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The reactions of polyhalogenated-2-nitro-1,3-butadiene with alkylthio, thiomorpholine and piperazine derivatives

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Mono(thio)substituted-1,3-nitrodiene compounds **3a-c** give **5a, 5c, 7a, 7c, 9a, 9c, 11a, 11c, 13a, 13b** with thiomorpholine **4** and piperazine derivatives **6**, **8**, **10**, **12**. The new compound **3a** is synthesized from reaction of **1** with **2a**. The compound **7b** crystallizes in the monolinic crystal system (space group $P2_{1/n}$) with the *n*-butyl group attached to S1 and C2Cl3 group disordered. The butadiene unit is not completely planar as can be expected if the two double bonds are fully conjugated. The structure has been solved by direct methods by using SHELXS-97 program and refined by using SHELXL-97 to the residul index R_1= 0.048.

Keywords: N,S-substituted nitrodiene, thioether, piperazine derivatives, thiomorpholine, crystal structure

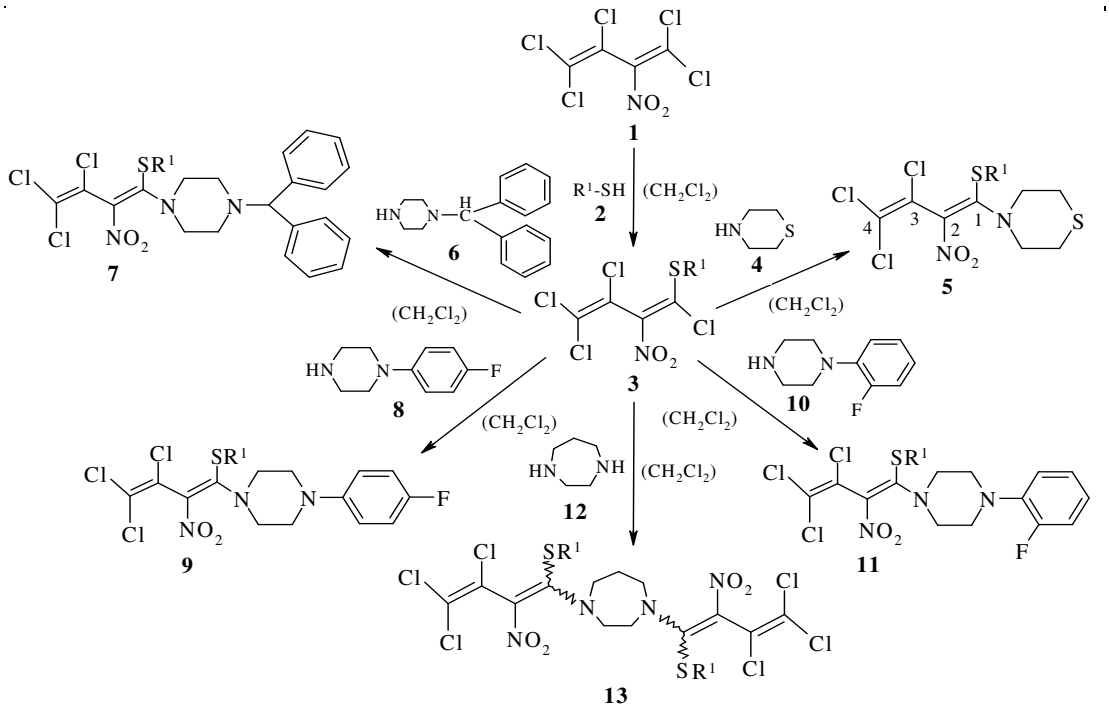
Substituted piperazine compounds are important for clinical chemistry[1] and have also been subject to medicinal applications and gene transfer studies due to their interesting biological activity and chemical effects[2]. Some piperazine derivatives possess high biological activity for multidrug resistance in cancer[3] and malaria[4]. Polycationic ligands, including piperidine and piperazine rings, exhibit a substantial degree of selective RNA binding[5]. Thiomorpholine analogues have found applications in medicine and agriculture[6]. Several investigators have prepared derivatives of thiomorpholine but little attention has been paid to their pharmacological properties[7,8]. Substituted thiomorpholino, piperidino and morpholino compounds enhanced the activity against Gram-positive bacteria, but reduced the activity against Gram-negative bacteria[9]. Nitro-1,3-butadienes, especially their halogen derivatives, have proved to be useful precursors for synthesizing new complex polyfunctional derivatives of different classes and to synthesize diversified functionalized heterocyclic compounds showing antibacterial, antiarrhythmic, antihypoxic, antiviral, antelmintic activity, anti-HIV-1, and antitumor activity[10]. In recent years, some N,S-substituted nitrodienes were obtained from the reactions of nitrodienes with thiols, dithiols and also amines[11-14].

The aim in this study was the synthesis and characterization of new S-, N,S-subtituted nitrodiene compounds and determination of the crystal structure of 2-nitro-3,4,4-trichloro-1-(butylthio)-1-[4-(diphenyl-methyl)piperazin-1-yl]-1,3-butadiene **7b**. The synthesis of compound **7b** have been published before[14].

