Ж У Р Н А Л   С Т Р У К Т У Р Н О Й   Х И М И И

2010. Том 51, № 2 *Март – апрель* *С. 410 – 412*

КРАТКИЕ СООБЩЕНИЯ

UDC 548.737;544.142.4

CRYSTAL STRUCTURE OF 2-(6-CHLORO-4-(*P*-TOLYLAMINO)PYRIDO[3,2-D]PYRIMIDIN-1-IUM-1-YL)ACETATE OXONIUM BROMIDE

© 2010 **L. Shen*, F.L. Zhang**

College of Material Chemistry and Chemical Engineering, Key Laboratory of Organosilicon Chemistry and Material Technology, Ministry of Education, Hangzhou Normal University, Hangzhou 310036, P. R. China

Received Yune, 15, 2009

The crystals of 2-(6-chloro-4-(*p*-tolylamino)pyrido[3,2-d]pyrimidin-1-ium-1-yl)acetate (zwitterionic form) oxonium bromide, $C_{16}H_{13}ClN_4O_2 \cdot Br^- \cdot H_3O^+$ (**I**) were prepared and studied by single-crystal X-ray diffraction method. The compound crystallizes in the triclinic space group *P*-1 with $a = 8.3121(8)$, $b = 9.3885(8)$, $c = 13.2903(12)$ Å, $\alpha = 106.788(2)$, $\beta = 95.204(3)$, $\gamma = 110.871(2)°$, $V = 905.81(14)$ Å^3, $Z = 2$; final $R = 0.053$, $wR2 = 0.150$. It is interesting that methylene C in the $BrCH_2COOH$ molecule binds to the N1 of the pyrimidine ring. In the crystal studied, two neighboring organic molecules are connected by hydrogen bonds through carboxylate oxygen, oxonium and bromide ions to form a dimer.

Keywords: pyridopyrimidine derivatives, quaternary ammonium salts, crystal structure, hydrogen bond.

Pyridopyrimidine derivatives have been intensively investigated due to analgesic, antiinflammatory and central nervous system depressing activities [1, 2]. In particular, their potent activities as anticancer agents are of great interest. The pyridopyrimidine derivatives were included in anticancer selective kinase inhibitors acting as ATP binding site. The recent development of anticancer agents led to some pyridopyrimidines analogues such as PD166285 [3, 4] and PD173074 [5], which were described as very promising PDGF kinase inhibitors. Pyridopyrimidinium derivatives also exhibit antibacterial and fungicidal activities [6, 7]. A few crystal structures of protonated pyridinium and pyrimidinium derivatives were reported in the literature [8—10]. In this work, we report on the preparation and a crystal structure study of a new pyridopyrimidine derivative.

Experimental. Synthesis. 4,6-dichloropyrido[3,2-d]pyrimidine was prepared as reported elsewhere [11]. 6-Chloro-4-(*p*-tolylamino)pyrido[3,2-d]pyrimidine was synthesized by the reaction of 4,6-dichloropyrido[3,2-d]pyrimidine and 4-methylaniline in 2-propanol in a molar ratio of 1:1.25 and was confirmed by the means of elemental analysis, IR, NMR and MS. The title compound **I** (2-(6-chloro-4-(*p*-tolylamino)pyrido[3,2-d]pyrimidin-1-ium-1-yl)acetate (zwitterionic form) oxonium bromide) was obtained as a yellow product by mixing 6-chloro-4-(*p*-tolylamino)pyrido[3,2-d]pyrimidine and bromoacetic acid (1:1.1) in ethanol/water at room temperature. Single crystals were grown by slow evaporation of the reaction solution.

X-Ray diffraction analysis. For X-ray data collection, a single crystal with dimensions 0.32× ×0.20×0.11 mm was mounted on a Rigaku RAXIS-RAPID diffractometer with MoK_α radiation source (0.71073 Å). The crystal structure was solved by direct methods using SHELXS-97 [12]. The refinement method involved the full-matrix least-squares procedure on F^2. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were treated as riding atoms but included in the structure factor calculations. **Crystal data for I**: $C_{16}H_{16}BrClN_4O_3$, $M = 427.69$, triclinic, *P*-1, $a = 8.3121(8)$ Å,

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* E-mail: shenchem@hotmail.com

Table 1

Selected Bond Lengths (Å) *in the Title Compound*

Cl(1)—C(1)	1.727(5)	N(2)—C(5)	1.309(6)	C(1)—C(2)	1.391(7)	C(8)—C(13)	1.383(6)
O(1)—C(16)	1.299(6)	N(2)—C(6)	1.337(6)	C(2)—C(3)	1.352(7)	C(9)—C(10)	1.386(6)
O(2)—C(16)	1.224(7)	N(3)—C(1)	1.311(5)	C(3)—C(4)	1.402(6)	C(10)—C(11)	1.373(7)
N(1)—C(4)	1.385(6)	N(3)—C(7)	1.346(6)	C(4)—C(7)	1.390(6)	C(11)—C(12)	1.381(7)
N(1)—C(5)	1.330(5)	N(4)—C(6)	1.325(5)	C(6)—C(7)	1.451(5)	C(11)—C(14)	1.510(6)
N(1)—C(15)	1.465(6)	N(4)—C(8)	1.428(5)	C(8)—C(9)	1.379(6)	C(12)—C(13)	1.381(6)

Table 2

Hydrogen Bonds Found in the Title Compound: *Bond Lengths* (Å) *and Angles* (deg.)

