Synthesis and Properties of 2-(2-Pyridyl)-1-azaazulene

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Abstract: The title azaazulene **3** was synthesized either by reaction of tropone with *N*-{(2-pyridyl)acetyl}pyridinium iodide in the presence of ammonium acetate or by palladium-catalyzed cross-couplings between 2-halo-1-azaazulene and 2-substituted pyridine. The compound shows relatively stronger basicity compared with 2,2’-bipyridyl. While **3** showed no emission from the S_1 state but from the S_2 state like azulene does, the diprotonated species of **3**, generated in 50% H_2SO_4, exhibited emission from the S_1 state. Cationic metal-dependent absorption and emission were also studied.

Keywords: Basicity; UV-Vis absorption spectrum; Emission spectrum; Cross-coupling reaction; Metal complexation.

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To date, synthetic studies of pyridyl-azaazulene and -diazaazulenes[1] which can be used a bidentate ligand like 2,2’-bipyridyl[2] have been limited to two cases reported by Abe et al. and Nakano et al. The former authors prepared 2-chloro-8-(2-pyridyl)-1-azaazulene (**1**)[3] by addition of 2-pyridylmagnesium reagent to 2-chloro-1-azaazulene and subsequent oxidation, and Nakano et al. synthesized 2-(2-pyridyl)-1,3-diazaazulene (**2**)[4] by the reaction of 2-methoxytropone with pyridylamidine. However, their basic physical properties have not been disclosed fully and also application of **1** to metal complexation is restricted. Abe et al. reported that with copper ion **2** provided a transition-metal complex in which **2** served as a bidentate ligand in a whole shape of the trigonal bi-pyramidal structure but not of a square plane structure probably because of steric interaction between the pyridyl 3’ and azulenyl 7 protons in its planar structure. Indeed, DFT calculations[5] predict the severe interaction in a planar structure of **2**.[6] In this paper we describe the synthesis and basic physical properties of the title compound **3** which is expected to behave as a bidentate ligand in a different way from **2**.

<Insert Chart 1 >

The synthesis of **3** was achieved by two methods as shown in Scheme 1. One method is based on the azaazulene synthesis of Sugimura et al.[7] The reaction of tropone (**4**) with the ylide, generated from *N*-{(2-pyridyl)acetyl}pyridinium iodide (**5**)[8], in the presence of ammonium acetate provided **3**. After an exploration of the reaction conditions in this intricate multi-step reaction, the optimal yield of **3** (58%) was realized when refluxed in acetic acid with 7.5 equivalents of ammonium acetate.[10] The other method is a Pd-catalyzed cross-coupling reaction between 2-halo-1-azaazulenes (**6a-c**)[9] and 2-substituted pyridines **7**. Results of the cross-coupling reactions are listed in Table 1. The Suzuki-Miyaura coupling[11] of **6** was examined with 2-pyridineboronic acid *N*-phenyldiethanolamine (NPDEA) ester[12] and the yields of **3** were low (entry 1-3). The Negishi coupling with 2-pyridylzinc bromide required a greater amount of the palladium catalyst and resulted in much better yields; while **6a** and **6b** were not consumed completely even in a longer reaction period (entry 4-5), the results with **6c** gave the highest yield (92%) of **3** (entry 6). The Stille coupling (entry 7-9) with tributylstannylpyridine **7c** was found to proceed faster than the other couplings and provided moderate yields of **3**. In contrast to the other couplings, the Stille coupling with **6c** was hampered by formation of by-products, affording **3** in 14% yield.

