Angewandte Highlights

Atom Tunneling

DOI: 10.1002/anie.201200991

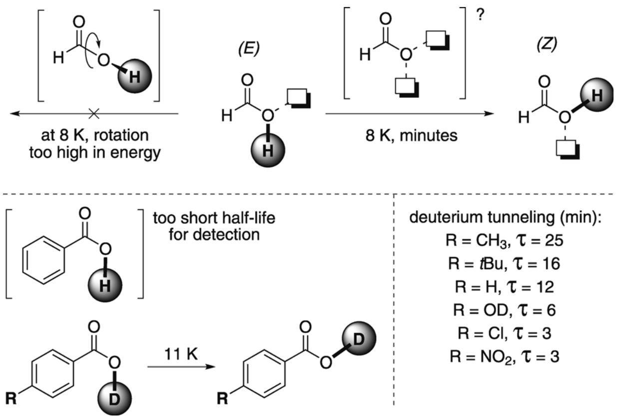
Atom Tunneling in Organic Transformations**

*Frederic W. Patureau**

atom tunneling · kinetic isotope effects ·
transition states

“*Rien ne se perd, rien ne se crée, tout se transforme.*”[1] Had Lavoisier known of today’s quantum physics and chemistry, of the tunneling behavior of atoms, would he still formulate his famous quote unchanged? The classical transition-state theory, in which chemical reactions are depicted as the result of the “gliding” movement of atoms through space, breaking selected covalent bonds in the substrates and forming new ones in the products is a well-established model in organic transformations, on which the concepts of kinetic and thermodynamic control commonly rely.[2] Although it is a very intuitive, visual, and, therefore, practical theory, many inspired scientists have expressed their suspicions throughout modern times that atoms may possess other modes of traveling.[3] Atom tunneling, that is, the disappearance of an atom from a given location and its simultaneous reappearance at another, simply obviating an otherwise high-energy transition state, is a consequence of the wave–particle duality paradox.[4] Until recently though, tunneling effects did not receive much attention from the organic chemistry community. In this respect, the discovery in 2002 by Pettersson et al. that (*E*)-formic acid could isomerize to the more stable and ubiquitous *Z* isomer through a tunneling event of the acidic proton is very significant.[5] More recently, in a brilliant series of reports between 2008 and 2012, Schreiner, Allen et al. have accurately measured tunneling events by comparing the isomerization rates of some hydroxycarbenes[6] as well as a series of carboxylic acid derivatives[7] as a function of the isotope involved (hydrogen or deuterium). The overwhelming evidence they offer us today is that tunneling events are in fact not rare at all in organic transformations, and deserve to be understood by organic chemists, at least as far as the hydrogen atom is involved. A short list of illustrative examples is highlighted herein, in the hope that the reader will concur with the significance of tunneling events in understanding organic transformations.

In a pioneering report about atom tunneling in small organic molecules, Pettersson et al. isolated and characterized by IR spectroscopy the *E* isomer of formic acid, which is only possible at very low temperature because of its intrinsic high reactivity for isomerization to the *Z* isomer. This event occurs within minutes, even at 8 K.[5] Their calculations showed, however, that the rotational transition state between the *E* and *Z* isomers was so high in energy that the isomerization rate should be some ten trillion times slower than observed experimentally, thus making it fairly certain that the H atom displaces itself through tunneling (Scheme 1). Furthermore, the isomerization of (*E*)-[D$_1$]formic acid (HCO$_2$D) is at least three orders of magnitude slower, which confirms the tunneling mechanism.[8] Later, in 2010, Schreiner et al. developed the understanding of H tunneling in carboxy moities considerably by comparing the tunneling rates of a series of substituted benzoic acid derivatives.[7] Unlike the formic acid case, the authors discovered that (*E*)-benzoic acids are undetectable on the time scale of the reaction (minutes), even at 11 K. Calculations suggest that the width of the energy barrier between the *E* and *Z* isomers is in fact narrower, such that the gap or distance (expressed, for example, in Å) between the locations of departure and destination is smaller. Thus, tunneling occurs faster. This observation intuitively implies that tunneling is facilitated by space proximity. Switching to the [D$_1$]-deuterated analogues proved rewarding, however, as the half-lives of the *E* isomers (τ) became experimentally measurable—from 3 to 25 min depending on the electronic substitution pattern on the benzene ring. Temperature variation (11 to 20 K) does not



Scheme 1. Isomerization of (*E*)-formic acid at 8 K (top) and of (*E*)-[D$_1$]benzoic acids (11 K, beneath). τ: half-life of *E* isomers (in min).

