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# An unexpected skeletal transformation of 1,4-dihydroxythioxanthen-9-one on treatment with iodic acid: the first construction of the 2-(5-oxofuran-2-ylidene)-1-benzothienyl-3-one core

Vladimir A. Loskutov *, Yurii V. Gatilov, Vitalij D. Shteingarts *

*N. N. Vorozhtsov Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, Lavrentiev Ave. 9, Novosibirsk 630090, Russia*

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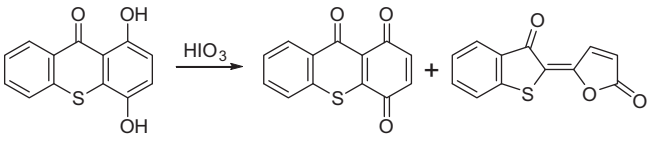
ABSTRACT

Treatment of 1,4-dihydroxythioxanthen-9-one with iodic acid gives, depending on the reaction conditions, predominantly either thioxanthen-1,4,9-trione or, unexpectedly, 2-(5-oxofuran-2(5*H*)-yliden)-1-benzothienyl-3(2*H*)-one. The latter is obtained in 60% yield.



Iodic acid ($HIO_3$) is used as a reagent in various organic reactions[1] including mild oxidation and aromatic iodination, in the latter case acting as an iodine-centered electrophile—an equivalent of the synthon $IO_2^+$.[2] Earlier 1,4-dihydroxythioxanthen-9-one (**1**) was shown to be oxidized quantitatively by potassium bromate[3] or cerium ammonium nitrate[4] into thioxanthen-1,4,9-trione (**2**). Attempting to perform this reaction using $HIO_3$ as the oxidant, we found that, in addition to **2**, the red-colored substance **3** was formed which was easily separated by TLC on silica gel (Scheme 1). The IR spectrum of **3** demonstrated vibration bands due to conjugated C=C (1611 $cm^{-1}$) and C=O (1678 and 1778 $cm^{-1}$) bonds, the latter indicating the presence of an ester group. The $^1H$ NMR spectrum of **3** contained six signals, the most characteristic being two doublets at 6.44 and 8.57 ppm, mutually coupling with $J(HH) = 5.4$ Hz. The $^{13}C$ NMR spectrum indicated that compound **3** possessed one carbon atom less than the starting material and two of the 12 carbons present, judging from their chemical shifts (167.3 and 188.0 ppm), were carbonyl carbons. Accordingly, the mass spectrum of **3** displayed a molecular ion with $m/z = 230$, being 14 amu less compared to the starting compound. Since the structure of **3** could not be proved on the basis of the above analytical and spectral data, an X-ray study[5] was carried out. This revealed that **3** was the previously unknown 2-(5-oxofuran-2(5*H*)-yliden)-1-benzothienyl-3(2*H*)-one (**3**) (Fig. 1) which was present as the *Z*-isomer. This isomer was calculated (DFT/PBE/3z) to be 6.1 kcal/mol more stable compared to the *E*-isomer.[6,7]




**Scheme 1.** Oxydation of 1,4-dihydroxythioxanthen-9-one (**1**) by $HIO_3$.

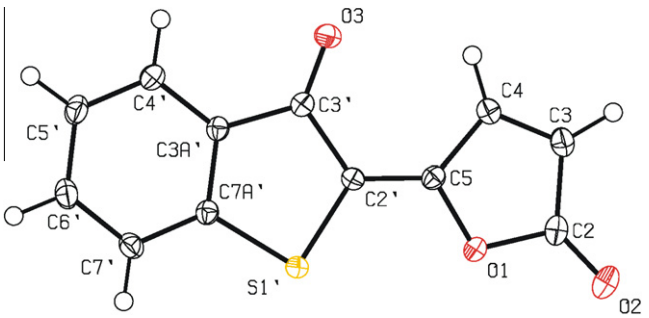



**Figure 1.** ORTEP view of compound **3** (*Z*-isomer).

* Corresponding authors. Fax: +7 383 330 97 52.
*E-mail addresses:* val@nioch.nsc.ru (V.A. Loskutov), shtein@nioch.nsc.ru, vshteingarts@mail.ru (V.D. Shteingarts).

