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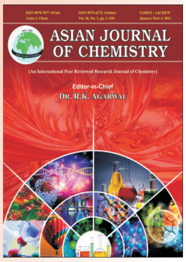

Synthesis, Characterization and Crystal Structure of 4-Dichloroacetyl-2,5-dimethyl-8-oxo-1,4-diazabicyclo[3.3.0]octane

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4-Dichloroacetyl-2,5-dimethyl-8-oxo-1,4-diazabicyclo[3.3.0]octane was synthesized by cycloaddition and acylation reaction. The molecular structure was characterized by IR, NMR, MS, elemental analysis and further confirmed by X-ray diffraction analysis. The title compound, $C_{10}H_{14}N_2O_2Cl_2$, crystallized in the monoclinic $P2_1/c$ space group with unit cell parameters a = 10.286(2) Å, b = 11.513(2) Å, c = 12.234(5) Å, Z = 4, V = 1223.5(6) $Å^3$, Dc = 1.439 g/cm^3, F (000) = 552, R_1 = 0.0405 and wR_2 = 0.1020. In the crystal structure, the molecule was linked through intermolecular C(7)-H(7)...O(2) hydrogen bond forming a one dimension chain conformation.

Keywords: Synthesis, X-ray structure, 4-Dichloroacetyl-2,5-dimethyl-8-oxo-1,4-diazabicyclo[3.3.0]octane.

INTRODUCTION

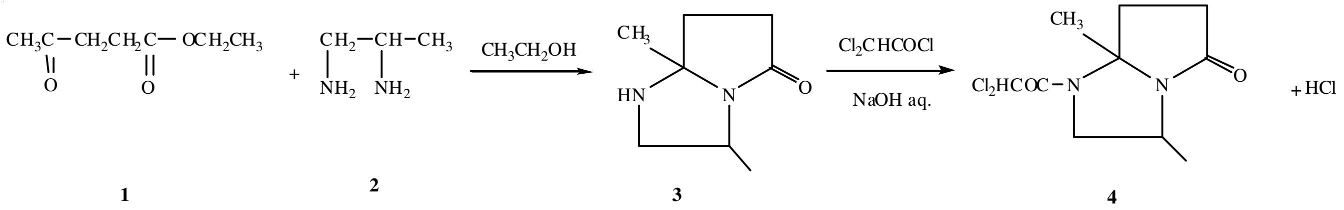
Diazabicyclo derivatives attracted more attention in organic synthesis for their widely used as a structure-directing agent[1], synthons[2,3], catalysts[4], *etc*. They were also the target compounds for their versatile bioactivity [5-8]. Since BASF employed BAS-145138 as safeners which increased the toleration of crops to herbicidal acetanilides[9], dichloroacetyl diazabicyclo derivatives were reported as a novel kind of herbicide safener protecting crops from injury by chlorine acetamide herbicides, sulfonylurea herbicides and imidazolinone herbicides[10,11].

In connection with our previous studies on the synthesis of nitrogen and oxygen containing heterocyclic compounds[12,13], we have described a convenient synthetic route to construct bridged ring skeleton with nitrogen as the bridgehead atom, from the readily available diamine, levulinic acid and dichloroacetyl chloride through cycloaddition and acylation[14-16]. As part of a progress to discover novel herbicide safeners with better bioactivity and to explore the relationship of structure and activity, we reported the synthesis and crystal structure of 4-dichloroacetyl-2,5-dimethyl-8-oxo-1,4-diazabicyclo[3.3.0]-octane (**4**) by employed the above synthetic route starting from 1,2-propane diamine, ethyl levulinate and dichloroacetyl chloride.

EXPERIMENTAL

The infrared spectra were taken on a KJ-IN-27G infrared spectrophotometer (KBr). HPLC-MS spectrometry was Waters Xevo-TQMS. The ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker AVANVE 400 MHz nuclear magnetic resonance spectrometer with DMSO-d_6 as the solvent and TMS as the internal standard. The elemental analysis was performed on FLASH EA1112 elemental analyzer. The melting points were determined on Beijng Taike melting point apparatus (X-4) and uncorrected.

