BASICITIES AND TAUTOMERISM OF SUBSTITUTED METHANO-BRIDGED AZA[10]ANNULENES: 10π-ANALOGUES OF PYRIDINE

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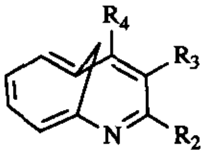
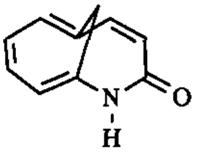
Abstract *- pKa values of substituted 2,7-methanoaza[10]annulenes are measured and compared with similarly substituted pyridines. The tautomerism of 2-azabicyclo-[4,4,1]undeca-4,6,8,10-tetraen-3-one is discussed.*

INTRODUCTION

In this comunication we describe the measurement of the basicities of some 2,7-methano- aza[10]annulenes (compounds **1** to **7**). The pKa values and the tautomerism of compound (**6**) are discussed with reference to their pyridine analogues.



	R_2	R_3	R_4
1	H	H	H
2	Me	H	H
3	H	Me	H
4	H	H	Me
5	MeO	H	H



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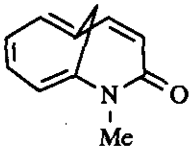

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EXPERIMENTAL

The pKa values were determined in water (with 0.3% MeOH) by a spectrophotometric method[1] using Pye-Unicam SP8-200 and Perkin-Elmer 330 UV/visisible spectrophotometers. The pH of solutions were measured in the cuvet with a Corning 130 pH-meter and a micro combination electrode calibrated with standard buffer solutions inmediately prior to use. Buffer solutions were prepared by known methods[2] using 0.1M HCOOH and 0.1M NaOH (pH 3-4), 0.2M NaCl (pH 1-1.5) and 0.02M $NaHCO_3$ and 0.01M Na_2CO_3 (pH 9-10) with constant ionic strength of 0.01. Sulphuric acid solutions of known molarity were prepared by diluting reagent grade sulphuric acid and the exact molarity was determined by titration with standard 1M NaOH prior to use. H_0 values were estimated from a calibration curve drawn from known values.[3]

Buffer solution (3 ml) was added by pipette into a cuvet in a thermostat controlled cell holder for equilibration. A stock solution was prepared by dissolving the aza[10]annulene (2-3 mg) in MeOH (1 ml) and 10 µl of the stock solution was added into the buffer solution by syringe to give a concentration of the aza[10]annulene between 4 and 7 x 10^{-5}M. The mixture was shaken and the spectrum was recorded against a solution of the same buffer containing 10 µl of MeOH.

Since the pyridone analog (**6**) was found to be unstable in solutions of low pH, values of absorbance at the analytical wavelength were estimated by following the decrease in absorbance at 340 nm and extrapolating the initial rate back to zero time. The pKa's of **5**, **6** and **7** were checked by superimposing full spectra of neutral and protonated forms as well as a 1:1 mixture at pH = pKa which in each case gave an intermediate spectrum and isobestic points as expected. All measurements were done at 25 ± 0.1°C.

Compounds (**1**) to (**4**) and (**6**) were kindly supplied by Professor E. Vogel, and were prepared by previously published methods.[4] Compounds (**5**) and (**7**) were prepared in moderate yield by reaction of **6** with diazomethane followed by chromatographic separation.

RESULTS

The pKa values and UV/visible spectroscopic data are recorded in Tables 1 and 2.

Table 1. pKa values of bridged methanoaza[10]annulenes.

Cmpd.	λ	ϵ^{+a}	ϵ^{a}	ϵ^{-a}	n^{b}	pKa	s.d.	Δ^{c}
1	*d*	-	-	-	-	3.20	-	0.00
2	239	13.70	22.70	-	5	3.78	0.02	0.15
3	244	21.70	39.10	-	6	3.55	0.04	0.12
4	252	21.20	33.80	-	6	3.99	0.04	-0.03
5	*e*	-	-	-	9	0.73	0.11	0.62
6	340	6.68	3.39	-	5	pKa_1= 0.03	0.07	-1.29
	274	-	36.90	17.80	7	pKa_2= 9.74	0.12	-0.07
7	338	6.82	3.39	-	6	-0.64	0.06	-1.07

[a] Extinction coefficients at analytical wavelength of protonated, neutral and deprotonated forms. [b] Number of measurements used in pka calculations. [c] *See text.* [d] *Reference 4.* [e] *Average value from* λ *370 nm, 340 nm and 277.5 nm.*

Table 2. uv Spectral data for bridged methanoaza[10]annulenes.

