

## Supplementary Information

### Surface-enhanced stereoselectivity in Mukaiyama aldol reactions catalyzed by clay-supported bis(oxazoline)-copper complexes

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**General remarks:** Bis(oxazoline) bearing phenyl groups was prepared from (*R*)-phenylglycinol and dimethylmalononitrile by a modified procedure.<sup>1</sup>

**Preparation of immobilized catalysts by cation exchange:** Laponite was dried under vacuum at 140°C for 24 h prior to use. The chiral ligand (0.11 mmol) and Cu(OTf)<sub>2</sub> (40 mg, 0.11 mmol) were dissolved in the minimum amount of anhydrous dichloromethane under an argon atmosphere. The solution was stirred for 15 min and filtered through a PTFE microfilter. The solvent was removed under reduced pressure, the complex was redissolved in methanol (4 mL), dry Laponite (375 mg) was added and the suspension was stirred for 24 h at room temperature. The solid was filtered off, washed with methanol (10 mL) and dichloromethane (20 mL) and then dried under vacuum for 24 h.

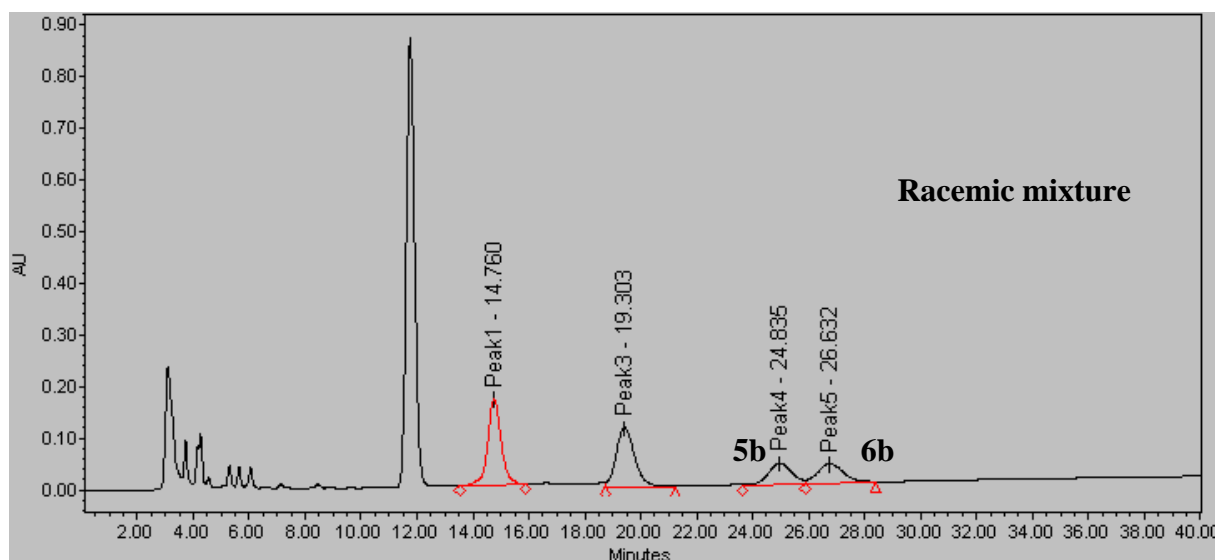
**Homogeneous Mukaiyama aldol reactions with methyl pyruvate (1a):** A suspension of the bis(oxazoline) ligand (0.05 mmol) and Cu(OTf)<sub>2</sub> (0.05 mmol) in anhydrous dichloromethane (1 mL) was stirred for 15 min under an inert atmosphere. The mixture was filtered through a microfilter and the solvent was evaporated under vacuum. Anhydrous CH<sub>2</sub>Cl<sub>2</sub> (2 mL), methyl pyruvate (**1a**, 0.5 mmol) and 2-(trimethylsilyloxy)furan (**2**, 0.6 mmol) were added by syringe and the reaction mixture was stirred at room temperature under an inert atmosphere. The

