Preparation and Reactions of 5H-1, 2-Dithiepin-5-thiones

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Summary: A new series of 5H-1,2-dithiepin-5-thiones were prepared from the reaction of 1,5-diarylpent-1-yne-3,5-diones and phosphorus pentasulfide. Some reactions of these dithiepins were studied and the structure of the parent compounds as well as all the products was confirmed from their spectral characteristics.

Relatively few examples of 5H-1,2-dithiepin-5-thiones are reported in literature. The synthesis of these thiones involve the reaction of phosphorus pentasulfide with 1,3,5-triones [1-3] or 5H-1,2-dithiepin-5-one derivatives [4,5]. They were also formed from the reaction of 4H-pyran-4-thiones and potassium hydrogen sulfide [6]. In the present study, a new route to these cyclic disulfides is described. A series of 3-aryl-7-phenyl-5H-1,2-dithiepin-5-thiones (5a-g) were obtained from 1,5-diarylpent-1-yne-3,5-diones (1a-g) [7,8] and phosphorus pentasulfide in dry benzene.

The mechanism of the formation of the 1,2-dithiepins (5) is assumed to proceed by initial formation of 1,5-diarylpent-1-yne-3, 5-dithiones (2) followed by addition of hydrogen sulfide molecule on the triple bond leading to the trithiones (4). Subsequent oxidation of the latter affords the 1,2-dithiepins. The intermediacy of the trithiones in the above reaction is supported by the fact that 1,2-dithiepins (5a-c) were also formed from the reaction of triketones (3a-c) [9] and phosphorus pentasulfide (Scheme I).

The structure of the 5H-1,2-dithiepin-5-thiones was confirmed from their analytical and spectral data. The ^{1}H-NMR spectra of these compounds showed a singlet at δ 8.20-8.69 for the C-4 and C-6 ring protons (Table-I).

The significant deshielding in the signals of the α-vinylic protons can be attributed to increased magnetic anisotropy of the thione over carbonyl. Such behaviour was also reported for 2H-pyran-2-thiones [10,11], 4H-pyran-4-thiones [7,12] and 2-pyridthiones [13]. The electronic spectra of these dithiepins (5a-g) are characterized by three absorption maxima in the ranges 251-255, 294-314, and 504-512 nm, besides a shoulder in the region 346-360 nm. The position as well as the intensity of these absorptions were not affected in the presence of 0.1 M sodium methoxide or 0.1 M sulfuric acid (Table-I).

