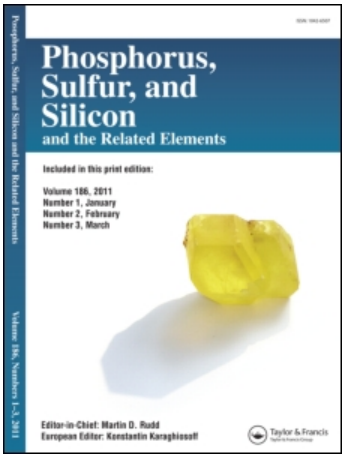

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THE SYNTHESIS OF NEW S- AND N,S-SUBSTITUTED HALO NITRO DIENES BY THE REACTIONS OF 1-BROMO-1,2,4,4-TETRACHLORO-3-NITROBUTA-1,3-DIENE WITH THIOLS AND CYCLIC AMINES

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The substituted products alkyl(aryl)thio-tetrahalo-3-nitrobuta-1,3-dienes 3a–b were obtained from the reactions of 1-bromo-1,2,4,4-tetrachloro-3-nitrobuta-1,3-diene (1) with thiols. Further reactions of the substituted product alkyl(aryl)thio-tetrahalo-3-nitrobuta-1,3-dienes 3a–b in dichloromethane reacted with piperazine derivatives and morpholine to generate 5a–b and 7a–l. The structures of the new compounds were determined by microanalysis and spectroscopic data.

Keywords Halides; nitro compounds; nucleophilic substitutions; piperazine derivatives; thiols

INTRODUCTION

Nitro-substituted polyhalogenatedbuta-1,3-dienes are useful and valuable precursors for versatile synthetic applications, which have in the last decade become the subject of investigations due to their rich chemistry as well as biological properties of the molecules.[1–3] Apart from the synthetic point of view, it is interesting to note that a number of highly chlorinated organic compounds, with additional nitro substituents, are pesticides.[4] They are important because of their biological activity as insecticides and fungicides.[5] Nitrobuta-1,3-dienes, especially their halogen derivatives, have proven to be excellent precursors to synthesize new complex polyfunctional derivatives of different classes and to synthesize diversified functionalized heterocyclic compounds showing antibacterial,[6] antiarrhythmic,[7] antihypoxic,[8] antiviral,[9] anthelmintic,[10] anti–HIV-1,[11] and antitumor activity.[12]

A number of publications dealing with the reactions of versatile soft and hard nucleophilic reagents such as thiols, dithiols, piperazine, and piperidine derivatives with perhalo-3-nitrobuta-1,3-diene,[13–16] perhalobuta-1,3-diene,[17] and 2*H*-perchlorobuta-1,3-diene[18] to obtain S-, N-, S,S-, S,S,S-, and N,S-substituted diene compounds are available in the

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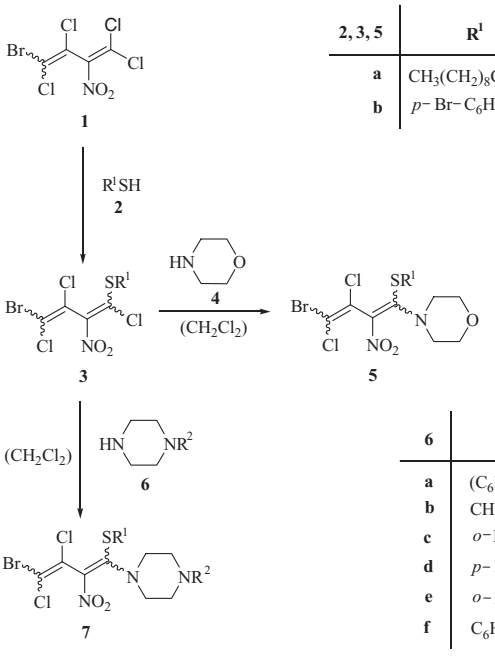
literature. Previously, the reactions of polyhalodienes, polybutenynes, and halobutenes with thiols were studied in different solvents such as DMSO, DMF, and EtOH.[19–22] Tetra- and penta-alkyl(aryl)thio-2-nitrobuta-1,3-dienes have been reported from a reaction in DMF containing triethylamine.[23]

It is well known that the reaction of **1** with nucleophiles, such as thiols and piperazine derivatives, follows a classical nucleophilic vinylic substitution (S_NV)[24] pathway via the addition–elimination route that leads to the formation of new products. In compound **1**, the profound electrophilic character of the C-4 position, due to the powerful electron-withdrawing properties of the α-nitro group, allows regioselective substitution of the either one or two terminal vinylic chlorine substituents in the nitrodichlorovinyl moiety of the dienes. In this article, the interaction of 1-bromo-1,2,4,4-tetrachloro-3-nitrobuta-1,3-diene[25–27] (**1**) with thiols **2a–b** leads to the substituted products alkyl(aryl)thio-tetrahalo-3-nitrobuta-1,3-dienes **3a–b** under mild conditions (without a catalyst, at room temperature).

Additionally, not only for reactivity advantages but also owing to our interest in active compounds, we have attempted some subsequent reactions of the alkyl(aryl)thio-perhalo-3-nitrobuta-1,3-dienes, namely with **3a–b** as the exemplary starting compounds. Analogously, the subsequent vinylic substitution of the monothio compounds **3a–b** in dichloromethane by means of hard nucleophiles, e.g., piperazine derivatives and morpholine, have given N,S-substituted nitrodiene compounds **5a–b** and **7a–l** (Scheme 1).

