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THE AZALOGUES OF PYRROLOTETRAZOLE – AN OVERVIEW

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Abstract – This overview is dealing with the seven azalogues of pyrrolotetrazole, *i.e.*, the systems **A**–**G**, in all their manifold forms. Major interest is directed to the preparative chemistry, but theoretical work, in particular on the azolotetrazole–azidoazole isomerism ('ring–chain tautomerism'), will be looked at as well.

INTRODUCTION

The chemistry of the title systems comprising the structures **A**–**G** has developed gradually since the mid-1960s (Figure 1) but lacks a specific review. While material on **A**–**C** has been gathered in three handbook articles that, in a wider context, are treating also bicycles with heteroatoms other than nitrogen,[1,2] the high-nitrogen representatives **D**–**G** have not been surveyed at all. The present work will draw a global picture, therewith complementing the preceding review on pyrrolotetrazoles.[3] Material will be organized in three major Sections (II, III, IV) as outlined overleaf.

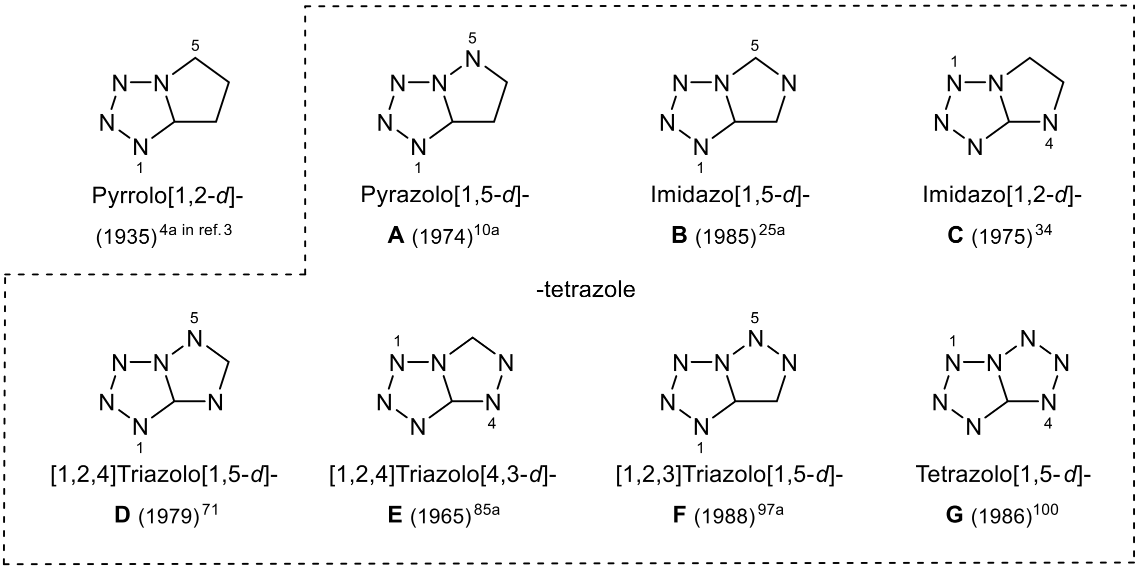


Figure 1. The title systems **A**– **G**: framework, nomenclature, ring numbering, year of first record

CONTENTS

I) GENERAL

a) Preparative work on **A**–**G** has led to a plethora of individual types (Figure 2). Synthesis usually started with a preformed, suitably functionalized α or β half-ring (Scheme 1: methods I–XI); only in rare cases, by using a linear precursor, both rings arose simultaneously (methods XII, XIII). Quite importantly, method I

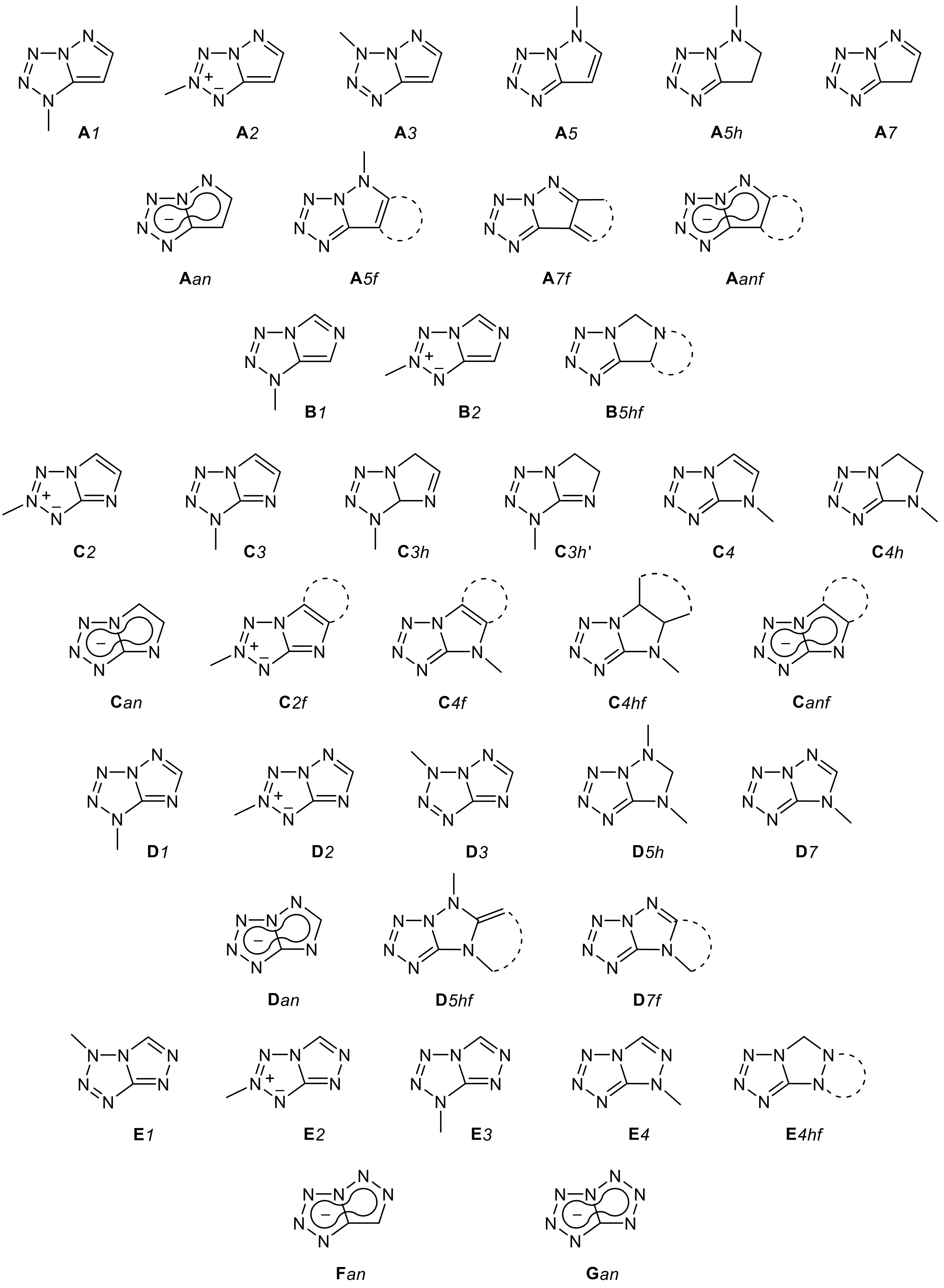
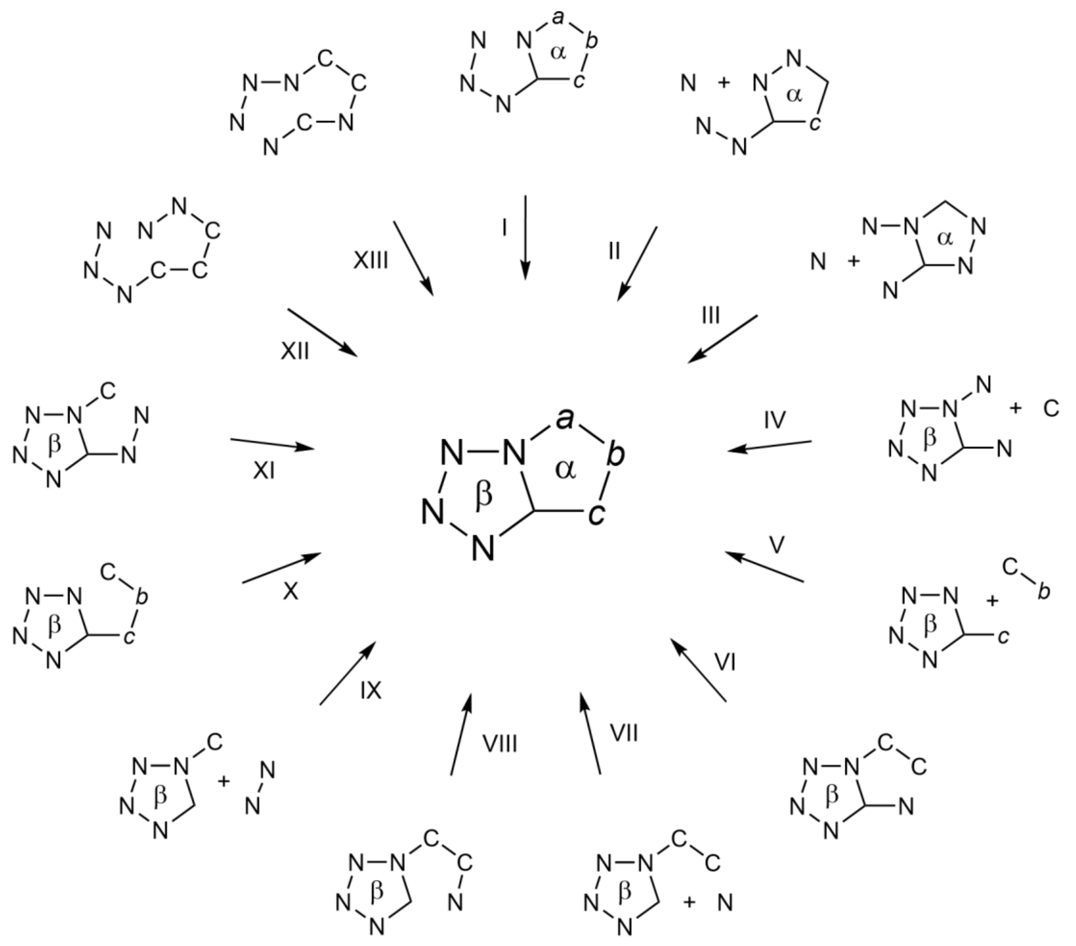
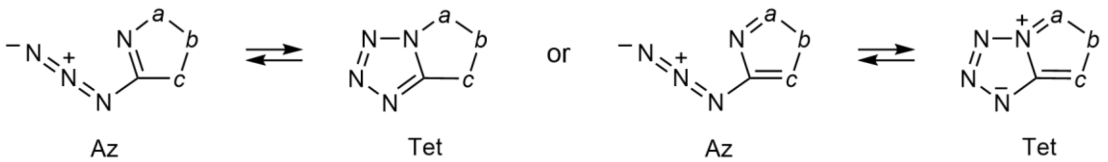


Figure 2. Types of azolotetrazoles **A**– **G** in preparative work
(numerals refer to indicated hydrogen; letters *h* and *f* signify hydrogenation and ring fusion, respectively)



method	products	method	products	method	products
I [a]	**A***an* [b], *5*, *anf* [c], *7* [d], *7f*;	III	**E***1*	IX	**E***4*
	C*4*, *4f*, *4h*, *an* [e], *anf*;	IV	**D***5h*, *7*	X	**B***5hf*; **C***4h*; **E***2*, *3*, *4*
	D*an* [f], *5*, *5hf*, *7*, *7f*;	V	**B***1*, *2*; **C***4*, *4hf*	XI	**E***4hf*
	F*an*; **G***an*	VI	**C***2*, *2f*, *3*, *3h*, *4*, *4hf*	XII	**A***5h*
II	**A***3*; **D***3*	VII, VIII	**C***3h*	XIII	**C***3h'*, *4f*, *4h*, *4hf*

[a] Azides partly generated *in situ*. [b-f] Converted to: **A***1*, *2*, *5* [b], **A***5f* [c], **A***1* [d], **C***4* [e], **D***1*, *2* [f].



Scheme 1. Synthetic principles for the species of Figure 2 and azido – tetrazole tautomerism

often did not work, as the azido–tetrazole equilibrium (Az $\rightleftharpoons$ Tet), governed by several factors,[1] is entirely on the azide side. For the same reason, certain attempts at getting azolotetrazoles from β half-rings that contain three pyridine-like nitrogens ended up with azidoazoles as final products.

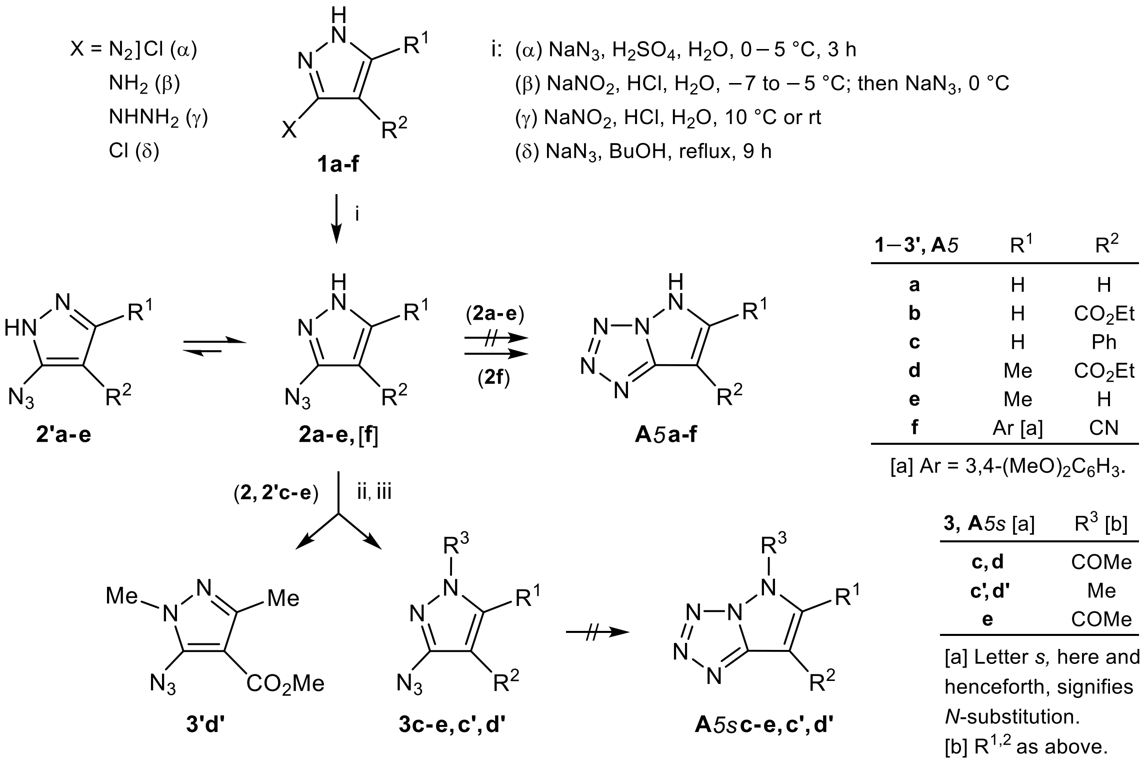
b) Because of the central role in azolotetrazole chemistry, the Az $\rightleftharpoons$ Tet tautomerism has been the subject of thorough theoretical studies [Sections (II / 4), (III / 5)].

II) DIAZOLOTETRAZOLES (A–C)

1) PYRAZOLO[1,5-*d*]TETRAZOLES (A)

a) Derivatives A*1, 2, 3* [II]*, ***5*** [I]*, ***an*** [I]* **Roman numerals, here and henceforth, refer to methods of Scheme 1.*

The first claim of a derivative **A** dates from the mid-1950s when the hydrazinopyrazole **1**(γ)**d** was reacted with nitrous acid (Scheme 2).[4a] But after IR spectroscopy had become a routine method, the putative bicycle **A***5***d** turned out to be the azide **2d**.[4b] Accordingly, further experiments with **1a-e** gave azides as the sole products (**2a-e**)[4c,5] which, inferred from spectral data, are favoured over the tautomers **2'**.[5] The absence of a species **A***5*[6a,7a] and the predominance of **2**[7a] are in line with DFT calculations [*cf.* Sections (II / 4. a,b), Tables 2 and 3]. Just as **2a-e**, *N*-substituted derivatives of **2** such as **3c-e** and **3c',d'** failed to cyclize.[5] Therefore, the report of a bicycle **A***5***f** seems surprising.[8] But provided that cyclization of the intermediary



i: (α) NaN_3, H_2SO_4, H_2O, 0 – 5 °C, 3 h
(β) $NaNO_2$, HCl, H_2O, –7 to – 5 °C; then NaN_3, 0 °C
(γ) $NaNO_2$, HCl, H_2O, 10 °C or rt
(δ) NaN_3, BuOH, reflux, 9 h

1–3', A*5*	R^1	R^2
a	H	H
b	H	CO_2Et
c	H	Ph
d	Me	CO_2Et
e	Me	H
f	Ar [a]	CN

[a] Ar = 3,4-$(MeO)_2C_6H_3$.

3, A*5s* [a]	R^3 [b]
c, d	COMe
c', d'	Me
e	COMe

[a] Letter *s*, here and henceforth, signifies *N*-substitution.
[b] $R^{1,2}$ as above.

ii: Ac_2O, pyridine (with **2c**) or benzene (with **2d,e**), reflux, 30 min
iii: MeI, EtONa, EtOH, 0 °C to reflux, 90 min (with **2c**) or CH_2N_2, Et_2O, some d, rt (with **2d**)

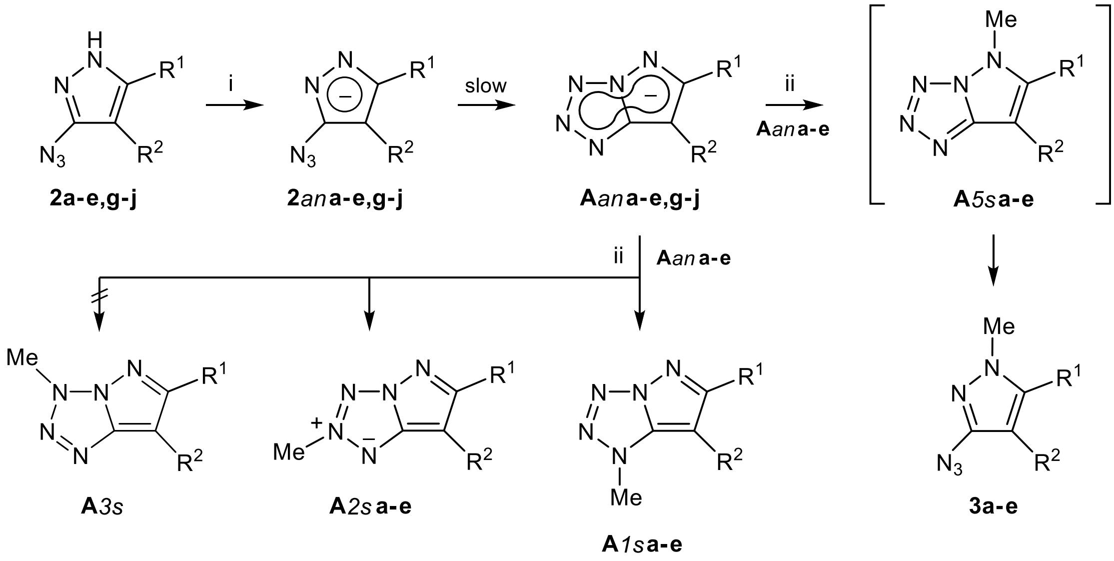
products formed [a]	yield	mp (°C)	ref.
2a (α; β)	52; 85	55–57; 60	4c; 5
2b (β)	89	110–111	5
2c (β; γ) // **3c** / **3c'**	94; 73 // 70 / 58	157–158 // 115–116 / 70–73	5
2d (γ) [b] // **3d** [b] / **3d'** [c]	60; 78 // 84; 85 / [d]	135; 135–136 // 75; 75 / 48–60	4a; 5
2e (β; γ) // **3e**	81; 80 // 90	78–79 // 50–51	5
A*5*f (δ)	83	260	8

[a] Greek letters refer to the class of starting material **1**. [b] In ref. 4a material viewed as a derivative of **A** (tacitly corrected in refs. 4b and 5). [c] In ref. 5 mixture of **3d'** and **3'd'** obtained. [d] Unreported.

Scheme 2

azide **2f** has occurred indeed, the product should exist as the **A***1* tautomer rather than **A***5* since the latter, because of the two adjacent pyrrole-like nitrogens, is higher in energy [for the relationship **A***1* to **A***5*, see Section (II / 4. c), Table 4].[6a] – A plethora of **A***1* tautomers appeared in the patent literature (no data).[9a–d] The materials which were prepared from substrates **1**(γ) are likely to be azides (**2**), they served as dye-forming couplers to afford bicycles of the type **A***7* (*vide infra*).

Contrasting with the neutral azides **2**, their anions **2***an*, generated in a strongly basic medium, are prone to cyclization to give the species **A***an* (Scheme 3).[5,10a,b] According to kinetics, electronegative substituents accelerate the process.[5,10b] Towards electrophiles the anions **A** *an* behave as multidentate substrates: methylation of **A***an***a-e** gave the bicycles **A***1s***a-e**, **A***2s***a-e**, and **A***5s***a-e**, but the latter ring-opened to the pyrazoles **3a-e**. While the products **A***2s* were erroneously viewed as **A***3s*,[11a,b] it was shown theoretically that methylation of **A***an* at N(3) is thermodynamically disfavoured and derivatives **A***3s* are only available



i: EtONa (excess), abs. EtOH, rt

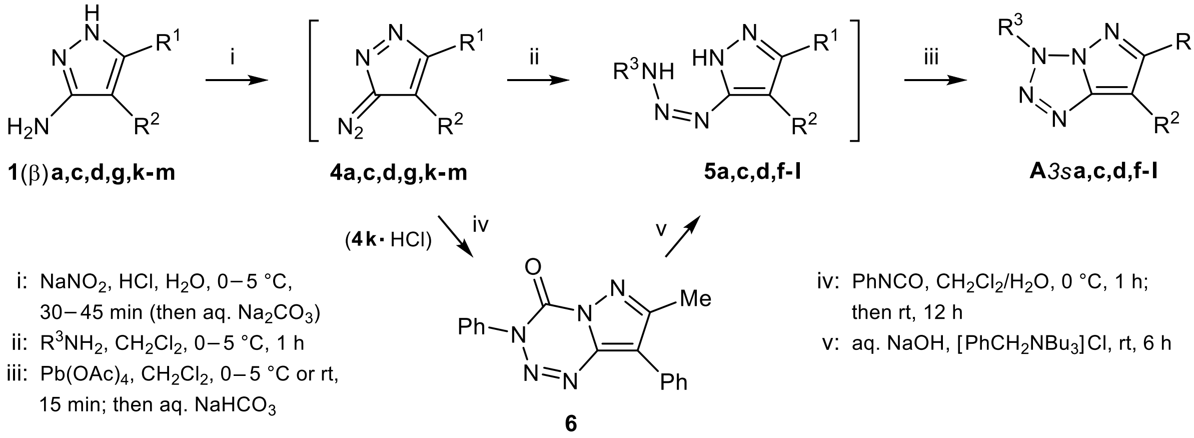
ii: MeI, reflux, 5 − 10 h

2, **2***an*, **3**, **A***an*,*1s*,*2s*,*5s*	R^1	R^2	− log *k* [a]	ref.	attack at **A***an*: ratio N(5) / N(1) / N(2) [b]	yield (%) [c] **3** / **A***1s* / **A***2s*	mp (°C) [d] **3** / **A***1s* / **A***2s*	ref.
a	H	H	4.65	10b		15 / 48 / [h]	oil / 115 − 116 / oil	11b
b	H	CO$_2$Et	3.27	10b	< 5 / 90 / > 5	[i] / 70 / [i]	--- / 67 − 68 / ---	11a
c [e]	H	Ph	4.30	10b	35 / 45 / 20	28 / 36 / 15, 16	70 − 73 / 101 − 103 / 139 − 140	11a,b
d [f]	Me	CO$_2$Et	3.20	10b	< 5 / 90 / > 5	[i] / 70 [j] / [i]	--- / 97 − 98 / ---	11a
e	Me	H	4.75	10b	40 / 50 / 10	[i] / 40 / [i]	--- / 88 − 91 / ---	11a
g	H	Br	4.70	10b				
h	H	NO$_2$	2.80	10b				
i	Me	NO$_2$	2.64	10b				
j [g]	[CH=CH]$_2$		3.43	10b				

[a] Reaction (**2***an* → **A***an*) in C_2D_5OD at 27 °C; monitored by IR. [b] Attack at N(2) thought to occur at N(3); hence, **A***2s* viewed as **A***3s*; for revision, see ref. 12b. [c] Ref. 12b: derivatives **c**: 40 / 20 / 12. [d] Ref. 12b: derivatives **c**: 63 − 65 / 92 − 94 / 138 − 139. [e] **A***2s***c** with X-ray crystal structure.[12b] [f] **A***1s***d** with X-ray crystal structure.[11b] [g] **A***an***j** = **A***an***fa**. [h] Unreported. [i] Not isolated. [j] Hydrolysis of **A***1s***d** in boiling aq. NaOH gave corresponding carboxylic acid (yield 90%, mp 224 − 225 °C).

Scheme 3

as follows (Scheme 4): *In situ* generated diazopyrazoles **4a,c,d** were converted to the triazenes **5** which on treatment with an oxidant cyclized to **A**_3s_.[12b] Originally, this method had served as an approach to special *N*-glycosides (*e.g.*, **A**_3s_**f,g**),[12a] but its synthetic potential became soon apparent such as to initiate syntheses like those of **A**_3s_**k**[9a] and **A**_3s_**l**[13] (the latter material was prepared for pesticidal studies). Regarding **A**_3s_**j**, a detour had to be made for providing the triazene **5j**: here **4k** was reacted with phenyl isocyanate (rather than aniline) to give the fused tetrazinone **6** which on alkaline hydrolysis converted to **5j**.[12c]

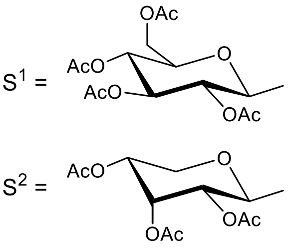


1(β)**a,c,d,g,k-m** **4a,c,d,g,k-m** **5a,c,d,f-l** **A**_3s_**a,c,d,f-l** **6**

i: $NaNO_2$, HCl, H_2O, 0−5 °C, 30−45 min (then aq. Na_2CO_3)
ii: R^3NH_2, CH_2Cl_2, 0−5 °C, 1 h
iii: $Pb(OAc)_4$, CH_2Cl_2, 0−5 °C or rt, 15 min; then aq. $NaHCO_3$
iv: PhNCO, CH_2Cl_2/H_2O, 0 °C, 1 h; then rt, 12 h
v: aq. NaOH, $[PhCH_2NBu_3]Cl$, rt, 6 h

1(β), **4**	R^1	R^2	**5**, **A**_3s_	R^1	R^2	R^3	yield (%)	mp (°C)	ref.
a	H	H	**a**	H	H	Me	31	39−40	12b
c	H	Ph	**c** [a]	H	Ph	Me	53	152−154	12b
d	Me	CO_2Et	**d** [a]	Me	CO_2Et	Me	34	94	12b
g	H	Br	**f**	H	Br	S^1	61	133−136	12a
k	Me	Ph	**g**	Me	Ph	S^2	21	122−124	12a
l	X	H	**h**	Me	Ph	$[CH_2]_2OH$	65	126−128	12a
m	H	4-pyridyl	**i**	Me	Ph	$4\text{-}NO_2C_6H_4$	69	215−217	12a
			j	Me	Ph	Ph	31	148−149	12c
			k	Q [c]	H	CH_2Ph	[d]	[d]	9a
			l [b]	H	4-pyridyl	Me	[d]	[d]	13

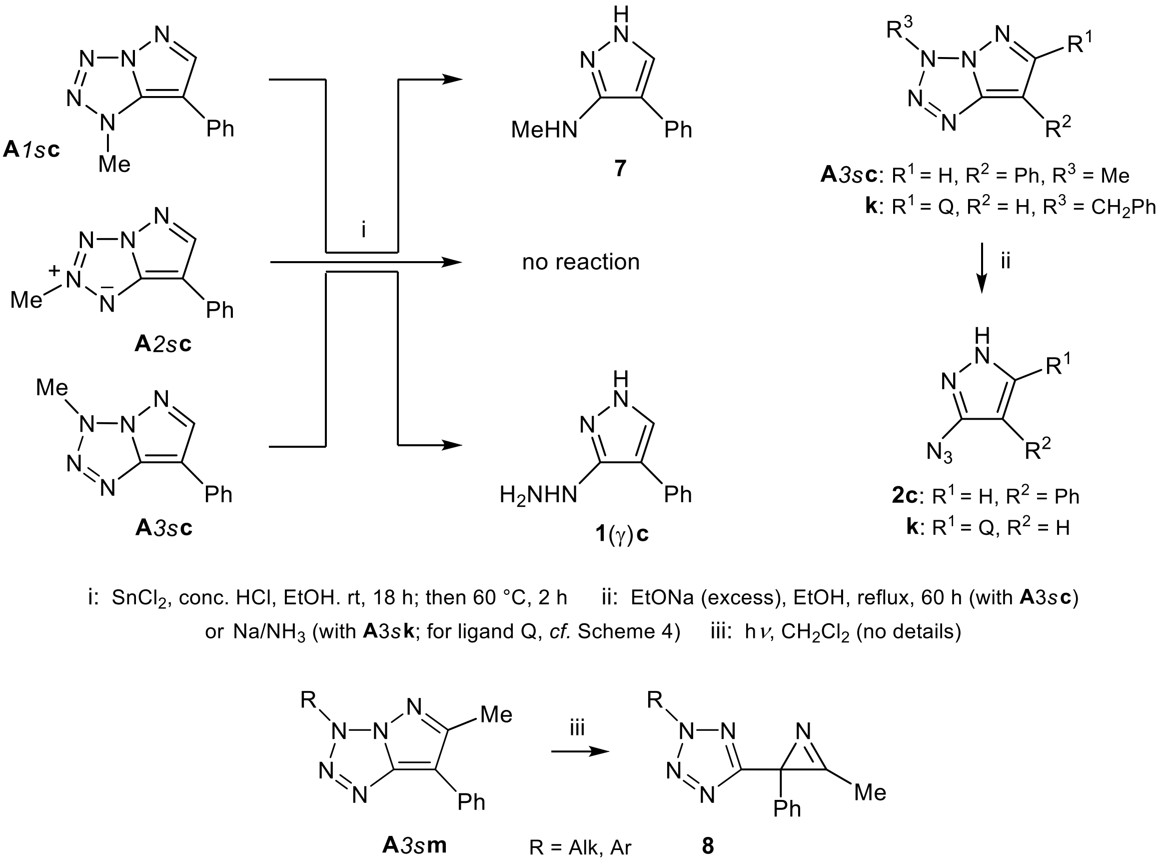
S^1 =
S^2 =



[a] **A**_3s_**c,d** with X-ray crystal structure. [b] **A**_3s_**l** in turn quaternized at pyridyl ligand with $Br[CH_2]_2CO_2H$. [c] Q = unspecified substituent. [d] Unreported.

