

ULTRAVIOLET AND INFRARED SPECTROSCOPIC STUDY OF 9-SUBSTITUTED 4-H-PYRIDO[1,2a]PYRIMIDIN-4-ONE DERIVATIVES

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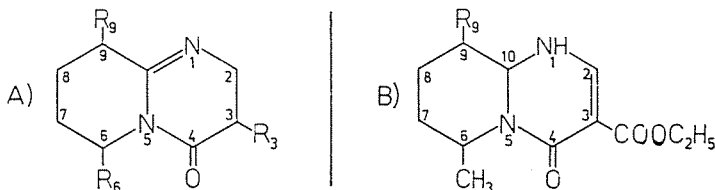
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Introduction

In recent years several new 4H-pyrido[1,2a]pyrimidin-4-one derivatives have been synthesized [1] and many of them exhibit an important biological activity [2]. A systematic study on the electronic spectra of substituted derivatives has been published by HORVÁTH et al. [3].

In the present work UV and IR spectra of the following 9-substituted 3-ethoxycarbonyl-4-H-pyrido[1,2a]pyrimidin-4-ones have been investigated:



	R ₁	R ₂	R ₃		R ₄
A1	H	CH ₃	H	B1	CHO
A2	COOC ₂ H ₅	H	H	B2	CSSCH ₃
A3	COOC ₂ H ₅	CH ₃	H	B3	COOCH ₃
A4	COOC ₂ H ₅	CH ₃	Cl	B4	COOC ₂ H ₅
A5	COOC ₂ H ₅	CH ₃	=NOH		
A6	COOC ₂ H ₅	CH ₃			
A7	COOC ₂ H ₅	CH ₃	=CHN(CH ₃) ₂		
A8	COOC ₂ H ₅	CH ₃	=CHNHC ₆ H ₅		

Molecular structure — spectrum correlations seemed to be interesting as the double bonds of the 9-substituents were expected to extend the conjugation.

Experimental

A separate communication will be published on the syntheses of the investigated compounds.

UV spectra were recorded on a Zeiss Specord UV-Vis spectrometer. The IR spectra of samples in KBr pellets and in CHCl_3 solutions were measured using a Zeiss Specord 75 IR spectrometer.

The pH dependence of the electronic spectra was investigated in 1 M HCl and 1 M NaOH solutions and in citrate-phosphate buffers.

Results and Discussion

Effect of conjugation

The effect of substitution on the conjugated systems A and B was studied by comparing the electronic spectra taking A1 as parent compound. The spectral data measured in ethanolic solutions have been compiled in Table 1.

Table 1
Electronic spectral data of compounds in ethanol

Band Compound	I.		II.		III.		IV.	
	$\lambda_{\text{max}}(\text{nm})$	$\lg \epsilon$	$\lambda_{\text{max}}(\text{nm})$	$\lg \epsilon$	$\lambda_{\text{max}}(\text{nm})$	$\lg \epsilon$	$\lambda_{\text{max}}(\text{nm})$	$\lg \epsilon$
A1			280	3.67			227	3.78
A2			304	3.96			230	3.88
A3			305	3.92			230	3.83
A4			315	3.83			231	3.60
A5			332	4.03			254	3.99
A6	392	4.54	319	4.04	297	4.01	229	4.16
A7	401	4.73	301	3.41	278	3.53	234	4.11
A8	415	4.93	300	3.69			244	3.91
B1	382	4.10	323	sh			226	4.09
B2*	422	2.65**	336	1.12**			235	1.55**
B3			337	4.11	301	4.34		
B4			337	3.88	301	4.11		

* Saturated solution

** Absorbances for 1 cm cell length

The two bands in the electronic spectra of compounds A1-A5 may be assigned to $\pi\text{-}\pi^*$ transitions of the conjugated system [3]. In the spectra of A2 and A3 the significant red shifts of the bands II are due to the more exten-

sive conjugated systems caused by the R_9 ethoxycarbonyl groups. The still stronger red shift in the case of compound A4 may be attributed to the partly delocalized nonbonding electrons of the halogen atom, contributing to the effect of ethoxycarbonyl group. In case of A5 the very strong red shift (~ 50 nm) is due to the effect of ethoxycarbonyl group as well as the π -electrons and the partly delocalized nonbonding electrons of oxygen atom in the R_9 substituent.

The new intensive longest-wavelength band of compounds A6, A7, A8 may be assigned to the R_9 substituents and the band splitting near 300 nm shows the widely spread conjugated system. In these molecules the nonbonding electrons of sulphur and nitrogen atoms are partly delocalized and so the d-orbitals of sulphur atoms can take part in the π -system. At A8, not only the first band, but the short-wavelength band (244 nm) is shifted to the visible region. This shows the extension of conjugation to the NH group and the existence of an intramolecular hydrogen bond between the imino group and the nitrogen atom of the pyrimidine ring. This latter supposition has been confirmed by the IR spectrum.

The electronic spectra of B1 and B2 are similar to that of compound A6 which refers to similar conjugation and to an intramolecular hydrogen-bond between the R_9 substituent and pyrimidine ring, also confirmed by the infrared spectra. The first band of compound B2 may be assigned to $n-\pi^*$ transition because of its very high wavelength (422 nm) though its intensity is higher than expected. The missing band at about 400 nm in the spectra of B3 and B4 may be explained by the hindrance effect of the R_9 ester groups to $n-\pi^*$ transition of carbonyl oxygen, as its nonbonding electron pair is dispersed within the ester group. This confirms the supposition that the first band in the spectrum of B2 is a $n-\pi^*$ transition.

pH dependence

The pH dependence of the spectra was investigated in the pH interval 0.1–14. The spectra were compared to those recorded in a neutral solution rather than in alcohol to avoid the disturbing effects of the solvents.