Results and Discussion

The new compound 2-nitro-1,3,4,4-tetrachloro-1-(propylthio)-1,3-butadiene **3a** and the known 2-nitro-1,3,4,4- tetrachloro-1-(octadecylthio)-1,3-butadiene **3c** (Ref.13) gave new compounds **5a, 5c, 7a, 7c, 9a, 9c, 11a, 11c** with thiomorpholine **4**, *n*-(diphenyl-methyl)-piperazine **6**, 4-(fluorophenyl)piperazine **8** and 2-(fluorophenyl)piperazine **10**. The new compound **3a** was synthesized from reaction of **1** with **2a**. Compounds **13a** and **13b** were obtained from the reactions of **3a** and **3b** with homopiperazine **12**. Disubstituted butadienyl homopiperazine **13a** and **13b** are unsaturated interesting compounds (**Scheme I**).

The ^{1}H NMR spectra of **7a, 7c, 9a, 9c, 11a, 11c** showed the piperazine ring, the piperazine protons are observed as broad singlets between δ 2.5 and 3.8. The aromatic protons are observed as multiplet at δ 6.8-7.5 for the compounds of **7a, 7c, 9a, 9c, 11a** and **11c**. ^{1}H NMR spectra of **5a** and **5c** showed thiomorpholine ring as triplets at δ 2.8 and 2.6 and broad singlets at δ 3.7 and 3.4. The ^{13}C NMR shift of the C-1 carbon atom of compound **5a** (the atom numbering of this compound follows the example in **5**, **Scheme I**) appear relatively downfield around δ 170.07, whereas the NO_2-bearing carbon atom C-2 show resonance, a broadened less intense peak at δ 130.12. The



2, 3, 5, 7, 9, 11, 13	R^1
a	CH_3-CH_2-CH_2-
b	CH_3-$(CH_2)_2$-CH_2-
c	CH_3-$(CH_2)_{16}$-CH_2-

Scheme I

individual C-3 and C-4 carbon atoms each provide chemical shift values around δ 117.47 and 124.32, respectively.

The ESI mass spectrum of the compound **5c** the respective molecular ion peak is observed at *m/z* (%) 589 (100). Major fragment F_1 of compound **5c** was found at *m/z* (%) 507 $[M-81]^+$ (100). It is likely that this corresponds to the nitronium $[NO_2]^+$ and chlorine $[Cl]^+$ ions. The respective molecular ion peak is observed at *m/z* (%) 379 (100) for compound **5a** in the mode of ESI. The cleavage of chlor ion from the compound **5a** of the molecular ion gives rise to fragment F_1 at *m/z* (%) 342 (100). The peak at *m/z* (%) 296 (65) is due to F_2 fragment obtained from the molecular ion by the loss of a nitronium ion.

Some characteristic bands in the IR spectra of compounds **9a, 9c, 11a** and **11c** should be mentioned: The C=C stretching band is observed within the range 1527-1657 cm^{-1}, and the NO_2 groups are observed in the range 1453-1512 cm^{-1} (asymmetric stretching) and 1274-1282 cm^{-1} (symmetric stretching). In the IR spectra of **13a** and **13b** no band is observed in the region 3200-3450 cm^{-1} attributable to the streching vibration of the bonded NH group, indicating the formation of a disubstituted butadienyl homopiperazine compound. In the ^1H NMR spectra of compounds **13a** and **13b** which contain the homopiperazine ring, the homopiperazine protons are observed as broad singlet at δ 2.10 and as multiplet at δ 3.90, respectively. In the ^{13}C NMR spectrum of the compound **13b,** the signals at δ 14.04 (CH_3-), 21.83 (-CH_2-), 32.10 (S-CH_2-*C*H_2-) and 35.54 (S-CH_2-) are characteristic of the carbon atoms of the *n*-butyl chain.

The substitution reaction proceeds by an addition-elimination mechanism[15]. First, an addition of the attacking reagent to the C,C double bond occurs, and in a second step the intermediate product is stabilized by elimination of hydrogen chloride.

The obtained products were stable compounds and some of them are yellow in color. The structures of the products were determinated by microanalysis and spectroscopic data such as IR, ^1H and ^{13}C NMR, MS and crystal structure of **7b** was determinated by X-ray diffraction method. Crystal stuctures of compounds **5a** and **7a** had been reported[16,17]. All these new compounds gave spectroscopic data in accordance with the proposed structure.

Discussion of the X-ray analysis for 7b

The title compound, $C_{25}H_{28}N_3O_2SCl_3$, contains the expected N,S-substituted butadienyl skeleton, piperazine and phenyl rings. The butadiene unit is not completely planar as can be if the two double bonds are fully conjugated. The C-C bond lengths of the butadiene unit are similar to those in related compounds[16-19].

The C_2Cl_3 group is disordered such that the C atoms have two possible positions inside the rectangle described by C_2 and the three chloro atoms. The occupancy of the "A" pair refined to 0.47(7). Likewise the *n*-butyl group attached to S_1 is disordered; the "A" group has a refined occupancy of 0.53(1). The torsion angles of C1-C2-C7A-C8A and C1-C2-C7B-C8B are -94.51(1)°, 107.07(1)°, respectively. The maximum electron-density peak is located 1.12 Å from atom Cl3. Hydrogen atoms were placed in calculated positions, although the rotational positions of methyl groups were allowed to refine with C-H distances and C-C-H angles fixed.

