RESEARCHES ON PYRAZOLES

LII. IR Spectra and Lactim-Lactam Tautomerism of Pyrazolopyridones*

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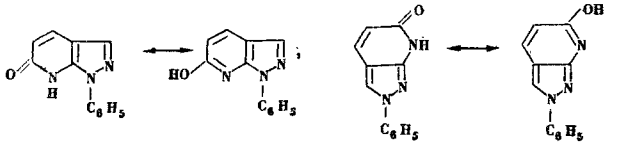
The IR spectra of the previously synthesized pyrazolo[3, 4-b]-and pyrazolo [4, 5-b] pyridones are investigated. From analysis of the IR spectra of the pyrazolopyridones themselves, and of complexes with heavy metal salts, as well as of some model compounds, conclusions are drawn regarding their lactam structure.

Continuing a study of the effect of chemical structure of molecules on lactim-lactam tautomerism [1], we have investigated the IR spectra of pyrazolopyridones which we previously synthesized [2] (see Table).



In unsubstituted α-and γ-hydroxypyridines, the tendency to aromatize does not secure stability of the lactim form. A lactam structure for these compounds is indicated by IR spectra data [3–5], dipole moments [6], and interatomic distances [4, 8]. The presence of alkyl and aryl groups and halogen atoms in the ring does not affect lactim-lactam groups in the crystalline state [9]. Obviously this is because in the solutions from which these compounds crystallize, equilibrium is rather largely shifted towards the lactam form. The presence of condensation polymerized rings (α-and γ-quinolines, 9-hydroxyacridine) also gives rise to further stabilization of the lactam form [10].

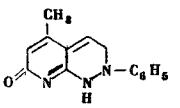
a) IR spectra in chloroform and dioxane solutions. With the spectra of model compounds and α-pyridinopyrazoles in $CHCl_3$ and dioxane solution (Table, Fig. 1), as well as in the crystalline state, (Fig. 4), three groups of bands can be separated in the 1500–1700 cm^{-1} region.

The first of them, at 1495–1507 cm^{-1}, is connected with benzene ring vibrations. The frequency is practically unaltered on passing from one compound to another. The greatest, but on the whole fluctuating value of the intensity (about 1.5 practical units) for this band is with compounds, containing an OMe group in the pyridine ring.

The second group of bands, at 1536–1600 cm^{-1}, contains, in addition to the component one on the average at the position at 1600 cm^{-1} (spread over 1611–1594 cm^{-1}), and obviously also relating to the benzene ring, a series of bands connected with vibrations of double bonds of the aromatic pyrazolo-pyridine system. In the model compounds, increase in the number of electron-donating substituents results in increase in the intensity of this group of bands (from 1.8 to 4.5 practical units). Furthermore, the maximum value (4.5) is shown by the compound with the electron-donating OMe group in the pyridine ring. In α-pyridine systems the intensity of this band is somewhat decreased (3.0 and 4.1 practical units), probably because of the electron-accepting effect of the C=O group.

The third, highest frequency group of the bands in α-pyridine systems, at 1673–1654 cm^{-1}, indicates that these compounds exist in the amide form.

In the case of compound 4 (Table), yet another tautomeric form is theoretically possible:

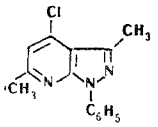
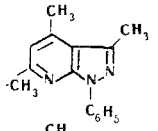
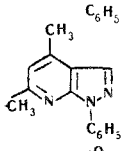
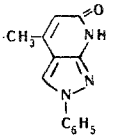
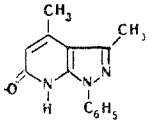
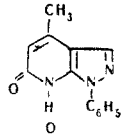
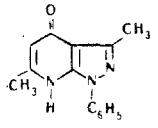
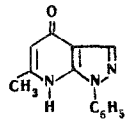
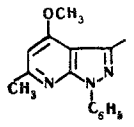


There the frequency of its C=O group should, under the action of the conjugated C=N bond be lowered in comparison with the range indicated, by 60–70 cm^{-1} [13], but that is not observed ($\nu_{C=O}$ at 1673 cm^{-1}). In this compound the C=N bond belonging to the nitrogen atom of the lactam group greatly increases $\nu_{C=O}$ in comparison with the effect of the similarly situated C=C bond in compounds 5 and 6. This fact is in agreement with the literature data regarding the effect of the C=N bond on the lactam group in 6-membered heterocyclic rings [14] (3-hydroxypyridazines, 2-hydroxypyrazines). The total intensity values (5.25 and 4.77 practical units) are also in agreement with those for amide structures [15].

