

Synthesis and Properties of 2,6-Bis(1-Azaazulen-2-yl)-Pyridine

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Abstract: The title compound, 2,6-bis(1-azaazulen-2-yl)pyridine (5), was synthesized by condensation between tropone (6) and 2,6-bis(pyridinioacetyl)pyridinium salt (7) in the presence of ammonium acetate. By slow addition of an acetic acid solution of the pyridinium salt 7 to a mixture of 6 and ammonium acetate the yield of 5 was improved. Physical properties of 5 were investigated. It is worthy to note that upon irradiation 5 shows strong emission in acidic media in contrast to very weak emission in neutral media.

Keywords: Pincer-Type Ligand, Azaazulene, Pyridine, Tropone, Basicity, Emission Behavior

1. Introduction

A pincer-type ligand works to stabilize metal-complexes singly by multiple rigid chelation onto a metal ion.[1–2] The uses of pincer complexes as a catalyst are emerging in various kinds of organic syntheses.[3–4] The pincer ligands having amine donors, such as pyridine and a dialkylamino group, in the side arms are easily accessible, and therefore most studied.[5] Meanwhile, we have synthesized various 1-azaazulene derivatives (1–4), shown in Fig. 1, and studied ability of 1-azaazulenes[6–9] as a ligand for metal ions and as a base for Brønsted acids.[10–12]

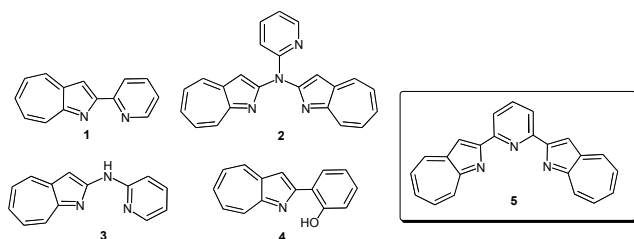


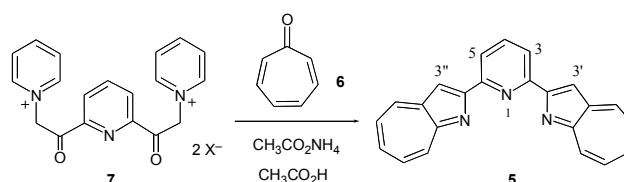
Fig. 1. 1-Azaazulene derivatives.

It was found that 2-(pyrid-2-yl)-1-azaazulene (1) chelated with metal ions and bound with proton and, then, showed the enhanced emission upon photoexcitation.[10] During a course of our study, we have been interested in a pincer ligand having 1-azaazulenyl groups. In this paper we describe synthesis of

the title compound 5, which has two 1-azaazulenyl groups at the 2,6-positions of pyridine, and its physical and spectroscopic properties.

2. Results and Discussion

Synthesis of the title compound 5 was examined by condensation between tropone (6) and 2,6-bis(pyridinioacetyl)pyridinium salt (7) [5,13] in the presence of ammonium acetate (Scheme 1). The synthetic method of 1-azaazulenes from 6 and various pyridinioacetyl salts was developed by Sugimura *et al.* [14] and we applied it to the synthesis of 1 and 4. [10,11] However, under the reported reaction conditions with a mixture of 2:1 ratio of 6 and 7 in refluxing acetic acid, 5 was not obtained at all (Table 1, entry 1–4).



Scheme 1. Synthesis of 5.

Sugimura *et al.* pointed out that the pyridinium ylide formed under the conditions added not only to tropone (6) to lead the azazulene product *via* several reaction intermediates but also added to the intermediates to reduce yield of the

1-azaazulene product. Therefore, slow addition of 7 to a reaction mixture was applied in order to prevent the unfavorable second addition of the ylide. First, solids of the pyridinium salt 7 ($X=I$) were added in many portions (once an hour) during a time of several hours and then the reaction mixture was refluxed to give low yields of 5 (entry 5–6). Further improvement was achieved by slow addition of an acetic acid solution of the pyridinium salt 7 ($X=O_2CCH_3$) to give a 41% yield of 5 (entry 7). Compound 5 was isolated as dark red prisms and its structure was confirmed by spectroscopic and combustion analyses. UV-vis spectra of 5 in CH_3CN and ethanol (EtOH) are shown in Fig. 2. Slight difference between two spectra may be attributed to its conformational change by hydrogen bond in the protic solvent, as seen in 1. [12]

Table 1. Results of the reaction of 6 and 7 (2:1 ratio) in refluxing acetic acid under various reaction conditions.

