Thermolysis of 6-Hydroxy-3,4,5-tris-methoxycarbonyl-2*H*-benzo[*b*]thiocin

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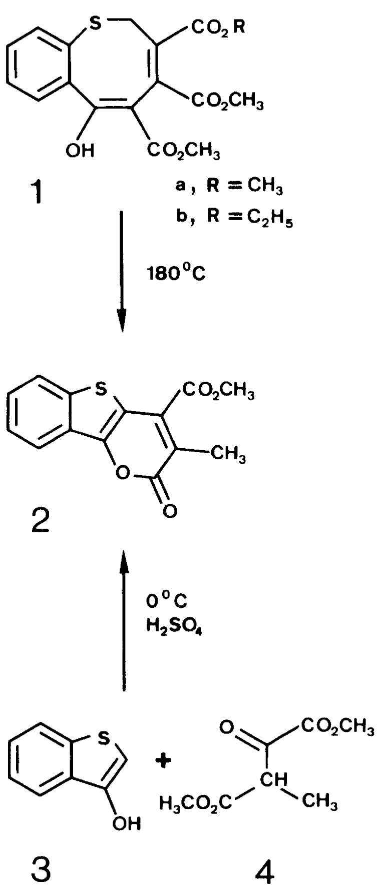
In a previous publication,[1] the syntheses of some eight-membered ring compounds belonging to the benzo[*b*]thiocin system have been described. One of these compounds, 6-hydroxy-3,4,5-tris-methoxycarbonyl-2*H*-benzo[*b*]thiocin, *1a*, melts at 146 – 150 °C.[1] Upon heating to 180 °C, it decomposes, but from the cooled melt, a crystalline, strongly fluorescent compound can be isolated. We were intrigued by this decomposition, particularly since a similarly fluorescent compound had been obtained as a by-product in the reaction between 3-hydroxy-2-methoxycarbonylbenzo[*b*]thiophene and dimethyl acetylenedicarboxylate, and characterized as an α-pyrone, 3,4-bis-methoxycarbonyl-2-oxo-2*H*-[1]benzothieno[3,2-*b*]pyran.[1] We suspected that the present thermolysis product might have a similar structure and decided to identify it.

The present paper will describe the structure determination of the fluorescent compound by spectral methods, verification by independent synthesis and a suggestion of its formation through thermolysis. As an aid in this work, the ethyl dimethyl ester *1b* (Scheme 1) was also synthesized and studied. Heating of *1b* gave the same product as was obtained from *1a*.

The pyrolysis product from *1a* or *1b* was purified through medium-pressure liquid chromatography. Its empirical formula was determined by high-resolution MS to be $C_{14}H_{10}SO_4$, indicating the loss of $C_3H_6O_3$ from *1a*. Since the same compound, *2*, is also obtained from *1b*, it appears that the alkoxycarbonyl or possibly the alkyl group in the 3 position of *1* is split off. Instead of trying to determine the structure of *2* from the MS fragmentation pattern, we next turned to the 270 MHz ^{1}H NMR spectrum. Peaks corresponding to four aromatic hydrogen atoms, one methoxy group (δ 4.05) and one methyl group (δ 2.50) were present. All hydrogens are thus accounted for. The shift of 2.50 is too much upfield for an $-OCH_3$, so we must consider methyl bound to sulfur or an sp^2-hybridized carbon.[2]

Two compounds that fit the above data are 4-methoxycarbonyl-3-methyl-2-oxo-2*H*-[1]benzothieno[3,2-*b*]pyran, *2*, or the 3-methoxycarbonyl-4-methyl isomer. At this point, rather than speculate about which of these is the more probable one from a mechanistic point of view, we decided to make independent syntheses. Luckily, our first choice, the 4-methoxycarbonyl isomer, obtained as shown in Scheme 1, turned out to be identical to the thermolysis product from *1*.



Scheme 1. Formation of 4-methoxycarbonyl-3-methyl-2-oxo-2*H*-[1]benzothieno[3,2-*b*]pyran *via* thermolysis and condensation, respectively.

The analogue of *2* without the 3-methyl group has been synthesized *via* a sulfuric acid-catalyzed reaction between 3-hydroxybenzo[*b*]thiophene and hydroxymaleic acid.[3] We decided to apply this condensation to 3-methyl-2-hydroxymaleic acid, but instead of the free acid, its dimethyl ester was employed. The diester was prepared from dimethyl oxalate and methyl propionate following a method described for the corresponding ethyl esters.[4] The von Pechmann reaction was carried out in conc.

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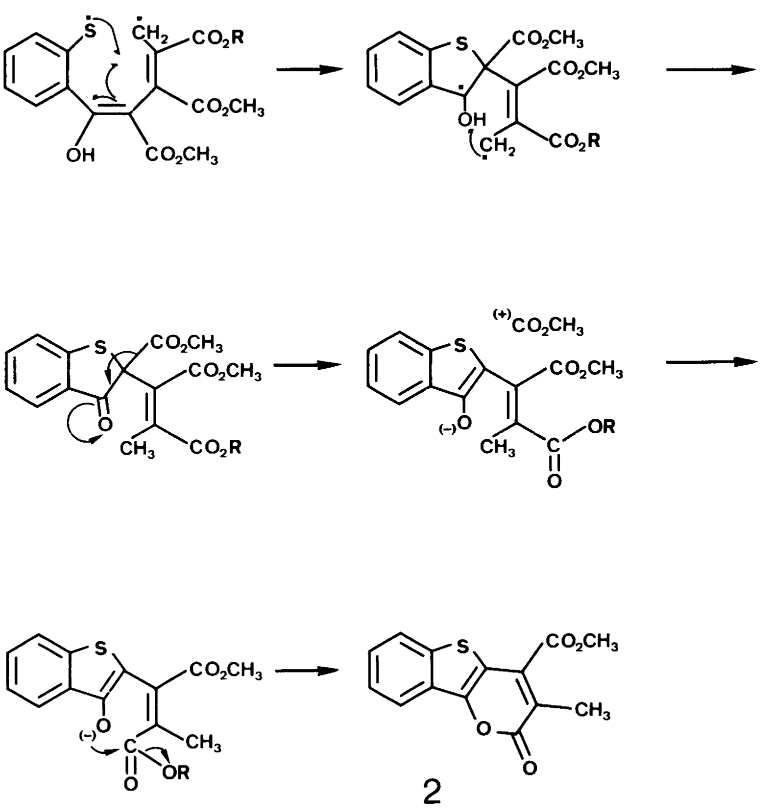

