4*H*-Imidazoles and Imidazoles from Anionic and Dipolar Electrocyclization Reactions of 2,4-Diazapenta-1,3-dienes

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Dedicated to Prof. Dr. Christian Reichardt on the occasion of his 70th birthday

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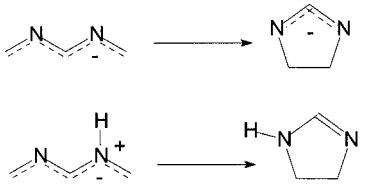
1-Amino-2,4-diazapenta-1,3-dienes **5** are synthesized by the activation of *N*-acylamidines **2** with trifluoromethanesulfonic anhydride and subsequent condensation with amino compounds **4**. When the amino compounds **4** possess electron-withdrawing substituents (e.g. alkoxycarbonyl groups, fluorenyl derivatives) this condensation leads instead to 4*H*-imidazoles **6** and imidazoles **7**. These reactions are considered to be 1,5-dipolar electrocyclization reactions of 1,5-dipoles that are tautomers of the 2,4-diazapenta-1,3-dienes **5**. Deprotonation of **5b**,**f** by the use of strong organic bases yields the corresponding imidazoles **7b**,**c** after amine elimination during the anionic 1,5-electrocyclization reaction. Results of quantum chemical model calculations (RHF, MP2, SCS-MP2, G3, DFT) performed on the parent 2,4-diazapentadienyl anion **9a**, its lithium compound **9a-Li**, the corresponding 1,5-dipole **12** and their substituted derivatives are in accordance with the suggested reaction mechanism. X-ray data are given for the 2,4-diazapenta-1,3-dienes **5a**·F_3CSO_3H, **5c**, **5d**·F_3CSO_3H, **5e**,**f** and the spirocyclic 4*H*-imidazole derivatives **6b–d**.

Introduction

The cyclization of open-chain compounds presents a straightforward and versatile method for the synthesis of carbo- and heterocyclic compounds. From the mechanistic and stereochemical points of view, pericyclic reactions, in this case electrocyclization reactions, are of special interest because of the sterically defined mode in which the ring-closure reactions proceed.[1,2] Whereas neutral compounds often require higher temperatures, anionic and dipolar intermediates are sufficiently reactive to allow the formation of cyclic products under well-controlled mild reaction conditions.

In earlier work, we developed a set of rules that allows to predict the thermodynamics of electrocyclization reactions of open-chain compounds that contain heteroatoms depending on the position of the heteroatoms.[3,4] Thus, anionic azapolyenyl-type precursors readily cyclize if the nitrogen atom is at an even-numbered position within the unsaturated chain. In contrast, cationic precursors lead to heterocycles if the nitrogen atom occupies an odd-numbered position.[5] On the other hand, if the thermodynamic barriers are not prohibitive, ring-opening reactions are predicted for anionic cyclic polyenyl systems with heteroatoms in even-numbered positions and for cations with heteroatoms in odd-numbered positions.

In this report we describe the results of the ring-closure reactions of 2,4-diazapentadienyl anions and the corresponding dipoles. The aim of this work was to investigate the scope and limitations of this approach, for example, in the synthesis of non-aromatic heterocycles such as 4*H*-imidazoles. Furthermore, we have studied the influence of electron-withdrawing substituents on the mechanism of these cyclization reactions; there are two mechanisms that seem reasonable, the anionic mode and the 1,5-dipolar mode (Scheme 1).



Scheme 1

There are only a few publications that report such reactions. Hunter and Sim[6,7] observed the formation of 4,5-dihydro-2,4,5-triphenylimidazole ("amarine") from 1,3,5-triphenyl-2,4-diazapenta-1,4-diene ("hydrobenzamide") via intermediate 2,4-diazapentadienyl anions[8,9] after depro-

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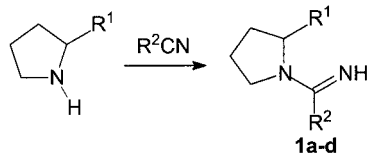
tonation with phenyllithium and subsequent work up with acetic acid. For 2-azapentadienyl anions[10] Hunter and co-workers also observed similar ring-formation reactions that produced dihydropyrroles.[11,12] Later, this reaction was applied to the synthesis of 2,3-dihydroindoles[13,14] and pyrrolizines.[15] 2-Azapentadienes also undergo thermal cyclization reactions to yield five-membered ring systems. Grigg and co-workers[16,17] attributed this behavior to an intermediate proton shift which leads to transient 1,5-dipoles that cyclize readily or may be trapped by appropriate dienophiles.[18]



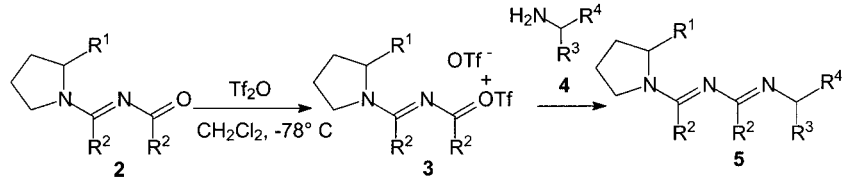
	R^1	R^2	Yield (%)
1a	H	Ph	80
1b	H	4-Tol	57
1c	H	4-MeOPh	82
1d	CH_2OCH_3	Ph	64

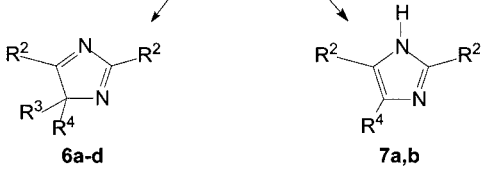
Scheme 2

Results and Discussion

2,4-Diazapenta-1,3-dienes **5** and 2,4-diazapenta-1,4-dienes may be envisaged as precursors for 2,4-diazapentadienyl anions and the corresponding lithium compounds. To allow the formation of doubly unsaturated (aromatic) heterocycles an amino functionality was incorporated into the 1-position as a potential leaving group.

From our experience of oligonitrile synthesis we designed the following pathway to synthesize the 1-amino-substituted 2,4-diazapenta-1,3-dienes **5**.[19] The preparation of **5** is summarized in Schemes 2−4. The secondary amidines **1** were prepared by the nucleophilic addition of amines to nitriles, which were subsequently acylated to yield the *N*-acylamidines **2**, as described by Katritzky and co-workers.[20] For the subsequent condensation with primary amines the *N*-acylamidines **2** were activated by use of trifluoro-





	R^3	R^4
4a	Ph	Me
4b	Ph	H
4c	Ph	Ph
4d	H	CF_3
4e	Ph	CF_3
4f	Me	CO_2Et
4g	*i*Pr	CO_2Et
4h	Ph	Me

	R^1	R^2	R^3	R^4	Yield (%)
5a	H	Ph	Ph	Me	54
5b	H	Ph	Ph	H	47
5c	H	Ph	Ph	Ph	50
5d	H	Ph	H	CF_3	51
5e	H	Ph	Ph	CF_3	57
5f	H	Ph	Me	CO_2Et	45
5g	H	Ph	*i*Pr	CO_2Et	57
5h	CH_2OCH_3	Ph	Ph	Me	14

	R^2	$R^3 = R^4$	Yield (%)
6a	Ph	CO_2Et	15
6b	Ph	fluorene*	41
6c	4-Tol	fluorene*	80
6d	4-MeOPh	fluorene*	74

	R^2	R^4	Yield (%)
7a	Ph	CO_2Et	72
7b	Ph	Ph	43

* spiro compound

Scheme 4

methanesulfonic anhydride[21] to give the cationic intermediates **3**, which were then treated at a low temperature with primary amines **4** (or with equimolar mixtures of the ammonium hydrochlorides **4**·HCl and triethylamine) to give the 1-amino-2,4-diazapenta-1,3-dienes **5a**−**g** in 45−57% yield (**5a** was isolated as the corresponding triflate, protonated at N4) (Scheme 4). This reaction works well for aromatic amines as well as for trifluoromethylamines and amino acids, for example, alaninates and valinates. The (*R*)-methoxymethyl-pyrrolidine (RMP) derivative **5h** was formed in a low yield.

The molecular structures of the new 1-amino-2,4-diazapenta-1,3-dienes **5a**·F_3CSO_3H, **5c**, **5d**·F_3CSO_3H, **5e**,**f** were determined by X-ray crystallography.[22] The neutral compounds **5c**,**e**,**f** have non-planar C=N−C=N skeletons (C1=N2−C3=N4 torsional angles: **5c**: 132.9°; **5e**: 129.4°; **5f**: 81.8°), which is a characteristic feature of 1,3-diazabuta-1,3-dienes[23,24] (see Figure 1 for **5c**). The CN bonds differ in length (e.g. **5c**: C1=N2 1.303 Å, N2−C3 1.393 Å, C3=N4 1.287 Å) as is expected for such an alignment of amidine and imine functions. The protonated compounds **5a** and **5d** are less twisted [C1=N2−C3=N4 torsional angles: **5a**: 155.9° (see Figure 1); **5d**: 159.1°] and the differences in the CN bond lengths (e.g. **5a**: C1=N2 1.341 Å, N2−C3 1.313 Å, C3=N4 1.330 Å) are not as pronounced due to better π-conjugation in the cationic species.

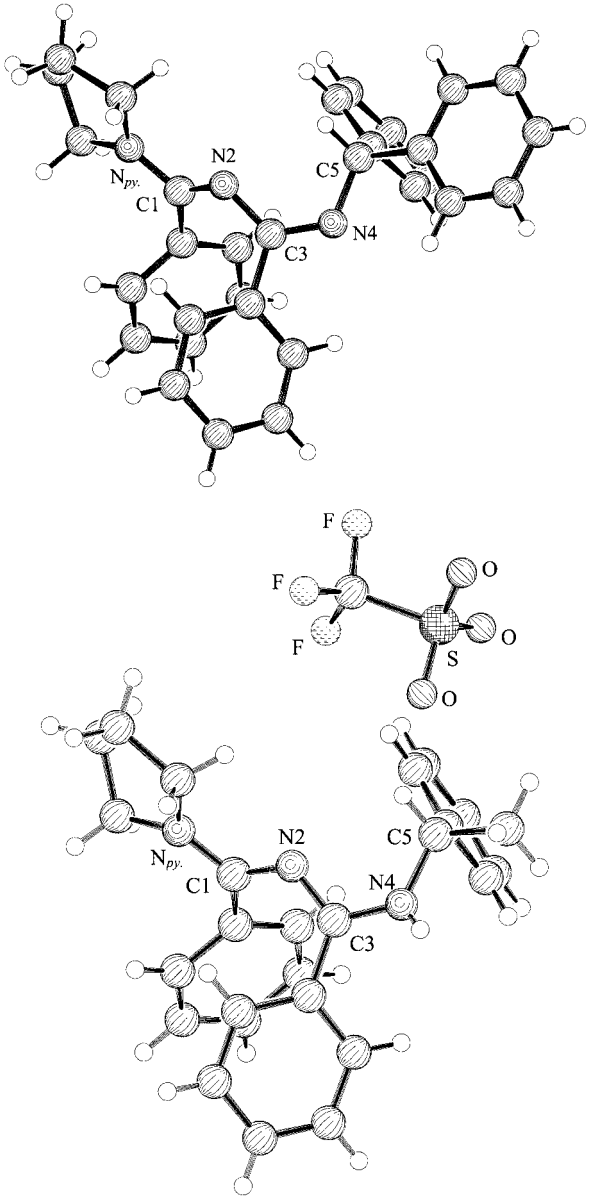


Figure 1. Molecular structures of **5c** (top) and of **5a**·F_3CSO_3H (bottom) (determined by X-ray crystallography)

In several cases, however, the condensation reactions of **3** and **4** took a surprising alternative route. Instead of the 2,4-diazapentadienes **5**, 4*H*-imidazole derivatives **6** and imidazoles **7** were obtained in moderate (15%) to good (80%) yields. The 4*H*-imidazoles deserve special attention because their non-aromatic cyclic structure, with a fixed *s*-*cis*-1,3-diazabutadiene subunit, makes them attractive starting materials for further transformations, for example, in hetero-Diels−Alder reactions. Inspection of the substitution patterns of the reagents shows that the condensation reactions occur mainly when the primary amines contain strongly acidifying functions, such as two ester functionalities (aminomalonate) or a fluorenyl group (Scheme 4). From the products obtained it is clear that after the condensation step a cyclization reaction must occur in the presence of the two moles of trifluoromethanesulfonic acid that are liberated during the condensation reaction. Finally elimination of the secondary amine leads to the protonated imidazole derivatives **6** and **7** and the corresponding ammonium salts. Imidazole **7b**, which was obtained from **2a** after triflate anhydride activation and reaction with ethyl phenylglycinate, deserves special attention. Its formation requires the complete loss of an ethoxycarbonyl group in order to achieve the aromatic electron sextet of the imidazole. It is surprising that this unusual reaction (43% yield) occurs under the mild reaction conditions (−78 °C, room temperature) applied. In contrast, the aminomalonate-derived compound **6a** was isolated as the corresponding 4*H*-imidazole.

