organic compounds

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N,*N*'-(1,2-phenylene)bis(pyridine-2carboxamide) and *N*,*N*'-(1,2-cyclohexanediyl)bis(pyridine-2-carboxamide) toluene hemisolvate

Jun Lin, Jun-Yong Zhang, Yan Xu, Xiao-Kang Ke and Zijian Guo*

Coordination Chemistry Institute, State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing 210093, People's Republic of China Correspondence e-mail: zguo@netra.nju.edu.cn

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The crystal structures of N,N'-(1,2-phenylene)bis(pyridine-2carboxamide), $C_{18}H_{14}N_4O_2$, (I), and N,N'-(1,2-cyclohexanediyl)bis(pyridine-2-carboxamide) have been determined, the latter compound as the toluene hemisolvate, $C_{18}H_{20}N_4O_2\cdot 0.5C_7H_8$, (II). In (I), the benzene ring is nearly coplanar with one of the pyridine rings and forms a dihedral angle of 59.4 (1)° with the other. However, in (II), the dihedral angle of the two pyridine rings is 70.0 (1)°.

Comment

Functional mimics of manganese superoxide dismutase (Mn-SOD) are of great potential as therapeutic agents (Riley, 1999), for example, manganese porphyrin derivatives, which show powerful anti-inflammatory effects due to their multiple scavenging activities (Cuzzocrea et al., 1999), and N-containing macrocyclic manganese complexes, which have high catalytic SOD activity and are chemically and biologically stable in vivo (Salvemini et al., 1999). In the latter case, the introduction of a fused cyclohexane group enhances the kinetic and thermodynamic stabilities of the manganese complexes. Therefore, we designed and synthesized the title compounds, (I) and (II), which each contain two pyridine and two amide moieties. The Mn^{II} and Mn^{III} complexes of the title compounds were also synthesized, and preliminary data showed that the Mn^{III} complexes possess potent SOD activity in human blood plasma and platelet.



The molecular structures of (I) and (II) are shown in Figs. 1 and 2, respectively. It is notable that the orientations of the

pyridine rings in (I) and (II) are quite different. In compound (I), the N1-pyridine ring is nearly coplanar with the benzene ring, with a dihedral angle of $18.6 (1)^{\circ}$, which may be due to stabilization *via* an intramolecular C—H···O hydrogen bond between C8 and O1 (see Table 2). The N4-pyridine ring forms a dihedral angle of 59.4 (1)° with the benzene ring. Such an arrangement is similar to that found in *N*,*N*'-(4,5-dichloro-*o*-phenylene)bis(4-*tert*-butylpyridine-2-carboxamide) (Fun *et al.*, 1999).

In (I), N2-H2B acts as a donor in the three-centre (bifurcated) N2-H2B···O2 and N2-H2B···N1 interactions, the former being responsible for the reciprocal orientation of the two oxamide groups that form a dihedral angle of $64.1 (1)^\circ$, the latter for the orientation of the O1-carboxamide plane with respect to that of the N1-pyridine, the C4-C5-C6-O1 torsion angle being $-7.8 (4)^\circ$. The N3-H3B···N4 interaction determines the orientation of the O2-carboxamide plane with respect to that of the N4-pyridine, the N3-C13-C14-N4 and O2-C13-C14-C15 torsion angles being -9.5 (3) and -11.6 (4)°, respectively. The orientation of the two carboxamide-2-pyridine substituents with respect to the benzene plane is defined by the C6-N2-C7-C8 and C13-N3-C12-C11 torsion angles of 23.7 (4) and 130.3 $(3)^{\circ}$, respectively. The weak $C11 - H11A \cdot \cdot \cdot O2^{i}$ interaction (Table 2) contributes to the crystal packing [symmetry code: (i) x, y - 1, z].

