PHOTOCHEMICAL HYDROXYLATION OF SALICYLIC ACID DERIVATIVES WITH HYDROGEN PEROXIDE, CATALYZED WITH Fe(III) AND SENSITIZED WITH METHYLENE BLUE

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Substitution of hydrogen in the carboxy or hydroxy group of a salicylic acid molecule with a methyl group, which hinders the coordination of Fe(III), results in a pronounced reduction of photocatalytic effects. The complex of Fe(III) with salicylic acid is the precursor of the thermal catalyst arising on irradiation.

In our previous papers we described the marked photocatalytic effects of Fe(III) compounds in photo-initiated hydroxylation of salicylic^{1,2} and benzoic^{3,4} acids. We demonstrated¹ that a thermal hydroxylation catalyst, viz. Fe(II), is photochemically generated during the reaction.

Two alternative explanations of iron-catalyzed hydroxylations have been suggested in the literature:

1. Conventional explanation in terms of the Fenton reaction with the participation of free hydroxyl radicals, which are active hydroxylation agents⁵ (Eq. (A)).

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + OH^- + OH^{\bullet}$$
 (A)

The same hydroxylation agent, however, must be taken into account in the photoinitiated dissociation of hydrogen peroxide⁶.

$$H_2O_2 \xrightarrow{hv} 2OH^{\bullet}$$
(B)

For the hydroxylation of benzoic acid, Ogata and coworkers⁶ suggest Eqs (C) and (D).



It is, however, questionable whether a reaction of two radical intermediates (reaction (D)) can play a major role.

2. The alternative mechanism suggested involves the formation of ferryl ions, FeO^{2+} (Eq. (*E*)), which interact with the hydroxyl substrate, often giving a complex.

$$Fe^{2+} + H_2O_2 \longrightarrow FeO^{2+} + H_2O$$
 (E)

For instance, Groves and coworkers^{7,8} used reaction (*F*) to describe the hydroxylation of cyclohexanol.



This mechanism is strongly supported by the occurrence of stereoselective hydroxylation products but it fails to account for the occurrence of free hydroxyl radicals.

The aim of the present work was to contribute to the insight into the mechanism by examining the role of coordination of the catalyzing iron ion by the substrate hydoxylated. Salicylic acid was chosen as the substrate, and the effect of decrease in the coordination affinity as a result of substitution of the hydrogen atom in the carboxy and/or hydroxy group by a methyl group was investigated.

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EXPERIMENTAL

Chemicals

Hydrogen peroxide p.a. (Chemical Works, Sokolov), FeCl₃ p.a. (Cambrian Chemicals), Fe(III) acetylacetonate (Merck, Darmstadt), methylene blue (Merck, Darmstadt), salicylic acid (Reanal, Budapest), and 2,3- and 2,5-dihydroxybenzoic acids (Merck, Suchhardt) were used as received. Redistilled water was additionally purified by a process involving photooxidative degradation of organic impurities as described previously¹.

Apparatus

The photochemical reaction was conducted in a 1 cm cell accommodated in an aluminium block thermostatted to 25 °C. An SHC 250 W sodium high-pressure discharge lamp (Tesla Holesovice) with the luminous flux maximum at 589 nm was used for irradiation. In the solutions studied, radiation of 589 nm wavelength is predominantly absorbed by methylene blue; Fe(III) compounds absorb a minor fraction, whereas the hydroxylated derivatives do not absorb radiation in this spectral region. Absorption spectra of methylene blue, hydrogen peroxide and salicylic acid and its derivatives are shown in Fig. 1.

Irradiation was discontinued periodically and the reaction mixture was analyzed on a liquid chromatograph equipped with a column 150×3.2 mm packed with Separon SCX C18, 7 μ m (Tessek, Prague). A UV detector (Unicam Philips) was used, measuring absorbance at 300 nm. The mobile phase was constituted by a methanol–water–1 M phosphoric acid 53 : 46 : 1 mixture. Its flow rate was 0.5 ml min⁻¹ at a pressure of 2.5 – 3 MPa. A volume of 5 μ l was invariably injected.