Preparation of 4-dichloroacetyl-2,5-dimethyl-8-oxo-1,4-diazabicyclo[3.3.0]octane (4): Ethyl levulinate (10.1 g, 0.07 mol) and 1,2-diamino propane (18.5 g, 0.25 mol) were mixed with 20 mL ethanol. The mixture was heated to reflux for 8 h, then vacuum distillation. The intermediate **3** was purified by column chromatography on silica gel eluting with ethyl acetate and light petroleum (1:15). Dichloroacetyl chloride (7.4 g, 0.05 mol) was added dropwise slowly into of diazabicyclo **3** (7.7 g, 0.05 mol) dissolved in 50 mL toluene at -10-5 °C. Stirring was continued for 2h. Then regulated the pH 8-9 with sodium hydroxide solution. The reaction system was stirred at 25 °C for 1h. Organic phase was rinsed with water until pH = 7. The organic layer was dried over anhydrous magnesium sulfate and the solvent was removed under vacuum (**Scheme-I**). The product **4** was recrystallized with ethanol and light petroleum. Compound **4** was obtained as white solid in 68 % yield. Anal. calcd. for $C_{10}H_{14}Cl_2N_2O_2$ (%): C, 45.45; H, 5.34; N, 10.61. Found, %: C, 45.61; H, 5.32; N, 10.51. IR spectrum, ν, cm^{-1}: 3001-2970 (C-H), 1679 (C=O), 1674 (C=O). ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 1.24 (d, J = 6.8 Hz, 3H, CH_3), 1.62 (s, 3H, CH_3), 2.18-2.76 (m, 4H, C-CH_2-CH_2-C), 3.57-4.10 (m, 2H, CH_2-N), 4.24-4.29 (m, 1H, N-CH), 6.89 (s, 1H, Cl_2CH). ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 21.67, 24.64,



Scheme-I: Synthetic route to the title compound

32.26, 35.71, 48.48, 53.46, 67.18, 84.49, 160.47, 175.41. Mass spectrum, (MS EI$^+$)[M + 1] = 265.

Crystal data and structure determination: The block colorless single crystal of the title compound was grown from ethanol solution at room temperature. The crystal with dimensions of 0.28 × 0.26 × 0.22 mm was mounted on a Brukcr AXSII CCD area-detector diffractometer using graphite monochromated MoK$_\alpha$ radiation ($\lambda = 0.071073$ nm) at 293(2) K. A total of 11679 reflections were collected in the range of $3.34 < \theta < 27.47°$, of which 2788 were independent and 2188 were observed with $I > 2\sigma(I)$. Lattice determination and data collection were carried out using SMART version 5.628 software[17]. Date reduction and absorption corrections were per. formed with SAINT version 6.02[17]. The structure was solved by direct methods using SHELXS-97 and refined by full matrix least squares on F^2, SHELXL-97[18]. 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 = 0.0405 and wR = 0.1020 ($w = 1/[\sigma^2(F_o^2) + (0.0584P)^2 + 0.1879P]$) where $P = (F_o^2 + 2F_c^2)/3$, S = 1.040, ($\Delta/\sigma_{max} = 0.001$, $\Delta\rho_{max} = 0.243$ eÅ^{-1} and $\Delta\rho_{min} = -0.233$ eÅ^{-1}. CIF file containing complete information on the studied structure was deposited with CCDC, deposition number 892496 and is freely available upon request from the following web site: www.ccdc.cam.ac.uk/data_request/cif

TABLE-1
PARAMETERS OF CRYSTAL STRUCTURE

Item	Value
Empirical formula	$C_{10}H_{14}Cl_2N_2O_2$
Formula weight	265.13
Temperature (K)	293(2) K
Wavelength (Å)	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a =10.286 (2)Å α = 90°
	b =11.513 (2)Å β = 122.38 (2)°
	c =12.234 (5)Å γ = 90°
Volume (Å^3)	1223.5 (6) Å^3
Z	4
Calculated density	1.439 g/cm^3
Absorption coefficient	0.518 mm^{-1}
F(000)	552
Crystal size	0.28 × 0.26 × 0.22 mm^3
Theta range for data collection	3.34 to 27.47°
Limiting indices	-13 < = h < = 13, -14 < = k < = 14, -15 < = l < = 14
Reflections collected / unique	11679/2788 [R(int) = 0.0296]
Completeness to theta = 27.47	99.6 %
Absorption correction	Semi-empirical from equivalents
Data / restraints / parameters	2788/0/147
Goodness-of-fit on F^2	1.040
Final R indices [I > 2sigma (I)]	$R_1 = 0.0405$, $wR_2 = 0.1020$
R indices (all data)	$R_1 = 0.0512$, $wR_2 = 0.1070$
Largest diff. peak and hole (eÅ^{-3})	0.243 and -0.233 eÅ^{-3}

