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Synthesis and crystal structure of a phenazine N-oxide

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Abstract

The preparation and crystal structure of 8-chloro-1H-pyrrolo[2,3-b]phenazine 5-oxide (**1**) are described. Compound **1** formed dark purple crystals from deeply colored solution in methanol. Crystal plates were in the triclinic system, P-1 space group with unit cell parameters $a = 6.9514(8)$, $b = 9.1568(10)$, $c = 10.2067(11)$, $\alpha = 84.509(2)^\circ$, $\beta = 82.936(2)^\circ$, $\gamma = 72.357(2)^\circ$ and a cell volume of $613.25(12) \text{ \AA}^3$. The title compound which contains the first example of the extensively conjugated pyrrolo-phenazine N-oxide system exhibits strong light absorption in the green to cyan wavelength range which disappears upon protonation.

Keywords

Phenazine; Wohl-Aue reaction

Introduction

An attempted nucleophilic substitution of an aryl chloride in the precursor **2** under basic conditions led to the formation of the title compound **1** instead (Scheme 1). This condensation is an intramolecular variant of the Wohl-Aue reaction in which an aromatic nitro compound is condensed with an aniline in the presence of base to furnish a phenazine [1]. Investigations of the mechanism of the Wohl-Aue reaction have shown that the N-oxide, which is present in compound **1**, is an intermediate in the formation of phenazines which may become the main product depending on the reaction conditions [2]. Since formation of the phenazine from the N-oxide in basic media may be a thermal deoxygenation process, the title compound **1** likely was isolated due to the mild conditions applied in our synthetic procedure. The Boc protection group at the indole was concomitantly removed under the alkaline reaction conditions. The compound **1** is the first representative of the linear pyrrolo-phenazine N-oxide heterocyclic system whose extensive conjugation gives rise to strong light absorption in the range of green to cyan light.

Experimental

A solution of 2-nitrodiphenylamine (**2**) (977 mg, 2.5 mmol) in dry DMF (120 mL) was stirred at 0 °C under argon atmosphere, while a mixture of 3-dimethylamino-1-propanol (292 μL , 2.5 mmol) and NaOtBu (482 mg, 5.0 mmol) in dry DMF (10 mL) was added dropwise via syringe. The reaction was warmed up to rt and stirred for 20 hrs. The solvent was removed under vacuum and the resulting residue was extracted using DI H₂O (150 mL) and dichloromethane ($2 \times 150 \text{ mL}$). The combined organic layers were washed with brine (100 mL) and dried over Na₂SO₄. After evaporating the solvent, phenazine oxide **1** was

purified by column chromatography (10 % MeOH in DCM) and eventually isolated as dark purple crystals. **1**: ^1H NMR (400 MHz, CD_3OD) δ 8.80 (s, 1H), 8.60 (d, J = 9 Hz, 1H), 8.09 (m, 2H), 7.80 (d, J = 3 Hz, 1H), 7.67 (dd, J = 9 Hz, J = 2 Hz, 1H), 6.78 (dd, J = 3 Hz, J = 1 Hz, 1H); MS ($\text{M}+\text{H}$) calculated 271.0, found 271.0

X-ray Crystallography

X-ray diffraction data of the title compound were collected on a Bruker Kappa diffractometer equipped with an APEX CCD II area detector using graphite-monochromated Mo K α radiation (λ = 0.71073 Å radiation). Dark purple plate (0.2 $\times$ 0.3 $\times$ 0.5 mm) was mounted on a cryoloop with paratone oil. Data were collected in a nitrogen gas stream at 173(2) K using ϕ and ω scans. The data were integrated using the Bruker SAINT [4] software and scaled using the SADABS [5] program. Solution by direct methods (SHELXS) [6] produced 1024 complete phasing models consistent with the unique proposed structure which was refined by least square methods on F^2 using the SHELXL-97 [6] program package. The refinement was continued until the maximum shift/e.s.d was 0.000. The final difference map was featureless with maximum and minimum electron densities at 0.373 and $-0.232 \text{ e}\text{\AA}^{-3}$. The crystal data, intensity collection conditions and refinement parameters are presented in Table 1. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares. Selected bond lengths and bond angles are given in Table 2. Hydrogen atoms H7, H10 and H11 were allowed to refine freely. All other H atoms were located geometrically, with C–H = 0.95 Å and treated using a riding model, with isotropic U set to 1.2 times the isotropic equivalent of that of the attached parent atom.

