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1,7-Dithioxo Systems. Reaction of 3-[(5,5-Dimethyl-3-thioxocyclohex-1-en-1yl)sulfanyl]-5,5-dimethylcyclohex-2-ene-1-thione with 2-Aminoethanol and Ethane-1,2-diamine

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Abstract—The reaction of 3-[(5,5-dimethyl-3-thioxocyclohex-1-en-1-yl)sulfanyl]-5,5-dimethylcyclohex-2-ene-1-thione with 2-aminoethanol involves cleavage of the sulfide bond with formation of 3-[(2-hydroxyethyl)-amino]-5,5-dimethylcyclohex-2-ene-1-thione as the major product. The reaction of the same sulfide with ethane-1,2-diamine gave previously unknown 3-({2-[(5,5-dimethyl-3-thioxocyclohex-1-en-1-yl)amino]ethyl}-amino)-5,5-dimethylcyclohex-2-ene-1-thione.

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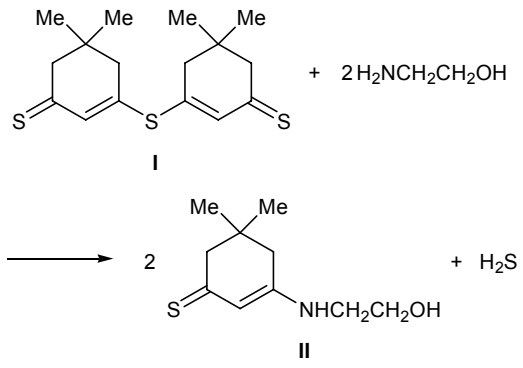
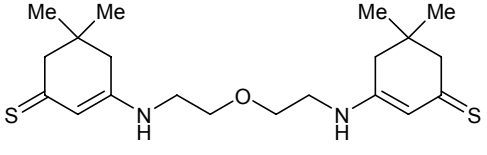
In continuation of our studies on the chemical properties of compounds containing an S=CC=CSC=CC=S fragment [1, 2], in the present work we examined reactions of 3-[(5,5-dimethyl-3-thioxocyclohex-1-en-1-yl)sulfanyl]-5,5-dimethylcyclohex-2-ene-1-thione (**I**) with N,O- and N,N-binucleophiles. The reactions of dithioxo sulfide **I** with 2-aminoethanol and ethane-1,2-diamine were carried out in acetonitrile in an inert atmosphere. Like aminolysis of compound **I** reported previously [2], these reactions involved cleavage of the sulfide bond in the substrate.

The reaction of **I** with 2-aminoethanol resulted in the formation of 3-[(2-hydroxyethyl)amino]-5,5-dimethylcyclohex-2-ene-1-thione (**II**) as the major product (Scheme 1). Enamino thioketone **II** was synthesized previously by reaction of 2-aminoethanol with 3-methoxy-5,5-dimethylcyclohex-2-ene-1-thione [3]. In the present article we report for the first time detailed spectral parameters of compound **II**. Its ^{1}H NMR spectrum contained signals at δ 6.49 ppm typical of =CH protons and NH signal at δ 8.08 ppm; protons of the methylene groups in the CH_2CH_2OH fragment resonated at δ 3.39 and 4.74 ppm, respectively, and broadened signal at δ 4.84 ppm was assigned to the hydroxy proton. In the ^{13}C NMR spectrum of **II**, the CH_2OH signal was located at δ_C 58.62 ppm, and the =C–N carbon atom gave a signal at δ_C 161.48 ppm.

Analysis of the ^{1}H ans ^{13}C NMR spectra showed that the reaction of dithioxo sulfide (**I**) with 2-aminoethanol at 20°C, apart from enamino thioketone **II**, produced a small amount of 3-[(2-{2-[(5,5-dimethyl-3-thioxocyclohex-1-en-1-yl)amino]ethoxy}ethyl)amino]-5,5-dimethylcyclohex-2-ene-1-thione (**III**).

Scheme 1.

