PYRIMIDINES AND CONDENSED DERIVATIVES, I.*

UV AND IR SPECTRA OF ISOCYTOSINES AND RELATED IMIDAZO[1,2-a]—PYRIMIDINONES**

By

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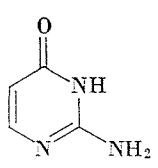
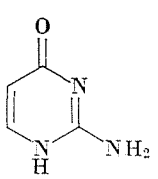
In the series starting with the present paper, ring closure reactions of isocytosine derivatives will, *inter al.*, be described. Most of the starting compounds (as well as isocytosine itself) were potentially tautomeric compounds of potential double reactivity. As a consequence, one had to reckon with two alternate orientations in the course of the cyclizations. Thus, there arose problems of tautomeric structures and orientations similar to those which had to be solved during our previous studies in the 1,2,4-triazine series [1—7]. The solution for both types of problems consisted in establishing the actual distribution of double bonds which, in principle, could be situated in different positions of or exocyclic to the triazine ring. For this purpose UV and IR spectroscopic methods proved to be very suitable and, therefore, the same methods were applied also in the course of our studies in the pyrimidine series.

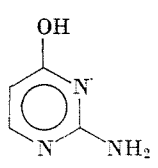
Isocytosine could principally exist in seven [8] different tautomeric forms. Among these, according to general experience [9] the two amino-oxo forms **1a** (conjugated form) and **1b** (cross conjugated form) are the most likely ones.



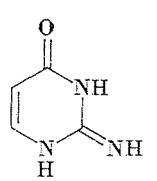
1a



1b



1c



1d

According to UV spectroscopic studies of Australian authors [10] (*cf.* also below) isocytosine exists in approximately neutral aqueous buffer solutions as a mixture of the tautomeric forms **1a** and **1b**; the presence of the aromatic form **1c** may, however, not be excluded

* Dedicated to Prof. Z. CSŰRÖS on the occasion of his 70th birthday.

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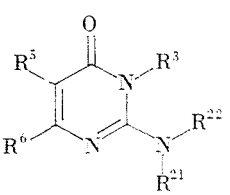
with complete certainty. Moreover, according to UV spectroscopic studies of French authors [11], the position of the equilibrium **1a** ⇄ **1b** depends on the solvent, as well as on the temperature while, according to X-ray studies [12], in crystalline state the two amino-oxo tautomers form a 1 : 1 complex.

In the IR spectra of the majority of monocyclic and condensed bicyclic derivatives of isocytosine prepared by us an intensive amide I band could easily be recognized; thus, the presence of a product containing a chromophore system identical with that of either **1a** or **1b** or perhaps with that of the form **1d** (containing an exocyclic double bond) could be taken as verified. In order to be able to distinguish between these three possibilities, characteristic differences in the UV and IR spectra corresponding to the three double bond distributions represented by formulas **1a, 1b** and **1d** had, however, to be recognized in addition to the demonstration of a carbonyl band.

As a result of a study of more or less "fixed", *i.e.* of such derivatives of the tautomeric forms **1a, 1b** and **1d** in which as many of the mobile hydrogen atoms attached to nitrogen as possible had been replaced by groups incapable of tautomeric shifts, the UV spectra of compounds containing a conjugated



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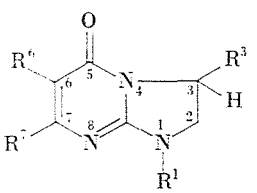

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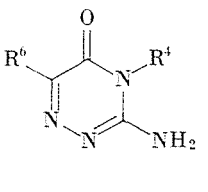
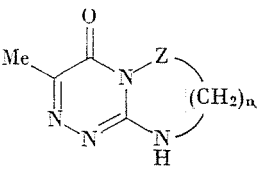
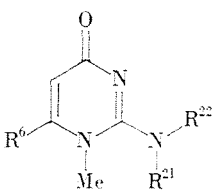


2A



3A



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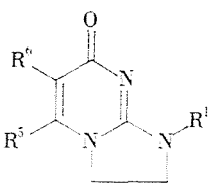

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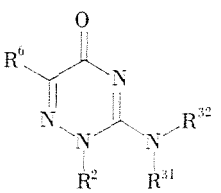
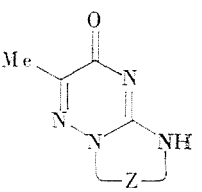
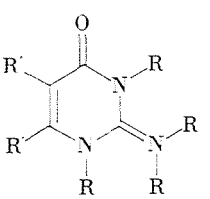


4A



5A



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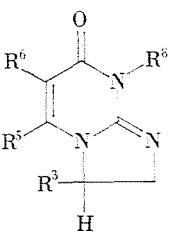

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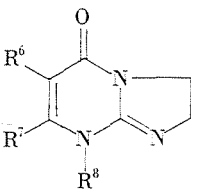

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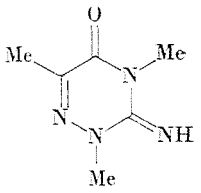


6A

(types **2** and **3**), a cross conjugated double bond system (types **4** and **5**)* and an exocyclic double bond (types **6**—**8**), respectively, can be stated to differ characteristically from each other; differences were found in the IR spectra as well, namely in the positions of the amide I bands (see Fig. 1).