Scheme 4

Comparing the reactivity of the isomers **A**_1–3_, conspicuous differences were observed (Scheme 5).[12b] As for the behaviour of the methyl derivatives **A**_1s_**c**–_3s_**c** towards stannous chloride, the representative **A**_1s_**c** was reduced to the aminopyrazole **7**, whereas the mesoion **A**_2s_**c** remained unaffected. Compound **A**_3s_**c**, however, expelled methylamine to give the hydrazinopyrazole **1**(γ)**c**, while treatment with sodium ethoxide caused demethylation, followed by ring opening to the azidopyrazole **2c**. Conceivably, compound **A**_3s_**k** underwent debenzylation on exposure to sodium/liquid ammonia.[9a] But an unexpected course was observed on photolysis of **A**_3s_**m**: the pyrazole moiety suffered ring contraction to give a 2*H*-azirine (→ **8**).[12d]

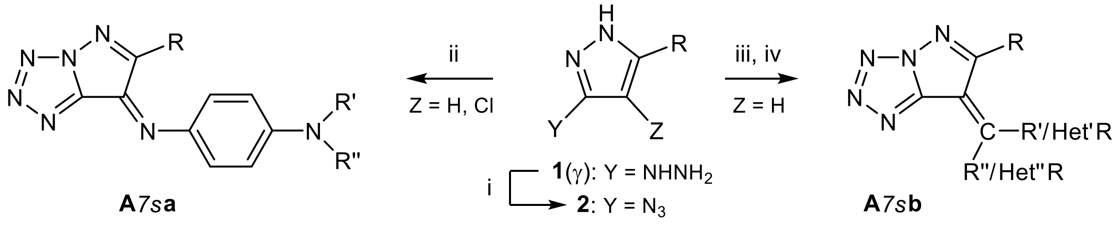


i: $SnCl_2$, conc. HCl, EtOH. rt, 18 h; then 60 °C, 2 h ii: EtONa (excess), EtOH, reflux, 60 h (with **A**3*s***c**) or Na/NH_3 (with **A**3*s***k**; for ligand Q, *cf.* Scheme 4) iii: h*ν*, CH_2Cl_2 (no details)

Scheme 5

b) Derivatives A*7* [I]

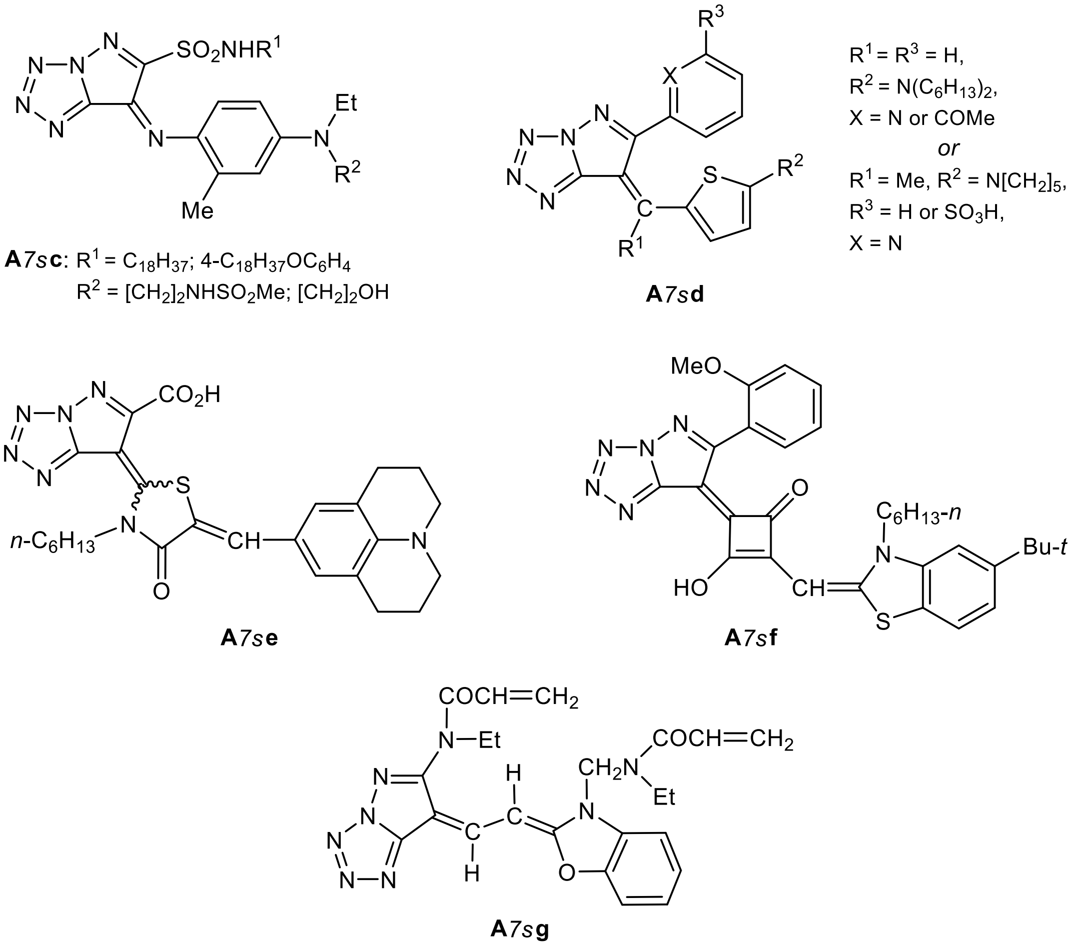
Contrasting with the pyrazolotetrazoles **A***5*, the derivatives **A***7* are energetically favoured over the isomeric azides [*cf.* Section (II / 4. a), Table 2].[6a] They arose when azidopyrazoles (**2**), or the putative bicycles (*vide supra*), undergo oxidative coupling with a *p*-phenylenediamine (→ **A***7s***a**) or condensation with either a carbonyl compound or a thiuronium salt (→ **A***7s***b**) (Scheme 6). Out of the plethora of the types **A***7s***a,b**, Figure 3 gives a selection. All the materials are dyes to serve in photography (**A***7s***c**[14]), electrophotography



i: HNO_2 ii: $4\text{-}NH_2C_6H_4NR'R''$, [O] iii: R'R"CO, base, Δ iv: RHet'RHet"CSAlk]X, base

Scheme 6

(**A***7s***d**[15]), inkjet technology (**A***7s***d**[16a,b], **A***7f* **f**[17]), and photoelectric conversion (**A***7s***e**[18]). A novel structure having polymerizable groups has recently been introduced through compounds of the type **A***7s***g**.[19]



A*7s***c**: $R^1 = C_{18}H_{37}$; $4\text{-}C_{18}H_{37}OC_6H_4$
$R^2 = [CH_2]_2NHSO_2Me$; $[CH_2]_2OH$

$R^1 = R^3 = H$,
$R^2 = N(C_6H_{13})_2$,
X = N or COMe
or
$R^1 = Me$, $R^2 = N[CH_2]_5$,
$R^3 = H$ or SO_3H,
X = N

A*7s***d**

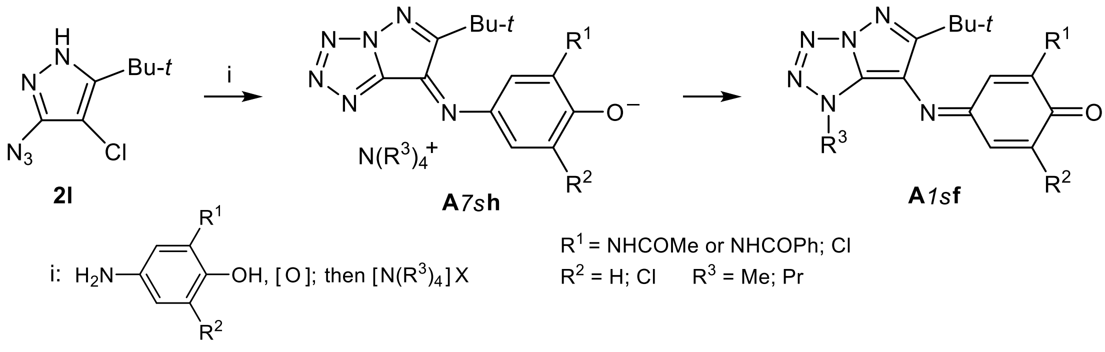
A*7s***e**

A*7s***f**

A*7s***g**

Figure 3. Selection of **A***7* dyestuffs

Salt-like coupling products of the type **A***7s***h** undergo 'intramolecular' *N*-alkylation to give **A***1* derivatives, as exemplified by the formation of **A***1s***f** (Scheme 7). These compounds represent additional inkjet dyes.[20]



2l

A*7s***h**

A*1s***f**

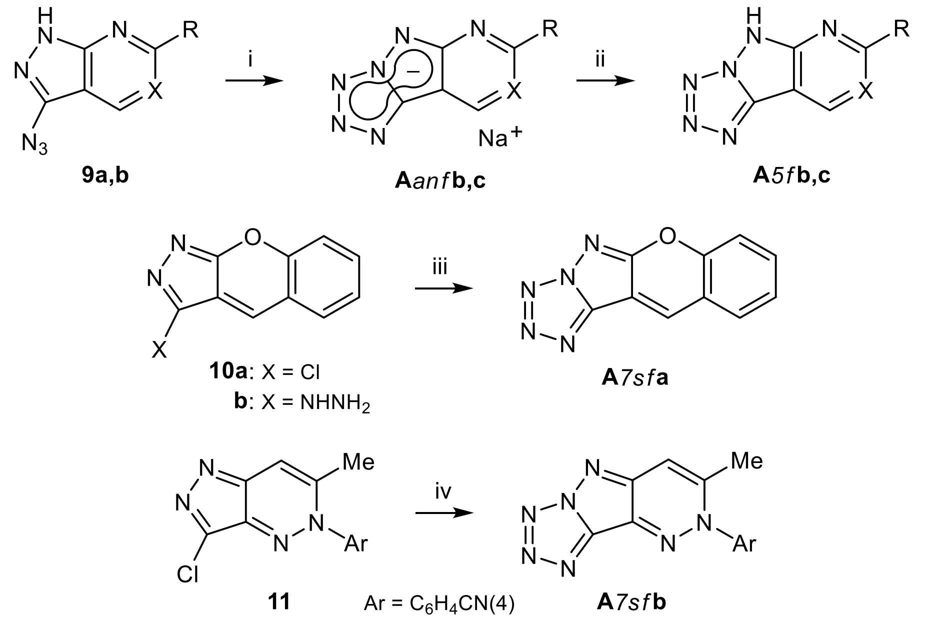
i: H_2N–C6H2(R1)(R2)–OH, [O]; then $[N(R^3)_4]X$

R^1 = NHCOMe or NHCOPh; Cl
R^2 = H; Cl R^3 = Me; Pr

Scheme 7

c) Derivatives A5*f* [I], 7*f* [I], *anf* [I]

In Section (a) it was shown that 3-azidoindazolide ion (**2***an***j**) is capable of cyclizing to the species **A***anf***a**, whereas the neutral azide (**2j**) does not change. This difference is well reflected by DFT calculated energy values [*cf.* Section (II / 4. a), Table 2].[6a,7a] A behaviour fully parallel to that of **2***an***j** was found on treatment of the azalogues **9a,b** with sodium methoxide (Scheme 8).[21a,b] However, when the separated salts **A***anf* **b,c** were exposed to acid, the neutral tetrazoles **A**5*f* **b,c** could be isolated. The same experiment with the tetrazolic species **A***anf***a** of Scheme 3 would have been interesting but is lacking. – Also derivatives of the type **A**7*f* were made: Compound **A**7*sf***a** resulted from both **10a** and **10b**,[22a] as did **A**7*sf* **b** from **11**.[22b] The first material showed biological activity against a number of bacteria, with a maximun against *S. albus*.



i: MeONa, MeOH, rt, 2−3 h (with **9a**) or 45−50 °C, 1 h (with **9b**)
ii: → dryness; then H_2O, 2 M AcOH or 2 M HCl → pH 6−7, 0−5 °C
iii: NaN_3, dioxane, reflux, 2 h (with **10a**) or $NaNO_2$, aq. HCl, 0 °C, 1 h (with **10b**)
iv: NaN_3, AcOH, reflux, 4 h

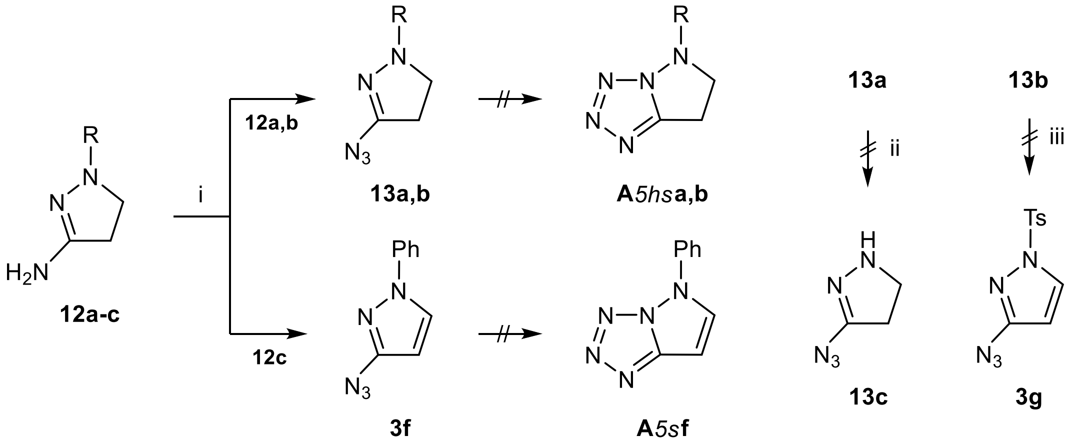
9	**A***anf*, 5*f*	X	R		yield (%)	mp (°C)	ref.
a	**b**	CH	H	**A**5*f***b**	94 [a]	178−180 [b]	21a
b	**c**	N	Ph	**A**5*f***c**	72	[c]	21b
				A7*sf***a**	60	320	22a
				A7*sf***b**	71	179−180	22b

[a] **A***anf***b**: yield 80%, mp ~100 °C. [b] Decomp. [c] Unreported.

Scheme 8

d) Derivatives A5*h* [XI]

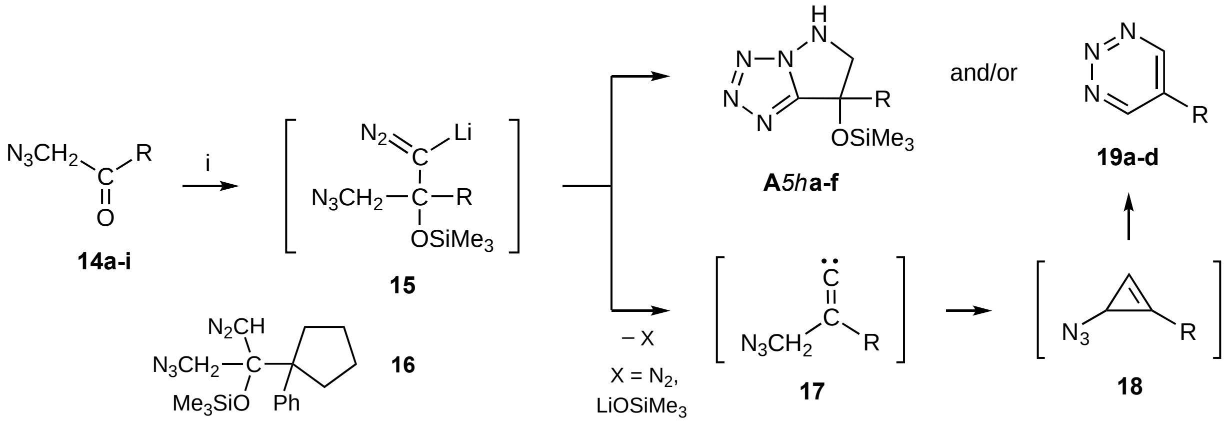
Starting materials for this study were the dihydropyrazolamines **12a-c** (Scheme 9); attempts to get also ring-unsubstituted precursors **12** failed.[23] Two-step azidation of **12a,b** gave the azido derivatives **13a,b**,



i: NaNO$_2$, aq. HCl, then NaN$_3$, < 0 °C throughout
ii: aq. HCl, reflux, 2 h iii: aq. NaOH, 85 °C, 1 h

12	13, A*5hs*	R		yield (%)	mp (°C)	ref.
a	**a**	COMe	**13a**	49	42–45	23
b	**b**	Ts	**13b**	42	104–105	23
c		Ph	**3f**	47	102–104	23

Scheme 9



i: Me$_3$SiCHN$_2$, BuLi, THF, –78 °C, 1 h; then rt, 1 h

14	R	A*5h*	yield (%)	19	yield (%)	ref.
a	*t*-Bu	**a**	71			24
b	CMe$_2$Ph	**b** [a]	88			24
c	CEt$_2$Ph			**a**	53	24
d	C[CH$_2$]$_5$Ph	**c**	66			24
e	C[CH$_2$]$_5$OSiMe$_2$Bu-*t*	**d**	94			24
f	C[CH$_2$]$_5$Pr	**e**	33	**b**	31	24
g	C[CH$_2$]$_4$Ph			**c**	22 [c]	24
h	1-adamantyl	**f**	86			24
i	2-R'-2-adamantyl [b]			**d**	42	24

[a] With X-ray crystal structure. [b] R' = OSiMe$_3$. [c] Besides 78% **16**.

Scheme 10

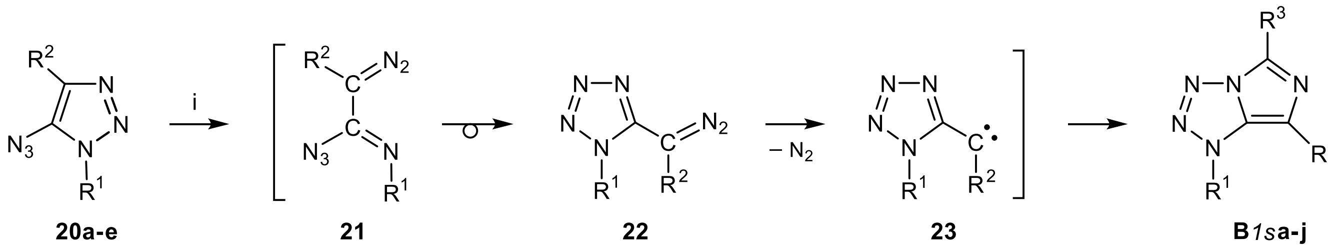
while the phenyl representative **12c** was directly converted to **3f** – a material that was assumed to result from oxidation of **12c** by excess nitrous acid. All these azides did not give indications of ring closure to **A**5, 5*h*, as in accord with DFT calculations [*cf.* Section (II / 4. a), Table 2].[6a,7a] Complementary experiments directed to deacetylation of **13a** and aromatization of **13b** met with failure: the substrates were recovered unchanged [the latter together with a trace of the azide **2a** (Scheme 2)].[23]

In contrast to the foregoing, a novel anionic [3+2] cycloaddition gave true **A**5*h* derivatives (Scheme 10).[24] Lithiated diazo(trimethylsilyl)methane and certain azidoketones **14** combined to adducts **15** that readily cyclized to the respective bicycles **A**5*h*. But with increasing steric bulk of the R ligand the formation of triazines **19** (*via* carbene **17** and azidocyclopropene **18**) became predominating. This influence is visible on going, for example, from **14b** to **14c** and from **14h** to **14i**. Should, exceptionally, protonation of **15** occur prior to ring closure (as in the reaction of **14g**), then compound **16** was the main product.

2) IMIDAZO[1,5-*d*]TETRAZOLES (B)

a) Derivatives B*1* [V], *2* [V]

1-Substituted 5-azido-1,2,3-triazoles **20** having an acceptor group at C(4) rearrange on being heated *via* **21** to 5-(diazoalkyl)tetrazoles **22** – a process resembling the Dimroth rearrangement. Using a nitrile as solvent and maintaining the reaction for a longer period of time, the diazo compound **22** expels dinitrogen and the residual carbene **23** is trapped by the nitrile to give bicycles of the **B***1* series (Scheme 11).[25a–c]



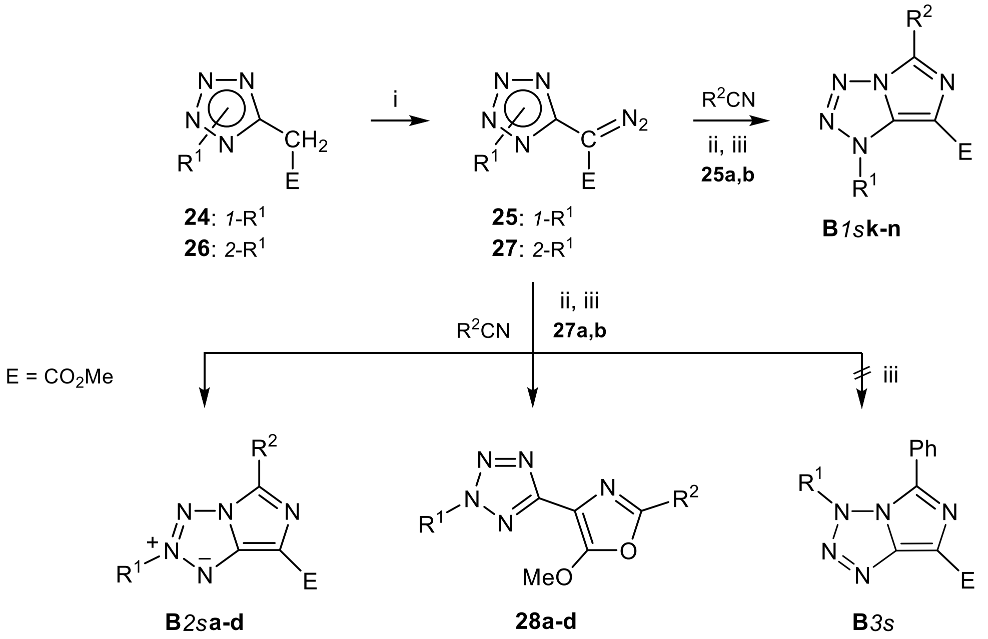
i: R^3CN (excess), 70−80 °C, 2−5 d

20	R^1	R^2	R^3	B*1s*	yield (%)	mp (°C)	ref.
a	Ph	CO_2Me	Me	a	42	210−212	25a
	Ph	CO_2Me	Ph	b	51	205 [a]	25a
b	4-$NO_2C_6H_4$	CO_2Me	Me	c	62	214	25b
	4-$NO_2C_6H_4$	CO_2Me	Ph	d	61	206	25b
c	4-pyridyl	CO_2Me	Me	e	65	180	25b
	4-pyridyl	CO_2Me	Ph	f	60	208	25b
d	4-$NO_2C_6H_4$	CN	Me	g	51−55 [b]	172	25c
	4-$NO_2C_6H_4$	CN	Ph	h		206	25c
e	4-pyridyl	CN	Me	i		202	25c
	4-pyridyl	CN	Ph	j		209	25c

[a] Decomp. [b] No individual figures reported.

Scheme 11

The foregoing synthetic principle (**22** → **23** → **B***1*) using aceto- and benzonitrile is fully applicable to the preparation of 1-*alkyl*-substituted derivatives such as **B***1***k-n** (Scheme 12).[26a] Since the substrates **25** were not available through a Dimroth rearrangement like **22**, they had to be provided by diazo transfer to **24**. However, extending the study to the isomers **27** (similarly prepared from **26**), major differences became apparent: (i) Regarding thermal stability, the decomposition of **27a** studied in benzene at 70 °C was *ca.* two times slower than that of **25a**–an observation matching a preceding finding with (diazomethyl)tetrazoles.[27a] (ii) Using acetonitrile for carbene trapping, instead of imidazotetrazoles like **B***2s***a,b** the oxazoles **28a,b** were found.[26a] Only employment of benzonitrile gave rise to bicycles (→ **B***2s***c,d**), but also here oxazoles (**28c,d**) arose. The formation of compounds **B***3s* as a consequence of an attack of the benzonitrile carbon at N(1) of the tetrazole could be excluded spectroscopically.[26b]

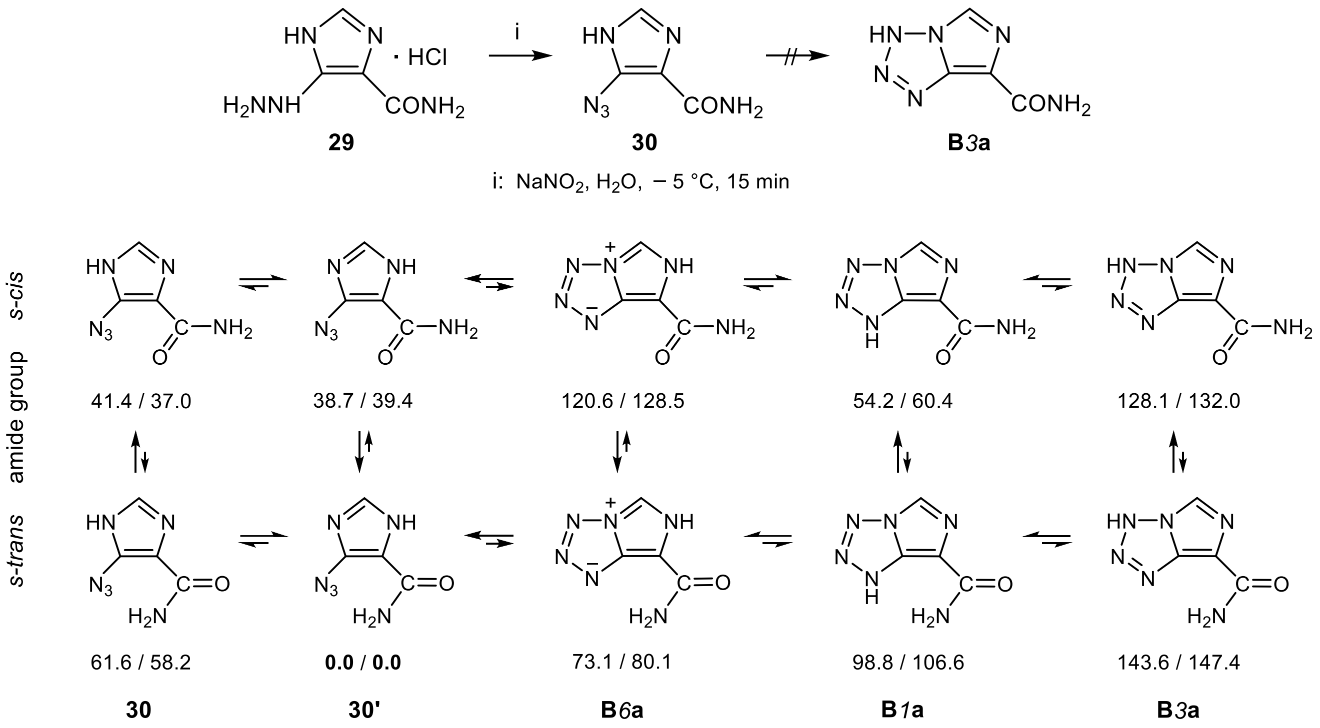


i: TsN_3, Et_3N, MeCN, rt: 12 h for **25a,b**, 3 weeks for **27a,b**
ii: MeCN (excess), 70–80 °C: 2 weeks for **B***1s***k**, 2 d for **B***1s***l**, 5 d for **28a,b**
iii: PhCN (excess), 70–80 °C: 2 weeks for **B***1s***m,n**, 5 d for **B***2s***c** and **28c**, 5 weeks for **B***2s***d** and **28d**

24–27	R^1	R^2	B*1s*	yield (%)	mp (°C)	B*2s*	yield (%)	mp (°C)	28	yield (%)	mp (°C)	ref.
a	Me	Me	**k**	56	199	**a**	0		**a**	75	138	26a
b	Et	Me	**l**	55	107	**b**	0		**b**	28	63	26a
	Me	Ph	**m**	75	185	**c**	15	184	**c**	25	128	26b
	Et	Ph	**n**	62	132	**d**	23	165	**d**	26	96	26b

Scheme 12

Also no **B***3* derivative was formed on reaction of the hydrazinoimidazole **29** with nitrous acid; as the sole product, the azide **30** was isolated (Scheme 13).[28] Yet, the authors' formulations "**30**" and "**B***3***a**" deserve



i: $NaNO_2$, H_2O, − 5 °C, 15 min

Values shown:[6a] $\Delta E / \Delta G$ (B3LYP/6-31G*, gas phase; kJ mol^{-1}); **30**, **30'** with *Z* configured azido group

Scheme 13

a short comment: From the mechanistic point of view, ring closure can occur only with the tautomeric azide **30'** (not with **30**), and this species would lead to the mesoionic bicycle **B***6***a** rather than to **B***3***a**. However, the observed failure of cyclization is consistent with DFT calculations that showed **B***6***a** to be distinctly higher in energy than the azide **30'** (regardless of the conformation of the amide function). This applies also to the parent bicycle **B**6 with respect to 4-azido-1*H*-imidazole [*cf.* Section (II/4. a), Table 2].[6a,7a] Moreover, when comparing the energies of the three tautomers **B***6***a**, **B***1***a**, and **B***3***a**, the latter turned out to be the least favoured one (as a result of the adjacent pyrrole-like nitrogens).[6a]

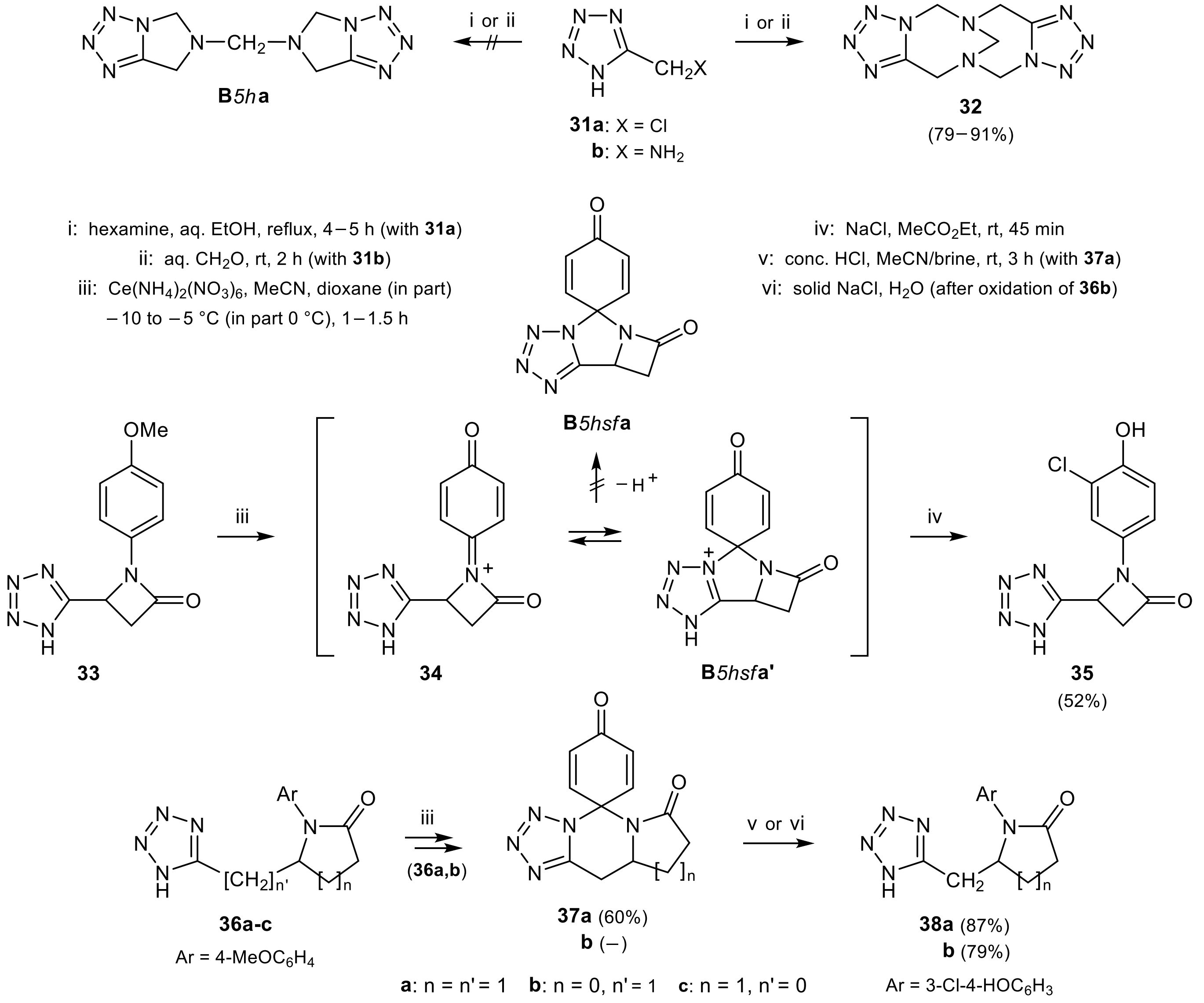
b) Derivatives B*5*, *7*

Some *N*-unsubstituted **B***1* representatives have been mentioned in the patent literature, showing ligands like $[CH_2]_2NHSO_2C_{16}H_{33}$ or $S[CH_2]_2OH$ at C(5) and Cl or 4-$(C_{12}H_{25})C_6H_4$ at C(7), but experimental details were not disclosed.[29] These materials should be azides; they act as dye forming couplers capable of giving imines of the **B***5* and **B***7* series, *i.e.*, derivatives related to the compounds **A***7sc* of Figure 3. Indeed, the azidoazole/azolotetrazole energy difference within both the **B***5* and **B***7* series is fairly small compared to that within the **B***6* series, although not to the same extent as calculated for the **A***7* series relative to **A***5* [*cf.* Section (II/4. a), Table 2].[6a,7a]

c) Derivatives B*5h*, *5hf* [X]

The reaction of *N*-unsubstituted 5-(chloromethyl)- (**31a**) or 5-(aminomethyl)tetrazole (**31b**) with hexamine and formaldehyde, respectively, might be envisaged as an entry to the series **B***5h* (Scheme 14). In either case a conversion took place readily, but the product (formed from substrate and reagent in the ratio 2 : 3) turned out be the bridged tricycle **32** rather than the sought compound **B***5h***a**.[30]

A ring-fused derivative of **B***5h*, *viz.* the spirane **B***5hsf***a**/**a'**, occurred as an intermediate in the cerium(IV)-mediated transformation of the tetrazolyl substituted β-lactam **33** into its congener **35**.[31a] Instead of causing *N*-deprotection, the reagent generates the quinone iminium species **34** which cyclizes to **B***5hsf***a'**. Sodium chloride, added in turn, affects the quinonoid moiety whereupon the central ring opens to the product **35**. Attempts to isolate the free base **B***5hsf***a** were vitiated, whereas with the process (**36a** → **38a**) the respective



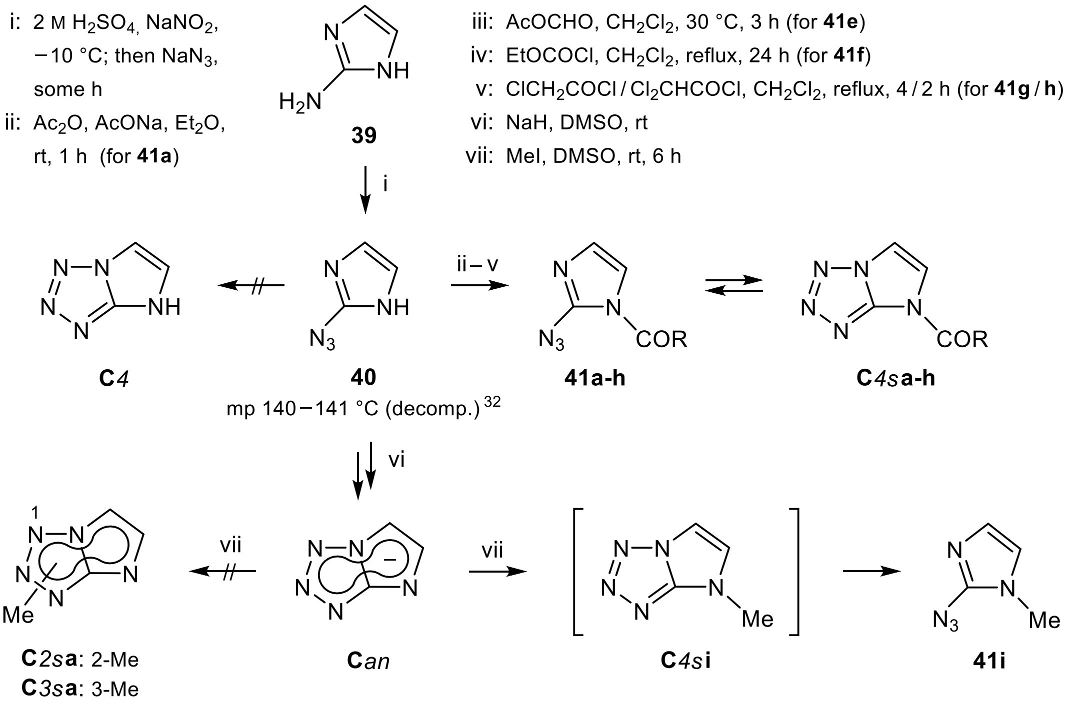
Scheme 14

compound **37a** could be separated. On the other hand, isolation of the free base (**37b**) failed too when the substrate **36b** having a β-lactam instead of the pyrrolidinone ring was reacted.[31b] A comparitive experiment with **36c** would have been interesting but has not been reported.

