Supporting Information
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Supporting Information

Stereoselective Synthesis of Orthogonally Protected β-Hydroxy-α-,γ-Diamino Butyric Acids

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VCD spectra for diols from dihydroxylation of cis-4
VCD spectra for diols from dihydroxylation of trans-4
VCD spectra for syn-9 and ent-syn-9
Data for compound A
Data for compound B
VCD spectra for diols from dihydroxylation of cis-4

Experimental:

‘Peak 1’ and ‘Peak 2’ were dissolved in DMSO-d_6 (7mg/0.2mL and 3.5mg/0.1mL respectively) and placed in a 100 μm pathlength cell with BaF_2 windows. IR and VCD spectra were recorded on a ChiralIR™ VCD spectrometer (BioTools, Inc.) equipped with DualPEM accessory, with 4 cm⁻¹ resolution, 6 h collection for both samples, and instrument optimized at 1400 cm⁻¹. The IR of the solvent was collected for 150 scans. The solvent-subtracted IR and enantiomer subtracted VCD spectra are shown in Figure 1.

The optical rotation (OR) of ‘peak 1’ and ‘peak 2’ were measured in ethanol using a Jasco DIP-370 Polarimeter at 590 nm and 25 °C. The measure specific OR values of ‘peak 1’ and ‘peak 2’ are listed below:

‘peak 1’: [α]_D = −18.85°, C=0.175

‘peak 2’: [α]_D = +21.00°, C= 0.2

Theoretical Calculations:

The (2R,3R) configuration shown above was built with Hyperchem (Hypercube, Inc., Gainesville, FL). A conformational search was carried out with Hyperchem for the entire structure at the molecular mechanics level. Geometry optimization, frequency, IR and VCD intensity calculations were carried out at the DFT level (B3LYP functional/ 6-31G(d) basis set) with Gaussian 09 (Gaussian Inc., Wallingford, CT). The calculated frequencies were scaled by 0.97 and the IR and VCD intensities were converted to Lorentzian bands with 6 cm⁻¹ half-width for comparison to experiment.

Gaussian calculations resulted in twelve conformers that have energies within 2 kcal/mol from the lowest-energy conformer. The other conformers have energies more than 3 kcal/mol higher than the lowest-energy conformer. The optimized geometries of the twelve low-energy conformers of the (2R,3R) configuration are shown in Figure 2, and the comparison of the observed VCD and IR spectra with those of the twelve low-energy conformers are shown in Figure 3. Based on the overall agreement in VCD pattern for the observed and the Boltzmann sum of the calculated spectra of the twelve lowest-energy conformers (Figure 4), the absolute configuration of ‘peak 1’ is assigned as (2R,3R) and ‘peak 2’ is assigned as (2S,3S).
Figure 1. IR (lower frame) and VCD (upper frame) spectra of ‘peak 1’ and ‘peak 2’ in DMSO-d6 (7mg/0.2mL and 3.5mg/0.1mL respectively); 100 µm path-length cell with BaF2 windows; 6 h collection for both samples; instrument optimized at 1400 cm⁻¹. Solvent-subtracted IR and enantiomer subtracted VCD spectra are shown. Uppermost traces are the VCD noise curves.
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<th>Boltzmann Population (%)</th>
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*Figure 2.* Optimized geometries, relative energies and Boltzmann populations of the twelve calculated lowest-energy conformers of the (2R,3R) configuration.
Figure 3. IR (lower frame) and VCD (upper frame) spectra observed for ‘peak 1’ (right axes) compared with calculated spectra for the twelve calculated lowest-energy conformations for the (2R,3R) configuration (left axes).
Figure 4. IR (lower frame) and VCD (upper frame) spectra observed for ‘peak 1’ (right axes) compared with the Boltzmann-population-weighted calculated spectra for the twelve lowest-energy conformations of the (2R,3R) configuration (left axes).
VCD spectra for diols from dihydroxylation of trans-4

\[
\begin{align*}
\text{HO} & \quad \text{O} \quad \text{Me} \\
\text{PMB} & \quad \text{N} \quad \text{Boc} \\
\text{peak 1} & \\
\text{HO} & \quad \text{O} \quad \text{Me} \\
\text{PMB} & \quad \text{N} \quad \text{Boc} \\
\text{peak 2}
\end{align*}
\]

**Experimental:**

‘Peak 1’ and ‘peak 2’ were dissolved in DMSO-d\textsubscript{6} (2.8mg/0.1mL and 3.3mg/0.11mL respectively) and placed in a 100 µm pathlength cell with BaF\textsubscript{2} windows. IR and VCD spectra were recorded on a ChiralIR\textsuperscript{TM} VCD spectrometer (BioTools, Inc.) equipped with DualPEM accessory, with 4 cm\textsuperscript{-1} resolution, 6 h collection for both samples, and instrument optimized at 1400 cm\textsuperscript{-1}. The IR of the solvent was collected for 150 scans. The solvent-subtracted IR and enantiomer subtracted VCD spectra are shown in Figure 5.

