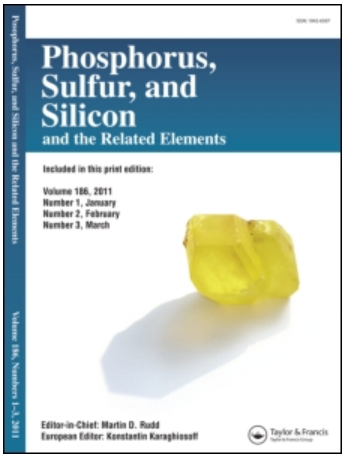

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Mieczysław Mąkosza[a]; Michał Sypniewski[a]
[a] Institute of Organic Chemistry, Polish Academy of Sciences, Warszawa, Poland

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NUCLEOPHILIC SUBSTITUTION OF HYDROGEN IN NITROARENES WITH CARBANIONS OF BENZODITHIOLANE SULFOXIDES VIA INTRAMOLECULAR REDOX PROCESS[1]

MIECZYSŁAW MĄKOSZA and MICHAŁ SYPNIEWSKI
Institute of Organic Chemistry, Polish Academy of Sciences, ul. Kasprzaka 44/52, 01-224 Warszawa, Poland

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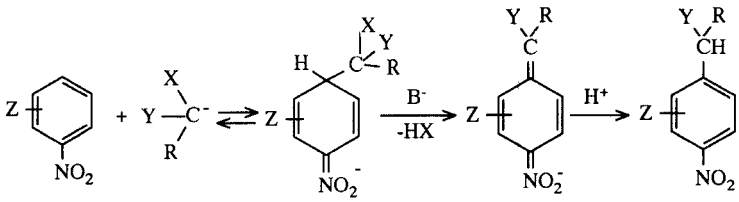
Carbanions of benzodithiolane monosulfoxides in the reaction with nitroarenes replace hydrogen *o*-/*p*-to the nitro group via oxidation of the σ^H adducts with the sulfoxide oxygen atom, whereas open chain analogue reacts along the vicarious nucleophilic substitution pathway.

Key words: Benzodithiolanes monoxides; oxidative nucleophilic substitution of hydrogen; vicarious nucleophilic substitution.

Carbanions containing leaving group X at the carbanion center react with nitroarenes according to the vicarious nucleophilic substitution (VNS) pathway Scheme 1.[2] The reaction consists in addition followed by the base induced β-elimination of HX from the intermediate σ^H adduct.[3]

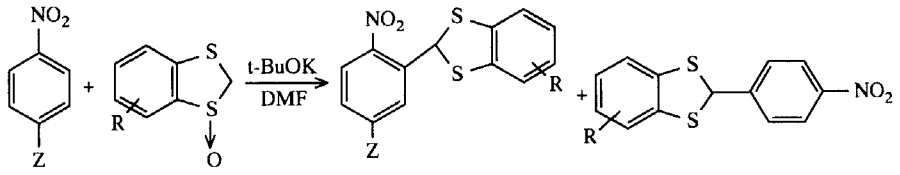


Scheme 1

Although this process is well recognized and of general character in respect to the nitroarenes and carbanions, very little is known about such reactions of carbanions in which the leaving group forms a heterocyclic ring incorporating the carbanion center. In such cases the second step of the VNS reaction-base induced β-elimination should proceed with the heterocyclic ring opening. The only reported example of such process is base promoted reaction of substituted α-cyanooxiranes (glycidonitriles) with 1-nitronaphthalene resulting in the formation of the corresponding cyanomethyl derivatives obviously via the oxirane ring opening VNS, followed by the retro aldol reaction of the initially formed β-hydroxynitriles.[4]

Since knowledge of the ring opening elimination should clarify some general questions of the VNS reaction we have decided to study this process. As one of the model carbanion precursor benzodithiolane was selected because its open chain analogue-diphenyl dithioacetal of formaldehyde enters the VNS reaction satisfactorily.[5] However, treatment of a mixture of benzodithiolane with nitrobenzene or

p-chloronitrobenzene with strong base under a variety of conditions did not provide the expected VNS products. Majority of the nitroarenes was recovered and the mixtures contained some tars. In this situation corresponding monosulfoxide **1a** was used as the carbanion precursor in this process, because it was anticipated that higher acidity of this compound would facilitate formation of the carbanion and the overall process. Indeed treatment of **1a** and nitrobenzene with *t*-BuOK in DMF resulted in the formation of two products of replacement of hydrogen (Scheme 2).



