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HETEROCYCLIC ANALOGS OF PLEIADIENE. 68*. UNUSUALLY SLOW (ON THE NMR TIME SCALE) ANNULAR PROTOTROPY IN THE 6(7)-FORMYL- AND 6(7)-ACETYL-2-TRIFLUOROMETHYL-PERIMIDINE SERIES

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The case of extremely slow (on the NMR time scale) annular prototropy rare in azole systems has been observed. According to ^{1}H NMR spectral data, both NH tautomers are observed in solutions of 6(7)-formyl- and 6(7)-acetyl-2-trifluoromethylperimidines in $CDCl_3$ and C_6D_6 at room temperature and even on heating to 60-70°C. The rate of interconversion of the tautomers in DMSO-d_6 and CD_3CN is sufficiently great that only averaged signals are observed in their ^{1}H NMR spectra. The main reason of the slow tautomerism is the cooperative effect of the 2-CF_3 group and the carbonyl substituent which decreases the basicity of the pyridine hetero atom to such an extent that a transfer of a proton between molecules in a nonpolar medium becomes strongly hindered.

Keywords: 6(7)-acetyl-2-trifuoromethylperimidine, 2-trifluoromethylperimidine, 2-trifluoromethyl-perimidine-6(7)-carbaldehyde, perimidine, annular tautomerism.

In the preceding paper, concerned with the synthesis of aldehydes of the perimidine series, we mentioned that in the ^{1}H NMR spectrum of 6(7)-formyl-2-trifluoromethylperimidine in $CDCl_3$ at room temperature the signals of both NH-tautomers **1A** and **1B** were observed simultaneously [1]. Since annular prototropy in the azole series under normal conditions is a very rapid process [2, 3] which has been slowed successfully only by strongly reducing the temperature [4], it appeared of interest to investigate this phenomenon more thoroughly. Consequently we have studied compound **1** and its acetyl analog **2** in this work.

* For paper 67 see [1].

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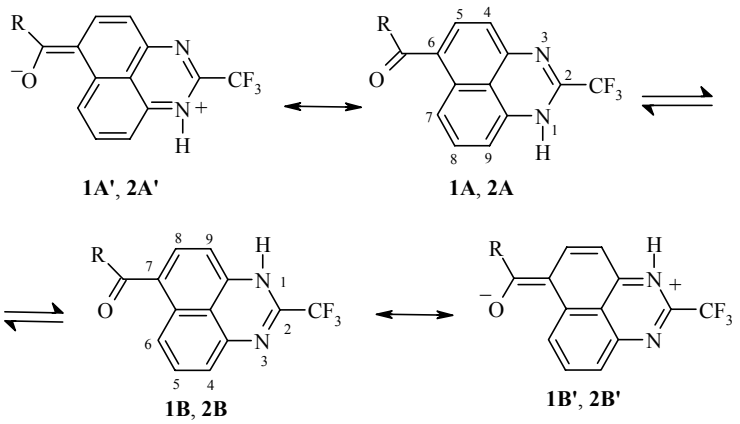


Peculiarities of the ^{1}H NMR spectra of tautomeric perimidines and designation of the cycle atoms. Since the analysis of the tautomeric equilibria in this paper is entirely based on ^{1}H NMR spectra, it is expedient to analyze first the spectra of simple perimidines without substituents in the naphthalene ring. Table 1 contains characteristics of the ^{1}H NMR spectra of 2-methyl- (**3**) and 2-trifluoromethylperimidines (**4**) and also of their 1-methyl derivatives (**5** and **6** respectively). The noteworthy characteristic of **5**, **6**, as well as of other 1-substituted perimidines [5], is high-field shift of the signals of both *ortho* protons. This is noted especially for the signal of 9-H which is a doublet of doublets in the 6.2-6.3 ppm region. The doublet of doublets of 4-H signal is found at 6.9-7.0 ppm. The position of the 9-H signal is determined principally by the decreased aromaticity of the heterocycle in perimidines [6] which formally contains 7 π electrons rather than 6. As a result the paramagnetic contribution of the ring current is increased. It has a lesser effect on the 4-H which undergoes a deshielding effect of the lone electron pair of the pyridine nitrogen atom 3-N. In compounds **3** and **4,** without the N-methyl group, the two *ortho* protons give an averaged signal at room temperature as a result of rapid interconversion. The signal position is close to the average value for the chemical shifts for 4-H and 9-H in compounds **5** and **6**.

