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INVESTIGATION OF FREQUENCY COUPLING IN THE IR SPECTRA OF 4H-PYRIDO(1,2a)PYRIMIDIN-4-ONE DERIVATIVES

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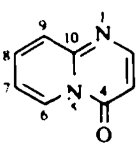
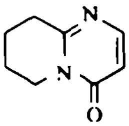
Abstract—The IR spectra of 4H-pyrido(1,2a)pyrimidin-4-one derivatives have been investigated in solid state and different solvents, at different temperatures. The experimental data of several keto-ester derivatives with an ester group in position 3 suggest coupling of the CO stretching frequencies. The CO band of higher frequency is more intense, the separation being 30–80 cm^{-1}. The force constants of the CO bonds have been calculated by the CNDO/2 method. The results of computation are in good accordance with the experimental data: the frequency separation arises mainly from the different CO vibrations, the intensities can be explained only by frequency coupling.

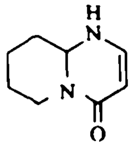
In recent years many new 4H-pyrido(1,2a)pyrimidin-4-one derivatives have been synthesised[1] which show important biological activity.[2] According to their ring system three different types of the compounds investigated can be distinguished (I–III).



I



II



III

In the course of the structural investigations the IR spectra have been thoroughly studied. A remarkable feature of the CO stretching vibrations has been observed, the spectra of several molecules show a less common type of frequency coupling. In order to study this interesting problem, detailed experimental investigations and theoretical calculations have been performed and the results are reported in this paper.

Experimental results

As the most interesting part of the spectra is the region of 1400–1800 cm^{-1}, only these frequencies will be considered. The results given in Tables 1–4 refer to measurements in KBr discs. Figure 1 shows the spectra of compounds 1 and 3 between 400 and 4000 cm^{-1} as examples.

The band assignment was given according to substituent effects. The stretching vibration of the 4-CO group is shifted to lower frequencies by +I substituent

