Persistent Radical Pairs Between *N*-Substituted Naphthalimide and Carbanion Exhibit pK_a -Dependent UV-vis Absorption

Xiancheng Nie,^a Tao Wang,^{*a} Xiaoyu Chen,^a Wenhuan Huang,^a Linkun Huang,^a Biao Chen^a and Guoqing Zhang^{*a}

A new strategy is constructed for estimating and screening pK_a values among different carbon acids under ambient conditions via the UV-vis absorption spectrum of persistent radical pair originating from an *N*-substituted naphthalimide (NNI) derivative in the presence of various carbanions in organic solutions.

Knowing the pK_a value of a deprotonatable carbon atom attached to a functional group (CH_XR_Y , $X>0$, a carbon acid, CA) is critical in organic chemistry since it foretells the reactivity and selectivity of reactions participated by the α -carbon. Over the past century, a plethora of experimental techniques, including potentiometry,^{1,2} spectrometry,³⁻⁵ conductometry,^{6,7} electrophoresis,^{8,9} nuclear magnetic resonance (NMR),^{10,11} voltammetry,^{12,13} high performance liquid chromatography (HPLC),^{14,15} fluorometry,¹⁶⁻¹⁸ and more recently, theoretical calculations,^{19,20} have been employed to measure or estimate pK_a . Among these techniques, the UV-vis spectrometry method, similarly to pH indicators, is particularly favoured due to its wide accessibility, high throughput, and easy operation for non-experts.

In organic solvents, however, measuring the pK_a value of CAs can be very challenging, mainly due to the complicated preparation in non-aqueous environments. Usually, a coloured indicator acid (InA, e.g., fluorene anion, $pK_a = 22.6$ in DMSO^{21,22}) of known acidity is used, the pK_a of which cannot differ by two units compared to that of the CA to be measured. For this specific reason, numerous InAs must be first selected and a guess must be made on the pK_a value of the target CA. Furthermore, most of the InA ions readily oxidize in the presence of oxygen and quench in water so that the whole experimental has to be performed in a concealed environment, which significantly reduces its usefulness. Consequently, a fast screening of pK_a values, sufficient for most organic reactions, is not economical with this method and a more convenient one that can be operated in ambient conditions is highly desired. Here we propose a potential method that can quickly estimate the pK_a range of a CA in organic solvents with good relative accuracy. Most importantly of all, the conditions are relatively mild which can dramatically speed up the screening process.

The application is based on our recent discovery that when an organic anion, such as a carbanion, comes in close contact with an electron-deficient aromatic compound, such as *N*-substituted naphthalimide (NNI), a persistent radical pair (PRP) forms.²³ The pair apparently lacks reactivity towards any reactions generally involving anions or radicals in the ambient condition. More interestingly, the PRP exhibits an absorption spectrum in the visible range. Based on the observation, we reason that the energy of the PRP absorption should be

Scheme 1. Reprehensive protocol to correlate pK_a of a carbon acid with the electronic paramagnetic resonance (EPR) and absorption spectrum.

dependent on the energy of carbanion if the aromatic acceptor is kept unchanged. As a result, it is possible that various CAs in basic condition exhibit different absorption patterns which are related to the energy difference of the carbanions formed. Since the electronic potential energy of the carbanion is also related to their pK_a values, it is believed that *there is the possibility that some kind of correlation may be found between the pK_a of the CA and the absorption spectrum of the PRP* (Scheme 1).

To test the hypothesis, a series of CAs with published pK_a ²⁴⁻²⁷ values are first selected with photos showing various colours in DMSO solutions in the presence of NNI-Br and excess *t*-BuOK (Fig. 1a), resulting from the formation of PRPs. The detailed experiments are described as follows: To DMSO solution (20 mL) of CAs (2.5×10^{-4} mol/L) was added *t*-BuOK (200 mg), followed by adding NNI-Br (equivalent molar ratio vs. CA) into the system. The stock solutions of DMSO were the subject to EPR experiments as recently established, which give rise to conspicuous EPR signals, indicative of the formation of radicals (Fig. 2). It is noteworthy that the lifetimes of as-prepared carbanion radicals are over 15 days.