The optical rotation (OR) of ‘peak 1’ and ‘peak 2’ were measured in ethanol using a Jasco DIP-370 Polarimeter at 590 nm and 25 °C. The measure specific OR values of ‘peak 1’ and ‘peak 2’ are listed below:

- ‘peak 1’: [\(\alpha\)]\textsubscript{D} = −37.89°, C=0.095
- ‘peak 2’: [\(\alpha\)]\textsubscript{D} = +28.89°, C=0.135

**Theoretical Calculations:**

The (2S,3R) configuration shown above was built with Hyperchem (Hypercube, Inc., Gainesville, FL). A conformational search was carried out with Hyperchem for the entire structure at the molecular mechanics level. Geometry optimization, frequency, IR and VCD intensity calculations were carried out at the DFT level (B3LYP functional/ 6-31G(d) basis set) with Gaussian 09 (Gaussian Inc., Wallingford, CT). The calculated frequencies were scaled by 0.97 and the IR and VCD intensities were converted to Lorentzian bands with 6 cm\textsuperscript{-1} half-width for comparison to experiment.

Gaussian calculations resulted in 9 conformers that have energies within 1 kcal/mol from the lowest-energy conformer. The other conformers have energies more than 1.5 kcal/mol higher than the lowest-energy conformer. The optimized geometries of the nine low-energy conformers of the (2S,3R)-configuration are shown in Figure 6, and the comparison of the observed VCD and IR spectra with those of the nine low-energy conformers are shown in Figure 7. Based on the overall agreement in VCD pattern for the observed and the Botlzmann sum of the calculated spectra of the nine lowest-energy conformers (Figure 8), the absolute configuration of 00702554-0404-peak1’ is assigned as (2R,3S) and 00702554-0404-peak2’ is assigned as (2S,3R).
Figure 5. IR (lower frame) and VCD (upper frame) spectra of ‘peak 1’ and ‘peak 2’ in DMSO-d$_6$ (2.8mg/0.2mL and 3.3mg/0.1mL respectively); 100 µm path-length cell with BaF$_2$ windows; 6 h collection for both samples; instrument optimized at 1400 cm$^{-1}$. Solvent-subtracted IR and enantiomer subtracted VCD spectra are shown. Uppermost trace is the VCD noise.
Figure 6. Optimized geometries, relative energies and Boltzmann populations of the nine calculated lowest-energy conformers of the (2S,3R) configuration.
Figure 7. IR (lower frame) and VCD (upper frame) spectra observed for ‘peak 2’ (right axes) compared with calculated spectra for the nine calculated lowest-energy conformations for the (2S,3R) configuration (left axes).
Figure 8. IR (lower frame) and VCD (upper frame) spectra observed for ‘peak 2’ (right axes) compared with the Boltzmann-population-weighted calculated spectra for the nine lowest-energy conformations of the (2S,3R) configuration (left axes).
VCD spectra for syn-9 and ent-syn-9

![Chemical structures](image)

**Experimental:**

‘Peak 1’ and ‘Peak 2’ were dissolved in DMSO-d₆ (unknown/0.1mL and 3.3mg/0.1mL respectively) and placed in a 100 μm pathlength cell with BaF₂ windows. IR and VCD spectra were recorded on a ChiralIR™ VCD spectrometer (BioTools, Inc.) equipped with DualPEM accessory, with 4 cm⁻¹ resolution, 6 h collection for both samples, and instrument optimized at 1400 cm⁻¹. The IR of the solvent was collected for 150 scans. The solvent-subtracted IR and enantiomer subtracted VCD spectra are shown in Figure 9.

