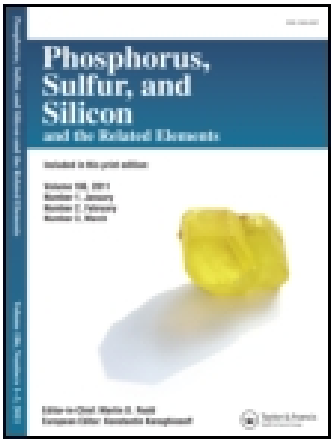

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

A Facile and Convenient Method for the Synthesis of Bis-Hydrazonoyl Halides and Bis-(1,3,4-Thiadiazol-3-ylphenoxy)Ethers

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Published online: 21 Dec 2010.

To cite this article: Ashraf A. Abbas & Nora M. Rateb (2005) A Facile and Convenient Method for the Synthesis of Bis-Hydrazonoyl Halides and Bis-(1,3,4-Thiadiazol-3-ylphenoxy)Ethers, Phosphorus, Sulfur, and Silicon and the Related Elements, 180:2, 497-511, DOI: 10.1080/104265090517226

To link to this article: http://dx.doi.org/10.1080/104265090517226

Phosphorus, Sulfur, and Silicon, 180:497–511, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090517226

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A Facile and Convenient Method for the Synthesis of Bis-Hydrazonoyl Halides and Bis-(1,3,4-Thiadiazol-3-ylphenoxy)Ethers

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*New bis(thiadiazole) derivatives **7a–m** were prepared in good yields by the reaction of the appropriate hydrazonoyl halides **4a–e** with the bis-Schiff bases **9a–c**. Similarly, the bis(thiadiazole) derivatives **17a–g** were prepared by the reaction of the novel bis-hydrazonoyl halides **13a–d** with schiff bases **3a–d**.*

Keywords Bis-thiadiazol(phenoxy) alkanes; bis-hydrazonoyl halides; bis-aldehydes

INTRODUCTION

There is an intensive development in the synthesis of new derivatives of thiazdiazole designed for uses ranging from routine to sophisticated applications. Various series of thiadiazoles and their annelated derivatives are reported to have diverse biological activities as antibacterial,[1–4] antimicrobial,[5,6] antifirinolytic and antiinflammatory,[7] antihistamine agents and muscarinic agonists.[8] In addition, some thiadiazole derivatives are useful as inhibitors of the neutral endopeptidase[9] carbonic anhydrase,[10] anticarcenogenic[11] and kainic acid neurocytotoxicity.[12] Also, some substituted thiadiazoles are used as corrosion inhibitor for copper,[13] complexing agent for Hg[14] as well as additives to improve the properties of many lubricating greases and oils.[15–17] Recently, bis(compounds) attracted the attention of a large group of authors due to their successful utility as building units for many chain polymers.[18–23] The biological activity of natural and synthetic compounds increases as the molecular symmetry increases.[24] This is based on the above facts and with continuation of our interest

Received May 11, 2004; accepted in inal form July 25, 2004.
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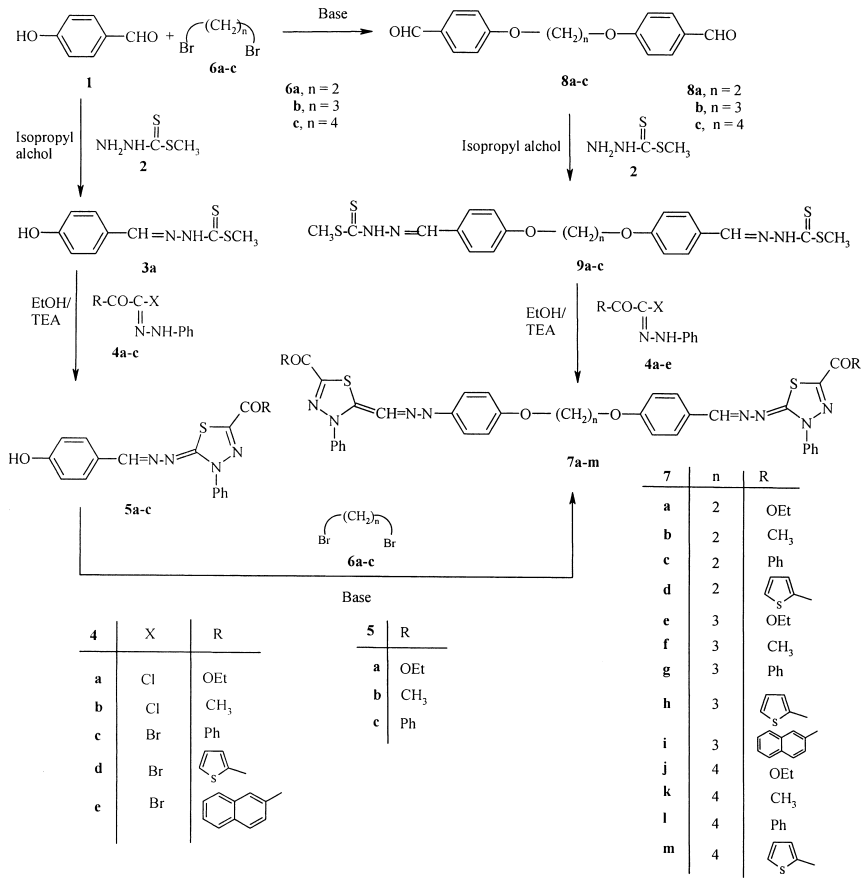
in the synthesis of novel bis-heterocycles.[25–27] The present work investigates the synthesis of some new bis-1,3,4-thiadiazoles as well as novel bis-hydrazonoyl halides as key intermediates for the synthesis of some new bis-heterocycles.

