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Synthesis, Crystal Structure and Antibacterial Properties of N-(2-Hydroxy-1-naphthalidene)-4-aminoantipyrine

FENG GUO†, CAI-FENG BI*, YU-HUA FAN, YAN XIAO,
XUE-TAO HE and JIA-KUN XU
Key Labaoratory of Marine Chemistry, Theory and Technology,
Ministry of Education, Ocean University of China, Qingdao-266 003, P.R. China
E-mail: bcfeng@ouc.edu.cn, guofeng1510@yeah.net

The structral features of Schiff base (N-(2-hydroxy-1-naphthalidene)-4-aminoantipyrine) formed by the interaction of 4-aminoantipyrine and 2-hydroxy-1-naphthaldehyde with the formula $C_{22}H_{19}N_3O_2$ has been determined by X-ray diffraction method and elemental analysis. The crystal belongs to orthorhomic system with space group P2(1)2(1) 2(1), a = 8.8170(18) Å, b = 14.605(3) Å, c = 14.734(3) Å, V = 1897.3(7) $Å^{-3}$, Z = 4, R_1 = 0.0414, wR_2 = 0.1063, F(000) = 752, respectively for 2306 observed reflections. In addition, the compound has been tested for its antibacterial active. The compound showed antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and had no antibacterial activity against *Bacillus subtilis*.

Key Words: Schiff base, Crystal structure, Antibacterial activity.

INTRODUCTION

The Schiff bases possess anticancer, antibacterial properties[1-3] and have important effect to simulate enzyme[4-6], so it is important part for coordination chemistry[7]. 4-Aminoantipyrine is good effective defervescent. It's derivatives have unique pharmacology property, so it attract much attention. People presumed its derivatives have potence to coordinate with metal which can generate its biological activity[8-10].

EXPERIMENTAL

All chemicals were analytical reagent grade and used without further purification. 2-Hydroxy-1-naphthaldehyde (0.01 mol) were added with stirring to anhydrous ethanol (30 mL) to make a clear solution. It was slowly added into the anhydrous ethanol solution of 15 mL of 4-aminoantipyrine (0.01 mol) at 50ºC and mixture was stirred at 50ºC for 4 h. A mass of

†College of Medicine and Pharmacy, Theory and Technology, Ministry of Education, Ocean University of China, Qingdao-266 003, P.R.China

golden grain was separated out. The product was collected by filtration and washed several times with anhydrous ethanol and dried under vacuum. Yellow single crystal suitable for X-ray diffraction analysis were obtained by slow evaporation at room temperature from anhydrous ethanol solution after 7 d. % Anal. Calcd. for $C_{22}H_{19}N_3O_2$, C: 73.93; H: 5.36; N: 11.76. Found: C: 74.42; H: 5.11; N: 11.72.

Crystal structure determinations and refinements

The selected crystal of dimensions 0.30 × 0.25 × 0.20 mm was mounted on a Brucker Smart CCD X-ray single-crystal diffractometer. Reflection data were at 293(2) K using graphite monochromated MoKα radiation (λ = 0.71073 Å), ω-2θ scan mode. A total of 2603 independent reflections were collected in the range of $1.49^o \leq \theta \leq 26.97^o$, of which 2603 reflections with $I>2\sigma(I)$ were considered to be observed and used in the subsequent refinement. Intensities were corrected for Lorentz and polarization effects and empirical absorption and the data reduction using SADABS program[11].

The structure was solved by direct methods using SHELXS-97[12]. Positional and thermal parameters were refined by full-matrix least-squares method using the SHELXTL software package[13]. The final least-square cycle of refinement gave R = 0.0414, wR = 0.1063, the weighting scheme $w = 1/[[\sigma^2(F_o^2) + (0.0725P)^2 + 0.0901P]$ where $P = (F_o^2 + 2F_c^2)/3$.

RESULTS AND DISCUSSION

The compound crystallizes in the orthorhombic system, space group P2(1)2(1)2(1), with cell dimensions of a = 8.8170(18) Å, b = 14.605(3) Å, c = 14.734(3) Å,V = 1897.3(7) $Å^{-3}$ and Z = 4. Crystal data and structure refinement for the compound are shown in Table-1. Selected bond lengths and bond angles of the Schiff base are listed in Tables 2 and 3, respectively. Figs. 1 and 2 show the molecular structure of the compound and view of the crystal packing for the Schiff base.