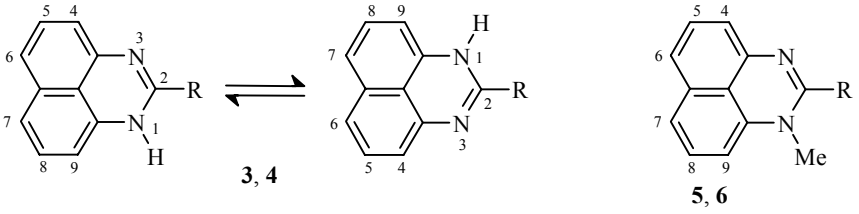


TABLE 1. ^{1}H NMR Spectra of Compounds **3-6**

Com-pound	δ, ppm					*J*, Hz			
	4-H	9-H	5-8-H, m	NH	CH_3, s	J_{45}	J_{46}	J_{89}	J_{79}
3	6.46 br. d	6.46 br. d	7.03-7.13	5.41 br. s	2.12	6.8	*	6.8	*
4	6.58 br. s	6.58 br. s	7.11-7.18	*	—	*	*	*	*
5	6.86 dd	6.21 dd	7.12-7.30	—	2.36 (2-CH_3) 3.20 (1-CH_3)	7.3	1.0	6.8	1.8
6	6.98 dd	6.31 dd	7.17-7.30	—	3.23	5.3	3.2	5.0	3.5

* Not recorded.

TABLE 2. ^{1}H NMR Spectra (δ, ppm, *J*, Hz) of the Tautomeric Compounds **1** and **2** and Their Fixed Forms

Compound (tautomer)	Solvent	*ortho* Protons		*meta* Protons		*para* Protons		CHO and (or) CH_3	NH
		4-H	9-H	5-H	8-H	6-H	7-H		
1	2	3	4	5	6	7	8	9	10
1A	$CDCl_3$	7.04 d J_{45} = 7.7	6.66 br. d J_{98} = 7.1	7.79 d J_{54} = 7.8	7.46 dd J_{87} = 8.9 J_{89} = 7.1	—	8.77 br. d J_{78} = 8.9	10.04 s	8.23 br. s
1B	$CDCl_3$	7.25 br. d J_{45} = 7.6	6.49 d J_{98} = 7.9	7.62 dd J_{54} = 7.6 J_{56} = 8.7	7.68 d J_{89} = 7.8	8.82 br. d J_{65} = 8.7	—	9.97 s	8.23 br. s
1A	C_6D_6	6.9-7.55 *	5.54 br. d J_{98} = 7.7	6.9-7.55 m*	6.9-7.55 m*	—	9.25 dd J_{78} = 8.8 J_{79} = 0.9	9.89 s	6.80 br. s
1B	C_6D_6	6.9-7.55 m*	5.20 d J_{98} = 7.8	6.9-7.55 m*	6.9-7.55 m*	9.27 dd J_{65} = 8.2 J_{64} = 1.3	—	9.95 s	6.80 br. s
1	CD_3CN*[2]	7.04 br. d	6.72 br. d	7.57 dd J_{54} = 8.0 J_{56} = 8.1	7.78 d J_{89} = 7.8	8.74 d J_{65} = 8.7	—	9.93 s	10.40 br. s
1	DMSO-d_6*[2]	7.03 br. dd	6.75 br. d	7.55 dd J_{54} = 7.9 J_{56} = 8.2	7.85 d J_{89} = 8.0	8.64 br. d J_{65} = 8.5	—	9.89 s —	12.40 br. s
2A	$CDCl_3$	6.92 d J_{45} = 8.0	6.55 dd J_{98} = 7.6 J_{97} = 0.7	7.92 d J_{54} = 8.0	7.35 dd J_{87} = 8.9 J_{89} = 7.6	—	8.55 dd J_{78} = 8.9 J_{79} = 0.8	— 2.63 s	8.10 br. s
2B	$CDCl_3$	7.16 dd J_{45} = 7.5 J_{46} = 0.8	6.35 d J_{98} = 8.0	7.52 dd J_{54} = 7.5 J_{56} = 8.8	7.83 d J_{89} = 8.1	8.72 dd J_{65} = 8.8 J_{64} = 0.8	—	— 2.60 s	8.10 br. s

TABLE 2 (continued)

