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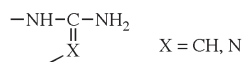
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The reactions of α,β -unsaturated nitriles (**1**, **9**, **12**) as bielectrophiles with aminoazoles (**2**, **4**, **6**) as binucleophiles were investigated. Acrylonitrile (**1**) reacts almost exclusively in a chemoselective Michael-type addition yielding the substituted azoles **3**, **5** and **7**, respectively. Cinnamonnitriles **9a,b** behave in a similar way, but the free CN group adds a second molecule **4** yielding **10a,b** and its cyclocondensation product **11a,b** as minor component. The attempted formation of azolopyrimidines is best achieved by the reaction of the benzylidenemalononitriles **12a-f** with **2** or **4**. The process is chemo- and regioselective. The structure determinations were based on NMR measurements including DEPT, COSY, ROESY, HMQC and HMBC techniques and correct earlier suggestions.

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Introduction.

Various physiological activities were found for natural and synthetic azolopyrimidines [1]. Therefore the preparation of new azolopyrimidine derivatives and their chemical modification represent a perspective trend and a promising goal. The most common method of dihydroazolopyrimidine synthesis is the cyclocondensation of aminoazoles, which contain an amidine substructure with α,β -unsaturated ketones [2]. Aminoazoles are bifunctional nucleophiles which should react with other bifunctional electrophiles like α,β -unsaturated nitriles as well. Cyclic products, obtained in the reaction of α,β -unsaturated nitriles and dinucleophiles as for example hydrazines, have been reported [3]. Thus, in continuation of our study on dihydroazolopyrimidines with active functional groups [4], we investigated the reaction of α,β -unsaturated nitriles with azoles containing the segment:



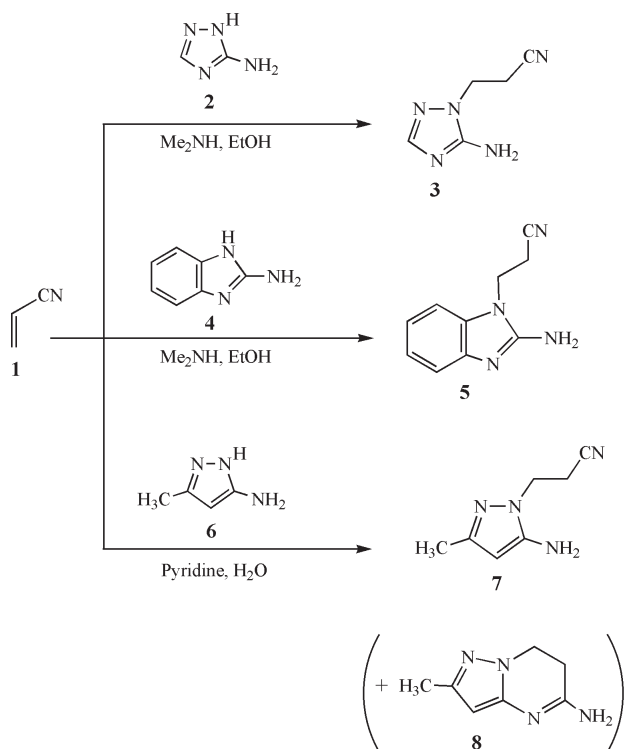
Due to the unsymmetric nitriles, two regioisomers can be expected for X = CH. If additionally three reactive centers (X = N) in an unsymmetric unit are present, altogether four isomers could be generated. Several examples of reaction products of α,β -unsaturated nitriles and aminoazoles were published by Elnagdi and coworkers [5], Ibrahim [6], Elgemeie [7] and Abdelhamid [8]; however, the reported product structures are not in agreement [6,8]. A profound structure determination, applying modern NMR techniques, seemed us to be necessary.

Results and Discussion.

The reaction of α,β -unsaturated nitriles and aminoazoles starts with a Michael-type addition. Acrylonitrile and

3-amino-5-phenylpyrazole for example yield in pyridine/water the β -adduct [9], the respective pyrazolopyrimidine is not formed. We found now a similar behavior of acrylonitrile (**1**) and 3-amino-1,2,4-triazole (**2**) [10] or **1** and 2-aminobenzimidazole (**4**) [11]. The products **3** and **5**, respectively, show the typical IR band for the CN group at $2250 \pm 5 \text{ cm}^{-1}$ and the δ value of $118.4 \pm 0.1 \text{ ppm}$ for the CN group in the ^{13}C NMR spectrum. Scheme 1 demonstrates the attack of an endocyclic nitrogen atom of the amidine