In the spectra of compounds containing the γ-pyridone system of bonds (Table, Fig. 1), the maximum intensity (4.55 practical units) is exhibited by a wide band with a complex contour near 1596–1594 cm^{-1}. In dioxane solution (Fig. 1) this band is split into two components, at 1582 and 1600 cm^{-1}. The higher frequency and more intense of these corresponds to the carbonyl of the γ-pyridine ring. The band at 1635 cm^{-1} undergoes a reverse displacement (to 1630 cm^{-1}) on changing to solution in dioxane. This band is half as intense (2.1 practical units), and it can be assigned to vibrations of double bonds in the ring. Such an interpretation, though it contradicts what is generally accepted [4, 14, 16], is in agreement with an interpretation based on calculation of the effect of solvents on the IR spectra of α- and γ-pyridones [17].

*For Part LI see [20].

Frequencies and Intensities of Individual Bands in the IR Spectra of the Pyrazolopyridines Synthesized*

Compound	ν, cm^{-1}	A · 10^{-4} practical units	ν, cm^{-1}	A · 10^{-4} practical units	ν, cm^{-1}	A · 10^{-4} practical units	ν_{NH}, cm^{-1}
	1506	1.3	1560 1600	3.2	—	—	—
	1507 1506**	1.1	1585—1592 1582—1596**	2.5	—	—	—
	1505	1.1	1600	1.8	—	—	—
	1496	—	1536—1566	3.0	1673	5.25	—
	1505	—	1583	4.1	1654	4.77	3400
	1505	—	1585	4.1	1645— 1657	4.77	3400
	1505	—	1596 1582, 1600**	4.55	1635 1630**	2.1	3420
	1505	—	1594	4.55	1632	2.0	3420
	1507 1506**	1.5	1560, 1580, 1594 1580, 1594** 1611	4.5	—	—	—

*In $CHCl_3$ solution, C = 0.025 M, d = 0.25 mm.

**In dioxane solution.

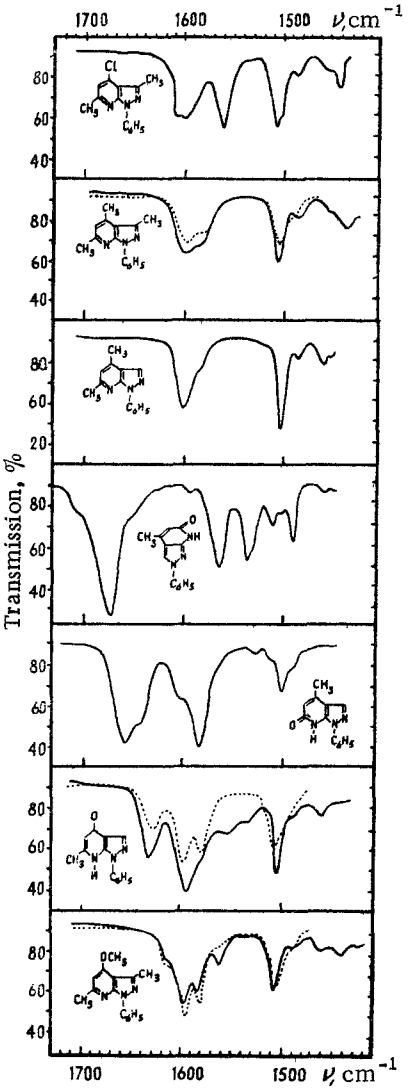


Fig. 1. IR spectra of pyrazolopyridines in $CHCl_3$ (———) and cyclohexane (· · · · · · · · · ·) solutions. C = 0.025 M, d = 0.25 mm.

