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Synthesis and Stereochemistry of 1*H*,5*H*-Naphtho[1,8-*ef*][1,3]dithiocine 2-Oxides

P. A. Kikilo, B. I. Khairutdinov, Yu. G. Shtyrlin, V. V. Klochkov, and E. N. Klimovitskii

Butlerov Chemical Institute, Kazan State University, P.O. Box 115, Kazan, 420111 Tatarstan, Russia
e-mail: Evgenii.Klimovitskii@ksu.ru

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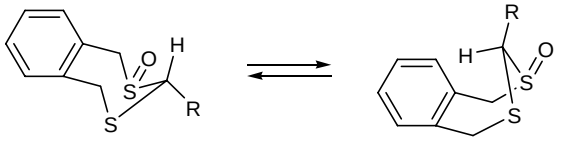
Abstract—3-Substituted 1*H*,5*H*-naphtho[1,8-*ef*][1,3]dithiocines (R = H, Me, Ph, *t*-Bu) were oxidized with *m*-chloroperoxybenzoic acid to the corresponding 2-oxides having *trans* configuration (R ≠ H). According to the ^{1}H and ^{13}C NMR data (including NOESY experiments), the disubstituted compounds at room temperature exist in a *boat* conformation with equatorial orientation of the substituent on C^3 and oxygen atom on S^2. The compound with no substituent on C^3 gives rise to a mixture of *boat* conformers with axial and equatorial sulfoxide oxygen atoms at a ratio of 83:17.

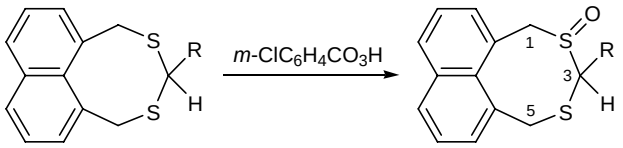
We previously showed that seven-membered cyclic dithio acetals with a planar fragment, 2-substituted 1,3-dithia-5,6-benzocycloheptenes **I**, are oxidized with *m*-chloroperoxybenzoic acid to the corresponding monosulfoxides **II** with high stereoselectivity [1, 2]. According to the data of dynamic ^{1}H and ^{13}C NMR spectroscopy, sulfoxides **II** exist as equilibrium mixtures of *chair* (C) and *boat* (B) conformers with equatorial orientations of the substituents in the seven-membered ring. Axial orientation of the R substituent (R = alkyl, phenyl) is unfavorable for steric reasons.



Chair **II** *Boat*

In continuation of these studies, we examined the stereochemistry of eight-membered cyclic monosulfoxides **IV** with a fused planar naphthalene fragment. Initial dithio acetals **IIIa**–**IIId** were synthesized by us for the first time by condensation of 1,8-bis(sulfanylmethyl)naphthalene with carbonyl compounds [3]. Compounds **IIIa**–**IIIc** were later reported in [4]. Like seven-membered analogs **I**, compounds **III** were oxidized with *m*-chloroperoxybenzoic acid (Scheme 1); the oxidation occurred at an appreciably lower rate. The products, compounds **IVa**–**IVd**, were purified by column chromatography; compounds **IIIb**–**IIId** (R ≠ H) were isolated as a single isomer. Their steric structure was elucidated by ^{1}H and ^{13}C NMR spectroscopy.

Scheme 1.



IIIa–**IIId** **IVa**–**IVd**

R = H (**a**), Ph (**b**), Me (**c**), *t*-Bu (**d**).

Compounds **IIIb**–**IIId** having a substituent on C^3 can be regarded as conformationally homogeneous: their ^{1}H NMR spectra did not change upon variation of the temperature from 20 to –60°C. By contrast, the ^{1}H (see figure) and ^{13}C NMR spectra of compound **IVa** even at room temperature showed a superposition of signals from two forms at a ratio of 83:17 (in $CDCl_3$). Raising the temperature to 140°C (DMSO-d_6) leads to a spectral pattern corresponding to fast exchange (on the NMR time scale).