The optical rotation (OR) of peak1 and peak2 were measured in ethanol using a Jasco DIP-370 Polarimeter at 590 nm and 25 °C. The measure specific OR values of ‘peak 1’ and ‘peak 2’ are listed below:

- ‘peak 1’: [α]₀ = +93.42°, C = 0.037
- ‘peak 2’: [α]₀ = −22.40°, C = 0.125

**Theoretical Calculations:**

The (2R,3S) configuration shown above was built with Hyperchem (Hypercube, Inc., Gainesville, FL). A conformational search was carried out with Hyperchem for the entire structure at the molecular mechanics level. Geometry optimization, frequency, IR and VCD intensity calculations were carried out at the DFT level (B3LYP functional/ 6-31G(d) basis set) with Gaussian 09 (Gaussian Inc., Wallingford, CT). The calculated frequencies were scaled by 0.97 and the IR and VCD intensities were converted to Lorentzian bands with 6 cm⁻¹ half-width for comparison to experiment.

Gaussian calculations resulted in six conformers that have energies within 2 kcal/mol from the lowest-energy conformer. The other conformers have energies more than 3 kcal/mol higher than the lowest-energy conformer. The optimized geometries of the six low-energy conformers of the (2R,3S)-configuration are shown in Figure 10, and the comparison of the observed VCD and IR spectra with those of the six low-energy conformers are shown in Figure 11. Based on the overall agreement in VCD pattern for the observed and the Botzmann sum of the calculated spectra of the six lowest-energy conformers (Figure 12), **the absolute configuration of ‘peak 1’ is assigned as (2R,3S) and ‘peak 2’ is assigned as (2S,3R)**.

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Figure 9. IR (lower frame) and VCD (upper frame) spectra of ‘peak 1’ and ‘peak 2’ in DMSO-d$_6$ (unknown/0.1mL and 3.3mg/0.1mL respectively); 100 µm path-length cell with BaF$_2$ windows; 6 h collection for both samples; instrument optimized at 1400 cm$^{-1}$. Solvent-subtracted IR and enantiomer subtracted VCD spectra are shown. Uppermost traces are the VCD noise curves.
Figure 10. Optimized geometries, relative energies and Boltzmann populations of the six calculated lowest-energy conformers of the (2R, 3S) configuration.
Figure 11. IR (lower frame) and VCD (upper frame) spectra observed for ‘peak 1’ (right axes) compared with calculated spectra for the six calculated lowest-energy conformations for the (2R, 3S) configuration (left axes).
Figure 12. IR (lower frame) and VCD (upper frame) spectra observed for ‘peak 1’ (right axes) compared with the Boltzmann-population-weighted calculated spectra for the six lowest-energy conformations of the (2R,3S) configuration (left axes).
Data for compound A

IR (neat): 2974, 1729, 1686 cm⁻¹. ¹H NMR (500 MHz, DMSO-d₆, 27 K): δ = 7.15 (dm, J = 8.3 Hz, 2H), 6.89 (dm, J = 8.3 Hz, 2H), 4.29 (s, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 3.35 (br, 2H), 2.93 (t, J = 6.4 Hz, 2H), 1.37 (s, 9H). ¹³C NMR (125 MHz, DMSO-d₆, 27 K): δ = 191.4, 159.9, 158.0, 154.3, 130.0, 128.2, 113.5, 79.0, 54.7, 52.3, 48.7, 41.2, 37.6, 27.5. ESI-HRMS: m/z calcd for C₁₈H₂₅NNaO₆ [M+Na]^+: 374.1580; found: 374.1539.

Data for compound B

IR (neat): 2975, 1780, 1747, 1685 cm⁻¹. ¹H NMR (500 MHz, DMSO-d₆, 70 °C): δ = 10.33 (br, 1H), 7.16 (dm, J = 8.5 Hz, 2H), 7.12 (dm, J = 8.5 Hz, 2H), 6.89 (dm, J = 8.5 Hz, 2H), 6.87 (dm, J = 8.5 Hz, 2H), 4.30 (m, 3H), 4.04 (m, 3H), 3.75 (s, 3H) 3.73 (s, 3H), 3.68 (s, 3H), 3.09 (m, 2H), 2.43 (ddd, J = 13.0, 9.8, 5.3 Hz, 1H), 2.03 (m, 1H), 1.37 (s, 18H). ¹³C NMR (125 MHz, DMSO-d₆, 70 °C): δ = 170.6, 167.8, 158.5, 158.3, 154.5, 154.3, 140.9, 130.0, 129.6, 128.1, 127.9, 126.4, 113.4, 113.3, 84.0, 79.4, 79.3, 54.4, 54.4, 52.4, 48.7, 48.2, 40.2, 38.6, 30.8, 27.3, 27.2. ESI-HRMS: m/z calcd for C₃₅H₄₆N₂NaO₁₁ [M+Na]^+: 693.2999; found: 693.3000.