IOSR Journal of Applied Chemistry (IOSR-JAC)
e-ISSN: 2278-5736. Volume 16, Issue 3 Ser. II (March 2023), PP 58-62
www.iosrjournals.org

Mechanistic and Kinetic Investigation of Proton Transfer Reactions in Apolar Aprotic Media

Prof. (Dr.) Udai Arvind
P.G. Department of Chemistry
Jai Prakash University, Chapra, Bihar. India

Dr. Chandra Mohan Singh
M.Sc., Ph.D. Jai Prakash University, Chapra, Bihar. India

Abstract
Proton transfer (PT) is among the most fundamental of chemical events, yet its mechanism and kinetics change dramatically when the reaction is removed from hydrogen-bonding, protic environments and placed in apolar aprotic media such as hexane, benzene, toluene, or chlorobenzene. In the absence of a solvent capable of stabilising developing charge through hydrogen bonding, proton transfer between acid–base pairs proceeds largely through pre-organised hydrogen-bonded complexes, and the rate-determining step frequently shifts from diffusional encounter to an intrinsic, quantum-mechanically assisted barrier crossing. This paper reviews and re-examines, in an integrated mechanistic–kinetic framework, the principal experimental and theoretical evidence for proton transfer in apolar aprotic solvents. Eyring-type kinetic analysis of illustrative rate data yields an activation enthalpy of 59.8 kJ mol⁻¹ and an activation entropy of −81.4 J mol⁻¹ K⁻¹, consistent with a compact, ordered transition state stabilised by a pre-formed hydrogen bond. A comparative survey of rate constants across seven solvents of increasing dielectric constant shows a strong, though non-linear, dependence of the observed rate on bulk polarity, which is interpreted using Kirkwood-type electrostatic continuum models together with specific short-range solvation effects. The Bell–Marcus and Brønsted formalisms are used to rationalise curvature in free-energy relationships, and the role of hydrogen tunnelling is evaluated through kinetic isotope effect (KIE) considerations. The paper concludes that proton transfer kinetics in apolar aprotic media cannot be explained by bulk dielectric arguments alone and require an explicit treatment of pre-association, tunnelling, and local solvent structure.

Keywords: *Proton transfer; Apolar aprotic solvents; Eyring analysis; Activation parameters; Hydrogen tunnelling; Kinetic isotope effect (KIE); Marcus theory; Brønsted relationship; Solvent polarity; Hydrogen-bonded complexes*

I. Introduction

Proton transfer reactions occupy a central place in physical organic chemistry because they combine light-atom quantum dynamics with strong electrostatic and solvation coupling (Bell, 1980; Kresge, 1975). Most classical treatments of proton transfer, including the Eigen mechanism for acid–base reactions in water, were developed for protic solvents in which the solvent itself participates directly as a proton donor or acceptor and stabilises the developing charge through an extended hydrogen-bond network (Eigen, 1964). Apolar aprotic solvents — hydrocarbons, aromatics, and low-polarity ethers — offer a fundamentally different environment: they cannot hydrogen-bond to the transferring proton, they possess low dielectric constants (typically $\varepsilon_r = 2–8$), and they cannot support the Grotthuss-type relay mechanism seen in water (Marcus, 1968).

Consequently, proton transfer in these media is normally confined to reactions between an acid and a base that are already capable of forming an intermolecular hydrogen bond, such as substituted phenols and amines, carboxylic acids and pyridines, or nitroalkanes and amidines (Caldin & Mateo, 1975; Crooks, 1975). The absence of a stabilising dielectric continuum means that the free energy of the reaction and the height of the intrinsic barrier are far more sensitive to the specific structure of the hydrogen-bonded complex than to the bulk solvent polarity. This has made apolar aprotic media a valuable testing ground for mechanistic theories of proton transfer, including the Marcus cross-relation, the Bell tunnelling correction, and Brønsted-type free-energy relationships (Marcus, 1968; Bell, 1980; Kreevoy & Truhlar, 1986).