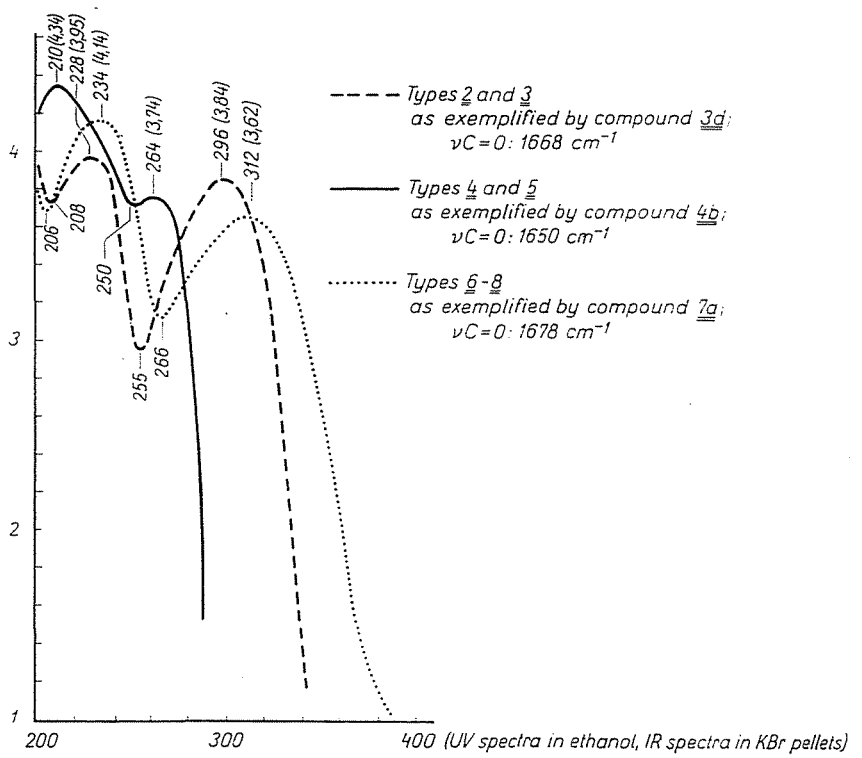


Fig. 1. UV spectra and carbonyl frequencies of representatives of types **2** and **3**, **4** and **5**, and **6**—**8**, respectively

The UV spectra of monocyclic (type **2**) and bicyclic (type **3**) compounds, containing a conjugated chromophore system of the 2-amino-4(3*H*)-pyrimidinone type, exhibit two absorption bands similarly to those of the isomeric monocyclic (type **6**) and bicyclic compounds (types **7** and **8**) containing a chromophore system of the 2,3-dihydro-2-imino-4(1*H*)-pyrimidinone type with an exocyclic double bond. An inspection of Fig. 1 and especially of the pertinent tables reveals that these two chromophore systems *cannot be dis-*

* Differences in the UV spectra corresponding to the conjugated and cross conjugated chromophores were pointed out previously by BROWN and TEITEI [10].

tinguished by the positions of the absorption bands with certainty. They may, however, be unequivocally distinguished on the basis of *the relative intensity of the maxima:* while the longer wave band of compounds containing either of the chromophores **6**—**8** is of much lower intensity than that at smaller wave lengths ($\Delta\log\varepsilon = -0.52 - -0{,}75$), the corresponding difference is much smaller in the case of compounds containing chromophores **2** or **3**; moreover, the longer wave maximum is quite often the more intense ($\Delta\log\varepsilon = -0.24 - +0.18$).

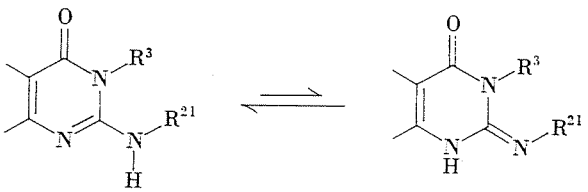
The tautomeric structure of compound **4b,** representing the compounds with cross conjugated chromophores in Fig. 1, is, in principle, not completely fixed because a potentially mobile hydrogen atom (attached to nitrogen) is present. The possibility that a mixture of **4b** and its tautomeride containing an exocyclic double bond is present in the ethanolic solution could, therefore, not be excluded in advance. Since, however, both UV absorption maxima of the compound in question coincide with the minima of model compound **7a** containing an exocyclic double bond and, furthermore, our compound was found to be practically transparent at wave lengths where **7a,** as well as its analogues shown in Table 5, have their longer wave absorption band, the tautomeric equilibrium mentioned above must be shifted considerably towards the cross conjugated form **4b** and, thus, the spectrum of this compound may be taken as to belong to the cross conjugated double bond system.

On the basis of their IR spectra, compounds containing a conjugated double bond system (types **2** and **3**) and an exocyclic double bond (types **6**—**8**), respectively, cannot be distinguished because the amide I band is found in both cases at approximately the same wave numbers. Compounds containing a cross conjugated double bond system (types **4** and **5**) may, however, in most cases be distinguished by the lower wave numbers of their amide I bands from the above two types of compounds (*c.f.* [25]).

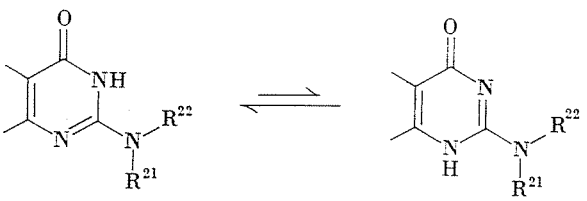
In the following a detailed discussion — mostly in tabular form — of the UV and IR characteristics of the three different chromophore systems will be presented.

The UV and IR spectra of the 2-amino-4(3*H*)-pyrimidinone chromophore (types 2 and 3)

The monocyclic variant (type **2**) of the chromophore under discussion was available in form of model compounds of not completely fixed tautomeric structures (**2**, R^{22} *or* R^3=H). The structures of these compounds, therefore, do not follow unequivocally from their syntheses, and the possible existence of the following tautomeric equilibria had to be taken into consideration:



Type **2** Type **6**



Type **2** Type **4**

From the fact, however, that the UV spectra of the compounds belonging into the subgroups R^{22}=H and R^3=H, respectively, were found — apart from a few exceptions (see below) — to be practically identical (see Table 1), it follows that both equilibria are strongly shifted to the left, *i.e.* that the compounds in question exist mainly as the tautomerides containing the chromophore **2.**

The situation with the bicyclic model compounds **3** is similar because, owing to R^1=H, the presence of the tautomeric form **8** (R^8=H) may not be excluded a priori either. Since, however, the spectra (see Table 2) of the compounds studied were found practically identical with those of compounds **2**, it could be taken as verified that, again at least predominantly, the tautomerides **3** were present.

