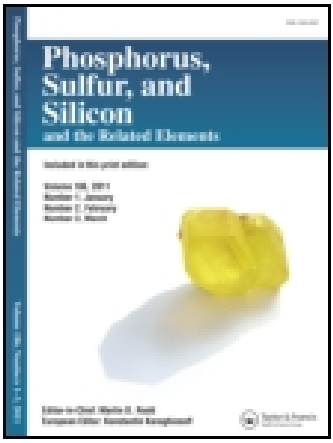

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SYNTHESIS OF SOME NEW FUSED AND POLYFUSED QUINOXALINES

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SYNTHESIS OF SOME NEW FUSED AND POLYFUSED QUINOXALINES

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2,3-Dimercaptoquinoxaline **1** was allowed to react with some dihalo compounds and chloroanil using PTC technique to afford the corresponding polyfused quinoxalines **2a-d**. The reaction of compound **1** with different monohalo compounds under the same PTC conditions or in refluxing ethanol in presence of piperidine catalyst gave (1,4)dithiino-, thieno-, (1,4)thiazino-, and pyrroloquinoxalines **3a-5b**. The addition of compound **1** to α,β-unsaturated nitriles was investigated to give the corresponding (1,5)dithiapinoquinoxalines **6a-7b** and thiapinoquinoxalines **8a,b**. The treatment of compound **1** with active nitriles furnished the corresponding thienoquinoxalines **9a-c** and pyridazinoquinoxaline **10**.

Keywords: quinoxalines; Phase-Transfer Catalysis; (1,4)dithiinoquinoxaline; thienoquinoxaline; (1,4)thiazinoquinoxaline; pyrroloquinoxaline; (1,5)dithiapinoquinoxaline

INTRODUCTION

The fungicidal, bactericidal and insecticidal activity[1–3]of some quinoxalines motivated us to synthesis some new fused and polyfused quinoxalines through the reaction of 2,3-dimercaptoquinoxaline with active halo compounds, active nitriles and the addition to α,β-unsaturated nitriles.

RESULTS AND DISCUSSION

In connection to our previous work[4–7] the application of PTC technique in the heterocyclic synthesis, 2,3-dimercaptoquinoxaline (quinoxa-

