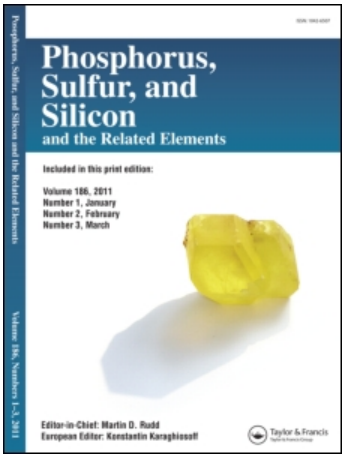

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

The Novel N, S-Substituted Halonitrodienes from the Reactions of Thiosubstituted Nitrodiene with Piperazine and Morpholine

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To cite this Article İbiş, Cemil and Onul, Nihal(2005) 'The Novel N, S-Substituted Halonitrodienes from the Reactions of Thiosubstituted Nitrodiene with Piperazine and Morpholine', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 12, 2787 — 2792
To link to this Article: DOI: 10.1080/104265090968163
URL: http://dx.doi.org/10.1080/104265090968163

Phosphorus, Sulfur, and Silicon, 180:2787–2792, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090968163

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*The substituted 1,2-dibromomethanethio nitrodiene **2** was obtained from the addition of bromine to S-substituted nitrodien **1** in carbon tetrachloride. N,S-substituted compounds **4a–h** were synthesized from the reactions of compound **2** with several substituted piperazine derivatives **3a–h** in dichloromethane. N,S-substituted compounds **6** and **8** were synthesized from the reaction of **2** with morpholine (**5**) and thiomorpholine (**7**) in dichloromethane, respectively. Dibutadienyl piperazines **10**, **12**, and **14** were synthesized from the reactions of **2** with homopiperazine (**9**), piperazine (**11**), and 2,5-dimethylpiperazine (**13**), respectively.*

Keywords Halobutadiene; morpholine; piperazine; polyhalobutadiene; thiosubstituted

Piperazine derivatives exhibit biological and pharmacological activity.[1–3] It has been reported that some piperazine compounds are useful in gen-transfer reactions.[4] Thiomorpholine compounds exhibit biological activity against respiratory tract-infection.[5–7]

It was reported that N-, N,N-substituted dienes were obtained from the reactions of nitrodienes and some nitrogen nucleophiles.[8–12]

Previously, the synthesis of mono(thio)- and dihalobutadienyl substituted piperazines have been reported.[12–20]

The aim of this work was to synthesize novel monobutadienyl and disubstituted butadienyl compounds from the reactions of **2** with piperazine, piperazine derivatives, and morpholine derivatives and also to establish the structure of these novel compounds.

Compound **1** with bromine gave the novel compound **2**. N,S-substituted compounds **4a–h** were obtained from the reactions of **2**

Received February 15, 2005; in final form March 8, 2005.
We thank the Reseach Fund (Project Number: 103/15052003) of the University of Istanbul for financial support of this work.
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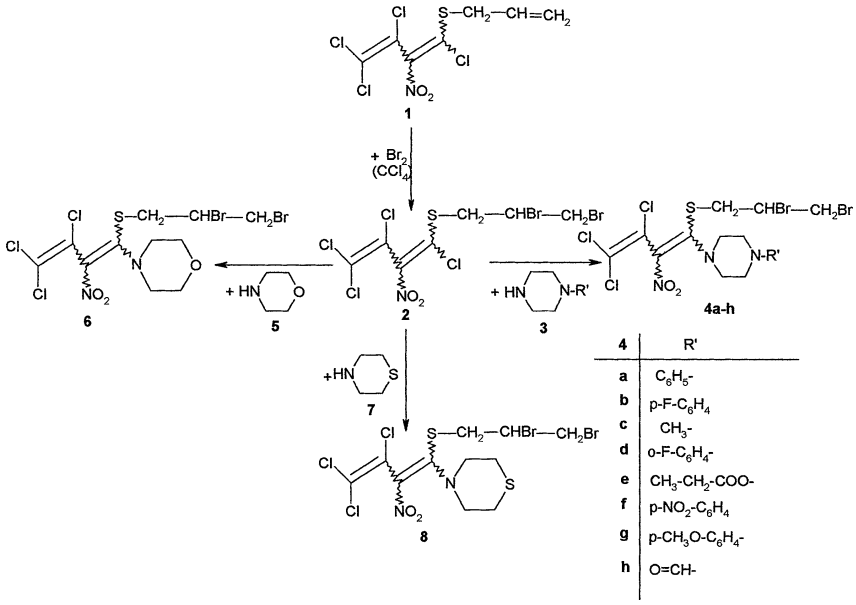
with **3a–h**. Compound **2** gave **6** and **8** with morpholine (**5**) and thiomorpholine (**8**), respectively (Scheme 1). The structure of these novel compounds **2** and **3a–h** were determined by microanalysis and spectroscopic data.