Both the phenyl rings are planar with a maximum deviations of 0.0004 Å (C14-C15-C16-C17-C18-C19) and 0.0053 Å (C20-C21-C22-C23-C24-C25). The piperazine ring adopts a chair conformation and is planar with a maximum deviation of 0.0154 Å ; the distances of two chair atoms in the *para* positions (N2 and N3) from the plane of the other four atoms of the six-membered piperazine ring are -0.576(1) Å and 0.735(2) Å. Both the planar phenyl rings are inclined at an angle of 85.1°(1). Dihedral angle is 60.5°(1) between planes of phenyl (C14-C15-C16-C17-C18-C19) and piperazine rings.

Material and Methods

General procedure 1. Synthesis of S-substituted polyhalonitrodienes 3a, 3b (Ref.12), 3c (Ref.13): Equimolar amounts of 1,1,3,4,4-pentachloro-2-nitro-1,3-butadiene **1** (2 g, 7.37 mmol) and thiols **2a** (0.56 g, 7.37 mmol), **2b** (0.66 g, 7.37 mmol) or **2c** (2.11 g, 7.37 mmol) in 20 mL dichloromethane were mixed at RT. The mixture was stirred for 24 hr. Chloroform (30 mL) was added to the reaction mixture. The organic layer was separated and washed with water (4 × 30 mL), and dried with anhyd. Na_2SO_4. After the solvent was evaporated the residue was purified by column chromatography over silica gel.

General procedure 2. Synthesis of *N,S*-substituted polyhalonitrodienes 5a, 5c, 7a, 7c, 9a, 9c, 11a, 11c, 13a, 13b: Equimolar amounts of S-substituted polyhalonitrodienes **3a-c** and thiomorpholine **4** or piperazine derivatives **6**, **8**, **10**, **12** were mixed in 20 mL dichloromethane at RT. The mixture was stirred for 24 hr. Chloroform (30 mL) was added to the reaction mixture. The organic layer was separated and washed with water (4×30 mL) and dried with anhyd. Na_2SO_4. After the solvent was evaporated the residue was purified by column chromatography over silica gel.

Experimental Section

Melting points were measured on a Buchi B-540 melting point apparatus and are uncorrected. Elemental analyses were performed on a Thermo Finnigan Flash EA 1112 elemental analyser. Infrared (IR) spectra were recorded in KBr pellets and in Nujol mulls on a Perkin Elmer Precisely Spectrum One FTIR spectrometry. ^1H and ^{13}C NMR spectra were recorded on Varian UNITYINOVA operating at 500 MHz. Mass spectra were obtained on a Thermo Finnigan LCQ Advantage MAX LC/MS/MS spectrometer according to ESI probe. Crystal structure of **7b** was determined on Rigaku R-Axis RAPID-S X-Ray Single Crystal diffractometer. Products were isolated by column chromatography over silica gel (Fluka silica gel 60, particle size 63-200 μm). TLC plates (silica $60F_{254}$, Merck, Darmstadt), spots were detected with ultraviolet light (254 nm). All chemicals were of reagent grade and used as received. Moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes.

X-Ray Structure Determination

A yellow block crystal of $C_{25}H_{28}N_3O_2SCl_3$ having approximate dimensions of 0.40 × 0.30 × 0.20 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID curved imaging plate area detector with graphite monochromated Mo-Kα radiation (λ=0.71093 Å). Experimental conditions are summarized in **Table I**. The structure was solved

Table I — Experimental details of the X-ray analysis for **7b**

Sum formula	$C_{25}H_{28}N_3O_2SCl_3$
M_w (g.mol^{-1})	540.91
Space group	$P2_1/n$ (No. 14)
	a = 8.4097(2) Å, b = 14.2018(4) Å, c = 22.6832(8) Å
	β = 94.679(2)°
V/Å^3	2700.09(14)
Z	4
D_c(g.cm^{-3})	1.331 g/cm^3
μ [mm^{-1}]	0.44
F(000)	1128.00
h,k,l ranges	0/10, 10/17, -27/27
Reflections collected	53074
Independent reflections	4930 (R_{int} = 0.030)
Data / restraints / parameters	4062 / 0 /365
Goodness-of-fit on F^2	1.160
Final R indices [$I>2\sigma(I)$]	R =0.048, wR = 0.133
Largest diff. peak and hole	0.19 and -0.28 e·Å^{-3}
Refine_ls_weighting_details;	
calc w=1/[\s^2^(Fo^2^)+(0.0540P)^2^] where P=(Fo^2^+2Fc^2^)/3'	

by direct method using SHELXS-97 (Ref.20) and refined with SHELXL-97 (Ref.21). The non-hydrogen atoms were refined anisotropically. Selected bond distances and bond angles for **7b** are listed in **Table II**. The molecular structure of the title compound, $C_{25}H_{28}N_3O_2SCl_3$, is shown in **Figure 1** (Ref.22). Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-653508 for **7b** (Ref.23).

