BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 1437—1441 (1973)

A Study on Restricted Rotation in 1-Acylpyrroles[1]

Taku MATSUO, Hideto SHOSENJI,* and Reiji MIYAMOTO**
Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Hakozaki, Fukuoka 812

(Received July 4, 1972)

Restricted rotation of the *N*-acyl group in 1-acylpyrroles was studied by means of NMR spectroscopy. The free energy of activation ($\Delta F_c^{\ddagger}$) for 1-formylpyrrole is 14.1 kcal/mol, which is less than that for DMF by 6.8 kcal/mol. The value of $\Delta F_c^{\ddagger}$ decreases in the order 1-formyl-, 1-acetyl-, and 1-benzoyl-pyrrole in exactly the same manner as is found in the series of *N,N*-dimethylamides with the corresponding acyl group: the difference in $\Delta F_c^{\ddagger}$ between a pair of compounds with the same acyl group in the two series remains constant (*ca.* 6 kcal/mol). The $\Delta F_c^{\ddagger}$-value for 3,4-dimethyl-1-acetylpyrrole is larger than that for 1-acetylpyrrole by 1 kcal/mol. In this particular case, the entropy of activation was found to be responsible for the difference in barrier height.

Restricted rotation about the C–N bond in 1-acylpyrroles was studied by two groups.[2] The origin of restricted rotation has been suggested to be the partial double bond character of the C–N bond between the pyrryl and carbonyl groups as in the case of dimethylformamide and its analogues. Since the ionization potential of pyrrole (8.97 eV) is close to that of dimethylamine (8.93 eV),[3] the significance of the ionic structure (I) may be as great as that in the case of dimethylformamide.

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* Present address: Department of Synthetic Chemistry, Faculty of Engineering, Kumamoto University, Kurokami-cho, Kumamoto.

** Present address: Institute of Service Engineering, Mitsui Polychemicals Co. Ltd., Ichihara-shi, Chiba.

[1] Contribution No. 258 from the Department of Organic Synthesis, Faculty of Engineering, Kyushu University.

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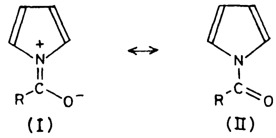

(I) (II)

A study of the electronic spectra of 1-acylpyrroles has also revealed that the π electron system of the carbonyl group strongly interacts with that of the pyrryl group.[4] Hence, the suggested origin of the barrier to the internal rotation is a very reasonable explanation. In order to study the nature of the barrier further in detail, the temperature dependence of the NMR spectra of a series of 1-acylpyrroles was investigated.

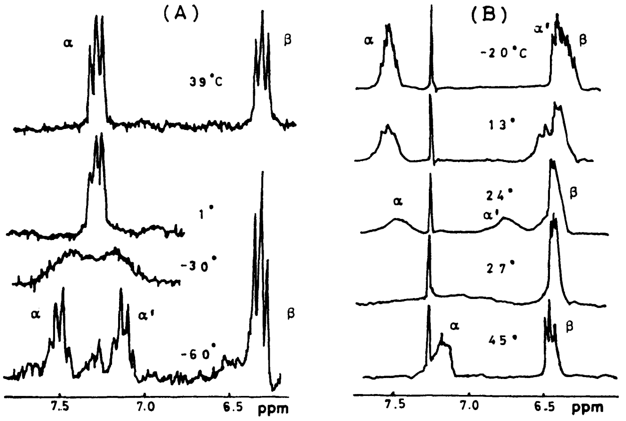

Fig. 1. The temperature dependence of the ring proton signals of 1-acetylpyrrole (A) and 1-pentachlorobenzoylpyrrole (B).