<Insert Scheme 1 and Table 1>

The title compound **3** was isolated as fine red needles after sublimation and was characterized by spectroscopic and combustion analyses. Although allowing a sample of **3** to stand at room temperature under air resulted in a slight change of color from fine to dull red, the sample can be stored under inert gas atmosphere in a refrigerator without any change for at least more than a couple of months. In the UV-Vis spectrum in acetonitrile the longest wavelength absorption maximum of **3** was observed at λ_{max} = 512 nm which showed a bathchromic shift in less polar solvents, suggesting significant contribution of the dipolar resonance forms, **3A** and **3B**, at the ground state. A hypochromic shift was observed in acidic solutions of **3**. In 50% H_2SO_4 the maximum was observed at λ_{max} = 429 nm with a hyperchromic effect and thus the solution appeared in yellow. Mono- and diprotonated species of **3** with hydrogen bromide were also isolated.[13] The pK_a values of the salts were determined by pH measurements of arbitrary solutions prepared by mixing **3** with these salts[14,15] to be 2.42 ± 0.12 (pK_{a2}) for the proton dissociation of **3**H_2^{2+} and 6.02 ± 0.06 (pK_{a1}) for the dissociation of **3**H^+ (Table 2). Both values are greater than the reported values of 2,2'-pyridyl;[15-17] *id est*, both the imino groups of **3** are stronger bases than those of 2,2'-pyridyl. The major reason can be drawn from the stabilized resonance structures[18] of **3A** and **3B** with the negatively charged five-membered ring. The pK_{a1} value of **3** is slightly less than that of 2-phenyl-1-azaazulene (**8**).[8,19] The phenomenon is rationalized by a fact that a pyridyl group shows a greater electron-withdrawing resonance effect than a phenyl group does. Therefore, the monoprotonated species **3**H^+ is thermodynamically destabilized by the pyridyl group much more than **8**H$^+$ is by the phenyl group.[20]

<Insert Table 2>

An outstanding feature of physical properties of **3** is its pH-dependent emission spectrum at room temperature. The free base **3** in acetonitrile showed an emission, assumed to be $S_2 \rightarrow S_0$ relaxation, at 434 nm upon excitation at 368 nm (Φ = 5.26 x 10^{-3})[21] and no emission upon excitation at the longest wavelength maximum of 512 nm (Fig. 1),[22] similarly seen in the case of azulene.[23] On the other hand, the diprotonated species **3**H_2^{2+} in 50% H_2SO_4 exhibited an emission of 484 nm upon excitation at the longest wavelength maximum of 429 nm (Φ = 4.10 x 10^{-4}),[21] assumed to be $S_1 \rightarrow S_0$ relaxation (Fig. 2).[24] Noteworthily this paper reports at a first time that 1-azaalulenes show a clear emission upon excitation at the longest wavelength absorption in acidic media at room temperature,[25] though the quantum yield is low.

<Insert Figure 1 and 2>

The absorption and emission spectra of **3** were found also dependent on a metal cation present in a solution. While the longest wavelength absorption maximum of **3** in the presence of a large excess amount of sodium perchlorate in acetonitrile indicated a slight hypochromic shift of 14 nm, the maximum of **3** in the presence of the same amount of magnesium perchlorate showed a greater hypochromic shift of 34 nm with a greater coefficient. Besides, while an emission centered at 543 nm upon excitation of 478 nm was observed in the presence of magnesium perchlorate, no emissions upon excitation of 498 nm in the presence of sodium perchlorate was obsereved but an emission of 434 nm seen in the free base (Figs 3 and 4). It is assumed that **3** forms a rigid complex with magnesium ion, probably in a tetrahedral shape,[26] but not like with sodium ion.

<Insert Figure 3 and 4>

As a summary, we have synthesized a novel 1-azaazulene derivative, 2-(2-pyridyl)-1-azaazulene (**3**), either by reaction of tropone with *N*-{(2-pyridyl)acetyl}pyridinium iodide in the presence of ammonium acetate or by cross-couplings between 2-halo-1-azaazulene and 2-substituted pyridine. The compound exhibits relatively stronger basicity and it should be emphasized that **3** showed the pH dependent spectra and also the distinctive absorption and emission spectra for cationic metal. Further a study on chelation of this novel ligand with various metal cations including transition metals is under a progress.

