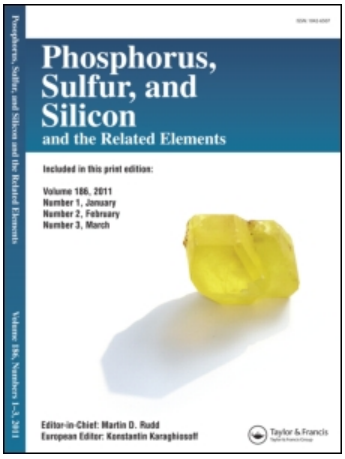


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Synthesis of Novel Bis-2-(1,3,4-thiadiazolin-3-ylphenoxy) Alkane Derivatives

Mohamed A. A. Elneairy[a]; Ashraf A. Abbas[a]; Yehia N. Mabkhout[a]
[a] Cairo University, Giza, Egypt

Online publication date: 27 October 2010

To cite this Article Elneairy, Mohamed A. A. , Abbas, Ashraf A. and Mabkhout, Yehia N.(2003) 'Synthesis of Novel Bis-2-(1,3,4-thiadiazolin-3-ylphenoxy) Alkane Derivatives', Phosphorus, Sulfur, and Silicon and the Related Elements, 178: 8, 1747 — 1757
To link to this Article: DOI: 10.1080/10426500307823
URL: http://dx.doi.org/10.1080/10426500307823

Phosphorus, Sulfur, and Silicon, 178:1747–1757, 2003

ISSN: 1042-6507 print
DOI: 10.1080/10426500390220989

Taylor & Francis
Taylor & Francis Group

SYNTHESIS OF NOVEL BIS-2-(1,3,4-THIADIAZOLIN-3-YLPHENOXY) ALKANE DERIVATIVES

Mohamed A. A. Elneairy, Ashraf A. Abbas, and Yehia N. Mabkhout
Cairo University, Giza, Egypt

(Received December 2, 2002; accepted February 24, 2003)

A novel synthesis of bis(thiadiazolin-3-yl)ethers ***6a–f*** *and bis(thiadiazolin-2-on-3-yl)ethers* ***10a–f*** *via the reaction of the bis (diazonium) salts* ***2a–c*** *with the appropriate ω-thiocyanatoacetophenone derivatives* ***4a–c****.*

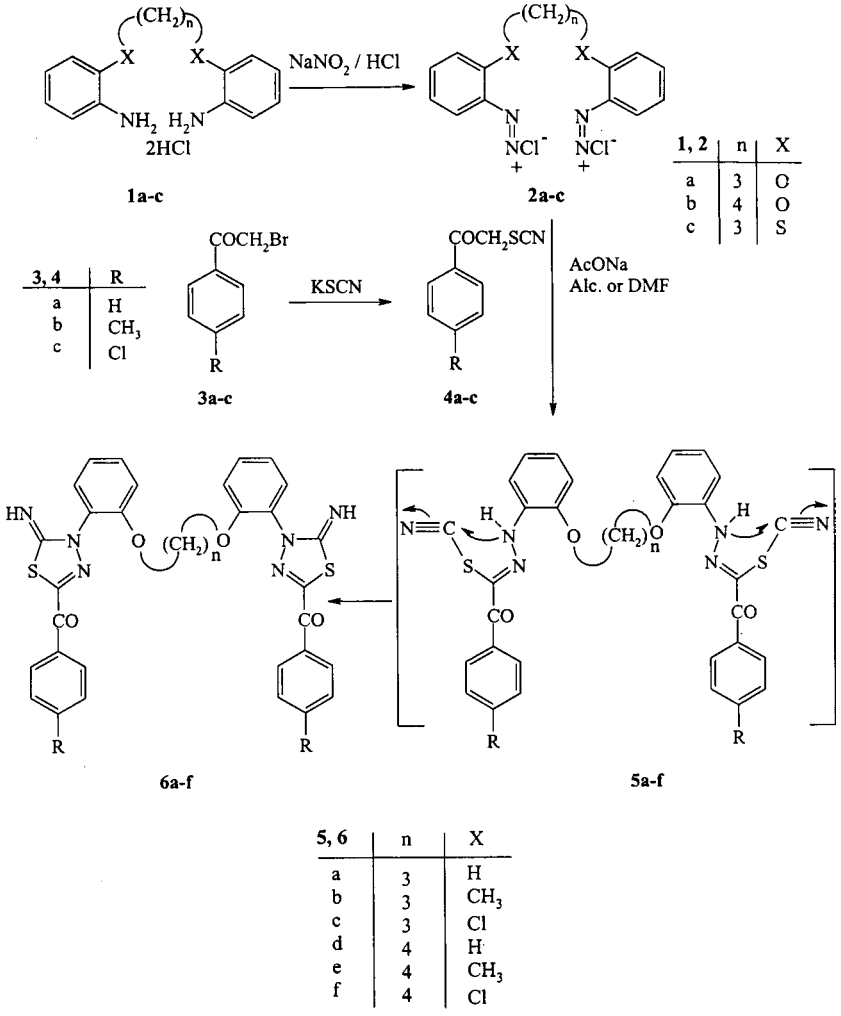
Keywords: Bis(diazonium) salts; thiadiazoline