SCHEME 1

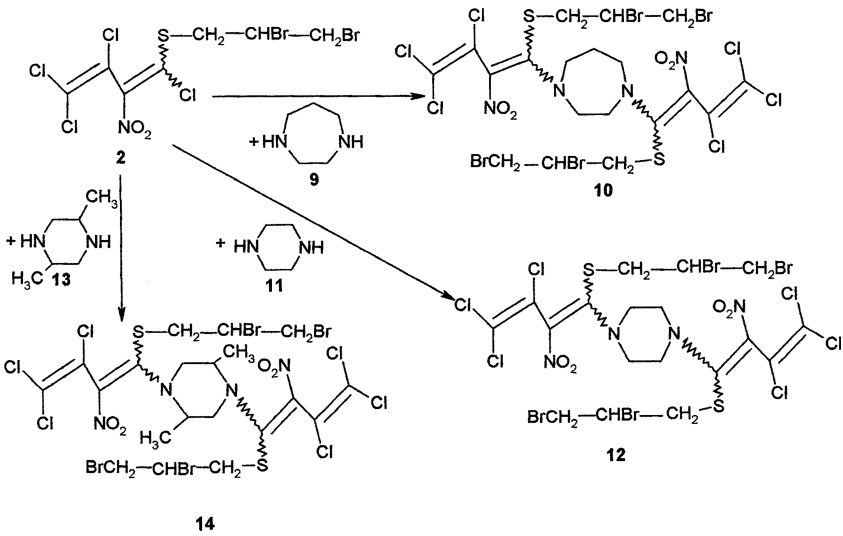
The IR spectra of the butadienylpiperazine **4e** shows a characteristic band for the C=O group of the ester at 1700 cm^{-1} and **4h** shows a characteristic band for the aldehyde group at 1630 cm^{-1}.

These compounds show no optical rotation, because these are rasemic mixtures.

Compound **2** gave **12** and **14** with the piperazines **11** and **13** in dichloromethane, respectively. Also **2** gave **10** when treated with homopiperazine (**9**) in dichloromethane (Scheme 2). It is known that substituted homopiperazines exhibit characteristic biological activity. The reactions occurred according to the addition-elimination mechanism. All compounds are stable, yellow, new dibutadienyl piperazine derivatives.

EXPERİMENTAL SECTİON

–^{1}H-NMR: Varian (Inova) 500 MHz. –IR: Shimadzu FTIR-8101. – Microanalyses: Carlo-Erba 1106 Elemental Analyser. –Melting Points:



SCHEME 2

Büchi SMP 20. Products were isolated by column chromatography on SiO_2 (Fluka Kieselgel 60, particle size 0.063–0.2 mm). TLC plates silica 60 F_{254} (Merck, Darmstadt), detection with ultraviolet light (254 nm).

Preparation of 1(1,2-Dibromoethanethio)-1,3,4,4-tetrachloro-2-nitro-1,3-butadiene (2)

1 g of (3.2 mmol) 1-(allylthio)-1,3,4,4-tetrachloro-2-nitro-1,3-butadiene (**1**) and 0.52 g (3.2 mmol) of bromine were stirred in carbon tetrachloride for 3 h until completion of the reaction (TLC). Ether and a solution of sodium sulfide were added to the reaction mixture. The organic layer was separated, washed with water (4 × 30 mL), and dried with anhydrous Na_2SO_4. The solvent was evaporated.