From Fig. 1 we can conclude that the compound form C-N bond, the N(3)-C(12) instance is 1.291 Å, which is shorter than N(3)-C(11) instance (1.400 Å) and other C-N instance in the same molecule that indicated N(3)-C(12) formed double bond, the compound exists in the form of imine.

The bond angle showed in Table-3 of O(1)-C(14)-C(13), C(14)-C(13)-C(12), C(13)-C(12)-N(3) are 122.7°, 119.6° and 121.1°, respectively. The difference of angle is small and approach to 120° of inner angle of hexagon which is due to occur hydrogen bond O(1)-H and N(3)(bond length 1.831Å, bond angle 147.79° and symmetry operation (1/2-x, 1-y, 1/2+z). The torsion angle of C(18)-C(13)-C(12)-N(3), C(14)-C(13)-C(12)-N(3) are 175.93° and 4.72°, respectively. All of these indicate that 2-hydroxy-1-naphthaldehyde and C(12)-N(3) had almost co-planar (The planar equation is -3.310x + 13.7086y - 0.4185z = 6.0715, the maximal and mean deviation are 0.069 Å and 0.028Å).

TABLE-1
CRYSTAL DATA AND STRUCTURE REFINEMENT
PARAMETERS FOR THE SCHIFF BASE

Empirical formula	$C_{22}H_{19}N_3O_2$
Formula weight	357.40
Temperature (K)	293 ± 2
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
space group	P2(1)2(1)2(1)
a (Å)	8.8170(18)
b (Å)	14.605(3)
c(Å)	14.734(3)
V (Å^3)	1897.3(7)
Calculated density (mg m^{-3})	1.251
Z	4
Absorption coefficient (mm^{-1})	0.082
Crystal size (mm)	0.30 × 0.25 × 0.20
θ Range (°)	1.49 - 26.97
h/k/l	0,10/0,17/0,17
Reflections collected	2603
Indpendent reflections	2603
Final *R* indices [I > 2σ(I)]	R_1 = 0.0414, wR_2 = 0.1063
Largest diff. peak and hole (e Å^{-3})	0.157 and -0.191

TABLE-2
SELECTED BOND LENGTHS (Å)

Bond	Distance	Bond	Distance
O(1)-C(14)	1.345(4)	C(8)-C(9)	1.492(4)
O(2)-C(10)	1.241(3)	C(9)-C(11)	1.377(3)
N(1)-C(9)	1.363(4)	C(10)-C(11)	1.437(4)
N(1)-N(2)	1.398(3)	C(12)-C(13)	1.473(4)
N(1)-C(7)	1.457(4)	C(13)-C(14)	1.399(4)
N(2)-C(10)	1.404(3)	C(13)-C(18)	1.437(4)
N(2)-C(6)	1.437(3)	C(14)-C(15)	1.442(4)
N(3)-C(12)	1.291(3)	C(15)-C(16)	1.341(5)
N(3)-C(11)	1.400(4)	C(16)-C(17)	1.413(5)
C(1)-C(2)	1.378(5)	C(17)-C(22)	1.404(5)
C(1)-C(6)	1.383(4)	C(17)-C(18)	1.443(4)
C(2)-C(3)	1.378(5)	C(18)-C(19)	1.421(4)
C(3)-C(4)	1.368(5)	C(19)-C(20)	1.370(4)
C(4)-C(5)	1.389(4)	C(20)-C(21)	1.420(6)
C(5)-C(6)	1.382(4)	C(21)-C(22)	1.357(5)

TABLE-3
SELECTED BOND ANGLES (°)