RESULTS AND DISCUSSION

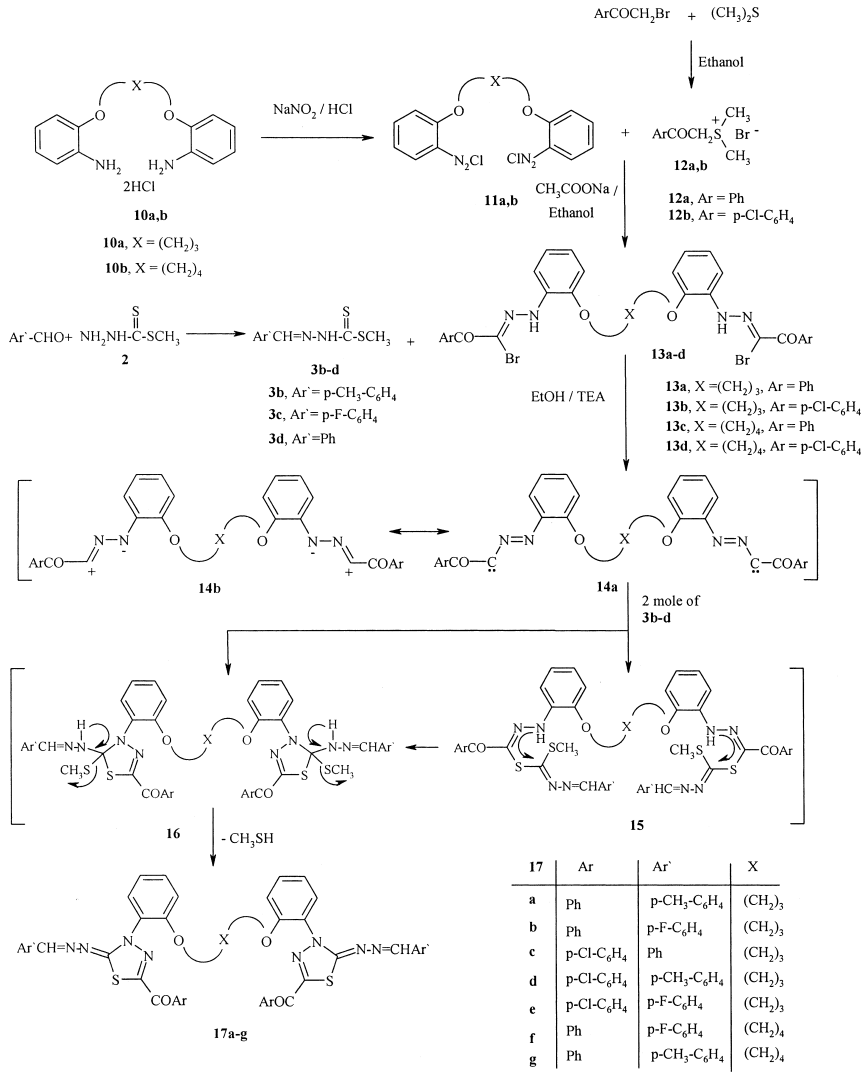
We constructed the new bis(1,3,4-thiadiazol-5-aminobenzylidinephenoxy) alkanes **7a–m** by two strategies outlined in Scheme 1. In the first strategy, we investigated the synthesis of the bis-compounds **7a–m** using p-hydroxybenzaldehyde (**1**) as starting material. Thus, condenstaion of latter compound with hydrazincarbodithioate (**2**) in isopropyl



SCHEME 1 Synthesis of bis(1,3,4-thiadiazol-5-aminobenzylidinephenoxy) alkanes **9a–m** from *p*-hydroxybenzaldehyde.

