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2-Amino-4-aryl-1-arylideneaminoimidazoles and Acylation Products: A Multinuclear (^{1}H, ^{13}C, ^{15}N) NMR Study

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Summary. The structure of 2-amino-4-aryl-1-arylideneaminoimidazoles in *DMSO*-d_6 solution was investigated by means of NMR spectroscopic methods (^{1}H, ^{13}C, ^{15}N). From these data the (*E*)-configuration at the excocyclic C=N bond and a strong preference for the conformer with the imidazole H-5 and the N=CH proton being spatially close (s-*trans* regarding the N–N bond) can be concluded. Reaction of the title compounds with acetic anhydride leads to mono and diacylation at the 2-amino group, whereas treatment with pivalic anhydride exclusively affords the corresponding monoacyl product. The mono- and diacylation products exhibit similar configurational and conformational properties as the parent compounds.

Keywords. Heterocycles; 2-Aminoimidazoles; *Schiff* bases; Acylation; NMR spectroscopy.

Introduction

Guanylhydrazones (*GH*s) – reaction products of oxo compounds with aminoguanidines [1] – are of considerable interest due to various biological activities found with many representatives [2, 3]. Moreover, such compounds represent valuable synthetic building blocks for the construction of different nitrogen-containing heterocycles. Thus, *e.g.*, guanylhydrazones derived from aromatic aldehydes can be transformed into 3-acylamino-5-aryl-1,4-diacetyl-4,5-dihydro-1,2,4-triazoles [4], N^1-(glycopyranosylamino)guanidines into 3-acetylamino-N^1-glycopyranosyl-5-methyl-1*H*-1,2,4-triazoles [5], and guanylhydrazones of cyclic ketones give 3-acetylamino-1-cycloalkenyl-5-methyl-1*H*-1,2,4-triazoles [6]. Many of these reactions proceed under the influence of hot, excessive acetic anhydride. However, some related guanylhydrazone educts (camphor-*GH*, isatin-*GH*, 2,6-dichlorobenzaldehyde-*GH*, *GH*s

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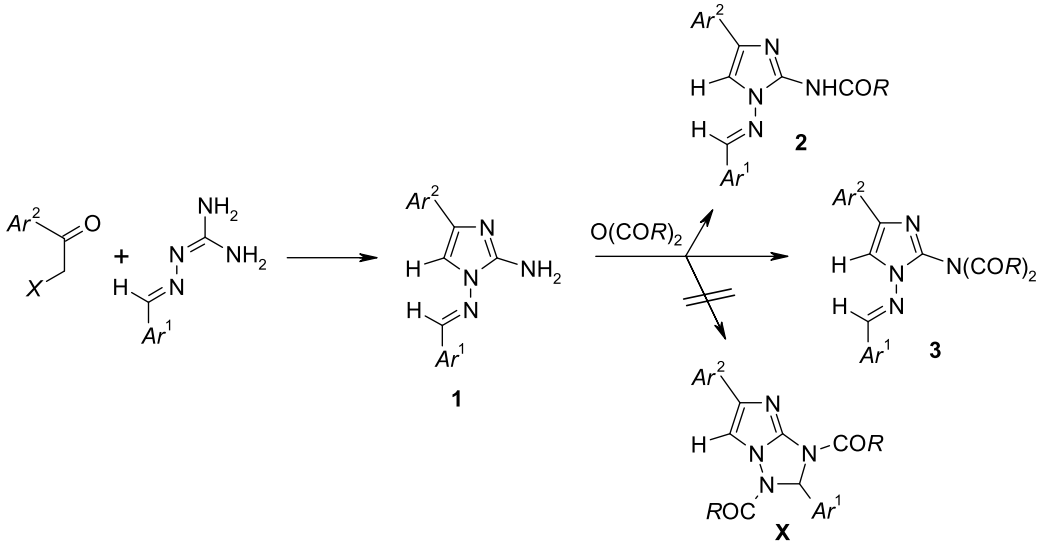
derived from (hetero)aryl methyl ketones) show a different reaction behavior and 'only' afford the corresponding *N*,*N*′-diacetyl derivatives upon treatment with acetic anhydride [6–9]. In addition to these cyclizations into substituted 1,2,4-triazoles *Beyer et al*. have described a straightforward approach to 2-amino-4-aryl-1-arylideneaminoimidazoles (**1**) *via* reaction of *GH*s derived from aromatic aldehydes (or acetophenones) with aryl α-halogenoalkyl ketones [10] (Scheme 1). It should be mentioned that compounds **1** are also available *via* several steps including ring transformation of 2-amino-3-phenacyl-1,3,4-oxadiazolium halides with appropriate amines [11]. However, the former method is much more convenient than the latter and thus it was exclusively employed in the following (for instance, see Refs. [12–19]). Compounds of type **1** are of considerable interest as in the recent patent



