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Synthesis and Crystal Structure of 4-Dichloroacetyl-3-phenyl-3,4-dihyro-2*H*-1,4-benzoxazine

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A new compound 4-dichloroacetyl-3-phenyl-3,4-dihyro-2*H*-1,4-benzoxazine with m.f. $C_{16}H_{13}NO_2Cl_2$ was synthesized and characterized. The crystal structure of the compound has been determined by single-crystal X-ray diffraction. The crystal is of monoclinic, space group $P2_1/c$ with a = 15.105(3), b = 6.2685(13), c = 16.084(3) Å, α = 90°, β = 103.79(3)°, γ = 90°, V = 1479.1(5)Å^3, Z = 4, F(000) = 664, D_c = 1.447 g/cm^3, μ = 0.442 mm^{-1}, the final R_1 = 0.0507 and wR_2 = 0.1435 for 2417 observed reflections with I > 2σ(I). A total of 13533 reflections were collected, of which 3362 were independent (R_{int} = 0.0307). Benzoxazine ring and the benzene plane were almost perpendicular with the dihedral angle of 91.7º with each other.

Keywords: Benzoxazine, Synthesis, X-ray crystallography.

INTRODUCTION

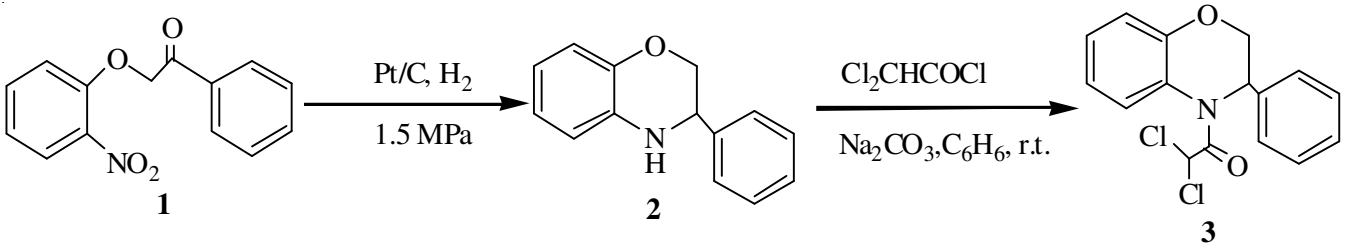
Benzoxazines are promising agents as a starting material for the synthesis of large structures that have properties such as potassium channel activator or antibacterial agents[1,2]. They were also been employed as the synthon of chiral compounds, pharmaceutical intermediates and polymer[3-5]. *N*-Dichloroacetyl benzoxazine is a significant safener for chlorinated amide herbicides and thiocarbamate herbicides. These aspects prompted us to synthesis, characteristics and biological activity of novel *N*-dichloroacetyl benzoxazine derivatives with better safety and efficacy, we introduced different groups substitution on the oxazine[6,7]. As part of our search for bioactive compounds, here we report the synthesis and crystal structure of 4-dichloroacetyl-3-phenyl-3,4-dihyro-2*H*-1,4-benzoxazine.

EXPERIMENTAL

The melting point was measured on a Beijing Taike point apparatus (X-4) and uncorrected. The IR of KBr discs were recorded on FTIR-8400S spectrometer. The ^{1}H NMR and ^{13}C NMR spectrum was recorded on a Bruker AV-300 spectrometer in DMSO-d_6, internal standard TMS. The mass spectrum was recorded on a Xevo TQ spectrometer. The elemental analysis was performed on FLASH EA1112 elemental analyzer. All the reagents were analytical reagent grade.

Synthesis and characterization: 4-Dichloroacetyl-3-phenyl-3,4-dihyro-2*H*-1,4-benzoxazine (**3**) was prepared following **Scheme-I**.