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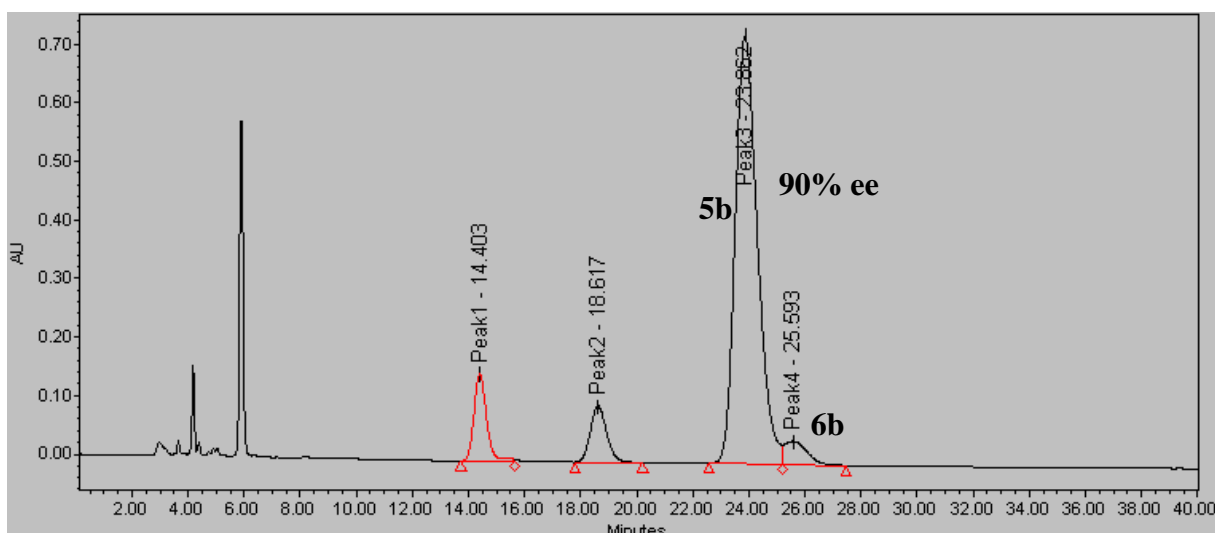
<sup>1</sup> A. Cornejo, J. M. Fraile, J. I. García, M. J. Gil, V. Martínez-Merino, J. A. Mayoral, E. Pires, I. Villalba, *Synlett* **2005**, 2321.

consumption of the cyclic silane was monitored by GC. The mixture was filtered through a silica pad (2 cm), which was washed with dichloromethane. The resulting solution was concentrated under vacuum and the mixture analyzed by HPLC (Chiralpak AD-H column, hexane/isopropanol (90:10), 1 mL min<sup>-1</sup>, UV detector at  $\lambda=210$  nm). A previous calibration was necessary to determine the yield. The retention times were for the *anti* enantiomers:  $t_r$  (**5a**) = 13.2 min and  $t_r$  (**6a**) = 14.0 min; and for the *syn* enantiomers:  $t_r$  = 19.1 min and  $t_r$  = 25.4 min. The absolute configurations of the *anti* enantiomers were assigned by comparison with the results reported by Evans et al.<sup>2</sup>

**Homogeneous Mukaiyama aldol reactions with methyl 2-oxo-2-phenylacetate (1b):** The procedure is the same as in the case of using methyl pyruvate with the following reagents: methyl 2-oxo-2-phenylacetate (**1b**, 0.5 mmol) and 2-(trimethylsilyloxy)furan (**2**, 0.6 mmol). At the end of the reaction and after the filtration through the silica pad, the solvent was eliminated under vacuum and the mixture analyzed by HPLC (Chiralcel OD-H column, hexane/isopropanol (90:10), 1 mL min<sup>-1</sup>, UV detector at  $\lambda=209$  nm). The retention times were for the *syn* enantiomers:  $t_r$  = 14.8 min and  $t_r$  = 19.3 min and for the *anti* enantiomers:  $t_r$  (**5b**) = 24.8 min and  $t_r$  (**6b**) = 26.6 min.



