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Short Note

8-(Pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane

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Abstract: Heptasulfur imides substituted by hereterocycle may be of interest as biologically active compounds. In this communication, the reaction of pyrimidin-2-amine **1** with disulfur dichloride was carefully investigated to give 8-(pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane in good yield. The structure of the newly synthesized compound was established by means of elemental analysis, high resolution mass-spectrometry, ^{1}H, ^{13}C NMR and IR spectroscopy and mass-spectrometry.

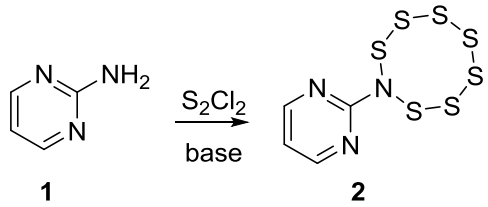
Keywords: heptasulfur imides; pyrimidin-2-amine; disulfur dichloride

1. Introduction

From cyclic sulfur imides with the general formula $S_{8-x}(NH)_x$ heptasulfur imide (S_7NH) is easily available and the most investigated representative of this class [1]. The chemical properties of S_7NH affording *N*-alkylated [2], *N*-acetylated [3] and *N*-metallated [4] derivatives are well investigated. 4-((1,2,3,4,5,6,7,8-Heptathiazocan-8-yl)methyl)morpholine showed valuable fungistatic and fungicidal activity [5]. There is only one example of heterocyclic derivatives of heptasulfur imide; methyl 7-(1,2,3,4,5,6,7,8-heptathiazocan-8-yl)-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate was obtained in low (8%) yield in the reaction of the corresponding heterocyclic amine and disulfur dichloride [6]. Herein, we report the synthesis of previously unknown 8-(pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane and study of conditions of its formation.

2. Results and Discussion

It is known that disulfur dichloride is an important reagent in the synthesis of heterocycles with various numbers of sulfur atoms [7–9]. The formation of every heterocycle from S_2Cl_2 requires precise selection of the reaction conditions—an appropriate base, solvent, and temperature, which can significantly improve the yields of the target compounds. In order to develop the synthesis of heptasulfur imides substituted by hereterocycle, which may be of interest as biologically active compounds, the reaction of pyrimidin-2-amine **1** with disulfur dichloride in the presence of a base was examined (Scheme 1). It was found that DCM as a solvent gave a bit better yield than chloroform (Entries 1,2, Table 1). Moreover, DABCO (1,4-diazabicyclooctane) showed better results than other bases such as triethylamine or pyridine for the formation of heptathiazocane cycle (Entries 2–4). Careful selection of other conditions (ratio of reagents, temperature, and reaction time) led to the best yield of heptathiazocane **2** (78%). The results were summarized in Table 1.



Scheme 1. Synthesis of 8-(pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane **2**.

Table 1. Reaction of pyrimidin-2-amine (1 equiv.) with disulfur dichloride.

Entry	S_2Cl_2 (equiv.)	Base (equiv.)	Solvent	Temperature, °C	Time, h	Yield of 2, %
1	4	DABCO (4)	CH_2Cl_2	5	12	78
2	4	DABCO (4)	$CHCl_3$	5	12	66
3	4	Et_3N (4)	CH_2Cl_2	5	12	48
4	4	Pyridine (4)	CH_2Cl_2	5	12	42
5	4	DABCO (4)	CH_2Cl_2	Rt	12	43
6	4	DABCO (4)	CH_2Cl_2	5	6	65
7	4	DABCO (4)	CH_2Cl_2	5	24	76
8	4	DABCO (4)	CH_2Cl_2	-18	12	12
9	2	DABCO (2)	CH_2Cl_2	5	12	26
10	6	DABCO (6)	CH_2Cl_2	5	12	77

8-(Pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane **2** is perfectly stable during storage at room temperature in solid state or in DCM solution for a week and decomposed in dipolar solvents such as DMSO. The structure of heptasulfur imide **2** was confirmed by means of elemental analysis, high resolution mass-spectrometry, ^{1}H, ^{13}C NMR and IR spectroscopy and mass-spectrometry (see Supplementary Materials).

