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**CRYSTAL STRUCTURE OF (2-CHLORO-4-(PHENYLTHIO)PHENYL)(3-METHYL-1-PHENYL-5-(PHENYLTHIO)-1H-PYRAZOL-4-YL)METHANONE****G.-X. Sun<sup>1</sup>, Z.-W. Zhai<sup>2</sup>, Z.-H. Sun<sup>2</sup>, C.-X. Tan<sup>2</sup>, J.-Q. Weng<sup>2</sup>, X.-H. Liu<sup>2</sup>**<sup>1</sup>*School of Chemistry and Chemical Engineering, Yancheng Institute of Technology, Jiangsu, Yancheng, P. R. China*<sup>2</sup>*College of Chemical Engineering, Zhejiang University of Technology, Hangzhou, Zhejiang, P. R. China*

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(2-Chloro-4-(phenylthio)phenyl)(3-methyl-1-phenyl-5-(phenylthio)-1H-pyrazol-4-yl)methanone was obtained by accident. In order to know the structure of this product, the compound was isolated by column chromatography and recrystallized from EtOH. The compound was characterized by X-ray diffraction. The compound crystallized in the triclinic space group *P*-1 with  $a = 9.909(2)$ ,  $b = 11.824(2)$ ,  $c = 13.056(3)$  Å,  $\alpha = 63.309(3)^\circ$ ,  $\beta = 89.964(4)^\circ$ ,  $\gamma = 67.727(3)^\circ$ ,  $V = 1237.7(4)$  Å<sup>3</sup>,  $Z = 2$  and  $R = 0.0414$ .

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**Key words:** aryl sulfide, synthesis, crystal structure.**INTRODUCTION**

Nowadays, sulfur chemistry has received considerable attention because of their medicinal, pesticidal, and industrial importance [1–5]. Thioether derivatives (especially aryl sulfide) are important sulfur compounds [6–10] because they have been widely used in pharmaceutical, polymer materials, flavor and fragrance. These compounds exhibit good biological activities, such as herbicidal [11], GPR119 agonist [12], antiplatelet aggregation [13], antibacterial [14], anticancer [15], antiviral [16] and are HIV-1 reverse transcriptase inhibitors [17]. For instance, pyrithiobac-sodium had been developed as a commercial herbicide.

In view of these facts mentioned above, many references [18–20] reported the synthesis method for aryl sulfide. Generally, aryl sulfide was synthesized from aryl halides and thiophenol under transition metal catalyst, such as Pd [21], Cu [22], Co [23], Ni [24]. Recently, we have reported the synthesis of aryl sulfide using NaH/THF system [25]. As a part of our work on the synthesis of bioactive lead compounds for drug discovery, a new aryl sulfide derivative was found through TLC. In order to investigate the new structure of this aryl sulfide derivative, it was characterized by <sup>1</sup>H NMR, MS, elemental analysis, and X-ray diffraction.

**RESULTS AND DISCUSSION**

**Synthesis.** Intermediate **3** was synthesized from start material **1** and 2,4-dichloro phenyl acyl chloride by the base-catalyzed method reported by Wu *et al.* [26] for the successful preparation of intermediate **3**. In this paper, intermediate **3** was synthesized in the presence of K<sub>2</sub>CO<sub>3</sub> catalyst and 1,4-dioxane at the reflux for 2–3 h with a high yield. Then intermediate **3** reacted with POCl<sub>3</sub> to give intermediate **4**. Thioether intermediate **5** was synthesized by treating intermediate **4** with benzenethiol

Table 1

## Products obtained under different conditions

Entry	Reaction condition	Compound	Entry	Reaction condition	Compound
1	NaH/THF	<b>5a</b>	2	KOH/DMF	<b>5a</b> and <b>5b</b>