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**Table 1**
Optimization of the transformation of **1** into **3**[a]

| Entry | $HIO_3$ (equiv) | Temp. (°C) | Time | **1**:**2**:**3**[b] |
|---|---|---|---|---|
| 1 | 1.2 | 20 | 50 min | 1:15:30 |
| 2[c] | 1.2 | 20 | 50 min | 1:50:97 |
| 3 | 1.2 | 0 | 4 h | 1:11:33 |
| 4 | 3.4 | 0 | 40 min | 1:4.5:11 |
| 5[d] | 3.5 | 0 | 50 min | 1:50:3 |

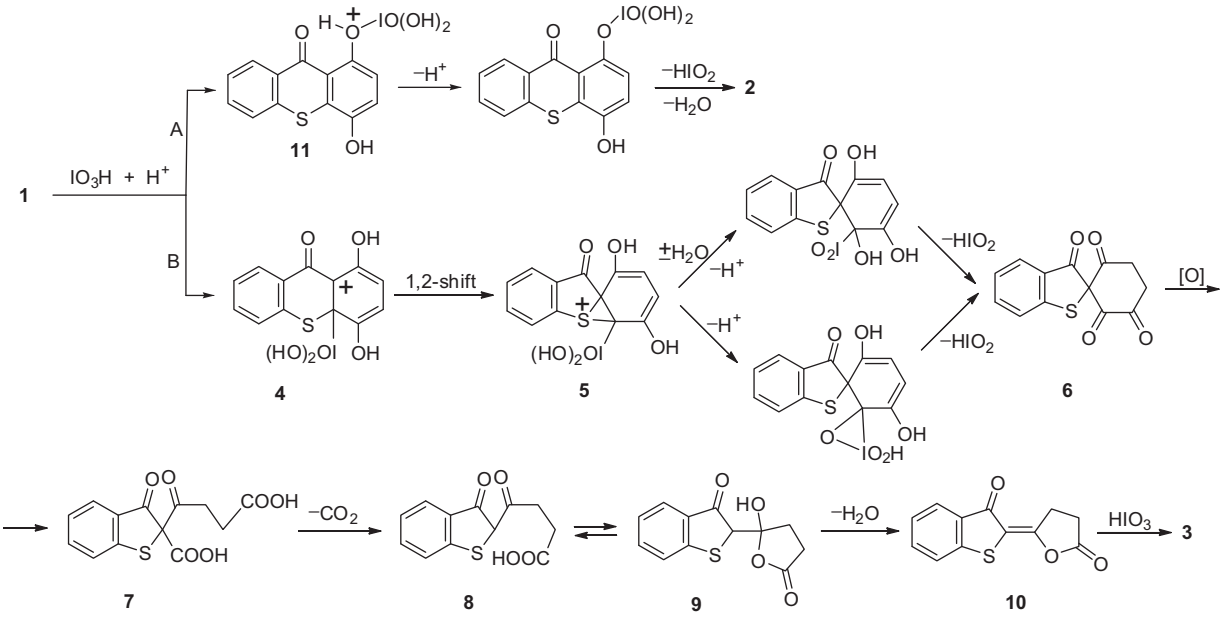
[a] In all experiments 0.12 mmol of **1** and 6 mL of the acetone–water (5:1) were used.
[b] Ratio determined by $^1$H NMR spectroscopy in DMSO-$d_6$.
[c] Under argon.
[d] Using **2** as the starting material.

The molecule **3** is planar within ±0.046 Å. The furanone ring bond lengths are similar to those of 3-(5-oxofuran-2(5*H*)-ylidene)-1-benzofuran-2(3*H*)-one[8] and the thiophene geometry is identical to that of 4,4′,5,5′,7,7′-hexachlorothioindigo.[9] Crystals of **3** are packed into stacks due to π···π interactions between the benzene-furan and thiophene-thiophene moieties; the interplanar distance is 3.36 Å and the intercentroid distances are 3.558 and 3.659 Å. Weak C–H···O hydrogen bonds, C4–H···O3 (intramolecular, C–H 0.97(2), H···O 2.47 Å, C–H···O 114(2)°) and C7′–H···O3 (interstack, C–H 0.93(2), H···O 2.38(2) Å, C–H···O 142(2)°) were observed. The short interstack S1′···S1′ contact of 3.4857(5) Å is noteworthy.