entry	reaction conditions		yield of 5 (%)
	equivalent of $CH_3CO_2NH_4$ to 6	reaction time	
1	5 eq.	22 hr	0
2	12 eq.	22 hr	0
3	15 eq.	22 hr	0
4	20 eq.	22 hr	0
5 ^a	7.5 eq.	22 hr	16
6 ^b	5 eq.	23 hr	17
7 ^c	7.5 eq.	23 hr	41

a) 7 ($X=I$) was added to the reaction mixture in portions during a time of 6 hr.
b) 7 ($X=I$) was added to the reaction mixture in portions during a time of 9 hr.
c) A solution of 7 ($X=O_2CCH_3$) in acetic acid was slowly added during a time of 8 hr

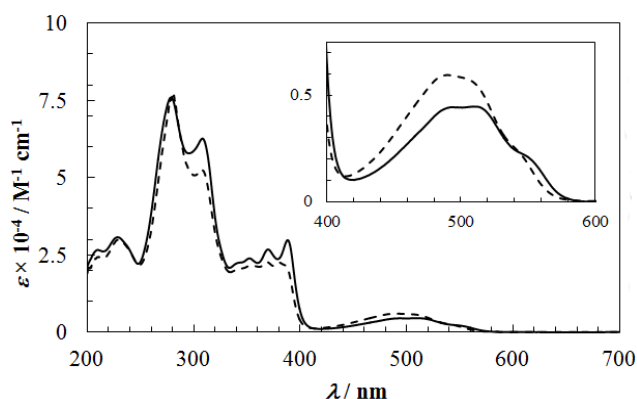


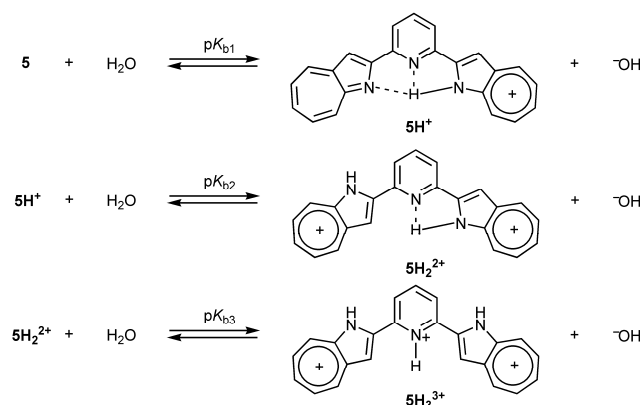
Fig. 2. UV-vis spectra of 5 in CH_3CN (solid line) and EtOH (broken line). Inset is expanded spectra in a range of 400–600 nm.

Change of the UV-vis spectrum of 5 in acidic to weak basic media was observed (Scheme 2) and basicity of 5 was determined by the change in a range of pH 4–9 in 50% aqueous EtOH. The results were shown in Table 2, indicating that 5 is more basic than 1 and 2-phenyl-1-azaazulene (8) but less than 3.[15] The relatively strong basicity of 5 can be ascribed to stabilization by hydrogen bonds with nitrogen atoms of the imino groups in $5H^+$.

Table 2. Basicity of 1, 3, 5 and 8.

Compound	pK_{b1}	pK_{b2}
1 ^a	7.98	11.58
3 ^b	6.47	7.11
5	6.85	8.20
2-phenyl-1-azaazulene (8) ^a	7.19	

a) Measured in 50% aqueous CH_3CN ; taken from ref. 10. b) Measured in 50% aqueous EtOH; taken from ref. 11.



Scheme 2. Stepwise protonation of 5 and pK_b .

The spectrum of 5 in strong acid, H_2SO_4 , also changes depending on its concentration (Fig. 3). The long wavelength absorption shows a blue-shift with a hyperchromic effect; the more H_2SO_4 concentration, the greater blue-shift with the greater hyperchromic effect.

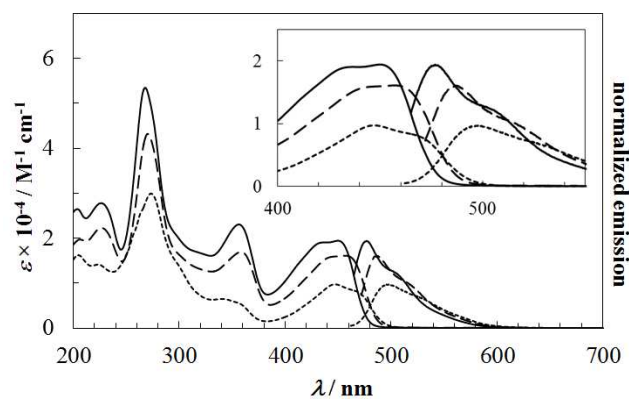


Fig. 3. UV-vis absorption and normalized emission spectra of 5 in 97% H_2SO_4 (solid line), 50% H_2SO_4 (broken line) and 20% H_2SO_4 (dotted line). Inset is expanded spectra in a range of 400–580 nm.

