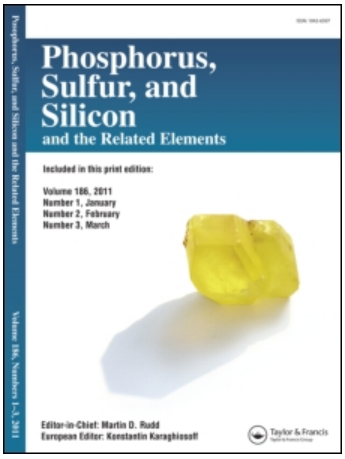

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Synthesis of Dibutadienyl Piperazines, 1,1-Dithio and 1,4-Dithio Substituted Dienes from Nitrodienes

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SYNTHESIS OF DIBUTADIENYL PIPERAZINES, 1,1-DITHIO AND 1,4-DITHIO SUBSTITUTED DIENES FROM NITRODIENES

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*Nitrodiene **1a**, **1b** reacted with 1,4-dithiolbutan and gave the heterocyclic compounds **3a**, **3b**. **1b** gave with 1,3-acetonedithiol the compound **5b**. The nitrodiene compound **1b** reacted with o-dithiolbenzene (**6**) and yielded the ketene dithioacetal (**7b**). Heterocyclic compounds **11a**, **11b**, **12a**, and **12b** were prepared from the reactions of **9a** with 2,2′-oxydiethanethiol. The compounds **9a**, **9b** were prepared from 2-nitropentachloro-1,3-butadiene and alkylthiols (**8a**, **8b**). Mono(thio) substituted diene compound **9b** gave dibutadienyl piperazine **14b** with piperazine in diethylether.*

Keywords: 1,1- and 1,4-Dithio dienes; dibutadienyl piperazines; nitrodienes

Reactions of 1H- and 2H-pentachlorobutadienes, perchlorobutadiene, nitrodienes and hexachlorobuta dienes with some thiols have previously been reported.[1–4] It is known that N,N- and S,N-substituted nitrodienes are synthesized by the treatment of nitrodienes and some mono(thio)substituted nitrodienes with amines.[5–10]

In this study, we synthesized some unknown heterocyclic compounds from the reactions of nitrodienes with dithiols and determined their structure.

The reason for the formation of 1-thio substituted compounds is the inductive effect of the nitro group. In our previous studies it was shown that cyclized compounds are obtained from the chlorine substitution of nitrovinyl groups with dithiols.

