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TETRAZOLIUM *N*-AMINIDES: COMPLEMENTARY STUDIES ON SYNTHESIS AND PROPERTIES [1]

Dietrich Moderhack* and Matthias Noreiks

Institute of Pharmaceutical Chemistry, Technical University,
D-38106 Braunschweig, Germany
e-mail: d.moderhack@tu-bs.de

Dedicated to Professor Gerwalt Zinner on the occasion of his 85th birthday

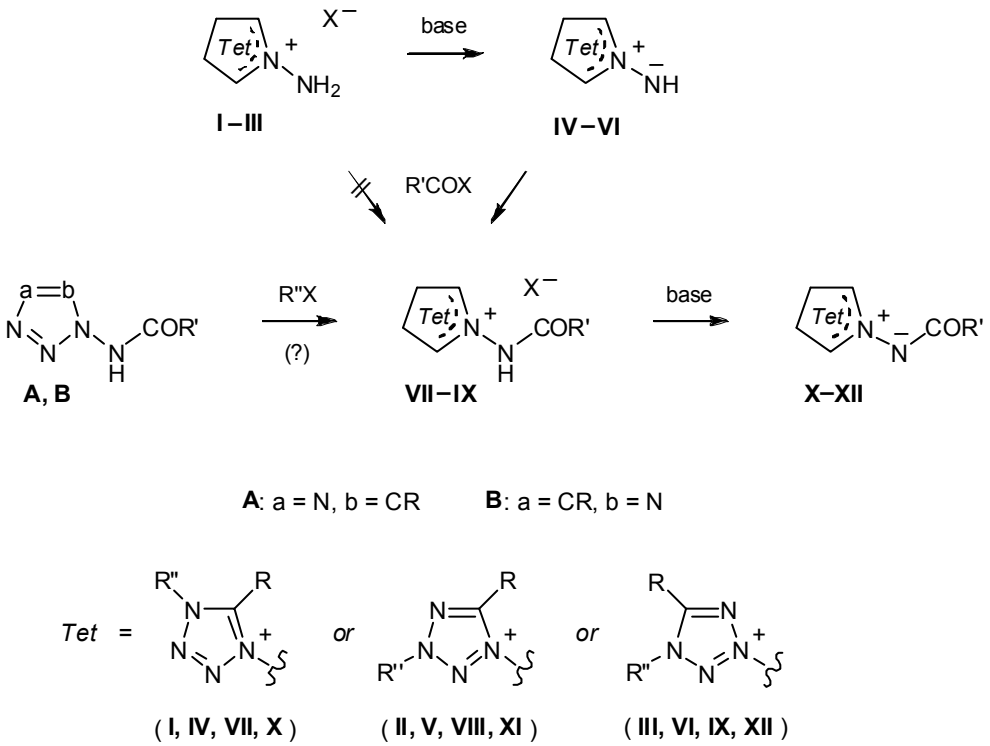
Abstract – Attempts are made to access the title compounds from *N*-amido/ureidotetrazoles (**A**, **B**; 1*H*- / 2*H*-system). These materials are provided by acylation of the respective *N*-aminotetrazoles (**A** in one step, **B** partly by hydrolysis of diacylated derivatives which are obtained directly). On treatment with excess dimethyl sulfate only **A** undergoes the necessary ring quaternization, giving rise to two isomers (ratio *ca.* 4 : 1); work-up with base allows isolation of the major aminide (**X**). This technique requires that the (slow) quaternization process be fully completed, since at pH > 7 dimethyl sulfate rapidly affects the side chain of **A**. Concluding experiments pertain to protonation and methylation of the title compounds (**X–XII**).

INTRODUCTION

Three series of tetrazolium *N*-aminides (**X–XII**) stabilized by an electron-withdrawing group have been recently prepared in straightforward manner from the respective aminotetrazolium salts (**I–III**) (Scheme 1).[1] The conversion, performed as one-pot synthesis, proceeded as follows: (i) deprotonation of **I–III** to generate the parent aminides (**IV–VI**), (ii) acylation of the latter to yield the amidotetrazolium salts (**VII–IX**), and (iii) deprotonation of **VII–IX** to afford the target aminides (**X–XII**). The abridgment (**I–III** → **VII–IX**) was not feasible because of insufficient nucleophilicity of the amino group.[1,2] This contrasts with the reactivity of 1(3)-aminoimidazolium [3] and both 4- and 1-amino-1,2,4-triazolium salts [4] which can be directly acylated. An alternate approach constitutes quaternization of *N*-amidotetrazoles like **A** and **B** — a principle that has been verified with 4-amido-[4a,5] and 1-amido-1,2,4-triazoles.[4d] Having pointed to the viability of the route (**A** → **VII** → **X**) marginally,[1] we provide a detailed account which includes the

sequences (**A** → **VIII** → **XI**) and (**B** → **IX** → **XII**) and, finally, describes properties of **X–XII** not dealt with in our previous paper.[1]

