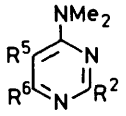
Proton and Carbon-13 Nuclear Magnetic Resonance Studies of Substituted Pyrimidines. Part 3.[1] Hindered Internal Rotation in Some 4-(*NN*-Dimethylamino)pyrimidines

By **Jacques Riand,* Marie-Thérèse Chenon,** and **Nicole Lumbroso-Bader,** Université Paris VI, Laboratoire de Spectrochimie, CNRS, 2 rue Henri Dunant, 94320 Thiais, France

The free energy of activation for internal rotation about the C–N exocyclic bond of some substituted 4-(*NN*-dimethylamino)pyrimidines has been determined using ^1H and ^{13}C n.m.r. line-shape analysis. Substituent effects on the rotational barrier of the dimethylamino group are evaluated. The influence of the position of the dimethylamino group with respect to the nitrogen atoms is discussed, the rotational barrier being higher in the 4- than in the 2-position. An interesting linear correlation between free energies of activation and ^1J(C,H) coupling constants for the 4-dimethylamino group has been found.

THE hindered internal rotation of the dimethylamino group in a series of 4-(*NN*-dimethylamino)pyrimidines has been investigated in order to study amino group conjugation with the ring quantitatively. Only few data [2-5] concerning restricted rotation in these compounds are known and a systematic study of these barriers, under the same conditions of concentration and solvent, appeared necessary. The thermodynamic parameters $\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ were determined by ^1H and ^{13}C n.m.r. line-shape analysis. For some compounds the free energy of activation $\Delta G^{\ddagger}$ could be obtained only at the coalescence temperature.

The influence of the substituent on the restricted rotation of the dimethylamino group has been studied for 4-(*NN*-dimethylamino)pyrimidine (I) and some methyl (III), chloro (II), (IV), nitro (V), and amino (VI)—(VIII) derivatives. Compounds (VI) and (VII), in



(I) $R^2 = R^5 = R^6 = H$
(II) $R^2 = Cl, R^5 = R^6 = H$
(III) $R^2 = R^6 = Me, R^5 = H$
(IV) $R^2 = Cl, R^5 = Me, R^6 = H$
(V) $R^2 = Cl, R^5 = NO_2, R^6 = H$
(VI) $R^2 = NMe_2, R^5 = R^6 = H$
(VII) $R^2 = NMe_2, R^5 = H, R^6 = Me$
(VIII) $R^2 = R^6 = NMe_2, R^5 = H$

particular, gave some information about the influence of the position of the dimethylamino group on its conjugation with the ring. Methanol was chosen as solvent because of the large temperature range (−90 to 65°) and the solubility of the pyrimidines. Moreover, total line-shape analysis was performed for 2-chloro-4-(*NN*-dimethylamino)pyrimidine (II) in $CDCl_3$–CH_2Cl_2 (2 : 1 v/v) to compare our results with previous data from Almog *et al.*[5] obtained at the coalescence temperature only.

The carbon-13 n.m.r. spectra of some compounds were recorded in order to look for a possible correlation between the free energies of activation and (i) substituent chemical shift parameters and (ii) ^1J(C,H) coupling constants of the 4-dimethylamino group.

RESULTS

The Eyring equation [6] allows the activation parameters $\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ to be obtained from the dependence of the rate constant k on temperature. At each temperature, the only parameters necessary for the total line-shape analysis are (i) the rate constant k, (ii) the effective transverse relaxation time T_2^* in the absence of exchange, and (iii) the difference $\Delta\nu_\infty$ between the chemical shifts of the two exchanging sites in the absence of exchange. The rotation of the dimethylamino group about the exocyclic C–N bond was assumed to be an exchanging, equally populated, and uncoupled two-site system. Moreover, we have considered the relaxation time T_2^* of the methyl group in the two sites to be identical. Line-shapes are particularly sensitive to the values [4,7-10] of T_2^* and $\Delta\nu_\infty$ and details of these measurements are given in the Experimental section.