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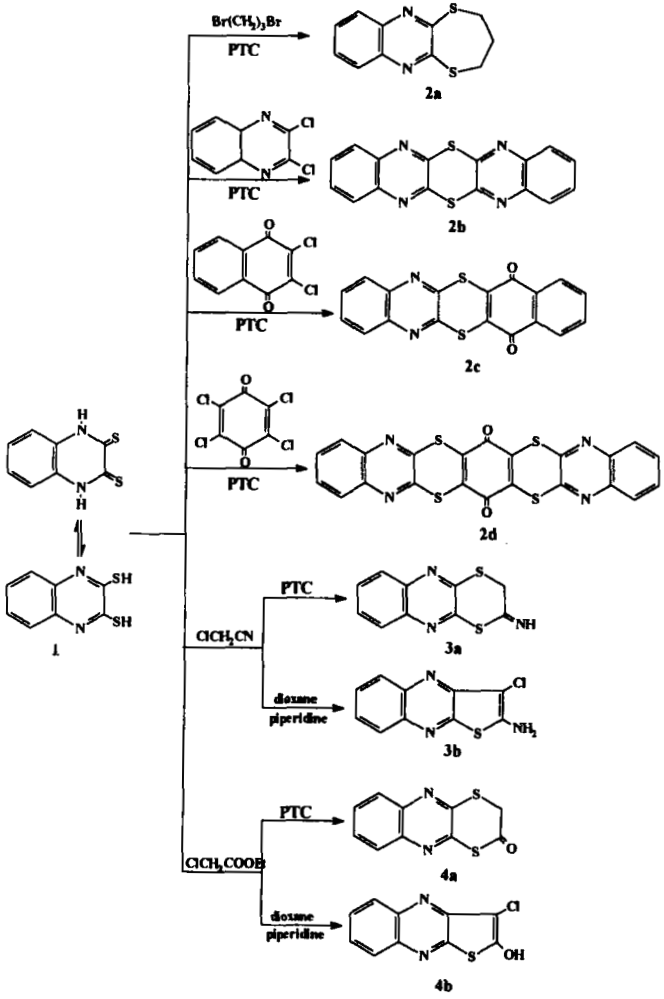
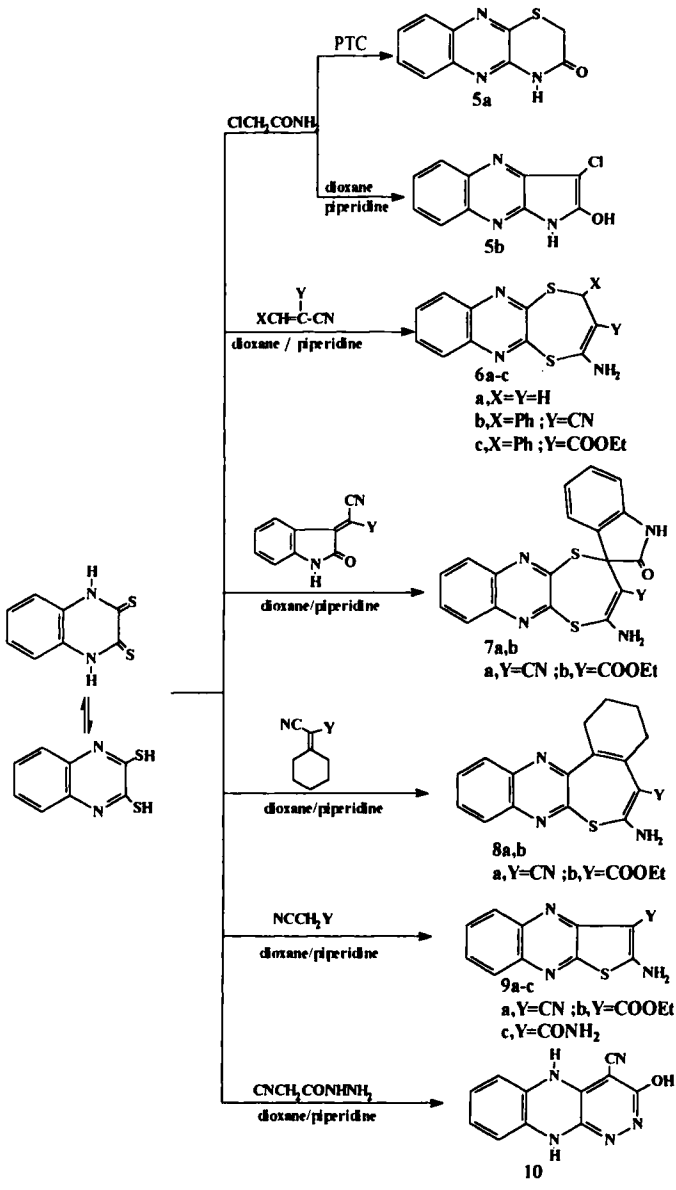
lin-2,3-dithione) **1** was allowed to react with 1,3-dibromopropane, 2,3-dichloroquinoxaline[8], 2,3-dichloro-1,4-naphthoquinone in 1:1 molar ratio or with chloroanil in 2:1 molar ratio under solid-liquid phase-transfer catalysis (PTC) conditions [dioxan/k_2CO_3/tetrabutylammonium bromide (TBAB)] to give the corresponding polyfused quinoxalines **2a-d**, respectively (cf. Scheme **1**, Table I). The mechanism cycle was explained in our previous work[7].



SCHEME 1



SCHEME 1 (continued)