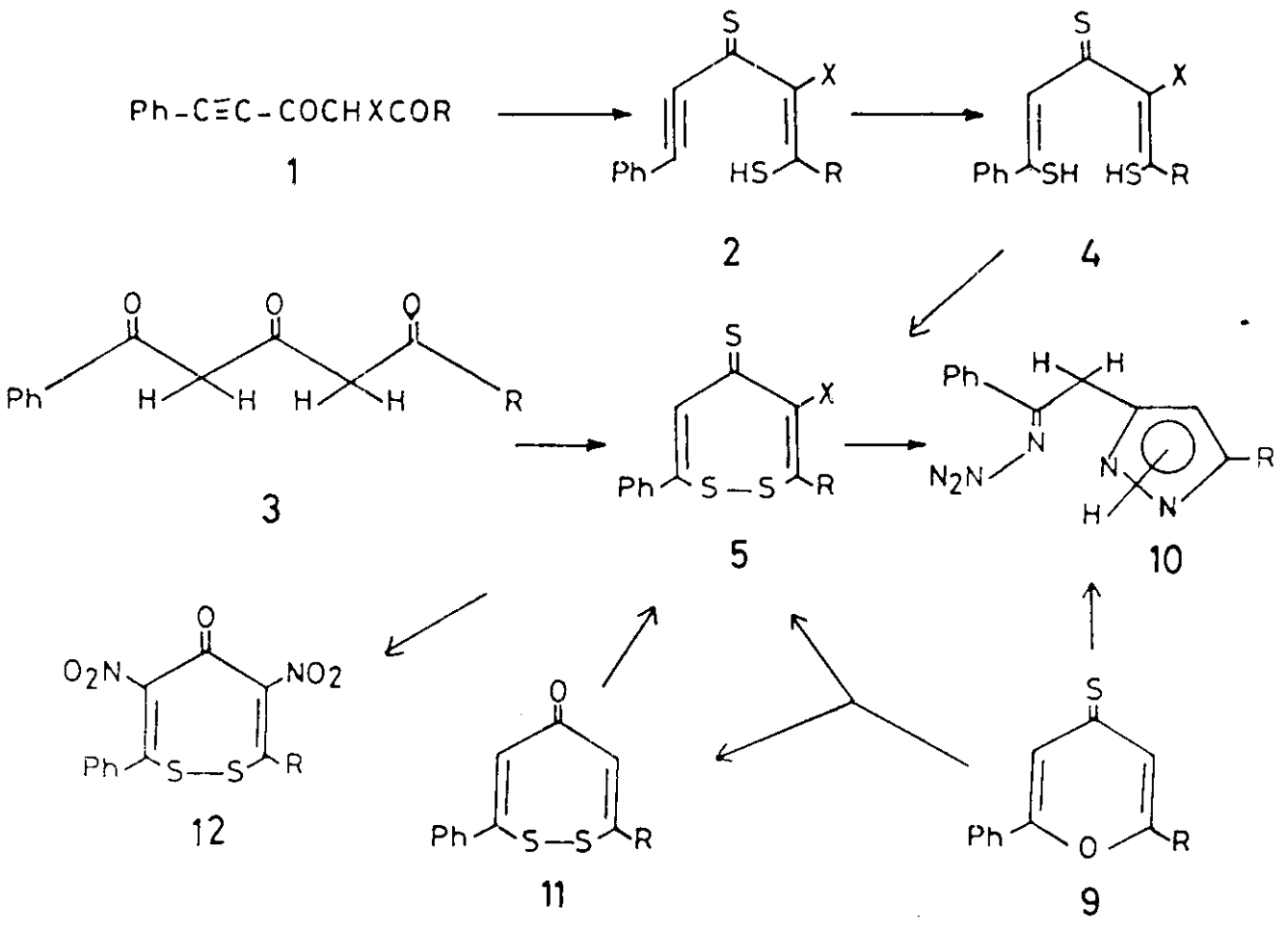
The structure of the dithiepins (5) was further confirmed from their mass spectral data. The relative intensities of the most prominent peaks in their spectra are listed in Table-II and their probable structures are shown in Scheme-II. Strong molecular ion peaks were observed for all the studied 1,2-dithiepins (5a-c, e-g). A major fragmentation route in the spectra of (5a-c,e) was the (M-H) species (6) arising by loss of a hydrogen, while in the

Table-1: Infrared, Electronic and ^{1}H-NMR Spectral Data of 5H-1,2-Dithiepin-5-thiones

	IR(cm^{-1})	UV λ_{max}, nm (δ) (a)				^{1}H-NMR chemical shift (δ/ppm) (b)			
	C=S					Solvent	H-4 & H-6 (s)	Ar-H (m)	Others (s)
5a	1190	252 (51316)	304 (21758)	350* (6568)	510 (14779)	DMSO-d_6	8.69	7.56	
5b	1191	251 (61474)	310 (25149)	352* (10246)	508 (18163)	DMSO-d_6	8.66	7.63	2.38 (CH_3)
5c	1185	255 (54474)	314 (20868)	360* (8688)	512 (15024)	DMSO-d_6	8.62	7.50	3.50 (OCH_3)
5d	1200	251 (42074)	309 (22579)	352* (7498)	510 (13164)	$CDCl_3$	8.20	7.66	
5e	1200	252 (50474)	308 (25230)	350* (8232)	512 (14239)	DMSO-d_6	8.68	7.65	
5f	1205	253 (48373)	300 (23389)	350* (9794)	505 (16657)	$CDCl_3$	8.60	7.64	
5g	1180	251 (47218)	294 (19382)	346* (7794)	504 (15657)	$CDCl_3$	8.53	7.59	