In compound (II), the two pyridine rings form a dihedral angle of 70.0 (1)° and the cyclohexane ring adopts a chair conformation, with a total puckering amplitude (Cremer & Pople, 1975) $Q_T = 0.559$ (2) Å. The two pyridine-2-carbox-amide substituents are approximately perpendicular to the cyclohexane ring, the dihedral angles they form with the least-squares plane through cyclohexane being 84.8 (1) and



Figure 1

The structure of (I) showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms are drawn as small spheres of arbitrary radii.

 $73.7 (1)^{\circ}$ for the N3- and N4-pyridine rings, respectively. The substituents occupy the equatorial position of the cyclohexane ring and adopt a *trans* conformation so that the energy of (II) is minimized.

In (II), N1-H1B is involved in two three-centre (bifurcated) interactions. One, N1-H1B···N4, is intramolecular, determining the coplanarity of the N4-pyridine and O1-oxamide [C15-C14-C13-O1 4.9 (2), O1-C13-N1-C12 1.4 (2) and N4-C14-C13-N1 5.2 (2)°]. The other, N1- $H1B \cdots O2^{ii}$ (Table 4), is intermolecular, connecting the molecule to a centrosymmetric one displaced along z [symmetry code: (ii) -x, -y, 2 - z]. Similar behaviour is shown by the N2-H2B group which, with the N2-H2B \cdots N3 interaction, causes coplanarity of the N3-pyridine and O2-oxamide [C4-C5-C6-O2 -5.4 (2), O2-C6-N2-C7 -2.4 (2) and N3-C5-C6-N2 $-5.0(2)^{\circ}$], while the intermolecular N2- $H2B \cdots O1^{iii}$ bond (Table 4) contributes to the crystal packing [symmetry code: (iii) 1 - x, -y, 2 - z]. The weak C4– $H4A \cdots O2$ and $C7 - H7A \cdots O2$ interactions contribute to the coplanarity of the N3-pyridine with O2-oxamide, which are approximately orthogonal to the cyclohexane ring [C6-N2-C7-C12 129.6 (2)°], and similarly, C12-H12A···O1 and C15-H15A...O1 are responsible for the coplanarity and orthogonality of the N4-pyridine and O1-oxamide system $[C13-N1-C12-C11-108.1 (2)^{\circ}]$. The weak intermolecular $C8-H8A\cdots O1^{iii}$ and $C11-H11B\cdots O2^{ii}$ interactions (Table 4) contribute to the molecular packing in the crystal. Compound (II) contains a molecule of toluene, disordered over two sites related by centrosymmetry, with occupancy factors of 0.5.

The mean C–N lengths of the pyridine rings are 1.336 (3) and 1.335 (2) Å in (I) and (II), respectively. The amide N–C



Figure 2

The structure of (II) showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms are drawn as small spheres of arbitrary radii. Only one of the two disordered toluene molecules is represented [symmetry code: (iv) -x, -1 - y, 3 - z].

distances towards the bridging ring [N2-C7 and N3-C12 in (I), and N2-C7 and N1-C12 in (II)] are longer than those towards the pyridine rings [N2-C6 and N3-C13 in (I), and N2-C6 and N1-C13 in (II)] in both compounds. These values are within the normal range expected (Allen *et al.*, 1987).

Experimental

Compounds (I) and (II) were synthesized by the reaction of pyridine-2-carboxylic acid and 2-phenylenediamine (or 1,2-cyclohexanediamine) in a 2:1 ratio in the presence of triphenyl phosphite in pyridine at 373 K for 2 h (Leung *et al.*, 1991). Crystals of both compounds suitable for X-ray structure analysis were obtained by slow evaporation from toluene solutions at room temperature.

