Biochemistry. 1998 Dec 22;37(51):17923-30. doi: 10.1021/bi9818772.

Reaction of myeloperoxidase compound I with chloride, bromide, iodide, and thiocyanate

P G Furtmüller [1], U Burner, C Obinger

Affiliations

Affiliation

1 Institute of Chemistry, University of Agricultural Sciences, Vienna, Austria.

PMID: 9922160 DOI: 10.1021/bi9818772

Abstract

Myeloperoxidase plays a fundamental role in oxidant production by neutrophils. The enzyme uses hydrogen peroxide to oxidize chloride (Cl-), bromide (Br-), iodide (I-), and the pseudohalide thiocyanate (SCN-) to their respective hypohalous acids. This study for the first time presents transient kinetic measurements of the oxidation of these halides and thiocyanate by the myeloperoxidase intermediate compound I, using the sequential mixing stopped-flow technique. At pH 7 and 15 degrees C, the two-electron reduction of compound I to the native enzyme by Cl- has a second-order rate constant of (2.5 +/- 0.3) x 10(4) M(-1) s(-1), whereas reduction of compound I by SCN- has a second-order rate constant of (9.6 +/- 0.5) x 10(6) M(-1) s(-1). Iodide [(7.2 +/- 0.7) x 10(6) M(-1) s(-1)] is shown to be a better electron donor for compound I than Br- [(1.1 +/- 0.1) x 10(6) M(-1) s(-1)]. The pH dependence studies suggest that compound I reduction by (pseudo-)halides is controlled by a residue with a pKa of about 4.6. The protonation of this group is necessary for optimum (pseudo-)halide anion oxidation. These transient kinetic results are underlined by steady-state spectral and kinetic investigations. SCN- is shown to be most effective in shifting the system myeloperoxidase/hydrogen peroxide from the peroxidatic cycle to the halogenation cycle, whereas iodide is shown to be more effective than bromide which in turn is much more effective than chloride. Decreasing pH increases the rate of this transition. Our results show that thiocyanate is an important substrate of myeloperoxidase in most environments and that hypothiocyanate is likely to contribute to leukocyte antimicrobial activity.

Related information

MedGen
Protein
PubChem Compound (MeSH Keyword)
Taxonomy via GenBank

LinkOut - more resources

Other Literature Sources
The Lens - Patent Citations