RESULTS AND DISCUSSION

The ^{13}C NMR shifts of the C-4 carbon atoms of compounds **3a** and **3b** have appeared downfield around 160 ppm, while the NO_2-bearing carbon atoms C-3 have resonances



2, 3, 5	R^1
a	$CH_3(CH_2)_8CH_2-$
b	p-Br-C_6H_4-

7	R^1	R^2
a	$CH_3(CH_2)_8CH_2-$	$(C_6H_5)_2CH-$
b	$CH_3(CH_2)_8CH_2-$	CH_3CH_2COO-
c	$CH_3(CH_2)_8CH_2-$	o-H_3CO-C_6H_4-
d	$CH_3(CH_2)_8CH_2-$	p-F-C_6H_4-
e	$CH_3(CH_2)_8CH_2-$	o-F-C_6H_4-
f	$CH_3(CH_2)_8CH_2-$	C_6H_5-
g	p-Br-C_6H_4-	$(C_6H_5)_2CH-$
h	p-Br-C_6H_4-	CH_3CH_2COO-
i	p-Br-C_6H_4-	o-H_3CO-C_6H_4-
j	p-Br-C_6H_4-	p-F-C_6H_4-
k	p-Br-C_6H_4-	o-F-C_6H_4-
l	p-Br-C_6H_4-	C_6H_5-

6	R^2
a	$(C_6H_5)_2CH-$
b	CH_3CH_2COO-
c	o-H_3CO-C_6H_4-
d	p-F-C_6H_4-
e	o-F-C_6H_4-
f	C_6H_5-

Scheme 1 Synthesis of target compounds.

between 137 ppm and 141 ppm. The particular C-4 carbon atoms of the heterocyclic compounds **5a–b** and **7a–l** have exhibited resonances in a range between 161 ppm and 169 ppm, depending on the structure of the molecule, whereas the NO_2-bearing carbon atoms C-3 showed resonances between 124 ppm and 129 ppm. The individual C-2 and C-1 carbons in each molecule of the library provided chemical shift values around 110 ppm and 120 ppm, respectively. Additionally, employing the information from the APT ^{13}C spectrum of the **3b**, we have unambiguously assigned two of four signals at −132.99 ppm and −136.82 ppm, due to −CH− of the aromatic carbons, while at 125.05 ppm and 130.13 ppm are assigned to quaternary carbons of the aromatic rings. The APT ^{13}C spectrum of the **7c** indicated that the peak at −54.55 ppm was the methyl carbon signal adjacent to the oxygen atom. We could readily deduce that the peak at 155.09 ppm and 154.89 ppm of **7b** and **7h** was due to ester carbonyl carbon. The chemical shift at 62.12 ppm and 62.09 ppm of **7b** and **7h** suggested the methylene carbon attached to the ester oxygen.

In the ^1H NMR spectra of **3b** and **7g–l**, the aromatic protons showed typical ppm values within the range 6.72–7.59 ppm as multiplets characteristic of aromatic rings with a splitting pattern AA′BB′. The piperazine protons of the substituted product **5b** and **7g–l** were observed as multiplets around 2.2 ppm and 3.8 ppm. The piperazine protons of the substituted product **5a** and **7a–h** were observed as broad singlets around 2.5 ppm and 4.0 ppm. The spectra of the **5b** and **7g–l** exhibited some splitting of signal at room temperature for the protons of the piperazine hydrogens, while we were unable to observe any signal splitting in compounds **5a** and **7a–f**.

Some characteristic bands in the IR spectra of the compounds should be mentioned. The asymmetric stretching of the NO_2 groups was observed ranging from 1520 cm^{-1} to 1540 cm^{-1}, and symmetric stretching of the NO_2 groups ranged from 1270 cm^{-1} to 1310 cm^{-1}. The IR spectra of the molecule **7b** and **7h** showed characteristic C=O bands at 1710 cm^{-1} and 1700 cm^{-1}, respectively.

After acquiring a full MS scan for preliminary information, a full MS_1 scan acquisition was performed to obtain structural information on the selected peak of the full MS spectra by using isolation in an ion trap and fragmentation at various collision energies. The APCI mass spectrum of **7e** is given in Figures 1 and 2. The molecular ion peak $[M]^+$ was detected at *m/z* 597.90 with strong abundance (Figure 1). Fragmentation of *m/z* 597 yielded fragment rich product ions (Figure 2). The presence of a nitro group was indicated by an appreciable peak at mass 46 $(NO_2)^+$ with 100% at *m/z* 548.94. Notably, cleavage of the C−Cl bond led to a small Cl^+ peak and to a R^+ peak, which was prominent with low relative abundance at *m/z* 560.39; the pattern appeared to be a characteristic of the ion corresponding to $[M-Cl]^+$. The main clue was the peak of compound **7e** at *m/z* 514.88 due to loss of both nitro and chlorine ions. Similarly, in the mass spectrum of the compounds **3a**, **5b**, **7a**, **7g**, **7j**, and **7l**, the accurate mass measurements of the molecular ion peaks were noticed at *m/z* 453.65 $[M]^+$, 520.74 $[M]^+$, 669.88 $[M]^+$, 683.50 $[M]^+$, 613.72 $[M]^+$, and 595.78 $[M]^+$, respectively. Major fragment of compound **3a** was found at *m/z* 406.86, corresponding most likely to $[M-NO_2]^+$. The peak of the compound **7a** at *m/z* 632.73 was caused by successive losses of a chlorine ion.

