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A NOVEL SOLVENT DIPOLE-INDUCED ROTATIONAL ISOMERISM OF 1-HYDROXY-2-PYRIDONE IN THE EXCITED SINGLET STATE

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Summary: The title compound shows dual fluorescence depending on polarity of the solvent used. The fluorescence in the nonpolar solvent, cyclohexane, has a maximum at 370 nm, while the fluorescence in the polar solvent, methanol, has a maximum at 400nm. The short and long wavelength fluorescences were assigned to the syn and anti conformers, respectively. From these observations one is allowed to conclude that a novel solvent dipole-induced rotational isomerism takes place in the excited singlet state.

The discovery of aspergillic acid with antibacterial properties has stimulated studies on the biological activity of its synthetic analogs.[1] Of the analogs of aspergillic acid prepared, 1-hydroxy-2-pyridone(HP) has been indicated to have significant antibacterial activity.[2] Spectroscopic studies of HP gave no evidence for the existence of dimer and the enol isomer, 2-hydroxypyridine-1-oxide, in solution.[3] Despite widespread investigations on the ground state behavior of the cyclic hydroxamic acids in the past, there has been only a few preliminary studies on the excited state behavior of these compounds.[4] Thus, a more detailed study is needed to characterize the photochemical and photophysical processes of hydroxamic acids. In the present communication, we report the first observation of rotational isomerism of HP in the excited singlet state. For comparison, spectroscopic data for 1-ethoxy-2-pyridone(EP) and 2-ethoxypyridine-1-oxide(EPO) were obtained under the same condition as HP.

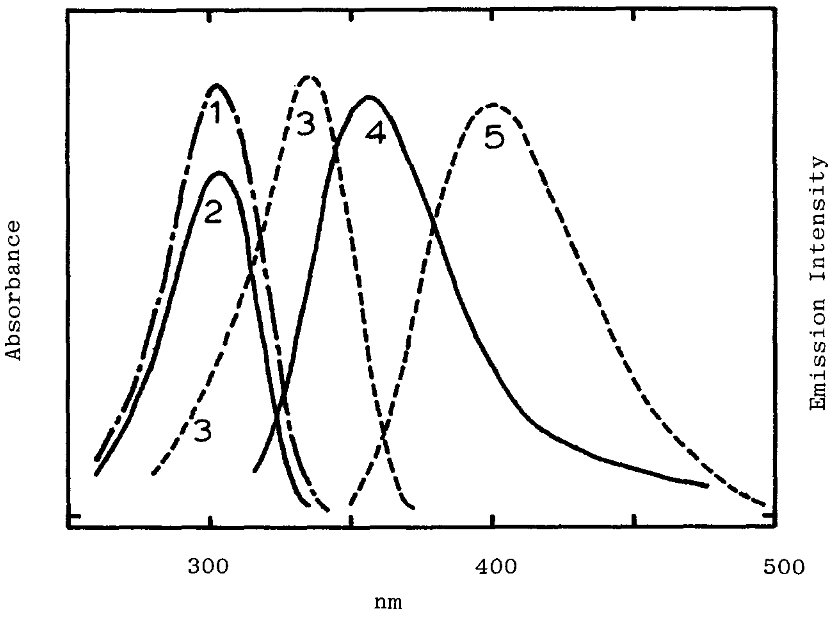
The results are given in the Table and Figure. The fluorescence of HP in methanol appears at 400nm and shows a large Stokes shift of 8000 cm^{-1} relative to the long wavelength absorption maximum, whereas normal fluorescence with a maximum at 370 nm is observed in cyclohexane. Clearly, the large Stokes shift is not due to the formation of the enol isomer, 2-hydroxypyridine-1-oxide, in the excited state because the fluorescence behavior of HP is not similar to that of EPO but to that of EP in aprotic solvents. The fluorescence maxima of HP in methanol and cyclohexane are independent of excitation wavelength. On the contrary, EP in cyclohexane shows an excitation wavelength-dependent fluorescence spectrum whose maximum varies from about 370 nm to about 410 nm at room temperature. The short wavelength fluorescence maximum of EP is close to that of HP in cyclohexane, while the long wavelength fluorescence spectrum resembles that of HP in polar solvents, methanol and acetonitrile. Furthermore, the fluorescence excitation spectrum of EP in cyclohexane can be interpreted as the superposition of the short and long wavelength fluorescence excitation spectra of HP. This means that an increase in excitation wavelength increases [long wavelength component]/[short wavelength component] ratios in the