Preparation of compound 2: Pt/C (2g) was added to a solution of 2-(*o*-nitrophenoxy)-phenylethanone **(1)** (0.05 mol, 12.9 g) in toluene (200 mL) and isopropanol (100 mL). The reaction mixture was stirred under H_2 at 60 °C at 1.5 Mpa for 10 h. Then the mixture was filtered. The toluene was removed under vacuum. The 3-phenyl-3,4-dihyro-2*H*-1,4-benzoxazine **(2)** was obtained as yellow oil with the yield of 93.3 %. Anal. calcd. for $C_{14}H_{13}NO$ (%): C, 79.58; H, 6.21; N, 6.63. Found: C, 79.52; H, 6.28; N, 6.59. IR (KBr, ν_{max}, cm^{-1}): 3363 (NH), 3060 (C-H), 1608, 1427 (C=C). ^{1}H NMR (300 M, DMSO-d_6):



Scheme-I: Synthetic route to the title compound

3.88-3.94, 4.20-4.24 (2H, m, O-CH_2); 4.46-4.48 (1H, t, *J* = 2.7 Hz, NCH); 6.25 (1H, s, NH); 6.50-6.55 (1H, m, H Ar); 6.69-6.71 (3H, m, H Ar); 7.22-7.46 (5H, m, H Ar); ^{13}C NMR (75M, DMSO-d_6): 53.3, 70.4, 115.4, 116.2, 117.4, 121.7, 127.6, 127.6, 128.1, 128.9, 128.9, 135.4, 140.7, 143.2.

Preparation of compound 3: Dichloroacetyl chloride (17.6 nmol, 2.59 g) was added in a mixture containing 3-phenyl-3,4-dihydro-2*H*-1,4-benzoxazine **(2)** (14 nmol, 2.95 g), K_2CO_3 (15.2 nmol, 2.08 g) and benzene (25 mL). The reaction mixture was stirred at room temperature for 2 h. The organic phase was dried over anhydrous magnesium sulfate and the benzene was removed under vacuum, the 4-dichloroacetyl-3-phenyl-3,4-dihyro-2*H*-1,4-benzoxazine **(3)** was recrystallized from ethanol and light petroleum. The yield was 74.2 % (3.34 g); m.p. 136-138 °C. Anal. calcd. for $C_{16}H_{13}NO_2Cl_2$ (%): C, 59.81; H, 4.08; N, 4.36. Found, %: C, 59.78; H, 4.16; N, 4.32. IR (KBr, ν_{max}, cm^{-1}): 3045 (C-H), 1689 (C=O), 1591, 1492 (C=C). ^{1}H NMR (300 M, DMSO-d_6): 4.47-4.52, 4.99-5.03 (2H, m, O-CH_2-C); 5.82 (1H, s, N-CH-); 6.79-7.75 (9H, m H Ar), 7.24 (1H, s, Cl_2CH); ^{13}C NMR (75 M, DMSO-d_6): 66.8, 68.2, 117.4, 121.2, 124.0, 124.9, 127.0, 127.9, 127.9, 128.9, 128.9, 129.2, 129.2, 136.4, 147.1, 163.1. Mass spectrum: $[M-1]^+$ = 321.

Crystal data and structure determination: The block-shaped single crystal of the title compound was grown by slow cooling from a hot saturated solution in ethanol. The crystal with dimensions of 0.62 × 0.23 × 0.20 mm was mounted on a Bruker AXSII CCD area-detector diffractometer using graphite monochromated M Ka radiation (λ = 0.71073 Å) at 293 (2) K. A total of 13533 reflections were collected in the range of $3.48 < \theta < 27.48°$, of which 3362 were independent and 2417 were observed with $I > 2\sigma(I)$. The structure was solved by direct methods using SHELXS-97 program[8] and the semi-empirical from equivalents absorption corrections were applied to all intensity data. All nonhydrogen atoms were refined an isotropically by the full-matrix least square method on F^2 using SHELXL-97[9]. The hydrogen atoms were determined with theoretical calculations and refined isotropically. A summary of the key crystallographic information is given in Table-1. The final full-matrix least squares refinement gave R = 0.0507 and wR = 0.1435 ($w = 1/[\sigma^2(F_o^2) + (0.0912P)^2 + 0.1416\ P]$) where $P = (F_o^2 + 2F_c^2)/3$, S = 1.122, ($\Delta/\sigma_{max} = 0.000$, $\Delta\rho_{max}$ = 0.598 and $\Delta\rho_{min}$ = -0.445 eÅ^{-1}. CIF file containing complete information on the studied structure was deposited with CCDC, deposition number 928571 and is freely available upon request from the following web site: www.ccdc.cam.ac.uk/data_request/cif.