	Ar^1	Ar^2	*R*
1a	*Ph*	*Ph*	—
1b	4-Cl-C_6H_4	*Ph*	—
1c	4-*Me*O-C_6H_4	*Ph*	—
1d	3,4,5-(*Me*O)$_3$-C_6H_2	*Ph*	—
1e	4-*Me*O-C_6H_4	4-Br-C_6H_4	—
2α	*Ph*	*Ph*	*t-Bu*
2b	4-Cl-C_6H_4	*Ph*	*Me*
2β	4-Cl-C_6H_4	*Ph*	*t-Bu*
2c	4-*Me*O-C_6H_4	*Ph*	*Me*
2γ	4-*Me*O-C_6H_4	*Ph*	*t-Bu*
2δ	3,4,5-(*Me*O)$_3$-C_6H_2	*Ph*	*t-Bu*
2e	4-*Me*O-C_6H_4	4-Br-C_6H_4	*Me*
2ε	4-*Me*O-C_6H_4	4-Br-C_6H_4	*t-Bu*
3a	*Ph*	*Ph*	*Me*
3α	*Ph*	*Ph*	*Et*
3b	4-Cl-C_6H_4	*Ph*	*Me*
3c	4-*Me*O-C_6H_4	*Ph*	*Me*
3d	3,4,5-(*Me*O)$_3$-C_6H_2	*Ph*	*Me*
3e	4-*Me*O-C_6H_4	4-Br-C_6H_4	*Me*

Scheme 1

literature they were claimed to exhibit promising anti-cancer activities [19] (for instance **1c**). Treatment of **1a** with refluxing acetic anhydride was described to lead to the *N,N*-diacetyl derivative [10], whereas *Yamazaki et al.* reported the formation of the monoacetyl product [14] upon 'acylation' of **1a** (no experimental details given). It should be emphasized that, in principle, also cyclization into bicyclic systems of type **X** should be possible (Scheme 1). In this regard it is refered to a closely related reaction which smoothly proceeds with related *GH*s to afford 1,2,4-triazole derivatives [4–6].

With respect to the fact that no detailed investigations regarding the stereochemistry of **1** are hitherto available and in continuation of our previous investigations on the structure and reactivity of *GH*s and related structures [4–9] we here present NMR (^{1}H, ^{13}C, ^{15}N) studies concerning the determination of structural features of 2-amino-4-aryl-1-arylideneaminoimidazoles **1** as well as their reaction products **2** and **3** with aliphatic carboxylic acid anhydrides.

Results and Discussions

Synthesis

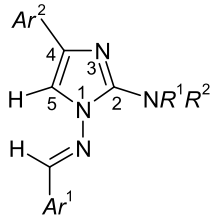
Compounds **1** were prepared by ring closure starting from known *GH*s [9] and substituted phenacyl bromides using potassium bicarbonate as base (Scheme 1). Refluxing equimolar amounts of the reactants in methanol afforded products **1**. In the following, the colored, high-melting *Schiff* bases **1** were heated with an excess of the appropriate anhydride for 30–50 minutes at 100°C. Whereas reaction of **1** with pivalic anhydride exclusively afforded the monoacyl derivatives **2**α, **2**β, **2**γ, **2**δ, and **2**ε, treatment with the sterically less hindered acetic anhydride led to mixtures of *N*-monoacetyl (**2b**, **2c**, **2e**) and the corresponding *N,N*-diacetyl derivatives (**3a**, **3b**, **3c**, **3d**, **3e**) which was also observed in the reaction with propionic anhydride (**3**α). Potential ring closure to bicyclic systems of type **X** could not be observed.

NMR Spectroscopic Investigations

The NMR data are summarized in Tables 1–4. Full and unambiguous assignment of ^{1}H and ^{13}C resonances was achieved by combined application of standard NMR techniques such as N*O*E difference experiments, 1D-TOCSY, APT, gated decoupling, and HMQC. Moreover, selective long-range INEPT experiments [20] were used for the unequivocal assignment of quaternary carbon atoms and a corresponding two-dimensional version of this technique [21] served for the discrimination of long-range ^{13}C,^{1}H coupling constants. For the determination and assignment of ^{15}N chemical shifts a sensitivity-enhanced gradient selected gs-HSQC technique [22–24] and – mainly – gs-HMBC experiments [25] were employed.

The ^{1}H NMR spectra of 2-aminoimidazoles **1** exhibit – besides the signal due to the NH_2 protons between 6.1 and 6.3 ppm – one singlet signal at $\delta \sim 8.0$ ppm and another in the range between $\delta = 8.5$–8.6 ppm. The former can be assigned to the imidazole H-5 resonance, whereas the latter originates from the N=CH substructure. Monoacylation of the 2-amino group (compounds **2**) leads to a downfield shift