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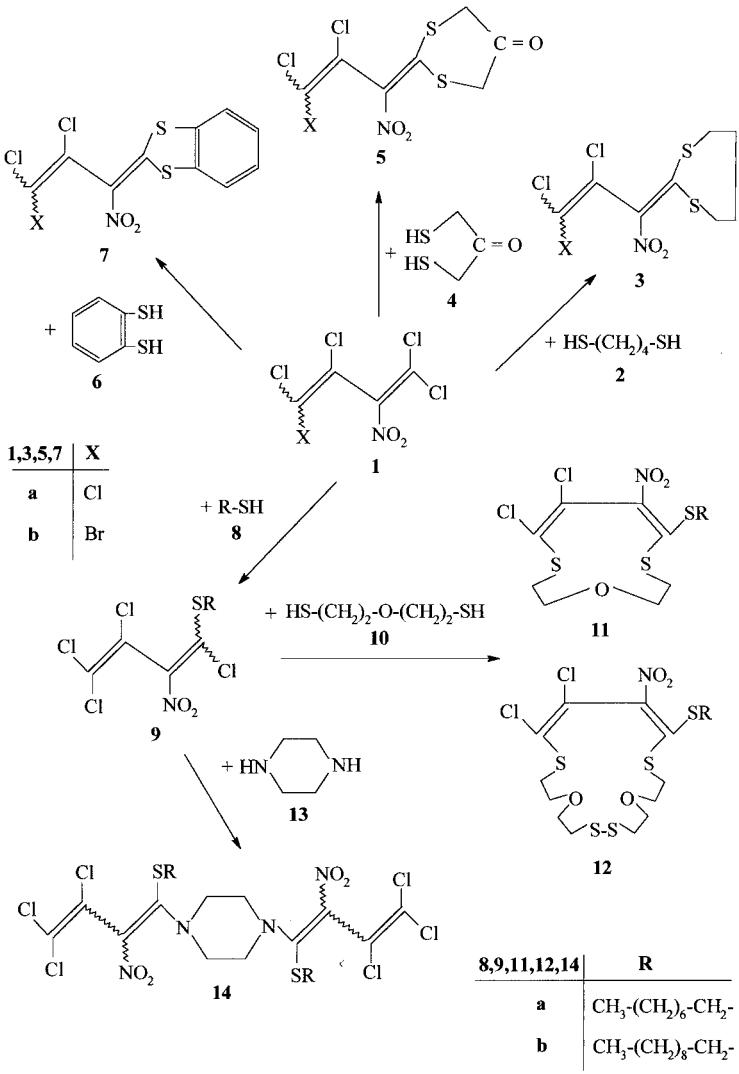
Reactions of **1a** and **1b** with some dithiols have been reported before.[11–13] In this study, **3a** and **3b** were formed when **1a** and **1b** were stirred with 1,4-butanedithiol for 30–35 h at room temperature. Under the same conditions reactions of compound **1b** with o-dithiolbenzene gave the compound **7b**, and with 1,3-acetonedithiol ($HS{-}CH_2{-}CO{-}CH_2{-}SH$), the compound **5b**. The compounds **3**, **5**, and **7** are new, stable heterocyclic compounds (Scheme 1).



SCHEME 1

It previously has been reported that mono(thio)substituted diene compounds were obtained when compound **1a** is stirred with thiols for a long time.[12–17] It is also known that reaction of compound **1a** with thiols in alcohol in the presence of NaOH gives mono-, di-, tris-, and tetrakis(thio)substituted thioethers.[17,18]

Mono(thio)substituted nitrodiene compounds **9a** and **9b** were obtained from the reaction of compound **1a** with thiols (**8a**, **8b**). Heterocyclic compounds **11a**, **11b**, **12a**, and **12b** formed when compounds **9a** and **9b** reacted with oxyethandithiol in ethyl alcohol in the presence of NaOH. These compounds are heterocyclic compounds with interesting structure. In these reactions, formation of compounds with open chain structure is also possible. The structures of these compounds were determined by microanalysis and spectroscopic data.

MS-spectral data of compounds **11a** and **12a** is as follows: Compound **11a** showed a mol peak at 445.8 (M^+)(molecular weight of compound **11a** = 446.4), while **12a** showed a mol peak at 582.4 (M^+)(molecular weight of compound **12a** = 582.7). These values verify the structure of the compounds.

Formation of compounds **11** and **12** is probably as follows: Reaction of compound **9** with compound **10** gives an intermediate ($Cl_2C{=}CCl{-}C(NO_2){=}C(SR){-}S{-}(CH_2){-}O{-}(CH_2)_2{-}S^-Na^+$). Compound **11** is formed by the cyclization of this intermediate. Compound **12** is formed by the cyclization of the intermediate ($Na^+S^-(CH_2)_2{-}O{-}(CH_2)_2{-}S{-}ClC{=}CCl{-}C(NO_2)_2{=}C(SR){-}S(CH_2)_2{-}O{-}(CH_2)_2{-}S^-Na^+$ or $Cl_2C{=}CCl{-}C(NO_2)_2{=}C(SR){-}S(CH_2)_2{-}O{-}(CH_2)_2{-}S{-}S{-}(CH_2)_2{-}O{-}(CH_2)_2{-}S^-Na^+$) which have been obtained by the reaction of compound **9** with compound **10**.

Monoaryl- and diarylpiperazines are important for clinical chemistry.[19–21] Some piperazine compounds were used in gen transfer reactions.[22]

We have synthesized compound **14a** previously.[18] Reaction of compound **9b** with piperazine in ether (or in CH_2CI_2) gave dibutadienyl compound **14b**. Compound **14b** is a new, stable, yellow colored compound.

