THE TAUTOMERISM OF 5-AMINOTETRAZOLE

VII. Synthesis, Structure, and Spectra of Diacyl Derivatives of 5-Amino-1-Methyltetrazole and 5-Amino-2-Methyltetrazole*

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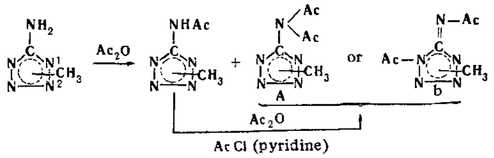
In the reaction of 5-amino-1-methyltetrazole and 5-amino-2-methyltetrazole with carboxylic acid anhydrides or chlorides, diacylamides are obtained in addition to monoacyl derivatives. The results of independent synthesis and a study of IR and PMR spectra have shown that in the diacylamides considered both acyl groups are attached to the same (the exocyclic) nitrogen atom.

The present work is devoted to a study of the structure of the products of the reaction of 5-acylamino-1-methyltetrazole and 5-acylamino-2-methyltetrazole—tautomeric compounds [2–4] capable of dual reactivity [5]—with carboxylic acid anhydrides and chlorides. The diacyl amides so obtained may theoretically have either of structures A or B.

It has been shown previously that the diarylsulfonyl derivaties of 5-amino-1-methyltetrazole and 5-amino-2-methyltetrazole (1- and 2-methyl-5-AT) have structure A [6]. But while the disulfonamides of N-heterocyclic amines (with heterocycles capable of amino-imino tautomerism) have been studied extremely intensively [7, 8], diacyl derivatives containing carboxylic acid residues have been studied to an incomparably smaller extent.

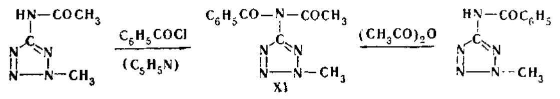
Diacyl derivatives of 1- and 2-methyl-5-AT are obtained together with the monoacyl derivatives by the reaction of these amines with acid anhydrides. The reaction of the monoacyl derivatives with the corresponding acyl chlorides in pyridine gives the same diacylamides.



$Ac_2O = (CH_3CO)_2O$, $(C_2H_5CO)_2O$; $AcCl = CH_3COCl$, C_6H_5COCl

Structure of the diacyl derivatives of 2-methyl-5-AT was established by the independent synthesis of diacylamides having different acyl residues. The reaction of 5-acetylamino-2-methyltetrazole with benzoyl chloride in pyridine gave compound XI, mp 109–110° C. A substance with the same melting point is formed by heating 5-benzoylamino-2-methyltetrazole with acetic anhydride.

The two substances proved to be identical with one another in respect to their elementary analyses, IR spectra, and a mixed-melting point test, which is possible only if the two acyl groups are attached to the exocyclic nitrogen atom.



In the case of the diacyl derivatives of 5-amino-1-methyltetrazole, it was impossible to effect the synthesis of a diacylamide containing different acyl residues. When 5-acetylamino-1-methyltetrazole and 5-propionylamino-2-methyltetrazole were treated with benzoyl chloride in the presence of pyridine, a transacylation reaction took place with the formation of the mono- and dibenzoyl derivatives of 5-amino-1-methyltetrazole. In exactly the same way, the reaction of 5-benzoylamino-1-methyltetrazole with acetic anhydride formed the mono- and diacetyl derivatives of 5-amino-1-methyltetrazole. In the case of the diacylamides of 5-amino-1-methyltetrazole, the transacylation reaction gives grounds for assuming a structure in form A for these compounds. In actual fact, if the second acyl group were attached to a ring nitrogen atom (structure B), transacylation would most probably not take place since of two acyl groups attached to the exocyclic and to a ring nitrogen atom the acyl group attached to the ring nitrogen atom would split out first (this has been shown for the case of disulfonamide derivatives of 2-aminothiazole [9]).

The transacylation reaction also takes place in the case of 5-amino-2-methyltetrazole derivatives, but to a smaller extent. Consequently, it is possible to isolate—in low yield (25–35%), it is true—diacylamides containing different acyl groups (benzoyl and acetyl). However, in attempts to obtain a diacyl derivative containing acetic and chloroacetic residues, for example by the reaction of the chloroacetyl derivative of 5-amino-2-methyltetrazole with acetic anhydride, only 5-diacetylamino-2-methylaminotetrazole was isolated.

In the carbonyl region, the IR spectra of the diacyl derivatives of 5-amino-1-methyl- and 5-amino-2-methyltetrazoles (Table 1) taken in the crystalline state and in CH_3Cl solution there is a single band, which shows the structure of the diacyl derivatives as form A for both 5-amino-2-methyl- and 5-amino-1-methyltetrazoles. It could be assumed that if the diacylamides have the structure of form B, there should be two carbonyl bands in the IR spectrum corresponding to the presence of acyl groups both in the ring

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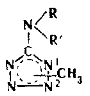
*For part VI, see [1].