Scheme 1



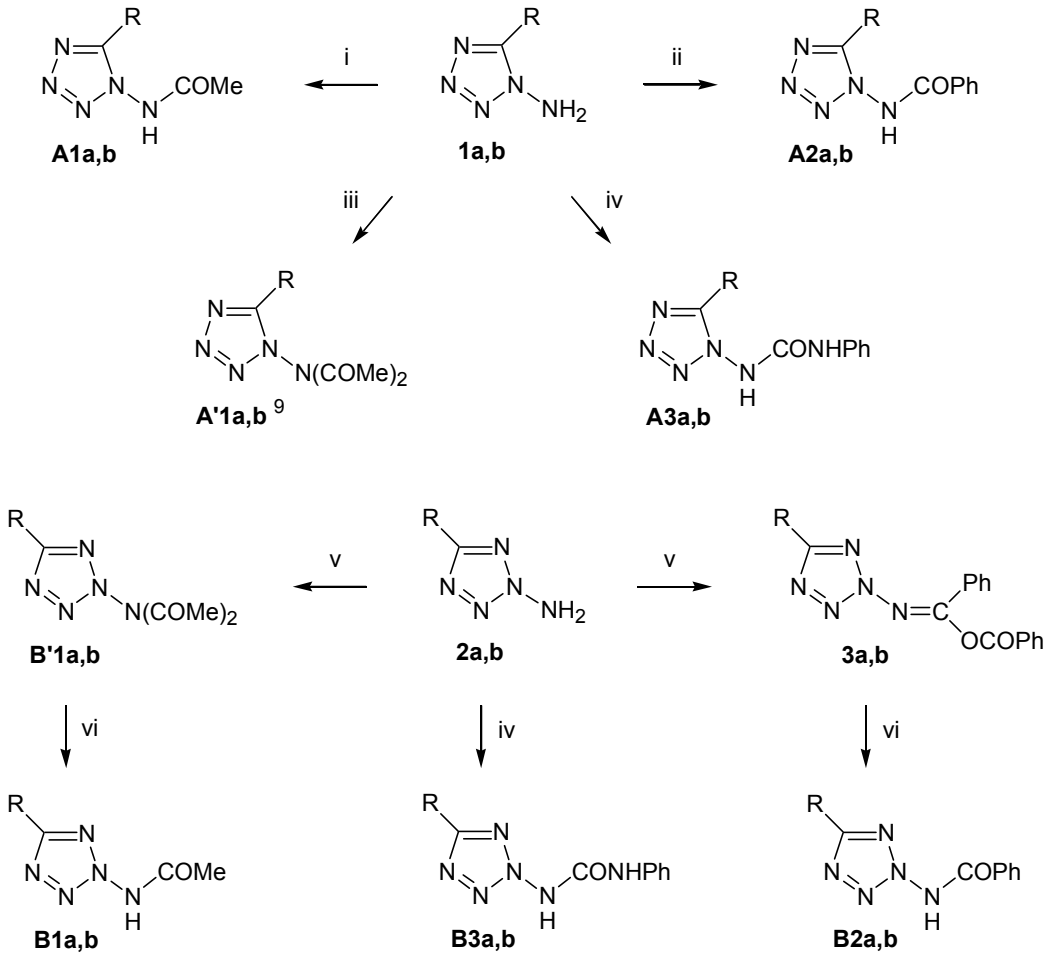
RESULTS AND DISCUSSION

N-Amido/Ureidotetrazoles

As candidates we chose derivatives having R = Me / Ph and R' = Me / Ph / NHPh most of which were unknown materials. Access was sought by acylation of the respective *N*-aminotetrazoles (**1**, **2**) (Scheme 2). While this kind of functionalization is amply documented for *N*-aminoazoles in general,[6] the experience with tetrazoles is scarce. Directly relevant examples are limited to the reactions of 1-aminotetrazole (**1**; R = H) with phenyl isocyanate [7] and of 2-amino-5-phenyltetrazole (**2b**) with phthaloyl chloride.[8]

Regarding acetylation, **1a,b** were treated at elevated temperature with a slight excess of acetic anhydride in acetic acid. While the derivative (**A1a**) was formed smoothly, the 5-phenyl congener (**A1b**) arose less readily (heating with the neat reagent proved inappropriate as this modification caused twofold acetylation giving **A'1a,b** [9,10]). However, when submitting the isomeric tetrazoles (**2a,b**) to the conditions suitable for **A1a,b**, no reaction occurred. This lack of nucleophilicity reflects the stronger electron-withdrawing influence exerted by the 2*H*-tetrazol-2-yl system.[11] Thus, to prepare **B1a,b** we attempted acetyl chloride in diethyl ether in the presence of triethylamine and commenced using an equimolar amount of the

Scheme 2



a: R = Me **b**: R = Ph

Reagents and conditions: i, Ac_2O (1.2 equiv.) / AcOH: 120 °C, 6 h; ii, PhCOCl / pyridine: for **A2a** 20 °C, 1 h; for **A2b** 115 °C, ≥ 6 h; iii, Ac_2O (neat): 140 °C, 4 h; iv, PhNCO: for **A3a** CH_2Cl_2, 20 °C, 1 h; for **A3b** pyridine, 115 °C, 6 h; for **B3a,b** pyridine, 20 °C, 1-2 h; v, MeCOCl or PhCOCl (2 equiv.) / Et_3N: 20 °C, 1 h; vi, 2 N KOH, 80 °C: for **B1a,b** 2 h, for **B2a,b** 4 h; then 12 N HCl

reagent. But since this led to a mixture of mono- and diacetyl derivatives accompanied by starting material, we sought for exhaustive acetylation by adjusting the proportions. The diacetyl derivatives (**B'1a,b**), now formed exclusively, could be in turn hydrolyzed to the required amides (**B1a,b**).

Benzoylation of **1a,b** was achieved with benzoyl chloride using pyridine as solvent (→ **A2a,b**);[12] again, the 5-phenyl substituted derivative (**1b**) proved less reactive. The two isomeric amines (**2a,b**), by contrast, turned out to be fully inert. In parallel to acetylation, reactivity was observed only on employing triethylamine and here too the process did not stop at the stage of monoacylation: as final products the isoimides (**3a,b**) were formed (instead of dibenzamides of type **B'**); their structure was deduced from comparison of the ^{13}C NMR data with those of analogous compounds of the 1,2,3-triazole series.[13] On hydrolysis of these materials (made by use of excess reagent) the target benzamides (**B2a,b**) arose in good yield.

Phenylcarbamoylation by the treatment with phenyl isocyanate proceeded well at room temperature in the cases of **1a** and **2a,b** to afford the ureas (**A3a**) and (**B3a,b**), respectively. With **1a** the reaction could be accomplished in dichloromethane as solvent, whereas pyridine was compulsory for the conversion of **2a,b**. This applies to **1b** as well, but here also heating was required because of the poor solubility.