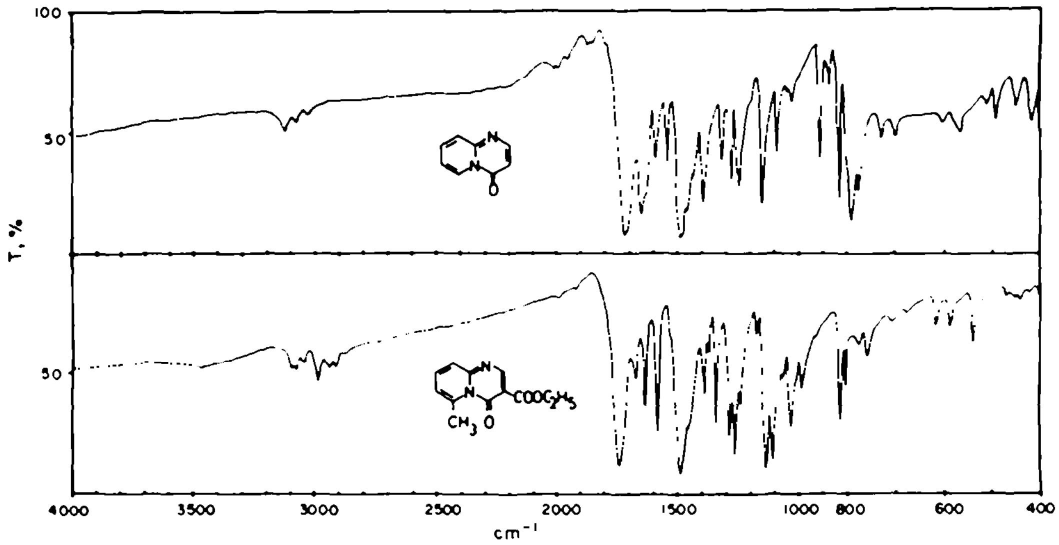


Fig. 1. The IR spectra of the compounds 1 and 3 in KBr discs

Table 1. The carbonyl bands of compounds I and II in KBr discs

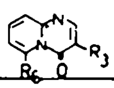
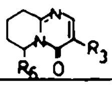
				Substituents	
	νC=O cm^{-1}		νC=O cm^{-1}	R_3	R_6
1.	- 1712 vs	7.	- 1670 vs	-H	-H
2.	1750 vs 1684 m	8.	1748 vs 1676 m	$-COOC_2H_5$	-H
3.	1738 vs 1670 m	9.	1750 vs 1680 m	$-COOC_2H_5$	$-CH_3$
4.	1750 vs 1690 m	10.	1755 vs 1678 m	$-COOCH^{CH_3}_{CH_3}$	$-CH_3$
5.	1710 vs 1692 s		- -	$-COCH_3$	$-CH_3$
6.	1746 vs 1682 vs	11.	1740 vs 1665 vs	$-CH_2COOC_2H_5$	-H

Table 2. The carbonyl bands of hydrochloride salts of compounds I and II in KBr discs

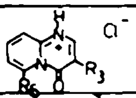
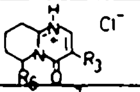
				Substituents	
	νC=O cm^{-1}		νC=O cm^{-1}	R_3	R_6
12.	- 1724 vs	15.	- 1710 vs	-H	-H
13.	1740 vs 1720 vs	16.	1755 vs 1719 s	$-COOC_2H_5$	-H
14.	1752 vs 1705 s	17.	1750 vs 1720 m	$-COOC_2H_5$	$-CH_3$

Table 3. The carbonyl bands of 1-methyl compounds of I and II in KBr discs

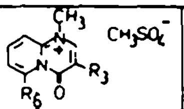
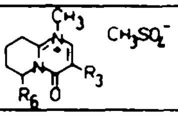
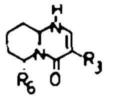
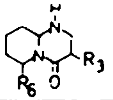
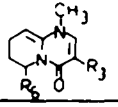
				Substituents	
	νC=O cm^{-1}		νC=O cm^{-1}	R_3	R_6
-	- -	20.	- 1725 vs	-H	$-CH_3$
18.	1780 vs 1710 m	21.	1770 vs 1720 m	$-COOC_2H_5$	-H
19.	1775 vs 1702 w	22.	1770 vs 1715 m	$-COOC_2H_5$	$-CH_3$

Table 4. The carbonyl bands of different saturated compounds in KBr discs

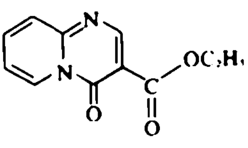
Compound	Substituents				
	R_3	R_6		νC=O /R_3/	νC=O /4/
	$-COOC_2H_5$	-H	23.	1700 vs	1610 vs
	$-COOC_2H_5$	$-CH_3$	24.	1690 vs	1620 vs
	-H	$-CH_3$	25.	-	1640 vs
	$-COOC_2H_5$	-H	26.	1730 vs	1640 s
	$-COOC_2H_5$	$-CH_3$	27.	1745 s	1634 vs
	$-COOC_2H_5$	-H	28.	1698 s	1645 vs
	$-COOC_2H_5$	$-CH_3$	29.	1725 vs	1665 vs 1642 vs

effect, and to higher frequencies by −I effect, the skeletal vibrations, on the other hand, are not much influenced by the substituent effects. This different behaviour can be used to distinguish between skeletal and group vibrations.

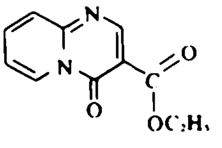
The solid state spectra of molecules of type I and II containing ester or acyl group in position 3 show radical changes in the considered spectral region. The frequency and intensity of the vibration assigned to the 4-CO group considerably decreases, the $\nu_{C=O}$ vibration originating from the ester group appears at higher frequencies with high intensity (Fig. 2). The latter vibration appears in the region 1712–1765 cm^{-1}, the former between 1670 cm^{-1} and 1710 cm^{-1}, the separation of the two bands being 30–80 cm^{-1}. The large intensity difference can be explained by frequency coupling of the two CO stretching vibrations.

