH_2N]; 60.9 [CHN]; 127.4 [CH ortho to SO_2]; 127.5 and 128.6 [CH para of benzyl and CH meta to $\text{C}=\text{O}$]; 127.8, 128.7 [CH ortho and meta of benzyl]; 129.5 [CH meta to SO_2 + CH meta to $\text{C}=\text{O}$]; 130.1 [CH ortho to $\text{C}=\text{O}$]; 131.8 [CH para to $\text{C}=\text{O}$]; 134.4, 135.2, 136.9, 137.8, 143.6 [quaternary aromatic]; 169.4, 169.8 [$\text{C}=\text{O}$]. I.R.: ν_{max} 3426, 3426 2926, 2854, 1669, 1635, 1599, 1451, 1406, 1349, 1286, 1156, 1118, 1091, 964, 908 cm^{-1} .

1d: White solid. M.p.: 217.5-218.0°C. *R*_f: 0.47 (PE/AcOEt 7:3). Found: C, 69.4; H, 8.0; N, 4.95. C₃₂H₄₄N₂O₄S requires C, 69.53; H, 8.02; N, 5.07. ¹H-NMR: δ 0.77-1.44 [6H, m, CH₂ cyclohexyl]; 0.97 [9 H, s, (CH₃)₃]; 1.41 and 1.42 [2 × 3 H, 2 s, (CH₃)₂C]; 1.62 [1 H, d, CHH*t*Bu, J 14.9]; 1.78 [1 H, d, CHH*t*Bu, J 14.9]; 2.38 [3 H, s, CH₃]; 3.45 [1 H, ddd, CHHN, J 4.5, 7.2, 15.3]; 3.59 [1 H, dt, CHHN, J_t 5.5, J_d 15.3]; 3.87 [1 H, ddd, CHHN, J 4.5, 7.5, 11.7]; 3.99 [1 H, dt, CHHN, J 5.5, 11.7]; 4.54 [1 H, d, CHN, J 10.5]; 5.91 [1 H, s, NH]; 7.21 [2 H, d, *H* ortho to CH₃, J 8.1]; 7.33-7.48 [3 H, m, CH of anthranilic group]; 7.55 [2 H, d, *H* ortho to SO₂, J 8.1]; 7.59 [1 H, dd, *H* ortho to C=O, J 1.2, 7.8]. ¹³C-NMR: δ 21.6 [CH₃Ar]; 25.66, 25.72, 26.2, 29.1, 29.7 [CH₂ cyclohexyl]; 28.5, 28.9 [(CH₃)₂C]; 31.5 [C(CH₃)₃]; 31.6 [C(CH₃)₃]; 36.8 [CH cyclohexyl]; 41.5 [CH₂N]; 52.0 [CH₂*t*Bu]; 52.7 [CH₂N]; 55.7 [N-C(CH₃)₂]; 62.3 [CHN]; 127.5 [CH ortho to SO₂]; 128.3, 129.0 [CH meta to C=O]; 129.6 [CH meta to SO₂]; 130.3 [CH ortho to C=O]; 131.7 [CH para to C=O]; 134.6, 134.8, 136.7, 143.7 [quaternary aromatic]; 168.4, 170.0 [C=O]. I.R.: *v*_{max} 3420, 3026, 2991, 2926, 2854, 1669, 1634, 1597, 1448, 1348, 1233, 1190, 1158, 1117, 1046, 966, 944 cm⁻¹.

1e: White solid. M.p.: 135.8-139.9°C. *R*_f: 0.52 (CH₂Cl₂/PE/acetone 85:5:10). Found: C, 55.5; H, 4.55; N, 7.7. C₂₅H₂₄BrN₃O₄S requires C, 55.35; H, 4.46; N, 7.75. ¹H-NMR: δ 2.76 [3 H, s, CH₃SO₂]; 3.24-3.57 [3 H, m, CHHN]; 4.22-4.34 [1 H, broad m, CHHN]; 4.48 and 4.54 [2 H, AB part of ABX syst, CH₂Ph, J_{AB} 14.8, J_{AX} 6.0, J_{BX} 5.7]; 6.51 [1 H, s, CHN]; 6.71 [1 H, t, NH, J 5.6]; 7.22-7.38 [7 H, m, aromatics]; 7.41-7.49 [2 H, m, aromatics]; 7.50-7.58 [3 H, m, aromatics]; 7.66 [1 H, dd, *H* ortho to C=O, J 1.5, 7.5]. ¹³C NMR: δ 38.6 [CH₃SO₂]; 43.3 [CH₂N]; 43.8 [CH₂Ph]; 52.8 [CH₂N]; 60.1 [CHN]; 123.3 [aromatic quat.]; 127.7 [benzyl CH ortho or meta]; 128.8 [benzyl CH ortho or meta]; 127.6, 127.7, 129.1, 130.3, 130.8, 131.4, 132.0, 132.3, 132.6 [other aromatic CH]; 134.1, 134.3, 137.0, 137.4; 168.4, 170.1 [C=O]. I.R.: *v*_{max} 3421, 3005, 2930, 1677, 1638, 1600, 1566, 1455, 1406, 1344, 1259, 1150, 1110, 1043, 968 cm⁻¹.