Shoulder. (a) Spectra carried out in methanol. (b) s: Singlet. m: Multiplet.

spectra of (5f, g) the base peak was the (M-Cl) cation. The ease of loss of a halogen radical had been also reported in the mass spectra of other halo-heterocyclic systems like 3-bromo-2-pyrones [14], 2,5-dichlorothiophene [15], 2,3,4-tribromo-pyrroles [16], and 3-iodo-4-pyrones [17]. Subsequent loss of a sulfur atom from (6) gave rise to an intense peak formulated as 4H-thiopyran-4-thione cation (7), the fragmentation of which gave the characteristic peaks reported in the mass spectra of this compound [18]. On the other hand, loss of S_2 from the molecular ion (5) leads to a moderately intense peak which was formulated as the cyclopentadiene species (8). It is worthy to mention that elimination of HS_2 or S_2 characterizes the mass spectra of 1,2-dithiacyclohexane, 1,2-dithiacyclopentane



	R	X
a,	Ph	H
b,	p-CH_3-C_6H_4	H
c,	p-CH_3O-C_6H_4	H
d,	p-Br-C_6H_4	H
e,	p-Cl-C_6H_4	H
f,	Ph	Cl
g,	p-Cl-C_6H_4	Cl

Scheme I

Table-II: Relative Intensity of the most prominent peaks in the mass spectra of the 5H-1,2-ithiepin-5- thiones

	M^+	6	7	8
5a	75	43	11	18
5b	100	55	14	22
5c	456	45	13	
5e	11,45	49.99	3.10	2,6
5f	3,13	100	6	2,6
5g	3,16	35,100	3,7	1,3

[19], and 1,2,5-trithiepane derivatives [20].

The chemistry of the 5H-1,2-dithiepin-5-thiones has been very little explored. While 3,7-dimethyl-5H-1,2-dithiepin-5-thione is susceptible to ring opening and subsequent recyclization by methanolic potassium hydroxide leading to thiepin derivative [21], the 1,2-dithiepins (5a-e) were recovered unchanged under the same reaction conditions. 3-Aryl-4-chloro-7-phenyl-5H-1,2-dithiepin-5-thiones, (5f, g) readily react with hydrazine hydrate in ethanol to give 5(3)-aryl-3(5)-[β-hydrazonophenylethyl] pyrazoles (10f, g) [22].

However, the non-chlorinated dithiepins (5a-e) are inert under the same conditions. The formation of the pyrazole hydrazones (10f, g) from the thiones (5f, g) is assumed to involve cleavage of the S-S bond of the 1,2-dithiepin ring and subsequent cyclization to pyrazoles (10) with the expulsion of chlorine atom [17] (Scheme 1).

Three different methods are reported for the synthesis of 1,2-dithiepin-5-ones : 1) the conversion of an appropriately substituted 1,2-dithiepin-5-thiones into the corresponding 5-ones by acids [2,4], 2) the reaction of potassium hydrogen sulfide with 4H-pyran-4-thiones [4,5a,b] or 4H-thiopyran-4-ones [5c] and 3) treatment of 4H-thiophran-4-thiones with mercuric chloride and sodium carbonate [5b]. In the present study, attempts to convert 1,2-dithiepin-5-thiones (5a-e) to the corresponing 5-ones by action of concentrated sulfuric acid, hydroxylamine or hydrazine in methanol in the presence of sulfuric acid failed in every case. However, the reaction of sodium sulfide in acetone with 2,6-diaryl-4H-pyran-4-thiones (9a-d) led to formation of 3,7-diaryl-1,2-di-thiepin-5-ones(11a-d) beside small amounts of the corresponding 5-thiones (5a-d). Treatment of the ketones 11a-d with phosphorus pentasulfide afforded the corresponding thiones (5a-d) (Scheme I).