Frequency coupling of two identical 1,3-CO groups results in a higher-frequency symmetric and a lower-frequency antisymmetric vibration.[1] This less frequent reversed frequency coupling occurs, e.g. $(CN)_2$, 1,3-butadiene, when the interaction is strong between identical groups. In planar open-chain systems generally the high-frequency symmetric band has larger intensity (e.g. acetic anhydride, diacyl amines),[4] in cyclic anhydrides, (with deformed COOCO group), on the other hand, the low-frequency antisymmetric band has higher intensity.[5] In our 1,3-ketoesters the high-frequency band has larger intensity (Table 1).

The large frequency separation suggests strong interaction between the CO bands. The strongly delocalized π-electron system proved by the UV spectra[6] explains the stability of the planar form and the interaction of the CO groups. Strong interaction of the CO groups is only possible in the O-*cis* form, and frequency coupling is observed only with this conformer, which is supported by the following results.



O-*cis*



O-*trans*

1. X-ray diffraction measurements of compounds **3** and **9** show that the ester C=O group is in O-*cis* position.[7,8]

2. The frequency coupling of the CO groups is stopped by heating, the separation of the band maxima is smaller and their intensities become equal, since the CO group of the ester (or acyl) substituent moves from O-*cis* to O-*trans* position (Fig. 2). This process is reversible.

3. In the IR solution spectra (in chloroform, carbon tetrachloride, dioxan, dimethylformamide) there is no coupling which demonstrates the presence of the O-*trans* form (Fig. 2).

4. DSC measurements show that the O-*cis*-O-*trans* isomerization and the decoupling needs about 5.0 kcal/mole energy.

The salts of type I and II with HCl are similar in behaviour to the corresponding bases; coupling is observed with most salts. The CO frequencies, especially those of the 4-CO band, are larger in the salts than in the bases. This may be explained by the polarization caused by the anions in the crystal lattice. It could be demonstrated that derivatives showing no frequency coupling (compounds **13**, **14** and **16** in Table 2) are in the O-*trans* form. X-ray diffraction measurements show[9] that compound **14** exists in O-*trans* form. In solution there is no coupling either with the salts or with the bases.

With a CH_2–COOEt group in position 3 no coupling occurs because of the larger separation of the CO groups (Table 1). Strong coupling was observed with molecules of type I and II containing a quaternary N atom in position 1. The positive charge produces a high-frequency shift of both CO bands (Table 3). No decoupling occurs either by heating or by solvents. It can be assumed that the −I effect of the delocalized positive charge stabilizes the O-*cis* form.

There is no frequency coupling with molecules of type III (hexahydro derivatives) or with the octahydro compounds (Table 4).

Because of the large frequency difference of the CO vibrations (4-CO band 1610–1640 cm^{-1}, ester band 1690–1740 cm^{-1}) coupling cannot occur with their derivatives.

No coupling can be observed in the spectra of products obtained by neutralization of type II quaternary salts (e.g. **21** and **22**) because the 1:10 double bond migrates to 9:10 position, thus these derivatives are in fact, of type III.

The IR spectra were recorded on a Zeiss UR-20 spectrophotometer between 400 and 4000 cm^{-1} in KBr discs and different solvents.

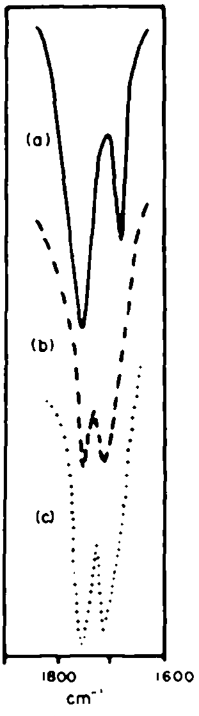


Fig. 2. The $\nu C{=}O$ bands of the compound **9**. (a) In KBr disc at room temperature; (b) in KBr disc at 140°C; (c) in $CHCl_3$ solution at room temperature.