RESULTS AND DISCUSSION

The structures of compound **2** and the title compound **3** were confirmed by elemental analysis, IR, ^{1}H NMR, ^{13}C NMR, MS and X-ray diffraction analysis. The IR spectrum of the title compound shows absorption band at 1689 cm^{-1} originated from the stretching vibration of C=O stretching vibration. The proton magnetic resonance spectra of compounds **2** and **3** have been recorded in DMSO-d_6. In the ^{1}H NMR spectrum the singlet at 3.8-5.8 ppm corresponds to the O-CH_2-CH-N proton indicating the formation of benzoxazine. The signals at 6.25 ppm range are N-H of compound **2**. And it is replaced by a single sharp peak at 7.24 ppm for the Cl_2CH of the title compound. With regard to the mass spectra, the title compound show M-1 signals. The measured data of elemental analytical results is in accord with the theoretical values.

TABLE-1
CRYSTAL STRUCTURE AND DATA REFINEMENT PARAMETERS

Empirical formula	$C_{16}H_{13}Cl_2NO_2$
Formula weight	322.17
Crystal system, space group	Monoclinic, $P2_1/c$
a (Å)	15.105(3)
b (Å)	6.2685(13)
c (Å)	16.084(3)
α (°)	90
β (°)	103.79(3)
γ (°)	90
V (Å^3)	1479.1(5)
Z	4
D_c (g/cm^3)	1.447
μ (mm^{-1})	0.442
F (000)	664
Crystal size (mm)	0.62 × 0.23 × 0.20
Color/shape	Colorless/block
Temp (K)	293(2)
Theta range for collection	3.48 - 27.48
Reflections collected	13533
Independent reflections	3362
Data/restraints/parameters	3362 / 0 / 190
Goodness-of-fit on F^2	1.122
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0507$, $wR_2 = 0.1435$
R indices (all data)	$R_1 = 0.0691$, $wR_2 = 0.1604$
Largest difference peak/hole (eÅ^{-3})	0.598 and -0.445

Crystal structure: The molecular structure with atom-numbering scheme and the packing diagram of the title compound are shown in Figs. 1 and 2, respectively. The selected bond lengths and bond angles are shown in Table 2.

According to X-ray analysis of the structure, the bond lengths of C(8)-N(1), C(1)-N(1) and C(7)-O(1) were close to the typical C-N and C-O bond length. The C(15)-O(2) (1.206 Å) indicated a double bond C=O (1.19-1.23 Å). However, compared with the normal aliphatic bond value, bond length C(15)-N(1) (1.359 Å) and C(6)-O(1) (1.370 Å) were shorter than normal.

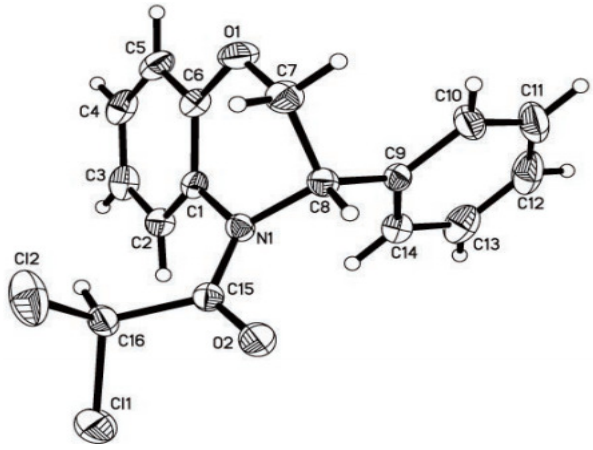


Fig. 1. Molecular structure of 4-dichloroacetyl-3-phenyl-3,4-dihyro-2*H*-1,4- benzoxazine, showing displacement ellipsoids drawn at the 30 % probability level