The molecular structures of the spiro-fluorene compounds **6b**−**d** were obtained by X-ray crystallography (for **6b**, see Figure 2) and exhibit features typical of spiro com-

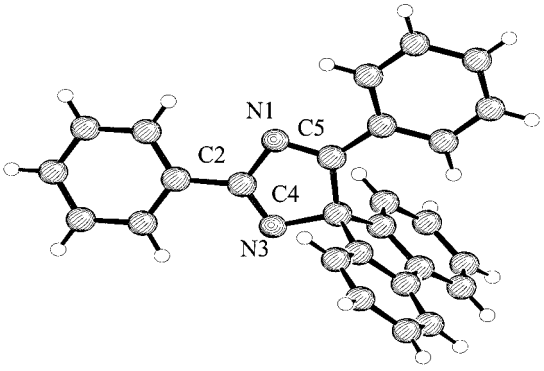
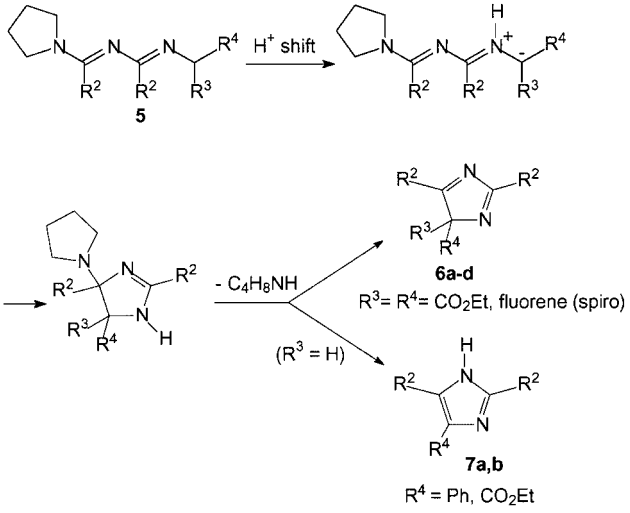


Figure 2. Molecular structure of **6b** (determined by X-ray crystallography)

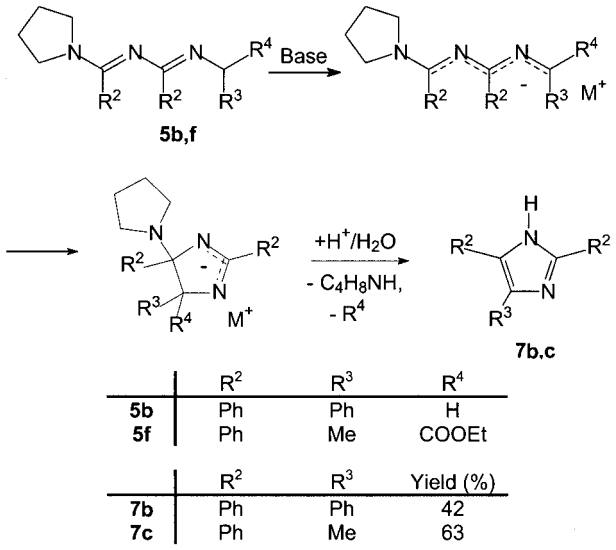
pounds. The additional aromatic substituents lie in the plane with the 4*H*-imidazole ring system.

With regard to the mechanism of such cyclization reactions, in the absence of base we assume an equilibrium between **5** and its tautomeric 1,5-dipolar form (azavinylogous azomethine ylide, in the presence of trifluoromethanesulfonic acid), which has the ability to undergo 1,5-dipolar electrocyclizations (Scheme 5).[16] Note that CF_3 groups are not sufficiently active as acidifying functionalities to induce proton shift and subsequent cyclization. On the other hand, it is surprising that the corresponding 2,4-diazapentadienes **5** are accessible from ethyl alaninate and ethyl valinate, but not from the glycinate; the presence of alkyl groups seems to reduce the CH acidity sufficiently to prevent the proton shift and the subsequent cyclization.



Scheme 5

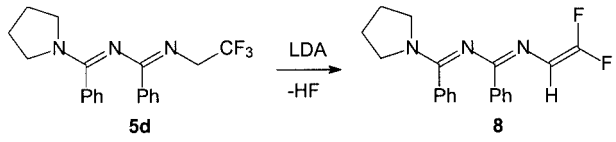
In order to convert the 2,4-diazapenta-1,3-dienes **5** into the corresponding lithium compounds, **5b** and **5f** were treated at a low temperature with strong base (1:1 KO*t*Bu/*n*BuLi for **5b**, lithium diisopropylamide for the more acidic **5f**) (Scheme 6). At first, a deep purple color was observed, which we attribute to the intermediate anion. After a few minutes, the color disappeared, and after aqueous work up the imidazoles **7a** and **7c** were obtained in 42 and 63% yield. The formation of these compounds is interpreted as being the result of an anionic 6π-cyclization with subsequent β-elimination of the heterocyclic amine to realize the energetically favorable aromatic 6π-electron system of the imidazole. Deprotonation of **5d** did not lead to the corresponding imidazole, but to the elimination of HF to furnish the corresponding 2,4-diazahexa-1,3,5-triene **8** (Scheme 7). The other 2,4-diazapenta-1,3-dienes (**5a**, **5c**, **5e**, **5h**, **5i**) were recovered in 30−80% yield after deprotonation and aqueous work up without cyclization, although the deep purple color of the intermediate anions was always observed at low temperatures.



	R2	R3	R4
5b	Ph	Ph	H
5f	Ph	Me	COOEt

	R2	R3	Yield (%)
7b	Ph	Ph	42
7c	Ph	Me	63

Scheme 6



Scheme 7

Quantum Chemical Calculations

In order to understand and interpret the experimentally observed cyclization reactions the thermodynamics and kinetics of the ring-closing step were calculated by means of quantum chemical model calculations. Based on previous experience[25] we have used RHF theory (6-31G* basis set) and MP2 single points to evaluate the relative energies of the species in question. The SCS-MP2 single points[26] proved to be especially useful, and are available at no extra cost from the MP2-outputs. To calibrate the unsubstituted systems we employed the G3 theory,[27] which indeed demonstrated the superior performance of the SCS-MP2 data (see below). The DFT method B3LYP/6-31G* was also used, but, according to our findings, it seems to be less well suited to anionic systems since it both overestimates activation barriers and underestimates heats of reaction.[25] All stationary points were checked by frequency analyses (minimum or transition state); the relative energies include zero point corrections (unscaled, except for G3). These calculations were performed using the Gaussian98 suite of programs.[28] For comparison, semiempirical PM3[29,30] data, obtained from the MOPAC93 package, are included.[31]

First, we discuss the results of the quantum chemical calculations performed on the anionic cyclization of the unsubstituted model system 2,4-diazapentadienyl anion **9a**. The results for the parent system **9a** in three configurations (W-shape, sickle-shape and U-shape), the transition states

Table 1. Relative energies (kcal·mol^{-1}) of the stationary points of the cyclization of the 2,4-diazapentadienyl anion **9a** at various levels of theory

Method	W	TS (W−S)	Sickle	TS (S−U)	U	TS (U−Cycle)	Cycle
PM3	1.05	13.47	0.59	14.38	0.00	28.91	−24.90
RHF/6-31G*	0.00	22.35	1.69	20.69	4.48	25.52	−32.60
MP2/6-31G*	0.00	24.06	1.41	22.13	3.04	9.51	−30.14
SCS-MP2/6-31G*	0.00	22.56	1.43	20.75	3.66	12.34	−29.90
G3	0.00	20.71	1.13	17.67	1.10	11.14	−25.34
B3LYP/6-31G*	0.00	27.30	2.08	25.60	4.77	19.41	−17.81

Table 2. Relative energies (kcal·mol^{-1}) of the stationary points in the cyclization of the 2,4-diazapentadienyllithium compound **9a-Li** at various levels of theory

Method	W	TS (W−S)	Sickle	TS (S−U)	U	TS (U−Cycle)	Cycle
PM3	0.00	20.32	12.08	23.46	20.87	38.60	−12.52
RHF/6-31G*	0.00	19.45	6.38	15.58	13.13	23.47	−24.26
MP2/6-31G*	0.00	29.33	9.21	19.74	11.79	12.54	−15.88
SCS-MP2/6-31G*	0.00	26.77	9.17	19.40	13.50	15.59	−16.05
G3	0.00	30.05	9.85	—[a]	14.46	17.11	−12.72
B3LYP/6-31G*	0.00	31.68	8.98	21.72	14.46	20.66	−6.90
B3LYP/6-311++G**	0.00	33.27	11.25	24.74	17.60	24.21	−4.92

[a] No transition state could be localized using G3 theory (M2/6-31G* optimization).

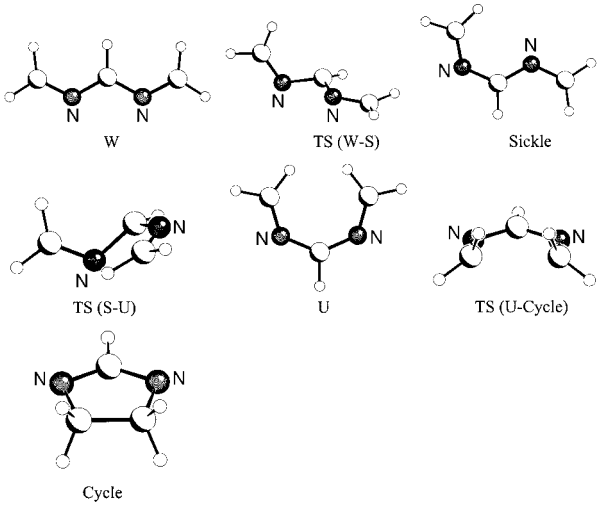


Figure 3. Molecular structures corresponding to the stationary points in the cyclization of the 2,4-diazapentadienyl anion **9a** (MP2/6-31G*//MP2/6-31G*)

of the internal rotations and the pericyclic (disrotatory) electrocyclization, and for the cyclic isomer are summarized in Table 1 and Figure 3. The lowest energy form of the 2,4-diazapentadienyl anion is predicted to be a W-shaped structure, followed by sickle- and U-shaped forms. To convert the lowest energy W-form into the ring isomer two internal rotations have to take place. For the W−sickle interconversion we calculate an activation barrier of 20.7 kcal·mol^{-1} (G3), which is the highest barrier en route to the cyclic isomer. The sickle- and U-forms are only slightly higher in energy than the W-form (ca. 1.1 kcal·mol^{-1}). For the rather exothermic cyclization ($\Delta H_r \approx -25.3$ kcal·mol^{-1}) of the U-form a surprisingly small barrier has been calculated (11.1 kcal·mol^{-1}). As seen in Table 1 the relative energies are strongly dependent on the method employed. The MP2 results, especially the SCS-MP2 data, are not far off the G3 values, but the B3LYP data overestimate the barriers and underestimate the heat of reaction. The semiempirical PM3 method predicts the reaction enthalpy quite well, but has problems with the relative energies of the conformers and with the activation barriers. In summary, from the calculations performed on the unsubstituted anion **9a** without a counterion, an exothermic cyclization reaction of the U-shaped form is expected, but substantial barriers may delay the interconversion of the different isomers.

The calculated energies for all stationary points in the electrocyclization of 2,4-diazapentadienyllithium **9a-Li**, which is taken as a model for the contact ion pair (without further coordination by aggregation or solvation), are summarized in Table 2, Figure 4. The best structure corresponds to a W-shaped form with Li^+ coordinating to both nitrogen lone pairs; the sickle- and U-forms have significantly higher energies. According to the G3 data, the barriers for internal rotations and for the electrocyclization are predicted to be higher than those of the anion by ca. 6 to 10 kcal·mol^{-1}, probably due to the less favorable coordination of lithium. For the same reason the ring closure is less exothermic since lithium is only mono-hapto coordinated in this model structure. Nevertheless, these data are in accordance with the experimental results under the conditions employed.

We also investigated the influence of substituents on the structures, thermodynamics and kinetics of the electrocyclization reaction of substituted model anions **9a**−**h** (in the absence of a counterion, see Table 3, Figure 5). Since G3

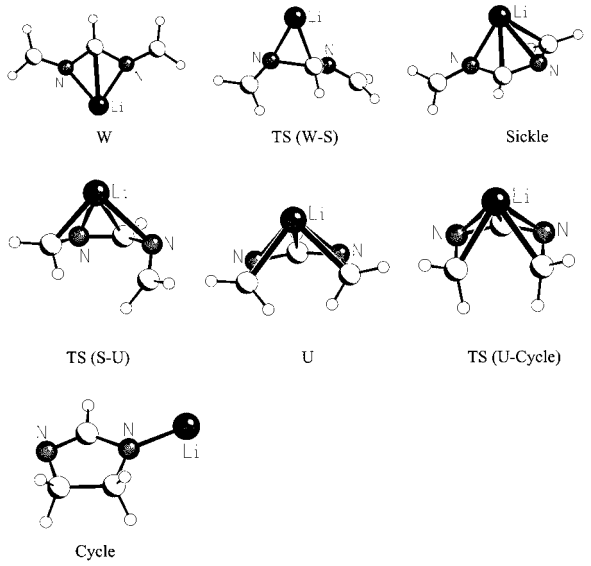


Figure 4. Molecular structures corresponding to the stationary points in the cyclization of the 2,4-diazapentadienyllithium compound **9a-Li** (MP2/6-31G*//MP2/6-31G*)

Table 3. Relative energies (kcal·mol^{-1}) of the stationary points in the cyclization of substituted 2,4-diazapentadienyl anions **9a**−**h** at the MP2/6-31G*, SCS-MP2/6-31G* and B3LYP/6-31G* levels

