*Chemistry of Heterocyclic Compounds, Vol. 37, No. 4, 2001*

# PREPARATION AND PROPERTIES OF A REPRESENTATIVE OF A NEW SERIES OF CHALCOGEN-CONTAINING 1,5-DIKETONES, DI(1-OXO-1,2,3,4-TETRAHYDRO-2-NAPHTHYL) SULFIDE

**A. V. Barabanova, O. V. Fedotova, V. G. Kharchenko, and V. A. Samokhvalov**

*Di(1-oxo-1,2,3,4-tetrahydro-2-naphthyl) sulfide has been obtained and its behavior towards hydrogen sulfide in situ, ammonium acetate, hydrazine hydrate, and hydrogen peroxide has been studied. The structure of the compounds synthesized was established by IR and by $^{1}H$ and $^{13}C$ NMR spectroscopy and by chromato-mass spectrometry.*

**Keywords:** 5,6,6a,7a,8,9-hexahydrodinaphtho[2,1-*b*;1,2-*f*]-4,5-thiadiazepine, di(1-oxo-1,2,3,4-tetrahydro-2-naphthyl) sulfide, di(1-oxo-1,2,3,4-tetrahydro-2-naphthyl) sulfone, 1,2,7,8-tetrahydrodibenzothianthrene S,S,S',S'-tetroxide, 1,2,7,8-tetrahydrodibenzothianthrene, 1,2,7,8-tetrahydro-3,4,5,6-dibenzophenothiazine.

It was shown by us previously that methylene-2,2'-bis(1-oxo-1,2,3,4-tetrahydronaphthalene) is notable for a reduced inclination towards S-heterocyclization under the action of hydrogen sulfide and acids [1]. It seemed of interest to us to synthesize and compare the behavior in nucleophilic substitution reactions of its thioanalog, the previously unknown di(1-oxo-1,2,3,4-tetrahydro-2-naphthyl) sulfide (**1**). The introduction of a sulfur atom creates a new reaction center in the molecule, which enables the range of conversions of diketone **1** to be broadened and thereby yield compounds valuable in practice, containing a tetrahydronaphthalenone fragment. This fragment is encountered in natural and biologically active substances, steroids, vitamin E, etc. [2].

Diketone **1** was obtained by the action of sodium sulfide on 2-bromo-1-oxotetrahydronaphthalene in methanol or 2-propanol in yields of 20 and 74% respectively (Scheme 1).

The yield of product **1** was increased when using 2-propanol and the reaction time was reduced from 3 h to 30 min. In this way diketone **1** did not require additional purification and was stable in the air, unlike di(1-oxodi-2-cyclohexyl) sulfide which is stored in the refrigerator [3].

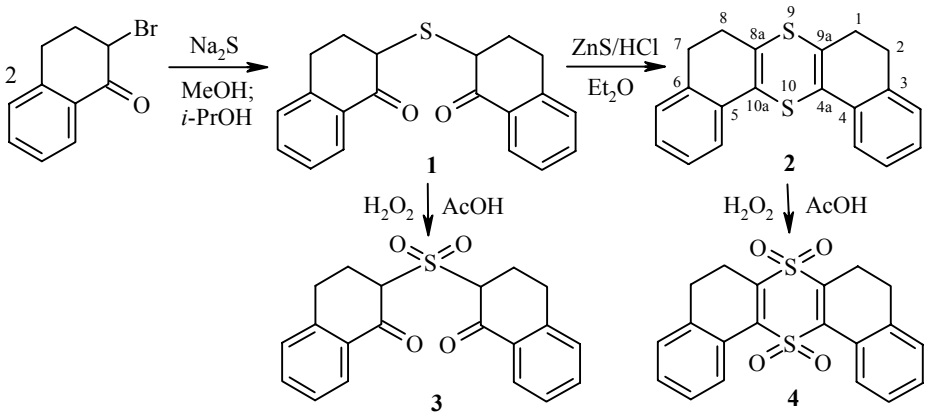
It was established by us that under the action of hydrogen sulfide *in situ* diketone **1**, like its C-analog [1], gives the product of S-heterocyclization, *viz*. 1,2,7,8-tetrahydrodibenzothianthrene (**2**). Its formation (70% yield) was facilitated due to benzannelation.

