## Photosensitized Oxygenation of 3-Hydroxyflavones. A Possible Model for Biological Oxygenation[1]

*Sir:*

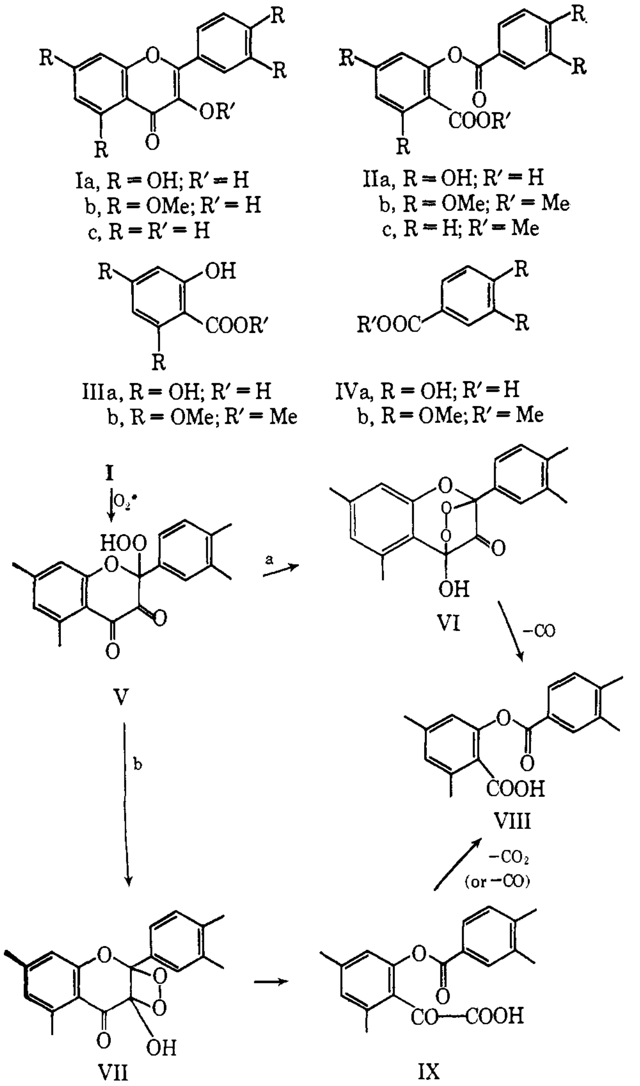
It has been reported that rutin is aerobically degraded to carbon monoxide and water-soluble products by extracellular enzymes from *Aspergillus* species.[2] Rutin is first hydrolyzed to quercetin (Ia) and rutinose, then Ia is oxidatively decarbonylated to give depside IIa and carbon monoxide. In the last step, IIa is hydrolyzed to 2,4,6-trihydroxybenzoic acid (IIIa) and protocatechuic acid (IVa). Among these steps, conversion of Ia into IIa was examined by tracer experiments, and it was found that C-3 is liberated as carbon monoxide[2b] and that an oxygen molecule is incorporated into IIa and its hydrolyzed products, IIIa and IVa, but not into carbon monoxide.[3] The results indicate that a dioxygenase catalyzes these reactions. In view of the resemblance between action of some oxygenases and photosensitized oxygenation,[4] we have carried out the photosensitized oxygenation of 3-hydroxyflavones.

In a typical run, a solution of quercetin 5,7,3′,4′-tetramethyl ether (Ib; 2.0 g) and bengal rose (50 mg) in pyridine (150 ml) was irradiated with a 300-w tungsten lamp under bubbling oxygen for 14 hr. The carbon dioxide (17%) liberated was determined as barium carbonate; carbon monoxide (31%) was determined by vpc analysis. Methylation of the crude products with diazomethane[5] followed by column chromatography on silica gel afforded depside IIb (77%), methyl 2-hydroxy-4,6-dimethoxybenzoate (IIIb, 2%), and methyl veratrate (IVb, 11%).[6] Depside IIb was identical with the pentamethyl derivative of depside IIa obtained enzymatically;[2d] the structure IIb was confirmed by synthesis from IIIb and veratroyl chloride. Similar degradations were observed with 3-hydroxyflavone (Ic) itself, which after methylation of the crude products gave a corresponding depside, IIc (44%), along with methyl salicylate (9%), and methyl benzoate (11%), carbon dioxide (19%) and carbon monoxide (88%) were also detected. On irradiation in the absence of sensitizer, Ic was recovered unchanged.