3) IMIDAZO[1,2-*d*]TETRAZOLES (C)

a) Derivatives C*1*, *2* [VI], *3* [VI], *4* [I, V, VI], *an* [I]

Sequential treatment of 2-aminoimidazole (**39**) with nitrous acid and sodium azide produced the azide **40** (Scheme 15; quantitative yield).[32] As with the pyrazole congener **1a** [*cf.* Section (II / 1. a)], there were no indications of ring closure (→ **C***4*). This failure is in accordance with DFT calculations which showed **C***4* to be higher energy [*cf.* Section (II / 4. a), Table 2].[6a,7a] But interestingly, the difference between **C***4* and **40**



41, **C***4s*	R	**41**: yield (%)	mp [bp$_1$] (°C)	*K* [**C***4s*] : [**41**]	solvent [a]	temp. (°C)	ref.
a	Me			0.67	A	[b]	34
		90	78 − 79	0.59 / 0.53 / 0.48 [c] / 0.42	A	15 / 25 / 35 / 45	35a
b	Et			0.60	A	35	35b
c	*i*-Pr			0.95	A	35	35b
d	*t*-Bu			1.7 [d]	A	35	35b
e	H	75	[120 − 122]	0.03	A	35	35c
f	OEt	85	[150 − 152]	0.16	A	35	35c
g	CH_2Cl	50	77 − 78	0.33 / 0.09	A / B	20 / 0	35c
h	$CHCl_2$	65	[135 − 137]	0.24 / 0.03	A / B	20 / 0	35c

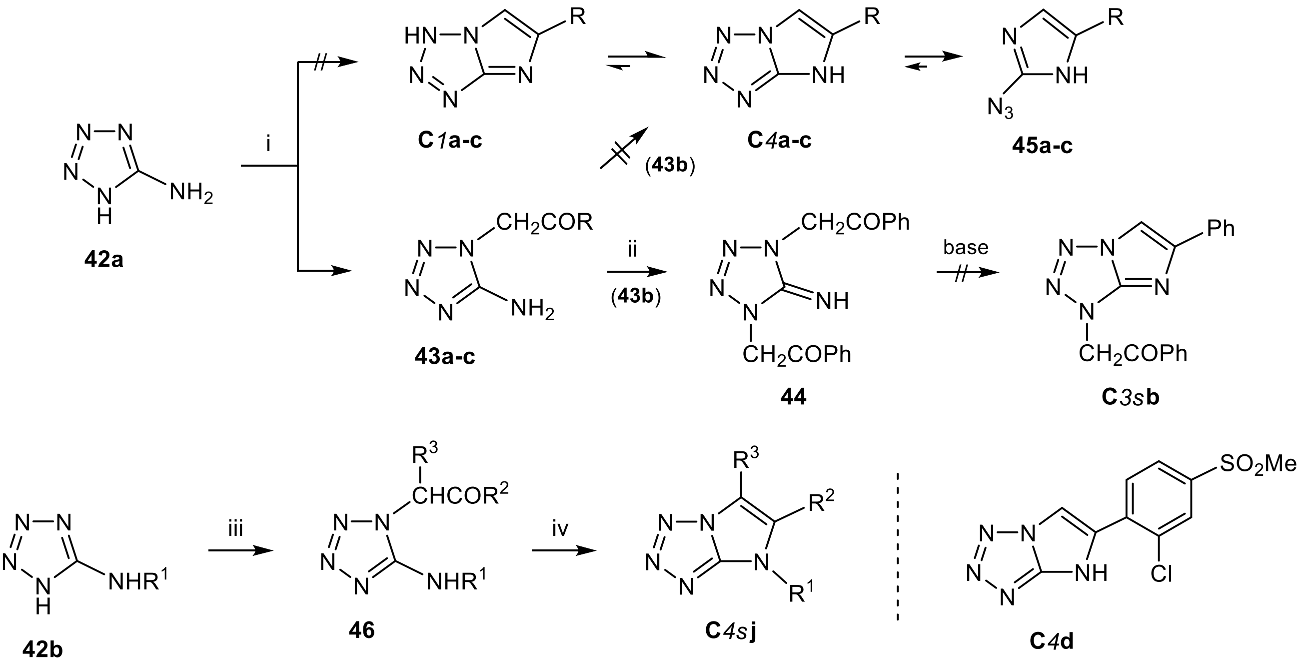
[a] A = $(CD_3)_2SO$, B = $(CD_3)_2CO$. [b] Unspecified. [c] See also ref. 35b. [d] High value entropy-controlled: $\Delta S = -4.8 \pm 1.0$ e.u.; compare case **a** showing $\Delta S = -8.0 \pm 0.6$ e.u. (refs. 35a,b).

Scheme 15

is reduced considerably on coordination with copper(I) chloride.[33a] Also a change of the medium from gas phase over carbon tetrachloride and acetonitrile to water has a levelling effect.[33b] In contrast to these DFT computations earlier HMO[7b] and MNDO calculations[33c] did not reflect the experimental finding.

Acylation with a variety of acid chlorides afforded the derivatives **41a-h**.[34,35a–c] These compounds, clearly differing from the pyrazole analogues **3** [*cf.* Section (II / 1. a)], equilibrate with the cyclic isomers **C**_4s_**a-h**, as detailed in the Scheme. But there exists a parallel to the pyrazolides **2**_an_ in the behaviour of anionized **40**: this species, generated accordingly, cyclized to **C**_an_.[11a] Methylation of the latter did not affect the tetrazolic half-ring (as observed with **A**_an_); only the imidazole part reacted giving **C**_4s_**i** which immediately ring-opened to the azide **41i**.

As for the synthesis of class **C** using the Chichibabin method – *i.e.*, the reaction of 5-aminotetrazole (**42a**) with phenacyl halides – , the first report relates to the derivative **C**_1_**a** (Scheme 16).[36] However, on repeating the experiment (with extension to phenacyl and 4-bromophenacyl bromides), it turned out that the process stops at the stage of the *N*-phenacylated tetrazole (**43a-c**).[37] Various attempts to cyclize the derivative **43b** failed, and also the doubly phenacylated substrate **44** resisted ring closure.[37,38] This contrasts with a patent claim, according to which the above synthesis is feasible, generalized as **42b** → **46** → **C**_4s_**j**; in this manner,



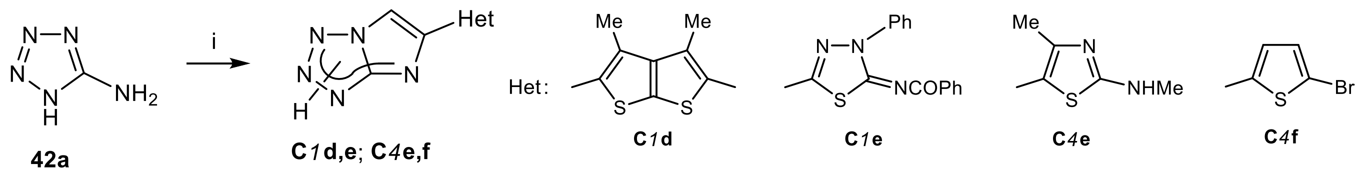
i: $BrCH_2COR$, EtOH, 60 °C, 3 h ii: $BrCH_2COPh$, EtOH, reflux, 50 h iii: $ClCHR^3COR^2$, KOH, MeOH, rt iv: AcOH/AcONa, rt

	R	yield (%)	mp (°C) [a]	ref.		R	yield (%)	mp (°C) [a]	ref.
43a	4-$(MeSO_2)C_6H_4$	50	220 [b]	37	**43c**	4-BrC_6H_4	85	226–227	37
43b	Ph	70 [c]	232–233	37	**44**		60 [d]	154 [e]	37

[a] Decomp. [b] Mp of '**C**_1_**a**' in ref. 36: 235–238 °C. [c] Mixture with 5% **44**. [d] Hydrobromide salt. [e] Free base.

Scheme 16

the agrochemical **C***4***d** has been made.[39] Also heterocyclic analogues of phenacyl bromide were said to give derivatives **C** very readily (in a one-pot procedure), *viz.* **C***1***d,e** and **C***4***e,f** – materials that exhibit divers biological activities.[40a,b, 41a,b]



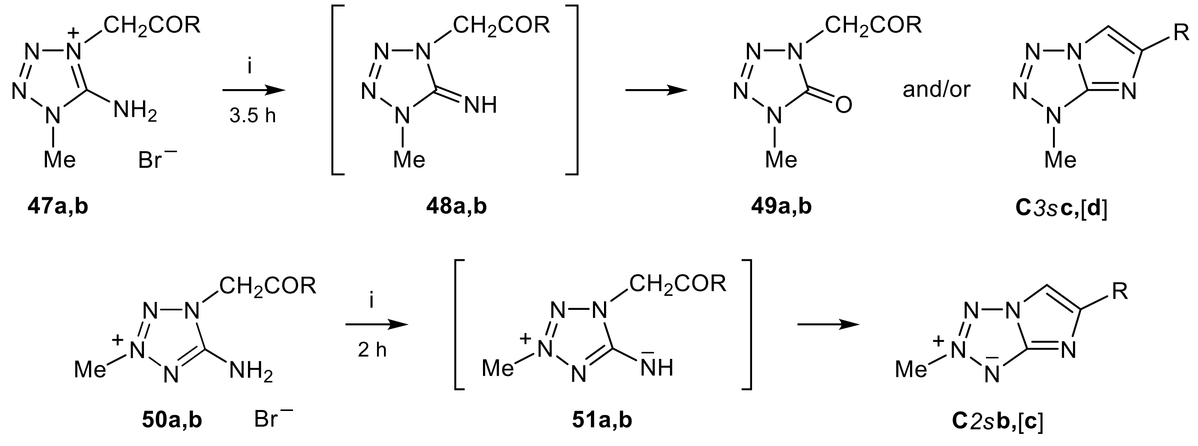
i: $BrCH_2COHet$, EtOH or abs. EtOH, reflux, 4−12 h

C*1* [a]	yield (%)	mp (°C)	ref.	**C***4*	yield (%)	mp (°C)	ref.
d	74	279	40a	**e**	76	155−157	41a
e	75	141−143	40b	**f**	50	212−213	41b

[a] Products arbitrarily formulated as **C***1* tautomers.

Scheme 17

To overcome the failure of getting *N*-substituted bicycles **C***3s* and **C***2s* by alkylation of **C***an* (*vide supra*), the Chichibabin method was attempted with the tetrazolium salts **47** and **50** (Scheme 18).[42,43] After a series of fruitless runs with **47a**,[43] only heating in a slightly acidic buffer gave the desired compound **C***3s***c** but accompanied by substantial amounts of the tetrazolone **49a**, whereas under the same conditions the isomeric salt **50a** reacted satisfactorily (→ **C***2s***b**). This difference can be rationalized as follows: Of the intermediary imines **48a** and **51a** the latter is more nucleophilic and, in addition, less sensitive to hydrolysis. Surprisingly,



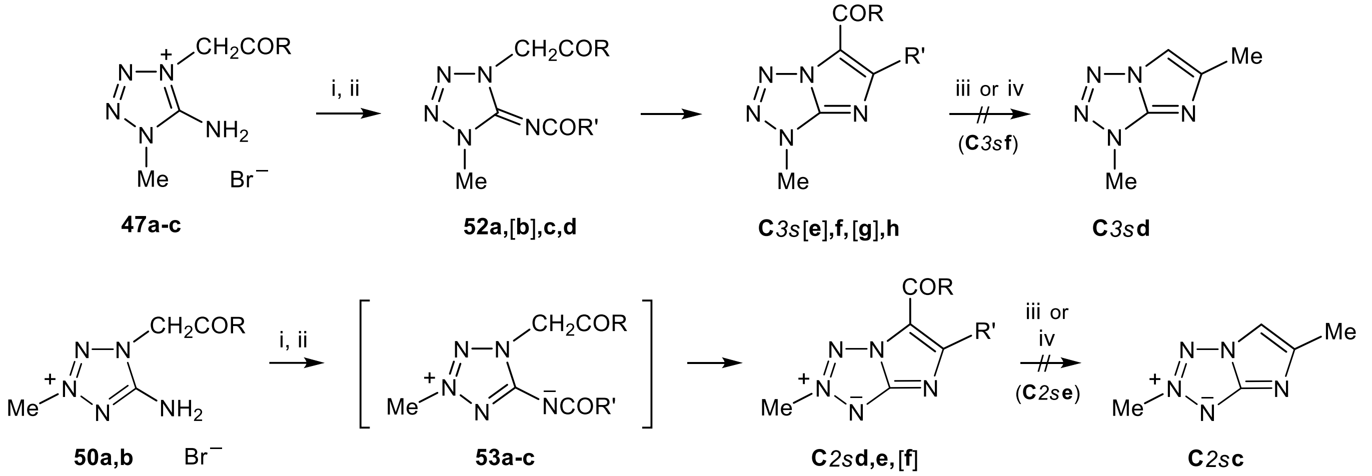
i: AcONa/AcOH/NH_3 (pH 6.5), 100−110 °C

				yield (%)			mp (°C)			
47−51	**C***3s*	**C***2s*	R	**49**	**C***3s*	**C***2s*	**49**	**C***3s*	**C***2s*	ref.
a	**c**	**b**	Ph	89 [a]	11 [a,b]	57	122−124 [d]	118−119	198−200	42
b	**d**	**c**	Me	13	0	0 [c]	oil			42, 43

[a] By ^{1}H NMR. [b] Compound **C***3s***c** separated as picrate (mp 156−157 °C). [c] Compound **50b** (**51b**) decomposed. [d] Authentic sample by alkaline hydrolysis of **47a**.

Scheme 18

the extension of these experiments to the acetonyl salts **47b** and **50b** met with failure: the sought bicycles **C**3*s***d** and **C**2*s***c** did not form; also working with propargyl groups instead of the acetonyl ligands was futile.



i: Ac_2O/Et_3N, 110 °C, 0.5 h (for **52a,b,d**; **53a,b**; **C**3*s***e,f,h**; **C**2*s***d,e**) ii: $AcOCHO/Et_3N$, rt, 2 h (for **52c**; **53c**; **C**3*s***g**; **C**2*s***f**)
iii: 12 M HCl, reflux, 2.5 h iv: 6 M NaOH, 90 °C, 2.5 h

							yield (%)			mp (°C)			
47, 50	R	**52, 53**	R	R'	**C**3*s*	**C**2*s*	**52**	**C**3*s*	**C**2*s*	**52**	**C**3*s*	**C**2*s*	ref.
a	Ph	**a**	Ph	Me	**e**	**d**	61 [a]	0	16 [c]	124–126	0	153–155	42
b	Me	**b**	Me	Me	**f**	**e**	0	51	86	0	124–125	129–130	42
c	OMe	**c**	Ph	H	**g**	**f**	53 [b]	0	0	42–45	0	0	43
		d	OMe	Me	**h**		25	trace		oil			43

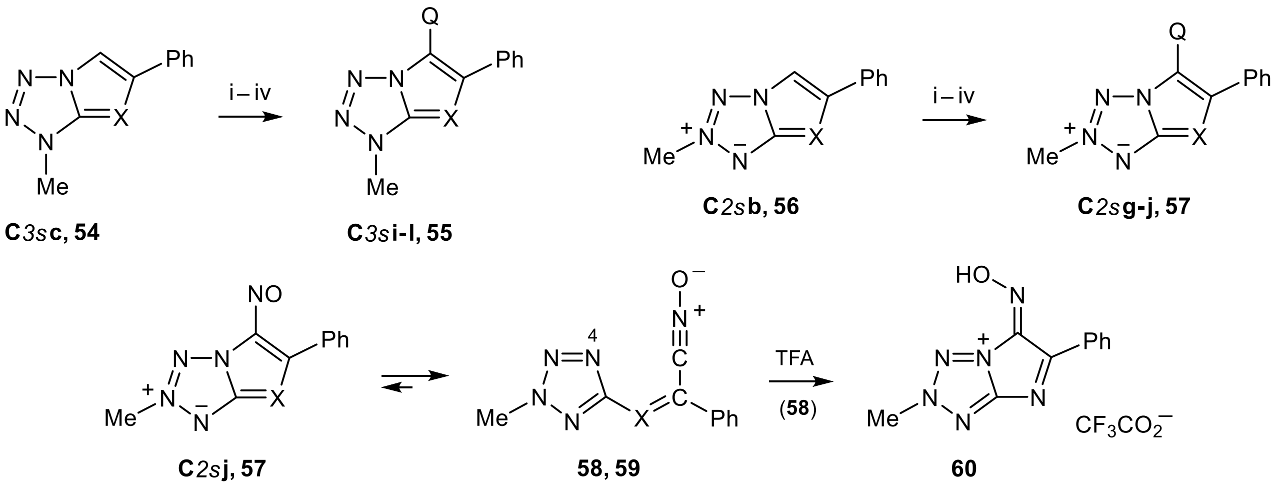
[a] Refluxing AcOH (0.5 h) caused deacetylation to give **48a** (Scheme 18). [b] Along with a trace of **52a**. [c] Besides 77% **C**2*s***e**.

Scheme 19

Depending on the R ligand and the position of the methyl group, cyclization with acetic anhydride allowed the salts **47** and **50** to be converted to 6-acyl derivatives of **C**3*s* and **C**2*s*, respectively (Scheme 19).[42,43] Thus, in the case of the phenacyl representatives **47a** and **50a**, only the latter reacted (→ **C**2*s***d**), whereas the former furnished the acetylimine **52a** which, on attempting ring closure, underwent deacetylation to afford **48a**. As for **C**2*s***d**, this product was accompanied by major amounts of the 6-acetyl derivative **C**2*s***e**; it resulted from benzoyl–acetyl exchange which obviously occurred at the stage of **53a** (*cf.* the synthesis of 5-acyl-1*H*/2*H*-pyrrolotetrazoles[3]). However, attempts to get 5-unsubstituted species like **C**3*s***g** and **C**2*s***f** by using a formylating agent failed, as did deacylation of **C**3*s***f** and **C**2*s***e** to give the missed products **C**3*s***d** and **C**2*s***c**.[43] – Concerning the behaviour of the acetonyl salts **47b** and **50b** towards acetic anhydride, both substrates reacted readily to give the products **C**3*s***f** and **C**2*s***e** (the latter in excellent yield). But an additional reaction with the ester-substituted salt **47c** did scarcely go beyond the imine **52d**.[43]

Finally, it should be mentioned that in the preceding review[2a] the synthesis of **C**3*s* and **C**2*s* was summarized erroneously as the authors failed to realize the difference between the routes followed in Scheme 18 *vs.* 19.

Regarding S_E reactions, the derivatives **C***3s***c** and **C***2s***b** are susceptive to standard electrophiles, as shown by the products **C***3s***i-l** and **C***2s***g-j** (Scheme 20).[42] The enhanced reactivity of **C***2s***b** (*cf.* reaction times) is consistent with the higher electron density at C(6) as found through model calculations (Table 1). The same



C*3s***c, 54** **C***3s***i-l, 55** **C***2s***b, 56** **C***2s***g-j, 57**

C*2s***j, 57** **58, 59** **60**

C*3s*, **C***2s*, **58**: X = N **54–57, 59**: X = CCOMe

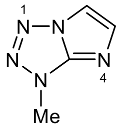
i: Br_2, $CHCl_3$, 0 °C (for **C***3s***i**, **C***2s***g**) ii: Ac_2O/AcONa, 130–140 °C (for **C***3s***j**) or 120–130 °C (for **C***2s***h**)
iii: AcOCHO, 85 °C (for **C***3s***k**, **C***2s***i**) iv: $NaNO_2$, AcOH, 0 °C (for **C***3s***l**, **C***2s***j**, **55**, **57**)

C*3s*	time (h)	yield (%)	mp (°C)	Q	**C***2s*	time (h)	yield (%)	mp (°C)	ref.
i	0.5	86	149 [a]	Br	**g**	0.5	93	150–151	42
j	25	66	113–114	COMe	**h**	3	58	152–154	42
k	2.5	62	150–152	CHO	**i**	1.5	69	229–231	42
l	0.75	44	149–150	NO	**j** [b]	0.25	58	105–107	42

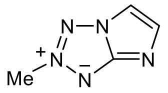
[a] Decomp. [b] Exists predominantly as **58** (%/°C): 96.2/25, 94.8/0, 94.3/−20, 93.3/−40 (CD_2Cl_2, ^1H NMR).

Scheme 20

Table 1. Calculated atomic charges for the models **C***3s***a** and **C***2s***a** [a,b]



C*3s***a**



C*2s***a**

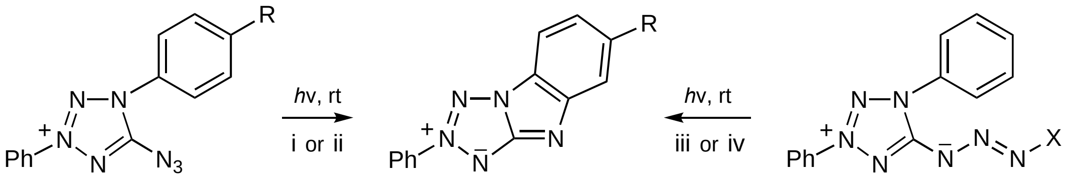
AM1		B3LYP/6-311+G**			AM1		B3LYP/6-311+G**	
total	π	total	π		total	π	total	π
0.033	1.171	–0.148	1.182	N(1)	–0.010	1.319	0.036	1.317
0.019	1.131	0.007	1.157	N(2)	–0.073	1.445	0.104	1.427
–0.182	1.658	–0.111	1.505	N(3)	–0.046	1.291	–0.237	1.204
0.005	1.051	–0.016	1.084	C(3a)	–0.048	1.059	–0.003	1.091
–0.121	1.259	–0.258	1.228	N(4)	–0.123	1.267	–0.245	1.214
–0.145	1.043	–0.026	1.021	C(5)	–0.089	0.979	0.010	0.995
–0.121	1.143	–0.146	1.162	C(6)	–0.209	1.235	–0.212	1.189
–0.160	1.535	0.077	1.443	N(7)	–0.081	1.409	–0.062	1.401

[a] Gas phase. [b] AM1 data obtained using HyperChem, version 4.5,[42,43] B3LYP/6-311+G** data obtained using Gaussian 98.[6a]

relationship applies to the isomeric pyrrolotetrazoles.[3] On the whole, the reactivity of **C3*s*c** and **C2*s*b** can be compared to that of the pyrrolotetrazoles **54** and **56**, since the electron-withdrawing influence exerted by a pyridine-like nitrogen [here N(4) of system **C**] resembles that of an acyl group; for example, acetylation of **C3*s*c** (and also of **C2*s*b**) could be achieved only after addition of sodium acetate, as observed with **54**.[3] Regarding the nitroso derivatives **C3*s*l** and **C2*s*j**, the parallel is twofold: **C3*s*l** retained its bicyclic form as did **55**,[3] whereas both **C2*s*j** and **57** ring-opened to give the nitrile oxides **58** and **59**. In this second case the ring-stabilizing influence of the acceptor X is offset by the less nucleophilic N(4) atom of the 2*H*-tetrazoles **58** and **59**. However, protonation of the oxide function caused recyclization to give the oxime **60**[43] – a kind of ring closure the nitrile oxide **59** (X = CH) was shown to undergo too.[3]

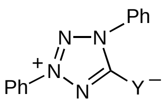
b) Derivatives C2*f* [VI], 4*f* [I, XIII], *anf* [I]

Photolysis of the azidotetrazolium salts **61a,b** gave rise to benzo-fused imidazotetrazoles the **C2*sf*a,b**,[44a] the former tricycle was formed also on irradiation of the triazenides **62a,b** (Scheme 21).[44b] Cyclization was thought to proceed *via* a singlet nitrene, while the triplet state led to tetrazolium aminides (**63**) as major side products.[44a] – Two interesting reactions of **C2*sf*a** were reported (Scheme 22).[45] (i) Benzyne produced the tetrazolium oxide **63e** that arose through nucleophilic addition to N(4) to be followed by C(3a)–N(4) bond breaking and uptake of water. (ii) DMAD (2 moles) added to the C(3a)–N(4) bond to give an intermediary tetracycle that rearranged to compound **64**. The process could not be extended to other unsaturated agents.



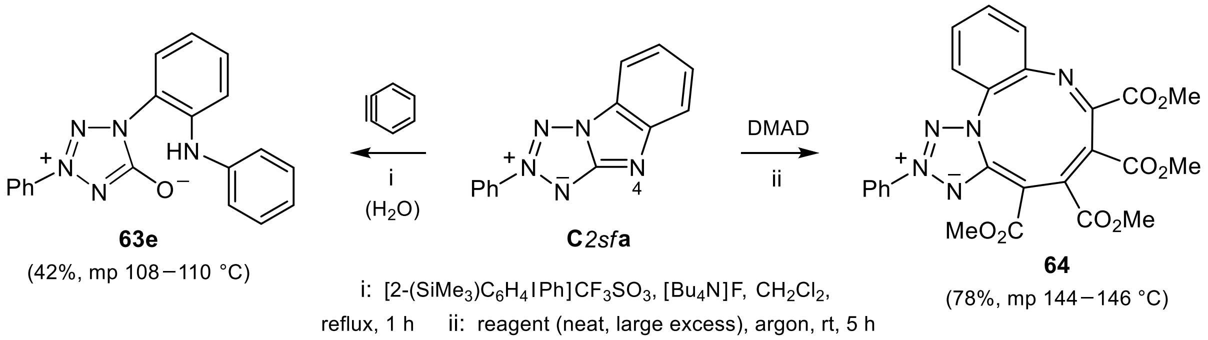
61a,b BF$_4^-$ **C2*sf*a,b** **62a,b**

i: MeOH, 80 min; then M NaOH ii: MeCN, 30 min iii: MeOH, 45 min (with **62a**), 5 h (with **62b**)
iv: MeCN, 40 min (with **62a**), 3 h (with **62b**)

61, C2*sf*	R	**62**	X	**C**2*sf*	from	method	yield (%)	mp (°C)	ref.
a	H	**a**	Ts	**a**	**61a**	i	20 [a]	216−217	44a
b	Me	**b**	CN	**a**	**61a**	ii	35 [b]		44a
				a	**62a**	iii	5 [c]		44b
63		**a**: Y = NH **b**: Y = NTs **c**: Y = NCN **d**: Y = O		**a**	**62a**	iv	32 [d]		44b
				a	**62b**	iii	0 [e]		44b
				a	**62b**	iv	9 [f]		44b
				b	**61b**	ii	22 [g]	219−220	44a

[a] Besides 23% **63a**. [b] Besides 30% acetanilide. [c] Besides 53% **63a** and 1% **63b**. [d] Besides 12% **63b** and 12% acetanilide. [e] Instead of **C**2*sf***a**: 6% **63a**, 21% **63c**, and 43% **63d**. [f] Besides 34% **63c**. [g] Besides 23% aceto-*p*-toluide.

Scheme 21



63e (42%, mp 108−110 °C)

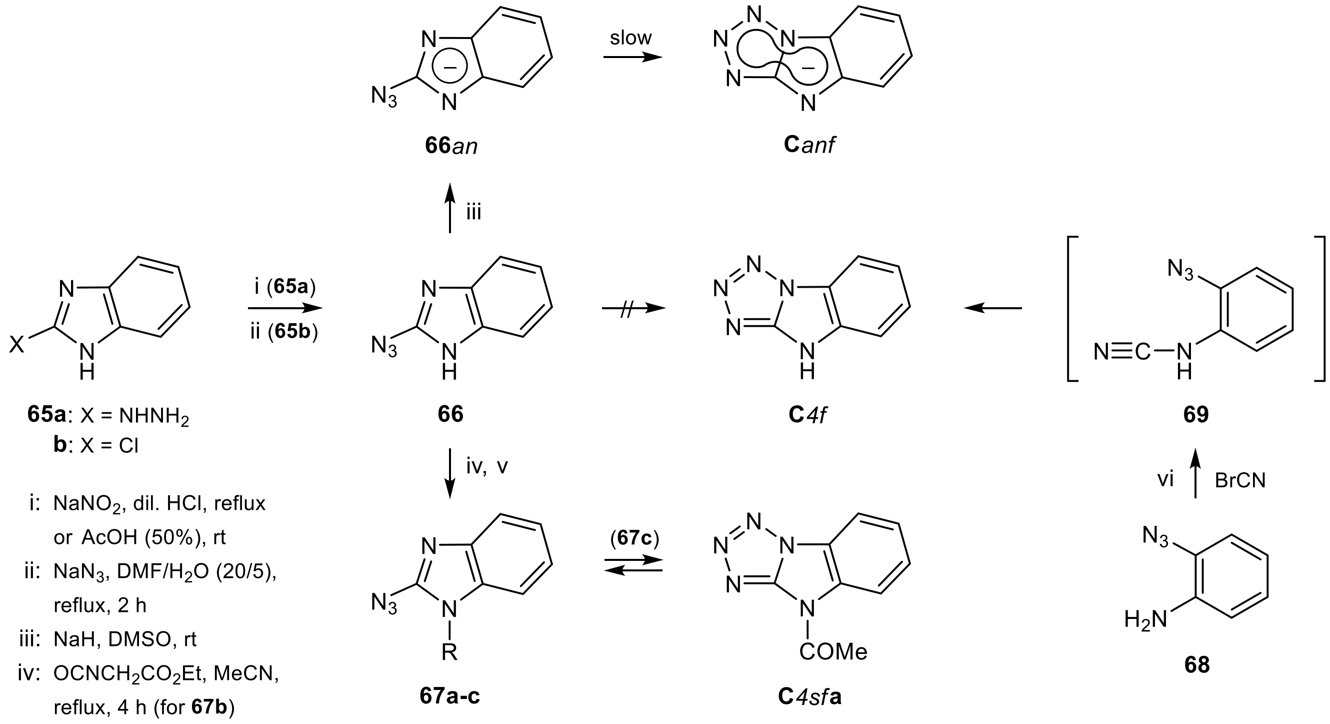
C2*sf***a**

64 (78%, mp 144−146 °C)

i: [2-(SiMe$_3$)C$_6$H$_4$IPh]CF$_3$SO$_3$, [Bu$_4$N]F, CH$_2$Cl$_2$, reflux, 1 h ii: reagent (neat, large excess), argon, rt, 5 h

Scheme 22

The earliest report on a ring-fused derivative of the parent **C**4, *viz.* compound **C**4*f*, dates from the mid-1950s when 2-hydrazinobenzimidazole (**65a**) was reacted with nitrous acid (Scheme 23).[46a] However, an experiment conducted shortly thereafter under IR control revealed the product to be the azide **66**.[46b] This



66*an* **C***anf*

65a: X = NHNH$_2$
b: X = Cl

66 **C**4*f* **69** **67a-c** **C**4*sf***a** **68**

i: NaNO$_2$, dil. HCl, reflux or AcOH (50%), rt
ii: NaN$_3$, DMF/H$_2$O (20/5), reflux, 2 h
iii: NaH, DMSO, rt
iv: OCNCH$_2$CO$_2$Et, MeCN, reflux, 4 h (for **67b**)

v: Ac$_2$O, no details (for **67c**) vi: THF, rt, 4 h (ref. 48a) or 60 °C, reaction time unspecified (ref. 48b)

	from	yield (%)	mp (°C)	IR (azide)	ref.
C4*f*	**65a**	[a]	189 [b]	[c]	46a
66	**65a**	66	192 [b]	yes	46b
66	**65a**	[a]	[a]	yes	34
C4*f*	**65b**	60	178	no	47
C4*f*	**68**	71	> 100 [b]	[c]	48a
C4*f*	**68**	[a]	[a]	[c]	48b

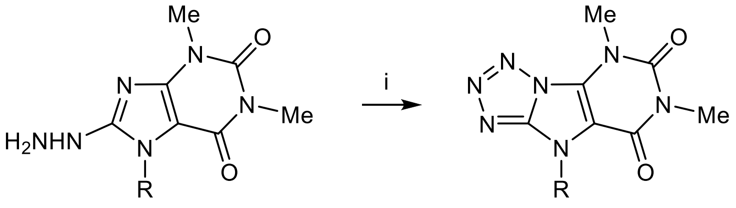
67	R	ref.
a	[CH$_2$]$_2$OH	46b
b	CONHCH$_2$CO$_2$Et	4b
c	COMe	34
67c : **C**4*sf***a**	10 : 1 [d]	34
(ratio)	3 : 2 [e]	34

[a] Unreported. [b] Decomp. [c] IR unreported. [d] Solvent CDCl$_3$. [e] Solvent (CD$_3$)$_2$SO.

