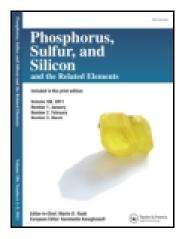
This article was downloaded by: [University of Auckland Library] On: 08 October 2014, At: 13:25 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/gpss20</u>

SYNTHESIS OF SOME NEW FUSED AND POLYFUSED QUINOXALINES

H. Abdel-Ghany ^a

^a Department of Chemistry, Faculty of Science , South Valley University , Sohage, Egypt Published online: 27 Oct 2006.

To cite this article: H. Abdel-Ghany (2000) SYNTHESIS OF SOME NEW FUSED AND POLYFUSED QUINOXALINES, Phosphorus, Sulfur, and Silicon and the Related Elements, 164:1, 259-268, DOI: <u>10.1080/10426500008045251</u>

To link to this article: http://dx.doi.org/10.1080/10426500008045251

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions Phosphorus, Sulfur and Silicon, 2000, Vol. 164, pp. 259-268 Reprints available directly from the publisher Photocopying permitted by license only © 2000 OPA (Overseas Publishers Association) Amsterdam N.V. Published under license by the Gordon and Breach Science Publishers imprint. Printed in Malaysia

SYNTHESIS OF SOME NEW FUSED AND POLYFUSED QUINOXALINES

H. ABDEL-GHANY*

Department of Chemistry, Faculty of Science, South Valley University, Sohage, Egypt

(Received March 23, 1999; In final form April 20, 2000)

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

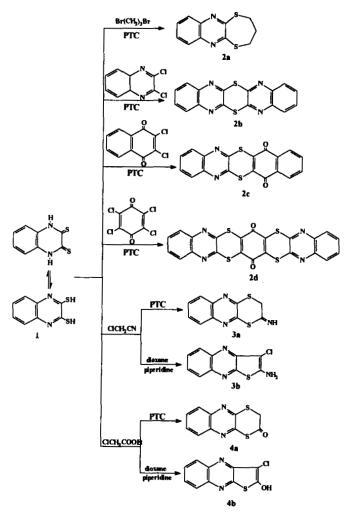
The fungicidal, bactericidal and insecticidal activity¹⁻³ of some quinoxalines motivated us to synthesis some new fused and polyfused quinoxalines through the reaction of 2,3-dimercaptoquinoxaline with active halo compounds, active nitriles and the addition to α , β -unsaturated nitriles.

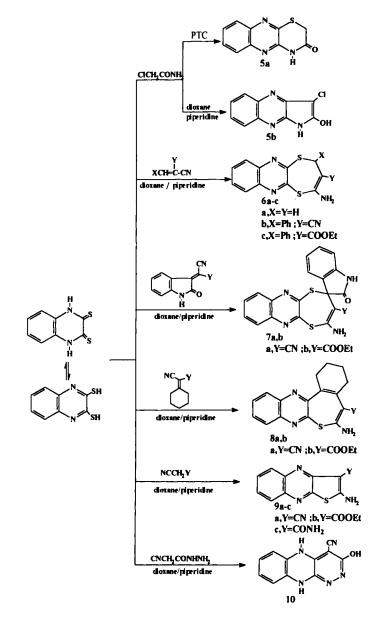
RESULTS AND DISCUSSION

In connection to our previous work⁴⁻⁷ the application of PTC technique in the heterocyclic synthesis, 2,3-dimercaptoquinoxaline (quinoxa-

^{*} Corresponding Author.

lin-2,3-dithione) 1 was allowed to react with 1,3-dibromopropane, 2,3-dichloroquinoxaline⁸, 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/k₂CO₃/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 work⁷.