2-Nitro-1,3,4,4-tetrachloro-1-(propylthio)-1,3-butadiene, 3a: Compound **3a** was synthesized from **1** (2 g, 7.37 mmol) and propanethiol **2a** (0.56 g, 7.37 mmol) according to the general procedure 1. Yield 0.62 g (27%); m.p. 62-63°C. R_f (CCl_4): 0.42; IR (KBr): 2875, 2933, 2967 (C-H), 1461, 1603 (C=C), 1291, 1534 cm^{-1} (C-NO_2); ^{1}H NMR (499.74 MHz, $CDCl_3$): δ 1.1 (t, J = 7.32 Hz, 3H, CH_3), 1.8 (m, 2H, S-CH_2-CH_2), 3.1 (t, J = 7.32 Hz, 2H, S-CH_2); ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 12.31 (CH_3), 21.03 (S-CH_2-CH_2), 36.84 (S-CH_2), 120.61, 127.62, 138.05, 156.84 (C_{butad}). Anal. $C_7H_7N_1O_2S_1Cl_4$ (M, 311.01). Calcd. C, 27.03; H, 2.26; N, 4.50; S, 10.30. Found C, 27.35; H, 2.13; N, 4.42; S, 10.13%.

Table II — Selected bond lengths [Å] and angles [°] with e.s.d. in parentheses for **7b**

Cl1-C8A	1.664(8)	C1-C2	1.384(3)	Cl2-C8B	1.701(6)
Cl2-C8A	1.805(8)	Cl3-C8B	1.693(6)	Cl3-C7A	1.802(9)
S1-C1	1.762(2)	S1-C3A	1.769(9)	S1-C3B	1.871(8)
N1-C2	1.431(3)	N2-C1	1.342(3)	N2-C9	1.459(3)
N2-C11	1.481(3)	N3-C10	1.465(3)	N3-C12	1.465(3)
N3-C13	1.472(3)	Cl1-C7B	1.766(8)	C2-C7A	1.469(9)
C2-C7B	1.546(9)	C3A-C4A	1.518(9)	C4A-C5A	1.507(7)
C5A-C6A	1.411(9)	C3B-C4B	1.471(8)	C4B-C5B	1.501(8)
C5B-C6B	1.456(8)	C7A-C8A	1.302(7)	C7B-C8B	1.315(8)
C9-C10	1.503(3)	C11-C12	1.502(3)	C13-C20	1.520(3)
C8A-Cl1-C7B	28.2(2)	C8B-Cl2-C8A	33.3(2)	C3A-S1-C3B	7.3(8)
C1-S1-C3A	106.9(5)	C1-S1-C3B	99.8(6)	C7A-C2-C7B	32.1(3)
N2-C1-C2	125.5(2)	N2-C1-S1	119.5(1)	C8B-Cl3-C7A	34.1(9)
C1-C2-N1	122.7(2)	C1-C2-C7A	124.3(3)	N1-C2-C7A	108.5(3)
C1-C2-C7B	120.6(3)	N1-C2-C7B	115.8(3)	C2-C1-S1	114.9(9)
C4A-C3A-S1	113.0(7)	C5A-C4A-C3A	114.0(8)	C6A-C5A-C4A	117.9(9)
C4B-C3B-S1	116.2(8)	C3B-C4B-C5B	118.1(9)	C6B-C5B-C4B	120.7(9)
C8A-C7A-C2	118.3(9)	C8A-C7A-Cl3	116.8(7)	C2-C7A-Cl3	124.8(6)
C7A-C8A-Cl1	121.6(8)	C7A-C8A-Cl2	118.7(7)	Cl1-C8A-Cl2	119.7(5)
C8B-C7B-C2	120.5(7)	C8B-C7B-Cl1	119.3(7)	C2-C7B-Cl1	120.2(5)

