Coordination chemistry of disulfoxides is of interest in inorganic chemistry given the well-known metal coordination through oxygen or sulfur atoms. Ethylene and propylene bridged disulfoxide pro-ligands, coordinate to metals, forming coordinated and chelated complexes, demonstrating its flexibility in the formation of such complexes. Some of these compounds have demonstrated interesting properties in medicinal chemistry and asymmetric catalysis and their synthesis is of importance for bioorganic studies. The presence of two stereogenic centers allows the existence of the meso and racemic forms in disulfoxides. Previous studies on b-disulfoxides in our laboratories have led to the synthesis and spectroscopic study of both diastereomeric forms. In this work we report the synthesis and structural analysis of meso-(2) and racemic-(3)-1,1-bis(benzylsulfinyl)-2-ethylbutane (Scheme1), with high steric requirement around both sulfinyl groups when a branched aliphatic carbon chain is introduced in the a-carbon. An increase in selectivity for small radius metal ions was achieved by compression of the pro-ligand coordination radius. These kind of compounds have not been previously studied.

EXPERIMENTAL

\[^{1}\text{H} \text{and } ^{13}\text{C} \text{ NMR spectra were recorded on a Bruker AC 250 spectrometer (250 MHz for } ^{1}\text{H} \text{ and 62.4 MHz for } ^{13}\text{C}) \text{ in CDCl}_3 \text{ and TMS as internal standard. Chemical shifts are expressed in delta units (ppm) and coupling constants in Hertz (Hz). FT-IR spectra were recorded on a Nicolet 550 IR spectrometer.} \]

1,1-bis(benzyl)-2-ethylbutyl dithioacetal (1)

To a mixture of 25 g (0.25 mol) of 2-ethylbutanal, 1 mL of HCl (c) and 200 mg of AlCl\(_3\), was slowly added 0.55 mol of benzyl alcohol. The mixture was kept at room temperature and stirred for 6 h. After that, water (20 mL) and CH\(_2\)Cl\(_2\) (3x20 mL) was added to extract the product. The organic phase was treated with NaOH 3.0 M (2x20 mL) and dried over anhydrous sodium sulfate. Removal of the solvent and vacuum distillation (99-102 °C/ 0.1 mmHg) gave a residue containing 70.1 g, 85 % yield. Anal. Found (calcd.): S 19.4(19.4).

1,1-bis(benzylsulfinyl)-2-ethylbutane (2)

To a solution of 33.0 g of 1,1-bis(benzylsulfinyl)-2-ethylbutane (2) was slowly added 0.55 mol of benzylthiol. The mixture was poured on ice and slowly neutralized with 1.0 M NaOH solution. The mixture was extracted three times with CH\(_2\)Cl\(_2\) (25 mL) and dried with anhydrous sodium sulfate rendering a residue containing 66.6 g, 70 % yield. Pure meso (2) and racemic (3) was obtained after medium pressure column chromatography (silica gel 60G, particle size 0.2-0.5 mm) with a mixture of ethyl acetate/n-hexane, 5:2, 5:3, 3:1 respectively. Pure meso (d) and racemic (d) were isolated and purified by column chromatography (silica gel 60G, particle size 0.2-0.006) with 40 % ethyl acetate in n-hexane.

Meso 1,1-bis(benzylsulfinyl)-2-ethylbutane (2)

Solid, m.p. 108 -109°C. \[^{1}\text{H-NMR (d ppm) 7.24-7.10 (10H, m), 4.72 (1H, d, J= 12.9 Hz), 3.96 (1H, d, J= 12.9), 3.47 (1H, d, J= 2.7 Hz), 1.71 (1H, m), 1.47 (4H, m), 0.53 (6H, t, J= 7.4 Hz). \]^{13}\text{C-NMR (d ppm) 130.79 (s), 129.07 (d), 127.97 (d), 71.99(d), 55.30 (t), 40.63 (d), 40.06 (t), 11.07 (q).} \]

Racemic 1,1-bis(benzylsulfinyl)-2-ethylbutane (3)

Solid, m.p. 112-113°C. \[^{1}\text{H-NMR (d ppm) 7.33 (5H, m), 4.23 (1H, d, J=12.87 Hz), 3.96 (1H, d, J=12.86 Hz), 3.83 (1H,d, J=2.21 Hz), 1.93 (2H, m), 1.56(m), 1.29 (1H, m), 0.89 (3H, t, J=7.17 Hz), 0.70 (3H, 7.39 Hz). \]^{13}\text{C-NMR (d ppm) 130.79 (s), 130.52 (d), 130.45 (d), 129.11 (s), 128.99 (d), 128.83 (d), 128.69 (d),128.48 (d), 73.81 (d), 58.72 (t), 39.56 (d), 24.59 (t), 23.04 (t), 12.18 (q), 11.85 (q).} \]

Computing calculations

The neutral structure was full optimized using B3LYP/6-31+(d,p) level of theory. A vibrational frequency calculation is used to determine whether the structure is a minimum or saddle point on the potential energy surface and to compute the zero-point energy, ZPE. The computations were carried out with the Gaussian 09 suite of programs.

