Synthesis, Structure and Properties of *N*-Acetylated Derivatives of Methyl 5-Amino-1*H*-[1,2,4]triazole-3-carboxylate

Anetta Dżygiel,[a] Barbara Rzeszotarska,*[,a] Elżbieta Masiukiewicz,[a] Piotr Cmoch,[b] and Bohdan Kamieński[b]

[a] *Institute of Chemistry, University of Opole; Oleska 48, 45–052 Opole, Poland: and* [b] *Institute of Organic Chemistry, Polish Academy of Sciences; Kasprzaka 44/52, 01-224 Warsaw, Poland.*

Received August 4, 2003; accepted November 1, 2003

Methyl 5-amino-1*H*-[1,2,4]triazole-3-carboxylate hydrochloride (1) and free ester (2) were obtained and 2 was reacted with Ac_2O to give the acetylated products 3—6. Compounds 1—6 were studied using HPLC, GC-MS, FTIR and multinuclear NMR spectroscopy, including the cross-polarisation magic angle spinning (CPMAS) technique. The results of the acetylation of 2 were compared to those of the acetylation of 5-amino-1*H*-[1,2,4]triazole, and for 2 a significant decrease in the susceptibility to acetylation was found. The reaction of 2 with Ac_2O at 20 °C, regardless of the amount and the concentration of the latter, including neat Ac_2O, proceeds fully regioselectively and leads to one product: methyl 1-acetyl-5-amino-1*H*-[1,2,4]triazole-3-carboxylate (3). In sharp contrast to 5-amino-1*H*-[1,2,4]triazole, neither an additional monoacetylated isomer, whether annular or exocyclic, nor any diacetylated derivative could be detected. The diacetylation of 2 requires the process to be carried out in neat boiling Ac_2O and, as in the case of 5-amino-1*H*-[1,2,4]triazole, gives two diacetylated isomers. These are methyl 1-acetyl-3-(acetylamino)-1*H*-[1,2,4]triazole-5-carboxylate (4) and 1-acetyl-5-(acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate (5). Hypothetical pathways of their formation have been suggested. A mixture of 4 and 5 upon hydrolysis of the ring acetyl group gives the monoacetylated derivative methyl 5-(acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate (6). The spectroscopic, structural and conformational characteristics of compounds 1—6 have been given and methods for their preparation have been provided.

Key words acylation; hetareneamino acid; intramolecular hydrogen bonding; FTIR spectrum; ^1H, ^{13}C, ^{15}N spectrum; cross-polarisation magic angle spinning (CPMAS) spectrum

Azoleamino acids have the potential to form hetarene oligoamides, which belong to the most promising small molecules controlling gene expression[1—3] and, moreover, to be the constituents of natural,[4] modified[5] and artificial[6,7] peptides useful for biological and non-biological purposes. Furthermore, they can serve as external, molecular scaffolds for the stabilisation of secondary peptide structures.[8—11] Their usefulness results from the flat, rigid ring system capable of acting as both a hydrogen bond acceptor and/or donor. It seems that the readily accessible *C*-amino-[1,2,4]triazole-carboxylic acid[12] could also be applied to the above ends. However, its chemistry, including the structural and spectral properties of its derivatives, of which only the methyl ester **2**[12] and its 1-acetyl congener **3**[13] are mentioned in the literature, is little recognised.

The exocyclic amino group of azoleamino acids offers a significant resistance to acylation and makes the synthesis of the carboxamides difficult.[14] The ability of *C*-amino-[1,2,4]triazole-carboxylic acid to undergo acylation is unexplored. In this paper, we present the studies on the acetylation of methyl 5-amino-1*H*-[1,2,4]triazole-3-carboxylate (**2**) with neat Ac_2O. The ester **2** is the simplest protected form of *C*-amino-[1,2,4]triazole-carboxylic acid allows one to avoid undesired side reactions at its free carboxyl group. As tools for structure determination we used various analytical methods: HPLC, GC-MS, FTIR, and multinuclear NMR spectroscopy, including the cross-polarisation magic angle spinning (CPMAS) technique. The results were compared to those from the acetylation of the parent substance of the investigated acid, *i.e.* 5-amino-1*H*-[1,2,4]triazole (AT).[15] The structures of compounds **1**—**6** obtained in this work are given in Chart 1.

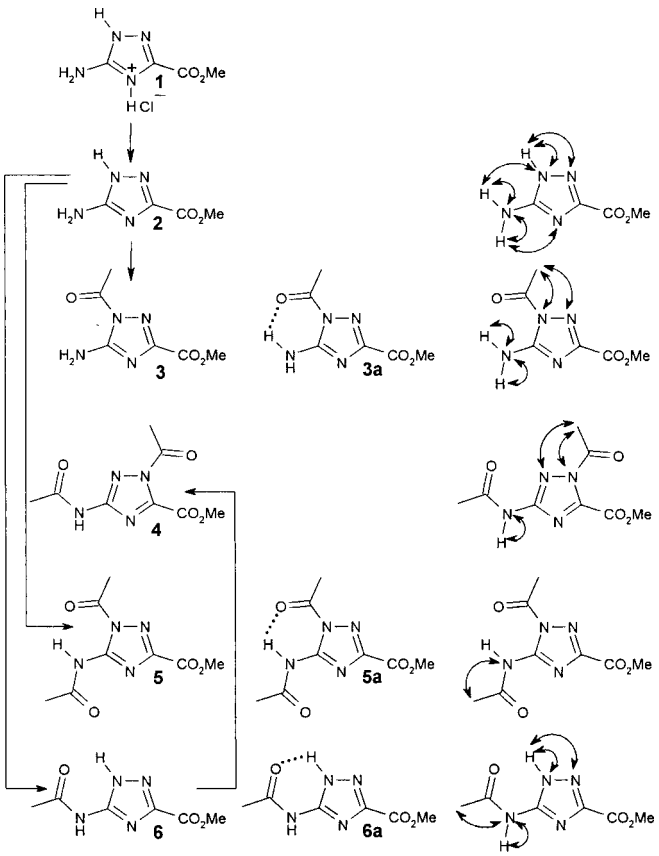

Chart 1. Structure of the Obtained Compounds **1**—**6** together with Their Preparative and NMR Connectivity

⋯: Intramolecular hydrogen bonds.

* To whom correspondence should be addressed. e-mail: rzeszot@uni.opole.pl

Results and Discussion

Methyl 5-Amino-1*H*-[1,2,4]triazole-3-carboxylate Hydrochloride (1) and Free Ester (2) Ester **2** was obtained in 42% yield by direct esterification of the corresponding acid in the presence of gaseous HCl, and subsequent neutralisation.[12] We applied the $SOCl_2$–MeOH method, highly recommended for efficient esterification in peptide chemistry[16] and used the advised threefold excess of $SOCl_2$, which produced the hydrochloride **1** in an 87% isolated yield. The crude **1** was neutralised to furnish 77% of free ester **2** based on the initial acid (Table 1).