Seeking optimized conditions to transform **1** into **3**, it was found that furanone **3** was not formed when using wet $HIO_3$ at room temperature without solvent or in water, with only oxidation of **1** to **2** occurring. The reaction in aqueous organic solvents (DMSO, DMF, acetone, ethanol, acetonitrile, THF, acetic acid) led to mixtures of quinone **2** and furanone **3**, the latter being formed predominately in a 5:1 acetone–water mixture (see Table 1). Thus, using this system at room temperature for 40–50 min and employing a nearly equimolar reagent ratio, compound **3** was formed in twice the amount compared to **2** (entry 1). Carrying out the reaction under argon somewhat accelerated the transformation but did not change the ratio of **2** to **3** (entry 2). This ratio changed in favor of **3** on lowering the temperature to 0 °C (entry 3) but a three-fold increase in $HIO_3$ quantity did not affect the result appreciably (entry 4). It should be noted that reaction of **2** with $HIO_3$ gave only traces of **3**, probably, owing to partial reduction of **2** into **1** and subsequent transformation of the latter into **3** (entry 5), thus testifying that **2** was not an intermediate en route from **1** to **3**. The optimized reaction conditions afforded **3** in 60% yield.[10]

Thus, the conversions of **1** into **2** and **3** are, apparently, parallel competing reactions both involving either $HIO_3$ (activated additionally by protonation) per se, or different species of similar type, produced by $HIO_3$ and more active than it, operating as iodine-centered electrophiles. It can be assumed that the first of these reactions proceeds via a mechanism similar to that suggested for the oxidation of 1-naphthol by benzeneseleninic anhydride,[11] or pyrocatechol by a succinimidodimethylsulfonium cation,[12] and also phenols,[13] and saturated alcohols and ketones by *ortho*-iodoxybenzoic acid,[14] involving substitution of the hydroxy hydrogen with a fragment which behaves as an electron-withdrawing leaving group in the following stage (route A, Scheme 2).

Transformation of thioxanthenone **1** into furanone **3** involves an unexpected and complex rearrangement of the molecular skeleton. Comparing the structures of **1** and **3**, it can be seen that the reorganization consists of three principal changes of the structure: (a) contraction of the heterocyclic fragment; (b) removal of one carbon atom; and (c) formation of the furan ring, the changes (b) and (c) both involving the hydroquinone fragment. It seems reasonable that change (a) is the result of a cation rearrangement with contraction of the heterocycle via a 1,2-shift of either a phenylthiol or benzoyl migrant group. For this to happen, protonation or addition of an electrophile *ipso* to one of the potential migrants should occur. To check whether $HIO_3$ operates as a protic acid in the first stage, trifluoroacetic acid was used instead, being somewhat stronger than $HIO_3$ ($pK_a$ 0.23 and 0.77, respectively[15]). Compound **1** remained intact thus indicating that $HIO_3$ (or any other active equivalent of $IO_2^+$ generated by this acid) acts as an iodine-centered electrophile. More probable, as indicated in Scheme 2 (route B), is the addition of $HIO_3$ *ipso* to the sulfur atom followed by a 1,2-shift of the phenylthiol fragment to give episulfonium cation **5** via the intermediacy of arenium cation **4**. The alternative migration of the benzoyl group cannot be excluded but seems less likely due to the following reasons. Addition of an electrophile *ipso* to the phenylthiol group would appear not to be significantly more difficult, albeit easier than *ipso* to the benzoyl group. In this respect,




**Scheme 2.** Suggested mechanism of the transformation of thioxanthenone **1** into quinone **2** and furanone **3**.

isomerization of arenesulfonic acids generally requires less acidic conditions than for aromatic ketones,[16] being even more likely for an arylthiol group. The phenylthiol group is a more efficient 1,2-migrant compared to the methyl group.[17,18] At the same time, and judging from a literature set of data,[19] the migratory ability of acyl groups can be estimated as being comparable to those of primary alkyl groups but less than $PhSO_n$ ($n$ = 1, 2)[20] and phenylthiol groups.

