J Chem Crystallogr (2011) 41:801–805
DOI 10.1007/s10870-010-9981-6

ORIGINAL PAPER

Crystal Structure and Energy Optimization of Dichlorobis(ethylanthranilatonicotinamide)Zinc(II)

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Received: 8 June 2009 / Accepted: 31 December 2010 / Published online: 19 January 2011

Abstract The title compound, $C_{30}H_{28}Cl_2N_4O_6Zn$, dichlorobis(ethylanthranilatonicotinamide)zinc(II) crystallized in a triclinic space group, $P-1$, with cell parameters a = 7.787(3), b = 13.468(1), c = 15.735(1), $\alpha = 110.25(1)$, $\beta = 95.11(1)$, $\gamma = 99.32(1)$ and Z = 2, with the whole molecule being the asymmetric unit. In this compound, zinc is bound to two ethylanthranilatonicotinamide (EAN) ligands and two chloride ligands in a distorted tetrahedral configuration. The nitrogen of the nicotinamide ring participates in bonding with zinc through its lone pair while the anthranilate nitrogen remains free. In one of the two EAN ligands, the anthranilate and nicotinamide groups are nearly co-planar while in the other, the angle between the two is ~35.5°. The complex shows three hydrogen bonds, two being C–H···O bonds and the other being C–H···Cl bond. The amidic N–H groups do not participate in hydrogen bond formation as they are buried in the core structure and are not accessible for other groups for association. Both the C–H···O bonds occur from C–H bonds present on the twisted EAN moiety.

Keywords Ethylanthranilatonicotinamide · Zinc complex · Energy optimization · MOPAC · Crystal structure

The contributions by author Dr. Debojit Chakrabarty were done when he was affiliated with Unilever R&D Bangalore.

Electronic supplementary material The online version of this article (doi:10.1007/s10870-010-9981-6) contains supplementary material, which is available to authorized users.

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Introduction

Zinc is a relatively abundant element in biological systems and plays a vital role in various enzymatic reactions [1]. Nicotinamide has significant pharmacological importance like anti-aging benefits [2]. Derivatives of anthranilic acid have been used as sunscreens for a long time [3]. Complexes of zinc and niacinamide have been prepared to exploit the potential benefits of both niacinamide and zinc [4–6]. Complexes of zinc and anthranilic acid have been prepared as well [7]. The current paper describes the synthesis of an ethyl anthranilate derivative of nicotinic acid [8] and its consequent complexation with zinc chloride to form a bis-complex.

Experimental

All NMR spectra were recorded on a Bruker 400 MHz instrument. Mass spectra were recorded on a Bruker (Esquire 3000) Ion Trap Mass analyzer.

Synthesis

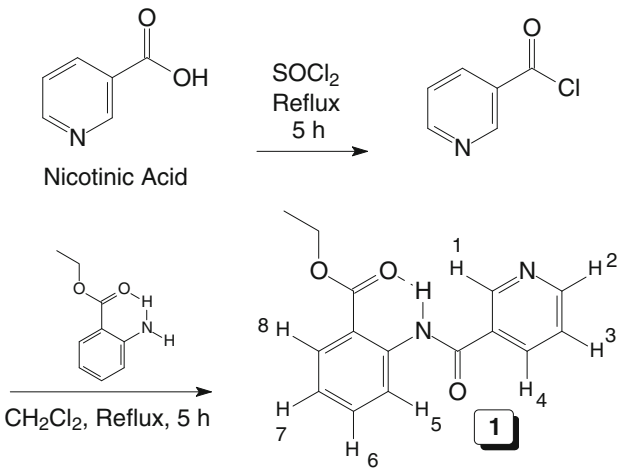
All chemicals were reagent grade (Sigma) and were used without further purification. Nicotinic acid was refluxed in

thionyl chloride for 5 h. The reaction mixture was rotor-evaporated to dryness in vacuum to obtain nicotinyl chloride in quantitative yield.