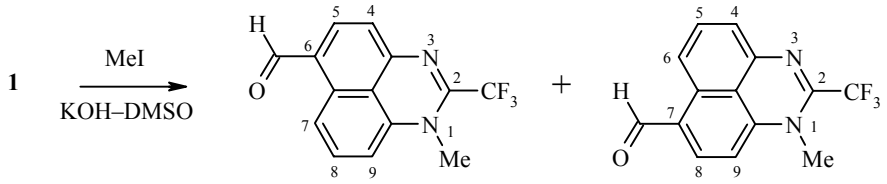
1	2	3	4	5	6	7	8	9	10
2A	C_6D_6	6.9-7.55 m*	5.54 br. d J_{98} = 7.3	6.9-7.55 m*	6.9-7.55 m*	—	9.22 dd J_{78} = 8.7 J_{79} = 0.8	— 2.25 s	6.83 br. s
2B	C_6D_6	6.9-7.55 m*	5.25 d J_{98} = 8.1	6.9-7.55 m*	6.9-7.55 m*	9.31 dd J_{65} = 8.3 J_{64} = 1.3	—	— 2.31 s	6.83 br. s
2	C_6D_6	6.95 br. s	6.65 br. s	7.48 dd	8.00 d J_{89} = 8.1	8.62 br. d J_{65} = 8.1	—	— 2.60 s	9.96 br. s
2	DMSO-d_6*[2]	6.96 br. dd	6.69 br. d J_{98} = 8.0	7.48 dd J_{56} = 8.7 J_{54} = 7.6	8.07 d J_{89} = 8.1	8.57 br. dd	—	2.57 s	12.2 br. s
7	$CDCl_3$	7.12 d J_{45} = 7.7	6.71 dd J_{98} = 8.0 J_{97} = 0.7	7.84 d J_{54} = 7.8	7.57 dd J_{87} = 8.7 J_{89} = 8.0	—	8.86 dd J_{78} = 8.7 J_{79} = 0.7	10.08 s 3.42 s	—
7	DMSO-d_6	7.04 d J_{45} = 7.8	7.00 dd J_{98} = 8.0 J_{97} = 0.9	8.00 d J_{54} = 7.8	7.67 dd J_{87} = 8.7 J_{89} = 8.0	—	8.72 dd J_{78} = 8.7 J_{79} = 0.9	10.05 s 3.45 s	—
8	$CDCl_3$	7.32 dd J_{45} = 7.6 J_{46} = 0.8	6.50 d J_{98} = 8.2	7.66 dd J_{56} = 8.6 J_{54} = 7.6	7.76 d J_{89} = 8.2	8.95 dd J_{65} = 8.6 J_{64} = 0.9	—	10.01 s 3.43 s	—
8	C_6D_6	7.33 m	5.42 d J_{98} = 8.1	7.37 dd J_{54} = 7.6	7.16 d J_{89} = 8.3	9.40 dq J_{65} = 7.6 J_{64} = 1.3 $^5J_{6\text{-H-CHO}}$ = 0.4	—	10.04 d $^5J_{\text{CHO-6-H}}$ = 0.4 2.30 q $^5J_{\text{CH3-CF3}}$ = 0.85	—
8	DMSO-d_6	7.23 dd J_{45} = 7.5 J_{46} = 0.9	6.83 d J_{98} = 8.3	7.68 dd J_{56} = 8.5 J_{54} = 7.5	8.00 d J_{89} = 8.2	8.82 dd J_{65} = 8.5 J_{64} = 0.9	—	9.98 s 3.42 q $^5J_{\text{CH3-CF3}}$ = 0.72	—

* Signal overlapped by the residual solvent peaks and their satellites.

*[2] Because of the rapid tautomerism in the given solvent the numbering of the pairs of *ortho*-, *meta*-, and *para*- protons is provisional.

There are considerable changes in the ^{1}H NMR spectra of the 6-substituted perimidines **1** and **2** with free NH groups since the tautomers are no longer degenerate. In addition the substituents, in this case aldehyde and acetyl, influence the position of the proton signals significantly. Their anisotropic deshielding effect particularly influences on the *ortho* hydrogen atom (the term "*ortho*" is used here relative to the substituent and not the heterocycle) and the *peri* hydrogen of the neighboring ring. The chemical shift of the latter is near to 9 ppm.