It is worthy to note that in acidic media 5 shows strong emission upon excitation at the longest wavelength absorption. While in neutral organic solvents emission of 5 is very weak [16], emission quantum yields of 5 in 20% H_2SO_4 , 50% H_2SO_4 , and 97% H_2SO_4 are 7, 63 and 98%, respectively. Under the strong acidic conditions 5 should be fully protonated to exist as a form of $5H_3^{3+}$ as shown in Scheme 2. Circumstance around the C–C single bonds in $5H_3^{3+}$ is crowded by the hydrogen atoms of N–H, C3–H, C3'–H, C3''–H and C5–H bonds and rotation around the bonds must be restricted. Therefore, $5H_3^{3+}$ indicates better emission quantum yield without loss of excitation energy by their rotation, besides

increased viscosity of the medium used. Preparation of transition-metal complexes of **5** and their use in cross-coupling reactions are now under investigation.

3. Experimental

3.1. General Remarks

Melting points were measured on a Yanaco MP-3 and are uncorrected. IR spectra were recorded on a JEOL Diamond-20 spectrometer. UV-vis spectra were measured on a Shimadzu UV-2550 spectrometer. Emission spectra were measured on a Shimadzu RT-5300PC spectrometer. ^1H - and ^{13}C -NMR spectra were recorded on a JEOL λ 400 spectrometer. Chemical shift values of tetramethylsilane ($\delta = 0$ ppm) for ^1H -NMR spectra and CDCl_3 ($\delta = 77.0$ ppm) for ^{13}C -NMR spectra were used as internal standard. Mass spectra were measured on a JMS-700 mass spectrometer. Column chromatography was performed with aluminium oxide 90 from Merck KGaA. Acetic acid, pyridine, iodine, 1,3,5-cycloheptatriene, selenium dioxide, and 2,6-diacetylpyridine were purchased from Tokyo Chemical Industry and used without purification. Silver acetate was purchased from Wako Chemical Co. and used without purification. 2,6-Bis(pyridinioacetyl)pyridinium diiodide (**7**, $\text{X}=\text{I}$) was prepared from 2,6-diacetylpyridine by reaction with iodine in pyridine according to the method reported by Sasaki *et al.*[13]. Tropone was prepared by oxidation of 1,3,5-cycloheptatriene with selenium dioxide.[17]

3.2. Synthesis of 2, 6-Bis(1-azaazulen-2-yl)pyridine (**5**) with 2, 6-Bis(pyridinioacetyl)pyridinium Diiodide

To a refluxing solution of tropone (**6**, 212 mg, 2.00 mmol) and ammonium acetate (385 mg, 5.00 mmol) in 10 mL of acetic acid was added 573 mg (1.00 mmol) of 2,6-bis(pyridinioacetyl)pyridinium diiodide (**7**, $\text{X}=\text{I}$) in nine portions during a time of 9 hr. The reaction mixture was refluxed further for 14 hr and was cooled to room temperature. The resulted reaction mixture was carefully poured into water and was extracted with chloroform (20 mL x 3). The combined organic layer was washed with a saturated NaHCO_3 aqueous solution, a saturated $\text{Na}_2\text{S}_2\text{O}_5$ aqueous solution and brine, and was dried over Na_2SO_4 . The solvent was removed under vacuum and the residue was purified by Al_2O_3 chromatography with a mixture of EtOH/chloroform (0.5/99.5) to give 57 mg (17% yield) of **5** as dark red solids. An analytical sample was obtained by recrystallization from dichloromethane-hexane. **2**: Dark red prisms, m.p. 243–246 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) $\delta = 7.64$ (t, $J = 9.7$ Hz, 2H, H-5',5''), 7.76 (t, $J = 9.7$ Hz, 2H, H-7',7''), 7.84 (t, $J = 9.7$ Hz, 2H, H-4',4''), 8.02 (t, $J = 7.8$ Hz, 1H, H-4), 8.40 (s, 2H, H-3',3''), 8.64 (d, $J = 7.8$ Hz, 2H, H-3,5), 8.65 (d, $J = 9.7$ Hz, 2H, H-6',6''), 8.75 (d, $J = 9.7$ Hz, 2H, H-8',8'') ppm; ^{13}C NMR (400 MHz, CD_3CN) $\delta = 7.75$ (t, $J = 10.0$ Hz, 2H, H-5',5''), 7.86 (t, $J = 10.0$ Hz, 2H, H-7',7''), 7.98 (t, $J = 10.0$ Hz, 2H, H-6',6''), 8.10 (t, $J = 7.8$ Hz, 1H, H-4), 8.38 (s, 2H, H-3',3''), 8.62 (d, $J = 7.8$ Hz, 2H, H-3,5), 8.72 (d, $J = 10.0$ Hz, 2H,