As can be expected, the single-electron transfer process readily takes place between a deprotonated CA donor (or carbanion) and the NNI-Br acceptor and gives rise to a coloured solution as has been recently verified in both intramolecular and intermolecular systems. However, *it is the first time that we have ever observed the dramatical difference in colour variations among different CAs*, further confirming that the resulting species posting charge transfer are donor-acceptor radical pairs instead of isolated NNI radical anions, which should in theory have given an identical colour. The representative UV-vis absorption spectra of these radical pairs are shown in Fig. 1b (Table S1). The result reveals more than one absorption peaks could be recorded for every different CA (it has to be noted that CAs instable in the presence of cyano group, such as 3-trifluoromethyl benzyl cyanide, are excluded from the experiment, given we noticed a visual colour change over time, Fig. S1). While the spectra may be complex for direct

Fig. 1 (a) Chemical structures of CAs and NNI-Br; the numbers below the structures is the corresponding pK_a values in DMSO; inset: digital photos of related carbanion radicals in DMSO after combination of CAs and NNI-Br. (b) UV-vis absorption spectra of PRPs in the presence of various CAs; red arrow represents shift tendency of the reddest absorption maximum. (c) Linear fitting Plotting of pK_a and wavenumber. (d) Schematic illustration for explaining linear dependence between the absorption energy and pK_a value.

interpretation, it was noted that the absorption maximum for the most red-shifted band appears to be correlated to the pK_a value of the CA used. A closer examination, shown in Fig. 1c, by plotting the increasing energy of the absorption of the maximum of the reddest band (in cm⁻¹) against the descending pK_a value of the CA, reveals a roughly linear dependence within a specific range (~10 pK_a units). The linear relationship derivation 470–480 nm is caused by the absorption overlap between carbanion radicals and NNI-Br (Fig. S2). To demonstrate that the visible-light absorptions (over 450 nm) originate from the carbanion radical pair, the UV-vis absorption spectra of the CA and t-BuOK in DMSO in the absence of NNI-Br were collected (Fig. S3). The results confirm the absorption over 450 nm does not solely derive from CA carbanion, which further indicates that absorption in the visible range is mainly contributed by PRPs. While the contributing factors can be complicated, a simplified model is proposed (Fig. 1d) to explain the main cause of the linear dependence. In Fig. 1d, the basic concept of molecular orbital (MO) theory is employed, where

Fig. 2 Liquid-phase EPR spectra of carbanion radicals originating from CAs and NNI-Br in the presence of t-BuOK.

Fig. 3 Chemical structures of CAs and NNI-Br; the numbers below the structures is the corresponding pK_a values in DMSO; inset: digital photos of related carbanion radicals in DMSO after combination of CAs and NNI-Br. (b) UV-vis absorption spectra of PRPs in the presence of various CAs; red arrow represents shift tendency of the reddest absorption maximum. (c) Linear fitting Plotting of pK_a and wavenumber.

the solid lines represent half-occupied MOs, the double arrows represent an electron with an indeterminable spin state, and the coloured single arrows stand for the optical absorption process. In order for the electron transfer to happen spontaneously, the energy of the carbanion must be higher than that of the NNI acceptor. After electron transfer occurs, the two electrons on the donor and acceptor, respectively, are "bonded" via the spin-pairing interactions. However, the energy difference between the "bonding state" and "anti-bonding state" should be related to the carbanion, i.e., a large energy disparity between the carbanion and NNI-Br should lead to smaller splitting which gives rise to more red-shifted electronic absorption in spectroscopy.

Next, to test whether such a method could exhibit any resolution within very close pK_a values, we then chose a series of nine well-documented aromatic α -ketones whose pK_a values are already published in the literature (Fig. 3a).²⁶ The ketones were subject to the same experimental condition as well: 200 mg t-BuOK was added into a DMSO solution with the target α -aromatic ketone concentration of 2.5×10^{-3} mol/L and equivalent NNI-Br as acceptor was added into the system. In this case, the UV-vis absorption spectra in DMSO are relatively similar to one another with one major absorption band in between 400–500 nm and a red-shifted shoulder peak beyond 550 nm (Fig. 3d, Table S2), which is used as the energy value to plot against pK_a of the aromatic ketone (Fig. 3c). The correlation is roughly linear except for an anomaly point for 4-trifluoromethyl acetophenone with a published pK_a value of 22.7. At this point, it is not immediately obviously why this particular ketone deviates more significantly from the others. It is possible that the value is also within the error range due to the very close pK_a values and absorption maxima.

