

A Synthesis of 2-Hydroxyxanthone

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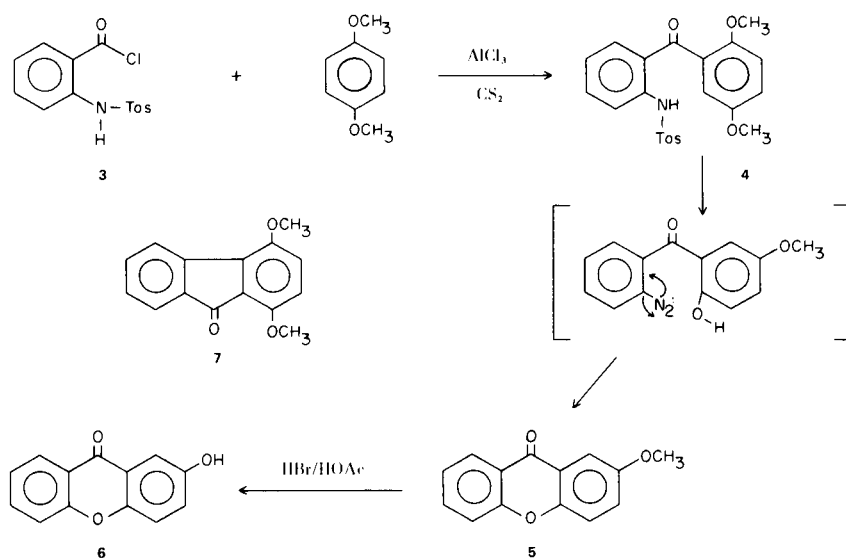
We wish to report a novel synthesis of 2-hydroxyxanthone (1) and its pmr and mass spectral characterization.

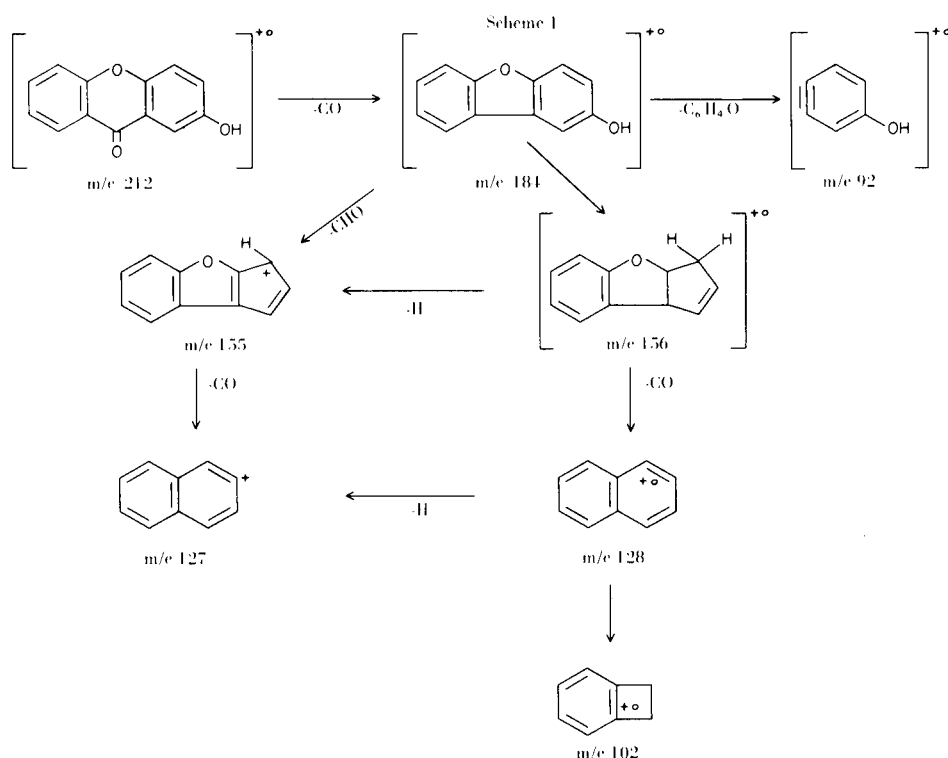
Anthranilic acid (1) when treated with *p*-toluenesulfonyl chloride (4) gave the *N*-tosylanthranilic acid (2). Treatment of 2 with phosphorus pentachloride gave the acid chloride (3) which readily reacted with *p*-dimethoxybenzene under the Friedel-Crafts conditions giving the benzophenone derivative (4) in 60-65% yield. When 4 was treated with 50% sulfuric acid at 45-50°, followed by diazotization with sodium nitrite at 0-5°, 2-methoxyxanthone (5) was formed. Further treatment of 5 with a mixture of hydrobromic acid:acetic acid, for 20 hours under reflux over nitrogen gave the phenol (6).