---

Saratov N. G. Chernyshevskii State University, Saratov 410600, Russia; e-mail: BarabanovaAV@info.sgu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 511-514, April, 2001. Original article submitted June 22, 2000.

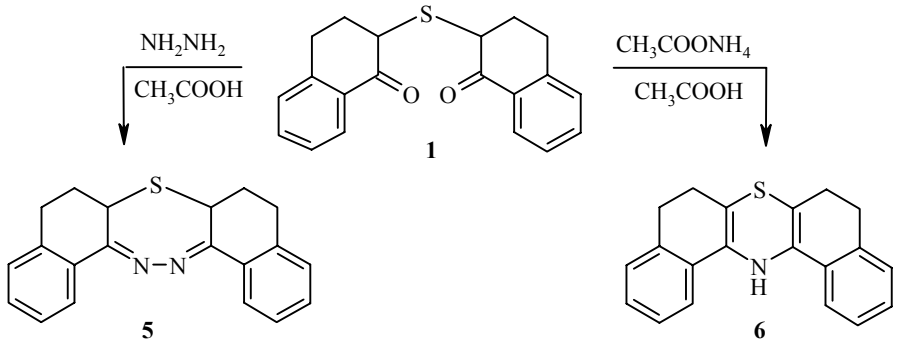
0009-3122/01/3704-0463$25.00 

Scheme 1




Chemical conversions, spectral characteristics, and data of chromato-mass spectrometry unequivocally confirmed the structures of compounds **1** and **2**. Oxidation of the sulfur atoms takes place under the action of hydrogen peroxide with the formation of the sulfone **3** and disulfone **4** respectively.

Nucleophilic reactions at the carbonyl function of diketone **1** with hydrazine hydrate and ammonium acetate occur with the formation of the previously unknown thiadiazepine **5** and phenothiazine **6**.




Characteristic absorption bands were present in the IR spectra of compounds **1** and **3** for conjugated carbonyl groups at 1670 $cm^{-1}$. The presence of a S=O bond in sulfones **3** and **4** was confirmed by the presence of intense absorption bands at 1100-1130 $cm^{-1}$, and the stretching vibrations of the N-H bond in thiazine **6** were displayed as an absorption band with a maximum at 3400 $cm^{-1}$.

Signals were present in the $^1H$ NMR spectra of compounds **1-5** for the aromatic protons as a multiplet in the region of 7.13-8.50 ppm and for the methylene protons as a multiplet and quartet at 2.81-3.17 and 2.20-2.71 ppm. The methine protons of diketone **1** and its sulfone **3** were observed as a triplet at 4.02 and 5.11 ppm respectively. Displacement of the methine protons of sulfone **3** towards low field is probably linked with the presence of the $SO_2$ acceptor group. In the $^1H$ NMR spectrum of thiadiazepine **5**, which is a conformationally more rigid structure than compounds **1** and **3**, the methine group protons correspond to the twin doublet at 3.76 ppm. The chromato-mass spectra of compounds **2** and **4** contain peaks for molecular ions with *m/z* 320 and 384 respectively, confirming their homogeneity.

TABLE 1. Physicochemical Characteristics of the Compounds Synthesized

| Compound | Empirical formula | Found, % / Calculated, % | | | | mp, °C | Yield, % |
|---|---|---|---|---|---|---|---|
| | | C | H | N | S | | |
| **1** | $C_{20}H_{18}O_2S$ | 75.01 / 74.54 | 5.45 / 5.59 | | 9.64 / 10.04 | 125-126 | 74 |
| **2*** | $C_{20}H_{16}S_2$ | | | | | 169.5-170 | 70 |
| **3** | $C_{20}H_{18}O_4S$ | 68.31 / 67.79 | 4.86 / 5.08 | | 8.64 / 9.04 | 205-206 | 73 |
| **4*** | $C_{20}H_{16}O_4S_2$ | | | | | 201-202 | 54 |
| **5** | $C_{20}H_{18}N_2S$ | 75.92 / 75.47 | 5.51 / 5.66 | 9.30 / 8.81 | 9.67 / 10.06 | 192-193 | 60 |
| **6** | $C_{20}H_{17}NS$ | 79.00 / 79.20 | 5.43 / 5.61 | 4.02 / 4.62 | 10.88 / 10.56 | >300 | 46 |