The parameters of the spectra of the compounds under discussion are given in Table 2. Fig. 1 shows the ^{1}H NMR spectra of aldehyde **1** in DMSO-d_6 and $CDCl_3$ and also the mixture of fixed (N-methylated) tautomers **7** and **8**. 1-Methyl-2-trifluoromethylperimidine-7-carbaldehyde (**8**) was isolated from this mixture (prepared by the formylation of 1-methyl-2-trifluoromethylperimidine (**6**) [1] and by methylation of aldehyde **1** with methyl iodide in DMSO-KOH) in pure form by fractional crystallization.



It should be noted that on going from one tautomer to the other the numbering of the ring atoms changes since, according to the IUPAC rules, numbering begins from the pyrrole nitrogen atom, which is changed relative to the proton. For example, when the tautomers **1A** and **2A** change to the tautomers **1B** and **2B** 9-H becomes 4-H and *vice versa*. However significantly the multiplicity of the corresponding signals does not change since one of the atoms in either case is in an unsubstituted benzene ring and appears as a doublet of doublets, while the other is in a substituted ring and appears as a doublet.

In light of this it is evident that if at high field of the tautomer spectrum a doublet with a characteristic constant for an *ortho* proton appears it should be assigned to the 7-COR form of **1B** or **2B**, whereas if a doublet of doublets appears in the same region it should belong to the 6-COR form of **1A** or **2A**. Additionally the tautomers should be identified by the spin-spin coupling constants for both doublet signals J_{45} and J_{54} (for **1A** and **2A**) and J_{89} and J_{98} (for **1B** and **2B**). This coupling constant is somewhat larger for tautomers **1B** and **2B** due to conjugation of the pyrrole nitrogen atom with the carbonyl group, and consequently the C=C bond order in **1B** and **2B** should be greater than in tautomers **1A** and **2A**. The latter stems from the assumption that the contribution of the bipolar structures **1B'** and **2B'** to the resonance hybrid is greater than of the structures **1A'** and **2A'**, i.e, conjugation between the substituents in the same benzene ring of naphthalene should be higher than between the same substituents in different rings [7]. This can be illustrated in the isomeric compounds **7** and **8**. In the 1-methyl-7-carbaldehyde **8** J_{89} = 8.1 Hz, whereas in the 1-methyl-6-carbaldehyde **7** J_{45} = 7.8 Hz. It is also very noteworthy that the difference between the chemical shifts of 9-H and 4-H for isomer **8** is much larger (0.8 in $CDCl_3$ and 0.4 ppm in DMSO-d_6) than for isomer **7** (0.4 and 0.04 ppm respectively). Analogous differences were observed for the 7- and 6-tautomers of **1** and **2**.

Different protons in the perimidine system react differently to the anisotropic influence of substituents. This too may be used for their identification by ^{1}H NMR spectra. For example the benzene molecule forms a complex with perimidines, placed above the pyrrole nitrogen atom and 9-H, with the planes of the two aromatic systems approximately parallel. This is confirmed by the strong paramagnetic shift of the 9-H and N-methyl signals in the spectrum of compound **8** in C_6H_6. Another characteristic example is the sharp decrease in the difference between the chemical shifts of 9-H and 4-H in the spectra of the compounds studied in DMSO-d_6 in comparison with solutions in $CDCl_3$ (see above).

Tautomerism of 6(7)-formyl- and 6(7)-acetyl-2-trifluoromethylperimidines. ^{1}H NMR spectra of compound **1** in $CDCl_3$ and C_6H_6 solutions show two sets of signals assigned to the tautomers **1A** and **1B**. Surprising similarity of the spectra of the tautomeric mixtures with the spectrum of the mixture of the N-methylated model compounds **7** and **8** (Fig, 1, b and c) confirms the above mentioned. Subsequent analysis of the spectra considering the mentioned observations, leaves no doubt that the 1-H-7-formyl tautomer **1B** predominates, and its concentration in $CDCl_3$ exceeds 60% (Table 3). It is interesting that the ratio of the 1-methyl-7-formyl- (**8**) and 1-methyl-6-formyl- (**7**) derivatives formed by methylation of compound **1** with methyl iodide in DMSO-KOH is approximately the same.

A similar pattern was observed for 6(7)-acetyl-2-trifluoromethylperimidine (**2**) which we obtained along with the 4(9)-acetyl derivative **9** by acetylation of compound **4** with acetic acid in polyphosphoric acid (PPA) [8]. In this case too the prototropy in $CDCl_3$ and C_6D_6 was slowed considerably, and the 1H-7-acetyl tautomer (**2B**) predominated in the reaction mixture (Table 3).

