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# An Acidity Scale of Triazolium-Based NHC Precursors in DMSO

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#### Abstract

An acidity scale of triazolium-based N-heterocyclic carbene precursors was established by measuring 25 compounds' (**10a** – **15b**) equilibrium acidities in dimethyl sulfoxide (DMSO) solution using overlapping indicator method. The p $K_a$  values ranged from 12.08 to 15.5, responding not only to the *N*-aryl motif, but also to the core structure. Excellent correlation was observed between the p $K_a$  values and the Hammett substituent constants ( $\sigma_p$ ).

# Introduction

N-heterocyclic carbenes (NHCs) have emerged as efficient organocatalysts over the past decades for various asymmetric C-C bond formations.<sup>1</sup> The genesis of this reactivity of stable carbenes dates back to 1943 when Ukai demonstrated that thiazolium salts could be used as efficient catalysts for benzoin transformation<sup>2</sup> and Breslow's subsequent determination of its mechanism<sup>3</sup>. In 1966, Sheehan and Hunneman rendered benzoin reaction enantioselective employing chiral thiazolium as precatalyst.<sup>4</sup> Today, organocatalytic reactions enabled by stable carbenes are dominated not only by thiazolium or imidazolium derived carbenes, but also triazolylidene carbenes, which were first described in 1995 by Enders and Teles.<sup>5</sup> Since then, much efforts were devoted to the development of chiral variants of triazolylidene carbenes, resulting in the discovery of chiral bicyclic triazolylidene scaffolds by Knight and Leeper<sup>6</sup> that significantly improved the achievable stereoselectivity in a series of NHC

catalyzed reactions. Nowadays, chiral bicyclic triazolylidene carbenes have proven to be broadly efficacious in great number of transformations, including umpolung reactions,<sup>1</sup> acylazolium intermediates and oxidants mediated reactions.<sup>7</sup>

Scheme 1 Representive activation mode enabled by NHC



It is a commonly used procedure to generate the active NHC species *in situ* in many synthetic transformations by deprotonating the conjugate acid azolium salts precursor of corresponding NHC using proper base (Scheme 1).<sup>8</sup> Remarkably, despite the emerging application of triazolylidene carbenes in organic synthesis, few reports focused on the equilibrium acidities of triazolium salt precatalysts, although there have been studies on NHCs' nucleophilicities,<sup>9</sup> gas-phase proton affinities<sup>10</sup> and kinetic acidities<sup>11</sup> in water. Bordwell and co-workers<sup>12</sup> reported the equilibrium acidities of  $C2\alpha/C2$  hydrogen atoms in thiazolium cations in DMSO solution by overlapping indicator method and they carried out NMR and cyclic voltammetry experiments to establish the existence of acid-base equilibrium. Alder et al. measured the  $pK_a$  of 1,3-diisopropyl-4,5-dimethyl-imidazol-2-ylidene to be 24.0 in DMSO-*d*<sub>6</sub> by NMR method.<sup>13</sup> Streitwieser et al. reported a DMSO  $pK_a$  value of 22.7 for 1,3-diitertbutylimidazol-2-ylidene.<sup>14</sup> Yates et al. predicted the basicity of nucleophilic

carbenes in DMSO and acetonitrile by theoretical computation.<sup>15</sup> Cheng determinated the  $pK_a$  values of sixteen 1,3-dialkylimidazolium-type room temperature ionic liquid (RTIL) molecules by overlapping indicator method, providing a direct measurement of stability of corresponding N-heterocyclic carbenes that were derived from deprotonation of imidazolium salts.<sup>16</sup> NMR experiments and UV titrations indicated that imidazolylidene carbenes were quite stable in dilute DMSO solution (millimole concentration) at least for hours at room temperature, although there were reports on carbenes' dimerization<sup>17</sup> or insertion of acidic C-H bond.<sup>18</sup> Recently, Harper et al reported their systematic study of  $pK_a$  values of imidazolium salts in dimethyl sulfoxide using the bracketing/overlapping indicator method.<sup>19</sup>