Only compounds (I)—(III) were studied by total line-shape analysis. Such a study was not possible for compounds (IV) and (VIII) because their coalescence temperature was too low ($T_c < 173$ and 195 K, respectively). For compounds (VI) and (VII), substituted by dimethylamino groups at the 2- and 4-positions, the proximity or overlap of signals for these groups did not allow total line-shape analysis at present.† For pyrimidine (V) the free energy of activation was determined only at the coalescence temperature, the line-shape being less sensitive to errors on $\Delta\nu_\infty$ and W (linewidth) when $\Delta\nu_\infty/W$ is large.[11] This occurred for compound (V) ($\Delta\nu_\infty$ 42.6 Hz, W 0.85 Hz) and $\Delta G^{\ddagger}_{T_c}$ was obtained with good accuracy. For compounds (IV)—(VIII) the rate constant at coalescence temperature k_{T_c} was determined by the relationship given by Schmid *et al.*[12] and the corresponding free energy of activation $\Delta G^{\ddagger}_{T_c}$ was calculated by the Eyring equation.

The thermodynamic activation parameters and the different parameters relevant to hindered internal rotation of the exocyclic bond C–N in the pyrimidines are summarized in Table 1. Data previously reported for pyrimidines (I) and (II) are also given for the sake of comparison.

DISCUSSION

It is well known that the free energies of activation in substituted compounds depend upon the electronic and

† A computation program in preparation should improve the data for these compounds.

TABLE 1

Thermodynamic parameters [a] for hindered internal rotation of the dimethylamino group in (*NN*-dimethylamino)-pyrimidines

Compound	Nucleus	MHz	Solvent	ΔT [b]/K	$\Delta\nu_{\infty T_c}$ [c]/Hz	T_c/K	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J mol^{-1} K^{-1}	$\Delta G^{\ddagger}_{T_c}$/kJ mol^{-1}	Ref.
(I)	^{1}H	100	CD_3OD	225.0—269.4	13.35	247 ± 1	52 ± 1	−8 ± 4	53.5	
	^{13}C	20	CD_3OD	221.2—268.7	13.64	250 ± 1	52.3 ± 0.8	−8 ± 4	54.0	
	^{1}H	100	$CHCl_3$	210.7—282.2	17.8	240.2	45 ± 2	−21 ± 4	49.8	2
	^{1}H	100	Bu^tNH_2	211.7—257.2	17.7	230.2	49 ± 2	46 ± 6	38.5	2
(II)	^{1}H	100	CD_3OD	251.8—283.8	10.2	268.2 ± 0.5	59 ± 2	4 ± 8	58.6	
	^{1}H	100	$CDCl_3$–CH_2Cl_2 (2:1)	243.6—276.5	14.3	266.2 ± 0.5	52 ± 3	−21 ± 16	57.3	
	^{1}H	100	$CDCl_3$–CH_2Cl_2 (2:1)		15.6	264.2			56.5	5
(III)	^{1}H	100	CD_3OD	229.1—248.7	16.2	241 ± 1	54 ± 1	12 ± 8	51.4	
(IV)	^{1}H	100	$CDCl_3$–CH_2Cl_2 (2:1)		(14)	<151			<(32) [d]	
(V)	^{1}H	100	$CDCl_3$–CH_2Cl_2 (2:1)		42.6	253 ± 2			51.9	
(VI)	^{1}H	100	CD_3OD		15.2	232 ± 2			49.4 [e]	
					8.2	200 ± 2			43.5 [f]	
(VII)	^{1}H	100	CD_3OD		16.2	222 ± 2			47.3 [e]	
						<201				

[a] Errors are the standard deviations from the least squares plot. [b] Temperature range used for the determination of activation parameters. [c] Difference between the chemical shifts of two methyl groups at the coalescence temperature, extrapolated from data obtained in the absence of exchange. [d] Value evaluated at 151 K with $\Delta\nu_\infty$ 14 Hz. [e] Parameters for 4-dimethylamino group. [f] Parameters for 2-dimethylamino group.

