MANIFESTATION OF AZA-EFFECT IN ^{13}C NMR SPECTRA OF ACETYLDIAZINES

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Carbon magnetic resonance spectra are reported for isomeric acetyldiazines, and an analysis is made of the changes in chemical shifts of the acetyl-group and ring carbon atoms due to the aza-effect in the isomers. In the α-acetylazine series, special features of spectral properties have been revealed for 2-acetylpyrimidines.

In an earlier study of the equilibrium CH-acidity of methyl ketones of the azine series, it was noted that additivity in manifestation of the aza-effect breaks down in the case of 2-acetylpyrimidine [1]. This peculiarity was related to the observation of a molecular conformation for 2-acetylpyrimidine with a torsion angle on the order of 90°, which was observed in a study of the conformational structure of acetylpyrimidines, using the dipole moment method [2]. In order to obtain additional data, we turned to the carbon resonance method, which is widely used in studying conformations of aromatic methyl ketones [3-5], since it reflects the distribution of charges and is sensitive to substitution effects. In the past, however, ^{13}C NMR studies of acetylazines have been limited to obtaining data on isomeric acetylpyrimidines [6-11], among which the 2-isomer has certain special features: an unusually weak influence of the substituent on the CS (chemical shift) of the C_2 ring atom ($\Delta\delta C_{ipso}$) and an unexpected upfield shift of the signal of the methyl group [7, 10].

We have examined the ^{13}C NMR spectra of acetyldiazines in order to reveal differences among the isomers in the CSs of the C=O and CH_3 groups of the substituent, and also in the relative CSs of the ring carbon atoms (C_{ipso} and C_p), reflecting both the electronic structure of the substituent and the intramolecular interaction of the substituent with the aromatic ring. Here, because of the generally complex character of the influence of isomeric diazine rings on the CS, our data have permitted us to examine only the most general relationships.

For pyridines that have carbon-containing substituents (CH_3, CHO, CN, $COCH_3$), it has been noted that the carbon atom is the least shielded when it is attached to position 2 of the ring [7]. We observed an analogous situation in the spectra of other acetyldiazines: The signal of the C=O group in the α-isomers is shifted ~2 ppm downfield in comparison with the other isomers (Table 1). The only exceptions are the 2-acetylpyrimidines, in which, despite the presence of two α-nitrogen atoms, the carbonyl signal remains in the region that is characteristic for the β- and γ-isomers and acetophenone. Moreover, this trend is also observed in the CS of the CH_3 group: The same as in the 2-acetylpyridines [7, 10], we find that in all α-acetyldiazines the signal of the methyl group is shifted upfield by as much as ~1.5 ppm; and only for the 2-acetylpyrimidines do we fail to observe such a change.

In acetophenone, the positions of the C_p and C_{ipso} signals are considerably different from those in benzene (by ~4 and ~9 ppm, respectively) [6, 12]. The change of C_p in acetylazines is less pronounced than in the aromatic series; but even within the framework of variations of $\Delta\delta C_p$ (depending on the type of diazine ring), the smallest changes of CS pertain to the 2-acetylpyrimidines (Table 2). In the β- and γ-acetylpyrimidines [6, 8, 10] and the corresponding diazines (Table 2), the influence of the acetyl group on the CS of C_{ipso} (the same as in acetophenone) amounts to approximately 6 to 8 ppm. Of special interest, however, are the shifts of the C_{ipso} atom of the ring in the α-acetylazines, since the influence of the substituent in these compounds is unusually weak (some 2 to 3 ppm; compare [7, 10]). Of the α-acetyldiazines that have been examined,

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TABLE 1. ^{13}C NMR Spectra of Acetyldiazines

Compound	Chemical shift, δ, ppm (from TMS)						
	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	C=O	CH_3
Acetophenone*	128,56	128,05	133,04	128,05	128,56	197,76	26,55
2-Acetylpyridine	152,96	121,03	137,31	127,53	149,10	199,33**	25,46
3-Acetylpyridazine	—	153,78	124,43	128,05	155,66	198,17	25,88
4-Acetylpyridazine	—	148,22	132,25	124,27	152,81	197,47	27,01
2-Acetylpyrimidine	159,76	—	157,71	123,46	157,71	197,04	26,91
4,6-Dimethyl-2-acetyl-pyrimidine	159,44	—	167,05	121,79	167,05	197,47	26,90
4,6-Diphenyl-2-acetyl-pyrimidine	160,19	—	164,51	113,80	164,51	197,47	27,17
4-Acetylpyrimidine	159,49	—	158,68	117,04	158,13	198,95	25,39
5-Acetylpyrimidine	160,90	—	156,60	129,52	156,60	196,35	27,01
Acetylpyrazine	148,11	142,61	—	147,25	144,01	198,87	25,61

*C_{ipso} 136.77 ppm.