Results and Discussion

NMR spectra of most 1-acylpyrroles are temperature dependent. Two examples are shown in Fig. 1. At low temperature, the signals due to the protons at the 2- and 5-positions split into two peaks which indicate that the two methine protons are under nonequivalent electromagnetic environments. The nonequivalence is ascribed to the fact that the rotation of the carbonyl group about the C–N bond is restricted. Since the spin systems of most of the 1-acylpyrroles under investigation are rather complex, an accurate value for the rate of rotation at various temperatures can be obtained only through a complete line-shape analysis including the effects of spin-spin couplings. It is known, however, that the free energy of activation ($\Delta F_C^{\ddagger}$) at the coalescence temperature (T_C) can be obtained with reasonable accuracy by the use of an approximate method based on Gutowsky and Holm's equation and absolute rate theory:

$$\Delta F_C^{\ddagger} = R\cdot T_C \ln (k\cdot T_C\cdot \tau_C/h) \tag{1}$$

where

$$\tau_C = \sqrt{2}/(\pi\delta\nu_0) \tag{2}$$

The values of $\Delta F_C^{\ddagger}$ thus obtained are practically good enough to be used for comparing the barrier heights between various amides.[5] The results are summarized in Table 1. The barrier to the internal rotation decreases in the order 1-formyl-, 1-acetyl-, and 1-benzoylpyrrole. The same trend is also observed with *N,N*-dimethylamides, when the acyl group is changed in the order formyl, acetyl, and benzoyl group.[5] In order to examine the relationship between these two series of compounds, the barriers to the restricted rotation in *N,N*-dimethylamides are compared with those for 1-acylpyrroles with the corresponding acyl group (Table 2).[6] The difference in $\Delta F_C^{\ddagger}$ between a pair of compounds with the same acyl group in the two series is defined as $\delta\Delta$. We should notice that the $\delta\Delta$-values are nearly the same among the investigated three acyl groups.

Table 1. Spectral data for the restricted rotations of 1-acylpyrroles

Compound	$\delta\nu_0$a)	T_c b)	$\Delta F_C^{\ddagger}$ c)
1-Formylpyrrole	21.0	5	14.1
1-Acetylpyrrole	22.9	−28	12.5
3,4-Dimethyl-1-acetylpyrrole	24.7	−5	13.5
1-Benzoylpyrrole		<−70	
3,4-Dimethyl-1-benzoylpyrrole	38$^{d)}$	−56	11$^{e)}$
1-(2′,4′,6′-trimethylbenzoyl)pyrrole	73	65	16.5
1-Pentachlorobenzoylpyrrole	67	27	14.6

a) Peak separation (Hz) at the temperature where the rate of rotation is slow enough in NMR time scale. The errors are within 0.5 Hz unless specified.
b) Coalescence temperature in °C.
c) Free energy of activation in kcal/mol for the restricted rotation. Accuracies are estimated to be 0.1 kcal/mol.
d) The error is less than 2 Hz.
e) The error is less than 0.2 kcal/mol.

Table 2. Difference in barrier heights between *N,N*-dimethylamides and 1-acylpyrroles

Barrier	*N,N*-Dimethylformamide	*N,N*-Dimethylacetamide	*N,N*-Dimethylbenzamide
$\Delta F_C^{\ddagger\,a)}$	20.9	18.1	16.0
$\delta\Delta^{b)}$	6.8	5.6	6$^{c)}$

a) The free energy of activation (kcal/mol) for *N,N*-dimethylamides as summarized by Stewart and Siddall[5].
b) The difference in $\Delta F_C^{\ddagger}$ between *N,N*-dimethylamides and 1-acylpyrroles with the corresponding acyl group.
c) The barrier in 1-benzoylpyrrole is estimated to be 10 kcal/mol as described in Footnote 6.

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4) T. Matsuo and H. Shosenji, This Bulletin, **45**, 1349 (1972).

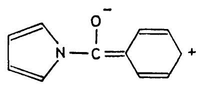
5) W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, **70**, 517 (1970).