TABLE 1 (continued)

| Compound | IR spectrum, ν, $cm^{-1}$ | $^1H$ NMR spectrum, δ, ppm |
|---|---|---|
| **1** | 1598 (C–C arom.), 1674 (C=O), 2932 (C–H aliph.), 3024 (C–H arom.) | 7.25-8.07 (8H, m, $2C_6H_4$); 4.02 (2H, t, 2CH); 2.95 (4H, q, $2CH_2$); 2.30 (4H, m, $2CH_2$) |
| **2*** | 1598 (C–C arom.), 2932 (C–H aliph.), 3072 (C–H arom.) | 7.13-8.07 (8H, m, $2C_6H_4$); 2.82 (4H, m, $2CH_2$); 2.56 (4H, m, $2CH_2$) |
| **3** | 1480 (C–C arom.), 1668 (C=O), 2929 (C–H aliph.) | 7.19-8.04 (8H, m, $2C_6H_4$); 5.11 (2H, t, 2CH); 3.17 (4H, q, $2CH_2$); 2.71 (4H, m, $2CH_2$) |
| **4*** | 1573 (C–C arom.), 2928 (C–H aliph.), 3035 (C–H arom.) | 7.25-8.50 (8H, m, $2C_6H_4$); 3.00 (8H, m, $2CH_2$) |
| **5** | 1560 (C–C arom.), 2968 (C–H aliph.) | 7.13-8.30 (8H, m, $2C_6H_4$); 3.76 (2H, dd, 2CH); 2.81 (4H, m, $2CH_2$); 2.20 (4H, m, $2CH_2$) |
| **6** | 1500 (C–C arom.), 3032 (C–H arom.), 3400 (N–H) | |

* Characterized by chromato-mass spectrometry.

Considering that compounds containing a hydronaphthalenone fragment possess, as was shown by us, DNA tropic, antitumor (in relation to Jensen sarcoma), and antibacterial (exceeding known antibiotics) activity [1], and are less toxic, it seemed of particular interest to carry out screening investigations in series of similar substances.

We detected a prooxidant effect in the action of diketone **1** by polarography using the autooxidation of adrenaline [4] and found a concentration dependent effect. The autooxidation of adrenaline was accelerated at a concentration of diketone **1** of ~$7.71.10^{-5}$ M in DMSO and an antioxidant effect developed at a tenfold reduction of concentration. This is characteristic of natural antioxidants, particularly ascorbic acid. Suppression of the peroxidase activity of hemoglobin by 65% was also detected in the presence of diketone **1**, which probably indicates its membrane-protective action.

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were recorded on Varian FT 80 A and Bruker DPX 200 spectrometers (operating frequencies 80 and 50 MHz respectively) in $CDCl_3$, internal standard was TMS. The IR spectra were recorded on a Specord M 80 spectrometer in nujol and hexachlorobutadiene. Chromato-mass spectra were

taken on a Hewlett-Packard 5890A gas-liquid chromatograph with a 5872A mass-selective detector and a column (30 m × 0.25 mm) of 5% methylphenylsilicone. Carrier gas was nitrogen, energy of ionizing electrons 70 eV. A check on the progress of reactions and the homogeneity of substances obtained was effected by TLC (Silufol UV 254, hexane–ether–chloroform, 3:1:1, detection with iodine vapor). The autooxidation of adrenaline was carried out by the procedure described in [4].