Scheme 1



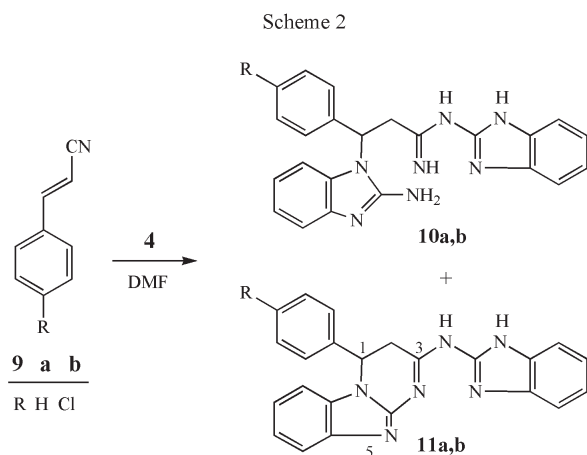
structure of **2** or **4** on the β -carbon atom of **1**. Whereas **4** is a symmetrical species, **2** has principally two different reactive sites. The attachment of the 2-cyanoethyl group on N-4 of **2** can be excluded since the ring proton does not show a 3J (H,C) coupling to a saturated carbon atom. Dimethylamine in ethanol was used as catalyst for both reactions. A cyclization of **3** or **5** to bicyclic systems could not be found.

3-Amino-5-methylpyrazole (**6**) [12] reacted with **1** to the β -adduct **7**; however, the ^1H NMR spectrum of the raw product revealed the presence of the bicyclic compound **8** as minor component (ratio **7**:**8** = 3:1). The yields of **3**, **5** and **7** were low (10, 35, 37 %), so we refrained from an isolation of **8**.

On the whole, the reactions shown in Scheme 1 are not suitable for the formation of azolopyrimidines.

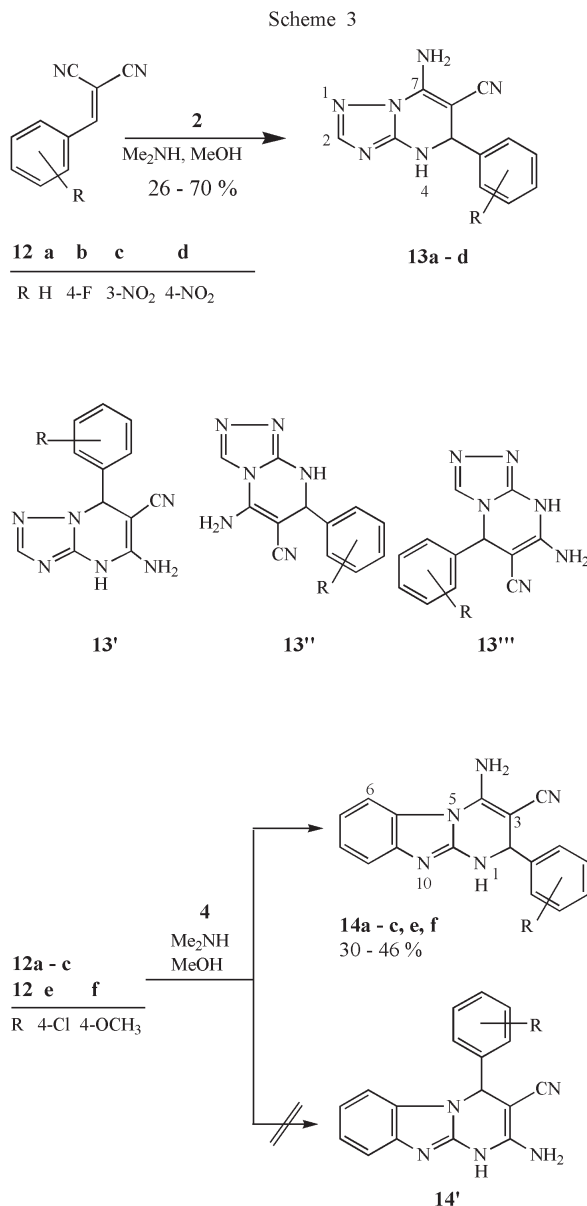
The next attempt was focused on cinnamitrile **9a** and its 4-chloro derivative **9b** which were reacted with **4** in DMF (Scheme 2). The major products **10a,b** are 1:2 adducts, whereby one 2-aminobenzimidazole molecule **4** attacks with N-1 in β -position of the nitrile, whereas the second molecule **4** attacks with the exocyclic amino group at the nitrile carbon atom. The minor reaction products **11a,b** are cyclocondensation products formed by the elimination of NH_3 . Equimolar mixtures of **9a** and **4** gave in boiling DMF 19 % of **10a** and 4 % of **11a**; analogously 51 % of **10b** and 11 % of **11b** were obtained. Excess amounts of nitriles did not yield 1:1 adducts. This result is in contrast to the reaction of **4** with α,β -unsaturated ketones as bielectrophiles, which furnished 1:1 adducts [10,11].

Apart from tautomeric equilibria in the amidine unit, one benzimidazole substructure is symmetric (due to a fast proton transfer), the other appears to be unsymmetric in the ^1H and ^{13}C NMR spectra of **9a,b** and **10a,b**.