TABLE I Analytical and spectral data of the prepared compounds

action ditions (mL)/ ap.(°C)	*M.P.*[a] *(cryst. solv.)*	*Yield %*	*Mol. formula (Mol. wt.)*	*Analytical Data*[b] *Cal./Foumd*				*IR (Kbr)*[c] *ν (Cm^{-1})*	*^{1}H-NMR (DMSO-d_6)*[d] *δ (ppm)*
				C	*H*	*N*	*S*		
2/65	277.79	85	$C_{11}H_{10}N_2S_2$	56.38	4.30	11.95	27.36		8.10–7.35 (m, 4H, arm.); 2.65–2 25 (t,
	(aq.dioxan)		(234.34)	56.21	4.43	11.78	27.51		$2CH_2$); 1.20–0.85 (m, 2H, CH_2).
3/65	> 300	90	$C_{18}H_8N_2O_2S_4$	62.05	2.31	8.04	18.41	1683 (CO).	8.15–6.90 (m, 8H, arm.).
	(aq. DMSO)		(348.40)	62.31	2.19	8.28	18.20		
4/75	> 300	83	$C_{20}H_8N_4O_2S_4$	51.71	1.74	12.06	27.61	1678 (CO).	8.15–7.25 (m, 8H, arm.).
	(aq. DMSO)		(464.57)	51.50	1.91	12.19	27.43		
2/50	199–200	72	$C_{10}H_7N_3S_2$	51.48	3.02	18.01	27.49	3238,(NH).	10.85 (s, 1H, NH); 8.15–7.25 (m, 4H, a
	(chloroform)		(233.32)	51.72	3.19	17.82	27.29		4.10 (s, 2H, CH_2).
v/ref.	174–75	68	$C_{10}H_6Cl\,N_3S$	50.96	2.57	17.83	13.60	3256,3148 (NH_2).	8.10–7.30 (m, 4H, arm.); 4.65 (s, 2H, N
	(chloroform/ pet. ether)		(235.70)	50.72	2.78	17.64	13.39		
3/65	651–52	76	$C_{10}H_7N_2OS_2$	51.04	2.10	11.90	27.25	3320(NH); 1701 (CO).	8.20–7.35 (m, 4H, arm.); 4.25 (s, 2H C
	(chloroform /benzene)		(235.31)	51.28	2.29	11.71	27.51		
v/ref.	164–65	74	$C_{10}H_6ClON_2S$	50.53	2.54	11.79	13.49	3342 (NH); 3420 (OH).	11.15 (s, 1H, NH); 8.15–7.25 (m, 4H, a
	(ethanol)		(237.69)	50.30	2.35	11.98	13.21		3.85 (s, 1H, OH).

action ifibns n(h)/ p.(°C)	M.P.[a] (cryst. solv.)	Yield %	Mol. formula (Mol. wt.)	Analytical Data[b] Cal./Foumd				IR (Kbr)[c] ν (Cm^{-1})	^{1}H-NMR (DMSO-d_6)[d] δ (ppm)
				C	H	N	S		
/7a	261–62	69	$C_{10}H_7N_3OS$	55.29	3.25	19.34	14.76	3235 (NH).	9.95 (s, 1H, NH), 8.10–7.35 (m, 4H, aro 4.25 (s, 2H, CH_2).
	(methanol)		(217.25)	55.51	3.49	19.13	14.57		
/ref.		69	$C_{10}H_6ClN_3O$	54.69	2.75	19.13		3420 (OH), 3132 (NH).	10.75 (s, 1H, NH); 8.15–7.35 (m, 4H, ar 3.45 (s, 1H, OH).
			(219.63)	54.48	2.54	19.27			
/ref.	230–32	78	$C_{11}H_9N_3S_2$	53.42	3.67	16.99	25.93	3252, 3149 (NH_2).	8.10–7.25 (m, 4H, arom.); 5.45 (s, 2H, N 3.75–3.35 (t, 1H, CH); 3.15–2.95 (d, 2H
	(methanol)		(247.34)	53.58	3.49	16.71	25.78		
/ref.	154–56	73	$C_{18}H_{12}N_4S_2$	62.05	3.47	16.08	18.40	3279, 3175 (NH_2): 2210 (CN).	8.15–6.75 (m, 9H, arom.); 5.60 (s. 2H. N 3.85–3.65 (d. 1H, CH).
	(chloroform /benzene)		(348.45)	62.29	3.31	16.25	18.58		
/ref.	130–32	68	$C_{20}H_{17}N_3O_2S_2$	60.74	4.33	10.62	16.21	3343, 3251 (NH_2); 1710 (CO).	8.30–6.95 (m, 9H, arom.); 5.75 (s, 2H. N 4.35–4.10 (q, 2H, CH_2); 1.10-0.85 (t, 3H CH_3).
	(chloroform/ benzene)		(395.51)	60.51	4.57	10.81	16.09		
/ref.	215–17	63	$C_{19}H_{11}N_5OS_2$	58.60	2.85	17.98	16.47	3378, 3289, 3178 (NH, NH_2); 2198 (CN); 1723 (CO).	11.35 (s. 1H, NH); 8.10–6.95 (m, 8H, ar 6.15 (s, 2H, NH_2).
	(aq. dioxan)		(389.46)	58.39	2.67	18.14	16.66		
/ref.	185–87	65	$C_{21}H_{16}N_4O_3S_2$	57.78	3.69	12.84	14.69	3363, 3275, 3172 (NH, NH_2); 1723, 1715 (CO).	11.25 (s, 1H, NH); 8.20–6.95 (m, 8H. ar 5.85 (s, 2H, NH_2); 4.25–3.95 (q, 2H, CH 1.15–0.95 (t, 3H, CH_3).
	(aq. dioxan)		(436.51)	57.99	3.52	12.98	14.52		