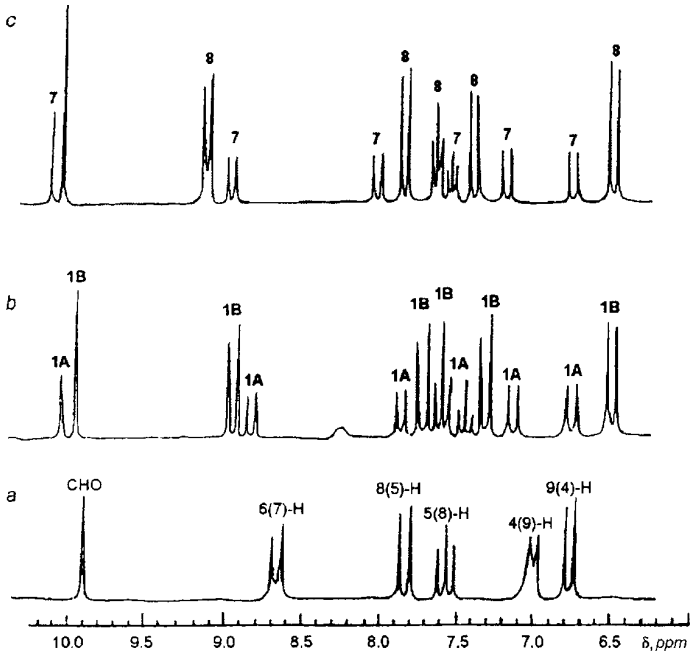
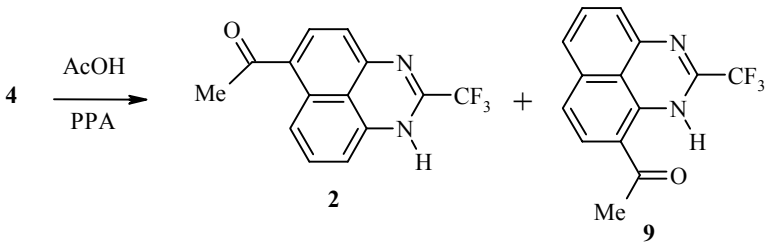


Fig.1. ^{1}H NMR spectra of the 6-aldehyde **1A** in DMSO-d_6 (a) and $CDCl_3$ (b) and the mixture of N-methylated isomers **7** and **8** in $CDCl_3$ (c).

TABLE 3. Content of Tautomers **A** and **B** in Equilibrium Mixtures at 25°C

Compound	Solvent	6-COR (**1A, 2A**)	7-COR (**1B, 2B**)	Equilibrium constant K_T = **1A/1B** or **2A/2B**
1	$CDCl_3$	37	63	0.59
1	C_6D_6	38	62	0.62
1	DMSO-d_6	34*	66*	0.52
1	CD_3CN	*	*	—
2	$CDCl_3$	40	60	0.67
2	C_6D_6	47	53	0.89
2	DMSO-d_6	*	*	—
2	CD_3CN	*	*	—

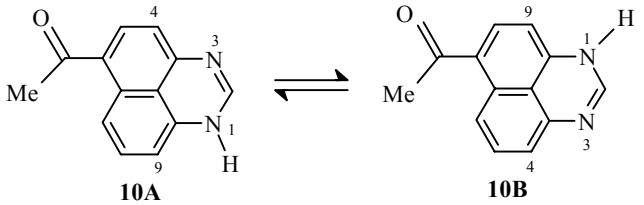
* Rapid equilibrium.



Quantum-chemical calculations revealed that tautomer **1B** is somewhat more stable than tautomer **1A** in the gas phase. The calculated (AM1 and PM3) heats of formation for tautomer **1B** (-111.62 and -129.66 kcal mol^{-1} respectively) and **1A** (-111.07 and -129.26 kcal mol^{-1}) probably explain the slight predominance of tautomers **1B** and **2B** in nonpolar solvents. In our opinion the reason for the hindered interconversion of the tautomers is the low basicity of compounds **1** and **2** resulting from the electron-withdrawing effect of the CF_3 and CHO (COMe)* groups.