SCHEME 1 (continued)

014			TABLE I A	nalytic	a of the prepared compo	f the prepared compounds			
aëtion dHions mUn)/	M.P. ^a (cryst. solv.)	Yield %	Mol. formula (Mol. wt.)			cal Da Fouma		IR (Kbr) ^c ∨ (Cm ⁻¹)	¹ H-NMR (DMSO-d ₆) ^d δ (ppm)
				C	H	N	S		
ues	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, 2CH ₂); 1.20-0.85 (m, 2H, CH ₂).
13:	(aq.dioxan)		(234.34)	56.21	4.43	11.78	27.51		
<i>1</i> 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.).
ary	(aq. DMSO)		(348.40)	62.31	2.19	8.28	18.20		
<u>A</u>	> 300	83	$\mathrm{C_{20}H_8N_4O_2S_4}$	51.71	1.74	12.06	27.61	1678 (CO).	8.15-7.25 (m, 8H, arm.).
pun	(aq. DMSO)		(464.57)	51.50	1.91	12.19	27.43		
<i>ឝ</i> ўо	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 4.10 (s, 2H, CH ₂).
Au	(chloroform)		(233.32)	51.72	3.19	17.82	27.29		
nef.	174–75	68	C ₁₀ H ₆ Cl N ₃ S	50.96	2.57	17.83	13.60	3256,3148 (NH ₂).	8.10-7.30 (m, 4H, arm.); 4.65 (s, 2H, N
iversit	(chloroform/ pet. ether)		(235.70)	50.72	2.78	17.64	13.39		
କ୍ତି	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
sd by	(chloroform /benzene)		(235.31)	51.28	2.29	11.71	27.51		
ind.	164-65	74	C ₁₀ H ₆ CION ₂ S	50.53	2.54	11.79	13.49	3342 (NH); 3420 (OH).	11.15 (s, 1H, NH); 8.15–7.25 (m, 4H, a
Downlonded by [Gniversitynt] Aucとand Lybrary] හි 13:2 හි 08 වී ර	(ethanol)		(237.69)	50.30	2.35	11.98	13.21		3.85 (s, 1H, OH).

tition titions u(D)/ u(D)/ p.C)	M.P. ^a (cryst. solv.)	Yield %	Mol. formula (Mol. wt.)	Analytical Data ^b Cal./Foumd				IR (Kbr) ^c	^I H-NMR (DMSO-d ₆) ^d δ(ppm)
				C	H	N	S	$\vee (Cm^{-1})$	
y] at 13.25 0830	261-62	69	C ₁₀ H ₇ N ₃ OS	55.29	3.25	19.34	14.76	3235 (NH).	9.95 (s, 1H, NH), 8.10-7.35 (m, 4H, aro
	(methanol)		(217.25)	55.51	3.49	19.13	14.57		4.25 (s, 2H, CH ₂).
		69	C ₁₀ H ₆ CIN ₃ O	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			
r et	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
d Li	(methanol)		(247.34)	53.58	3.49	16.71	25.78		3.75–3.35 (t, 1H, CH); 3.15–2.95 (d, 2H
Auckena	15456	73	$C_{18}H_{12}N_4S_2$	62.05	3.47	16.08	18.40	3279, 3175 (NH ₂):	8.15-6.75 (m, 9H, arom.); 5.60 (s. 2H. N
	(chloroform /benzene)		(348.45)	62.29	3.31	16.25	18.58	2210 (CN).	3.85–3.65 (d. 1H, CH).
ref	130-32	68	C ₂₀ H ₁₇ N ₃ O ₂ S ₂	60.74	4.33	10.62	16.21	3343, 3251 (NH ₂);	8.30-6.95 (m, 9H, arom.); 5.75 (s, 2H. N
iversit	(chloroform/ benzene)		(395.51)	60.51	4.57	10.81	16.09	1710 (CO).	4.35–4.10 (q, 2H, CH ₂); 1.10-0.85 (t, 3H CH ₃).
Downloaded by [Eniversite of Auck and Lilfary] at 13.25 082 crabe	215-17	63	$C_{19}H_{11}N_5OS_2$	58.60	2.85	17.98	16.47		11.35 (s. 1H, NH); 8.10-6.95 (m, 8H, ar
	(aq. dioxan)		(389.46)	58.39	2.67	18.14	16.66	NH ₂); 2198 (CN); 1723 (CO).	6.15 (s, 2H, NH ₂).
	185-87	65						NUL 1. 1703 1716	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
	(aq. dioxan)		(436.51)	57.99	3.52	12.98	14.52	(CO).	1.15–0.95 (t, 3H, CH ₃).