2: Yield: 1.3 g (86%); dark yellow, viscose oil. $R_f = 0.3500$ (CCl_4). – IR (film): $\nu = 3000$, 2950 cm^{-1} (C—H), 1600 (C=C), 1300, 1520 (NO_2). -^{1}HNMR ($CDCl_3$): $\delta =$ 4.3–4.5 ppm (m, 1H, CH), 3.9–4.1 (m, 2H, CH_2—Br), 3.6–3.8 (m, 2 H, CH_2—S). –$C_7H_5Br_2Cl_4NO_2S$ (468.745): Calcd. C, 17.93; H, 1.08; N, 2.99; S, 6.84; found C, 17.94; H, 1.10; N, 2.70; S 6.36.

Preperation of N,S-Substituted Polyhalonitrodienes General Procedure

1 mol of **2** and 1 mol of piperazine derivative or morpholine or thiomorpholine were stirred in dichloromethane until completion of the reaction

TABLE I Characteristics of the Novel N,S-Substituted Polyhalonitrodienes

Compound number	Molecular formula (% yield)	m.p. (°C)	Microanalyses found (calcd.) C %	H %	N %	S %	IR (cm^{-1})	^{1}H-NMR (ppm) DMSO
4a	$C_{17}H_{18}Br_2Cl_3N_3O_2S$ (79)	235–236	34.60 (34.34)	2.94 (3.05	7.7 (7.07	5.21 (5.39	3050 (Ar—CH), 2800, 2900, 2950 (C—H), 1600 (C═C), 1295, 1520 (NO_2)	6.8–7.3 (m, 5H, Ar—**H**), 4.6 (s, H, C**H**), 3.9–4.1 (m, 2H, C**H**$_2$-Br), 3.5–3.8 (m, 10H, 5C**H**$_2$).
4b	$C_{17}H_{17}Br_2Cl_3FN_3O_2S$ (77)	Oil	33.64 (33.33)	2.21 (2.80)	7.1 (6.86)	5.35 (5.23)	3050 (Ar—CH), 2900, 2950 (C—H), 1600 (C═C), 1290, 1510 (NO_2)	6.9–7.2 (m, 4H, Ar—**H**), 4.6 (s, 1H, C**H**), 3.9–4.1 (m, 2H, C**H**$_2$-Br), 3.0–3.8 (m, 10H, 5C**H**$_2$).
4c	$C_{12}H_{16}Br_2Cl_3N_3O_2S$ (86)	Oil	27.41 (27.07)	3.16 (3.03)	7.86 (7.89)	6.77 (6.02)	2900, 2990 (C—H) 1600 (C═C), 1290, 1510 (NO_2)	4.6 (s, 1H, C**H**), 4.0–4.2 (m, 2H, C**H**$_2$-Br), 3.0–4.0 (m, 10H, 5C**H**$_2$), 2.8 (s, 3H, C**H**$_3$).
4d	$C_{17}H_{17}Br_2Cl_3FN_3O_2S$ (77)	Oil	33.33 (33.58)	2.80 (2.79)	6.86 (6.91)	5.23 (5.6)	3050 (Ar—CH), 2900, 2950 (C—H), 1600 (C═C), 1290, 1530 (NO_2)	6.9–7.2 (m, 5H, Ar—**H**), 4.6 (s, 1H, C**H**), 4.0–4.1 (m, 2H, C**H**$_2$-Br), 3.2–3.9 (m, 10H, 5C**H**$_2$).
4e	$C_{14}H_{18}Br_2Cl_3N_3O_4S$ (75)	Oil	28.18 (28.47)	3.71 (3.07)	7.65 (7.12)	5.38 (5.43)	2950, 2990 (C—H) 1700 (C═O), 1600 (C═C) 1290, 1510 (NO_2)	4.6 (s, 1H, C**H**), 3.8–4.2 (m, 2H, C**H**$_2$-Br), 3.3–3.7 (m, 12H, 6C**H**$_2$).
4f	$C_{17}H_{17}Br_2Cl_3N_4O_4S$ (64)	130–132	31.90 (31.93)	2.67 (2.68)	8.41 (8.76)	5.26 (5.01)	3050 (Ar—CH), 2900, 2950 (C—H) 1600 (C═C), 1300, 1510 (NO_2)	7.0–8.0 (m, 4H, Ar—**H**), 4.6 (s, 1H, C**H**), 3.2–4.2 (m, 12H, 6C**H**$_2$).

