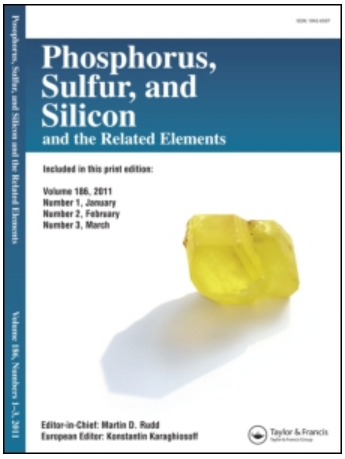

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New N,S-Derivatives of Nitrodienes from Thioallyl-and Thiodibromopropyl Nitrodienes

Cemil İbiş[a]; Nihal Onul[a]
[a] Department of Chemistry, Istanbul University, Avcılar, Istanbul, Turkey

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New N,S-Derivatives of Nitrodienes from Thioallyl- and Thiodibromopropyl Nitrodienes

Cemil İbiş
Nihal Onul
Istanbul University, Department of Chemistry, Avcılar, Istanbul, Turkey

*Compound **3** and **5a**,**b** were obtained from the reaction of 1,3,4,4-tetrachloro-1-thioallyl-2-nitro-1,3-butadiene (**1**) with thiomorpholine (**2**) and piperazine derivatives **4a**,**b** in dichloromethane. The reaction of compound **1** and bromine gave compound **6**. Compounds **8** and **10** were obtained from the reaction of **6** with 1-(diphenylmethyl)piperazine (**7**) and piperidine (**9**) in dichloromethane. The derivative **13** was synthesized from the reaction of 4-bromo-1,1,3,4-tetrachloro-2-nitro-1,3-butadiene (**11**) and allylmercaptane (**12**). Compounds **15** and **16a**,**b** were obtained from the reaction of 1-allyl-4-bromo-1,3,4-trichloro-2-nitro-1,3-butadiene (**13**) with morpholine (**14**) and the piperazine derivatives **16a**,**b**, in dichloromethane, respectively.*

Keywords Morpholine; piperazine; polyhalobutadiene; thiomorpholine

It is known that *S*-, *S*,*S*-, *N*,*S*-, and *N*, *N*-substituted polyhalobutadienes and polyhalonitrobutadienes can be synthesized from the reaction of polyhalobutadienes and polyhalonitrobutadienes with various thiols and amines.[1–4]

Previously, we have reported the synthesis of mono-, di-, tri-, and tetrathiosubstituted polyhalonitrobutadienes from the reaction of polyhalonitrobutadienes with thiols.[5–9] Also we have reported that *N*, *S*-substituted dienes were obtained from the reaction of *S*-substituted polyhalonitrodienes with primary and secondary amines and piperazine derivatives.[10–14]

Piperazine and morpholine derivatives are important for therapeutical use.[15–19] Some piperazine derivatives were used in gen transfer.[20]

The aim of this work is to synthesize new *N*,*S*-substiuted compounds from the reaction of monothiosubstituted polyhalonitrobutadienes with

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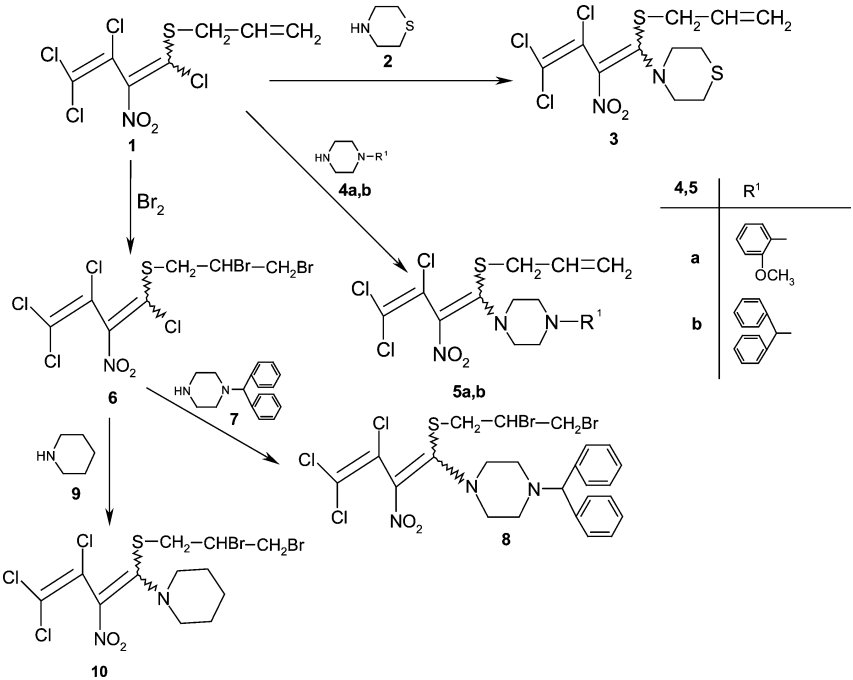
Address correspondence to Cemil İbiş, Istanbul Universitesi, Mühendislik Fakültesi, Kimya Bölümü, Avcılar, Istanbul, Turkiye. E-mail: cmlibis@istanbul.edu.tr

