700 RESEARCH PAPER NOVEMBER, 700–702 JOURNAL OF CHEMICAL RESEARCH 2005

A new synthesis and crystal structure of the ethyl 4,6-dibromobenzothiazol-2-ylcarbamate

Li-Zi Yang, Tai-Bao Wei and You-Ming Zhang*

College of Chemistry and Chemical Engineering , Gansu Key Laboratory of Polymer Materials, Northwest Normal University, Lanzhou, Gansu, 730070, P. R. China

The title compound was synthesised by the reaction of *N*-ethoxycarbonyl-*N'*-(2,4,6–tribromo-phenyl)thiourea with copper chloride in ethanol solution. Cyclisation of the ethoxycarbonylthiourea formed the ethyl 4,6-dibromo benzothiazol-2-ylcarbamate.

Keywords: aminobenzothiazoles, cyclisation, crystal structure

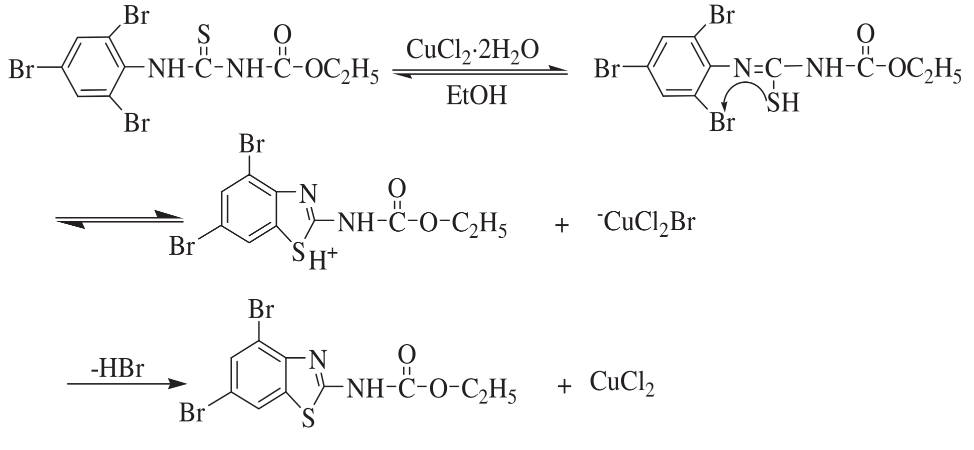
Benzothiazoles comprise a class of therapeutic compounds with antitumor activity at nanomolar levels causing inhibitory activity against a range of human breast, ovarian, colon and renal cell lines *in vitro*[1-3]. Moreover benzothiazoles are synthesised in solution by the condensation of *o*-aminothio-phenols with carboxylic acid derivatives[4], the radical cyclisation of thioacylbenzanilides, the base-induced cyclisation of the corresponding *o*-haloanilides[5-7], or the cyclisation by standing in a solution of dithiothreitol in DMF or ethanol[8]. In order to study the structures and biological functions of *N*-substituted-*N'*-ethoxycarbonylthiourea and their metal complexes, we have synthesised some metal complexes with these thiourea ligands[9-15]. Yet in this experiment we did not obtain the copper(II) complex of thiourea, but got the title compound. This procedure provides a new way to synthesise aminobenzothiazole. We now report this efficient method for the preparation of aminobenzothiazole and the structure of title compound.

The *N*-ethoxycarbonyl-*N'*-(2,4,6–tribromophenyl)thiourea (HL) was prepared according to our previous work[15]. To ethanol (30ml) containing the compound(HL) (2mmol) was added an ethanol solution of copper(II) chloride (2mmol). After stirring the solution at room temperature for 2h, the mixture was filtered to obtained solid product, which was then dried in air. The solid was dissolved in ethanol solvent, heated for a while, and then filtered after cooling down. Single crystals of the title compound were obtained after two weeks, by slow evaporation of the ethanol solution. Yield 60%. M.p. 180-182 °C Anal. Calc. For $C_{10}H_8Br_2N_2O_2S$: C, 31.60; H, 2.12; N, 7.37; Found: C, 31.32 H, 2.01; N, 7.19.