Table 1. ^{1}H NMR chemical shifts (δ/ppm) of **1–3** in *DMSO*-d_6



No.	Imidazole		H of Ar^1			H of Ar^2			H of NR^1R^2
	H-5	–N=CH	H-2,6	H-3,5	H-4	H-2,6	H-3,5	H-4	
1a	8.03	8.59	7.94	7.48	7.48	7.73	7.35	7.18	6.21 (NH_2)
1b	7.96	8.55	7.95	7.55	–	7.70	7.35	7.19	6.25 (NH_2)
1c	7.96	8.50	7.87	7.05	3.81 (O*Me*)	7.71	7.34	7.17	6.11 (NH_2)
1d	7.96	8.49	7.25	3.87 (O*Me*)	3.72 (O*Me*)	7.71	7.35	7.18	6.33 (NH_2)
1e	8.04	8.50	7.86	7.05	3.82 (O*Me*)	7.63	7.52	–	6.21 (NH_2)
2α	8.50	8.84	7.81	7.53	7.53	7.81	7.41	7.26	9.72 (NH), 1.28 (*tBu*)
2b	8.43	8.84	7.87	7.61	–	7.78	7.41	7.26	10.14 (NH), 2.13 (*Me*)
2β	8.47	8.83	7.79	7.61	–	7.79	7.41	7.26	9.73 (NH), 1.27 (*tBu*)
2c	8.42	8.78	7.83	7.10	3.84 (O*Me*)	7.80	7.41	7.26	10.09 (NH), 2.13 (*Me*)
2γ	8.46	8.77	7.77	7.11	3.84 (O*Me*)	7.82	7.42	7.26	9.70 (NH), 1.30 (*tBu*)
2δ	8.46	8.76	7.12	3.82 (O*Me*)	3.74 (O*Me*)	7.79	7.41	7.25	9.73 (NH), 1.28 (*tBu*)
2e	8.47	8.74	7.80	7.08	3.82 (O*Me*)	7.71	7.58	–	10.13 (NH), 2.11 (*Me*)
2ε	8.49	8.73	7.74	7.09	3.82 (O*Me*)	7.73	7.59	–	9.68 (NH), 1.30 (*tBu*)
3a	8.72	8.97	7.81	7.54	7.54	7.83	7.44	7.30	2.28 (*Me*)
3α	8.71	8.96	7.79	7.53	7.53	7.83	7.44	7.29	2.60 (CH_2), 1.03 (*Me*)
3b	8.70	8.98	7.81	7.61	–	7.82	7.44	7.30	2.28 (*Me*)
3c	8.66	8.89	7.76	7.09	3.83 (O*Me*)	7.82	7.43	7.29	2.27 (*Me*)
3d	8.64	8.87	7.10	3.84 (O*Me*)	3.74 (O*Me*)	7.82	7.43	7.29	2.29 (*Me*)
3e	8.71	8.86	7.75	7.10	3.83 (O*Me*)	7.75	7.62	–	2.26 (*Me*)

for both imidazole H-5 ($\delta \sim 8.5$ ppm) and N=CH ($\delta = 8.7$–8.8 ppm) signals. Diacylation (compounds **3**) results in an additional – albeit small – shift to lower frequencies ($\delta = 8.7$ and 8.9–9.0 ppm, respectively).

Concerning the stereochemistry of compounds **1**, diastereomerism at the C=N bond as well as the possible preference of specific rotameric forms with respect to the N–N bond has to be considered (the thus resulting four possible species are displayed in Fig. 1). In the course of N*O*E-difference experiments with **1** intensive N*O*Es were detected between imidazole H-5 and N=CH, no through-space interactions emerged between the amino protons and the N=CH proton. From this spatial closeness of imidazole H-5 and N=CH as well as from the complete absence of an N*O*E between NH_2 and N=CH the (*E*)-configuration at the C=N double bond and a preferential occurrence of the s-*trans* conformation can be concluded (Fig. 1). Similar experiments with monoacylation products **2** (complete absence of N*O*Es between NHAc and N=CH as well as strong through-space

Table 2. ^{13}C NMR chemical shifts (δ/ppm) of **1–3** in *DMSO*-d_6

No.	Imidazole-C				C of Ar^1			
	C-2	C-4	C-5	N=CH	C-1	C-2,6	C-3,5	C-4
1a	149.5	136.6	101.3	146.5	133.8	127.6	128.7	130.5
1b	149.7	136.9	101.2	145.2	132.8	129.2	128.9	134.9
1c	149.3	136.3	101.2	146.4	126.3	129.3	114.3	161.2
1d	149.6	136.6	101.1	146.4	129.3	105.0	153.2	139.6
1e	149.2	134.7	102.0	147.0	126.2	129.4	114.3	161.3
2α	138.9	137.0	106.7	151.4	133.1	127.7	129.0	131.4
2b	138.9	137.0	106.1	150.2	132.0	129.6	129.1	135.9
2β	139.0	137.0	106.7	150.3	132.1	129.3	129.2	135.9
2c	138.4	136.7	106.3	151.4	125.5	129.8	114.5	161.9
2γ	138.5	136.7	106.8	151.4	125.6	129.5	114.6	161.9
2δ	138.9	137.0	106.5	151.0	128.5	105.0	153.2	140.3
2e	138.6	135.6	106.9	151.8	125.5	129.9	114.6	162.0
2ε	138.6	135.6	107.4	151.7	125.5	129.5	114.6	161.9
3a	138.0	138.0	108.0	153.6	132.4	128.1	129.1	131.9
3α	137.8	138.0	107.9	153.5	132.4	128.0	129.1	131.9
3b	138.1	138.1	108.0	152.5	131.3	129.7	129.3	136.5
3c	137.7	137.8	108.0	153.4	124.9	130.0	114.7	162.3
3d	138.0	138.0	107.8	153.1	127.7	105.3	153.2	140.8
3e	137.8	136.7	108.6	153.7	124.8	130.0	114.7	162.3