In the last decades much attention have been devoted to the construction of new derivatives of thiadiazole and thiadiazolone on account of their reported biological activities. Various series of thiadiazoles, thiadiazolones and their annelated derivatives are reported to have diverse biological activities as antibacterial,[1–4] antimicrobial,[5,6] antifirinolytic and antiinflammatory,[7] antihistamines, and muscarinic agonists.[8] Some thiadiazole derivatives also were used as inhibitors of the neutral endopeptidase[9] carbonic anhydrase,[10] anticarcenogenic.[11] Recently, bis(compounds) have received great attention not only for being model compounds for main chain polymers[12–17] but also because many biologically active natural and synthetic products have molecular symmetry.[18] We recently[19] have described the synthesis of some new bis (activated styrene) derivatives and studied their synthetic potential as starting materials for novel bis(pyridin-4-yl) ethers and bis(thieno[2,3-b]-pyridine) derivatives. In continuation of our interest in this field, we report here on the synthesis of some new bis(hydrazones) to explore their synthetic utility as intermediates in the synthesis of novel bis(thiadiazolyl) ethers of expected biological activities.

Address correspondence to Mohamed A. A. Elneairy, Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt. E-mail: elneairy@hotmail.com

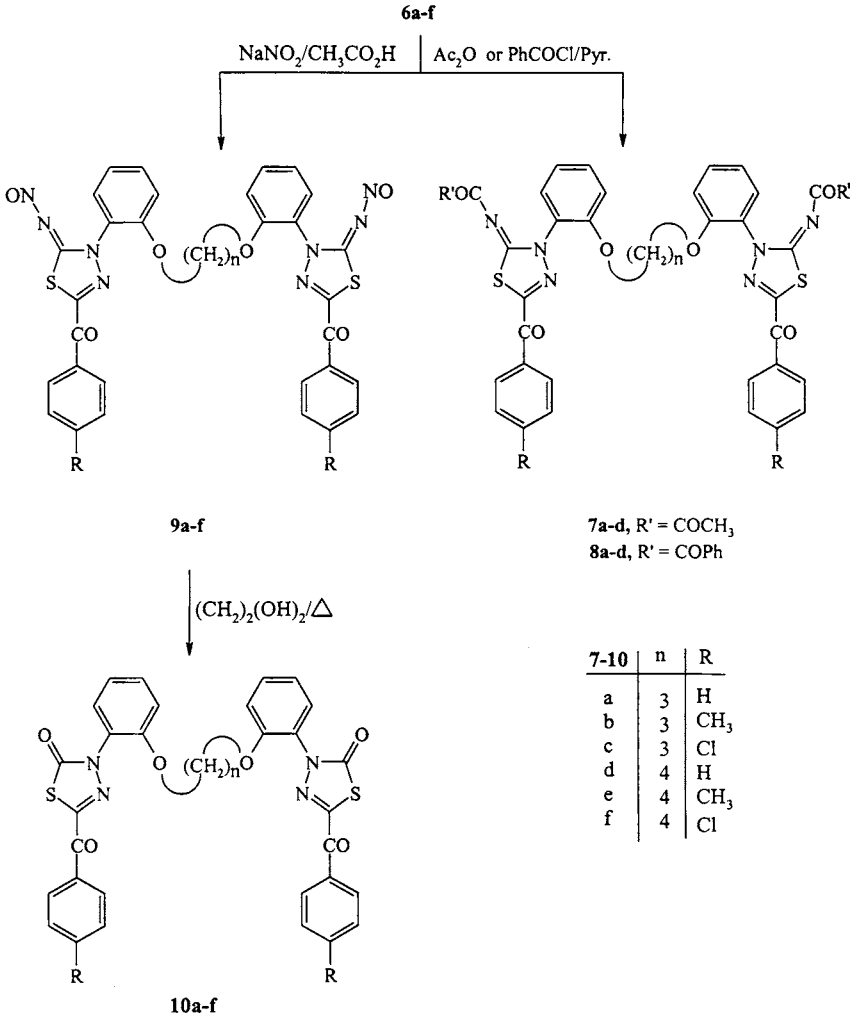
RESULT AND DISCUSSION

The synthetic route described for the synthesis of the bis(2-iminothiadiazolin-3-yl)ethers **6a–f** is outlined in Scheme 1. Thus, the diamine dihydrochloride **1a–c** were diazotized with sodium nitrite in hydrochloric acid to give the corresponding bis(diazonium) salts **2a–c**. The diazonium salts **2a**,**b** were then reacted with ω-thiocyanatoacetophenone **(4a)** to give the corresponding bis(iminothiadiazole) derivatives **6a**,**d**.



