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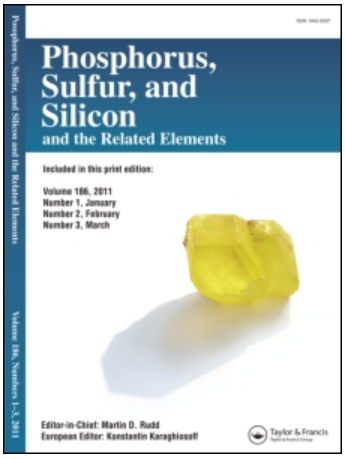

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SYNTHESIS OF SOME CONDENSED *s*-TRIAZOLE HETEROCYCLES USING PHASE-TRANSFER CATALYSIS TECHNIQUE

Adel A. Sultan[a]
[a] Chemistry Department, Faculty of Science, Sohag, Egypt

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SYNTHESIS OF SOME CONDENSED *s*-TRIAZOLE HETEROCYCLES USING PHASE-TRANSFER CATALYSIS TECHNIQUE

ADEL A. SULTAN
Chemistry Department, Faculty of Science, Sohag, Egypt

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Some condensed heterocyclic systems were obtained by reacting 3-phenyl-4-amino-*s*-triazole-5-thiol 1 as a dianionic ambident compound containing N^- and S^- poles with some tetrahalo- and dihalo derivatives as well as α-haloketones and α-halonitrile derivatives under solid-liquid phase-transfer catalysis conditions.

Key words: 3-Phenyl-4-amino-5-mercapto-*s*-triazole, mono, di- and tetrahalogeno compounds, phase transfer catalysis.

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INTRODUCTION

The use of 3-substituted-4-amino-5-mercapto-*s*-triazole in preparation of fused heterocyclic systems was studied under ordinary conditions; in some of these cases the desired product (e.g.; compound 2 and 3)[1] was isolated in one step, but sometimes (e.g., compound 6a)[2,3] separated in two steps in poor yields.

Phase-transfer catalysis (PTC), or more generally, application of two-phase systems is one of the most important recent techniques in organic synthesis.[4–17] It is important because it simplifies procedure, eliminates expensive, inconvenient, and dangerous reactions that otherwise proceed unsatisfactorily or do not proceed at all. PTC has been reviewed but only two reviews concern the chemistry of heterocyclic systems.[18,19] Thus owing to the important development of PTC technique, especially solid-liquid two-phase systems in heterocyclic chemistry,[20,21] we tried to apply this simple and rapid method to synthesize previously reported molecules as well as some new condensed systems.

RESULTS AND DISCUSSION

Our main substrate, namely, 3-phenyl-4-amino-*s*-triazole-5-thiol (1) reacted with four main groups of compounds, tetrahalogeno compounds (e.g. chloroanil (a)), dihalogeno compounds (e.g. 2,3-dichloroquinoxaline (b), 2,3-dichloronaphthoquinone (c) and dibromomethane (d)), α-haloketones (e.g. phenacyl bromide and its derivatives (e), ethyl chloroacetate (f)) and α-halonitrile (chloroacetonitrile (g)). A summary of the experimental conditions and results are listed in Table I and the general reaction types are summarized in Scheme I.

These reactions were carried out by stirring the substrates for 2 h at room temperature and for 2–4 h at 60°C under solid-liquid phase-transfer catalysis con-

TABLE I

Synthesis of some condensed *s*-triazole heterocycles using phase-transfer catalysis technique

Comp.	M.P.(°C)[a] (Cryst.Solv.)	Yield (%)	Time (hrs.)	Mol.F[b] (Mol.Wt.)	IR (KBr) λmax(cm^{-1})	^{1}H-HMR (DMSO-d_6), δ(ppm)
2	266 (EtOH)	85	4	$C_{22}H_{12}N_8S_2O_2$ (484.52)	1775(C=O), 3250(NH).	10.90(s,2H,2NH), 8.30-7.10(m,10H,arom.).
3	287 (EtOH)	77	5	$C_{16}H_{10}N_6S$ (318.35)	1600(C=N), 3180(NH).	9.80(s,1H,NH), 8.40-7.20(m,9H,arom.).
4	227 (benzene)	88	4	$C_{18}H_{10}N_4SO_2$ (346.35)	1670(C=O), 3220(NH).	10.60(s,1H,NH), 8.60-7.35(m,9H,arom.).
5	219 (Dioxan)	83	5	$C_9H_8N_4S$ (204.25)	1610(C=N), 3230(NH).	11.10(s,1H,NH), 8.20-7.25(m,5H,arom.), 5.25(s,2H,CH_2).
6a	248 (EtOH)	75	5	$C_{16}H_{12}N_4S$ (292.35)	1618(C=N).	8.10-7.15(m,10H,arom.), 4.60(s,2H,CH_2)
6b	293 (EtOH)	90	4	$C_{16}H_{11}N_5SO_2$ (337.35)	1620(C=N), 1560-1355 (NO_2)	8.90-7.60(m,9H,arom.), 4.60(s,2H,CH_2).
6c	230 ($CHCl_3$)	65	6	$C_{17}H_{14}N_4SO$ (322.37)	1600(C=N).	8.10-6.90(m,9H,arom.), 4.35(s,2H,CH_2),3.90 (s,3H,OCH_3).
7	173 (benzene)	85	4	$C_{12}H_{14}N_4SO_2$ (278.32)	1740-1725 (CO,ester), 3485-3315 (NH_2)	8.20-7.30(m,5H,arom.), 5.70(s,2H,NH_2),4.30-4.10(9,2H,CH_2CH_3), 4.00(s,2H,S-CH_2), 2.10-1.50(t,3H,CH_3).
8	280 (MeOH)	95	1	$C_{10}H_8N_4SO$ (232.26)	1780(C=N), 3200(NH)	12.00(s,1H,NH),8.15-7.30(m,5H,arom.), 4.50(s,2H,CH_2).
9	273 (EtOH)	73	5	$C_{10}H_9N_5S$ (231.27)	3440-3330 (NH_2)	8.40-7.30(m,5H,arom.), 7.10(s,2H,NH_2),3.90 (s,2H,CH_2).