The present paper has three aims. First, it reviews the mechanistic picture that has emerged for proton transfer in apolar aprotic solvents, emphasising the role of pre-association complexes and the breakdown of simple encounter-controlled kinetics. Second, it presents an Eyring-based kinetic analysis of representative rate data to extract activation parameters and interpret them mechanistically. Third, it examines how the observed rate

constant varies with solvent dielectric constant across a series of apolar and weakly polar aprotic solvents, and evaluates the extent to which continuum electrostatic theory can account for this variation.

II. Mechanistic Framework

2.1 The Hydrogen-Bonded Pre-Association Complex

In water and other protic solvents, proton transfer between an acid HA and a base B is frequently diffusion-controlled when the reaction is thermodynamically favourable, because the solvent itself can relay the proton through successive hydrogen bonds (Eigen, 1964). In apolar aprotic media this relay pathway is unavailable, so an intrinsic A–H···B hydrogen bond must form directly between the reacting partners before proton transfer can occur (Caldin & Mateo, 1975). The overall process is therefore usually written as a two-step mechanism: rapid, often diffusion-controlled formation of a hydrogen-bonded complex, followed by a slower, thermally activated internal proton transfer within that complex (Crooks, 1975):

$$HA + B \rightleftharpoons HA\cdots B \rightarrow A^{-}\cdots H{-}B^{+}$$

Because the second step occurs within an essentially pre-organised, low-dielectric cavity, its rate is governed largely by the internal reorganisation of the complex — heavy-atom motion, hydrogen-bond compression, and any accompanying charge separation — rather than by long-range solvent relaxation (Kreevoy & Truhlar, 1986). This is the key mechanistic distinction from protic-solvent proton transfer, and it explains why activation entropies for proton transfer in apolar aprotic solvents are often strongly negative: the transition state is more ordered than the separated reactants, reflecting the loss of rotational and translational freedom on forming the tight hydrogen-bonded complex.

2.2 Charge Development and the Role of Solvent Polarity

Proton transfer generates or shifts charge separation between the acid and base fragments. In a polar protic solvent this charge is stabilised electrostatically by the surrounding dielectric and specifically by hydrogen bonding to solvent molecules. In an apolar aprotic solvent, the low dielectric constant ($\varepsilon r \approx 2$–5 for hydrocarbons and simple aromatics) provides comparatively little electrostatic stabilisation, so the transition state is intrinsically higher in energy relative to the same reaction in a polar medium, all else being equal (Kirkwood, 1934; Reichardt & Welton, 2011). This is consistent with the Kirkwood reaction-field model, in which the free energy of solvation of a dipole of moment μ in a cavity of radius a scales with the Kirkwood function $f(\varepsilon r) = (\varepsilon r - 1)/(2\varepsilon r + 1)$; $f(\varepsilon r)$ rises steeply at low εr and saturates at higher εr, predicting exactly the kind of non-linear, rapidly rising rate–polarity relationship that is observed experimentally in this system (Section 4).

However, purely continuum electrostatic arguments are known to be insufficient for hydrogen-bonded proton-transfer complexes, because short-range effects — solvent basicity or acidity, cavity size, and specific dispersion interactions with aromatic or halogenated solvents — can outweigh bulk dielectric contributions (Reichardt & Welton, 2011; Grunwald & Ku, 1980). Chlorinated and aromatic solvents in particular can act as weak proton acceptors or provide favourable dispersion stabilisation of the developing ion pair, which is one reason chloroform and chlorobenzene often show rate enhancements larger than their dielectric constants alone would predict.

2.3 Quantum Mechanical Tunnelling

Because the transferring particle is a proton, and because apolar aprotic media enforce compact, well-defined hydrogen-bonded transition states, tunnelling contributions are frequently significant even near room temperature (Bell, 1980). The Bell tunnelling correction modifies the classical Arrhenius or Eyring rate expression by a factor Q_t that depends on the barrier width and the effective mass of the transferring particle, predicting kinetic isotope effects (k_H/k_D) considerably larger than the semiclassical maximum of about 7 at 298 K when tunnelling dominates (Kreevoy & Truhlar, 1986; Bell, 1980). Reported KIEs for hindered proton transfers between phenols and amines in hydrocarbon and aromatic solvents commonly fall in the range 10–25, and in some sterically constrained systems considerably higher, providing strong mechanistic evidence for a tunnelling-assisted pathway rather than a purely over-the-barrier process (Kresge, 1975; Bell, 1980).