SCHEME 1

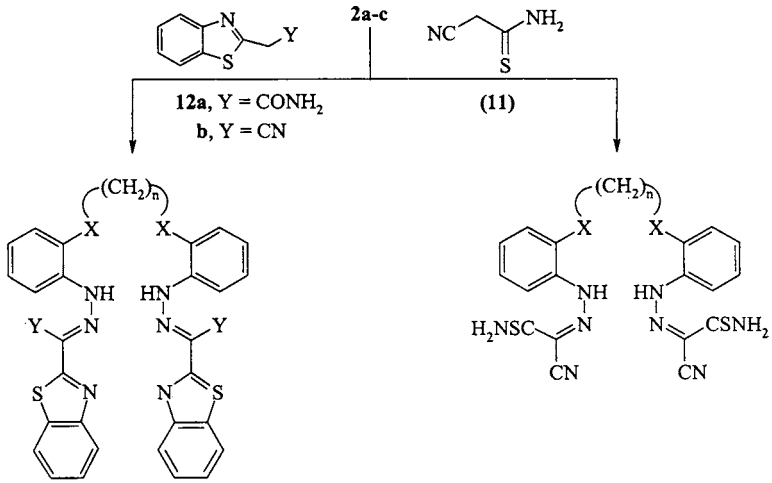
The reaction proceed via initial formation of the bis(hydrazone) derivatives **5a**,**d** followed by the addition of the hydrazone NH to the nitrile function to afford the target molecules **6a**,**d**. The IR(cm^{-1}) spectra of the latter products showed absorption bands of NH and C=O groups near $\nu = 3290\ cm^{-1}$ and $\nu = 1640\ cm^{-1}$, respectively. The structures of compounds **6a**,**d** were further supported via their reactions with acetic anhydride and benzoyl chloride to give the corresponding bis-*N*-(acetylimino) and bis-*N*-(benzoylimino) derivatives **7a**,**d** and **8a**,**d** respectively, (Scheme 2). The IR spectra of compounds **7a**,**d** and



7-10	n	R
a	3	H
b	3	CH_3
c	3	Cl
d	4	H
e	4	CH_3
f	4	Cl

SCHEME 2

8a,**d** revealed the absence of bands characteristic for the NH absorption. Moreover, their ^{1}H-NMR did not reveal any signal corresponding to NH proton. The structures **6a**,**d** were further confirmed by their reaction with nitrous acid to give the corresponding bis-*N*-(nitrosoimino-1,3,4-thiadiazolyl) derivatives **9a**,**d** (Scheme 2). Heating of compounds **9a**,**d** in refluxing ethylene glycol afforded 60% of the corresponding bis(thiadiazolone) derivatives **10a**,**d** via the loss of one molecule of nitrogen. The IR (cm^{-1}) of compounds **10a**,**d** showed C=O absorption band near 1650 cm^{-1}. In the same manner, compounds **2a**,**b** were reacted with *p*-methyl-ω-thiocyanatoacetophenone (**4b**) and*p*-chloro-ω-thiocyanatoacetophenone (**4c**) to give the corresponding bis(iminothiadiazole) derivatives **6b**,**c**,**e**,**f** in a respective manner. The latter products reacted with acetic anhydride and benzoyl chloride to yield 45–60% of the corresponding bis-*N*-(acetylimino) and bis-*N*-(benzoylimino) derivatives **7b**,**c**,**e**,**f** and **8b**,**c**,**e**,**f** respectively. Compounds **6b**,**c**,**e**,**f** also reacted with nitrous acid to afford the corresponding bis-*N*-(nitrosoimino-1,3,4-thiadiazole) derivatives **9b**,**c**,**e**,**f**. Heating of the latter compounds in boiling ethylene glycol afforded the corresponding bis(thiadiazolone) derivatives **10b**,**c**,**e**,**f** respectively,



14a-d

14a, n = 3, X = O, Y = $CONH_2$
14b, n = 3, X = O, Y = CN
14c, n = 4, X = O, Y = $CONH_2$
14d, n = 4, X = O, Y = CN

13a-b

13	n	X
a	3	O
b	3	S

SCHEME 3

(Scheme 2). The structures of compounds **6a–f**, **7a–f**, **8a–f**, **9a–f**, and **10a–f** were established on the basis of their elemental analyses and spectral data.

Our studies have also extended to include the synthesis of the new bis(hydrazones) **13a**,**b** and **14a–d** as outlined in Scheme 3. Thus, coupling of the diazonium salts **2a–c** with a series of active methylene compounds namely, 2-cyanothioacetamide (**3**)[20] benzothiazol-2-ylacetamide (**4a**)[21] and benzothiazol-2-yl-acetonitrile (**4b**)[22] in ethanolic solution containing sodium acetate afforded **13a**,**b** and **14a–d** in 60–75% yield (cf. Scheme 3). The existance of compounds **13a**,**b**, **14a–d** in the hydrazone form was confirmed by the following facts: a) the absence of signals characteristic for the methine protons in their ^{1}H NMR spectra, b) the presence of NH absorption near $\nu = 3275$ cm^{-1} in their IR spectra, and c) the fact that the hydrazone is the most stable form whenever condensation occur at a methylene group.[23] Unfortunately, attempts to react **13a**,**b** and **14a–d** with a series of amino nucleophiles to give the corresponding bis(heterocycles) were unsuccessful. This may be attributed to the inherent insolubility of the new bis(hydrazones) in the reaction media.