RESULTS AND DISCUSSION

The structure of the title compound was elucidated by elemental analysis and spectroscopic technique data. In the IR spectra a characteristic carbonyl band at around 1650-1700 cm^{-1} splitted two sharp peaks which proved the presence of two p-π conjunction between N atom and O=C in the molecular. ^{1}H NMR spectra of the compound gave a characteristic of Cl_2CH- with single signal in the δ 6.89 ppm range. In the ^{13}C NMR spectra of compound **4**, the signals observed in the region δ 175.41 ppm and δ 160.47 ppm accounting for the two carbon of O=C-N, δ 84.49 ppm accounting for the signals of the Cl_2C and δ 67.18 ppm accounting for the bridgehead carbon, which also confirmed the formation of diazabicyclo.

Crystal structure: A perspective view of 4-dichloroacetyl-2,5-dimethyl-8-oxo-1,4-diazabicyclo[3.3.0]octane, showing the atomic numbering scheme, was depicted in Fig. 1. The title compound crystallized in the monoclinic space group $P2_1/c$, with four molecules in the unit cell. The title compound was a bridged compound with N(1) and C(4) as the bridge carbon atoms. The C(1)=O(1) and C(9)=O(2) bond distances [1.2213(19) and 1.2178(19) Å, respectively] confirmed the existence of the carbonyl. The bond distances of C(1)-N(1) and C(9)-N(2) [1.361(2) Å and 1.341(2) Å, respectively] were shorter than the normal C-N distance [C-N = 1.472 Å], which indicated the existence of p-π conjunction effect between N atom and carbonyl. All the bond lengths and bone angles were in their normal range (Table-2). The compound lied in two planes with plane I[C(4), C(3), C(2), C(1) and N(1)] making a dihedral angle of 42.6° with plane II[N(1), C(4), N(2), C(6) and C(7)]. Plane I was in an envelope conformation with the C(2) atom forming the flap and N(1) atom for plane II. The

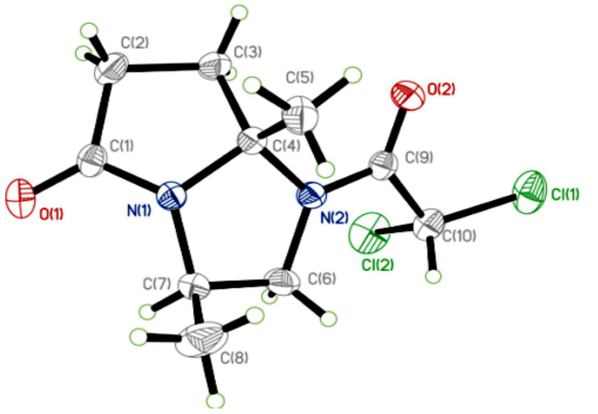


Fig. 1. Molecular diagram of compound **4**, showing atom labeling scheme 30 % probability amplitude displacement ellipsoids are shown