The correctness of these reasonings was fully supported by the UV spectral data of a completely fixed representative (**2j** and **3d**, respectively) both of the mono- and bicyclic variant described in the literature and also presented in Tables 1 and 2, respectively.

Among the compounds of Table 1 deviations from the rule concerning the extremes of the $\Delta\log\varepsilon$ values (see p. 46) were found only in the cases of isocytosine (**2a**) itself as well as of a limited number of its *N*(2), *N*(2)-dimethyl derivatives (**2f—i**); the $\Delta\log\varepsilon$ values of these compounds were < -0.36 [10] and -0.79 — -0.30 [10,13], respectively. Since the UV spectrum of isocytosine was found to be intermediate between those corresponding to compounds containing the fixed chromophores **2** and **4**, respectively, according to Australian authors, a tautomeric equilibrium of forms **1a** and **1b** must be present in solutions of isocytosine [10]. The anomalously small value of $\Delta\log\varepsilon$ may be rationalized also by assuming a tautomeric equilibrium: as may readily be seen from Fig. 1,

Table 1

UV and IR spectra of

Compound	R^{21}	R^{22}	R^3	R^5	R^6
a [10]	H	H	H	H	H
b	H	H	H	H	Me
c [10]	H	H	Me	H	H
d	H	H	Me	H	Me
e	H	H	Me	Br	Me
f [10]	Me	Me	H	H	H
g [13]	Me	Me	H	Et	Me
h [13]	Me	Me	H	n—Pr	Me
i [13]	Me	Me	H	n—Bu	Me
j [10]	Me	Me	Me	H	H
k	$-(CH_2)_4-$		H	H	$CH_2=CH-(CH_2)_2-$
l	$-(CH_2)_5-$		H	H	$CH_2=CH-(CH_2)_2-$
m	$-(CH_2)_5-$		H	H	$Me-\underset{\displaystyle Br}{\underset{\vert}{CH}}-(CH_2)_2-$
n	$-(CH_2)_5-$		H	allyl	Me
o	$-(CH_2)_5-$		H	Br	$CH_2=CH-(CH_2)_2-$
p	$-(CH_2)_5-$		H	Br	$CH_2(Br)-CH(Br)-(CH_2)_2-$
q	HOC_2H_4-	H	H	H	Me
r	HOC_2H_4-	H	H	$-(CH_2)_4-$	
s	HOC_2H_4-	H	H	Br	Me
t	HOC_2H_4-	H	Me	H	Me
u	HOC_2H_4-	H	Et	$-(CH_2)_4-$	
v	HOC_2H_4-	H	$-CH_2-C(=O)NHC_2H_4OH$	$-(CH_2)_4-$	
w	HOC_3H_6-	H	H	H	Me
z	$PhCH_2-$	H	H	$-(CH_2)_4-$	
x	$PhCH_2-$	H	$-CH_2-C(=O)NHCH_2Ph$	$-(CH_2)_4-$	
y	HOC_2H_4NH-	H	H	$-(CH_2)_4-$	

the presence of either of the tautomerides **1b** and **1d** besides **1a** in the solution should cause the lowering of the value of $\Delta\log\varepsilon$. With the $N(2)$,$N(2)$-dimethyl derivatives the situation is analogous (tautomeric equilibrium between the forms corresponding to **1a** and **1b**, respectively).

The UV data of compounds of types **2A** and **3A**, the aza analogues of types **2** and **3**, are presented in Tables 3 and 4.

By comparing the data of the corresponding tables it becomes evident that the introduction of a further nitrogen atom into the cyclic skeleton does

compounds of type **2**

Solvent	λ_{max} (log ε)		Δ log ε	IR (KBr) Amide I (cm^{-1})
buffer, pH = 7	< 220 (> 4.0);	280 (3.64)	< −0.36	
EtOH	226 (3.96);	283 (3.97)	0.01	1665
buffer, pH = 9.8−13.3	225 (3.86);	284 (3.94)	0.08	
EtOH	228 (3.88);	284 (4.01)	0.13	1665
EtOH	231 (3.88);	298 (4.05)	0.17	1655
buffer, pH = 7	224 (4.30);	297 (3.51)	−0.79	
**	227 (4.15);	300 (3.84)	−0.31	
**	228 (4.15);	304 (3.85)	−0.30	
**	229 (4.19);	304 (3.89)	−0.30	
buffer, pH = 9.8	237 (3.89);	297 (4.04)	0.15	
EtOH	232 (4.14);	300 (4.04)	−0.10	1650
EtOH	234 (4.16);	300 (4.05)	−0.11	1650
EtOH	233 (4.20);	301 (3.96)	−0.24	1650
EtOH	236 (4.20);	304 (4.03)	−0.17	1635
EtOH	240 (4.15);	312 (4.11)	−0.04	1665
EtOH	240 (4.14);	315 (4.14)	0	1648
EtOH	224 (4.02);	290 (3.97)	−0.05	1635
EtOH	226 (4.03);	293 (3.88)	−0.15	1670
EtOH	229 (4.04);	304 (4.04)	0	1645
EtOH	228 (3.86);	289 (4.04)	0.18	1650
EtOH	233 (3.92);	292 (4.02)	0.10	1630
EtOH	232 (3.92);	293 (4.00)	0.08	1655
EtOH	224 (4.00);	290 (3.96)	−0.04	1680
EtOH	224 (4.14), sh.;	294 (3.96)	0.18	1650
EtOH	226 (3.98), sh.;	296 (4.04)	−0.06	1650
EtOH	230 (4.04);	291 (3.80)	−0.24	

* The UV spectra of isocytosine derivatives are strongly dependent on the pH of the solutions examined, *i.e.* on the actual form of the compound (neutral, anionic or cationic species) present in the solution. Therefore it has become common practice in the literature to state — in addition to the spectral characteristics of these compounds — also their pK_a values and the pH of the aqueous buffer solutions used. According to experience, in ethanolic solutions the spectra of the neutral species are always observed; therefore the pK_a values could be omitted in the above as well as in the subsequent tables.