alcohol, afforded exclusively the Schiff base **3** in good to excellent yields. Compound **3** consequently reacted with hydrazonoyl halides **4a–c** and gave the corresponding 2-*p*-hydroxybenzaldehydehydrazono-3-phenyl-5-substituted-2,3-dihydro-1,3,4-thiadiazoles **5a–c** in 80–90% yields. We tried several attempts to react different derivatives of thiadiazoles **5a–c** with 1,ω-dibromoalkanes **6a–c** in different basic mediums [EtONa, KOH/DMF, K_2CO_3/DMF) to obtain the target bis heterocycles **7a**, **e**, and **g** in good yields, but unfortunately all attempts lead to the formation of an oily residue that cannot easily be handled with the formation of minor products (2∼3% ^{1}H NMR and TLC) of **7a**, **e**, and **g**. In view of the low yields of the above strategy, we tried a second route. Thus, condensation of 1,ω-bis(4-formaylphenoxy)alkanes **8a–c** (obtained by reaction of **1** with 1,ω-dibromoalkanes in basic medium) with **2** in isopropyl alcohol, furnished the corresponding bis-Schiff bases **9a–c** in 70–90% yields. The reaction of equimolecular amounts of C-ethoxycarbonyl-N-phenylhydrazonoyl chloride (**4a**) with **9a** in ethanolic triethylamine solution afforded **7a** which was assigned as bis-(1,3,4-thiadiazole-5-aminobenzylidinephenoxy)alkane based on the spectral and elemental analysis data of the reaction product. The ^{1}H NMR spectrum of compound **7a** showed signals at δ 1.3 (t, 6H, $J = 6$Hz, CH_3), 4.40 (q, 4H, $J = 7.6$Hz, 7.6Hz, $\underline{CH_2}CH_3$), 4.48 (s, 4H, OCH_2), 7.06–8.40 (m, 20H, ArH's and $\underline{CH}$=N); IR spectrum also revealed absorption bands at 1742 and 1712 (cm^{-1}) for (2 CO ester). Similarly, the hydrazonoyl halides **4b–e** reacted with compounds **9a–c** to furnish the corresponding novel bis(thiadiazole) derivatives **7a–m** in 60–85% yields. Our efforts were also extended to include the synthesis of new derivatives of bis-thiadiazole (2-arylaldehydehydrazono-3-phenoxy)ethers where the phenoxy alkanes moiety are connected to the position 3 in the thiadiazole ring instead of position **2** as in **7a–m**. For this purpose we choose 1,ω-bis(2-aminophenoxy)alkane hydrochloride **10a**, **b** as starting material as depicted in Scheme 2. Thus, diazotization of the diamine dihydrochloride **10a**, **b** with sodium nitrite in hydrochloric acid gave the corresponding bis-diazonium salts **11a**, **b** which subsequently reacted with the sulphonium bromides **12a**, **b** (obtained by reacting arylphenacylbromide with dimethylsulphide in absolute ethanol) in ethanolic sodium acetate solution to afford the novel bis-hydrazonoyl halides **13a–d** in 60–75% yields. By analogy and under the same conditions, the reaction of bis-hydrazonoyl halides **13a–d** with methylcarbodithioate derivatives **3b–d**, afforded the target bis-thiadiazole derivatives **17a–f** in 50–65% yields.

It is noteworthy that the formation of the bis(thiadiazole) derivatives can proceed either by initial addition of the thiol tautomer **3** to the intermediate **14**, formed *in situ* by treatment of hydrazonoyl bromid **13** with



17	Ar	Ar`	X
a	Ph	p-CH_3-C_6H_4	$(CH_2)_3$
b	Ph	p-F-C_6H_4	$(CH_2)_3$
c	p-Cl-C_6H_4	Ph	$(CH_2)_3$
d	p-Cl-C_6H_4	p-CH_3-C_6H_4	$(CH_2)_3$
e	p-Cl-C_6H_4	p-F-C_6H_4	$(CH_2)_3$
f	Ph	p-F-C_6H_4	$(CH_2)_4$
g	Ph	p-CH_3-C_6H_4	$(CH_2)_4$

SCHEME 2 Synthesis of bis-thiadiazole (2-arylaldehydehydrazono-3-phenoxy)ethers **17a–g** from bis-amines.

TEA (which can exist in the mesomeric forms **14a** and **14b**)[28] to give the intermediate **15** which undergoes nucleophilic cyclization to yield **16**. This affords **17** by loss of methyl mercaptan or by 1,3 cycloaddition of **14b** to the C=S of **3** to give **16** directly[29,30] (Scheme 2). By the same mechanism, bis(thiadiazole) derivatives **7a–m** can be obtained.

The structures of all compounds were confirmed by IR, ^{1}H NMR and elemental analyses data. From the IR and ^{1}H NMR spectra of compounds **13a–d** it could be concluded that compounds **13a–d** exist exclusively in the hydrazone form due to 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 $\nu = 3325$ (cm^{-1}) in their IR spectra, and (c) the fact that the hydrazone is the most stable form whenever condensation occurs at a methylene group.[25]

In conclusion, we succeeded to prepare new derivatives of bis(thiadiazole) ring systems using bis(aldehydes) and bis(diamines) and we prepared novel bis(hydrazonoyl halides) which are considered key intermediates for the synthesis of a wide variety of new bis(heterocycles) of expected useful applications.[31–33] The utility of these new bis(hydrazonoyl halides) for preparing new ring systems are now in progress.

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded in (KBr disk) on a Bruker, vector 22, Germany or on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ on a Varian Gemini 200 MHz or on a Varian Mercury 300 MHz spectrometer and shifts were expressed in δ units using tetramethylsilane (TMS) as internal reference. Mass spectra were recorded on Hewlett-Packard (HP) 5988A (EI, 15 eV). 1,2-Dibromoethane, 1,3-diaminopropane and 1,4-dibromobutane were used (from Aldrich). Compounds **2**,[34] **3a–d**,[35] **4a–c**,[36–40] **8a–c**,[41] **10a**,[42] **10b**,[43] were prepared as reported.

Synthesis of Bis Schiff Bases 9a–c

General Procedure

A mixture of hydrazine carbodithioate **2** (0.01 mole) and the appropriate aldehydes **8a–c** (0.005 mole) were stirred in isopropyl alcohol (20 mL) at room temperature for 2 hr. The solid was obtained and collected by filtration and crystallized from acetic acid as pale yellow crystals to give **9a–c** respectively.