On the other hand, the structure and electronic nature of NHC have a profound effect on catalytic activities within many organocatalytic transformations. For example, Bode and co-workers<sup>20</sup> have reported that electronic-rich imidazolium-derived catalyst deprotonated by strong base such as DBU favor the homoenolate pathway; while triazolium-derived structures in combination with weak base such as DMAP enhance protonation and lead to enolate outcome. *N*-aryl motif also plays a crucial role in determining the product outcome.<sup>21</sup> Generally, *N*-mesityl substituted triazolium salts are preferred precatalysts in reactions involving  $\alpha$ , $\beta$ -unsaturated aldehydes,<sup>22</sup> while *N*-pentafluorophenyl triazolium salts are efficient precatalysts for benzoin and Stetter reaction.<sup>23</sup> Further experiments by Bode et al.<sup>24</sup> lead to the conclusion that the effect of *N*-mesityl group is to render the initial addition of NHC to the aldehyde irreversible, thus accelerating the formation of Breslow intermediate. Qualitative experiments have

shown that *N*-pentafluorophenyl triazolium salts are more acidic than the corresponding *N*-mesityl salts. Given the aforementioned aspects and our continuous interest in experimental  $pK_a$  study of organocatalysts,<sup>25</sup> herein, we report the determination of the acidities of triazolium-based N-heterocyclic carbene precursors by classical overlapping indicator method, which help us establish the  $pK_a$  scale of NHC precursors in DMSO.<sup>26</sup>

#### **Results and Discussion**

The indicator overlapping method used in this work does not measure the equilibrium acidity of triazolium salts directly, instead it measures the differences of the equilibrium acidities of the unknown acid relative to that of an indicator acid whose  $pK_a$  is known by monitoring the change of UV/vis absorbance-readings of colored species, either the indicator anion in a normal titration or the unknown acid anion in a back titration. The concentration of each species can be calculated with gravimetrically determined total mass of indicator and the unknown acid in combination with Beer's law plot and the  $pK_a$  is obtained as equations in Figure **1**.

$$PK_{HA} = PK_{HIn} - \log_{10}K_{eq}$$

 $= pK_{HIn} - log_{10}([HIn][A^-]/[In^-][HA])$ 

Figure 1 Formation of NHC by deprotonation

One of the major problems encountered in this work was that the absorbancereading of conventional indicators containing C-S bond, whose  $pK_a$  values cover the range from 10.55 to 15.4, such as 9-*t*BuSO<sub>2</sub>-FH, 9-PhS-FH et al. continued to decrease

slowly (see Figure S1, S2, Supporting Information) after the initial drop of triazolium salt solution instead of remaining constant, as in a successful titration. Bordwell et al. ascribed this to dimerization of thiazolylidene carbene and performed one-point run titration at a rather low concentration followed by extrapolation of the absorbance back to to and gave a rough estimation by assuming the rate of establishment of acid-base equilibrium faster than the rate of dimerization.<sup>12b</sup> Inspired by earlier work of our group<sup>16</sup> and further experiments on decomposition of C-S containing indicators under basic conditions,<sup>27</sup> we reasoned that indicators without C-S bond would be appropriate. This idea was first tested by experiments carried out between triazolium salt 10a and indicator 2, which was designed by introducing one bromine atom to the 2-position of 9-(m-ClPh)-FH resulting in 2 pK units increase as expected. As a result, the absorbancereading remained constant (see Figure S3, Supporting Information). Then another electron withdrawing group (to give 2,7-Br2-9-Ph-FH or 2-Br-9-(3,5-Cl2-Ph)-FH, for example) was introduced to the indicator. However, the solubility of 2,7-Br<sub>2</sub>-9-Ph-FH or 2-Br-9-(3,5-Cl<sub>2</sub>-Ph)-FH in DMSO are poor. To our delight, we found that 2,7dibromo-9-naphthalen-2-yl-9H-fluorene 4 had better solubility in DMSO and its  $pK_a$  is determined to be 13.50 by a back titration method (see Table S1, Supporting Information). 9-Fluorenonephenylhydrazone 5 and its deritives were found to be good indicators (see Figure S4, S5, S6, Supporting Information) as previously described,<sup>12,28</sup> which introducing more electron withdrawing groups rendered its  $pK_a$  as low as 12.20 (indicator 8, see Table S1, Supporting Information).