The multinuclear NMR, the ^1H–^{15}N gradient heteronuclear single quantum coherence (g-HSQC), the gradient heteronuclear multiple bond connectivity (g-HMBC) in DMF-d_7 and the CPMAS experiment (Tables 2, 3; Chart 1) reveal that in both solutions and the solid state, **2** has the structure of methyl 5-amino-1*H*-[1,2,4]triazole-3-carboxylate and its hydrochloride **1** has an 1H,4H$^+$-triazolium cation. The cations of this tautomeric type are commonly found in the crystals of 5-amino-1*H*-[1,2,4]triazolium salts.[17—21] The CCl_4 FTIR spectrum of **2** contains the broad multiplet band in the region of the bonded NH and the broad C=O band centred at

Table 1. Methyl 5-Amino-1*H*-[1,2,4]triazole-3-carboxylates **1** and **2** and Acetylated Derivatives **3**—**6**

Compd.	mp[a] (°C)	TLC[b] *Rf*				HPLC		Molecular formula (mass)	Elemental analysis Calcd. (Found) (%)			Yield (%)
		A	B	C	D	t_R (min)	Purity (%)		C	H	N	
1	180	0.78	0.44	0.18		2.47	99.6	$C_4H_6N_4O_2 \cdot HCl$ (178.58)	26.90 (26.91)	3.95 (3.83)	31.35 (31.29)	87.2
2	233[c]	0.78	0.44	0.18		2.47	100.0	$C_4H_6N_4O_2$ (142.13)	33.80 (34.10)	4.26 (4.11)	39.42 (39.28)	76.8[d,e]
3a	214[f] 226[g]	0.72	0.62	0.57		8.22	99.7	$C_6H_8N_4O_3$ (184.15)	39.14 (39.10)	4.38 (4.43)	30.41 (30.28)	100.0
4	247	0.82		0.59	0.42	9.27	95.5	$C_8H_{10}N_4O_4$ (226.19)	42.48 (42.67)	4.46 (4.58)	24.77 (24.77)	58.4
5a	159	0.82	0.54	0.59	0.42	7.83	99.3	$C_8H_{10}N_4O_4 \cdot 0.25H_2O$ (230.69)	41.65 (41.84)	4.59 (4.38)	24.28 (24.19)	60.0
6a	229	0.72	0.80	0.63	0.17	4.13	99.5	$C_6H_8N_4O_3$ (184.15)	39.14 (39.11)	4.38 (4.56)	30.41 (30.18)	98.0

a) Recorded on a DSC-2010 calorimeter (Thermal Analysis Instruments) under nitrogen in a closed copper vessel with a heating rate of 10 °C·min^{-1}. *b*) TLC aluminum sheets covered with silica gel 60 (Merck 105553); A, *n*-BuOH–AcOH–AcOEt–H_2O (1 : 1 : 1 : 1 v/v/v/v); B, $CHCl_3$–MeOH–dioxane–NH_4OH concd. (12 : 7 : 5 : 1 v/v/v/v); C, $CHCl_3$–MeOH–AcOH (95 : 5 : 3 v/v/v); D, AcOEt. Visualised with ninhydrin and Cl_2-tolidine reagent. *c*) mp 220 °C.[12] *d*) Based on the initial acid. *e*) Yield 41.5%.[12] *f*) mp 216 °C.[13] *g*) Mp upon crystallization from methanol–diethyl ether.

Table 2. Chemical Shifts (ppm) of ^1H, ^{13}C and the Half-Height Width of ^1H-NMR Signals (Hz) for Methyl 5-Amino-1*H*-[1,2,4]triazole-3-carboxylates **1** and **2** and Acetylated Derivatives **3**—**6**

Compd.	N**H**$_2$	N**H** amide	N**H** ring	**H**$_3$**C**–O–**C**O ester			**H**$_3$**C**–**C**O–N amide			**H**$_3$**C**–**C**O–N ring			C-3	C-5
1[a]	10.70		10.70	4.11	53.2	157.8							143.7	154.6
CPMAS					55.0	158.5							141.1	151.5
2[b]	7.15 [8.20]		13.40 [5.50]	3.80	52.0	161.6							152.4	158.7
2[a]	6.45		12.90	3.80	51.9	161.7							152.9	158.7
CPMAS	7.62				53.3	161.5							150.5	156.9
3a[b]	8.63 [16.8]			3.96	52.8	160.9				2.56	23.1	172.5	152.6	158.2
3a[a]	7.70 [12.7]			3.90	52.6	161.0				2.62	23.1	172.6	153.2	158.5
CPMAS					53.4	160.7					21.2	172.9	152.8	157.9
4[a]		10.40 [12.3]		3.96	53.0	162.0	2.37	24.2	169.2	2.73	23.6	172.0	152.5[c]	151.3[d]
CPMAS[e]					55.2	158.8		21.9	169.2		25.5	172.8	150.9[c]	152.5[d]
					56.6	160.1		23.9	172.1		26.9	173.5		
5a[b]		16.70 [50.7]		3.98	53.5	[f]	2.46	[f]	[f]	2.46	[f]	172.7	[f]	[f]
5a[a]		15.90 [268.0]		4.16	53.2	158.4	2.44	25.7	[f]	2.44	25.7	172.4	149.4	156.6
CPMAS					54.2	158.2		26.3[g]	172.8[g]		22.9[g]	171.4[g]	149.5	156.4
6a[b]		12.15 [5.4]	14.58 [7.2]	3.90	52.5	161.2	2.24	23.0	170.3				151.8	150.6
6a[a]		11.70 [68.0]	14.12 [91.6]	3.90	52.2	161.2	2.24	22.9	170.2				152.1	150.8
CPMAS					53.0	160.9		24.0	171.0				150.2	150.2

a) Measured at 30 °C. *b*) Measured at −50 °C. *c*) The C atom connected with the COOMe group. *d*) The C atom connected with the NH group. *e*) Doubled signals probably owing to two solid state forms. *f*) Not recorded in a ^{13}C-NMR spectrum. *g*) The signals could be reversed in the corresponding pairs.

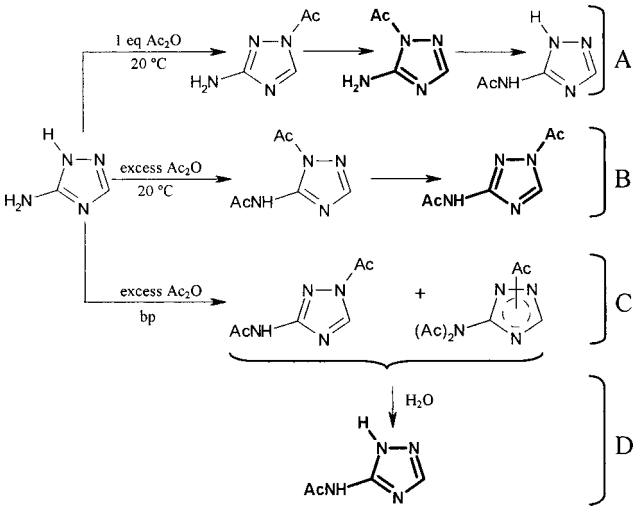

Fig. 1. Reactivity of AT with Neat Ac_2O and Products Obtained (in Bold)[15]

$1734\,cm^{-1}$, thus proving some degree of association. The latter band has a high-frequency inflexion and was decomposed into two curve-fitted components to obtain the stretching frequency for the carbonyl free $C{=}O_{ester\text{-}f}$, $1744\,cm^{-1}$, and bonded $C{=}O_{ester\text{-}b}$, $1730\,cm^{-1}$ (Table 4).