** The solvent has not been stated, but the actual form present was explicitely denoted as the neutral species.

Table 2

UV and IR spectra of compounds of type **3**

	R^1	R^3	R^6	R^7	Solvent	λ_{max} (log ε)	Δ log ε	IR (KBr) Amide I (cm^{-1})
a	H	H	$(CH_2)_4$		EtOH	231 (4.32); 288 (4.20)	−0.12	1690
b	H	OH	H	Me	EtOH	226 (4.00); 290 (3.95)	−0.05	1680
c	H	OH	Br	Me	EtOH	230 (3.94); 304 (3.94)	0	1675
d [14]	Me	H	Me	H	EtOH	228 (3.95); 296 (3.84)	−0.11	1668

Table 3

UV and IR spectra of compounds of type **2A**

	R^4	R^5	Solvent	λ_{max} (log ε)	Δ log ε	IR (KBr) Amide I (cm^{-1})
a [15]	Me	H	EtOH	220 (3.82); 301 (3.80)	−0.02	
			buffer, pH=9.3	219 (3.90); 297 (3.82)	−0.08	
b [15]	Me	Me	EtOH	222 (3.90); 299 (3.89)	−0.01	
			buffer, pH=7.0	222 (3.91); 296 (3.85)	−0.06	
c [16]	$-NH_2$	Me	EtOH	218 (3.93); 298 (3.84)	−0.09	1685
d [7]	$-NHC_2H_4OH$	Me	EtOH	220 (3.88); 300 (3.78)	−0.10	1690
e [7]	$-NHC_2H_4Cl$	Me	EtOH	218 (3.93); 302 (3.83)	−0.10	1690

Table 4

UV and IR spectra of compounds of type **3A** [7]

	Z	n	Solvent	λ_{max} (log ε)	Δ log ε	IR (KBr) Amide I (cm^{-1})
a	CH_2	1	EtOH	220 (4.05); 300 (3.70)	−0.35	1680
b	CH_2	2	EtOH	231 (4.05); 316 (3.85)	−0.18	1680
c	NH	2	EtOH	226 (4.11); 311 (3.84)	−0.27	1665

not change the shape of the UV spectra, and at most as a result of the transition **2** → **2A** may a rather small hypsochromic shift of the short-wave band be observed.

These findings support, on the one hand, the correctness of the above considerations and, on the other, they demonstrate that the UV spectrum corresponding to the 2-amino-4(3*H*)-pyrimidinone chromophore is rather insensitive to variations in the skeleton of the chromophore. The same will be found below when discussing the effects of replacing the 2-amino by a 2-alkylthio group.

*

In the last columns of Tables 1—4 the positions of the amide I bands in the IR spectra of the respective compounds are shown. With the exception of five compounds (**2n, 2p, 2q, 2s** and **2u**) in Table 1 — in which the amide I band is found at 1648—1630/cm — the IR spectra (taken in KBr pellets) exhibit amide I bands in the region of 1680—1650/cm. Thus, comparatively high wave numbers may be accepted as typical for the amide I bands or 2-amino-4(3*H*)-pyrimidinones, this being a significant difference from the 2-amino-4(1*H*)-pyrimidinones to be discussed below*. The amide I bands of compounds of type **3** are found without exception in the region 1690—1668/cm (Table 2), and the amide bands of the aza analogues **2A** (1690—1685/cm) and **3A** (1680—1665/cm) are also found at comparatively high wave numbers.

The UV and IR spectra of the 2-amino-4(1*H*)--pyrimidinone chromophore (types 6—8)

According to our findings the double bond distribution corresponding to this chromophore is the least stable: if the possibility for prototropy exists in principle, it will be realized. Therefore this chromophore can be studied only if completely "fixed" derivatives are available. Representatives of this class were available only in the bicyclic imidazo[1,2-a]pyrimidine series (types **7** and **8**), their spectral characteristics being compiled in Table 5.

The UV spectrum corresponding to the chromophore in question has two absorption maxima, their actual positions being strongly dependent on the quality of the substituents, above all whether the 2,3-imidazo[1,2-a]-pyrimidin-7(8*H*)-one (**7**) or the -5(8*H*)-one system (**8**) is concerned. (For the possibility of distinguishing these spectra from those corresponding to the 2-amino--4(3*H*)-pyrimidinone chromophore system already discussed and also exhibiting two maxima, see p. 46).

The spectral characteristics of the compounds containing a double bond, exocyclic to the pyrimidine ring, are essentially retained also in the case of the aza analogue **6A** but both bands suffer hypsochromic shifts and the value of $|\Delta \log \varepsilon|$ diminishes (see Table 5).

Although final conclusions can not be drawn from the comparatively few data available, it may at least be pointed out that the UV spectra of com-

* Though the anomalously low wave numbers of the amide I bands of compounds **2n, 2p, 2q** and **2s** could be explained by assuming that *in crystalline state* these compounds exist as the corresponding cross-conjugated 2-amino-4(1*H*)-pyrimidinones, in the case of compound **2u**, owing to $R^3 \neq H$, a tautomerization of this type would be impossible. Thus, the shift of the amide I band towards lower wave numbers must be caused by different and still uncleared structural features.