<sup>a</sup> FH, fluoreno<sup>b</sup> 9-Fluorenonephenylhydrazone<sup>c</sup> 9-Fluorenone(4-chlorophenyl)hydrazone <sup>d</sup> 9-Fluorenone(2-chlorophenyl)hydrazone<sup>e</sup> 2,7-dibromo-9-Fluorenonephenylhydrazone <sup>f</sup> 1,4,5-triphenyl-2,3-(*para*-chlorophenyl)-cyclopenta-1,3-diene

Figure 2 Indicators involved in this work

With indicators **1-9** in hand (Figure **2**), among which compounds **2**, **3**, **4**, **8**, **9** were first reported as indicators, we were able to perform precise measurements with classical indicator overlapping method. For each triazolium precatalyst, at least two indicators were chosen to carry out two independent five or six-point runs, for the purpose of accuracy and precision. For each point, at least two UV/vis scans were required to make sure the establishment of acid-base equilibrium. The p $K_a$  values were obtained with small uncertainty (SD < 0.1 p*K*) and the results were listed in **Table 1** and **2**.

Generally, the p $K_a$  values of triazolium salts covered the range from 12.08 to 15.5, which were more acidic than imidazolium salts by 5-12 pK units or thiazolium salts by as much as 4.5 pK units. Among the different core structures measured in this work, pyrrolidine-based triazoliums were least acidic (**10a**, p $K_a$  = 14.55). Replacement of Nphenyl with electron withdrawing or donating groups caused appreciable change on equilibrium acidity. In order to investigate the substituent effect, the p $K_a$  values of triazoliums **10a-f** was plotted against the corresponding Hammett substituent values ( $\sigma_p$ )

 and a good linear correlation ( $R^2 = 0.99$ ) was obtained (Figure **3a**). The slope ( $\rho = 2.2$ ) was slightly smaller than that of benzoic acid system ( $\rho = 2.4$ ) in DMSO.<sup>29</sup> On the other hand, *N*-mesityl brought about nearly 1 p*K* unit (**10g**, p*K*<sub>a</sub> = 15.52) decrease in equilibrium acidity. This might be explained by *ortho* steric effect preventing aryl ring from being in the same plane with triazolium ring thus resulting in an increase in electron density and making it less stable, as an electron donating group would do. Introducing strong electron withdrawing groups would greatly increase acidity as expected and triazolium **10i** ( $pK_a = 12.08$ ) bearing a *N*-pentafluorophenyl was more acidic than acetic acid ( $pK_a = 12.6$ ).<sup>30</sup> The counter anion effect was also investigated and triazolium **10h** was synthesized with chloride as counter anion. As a result, **10h**'s  $pK_a$  almost identical with that of **10g** suggesting that the influence of counter anion on the acidity of NHC precursor is small.



**Figure 3** Correlation between the  $pK_a$  values of triazoliums in DMSO and Hammett substituent constants ( $\sigma_p$ ).

As shown in Table 2, morpholine-based triazolium salts (**12a-f**) covered the p $K_a$  range of 12.55 – 14.34. LEFR examination of substituent effect showed a good linear correlation ( $R^2 = 0.97$ ) with even smaller slope (Figure **3b**,  $\rho = 2.0$ ), indicating it's less sensitive to the change of charge by substituents. *N*-mesityl substituted NHC **12f** 

brought about only 0.9 pK unit decrease in equilibrium acidity in equilibrium acidity than **12a**, which was not unexpected considering its smaller  $\rho$  value. For triazoliums **13b-d**, side chain on the 5-position of morpholine ring did not cause appreciable change on equilibrium acidity ( $\Delta pK_a < 0.1$ ). Aminoindane-based triazolium **14a** ( $pK_a = 13.15$ ) was further enhanced by 0.7 pK unit compared to **12a**. Again, it seems that the effect of the counter anion on the acidity can be negligible by comparison of the  $pK_a$  values of triazolium **14b** and **14c**.