steric effects of the substituents.[8] In dynamic rotation, the value of the entropy of activation is close to zero [8,10,13] as confirmed by our study. We discuss our results on the basis of $\Delta G^{\ddagger}$ rather than $\Delta H^{\ddagger}$ values because $\Delta G^{\ddagger}$ is less sensitive to errors in T_2*, $\Delta\nu_\infty$,[7,9] and temperature.[11] Furthermore, Krug *et al.* have emphasized the possibility of compensation between the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values.[14] Finally, it is better to compare the $\Delta G^{\ddagger}$ values estimated by total line-shape analysis at the coalescence temperature than at 298 K in order to avoid possible error due to extrapolation over a large range of temperature.[15]

Solvent Effects.—Several investigations indicate that free energies of activation increase with the polarity of the solvent taking the dielectric constant ε as the standard.[16,17] Nevertheless, our data show no significant influence of solvent on $\Delta G^{\ddagger}$: for compound (II) in $CDCl_3$–CH_2Cl_2 ($\varepsilon_{CH_2Cl_2}$ 9.08, ε_{CHCl_3} 4.8) we have $\Delta G^{\ddagger}_{T_c}$ 57.3 and in CD_3OD (ε_{CH_3OH} 32.6) 58.6 kJ mol^{-1}. A significant solvent effect on $\Delta G^{\ddagger}$ has been found only for Bu^tNH_2 compared with $CHCl_3$ for pyrimidine (I) due to differences in solute–solvent interactions between the two systems.[2]

Substituent Effects.—Our results show that substitution of a hydrogen by a Me, Cl, NMe_2, or NO_2 group significantly affects the hindered internal rotation of the dimethylamino group in the 4-position. The free energy of activation changes from 47.3 to 58.6 kJ mol^{-1} according to the nature and position of the substituent. For 2- and 6-substitution, only an electronic effect occurs to which a steric effect is added in the case of 5-substitution.

To discuss the electronic effect of 2-substitution, one has to take into account the possible presence of a 6-substituent [in the case of pyrimidines (III) and (VII) for example]. A comparison of the results obtained for the pyrimidines (VI) and (VII) shows that substitution by a methyl group in the 6-position lowers $\Delta G^{\ddagger}_{T_c}$ by *ca.* 2 kJ mol^{-1}.

Taking into account the effect of a 6-methyl group the $\Delta G^{\ddagger}_{T_c}$ value increases according to the following order of substituents in the 2-position: NMe_2 < Me, H < Cl.

The rotational barrier increases with increasing electron-withdrawing power. The results for the 4-(*NN*-dimethylamino)pyrimidines are identical with those for the benzene series and based on Taft's constants.[18] This is consistent with earlier ^{1}H n.m.r. data which pointed out that the order of electron-withdrawing power of substituents is the same in the benzene and pyrimidine series.[19]

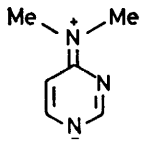
When an electron-donor group is *ortho* to the dimethylamino group, both the electronic and steric effects of the substituent will contribute to a decrease of the free energy of activation. This is observed for 2-chloro-4-(*NN*-dimethylamino)-5-methylpyrimidine (IV). The rotational barrier is reduced to such an extent that the coalescence temperature could not be determined experimentally. At the lowest temperature measured (181 K) the dimethylamino group is still in the fast exchange region and its signal does not undergo any broadening compared with that of the 5-methyl group (2 : 1 $CDCl_3$–CH_2Cl_2). The coalescence temperature for this compound should be at least 30 K lower than the lowest temperature (181 K) and the chemical shift difference $\Delta\nu_\infty$ should be *ca.* 14 Hz [see data for (II)]. The reduced relation $k = \pi\Delta\nu_\infty/\sqrt{2}$ at the coalescence temperature [20] leads to a maximum value of 32 kJ mol^{-1} for $\Delta G^{\ddagger}$ at 151 K for the pyrimidine (IV). This result shows that a methyl group reduces the energy barrier by at least 25 kJ mol^{-1}. MO Calculations on cytosine, using the CNDO/2 method, confirm the influence of a 5-methyl group on the hindered internal rotation of a 4-dimethylamino group ($\Delta G^{\ddagger}$ decreases by *ca.* 42 kJ mol^{-1}).[21]