Bis Methyl Carbodithioate 9a

With the use of the general procedure, reaction of **2** with **8a** gave **9a** in (85%) yield, m.p. 188–90°C. IR (cm^{-1}) 3448, 3131 (NH); ^{1}H NMR

(DMSO) δ 2.48 (s, 6H, S$\underline{CH_3}$), 4.43 (s, 4H, O$\underline{CH_2}$), 7.05 (d, 4H, $J = 8.7$ Hz, ArH's), 7.65 (d, 4H, $J = 8.7$ Hz, ArH's), 8.20 (s, 2H, $\underline{CH}$=N) 12.84 (s, 2H, NH). Calcd. for $C_{20}H_{22}N_4O_2S_4$ (478.68): C, 50.18; H, 4.63; N, 11.70; S, 26.79. Found: C, 50.30, H, 4.80; N, 11.60; S, 26.60.

Bis Methyl Carbodihtioate 9b

With the use of the general procedure, reaction of **2** with **8b** gave **9b** in (78%) yield, m.p. 178–81°C. IR (cm^{-1}) 3449, 3116 (NH); ^{1}H NMR (DMSO) δ 2.38 (quintet, 2H, $J = 8.4$ Hz, OCH$_2\underline{CH_2}$), 2.48 (s, 6H, S$\underline{CH_3}$), 4.18 (t, 4H, $J = 8.4$ Hz, O$\underline{CH_2}$), 7.03 (d, 4H, $J = 9$ Hz, ArH's), 7.65 (d, 4H, $J = 9$ Hz, ArH's), 8.17 (s, 2H, $\underline{CH}$=N) and 13.02 (s, 2H, NH). Calcd. for $C_{21}H_{24}N_4O_2S_4$ (492.71): C, 51.19; H, 4.91; N, 11.37; S, 26.03. Found: C, 50.90, H, 4.70; N, 11.40; S, 26.10.

Bis Methyl Carbodithioate 9c

With the use of the general procedure, reaction of **2** with **8c** gave **9c** in (83%) yield, m.p. 175–77°C. IR (cm^{-1}) 3448, 3101, (NH); ^{1}H NMR (DMSO) δ 1.88 (brs, 4H, OCH$_2\underline{CH_2}$), 2.47 (s, 6H, S$\underline{CH_3}$), 4.08 (brs, 4H, O$\underline{CH_2}$), 7.02 (d, 4H, $J = 8.7$ Hz, ArH's), 7.65 (d, 4H, $J = 8.7$ Hz, ArH's), 8.17 (s, 2H, $\underline{CH}$=N) and 13.16 (s, 2H, NH). Calcd. for $C_{22}H_{26}N_4O_2S_4$ (506.73): C, 52.15; H, 5.17; N, 11.06; S, 25.31. Found: C, 52.30, H, 4.90; N, 11.00; S, 25.20.

Synthesis of 2,3-Dihydro-1,3,4-thiadiazoles 5a–c and bis(1,3,4-thiadiazol-5-aminobenzylidinephenoxy)alkanes 7a–m

General Procedure

To a stirred solution of the appropriate hydrazonoyl halides **4a–e** (0.01 mole) and **3a** (0.01 mole) or the appropriate bis methyl carbodithioate derivatives **9a–c** (0.005 mole) in ethanol (20 ml) triethylamine (0.01 mole) was added dropwise at room temperature and the reaction mixture was further stirred for 2 hr. The solid was obtained, collected, and crystallized from the proper solvent to give **5a–c** and **7a–m**, respectively.

Synthesis of 2,3-Dihydro-1,3,4-thiadiazole 5a

With use of the general procedure, reaction of **3a** with **4a** gave crude **5a** which was crystallized from ethanol as yellow crystals (65%) m.p. 157–60°C. IR (cm^{-1}) 3340 (OH), 1723 (C=O). ^{1}H NMR ($CDCl_3$) δ 1.43

(t, 3H, $J = 6.5$ Hz, $CH_2\underline{CH_3}$), 4.49 (q, 2H, $J = 6.9$ Hz, $\underline{CH_2}CH_3$), 5.45 (s, 1H, $\underline{CH}$=), 6.83–7.98 (m, 9H, ArH's), 8.31 (s, 1H, OH). Calcd. For: $C_{18}H_{16}N_4O_3S$ (368.42): C, 58.68: H, 4.38; N, 15.21; S, 8.70. Found: C, 58.50; H, 4.20; N, 15.00; S, 8.60.

Synthesis of 2,3-Dihydro-1,3,4-thiadiazole 5b

With use of the general procedure, reaction of **3a** with **4b** gave crude **5b** which was crystallized from acetic acid as orange crystals (75%) m.p. 229–30°C. IR (cm^{-1}) 3345 (OH), 1656 (C=O). ^{1}H NMR (DMSO) δ 2.35 (s, 3H, $\underline{CH_3}$), 6.82–8.07 (m, 10H, ArH's and $\underline{CH}$=), 10.01 (s, 1H, OH). Calcd. for: $C_{17}H_{14}N_4O_2S$ (338.39): C, 60.34; H, 4.17; N, 16.56; S, 9.48. Found: C, 60.20; H, 4.00; N, 16.50; S, 9.30.