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References and Notes

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5. DFT calculations were carried out at the B3LYP/6-31G(d) level of theory by using the Mulliken program (ver. 2.0.0, IBM Inc.).
6. Total energy difference between the planar structure with the two nitrogen atoms at the same side and the most stable structure with a dihedral angle through 1’-2’-8-8a of 148.8˚ is 0.21619 a.u (13.521 kcal mol^{-1}). The distance between the pyridyl H-3’ and azulenyl H-7 protons in the planar structure is 1.756 Å (175.6 pm).
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9. For the chloride and bromide, see; Nozoe, T.; Seto, S.; Matsuura, S.; Terasawa, T. *Chem. Ind.* **1954**, 1357-1358. The iodide was obtained in 66% yield from the bromide by treating with magnesium and subsequently with iodine.
10. The details of this reaction were as follows; A solution of **4** (1.06 g,10.0 mmol), **5** (3.65 g, 11.2 mmol), ammonium acetate (5.77 g, 75 mmol) in 100 mL of acetic acid was refluxed for 6 hr. The reaction mixture was cooled and carefully poured into a $NaHCO_3$ aq. solution, and was passed through a Celite pad. The filtrate was diluted with ethyl acetate (100 mL), and the organic layer was separated and washed with a thiosulfate aq. solution and brine. After dryness over anhydrous Na_2SO_4, evaporation gave red solids, which were chromatographed on alumina (eluted with AcOEt/hexane = 3/1) and then sublimed (150 ˚C/ 3 mmHg) to give 1.20 g (58% yiled) of **3** as fine red needles: Mp 160-161 ˚C. ^{1}H-NMR ($CDCl_3$) δ = 8.80 (m, dm, J = 4.8 Hz, 1H, H-6’), 8.75 (d, J = 9.6 Hz, 1H, H-8), 8.62 (d, J = 9.6 Hz, 1H, H-4), 8.57 (dm, J = 7.2 Hz, 1H, H-3’), 8.14 (s, 1H, H-3), 7.87 (td, J = 7.2, 1.2 Hz, 1H, H-4’), 7.86 (tt, J = 9.6, 1.1 Hz, 1H, H-6), 7.77 (t, J = 9.6 Hz, 1H, H-7), 7.65 (t, J = 9.6 Hz, 1H, H-5), 7.31 (ddd, J = 7.2, 4.8, 1.2 Hz, 1H, H-5’) ppm; ^{13}C-NMR ($CDCl_3$) δ = 112.7, 123.0, 124.1, 128.9, 129.7, 136.3, 136.7, 136.9,

137. 8, 148.0, 150.1, 153.8, 158.7, 166.4 ppm.

11. For the Suzuki-Miyaura cross-coupling reactions of 1-azaazulene at the 3-position, see ref 1b.
12. Bouillon, A.; Lancelot, J.-C.; Santos, J. S. d. O.; Collot, V.; Bovy, P. R.; Rault, S. *Tetrahedron*, **2003**, *59*, 10043-10049.
13. Salt **3**·HBr: Yellow crystals, mp 223-225 ˚C. Salt **3**·2(HBr): Yellow crystals, mp 219-221 ˚C.
14. Measurements were carried out in the presence of 0.5 M $NaClO_4$ in 50% aqueous ethanol.
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21. The quantum yield of **3** was obtained with anthracene as a standard ($\Phi = 2.7 \times 10^{-1}$) in ethanol and that of **3**H_2^{2+} with 2-aminopyridine as a standard ($\Phi = 3.7 \times 10^{-1}$) in 0.5M H_2SO_4.
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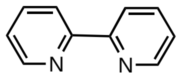
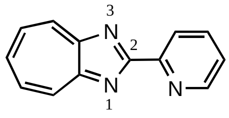
24. The monoprotonated species **3**H^+ also exhibited the $S_1 \rightarrow S_0$ emission with a quantum yield of 0.027, which was measured with 2-aminopyridine as a standard ($\Phi = 0.48$) in acetonitrile.
25. We also found that 2-phenyl-1-azaazulene (**8**) behaved similarly.
26. The Job plot of **3** with magnesium perchlorate using absorption changes indicated the binding mode of two of **3** to one of magnesium ion.