Scheme 2. Proposed mechanism for the thermolysis of 6-hydroxy-3,4,5-tris-methoxycarbonyl-2*H*-benzo[*b*]thiocin.

sulfuric acid at 0 °C and gave 13% yield of a compound that was identical to *2* (270 MHz ^{1}H NMR, m.p., mixed m.p.). The 3-methoxycarbonyl-4-methyl isomer of *2* was not synthesized, since the authenticity of *2* was considered to be established beyond doubt.

Possible mechanism of thermolysis. The driving force for the reaction is no doubt the formation of the non-strained benzothieno[3,2-*b*]pyran system from the eight-membered compound *1*. The origin of the 3-methyl group in *2* is probably neither the 4- nor the 5-methoxycarbonyl methyls of *1*, but rather the ring methylene in 2 position. It was brought to our attention by Professor D. Neckers that certain photochemical rearrangements of [2+2] adducts involve radicals.[5] We argued that initial homolytic fragmentation of the sulfur–methylene bond in *1* would be a comparatively facile process, since a phenylmercapto and an allyl radical, both resonance-stabilized, are formed. The process is outlined in Scheme 2. Attack of the sulfur radical on the 5-carbon atom gives the thiophene ring. Hydrogen atom transfer from the hydroxy group to the allyl radical gives the 3-methyl group of *2*. For the later steps of Scheme 2, an ionic mechanism is suggested, but the details are open to discussion.

Experimental. *6-Hydroxy-3,4,5-tri-methoxycarbonyl-2*H*-benzo*[b]*thiocin* (*1a*) and 3-hydroxybenzo[*b*]thiophene (*3*) were prepared according to the literature.[1,6] Compound *1b* was prepared in analogy with compound *1a*, starting with diethyl oxalate.[7]

3-Methyl-2-oxo-butane-1,4-dioic acid dimethyl ester (4). To a heterogeneous mixture of 2.3 g finely divided sodium (100 mmol) in 200 ml of benzene was added 11.8 g dimethyl oxalate (100 mmol) and 9.7 g methyl propionate (110 mmol). The mixture was refluxed for 20 h. Benzene was removed under reduced pressure and ether was added to the crystalline mass. Upon stirring, a yellow salt was left as a precipitate. This salt was filtered off and acidified with dilute sulfuric acid and extracted with ether. The ether solution was washed with water and dried over anhydrous magnesium sulfate. The residue was distilled to give a dark-yellow oil (b.p. 115 °C at 1 mmHg). The yield was 9.5 g (55 %). In deuterochloroform the keto – enol ratio is 6.5 : 1. ^{1}H NMR (Keto) (270 MHz, $CDCl_3$) δ 1.41 (3 H, d, J 7 Hz), 3.74 (3 H, s), 3.89 (3 H, s) and 4.12 (1 H, q, J 7 Hz). ^{1}H NMR (Enol) (270 MHz, $CDCl_3$) δ 2.00 (3 H, s), 3.85 (3H, s), 3.87 (3H, s) and 12.35 (1 H, s).

*4-Methoxycarbonyl-3-methyl-2-oxo-2*H-*[1] benzothieno[3,2-*b*]pyran (2). Thermolysis.* Compound *1a*, 1 g, was heated in a tube at 180 – 190 °C for 6 h with stirring. The residue was taken up in dichloromethane and chromatographed on silica gel – dichloromethane with medium-pressure equipment to give 150 mg of compound *2* (18 %). Yellow needles from ether, m.p. 191 – 192 °C. ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.50 (3H, s), 4.05 (3H, s), 7.45 – 7.49 (2H, m), 7.78 – 7.82 (1 H, m) and 7.99 – 8.03 (1 H, m). MS: M^+ 274.0300. Calc. for $C_{14}H_{10}O_4S$, 274.0320. Fragments: *m/e* 274 (100), 247 (5.3), 246 (34.2), 245 (7.8), 231 (19.2), 218 (10.8), 214 (25.6), 187 (39.2), 186 (16.6) and 115 (25.9). Solutions of compound *2* are fluorescent (green), particularly in dilute ethereal solution.

Independent synthesis. To a mixture of 4.2 g of 3-hydroxybenzo[*b*]thiophene (*3*) (28 mmol) and 5.65 g of 3-methyl-2-oxo-butane-1,4-dioic acid dimethyl ester (*4*) (28 mmol) at 0 °C was added 40 ml of conc. sulfuric acid at 0 °C with stirring. The resulting mixture was kept at 0 °C for 1.5 h and poured onto ice-water. After extraction into dichloromethane, the organic phase was washed with water and dried over magnesium sulfate. Evaporation yielded a red oil, which was flash chromatographed on silica gel – dichloromethane to yield 1.0 g of pure compound (*2*) (13 %). All physical data are identical with those of the thermolysis product.

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