In conclusion, the synthesis of previously unknown 8-(pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane **2** from pyrimidin-2-amine and disulfur dichloride with maximum yield was achieved. The described experimental procedure may serve as an efficient basis for the synthesis of other heptasulfur imides substituted by hereterocycle.

3. Experimental Section

3.1. General Information

The solvents and reagents were purchased from commercial sources and used as received. Elemental analysis was performed on a 2400 Elemental Analyzer (Perkin Elmer Inc., Waltham, MA, USA). Melting point was determined on a Kofler hot-stage apparatus and is uncorrected. ^{1}H were taken with a Bruker AM-300 machine (Bruker AXS Handheld Inc., Kennewick, WA, USA) (at frequencies of 300.1 MHz) and ^{13}C NMR spectra were taken with a Bruker DRX-500 machine (Bruker AXS Handheld Inc., Kennewick, WA, USA) (125.8 MHz) in DMSO-d_6 solution, with TMS as the standard. J values are given in Hz. MS spectrum (EI, 70 eV) was obtained with a Finnigan MAT INCOS 50 instrument (Hazlet, NJ, USA). IR spectrum was measured with a Bruker "Alpha-T" instrument in KBr pellet. High-resolution MS spectrum was measured on a Bruker micrOTOF II instrument (Bruker Daltonik Gmbh, Bremen, Germany) using electrospray ionization (ESI). The measurement was performed in a positive ion mode (interface capillary voltage—4500 V) or in a negative ion mode (3200 V); mass range was from *m/z* 50 to *m/z* 3000 Da; external or internal calibration was done with electrospray calibrant solution (Fluka). Syringe injection was used for solutions in acetonitrile, methanol, or water (flow rate 3 L/min^{-1}). Nitrogen was applied as a dry gas; interface temperature was set at 180 °C.

3.2. Synthesis of 8-(pyrimidin-2-yl)-1,2,3,4,5,6,7,8-heptathiazocane **2**

At −20 °C and under argon, S_2Cl_2 (3.2 mL, 40 mmol) was added dropwise to a stirred solution of pyrimidin-2-amine (0.95 g, 10 mmol) and DABCO (4.48 g, 40 mmol) in dry CH_2Cl_2 (50 mL). The mixture was stirred for 15 min at −20 °C, left for 12 h at 5–6 °C. The solvent was distilled off under reduced pressure. The residue was separated by column chromatography (silica gel Merck 60, CH_2Cl_2/hexane 1:1). Yield 2.47 g (78%), white crystals, mp 118–120 °C. Rf = 0.15 (CH_2Cl_2:hexane 1:1). IR (KBr), ν, cm^{-1}: 3421, 3080, 3037(C-H), 1670, 1627, 1559(C=N), 1391, 1266, 1108, 1075, 1027, 966, 922, 808, 781, 615. ^{1}H-NMR ($CDCl_3$, ppm, *J*/Hz): δ 7.06 (t, 1H, *J* = 4.8), 8.71 (d, 2H, *J* = 4.8). ^{13}C-NMR (DMSO-d_6, ppm): δ 115.6 (1C, CH), 158.6 (2C, >C=N), 160.9 (1C, N(N)>C=N). MS (EI, 70 Ev), *m/z* (I, %): 317 (M^+, 22), 285 (M^+-S, 3), 253 (M^+-2S, 7), 221 (M^+-3S, 5), 189 (M^+-4S, 7), 157 (M^+-5S, 100), 125 (M^+-6S, 40), 96 (7), 79 (30), 64 (42), 32 (14). HRMS (ESI-TOF): calcd for $C_4H_3N_3S_7$ $[M + H]^+$ 317.8445; found *m/z* 317.8443. Anal. Calcd. for $C_4H_3N_3S_7$: C, 15.13; H, 0.95; N, 13.23; found: C, 15.25; H, 1.03; N, 12.95%.

Supplementary Materials: The following are available online, ^{1}H, ^{13}C NMR, IR, and mass-spectra for compound **2**.

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Conflicts of Interest: The authors declare no conflict of interest.

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