[a] Reported melting points for compounds 2, 3 and 6a are 264 °C, 286 °C and 246 °C, respectively.

[b] Satisfactory microanalyses obtained; C; ±0.4%, N; ±0.4%, S; ±0.2%.

ditions; e.g. anhydrous potassium carbonate, with dry benzene as organic solvent and tetrabutylammonium bromide (TBAB) as catalyst.

The reactions were monitored by TLC. The structures of all products were investigated on the basis of microanalysis, ^{1}H-NMR and IR spectra (cf. Table I).

The reaction of compound 1 with chloroanil was carried out with two moles of

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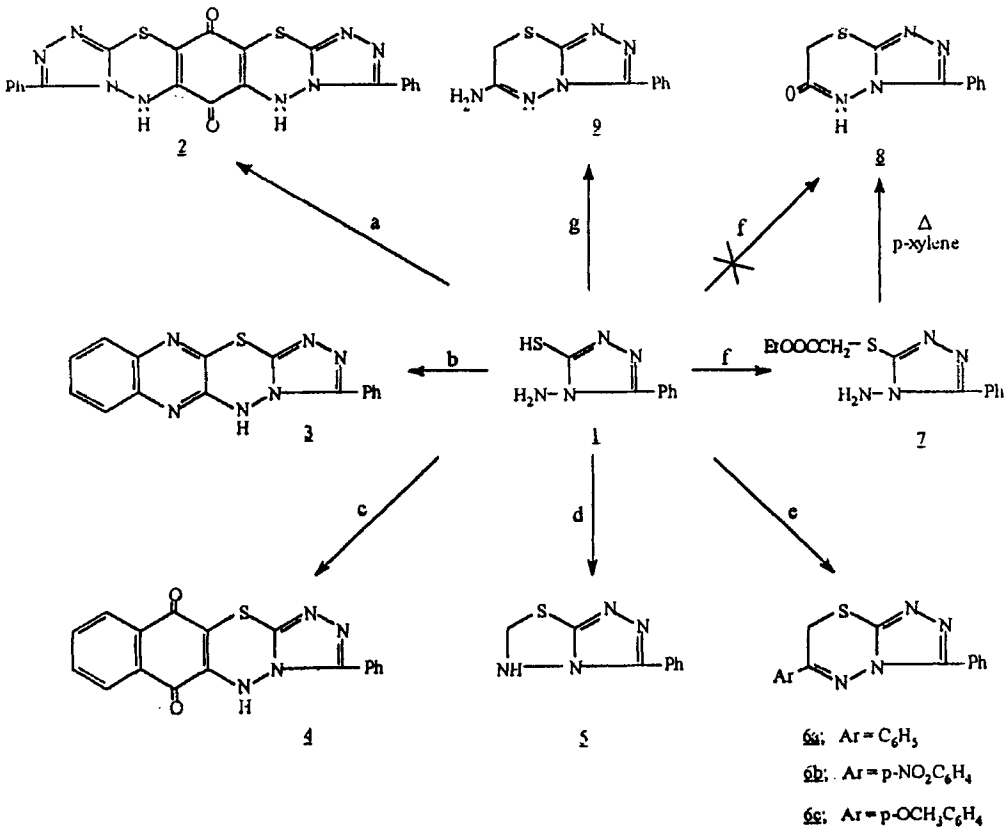

SCHEME I a; Chloroanil, b; 2,3-dichloroquinoxaline, c; 2,3-dichloronaphthoquinone, d; dibromomethane, e; $ArCOCH_2Br$, f; $ClCH_2COOEt$, g; $ClCH_2CN$.

the latter to give the expected product 2. In this case and with 2,3-dichloroquinoxaline (b) as well as 2,3-dichloronaphthoquinone (c) the reaction mechanism was assumed to involve addition to the double bond followed by attack of the carbanion generated to expel the halid ion.