It is well known that the typical mechanism of prototropy includes the transfer of a proton from one particle to another with the help of a solvent molecules or the other molecules of the prototropic compound. In the latter case the formation of associates *via* intermolecular hydrogen bonds with a proton transfer plays an important role [10]. It is clear that in the case of compounds **1** and **2** in nonpolar media neither the solvent nor the molecules of the prototropic compound are able to play the part of an effective proton carrier.

We have demonstrated with 6(7)-acetylperimidine (**10**) [8] the considerable role of the 2-CF_3 group in slowing tautomerism. As would be expected, the process of prototropy in this compound both in polar (DMSO-d_6) and in nonpolar ($CDCl_3$) media occurs relatively rapidly and results in averaging of the ^{1}H NMR spectral features. Outwardly the spectrum may be interpreted in terms of the presence of only one of the two tautomers, but the considerable broadening of the signals of 4-H and 9-H, which disappears upon heating to 120°C (in DMSO-d_6) shows that we are dealing with an equilibrium between the two forms **10A** and **10B**.



Rapid prototropic equilibrium is observed in DMSO-d_6 and CD_3CN for compounds **1** and **2**. Both solvents are highly polar and are capable to lower the activation barrier for tautomerism by effectively solvating the polar transition state. In addition dimethylsulfoxide may also play the role of proton carrier as a rather strong base (pK_a = 0) [11]. The latter is much less likely in the case of acetonitrile (pK_a = -10.11) [11], but in this case microimpurities of water and basic substances which are generally present in it may play the role of catalysts.

The content of tautomers **A** and **B** in the equilibrium mixture in solutions of the aldehyde **1** in DMSO-d_6 was estimated from the formula [12]:

$$p_1 = \chi_{1A}\, p_7 + \chi_{1B}\, p_8$$

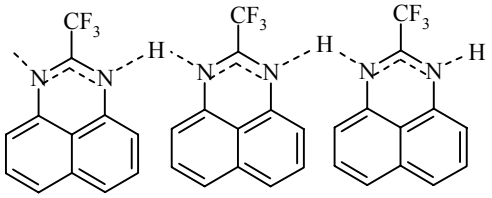
* Although we have not measured the ionization constants of compounds **1** and **2**, it is known that pK_a value for 1-methyl-2-trifluoromethylperimidine **6** in CH_3CN is 6.64 [9]. Extrapolating this to water corresponds to a value of pK_a within the limits from -0.5 to -1. Clearly the basicity of compounds **1** and **2** should be even lower than this.

where p_1 is the observed difference in the chemical shifts of 4-H and 9-H for the tautomers of compound **1**, p_7 and p_8 are the analogous difference for the fixed forms **7** and **8**, χ_{1A} and χ_{1B} are the mole fractions of tautomers **1A** and **1B**.

Taking into account the results in Table 2 (p_1 = 0.28, p_7 = 0.04, and p_8 = 0.40 ppm) the ratio of **1A**:**1B** is 34:66, i.e, it is almost unchanged in comparison with nonpolar solvents. In these calculations corrections for the methyl group in the model compounds **7** and **8** were ignored, however, as it follows from the data for chloroform solutions (Table 2), this correction is very small and cannot lead to a principal correction of the results.

Unfortunately because of the limitations imposed by the specific of the solvents used we were unable to attain the coalescence temperatures and to measure the free energy of activation for the annular prototropy of compounds **1** and **2**. For example, when solutions of these compounds in CD_3CN were cooled to -40°C no broadening of the signals was observed. On the other hand when a solution of the aldehyde **1** in C_6D_6 was heated to 70°C, the indicator signals, e.g., that of the CHO group, broadened considerably and their chemical shifts difference was halved. We suggested that replacement of deuterobenzene by deuterotoluene would permit the coalescence temperature to be achieved. However, it was found unexpectedly that the ^{1}H NMR spectra of compounds **1** and **2** in $C_6D_5CD_3$ show only one set of signals which did not change on increasing the temperature to 100°C. The reason for this difference in the behavior of compounds **1** and **2** in two closely similar solvents (C_6D_6 and $C_6D_5CD_3$) is not clear. Nevertheless these observations let us conclude that the value of $\Delta G^{\neq}$ for tautomerization of compounds **1** and **2** in nonpolar solvents is at least not smaller than 18-19 kcal·mol^{-1}.