Synthesis of 2,3-Dihydro-1,3,4-thiadiazole 5c

With the use of the general procedure, reaction of **3a** with **4c** gave crude **5c** which was crystallized from acetic acid as yellow crystals (85%) m.p. 248–50°C. IR spectra (cm^{-1}) 3340 (OH), 1645 (C=O). ^{1}H NMR (DMSO) δ 6.85–8.39 (m, 15H, ArH's and $\underline{CH}$=), 10.06 (s, 1H, OH). Calcd. for: $C_{22}H_{16}N_4O_2S$ (400.46): C, 65.99: H, 4.03; N, 13.99; S, 8.01. Found: C, 65.60; H, 4.30; N, 14.00; S, 8.00.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7a

With the use of the general procedure, reaction of **4a** with **9a** gave crude **7a** which was crystallized from acetic acid as yellow crystals (75%) m.p. 185–87°C. IR (cm^{-1}) 1742, 1712 (2 C=O). ^{1}H NMR (DMSO) δ 1.31 (t, 6H, $J = 6$ Hz, $CH_2\underline{CH_3}$), 4.40 (q, 4H, $J = 6$ Hz, $\underline{CH_2}CH_3$) 4.48 (s, 4H, $O\underline{CH_2}$), 7.06–8.40 (m, 20H, ArH's and $\underline{CH}$=). Calcd. for $C_{38}H_{34}N_8O_6S_2$ (762.87): C, 59.83; H, 4.49; N, 14.69; S, 8.41. Found: C, 59.70, H, 5.00; N, 14.60; S, 8.30.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7b

With the use of the general procedure, reaction of **4b** with **9a** gave crude **7b** which was crystallized from acetic acid as yellow crystals (85%) m.p. 235–37°C. IR (cm^{-1}) 1686, 1610 (2 C=O). ^{1}H NMR (DMSO) δ 2.51 (s, 6H, $\underline{CH_3}$), 4.40 (s, 4H, $O\underline{CH_2}$), 7.08–8.44 (m, 20H, ArH's and $\underline{CH}$=). Calcd.

for $C_{36}H_{30}N_8O_4S_2$ (702.82): C, 61.52; H, 4.30; N, 15.94; S, 9.12. Found: C, 61.60, H, 4.40; N, 16.00; S, 9.00.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7c

With the use of the general procedure, reaction of **4c** with **9a** gave crude **7c** which was crystallized from acetic acid as orange crystals (75%) m.p. 232–35°C. IR (cm^{-1}) 1640, 1610 (2 C=O). ^{1}H NMR ($CDCl_3$) δ 4.41 (s, 4H, O$\underline{CH_2}$), 6.99–8.39 (m, 30H, ArH's and $\underline{CH}$=). Calcd. for $C_{46}H_{34}N_8O_4S_2$ (826.96): C, 66.81; H, 4.14; N, 13.55; S, 7.75. Found: C, 66.70, H, 4.10; N, 13.50; S, 7.60.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7d

With the use of the general procedure, reaction of **4d** with **9a** gave crude **7d** which was crystallized from DMF as orange crystals (70%) m.p. 260–62°C. IR (cm^{-1}) 1620, 1615 (2 C=O). ^{1}H NMR (DMSO) δ 4.43 (s, 4H, O$\underline{CH_2}$), 7.08–8.44 (m, 26H, ArH's and $\underline{CH}$=). Calcd. for $C_{42}H_{30}N_8O_4S_4$ (839.01): C, 60.13; H, 3.60; N, 13.36; S, 15.29. Found: C, 59.90, H, 3.50; N, 13.30; S, 15.20.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7e

With the use of the general procedure, reaction of **4a** with **9b** gave crude **7e** which was crystallized from acetic acid as yellow crystals (85%) m.p. 130–33°C. IR (cm^{-1}) 1741, 1710 (2 C=O). ^{1}H NMR (DMSO) δ 1.31 (t, 6H, J = 6.9 Hz, $CH_2\underline{CH_3}$), 2.19 (quintet, 2H, J = 7.2 Hz, $OCH_2\underline{CH_2}$) 4.18 (t, 4H, J = 7.2 Hz, O$\underline{CH_2}$), 4.38 (q, 4H, J = 7.2 Hz, $\underline{CH_2}CH_3$) 7.00–8.37 (m, 20H, ArH's and $\underline{CH}$=). Calcd. for $C_{39}H_{36}N_8O_6S_2$ (776.90): C, 60.30; H, 4.67; N, 14.42; S, 8.25. Found: C, 59.90, H, 4.80; N, 14.60; S, 8.30.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7f

With the use of the general procedure, reaction of **4b** with **9b** gave crude **7f** which is crystallized from acetic acid as orange crystals (83%) m.p. 188–90°C. IR (cm^{-1}) 1683, 1620 (2 C=O); Ms: m/z 716 (M^+, 4.2%), 498 (19%), 396 (1.5%), 380 (1.4%), 266 (43%), 91 (100%), 77 (37%); ^{1}H NMR (DMSO) δ 2.17 (quintet, 2H, J = 6 Hz, $OCH_2\underline{CH_2}$), 2.30 (s, 6H, $\underline{CH_3}$), 4.20 (t, 4H, J = 5.4Hz, O$\underline{CH_2}$), 7.01–8.37 (m, 20H, ArH's and $\underline{CH}$=).