Cmpd.	Protonated form		Neutral form		Cmpd.	Protonated form		Neutral form		Deprotonated form	
	λ^{a}	ϵ^{b}	λ^{a}	ϵ^{b}		λ^{a}	ϵ^{b}	λ^{a}	ϵ^{b}	λ^{a}	ϵ^{b}
1[c]			238	33.00	**5**	225	16.90	235	23.60		
			292	2.65		238	19.90	262	27.40		
			343	5.00		275	27.50	295	5.41		
						345	6.90	370	4.87		
2	232	13.70	239	22.70		370	7.14				
	270	19.80	310	14.20							
	345	4.45	365	3.30	**6**	223	28.60	223	15.00	274	46.90
						274	30.10	270	26.20	300	8.04
3	238	23.40	244	39.10		330	8.23	302	4.63	386	9.30
	264	30.00	310	4.15		370	6.47	370	4.55		
	345	6.15	367	3.87							
					7	230	10.30	227	11.10		
4	252	21.20	252	33.80		243	10.90	245	11.70		
	278	33.90	315	2.01		272	18.50	273	20.70		
	355	2.77	370	1.46		336	4.70	302	3.91		
						370	3.99	375	2.92		

[a] λ in nm. [b] $\epsilon \times 10^{-4}$ ($mol^{-1}\ cm^{-1}$). [c] Ref. 4.

All the aza[10]annulenes are 2 or more pKa units less basic than their pyridine analog. This suggests that the electron density on nitrogen in the aza[10]annulene is less than that in the analogous pyridine. This presumably arises from the lower polarizability of the annulene π-system to electron withdrawal. Evidently, polarization of the π-electrons towards nitrogen, and the concomitant reduction in π-bonding overlap leads to a greater destabilization of the inherently non-planar aza[10]annulene than that occurring in pyridine. The value Δ is defined acording to Equation 1, where $pKa^{(10\pi)}$ = pKa of the particular aza[10]annulene and $pKa^{(6\pi)}$ = pKa of the analogous pyridine; Δ is thus zero for the parent compound.

$$\Delta = [pKa^{(6\pi)} - 2.03] - pKa^{(10\pi)} \qquad \text{Eq 1}$$

We find that Δ is less than 0.2 for the methyl substituted aza[10]annulenes (**2**, **3** and **4**). However, Δ is significant for the methoxy substituted **5** (0.54), the 2-pyridone analogue (**6**) (-1.29) and the *N*-methyl-2-pyridone analogue (**7**) (-1.07). This may reflect differences in the overlap and/or hybridization in the two series of compounds.

The *N*-methylaza[10]annulenone (**7**), is a weaker base by 0.67 pka units than **6**. This effect is similar in magnitude and direction to that in the 2-pyridone series (ΔpKa = 0.45).

Comparison of the pKa of **6** (0.03) with that of **5** (0.73) suggests that **6** exists in the aza[10]annulenone form as drawn, and is protonated on oxygen in strongly acidic media. The ratio of the oxy-form (**6**), to the 2-hydroxyaza[10]annulene form pK_T = -0.70 is calculated from Equation 2. This shows a significantly diminished preference for the oxy-form in **6** compared to 2-pyridone (pK_T = -3.0).

$$pK_T = pKa(\mathbf{6}) - pKa(\mathbf{5}) \qquad \text{Eq. 2}$$

The results suggest that the aza[10]annulenones (**6**) and (**7**) should be rightlyviewed as 6π-homoaromatic species. ^{1}H Nmr spectra support this view. For **7**, one proton from the methylene bridge resonates at δ 0.15 (dd, J_{ab}= 11Hz, J_{ax}= 1 Hz) due to the diamagnetic current of the 6π homoaromatic system while the other appears at δ 2.00 (dd, J_{ab}= 11 Hz, J_{ax}= 1 Hz), deshielded by through-space inductive effects. These results are in accord with that previously observed for **6**[4] and contrast with that obtained for **5**[4] where the protons of the bridge are shifted upfield by the diamagnetic ring current of the aromatic system.