No.	C of Ar^2				C of NR^1R^2	Other C of Ar^1
	C-1	C-2,6	C-3,5	C-4		
1a	134.4	124.1	128.3	126.3	–	–
1b	134.4	124.1	128.3	126.3	–	–
1c	134.6	124.0	128.3	126.1	–	55.3 (4-O*Me*)
1d	134.5	124.0	128.5	126.4	–	60.2 (4-O*Me*), 56.0 (3,5-O*Me*)
1e	133.6	125.9	131.3	118.9	–	55.3 (4-O*Me*)
2α	133.7	124.1	128.6	126.9	178.2 (CO), 38.7, 27.1 (*tBu*)	–
2b	133.5	124.2	128.8	127.0	169.7 (CO), 22.7 (*Me*)	–
2β	133.6	124.1	128.6	126.9	178.2 (CO), 38.7, 27.1 (*tBu*)	–
2c	133.7	124.1	128.6	126.8	169.8 (CO), 22.6 (*Me*)	55.4 (4-O*Me*)
2γ	133.8	124.1	128.6	126.8	178.2 (CO), 38.6, 27.1 (*tBu*)	55.4 (4-O*Me*)
2δ	133.7	124.1	128.6	126.9	178.2 (CO), 38.7, 27.1 (*tBu*)	60.2 (4-O*Me*), 55.8 (3,5-O*Me*)
2e	133.1	126.1	131.6	119.7	169.9 (CO), 22.7 (*Me*)	55.4 (4-O*Me*)
2ε	133.1	126.0	131.5	119.6	178.1 (CO), 38.6, 27.1 (*tBu*)	55.4 (4-O*Me*)
3a	133.0	124.3	128.7	127.4	171.7 (CO), 25.2 (*Me*)	–
3α	133.0	124.3	128.7	127.4	175.3 (CO), 30.3, 8.6 (*Et*)	–
3b	132.9	124.3	128.7	127.4	171.7 (CO), 25.2 (*Me*)	–
3c	133.1	124.3	128.7	127.3	171.7 (CO), 25.2 (*Me*)	55.4 (4-O*Me*)
3d	133.0	124.3	128.7	127.4	171.8 (CO), 25.1 (*Me*)	60.2 (4-O*Me*), 55.8 (3,5-O*Me*)
3e	132.4	126.2	131.6	120.1	171.7 (CO), 25.2 (*Me*)	55.4 (4-O*Me*)

Table 3. Selected $^{13}C,^{1}H$ spin coupling constants (J/Hz) of **1–3** in *DMSO*-d_6

No.	Imidazole-C				
	^{3}J(C2,H5)	^{2}J(C4,H5)	^{3}J(C4,Ph2,6)	^{1}J(C5,H5)	^{1}J(N = CH)
1a	7.5	6.7	4.2	193.6	165.4
1b	7.5	6.6	4.4	193.6	166.8
1c	7.6	6.7	4.5	193.2	163.9
1d	7.3	[a]	[a]	193.5	165.2
1e	7.5	6.8	[a]	194.1	163.9
2α	8.0	6.5	4.4	193.8	165.7
2b	8.4	6.5	4.6	194.2	167.2
2β	7.9	6.3	4.4	193.9	167.3
2c	7.2	6.4	4.6	193.5	164.5
2γ	8.0	6.4	4.6	193.5	164.2
2δ	7.6	6.1	[a]	193.9	166.0
2e	8.0	6.4	4.0	194.6	164.6
2ε	8.1	6.5	4.3	193.7	164.1
3a	8.3	[a]	4.6	195.5	166.5
3α	8.3	6.4	4.6	195.3	166.7
3b	8.1	[a]	4.5	195.6	168.2
3c	8.3	6.5	4.5	195.1	165.4
3d	8.1	[a]	[a]	195.2	167.4
3e	8.3	6.8	4.4	195.6	165.4

No.	Imidazole-C	Other couplings
	^{3}J(=NCH,Ph2,6)	
1a	4.8	–
1b	4.6	–
1c	4.6	^{1}J(4-O*Me*) = 144.8
1d	[a]	^{1}J(4-O*Me*) = 144.5, ^{1}J(3,5-O*Me*) = 144.7
1e	4.4	^{1}J(4-O*Me*) = 144.8
2α	4.7	^{1}J(*Me*) = 126.8, ^{3}J($\underline{C}H_3$,C$\underline{H}_3$) = 4.7
2b	4.6	^{1}J(*Me*) = 128.5
2β	4.4	^{1}J(*Me*) = 126.9, ^{3}J($\underline{C}H_3$,C$\underline{H}_3$) = 4.7
2c	4.5	^{1}J(4-O*Me*) = 144.9, ^{1}J(*Me*) = 128.2
2γ	4.6	^{1}J(4-O*Me*) = 144.9, ^{1}J(*Me*) = 126.8, ^{3}J($\underline{C}H_3$,C$\underline{H}_3$) = 4.7
2δ	5.1	^{1}J(4-O*Me*) = 144.8, ^{1}J(3,5-O*Me*) = 144.7, ^{1}J(*Me*) = 126.7, ^{3}J($\underline{C}H_3$,C$\underline{H}_3$) = 4.7
2e	[a]	^{1}J(4-O*Me*) = 144.8
2ε	4.6	^{1}J(4-O*Me*) = 144.9, ^{1}J(*Me*) = 126.8, ^{3}J($\underline{C}H_3$,C$\underline{H}_3$) = 4.7
3a	4.8	^{1}J(*Me*) = 130.4, ^{2}J(CO,*Me*) = 6.6
3α	4.6	^{1}J(CH_2) = 129.3, ^{2}J($\underline{C}H_2$,C$\underline{H}_3$) = 4.4, ^{1}J(*Me*) = 128.3, ^{2}J($\underline{C}H_3$,C$\underline{H}_2$) = 4.4
3b	4.5	^{1}J(*Me*) = 130.5, ^{2}J(CO,*Me*) = 6.7
3c	4.5	^{1}J(*Me*) = 130.4, ^{2}J(CO,*Me*) = 6.7, ^{1}J(4-O*Me*) = 145.0
3d	5.2	^{1}J(4-O*Me*) = 144.8, ^{1}J(3,5-O*Me*) = 144.8, ^{1}J(*Me*) = 130.4, ^{2}J(CO,*Me*) = 6.6
3e	4.4	^{1}J(*Me*) = 130.5, ^{2}J(CO,*Me*) = 6.7, ^{1}J(4-O*Me*) = 145.0