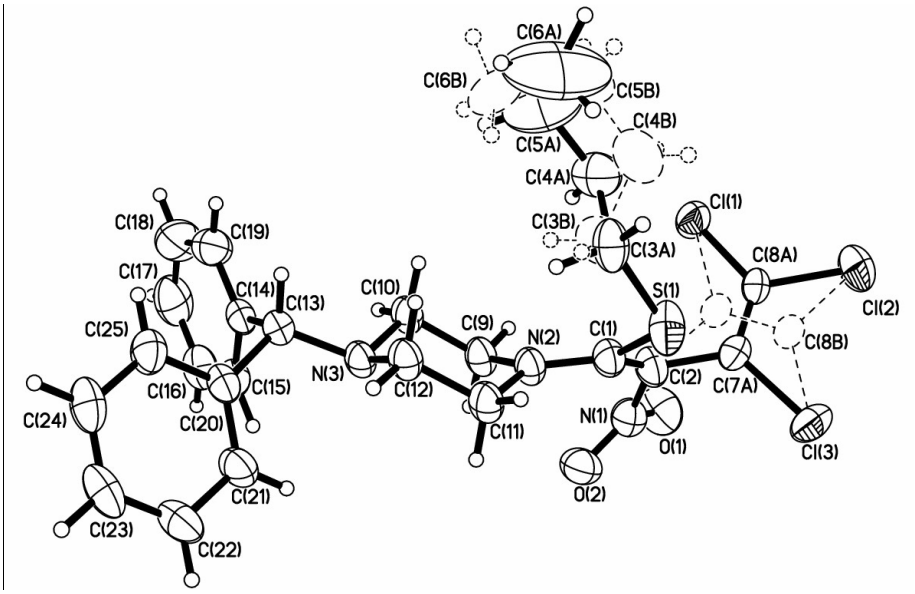


Figure 1 — X-ray analysis of **7b**. Displacement ellipsoids are plotted at the 50% probability level (Symmetry transformations used to generate equivalent atoms: (i)- x, -y, -z).

2-Nitro-3,4,4-trichloro-1-(propylthio)-1-(thiomorpholinly)-1,3-butadiene, 5a: Compound **5a** was synthesized from **3a** (0.4 g, 1.28 mmol) and thiomorpholine **4** (0.13 g, 1.28 mmol) according to the general procedure 2. Yield 0.26 g (54%); m.p. 151-53°C. R_f ($CHCl_3$): 0.45; IR (KBr): 2895, 2900 (C-H), 1580, 1650 (C=C), 1290, 1550 cm^{-1} (C-NO_2); ^1H NMR (499.74 MHz, DMSO-d_6): δ 0.95 (t, J = 7.32 Hz, 3H, CH_3), 1.65 (m, 2H, S-CH_2-CH_2), 3.00 (t, J = 7.32 Hz, 2H, S-CH_2), 2.86 (t, J = 4.88 Hz, 4H, $H_{thiomorp}$), 3.76 (s, br, 4H, $H_{thiomorp}$); ^{13}C NMR (125.66 MHz, DMSO-d_6): δ 13.60 (CH_3), 23.30 (S-CH_2-CH_2), 37.41 (S-CH_2), 40.79, 56.68 ($C_{thiomorp}$), 117.47, 124.32, 130.12, 170.07 (C_{butad}); MS (+ESI): *m/z* 379 $(M+1)^+$, 297 $(M-81)^+$. Anal. $C_{11}H_{15}N_2O_2S_2Cl_3$ (M, 377.73). Calcd. C, 34.98; H, 4.00; N, 7.41; S, 16.97. Found C, 35.05; H, 4.17; N, 7.33; S, 16.80%.

2-Nitro-3,4,4-trichloro-1-(octadecylthio)-1-(thiomorpholinly)-1,3-butadiene, 5c: Compound **5c** was synthesized from **3c** (0.3 g, 0.57 mmol) and thiomorpholine **4** (0.059 g, 0.57 mmol) according to the general procedure 2. Yield 0.18 g (53%); Oil, R_f [CCl_4/$CHCl_3$(1:1)]: 0.30; IR (KBr) 2875, 2900 (C-H), 1580, 1650 (C=C), 1290, 1530 cm^{-1} (C-NO_2); ^1H NMR (499.74 MHz, $CDCl_3$): δ 0.88 (t, J = 7.32 Hz, 3H, CH_3), 1.2-1.5 (m, 30H, CH_2), 1.65 (m, 2H, S-CH_2-CH_2), 3.12 (t, J = 7.32 Hz, 2H, S-CH_2), 2.69 (t, J = 4.88 Hz, 4H, $H_{thiomorp}$), 3.45 (s, br, 4H, $H_{thiomorp}$); ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 13.08 (CH_3), 21.67, 27.73, 28.02, 28.23, 28.25, 28.28, 28.34, 28.36, 28.41, 28.50, 28.52, 28.56, 28.59, 28.64, 28.68 (CH_2), 30.91 (S-CH_2-CH_2), 34.49 (S-CH_2), 39.67, 50.80 ($C_{thiomorp}$), 118.46, 124.41, 125.48, 168.17 (C_{butad}); MS (+ESI): *m/z* 589 $(M+1)^+$, 507 $(M-81)^+$. Anal. $C_{26}H_{45}N_2O_2S_2Cl_3$ (M, 588.14). Calcd C, 53.08; H, 7.71; N, 4.76; S, 10.90. Found C, 52.99; H, 7.79; N, 4.64; S, 10.86%.