Nicotinyl chloride (2.1 g, 1.46 mmol) was treated with equimolar amounts of ethyl anthranilate (2.4 g) and two equivalents of triethylamine as the base and dichloromethane as the solvent under reflux conditions for 5 h. The product mixture was cooled to 25 °C and washed with dil. HCl followed with water and brine. The solvent was evaporated in vacuo and the residue chromatographed on silica gel using hexane and ethylacetate as the eluant system (refer Scheme 1). The product '**1**' obtained (3.2 g, 80% yield) was further characterized by ^{1}H-NMR $CDCl_3$ (δ 1.45 CH_2CH_3, 4.45 CH_2CH_3, 12.23, CONH, Ar 1Hs, 7.00 to 9.40 ppm), UV–Vis λ-max 278, and 322 nm and MS (m/z 270, M^+).

'**1**', niacinamide, and $ZnCl_2$ were mixed in a ratio of 1:1:0.5 in methanol and stirred overnight at 25 °C. The reaction mixture was concentrated to 15 mL volume and allowed to cool at 4 °C for 48 h. Compound '**2**' crystallized out (Fig. 1) and was characterized by X-ray crystallography. The ^{1}H NMR spectra of '**1**' & '**2**' are similar in appearance but for the aromatic region (refer Table 1). The signals for the protons H1, H2 and H3 are down shifted in '**2**' as compared to '**1**' and this is expected since complexation with zinc would decrease the electron density in the pyridine ring (refer to Table 1 for chemical shift values). The signals for the aromatic protons UV–Vis peak maxima for '**2**' (λmax: 276 and 316 nm) show blue shifts as compared to that of the free ligand '**1**'. The MS spectrum for '**2**'shows intense peaks for M-(HCl), (m/z 639); and M-2 (HCl), (m/z 603) fragments.

The crystals obtained were examined under an optical microscope and high quality crystals suitable for single-crystal diffraction were separated out. X-ray diffraction intensities were measured at room temperature (298 K) on



Scheme 1 Synthesis of Ethylanthranilatonicotinamide (EAN)

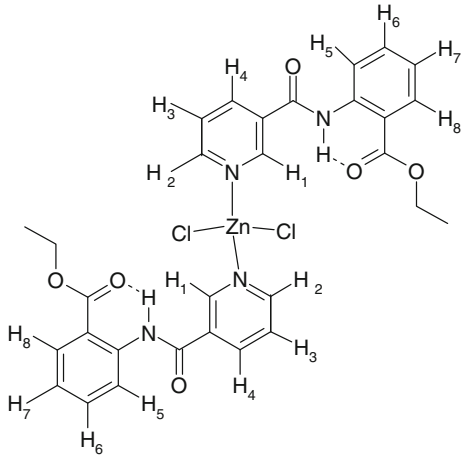


Fig. 1 Chemical structure of **2** showing hydrogen labels

a Enraf–Nonius Mach-3 diffractometer using a graphite monochromator for the Mo-Kα radiation (λ = 0.71071 Å). The crystal structure was solved by direct methods using the SHELXTL program [9] and refined by full matrix least squares on F^2 (CCDC 690286). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were fixed using HFIX and were refined isotropically. Hydrogen bond analysis was carried out using the PLATON routine [10]. Crystal structure data of the complex is given in Table 2. Energy calculation and energy minimization were carried out using PM6 routine on the title compound using MOPAC 2007 [11]. The geometric coordinates obtained from X-ray structure was used as the starting coordinates for energy minimization.