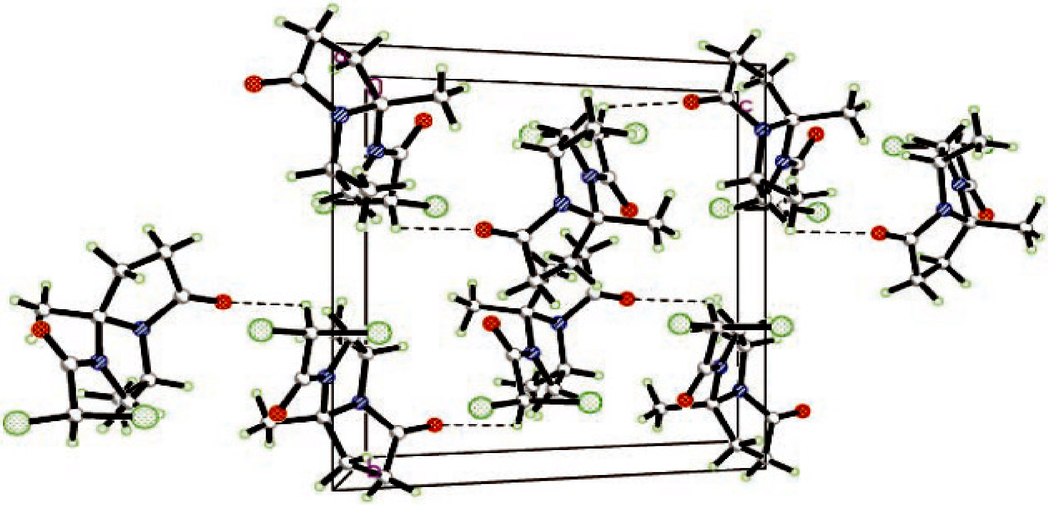


Fig. 2. Packing of the title compound

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

	Bond lengths(Å)		Bond angles (°)
Cl(1)-C(10)	1.7598(18)	C(1)-N(1)-C(4)	114.25(13)
Cl(2)-C(10)	1.7836(19)	C(1)-N(1)-C(7)	124.59(13)
O(1)-C(1)	1.2213(19)	C(4)-N(1)-C(7)	113.29(12)
O(2)-C(9)	1.2178(19)	C(9)-N(2)-C(6)	127.17(13)
N(1)-C(1)	1.361(2)	C(9)-N(2)-C(4)	120.76(12)
N(1)-C(4)	1.4563(19)	C(6)-N(2)-C(4)	111.80(12)
N(1)-C(7)	1.461(2)	O(1)-C(1)-N(1)	124.61(15)
N(2)-C(9)	1.341(2)	O(1)-C(1)-C(2)	128.13(15)
N(2)-C(6)	1.476(2)	N(1)-C(1)-C(2)	107.26(13)
N(2)-C(4)	1.4888(19)	C(1)-C(2)-C(3)	104.13(13)
C(1)-C(2)	1.508(2)	C(2)-C(3)-C(4)	104.10(12)
C(2)-C(3)	1.531(2)	N(1)-C(4)-N(2)	100.64(11)
C(3)-C(4)	1.540(2)	N(1)-C(4)-C(5)	112.38(13)
C(4)-C(5)	1.521(2)	N(2)-C(4)-C(5)	111.01(12)
C(6)-C(7)	1.533(2)	N(1)-C(4)-C(3)	103.63(12)
C(7)-C(8)	1.513(3)	N(2)-C(4)-C(3)	114.56(12)
C(9)-C(10)	1.543(2)	C(5)-C(4)-C(3)	113.66(14)
		N(2)-C(6)-C(7)	105.34(13)
		N(1)-C(7)-C(8)	113.16(15)
		N(1)-C(7)-C(6)	102.72(12)
		C(8)-C(7)-C(6)	114.16(16)
		O(2)-C(9)-N(2)	124.06(15)
		O(2)-C(9)-C(10)	121.30(14)
		N(2)-C(9)-C(10)	114.63(14)
		C(9)-C(10)-Cl(1)	110.92(12)
		C(9)-C(10)-Cl(2)	108.72(11)
		Cl(1)-C(10)-Cl(2)	109.90(9)

molecular packing diagram (Fig. 2) showed molecules connected with weak intermolecular (C-H)…O hydrogen bonds (Table-3) forming chains along the a-axis direction, which were independently arranged in the unit cell. These hydrogen bonds stabilized the crystal structure.

TABLE-3
HYDROGEN BONDS GEOMETRY (Å, °)

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(7)-H(7)...O(2)	0.98	2.60	3.454(3)	145.8

Symmetry transformations used to generate equivalent atoms: *x*,-*y*-1/2, *z*+1/2

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