The >NH band was not observed in the IR-spectrum of compound **14b**. This result shows that this compound is a disubstituted butadienyl piperazine. MS-spectral data verifies this structure.

EXPERIMENTAL

Melting points are uncorrected: Büchi SMP-510 capillary apparatus.

- IR-spectra: Perkin-Elmer 983 or Shimadzu FTIR-8101. -^{1}H-NMR-Spectra: Bruker AC 200 L. -MS: VG-ZAB-SPEC-Spectrophotometer. Elemental analyses: Elemental Analyzer 1106 Carlo Erba.
- Thin-layer chromatography: TLC plates silica 60 F_{254} (Merck, Darmstadt) detection with ultraviolet light (254 nm).
- Column chromatography: Silica 60 (Merck), particle size 0.063–0.20 mm.

Standart Work Up Procedure

A-) Equimolar amounts of 2-nitrodiene **1a** (or **1b**) and dithiols (or thiols) were stirred for 36 h at room temperature. Then, dichloromethane was added to the reaction mixture. The layer of dichloromethane was separated and washed with water (4 × 30 ml) and dried with magnesium sulfate.

B-) To a mixture of **9a** (or **9b**) and **10** in 30 ml of ethanol 2 g of NaOH (in 8 ml water) was added at room temperature. The mixture was stirred for 1 h. 40 ml of dichloromethane were added to the mixture, and the organic phase was separated, washed with water, dried with $MgSO_4$, and concentrated in vacuo. The residue was purified by chromatography on silica gel 60 (Merck, particle size 0.063–0.20 mm).

2-(1-Nitro-2,3,3-trichloro-2-propenylidene)-1,3-dithia-cycloheptane (3a)

Synthesized from **1a** (0.5 g, 1.84 mmol) and 1,4-butanedithiol (0.225 g, 1.84 mmol) according to the general procedure A. The crude product was purified by recrystallization from methanol (20 ml);

3a: Yield 0.40 g (68%); mp 139–141°C; -IR (KBr): $\upsilon = 2870$, 2930, 2995 cm^{-1} (C—H), 1595 (C=C), 1295, 1520 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 2.4$–3.8 ppm (m, 8 H, 4 CH_2). -^{13}C-NMR ($CDCl_3$, TMS int.): $\delta = 163.48$ ppm (=C$\langle^{S}_{S}$). $C_8H_8S_2Cl_3NO_2$ (320.6) calc. C 29.96; H 2.51; N 4.36; S 19.99; found C 29.69; H 2.64; N 4.49; S 20.23.

2-(1-Nitro-2,3-dichloro-3-bromo-2-propenylidene)-1,3-dithia-cycloheptane (3b)

Synthesized from **1b** (0.5 g, 1.58 mmol) and 1,4-butanedithiol (0.193 g, 1.58 mmol) according to the general procedure A.

3b: Yield 0.49 g (85%); mp 169–171°C; -IR (KBr): $\upsilon = 2875$, 2930, 2990 cm^{-1} (C—H), 1595 (C=C), 1290, 1525 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 2.9$–3.4 ppm (m, 4 H, 2 S—CH_2), 2.0–2.3 (m, 4 H, 2 CH_2). -^{13}C-NMR ($CDCl_3$, TMS int.): $\delta = 163.46$ ppm (=C$\langle^{S}_{S}$), 123.2

(=CCl), 126.4 (=CClBr), 142.3 (=C—NO_2), 134.4 (S—C), 31.8 (S—C—C). $C_8H_8S_2NCl_2BrO_2$ (365.0) calc. C 26.31; H 2.20; N 3.83; S 17.56; found C 26.10; H 1.90; N 3.67; S 17.44.