Scheme 23

finding was confirmed later[34] and is consistent with DFT computations that showed the tetrazole form **C***4f* to be distinctly higher in energy [*cf.* Section (II/4. a), Table 2].[6a,7a]. On the other hand, and in direct parallel to the behaviour of the couple of anionized **40** and **C***an* (Scheme 15), the equilibrium between the species **66***an* and **C***anf* is completely on the tetrazole side,[34] as confirmed theoretically [*cf.* Section (II/4. a), Table 2].[6a,7a] Acylation of **66** gave azides such as **67a-c**, the latter of which was shown to equilibrate with the tetrazole form **C***4sf***a**, with the extent of ring closure depending on the polarity of the solvent. Remarkably, the transformation (**67c** → **C***4sf***a**) proceeded also in the solid state, but **C***4sf***a** reverted to the azide **67c** on melting.[34]

Contrasting with the process (**65a** → **66**), 2-chlorobenzimidazole (**65b**) was said to give **C***4f* on treatment with sodium azide under forcing conditions.[47] Alternatively, compound **C***4f* arose through intramolecular [2 + 3] cycloaddition of *in situ* formed (2-azidophenyl)cyanamide (**69**),[48a] a process that has also been studied by DFT calculations.[49] Some time later, this synthesis has been duplicated in conjunction with the discovery of a novel procedure for azidoanilines (including **68**) that works under mild conditions by using copper catalysts.[48b]



70a-g **C***4sf***b-h**

i: $NaNO_2$, dil. H_2SO_4 (with **70a**) or HCl (with **70b-g**)

70	C4sf	R	yield (%)	mp (°C)	ref.	70	C4sf	R	yield (%)	mp (°C)	ref.
a	**b**	Me	95	250	50a	**e**	**f**	CH_2Ph	68	148−149	50b
b	**c**	n-C_6H_{13}	71	70−72	50b	**f**	**g**	$CH_2C_6H_4F(4)$ [a]	65	134−136	50b
c	**d**	n-C_9H_{19}	72	44−46	50b	**g**	**h**	$CH_2C_6H_4Cl(4)$ [b]	68	130−132	50b
d	**e**	n-$C_{12}H_{25}$	72	46−48	50b						

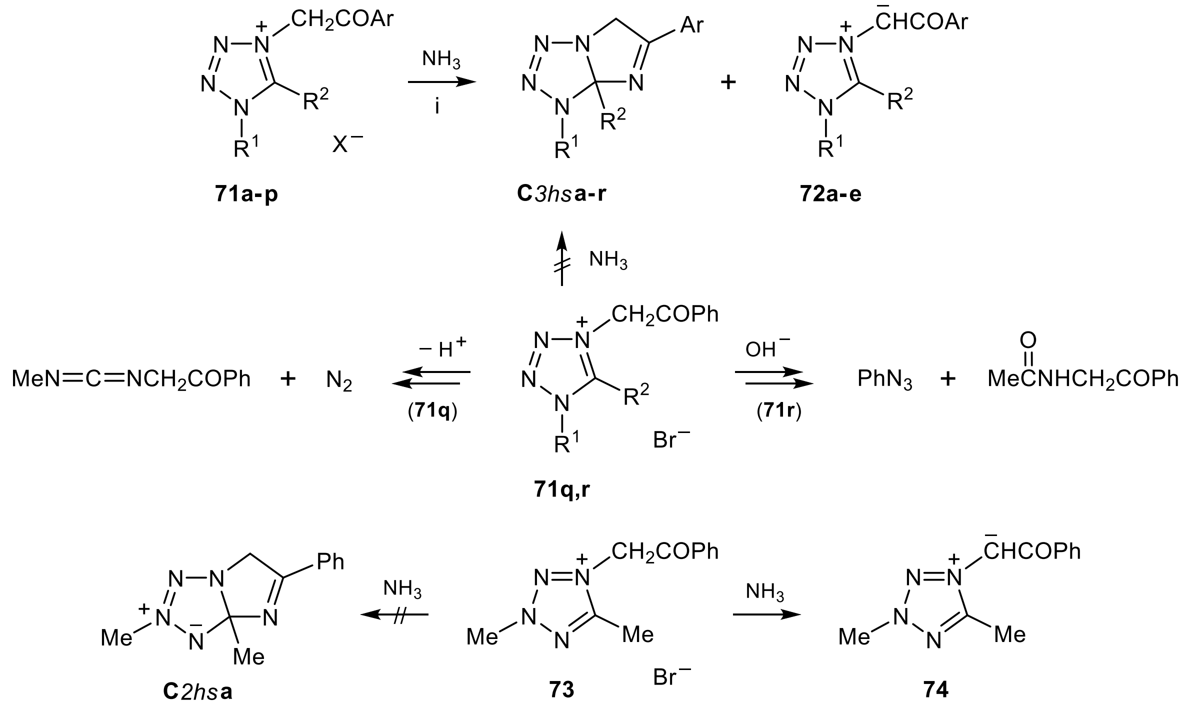
[a] Including derivatives having R = $CH_2C_6H_4F(2)$ and $CH_2C_6H_4F(3)$; similar yields. [b] Including derivatives having R = $CH_2C_6H_4Cl(2)$ and $CH_2C_6H_4Cl(3)$; yields similar.

Scheme 24

Out of representatives **C***4* that are fused to heterocycles, a range of purine derivatives have been mentioned (Scheme 24). An early claim of the caffeine example **C***4sf***b** which was said to arise on nitrosation of the hydrazine **70a** waits for confirmation of its tetrazolic structure.[50a] However, based on spectroscopic data, the tetrazole state residing in the theophylline derivatives **C***4sf***c-h** appears rather probable.[50b] The materials were prepared in like manner; they were studied for anticonvulsant properties, the most active species being compound **C***4sf***d**.[50b]

c) Derivatives C*3h* [VII, VIII], *3h'* [XIII], *4h* [I, VI, X, XIII], *4hf* [V, VI]

A unique formation of partially saturated derivatives **C** consists in the reaction of phenacyltetrazolium salts **71** with concentrated ammonia: Acting as a nucleophile, the reagent gave rise to bicycles such as **C*3hs*a-p** (Scheme 25).[51a,b] The scope of the reaction, which is an implementation of Scheme 1 / pattern VII, strongly depends on the substituents. Thus, substrates **71** having small R^1 rests gave high yields of these bicycles, irrespective of the size of the R^2 ligand (→ **C*3hs*a-h**); but with R^1 becoming bulkier, the amounts gradually decreased (→ **C*3hs*j-m**), while ylides began to arise (→ **72a-d**). This is explained with the folded geometry of **C***3hs* [*cf.* Section (IV. a)], showing that sterically demanding ligands are hindered when attached to N(3)



i: 13−14 M NH_3, −10 °C, 16−24 h (with **71a,b,e,h,k-m,o,p**) or 0 °C, 5−6 d (with **71c,d,f,g,i,n**)

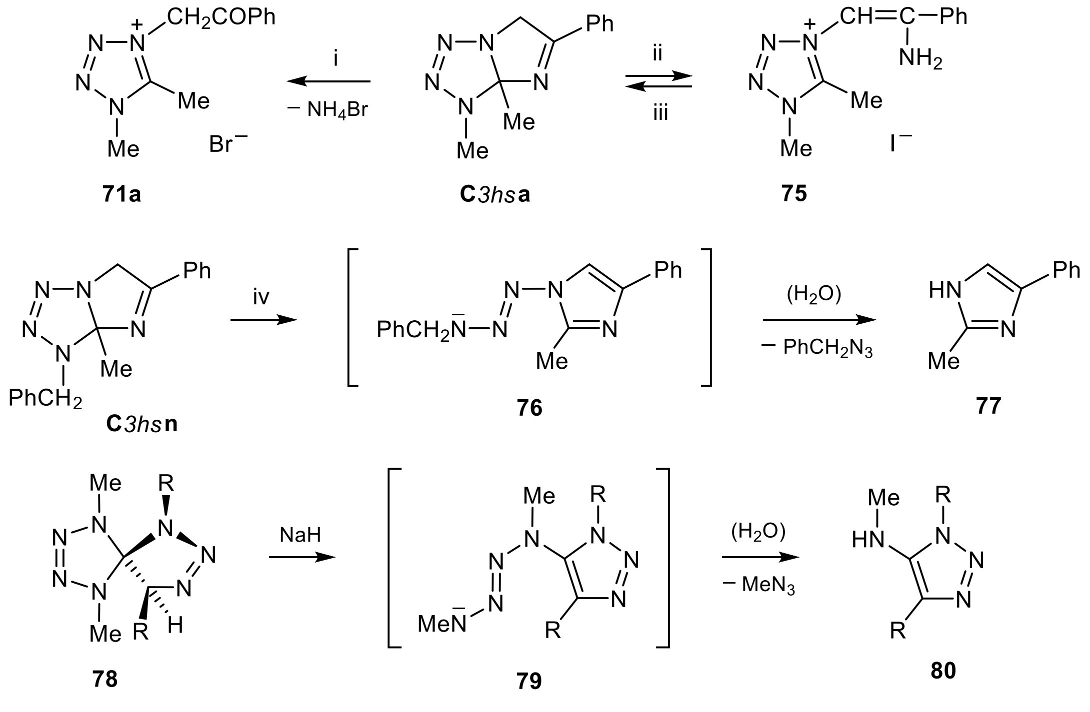
71,					C*3hs*		**71,**					C*3hs*		
C*3hs*	R^1	R^2	Ar	X	yield (%)	mp (°C)	C*3hs*	R^1	R^2	Ar	X	yield (%)	mp (°C)	**72**
a [a]	Me	Me	Ph	Br	95	68	**j**	Pr	Me	Ph	Br	32 [e]	51	**a**
b	Me	Et	Ph	Br	93	94−95	**k**	*i*-Pr	Me	Ph	Br	13 [f]	78	**b**
c	Me	Pr	Ph	ClO_4	90	71	**l**	*i*-Bu	Me	Ph	Br	10 [g]	83−84	**c**
d	Me	*i*-Pr	Ph	$SbCl_6$	96	76	**m**	CH_2Bu-*t*	Me	Ph	Br	2 [h]	128	**d**
e	Me	*c*-C_6H_{11}	Ph	I	91	140	**n**	CH_2Ph	Me	Ph	PF_6	73	99	
f	Me	CH_2Ph	Ph	$SbCl_6$	98	91−92	**o**	Me	Me	[c]	Br	67	53−57	
g	Me	[b]	Ph	$SbCl_6$	89	139−140	**p**	Me	Me	[d]	Br	4 [i]	139−140	**e**
h	Me	Ph	Ph	Br	97	133	**q**	Me	H			0		
i	Et	Me	Ph	ClO_4	72	55−56	**r**	Ph	Me			0		

[a] **C***3hs***a** with X-ray crystal structure.[51a] [b] $R^2 = CH_2C_6H_4NO_2(4)$. [c] Ar = 4-MeC_6H_4. [d] Ar = 4-BrC_6H_4. [e] Besides 60% **72a**. [f] Besides 79% **72b**. [g] Besides 80% **72c**. [h] Besides 90% **72d**. [i] Besides 83% **72e**.

Scheme 25

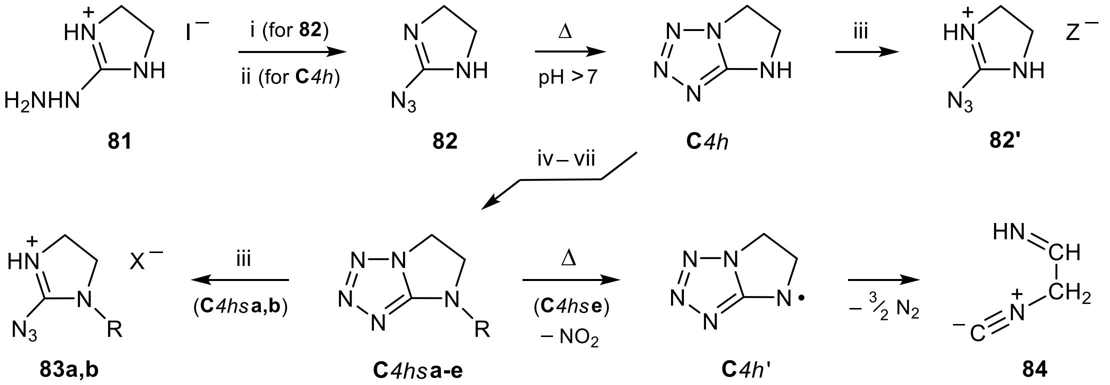
but not to the bridgehead C(3a). To rationalize the low yield of **C**_3hs_**p**: ylides with substituted phenacyl groups like **72e** are sparingly soluble in water and precipitated from the reaction mixture once the reagent had been added, thereby reducing the stock of **71p** for the (much slower) formation of the sought bicycle. Expectedly, no derivatives **C**_3hs_ (or, alternatively, ylides **72**[52a]) were obtained from the salts **71q,r**: the substrate **71q** was deprotonated at C(5) to generate a carbenoid tetrazole that fragmented into dinitrogen and *N*-methyl-*N'*-phenacylcarbodiimide, whereas with compound **71r** hydroxide ion added to C(5) to form an intermediary 4,5-dihydro-1*H*-tetrazole derivative that underwent [3 + 2] cycloreversion into phenyl azide and *N*-phenacylacetamide.[52b] Likewise, no cyclization of 2*H*-tetrazolium salts such as **73** took place with ammonia; instead of the mesoionic derivative **C**_2hs_**a**, only the ylide **74** was obtained.[53]

The behaviour of compounds **C**_3hs_ is dominated by the proclivity to release a five-membered aromatic ring, depending on the reagent (Scheme 26): Thus, aqueous hydrogen bromide converted the derivative **C**_3hs_**a** to the starting salt **71a** along with ammonium bromide, whereas the weaker acid ammonium iodide led to the enamine **75** which, on addition of base, reverted to the bicycle. Treatment of **C**_3hs_**n** with butyllithium caused deprotonation of C(6) to be followed by N(3)–C(3a) bond breaking to generate the triazenide ion **76** which disintegrated into benzyl azide and the imidazole **77**.[51a,b] Formally, this process resembles the base-induced cleavage of the dihydrotetrazole ring in spiro compounds such as **78** to form tetrazenide ions **79** that fragmented into methyl azide and 5-(methylamino)-*v*-triazoles **80**.[54a,b]



i: aq. HBr, rt ii: aq. NH_4I, Et_2O, rt, 30 min iii: K_2CO_3, H_2O, 60 °C, 10 – 15 min
iv: BuLi, THF, – 70 to – 80 °C, 1 h; then 0 °C, 12 – 16 h

Scheme 26



i: H_2O/conc. HNO_3 (10/1), 50 °C, $AgNO_3$, then $NaNO_2$/conc. HCl, – 10 °C to 0 °C, 30 min, neutralization to pH 6.5
ii: procedure (i) without isolating **82**, then Na_2CO_3 until pH 8, reflux, 1 h (ref. 23) or Na_2CO_3 until pH 9, rt,1 h, then 60 °C, 10 min (ref. 56)
iii: picric acid or TFA iv: $(MeO)_2SO_2$ or $PhCH_2Cl$, aq. NaOH (40 – 50%), CH_2Cl_2, $PhCH_2NEt_3$]Cl, reflux, 27 h (for **C**4*hs***a**) or 40 h (for **C**4*hs***b**)
v: Ac_2O (neat), 100 °C, 2 h (for **C**4*hs***c**) vi: $NaNO_2$, 2 M HCl, 0 to 10 °C, 30 min, then K_2CO_3 until pH 8 (for **C**4*hs***d**)
vii: HNO_3/Ac_2O, 0 °C to rt, 30 min (for **C**4*hs***e**)

	R	yield (%)	mp (°C)	ref.	**C**4*hs*	R	yield (%)	mp (°C)	ref.
82		30	128	23	**a**	Me	19	90 – 92	23
82' [a]			177 – 178	23	**b**	CH_2Ph	89	89 – 91	23
C4*h* [b]		74 / 74.5 / 75	159 – 163 / 163 – 164 [c] / [d]	23 / 55 / 56a	**c**	COMe	80	127 – 130	23
83a [a]	Me		161 – 163	23	**d** [b]	NO	94	110 – 110.5	56a
83b [a]	CH_2Ph		134 – 136	23	**e** [b]	NO_2	68 / 75	150 / 160 [c]	56a / 57

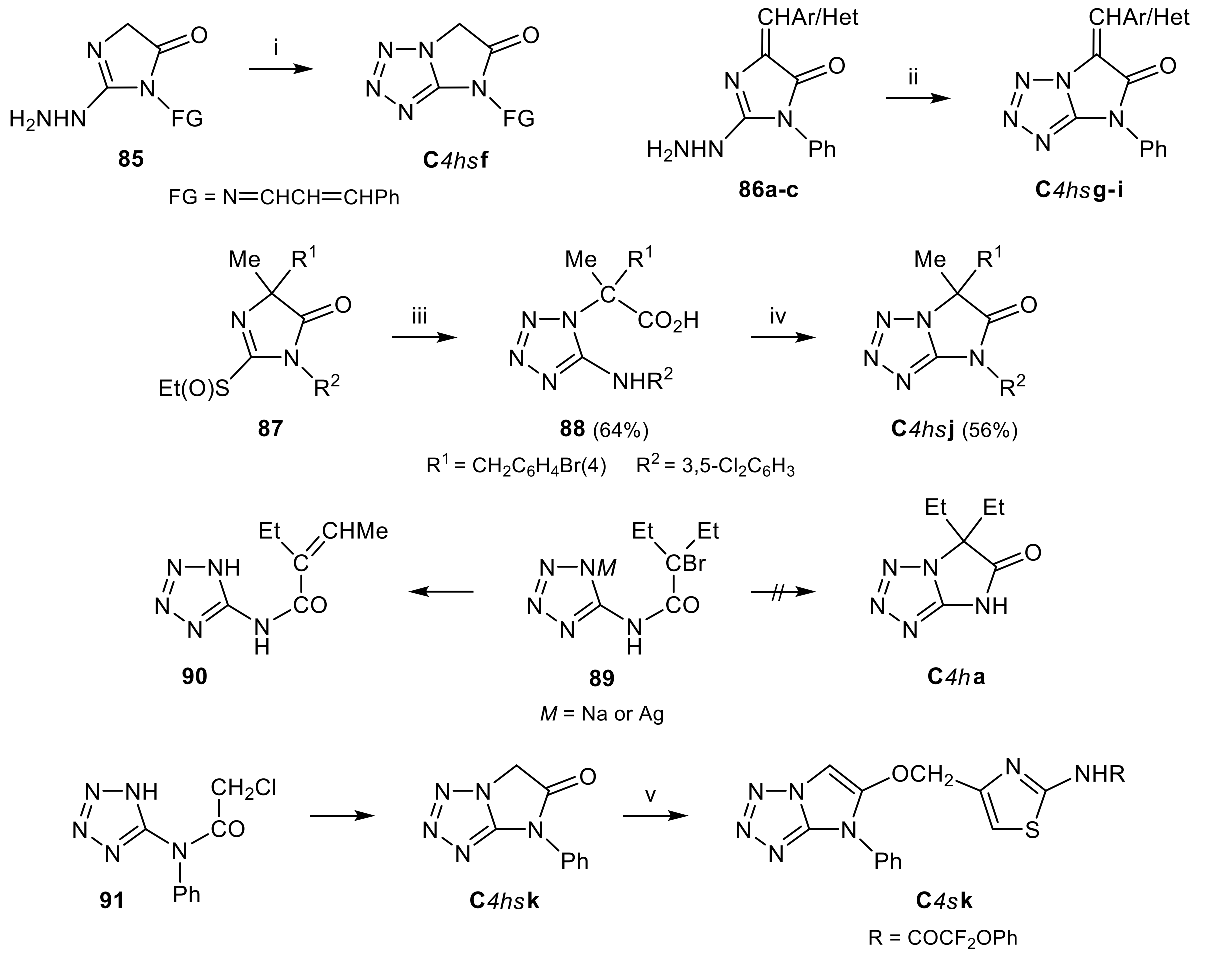
[a] Z = picrate. [b] With X-ray crystal structure.[56a] [c] Decomp. [d] Mp 160 °C (decomp.; from Supporting Information), value differs from main text showing mp 175 – 175.5 °C.

Scheme 27

In contrast to the fully conjugated bicycle **C**4 (Scheme 15) its partly hydrogenated congener **C**4*h* exists as such (solid state), while DFT calculations (gas phase) show azido and tetrazole form to be close in energy [*cf.* Section (II / 4. a), Table 2].[6a] Compound **C**4*h* was directly available from 2-hydrazino-4,5-dihydro-imidazolium iodide (**81**) or through heating of the separately prepared azide **82** in a weakly basic medium (Scheme 27).[23,55,56a] Alkylation and acylation of **C**4*h* affected N(4) (*cf.* Scheme 15) to give derivatives like **C**4*hs***a-c**. On treatment with strong acids such as TFA and picric acid the products **C**4*hs***a,b** (including the substrate **C**4*h*) ring-opened to furnish, for example, the salts **82'** and **83a,b**.[23]

During the search for high energy materials, **C**4*h* was submitted to nitrosation and nitration to afford the derivatives **C**4*hs***d**[56a] and **C**4*hs***e**.[56a, 57] The latter arose also from treatment of **C**4*hs***d** with trifluoroperoxy-acetic acid or from **82'** (Z = NO_3) and sulfuric acid.[56a,b] Apart from their thermochemistry, the molecular structures of these materials were studied by X-ray diffraction, DFT methods, and natural bond analysis (NBO).[56] Interestingly, when **C**4*hs***e** was heated at 120 °C/s under 2 psia Ar, the first products to be detected were nitrogen dioxide and the isocyanide **84**, the latter arose from the radical species **C**4*h'*.[58]

A number of oxo derivatives of the **C**4*hs* type, most of which were studied for biological activities, have been prepared (Scheme 28). Nitrous acid converted the hydrazine **85** to the antibacterial compound **C**4*hs***f**.[59]



i: $NaNO_2$, HCl, AcOH, 50 °C, 3 h ii: $NaNO_2$, 2 M HCl, 10 °C, 15 min; then rt, 2 h

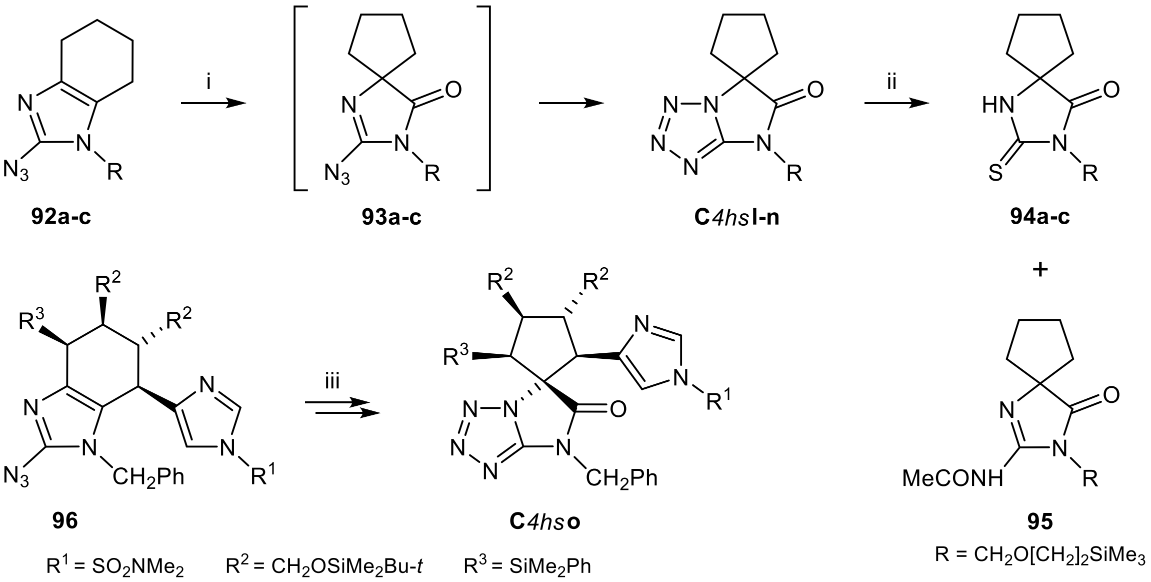
iii: NaN_3, DMF, rt, 20 h iv: $EtN{=}C{=}N[CH_2]_3NMe_2 \cdot HCl$, 1-hydroxybenzotriazole, DMF, rt, 2 h; then *i*-Pr_2NEt, rt, 10 h

v: 4-(bromomethyl)-2-[difluoro(phenoxy)acetamido]thiazole

86	Het	**C**4*hs*	yield (%)	mp (°C)	ref.	**86**	Ar	**C**4*hs*	yield (%)	mp (°C)	ref.
		f	61	117	59	**b**	4-ClC_6H_4	**h**	60	150−152	60
a	2-thienyl	**g**	65	235−237	60	**c**	4-$NO_2C_6H_4$	**i**	50	130−132	60

Scheme 28

Similarly, the substrates **86a-c** were transformed into the materials **C**4*hs***g-i**, two of which (**g,h**) showed antimicrobial properties.[60] The preparation of the anti-inflammatory agent **C**4*hs***j** succeeded only in two steps: (i) tetrazole formation through azidation of the sulfoxide **87** was accompanied by hydrolytic cleavage of the adjacent half-ring to give the α-(5-aminotetrazol-1-yl)carboxylic acid **88**; (ii) obeying an elaborate protocol, the latter compound was cyclized[61a,b] – *i.e.*, in a process following pattern VI of Scheme 1. An early attempt to utilize the related pattern X for providing a **C**4*h* derivative, such as **C**4*h***a**, failed since the substrate **89** split out hydrogen bromide from the side chain to give the crotonamide **90**.[62] However, exactly this principle was recently exemplified by the reaction (**91** → **C**4*hs***k**); sequential *O*-substitution gave the (fully conjugated) bicycle **C**4*s***k** that served as an agrochemical.[63]



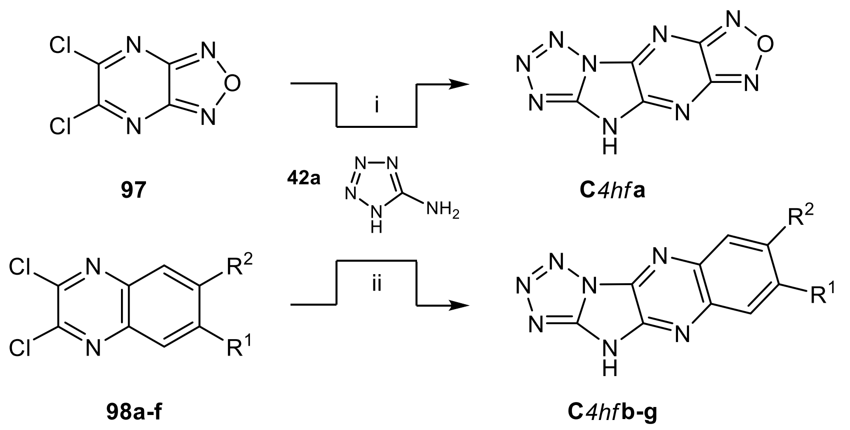
i: DMDO, Me_2CO, CH_2Cl_2 (no details) ii: MeCOSH, 2,6-lutidine, MeOH, rt, 4 h
iii: DMDO, Me_2CO, CH_2Cl_2, 0 °C, 10 min; then rt, 2 h

92–**94**	**C**4*hs*	R	**C**4*hs*: yield (%)	**94**: yield (%)	ref. [a]
a	**l** [b]	CH_2Ph	70 [c] / 80	95	64b,c / 64d
b	**m**	CH_2OMe	40 [d]	80	64d
c	**n**	$CH_2O[CH_2]_2SiMe_3$	41	70 [e]	64d
	o [f]		69		64e

[a] No mps. [b] With X-ray crystal structure.[64c,d] [c] Reagent instead of DMDO: 3-(4-nitrophenyl)-2-phenylsulfonyloxaziridine; in ref. 64b product erroneously viewed as **93a** (corrected to **C**4*hs***l** in ref. 64c). [d] In ref. 64a viewed as **93b** (uncorrected). [e] Besides 7% **95** (from small amounts of **93c**). [f] With X-ray crystal structure.

Scheme 29

The formation of another series of oxo derivatives of the **C**4*hs* type is preceded by a fused to spiro skeletal change of widespread application: the oxidative rearrangement of 4,5,6,7-tetrahydrobenzimidazoles (THB) to spiro imidazol-5-ones.[64a] So, THBs having an azide group at C(2), such as **92a-c**, were converted to the species **93a-c** which, because of the transformation of the fully conjugated imidazole core into a dihydro form, underwent tetrazole ring closure (→ **C**4*hs***l-n**) (Scheme 29).[64b–e] The first oxidation of **92a** was carried out with an *N*-sulfonyloxaziridine; however, the product was erroneously viewed as the azide **93a**[64b] and its structure corrected only recently (→ **C**4*hs***l**).[46c] Apart from this single experiment, dimethyldioxirane (DMDO) was used as oxidant throughout.[64d,e] The conversion of the more elaborate substrate **96** to the bicycle **C**4*hs***o** was performed during model studies on palau'amine (a dimer of the alkaloid oroidin).[64e] Investigating the behaviour of the starting materials **92a-c** and the products **C**4*hs***l-n** towards thio acids (mainly thio acetic acid), the former substrates gave, expectedly, *N*-imidazolyl(acet)amides, whereas the latter were converted to the thiohydantoins **94a-c** which may result from an addition elimination pathway. The formation of a small amount of **95** indicates the presence of some azide **93c** in the equilibrium.[64d]



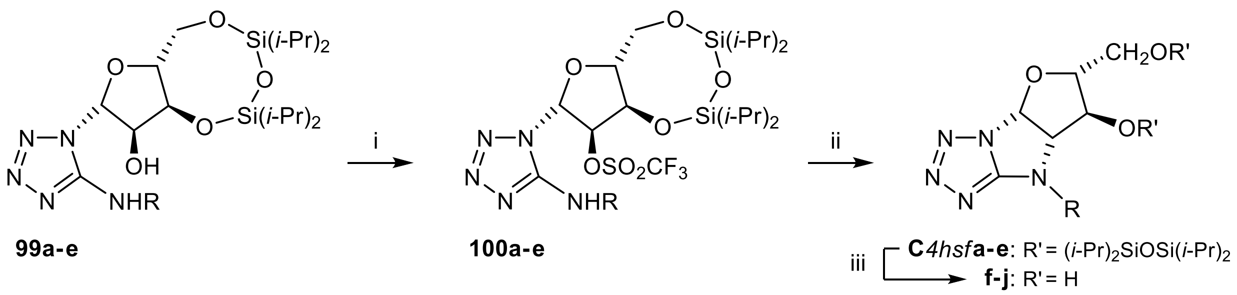
i: MeCN, rt, 1 h ii: DMF, Na_2CO_3 (trace), reflux, 12−15 h

98	C*4hf* [a]	R^1	R^2	yield (%)	mp (°C)	ref.	98	C*4hf* [a]	R^1	R^2	yield (%)	mp (°C)	ref.
	a			36	> 260	65	**d**	**e**	NO_2	H	71	245−246	66
a	**b**	H	H	78	223−224	66	**e**	**f**	Br	H	74	267−269	66
b	**c**	Me	H	65	215−216	66	**f**	**g**	Cl	H	70	223−224	66
c	**d**	Me	Me	69	202−203	66							

[a] With the products **C***4hf***c,e-g** the position of R^1 and R^2 was not proved.

Scheme 30

Pyrazino-fused derivatives **C***4hf* resulted from fusion with 5-aminotetrazole (**42a**) (Scheme 30). Thus, the dichlorofurazanopyrazine **97** gave rise to the tetracycle **C***4hf***a** under mild conditions,[65] whereas the harsher reaction with the quinoxalines **98a-f** led to the analogues **C***4hf***b-g** which showed antimicrobial activity.[66] Except for the derivatives **C***4hf***b,d**, the distribution of R^1 and R^2 seems open.



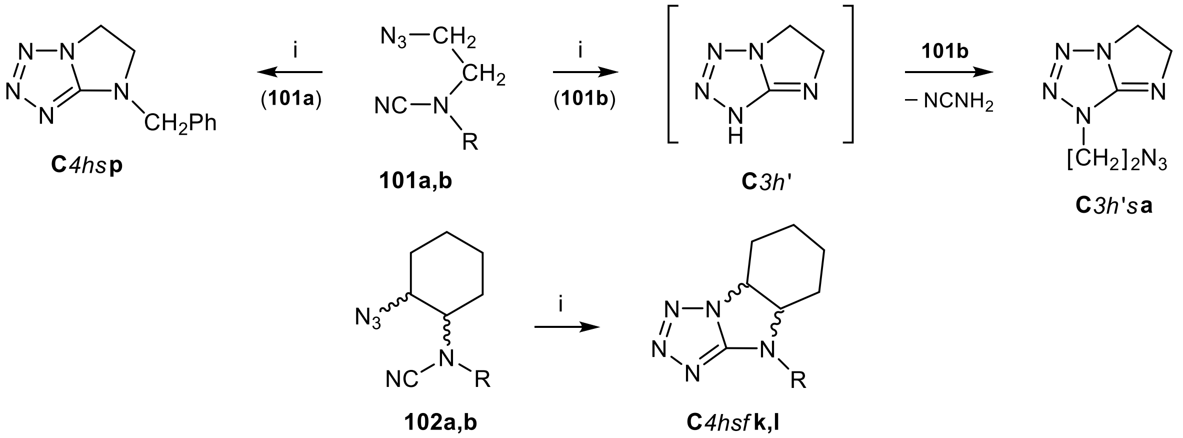
i: CF_3SO_2Cl, pyridine, Et_3N, 4-(dimethylamino)pyridine, 0 °C to rt, 30 min ii: $MeCO_2Na$, $PO(NMe_2)_3$, rt, 2 h
iii: $[Bu_4N]F$, THF, rt, 15 min

99, 100	R	C*4hsf*	yield (%)	mp (°C)	C*4hsf*	yield (%)	mp (°C)	ref.
a	Me	**a**	84	64−65	**f**	92	oil	67
b	*i*-Pr	**b**	79	99	**g**	85	98	67
c	*t*-Bu	**c**	91	90−91	**h**	98	125−127	67
d	$CH_2CH{=}CH_2$	**d**	81	oil	**i**	95	104	67
e	(*S*)-CH(Me)CO_2Et	**e**	97	oil	**j** [a]	87	oil	67

[a] Mixture of epimers.

Scheme 31

Derivatives of the **C**4*hsf* type such as *ara*-tetrazole nucleosides **C**4*hsf***f-j** were obtained after pattern VI of Scheme 1 (Scheme 31): Reaction of the silyl protected substrates **99a-e** with triflic chloride gave the triflates **100a-e** which were treated with sodium azide. Contrary to the authors' expectation, this agent did not enter the arabinose ring but caused intramolecular cyclization by the 5-NHR group [with inversion at C(2')] to afford the derivatives **C**4*hsf***a-e**; ensuing deblocking of the latter with a fluoride salt provided the target materials in excellent yields.[67]



i: DMF, 130–140 °C, 24–64 h

	R		yield (%)	mp (°C)	ref.
101a	CH_2Ph	**C**4*hs***p**	96	[a]	48a
101b	H	**C**3*h*'*s***a**	68	[b]	48a
cis-**102a**	CH_2Ph	*cis*-**C**4*hsf***k**	96	[a]	48a
trans-**102a**	CH_2Ph	*trans*-**C**4*hsf***k**	53	[b]	48a
trans-**102b**	Ts	*trans*-**C**4*hsf***l**	24 [c]	> 200 [d]	48a

[a] Light brown oil. [b] Clear oil. [c] 60% conversion. [d] Decomp.

