

## Cover Picture

**Ashraf Brik, Lawrence J. D'Souza, Ehud Keinan, Flavio Grynszpan, and Philip E. Dawson**

**The cover picture shows** a schematic representation of the mechanistic and catalytic diversity exhibited by mutants of 4-oxalocrotonate tautomerase (4-OT). A designed single amino acid substitution can alter the catalytic activity and mechanism of this enzyme. While the wild-type 4-OT catalyzes only the tautomerization of oxalocrotonate through a general acid/base mechanism, the Pro1Ala mutant catalyzes two reactions—the original tautomerization reaction through an acid/base mechanism and the decarboxylation of oxaloacetate by a nucleophilic mechanism. This bifunctional mutant suggests that a new synthetic family of nucleophilic catalysts could be generated on the basis of the 4-OT scaffold through selection methods and rational protein engineering. For more details, see the article by Brik et al. on p. 845 ff.

