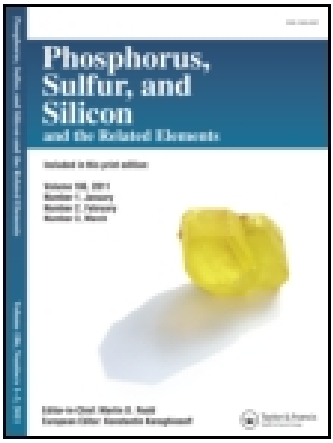

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Some Reactions of 4,6-Diaminopyrimidinethione

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Some Reactions of 4,6-Diaminopyrimidinethione

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*Reaction of 4,6-diamino-2(1H)-pyrimidinethione (**1**) with p-toluene-sulfonyl hydrazine, nitrous acid and carbon disulfide afforded the compounds (**2, 3**) and (**4**) respectively. Compound (**3**) easily reacted with anthranilic acid, semicarbazide thiosemicarbazide and acid hydrazides and gave the polynuclearheterocyclic compounds (**5, 6**$_{a,b}$) and (**8**$_{a,b}$) respectively. Also, compound (**4**) yielded the tricyclic compound **7** when reacted with ethylchloroformate. The purpose of this article is synthesis of biologically active polynuclear heterocyclic compounds.*

Keywords Tetrazopyrimidinethione; triazolopyridine; polynuclear heterocycle

INTRODUCTION

As an extension of our studies on pyrimidine and pyrimidine thione derivatives, as synthons to prepare fused heterocyclic compounds,[1,2] we have synthesized new compounds for use as antischitosomal, such as tricyclic and hexacyclic compounds, since some of pyrimidine and pyrimidinethione derivatives have provided to be active antiviral,[3,4] antimicrobial,[5,6] and anticancer.[7]

CHEMISTRY

Heating a ternary mixture of malononitrile and thiourea in presence of sodium ethoxide in ethanol under reflux yielded 4,6-diamino-2(1H)-pyrimidinthione **(1)**.[8]

Reaction of **(1)** with p-toluenesulfonyl hydrazine gave 4,6-diamino-(3-oxo-3-p-tolyl)-thia-(1,2,4)-triazolo-[5,4a]pyrimidine **(2)**. The structure of (**2**) was elucidated from its correct spectral data (Table I).

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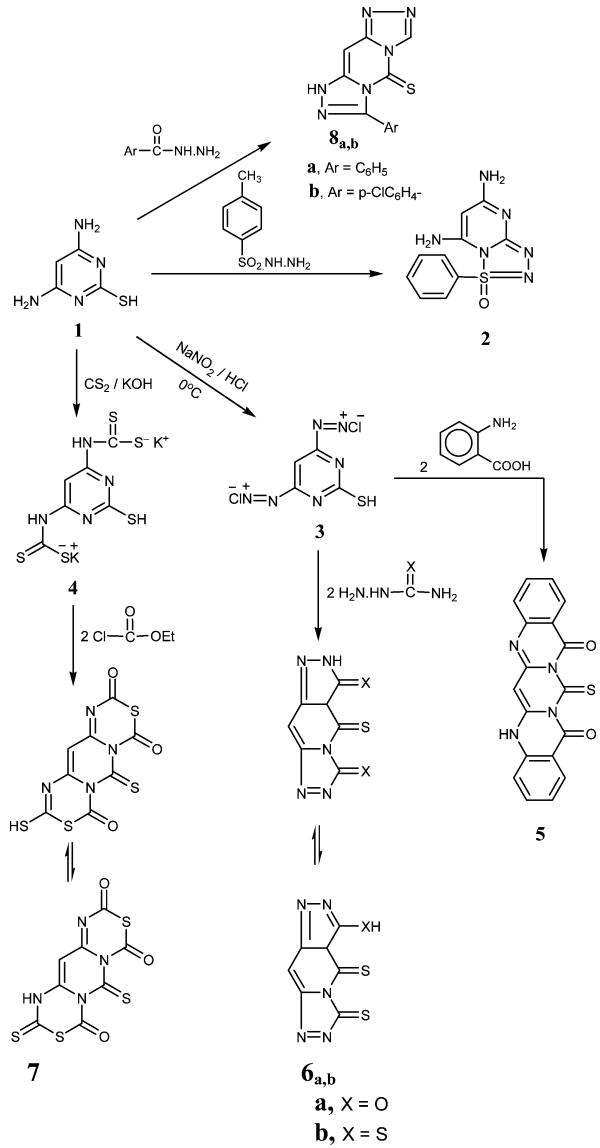

SCHEME 1

On the other hand, when compound (**1**) was allowed to react with nitrous acid and carbon disulfide, it afforded the unseparated intermediates (**3**) and (**4**), respectively.[1,2] Treatment of the tetrazonium salt (**3**) with anthranilic acid yielded the polynuclear heterocyclic compound **5** (Table I).

