Direct observation of enantiomer discrimination of epoxides by chiral salen complexes using ENDOR


School of Chemistry, Cardiff University, PO Box 912 Cardiff, CF10 3TB, UK

SUPPLEMENTARY DATA

LIGAND/COMPLEX STRUCTURES

\[
\begin{align*}
\text{[VO(1)]} & \\
\text{[VO(2)]} & \\
\text{[VO(3)]} & \\
\text{[VO(4)]} & \\
\end{align*}
\]

PREPARATION OF MATERIALS

All reagents were purchased (Aldrich, Avocado, Lancaster) and used as received. Solvents were purified by standard literature methods [1]. Mass spectra were obtained in FAB (Fast Atom Bombardment) mode in a 3-nitrobenzyl alcohol matrix, or APCI (Atmospheric Pressure Chemical Ionisation) mode. IR spectra were recorded in KBr or on NaCl discs using a Nicolet 510 series spectrometer and electronic spectra in appropriate solvents using Perkin-Elmer Lambda 20, Lambda 900 or Jasco V-570 spectrophotometers. NMR spectra were obtained on Bruker Avance AMX 400, AMX 500 or JEOL Eclipse 300 spectrometers and referenced to external TMS. Gas chromatography was performed using a VG trio-1 machine with a mass spectrometer detector or a Perkin Elmer 8700 series machine with a FID detector, a Beta Dex 120 capillary column (Supelco, 30m x 0.25mm x 0.25 µm film thickness) was used on both instruments.

(R, R)-[VO(1)] - (R, R)-N,N'-bis(3,5-di-tert-butylsalicylidene)-1,2- cyclohexanediamino vanadium (IV) oxide.
(R,R)-H₂(1) was prepared by a literature method [2]. To a solution of (R, R)-H₂(1) (2.00 g (3.6 mmol) in chloroform (50 ml) was added an aqueous solution (20 ml) containing a large excess of vanadyl sulphate hydrate. Ethanol (30 ml) containing 0.81 g (2.2 mmol) of triethylamine was added slowly over a period of 1 hour. The resulting homogeneous reaction mixture was stirred overnight and subsequently diluted with chloroform (50 ml). This solution was washed three times with water (20 ml). The organic layer was dried (MgSO₄), filtered and the solvent removed in vacuo. The crude complex was recrystallised by dissolution in a small volume of chloroform followed by the addition of ethanol and subsequent slow evaporation. Further purification was achieved by dissolution in dichloromethane followed by reprecipitation by the addition of n-pentane. Yield 2.05 g (92 %). MS (APCI): m/z = 612.0 (calc. 611.3). IR (KBr disc, cm⁻¹) 3407, 2945, 2855, 1609, 1533, 1458, 1433, 1388, 1342, 1312, 1247, 1197, 1172, 1031, 981, 830, 745. Anal. Calcd for C₃₆H₅₂N₂O₃V (Mr = 611.76): C, 70.7; H, 8.6; N, 4.6. Found: C, 70.3; H, 8.3; N, 4.5.

S, S-[VO(1)] – (S, S)-N, N'-bis(3,5-Di-tert-butylsalicylidene)-1,2-cyclohexanediamino-vanadium (IV) oxide.

This complex was prepared from and (S, S)-1H₂ using the procedure described for (R, R)-[VO(1)] and had identical spectroscopic properties. Anal. Calcd for C₃₆H₅₂N₂O₃V (Mr = 611.76): C, 70.7; H, 8.6; N, 4.6. Found: C, 70.4; H, 8.2; N, 4.2.

H₂(2) - N,N'-bis(3,5-di-tert-butylsalicylidine)-1,2-ethylenediamine.