When Ib and Ic were submitted to photosensitized oxygenation using a 100-w high-pressure mercury lamp (Pyrex filter), similar results were obtained. Thus, Ib gave IIb (51%), IIIb (2.5%), IVb (13%), and carbon dioxide (107%),[7] and Ic gave IIc (48%), methyl salicylate (17%), methyl *o*-methoxybenzoate (5%), methyl benzoate (24%), carbon dioxide (43%), and carbon monoxide. On the other hand, the photosensitized oxygenation of quercetin 3,7,3′,4′-tetramethyl ether proceeded very slowly and 88% of the starting material was recovered.[8] These results indicate that the presence of a 3-hydroxyl group is the prerequisite to the present degradation reaction.[9]

Two possible sequences, involving a common hydroperoxide intermediate (V), for the photochemical formation of depside II from 3-hydroxyflavones (I) are illustrated in Chart I. Such a hydroperoxide is known to be formed in the photosensitized oxygenation of allylic compounds, *i.e.*, >C=C(XH)– → >C(OOH)–C(=X) (X = –C– or –N).[10] Hydroperoxide V can undergo rearrangement either to a five-membered cyclic

**Chart I**



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(1) Photoinduced Reactions. XIII. Part XII: T. Matsuura and Y. Kitaura, *Tetrahedron Letters*, 3311 (1967).

(2) (a) D. W. S. Westlake, G. Talbot, E. R. Blakley, and F. J. Simpson, *Can. J. Microbiol.*, **5**, 621 (1959); (b) F. J. Simpson, G. Talbot, and D. W. S. Westlake, *Biochem. Biophys. Res. Commun.*, **2**, 15 (1960); (c) S. Hattori and I. Noguchi, *Nature*, **184**, 1145 (1959); (d) H. Sakamoto, 36th Annual Meeting of Japanese Biochemical Society, Tokyo, April 1963; *cf.* Seikagaku, *J. Japan. Biochem. Soc.*, **35**, 633 (1963).

(3) H. Sakamoto, unpublished results.

(4) Photosensitized oxygenation of tryptophan results in the same type of cleavage as tryptophan pyrrolase, a dioxygenase. *Cf.* Z. Yoshida and M. Kato, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **75**, 106, 109, 112 (1954); O. Hayaishi, S. Rothberg, A. H. Mehler, and Y. Saito, *J. Biol. Chem.*, **229**, 889 (1957). Photosensitized oxygenation of 1-ribityl-2,3-diketo-6,7-dimethyl-1,2,3,4-tetrahydroquinoxaline gives 6,7-dimethylquinoxaline-2,3-diol, which is considered to be formed from the former by the action of an oxygenase. *Cf.* I. Saito and T. Matsuura, unpublished results; D. R. Harkness, L. Tsai, and E. R. Stadtman, *Arch. Biochim. Biophys.*, **108**, 323 (1964).

(5) Direct chromatography of the crude products on silica gel resulted in products which are formed by hydrolysis of the depside.

(6) All products were identified by direct comparison with authentic samples, unless otherwise indicated.

(7) Determination of carbon monoxide was not done in this case.

(8) Photooxidation of 3-methoxyflavone caused a different type of reaction. The results will be published elsewhere.

(9) In accordance with this observation, the enzymes from *Aspergillus* species are specific for 3-hydroxyflavones but not for other flavonoids such as flavones, flavanones, and 3-hydroxyflavanones. *Cf.* J. J. Child, F. J. Simpson, and D. W. S. Westlake, *Can. J. Microbiol.*, **9**, 653 (1963); H. Sakamoto, unpublished results.

(10) For allylic compounds (X = –C–) see G. O. Schenck, *Angew. Chem.*, **69**, 579 (1957); A. Nickon, N. Schwartz, J. B. DiGiorgio, and D. A. Widdowson, *J. Org. Chem.*, **30**, 1711 (1965), and references cited therein. For N-heterocycles (X = –N) see C. Rio, A. Ranjon, and O. Pouchot, *Compt. Rend., Ser. C.*, **263**, 639 (1966); E. H. White and M. J. C. Harding, *Photochem. Photobiol.*, **4**, 1129 (1965).

peroxide (VI) in path a or to a four-membered one (VII) in path b.[11] Decarbonylation of VI to depside VIII in path a has an analogy.[12] In path b, keto acid IX which was derived from VII might be transformed into VIII by decarbonylation or by oxidative decarboxylation. In order to distinguish between the two modes of elimination of one carbon atom from keto acid IX, *p*-anisylglyoxylic acid was photooxidized in the presence of bengal rose. After irradiation with visible light, *p*-anisic acid (19%) and carbon dioxide (30%) were obtained, in addition to recovery (54%) of *p*-anisylglyoxylic acid, but no carbon monoxide could be detected.[13] These results suggest that the photosensitized oxygenation of 3-hydroxyflavones may proceed through path a simultaneously with path b. It seems reasonable to assume that the enzymatic cleavage of quercetin leading to depside IIa and carbon monoxide may proceed by a mechanism similar to path a.

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(11) Concerted cleavage processes in which a cyclic peroxide (VI or VII) is not involved may also be possible, instead of path a and path b.

(12) N. M. Bikales and E. I. Becker, *J. Org. Chem.*, 21, 1405 (1956).

(13) On irradiation with a high-pressure mercury lamp (Pyrex filter) in the presence and in the absence of sensitizer, *p*-anisylglyoxylic acid reacted with oxygen much faster to yield anisic acid and carbon dioxide. However, it was recovered unchanged when irradiated by visible light under oxygen without sensitizer.