In a strong alkaline medium the spectrum of A1 does not differ significantly from that measured in neutral solution but both bands have a strong blue shift for compounds A2 and A3. This may refer to hydrolysis of the ester group. The spectra of A4–A8 and B1–B2 indicate a similar decomposition. Bands I of A6 and A7 have also a blue shift but no shift of this band is found for compound A8. It shows that in this case the conjugation through the imino group subsists and so existence of the hydrogen bond may be supposed.

In alkaline medium the first bands of B3 and B4 vanish probably because of the splitting of R_9 methoxycarbonyl and ethoxycarbonyl groups, respectively. The spectra of the reacidated solutions are very similar to that of A3 in acidic medium, confirming our supposition.

In acidic medium blue shift of band II is observed for compound A1—A5 and this refers to protonation on 1-nitrogen [2]. For A6, the blue shift of the 229 nm band indicates the protonation and the red shift of the band I belonging to the substituent R_9 shows that the protonation increases conjugation. Protonation occurs also for A7 and A8. The spectra in the neutral acidic medium for B3 and B4 are nearly identical, demonstrating the absence of protonation.

In strong acidic medium the blue shift of bands IV of B1 and B2 indicates the protonation while that of band I shows reduced conjugation for B1.

Hydrogen bonding

Hydrogen bonding was studied by IR spectroscopy. The most characteristic IR frequencies are given in Table 2.

In the spectra of crystalline A8 and its concentrated solution, three ν_{N-H} bands have been observed. Upon diluting the solution, the band of the lowest frequency disappeared, demonstrating the decomposition of intermolecular hydrogen bonds. The two other bands may be derived from NH groups intramolecularly hydrogen bonded to the 1-nitrogen atom and from free ones.

In the solid state spectra of B1, B2, B3 and B4 both the $\nu_{C=O}$ bands of R_9 aldehyde and ester groups and the ν_{N-H} bands have been found at extremely low wave numbers. These bands appeared at almost the same frequencies in the spectra in dilute solutions. These results give evidence to very strong intramolecular hydrogen bonds between the NH groups and the R_9 substituents. Similarly low frequencies of the $\nu_{C=O}$ and ν_{N-H} bands were observed in the case of β -amino α - β unsaturated ketones [4].

O-cis-O-trans conformation, coupling of vibrations, tautomerism

In the solid state IR spectra of compounds A a strong coupling between the $\nu_{C=O}$ vibrations of the 3-ester and 4-lactame carbonyl groups may occur if the molecules are in "O-cis" conformation [5]. In the case of A1, A2, A3, A4 and B1 the intenseness of the bands of the coupled vibrations shows the dominance of the "O-cis" form.

Comparing the 1600—1400 cm^{-1} regions in the spectra of A6, A7 and A8, the frequencies and intensities of the bands have been found very similar, but they differ very much from those in the spectra of A3 and A4. This suggests that in the A6, A7 and A8 molecules the stretching vibrations of the double bonds between the 9-carbon atom and the R_9 substituents are strongly coupled with the vibrations of the pyrido-pyrimidinone skeletons. In the spectra of A3 and A4 no such coupling has been observed.

In the IR spectrum of B2 two weak bands appear around 2500 cm^{-1} likely to belong to the ν_{S-H} vibration of a tautomeric form resulting from the transposition of proton from the 1-nitrogen to the R_9 group.

Table 2

Some characteristic frequencies in the IR spectra of the crystalline compounds (cm⁻¹)*

Compound	A3	A4	A5	A6	A7	A8
$\nu_{C=O}$ (3-ester and 4-lactame carbonyl groups)	1740 m 1704 } 1692 } 1680 } s	1736 vs 1710 sh 1672 m	1744 m 1690 vs	1729 m 1689 s 1670 m	1680 s 1658 m	1715 m 1682 s 1660 m
Skeletal vibrations	1574 m 1505 vs	1575 m 1504 vs	1611 w 1568 m 1497 vs	1565 s 1530 m 1468 vs 1450 vs	1550 s 1470 vs 1465 vs 1438 vs	1552 s 1469 vs

Compound	B1	B2	B3	B4
ν_{N-H}	3093 w 3080 w	3090 m	3070 m	3090 m
ν_{S-H} (partly)		2400 m 2400 vb		
$\nu_{C=O}$ (3-ester and 4-lactame carbonyl groups)	1736 ws 1710 w 1673 m	1740 w 1700 s 1690 w	1730 sh 1696 s 1672 w	1740 sh 1688 s
$\nu_{C=O}$ and $\nu_{C=S}$ resp. (R_3)	1615 s	1196 s	1642 m	1648 m
Skeletal vibrations	1575 vs, b 1482 m	1560 vs, b 1474 m	1585 vs, b 1480 m	1578 vs, b 1480 m

* For spectral data of A1 and A2 see ref. [5]

vs: very strong,
m: medium,
sh: shoulder,
b: broad.

s: strong,
w: weak,
vb: very broad,

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Summary

UV and IR spectra of 9-R-3-etoxy carbonyl-6-methyl-4-H-pyrido[1,2a]pyrimidin-4-ones ($R = Cl, NOH, CS_2(CH_2)_2, CHNH(CH_3)_2, CHNHC_6H_5, CHO, CSSCH_3, COOCH_3, COOC_2H_5$) have been studied. In the UV region the effect of substitution, the protonation and the decomposition were investigated in the pH interval 0.1–14. The IR spectra were used for studying hydrogen bond, molecular conformation and tautomerism.

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