Results and discussion. The synthetic aflatoxicol was found to have the same R_f-value as that of an authentic aflatoxicol standard provided to us by Professor Dennis P. H. Hsieh of University of California, Davis. The UV-spectrum was identical to the standard. The mass spectrum contained the following major ions which are consistent with the structure of alfatoxicol: m/e 314 (M^+, base peak), 313, 297, 296, 268 and 267. The fragmentation patterns for both synthetic and natural aflatoxicols were identical.

Chemical reduction of afla B_1 by sodium borohydride has been reported to give either low yield of aflatoxicol[6] or quantitative conversion to the trihydroxy derivative (**III**)[11]. These results must be related to the sensitivity of afla B_1 toward the hydroxide or ethoxide ions present in alcoholic borohydride. In the preparation of ^{3}H-aflatoxicol, essentially equal radioactivity was found for each diastereomer. Thus, a 50:50 mixture was obtained from this reduction, indicating no steric preference for the hydride attack. Therefore, our present procedure represents an efficient preparation for obtaining quantities of synthetic aflatoxicol under essentially neutral conditions. We are presently investigating the synthesis of a protein-mycotoxin conjugate starting with labeled aflatoxicol and succinic anhydride.

11 S. H. Ashoor and F. S. Chu, J. Ass. off. analyt. Chem. *58*, 492 (1975).

Fe(II)-induced decomposition of epidioxides. A chemical model for prostaglandin E, prostacyclin and thromboxane biosynthesis

J. A. Turner and W. Herz[1]

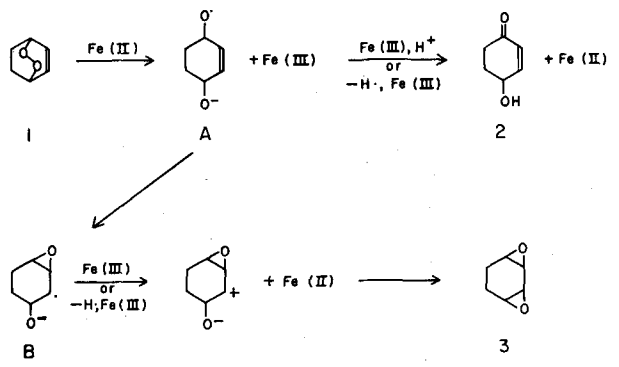
Department of Chemistry, The Florida State University, Tallahassee (Florida 32306, USA), 14 February 1977

Summary. A chemical model for biosynthesis of PGE, PGX and the thromboxanes from the prostaglandin endoperoxides is presented which is based on known reactions of other endoperoxides with the Fe(**II**)-Fe(**III**) redox system in vitro.

The peroxy radical cyclization mechanism for the cyclooxygenase-mediated[2–4] conversion of arachidonic acid to the prostaglandin endoperoxides (PPG_2 and PGH_2)[5] has been supported by di-tert-butyl peroxyoxalate-initiated reactions of lipid hydroperoxides[6] and by a recent model study[7]. We now suggest that Fe(II)-induced isomerizations of epidioxides[8] provide not only a model for the transformation of PGG_2 and PGH_2 to the PGE's in vivo as already pointed out briefly by us earlier[8b], but also a model for the biosynthesis of the thromboxanes[4,9,10] and prostacyclin (PGX)[11,12]. This is in line with recent suggestions[13,14] that the in vivo fragmentation of PG-endoperoxides is probably a catalyzed process.

We have provided evidence[8] that the previously little-studied isomerization of epidioxides of type **1** to ketols **2** or diepoxides **3** by $FeSO_4$ in H_2O-THF actually involves a redox process in which the first step is reduction of **1** by Fe(II) to anion radical A (Scheme I). The latter may be oxidized by Fe(III), generated in the first step, to ketol **2** or, if a double bond is present can isomerize to B which is oxidized to **3**[15]. In appropriately constituted anion radicals A, intramolecular 1,5-hydrogen transfer from remote carbon to oxygen may intervene prior to oxidation by Fe(III)[8a,c].