^{13}C NMR spectroscopy turned out to be very informative from the viewpoint of revealing conformational composition of nonrigid seven-membered heterocycles **I** and **II** [1, 2, 5, 6] which exist in solution as equilibrium mixtures of *chair* and *boat* conformers. Their spectra are characterized by relatively upfield positions of signals from both benzylic and dithioacetal carbon atoms in the *boat* conformer. Comparison of the chemical shifts of C^1 (C^5) (δ_C 37.51–38.94 ppm [3]) in compounds **IIIa**–**IIId** (which adopt a *boat* conformation in CS_2 and CCl_4 at room tempera-

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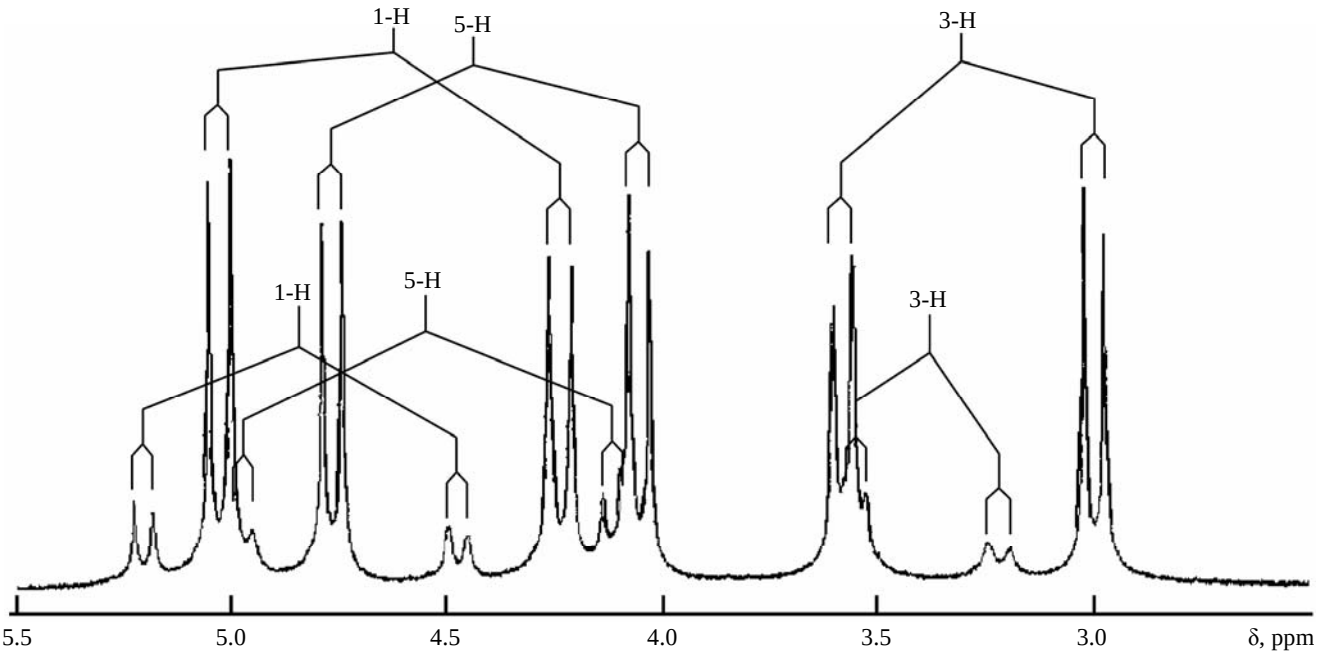
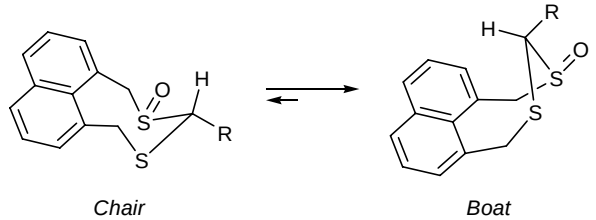


^{1}H NMR spectrum of 1*H*,5*H*-naphtho[1,8-*ef*][1,3]dithiocine 2-oxide (**IVa**) (20°C, $CDCl_3$). Major signals belong to the *boat-eq* conformer, and minor, to the *boat-ax* conformer.