Calcd. for $C_{37}H_{32}N_8O_4S_2$ (716.85): C, 62.08; H, 4.50; N, 15.63; S, 8.95. Found: C, 61.80, H, 4.80; N, 15.60; S, 8.80.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7g

With the use of the general procedure, reaction of **4c** with **9b** gave crude **7g** which was crystallized from acetic acid as yellow crystals (85%) m.p. 160–63°C. IR (cm^{-1}) 1638, 1612 (2 C=O); Ms: m/z 840 (M^+, 8.5%), 560 (12.47%), 533 (17%), 457 (13.9%), 281 (23.3%), 110 (100%), 105 (5.4%); ^1H NMR (DMSO) δ 2.19 (quintet, 2H, $J = 6.3$ Hz, $OCH_2\underline{CH_2}$) 4.24 (t, 4H, $J = 6.3$ Hz, $O\underline{CH_2}$), 7.01–8.39 (m, 30H, ArH's and $\underline{CH}$=). Calcd. for $C_{47}H_{36}N_8O_4S_2$ (840.99): C, 67.13; H, 4.31; N, 13.32; S, 7.63. Found: C, 67.00, H, 4.20; N, 13.10; S, 7.80.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7h

With the use of the general procedure, reaction of **4d** with **9b** gave crude **7h** which was crystallized from acetic acid as red crystals (75%) m.p. 197–200°C. IR (cm^{-1}) 1684, 1610 (2 C=O). ^1H NMR (DMSO) δ 2.23 (quintet, 2H, $J = 6.3$ Hz, $OCH_2\underline{CH_2}$) 4.24 (t, 4H, $J = 6.3$ Hz, $O\underline{CH_2}$), 7.01–8.39 (m, 26H, ArH's and CH=). Calcd. for $C_{43}H_{32}N_8O_4S_4$ (853.04): C, 60.55; H, 3.78; N, 13.14; S, 15.04. Found: C, 60.30, H, 3.80; N, 13.00; S, 14.90.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7i

With the use of the general procedure, reaction of **4e** with **9b** gave crude **7i** which was crystallized from DMF as orange crystals (70%) m.p. 230–32°C. IR (cm^{-1}) 1624, 1610 (2 C=O). ^1H NMR (DMSO) δ 2.23 (quintet, 2H, $J = 6.3$ Hz, $OCH_2\underline{CH_2}$), 4.24 (t, 4H, $J = 6.3$ Hz, $O\underline{CH_2}$), 7.03–8.91 (m, 34H, ArH's and $\underline{CH}$=). Calcd. for $C_{55}H_{40}N_8O_4S_2$ (941.11): C, 70.20; H, 4.28; N, 11.91; S, 6.81. Found: C, 70.00, H, 4.10; N, 12.00; S, 6.90.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7j

With the use of the general procedure, reaction of **4a** with **9c** gave crude **7j** which was crystallized from acetic acid as yellow crystals (82%) m.p. 180–83°C. IR (cm^{-1}) 1743, 1714, (2 C=O). ^1H NMR (DMSO) δ 1.38 (t, 6H, $J = 7$ Hz, $CH_2\underline{CH_3}$), 1.94 (brs, 4H, $OCH_2\underline{CH_2}$), 4.11 (brs, 4H, $O\underline{CH_2}$),

4.42 (q, 4H, $J = 7$ Hz, $\underline{CH_2}CH_3$) 7.02–8.42 (m, 20H, ArH's and $\underline{CH}$=). Calcd. for $C_{40}H_{38}N_8O_6S_2$ (790.93): C, 60.74; H, 4.84; N, 14.17; S, 8.11. Found: C, 60.50, H, 4.80; N, 14.10; S, 8.00.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7k

With the use of the general procedure, reaction of **4b** with **9c** gave crude **7k** which was crystallized from acetic acid as yellow crystals (83%) m.p. 215–18°C. IR (cm^{-1}) 1683, 1613, (2 C=O). ^{1}H NMR (DMSO) δ 1.92 (brs, 4H, $OCH_2\underline{CH_2}$), 2.34 (s, 6H, $\underline{CH_3}$), 4.11 (brs, 4H, $O\underline{CH_2}$), 7.02–8.42 (m, 20H, ArH's and $\underline{CH}$=). Calcd. for $C_{38}H_{34}N_8O_4S_2$ (730.87): C, 62.45; H, 4.69; N, 15.53; S, 8.77. Found: C, 62.30, H, 4.60; N, 15.30; S, 8.60.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7l

With the use of the general procedure, reaction of **4c** with **9c** gave crude **7l** which was crystallized from acetic acid as orange crystals (73%) m.p. 225–27°C. IR (cm^{-1}) 1683, 1620, (2 C=O). ^{1}H NMR (DMSO) δ 1.92 (brs, 4H, $OCH_2\underline{CH_2}$), 4.13 (brs, 4H, $O\underline{CH_2}$), 7.02–8.42 (m, 30H, ArH's and $\underline{CH}$=). Calcd. for $C_{48}H_{38}N_8O_4S_2$ (855.02): C, 67.43; H, 4.48; N, 13.11; S, 7.50. Found: C, 67.30, H, 4.30; N, 13.00; S, 7.50.

Synthesis of bis(1,3,4-Thiadiazol-5-aminobenzylidinephenoxy) Alkane 7m

With the use of the general procedure, reaction of **4d** with **9c** gave crude **7m** which was crystallized from DMF as orange crystals (70%) m.p. 245–48°C. IR (cm^{-1}) 1685, 1613, (2 C=O); Ms: m/z 867 (M^+, 14%), 581 (100%), 554 (26%), 463 (3.5%), 287 (4.7%); ^{1}H NMR (DMSO) δ 1.93 (brs, 4H, $OCH_2\underline{CH_2}$), 4.11 (brs, 4H, $O\underline{CH_2}$), 7.01–8.43 (m, 26H, ArH's and $\underline{CH}$=). Calcd. for $C_{44}H_{34}N_8O_4S_4$ (867.07): C, 60.95; H, 3.95; N, 12.92; S, 14.79. Found: C, 60.80, H, 4.00; N, 13.00; S, 14.60.