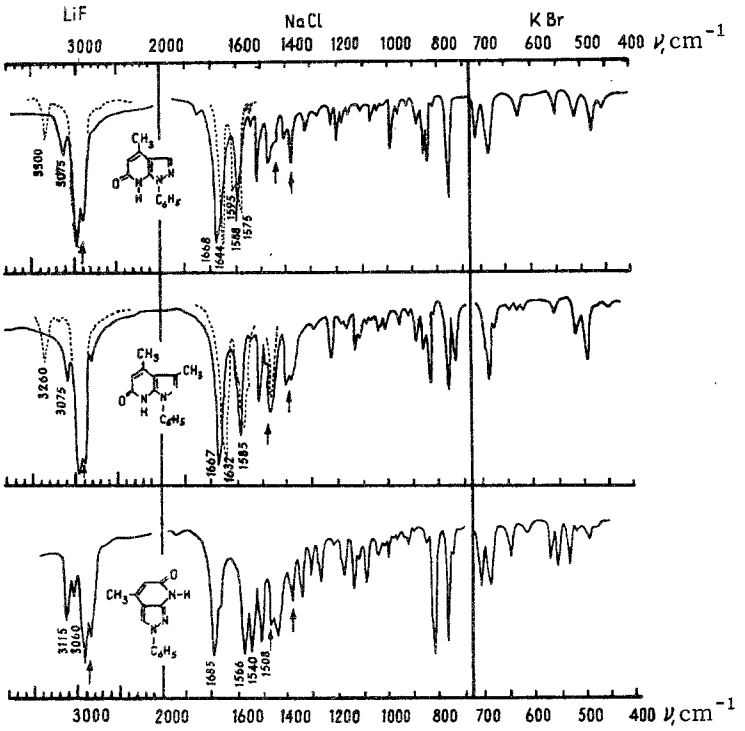


Fig. 2. IR spectra of pyrazolo-α-pyridones (———) and their complexes (· · · · · · · · · ·) with $CdCl_2$ (in the crystalline state).

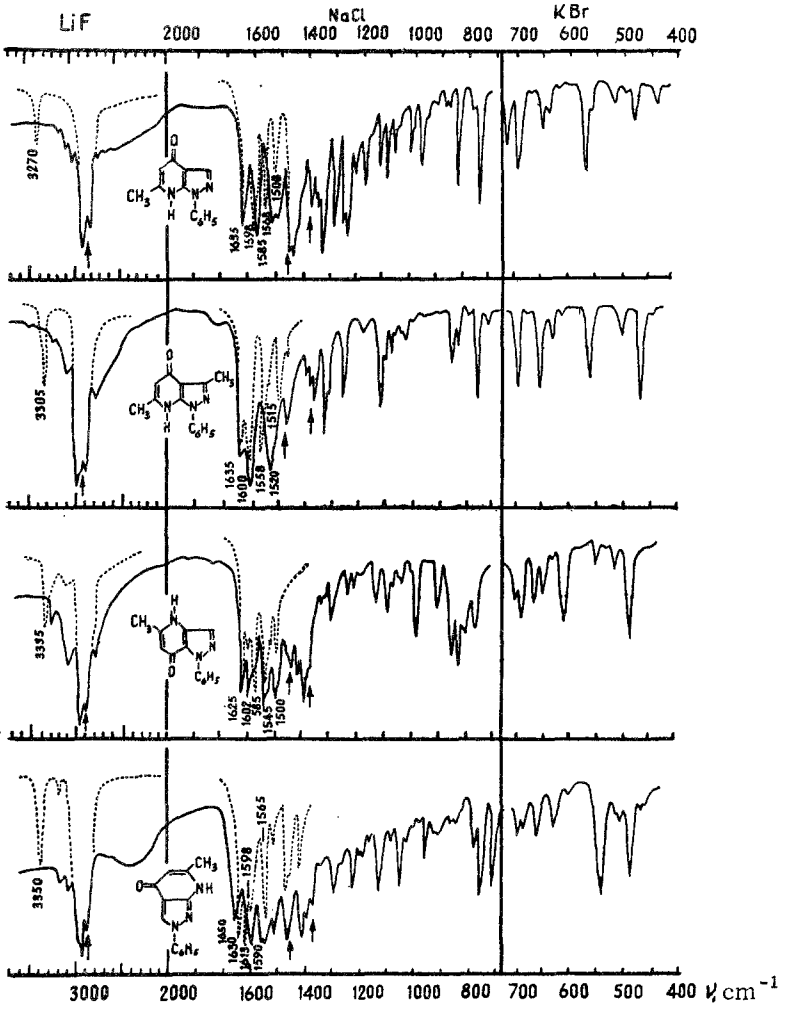


Fig. 3. IR spectra of pyrazolo-γ-pyridones (———) and their complexes (· · · · · · · · · ·) with $CdCl_2$ (in the crystalline state).