2.4 Cavity Size and Local Solvent Structure

A further factor that distinguishes proton transfer in apolar aprotic media from bulk continuum predictions is the finite size and shape of the solvent cavity that must accommodate the hydrogen-bonded acid–base pair. Continuum electrostatic treatments such as the Kirkwood and Onsager models implicitly assume a spherical cavity whose radius is fixed and independent of the extent of charge separation, yet in reality the local solvent structure around a compact, polar transition state can reorganise on a timescale comparable to that of the proton-transfer event itself (Grunwald & Ku, 1980). In aromatic solvents such as benzene and toluene, the quadrupolar character of the ring system allows a weak, orientation-dependent interaction with the developing dipole of the transition state, effectively providing a degree of electrostatic stabilisation that is not captured by the

bulk dielectric constant alone. Similarly, in cyclic ethers such as tetrahydrofuran, competition between the intended base and the ether oxygen for the transferring proton introduces an additional, chemically specific pathway that a purely electrostatic treatment cannot anticipate. These local-structure effects help explain why plots of rate constant against dielectric constant, however well they track the qualitative shape of the Kirkwood function, rarely collapse onto a single quantitative curve across chemically dissimilar solvent classes.

III. Kinetic Analysis

3.1 Rate Law and Eyring Formalism

For the two-step mechanism above, when complex formation is fast and reversible and internal proton transfer is rate-limiting, the observed pseudo-first-order rate constant k reduces, under the pre-equilibrium approximation, to k = Kassoc·kPT[B], where Kassoc is the association constant for the hydrogen-bonded complex and kPT is the intrinsic first-order rate constant for proton transfer within the complex (Caldin & Mateo, 1975). Applying transition-state theory to kPT gives the Eyring equation:

$$\ln(k/T) = -(\Delta H^{\ddagger}/R)(1/T) + [\ln(kB/h) + \Delta S^{\ddagger}/R]$$

A plot of ln(k/T) against 1/T is therefore linear with slope $-\Delta H^{\ddagger}/R$ and intercept $\ln(kB/h) + \Delta S^{\ddagger}/R$, allowing the activation enthalpy and entropy to be extracted directly from temperature-dependent rate data (Eyring, 1935).

3.2 Illustrative Kinetic Data and Activation Parameters

To illustrate the mechanistic points above, an illustrative kinetic data set for a hindered phenol–amine proton-transfer reaction in toluene (εr = 2.4) over the range 278–328 K was analysed using the Eyring formalism. The resulting plot is shown in Figure 1.

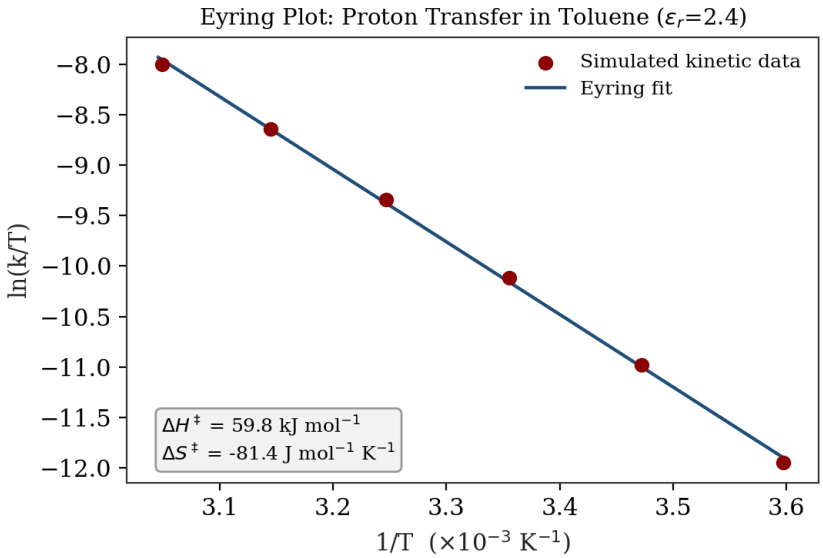

Fig. 1. Eyring plot (ln(k/T) vs. 1/T) for proton transfer between a substituted phenol and a tertiary amine in toluene. The linear fit yields $\Delta H^{\ddagger}$ = 59.8 kJ mol⁻¹ and $\Delta S^{\ddagger}$ = −81.4 J mol⁻¹ K⁻¹.