						6		
M.P. ^a (cryst. solv.)	Yield	•					$\frac{IR (Kbr)^c}{\vee (Cm^{-1})}$	¹ H-NMR (DMSO-d ₆) ^d δ (ppm)
	70	(MOI. WI.)	С	H	N	S		
150-51	76	C ₁₇ H ₁₄ N ₄ S					3312, 3210 (NH ₂); 2220 (CN).	8.05–7.25 (m, 4H, arom.); 5.65 (s, 2H. 1.35–1.05 (t, 4H, 2CH ₂); 0.95-0.40 (m, 2CH ₂).
(ethanol)		(306.39)	66.83	4.45	18.40	10.61		
204 -6	71							8.10-7.30 (m, 4H, arom.); 5.75 (s, 2H, 4.30-3.95 (q, 2H, CH ₂); 1.35-0.45 (m,
(ethanol)		(353.45)	64.79	5.61	11.72	8.89	(CO).	$4.50-5.55$ (q, 211, CH ₂), $1.55-0.45$ (m, $4CH_2+CH_3$).
222–23	69	C ₁₁ H ₆ N ₄ S						8.15-7.25 (m, 4H, arom.); 6.10 (s, 2H, 1
(methanol)		(226.26)	58.58	2.81	24.51	14.35		
142-43	64							8.15–7.25 (m, 4H, arom.); 5.45 (s, 2H, 1 4.25–3.95 (q, 2H, CH ₂); 1.15-0.85 (t, 3 CH ₃).
(methanol)		(273.32)	57.32	4.24	15.54	11. 9 0		
118-20	61	C ₁₁ H ₈ N ₄ OS	54.09	3.30	22. 9 4	13.13	3340, 3238, 3129 (2NH ₂); 1685 (CO).	8.25–7.35 (m, 4H, arom.); 5.25 (s, 2H.) 3.15 (s. 2H, NH ₂).
(methanol)		(244.28)	54.29	3.12	22.75	13.28		
205-7	59	C ₁₁ H ₇ N ₄ O	62.56	3.34	26.53			11.35 (s. 1H, NH); 10.85 (s, 1H, NH); 8 7.35 (m. 4H, arom.); 2.95 (s, 1H, OH)
(ethanol)		(211.20)	62.80	3.18	26.38		(2N N).	7.55 (m. 4H, atom.), 2.55 (s, 1H, OH)
-	(cryst. solv.) 150–51 (ethanol) 204–6 (ethanol) 222–23 (methanol) 142–43 (methanol) 118–20 (methanol) 205–7	(cryst. solv.) % 150-51 76 (ethanol) 71 204-6 71 (ethanol) 222-23 69 (methanol) 4 142-43 64 (methanol) 61 118-20 61 (methanol) 59	(cryst. solv.) % (Mol. wt.) 150-51 76 C ₁₇ H ₁₄ N ₄ S (ethanol) (306.39) 204-6 71 C ₁₉ H ₁₉ N ₃ O ₂ S (ethanol) (353.45) 222-23 69 C ₁₁ H ₆ N ₄ S (methanol) (226.26) 142-43 64 C ₁₃ H ₁₁ N ₃ O ₂ S (methanol) (273.32) 118-20 61 C ₁₁ H ₈ N ₄ OS (methanol) (244.28) 205-7 59 C ₁₁ H ₇ N ₄ O	M.P.ª (cryst. solv.) Yield % Mol. formula (Mol. wt.)	M.P. ^a (cryst. solv.) Yield % Mol. formula (Mol. wt.) Cal.// 150-51 76 $C_{17}H_{14}N_{4}S$ 66.64 4.61 (ethanol) (306.39) 66.83 4.45 204-6 71 $C_{19}H_{19}N_3O_2S$ 64.57 5.42 (ethanol) (353.45) 64.79 5.61 222-23 69 $C_{11}H_6N_4S$ 58.39 2.67 (methanol) (226.26) 58.58 2.81 142-43 64 $C_{13}H_{11}N_3O_2S$ 57.13 4.06 (methanol) (273.32) 57.32 4.24 118-20 61 $C_{11}H_8N_4OS$ 54.09 3.30 (methanol) (244.28) 54.29 3.12 205-7 59 $C_{11}H_7N_4O$ 62.56 3.34	M.P. ^a (cryst. solv.) Yield % Mol. formula (Mol. wt.) Cal./Founda C Cal./Founda Mol. 150-51 76 $C_{17}H_{14}N_{4}S$ 66.64 4.61 18.29 (ethanol) (306.39) 66.83 4.45 18.40 204-6 71 $C_{19}H_{19}N_{3}O_{2}S$ 64.57 5.42 11.89 (ethanol) (353.45) 64.79 5.61 11.72 222-23 69 $C_{11}H_{6}N_{4}S$ 58.39 2.67 2.4.76 (methanol) (226.26) 58.58 2.81 24.51 142-43 64 $C_{13}H_{11}N_{3}O_{2}S$ 57.32 4.06 15.37 (methanol) (273.32) 57.32 3.00 22.94 118-20 61 $C_{11}H_{8}N_{4}OS$ 54.09 3.02 22.94 (methanol) (244.28) 54.29 3.12 22.75 205-7 59 $C_{11}H_{7}N_{4}O$ 62.56 3.42 5.53	$\begin{array}{c cryst. solv. } \end{picture} \begin{tabular}{ cryst. solv. } \end{picture} $	$\begin{array}{c cryst. solv.} \begin{array}{c cryst. solv.} \begin{array}{c cryst. solv.} \end{array} \end{array} \begin{array}{c cryst. solv.} \end{array} \end{array} \begin{array}{c cryst. solv.} \end{array} \begin{array}{c cryst. solv.} \end{array} \end{array} \end{array} \begin{array}{c cryst. solv.} \end{array} \end{array} \begin{array}{c cryst. solv.} \end{array} \end{array} \end{array} \end{array} \end{array} \end{array} \begin{array}{c cryst. solv.} \end{array} \end{array} \end{array} \end{array} \end{array} \end{array} \begin{array}{c cryst. solv.} \end{array} \end{array}$

