

CHEMICAL AND BIOLOGICAL REACTIONS OF REDUCED PTERINS

W.L.F. ArmaregoJohn Curtin School of Medical Research,
The Australian National University, Canberra, A.C.T., Australia.

Among the most abundant pteridines in nature are the 2-aminopteridin-4-ones which are collectively called 'pterins' after Pfeleiderer's suggestion. The biologically active members of this class of pteridines are the 7,8-dihydro(3H), 7,8-dihydro(6H), and the 5,6,7,8-tetrahydro derivatives. Enzyme cofactors in these three reduced states are known. Typical respective examples are 7,8-dihydrofolic acid (for dihydrofolate reductase), 7,8-dihydro(6H)biopterin (for dihydropteridine reductase), and 5,6,7,8-tetrahydrobiopterin (for aromatic amino acid hydroxylases). The biological importance of reduced pterin cofactors has stimulated many purely chemical studies on the physical properties and reactions of reduced pteridines. Several of these will be discussed.

The nature of the reactions of 5,6,7,8-tetrahydropterins with oxygen and other specific oxidising media, the tautomeric structure of 7,8-dihydro(6H)pterins and their ability to oxidise NADH have been examined to provide a better understanding of the structures and reactivity of the natural analogues. Similar studies with the natural cofactors, however, have shown that their reactions are not entirely similar to those of simpler pterins. These studies have assisted in resolving part of the mechanism of the enzymic reaction of dihydropteridine reductase.

Detailed ^1H and ^{13}C n.m.r. spectroscopy of reduced pterins in solution has revealed important features about the conformations of the reduced hydropyrazine ring and of the substituents in that ring. These features are important in the enzymic reactions with dihydropteridine reductase but not so important in the enzymic reactions with aromatic amino acid hydroxylases.

Chemical studies of this kind are very useful for understanding biological reactions, and may lead to improved assay procedures, understanding the mechanism of the diseased state, and hopefully for developing more effective drugs.