Compound	Method	W	Sickle	U	TS (U−Cycle)	Cycle
9a	MP2	0.00	1.41	3.04	9.51	−30.41
	SCS-MP2	0.00	1.43	3.66	12.34	−29.90
	B3LYP	0.00	2.08	4.77	19.41	−17.81
9b	MP2	8.41	2.70	0.00	9.43	−27.48
	SCS-MP2	8.41	2.47	0.00	12.10	−27.97
	B3LYP	9.61	2.90	0.00	18.10	−17.11
9c	MP2	0.00	0.71	5.24	11.76	−6.53
	SCS-MP2	0.00	0.82	5.71	14.47	−6.81
	B3LYP	0.00	1.64	6.92	24.73	12.14
9d	MP2	3.84	0.43	0.00	6.33	−10.85
	SCS-MP2	3.58	0.30	0.00	8.73	−11.91
	B3LYP	4.64	0.65	0.00	17.46	4.37
9e	MP2	0.00	0.09	4.58	15.04	−14.54
	SCS-MP2	0.00	0.03	5.06	17.43	−14.22
	B3LYP	0.00	1.49	6.19	22.63	−0.41
9f	MP2	0.00	0.69	2.86	11.60	−27.96
	SCS-MP2	0.00	0.70	3.42	13.66	−27.52
	B3LYP	0.00	1.20	4.90	18.91	−14.35
9g	MP2	0.00	0.75	3.72	13.73	−18.83
	SCS-MP2	0.00	0.78	4.22	15.88	−18.76
	B3LYP	0.00	1.24	5.61	21.12	−4.91
9h	MP2	0.26	0.00	6.95	11.82	−5.58
	SCS-MP2	0.28	0.00	7.07	14.72	−5.57
	B3LYP	0.00	1.09	9.65	21.20	8.25

calculations on these species are not feasible due to the size of the molecules, we consider the SCS-MP2 data to be the most reliable. All substituents lead to a less exothermic cyclization reaction, probably due to a better stabilization of the open form relative to the cyclic structure, as seen for the 1-methoxycarbonyl (**9e**), phenyl (**9b**−**d**) and fluorenyl (**9h**) derivatives. Phenyl groups in the 3-position exert a strong steric effect, which destabilizes the W- and sickle-

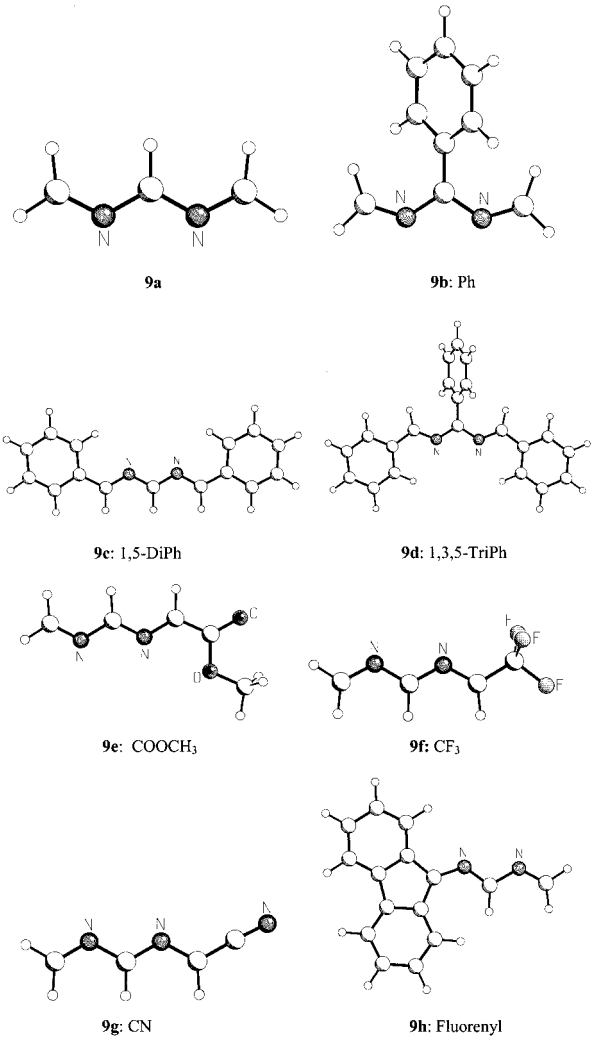


Figure 5. Molecular structures of various substituted 2,4-diazapentadienyl anions **9a**−**h** (MP2/6-31G*//RHF/6-31G*)

shaped forms, and consequently the U-shaped structure is favored. According to the calculations, the barrier to ring closure is strongly reduced for the 1,3,5-triphenyl-2,4-diazapentadienyl anion **9d** (SCS-MP2: 8.7 kcal·mol^{-1}), both for steric and electronic reasons; otherwise there is little variation (12−18 kcal·mol^{-1}) in this barrier.

To model the 1,5-dipolar electrocyclization reaction, we performed calculations on the 2,4-diazapenta-1,3-diene **10a**, its isomer the 2,4-diazapenta-1,4-diene **11a**, the 1,5-dipole **12a** and the transition states for its internal rotations and cyclization, and the ring form **13a** (see Table 4, Figure 6). Again we find a strong dependence on the method employed. Here, SCS-MP2/6-31G* single point data are not as close to the G3 values as was the case for the anions (Table 1), which might be due to the relatively poor description of the electronic structure of such 1,5-dipoles by this basis set. In this case, B3LYP is not far off the G3 data. The best structure for the 2,4-diazapenta-1,3-dienes **10a** is not a planar penta-1,3-diene-like structure but a strongly twisted *gauche* conformation, as found in 1,3-diazabutadi-

Table 4. Relative energies (kcal·mol^{-1}) of 2,4-diazapenta-1,3-diene **10a**, 2,4-diazapenta-1,4-diene **11a** and the corresponding 1,5-dipole **12a**, the stationary points in the cyclization of **12a** and for dihydroimidazole (**13a**) at various levels of theory

Method	1,3-Diene **10a**	1,4-Diene **11a**	1,5-Dipole W **12a**	TS (W−S1)	TS (W−S2)	Sickle 1	Sickle 2	TS (S1−U)	TS (S2−U)	U	TS (U−Cycle)	Cycle **13a**
PM3	0.00	6.77	17.08	25.65	41.46	22.83	20.11	46.49	26.39	22.41	44.80	−18.36
AM1	0.00	2.86	21.12	27.95	45.91	19.76	22.27	42.61	28.00	19.78	35.69	−12.43
RHF/6-31G*	0.00	9.19	48.24	64.79	71.38	56.28	50.45	73.45	62.87	55.44	62.72	−13.90
MP2/6-31G*//6-31G*	0.00	9.63	31.00	48.27	69.23	37.93	33.55	68.48	45.87	37.31	40.38	−17.20
SCS-MP2	0.00	8.96	33.21	49.40	69.25	40.33	35.70	69.27	47.21	40.26	44.57	−15.38
G3	0.00	8.52	27.05	42.64	60.76	32.99	28.47	59.92	39.53	31.64	35.38	−17.42
B3LYP/6-31G*	0.00	10.21	26.09	46.01	63.48	33.08	28.71	61.68	44.21	33.04	38.23	−13.36
B3LYP/6-311++G**	0.00	9.53	22.03	40.84	56.69	29.15	24.09	55.87	38.24	28.02	33.45	−14.53

enes.[23] It is more stable than the non-conjugated 2,4-diazapenta-1,4-diene **11a** by approximately 8.5 kcal·mol^{-1}. The best corresponding 1,5-dipolar form **12a** is predicted to be planar, but is about 27 kcal·mol^{-1} more energy rich than the 2,4-diazapenta-1,3-diene **10a**. Thus, it is unlikely that such an intermediate will exist in equilibrium with the other $C_3N_2H_6$ compounds under experimental conditions. If such a W-shaped 1,5-dipole was formed, barriers to internal rotation (of the iminium moiety) would amount to an additional 33 kcal·mol^{-1}, whereas only a small barrier (ca. 8 kcal·mol^{-1}) is associated with the formation of the cyclic tautomer imidazoline **13a**, which is predicted to have a lower energy (by ca. 44 kcal·mol^{-1}) than the 1,5-dipole. However, one can also envisage the direct formation of the U-shaped 1,5-dipole **12a** from an appropriate conformer of the 2,4-diazapenta-1,3-diene **10a** without involving internal rotations of the 1,5-dipole.

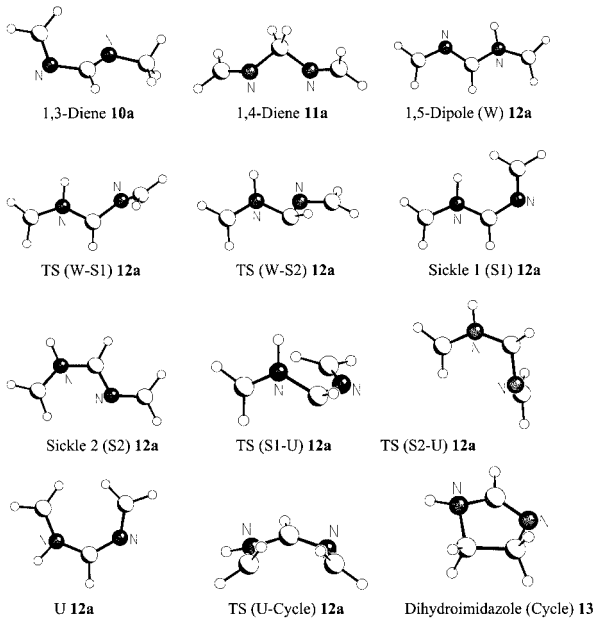


Figure 6. Molecular structures of 2,4-diazapenta-1,3-diene **10a**, 2,4-diazapenta-1,4-diene **11a** and the corresponding 1,5-dipole **12a**, the stationary points in the cyclization of **12a** and for 4,5-dihydroimidazole (**13a**) (RHF/6-31G*)

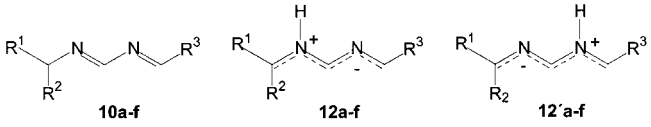


Figure 7. Various substituted 2,4-diazapenta-1,3-dienes **10** and the corresponding 1,5-dipoles **12**, **12′**

The accessibility of the 1,5-dipoles **12** under experimental conditions depends very much on the nature of the electron-withdrawing groups present in the 2,4-diazapenta-1,3-dienes **10** (Figure 7, Table 5). We present model calculations for some of the experimentally investigated systems in Table 5. In all cases the 1,5-dipoles **12**, which have the protonated nitrogen atom close to the electron-withdrawing group, are more stable than the tautomeric 1,5-dipoles **12′**. It is clear that a trifluoromethyl group (**10d**, **12d**) has relatively little effect on the possible tautomeric (intermolecular) equilibrium between the 2,4-diazapenta-1,3-diene **10d** and the corresponding dipoles **12d**. Two phenyl groups in the 1,5-positions (**10b**, **12b**), or a cyano group (**10e**, **12e**), acidify the respective compounds considerably; the effect is even more pronounced for the methoxycarbonyl and fluorenyl moieties (**10c**,**f**, **12c**,**f**). If the additional substituents that are present in the experimentally investigated compounds are taken into account, these qualitative data agree well with the experimental results.

Experimentally, the spiro-fluorene-4*H*-imidazoles **6b**−**d** are formed in a fast cyclization process even in the absence of base; the intermediate 2,4-diazapenta-1,3-dienes **5** could not be isolated under the reaction conditions employed (see above). Therefore, we have studied this system in more detail. Based on the SCS-MP2 data (Figure 8, Table 6), which are possibly too high by 6−8 kcal·mol^{-1} for the 1,5-dipole and its transition states, as estimated from the data in Table 4, we have calculated an energy difference between the fluorenyl-substituted 1,3-diene **10f** and the better of its two 1,5-dipolar forms **12f** (ca. 14 kcal·mol^{-1}) that is drastically reduced compared with the parent system **10a** (Table 4). Phenyl groups, present in the experimentally studied system, will further reduce this energy difference. From the calculated transition state energy for cyclization (27.7 kcal·mol^{-1}) we estimate a barrier of ca. 20 kcal·mol^{-1},

Table 5. Relative energies (kcal·mol^{-1}) of various substituted 2,4-diazapenta-1,3-dienes **10** and its 1,5-dipoles **12** and **12′** at three levels of theory

Nr.	R^1	R^2	R^3	Method	1,3-Diene **10**	Dipole **12**	Dipole **12′**
a	H	H	H	MP2	0.00	31.00	31.00 [a]
				SCS-MP2	0.00	33.21	33.21 [a]
				B3LYP	0.00	26.09	26.09 [a]
b	Ph	H	Ph	MP2	0.00	18.21	18.21 [a]
				SCS-MP2	0.00	21.97	21.97 [a]
				B3LYP	0.00	13.24	13.24 [a]
c	CO_2Me	H	H	MP2	0.00	14.88	23.60
				SCS-MP2	0.00	17.76	26.69
				B3LYP	0.00	8.03	17.06
d	CF_3	H	H	MP2	0.00	27.43	28.73
				SCS-MP2	0.00	29.85	31.21
				B3LYP	0.00	22.31	22.92
e	CN	H	H	MP2	0.00	18.23	19.68
				SCS-MP2	0.00	21.17	22.98
				B3LYP	0.00	11.96	13.88
f	*N*-fluorenyl		H	MP2	0.00	9.58	15.05
				SCS-MP2	0.00	13.83	19.01
				B3LYP	0.00	3.95	8.19

[a] Owing to symmetry the energies are equal to those of dipole **12**.

