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PRODUCTS FROM ENZYMIC OXIDATION OF 2',4,4'-TRIHYDROXYCHALCONE: STRUCTURAL RECONSIDERATIONS

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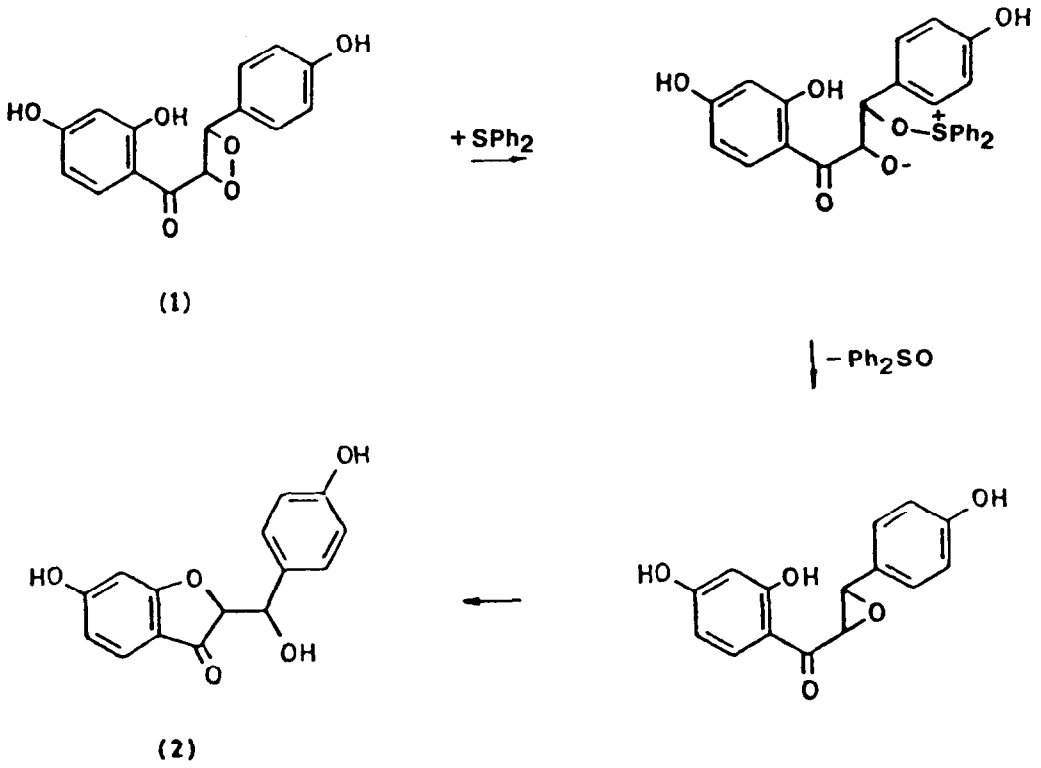
Abstract: The enzymic products from peroxidase-catalysed oxidation of 2',4,4'-trihydroxychalcone react with diphenylsulphide to form diastereoisomers of 4',6-dihydroxy-2-(α-hydroxybenzyl)-coumaranone, consistent with their previously assigned dioxetane structure.

In a previous work[1] we proposed the dioxetane structure (1) for the various forms of the labile enzymic product (EP) isolated from the peroxidase-catalysed oxidation of 2',4,4'-trihydroxychalcone; together with structures for their two spontaneous transformation products, designated OC (Oxidised Chalcone) and ψOC. Recently, a product identical to OC was isolated from independent enzymic oxidation of the same chalcone, and its structure established as the quinol ether (4) from X-ray diffraction studies by Begley et al.[2] These authors postulated a rearrangement step taking place via the spiro-epoxide intermediate (3), and further suggested that the latter structure could more appropriately represent our product EP. In view of all the physical, chemical and biochemical data already presented by us[1,9] for EP this view is clearly untenable. However, in the light of the revised structure for OC, our previously proposed structure for ψOC, its closely related intermediate, must now also need modification. We wish to point out that the spiro-epoxide structure (3) invoked by Begley et al. is in fact compatible with all the properties of ψOC recorded by us,[1] and suggest that this structure be now taken to represent the revised structure for ψOC.