action ditions n(h)/ p(°C)	M.P.[a] (cryst. solv.)	Yield %	Mol. formula (Mol. wt.)	Analytical Data[b] Cal./Foumd				IR (Kbr)[c] ν (Cm^{-1})	^{1}H-NMR (DMSO-d_6)[d] δ (ppm)
				C	H	N	S		
/ref.	150–51	76	$C_{17}H_{14}N_4S$	66.64	4.61	18.29	10.47	3312, 3210 (NH_2); 2220 (CN).	8.05–7.25 (m, 4H, arom.); 5.65 (s, 2H.
	(ethanol)		(306.39)	66.83	4.45	18.40	10.61		1.35–1.05 (t, 4H, $2CH_2$); 0.95-0.40 (m, $2CH_2$).
/ref.	204–6	71	$C_{19}H_{19}N_3O_2S$	64.57	5.42	11.89	9.07	3313, 3210 (NH_2) 1717 (CO).	8.10–7.30 (m, 4H, arom.); 5.75 (s, 2H,
	(ethanol)		(353.45)	64.79	5.61	11.72	8.89		4.30–3.95 (q, 2H, CH_2); 1.35-0.45 (m, $4CH_2$+ CH_3).
/ref.	222–23	69	$C_{11}H_6N_4S$	58.39	2.67	24.76	14.17	3320, 3221 (NH_2) 2210 (CN).	8.15–7.25 (m, 4H, arom.); 6.10 (s, 2H,
	(methanol)		(226.26)	58.58	2.81	24.51	14.35		
/ref.	142–43	64	$C_{13}H_{11}N_3O_2S$	57.13	4.06	15.37	11.73	3319, 3217 (NH_2) 1715 (CO).	8.15–7.25 (m, 4H, arom.); 5.45 (s, 2H,
	(methanol)		(273.32)	57.32	4.24	15.54	11.90		4.25–3.95 (q, 2H, CH_2); 1.15-0.85 (t, 3H CH_3).
/ref.	118–20	61	$C_{11}H_8N_4OS$	54.09	3.30	22.94	13.13	3340, 3238, 3129 ($2NH_2$); 1685 (CO).	8.25–7.35 (m, 4H, arom.); 5.25 (s, 2H.
	(methanol)		(244.28)	54.29	3.12	22.75	13.28		3.15 (s. 2H, NH_2).
/ref.	205–7	59	$C_{11}H_7N_4O$	62.56	3.34	26.53		3425 (OH); 3155, 3135 (2NH).	11.35 (s. 1H, NH); 10.85 (s, 1H, NH); 8
	(ethanol)		(211.20)	62.80	3.18	26.38			7.35 (m. 4H, arom.); 2.95 (s, 1H, OH)

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The reaction of compound **1** with chloroacetonitrile, ethyl chloroacetate or chloroacetamide proceeds differently according to the reaction conditions. When the reaction was carried out under PTC conditions it gave the corresponding (1,4)dithiinoquinoxalines **3a, 4a** or (1,4)thiazinoquinoxaline derivative **5a**. But, when the reaction was carried out in refluxing dioxan in the presence of piperidine as catalyst it yielded the corresponding thienoquinoxalines **3b, 4b** or pyrroloquinoxaline derivative **5b** In case of PTC conditions the postulated reaction mechanism was assumed to follow alkylation to one of the SH groups followed by nucleophilic attack of the second SH group to the cyano group or the carbonyl ester with elimination of ethanol to give **3a** or **4a**. Compound **5a** was formed via alkylation of the SH group followed by condensation between the thiono group and the amidic NH_2group. While in the case when using piperidine as catalyst, formation of compounds **3b** and **4b** may be rationalized in terms of a condensation between the thiono group and the active methylene group followed by nucleophilic attack of the SH group to the cyano group or the carbonyl ester group. Compound **5b** was formed through the condensation of the two thiono groups with the active methylene group and the amidic NH_2 group (cf. Scheme 1, Table I).

The addition of compound **1** to α,β-unsaturated nitriles was investigated where compound **1** was treated with acrylonitrile, benzylidenemalononitrile, ethyl benzylidenecyanoacetate, 2-(2-oxo-2,3-dihydro-1H-indolid-3-ene)malononitrile, ethyl 2-(2-oxo-2,3-dihydro-1H-indolid-3-ene)cyanoacetate, cyclohexylidenemalononitrile or ethyl cyclohexylidenecyanoacetate to give the cyclized compounds **6a-c – 8a,b**. It may be suggested that the formation of compounds **6a-c** and **7a,b** should proceed through the addition of the SH group of compound **1** to the C-C double bond followed by cycloaddition of the second SH group to the cyano group. While the formation of compounds **8a,b** was assumed to proceed via firstly a condensation between the thiono group of compound **1** and the active methylene group in the 2-position of cyclohexylidenemalononitrile or ethyl cyclohexylidenecyanoacetate followed by addition of the SH group of compound **1** to the cyano group.