RESULTS AND DISCUSSION

The synthesis of disulfoxides 1,1-bis(benzylsulfinyl)-2-ethylbutane (2 and 3) was achieved by controlled oxidation of dithioacetal (1), with sodium perborate in glacial acetic acid, producing a 1:1 mixture of meso (2) and racemic (3) modifications, quantified by \[^{1}\text{H-NMR. This synthesis is summarized in Scheme 1:} \]

![Scheme 1](image)

Both compounds were isolated and purified by column chromatography. The expected goal of this work was to incorporate a branched hydrocarbon chain in the a-carbon of the b-disulfoxide to reduce the coordination sphere of the pro-ligand to increase the coordination selectivity for small radius metal ions. See Figure 1. Previously we have reported \[^{1}\text{H-NMR studies to demonstrate that in 1,1-bis(phenylsulfinyl)-methane both sulfinyl oxygens and the phenyl groups are located in an anti orientation.} \]

In the case of meso 1,1-bis(benzylsulfinyl)-2-ethylbutane an anti orientation for both sulfinyl oxygens and benzyl groups it is to be expected for the free pro-ligand in solution. However, oxygen coordination to a metal ion makes both coplanar benzyl groups closer together, introducing an important steric strain. This steric factor makes coordination less likely. The most probable conformation of meso-1,1-bis(benzylsulfinyl)-2-ethylbutane is indicated in Figure 2. Table 1 shows some selected distances and angles...
Fig. 1. Disulfoxide model of high steric compression.

Fig. 2. Proposed structure for Meso-1,1-bis(benzylsulfinyl)-2-ethylbutane

Table 1: selected distances and angles.

<table>
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<th>Distance</th>
<th>Å</th>
<th>Angle</th>
<th>°</th>
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<tbody>
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<td>S1-C8-S2</td>
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<tr>
<td>S2-O2</td>
<td>1.522</td>
<td>C7-S1-C8</td>
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<td>S1-C7</td>
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<td>S2-C9</td>
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<td>O1-S1-S2-O2</td>
<td>97.59</td>
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<tr>
<td></td>
<td></td>
<td>C17-C18-C19-C20</td>
<td>32.46</td>
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</table>

A ¹H-NMR analysis of 1,1-bis(benzylsulfinyl)-2-ethylbutane clearly distinguishes meso from the racemic pair. Figure 3, shows the ¹H-NMR spectrum for the mixture of diastereomers, dl and meso compounds (a) and that of meso compound (b).

Two AB quartets centered at 4.72 and at 3.96 (ppm) with, J= 12.93 Hz for the meso and 4.23 and at 3.83 (ppm) with J= 12.87 Hz for the dl pair. The coupling constant between hydrogens in carbons C₈ and C₁₆, JH₈H₁₆ = 2.7 Hz is small, indicating a dihedral angle smaller or more than 90° between H₈ and H₁₆. Methyl groups have been shifted to high field, appearing at 0.53 ppm in the meso compound and 0.89 and 0.70 (ppm) respectively in the racemic form. These values suggest a fairly perpendicular orientation of both phenyl groups with respect to the alkyl chain. However, the high steric hindrance introduced by both coplanar benzyl results in a closer proximity of both oxygens promoting rotation to minimize steric hindrance. In this conformation, shown as structure Figure 2, ethyl groups should appear at high field and hydrogens in C₈ and C₁₆ should be synperiplanar with a small value for JH₈H₁₆. This analysis is consistent with ¹H-NMR data.

In conclusion methyl and methylene groups have been shifted to high field; 0.53 (ppm) for “meso methyl” and 0.89 and 0.70 (ppm) for “racemic methyl groups” due to the proximity of aromatic’s rings anisotropy. An ¹H-NMR analysis of JH₈H₁₆ for meso and racemic compounds indicates small values for both constants (2.7 and 2.1 Hz, respectively). ¹C-NMR data, on the other hand, confirm the shielding experienced by methyl and methylene groups due to the proximity of both benzyl groups, shifting their resonances to 40.6 and 11.0 ppm respectively in meso and 24.6; 24.0 and 12.2; 11.8 ppm respectively in the racemic pair. This shielding effect has not been observed in other b-disulfoxides studied so far.

CONCLUSION

It has carried out the synthesis of a new disulfoxide compound with a branched aliphatic carbon chain introduced into the alpha carbon. It has obtained and resolved the Meso and Racemic forms of the disulfoxide 1,1-bis(benzylsulfinyl)-2-ethylbutane. The ¹H-NMR analysis has clearly differentiate these forms and theoretical calculus are in agreement with the experimental data.

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REFERENCES