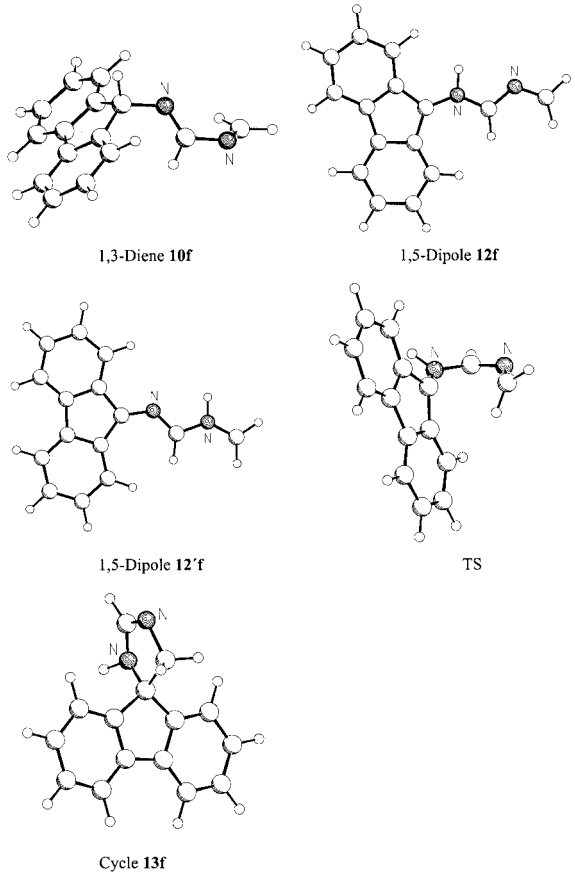


Figure 8. Molecular structures of the fluorenyl-substituted 2,4-diazapenta-1,3-diene **10f**, its 1,5-dipoles **12f** and **12′f**, the transition state of the cyclization and the corresponding cyclic product **13f** (4,5-dihydroimidazole) (RHF/6-31G*)

which is easily overcome even under mild experimental conditions, assuming an intermolecular proton shift occurs. Again, the cyclization to form **13f** is predicted to be rather exothermic (−18 kcal·mol^{-1}).

Conclusions

A new synthetic route to 1-amino-2,4-diazapenta-1,3-dienes **5** has been developed, that is based on the activation of *N*-acylamidines **2** by trifluoromethanesulfonic anhydride and subsequent condensation with amino compounds **4**. If the amino compounds **4** are substituted with electron-withdrawing substituents (e.g. alkoxycarbonyl groups, fluorenyl derivatives) the condensation reaction surprisingly gives 4*H*-imidazoles **6** and imidazoles **7** instead of the 2,4-diazapenta-1,3-dienes **5**. We consider these reactions to occur by 1,5-dipolar electrocyclization of 1,5-dipoles, which are formed from the relatively acidic 2,4-diazapenta-1,3-dienes **5** by tautomerism. In the case of **5b**,**f**, electrocyclization could be achieved by using strong organic bases to yield the corresponding imidazoles **7b**,**c** after amine elimination in an anionic ring-closure reaction. The anionic and the 1,5-dipolar reaction mechanisms have been studied by performing quantum chemical model calculations (RHF, MP2, SCS-MP2, G3, DFT) on the parent 2,4-diazapentadienyl anion **9a**, its lithium compound **9a-Li**, the corresponding 1,5-dipole **12**, and substituted derivatives as model systems for the experimentally studied species. We have supplemented our experimental and theoretical work by X-ray analyses of the 2,4-diazapenta-1,3-dienes **5a**·F_3CSO_3H, **5c**, **5d**·F_3CSO_3H, **5e**,**f** and the spirocyclic 4*H*-imidazole derivatives **6b**−**d**.

Experimental Section

Materials and Methods: IR: Nicolet 5DXC. ^{1}H NMR: Bruker WM 300 (300.13 MHz), Bruker AMX 400 (400.13 MHz) and Varian Unity plus (599.86 MHz), internal reference tetramethylsilane. ^{13}C NMR: Bruker WM 300 (75.47 MHz), Bruker AMX 400 (100.61 MHz) and Varian Unity plus (150.85 MHz), internal reference tetramethylsilane or solvent. ^{19}F NMR: Bruker WM 300

Table 6. Relative energies (kcal·mol^{-1}) of the fluorenyl-substituted 2,4-diazapenta-1,3-diene **10f**, its 1,5-dipoles **12f** and **12′f**, the transition state of the cyclization and the corresponding cyclic product (4,5-dihydroimidazole **13f**) at various levels of theory

Method	1,3-Diene **10f**	Dipole **12f**	Dipole **12′f**	TS (U−Cycle)	Cycle **13f**
PM3	0.00	4.05	8.99	33.42	−20.27
AM1	0.00	5.91	10.59	19.54	−15.82
RHF/6-31G*	0.00	29.93	35.24	42.97	−17.62
MP2/6-31G*//6-31G*	0.00	9.58	15.05	21.88	−23.71
SCS-MP2	0.00	13.83	19.01	27.69	−21.22
B3LYP/6-31G*	0.00	3.95	8.19	17.50	−17.86

(282.37 MHz), internal reference trichlorofluoromethane. CHN elemental analysis: Elementar Vario El III. Melting points are uncorrected. All solvents were rigorously dried by standard methods. When necessary, the experiments were carried out with complete exclusion of moisture (argon, septum-syringe technique) in glassware that had been thoroughly dried by repeated heating under argon and subsequent evacuation.

Amidines 1a−d. General Procedure: An equimolar amount of the appropriate amine was added to a solution of *n*-butyllithium (1.6 M in *n*-hexane) in dry tetrahydrofuran at −78 °C. This solution was stirred at room temperature for 15 min. At −78 °C an equimolar amount of nitrile was added. The reaction mixture was warmed slowly to room temperature and stirred for 2 h. For hydrolysis methanol (80 mL) and water (80 mL) were subsequently added. The aqueous layer was separated from the organic layer and extracted three times with *tert*-butyl methyl ether. The combined organic layers were dried with sodium sulfate and the solvent was removed in vacuo.

1-Benzimidoylpyrrolidine (1a): Following the general procedure **1a** was prepared from pyrrolidine (5.0 mL, 60.0 mmol) in dry tetrahydrofuran (100 mL), *n*-butyllithium (37.5 mL, 1.6 M in *n*-hexane) and benzonitrile (6.2 mL, 60.0 mmol). The crude product was purified by distillation (100 °C, 1 mbar). Yield 8.37 g (80%) (ref.[32] 70%, 104 °C/1 hPa), colorless oil. $C_{11}H_{14}N_2$ (174.24): calcd. C 75.82, H 8.10, N 16.08; found C 75.61, H 8.09, N 15.86.

1-(4-Methylbenzimidoyl)pyrrolidine (1b): Following the general procedure **1b** was prepared from pyrrolidine (5.3 mL, 64.0 mmol) in dry tetrahydrofuran (100 mL), *n*-butyllithium (40.0 mL, 1.6 M in *n*-hexane) and 4-methylbenzonitrile (7.49 g, 64.0 mmol). The crude product was purified by distillation (105 °C, 1 mbar). Yield 6.83 g (57%), pale-yellow oil. IR (film): $\tilde{\nu}$ = 3312 (m, NH), 3022 (m, $CH_{arom.}$), 2968 (m, $CH_{aliph.}$), 2868 (m, $CH_{aliph.}$), 1583 (s, C=N), 1560 (s, C=N), 1445 (s), 1344 (s), 1215 (s), 1176 (m), 827 (s), 789 (m), 734 (m) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.76 (m, 4 H, NCH_2CH_2), 2.23 (s, 3 H, CH_3), 3.23 (m, 4 H, NCH_2CH_2), 5.92 (br. s, 1 H, NH), 7.03 (m, 2 H, $CH_{arom.}$), 7.13 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 20.8 (CH_3), 25.3 (NCH_2CH_2), 47.7 (NCH_2CH_2), 126.0, 128.6 ($C_{arom.}$), 136.5, 138.2 (*i*-$C_{arom.}$), 167.1 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 188 (81) [M$^+$], 187 (90) [M$^+$ − H], 159 (66), 145 (54), 118 (79) [TolCN$^+$], 91 (33) [Tol$^+$], 70 (100) [$(CH_2)_4N^+$]. $C_{12}H_{16}N_2$ (188.27): calcd. C 76.56, H 8.57, N 14.88; found C 76.22, H 8.90, N 14.73.

1-(4-Methoxybenzimidoyl)pyrrolidine (1c): Following the general procedure **1c** was prepared from pyrrolidine (5.3 mL, 64.0 mmol) in dry tetrahydrofuran (100 mL), *n*-butyllithium (40.0 mL, 1.6 M in *n*-hexane) and 4-methoxybenzonitrile (8.51 g, 64.0 mmol). The crude product was purified by distillation (115 °C, 1 mbar). Yield 10.71 g (82%), pale-yellow oil. IR (film): $\tilde{\nu}$ = 3312 (m, NH), 2966 (m, $CH_{aliph.}$), 2869 (m, $CH_{aliph.}$), 1609 (s, C=N), 1585 (vs, C=N), 1562 (s, C=N), 1516 (s, C=C), 1437 (s), 1344 (s), 1296 (s), 1250 (vs), 1175 (s), 1111 (m), 1030 (s), 839 (s), 793 (m) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.76 (m, 4 H, NCH_2CH_2), 3.22 (m, 4 H, NCH_2CH_2), 3.67 (s, 3 H, OCH_3), 5.94 (br. s, 1 H, NH), 6.74 (m, 2 H, $CH_{arom.}$), 7.17 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 25.3 (NCH_2CH_2), 47.8 (NCH_2CH_2), 54.9 (OCH_3), 113.3 (*m*-$C_{arom.}$), 127.6 (*o*-$C_{arom.}$), 131.8 (*i*-$C_{arom.}$), 159.6 (*i*-$COCH_3$), 166.8 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 204 (88) [M$^+$], 203 (78) [M$^+$ − H], 175 (80), 134 (87) [M$^+$ − $(CH_2)_4N$], 91 (23), 70 (100) [$(CH_2)_4N^+$]. $C_{12}H_{16}N_2O$ (204.27): calcd. C 70.56, H 7.89, N 13.71; found C 70.58, H 7.83, N 13.50.

(*R*)-1-Benzimidoyl-2-methoxymethylpyrrolidine (1d): Following the general procedure **1d** was prepared from (*R*)-2-methoxymethylpyrrolidine (3.7 mL, 30.0 mmol) in dry tetrahydrofuran (100 mL), *n*-butyllithium (18.8 mL, 1.6 M in *n*-hexane) and benzonitrile (3.1 mL, 30.0 mmol). The crude product was purified by distillation (104 °C, 1 mbar). Yield 4.17 g (64%), colorless oil. IR (film): $\tilde{\nu}$ = 3312 (s, NH), 3059 (m, $CH_{arom.}$), 2972 (s, $CH_{aliph.}$), 2874 (s, $CH_{aliph.}$), 2826 (s, $CH_{aliph.}$), 1585 (vs, C=N), 1566 (vs, C=N), 1499 (s, C=C), 1447 (vs, C=C), 1344 (s), 1310 (m), 1223 (s), 1188 (s), 1111 (vs), 1028 (m), 972 (m), 872 (m), 775 (vs), 704 (vs) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.72−1.96 (m, 4 H, NCH_2CH_2), 3.18 (s, 3 H, OCH_3), 3.20−3.40 (m, 4 H, NCH_2, OCH_2), 4.09 (m, 1 H, NC*H*), 5.98 (br. s, 1 H, NH), 7.26 (m, 5 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 23.6, 28.2 (NCH_2CH_2), 48.9 (NCH_2), 56.7 (OCH_3), 58.7 (NCH), 72.7 (OCH_2), 126.2, 128.1 (*o*-, *m*-$C_{arom.}$), 128.4 (*p*-$C_{arom.}$), 139.5 (*i*-$C_{arom.}$), 167.1 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 218 (9) [M$^+$], 203 (44) [M$^+$ − CH_3], 187 (15) [M$^+$ − OCH_3], 173 (6) [M$^+$ − CH_2OCH_3], 104 (39) [PhCNH$^+$], 77 (20) [Ph$^+$], 70 (100) [$(CH_2)_4N^+$]. $C_{13}H_{18}N_2O$ (218.29): calcd. C 71.53, H 8.31, N 12.83; found C 71.37, H 8.35, N 12.69.

***N*-Acylamidines 2a−d. General Procedure. Method A:** An excess of 2 M sodium hydroxide solution (100 mL) was added to *N*,*N*-dialkylamidine **1** (30.0 mmol). The mixture was stirred and cooled to 0 °C. A solution of acyl chloride (30.0 mmol) in acetone (15 mL) was added dropwise to the reaction mixture using a dropping funnel. Then the suspension was warmed to 10 °C over the course of 1.5 h. The remaining solid was filtered off, washed with water (50 mL), and the solvent removed in vacuo.

Method B: An excess of 2 M sodium hydroxide solution (100 mL) was added to *N*,*N*-dialkylamidine **1** (30.0 mmol). The mixture was stirred and cooled to 0 °C. A solution of acyl chloride (30.0 mmol) in acetone (15 mL) was added dropwise to the reaction mixture using a dropping funnel. Then the solution was warmed to 10 °C over the course of 1.5 h. The solution was extracted with chloroform (3 × 30 mL). The combined organic layers were dried with sodium sulfate, and the solvent removed in vacuo.

***N*-[(Phenyl)(pyrrolidin-1-yl)methylene]benzamide (2a):** Following method A **2a** was prepared from **1a** (10.44 g, 60.0 mmol) and ben-

zoyl chloride (6.9 mL, 60.0 mmol). Yield 14.10 g (85%), colorless solid; m.p. 119 °C (ref.[32] 96.5%, 119 °C). $C_{18}H_{18}N_2O$ (278.35): calcd. C 77.67, H 6.52, N 10.06; found C 77.61, H 6.28, N 9.99.