1f: White solid. M.p.: 161.1-161.9°C. *R*_f: 0.33 (PE/acetone 75:25). Found: C, 59.65; H, 7.35; N, 9.75. C₂₁H₃₁N₃O₄S requires C, 59.83; H, 7.41; N, 9.97. ¹H-NMR: δ 0.90 [3 H, d, CH₃CH, J 6.6]; 1.02 [3 H, d, CH₃CH, J 6.3]; 1.02-1.22 [2H, m, cyclohexyl]; 1.23-1.44 [2H, m, cyclohexyl]; 1.55-1.76 [2H, m, cyclohexyl]; 1.79-1.99 [2H, m, cyclohexyl]; 2.28 [1 H, d of septuplet, CH(CH₃)₂, J_s 6.45, J_d 11.1]; 2.76 [3 H, s, CH₃]; 3.35 [1 H, ddd, CHHN, J 3.9, 11.4, 15.0]; 3.66-3.92 [3 H, m, 2 CHHN, cyHexCHN]; 4.28 [1 H, ddd, CHHN, J 4.8, 11.4, 13.2]; 4.79 [1 H, d, *i*PrCHN, J 10.8]; 6.33 [1 H, broad d, NH]; 7.43-7.59 [3 H, m, aromatic CH]; 7.64-7.70 [1 H, m, CH ortho to C=O]. ¹³C-NMR: δ 18.8, 19.3 [(CH₃)₂CH]; 24.8, 24.8, 25.3, 32.7, 33.1 [CH₂ cyclohexyl]; 28.1 [CH(CH₃)₂]; 38.3 [CH₃SO₂]; 41.8 [CH₂N]; 48.5 [CHN cyclohexyl]; 52.8 [CH₂N]; 62.5 [*i*Pr-CHN]; 129.1, 131.3, 132.3 [CH anthranilic group]; 129.9 [CH ortho to C=O]; 133.7, 135.0 [quaternary anthranilic group]; 168.9, 170.2 [C=O]. I.R.: *v*_{max} 3415, 3008, 2931, 2855, 1667, 1632, 1601, 1505, 1453, 1408, 1346, 1191, 1151, 1107, 1042, 970 cm⁻¹.

1g: White solid. M.p.: 87.0-88.0°C. *R*_f: 0.33 (PE/acetone 7:3). Found: C, 61.4; H, 6.3; N, 9.7. C₂₂H₂₇N₃O₄S requires C, 61.52; H, 6.34; N, 9.78. ¹H-NMR: δ 0.91 [3 H, t, CH₃CH₂, J 7.3]; 1.32 [2 H sextuplet, CH₃CH₂, J 7.5]; 1.42-1.54 [2 H, m, CH₃CH₂CH₂]; 2.87 [3 H, s, CH₃SO₂]; 3.24-3.54 [5 H, m, CH₂N]; 4.16-4.32 [1 H, broad m, CHHN]; 5.80 [1 H, broad s, NH]; 6.42 [1 H, s, CHN]; 7.42 [5 H, s, Ph CH]; 7.43-7.57 [3 H, m, anthranilic CH]; 7.72-7.77 [1 H, m, CH ortho to C=O]. ¹³C NMR: δ 13.7 [CH₃CH₂]; 20.0 [CH₂CH₃]; 31.5 [CH₂CH₂CH₃]; 38.5 [CH₃SO₂]; 39.6, 43.4, 53.0 [CH₂N]; 61.2 [CHN]; 129.0 [CH para to CHN]; 129.1, 129.4 [CH ortho and meta to CHN]; 130.3 [CH ortho to C=O]; 129.2, 131.6, 132.4 [other CH of anthranilic group]; 134.0, 134.6, 134.9 [aromatic quat.]; 168.9, 169.9 [C=O]. I.R.: *v*_{max} 3426, 3046, 2926, 2854, 1669, 1635, 1599, 1451, 1406, 1349, 1286, 1156, 1118, 1091, 964, 908 cm⁻¹.

1h: White solid. M.p.: 136.5-138.9°C. R_f : 0.61 (PE/AcOEt 50:50). Found: C, 59.55; H, 6.25; N, 9.25. $C_{22}H_{27}N_3O_5S$ requires C, 59.31; H, 6.11; N, 9.43. 1H -NMR: δ 1.08-1.28 [2H, m, cyclohexyl]; 1.28-1.45 [2H, m, cyclohexyl]; 1.56-1.77 [4H, m, cyclohexyl]; 1.85-1.98 [2H, m, cyclohexyl]; 2.89 [3 H, s, CH_3]; 3.34-3.47 [1 H, m, $CHHN$]; 3.50-3.62 [1 H, m, 2 $CHHN$]; 3.75-3.90 [2 H, m, 1 $CHHN$ + cyclohexyl CHN]; 5.91 [1 H, d, NH , J 7.8]; 6.34 [1 H, s, $ArCHN$]; 6.46 [1 H, dd, furyl H -4, J 1.8, 3.3]; 6.66 [1 H, d, furyl H -5, J 3.3]; 7.45-7.60 [4 H, m, furyl H -3 + H para and meta to $C=O$]; 7.73-7.78 [1 H, m, H ortho to $C=O$]. ^{13}C -NMR: δ 24.6, 24.7, 25.4, 32.7, 32.8 [CH_2 cyclohexyl]; 38.1 [CH_3]; 43.5 [CH_2N]; 48.8 [CHN cyclohexyl]; 52.6 [CH_2N]; 54.8 [$Ar-CHN$]; 111.1 [C -4 furyl]; 112.2 [C -5 furyl]; 129.3, 132.1, 132.7 [CH anthranilic group]; 130.4 [CH ortho to $C=O$]; 133.8, 134.2 [quaternary anthranilic group]; 143.9 [C -3 furyl]; 148.0 [C -1 furyl]; 165.8, 169.7 [$C=O$]. I.R.: ν_{max} 3419, 3043, 2928, 2855, 1678, 1641, 1599, 1511, 1466, 1413, 1363, 1331, 1246, 1158, 1094, 1013, 964, 908 cm^{-1} .