R = H, **1a**; Me, **1b**

Z: H, Cl, OMe, CF_3

$ArNO_2$ = 1-nitronaphthyl

2a, 2b; **4b**; **5a**; **6a**; **7a**

3a, 3b

8a - dithiolane monoxide

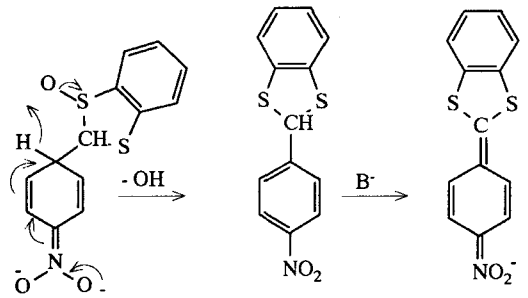
Scheme 2

They were identified as 2-(2-nitrophenyl)- and 2-(4-nitro-phenyl)-benzodithiolanes **2a, 3a** total yield 24% ratio *o*-:*p*- 69:31. No starting materials or other products besides of dark tars were found in the reaction mixture. Obviously the σ^H adducts of the carbanions **1a** to nitrobenzene did not react along the ring opening β-elimination pathway but underwent unprecedented intramolecular redox process to form the products. Oxidative conversion of the σ^H adducts to products of nucleophilic replacement of hydrogen is a well known process.[6,7] There are also known examples of intramolecular redox processes in which the reactions of nitrophenazine *N*-oxides with carbanions, *N*-oxide function acts as oxidant of the σ^H adducts.[8] To our knowledge, however, no example of an intramolecular redox process in which sulfoxide function oxidizes σ^H-adduct, being reduced to sulfide was reported. This reaction took place with some other nitroarenes, also 5-methyl and 6-methylbenzodithiolane monosulfoxide **1b** reacted in a similar way. This compound was used as a mixture of isomers because oxidation of 5-methyl-1,3-benzodithiolane proceeds on both S-1 and S-3 sulfur atoms. In some cases however we have observed that the initial σ^H adducts were oxidized by an external oxidant (unidentified) to form nitrophenyl-1,3-benzodithiolane-1-oxide derivatives. For example the reaction of **1a** with *p*-trifluoromethylnitrobenzene gave products **8a** and **7a** in yield 29% and 11%, respectively. Because of the presence of two chiral centers in **8a** it forms two diastereoisomers readily separated by chromatography.

In order to clarify whether the elimination process is hindered because of the rigid five-membered ring structure of the dithiolane derivate, hence the intra- and inter-molecular oxidation of the σ^H adducts is observed instead of the VNS reaction, we have prepared corresponding open chain analogue of **1a,b** namely sulfoxide of bis(4-tolylthio)methane **9**. The reaction of this sulfoxide with *p*-chloronitrobenzene, chosen in order to avoid formation of regioisomers, in the presence of *t*-BuOK in

DMF proceeded along the VNS pathway to give 5-chloro-2-nitrobenzyl-*p*-tolyl sulfide **10** and di-*p*-tolyl-disulfide **11**. No other products were detected via TLC analysis of the reaction mixture. Thus in this case further transformation of the σ^H adduct occurs via base-induced β-elimination of *p*-toluenesulfenic acid, without participation of the oxidative processes or elimination of thiocresole. Taking into account our earlier observations that open chain bis(phenylthio)methane also reacted via the elimination pathway[5] it appears that in the σ^H adduct the rigid 5-membered ring structure hinders the elimination, therefore competing intra- or inter-molecular redox processes dominate.