Methyl 1-Acetyl-5-amino-1*H*-[1,2,4]triazole-3-carboxylate (3) We have previously found[15] the acetylation of AT in DMF or DMSO solutions with 1 eq Ac_2O at 20 °C to be almost instantaneous. Firstly the kinetic product 1-acetyl-3-amino-1*H*-[1,2,4]triazole was formed (Fig. 1A), which we could not isolate. This quickly was transformed into the thermodynamic compound 1-acetyl-5-amino-1*H*-[1,2,4]triazole. The latter is also unstable at room temperature and easily isomerises into the 5-acetylamino derivative, both in solutions and in the solid state.

The monoacetylation of ester **2** is slower than that of AT. Under the same conditions, AT reacts with 1 eq Ac_2O in 74%, whereas **2** reacts merely in 15% (dilute DMSO solution, 20 °C, 2 min). In sharp contrast to AT, the reaction of **2** with acetic anhydride at 20 °C, whatever amount and concentration of the latter, including neat Ac_2O, proceeds fully regioselectively and only results in compound **3**. Neither an additional monoacetylated isomer, whether annular or exocyclic, nor any diacetylated derivative could be detected. Hence, preparing the compound **3** in quantitative yield is feasible when neat anhydride is used as a medium. Compound **3**, unlike monoacetylated amino-1*H*-[1,2,4]triazoles, is stable with a long shelf-life. After one year of storage at room temperature, we observed neither the formation of the 5-acetylamino isomer **6** nor any other change. In a saturated DMF or Py solution up to 70 °C, the acetyl transfer is rather slow but it is much quicker at higher temperatures. For example, after heating **3** at 120 °C for 15 min, it reaches several percentages. Deacetylation accompanies this isomerisation unless a special moisture proofing is applied. In general, the higher the temperature the larger amount of **2** produced. Upon quick heating of **3** to the melting point (214 °C), 61% of **6** is formed, but longer heating causes some significant decomposition. So, the thermal rearrangement of **3** would not be the best way to prepare the compound **6**.

The ^{1}H- and ^{13}C-NMR spectra of **3** in DMSO-d_6 and the FTIR spectrum in KBr (Tables 2, 4) correspond to those of the methyl 1-acetyl-5-amino-1*H*-[1,2,4]triazole-3-carboxylate that was obtained *via* univocal linear substrate cyclisation.[13] The analysis of ^{15}N-NMR data in DMF-d_7, based on **2** and the effect of the *N*-acetylation in the pyrrole molecule,[22,23] indicates that it is the N-1 atom which bears the acetyl group (Table 3, Chart 1). The X-ray crystal analysis[24] confirms **3** to be the 1-acetyl-5-amino isomer and reveals that its NH_2 group is hydrogen-bonded intermolecularly with the $C{=}O_{ester}$ and intramolecularly with the $C{=}O_{N\text{-}ring}$. So, in the solid state the compound has the conformation **3a**. This enables us to consider the band at $1736\,cm^{-1}$ in its FTIR spectrum in KBr as the coincidental singlet originating from two indistinguishable frequencies, *viz.*, of the $C{=}O_{ester\text{-}b}$ and the $C{=}O_{N\text{-}ring\text{-}b}$ (Table 4).

Table 3. Chemical Shifts (ppm) of ^{15}N-NMR for Methyl 5-Amino-1*H*-[1,2,4]triazole-3-carboxylates **1** and **2** and Acetylated Derivatives **3**—**6**

Compound	NH_2	NH_{amide}	N-1	N-2	N-4
1[a]	−321.5		−198.4	−94.1	−222.6
CPMAS	−311.0		−208.2	−98.3	−230.1
2[b]	−333.0[c]		−200.0[c]	−93.6[c]	−169.0[c]
2[a]	−333.0[d]		−198.1[d]	−91.0[d]	−164.3[d]
CPMAS	−334.3		−189.8	−99.3	−173.9
3a[b]	−313.5		[e]	[e]	[e]
3a[a]	−314.3		−164.3	−97.3	−167.8
CPMAS	−309.8		−165.4	−105.2	−174.5
4[a]		−254.0[d]	−88.0[d,g]	−155.0[d,g]	−145.8
CPMAS[h]		−253.9	−93.4[f]	−158.7[g]	−153.6
		−252.8	−92.1[f]	−161.3[g]	−156.2
5a[a]		−204.6	[i]	[i]	−123.6
CPMAS		−205.5	−166.3	−89.4	−134.8
6a[b]		−253.9	−186.9	−86.9	[e]
6a[a]		−253.3	[e]	[e]	−152.9
CPMAS		−250.7	−189.3	−93.7	−163.0

a) Measured at 30 °C. *b*) Measured at −50 °C. *c*) Measured using ^{1}H–^{15}N NMR g-HMBC or g-HSQC correlation experiments. *d*) Measured using ^{15}N-NMR invgate sequence. *e*) Lack of correlation signals in the ^{15}N-NMR g-HMBC experiment. *f*) The –N=atom. *g*) The N atom substituted with the MeCO group. *h*) Doubled signals probably owing to two solid state forms. *i*) Not recorded in the ^{15}N-NMR spectrum obtained using invgate sequence.

The solution FTIR spectra point to compound **3** as being in form **3a**, *i.e.* monomer with the intramolecular hydrogen bond. The stretching frequencies of its amino group, 3516 and $3394\,cm^{-1}$ in CCl_4 and 3504 and $3388\,cm^{-1}$ in CH_2Cl_2, correspond to those of the methyl anthranilate amino group, 3509 and $3380\,cm^{-1}$, measured in the latter solvent.[25] The anthranilate is a well-known molecule with the bonded $H_2N{\cdots}C{=}O_{ring}$ intramolecularly. The broad carbonyl band centred at $1737\,cm^{-1}$, found in the CCl_4 solution of **3a**, shows a high-frequency inflexion. The curve fitting procedure results in two components, one of the $C{=}O_{ester\text{-}f}$ at $1751\,cm^{-1}$ and the other of the $C{=}O_{N\text{-}ring\text{-}b}$ at $1736\,cm^{-1}$. In the CH_2Cl_2 solution, these bands are clearly separated and the stretching frequency of the $C{=}O_{ester\text{-}f}$ is several cm^{-1} red-shifted. However, the $C{=}O_{N\text{-}ring\text{-}b}$ frequency remains the same in each of these solvents as well as in DMSO, indicating the inaccessibility of this carbonyl to solvents.[26,27] The resonance of the NH_2 protons of **3a** at −50 °C appears as two clearly separated singlets down field shifted as compared to the corresponding signals of **2** (Table 2). At 30 °C, both protons give only one signal, however also down field shifted. The NH_2 nitrogen signal is at about −314 ppm, *i.e.* down