**In [10], an erroneous value was given.

TABLE 2. Relative CSs in ^{13}C NMR Spectra of Acetyldiazines

Compound	i-N	$\Delta\delta_{C_i}^{exp}$, ppm		$\Delta\Delta\delta_{C_i}^{add}$, ppm		$\Delta\delta_{COCH_3}^{add}$, ppm		$\Delta\delta_{\alpha\text{-N}}$, ppm	
		C_p	C_{ipso}	C_p	C_{ipso}	C=O	CH_3	C=O	CH_3
I	α,β	3,77	1,89	+0,86	-1,29	-0,77	-0,44	+0,80	-0,99
II	α,β	2,03	2,89	-0,88	-0,29	-0,07	-0,31	+1,50	-1,26
III	α,γ	—	1,56	—	+0,03	-0,67	-0,46	+0,90	-1,41
IV	α,α	1,42	1,16	-1,39	+2,74	-4,36	+2,26	-2,29	+1,41
V	β,β	2,30	7,48	-0,71	-0,46	-0,63	-0,18	—	—
VI	β,γ	—	5,39	—	-0,90	-0,19	-0,11	—	—
VII**	—	4,63	8,36	—	—	—	—	—	—

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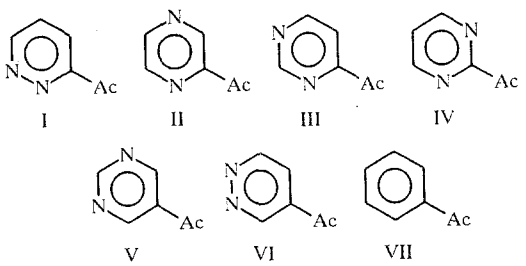

I II III IV V VI VII

**$\delta C_{benzene}$ in DMSO-d_6 128.41 ppm [13].

2-acetylpyrimidine is distinguished by the smallest values of $\Delta\delta C_{ipso}$. The 4,6-dimethyl-2-acetylpyrimidine has respective CSs of 1.8 ppm ($\Delta\delta C_p$) and 1.9 ppm ($\Delta\delta C_{ipso}$). Thus, the changes we have examined in both C_p and C_{ipso} signals in isomeric acetyldiazines indicate that the acetyl group in 2-acetylpyrimidines has a very small perturbing effect on the azine system as a whole.

Aza-effects in derivatives of azines can often be analyzed successfully on the basis of additivity of the influence of aza groups [1, 14]. Since a rather extensive set of acetylazines is available, it is feasible to examine the question of additivity of the influence of aza groups on CSs in ^{13}C NMR spectra. To this end, we calculated changes in CSs of the ring carbon atoms and of the substituent, using the equations

$$\Delta\delta_{Ci}^{calc} = \Delta\delta_{\text{acetophenone}} + \sum_{N_i} [\Delta\delta_{\text{i-pyridine}} - \Delta\delta_{\text{acetophenone}}]$$

and

$$\delta_{COCH3}^{calc} = \delta_{\text{acetophenone}} + \sum_{N_i} [\delta_{\text{i-pyridine}} - \delta_{\text{acetophenone}}],$$

where the summation is performed relative to the number and position of the nitrogen atoms in the ring. Then we determined the deviations from additivity $\Delta\Delta\delta_{Ci}^{add}$ and $\Delta\delta_{COCH3}^{add}$ as the differences between the experimental and calculated values.

We also used another approach in which we examined changes in CS of the carbon atoms of the substituent due to the introduction of an additional α-nitrogen atom into the isomeric acetylpyridines

$$\Delta\delta_{\alpha\text{-N}} = \delta_{\alpha\text{-acetyldiazine}} - \delta_{\text{i-pyridine}}$$

When we analyze the relative CS values obtained on the basis of different initial premises, we still arrive at a fairly clear-cut situation: In all cases, the greatest deviations from additivity are characteristic for the α,α-position of the aza groups, i.e., for 2-acetylpyrimidine. Moreover, for $\Delta\Delta\delta_{Cipso}$, $\Delta\delta_{CH3}$, and $\Delta\delta_{\alpha-N}$, we observe effects from two α-nitrogen atoms that are opposite in sign in comparison with the effect from a single nitrogen atom, indicating a different intramolecular interaction of the substituent with the ring in these cases.

Thus, on the basis of the entire set of data that we have obtained on the character of changes in the carbon magnetic resonance spectra of 2-acetylpyrimidine in comparison with other acetyldiazines, we are justified in speaking of fundamental differences between the 2-acetylpyrimidine and its analogs, primarily as a result of the less intense interaction of the acetyl group and the pyrimidine ring. In turn, this may reflect deviation of the acetyl group from the plane of the ring, as well as the presence of a large torsion angle at the C_2—CO bond; this is consistent with data obtained previously on its conformational structure [2].

EXPERIMENTAL

The ^{13}NMR spectra were recorded in a Bruker HX-90 spectrometer (working frequency 22.63 MHz) and a VP-200 spectrometer (working frequency 50.32 MHz), in solution in DMSO-d_6 at a concentration of 0.5-1.0 M.* The acetyldiazines were obtained by known methods, and their constants matched the literature values. Data on ^{13}C NMR spectra of unsubstituted azines in DMSO-d_6 were taken from the following sources: pyridine [10]; 4,6-dimethylpyrimidine [15]; isomeric diazines [14, 16].

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