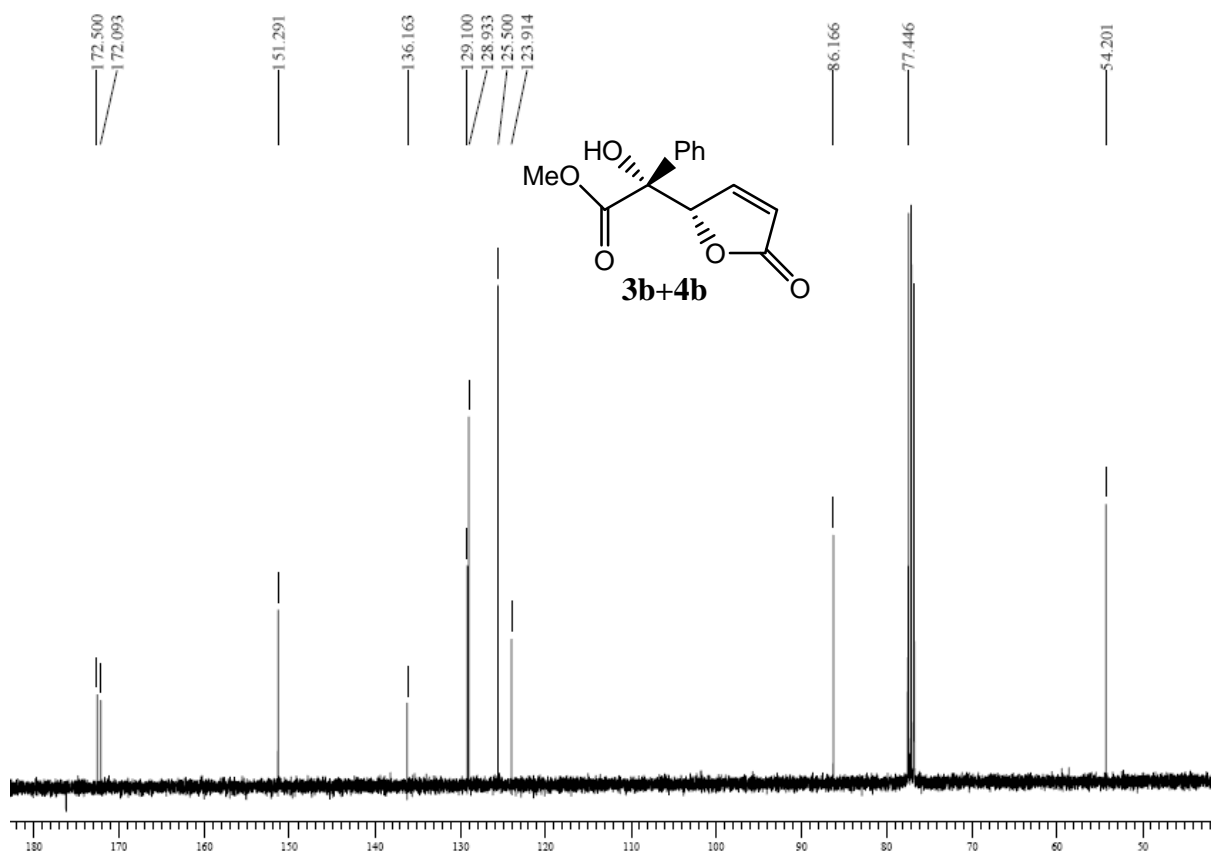
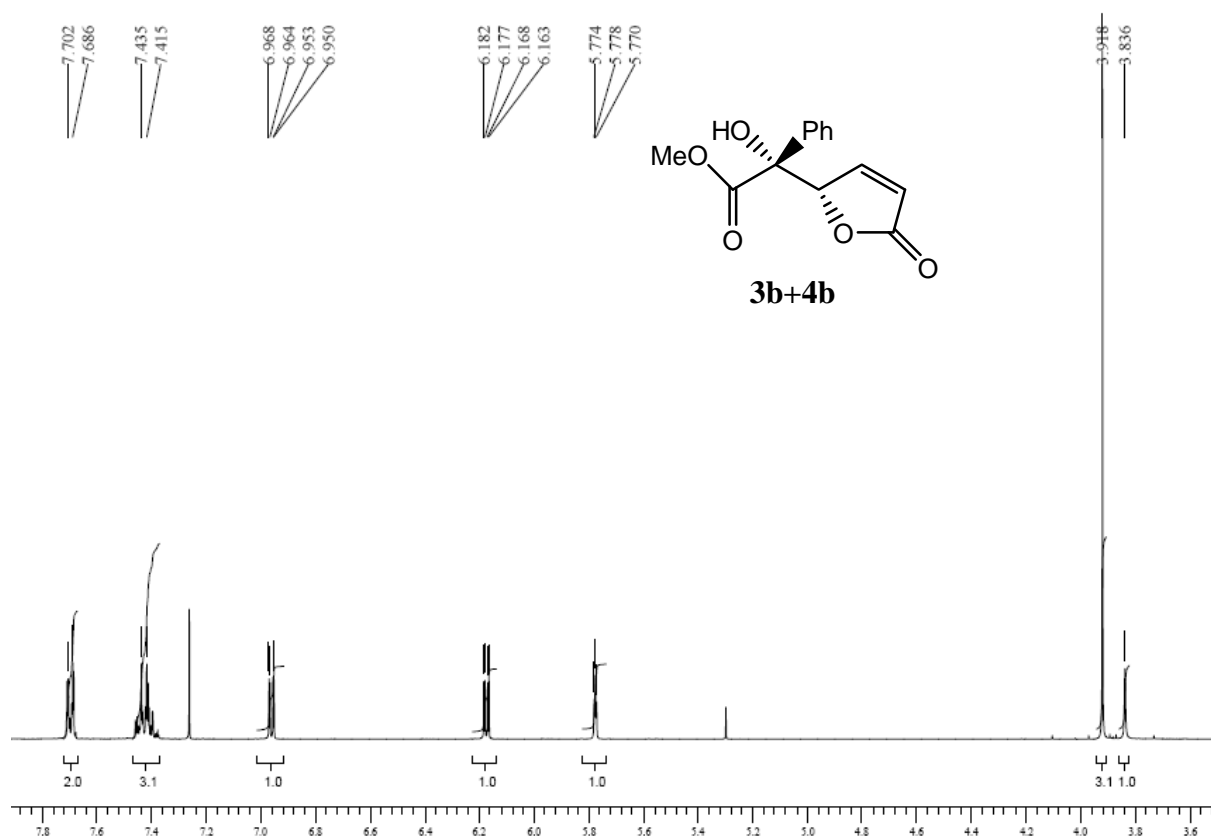
<sup>2</sup> D. A. Evans, C. S. Burgey, M. C. Kozlowski, S. W. Tregay, *J. Am. Chem. Soc.* **1999**, *121*, 686.