Concerning the formation of dihydroazolopyrimidines, the cinnamitriles in Scheme 2 are an improvement in comparison to acrylonitrile in Scheme 1, but they are not good enough for preparative purposes. Therefore we studied the behavior of benzylidenemalonodinitriles **12a - f**. Their reactivity towards the aminoazoles **2** and **4** proved to

be much higher so that mild conditions by heating in methanol in the presence of dimethylamine could be used. Scheme 3 shows the generation of the desired azolopyrimidine derivatives **13** and **14** in reasonable yields.



The ^1H and ^{13}C NMR data of **13** and **14** are summarized in Tables 1 and 2. The δ values reveal a pyrimidine ring structure which is common to **13** and **14**; nevertheless, there are four possible isomeric structures for the product of **12** and **2**, and two possible structures for the product of **12** and **4** (Scheme 3). A detailed NMR study including one-dimensional NOE, ROESY, COSY, HMQC and HMBC measurements was performed for **14f** for which structure **14'** (R = 4-OCH₃) was claimed [6]. Figure 1 shows the HMBC con-

tour plot with particular emphasis on the crosspeaks for 2-H ($\delta = 5.14$). Six correlations can be seen: 2J (2-H, C-3), 3J (2-H, CN), 3J (2-H, *o*-C, Phenyl), 2J (2-H, *i*-C, Phenyl), 3J (2-H, C-4) and 3J (2-H, C-10a). The Nuclear Overhauser effect between the protons of the NH₂ group and the aromatic proton 6-H rules structure **14'** out. Thus, the regioselectivity of the addition **12** + **4** is established – in so far as the exocyclic amino group and not the endocyclic nitrogen atom attacks in β -position of the nitrile **4**. A tautomeric form, in which N-10 bears a hydrogen atom instead of N-1 cannot be excluded a priori – particularly not a fast equilibration with **14** – but the NOE between 1-H and 2-H favors strongly structure **14**. Due to a torsional angle close to 90°, the coupling constant between NH and 2-H is small. The signal of 2-H is a singlet, for some compounds a broadened singlet, the largest 3J value amounts to 2.0 Hz measured for

12d. A complete assignment of all ^1H and ^{13}C NMR signals for **14f**, together with the most important NOEs is given in Scheme 4.

The neighborhood (NOE) of 4-NH and 5-CH in the compounds **12** rules the alternative structures **13'** and **13'''** out, **13''** can be excluded by the absence of an NOE between the amino group and the proton on the triazole ring.

The result of the structure elucidation of **13** and **14** which includes the attack of the NH₂ group on the β -position of **2** and **4**, respectively, is surprising; it is not only in contrast to the reactivity of **2** and **4** in the presence of **1**, it disproves also the structure of the type **14'** (R = 4-OCH₃) which was suggested as reaction product of **12f** and **4** [6]. Recently a three-component reaction of 2-aminobenzimidazole, aromatic aldehydes and malononitril was studied [13]. The published product structures correspond to **14**.

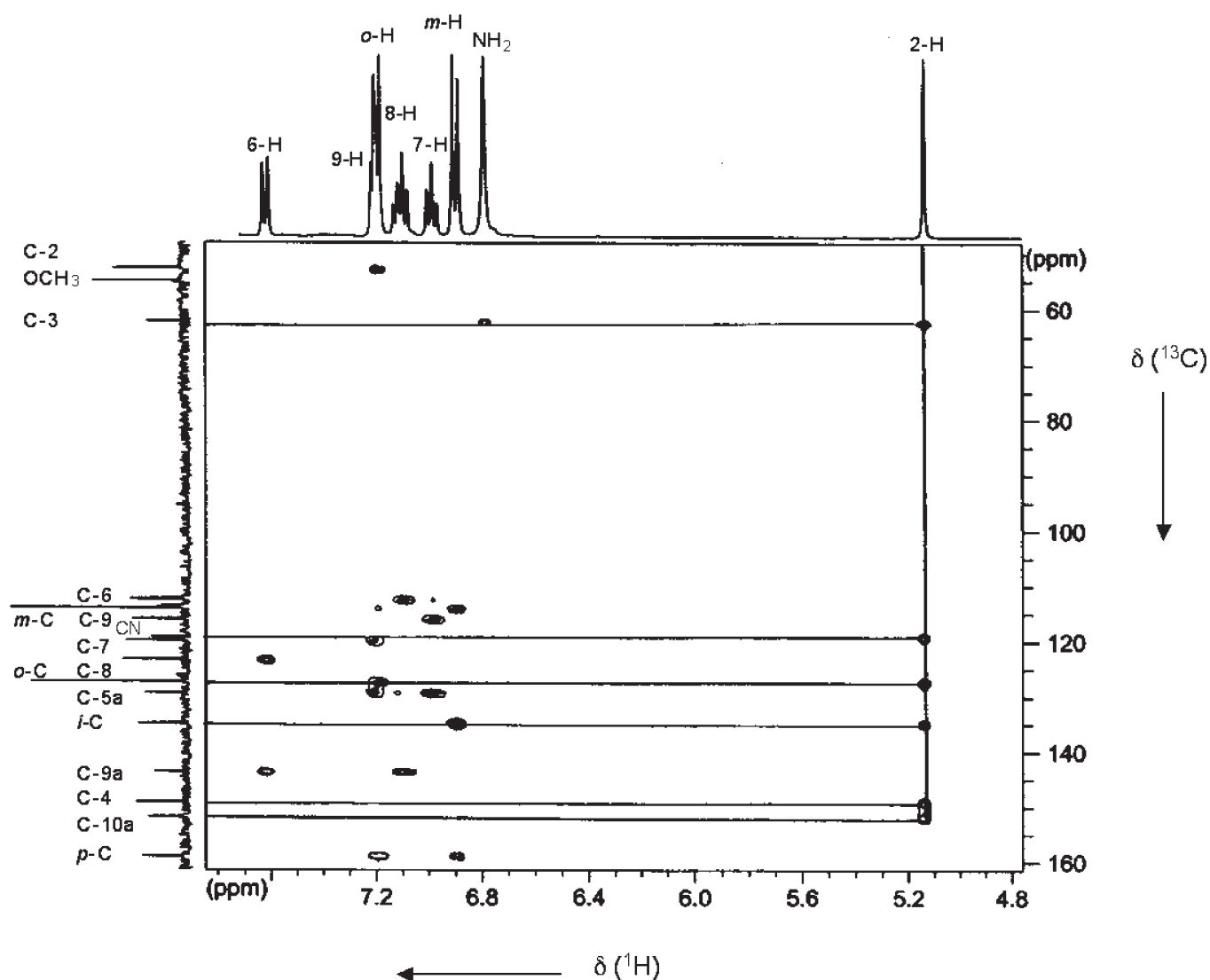
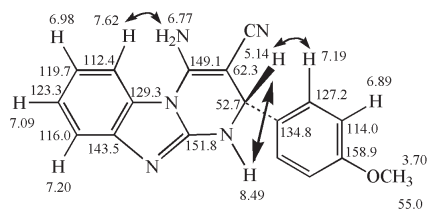


