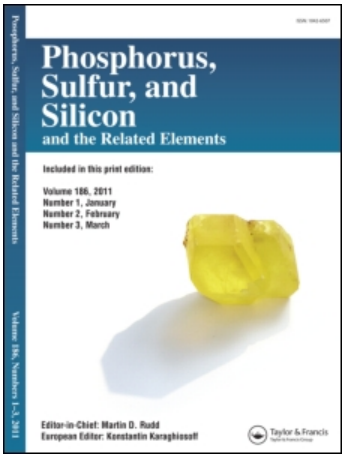

Phosphorus, Sulfur, and Silicon and the Related Elements

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A Novel Synthesis of Some Naphtho[2,3-d]Thiazole-4,9-Diones From Lawsone

G. Brahmeshwari[a]; V. Rajeswar Rao[a]; T. Surya Kumari[a]; T. V. Padmanabha Rao[a]
[a] Department of Chemistry, Kakatiya University, Warangal, Andhra Pradesh, India

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A NOVEL SYNTHESIS OF SOME NAPHTHO[2,3-d]THIAZOLE-4,9-DIONES FROM LAWSONE

G. BRAHMESHWARI, V. RAJESWAR RAO, T. SURYA KUMARI and T. V. PADMANABHA RAO*

Department of Chemistry, Kakatiya University, Warangal - 506 009, Andhra Pradesh, India

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A series of naphtho[2,3-d]thiazole-4,9-diones (**IV**) have been prepared by the condensation of bromolawsone (**II**) with thiosemicarbazones derived from aldehydes and ketones in dry DMF. The products (**V**) are also obtained by the cyclization of the intermediate 2-chlorobenzaldehyde thiosemicarbazone of 1,4-naphthoquinone (**IV**) in ethanol containing $KHCO_3$ obtained from 2,3-dichloronaphthoquinone.

Key words: Bromolawsone, thiazole, 2,3-dichloronaphthoquinone and naphthothiazoles.

INTRODUCTION

Numerous reports have appeared in the literature describing antimicrobial,[1,2] antiradiation[3,4] and antiparasitic[5] properties of the thiazole ring. The discovery that quinones are also endowed with antimalarial,[6] antiprotozoal[7] and antitumor[8] properties has directed attention to the synthesis of fused thiazoloquinones ring system, with the hope that a combination of favorable properties of both the quinone and the thiazole moiety may be achieved. The present work deals with a novel preparation of naphthothiazole diones.

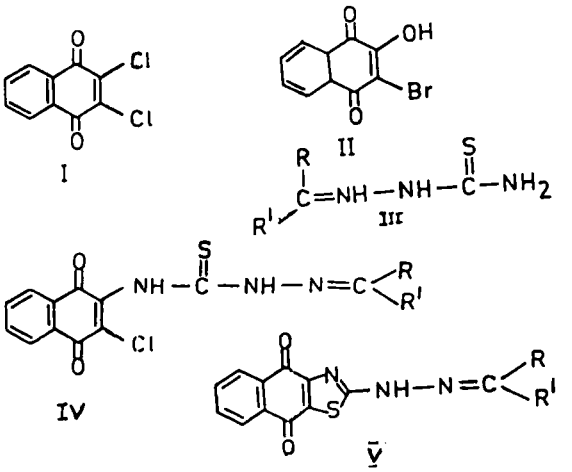
RESULTS AND DISCUSSION

A series of naphtho[2,3-d]thiazole-4,9-diones (**IV**), have been prepared by the condensation of bromolawsone (**II**) with thiosemicarbazones derived from aldehydes and ketones in dry DMF. The products (**V**) are also obtained by the cyclization of the intermediates 2-chlorobenzaldehyde thiosemicarbazone of 1,4-naphthoquinone (**IV**) in ethanol containing $KHCO_3$ obtained from 2,3-dichloronaphthoquinone.

In continuation of the earlier work on the synthesis of heterocyclic system derived from natural quinones, the synthesis of heterocyclic system naphtho[2,3-d]thiazole-4,9-diones (**V**) from 2,3-dichloronaphthoquinones (**I**) in two steps in good yields (60–80%) is reported. The configuration of the uncyclized (**IV**) and cyclized (**V**) compounds was found to be E on the basis of the fact that there is no change in the MP after their melting and resolidification.

The products (**V**) are also synthesized from bromolawsone in one step.