4g	$C_{18}H_{20}Br_2Cl_3N_3O_3S$ (77)	Oil	34.59 (34.61)	3.43 (3.23)	6.75 (6.73)	5.26 (5.13)	3050 (Ar—CH), 2990, 2950 (C—H), 2830 (OCH_3), 1600 (C=C) 1290, 1510 (NO_2)	6.8–7.2 (m, 4H, Ar—**H**), 4.6 (s, 1H, C**H**), 4.0–4.2 (m, 2H, C$\mathbf{H}_2$-Br), 3.4–3.8 (m, 10H, 5C$\mathbf{H}_2$), 2.5 (s, 3H, C$\mathbf{H}_3$).
4h	$C_{12}H_{14}Br_2Cl_3N_3O_3S$ (79)	Oil	26.88 (26.37)	2.82 (2.58)	7.38 (7.69)	5.6 (5.87)	2900, 2950 (C—H), 1630 (C=O), 1600 (C=C), 1230, 1520 (NO_2)	8.2 (s, H, C**H**O), 4.6 (s, 1H, C**H**), 3.2–4.0 (m, 12H, 6C$\mathbf{H}_2$).
6	$C_{11}H_{13}Br_2Cl_3N_2O_3S$ (86)	120–121	25.94 (25.43)	2.37 (2.52)	5.53 (5.39)	6.01 (6.17)	2990, 2950 (C—H), 1610 (C=C), 1300, 1510 (NO_2)	4.6 (s, 1H, C**H**), 3.9–4.1 (m, 2H, C$\mathbf{H}_2$-Br), 3.5–3.9 (m, 10H, 5C$\mathbf{H}_2$).
8	$C_{11}H_{13}Br_2Cl_3N_2O_2S_2$ (88)	Oil	24.35 (24.67)	2.64 (2.45)	5.31 (5.23)	11.26 (11.97)	2900, 2950 (C—H), 1600 (C=C), 1280, 1510 (NO_2)	4.6 (s, 1H, C**H**), 4.0–4.1 (m, 2H, C$\mathbf{H}_2$-Br), 3.3–4.0 (m, 10H, 5C$\mathbf{H}_2$).
10	$C_{12}H_{16}Br_2Cl_3N_3O_2S$ (45)	145–146	23.00 (23.65)	2.06 (2.09)	5.42 (5.81)	6.38 (6.65)	2900 (C—H), 1600 (C=C), 1290, 1510 (NO_2)	4.6 (s, 1H, C**H**), 3.0–4.2 (m, 18H, 9C$\mathbf{H}_2$).
12	$C_{18}H_{18}Br_4Cl_6N_4O_4S_2$ (25)	175–180	22.94 (22.74)	1.96 (1.91)	6.09 (5.89)	6.12 (6.74)	2990, 2950 (C—H), 1600 (C=C), 1295, 1520 (NO_2)	4.2–4.4 (m, 2H, 2C**H**), 3.4–4.0 (m, 16H, 8C$\mathbf{H}_2$).
14	$C_{20}H_{22}Br_4Cl_6N_4O_4S_2$ (62)	140–142	24.19 (24.54)	2.65 (2.27)	5.89 (5.72)	5.91 (6.55)	2990, 2950 (C—H), 1600 (C=C), 1280, 1510 (NO_2)	4.8–4.9 (m, 2H, 2C**H**), 4.6 (s, 2H, 2C**H**), 3.9–4.2 (m, 4H, 2C$\mathbf{H}_2$-Br), 3.2–4.0 (m, 8H, 4C$\mathbf{H}_2$), 1.2–1.5 (m, 6H, 2C$\mathbf{H}_3$).