6) The barrier for 1-benzoylpyrrole itself could not be obtained, since the coalescence temperature was below −70°C which was the lowest limit accessible in the present experiment. The approximate barrier height, however, may be estimated as follows. Assuming that the $\delta\nu_0$ value for 1-benzoylpyrrole is equal to that for 3,4-dimethyl-1-benzoylpyrrole, and that Tc is −75 °C, the barrier height is calculated to be 10 kcal/mol, which may be taken to be an approximate value for the upper limit of $\Delta F_C^{\ddagger}$ for 1-benzoylpyrrole. On the basis of the $\Delta F_C^{\ddagger}$ value for 3,4-dimethyl-1-benzoylpyrrole (11 kcal/mol), we can also estimate $\Delta F_C^{\ddagger}$ for 1-benzoylpyrrole to be approximately 10 kcal/mol, provided that the effect of the methyl groups on the 3- and 4-positions is assumed to lower the barrier by 1 kcal/mol as in the case of 1-acetylpyrrole and 3,4-dimethyl-1-acetylpyrrole.

The barrier to the internal rotation is mainly determined by two factors: the electronic state of the molecule as represented by its double bond character, and the steric hindrance during the rotation. The relative importance of these two factors is expected to vary considerably depending on the nature of the substituent on the amide group. Let us first consider the case of 1-formylpyrrole and *N*,*N*-dimethylformamide. By the use of molecular models, it is easily understood that no steric strain is expected during the internal rotation around the C–N bond. The barrier height in this case should therefore be determined by purely electronic factors alone. The difference in $\Delta F^{\ddagger}_{\mathrm{C}}$, 6.8 kcal/mol, is thus taken to represent the fact that the double bond character of the C–N bond in 1-formylpyrrole is less than that in *N*,*N*-dimethylformamide.

In the case of 1-acetylpyrrole, a completely planar configuration can not be assumed because the presence of steric strain is indicated by the molecular model. The plane of the acetyl group should be twisted with respect to that of the pyrryl group in the ground state. In other words, the valley of the potential energy curve for 1-acetylpyrrole should be shallower than that for 1-formylpyrrole. Thus, the decrease in the rotational barrier in 1-acetylpyrrole is ascribed to the decrease in the double bond character due to the presence of steric strain in the ground state as in the case of *N*,*N*-dimethylacetamide.⁵⁾ In addition, it is also understood that the effect of the pyrryl group is very close to that of the *N*,*N*-dimethylamino group, since the decrease in $\Delta F^{\ddagger}_{\mathrm{C}}$ on going from 1-formylpyrrole to 1-acetylpyrrole is almost the same as the difference in the rotational barrier between *N*,*N*-dimethylformamide and *N*,*N*-dimethylacetamide.

The case of 1-benzoylpyrrole is an example where both electronic and steric factors are equally important. In analogy to the case of *N*,*N*-dimethylbenzamide,[5)] the contribution of cross conjugation between the phenyl and carbonyl groups as represented by III is expected to be effective in reducing the barrier height in 1-benzoylpyrrole. In addition, we can not disregard the fact that 1-benzoylpyrrole is not expected to take a completely planar configuration because of the large steric hindrance between the phenyl and the pyrryl groups. As a consequence, the C–N bond is expected to be slightly twisted already in the ground state so that its double bond character is reduced. This might be another reason for the barrier height in 1-benzoylpyrrole being so much lower than that in 1-formylpyrrole.



(III)