Scheme 32

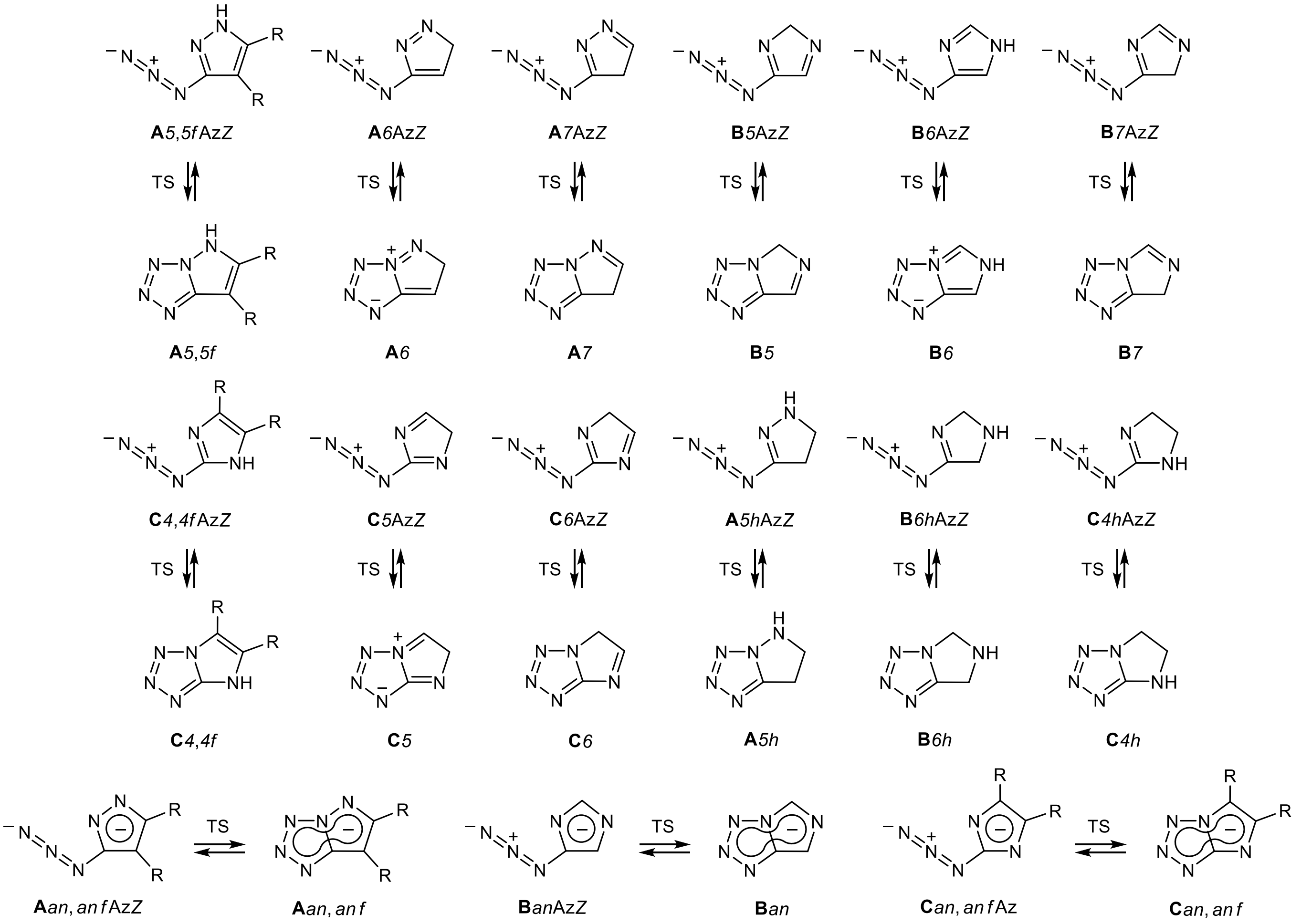
An intramolecular [2 + 3] cycloaddition as operative in Scheme 23 (**69** → **C**4*f*) gave derivatives of the **C**4*hs* and **C**4*hsf* types when the azidocyanamides **101a** and **102a,b** were heated in DMF (→ **C**4*hs***p**, **C**4*hsf***k,l**) (Scheme 32).[48a] Electronegative R ligands, as in *trans*-**C**4*hsf***l**, decrease the thermal stability so as to reduce the yield. On reacting the monosubstituted azidocyanamide **101b**, the regular product **C**3*h*' eluded isolation: it took up another molecule of the substrate to give, after extrusion of cyanamide, the bicycle **C**3*h*'*s***a**. The tetrazole forming cycloadditions of **101a** and **102a,b** have also been investigated by DFT calculations.[49]

4) THEORETICAL STUDIES

a) Azido–tetrazole tautomerism with diazolotetrazoles (A–C)

Four categories of model compounds have been studied: substrates that are (i) fully conjugated and neutral, (ii) nonconjugated, (iii) hydrogenated, and (iv) fully conjugated but anionic (Table 2).

Table 2. Azido–tetrazole tautomerism with Series **A**–**C**:
Relative energies (Δ*E*) / relative free energies (Δ*G*) of azidodiazoles (Az*Z*), diazolotetrazoles (Tet), and transition states (TS) [a]



A*5*, *an*; **C***4*, *an*: R = H **A***5f*, *anf*; **C***4f*, *anf*: RR = $[CH{=}CH]_2$

Series	**A***5* [b]	**A***6*	**A***7*	**B***5*	**B***6*	**B***7*	**C***4*	**C***5*	**C***6*
Ref.	6a / 7a [c,d]	6a	6a	6a	6a	6a	6a / 7a [d]	6a	6a
Az*Z*	48.9 / 48.9	153.1 / 146.8	125.3 / 120.0	47.9 / 46.3	2.5 / 2.5	42.3 / 40.5	**0.0 / 0.0**	51.4 / 48.8	50.5 / 48.1
TS	174.2 / 169.7	286.2 / 281.2	207.7 / 203.7	139.5 / 139.6	123.2 / 125.7	127.9 / 127.2	97.6 / 99.8	204.0 / 201.1	146.8 / 145.9
Tet	121.7 / 129.1	227.1 / 229.0	107.9 / 113.2	47.0 / 55.1	82.3 / 89.8	45.9 / 52.7	34.1 / 41.7	168.0 / 169.7	56.8 / 63.4

A*5f*	**C***4f*	**A***5h*	**B***6h*	**C***4h*	**A***an* [f]	**B***an*	**C***an*	**A***anf* [f]	**C***anf*
6a / 7a [d,e]	6a / 7a [d]	6a	6a	6a	6a / 7a [d,g]	6a	6a / 7a [d]	6a / 7a [d,h]	6a / 7a [d]
70.5 / 69.4	**0.0** / **0.0**	83.9 / 75.5	37.6 / 30.6	6.9 / **0.0**	84.9 / 72.2	13.5 / 4.5	12.7 / 3.5	106.7 / 97.5	6.5 / **0.0**
186.9 / 187.8	93.2 / 95.2	178.3 / 171.4	118.0 / 112.5	89.5 / 84.2	159.7 / 150.3	101.3 / 94.0	101.6 / 93.6	185.5 / 178.1	94.7 / 89.2
118.6 / 126.8	26.3 / 33.7	85.0 / 86.7	17.2 / 20.5	**0.0** / 2.3	40.3 / 40.8	13.2 / 12.9	**0.0** / **0.0**	59.5 / 62.1	**0.0** / 2.4

[a] Gas phase; theory: B3LYP/6-31G*; values in kJ mol^{-1}. [b] See also Section (III/5), Scheme 50, for series **A'***5*. [c] **A***5* values of ref. 7a (*i.e.*, **0.0**, 120.9, 80.2) here related to **C***4*Az*Z*. [d] See also for Δ*G* values determined at the G3B3 level. [e] **A***5f* values of ref. 7a (*i.e.*, **0.0**, 118.4, 57.4) here related to **C***4f*Az*Z*. [f] In ref. 7a: values of series **A***an* and **A***anf* to be exchanged. [g] **A***an* values of ref. 7a (*i.e.*, 31.4, 109.5, **0.0**) here related to **C***an*. [h] **A***anf* values of ref. 7a (*i.e.*, 35.4, 116.0, **0.0**) here related to **C***anf*Az.

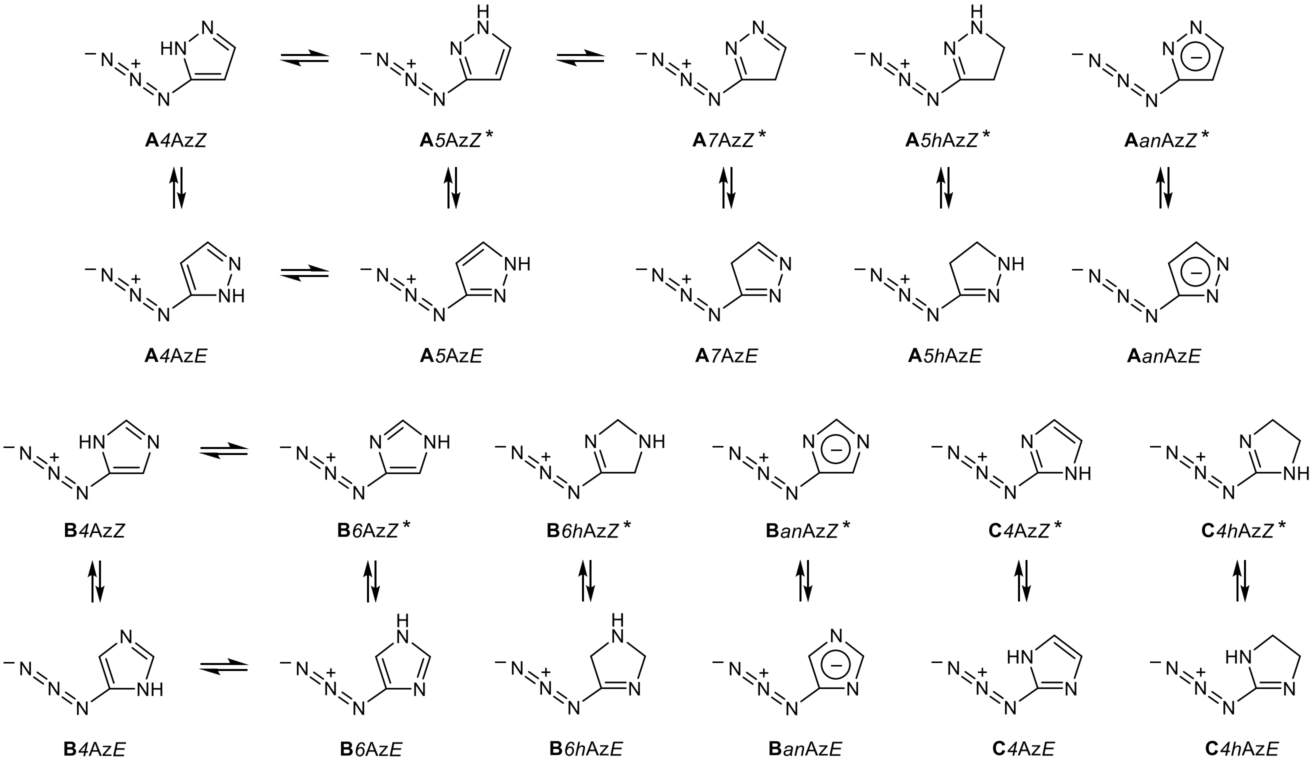
(i) Series **A***5*, **B***6*, **C***4* and **A***5f*, **C***4f*: Here the azide (Az*Z*) is energetically favoured over the bicycle (Tet), with the difference increasing in the order: **C***4* < **A***5* < **B***6* and **C***4f* < **A***5f*, respectively.

(ii) Series **A**6, **A**7, **B**5, **B**7, **C**5, **C**6: Except for **A**6 and **C**5, the difference between (Tet) and (Az*Z*) is small; it inceases as follows: **B**5 < **B**7 < **C**6 < **A**6 < **C**5; only with **A**7 the bicyle (Tet) is favoured over (Az*Z*).
(iii) Series **A**5*h*, **B**5*h*, **C**4*h*: As with **B**5, **B**7, and **C**6 (preceding paragraph), the species (Tet) and (Az*Z*) are energetically similar with **A**5*h* and **C**4*h*; but with **B**5*h* the bicycle (Tet) is clearly favoured over (Az*Z*).
(iv) Series **A***an*, **B***an*, **C***an*, **A***anf*, **C***anf*: With **A***an* and **C***an*, and also with **A***anf*, the bicycle (Tet) is favoured over (Az*Z*), *i.e.*, distinctly with **A***an* and **A***anf* but to a less extent with **C***an* and (partly) with **C***anf*, whereas with **B***an* the bicycle (Tet) appears energetically either similar or slightly disfavoured with respect to (Az*Z*).

b) Annular tautomerism and *E*/*Z* isomerism of azidodiazoles (AAz−CAz)

Complementing the foregoing study, various azide structures have been calculated to show that, out of all annular tautomers and *E*/*Z* isomers, those directly equilibrating with (Tet) are lower in energy (Table 3). For an overview of conformational preferences with **A**Az−**C**Az, see also Section (III/5), Scheme 51.

Table 3. Annular tautomerism (horizonzal) and *E*/*Z* isomerism (vertical) of azidodiazoles (**A**Az–**C**Az): Relative energies (Δ*E*) / relative free energies (Δ*G*) [a,b]



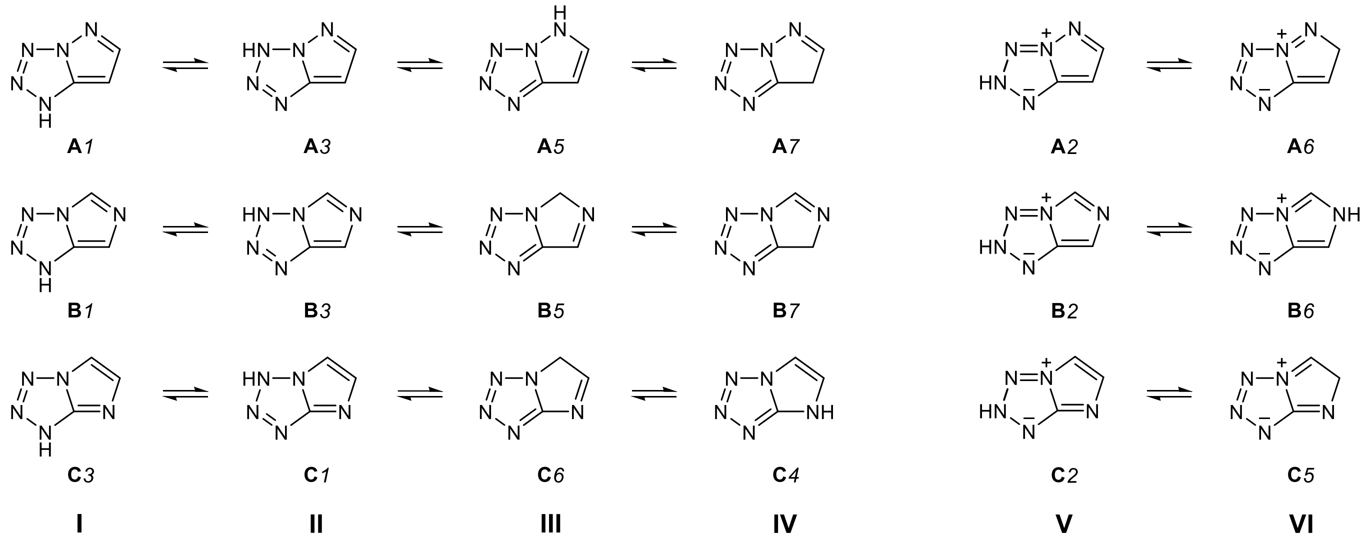
Ref.	6a / 7a [c,d]		6a		6a / 7a [d]		6a		6a
A4Az*Z*	17.6 / 16.3			**C**4Az*Z**	**0.0 / 0.0**	**A**5*h*Az*Z**	**0.0 / 0.0**	**B**6*h*Az*Z**	**0.0 / 0.0**
A4Az*E*	8.0 / 7.7	**B**4Az*Z*	23.2 / 21.5	**C**4Az*E*	20.0 / 18.5	**A**5*h*Az*E*	7.6 / 7.3	**B**6*h*Az*E*	12.3 / 11.6
A5Az*Z**	**0.0 / 0.0**	**B**4Az*E*	13.7 / 13.1						
A5Az*E*	6.7 / 6.6	**B**6Az*Z**	**0.0 / 0.0**						
A7Az*Z**	76.4 / 71.1	**B**6Az*E*	11.5 / 10.9	**A***an*Az*Z**	**0.0 / 0.0**	**B***an*Az*Z**	**0.0 / 0.0**	**C**4*h*Az*Z**	**0.0 / 0.0**
A7Az*E*	90.7 / 84.8			**A***an*Az*E*	6.5 / 6.1	**B***an*Az*E*	7.9 / 7.3	**C**4*h*Az*E*	16.9 / 15.6

[a] Gas phase; theory: B3LYP/6-31G*; values in kJ mol^{-1}. [b] Species starred (*) equilibrates with (Tet) of Table 2. [c] Δ*G* values of **A**7Az*Z* and **A**7Az*E*: Ref. 6a. [d] See also for Δ*G* values determined at the G3B3 level.

c) Annular tautomerism of diazolotetrazoles (A–C)

A global look at all conceivable tautomers of the series **A**–**C** shows that the model **C***4* is lowest in energy, followed by **C***3* (Table 4). Viewing **A**–**C** separately, the **B** family displays the nonconjugated models **B***5* and **B***7* as the most favoured, whereas with the **A** series this applies to the fully conjugated tautomer **A***1*. Expectedly, all fully conjugated models having two adjacent pyrrole-type nitrogens are much disfavoured (**A***3*, **A***5*, **B***3*, **C***1*). As to the effect of the electronegative pyridine-like nitrogen in the α half-ring of **A** and **C**, there is some parallel to the influence of acceptor substituents on the tautomerism of pyrrolotetrazoles.[3]

Table 4. Annular tautomerism of diazolotetrazoles (**A**–**C**):
Relative energies (Δ*E*) / relative free energies (Δ*G*) [a,b]



Series ↓ Type →	I	II	III	IV	V	VI
A*1, 3, 5, 7, 2, 6*	56.8 / 57.6	108.5 / 107.9	88.5 / 87.8	80.7 / 77.9	78.7 / 82.0	199.7 / 193.4
B*1, 3, 5, 7, 2, 6*	29.6 / 29.5	76.9 / 76.1	20.9 / 20.6	19.2 / 17.7	57.2 / 59.7	48.1 / 48.0
C*3, 1, 6, 4, 2, 5*	7.3 / 8.4	67.1 / 66.3	30.1 / 28.5	**0.0** / **0.0**	33.0 / 36.0	140.6 / 134.1

[a] Gas phase; theory: B3LYP/6-31G**; values in kJ mol^{-1}. [b] Ref. 6a.

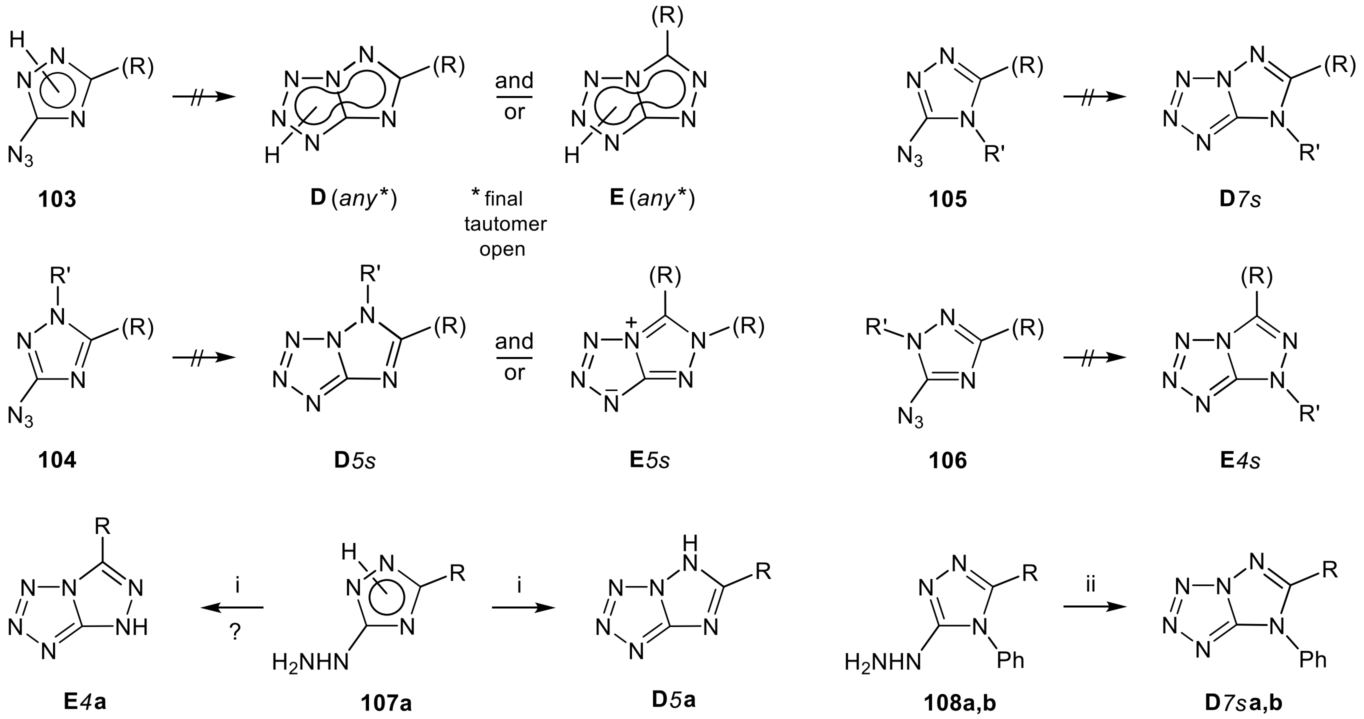
III) HIGH NITROGEN AZOLOTETRAZOLES (D–G)

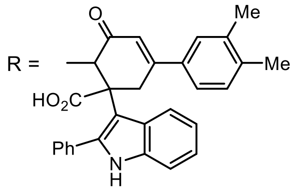
1) [1,2,4]TRIAZOLO[1,5-*d*]TETRAZOLES (D)

a) Derivatives D*1, 2, 3* [II], *5* [I], *5h* [IV], *7* [IV], *an* [I]

Azido-1,2,4-triazoles of the types **103**–**106** (made from the respective amino- and/or hydrazinotriazoles) are known to exist as such and to lack any tendency to cyclize to the systems **D** and/or **E** (Scheme 33). The absence of **D** and **E** is consistent with DFT calculations that were performed for R = R' = H, showing the bicycles to be higher in energy than the corresponding azides [*cf.* Section (III / 5. a), Table 6].

Two recent reports contrast with the above experience: (i) Nitrosation of the hydrazino group in **107a** was said to produce the bicycle **D***5***a** (a material showing antitumor activity); the formal possibility that, instead





108	D	R	yield (%)	mp (°C)	ref.
	*5*a	[a]	[b]	[b]	68
a	*7s*a	Ph	80	145	69
b	*7s*b	4-ClC$_6$H$_4$	74	129	69

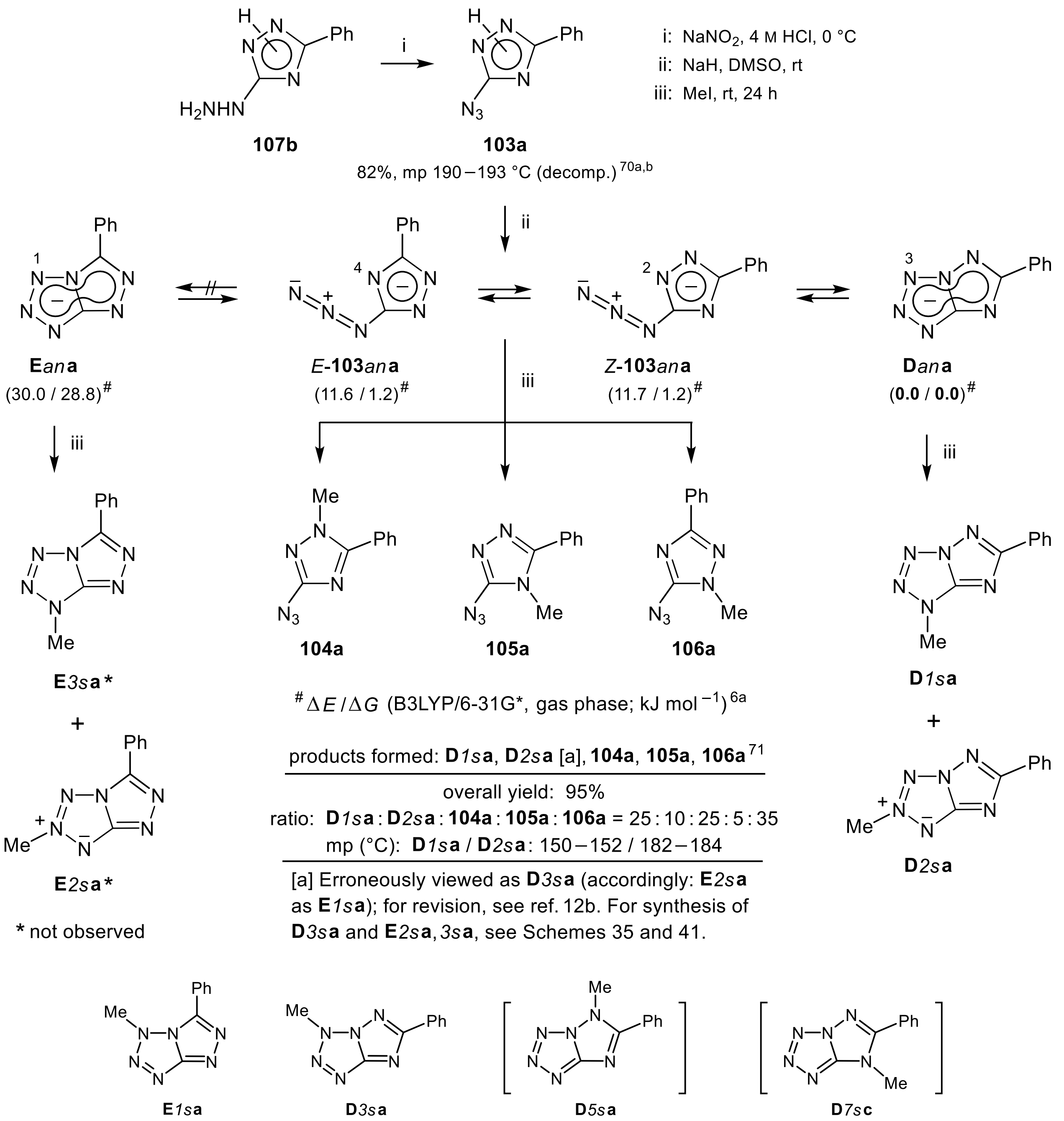
[a] See left. [b] No clear-cut protocol.

i: NaNO$_2$, AcOH, EtOH, rt, 4 h
ii: NaNO$_2$, conc. HCl, 0 °C, 40 min

Scheme 33

of **D***5***a**, the isomer **E***4***a** might have arisen has not been considered.[68] Beyond this point, the claimed product **D***5***a** should adopt the tautomeric form **D***1***a** to avoid adjacent pyrrole-like nitrogens [*cf.* the relationship of **A***5* and **A***1* in Section (II/1. a); see also Tables 4 and 9 in Sections (II/4) and (III/5)]. (ii) The same method of nitrosation applied to the hydrazino-4*H*-triazoles **108a,b** gave rise to the bicycles **D***7s***a,b**.[69]

In line with the behaviour of 3-azidopyrazoles (**2**; Scheme 3) and 2-azidoimidazole (**40**; Scheme 15), the azidotriazole **103a** (made from **107b**) cyclized in a strongly basic medium to give an *s*-triazolotetrazolide ion (Scheme 34).[71] Of the possible structures **D***an***a** and **E***an***a**, the anion **E** could be excluded as treatment with methyl iodide gave two bicycles that differed from earlier prepared samples of **E***1s***a** and **E***2s***a** [see Section (III/2. a)] and, hence, represent the derivatives **D***1s***a** and **D***2s***a** (the latter was erroneously viewed as **D***3s***a**). This shows that only the rotamer *Z*-**103***an***a** had cyclized as a consequence that ring position N(2) is more nucleophilic than N(4) because of the adjacent nitrogen (so-called α-effect). Complementary DFT calculations showed the bicycle **E***an***a** to be higher in energy than the open-chain isomer *E*-**103***an***a** (in contrast to **D***an***a** *vs.* *Z*-**103***an***a**) [*cf.* also Section (III/5. a), Table 6 (H for Ph)].[6a] – Besides the products **D***1s***a** and **D***2s***a** methylated triazoles such as **104a**–**106a** were isolated. Indeed, cyclization of *Z*-**103***an***a** was



$^{\#}\Delta E/\Delta G$ (B3LYP/6-31G*, gas phase; kJ mol^{-1})[6a]

products formed: **D***1s***a**, **D***2s***a** [a], **104a**, **105a**, **106a**[71]

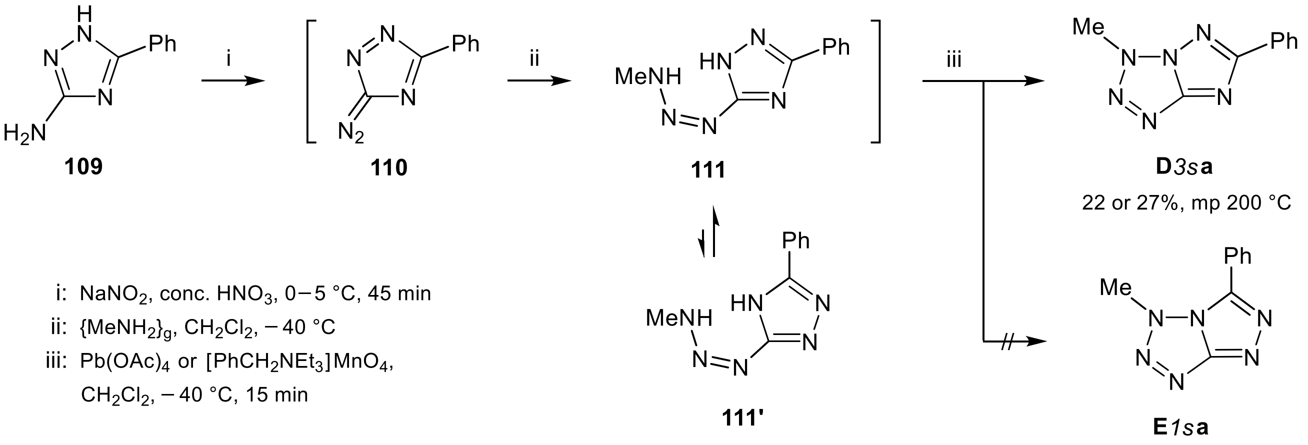
overall yield: 95%
ratio: **D***1s***a** : **D***2s***a** : **104a** : **105a** : **106a** = 25 : 10 : 25 : 5 : 35
mp (°C): **D***1s***a** / **D***2s***a**: 150−152 / 182−184

[a] Erroneously viewed as **D***3s***a** (accordingly: **E***2s***a** as **E***1s***a**); for revision, see ref. 12b. For synthesis of **D***3s***a** and **E***2s***a**, *3s***a**, see Schemes 35 and 41.

Scheme 34

found only partial: the azido–tetrazole equilibrium determined in $(CD_3)_2SO$ gave $K_{[Z\text{-}\mathbf{103}ana]/[\mathbf{D}ana]}$ = 0.78 (23 °C) and 1.60 (80 °C), and for the parents (H for Ph) *K* = 0.45 (27 °C).[71] Yet, the triazoles **104a** and **105a** might have formed also *via* **D***5s***a** and **D***7s***c** [*cf.* Scheme 3: → **3a-e**; Scheme 15: → **41i**].

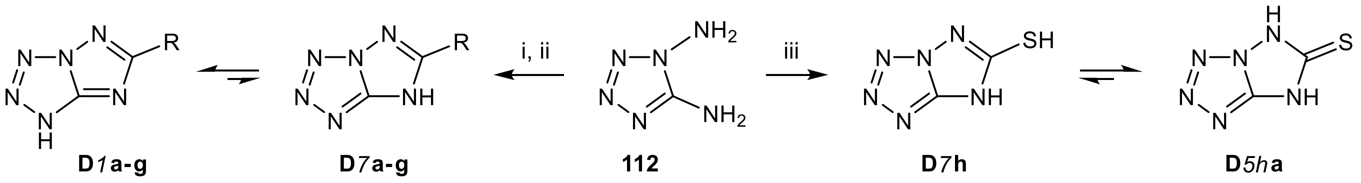
Finally, the putative bicycle **D***3s***a** obtained from methylation of **D***an***a**[71] was provided by the synthetic principle applied to the pyrazole analogues **A***3s* [see Section (II / 1. a)], *i.e.*, by oxidative ring closure of the triazolyltriazene **111**; this intermediate was generated *in situ* from the precursors **109** and **110**.[12b] The isomer



Scheme 35

E*1s***a** was not observed;[12b] this reflects the rules of annular tautomerism of *N*-unsubstituted 1,2,4-triazoles: all 4*H* forms (here **111'**) are found energetically disfavoured (Scheme 35).[72a,b]

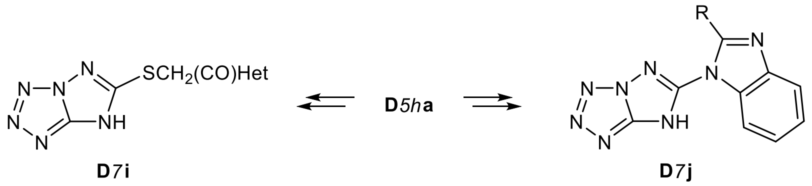
A range of derivatives **D***7* (possibly **D***1*), such as **a-g**, allegedly arose on heating 1,5-diaminotetrazole (**112**) with carboxylic acids (Scheme 36).[73] The reaction should be revisited since in an attempt to duplicate, for instance, the process (**112** → **D***7***b**) the starting material was recovered.[74] Treatment with carbon disulfide led to the thioxo compound **D***5h***a** which served as a building block for a plethora of derivatives having elaborate structures like **D***7***i** and **D***7***j** that exhibit biological activities.[75a–e]



i: RCO_2H (neat), reflux (1 h for **D***7***a**, 30 min for **D***7***b**) ii: RCO_2H, EtOH, reflux, 1 h (for **D***7***c-g**) iii: CS_2, pyridine, reflux, 3 h

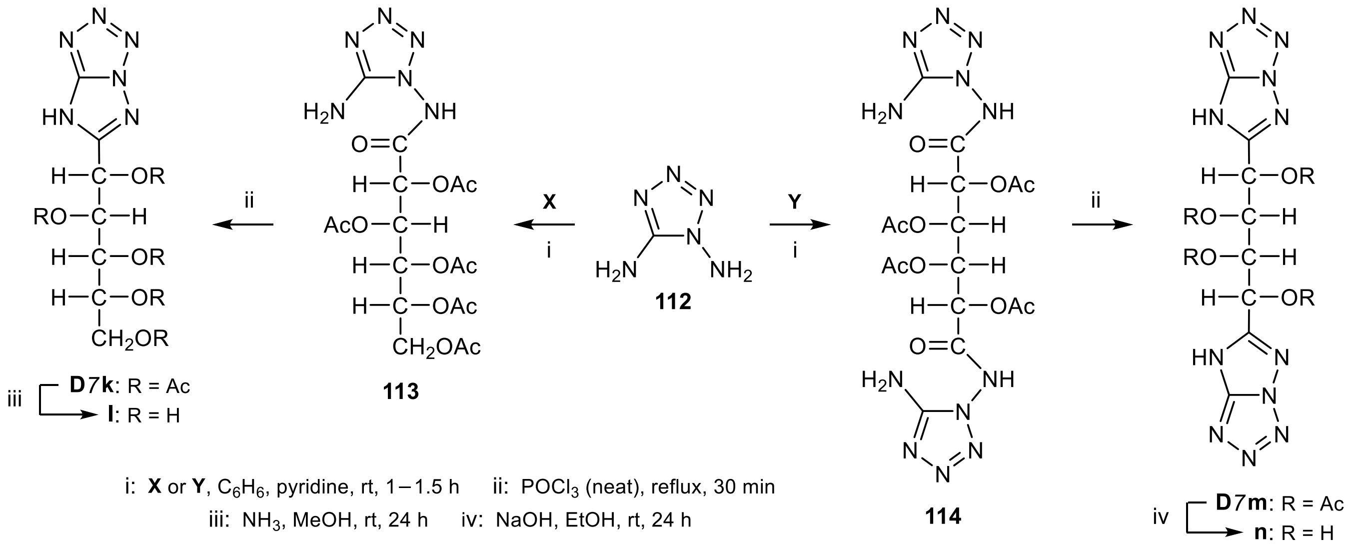
D*1*/*7*	R	yield (%)	mp (°C)	ref.	**D***1*/*7*	R	yield (%)	mp (°C)	ref.
a [a]	H	73	195	73	**e**	4-BrC_6H_4	72	210	73
b	Me	57	185	73	**f**	4-$MeOC_6H_4$	64	225	73
c	Ph	48	230	73	**g**	4-$NO_2C_6H_4$	65	240	73
d	4-ClC_6H_4	73	190	73	**h** [b]		57	240	73

[a] **D***7***a** higher in energy than **D***1***a** by 11.7 / 10.3 kJ mol^{-1} [see Section (III/5, Table 9)]. [b] In ref. 73 shown as such; energetically higher than **D***5h***a** by 9.9 / 0.1 kJ mol^{-1} ($\Delta E / \Delta G$; B3LYP/6-31G**, gas phase).[6a]

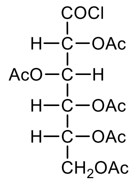


Scheme 36

The foregoing principle of ring closure of diaminotetrazole (**112**) using RCO_2H reagents was extended to acid chlorides (RCOCl) for making acyclic *C*-nucleosides of the type **D***7* such as **D***7***k-n** (Scheme 37).[76] The two-step procedure started with the formation of the amides **113** and **114** (yields 78 and 65%, respectively), which smoothly cyclized to **D***7***k** and **D***7***m** on treatment with phosphoryl chloride.