2-Nitro-3,4,4-trichloro-1-(propylthio)-1-[4-(diphenylmethyl)piperazin-1-yl]-1,3-butadiene, 7a: Compound **7a** was synthesized from **3a** (0.6 g, 1.92 mmol) and *N*-(diphenylmethyl)-piperazine **6** (0.48 g, 1.92 mmol) according to the general procedure 2. Yield 0.52 g (51%); m.p. 143-45°C. R_f ($CHCl_3$): 0.52; IR (KBr): 2900 (C-H), 1580, 1650 (C=C), 1280, 1520 (C-NO_2), 3100 cm^{-1} (Ar-H); ^1H NMR (499.74 MHz, DMSO-d_6): δ 0.95 (t, J = 7.32 Hz, 3H, CH_3), 1.60 (m, 2H, S-CH_2-CH_2), 2.95 (t, J = 6.84 Hz, 2H, S-CH_2), 2.5 (s, br, 4H, H_{piper}), 3.6 (s, br, 4H, H_{piper}), 4.3 (s, 1H, -CH<), 7.0-7.5 (m, 10H, $H_{arom.}$); ^{13}C NMR (125.66 MHz, DMSO-d_6): δ 17.00 (CH_3), 23.32 (S-CH_2-CH_2), 37.43 (S-CH_2), 40.88, 51.51 (N-CH_2), 74.85 (-CH<), 128.08, 128.36, 129.47 (CH_{arom}), 142.92 (C_{arom}), 124.26, 128.36, 129.47, 167.70 (C_{butad}); MS (+ESI): *m/z* 528 $(M+1)^+$. Anal. $C_{24}H_{26}N_3O_2S_1Cl_3$ (M, 526.91). Calcd. C, 54.70; H, 4.97; N, 7.97; S, 6.08. Found C, 54.98; H, 4.89; N, 7.99; S, 5.96%.

2-Nitro-3,4,4-trichloro-1-(octadecylthio)-1-[4-(diphenylmethyl)piperazin-1-yl]-1,3-butadiene, 7c: Compound **7c** was synthesized from **3c** (0.6 g, 1.15 mmol) and *N*-(diphenylmethyl)-piperazine **6** (0.29 g, 1.15 mmol) according to the general procedure 2.

Yield 0.38 g (45%); Oil, R_f ($CHCl_3$): 0.32; IR (KBr): 2853, 2924 (C-H), 1590, 1660 (C=C), 1286, 1531 (C-NO_2), 3027 cm^{-1} (Ar-H); ^1H NMR (499.74 MHz, DMSO-d_6): δ 0.85 (t, J = 6.83 Hz, 3H, CH_3), 1.1-1.4 (m, 30H, CH_2), 1.55 (m, 2H, S-CH_2-CH_2), 2.94 (t, J = 6.84 Hz, 2H, S-CH_2), 2.5 (s, br, 4H, H_{piper}), 3.55 (s, br, 4H, H_{piper}), 4.2 (s, 1H, -CH<), 7.0-7.5 (m, 10H, $H_{arom.}$); ^{13}C NMR (125.66 MHz, DMSO-d_6): δ 14.59 (CH_3), 14.61, 23.75, 28.48, 28.59, 28.81, 29.08, 29.16, 29.36, 29.40, 29.55, 29.64, 29.68, 29.82, 30.35, 31.95 (CH_2), 32.75 (S-CH_2-CH_2), 35.57 (S-CH_2), 40.74, 51.55 (N-CH_2), 74.91 (-CH<), 127.86, 128.15, 129.24 (CH_{arom}), 142.81 (C_{arom}), 124.19, 128.30, 129.38, 167.56 (C_{butad}); MS (+ESI): *m/z* 738 $(M+1)^+$, 657 $(M-81)^+$. Anal. $C_{39}H_{56}N_3O_2S_1Cl_3$ (M, 737.32). Calcd. C, 63.79; H, 7.65; N, 5.69; S, 4.34. Found C, 63.88; H, 7.64; N, 5.64; S, 4.14%.

2-Nitro-3,4,4-trichloro-1-(propylthio)-1-[4-(fluorophenyl)piperazin-1-yl]-1,3-butadiene, 9a: Compound **9a** was synthesized from **3a** (0.65 g, 2.05 mmol) and 4-(fluorophenyl)piperazine **8** (0.37 g, 2.05 mmol) according to the general procedure 2. Yield 0.55 g (59%); m.p. 118-19°C. R_f (CH_2Cl_2): 0.45; IR (KBr): 2931, 2823 (C-H), 1527, 1657 (C=C), 1276, 1453 (C-NO_2), 2965 cm^{-1} (Ar-H); ^1H NMR (499.74 MHz, $CDCl_3$): δ 1.0 (t, J = 7.32 Hz, 3H, CH_3), 1.7 (m, 2H, S-CH_2-CH_2), 2.96 (t, J = 7.32 Hz, 2H, S-CH_2), 3.2 (s, br, 4H, H_{piper}), 3.8 (s, br, 4H, H_{piper}), 6.8-7.1 (m, 4H, H_{arom}); ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 12.27 (CH_3), 22.29 (S-CH_2-CH_2), 36.42 (S-CH_2), 49.50, 52.06 (N-CH_2), 114.85, 115.03, 117.75, 117.82 (CH_{arom}), 123.83, 125.78 (C_{arom}), 145.64, 156.11, 158.03, 168.01 (C_{butad}). Anal. $C_{17}H_{19}N_3O_2S_1Cl_3F_1$ (M, 454.78). Calcd. C, 44.89; H, 4.21; N, 9.23; S, 7.05. Found C, 44.85; H, 4.29; N, 9.11; S, 7.18%.