4-Methyl-*N*-[(4-methylphenyl)(pyrrolidin-1-yl)methylene]benzamide (2b): Following method A **2b** was prepared from **1b** (5.65 g, 30.0 mmol) and 4-methylbenzoyl chloride (4.0 mL, 30.0 mmol). Yield 8.22 g (90%), colorless solid; m.p. 142 °C. IR (KBr): $\tilde{\nu}$ = 3022 (m, $CH_{arom.}$), 2974 (s, $CH_{aliph.}$), 2947 (s, $CH_{aliph.}$), 2920 (m, $CH_{aliph.}$), 2876 (s, $CH_{aliph.}$), 1634 (vs, C=O/C=N), 1606 (s, C=O/C=N), 1545 (vs, C=C), 1477 (vs, C=C), 1339 (s), 1308 (vs), 1285 (vs), 1209 (s), 1167 (vs), 1069 (vs), 1018 (s), 951 (s), 916 (s), 825 (vs), 779 (s), 758 (vs), 729 (s), 696 (s) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.90−1.97 (br. m, 4 H, NCH_2CH_2), 2.30 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 3.31 (br. s, 2 H, NCH_2CH_2), 3.76 (br. s, 2 H, NCH_2CH_2), 7.09−7.21 (m, 6 H, $CH_{arom.}$), 7.99 (m, 2 H, *o*-$CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 21.2, 21.3 (CH_3), 24.5, 25.7 (NCH_2CH_2), 48.1, 49.5 (NCH_2CH_2), 127.0, 128.4, 128.9, 129.4 (*o*-, *m*-$C_{arom.}$), 132.3, 134.6 (*i*-$C_{arom.}$), 139.2, 141.3 (*i*-CCH_3), 163.0 (C=N), 176.1 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 306 (51) [M^+], 237 (17), 215 (22) [M^+ − Tol], 119 (83) [$TolCO^+$], 91 (53) [Tol^+], 70 (100) [$(CH_2)_4N^+$]. $C_{20}H_{22}N_2O$ (306.40): calcd. C 78.40, H 7.24, N 9.14; found C 78.11, H 6.97, N 9.09.

4-Methoxy-*N*-[(4-methoxyphenyl)(pyrrolidin-1-yl)methylene]-benzamide (2c): Following method B **2c** was prepared from **1c** (6.12 g, 30.0 mmol) and 4-methoxybenzoyl chloride (4.1 mL, 30.0 mmol). The crude product was purified by column chromatography (SiO_2) using *tert*-butyl methyl ether as eluent (R_f = 0.08). Yield 5.80 g (57%), colorless solid; m.p. 110 °C. IR (KBr): $\tilde{\nu}$ = 3070 (m, $CH_{arom.}$), 2972 (s, $CH_{aliph.}$), 2878 (m, $CH_{aliph.}$), 2837 (m, $CH_{aliph.}$), 1728 (m), 1607 (vs, C=O/C=N), 1516 (vs, C=C), 1458 (vs), 1364 (m), 1339 (s), 1283 (vs), 1248 (vs), 1205 (s), 1178 (vs), 1153 (vs), 1069 (s), 1028 (vs), 933 (m), 848 (s), 783 (s), 766 (s), 700 (m) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.94 (br. s, 4 H, NCH_2CH_2), 3.33−3.63 (m, 4 H, NCH_2CH_2), 3.77 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 6.81−6.88 (m, 4 H, $CH_{arom.}$), 7.24 (m, 2 H, $CH_{arom.}$), 8.04 (m, 2 H, *o*-$CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 24.6, 25.7 (NCH_2CH_2), 48.1, 49.6 (NCH_2CH_2), 55.0, 55.2 (OCH_3), 112.9, 113.7 (*m*-$C_{arom.}$), 127.5 (*i*-$C_{arom.}$), 128.7 (*o*-$C_{arom.}$), 129.0 (*i*-$C_{arom.}$), 131.3 (*o*-$C_{arom.}$), 160.2, 162.1 (*i*-$COCH_3$), 162.7 (C=N), 176.0 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (60) [M^+], 269 (20), 231 (10) [M^+ − PhOMe], 136 (23), 135 (90) [$MeOPhCO^+$], 134 (35), 107 (8) [$PhOMe^+$], 77 (13) [Ph^+], 70 (100) [$(CH_2)_4N^+$]. $C_{20}H_{22}N_2O_3$ (338.40): calcd. C 70.99, H 6.55, N 8.28; found C 70.85, H 6.36, N 8.28.

(*R*)-*N*-{[2-(Methoxymethyl)pyrrolidin-1-yl]phenylmethylene}-benzamide (2d): Following method B **2d** was prepared from **1d** (3.93 g, 18.0 mmol) and benzoyl chloride (2.1 mL, 18.0 mmol). The crude product was purified by column chromatography (SiO_2) using *tert*-butyl methyl ether/petroleum ether (1:1) as eluent (R_f = 0.11). Yield 4.12 g (71%), colorless oil. IR (film): $\tilde{\nu}$ = 3059 (m, $CH_{arom.}$), 3028 (m, $CH_{arom.}$), 2974 (s, $CH_{aliph.}$), 2928 (s, $CH_{aliph.}$), 2878 (s, $CH_{aliph.}$), 2827 (s, $CH_{aliph.}$), 1678 (s, C=O/C=N), 1632 (vs, C=O/C=N), 1539 (vs, C=C), 1456 (vs), 1337 (s), 1310 (vs), 1277 (vs), 1161 (s), 1113 (vs), 1059 (vs), 1024 (s), 974 (m), 927 (m), 802 (s), 777 (vs), 723 (vs), 702 (vs) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.97−2.09 (m, 4 H, NCH_2CH_2), 3.20 (s, 3 H, OCH_3), 3.30−3.50 (m, 4 H, NCH_2, OCH_2), 4.67 (m, 1 H, NC*H*), 7.25−7.42 (m, 8 H, $CH_{arom.}$), 8.03 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 24.3, 27.9 (NCH_2CH_2), 50.5 (NCH_2), 58.0 (OCH_3), 59.0 (NCH), 72.3 (OCH_2), 127.1, 127.7 (*o*-, *m*-$C_{arom.}$), 128.1 (*p*-$C_{arom.}$), 128.2, 129.3 (*o*-, *m*-$C_{arom.}$), 131.2 (*p*-$C_{arom.}$), 135.3, 137.2 (*i*-$C_{arom.}$), 163.2 (C=N), 176.2 (C=O) ppm. MS (EI, 70 eV): *m*/*z* (%) = 322 (13) [M^+], 307 (9) [M^+ − CH_3], 237 (12) [M^+ − PhCO], 174 (10), 105 (100) [$PhCO^+$], 77 (30) [Ph^+]. $C_{20}H_{22}N_2O_2$ (322.40): calcd. C 74.51, H 6.88, N 8.69; found C 74.60, H 7.08, N 8.21.

2,4-Diazapenta-1,3-dienes 5a−h and Imidazoles 6 and 7. General Procedure. Method A: An equimolar amount of *N*-acylamidine **2**, dissolved in dichloromethane, was added to a solution of trifluoromethanesulfonic anhydride in dry dichloromethane at −78 °C. This solution was stirred for 1.5 h at −50 °C. At −78 °C an equimolar amount of amine **4** was added. The reaction mixture was stirred at −78 °C for 1 h and additionally for 3 h at room temperature. The reaction mixture was washed with saturated sodium hydrogen carbonate solution (3 × 30 mL), dried with sodium sulfate, and the solvent removed in vacuo.

Method B: An equimolar amount of *N*-acylamidine **2**, dissolved in dichloromethane, was added to a solution of trifluoromethanesulfonic anhydride in dry dichloromethane at −78 °C. This solution was stirred for 1.5 h at −50 °C. Subsequently, equimolar amounts of the appropriate ammonium salt and triethylamine were added at −78 °C. The reaction mixture was warmed slowly to room temperature and was stirred for 16 h. The reaction mixture was washed with saturated sodium hydrogen carbonate solution (3 × 30 mL), dried with sodium sulfate, and the solvent removed in vacuo.

***N*-(1-Phenylethyl)-*N′*-[(phenyl)(pyrrolidin-1-yl)methylene]benzamidine Hydrotrifluoromethanesulfonate (5a):** Following the general procedure (method A) **5a** was prepared from **2a** (5.56 g, 20.0 mmol), trifluoromethanesulfonic anhydride (3.4 mL, 20.0 mmol) and DL-1-phenylethylamine (2.6 mL, 20.0 mmol) in dry dichloromethane (60 mL). The crude product was purified by crystallization from dichloromethane/petroleum ether. Yield 5.73 g (54%), colorless crystals; m.p. 194 °C. IR (KBr): $\tilde{\nu}$ = 3258 (s, NH), 3065 (m, $CH_{arom.}$), 2990 (m, $CH_{aliph.}$), 2888 (w, $CH_{aliph.}$), 1584 (vs, C=N), 1539 (vs, C=C), 1459 (vs), 1339 (s), 1280 (vs), 1256 (vs), 1157 (vs), 1029 (vs), 774 (s), 709 (s), 643 (s) cm^{-1}. ^1H NMR (300.13 MHz, CD_3CN): δ = 1.68 (d, ^3J = 6.9 Hz, 3 H, CH_3), 2.08−2.14 (m, 4 H, NCH_2CH_2), 3.38 (m, 1 H, NCH_2CH_2), 3.55 (m, 1 H, NCH_2CH_2), 3.77 (m, 1 H, NCH_2CH_2), 3.91 (m, 1 H, NCH_2CH_2), 5.40 (q, ^3J = 6.9 Hz, 1 H, CH), 6.54 (m, 2 H, $CH_{arom.}$), 7.01 (m, 2 H, $CH_{arom.}$), 7.15−7.27 (m, 5 H, $CH_{arom.}$), 7.39 (m, 2 H, $CH_{arom.}$), 7.44−7.55 (m, 4 H, $CH_{arom.}$), 8.30 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.47 MHz, CD_3CN): δ = 22.0 (CH_3), 25.1, 26.5 (NCH_2CH_2), 51.3, 53.1 (NCH_2CH_2), 55.0 (CH), 127.9, 128.7, 128.8, 129.1, 129.2, 129.6, 129.9 (*o*-, *m*-, *p*-$C_{arom.}$), 132.0, 133.2 (*p*-$C_{arom.}$), 134.1, 134.5, 144.1 (*i*-$C_{arom.}$), 168.1, 168.5 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 382 (23) [M − $F_3CSO_3^-$], 381 (45) [M^+ − F_3CSO_3H], 366 (25) [M^+ − F_3CSO_3H − CH_3], 276 (5) [$(CH_2)_4NPhCNPhCN^+$], 207 (100) [$PhCNPhCNH^+$], 194 (12), 158 (12), 105 (54) [$PhCHCH_3^+$], 104(50) [$PhCNH^+$], 70 (12) [$(CH_2)_4N^+$]. $C_{27}H_{28}F_3N_3O_3S$ (531.58): calcd. C 61.00, H 5.31, N 7.90; found C 61.00, H 5.20, N 7.76.

X-ray Crystal Structure Analysis of 5a: formula $C_{26}H_{28}N_3{\cdot}CF_3SO_3$, M = 531.58, colorless crystal, 0.35 × 0.25 × 0.10 mm, a = 25.279(1), b = 11.379(1), c = 19.037(1) Å, β = 105.13(1)°, V = 5286.2(6) $Å^3$, $\rho_{calcd.}$ = 1.336 $g{\cdot}cm^{-3}$, μ = 15.65 cm^{-1}, empirical absorption correction (0.610 ≤ T ≤ 0.859), Z = 8, monoclinic, space group $C2/c$ (No. 15), λ = 1.54178 Å, T = 223 K, ω and scans, 13421 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.59 $Å^{-1}$, 4427 independent (R_{int} = 0.041) and 3184 observed reflections [$I \geq 2\sigma(I)$], 340 refined parameters, R = 0.045, wR^2 = 0.110, max. residual electron density 0.41 (−0.28) $e{\cdot}Å^{-3}$, hydrogen at N3

from difference Fourier map, other hydrogens calculated and all refined as riding atoms.

***N*-Benzyl-*N*′-[(phenyl)(pyrrolidin-1-yl)methylene]benzamidine (5b):** Following the general procedure (method A) **5b** was prepared from **2a** (5.56 g, 20.0 mmol), trifluoromethanesulfonic anhydride (3.4 mL, 20.0 mmol) and benzylamine (2.2 mL, 20.0 mmol) in dry dichloromethane (60 mL). The crude product was purified by column chromatography (SiO_2) using *tert*-butyl methyl ether/*n*-pentane/triethylamine (10:10:1) as eluent (R_f = 0.20). Yield 3.45 g (47%), pale-yellow oil. IR (film): $\tilde{\nu}$ = 3061 (m, $CH_{arom.}$), 3026 (m, $CH_{arom.}$), 2976 (s, $CH_{aliph.}$), 2878 (m, $CH_{aliph.}$), 1622 (vs, C=N), 1502 (s, C=C), 1463 (s), 1253 (s), 1155 (s), 1061 (m), 1030 (s), 939 (m), 849 (m), 766 (s), 710 (s) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.99 (s, 4 H, NCH_2CH_2), 3.28 (br. s, 2 H, NCH_2CH_2), 3.76 (br. s, 2 H, NCH_2CH_2), 4.62 (s, 2 H, CH_2), 6.66 (m, 1 H, $CH_{arom.}$), 7.00 (m, 2 H, $CH_{arom.}$), 7.10−7.20 (m, 3 H, $CH_{arom.}$), 7.25−7.35 (m, 5 H, $CH_{arom.}$), 7.37−7.42 (m, 3 H, $CH_{arom.}$), 8.05 (m, 1 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 24.6, 25.8 (NCH_2CH_2), 48.2, 49.6 (NCH_2CH_2), 50.4 (CH_2), 126.7, 126.9, 127.0, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3 (*o*-, *m*-, *p*-$C_{arom.}$), 134.4, 136.7, 139.7 (*i*-$C_{arom.}$), 162.0, 166.2 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 367 (51) [M^+], 297 (12) [$M^+ - (CH_2)_4N$], 194 (27) [$PhCNCH_2Ph^+$], 193 (100), 104 (26) [$PhCNH^+$], 91 (79) [$PhCH_2^+$], 70 (14) [$(CH_2)_4N^+$]. $C_{25}H_{25}N_3$ (*M* = 367.49)

