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Hydrogen-bonding controls the solid-state and enantiomeric comformations of the amino alcohol ligand 2-[(2-hydroxyethyl)amino]cyclohexanol

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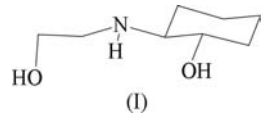
The crystal structure of the title compound, $C_8H_{17}NO_2$, consists of (*R*,*R*) and (*S*,*S*) enantiomeric pairs packed in adjacent double layers which are characterized by centrosymmetric hydrogen-bonded dimers, generated *via* N—H···O and O—H···O interactions, respectively. Intermolecular interactions, related to acceptor and donor molecule chirality, link the achiral double layers into tubular columns, which consist of a staggered hydrophilic inner core surrounded by a hydrophobic cycloalkyl outer surface and extend in the [011] direction.

Comment

Our investigation of reinforced β-amino alcohols as potential metal chelators has highlighted the need for a detailed understanding of the hydrogen-bonding topology associated with these compounds. The relationship between ligand backbone architecture and complex stability indicates that metal ions of smaller ionic radii are preferred upon grafting of cyclohexyl groups across donor atoms (de Sousa *et al.*, 1991; de Sousa & Hancock, 1995). Short nonbonding hydrogen contacts have been reported to cause the observed dependency on metal ion radius (de Sousa *et al.*, 1997*a*; Hancock *et al.*, 1996), with complexes of larger metal ions being destabilized by H···H repulsions. The conformations of amino alcohol chelates and their respective inter- and intramolecular interactions in the solid state may contribute towards a better understanding of this observation. Solid-state analysis of a cycloalkyl-reinforced amino alcohol in which all donor atoms are linked *via* cyclohexyl bridges suggests that stronger intramolecular hydrogen bonding within the chelating cavity is accompanied by a weakening of the H···H repulsions (de Sousa & Fernandes, 2003; de Sousa *et al.*, 1997*b*). The presence of intramolecular hydrogen bonds (Varadwaj *et al.*, 2009), typically defined by string motifs $S(n)$, is implied as relevant in rationalizing the observed trends in the relative stabilities of amino alcohol metal ion complexes. Recent studies of hydrogen-bonding arrays prevalent in a series of *N*-alkyldiethanolamine ligands relate intramolecular interactions to the steric constraints imposed by ligand backbone architectures (Churakov *et al.*, 2009). Ligand backbone alterations include *C*-alkyl substitution of hydroxyethyl pendents and varied substituents on the amine N-donor atom.



(I)

We report here a solid-state study of the title reinforced diethanolamine derivative, (I), comprising a cyclohexyl bridge between the amine N atom and a single hydroxy O-donor atom, representing *C*-alkyl substitution across a hydroxyethyl bridge in diethanolamine. Based on a previous study of *N*,*N*′-bis(2-hydroxycyclohexyl)-*trans*-cyclohexane-1,2-diamine (de Sousa & Fernandes, 2003), a crystal structure of (I) containing enantiomeric layers might be expected. In fact, both *syn* and *anti* conformations of (I) (Fig. 1), the latter disordered, occur in the structure, with alternating *anti*- and *syn*-enantiomeric double layers. The *syn* O1—C1—C2—N1 torsion angle of 58.98 (10)° suggests minimal torsional strain for the hydroxycyclohexyl pendent, accommodating an N1—C7—C8—O2 torsion angle of −65.06 (13)° for a *gauche* orientation of the hydroxyethyl pendent. In the *anti* conformer, the corresponding O11—C11—C12—N11 torsion angle of −54.15 (10)° deviates from that of minimal strain for a cyclohexyl bridge (de Sousa *et al.*, 1991; Kemp & Vellaccio, 1980). In addition, a distorted *gauche* hydroxyethyl pendent has an N11—C17—C18—O12 torsion angle of −68.9 (5)°. The hydroxyethyl group of the predominantly *anti* conformer is