NHC Precursors	Ar	Indicator (p <i>K</i> <sub>a</sub> )	Measured $pK_a$	Assigned pK <sub>a</sub>				
$ \begin{array}{c}                                     $	Ph <b>10a</b>	<b>5</b> (14.90)	$14.53\pm0.03$					
		<b>2</b> (14.83)	$14.61\pm0.03$	$14.55\pm0.04$				
		<b>6</b> (14.15)	$14.53\pm0.01$					
	p-MeOPh	<b>3</b> (15.48)	$15.14\pm0.02$	$15.08 \pm 0.06$				
	10b	<b>5</b> (14.90)	$15.02\pm0.03$					
	<i>p</i> -MePh	<b>5</b> (14.90)	$14.85\pm0.02$	$14.83 \pm 0.03$				
	10c	<b>2</b> (14.83)	$14.82{\pm}~0.02$					
	<i>p-</i> FPh <b>10d</b>	<b>2</b> (14.83)	$14.32\pm0.02$	$14.28 \pm 0.03$				
		<b>6</b> (14.15)	$14.27\pm0.02$					
		4 (13.50)	$14.24\pm0.01$					
	<i>p</i> -ClPh	<b>6</b> (14.15)	$13.99\pm0.01$	$13.98 \pm 0.02$				
	10e	4 (13.50)	$13.97\pm0.02$					
	<i>p</i> -BrPh	<b>6</b> (14.15)	$13.97\pm0.01$	$13.96 \pm 0.02$				
	10f	4 (13.50)	$13.96\pm0.01$					
	Mes	<b>1</b> (15.65)	$15.48\pm0.02$	$15.52 \pm 0.05$				
	10g	<b>5</b> (14.90)	$15.57\pm0.01$					
	Mes <sup>a</sup>	<b>1</b> (15.65)	$15.45\pm0.02$	$15.46 \pm 0.03$				
	10h	<b>5</b> (14.90)	$15.47\pm0.02$					
	C <sub>6</sub> F <sub>5</sub>	8 (12.20)	$12.08\pm0.03$	$12.08 \pm 0.02$				
	10i	<b>9</b> (11.15)	$12.07\pm0.05$	$12.00 \pm 0.03$				
Ph- Ph- Ph BF <sub>4</sub>	Ph	<b>2</b> (14.83)	$14.30 \pm 0.02$	$14.25 \pm 0.05$				
	11	<b>6</b> (14.15)	$14.21\pm0.01$					

Table 1 Equilibrium Acidity Measurements of Pyrrolidine-Based Triazolium Salts in DMSO

<sup>a</sup> Cl<sup>-</sup> as counter anion

Furthermore, the Enders-type triazoliums<sup>31</sup> **15a** and **15b** were also examined in this study. The  $pK_a$  value of **15a** was nearly the same as BINOL ( $pK_a = 12.98$ ).<sup>25e</sup> Introducing another *N*-mesityl motif only brought about 0.3 pK unit decrease in equilibrium acidity, which may be explained by multiple aromatic rings attached to the triazolium ring.

 

 Table 2 Equilibrium Acidity Measurements of Morpholine-Based, Aminoindane-Based and Acyclic Triazolium Salts in DMSO

NHC Precursors	Ar	Indicator (pKa)	Measured $pK_a$	Assigned pK <sub>a</sub>
$ \begin{array}{c}                                     $	Ph	<b>6</b> (14.15)	$13.85 \pm 0.02$	$13.84 \pm 0.02$
	12a	4 (13.50)	$13.83 \pm 0.01$	
	p-MeOPh	<b>2</b> (14.83)	$14.38\pm0.02$	$14.34 \pm 0.04$
	12b	<b>6</b> (14.15)	$14.30\pm0.03$	
	<i>p</i> -FPh	<b>6</b> (14.15)	$13.64\pm0.02$	$13.64 \pm 0.04$
	12c	4 (13.50)	$13.60\pm0.03$	
	p-ClPh	4 (13.50)	$13.16\pm0.03$	$13.15 \pm 0.03$
	12d	7 (12.95)	$13.15\pm0.03$	
	p-CNPh	7 (12.95)	$12.59\pm0.01$	$12.55 \pm 0.04$
	12e	8 (12.20)	$12.50\pm0.02$	
	Mes	2 (14.83)	$14.80\pm0.02$	$14.75 \pm 0.04$
	12f	<b>6</b> (14.15)	$14.72\pm0.02$	
$ \begin{array}{c}                                     $	R=s-Bu	<b>6</b> (14.15)	$13.78\pm0.02$	13.73 ± 0.05
	Ar=Ph	<b>4</b> (13.50)	$13.66 \pm 0.02$	
	13a			
	R=t-Bu	<b>2</b> (14.83)	$14.43\pm0.02$	
	Ar=Mes	<b>6</b> (14.15)	$14.41 \pm 0.01$	$14.43 \pm 0.02$
	13b			
	R= <i>i</i> -Pr	<b>2</b> (14.83)	$14.55\pm0.02$	
	Ar=Mes	<b>6</b> (14.15)	$14.49 \pm 0.01$	$14.53 \pm 0.03$
	13c			
	R=Bn	<b>2</b> (14.83)	$14.54\pm0.01$	14.51 ± 0.03
	Ar=Mes	<b>6</b> (14.15)	$14.48\pm0.01$	
	13d			
N BF <sub>4</sub> N BF <sub>4</sub>	Ph	4 (13.50)	$13.16\pm0.02$	$13.15 \pm 0.03$
	14a	7 (12.95)	$13.13\pm0.01$	
	Mes	<b>6</b> (14.15)	$13.75\pm0.02$	$13.72 \pm 0.04$
	14b	4 (13.50)	$13.68\pm0.01$	
14	Mes <sup>a</sup>	<b>6</b> (14.15)	$13.85\pm0.02$	$13.85 \pm 0.02$
	14c	4 (13.50)	$13.84\pm0.01$	