TABLE I Characterization Data of Products 2-8$_b$

Compound	M.P.°C solvent	Yield %	IR cm^{-1}	^{1}H NMR (ppm)
2	280–281 n-butanol	52	1590 (C═N), 1335 (S═O), 1370–1325 (S═N), 3300–3200 (NH_2)	2.5 (s, 3H, CH_3), 7.5–8 (m, 4H, aromatic), 5.1–5.6 (broad, 4H, $2NH_2$)
5	268–70 DMF	47	1660 (C═O), 3190 (NH), 1460 (C═S)	6.1 (s, 1H, NH), 7.2–7.9 (m, 8H, 2Ph), 6.8 (s, 1H pyrimidyl)
6$_{a=}$	229 n-butanol	55	1450 (C═S), 1470 (C═S), 3195 (NH)	7.2 (s, 1H pyrimidyl), 6.8 (broad, 1H, NH)
6$_b$	253 n-butanol	58	1440 (C═S), 1650 (C═O), 3180 (NH)	7.1 (s, 1H pyrimidyl), 10.1 (broad, 1H, NH)
7	218–20 ethanol	61	1670 (C═O), 1650 (C═O), 1635 (C═O), 1455 (C═S), 3180 (NH)	6.8 (broad, 1H, NH), 7.2 (s, 1H pyrimidyl)
8$_a$	261 A.A.	43	1450 (C═S), 3200 (NH), 1580 (C═N)	7.1 (s, 1H pyrimidyl), 6.8 (broad, 1H, NH), 7–7.8 (m, 5H, phenyl)
8$_b$	273–5 A.A.	49	1455 (C═S), 1590 (C═N), 3190 (NH)	7.2 (s, 1H, pyrimidyl), 6.2 (broad, 1H, NH), 7.2–7.9 (m, 4H, phenyl)

DMF: dimethyl formate; A.A.: acetic acid.

Also, compound (**3**) reacted with semicarbazide and thiosemicarbazide and gave the tricyclic compounds (**6$_{a,b}$**); the structure of these compounds was confirmed from their correct spectral data (Table I).

On the other hand when the dipotassium salt (**4**) was allowed to react with ethylchloroformate it gave the tricyclic compound (**7**) (Table I).

Reaction of the tetrazonium salt (**4**) with benzoylhydrazine and p-clorobenzoylhydrazine afforded the tricyclic compounds (**8$_{a,b}$**) (Table I).

EXPERIMENTAL

All melting points were uncorrected and were determined on electric melting point apparatus. ^{1}H NMR spectra (DMSO-d_6 and $CDCl_3$), were carried out on a Bruker Avance 300 MHz spectrometer using TMS as internal reference chemical shift in δ, ppm).

Reaction of Compound (1) with p-Toluenesulfonyl Hydrazine—Formation of (2)

A mixture of compound **1** (1.42 g, 0.01 mol) and p-toluenesulfonyl hydrazine (1.86 g, 0.01 mol) in n-butanol (30 ml) was heated under reflux for 15 h; the solid produced after cooling was collected and crystallized from n-butanol into compound (**2**) m.p. 289–80°C.

Reaction of Compound (1) with Nitrous Acid—Formation of the Intermediate (3)

To an ice-cold solution of (**1**) (3 g) in dilute hydrochloric acid (35 ml), contained in 250 ml beaker, a solution of sodium nitrite (2.5 g) in cold water (20 ml) was added slowly. The resulting tetrazonium salt solution was stirred for 15 min at 0°C and used in the next experiments without isolation.

Reaction of 3 with Anthranilic Acid—Formation of (5)

To the tetrazonium salt solution **3** (2.2 g, 0.01 mol) anthranilic acid was added (1.37 g, 0.01 mol) and the mixture was stirred for 8 h, concentrated by evaporation under vacuum. The solid produced was collected and crystallized from dimethylformamide into compound (**5**), m.p 268°C.

Reaction of (3) with Semicarbazide and Thiosemicarbazide—Formation of ($\mathbf{6_{a,b}}$)

To the tetrazonium salt solution (**3**) (2.2 g, 0.01 mol), semicarbazide (0.75 g, 0.01 mol) and/or thiosemicarbazide (0.91 g, 0.01 mol) was added, and the reaction mixture was stirred for 12 h; the solid produced was collected and crystallized from n-butanol, $\mathbf{6_a}$, m.p. 229°C, $\mathbf{6_b}$, m.p. 253°C.

Reaction of 1 with Carbon Disulfide—Formation of the Dipotassium Salt (4)

A mixture of (**1**), (1.42 g, 0.01 mol) and potassium hydroxide (0.39 g, 0.01 mol) in carbon disulfide (60 ml) was heated on water bath at 60°C for 1 h; the reaction mixture was left to cool and used in the next experiment without separation.

Reaction of the Dipotassium Salt (4) with Ethylchloroformate—Formation of (7)

A mixture of (**4**), (3.7 g, 0.01 mol) and ethylchlorformate (0.96 g, 0.01 mol) was heated on water bath for 2 h; the solid produced after cooling was collected and crystallized from ethanol into compound (**7**), m.p. 218°C.

Reaction of the Tetrazonium Salt with Acid Hydrazide, Formation of ($8_{a,b}$)

To the tetrazonium salt solution (**4**) (3.7 g, 0.01 mol), benzoylhydrazine (1.3 g, 0.01 mol) and/or p-chlorobenzoylhydrazine (1.7 g, 0.01 mol) was added, and the reaction mixture was stirred for 18 h at room temperature, then concentrated by evaporation under reduced pressure, the solid produced was collected, washed with water and recrystallized from acetic acid into compounds $\mathbf{8_{a,b}}$, m.p. of $\mathbf{8_a}$ 261°C, m.p. of $\mathbf{8_b}$ 284°C.

CONCLUSION

The above work enables us to synthesize some new biologically active polynuclear heterocyclic compounds from simple monocyclic heteroyclic compounds.

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