EXPERIMENTAL

All reagents and solvents were commercially available and used without further purification. Melting points were determined with a Buchi apparatus B-540 and were uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded with Varian UNITY INOVA

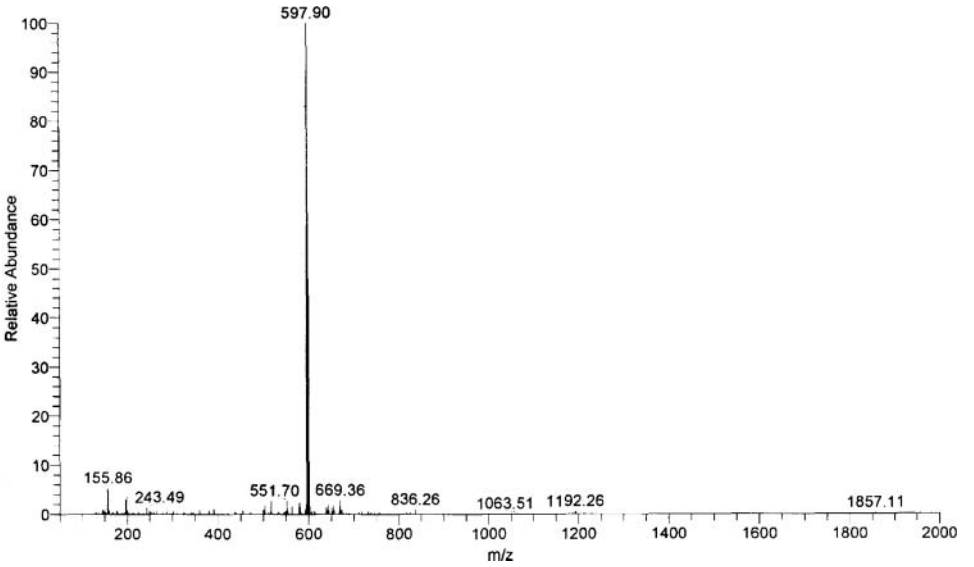


Figure 1 Mass spectrum of compound **7e**.

spectrometers with 500 MHz frequency for ^{1}H and 125 MHz frequency for ^{13}C NMR. ^{1}H NMR spectra and ^{13}C NMR spectra in $CDCl_3$ refer to the solvent signal center at $\delta = 7.26$ and $\delta = 77.0$ ppm, respectively. Other solvents are as follows: DMSO-d_6: 2.49, 3.30 ppm (^{1}H), 40.27 ppm (^{13}C). IR spectra were recorded for liquids as film and for solids as KBr discs on a Shimadzu FT-IR 8101 spectrometer. Microanalyses were carried out with a Carlo Erba Elemental Analyzer 1106. UV spectra were recorded in UV-vis

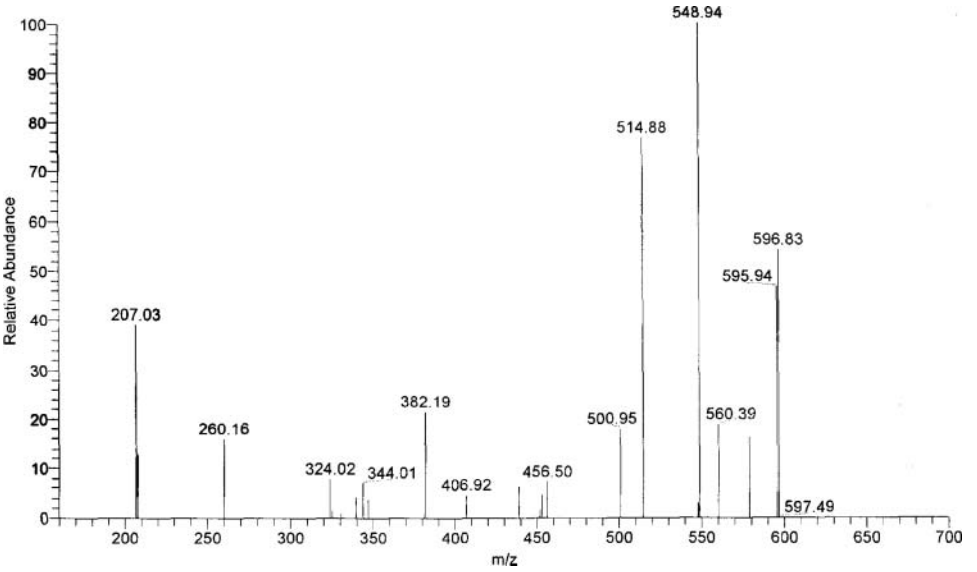


Figure 2 Fragmentation pattern of compound **7e**.

spectrophotometer TU-1901. Mass spectra were obtained on a Thermo Finnigan LCQ Advantage MAX MS/MS spectrometer equipped with an electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) sources. Nitrogen was used as the nebulizing gas. In the MS_1 experiment, helium was used as collision gas. TLC was carried out on Merck DC-plates (aluminum based) silica gel (60 F_{254}) for monitoring reactions, available from Merck. Column chromatographic separations were carried out on silica gel 60 (Merck, particle size 63–200 μm). PE had a boiling range 40–60°C. All chemicals were reagent grade and were used without further purification, and moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes.