The steric factors become extremely important in the case of 1-(2′,4′,6′-trimethylbenzoyl)pyrrole and 1-pentachlorobenzoylpyrrole. The steric hindrance due to the substituents at the *ortho* positions forces the carbonyl group to take an almost perpendicular position with respect to the plane of the phenyl group. The pyrryl group, on the other hand, seems to remain coplanar with the carbonyl group. This is strongly supported by the fact that the electronic spectra of 1-(2′,4′,6′-trimethylbenzoyl)pyrrole is found to be close to that of 1-acetylpyrrole than that of 1-benzoylpyrrole (Fig. 2). In correspondence with this, the barrier heights in 1-(2′,4′,6′-trimethylbenzoyl)pyrrole and 1-pentachlorobenzoylpyrrole are surprisingly large as compared with that in 1-benzoylpyrrole (Table 1). Due to the above steric factors, the contribution of cross conjugation as represented by III is considered to be negligible in the electronic structures of 1-(2′,4′,6′-trimethylbenzoyl)pyrrole and 1-pentachlorobenzoylpyrrole. As a consequence, the double bond character of the C–N bond in 1-benzoylpyrrole is expected to increase on the introduction of substituents at both *ortho* positions. In other words, the valley of the potential energy curve for the restricted rotation becomes deeper than in the case without substituents. The present results are in agreement with this expectation. However, we should further notice that the barrier in 1-(2′,4′,6′-trimethylbenzoyl)pyrrole exceeds that in 1-formylpyrrole by more than 2 kcal/mol. This is unlikely to be explained by the change in the electronic factor alone. On the other hand, it is easily understood from the molecular model that the internal rotation of the pyrryl group with respect to the carbonyl group is strongly hindered in the transition state by the presence of substituents at the *ortho* positions. In other words, the top of the potential energy curve for the restricted rotation of the C–N bond in 1-(2′,4′,6′-trimethylbenzoyl)pyrrole is considered to be appreciably raised by the steric hindrance due to the two methyl groups. This steric hindrance may be mainly responsible for the extraordinary large $\Delta F^{\ddagger}_{\mathrm{C}}$-value for 1-(2′,4′,6′-trimethylbenzoyl)pyrrole. The data for 1-pentachlorobenzoylpyrrole may be analogously explained as due to the combined influence of the two different effects of the substituents at the *ortho* position: the increase in the double bond character of the C–N bond in its

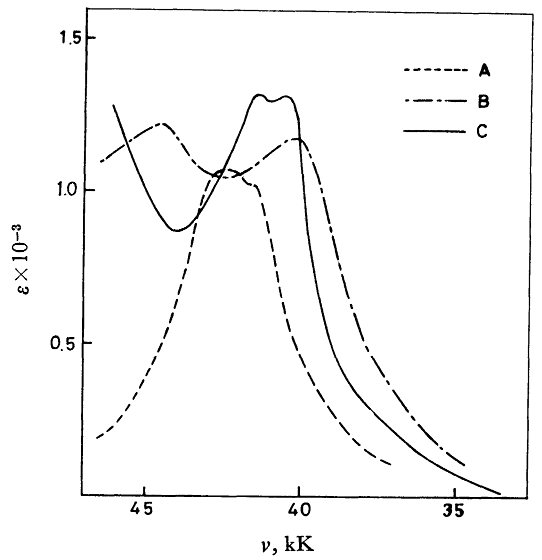


Fig. 2. Electronic absorption spectra of 1-acetylpyrrole (A), 1-benzoylpyrrole (B), and 1-(2′,4′,6′-trimethylbenzoyl)-pyrrole (C) in *n*-hexane.

ground state and the presence of large steric hindrance to the internal rotation in the transition state. The slightly lower barrier height in 1-pentachlorobenzoylpyrrole, in comparison with that in 1-(2′,4′,6′-trimethylbenzoyl)pyrrole, can be correlated with the fact that the van der Waals radius of chlorine atom (1.8 Å) is less than that for the methyl group (2.0 Å). Exactly the same type of *ortho*-substituent effects as described above have also been known in the study of internal rotation of *N,N*-dimethylbenzamide.[7] The difference in $\Delta F_{\mathrm{c}}^{\ddagger}$ between 1-(2′,4′,6′-trimethylbenzoyl)pyrrole and *N,N*-dimethyl-2,4,6-trimethylbenzamide (6.0 kcal/mol) is not far from the corresponding difference between 1-formylpyrrole and *N,N*-dimethylformamide (6.8 kcal/mol). On the basis of this result together with the data in Table 2, it is concluded that the double bond character of the C–N bond in 1-acylpyrrole is invariably less than that in the corresponding *N,N*-dimethylamide by an almost constant amount irrespective of the nature of the acyl group.