Bromolawsone (**II**) on treatment with thiosemicarbazones (**III**) in dry DMF gave



the corresponding naphtho[2,3-d]thiazole-4,9-diones (**V**). Attempts have been made to isolate the intermediate 2-hydroxy-3-thioamido-1,4-naphthoquinones, but the attempts did not meet with success. An inseparable mixture has been obtained. Refluxing equimolar amounts of 2,3-dichloro-1,4-naphthoquinone (**I**) and thiosemicarbazone (**III**) in ethanol, acetonitrile, or an ethanol and acetonitrile mixture resulted in a dark violet crystalline solid. Formation of the solid was enhanced by addition of an aqueous solution of $KHCO_3$ to the refluxing mixture. Elemental analysis showed the absence of halogen in these compounds and the participation of only one molecule of thiosemicarbazone in their formation. Warming the compounds in concentrated sulfuric acid gave a yellow to brownish red solution from which they were precipitated on dilution without eliminating the thioamide. This suggested the incorporation of the latter in a stable structure. In these compounds a quinonoid structure was found to be intact as indicated by the discharge of their colors on treatment with stannous chloride/acetic acid and on exposure to air ready oxidation to the original colors. Moreover, the IR spectra consistently show bands in the range 1650 and 1640 cm^{-1} characteristic of (C=O) and 1600 (C=C) conjugated with C=O in quinones respectively.

These characteristics are consistent with a naphthothiazole dione structure (**V**).

TABLE I

Yields, mps and elemental analysis

Compd	R	R^1	Yield (%)	m.p.[a] (°C)	Elemental Analysis Cald. (Found)			
					C	H	N	S
IVa	p-N,N-dimethyl aminophenyl	H	70	162	58.18 (58.14)	4.12 (4.10)	13.57 (13.54)	7.75 (7.72)
IVb	phenyl	H	60	139	58.45 (58.42)	3.24 (3.21)	11.36 (11.34)	8.66 (8.61)
IVc	methyl	H	68	182	50.73 (50.70)	3.25 (3.20)	13.65 (13.64)	10.40 (10.39)

TABLE I (*Continued*)

Compd	R	R^1	Yield (%)	m.p.[a] (°C)	Elemental Analysis Cald. (Found)			
					C	H	N	S
IVd	3,4-dimethoxy phenyl	H	70	194	55.87 (55.74)	3.72 (3.71)	9.77 (9.72)	7.45 (7.41)
IVe	o-hydroxyphenyl	H	62	152	56.03 (56.00)	3.11 (3.10)	10.89 (10.85)	8.30 (8.28)
IVf	p-methoxyphenyl	H	58	155	57.07 (57.00)	3.50 (3.48)	10.51 (10.49)	8.01 (8.00)
IVg	2-hydroxy 3-methoxyphenyl	H	75	185	54.87 (54.84)	3.36 (3.32)	10.10 (10.08)	7.70 (7.68)
IVh	Naphthyl	H	70	129	62.93 (62.90)	3.33 (3.31)	10.01 (10.00)	7.62 (7.60)
IVi	m-nitrophenyl	H	60	162	52.11 (52.10)	2.65 (2.62)	13.51 (13.50)	7.72 (7.68)
IVj	p-hydroxyphenyl	H	60	175	56.03 (56.00)	3.11 (3.10)	10.89 (10.82)	8.30 (8.21)
IVk	p-chlorophenyl	H	65	126	53.46 (53.42)	2.72 (2.70)	10.39 (10.35)	7.92 (7.90)
Va	p-N,N-dimethyl aminophenyl	H	80	242	63.82 (63.79)	4.25 (4.20)	14.89 (14.82)	8.51 (8.49)
Vb	phenyl	H	65	231	64.86 (64.84)	3.30 (3.10)	12.61 (12.58)	9.60 (9.56)
Vc	methyl	H	60	284	57.56 (57.52)	3.32 (3.31)	15.49 (15.44)	11.80 (11.78)
Vd	3,4-dimethoxy phenyl	H	65	289	61.06 (61.00)	3.81 (3.67)	10.68 (10.62)	8.14 (8.10)
Ve	o-hydroxyphenyl	H	65	240	61.89 (61.77)	3.15 (3.12)	12.03 (12.00)	9.16 (9.14)
Vf	p-methoxyphenyl	H	60	232	62.80 (62.77)	3.58 (3.56)	11.57 (11.54)	8.82 (8.78)
Vg	2-hydroxy 3-methoxyphenyl	H	60	225	60.15 (60.00)	3.43 (3.40)	11.08 (11.00)	8.44 (8.41)
Vh	Naphthyl	H	60	235	69.92 (69.90)	3.94 (3.93)	10.96 (10.97)	8.35 (8.34)
Vi	m-nitrophenyl	H	65	229	57.14 (57.13)	2.64 (2.63)	14.81 (14.80)	8.46 (8.44)
Vj	p-hydroxyphenyl	H	65	231	61.89 (61.82)	3.15 (3.12)	12.03 (12.00)	9.16 (9.14)
Vk	p-chlorophenyl	H	70	223	58.77 (58.74)	2.72 (2.70)	11.42 (11.41)	8.70 (8.69)

a - Compounds IVa-k were crystallised from chloroform.

b - Compounds Va-k were crystallised from benzene.

c - All the yields are based upon after recrystallisation.

d - All the compounds IV and V are existing in the E configuration around -C=N-

TABLE II

Spectral data of compounds (IV) and (V)