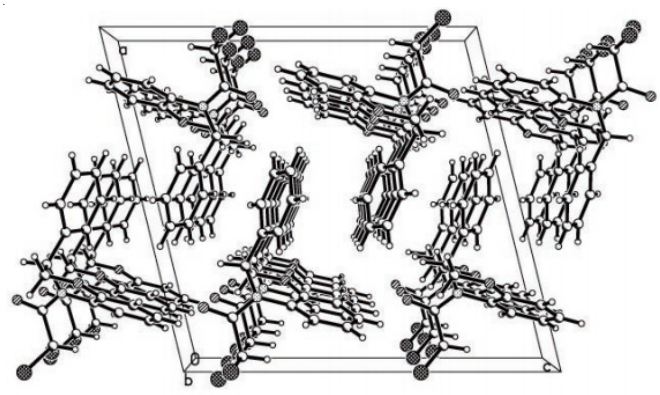


Fig. 2. Packing of the title compound

TABLE-2
SELECTED BOND LENGTHS (Å) AND BOND ANGLES (°)

Atom	Distance	Atom	Angle
C(1)-C(6)	1.387(3)	C(6)-C(1)-C(2)	119.53(18)
C(1)-C(2)	1.394(3)	C(6)-C(1)-N(1)	118.30(17)
C(1)-N(1)	1.430(2)	C(2)-C(1)-N(1)	121.86(18)
C(2)-C(3)	1.372(3)	O(1)-C(6)-C(1)	122.98(18)
C(3)-C(4)	1.379(4)	O(1)-C(6)-C(5)	117.2(2)
C(4)-C(5)	1.383(4)	C(1)-C(6)-C(5)	119.8(2)
C(5)-C(6)	1.390(3)	O(1)-C(7)-C(8)	112.73(17)
C(6)-O(1)	1.370(3)	N(1)-C(8)-C(9)	112.41(16)
C(7)-O(1)	1.433(3)	N(1)-C(8)-C(7)	105.24(17)
C(7)-C(8)	1.523(3)	C(9)-C(8)-C(7)	115.24(17)
C(8)-N(1)	1.477(2)	C(14)-C(9)-C(10)	118.6(2)
C(8)-C(9)	1.518(3)	C(14)-C(9)-C(8)	121.58(19)
C(9)-C(14)	1.388(3)	C(10)-C(9)-C(8)	119.7(2)
C(9)-C(10)	1.393(3)	O(2)-C(15)-N(1)	123.31(19)
C(10)-C(11)	1.382(4)	O(2)-C(15)-C(16)	120.01(18)
C(11)-C(12)	1.357(5)	N(1)-C(15)-C(16)	116.53(17)
C(12)-C(13)	1.385(5)	C(15)-C(16)-Cl(1)	110.06(15)
C(13)-C(14)	1.388(3)	C(15)-C(16)-Cl(2)	106.64(14)
C(15)-O(2)	1.206(2)	Cl(1)-C(16)-Cl(2)	110.83(12)
C(15)-N(1)	1.359(3)	C(15)-N(1)-C(1)	127.04(16)
C(15)-C(16)	1.542(3)	C(15)-N(1)-C(8)	118.52(16)
C(16)-Cl(1)	1.756(2)	C(1)-N(1)-C(8)	113.17(16)
C(16)-Cl(2)	1.769(2)	C(6)-O(1)-C(7)	117.11(17)

It was obvious that there was p_{π}-p_{π} large conjunctive effect between O(1), benzene ring [C(1), C(3), C(4), C(5), C(6) and C(2)], N(1), C(15)-O(2) [C=O], which resulting in shorter bond length than the typical C-N bond length and C-O bond length. The title compound contained two benzene rings and an oxazine ring. The torsion angle of O(1)-C(7)-C(8)-N(1) was -59.0(2)°, forming 7,8-half-chair conformation. Benzene ring plate I[C(1), C(3), C(4), C(5), C(6) and C(2)] made a dihedral angle of 2.6º with oxazine plane II[O(1), C(6), C(1), N(1), C(8), C(7)]. It means that they were almost coplanar because of the conjunctive effect. Benzoxazine ring and plan III[C(9), C(10), C(11), C(12), C(13) and C(14)] were almost perpendicular with the dihedral angle being 91.7º.

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