1i: White solid. M.p.: 85.0-86.0°C. R_f : 0.38 (PE/AcOEt 7:3). Found: C, 64.2; H, 7.15; N, 6.5. $C_{34}H_{45}N_3O_5SSi$ requires C, 64.22; H, 7.13; N, 6.61. 1H -NMR: δ 0.16, 0.21 [2×3 H, 2 s, $(CH_3)_2Si$]; 0.84 [1 H, d, CH_3CH , J 6.6]; 0.99 [3 H, s, $SiC(CH_3)_3$]; 1.05 [3 H, d, CH_3CH , J 6.6]; 2.12 [3 H, s, CH_3Ar]; 2.22 [1 H, d of septuplet, $CH(CH_3)_2$, J_s 6.6, J_d 11.1]; 3.36-3.50 [1 H, m, $CHHN$]; 3.73-3.84 [2 H, m, $CHHN$]; 4.15-4.27 [1 H, m, $CHHN$]; 4.70 [1 H, d, CHN , J 11.1]; 4.73 and 4.76 [2 H, AB syst. CH_2O , J 12.3]; 6.96 [2 H, d, H ortho to CH_3 , J 8.1]; 7.11 [1 H, H para to $C=O$, dt, J_d 0.9, J_t 7.4]; 7.16 [1 H, dd, H ortho to NSO_2 , J 1.5, 7.2]; 7.32-7.43 [2 H, m, H para to NSO_2 + 1 CH Linderman's group]; 7.42-7.52 [4 H, m, H ortho to SO_2 + 2 CH Linderman's group]; 7.64 [1 H, d, CH of Linderman's group]; 8.09 [1 H, d, H ortho to $C=O$, J 8.1]; 8.95 [1 H, s, NH]. ^{13}C NMR: δ -5.2, -5.1 [$(CH_3)_2Si$]; 18.4 [$C(CH_3)_3$]; 19.0, 19.5 [$(CH_3)_2CH$]; 21.3 [CH_3Ar]; 26.0 [$C(CH_3)_3$]; 28.5 [$CH(CH_3)_2$]; 41.6, 52.7 [CH_2N]; 63.3 [CHN]; 65.2 [CH_2O]; 122.2 [CH ortho to $C=O$]; 124.3 [CH para to $C=O$]; 127.3 [CH ortho to SO_2]; 127.9 [CH ortho to NSO_2]; 128.4, 128.5 [CH para to NSO_2 and CH Linderman]; 129.5 [CH meta to SO_2]; 129.5 [quat.]; 130.2 ($\times 2$), 131.7 [CH Linderman]; 134.5, 134.7, 136.4, 137.0, 143.3 [quat.]; 168.2, 169.6 [$C=O$].

1j: White solid. M.p.: 95.0-95.9°C. R_f : 0.47 (PE/acetone 7:3). Found: C, 58.55; H, 7.2; N, 8.4. $C_{24}H_{35}N_3O_6S$ requires C, 58.40; H, 7.15; N, 8.51. 1H -NMR: δ 0.98-1.33 [5 H, m, cyclohexyl CH_2]; 1.47 [9 H, s, $C(CH_3)_3$]; 1.50-1.82 [5 H, m, cyclohexyl CH_2]; 1.90-2.03 [1 H, m, CH cyclohexyl]; 2.76 [3 H, s, CH_3SO_2]; 3.31 [1 H, ddd, $CHHN$, J 4.0, 11.8, 15.0]; 3.63 [1 H, ddd, $CHHN$, J 2.4, 4.2, 12.6]; 3.75 [1 H, ddd, $CHHN$, J 2.7, 4.6, 15.0]; 3.94 and 3.99 [2 H, AB part of ABX syst., CH_2CO , J_{AB} 16.9, J_{AX} 3.6, J_{BX} 4.0]; 4.22 [1 H, ddd, $CHHN$, J 4.6, 11.8, 12.6]; 4.95 [1 H, d, CHN , J 11.4]; 6.55 [1 H, t, NH , J 5.1]; 7.43-7.58 [3 H, m, aromatic CH]; 7.70 [1 H, dd, CH ortho to $C=O$, J 1.8, 7.5]. ^{13}C NMR: δ 25.58, 25.61, 26.1, 28.7, 29.8 [cyclohexyl CH_2]; 28.0 [$C(CH_3)_3$]; 36.6 [cyclohexyl CH]; 38.5 [CH_3SO_2]; 41.8 [CH_2N]; 42.0 [CH_2CO]; 52.5 [CH_2N]; 60.9 [CHN]; 82.6 [$C(CH_3)_2$]; 129.1, 130.1, 130.9, 132.3 [aromatic CH]; 133.7, 135.0 [aromatic quat.]; 169.9, 168.3 [$C=O$]. I.R.: ν_{max} 3411 (broad), 3002, 2928, 2854, 1738, 1676, 1636, 1454, 1388, 1367, 1342, 1190, 1152, 1046, 967, 821 cm^{-1} .

Characterization data of diazepanones 2

2b: White solid. M.p.: 197.4-198.1°C. R_f : 0.51 (PE/AcOEt 55:45). Found: C, 64.95; H, 7.2; N, 8.25. $C_{27}H_{35}N_3O_4S$ requires C, 65.16; H, 7.09; N, 8.44. 1H -NMR: δ 0.74-0.98 [2 H, m, 2 CHH cyclohexyl]; 1.03-1.33 [2 H, m, 3 CHH cyclohexyl]; 1.42 [1 H, d, CHH cyclohexyl]; 1.55-1.76 [4 H, m, 3 CHH cyclohexyl]; 1.76-1.94 [1 H, m, CH cyclohexyl]; 2.42 [3 H, s, CH_3Ar]; 2.42-2.63 [3 H, m, H -3, H -6, H -7]; 2.66-2.78 [1 H, m, H -6]; 3.53 [1 H, dd, H -3, J 9.0, 15.6]; 3.62-3.76 [2 H, m, H -7, H -3]; 3.82 [1 H, dd, H -2, J 9.3, 15.6]; 4.23 and 4.28 [2 H, AB part of ABX system, CH_2Ph , J_{AB} 15.0, J_{AX} 6.4,

J_{BX} 5.6]; 4.57 [1 H, d, CHN, J 11.4]; 6.68 [1 H, broad t, NH]; 7.05-7.12 [2 H, m, benzyl CH]; 7.12-7.18 [3 H, m, benzyl CH]; 7.31 [2H, CH ortho to CH₃, J 8.1]; 7.60 [2 H, d, CH meta to CH₃, J 8.1]. ¹³C NMR: δ 21.5 [CH₃Ar]; 25.40, 25.45, 26.1, 28.9, 29.7 [cyclohexyl CH₂]; 35.4 [cyclohexyl CH]; 38.2 [C-6]; 43.2 [PhCH₂]; 43.3 [C-7]; 44.4 [C-2]; 48.9 [C-3]; 61.5 [CH-N]; 127.3 [CH ortho to SO₂]; 127.4 [CH benzyl para]; 127.6, 128.5 [CH benzyl meta and ortho]; 129.8 [CH ortho to CH₃]; 134.4, 137.8, 143.8 [aromatic quaternary]; 169.6, 174.3 [C=O]. I.R.: ν_{max} 3429, 3024, 3011, 2988, 2928, 2851, 1668, 1633, 1512, 1462, 1363, 1341, 1319, 1306, 1238, 1154, 1096, 1042, 968, 907 cm⁻¹.