Table 1

IR Spectra (cm^{-1}) of Diacyl and Monoacyl Derivatives of 5-Amino-1-methyltetrazole and 5-Amino-2-methyltetrazole



Compound	R	R′	Crystals		Solution in $CHCl_3$	
			ν_{CO}	vibrations of the C=N and N=N bonds of the ring	ν_{CO}	vibrations of the C=N and N=N bonds of the ring
			1-Methyl derivatives			
I	$COCH_3$	$COCH_3$	1718, 1770	1537	1744 1748*	1530 1533*
II	H	$COCH_3$	1709	1582	—	—
III	COC_2H_5	COC_2H_5	1730 1813 V. W.	1528	1737 —	1522 —
IV	H	COC_2H_5	1720	1584		
V	COC_6H_5	COC_6H_5	1714	1538	1711	1527
VI	H	COC_6H_5	1692	1576	—	—
			2-Methyl derivatives			
VII	$COCH_3$	$COCH_3$	1725	1505	1732	1501
VIII	H	$COCH_3$	1726	1577	—	—
IX	COC_6H_5	COC_6H_5	1703	1499	1708	1498
X	H	COC_6H_5	1711	1567	—	—
XI	$COCH_3$	COC_6H_5	1702, 1723	1499	1719	1498

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*In CCl_4 solution

Table 2

5-(Diacylamino)-1-methyl- and -2-methyltetrazoles

Compound	Method	Reaction time, min	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
					C	H	C	H	
I	a	90	79	$C_6H_9N_5O_2$	39.32	5.01	39.34	4.91	30
III*	a	180	95—96	$C_8H_{13}N_5O_2$	46.01	5.90	45.48	6.20	0.96
V	b	60	176	$C_{19}H_{13}N_5O_2$	62.40	4.34	62.53	4.26	66
VII	a	30	68—69	$C_6H_9N_5O_2$	39.67	4.99	39.34	4.91	48
IX**	b	150	129—130	$C_{19}H_{13}N_5O_2$	62.28	4.19	62.53	4.26	50
XI	a, b	60	109—110	$C_{11}H_{11}N_5O_2$	54.09	4.52	53.87	4.52	37

*The main product (yield 67%) was 1-methyl-5-propionylaminotetrazole (IV), mp 85-86° C (needles, from benzene). Found, %: C 38.87; H 6.07. Calculated for $C_5H_9N_5O$, %: C 38.70; H 5.84.

**The reaction was carried out at the boil in a tenfold excess of pyridine.

and on the exocyclic nitrogen atom. Just such a pattern was observed, for example, in the IR spectra of diacyl derivatives of 2-aminothiadiazolidine (structure B), which showed two carbonyl bands in the crystalline state and in solution, the difference between these bands being 20–30 cm^{-1} [10].

Among the diacylamides considered, an exception is formed by the diacetyl derivative of 5-amino-1-methyltetrazole which, in the crystalline state, shows two equally strong bands in the carbonyl region, at 1718 and 1770 cm^{-1}. But in solution this compound, like all the other diacylamides, has a single band in the 1744 cm^{-1} region. The phenomenon observed, the existence of two carbonyl bands in the crystalline state and one band in solution, is similar to the analogous phenomenon, also difficult to explain, in the case of some carboxylic acid anhydrides [11]. The splitting of the carbonyl band in the case of the diacylamide XI is completely natural, since it is apparently connected with the different nature of the acyl groups present.

The PMR spectrum of 5-(diacetylamino)-1-methyltetrazole has two sharp singlets at 3.10 and 1.59 ppm which, from their position and intensity ratio (1: 2) can be ascribed to the N-methyl group and two chemically equivalent methyl groups of acetyl residues. Similarly, in the spectrum of 5-(diacetylamino)-2-methyltetrazole there are two signals at 3.61 and 1.32 ppm, assigned, respectively, to the absorption of the three protons of a N—CH_3 group and the six protons of two equivalent acetyl groups. It is understandable that if the acyl groups were present on different nitrogen atoms, their methyl groups could not be equivalent and then the signal corresponding to the protons of these methyl groups would be split.

The observed features of the NMR spectra, and also those of the IR spectra, permit the conclusion that the diacylated 5-amino-1-methyl- and 5-amino-2-methyltetrazoles have structure A, i.e., the diacylamides of 5-amino-1-methyl- and 5-amino-2-methyltetrazoles have the same structure as the diarylsulfonyl derivatives of the same amines [6]. Thus, a decrease in the electrophilicity of the acyl residue involves no change in the nature of the structure of the diacylaminotetrazoles.

EXPERIMENTAL

The IR spectra* were obtained on an IKS-14 instrument with the substances in the crystalline state in the form of mulls in paraffin oil and in solution in $CHCl_3$ (concentration 1%, layer thickness 0.25 mm). The PMR spectra* were recorded on a JMH-3 instrument at 40 MHz. The substances were studied in the form of 10% solutions in $CHCl_3$. The chemical shifts were measured in $CHCl_3$ and calculated relative to tetramethylsilane.

For the syntheses of the 5-acylamino-1-methyl- and -2-methyltetrazoles, see [2].

The diacylaminotetrazoles were obtained: a) by boiling the corresponding amine with anhydride of the acid; or b) by the reaction of an acylamino derivative with an acyl chloride in the presence of pyridine. Examples of the procedures are given below.

5-Diacetylamino-1-methyltetrazole (I). A) A mixture of 6.3 g of 5-amino-1-methyltetrazole and 31 ml of acetic anhydride was boiled for 1.5 hr. After cooling, the precipitate of 5-acetylamino-1-methyltetrazole (II) was filtered off and was washed with benzene. Yield 4 g, mp 164° C (from ethanol). The filtrate was evaporated, and the residue was washed with water and recrystallized from ethanol. This gave 3.5 g (30%) of **I**, mp 79° C (prisms.)

B) Equimolar amounts (0.01 mole) of II, pyridine, and acetyl chloride were heated at 80° C for 1 hr. After cooling, 5 ml of water was added and the colorless precipitate was filtered off. The yield of I was 0.5 g (27%), mp 78–79° C (from ethanol). The substance was identical with the diacylamine obtained in the preceding experiment. All the diacylamines obtained, unlike the monoacylamines, were readily soluble in benzene and insoluble in water and alkalis in the cold.

The experimental details and characteristics of the diacylamines are given in Table 2.

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