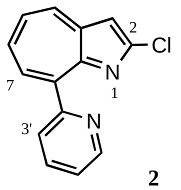
Chart 1



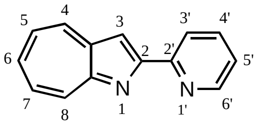
2,2'-bipyridyl



1



2



3

Scheme 1. Synthetic methods of **3**.

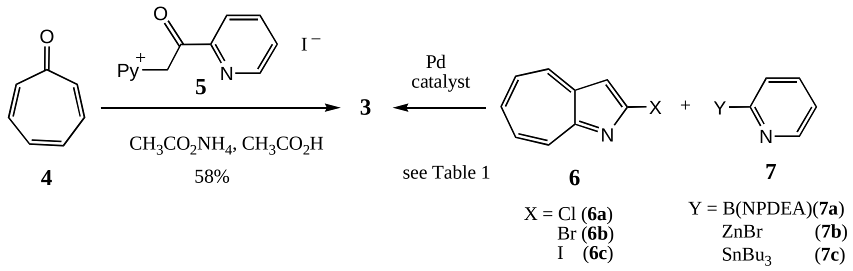
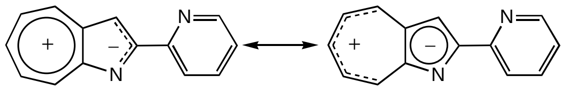


Table 1. Results of cross-coupling reactions of. 2-halo-1-azaazulene **6**.

entry	**6**	**7**	reaction conditions	yield (%) of **3** [a]	recovery of **6**
1	**6a**	**7a**[b]	5%Pd(PPh_3)$_2$$Cl_2$, CuI, Cs_2CO_3, THF, refl, 4 h	0	95
2	**6b**	**7a**[b]	5%Pd(PPh_3)$_2$$Cl_2$, CuI, Cs_2CO_3, THF, refl, 4 h	20 (22)	7
3	**6c**	**7a**[b]	5%Pd(PPh_3)$_2$$Cl_2$, CuI, Cs_2CO_3, THF, refl, 4 h	25	0
4	**6a**	**7b**[c]	10%Pd(PPh_3)$_4$, THF, 60˚ C, 48 h	47 (68)	32
5	**6b**	**7b**[c]	10%Pd(PPh_3)$_4$, THF, 60˚ C, 48 h	51(80)	36
6	**6c**	**7b**[c]	10%Pd(PPh_3)$_4$, THF, 60˚ C, 48 h	92	0
7	**6a**	**7c**[d]	5%Pd(PPh_3)$_4$, CuO, DMF, 120 ˚C, 3 h	44	0
8	**6b**	**7c**[d]	5%Pd(PPh_3)$_4$, CuO, DMF, 120 ˚C, 3 h	47	0
9	**6c**	**7c**[d]	5%Pd(PPh_3)$_4$, CuO, DMF, 120 ˚C, 3 h	14[e]	0

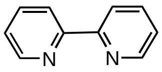
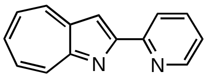
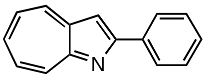
[a] The yields in parentheses are based on the consumed starting material. [b] An excess of the reagent (3 eq.) were used. [c] An excess of the reagent (2.7 eq.) were used. [d] A slightly excess of the reagent (1.2 eq.) was used. [e] The desired product **3** was obtained with a mixture of by-products whose structures were not clarified yet.