piperazine and morpholine derivatives and to establish the structure of these novel compounds.

Previously, we reported that mono-, di-, and tris(thioallyl)butadienes were obtained from the reaction of polyhalobutadienes and polyhalonitrobutadienes with allylmercaptans.[21,22]

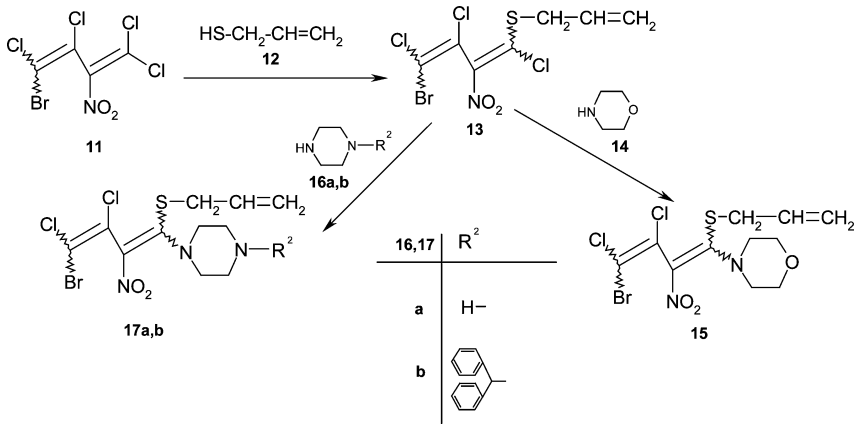
The thioallyl substituted nitrobutadiene **1**[21] gave with thiomorpholine the *N*,*S*-substituted derivative **3**. Dienes **5a**,**b** were obtained from the reaction of compound **1** with **4a**,**b**. Compound **6**[23] resulted from the addition of bromine to compound **1**. The reaction of **6** with the amines **7** and **9** resulted with the formation of dienes **8** and **10**, respectively (Scheme 1).



SCHEME 1

Compound **11** with allylthiol gave **13**. The morpholine derivative **15** was obtained from the reaction of **13** with morpholine **(14)**. The reaction of **13** with the piperazine derivatives **16a**,**b** yielded the dienes **17a**,**b** (Scheme 2).

The infrared spectrum of 1-thioallyl-4-bromo-3,4-dichloro-1-piperazine-2-nitro-1,3-butadiene (**17a**) showed a characteristic band for >NH at 3490 cm^{-1}. Its mass spectrum showed the molecular ion peak at 403.84.



SCHEME 2

Previously, we reported that compound **6**[16] shows no optical rotation because of the presence of a racemic mixture. The same was observed also for compounds **8** and **10**.

Compounds **3**, **5a**, **5b**, **8**, **10**, **15**, **17a**, and **17b** are new *N*,*S*-substituted nitrodienes. Compound **13** is a new *S*-substituted nitrodiene. These compounds are yellow. The structures of these new compounds were determined by elemental analysis and ^{1}H NMR spectroscopy (Table I).

The reactions of these novel compounds occurred according to the addition-elimination mechanism.[3,24]

EXPERIMENTAL SECTION

^{1}H-NMR: Varian (Inova) 500MHz. Mass spectra: Finnigan Max LCMS. IR: Shimadzu FTIR-8101. Microanalyses: Carlo-Erba 1106 elemental analyzer. Melting points: Büchi B-540. 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). 4-bromo-1,1,3,4-tetrachloro-2-nitro-1,3-butadiene was obtained from the reaction of 4-bromo-1,1,3,4-tetrachloro-1,3-butadiene and 58% HNO_3. B.p. 69–71°C; yield: 35%. (b.p. 68–70°C; yield: 40%[25]).