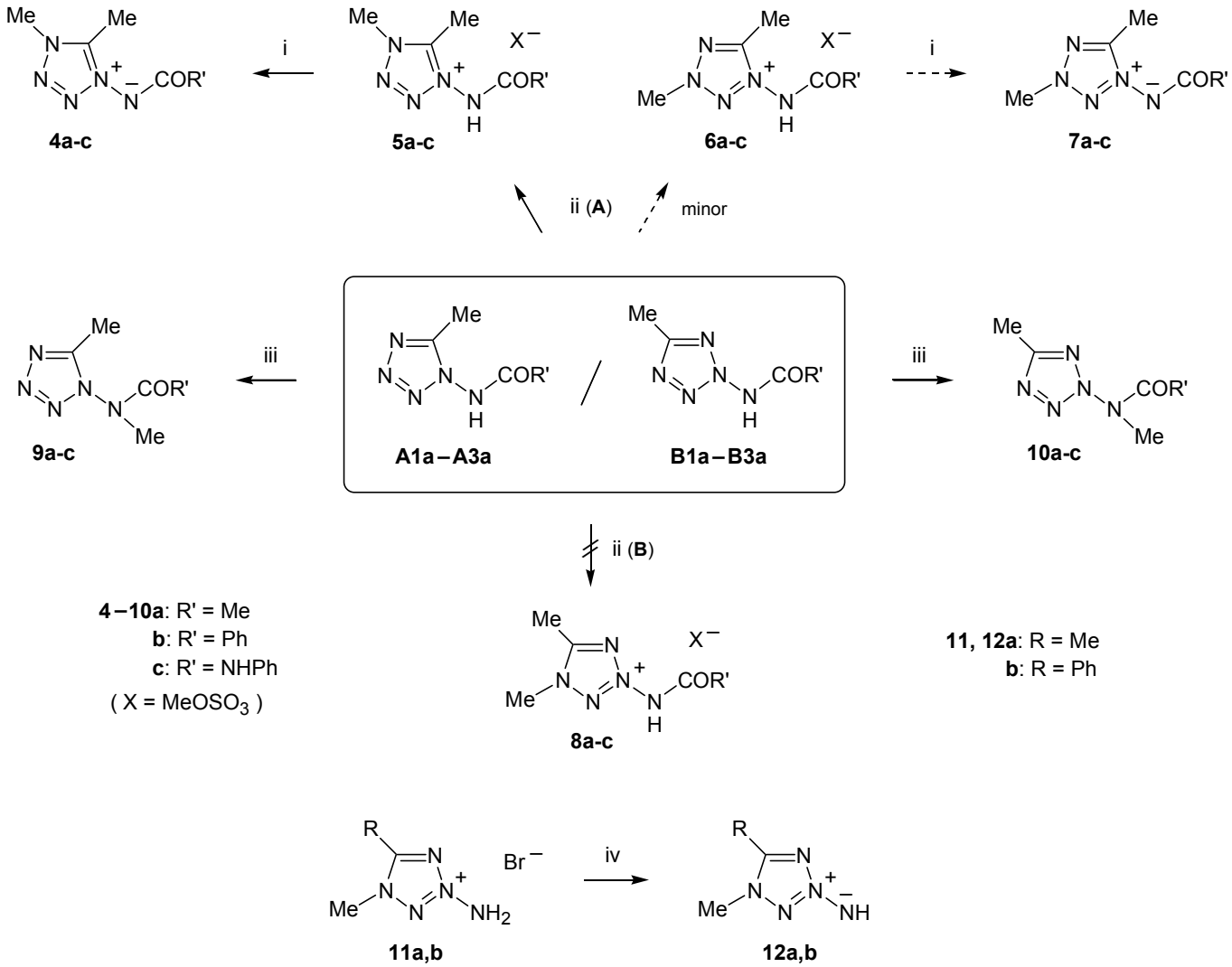
Tetrazolium *N*-Aminides

Exploring to what extent the above tetrazoles (**A**) and (**B**) are suitable materials for aminide making, we first studied the 5-methyl derivatives (**A1a–A3a**) and (**B1a–B3a**). Since in preliminary experiments[1] methyl iodide has proved inappropriate for ring quaternization,[14] dimethyl sulfate was used throughout to effect the following (Scheme 3):

The isomers (**A1a–A3a**), while reacting more slowly than the parent (**1a**),[1] gave, in line with the ambident behavior of 1*H*-tetrazoles, *ca.* 4 : 1 mixtures of the quaternary salts (**5a-c**) and (**6a-c**). Attempts to isolate them were vitiated: In the case of **5a** / **6a** the acidic medium arising on removal of excess reagent with water–diethyl ether induced hydrolysis of the acetamido group to leave behind the respective amino salts of type (**I** / **II**) (R = R" = Me). The side chains of **5b** / **6b** and **5c** / **6c** withstood this work-up, but when, for convenience, the solution of **5b** / **6b** was submitted to an anion exchange procedure ($MeOSO_3 \rightarrow Br$), in addition to the target bromides substantial amounts of the aminides (**4b** / **7b**) were formed and separated as solids on the exchange resin. Hence we treated the original reaction mixtures (**5b** / **6b**) and (**5c** / **6c**) with aqueous alkali carbonate. This immediately caused precipitation of the pure aminides (**4b**) and (**4c**);[15] the minor components (**7b**) and (**7c**), however, eluded isolation. The same technique was then applied to the couple (**5a** / **6a**). But here the liberated aminides (**4a** / **7a**) proved susceptive of alkylation by the dimethyl sulfate still present in the reaction mixture, giving rise to irremovable by-products identified as the methyl sulfate analogues of the iodide salts (**14a** / **15a**) which were prepared separately (see later). Yet another impurity, the *N*-methylacetamide (**9a**), will form if that base-assisted work-up is set about untimely, *i.e.* before the initial quaternization process (which is very slow !) has been fully completed: According to a model experiment dimethyl sulfate at pH > 7 rapidly attacks unconsumed starting material at the functional group.[16, 17] Since the educts (**A2a**) and (**A3a**) are likewise susceptible to this kind of conversion giving **9b** and **9c**, respectively, an appropriate check should precede isolation of the aminides (**4b**) and (**4c**).

In striking contrast to the behavior of **A1a–A3a** towards dimethyl sulfate, no reaction took place with the isomers (**B1a–B3a**), even on prolonged exposure. These substrates, like all 2*H*-tetrazoles, are extremely weak nucleophiles, and here the acyl moiety further impairs reactivity so as to prevent the formation of the desired salts (**8a–c**). The only conversion of which **B1a–B3a** were found capable was side chain methylation yielding the derivatives (**10a-c**).[18]

Scheme 3



Reagents and conditions: i, K_2CO_3, H_2O; ii, $(MeO)_2SO_2$, 20 °C: for **5a-c** and **6a-c** 3 d, for **8a-c** 6 d; iii, $(MeO)_2SO_2$ / K_2CO_3: for **9a** and **10a** $CHCl_3$, 60 °C, 4 h; for **9b,c** and **10b,c** H_2O, 20 °C, 0.5 h; iv, K_2CO_3, H_2O; then CH_2Cl_2

Turning to substrates having R = Ph, we treated the urea (**A3b**) with dimethyl sulfate. Unlike its methyl congener (**A3a**) it displayed only negligible reactivity. This resembles our earlier observation in which the quaternization of the parent (**1b**) proceeded considerably more slowly than that of **1a**.[1] In view of this inertness the experiments with the 5-phenyl-2*H*-tetrazoles (**B1b–B3b**) were unpromising and omitted.

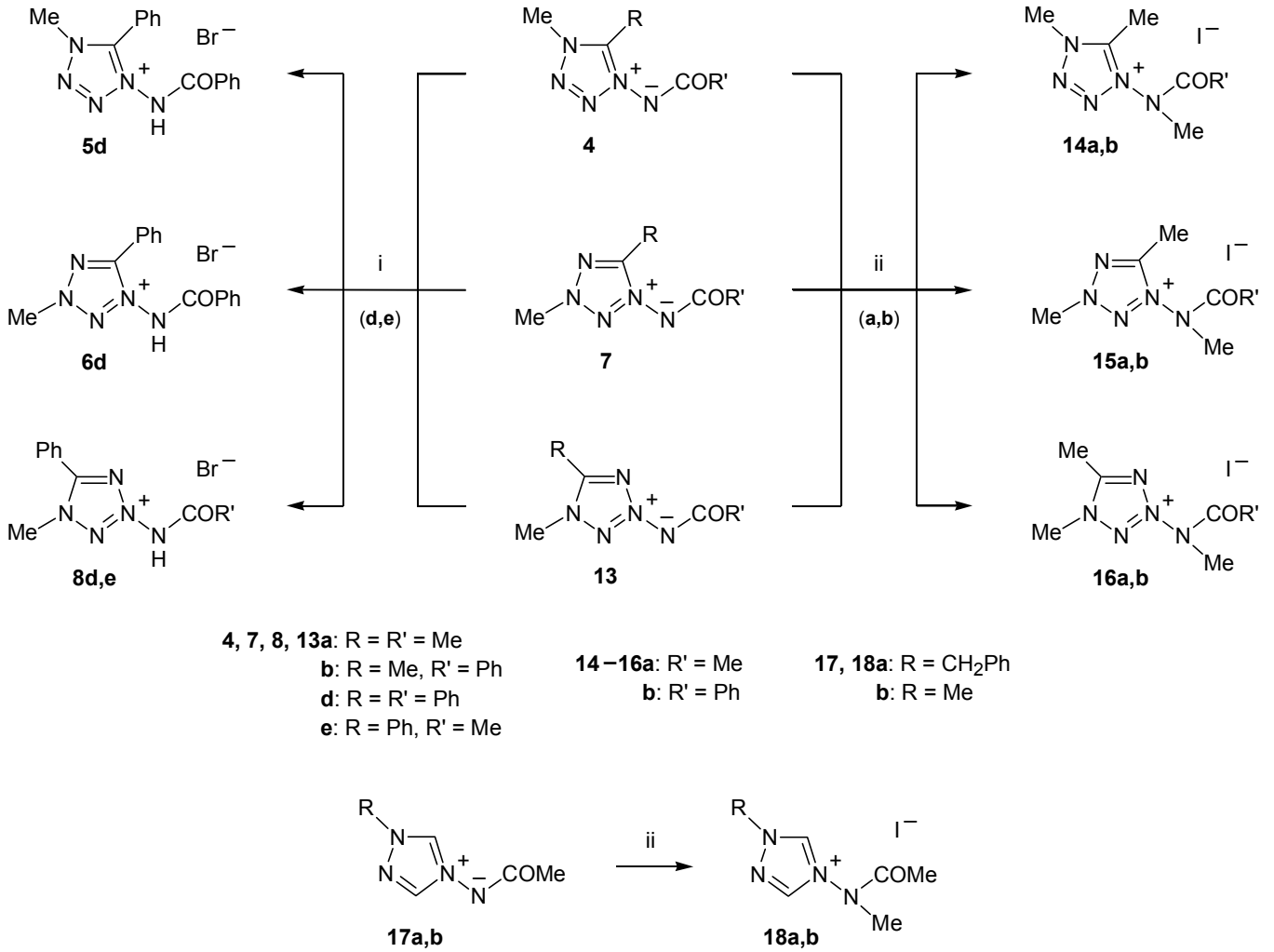
Addendum to aminide synthesis from **I–III**: In pursuit of our former aminide synthesis [1] we have found that intermediates of type (**VI**), *viz.* the derivatives (**12a,b**), are isolable compounds.[19] The corresponding representatives of type (**IV**) and (**V**), however, proved elusive. The obtained substances form slightly hygroscopic crystals. Their relative stability is rationalized in terms of the stronger electron-withdrawing effect (inductively and by resonance) of the 1*H*-tetrazolium-3-yl system (*cf.* ref.[20]). Basicity measure-