[a] not unequivocally determined

Table 4. ^{15}N NMR chemical shifts (δ/ppm)[a] of **1–3** in *DMSO*-d_6

No.	N-1	N-3	CH=N	NR^1R^2
1a	– 191.9	– 179.5	– 76.0	– 329.3
1b	– 191.7	– 179.1	– 74.4	– 329.4
1c	– 192.2	– 178.5	– 81.7	– 330.0
1d	– 192.2	– 179.5	– 77.9	– 328.8
1e	– 191.9	– 179.2	– 82.2	– 329.6
2α	– 173.6	– 134.6	– 72.7	– 271.0
2b	– 176.1	[b]	– 73.0	– 261.4
2β	– 173.7	– 134.6	– 71.7	– 270.9
2c	– 175.6	[b]	– 80.2	– 261.4
2γ	– 173.3	– 135.0	– 78.8	– 270.9
2δ	– 173.7	– 134.7	– 75.2	– 270.9
2e	– 175.3	[b]	– 80.4	– 261.5
2ε	– 172.8	– 135.3	– 79.2	– 271.1
3a	– 172.5	– 128.7	– 79.9	– 208.0
3α	– 172.5	– 128.5	– 79.8	[b]
3b	– 172.7	– 128.0	– 79.1	– 207.4
3c	– 172.5	– 129.5	– 86.3	– 207.6
3d	– 173.2	– 129.1	– 81.3	– 207.6
3e	– 171.9	– 129.6	– 86.2	– 207.8

[a] error margins ± 1.56 ppm; [b] not unequivocally determined

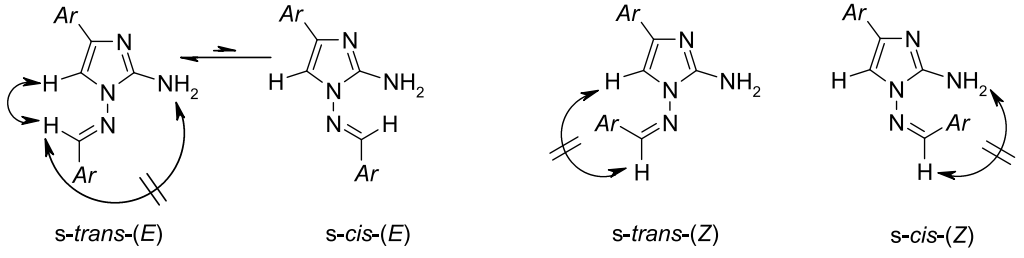


Fig. 1. Configurational and conformational assignment in **1** *via* a strong N*O*E between imidazole H-5 and N=CH (preference of the s-*trans*-(*E*) form)

interactions beetween imidazole H-5 and N=CH) and with *N*,*N*-diacyl derivatives **3** also reveal the corresponding s-*trans*-(*E*) forms to be highly probable for these compounds. It should be mentioned that similar steric situations were found recently with somewhat related structures [26].

The ^{13}C NMR chemical shifts of compounds **1–3** are displayed in Table 2, whereas selected ^{13}C,^{1}H spin coupling constants are given in Table 3. The obtained data exhibit a high degree of consistency, particularly within the 1-arylideneaminoimidazole system. Switching from parent compounds **1** to the corresponding monoacyl derivatives **2** leads to a marked upfield shift (approximately 10 ppm) for the imidazole C-2 resonance. In contrast, the imidazole C-5 signal receives a downfield shift (~5 ppm), whereas the position of the imidazole C-4 line is nearly