(TLC). Chloroform was added to the reaction mixture. The organic layer was separated and washed with water (4 × 30 mL), and dried with anhydrous Na_2SO_4. The solvent was evaporated and the residue was either crystallized in methanol or purified by column chromatography on silica gel.

REFERENCES

[1] A. Foster, H. Wu, W. Chen, W. Williams, W. D. Bowen, R. R. Matsumoto, and A. Coop, *Biorg Med. Chem. Lett.*, **13,** 749 (2003).
[2] K. Isomae, S. Morimoto, H. Hasegawa, K. Morita, and J. Kamei, *Eur. J. Pharm.*,**465,** 97 (2003).
[3] L. Neuville and J. Zhu, *Tetrahedron Lett.*, **38,** 4091 (1997).
[4] I. Solodin and T. D. Heath, *Synlett*, **7,** 619 (1996).
[5] P. Besse, B. Combourieu, P. Poupin, M. Sancelme, N. Truffaut, H. Veschambre, and A. M. Delart, *Journal. Molecular Catalysis B. Enzymatic*, **5,** 403 (1998).
[6] U. Singh, B. Raju, S. Lam, J. Zhou, R. C. Gadwood, C. W. Ford, G. E. Zurenko, R. D. Schaadt, S. E. Marin, W. J. Adams, J. M. Friis, M. Courtney, J. Palandro, C. J. Hackbarth, S. Lopez, C. Wu, K. H. Mortel, J. Trias, Z. Yuan, D. V. Patel, and M. F. Goraew, *Biorg Med. Chem. Lett.*, **13,** 4209 (2003).
[7] J. Ong, V. Marino, D. A. S. Porker, D. I. B. Kerr, and D. J. Blythin, *Eur. J. Pharm.*, **369,** 33 (1999).
[8] R. V. Kaberdin, V. I. Potkin, and V. A. Zapol'skii, *Russ. Chem. Rev.*, **22,** 1389 (1986).
[9] R. V. Kaberdin, V. I. Potkin, and V. A. Zapol'skii, *Russ. Chem. Rev.*, **68,** 765 (1999).
[10] Yu. A. Ol'dekop, R. V. Kaberdin, and V. I. Potkin, *Zh. Org. Khim.*, **16,** 543 (1980).
[11] R. V. Kaberdin, V. I. Potkin, and V. P. Suboch, *Zh. Org. Khim.*, **29,** 1069 (1983).
[12] Yu. A. Ol'dekop, R. V. Kaberdin, and V. I. Potkin, *Zh. Org. Khim.*, **12,** 2039 (1976).
[13] C. Ibiş and N. B. Yilmaz, *Phosphorus, Sulfur, and Silicon*, **177,** 695 (2002).
[14] C. Ibiş, N. Yilmaz, and Ö. H. Ataseven, *Phosphorus, Sulfur, and Silicon*, **179,** 1897 (2004).
[15] C. Ibiş and Z. Gökmen, *Phosphorus, Sulfur, and Silicon*, **178,** 2297 (2003).
[16] C. Ibiş, Z. Gökmen, and F. S. Göksel, *Chim. Acta Turc.* **32**(1, 2, 3) 32 (2004).
[17] C. Ibiş, F. S. Göksel, and G. Aydinli, *Phosphorus, Sulfur, and Silicon*, **178,** 777 (2003).
[18] C. Ibiş and F. S. Göksel, *Phosphorus, Sulfur, and Silicon*, **97,** 87 (1994).
[19] C. Ibiş und N. Yilmaz, *Phosphorus, Sulfur, and Silicon*, **159,** 87 (2000).
[20] C. Ibiş und M. Onul, *Phosphorus, Sulfur, and Silicon*, **178,** 1881 (2003).