EXPERIMENTAL

All melting points were measured on a Gallenkamp electrothermal melting point apparatus and are uncorrected. The infrared spectra were recorded in potassium bromide on a Pye Unicam SP 3-300 infrared and FT-IR 8101PC Schimadzu spectrophotometers.

The ^{1}H NMR spectra were recorded in deuterated chloroform or dimethyl sulphoxide on a Varian Gemini 200 NMR and varian Mercury 300 MHz spectrometer using tetramethysilane(TMS) as an internal reference; mass spectra were recorded on a GCMS-QP 1000 EX Shimadzu mass spectrumeter at 70 eV. Elemental analysis were carried out at the Microanalytical Center of Cairo University, Giza, Egypt.

Compounds **1a**, **b**,[24] **1c**,[23] **11**,[20] **12a**,[21] **12b**,[22] and **4a–c**[25] were prepared according to the literature procedure.

Synthesis of Compounds 13a,c, 14a–d, and 6a–f

General procedure: A stirred cold solution (0–5°C) of the appropriate diamine dihydrochloride **1a–c** (1 mmol) in water (10 ml) and concentrated hydrochloric acid (5 ml) was added a solution of sodium nitrite (0.23 g in 5 ml of water) over 30 min. Stirring was continued for 40 min at 0–5°C. The solution was then added dropwise with stirring to a solution containing the appropriate active methylene compounds

TABLE I Characterization Data of the Newly Synthesized Compounds

Comp.	Mol. formula colour	Yield % m.p.°C	Solvent of cryst.	Elemental analyses calc./found				
				C	H	N	S	Cl
6a	$C_{33}H_{26}N_6O_4S_2$	75	Ethanol	62.45	4.13	13.24	10.10	
	Yellow	125–127		62.20	3.90	13.50	10.40	
6b	$C_{35}H_{30}N_6O_4S_2$	60	Ethanol	63.43	4.56	12.68	9.68	
	Yellow	95–97		63.70	4.70	12.90	9.90	
6c	$C_{33}H_{24}N_6O_4S_2Cl_2$	50	Ethanol	56.33	3.44	11.94	9.11	10.08
	Yellow	215–217		56.60	3.20	12.10	8.90	10.30
6d	$C_{34}H_{28}N_6O_4S_2$	60	Ethanol	62.95	4.35	12.95	9.89	
	Yellow	145–147		63.10	4.50	13.10	9.60	
6e	$C_{36}H_{32}N_6O_4S_2$	66	Acetic acid	63.89	4.77	12.42	9.48	
	Yellow	90–92		64.00	4.50	12.20	9.60	
6f	$C_{34}H_{26}N_6O_4S_2Cl_2$	70	Ethanol	56.90	3.65	11.71	8.94	9.88
	Yellow	Semisolid		57.20	3.90	11.40	8.70	10.0
7a	$C_{37}H_{30}N_6O_6S_2$	60	Acetic acid	61.83	4.21	11.69	8.92	
	Yellowish-white	238–240		62.00	4.50	11.40	9.10	
7b	$C_{39}H_{34}N_6O_6S_2$	60	Acetic acid	62.72	4.59	11.25	8.59	
	Yellowish-white	255–257		63.00	4.30	11.50	8.30	
7c	$C_{37}H_{28}N_6O_6S_2Cl_2$	55	Acetic acid	56.42	3.58	10.67	8.14	9.0
	Yellowish-white	275–277		56.20	3.30	10.90	8.40	8.7
7d	$C_{38}H_{32}N_6O_6S_2$	60	Acetic acid	62.28	4.40	11.47	8.75	
	Yellowish-white	205–207		62.00	4.70	11.70	9.00	
7e	$C_{40}H_{36}N_6O_6S_2$	60	Acetic acid	63.14	4.77	11.04	8.43	
	Yellowish-white	165–167		63.40	4.90	10.90	8.20	
7f	$C_{38}H_{30}N_6O_6S_2Cl_2$	50	Acetic acid	56.93	3.77	10.48	8.00	8.84
	Yellowish-white	110–112		57.10	4.00	10.20	8.30	8.60
8a	$C_{47}H_{34}N_6O_6S_2$	65	DMF	66.97	4.07	9.97	7.61	
	White	245–246		67.10	3.90	10.10	7.40	
8b	$C_{49}H_{38}N_6O_6S_2$	55	DMF	67.57	4.40	9.65	7.36	
	White	305–307		67.30	4.70	9.80	7.10	
8c	$C_{47}H_{32}N_6O_6S_2Cl_2$	65	DMF	61.91	3.54	9.22	7.03	7.78
	White	302–304		62.10	3.80	9.00	7.30	8.0
8d	$C_{48}H_{36}N_6O_6S_2$	60	Acetic acid	67.27	4.23	9.81	7.48	
	Yellow	210–212		67.50	4.50	10.00	7.20	
8e	$C_{50}H_{40}N_6O_6S_2$	70	Acetic acid	67.86	4.56	9.50	7.25	
	Reddish-brown	140–142		68.00	4.80	9.20	7.50	
8f	$C_{48}H_{34}N_6O_6S_2Cl_2$	55	Acetic acid	62.27	3.70	9.08	6.93	7.66
	Yellowish-white	230–232		62.00	3.40	9.30	7.10	7.90
9a	$C_{33}H_{24}N_8O_6S_2$	70	Acetic acid	57.22	3.49	16.18	9.26	
	Reddish-brown	140–142		57.50	3.20	16.40	9.50	
9b	$C_{35}H_{28}N_8O_6S_2$	60	Acetic acid	58.32	3.92	15.55	8.90	
	Reddish-brown	154–156		58.50	3.70	5.80	9.10	
9c	$C_{33}H_{22}N_8O_6S_2Cl_2$	65	Acetic acid	52.04	2.91	14.71	8.42	9.31
	Reddish-brown	138–140		51.80	2.70	15.00	8.20	9.10
9d	$C_{34}H_{26}N_8O_6S_2$	60	Acetic acid	57.78	3.71	15.85	9.07	
	Reddish-brown	250–252		58.00	3.90	15.60	9.30	