Table 4. Selected Frequencies (cm^{-1}) of 5-Amino-1*H*-[1,2,4]triazole (AT), 5-Amino-3-carbomethoxy-1*H*-[1,2,4]triazole (**2**) and Acetylated Derivatives **3**—**6**

Compd.	Medium	$\nu_{as}NH_2$	ν_sNH_2	NH ring free	NH ring bonded	δ_sNH_2	NH amide free	NH amide bonded	C=O ester free	C=O ester bonded	C=O N-ring free	C=O N-ring bonded	C=O amide free	C=O amide bonded
AT	CH_2Cl_2	3486[a]	3396	3453[b]	3163	1625								
2[d]	KBr[c]	3425	3346		3225	1653				1722				
	CCl_4	[e]	[e]		[f]	[e]			1744[a]	1730[a]				
	DMSO	[g]	[g]		3201	[g]			1730					
3a	KBr[h]	(3434, 3275, 3219, 3143)				1635				1736[i]		1736[i]		
	CCl_4	3516	3394			1628			1751[a]			1736		
	CH_2Cl_2	3504	3388			1630			1744			1736		
	DMSO	[g]	[g]			1641			1735			1735		
4	KBr							3319, 3265	1738			1746	1714	
	CCl_4							3330	1754			1746	1724	
	CH_2Cl_2							3337	1743			1743	1716	
	DMSO							[g]	1743		1771		1710	
5a	KBr						(3449, 3416, 3126)		1737			1737	1716	
	CCl_4							3419	1743[a]			1735	1735	1705
	CH_2Cl_2						3422[a]	3396[a]	1735		1767	1735	1723[a]	
	DMSO							[g]	1729		1751[a]	1729	1714[a]	
6a	KBr				3208			3208		1733				1703
	CCl_4				3397		3434	3305—3221	1751[a]	1737				1707
	CH_2Cl_2				3392[a]		3409[a]		1742					1707
	DMSO				[g]			[g]	1735					1700

a) The position of the band obtained by a curve-fitting procedure. *b*) The $NH_{ring\text{-}f}$ vibration of [1,2,4]triazole in CCl_4 is at 3464 cm^{-1}. *c*) For AT in KBr ν=3416, 3351, 3216, 1660 cm^{-1}.[17] *d*) Insoluble in CH_2Cl_2. *e*) Not detectable owing to poor solubility. *f*) A broad multiplet band. *g*) Not given owing to the presence of the bands of DMSO and water. *h*) 3425, 3280, 3220, 3145, 1730, 1635 cm^{-1}.[13] *i*) The assignment of the C=O frequencies for the free and bonded group, based on the X-ray structure.[24]

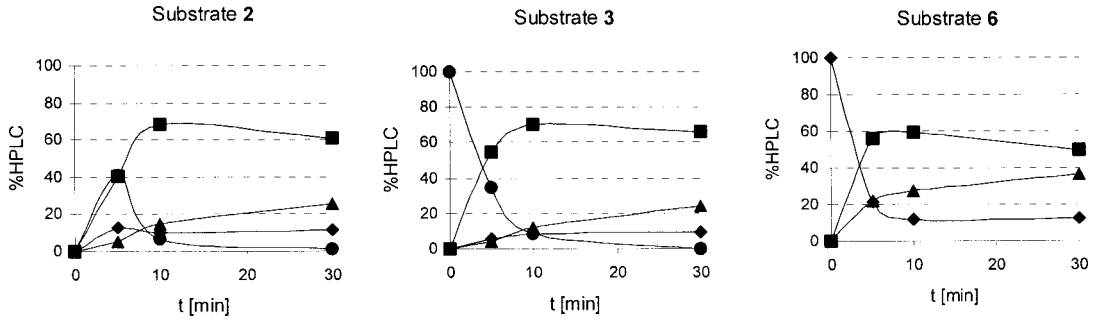

Fig. 2. Incipient Time Courses of the Reaction of **2**, **3** and **6** as Starting Substrates with Neat Boiling Ac_2O

●: Compound **3**, ■: compound **4**, ▲: compound **5**, ◆: compound **6**.

field shifted by *ca.* 20 ppm in relation to **3** (Table 3), is invariable with temperature change and in the CPMAS spectrum also appears at −309.8 ppm.

Methyl 1-Acetyl-3-(acetylamino)-1*H*-[1,2,4]triazole-5-carboxylate (4) and Methyl 1-Acetyl-5-(acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate (5) AT with neat Ac_2O at room temperature after a few days yields quantitatively the diacetylated derivative 1-acetyl-3-(acetylamino)-1*H*-[1,2,4]-triazole. In parallel to monoacetylation, firstly the kinetic product 1-acetyl-5-(acetylamino)-1*H*-[1,2,4]triazole appears, which was unable to be isolated, as during the reaction it converts completely into the final isomer (Fig. 2B). AT in boiling anhydride also forms in addition to the diacetylated compound a triacetylated species, 1-acetyl-3(5)-(diacetylamino)-1*H*-[1,2,4]triazole[15] (Fig. 2C).

The exoamino group of **2** does not react with neat Ac_2O at 20 °C at all. It took 10 d for the diacetylated compound **4** to appear and then it was only a minute quantity. The long-lasting acetylation of the separate monoacetylated derivative **3** and **6** at room temperature shows that whereas **3** practically does not react, **6** under the same conditions relatively quickly yields a significant amount of the diacetylated derivative **4** and a small amount of its isomer **5** (data not included). The diacetylation of **2** and the second acetylation of the monoacetylated **3** require the process to be carried out at boiling point and Fig. 2 presents the incipient time courses of such reactions with **2**, **3** and also with **6**. Expectedly, the first product of acetylation of **2** is the compound **3**. This is converted primarily into the diacetylated derivative **4**. Moreover, **5** and **6** appear in a small amount. Later, the amount of **4** decreases, that of **5** increases while that of **6** remains constant. As we started with **3**, this disappears quickly and the remaining picture is similar to the above described, but the summary amount of two products **4** and **5** upon 5 min reaction is larger. Compound **6** as a substrate rapidly vanishes to a constant level. The summary amount of the two products upon 5 min reaction is the largest and the further picture is similar to the two previous. The equilibrium between **4** (27%), **5** (65%) and **6** (7%) is reached upon the reflux of **2** in neat Ac_2O within 6 h, and no triacetylation was observed. The isomerisation

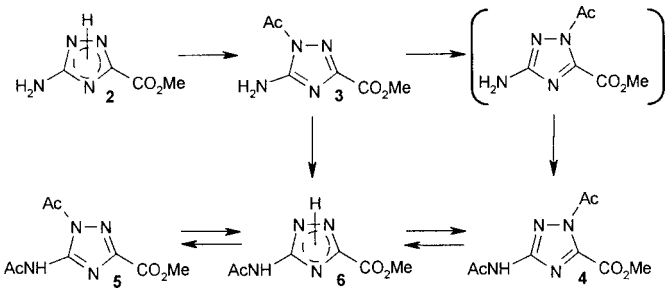

Chart 2. Hypothetical Pathways of the Acetylation of **2** with Neat Boiling Ac_2O

4→5 should be therefore considered a process mediated by **6**, but not an intramolecular rearrangement. All together suggests the pathways of the acetylation of **2** with boiling Ac_2O, shown in Chart 2. The firstly-formed monoacetylated **3** undergoes transacetylation to the isomeric **6** that in turn is acetylated to the kinetic diacetylated product **4** and this is converted into the thermodynamic product **5**. However, the hypothetical methyl 1-acetyl-3-amino-1*H*-[1,2,4]triazole-5-carboxylate cannot be completely ruled out as an intermediate between **3** and **4**.

