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N,*N*′-(1,2-phenylene)bis(pyridine-2-carboxamide) 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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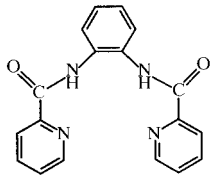
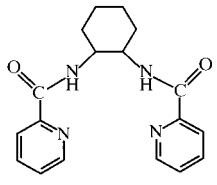
The crystal structures of *N*,*N*′-(1,2-phenylene)bis(pyridine-2-carboxamide), $C_{18}H_{14}N_4O_2$, (I), and *N*,*N*′-(1,2-cyclohexanediyl)bis(pyridine-2-carboxamide) have been determined, the latter compound as the toluene hemisolvate, $C_{18}H_{20}N_4O_2{\cdot}0.5C_7H_8$, (II). In (I), the benzene 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.



(I)



(II)

$\cdot 0.5C_7H_8$

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)°, 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—H2*B* acts as a donor in the three-centre (bifurcated) N2—H2*B*···O2 and N2—H2*B*···N1 interactions, the former being responsible for the reciprocal orientation of the two oxamide groups that form a dihedral angle of 64.1 (1)°, 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)°. The N3—H3*B*···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)°, respectively. The weak C11—H11*A*···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-carboxamide 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

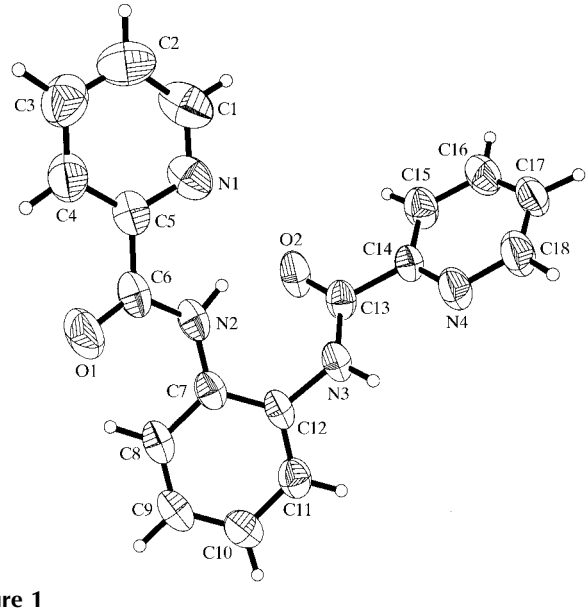


Figure 1
The structure of (I) showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms are drawn as small spheres of arbitrary radii.

73.7 (1)° 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—H1*B* is involved in two three-centre (bifurcated) interactions. One, N1—H1*B*···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—H1*B*···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—H2*B* group which, with the N2—H2*B*···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)°], while the intermolecular N2—H2*B*···O1^{iii} bond (Table 4) contributes to the crystal packing [symmetry code: (iii) $1-x, -y, 2-z$]. The weak C4—H4*A*···O2 and C7—H7*A*···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—H12*A*···O1 and C15—H15*A*···O1 are responsible for the coplanarity and orthogonality of the N4-pyridine and O1-oxamide system [C13—N1—C12—C11 −108.1 (2)°]. The weak intermolecular C8—H8*A*···O1^{iii} and C11—H11*B*···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 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).