If an electron-donating group is substituted on the pyrryl group, the significance of the ionic structure (I) increases and the barrier height will be raised as long as the steric factors are not affected by the substitution. In expectation of these effects, the restricted rotation of 3,4-dimethyl-1-acylpyrroles was further investigated in detail. On the introduction of methyl groups at the 3- and 4-positions of 1-acylpyrrole, $\Delta F_{\mathrm{c}}^{\ddagger}$ is found to increase by 1 kcal/mol in comparison with the case without the methyl groups (Table 1). Analogously, the barrier to the internal rotation in 1-benzoylpyrrole is clearly raised by the introduction of methyl groups at the 3- and 4-positions of the pyrryl group.[6] These effects of the methyl groups on the 3- and 4-positions of the pyrryl group are surprisingly large, if we recall the fact that the difference in $\Delta F_{\mathrm{c}}^{\ddagger}$ between 1-acylpyrroles and *N,N*-dimethylamide is no more than 6 kcal/mol. In order to clarify the methyl substitution effect on the barrier height in detail, the temperature dependence of the proton signals of 3,4-dimethyl-1-acetylpyrrole was studied by the use of total line-shape analysis. The ring proton signals of this compound should be analyzed as a part of a ABX_3Y_3 system in principle. No one has analyzed the NMR spectra of such a complex system under chemical exchange. On the other hand, the method of analysis for AB spin system with chemical exchange between A and B has been well established.[8] Thus the present data were analyzed by the use of the line shape comparison method for the AB spin system with a slight modification. The signals for the ring protons at the 2- and 5-positions were calculated at first by the use of Heidbergs' line shape equation for the AB spin system.[8] The contribution of the methyl protons at the 3- and 4-positions was then taken into consideration by assuming that each ring proton signal was split into a quartet

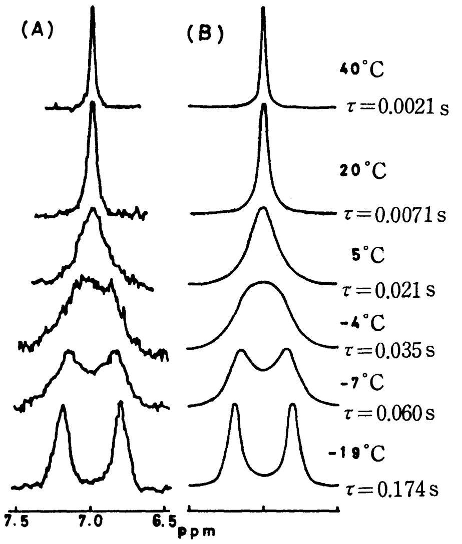


Fig. 3. The temperature dependence of the ring proton signals of 3,4-dimethyl-1-acetylpyrrole.
(A), The observed spectra; (B), The theoretical spectra.

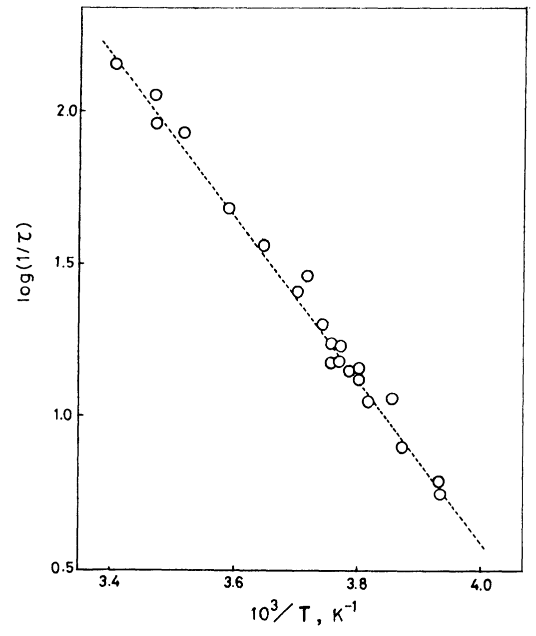


Fig. 4. An Arrhenius plot of the rate of the restricted rotation in 3,4-dimethyl-1-acetylpyrrole.