The oxidations of A and B by Fe(III) can be viewed[8b] as equivalent to loss, by fragmentation, of H which is subject to oxidation by Fe(III). Such fragmentations, with loss of an isopropyl radical which migrates intra- or intermolecularly (the latter if a radical trap is introduced) or is subsequently oxidized to propylene, have been observed on treatment of ascaridole[17] or dihydroascaridole[18] with $FeSO_4$.



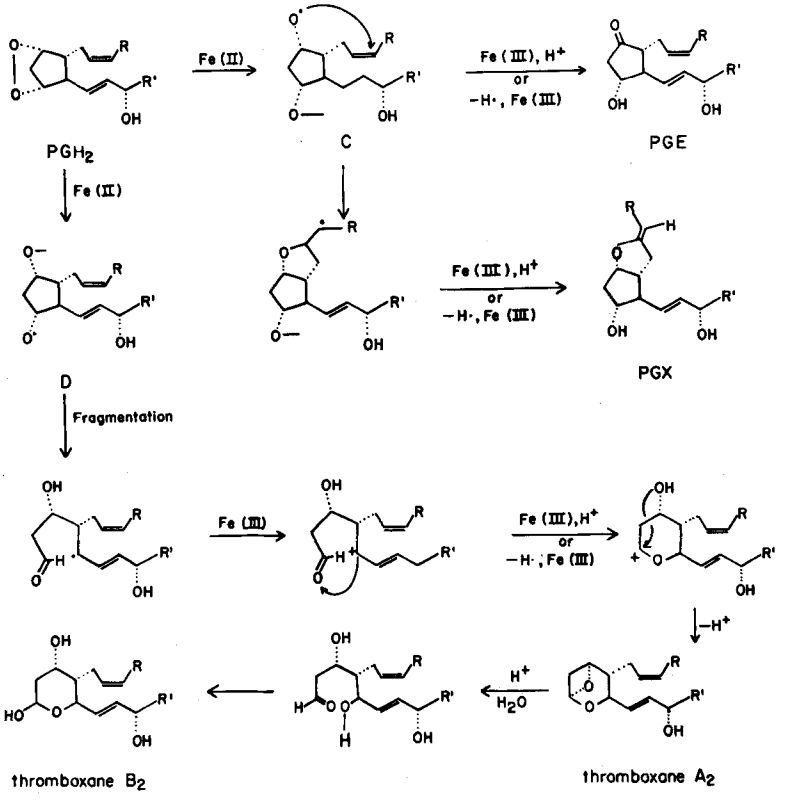
1 Supported in part by USPH grant CA-13121 through the National Cancer Institute.

2 M. Hamberg and B. Samuelsson, Proc. nat. Acad. Sci. USA, *70*, 899 (1973).
3 D. H. Nugteren and E. Hazelhof, Biochem. biophys. Acta. *326*, 448 (1973).
4 M. Hamberg and B. Samuelsson, Proc. nat. Acad. Sci. USA *71*, 3400 (1974).
5 M. Hamberg, J. Svensson, T. Wakabayashi and B. Samuelsson, Proc. nat. Acad. Sci. USA *71*, 345 (1974).
6 N. A. Porter and M. Funk, J. org. Chem. *40*, 3614 (1975).
7 N. A. Porter, M. O. Funk, D. Gilmore, R. Isaac and J. Nixon, J. Am. chem. Soc. *98*, 6000 (1976).
8 a) J. A. Turner and W. Herz, J. org. Chem. *42*, 1885 (1977); b) J. A. Turner and W. Herz, J. org. Chem. *42*, 1895 (1977); c) J. A. Turner and W. Herz, J. org. Chem. *42*, 1900 (1977).
9 M. Hamberg, J. Svensson and B. Samuelsson, Proc. nat. Acad. Sci. USA *77*, 2994 (1975); J. org. Chem. *72*, 2994 (1976).
10 P. Needleman, S. Moncada, S. Bunting, J. R. Vane, M. Hamberg and B. Samuelsson, Nature *261*, 550 (1976).
11 S. Moncada, R. Gryglewski, S. Bunting and J. R. Vane, Nature *263*, 663 (1976).
12 Chem. Eng. News, Report on Intra-Science Research Foundation Symposium, Santa Monica, Dec. 20, 1976, p. 17.
13 W. A. Pryor and J. P. Stanley, J. org. Chem. *40*, 3615 (1975).
14 D. J. Coughlin and R. G. Salomon, J. Am. chem. Soc. *99*, 655 (1977).
15 This contrasts with the thermally or photolytically induced isomerization 1→3 which presumably proceeds by a radical mechanism (for citations, see Turner and Herz[8] and the base-catalyzed isomerization 1→2 characteristic of dialkyl peroxides[16].
16 N. Kornblum and H. B. De La Mare, J. Am. chem. Soc. *73*, 880 (1951).
17 D. Brown, B. T. Davis, T. G. Halsall and A. P. Hands, J. chem. Soc. 4492 (1962).
18 D. Brown, B. T. Davis and T. G. Halsall, J. chem. Soc. 1095 (1963).