UV Spectroscopy

UV studies have been performed on a UV-2401PC spectrofluorometer (Shimadzu, Columbia, MD) at 23°C.

Results and Discussion

Crystal Structure

Compound **1** crystallized in the triclinic P-1 space group with one molecule of water in the asymmetric unit. An ORTEP drawing of the asymmetric unit with atom numbering scheme is shown in Fig. 1. The molecule of compound **1** is essentially planar with the mean deviation from the plane for all non-hydrogen atoms of 0.0168(3) Å. The largest deviation from the plane was observed for O1 at 0.0515(3) Å. Surprisingly, the Cambridge Crystallographic Data Centre and only one [3] was solved using data obtained at 173K. This limits our abilities to compare the structural features of our compound to similar structures obtained previously. The N(1)–O(1) bond in our structure (1.295(3) Å) is longer than the one determined earlier for the 1-*t*-butyl-9-methylphenazine-5-oxide in which this bond measures 1.285 Å (s. u. unknown). All bonds in our structure in the O(1)–N(1)–C(8)–C(7)–N(2)–C(5) system within the six-membered heterocyclic ring are longer than the corresponding bonds for the 1-*t*-butyl-9-methylphenazine-5-oxide structure. Hydrogen atoms H7, H10 and H11 were easily located from the electron density map. All three atoms of the water molecule participate in a formation of a hydrogen bond network (Table 3) in **1**. The oxygen atom forms a hydrogen bond with the H(7) atom with the distance of H(7) $\cdots$ O(2), water hydrogen atoms also form bonds with H(10) $\cdots$ O(1) and H(11) $\cdots$ N(2), respectively. In the crystal lattice molecules are arranged in dimeric units with a face-to-back orientation within dimers. These dimers exhibit a strong π – π interaction with the interplanar distance of 3.431 Å and an off-center angle of 20.7°. These dimeric units are stapled by neighboring water molecules which engage in a network of hydrogen bonds. The dimeric chains propagate along the $[-1\ 1\ 0]$ direction and are stacked along the *a*-axis with the interplanar distance of 3.374 Å. Molecules from adjacent dimeric units also exhibit π – π interaction but their centers

of mass are more shifted with respect to each other. These π – π and hydrogen bonding interactions lead to the formation of the pattern shown in Fig. 2.

Photophysical Properties

Compound **1** contains an extensive conjugated heterocyclic system and exhibits a strong broad light absorption band in various organic solvents. Its peak position varies from 528nm in acetonitrile to 541nm in methanol. The extinction coefficient of this absorption in common organic solvents is around 1000 L/(mole•cm). Upon treatment of the solution of **1** in methanol with 0.1M solution of hydrochloric acid this band decreased its intensity and broadened towards the lower energy region. At the same time a narrow sharp absorption band appeared at 420nm. We attributed this effect to the protonation of compound **1** at N(2). A similar effect was observed in chloroform under ultrasound treatment which leads to acid generation by sonodegradation of the solvent.

Acknowledgments

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Figure 1.
ORTEP plot of compound **1**. Thermal ellipsoids are shown at 50% probability.

Figure 2. Intermolecular hydrogen bonds (**1**) are shown as dashed lines. The hydrogen atoms involved in the hydrogen-bonding network are shown, while the others are omitted for clarity.

Scheme 1.

Formation of the 8-chloro-1H-pyrrolo[2,3-b]phenazine 5-oxide.

Table 1Crystal data and structure refinement for compound **1**.