Figure 4 Comparison of  $pK_a$  values of some triazolium salts in DMSO and water

O'Donoghue reported the  $pK_a$  values of twenty triazolium salts in aqueous solution by deuterium exchange method.<sup>11f</sup> Remarkably, their results remained constant with regard to *N*-substituent, ring size and substituent pattern (Figure 4). In both solvents, the  $pK_a$  values of most triazolium salts showed similar trend except for the aminoindane-based triazolium salt **14a**, which was most acidic in DMSO but not in water among the three different core structures. Correlation between the  $pK_a$  values of these triazolium salts in DMSO and in water became poor due to this exception (see Figure **S7**, **S8**, Supporting Information). Previous reports have shown that the  $pK_a$  values for thiazolium salts, imidazolium salts or alkylammonium ions in DMSO were close to the values in water within ±1 pK unit.<sup>11d,12,16,32</sup> The small differences can be explained by

subtle changes in solvation effect between DMSO and water. For example, water is known to solvate (or stabilize) cations better than nonhydroxylic solvents such as DMSO through hydrogen bonding, while the solvation effect on deprotonated product, neutral carbene, should be more or less the same. Therefore, the stronger solvated thiazolium or imidazolium cations has to overcome greater energetic barrier during deprotonation in water than they do in DMSO thus result in higher  $pK_a$  values. Amyes et al. had examined the effect of heteroatom substituent on the kinetic and thermodynamic acidity of the C(2)-proton of simple azolium cations.<sup>11d</sup> For triazolium salts, the third nitrogen atom in the azolium ring may make hydrogen bonding predominate before and after the deprotonation in water to DMSO, in which the triazolium cations and triazolylidene carbenes are solvated by electrostatic effect, causes  $pK_a$  to increase by as much as 3-4 pK units.

Since a great number of NHC enabled organocatalytic reactions were performed in nonhydroxylic solvents such as tetrahydrofuran or toluene, it would be useful to compare the acidity of triazolium salts in these solvents with that of DMSO; however, to the best of our knowledge, no such  $pK_a$  values have been reported in tetrahydrofuran or toluene. Over the past decades,  $pK_a$  data in DMSO has been extensively studied and accumulated which makes it one of the biggest fundamental database for organic chemistry and easy access through *i*Bond 2.0.<sup>30</sup> The relative acidity strength obtained in DMSO for triazolium salts and other bases should hold in other nonhydroxylic solvents thus help choosing proper bases in NHC enabled reactions employing

triazolium salts as precatalysts.

In summary, we have measured the equilibrium acidities of a number of triazolium-based NHC precursors in DMSO by overlapping indicator method. The  $pK_a$  values cover the range from 12.08 to 15.52, which are more acidic than imidazolium salts by 5-12 pK units or thiazolium salts by as much as 4.5 pK units. Substituent effect on equilibrium acidity is examined. Moreover, comparisons of  $pK_a$  values between DMSO and water are also discussed.

#### EXPERIMENTAL SECTION

**General.** All commercial reagents were used as received, unless otherwise noted. NMR spectra were recorded on a Bruker AV400 spectrometer at 400 MHz for <sup>1</sup>H and 101 MHz for <sup>13</sup>C, respectively. Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. Melting points were measured using a micro melting point apparatus and were not corrected. Elemental Analysis was performed using an elementar CHONS Elemental Analyzer (vario EL CUBE) with standard deviation less than 0.4%. Anhydrous solvents were prepared according to standard procedure. Ethyl ether, tetrahydrofuran and toluene were distilled from sodium and benzophenone; CH<sub>2</sub>Cl<sub>2</sub> were distilled from CaH<sub>2</sub>; Methanol and ethanol were treated with magnesium and iodine prior to distillation.