Figure 1: HMBC measurement of **14f** in CD₃SOCD₃. (The correlation lines indicate all 2J (2-H, C) and 3J (2-H, C) couplings.)

Scheme 4



cyclization with the endocyclic N atom of the azole **2** or **4**. Thus, the structures published earlier for the reaction products of **2** and **12** [6] and **4** and **12** [6,8] are not correct and the reactions of related aminoazoles [5,7] with **12** should be checked in the light of the new results.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were measured with the

Table 1

^1H NMR data of **13a - d** and **14a - c, e, f** (δ values in CD_3SOCD_3 , TMS as internal standard).

13	2-H	4-H	5-H	5-Aryl <i>o</i> -H	<i>m</i> -H	<i>p</i> -H	7-NH ₂						
14		1-H	2-H	2-Aryl <i>o</i> -H	<i>m</i> -H	<i>p</i> -H	4-NH ₂	6-H	7-H	8-H	9-H	OCH ₃	
13a	7.71	8.79	5.32	7.25	—	7.38	7.23						
13b	7.70	8.76	5.36	7.16	7.36	—	7.23						
13c	7.74	8.94	5.60	7.66	—	8.21	7.37						
13d	7.75	8.93	5.55	7.56	8.26	—	7.35						
14a		8.61	5.20	7.24	—	7.34	6.84	7.61	6.99	7.10	7.22		
14b		8.59	5.24	7.17	7.36	—	6.85	7.62	6.99	7.10	7.22		
14c		8.77	5.49	7.62	—	8.18	6.98	7.63	7.00	7.11	7.24		
14e		8.61	5.25	7.29	7.42	—	6.86	7.62	6.98	7.10	7.22		
14f		8.49	5.14	7.19	6.89	—	6.77	7.62	6.98	7.09	7.20	3.70	

Table 2

^{13}C NMR data of **13a - d** and **14a - c, e, f** (δ values in CD_3SOCD_3 , TMS as internal standard).

13	C-2	C-3a	C-5	5-Aryl <i>i</i> -C	<i>o</i> -C	<i>m</i> -C	<i>p</i> -C	C-6	6-CN	C-7						
14		1-H	2-H	2-Aryl <i>i</i> -C	<i>o</i> -C	<i>m</i> -C	<i>p</i> -C	C-3	3-CN	C-4	C-5a	C-6	C-7	C-8	C9	OCH ₃
13a	146.8	151.7	54.0	143.0	125.9	128.5	127.8	56.1	118.8	153.8						
13b ^[a]	147.0	151.8	53.3	139.3	128.2	115.4	161.7	55.9	118.8	153.8						
13c	147.3	152.0	53.0	145.2	132.9	147.8	120.7	54.9	118.7	153.7						
13d	147.1	152.0	53.2	147.2	127.3	124.0	150.1	54.9	118.7	153.8						
14a	143.6	151.8	53.2	142.9	125.9	128.7	127.8	62.0	119.2	149.1	129.3	112.4	119.9	123.3	116.1	
14b ^[a]	143.5	151.6	52.5	139.0	128.1	115.4	162.1	61.8	119.0	149.1	129.2	112.4	119.8	123.3	116.0	
14c	143.5	151.3	52.3	145.0	132.7	147.8	120.8	60.6	118.9	149.5	129.2	112.5	120.0	123.4	116.2	
14e	143.5	151.5	52.5	141.7	127.9	128.6	132.4	61.5	119.0	149.2	129.2	112.3	119.9	123.3	116.1	
14f	143.5	151.8	52.7	134.8	127.2	114.0	158.9	62.3	119.1	149.1	129.3	112.4	119.7	123.3	116.0	55.0