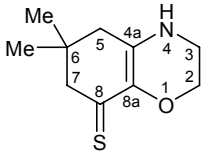




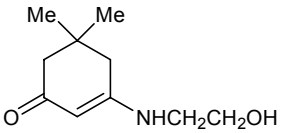
The minor product displayed in the ^{13}C NMR spectrum nine signals whose position was similar to the position of signals in the spectrum of **II**. In particular, signals at δ_C 166.34 (=C–N), 114.22 (=CH), and 59.94 ppm (CH_2OCH_2) were present. In addition, the

^{1}H NMR spectrum contained signals at δ 8.51 and 6.64 ppm, typical of NH and =CH protons, respectively, while no signal assignable to hydroxy proton was present. The molar ratio of compounds **II** and **III**, calculated from signal intensities in the ^{1}H NMR spectrum, was 1.00:0.09. An indirect support to the assumed structure of **III** may be elemental composition of the product mixture, calculated on the basis of the ^{1}H NMR data, which coincided with the results of chemical analysis (see Experimental).

When the reaction of dithioxo sulfide **I** with 2-aminoethanol was carried out at reduced temperature (–10 to 0°C) in a more concentrated solution (2 mmol of **I** in 10 ml of acetonitrile against 0.65 mmol in 30 ml of acetonitrile in the reaction performed at 20°C), the products were enamino thioketone **II** and previously unknown 6,6-dimethyl-3,4,5,6,7,8-hexahydro-2*H*-1,4-benzoxazine-8-thione (**IV**). The ^{1}H NMR spectrum of the product mixture contained minor signals indicating the presence of a compound structurally related to **II** but lacking hydroxy proton and proton at double C=C bond. Unlike thioketone **II**, in the ^{13}C NMR spectrum of the other product we observed signals at δ_C 138.95 and 159.73 ppm, whereas the C=S signal was displaced appreciably upfield ($\Delta\delta_C$ ~10 ppm). These findings suggest the presence of a $CH_2OC{=}CN$ fragment which could be formed via intramolecular cyclization of enamino thioketone **II** at position *2* of the cyclohexene ring (structure **IV**). The presence of a vinyl ether fragment (C–O–C=C) in molecule **IV** should led to considerable electron density redistribution over the cyclohexene ring, i.e., delocalization over the S=CC=CN bond system. As a result, the carbon atom in the thiocarbonyl group in **IV** should be shielded to a greater extent as compared to compound **II**, and the C^{8a} atom should be shielded more strongly than quaternary C^{α} atom in $O–C^{\alpha}=C^{\beta}$ fragment; the chemical shifts of the latter generally range from δ_C 145 to 152 ppm provided that there are no conjugated bonds [4]. In addition, the C^{4a} atom in molecule **IV** resonates in a stronger field than does analogous carbon atom in **II**, though the corresponding $\Delta\delta_C$ value is smaller than that observed for C=S.



IV

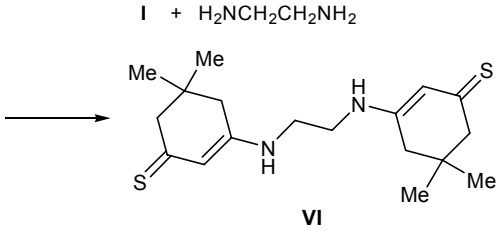


V

The ^{13}C NMR spectrum of the product mixture also contained signals with lower intensity at δ_C 195.26, 166.33, 115.29, 57.16, 55.30, and 45.16 ppm; taking into account the corresponding signals in the ^{1}H NMR spectrum, we identified the third product as 3-[(2-hydroxyethyl)amino]-5,5-dimethylcyclohex-2-en-1-one (**V**). According to the signal intensity ratio in the ^{1}H NMR spectrum, the molar ratio of compounds **II**, **IV**, and **V** was estimated at 1.00:0.57:0.11. The elemental composition calculated for that mixture was consistent with that found experimentally.

By reaction of dithioxo sulfide **I** with ethane-1,2-diamine in acetonitrile at –10 to 0°C under argon we obtained a new dithiocarbonyl compound, 3-({2-[(5,5-dimethyl-3-thioxocyclohex-1-en-1-yl)amino]ethyl}-amino)-5,5-dimethylcyclohex-2-ene-1-thione (**VI**) (Scheme 2).

Scheme 2.