Indicators **1**, **5**, **6**, **7** were synthesized according to literature procedure and characterization data were in agreement with previous report.<sup>12,28</sup> All indicators were carefully recrystallized from methanol or ethanol or dichloromethane threes time and dried in high vacuum before the measurement. Triazolium salts **13a-d**, **14b** were

commercial available. Other were synthesized according to literature and all analytical data agreed well with reported values.<sup>11f, 13b, 31</sup>

**Synthesis. 2-bromo-9-(meta-chlorophenyl)-9H-fluorene (2)** A solution of 2-bromo-9-fluorenone (5g, 19.3 mmol, 1.0 eqiv) in dry ether (80 ml) was cooled with an icewater bath for 10 minutes before the addition of 60 ml of phenyl magnesium bromide ether solution prepared from 1-bromo-3-chloro-benzene (7.66g, 40 mmol, 2.1 eqiv), magnesium (0.96g, 40 mmol, 2.1eqiv) and a small amount of iodine. The reaction mixture was stirred and slowly warmed to room temperature until TLC indicated complete conversion of 2-bromo-9-fluorenone. The reaction was quenched with ammonium chloride and extracted with ether (60ml) three times. The combined organic phase was dried with Na<sub>2</sub>SO<sub>4</sub>, then the solvent was removed in vacuo. The crude product was used in next step without further purification.

The crude product was placed into a 250 ml round bottom flask and 80 ml dry CH<sub>2</sub>Cl<sub>2</sub> was added. The flask was chilled in an ice-water bath and Et<sub>3</sub>SiH (4.5g, 38.6 mmol, 2.0 eqiv) was added in one portion. A solution of BF<sub>3</sub>Et<sub>2</sub>O(5.5g, 38.6 mmol, 2.0 eqiv) was added dropwise and the reaction mixture was maintained 0 °C for 1 h then warmed to room temperature. The reaction was stirred overnight and quenched with water and extracted with CH<sub>2</sub>Cl<sub>2</sub>, the combined organic phase was dried with Na<sub>2</sub>SO<sub>4</sub>, then the solvent was removed in vacuo. The product was recrystallized from ethanol three times and obtained as white needles 2.7 g (two step yield: 40%) with melting point of 91-93 °C.

<sup>1</sup>**H NMR** (400 MHz, DMSO-*d*<sub>6</sub>) δ 7.95 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 8.2 Hz, 1H),

7.58 (dd, J = 8.2, 1.9 Hz, 1H), 7.49 – 7.35 (m, 2H), 7.29 (d, J = 4.9 Hz, 4H), 7.16 (s, 1H), 7.01 – 6.91 (m, 1H), 5.29 (s, 1H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 149.3, 146.7, 143.3, 139.7, 139.4, 133.3, 130.7, 130.6, 128.0, 127.8, 127.0, 126.6, 125.2, 122.2, 120.6, 120.4, 52.6.

Anal. calcd for C19H12BrCl: C, 64.17; H, 3.40. Found: C, 64.63; H, 3.52.

**2-bromo-9-(naphthalen-2-yl)-9H-fluorene (3)** This compound was synthesized from 2-bromo-9-fluorenone, 2-Bromonaphthalene and magnesium as previous described. Recrystallization from ethanol afforded compound **3** as white solid with melting point of 140-142 °C.

<sup>1</sup>**H NMR** (400 MHz, Chloroform-*d*) δ 7.89 – 7.80 (m, 4H), 7.72 (dd, *J* = 8.2, 1.6 Hz, 2H), 7.59 – 7.42 (m, 5H), 7.37 – 7.29 (m, 2H), 6.91 (dd, *J* = 8.5, 1.8 Hz, 1H), 5.21 (s, 1H).

<sup>13</sup>C NMR (101 MHz, Chloroform-*d*) δ 150.0, 147.7, 140.2, 140.2, 138.2, 133.7, 132.8, 130.7, 128.8, 128.8, 127.9, 127.8, 127.8, 127.7, 127.5, 126.4, 126.1, 125.9, 125.6, 121.4, 121.2, 120.1, 54.6.

**HRMS** (**ESI**<sup>+</sup>) calculated for [C<sub>23</sub>H<sub>15</sub>Br+NH<sub>4</sub><sup>+</sup>]: 388.0695; found: 388.0684.