ture) with those of C^5 in heterocycles **IVb**–**IVd** and in the predominant conformer of **IVa** (δ_C 36.72–38.18 ppm) indicates that monosulfoxides **IV** occur in a *boat* conformation (Scheme 2). Taking into account β-effect of the sulfinyl oxygen atom [1, 2, 5], the chemical shifts of C^1 in these compounds (δ_C 55.08–56.40 ppm) suggest that 3-substituted compounds **IVb**–**IVd** are *trans* isomers with diequatorial orientation of the substituents. A useful information may be obtained from the substituent α-effects which are well consistent with those typical of *boat* conformers of seven-membered monosulfoxides **II** [1].

The ^{1}H NMR spectral parameters are given in Experimental. The differences Δδ in the chemical shifts of the benzylic protons on C^1 and C^5 in the spectra of diastereoisomers **IVb** and **IVc**, on the one hand, and predominant conformer of **IVa**, on the other, as well as the corresponding geminal coupling constants $^2J_{HH}$, were similar. These data indicate similarity in the stereochemical structure of these compounds.

Scheme 2.



The most complex problem was to determine the structure of the minor conformer of **IVa**. Here, β-effect of the sulfoxide oxygen atom in the *chair* conformer cannot be taken into consideration, for that conformer was not detected for compound **IIIa** [3]. Repeated examination of the structure of **IIIa** by dynamic ^{1}H NMR spectroscopy has confirmed the conclusions drawn previously. As in the spectra of **IIb** and **IIc**, the C^1, C^3, and C^5 signals of the major conformer are located in a stronger field. However, we cannot assign with certainty *chair* structure to the minor conformer of **IVa** since the chemical shifts of the corresponding carbon atoms in the spectrum of compound **IIa** (*boat* conformer) with axial and equatorial orientation of the oxygen atom are different, and their signals appear in a relatively stronger field (as compared to the *chair* conformer) [5]. According to the PM3 calculations, the heats of formation of the *boat* and *chair* conformers with equatorial and axial orientation of the sulfinyl oxygen atom are as follows, kJ/mol: 27.17 (B-*eq*), 29.16 (B-*ax*), 28.80 (C-*eq*), and 32.36 (C-*ax*). These data did not allow us to distinguish between C-*eq* and B-*ax*, but C-*ax* conformer can be excluded.

In order to determine the structure of the minor conformer more rigorously, we recorded the NOESY spectrum of **IVa** at –60°C in $CDCl_3$. These conditions ensured slow exchange on the NMR time scale, and we observed cross peaks from spatially close nuclei. Analysis of the NOESY spectrum allowed us to assign

equatorial orientation to the 1-H and 5-H protons which showed NOEs with the nearest aromatic protons. In fact, in keeping with the X-ray diffraction data for dithioacetal **IIId** [7], the equatorial C–H bonds at the benzylic carbon atoms form an angle of 9° with the benzene ring plane, while the corresponding angle for the axial C–H bonds is 140°. Insofar as 3-H and 1-H, as well as 3-H and 5-H, in both minor and major conformers give no cross peak, *chair* conformation may be ruled out. Otherwise, strong cross peaks should be observed for *syn*-axial protons in the *chair* conformer.

One more spectral criterion which may be used to distinguish *chair* and *boat* conformers of seven-membered compounds **I** and **II** and eight-membered analogs **III** is a relatively upfield position of signals from the axial dithioacetal protons in the *boat* conformer due to appreciable shielding effect of the aromatic rings [1, 3, 5, 7]. The Δδ value for compounds **III** is 0.85±0.1 ppm [7]. In the ^{1}H NMR spectrum of **IVa**, the parameters of both *AB* quartets (δ 3.00, 3.59 and 3.22, 3.56 pm) are very similar. An analogous weak stereochemical dependence of the chemical shifts of the methylene protons in the SCH_2SO fragment was observed previously for the *chair*-like conformers of 1,3-dithiane 1-oxide with axial and equatorial orientation of the sulfoxide group [8–11]. Thus we can conclude that the minor conformer of **IVa** has a *boat* structure with axial orientation of the sulfoxide oxygen atom.

