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ARTICLE

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Determination of pK_a values for (*E*)-2-hydroxy-5-(aryldiazenyl) benzaldehydes in dimethyl sulfoxide: Cyclic voltammetry and density functional theory calculations

Forouzan Zonouzi¹ | Alireza Shayesteh² | Taher Alizadeh² | Hamid Dezhampanah^{1,3} | Bahram Ghalami-Choobar^{1,3} | Afsaneh Zonouzi^{2,4}

¹Department of Chemistry, University campus 2, University of Guilan, Rasht, Iran

²School of Chemistry, College of Science, University of Tehran, Tehran, Iran

³Department of Chemistry, Faculty of Science, University of Guilan, Rasht, Iran

⁴Pharmaceutical and Cosmetic Research Center (PCRC), University of Tehran, Tehran, Iran

Correspondence

Bahram Ghalami-Choobar, Department of Chemistry, Faculty of Science, University of Guilan, Rasht, Iran. Email: b-ghalami@guilan.ac.ir

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1 | INTRODUCTION

Knowledge of dissociation constants and proton transfer reactions for organic compounds is critical in many fields including biology and chemistry, as well as industrial processes.^[1,2] Azo dves are an important class of synthetic industrial compounds that have been used for many years^[3] in applications including but not limited to coloring processes in textile industry, data storage,^[4] inkjet printing,^[5] dye-sensitized solar cells,^[6] sensors,^[7] and pharmaceuticals.^[8] In 1889, Tummeley reported the synthesis of aryl azo salicylaldehydes.^[9] Since then, these compounds have been used to obtain a wide variety of more complex dyes.^[10] In this project, (E)-2-hydroxy-5-(aryldiazenyl) benzaldehydes **1–4** (Scheme 1) are considered model representative azo dyes for pK_a calculations. These dyes were synthesized in their pure form using a double-solvent catalyzed procedure, which was recently reported by our team^[11]; thus, these azo

The (*E*)-2-hydroxy-5-(aryldiazenyl) benzaldehydes (azo dyes **1–4**) were synthesized in high purity. As they are insoluble in water, the usual analytical methods cannot be utilized to determine their pK_a values. Cyclic voltammetry was experimentally used to determine their pKa values in DMSO solvent. In addition, computational methods and a conductor-like screening model (COSMO) were used to calculate the solvent effect. $\Delta U_{exchange}^{\circ}$, $\Delta G_{exchange}^{\circ}$, $K_{exchange}$, and pK_a values were estimated for the azo dyes being studied using the BP86, TPSS, B3LYP, PBE0, TPSSh, and PW6B95 density functionals in def2-TZVP basis sets. The obtained mean absolute deviations (MADs) indicate that the results of BP86, PBE0, and PW6B95 functionals are in good agreement with experimental values.

KEYWORDS

azo dyes, cyclic voltammetry, DFT calculations, dimethyl sulfoxide, pKa

compounds are insoluble in water, and conventional experimental procedures cannot be used to determine their pK_a values. In order to evaluate the theoretical results, we also used cyclic voltammetry (CV) in dimethyl sulfoxide (DMSO) to experimentally report the related pKa values for the first time (Table 1).

In addition, the measurement of pK_a may not be easy and would turn into a significant experimental challenge for some compounds, including azo dyes. Thus, experiments should be performed carefully under standard conditions. Furthermore, theoretical calculations provide a proper way to gain a first idea about pK_a values. However, developing computational methods to determine the pK_a values is of particular interest. The goal of these methods is to improve the reliability of the computational approach through comparison with the available experimental data and to predict unknown values. In continuation of our quest for the theoretical calculation of pK_a values,^[12–16] here, we performed

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1 (R=H), 2 (R=CI), 3 (R=Br), 4 (R= Et)