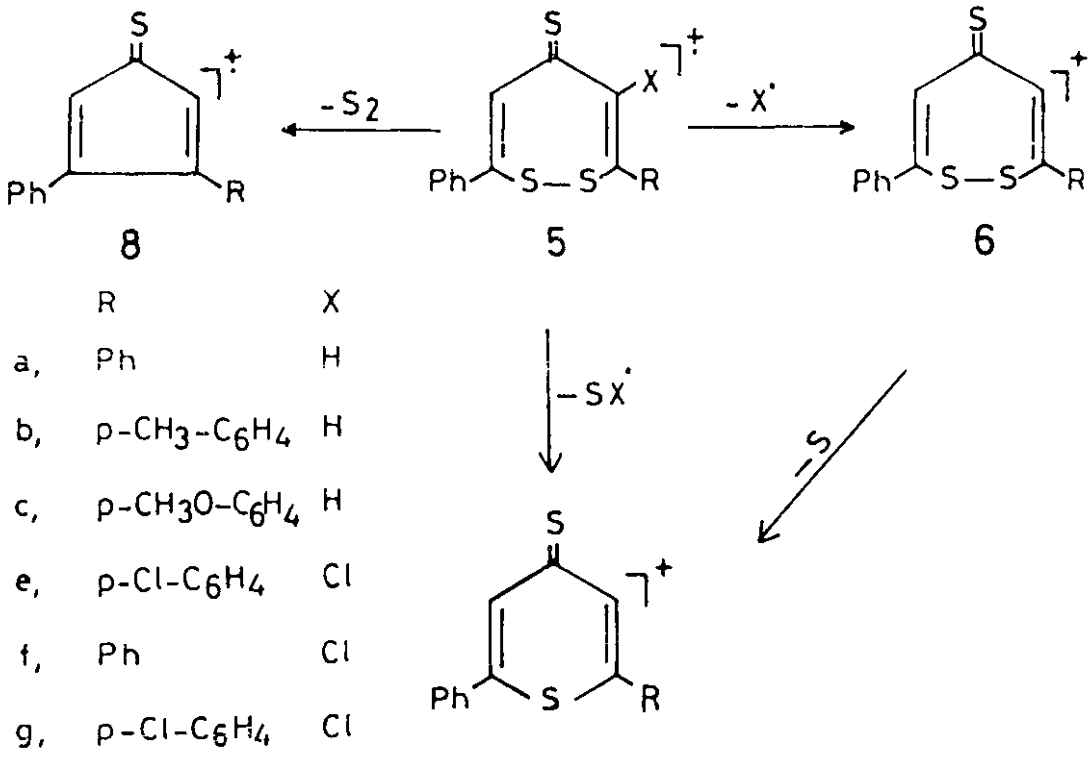
The infrared spectra of the 1,2-dithiepin-5-ones (11) gave the carbonyl absorption at 1660-1685 cm^{-1}. It is observed that the H-4 and H-6 protons of these compounds resonated at much higher field (δ 7.43-7.60) relative to the analogous 5-thiones (5). Their electronic spectra exhibited three absorption maxima in the regions 230-260, 294-314 and 450-568 nm. In the presence of 0.1 M sodium methoxide, the position as well as the intensity of these absorptions were not affected. However, a shoulder appeared at 357-360 nm in the presence of 0.1 M sulfuric acid which may be due to the protonated dithiepin-5-one species (Table-III).

1,2-Dithiepin-5-thiones (5a,b,d) were shown to undergo nitration as well as oxidation into the correspon-

Table-III: Infrared, Electronic and ^{1}H-NMR Spectral Data of 5H-1,2-Dithiepin-5-one Derivatives

