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A synthesis of vinylic bis-thioethers from α-bromoketones

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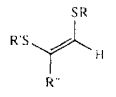
Summary – Reaction of 2-bromoacetophenone and 2-bromo-4′-nitroacetophenone with propane-1-thiol in the presence of 2,6-lutidine gave (*E*) and (*Z*) vinylic bis-thioethers. The intermediate α-thioether ketone was treated with an excess of propane-1-thiol in the presence of various acids. Vinylic bis-thioethers were only formed in the presence of hydrobromic acid. Reaction of ethane-1,2-dithiol with 2-bromo-4′-nitroacetophenone gave the dithiine **8**.

bromoketone / bis-thioether/ dithiine

Vinylic bis-thioethers **1** have been synthesized by the reaction of thiols with a number of substrates including *cis*-bis-chloroethylene [1, 2], acetylenic sulfones (by addition-elimination) [3] and α-bromoacetals [4, 5]. We present here a method of synthesis of these vinylic bis-thioethers **1** starting from α-bromoketones.



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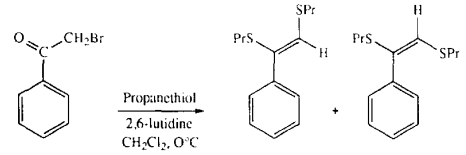
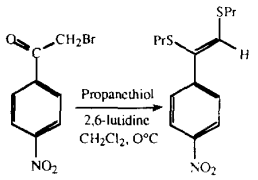


2 **3** **4**

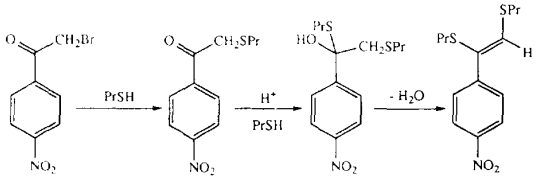
The reaction of bromoacetophenone **2** with an excess of propanethiol in the presence of a catalytic amount of 2,6-lutidine (0.35 equiv) at 0°C gave within 15 min a mixture of *Z*/*E* isomers **3** and **4**. The reaction product was isolated in 79% yield as a mixture of *Z*/*E* isomers, which could not be separated by column chromatography. They could be distinguished by gas chromatography coupled to mass spectrometry and were shown to have the molecular weight expected for structures **3** and **4**. The substitution pattern was deduced from the reaction mechanism.

We extended the reaction to 2-bromo-4′-nitroacetophenone **5**. This bromoketone **5** was treated with an excess of propane-1-thiol (10 equiv) and a catalytic amount of 2,6-lutidine (0.35 equiv) in dichloromethane under argon as above. The vinylic bis-thioether **6** was isolated as the major product after 0.5 h by chromatography in 60% yield. The *Z* stereochemistry of the double bond was determined using the NOE effect observed on the *ortho* aromatic protons on irradiation of the vinylic proton. Upon longer reaction times other thioethers appeared, but these were not studied further. The following reaction scheme can be proposed. Reaction of the bromoketone **5** with the thiol gave the intermediate α-thioether ketone **7**, which gave on further reaction the vinylic bis-thioether **6**.



5 **6**

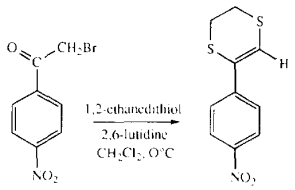
The α-thioether ketone **7** was obtained in high yield by reaction of the 2- bromo-4′-nitroacetophenone **5** with an excess of propane-1-thiol in presence of three equivalents of 2,6-lutidine. Therefore, in the presence of an excess of base the substitution product did not un-



5 **7** **6**

* Correspondence and reprints

dergo further reaction. Further reactions were catalyzed by hydrobromic acid. In order to clarify the reaction mechanism, reaction of the α-thioether ketone **7** with propanethiol was attempted in the presence of acids at 20°C. In the presence of hydrochloric acid (gas) or *p*-toluenesulfonic acid, no reaction was observed. The vinylic bis-thioether **6** was obtained only in the presence of hydrobromic acid as a gas or as an aqueous solution.



5 **8**

This reaction was used to prepare 1,4-dithiine **8** starting with 2-bromo-4′-nitroacetophenone **5** and ethane-1,2-dithiol under the same experimental conditions (10 min at 0°C). The product **8** was obtained in 70% yield as orange crystals. A structurally related compound has been prepared previously by pyrolysis of 2,5-diethoxy-1,4-dithiane [6].