1,3-Dithio-2-(1-nitro-3,4-dichloro-4-bromo-propenylidene)-5-oxocyclohexane (5b)

Synthesized from **1b** (0.5 g, 1.58 mmol) and 1,3-acetonedithiol (0.193 g, 1.58 mmol) according to the general procedure A.

5b: Yield 0.50 g (87%); mp 176–178°C; -IR (KBr): $\upsilon = 2955$, 2995 cm^{-1} (C—H), 1600 (C=C), 1705 (C=O). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 3.5$–4.1 ppm (m, 4 H, 2 CH_2). -^{13}C-NMR ($CDCl_3$, TMS int.): $\delta = 39.94$, 40.48 ppm (2 C—S), 124.10 (=C—Cl), 129.10 (=CClBr), 143.11 (=C—NO_2), 163.16 ppm (=C$\begin{smallmatrix}\diagup\mathrm{S}\\ \diagdown\mathrm{S}\end{smallmatrix}$), 197.67 (C=O), 138.4 (S—C). $C_7H_4S_2Cl_2NBrO_3$ (365.0) calc. C 23.03; H 1.10; N 3.83; S 17.56; found C 22.95; H 1.20; N 3.57; S 17.33.

2-(1-Nitro-3,4-dichloro-4-bromo-propenylidene)-benzo-1,3-dithiol (7b)

Synthesized from **1b** (0.5 g, 1.58 mmol) and o-dithiophenole according to the general procedure A.

7b: Yield 0.52 g (85%); mp 158–159°C; -IR (KBr): $\upsilon = 3070$ cm^{-1} (C—H_{arom}), 1577, 1600 (C=C), 1295, 1465, 1500 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 7.1$–8.2 ppm (m, 4 H, H_{arom}). -^{13}C-NMR ($CDCl_3$, TMS int.): $\delta = 123.90$ (=C—Cl), 128.42 (=CClBr), 134.12 (S—C_{arom}) 139.20 (=C—NO_2), 165.03 ppm (=C$\begin{smallmatrix}\diagup\mathrm{S}\\ \diagdown\mathrm{S}\end{smallmatrix}$). $C_{10}H_4S_2Cl_2NBrO_2$ (385.0) calc. C 31.19; H 1.04; N 3.63; S 16.65; found C 30.98; H 1.10; N 3.47; S 16.43.

1,3,4,4-Tetrachloro-1-(octylthio)-2-nitro-1,3-butadiene (9a)

Synthesized from **1a** (0.5 g, 1.84 mmol) and octylthiol **8a** (0.269 g, 1.84 mmol) according to the general procedure A.

9a: Yield 0.60 g (85%) (Lit.[10] 75%).

1,3,4,4-Tetrachloro-1-(decanethio)-2-nitro-1,3-butadiene (9b)

Synthesized from **1a** (0.5 g, 1.84 mmol) and decanethiol **8b** (0.319 g, 1.84 mmol) according to the general procedure A.

9b: Yield 0.58 g (77%); yellow oil; -IR (film): $\upsilon = 2880$, 2960 cm^{-1} (C—H), 1600 (C=C), 1290, 1520 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 0.9$–1.1 ppm (m, 3 H, CH_3), 1.3–1.8 (m, 16 H, 8 CH_2), 2.6–2.9 (m, 2 H, S—CH_2). $C_{14}H_{21}SNCl_4O_2$ (409.2) calc. C 41.09; H 5.17; N 3.42; S 7.83; found C 41.20; H 4.98; N 3.19; S 7.53.

5-(Octylthio)-6-nitro-7,8-dichloro-4,9-dithia-1-oxa-cyclo-undecane-5,7-diene (11a) and 5-(octylthio)-6-nitro-7,8-dichloro-4,9,15,16-tetrathia-1,12-dioxa-cyclo-octadecane-5,7-diene (12a)

Synthesized from **9a** (0.5 g, 1.31 mmol) and **10** (0.181 g, 1.31 mmol) according to the general procedure B.