SCHEME 1 The structure of the azo dyes under study

TABLE 1 The structure, name, and experimental pK_a values of compounds 1–4 obtained from cyclic voltammetry (CV) in DMSO

| Comp. | Name | pK_a (CV) |
|-------|--|-------------|
| 1 | (E)-2-hydroxy-5-(phenyldiazenyl) benzaldehyde | 8.62 |
| 2 | (E)-5-([4-chlorophenyl] diazenyl)-2-hydroxybenzaldehyde | 8.29 |
| 3 | (E)-5-([4-bromophenyl] diazenyl)-2-hydroxybenzaldehyde | 8.33 |
| 4 | (E)-5-([4-ethylphenyl] diazenyl)-2-hydroxybenzaldehyde | 8.95 |

density functional calculations to complement experimentally measured pK_a values. This approach is hopefully general to many organic compounds, especially azo dyes, which are usually insoluble in water, and their hue color intensity are highly *p*H dependent.

2 | METHOD

2.1 | Synthesis of azo dyes 1–4

The azo dyes under study were obtained in pure form via our recently reported double-solvent catalyzed method.^[11] Briefly, 8 mL of HCl (37%) was added dropwise to a stirred solution of aniline derivatives maintained at 0°C, and 20 mL of NaNO₂ solution (4 g in 20 mL of H₂O) was then added. Separately, 0.05 mol of salicylaldehyde was dissolved in 10 mL of petroleum ether, a regioselective catalyst based on zinc (Zn/SBA-15), and then, 5 mL of 10% aq NaOH were added. The new mixture was added to the first aqueous solution. After 45 min of vigorous stirring, a yellow to brown organic precipitate can be separated easily, which contains azo dyes **1–4** that can be purified by aqueous washing and are obtained by solvent evaporation.

2.2 | Electrochemical measurements

CV experiments were carried out via a computerized handheld potentiostat/galvanostat (Palm Instruments BV, the Netherlands) interfaced with a laptop. Analytical procedure was controlled by Drop Sens PC software, Drop view. A conventional three-electrode system, including a glassy carbon electrode (working electrode), platinum rod (counter electrode,) and Ag/Ag + electrode (reference electrode), was used for the electrochemical experiment. Dry DMSO was used for the preparation of solutions of the dyes under study and benzoquinone (BQ). Tetra butyl ammonium bromide (TAB) was used as a supporting electrolyte.

2.3 | Computational details

In this section, pKa values of compounds **1–4** using density functional theory (DFT) were calculated. All calculations were performed using the ORCA 3.0.3 program,^[17] and the solvent effects were included by the conductor-like screening model (COSMO).^[18] The structures were optimized in the DMSO solvent using the BP86,^[19,20] TPSS,^[21] B3LYP,^[22] PBE0,^[23] TPSSh,^[24] and PW6B95^[25] density functionals with the def2-TZVP basis sets.^[26] Vibrational frequency calculations and thermochemical analyses were carried out using the BP86 functional.^[19,20] Single-point energies were obtained for all six density functionals with the def2-TZVPP basis sets.

3 | **RESULTS AND DISCUSSION**

The azo dye compounds under study are important precursors in the dyeing industry, and having precise information about their pK_a values will play a crucial role in color control and stability. Although measuring the pK_a seems to be easy, azo dyes 1–4 are not soluble in water; therefore, we tried using CV in DMSO, followed by theoretical calculations, to measure and estimate the pK_a values.

3.1 | Cyclic voltammetry

Figure 1 shows the electrochemical behavior of BQ in the absence and presence of azo dyes **1–4** in DMSO. As can be seen, new reduction peaks appear at more positive potentials (-0.04, -0.03, -0.03, and -0.05 V for 1-4, respectively) than the peak potential due to the first reduction of BQ alone (about -0.2 V). Based on the depicted data, the *pK_a* values of **1–4** were estimated to be 8.62, 8.29, 8.33, and 8.95 respectively (Figure 1).