D—H---A	D—H	H---A	D---A	D—H---A
O(3)—H(301)---O(1)	0.82	1.72	2.505(8)	159
O(3)—H(302)---Br(1)^{i}	0.82	2.58	3.280(6)	144
N(4)—H(4)---N(3)	0.82	2.30	2.718(7)	110

Symmetry code i: $-x, -y+1, -z+2$.

$b = 9.3885(8)$ Å, $c = 13.2903(12)$ Å, $\alpha = 106.788(2)°$, $\beta = 95.204(3)°$, $\gamma = 110.871(2)°$, $V = 905.81(14)$ Å^3, $Z = 2$. 7949 reflections were measured with ω-scans, in the range of $3.1° \le \theta \le 27.4°$ ($-10 \le h \le 10$, $-11 \le k \le 10$, $-16 \le l \le 16$) to yield 3567 independent reflections ($R_{\text{int}} = 0.031$). Final $R_1 = 0.053$, $wR_2 = 0.150$ [$I > 2\sigma(I)$], and the goodness-of-fit on F^2 was 1.001.

Selected bond lengths for the title compound are given in Table 1. The parameters of hydrogen bonds are listed in Table 2. The CIF file with complete information about the structure was deposited with CCDC (Deposition no. 737932), from which it is available free of charge on request at www.ccdc.cam.ac.uk/data_request/cif.

Results and discussion. As shown in Fig. 1, the main molecule of **I** is flat; it comprises connected through NH-group pyrimidine and benzene moieties as well as side substituent groups. Presumably, the main molecule is in zwitterionic form with a positive charge on N1 and negative charge on the C16O1O2 group. The ring atoms in the pyridopyrimidine ring are co-planar within ±0.004 Å and the bonded to it Cl1, C15 and N4 atoms are in the same plane within 0.000, 0.037 and 0.014 Å, respectively. The atoms of the benzene ring are co-planar within ±0.001 Å and the bonded to it N4 and C14 atoms are in the same plane within 0.046 and 0.065 Å, respectively. The dihedral angle between the two planes is 7.9°. It is interesting that methylene C in the $BrCH_2COOH$ molecule bonds to the N1 atom of the pyrimidine ring (N1—C15 bond). The N1—C15 distance of 1.465(6) Å is longer

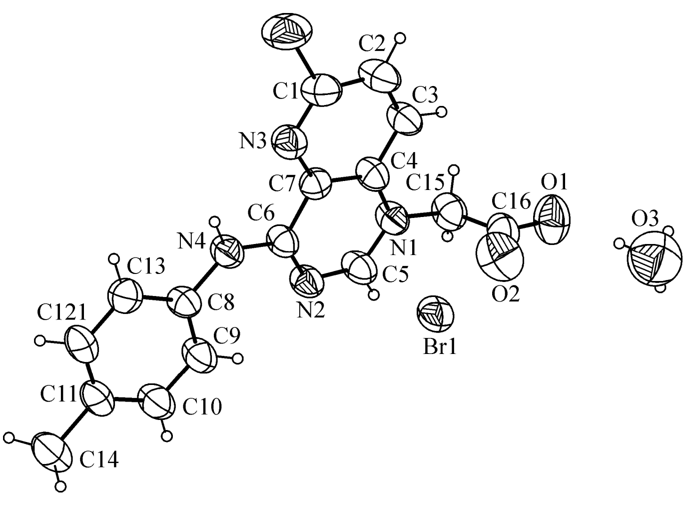

Fig. 1. Asymmetric unit of $C_{16}H_{13}ClN_4O_2 \cdot Br^{-} \cdot H_3O^{+}$ with atom numbering scheme (50 % probability displacement ellipsoids)

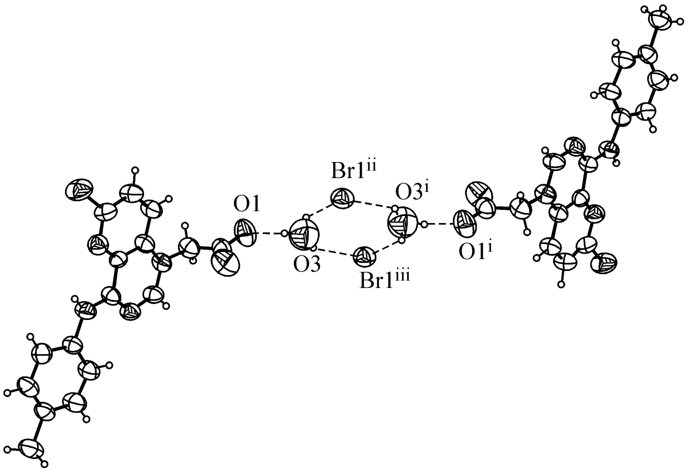

Fig. 2. View of a dimer formed by hydrogen bonds in the crystal studied (the two halves are related by centrosymmetry)

than the N1—C4 and N1—C5 distances of 1.385(6) and 1.330(5) Å, respectively. A similar feature is also observed in 4-aminopyridinium-N-acetate [13]. The dihedral angle between the planes of pyridopyrimidine ring and carboxymethylene fragment is 84.7°.

Hydrogen bonding interactions (Table 2) play an important role in the crystal structure. As shown in Fig. 2, two adjacent molecules are linked by intermolecular hydrogen bonds through carboxylate oxygen, oxonium and bromide, with O1---O3 (2.505(8) Å) and O3---Br1($-x$, $-y+1$, $-z+2$) (3.280(6) Å) contacts. There also exist an intramolecular hydrogen bond between pyridine N3 atom and amine N4 atom.

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