The speculative "electron pushing" mechanistic pathway of the intramolecular redox process is shown on Scheme 3.



Scheme 3

It appears that there is a substantial similarity of this process to intramolecular redox transformation of the σ^H adducts formed in reactions of nucleophiles with nitrophenazine *N*-oxides.[8]

EXPERIMENTAL

NMR spectra were recorded on a Varian Gemini 200 (200 MHz) and Bruker AMX (500 MHz) in $CDCl_3$, using tetramethysilane as an internal standard. Coupling constants are expressed in Hz. M.p. are uncorrected, TLC analyses were carried out on foil plates, silica gel Merck $60F_{254}$. Starting materials **1a**, **1b** and **9** were prepared in standard way,[9] via condensation of 1,2-benzenedithiol, 4-methyl-1,2-benzenedithiol and 4-methylphenylthiol with dibromomethane and subsequent oxidation of benzodithiolane, methyl-benzodithiolane and bis(4-tolylthio)methane to **1a**, **1b** and **9** correspondingly.

1,3-Benzodithiolane. A solution of 1,2-benzenedithiole (5.19 g, 0.0332 mole) and dibromomethane (6.07 g, 0.0349 mode) in DMF (5 ml) was added to a stirred suspension of anhydrous K_2CO_3 (22.3 g, 0.16 mole) in DMF (75 ml). During the addition which lasted ca. 5 min the reaction mixture was kept at 0–5°C. After 15 min it was diluted with water (400 ml) and extracted with dichloromethane (4 × 50 ml). The combined extract was washed with water and dried over $MgSO_4$. The solvent was evaporated, the residue dissolved in ethyl acetate-heptane and passed through a short layer of silica gel. The solvent was evaporated to give a colourless oil which solidified upon cooling. Yield 3.65 g, (71%) lit[9] mp. 21°C.

5-Methyl-1,3-benzodithiolane was prepared in the same way from 3,4-toluene-dithiol (yield 70%), oil.

bis(4-Tolylthio)methane.[10] A solution of 4-methylphenylthiol (3.1 g, 0.025 mole) and dibromomethane (2.39 g, 0.0138 mole) in acetone (8 ml) was added to a stirred suspension of anhydrous K_2CO_3 (8.6 g, 0.0625 mole) in acetone (42 ml). The reaction mixture was stirred at room temperature for 5 h. Then acetone was evaporated the residue dissolved in water and extracted with dichloromethane (4 × 30 ml). The combined extract was dried over $MgSO_4$. The solvent was evaporated to give the crude product (3.2 g, 98%), which was used in the next step without purification.

Synthesis of monosulfoxides (**1a**) *and* (**1b**). *General Procedure.* To a solution of the corresponding sulfides (0.023 mole) in methanol (170 ml) a solution of sodium periodate (5.15 g, 0.024 mole) in water

(48 ml) was added at 20°C. After the addition was completed (~30 min) the reaction was carried out for 1 h, then solvent was evaporated, the residue was dissolved in chloroform and after drying, the solvent evaporated. The residue was dissolved in heptane-ethyl acetate, the solution passed through short layer of silica gel and the solvent was evaporated to give a solid which was recrystallized from heptane-ethyl acetate.

Benzo-1,3-dithiolane-1-oxide (**1a**), *yield 70%, mp. 96°C (ethyl acetate-heptane).* ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.18 (d, J = 13.1, 1H); 4.20 and 4.33 (AB, J = 13.0, 2H); 7.28–7.37 (m, 1H); 7.45–7.57 (m, 2H); 7.87–7.94 (m, 1H)

$C_7H_6OS_2$ (170.24) Calcd. C 49.38, H 3.55, S 37.66
Found C 49.31, H 3.31, S 37.79