Condensation of aryl aldehydes with active methylene was reported[21,22] to be easily performed using PTC conditions; similarly when compound 1 allowed to react with phenacyl bromide derivatives it gives the cyclized products 6a–c, most probably through S-alkylation followed by condensation of the amino group with the carbonyl group; the rate of the reaction was increased by introduction of electron-withdrawing group on the phenacyl bromide benzene ring (cf. Table I).

Cyclization in one step under PTC condition failed in the reaction of compound 1 with ethyl chloroacetate; thus we obtained the cyclized product 8 by heating its uncyclized form in high-boiling solvent e.g. *p*-xylene, in good yield.

The reaction of our substrate 1 with chloroacetonitrile was firstly also S-alkylation, then nucleophilic attack of the NH_2 group on the cyano group in one step under the same conditions.

The mechanisms leading to all heterocyclic systems containing bridgehead nitrogen atom were suggested in Scheme II, which indicate that compound 1 reacted

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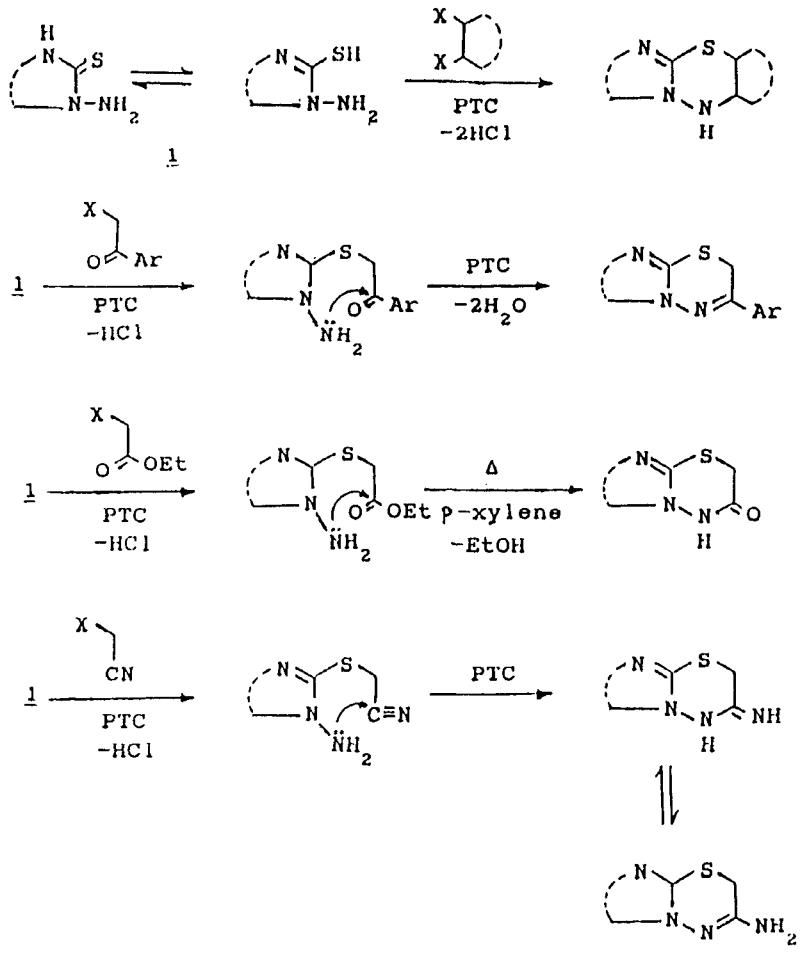

SCHEME II

with its thiol form under PTC conditions. These results were in accordance with those of Dou[23,24] as he arranged reactivity of the anionic poles in the order $S^- > N^- \simeq C^- > 0^-$.

EXPERIMENTAL

Melting points were determined using a Kofler bank and are uncorrected. The IR spectra were recorded on a Pye Unicam SP 1200 spectrophotometer. ^{1}H-NMR spectra were measured on a Varian EM 360L spectrometer using TMS as internal standard. Qualitative thin-layer analysis were carried out using nanoplates HPLC silica 5μ with methyl acetate-benzene (9:1) as eluent.

Synthesis of 3-phenyl-4-amino-s-triazole-5-thiol 1: This compound was prepared according to the method reported by Reid.[25]

Synthesis of Condensed s-triazoles 2–8

General procedure: To a suspension of 5 mmol of anhydrous K_2CO_3 in dry benzene (50 ml), compound 1 (3 mmol) was added and a catalytic amount of TBAB (0.05 g., ≃ 6% mol/mol of substrate) was

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added. The mixture was stirred and a solution of the appropriate reactant a–g (3 mmol) in dry benzene was added dropwise. The reaction was stirred for 2 h at room temperature, then at 60°C for 2–4 h whereby a noticeable change in color was observed. After completion of the reaction monitored by TLC the mixture was filtered, the organic layer was washed thoroughly with water, dried over magnesium sulfate overnight and evaporated *in vacuo*. The solid products thus obtained were recrystallized from the proper solvent (cf. Table I and Scheme I). Compound 8 was obtained by heating its uncyclized form 7 in *p*-xylene for 1 h.

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