Supporting Information

Chemometric Analysis of Enantioselective Raman Spectroscopy Data Enables

Enantiomeric Ratio Determination

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Nomenclature:

- (5*R*,6*S*): (5*R*,6*S*)-(-)-5,6-diphenylmorpholin-2-one
- (5S,6R): (5S,6R)-(+)-5,6-diphenylmorpholin-2-one
- 5,6: racemic 5,6-diphenylmorpholin-2-one

1. Experimental setup for esR spectroscopy



Fig. S1: Schematic of polarization-resolved Raman setup for esR spectroscopy. (A: aperture, AC: achromatic lens, BD: beam dump, HWP: achromatic zero-order half-wave plate, FR: double Fresnel rhomb, L: lens, LPF: dichroitic long-pass filter, PD: photodiode, PBS: polarizing beam splitter cube, SM: stepper motor. The oscilloscope, the stepper motor and the CCD camera are connected to a laptop via USB 2.0 and are controlled by a self-built LabVIEW application.



2. Principal Component Analysis (PCA) to estimate a suitable sample concentration

Fig. S2: Principal component analysis (PCA) of (5R,6S)-1 and (5S,6R)-1 in DMSO (c = 0.010 g mL⁻¹) normalized with respect to the symmetric CH stretching vibration (of one data set): -40.0° $\leq \theta \leq -20.0^{\circ}$ (a) and (b), and $20.0^{\circ} \leq \theta \leq 40.0^{\circ}$ (c) and (d). Data sets are taken from two Raman experiments at different days.



Fig. S3: Loadings of the principal component analysis (PCA) of (**5R,6S)-1** and (**5S,6R)-1** in DMSO ($c = 0.010 \text{ g mL}^{-1}$) for the spectra recorded at -46.0° $\leq \theta \leq 46.0^{\circ}$. The spectra are normalized with respect to the symmetric CH stretching vibration (of one data set) prior to subtraction. The explained variances for the first three components are 62.98%, 11.80%, and 3.00%, respectively. The corresponding scores are displayed in Fig. S4.



Fig. S4: PCA of (5R,6S)-1 and (5S,6R)-1 in DMSO ($c = 0.010 \text{ g mL}^{-1}$) normalized with respect to the symmetric CH stretching vibration (of one data set) prior to subtraction. The labels (-) and (+) indicate the scores for the difference spectra of (5R,6S)-1 and (5S,6R)-1 in DMSO, respectively. For clarity the PCA of -46.0° $\leq \theta \leq 46.0°$ is divided into two ranges: the negative range -46.0° $\leq \theta \leq 0.0°$ (a), (c), (e), and the positive range $0.0° \leq \theta \leq 46.0°$ (b), (d), (f).



Fig. S5: PCA of (5R,6S)-1 and (5S,6R)-1 in DMSO (w = 0.10) separately in the negative range $-40.0^{\circ} \le \theta \le -20.0^{\circ} \ 0^{\circ}$ (a), (c), (e) and in the positive range $20.0^{\circ} \le \theta \le 40.0^{\circ}$ (b), (d), (f) over the full Raman spectra (563 cm⁻¹to 3358 cm⁻¹). The initial spectra were normalized with respect to the symmetric CH stretching vibration (of one data set). The corresponding explained variances are displayed in Tab. S1.



Fig. S6: PCA of (5R,6S)-1 and (5S,6R)-1 in DMSO (w = 0.10) separately in the negative range $-40.0^{\circ} \le \theta \le -20.0^{\circ} 0^{\circ}$ (a), (c), (e) and in the positive range $20.0^{\circ} \le \theta \le 40.0^{\circ}$ (b), (d), (f) of the CH stretching region. The initial spectra were normalized with respect to the symmetric CH stretching vibration (of one data set). PC1 loadings are dominated by symmetric CH str. vibration, whereas the loadings of PC2 have main contributions for the antisymmetric CH str. vibration. The corresponding explained variances are displayed in Tab. S1.

	full spectrum		CH str. vib. region	
	$-40.0^{\circ} \le \theta \le -20.0^{\circ}$	$20.0^\circ \le \theta \le 40.0^\circ$	$-40.0^\circ \le \theta \le -20.0^\circ$	$20.0^\circ \le \theta \le 40.0^\circ$
variance expl. by PC1 /%	99.35	99.13	99.62	99.57
variance expl. by PC2 /%	0.44	0.70	0.28	0.35
variance expl. by PC3 /%	0.03	0.03	0.03	0.02

Tab. S1 Variance explained (expl.) by the first three principal components for the PCA shown in Fig. S5 (full spectrum) and Fig. S6 (CH stretching vibrational region).

3. Partial Least-Squares Regression (PLSR) for enantiomeric ratio discrimination



Fig. S7: Normalized esR-spectra recorded at $\theta = 30.0^{\circ}$ of (5R,6S)-1 and (5S,6R)-1 in DMSO (w = 0.10) with enlarged CH-stretching region. These spectra are used to conduct the PLSR.



Fig. S8: PLS weights of the first three PLS components (PLSC) obtained by PLSR with 11 data sets covering the whole enantiomeric ratio range of (**5R,6S)-1** and (**5S,6R)-1** in DMSO (w = 0.10) of the full spectra recorded at $\theta = 30.0^{\circ}$. The vibrational bands at around 350 cm⁻¹ and 850 cm⁻¹) attribute to the PLS weights in an unreasonable manner.



Fig. S9: PLS weights of the first three PLS components (PLSC) obtained by PLSR with 11 data sets covering the whole enantiomeric ratio range of (**5R,6S)-1** and (**5S,6R)-1** in DMSO (w = 0.10) excluding the regions around 350 cm⁻¹ and 850 cm⁻¹ at $\theta = 30.0^{\circ}$.