Tetrahedron Letters No. 5, pp 389 - 392, 1973. Pergamon Press. Printed in Great Britain.

VIBRATIONAL ACTIVATION I. A SOURCE FOR THE CATALYTIC POWER OF ENZYMES

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(Received in USA 28 September 1972; received in UK for publication 2 January 1973)

Intramolecular reactions and, to a greater extent, reactions within enzyme-substrate complexes, exhibit rate accelerations over their intermolecular counterparts. Many explanations have been offered, such as orbital steering, rotational and translational entropy reduction, and other steric effects.[1] However, the proponents of each theory have convincingly shown that all the other theories could not account for the sometimes enormous magnitude of enzyme catalysis.

We therefore suggest a new factor in chemical transformations. (1) Reactions of complex molecules requiring significant activation energy take place only through vibrational, not translational, activation. Thus, the reacting molecule (or one of them if there are two) must possess enough vibrational energy to surmount the barrier. (2) The formation of a new bond must be vibrationally coupled to the breaking of the old, vibrationally exicted, bond, and this coupling requires sufficient time for several vibrations, not just one. If a single bond breaks, it too needs vibrational excitation and time enough for several vibrations; and, of course, the microscopic reverse holds as well.

Principle (1) is not new, having been proposed long ago,[2] though perhaps not yet as a completely general one. It has considerable experimental and theoretical support. Bauer, Lifshitz and co-workers[3] have discovered several reactions, *e.g.*, H-D exchange between D_2 and NH_3, which require only vibrational and not translational energy. Other groups, too, have reported this phenomenon,[4] and an example is known[5] in which ample translational energy was unable to induce reaction between vibrationally cold partners (HI and DI). In the exothermic direction, which is the microscopic reverse of (1), the formation of products in high vibrational, rather than translational, energy states has long been known.[6] Extensive theoretical studies by Polanyi and co-workers also support the general idea that endothermic reactions require vibrational energy, and exothermic ones give vibrationally excited products.[7]

Principle (2) is, to our knowledge, novel,[8,9] and it is the heart of the matter because it leads to the concept that not only is translational energy of little use in promoting chemical change, but it actually <u>inhibits</u> when present in excess. This comes about because molecules undergoing hard collisions rebound in less time than it takes for vibrational coupling to take place. Thus, soft collisions are most effective, and the harder the collision, the less likely the reaction.

It follows, then, that any agency, such as intramolecularity or association with an enzyme, which <u>immobilizes</u> the reactants will increase the reaction rate by permitting only soft collisions, and the degree of catalysis will be related to the degree of immobility. It is obvious that the reactants must be held within bonding distance, but the exact placement associated with orbital steering is not needed. Immobility includes the reduction of rotational and translational entropy, but goes far beyond these effects.

The role of the enzyme is to insure that energy bound substrate molecule reacts the moment it acquires, through thermal agitation, sufficient vibrational energy to surmount the activation barrier. In contrast, free-floating molecules may acquire vibrational energy as often as bound ones do, but comparatively few react before losing their excess vibrational energy because they are moving too fast. It may be that the enzyme exerts an additional ponderal effect in that the massive complex receives energy primarily as vibration, while small molecules do so primarily as translation. Conceivably, the vibrational modes of the complex are even such as to channel energy into the active site.[10]

This proposal might also serve to rationalize the Lindemann-Hinshelwood theory, which was invoked to account for the first-order kinetic anomaly,[11] although other explanations are not lacking.[12]

A further result of the vibrational-activation theory is the imposition on all reactions of a small negative activation energy factor, arising from the reduction in the number of soft collisions with rise in temperature, and causing the experimental Ea to be less than the "true" Ea. Normally masked, this effect emerges only for simple reactions with very small barriers, such as atom recombinations.[9]

Further ramifications of the vibrational-activation theory[13] will appear in due course.

Footnotes and References

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