2c: White solid. M.p.: 146.5-147.9. R_f: 0.48 in CH₂Cl₂/Me₂CO 9:1. Found: C, 59.75; H, 7.95; N, 9.85. C₂₁H₃₃N₃O₄S requires C, 59.55; H, 7.85; N, 9.92. ¹H-NMR: δ 0.75 & 0.89 [2 × 3H, 2d, (CH₃)₂CH, J 6.6 and 6.3]; 1.10 [9H, s, (CH₃)₃C]; 2.14 [1H, d of septuplet, CH(CH₃)₂, J_s 6.6, J_d 11.1]; 2.40 [3H, s, ArCH₃]; 2.30-2.43 [1H, m, H-3]; 2.49 [1 H, t, H-7, J 11.5]; 2.72 [1 H, dd, H-6, J 6.9, 14.4]; 2.86 [1 H, ddd, H-6, J 1.5, 10.8, 14.7]; 3.49-3.60 [1H, m, H-2]; 3.70-3.92 [3H, m, (in order of increasing δ): H-2, H-3, H-7]; 4.25 [1H, d, CHN, J 11.1]; 5.74 [1H, s, NH]; 7.28 [2H, CH ortho to CH₃, J 8.1]; 7.58 [2 H, d, CH meta to CH₃, J 8.1]. ¹³C-NMR: δ 18.4 and 19.3 [(CH₃)₂CH]; 21.5 [CH₃ aryl]; 25.9 [CH(CH₃)₂]; 28.3 [(CH₃)₃C]; 37.7 [C-6 of the ring]; 43.6 [C-2 of the ring]; 43.8 [C-7 of the ring]; 49.2 [C-3 of the ring]; 51.1 [C(CH₃)₃]; 63.1 [CHN]; 127.4 and 129.8 [aromatic CH]; 133.2 [CSO₂]; 143.8 [CCH₃]; 169.0 & 174.2 [2 × C=O]. I.R.: ν_{max} 3682; 3418; 2960; 2926; 2869; 2401; 1673; 1641; 1505; 1460; 1364; 1340; 1312; 1159; 1094; 1044; 971; 902 cm⁻¹.

2d: Foam. R_f: 0.46 in CH₂Cl₂/Me₂CO 9:1. Found: C, 63.45; H, 7.05; N, 8.75;. C₂₅H₃₃N₃O₄S requires C, 63.67; H, 7.05; N, 8.91. ¹H-NMR: δ 0.85 [3H, t, CH₃CH₂, J 7.0]; 1.08-1.36 [4H, m, CH₂CH₂]; 1.45-1.58 [1H, m, CHHCHN]; 1.78-1.93 [1H, m, CHHCHN]; 2.64-2.82 [2 H, m, H-6]; 2.92-3.06 [2 H, m, H-7 + H-2 or H-3] 3.29-3.43 [2 H, m, H-7 + H-2orH-3] 3.49-3.68 [2 H, m, H-2orH-3]; 4.30 [2H, d, CH₂Ph, J=6.0]; 4.86 [1H, t, CHN, J=7.5]; 6.49 [1H, t broad, NH, J=5.4]; 7.10-7.16 [2 H, m, CH benzyl]; 7.18-7.24 [3H, m, CH benzyl]; 7.33 [2H, d, CH ortho to CH₃, J=7.8]; 7.61 [2H, d, CH meta to CH₃, J=8.4]. ¹³C-NMR: δ 13.9 [CH₂CH₃]; 21.5 [CH₃ tolyl]; 22.4 [CH₂CH₃]; 28.0 and 28.1 [CH₂CH₂]; 38.3 [CH₂C=O]; 43.3 [PhCH₂N]; 43.4 [C-7 or C-2 or C-3]; 44.2 [C-2 or C-3]; 49.1 [C-7 or C-2 or C-3]; 56.4 [CHN]; 127.3 [CH meta to CH₃]; 127.5 [CH benzyl para]; 127.5 and 128.6 [CH benzyl ortho and meta]; 129.9 [CH ortho to CH₃]; 134.2 [CSO₂]; 137.8 [CCH₂ benzyl]; 143.9 [CCH₃ tolyl]; 170.2 and 174.4 [C=O]. I.R.: ν_{max} 3671; 3594; 3426; 3062; 2956; 2926; 2860; 2394; 1672; 1635; 1516; 1455; 1429; 1363; 1340; 1158; 1094; 967; 904 cm⁻¹.