(4-Bromo-1,3,4-trichloro-2-nitrobuta-1,3-dienyl)(decyl)sulfane (3a)

1-Decanethiol (1.66 g, 9.5 mmol) was added to a stirred solution of nitrodiene **1** (3 g, 9.5 mmol). After stirring for 24 h, chloroform (30 mL) was added to the reaction mixture at room temperature. The organic layer was separated, washed with water (4 × 30 mL), and dried over $CaCl_2$ or $MgSO_4$. After evaporation of the solvent, the crude product was purified via column chromatography on silica gel. Yield: 1.14 g (26.5%); light orange oil; R_f (CCl_4): 0.59; IR (neat, cm^{-1}) = 2900 (C—H_{aliph}), 1580 (C=C), 1300, 1540 (NO_2); UV ($CHCl_3$) λ = 242, 349 nm; ^{1}H NMR (500 MHz, $CDCl_3$) ppm = 0.88 (t, ^3J = 6.84 Hz, 3H, C***H*****$_3$**), 1.27–1.48 (m, 14H, (C***H*****$_2$)$_7$**), 1.75 (m, 2H, SCH_2C***H*****$_2$**), 3.13 (t, ^3J = 7.32 Hz, 2H, SC***H*****$_2$**); ^{13}C NMR (125 MHz, $CDCl_3$) ppm = 13.07 (***C***H_3), 21.65, 27.46, 27.75, 28.04, 28.24, 28.36, 28.46, 30.85, 35.04 ((***C***H_2)$_9$), 113.91 (***C***ClBr), 122.07 (***C***Cl), 137.67 (***C***NO_2), 156.27 (***C***SCl); MS (APCI) *m/z* (%): 453.65 [M^+] (100), 406.86 [M^+—NO_2] (29.07), 372.30 [M^+—NO_2—Cl] (19.71), 313.66 (34.87), 293.92 [M^+—NO_2—Cl—Br] (15.63), 280.16 (8.07), 246.10 (12.5); $C_{14}H_{21}BrCl_3NO_2S$ (M_W = 453.66 g/mol); Calcd C:% 37.07, H:% 4.66, N:% 3.09, S:% 7.06; Found C:% 37.29, H:% 4.95, N:% 3.08, S:% 6.78.

(4-Bromo-1,3,4-trichloro-2-nitrobuta-1,3-dienyl)(4-bromophenyl)sulfane (3b)

At room temperature, 4-bromothiophenol (1.80 g, 9.5 mmol) was added dropwise to a stirred solution of nitrodiene **1** (3 g, 9.5 mmol) for 24 h. Subsequent addition of the methanol (15 mL) afforded a solid, which was filtered off and washed with petroleum ether and cold methanol twice (2 × 20 mL). Recrystallization from methanol gave the thiodiene **3b**. Yield: 1.43 g (32%); Yellow crystal; mp: 168–169°C; R_f (CCl_4): 0.46; IR (KBr, cm^{-1}) = 3100 (C—H_{arom}), 1595, 1580 (C=C), 1300, 1530 (NO_2); UV ($CHCl_3$) λ = 243, 362 nm; ^{1}H NMR (500 MHz, DMSO-d_6) ppm = 6.98–7.00 (m, 2H, C***H***$_{arom}$), 7.15–7.20 (m, 2H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, DMSO-d_6) ppm = 116.44 (***C***ClBr), 123.46 (***C***Cl), 125.05, 130.13 (***C***$_{arom}$), 132.99, 136.82 (***C***H_{arom}), 141.71 (***C***NO_2), 160.31 (***C***SCl); $C_{10}H_4Br_2Cl_3NO_2S$ (M_W = 468.38 g/mol); Calcd C:% 25.64, H:% 0.86, N:% 2.99, S:% 6.84; Found C:% 25.71, H:% 1.20, N:% 2.78, S:% 7.20.

4-(4-Bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)morpholine (5a): Typical Procedure

A solution of morpholine **4** in dichloromethane (10 mL) was added to a solution of (4-bromo-1,3,4-trichloro-2-nitrobuta-1,3-dienyl)(decyl)sulfane (**3a**) in dichloromethane

(10 mL) at room temperature at the same molar ratio. After stirring for 4 h, chloroform or dichloromethane (15 mL) was added to the reaction mixture. The organic layer was separated, washed with water (4 × 30 mL), and dried over $CaCl_2$ or $MgSO_4$. After evaporation of the solvent, the crude product was purified by column chromatography on silica gel. Yield: 170 mg (73%); Yellow crystal; mp 80–81°C; R_f (CH_2Cl_2): 0.32; IR (KBr, cm^{-1}) = 2900 (C—H_{aliph}), 1580 (C=C), 1290, 1530 (NO_2); UV ($CHCl_3$): λ = 242, 394 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.83 Hz, 3H, C***H*****$_3$**), 1.26–1.41 (m, 14H, (C***H*****$_2$)$_7$), 1.64–1.70 (m, 2H, SCH_2C***H*****$_2$**), 2.96 (t, ^{3}J = 7.32 Hz, 2H, SC***H*****$_2$**), 3.66 (bs, 4H, NC***H*****$_{2\,piperazine}$**), 3.81 (s, 4H, OC***H*****$_{2\,piper}$**); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 13.07 (***C***H_3), 21.65, 27.70, 28.01, 28.23, 28.35, 28.45, 28.81, 30.85, 34.52 ((***C***H_2)$_9$), 52.61 (N***C*****$H_{2\,piper}$**), 65.40 (O***C*****$H_{2\,piper}$**), 111.22 (***C***ClBr), 119.20 (***C***Cl), 129.16 (***C***NO_2), 167.81 (***C***SN); $C_{18}H_{29}BrCl_2N_2O_3S$ (M_W = 504.32 g/mol); Calcd C:% 42.86, H:% 5.80, N:% 5.55, S:% 6.35; Found C:% 42.79, H:% 5.98, N:% 5.63, S:% 6.17.