The isomer **5** is stable with a long shelf life. After half a year of storage at 20 °C, we observed no change in its chromatographic purity. The isomer **4**, after half a year of storage in a refrigerator, was converted into **6** in about 30%, but compound **5** was not detected. However, after storage at room temperature for the same time, **4** disappears completely and the residue contains **6** and **5** (*ca.* 80 : 20). Considering the stability of **5**, the hydrolysis and transacetylation of **4** has to proceed simultaneously. In neutral water at ambient temperature, **4** totally hydrolyses into **6** after 10 min. In contrast, compound **5** is more resistant and its hydrolysis into **6** requires 24 h before it is completed. It is interesting to note, that no difference in the susceptibility to hydrolysis of both isomeric diacetylated amino-[1,2,4]triazoles has been found.[15)]

The study brings the following suggestions for preparing **4** and **5**. Because isomer **4** is the kinetic product of the acetylation of **6** (Chart 2), its highest yield can be reached through the reaction of **6** with Ac_2O under mild conditions. The short warming to 45—50 °C of the suspension of this substrate in Ac_2O only for dissolving proved to be enough to obtain a mixture with 82% of isomer **4**. This still contains 16% of compound **6**, but only 2% of isomer **5**. One crystallisation from ethyl acetate removes the latter completely and the former partially, leaving 58% of **4** of 96% purity. Because isomer **5** is the thermodynamic product of the acetylation of **6**, its formation demands heating, and **2** can be used as the starting material to give the mentioned above equilibrium mixture of **5**, **4** and **6** (65 : 27 : 7). Physicochemical properties of the closely related isomers **4** and **5** are similar in the majority. However, due to their different susceptibilities to hydrolysis, compound **4** can be hydrolysed into **6**, without the loss of **5** and then the separation of **5** from **6** succeeds simply by silica gel column chromatography.[28)]

The NMR data (Tables 2, 3) gives the unequivocal structures of compound **4** and **5**. The N-2 nucleus of **4** is the most shielded out of the ring nitrogen nuclei in this compound. This proves its pyrrole character. The molecule of **4** cannot form an intramolecular hydrogen bond and the chemical shift of its N**H**$COCH_3$ proton amounts to 10.40 ppm against 15.90 ppm in molecule **5** with such a hydrogen bond. All signals in the CPMAS spectra of **4** are very similar to those in the solution spectra. However, they occur as doublets showing two independent molecules with different spatial arrangements. The cause may be overcrowding with two sterically demanding vicinal substituents, the carbomethoxy and acetyl, as was observed in the crystal of a related [1,2,4]triazole derivative.[24)] In sum, this proves that we are dealing with methyl 1-acetyl-3-(acetylamino)-1*H*-[1,2,4]triazole-5-carboxylate. In the stable compound **5**, the CPMAS spectrum indicates the N-2 atom has the pyridine character and that it is the N-1 atom, which bears the acetyl group. So, we are dealing with methyl 1-acetyl-5-(acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate. The difference, *ca.* 80 ppm, in nitrogen shift between the NH_2 group in compound **2** (−333.0 ppm) and the $NHCOCH_3$ group in **4** or **6** (*ca.* −254.0 ppm) gives a deshielding effect of the acetyl group. For compound **5**, this deshielding effect amounts to as much as *ca.* 130 ppm. The mentioned N**H**$COCH_3$ proton at 15.90 ppm, is also strongly deshielded, and moreover the signal is broad even at low temperature. Collectively this documents the structure of **5a** with the intramolecular hydrogen bond. The CPMAS spectra are very similar to those in solution, so the bond occurs in the solid state, too.

In the spectra of **4** in both chlorinated solvents, the vibration of the NH group lies at 3330/3337 cm^{-1} and that of the $C{=}O_{N\text{-}ring}$ group at 1746/1743 cm^{-1} depending on the solvent (Table 4). The spectra do not change with the dilution of solutions even to the limit of detection, which means that compound **4** probably forms the cyclic dimer linked by these groups. In DMSO solution, the $C{=}O_{N\text{-}ring}$ becomes free and appears at 1771 cm^{-1}. Compound **5** populates chlorinated solvents most largely as a monomer with the intramolecular hydrogen bond, *i.e.* **5a**, as was seen from the NMR data. The $NH_{amide\text{-}b}$ frequency is found at 3419/3396 cm^{-1} depending on the solvent. The corresponding $C{=}O_{N\text{-}ring\text{-}b}$ vibration occurs at 1735 cm^{-1} and is invariable by the solvent change. This band is massive and overwhelming in intensity in both solvents. In CCl_4, it coincides with the $C{=}O_{amide\text{-}f}$ band and in CH_2Cl_2 with the $C{=}O_{ester\text{-}f}$ band. There are also other chemical entities. In CCl_4, some association is documented by the $C{=}O_{amide\text{-}b}$ vibration at 1705 cm^{-1} and in CH_2Cl_2 we have found some population of the molecules **5** with no intramolecular hydrogen bond. This population shows the curve-fitted $NH_{amide\text{-}f}$ absorption at 3422 cm^{-1} and the respective $C{=}O_{N\text{-}ring\text{-}f}$ absorption at 1767 cm^{-1}. The DMSO spectrum contains the very broad, strong band at 1729 cm^{-1}, which originates primarily from the coincidental $C{=}O_{ester\text{-}f}$ and $C{=}O_{N\text{-}ring\text{-}b}$ vibrations. The band has a high-frequency inflexion from the component $C{=}O_{N\text{-}ring\text{-}f}$ band positioned at 1751 cm^{-1} and is derived from the fraction of molecules **5** with no intramolecular hydrogen bond. At the low-frequency edge of this combined band (1729 cm^{-1}), there is the component at 1714 cm^{-1} ascribable to the vibration of the $C{=}O_{amide\text{-}f}$.

Methyl 5-(Acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate (6) The most convenient way for preparing 5-(acetylamino)-1*H*-[1,2,4]triazole relies on the exhaustive diacetylation of AT followed by hydrolysis of the labile acetyl

groups[15] (Figs. 1C, D). The same concerns the preparation of **6** that can simply be obtained *via* diacetylation of **2**. The process of acetylation and hydrolysis is quantitative and its final product needs no purification.