2e: White solid. M.p.: 246.6-247.4°C. R_f: 0.40 in petroleum ether/AcOEt 4:6. Found: C, 60.3; H, 6.3; Cl, 6.77; N, 8.0. C₂₆H₃₂ClN₃O₄S requires C, 60.28; H, 6.23; N, 8.11. ¹H-NMR: δ 0.98-1.44 [5H, m, cyclohexyl]; 1.52-1.96 [5H, m, cyclohexyl]; 2.43 [3H, s, CH₃Ar]; 2.82 [2H, t, CH₂C=O (H-6) J 5.4]; 2.98-3.09 [1 H, m, H-7]; 3.09-3.42 [3 H, m, H-2 and H-3]; 3.47-3.65 [2 H, m, H-7 and H-2 or H-3]; 5.68 [1H, d, NH J 8.1]; 6.15 [1H, s, ArCHN]; 7.20 [2H, d, CH in meta to SO₂ J 8.4]; 7.26-7.38 [4H, m, CH chlorofenile]; 7.57 [2H, d, CH in ortho to SO₂ J 8.1]. ¹³C-NMR: δ 21.5 [CH₃]; 24.7, 24.7 and 25.3 [3 × CH₂ cyclohexyl]; 32.7 and 32.8 [2 × CH₂ cyclohexyl]; 38.4 [CH₂C=O]; 43.4 [C-7]; 46.1 and 49.0 [C-2 and C-3]; 48.6 [CHN cyclohexyl]; 59.5 [ArCHN]; 127.2 [CH in ortho to SO₂]; 129.2 and 129.8 [aromatic CH]; 130.1 [CH in meta to SO₂]; 133.8, 134.2, 134.6 [C aromatic quat., CSO₂, CCl, CCN]; 143.8 [CCH₃]; 167.9 and 174.1 [2 × C=O]. I.R.: ν_{max} 3670; 3418; 3005; 2932; 2854; 2392; 1912; 1674; 1643; 1597; 1489; 1464; 1425; 1363; 1327; 1157; 1093; 1015; 986; 965; 909 cm⁻¹.

2f: Foam. R_f: 0.55 in CH₂Cl₂/Me₂CO 8:2. Found: C, 61.4; H, 6.7; N, 8.45;. C₂₅H₃₃N₃O₅S requires C, 61.58; H, 6.82; N, 8.62. ¹H-NMR: δ 1.31 [9H, s, C(CH₃)₃]; 2.43 [3H, s, CH₃Ar]; 2.74-2.90 [2H, m, CH₂C=O]; 3.03 [1H, dd, H-2, J 7.5 13.5]; 3.13-3.25 [2 H, m, H-2 and H-7]; 3.33-3.46 [2 H, m, H-7 and

H-3]; 3.58 [1H, dd, *H*-3, *J* 7.2 15.9]; 3.74 [3H, s, CH₃O]; 5.54 [1H, broad, NH]; 6.06 [1H, s, ArCHN]; 6.76-6.90 [3H, m, CH in ortho and in para to OCH₃]; 7.26 [1 H, t, CH in meta to OCH₃, *J* 8.1]; 7.29 [2H, d, CH in meta to SO₂, *J* 8.1]; 7.56 [2H, d, CH in ortho to SO₂ *J* 8.1]. ¹³C-NMR: δ 21.5 [CH₃Ar]; 28.6 [C(CH₃)₃]; 38.3 [C-6]; 43.4 [C-7], 46.1 [C-3]; 49.1 [C-2]; 51.8 [C(CH₃)₃]; 55.2 [OCH₃]; 60.7 [NHCHAr]; 114.1 and 114.4 [CH in ortho to OCH₃]; 121.0 [CH in para to OCH₃]; 127.2 [CH in ortho to SO₂]; 129.8 [CH in meta to SO₂]; 130.0 [CH in meta to OCH₃]; 134.4 [CSO₂]; 136.9 [CCHN aromatic]; 143.7 [CCH₃]; 160.0 [COCH₃]; 168.4 and 174.1 [2 × C=O]. I.R.: ν_{max} 3668; 4315; 2958; 2836; 2734; 2401; 1931; 1671; 1632; 1600; 1452; 1366; 1328; 1259; 1155; 1091; 1042; 930 cm⁻¹.

2g: White solid. M.p.: 180.5-181.6°C R_f: 0.63 in PE/Me₂CO 65:35. Found: C, 64.25; H, 7.65; N, 7.65. C₂₉H₄₁N₃O₅S requires C, 64.06; H, 7.60; N, 7.73. ¹H-NMR: δ 0.89 [9H, s, C(CH₃)₃]; 1.34 and 1.39 [2 × 3 H, 2s, (CH₃)₂C]; 1.47 [1 H, d, CHHtBu, *J* 14.7]; 1.84 [1 H, d, CHHtBu, *J* 14.7]; 2.75-2.87 [2 H, m, CH₂CO]; 3.04-3.20 [3 H, m, CH₂N]; 3.41 [1 H, dt, CHHN, *J*_t 4.5, *J*_d 16.5]; 3.40-3.52 [1 H, m, CHHN]; 3.61 [1 H, dt, CHHN, *J*_t 4.3, *J*_d 16.5]; 3.76 [3H, s, CH₃O]; 5.52 [1H, broad, NH]; 6.01 [1H, s, ArCHN]; 6.76-6.90 [3H, m, CH in ortho and in para to OCH₃]; 7.26 [1 H, t, CH in meta to OCH₃, *J* 8.1]; 7.29 [2H, d, CH in meta to SO₂, *J* 8.1]; 7.58 [2H, d, CH in ortho to SO₂ *J* 8.1]. ¹³C-NMR: δ 21.5 [CH₃Ar]; 28.6 and 29.0 [(CH₃)₂]; 31.4 [C(CH₃)₃]; 31.6 [C(CH₃)₃]; 38.3 [C-6]; 43.5 [C-7], 46.1 [C-3]; 49.1 [C-2]; 52.1 [CH₂tBu]; 55.2 [NC(CH₃)₂]; 55.8 [OCH₃]; 60.9 [NHCHAr]; 114.1 and 114.4 [CH in ortho to OCH₃]; 121.0 [CH in para to OCH₃]; 127.3 [CH in ortho to SO₂]; 129.8 [CH in meta to SO₂]; 130.0 [CH in meta to OCH₃]; 134.3 [CSO₂]; 136.7 [CCHN aromatic]; 143.7 [CCH₃]; 160.0 [COCH₃]; 168.1 and 173.9 [2 × C=O]. I.R.: ν_{max} 2393, 3066, 2998, 2960, 2901, 1677, 1639, 1599, 1536, 1465, 1427, 1364, 1322, 1306, 1157, 1095, 1040, 967, 908 cm⁻¹.

