OXYGENATION OF SULFUR HETEROCYCLES WITH HEPATIC CYTOCHROME P-450

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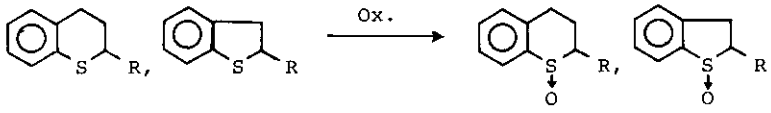
Stereochemistry of the enzymatic oxygenation of cyclic sulfides, benzothianes and 2,3-dihydrobenzothiophenes, to the corresponding sulfoxides with hepatic cytochrome P-450 obtained from phenobarbital pretreated rabbit has been investigated in comparison with that with the nonenzymatic oxidation by m-chloroperbenzoic acid and sodium metaperiodate.



(R = H, CH_3, C_8H_{17})

The formation of trans-2-methylbenzothiane 1-oxide predominated over that of cis-isomer in the enzymatic oxygenation of 2-methylbenzothiane (cis : trans = 18 : 82). On the other hand, nearly same amounts of both cis and trans isomers were obtained in the nonenzymatic oxidation of same compound (cis : trans = 45 : 55). Same trend was also observed in the same reactions of 2-methyl-2,3-dihydrobenzothiophene. Further stereochemical remark observed in the enzymatic oxygenation is the asymmetric induction on sulfur, i.e. the enzymatic oxygenation of 2,3-dihydrobenzothiophene afforded optically active 2,3-dihydrobenzothiophene 1-oxide ($[\alpha]_D^{25}$ = -7.3°, enantiomer excess = 3.0 %) whose absolute configuration is known to be R. The oxygenation of benzothiane also gave optically active sulfoxide ($[\alpha]_D^{25}$ = -21.8°, e.e. = 10.8 %) which showed same CD spectrum as (-)-2-methyl-2,3-dihydrobenzothiophene 1-oxide suggesting that its sulfur atom has R-configuration. The enzymatic oxygenation of benzothiane substituted by bulky alkyl group at 2-position such as n-octyl hardly proceeded in spite of its increased hydrophobicity.