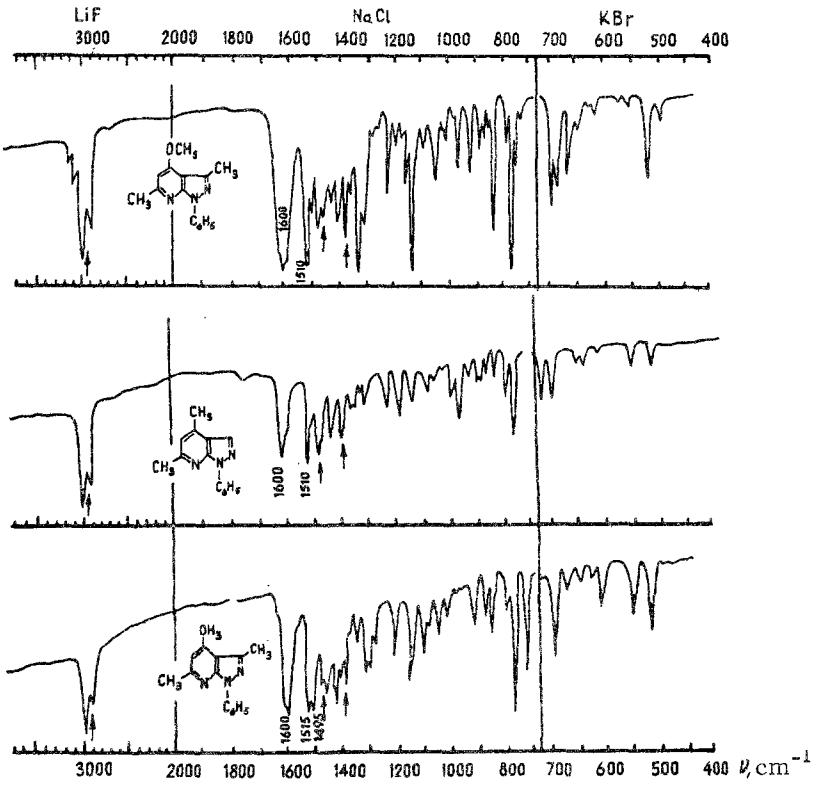
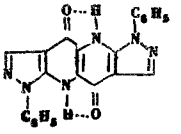


Fig. 4. IR spectra of model pyrazolopyridines (in the crystalline state).

Independent confirmation of an amide structure for the compounds under consideration is the presence of absorption in the 3420 cm^{-1} region for γ-pyridone systems, and in the 3400 cm^{-1} region for α-pyridone ones (dilute solutions in $CHCl_3$), which we assign to NH bonds of amide groups. A similar picture of α-and γ-pyridones was observed in a paper [14].

b) IR spectra in the crystalline state. The spectra of all α-pyridone systems (Fig. 2) have an intense band at 1685–1667 cm^{-1}, belonging to an amide type carbonyl group. Bands of associated NH bonds appear at 3115–3075 cm^{-1}. As expected, the corresponding absorption was lacking in the IR spectra of the model compounds (Fig. 4). In γ-pyridone systems there are more powerful intermolecular bonds, as absorption by the NH bond in the spectra of these compounds is considerably displaced towards the lower frequency side (2700–3000 cm^{-1}, Fig. 3). This fact is also reflected in the higher melting points of the appropriate isomers [2]. It is evident that there is association between NH bonds and the more electrophilic centers in the molecules, the carbonyl group for example, in the case of the γ-isomer.



It might be expected that hydrogen bonds of this type will weaken (or break altogether) if a donor of cations (HCl, $CdBr_2$, $CdCl_2$, etc) which is more readily accessible (to the electrophilic center in the molecule) is introduced. This can occur if a new type of interaction (C=O... cation) is energetically more favored. Then one could expect, along with increase in the NH bond force constant (LiF region), decrease also in the corresponding constant for the C=O bond. The latter circumstance should have led to lowering of the frequency of the valence vibration of the C=O group, and would have served as additional confirmation of the assigning of the bands to the region of double bonds. A series of heterocyclic systems, e.g. and some of its derivatives, had previously been similarly reviewed [12,18,19].

Actually, bands at 3300–3400 cm^{-1} belonging to weakly associated NH bonds, arise in the spectra of complexes of the γ-pyridone system (Fig. 3). In the hydrochloride spectrum they are close to free NH (near 3400 cm^{-1}). In the double bonds region, the intensity of the complex band near 1602 cm^{-1} decreased sharply, and a new band arose at 1558–1585 cm^{-1}, corresponding to the carbonyl group in the new complex. This confirms our deductions regarding the lactam structure of the compounds studied. Bands at 1625–1630 cm^{-1} and some others in the spectra of α-pyridone complexes do not undergo substantial changes as compared with those in the spectra of the actual γ-pyridine system.

The position of the high-frequency C=O bond also changed markedly in the spectrum of a complex of the α-pyridine system.

EXPERIMENTAL

To solve the problem of the structure of the pyrazolopyridine derivatives investigated, we investigated the IR spectra of model and complex compounds, as well as total intensities of some bands in the region of double bonds (1500–1700 cm^{-1}). The spectra were observed with a UR-10 double beam spectrophotometer. The compounds were investigated either as mulls with vaseline or in some cases with polyfluorinated oil (Figs. 2–4), or dissolved in $CHCl_3$ or dioxane. (Fig. 1, Table). The arrow (↑) in Figs. 2–4 means absorption by the vaseline. Total intensities were measured by Burzhen's method [11], areas being measured with a PP-2K type planimeter. The complexes with pyrazolopyridones and $CdCl_2$ or CdBr were obtained by mixing equimolecular EtOH solutions of the pyrazolopyridones and the appropriate salts. The salts precipitated were recrystallized EtOH.

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