Vinylic bis-thioethers are now easily accessible in good yield starting from the corresponding bromoketones.

Experimental section

Chemicals were purchased from Aldrich. Anhydrous dichloromethane was obtained by distillation under argon with calcium hydride. Melting points were recorded with a Reichert hot-stage microscope and are uncorrected. Thin layer chromatography (TLC) was performed on silica analytical plates (Merck, Kieselgel 60 F_{254}) and visualized under UV or with iodine. UV spectra were recorded with a Hewlett-Packard 8451A spectrophotometer. Infrared spectra (IR) were recorded on a Bruker FTIR spectrophotometer. Mass Spectra (EIMS) were recorded on a LKB 9000S apparatus by electronic impact (EI, 70 eV). ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on a Bruker WP-200 SY spectrometer. The residual protonated solvent was used as an internal reference. Chemical shifts (δ) are given in parts per million (ppm) with regard to tetramethylsilane. The letters s, d, q and m denote the multiplicity of the signals, respectively singlet, doublet, quartet and multiplet. The coupling constants (J) are given in hertz (Hz).

(Z) *and* (E)-*1,2-Bis(propylthio)-1-phenylethene* **3** *and* **4**

To a solution of 2-bromoacetophenone **2** (200 mg; 1 mmol) and 2,6-lutidine (0.04 mL; 0.35 mmol) in anhydrous dichloromethane (1 mL) under argon at 0°C was added propane-1-thiol (0.9 mL; 10 mmol). The temperature was slowly raised to 20°C. After 15 min solvent and excess of reagent were evaporated under reduced pressure. The resulting solid was dissolved in dichloromethane (20 mL) and the organic phase was washed with water (3 × 10 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure. Chromatography (silica gel, hexane/ether: 500:1) gave a mixture of the isomers **3** and **4** in the ratio 8:2 or 2:8 as a colorless oil (200 mg, 79%).

UV ($CHCl_3$): λ_{max} (ε) 234 nm (12 700 M^{-1} cm^{-1}), 310 nm (12 300 M^{-1} cm^{-1}).

IR ($CHCl_3$): 2 878; 2 950 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.91 (t; J = 7 Hz), 1.03 (t; J = 7 Hz), 1.03 (m), 1.47 (m), 2.39 (t; J = 7 Hz), 2.48 (t; J = 7 Hz), 2.66 (t; J = 7 Hz), 2.79 (t; J = 7 Hz), 6.54 (s), 7.30 (m), 7.49 (m).

^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.3, 22.6, 23.2, 23.6, 23.9, 34.7, 35.0, 36.9, 37.0, 127.2, 127.8, 128.1, 128.2, 128.4, 129.1, 130.9, 130.7, 132.4, 137.9, 139.4.

EIMS (70 eV, m/z, rel intensity): 252 (M^+, 78); 134 (100); 252 (M^+, 71); 134 (100).

Anal calc for $C_{14}H_{20}S_2$: C, 66.61; H, 7.93. Found: C, 66.70; H, 7.63.

2-(Propylthio)-4′-nitroacetophenone **7**

To a solution of 2-bromo-4′-nitroacetophenone **5** (490 mg; 2 mmol) and 2,6-lutidine (0.7 mL; 6 mmol) in anhydrous dichloromethane (2 mL), was added 10 equiv of propane-1-thiol (1.8 mL; 20 mmol). The reaction was followed by TLC (ether/hexane: 1:1). After 20 h at 20°C, excess reagent and solvent were evaporated. The product was dissolved in dichloromethane (20 mL) and washed with water (60 mL). The organic phase was dried with magnesium sulfate, filtered and the solvent evaporated. Product **7** was obtained as a yellow oil (430 mg, 95%).

UV ($CHCl_3$): λ_{max} (ε) 266 nm (12 200 M^{-1} cm^{-1}).

IR ($CHCl_3$): 1 680; 856 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.96 (t; J = 7 Hz; 3H), 1.66 (m; J = 7 Hz; 2H), 2.52 (t; J = 7 Hz; 2H), 3.78 (s; 2H), 8.13 (m; 2H), 8.31 (m; 2H).

EIMS (70 eV, m/z, rel intensity): 239 (M^+, 28); 150 (45); 89 (100).

Anal calc for $C_{11}H_{13}NO_3S$: C, 55.23; H, 5.44; N, 5.86. Found: C, 54.99; H, 5.25; N, 5.84.