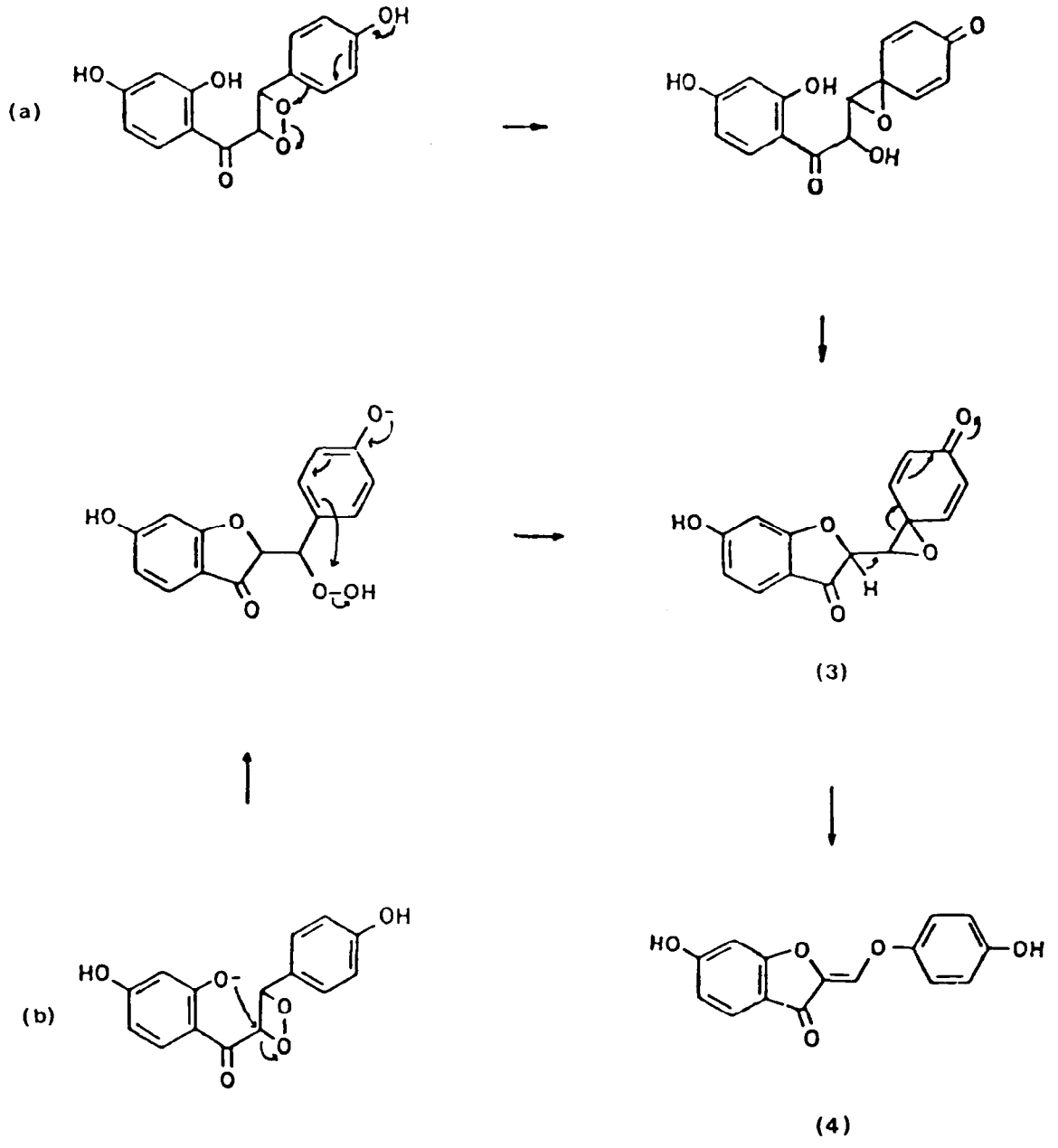
At the time when structure (1) was proposed, dioxetane chemistry was still in a fairly novel state. Since then there has been much progress made in the better understanding of such compounds.[3,4,5,6] In the area of photochemistry involving singlet oxygen, the usefulness of diphenylsulphide as trapping agents for dioxetane intermediates has been demonstrated[7] and recommended.[6] We have now carried out this diagnostic test on the EP compounds in order to verify their dioxetane nature. Reaction of a mixture of EP compounds from enzymic oxidation of the chalcone (5.7 mg) at pH 8, with diphenylsulphide (50 mg) in methanol at 0^{o} for 6 days, yielded two products which were isolated by C_{18}-reversed-phase h.p.l.c. (yield 70%). Chromatographic and spectral evidence (u.v.,i.r.) enabled

the products to be identified as the diastereoisomers of 4',6-dihydroxy-2-(α-hydroxybenzyl)coumaranone (2) previously encountered as minor products in the enzymic reaction.[8,9] The formation of diphenylsulphoxide as the other product of the reaction was also demonstrated by h.p.l.c. analysis. A plausible rationalisation of these transformations, based on the original dioxetane structure for EP, and on the epoxide mechanism of Wasserman and Saito,[7] is shown in Scheme 1.



Scheme 1

The salient feature of the EP compounds - their facile transformation to the more stable product OC - can also be readily accommodated by the original dioxetane structure (1), regard being taken of the revised structure for OC. Two possible transformation pathways are shown in Schemes 2(a) and 2(b).


(a)
HO
OH
OH
O
O
O
HO
OH
O
O
OH
O
O-
HO
O
O
O-OH
O
HO
O
O
O
H
O
(3)
(b)
HO
O-
OH
O
O
O
HO
O
O
OH
O
(4)

Scheme 2

Although oxidation of diphenylsulphide does not in itself provide unique proof of a dioxetane structure, this reaction with EP, together with evidence from the stoichiometry of molecular oxygen uptake and the radical-chain features found in our original biochemical studies,[9] lends strong support to the proposal of the dioxetane structure (1) for the EP compounds. Taken singly, many of the chemical and physical properties of the EP compounds can be satisfactorily accounted for also by other structural proposals. Collectively however, the known properties of EP are best accommodated as a whole by the dioxetane structure (1). Among other key chemical properties of EP needing to be accounted for in any structural representation are conversion to 4',7-dihydroxyflavonol and fragmentation to p-hydroxybenzaldehyde. The dioxetane structure (1) accounts for these readily. The probable involvement of dioxetane intermediates in other peroxidase-catalysed reactions has in recent years been well documented.[5,10]

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