Tautomerization of 2-trifluoromethylperimidine. Considering the evident role of the CF_3 group in slowing annular tautomerism in compounds **1** and **2**, it appeared interesting to investigate its influence on tautomerization of 2-trifluoromethylperimidine **4**. Even at room temperature the averaged signal of the 9-H and 4-H protons in the ^{1}H NMR spectrum of compound **4** in $CDCl_3$ was considerably broadened, indicating slow tautomerism (compare with 2-methylperimidine, **3**, for example). When the temperature was lowered to -20°C this signal split into two broad peaks and the signal of the NH proton appeared at about 8 ppm at the same time. However further temperature decrease unexpectedly did not lead to narrowing of the separated signals of 4-H and 9-H, but to a second coalescence and narrowing. The peak of the NH proton broadened considerably and shifted to lower field (to ~9 ppm at -60°C). Apparently another dynamic process is superimposed on the freezing of the annular tautomerism under the influence of the CF_3 group. Although the elucidation of its nature requires a special investigation, it may be suggested that a decrease in temperature facilitates the formation of the intermolecular associates **11**, within which the proton transfer between the nitrogen atoms of neighboring molecules proceeds quite freely as a result of its increased acidity. This should lead to symmetrization of the pairs of *ortho*, *meta*, and *para* protons which becomes all the more expressed as the temperature is lowered further. The behavior of the NH proton signal with change in temperature corresponds completely to this description [4].



11

Independently of the details of the process described, all of the data indicate that the cooperative electron-withdrawing effects of the 2-CF_3 group and the carbonyl containing substituent in the naphthalene ring is responsible for slowing down of the tautomerism in compounds **1** and **2**. The importance of this effect is

evident from the following observation. If 2-trifluoromethylperimidine **4** gave compound **6** in almost quantitative yield on methylation with methyl iodide in DMSO-KOH at room temperature, methylation of the aldehyde **1** under the same conditions did not occur, but only gave a yield of no more than 43% of a mixture of the N-methyl derivatives **7** and **8** on prolonged heating.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Unity-300 (300 MHz) instrument with TMS as internal standard, UV spectra on a Specord M-40 spectrophotometer, IR spectra on a UR-20 spectrometer, and mass spectra were recorded with an MX-1321A machine with direct insertion of the sample, the temperature of ionization chamber was 50-100°C, and an ionizing voltage was 70 eV. Chromatography was carried out on aluminum oxide (activity III by Brockman), or as well as on Chemapol L 40/100 silica gel. Melting points were determined in sealed glass capillaries with a PTP apparatus and were uncorrected.

1-Methyl-2-trifluoromethylperimidine (6). Finely divide potassium hydroxide (0.34 g, 6 mmol) was added to a solution of 2-trifluoromethylperimidine (**4**) [13] (1.2 g, 5 mmol) in DMSO (10 ml) which was blowed out with an inert gas. The mixture was stirred for 5 min, methyl iodide (0.8 g, 5.5 mmol) was added, and stirring was continued for 30 min in an inert atmosphere at room temperature. The mixture was poured into cold water (200 ml), the precipitate formed was separated, washed on the filter with hot water (200 ml), pressed out, and dried in air. The yield of chromatographically pure **6** was 1.05 g (83%) of light yellow crystals, m.p. 130-131°C (octane), which corresponds to the results of [7].

Methylation of 2-Trifluoromethylperimidine-6(7)-carbaldehyde (1). A mixture of aldehyde **1** (0.11 g, 0.42 mmol), finely divide potassium hydroxide (0.03 g, 0.53 mmol), and methyl iodide (0.15 ml) in DMSO (4 ml) was stirred under an inert atmosphere at 70-80°C for 4 h, adding after each hour more CH_3I (0.1 ml, for a total of 0.45 ml, 7.2 mmol CH_3I). At the end of the reaction the mixture was poured into water (70 ml) and extracted with chloroform (3 × 40 ml). The extract was evaporated to small volume (~25 ml) and passed through an Al_2O_3 column (l = 15 cm, d = 1.5 cm) with $CHCl_3$ as eluant. The yellow green fraction with R_f 0.78 which was collected contained 0.05 g (43 %) of a mixture (37:63) of the isomeric N-methyl derivatives **7** and **8**. After three recrystallizations from octane practically pure 1-methyl-2-trifluoromethylperimidin-7-carbaldehyde **8** was obtained as greenish-yellow crystals; mp 181-184°C. Found %: C 60.15; H 3.41; N 9.80. $C_{14}H_9F_3N_2O$. Calculated, %: C 60.43; H 3.24; N 10.07.