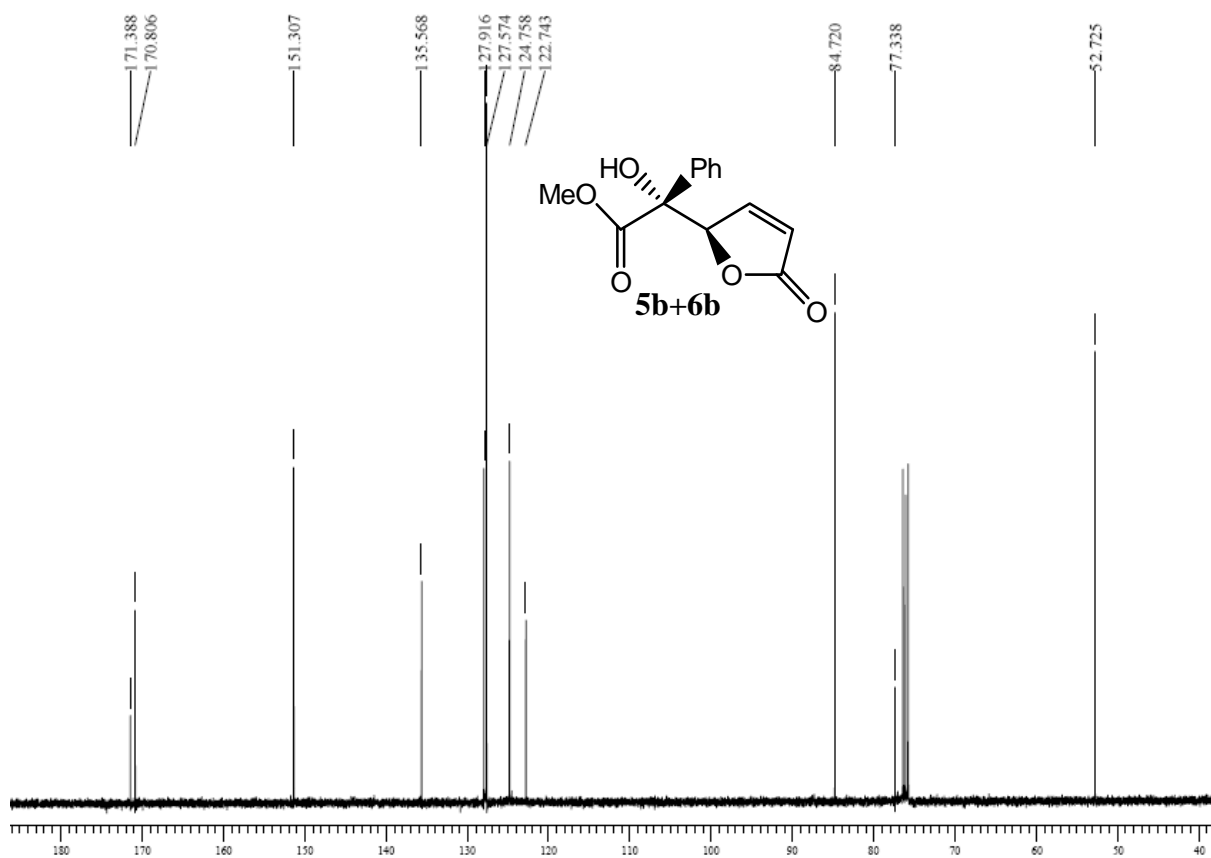
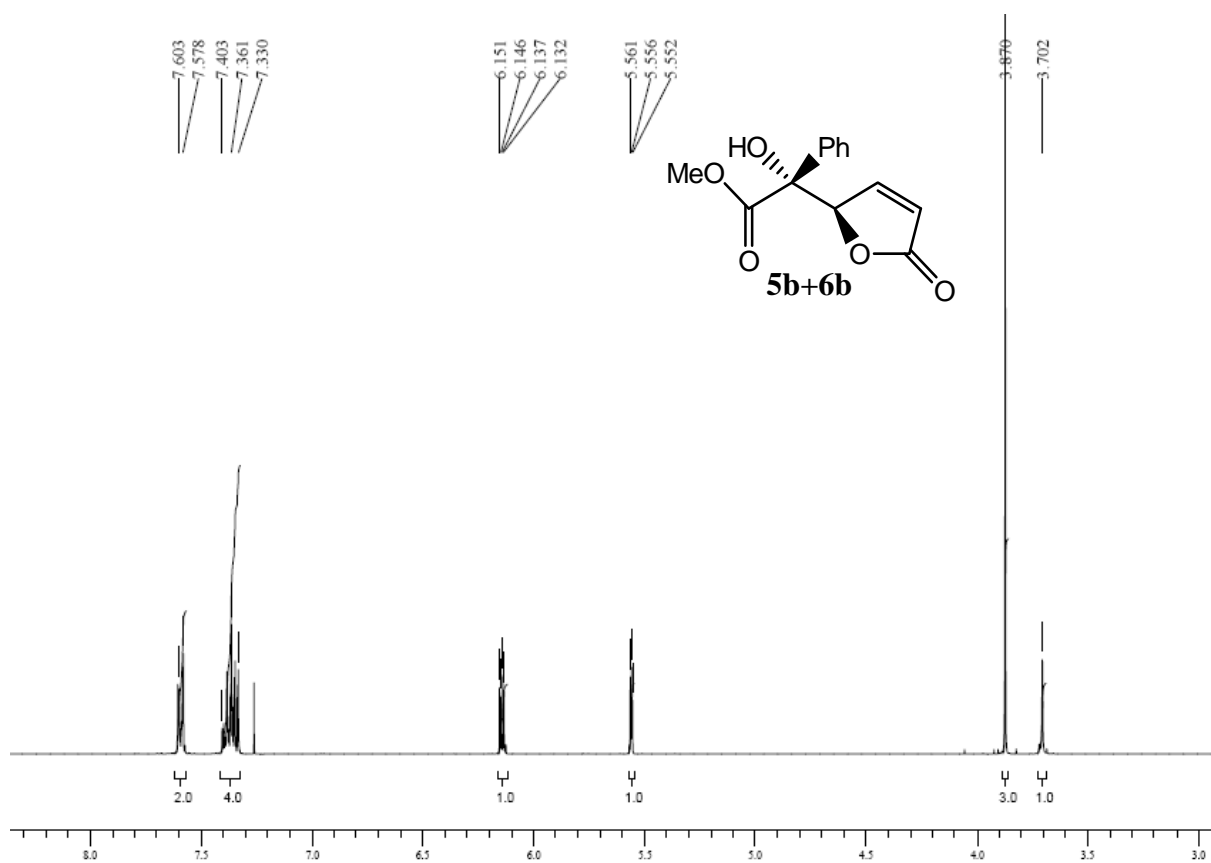