(Continued on next page)

TABLE I Characterization Data of the Newly Synthesized Compounds *(Continued)*

Comp.	Mol. formula colour	Yield % m.p.°C	Solvent of cryst.	Elemental analyses calc./found C	H	N	S	Cl
9e	$C_{36}H_{30}N_8O_6S_2$	70	Acetic acid	58.84	4.11	15.25	8.73	
	Reddish-brown	140–142		59.00	4.40	15.50	8.40	
9f	$C_{34}H_{24}N_8O_6S_2Cl_2$	60	Acetic acid	52.65	3.12	14.45	8.27	9.14
	Reddish-brown	140–142		52.40	3.40	14.20	8.50	8.90
10a	$C_{33}H_{24}N_4O_6S_2$	55	Ethanol	62.25	3.80	8.80	10.07	
	Yellowish-white	80–82		62.40	3.90	9.00	9.90	
10b	$C_{35}H_{28}N_4O_6S_2$	40	Ethanol	63.24	4.25	8.43	9.65	
	Yellowish-white	145–147		63.50	4.00	8.20	9.90	
10c	$C_{33}H_{22}N_4O_6S_2Cl_2$	40	Ethanol	56.17	3.14	7.94	9.09	10.05
	Yellow	95–97		55.90	3.40	7.10	8.80	10.30
10d	$C_{34}H_{26}N_4O_6S_2$	40	Ethanol	62.76	4.03	8.61	9.86	
	Yellow	166–168		63.00	4.30	8.80	9.60	
10e	$C_{36}H_{30}N_4O_6S_2$	50	Ethanol	63.70	4.45	8.25	9.45	
	Yellowish-white	145–147		64.00	4.20	8.50	9.70	
10f	$C_{34}H_{24}N_4O_6S_2Cl_2$	40	Ethanol	56.75	3.36	7.79	8.91	9.85
	Yellow	218–220		57.00	3.10	8.80	9.10	10.1
13a	$C_{21}H_{20}N_8O_2S_2$	75	Acetic acid	52.49	4.19	23.32	13.34	
	Yellow	225–227		52.10	4.00	23.10	13.60	
13b	$C_{21}H_{20}N_8S_4$	75	Acetic acid	49.20	3.93	21.86	25.02	
	Yellow	215–217		49.50	3.70	22.00	25.3	
14a	$C_{33}H_{28}N_8O_4S_2$	80	DMF	59.62	4.25	16.86	9.65	
	Yellow	240–242		59.40	4.11	16.75	9.70	
14b	$C_{33}H_{24}N_8O_2S_2$	75	DMF	63.04	3.85	17.82	10.20	
	Yellow	255–257		62.80	4.00	17.50	9.90	
14c	$C_{34}H_{30}N_8O_4S_2$	80	DMF	60.16	4.45	16.51	9.45	
	Yellow	290–292		59.80	4.19	16.65	9.30	
14d	$C_{34}H_{26}N_8O_2S_2$	75	DMF	63.53	4.08	17.43	9.98	
	Yellow	265–267		63.30	3.80	17.70	10.20	

namely; 2-cyanothioacetamide (**11**) benzothiazol-2-ylacetamide (**12a**), benzothiazol-2-ylacetonitrile (**12b**), and ω-thiocyanatoacetophenone derivatives **4a–c** (2 mmol), in ethanol (20 ml) and dimethylformamide (10 ml) containing sodium acetate (3 g) over a period of 50 min. The reaction mixture was then allowed to stand at 0°C for 3 h. The solid obtained was collected by filtration and crystallized from the proper solvent.