**2,7-dibromo-9-(naphthalen-2-yl)-9***H***-fluorene (4)** This compound was synthesized from 2,7-dibromo-9-fluorenone, 2-Bromonaphthalene and magnesium as previous described. Recrystallization from ethanol afforded compound **4** as white solid with melting point of 171-173 °C.

<sup>1</sup>**H NMR** (400 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  7.99 (d, *J* = 8.2 Hz, 2H), 7.93 – 7.84 (m, 3H), 7.79

(d, *J* = 8.5 Hz, 1H), 7.64 (dt, *J* = 8.2, 1.2 Hz, 2H), 7.56 – 7.42 (m, 4H), 6.89 (dd, *J* = 8.5, 1.7 Hz, 1H), 5.48 (s, 1H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 149.7, 138.8, 137.5, 133.1, 132.2, 130.7, 128.7, 128.2, 127.6, 127.6, 127.2, 126.4, 126.0, 125.7, 122.6, 120.9, 53.3.

Anal. calcd for C23H14Br2: C, 61.37; H, 3.13. Found: C, 61.42; H, 2.97.

**2,7-dibromo-9-Fluorenonephenylhydrazone (8)** To a 100 ml round bottom flask was added 2,7-dibromo-9-fluorenone (3.75 g, 11.1 mmol, 1.0 eqiv), ethanol (20 ml), phenylhydrazine (1.2g, 11.1 mmol, 1.0 eqiv) and H<sub>2</sub>SO<sub>4</sub> (0.4 ml). The mixture was refluxed for 30 minutes and then cooled to room temperature and yellow precipitate formed. The yellow solid was filtered and recrystallized from CH<sub>2</sub>Cl<sub>2</sub> twice to afford title compound as yellow needles (1.6g, yield 34%) with melting point 181-182 °C.

<sup>1</sup>**H NMR** (400 MHz, DMSO-*d*<sub>6</sub>) δ 10.59 (s, 1H), 8.62 (d, *J* = 1.7 Hz, 1H), 7.90 (d, *J* = 1.8 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.60 (ddd, *J* = 8.7, 7.2, 1.4 Hz, 3H), 7.47 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.37 (dd, *J* = 8.6, 7.3 Hz, 2H), 7.01 (dd, *J* = 8.0, 6.7 Hz, 1H).

<sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 144.7, 139.8, 137.6, 135.5, 135.0, 131.5, 130.3, 130.2, 129.0, 127.7, 122.8, 122.2, 122.0, 121.9, 121.0, 114.6.

**HRMS (ESI**<sup>+</sup>) calculated for [C<sub>19</sub>H<sub>12</sub>Br<sub>2</sub>N<sub>2</sub>+H<sup>+</sup>]:428.9420; found: 428.9412. Anal. calcd for C19H12Br2N2: C, 53.30; H, 2.83; N, 6.54. Found: C, 53.61; H, 2.67; N, 6.66.

1,4,5-triphenyl-2,3-(para-chlorophenyl)-cyclopenta-1,3-diene (9) To a 250 ml round bottom flask was added 4,4'-dichlorobenzil (4.02 g, 14.4 mmol, 1.0 eqiv), 1,3diphenylpropan-2-one (3.02 g, 14.4 mmol, 1.0 eqiv), KOH (0.81 g, 14.4 mmol, 1.0 eqiv) and ethanol (100 ml). The reaction mixture was heated to reflux for 30 minutes and the solution turned into dark red. The reaction mixture was poured into 100 ml ice-water mixture and stirred for another 15 minutes. The solution was filtered and the precipitate was washed with cold water and cold methanol subsequently and dried in vacuo to yield 3,4-bis(4-chlorophenyl)-2,5-diphenylcyclopenta-2,4-dien-1-one (5.08 g, yield 78%) as purple power.<sup>1</sup>H NMR (400 MHz, Chloroform-*d*)  $\delta$  7.30 (dd, J = 5.4, 2.0 Hz, 6H), 7.26 -7.19 (m, 8H), 6.89 (d, J = 8.5 Hz, 4H).<sup>13</sup>C NMR (101 MHz, Chloroform-d)  $\delta$  199.7, 152.7, 134.9, 131.3, 130.8, 130.3, 130.2, 128.7, 128.3, 127.9, 126.0. To a flame-dried round bottom flask was added 3,4-bis(4-chlorophenyl)-2,5-diphenylcyclopenta-2,4dien-1-one (2.31 g, 5.1 mmol, 1.0 eqiv) and 50 ml dry ether under Ar, then a solution of phenyl magnesium bromide (10 mmol) was added dropwise through a syringe. After complete addition of PhMgBr, the dark red reaction solution turned into yellow. After stirring for another 10 minutes, the reaction was quenched with 1 M HCl and extracted with ether (50 ml) three times. The combined organic phase was washed with water dried with Na<sub>2</sub>SO<sub>4</sub>, then the solvent was removed in vacuo. The crude product was used in next step without further purification. The crude product was placed into a 100 ml round bottom flask and 50 ml dry CH<sub>2</sub>Cl<sub>2</sub> was added. The flask was chilled in an icewater bath for 10 minutes before Et<sub>3</sub>SiH (1.74g, 15 mmol, 3.0 eqiv) was added in one portion. A solution of BF<sub>3</sub>Et<sub>2</sub>O (2.13g, 15 mmol, 3.0 eqiv) was added dropwise and the reaction mixture was maintained 0 °C for 1 h then warmed to room temperature. The reaction was stirred overnight and quenched with water, extracted with CH<sub>2</sub>Cl<sub>2</sub>, the