It should be noted that the oxidation of dithioacetals **Ib**–**Id** and **IIIb**–**IIId** to the corresponding sulfoxides **IIb**–**IId** and **IVb**–**IVd** is characterized by high stereoselectivity with respect to equatorial lone electron pairs with formation of *trans* isomers. In both cases, introduction of a sulfinyl moiety leads to displacement of the conformational equilibrium *chair–boat* toward the latter.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded at 300 and 75.43 MHz, respectively, on a Varian Unity-300 spectrometer equipped with a B-VT-1000 temperature control unit. The chemical shifts were measured relative to HMDS. While performing two-dimensional NMR experiments (NOESY), the pulse delay was set at a value exceeding by a factor of 3 the average longitudinal relaxation period (T_1). The spectra were recorded using the phase-sensitive technique for 1024 points along the F2 coordinate and 256 points along the F1 coordinate with exponential filtration along both coordinates. The time shift parameter τ_m was set at 0.2, 0.4, 0.6, and 0.8 s.

1*H*,5*H*-Naphtho[1,8-*ef*][1,3]dithiocine 2-oxide (IVa). A solution of 1 g of 1*H*,5*H*-naphtho[1,8-*ef*][1,3]-dithiocine (**IIIa**) in 20 ml of methylene chloride was cooled, and a solution of 0.82 g of *m*-chloroperoxybenzoic acid in 15 ml of methylene chloride was added over a period of 0.5 h under stirring. The mixture was stirred for 6 h at room temperature, washed with a 10% aqueous solution of sodium hydroxide (3× 50 ml) and water, and dried over $MgSO_4$. The product was isolated by column chromatography on silica gel (Chemapol L, 100/160 μm) using $CDCl_3$–ethyl acetate (6:1) as eluent. Yield 0.43 g (40%), mp 183–185°C. ^{1}H NMR spectrum ($CDCl_3$, 20°C), δ, ppm: *boat-eq*: 4.24 and 5.03 (2H, 1-H, *AB* quartet, J = –15.1 Hz), 3.00 and 3.59 (2H, 3-H, *AB* quartet, J = –14.0 Hz), 4.06 and 4.77 (2H, 5-H, *AB* quartet, J = –13.9 Hz); *boat-ax*: 4.48 and 5.21 (2H, 1-H, *AB* quartet, J = –13.4 Hz), 3.22 and 3.56 (2H, 3-H, *AB* quartet, J = –14.4 Hz), 4.13 and 4.97 (2H, 5-H, *AB* quartet, J = –14.3 Hz); 7.35–7.60 m (6H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$, 20°C), δ_C, ppm: *boat-eq*: 55.87 (C^1), 43.81 (C^3), 36.72 (C^5); *boat-ax*: 58.34 (C^1), 48.36 (C^3), 39.13 (C^5). Found, %: C 62.20; H 4.80. $C_{13}H_{12}OS_2$. Calculated, %: C 62.87; H 4.87.

3-Phenyl-1*H*,5*H*-naphtho[1,8-*ef*][1,3]dithiocine 2-oxide (IVb) was synthesized in a similar way from 1.20 g of compound **IIIb** and 0.74 g of *m*-chloroperoxybenzoic acid. Yield 0.48 g (38%), mp 217°C. ^{1}H NMR spectrum ($CDCl_3$, 20°C), δ, ppm: 4.26 and 5.32 (2H, 1-H, *AB* quartet, J = –15.4 Hz), 3.90 s (3-H), 4.05 and 4.84 (2H, 5-H, *AB* quartet, J = –13.8 Hz), 7.04–7.88 m (6H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$, 20°C), δ_C, ppm: 55.24 (C^1), 61.46 (C^3), 38.18 (C^5). Found, %: C 70.05; H 5.07. $C_{19}H_{16}OS_2$. Calculated, %: C 70.34; H 4.97.