Synthesis of Bis Hydrazonoyl Halides 13a–d

General Procedure

To a stirred solution of the appropriate dimethylsulfonium bromides **12a**, **b** (0.01 mole) in ethanolic sodium acetate solution (20 mL ethanol, 4 g CH_3COONa) a cold solution of the appropriate diazonium chlorides **11a**, **b** (0.005 mole) (which was prepared by reaction of the appropriate diamine dihydrochlorides **10a**, **b** with concentrated HCl followed by

addition of a solution of sodium nitite at 0–5°C) was added dropwise with stirring (0–5°C) and the reaction mixture was stirred for 2–3 hr. The solid obtained was collected and crystallized from acetic acid as yellow-brown crystals to give **13a–d**, respectively.

Bis Hydrazonoyl Halide 13a

With the use of the general procedure, reaction of **11a** with **12a** gave **13a** in (80%) yield, m.p. 138°C. IR (cm^{-1}) 3325 (NH), 1651 (C=O). ^1H NMR ($CDCl_3$) δ 2.48 (quintet, 2H, $J = 5.8$ Hz, $OCH_2\underline{CH_2}$), 4.41 (t, 4H, $J = 5.8$Hz, $\underline{OCH_2}$), 6.94–8.04 (m, 18H, ArH's) 9.08–9.18 (2s, 2H, NH). Calcd. for $C_{31}H_{26}Br_2N_4O_4$ (678.39): C, 54.89; H, 3.86; N, 8.26. Found: C, 55.00, H, 4.10; N, 8.30.

Bis Hydrazonoyl Halide 13b

With the use of the general procedure, reaction of **11a** with **12b** gave **13b** in (75%) yield, m.p. 170°C. IR (cm^{-1}) 3325 (NH), 1651 (C=O). ^1H NMR ($CDCl_3$) δ 2.49 (quintet, 2H, $J = 5.4$ Hz, $OCH_2\underline{CH_2}$), 4.40 (m, 4H, $J = 5.4$ Hz, $\underline{OCH_2}$), 6.94–8.04 (m, 16H, ArH's) 9.09–9.19 (2s, 2H, NH). Calcd. for $C_{31}H_{24}Br_2\ Cl_2N_4O_4$ (747.28): C, 49.83; H, 3.24; N, 7.50. Found: C, 50.00, H, 3.10; N, 7.30.

Bis Hydrazonoyl Halide 13c

With the use of the general procedure, reaction of **11b** with **12a** gave **13c** in (73%) yield, m.p. 198°C. IR (cm^{-1}) 3325 (NH), 1658 (2 C=O). ^1H NMR ($CDCl_3$) δ 2.18 (brs, 4H, $OCH_2\underline{CH_2}$), 4.24 (brs, 4H, $\underline{OCH_2}$), 6.94–8.04 (m, 18H, ArH's) 9.09–9.21 (2s, 2H, NH). Calcd. for $C_{32}H_{28}Br_2N_4O_4$ (692.41): C, 55.51; H, 4.08; N, 8.09. Found: C, 55.30, H, 4.10; N, 8.00.

Bis Hydrazonoyl Halide 13d

With the use of the general procedure, reaction of **11b** with **12b** gave **13d** in (75%) yield, m.p. 196–98°C. IR (cm^{-1}) 3302 (NH), 1666 (C=O). ^1H NMR ($CDCl_3$) δ 2.17 (brs, 4H, $OCH_2\underline{CH_2}$), 4.24 (brs, 4H, $\underline{OCH_2}$), 6.91–8.00 (m, 16H, ArH's) 9.10–9.21 (2s, 2H, NH). Calcd. for $C_{32}H_{26}Br_2$-$Cl_2N_4O_4$ (761.30): C, 50.49; H, 3.44; N, 7.36. Found: C, 50.30, H, 3.30; N, 7.20.

Synthesis of Bis 1,3,4-Thiadiazoles 17a–g

General Procedure

To a stirred solution of the appropriate hydrazonoyl halides **13a–c** (0.005 mole) and the appropriate methyl carbodithioate derivatives **3b–d** (0.01 mole) in ethanol (20 mL) triethylamine (0.01 mole) was added dropwise at room temperature and the reaction mixture was further stireed for 2 hr. The solid was obtained, collected, and crystallized from acetic acid as yellow-brown crystals to give **17a–g**, respectively.

Bis 1,3,4-Thiadiazole 17a

With the use of the general procedure, reaction of **13a** with **3b** gave **17a** in (55%) yield, m.p. 170–73°C. IR (cm^{-1}) 1635, 1605, (2 C=O); Ms: m/z 869 (M^+, 3%), 764 (3%), 548 (23%), 536 (30%), 296 (100%); ^{1}H NMR ($CDCl_3$) δ 2.05 (quintet, 2H, $J = 6.3$ Hz, $OCH_2\underline{CH_2}$), 2.38 (s, 6H, $\underline{CH_3}$), 4.07 (t, 4H, $J = 5.7$ Hz, $O\underline{CH_2}$) 6.83–8.25 (m, 28H, ArH's and $\underline{CH}$=) Calcd. for $C_{49}H_{40}N_8O_4S_2$ (869.04): C, 67.72; H, 4.64; N, 12.89; S, 7.38. Found: C, 67.50, H, 4.60; N, 12.90; S, 7.30.