unaffected. Attachment of a second acyl group at the excocyclic 2-amino function (**2** → **3**) has only little influence. In diacyl derivatives **3** the imidazole C-2 and C-4 resonances are very close or – accidentally – isochronous. For this reason, the corresponding coupling constant ^{2}J(C4,H5) could not be unequivocally determined in all cases. The characteristic ^{13}C,^{1}H spin coupling constants in the 1-arylidene-aminoimidazole system are nearly of the same size with structures **1**, **2**, and **3** and thus they remain unaffected upon acylation. The ^{15}N NMR chemicals shifts of compounds **1**–**3** (Table 4) represent a valuable set of data as very little is known regarding nitrogen-15 NMR spectroscopy of such (and related) type of compounds. A comparison between structures **1**, **2**, and **3** reveals the imidazole N-3 resonance to be most sensitive upon acylation of the 2-amino function, even the introduction of a second acetyl group (**2** → **3**) leads to an additional, distinct downfield shift. ^{1}H Coupled INEPT spectra of **1d** and **3a** show only a small splitting (∼3 Hz) for the CH=**N** signal. This finding supports the above assignment of the (*E*)-configuration at the C=N bond as it is known that in such systems the *trans*-position of the nitrogen's lone-pair and the geminally coupled H-atom leads to a small (positive) ^{2}J coupling constant, whereas a *cis*-position (and thus (*Z*)-configuration) should result in a considerably larger (∼10–16 Hz), negative geminal coupling, as observed in (*Z*)-aldoximes or in different heterocyclic systems [27–29].

Experimental

Melting points were determined on a *Boëtius*-type hot-stage microscope and are uncorrected. MS spectra were obtained on a Shimadzu QP 1000 spectrometer (EI, 70 eV). ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unityplus 300 spectrometer (300 MHz for ^{1}H, 75.4 MHz for ^{13}C) from *DMSO*-d_6 solutions (approximately 0.2 *M*) at 28°C. The solvent signal was used as an internal standard which was related to *TMS* with $\delta = 2.49$ ppm (^{1}H) and $\delta = 39.5$ ppm (^{13}C). The digital resolutions were 0.25 for the ^{1}H NMR spectra, 0.5 for the broadband decoupled ^{13}C NMR spectra, and 0.33 Hz/data point for the gated decoupled ^{13}C NMR spectra. All ^{15}N NMR spectra were obtained at 300 K on a Bruker Avance 500 spectrometer (50.69 MHz for ^{15}N) equipped with a 5 mm broadband observe probe using gradient-selected inverse techniques (sensitivity enhanced gs-HSQC and gs-HMBC) and, occasionally, the INEPT sequence. HMBC Spectra were acquired as 4096 × 256 data matrices (10 ppm for ^{1}H and 400 ppm for ^{15}N) with 24 transients accumulated per t_1 increment; the delay for the evolution of the ^{15}N,^{1}H long-range coupling was set to 83 ms (optimized for $J = 6$ Hz). Processing was performed using zero-filling to 1K data points in the F1 dimension and sine multiplication in both dimensions. HSQC Spectra were recorded as 1024 × 64 data matrices (3 ppm for ^{1}H and 50 ppm for ^{15}N) with 8 transients per t_1 increment and were optimized to a $^{1}J(^{15}\text{N},^{1}\text{H})$ coupling constant of 90 Hz. Processing was performed in the echo-antiecho mode using squared sine window functions in both dimensions. Referencing of the ^{15}N NMR spectra was performed against external nitromethane (coaxial capillary). Elemental analyses (C, H, N) were performed by Microanalytical Laboratory, Department of Physical Chemistry, University of Vienna; the results for the novel compounds agreed satisfactorily (±0.4%) with the calculated values. Compounds **1b** and **3c** have a registry number in Chemical Abstracts, however, no references and thus no data are available.

*General Method for the Preparation of Compounds **1a–1e***

A solution of 3 mmol of the appropriate guanylhydrazone in 7 cm^3 of methanol was treated with 300 mg of $KHCO_3$ (3 mmol) and 3 mmol of the corresponding phenacyl bromide. The resulting suspension was refluxed for 3 h, cooled, and then diluted with ∼80 cm^3 of H_2O. The precipitation

of the reaction product was promoted by sonication. The products were filtered, crystallized from the solvents given below, and dried *in vacuo*.

(E)-4-Phenyl-N^{1}-(phenylmethylene)-1H-imidazole-1,2-diamine (**1a**)

Yield: 90%; mp 201–204°C (*Et*OH) (Ref. [18] 200–203°C, Refs. [10, 11] 213°C); MS (180°C): m/z (%) = 262 ($M^{+\bullet}$, 10), 223 (16), 158 (51), 131 (11), 117 (33), 105 (100), 104 (17), 103 (14), 90 (18), 89 (20), 85 (11), 77 (81), 51 (40), 50 (12).

(E)-N^{1}-[(4-Chlorophenyl)methylene]-4-phenyl-1H-imidazole-1,2-diamine (**1b**, $C_{16}H_{13}ClN_4$)

Yield: 86%; mp 230–234°C (*DMF*-H_2O); MS (180°C): m/z (%) = 296/298 ($M^{+\bullet}$, 9/3), 158 (100), 131 (17), 117 (55), 104 (22), 89 (21), 77 (21), 75 (11), 51 (11), 43 (11).

(E)-N^{1}-[(4-Methoxyphenyl)methylene]-4-phenyl-1H-imidazole-1,2-diamine (**1c**)

Yield: 83%; mp 192–195°C (*DMF*-H_2O) (Ref. [16] 197–198°C); MS (175°C): m/z (%) = 292 ($M^{+\bullet}$, 14), 159 (14), 158 (100), 134 (12), 131 (14), 117 (48), 105 (14), 104 (21), 89 (10), 77 (33), 73 (23), 51 (14), 44 (25), 42 (12).