Table. The first absorption and fluorescence maxima of HP, EP, and EPO at room temperature(RT) and 77K.

Compd.	Solv.	Abs./nm,RT	Fluo./nm(λex),RT	Fluo./nm(λex),77K
HP	CH_3OH	303	400[a](337)	356(308),381(340)[c]
	CH_3CN	308	409[a](341)	-----
	$c\text{-}C_6H_{12}$	314	370[a](307)	365[a](312)[d]
EP	CH_3OH	300	399[a](332)	356(308),378(340)[c]
	CH_3CN	302	407[a](340)	-----
	$c\text{-}C_6H_{12}$	305	377(300),384(320),414(342)	370[a](313)[d]
EPO	CH_3CN	316	ca.360[b](310)	-----
	$c\text{-}C_6H_{12}$	325	ca.350-370[b](310)	367[e](313)[d]

[a] Excitation wavelength-independent fluorescence maxima.
[b] Very weak fluorescence. [c] $CH_3OH\text{-}C_2H_5OH$(1:1 by volume) as a solvent.
[d] Methylcyclohexane as a solvent. [e] Weak fluorescence.
Concentrations of HP, EP, and EPO ranged between 1.5×10^{-4} and 2.0×10^{-4}M.

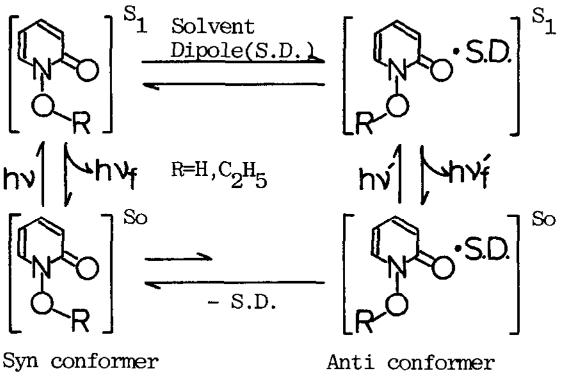
Figure. The first absorption, emission, and excitation spectra of HP at room temperature(RT) and 77K.



Curve 1, absorption in CH_3OH at RT; curve 2, fluorescence excitation spectrum in an alcohol glass at 77K; curve 3, fluorescence excitation spectrum in CH_3OH at RT; curve 4, emission spectrum in an alcohol glass at 77K; curve 5, fluorescence in CH_3OH at RT.

excited singlet state, thus populating the long wavelength component in preference to the short wavelength component, and causing a red shift in the fluorescence maximum of EP as observed. These spectral observations for EP indicate the existence of an equilibrium between two different excited species at room temperature. Based on these experimental results, one can assume the rotational isomerism between the syn and anti conformers in the excited singlet state as well as in the ground state to explain the fluorescence behavior of HP in polar and nonpolar solvents.

HP in cyclohexane exhibits single fluorescence whose excitation spectrum agrees well with the absorption spectrum of HP, suggesting that the excited state conformation of HP is the same as the ground state one, i.e., the syn conformation, which is supported from the observation that HP is strongly hydrogen bonding intramolecularly as monomer in nonpolar solvents.[3] The planarity of the hydroxamic acid groups[5] and repulsive interaction between lone pair electrons in the molecule indicate that the ground state conformation of EP is the same as or similar to that of HP. Thus, the short and long wavelength fluorescences of HP and EP are tentatively assigned to the syn and anti conformers, respectively.