VI

Its structure was determined on the basis of the IR and NMR spectra and elemental analysis. In the IR spectrum of dithione **VI**, stretching vibrations of the C=S groups gave rise to a strong absorption band at 1050 cm^{-1}, and vibrations the C=C bonds were characterized by a frequency of 1525 cm^{-1}. The NH absorption band was located at 3201 cm^{-1}. The ^{1}H NMR spectrum of **VI** contained signals from methylene protons in the NCH_2CH_2N fragment (δ 3.82 ppm), the NH signal appeared as a broadened singlet at δ 7.84 ppm, and olefinic protons resonated at δ 6.29 ppm. In the ^{13}C NMR spectrum of **VI** we observed characteristic signals from carbon atoms in the C=S (δ_C 217.67 ppm), =C–NH (δ_C 161.54 ppm), and =CH fragments (δ_C 110.81 ppm).

EXPERIMENTAL

The IR spectra were recorded in KBr on an IFS 25 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker DPX-400 instrument at 400.1 and 100.4 MHz, respectively, using hexamethyldisiloxane as internal reference. The progress of reactions and the purity of products were monitored by TLC on

Silufol UV-254 plates using chloroform–ethyl acetate (3 : 1) as eluent.

3-[(5,5-Dimethyl-3-thioxocyclohex-1-en-1-yl)sulfanyl]-5,5-dimethylcyclohex-2-ene-1-thione (**I**) was synthesized according to the procedure reported in [5].

Reaction of dithioxo sulfide I with 2-aminoethanol. *a*. A solution of 0.079 g (1.3 mmol) of 2-aminoethanol in 3 ml of acetonitrile was added dropwise over a period of 10 min to a solution of 0.2 g (0.65 mmol) of compound **I** in 30 ml of anhydrous acetonitrile under stirring in an argon atmosphere. The color of the mixture changed from dark green to dark orange, and vigorous evolution of hydrogen sulfide was observed [test with a solution of $Pb(OAc)_2$]. The mixture was stirred for 12 h while continuously bubbling argon until hydrogen sulfide no longer evolved, evaporated to 1/3 of the initial volume, and left overnight at 5°C. The precipitate was filtered off, washed with acetonitrile, and dried under reduced pressure. We isolated 0.15 g of a mixture of 3-[(2-hydroxyethyl)amino]-5,5-dimethylcyclohex-2-ene-1-thione (**II**) and 3-[(2-{2-[(5,5-dimethyl-3-thioxocyclohex-1-en-1-yl)amino]ethoxy}ethyl)amino]-5,5-dimethylcyclohex-2-ene-1-thione (**III**) as orange powder. IR spectrum, ν, cm^{-1}: 3217, 3057 (NH); 1585, 1545 (C=C); 1048 (C=S). ^1H NMR spectrum, δ, ppm: compound **II** (in CD_3OD): 1.02 s (6H, CH_3), 2.32 s (2H, 4-H), 2.65 s (2H, 6-H), 3.39 t (2H, NCH_2, ^3J = 5.64 Hz), 4.74 t (2H, OCH_2, ^3J = 5.64 Hz), 6.49 s (1H, 2-H), 8.08 br.s (in DMSO-d_6; 1H, NH); compound **III** (in DMSO-d_6): 0.92 s (12H, CH_3), 2.32 s and 2.49 s (4H each, 4-H, 6-H), 3.22 t (4H, OCH_2), 3.27 t (4H, NCH_2), 8.51 br.s (2H, NH), 6.64 s (2H, 2-H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: compound **II**: 27.30 (CH_3), 32.98 (C^5), 42.03 (C^4), 45.28 (NCH_2), 51.12 (C^6), 58.62 (CH_2O), 110.00 (C^2), 161.48 (C^3), 215.12 (C=S); compound **III**: 27.64 (CH_3), 32.62 (C^5), 41.04 (C^4, C^6), 45.11 (NCH_2), 56.53 (C^4, C^6), 59.94 (CH_2O), 114.22 (C^2), 166.34 (C^1, C^3), 210.02 (C=S). Found, %: C 59.40; H 8.68; N 7.30; S 16.98. $C_{10}H_{17}NOS$ (**II**), $C_{20}H_{32}N_2OS_2$ (**III**). Calculated, %: C 60.73; H 8.52; N 7.09; S 16.19 (according to the product ratio determined on the basis of the ^1H NMR data).

