Restricted Rotation in the *NN*-Dimethylamides of the Pyridinecarboxylic Acids

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The free energies of activation at 25 °C for rotation about the amide bond in *NN*-dimethylbenzamide, and *NN*-dimethylpyridine-2-, -3-, and -4-carboxamides, have been found to be 61·5, 74·9, 66·6, and 69·5 kJ mol^{-1} respectively. These values are interpreted in terms of (Jaffé) substituent constants.

THERE has been a continuing interest in the barrier to rotation about the amide bond.[1,2] Since such barriers are usually in the 60—100 kJ mol^{-1} range, lineshape analysis of n.m.r. spectra is a convenient way of studying this phenomenon. Recently we have reported[3] a computational method of lineshape analysis, incorporating a least-squares approach to curve fitting, designed to reduce the errors involved in a visual matching of calculated and experimental spectra. We now report the use of this method in the study of the rotational barriers of the *NN*-dimethylamides of pyridine-2-, -3-, and -4-carboxylic acids and benzoic acid.

EXPERIMENTAL

All the amides were prepared by treatment of the corresponding pyridinecarboxylates with aqueous dimethylamine solution. Their properties corresponded with those reported in the literature.

N.m.r. spectra of 15% w/v solutions of the amides in deuteriochloroform were run on a Perkin-Elmer R.10 instrument fitted with the standard variable temperature probe. Paper tape output of spectra from a Digiac computer on line to the spectrometer were processed on an Elliott 4100 computer.

The temperatures of the sample were measured by a copper–constantan thermocouple fitted close to the spinning sample, and were considered to be internally consistent to ±1 °C.

The chemical shift difference (C.S.D.) between exchanging peaks around the coalescence temperature (T_c) was obtained by extrapolation from a linear plot of C.S.D. against temperature well below the coalescence temperature. The extrapolated values are indicated in Table 1.

Six or seven spectra, ranging around the coalescence temperature, were recorded for each amide. The best-fit curve, and consequently the rate of exchange was obtained as previously described.[3]

RESULTS AND DISCUSSION

The experimental rates of exchange for the amides are given in Table 1, and the calculated rates are those obtained from the best-fit Arrhenius plots. Table 2 gives the activation parameters associated with the rotational barrier. Since the principal source of error is probably temperature measurement, and since these

TABLE 1

Rates of rotation of amide groups

T/K	$k_{exp.}$/s^{-1}	$k_{calc.}$ */s^{-1}	C.S.D./Hz
NN-Dimethylbenzamide			
274·0	10	9·14	8·50
278·9	13·9	14·1	8·59
281·7	16·3	18·8	8·65
290·1	39·5	38·8	8·85
294·2	58·1	55·7	8·93
299·4	89·3	86·0	9·05
NN-Dimethylpyridine-2-carboxamide			
308·7	1·53	1·49	3·40
313·7	2·75	2·67	3·28
316·7	3·56	3·77	3·17
319·6	4·98	5·27	3·10
323·7	8·93	8·34	2·99
330·7	16·4	17·6	2·80
NN-Dimethylpyridine-3-carboxamide [3]			
283·2	2·08	2·22	6·60
288·9	4·57	4·30	6·87
294·7	8·24	8·20	6·96
300·7	15·9	15·6	7·05
306·4	28·4	28·1	7·14
311·7	46·1	47·6	7·23
318·9	93·5	94·6	7·34
NN-Dimethylpyridine-4-carboxamide			
306·7	8·80	8·69	10·85
311·4	13·95	13·98	10·95
314·9	19·4	19·5	11·00
318·2	26·4	26·7	11·07
321·9	37·2	37·7	11·15
329·2	73·8	72·6	11·30

* From best-fit Arrhenius plot.

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parameters are determined over a fairly small range of temperature, there are significant errors associated with enthalpies and entropies. Thus, discussion is in terms

TABLE 2

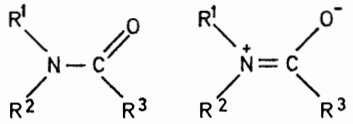
Thermodynamic data for the *NN*-dimethylpyridine-carboxamides and *NN*-dimethylbenzamide

Amide	E_A/kJ mol^{-1} [a,b]	log A [a]	$\Delta G^{\ddagger}_{298}$/ kJ mol^{-1} [b]	T_c/K [c]
Benzamide	64·0	13·2	61·5	283
2-Amide	92·9	15·9	74·9	319
3-Amide	79·1	14·9	66·6	298
4-Amide	78·7	14·4	69·5	318

[a] Energy of activation and frequency factor from Arrhenius plots. [b] $\pm$0·5 kJ mol^{-1}. [c] Coalescence temperature.

of the free energy parameter, $\Delta G^{\ddagger}$, at 298 K. Standard statistical methods suggest the error on $\Delta G^{\ddagger}_{298}$ values to be of the order of 0·5 kJ mol^{-1}.

The barrier to rotation in amides is considered to arise from the partial double bond character of the carbon–nitrogen bond. Pauling [4] suggested the dipolar form contributes about 40% to the overall structure, or in



energy terms there should be a barrier of *ca.* 80 kJ mol^{-1}. The exact value, however, will depend on the various steric and electronic effects of the substituent groups. Thus, *NN*-dimethylbenzamide has a lower rotational barrier (64·1 kJ mol^{-1}, *cf.* 61·5 in this work) [5] than *NN*-dimethylacetamide [6] (92·1 kJ mol^{-1}), since the aromatic π electrons compete with the nitrogen p electrons for conjugation with the carbonyl group. Considering the nitrogen atom of pyridine as a group with a positive inductive effect, the presence of the nitrogen in the *ortho*- or *para*-position with respect to the amide group should decrease the ability of aromatic ring to conjugate with the carbonyl group. Thus, a barrier increase over that of benzamide is expected, and found (pyridine-2- and -4-carboxamide values). With nitrogen in the *meta*-position there is less effect, and the barrier increases to a lesser extent (the pyridine-3-carboxamide value).

Jackman *et al.*[2] have found a linear relationship between the free energies of activation for rotation about the amide bond in a series of *meta*- and *para*-substituted benzamides and the corresponding σ^+ substituent constants. Considering the nitrogen in pyridine as a substituent, Jaffé found the values for aza-substitution being *ortho*, *meta*, and *para* to a substituent group to be 0·81, 0·62, and 0·93 respectively.[6] Favini and Simonetta [7] did not find good agreement either theoretically or empirically with these values when they studied the alkaline hydrolysis of the pyridinecarboxylates, but they did find reasonable agreement when studying the hydrolysis of the corresponding amides. In this case, using these parameters, the observed barriers for *NN*-dimethylpyridine-4- and -3-carboxamide agree well with Jackman's correlation. A position ρ^+ value (1·13) was found and confirms the idea of a barrier increase with increasing electron withdrawal, and shows the barrier to be dependent on conjugation between the carbonyl and aromatic functions.

Using Jaffé's value for nitrogen in the *ortho*-position for *NN*-dimethylpyridine-2-carboxamide a large deviation from the line is observed suggesting the presence of an *ortho* 'proximity' effect. Assuming Jaffé's value of σ to be reasonable a direct steric origin to this effect seems unlikely, as does a specific electronic interaction between the nitrogen lone pair and the amide function. A possible explanation may lie with a solvation effect; the lone pair may associate with a solvent molecule and thereby increase its spatial requirement.

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