The experiment was difficult to reproduce and in a number of other trials the total yield of compounds **7** and **8** was considerably lower.

Acetylation of 2-Trifluoromethylperimidine (4). A mixture of compound **4** (0.47 g, 2 mmol), glacial acetic acid (0.17 ml, 3 mmol), and polyphosphoric acid (6 g, 84% P_2O_5) was stirred for 4 h at 60-65°C, poured with stirring into cold water (100 m), ammonia was added to pH ~3-4, and the mixture was extracted with ethyl acetate (3 x 20 ml). The solvent was evaporated to minimal volume (~ 7 ml), and the residue was placed on a silica gel column, the first pale yellow fraction was eluted with benzene, and the second orange-yellow fraction with ethyl acetate. 4(9)-Acetyl-2-trifluoromethylperimidine (**9**) (0.05 g, 9%) was obtained from the first fraction after evaporating the solvent as lemon yellow crystals; mp 166-167°C (decane). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, J (Hz): 2.61 (3H, s, CH_3); 7.10 (1H, d, J_{78} = 9.1, 7-H); 7.24 (1H, dd, J_{45} = 7.6, J_{56} = 0.8, 4-H); 7.38 (1H, dd, J_{65} = 8.2, J_{64} = 0.8, 6-H); 7.52 (1H, d, J_{87} = 9.1, 7-H); 7.57 (1H, dd, J_{54} = 7.6, J_{56} = 8.2, 6-H); 13.2 (1H, br. s, NH). ^{1}H NMR spectrum (DMSO-d_6, 20°C), δ, ppm, J (Hz): 2.62 (3H, s, CH_3); 7.20 (1H, br. d, J_{45} = 7.3, 4-H); 7.27 (1H, d, J_{78} = 9.1, 7-H); 7.55 (1H, br. d, J_{65} = 8.0, 6-H); 7.66 (1H, dd, 5-H); 7.77 (1H, d, J_{87} = 9.1, 8-H); 13.2 (1H, br. s, NH). IR spectrum (nujol mull), ν, cm^{-1}: 1633 (C=O), 1620, 1580 (cyclic system). Found, %: C 60.60; H 3.37; N 9.92. $C_{14}H_9F_3N_2O$. Calculated, %: C 60.43; H 3.24; N 10.07.

6(7)-Acetyl-2-trifluoromethylperimidine **2** was obtained as orange crystals (0.42 g, 76%); mp 218-219°C (decane) from the second fraction. IR spectrum (nujol mull), n, cm^{-1}: 3180-3093 (NH), 1633 (C=O), 1613, 1580 (cyclic systems). Found, %: C 60.28; H 3.40; N 10.20. $C_{14}H_9F_3N_2O$. Calculated, %: C 60.43; H 3.24; N 10.07.

6(7)-Acetylperimidine (10) was obtained by a known method [8]. ^{1}H NMR spectrum ($CDCl_3$, 20°C), δ, ppm, *J* (Hz): 2.58 (3H, s, CH_3); 6.45 (1H, br. d, 9(4)-H); 6.74 (1H, br. dd, 4(9)-H); 7.36 (1H, s, 2-H); 7.38 (1H, dd, $J_{8(5)9(4)}$ = 8.0, $J_{8(5)7(6)}$ = 8.3, 8(5)-H); 7.84 (1H, d, $J_{5(8)4(9)}$ = 8.0, 5(8)-H), 8.62 (1H, dd, $J_{7(6)8(5)}$ = 8.3, $J_{7(6)9(4)}$ = 0.7, 7(6)-H). ^{1}H NMR spectrum (DMSO-d_6, 120°C), δ, ppm, *J* (Hz): 2.52 (3H, s, CH_3); 6.48 (1H, d, $J_{9(4)8(5)}$ = 8.1, 9(4)-H); 6.83 (1H, br. dd, 4(9)-H); 7.39 (1H, dd, $J_{8(5)9(4)}$ = 8.0, $J_{8(5)7(6)}$ = 8.7, 8(5)-H); 7.62 (1H, s, 2-H); 8.00 (1H, d, $J_{5(8)4(9)}$ = 8.1, 5(8)-H); 8.52 (1H, dd, $J_{7(6)8(5)}$ = 8.7, $J_{7(6)9(4)}$ = 0.7, 7(6)-H); 11.36 (1H, br. s, NH).

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