In conclusion, the UV-Vis absorption spectrum of an NNI derivative in the presence of various carbanion radicals in organic solutions was found to be highly dependent on the pK_a value of CA, which was proposed as a potentially useful method to help organic chemists estimate, compare or fast screen pK_a values among different carbon acids under ambient conditions. This simple design method opened a new door to pK_a measurement.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- 1 Z. Qiang and C. Adams, *Water Res.*, 2004, **38**, 2874–2890.
- 2 Z. Wang, Y. Xie, Z. Lei, Y. Lu, G. Wei, S. Liu, C. Xu, Z. Zhang, X. Wang and L. Rao, *Anal. Chem.*, 2019, **91**, 9690–9697.
- 3 S. Radunz, H. R. Tschiche, D. Moldenhauer and U. Resch-Genger, *Sensor Actuat. B- Chem.*, 2017, **251**, 490–494.
- 4 C. G. Frankær, K. J. Hussain, T. C. Dörge and T. J. Sørensen, *ACS sensors*, 2018, **4**, 26–31.
- 5 L. Huang, B. Chen, X. Zhang, C. O. Trindle, F. Liao, Y. Wang, H. Miao, Y. Luo and G. Zhang, *Angew. Chem. Int. Ed.*, 2018, **57**, 16046–16050.
- 6 F. Maran, D. Celadon, M. G. Severin and E. Vianello, *J. Am. Chem. Soc.*, 1991, **113**, 9320–9329.
- 7 I. Salma and G. Láng, *Atmos. Chem. Phys.*, 2008, **8**, 5997–6002.
- 8 J. Cleveland Jr, M. Benko, S. Gluck and Y. Walbroehl, *J. Chromatogr. A*, 1993, **652**, 301–308.
- 9 A. R. Ribeiro and T. C. Schmidt, *Chemosphere*, 2017, **169**, 524–533.
- 10 B. Liang and L. K. Tamm, *Nat. Struct. Mol. Biol.*, 2016, **23**, 468–474.
- 11 F. V. C. Kock and L. A. Colnago, *Carbohydr. Polym.*, 2016, **150**, 1–4.
- 12 J. Věžník, M. Konhefr, L. Trnková, P. Skládal and K. Lacina, *Electrochim. Acta*, 2019, **318**, 534–541.
- 13 S. J. Cobb, Z. J. Ayres, M. E. Newton and J. V. Macpherson, *J. Am. Chem. Soc.*, 2018, **141**, 1035–1044.
- 14 S.-Y. Han, C. Liang, K. Zou, J.-Q. Qiao, H.-Z. Lian and X. Ge, *Talanta*, 2012, **101**, 64–70.
- 15 I. Canals, J. A. Portal, E. Bosch and M. Rosés, *Anal. Chem.*, 2000, **72**, 1802–1809.
- 16 P. M. Gosavi, Y. S. Moroz and I. V. Korendovych, *Chem. Commun.*, 2015, **51**, 5347–5350.
- 17 Y. Urano, D. Asanuma, Y. Hama, Y. Koyama, T. Barrett, M. Kamiya, T. Nagano, T. Watanabe, A. Hasegawa and P. L. Choyke, *Nat. Med.*, 2009, **15**, 104–109.
- 18 H.-Y. Li, Y.-L. Wei, X.-Y. Dong, S.-Q. Zang and T. C. Mak, *Chem. Mater.*, 2015, **27**, 1327–1331.
- 19 B. Thapa and H. B. Schlegel, *J. Phys. Chem. A*, 2016, **120**, 8916–8922.
- 20 W. L. Jorgensen, J. M. Briggs and J. Gao, *J. Am. Chem. Soc.*, 1987, **109**, 6857–6858.
- 21 F. G. Bordwell and X. M. Zhang, *J. Am. Chem. Soc.*, 1994, **116**, 973–976.
- 22 J. E. Bartmess, J. A. Scott and R. T. McIver Jr, *J. Am. Chem. Soc.*, 1979, **101**, 6046–6056.
- 23 W. Huang, B. Chen and G. Zhang, *Chem- A Eur. J.*, 2019, **25**, 12497 – 12501.
- 24 F. G. Bordwell, *Acc. Chem. Res.*, 1988, **21**, 456–463.
- 25 S. E. Denmark and M. Harmata, *J. Am. Chem. Soc.*, 1982, **104**, 4972–4974.
- 26 F. Bordwell and F. J. Cornforth, *J. Org. Chem.*, 1978, **43**, 1763–1768.
- 27 F. G. Bordwell and H. E. Fried, *J. Org. Chem.*, 1991, **56**, 4218–4223.