2-Nitro-3, 4, 4-trichloro-1-(octadecylthio)-1-[4-(fluorophenyl)piperazin-1-yl]-1,3-butadiene, 9c: Compound **9c** was synthesized from **3c** (0.65 g, 1.24 mmol) and 4-(fluorophenyl)piperazine **8** (0.22 g, 1.24 mmol) according to the general procedure 2. Yield 0.52 g (64%); m.p. 74-75°C; R_f ($CHCl_3$): 0.46; IR (KBr): 2849 (C-H), 1531, 1596 (C=C), 1282, 1512 (C-NO_2), 2918 cm^{-1} (Ar-H); ^1H NMR (499.74 MHz, $CDCl_3$): δ 0.88 (t, J = 7.32 Hz, 3H, CH_3), 1.2-1.5 (m, 30H, CH_2), 1.7 (m, 2H, S-CH_2-CH_2), 2.97 (t, J = 7.32 Hz, 2H, S-CH_2), 3.2 (s, br, 4H, H_{piper}), 3.8 (s, br, 4H, H_{piper}), 6.8-7.0 (m, 4H, H_{arom}); ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 13.06 (CH_3), 21.67, 21.78, 22.15, 22.45, 23.10, 27.71, 27.89, 28.03, 28.34, 28.37, 28.51, 28.60, 28.65, 28.68, 28.80 (CH_2), 30.92 (S-CH_2-CH_2), 34.59 (S-CH_2), 49.48, 52.07 (N-CH_2), 114.84, 115.01, 117.73, 117.79 (CH_{arom}), 123.79, 125.81 (C_{arom}), 145.69, 156.08, 158.00, 168.09 (C_{butad}). Anal. $C_{32}H_{49}N_3O_2S_1Cl_3F_1$ (M, 665.18). Calcd. C, 57.78; H, 7.42; N, 6.31; S, 4.82. Found C, 57.62; H, 7.50; N, 6.34; S, 4.85%.

2-Nitro-3,4,4-trichloro-1-(propylthio)-1-[2-(fluorophenyl)piperazin-1-yl]-1,3-butadiene, 11a: Compound **11a** was synthesized from **3a** (0.5 g, 1.60 mmol) and 2-(fluorophenyl)piperazine **10** (0.28 g, 1.60 mmol) according to the general procedure 2. Yield 0.41g (58%); Oil, R_f ($CHCl_3$): 0.36; IR (KBr): 2828, 2927 (C-H), 1530, 1612 (C=C), 1275, 1502 (C-NO_2), 2965 cm^{-1} (Ar-H); ^1H NMR (499.74 MHz, $CDCl_3$): δ 1.0 (t, J = 7.32 Hz, 3H, CH_3), 1.7 (m, 2H, S-CH_2-CH_2), 2.97 (t, J = 7.32 Hz, 2H, S-CH_2), 3.2 (s, br, 4H, H_{piper}), 3.8 (s, br, 4H, H_{piper}), 6.9-7.2 (m, 4H, H_{arom}); ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 12.27 (CH_3), 22.27 (S-CH_2-CH_2), 36.39 (S-CH_2), 49.39, 52.37 (N-CH_2), 115.41, 115.57, 117.69, 118.45 (CH_{arom}), 122.76, 123.68 (C_{arom}), 125.87, 137.51, 153.85, 168.13 (C_{butad}). Anal. $C_{17}H_{19}N_3O_2S_1Cl_3F_1$ (M, 454.78). Calcd. C, 44.89; H, 4.21; N, 9.23; S, 7.05. Found C, 44.93; H, 4.12; N, 9.19; S, 6.98%.

2-Nitro-3,4,4-trichloro-1-(octadecylthio)-1-[2-(fluorophenyl)piperazin-1-yl]-1,3-butadiene, 11c: Compound **11c** was synthesized from **3c** (0.3 g, 0.57 mmol) and 2-(fluorophenyl)piperazine **10** (0.1 g, 0.57 mmol) according to the general procedure 2. Yield 0.25 g (67%); m.p. 98-99°C; R_f ($CHCl_3$): 0.35; IR (KBr): 2850 (C-H), 1530, 1581 (C=C), 1274, 1500 (C-NO_2), 2915 cm^{-1} (Ar-H); ^1H NMR (499.74 MHz, $CDCl_3$): δ 0.88 (t, J = 7.32 Hz, 3H, CH_3), 1.1-1.5 (m, 30H, CH_2), 1.7 (m, 2H, S-CH_2-CH_2), 2.98 (t, J = 7.32 Hz, 2H, S-CH_2), 3.2 (s, br, 4H, H_{piper}), 3.8 (s, br, 4H, H_{piper}), 6.8-7.1 (m, 4H, H_{arom}); ^{13}C NMR (125.66 MHz, $CDCl_3$): δ 13.06 (CH_3), 21.67, 22.73, 22.89, 23.51, 24.12, 27.71, 28.03, 28.34, 28.37, 28.51, 28.60, 28.65, 28.67, 28.68, 28.80 (CH_2), 30.92 (S-CH_2-CH_2), 34.57 (S-CH_2), 49.39, 52.37 (N-CH_2), 115.41, 115.58, 117.72, 118.43 (CH_{arom}), 122.73, 123.64 (C_{arom}), 125.91, 137.64, 155.83, 168.16 (C_{butad}). Anal. $C_{32}H_{49}N_3O_2S_1Cl_3F_1$ (M, 665.188). Calcd. C, 57.78; H, 7.42; N, 6.31; S, 4.82. Found C, 57.65; H, 7.38; N, 6.29; S, 4.90%.