Methyl-benzo-1,3-dithiolane-1-oxides (**1b**), *yield 70%, mixture of 5-methyl- and 6-methyl-isomers ratio 7:5 (NMR).* ^{1}H NMR (200 MHz, $CDCl_3$): Major isomer δ = 2.40 (s, 3H); 4.18 and 4.30 (AB, J = 13.0, 2H); 7.10 (br.d, J = 7.9, 1H); 7.33 (br.s, 1H); 7.77 (d, J = 7.9, 1H). Minor isomer δ = 2.39 (s, 3H), 4.22 and 4.31 (AB, J = 13.0, 2H); 7,30 (br.d, J = 8.1, 1H); 7.41 (d, J = 8.1, 1H); 7.69 (br.s, 1H)

Sulfoxide of bis(4-Tolylthio)methane (**9**). Solution of sodium periodate (2.94 g, 0.137 mole) in water (25 ml) was added to the stirred solution of bis(4-tolylthio)methane (3.25 g, 0.0125 mole) in methanol (200 ml) during 30 min at 20°C and left overnight. Work-up procedure was analogous to the described above for (**1a**) and (**1b**). Yield 71%, M.p. 56–58°C (ethyl acetate-heptane). ^{1}H NMR (200 MHz, $CDCl_3$) δ = 2.34 (s, 3H); 2.41 (s, 3H); 4.01 and 4.14 (AB, J = 13.1, 2H); 7.11 (d, J = 7.9, 2H); 7.29 (d, J = 7.9, 2H); 7.43 (d, J = 8.2, 2H); 7.58 (d, J = 8.2, 2H).

$C_{15}H_{16}OS_2$ (276.40) Calcd. C 65.18, H 5.84, S 23.20
Found C 65.27, H 5.82, S 22.95

Reaction of Benzodithiolane Oxides (**1a**) *and* (**1b**) *with Nitroarenes.* General Procedure. A solution of benzodithiolane oxide (3 mmole) and nitroarene (3 mmole) in DMF (1.5 ml) was added dropwise to a solution of *t*-BuOK (1 g, 9 mmole) in DMF (7 ml). The reaction was carried out under argon (temp. and time given in Table I). Then the reaction mixture was poured into water (100 ml) containing hydrochloric acid (2 ml), the products were extracted with ethyl acetate, the extracts washed, dried over $MgSO_4$, the solvent was evaporated and the residue chromatographed on silica gel, heptane-ethyl acetate in a variable ratio 95:5 for sulfides and 83:17 to 75:25 for sulfoxides as eluent. Finally the products were recrystallized.

Reaction of Sulfoxide of bis(4-Tolylthio)methane (**9**) *with* p-*Chloronitrobenzene.* The procedure was analogous to the described above; reaction was carried out for fourty minutes. 2-Nitro-5-chlorobenzyl-*p*-tolylsulfide (**10**) yield 37%, di-*p*-tolyldisulfide (**11**) yield 10%.

2-(2-Nitrophenyl)-1,3-benzodithiolane (**2a**). M.p. 102–103°C (ethyl acetate). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.58 (s, 1H); 7.04–7.14 (m, 1H); 7.20–7.30 (m, 2H); 7.37–7.49 (m, 1H); 7.52–7.63 (m, 1H); 7.97–8.06 (m, 2H).

$C_{13}H_9NO_2S_2$ (275.33) Calcd. C 56.71, H 3.29, S 5.09
Found C 56.56, H 3.10, S 5.93

2-(4-Nitrophenyl)-1,3-benzodithiolane (**3a**). M.p. 86–87°C (ethyl acetate). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.06 (s, 1H); 7.06–7.16 (m, 2H); 7.18–7.28 (m, 2H); 7.66 (d, J = 8.8, 2H); 8.17 (d, J = 8.8, 2H).