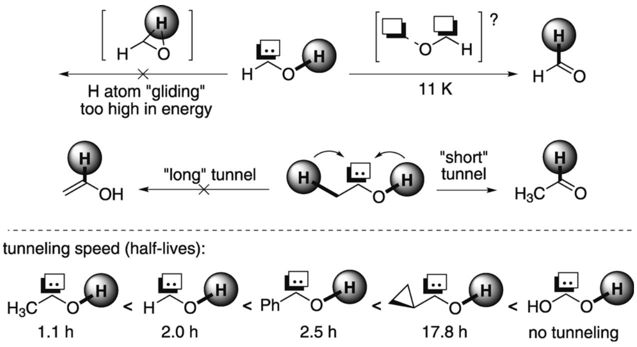
---

[*] Prof. Dr. F. W. Patureau
Fachbereich Chemie, Technische Universität Kaiserslautern
Erwin-Schrödinger-Str., Geb. 52, 67663 Kaiserslautern (Germany)
E-mail: patureau@chemie.uni-kl.de
Homepage: http://www.chemie.uni-kl.de/index.php?id=patureau

[**] The work was supported by the DFG-funded trans-regional collaborative research center SFB/TRR 88 “Cooperative effects in homo- and heterometallic complexes (3MET)”. Corinna Nimphius is acknowledged for discussions.

affect these rates, and thus excludes a rotational transition-state mechanism (over the barrier). This discovery is very significant because it shows that the acidic deuterium atom of an electron-poor carboxylate will tunnel faster than that of an electron-donating one. The authors argue that variations in the width of the energy barrier are the main cause of this effect. It should be noted, however, that deuterium, although twice as heavy, still tunnels at substantial rates in those transformations. Therefore, the simultaneous disappearance of two nucleons (or more) is not to be underestimated in organic transformations.[9]

Schreiner et al. also studied thoroughly the prototropic isomerization of several classes of hydroxycarbenes to the more stable aldehyde isomers.[6] This transformation is particularly interesting because, unlike the previous one, the H atom shifts to a different atom in the molecule. In 2008, Schreiner, Allen et al. reported the isolation and characterization of the elusive hydroxymethylene at 11 K and its isomerization to the more stable formaldehyde isomer through a tunneling mechanism ($\tau = 2$ h). On the other hand, the deuterated analogue is stable, which excludes all forms of the "gliding" mechanism (Scheme 2). In 2011, the authors tackled the subtle case of methylhydroxycarbene. This case is particularly interesting because a competition can now take place between H tunneling of the hydroxy proton (acetaldehyde product) and H tunneling of a methyl proton (vinyl alcohol product). Calculations predict that the classical transition-state energy is $5\,\mathrm{kcal\,mol^{-1}}$ lower for the latter than for the former, but the experiment leads exclusively to the acetaldehyde product, because the tunneling distance is shorter. This experiment is remarkable because it formally establishes a tunneling event, which overrides kinetic and thermodynamic considerations. Thus, the chemoselectivity is controlled by the tunneling event. What is also very instructive is that the tunneling rate is heavily dependent on the electronic character of the hydroxycarbene substituent. The π-donating or withdrawing character of substituents (such as methyl, through hyperconjugation of C$-$H σ bonds, or conjugation with an arene, etc), seems to be important.[6e] Nevertheless, it remains difficult to draw a direct and general correlation between remote electronic substitution and the tunneling rate, simply because the atom tunneling mechanism is not well understood and may also involve other local physical parameters. Another intriguing question is where does the atom disappear from and reappear on the potential energy surface, and how. The speed of this process (tunneling time) is also the subject of intense debate.[10] Nevertheless, these experiments open the way for new exciting discoveries regarding the nature of atoms and their surroundings, through the experimental study of organic reactions.



Scheme 2. Isomerization of hydroxycarbene derivatives at 11 K.

In summary, hydrogen and deuterium atom tunneling are common in prototropic organic reactions. It is helpful to study these events in cryogenic conditions to minimize thermal side reactions. There is no reason, however, to believe that these events should not take place in any average organic reaction. Analysis of room temperature tunneling events in organic transformations will probably develop in the coming years, as a result of the awareness of the scientific community. It might also be taking place in many transition-metal-catalyzed reactions, at least those involving metal-hydride intermediates (hydrogenations, C$-$H activations),[11] and thus will have profound consequences on catalyst design and optimization.