Table 2

## Selected bond lengths (Å) and angles (deg.) for the title compound

Bond	X-ray crystal	Bond	X-ray crystal	Bond	X-ray crystal
S(1)—C(7)	1.751(2)	N(1)—N(2)	1.366(2)	C(8)—C(17)	1.462(3)
S(1)—C(11)	1.769(2)	N(1)—C(1)	1.438(3)	C(9)—C(10)	1.498(3)
S(2)—C(21)	1.776(2)	N(2)—C(9)	1.321(3)	C(11)—C(16)	1.379(3)
S(2)—C(24)	1.782(2)	C(1)—C(2)	1.377(3)	C(17)—C(18)	1.510(3)
Cl(1)—C(23)	1.739(2)	C(1)—C(6)	1.378(3)	C(18)—C(23)	1.381(3)
O(1)—C(17)	1.220(2)	C(7)—C(8)	1.400(3)	C(24)—C(25)	1.378(4)
N(1)—C(7)	1.356(2)	C(8)—C(9)	1.421(3)		
Angle	X-ray crystal	Angle	X-ray crystal	Angle	X-ray crystal
C(7)—S(1)—C(11)	104.05(10)	C(2)—C(1)—N(1)	120.2(2)	C(8)—C(9)—C(10)	129.54(19)
C(21)—S(2)—C(24)	102.34(11)	C(1)—C(2)—C(3)	118.3(3)	C(16)—C(11)—S(1)	124.62(17)
C(7)—N(1)—N(2)	112.27(16)	N(1)—C(7)—C(8)	106.18(17)	C(13)—C(12)—C(11)	119.5(3)
C(7)—N(1)—C(1)	129.96(17)	N(1)—C(7)—S(1)	120.40(15)	O(1)—C(17)—C(8)	120.90(19)
N(2)—N(1)—C(1)	117.70(16)	C(8)—C(7)—S(1)	132.81(15)	C(23)—C(18)—C(19)	118.24(19)
C(9)—N(2)—N(1)	105.52(16)	C(7)—C(8)—C(17)	129.98(18)	C(22)—C(21)—S(2)	117.72(18)
C(2)—C(1)—C(6)	121.7(2)	N(2)—C(9)—C(8)	111.34(18)		

under basic conditions at room temperature for 24 h, as shown in Scheme 1. Interestingly, in the KOH/DMF system, two products were obtained. One was recognized as the title compound (2,4-dichlorophenyl)(3-methyl-1-phenyl-5-(phenylthio)-1H-pyrazol-4-yl)methanone, the other one is (2-chloro-4-(phenylthio)phenyl)(3-methyl-1-phenyl-5-(phenylthio)-1H-pyrazol-4-yl)methanone that was produced by double coupling, and its structure was characterized by single crystal X-ray diffraction. When the NaH/THF system was tried in this procedure, it worked well and yielded one product **5a** in our experiment (Table 1).

**Crystal structure.** The selected bond lengths and bond angles are listed in Table 2. The molecular structure of the title compound is shown in Fig. 1.