	IR (cm^{-1})			UV λ_{max}, nm ( )				^{1}H-NMR Chemical Shift (δ/ppm) (c)	
	C=O	NO_2						Ar-H	Others
								(m)	(s)
11a	1680		netural (a)	254 (21400)	310 (11571)		454 (8457)	7.50	
			cationic (b)	254 (21400)	310 (11571)	360* (6332)	454 (8457)		
11b	1685		neutral	256 (20412)	(11941)	314	468 (8206)	7.46	2.33 (CH_3)
			cationic	257 (20412)	314 (11941)	357* (7339)	468 (8206)		
11c	1660		neutral	230 (21733)	294 (112065)		450 (10806)	7.43	3.76 (OCH_3)
			cationic	232 (21486)	294 (12065)	358* (7539)	450 (11300)		
11d	1675		netural	260 (21635)	312 (12500)		462 (9375)	7.60	
			cationic	261 (20992)	312 (12492)	360* (7635)	462 (9375)		
12a	1710	1345,1535	neutral	258 (30302)	305* (13789)	475 (2632)		7.93	
12b	1707	1355,1545	netural	254 (33125)	298* 12051)	470 (2795)		8.00	
12c	1710	1355,1541	neutral	260 (29789)	306* (15984)	478 (2906)		8.01	

*Shoulder. (a) Spectra carried out in methanol. (b) Spectra carried out in 0.1. M methanolic sulfuric acid. (c) Spectra carried out in DMSO-d_6, s: Singlet, m:Multiplet.



	R	X
a,	Ph	H
b,	p-CH_3-C_6H_4	H
c,	p-CH_3O-C_6H_4	H
e,	p-Cl-C_6H_4	Cl
f,	Ph	Cl
g,	p-Cl-C_6H_4	Cl

Scheme II

ding 4,6-dinitro-1,2-dithiepin-5-ones (12a,b,d). The latter compounds were also obtained by nitration of 3,7-diaryl-1,2-dithiepin-5-ones (11a,b,d). The infrared spectra of (12) showed, besides the carbonyl absorption at 1707-1710 cm^{-1}, two absorptions at 1345-1355 and 1535-1545 cm^{-1} for the nitro group [23]. Their electronic spectra showed three absorption maxima in the regions 254-260, 298-306 (sh), and 470-478 nm.

Experimental

Microanalyses were performed by the Microanalysis Unit, Cairo University, Cairo. Infrared spectra were measured with a Unicam SP 1025 spectrophotometer for potassium bromide pellets and electronic spectra were measured with a Unicam SP 1750 spectrophotometer for solutions in methanol. The ^{1}H-NMR spectra were recorded on a Varian EM-390 90 MHz spectrometer with TMS as internal standard. Mass spectra were recorded on an AEI MS 30 spectrometer. TLC were done on Merck Kieselgel 60-F 254 precoated plastic plates.

3-Aryl-7-phenyl (5a-e) and 3-aryl-4-chloro-7-phenyl-(5f,g) 5H-1,2-dithiepin-5-thiones (Tables I, II, IV)

A solution of the acetylenic β-diketone (1a-g) [7,8] or the triketone (3a-c) [9] (4 mmol) in dry benzene (30 ml) was refluxed with phosphorus pentasulfide (9 mmol) for one hour. The reaction mixture was worked up

Table-IV: Analytical Data of the 5H-1,2-Dithiepin Derivatives.

	mp °C	Formula	C% Calcd.	C% Found	H% Calcd.	H% Found	N% Calcd.	N% Found	S% Calcd.	S% Found	X% Calcd.	X% Found
5a	180	$C_{17}H_{12}S_3$	65.4	65.5	3.9	3.8			30.8	30.9		
5b	202	$C_{18}H_{14}S_3$	66.3	66.5	4.3	4.4			29.5	29.7		
5c	220	$C_{18}H_{14}OS_3$	63.2	63.3	4.1	4.3			28.1	28.0		
5d	212	$C_{17}H_{11}BrS_3$	52.2	52.1	2.8	3.0			24.6	24.5	20.5	20.7
5e	210	$C_{17}H_{11}ClS_3$	58.9	59.0	3.2	3.3			27.7	27.9	10.3	10.2
5f	170	$C_{17}H_{11}ClS_3$	58.9	59.0	3.2	3.3			27.7	27.5	10.3	10.5
5g	200	$C_{17}H_{10}Cl_2S_3$	53.7	53.8	2.6	2.8			25.3	25.2	18.4	18.3
11a	132	$C_{17}H_{12}OS_2$	68.9	68.9	4.1	4.0			21.6	21.4		
11b	137	$C_{18}H_{14}O_2S_2$	69.7	69.9	4.5	4.3			20.7	20.3		
11c	150	$C_{18}H_{14}O_2S_2$	66.3	66.5	4.3	4.2			19.6	19.8		
11d	145	$C_{17}H_{11}BrOS_2$	54.4	54.3	2.9	3.0			17.1	17.0	21.3	21.7
12a	162	$C_{17}H_{10}N_2O_5S_2$	52.9	52.9	2.6	2.6	7.3	7.3	16.6	16.8		
12b	165	$C_{18}H_{12}N_2O_5S_2$	54.0	54.2	3.0	3.1	7.0	7.1	16.0	16.2		
12d	170	$C_{17}H_9BrN_2O_5S_2$	43.9	43.8	1.9	2.0	6.0	5.7	13.8	13.7	17.2	17.0