To a solution of 3,5-di-tert-butylsalicylaldehyde (5.00g, 21mmol) in ethanol (100ml) was added 1,2-diaminoethane (0.60g, 10mmol) slowly over 10 minutes and the mixture refluxed overnight. Heating was discontinued and the solution cooled to 0°C.
and maintained for 1 hour. The yellow precipitate was filtered and washed with cold ethanol (20ml). The material required no further purification. Yield 4.4g (90%). 1H NMR (400MHz, CDCl3): δ 13.60 [s, 2H, OH], 8.40 [s, 2H, NCH], 7.40 [s, 2H of Ar], 7.10 [s, 2H of Ar], 3.90 [s, 4H, CH2], 1.45 [s, 18H, CCH3] and 1.30 [s, 18H, CCH3]. 13C NMR (100MHz, CDCl3): δ 168 [C of Imine], 158 [C of Ar], 137 [C of Ar], 128 [C of Ar], 127 [C of Ar], 118 [C of Ar], 60 [CH2N], 34 [CCH3], 33 [CCH3], 32 [CH3] and 30 [CH3]. Mass spectrum: molecular ion peak at m/z = 493.6 (calc. 492.7). IR (KBr disc, cm⁻¹): 3437, 2963, 2869, 1628, 1466, 1438, 1270, 1041, 879 and 830.

H2(d4-2) - N,N'-bis(3,5-di-tert-butylsalicylidine)-1,2-d4-ethylenediamine.

This material was prepared in a similar manner to that of H2(2) using ethylene-d4-diamine (1.0g, 16mmol) and 3,5-di-tert-butylsalicylaldehyde (7.80g, 33mmol) to yield the product as a yellow solid. Yield 7.91g (83%). 1H NMR (400MHz, CDCl3): δ 13.60 [s, 2H, OH], 8.38 [s, 2H, NCH], 7.40 [s, 2H of Ar], 7.15 [s, 2H of Ar], 1.40 [s, 18H, CCH3] and 1.30 [s, 18H, CCH3]. 13C NMR (100 MHz, CDCl3): δ 170 [C of Imine], 158 [C of Ar], 137 [C of Ar], 128 [C of Ar], 127 [C of Ar], 118 [C of Ar], 59 [CD2N, q, JCD = 20 Hz], 34 [CCH3], 33 [CCH3], 32 [CH3] and 31 [CH3]. Mass spectrum: molecular ion peak at m/z = 496.8 (calc. 496.5). IR (KBr disc, cm⁻¹): 3432, 2961, 2865, 2212, 2091, 1628, 1466, 1439, 1273, 1045, 877 and 830.

[VO(2)] - N,N'-Bis(3,5-di-tert-butylsalicylidene)-1,2-ethylenediamine vanadium (IV) oxide.

H22 was converted to [VO(-2)] using the procedure described for (R, R)-[VO(1)]. H22 was converted to [VO(2)] using the procedure described for (R, R)-[VO(1)]. Mass spectrum: molecular ion peak at m/z = 558.4 (calc. 557.3). IR (KBr disc, cm⁻¹): 3427, 2959, 2856, 1628, 1476, 1434, 1270, 1150, 1041, 971, 840, and 775. Anal. Calcd for C32H46N2O3V (Mᵣ = 557.67): C, 68.9; H, 8.3: N, 5.0. Found: C, 68.6; H, 8.4; N, 5.1.

[VO(d4-2)] - N,N'-Bis(3,5-di-tert-butylsalicylidene)-1,2-d4-ethylenediamine vanadium (IV) oxide.
\[ d_4H_22 \] was converted to \([\text{VO}(d_4-2)]\) using the procedure described for \((R, R)-[\text{VO}(1)]\).

Mass spectrum: molecular ion peak at \(m/z = 562.4\) (calc. 561.3). IR (KBr disc, cm\(^{-1}\)):
3052, 2959, 2866, 1628, 1476, 1441, 1273, 1042, 970, 877, 829.

\(H_2(3)\) - \(N,N'\)-bis(salicylidine)-1,2-ethylenediamine.

To a solution of salicylaldehyde (4.91g, 21mmol) in ethanol (100ml) was added 1,2-diaminoethane (0.60g, 10mmol) slowly over 10 minutes and the mixture brought to reflux. After 24 hours heating was discontinued and the solution cooled to 0\(^\circ\)C and maintained for 1 hour. The yellow precipitate was filtered and washed with cold ethanol (20ml). The material required no further purification. Yield 2.5g (93%). \(^1\)H NMR (400MHz, CDCl\(_3\)):
\[ \delta 13.15 \text{ [s, 2H, OH]}, 8.25 \text{ [s, 2H, NCH]}, 7.20 \text{ [m, 2H of Ar]}, 7.15 \text{ [d, 2H of Ar]}, 6.90 \text{ [d, 2H of Ar]}, 6.80 \text{ [m, 2H of Ar]} \text{ and 3.90 \text{ [s, 4H, CH\(_2\)}].} \]