[a] The CF coupling constants have the usual size: $^1J = 242$ Hz, $^2J = 22$ Hz, $^3J = 8$ Hz, $^4J = 3$ Hz.

Conclusion.

Acrylonitrile (**1**) and cinnamionitriles (**9a,b**) react with aminoazoles (**2**, **4** or **6**) to linear adducts (**3**, **5**, **7**, **10**) as major products. Cyclic products as **8** and **11a,b** are at most minor components. The preferred interaction consists of an attack of an endocyclic nitrogen atom as electrophile on the β -position of the unsaturated nitrile as nucleophile. The opposite chemoselectivity is observed for the reactions of **2** or **4** with the benzylidenemalononitriles **12a - f**. In these cases the exocyclic nitrogen of the amino group attacks on the β -position of **12a - f** and a cyano group serves for the

Bruker machines AM 400 and AMX 400 and with a Varian Mercury VX-200 spectrometer using CD_3SOCD_3 as solvent and TMS as internal standard. Mass spectra (EI) were recorded on a Varian CH7A (70 eV ionization energy) and FD MS on a Finnigan MAT 95.

3-(5-Amino[1.2.4]triazol-1-yl)propionitrile or 5-Amino-1-(2-cyanoethyl)-1,2,4-triazole (**3**).

Acrylonitrile (**1**, 0.35 g, 6.5 mmol) and 3-amino-1,2,4-triazole (**2**, 0.42 g, 5.0 mmol) were refluxed in a mixture of 30 % dimethylamine in ethanol for 2 h. The volatile parts were evaporated and the residue triturated with 3 mL acetonitrile. Filtration and recrystallization from acetonitrile yielded 0.07 g (10 %) of **3**

which melted at 136 - 138 °C. ^1H NMR (CD_3SOCD_3): δ = 2.97 (t, 3J = 6.4 Hz, 2 H, β -CH $_2$), 4.18 (t, 3J = 6.4 Hz, 2 H, α -CH $_2$), 5.36 (s, 2 H, NH $_2$), 8.01 (s, 1 H, 4-H); ^{13}C NMR (CD_3SOCD_3): δ = 18.1 (β -CH $_2$), 43.7 (α -CH $_2$), 118.3 (CN), 143.0 (HC-3), 164.4 (C-5). EI MS: m/z (%) = 137 (52, M $^+$), 97 (88), 70 (100).

Anal. Calcd. for $\text{C}_5\text{H}_7\text{N}_5$ (137.1): C, 43.79; H, 5.14; N, 51.07. Found: C, 43.56; H, 5.03; N, 50.85.

3-(2-Aminobenzimidazol-1-yl)propionitrile or 5-amino-1-(2-cyanoethyl)benzimidazole (**5**).

The procedure described above for **3** yielded from 0.35 g (6.5 mmol) **1** and 0.67 g (5.0 mmol) **4** 0.33 g (35 %) of **5** which melted at 174 - 176 °C (recrystallization from CHCl_3). ^1H NMR (CD_3SOCD_3): δ = 2.89 (t, 3J = 6.8 Hz, 2 H, β -CH $_2$), 4.30 (t, 3J = 6.8 Hz, 2 H, α -CH $_2$), 6.54 (s, 2 H, NH $_2$), 6.91 (m, 2 H, 5-H, 6-H), 7.12, m, 1 H / 7.26, m, 1 H (4-H, 7-H). ^{13}C NMR (CD_3SOCD_3): δ = 17.0 (β -CH $_2$), 37.2 (α -CH $_2$), 107.7, 114.7, 118.1, 120.6 (C-4, C-5, C-6, C-7), 118.5 (CN), 133.7, 142.7 (C-3a, C-7a), 154.4 (C-2). EI MS: m/z (%) = 186 (84, M $^+$), 146 (63), 133 (49), 119 (27), 91 (100).

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{N}_4$ (186.2): C, 64.50; H, 5.41; N, 30.09. Found: C, 64.21; H, 5.18; N, 29.81.

3-(5-Amino-3-methylpyrazol-1-yl)propionitrile or 5-Amino-1-(2-cyanoethyl)-3-methylpyrazole (**7**).

