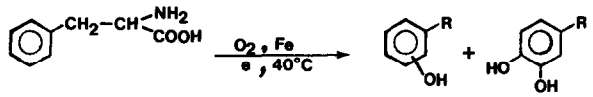
Tetrahedron Letters,Vol.29,No.18,pp 2177-2178,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

OXIDATION OF L-PHENYLALANINE BY THE MODIFIED UDENFRIEND SYSTEM

M. Blanchard*, C. Bouchoule, G. Djaneye-Boundjou and P. Canesson
Université de Poitiers
Laboratoire de Catalyse en Chimie Organique, associé au CNRS
40, Avenue du Recteur Pineau
86022 POITIERS (France)

L-phenylalanine is oxidized by oxygen into 3,4-dihydroxyphenylalanine (DOPA) at 40°C with Fe^{2+} EDTA as a catalyst. For the reduction of Fe^{3+} species, electrons are released from the cathode of an electrochemical cell.

A few years ago we showed that aromatic compounds could be hydroxylated by an Udenfriend system (Fe^{2+}, EDTA, ascorbic acid) in which the reducing agent was replaced by the cathode of an electrochemical cell (1,2). This electrochemical modification revealed itself to be very efficient and has since been applied by other researchers in the oxidation of aromatics or of alkanes (2,3).



In this paper, we report the results obtained with L-phenylalanine. Oxidation of this substance could lead to DOPA (3,4-dihydroxyphenylalanine) which up to now has been prepared essentially by biochemical methods, and it was interesting to compare the selectivity of this quite simple system to the selectivity of oxygenases (5-7).

Oxidation of L-phenylalanine

The reactions were carried out at 40°C in an electrochemical cell already described (1) in which the cathode was constituted by a 45 cm braided carbon fiber cord. The substrate was in a buffered aqueous solution at pH 3. The analyses were carried out at regular intervals by HPLC in a C18 Rosil column by eluting with a 1/1 (v./v.) methanol-phosphoric acid 0.05M solution containing 0.005 mole l^{-1} of sodium dodecyl hydrogenosulfate. The identification of the products ensued from the reaction carried out under the same conditions with various isomers : there were 3 monohydroxylated phenols, ortho, meta and para tyrosines, all of which are obtainable commercially. One of the dihydroxyphenylalanines, namely the 3,4 isomer (DOPA) is also obtainable, so that by treating separately each tyrosine and comparing the chromatograms, all the dihydroxyphenylalanines could be identified by cross-checking since some of them could be found among the oxidation products of two of the three tyrosines. In normal

conditions (substrate 1.5mmole, buffer pH 3 : 100ml, Fe^{2+}-EDTA : 1.5mmole) the main products resulting from the oxidation of phenylalanine are the three tyrosines, DOPA and products which could not be identified resulting from a further oxidation. The catalytic system was quite active : after 4h, all the substrate was consumed but the lower the conversion the higher the selectivity for DOPA (see Table 1)

Table 1

Oxidation of phenylalanine (1.5mmole) in 100ml of buffer pH=3, T=40°C, catalyst Fe^{2+}/EDTA (1.5mmole)

Phenylalanine transformation extent (%)	Selectivities (%)	
	Tyrosines	DOPA
33	21	16
11	24	25

By operating in conditions where the transformation extent was low, the subsequent reactions could be limited and the initial rate measured (see Table 2).

Table 2

Initial hydroxylation rates (operating conditions as in Table 1)

Substrate	Initial transformation rate (mmole.h^{-1})
Phenylalanine	0.13
o.Tyrosine	0.28
p.Tyrosine	0.24
m.Tyrosine	0.40
DOPA	0.14

All the tyrosines are more reactive than phenylalanine, meta-tyrosine being the most reactive of all. Yet the oxidation rate of DOPA cannot be neglected as it is practically equal to the oxidation rate of phenylalanine so that to improve the performances of the system it would be necessary to develop a continuous process working at low conversion with recycling of the substrate.

References

(1) J.M. Maissant, C. Bouchoule, P. Canesson and M. Blanchard. J. Mol. Catal., 1983, 18, 189.
(2) J.M. Maissant, C. Bouchoule and M. Blanchard. J. Mol. Catal., 1982, 14, 333.
(3) G. Balavoine, D.H.R. Barton, J. Boivin, A. Gref, N. Ozobalik and H. Rivière. Tetrahedron Lett. 1986, 27, 2849. J. Chem. Soc., Chem. Commun., 1986, 1727.
(4) T.L. Kinoshita, J. Harada, S. Ito and K. Sasaki. Angew. Chem., 1983, 22, 502.
(5) H. Kumagai, H. Matsvi, H. Ougishi, K. Ogata, H. Yamada, T. Veno and H. Fukami. Biochem. Biophys. Res. Commun., 1969, 34, 266.
(6) H.J. Huizing and H.J. Wichers, Prog. Ind. Microbiol., 1984, 20, 217.
(7) J.R. Wykes, P. Dunnill and D. Lilly.Nature, (London) New Biol., 1971, 230, 187.

(Received in France 26 February 1988)