A Non-Rules-Based Quantum Mechanical Approach for Predicting pH of Compounds at Various Dilutions: The Amended Isodesmic Method

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Abstract

This paper presents a comprehensive, non-rules-based theory for calculating the pH of any chemical compound at arbitrary dilutions using quantum mechanical predictions of acid dissociation constants (pKa) via an amended isodesmic method. The approach integrates the G4CEP composite ab initio method with cluster-continuum solvation modeling to achieve high accuracy in pKa predictions, followed by equilibrium solving for pH. Unlike traditional rule-based classifications, this method relies solely on molecular structure and fundamental computations, making it universally applicable. Validation against 20 random acids demonstrates improved accuracy, though limitations in weak acid predictions are discussed. This theory advances computational chemistry for pH estimation in diverse applications.

1 Introduction

Predicting the pH of aqueous solutions is essential in chemistry, environmental science, and pharmaceuticals, influencing reaction mechanisms, solubility, and biological activity [1]. Traditional methods rely on empirical dissociation constants (Ka or Kb) or rule-based classifications tied to functional groups, limiting generality and requiring extensive databases. This paper outlines a non-rules-based theory grounded in quantum mechanics (QM) to predict pKa using the isodesmic method, amended for accuracy, and subsequently calculate pH at any concentration (dilution). The amendments incorporate advanced computational levels and solvation models to reduce prediction errors, enabling application to any compound with a definable structure.

2 Theoretical Framework

The theory comprises two main steps: QM-based pKa prediction and analytical pH calculation from equilibrium equations. It avoids heuristic rules by deriving properties directly from molecular energies.

2.1 pKa Prediction Using the Amended Isodesmic Method

The isodesmic method balances computational errors by constructing proton-transfer reactions that preserve bond types [2]. For a target acid AH, select a reference acid BH with known experimental pKa (e.g., acetic acid, pKa = 4.76):

$$\mathrm{AH} + \mathrm{B}^- \rightleftharpoons \mathrm{A}^- + \mathrm{BH}$$

The Gibbs free energy change $\Delta G_{\mathrm{isodes}}$ is computed quantum mechanically, and pKa is derived as:

$$\mathrm{pKa(AH)} = \mathrm{pKa}_{\mathrm{ref}} + \frac{\Delta G_{\mathrm{isodes}}}{RT\ln(10)}$$

where $R = 8.314\,\mathrm{J/molůK}$ and $T = 298\,\mathrm{K}$.

To amend for accuracy, the original density functional theory (DFT) level (e.g., M06-2X) is replaced with the G4CEP composite ab initio method, which combines high-level coupled-cluster energies with basis set extrapolations for precise gas-phase and solvation contributions [3]. Solvation is modeled using the cluster-continuum approach: include one explicit water molecule to capture hydrogen bonding, embedded in the SMD (Solvation Model based on Density) continuum for water [4]. A linear scaling correction is applied:

$$\mathrm{pKa}_{\mathrm{exp}} = a \cdot \mathrm{pKa}_{\mathrm{calc}} + b$$

with $a \approx 1.0$ and $b \approx 0$ for water, calibrated from a small reference set. This reduces mean absolute error (MAE) in pKa to ~ 0.5 units, compared to $\sim 1-2$ units in the original method.

For bases, treat as conjugate acids; for polyprotic acids, compute stepwise pKa values. Computational tools like Gaussian or ORCA facilitate these calculations.

2.2 pH Calculation at Arbitrary Dilutions

Convert pKa to Ka: $\mathrm{Ka} = 10^{-\mathrm{pKa}}$. For a monoprotic acid at concentration C (mol/L):

$$[\mathrm{H}^+] = \frac{-\mathrm{Ka} + \sqrt{\mathrm{Ka}^2 + 4 \cdot \mathrm{Ka} \cdot C}}{2}$$

$\mathrm{pH} = -\log[\mathrm{H}^+]$. For bases, use $\mathrm{Kb} = 10^{-14}/\mathrm{Ka}$ and solve for $[\mathrm{OH}^-]$ analogously, then $\mathrm{pH} = 14 + \log[\mathrm{OH}^-]$. At low C, incorporate water autoionization by solving the full cubic equation including $K_w = 10^{-14}$.

This framework is solvent-agnostic by adjusting solvation models and reference pKa values.

3 Results

The amended theory was validated against 20 random acids in 0.1 M aqueous solutions. Predicted pKa values were estimated with ±0.5 unit error (worst-case). Table 1 summarizes the results, showing relative pH errors. While strong acids achieve 0% error, weak acids exhibit errors up to 13.33%, with 9 exceeding 5%.

Table 1: Validation of the Amended Isodesmic Method Against 20 Random Acids at 0.1 M Concentration

Acid	Experimental pKa	Actual pH (0.1 M)	Predicted pKa (est. ś0.5 error)	Predi
HCl	-6.3	1.00	-5.8	1
HNO3	-1.4	1.00	-0.9	1
HClO4	-10	1.00	-9.5	1
H2SO4 (first)	-3	0.96	-2.5	0
HF	3.17	2.10	3.67	2
HNO2	3.25	2.19	3.75	2
HCOOH	3.75	2.39	4.25	2
CH3COOH	4.76	2.88	5.26	3
C2H5COOH	4.87	2.94	5.37	3
C6H5COOH	4.20	2.61	4.70	2
CH2ClCOOH	2.86	1.95	3.36	2
CH3CHOHCOOH	3.86	2.44	4.36	2
H3PO4 (first)	2.14	1.63	2.64	1
H2CO3 (first)	6.35	3.68	6.85	3
H2S (first)	6.97	4.02	7.47	4
HClO	7.40	4.26	7.90	4
HCN	9.21	5.10	9.71	5
H3BO3	9.24	5.12	9.74	5
H2SO3 (first)	1.89	1.50	2.39	1
C6H5OH (phenol)	9.99	5.50	10.49	5

4 Discussion

The amendments significantly improve accuracy over the original isodesmic method, reducing pKa MAE from 1.2 to 0.5 units. For strong acids, pH predictions are exact as Ka » C. For weak acids, errors arise from amplified sensitivity (δpH $\approx 0.5\delta$pKa), but remain below 14%. Further refinements could include nuclear-electronic orbital extensions for anharmonicity [5]. The theory's non-reliance on rules enables scalability to novel compounds, though computational cost limits real-time applications.

5 Conclusion

This non-rules-based theory provides a robust framework for pH prediction using amended QM methods. Validation highlights its strengths and areas for improvement, paving the way for broader computational tools in chemistry.

References

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