As shown in scheme 1, we found that ethyl 4,6-dibromobenzothiazol-2-ylcarbamate was formed in this reaction. The reason for this was presumably due to the fact that electrons of copper (II) transferred into the vacant p orbital of bromine atom and the delocalisation of p orbital and π system were weakened by this electrons transferred. Then the lone pair electrons on the sulfur atom were also easily to transfer into the vacant p orbital of carbon atom, which led to the formation of benzothiazoles ring and hydrogen bromide was formed at the same time. Thus the formation of title compound could be easily understood.

Table 1 Crystal data and structure refinement for $C_{10}H_8Br_2N_2O_2S$

Empirical formula	$C_{10}H_8Br_2N_2O_2S$
Formula weight	380.06
Temperature	298(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2/c
Unit cell dimensions	a=19.92(18) Å α=90°
	b=7.68(6) Å β=93.91(2)°
	c=16.48(14) Å γ= 90°
Volume	2514(4) Å^3
Z	8
Density (calculated)	2.008mg/m^3
Absorption correction	Semi-empirical from equivalents
F(000)	464
Absorption coefficient	6.604 mm^{-1}
Theta range for data collection	2.48 to 25.05°
Reflections collected	5775
Independent reflections	2105 [R(int) = 0.3655]
Data / restraints / parameters	2105/78/154
Final R indices [I>2σ(I)]	R1=0.0746, wR2=0.1568
	R1=0.1605, wR2=0.2083
Goodness of fit on F^2	0.666
Largest diff. Peak and hole	0.886 and -0.689 e. Å^{-3}



Scheme 1

---

* Correspondent. E-mail: zhangnwnu@126.com

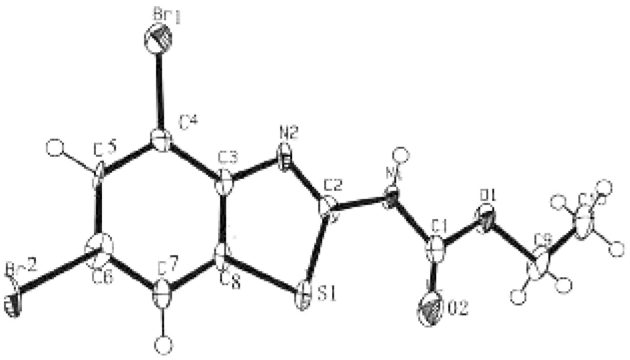


Fig. 1 An ORTEP plot of title compound drawn 50% probability level.

The C=S and one N–H absorption characteristic peaks at 1247cm^{-1} and 3175cm^{-1} are not observed in the IR spectrum of title compound. The benzene ring characteristic vibration are at 1589 and 1423cm^{-1}. One strong band at 1551cm^{-1} attributed to ν (C=N), the other at 629cm^{-1} attributed to ν (C–S). The existence of intermolecular hydrogen bonding (N(1)–H(1)–N(2)), the N–H group characteristic peak has blue shift to 3441cm^{-1}. In its ^{1}H NMR spectrum, δ=7.45 is the proton peak of the benzene ring. Two proton peaks for N–H of the compound (HL) at δ=10.95 and 8.65, disappeared one proton N–H (δ=10.95). And this phenomenon also confirms the formation of the benzothiazoles ring.

The title compound was subjected to single crystal X- ray crystallography[16] and intensity data were collected 298(2) K on the Bruker SMART diffractometer and use graphite monochromatic MoKα radiation (λ=0.71073 Å). The structure was solved directly using the SHELXL-97 program[17] and refined with the SHELXL-97 program[18]. Selected crystal data and structure refinement details are presented in Table 1. The molecular structure is shown in Fig. 1. Selected bond distances and angles are listed in Table 2. As presented in Fig. 1, the C(1)–C(2)–N(1)–S(1)–O(2) group is nearly planar (the mean deviation from plane is 0.0156Å) and forms with the benzothiazoles ring a dihedral angle of 3.2°.The dihedral angle between the phenyl ring and thiazoles ring is 1.5°. The S(1)–C(2) bond length in the title compound is 1.749(11) Å, which is shorter than C–S (1.820 Å) and longer than C=S (1.560 Å). Thus the S(1)–C(2) has a double bond character, which may be explained by some π-electron density delocalisation in the region of thiazoles ring. Packing is mainly determined by two mutual intermolecular hydrogen bonds occurring between the N(1)–H(1) and N(2) atoms of centrosymmetric molecules (N(1)–H(1), 0.860 (2) Å; N(1)… N(2)', 2.942 (1) Å, H(1)…N(2), 2.115 (1) Å; N(1)–H(1), N(2)', 161.13°=$-x+2$, y, $-z+3/2$).