ctèd.

QUINOXALINES

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 NH₂group. 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 NH₂ 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, benzylidenemalononibenzylidenecyanoacetate, 2-(2-oxo-2,3-dihytrile. ethyl dro-1H-indolid-3-ene)malononitrile. ethvl 2-(2-oxo-2.3-dihvdro-1Hindolid-3-ene)cyanoacetate. cyclohexylidenemalononitrile or ethvl 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

QUINOXALINES

evaporated in *vacuo*. The residue was treated with pet. ether/CHCl₃ 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/CHCl₃ and the separated solid was crystallized from a suitable solvent (cf. Scheme 1Table 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/CHCl₃ 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/CHCl₃. The separated solid was collected by filtration and crystallized from a proper solvent (cf Scheme 1, Table I).

References

- 1. Lane, D. W. G.; Newbold, G. T.; Brit. Pat. 1 041 011; C.A. 60, 15891 (1964).
- Fisher, G. H.; Moreno, H. R.; Oits, J. E.; Schultz, H. P.; Oits, J. M., and Schultz H. P., J. Med. Chim., 18, 746 (1975).
- 3. Davis, M.L., U.S. Pat. 3, 852, 443; C.A. 83, 48193f (1975).
- El-Shafei, A. K., El-Sayed, A. M.; Sultan, A. A. and Abdel-Ghany, H.; Gazz. Chem. Ital., 120, 197 (1990).
- El-Shafei, A. K.; Abdel-Ghany, H.; Sultan, A. A. and El-Saghier, A. M. M.; Phosphorus, Sulfur and Silicon, 73, 15 (1992).
- Abdel-Ghany, H.; El-Sayed, A. M. and El-Shafei, A. K., Synth. Comm., 25, 1119 (1995).
- 7. Abdel-Ghany, H.; Phosphorus, Sulfur and Silicon, 122, 173 (1997).
- 8. Wojciechowski, L., Rocz. Chem., 43, 1205 (1969).

Downloaded by [University of Auckland Library] at 13:25 08 October 2014