Compound (I)

Crystal data	
$C_{18}H_{14}N_4O_2$	$D_x = 1.368 \text{ Mg m}^{-3}$
$M_r = 318.33$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 30
$a = 12.346 (2) \text{\AA}$	reflections
b = 5.567 (1) Å	$\theta = 4.92 - 12.44^{\circ}$
c = 22.578 (6) Å	$\mu = 0.093 \text{ mm}^{-1}$
$\beta = 95.20 \ (1)^{\circ}$	T = 293 (2) K
V = 1545.4 (6) Å ³	Block, colourless
Z = 4	$0.5 \times 0.2 \times 0.2$ mm

Data collection

Bruker P4 diffractometer	$h = -1 \rightarrow 14$
θ/ω scans	$k = -1 \rightarrow 6$
821 measured reflections	$l = -26 \rightarrow 26$
726 independent reflections	3 standard reflections
624 reflections with $I > 2\sigma(I)$	every 97 reflections
$R_{\rm int} = 0.078$	intensity decay: 5.38%
$m_{\rm max} = 24.99^{\circ}$	

Table 1

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Selected geometric parameters (Å, °) for (I).

N1-C1	1.338 (4)	N3-C12	1.432 (3)
N1-C5	1.340 (3)	N4-C14	1.324 (3)
N2-C6	1.356 (3)	N4-C18	1.342 (3)
N2-C7	1.406 (3)	O1-C6	1.229 (3)
N3-C13	1.343 (3)	O2-C13	1.222 (3)
C1-N1-C5	116.2 (3)	O1-C6-N2	124.4 (3)
C6-N2-C7	128.7 (2)	O1-C6-C5	120.7 (3)
C13-N3-C12	126.7 (2)	O2-C13-N3	124.9 (2)
C14-N4-C18	116.6 (2)	O2-C13-C14	120.9 (2)

able 2			
Hydrogen-bonding geometr	y (Å,	°) for	(I).

$D - H \cdots A$	D-H	$H \cdot \cdot \cdot A$	$D \cdots A$	$D - \mathbf{H} \cdots A$
N2-H2 B ···O2	0.86	2.13	2.840 (3)	140
$N2-H2B\cdots N1$	0.86	2.24	2.673 (4)	111
N3−H3 <i>B</i> ···N4	0.86	2.25	2.674 (3)	110
C8-H8A···O1	0.93	2.37	2.898 (4)	116
$C11 - H11A \cdots O2^{i}$	0.93	2.45	3.161 (3)	133

Symmetry code: (i) x, y - 1, z.

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Refinement

Refinement on F^2 $R[F^2 > 2\sigma(F^2)] = 0.053$ $wR(F^2) = 0.139$ S = 1.0312726 reflections 217 parameters H-atom parameters constrained

Compound (II)

Crystal data

 $\begin{array}{l} C_{18}H_{20}N_4O_2{\cdot}0.5C_7H_8\\ M_r = 370.45\\ \text{Triclinic, P}\\ a = 9.899 (2) \text{ Å}\\ b = 10.492 (2) \text{ Å}\\ c = 10.795 (2) \text{ Å}\\ \alpha = 88.52 (3)^{\circ}\\ \beta = 64.39 (3)^{\circ}\\ \gamma = 89.70 (3)^{\circ}\\ V = 1010.7 (4) \text{ Å}^3 \end{array}$

Data collection

Enraf–Nonius CAD-4 diffractometer $2\theta/\omega$ scans 3764 measured reflections 3539 independent reflections 2552 reflections with $I > 2\sigma(I)$ $R_{\rm int} = 0.007$

Refinement

Refinement on F^2 $w = 1/[\sigma^2(F_o^2) + (0.0904P)^2]$ $R[F^2 > 2\sigma(F^2)] = 0.049$ + 0.3004P] where $P = (F_o^2 + 2F_c^2)/3$ $wR(F^2) = 0.173$ $(\Delta/\sigma)_{\rm max} = 0.006$ S = 1.062-3 $\Delta \rho_{\rm max} = 0.27 \ {\rm e} \ {\rm \AA}^2$ 3539 reflections $\Delta \rho_{\rm min} = -0.16 \text{ e } \text{\AA}^{-3}$ 263 parameters Extinction correction: SHELXTL H-atom parameters constrained (Sheldrick, 1997)