A mixture of 265 mg (5.0 mmol) **1** and 485 mg (5.0 mmol) **6** [14] in 7.5 mL pyridine/15 mL H_2O was refluxed for 12 h. The volatile parts were evaporated *in vacuo* and the residue triturated with ethanol. The raw product was collected by filtration and washed with ethanol and acetonitrile. Recrystallization from ethyl acetate yielded 280 mg (37 %) of pure **7** which melted at 94 - 96 °C. ^1H NMR (CD_3SOCD_3): δ = 2.13, (s, 3 H, CH $_3$), 2.83 (t, 3J = 6.8 Hz, 2 H, β -CH $_2$), 3.57 (s, 2 H, NH $_2$), 4.18 (t, 3J = 6.8 Hz, 2 H, α -CH $_2$), 5.40 (s, 1 H, 4-H); ^{13}C NMR (CD_3SOCD_3): δ = 13.9 (CH $_3$), 18.7 (β -CH $_2$), 42.5 (α -CH $_2$), 92.9 (C-4), 118.1 (CN), 145.1, 148.9 (C-3, C-5). EI MS: m/z (%) = 150 (31, M $^+$), 98 (100).

Anal. Calcd. for $\text{C}_7\text{H}_{10}\text{N}_4$ (150.2): C, 55.98; H, 6.71; N, 37.31. Found: C, 55.65; H, 6.39; N, 37.10.

The raw product contained a second component **8** which showed in the ^1H NMR spectrum in CD_3SOCD_3 signals at δ = 2.19 (s, 3 H, CH $_3$), 2.81 (t, 3J = 6.3 Hz, 2 H, CH $_2$), 3.49 (s, 2 H, NH $_2$), 4.09 (t, 3J = 6.3 Hz, 2 H, CH $_2$), 5.40 (s, 1 H, CH). Signal integration gave a ratio **7**:**8** = 3:1.

3-(2-Aminobenzimidazol-1-yl)-3-phenylpropionic Acid Benzimidazol-2-ylamidine (**10a**) and 3-(Benzimidazol-2-yl-amino)-1-phenyl-1,2-dihydropyrimido[1,2-*a*]benzimidazole (**11a**).

A mixture of 0.39 (3.0 mmol) cinnamionitrile (**9a**) and 0.40 g (3.0 mmol) **4** was refluxed in 0.4 mL DMF for 15 min, diluted with 10 mL ethyl acetate and chromatographed on neutral Al_2O_3 (20 x 3 cm). The first fraction obtained with ethyl acetate as eluent consisted of small amounts of unreacted **4** and **9a**. A 4:1 mixture of ethylacetate and methanol gave then 110 mg (19 %) of **10a** and 20 mg (4 %) of **11a**. Compound **10a** decomposes at 230 °C and compound **11a** does not melt below 310 °C.

10a: ^1H NMR (CD_3SOCD_3): δ = 3.15 (dd, 2J = 16.4 Hz, 3J = 3.5 Hz, 1 H, 2-H), 3.50 (dd, 2J = 16.4 Hz, 3J = 7.6 Hz, 1 H, 2-H), 6.01 (dd, 3J = 3.5 Hz, 3J = 7.6 Hz, 1 H, 3-H), 7.10 (m, 1 H, aromat. H), 7.12 - 7.21 (m, 5 H, aromat. H), 7.24 (m, 1 H, aromat. H), 7.31 - 7.40 (m, 5 H, aromat. H), 7.48 (m, 1 H, aromat. H), 8.40 (br. s, 3 H, NH $_2$, NH), 9.10 (br. s, 1 H, NH), 9.30 (br. s, 1 H, NH); ^{13}C

NMR (CD_3SOCD_3): δ = 32.2 (CH $_2$), 51.5 (CH), 110.1, 111.3, 111.3, 113.0, 122.4, 122.4, 122.9, 123.4 (CH, benzimidazole) 125.8, 128.5, 129.1 (CH, phenyl), 129.7, 130.2, 131.2, 138.1 (aromat. C $_q$), 150.9, 152.4 (C $_q$, imidazole), 168.2 (C $_q$, amidine). EI MS: m/z (%) = 262 (100, [M $^+$ - 133]), 133 (56, [M $^+$ - 262]) [15].

Anal. Calcd. for $\text{C}_{23}\text{H}_{21}\text{N}_7$ (395.5): C, 69.85; H, 5.35; N, 24.79. Found: C, 69.53; H, 5.47; N, 24.55.

11a: ^1H NMR (CD_3SOCD_3): δ = 3.16 (dd, 2J = 16.6 Hz, 3J = 2.4 Hz, 1 H, 2-H), 3.72 (dd, 2J = 16.6 Hz, 3J = 7.3 Hz, 1 H, 2-H), 6.00 (dd, 3J = 2.4 Hz, 3J = 7.3 Hz, 1 H, 1-H), 6.95 - 7.20 (m, 7 H, aromat. H), 7.21 - 7.39 (m, 3 H, aromat. H), 7.42 - 7.58 (m, 3 H, aromat. H), 12.50 (br. s, 2 H, 2 NH); ^{13}C NMR (CD_3SOCD_3): δ = 35.6 (CH $_2$), 51.9 (CH), 109.3, 114.0, 114.0, 117.7, 121.1, 121.6, 121.6, 125.4, 125.7, 128.2, 129.0 (aromat. CH), 132.5, 135.7, 139.3, 142.1 (aromat. C $_q$), 148.8, 151.4, 157.7 (C $_q$ N $_x$, x = 2,3). EI MS: m/z (%) = 378 (79, M $^+$), 301 (100), 189 (25).