4-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)morpholine (5b)

Followed the typical procedure for **5a**. Yield: 58 mg (35%); Orange crystal; mp 171–172°C; R_f (CH_2Cl_2): 0.28; IR (KBr, cm^{-1}) = 3000 (C—H_{arom}), 1580, 1560 (C=C), 1280, 1520 (NO_2); UV ($CHCl_3$): λ = 251, 387 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 3.35–3.51 (m, 8H, C***H*****$_{2\,piper}$**), 7.25–7.30 (m, 2H, C***H*****$_{arom}$**), 7.40–7.59 (m, 2H, C***H*****$_{arom}$**); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 52.30 (N***C***$H_{2\,piper}$), 64.46 (OC***H*****$_{2\,piper}$**), 112.22 (***C***ClBr), 123.32, 128.85 (***C***$_{arom}$), 126.74 (***C***Cl), 129.85 (***C***NO_2), 132.44, 133.06 (***C***H_{arom}), 162.93 (***C***SN); MS (APCI) *m/z* (%): 520.74 [M^+] (100), 474.69 (16), 441.77 [M^+—Br] (9.20), 389.19 (10.2); $C_{14}H_{12}Br_2Cl_2N_2O_3S$ (M_W = 519.04 g/mol); Calcd C:% 32.40, H:% 2.33, N:% 5.40, S:% 6.18; Found C:% 32.75, H:% 2.52, N:% 5.56, S:% 6.58.

1-Benzhydryl-4-(4-bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)piperazine (7a)

Followed the typical procedure for **5a**. Yield: 89 mg (42%); Light orange thick oil; R_f ($CHCl_3$): 0.53; IR (neat, cm^{-1}) = 3100 (C—H_{arom}), 2900 (C—H_{aliph}), 1590 (C=C), 1310, 1525 (NO_2); UV ($CHCl_3$): λ = 240, 392 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.83 Hz, 3H, C***H*****$_3$**), 1.26–1.37 (m, 14H, (C***H*****$_2$)$_7$**), 1.59–1.67 (m, 2H, SCH_2C***H*****$_2$**), 2.54 (s, 4H, C***H*****$_{2\,piper}$**), 2.91 (t, ^{3}J = 7.32 Hz, 2H, SC***H*****$_2$**), 3.64 (bs, 4H, C***H*****$_{2\,piper}$**), 4.28 (s, 1H, (C_6H_5)$_2$C***H***), 7.19–7.42 (m, 10H, (C_6***H*****$_5$)$_2$**); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 14.09 (***C***H_3), 22.65, 28.65, 29.02, 29.25, 29.36, 29.46, 29.81, 31.86, 35.46 ((***C***H_2)$_9$), 51.65, 53.52 (N***C***H_2), 75.69 ((C_6H_5)$_2$***C***H), 111.17 (***C***ClBr), 119.94 (***C***Cl), 127.48, 127.73, 128.81 (***C***H_{arom}), 130.36 (***C***NO_2), 141.58 (***C***$_{arom}$), 168.38 (***C***SN); MS (APCI) *m/z* (%): 669.88 [M^+] (100), 632.73 [M^+—Cl] (62.18), 426.81 (13.91); $C_{31}H_{40}BrCl_2N_3O_2S$ (M_W = 669.56 g/mol); Calcd C:% 55.61, H:% 6.02, N:% 6.27, S:% 4.79; Found C:% 55.91, H:% 6.33, N:% 5.98, S:% 5.03.

Ethyl 4-(4-Bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)piperazine-1-carboxylate (7b)

Followed the typical procedure for **5a**. Yield: 128 mg (48%); Light orange thick oil; R_f (CH_2Cl_2): 0.27; IR (neat, cm^{-1}) 2850 (C—H_{aliph}), 1710 (C=O), 1595 (C=C), 1280,

1525 (NO_2); UV ($CHCl_3$): λ = 240, 393 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.83 Hz, 3H, C***H₃***), 1.26–1.40 (m, 14H, (C***H₂***)$_7$; 3H, OCH_2C***H₃***), 1.64–1.70 (m, 2H, SCH_2C***H₂***), 2.95 (t, ^{3}J = 7.32 Hz, 2H, SC***H₂***), 3.64 (bs, 8H, C***H₂***$_{piper}$), 4.19 (q, 2H, OC***H₂***); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 14.09 (***C***H_3), 14.60 (OCH_2***C***H_3), 22.66, 28.71, 28.73, 29.03, 29.25, 29.37, 29.46, 31.86, 35.56 ((***C***H_2)$_9$), 43.29, 52.84 (N***C***H_2), 62.12 (O***C***H_2), 111.67 (***C***ClBr), 118.87 (***C***Cl), 128.14 (***C***NO_2), 155.09 (***C***=O), 169.22 (***C***SN); $C_{21}H_{34}BrCl_2N_3O_4S$ (M_W = 575.40 g/mol); Calcd C:% 43.84, H:% 5.96, N:% 7.30, S:% 5.57; Found C:% 44.10, H:% 6.22, N:% 7.10, S:% 5.26.

