It will be remembered that in the original Lewis definitions we used the words electrophile and nucleophile interchangeably with acid and base, and this often tends to be the case in general usage. However, it also is true that a distinction frequently is made to the extent that the terms basicity and acidity are used in situations which are thermodynamically determined, and the terms nucleophilicity and electrophilicity in situations which are kinetically determined. For example, while methylate anion, H_3CO^- is a considerably stronger base than methanethiolate anion, H_3CS^- (the pK_A of methanol is 16, that of methanethiol is 10), methanethiolate is said to be the better nucleophile, or more nucleophilic, than methylate (in protic solvents), because displacement reactions in protic solvents carried out with methanethiolate ordinarily proceed at faster rates — often faster by as much as a factor of a million — than the corresponding reactions initiated by methylate. As a general rule for protic solvents, while nucleophilicity increases with basicity as one moves from right to left in the periodic table, nucleophilicity increases as one moves down a column — that is, from oxygen to sulfur, or from nitrogen to phosphorous. This is in contrast to basicity, which tends to increase as one moves up a column in the periodic table. Perhaps it should not be surprising that enzymes, which function to increase reaction rates in living systems, yet which, by the same token, must be able to operate at cellular pH values fairly near to neutral, have evolved to employ sulfur to initiate displacement reactions.