**Di(1-oxo-1,2,3,4-tetrahydro-2-naphthyl) Sulfide (1).** A solution of $Na_2S·9H_2O$ (4.05 g, 16 mmol) in $H_2O$ (10 ml) was added dropwise to a solution of 2-bromo-1-oxotetrahydronaphthalene (6.8 g, 30 mmol) in 2-propanol (35 ml). The reaction mixture was stirred for 30 min at room temperature. The crystals formed were filtered off, washed with water, and with diethyl ether. Product **1** (3.9 g, 74%) was obtained.

**1,2,7,8-Tetrahydrodibenzothianthrene (2).** Zinc sulfide (0.7 g, 7 mmol) and diketone **1** (2.1 g, 6 mmol) were added with stirring to a mixture of hydrochloric acid (d = 1.19, 4 ml) and diethyl ether (4 ml) cooled with ice. The reaction mixture was stirred at room temperature for 20 h. The precipitate was filtered off, washed with water, and with 2-propanol. Product **2** (1.4 g, 70%) was obtained. $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 30.37 (C-1); 29.01 (C-2); 133.52 (C-3); 127.21 (C-4); 135.91 (C-9a); 135.52 (C-4a); 127.43, 127.38, 126.70, 123.73 ($C_{A2}$).

**Di(1-oxo-1,2,3,4-tetrahydro-2-naphthyl) Sulfone (3).** A 30% solution of $H_2O_2$ (10 ml) was added dropwise to a solution of diketone **1** (1.61 g, 5 mmol) in acetic acid (30 ml). The reaction mixture was stirred for 3 h at 18°C. The crystals formed were filtered off, washed with water, and with ethanol. Product **3** (1.3 g, 73%) was obtained.

**1,2,7,8-Tetrahydrodibenzothianthrene S,S,S',S'-Tetroxide (4).** A 30% solution of $H_2O_2$ (12 ml) was added dropwise to a solution of thianthrene **2** (1 g, 3 mmol) in acetic acid (20 ml). The reaction mixture was stirred for 20 h at room temperature. The precipitate was filtered off, washed with acetic acid, and with 2-propanol. Product **4** (0.65 g, 54%) was obtained.

**5,6,6a,7a,8,9-Hexahydrodinaphtho[2,1-*b*;1,2-*f*]-1,4,5-thiadiazepine (5).** A mixture of diketone **1** (0.8 g, 2 mmol) and hydrazine hydrate (0.62 g, 12 mmol) in acetic acid (15 ml) was stirred for 15 h at room temperature. The precipitate was filtered off, and washed with acetic acid. Product **5** (0.48 g, 60%) was obtained. $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 24.57 (C-1); 26.09 (C-2); 129.29 (C-3); 129.30 (C-4); 36.68 (C-9a); 148.13 (C-4a); 128.60, 129.88, 125.92, 126.62 ($C_{A2}$).

**1,2,7,8-Tetrahydro-3,4,5,6-dibenzophenothiazine (6).** A mixture of diketone **1** (0.4 g, 1 mmol) and ammonium acetate (0.2 g, 2 mmol) in acetic acid (20 ml) was boiled for 10 h. The precipitated crystals were filtered off, and washed with diethyl ether. Product **6** (0.18 g, 46%) was obtained.

## REFERENCES


1. L. K. Kulikova, V. G. Kharchenko, A. P. Kriven'ko, O. V. Fedotova, and G. K. Kravtsova, *Khim.-farm. Zh.*, 545 (1982).
2. S. N. Petrakov, B. I. Drevko, V. G. Kharchenko, L. A. Fomenko, and O. V. Fedotova, USSR Inventor's Certificate 1583421; *Byull. Izobret.*, No. 29, 34 (1990).
3. A. A. Usol'tsev, E. S. Karaulov, and M. N. Tilichenko, USSR Inventor's Certificate 638592; *Byull. Izobret.*, No. 47, 53 (1978).
4. T. V. Sirota, *Vopr. Med. Khim.*, **45**, 263 (1999).