1-(4-Bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)-4-(2-methoxyphenyl)piperazine (7c)

Followed the typical procedure for **5a**. Yield: 140 mg (48.5%); Orange thick oil; R_f (CH_2Cl_2): 0.56; IR (neat, cm^{-1}) = 3020 (C−H_{arom}), 2900 (C−H_{aliph}), 2815 (OCH_3), 1595 (C=C), 1285, 1520 (NO_2); UV ($CHCl_3$): λ = 245, 393 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.83 Hz, 3H, C***H₃***), 1.26–1.44 (m, 14H, (C***H₂***)$_7$), 1.64–1.72 (m, 2H, SCH_2C***H₂***), 2.98 (t, ^{3}J = 7.32 Hz, 2H, SC***H₂***), 3.23 (s, 4H, C***H₂***$_{piper}$), 3.82–4.03 (m, 4H, C***H₂***$_{piper}$), 3.88 (s, 3H, OC***H₃***), 6.90–7.08 (m, 4H, C_6***H₄***); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 13.07 (***C***H_3), 21.65, 27.72, 28.04, 28.24, 28.37, 28.46, 28.81, 30.85, 34.54 ((***C***H_2)$_9$), 49.47, 52.56 (N***C***H_2), 54.55 (O***C***H_3), 110.26 (***C***ClBr), 117.64 (***C***Cl), 110.73, 120.15, 123.20, 127.46 (***C***H_{arom}), 129.37 (***C***NO_2), 139.45 (N-***C***$_{arom}$), 151.33 (H_3CO−***C***$_{arom}$), 168.27 (***C***SN); $C_{25}H_{36}BrCl_2N_3O_3S$ (M_W = 609.46 g/mol); Calcd C:% 49.27, H:% 5.95, N:% 6.90, S:% 5.26; Found C:% 49.54, H:% 5.90, N:% 7.14, S:% 5.47.

1-(4-Bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)-4-(4-fluorophenyl)piperazine (7d)

Followed the typical procedure for **5a**. Yield: 166 mg (63%); Orange thick oil; R_f ($CHCl_3$): 0.45; IR (neat, cm^{-1}) = 3020 (C−H_{arom}), 2900 (C−H_{aliph}), 1590 (C=C), 1280, 1530 (NO_2); UV ($CHCl_3$): λ = 242, 394 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.91 Hz, 3H, C***H₃***), 1.26–1.41 (m, 16H, (C***H₂***)$_7$), 1.65–1.71 (m, 2H, SCH_2C***H₂***), 2.98 (t, ^{3}J = 7.08 Hz, 2H, SC***H₂***), 3.24 (s, 4H, C***H₂***$_{piper}$), 3.61–3.99 (m, 4H, C***H₂***$_{piper}$), 6.88–7.00 (m, 4H, C_6***H₄***); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 13.09 (***C***H_3), 21.64, 27.70, 28.03, 28.23, 28.35, 28.45, 28.80, 30.85, 34.58 ((***C***H_2)$_9$), 49.37, 52.10 (N***C***H_2), 110.43 (***C***ClBr), 114.95, 117.69 (***C***H_{arom}), 119.42 (***C***Cl), 129.81 (***C***NO_2), 145.68 (N−***C***$_{arom}$), 155.93, 157.84 (F−***C***$_{arom}$), 167.68 (***C***SN); $C_{24}H_{33}BrCl_2FN_3O_2S$ (M_W = 597.41 g/mol) Calcd C:% 48.25, H:% 5.56, N:% 7.03, S:% 5.36; Found C:% 48.18, H:% 5.31, N:% 7.03, S:% 5.12.

1-(4-Bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)-4-(2-fluorophenyl)piperazine (7e)

Followed the typical procedure for **5a**. Yield: 120 mg (45.6%); Orange crystal; mp 75–76°C; R_f ($CHCl_3$): 0.56; IR (KBr, cm^{-1}) = 3050 (C−H_{arom}), 2900 (C−H_{aliph}), 1580, 1565 (C=C), 1310, 1530 (NO_2); UV ($CHCl_3$): λ = 243, 392 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.83 Hz, 3H, C***H₃***), 1.27–1.42 (m, 14H, (C***H₂***)$_7$), 1.66–1.72 (m, 2H, SCH_2C***H₂***), 2.98 (t, ^{3}J = 7.32 Hz, 2H, SC***H₂***), 3.24 (s, 4H, C***H₂***$_{piper}$), 3.82 (bs, 4H, C***H₂***$_{piper}$), 6.92–7.10 (m, 4H, C_6***H₄***); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 14.09 (***C***H_3), 22.66, 28.73, 29.05, 29.26, 29.38, 29.47, 29.81, 31.87, 35.56 ((***C***H_2)$_9$), 50.38,

53.39 (N***C***H_2), 111.42 (***C***CBr), 118.32 (***C***Cl), 116.40, 119.41, 123.75, 124.65 (***C***H_{arom}), 128.38 (***C***NO_2), 138.53 (N—***C***$_{arom}$), 154.80, 156.77 (F—***C***$_{arom}$), 168.86 (***C***SN); MS (APCI) *m/z* (%): 597.90 [M^+] (100), 560.39 [M^+—Cl] (18.88), 548.94 [M^+-NO_2] (100), 514.88 [M^+—NO_2—Cl] (76.76); $C_{24}H_{33}BrCl_2FN_3O_2S$ (M_W = 597.41 g/mol); Calcd C:% 48.25, H:% 5.57, N:% 7.03, S:% 5.36; Found C:% 48.50, H:% 6.06, N:% 7.02, S:% 5.07.