Synthesis of 7a–f

General procedure: The appropriate of bis imino-1,3,4-thiadiazole derivative of **6a–f** (10 mmol) and acetic anhydride (20 ml) was heated

TABLE II IR and ^{1}H-NMR Data

Comp.	IR(cm^{-1})	H-NMR(δ)
6a	3290, (NH), 1640 (C═O)	2.32 (quintet, 2H, $J = 5.8$ Hz, $OCH_2\underline{CH_2}$), 4.16 (t, 4H, $J = 5.8$ Hz, OCH_2), 6.98–8.22 (m, 20H, ArH's, NH)
6b	3205, (NH), 1697 (C═O)	2.17 (quintet, 2H, $J = 5.6$ Hz, $OCH_2\underline{CH_2}$), 2.37 (s, 6H, CH_3), 4.16 (t, 4H, $J = 5.8$ Hz, OCH_2), 6.99–8.16 (m, 18H, ArH's and NH)
6c	3320, (NH), 1635 (C═O)	2.09 (brs, 2H, $OCH_2\underline{CH_2}$), 3.4 (brs, 2H, NH), 4.20 (t, 4H, $J = 4$ Hz, OCH_2), 7.17–8.19 (m, 16H, ArH's)
6d	3288, (NH), 1635 (C═O)	1.81 (brs, 4H, $OCH_2\underline{CH_2}$), 2.71 (brs, 2H, NH), 3.95 (brs, 4H, OCH_2), 6.95–8.24 (m, 18H, ArH's)
6e	3270, (NH), 1690 (C═O)	1.81 (brs, 4H, $OCH_2\underline{CH_2}$), 2.38 (s, 6H, CH_3), 3.94 (brs, 4H, OCH_2), 6.98–8.16 (m, 18H, ArH's and NH)
6f	3292, (NH), 1635 (C═O)	1.82 (brs, 4H, $OCH_2\underline{CH_2}$), 3.6 (brs, 2H, NH), 3.94 (brs, 4H, OCH_2), 6.97–8.21 (m, 16H, ArH's)
7a	1705, 1628 (two C═O)	1.92 (quintet, 2H, $J = 5.6$ Hz, $OCH_2\underline{CH_2}$), 1.9 (s, 6H, CH_3), 3.86 (t, 4H, $J = 5.8$ Hz, OCH_2), 6.85–8.28 (m, 18H, ArH's)
7b	1703, 1659 (two C═O)	1.91 (m, 2H, $OCH_2\underline{CH_2}$), 1.95 (s, 6H, CH_3), 2.34 (t, 4H, $J = 5.2$ Hz, OCH_2), 7.02–8.09 (m, 16H, ArH's)
7c	1702, 1661 (two C═O)	1.86 (brs, 2H, $OCH_2\underline{CH_2}$), 1.92 (s, 6H, CH_3), 3.94 (brs, 4H, OCH_2), 7.03–8.16 (m, 16H, ArH's)
7d	1710, 1665 (two C═O)	1.53 (brs, 4H, $OCH_2\underline{CH_2}$), 2.21 (s, 6H, CH_3), 3.84 (brs, 4H, OCH_2), 6.95–8.32 (m, 18H, ArH's)
7e	1705, 1627 (two C═O)	1.49 (brs, 4H, $OCH_2\underline{CH_2}$), 2.1 (s, 6H, CH_3), 2.36 (s, 6H, Ar-CH_3), 3.92 (brs, 4H, OCH_2), 7.1–8.1 (m, 16H, ArH's)
7f	1701, 1658 (two C═O)	1.53 (brs, 4H, $OCH_2\underline{CH_2}$), 2.51 (s, 6H, CH_3), 3.86 (brs, 4H, OCH_2), 6.99–8.28 (m, 16H, ArH's)
8a	1676, 1641 (two C═O)	1.80 (brs, 2H, $OCH_2\underline{CH_2}$), 3.91 (t, 4H, $J = 4.4$ Hz, OCH_2), 6.85–8.22 (m, 28H, ArH's)
8b	1657, 1620 (two C═O)	2.34 (m, 8H, CH_3-Ar, $OCH_2\underline{CH_2}$), 3.92 (brs, 4H, OCH_2), 6.8–8.15 (m, 26H, ArH's)
8c	1663, 1615 (two C═O)	1.79 (brs, 2H, $OCH_2\underline{CH_2}$), 3.92 (t, 4H, $J = 5$ Hz, OCH_2), 6.9–8.20 (m, 26H, ArH's)
8d	1645, 1618 (two C═O)	1.36 (brs, 4H, $OCH_2\underline{CH_2}$), 3.53 (brs, 4H, $J = 5.8$ Hz, OCH_2), 6.5–8.34 (m, 28H, ArH's)
8e	1650, 1620 (two C═O)	1.33 (brs, 4H, $OCH_2\underline{CH_2}$), 2.73 (s, 6H, CH_3), 3.67 (brs, 4H, OCH_2), 6.8–8.13 (m, 26H, ArH's)