On the basis of these observations we suggested[8b] that the Fe(II)-induced isomerization **1**→**2** might serve as a model for the transformation of the prostaglandin endoperoxides to the PGE's in vivo under the influence of Fe(II)-based enzyme systems as shown in the first row of Scheme II. The lower part of the Scheme adumbrates our suggestion for the biosynthesis of PGX and the thromboxanes, using as a model the 2 other reactions of endoperoxides induced by the Fe(II)-Fe(III) redox system which have been discussed in the preceding paragraphs.

Thus in the anion radical C, produced by one-electron reduction of PGH_2, an alternative to oxidation to PGE is attack by the C-9 oxyradical on the double bond of the side chain attached to C-9 in a manner analogous to the reaction A→B of Scheme I. This is consistent with the alteration of double bond geometry (cis→trans). Subsequent oxidation by the enzyme-based redox system would explain the formation of PGX.

Thromboxane biosynthesis requires cleavage of the 11, 12-bond of a precursor derived from PGH_2[4,9,10]. This can be rationalized by invoking one-electron reduction of PGH_2 to the isomeric anion radical D whose fragmentation (arrows) and subsequent oxidation by the enzyme-based redox system is analogous to the loss of an isopropyl group (and oxidation of the latter) exhibited by dihydroascaridole on treatment with $FeSO_4$[18]. The circumstance that ring cleavage leads to an allylic radical may conceivably assist the mode of fragmentation of D. The subsequent steps leading to thromboxane A_2 and A_3 are self-explanatory.



Reductive dechlorination of chlorobiphenylols by rats

M. Th. M. Tulp[1], W. A. Bruggeman and O. Hutzinger

Laboratory of Environmental Chemistry, University of Amsterdam, Nieuwe Achtergracht 166, Amsterdam (the Netherlands), 17 December 1976

Summary. Dechlorinated products were isolated from the urine of rats that were administered chlorobiphenylols, the primary hydroxylated metabolites of PCB in mammals. The mechanism of chlorine loss from chlorobiphenylols is different from the mechanism of dechlorination via arene oxides whereby concomitant hydroxylation is always observed.

Although extensive metabolic dechlorination is known to occur with compounds in which chlorine is not bound to an aromatic carbon[2], this reaction is much less important in aromatic chlorine compounds[3]. The possibility of reductive dechlorination of an aromatic chlorine compound was firstly reported in 1973[4] for hexachlorobenzene (HCB), and recently unambiguously demonstrated: pentachlorobenzene, tetrachlorobenzene and a number of polychlorophenols were found as metabolites from HCB in rats[5,6]. This reductive dechlorination was shown to be catalysed by an enzyme located in the microsomal fraction of liver, lung, kidney and intestine[5].

Reductive dechlorination of polychlorinated biphenyls (PCB) is known only as a photochemical pathway[7]. All documented cases of metabolic chlorine loss from PCB involve concomitant hydroxylation via an arene oxide