3-Methyl-1*H*,5*H*-naphtho[1,8-*ef*][1,3]dithiocine 2-oxide (IVc) was synthesized in a similar way from 1.45 g of compound **IIIc** and 1.12 g of *m*-chloroperoxybenzoic acid. Yield 0.68 g (44%), mp 193–195°C. ^{1}H NMR spectrum ($CDCl_3$, 20°C), δ, ppm: 1.43 d (CH_3, J = 7.2 Hz) 4.20 and 5.17 (2H, 1-H, *AB* quartet, J = –14.5 Hz), 3.03 q (3-H, J = 7.2 Hz), 4.02 and 4.76 (2H, 5-H, *AB* quartet, J = –12.2 Hz), 7.27–7.91 m (6H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$, 20°C), δ_C, ppm: 14.53 (CH_3), 55.08 (C^1), 51.81 (C^3), 37.58 (C^5). Found, %: C 64.07; H 5.39. $C_{14}H_{14}OS_2$. Calculated, %: C 64.58; H 5.42.

3-*tert*-Butyl-1*H*,5*H*-naphtho[1,8-*ef*][1,3]dithiocine 2-oxide (IVd) was synthesized in a similar way from 1.34 g of compound **IIId** and 0.88 g of *m*-chloroperoxybenzoic acid. Yield 0.45 g (32%), yellowish oily substance. ^{1}H NMR spectrum ($CDCl_3$, –60°C), δ, ppm: 0.93 s (CH_3), 2.67 s (3-H), 3.98 and 5.22 (2H, 1-H, *AB* quartet, J = –14.8 Hz), 4.06 and 4.51 (2H, 5-H, *AB* quartet, J = –13.0 Hz), 7.26–7.81 m (6H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$, 20°C), δ_C, ppm: 29.80 (CH_3), 36.27 (**C**Me_3), 56.40 (C^1), 68.73 (C^3), 37.73 (C^5). Found, %: C 67.72; H 6.39. $C_{17}H_{20}OS_2$. Calculated, %: C 67.06; H 6.62.

REFERENCES

1. Kikilo, P.A., Khairutdinov, B.I., Shaikhutdinov, R.A., Shtyrlin, Yu.G., Klochkov, V.V., and Klimovitskii, E.N., *Russ. J. Gen. Chem*., 2001, vol. 71, p. 960.
2. Klimovitskii, E.N., Kikilo, P.A., Dobrynin, A.B., Kataeva, O.N., Litvinov, I.A., Fedorenko, V.Yu., and Shtyrlin, Yu.G., *J. Mol. Struct*., 2004, vol. 688, p. 191.
3. Klimovitskii, E.N., Sergeeva, G.N., Il'yasov, K.A., Latypov, Sh.K., Klochkov, V.V., Al'myanova, R.Kh., and Arbuzov, B.A., *Zh. Obshch. Khim*., 1987, vol. 57, p. 2207.
4. Kamada, T., Gama, Y., and Wasada, N., *Bull. Chem. Soc. Jpn*., 1989, vol. 62, p. 3024.
5. Klimovitskii, E.N., Shaikhutdinov, R.A., Kikilo, P.A., Shtyrlin, Yu.G., Klochkov, V.V., and Aminova, R.M., *Russ. J. Gen. Chem*., 1998, vol. 68, p. 1785.
6. Klimovitskii, E.N., Strel'nik, D.Yu., Klochkov, V.V., and Latypov, Sh.K., *Zh. Org. Khim*., 1992, vol. 28, p. 1587.
7. Klimovitskii, E.N., Litvinov, I.A., Kataeva, O.N., Strelnik, D.Yu., and Sergeeva, G.N., *J. Mol. Struct*., 1989, vol. 197, p. 1.
8. Van Acker, L. and Anteunis, M., *Tetrahedron Lett*., 1974, p. 225.
9. Khan, S.A., Lambert, J.B., Hernandez, O., and Carey, F.A., *J. Am. Chem. Soc*., 1975, vol. 97, p. 1468.
10. Juaristi, E., Guzman, J., Kane, V.V., and Glass, R.S., *Tetrahedron*, 1984, vol. 40, p. 1477.
11. Klimovitskii, E.N., Shaikhutdinov, R.A., Kikilo, P.A., and Klochkov, V.V., *Russ. J. Gen. Chem*., 1999, vol. 69, p. 5.