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## The Hydration Number and Rate of Water Exchange of the Trimethylplatinum(IV) Ion in Aqueous Solution Determined by Oxygen-17 Nuclear Magnetic Resonance[1]

*Sir:*

Recently we made a study of the hydration of organometallic ions in aqueous solution. Among the ions investigated was an unusual $d^6$ platinum(IV) complex whose properties are in marked contrast to those of other octahedral complexes of tetravalent platinum. Trimethylplatinum(IV) halides react with aqueous solutions of $AgNO_3$ or $AgClO_4$ to yield electrolyte solutions containing the trimethylplatinum(IV) cation. The pmr spectra of these solutions show a triplet (1:4:1) centered at $\tau$ 8.90 ppm. The similarity of the coupling constant $J_{^{195}Pt-CH_3}$ for the aquo ion to that of $[Pt(CH_3)_3(OH)]_4$ suggests that the aquo ion is probably *cis*-$[Pt(CH_3)_3(OH_2)_3]^+$.[2]

The $^{17}O$ nmr spectra of solutions of $(CH_3)_3PtClO_4$ indicate that the exchange of coordinated water molecules is *fast* at room temperature. The time scale of the $^{17}O$ resonance experiment was shortened by using $Dy(ClO_4)_3$ concentrations of up to 1.2 *m* to shift the bulk water signal as much as 3500–4000 cps upfield from the bound water resonance. At 5°, a signal for the water molecules bound in the first coordination sphere of the platinum(IV) is recorded clearly. As the sample is warmed to 29°, the bound-water signal disappears because of exchange. This is illustrated in Figure 1. By measuring the shift of the bulk water signal with respect to an external water standard for $Dy(ClO_4)_3$ solutions with and without $(CH_3)_3PtClO_4$, the hydration number of the trimethylplatinum(IV) ion has been found to be 3.0 ± 0.1 by the molal shift method.[3,4] The data are listed in Table I, and the hydration number, *n*, was calculated using the relation

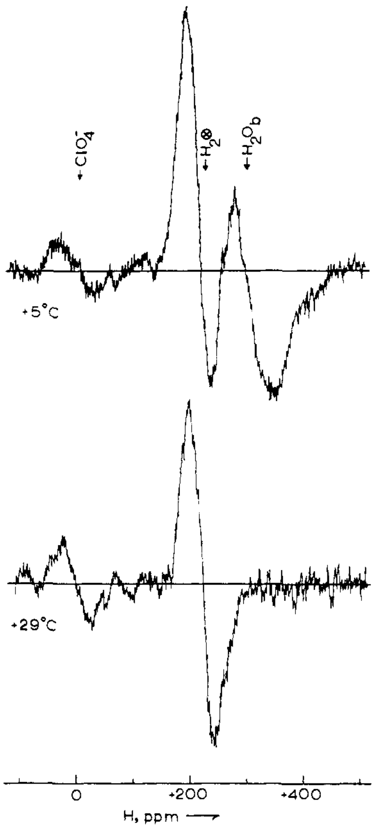

Figure 1. Oxygen-17 nmr spectra showing the bound-water resonance with respect to an external water sample. Solution composition: 1.969 *m* $(CH_3)_3PtClO_4$, 0.802 *m* $Dy(ClO_4)_3$, 0.486 *m* $HClO_4$.

$$n = \frac{55.5}{[(CH_3)_3Pt^{IV}]}\left[1 - \frac{(\delta_{H_2O}/[Dy^{+3}])_{ref}}{(\delta_{H_2O}/[Dy^{+3}])_{sample}}\right]$$

The bulk-water signal in these solutions is broadened considerably because of the exchange process. While the $^{17}O$ water resonance of a pure $Dy(ClO_4)_3$ solution sharpens as the temperature is raised from 5 to 29°, the signal for a solution containing $[Pt(CH_3)_3(OH_2)_3]^+$ broadens (see Figure 2). Using the relation for slow exchange together with the line-width measurements and considering the $Dy(ClO_4)_3$ solution as the solvent, the mean half-life of the water-exchange process has been estimated to be $1.4 \times 10^{-3}$ sec at 5°.[5]

The very high rate of exchange of the coordinated water ligands in this complex compared with other octa-

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(1) Research sponsored by AFOSR (SRC)-OAR, USAF Grant No. AF-AFOSR-691-65 and -67.

(2) K. Kite, J. A. S. Smith, and E. J. Wilkins, *J. Chem. Soc., Sect. A*, 1744 (1966).

(3) M. Alei and J. A. Jackson, *J. Chem. Phys.*, 41, 3402 (1964).

(4) J. A. Jackson, J. F. Lemons, and H. Taube, *ibid.*, 32, 553 (1960).

(5) The experimental details of the oxygen-17 resonance measurements and the kinetic studies will be published elsewhere.