Anal. Calcd. for $\text{C}_{23}\text{H}_{18}\text{N}_6$ (378.4): C, 73.00; H, 4.79; N, 22.21. Found: C, 72.65; H, 4.42; N, 21.95.

3-(2-Aminobenzimidazol-1-yl)-3-(4-chlorophenyl)propionic Acid Benzimidazol-2-ylamidine (**10b**) and 3-(Benzimidazol-2-ylamino)-1-(4-chlorophenyl)-1,2-dihydropyrimido[1,2-*a*]benzimidazole (**11b**).

The preparation according to the procedure described for **10a** and **11a** yielded 0.33 g (51 %) **10b** 0.07 g (11 %) of **11b** from 0.40 g (3.0 mmol) of **4** and 0.49 g (3.0 mmol) of 4-chlorocinnamionitrile (**9b**). The crystals of **10b** decompose at 215 °C; **11b** does not melt below 310 °C.

10b: ^1H NMR (CD_3SOCD_3): δ = 3.10 (dd, 2J = 16.4 Hz, 3J = 3.1 Hz, 1 H, 2-H), 3.46 (dd, 2J = 16.4 Hz, 3J = 7.8 Hz, 1 H, 2-H), 6.01 (dd, 3J = 7.8 Hz, 3J = 3.1 Hz, 1 H, 3-H), 7.09 - 7.16 (m, 4 H, aromat. H), 7.19 (m, 2 H, aromat. H), 7.21 (m, 1 H, aromat. H), 7.31 - 7.37 (m, 2 H, aromat. H), 7.43 (m, 2 H, aromat. H), 7.47 (m, 1 H, aromat. H), 8.34 (br. s, 3 H, NH $_2$, NH), 8.88 (br. s, 1 H, NH), 9.03 (br. s, 1 H, NH); ^{13}C NMR (CD_3SOCD_3): δ = 32.2 (CH $_2$), 50.8 (CH), 109.8, 111.3, 111.3, 113.6, 122.3, 122.3, 122.5, 123.1 (CH, benzimidazole), 127.8, 129.1 (CH, aryl), 130.0, 130.6, 132.9, 133.1, 137.4 (aromat. C $_q$), 151.1, 152.7 (C $_q$, imidazole), 167.5 (C $_q$, amidine). EI MS: m/z (%) = 296 (10, [M $^+$ - 133]), 133 (100, [M $^+$ - 296]) [15].

Anal. Calcd. for $\text{C}_{23}\text{H}_{20}\text{ClN}_7$ (429.9): C, 64.26; H, 4.69; N, 22.81. Found: C, 64.29; H, 4.75; N, 22.58.

11b: ^1H NMR (CD_3SOCD_3): δ = 3.15 (dd, 2J = 16.1 Hz, 3J = 2.7 Hz, 1 H, 2-H), 3.73 (dd, 2J = 16.1 Hz, 3J = 7.2 Hz, 1 H, 2-H), 6.03 (dd, 3J = 7.2 Hz, 3J = 2.7 Hz, 1 H, 1-H), 7.03 - 7.19 (m, 7 H, aromat. H), 7.40 (m, 2 H, aromat. H), 7.48 - 7.55 (m, 3 H, aromat. H), 12.6 (br. s, 2 H, NH); ^{13}C NMR (CD_3SOCD_3): δ = 35.5 (CH $_2$), 51.3 (CH), 109.3, 113.9, 113.9, 117.6, 121.3, 121.7, 121.7, 127.7, 128.2, 129.0 (aromat. CH), 132.3, 132.8, 135.5, 138.3, 141.8 (aromat. C $_q$), 148.9, 151.2 (C $_q$, imidazole), 167.9 (C $_q$, amidine). EI MS: m/z (%) = 412 (74, M $^+$), 301 (100).

Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{ClN}_6$ (412.9): C, 66.91; H, 4.15; N, 20.35. Found: C, 66.68; H, 3.94; N, 20.04.

General Procedure for the Preparation of the 7-Amino-5-aryl-4,5-dihydro-(1,2,4)-triazolo[1,5-*a*]pyrimidine-6-carbonitriles (**13a-d**).

A mixture of 0.17 g (2.0 mmol) **2** and 2.0 mmol of malonodinitrile **12a-d** was refluxed in 2 mL 30 % dimethylamine in ethanol for 5 min. The precipitate formed after cooling was collected by filtration and recrystallized from ethanol.