b. A suspension of 0.62 g (2 mmol) of dithioxo sulfide **I** in 10 ml of anhydrous acetonitrile was cooled to –14°C, a solution of 0.24 g (4 mmol) of 2-aminoethanol in 5 ml of acetonitrile was added dropwise under stirring over a period of 20 min in an argon atmosphere, and the mixture was stirred for 2 h at –10 to 0°C (hydrogen sulfide evolved, and the mixture changed from dark green to dark orange). The mixture was then kept for 20 h at 5°C, and the precipitate was filtered off, washed with acetonitrile, and dried under reduced pressure. We thus isolated 0.57 g of a mixture of 3-[(2-hydroxyethyl)amino]-5,5-dimethylcyclohex-2-ene-1-thione (**II**), 6,6-dimethyl-3,4,5,6,7,8-hexahydro-2*H*-1,4-benzoxazine-8-thione (**IV**), and 3-[(2-hydroxyethyl)amino]-5,5-dimethylcyclohex-2-en-1-one (**V**) as yellow powder. IR spectrum, ν, cm^{-1}: 3218, 3143, 3057 (NH); 1586, 1546 (C=C); 1048, 1025 (C=S). ^1H NMR spectrum (CD_3OD), δ, ppm: compound **IV**: 0.97 s (6H, CH_3), 2.52 br.s (4H, 5-H, 7-H), 3.04 t (2H, 3-H, $^3J_{HH}$ = 5.12 Hz), 3.75 t (2H, 2-H, $^3J_{HH}$ = 5.12 Hz), 7.35 s (1H, NH); compound **V**: 1.05 s (6H, CH_3), 2.44 s (2H, 4-H), 2.59 s (2H, 6-H), 3.46 t (2H, NCH_2, $^3J_{HH}$ = 5.00 Hz), 3.69 t (2H, OCH_2, $^3J_{HH}$ = 5.00 Hz), 8.99 s (1H, 2-H). ^{13}C NMR spectrum (CD_3OD), δ_C, ppm: compound **IV**: 26.74 (CH_3), 33.92 (C^6), 41.54 (C^5), 56.44 (C^7), 57.61 (C^2), 138.95 (C^{8a}), 159.73 (C^{4a}), 205.05 (C=S); compound **V**: 27.87 (CH_3), 45.16 (NCH_2), 55.30 (C^6), 57.16 (CH_2O), 115.29 (C^2), 166.33 (C^3), 195.26 (C=O). Found, %: C 63.18; H 9.00; N 6.19; S 13.87. $C_{10}H_{17}NOS$ (**II**), $C_{10}H_{15}NS$ (**IV**), $C_{10}H_{17}NO$ (**V**). Calculated, %: C 60.83; H 8.27; N 7.10; S 15.16 (according to the product ratio determined on the basis of the ^1H and ^{13}C NMR data).

3-({2-[(5,5-Dimethyl-3-thioxocyclohex-1-en-1-yl)amino]ethyl}amino)-5,5-dimethylcyclohex-2-ene-1-thione (VI). The reaction was carried out as described above in *b* using 0.31 g (1 mmol) of compound **I** in 10 ml of anhydrous acetonitrile and 0.12 g (2 mmol) of ethane-1,2-diamine in 4 ml of acetonitrile. Yield 0.23 g (68%), yellow powder, mp 194–196°C. IR spectrum, ν, cm^{-1}: 3201 (NH), 1525 (C=C), 1050 (C=S). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.94 s (12H, CH_3), 2.19 s and 3.18 s (4H each, 4-H, 6-H), 3.82 br.s (4H, NCH_2), 6.29 s (2H, 2-H), 7.84 br.s (2H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 27.82 (CH_3), 33.25 (C^5), 41.69 (C^4, C^6), 42.91 (NCH_2), 58.00 (C^4, C^6), 110.81 (C^2), 161.54 (C^1, C^3), 217.67 (C=S). Found, %: C 63.50; H 8.37; N 8.09; S 18.84. $C_{18}H_{18}N_2S_2$. Calculated, %: C 64.29; H 8.33; N 8.33; S 19.05.

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