The possibility of the subsequent stages depicted in Scheme 2 relies on literature analogies. The product of the 1,2-shift, cation **5**, is transformed into compound **6** by either of the routes shown in Scheme 2. Oxidation of the 1,2-diketone gives β,β′-diketocarboxylic acid **7**, which decarboxylates readily to produce diketo acid **8**. As a result of ring-chain tautomerism, lactone-aldol **9** forms and undergoes dehydration into diketone **10**, which being a dihydro precursor of the final product, gives **3** upon further reaction with $HIO_3$. The latter is known as an efficient reagent for the dehydrogenation of ketones.[21] Overall, in conformity with Scheme 2, the conversion of **1** into **3** consumes not less than 2 mol of $HIO_3$, while in the actual experiment 1.2 mol is used. However, one should bear in mind that a significant amount of $HIO_3$ is recycled via redox dismutation of $HIO_2$ formed during the course of reaction.[22]

As to the reasons why the competing formation of **2** and **3** changes in favor of the latter in going from water to aqueous organic media, two assumptions can be put forward. First, interaction of $HIO_3$ with an organic solvent (S) can produce the adduct $(HO)_2OI–S^+$[21] which is probably a softer electrophile compared with $HIO_3$ and, accordingly, may prefer to attack the carbon atom (route B) as a softer nucleophilic center compared with the hydroxy oxygen atom (route A). Secondly, the decreased polarity of the reaction medium favors route B, because, in intermediate **4** the positive charge is more or less dispersed, while in cation **11** it is virtually concentrated on the oxygen atom.

In conclusion, treatment of 1,4-dihydroxythioxanthen-9-one with $HIO_3$ leads to rearrangement of the thioxanthen-9-one skeleton to give the benzothiophenylidenfuranone and 2-(5-oxofuran-2(5*H*)-yliden)-1-benzothienyl-3(2*H*)-one (**3**) for the first time. Compound **3** represents a basic molecular scaffold which can undergo further structural modifications and investigation of the properties of its functional derivatives.

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5. Crystallographic data for **3**: $C_{12}H_6O_3S$, $M$ = 230.23, triclinic, space group $P\bar{1}$, $a$ = 6.9531(3), $b$ = 7.1172(3), $c$ = 11.3211(4) Å, $\alpha$ = 79.378(2), $\beta$ = 78.671(2), $\gamma$ = 62.329(2), $V$ = 483.70(3) Å$^3$, $Z$ = 2, $D_c$ = 1.581 g cm$^{-3}$, $\mu$(Mo Kα) = 0.319 cm$^{-1}$, 9776 reflections measured, 2809 unique ($R_{int}$ = 0.0352), final $R_1$ = 0.0317 (2463 $I \geqslant 2\sigma(I)$), $wR_2$ = 0.0880 and $S$ = 1.081 (all data). CCDC 777291. Crystallographic data can be obtained free of charge via www.ccdc.cam.uk/conts/retrieving.html.
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10. *Synthesis of furanone* **3**: To a stirred mixture of **1** (0.093 g, 0.38 mmol), $HIO_3$ (0.079 g, 0.45 mmol) and acetone (15 ml), at 0 °C, $H_2O$ (3 ml) was added dropwise and stirring was continued for 4 h. The resulting red precipitate was filtered and washed with $H_2O$ to afford chromatographically pure **3** (0.034 g). The filtrate was extracted with $CH_2Cl_2$ (3 × 10 mL), dried over $Na_2SO_4$, and the solvent evaporated to give a residue which was purified by column chromatography (silica gel, $CH_2Cl_2$) to give additional product **3** (0.019 g) (mobile orange zone). The overall product yield was 0.053 g (60%). Mp: 201–204 °C ($CH_2Cl_2$–$Et_2O$). IR $\nu$ (KBr): 1778 (C=O ester group), 1678 (C=O thioxanthene moiety), 1611 cm$^{-1}$ (C=C). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 6.44 (d, *J* 5.4 Hz, 1*H*), 7.31 (t, *J* 8.0 Hz, 1*H*), 7.46 (d, *J* 8.0 Hz, 1*H*), 7.60 (t, *J* 8.0 Hz, 1*H*), 7.83 (d, *J* 8.0 Hz, 1*H*), 8.57 (d, *J* 5.4 Hz, 1*H*). $^{13}$C NMR (100 MHz, $CDCl_3$–DMSO-$d_6$): $\delta$ 116.18, 123.45, 124.91, 126.60, 126.64, 131.09, 136.73, 140.73, 143.64, 152.91, 167.27, 188.00. HRMS (EI). Calcd for $C_{12}H_6O_3S$: 230.00376. Found: 229.99878. Anal. found C, 62.82; H, 2.64; S, 14.02; $C_{12}H_6O_3S$ requires C, 62.61; H, 2.61; S, 13.91.
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