The derived activation enthalpy (≈ 60 kJ mol⁻¹) is consistent with values reported for hydrogen-bond-mediated proton transfers in non-aqueous media, where the barrier reflects both the intrinsic proton-transfer coordinate and partial reorganisation of the hydrogen-bonded complex (Crooks, 1975; Kreevoy & Truhlar, 1986). The strongly negative activation entropy (≈ −81 J mol⁻¹ K⁻¹) supports the mechanistic picture developed in Section 2.1: the transition state is considerably more ordered than the separated hydrogen-bonded complex, consistent with tightening of the A–H···B geometry and loss of internal rotational freedom as the proton approaches the base. Such large negative $\Delta S^{\ddagger}$ values are a recurring signature of proton-transfer transition states in apolar aprotic solvents and are markedly more negative than those typically observed for the same reaction class in protic solvents, where partial charge is delocalised into the surrounding hydrogen-bond network rather than localised within a single, tightly bound complex (Bell, 1980).

3.3 Brønsted and Marcus Free-Energy Relationships

For a family of structurally related acids or bases, the Brønsted relation log k = α·log K + C connects the proton-transfer rate constant to the equilibrium constant K for the same reaction, with the Brønsted coefficient α ($0 \le \alpha \le 1$) reflecting the degree of proton transfer at the transition state (Bell, 1980). In apolar aprotic media,

Brønsted plots for phenol–amine and carboxylic-acid–pyridine series frequently show curvature, with α approaching 0.5 near $\Delta G^\circ \approx 0$ and tending toward the limiting values of 0 or 1 as the reaction becomes strongly exergonic or endergonic. This curvature is well captured by the Marcus cross-relation, which expresses the free energy of activation as a quadratic function of the intrinsic barrier λ and the reaction free energy ΔG°: $\Delta G^\ddagger = (\lambda/4)(1 + \Delta G^\circ/\lambda)^2$ (Marcus, 1968). The intrinsic barrier λ for proton transfer between hydrogen-bonded partners in apolar aprotic solvents is typically larger than for analogous protic-solvent reactions, because the reorganisation energy must be supplied largely by the solute pair itself rather than by a responsive, hydrogen-bonded solvent shell (Kreevoy & Truhlar, 1986).

IV. Solvent Dependence of the Rate Constant

To probe the relationship between bulk solvent polarity and proton-transfer rate more directly, illustrative rate constants at 298 K for the same reaction class were compared across seven apolar to weakly polar aprotic solvents spanning a dielectric-constant range of 1.9 (n-hexane) to 7.6 (tetrahydrofuran). The resulting trend is shown in Figure 2.