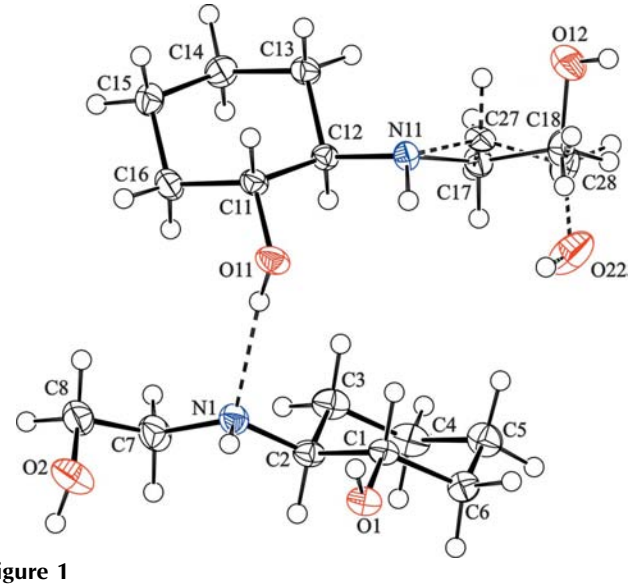


Figure 1
The molecular structure of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Dashed lines indicate hydrogen bonds and the minor disordered conformation of one molecule.

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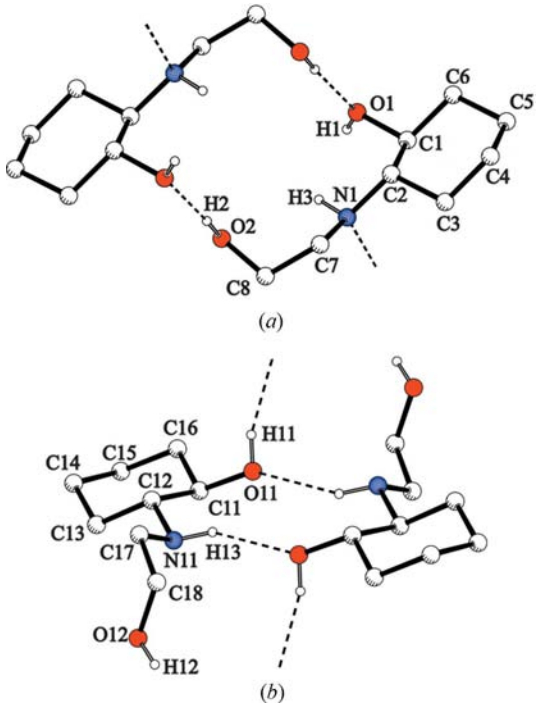

Figure 2
(*a*) The $R_2^2(16)$ dimers for *syn* enantiomeric pairs of (I) and (*b*) the $R_2^2(10)$ dimers for *anti* enantiomeric pairs of (I). Dashed lines indicate hydrogen bonds.

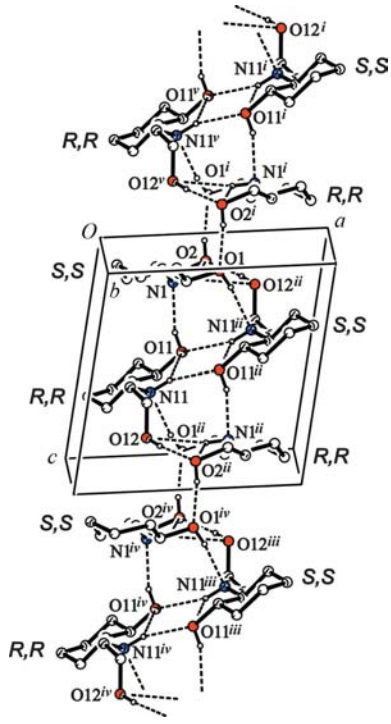

Figure 3
Intermolecular O—H···N and O—H···O interactions (dashed lines) linking $R_2^2(10)$ and $R_2^2(16)$ dimers of (I) into tubular columns along [011]. [Symmetry codes: (i) $1-x, -y, -z$; (ii) $1-x, 1-y, 1-z$; (iii) $1-x, 2-y, 2-z$; (iv) $x, 1+y, 1+z$; (v) $x, y-1, z-1$.]