Table 5

UV and IR spectra of compounds of types **7**, **8** and **6A**

Type	Compound	R^5, or R^7	R^6	R^8	Solvent	λ_{max} (log ε)	$\Delta \log \varepsilon$	IR (KBr) Amide I (cm^{-1})
7	a	$(CH_2)_4$		Et	EtOH	234 (4.14); 312 (3.62)	−0.52	1678
7	b [14]	H	Me	Me	EtOH	234 (4.15); 314 (3.58)	−0.57	1670
8	c	Me	H	Me	EtOH	226 (4.26); 297 (3.55)	−0.71	1695 + 1675 (d)
8	d [14]	H	Me	Me	EtOH	225 (4.15); 302 (3.40)	−0.75	1685
6A	e [15]				buffer, pH = 7	217 (4.05); 262 (3.57)	−0.48	
					EtOH	216 (3.88); 266 (3.58)	−0.30	

Table 6

UV and IR spectra of compounds of type **4** and **5**

	R^{21}	R^{22}	R^6	Solvent	λ_{max} (log ε)	IR (KBr) Amide I (cm^{-1})
4a [10]	H	H	H	buffer, pH = 13.0	< 220 (> 4.1); 260 (3.74)	
4b	H	Me	Me	EtOH	210 (4.34); 264 (3.74), shoulder	1650
4c	H	$-C_2H_4OH$	Me	EtOH	213 (4.36); 264 (3.74)	1645
4d	H	$-CH_2COOH$	Me	EtOH	213 (4.31); 263 (3.75), shoulder	1650
4e	Me	Me	Me	EtOH	216 (4.26); 282 (3.74)	1650
5 [14]	$R^1 = R^6 = Me$, $R^5 = H$			EtOH	210 (4.22); 232 (4.17); 277 (3.58)	1660

pounds containing the 2,3-dihydro-2-imino-4(1*H*)-pyrimidinone chromophore are considerably more sensitive to structural variations than are the spectra of 2-amino-4(3*H*)-pyrimidinones.

*

In the last column of Table 5 the positions of the amide I bands in the IR spectra of the individual compounds are shown. The amide I band of the bicyclic 2,3-dihydro-2-imino-4(1*H*)-pyrimidinones containing a double bond exocyclic with respect to the pyrimidine ring is also found at comparatively high wave numbers (in the region 1695—1660/cm) and, therefore, on the basis of the positions of the amide I bands the 2,3-dihydro-2-imino-4(1*H*)-pyrimidinone and the 2-amino-4(3*H*)-pyrimidinone systems can not be told apart.

The UV and IR spectra of the 2-amino-4(1*H*)--(pyrimidinone chromophore (types 4 and 5)

Most representatives of the monocyclic variant (4) of the compounds, containing the cross conjugated chromophore system, available to us were of the non completely "fixed" type (R^{21}=H). Therefore the possible existence of a tautomeric equilibrium of the type 4 ⇌ **6** could not be denied in advance. On the basis of a reasoning similar to that on p. 47 it may, however, be realized that, in any case, this equilibrium must be strongly shifted towards the cross conjugated tautomeride (4). The spectral data are presented in Table 6.

The long-wave absorption bands in the spectra of compounds **4a**—**4d** are considerably hypsochromically shifted (by 20—40 nm) as compared to those of compounds **2** and **6**; moreover, in two of a total of four examples their shapes are almost shoulder-like, pointing to the fact that cross conjugation is less "effective".

The considerable change in the spectrum caused by the introduction of a second alkyl group at the exocyclic nitrogen atom of 4 is striking. The long-wave band in the spectra of the completely "fixed" compounds (**4e** and **5**) is found to be bathochromically shifted by 15—20 nm as compared to the corresponding bands in the spectra of compounds **4a**—**d** and, at the same time, the band has lost its shoulder-like appearance and become more pronounced. Furthermore, in the spectrum of the bicyclic compound **5** a further maximum is found (at 232 nm) between the above two bands. Thus, the UV spectra of compounds of type 4 are by far more sensitive to variations of the substituents than those of compounds **2** and **6**. The same will be found below when discussing the effects of replacing the 2-amino by a 2-alkylthio group.

The spectral data of the aza analogues **4A** and **5A** are compiled in Table 7. Among the monocyclic compounds (type **4A**) listed no completely "fixed" derivative may be found: at least one of the ligands R^2, R^{31} and R^{32} is hy-

Table 7

UV and IR spectra of compounds

Type	Compound	R^2	R^{31}	R^{32}	R^6
4A	a [15]	H	H	H	H
	b	H	H	H	Me
	c [7]	H	H	H	HOC_2H_4—
	d [7]	H	H	H	HOC_3H_6—
	e [15]	H	H	Me	Me
	f [7]	H	H	HOC_2H_4—	Me
	g [7]	H	H	HOC_3H_6—	Me
	h [7]	H	H	HOC_2H_4NH—	Me
	i [15]	H	Me	Me	Me
	j	H	$(CH_2)_4$		Me
	k [15]	Me	H	H	Me
	l [15]	Me	Me	H	Me
	m [7]	$-CH_2C(=O)NHBu$	H	n—Bu	Me
5A	n [7]	Z = C_2H_4	(monohydrate)		
	o [7]	Z = C_3H_6			

drogen. From the identity of the UV spectra it follows, however, unequivocally that the potentially tautomeric compounds studied all exist, at least predominantly, as the cross conjugated tautomerides. This statement holds, on similar grounds, for the bicyclic representatives (type **5A**) as well.

Comparison of the data in Tables 6 and 7 shows that, as a consequence of the replacement of the pyrimidine by the 1,2,4-triazine ring, the long-wave absorption band has been hypsochromically shifted by about 20 nm but the shapes of the spectra are scarcely changed. In any case, the shift of the long-wave band supports the correctness of our conclusion that the spectra of the cross conjugated compounds are highly sensitive to variations of structure.