Deshielding the exocyclic nitrogen nucleus of **6**, *ca.* 80 ppm, compared to the respective nucleus of **2**, points to the NH_2 group as bearing the acetyl group. The chemical shift of the N-1 nucleus proves its pyrrole type. The ring NH proton, at 14.12 ppm and the N-1 nucleus, at −186.9 ppm are deshielded in relation to the respective 12.90 and −200.0 ppm in the spectra of **2** and argue for structure **6a** with the intramolecular hydrogen bond. The CPMAS data indicate the same molecular structure **6a** in the solid state (Tables 2, 3). No FTIR spectra of **6** (Table 4) reveal a frequency near 3464 or 3453 cm^{-1} (the $NH_{ring\text{-}f}$ group of triazole or AT, respectively). The NH_{ring} and $C{=}O_{amide}$ are observed only as hydrogen-bonded. In CCl_4, a population of the molecules exist with the $NH_{amide\text{-}f}$ vibration at 3434 cm^{-1} and the $C{=}O_{ester\text{-}f}$ vibration at 1751 cm^{-1}. The latter band is localised upon decomposition of the strong, asymmetric $C{=}O_{ester\text{-}b}$ band with the maximum at 1737 cm^{-1} and with a high-frequency inflexion, into two curve-fitted components, at 1737 and 1751 cm^{-1}. The intramolecular hydrogen bond in the above chemical species may be identified by the frequency of the $NH_{ring\text{-}b}$ at 3397 cm^{-1} and the $C{=}O_{amide\text{-}b}$ at 1707 cm^{-1}. In addition, the multiplet NH-band at 3305—3221 cm^{-1} proves numerous associates. The main entity represented by band 3305 cm^{-1} may be a cyclic dimer similar to the cyclic dimer of **4**. Fortunately, no visible association of **6** happens in CH_2Cl_2 solution. The spectra in the sample regions exhibit only three well-shaped bands, at 3400 (broad, combined), 1742 (the $C{=}O_{ester\text{-}f}$) and 1707 (the $C{=}O_{amide\text{-}b}$) cm^{-1}. This first consists of two curve-fitted components, at 3409 cm^{-1} for the $NH_{amide\text{-}f}$ and at 3392 cm^{-1} for the $NH_{ring\text{-}b}$. The DMSO spectrum shows the absorption originating from the $C{=}O_{ester\text{-}f}$ at 1735 cm^{-1} and the $C{=}O_{amide\text{-}b}$ at 1700 cm^{-1}. So, compound **6** presents itself in CH_2Cl_2 and DMSO as the monomer with the intramolecular hydrogen bond, *i.e.* as **6a**.

Conclusion

The acetylation by means of neat Ac_2O of *C*-amino-1*H*-[1,2,4]triazole-carboxylic acid protected with the methyl ester (**2**) has been investigated and compared to the acetylation of 5-amino-1*H*-[1,2,4]triazole (AT). For **2**, a significant decrease in the susceptibility to acetylation was found. However, two monoacetylated derivatives **3** and **6** and two diacetylated derivatives **4** and **5** (Chart 1) can be obtained. Compound **3** has been synthesised regioselectively and quantitatively by mild acetylation of **2** in a suspension in Ac_2O at 20 °C. Whereas **6** undergoes the second acetylation at room temperature, diacetylation of **2** and the second acetylation of **3** requires boiling Ac_2O. All these processes furnish a mixture of primarily two products, one kinetic **4** and one thermodynamic **5** (Chart 2). Both have been obtained in a moderate yield, the former by mild, very short solution acetylation of **6** with Ac_2O warmed to 45—50 °C, the latter from an equilibrium mixture of **4** and **5** upon a prior hydrolysis of **4**. Compound **4** in contrast with its stable AT counterpart, left standing undergoes, simultaneously, hydrolysis to give **6**, and isomerisation to give **5**. The other monoacetylated derivative **6** can be gained quantitatively *via* the diacetylation of **2** and the hydrolysis of a ring acetyl group. Compounds **3**, **5** and **6** are intramolecularly hydrogen-bonded (**3a**, **5a**, **6a**) both in solutions and in the solid state, which was documented by FTIR, multinuclear NMR and CPMAS spectroscopy. The hydrogen bond is a stabilising factor and these compounds have a long shelf life, whereas the AT counterpart of **3** is very unstable and that of **5** has so far been unable to be isolated.

Experimental

C-Amino-[1,2,4]triazole-carboxylic acid hemihydrate of 98% purity (Aldrich # 28,207,3) was used without further purification. A good many broad, unsymmetrical signals in CPMAS spectra (^{13}C-CPMAS δ: 146.6, 151.4, 158.7, 160.0 ppm and ^{15}N-CPMAS δ: −113.5, −122.2, −206.5, −211.6, −216.9, −220.7, −238.9, −313.7, −318.3 ppm) does not allow an univocal structure to be ascribed to this compound. Volatiles from reaction mixtures and fractions after column chromatography separation were removed in vacuum on a rotary evaporator, and unless otherwise indicated, at a bath temperature not exceeding 40 °C. Details about mps' determination and TLC are given in Table 1.

Analytical Chromatography The purity of final products (Table 1) was checked and the results of acetylation experiments (Fig. 3) were followed using a Beckman chromatographic system. The separations were performed on an Alltech Alltima, C-18 RP, 5 μm, 150×4.6 mm column. The mobile phase was 0.1% aqueous trifluoroacetic acid–acetonitrile (90 : 10 v/v) at a flow rate of 1 ml min^{-1}. Detection was made at 210 nm.

The GC-MS analyses were performed on an HP 6890 gas chromatograph with an HP-5 column and an MS 5973 (EI) mass spectrometer as detector.

Multinuclear NMR Spectra The ^{1}H- and ^{13}C-NMR spectra in DMSO-d_6 were recorded on a Bruker Avance DRX 300 with TMS as internal standard. The ^{1}H-, ^{13}C- and ^{15}N-NMR spectra in DMF-d_7 solution were performed on a Bruker Avance DRX 500 spectrometer. A Bruker TBI 500SB H-C/BB-D-05ZG probehead, which is 5 mm, inverse, variable temperature, and PFG were used for the liquid-phase experiments. The ^{13}C- and ^{15}N-NMR spectra were recorded using power-gated decoupling and inverse-gated decoupling sequence, respectively.

The ^{1}H–^{13}C g-HMBC spectra were obtained with an acquisition time of 0.2 s, spectral windows of 9000 Hz (*F2*) and 22000 Hz (*F1*), 2048 data points, 512 time increments (zero filled to 1024), a 1.5 s relaxation delay and 8 transients per increment. The proton and carbon $\pi/2$ pulse lengths were *ca.* 8.0 and 12 μs, respectively. The ^{1}H–^{15}N g-HSQC and g-HMBC spectra were optimised for coupling constants of 100 Hz or 2 Hz, respectively. The experimental conditions were as follows: an acquisition time *ca.* 0.3 s, spectral windows of 9000 Hz (*F2*) and 16000 Hz (*F1*), 2048 data points, 512 time increments (zero filled to 1024), a 1.4 s relaxation delay and 16 transients per increment. For the ^{1}H- and ^{13}C-NMR spectra, TMS was used as internal standard, whereas for ^{15}N-NMR spectra CH_3NO_2 was applied as external standard. The spectra measured at −50 °C were calibrated using spectral reference taken from measurements at 30 °C.