RESULTS AND DISCUSSION

The photocatalytic effect of Fe(III) compounds is most marked in the hydroxylation of salicylic acid with hydrogen peroxide initiated by visible radiation and sensitized with methylene blue. The photocatalytic effect of iron(III) acetylacetonate ($Fe(acac)_3$) is



Fig. 1

Absorption spectra (substance, concentration in mmol l^{-1}): 1 methylene blue, 0.04; 2 hydrogen peroxide, 10; 3 methyl salicylate, 1; 4 salicylic acid, 1; 5 methyl *o*-methoxybenzoate, 1; 6 *o*-methoxybenzoic acid, 1 demonstrated in Fig. 2. As in the case of FeCl_3 described previously, a high photocatalytic activity and an autocatalytic reaction course were also observed in the present study. The autocatalytic nature is due to a gradual accumulation of Fe(II) which is the photochemically generated thermal reaction catalyst. A photocatalytic effect was also found, as expected, in the photochemical interactions of the other salicylic acid derivatives examined. The photocatalytic effect of Fe(acac)₃ on the hydroxylation of methyl salicylate is documented by Fig. 3.

When considering the reaction mechanism, the high stability constants of Fe(II) (ref.⁹) and, in particular, Fe(III) (refs^{10,11}) with salicylic acid must be taken into account. In the reaction conditions where virtually all Fe(III) (as well as the generated Fe(II)) is bonded in complexes with salicylic acid, the complexes apparently play a decisive role in the hydroxylations studied. This assumption is borne out by the results shown in Fig. 4, comparing the courses of hydroxylations, under identical conditions, of salicylic acid and of its derivatives in which the hydrogen atoms in the carboxy and/or hydroxy groups are replaced by methyl groups. The results indicate unambiguously that the hydroxylation rate increases with increasing strength of Fe(III)/Fe(II) coordination.





Effect of photocatalyst (Fe(acac)₃) concentration on salicylic acid (S) loss. Starting concentrations (mmol l^{-1}): salicylic acid 0.7, methylene blue 0.01, hydrogen peroxide 10. Fe(acac)₃ concentration (µmol l^{-1}): 1 1, 2 2.5, 3 5, 4 7.5, 5 10





Effect of photocatalyst (Fe(acac)₃) concentration on methyl salicylate (S) loss. Starting concentrations (mmol 1^{-1}): methyl salicylate 0.7, methylene blue 0.01, hydrogen peroxide 10. Fe(acac)₃ concentration (µmol 1^{-1}): 1 0, 2 3, 3 10, 4 50

Substitution of the hydrogen atom in the carboxy group by a methyl group not only affects reactivity (photocatalyst activity) but also has a significant effect on the reaction products. Hydroxylation of salicylic acid under the conditions applied (visible radiation, sensitization with methylene blue, Fe(III) photocatalyst) provides 2,3-dihydroxybenzoic acid as the main products, with a significant fraction of 2,5-dihydroxybenzoic acid (Table I). On the other hand, hydroxylation of methyl salicylate in position 3 does not occur, the -OH group entering into positions 4 and 5. The 2,6-dihydroxy derivative is not formed either, this compound, however, was also nearly absent in the case of salicylic acid. The effect of the Fe(acac)₃ photocatalyst concentration on the formation of the 2,4- and 2,5-dihydroxy derivatives is illustrated by Figs 5 and 6, respectively. While the formation of the 2,5-dihydroxy derivative can be observed in the absence of Fe(III), the 2,4-dihydroxy derivative is not detected. This is consistent with the fact that the 2,5-derivative is a typical product of direct interaction of excited hydrogen peroxide with salicylic acid, whereas the 2,4-derivative is not formed in appreciable quantities during that interaction. Hence, 2,4-dihydroxybenzoic acid can be regarded as a product of the reaction catalyzed by the photochemically generated catalyst.



FIG. 4

Effect of substitution of the hydrogen atom in the hydroxy/carboxy group by a methyl group on the loss of substrate. Starting concentrations (mmol l^{-1}): substrate 0.7, methylene blue 0.01, hydrogen peroxide 10, Fe(acac)₃ 0.01. Substrate: 1 methyl *o*-methoxybenzoate, 2 methyl salicylate, 3 *o*-methoxybenzoic acid, 4 salicylic acid