*

In the last columns of Tables 6 and 7 we have listed the wave number of the amide I bands in the IR spectra of the individual compounds. The amide I band of the compounds of types 4 and 5 is found in the region 1660—1645, that of the aza analogues (types **4A** and **5A**) in the region 1668—1635/cm. The regions of the amide I bands of the different types are listed in Table 8.

The regions of the amide I bands are seen to overlap partly. Therefore the differentiation of the cross conjugated forms from the other ones on the

of types **4A** and **5A**

Solvent	λ_{max} (log ε)	IR (KBr) Amide I (cm^{-1})
EtOH	248 (3.75)	
buffer, pH = 5.1	247 (3.71)	
EtOH	204 (4.52); 246 (3.87), shoulder	1665 + 1650 (d)
buffer, pH = 5.1	243 (3.78) [15]	
EtOH	205 (4.43); 249 (3.78), shoulder	1668
		1665
EtOH	214 (4.25); 241 (3.88), shoulder	
buffer, pH = 5.6	213 (4.22); 243 (3.80), shoulder	
EtOH	210 (4.42); 240 (3.86), shoulder	1658
EtOH	211 (4.40); 240 (3.86), shoulder	1665
EtOH	211 (4.36); 244 (3.85), shoulder	1673
EtOH	220 (4.27); 247 (3.80), shoulder	
buffer, pH = 4.0	223 (4.28); 247 (3.84), shoulder	
EtOH	218 (4.42); 246 (3.94), shoulder	1665
EtOH	257 (3.73)	
buffer, pH = 5.1	248 (3.73)	
EtOH	250 (3.85)	
buffer, pH = 7.0	218 (4.19), shoulder; 245 (3.86), shoulder	
EtOH	212 (4.43); 248 (3.94), shoulder	1675 (acycl.)
		1648 (ring)
EtOH	210 (4.42); 244 (3.86), shoulder	1660
EtOH	212 (4.42); 255 (3.82), shoulder	1635

Table 8

Region of the amide I band as a function of the distribution of the double bonds in the pyrimidine ring

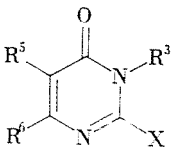
Type of distribution of the double bonds	Types of compounds	Amide I (cm^{-1}) (KBr)	Number of compounds
Conjugated	**2**, **3**	1690—1630	22
		typical: 1690—1650	17
Aza analogues	**2A**, **3A**	1690—1665	6
Cross conjugated	**4**, **5**	1660—1645	5
Aza analogues	**4A**, **5A**	1673—1635	11
Exocyclic	**7**, **8**	1695—1660	4

basis of the wave numbers of the amide I bands seems more questionable than in the cases of the alkylthio analogues and the aza analogues of the latter (see below).

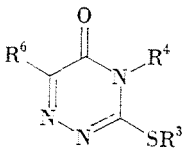
In any case, it may be accepted as established that an amide I band at or above 1675/cm excludes the possibility of dealing with a 2-amino-4-pyrimidinone derivative.

*

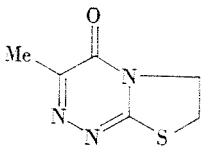
In the following a comparison of the spectra of isocytosine and imidazopyrimidinone derivatives with those of some analogues will be presented.



9: X = MeS–
11: X = H



9A



10A

The UV and IR spectra of the methylthio analogues (**9**) of the compounds of type **2** containing a conjugated double bond system and those of their aza analogues (**9A**) are listed in Table 9 and in Table 10, respectively. In the latter we have listed also the data of the bicyclic compound **10A** which contains the same chromophore system. As a supplement, the UV spectral data (taken from literature) of compounds of type **11** have been also listed in Table 11.

The spectra of the methylthio analogues **9** are seen to be practically identical with those of the compounds **2** and their bicyclic variants **3**; the same holds for the positions of the amide I bands in the IR spectra. Only in the case of a single compound, **9k**, could a slight difference be registered: the short-wave absorption band in the UV spectrum run in ethanol of this compound was found, in contrast to the corresponding bands of the fundamental types **2** and **3** or even to those of the rest of the compounds **9**, to be split. This splitting was found in the UV spectra of the sulphur-containing aza analogues **9A** and **10A** to be general. At the same time, this split band system — especially its more pronounced shorter-wave part upon which the longer-wave part is superposed as a shoulder — has been rather considerably hypsochromically shifted. On the other hand, the second band system retains its position unaltered with respect to the compounds of type **2** and in all these cases the value of $\Delta \log \varepsilon$ falls between the limits found for the case of compounds **2**.

The wave numbers of the amide I bands in the IR spectra of compounds **9A** and **10A** fluctuate between less broad limits than found for the case of the other types discussed above and, at the same time, are shifted towards higher wave numbers.

In the UV spectra of the 4(3*H*)-pyrimidinones **11**, unsubstituted in position 2, the second band is shifted by approximately 20—40 nm towards lower wave lengths in harmony with the fact that, in the absence of a substituent in position 2, the extension of the chromophore system decreases. Apart from this, however, the UV spectra of the compounds **11** are very similar to those of the other related systems. All these data, summarized in Table 12, support