Empirical formula	C14 H10 Cl N3 O2
Formula weight	287.70
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	$a = 6.9514(8) \text{ Å}$ $b = 9.1568(10) \text{ Å}$ $c = 10.2067(11) \text{ Å}$ $\alpha = 84.509(2)^\circ$ $\beta = 82.936(2)^\circ$ $\gamma = 72.357(2)^\circ$
Volume	$613.25(12) \text{ Å}^3$
Z	2
Density (calculated)	1.558 Mg/m^3
Absorption coefficient	0.316 mm^{-1}
F(000)	296
Crystal size	$0.50 \times 0.30 \times 0.20 \text{ mm}^3$
Theta range for data collection	2.01 to 25.35°
Index ranges	$-8 \leq h \leq 8$, $-11 \leq k \leq 11$, $-12 \leq l \leq 12$
Reflections collected	8261
Independent reflections	2232 [R(int) = 0.0313]
Completeness to theta = 25.35°	99.5 %
Absorption correction	None
Max. and min. transmission	0.9395 and 0.8580
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2232/0/193
Goodness-of-fit on F^2	1.092
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0451$, $wR2 = 0.1131$
R indices (all data)	$R1 = 0.0543$, $wR2 = 0.1170$
Largest diff. peak and hole	0.373 and -0.232 e Å^{-3}

Table 2Selected bond lengths [Å] and angles [°] for **1**.

Cl(1)-C(1)	1.742(3)	N(1)-C(4)-C(3)	120.0(2)
O(1)-N(1)	1.295(3)	N(1)-C(4)-C(5)	118.7(2)
N(1)-C(4)	1.365(4)	C(3)-C(4)-C(5)	121.3(3)
N(1)-C(8)	1.383(4)	C(1)-C(6)-C(5)	119.7(3)
N(2)-C(5)	1.344(4)	C(14)-C(13)-C(10)	106.9(3)
N(2)-C(7)	1.354(4)	C(10)-C(9)-C(8)	118.1(3)
N(3)-C(11)	1.374(4)	N(2)-C(7)-C(12)	118.9(2)
N(3)-C(14)	1.377(4)	N(2)-C(7)-C(8)	122.7(3)
N(3)-H(7)	0.90(4)	C(12)-C(7)-C(8)	118.5(2)
C(4)-C(3)	1.421(4)	C(12)-C(11)-N(3)	130.1(3)
C(4)-C(5)	1.424(4)	C(12)-C(11)-C(10)	122.9(3)
C(6)-C(1)	1.359(4)	N(3)-C(11)-C(10)	107.1(2)
C(6)-C(5)	1.426(4)	N(2)-C(5)-C(4)	123.4(3)
C(13)-C(14)	1.354(4)	N(2)-C(5)-C(6)	119.2(2)
C(13)-C(10)	1.434(4)	C(4)-C(5)-C(6)	117.5(2)
C(9)-C(10)	1.377(4)	N(1)-C(8)-C(9)	119.4(2)
C(9)-C(8)	1.394(4)	N(1)-C(8)-C(7)	117.8(2)
C(7)-C(12)	1.416(4)	C(9)-C(8)-C(7)	122.8(3)
C(7)-C(8)	1.442(4)	C(11)-C(12)-C(7)	118.2(3)
C(11)-C(12)	1.369(4)	C(2)-C(3)-C(4)	119.5(3)
C(11)-C(10)	1.448(4)	C(3)-C(2)-C(1)	119.7(3)
C(3)-C(2)	1.354(4)	C(6)-C(1)-C(2)	122.3(3)
C(2)-C(1)	1.421(4)	C(6)-C(1)-Cl(1)	120.2(2)
		C(2)-C(1)-Cl(1)	117.5(2)
O(1)-N(1)-C(4)	120.1(2)	C(9)-C(10)-C(13)	134.1(3)
O(1)-N(1)-C(8)	119.8(2)	C(9)-C(10)-C(11)	119.6(3)
C(4)-N(1)-C(8)	120.2(2)	C(13)-C(10)-C(11)	106.3(2)
C(5)-N(2)-C(7)	117.2(2)	C(13)-C(14)-N(3)	111.2(3)
C(11)-N(3)-C(14)	108.6(2)		

Table 3Hydrogen bonds for **1** [Å and °].

D-H...A	d(D-H)	d(H····A)	d(D····A)	<(DHA)
N(3)-H(7)...O(2)#1	0.90(4)	1.90(4)	2.792(3)	169(3)
O(2)-H(10)...O(1)#2	0.81(4)	2.00(4)	2.805(3)	173(4)
O(2)-H(11)...N(2)#3	0.82(5)	2.11(5)	2.877(3)	157(5)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y,-z+1

#2 -x,-y+1,-z+1

#3 x,y+1,z