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Synthesis and Structure of New Derivatives of Thieno[2,3–*b*]thiocine. Unusual Intramolecular Cycloaddition Product of 2-Homomethallyl-3-thiophenecarbonitrile Oxide

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For the first time 9-methyl-3,3a,4,5,6-hexahydrothieno[2,3-*b*]thiocine[4,5-*c*]isoxazole and 9-methyl-7-hydroxyimino-3,4,6-hexahydro-5-methylenethieno[2,3–*b*]thiocine have been prepared by NaOCl oxidation of 2-ω-alkenylthio-3-thiophenecarbaldoximes. The structure of these products has been confirmed by mass, ^{1}H NMR and ^{13}C NMR spectroscopy, and of the second, also by X-ray analysis.

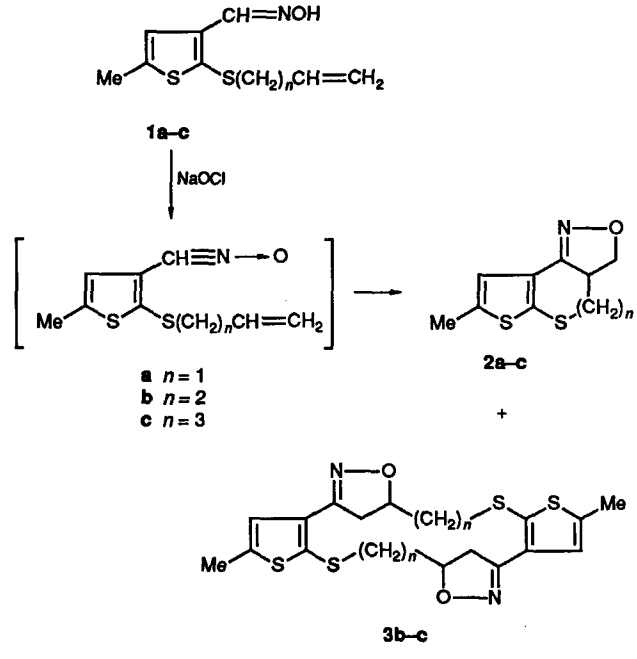
During our investigations into intramolecular cycloaddition (IMCA) we have shown that the only product in the cyclization of oximes such as **1** by oxidation was isoxazoline **2a**.[1]

The oxidation of the longer unsaturated chain oxime ($n=2$) led to the product of intermolecular interaction, bis(isoxazoline) **3b**, as well as **2b**. The quantitative ratio of these products depends on the dilution degree.[2]

It was interesting to study the effect of increase in side-chain length and structure on the reaction process and the distribution of these products.

The aim of the present study was therefore to examine the interaction of NaOCl with oxime **1c** ($n=3$) and its isomer **4**, containing a methyl group linked to a double bond. Compounds **1c** and **4** were obtained from 2-methylthio-5-methyl-3-thiophenecarbaldoxime and the corresponding ω-halogenoalkenes according to the method given in ref. 3.

In the case of **1c** at concentration 0.11 mol dm^{-3} the only product of intermolecular interaction, thiophene **3c**, was separated in 30% yield by typical IMCA conditions. 11% of 9-methyl-3,3a,4,5,6-hexahydrothieno[2,3-*b*]thiocine[4,5-*c*]isoxazole (**2c**, $n=3$) as well as **3c** were isolated in the diluted solution (0.011 mol dm^{-3}). The structure of these compounds was confirmed by mass, ^{1}H and ^{13}C NMR spectroscopy.†



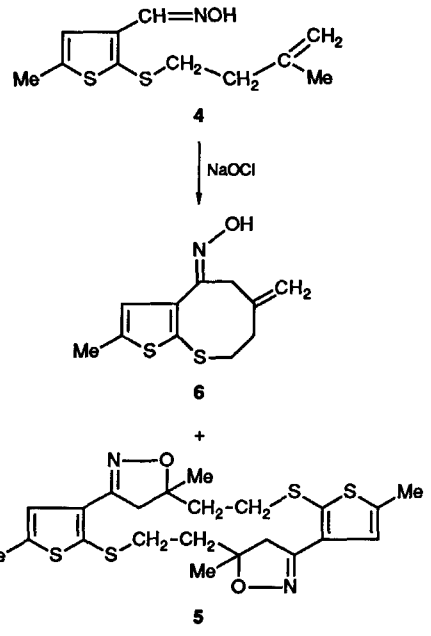
Using homomethallylthioxime **4**, 10% of dimethyl-substituted bis(isoxazoline) **5** was separated together with 15% of a compound identified as 9-methyl-7-hydroxyimino-3,4,6-hexahydro-5-methylenethieno[2,3-*b*]thiocine **6** by IR, ^{1}H NMR and mass spectroscopy.‡ The yield of **6** was 5% and