Angle	(°)	Angle	(°)
C(9)-N(1)-N(2)	107.76(19)	C(9)-C(11)-N(3)	122.6(2)
C(9)-N(1)-C(7)	128.6(2)	C(9)-C(11)-C(10)	108.4(2)
N(2)-N(1)-C(7)	119.5(2)	N(3)-C(11)-C(10)	128.7(2)
N(1)-N(2)-C(10)	109.4(2)	N(3)-C(12)-C(13)	121.1(3)
N(1)-N(2)-C(6)	121.1(2)	C(14)-C(13)-C(18)	119.1(2)
C(10)-N(2)-C(6)	127.0(2)	C(14)-C(13)-C(12)	119.6(3)
C(12)-N(3)-C(11)	122.2(2)	C(18)-C(13)-C(12)	121.3(2)
C(2)-C(1)-C(6)	118.9(3)	O(1)-C(14)-C(13)	122.7(3)
C(1)-C(2)-C(3)	121.2(3)	O(1)-C(14)-C(15)	117.1(3)
C(4)-C(3)-C(2)	119.4(3)	C(13)-C(14)-C(15)	120.2(3)
C(3)-C(4)-C(5)	120.5(3)	C(16)-C(15)-C(14)	120.1(3)
C(6)-C(5)-C(4)	119.4(3)	C(15)-C(16)-C(17)	122.8(3)
C(5)-C(6)-C(1)	120.5(3)	C(22)-C(17)-C(16)	122.4(3)
C(5)-C(6)-N(2)	118.8(2)	C(22)-C(17)-C(18)	119.3(3)
C(1)-C(6)-N(2)	120.7(3)	C(16)-C(17)-C(18)	118.2(3)
N(1)-C(9)-C(11)	109.4(2)	C(19)-C(18)-C(13)	123.3(2)
N(1)-C(9)-C(8)	121.8(2)	C(19)-C(18)-C(17)	117.1(3)
C(11)-C(9)-C(8)	128.7(3)	C(13)-C(18)-C(17)	119.5(3)
O(2)-C(10)-N(2)	123.2(2)	C(20)-C(19)-C(18)	121.8(3)
O(2)-C(10)-C(11)	132.0(3)	C(19)-C(20)-C(21)	120.0(4)
N(2)-C(10)-C(11)	104.7(2)	C(22)-C(21)-C(20)	119.8(3)
		C(21)-C(22)-C(17)	121.9(3)

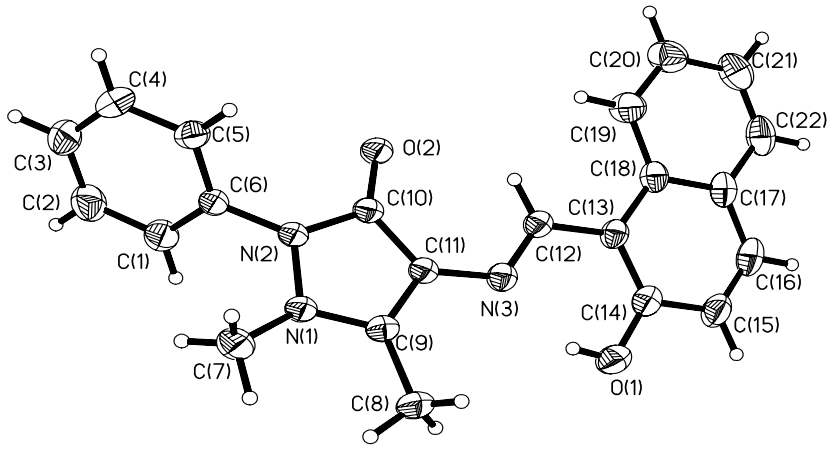

Fig. 1. Molecular structure of the compound with the atomic numbering scheme

The bond length of O(1)-C(14) is 1.345Å, which is shorter than normal phenol (1.361 Å). The bond length of C(12)-C(13), N(3)-C(12), C(13)-C(18) and C(13)-C(14) are longer than double bond and shorter than single bond. All of these are due to formation of the large delocalized π bond.

From Fig. 2, it is concluded that the Schiff base compound interact through hydrogen bond (bond length 2.579 Å) and weak π-π stacking two-dimension layered structure.