CCDC 690286 contains the supplementary crystallographic data for this complex. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Results and Discussion

The complex crystallizes in centrosymmetric triclinic system (lattice parameters, a = 7.787(3), b = 13.468(1), c = 15.735(1), α = 110.25(1), β = 95.11(1), γ = 99.32(1)) with two molecules per unit cell. The asymmetric unit comprises of the whole molecule (see Fig. 2.). During the synthesis, both EAN and nicotinamide were added in equimolar concentrations to form a co-complex with zinc. However, only EAN forms complex with zinc, possibly indicating stronger binding power of EAN over nicotinamide. Important structural parameters are given in the Table 2. Like most zinc complexes, this complex exhibits a

Table 1 NMR of aromatic protons in compounds **1** and **2**

Aromatic proton no.	Chemical shift (ppm) **'1'**	Chemical shift (ppm) **'2'**
H1	9.30	9.47
H2	8.89	9.15
H3	8.33	8.57
H4	8.79	8.79
H5	7.47	7.77
H6	7.62	7.62
H7	7.16	7.19
H8	8.11	8.08

Table 2 Crystal data for dichlorobis(ethylanthranilatonicotinamide)-zinc(II)

	Compound 2
Empirical formula	$C_{30}H_{28}Cl_2N_4O_6Zn$
Formula weight	676.860
T (K)	298
Wavelength (Å)	0.71073
Crystal system	Triclinic
Space group	$P-1$
Unit cell dimensions	
a (Å)	7.787(3)
b (Å)	13.468(1)
c (Å)	15.735(1)
α (°)	110.25(1)
β (°)	95.11(1)
γ (°)	99.32(1)
Z	2
V (Å^3)	1508.84(0.54)
ρ_{calc} (Mg/m^3)	1.4898
μ (mm^{-1})	1.041
F(000)	696
θ range for data collection (°)	1.40–24.97
hkl range	$0 \le h \le 9$
	$-15 \le k \le 15$
	$-18 \le k \le 18$
Reflections	
Collected	5299
Unique (R_{int})	5299
Observed ($I > 2\sigma$)	3378
Data/restraints/parameters	5299/0/398
R (F) ($I > 2\sigma$)	0.0477
wR (F^2) (all data)	0.1106
S	1.032
Max./min. $\Delta\rho$ (e/Å^3)	0.313/−0.307

tetrahedral geometry about the metal. The tetrahedron is distorted with bond angle Cl–Zn–Cl (124.8°) larger than the N–Zn–N (102.2°) bond. Other angles about the zinc centre are closer to the tetrahedral angles (105.5–108.3°). This is expected based on the sizes of the atoms bonded to zinc. As expected, the bonding to zinc is through the more basic pyridyl nitrogen instead of amidic nitrogen. The Zn–Cl (2.204 and 2.199 Å) and Zn–N (2.057 and 2.057 Å) bond lengths in the complex are close to the average values reported in CSD [12] viz., 2.184 (Zn–Cl, 1087 hits) and 2.112 Å (1706 hits, Zn–N, where N is a pyridine nitrogen) respectively. However, the Cl–Zn–Cl bond angles (124.79°) and N–Zn–N bond angles (102.19°) in the complex are much larger than the average values (∠Cl–Zn–Cl = 117.54°, 1087 hits; ∠N–Zn–N = 100.93°, in which both N were pyridine nitrogen, 1706 hits) reported in CSD [12]. These values are however closer to values reported in dichlorobis(nicotinamide)zinc(II) complex[4] (Zn–Cl = 2.221(1) and 2.209(1) Å; Zn–N = 2.058(3) and 2.057(4) Å; ∠N–Zn–N = 101.8° and ∠Cl–Zn–Cl = 121.81°). The two ethylanthranilatonicotinamide (EAN) ligands have different geometries. In one EAN ligand, the anthranilate and nicotinamide groups are nearly co-planar (The angle between the two groups is 5.18°, torsion angle ∠C18–C19–C21–N4 = −4.52°, ∠C20–C19–C21–N4 = 174.67°). In the other EAN ligand, the two groups are at an angle to each other. The angle between the two planes being 35.5° (Torsion angle ∠C3–C4–C6–N2 = −35.20°, ∠C5–C4–C6–N2 = 145.38°). The torsion angles between the phenylene and pyridyl rings of the two EAN moieties (∠C4–C6–N2–C7 = 176.88° and ∠C19–C21–N4–C22 = 77.71°) and those between the ethoxy group and pyridyl rings (∠C29–O6–C28–C27 = 178.64° and ∠C14–O3–C13–C12 = 177.49°) are quite similar while those of the ethoxy groups themselves (∠C13–O3–C14–C15 = 178.62° and ∠C28–O6–C29–C30 = −166.03°) are significantly different (Fig. 2).