disordered over two positions (Fig. 1), corresponding to *anti* and *syn* conformations [N11—C27—C28—O22 = 65.7 (16)° for the latter], with site occupancies of 0.736 (2) and 0.264 (2), respectively. The minor *syn* conformation affords a hydrogen-bonding pattern very similar to that observed for diethanolamine (Mootz *et al.*, 1989) and is not included in this discussion.

Pairs of *syn* enantiomers related by the inversion centre at ($\frac{1}{2}$, 0, 0) generate an $R_2^2(16)$ dimer (Bernstein *et al.*, 1995) *via* strong O—H···O hydrogen bonds (Table 1 and Fig. 2*a*), while *anti* enantiomeric pairs related by the inversion centre at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) generate an $R_2^2(10)$ dimer *via* N—H···O hydrogen bonds (Table 1 and Fig. 2*b*). The mean planes through each molecule of *syn* molecule pairs are separated by 3.2 Å, which reveals significant puckering in the centrosymmetric 16-membered rings compared with the corresponding plane separation of 0.72 Å in the structure of diethanolamine (Mootz *et al.*, 1989).

Puckering of the $R_2^2(10)$ dimers is minimal, as evidenced by the molecular plane separation of 0.91 Å for pairs of *anti* molecules. The inversion centres of the $R_2^2(10)$ and $R_2^2(16)$ dimers are separated by 5.66 Å. Alternating $R_2^2(16)$ dimers are therefore significantly separated (11.32 Å) compared with their counterparts in the diethanolamine structure (4.46 Å), largely as a consequence of enantiomeric crystallization into separate layers. The tubular stacks observed in the structure of diethanolamine result from $R_2^2(16)$ dimers weakly linked *via* N—H···O hydrogen bonds.

The hydrogen bonding in (I) links $R_2^2(16)$ and $R_2^2(10)$ dimers, predominantly *via* O—H···O and O—H···N hydrogen bonds, to generate a tubular column extending in the [011] direction (Table 1 and Fig. 3). Hydroxyethyl atom O12 acts as a hydrogen donor *via* atom H2 to hydroxyethyl atom O2^{ii} (see Table 1 for details and symmetry codes) in an O—H···O interaction between *anti* and *syn* molecules of $R_2^2(10)$ and $R_2^2(16)$ dimers centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) and ($\frac{1}{2}$, 1, 1), respectively. A symmetrically equivalent hydrogen bond involving atoms O12^{ii} and O2 links $R_2^2(10)$ and $R_2^2(16)$ dimers centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) and ($\frac{1}{2}$, 0, 0), respectively. These O12—H12···O2^{ii} hydrogen bonds are stereospecific, occuring only between molecules of like chirality.

O—H···N hydrogen bonds between centrosymmetric dimers are restricted to the N and O atoms connected *via* the cyclohexyl bridge (Fig. 3). Stereospecificity originates from the conformation of the O-donor atom. O11—H11···N1 hydrogen bonds occur only between *syn* and *anti* molecules of opposite chirality where the donor atom, O11, originates from an *anti* conformer. Hydroxycyclohexyl atom O11 of an *anti* (*R*,*R*) molecule acts as a donor *via* atom H11 to amine atom N1 of a *syn* (*S*,*S*) molecule (see Fig. 1), linking $R_2^2(10)$ and $R_2^2(16)$ dimers centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) and ($\frac{1}{2}$, 0, 0), respectively. An equivalent interaction, between atom O11 of an *anti* (*S*,*S*) molecule and atom N1 of a *syn* (*R*,*R*) molecule, both at ($1-x$, $1-y$, $1-z$), links $R_2^2(10)$ and $R_2^2(16)$ dimers centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) and ($\frac{1}{2}$, 1, 1), respectively. O1—H1···N11^{ii} hydrogen bonds occur between *syn* and *anti* molecules of like chirality, where donor atom O1 originates from a *syn* conformer. The $R_2^2(16)$ dimer centred at ($\frac{1}{2}$, 0, 0) is linked to the $R_2^2(10)$ dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) *via* atom O1 of a *syn* (*S*,*S*) molecule, hydrogen