The melting points of 5 and 6 were quite different from those reported for the expected 1,4-dimethoxy- or 1,4-dihydroxyfluorenones (2,3). However, values given in the literature for 2-methoxy and 2-hydroxyxanthone correspond to those obtained for 5 and 6. To conclusively characterize 6, pmr and mass spectral methods were employed.

The structural elucidation of 6 was rapidly reduced to a decision between isomeric forms of the molecular formula $C_{13}H_8O_3$ by high resolution mass spectrometry which indicated a pure compound of molecular weight 212 corresponding to the unique formula $C_{13}H_8O_3$. These measurements showed, in addition to the molecular ion $[M]^+ C_{13}H_8O_3$, fragment ions at m/e 184 $[M-CO]^+$, 155 $[M-(CO + CHO)]^+$, 128 $[M-3CO]^+$, and 127 $[M-(2CO + CHO)]^+$.

The low resolution mass spectrum of the product is shown in Figure 1. Scheme 1 is suggested as a reasonable fragmentation pathway to explain the origin of those ions prominent in the spectrum. The expulsion of carbon monoxide and CHO from cyclic ketones or from phenolic compounds is well documented (5-8). The mass spectra of fluorenones show peaks at m/e 76 (benzyne) and at m/e 92 (presumably due to the monohydroxy benzyne fragment). A further peak of interest in the spectrum (Figure 1) is that found at m/e 106 (shown to be the doubly-charged molecular ion by the ^{13}C isotope peak appearing at m/e 106.5).





Derivatization of the compound with *bis*-trimethylsilyl acetamide (BSA) yielded a monotrimethylsilyl (TMSi) derivative with a molecular weight of 284 by mass spectroscopy, giving further evidence for **6**.

TABLE I

Pmr Parameters of 2-Hydroxyxanthone

(a)	Relative No. H	Assignment
0.16	1	Active
1.95 (J, 8.0, 1.5) (b)	1	C ₈ H
2.36 (J, 8.5, 7.0, 1.5)	1	C ₆ H
2.60 (J, \approx 2.5)	1	C ₁ H
2.61 (J, \approx 8.5)	1	C ₅ H
2.67 (J, \approx 8.5)	1	C ₄ H
2.72 (J, \approx 8.0, 7.0, 1.0)	1	C ₇ H
2.80 (J, \approx 8.5, 2.5)	1	C ₃ H

(a) Spectrum determined in DMSO (*ca.* 10% w/v; chemical shifts are relative to internal TMS). (b) Coupling constants in Hertz.

Comparison of Figures 1 and 2 show the striking difference between the spectrum of 2-hydroxyxanthone and that of authentic 1,4-dihydroxyfluorenone. In addition, derivatization of this compound with BSA yielded a di-TMSi derivative of molecular weight 356 (by mass spectroscopy).

Similarly, the pmr data are consistent with the 2-hydroxyxanthone structure. Although five of the seven aromatic proton resonances overlap in varying degrees, individual signals can be assigned as in Table I.

The alternate 1,4-dihydroxyfluorenone can be excluded because of the absence of signals above 2.8 τ and the presence of seven rather than six aromatic protons. The observation of only one active hydrogen is supportive but not compelling evidence against the fluorenone proposal, since active hydrogen signals are occasionally broadened beyond detectability. The unusually low field position of the C₃ proton (2.80 τ) is attributed to the carbonyl group. The C₆ proton, also disposed para to the ketone, exhibits a comparable downfield shift (2.36 τ).

On the basis of these observations, **5** is assigned the structure 2-methoxyxanthone (9) and **6** is 2-hydroxyxanthone.

It is interesting to note that during the hydrolysis of the tosyl group with 50% sulfuric acid one of the methoxy groups was selectively demethylated to give an intermediate which readily coupled to give product **5**. This reaction sequence affords a convenient synthesis for 2-hydroxyxanthones.

EXPERIMENTAL

High resolution mass measurements were obtained *via* the peak matching technique on a CEC 21-110 mass spectrometer; introduction of the sample was accomplished through a direct probe

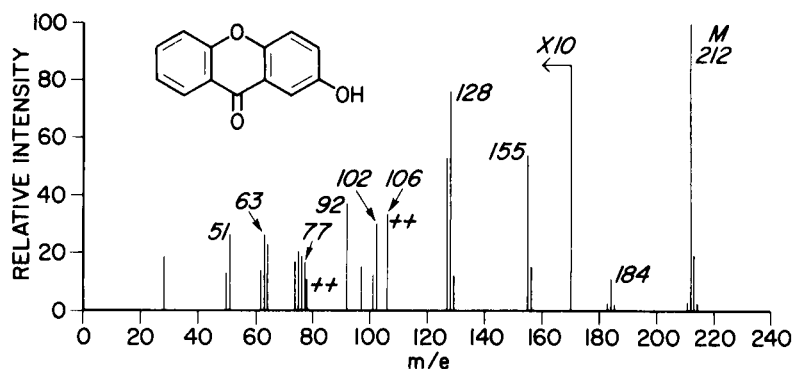


Figure 1. Mass spectrum (70 eV) of 2-hydroxyxanthone.