The Preparation of S-Substituted Polyhalonitrodienes: 1-Allylthio-4-bromo-1,3,4-trichloro-2-nitro-1,3-butadiene (13)

5.0 g (15.82 mmol) of 4-bromo-1,1,3,4-tetrachloro-2-nitro1,3-butadiene (**11**) and 1.17 g (15.82 mmol)allylmercaptan (**12**) were stirred at r.t.

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

Compound No.	Molecular Formula Yield (%)	M.P. (°C)	Elemental Analysis Found (calcd.) (%) C	H	N	S	Selected IR Data (cm^{-1})	^{1}H-NMR, δ (ppm) $CDCl_3$
3	$C_{11}H_{13}Cl_3N_2O_2S_2$ (44)	132–134	35.12 (35.16)	3.54 (3.49)	7.47 (7.46)	17.83 (17.07)	2950,2800 (C—H) 1595 (C=C), 1260,1530 (NO_2)	5.6–5.8 (M,1H,C**H**=), 5.1–5.3 (M,2H,=C**H**$_2$), 3.4–4.0 (M,8H,C**H**$_2$), 2.4–2.6 (M,2H,C**H**$_2$)
5a	$C_{18}H_{20}Cl_3N_3OS$ (47)	Oil	46.03 (46.51)	4.11 (4.34)	9.56 (9.04)	6.40 (6.90)	3100 (Ar—H), 2900, 2950 (C—H), 2800 (OCH_3), 1600 (C=C), 1590,1520 (NO_2)	6.8–7.1 (m,4H,Ar—**H**), 5.7–5.9 (m, 1H, C**H**=), 5.1–5.4 (M,2H,=C**H**$_2$5), 3.4–4.0 (m,10H,C**H**$_2$), 3.0 (S,3H,C**H**$_3$)
5b	$C_{24}H_{24}Cl_3N_3O_2S$ (47)	149–150	55.04 (54.92)	4.74 (4.61)	8.16 (8.01)	6.04 (6.11)	3050 (Ar—H), 2950,2900 (C—H), 1600 (C=C), 1295,1510 (NO_2)	7.1–7.4 (M,10H, Ar**H**), 5.6–5.8 (M,1H,C**H**=), 5.1–5.2 (M,2H,=C**H**$_2$), 4.2 (s,1H, C**H**—N), 3.4–3.8 (m,8H, C**H**$_2$), 2.4–2.6 (m, 2H, C**H**$_2$)
8	$C_{24}H_{24}Br_2Cl_3N_3O_2S$ (33)	Oil	42.60 (42.10)	3.54 (3.53)	6.64 (6.14)	4.09 (4.68)	3050 (Ar—CH), 2990, 2950 (C—H), 1600 (C=C), 1290, 1520 (NO_2)	7.1–7.6 (m,10H, Ar—**H**), 4.2–4.3 (m, 2H, C**H**), 3.2–4.0 (m, 12H, C**H**$_2$)
10	$C_{12}H_{15}Br_2Cl_3N_2O_2S$ (64)	Oil	27.53 (27.65)	2.79 (2.92)	5.59 (5.41)	6.51 (6.20)	2950, 2990 (C—H), 1620 (C=C), 1290, 1530 (NO_2)	4.6–4.7 (m, 1H, C**H**), 4.0–4.1 (m,2H, C**H**$_2$-Br), 2.0–3.0 (m,12H, C**H**$_2$)