**Methyl 2-hydroxy-2-[5-oxofuran-2(2*H*)-yl]-2-phenylacetate (3b, 4b, 5b, 6b):** The products were prepared according to the typical procedure. Then, the crude of the reaction was purified by silica gel column chromatography (30% ethyl acetate/hexane) to afford in both cases a white solid.

*Syn* isomers (**3b+4b**):  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ,  $\delta$  ppm): 7.70-7.68 (m, 2H), 7.45-7.39 (m, 3H), 6.95 (dd,  $J=1.6$  Hz,  $J=5.8$  Hz, 1H), 6.17 (dd,  $J=2.0$  Hz,  $J=5.8$  Hz, 1H), 5.77 (t,  $J=1.6$  Hz, 1H), 3.9 (s, 3H), 3.83 (s, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ,  $\delta$  ppm): 172.5, 172.1, 151.3, 136.2, 129.1, 128.9, 125.5, 123.9, 86.2, 77.4, 54.2.

*Anti* isomers (**5b+6b**):  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ,  $\delta$  ppm): 7.60-7.57 (m, 2H), 7.41-7.33 (m, 4H), 6.14 (dd,  $J=2.0$  Hz,  $J=5.6$  Hz, 1H), 5.55 (m, 1H), 3.87 (s, 3H), 3.70 (br, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ,  $\delta$  ppm): 171.4, 170.8, 151.3, 135.6, 127.9, 127.6, 124.8, 122.8, 84.7, 77.4, 52.7.