Table 3. Activation parameters for the restricted rotation of 3,4-dimethyl-1-acetylpyrrole and 1-acetylpyrrole[a]

Compound	E_a	$\Delta F^{\ddagger}_{298\mathrm{K}}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$
3,4-Dimethyl-1-acetylpyrrole	12.2±0.9	14.3±0.9	11.7±0.9	−8.7±3.7
1-Acetylpyrrole	12.6±0.1	12.1±0.1	12.0±0.1	−0.6±0.6

a) The values for 1-acetylpyrroles are those given by Dahlqvist and Forsén[2b]. They are given in kcal/mol except for the case of $\Delta S^{\ddagger}$ which is expressed in e.u.

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[8] J. Heidberg, J. A. Weil, G. A. Janusonis, and J. K. Andersen, *J. Amer. Chem. Soc.*, **41**, 1033 (1964).

due to the spin-spin interactions with the methyl protons. The longitudinal relaxation time was taken to be 0.53 sec as estimated from the line width of the internal TMS standard. The coupling constant (J_{AB}) between the ring protons was taken to be 2.2 Hz. The calculated spectra reproduced the observed spectra very well as shown in Fig. 3. An Arrhenius plot of the rate constants for the restricted rotation afforded a very good linear relationship as shown in Fig. 4. The activation parameters were then evaluated from the linear relationship. They are given in Table 3, together with the parameters for 1-acetylpyrrole studied by Dahlqvist and Forsén by use of the density matrix method.[2b] It is interesting that the difference in ΔS^{*} between 1-acetylpyrrole and 3,4-dimethyl-1-acetylpyrrole exceeds experimental errors although ΔH^{*}-values do not differ appreciably. The origin of the difference in ΔS^{*} is not known at present. It should be emphasized, however, that the increase of barrier height in 3,4-dimethyl-1-acetylpyrrole can not be simply explained as due to the increase of the double bond character in the C–N bond.

Experimental

Materials. The syntheses of 1-formyl- and 1-acetylpyrroles were described previously.[4] Jones and Laslett's procedure was applied to obtain 1-benzoylpyrrole (bp 122—125 °C/6.5 mmHg) and 3,4-dimethyl-1-benzoylpyrrole (bp 135—139 °C/3 mmHg).[9] 1-(2′,4′,6′-trimethylbenzoyl)pyrrole (bp 126—129 °C/7 mmHg) and 1-pentachlorobenzoylpyrrole (mp 172—174 °C) were prepared either by the method of Rainey and Adkins[10] or by that of Jones and Laslett.[9] Found: C, 78.41; H, 6.49; N, 6.73%. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.57; N, 7.02%. Found: C, 78.69; H, 6.99; N, 6.41%. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57%. Found: C, 38.16; H, 0.92; N, 4.06%. Calcd for $C_{11}H_4Cl_5NO$: C, 38.47; H, 1.17; N, 4.08%.

Measurement of NMR Spectra. The NMR spectra were measured with 4 mol% $CDCl_3$ solution of each compound, containing a small amount of TMS as an internal standard. Oxygen was removed from the solution by bubbling purified nitrogen. The NMR signals obtained by four, repeated scans of a Varian A-60 NMR spectrometer were accumulated on a time averaging computor (JRA-1). The temperature was regulated with a variable temperature attachment V-6057, calibrated by the use of copper-constantan thermocouples in advance. The resolution was checked by the use of the half-height width of the internal TMS signal, no significant change being noticed during the measurement in the temperature region.

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