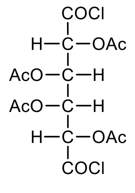


i: **X** or **Y**, C_6H_6, pyridine, rt, 1 – 1.5 h ii: $POCl_3$ (neat), reflux, 30 min
iii: NH_3, MeOH, rt, 24 h iv: NaOH, EtOH, rt, 24 h



X

D*7*	yield (%)	mp (°C)	ref.
k	65	290	76
l	68	> 300	76
m	55	> 300	76
n	60	> 300	76

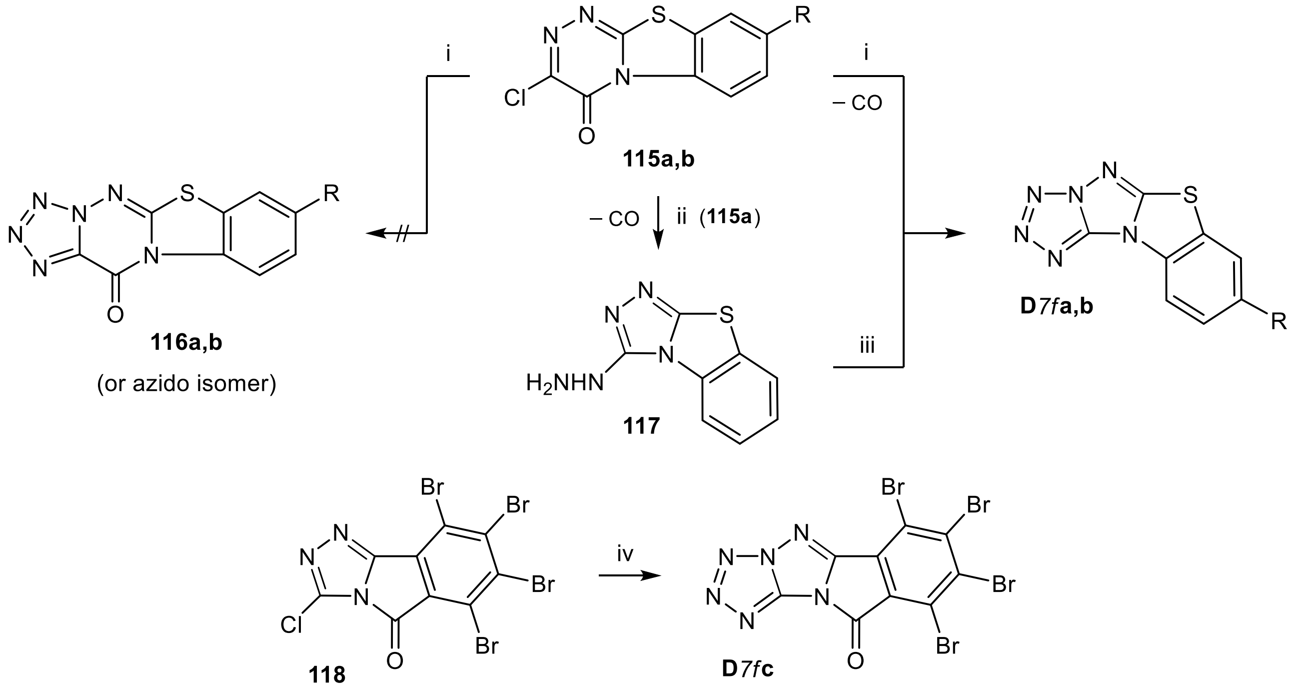


Y

Scheme 37

b) Derivatives D*5hf* [I], *7f* [I]

In conjunction with studies on *as*-triazinobenzothiazoles like **115a,b** it was surprisingly found that heating of these substrates with sodium azide did not give the anticipated compounds **116a,b** rather than the fused triazolotetrazoles **D***7f***a,b** (Scheme 38).[77a,c] The same triazine → triazole ring transfomation (extrusion of CO) took place when **115a** was heated with hydrazine to produce compound **117** (which could easily be converted to **D***7f***b**).[77b] This shows that ring transformation occurs already in the course of nucleophilic displacement of chlorine, *i.e.*, the products **D***7f***a,b** do not arise from transient **116a,b** rather than from azido tricycles **117** (N_3 instead of $NHNH_2$). Less spectacular, however, did proceed the conversion of another chloro-4*H*-*s*-triazole fused to a five-member ring: azidolysis of **118** gave the product **D***7f***c** very readily.[78] In contrast to the above substrate **117**, hydrazino-'4*H*'-*s*-triazoles that are fused to six-member rings could be transformed to compounds **D***7f* only partially (Scheme 39): While the isoquinoline representative **119** afforded an azide **120** that resisted cyclization to **D***7f***d**,[79] substrates **121** having azine moieties yielded the



i: NaN_3, DMF, pyridine, reflux, 3 h ii: $NH_2NH_2 \cdot H_2O$, reflux, 3 h iii: $NaNO_2$, conc. H_3PO_4, rt, 12 h iv: NaN_3, AcOH, reflux, 3 h

115, 116, D_7f_	R	from	yield (%)	mp (°C)	ref.
a	H	**115a / 117**	50 / 30	110	77a / 77b
b	Cl		60	305 (!)	77c
c			60	168–170	78

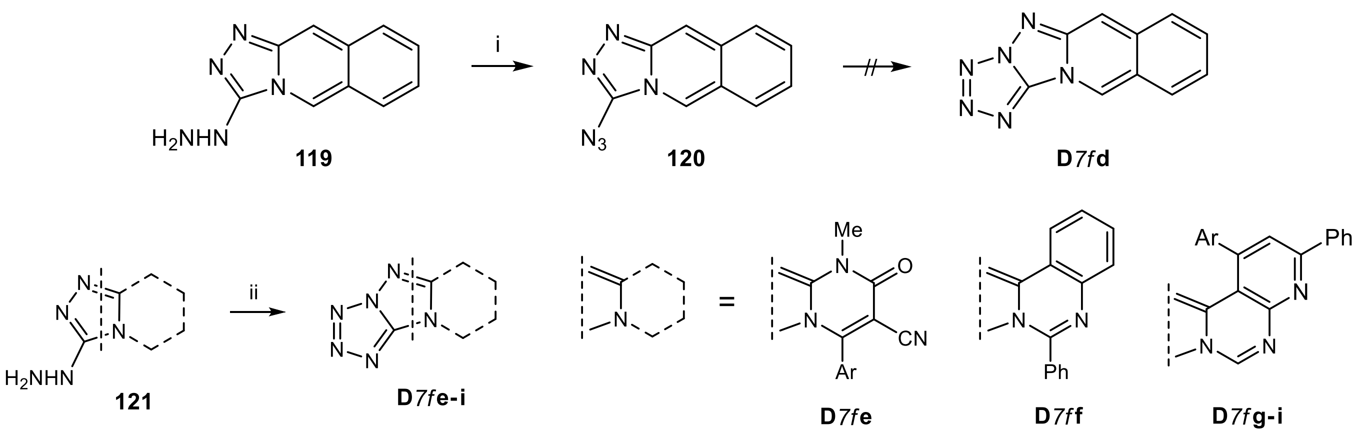
Scheme 38

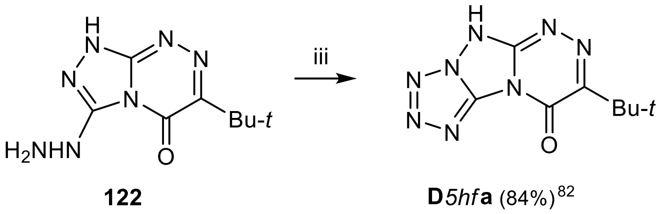
expected products throughout (*i.e.*, **D**_7f_**e-i**) and none of the respective azides was observed.[80, 81a,b] In the same way also a derivative of the type **D**_5hf_ was available, as exemplified by the process (**122** → **D**_5hf_**a**).[82]

2) [1,2,4]TRIAZOLO[4,3-*d*]TETRAZOLES (E)

a) Derivatives **E**_1_ [III], _2_ [X], _3_ [X], _4_ [IX, X]

As shown in Section (III/1. a), 5-azido-1*H*-1,2,4-triazoles resist ring closure to the respective bicycles **E**. In divergence from this experience, the (intermediary) azide formed from **107b** and nitrous acid was said to afford compound **E**_3_**a** (Scheme 40).[83] The material, however, differed from the product obtained from the reaction of the tetrazole **123** with hydrazine.[84] Therefore, it may represent the bicycle **D**5**b** which, prior to melting, ring-opens to the azide **103a**. Authentic samples of **103a** had been made earlier from the same substrate **107b** (*cf.* Scheme 34).[70a,b] This azide also arose in three steps from the diaminotriazole **124**: ring closure with nitrous acid (→ **E**_1s_**d**), hydrolytic removal of the ester group, and ring opening.[70b] The instability of the defunctionalized bicycle contrasts with the properties of **E**_4_**a**[84] but is in line with the findings detailed in Scheme 43 (*vide infra*).

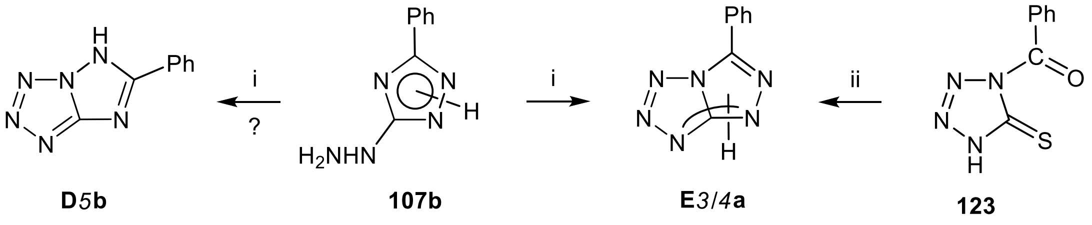




D*7f*	Ar	yield (%)	mp (°C)	ref.
e	3,4,5-(MeO)$_3$C$_6$H$_2$	55	242−244	80
f		93	257−258	81a
g	Ph	58	> 320	81b
h	4-MeC$_6$H$_4$	64	> 320	81b
i	4-NO$_2$C$_6$H$_4$	69	> 320	81b

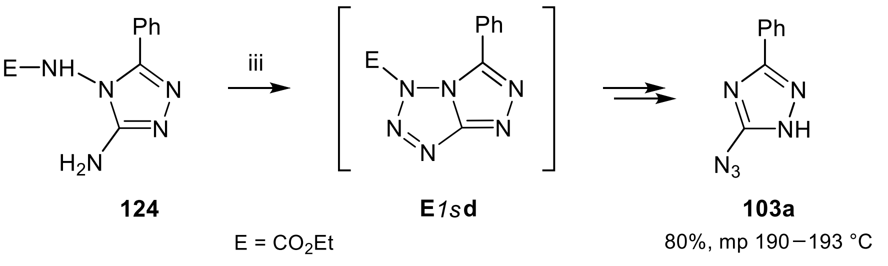
i: NaNO$_2$, AcOH (50%), 0 to 3 °C, 90 min ii: (α) NaNO$_2$, 2 M HCl, 10 °C, 15 min; then rt, 2 h (for **D***7f***e**); (β) reagents as in (α), rt, 1 h (for **D***7f***f**); (γ) NaNO$_2$, AcOH, 0 °C, 3 h (for **D***7f***g-i**) iii: NaNO$_2$, H$_3$PO$_4$, H$_2$O, 0 to 3 °C, 2 h

Scheme 39



	yield (%)	mp (°C)	ref.
E*3***a** [a]	60	190−192	83
E*4***a** [a]	50	232	84

[a] Arbitrarily formulated tautomer.



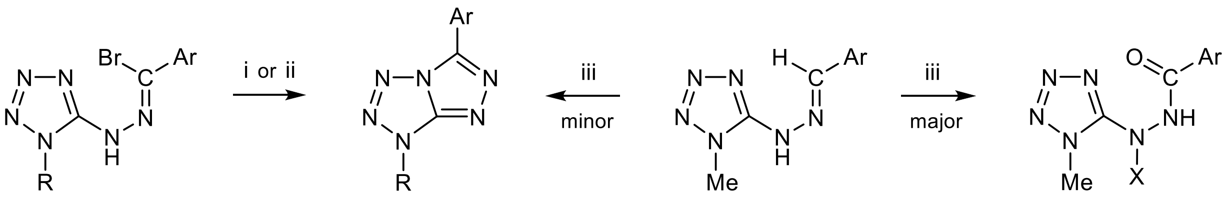
E = CO$_2$Et

80%, mp 190−193 °C

i: NaNO$_2$, HCl/AcOH (2/1), rt, 2 h ii: NH$_2$NH$_2$, DMF, reflux, 2 h iii: NaNO$_2$, HCl (20%), 0 °C

Scheme 40

An important entry to the class **E***3s* consists in solvolysis of hydrazonoyl bromides **125** in aqueous acetone (or dioxane) under mild conditions (Scheme 41). In this reaction the tetrazole ring acts as an internal nucleophile to successfully compete with the water to give derivatives such as **E***3s***a-e** in reasonable to good yields.[85a,b] The derivatives **E***3s***a-d** were also formed *via* oxidative ring closure of the hydrazones **126** using

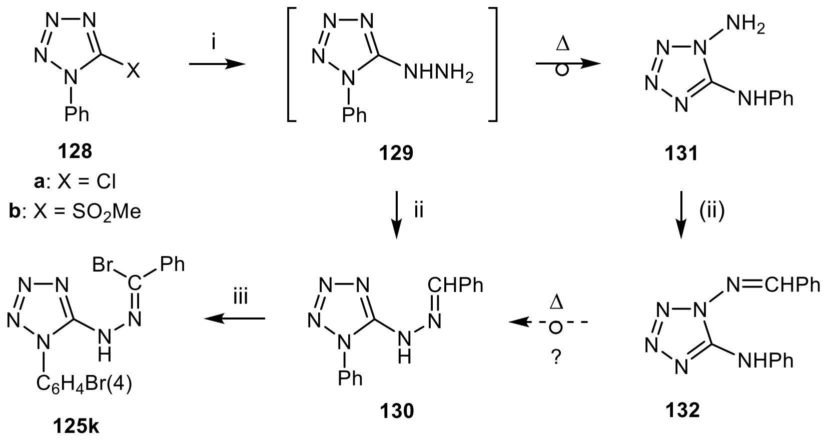


125a-n **E***3s***a-n** **126a-d** **127a-d**

i: Me$_2$CO/H$_2$O (1 + 1), 50 °C, 3–30 min; then rt, 60–100 min (for **E***3s***a-e**) or rt, 2 h (for **E***3s***k-n**)
ii: Et$_3$N, C$_6$H$_6$, reflux, 5 h iii: Pb(OAc)$_4$, AcOH, Ac$_2$O (with **126c** only), 50 °C, 5 min; then rt, 90–100 min

125–127, E*3s*	R	X	Ar	method	**E***3s*: yield (%)	mp (°C)	ref.
a	Me	COMe	Ph	i / iii	70, 50 / 26 [a]	157 / 157	85a,b / 86a
b	Me	COMe	4-MeC$_6$H$_4$	i / iii	82, 74 / 22 [b]	156–158 / 156–157	85a,b / 86a
c	Me	H	4-*i*-PrC$_6$H$_4$	i / iii	37 / 26 [c]	120 / 119 –120	85b / 86b
d	Me	COMe	4-ClC$_6$H$_4$	i / iii	84 [d] / 20 [e]	173 / 172	85a,b / 86a
e	Me		4-BrC$_6$H$_4$	i	50 [f]	174	85b
f	CH$_2$Ph		Ph	ii	quant.	144	87
g	CH$_2$Ph		4-MeC$_6$H$_4$	ii	quant.	147	87
h	CH$_2$Ph		4-ClC$_6$H$_4$	ii	quant.	154	87
i	CH$_2$Ph		4-BrC$_6$H$_4$	ii	quant.	183–185	87
j	CH$_2$Ph		4-NO$_2$C$_6$H$_4$	ii	quant.	247	87
k [g]	4-BrC$_6$H$_4$		Ph	i	85	205–207	88
l [g]	4-BrC$_6$H$_4$		4-BrC$_6$H$_4$	i	90	268–270	88
m [g]	4-BrC$_6$H$_4$		4-ClC$_6$H$_4$	i	90	244–246	88
n [g]	4-BrC$_6$H$_4$		[h]	i	80	270–272	88

[a] Besides 39% **127a**. [b] Besides 41% **127b**. [c] Besides 50% **127c**. [d] Ref. 85b: Besides 2.5% **127** (X = H, Ar = 4-ClC$_6$H$_4$). [e] Besides 37% **127d**. [f] Besides 12% **127** (X = H, Ar = 4-BrC$_6$H$_4$). [g] Preparation of **125** to be revisited. [h] Ar = 5-bromo-2-thienyl.



	mp (°C)	ref.
129	140–141 [a] // 125 [b]	89a // 89b
129	213 (!) [c]	88
131	210 [d/e] // 215–216 [f]	89a/c // 89d

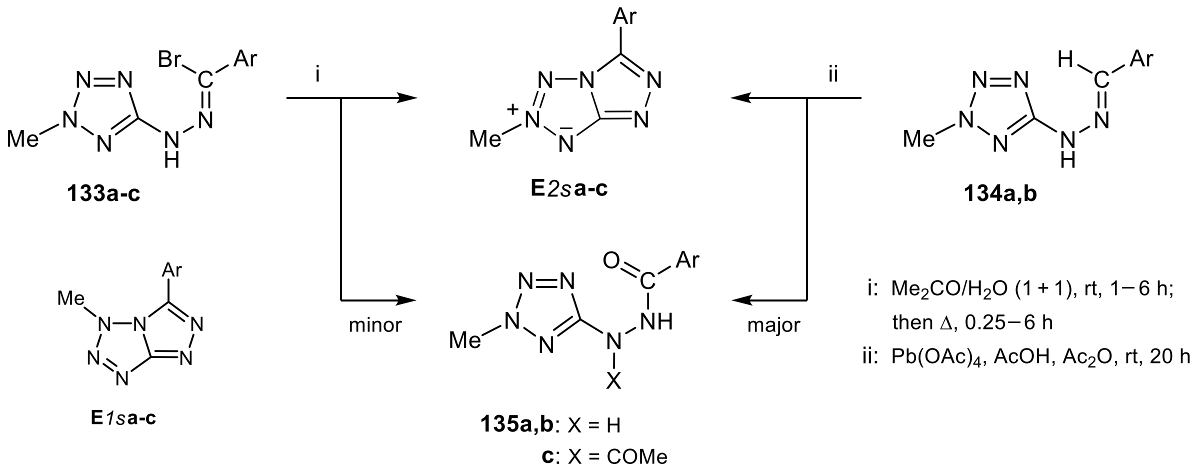
[a] Material obtained by brief heating (2–3 min) of **128b** with NH$_2$NH$_2$ • H$_2$O. [b] By reduction of **128** (X = NHNO). [c] From **128a** by method i. [d] By brief heating of **129** in xylene. [e] From 4-phenylthiosemicarbazide and PbO/NaN$_3$. [f] By heating (10 h) of **128a** with NH$_2$NH$_2$ • H$_2$O; wrong mp 247 °C here corrected (*cf.* ref. 90).

i: NH$_2$NH$_2$ • H$_2$O, reflux, 24 h ii: PhCHO, EtOH (reflux, 2 h) iii: Br$_2$, AcOH, rt, 1 h

Scheme 41

lead tetraacetate, but this variant was less productive since it favoured the formation of benzohydrazides such as **127**.[86a,b] Another range of compounds **E**_3s_, *viz.* the bicycles **E**_3s_**f-j**, were obtained through heating the bromides **125f-j** with triethylamine in an inert solvent; conceivably, in this case there were no side products.[87] However, a further report dealing with derivatives **E**_3s_ such as **E**_3s_**k-n** should be regarded with care as there is a discrepancy concerning the preparation of the precursors **125k-n** from the chlorotetrazole **128a** as starting material.[88] It is known that hydrazinolysis of **128a** under forcing conditions (prolonged heating) gives the diaminotetrazole **131** rather than the hydrazinotetrazole **129** since the latter undergoes the Dimroth rearrangement.[89a,d] Indeed, from the authors' mp[88] it is evident that, instead of **129**, the *N*-amine **131** was in hand (see Table). Thus, the ensuing reaction with benzaldehyde would lead to the imine **132**, not to the hydrazone **130** (the precursor to **125k**). This follows from the ^{1}H NMR data,[88, 89e, 90] while the mps of **130** and **132** are too close for allowing a decision.[88, 89c,f] However, since also compounds of the type **132** are susceptible to the Dimroth rearrangement,[90] the hydrazone **130** might have occurred as an intermediate in the course of bromination. On the other hand, bromination of the imine function of **132** giving an imidoyl bromide that cyclizes to the adjacent (brominated) anilino group (so as to give derivatives **D**_7_) would constitute an unprecedented process. Hence, the preparative protocol[88] may be revisited.

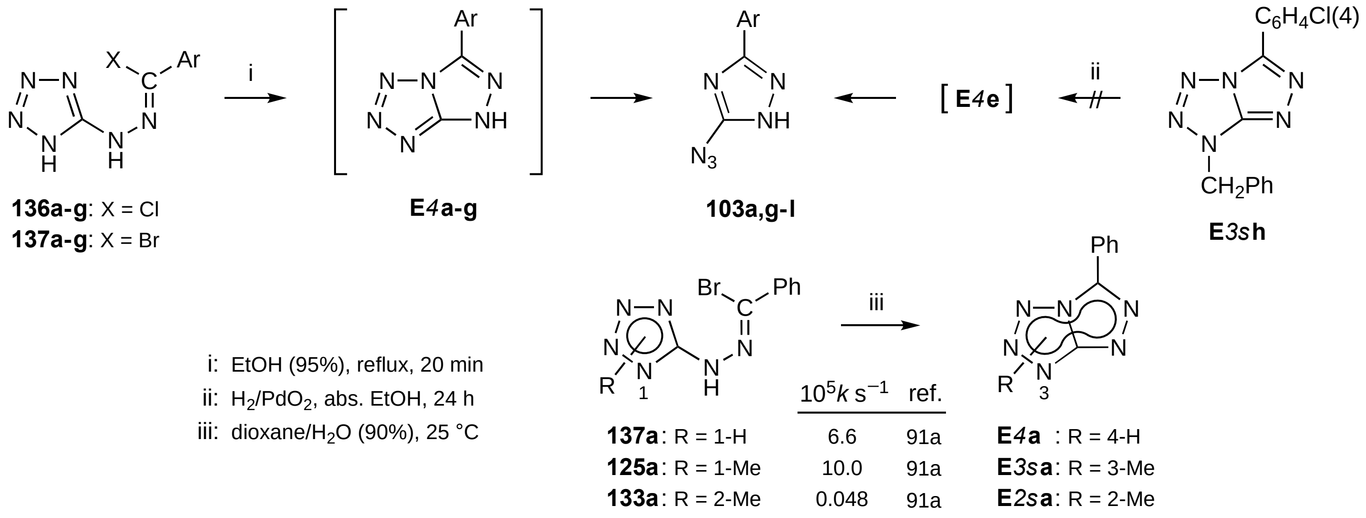
In a manner corresponding to the conversion (**125** → **E**_3s_), the isomeric substrates **133** could be transformed into the bicycles **E**_2s_ (Scheme 42).[91a,b] Being first viewed as **E**_1s_ derivatives,[91a] the structure of the products was corrected later[12b] [*cf.* the case **D**_2s/3s_ (Scheme 34)] and confirmed by an X-ray analysis of **E**_2s_**c**.[91b] A



133, **E**_2s_ [a]	**134**	**135**	Ar	method	**E**_2s_: yield (%)	mp (°C)	ref.
a			Ph	i	73	173−174	91a
b	**a**	**a**	4-ClC$_6$H$_4$	i / ii	66 [b] / 2 [c]	235−237	91a
c [e]	**b**	**b, c**	4-BrC$_6$H$_4$	i / ii	60 [d] / 2 [f]	235−236	91a

[a] **E**_2s_**a-c** erroneously viewed as **E**_1s_**a-c**; for revision, see ref. 12b. [b] Besides 11.5% **135a**-monohydrate. [c] Besides 27% **135a**. [d] Besides 20% **135b**-monohydrate. [e] **E**_2s_**c** with X-ray crystal structure (see ref. 91b). [f] Besides 20% **135b**-monohydrate and 19% **135c**.

Scheme 42



136a-g: X = Cl
137a-g: X = Br

E4a-g

103a,g-l

E3sh

i: EtOH (95%), reflux, 20 min
ii: H_2/PdO_2, abs. EtOH, 24 h
iii: dioxane/H_2O (90%), 25 °C

	$10^5 k$ s^{-1}	ref.
137a: R = 1-H	6.6	91a
125a: R = 1-Me	10.0	91a
133a: R = 2-Me	0.048	91a

E4a : R = 4-H
E3sa: R = 3-Me
E2sa: R = 2-Me

136, 137, E4	Ar	**103**	yield (%) [from **136/137**]	mp (°C)	**136/137** → **103**: $10^5 k$ s^{-1} (**136/137**: 50/25 °C)	ref.
a	Ph	**a**	85 / 65	181−182	7.5 / 29.2	93a
b	4-MeC_6H_4	**g**	84 / 72	181−182	11.2 / 55.0	93a
c	4-*i*-PrC_6H_4	**h**	86 / 65	178−179	10.5 / 66.0	93a
d	4-$MeOC_6H_4$	**i**	--- / 69 [a]	[b]	30.4 / 860	93a
e	4-ClC_6H_4	**j**	86 / 72	195−196	4.4 / 10.7	93a
f	4-BrC_6H_4	**k**	85 / 61	186−187	4.1 / 14.6	93a
g	4-$NO_2C_6H_4$	**l**	93 / 88	196−197	[c] / 8	93a

[a] Ref. 93b. [b] Unreported. [c] Undetermined.

Scheme 43

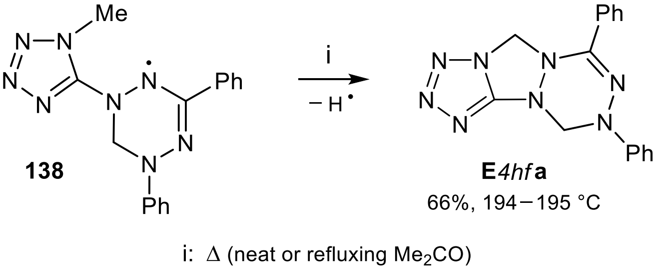
preparative entry to the alleged compounds **E***1s* (as successfully applied to **D***2s*) is not viable as reasoned in Scheme 35. In contrast to the hydrazonoyl bromides **125**, their congeners **133** were solvolyzed much more slowly (*cf.* Scheme 43, Table). The higher reactivity of **125** is not owing to the enhanced electron withdrawal of the 1*H*-tetrazol-5-yl moiety,[92] but due to the following: (i) The cyclization of **125** and **133** is thought to involve the formation of intermediates like [Tet–NH–N=C$^+$–Ar] (a) $\rightleftharpoons$ [Tet–N=N–CH$^+$–Ar] (b); (ii) of these two species, the azocarbenium tautomer (b) – which is structurally closer to **E***3s* and **E***2s* than the tautomer (a) – is distinctly favoured in the case of **125** because the positive charge of (b) can be better delocalized over the heterocycle.[91a]

Complementary attempts at getting compounds **E***2s* through oxidative cyclization of the hydrazones **134** resulted almost exclusively in the formation of the hydrazides **135** (Scheme 42).[91a]

In contrast to the stable bicycles **E***3s* and **E***2s*, their *N*-unsubstituted congeners **E***4* which were formed in the same way from hydrazonoyl halides like **136** or **137** ring-opened to the respective azidotriazoles **103** (Scheme 43).[93a,b,94] Therefore, debenzylation of the bicycle **E***3s***h** was expected to give the triazole **103j**, but the experiment failed.[87] Comparative kinetic studies with both halides showed the bromides **137** to be more reactive; in addition, the rate-determining effect of various aryl-attached groups was demonstrated.[93a]

b) Derivatives E*4hf* [XI]

A single example of this type, the unique tricyclic compound E*4hf***a**, arose when the verdazyl radical **138** was heated in the crystalline state or in solution.[95]



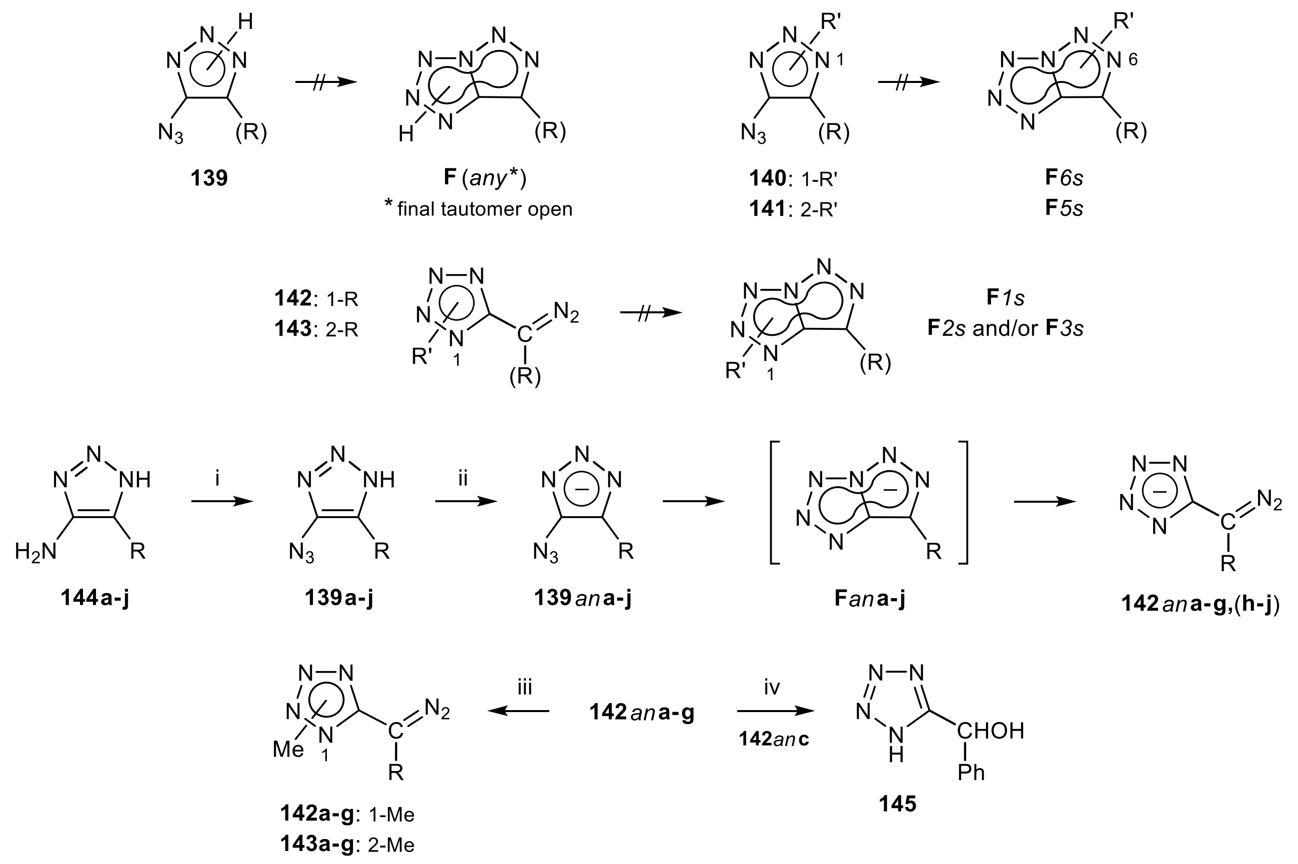
Scheme 44

3) [1,2,3]TRIAZOLO[1,5-*d*]TETRAZOLES (F)