Received: February 6, 2012

---

[1] This conservation-law statement is commonly attributed to A. L. de Lavoisier, and means roughly: "nothing appears, nor disappears, but it all transforms." It is sometimes considered by scholars to mark the end of the alchemist era and the dawn of modern chemistry, see A. L. de Lavoisier, *Traité Elémentaire de Chimie* **1789**.

[2] a) H. Eyring, *J. Chem. Phys.* **1935**, *3*, 107; b) M. G. Evans, M. Polanyi, *Trans. Faraday Soc.* **1935**, *31*, 875.

[3] a) See Ref. [2a] and also: b) R. P. Bell, *The Tunnel Effect in Chemistry*, Chapman and Hall, London, **1980**.

[4] a) L. de Broglie, *Nature* **1923**, *112*, 540; b) the term "tunneling" accommodates well the particulate character of atoms, but this event seems more in accordance with their wave character.

[5] a) M. Pettersson, J. Lundell, L. Khriachtchev, M. Räsänen, *J. Am. Chem. Soc.* **1997**, *119*, 11715, and references therein; b) M. Pettersson, E. M. S. Maçôas, L. Khriachtchev, J. Lundell, R. Fausto, M. Räsänen, *J. Chem. Phys.* **2002**, *117*, 9095.

[6] For some of the related studies on hydroxycarbenes, see a) P. R. Schreiner, H. P. Reisenauer, F. C. Pickard IV, A. C. Simmonett, W. D. Allen, E. Mátyus, A. G. Császár, *Nature* **2008**, *453*, 906; for early highlights, see b) M. Räsänen, *Nature* **2008**, *453*, 862; c) G. Bucher, *Angew. Chem.* **2008**, *120*, 7064; *Angew. Chem. Int. Ed.* **2008**, *47*, 6957; d) D. Gerbig, H. P. Reisenauer, C.-H. Wu, D. Ley, W. D. Allen, P. R. Schreiner, *J. Am. Chem. Soc.* **2010**, *132*, 7273; e) P. R. Schreiner, H. P. Reisenauer, D. Ley, D. Gerbig, C.-H. Wu, W. D. Allen, *Science* **2011**, *332*, 1300; f) D. Ley, D. Gerbig, J. P. Wagner, H. P. Reisenauer, P. R. Schreiner, *J. Am. Chem. Soc.* **2011**, *133*, 13614.

[7] S. Amiri, H. P. Reisenauer, P. R. Schreiner, *J. Am. Chem. Soc.* **2010**, *132*, 15902.

[8] A kinetic isotope effect (KIE $= k_H/k_D$) above 7 usually implies an atom tunneling control of the rate.

[9] For selected examples of heavy atom tunneling, see a) B. K. Carpenter, *J. Am. Chem. Soc.* **1983**, *105*, 1700; b) P. S. Zuev, R. S. Sheridan, T. V. Albu, D. G. Truhlar, D. A. Hrovat, W. Thatcher Borden, *Science* **2003**, *299*, 867; c) R. A. Moss, R. R. Sauers, R. S. Sheridan, J. Tian, P. S. Zuev, *J. Am. Chem. Soc.* **2004**, *126*, 10196; d) O. M. Gonzalez-James, X. Zhang, A. Datta, D. A. Hrovat, W. Thatcher Borden, D. A. Singleton, *J. Am. Chem. Soc.*

2010, *132*, 12548; e) D. Gerbig, D. Ley, P. R. Schreiner, *Org. Lett.* **2011**, *13*, 3526, and references therein.

[10] P. C. W. Davies, *Am. J. Phys.* **2005**, *73*, 23, and references therein.

[11] a) P. W. N. M. Van Leeuwen, *Homogeneous Catalysis: Understanding the Art*, Kluwer, Dordrecht, **2004**; b) *C-H activation* (Eds.: J.-Q. Yu, Z.-J. Shi), *Top. Curr. Chem.* **2010**, *292*. See also: c) J. E. Bercaw, G. S. Chen, J. A. Labinger, B.-L. Lin, *J. Am. Chem. Soc.* **2008**, *130*, 17654; d) Z. Pan, J. H. Horner, M. Newcomb, *J. Am. Chem. Soc.* **2008**, *130*, 7776; e) E. J. Klinker, S. Shaik, H. Hirao, L. Que, Jr., *Angew. Chem.* **2009**, *121*, 1317; *Angew. Chem. Int. Ed.* **2009**, *48*, 1291; f) S. Fukuzumi, T. Kobayashi, T. Suenobu, *J. Am. Chem. Soc.* **2010**, *132*, 1496, and references therein.