ments, performed by UV spectrometry at 260 nm and 20 °C in water, showed pK_a = 9.27 (**12a**) and 8.76 (**12b**).[21] On addition of hydrobromic acid to **12b**, the starting salt (**11b**) was recovered in 78% yield.

N-Amidotetrazolium Salts

Isolation of the intermediary salts (**5**) and (**6**), dispensible in the preceding part, was required for comparative purposes. We therefore tried to approach the species from the aminide side and extended the method to the isomer (**8**). When the acetyl derivatives (**4a,e**) and (**7e**) were treated in ethanol with hydrobromic acid, followed by addition of diethyl ether, instead of the respective acetamido salts (**5**) and (**6**) the products of hydrolysis [*i.e.* type (**I**) and (**II**)] were found. This confirms the sensitivity experienced above with **5a**/**6a** after having quaternized **A1a**. Complete hydrolysis of the functionality also occurred on the

Scheme 4



Reagents and conditions: i, 9 N HBr (1.5 equiv.): for **5d** H_2O –CH_2Cl_2, for **6d** and **8d,e** EtOH –Et_2O; ii, MeI / DMF, 20 °C: for **14a,b**, **15a,b**, and **18a,b** 24 h; for **16a,b** 3d

attempt to prepare the benzamido salt (**5b**). Stability was encountered only with its congeners having R = Ph, *i.e.* the derivatives (**5d**), (**6d**), and (**8d**) (X = Br; made accordingly from **4d**, **7d**, and **13d**).[22] As expected, these compounds are strong acids; we determined pK_a = 2.92 (**5d**), 2.87 (**6d**), and 3.19 (**8d**) (all values by potentiometric titration of 0.002 molar solutions with 0.01 N NaOH in water at 20 °C). Judging from the pK_a's of the (5-methylated) phenacyltetrazolium bromides which show 10.17, 9.64, and 9.05, respectively,[20] the tetrazolium *N*-aminides are by 10^6–10^7 less basic than their *N*-ylidic counterparts.[23] But while the pK_a's of the phenacyl salts follow the electron-withdrawing effect of the tetrazolium moieties [20] (which increases in the order as these units are grouped in Scheme 1), the pK_a's of **5d**, **6d**, and **8d** do not.

To provide the remaining reference material (**14** / **15**) (*cf.* above) we adopted the method that has proved fruitful with tetrazolium *N*-phenacylides,[20] *i.e.* treatment of the aminides (**4**) and (**7**) with methyl iodide in dimethylformamide as solvent.[24] At room temperature the derivatives (**14a,b**) and (**15a,b**) were obtained within 24 hours. Yet, applying the procedure to **13**, several days were required for the products (**16a,b**). This again reflects the enhanced acceptor character of the 1*H*-tetrazolium-3-yl system: for the total atomic charge of the aminide nitrogen of **13a** we found –0.382, compared to –0.422 (**4a**) and –0.418 (**7a**) [values refer to optimized geometries calculated at the B3LYP/6-31G(d) level of theory (*cf.* ref.[1])]. Apart from **15b** which could not be isolated pure because of extreme hygroscopicity, all of the methylation products are stable solids. This led us to doubt a literature note [26] stating that the triazolium *N*-aminide (**17a**) forms a 'very unstable salt with methyl iodide' — apparently compound (**18a**) — which releases the reagent 'even at room temperature.' Preparing this derivative, we could not confirm the alledged sensitivity, but found that the substance, including its congener (**18b**), matches the stability of the above tetrazolium salts.

EXPERIMENTAL

Mp: Linström apparatus; elemental analysis: CHN Analyzer 1106 Carlo Erba; IR: Philips PU-9800 FTIR, Thermo Nicolet FT-IR 200; NMR: Bruker DRX-400 (400.1 and 100.6 MHz for ^{1}H and ^{13}C, respectively); UV/VIS: Philips PU-8730, Analytik Jena Specord 200; MS: Finnigan-MAT 90 (70 eV).

The following compounds were prepared by reported procedures: (i) Tetrazolamines (**1a**),[1] (**1b**),[9b] (**2a**),[1] and (**2b**);[9b] (ii) tetrazolium aminides (**4a,b,d**), (**7a,b,d**), and (**13a,b,d,e**);[1] (iii) aminotetrazolium bromides (**11a,b**);[1] (iv) 1,2,4-triazolium aminides (**17a**) [4a] and (**17b**).[4d]

***N*-(5-Methyl/5-Phenyl-1*H*-tetrazol-1-yl)acetamide (A1a,b)**. General procedure: Adopting the method of ref.,[4a] a mixture of the appropriate tetrazol-1-amine (**1a**) or (**1b**) (5 mmol), acetic anhydride (0.61 g, 6 mmol), and acetic acid (5 mL) was heated at reflux for 6 h. Removal of the solvent left an oil that slowly solidified; in the case of **A1b**, it was purified on silica gel (Et_2O). For data, see Tables 1 and 2.

