

Selective Nucleophilic Attack by Peroxy-acid Anions on Nucleic Acid Components

By L. R. SUBBARAMAN, JIJI SUBBARAMAN, and E. J. BEHRMAN*

(Department of Biochemistry, The Ohio State University, Columbus, Ohio 43210)

ALTHOUGH electrophilic attack by peroxy-acids on cytosine, adenine, and their nucleosides and nucleotides leading to the *N*-oxides has been recognized for some time,¹ it has not been realized that the anions of the same peroxy-acids are capable of nucleophilic attack on uracil, thymine, guanine, and their derivatives. In a study of the rate dependence on pH for the reaction of all of the common nucleic acid components with *m*-chloro-peroxybenzoic acid, reactions were run at 40° with equimolar concentrations of the peroxy-acid and substrate. The kinetics were second-order in all cases. The rate constants have been corrected for the rate of autodecomposition of the peroxy-acid. The rate of reaction for each nucleic acid component showed a characteristic pH maximum. The Table gives the observed second-order rate constant at this maximum and the pH at which it is observed. The reactions fall into two groups: cytosine, adenine, and their derivatives show

The reaction of m-chloroperoxybenzoic acid with nucleic acid components

Component	$k_{\text{obs}}(\text{mole}^{-1}\text{min.}^{-1})$	pH
Adenine	4.7	6.2
Adenosine	4.0	5.5
Cytosine	13.2	6.6
Cytidine	4.2	6.0
Deoxycytidine	4.5	6.0
Guanosine	4.4	8.4
Uracil	8.3	8.8
Uridine	3.8	8.6
Deoxyuridine	3.2	8.5
5-Bromouracil	8.3	8.4
6-Methyluracil	4.3	8.6
Thymine	1.9	8.8
Thymidine	0.7	8.6

maxima on the acidic side of the $\text{p}K_{\text{a}}$ of the peroxy-acid (7.6), while uracil, thymine, guanosine, and their derivatives, show maxima on the alkaline side. The kinetic data for the first group are consistent either with attack by the un-ionized

peroxy-acid on the uncharged substrates or with attack by the peroxy-acid anion on the cationic form of the substrate. We favour the first possibility on the basis of substituent effects observed by Dondoni, Modena, and Todesco² for the reaction between peroxybenzoic acid and a series of substituted pyridines and the fact that the only products detected in our study were the expected *N*-oxides. However, the two mechanisms described³ for the oxidation of sulphoxides by peroxy-acids should be borne in mind. The kinetic results for the second group may be interpreted either as a reaction between the peroxy-acid anion and the uncharged substrate, or as a reaction between the un-ionized peroxy-acid and the substrate anion. We favour the first interpretation because of the substituent effects shown by

the uracil derivatives and because of the nature of the products. *N*-Oxides are not formed in the reactions of the second class. Instead, products that can only be attributed to ring-opening are found: from uracil, oxalic, and oxaluric acids and urea; from uridine, ribosylurea; from thymine, urea and hydroxyacetone; from thymidine, deoxyribosylurea; and from guanosine, ribosylurea and formic acid. In the case of the pyrimidines, we visualize attack by the peroxy-acid anion at the 5,6-double bond,⁴ epoxide formation, hydrolysis and subsequent reactions similar to those formulated by Jones and his co-workers⁵ for permanganate oxidation.

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