Bis 1,3,4-Thiadiazole 17b

With the use of the general procedure, reaction of **13a** with **3c** gave **17b** in (49%) yield, m.p. 180–83°C. IR (cm^{-1}) 1635, 1613, (2 C=O). ^{1}H NMR ($CDCl_3$) δ 2.08 (quintet, 2H, $J = 6.6$ Hz, $OCH_2\underline{CH_2}$), 4.07 (t, 4H, $J = 5.9$ Hz, $O\underline{CH_2}$) and 6.81–8.25 (m, 28H, ArH's and $\underline{CH}$=) Calcd. for $C_{47}H_{34}F_2N_8O_4S_2$ (876.97): C, 64.37; H, 3.91; N, 12.78; S, 7.31. Found: C, 64.20, H, 4.00; N, 12.90; S, 7.20.

Bis 1,3,4-Thiadiazole 17c

With the use of the general procedure, reaction of **13b** with **3d** gave **17c** in (45%) yield, m.p. 203–205°C. IR (cm^{-1}) 1635, 1605, (2 C=O); Ms: m/z 909 (M^+, 5.8%), 567 (10%), 491 (8%), 447 (8.7%), 416 (14.5%), 341 (1.2%), 69 (100%); ^{1}H NMR (DMSO) δ 1.98 (quintet, 2H, $J = 6$ Hz, $OCH_2\underline{CH_2}$), 4.07 (t, 4H, $J = 5.7$ Hz, $O\underline{CH_2}$) 6.93–8.24 (m, 28H, ArH's and $\underline{CH}$=) Calcd. for $C_{47}H_{34}Cl_2N_8O_4S_2$ (909.88): C, 62.04; H, 3.77; N, 12.32; S, 7.05. Found: C, 61.90, H, 3.50; N, 12.20; S, 7.00.

Bis 1,3,4-Thiadiazole 17d

With the use of the general procedure, reaction of **13b** with **3b** gave **17d** in (56%) yield, m.p. 180–82°C. IR(cm^{-1}) 1635, 1605, (2 C=O). ^{1}H

NMR ($CDCl_3$) δ 2.06 (quintet, 2H, $J = 6.2$ Hz, $OCH_2\underline{CH_2}$), 2.38 (s, 6H, $\underline{CH_3}$), 4.07 (t, 4H, $J = 6.3$ Hz, $O\underline{CH_2}$), 6.79–8.01 (m, 26H, ArH's and $\underline{CH}$=). Calcd. for $C_{49}H_{38}Cl_2N_8O_4S_2$ (937.93): C, 62.75; H, 4.08; N, 11.95; S, 6.84. Found: C, 62.70, H, 4.00; N, 12.00; S, 7.00.

Bis 1,3,4-Thiadiazole 17e

With the use of the general procedure, reaction of **13b** with **3c** gave **17e** in (73%) yield, m.p. 210–12°C. IR (cm^{-1}) 1635, 1605, (2 C=O). ^{1}H NMR ($CDCl_3$) δ 2.06 (quintet, 2H, $J = 6.2$ Hz, $OCH_2\underline{CH_2}$), 4.07 (t, 4H, $J = 5.6$ Hz, $O\underline{CH_2}$), 6.65–8.23 (m, 26H, ArH's and $\underline{CH}$=). Calcd. for $C_{47}H_{32}Cl_2F_2N_8O_4S_2$ (945.86): C, 59.68; H, 3.41; N, 11.85; S, 6.78. Found: C, 59.70, H, 3.20; N, 12.00; S, 6.90.

Bis 1,3,4-Thiadiazole 17f

With the use of the general procedure, reaction of **13c** with **3c** gave **17f** in (55%) yield, m.p. 209–10°C. IR (cm^{-1}) 1641, 1605, (2 C=O). ^{1}H NMR ($CDCl_3$) δ 1.68 (brs, 4H, $OCH_2\underline{CH_2}$), 3.84 (brs, 4H, $O\underline{CH_2}$) 6.80–8.26 (m, 28H, ArH's and $\underline{CH}$=) Calcd. for $C_{48}H_{36}F_2N_8O_4S_2$ (891.00): C, 64.71; H, 4.07; N, 12.58; S, 7.20. Found: C, 64.60, H, 4.00; N, 12.30; S, 7.00.

Bis 1,3,4-Thiadiazole 17g

With the use of the general procedure, reaction **13c** with **3b** gave **17g** in (50%) yield, m.p. 205–08°C. IR (cm^{-1}) 1635, 1605, (2 C=O); Ms: m/z 884 (M+1, 8%), 765 (11%), 562 (13%), 486 (19%), 471 (2.2%), 235 (100%); ^{1}H NMR ($CDCl_3$) δ 2.10 (brs, 4H, $OCH_2\underline{CH_2}$), 2.57 (s, 6H, $\underline{CH_3}$), 4.25 (brs, 4H, $O\underline{CH_2}$), 7.20–8.68 (m, 28H, ArH's and $\underline{CH}$=) Calcd. for $C_{50}H_{42}N_8O_4S_2$ (883.07): C, 68.01; H, 4.79; N, 12.69; S, 7.26. Found: C, 67.90, H, 4.60; N, 12.50; S, 7.20.

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