The complex shows three favorable hydrogen bonds (see packing diagram, Fig. 3), two of them between C–H and O at ~2.65 Å (H14A···O5 = 2.66 Å, C14···O5 = 3.368 Å, ∠C14–H14A···O5 = 131°; H14A···O1 = 2.63 Å, C14···O1 = 3.292 Å, ∠C14–H14A···O1 = 125°) and the third between aromatic C–H hydrogen and Cl ion at 2.81 Å (H(2)···Cl(2) = 2.81 Å, C(2)···Cl(2) = 3.646 Å, ∠C(2)–H(2) ···Cl(2) = 150°). In one of the C–H···O hydrogen bonds, amidic oxygen acts as the acceptor while in the other, the C=O of the carboxylic group acts as the acceptor. Both hydrogen bonds are formed between the C–H in the twisted EAN group with the carboxylic oxygen of the planar EAN group. The complex however does not form N–H···O hydrogen bonds even though two amidic N–H groups are present in the complex. This is understandable as these groups are buried in the core of the structure and are not accessible for other groups for association.

Energy minimization of the complex [11] shows some changes in the bond angles and torsion angles from that observed experimentally (Supplementary Information 1). Among the bond angles, major differences between X-ray

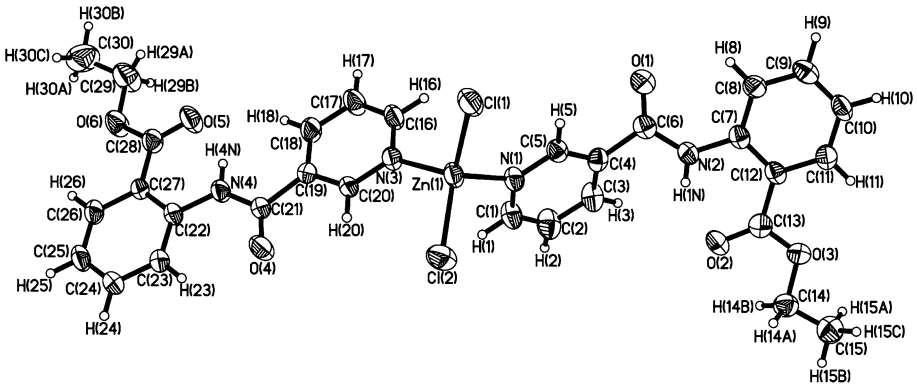


Fig. 2 ORTEP diagram of the title compound with the atom numbering scheme. Displacement ellipsoids are drawn at 50% probability level