$C_{13}H_9NO_2S_2$ (275.33) Calcd. C 56.71, H 3.29, S 5.09
Found C 56.60, H 3.06, S 4.80

2-(2-Nitrophenyl)-5-methyl-1,3-benzoadithiolane (**2b**). M.p. 136–138°C (ethyl acetate). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.29 (s, 3H); 6.55 (s, 1H); 6.91 (br.d, J = 7.9, 1H); 7.08 (br.s, 1H); 7.14 (d, J = 7.9, 1H); 7.38 (dd, J = 8.7, 2.3, 1H); 7.96 (d, J = 2.3, 1H); 8.00 (d, J = 8.7, 1H).

$C_{14}H_{11}NO_2S_2$ (289.36) Calcd. C 58.11, H 3.83, S 4.84
Found C 57.88, H 3.79, S 4.62

2-(4-Nitrophenyl)-5-methyl-1,3-dithiolane (**3b**). M.p. 135–136°C (isopropanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.30 (s, 3H); 6.03 (s, 1H); 6.93 (d, J = 7.9, 1H); 7.07 (s, 1H); 7.12 (d, J = 7.9, 1H); 7.65 (d, J = 8.7, 2H); 8.15 (d, J = 8.7, 2H).

TABLE I
Reactions of the sulfoxides with nitroarenes

Educts		Conditions		Products	
	Z in $ArNO_2$	temp. °C	time min.		yields %[a]
1a	H	-20	15	**2a**	17
				3a	8
1b	H	-10	15	**2b**	15
				3b	8
1b	Cl	-10	15	**4b**	13
1a	OMe	-15	7	**5a**	17.5
1a	1-nitronaphthalene	-33[b]	4	**6a**	17
1a	CF_3	-27	20	**7a**	11
				8a	29
9	Cl	-20	40	**10**	37

[a] Isolated, calculated on $ArNO_2$ used for the reaction

[b] in liquid ammonia

$C_{14}H_{11}NO_2S_2$ (289.36) Calcd. C 58.11, H 3.83, S 4.84
Found C 57.86, H 3.81, S 4.61

2-(5-Chloro-2-nitrophenyl)-5-methyl-1,3-benzodithiolane (**4b**). M.p. 141–143°C (ethyl acetate-heptane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.30 (s, 3H); 6.55 (s, 1H); 6.91 (d, J = 7.9, 1H); 7.08 (br.s, 1H); 7.14 (d, J = 7.9, 1H); 7.39 (dd, J = 8.7, 2.3, 1H); 7.96 (d, J = 2.3, 1H); 8.00 (d, J = 8.7, 1H).

$C_{14}H_{10}ClNO_2S_2$ (323.80) Calcd. C 51.93, H 3.11, S 4.33
Found C 52.00, H 2.91, S 4.50

2-(5-Methoxy-2-nitrophenyl)-1,3-benzodithiolane (**5a**). M.p. 137–138°C (ethyl acetate-heptane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.79 (s, 3H); 6.70 (s, 1H); 6.85 (dd, J = 9.1, 2.8, 1H); 7.02–7.13 (m, 2H); 7.20–7.31 (m, 2H); 7.52 (d, J = 2.8, 1H); 8.15 (d, J = 9.1, 1H).

$C_{14}H_{11}NO_3S_2$ (305.36) Calcd. C 55.06, H 3.63, S 4.59
Found C 55.10, H 3.45, S 4.41

2-[2-(1-Nitronaphthyl)]-1,3-benzodithiolane (**6a**). M.p. 172–173°C (isopropanol). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.20 (s, 1H); 7.09–7.12 (m, 2H); 7.22–7.25 (m, 2H); 7.57–7.67 (m, 2H); 7.77 (d, J = 8.2, 1H); 7.87 (d, J = 7.7, 1H); 7.93 (d, J = 8.8, 1H); 7.95 (d, J = 8.8, 1H).

$C_{17}H_{11}NO_2S_2$ (325.02) Calcd. C 62.75, H 3.41, S 4.30
Found C 62.53, H 2.97, S 3.98

2-(5-Trifluoromethyl-2-nitrophenyl)-1,3-benzodithiolane (**7a**). Oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.55 (s, 1H); 7.06–7.16 (m, 2H); 7.22–7.32 (m, 2H); 7.69 (dd, J = 8.3, 1.8, 1H); 8.11 (d, J = 8.3, 1H); 8.29 (d, J = 1.7, 1H).