Table 1. Yields, Melting Points, and Elemental Analyses (Calcd / Found) of New Compounds

Compd	Yield (%)	mp (°C)	Recryst. from	Formula	C	H	N
A1a	78	101	EtOH	$C_4H_7N_5O$	34.04 / 34.43	5.00 / 5.03	49.62 / 49.92
A1b	39	81	EtOH–(Q) [a]	$C_9H_9N_5O$	53.20 / 53.09	4.46 / 4.46	34.47 / 35.02
A2a	75	121	EtOH	$C_9H_9N_5O$	53.20 / 53.18	4.46 / 4.41	34.47 / 34.69
A3a	69	202	EtOH	$C_9H_{10}N_6O$	49.54 / 49.67	4.62 / 4.64	38.51 / 38.61
A3b	57	150–151	EtOH–H_2O	$C_{14}H_{12}N_6O$	59.99 / 59.96	4.32 / 4.34	29.98 / 29.80
A'1a	38	74–76	EtOH	$C_6H_9N_5O_2$	39.34 / 39.61	4.95 / 4.93	38.23 / 38.52
B1a	72 [b]	95–96	Et_2O–(Q) [a]	$C_4H_7N_5O$	34.04 / 33.86	5.00 / 5.02	49.62 / 49.60
B1b	79 [b]	87–89	EtOH	$C_9H_9N_5O$	53.20 / 53.31	4.46 / 4.53	34.47 / 34.66
B2a	95 [c]	124–125	EtOH	$C_9H_9N_5O$	53.20 / 53.37	4.46 / 4.47	34.47 / 34.28
B2b	90 [c]	147	EtOH	$C_{14}H_{11}N_5O$	63.39 / 63.04	4.18 / 4.13	26.40 / 26.13
B3a	78	214 [c]	EtOH	$C_9H_{10}N_6O$	49.54 / 49.68	4.62 / 4.63	38.51 / 38.88
B3b	43	156–158	EtOH	$C_{14}H_{12}N_6O$	59.99 / 60.18	4.32 / 4.18	29.98 / 29.66
B'1a	68	56–57	EtOH	$C_6H_9N_5O_2$	39.34 / 39.37	4.95 / 4.99	38.23 / 38.31
B'1b	73	68–69	MeOH	$C_{11}H_{11}N_5O_2$	53.87 / 53.78	4.52 / 4.58	28.56 / 28.59
3a	85	93–95 [d]	EtOH	$C_{16}H_{13}N_5O_2$	62.54 / 62.21	4.26 / 4.32	22.79 / 22.84
3b	95	114 [d]	EtOH	$C_{21}H_{15}N_5O_2$	68.28 / 68.29	4.09 / 4.18	18.96 / 19.20
5d	69	143–144	EtOH–Et_2O	$[C_{15}H_{14}N_5O]Br$	50.02 / 50.08	3.92 / 3.99	19.44 / 19.57
6d	72	125–127	EtOH–Et_2O	$[C_{15}H_{14}N_5O]Br$	50.02 / 50.03	3.92 / 3.91	19.44 / 19.22
8d	92	141–142	EtOH	$[C_{15}H_{14}N_5O]Br$	50.02 / 50.15	3.92 / 3.97	19.44 / 19.47
8e	40	152–153	EtOH	$[C_{10}H_{12}N_5O]Br$	40.29 / 39.83	4.06 / 4.05	23.49 / 23.56
9a	84	oil		$C_5H_9N_5O$	38.71 / 38.79	5.85 / 6.00	45.13 / 45.07
9b	37	89–90	EtOH	$C_{10}H_{11}N_5O$	55.29 / 55.14	5.10 / 5.10	32.24 / 32.39
9c	86	139–141	EtOH	$C_{10}H_{12}N_6O$	51.72 / 51.82	5.21 / 5.22	36.19 / 36.68
10a	71	oil		$C_5H_9N_5O$	38.71 / 38.95	5.85 / 5.83	45.13 / 45.05
10b	28	oil		$C_{10}H_{11}N_5O$	55.29 / 55.43	5.10 / 5.26	32.24 / 31.75
10c	82	94–96	EtOH	$C_{10}H_{12}N_6O$	51.72 / 51.63	5.21 / 5.12	36.19 / 36.66
14a	67	155–156	EtOH	$[C_6H_{12}N_5O]I$	24.26 / 24.21	4.07 / 4.06	23.57 / 23.51
14b	78	138–139	EtOH–Et_2O	$[C_{11}H_{14}N_5O]I$	36.78 / 36.52	3.93 / 3.92	19.50 / 19.51
15a	67	88–90	EtOH–Et_2O	$[C_6H_{12}N_5O]I$	24.26 / 24.12	4.07 / 4.08	23.57 / 23.66
16a	71	148–149	EtOH	$[C_6H_{12}N_5O]I$	24.26 / 24.04	4.07 / 4.10	23.57 / 23.60
16b	84	117	EtOH–Et_2O	$[C_{11}H_{14}N_5O]I$	36.78 / 36.63	3.93 / 4.06	19.50 / 19.59
18a	61	141–143	EtOH–Et_2O	$[C_{12}H_{15}N_4O]I$	40.24 / 40.20	4.22 / 4.25	15.64 / 15.51
18b	78	173–175	*i*-PrOH	$[C_6H_{11}N_4O]I$	25.55 / 25.50	3.93 / 3.94	19.86 / 19.77

[a] (Q) = light petroleum. [b] From **B'1a** and **B'1b**, respectively. [c] From **3a** and **3b**, respectively. [d] With decomp.

***N*-Acetyl-*N*-(5-methyl/5-phenyl-1*H*-tetrazol-1-yl)acetamide (A'1a,b)**. General procedure: Adopting the method of ref.,[9b] the appropriate tetrazol-1-amine (**1a**) or (**1b**) (5 mmol) and acetic anhydride (4.08 g, 40 mmol) were heated at reflux for 4 h. Evaporation of excess reagent *in vacuo* afforded an oil that slowly solidified. For the data of **A'1a**, see Tables 1 and 2; for **A'1b**, see below.