Table 3

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C - 1 +			/ A 0) f	(TT)
Selected	geometric	parameters	IA '	INT	()
Selected	Scometrie	parameters	(11,	, 101	(11)

C1-N3	1.336 (2)	C12-N1	1.455 (2)
C5-N3	1.335 (2)	C13-O1	1.229 (2)
C6-O2	1.233 (2)	C13-N1	1.325 (2)
C6-N2	1.321 (2)	C14-N4	1.335 (2)
C7-N2	1.457 (2)	C18-N4	1.335 (2)
O2-C6-N2	124.3 (1)	C13-N1-C12	124.2 (1)
O2-C6-C5	119.9 (1)	C6-N2-C7	123.6 (1)
O1-C13-N1	124.0 (2)	C5-N3-C1	116.9 (2)
O1-C13-C14	120.1 (1)	C14-N4-C18	117.0 (1)

For both compounds, H atoms were placed in calculated positions and refined with fixed isotropic displacement parameters (N–H = 0.86 Å and C–H = 0.93 Å). However, the H atoms of the toluene molecule in (II) were not located, because of disorder.

$u = 1/[\sigma^2(E^2) + (0.048P)^2]$
$w = 1/[0 (F_o) + (0.048F) + 0.0282B]$
+ 0.282F]
where $P = (F_o + 2F_c)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta \rho_{\text{max}} = 0.16 \text{ e A}$
$\Delta \rho_{\rm min} = -0.16 \ {\rm e} \ {\rm A}$

Z = 2

 $D_x = 1.217 \text{ Mg m}^{-3}$

Cell parameters from 25

Mo $K\alpha$ radiation

reflections

 $\begin{array}{l} \theta = 2.38 \text{--} 15.62^{\circ} \\ \mu = 0.080 \ \text{mm}^{-1} \end{array}$

T = 293 (2) K

 $\theta_{\rm max} = 24.96^{\circ}$

 $h = 0 \rightarrow 11$

 $k = -12 \rightarrow 12$

 $l = -11 \rightarrow 12$ 3 standard reflections

Block, colourless

 $0.30 \times 0.26 \times 0.24 \text{ mm}$

every 97 reflections

intensity decay: 4.2%

Extinction coefficient: 0.046 (4)

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Tab	e	4	

Hydrogen-bonding geometry (Å, °) for (II).

$D-\mathrm{H}\cdots A$	D-H	$H \cdot \cdot \cdot A$	$D \cdots A$	$D - H \cdots A$
$N1 - H1B \cdots N4$	0.86	2.31	2.710 (2)	108
$N1 - H1B \cdot \cdot \cdot O2^{ii}$	0.86	2.46	3.156 (2)	138
$N2 - H2B \cdot \cdot \cdot N3$	0.86	2.30	2.696 (2)	108
$N2 - H2B \cdot \cdot \cdot O1^{iii}$	0.86	2.36	3.068 (2)	140
$C4-H4A\cdots O2$	0.93	2.53	2.812 (2)	98
$C7-H7A\cdots O2$	0.98	2.43	2.828 (2)	104
$C8-H8A\cdots O1^{iii}$	0.97	2.55	3.357 (2)	140
$C11 - H11B \cdot \cdot \cdot O2^{ii}$	0.97	2.47	3.317 (3)	145
$C12-H12A\cdots O1$	0.98	2.45	2.835 (2)	103
$C15-H15A\cdots O1$	0.93	2.51	2.799 (3)	98

Symmetry codes: (ii) -x, -y, 2-z; (iii) 1-x, -y, 2-z.

For compound (I), data collection: *XSCANS* (Siemens, 1994); cell refinement: *XSCANS*; data reduction: *XSCANS*. For compound (II), data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *CAD-4 Software*. For both compounds, program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; 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: NA1486). Services for accessing these data are described at the back of the journal.

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