as described earlier [24]. The isolated thiones (5a-g) (78-86% yield) were crystallized from benzene-ethanol in violet needles.

5(3)-Aryl-3(5)-[β-hydrazonophenyl-ethyl]pyrazoles (10f,g)

A solution of the 5H-1,2-dithiepin-5-thione (5f,g) (2 mmol) in 95% ethanol (10 ml) was refluxed with 99% hydrazine hydrate (4 mmol) for 3 hours. After removal of most of the solvent and dilution with water, the separated pyrazoles (10f,g) (70-80% yield) were crystallized from benzene-petroleum ether (b.p. 60-80°) in needles. The pyrazole (10f) was found to be completely identical (m.p. mixed m.p., ir and ^{1}H-NMR spectra) with authentic sample prepared from 2,6-diphenyl-4H-pyran-4-one or 1,5-diphenylpent-1,3,5-trione with hydrazine hydrate [22]. 5(3)-p-Chloro-

phenyl-3(5)-[β-hydrazonophenylethyl] pyrazole (10g) has m.p. 180°, ν_{max} (cm^{-1}) : 1654 (C=N, hydrazone), 1598 (C=N, pyrazole ring), 3205, 3330 (NH_2); ^{1}H-NMR (δ /ppm, DMSO-d_6) : 3.98 (s, CH_2), 6.39 (s, H-4), 6.70 (s, NH_2), 12.90 (s, NH), 7.60 (m, Ar-H); MS : m/z (relative intens.) M^+ 312, 310 (4,15), 311, 309 (12,40), 296, 294 (35,100), 193, 191 (5,16), 151, 149 (7,22), 119 (30), 77 (18).

Anal.Calcd. for $C_{17}H_{15}ClN_4$: C, 65.7; H, 4.8; N, 18.0; Cl, 11.4. Found : C, 65.5; H, 4.9; N, 18.1; Cl, 11.2.

The pyrazole (10g) was also prepared (75% yield) from 2-p-chlorophenyl-6-phenyl-4H-pyran-4-thione (9g) [24] and 99% hydrazine hydrate in ethanol as described earlier [22b].

3,7-Diaryl-5H-1,2-dithiepin-5-ones (11) (Tables III,IV)

A solution of sodium sulfide (5 mmol) in water (2 ml) was added to a solution of the 2,6-diaryl-4H-pyran-4-thione (9a-d) (2 mmol) in acetone (10 ml) and the mixture was refluxed for 7-10 hours. The solution was then evaporated under reduced pressure, the residue mixed with ice-cold water and extracted with ether. After acidification of the alkaline solution, the separated yellow solid was subjected to fractional crystallization from methanol. The ketones (11a-d) (66-75% yield) separated first in dark brown needles, and from the mother liquors, 3,7-diaryl-1,2-dithiepin-5-thiones (5a-d) (15-20% yield) were obtained in violet needles.

The ketones 11a-d gave after refluxing their solutions in dry benzene with phosphorus pentasulfide, the corresponding thiones 5a-d in 80% yield.

3,7-Diaryl-4,6-dinitro-5H-1,2-dithiepin-5-ones (12) (Tables III,IV).