bonded to atom N11^{ii} of an *anti* (*S*,*S*) molecule. The $R_2^2(16)$ dimer centred at ($\frac{1}{2}$, 1, 1) is linked to the $R_2^2(10)$ dimer centred at ($\frac{1}{2}$, $\frac{1}{2}$, $\frac{1}{2}$) through an equivalent interaction between a *syn* (*R*,*R*) and an *anti* (*R*,*R*) molecule. The intricate hydrogen-bonding array within the tubular columns is completed by very weak N—H···O interactions (Fig. 3). In the N1—H3···O12^{ii} hydrogen bonds, donor atom N1 of a *syn* molecule is hydrogen bonded to hydroxyethyl atom O12^{ii} of an *anti* molecule with like chirality.

In conclusion, the *anti* conformation of (I), observed when grafting a cyclohexyl bridge across a hydroxyethyl pendent, facilitates stronger O—H···O hydrogen bonds between centrosymmetric dimers and favours the formation of tubular columns. Grafting of cyclohexyl bridges into the carbon backbone of amino alcohols may prove to be a useful synthetic strategy in designing self-assembled supramolecular structures of β-amino alcohols.

Experimental

Ethanolamine and cyclohexene oxide were used as obtained from Merck and Aldrich, respectively. Equimolar quantities of ethanolamine (1 g, 16.4 mmol) and cyclohexene oxide (1.61 g, 16.4 mmol) were added to a round-bottomed flask containing absolute ethanol (10 ml). A $CaCl_2$ drying tube and condenser were fitted to the flask and the mixture was refluxed with stirring at 358 K for 48 h. After completion of the reaction, the solvent was removed under reduced pressure to yield a yellow oil. The oil was dissolved in deionized water (15 ml) and washed with chloroform (30 ml). Upon removal of the solvent under reduced pressure, the aqueous layer yielded a light-yellow oil, which was characterized by NMR and FAB–MS to be the product 2-[(2-hydroxyethyl)amino]cyclohexanol, (I). Diffraction quality crystals of (I) formed from the crude oil and the extractant when left unattended for several days (yield 96%). ^{1}H NMR (D_2O, 300 MHz): δ 3.61 (2H, *m*, CH_2), 3.28 (1H, *m*, CH), 2.66 (2H, *m*, CH_2), 2.31 (1H, *m*, CH), 1.89 (2H, *m*, CH_2), 1.62 (2H, *m*, CH_2), 1.09 (4H, *m*, 2 × CH_2); ^{13}C NMR ($CDCl_3$, 300 MHz): δ 73.42, 63.15, 60.95, 48.30, 34.16, 30.13, 24.73, 24.63; MS, *m*/*z* (FAB): 160 (M^+, 100%).