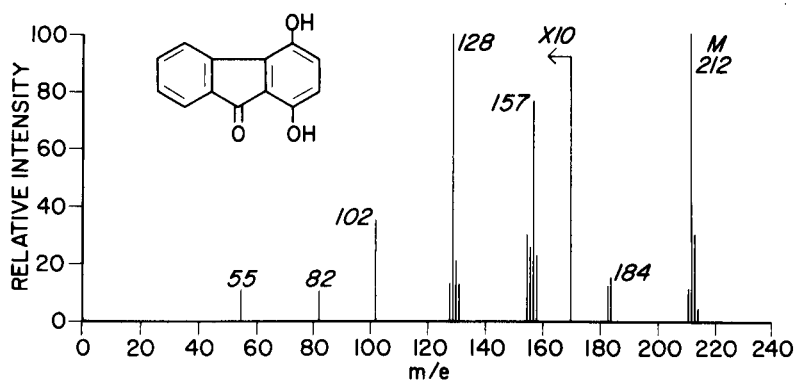


Figure 2. Mass spectrum (70 eV) of 1,4-dihydroxyfluorenone.

inlet. Source temperature, 200°; accelerating voltage, 8.12 kV; electron energy, 70 eV; ionizing current, 100 μ A. Low resolution mass spectra were obtained via a direct probe introduction on an LKB-9000 instrument. Source temperature, 290°; accelerating voltage, 3.5 kV; electron energy, 70 eV; trap current, 60 μ A.

TMSi derivatives were prepared by reaction of approximately 0.1 mg. of the parent compound with 100 μ l of *bis*-trimethylsilylacctamide at 45° for 30 minutes.

2,5-Dimethoxy-2'-toluenesulfonamidobenzophenone (4).

The *N*-tosyl anthranilic acid (2) (1), (15.0 g.) was dissolved in 300 ml. of carbon disulfide and treated under reflux for 2 hours with phosphorus pentachloride (12.0 g.). The reaction mixture was cooled, and 19.8 g. of *p*-dimethoxybenzene was added, followed by addition of 6.0 g. of aluminum chloride in small portions at room temperature and with vigorous stirring. Then the reaction mixture was heated under reflux for 2 hours, cooled rapidly and added to an excess of ice and 2.5*N* hydrochloric acid (300-400 ml.). The organic layer was separated, the aqueous solution was extracted three times with benzene, and combined with the organic layer. The organic phase was washed with water 3 x 200 ml. and then with 3 x 2.5*N* sodium hydroxide, then dried over sodium sulfate. Upon evaporation of benzene and carbon disulfide the residue, 8.0 g. was obtained. Recrystallization from methanol gave 6.5 g. of crystals, m.p. 155-157°, ir (Nujol) 3314 (N-H), 1620 (aromatic C=O), 1280 and 1155 cm^{-1} (*o*-tosyl).

Thin layer chromatography showed a single product in methanol: chloroform, 4:96 system.

2-Methoxyxanthone (5).

Product 4 (5.39 g.) was dissolved in a mixture of 10 ml. of glacial acetic acid and 10 ml. of concentrated sulfuric acid and heated on a steam bath for ½ hour. The reaction mixture was cooled to 0-3°, diluted with water (20 ml.) and diazotized with 15 ml. of 6% sodium nitrite solution. The reaction mixture was brought to room temperature, and placed on the steam bath until evolution of nitrogen ceased. The reaction mixture was further diluted with water and extracted 3 times with ether. The ether solution was washed 3 times with water, then with 2.5*N* sodium hydroxide, dried over sodium sulfate and evaporated *in vacuo* to give, after crystallization from ether, 2.0 g. of product, m.p. 128-130°.

Anal. Calcd. for $\text{C}_{14}\text{H}_{10}\text{O}_3$: C, 74.33; H, 4.46. Found: C, 73.99; H, 4.30.

2-Hydroxyxanthone (6).

A mixture of 5 (2.0 g.) with 25 ml. of acetic acid and 9 ml. of 47% hydrobromic acid was boiled for 22 hours. The product (1.6 g.) separated from methanol as red brick plates, m.p. 218-220°.

Anal. Calcd. for $\text{C}_{13}\text{H}_8\text{O}_3$: C, 73.58; H, 3.80. Found: C, 73.21; H, 3.84. M^+ (Calcd. 212.0473). Found: 212.047.

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