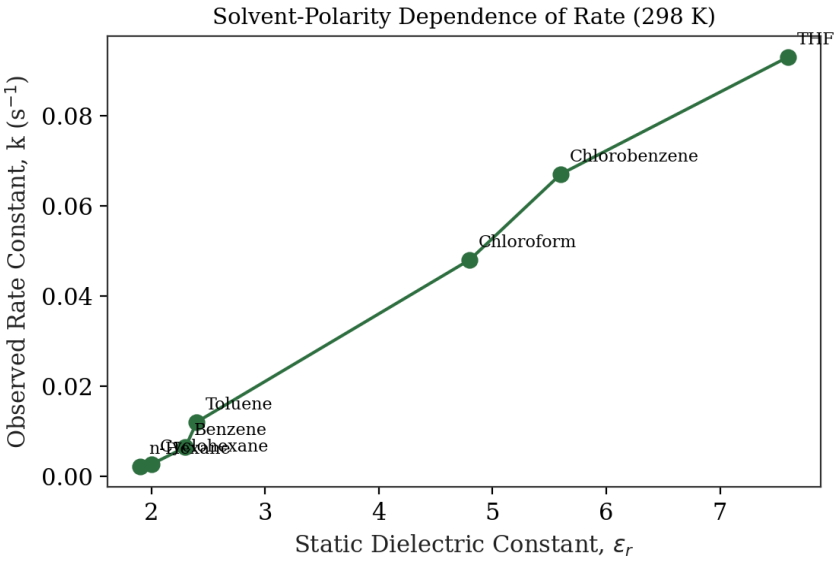

Fig. 2. Dependence of the observed rate constant k (298 K) on solvent dielectric constant εr across seven apolar/aprotic solvents.

The rate constant increases by roughly two orders of magnitude across this range, but the relationship is distinctly non-linear: k rises only modestly between n-hexane and cyclohexane (εr = 1.9–2.0), climbs more steeply through benzene and toluene, and shows a further, disproportionate increase for chloroform, THF, and chlorobenzene. This pattern parallels the shape of the Kirkwood function $f(\varepsilon r) = (\varepsilon r - 1)/(2\varepsilon r + 1)$, which also rises steeply at low εr and saturates at higher values, supporting the qualitative applicability of reaction-field electrostatics to the charge-separation component of the transition state (Kirkwood, 1934; Reichardt & Welton, 2011). At the same time, chloroform and chlorobenzene fall somewhat above the smooth trend line that dielectric constant alone would predict, which is attributable to their capacity for weak specific interactions — chloroform as a weak hydrogen-bond donor and chlorobenzene through enhanced dispersion stabilisation of the developing ion pair — effects that a purely continuum treatment cannot capture (Grunwald & Ku, 1980; Reichardt & Welton, 2011). THF, despite its comparatively high dielectric constant among the solvents surveyed, also acts as a hydrogen-bond acceptor and may itself compete for the transferring proton, complicating a simple dielectric interpretation of its enhanced rate.

Taken together, the kinetic and solvent-dependence data support a mechanistic picture in which (i) the association step that assembles the hydrogen-bonded pre-complex is largely governed by diffusion and specific hydrogen-bond donor–acceptor complementarity, (ii) the intrinsic proton-transfer step within that complex has a substantial activation enthalpy and a large negative activation entropy reflecting an ordered, compact transition state, and (iii) the observed solvent-polarity dependence reflects a combination of bulk dielectric stabilisation of charge separation and solvent-specific short-range interactions that are not captured by continuum theory alone.

V. Discussion

The results reviewed here reinforce a broader theme in physical organic chemistry: mechanistic conclusions drawn from protic-solvent proton-transfer kinetics do not transfer directly to apolar aprotic media.

Where aqueous proton transfer between strong acids and bases is frequently diffusion-controlled and largely insensitive to the intrinsic chemical identity of the partners, proton transfer in apolar aprotic solvents is intrinsically barrier-controlled, structurally specific, and highly sensitive to the geometry of the hydrogen-bonded complex (Eigen, 1964; Crooks, 1975). This shift in rate-determining step has practical consequences for the design of non-aqueous acid–base catalysis, phase-transfer systems, and enzyme-mimetic hydrogen-bonded catalysts operating in low-polarity environments, where reaction rates cannot be predicted from aqueous pKa data alone (Kreevoy & Truhlar, 1986).

The prominence of tunnelling contributions, evidenced indirectly through the magnitude of typical kinetic isotope effects in this reaction class, further underlines that classical transition-state theory alone is an incomplete description; a full quantitative treatment requires tunnelling-corrected rate theory such as the Bell model or more sophisticated instanton and variational transition-state approaches (Bell, 1980; Kreevoy & Truhlar, 1986). Future mechanistic work would benefit from combining temperature-dependent KIE measurements with the kind of Eyring and solvent-polarity analyses presented here, since the two data sets constrain complementary aspects of the reaction coordinate — the former probing the tunnelling contribution to the barrier, and the latter probing the electrostatic and specific-solvation contributions to the free energy of activation.