Table 2 Selected bond distances (Å) and angles (°) for $C_{10}H_8Br_2N_2O_2S$

Br(1)–C(6)	1.863(13)	Br(2)–C(8)	1.876(10)
N(1)–C(1)	1.380(14)	N(1)–C(2)	1.382(14)
N(2)–C(2)	1.301(13)	N(2)–C(3)	1.384(14)
S(1)–C(2)	1.749(11)	S(1)–C(4)	1.760(11)
C(3)–C(4)	1.390(14)	C(4)–C(5)	1.404(15)
C(5)–C(6)	1.398(16)	C(6)–C(7)	1.381(15)
C(1)–N(1)–C(2)	122.9(10)	C(1)–N(1)–H(1)	118.5
C(2)–N(1)–H(1)	118.5	C(2)–N(2)–C(3)	109.3(10)
C(2)–S(1)–C(4)	87.6(5)	N(2)–C(2)–S(1)	117.5(10)
N(2)–C(2)–N(1)	120.2(10)	N(1)–C(2)–S(1)	122.3(8)
N(2)–C(3)–C(4)	116.3(10)	N(2)–C(3)–C(8)	125.8(10)

This work was supported by the Natural Science Foundation of China (No.20371040), the Key Project of Chinese Ministry of Education (205161) and the Foundation of Gansu province (3ZS041-A25-007,031-A21-004)

Received 25 May 2005; accepted 13 July 2005
Paper 05/3271

References

1 T.D. Bradshaw, S. Wrigley, D.-F. Shi, R.J. Schultz, K.D. Paull and M.F.G. Stevens, *Br. J. Cancer.*, 1998, **77**, 745.
2 S.E. O'Brien, H.L. Browne, T.D. Bradshaw, A.D. Westwell, M.F.G. Stevens and C.A. Laughton., *Org. Biomolec. Chem.*, 2003, **1**, 493.
3 T.D. Bradshaw, M.C. Bibby, J.A. Double, I. Fichtne, P.A. Copper, M.C. Alley and S. Donohue, *Mol. Cancer Therapeutics.*, 2002, **1**, 239.
4 A. Ben-Alloum, S. Bakkas and M. Soufiaoui, *Tetrahedron Lett.*, 1997, **38**, 6395.
5 I. Hutchinson, M.F.G. Stevens and A.D. Westwell, *Tetrahedron Lett.*, 2000, **41**, 425.
6 M.J. Spitulnik, *Synthesis.*, 1976, 730.
7 A. Roe and W.P.J. Tucker, *J. Heterocycl. Chem.*, 1965, **2,** 148.
8 S. Mourtas, D. Gatos and K. Barlos, *Tetrahedron Lett.,* 2001, **42**, 2201.
9 Y.M. Zhang, T.B. Wei and L.M. Gao, *Synth.Commun.*, 2001, **31**, 3099.
10 Y.M. Zhang, L Xian, T.B. Wei and L.X. Cai, *Acta.Cryst.*, 2003, **E59,** 817.
11 Y.M. Zhang, T.B. Wei, L. Xian, Q. Lin and K.B. Yu, *Acta. Cryst.*, 2003, **E59**, 905.
12 Y.M. Zhang, L. Xian and T.B. Wei, *Acta Cryst.*, 2003, **C59**, 473.
13 L. Xian, T.B. Wei and Y.M. Zhang, *J. Coord. Chem.*, 2004, **57,** 453.
14 Y.M. Zhang, L. Xian, T.B. Wei and K.B. Yu, *J. Chem. Res (S)*, 2003, 798.
15 Q. Lin, Y.M. Zhang, T.B. Wei and H. Wang, *J. Chem. Res.*, 2004, 298.
16 All the X-ray crystal structural data are available in CCDC (CCDC No. 259198)
17 G.M. Sheldrick, *Acta Cryst.* A46, 1990, 467
18 G.M. Sheldrick, SHELXL97. University of Göttingen, Germany, 1997.