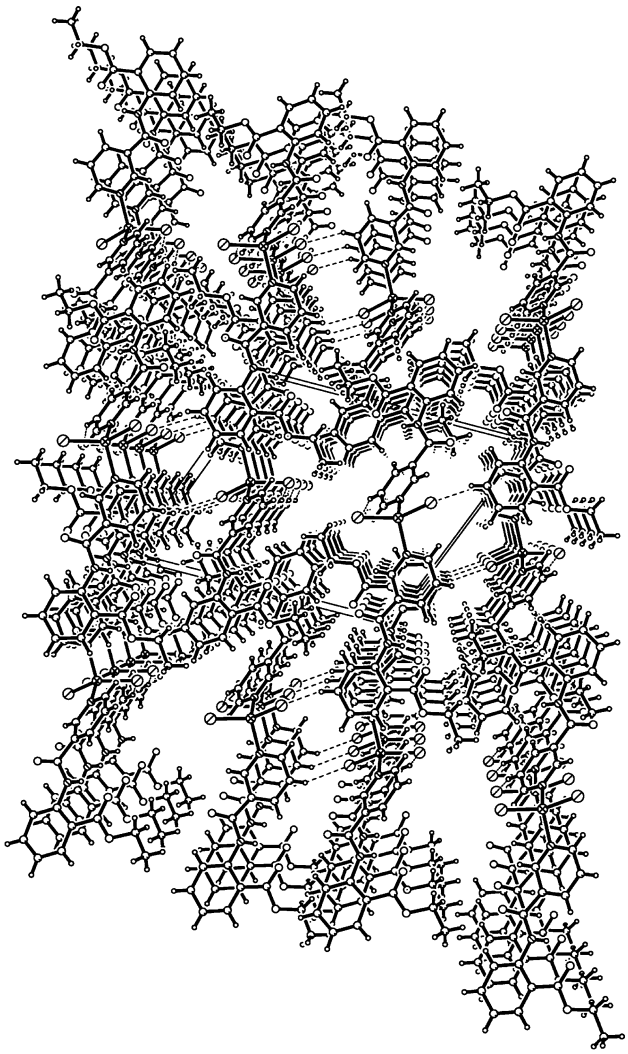


Fig. 3 Packing diagram of the title compound along b-axis showing hydrogen bonding and hydrophobic channels

structure and calculated structures occur around the zinc atom and near the ethyl group of ethyl anthranilate. The differences in torsion angles between the X-ray structure and calculated structure are however much higher (even as high as 70°). Major changes in torsion angles also occur around the zinc atom as well as near the ethyl group in ethyl anthranilate. In addition to the above, it is found that in the calculated structure both the EAN groups are twisted, the angle between the nicotinamide and ethylanthranilate in the two EAN groups being 22.5° and 29.2° respectively. In comparison, in the X-ray crystal structure, only one of the two EAN ligands is twisted while the other is nearly planar.

Heats of formation of the optimized geometry as well as the X-ray geometry were calculated [11] and were found to be −1051.84 and −675.61 kJ/mole respectively. Though the molecular configuration in the X-ray geometry is energetically higher than optimized geometry, probably packing in solid state, hydrogen bonds between aromatic hydrogen and Cl and those between C–H group of the twisted EAN group and oxygen of the carboxylic group in the planar EAN moiety are responsible for stabilization of this configuration in the solid state.

Conclusions

Zinc complex **2** was synthesized in the presence of equal concentrations of nicotinamide and EAN ligands. However, only EAN ligand binds to metal ions, possibly indicating superior binding ability of the EAN ligand. The two EAN ligands bound to zinc ion in the complex are significantly different; one is nearly co-planar while the other is twisted. The complex shows interesting hydrogen bonding patterns. The C–H hydrogens are involved in the hydrogen bonding while the N–H remains free. Energy minimization of the complex leads to a molecule in which both the EAN groups were twisted. Though the energy of the X-ray geometry is energetically unfavorable by 376 kJ/mole, it appears that packing in solid state and formation of hydrogen bonds are responsible for the stability of this configuration in the solid state.

Acknowledgment The authors thank the reviewer for his valuable comments and suggestions.

References

1. Raj SSS, Fun HK, Zhao PS, Jian FF, Lu LD, Yang XJ, Wang X (2000) Acta Crystallogr C 56:742
2. Brühlmann U, Hayon E (1974) J Am Chem Soc 96:6169
3. Giese AC, Christensen E, Jeppon J (1950) J Am Pharm Assoc 39:30
4. Ide S, Atac A, Yurdakul S (2002) J Mol Struct 605:103
5. Chakrabarty D, Nagase H, Kamijo M, Endo T, Ueda H (2005) Anal Sci 21:x167
6. Sahin E, Ide S, Atac A, Yurdakul S (2002) J Mol Struct 616:253
7. Boudreau SM, Boudreau RA, Haendler HM (1983) J Solid State Chem 49:379
8. Osselaere JP (1974) Eur J Med Chem 9:305
9. Sheldrick GM (2008) Acta Crystallogr A 64:112
10. Spek AL (2003) J Appl Crystallogr 36:7
11. Stewart JJP (2007) J Mol Mod 13:1173
12. Allen FR (2002) Acta Crystallogr B 58:380