Table 9

UV and IR spectra of methylthio analogues of type **9**

	R^a	R^b	R^c	Solvent	λ_{max} (log ε)	Δ log ε	IR (KBr) Amide I (cm^{-1})
a	H	H	Me	EtOH	232 (4.05); 285 (3.92)	−0.13	1655
b	H	Br	Me				1645
c	H	H	CH_2=CH−$(CH_2)_2$−	EtOH	236 (3.91); 286 (3.88)	−0.03	1665
d	H	H	CH_2(Br)−CH(Br)−$(CH_2)_2$−	EtOH	236 (3.88); 287 (3.85)	−0.03	1650
e	H	H	−C_2H_4COOH				1650
f	H	−$(CH_2)_3$−		EtOH	244 (3.93); 288 (3.95)	+0.02	
g	H	−$(CH_2)_4$−		EtOH	238 (3.99); 284 (3.92)	−0.07	1645
h	H	HOC_2H_4−	$HOOC-C_2H_4$−	EtOH	243 (3.90); 292 (3.98)	+0.08	
i	H	$AcOC_2H_4$−	$HOOC-C_2H_4$−	EtOH	241 (3.86); 292 (3.96)	+0.10	1650
j	H	HOC_2H_4−		EtOH	242 (3.92); 290 (4.00)	+0.08	1640 (broad)
k	Me	H	Me	EtOH buffer, pH=2—12 [17]	224 (3.79): ~241 (~3.8); ~286 (~3.9)	~+0.1	1685
				pH=2—12 [18]	241 (3.76); 288 (3.93)	+0.17	
l	Et	−$(CH_2)_4$−		EtOH	242 (3.83); 288 (3.97)	+0.16	1670
m	−CH_2COOEt	−$(CH_2)_4$−		EtOH	241 (3.81); 288 (3.99)	+0.18	1670
n	−CH_2CONH_2	−$(CH_2)_4$−		EtOH	242 (3.78); 288 (4.00)	+0.22	1670 (broad)

Table 10

UV and IR spectra of compounds of type **9A** and **10A**

Type	Compound	R^3	R^4	R^6	Solvent	λ_{max} (log ε)	$\Delta \log \varepsilon$	IR (KBr) Amide I (cm^{-1})
9A	a [1]	Me	Me	H	MeOH	208 (4.11); 226 (3.76), sh.; 298 (3.92)	—0.19	1695
	b [5]	Me	NH_2	Me	EtOH	212 (4.08); 228 (4.01); 298 (3.94)	—0.14	1695
	c [5]	$-CH_2COOEt$	NH_2	Me	EtOH	209 (4.06); 225 (3.9), sh.; 294 (3.90)	—0.16	1695
	d [5]	$-CH_2CN$	NH_2	Me	EtOH	207 (4.08); ~225 (~3.8), sh.; 290 (3.89)	—0.19	1695
	e [5]	$-CH_2CN$	NH_2	HOC_2H_4-	EtOH	206 (4.12); ~230 (~3.9), sh.; 291 (3.96)	—0.16	1695
10A	f[1]				EtOH	212 (4.07); 225 (3.96), sh.; 292 (3.83)	—0.24	1685

Table 11

UV spectra of compounds of type **11**

	R^3	R^5	R^6	Solvent	λ_{max} og ε)	Δ log ε	Ref.
a	Me	H	H	pH = 5.0	221 (3.83); 269 (3.59)	−0.24	[17]
b	Me	H	Me	pH = 7	224 (3.75); 268 (3.56)	−0.19	[18]
c	Me	Br	H	pH = 4.0	236 (3.60); 283 (3.77)	+0.17	[19]
d	Me	Me	H	pH = 7.0	226 (3.76); 270 (3.72)	−0.04	[19]

Table 12

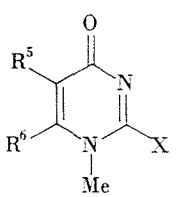
Comparison of the UV and IR spectra of some compounds containing a conjugated double bond system in the pyrimidine and 1,2,4-triazine ring, respectively

Type	λ_{max} [nm] I	λ_{max} [nm] II	Δ log ε	Number of compounds	IR (KBr) Amide I (cm^{-1})	Number of compounds
2	<220—240	280—315	−0.24 — +0.18*	26	1680—1650**	18
3	226—231	288—304	−0.12 — 0	4	1690—1668	4
2A	218—222	296—302	−0.10 — −0.01	5	1690—1685	3
3A	220—231	300—316	−0.35 — −0.18	3	1680—1665	3
9	225; 232—244	285—292	−0.13 — +0.22	14	1685—1640	12
9A	208—212; 225—230 (sh)	290—298	−0.19 — −0.14	5	1695	5
10A	212; 225 (sh)	292	−0.24	1	1685	1
11	221—226	268—270	−0.24 — −0.04	3***		

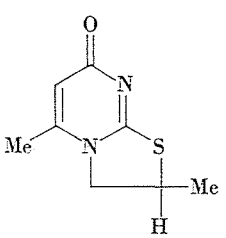
* The data of compounds **2a** and **2f—i** were neglected *(cf.* p. 47.)
** The data of compounds **2n, 2p, 2q, 2s** and **2u** were neglected *(cf.* p. 51.)
*** The data of the bromo derivative **11c** were neglected.

once more the correctness of our view that the UV spectra of 4(3*H*)-pyrimidinones containing a conjugated double bond system are comparatively insensitive to variations of chemical structure.

*



12: X = RS—
14: X = H



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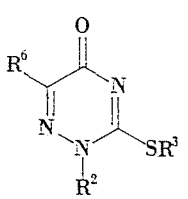
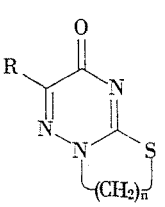


12A



13A

The spectral data of the cross-conjugated analogues **12, 13, 12A, 13A** and **14** of types **9, 9A, 10A** and **11,** have-been listed in Tables 13 and 14 respectively. The data of all cross-conjugated types of compounds studied by us are summarized in Table 15.

Table 13

UV and IR spectra of compounds of types **12—14**

Type	Compound	X	R^5	R^6	Solvent	λ_{max} (log ε)	IR (KBr) Amide I (cm^{-1})
12	a	MeS	H	Me	EtOH	233 (4.44); ~260 (~3.9) sh	1645
	b*	EtS	H	H	EtOH	233 (4.39); ~260 (~3.8) sh	1645
					buffer, pH=3.6—14	233.5 (4.43) [20]	
	c	$PhCH_2S$	H	Me	EtOH	236 (4.46); ~260 (~4.0) sh	1650
13	d				EtOH	230 (4.42); 258 (3.91) sh	1650
14	e	H	H	H	buffer, pH = 6.0	240 (4.16) [17]	
	f	H	Me	H	buffer, pH = 7.0	247 (4.07) [19]	

* Kindly furnished by Dr. J. J. Fox, c.f. [20].