combined organic phase was dried with Na<sub>2</sub>SO<sub>4</sub>, then the solvent was removed *in vacuo*. The product was washed with CH<sub>2</sub>Cl<sub>2</sub> several times and obtained as pale green power 0.8 g (1*H* and 2*H* mixture, two step yield: 30%) with melting point 105-108 °C. <sup>1</sup>H NMR (400 MHz, Methylene Chloride-*d*<sub>2</sub>) δ 7.33 – 6.90 (m, 23H), 5.16 (s, 1H). <sup>13</sup>C NMR (101 MHz, Methylene Chloride-*d*<sub>2</sub>) δ 147.2, 146.8, 146.0, 145.2, 145.0, 144.5, 143.8, 143.6, 137.6, 136.7, 136.0, 135.9, 135.8, 135.5, 135.4, 134.5, 134.1, 132.8, 132.3, 132.2, 132.2, 131.5, 131.5, 131.5, 130.3, 130.2, 130.1, 130.0, 129.8, 129.0, 128.9, 128.8, 128.7, 128.6, 128.4, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.1, 127.0, 127.0, 126.8, 126.7, 126.7, 126.7, 126.6, 62.3, 61.4.

**HRMS (ESI**<sup>+</sup>) calculated for [C<sub>35</sub>H<sub>24</sub>Cl<sub>2</sub>+H<sup>+</sup>]: 515.1328; found: 515.1316.

 $pK_a$  measurement. All manipulations were carried out under dry Argon according to literature.<sup>26</sup> Weights of indicators and acids were recorded to 0.01 mg, others 0.0001 g. DMSO was freshly distilled from NaNH<sub>2</sub> under reduced pressure. *K*-dimsyl solution was prepared by reaction of freshly distilled DMSO and KH, and the mineral oil was washed with freshly distilled pentane. UV/vis spectra were recorded on a Hitachi U-3000 spectrometer.

The p $K_a$  measurement was started by flame-drying and degassing the cuvette with a three-way stopcock on its top. After cooling under dry Argon atmosphere, the cuvette was weighed and 1.5 ml DMSO and dimsyl was added. Again the cuvette was weighed so that the exact amount of dimsyl solution could be calculated. The cuvette was then placed into the spectrometer and recorded a baseline at 25 °C. The solution of indicator

with known p $K_a$  and concentration was added and the weight and UV/vis spectrum were recorded. This operation was repeated several times before the addition of excess amount of indicator solution. A work calibration curve was obtained from Beer's Law plot of absorbance vs added amount of indicator solution. Then the solution of triazolium salt was added to the cuvette in several aliquots, and for each addition, both spectrum and weight of the cuvette were recorded. The equilibrium constant  $K_{eq}$  could be calculated for each addition of triazolium salt solution, thus the p $K_a$  of triazolium salt could be obtained. The p $K_a$  values measured in one run, between independent runs are usually reproducible to within  $\pm 0.05$  pK unit.

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#### Note

The authors declare no competing financial interest

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# **Supporting Information**

 $pK_a$  determination of new indicators, UV/vis spectra, <sup>1</sup>H and <sup>13</sup>C NMR spectra of indicators and triazolium salts. This material is available free of charge via the Internet at http://pubs.acs.org/

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