(E)-4-Phenyl-N^{1}-[(3,4,5-trimethoxyphenyl)methylene]-1H-imidazole-1,2-diamine
(**1d**, $C_{19}H_{20}N_4O_3$)

Yield: 47%; mp 193–194°C (*Me*OH-Et_2O-hexane); MS (190°C): m/z (%) = 352 ($M^{+\bullet}$, 16), 158 (100), 131 (10), 117 (34), 105 (24), 104 (12), 77 (22), 44 (11).

(E)-4-(4-Bromophenyl)-N^{1}-[(4-methoxyphenyl)methylene]-1H-imidazole-1,2-diamine
(**1e**, $C_{17}H_{15}BrN_4O$)

Yield: 82%; mp 220–224°C (*DMF*-H_2O); MS (220°C): m/z (%) = 370/372 ($M^{+\bullet}$, 21/19), 237/239 (12/12), 236/238 (75/76), 183/185 (48/44), 182/184 (12/13), 158 (13), 157 (100), 155 (18), 135 (26), 134 (37), 133 (18), 117 (14), 107 (11), 104 (15), 103 (18), 102 (21), 92 (22), 91 (19), 90 (18), 89 (18), 82 (11), 80 (12), 79 (12), 78 (10), 77 (54), 76 (34), 75 (31), 64 (19), 63 (19), 56 (11), 51 (31), 50 (25), 44 (21), 43 (21).

*General Method for the Preparation of Compounds **2** and **3***

Educt **1** (1 mmol) was mixed with 3 cm^3 of acetic anhydride, 3 cm^3 of propionic anhydride, or 1 cm^3 of pivalic anhydride (plus a catalytic amount of 4-pyrrolidinopyridine). Under stirring, the mixture was heated at 100°C for 30–50 min. Then the volatile components were distilled off *in vacuo* and the residue was subjected to column chromatography (silica gel, eluent: *Et*O*Ac*:*n*-hexane = 5:1) and/or it was directly crystallized from the solvents given below.

(E)-2,2-Dimethyl-N-[4-phenyl-1-[(phenylmethylene)amino]-1H-imidazol-2-yl]propanamide
(**2**α, $C_{21}H_{22}N_4O$)

Yield: 52%; mp 256–257°C (*Me*OH); MS (185°C): m/z (%) = 346 ($M^{+\bullet}$, 22), 290 (20), 289 (100), 243 (14), 186 (35), 185 (62), 159 (23), 158 (48), 131 (11), 118 (14), 117 (27), 104 (38), 103 (11), 77 (36), 57 (68), 51 (11), 41 (22).

(E)-N-[1-[[(4-Chlorophenyl)methylene]amino]-4-phenyl-1H-imidazol-2-yl]acetamide (**2b**, $C_{18}H_{15}ClN_4O$)

Yield: 60%; mp 228–229°C (*Et*OH-*Et*O*Ac*). MS (200°C): m/z (%) = 338/340 ($M^{+\bullet}$, 12/4), 296/298 (11/3), 159 (56), 158 (100), 131 (13), 117 (36), 104 (20), 89 (14), 77 (18), 43 (27).

(E)-2,2-Dimethyl-N-[1-[[(4-chlorophenyl)methylene]amino]-4-phenyl-1H-imidazol-2-yl]propanamide (**2**β, $C_{21}H_{21}ClN_4O$)

Yield: 67%; mp 270–273°C (*Et*O*Ac*); MS (195°C): m/z (%) = 380/382 ($M^{+\bullet}$, 5/2), 323/325 (35/11), 243 (12), 186 (26), 185 (58) 159 (27), 158 (45), 131 (11), 129 (11), 118 (12), 117 (32), 111 (17), 104 (36), 103 (13), 89 (17), 85 (11), 77 (18), 75 (13), 57 (100), 56 (12), 55 (17), 44 (14), 43 (19), 41 (30).

(E)-N-[1-[[(4-Methoxyphenyl)methylene]amino]-4-phenyl-1H-imidazol-2-yl]acetamide (**2c**, $C_{19}H_{18}N_4O_2$)

Yield: 36%; mp 180–181°C (*Et*O*Ac*); MS (250°C): m/z (%) = 334 ($M^{+\bullet}$, 26), 292 (11), 159 (75), 158 (100), 134 (15), 131 (11), 117 (33), 104 (14), 77 (22), 43 (51).

(E)-2,2-Dimethyl-N-[1-[[(4-methoxyphenyl)methylene]amino]-4-phenyl-1H-imidazol-2-yl]propanamide (**2**γ, $C_{22}H_{24}N_4O_2$)

Yield: 55%; mp 205–207°C (*Et*O*Ac*-hexane); MS (220°C): m/z (%) = 376 ($M^{+\bullet}$, 17), 320 (21), 319 (100), 243 (38), 187 (12), 186 (90), 185 (29), 159 (38), 158 (61), 134 (45), 118 (14), 117 (28), 106 (15), 104 (21), 92 (13), 91 (12), 77 (40), 57 (69), 41 (27).