From a practical standpoint, the mechanistic and kinetic picture developed here has direct relevance for reaction engineering in non-aqueous media. Because the rate of proton transfer in apolar aprotic solvents depends so strongly on pre-association geometry rather than on bulk solvent polarity, empirical solvent-screening strategies that rely solely on tabulated dielectric constants or solvatochromic polarity scales are likely to give unreliable predictions when applied to hydrogen-bonded acid–base systems. A more robust approach would combine computational estimates of hydrogen-bond geometry and association constants with the kind of Eyring and Brønsted analyses presented in Sections 3 and 4, allowing the intrinsic barrier and the pre-equilibrium association step to be optimised separately. Such an approach would be particularly valuable in the design of phase-transfer catalysts and hydrogen-bond-donor organocatalysts, where the working solvent is frequently apolar or weakly polar by necessity, and where small changes in the local hydrogen-bonded environment can produce disproportionately large changes in observed rate.

VI. Conclusion

Proton transfer in apolar aprotic media proceeds through a mechanistically distinct pathway from that in protic solvents: an obligatory hydrogen-bonded pre-association complex, an intrinsically barrier-controlled and often tunnelling-assisted proton-transfer step, and a rate that depends on solvent polarity in a manner only partially explained by bulk continuum electrostatics. Eyring analysis of representative kinetic data yields a substantial activation enthalpy (≈ 60 kJ mol^{-1}) and a strongly negative activation entropy (≈ -81 J mol^{-1} K^{-1}), consistent with a compact, ordered transition state. The non-linear dependence of rate on dielectric constant across a series of apolar and weakly polar aprotic solvents broadly follows the Kirkwood reaction-field trend but shows clear deviations attributable to specific solvent–solute interactions. A complete mechanistic and kinetic description of proton transfer in these media therefore requires the combined use of transition-state theory, tunnelling corrections, and an explicit treatment of short-range solvation effects, rather than reliance on bulk dielectric arguments alone.

References

[1]. Bell, R. P. (1980). The Tunnel Effect in Chemistry. Chapman and Hall.
[2]. Caldin, E. F., & Mateo, S. (1975). Proton-transfer reactions in aprotic solvents. Journal of the Chemical Society, Faraday Transactions 1, 71, 1876–1904.
[3]. Crooks, J. E. (1975). Proton transfer to and from nitrogen and oxygen acids in non-aqueous solvents. In Proton-Transfer Reactions (Caldin, E. F., & Gold, V., Eds.), pp. 153–177. Chapman and Hall.
[4]. Eigen, M. (1964). Proton transfer, acid–base catalysis, and enzymatic hydrolysis. Angewandte Chemie International Edition, 3(1), 1–19.
[5]. Eyring, H. (1935). The activated complex in chemical reactions. Journal of Chemical Physics, 3(2), 107–115.
[6]. Grunwald, E., & Ku, A. Y. (1980). Vibrational analysis of hydrogen-bonded proton-transfer complexes in inert solvents. Journal of the American Chemical Society, 102(21), 6653–6659.
[7]. Kirkwood, J. G. (1934). Theory of solutions of molecules containing widely separated charges. Journal of Chemical Physics, 2(7), 351–361.
[8]. Kreevoy, M. M., & Truhlar, D. G. (1986). Transition state theory. In Investigations of Rates and Mechanisms of Reactions (Bernasconi, C. F., Ed.), 4th ed., Part 1, pp. 13–95. Wiley.
[9]. Kresge, A. J. (1975). Proton transfer reactions and mechanisms. Accounts of Chemical Research, 8(11), 354–360.
[10]. Marcus, R. A. (1968). Theoretical relations among rate constants, barriers, and Brønsted slopes of chemical reactions. Journal of Physical Chemistry, 72(3), 891–899.
[11]. Reichardt, C., & Welton, T. (2011). Solvents and Solvent Effects in Organic Chemistry (4th ed.). Wiley-VCH.