1-(4-Bromo-3,4-dichloro-1-(decylthio)-2-nitrobuta-1,3-dienyl)-4-phenylpiperazine (7f)

Followed the typical procedure for **5a**. Yield: 179 mg (70%); Yellow thick oil; R_f ($CHCl_3$): 0.58; IR (neat, cm^{-1}) = 3020 (C-H_{arom}), 2850 (C-H_{aliph}), 1600, 1590 (C=C), 1280, 1525 (NO_2); UV ($CHCl_3$): λ = 249, 392 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 0.88 (t, ^{3}J = 6.81 Hz, 3H, C***H*****$_3$**), 1.26–1.55 (m, 14H, (C***H*****$_2$)$_7$**, 1.68 (m, 2H, SCH_2C***H*****$_2$**), 2.98 (t, ^{3}J = 7.42 Hz, 2H, SC***H*****$_2$**), 3.34 (s, 4H, C***H*****$_{2piper}$**), 3.61–4.00 (m, 4H, C***H*****$_{2piper}$**), 6.92–7.32 (m, 5H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 13.06 (***C***H_3), 21.64, 27.72, 28.03, 28.24, 28.36, 28.45, 28.76, 28.82, 30.85, 34.58 ((***C***H_2)$_9$), 48.44, 52.05 (N***C***H_2), 110.44 (***C***ClBr), 120.14 (***C***Cl), 115.64, 128.40 (***C***H_{arom}), 127.32 (***C***NO_2), 149.02 (N—***C***$_{arom}$), 165.70 (***C***SN); $C_{24}H_{34}BrCl_2N_3O_2S$ (M_W = 579.42 g/mol); Calcd C:% 49.75, H:% 5.91, N:% 7.25, S:% 5.53; Found C:% 49.98, H:% 5.75, N:% 7.14, S:% 5.77.

1-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)-4-benzhydrylpiperazine (7g)

Followed the typical procedure for **5a**. Yield: 71 mg (42%); Light orange thick oil; R_f (CH_2Cl_2): 0.71; IR (neat, cm^{-1}) = 3020 (C—H_{arom}), 1590 (C=C), 1275, 1540 (NO_2); UV ($CHCl_3$): λ = 242, 388 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 2.17 (s, 4H, C***H*****$_{2piper}$**), 3.41–3.62 (bd, 4H, C***H*****$_{2piper}$**), 4.13 (s, 1H, $(C_6H_5)_2C$***H***), 7.13–7.51 (m, 14H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 49.38, 52.33 (N***C***H_2), 74.43 (($C_6H_5)_2$***C***H), 111.20 (***C***ClBr), 120.66 (***C***Cl), 124.30 (***C***NO_2), 126.42, 126.79, 127.70 (S—***C***H_{arom}), 127.21, 128.02 (S—***C***$_{arom}$), 132.26, 133.19 (>CH—***C***H_{arom}), 140.23 (>CH—***C***$_{arom}$), 162.99 (***C***SN); MS (ESI) *m/z* (%): 683.50 [M^+] (100), 646.43 (13.14), 390.83 (16.85); $C_{27}H_{23}Br_2Cl_2N_3O_2S$ (M_W = 684.28 g/mol); Calcd C:% 47.39, H:% 3.39, N:% 6.14, S:% 4.69; Found C:% 47.53, H:% 3.71, N:% 5.95, S:% 4.49.

Ethyl 4-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)piperazine-1-carboxylate (7h)

Followed the typical procedure for **5a**. Yield: 99 mg (19.6%); Yellow crystal; mp 152–153 °C; R_f (CH_2Cl_2): 0.33; IR (KBr, cm^{-1}) = 3020 (C—H_{arom}), 1700 (C=O), 1580, 1570 (C=C), 1270, 1520 (NO_2); UV ($CHCl_3$): λ = 250, 388 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 1.25 (t, ^{3}J = 6.35 Hz, 3H, C***H*****$_3$**), 3.28–3.52 (m, 8H, NC***H*****$_{2piper}$**), 4.15 (q, 2H, OC***H*****$_2$**), 7.32–7.59 (m, 4H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 14.57 (OCH_2***C***H_3), 42.39, 52.66 (N***C***H_2), 62.09 (O***C***H_2), 113.38 (***C***ClBr), 124.43 (***C***Cl), 129.80 (***C***NO_2), 127.62, 133.93 (***C***$_{arom}$), 133.51, 134.04 (***C***H_{arom}), 154.89 (***C***=O), 164.19 (***C***SN); $C_{17}H_{17}Br_2Cl_2N_3O_4S$ (M_W = 590.12 g/mol); Calcd C:% 34.60, H:% 2.90, N:% 7.12, S:% 5.43; Found C:% 34.66, H:% 3.03, N:% 6.84, S:% 5.11.