^{13}C- and ^{15}N-CPMAS Spectra The natural abundance ^{13}C- and ^{15}N-CPMAS spectra of **1**—**6** were measured on a Bruker Avance DRX 500 spectrometer with a Bruker MASVTN500SB BL4 probehead using 4 mm zirconia rotors. The 10 kHz spinning speed was applied. The ramp[29] was implemented on proton channel of cross-polarisation pulse sequence. The ^{1}H decoupling rf field strength of 73.5 kHz (3.4 μs $\pi/2$ pulse length) was used and two pulse phase-modulation decoupling sequence[30] was applied. The following parameters were used for ^{13}C-spectra: a frequency 125.77 MHz, a spectral width 31 kHz; a contact time 4 ms; an acquisition time 30 ms; a relaxation delay was *ca.* 10—60 s. The spectra were referenced to solid glycine and recalculated to TMS scale [δ(**C**H_2 in glycine)=43.3 ppm]. The ^{15}N-CPMAS spectra were recorded at a frequency 50.68 MHz; a spectral width 20—31 kHz; a contact time 6 ms; an acquisition time 30—35 ms; a relaxation delay was *ca.* 20—60 s. The spectra were referenced to solid glycine and recalculated to CH_3NO_2 scale [δ(**N**H_2 in glycine)=−347.6 ppm].

FTIR Spectra These were recorded on a Philips Analytical PU9800 FTIR spectrometer at 2 cm^{-1} nominal resolution in a KBr pellet, moreover in CCl_4, CH_2Cl_2, and DMSO solutions using liquid cells (KBr) of 2.86 mm optical pathlength for the former two solvents and 0.1 mm for the latter one. Because of poor solubility, saturated solutions in chlorinated solvents were measured. Only the solutions of **4** were further diluted and measured to the limit of detection to verify solute-solute interactions. DMSO solutions were 10^{-2} M and for this concentration no association was observed. Attention

was focused on the frequency domain 3500—3100 cm^{-1} characteristic of the NH stretching vibrations and 1800—1600 cm^{-1} characteristic of the C=O stretching and NH_2 scissoring vibrations. If necessary, the spectra were analysed with the GRAMS/386 program and the curve fitting procedure with the mixed Gaussian–Lorentzian sum functions was applied.[31)]

Methyl 5-Amino-1*H*-[1,2,4]triazole 3-carboxylate Hydrochloride (1) Methanol (25 ml) was cooled to −15 °C, $SOCl_2$ (6.4 ml, 89.5 mmol) was added dropwise under stirring and followed by *C*-amino-[1,2,4]triazole-carboxylic acid hemihydrate (3.427 g, 25 mmol). Stirring was continued at room temperature for 24 h and volatiles were evaporated. The crude hydrochloride was crystallised from methanol–diethyl ether. White powder. Yield 3.89 g (87%). The analytical data is given in Table 1 and NMR data in Tables 2 and 3.

Methyl 5-Amino-1*H*-[1,2,4]triazole-3-carboxylate (2) The crude hydrochloride (**1**) was dissolved in MeOH (30 ml) and 5% aqueous $NaHCO_3$ (75 ml) was added in portions. The resulting precipitate was filtered and washed with water and acetone. White powder. Yield 2.73 g (77%). ^{1}H-NMR (DMSO-d_6) (δ: 3.78 (s, 3H, CH_3O), 6.22 (s, 2H, NH_2), 12.64 (s, 1H, NH_{ring}). ^{13}C-NMR (DMSO-d_6) δ: 51.5 (CH_3O), 151.8 (C-3), 157.5 (C-5), 160.7 (C=O). The analytical data is given in Table 1, the multinuclear NMR data in DMF-d_7 and CPMAS chemical shifts are collated in Tables 2 and 3. FTIR data is presented in Table 4. EI-MS *m*/*z* (%): 142 (M^+, 75), 125 (25), 110 (27), 98 (48), 84 (100), 69 (14), 57 (66), 42 (85).

Methyl 1-Acetyl-5-amino-1*H*-[1,2,4]triazole-3-carboxylate (3) (A) Ac_2O (2.83 ml, 30 mmol) was added to a stirred suspension of **2** (2.84 g, 20 mmol) in DMF (40 ml). Stirring was continued for 18 h and MeOH (35 ml) was added. After 1 h, the precipitate was filtered and washed with cold methanol. White powder. Yield 3.208 g (87%). Mp 214 °C. (B) A suspension of **2** (2.84 g, 20 mmol) in Ac_2O (20.68 ml, 220 mmol) was stirred for 4.5 h and volatiles were evaporated to leave the title compound. Yield 3.68 g (100%). ^{1}H-NMR (DMSO-d_6) δ: 2.60 (s, 3H, Ac), 3.87 (s, 3H, CH_3O), 7.69 (s, 2H, NH_2). ^{13}C-NMR (DMSO-d_6) δ: 22.7 (Ac), 52.0 (CH_3O), 151.8 (C-3), 157.1 (C-5), 159.7 ($C=O_{ester}$), 171.4 ($C=O_{N\text{-}ring}$) (^{1}H- and ^{13}C-data agreeable to the data from ref. 13). The analytical data is given in Table 1, the multinuclear NMR data in DMF-d_7 and CPMAS chemical shifts are collected in Tables 2 and 3. FTIR data are presented in Table 4. EI-MS *m*/*z* (%): 184 (M^+, 10), 142 (100), 111 (16), 84 (11), 43 (17).

Methyl 1-Acetyl-3-(acetylamino)-1*H*-[1,2,4]triazole-5-carboxylate (4) Compound **6** (1.84 g, 10 mmol), suspended in Ac_2O (34 ml, 360 mmol) and stirred was warmed to 45—50 °C until a clear solution formed. This was immediately evaporated at 20 °C to dryness and the residue was crystallised from EtOAc (50 ml). White powder. Yield 1.32 g (58%). ^{1}H-NMR (DMSO-d_6) δ: 2.22 (s, Ac_{amide}), 2.66 (s, 3H, Ac_{ring}), 3.90 (s, 3H, CH_3O), 10.60 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6) δ: 23.5 ($C=O_{N\text{-}ring}$), 23.6 (CH_{3amide}), 52.6 (CH_3O), 149.7 (C-5), 151.3 (C-3), 159.2 ($C=O_{ester}$), 168.5 ($C=O_{amide}$), 170.1 ($C=O_{N\text{-}ring}$). The analytical data is given in Table 1, the multinuclear NMR data in DMF-d_7, and CPMAS chemical shifts are collected in Tables 2 and. 3. FTIR data are presented in Table 4. EI-MS *m*/*z* (%): 226 (M^+, 8), 184 (40), 169 (50), 142 (83), 110 (12), 43 (100).