\(^{13}\)C NMR (100MHz, CDCl\(_3\)):
\[ \delta 166 \text{ [C of Imine]}, 160 \text{ [C of Ar]}, 131 \text{ [C of Ar]}, 130 \text{ [C of Ar]}, 118 \text{ [C of Ar]}, 116 \text{ [C of Ar]} \text{ and 58 \text{ [CH\(_2\)}].} \]
Mass spectrum: molecular ion peak at \(m/z = 269.4\) (calc. 268.3). IR (KBr disc, cm\(^{-1}\)):
3056, 2895, 1636, 1576, 1497, 1458, 1419, 1283, 1149, 1042, 1021, 857 and 749.

\(H_2(d_4-3)\) - \(N,N'\)-bis(salicylidine)-1,2-d\(_4\)-ethylenediamine.

This material was prepared in a similar manner to that of \(H_2(3)\) using ethylene-d\(_4\)-diamine (1.0g, 16mmol) and salicylaldehyde (4.0g, 33mmol) to yield the product as a yellow solid. Yield 3.95g (90%). \(^1\)H NMR (400MHz, CDCl\(_3\)):
\[ \delta 13.15 \text{ [s, 2H, OH]}, 8.25 \text{ [s, 2H, NCH]}, 7.20 \text{ [m, 2H of Ar]}, 7.15 \text{ [d, 2H of Ar]}, 6.90 \text{ [d, 2H of Ar]} \text{ and 6.80 \text{ [m, 2H of Ar].} \text{}} \]

\(^{13}\)C NMR (100MHz, CDCl\(_3\)):
\[ \delta 166 \text{ [C of Imine]}, 160 \text{ [C of Ar]}, 133 \text{ [C of Ar]}, 131 \text{ [C of Ar]}, 118 \text{ [C of Ar]} \text{ and 115 \text{ [C of Ar]} \text{ and 56 \text{ [CD\(_2\), q, J\(_{CD} = 21\text{ Hz.}} \]}} \text{.} \]
Mass spectrum: molecular ion peak at \(m/z = 273.3\) (calc. 272.3). IR (KBr disc,
cm\(^{-1}\): 3050, 2896, 2210, 1632, 1568, 1498, 1419, 1282, 1152, 1042, 1021, 852 and 740.

\[\text{[VO(3)]} \] \(N, N'\text{-bis(salicylidine)-1,2-ethylenediamine vanadium (IV) oxide.}\)

\[\text{[VO(3)]}\]

\(H_2\text{3}\) was converted to [VO(3)] using the procedure described for \((R, R)\text{-[VO(1)]}\). Mass spectrum: molecular ion peak at \(m/z = 334.4\) (calc. 333.0). IR (KBr disc, cm\(^{-1}\)): 3050, 2889, 1624, 1572, 1491, 1455, 1419, 1281, 1152, 1042, 1021, 982, 857, 749. Anal. Calcd for \(C_{16}H_{14}N_2O_3V\) (\(M_r = 333.24\)): C, 57.7; \(H\), 4.2; N, 8.4. Found: C, 57.3; \(H\), 4.0; N, 8.3.

\[\text{[VO(d4-3)]} \] \(N, N'\text{-bis(salicylidine)-1,2-d}_4\text{-ethylenediamine vanadium (IV) oxide.}\)

\[\text{[VO(d4-3)]}\]

d\(_4\)-\(H_2\text{3}\) was converted to [VO(d\(_4\)-3)] using the procedure described for \((R, R)\text{-[VO(1)]}\). Mass spectrum: molecular ion peak at \(m/z = 337.9\) (calc. 337.2). IR (KBr disc, cm\(^{-1}\)): 3048, 2880, 2220, 1631, 1570, 1496, 1450, 1423, 1279, 1151, 1042, 1019, 980, 851, 740.

