

## Supplementary Information for

### Consideration of molecular arrangements in regio- and enantioselective reduction of an NAD model compound controlled by carbonyl oxygen orientation

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#### Experimental

**X-ray crystallography.** Single crystals of (2*R*)-**6** and (2*S*)-**6** were covered by paraffin oil and mounted on a glass fiber. All data were collected at 173 K on a Rigaku Mercury CCD detector, with monochromated MoK $\alpha$  radiation, operating at 50 kV/40 mA. Data were processed on a PC using CrystalClear Software (Rigaku). Structures were solved by direct methods (SIR-92) and refined by full-matrix least-squares methods on  $F^2$  (SHELXS-97). Crystal data are summarized in Table S1.

**Preparation of Optically active 1.** To the solution of enantiomerically-pure **2**<sup>1</sup> (82.3 mg, 0.29 mmol) in anhydrous acetonitrile (145 mL), the solution (100 mL) of methyl benzoylformate (476 mg, 2.9 mmol) and magnesium perchlorate (64.7 mg, 0.29 mmol) in the same solvent was injected. The reaction was run for 1 h at room

temperature in the dark under argon atmosphere. After removal of the solvent, water was added and the inside of the flask was washed with ether three times to remove methyl mandelate. Then, the water layer was extracted with dichloromethane three times. The combined dichloromethane layer was dried and evaporated to give optically-active **1** as a perchlorate salt in ~50% yield. The enantiomer excess of **1** was checked by HPLC (column: Daicel CHIRALCEL OD 0.46φ x 25 cm; eluent: hexane/iPrOH/diethylamine = 70/30/0.1). The absolute configuration of **1** has been determined from their retention time in HPLC and comparison of CD spectra (Figure S1) with those of related compounds.<sup>2,3</sup>

**Reaction. (i) With Sodium Hydrosulfite.** To an argon-filled flask containing chiral **1**·ClO<sub>4</sub> (1.35 mg, 3.5 μmol), 0.5 mL solution of sodium hydrosulfite (6.1 mg, 35 μmol) in aqueous 0.5 M Na<sub>2</sub>CO<sub>3</sub> was injected under argon atmosphere at room temperature in the dark. After stirring for 15 min at room temperature, the reaction solution was extracted with dichloromethane, dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated, and the residue was subjected to <sup>1</sup>H NMR and HPLC analysis.

**(ii) With Sodium Borohydride.** To a methanol solution (0.2 mL) of chiral **1**·ClO<sub>4</sub> (1.35 mg, 3.5 μmol), 0.2 mL solution of NaBH<sub>4</sub> (0.26mg, 7.0 μmol) in the same solvent was injected under argon atmosphere at 0 °C in the dark. After stirring for 2 h at 0 °C, the solvent was evaporated and the residue was subjected to <sup>1</sup>H NMR and HPLC analysis.

**(iii) With Me<sub>2</sub>PNPH (4).** To an anhydrous acetonitrile solution (0.38 mL) of chiral

$1\cdot\text{ClO}_4$  (1.50 mg, 3.9  $\mu\text{mol}$ ), 0.40 mL solution of **4** (1.16 mg, 3.9  $\mu\text{mol}$ ) in the same solvent was injected under argon atmosphere at room temperature in the dark. After stirring for 36 h at room temperature, the solvent was evaporated and the residue was subjected to  $^1\text{H}$  NMR and HPLC analysis.

**(iv) With PNAH (5).** To an anhydrous acetonitrile solution (0.65 mL) of chiral  $1\cdot\text{ClO}_4$  (2.50 mg, 6.51  $\mu\text{mol}$ ), 0.65 mL solution of **5** (1.08 mg, 6.51  $\mu\text{mol}$ ) in the same solvent was injected under argon atmosphere at room temperature in the dark. After stirring for 1 h at room temperature, the solvent was evaporated and the residue was subjected to  $^1\text{H}$  NMR and HPLC analysis.

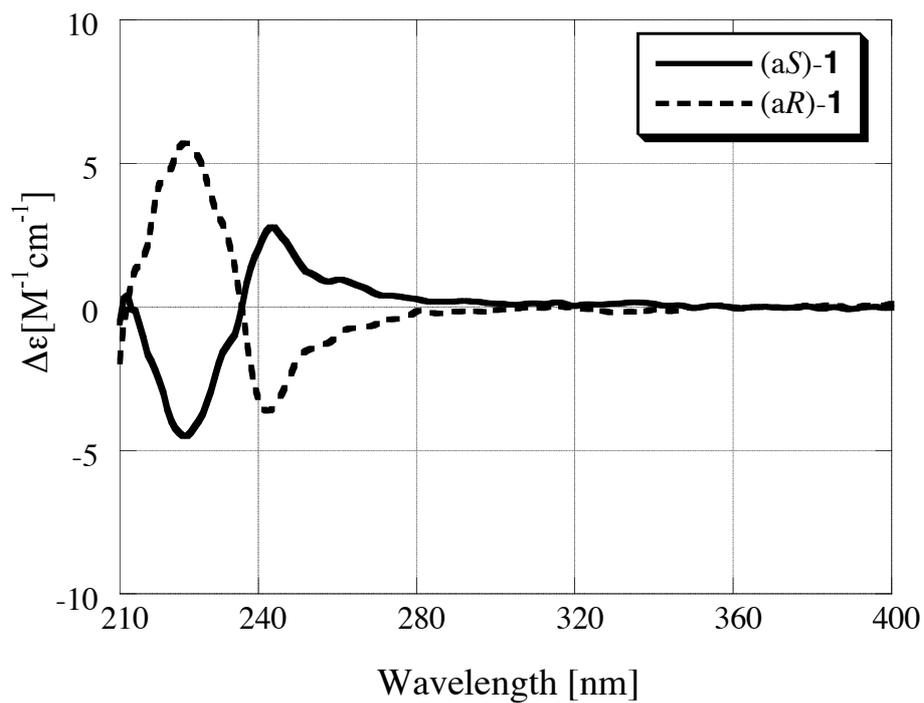
## References

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**Table S1.** Crystallographic Data for (2*R*)-6 and (2*S*)-6

	(2 <i>R</i> )-6	(2 <i>S</i> )-6
Formula	C <sub>21</sub> H <sub>24</sub> N <sub>2</sub> O	C <sub>21</sub> H <sub>24</sub> N <sub>2</sub> O
FW	320.43	320.43
Crystal System	monoclinic	orthorhombic
Space group	<i>P</i> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub>
<i>a</i> , Å	12.3636(10)	5.3478(10)
<i>b</i> , Å	5.2242(4)	13.519(3)
<i>c</i> , Å	13.3704(11)	23.990(5)
β, deg	97.482(2)	90
<i>V</i> , Å <sup>3</sup>	856.24(12)	1734.4(6)
<i>Z</i>	2	4
<i>D</i> <sub>calc</sub> , g cm <sup>-3</sup>	1.243	1.227
μ, cm <sup>-1</sup>	0.077	0.076
2θ <sub>max</sub> , deg	57.4	57.4
temp, K	173	173
no. reflns collected	7387	14708
no. reflns used	3768	3197
no. of params	314	314
final <i>R</i> 1 ( <i>I</i> > 2σ( <i>I</i> ))	0.051	0.039
<i>wR</i> 2 (all data)	0.102	0.115
GOF	1.133	1.155

$$R1 = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|} \quad wR2 = \left[ \frac{\sum w[(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right]^{1/2}$$



**Figure S1.** CD spectra of (aS)-1 (solid line) and (aR)-1 (broken line) in EtOH.