***N*-Benzhydryl-*N*′-[phenyl(pyrrolidin-1-yl)methylene]benzamidine (5c):** Following the general procedure (method A) **5c** was prepared from **2a** (5.56 g, 20.0 mmol), trifluoromethanesulfonic anhydride (3.4 mL, 20.0 mmol) and α-aminodiphenylmethane (3.4 mL, 20.0 mmol) in dry dichloromethane (60 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (20:1) as eluent (R_f = 0.17). Yield 4.47 g (50%), colorless crystals; m.p. 137 °C. IR (KBr): $\tilde{\nu}$ = 3059 (m, $CH_{arom.}$), 3022 (m, $CH_{arom.}$), 2976 (s, $CH_{aliph.}$), 2868 (m, $CH_{aliph.}$), 2854 (w, $CH_{aliph.}$), 1610 (s, C=N), 1584 (vs, C=N), 1489 (s, C=C), 1452 (vs), 1441 (vs), 1342 (s), 1296 (s), 1097 (m), 1069 (s), 1028 (m), 916 (m), 850 (m), 771 (s), 743 (s), 698 (vs) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.90 (s, 4 H, NCH_2CH_2), 3.37 (br. s, 4 H, NCH_2CH_2), 6.16 (s, 1 H, $CHPh_2$), 6.44 (m, 2 H, $CH_{arom.}$), 6.82 (m, 2 H, $CH_{arom.}$), 6.96 (m, 1 H, *p*-$CH_{arom.}$), 7.05−7.17 (m, 5 H, $CH_{arom.}$), 7.19−7.24 (m, 4 H, $CH_{arom.}$), 7.42 (m, 4 H, $CH_{arom.}$), 7.59 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 25.5 (NCH_2CH_2), 48.3 (NCH_2CH_2), 65.4 (CH), 126.0, 126.8, 127.3, 127.6, 127.8, 127.9, 128.2, 128.4 (*o*-, *m*-, *p*-$C_{arom.}$), 135.2, 140.7, 145.9 (*i*-$C_{arom.}$), 158.1, 162.2 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 443 (57) [M^+], 373 (12) [$M^+ - (CH_2)_4N$], 270 (35) [$PhCNCHPh_2^+$], 269 (100), 167 (50) [$CHPh_2^+$], 166 (53), 165 (54), 159 (29) [$(CH_2)_4NCPh^+$], 104 (24) [$PhCNH^+$], 70 (11) [$(CH_2)_4N^+$]. $C_{31}H_{29}N_3$ (443.57): calcd. C 83.94, H 6.59, N 9.47; found C 83.60, H 6.56, N 9.44.

X-ray Crystal Structure Analysis of 5c: Formula $C_{31}H_{29}N_3$, *M* = 443.57, colorless crystal, 0.25 × 0.15 × 0.10 mm, *a* = 10.415(1), *b* = 13.133(1), *c* = 18.964(1) Å, β = 104.72(1)°, *V* = 2508.8(3) $Å^3$, $\rho_{calcd.}$ = 1.174 g·cm^{-3}, μ = 0.69 cm^{-1}, empirical absorption correction (0.983 ≤ *T* ≤ 0.993), *Z* = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 0.71073 Å, *T* = 198 K, ω and scans, 15257 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.67 $Å^{-1}$, 6174 independent and 3384 observed reflections [$I \geq 2\sigma(I)$], 307 refined parameters, *R* = 0.058, wR^2 = 0.111, max. residual electron density 0.16 (−0.22) e·$Å^{-3}$, hydrogens calculated and refined as riding atoms.

***N*-[(Phenyl)(pyrrolidin-1-yl)methylene]-*N*′-(2,2,2-trifluoroethyl)benzamidine (5d):** Following the general procedure (method B) **5d** was prepared from **2a** (2.78 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), 2,2,2-trifluoroethylamine hydrochloride (1.21 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (20:1) as eluent (R_f = 0.17). Yield 1.83 g (51%), colorless crystals; m.p. 134 °C. IR (KBr): $\tilde{\nu}$ = 3053 (m, $CH_{arom.}$), 3024 (m, $CH_{arom.}$), 2972 (s, $CH_{aliph.}$), 2949 (s, $CH_{aliph.}$), 2878 (s, $CH_{aliph.}$), 1616 (vs, C=N), 1522 (vs, C=C), 1458 (vs), 1441 (vs), 1348 (vs), 1308 (vs), 1288 (vs, CF), 1204 (s), 1059 (s), 1024 (s), 947 (s), 922 (s), 804 (s), 781 (vs), 744 (s), 719 (vs), 704 (vs) cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 1.89 (s, 4 H, NCH_2CH_2), 3.13−3.58 (br. m, 4 H, NCH_2CH_2), 3.82 (q, $^3J_{H,F}$ = 10.2 Hz, 2 H, CH_2CF_3), 6.82 (m, 2 H, $CH_{arom.}$), 7.02−7.14 (m, 6 H, $CH_{arom.}$), 7.50 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ = 25.4 (br., NCH_2CH_2), 47.8, 49.5 (br., NCH_2CH_2), 51.8 (q, $^2J_{C,F}$ = 30.5 Hz, CH_2CF_3), 117.3 (q, $^1J_{C,F}$ = 336.5 Hz, CF_3), 126.5, 127.5, 127.7, 128.3 (*o*-, *m*-$C_{arom.}$), 129.1, 129.2 (*p*-$C_{arom.}$), 135.2, 139.3 (*i*-$C_{arom.}$), 158.4, 166.3 (C=N) ppm. ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −71.3 (t, $^3J_{F,H}$ = 9.5 Hz, CF_3) ppm. MS (EI, 70 eV): *m*/*z* (%) = 359 (60) [M^+], 290 (26) [$M^+ - CF_3$], 186 (78) [$PhCNCH_2CF_3^+$], 104 (100) [$PhCNH^+$], 77 (16) [Ph^+], 70 (40) [$(CH_2)_4N^+$]. $C_{20}H_{20}F_3N_3$ (359.39): calcd. C 66.84, H 5.61, N 11.69; found C 66.86, H 5.27, N 11.63.

From the crude reaction mixture a small crystal of the corresponding triflate was isolated, which was subjected to X-ray analysis.

X-ray Crystal Structure Analysis of 5d·CF_3SO_3H: Formula $C_{20}H_{21}F_3N_3{\cdot}CF_3SO_3$, *M* = 509.47, colorless crystal, 0.50 × 0.50 × 0.25 mm, *a* = 12.593(1), *b* = 14.028(1), *c* = 14.326(1) Å, β = 108.77(1)°, *V* = 2396.2(3) $Å^3$, $\rho_{calcd.}$ = 1.412 g·cm^{-3}, μ = 18.85 cm^{-1}, empirical absorption correction by ψ scan data (0.453 ≤ *T* ≤ 0.650), *Z* = 4, monoclinic, space group $P2_1/n$ (No. 14), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 5076 reflections collected (±*h*, +*k*, +*l*), [(sinθ)/λ] = 0.62 $Å^{-1}$, 4882 independent (R_{int} = 0.028) and 4229 observed reflections [$I \geq 2\sigma(I)$], 313 refined parameters, *R* = 0.043, wR^2 = 0.130, max. residual electron density 0.24 (−0.33) e·$Å^{-3}$, hydrogen at N4 from difference Fourier map, others calculated and all refined as riding atoms.

***N*-[(Phenyl)(pyrrolidin-1-yl)methylene]-*N*′-(2,2,2-trifluoro-1-phenylethyl)benzamidine (5e):** Following the general procedure (method B) **5e** was prepared from **2a** (2.78 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), 2,2,2-trifluoro-1-phenylethylamine hydrochloride (2.18 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (25:1) as eluent (R_f = 0.13). Yield 2.46 g (57%), colorless crystals; m.p. 152 °C. IR (KBr): $\tilde{\nu}$ = 3053 (m, $CH_{arom.}$), 3030 (m, $CH_{arom.}$), 2966 (m, $CH_{aliph.}$), 2928 (m, $Ch_{aliph.}$), 2868 (m, $CH_{aliph.}$), 1602 (s, C=N), 1555 (vs, C=N), 1499 (s, C=C), 1452 (vs), 1342 (s), 1250 (s, CF), 1161 (s), 1113 (s), 775 (m), 708 (s), 696 (s) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.93 (s, 4 H, NCH_2CH_2), 2.90−3.80 (br. m, 4 H, NCH_2CH_2), 5.49 (q, $^3J_{H,F}$ = 8.3 Hz, 1 H, $CHCF_3$), 6.27 (m, 2 H, $CH_{arom.}$), 6.85 (m, 2 H, $CH_{arom.}$), 7.00 (m, 1 H, $CH_{arom.}$), 7.05−7.14 (m, 3 H, $CH_{arom.}$), 7.28−7.36 (m, 3 H, $CH_{arom.}$), 7.40 (m, 2 H, $CH_{arom.}$), 7.55 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 25.4 (br., NCH_2CH_2), 47.6 (br., NCH_2CH_2), 64.3 (q, $^2J_{C,F}$ = 28.0 Hz, $CHCF_3$), 117.4 (q, $^1J_{C,F}$ = 337.0 Hz, CF_3), 126.7, 127.4, 127.7, 127.9 (*o*-, *m*-$C_{arom.}$), 128.0 (*p*-$C_{arom.}$), 128.1 (*o*-, *m*-$C_{arom.}$), 128.7, 128.8 (*p*-$C_{arom.}$), 129.7 (*o*-, *m*-$C_{arom.}$), 135.2, 137.1, 140.3 (*i*-$C_{arom.}$), 159.2, 166.4 (C=N) ppm. ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −74.1 (d, $^3J_{F,H}$ = 9.5 Hz, CF_3) ppm. MS (EI, 70 eV): *m*/*z* (%) =

435 (87) [M^+], 366 (44) [$M^+ - CF_3$], 261 (96), 194 (49), 159 (100) [$PhCHCF_3^+$], 131 (18), 109 (58), 104 (78) [$PhCNH^+$], 91 (30), 70 (38) [$(CH_2)_4N^+$]. $C_{26}H_{24}F_3N_3$ (435.48): calcd. C 71.71, H 5.55, N 9.65; found C 71.37, H 5.35, N 9.37.

X-ray Crystal Structure Analysis of 5e: Formula $C_{26}H_{24}F_3N_3$, M = 435.48, colorless crystal, 0.40 × 0.25 × 0.10 mm, a = 8.792(1), b = 9.332(1), c = 27.193(1) Å, β = 93.52(1)°, V = 2226.9(4) Å^3, $\rho_{calcd.}$ = 1.299 g·cm^{-3}, μ = 7.84 cm^{-1}, empirical absorption correction (0.744 ≤ T ≤ 0.926), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, T = 223 K, ω and scans, 14645 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.59 Å^{-1}, 3779 independent (R_{int} = 0.054) and 2618 observed reflections [$I \geq 2\sigma(I)$], 290 refined parameters, R = 0.043, wR^2 = 0.119, max. residual electron density 0.21 (−0.17) e·Å^{-3}, hydrogens calculated and refined as riding atoms.

Ethyl (*S*)-2-[({Phenyl[(phenyl)(pyrrolidin-1-yl)methylene]amino}-methylene)amino]propionate (5f): Following the general procedure (method B) **5f** was prepared from **2a** (5.56 g, 20.0 mmol), trifluoromethanesulfonic anhydride (3.4 mL, 20.0 mmol), ethyl L-alaninate hydrochloride (3.07 g, 20.0 mmol) and triethylamine (2.8 mL, 20.0 mmol) in dry dichloromethane (60 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (10:1) as eluent (R_f = 0.13). Yield 3.40 g (45%), colorless crystals; m.p. 101 °C. IR (KBr): ṽ = 3061 (m, $CH_{arom.}$), 2980 (m, $CH_{aliph.}$), 2881 (m, $CH_{aliph.}$), 1740 (s, C=O), 1533 (vs, C=N), 1452 (s), 1339 (s), 1275 (s), 1157 (s), 1032 (s), 735 (m), 698 (m) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.28 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.44 (d, ^3J = 6.7 Hz, 3 H, $CHCH_3$), 1.94 (s, 4 H, NCH_2CH_2), 3.30−3.70 (br. m, 4 H, NCH_2CH_2), 4.18 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 4.54 (q, ^3J = 6.7 Hz, 1 H, $CHCH_3$), 6.93 (m, 2 H, $CH_{arom.}$), 7.07−7.14 (m, 6 H, $CH_{arom.}$), 7.44 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.3 (OCH_2CH_3), 18.8 ($CHCH_3$), 25.4 (br., NCH_2CH_2), 48.0 (br., NCH_2CH_2), 57.2 ($CHCH_3$), 60.1(OCH_2CH_3), 126.9, 127.3, 127.7, 127.9 (*o*-, *m*-$C_{arom.}$), 128.5, 128.8 (*p*-$C_{arom.}$), 135.3, 140.2 (*i*-$C_{arom.}$), 158.2, 164.3 (C=N), 175.0 (*C*OOEt) ppm. MS (EI, 70 eV): *m*/*z* (%) = 377 (34) [M^+], 304 (100) [$M^+ - COOEt$], 176 (10), 132 (15), 130 (20), 104 (20) [$PhCNH^+$]. $C_{23}H_{27}N_3O_2$ (377.48): calcd. C 73.18, H 7.21, N 11.13; found C 73.08, H 7.32, N 11.16.

