From the viewpoint of enzyme technology, oxygenases, which incorporate molecular oxygen directly into organic substrates, are particularly intriguing since selective, direct oxygenation of organic substrates has traditionally been an unresolved challenge to organic chemistry. We have focused on oxygenase-catalyzed heteroatom oxygenation, epoxidation, hydroxylation, and ketonization of simple organic substrates (Fig. 1). These represent basic, synthetically important reactions. In all cases, the reactions involve highly stereo and regio selective insertions of molecular oxygen into organic substrates. Although we illustrate these three oxyfunctionalization reaction types for a few specific cases, work in progress indicates that several other enzymes, heretofore considered simple hydroxylases, also readily carry out these three processes with regio and stereo specificity.

Fig. 1. Basic types of enzymatic oxygenation reactions investigated.
Working with the copper-containing monooxygenase, dopamine-B-hydroxylase (DBH), we demonstrated for the first time sulfoxidation by an enzyme heretofore considered to be a hydroxylase (1,2). Sulfoxidation exhibits all the characteristics diagnostic of a monooxygenase reaction. For example, oxygen, substrate, and electron consumptions are stoichiometric with sulfoxide production. Product identities were established unequivocally by direct isolation and uv, ir, nmr, and mass spectral examination. Sulfoxidation is stereospecific, and the stereochemistry of oxygen attack is fully consistent with that established for DBH-catalyzed methylene hydroxylation (Fig. 2). On the basis of detailed kinetic experiments, we have established that sulfoxidation proceeds much more readily than hydroxylation for comparable substrates. In fact, DBH catalyzes sulfoxidation more rapidly than any other reaction; and designation of this enzyme as a hydroxylase is obviously misleading. Thus, preparative scale production of mg/ml quantities of essentially optically pure sulfoxides is easily accomplished, even with crude enzyme preparations. In sharp contrast, microsomal sulfoxidation has been reported to result in only the slightest (1%) enantiomeric enrichment.

Fig. 2. Stereochemical consistency of sulfoxidation and hydroxylation products produced by DBH.

Fig. 3. Pathway for ketonization.