Methyl 1-Acetyl-5-(acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate (5) Compound **2** (1.42 g, 10 mmol) in Ac_2O (34 ml, 360 mmol) was refluxed under dry nitrogen for 6 h. Volatiles were evaporated, water (60 ml) was added and the resulting suspension was stirred for 10 min. Again, volatiles were evaporated, EtOAc (50 ml) was added and evaporated. EtOAc was added once more (25 ml) and the insoluble precipitate of **6** filtered off. The filtrate was concentrated *in vacuo* and chromatographied on a short column[28)] (Silica gel 60H, Merck 107736; ϕ 30 mm, *l* 70 mm) equilibrated and eluted with EtOAc. The appropriate fractions (TLC) were collected and evaporated. White powder. Yield 1.356 g (60%). ^{1}H-NMR (DMSO-d_6) δ: 2.21 (s, 6H, Ac_{amide}, Ac_{ring}), 3.92 (s, 3H, CH_3O), 15.61 (s, 1H, NH). ^{13}C-NMR (DMSO-d_6) δ: 25.3 (Ac_{amide}, Ac_{ring}), 52.8 (CH_3O), 149.3 (C-3), 156.6 (C-5), 158.4 ($C=O_{ester}$), 171.5 ($C=O_{amide}$, $C=O_{N\text{-}ring}$). The analytical data is given in Table 1, the multinuclear NMR data in DMF-d_7 and CPMAS chemical shifts are collected in Tables 2 and 3. FTIR data are presented in Table 4. EI-MS *m*/*z* (%): 226 (M^+, 9), 184 (48), 169 (59), 142 (100), 110 (14), 43 (97).

Methyl 5-(Acetylamino)-1*H*-[1,2,4]triazole-3-carboxylate (6) A suspension of **2** (1.42 g, 10 mmol) in Ac_2O (30 ml, 320 mmol) was refluxed for 30 min until a clear solution formed. The solution was evaporated to dryness, water (40 ml) added, a suspension stirred for 24 h and water evaporated. White powder. Yield 1.80 g (98%). ^{1}H-NMR (DMSO-d_6) δ: 2.11 (s, 3H, Ac), 3.82 (s, 3H, CH_3O), 11.66 (br, 1H, NH_{amide}), 13.95 (br, 1H, NH_{ring}). ^{13}C-NMR (DMSO-d_6) δ: 22.7 (Ac), 52.0 (CH_3O), 149.3 (C-3), 150.9 (C-5), 160.2 ($C=O_{ester}$), 169.2 ($C=O_{amide}$). The analytical data is given in Table 1, the multinuclear NMR data in DMF-d_7 and ^{15}N-CPMAS chemical shifts are collected in Tables 2 and 3. FTIR data is presented in Table 4. EI-MS *m*/*z* (%): 184 (M^+, 11), 156 (33), 142 (72), 111 (18), 98 (11), 84 (18), 43 (100).

Acknowledgements We express our gratitude to The University of Opole for the financial support. We would like also to thank Prof. Paweł Kafarski for providing the access to a Bruker Avance DRX 300 MHz spectrometer and to Dr. Tomasz Cierpicki for recording and interpreting some ^{1}H-NMR spectra in DMSO-d_6.

References

1) Dervan P. B., *Bioorg. Med. Chem.*, **9**, 2215—2235 (2001).
2) Kopka M. L., Goodsell D. S., Han G. W., Chiu T. K., Lown J. W., Dickerson R. E., *Structure*, **5**, 1033—1046 (1997).
3) Johnson D. S., Boger D. L., "Comprehensive Supramolecular Chemistry," Vol. 4, ed. by Lehn J.-M., Atwood J. L., Davies J. E. D., Macnicol D. D., Vogtle F., Pergamon Press, Oxford, 1996, pp. 73—176.
4) Voyer N., "Topics in Current Chemistry," Vol. 184, ed. by Schmidtchen F. P., Springer Verlag, Berlin, 1997, pp. 1—37.
5) Janecka A., Janecki T., Shan S., Bowers C., Folkers K., *J. Med. Chem.*, **37**, 2238—2241 (1994).
6) Ishida H., Inoue Y., *Biopolymers* (*Peptide Science*), **55**, 469—478 (2000).
7) Kubik S., Goddard R., *Eur. J. Org. Chem.*, **2001**, 311—322 (2001).
8) Kirsten C. N., Schrader T. H., *J. Am. Chem. Soc.*, **119**, 12061—12068 (1997).
9) Saweczko P., Kraatz H.-B., *Coord. Chem. Rev.*, **190—192**, 185—198 (1999).
10) Saweczko P., Enright G. D., Kraatz H.-B., *Inorg. Chem.*, **40**, 4409—4419 (2001).
11) Unterberg C., Gerlach A., Schrader T., Gerhards M., *Eur. Phys. J. D.*, **20**, 543—550 (2002).
12) Cipen G. E., Grinstein V., *Latvijas PSR Zinatnu Akad. Vestis Kim. Ser.*, **1965**, 204—208 [*Chem. Abst.*, **63**, 13243*f* (1965)].
13) Saalfrank R. W., Wirth U., *Chem. Ber.*, **122**, 519—522 (1989).
14) Baird E. E., Dervan P. B., *J. Am. Chem. Soc.*, **118**, 6141—6146 (1996).
15) Dżygiel A., Masiukiewicz E., Rzeszotarska B., *J. Agric. Food Chem.*, **50**, 1383—1388 (2002).
16) Kohlbau H.-J., Thürmer R., Voelter W., "Synthesis of Peptides (Houben-Weyl Methods of Organic Chemistry)," Vol. E22a, ed. by Goodman M., Felix A., Moroder L., Toniolo C., George Thieme, Stuttgart, 2002, pp. 193—237.
17) Gabryszewski M., Wieczorek B., *Polish J. Chem.*, **73**, 2061—2066 (1999).
18) Byriel K. A., Kennard C. H. L., Lynch D. E., Smith G., Thompson J. G., *Aust. J. Chem.*, **45**, 969—981 (1992).
19) Lynch D. E., Smith G., Byriel K. A., Kennard C. H. L., *Acta Crystallogr.*, **C48**, 1265—1267 (1992).
20) Lynch D. E., Smith G., Byriel K. A., Kennard C. H. L., *Acta Crystallogr.*, **C50**, 1291—1294 (1994).
21) Smith G., Lynch D. E., Byriel K. A., Kennard C. H. L., *Acta Crystallogr.*, **C52**, 231—235 (1996).
22) McNab H., *J. Chem. Soc. Perkin Trans. 1*, **1987**, 657—660 (1987).
23) Claramunt R. M., López C., Sanz D., Alkorta I., Elguero J., *Heterocycles*, **55**, 2109—2121 (2001).
24) Wawrzycka-Gorczyca I., Rzeszotarska B., Dżygiel A., Masiukiewicz E., Kozioł A. E., *Z. Kristallogr.*, **218**, 480—487 (2003).
25) Denisov G. S., Kuzina L. A., *J. Mol. Struct.*, **271**, 9—18 (1992).
26) Parmentier J., De Wael K., Zeegers-Huyskens Th., *J. Mol. Struct.*, **270**, 217—227 (1992).
27) Pless M., Griehl C., Kolbe A., *J. Mol. Struct.*, **570**, 203—214 (2001).
28) Hunt B. J., Rigby W., *Chem. & Ind.*, **1967**, 1868—1869 (1967).
29) Metz G., Wu X., Smith S. O., *J. Magn. Reson.*, **A110**, 219—227 (1994).
30) Bennett A. E., Rienstra C. M., Auger M., Lakshimi K. V., Griffin R. G., *J. Chem. Phys.*, **103**, 6951—6958 (1995).
31) GRAMS/386 Version 3.01B, Galactic Industries Corp., Salem NH (1994).