When a nitro group is in the 5-position [compound (V)], the energy barrier should increase compared with the parent compound (II) on account of the large electron-

withdrawing effect of the nitro group. A decrease of *ca.* 5.4 kJ mol^{-1} for $\Delta G^{\ddagger}$ is observed and shows the predominance of a steric effect that suggests an increase in the angle of the dimethylamino group with the ring. This is in contrast with data for pyridine which indicate the major influence of the electronic effect.[2]

Influence of the Position of the Dimethylamino Group with Respect to the Nitrogen Atoms.—Data for 2,4-bis-(*NN*-dimethylamino)pyrimidine (VI) (*cf.* Table 1) show a difference between the two dimethylamino groups according to their position. The free energy of activation for the 2-dimethylamino group (43.5 kJ mol^{-1}) is 6 kJ mol^{-1} smaller than the corresponding value when this group is in the 4-position (49.4 kJ mol^{-1}). Conjugation between the lone pair electrons of the exocyclic nitrogen and the ring seems to be larger when the dimethylamino group is in the 4-position.

It is interesting to make a comparison with 2-(*NN*-dimethylamino)pyridine. The $\Delta G^{\ddagger}$ value [22] for a dimethylamino group α to one nitrogen atom is 32 kJ mol^{-1}. This value increases to 43.5 kJ mol^{-1} when the dimethylamino group is α to two nitrogen atoms [compound (VI)]. However, this last value is somewhat reduced by the substitution effect of 4-dimethylamino group. When the dimethylamino group is simultaneously α and γ to two nitrogen atoms [pyrimidine (I)] $\Delta G^{\ddagger}$ reaches 53.7 kJ mol^{-1}. In the pyrimidine ring the effect of a γ-nitrogen atom on the conjugation of the lone pair electrons of the exocyclic nitrogen atom with the ring seems therefore much larger than the effect of an α nitrogen atom. This result can be explained by the greater stability of the quinonoid form (IX).



(IX)

Linear Correlation of Free Energies of Activation with ^{13}C *Chemical Shift Parameters.*—We shall focus our attention on the change in ^{13}C chemical shifts due to the introduction of a 4-dimethylamino group. We have not taken into account the solvent effect, all the molecules being studied in CD_3OD when they are substituted by a 4-dimethylamino group and in Me_2SO when this substituent is absent.[23] The corresponding values are summarized in Table 2.

TABLE 2

Chemical shifts (p.p.m.) induced by the 4-dimethylamino group on the carbons of pyrimidines

Compound	C-2	C-4	C-5	C-6
(I)	−0.15	6.11	−17.76	−2.28
(II)	0.45	4.09	−18.1	−3.7
(III)	−0.05	7.44	−18.29	−2.38
(VI)	2.09	6.18	−15.96	−2.01
(VII) *	(2.63)	(7.23)	(−16.48)	(−1.02)

* 2-(*NN*-Dimethylamino)-4-methylpyrimidine not being available, the chemical shift parameters have been determined for 2-amino-4-methylpyrimidine and corrected for the substitution of hydrogen by a methyl group. These corrections, determined for 2-aminopyrimidine and 2-(*NN*-dimethylamino)-pyrimidine are: Δ(C-2) −2.89, Δ(C-4) −0.27, Δ(C-5) −1.01, and Δ(C-6) −0.27 p.p.m.

As shown in Table 2, C-2, -4, -5, and -6 are only weakly sensitive to the substituent effect of the dimethylamino group in 4-position. So, the slopes of correlation lines between the chemical shift parameters of the aromatic carbons and the free energies of activation for the 4-dimethylamino group are too steep to allow an evaluation of $\Delta G^{\ddagger}$ from these parameters.

Linear Correlation of Free Energies of Activation with ^{1}J(C,H) *Coupling Constants relative to the Dimethylamino Group.*—Haake *et al.* have pointed out that the ^1J(C,H) coupling constant for the dimethylamino group increases with the positive charge on the nitrogen atom bearing the methyl groups.[24] Therefore we could expect a relationship between ^1J(C,H) and $\Delta G^{\ddagger}$ within the same series of compounds. This is consistent with the results in Table 3. Figure 1 shows a linear correlation between these free energies of activation and the coupling constants for a 4-dimethylamino group. Such a correlation allows the estimation of the free energies of activation for compounds in this series for which experimental determination is impossible.