X-ray Crystal Structure Analysis of 5f: Formula $C_{23}H_{27}N_3O_2$, M = 377.48, light yellow crystal, 0.30 × 0.15 × 0.10 mm, a = 8.974(1), b = 14.361(1), c = 16.272(1) Å, V = 2097.1(3) Å^3, $\rho_{calcd.}$ = 1.196 g·cm^{-3}, μ = 0.77 cm^{-1}, empirical absorption correction (0.977 ≤ T ≤ 0.992), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 0.71073 Å, T = 198 K, ω and scans, 13808 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.66 Å^{-1}, 4901 independent (R_{int} = 0.045) and 3343 observed reflections [$I \geq 2\sigma(I)$], 255 refined parameters, R = 0.055, wR^2 = 0.125, max. residual electron density 0.22 (−0.17) e·Å^{-3}, hydrogens calculated and refined as riding atoms.

Ethyl (*S*)-3-Methyl-2-[({phenyl[(phenyl)pyrrolidin-1-ylmethylene]-amino}methylene)amino]butanoate (5g): Following the general procedure (method B) **5g** was prepared from **2a** (2.78 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), ethyl L-valinate hydrochloride (1.82 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (20:1) as eluent (R_f = 0.18). Yield 2.32 g (57%), pale-yellow oil. IR (film): ṽ = 3061 (w, $CH_{arom.}$), 2968 (s, $CH_{aliph.}$), 2871 (m, $CH_{aliph.}$), 1730 (s, C=O), 1609 (vs, C=N), 1587 (vs, C=N), 1568 (vs, C=N), 1448 (s), 1340 (m), 1310 (m), 1283 (m), 1246 (m), 1175 (m), 1033 (m), 771 (m), 698 (s) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 0.99 (d, ^3J = 6.7 Hz, 6 H, $CH(CH_3)_2$], 1.27 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 1.94 (s, 4 H, NCH_2CH_2), 2.23 [m, 1 H, $CH(CH_3)_2$], 3.43 (br. s, 4 H, NCH_2CH_2), 4.06 (d, ^3J = 7.6 Hz, 1 H, $CHCH(CH_3)_2$], 4.18 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 6.92 (m, 2 H, $CH_{arom.}$), 7.04−7.15 (m, 6 H, $CH_{arom.}$), 7.47 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 14.4 (OCH_2CH_3), 19.3, 19.5 [$CH(CH_3)_2$], 25.4 (br., NCH_2CH_2), 32.7 [$CH(CH_3)_2$], 48.2 (br., NCH_2CH_2), 59.8 [$CHCH(CH_3)_2$], 68.6 (OCH_2CH_3), 126.9, 127.2, 128.0 (*o*-, *m*-$C_{arom.}$), 128.5, 128.7 (*p*-$C_{arom.}$), 135.4, 140.4 (*i*-$C_{arom.}$), 157.8, 164.8 (C=N), 173.7 (*C*OOEt) ppm. MS (EI, 70 eV): *m*/*z* (%) = 405 (30) [M^+], 362 (100) [$M^+ - iPr$], 332 (84) [$M^+ - COOEt$], 158 (45), 104 (42) [$PhCNH^+$]. $C_{25}H_{31}N_3O_2$ (405.54): calcd. C 74.04, H 7.70, N 10.36; found C 73.33, H 8.02, N 10.12.

(*R*,*R*)-*N*-{[(2-Methoxymethyl)pyrrolidin-1-yl](phenyl)methylene}-*N*′-(1-phenylethyl)benzamidine (5h): Following the general procedure (method A) **5a** was prepared from **2d** (3.74 g, 11.6 mmol), trifluoromethanesulfonic anhydride (2.0 mL, 11.6 mmol) and (*R*)-1-phenylethylamine (1.5 mL, 11.6 mmol) in dry dichloromethane (40 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (20:1) as eluent (R_f = 0.25). Yield 0.70 g (14%), colorless oil. IR (film): ṽ = 3059 (m, $CH_{arom.}$), 3024 (m, $CH_{arom.}$), 2968 (s, $CH_{aliph.}$), 2924 (s, $CH_{aliph.}$), 2874 (s, $CH_{aliph.}$), 1722 (m), 1609 (vs, C=N), 1591 (vs, C=N), 1574 (vs, C=N), 1493 (s, C=C), 1447 (s), 1423 (s), 1310 (s), 1281 (s), 1113 (s), 1055 (s), 1026 (s), 756 (s), 723 (s), 700 (vs) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 1.33 (d, ^3J = 5.0 Hz, 3 H, $CHCH_3$), 1.70−2.10 (m, 4 H, $NCH_2CH_2CH_2$), 3.07 (s, 3 H, OCH_3), 3.10−3.70 (m, 4 H, OCH_2, NCH_2), 4.55 (m, 1 H, NCH), 4.92 (q, ^3J = 5.0 Hz, 1 H, $CHCH_3$), 6.83 (m, 2 H, $CH_{arom.}$), 6.96 (m, 1 H, $CH_{arom.}$), 7.02−7.07 (m, 3 H, $CH_{arom.}$), 7.10−7.25 (m, 5 H, $CH_{arom.}$), 7.40 (m, 4 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 24.5 (CH_3), 26.5, 28.2 ($NCH_2CH_2CH_2$), 46.3 (NCH_2), 56.9 (OCH_3), 57.1, 59.0 (CH), 72.8 (OCH_2), 125.9 (*p*-$C_{arom.}$), 126.9, 127.2, 127.4, 127.5, 127.6, 128.0 (*o*-, *m*-$C_{arom.}$), 128.3, 128.5 (*p*-$C_{arom.}$), 135.2, 140.7, 147.4 (*i*-$C_{arom.}$), 158.1, 161.7 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 425 (48) [M^+], 410 (19) [$M^+ - CH_3$], 320 (7) [$M^+ - PhCHCH_3$], 207 (100) [$PhCNPhCNH^+$], 194 (11), 105 (70) [$PhCHCH_3^+$]. $C_{28}H_{31}N_3O$ (425.57): calcd. C 79.02, H 7.34, N 9.87; found C 78.41, H 7.79, N 9.22.

Ethyl 2,5-Diphenyl-3*H*-imidazole-4-carboxylate (7a): Following the general procedure (method B) **7a** was prepared from **2a** (5.56 g, 20.0 mmol), trifluoromethanesulfonic anhydride (3.4 mL, 20.0 mmol), ethyl glycinate hydrochloride (2.77 g, 20.0 mmol) and triethylamine (2.8 mL, 20.0 mmol) in dry dichloromethane (60 mL). The crude product was purified by recrystallization from acetonitrile. Yield 4.21 g (72%), colorless solid; m.p. 168 °C (ref.[33] 166−167.5 °C). IR (KBr): ṽ = 3053 (m, $CH_{arom.}$), 2957 (m, $CH_{aliph.}$), 2901 (m, $CH_{aliph.}$), 1713 (vs, C=O), 1583 (m, C=N), 1531 (m, C=N), 1491 (s, C=C), 1383 (s), 1312 (s), 1236 (s), 1130 (vs), 1022 (s), 966 (s), 781 (m), 717 (s), 692 (s) cm^{-1}. ^{1}H NMR (300.13 MHz, [D_6]DMSO): δ = 1.24 (t, ^3J = 6.9 Hz, 3 H, OCH_2CH_3), 4.25 (q, ^3J = 6.9 Hz, 2 H, OCH_2CH_3), 7.37−7.52 (m, 6 H, $CH_{arom.}$), 7.83 (m, 2 H, $CH_{arom.}$), 8.18 (m, 2 H, $CH_{arom.}$), 13.08 (s, 1 H, NH) ppm. ^{13}C NMR (75.47 MHz, [D_6]DMSO): δ = 14.0 (CH_3), 59.8 (OCH_2), 126.0, 127.6, 128.2, 128.6, 129.1, 129.4, 129.5, 131.8 (*o*-, *m*-, *p*-, *i*-$C_{arom.}$, $C_{imidazol.}$), 146.9 (NCN), 161.3 (*C*OOEt) ppm. MS (EI, 70 eV): *m*/*z* (%) = 292 (100) [M^+], 246 (93) [$M^+ - EtOH$], 218 (33) [$M^+ - HCOOEt$], 115 (38), 89 (42). $C_{18}H_{16}N_2O_2$ (292.33): calcd. C 73.95, H 5.52, N 9.58; found C 73.66, H 5.26, N 9.60.

2,4,5-Triphenyl-1*H*-imidazole (7b): Following the general procedure (method B) **7b** was prepared from **2a** (5.56 g, 20.0 mmol), trifluoromethanesulfonic anhydride (3.4 mL, 20.0 mmol), ethyl DL-phenylglycinate hydrogen *p*-toluenesulfonate (7.02 g, 20.0 mmol) and triethylamine (2.8 mL, 20.0 mmol) in dry dichloromethane (60 mL). The crude product was purified by recrystallization from acetonitrile. Yield 2.53 g (43%), colorless solid; m.p. 278 °C (ref.[34] 278−279 °C). IR (KBr): $\tilde{\nu}$ = 3045 (m, $CH_{arom.}$), 2966 (m, $CH_{aliph.}$), 2853 (m, $CH_{aliph.}$), 1601 (m, C=N), 1587 (m, C=N), 1489 (s, C=C), 1460 (s, C=C), 1396 (m), 1202 (w), 1128 (m), 1070 (m), 1028 (m), 966 (m), 916 (m), 834 (m), 766 (s), 735 (s), 698 (vs) cm^{-1}. ^1H NMR (400.14 MHz, [D$_6$]DMSO): δ = 7.20−7.60 (m, 13 H, $CH_{arom.}$), 8.11 (m, 2 H, $CH_{arom.}$), 12.73 (s, 1 H, NH) ppm. ^{13}C NMR (100.63 MHz, [D$_6$]DMSO): δ = 125.2, 126.5, 127.1, 127.8, 128.2, 128.3, 128.5, 128.6, 128.7, 130.4 (*o*-, *m*-, *p*-$C_{arom.}$, $C_{imidazol.}$), 131.1, 135.2, 137.1 (*i*-$C_{arom.}$), 145.5 (NCN) ppm. MS (EI, 70 eV): *m*/*z* (%) = 296 (100) [M^+], 195 (29) [M^+ − H], 165 (30), 127 (30), 84 (11). $C_{21}H_{16}N_2$ (296.37): calcd. C 85.11, H 5.44, N 9.45; found C 84.64, H 5.48, N 9.25.

Diethyl 2,5-Diphenyl-4*H*-imidazole-4,4-dicarboxylate (6a): Following the general procedure (method B) **6a** was prepared from **2a** (2.78 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), ethyl 2-aminomalonate hydrochloride (2.12 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by column chromatography (SiO_2) using *tert*-butyl methyl ether/*n*-pentane/triethylamine (10:10:1) as eluent (R_f = 0.20). Yield 0.54 g (15%), colorless oil. IR (film): $\tilde{\nu}$ = 3063 (w, $CH_{arom.}$), 2982 (m, $CH_{aliph.}$), 2937 (w, $CH_{aliph.}$), 1738 (vs, C=O), 1605 (s, C=N), 1566 (s, C=N), 1448 (m, C=C), 1323 (s), 1283 (s), 1229 (vs), 1063 (s), 733 (m), 690 (s) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 1.19 (t, ^3J = 7.2 Hz, 6 H, OCH_2CH_3), 4.23 (q, ^3J = 7.2 Hz, 4 H, OCH_2CH_3), 7.46−7.59 (m, 6 H, $CH_{arom.}$), 8.25 (m, 2 H, $CH_{arom.}$), 8.46 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 13.7 (OCH_2CH_3), 63.0 (OCH_2CH_3), 95.3 (C_q), 128.4, 128.5, 129.7 (*o*-, *m*-$C_{arom.}$), 130.2 (*i*-$C_{arom.}$), 130.4 (*o*-, *m*-$C_{arom.}$), 130.9 (*i*-$C_{arom.}$), 132.1, 132.9 (*o*-$C_{arom.}$), 164.1 (*C*OOEt), 177.9, 187.8 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 364 (19) [M^+], 320 (27), 292 (100) [M^+ − $COOCH_2CH_2$], 291 (75) [M^+ − COOEt], 274 (11), 246 (99), 218 (38) [M^+ − 2 COOEt], 187 (51), 127 (17), 115 (38), 105 (81), 104 (62) [PhCNH^+], 89 (60), 77 (25) [Ph^+]. $C_{21}H_{20}N_2O_4$ (364.40): calcd. C 69.22, H 5.53, N 7.69; found C 68.24, H 6.00, N 7.55.

2′,5′-Diphenylspiro[9*H*-fluorene-9,4′-(4*H*)imidazole] (6b): Following the general procedure (method B) **6b** was prepared from **2a** (2.78 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), 9-aminofluorene hydrochloride (2.18 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (20:1) as eluent (R_f = 0.18). Yield 1.52 g (41%), colorless crystals; m.p. 187 °C. IR (KBr): $\tilde{\nu}$ = 3057 (w, $CH_{arom.}$), 3007 (w, $CH_{arom.}$), 1605 (m, C=N), 1595 (s, C=N), 1562 (s, C=N), 1531 (m, C=N), 1447 (s), 1317 (s), 1277 (s), 1173 (m), 1080 (s), 1059 (s), 1020 (m), 933 (m), 771 (s), 737 (s), 710 (vs), 689 (s) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 6.90 (m, 2 H, $CH_{arom.}$), 7.15 (m, 4 H, $CH_{arom.}$), 7.27 (m, 1 H, $CH_{arom.}$), 7.41 (m, 2 H, $CH_{arom.}$), 7.47−7.60 (m, 5 H, $CH_{arom.}$), 7.83 (m, 2 H, $CH_{arom.}$), 8.51 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 94.4 (C_q), 121.1, 123.9, 128.3, 128.4, 128.5, 128.7, 129.3, 129.4 (*o*-, *m*-$C_{arom.}$, $C_{fluoren.}$), 130.3 (*i*-$C_{arom.}$), 131.4 (*p*-$C_{arom.}$), 131.8 (*i*-$C_{arom.}$), 132.1 (*p*-$C_{arom.}$), 141.7, 141.8 (*i*-$C_{fluoren.}$), 175.4, 192.7 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 370 (29) [M^+], 267 (100) [M^+ − PhCN], 164 (59) [M^+ − 2 PhCN]. $C_{27}H_{18}N_2$ (370.45): calcd. C 87.54, H 4.90, N 7.56; found C 87.45, H 4.89, N 7.48.