**Representative procedure for heterogeneous Mukaiyama aldol reactions:** To a solution of methyl pyruvate (**1a**, 0.5 mmol) and 2-(trimethylsilyloxy)furan (**2**, 0.6 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was added the solid catalyst (217 mg, 10 mol%). The resulting suspension was stirred at room temperature under an inert atmosphere. The consumption of the cyclic silane was monitored by GC. The mixture was filtered and the filtrate was concentrated under vacuum and analyzed by HPLC. The solid catalyst was repeatedly washed with anhydrous dichloromethane, dried under vacuum and reused under the same conditions.

**X-ray analyses:** Intensity data for both molecules were collected at low temperature (100(2)K) on a Bruker SMART (**3b** and **4b**) or Oxford Diffraction Xcalibur Nova (**5b**) CCD area detector diffractometers. Graphite monochromated MoK<sub>α</sub> (**3b** and **4b**;  $\lambda = 0.71073 \text{ \AA}$ ) or CuK<sub>α</sub> (**5b**;  $\lambda = 1.54178 \text{ \AA}$ ) radiations (**5b**) were used. Cell parameters were refined from the observed setting angles and detector positions of strong reflections (2598 reflns,  $2\theta \leq 27.0^\circ$  for **3b** and **4b**; 4998 reflns,  $2\theta \leq 73.47^\circ$  for **5b**). Data were corrected for Lorentz and polarization effects, and multiscan absorption corrections were also applied. The structures were solved by direct methods (SHELXS86) and completed by successive difference Fourier synthesis. Refinement, by full-matrix least-squares on  $F^2$  was carried out with SHELXL97, including all non-hydrogen atoms in both structures with anisotropic displacement parameters. Hydrogen atoms were included in the refinement from observed positions and refined as free isotropic atoms. No significant residual ( $< 0.475 \text{ e\AA}^{-3}$ ) was observed in the final Fourier maps.

**Crystal data for the mixture of the *syn* enantiomers 3b and 4b:** C<sub>13</sub>H<sub>12</sub>O<sub>5</sub>,  $M = 248.23$ , monoclinic,  $P2(1)/c$ ;  $a = 11.5169(15)$ ,  $b = 7.9585(11)$ ,  $c = 13.1517(17) \text{ \AA}$ ,  $\beta = 94.033(2)^\circ$ ,  $V = 1202.5(3) \text{ \AA}^3$ ,  $Z = 4$ ,  $D_c = 1.371 \text{ g cm}^{-3}$ ,  $\mu (\text{Mo-K}\alpha) = 1.06 \text{ cm}^{-1}$ . Crystal dimensions  $0.164 \times 0.163 \times 0.161 \text{ mm}$ , 7457 reflections measured, 2602 unique ( $R_{\text{int}} = 0.0222$ ); number of data/restraints/parameters 2602/0/211; final GoF 1.046,  $R = 0.0425$  (2295 reflns,  $I > 2\sigma(I)$ ),  $wR2 = 0.1075$  for all data. **Crystal data for the *anti* enantiomer 5b:** C<sub>13</sub>H<sub>12</sub>O<sub>5</sub>,  $M = 248.23$ , monoclinic,  $P2(1)$ ,  $a = 7.5836(15)$ ,  $b = 5.7612(12)$ ,  $c = 13.331(3) \text{ \AA}$ ,  $\beta = 102.73(3)^\circ$ ,  $V = 568.1(2) \text{ \AA}^3$ ,  $Z = 2$ ,  $D_c = 1.451 \text{ g cm}^{-3}$ ,  $\mu (\text{Cu-K}\alpha) = 9.49 \text{ cm}^{-1}$ . Crystal dimensions  $0.124 \times 0.120 \times 0.074 \text{ mm}$ , 5624 reflections measured, 2199 unique ( $R_{\text{int}} = 0.0214$ ); number of data/restraints/parameters 2199/1/211; final GoF 1.127,  $R = 0.0316$  (2088 reflns,  $I > 2\sigma(I)$ ),  $wR2 = 0.0841$  for all data. CCDC-684313 and CCDC-684314 contain the supplementary

crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).