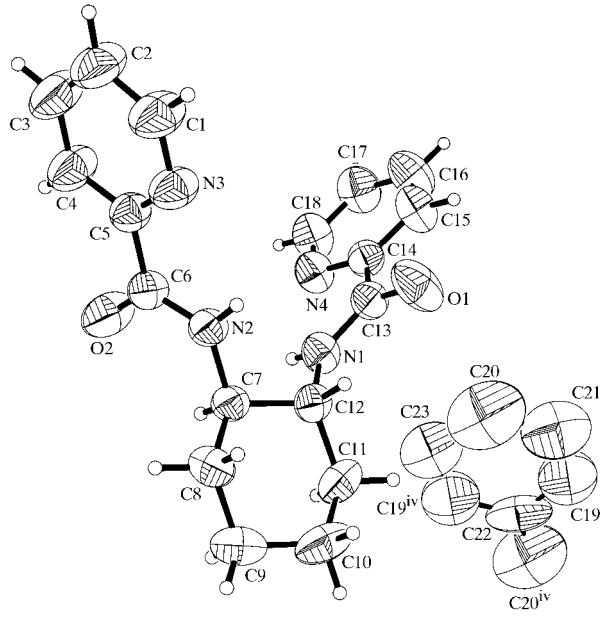


Figure 2
The structure of (II) showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms are drawn as small spheres of arbitrary radii. Only one of the two disordered toluene molecules is represented [symmetry code: (iv) $-x, -1-y, 3-z$].

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

$C_{18}H_{14}N_4O_2$
M_r = 318.33
Monoclinic, $P2_1/c$
a = 12.346 (2) Å
b = 5.567 (1) Å
c = 22.578 (6) Å
β = 95.20 (1)°
V = 1545.4 (6) Å^3
Z = 4
D_x = 1.368 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 30 reflections
θ = 4.92–12.44°
μ = 0.093 mm^{-1}
T = 293 (2) K
Block, colourless
0.5 × 0.2 × 0.2 mm

Data collection

Bruker *P*4 diffractometer
$2\theta/\omega$ scans
3821 measured reflections
2726 independent reflections
1624 reflections with $I > 2\sigma(I)$
R_{int} = 0.078
θ_{max} = 24.99°
$h = -1 \rightarrow 14$
$k = -1 \rightarrow 6$
$l = -26 \rightarrow 26$
3 standard reflections
every 97 reflections
intensity decay: 5.38%

Table 1
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)

Table 2
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2*B*···O2	0.86	2.13	2.840 (3)	140
N2—H2*B*···N1	0.86	2.24	2.673 (4)	111
N3—H3*B*···N4	0.86	2.25	2.674 (3)	110
C8—H8*A*···O1	0.93	2.37	2.898 (4)	116
C11—H11*A*···O2^{i}	0.93	2.45	3.161 (3)	133

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

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.048P)^2 + 0.282P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.053$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.139$	$\Delta\rho_{max} = 0.16$ e Å^{-3}
$S = 1.031$	$\Delta\rho_{min} = -0.16$ e Å^{-3}
2726 reflections	
217 parameters	
H-atom parameters constrained	

Compound (II)

Crystal data

$C_{18}H_{20}N_4O_2{\cdot}0.5C_7H_8$	$Z = 2$
$M_r = 370.45$	$D_x = 1.217$ Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
$a = 9.899$ (2) Å	Cell parameters from 25 reflections
$b = 10.492$ (2) Å	$\theta = 2.38$–$15.62°$
$c = 10.795$ (2) Å	$\mu = 0.080$ mm^{-1}
$\alpha = 88.52$ (3)°	$T = 293$ (2) K
$\beta = 64.39$ (3)°	Block, colourless
$\gamma = 89.70$ (3)°	0.30 × 0.26 × 0.24 mm
$V = 1010.7$ (4) Å^3	

Data collection

Enraf–Nonius CAD-4 diffractometer	$\theta_{max} = 24.96°$
$2\theta/\omega$ scans	$h = 0 \rightarrow 11$
3764 measured reflections	$k = -12 \rightarrow 12$
3539 independent reflections	$l = -11 \rightarrow 12$
2552 reflections with $I > 2\sigma(I)$	3 standard reflections every 97 reflections
$R_{int} = 0.007$	intensity decay: 4.2%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0904P)^2 + 0.3004P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.049$	$(\Delta/\sigma)_{max} = 0.006$
$wR(F^2) = 0.173$	$\Delta\rho_{max} = 0.27$ e Å^{-3}
$S = 1.062$	$\Delta\rho_{min} = -0.16$ e Å^{-3}
3539 reflections	Extinction correction: *SHELXTL* (Sheldrick, 1997)
263 parameters	Extinction coefficient: 0.046 (4)
H-atom parameters constrained	

Table 3
Selected geometric parameters (Å, °) for (II).

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.

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

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