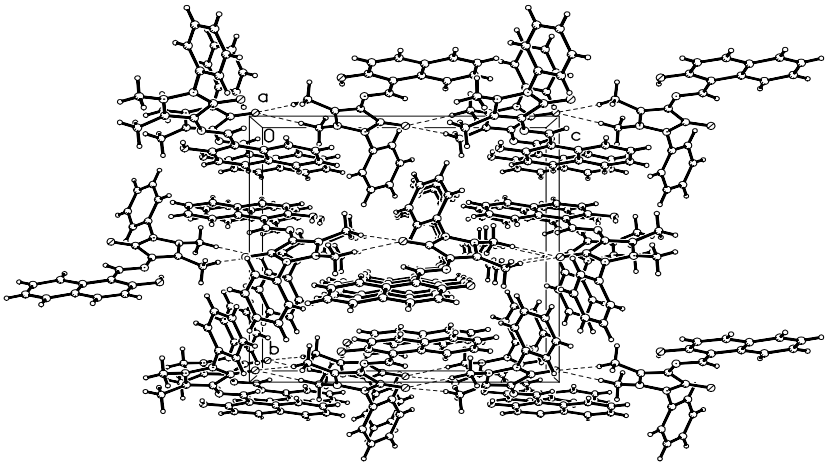

Fig. 2. A view of the crystal packing of $C_{22}H_{19}N_3O_2$

Antibacterial activity

All antibacterial properties were investigated at National Institute for the Control of Pharmaceutical and Biological Products.

Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa and *Bacillus subtilis* were cultured by inoculating in beef broth (which were sterilized by autoclaving at 121ºC for 20 min) and incubating at 37ºC for 24 h. Agar culture medium was prepared, by dissolving peptone, beef broth, agar and sodium chloride in distilled water and adjusted pH = 7.2-7.4, which were sterilized by autoclaving at 121ºC for 20 min. Cultured *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Bacillus subtilis* were added to the warm nutrient agar, which were poured into plate that were allowed to set in the refrigerator for at least 6 h.

The agar plate which were incubated at 37ºC overnight allowing the bacteria to grow where possible. Digital calipers were used to measure the diameter of the area of inhibition around the wells[14]. The compound The compound was divided into 10, 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}, 10^{-6}, 10^{-7} mg/mL and used to full soak scrip.

From Table-4, it is concluded that the compound showed moderately sensitive antibacterial activity against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and had no antibacterial activity against *Bacillus subtilis*. The effects on *Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeruginosa* of compound are shown in Figs. 3-5, respectively. The antibacterial active ring of agar culture medium is

transparent ring which doesn't grow bacterium. Figs. 3-5 showed that when the concentration of compound increase, the average diameter of the compound antibacterial active ring enlarged at certain range[15].

TABLE-4
AVERAGE DIAMETER OF THE COMPOUND ANTIBACTERIAL ACTIVE RING (mm)

Compound Concentration (mg/mL)	*Escherichia coli*	*Staphylococcus aureus*	*Pseudomonas aeruginosa*	*Bacillus subtilis*
10	15.1 ± 0.3	15.1 ± 0.2	12.1 ± 0.2	10.1 ± 0.2
10^{-1}	14.8 ± 0.2	11.2 ± 0.4	11.8 ± 0.1	–
10^{-2}	12.1 ± 0.5	10.2 ± 0.3	9.1 ± 0.5	–
10^{-3}	–	–	–	–

R (antibacterial active ring) < 10 mm no antibacterial effect, R > 16 mm highly sensitive, 11 mm < R < 16 mm moderately sensitive.

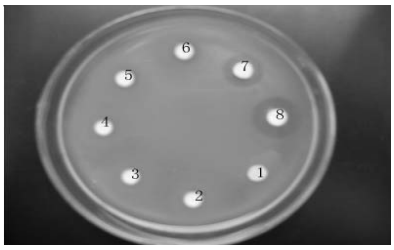

Fig. 3. Effect on *Escherichia coli* of compound

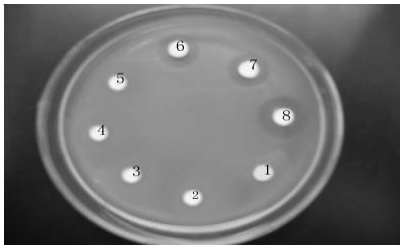

Fig. 4. Effect on *Staphylococcus aureus* of compound

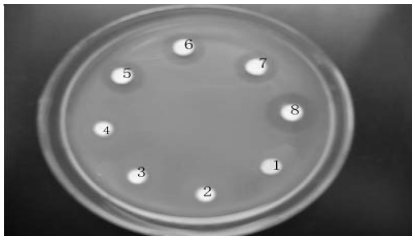

Fig. 5. Effect on *Pseudomonas aeruginosa* of compound

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