The reorientation of solvent dipole appears to be the major factor to lower the rotational barrier about the N-O single bond and to stabilize the anti conformation since the anti conformer is present predominantly in polar solvents. A weak solute-solvent dipole interaction in cyclohexane results in the isomerization of EP to the anti conformer in the excited singlet state to some extent, which reflected in an excitation wavelength-dependent fluorescence of EP. On the other hand, hydrogen bonding between the hydroxyl group and the carbonyl oxygen atom in HP does seem to contribute to raising the energy barrier to N-O bond rotation and thereby the occurrence of isomerization in the excited state is inhibited in cyclohexane. A similar fluorescence behavior can be expected to be observed for HP and EP in polar solvents owing to a negligible hydrogen bonding interaction in HP and an appreciable interaction between solute molecules and solvent dipole. In fact, the fluorescence spectra of HP are very similar to those of EP in polar solvents as indicated in the Table.

The excitation spectrum of HP with respect to the long wavelength fluorescence has its maximum at about 335 nm and is not identical with the absorption spectra of HP measured in any solvent, indicating that the ground state anti conformer is thermodynamically unstable and rapidly reverts back to the more stable syn conformer. Although the equilibrium for syn conformer $\rightleftharpoons$ anti conformer in polar solvents lies almost completely on the side of anti conformer in the excited state, the syn conformer seems to be present at steady-state concentration during illumination.

The rotational isomerization in the excited state can hardly be expected to occur at 77K, judging from the fact that the reorientation of solvent dipole in addition to rotation about the N-O single bond is suppressed at such a low temperature that the solvent becomes rigid. As expected, the fluorescence arising from the syn conformer becomes predominant even in a polar matrix at 77K. Both HP and EP show single fluorescence, i.e., the short wavelength fluorescence in methylcyclohexane glass, of course. Accordingly, these observations strongly suggest the rotational isomerization of HP to occur in the excited state, in polar solvents.

The excited state pK* values of the syn and anti conformers were evaluated to be 3.8 and 10.3 based on the Förster cycle,[6] respectively, indicating that the rotational isomerization to the anti conformation causes a considerable decrease in the singlet state acidity.[7]
An appreciable interaction between the syn conformer and solvent dipole might be responsible for dramatic change in charge density on the hydroxyl oxygen atom, resulting in the isomerization in the excited singlet state.

References and Notes

1. E. C. White and J. H. Hill, J. Bacteriol., 45, 433 (1943); J. D. Dutcher and O. Wintersteiner, J. Biol. Chem., 155, 359 (1944); J. D. Dutcher, ibid., 171, 321 (1947).
2. E. Shaw, J. Am. Chem. Soc., 71, 67 (1949).
3. K. G. Cunningham, G. T. Newbold, F. S. Spring, and J. Stark, J. Chem. Soc.,2091 (1949); J. N. Gardner and A. R. Katritzky, ibid., 4375 (1957).
4. H. Furrer, Tetrahedron Lett., 2953 (1974); A. R. Katritzky, A. V. Chapman, M. J. Cook, and G. H. Millet, J. Chem. Soc. Chem. Commun., 395 (1979).
5. D. Kost and E. Berman, Tetrahedron Lett., 1065 (1980); W. L. Smith and K. N. Raymond, J. Am. Chem. Soc., 102, 1252 (1980).
6. Th. Förster, Z. Elektrochem., 54, 43 (1950); A. Weller, Progr. React. Kinet., 1, 188 (1961).
7. The ground state pK value of HP was spectrophotometrically estimated to be 6.0 in Britton-Robinson buffer at 25°C (lit. 6.0[3] and 5.9[2]). The excited state pK* values of both conformers will be discussed in more detail in a full paper.

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