A solution of (5a, b,d) (2 mmol) in glacial acetic acid (12 ml) was refluxed with nitrating mixture (3 ml, 1 HNO_3 : 1 H_2SO_4) for 3-5 hours. The reaction mixture was then poured into ice-cold water; and the yellow solid (70-80% yield) which separated crystallized from methanol in yellow needles. The nitro compounds 12a,b,d were also obtained (55-65% yield), when the 1,2-dithiepin-5-ones (11a,b,d) were refluxed with nitrating mixture (conc. HNO_3 and H_2SO_4) in acetic acid for 2-3 hours.

References

1. F. Arndt, P.Nachtwey and J. Pusch, *Chem.Ber.*, **58**, *1633 (1925).*
2. F.Arndt, R.Schwarz, C. Martius, and E. Aron. *Rev.Facilte Sci. Univ. Istanbul A 13, 57 (1948).*
3. G. Traverso, *Ann. Chim.*, **45**, *687 (1955).*
4. G.Traverso, and M. Sanesi, *Ann. Chim.*, **43**, *795 (1953).*
5. (a) G.Traverso, *Ann. Chim.*, **44**, *1018 (1954).* (b) G.Traverso, *Chem.Ber.*, **91**, *1224 (1958).* (c) G.Traverso, *Ann.Chim. (Rome)*, **46**, *821 (1956).*
6. G.Traverso, *Ann.Chim.*, **45**, *687 (1955).*
7. I.E. EL-Kholy, M.G. Marei, M. M. Mishrikey, *Heterocyclic Chem.*, **16**, *737 (1979).*
8. M.G. Marei, M.M. Mishrikey and I.E. El-Kholy, *J.Chem.Soc.Pak.*, **9**, *539 (1987).*

9. (a) R.L. Light and C.R. Hauser, *J.Org.Chem.*, **25**, *538 (1960).* (b) G. Soliman and I.E. El-Kholy, *J. Chem.Soc.*, *1755 (1954).* (c) I.E. El-Kholy, M.M. Mishrikey and M.G. Marei, *Egypt. J. Chem.*, **27**, *767 (1984).*

10. W.H. Pirkle and W.V. Turner, *J.Org.Chem.*, **40**, *1617 (1975).*

11. I.E.El-Kholy, M.M.Mishrikey and H.M.Fuld-All *Heterocyclic Chem.*, **14**, *845 (1977).*

12. F.M. Dean, J. Goodchild, A.W. Hill, S.Murray, and A.Zahman, *J.Chem.Soc.Perkin Trans. I*, *1335 (1975).*

13. W.E.Stewart, and T.H.Siddal, *J.Phys.Chem.*, **69**, *1 (1965).*

14. H. Nakata, and A. Tatematsu, *Tetrahedron Letters*, *4101 (1967).*

15. J.H.Boeie, R.G.Cooks, S.-O. Bowiem Lawesson, and C.Nolde, *J.Chem.Soc., B., 616 (1967).*

16. S.Hannessian, and J.S.Kaltenbronn, *J.Amer.Chem.Soc.*, **88**, *4509 (1966).*

17. M.G.Marei, M.M. Mishrikey, and I.E.El-Kholy, *Heterocyclic Chem.*, **23**, *1849 (1986).*

18. *J.Bonham, E. McLeister, and P. Beak,* *J.Org.Chem.*, **32**, *639 (1967).*

19. T.J.Wallace, *J.Amer.Chem.Soc.*, **86**, *2018 (1964).*

20. L.Field, and C.H.Foster, *J.Org.Chem.*, **35**, *749 (1970).*

21. A. Bothner-By and G.Traverso, *Chem.Ber.*, **90**, *453 (1957).*

22. (a) C.Ainsworth and R.C. Jones, *J.Amer.Chem.Soc.*, **76**, *3172 (1954).* *(b) I.E.El-Kholy, F.K.Rafla, and G. Soliman,* *J.Chem.Soc., 1857 (1962).*

23. Bellamy, "The Infrared Spectra of Complex Molecules" Methuen and Co. Ltd., London, p. 298 (1964).

24. I.E.El-Kholy, F.K.Rafla, and G.Soliman, *J.Chem.Soc., 2588 (1959).*