1-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)-4-(2-methoxyphenyl)piperazine (7i)

Followed the typical procedure for **5a**. Yield: 21 mg (6.5%); Light orange thick oil; R_f (CH_2Cl_2): 0.23; IR (neat, cm^{-1}) = 3020 (C—H_{arom}), 2900 (O—CH_3), 1560 (C=C), 1280, 1540 (NO_2); UV ($CHCl_3$): λ = 244, 387 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 2.88 (s, 4H, C***H*****2**$_{piper}$), 3.64 (m, 4H, C***H*****2**$_{piper}$), 3.85 (s, 3H, OC***H*****3**), 6.72–7.57 (m, 8H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 48.51, 52.50 (N***C***H_2), 54.48 (O***C***H_3), 110.56 (***C***ClBr), 117.48 (***C***Cl), 129.02 (***C***NO_2), 120.13, 123.04, 123.15, 132.34 (N—***C***H_{arom}), 132.35, 133.19 (S—***C***H_{arom}), 138.62 (N—***C***$_{arom}$), 151.31 (H_3CO—***C***$_{arom}$), 162.80 (***C***SN); $C_{21}H_{19}Br_2Cl_2N_3O_3S$ (M_W = 624.18 g/mol); Calcd C:% 40.41, H:% 3.07, N:% 6.73, S:% 5.14; Found C:% 40.78, H:% 3.29, N:% 6.48, S:% 5.52.

1-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)-4-(4-fluorophenyl)piperazine (7j)

Followed the typical procedure for **5a**. Yield: 298 mg (35%); Orange thick oil; R_f ($CHCl_3$): 0.44; IR (neat, cm^{-1}) = 3050 (C—H_{arom}), 1600 (C=C), 1290, 1540 (NO_2); UV ($CHCl_3$): λ = 242, 386 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 2.90 (s, 4H, C***H*****2**$_{piper}$), 3.55–3.76 (m, 4H, C***H*****2**$_{piper}$), 6.77–7.57 (m, 8H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 48.70, 51.96 (N***C***H_2), 111.54 (***C***ClBr), 115.04, 117.85 (N—***C***H_{arom}), 126.18 (***C***Cl), 128.91 (***C***NO_2), 123.26, 128.82 (S—***C***$_{arom}$), 132.40, 133.14 (S—***C***H_{arom}), 145.68 (N—***C***$_{arom}$), 156.09, 158.01 (F—***C***$_{arom}$), 163.20 (***C***SN); MS (ESI) *m/z* (%): 613.72 [M^+] (100), 594.53 (16.8), 564.94 (89), 503.57 (13.7), 395.92 (64.9), 206.9 (29.1); $C_{20}H_{16}Br_2Cl_2FN_3O_2S$ (M_W = 612.14 g/mol); Calcd C:% 39.24, H:% 2.63, N:% 6.86, S:% 5.24; Found C:% 39.32, H:% 2.75, N:% 7.14, S:% 5.52.

1-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)-4-(2-fluorophenyl)piperazine (7k)

Followed the typical procedure for **5a**. Yield: 27 mg (14%); Orange crystal; mp 170–171 °C; R_f (CH_2Cl_2): 0.56; IR (KBr, cm^{-1}) = 3050 (C—H_{arom}), 1610, 1590 (C=C), 1280, 1530 (NO_2); UV ($CHCl_3$): λ = 245, 388 nm; ^{1}H NMR (500 MHz, $CDCl_3$) ppm = 2.90 (s, 4H, C***H*****2**$_{piper}$), 3.58–3.77 (bd, 4H, C***H*****2**$_{piper}$), 6.77–7.58 (m, 8H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 48.45, 52.22 (N***C***H_2), 112.06 (***C***ClBr), 115.50 (***C***Cl), 122.73 (N—***C***$_{arom}$), 123.22, 123.65, 123.68 (N—***C***H_{arom}), 128.92 (***C***NO_2), 132.37, 133.10 (S—***C***H_{arom}), 126.91, 137.50 (S—***C***$_{arom}$), 153.82, 155.77 (F—***C***$_{arom}$), 163.15 (***C***SN); $C_{20}H_{16}Br_2Cl_2FN_3O_2S$ (M_W = 612.15 g/mol); Calcd C:% 39.24, H:% 2.63, N:% 6.86, S:% 5.24; Found C:% 39.33, H:% 2.93, N:% 6.78, S:% 5.50.

1-(1-(4-Bromophenylthio)-4-bromo-3,4-dichloro-2-nitrobuta-1,3-dienyl)-4-phenylpiperazine (7l)

Followed the typical procedure for **5a**. Yield: 243 mg (32%); Orange thick oil; R_f ($CHCl_3$): 0.53; IR (neat, cm^{-1}) = 3100 (C—H_{arom}), 1600 (C=C), 1280, 1530 (NO_2); UV ($CHCl_3$): λ = 246, 386 nm; ^{1}H NMR (500 MHz, $CDCl_3$): ppm = 3.01 (s, 4H, C***H*****2**$_{piper}$), 3.56–3.78 (d, 4H, C***H*****2**$_{piper}$), 6.82–7.57 (m, 9H, C***H***$_{arom}$); ^{13}C NMR (125 MHz, $CDCl_3$): ppm = 48.70, 52.96 (N***C***H_2), 112.48 (***C***ClBr), 121.23, 127.93 (S—***C***$_{arom}$), 124.29 (***C***Cl), 129.91

(***C***NO_2), 116.79, 129.42 (N−***C***H_{arom}), 133.42, 134.10 (S−***C***H_{arom}), 150.01 (N−***C***$_{arom}$), 161.09 (***C***SN); MS (ESI) *m/z* (%): 595.78 [M^+] (100), 546.85 (94.54), 377.95 (61.7), 376.98 (17.15), 189.07 (16.5),; $C_{20}H_{17}Br_2Cl_2N_3O_2S$ (M_W = 594.15 g/mol); Calcd C:% 40.43, H:% 2.88, N:% 7.07, S:% 5.40; Found C:% 40.63, H:% 3.12, N:% 7.03, S:% 5.21.

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