H-4',4''), 8.79 (d, $J = 10.0$ Hz, 2H, H-8',8'') ppm; ^{13}C NMR (100 MHz, CDCl_3) $\delta = 113.13$, 123.19, 128.88, 129.65, 136.22, 136.53, 137.65, 137.66, 147.85, 153.9, 158.73, 166.76 ppm; IR (KBr) $\nu = 1566$ (m), 1448 (m), 1408 (s), 1032 (m), 799 (s), 742 (s), 723 (s), 677 (s) cm^{-1} ; UV (EtOH): $\lambda_{\text{max}} = 229$ (log $\epsilon = 4.48$), 278 (4.88), 280 (4.89), 307 (4.72), 342sh (4.31), 354 (4.33), 369 (4.35), 380 (4.35), 387sh (4.33), 490 (3.77), 504sh (4.75), 546sh (3.33) nm; UV (CH_3CN): $\lambda_{\text{max}} = 229$ (log $\epsilon = 4.49$), 279 (4.88), 308 (4.80), 340sh (4.35), 352 (4.38), 370 (4.43), 388 (4.47), 492sh (3.64), 510 (3.65), 552sh (3.30) nm; MS (70 eV): m/z (rel int) = 334 ($\text{M}^+ + 1$, 27), 333 (M^+ , 100), 332 (38), 307 (10), 205 (5), 178 (6), 167 (9), 77 (4). HRMS; Calcd for $\text{C}_{23}\text{H}_{15}\text{N}_3$; 333.1266, found 333.1267. EA ($\text{C}_{23}\text{H}_{15}\text{N}_3 \cdot \text{H}_2\text{O}$) Calcd C; 78.61, H; 4.88, N; 11.96%, Found C; 78.91, H; 4.82, N; 11.59%.

3.3. Synthesis of 2, 6-Bis(1-azaazulen-2-yl)pyridine (**5**) with 2, 6-Bis(pyridinioacetyl)pyridinium Diacetate

A solution of 2,6-bis(pyridinioacetyl)pyridinium diiodide (**7**, $\text{X}=\text{I}$) (573 mg, 2.00 mmol) in 20 mL of water added dropwise to a solution of silver acetate (334 mg, 2.00 mmol) in 16 mL of water under vigorous stirring at room temperature. The reaction mixture was heated at on an oil bath at 60 $^\circ\text{C}$ for 1 hr and, then, was cooled to room temperature. The solids (AgI) formed were removed by filtration and washed well with EtOH/water. The filtrate was concentrated under vacuum to give 2,6-bis(pyridinioacetyl)pyridinium diacetate, which was dissolved in 10 mL of acetic acid. This solution was added slowly to a refluxing solution of tropone (**6**, 212 mg, 2.00 mmol) and ammonium acetate (578 mg, 7.50 mmol) in 10 mL of acetic acid during a time of 8 hr. The reaction mixture was refluxed further for 14 hr and was cooled to room temperature. The resulted reaction mixture was carefully poured into water and was extracted with chloroform (20 mL x 3). The combined organic layer was washed with a saturated NaHCO_3 aqueous solution and brine, and was dried over MgSO_4 . The solvent was removed under vacuum and the residue was purified by Al_2O_3 chromatography with a mixture of EtOH/chloroform (99.5/0.5) to give 136 mg (41% yield) of **5** as dark red solids.

3.4. Determination of Basicity of **5**

The basicity of **5** was determined from a titration curve based on pH-dependent absorption spectra in 50% aqueous ethanol solutions by a curve fitting method using KaleidaGraph program. Isosbestic points were observed at 398 and 483 nm. The absorption peak at 446 nm was used for the titration. Boronic acid buffer solutions were used at a range of pH 2.0–9.0. A TPX-90Si glass electrode pH meter, available from TOKO Chemical Laboratories Co., was used for pH measurements.

4. Conclusion

It has been demonstrated that the title compound **5** bearing two 1-azaazulenyl groups at the 2,6-positions of the pyridinyl core can be synthesized from tropone and the easily accessible

pyridinium salt 7. Properties of 5 including basicity and absorption and emission behaviors were clarified. Noteworthy, 5 shows very strong emission in H₂SO₄.

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