7-Amino-4,5-dihydro-5-phenyl-(1,2,4)-triazolo[1,5-*a*]pyrimidine-6-carbonitrile (**13a**).

This compound was obtained in 70 % yield, mp 267 – 269 °C. EI MS: m/z (%) = 238 (31, M⁺), 161 (100).

Anal. Calcd. for C₁₂H₁₀N₆ (238.3): C, 60.50; H, 4.23; N, 35.27. Found: C, 60.38; H, 4.07; N, 35.13.

7-Amino-5-(4-fluorophenyl)-4,5-dihydro-(1,2,4)-triazolo[1,5-*a*]pyrimidine-6-carbonitrile (**13b**).

This compound was obtained in 27 % yield, mp 255 – 256 °C. FD MS: m/z (%) = 257 (100, [M + 1]⁺).

Anal. Calcd. for C₁₂H₉FN₆ (256.2): C, 56.25; H, 3.54; N, 32.80. Found: C, 56.18; H, 3.49; N, 32.59.

7-Amino-4,5-dihydro-5-(3-nitrophenyl)-(1,2,4)-triazolo[1,5-*a*]pyrimidine-6-carbonitrile (**13c**).

This compound was obtained in 42 % yield, mp 258 – 259 °C. FD MS: m/z (%) = 284 (100, [M + 1]⁺).

Anal. Calcd. for C₁₂H₉N₇O₂ (283.3): C, 50.88; H, 3.20; N, 34.62. Found: C, 50.99; H, 3.06; N, 34.67.

7-Amino-4,5-dihydro-5-(4-nitrophenyl)-(1,2,4)-triazolo[1,5-*a*]pyrimidine-6-carbonitrile (**13d**).

This compound was obtained in 26 % yield, mp 275 (decomp.). FD MS m/z (%) = 284 (100, [M + 1]⁺).

Anal. Calcd. for C₁₂H₉N₇O₂ (283.3): C, 50.88; H, 3.20; N, 34.62. Found: C, 51.05; H, 3.33; N, 34.85.

General Procedure for the Preparation of the 4-Amino-2-aryl-1,2-dihydro-pyrimido[1,2-*a*]benzimidazole-3-carbonitriles (**14a-c,e,f**).

A mixture of 266 mg (2.0 mmol) **4** and 2.0 mmol of malonodinitrile **12a-c,e,f** was refluxed in 2 mL 30 % dimethylamine in ethanol for 5 min. The precipitate formed after cooling was collected by filtration and recrystallized from ethanol.

4-Amino-1,2-dihydro-2-phenylpyrimido[1,2-*a*]benzimidazole-3-carbonitrile (**14a**).

This compound was obtained in 45 % yield, mp 205 – 207 °C, lit. [13] 218 °C. EI MS: m/z (%) = 287 (42, M⁺), 210 (66), 133 (100).

Anal. Calcd. for C₁₇H₁₃N₅ (287.3): C, 71.06; H, 4.56; N, 24.37. Found: C, 71.86; H, 4.46; N, 24.29.

4-Amino-2-(4-fluorophenyl)-1,2-dihydropyrimido[1,2-*a*]benzimidazole-3-carbonitrile (**14b**).

This compound was obtained in 46 % yield, mp 232 (decomp.). FD MS: m/z (%) = 306 (100, [M + 1]⁺).

Anal. Calcd. for C₁₇H₁₂FN₅ (305.3): C, 66.88; H, 3.96; N, 22.94. Found: C, 66.71; H, 3.73; N 22.86.

4-Amino-1,2-dihydro-2-(3-nitrophenyl)pyrimido[1,2-*a*]benzimidazole-3-carbonitrile (**14c**).

This compound was obtained in 37 % yield, 216 – 217 °C. FD MS: m/z (%) = 333 (100, [M + 1]⁺).

Anal. Calcd. for C₁₇H₁₂N₆O₂ (332.3): C, 61.44; H, 3.64; N, 25.29. Found: C, 61.27; H, 3.50; N 25.22.

4-Amino-2-(4-chlorophenyl)-1,2-dihydropyrimido[1,2-*a*]benzimidazole-3-carbonitrile (**14d**).

This compound was obtained in 37 % yield, mp 232 (decomp.), lit. 238 °C [13]. FD MS: m/z (%) = 322 (100, [M + 1]⁺).

Anal. Calcd. for C₁₇H₁₂ClN₅ (321.8): C, 63.46; H, 3.76; N, 21.77. Found: C, 63.25; H, 3.62; N, 21.71.

4-Amino-1,2-dihydro-2-(4-methoxyphenyl)pyrimido[1,2-*a*]benzimidazole-3-carbonitrile (**14f**).

This compound was obtained in 30 % yield, mp 212 – 213 °C, lit. [13] 197 °C. FD MS: m/z (%) = 318 (100, [M + 1]⁺).

Anal. Calcd. for C₁₈H₁₅N₅O (317.4): C, 68.13; H, 4.76; N, 22.07. Found: C, 67.82; H, 4.55; N, 21.91.

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