Formation and transfer of HCl in a macromolecular noncovalent complex: does the roaming atom mechanism play a role?

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In the last twenty years, the “roaming atom” mechanism emerged and gained enormous interest thanks to its success in explaining experimental results that are not accounted for by the widely accepted statistical transition state theory.[1] In the roaming atom mechanism, on the pathway from reactants to products of a given chemical reaction, there is no tight transition state, defined as a saddle point on the potential-energy surface (PES) of the system. Instead, the roaming atom (or group of atoms) explores large and relatively flat regions of the PES, bypassing saddle points. Along its trajectory, “frustrated bonds” between the roaming species and other atoms of the system are successively formed and cleaved.[2] A crucial characteristic is the low total energy required for the roaming atom mechanism to play a major role, once the roaming radical is formed. Another characteristic of the roaming atom mechanism is the asymmetric energy partitioning between the reaction products.

Despite intense efforts for describing this new mechanism, intriguing questions remain. A crucial one is: does it play a role in molecular systems larger than 25 atoms, in particular those relevant to life sciences and pharmacology? Here, we present data on HCl transfer within a noncovalent complex built upon vancomycin, an antibiotic containing more than 170 atoms, and a tripeptide, following UV-VUV photoabsorption in the gas phase. Our experimental results show that the energetics for HCl formation is unusually low, as compared to a straightforward direct abstraction mechanism governed by the transition state, which energy budget has been evaluated by quantum chemistry calculations.[3] Strikingly, we observe an asymmetric internal energy partitioning between the released product anions. Furthermore, the mechanism for HCl formation and transfer implies atypical motion of the reactive Cl radical. We believe that only a roaming atom mechanism can account for these observations. Our results provide a benchmark for future theoretical investigation, not only on HCl loss from molecules, but more broadly on the roaming atom mechanism itself. Moreover, they also raise other questions, for instance whether this mechanism is common in biological molecular systems, and even dominant in some cases.

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