\(H_2(4)\) – \((R,R)\text{-}N, N'\text{-bis(salicylidine)-1,2-cyclohexanediamine.}\)

\(H_2(4)\)

A 250ml 3-necked round bottomed flask equipped with an addition funnel and reflux condenser was charged with \((R,R)\text{-1,2-diammoniumcyclohexane mono-(-)-tartrate salt [ref 2]}\) (3.00g, 11mmol), potassium carbonate (6.30g, 22mmol) and distilled water (15ml). The mixture was stirred until dissolution was achieved and ethanol (60ml) was added. The mixture was heated to reflux and an ethanolic (25ml) solution of salicylaldehyde (2.80g, 23mmol) was added slowly over 10 minutes. The solution was refluxed for 1 hour. Heating was discontinued and the solution cooled to 0\(^\circ\)C and maintained for 1 hour. Ethanol was removed under reduced pressure to yield a yellow solution, the solution was extracted with dichloromethane (3x100ml) and the combined organic extracts washed with distilled water (2x10ml), dried (MgSO\(_4\)).
filtered and the solvent removed under reduced pressure to yield a yellow, low melting solid. Yield 3.2g (87%). 1H NMR (400MHz, CDCl3): δ 13.25 [s, 2H, O\(\text{O}H\)], 8.18 [s, 2H, NC\(\text{H}C\)], 7.18 [m, 2H of Ar], 7.08 [d, 2H of Ar], 6.80 [m, 2H of Ar], 6.70 [d, 2H of Ar], 3.25 [m, 2H, CH\(\text{C}H\)], 1.86 [m, 2H, CHC(H)H], 1.82 [m, 2H, CHCH(H)], 1.65 [m, 2H, CH\(\text{C}H\)(H)] and 1.40 [m, 2H, CH\(\text{C}H\)(H)]. 13C NMR (100MHz, CDCl3): δ 165 [C of Imine], 161 [C of Ar], 133 [C of Ar], 132 [C of Ar], 119 [C of Ar], 117 [C of Ar], 73 [CHN], 34 [C of Al], and 25 [C of Al]. Mass spectrum: molecular ion peak at \(m/\text{z}=323.5\) (calc. 322.4). IR (KBr disc, cm\(^{-1}\)): 3467, 2935, 2855, 1629, 1493, 1458, 1418, 1272, 1147, 1091, 840 and 755.

\[
\text{[VO(4)] - (R,R)-N,N’-bis(salicylidine)-1,2-cyclohexanediamine vanadium (IV) oxide.}
\]

H\(_2\)A was converted to [VO(4)] using the procedure described for (R, R)-[VO(1)]. Mass spectrum: molecular ion peak at \(m/\text{z}=388.4\) (calc. 387.1). IR (KBr disc, cm\(^{-1}\)): 3410, 2935, 2853, 1615, 1492, 1458, 1421, 1312, 1272, 1147, 1091, 979, 840, 755. Anal. Calcd for C\(_{20}\)H\(_{20}\)N\(_2\)O\(_3\)V (M\(_r\) = 387.33): C, 62.0; H, 5.2; N, 7.2. Found: C, 61.7; H, 5.0; N, 7.0.

**Propylene oxide** (5) - was resolved by the method of Jacobsen [3] and the optical purity was determined to be greater than 98% as determined by chiral GC-MS analysis (Supelco, Beta Dex 120 capillary column, 30m x 0.25mm x 0.25 \(\mu\)m film thickness) of the thiophenol adducts, the preparation of which is detailed below.

\[
\text{(R)-2-hydroxypropane-1-phenylsulphide.}
\]

To a stirred solution of thiophenol (0.20g, 2mmol) in ethanol (25ml) was added (S)-epoxypropane (0.10g, 1mmol) over 1 minute. A catalytic amount of triethylamine was added and the solution stirred overnight. All volatiles and solvent were removed under reduced pressure to yield the product as a white solid. Yield 0.14g (85%). 1H NMR (400MHz, CDCl3): δ 7.20 [m, 5H of Ar], 3.75 [m, 1H, C(OH)(H)], 3.05 [m, 1H, SC(H)(H)], 2.75 [m, 1H, SC(H)(H)], 2.35 [br s, 1H, OH] and 1.20 [d, 3H, CH\(_3\)]. 13C NMR (100MHz, CDCl3): δ 130 [C of Ar], 129 [C of Ar], 128 [C of Ar], 127 [C of Ar], 126 [C of Ar], 65 [COH], 43 [CH\(_2\)S] and 22 [CH\(_3\)]. Mass spectrum: molecular ion peak at \(m/\text{z}=151.0\) (calc. 151.2 for M-OH). IR (KBr disc, cm\(^{-1}\)): 3407, 3056, 2955, 1634, 1573, 1473, 1433, 1383, 1071, 1061, 735 and 685.
(S)-2-hydroxypropane-1-phenylsulphide.