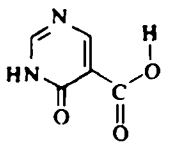
Theoretical calculations

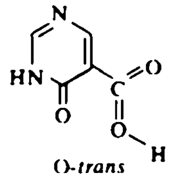
According to the above discussion, the most typical features of the CO vibrations can be summarized as follows: (1) In the solid state, two C=O stretching modes appear with a separation of 30–80 cm^{-1}, the higher frequency band showing higher intensity. By analogy with simpler 1,3-dicarbonyl systems, this was interpreted by the less frequent type of coupling of the two vibrations. (2) When the substances are heated or dissolved, the two C=O bands appear with approximately the same intensity and with smaller frequency separation, indicating that the coupling is suspended if the two CO groups are out-of-plane (free rotation) or even if they are in O-*trans* position.

To obtain a better understanding of the situation, an attempt was made to estimate the separation of the CO frequencies and their relative intensities on the basis of approximate quantum chemical calculations.

It has been shown in recent years that force constants can be obtained to a good approximation from *ab initio* calculations using the force method[10] and the results are acceptable on the semiempirical CNDO/2 level.[11] This CNDO force method was applied to the present problem in a simplified form. Because of the very large computing time needed for a complete calculation, we have only calculated the C=O force constants (diagonal and interaction). These data alone are sufficient for the approximate study of the C=O vibrations with two assumptions. First, we assume that the C=O vibrations can be treated independently of the other vibrations in the molecule. Secondly, we anticipated that the coupling of the C=O vibrations arises from the interaction force constant and we neglected the kinetic coupling. (The latter is certainly allowed as there can be only indirect coupling).

Considering the great dimensions and variety of the molecules under investigation, only one model was used in the theoretical calculations, but for this both conformers were considered:


O-*cis*


O-*trans*

We think that this is a good model for the molecules of type I and II, even if the pyridine ring is neglected and the ester alkyl group is substituted by hydrogen for simplicity. The effect of protonation on the N_1 atom was not investigated.

In the force method, beyond the usual quantities (energy, dipole moment etc.) the forces acting on the nuclei in a given nuclear configuration are also calculated analytically from the wavefunction and then transformed into internal coordinates. The force constants are obtained numerically as the difference of forces when the molecule is distorted according to the internal coordinates. In the present case, this distortion meant making the C=O bonds longer and shorter by 0.02 Å. The relative intensities are also calculated numerically from the squares of the dipole moment changes during the distortion. The equilibrium geometry used in the calculations was estimated from an X-ray study.[7] We quote here only the most important parameters: the C=O bond length is 1.225 and 1.199 Å for the ring CO and for the ester (actually in the calculations carboxyl) C=O bond, respectively. The results of the calculations are summarized in Table 5. Because the force constants are very strongly, but systematically overestimated in the CNDO approximation, they were scaled by a factor of 0.381. This was obtained as an average value on several molecules[12] and is also supported by some recent results. (This scaling is not crucial in the present case as we used only relative values.)

For the treatment of the C=O vibrations there are two extreme models. First, let us assume that there are two individual vibrations of different frequency. According to the calculations the ester force constant f_{r2} is significantly higher than f_{r1} (ring CO). From elementary calculations, if we take an experimental average C=O frequency of $\nu_0 = 1650\,cm^{-1}$ and use only the relative values of the calculated force constants for the estimation of the separation, the frequency difference is about $\Delta\nu = 120\,cm^{-1}$. As to the relative intensities, the calculated ratio of the absorption coefficients ϵ_1/ϵ_2 shows (Table 5) that in this model the higher frequency band should be of lower intensity. Between the O-*cis*