11a: Yield 0.131 g (22%); yellow oil; -IR (film): $\upsilon = 2860$, 2980, 2995 cm^{-1} (C—H), 1600 (C=C), 1290, 1530 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 0.6$–1.1 ppm (m, 3 H, CH_3), 1.1–2.1 (m, 12 H, 6 CH_2), 2.4–4.5 (m, 10 H, 3 S—CH_2 and 2 O—CH_2). $C_{16}H_{25}Cl_2NS_3O_3$ (446.4) calc. C 43.04; H 5.64; N 3.13; S 21.54; found C 42.90; H 5.88; N 2.88; S 22.20; MS m/z 445.8.

12a: Yield 0.20 g (26%); yellow oil; -IR (film): $\upsilon = 2865$, 2970, 2990 cm^{-1} (C—H), 1600 (C=C), 1300, 1520 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 0.8$–1.3 ppm (m, 3 H, CH_3), 1.3–2.4 (m, 12 H, 6 CH_2), 2.5–4.8 (m, 18 H, 5 S—CH_2, 4 O—CH_2). $C_{20}H_{33}Cl_2S_5NO_4$ (582.7) calc. C 41.22; H 5.70; N 2.40; S 27.51; found C 41.10; H 5.80; N 2.50; S 27.43; MS m/z 582.4.

5-(Decanethio)-6-nitro-7,8-dichloro-4,9-dithia-1-oxa-cyclo-undecane-5,7-diene (11b) and 5-(decanethio)-6-nitro-7,8-dichloro-4,9,15,16-tetrathia-1,12-dioxa-cyclo-octadecane-5,7-diene (12b)

Synthesized from **9b** (0.5 g, 1.22 mmol) and **10** (0.168 g, 1.22 mmol) according to the general procedure B.

11b: Yield 0.22 g (38%); yellow oil; -IR (film): $\upsilon = 2880$, 2960, 2995 cm^{-1} (C—H), 1610 (C=C), 1295, 1525 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 0.7$–1.2 ppm (m, 3 H, CH_3), 1.2–2.3 (m, 16 H, 8 CH_2), 2.5–4.7 (m, 10 H, 3 S—CH_2 and 2 O—CH_2). $C_{18}H_{29}NS_3Cl_2O_3$ (474.5) calc. C 45.56; H 6.15; N 2.95; S 20.27; found C 45.44; H 6.01; N 3.10; S 20.02; MS m/z 474.3.

12b: Yield 0.18 g (24%); yellow oil; -IR (film): $\upsilon = 2890$, 2960, 2985 cm^{-1} (C—H), 1595 (C=C), 1295, 1530 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 0.7$–1.3 ppm (m, 3 H, CH_3), 1.5–2.6 (m, 16 H, 8 CH_2), 2.3–4.4 (m, 18 H, 5 S—CH_2, 4 O—CH_2). $C_{22}H_{37}Cl_2S_5NO_4$ (610.7) calc. C 43.26; H 6.10; N 2.29; S 26.24; found C 43.33; H 5.96; N 2.19; S 26.02; MS m/z 610.6.

N,N′-Bis(3,4,4-trichloro-1-decylthio-2-nitro-1,3-butadienyl)piperazine (14b)

Synthesized from **9b** (0.5 g, 1.22 mmol) and piperazine **13** (0.105 g, 1.22 mmol) according to the general procedure A.

14b: Yield 0.86 g (85%); mp 144–145°C; -IR (KBr): $\upsilon = 2880$, 2960, 2980, 2990 cm^{-1} (C—H), 1595, 1600 (C=C), 1295, 1525 (C—NO_2). -^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 0.9$–1.2 ppm (m, 6 H, 2 CH_3), 1.3–1.7 (m, 16 H, 8 CH_2), 2.7–3.0 (m, 4 H, 2 S—CH_2), 3.4–4.3 (m, 8 H, piperazine-H). $C_{32}H_{50}Cl_6S_2N_4O_4$ (831.6) calc. C 46.21; H 6.06; N 6.73; S 7.71; found C 46.00; H 6.20; N 6.66; S 7.67; MS m/z 831.

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