![Chemical Structure](image)

This material was prepared in a similar manner to that of (R)-2-hydroxypropane-1-phenylsulphide using thiophenol (0.20g, 2mmol) and (R)-epoxypropane (0.10g, 1mmol). Yield 0.13g (79%). Spectroscopic data for this material was exactly the same as that of (R)-2-hydroxypropane-1-phenylsulphide.

**SPECTROSCOPIC (EPR/ENDOR) ANALYSES**

For EPR/ENDOR measurements a small quantity (ca. 10 mg) of the appropriate complex [VO(1-4)] was dissolved in neat solvent (CH₂Cl₂, DMF or S, R-5). A small amount of toluene was added to improve the quality of the glass in the frozen solution. The EPR/ENDOR spectra were recorded on a CW X-band Bruker ESP 300E series spectrometer equipped with an ESP360 DICE ENDOR unit, operating at 12.5 kHz field modulation in an X-band ENDOR cavity (Bruker EN 801). All spectra (EPR and ENDOR) were recorded at 10 K. The ENDOR spectra were obtained using 8 dB RF power from a ENI A-300 RF amplifier and 50 or 200 kHz RF modulation depth and 2 mW microwave power. Accurate g values were obtained using an NMR Gaussmeter (Bruker ER 035 M) calibrated using the perylene radical cation in concentrated H₂SO₄ (g = 2.002569). ENDOR simulations were performed using an in house program based on the resonance expressions of Hurst *et al.* [4] for ENDOR resonances in disordered systems.
Figure S1: X-band EPR spectrum of $(R,R)$-[VO-(1)] in epoxide solution $(R)$-5 (with a drop of toluene-d$_8$) recorded with a microwave power of 2.02 mW at 10 K. (a) Experimental spectrum; (b) simulated spectrum and (c) angular dependencies. The ENDOR spectra shown in the main article were recorded at the field position of 3290G corresponding to a pure perpendicular feature (dashed line) in the single crystal type ENDOR spectrum.

Spin Hamiltonian parameters used to simulate the EPR spectra of $(R,R)$-[VO-(1)] in $(R)$-5 (shown above) and $(S,S)$-[VO-(1)] in $(R)$-5 (not shown). The other enantiomers, $(S,S)$-[VO-(1)] in $(S)$-5 and $(R,R)$-[VO-(1)] in $(S)$-5 gave similar values.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>$A_{xx}/$MHz</th>
<th>$A_{yy}/$MHz</th>
<th>$A_{zz}/$MHz</th>
<th>$g_{xx}/$MHz</th>
<th>$g_{yy}/$MHz</th>
<th>$g_{zz}/$MHz</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR in R</td>
<td>152</td>
<td>167</td>
<td>479</td>
<td>1.9827</td>
<td>1.9775</td>
<td>1.9550</td>
</tr>
<tr>
<td>SS in R</td>
<td>155</td>
<td>168</td>
<td>480</td>
<td>1.9827</td>
<td>1.9775</td>
<td>1.9550</td>
</tr>
</tbody>
</table>

This table shows the spin Hamiltonian parameters used for different experiments involving $(R,R)$-[VO-(1)] in epoxide solution $(R)$-5 and its enantiomers in $(S)$-5.
Figure S2: Comparison of the EPR spectra of (a) \((R,R)\)-[VO(1)] in \((S)\)-5, and (b) \((R,R)\)-[VO(1)] in \((R)\)-5. The spectra are essentially identical and hence no chiral discrimination can be recognised by EPR. The corresponding enantiomeric experiment of \((S,S)\)-[VO(1)] in \((R)\)-5, and (b) \((S,S)\)-[VO(1)] in \((S)\)-5 affords essentially identical spectra.
To assist in the interpretation of the $^1H$ ENDOR spectra (and to subsequently differentiate the ligand derived peaks from the epoxide derived peaks), the ENDOR spectra of the following range of protic and deuterated Schiff base vanadyl complexes were measured. In a separate study, we have examined specifically the solvatochromic interactions in some of these complexes (using protic solvents). [5]