Table 5. Results of the quantumchemical calculations*

	O-cis	O-trans
f_{r1}(mdyn/Å) (ring carbonyl)	14.3	14.3
f_{r2}(mdyn/Å) (ester carbonyl)	16.4	16.4
f_{rr}(mdyn/Å) (interaction)	0.07	0.02
$\partial\|\mu\|/\partial$ r1 (D/Å)	8.20	8.55
$\partial\|\mu\|/\partial$ r2 (D/Å)	6.33	6.82
$\nu_1 - \nu_2$ (cm^{-1})	-120	-120
$\varepsilon_1 / \varepsilon_2$	1.67	1.57
$\nu_{sym} - \nu_{as}$ (cm^{-1})	8	2
$\varepsilon_{sym} / \varepsilon_{as}$	53.8	0.32

* Force constants are scaled, see text.

and O-*trans* conformers, there is no marked difference in either the frequency separation or the intensity relations. Thus, this model would result in just the opposite of the experimental findings. Some care should be taken. (Regarding the difference in the calculated force constants. Actually, this was experimentally introduced into the calculations because, on the basis of the X-ray study on *one* molecule, we took different C=O bond lengths; the force constants are, of course, very sensitive to this difference.)

As the other extreme model, let us take two equivalent C=O groups. In this case the separation arises from the splitting of the symmetric and antisymmetric vibrations. Taking now the theoretical average value of 15 mdyn/Å for the f_r force constant and again a value of 1650 cm^{-1} for ν_0, the splitting arising from the coupling through f_{rr} is 8 cm^{-1} for the O-*cis* form, and much less, about 2 cm^{-1} for the *trans* conformer. As to the intensities, the calculations show that the dipole moment changes are directed almost precisely along the C=O bonds. In this case, the intensity ratio (assuming equivalent C=O groups) can be simply calculated from the relative orientation of the C=O bonds. (In the geometry we used the angle between the C-O vectors was 13.0° for the *cis*-form and 121.0° for the *trans* form.) The result is that the symmetric mode is very much stronger than the antisymmetric one in the O-*cis* conformer, while in the O-*trans* form the intensity ratio is reversed, the difference being, however, much less (Table 5)

Qualitatively, this model is in agreement with the experiment: the symmetric vibration is of higher frequency and the corresponding band is more intense if, as it was assumed earlier, the substances exist in the O-*cis* form. It is also proved theoretically that the coupling is much smaller for the O-*trans* conformer. However, if we consider the results more quantitatively, it is clear that the splittings are very small as compared with the experimental values of 30–80 cm^{-1} and the experimental intensity relations are far less extreme than calculated. This indicates that the real situation is between the two extreme models: the individual C=O frequencies are obviously different but their coupling through a positive f_{rr} is also significant.

In order to estimate the combined effect, we assumed that the individual frequencies are separated by 50 cm^{-1}, e.g. 1650 and 1700 cm^{-1}, respectively. Assigning the calculated average force constant of 15 mdyn/Å to the first one, the corresponding force constant for the ester CO group is 15.92 mdyn/Å. The coupling of these two vibrations through the coupling force constant f_{rr} = 0.07 mdyn/Å can be calculated by solving a simple second order eigenvalue problem. The resulting normal vibrations are of the form:

$$Q_1(\nu_1 = 1700.3\ \mathrm{cm}^{-1}) = 0.07544\, r_1 + 0.99715\, r_2$$
$$Q_2(\nu_2 = 1649.7\ \mathrm{cm}^{-1}) = -0.99715\, r_1 + 0.07544\, r_2.$$

As anticipated, the coupling is now so small that the additional frequency separation is negligible. However, the intensity ratio is influenced significantly even by this small coupling. Starting with two uncoupled vibrations of the same intensity, the new intensity ratio, as a consequence of this coupling, is:

$$\epsilon(Q_1)/\epsilon(Q_2) = 1.34.$$

In accordance with the experiment, the higher frequency band is the more intense one.

In conclusion, we think that the frequency separation in the spectra arises mainly from the individual difference of the two C=O vibrations but the intensity relations can only be understood if the coupling is also taken into consideration.

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