2h: White solid. M.p.: 205.3-205.8°C. R_f: 0.51 in PE/AcOEt 35:65. Found: C, 61.3; H, 6.9; N, 8.4;. C₂₅H₃₃N₃O₅S requires C, 61.58; H, 6.82; N, 8.62. ¹H n.m.r.: δ 0.87 [3 H, t, CH₃CH₂, *J* 7.3]; 1.27 [2 H, sextuplet, CH₂CH₃, *J* 7.4]; 1.43 (mc) [2 H, m, CH₂CH₂CH₃]; 2.43 [3H, s, CH₃Ar]; 2.74-2.86 [2H, m, CH₂C=O]; 3.04-3.32 [5 H, m, CH₂NH, 2 *H*-2, 1 *H*-7]; 3.33-3.53 [2 H, m, 1 *H*-7, 1 *H*-3]; 3.59 [1 h, dt, 1 *H*-3, *J*_t 4.4, *J*_d 16.8]; 3.76 [3H, s, CH₃O]; 5.85 [1H, broad, NH]; 6.16 [1H, s, ArCHN]; 6.76-6.90 [3H, m, CH in ortho and in para to OCH₃]; 7.26 [1 H, t, CH in meta to OCH₃, *J* 7.8]; 7.29 [2H, d, CH in meta to SO₂, *J* 7.8]; 7.58 [2H, d, CH in ortho to SO₂ *J* 8.1]. ¹³C-NMR: δ 13.6 [CH₃CH₂]; 20.0 [CH₂CH₃]; 21.5 [CH₃Ar]; 31.3 [CH₂CH₂CH₃]; 38.4 [C-6]; 39.3 [CH₂NH]; 43.4 [C-7], 46.3 [C-3]; 49.0 [C-2]; 55.2 [OCH₃]; 60.7 [NHCHAr]; 114.1 and 114.5 [CH in ortho to OCH₃]; 121.0 [CH in para to OCH₃]; 127.2 [CH in ortho to SO₂]; 129.8 [CH in meta to SO₂]; 130.1 [CH in meta to OCH₃]; 134.5 [CSO₂]; 136.7 [CCHN aromatic]; 143.7 [CCH₃]; 160.0 [COCH₃]; 169.1 and 174.0 [2 × C=O].

2i: White solid. M.p.: 167.0-169.3°C. R_f: 0.56 in PE/Me₂CO 6:4. Found: C, 61.1; H, 6.7; N, 8.7;. C₂₄H₃₁N₃O₅S requires C, 60.87; H, 6.60; N, 8.87. ¹H-NMR: δ 1.00-1.42 [5H, m, CH₂ cyclohexyl]; 1.49-1.92 [5H, m, CH₂ cyclohexyl]; 2.74-2.90 [2H, m, *H*-6]; 3.09-3.30 [3H, m, *H*-7 + 2 *H*-2]; 3.38-3.53 [2H, m, *H*-7 and *H*-3]; 3.55-3.78 [2H, m, *H*-3 + CHN cyclohexyl]; 5.79 [1H, d, NH *J* 7.5]; 6.18 [1H, s, ArCHN]; 6.36 [1H, dd, *H* at position 5 of furyl, *J* 2.1, 3.3]; 6.50 [1H, d, *H* at position 3 of furyl *J* 3.3]; 7.30 [2H, d, CH in meta to SO₂ *J* 8.1]; 7.36 [1H, d, *H* at position 3 of furyl, *J* 2.1]; 7.59 [2H, d, CH in ortho to SO₂ *J* 8.1]. ¹³C-NMR: δ 21.5 [CH₃]; 24.6 (× 2), 25.3, 32.6 and 32.7 [CH₂ cyclohexyl]; 38.3 [C-6]; 43.4 [C-7]; 46.1 [C-3]; 48.6 [CHN cyclohexyl]; 48.9 [C-2]; 55.3 [ArCHN]; 110.7 [CH at position 4 of furyl]; 111.6 [CH at position 5 of furyl]; 127.2 [CH in ortho to SO₂]; 129.8 [CH in meta to SO₂]; 134.4 [C quat.]; 143.3 [CH at position 3 of furyl]; 143.7, 148.2 [2 × C quat.]; 166.2 and 173.9 [2 × C=O]. I.R.: ν_{max} 3668; 3415; 2958; 2836; 2734; 2401; 1931; 1671; 1632; 1600; 1452; 1366; 1328; 1259; 1155; 1091; 1042; 930 cm⁻¹.

2j: Foam. Note: it was not possible to separate completely this compound from the isomeric ketopiperazine 12j. Analysis was done on the enriched mixture. R_f : 0.29 in $\text{CH}_2\text{Cl}_2/\text{Me}_2\text{CO}$ 9:1. Found: C, 59.6; H, 6.5; N, 7.7; $\text{C}_{27}\text{H}_{35}\text{N}_3\text{O}_7\text{S}$ requires C, 59.43; H, 6.47; N, 7.70. $^1\text{H-NMR}$: δ 1.43 [9 H, s, $\text{C}(\text{CH}_3)_3\text{C}$]; 2.78-2.86 [2 H, m, $H-6$]; 3.08-3.29 [3 H, m, 2 $H-2$ and $H-7$]; 3.34-3.47 [2 H, m, $H-7$ and $H-3$]; 3.59 [1H, dd, $H-3$, J 7.2 15.9]; 3.77 [3 H, s, OCH_3]; 3.93-4.05 [2 H, m, $\text{NCH}_2\text{CO}_2t\text{Bu}$]; 6.27 [1 H, s, CH-N]; 6.32 [1 H, t broad, NH , J non determined]; 6.82-6.90 [3H, m, CH in ortho and in para to OCH_3]; 7.26 [1 H, t, CH in meta to OCH_3 , J 8.1]; 7.29 [2H, d, CH in meta to SO_2 , J 8.1]; 7.57 [2H, d, CH in ortho to SO_2 J 8.1].