The structure of the compounds under study contains a phenol group; phenolic compounds are organic acids without a carboxylic moiety. The acidity of such compounds change on substitution. For example, pK_a of phenol in water is 0.89, while for picric acid (2,4,6-trinitro phenol), it is 0.25.^[27] On the other hand, the pK_a values also depend on the solvent, that is, pK_a of picric acid in DMSO has been reported to be -1.0 by CV.^[27] For phenolic compounds **1–4**, deprotonating is made easy as a result of electron-



FIGURE 1 Cyclic voltammetry curves of BQ in the absence (BQ) and presence of various dyes **1–4**; *scan rate*: 50 mV/s; $[BQ] = 5 \times 10^{-3} \text{ M}$, $[dye] = 5 \times 10^{-3} \text{ M}$, $[TAB] = 1 \times 10^{-2} \text{ M}$

withdrawing groups (CHO, N₂-Ar). The presence of intramolecular H-bonding (proven by FTIR and ¹H NMR spectra) leads to distance between the proton and oxygen in the hydroxyl group; meanwhile, that proton becomes less available for the solvent. The range of experimental and calculated pK_a at about 8 seems logical. The presented CV approach may be generalized for the pK_a determination of organic azo compounds that are not soluble in water in order to provide valuable data for color control in dyeing processes.

3.2 | Theoretical calculations

Theoretical calculations had been proven to be significant complementary tools for pK_a estimation.^[28] There are some reports on computational methods for compounds that are soluble in water or other protic solvents.^[12–16] Following our quest for the pK_a estimation for organic compounds, here, we tried to calculate the pK_a values of compounds **1–4** using DFT methods. For this aim, the following thermodynamic cycle was considered (Figure 2).

Fu and coworkers predicted the principles of absolute pK_a of some small organic compounds in DMSO as an



FIGURE 2 The thermodynamic cycle

aprotic solvent.^[29] Based on their report, an advantage of using exchange reactions for the calculation of pK_a values is that their computational errors are usually small due to error cancellation; therefore, the following deprotonation reaction of azo dye molecules in DMSO can be considered for the simple calculation of pK_a values (Scheme 2).

The ΔG° values of the above reaction, that is, the proton exchange reaction, were calculated at 298.2 K using various density functionals, and the equilibrium constants were obtained:

$$K_{\text{exchange}} = \exp\left(\frac{-\Delta G^0}{RT}\right).$$
 (1)

In the next step, as pointed out by Fu,^[29] using the autoionization constant of DMSO, that is, 10^{-35} , the K_a values in DMSO were calculated as:

$$K_a = 10^{-35} K_{\text{exchange}}.$$
 (2)

In order to complement the results obtained from CV measurements, $\Delta U_{\text{exchange}}^{\circ}$, $\Delta G_{\text{exchange}}^{\circ}$, K_{exchange} , and pK_a values were calculated using the BP86, TPSS, B3LYP, PBE0, TPSSh, and PW6B95 density functionals with the def2-TZVP basis sets. The results of our calculations are summarized for azo dyes **1–4** in Table 2. It is obvious that the results obtained from PW6B95, BP86, and PBE0 functionals agree better (mean absolute deviation [MAD] = 0.26, 0.28, and 0.35, respectively) with the experimental pK_a values for azo dyes **1–4**, which were estimated by (CV) to be 8.62, 8.29, 8.33, and 8.95, respectively (Table 3).