Crystal data

$C_8H_{17}NO_2$
M_r = 159.23
Triclinic, $P\overline{1}$
a = 9.4334 (2) Å
b = 10.0280 (3) Å
c = 10.4651 (3) Å
α = 112.954 (1)°
β = 92.429 (1)°
γ = 102.055 (1)°
V = 883.02 (4) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 173 K
0.48 × 0.40 × 0.15 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
20934 measured reflections
4253 independent reflections
3495 reflections with $I > 2\sigma(I)$
R_{int} = 0.046

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.103
S = 1.03
4253 reflections
232 parameters
31 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.33 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2···O1^{i}	0.84	1.89	2.7270 (11)	172
N11—H13···O11^{ii}	0.92	2.37	3.1884 (11)	148
O12—H12···O2^{ii}	0.84	1.90	2.7299 (14)	170
O11—H11···N1	0.84	2.03	2.8379 (12)	162
O1—H1···N11^{ii}	0.84	1.94	2.7701 (11)	169
N1—H3···O12^{ii}	0.92	2.52	3.4051 (16)	163

Symmetry codes: (i) $-x+1, -y, -z$; (ii) $-x+1, -y+1, -z+1$.

H atoms were first located in a difference map and then positioned geometrically. They were allowed to ride on their respective parent atoms, with C—H = 1.00 (CH) or 0.99 Å (CH_2), N—H = 0.92 Å and O—H = 0.84 Å, and with U_{iso}(H) = 1.2U_{eq}(C). The disordered hydroxyethyl groups were refined over two positions with similarity restraints, of standard uncertainty 0.001 Å, applied to chemically equivalent bond lengths and angles for disordered hydroxyethyl groups C17—C18—O12 and C27—C28—O22. The N11—C17 and N11—C27 bonds were restrained to have similar lengths within an effective standard uncertainty of 0.001 Å. Atom C27 was restrained to approximate isotropic behaviour with a standard uncertainty of 0.003 Å^2. A rigid bond restraint with a standard uncertainty of 0.003 Å was applied to atoms C27, C28 and O22 of the minor conformation of the hydroxyethyl group, of site occupancy 0.264 (2), because the components of the displacement parameters along the bond directions between atoms C27 and C28 and between atoms C28 and O22 were irregular. In addition, similarity restraints were applied to the displacement parameters of the atoms of the minor conformation of the hydroxyethyl group with a standard uncertainty of 0.01 Å^2.

Data collection: *APEX2* (Bruker, 2005); cell refinement: *APEX2*; data reduction: *SAINT-Plus* (Bruker, 2005); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008) and *WinGX* (Farrugia, 1997); molecular graphics: *SHELXTL* and *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG3157). Services for accessing these data are described at the back of the journal.

References

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bruker (2005). *APEX2* (Version 2.0-1) and *SAINT-Plus* (Version 6.0). Bruker AXS Inc., Madison, Wisconsin, USA.
Churakov, A. V., Lermontova, E. K., Zaitsev, K. V., Huang, M., Karlov, S. S., Zaitseva, G. S. & Howard, J. A. K. (2009). *Acta Cryst.* C**65**, o587–o592.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Hancock, R. D., Maumela, H. & de Sousa, A. S. (1996). *Coord. Chem. Rev.* **148**, 315–347.
Kemp, D. S. & Vellaccio, F. (1980). *Organic Chemistry*, pp. 480–481. London: Worth Publishers.
Mootz, D., Brodalla, D. & Wiebcke, M. (1989). *Acta Cryst.* C**45**, 754–757.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Sousa, A. S. de, Croft, G. J. B., Wagner, C. A., Michael, J. P. & Hancock, R. D. (1991). *Inorg. Chem.* **30**, 3525–3529.

Sousa, A. S. de & Fernandes, M. A. (2003). *Acta Cryst.* E**59**, o1872–o1874.
Sousa, A. S. de & Hancock, R. D. (1995). *Chem. Commun.* pp. 415–416.
Sousa, A. S. de, Hancock, R. D. & Riebenspies, J. H. (1997*a*). *J. Chem. Soc. Dalton Trans.* pp. 939–944.
Sousa, A. S. de, Hancock, R. D. & Riebenspies, J. H. (1997*b*). *J. Chem. Soc. Dalton Trans.* pp. 2831–2836.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Varadwaj, P. R., Cukrowski, I. & Marques, H. M. M. (2009). *J. Mol. Struct. (THEOCHEM)*, **915**, 20–32.