(Continued on next page)

TABLE II IR and ^{1}H-NMR Data *(Continued)*

Comp.	IR(cm^{-1})	H-NMR(δ)
8f	1645 1620 (two C═O)	1.31 (brs, 4H, $OCH_2\underline{CH_2}$), 3.65 (brs, 4H, OCH_2), 6.71–8.23 (m, 26H, ArH's)
9a	1663 (C═O)	—
9b	1643 (C═O)	—
9c	1651 (C═O)	—
9d	1643 (C═O)	—
9e	1643 (C═O)	—
9f	1651 (C═O)	—
10a	1697, 1651 (two C═O)	2.17 (quintet, 2H, $J = 5.5$ Hz, $OCH_2\underline{CH_2}$), 4.2 (t, 4H, $J = 7.3$ Hz, OCH_2), 6.8–8.2 (m, 18H, ArH's)
10b	1697, 1643 (two C═O)	2.15 (quintet, 2H, $J = 5.8$ Hz, $OCH_2\underline{CH_2}$), 2.37 (s, 6H, CH_3), 4.14 (t, 4H, $J = 6$ Hz, OCH_2), 6.94–8.18 (m, 16H, ArH's)
10c	1695, 1643 (two C═O)	2.05 (brs, 2H, $OCH_2\underline{CH_2}$), 4.12 (brs, 4H, OCH_2), 7.01–8.41 (m, 16H, ArH's)
10d	1697, 1651 (two C═O)	1.68 (brs, 4H, $OCH_2\underline{CH_2}$), 3.99 (brs, 4H, OCH_2), 7.05–8.14 (m, 18H, ArH's)
10e	1720, 1643 (two C═O)	1.72 (brs, 4H, $OCH_2\underline{CH_2}$), 2.37 (s, 6H, CH_3), 4.08 (brs, 4H, OCH_2), 7.20–8.09 (m, 16H, ArH's)
10f	1697, 1651 (two C═O)	1.69 (brs, 4H, $OCH_2\underline{CH_2}$), 4.23 (brs, 4H, OCH_2), 7.2–8.15 (m, 16H, ArH's)
13a	3420, 3273, 3144 (NH_2 and NH), 2221 (CN), 1537 (C═S)	2.32 (quintet, 2H, $J = 5.2$ Hz, O $CH_2\underline{CH_2}$), 4.39 (t, 4H, $J = 5.4$ Hz, OCH_2), 6.98–7.97 (m, 8H, ArH's), 9.56 (brs, 2H, NH_2), 9.64 (s, 2H, NH), 9.81 (brs, 2H, NH_2)
13b	3410, 3290, 3200 (NH_2 and NH), 2206 (CN), 1520 (C═S)	1.66 (quintet, 2H, $J = 7$ Hz, $SCH_2\underline{CH_2}$), 2.96 (t, 4H, $J = 7$ Hz, SCH_2), 7.1–8.01 (m, 8H, ArH's), 9.567 (brs, 2H, NH_2), 9.87 (brs, 2H, NH_2), 10.13 (s, 2H, NH)
14a	3468, 3330, 3192 (NH_2 and NH), 1665 (C═O)	2.7 (brs, 2H, $OCH_2\underline{CH_2}$), 4.55 (brs, 4H, OCH_2), 6.92–8.17 (m, 16H, ArH's), 9.55 (brs, 4H, NH_2), 14.65 (brs, 2H, NH)
14b	3449, (NH), 2216 (CN)	2.65 (brs, 2H, $OCH_2\underline{CH_2}$), 4.54 (brs, 4H, OCH_2), 6.92–8.16 (m, 16H, ArH's), 14.14 (brs, 2H, NH)
14c	3464, 3248, 3171 (NH_2 and NH), 1659(C═O)	2.17 (brs, 4H, $OCH_2\underline{CH_2}$), 4.35 (brs, 4H, OCH_2), 6.8–8.3 (m, 16H, ArH's), 9.2 (brs, 4H, $2NH_2$), 14.7 (brs, 2H, NH).
14d	3420, (NH), 2208 (CN)	2.2 (brs, 4H, $OCH_2\underline{CH_2}$), 4.21 (brs, 4H, OCH_2), 6.70–8.0 (m, 16H, ArH's), 14.44 (brs, 2H, NH)

under reflux for 3 h. The excess of the acetic anhydride was evaporated in vacuo. The solid product was collected by filtration, washed with water, and crystallized from the acetic acid as yellowish white crystals to give **7a–f** respectively.

Synthesis of 8a–f

General procedure: A solution of the appropriate bis-imino-1,3,4-thiadiazole derivative each of **6a–f** (10 mmol) and benzoyl chloride (20 ml), in pyridine was stirred at room temperature for 1 h. The reaction mixture was then poured onto ice and acidified with hydrochloric acid. The solid product was collected by filtration, washed with water, and crystallized from the proper solvent to give **8a–f** respectively.