2l: Foam. R_f : 0.50 in $\text{CH}_2\text{Cl}_2/\text{Me}_2\text{CO}$ 9:1. Found: C, 56.75; H, 5.8; N, 11.25. $\text{C}_{23}\text{H}_{28}\text{N}_4\text{O}_6\text{S}$ requires C, 56.54; H, 5.78; N, 11.47. $^1\text{H-NMR}$: δ 0.81 and 0.95 [$2 \times 3\text{H}$, $2 \times \text{d}$, $(\text{CH}_3)_2\text{C}$ J 6.6 and 6.3]; 2.22 [1H, d of septuplet, $\text{CH}(\text{CH}_3)_2$, J_s 6.6, J_d 11.1]; 2.60-2.84 [3H, m, $H-6$ and $H-2$]; 2.86-3.04 [1H, m, $H-7$]; 3.57 [1H, dd, $H-3$, J 8.9, 15.2]; 3.64-3.88 [3H, m, $H-7$, $H-2$, $H-3$]; 4.31 and 4.38 [2H, AB part of ABX system, HNCH_2Ph , J_{AB} 14.7, J_{AX} 5.6 J_{BX} 6.4]; 4.52 [1H, d, $\text{NCHCH}(\text{CH}_3)_2$ J 11.1]; 6.71 [1H, t, NHCH_2Ph J 5.9]; 7.06-7.16 [1H, m, aromatic CH]; 7.16-7.36 [4H, aromatic CH]; 7.64-7.80 [3H, m, aromatic CH]; 7.92-8.04 [1H, m, aromatic CH]. $^{13}\text{C-NMR}$: δ 18.6 and 19.4 [$(\text{CH}_3)\text{CH}$]; 26.3 [$\text{CH}(\text{CH}_3)_2$]; 39.0 [$C-6$]; 43.3 and 43.1 [CH_2Ph and $C-7$]; 44.7 [$C-3$]; 48.6 [$C-2$]; 62.8 [$i\text{PrCHN}$]; 124.4, 131.1, 131.9 and 133.9 [CH of nitrobenzenesulfonyl]; 127.5 (para), 127.8 and 128.6 (ortho and meta) [aromatic CH of phenyl]; 132.5, 137.9 [C aromatic quat.]; 169.7 and 174.4 [$2 \times \text{C=O}$].

2m: Foam. R_f : 0.45 in $\text{CH}_2\text{Cl}_2/\text{Me}_2\text{CO}$ 9:1. Found: C, 58.4; H, 5.95; N, 10.75. $\text{C}_{25}\text{H}_{30}\text{N}_4\text{O}_6\text{S}$ requires C, 58.35; H, 5.88; N, 10.89. $^1\text{H-NMR}$: δ 1.00-1.40 [5H, m, cyclohexyl]; 1.50-2.00 [5H, m, cyclohexyl]; 2.78-2.92 [2H, m, 2 $H-6$]; 3.28-3.46 [3H, $H-2$, $H-3$, $H-7$]; 3.48-3.66 [2H, m, $H-2$ and $H-3$]; 3.67-3.85 [2H, m, $H-7$ + CHN cyclohexyl]; 5.65 [1H, d, NH J 8.1]; 6.25 [1H, s, CHPh]; 7.25- 7.44 [5H, m, CH fenile]; 7.60-7.75 [3H, m, CH in meta and para to NO_2]; 7.94 [1H, m, CH in ortho to NO_2]. $^{13}\text{C-NMR}$: δ 24.7, 24.8 and 25.4 [$3 \times \text{CH}_2$ cyclohexyl]; 32.8 and 32.8 [$2 \times \text{CH}_2$ cyclohexyl]; 39.3 [$C-6$]; 43.5 [$C-7$]; 46.8 and 48.9 [$C-2$ and $C-3$]; 48.7 [CHN cyclohexyl]; 60.8 [NCHPh]; 128.7 [CH para of phenyl]; 128.9 and 129.1 [CH in ortho and meta of phenyl]; 124.3, 130.8, 131.8 and 133.8 [CH of o-nitrobenzensulfonyl group]; 130.8 and 135.3 [$2 \times C$ aromatic quat.]; 147.9 [CNO_2]; 168.4 and 174.0 [$2 \times \text{C=O}$].

Data of compound 11a (main diastereoisomer)

R_f : 0.41 in $\text{CH}_2\text{Cl}_2/\text{Me}_2\text{CO}$ 9:1. Found: C, 61.5; H, 7.85; N, 9.3. $\text{C}_{23}\text{H}_{35}\text{N}_3\text{O}_4\text{S}$ requires C, 61.44; H, 7.85; N, 9.35 $^1\text{H-NMR}$: δ 0.80 and 1.01 [$2 \times 3 \text{H}$, 2 d, $(\text{CH}_3)_2\text{CH}$, J 6.9]; 1.10-1.30 [3 H, m, CH_2 cyclohexyl], 1.40-1.65 [3 H, m, CH_2 cyclohexyl], 1.70-1.90 [4 H, m, CH_2 cyclohexyl + $\text{CHH-CH}_2\text{NHS}$]; 2.00-2.22 [3 H, m, $\text{CH}(\text{CH}_3)_2$, $\text{CHH-CH}_2\text{NHS}$ + CH_2 cyclohexyl]; 2.76 [1 H, dd, OCH_2CHHN , J 4.5 e 12.0]; 2.89 [1 H, dt, OCH_2CHHN , J_t 12.0, J_d 5.7]; 2.95-3.08 [1 H, m, CHN]; 3.05 [1 H, d, $i\text{PrCHN}$, J 3.9]; 3.13 [2 H, q, CH_2NHS , J 5.7]; 3.53 [1 H, ddd, CHHO , J 5.1, 8.7, 11.4]; 3.82 [1 H, dd, CHHO , J 5.1, 8.7]; 5.87 [1 H, t, NH , J 5.3]; 7.32 [2 H, d, CH meta a SO_2 , J 7.8]; 7.76 [2 H, CH orto to SO_2 , J 7.8]. $^{13}\text{C-NMR}$: 17.2 e 19.5 [$(\text{CH}_3)_2\text{CH}$]; 21.5 [CH_3Ar]; 25.0, 26.06, 26.09, 29.5, 30.0, 36.1, 38.5 [CH_2 cicloesile + $\text{CH}_2\text{CH}_2\text{NH}$]; 30.7 [$\text{CH}(\text{CH}_3)_2$]; 54.2 [CHN]; 56.6 [CH_2N]; 63.2 [CH_2O]; 72.9 [CHN]; 112.0 [O-C(O)-N]; 127.1 e 129.6 [aromatic CH]; 136.9 e 143.4 [aromatic quat.]; 172.0 [C=O].