Table 2. Spectral Data of New Compounds

Compd	IR (ν, cm^{-1}; KBr // ^1H / ^{13}C NMR (δ, ppm; $CDCl_3$ or * DMSO-d_6)
A1a	3183, 1712 // * 2.15 (s, 3H), 2.39 (s, 3H), 12.26 (s, 1H) / 7.6 (q), 20.5 (q), 152.6 (s), 168.7 (s)
A1b	3215, 1730 // 2.13 (s, 3 H), 7.40–7.46 (m, 2H), 7.48–7.54 (m, 1H), 7.67–7.72 (m, 2H), 11.14 (s, 1H) / 20.9 (q), 121.7 (s), 128.1 (d, 2C), 129.1 (d, 2C), 132.1 (d), 153.9 (s), 169.5 (s)
A2a	3466, 1704 // 2.45 (s, 3H), 7.51–7.56 (m, 2H), 7.62–7.67 (m, 1H), 8.03–8.06 (m, 2H), 11.66 (br s, 1H) / 8.1 (q), 128.1 (d, 2C), 129.1 (d, 2C), 129.5 (s), 133.8 (d), 153.4 (s), 165.7 (s)
A3a	3332, 3194, 1676 // * 2.44 (s, 3H), 7.03–7.08 (m, 1H), 7.29–7.35 (m, 2H), 7.46–7.50 (m, 2H), 9.77 (s, 1H), 10.54 (s, 1H) / 7.8 (q), 119.1 (d, 2C), 123.1 (d), 128.9 (d, 2C), 138.5 (s), 152.6 (s), 153.2 (s)
A3b	3378, 3187, 1731 // * 6.95–7.05 (m, 1H), 7.20–7.35 (m, 2H), 7.40–7.48 (m, 2H), 7.57–7.67 (m, 3H), 7.90–8.05 (m, 2H), 9.84 (s, 1H), 10.82 (s, 1H) / 119.0 (d, 2C), 122.6 (s), 123.1 (d), 128.0 (d, 2C), 128.8 (d, 2C), 129.2 (d, 2C), 131.8 (d), 138.3 (s), 152.6 (s), 153.3 (s)
A'1a	1749 // 2.37 (s, 6H), 2.48 (s, 3H) / 8.0 (q), 24.5 (q, 2C), 152.8 (s), 168.2 (s, 2C)
B1a	3171, 1728 // 2.19 (br s, 3H), 2.54 (s, 3H), 10.24 (br s, 1H) / 11.2 (q), 20.7 (q), 162.5 (s), 169.4 (s)
B1b	3178, 1688 // 2.16 (s, 3H), 7.38–7.48 (m, 3H), 7.97–8.13 (m, 2H), 10.80 (br s, 1H) / 20.8 (q), 126.2 (s), 126.8 (d, 2C), 129.0 (d, 2C), 131.0 (d), 164.1 (s), 169.6 (s)
B2a	^1H: 2.42 (s, 3H), 7.38–7.47 (m, 2H), 7.54–7.64 (m, 1H), 7.81–7.89 (m, 2H), 11.31 (s, 1H); ^{13}C: 11.1 (q), 128.0 (d, 2C), 129.0 (d, 2C), 129.6 (s), 133.7 (d), 162.4 (s), 166.6 (s)
B2b	3182, 1680 // * 7.61–7.68 (m, 5H), 7.73–7.78 (m, 1H), 8.03–8.07 (m, 2H), 8.13–8.17 (m, 2H), 13.70 (br s, 1H) / 126.3 (s), 126.4 (d, 2C), 128.1 (d, 2C), 129.1 (d, 2C), 129.4 (d, 2C), 129.9 (s), 131.1 (d), 133.6 (d), 163.3 (s), 166.0 (s)
B3a	3300, 3184, 1663 // * 2.51 (s, 3H), 6.99–7.10 (m, 1H), 7.25–7.37 (m, 2H), 7.43–7.53 (m, 2H), 9.69 (s, 1H), 11.23 (s, 1H) / 10.7 (q), 119.2 (d, 2C), 123.1 (d), 128.8 (d, 2C), 138.4 (s), 152.9 (s), 161.3 (s)
B3b	3339, 3261, 1673 // * 7.04–7.09 (m, 1H), 7.31–7.35 (m, 2H), 7.50–7.53 (m, 2H), 7.59–7.62 (m, 3H), 8.11–8.14 (m, 2H), 9.82 (s, 1H), 11.43 (s, 1H) / 119.3 (d, 2C), 123.2 (d), 126.3 (d, 2C), 126.5 (s), 128.8 (d, 2C), 129.4 (d, 2C), 130.9 (d), 138.4 (s), 152.9 (s), 162.8 (s)
B'1a	1758, 1740 // 2.33 (s, 6H), 2.65 (s, 3H) / 11.4 (q), 24.2 (q, 2C), 163.3 (s), 168.4 (s, 2C)
B'1b	1762, 1742 // 2.37 (s, 6H), 7.50–7.55 (m, 3H), 8.16–8.22 (m, 2H) / 24.3 (q, 2C), 126.2 (s), 127.1 (d, 2C), 129.1 (d, 2C), 131.3 (d), 165.0 (s), 168.4 (s, 2C)
3a	1762, 1626 // 2.40 (s, 3H), 7.45–7.76 (m, 6H), 8.08–8.19 (m, 4H) / 11.1 (q), 127.5 (s), 128.6 (d, 2C), 128.9 (d, 2C), 129.0 (d, 2C), 129.3 (s), 130.7 (d, 2C), 133.6 (d), 134.7 (d), 154.2 (s), 161.6 (s), 162.3 (s)
3b	1748, 1678 // 7.23–7.31 (m, 2H), 7.33–7.38 (m, 1H), 7.48–7.65 (m, 5H), 7.72–7.76 (m, 3H), 8.15–8.18 (m, 2H), 8.21–8.24 (m, 2H) / 126.6 (s), 126.7 (d, 2C), 127.7 (s), 128.68 (d, 2C), 128.73 (d, 2C), 129.0 (d, 2C), 129.1 (d, 2C), 129.4 (s), 130.5 (d), 130.9 (d, 2C), 133.6 (d), 134.7 (d), 153.6 (s), 162.3 (s), 162.7 (s)
5d	1698 // * 4.44 (s, 3H), 7.55–7.58 (m, 2H), 7.68–7.73 (m, 1H), 7.76–7.82 (m, 2H), 7.83–7.88 (m, 1H), 7.98–8.02 (m, 2H), 8.04–8.08 (m, 2H), 8.5–10.0 (br, 1H) / 39.5 (q), 115.3 (s), 128.3 (d, 2C), 128.9 (d, 2C), 129.6 (d, 2C), 129.7 (s), 130.1 (d, 2C), 133.6 (d), 134.7 (d), 150.9 (s), 166.6 (s)
6d	1689 // * 4.83 (s, 3H), 7.53–7.78 (m, 6H), 8.06–8.21 (m, 4H), 10.84 (s, 1H) / 44.3 (q), 119.6 (s), 128.3 (d, 4C), 128.6 (d, 2C), 129.7 (d, 2C), 131.6 (s), 132.8 (d), 133.8 (d), 155.9 (s), 167.7 (s)
8d	1708 // * 4.44 (s, 3H), 7.48–7.62 (m, 3H), 7.68–7.82 (m, 3H), 8.00–8.12 (m, 4H), 11.06 (s, 1H) / 38.1 (q), 120.5 (s), 128.1 (d, 2C), 129.45 (d, 2C), 129.53 (d, 2C), 131.8 (d), 133.0 (d), 133.8 (s), 156.6 (s), 168.4 (s)
8e	1733 // * 2.22 (s, 3H), 4.46 (s, 3H), 7.72–7.78 (m, 2H), 7.81–7.86 (m, 1H), 7.98–8.02 (m, 2H), 9.96 (br s, 1H) / 20.9 (q), 39.5 (q), 119.8 (s), 129.6 (d, 2C), 129.7 (d, 2C), 133.5 (d), 157.9 (s) [a]
9a	1710 [b] // 1.78 (s, 3H), 2.58 (s, 3H), 3.44 (s, 3H) / 8.1 (q), 19.9 (q), 37.0 (q), 151.5 (s), 170.3 (s)
9b	1697 // 2.37 (s, 3H), 3.62 (s, 3H), 7.29–7.49 (m, 5H) / 8.1 (q), 38.9 (q), 127.3 (d, 2C), 128.7 (d, 2C), 131.3 (s), 131.8 (d), 151.3 (s), 169.6 (s)
9c	3353, 1708, 1688 // * 2.49 (s, 3H), 3.48 (s, 3H), 7.05–7.10 (m, 1H), 7.28–7.33 (m, 2H), 7.43–7.47 (m, 2H), 9.18 (s, 1H) / 7.9 (q), 39.5 (q), 121.0 (d, 2C), 123.7 (d), 128.5 (d, 2C), 138.2 (s), 157.9 (s), 153.3 (s)
10a	1716 [b] // 1.79 (s, 3H), 2.62 (s, 3H), 3.48 (s, 3H) / 11.3 (q), 19.8 (q), 37.0 (q), 162.9 (s), 170.2 (s)
10b	1698 [b] // 2.47 (s, 3H), 3.61 (s, 3H), 7.23–7.47 (m, 5H) / 11.1 (q), 38.9 (q), 127.6 (d, 2C), 128.3 (d, 2C), 131.6 (d), 131.9 (s), 162.4 (s), 170.1 (s)
10c	3287, 1709 // * 2.54 (s, 3H), 3.49 (s, 3H), 7.04–7.13 (m, 1H), 7.25–7.36 (m, 2H), 7.41–7.49 (m, 2H), 9.19 (s, 1H) / 11.0 (q), 39.5 (q), 121.0 (d, 2C), 123.8 (d), 128.5 (d, 2C), 138.1 (s), 153.5 (s), 161.9 (s)
12a	3511, 3234, 1368 // 2.35 (s, 3H), 3.66 (s, 3H), 6.20 (br s, 1H) / 8.6 (q), 32.8 (q), 150.3 (s)
12b	3270, 1381 // 3.81 (s, 3H), 4.0–6.0 (br, 1H), 7.52–7.64 (m, 5H) / 34.4 (q), 122.3 (s), 128.5 (d, 2C), 129.2 (d, 2C), 131.8 (d), 152.5 (s)
14a	1708 // * 2.32 (br s, 3H), 2.94 (s, 3H), 3.63 (br s, 3H), 4.35 (s, 3H) / 8.5 (q), 20.7 (q), 37.6 (q), 154.2 (s), 170.1 (s) [c]