Compound	R	R^1	^{1}H-NMR (ppm)			IR	
			NH	ArH	Other	NH	C=O Quinone
IVa	N,N-dimethyl aminophenyl	H	6.71(s,2H,b)	7.7 - 8.3 (m, 8H)	2.8-3.2(s,6H, $N(CH_3)_2$) 7.1(s, 1H, methine)	3400	1600 1630
IVb	phenyl	H	4.0 - 4.5 (s,2H,broad)	7.4 - 8.6 (m, 9H)	7.2 (s, methine)	3410	1620 1640
IVc	p-methoxy	H	5.2 - 5.5 (s, 2H)	7.2 - 7.4 (m, 8H)	7.1(s,methine), 2.8(s, 3H, methoxy)	3420	1620 1630
Va	N,Ndimethyl aminophenyl	H	6.2 - 6.4 (s, 1H)	7.0 - 7.8 (m, 8H)	2.8(s,6H Dimethyl amino) 6.9(s,1H methine)	3410	1620
Vb	phenyl	H	4.6 - 4.8 (s,1H,NH)	7.2 - 7.8 (m,9H)	7.0(s, 1H methine)	3420	1600 1630
Vc	p-methoxy	H	5.6 - 5.8 (s,1H,NH)	7.0 - 7.7 (m, 8H)	7.1(s, 1H methine), 2.8(s, 3H, methoxy)	3400	1610

a - NMR spectra of IVa,IVb,IVc were recorded in DMSO-d_6 while Va,Vb,Vc were recorded in $CDCl_3$

b - These protons disappeared on shaking with D_2O

c - Mass spectrum of compound IVa: m/e 412(10%), 375(40%), 373(80%), 372(50%), 338(40%), 316(20%), 295(98%), 176(78%), 105(100%), 77(90%) and 76(50%).

d - Mass spectrum of compound Va: m/e 376(10%), 373(10%), 294(30%), 250(38%), 147(86%), 148(100%), 145(40%), 105(42%) and 77(62%).

In the mechanism of the formation of (V) it is assumed that the thiosemicarbazone (III) undergoes a nucleophillic displacement of one chlorine atom in (II) to give 2-chlorothiosemicarbazone 1,4-naphthaquinone (IV), which loses a hydrogen chloride molecule giving (V). The formation of (IV) as intermediate was indicated by its isolation in the reaction medium and by the ready transformation to (V) on refluxing in aqueous ethanolic $KHCO_3$ or acetonitrile in $KHCO_3$.

Conducting the reaction between (I) and thiosemicarbazone in acetonitrile for a limited period (10–20 minutes) yielded only compounds (IV). The intermediates (IV) are soluble in most organic solvents. Their IR spectra exhibited two strong bands in the ranges 3400 (NH), 1070 (C=S) and 760 (C—Cl) cm^{-1} respectively.

EXPERIMENTAL

All melting points were determined in open capillary tubes using sulphuric acid bath and are uncorrected. IR spectra (ν_{max} cm^{-1}) were recorded in Nujol on Perkin-Elmer-282 instrument. The ^{1}H-NMR spectra were recorded on a Varian 90 MHz spectrometer using TMS as the internal standard. Chemical shifts are expressed in δ ppm. Mass spectra were scanned on a Jeol JMS 300 spectrometer at 70 eV. The purity of the compounds was monitered by TLC performed on silica gel plates (Merck) using chloroform-methanol as the eluent. Chemical analysis was done at each stage to confirm the presence or absence of bromine or chlorine by Bielstein's and Lassaigne's tests.

Lawsone was extracted from the fresh leaves of lawsonia inermis. Bromolawsone and aryl hydrazones were prepared according to the literature methods.[12,13]

Preparation of (V) *from* (I): A mixture of bromolawsone (II; 0.01 mole) and an appropriate thiosemicarbazone (III; 0.01 mole) was stirred in dry DMF (40 mL) at 85–90°C for a period of 4 hr. The reaction mixture was cooled and poured on crushed ice. The solid thus separated was recrystallized from suitable solvents (Table I).

Preparation of naphtho[2,3-d]thiazole-4,9-diones (II) *and 2-thioamido-3-chloro-1,4-naphthoquinones* (IV): A solution of 2,3-dichloronaphthoquinone (0.01 mole) in the minimum volume of ethanol or acetonitrile was stirred with 0.01 mole of thiosemicarbazone in the same solvent. The mixture was heated until a violet colored solid started to precipitate (30 minutes). Ethanol or acetonitrile (15 ml) containing 5% $KHCO_3$ were added and refluxing continued (1–2 hr) until precipitation of a dark solid was complete. The solid (V) was removed by filtration and recrystallized from the proper solvent (the compounds are included in Table I). The mother liquor after filtering off solid (V), was diluted with water and the corresponding (IV) separated out. These were collected and dried at 70°C.

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