parameters converged at $R = 0.044$ for 3122 observed reflections with $I > 2\sigma(I)$ and $wR2 = 0.096$ for all reflections. Min./max. residual electron density $-0.219/0.208\,\text{e}\,\text{Å}^{-3}$. The structure solution was carried out using SHELXS-86, the structure refinement with SHELXL-93. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-101494". Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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How Does the Intrinsic Barrier of Intermolecular Proton Transfer Depend on Molecular Parameters?**

Martin Goez* und Rainer Heun

Especially with regard to biological systems, intermolecular proton transfer must be counted among the most important elementary chemical processes; its significance is comparable with that of electron transfer.[1] These two reaction types also have much in common conceptually, because the two lightest chemical particles are transferred and the overall structural changes are not very large. Yet, the difference in their theoretical understanding is considerable. Well established for both is that the relationship between thermodynamics and kinetics—that is, between the driving force of the reaction $-\Delta G^{\ominus}$ and the activation barrier $\Delta G^{\ddagger}$—can be expressed in terms of a single parameter, the intrinsic barrier $\Delta G^{\ddagger}_{\text{int}}$, which is the activation barrier for the (often hypothetical) reaction with $\Delta G^{\ominus}$ equal to zero.[2] However, asking for the factors that govern the magnitude of the key quantity $\Delta G^{\ddagger}_{\text{int}}$ reveals a fundamental gap in our knowledge. While $\Delta G^{\ddagger}_{\text{int}}$ of electron transfer can be predicted numerically from molecular geometries, force constants, and charge densities,[3] much less is known about the dependence of $\Delta G^{\ddagger}_{\text{int}}$ on molecular parameters in the case of proton transfer.[4–6] Here we explore the influence of electronic factors on $\Delta G^{\ddagger}_{\text{int}}$ of proton transfer experimentally, and develop a valence bond configuration mixing (VBCM) model that is capable of explaining the results.

For the substrates we chose *para*-substituted *N,N*-dimethylanilines B, because these compounds lend themselves very well to a separation of electronic and steric effects: By changing the *para* substituent the electron density at the base center can be varied with negligible influence on the geometry of this site and the steric requirements for the reaction. Intermolecular proton transfer is often complicated by participation of the solvent (relay mechanism),[7] which causes the apparent (i.e., observed) activation barrier to be a compound quantity.[6] To avoid this, we carried out the experiments in water-free acetonitrile, which does not function as a hydrogen-bond donor and is a much weaker hydrogen-bond acceptor than is water.[8] The intrinsic barriers $\Delta G^{\ddagger}_{\text{int}}$ were obtained directly from measurements of the rates of proton self-exchange [Eq. (1)] between the unprotonated and protonated forms B and BH^+ of our substrates by means of dynamic NMR spectroscopy.

$$BH^+ + B \rightleftharpoons B + BH^+ \qquad (\Delta G^{\ominus} = 0,\ \Delta G^{\ddagger} = \Delta G^{\ddagger}_{\text{int}}) \qquad (1)$$

Not only is this approach more economical than the usual one—namely, using the Marcus theory[2b] to calculate $\Delta G^{\ddagger}_{\text{int}}$ from the activation barriers of a series of homologous cross reactions—it is also much more reliable because it circumvents the difficulties associated with the determination of $\Delta G^{\ominus}$, that is, the problem of acidities in a nonaqueous solvent.

All experimental details are given in a previous paper,[9] where the mechanism of these reactions was also cleared up in detail. As was shown there, thermally activated direct proton transfer between BH^+ and B is rate-determining; relayed proton transfer involving the solvent or residual water is absent, and formation of hydrogen bonds between BH^+ and B as well as tunnelling do not play a significant role. These findings mean that a unique and well-defined reaction mechanism is realized in these systems, which is an indispensible prerequisite for a study aiming to quantify the influence of molecular parameters on the intrinsic barrier of proton transfer.

As Figure 1 shows, there exists a good linear correlation between the values for $\Delta G^{\ddagger}_{\text{int}}$ obtained in this way and the Hammett parameter σ^+. While σ^+ is not a molecular property of our substrates, it is nevertheless related to such: It is well known that σ^+ is a quantitative measure of the electron density at the nitrogen atom in these compounds, and basicity as well as ionization potential I_v of B are linear functions of σ^+.[10] This correspondence will play a key role for the theoretical interpretation that follows. We stress that Figure 1 differs in its implications from a usual Hammett plot: The latter is either a linear relationship between free energies or—when it is of the type $\lg k$ versus Hammett parameter—reflects the influence of the driving force of a reaction on its rate. However, for our self-exchange reactions $\Delta G^{\ominus}$ is zero, and the plot reveals how the *intrinsic* activation barrier $\Delta G^{\ddagger}_{\text{int}}$ depends on an electronic parameter of the reactants. It is seen that the height of $\Delta G^{\ddagger}_{\text{int}}$ is a linear function of the electron density at the nitrogen atom, and the higher the latter, the lower the intrinsic barrier. As a qualitative general trend, this behavior has been reported,[4] but to the best of our knowledge a linear relationship has not been observed before.