Table 2 (continued)

14b	1716 // * 3.08 (s, 3H), 3.70 (s, 3H), 4.40 (s, 3H), 7.56–7.76 (m, 3H), 7.84–7.91 (m, 2H) / 8.7 (q), 37.7 (q), 41.8 (q), 128.6 (d, 2C), 128.8 (d, 2C), 130.0 (s), 132.7 (d), 154.2 (s), 169.4 (s)
15a	1712 // * 2.35 (s, 3H), 2.80 (s, 3H), 3.67 (s, 3H), 4.74 (s, 3H) / 8.5 (q), 20.6 (q), 44.7 (q), 159.7 (s), 169.9 (s) [c]
15b	1698 // * 2.91 (s, 3H), 3.72 (s, 3H), 4.79 (s, 3H), 7.59–7.64 (m, 2H), 7.70–7.74 (m, 1H), 7.85–7.88 (m, 2H) / 8.6 (q), 42.0 (q), 44.8 (q), 128.6 (d, 2C), 128.9 (d, 2C), 129.9 (s), 132.9 (d), 159.7 (s), 169.1 (s) [d]
16a	1723 // * 2.30 (br s, 3H), 2.88 (s, 3H), 3.67 (s, 3H), 4.41 (s, 3H) / 10.0 (q), 20.5 (q), 37.8 (q), 160.2 (s), 169.9 (s) [c]
16b	1715 // * 2.90 (s, 3H), 3.75 (s, 3H), 4.44 (s, 3H), 7.56–7.85 (m, 5H) / 9.9 (q), 37.9 (q), 42.1 (q), 128.5 (d, 2C), 129.1 (d, 2C), 129.6 (s), 133.1 (d), 160.3 (s), 169.5 (s)
18a	1696 // * 2.25 (br s, 3H), 3.60 (br s, 3H), 5.72 (s, 2H), 7.43–7.54 (m, 5H), 9.57 (s, 1H), 10.67 (br s, 1H) / 20.7 (q), *ca.* 39.0 (br q) [e], 55.6 (t), 128.9 (d, 2C), 129.1 (d, 2C), 129.2 (d), 132.2 (s), 144.0 (d), 145.1 (d), 170.2 (s)
18b	3071, 1691 // * 2.27 (br s, 3H), 3.59 (br s, 3H), 4.14 (s, 3H), 9.57 (s, 1H), 10.56 (s, 1H) / 20.7 (q), 39.7 (q), 144.0 (d), 144.5 (d), 170.2 (s) [c]

[a] CO not observed. [b] Neat. [c] N–Me of amido group not observed. [d] Impure material. [e] Detected by DEPT pulse technique only.

A'1b: 0.16 g (21%); mp 86–88 °C (benzene–Et_2O; lit.,[9a] mp 90 °C; lit.,[9b] mp 88–89 °C); IR (KBr): ν 1760, 1743 cm^{-1}; ^1H NMR (DMSO-d_6): δ 2.36 (s, 6H), 7.53–7.58 (m, 2H), 7.60–7.65 (m, 1H), 7.72–7.76 (m, 2H) [lit.,[9b] 2.38 (s, 6H), 7.6–8.0 (m, 5H)]; ^{13}C NMR (DMSO-d_6): δ 24.7 (q, 2C), 121.6 (s), 127.7 (d, 2C), 129.8 (d, 2C), 132.7 (d), 153.5 (s), 168.6 (s, 2C).

***N*-(5-Methyl/5-Phenyl-1*H*-tetrazol-1-yl)benzamide (A2a,b)**. General procedure: To a stirred solution of the respective tetrazol-1-amine (**1a**) or (**1b**) (4 mmol) in pyridine (10 mL) was added dropwise benzoyl chloride (0.56 g, 4 mmol) at 20 °C. In the case of **A2a**, the mixture was allowed to stand at room temperature for 1 h; for **A2b**, it was heated at reflux for ≥ 6 h. After concentration to dryness the resultant oil was treated with water (5 mL) and the solid formed was collected by filtration.

A2b: 0.99 g (93%); mp 135–136 °C (EtOH–water; lit.,[12a] mp 134–135 °C; lit.,[12b] mp 136–138 °C); IR (KBr): ν 3169, 1704 cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.58–7.64 (m, 5H), 7.70–7.75 (m, 1H), 7.94–8.03 (m, 4H), 13.27 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 122.2 (s), 127.8 (d, 2C), 127.9 (d, 2C), 129.1 (d, 2C), 129.4 (d, 2C), 129.9 (s), 132.0 (d), 133.5 (d), 153.2 (s), 165.6 (s). — For the data of **A2a**, see Tables 1 and 2.

1-(5-Methyl-1*H*/2*H*-tetrazol-1-yl/2-yl)-3-phenylurea (A3a / B3a), 1-phenyl-3-(5-phenyl-1*H*/2*H*-tetrazol-1-yl/2-yl)urea (A3b / B3b). General procedure: (i) To a stirred solution of 2 mmol of the appropriate tetrazolamine (**1a**) in CH_2Cl_2 (5 mL) or (**1b**), (**2a**), (**2b**) in pyridine (2 mL) was slowly added phenyl isocyanate (0.24 g, 2 mmol). After continued stirring at 20 °C (1 h for **A3a**, **B3a**; 2 h for **B3b**) or 115 °C (6 h for **A3b**) the solvent was evaporated. The derivative (**A3a**) was directly crystallized from the residue, whereas the other products were first purified on silica gel (EtOAc). For data, see Tables 1 and 2.

***N*-Acetyl-*N*-(5-methyl/5-phenyl-2*H*-tetrazol-2-yl)acetamide (B'1a,b), *N*-(5-methyl/5-phenyl-2*H*-tetrazol-2-yl)benzimidoyl benzoate (3a,b)**. General procedure: To a stirred solution of the appropriate tetrazol-2-amine (**2a**) or (**2b**) (10 mmol) and triethylamine (2.20 g, 22 mmol) in Et_2O (40 mL) was slowly

added in the same solvent (10 mL): acetyl chloride (1.57 g, 20 mmol) and benzoyl chloride (2.81 g, 20 mmol), respectively. After 1 h the mixture was cooled to 4 °C, the solid was filtered off and the filtrate concentrated. The resultant oil readily crystallized on scratching. For data, see Tables 1 and 2.