Synthesis of 9a–f

General procedure: A cold solution of the appropriate **6a–f** (0.5 g) in acetic acid (25 ml) was treated with a saturated aqueous solution of sodium nitrite with stirring for 30 min. The solid product that formed was collected by filtration and crystallized from acetic acid as reddish brown crystal to give **9a–f** respectively.

Synthesis of 10a–f

General procedure: The appropriate nitroso derivative **9a–f** was refluxed in ethylene glycol (20 ml) for 40 min. The solvent was then diluted with water. The solid product that formed was collected by filtration, washed with water, and crystallized from the proper solvent to give **10a–f** respectively.

REFERENCES

[1] T. Kamiya, T. Naito, T. Komatsu, Y. Kai, T. Nakamura, M. Sasho, and H. Yamashita, *Jpn. Kokai Tokyo Koho JP. 02*, **28,** 170 (1990); *Chem. Abstr.*, **113,** 40334 (1990).

[2] H. Watanabe, K. Sakurai, A. Yamashita, T. Fujiwara, and M. Yaso, *Jpn. Kokai Tokyo Koho JP. 03*, **193,** 786 (1991); *Chem. Abstr.*, **115,** 280058 (1991).

[3] C. S. Andotra and S. K. Sharma, *Proc. Natl. Acad. Sci.*, **61,** 145 (1991); *Chem. Abstr.*, **116,** 55404d (1992).

[4] L. M. Thomasco, R. C. Gadwood, and D. J. Anderson; PCT Int. Appl. WO, 99 02, 525 1997; *Chem. Abstr.*, **130,** 139334h (1999).

[5] F. A. Ashour, N. S. Habib, M. El Taibbi, and A. Shams ElDine, *Alexandria J. Pharm. Sci.*, **4**(1), 86 (1990); *Chem. Abstr.*, **114,** 81707h (1991).

[6] T. Shirasako, H. Ishikawa, K. Yasamura, K. Jitsukawa, S. Toyama, H. Tsubouchi, K. Sudo, and K. Tsuji, Eup. Pat. Appl. Ep., 435, 333 (1991); *Chem. Abstr.*, **115,** 279695s (1991).

[7] L. I. Shevchenko, T. A. Kutsenko, M. O. Lozinskji, T. A. Tatarova, and T. M. Shoroded, *Fiziol. Akt. Veshchestva*, **21,** 18 (1989); *Chem. Abstr.*, **113,** 126046q (1990).
[8] R. Brodin, D. Olliero, and P. Worms, Eur. Pat. Appl. Ep., 356, 333 (1990); *Chem. Abstr.*, **113,** 59198a.
[9] Y. Shiokawa, K. Tokimoto, K. Takenaka, Y. Tokutomi, O. Okitsu, and H. Mizuno, PCT Int. Appl. WO, 93 09, 101 (1993); *Chem. Abstr.*, **119,** 160297f (1993).
[10] C. Supuran, T. Clure, and W. Brain, *Eur. J. Med. Chem.*, **34**(I), 41–50 (1999).
[11] P. C. Tang, J. Y. Ramphal, G. D. Jr. Harlis, and A. S. Namatolla, PCT Int. Appl. WO, 9827, 092 (1998); *Chem. Abstr.*, **129,** 95500g (1998).
[12] A. G. Griffin and T. R. Britt, *J. Am. Chem. Soc.*, **193,** 4957 (1981).
[13] G. Galli, M. Laus, and A. S. Angeloni, *Makromol. Chem.*, **187,** 289 (1986).
[14] H. Ringsdorf, B. Schlarb, and J. Venzmer, *Angew. Chem., Int. Ed. Engl.*, **27,** 115 (1988).
[15] H. Finkelman, *Angew. Chem., Int. Ed. Engl.*, **26,** 816 (1987).
[16] C. Aguilera, M. Parra, and G. Fuentes, *Z. Naturforsch.*, **53b,** 367 (1998).
[17] D. Braun and R. Langendorf, *J. Prakt. Chem.*, **341,** 128 (1999).
[18] J. Ariens, *Drug Design*, Vol. 1, edited by E. J. Ariens (Academic Press, NewYork, 1971).
[19] A. A. Abbas, M. A. A. Elneairy, and Y. N. Mabkhout, *J. Chem. Res.(S)*, 124 (2001).
[20] E. G. Howard and J. R, U.S. Patent, 2733 260 (1956); *Chem. Abstr.*, **50,** 12104 (1956).
[21] N. M. Fathy and G. E. H. Elgemeie, *Sulfur Lett.*, **7**(5), 189 (1988).
[22] N. M. Fathy, F. M. Abdel Motti, and G. E. H. Elgemeic, *Arch. Pharam.* (Winheim), **321,** 509 (1988).
[23] A. H. M. Elwahy and A. A. Abbas, *Synth. Comm.*, **30,** 2903 (2000).
[24] Y. A. Ibrahim, A. H. M. Elwahy, and A. A. Abbas, *Tetrahedron*, **50,** 11489 (1994).
[25] L. Arapides, *Ann. Chem*., **249,** 10 (1888).