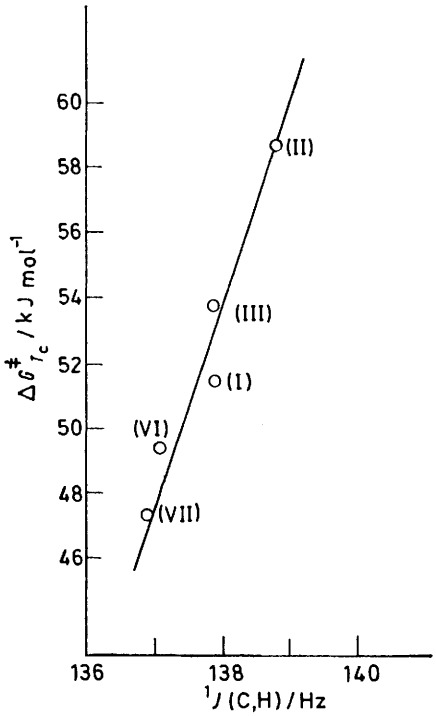


FIGURE 1 Correlation between free energies of activation $\Delta G^{\ddagger}_{T_c}$ and $^1J(NMe_2)$

The rotational barrier in 2,4,6-tris-(*NN*-dimethylamino)pyrimidine (VIII) could not be studied because

TABLE 3

Compound	2-Substituent	^1J(NMe-4)/ Hz	$\Delta G^{\ddagger}_{T_c}$/ kJ mol^{-1}
(VI)	NMe_2	137.1	49.4
(III)	Me	137.9	51.4
(I)	H	137.9	53.7
(II)	Cl	138.8	58.6

the coalescence temperature is too low ($T_c < 195$ K). The use of the correlation in Figure 1 gives $\Delta G^{\ddagger}$ for this compound (*ca.* 42 kJ mol^{-1}), the ^1J(NMe-4) coupling constant being 136.2 Hz. This result confirms the decrease of $\Delta G^{\ddagger}$ for the 4-dimethylamino group when a second group is introduced in the 6-position. The introduction of a group in the 2-position lowers $\Delta G^{\ddagger}$ by *ca.* 4.3 kJ mol^{-1} [comparison of pyrimidines (I) and (VI)]. The presence of a second dimethylamino group in the 6-position again lowers $\Delta G^{\ddagger}$ by *ca.* 7.6 kJ mol^{-1} [comparison of pyrimidines (VI) and (VIII)].

Conclusions.—2-Substituents have the following increasing electron-withdrawing effect in the pyrimidine ring: $NMe_2 < Me,H < Cl$. Substitution of the pyrimidine ring in the 5-position, *i.e. ortho* to the dimethylamino group, by a methyl or nitro group, involves a decrease of the free energy of activation larger in the case of the methyl group. For the nitro group, there is partial compensation between the electronic and steric effects.

Comparison of the rotational barriers for dimethylamino groups in the 2- and 4-positions shows that the double bond character of the amino–ring bond is larger for 4-substitution.

A good linear correlation has been found between the free energy of activation $\Delta G^{\ddagger}$ and ^1J(C,H) for the 4-dimethylamino group. This correlation allows an estimate of the free energy of activation of compounds in this series when experimental determination is not possible. A similar study of 2-(*NN*-dimethylamino)pyrimidines is in progress. If a similar correlation exists for these compounds, it should be possible to estimate the free energies of activation of dimethylamino groups in symmetric 2-(*NN*-dimethylamino)pyrimidines for which direct experimental determination of $\Delta G^{\ddagger}$ is impossible.