† *Selected spectroscopic data.* Coupling constant values J are given in Hz. **2c**: ^{1}H NMR ($CDCl_3$) δ 1.70–2.00 (m, 4H, CH_2–CH_2), 2.42 (s, 3H, CH_3–9), 2.52 (dt, 1H, CH–6, J 12.5, 3.5), 2.98 (dtd, 1H, CH′–6, J 12.5, 3.5, 1.25), 4.81–4.96 (dddd, 1H, CH–3a, J 11.0, 9.0, 7.0, 3.5), 4.19 (dd, 1H, CH–3, J 9.0, 3.5), 4.30 (dd, 1H, CH′–3, J 9.0, 9.0), 7.32 (s, 1H, H–10); ^{13}C NMR ($CDCl_3$) δ 15.54 (q, CH_3), 23.75 (t, C–5), 32.19 (t, C–4), 35.73 (t, C–6), 45.03 (d, C–3a), 77.23 (t, C–3), 125.79 (d, C–10), 128.86 (s, C–10a), 130.93 (s, C–7a), 142.87 (s, C–9), 157.17 (s, C–10b).

3c: MS m/z 478 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.63–1.93 (m, 8H, CH_2–1,2,15,16), 2.44 (s, 6H, CH_3–7,21), 2.86–2.98 (m, 4H, SCH_2), 3.30–3.60 (m, 4H, CH_2–14,28), 4.62–4.80 (m, 2H, CH–13,27), 7.02 (s 2H, H–8), 7.05 (s, 1H, H–22).

‡ *Selected spectroscopic data for* **6**: IR ($CHCl_3$) ν/cm^{-1} 3580 (OH), 1640 (C=C); ^{1}H NMR ($CDCl_3$) δ 2.42 (d, 3H, CH_3–9, J 1.25 Hz), 2.48 (m, 2H, CH_2–4), 2.86 (m, 2H, SCH_2), 4.19 (s, 2H, CH_2–6), 4.96 (m, 1H, CH=), 5.01 (m, 1H, CH′=), 7.08 (q, 1H, H–8, J 1.25 Hz), 9.12 (br s, 1H, OH).

of bis(isoxazoline) **5**, 15% in the concentrated solution, and the main part of the reaction mixture comprised unidentified compounds of a polymeric nature.



The appearance of oxime **6** in a typical IMCA experiment was surprising. Previously the formation of oximes by interaction of nitrile oxides with dipolarophiles containing a C=C double bond had been observed only in the intermolecular reaction of trifluoroacetonitrile oxide with conjugated olefins.[4,5] Thus, the molecular structure of compound **6** has been investigated by X-ray analysis as well as by spectroscopic methods.§

The conformation of molecule **6** is presented in Fig. 1. The skeleton of this molecule consists of fused rings of thiophene and thiocine. The eight-membered ring adopts a slightly skew boat (B) conformation.[6] The methylene group is *exo*-oriented with respect to the bicycle. Thiophene and atoms S(2) and C(7) linked to it form a planar fragment.

§ *Crystal data for* **6**: $C_{11}H_{13}NOS_2$, triclinic, space group $P\bar{1}$, $a=13.433(2)$, $b=8.771(1)$, $c=4.920(1)$ Å, $\alpha=89.48(1)$, $\beta=88.26(1)$, $\gamma=97.21(1)°$, $V=574.77$ Å^3, $Z=2$. The intensities of 760 independent reflections were measured with a RED-4 automatic diffractometer (λ CuK$_\alpha$ = 1.542 Å, $\omega-\theta/2\theta$ scan technique, $\theta \leqslant 60°$). Structure **6** was solved by a direct method using the program AREN-90. The coordinates of the heavy atoms were refined by a least-squares method in anisotropic approximation. Final value of $R=0.088$. Detailed results of an X-ray study will be published elsewhere.

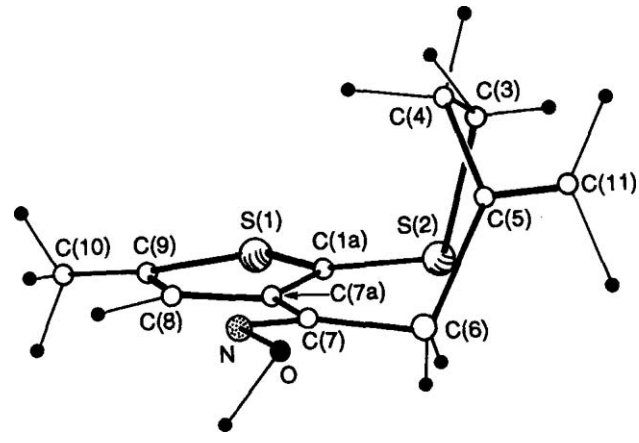


Fig. 1 Molecular structure of **6**

The plane of the hydroxyimine group is twisted out of it by 85 °. The H atom of the hydroxylic group takes part in the intermolecular hydrogen bond N···O (2.80 Å). All bond lengths and valency angles in thiophene and thiocine cycles are very close to standard values.[7]

We assume that the formation of oxime **6** is the result of electrophilic interaction of the nitrile oxide group either with the allylanionic fragment that appears in the reaction, or with a terminal methylene group.

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