These findings can be explained by a VBCM model (Figure 2). Such models were introduced by Pross and Shaik,

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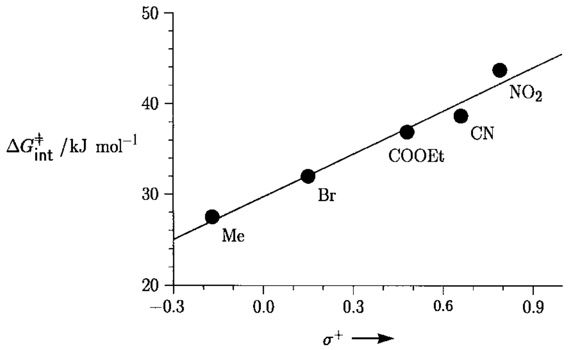

Figure 1. Proton self-exchange of *para*-substituted *N,N*-dimethylanilines in acetonitrile. The plot displays the intrinsic barrier $\Delta G^{\ddagger}_{\rm int}$ as a function of the Hammett parameter σ^+. The labels at the data points denote the *para* substituent.

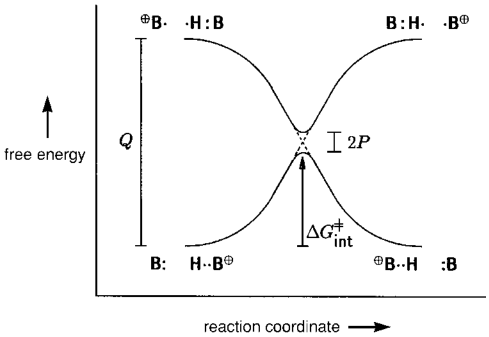

Figure 2. Valence bond configuration mixing (VBCM) model for proton self-exchange between a base B and its conjugated acid BH$^+$. For further explanation, see the text.

and have already been applied very successfully to many types of chemical reactions, for instance, nucleophilic aliphatic substitutions or cycloadditions.[11] The advantage of a valence bond (VB) description over a molecular orbital (MO) description is that VB configurations provide more chemical insight in the sense that they can be translated directly into a chemical picture and, above all, chemical notation (see below). On the other hand, in the limit of infinite basis sets and infinite configuration interaction, VB and MO models are completely equivalent.

The central idea of the VBCM approach is that the activation barrier of a chemical reaction arises from an avoided crossing of VB configurations. A minimum set of two configurations is very often sufficient: the reactant configuration, which provides the best VB description of the reacting sites in the reactants, and the product configuration, which is the analogue for the products. In our case, each configuration comprises the lone pair at the nitrogen atom in B and the N–H bond in BH$^+$; hence, the reactant configuration (lower left of Figure 2) is written as $B\colon H\cdots B^{\oplus}$, and the product configuration (lower right) as $^{\oplus}B\cdots H\ {:}B$. The free energies of these configurations are of course equal, which holds for every self-exchange reaction. The transfer of the proton in either direction is accompanied by an increase in the free energy of the respective starting configuration, because the N–H bond must be stretched and an unfavorable three-electron interaction arises between the lone pair and the approaching hydrogen atom. At the final geometry, the starting configuration is thus an excited configuration. The reactant configuration at the product geometry (upper right of Figure 2) can be represented as $B\colon H\cdots B^{\oplus}$, and the product configuration at the geometry of the reactants (upper left) as $^{\oplus}B\cdots H\ {:}B$. Owing to the symmetry of the reaction, both excitation energies are identical.

It is clear that the two configuration curves would cross during the reaction, as indicated by the dashed lines in Figure 2. However, around the crossing point they are degenerate or nearly degenerate in free energy, so any interaction between them—which is given by the matrix element $\langle\psi_{\rm p}|\boldsymbol{H}|\psi_{\rm e}\rangle$, where $\psi_{\rm e}$ and $\psi_{\rm p}$ are the configurations and $\boldsymbol{H}$ the Hamiltonian—causes a splitting of the levels. The amount of splitting $2P$ is determined by the ratio of $|\langle\psi_{\rm p}|\boldsymbol{H}|\psi_{\rm e}\rangle|$ to the difference $|G(\psi_{\rm p}) - G(\psi_{\rm e})|$ calculated in the absence of an interaction between the configurations; it is, therefore, largest at the crossing point and decreases monotoneously when the system moves away from it. Owing to this mixing of configurations, the resulting curves (the solid lines in the center part of Figure 2) no longer connect the same configurations on both sides of the diagram. Instead, a change of configurations occurs in the vicinity of the avoided crossing.