Figure S3: X-band $^1H$ ENDOR spectra (recorded at the parallel 2835G and perpendicular 3290G field positions) of a range of vanadyl-Schiff base complexes, recorded with a microwave power of 2 mW at 10 K. (a) [VO(d$_4$)-(3)], (b) [VO-(3)], (c) [VO-(1)], (d) [VO-(4)] and (e) [VO(d$_4$)-(2)].

*NB* Note the large couplings in (c) and (d) due to the cyclohexyl methine protons, and the smaller couplings due to the t-butyl groups in (e) when the cyclohexyl methine protons are deuterated.
Figure S4: Complete X-band $^1$H ENDOR spectra evidencing the diastereomeric states formed between enantiomers of [VO(1)], when dissolved in $R$- or $S$-(5). (a) (R,R)-[VO(1)] in (S)-5. (b) (S,S)-[VO(1)] in (R)-5. (c) (R,R)-[VO(1)] in (R)-5. (d) (S,S)-[VO(1)] in (S)-5. (e) racemic (R,R/S,S)-[VO(1)] in racemic (R,S)-5. Only the low frequency half of the spectra were shown in the main paper in order to highlight the changes in the epoxide related peaks.
**Figure S5:** X-band $^1$H ENDOR spectra (recorded at the perpendicular field position 3290G) of (R,R) - [VO-(1)] in (S)-5 (a) Experimental, (b) Simulation, illustrating the epoxide peaks only.

![X-band $^1$H ENDOR spectra (recorded at the perpendicular field position, 3290G) of (R,R) - [VO-(1)] in (S)-5. (a) Experimental, (b) Simulation illustrating the epoxide peaks only.](image)

**Figure S6:** X-band $^1$H ENDOR spectra (recorded at the perpendicular field position, 3290G) of (R,R) - [VO-(1)] in (R)-5. (a) Experimental, (b) Simulation illustrating the epoxide peaks only.

![X-band $^1$H ENDOR spectra (recorded at the perpendicular field position, 3290G) of (R,R) - [VO-(1)] in (R)-5. (a) Experimental, (b) Simulation illustrating the epoxide peaks only.](image)
Computational Details

Density Functional Theory (DFT) calculations were carried out using the ADF code [6], BLYP functionals and TZP STO level basis (ADF IV) for the inner part of the vanadyl complex described in the following chapter. The outer part, including the tert-butyl groups were optimised in MOPAC [7] PM3 with the central section held in the optimised DFT geometry.

DFT calculations lead to the optimum structure shown in figure 7 in which the closest epoxide H…V atom distances are 3.37 and 3.71Å and corresponding O=V..H angles of 142° and 146°, in good agreement with the value deduced from the ENDOR spectra.

Note: that the angles are larger than those determined from the ENDOR simulations which would suggest that the epoxide is arranged so that the CCO plane in the figure is more vertical than shown. This may result from steric interactions of the epoxide and extended salen ligand structure.

Note on Methodology: These calculations were carried out at the B3LYP level with a 631G(d) basis set using the Gaussian98 package. As commented on in the text the interaction between the vanadyl and epoxide is extremely weak. To gain an initial starting point a series of constrained optimisations at different O=V..O epoxide distances were undertaken and the relative energies plotted as shown in figure 8. The minimum structure from this plot was then optimised without constraints applied.

Figure S7. Calculated structure for the vanadyl(Salen) complex with a co-ordinated propylene oxide molecule. In these calculations, the [VO(1)] ligand was simplified to a Salen type structure in which the phenyl sections are represented by C=C double bonds.
Figure S8. Binding energy of model vanadyl / epoxide dimer as a function of O=V...O_{epox} distance. Binding energy was defined as the difference of total energy calculated for the dimer and that for separate optimisations of the vanadyl complex and epoxide at the same level of theory. BSSE was not calculated.

References