Treatment of compound **1** with malononitrile, ethyl cyanoacetate, cyanoacetamide or cyanoacetohydrazide in refluxing dioxan in the presence of piperidine as catalyst afforded thienoquinoxalines **9a-c** or pyridazinoquinoxaline **10**. The reaction pathway was suggested to proceed through the condensation between the thiono group of compound **1** and the

active methylene group followed by intramolecular cyclization via addition of the SH group to the cyano group to form compounds **9a-c**. While the formation of compound **10** was assumed to proceed through a condensation of the two thiono groups of compound **1** with the active methylene group and the amino group of the hydrazide compound.

EXPERIMENTAL

Reactions of compound 1 with di and polyhalo compounds

Synthesis of compounds 2a-d
General procedure

To a mixture of anhydrous potassium carbonate (4g), dry dioxan (50 ml), compound **1** (0.01 mol) and a catalytic amount of TBAB was added an equimolar amount of 1,3-dibromopropane, 2,3-dichloroquinoxaline or 2,3-dichloro-1,4-naphthoquinone or (0.005 mol) of chloroanil. The reaction mixtures were stirred over different periods of time at different temperatures (cf. Table I) till the completion of the reaction (TLC). The reaction mixtures were filtered, the filtrate was evaporated in *vacuo*. The solid residue was washed with water and crystallized from aq. dioxan where compound **2a** was obtained. The residual solid potassium carbonate was dissolved in distilled water (50 ml). The separated solid was collected by filtration and crystallized from the suitable solvent where compounds **2b-d** were obtained (cf. Table I, Scheme 1).

Reactions of compound 1 with monohalo compounds

A) Under PTC conditions

Synthesis of compounds 3a, 4a and 5a
General procedure:

A mixture of 4g anhydrous potassium carbonate, compound **1** (0.01 mol), dry dioxan (50 ml) and catalytic amount of TBAB was treated with 0.01 mole of chloroacetonitrile, ethyl chloroacetate or chloroacetamide. The reaction mixtures were stirred for a period of time 2–4 h at different temperatures. The reaction mixture was filtered, the filtrate was

evaporated in *vacuo*. The residue was treated with pet. ether/$CHCl_3$ to give a solid which was crystallized from chloroform when compound **3a** was obtained. The solid potassium carbonate was dissolved in distilled water (50 ml) and acidified with HCl and the separated solid was collected by filtration and crystallized from the proper solvent where compounds **4a** and **5a** were obtained (cf. Scheme 1, Table I).

B) In presence of piperedine catalyst

Synthesis of compounds 3b, 4b and 5b
General procedure

A solution of an equimolar amount (0.01 mol) of compound **1** and chloroacetonitrile, ethyl chloroacetate or chloroacetamide in dioxan (50 ml) was treated with catalytic amount of piperedine and refluxed for 6 h. The solvent was evaporated in *vacuo* and the residue treated with pet. ether/$CHCl_3$ and the separated solid was crystallized from a suitable solvent (cf. Scheme **1**Table I).

Addition of compound 1 to α,β-unsaturated nitriles

Synthesis of compounds 6a-c – 8a,b
General procedure

An equimolar amount (0.01 mol) of compound **1** and acrylonitrile, or the proper ylidenemalononitrile or ethyl ylidenecyanoacetate were dissolved in dioxan (50 ml), treated with two drops of pipredine and refluxed for different periods of time. The reaction mixtures were evaporated in *vacuo* and the residues were treated with pet. ether/$CHCl_3$ and the separated solids were collected by filtration and crystallized from a suitable solvent (cf. Scheme 1, Table I).

Reactions of compound 1 with active nitriles

Synthesis of compounds 9a-c and 10
General procedure

To a solution of compound **1** (0.01 mol) in dioxan (50 ml) was added an equimolar amount of malononitrile, ethyl cyanoacetate, cyanoacetamide

or cyanoacetohydrazide. The reaction mixture was treated with few drops of piperedine and refluxed over different periods of time. The solvent was evaporated in *vacuo* and the residue was treated with pet. ether/$CHCl_3$. The separated solid was collected by filtration and crystallized from a proper solvent (cf Scheme **1**, Table I).

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