SCHEME 2 Reaction of azo dyes in DMSO used in DFT calculations

| Comp. | def2-TZVPP | $\Delta U^{^{\circ}}_{\mathrm{exchange}} \; (\mathrm{kJ/mol})$ | $\Delta G_{\mathrm{exchange}}^{\circ}$ (kJ/mol) | Kexchange |
|-------|------------|--|---|------------------------|
| 1 | BP86 | -150.669 | -150.778 | 2.600×10^{26} |
| | TPSS | -158.015 | -158.125 | 5.036×10^{27} |
| | B3LYP | -155.136 | -155.245 | 1.576×10^{27} |
| | PBE0 | -148.856 | -155.245 | 1.252×10^{26} |
| | TPSSh | -155.726 | -155.245 | 2.000×10^{27} |
| | PW6B95 | -152.660 | -155.245 | 5.807×10^{26} |
| 2 | BP86 | -152.198 | -152.098 | 4.429×10^{26} |
| | TPSS | -159.237 | -159.136 | 7.575×10^{27} |
| | B3LYP | -156.944 | -156.843 | 3.003×10^{27} |
| | PBE0 | -150.507 | -150.407 | 2.239×10^{26} |
| | TPSSh | -157.549 | -157.449 | 3.834×10^{27} |
| | PW6B95 | -153.851 | -153.750 | 8.624×10^{26} |
| 3 | BP86 | -149.859 | -150.155 | 2.023×10^{26} |
| | TPSS | -156.876 | -157.171 | 3.428×10^{27} |
| | B3LYP | -154.160 | -154.456 | 1.147×10^{27} |
| | PBE0 | -147.856 | -148.152 | 9.014×10^{25} |
| | TPSSh | -155.043 | -155.339 | 1.637×10^{27} |
| | PW6B95 | -151.557 | -151.853 | 4.011×10^{26} |
| 4 | BP86 | -148.634 | -149.832 | 1.776×10^{26} |
| | TPSS | -155.606 | -156.805 | 2.957×10^{27} |
| | B3LYP | -153.399 | -154.597 | 1.214×10^{27} |
| | PBE0 | -147.140 | -148.339 | 9.720×10^{25} |
| | TPSSh | -153.886 | -155.084 | 1.477×10^{27} |
| | PW6B95 | -150.607 | -151.805 | 3.935×10^{26} |

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TABLE 2 Theoretical values for $\Delta U_{\text{exchange}}^{\circ}$, $\Delta G_{\text{exchange}}^{\circ}$, and K_{exchange} in DMSO solvent for compounds **1–4**, calculated using various density functionals with the def2-TZVPP basis sets

TABLE 3 Theoretical values for pK_a

for compounds 1-4 in comparison with

corresponding MADs

experimental values obtained from cyclic voltammetry (CV) in DMSO and

4 | CONCLUSIONS

 pK_a (cal.)

TPSS

7.30

7.12

7.46

7.53

1.19

B3LYP

7.80

7.52

7.94

7.92

0.74

PBE0

8.90

8.65

9.05

9.01

0.35

TPSSh

7.70

7.42

7.79

7.83

0.85

PW6B95

8.24

8.06

8.40

8.41

0.26

pK_a(exp.) CV

8.62

8.29

8.33

8.95

BP86

8.58

8.35

8.69

8.75

0.28

Comp.

1

2

3

4

MAD

In this work, first (*E*)-2-hydroxy-5-(aryldiazenyl) benzaldehydes **1–4** were synthesized in high purity. These compounds are soluble in DMSO rather than protic solvents or water. Thus, their pK_a values were measured by CV in DMSO and are being reported for the first time. This method could be generalized for pK_a measurement for organic azo compounds that are insoluble in water, which will provide valuable data for color control in the dyeing processes. In order to complement the results obtained from CV measurements, $\Delta U_{\text{exchange}}^{\circ}$, $\Delta G_{\text{exchange}}^{\circ}$, K_{exchange} , and pK_a values were calculated using DFT with various density functionals using the def2-TZVPP basis sets. Then, we calculated the pK_a values of azo dyes **1–4** for the first time and used the COSMO to apply the solvent effect. The structures were optimized in the DMSO, and the $\Delta U_{\text{exchange}}^{\circ}$, $\Delta G_{\text{exchange}}^{\circ}$, K_{exchange} , and pK_a values were estimated for azo dyes being studied using the BP86, TPSS, B3LYP, PBE0, TPSSh, and PW6B95 density functionals with the def2-TZVP basis sets. The results obtained from PW6B95, BP86, and PBE0 functionals are in good agreement (MAD = 0.26, 0.28, and 0.35, respectively) with the experimental pK_a values for azo dyes **1–4**, which were estimated by (CV) to be 8.62, 8.29, 8.33, and 8.95, respectively. We hope this approach can be generalized for organic compounds that are not soluble in water or protic solvents and would be helpful for industrial coloring procedure design and control.

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ORCID

Bahram Ghalami-Choobar D https://orcid.org/0000-0002-3599-1153

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