Derivatives F*1, 2, 3, 5, 6, an* [I]

Just as the azides of pyrazole (**2**, **3**), imidazole (**30'**, **40**, **41**), and 1,2,4-triazole (**103**–**106**) (*cf.* Schemes 2, 13, 15, and 33, respectively), their 1,2,3-triazole congeners **139**–**141** do not show any proclivity to cyclize, *i.e.*, to form derivatives **F** (Scheme 45). This is in agreement with DFT calculations performed for (R) = R' = H [*cf.* Section (III / 5. a), Table 6]. Cyclization of 5-(diazoalkyl)tetrazoles **142** and **143** as an alternative route to **F** can be ruled out as these materials exist as stable monocycles.[25a,b,26a,27a,b] Ring-chain tautomerism of this particular kind is only known from the thiazole[96a–d] and thiadiazole series.[96d]

None the less, in direct parallel to the anions **2***an*, **40***an*, and **103***an* (*cf.* Schemes 3, 15, and 34, respectively), the anions **139***an* generated *in situ* from **139** (the latter made easily from the amines **144**) cyclized to **F***an*. However, in marked contrast to **2***an*, **40***an*, and **103***an*, the bicycles **F***an* eluded detection: once formed they ring-opened to the (diazoalkyl)tetrazolides **142***an*.[97a,b] This process constitutes a rare type of 1,2,3-triazole ring transformation;[99a–c] formally, it resembles the degenerate rearrangement of azidotetrazolide (**G***an*) [see Section (III / 4)].[100] Regarding its scope, the anions **139***an***a-g** gave clean solutions of **142***an***a-g** (with minor restrictions in the case **142***an***b,g**), whereas the substrates **139***an***h-j** underwent extensive decomposition. Chemical characterization of **142***an***a-g** included (i) ring methylation to produce the derivatives **142a-g** and **143a-g** and (ii) diazo degradation of **142***an***c** to give the carbinol **145**. Kinetic studies showed the rate constants *k* to be largely independent from the electronic influence of the R substituent; compared to the process (**2***an* → **A***an*) [Section (II / 1. a)], they are distinctly smaller (especially in a protic medium[97b]).



i: $NaNO_2$, conc. HCl, – 5 to – 10 °C; then NaN_3, – 5 to 0°C (for **139a**) or $NaNO_2$, 6 M HCl, 0 °C; then NaN_3, –15 °C, 30 min (for **139b-j**)
ii: NaH, DMSO or DMSO-d_6, rt or 32 °C iii: MeI, rt iv: H_2SO_4 (10%), MeOH/H_2O, 50 °C, 1 h v: Me_2CO/H_2O (1 + 1), 50 °C, 30 min

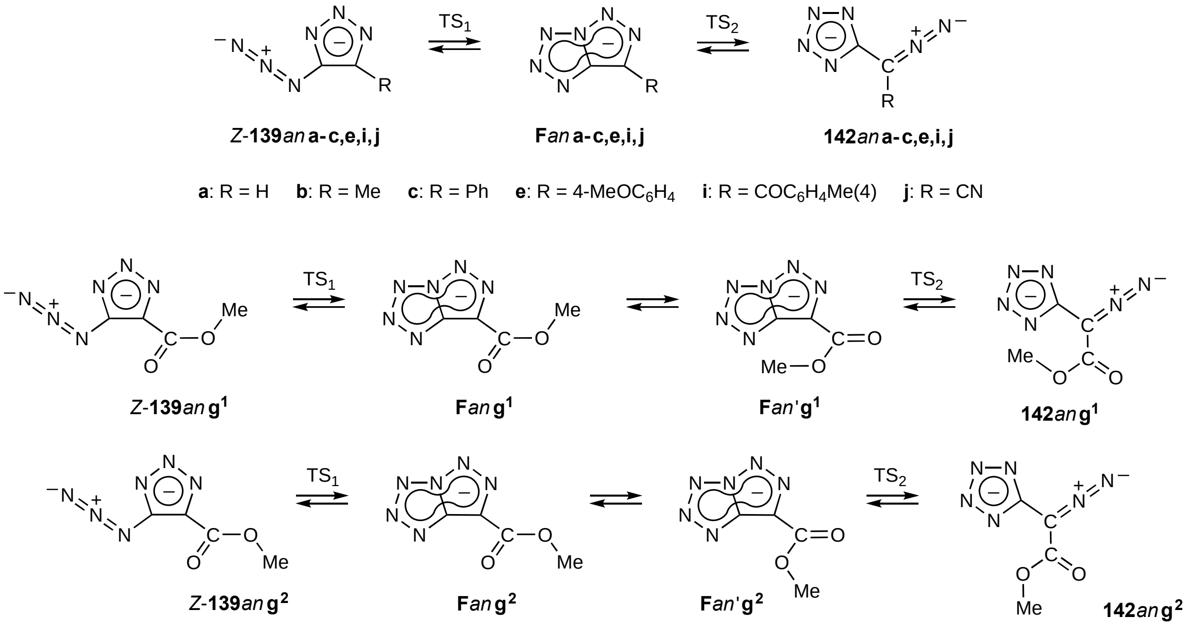
139(*an*), **F***an* **142**(*an*)–**144**	R	**139**: yield (%)	mp (°C) [a]	**139***an* → **142***an*: 10^5k s^{-1} (32 °C / 23 °C)	$t_{1/2}$ [min] (32 °C)	mixture **142** / **143** ratio [g]	ref.
a	H	60 [b,c]	76–78 [b]	9.20, 7.70 / 2.28	125, 149	45 / 55	97a,b
b	Me	83	133–136	9.80 / 3.30	117	35 / 65	97b
c	Ph	71	131–133	24.0 / [d]	48	18 / 82	97b
d	4-MeC_6H_4	68	119–120	25.5 / [d]	45	19 / 81	97b
e	4-$MeOC_6H_4$	84	114–115	24.5 / 7.75	47	17 / 83	97b
f	4-$(CO_2Me)C_6H_4$	89	146–147	26.1 / [d]	44	12 / 88	97b
g	CO_2Me	39	148–150	9.90 [e] / 2.18 [e]	116 [e]	48 / 52	97b
h	COMe	76	136–137	[d]			97b
i	$COC_6H_4Me(4)$	86	156–157	(3.30) [a,f] / [d]	(348)		97b
j	CN	45	129–131	[d]			97b

[a] Decomp. [b] Ref. 7b. [c] For a direct synthesis of the sodium salt (different method; low yield), see ref. 98. [d] Undetermined. [e] Value entropy-controlled. [f] Monitored over 1 half-life only. [g] Based on ^1H NMR (*N*-Me signal).

Scheme 45

Theoretical investigations of the transformation (*Z*-**139***an* → **F***an* → **142***an*) were performed at different levels (Table 5, Figure 4): Semiempirical (PM3)[97b] as well as DFT calculations at the B3LYP/6-311+G** level[6a] gave a nicely consonant picture in that the final product **142***an* is lower in energy than the starting triazolide *Z*-**139***an* to roughly the same extent, whereas the intermediary bicycle **F***an* is higher in energy than the former, especially when looking at the Δ*G* values. This parallel, however, was not found at the less elaborate B3LYP/6-31G* level (compare the Δ*E*/Δ*G* values of the derivatives **c** and **g**). Finally, as a good agreement with the experimental failure to launch the conversion of the cyano substituted azidotriazolide, *i.e.*, the process (*Z*-**139***an***j** → **F***an***j** → **142***an***j**), the energetical relationship *Z*-**139***an* *vs.* **142***an* turned out to be reversed.

Table 5. *v*-Triazolide–tetrazolide ring transformation:
Heats of formation (ΔH_f) and relative energies (Δ*E*) / relative free energies (Δ*G*) of (*Z*)-azido-*v*-triazolides (*Z*-**139***an*), *v*-triazolotetrazolides (**F***an*, **F***an*'), (diazoalkyl)tetrazolides (**142***an*), and transition states (TS_1, TS_2) [a]



ΔH_f [b]

	a	b	c	e	g^1	i	j
Z-**139***an*	396.1	358.7	484.1	325.4	16.2	299.2	498.2
TS_1	551.6	515.1	635.5	477.0	172.8	455.3	653.7
F*an*	427.7	389.6	513.1	354.9	58.7	335.6	539.2
F*an*'	---	---	---	---	54.1	---	---
TS_2	528.2	489.3	610.5	453.8	141.0	436.0	638.9
142*an*	375.3	344.6	475.7	318.3	5.8	280.1	506.1

Δ*E* / Δ*G* [c]

	a	b	c	g^2	j
Theory	[d] // [e]	[d] // [e]	[d] // [e]	[d] // [e]	[d] // [f]
Z-**139***an*	15.8 / 18.1 // 15.7 / 18.1	14.2 / 11.0 // 11.3 / 9.4	16.4 / 6.3 // 1.8 / 2.6	13.4 / 3.9 // 3.0 / 4.5	3.5 / **0.0** // **0.0** / **0.0**
TS_1	103.1 / 107.1 // 111.6 / 115.9	101.4 / 100.8 // 106.7 / 108.9	100.6 / 92.4 // [g] / [g]	102.9 / 94.9 // 100.6 / 104.3	93.9 / 92.1 // 98.9 / 100.8
F*an*	1.9 / 14.5 // 18.8 / 31.1	**0.0** / 8.9 // 13.2 / 24.6	**0.0** / **0.0** // 0.8 / 11.5	1.4 / 1.9 // 6.0 / 17.8	**0.0** / 6.2 // 12.4 / 21.8
F*an*'	---	---	---	**0.0** / **0.0** // 3.9 / 15.8	---
TS_2	75.8 / 80.1 // 85.2 / 89.9	75.3 / 76.2 // 83.0 / 87.1	68.8 / 61.5 // [g] / [g]	64.2 / 56.9 // 59.9 / 65.1	75.1 / 72.9 // 78.8 / 80.5
142*an*	**0.0** / **0.0 //** **0.0** / **0.0**	2.6 / **0.0** // **0.0** / **0.0**	16.3 / 5.0 // **0.0** / **0.0**	17.5 / 4.9 // **0.0** / **0.0**	30.5 / 23.7 // 24.7 / 21.1

[a] Gas phase, values in kJ mol^{-1}. [b] Ref. 97b; theory: PM3. [c] Ref. 6a. [d] B3LYP/6-31G*; for Δ*G* of derivatives **a** (*Z*-**139***an* / TS_1 / **F***an*), see also Section (III/5. a), Table 6 (ref. 7a). [e] B3LYP/6-311+G**. [f] B3LYP/6-311+G*. [g] Calculation failed.

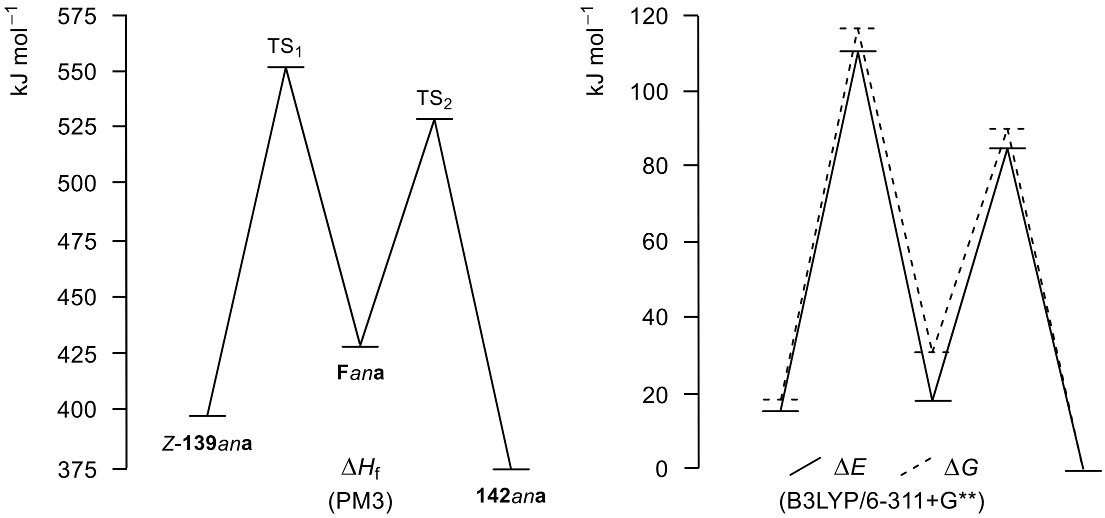
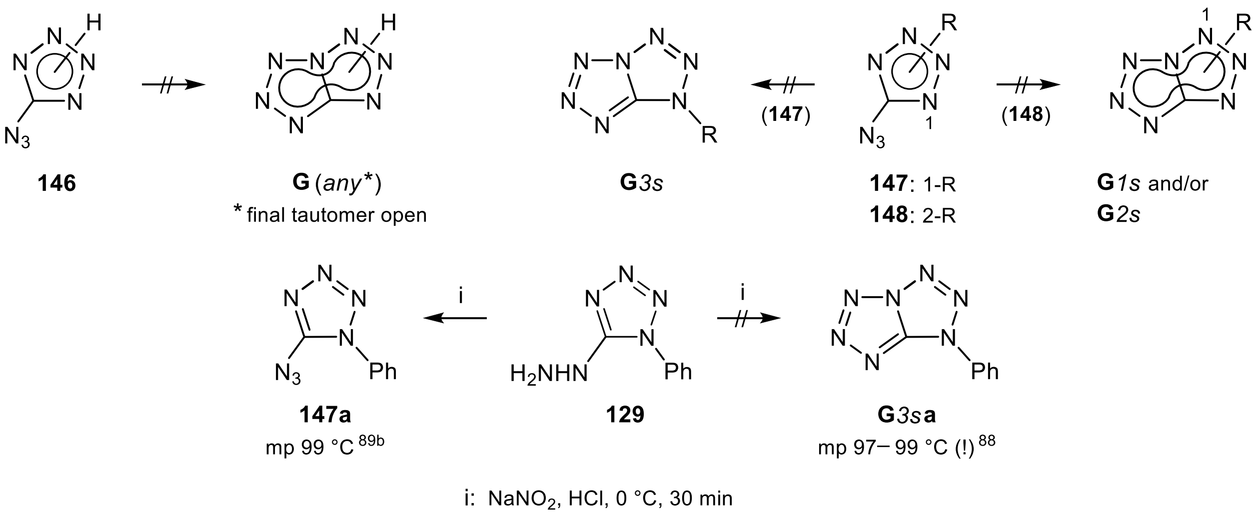


Figure 4. Energy profiles of the process {*Z*-**139***an***a** → TS$_1$ → **F***an***a** → TS$_2$ → **142***an***a**}

4) TETRAZOLO[1,5-*d*]TETRAZOLES (G)

Derivatives G*3*, *an* [I]

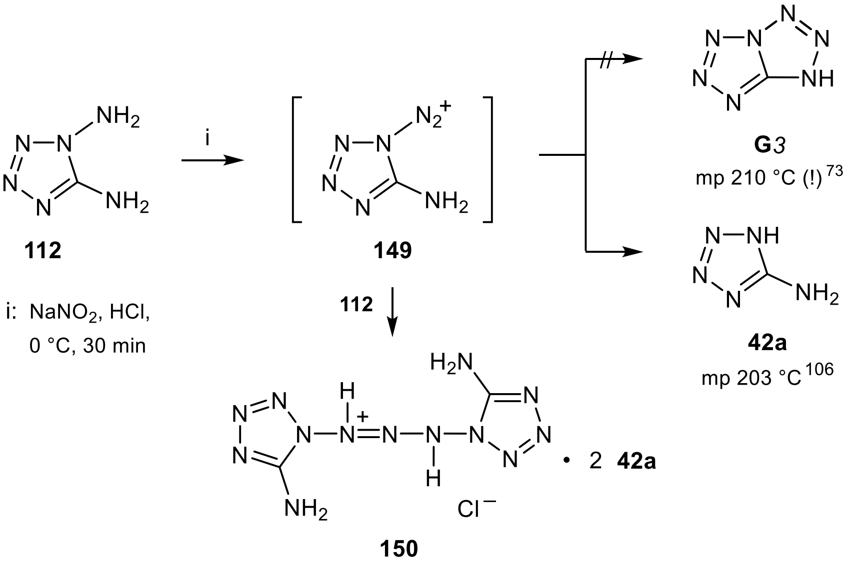
Azidotetrazoles of the types **146**–**148** exist as such and do not cyclize to derivatives **G** (Scheme 46) [*cf.* the X-ray crystal structures of **146**[101a] and **147a**[101b]]. This is consistent with DFT calculations for R = H and NH$_2$ that showed the cyclic isomers to be much higher in energy [*cf.* Section (III/5.a), Table 7].[6a,7a,102,103] Contrasting with this finding, treatment of the hydrazinotetrazole **129** with nitrous acid was said to give compound **G***3s***a**.[88] Yet, the mp of the product (though no azide band reported) points to **147a**. This material has been obtained earlier in the same manner[89b] and, alternatively, from 5-chloro-1-phenyltetrazole.[101b,104]



i: NaNO$_2$, HCl, 0 °C, 30 min

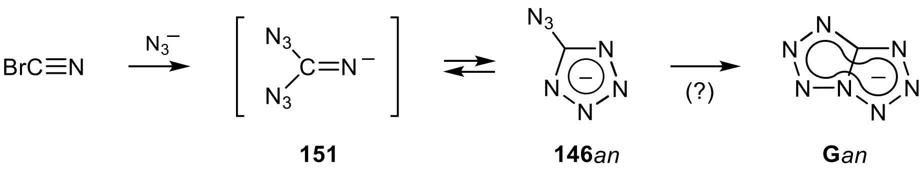
Scheme 46

A further example of the alleged formation of a representative **G**, *viz.* **G***3*, constitutes the reaction of 1,5-diaminotetrazole (**112**) with nitrous acid (Scheme 47).[73] Yet, *N*-aminotetrazoles undergo deamination when treated with this reagent;[105] hence, the product believed to be **G***3* was the long known 5-aminotetrazole (**42a**).[106] Indeed, in an attempt to remake **G***3*,[107] **42a** (2 mol) was found in an adduct that also contained the interesting triazenium salt **150** (from **112** and **149**); the material was studied by X-ray crystallography.



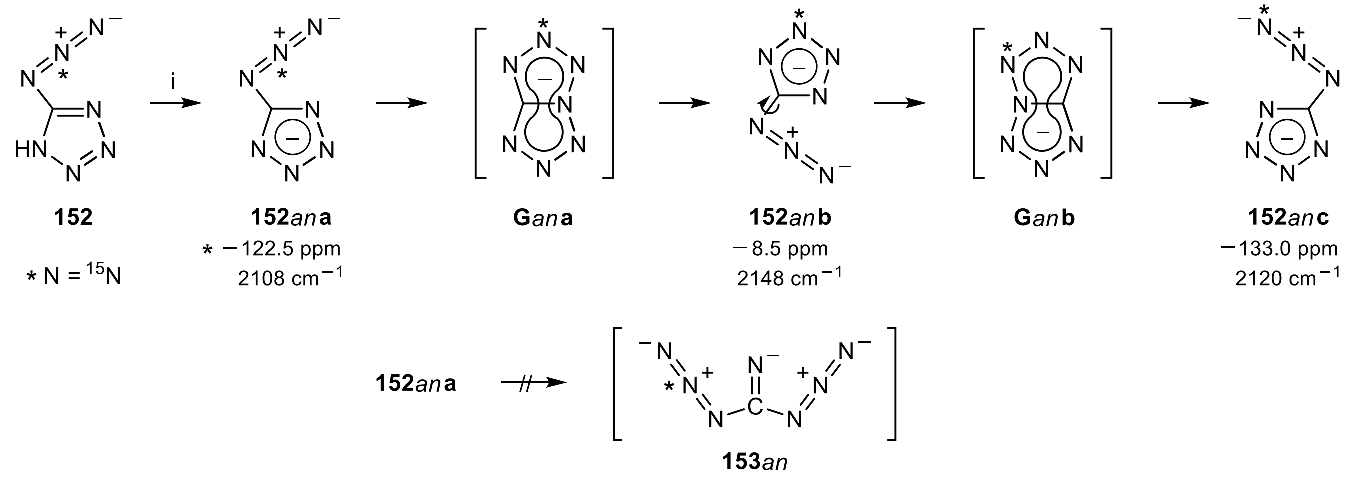
Scheme 47

5-Azidotetrazolide (**146***an*) was first mentioned as a component resulting from partial ring closure of the *gem*-diazide **151** that was formed through addition of sodium azide onto cyanogen bromide (Scheme 48). Yet, the possibility of an additional cyclization step leading to the species **G***an* was not considered.[108a] Later, theoretical work showed **G***an* to be higher in energy than **146***an* [*cf.* Section (III / 5. a), Table 7].[6a,7a,100,102]



Scheme 48

None the less, the occurrence of **G***an* could be inferred from an experiment using a labelled substrate like **152***an***a**: slow ^{15}N scrambling {**152***an***a** → **152***an***b** → **152***an***c**} showed the bicycles **G***an***a** and **G***an***b** to be true (albeit inobservable) intermediates. This finding excluded the involvement of the fully open structure **153***an*; in addition, compared to **G***an***a**, such a species is clearly disfavoured energetically (Scheme 49).[100]



i: $NaCH_2SOMe$, Me_2SO, rt

Scheme 49

5) THEORETICAL STUDIES

a) Azido–tetrazole tautomerism with triazolo- and tetrazolotetrazoles (D–G)

Three categories of model compounds have been studied: substrates that are (i) fully conjugated and neutral, (ii) nonconjugated, and (iii) fully conjugated but anionic (Tables 6, 7). – Partly hydrogenated structures have not been included since, for practice, they appear negligible [*cf.* Section (I), Figure 2].

(i) Series **D***5*, **D***7*, **E***5*, **E***4*, **F***5*, **F***6* and **G***1*, **G***2*, **G***3*: The azide (Az*Z*) is energetically favoured throughout over the bicycle (Tet), the difference between (Az*Z*) and (Tet) increases as follows: **D***7* ≪ **E***4* < **F***6* < **F***5* < **D***5* ≅ **E**5 and **G***3* < **G***2* < **G***1*. – See also Scheme 50 for the more complex structures **D'***7*, **F'***5*, **F'***6*, and **G'***3*.

(ii) Series **D***6*, **E***6*, **F***7*: All bicycles (Tet) are higher in energy, especially with **D***6*; the difference between (Az*Z*) and (Tet) increases as follows: **F***7* < **E***6* ≪ **D***6*.

(iii) Series **D***an*, **E***an*, **F***an*, and **G***an*: In this family the cyclic form (Tet) is slightly favoured over (Az) with **D***an* and **F***an*, whereas the opposite holds for **E***an* and **G***an*.

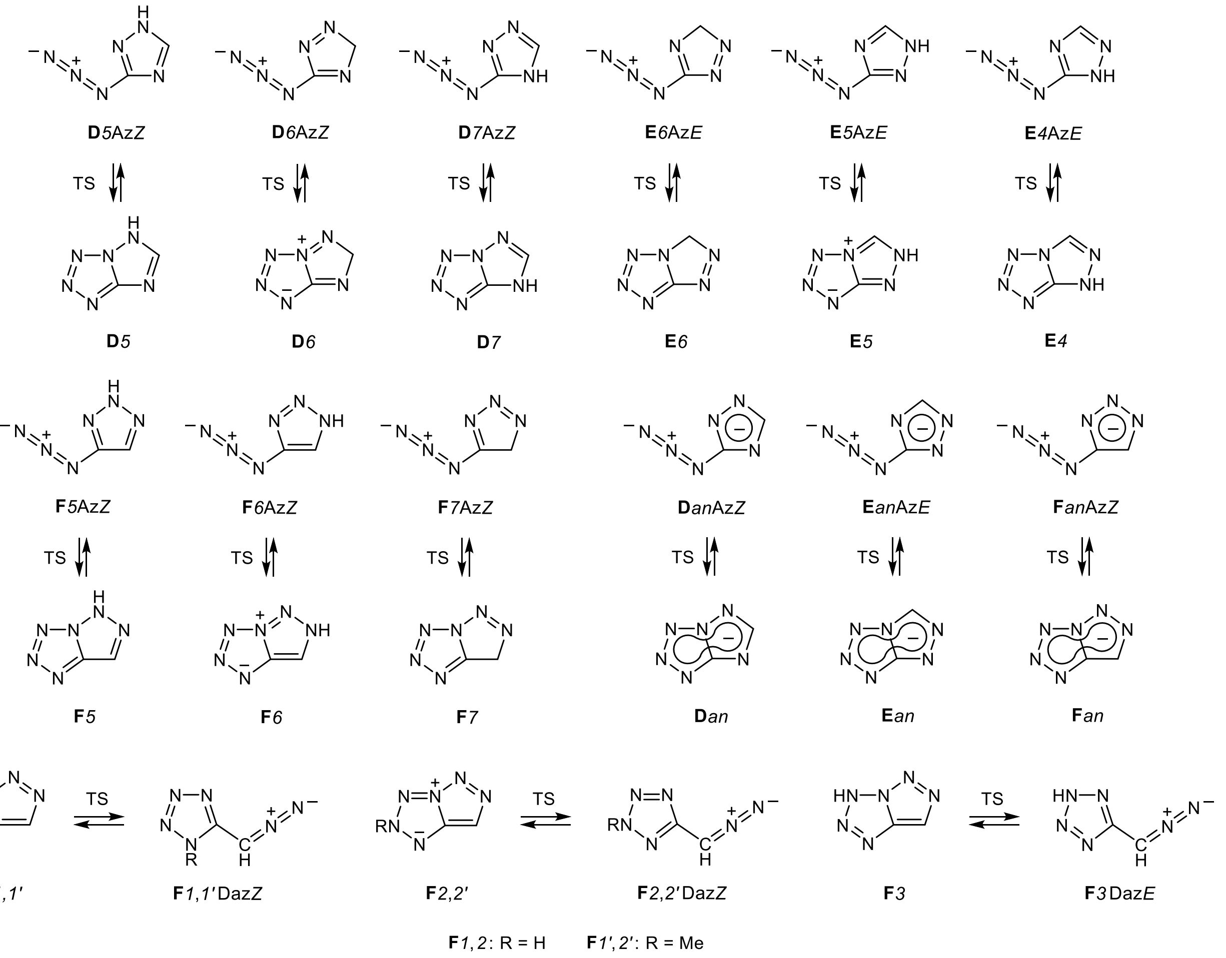
b) *v*-Triazole–diazomethyl tautomerism with *v*-triazolotetrazoles (F)

Studying the fully conjugated (neutral or mesoionic) substrates **F***1,1'*, **F***2,2'*, and **F***3*, all bicycles (*v*-Tri) have been found to be higher in energy than the diazomethyl forms (Daz). The difference between (Daz) and (*v*-Tri) increases as follows: **F***1* < **F***2* < **F***3* and **F***1'* < **F***2'* (Table 6).

c) Annular tautomerism and *E*/*Z* isomerism of azidotriazoles and -tetrazoles (DAz–GAz)

As observed with azidodiazoles [*cf.* Section (II/4. b)], species that directly equilibrate with (Tet) are lower in energy (Table 8). The conformational preferences are also shown in Scheme 51; they were rationalized electronically (lone pair–lone pair repulsion, as occurring in equilibria Ia, Ib, and III) or through pointing to the different acidity of NH and CH (equilibrium II).[7a]

Table 6. Azido–tetrazole and *v*-triazole–diazomethyl tautomerisms with Series **D** – **F** and **F**, respectively: Relative energies (Δ*E*) / relative free energies (Δ*G*) of azidotriazoles (Az*Z*,*E*), triazolotetrazoles (Tet, *v*-Tri), (diazomethyl)tetrazoles (Daz*Z*,*E*), and transition states (TS) [a,b]



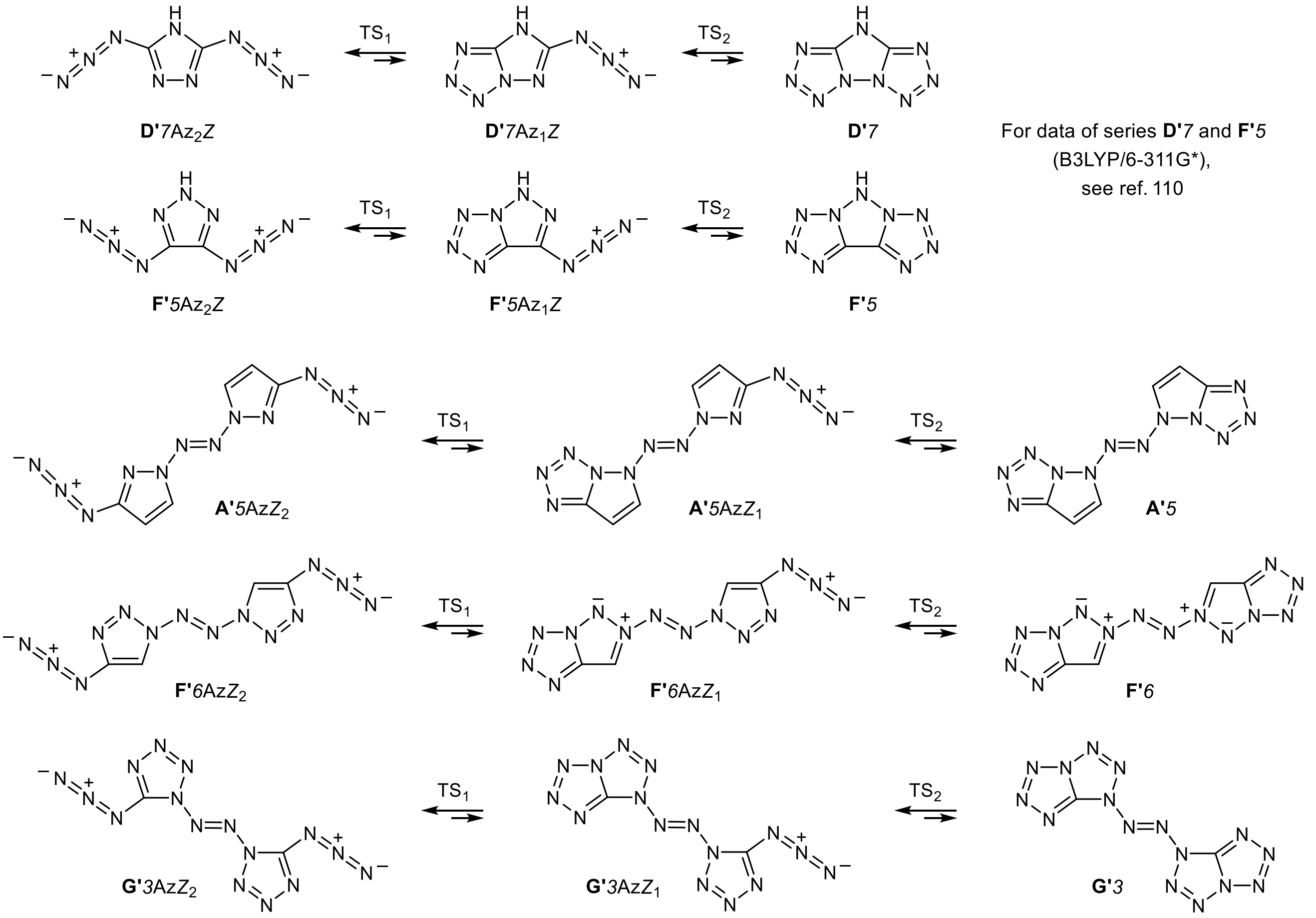
Series	**D***5*	**D***6*	**D***7* [c]	**E***6*	**E***5*	**E***4*	**F***5* [c]	**F***6* [c]	**F***7*
Ref.	6a / 7a [d]	6a	6a / 7a [d]	6a	6a / 7a [d]	6a / 7a [d]	6a / 7a [d,e]	6a / 7a [d,e]	6a
Az*Z*,*E*	5.7 / 5.4	105.7 / 100.0	31.2 / 28.9	105.2 / 99.8	2.9 / 2.9	**0.0** / **0.0**	61.9 / 60.9	79.0 / 76.4	156.2 / 148.6
TS	149.2 / 147.7	263.2 / 257.5	130.4 / 130.6	217.3 / 213.5	140.0 / 141.9	111.8 / 113.6	205.5 / 203.2	202.6 / 203.3	248.3 / 241.6
Tet	107.3 / 112.4	214.4 / 215.1	62.6 / 69.5	137.5 / 140.6	105.2 / 112.0	63.8 / 70.2	158.7 / 164.5	152.4 / 159.6	168.1 / 169.3

Series	**D***an*	**E***an*	**F***an*	Series [f]	**F***1*	**F***2*	**F***3*	**F***1'*	**F***2'*
Ref.	6a / 7a [d]	6a / 7a [d]	6a / 7a [d,g]	Ref.	6a	6a	6a	6a [h]	6a [h]
Az*Z*,*E*	22.6 / 11.9	22.3 / 11.6	89.1 / 76.0	*v*-Tri	58.9 / 68.4	80.3 / 92.6	106.9 / 115.3	76.0 / 83.4	88.1 / 96.0
TS	111.8 / 102.6	121.6 / 112.2	176.4 / 165.1	TS	101.6 / 105.1	117.1 / 123.1	138.8 / 140.2	117.7 / 120.7	123.4 / 128.9
Tet	**0.0** / **0.0**	40.2 / 37.5	75.2 / 72.5	Daz*Z*,*E*	12.3 / 10.0	**0.0** / **0.0**	0.08 / 0.03	20.1 / 18.0	**0.0** / **0.0**

[a] Gas phase; values in kJ mol^{-1}. [b] Theory: B3LYP/6-31G*, except for **F***1',2'*: B3LYP/6-311+G**. [c] See also Scheme 50 of this Section for series **D'***7*, **F'***5*, and **F'***6*. [d] *Cf.* ref. 7a also for Δ*G* values determined at the G3B3 level. [e] **F***5* and **F***6* values of ref. 7a (*i.e.*, **0.0**, 142.3, 103.5 and 15.5, 142.1, 98.7, respectively) here related to **E***4*Az*E*. [f] For Series **F***an* (*v*-Tri, TS, Daz), see Section (III/3, Table 5). [g] **F***an* values of ref. 7a (*i.e.*, 3.5, 92.6, **0.0**) here related to **D***an*. [h] Δ*E* values of *v*-Tri and Daz*Z* from ref. 109 (here converted into kJ mol^{-1}).

d) Annular tautomerism of triazolo- and tetrazolotetrazoles (D–G)

Looking globally at all triazolotetrazoles **D**–**F**, the tautomer **D***1* is lowest in energy, whereas **D***6* is least favoured. Quite small, however, appears the difference within the **F** series, while that within the **E** series is intermediate. As regards the tetrazolotetrazoles **G**, the tautomer **G***3* is most favoured, whereas **G***1* is highest in energy as a consequence of the adjacent pyrrolo-like nitrogen atoms (*cf.*, for example, the differences between **D***1* and **D***3* and between **D***5* and **D***7*).