EXPERIMENTAL

Compound (II) is commercially available and purified by sublimation prior to measurement. The other compounds were prepared according to literature methods,[25-31] (I),[25] (III),[26] (IV),[27] (V),[28] (VI),[29] (VII),[30] and (VIII).[31]

Dynamic ^{1}H n.m.r. experiments were carried out on a Varian HA–100 spectrometer with a variable temperature unit. For all solutions 5% Me_4Si was added as lock signal and internal reference. The chemical shifts are accurate to 0.002 p.p.m. The spectra of the *N*-methyl protons were recorded at a sweep rate of 0.2 Hz s^{-1}. The homogeneity was optimized at each temperature using dioxan (5% for all solutions) as internal standard. The temperatures, measured using the standard methanol sample and calibrated graphs of Van Geet,[32] are accurate to ±0.5 °C.

Carbon-13 n.m.r. spectra were recorded on a Varian CFT 20 spectrometer equipped with a variable temperature system. The size of the data memory is 8 K words. Solutions were made up in CD_3OD or $CDCl_3$–CH_2Cl_2 in the 0.3—1.5M concentration range. Chemical shifts were measured with respect to internal dioxan in CD_3OD, and CH_2Cl_2 in $CDCl_3$–CH_2Cl_2. The accuracies of the chemical shifts and of coupling constants are 0.0_5 p.p.m. and 0.5 Hz, respectively. For coupling constant determinations for the dimethylamino group [^1J(NMe-4), ^3J(MeNMe-4)] typical conditions are: spectral width 700 Hz, pulse width of 12 μs corresponding to a 72° pulse angle and a pulse repetition time of 1.5 s. The observed coupling constants are accurate to at least ±0.2 Hz under these conditions.

There is equivalence between the line-shapes obtained by Fourier transform and continuous mode n.m.r.[33] Nevertheless, in order to obtain well transcribed line-shapes in Fourier transform n.m.r. we have used a spectral width of 1 000 Hz (resolution of 0.25 Hz).

The temperature was measured by inserting thermometers inside the probe before and after each experiment, the thermometers being placed in a non-spinning sample tube with the bulbs carefully positioned. In the temperature range ($-100 \leqslant t \leqslant 64$ °C) alcohol and neopentane thermometers were used after calibration against a standard copper–constant thermocouple. The error is estimated to be ±1 °C.

^{13}C *N.m.r. Signal Assignments.*—Carbon-13 chemical shifts and coupling constants of the compounds are listed in Supplementary Publication No. SUP 22538 (4 pp.).* Assignments of the lines of compounds (I)—(IV), (VII), and (VIII) were based on coupling constants and comparison with data obtained for the aminopyrimidine parent compounds in Me_2SO solution.[23] For 2,4-bis-(*NN*-dimethylamino)pyrimidine (VI) the assignment of the C-2 line was based on an expected regular change of the C-2 chemical shift in 2-(*NN*-dimethylamino)pyrimidine (160.52 p.p.m.) and pyrimidines (VI) (162.61 p.p.m.) and (VIII) (163.08 p.p.m.) since the same trend is observed for the corresponding aminopyrimidines in Me_2SO. The signal for the 2-dimethylamino group, both in ^{1}H and ^{13}C n.m.r. spectra, was assigned on the same basis. This assignment is confirmed by the values of the ^1J(C,H) coupling constant (Table 4).

TABLE 4

Compound	δ(NMe$_2$-2)	δ(NMe$_2$-4)	^1J(NMe-2)/ Hz	^1J(NMe-4)/ Hz
2-(*NN*-Dimethylamino)-pyrimidine	3.142		137.3_5	
(I)		3.107		137.9
(VI)	3.071	3.014	136.9	137.1
(VII)	3.078	2.984	136.6	136.9
(VIII)	3.061	2.988	136.0	136.2_5