1, 1-Bis[3, 4, 4-trichloro-1-(propylthio)-2-nitro-1,3-butadienyl]homopiperazine, 13a: Compound **13a** was synthesized from **3a** (0.6 g, 1.92 mmol) and homopiperazine **12** (0.19 g, 1.92 mmol) according to the general procedure 2. Yield 0.55 g (44%); Oil, R_f (CH_2Cl_2): 0.35; IR (KBr): 2850, 2920 (C-H), 1644, 1698 (C=C), 1277, 1510 cm^{-1} (C-NO_2); ^1H NMR

(499.74 MHz, DMSO-d_6): δ 0.93 (t, J = 7.32 Hz, 3H, CH_3), 1.65 (m, 2H, S-CH_2-CH_2), 3.00 (t, J = 7.32 Hz, 2H, S-CH_2), 2.10 (s, br, 4H, $H_{homopiper}$), 3.90 (m, 6H, $H_{homopiper}$); ^{13}C NMR (125.66 MHz, DMSO-d_6): δ 13.63 (CH_3), 23.55 (S-CH_2-CH_2), 37.66 (S-CH_2), 29.37 ($CH_{2homopiper}$), 45.58, 54.34 (N-CH_2), 117.08, 124.07, 127.82, 171.39 (C_{butad}); MS (+ESI): *m/z* 535 $(M-116)^+$. Anal. $C_{19}H_{24}N_4O_4S_2Cl_6$ (M, 649.27). Calcd. 35.14; H, 3.72; N, 8.62; S, 9.87. Found C, 35.29; H, 3.55; N, 8.61; S, 9.85%.

1,1-Bis[3,4,4-trichloro-1-(butylthio)-2-nitro-1,3-butadienyl]homopiperazine, 13b: Compound **13b** was synthesized from **3b** (0.5 g, 1.53 mmol) and homopiperazine **12** (0.15 g, 1.53 mmol) according to the general procedure 2. Yield 0.47 g (46%); m.p. 132-33°C; R_f ($CHCl_3$): 0.50; IR (KBr): 2872, 2932, 2959 (C-H), 1570, 1648 (C=C), 1275, 1513 cm^{-1} (C-NO_2); ^{1}H NMR (499.74 MHz, DMSO-d_6): δ 0.86 (t, J = 7.32 Hz, 3H, CH_3), 1.35 (m, 2H, CH_2), 1.60 (m, 2H, S-CH_2-CH_2), 3.02 (t, J = 7.32 Hz, 2H, S-CH_2), 2.10 (s, br, 4H, $H_{homopiper}$), 3.90 (m, 6H, $H_{homopiper}$); ^{13}C NMR (125.66 MHz, DMSO-d_6): δ 14.04 (CH_3), 21.83 (CH_2), 32.10 (S-CH_2-CH_2), 35.54 (S-CH_2), 28.31 ($CH_{2homopiper}$) 40.87, 54.68 (N-CH_2), 117.06, 124.06, 127.81, 171.40 (C_{butad}). Anal. $C_{21}H_{18}N_4O_4S_2Cl_6$ (M, 667.24). Calcd. C, 37.80; H, 2.71; N, 8.39; S, 9.61. Found C, 37.69; H, 2.60; N, 8.47; S, 9.67%.

Conclusion

The new compound **3a** was synthesized from reaction of **1** with **2a**. The compound 2-nitro-3,4,4-trichloro-1-(propylthio)-1-(thiomorpholinly)-1,3-butadiene **5a** and 2-nitro-3,4,4-trichloro-1-(octadecylthio)-1-(thiomorpholinly)-1,3-butadiene **5c** were synthesized from the reactions of **3a** and **3c** with thiomorpholine **4**. Compounds **7a** and **7c** were obtained from **3a** and **3c** with *N*-(diphenylmethyl)-piperazine **6**. Compounds **3a** and **3c** gave new compounds **9a**, **9c**, **11a**, **11c** with 4-(fluorophenyl)piperazine **8** and 2-(fluorophenyl)-piperazine **10**. Compounds **13a** and **13b** were obtained from the reactions of **3a** and **3b** with homopiperazine **12**. The structures of these novel compounds were characterized by microanalysis and spectroscopic data such as IR, ^{1}H and ^{13}C NMR, MS and crystal structure of 2-nitro-3,4,4-trichloro-1-(butylthio)-1-[4-(diphenylmethyl)piperazin-1-yl]-1,3-butadiene **7b** was determinated by X-ray diffraction method.

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23 Further information may be obtained from: Cambridge Crystallographic Data Center (CCDC), 12 Union Road, Cambridge CB21EZ, UK, by quoting the depository number CCDC-653508 for **7b**. E-mail: deposit@ccdc.cam.ac.uk.