Supporting Information

Efficacious Preparation of Oppolzer’s Glycylsultam via the Delépine Reaction

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I. General Experimental Methods.

Nonaqueous reactions were carried out using oven-dried glassware under a Drierite drying tube. Dry tetrahydrofuran (THF) was distilled from Na/benzophenone ketyl under Ar. Hexamethylenetetraamine (HMTA) was recrystallized from 95% EtOH prior to use. All other commercial reagents were used as received. The progress of reactions was monitored by analytical thin-layer chromatography (TLC). Plates were visualized by charring with anisaldehyde (5% p-anisaldehyde 95/5/1 EtOH/AcOH/H₂SO₄). Melting points (mp) are uncorrected. Optical rotations were measured at 589 and 546 nm with a Jasco DIP-181 digital polarimeter, which was been calibrated with a sucrose standard.¹¹H-NMR spectra were recorded at 300 MHz in CDCl₃ and are reported in parts per million (ppm) on the δ scale downfield from tetramethylsilane δ 0.00.¹³C-NMR spectra were recorded at 75 MHz and are reported in parts per million (ppm) on the δ scale relative to CDCl₃ (δ 77.00). Proton and carbon NMR assignments for compounds 2, 3, and 6 were made using data from COSY, NOESY, and HMOC/HMBC 2D experiments. Matrix-assisted laser desorption (MALDI) high resolution mass spectra (HRMS) were obtained using an α-cyano-4-hydroxycinnamic acid matrix.

*The numbering system is based on the 3H-3a, 6-Methano-2,1-benzisothiazole, 1-(aminoacetyl)hexahydro-8,8-dimethyl-, 2,2-dioxide, (3aS, 6R, 7aR) core.

II. $^1$H NMR and $^{13}$C NMR Spectra of Compounds 2-8
75 MHz $^{13}$C NMR spectrum of compound 2 in CDCl$_3$
300 MHz $^1$H NMR spectrum of compound 3 in CDCl$_3$.
75 MHz 1H NMR spectrum of compound 3 in CDCl₃
300 MHz $^1$H NMR spectrum of compound 6 in CDCl$_3$
300 MHz $^1$H NMR spectrum (expansion) of compound 6 in CDCl$_3$ (from 0.5g scale reaction)
300 MHz $^1$H NMR spectrum (expansion) of compound 6 in CDCl$_3$ (from 10g scale reaction)
$75$ MHz $^{13}$C NMR spectrum of compound 6 in CDCl$_3$
300 MHz $^1$H NMR spectrum of compound 8 in CDCl$_3$
75 MHz $^{13}$C NMR spectrum of compound 8 in CDCl₃
300 MHz $^1$H NMR spectrum of compound 7 in CDCl$_3$.
75 MHz $^{13}$C NMR spectrum of compound 7 in CDCl$_3$
III. Detailed NMR Assignments for Compounds 2, 3, and 6

Chloroacetylsultam 2

$^1$HNMR (300 MHz, CDCl$_3$) δ4.50 (s, 2H, H2'), 3.92 (dd, J= 7.5, 5.1 Hz, 1H, H7a), 3.54 (d, J= 13.8 Hz, 1H, H3), 3.47 (d, J= 13.8 Hz, 1H, H3), 2.23-2.07 (m, 2H, H7exo & H7endo), 1.99-1.84 (m, 3H, H4exo, H5exo, & H6), 1.48-1.33 (m, 2H, H4endo & H5endo), 1.15 (s, 3H, 3 x H9), 0.98 (s, 3H, 3 x H10); $^{13}$C-NMR (75 MHz, CDCl$_3$) δ 164.6 (C1'), 65.5 (C7a), 52.6 (C3), 49.1 (C3a), 47.9 (C8), 44.5 (C6), 42.3 (C2'), 38.0 (C7), 32.7 (C4), 26.4 (C5), 20.7 (C9), 19.8 (C10).

Bromoacetylsultam 3

$^1$HNMR (300 MHz, CDCl$_3$) δ 4.35 (d, J= 12.9 Hz, 1H, H2'), 4.21 (d, J= 12.9 Hz, 1H, H2'), 3.92 (dd, J= 7.5, 5.1 Hz, 1H, H7a), 3.54 (d, J= 13.8 Hz, 1H, H3), 3.47 (d, J= 13.8 Hz, 1H, H3), 2.21-2.04 (m, 2H, H7exo & H7endo), 2.00-1.83 (m, 3H, H4exo, H5exo & H6), 1.49-1.31 (m, 2H, H4endo & H5endo), 1.16 (s, 3H, 3 x H9), 0.99 (s, 3H, 3 x H10); $^{13}$C-NMR (75 MHz, CDCl$_3$) δ 164.5 (C1'), 65.4 (C7a), 52.7 (C3), 49.0 (C3a), 47.8 (C8), 44.5 (C6), 37.9 (C7), 32.7 (C4), 27.5 (C2'), 26.4 (C5), 20.7 (C9), 19.8 (C10).

Glycylsultam 6

$^1$H-NMR (300 MHz, CDCl$_3$) δ 3.90 (d, J= 18.0 Hz, 1H, H2'), 3.88 (dd, J= 7.5, 5.1 Hz, 1H, H7a), 3.76 (d, J= 18.0 Hz, 1H, H2'), 3.50 (d, J= 13.8 Hz, 1H, H3), 3.43 (d, J= 13.8 Hz, 1H, H3), 2.20-2.04 (m, 2H, H7exo & H7endo), 1.95-1.83 (m, 3H, H4exo, H5exo & H6), 1.52 (br s, 2H, NH$_2$), 1.46-1.33 (m, 2H, H4endo & H5endo), 1.15 (s, 3H, 3 x H9), 0.98 (s, 3H, 3 x H10); $^{13}$C-NMR (75 MHz, CDCl$_3$) δ 172.9 (C1'), 65.05 (C7a), 52.7 (C2'), 49.1 (C3a), 47.8 (C8), 45.4 (C3), 44.6 (C6), 38.2 (C7), 32.8 (C4), 26.4 (C5), 20.7 (C9), 19.8 (C10).