Effect of photocatalyst (Fe(acac)₃) concentration of the formation of methyl 2,4-dihydroxybenzoate (P). Starting concentrations (mmol l^{-1}): methyl salicylate 0.7, methylene blue 0.01, hydrogen peroxide 10, Fe(acac)₃: 1 0, 2 0.003, 3 0.01, 4 0.05 TABLE I

c _{Fe(III)} μmol l ⁻¹	Product concentration, μ mol l ⁻¹ , in a time of				
	60 min	120 min	180 min	240 min	300 min
0	0	0	traces	traces	4
	0	0	traces	traces	6
1.0	0	0	traces	2	7
	0	0	traces	3	8
2.5	traces	7	24	37	44
	traces	7	29	51	67
5.0	2	30	43	46	47
	4	35	60	69	75
7.5	12	44	48	48	49
	13	61	73	76	78
10.0	28	_	36	38	38
	34	_	62	70	69

Photohydroxylation of salicylic acid ($c_0 = 0.7 \text{ mmol } l^{-1}$) with hydrogen peroxide ($c_0 = 10 \text{ mmol } l^{-1}$) sensitized with methylene blue ($c_0 = 0.01 \text{ mmol } l^{-1}$) and photocatalyzed by Fe(acac)₃. Products: 2,5-dihydroxybenzoic acid (upper values) and 2,3-dihydroxybenzoic acid (lower values)



Fig. 6

Effect of photocatalyst (Fe(acac)₃) concentration of the formation of methyl 2,5-dihydroxybenzoate (P). Starting concentrations (mmol I^{-1}): methyl salicylate 0.7, methylene blue 0.01, hydrogen peroxide 10, Fe(acac)₃: 1 0, 2 0.003, 3 0.01, 4 0.05 Based on published as well as our data we suggest that the hydroxylation proceeds by two different mechanisms in the reaction systems under study. In the absence of catalyst the excited substrate interacts directly with hydrogen peroxide. The noncatalyzed photohydroxylation is described by Eqs (G) - (I), where S is substrate (salicylic acid or its methyl derivative), S_{ox} is the substrate hydroxylation product, and MB is methylene blue.

$$MB \xrightarrow{h_V} (MB)^*$$
 (G)

 $(MB)^* + S \longrightarrow MB + S^*$ (H)

$$S^* + H_2O_2 \longrightarrow S_{ox} + H_2O$$
 (1)

It should be emphasized that the hydroxylation species which is most frequently considered, i.e. the hydroxyl radical, does not form by interaction according to Eqs (J) and (K). This conclusion is warranted by our results of investigation of hydrogen peroxide photolysis initiated by visible radiation and sensitized by methylene blue^{12,13}, which does not take place if no photocatalyst (such as Fe(III)) is present.

$$(MB)^* + H_2O_2 \longrightarrow MB + (H_2O_2)^*$$
 (J)

 $(\mathrm{H}_2\mathrm{O}_2)^* \longrightarrow 2 \mathrm{OH}^{\bullet}$ (K)

In the presence of $Fe(acac)_3$ the interaction of substrate with hydrogen peroxide involves, in addition to the above direct mechanism, also the photocatalytic mechanism, which starts to predominate even at low photocatalyst concentrations (see effect of $Fe(acac)_3$). The photocatalytic mechanism consists of photochemical generation of the thermal reaction catalyst (i.e. Fe(II)) which subsequently catalyzes the thermal interaction of substrate with hydrogen peroxide. This mechanism can be schematically described by Eqs (L) - (P) in which MB_{ox} is the oxidized leuco form of methylene blue.

1. Photochemical generation of catalyst, i.e. of Fe(II)

$$(MB)^* + Fe(III)S_n \longrightarrow MB_{ox} + Fe(II)S_n$$
 (L)

2. Catalyzed thermal reaction

$$Fe(II)S_n + H_2O_2 \longrightarrow Fe(II)S_{(n-2)}(S_{ox})_2 \qquad (M)$$

$$\operatorname{Fe}(\operatorname{II})\operatorname{S}_{(n-2)}(\operatorname{S}_{\operatorname{ox}})_{2} + 2\operatorname{S} \longrightarrow \operatorname{Fe}(\operatorname{II})\operatorname{S}_{n} + 2\operatorname{S}_{\operatorname{ox}} \qquad (N)$$

3. Catalyst deactivation

 $Fe(II)S_n + H_2O_2 \longrightarrow Fe(III)S_n + OH^- + OH^{\bullet}$ (*O*)

 $Fe(II)S_n + OH^{\bullet} \longrightarrow Fe(III)S_n + OH^{-}$ (P)

The hydroxyl radical formed by reaction (O) can, naturally, also attack the benzene ring and cause its hydroxylation (Eq. (C)).

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