Figure 1. Comparison of uv spectra of compounds (**5**, **6** and **7**)

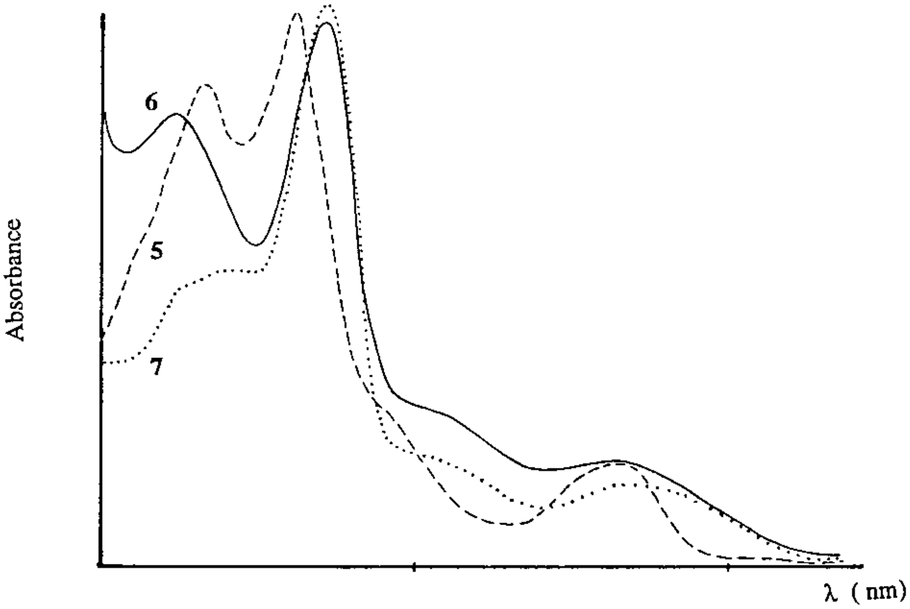
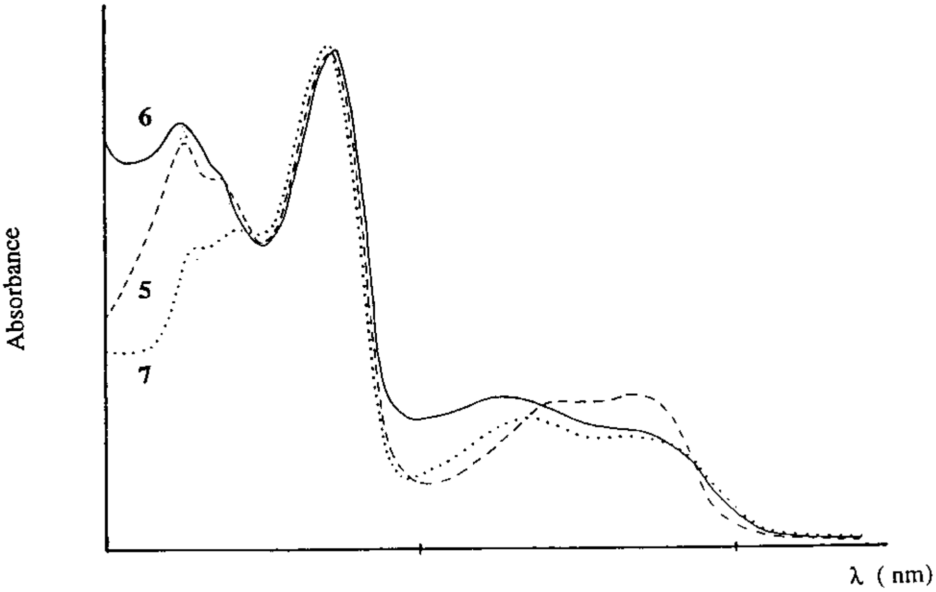


Figure 2. Comparison of uv spectra of protonated forms of compounds (**5**, **6** and **7**)



Comparison of the uv spectra of the neutral forms of **5**, **6** and **7** shows relatively little dissimilarity (Figure 1), although uv spectra of the protonated forms of these compounds are still more similar (Figure 2). Conclusions based on uv spectra in this series are not reliable indications of tautomeric composition because the spectra are too similar.

ACKNOWLEDGEMENTS

We thank Professor E. Vogel for supplying the compounds and the Dirección General de Investigación Científica y Técnica (DGICYT) of Spain for the financial support of Dr. Mancheño at the University of Florida.

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Received, 24th May, 1993