***N*-(5-Methyl/5-Phenyl-2*H*-tetrazol-2-yl)acetamide (B1a,b), *N*-(5-methyl/5-phenyl-2*H*-tetrazol-2-yl)-benzamide (B2a,b)**. General procedure: A suspension of the appropriate derivative (**B'1a**), (**B'1b**), (**3a**) or (**3b**) (5 mmol) in 2 N KOH (30 mL) was stirred at 80 °C (2 h with **B'1a,b**, 4 h with **3a,b**). The clear solution was acidified with 12 N HCl to afford the product which was isolated by filtration or extraction with CH_2Cl_2. For data, see Tables 1 and 2.

***N*-Benzoyl-1,5-dimethyl-1*H*-tetrazolium-4-aminide (4b), 1,5-dimethyl-*N*-(phenylcarbamoyl)-1*H*-tetrazolium-4-aminide (4c)**. General procedure: A suspension of the amide (**A2a**) or urea (**A3a**) (1 mmol) in dimethyl sulfate (1 mL, *ca.* 10 mmol) was allowed to stand at 20 °C for 3 d. Then the mixture was diluted with Et_2O (20 mL) and the solvent was decanted to afford *ca.* 0.3 g of a colorless oil [^{1}H NMR (DMSO-d_6): s (*N*-Me) at δ 4.34 (**5b**) / 4.61 (**6b**) or 4.35 (**5c**) / 4.73 (**6c**)]. On adding aqueous K_2CO_3 (10 mL, 5%) the pure aminide (**4b**) (0.08 g, 36%) or (**4c**) (0.16 g, 65%) precipitated and was filtered off. The data (mp, IR, ^{1}H and ^{13}C NMR) were consistent with those of ref.[1]

4-Benzamido-1-methyl-5-phenyl-1*H*-tetrazolium bromide (5d). The aminide (**4d**) (1 mmol) was dissolved in water (5 mL) followed by addition of *ca.* 9 N HBr (0.25 g). Then the mixture was extracted with CH_2Cl_2 (2 x 20 mL); the organic layer was concentrated to dryness and the residue was recrystallized. For data, see Tables 1 and 2.

4-Benzamido-2-methyl-5-phenyl-2*H*-tetrazolium bromide (6d), 3-benzamido/3-acetamido-1-methyl-5-phenyl-1*H*-tetrazolium bromide (8d,e). General procedure: The appropriate aminide (**7d**), (**13d**) or (**13e**) (1 mmol) was dissolved in EtOH (5 mL) followed by addition of *ca.* 9 N HBr (0.25 g). After the mixture had been cooled to 4 °C, it was cautiously diluted with Et_2O and set aside to allow crystallization of the product. For data, see Tables 1 and 2.

***N*-Methyl-*N*-(5-methyl-1*H*/2*H*-tetrazol-1-yl/2-yl)acetamide (9a / 10a)**. General procedure: To a solution of the appropriate acetamide (**A1a**) or (**B1a**) (0.18 g, 1 mmol) in $CHCl_3$ (50 mL) were added K_2CO_3 (1.00 g) and dimethyl sulfate (0.13 g, 1 mmol). The mixture was heated at reflux for 4 h with vigorous stirring. Then the solid was removed and the filtrate was concentrated. The residual mass was purified on silica gel (CH_2Cl_2). For data, see Tables 1 and 2.

***N*-Methyl-*N*-(5-methyl-1*H*/2*H*-tetrazol-1-yl/2-yl)benzamide (9b / 10b), 1-(5-methyl-1*H*/2*H*-tetrazol-1-yl/2-yl)-3-phenylurea (9c / 10c)**. General procedure: To a vigorously stirred solution of K_2CO_3 (1.00 g) in water (10 mL) were added, successively, the appropriate benzamide (**A2a**) or (**B2a**) or the phenylurea

(**A3a**) or (**B3a**) (1 mmol) and dimethyl sulfate (0.5 mL, *ca.* 5 mmol). After 30 min the solid was removed and the filtrate was concentrated to dryness. The residual material was purified on silica gel (CH_2Cl_2). For data, see Tables 1 and 2.

1,5-Dimethyl-1*H*-tetrazolium-3-aminide (12a), 1-methyl-5-phenyl-1*H*-tetrazol-3-aminide (12b). General procedure: The respective tetrazolium salt (**11a**) or (**11b**) (1 mmol) and K_2CO_3 (0.35 g, *ca.* 2.5 mmol) were dissolved in water (10 mL). The mixture was immediately extracted with CH_2Cl_2 (3 x 15 mL) and the organic layers were dried. Evaporation of the solvent afforded slightly hygroscopic crystals giving microanalytical figures only approximate (because of moisture and gradual decomposition); attempts to recrystallize the material failed.

12a: 0.04 g (49%); mp 56–57 °C; UV (MeOH / CH_2Cl_2): λ_{max} (log ε) 285 (*ca.* 3.47) / 287 (*ca.* 3.91) nm; MS (*m/z*, %): 113 (M^+, 100), 98 (29), 69 (76), 56 (44), 43 (50); for IR and ^1H / ^{13}C NMR, see Table 2.

12b: 0.10 g (57%); mp 75–76 °C; UV (MeOH / CH_2Cl_2): λ_{max} (log ε) 276 (*ca.* 3.76) / 287 (*ca.* 4.10) nm; MS (*m/z*, %): 175 (M^+, 25), 160 (54), 118 (41), 104 (62), 77 (100); for IR and ^1H / ^{13}C NMR, see Table 2.

1,5-Dimethyl-4-(*N*-methylacetamido/*N*-methylbenzamido)-1*H*-tetrazolium iodide (14a,b), 2,5-dimethyl-4-(*N*-methylacetamido/*N*-methylbenzamido)-2*H*-tetrazolium iodide (15a,b), 1-benzyl/1-methyl-4-(*N*-methylacetamido)-1*H*-1,2,4-triazolium iodide (18a,b). General procedure: To a solution of the appropriate aminide (**4a**), (**4b**), (**7a**), (**7b**), (**17a**) or (**17b**) (1 mmol) in anhydrous DMF (5 mL) was added methyl iodide (0.36 g, 2.8 mmol) and the mixture was allowed to stand for 24 h. After removal of the solvent *in vacuo* the residue was dissolved in EtOH, followed by addition of Et_2O for crystallization of the product which was filtered off (**15b** liquefied instantaneously). For data, see Tables 1 and 2.

1,5-Dimethyl-3-(*N*-methylacetamido/*N*-methylbenzamido)-1*H*-tetrazolium iodide (16a,b). General procedure: The appropriate aminide (**13a**) or (**13b**) (1 mmol) was treated as above except that work-up was performed after 3 d. For data, see Tables 1 and 2.

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15. In ref.,[1] p. 2608, instead of the process (**A2a** → **4b**), the conversion (**A1a** → **4a**) has been inadvertently quoted. — Additional corrections on p. 2612: (i) line 14 should read '**8d,f,h**, **9d,f,h**, and **10b,d,f,h**:,' (ii) line 17 should read 'After 1 h (4 h for **9f**) the.'
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