Chart 2



3A **3B**

Table 2. The pK_a values of 2,2'-bipyridyl, **3**, and **8**.

amines		pK_{a1}	pK_{a2}
 2,2'-bipyridyl		4.34[a] 4.12[b]	– 0.20[a] – 0.52[c]
	**3**	6.02[d]	2.42[d]
	**8**	6.81[d]	

[a] Taken from ref. 16. [b] Taken from ref. 15.
[c] Taken from ref. 17. [d] Measured in this study.

Figure 1. The UV-Vis absorption and normalized emission spectra of **3** in CH_3CN.

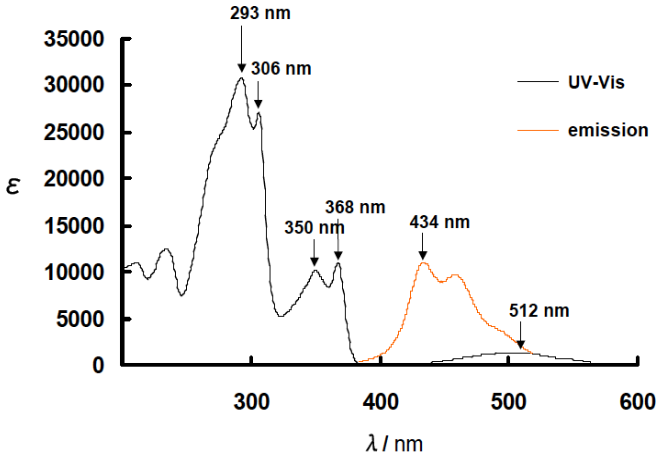


Figure 2. The UV-Vis absorption and normalized emission spectra of **3** in 50% H_2SO_4.

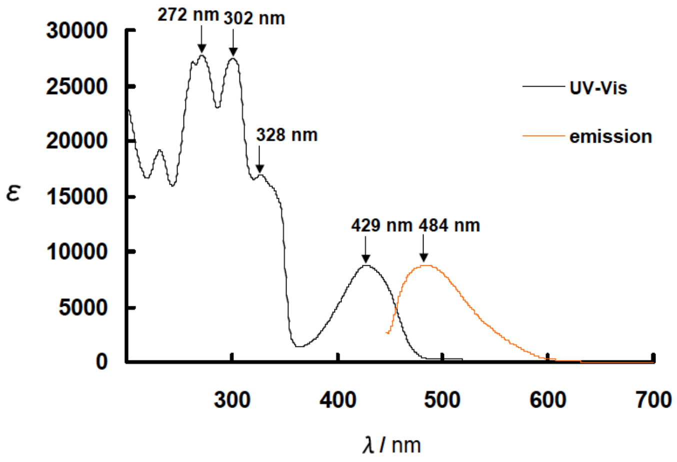


Figure 3. The UV-Vis absorption and normalized emission spectra of **3** in the presence of magnesium perchlorate (1000 eq. to **3**).

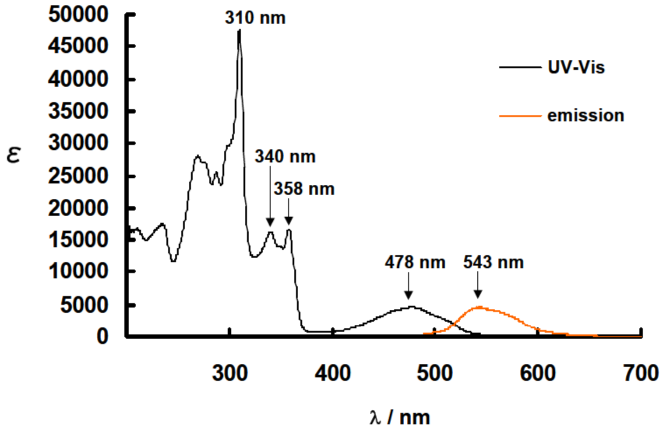


Figure 4. The UV-Vis absorption and normalized emission spectra of **3** in the presence of sodium perchlorate (1000 eq. to **3**).