Notes: the other diastereoisomer was formed in very small amounts (d.r. = 15:1) and was not obtained in pure form, but only in mixed fractions containing also **2a**. However its peaks at NMR were quite similar to those of the major diastereoisomer.

To compound **11a** the above reported structure was assigned for the following reasons: A) It is clearly an isomer of **2a** according to elemental analysis and to the fact that the number of protons and

carbon at NMR are the same. B) In the ^1H spectrum, the sulfonamide NH is still present at 5.87 ppm (triplet). C) On the contrary the NH derived from cyclohexyl isocyanide is no longer present. D) There are no OH peaks. E) The $(\text{CH}_3)_2\text{CH-CHN}$ proton falls at 3.05 ppm, a value remarkably lower than the one determined for **2a**. This suggests the fact that this nitrogen may not belong to an amide group. F) In ^{13}C there is only one carbonyl peak, at 172.02 ppm. On the other hand there is a quaternary signal at 112.00 ppm, compatible with a orthoester-like carbon. G) At ^{13}C a CH_2 at 63.25 ppm is present, compatible with a CH_2O . H) The compound gives a single set of signals at room temperature, indicating that it is a single diastereoisomer and that there are no partially restricted conformational equilibria.

Data of compound 12b: R_f : 0.27 (PE/AcOEt 55:45). Found: C, 65.3; H, 7.1; N, 8.2. $\text{C}_{27}\text{H}_{35}\text{N}_3\text{O}_4\text{S}$ requires C, 65.16; H, 7.09; N, 8.44 $^1\text{H-NMR}$ (at room temperature two conformations in a 1:1 ratio were observed): δ 1.10-1.30 [4 H, m, cyclohexyl CH_2]; 1.58-2.04 [4 H, m, cyclohexyl CH_2]; 2.42 [3 H (2 conf.), s, CH_3Ar]; 2.52-2.60 [2 H (2 conf.), m, $\text{CH}_2\text{C=O}$]; 3.00-3.14 [1 H (1 conf.), m, CHHN]; 3.12-3.33 [4 H (2 conf.), m, $\text{CH}_2\text{NHS} + 2 \text{CHHN}$]; 3.48 [1 H (1 conf.), ddd, CHHN , J 4.8, 8.7, 13.8]; 3.65 [1 H (1 conf.), dt, CHHN , J_d 13.5, J_t 3.9]; 3.97 [1 H (1 conf.), d, CHN , J 7.8]; 4.25 [1 H (1 conf.), d, CHHPh , J 14.7]; 4.41 [1 H (1 conf.), d, CHHPh , J 15.0]; 4.42-4.51 [1 H (1 conf.), m, CHHN]; 4.80 [1 H (1 conf.), d, CHHPh , J 14.7]; 4.89 [1 H (1 conf.), d, CHHPh , J 14.7]; 4.89 [1 H (1 conf.), d, CHN , J 6.6]; 5.46 [1 H (1 conf.), t, NHSO_2 , J 6.6]; 5.52 [1 H (1 conf.), t, NHSO_2 , J 6.6]; 7.18-7.38 [7 H, m, benzyl aromatics and H ortho to CH_3]; 7.73 [2 H (1 conf.), d, H ortho to SO_2 , J 8.7]; 7.74 [2 H (1 conf.), d, H ortho to SO_2 , J 8.4]. $^{13}\text{C-NMR}$: δ 21.5 [CH_3Ar (2 conf.)]; 25.9, 26.0, 26.1, 26.2, 26.3, 26.4 [3 C $\times$ 2 conf., CH_2 cyclohexyl]; 29.8, 30.2, 30.7, 30.9 [2 C $\times$ 2 conf., CH_2 cyclohexyl]; 33.0, 33.3 [$\text{CH}_2\text{C=O}$]; 36.3, 39.0, 39.1, 41.2, 44.6, 45.1, [3 CH_2N]; 41.2, 41.6 [CH cyclohexyl]; 49.9, 50.0 [CH_2Ph]; 59.9, 63.5 [CHN]; 126.96, 126.98 [CH benzyl meta]; 127.8 [CH benzyl para (2 conf.)]; 128.17, 128.23 [CH benzyl ortho]; 128.8 [CH ortho to SO_2 (2 conf.)]; 129.7 [CH ortho to CH_3 (2 conf.)]; 136.2, 136.3, 137.0 (2 conf.), 143.4 (2 conf.) [aromatic quat.]; 166.6, 167.4, 169.8, 170.4 [C=O].

To compound **12b** the above reported structure was assigned for the following reasons: A) It is clearly an isomer of **2b** according to an HPLC-MS analysis, and to the fact that the number of protons and carbon at NMR are the same. B) In the ^1H spectrum, the sulfonamide NH is still present at 5.46-5.52 ppm (triplet). C) On the contrary the NH derived from benzyl isocyanide is no longer present. D) There are no OH peaks. E) The CHN proton falls at 3.97-4.89 ppm, a value similar to that determined for **2b**. This suggests the fact that this nitrogen may belong to an amide group. F) In ^{13}C there are two carbonyl signals and no signal that may be attributed to an orthoester-type structure or to a structure deriving from O -cyclization of the secondary amide. Thus, according also to the absence of amidic NH group, this suggests the presence of two tertiary amides. G) At ^{13}C there are no CH_2 compatible with a CH_2O group. H) The compound gives two sets of signals at room temperature, indicating that a conformational equilibrium is operating, and therefore that one of the tertiary amide carbonyl is outside the ring.