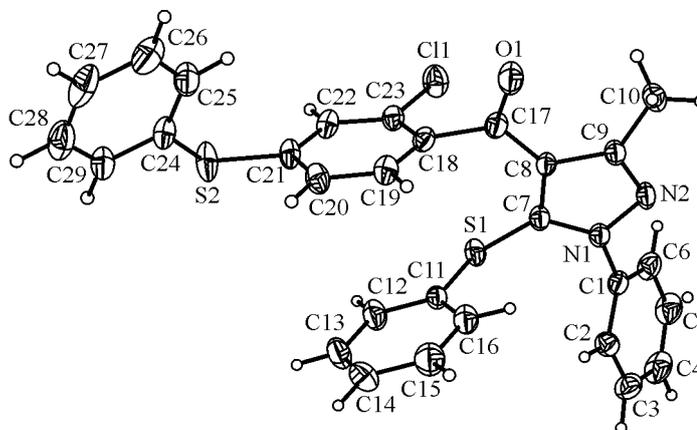


Fig. 1. Molecular structure of the title compound

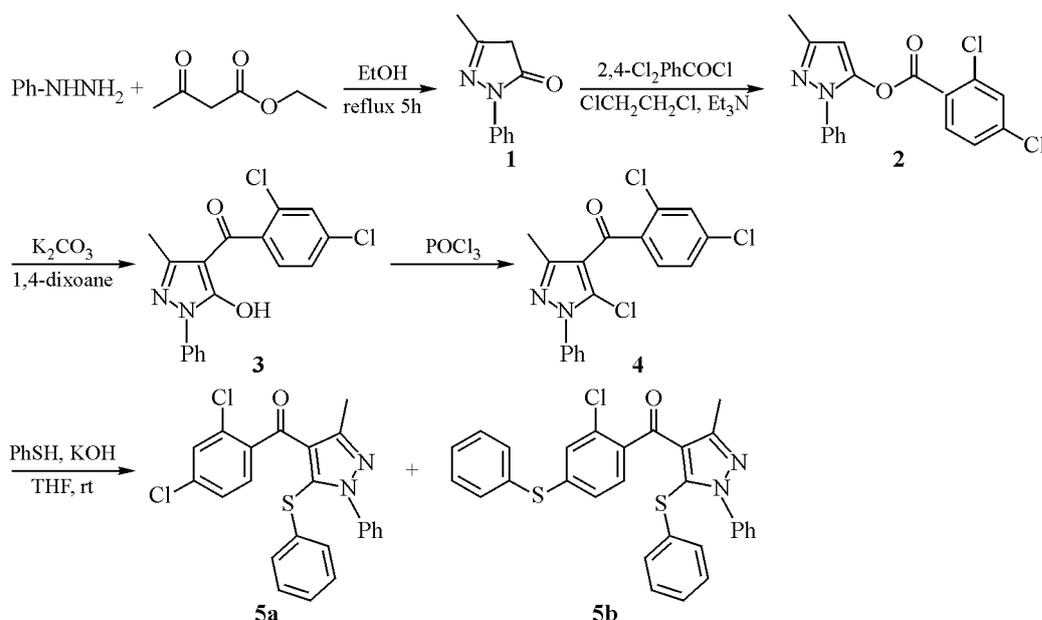
From Fig. 1 it is seen that the title compound consists of one pyrazole ring, four benzene rings, two thioether bonds, and one carbonyl group. Generally, the average bond lengths and bond angles of pyrazole and phenyl rings are in normal ranges [27–36]. In the pyrazole ring, the C9—N2 bond (1.321(3) Å) is significantly longer than the C=N bond (1.27 ~ 1.28 Å) [37, 38]. Meanwhile, the C7—N1 bond (1.356(2) Å) is shorter than the C—N bond (1.52 Å), which indicates significant electron delocalization in the pyrazole ring system. The bond angles of two thioether bonds are 104.05(10)° (C7—S1—C11) and 102.34(11)° (C21—S2—C24) respectively. The C8—C17—C18 torsion angle is 129.98(18)°.

As shown in Fig. 1, the pyrazole ring is nearly vertical with two benzene rings with dihedral angles ( $\theta$ ) of 80.5 and 82.9° respectively. The pyrazole ring (N1, N2, C9, C8, C7) and two benzene rings (C11 to C16, C18 to C23) are fairly planar with plane equations  $6.548x + 0.805y + 7.025z = 5.2853$ ,  $5.592x + 11.535y + 4.501z = 14.9192$  and  $6.395x + 10.902y + 2.154z = 11.0094$  respectively. As for the benzene ring (C1 to C6) connected to the pyrazole ring, it is also vertical with the other two benzene rings (C11 to C16 and C18 to C23). The dihedral angles ( $\theta$ ) are 87.1 and 97.8° respectively. However, among them, the two benzene rings are nearly parallel with a dihedral angle ( $\theta$ ) of 11.3°. The benzene ring (C24 to C29) held a certain twist angle with the other rings (41.0, 56.2, 64.1, and 37.3°). In addition, the length of the S(1)···Cl(1) contact (3.853 Å) allows for a specific interaction due to electronic factors. The latter interaction also contributes to the stabilization of the observed molecular conformation, especially for the parallel between the two benzene rings (C11 to C16, C18 to C23) [39].