$C_{14}H_8F_3NO_2S_2$ (342.99) Calcd. C 48.97, H 2.35, S 4.08
Found C 49.62, H 2.36, S 4.00

2-(5-Trifluoromethyl-2-nitrophenyl)-1,3-benzodithiolane-1-oxide (**8a**)—less polar diastereoisomer. M.p. 145–146°C (ethyl acetate-heptane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.33 (s, 1H); 7.35–7.46 (m, 1H); 7.50–7.61 (m, 2H); 7.82–7.92 (m, 2H); 8.19 (d, J = 8.3, 1H); 8.36 (d, J = 1.7, 1H).

$C_{14}H_8F_3NO_3S_2$ (359.33) Calcd. C 46.79, H 2.24, S 3.90
Found C 46.62, H 2.41, S 3.92

(**8a**)—more polar diastereoisomer. M.p. 166–168°C (ethyl acetate-heptane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.33 (s, 1H); 7.33–7.44 (m, 1H); 7.54–7.70 (m, 2H); 7.70–7.86 (m, 3H); 8.25 (d, J = 8.6, 1H).

$C_{14}H_8F_3NO_3S_2$ (359.33) Calcd. C 46.79, H 2.24, S 3.90
Found C 46.67, H 2.51, S 3.98

*2-Nitro-5-chloro-*p*-tolylsulfide* (**10**). M.p. 71–72°C (heptane). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.32 (s, 3H); 4.33 (s, 2H); 7.07 (d, J = 8.0, 2H); 7.15 (br.s, 1H); 7.17 (d, J = 8.0, 2H); 7.33 (dd, J = 8.8, 2.3, 1H); 7.95 (d, J = 8.8, 1H).

$C_{14}H_{11}ClNO_2S$ (293.76) Calcd. C 57.24, H 4.12, S 4.77
Found C 57.16, H 3.86, S 4.64

di(-p-*Tolyl)disulfide*[11] (**11**). M.p. 44–45°C (isopropanol). ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.32 (s, 6H); 7.10 (d, J = 8.0, 4H); 7.38 (d, J = 8.0, 4H).

$C_{14}H_{14}S_2$ (246.38) Calcd. C 68.25, H 5.73
Found C 68.15, H 5.51

REFERENCES

1. Reactions of Organic Anions, Part 198. Part 197: Z. Wróbel and M. Mąkosza, *Tetrahedron*, (submitted).
2. M. Mąkosza and J. Winiarski, *Acc. Chem. Res.*, **20,** 282 (1987). M. Mąkosza, W. Danikiewicz and K. Wojciechowski, *Phosphorus, Sulfur and Silicon*, **53,** 457 (1990).
3. M. Mąkosza and T. Glinka, *J. Org. Chem.*, **48,** 3860 (1983).
4. M. Mąkosza and J. Pankowski, *Bull. Soc. Chim. Belg.*, **94,** 235 (1985).
5. M. Mąkosza and J. Winiarski, *J. Org. Chem.*, **49,** 5272 (1984).
6. F. Terrier, Nucleophilic Aromatic Displacement (Verlag Chemie, Weinheim 1991) Chapt. 5.
7. M. Mąkosza, *Polish J. Chem.*, **66,** 3 (1992).
8. S. Pietra and G. Casiraghi, *Gazz. Chim. Ital.*, **96,** 1826 (1967).
9. D. Seebach, K.-H. Geiss, A. K. Beck, B. Graf and H. Daum, *Chem. Ber.*, **105,** 3280 (1972).
10. Fromm, Forster and v. Scherschewitzki, *Lieb. Ann. Chem.*, **394,** 348 (1912).
11. I. M. Dawson, A. McL. Mathieson and J. Monteath Robertson, *J. Chem. Soc.*, 322 (1948).