Total Line-shape Analysis.—In the absence of exchange the width of the dimethylamino resonance W_{NMe_2} can be obtained at each temperature from the width of a reference line $W_{ref}(T)$. The effective transverse relaxation time T_2^* can then be evaluated by the relationship (1). $\Delta W(T)$

$$T_2^*(T) = \frac{1}{\pi W_{NMe_2}} = \frac{1}{\pi[W_{ref}(T) + \Delta W(T)]} \quad (1)$$

should be determined both for no exchange and fast exchange conditions. Then $\Delta W(T)$ values necessary for the calculation of line-shape in the intermediate range are interpolated. However the solvent used (CD_3OD or $CDCl_3$–CH_2Cl_2) did not allow $\Delta W(T)$ to be determined in a temperature range large enough to cover both fast exchange and the absence of exchange. Consequently $\Delta W(T)$ was extrapolated from results obtained for only one of these limiting conditions. The values of ΔW for pyrimidine (I) are 0.20 and 0.07 Hz in the absence of exchange for ^{13}C and ^{1}H,

* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1978, Index issue.

respectively. For compound (III) in the absence of exchange, $\Delta W(T)$ is expressed for ^{1}H n.m.r. by $\Delta W = 0.17 - 0.002t$. We chose as reference compound dichloromethane or dioxan which have resonance lines close to those of the dimethylamino group, allowing the use of a narrow spectral width thus increasing the spectral resolution.

The dependence of the $\Delta\nu_\infty$ parameter on temperature was determined in the absence of exchange and the linear relationship obtained was extrapolated to the intermediate zone of exchange. The values for $\Delta\nu_\infty$ for pyrimidine (I) are

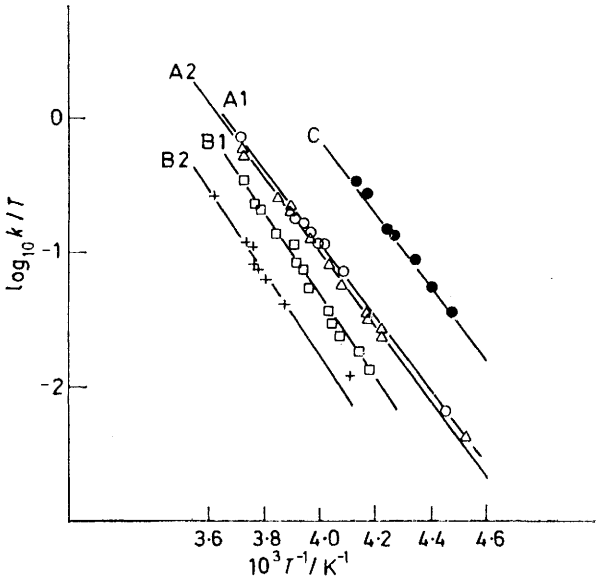


FIGURE 2 Eyring plots for hindered rotation of the dimethylamino group in 4-(*NN*-dimethylamino)pyrimidines: A_1, pyrimidine (I) in CD_3OD (^{1}H n.m.r.) (r 0.998); A_2, pyrimidine (I) in CD_3OD (^{13}C n.m.r.) (r 0.998); B_1, pyrimidine (II) in CD_3OD (^{1}H n.m.r.) (r 0.997); B_2, pyrimidine (II) in $CDCl_3$–CH_2Cl_2 (^{1}H n.m.r.) (r 0.987); C, pyrimidine (III) in CD_3OD (^{1}H n.m.r.) (r 0.998)

similar in ^{1}H (13.35 Hz) and ^{13}C (13.64 Hz) n.m.r. The change of $\Delta\nu_\infty$ with respect to temperature is not important for this compound: 0.02 and 0.2 Hz for 10° for ^{1}H and ^{13}C, respectively. For compounds (II)—(IV), (VI), and (VII) the values for $\Delta\nu_\infty$ in ^{1}H n.m.r. are 10.2—16.2 Hz (*cf.* Table 1), the change with temperature being 0.01—0.4 Hz for 10°.

The theoretical line-shapes were calculated on the basis of the Gutowsky–Holm equation [20] using a program written by Binsch and Kleier.[34] We have modified this program to include an iterative calculation of the rate constant k with graphical output corresponding to the optimum value. To calculate $\Delta H^\ddagger$, $\Delta S^\ddagger$, and $\Delta G^\ddagger$ from k using the Eyring equation we assumed a transmission coefficient of unity and took all experimental points with equal statistical weight. The Eyring plots for compounds (I)—(III) are shown in Figure 2.

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