#### EXPERIMENTAL

**Instruments.** Melting points were determined using an X-4 apparatus and were uncorrected.  $^1\text{H}$  NMR spectra were measured on a Bruker AV-400 instrument using TMS as the internal standard and  $\text{CDCl}_3$  as the solvent. Elemental analyses were performed on a Vario EL elemental analyzer. Crystallographic data on the compound were collected on a Rigaku Saturn diffractometer. All the reagents are of analytical grade or freshly prepared before the use.

**General procedure.** The synthesis procedure of title compound was outlined in Scheme 1. Intermediates **1**, **2**, **3**, **4** were synthesized according to our previous work [25]. Preparation of **5b**: to a mixture of KOH (69 mmol) in  $\text{H}_2\text{O}$  (5 ml) a thiophenol solution (63 mmol) in DMF (80 ml) was added dropwise at 45 °C. After being stirred for 1 h, the mixture was added dropwise to a solution of inter-



Scheme 1. The synthetic route of title compound

mediate **4** (60 mmol). The mixture was further stirred at 80 °C for 5 h, then water (25 mL) was added and extracted with ethyl acetate (3×15 mL). The organic layers were combined and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated in vacuo and the residue was purified by column chromatography and recrystallized from EtOH to give compound **5b**. White yellow crystals, yield 48 %, m.p. 128—131 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz), δ: 7.56 (s, 1H, Ph—H), 7.30—7.39 (m, 6H, Ph—H), 7.18—7.25 (m, 6H, Ph—H), 6.67—6.71 (m, 3H, Ph—H), 6.66 (m, 2H, Ph—H), 2.53 (s, 3H, pyrazol-CH<sub>3</sub>). MS (ESI), *m/z*: 514(M+1)<sup>+</sup>.

Elemental analysis. For C<sub>29</sub>H<sub>21</sub>ClN<sub>2</sub>OS<sub>2</sub> calculated, %: C 67.89, H 4.13, N 5.46; found: C 67.90, H 4.17, N 5.65.

**Structure determination.** A cube-shaped single crystal of the title compound was obtained by recrystallization from EtOH. The crystal with dimensions of 0.24×0.20×0.18 mm was mounted on a Rigaku Saturn diffractometer with graphite-monochromated MoK<sub>α</sub> radiation (λ = 0.71073 Å) and analyzed using φ scan modes at 294(2) K in the range 2.01 ≤ θ ≤ 26.44°. A total of 5808 reflections were collected, out of which 5003 were independent (*R*<sub>int</sub> = 0.0162) and 3475 were observed with *I* > 2σ(*I*). The calculations were performed using the SHELXS-97 program [40, 41] and the empirical absorption corrections were applied to all intensity data. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were determined by theoretical calculations and refined isotropically. The final full-matrix least squares refinement gave *R* = 0.0414 and *wR* = 0.1038 (*w* = 1/[σ<sup>2</sup>(*F*<sub>0</sub><sup>2</sup>) + (0.056*P*)<sup>2</sup> + 0.3781*P*] where *P* = (*F*<sub>0</sub><sup>2</sup> + 2*F*<sub>c</sub><sup>2</sup>)/3), *S* = 1.02, (Δ/σ)<sub>max</sub> = 0.003, Δρ<sub>max</sub> = 0.39 and Δρ<sub>min</sub> = -0.30 e/Å<sup>3</sup>.

## CONCLUSIONS

In summary, the crystal and molecular structure of the title compound (2-chloro-4-(phenylthio)phenyl(3-methyl-1-phenyl-5-(phenylthio)-1H-pyrazol-4-yl)methanone is reported. These data represent a crystallographically characterized example of a molecular compound. This synthetic method can be applied in building blocks of dithioether compounds.

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Crystallographic data for the structure reported in this article have been deposited with the Cambridge Crystallographic Data Center, CCDC 1453985. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge, CBZ IEZ, UK. Facsimile (44) 01223 336 033, E-mail: deposit@ccdc.cam.ac.uk or <http://www.ccdc.com.ac.uk/deposit>.

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