(Z)-*1,2-Bis(propylthio)-1-(4-nitrophenyl)ethene* **6**

To a solution of 2-bromo-4′-nitroacetophenone **5** (500 mg; 2 mmol) and of 2,6-lutidine (0.08 mL; 0.7 mmol) in anhydrous dichloromethane (2 mL), under argon, at 20°C, was added propane-1-thiol (1.8 mL; 20 mmol). After 15 min solvent and excess reagent were evaporated under reduced pressure. The same treatment as above was performed. Chromatography (silica gel, hexane/ether: 15:1) gave product **6** as an orange oil (200 mg, 59%).

UV ($CHCl_3$): λ_{max} (ε) 386 nm (11 200 M^{-1} cm^{-1}), 310 nm (12 300 M^{-1} cm^{-1}).

IR ($CHCl_3$): 2 877; 2 939; 2 968; 1 342; 1 510 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.96 (t; J = 7 Hz; 3H), 1.05 (t; J = 7 Hz; 3H), 1.49 (m; J = 7 Hz; 2H), 1.54 (m; J = 7 Hz; 2H), 2.50 (t; J = 7 Hz; 2H), 2.84 (t; J = 7 Hz; 2H), 6.92 (s; 1H), 7.65 (m; 2H), 8.18 (m; 2H).

^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.1, 23.1, 24.0, 36.5, 123.95, 127.2, 127.9, 139.2, 146.6, 145.8.

EIMS (70 eV, m/z, rel intensity): 297 (M^+, 100); 166 (74).

Anal calc for $C_{14}H_{19}NO_2S_2$: C, 56.56; H, 6.40; N, 4.71. Found: C, 56.34; H, 6.65; N, 4.55.

Preparation of (Z)-*1,2-bis(propylthio)-1-(4-nitrophenyl)ethene* **6** *from ketone* **7**

To a solution of ketone **7** (280 mg; 1.2 mmol) in anhydrous dichloromethane (2 mL), was added 2 equiv of propane-1-thiol (0.22 mL; 2.4 mmol). This solution was treated with hydrobromic acid (gas). The reaction was followed by TLC (ether/hexane: 1:1). After 18 h at 20°C, excess

reagent and solvent were evaporated. 1,2-Bis(propylthio)-1-(4-nitrophenyl)ethene **6** was obtained in a 24% yield.

5-(4-Nitrophenyl)-2,3-dihydro-1,4-dithiine **8**

Ethane-1,2-dithiol (1.7 mL; 20 mmol) was added at 0°C, under argon to a solution of 2-bromo-4′-nitroacetophenone **5** (500 mg; 2 mmol) and 2,6-lutidine (0.08 mL; 0.7 mmol) in anhydrous dichloromethane (2 mL). After 10 min solvent and excess reagent were evaporated. The same treatment as above was performed. The product was crystallized in ether/hexane. Product **8** was obtained as orange crystals (335 mg, 70%).

Mp 145–146°C.

UV (CH_2Cl_2): λ_{max} (ε) 274 nm (15 600 M^{-1} cm^{-1}), 394 nm (11 700 M^{-1} cm^{-1}).

^1H NMR (200 MHz, $CDCl_3$) δ: 3.30 (t; J = 7 Hz; 4H), 6.65 (s; 1H), 7.59 (m; 2H), 8.19 (m; 2H).

^{13}C NMR (50 MHz, $CDCl_3$) δ: 27.2, 117.6, 123.9, 125.7, 126.2, 146.2, 146.8.

EIMS (70 eV, m/z, rel intensity): 229 (M^+, 100).

Anal calc for $C_{10}H_9NO_2S_2$: C, 50.21; H, 3.76; N, 5.86. Found: C, 50.26; H, 3.66; N, 5.77.

References

1 Parham WE, Heberling J, *J Am Chem Soc* (1955) 77, 1175-1177

2 Lee SJ, Peng ML, Lee JC, Chou TS, *Chem Ber* (1992) 125, 499-504

3 Selling HA, *Tetrahedron* (1975) 31, 2387-2390

4 Rothstein E, Whitely R, *J Chem Soc* (1953) 4012-4018

5 Rothstein E, Standbank D, Whitely R, *J Chem Soc* (1968) 753-760

6 Parham NP, Gadsby B, Mikulec RA, *J Org Chem* (1959) 24, 1819-1823