13	$C_7H_5BrCl_3NO_3S$ (18)	Oil	23.79 (23.53)	1.43 (1.22)	3.96 (3.14)	9.07 (9.31)	2950, 2900 (C—H), 1600 (C=C), 1300, 1510 (NO_2)	5.8–6.0 (m, 1H, C**H**=), 5.2–5.5 (m,2H, =C**H**$_2$), 3.6–3.8 (m, 2H, C**H**$_2$)
15	$C_{11}H_{13}BrCl_2N_2O_3S$ (66)	157–158	32.87 (32.69)	3.37 (3.24)	6.83 (6.93)	7.30 (7.93)	2900, 2800 (C—H), 1590 (C=C), 1290, 1520 (NO_2)	5.7–5.9 (m, 1H, C**H**=), 5.1–5.3 (m, 2H, =C**H**$_2$), 3.2–4.0 (m, 10H, C**H**$_2$)
17a	$C_{11}H_{14}BrCl_2N_3O_2S$(403.13) (75)	Oil	32.77 (32.85)	3.50 (3.38)	10.42 (10.15)	7.95 (7.15)	3490 (NH), 2950,2900 (C—H), 1600 (C=C), 1290, 1510 (NO_2)	5.5–6.0 (m,1H, C**H**=), 5.0–5.4 (m,2H, =C**H**$_2$), 3.0–4.5 (M, 8h, C**H**$_2$), 2.5–3.0 (m,2H, C**H**$_2$), 2.0–2.5 (m, H, N**H**)
17b	$C_{24}H_{24}BrCl_2N_3O_2S$ (55)	14–125	50.69 (50.63)	4.47 (4.25)	7.41 (7.38)	5.99 (5.63)	3050 (Ar—H), 2950, 2900 (C—H), 1600 (C=C), 1290, 1510 (NO_2)	7.0–7.4 (m, 10H, Ar**H**), 5.6–5.8 (m, 1H, C**H**=), 5.1–5.2 (M, 2H, =C**H**$_2$), 4.2–4.4 (s, 1H, **CH**—N), 3.4–3.9 (m, 8H, C**H**$_2$), 2.3–2.6 (m, 2H, C**H**$_2$)

until the completion of the reaction (TLC). Fifty mL of 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 purified by column chromatography on silica gel. Compound **13** was obtained purely. **13**: Yield: 1.0 g (18%); viscose oil. $R_f = 0.5714$ (CCl_4).

The Preparation of N,S-Substituted Polyhalonitrobutadienes: General Procedure

One mol of the *S*-subtituted polyhalonitrobutadiene and 1 mol of the piperazine or morpholine derivative were stirred in dichloromethane until the completion of the reaction (TLC). Chloroform (50 mL) was 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, and the residue was either recrystallized from methanol or the compound was obtained pure as an oil.

1-Allylthio-3,4,4-trichloro-1-thiomorpholino-2-nitro-1,3-butadiene (3)

3: Yield: 52 mg, yellow crystals. $R_f = 0.6471$ ($CHCl_3$).

1-Allylthio-3,4,4-trichloro-1-(2-methoxyphenyl)piperazine-2-nitro-1,3-butadiene (5a)

5a: Yield: 70 mg, dark yellow, viscose oil. $R_f = 0.6956$ ($CHCl_3$).

1-Allylthio-3,4,4-trichloro-1-(1-(diphenylmethyl)piperazine)-2-nitro-1,3-butadiene (5b)

5b: Yield: 80 mg, yellow crystals. $R_f = 0.6087$ ($CHCl_3/CCl_4$ 1:1).

1-(1,2-Dibromoethanethio)-3,4,4-trichloro-1-(1-(diphenylmethyl)piperazine)-2-nitro-1,3-butadiene (8)

8: Yield: 50 mg, yellow oil. $R_f = 0.6260$ ($CCl_4/CHCl_3$ 1:1).

1-(1,2-Dibromoethanethio)-3,4,4-trichloro-1-piperidino-2-nitro-1,3-butadiene (10)

10: Yield: 70 mg, yellow oil, $R_f = 0.6400$ ($CCl_4/CHCl_3$ 1:2).

1-Allylthio-4-bromo-3,4-dichloro-1-morpholino-2-nitro-1,3-butadiene (15)

15: Yield: 75 mg; yellow crystals. $R_f = 0.4500$ ($CHCl_3$).

1-Allylthio-4-bromo-3,4-dichloro-1-piperazine-2-nitro-1,3-butadiene (17a)

17a: Yield: 114 mg, viscose oil. $R_f = 0.4117$ (CH_3OH).

1-Allylthio-4-bromo-3,4-dichloro-1-(1-(diphenylmethyl) piperazine)-2-nitro-1,3-butadiene (17b)

17b: Yield: 88 mg; yellow crystals. $R_f = 0.7727$ ($CHCl_3$).

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