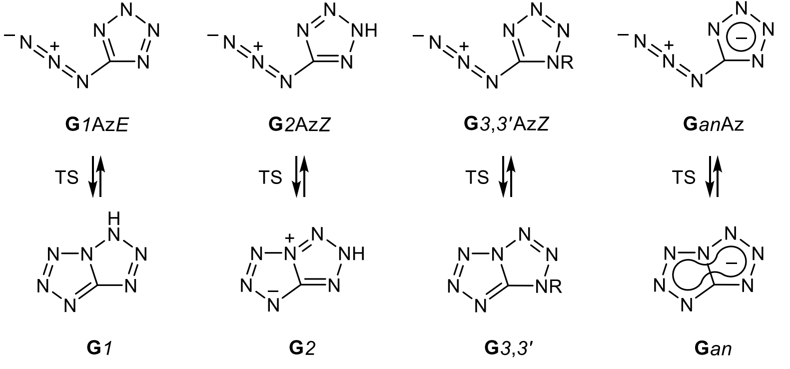


For data of series **D'***7* and **F'***5* (B3LYP/6-311G*), see ref. 110

For data of series **A'***5*, **F'***6*, and **G'***3* (throughout: B3LYP/6-311++G**, B3PW91/6-311++G**, and B3LYP/Aug-cc-PVDZ), see ref. 111

Scheme 50

Table 7. Azido–tetrazole tautomerism with Series **G**:
Relative energies (Δ*E*) / relative free energies (Δ*G*) of azidotetrazoles (Az*E*,*Z*), tetrazolotetrazoles (Tet), and transition states (TS) [a]



[continued overleaf]

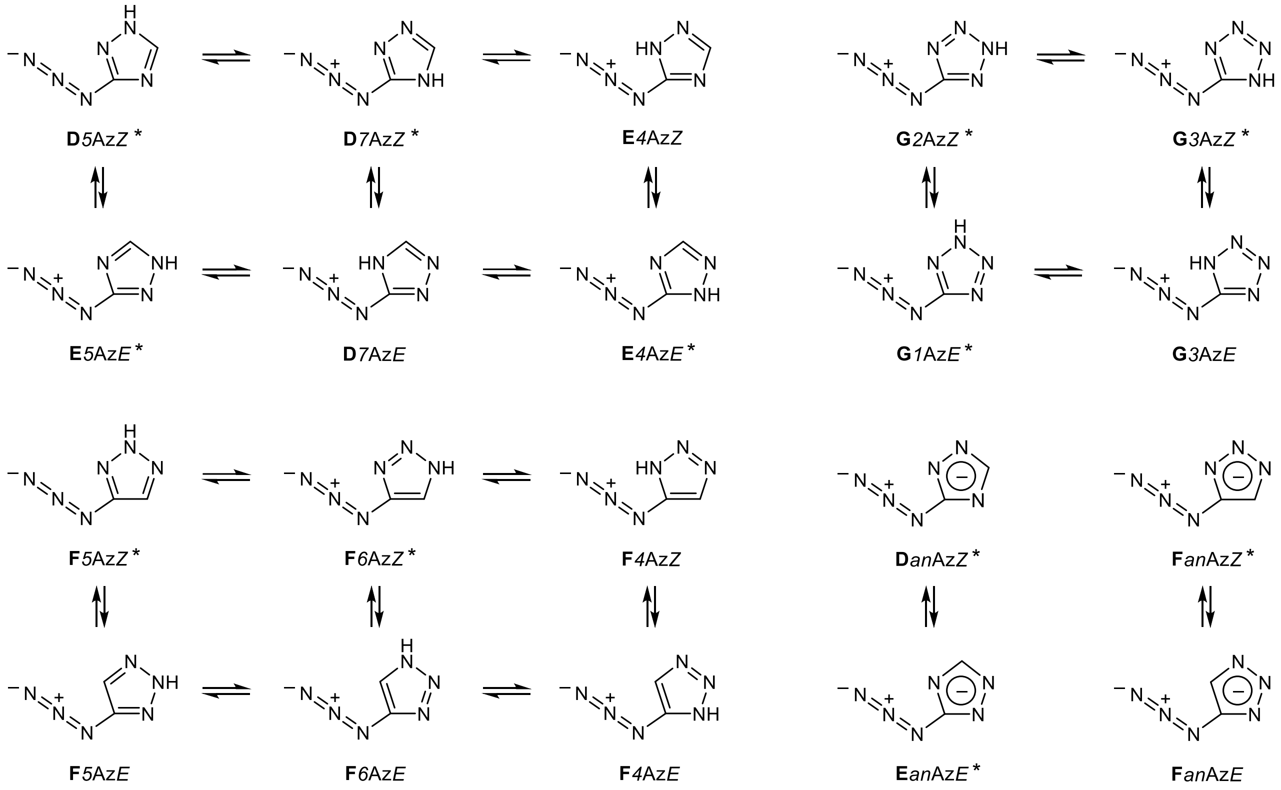
G*3* : R = H
G*3'*: R = NH_2

Table 7 (continued)

Series	**G***1*	**G***2*	**G***3* [b]	**G***3*	**G***3'*	**G***an*	**G***an*	**G***an*
Theory	[c]	[c]	[c]	[d]	[e]	[c]	[f]	[d]
Ref.	6a / 7a	6a / 7a	6a / 7a	102	103 / 6a	6a / 7a	100	102
Az*E*,*Z*	3.3 / 3.0	**0.0** / **0.0**	8.9 / 7.1	**0.0** / ---	**0.0** / **0.0**	**0.0** / **0.0**	**0.0** / ---	**0.0** / ---
TS	170.2 / 168.3	144.0 / 146.6	126.1 / 126.4	116.7 / ---	127.0 / 130.9	101.1 / 102.6	--- / ---	101.7 / ---
Tet	137.7 / 141.5	103.9 / 112.2	78.0 / 83.7	72.0 / ---	86.9 / 90.9	11.9 / 21.0	27.6 / ---	20.1 / ---

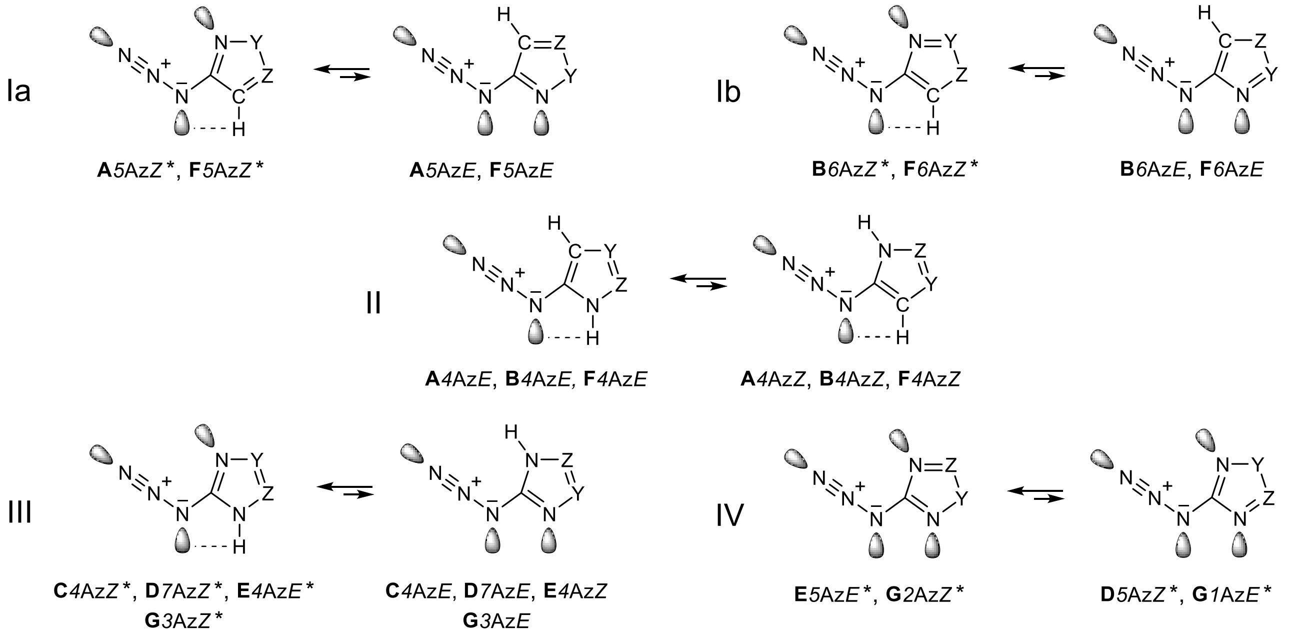
[a] Gas phase; values in kJ mol^{-1}. [b] See also Scheme 50 of this Section for series **G**'*3*. [c] B3LYP/6-31G*. [d] B3LYP/aug-cc-pVDZ (no ZPE correction). [e] B3LYP/6-311++G** (Δ*E* values: no ZPE correction, here converted into kJ mol^{-1}). [f] HF/4-31G (values here converted into kJ mol^{-1}).

Table 8. Annular tautomerism (horizontal) and *E*/*Z* isomerism (vertical) of azidotriazoles, -tetrazoles (**D**Az–**G**Az): Relative energies (Δ*E*) / relative free energies (Δ*G*) [a,b]



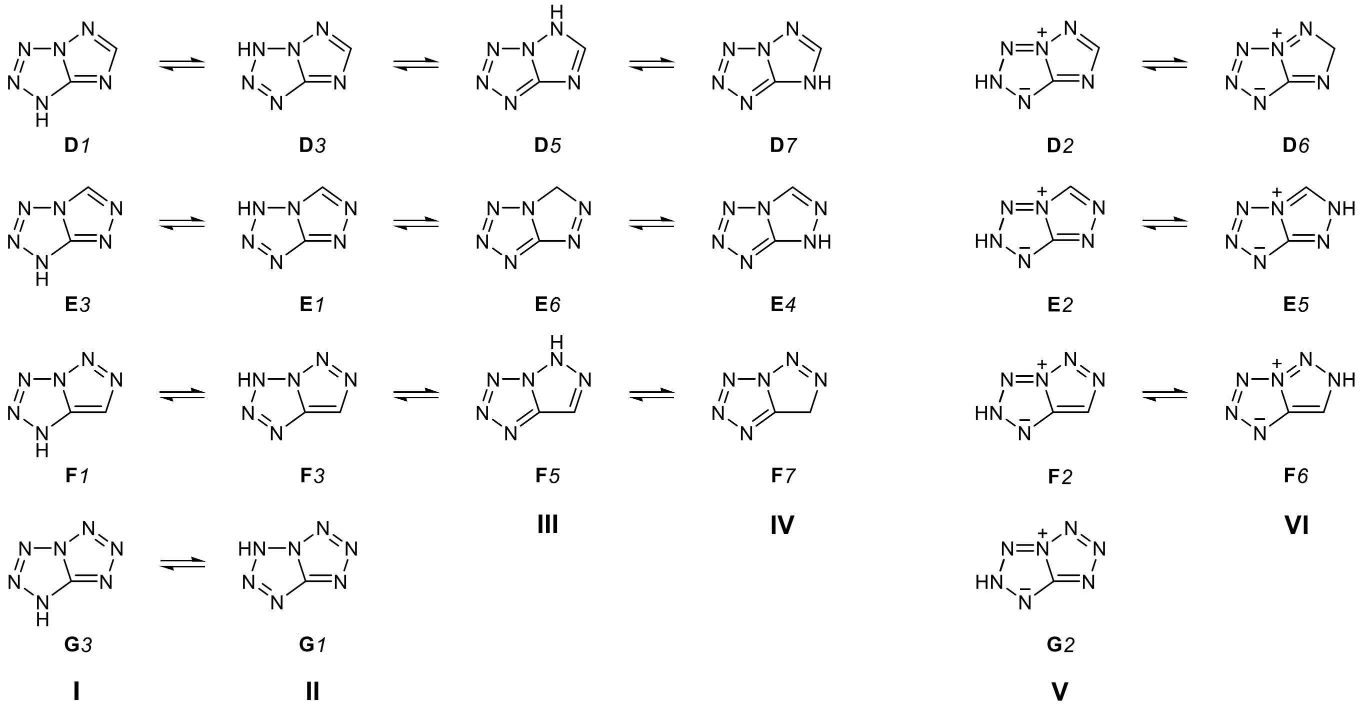
Ref.	6a / 7a [c]		6a / 7a [c]		6a / 7a [c]		6a / 7a [c,d]
D5AzZ*	5.7 / 5.4	**F**4AzZ	37.4 / 34.1			**D**anAzZ*	0.3 / 0.3
D7AzZ*	31.2 / 28.9	**F**4AzE	27.8 / 25.5	**G**1AzE*	3.3 / 3.0	**E**anAzE*	**0.0 / 0.0**
D7AzE	52.7 / 48.6	**F**5AzZ*	**0.0 / 0.0**	**G**2AzZ*	**0.0 / 0.0**		
E4AzZ	20.0 / 18.5	**F**5AzE	6.9 / 6.8	**G**3AzZ*	8.9 / 7.1		
E4AzE*	**0.0 / 0.0**	**F**6AzZ*	17.1 / 15.5	**G**3AzE	30.1 / 26.8	**F**anAzZ*	**0.0 / 0.0**
E5AzE*	2.9 / 2.9	**F**6AzE	28.7 / 26.4			**F**anAzE	7.0 / 6.6

[a] Gas phase; theory: B3LYP/6-31G*; values in kJ mol^{-1}. [b] Species starred (*) equilibrates with (Tet) of Table 6 and 7, respectively. [c] See also for Δ*G* values determined at the G3B3 level. [d] In ref. 7a: **D***an*Az*Z* and **E***an*Az*E* values related to **D***an* (*i.e.*, 11.9, 11.6, **0.0**); **F***an*Az*Z* and **F***an*Az*E* values related to **F***an* (*i.e.*, 3.5, 10.1, **0.0**).



Scheme 51. Conformational preferences of azides selected from Table 3 (**A**Az– **C**Az) and Table 8 (**D**Az– **G**Az)

Table 9. Annular tautomerism of triazolo- and tetrazolotetrazoles (**D** – **G**): Relative energies (Δ*E*) / relative free energies (Δ*G*) [a,b]



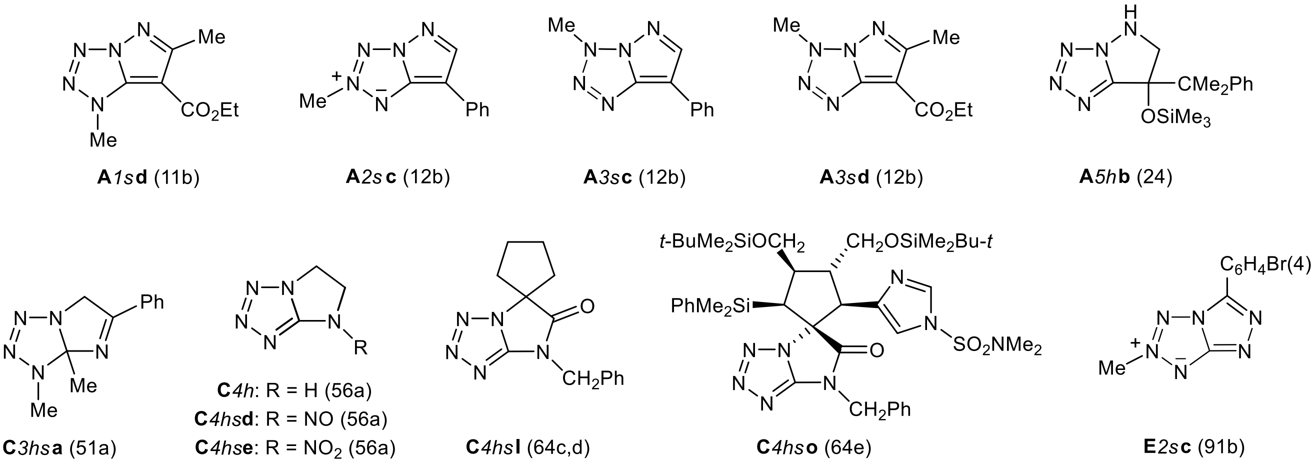
Series ↓ Type →	I	II	III	IV	V	VI
D *1, 3, 5, 7, 2, 6*	**0.0** / **0.0**	60.4 / 58.1	56.9 / 53.2	11.7 / 10.3	22.3 / 24.6	170.2 / 162.0
E *3, 1, 6, 4, 2, 5*	40.7 / 37.9	102.6 / 98.2	93.4 / 87.7	13.0 / 11.1	73.6 / 73.2	54.4 / 52.8
F *1, 3, 5, 7, 2, 6*	87.8 / 84.5	136.5 / 131.7	108.9 / 106.0	123.7 / 116.1	109.9 / 109.3	101.9 / 100.6
G *3, 1, 2*	**0.0** / **0.0**	60.2 [c] / 57.9			26.5 [c] / 29.0	

[a] Gas phase; theory: B3LYP/6-31G**; values in kJ mol^{-1}. [b] Ref. 6a. [c] *Cf.* B3LYP/6-311++G**: **II** 59.5, **V** 26.5 (ref. 112).

IV) EXPERIMENTAL STRUCTURAL METHODS

a) X-Ray diffraction

Azolotetrazoles that have been submitted to X-ray diffraction analysis are gathered in Figure 5. Regarding derivatives with an *N*-unsubstituted tetrazolic half-ring, fully conjugated (10π) structures have not been studied so far; there are only examples fused to a hydrogenated ring, such as **A***5h***b**, **C***4h*, and **C***4hs***d,e,l,o**.

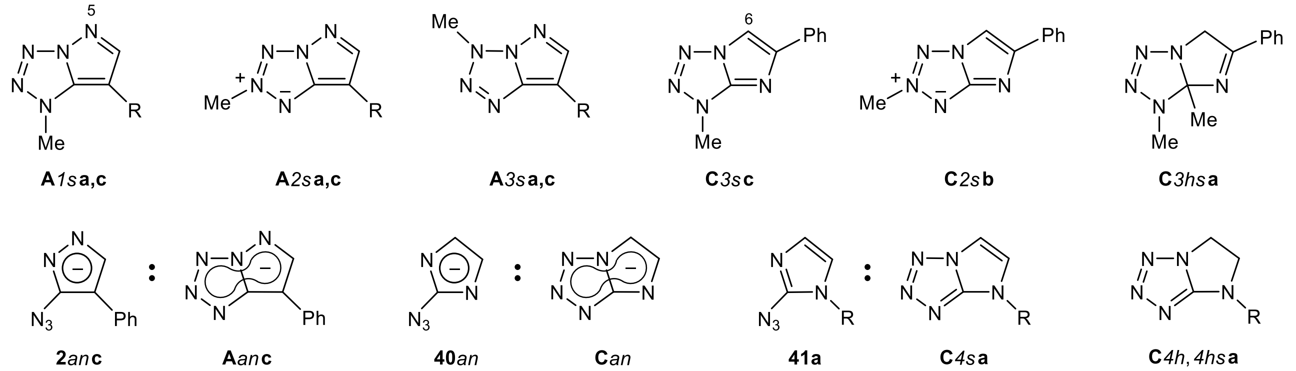


A*1s***d** (11b) **A***2s***c** (12b) **A***3s***c** (12b) **A***3s***d** (12b) **A***5h***b** (24)

C*3hs***a** (51a) **C***4h*: R = H (56a) **C***4hs***d**: R = NO (56a) **C***4hs***e**: R = NO_2 (56a) **C***4hs***l** (64c,d) **C***4hs***o** (64e) **E***2s***c** (91b)

Figure 5. Compounds **A**, **C**, and **E** studied by X-ray diffraction
(in parentheses: references)

Table 10. ^{1}H NMR data of selected compounds **A** and **C** (including corresponding azides) [a]



A*1s***a,c** **A***2s***a,c** **A***3s***a,c** **C***3s***c** **C***2s***b** **C***3hs***a**

2*an***c** **A***an***c** **40***an* **C***an* **41a** **C***4s***a** **C***4h,4hs***a**

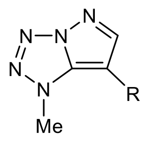
Compd. (ref.)	R	6-H	7-H	NMe	Solvent	Compd. (ref.)	R	5-H	6-H	NMe	Solvent
A*1s***a** (11b)	H	7.76	5.80	4.11	$CDCl_3$	**C***3s***c** (42)			7.79	4.12	$CDCl_3$
A*2s***a** (11b)	H	7.86	6.05	4.43	$CDCl_3$	**C***2s***b** (42)			7.80	4.41	$CDCl_3$
A*3s***a** (12b)	H	7.75	6.27	4.44	$CDCl_3$	**40***an* (35a)		6.89			[b]
A*1s***c** (11b)	Ph	7.93		4.20	$CDCl_3$	**C***an* (11a, 35a)		7.21	7.43		[b]
A*2s***c** (11b)	Ph	8.22		4.46	$CDCl_3$	**41a** (34)	COMe	7.51	6.89		DMSO-d_6
A*3s***c** (12b)	Ph	8.06		4.40	$CDCl_3$	**C***4s***a** (34)	COMe	8.32	8.06		DMSO-d_6
2*an***c** (5)		7.95			KOH/D_2O	**C***3hs***a** (51a)			[c]	3.33	$CDCl_3$
A*an***c** (5)		8.16			KOH/D_2O	**C***4h* (23)	H	4.19	4.39		DMSO-d_6
						C*4hs***a** (23)	Me	4.11	4.39	2.86	DMSO-d_6

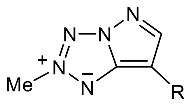
[a] Values (δ, ppm) from $SiMe_4$. [b] Solvent: $NaOH/D_2O$/DMSO-d_6 (ref. 35a) or NaH/DMSO-d_6 (ref. 11a). [c] 4.29, 5.04 (AB$_q$, J = 17 Hz).

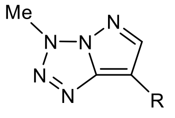
b) Spectroscopic methods

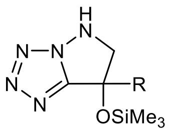
Almost all of the derivatives dealt with in Sections (II) and (III) have been characterized by IR, UV/Vis, NMR and/or MS spectra. For a selection of data, see Tables 10–12; some comments are included below.

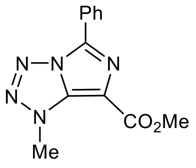
Table 11. ^{13}C and ^{15}N NMR data of selected compounds **A**–**E** [a]

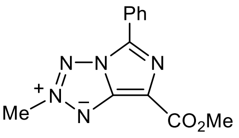

A*1s***a,c**

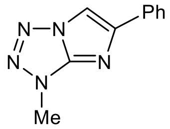

A*2s***a,c**

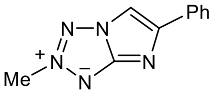

A*3s***a,c**

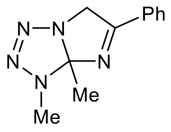

A*5h***b**

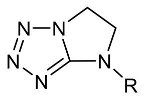

B*1s***m**

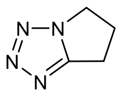

B*2s***c**

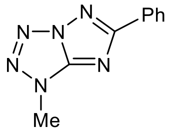

C*3s***c**

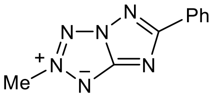

C*2s***b**

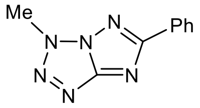

C*3hs***a**

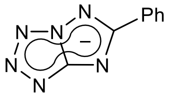

C*4h*; *4hs***a,e**

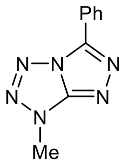

154

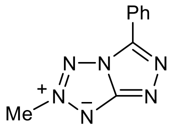

D*1s***a**


D*2s***a**


D*3s***a**


D*an***a**


E*3s***a**

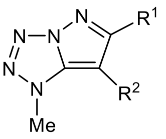

E*2s***a**

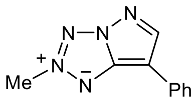
Compd. (ref.)	R	C(3a)	C(5)	C(6)	C(7)	C(7a)	NMe	N(1)	N(2)	N(3)	N(4)	N(6/7)	Solvent
A*1s***a** (11b)	H			146.9	78.2	138.4	35.7						$CDCl_3$
A*2s***a** (11b)	H			146.8	80.8	149.8	42.4						$CDCl_3$
A*3s***a** (12b)	H			145.18	86.58	152.04	36.11						$CDCl_3$
A*1s***c** (11b)	Ph			144.9	96.7	134.9	37.2						$CDCl_3$
A*2s***c** (12b) [b]	Ph			143.26	98.94	147.81	42.47						$CDCl_3$
A*3s***c** (12b)	Ph			141.17	104.05	149.33	35.85						$CDCl_3$
A*5h***b** (24)	[c]			45.32	65.81	156.97							$CDCl_3$
B*1s***m** (26b)			128.8		101.1	139.4	36.5	186.2	375.4	325.4	255.7	269.3	$CDCl_3$
B*2s***c** (26b)			127.0		105.4	150.4	43.1	280.8	276.4	311.3	242.5	277.3	$CDCl_3$
C*3s***c** (42)		145.3	150.4	101.9			33.9						$CDCl_3$
C*2s***b** (42)		156.3	151.4	99.2			42.4						DMSO-*d*$_6$
C*3hs***a** (51a)		109.7	166.9	60.8			33.2						$CDCl_3$
C*4h* (23, 56a) [d]	H	165.9	43.2	51.5				–29.2	21.0	–104.1	–349.2	–163.3	DMSO-*d*$_6$
C*4hs***a** (23)	Me	166.0	42.9	58.9			34.6						DMSO-*d*$_6$
C*4hs***e** (56a)	NO_2	158.6	42.9	58.2				–24.5	26.1	–83.2	–203.5	–156.8	[e]
154 (23) [f, g]			44.5	18.3	27.5	163.2							DMSO-*d*$_6$
D*1s***a** (71)				168.4		150.2	35.1						DMSO-*d*$_6$
D*2s***a** (71)				169.0		156.2	43.2						DMSO-*d*$_6$
D*3s***a** (12b)				167.98		161.94	37.92						DMSO-*d*$_6$
D*an***a** (71)				153.5		165.5							DMSO-*d*$_6$
E*3s***a** (71)		154.5		139.7			34.4						DMSO-*d*$_6$
E*2s***a** (71)		164.6		136.9			43.7						DMSO-*d*$_6$

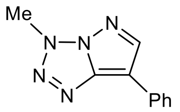
[a] Values (δ, ppm): ^{13}C from $SiMe_4$; ^{15}N from liquid NH_3 with $MeNO_2$ as external reference (ref. 26b) or from $MeNO_2$ (ref. 56a). [b] See also ref. 11b [value of C(7a) obviously misprinted]. [c] R = CMe_2Ph. [d] Ref. 23 refers to ^{13}C; ref. 56a refers to ^{15}N. [e] Solvent: acetone-*d*$_6$ (^{13}C), DMSO-*d*$_6$ (^{15}N). [f] Entry corrects ref. 3 / Table 6 (compound **Aa**) because of wrong assignment of C(6) and C(7) values and the erroneous footnote [b]. [g] In agreement with ref. 113: C(5) 44.18, C(6) 18.26, C(7) 27.21, C(7a) 162.5 [$CDCl_3$].

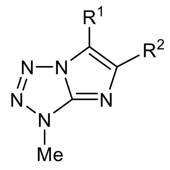
(i) ^{1}H NMR (Table 10): Analytically important is the downfield shift of the NMe signal observed on passing from **A***1s* to **A***2s* (and **A***3s*) and from **C***3s* to **C***2s* [in the case of **A***2s* and **A***3s* the distinction occurs *via* ^{13}C NMR, *i.e.*, NMe signal in conjunction with C(7a)]. Also remarkably: cyclization of the azides **2***an***c**, **40***an*, and **41a** to the bicycles **A***an***c**, **C***an*, and **C***4s***a** is associated with a downfield shift of the ring protons.
(ii) ^{13}C and ^{15}N NMR (Table 11): For discerning the isomers within the fully conjugated series **A***s*–**E***s*, the NMe and bridgehead signals C(7a) / C(3a) serve as diagnostic tools, *i.e.*, with the mesoions **A***2s*–**E***2s* both signals appear markedly downfield, whereas in the case of the types **A***3s* and **D***3s* only the bridgehead signal shows that phenomenon. Discrimination of **B***1s* from **B***2s* occurred also *via* ^{15}N signals.
(iii) IR, UV/Vis, and EIMS (Table 12): Typical of carbonyl groups attached to electron-rich azoles, the IR C=O absorptions of the respective derivatives **A***1s* and **C***3s*, *2s* are shown at low wave numbers. Comparing the UV/Vis spectra of **A***1s* / **A***2s* and **C***3s* / **C***2s*, those of the mesoions are characterized by a bathochromic

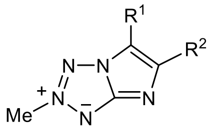
Table 12. IR, UV/Vis, and EIMS data of selected compounds **A**, **C**, and **D**

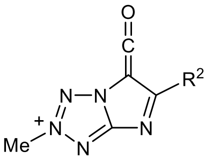

A*1s***b-d**

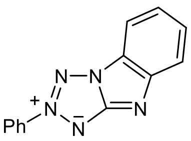

A*2s***c**

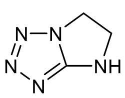

A*3s***c**

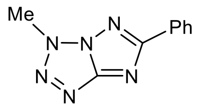

C*3s***c,f,i,j**


C*2s***b,d,e,g,h**


[**C***2s***e,h**−Me]


C*2sf***a**


C*4h*


D*3s***a**

Compd. (ref.)	R^{1} / R^{2}	$\tilde{\nu}$(cm^{-1}) [a]	Compd. (ref.)	R^{1} / R^{2}	$\tilde{\nu}$(cm^{-1}) [a]	Compd. (ref.)	R^{1} / R^{2}	$\tilde{\nu}$(cm^{-1}) [a]
A*1s***b** (11a)	H / CO$_2$Et	1680	**C***3s***c** (42)	H / Ph	3109	**C***2s***b** (42)	H / Ph	3135
A*1s***d** (11a)	Me / CO$_2$Et	1690	**C***3s***f** (42)	COMe / Me	1657	**C***2s***e** (42)	COMe / Me	1631
C*2s***d** (42)	COPh / Me	1663	**C***3s***j** (42)	COMe / Ph	1656	**C***2s***h** (42)	COMe / Ph	1663
		λ_{max} (nm) [b]			λ_{max} (nm) [b]			λ_{max} (nm) [b]
A*1s***c** (11b)	H / Ph	298sh (3.46)	**C***3s***c** (42)	H / Ph	289 (3.94)	**C***2s***b** (42)	H / Ph	328 (3.98)
A*2s***c** (11b) [c]		346 (3.15)	**C***3s***i** (42)	Br / Ph	296 (3.84)	**C***2s***g** (42)	Br / Ph	334 (3.88)
A*2s***c** (12b)		353 (3.56)	**C***3s***f** (42)	COMe / Me	279 (4.13)	**C***2s***e** (42)	COMe / Me	279 (4.16)
A*3s***c** (12b)		319 (3.81)	**C***3s***j** (42)	COMe / Ph	289 (4.06)	**C***2s***h** (42)	COMe / Ph	280 (4.08)
C*4h* (114)		232 (3.25)	**C***2sf***a** (44a)		393 (3.45)	**D***3s***a** (12b)		266 (4.18)
		m/z (%)			*m/z* (%)			*m/z* (%)
C*3s***c** (42)	H / Ph	199 (M^{+}, 18), 103 (100)	**C***3s***f** (42)	COMe / Me	179 (M^{+}, 24), 108 (100)	**C***3s***j** (42)	COMe / Ph	241 (M^{+}, 18), 170 (100)
C*2s***b** (42)	H / Ph	199 (M^{+}, 100), 103 (38)	**C***2s***e** (42)	COMe / Me	179 (M^{+}, 76), 164 (100) [d]	**C***2s***h** (42)	COMe / Ph	241 (M^{+}, 100), 226 (98) [d]

[a] In KBr; C=O and CH$_{imidazole}$, respectively. [b] Longest wavelength maximum (in parentheses: log ε); solvent: EtOH [**A***1s***c**, **A***2s***c** (ref. 11b), **C***4h*], CH$_2$Cl$_2$ [**A***2s***c** (ref. 12b), **A***3s***c**, **D***3s***a**], MeOH (**C***3s***c,f,i,j**; **C***2s***b,e,g,h**); MeCN (**C***2sf***a**). [c] Erroneously viewed as **A***3s***c**; for revision, see ref. 12b. [d] Corresponds to the ketenic species [**C***2s***e**/**h**−Me].

shift of the longest wavelength maximum. As to the EIMS data of **C***3s* and **C***2s*, the latter show a more intense molecular ion which, in two cases, represents the base peak. A salient feature of the ketones **C***2s***e** and **C***2s***h** constitutes an intense [M–15] peak which corresponds to the ketenic species [**C***2s***e,h** – Me].

A great number of the above spectroscopic properties match observations made earlier in the class of fully conjugated 1- and 2-substituted pyrrolotetrazoles.[3]

CONCLUSION

The material accumulated in the preceding Sections illustrates that studies on the seven title systems **A**–**G** are well advanced. Preparative work – started in the 1960s – established the basic knowledge till the turn of the century. Thereafter experimental work, more often, gave results that might be routinely predicted, although novel findings continued to be made, such as the formation of the pyrazolotetrazoles **A***5h***a-f** or the imidazotetrazoles **C***4hs***l-o** [Sections (II / 1. d), (II / 3. c); Schemes 10, 29]. But despite much progress there are preparative desiderata: Thus, no information exists whether azolotetrazoles of the type **A***1s*, *2s* and **D***1s*, *2s* can be obtained from 5-functionalized *N*-aminotetrazoliums, or whether derivatives **A***1s*–*3s* are capable of undergoing S_E reactions. "Care should be exercised" (*cf.* ref. 1) regarding fully conjugated azolotetrazoles that were said to have formed through ring closure of azidoazoles (isolable or intermediary ones); some of such claims may be revisited. Theoretical studies have been intensified during the last two decades, and here, for obvious reasons, the azido–tetrazole tautomerism is receiving much interest: quite a number of calculations in this field are consistent with experimental findings.

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