(E)-2,2-Dimethyl-N-[4-phenyl-1-[[(3,4,5-trimethoxyphenyl)methylene]amino]-1H-imidazol-2-yl]propanamide (**2**δ, $C_{24}H_{28}N_4O_4$)

Yield: 57%; mp 247–248°C (*Et*O*Ac*-hexane); MS (215°C): m/z (%) = 436 ($M^{+\bullet}$, 3), 379 (15), 243 (39), 186 (57), 185 (11), 167 (13), 159 (39), 158 (48), 117 (26), 104 (19), 77 (20), 57 (100), 56 (16), 43 (29), 41 (26).

(E)-N-[4-(4-Bromophenyl)-1-[[(4-methoxyphenyl)methylene]amino]-1H-imidazol-2-yl]acetamide (**2e**, $C_{19}H_{17}BrN_4O_2$)

Yield: 7%; mp 213–218°C; MS (205°C): m/z (%) = 412/414 ($M^{+\bullet}$, 3/3), 239 (27), 238 (28), 237 (29), 236 (26), 185 (21), 183 (16), 158 (21), 157 (41), 135 (16), 134 (27), 133 (17), 121 (53), 117 (11), 107 (11), 104 (13), 103 (11), 102 (15), 92 (18), 91 (16), 89 (11), 83 (11), 78 (11), 77 (54), 76 (19), 75 (15), 64 (14), 63 (12), 57 (30), 56 (10), 51 (21), 50 (14), 45 (12), 44 (19), 43 (100), 41 (12).

(E)-2,2-Dimethyl-N-[4-(4-bromophenyl)-1-[[(4-methoxyphenyl)methylene]amino]-1H-imidazol-2-yl]propanamide (**2**ε, $C_{22}H_{23}BrN_4O_2$)

Yield: 60%; mp 276–277°C (dioxane); MS (250°C): m/z (%) = 454/456 ($M^{+\bullet}$, 2/2), 397/399 (9/9), 264 (11), 157 (15), 134 (34), 107 (12), 92 (13), 77 (29), 57 (100), 44 (11), 41 (24).

(E)-N-Acetyl-N-[4-phenyl-1-[(phenylmethylene)amino]-1H-imidazol-2-yl]acetamide (**3a**)

Yield: 45%; mp 201–202°C (toluene) (Ref. [10] 206°C); MS (160°C): m/z (%) = 346 ($M^{+\bullet}$, 2), 304 (11), 201 (21), 160 (11), 159 (100), 158 (65), 131 (16), 117 (43), 104 (31), 103 (18), 91 (14), 89 (16), 77 (44), 76 (11), 51 (20), 43 (95).

(E)-N-(1-Oxopropyl)-N-[4-phenyl-1-[(phenylmethylene)amino]-1H-imidazol-2-yl]propanamide (**3**α, $C_{22}H_{22}N_4O_2$)

Yield: 43%; mp 197–203°C (*Et*OH); MS (190°C): m/z (%) = 374 ($M^{+\bullet}$, 2), 215 (22), 186 (12), 185 (17), 159 (100), 158 (43), 131 (11), 117 (29), 104 (22), 103 (12), 89 (13), 77 (37), 57 (70), 51 (14), 43 (10).

(E)-N-Acetyl-N-[1-[[(4-chlorophenyl)methylene]amino]-4-phenyl-1H-imidazol-2-yl]acetamide (**3b**, $C_{20}H_{17}ClN_4O_2$)

Yield: 18%; mp 206–211°C (*Et*OH); MS (200°C): m/z (%) = 380/382 ($M^{+\bullet}$, 4/1), 338/340 (13/4), 201 (24), 159 (100), 158 (61), 117 (34), 104 (14), 103 (11), 89 (11), 77 (11), 43 (48).

(E)-N-Acetyl-N-[1-[[(4-methoxyphenyl)methylene]amino]-4-phenyl-1H-imidazol-2-yl]acetamide (**3c**, $C_{21}H_{20}N_4O_3$)

Yield: 22%; mp 165–170°C (*Et*OAc); MS (190°C): m/z (%) = 376 ($M^{+\bullet}$, 1), 201 (28), 160 (11), 159 (100), 158 (40), 134 (16), 133 (10), 121 (24), 117 (26), 104 (15), 103 (11), 77 (36), 51 (11), 43 (83).

(E)-N-Acetyl-N-[4-phenyl-1-[[(3,4,5-trimethoxyphenyl)methylene]amino]-1H-imidazol-2-yl]acetamide (**3d**, $C_{23}H_{24}N_4O_5$)

Yield: 65%; mp 166–170°C (*Et*OAc-hexane); MS (190°C): m/z (%) = 436 ($M^{+\bullet}$, 3), 201 (35), 160 (12), 159 (100), 158 (38), 117 (18), 43 (40).

(E)-N-Acetyl-N-[4-(4-bromophenyl)-1-[[(4-methoxyphenyl)methylene]amino]-1H-imidazol-2-yl]acetamide (**3e**, $C_{21}H_{19}BrN_4O_3$)

Yield: 48%; mp 208–210°C (*Et*OAc); MS (210°C): m/z (%) = 454/456 ($M^{+\bullet}$, 4/4), 279/281 (19/18), 239 (50), 238 (24), 237 (53), 236 (19), 185 (20), 183 (22), 157 (35), 135 (17), 134 (32), 133 (24), 121 (25), 102 (11), 92 (18), 91 (11), 77 (36), 76 (15), 75 (12), 64 (11), 51 (11), 43 (100).

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