Table 14

UV and IR spectra of compounds of types **12A** and **13A**

Type	Compound	R^2	R^3	R^4	Solvent	λ_{max} (log ε)	IR (KBr) Amide I (cm^{-1})
12A	a [4]	H	$-CH_2COOH$	Me	EtOH	236 (4.26)	1620
					dioxane	233 (4.17)	
	b [4]	H	$-C_2H_4COOH$	Me	EtOH	236 (4.30)	
	c [1]	Me	Me	H	MeOH	235 (4.38)	1670
	d [7]	$-CH_2COOEt$	Me	Me	EtOH	238 (4.34)	1660
	e [21]	H	Me	$-C_2H_4COOH$	EtOH	236 (4.28)	
13A	f [1]*	n = 2,	R = Me		EtOH	232 (4.32)	1645
	g [1]**	n = 3,	R = Me		EtOH	238 (4.36)	1645

* For the spectra of compounds of analogous structures see [3].
** For the spectra of compound of analogous structures see [6].

Table 15

Comparison of the UV and IR spectra of some compounds containing a cross-conjugated double bond system in the pyrimidine and 1,2,4-triazine ring, respectively

Type	λ_{max} [nm]		Number of compounds	IR (KBr) Amide I (cm^{-1})	Number of compounds
	I	II			
4	210—220	260—282*	4	1650—1645	4
5	210	277**	1	1660	1
4A	204—223	241—257*	18	1673—1648	9
5A	210—212	244—255*	2	1660—1635	2
12	230—236	260 sh	3	1650—1645	3
13	230	258 sh	1	1650	1
12A	233—238	—	5	1670—1620	3
13A	232—238	—	2	1645	2
14	240—247	—	2		

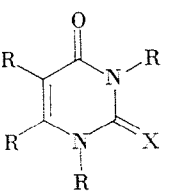
* This band is seldom well-developed and appears often as a shoulder on the first band.
** A third band at intermediate wave number (232 nm) is also found in this case.

A comparison of the data in Tables 12 and 15 readily reveals — in addition to the conclusion that the compounds containing one of the two different kinds of chromophores in question may, on the basis of their spectra, distinguished with certainty — that the UV spectra of the compounds containing a cross-conjugated chromophore are by far more sensitive to variations of chemical structure than those of the compounds containing an "ordinary" conjugated double bond system and, furthermore, that variation of the substitufent attached to position 2 of the pyrimidine ring results in two opposing effects on the UV spectra, depending on the type of chromophore present: replacement of the 2-NRR' group by the 2-SR and 2-H ligands of gradually decreasing conjugative ability results in a significant bathochromic shift of the main absorption band while, in the "ordinary" conjugated system, a

hypsochromic shift of the second* band is caused by the same variations, the shift caused by the exchange 2-NRR' → 2-SR being rather unimportant while that caused by the exchange 2-SR → 2-H is all the more significant.

*

The UV spectra of compounds **7, 8** and **6A** containing a double bond exocyclic to the pyrimidine ring resemble those of their thioxo (**15**) and even oxo analogues (**16**) only in that they have two absorption bands, considerable



15: X = S
16: X = O

differences being, however, found both in the band positions and the $\Delta \log \varepsilon$ values. Therefore, the spectra of the latter type of compounds are not discussed in detail and only the differences in the spectra are briefly summarized in Table 16.

Table 16

Comparison of the UV spectra in ethanol of some compounds containing an exocyclic double bond

Type	λ_{max} (log ε)		$\Delta \log \varepsilon$	Number of compounds
	I	II		
7	234 (4.14—4.15)	312—314 (3.58—3.62)	—0.57 — —0.52	2
8	225—226 (4.15—4.26)	297—302 (3.40—3.57)	—0.75 — —0.71	2
6A	217 (4.05)	262 (3.57)	—0.48	1
15	214—220 (4.08—4.26)	270—280 (4.13—4.27)	—0.08 — +0.17	8
16	206—215 (3.84—4.00)	260—268 (3.90—4.02)	—0.10 — +0.11	5

Experimental

UV spectra** were obtained using a Spectromom 201 spectrometer (Magyar Optikai Művek***, Budapest), the IR spectra were run in KBr pellets using UR-10 (Carl Zeiss, Jena), Model 221 (Perkin-Elmer & Co.) and Spec-

* The first band is less sensitive and reacts less uniformly to the same structural variations.

** The majority of the UV spectra has been published in [26].

*** Hungarian Optical Works.

tromom 2000 (Magyar Optikai Művek*, Budapest) spectrometers. The authors wish to express their gratitude to Miss Zs. FARAGÓ, Mrs. GY. KARSAI-SAS, Mrs. M. SZIRÁNYI-KISS and to Mr. M. VÖRÖS for their valuable assistance in obtaining the various spectra.

The compounds studied were partly prepared in conformity to literature and partly by methods to be described in subsequent papers of this series. Finally, part of the compounds was supplied by J. J. FOX, J. GUT and J. REITER to whom the authors wish to express their gratitude for their obligeance.

Summary

UV and IR spectra of a series of *C*- and *N*-alkylated isocytosines as well as of the corresponding derivatives of imidazo[1,2-a]pyrimidinones have been studied. Characteristic differences have been found between the spectra of the different types of compounds, which make possible the differentiation of compounds containing cross-conjugated and ordinary conjugated chromophores in and a semicyclic C=N double bond at the pyrimidine ring, respectively, on the one hand, and on the other the elucidation of the tautomeric structure of potentially tautomeric members of the above series by spectroscopic means.

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