The activated complex corresponds to the highest point on the lower curve in Figure 2. From simple geometric considerations,[11] the intrinsic barrier $\Delta G^{\ddagger}_{\rm int}$ is given by Equation (2).

$$\Delta G^{\ddagger}_{\rm int} = f\cdot Q - P \tag{2}$$

The factor f takes into account the location of the transition state. Hence, f depends on the thermodynamics of the reaction (not applicable in our case) and on the functional form of the potential curves. Within a homologous series of substrates this form can hardly change, so f should be constant in our systems. The initial gap Q describes the separation of the configuration curves before the reaction (reactants *and* products at the geometry of the reactants); that is, Q is the free energy needed to excite the reactant configuration vertically. The splitting parameter P is predominantly determined by symmetry (for instance, P is directly responsible for the Woodward–Hoffmann rules),[11] so it should also be constant within our homologous series.

We point out that this VBCM model is essentially identical to the Marcus theory of electron transfer[2a,3a] despite the differences in notation: The Marcus expression for the intrinsic barrier of electron transfer is given by Equation (3),

$$\Delta G^{\ddagger}_{\rm int} = \lambda/4 \tag{3}$$

where the reorganization energy λ is the free energy needed to distort the geometry of the reactants (including that of the solvent shell) to that of the products, without transferring the electron. It is evident that λ is identical to the initial gap Q of the VBCM treatment. Furthermore, in the Marcus model nonadiabatic electron transfer (i.e., negligible P) and parabolic potential curves are assumed. Owing to the latter condition, f becomes equal to 1/4, so Equation (2) is transformed into Equation (3).

Reverting to the discussion of Equation (2), the dependence of $\Delta G^{\ddagger}_{\rm int}$ on the electronic properties of our substrates obviously arises through the quantity Q. The vertical transition from the VB configuration of the reactants to that of the products can be associated with a concrete chemical picture: The lone pair in B must be oxidized vertically, and the liberated electron must be accommodated by the antibonding orbital of the N–H bond in BH^+. This notion immediately leads to a linear relationship [Eq. (4)] with constants a and b.

$$\Delta G^{\ddagger}_{\mathrm{int}} = a\cdot[I_{\mathrm{v}} - E(\sigma^{*}_{\mathrm{NH}})] + b \qquad (4)$$

As the oxidation potential of B in solution is unavailable for most of our compounds, because they are irreversible redox systems,[10b] the (vertical) gasphase ionization potential I_{v}, which is known to be proportional to the former,[11c] has been used in Equation (4). AM1 calculations indicate that the preferred geometry of the N–H bond in BH^+ is in the plane of the aromatic ring. Because the electronic influence of the *para* substituent is transmitted predominantly through the π system, only a negligible interaction between this substituent and the N–H bond is possible, and the energy $E(\sigma^{*}_{\mathrm{NH}})$ of the antibonding orbital of this bond is expected to be constant within our homologous series. This yields a linear relationship between $\Delta G^{\ddagger}_{\mathrm{int}}$ and I_{v} [Eq. (5)] and explains, by virtue of the known fact that I_{v} and σ^+ are linear functions of one another,[10d] the experimentally observed dependence (Figure 1) of the intrinsic barrier on the Hammett parameter σ^+.

$$\Delta G^{\ddagger}_{\mathrm{int}} = a'\cdot I_{\mathrm{v}} + b' = a''\cdot\sigma^+ + b'' \qquad (5)$$

The intrinsic activation barriers of proton transfer have frequently been rationalized with the principle of nonperfect synchronization (PNS),[4,5] which states that the barrier arises because charge delocalization and above all solvation lag behind the motion of the proton. Ab initio calculations,[5c] however, indicate that the effect should also be pronounced in the gas phase, that is, in the absence of solvation. Hence, as in the case of electron transfer a significant inner-sphere contribution to the intrinsic barrier must exist, which is consistent with previous experimental results for our systems.[9] Although the present work is concerned with this inner-sphere term only, the VBCM model is expected to cover the solvent dependence of $\Delta G^{\ddagger}_{\mathrm{int}}$ as well when I_{v} is measured in the medium used.

The PNS allows quantitative correlations between $\Delta G^{\ddagger}_{\mathrm{int}}$, the slopes of Brønsted plots, and thermodynamics, but its potential for quantitative predictions of $\Delta G^{\ddagger}_{\mathrm{int}}$ from molecular parameters of the reactants seems to be limited. It is our view that the VBCM approach is better suited for this task, while at the same time being just as intuitive and transparent as the PNS, and that for these reasons and because of its firm quantum mechanical basis the former should be preferred.

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