X-ray Crystal Structure Analysis of 6b: $C_{27}H_{18}N_2$, *M* = 370.45, colorless crystal, 0.35 × 0.20 × 0.05 mm, *a* = 10.959(1), *b* = 8.727(2), *c* = 11.191(1) Å, β = 109.31(1)°, *V* = 1010.1(3) $Å^3$, $\rho_{calcd.}$ = 1.218 g·cm^{-3}, μ = 5.51 cm^{-1}, no absorption correction (0.830 ≤ *T* ≤ 0.973), *Z* = 2, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, *T* = 223 K, ω/2θ scans, 2301 reflections collected (±*h*, +*k*, −*l*), [(sinθ)/λ] = 0.62 $Å^{-1}$, 2191 independent (R_{int} = 0.031) and 1542 observed reflections [$I \geq 2\sigma(I)$], 263 refined parameters, *R* = 0.069, wR^2 = 0.214, max. residual electron density 0.45 (−0.37) e·$Å^{-3}$, hydrogens calculated and refined as riding atoms.

2′,5′-Bis(4-methylphenyl)spiro[9*H*-fluorene-9,4′-(4*H*)-imidazole] (6c): Following the general procedure (method B) **6c** was prepared from **2b** (3.06 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), 9-aminofluorene hydrochloride (2.18 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by crystallization from chloroform/*n*-pentane. Yield 3.19 g (80%), colorless crystals; m.p. 223 °C. IR (KBr): $\tilde{\nu}$ = 3018 (w, $CH_{arom.}$), 2964 (w, $CH_{aliph.}$), 2920 (w, $CH_{aliph.}$), 1610 (s, C=N), 1593 (s, C=N), 1558 (s, C=N), 1497 (s, C=C), 1448 (s), 1315 (s), 1279 (s), 1175 (s), 1072 (s), 1028 (m), 835 (m), 764 (vs), 733 (vs) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 2.43 (s, 3 H, CH_3), 6.89 (m, 2 H, $CH_{arom.}$), 6.91 (m, 2 H, $CH_{arom.}$), 7.15 (m, 2 H, $CH_{arom.}$), 7.32 (m, 2 H, $CH_{arom.}$), 7.39 (m, 2 H, $CH_{arom.}$), 7.47 (m, 2 H, $CH_{arom.}$), 7.82 (m, 2 H, $CH_{arom.}$), 8.38 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 21.5, 21.6 (CH_3), 94.1 (C_q), 121.0, 124.0, 128.3, 128.8, 129.1, 129.2, 129.3, 129.4 (*o*-, *m*-$C_{arom.}$, $C_{fluoren.}$), 141.8, 141.9, 142.2, 142.8 (*i*-$C_{arom.}$), 175.6, 192.3 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 398 (35) [M^+], 281 (100) [M^+ − TolCN], 164 (44) [M^+ − 2 TolCN]. $C_{29}H_{22}N_2$ (398.49): calcd. C 87.41, H 5.56, N 7.03; found C 87.10, H 5.65, N 6.97.

X-ray Crystal Structure Analysis of 6c: Formula $C_{29}H_{22}N_2$, *M* = 398.49, colorless crystal, 0.30 × 0.20 × 0.05 mm, *a* = 12.881(1), *b* = 11.202(1), *c* = 15.664(1) Å, β = 108.69(1)°, *V* = 2141.0(3) $Å^3$, $\rho_{calcd.}$ = 1.236 g·cm^{-3}, μ = 5.54 cm^{-1}, empirical absorption correction (0.851 ≤ *T* ≤ 0.973), *Z* = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, *T* = 223 K, ω and scans, 12291 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.59 $Å^{-1}$, 3575 independent (R_{int} = 0.103) and 2026 observed reflections [$I \geq 2\sigma(I)$], 281 refined parameters, *R* = 0.060, wR^2 = 0.138, max. residual electron density 0.21 (−0.18) e·$Å^{-3}$, hydrogens calculated and refined as riding atoms.

2′,5′-Bis(4-methoxyphenyl)spiro[9*H*-fluorene-9,4′-(4*H*)imidazole] (6d): Following the general procedure (method B) **6d** was prepared from **2c** (3.38 g, 10.0 mmol), trifluoromethanesulfonic anhydride (1.7 mL, 10.0 mmol), 9-aminofluorene hydrochloride (2.18 g, 10.0 mmol) and triethylamine (1.4 mL, 10.0 mmol) in dry dichloromethane (30 mL). The crude product was purified by crystallization from chloroform/*n*-pentane. Yield 3.18 g (74%), colorless crystals; m.p. 206 °C. IR (KBr): $\tilde{\nu}$ = 3065 (w, $CH_{arom.}$), 3005 (w, $CH_{arom.}$), 2937 (w, $CH_{aliph.}$), 2833 (w, $CH_{aliph.}$), 1607(s, C=N), 1595 (s, C=N), 1564 (w, C=N), 1510 (s, C=C), 1319 (s), 1258 (vs), 1165 (s), 1074 (m), 1028 (m), 835 (m), 756 (m), 727 (m) cm^{-1}. ^1H NMR (300.13 MHz, $CDCl_3$): δ = 3.70 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 6.65 (m, 2 H, $CH_{arom.}$), 6.91 (m, 2 H, $CH_{arom.}$), 7.01 (m, 2 H, $CH_{arom.}$), 7.17 (m, 2 H, $CH_{arom.}$), 7.40 (m, 2 H, $CH_{arom.}$), 7.53 (m, 2 H, $CH_{arom.}$), 7.83 (m, 2 H, $CH_{arom.}$), 8.43 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 55.2, 55.4 (OCH_3), 93.7 (C_q), 113.9, 121.0, 123.2, 124.1, 124.8, 128.3, 129.1, 130.9, 131.2 (*o*-, *m*-$C_{arom.}$, $C_{fluoren.}$), 141.7, 142.8 (*i*-$C_{arom.}$), 162.3, 162.7 (*i*-$COCH_3$), 175.1, 191.5 (C=N) ppm. MS (EI, 70 eV): *m*/*z* (%) = 430 (26) [M^+], 297 (100) [M^+ − $MeOC_6H_4CN$], 164 (44) [M^+ −

2 $MeOC_6H_4CN$]. $C_{29}H_{22}N_2O_2$ (430.49): calcd. C 80.91, H 5.15, N 6.51; found C 80.23, H 5.15, N 6.44.

X-ray Crystal Structure Analysis of 6d: Formula $C_{29}H_{22}N_2O_2$, M = 430.49, colorless crystal, 0.70 × 0.10 × 0.05 mm, a = 9.331(1), b = 9.187(1), c = 14.522(1) Å, α = 90.74(1), β = 94.05(1), γ = 91.55(1)°, V = 1108.2(2) Å^3, $\rho_{calcd.}$ = 1.290 g·cm^{-3}, μ = 6.45 cm^{-1}, no absorption correction ($0.661 \leq T \leq 0.969$), Z = 2, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, T = 223 K, ω/2θ scans, 4856 reflections collected ($-h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.62 Å^{-1}, 4529 independent (R_{int} = 0.032) and 3830 observed reflections [$I \geq 2\sigma(I)$], 301 refined parameters, R = 0.044, wR^2 = 0.124, max. residual electron density 0.32 (−0.19) e·Å^{-3}, hydrogens calculated and refined as riding atoms.

2,4,5-Triphenyl-1*H*-imidazole (7b): A solution of **5b** (920 mg, 2.5 mmol) in dry tetrahydrofuran (10 mL) was added to a solution of potassium *tert*-butoxide (336 mg, 3.0 mmol) and *n*-butyllithium (1.9 mL, 1.6 M in *n*-hexane) in dry tetrahydrofuran (40 mL) at −78 °C. The reaction mixture was stirred at −40 °C for 3 h. After warming to room temperature the reaction mixture was washed with saturated sodium hydrogen carbonate solution (3 × 15 mL), dried with sodium sulfate, and the solvent removed in vacuo. The crude product was purified by crystallization from dichloromethane/diethyl ether. Yield 310 mg (42%), colorless solid; m.p. 278 °C (ref.[34] 278−279 °C). $C_{21}H_{16}N_2$ (296.37).

4-Methyl-2,5-diphenyl-1*H*-imidazole (7c): A solution of **5f** (950 mg, 2.5 mmol) in dry tetrahydrofuran (10 mL) was added dropwise at −78 °C over a period of 20 min to a solution of lithium diisopropylamide [3.0 mmol, prepared in situ from diisopropylamine (300 mg) and *n*-butyllithium (1.9 mL, 1.6 M in *n*-hexane)] in dry tetrahydrofuran (40 mL). The reaction mixture was stirred at −40 °C for 3 h. After warming to room temperature the reaction mixture was washed with saturated sodium hydrogen carbonate solution (3 × 15 mL), dried with sodium sulfate and the solvent removed in vacuo. The crude product was purified by column chromatography (SiO_2) using *tert*-butyl methyl ether/*n*-pentane (1:1) as eluent (R_f = 0.18). Yield 370 mg (63%), pale-yellow oil. IR (film): $\tilde{\nu}$ = 3211 (m, NH), 3063 (m, $CH_{arom.}$), 2978 (s, $CH_{aliph.}$), 2924 (m, $CH_{aliph.}$), 2876 (m, $CH_{aliph.}$), 1672 (s, C=N), 1591 (m, C=N), 1498 (m, C=C), 1462 (s, C=C), 1182 (m), 1128 (m), 1111 (m), 910 (s), 773 (s), 696 (vs) cm^{-1}. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ = 2.54 (s, 3 H, CH_3), 7.36−7.55 (m, 6 H, $CH_{arom.}$), 7.76 (m, 2 H, $CH_{arom.}$), 8.09 (m, 2 H, $CH_{arom.}$), 10.94 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 12.0 (CH_3), 125.3, 126.2, 126.9, 127.9, 128.2, 128.5, 130.4, 133.4 (C-5, $C_{arom.}$), 145.4 (C-4), 155.4 (NCN) ppm. MS (EI, 70 eV): m/z (%) = 234 (100) [M^+], 130 (22), 104 (23) [$PhCNH^+$], 103 (20) [$PhCN^+$], 89 (17), 77 (8) [Ph^+]. $C_{16}H_{14}N_2$ (234.30).

***N*-(2,2-Difluorovinyl)-*N'*-[(phenyl)(pyrrolidin-1-yl)methylene]benzamidine (8):** A solution of **5d** (1.80 g, 5.0 mmol) in dry tetrahydrofuran (20 mL) was added dropwise at −78 °C over a period of 20 min to a solution of lithium diisopropylamide [6.0 mmol, prepared in situ from diisopropylamine (600 mg) and *n*-butyllithium (3.8 mL, 1.6 M in *n*-hexane)] in dry tetrahydrofuran (80 mL). The reaction mixture was stirred at −40 °C for 3 h. After warming to room temperature, the reaction mixture was washed with saturated sodium hydrogen carbonate solution (3 × 30 mL), dried with sodium sulfate and the solvent removed in vacuo. The crude product was purified by column chromatography (SiO_2) using *n*-pentane/triethylamine (10:1) as eluent (R_f = 0.30). Yield 1.24 g (69%), colorless crystals; m.p. 139 °C. IR (KBr): $\tilde{\nu}$ = 3055 (w, $CH_{arom.}$), 3003 (w, $CH_{arom.}$), 2972 (m, $CH_{aliph.}$), 2870 (m, $CH_{aliph.}$), 1717 (vs), 1583 (vs, C=N), 1501 (m, C=C), 1448 (s), 1339 (s), 1310 (s), 1288 (s), 1234 (s), 1202 (m), 1047 (m), 1022 (m), 943 (m), 766 (m), 719 (s), 698 (s) cm^{-1}. ^{1}H NMR (300.13 MHz, $CHCl_3$): δ = 1.97 (s, 4 H, NCH_2CH_2), 3.22 (br. s, 2 H, NCH_2CH_2), 3.68 (br. s, 2 H, NCH_2CH_2), 6.38 [d, ^3J(H,F) = 19.6 Hz, 1 H, $CH{=}CF_2$], 6.94 (m, 2 H, $CH_{arom.}$), 7.10−7.25 (m, 6 H, $CH_{arom.}$), 7.66 (m, 2 H, $CH_{arom.}$) ppm. ^{13}C NMR (75.47 MHz, $CHCl_3$): δ = 25.4 (br., NCH_2CH_2), 47.5, 49.2 (br., NCH_2CH_2), 94.2 [dd, ^2J(C,F) = 43.2 Hz, ^2J(C,F) = 11.5 Hz, $CH{=}CF_2$], 115.1, 119.5 (i-$C_{arom.}$), 126.6, 127.6, 127.7, 128.2, 129.2 (*o*-, *m*-$C_{arom.}$), 135.0, 138.7 (*p*-$C_{arom.}$), 157.1 [dd, $1J$(C,F) = 300.1 Hz, $1J$(C,F) = 279.7 Hz, $CH{=}CF_2$], 158.7 (C=N), 162.3 [d, 4_J(C,F) = 7.6 Hz, C=N] ppm. ^{19}F NMR (282.37 MHz, $CHCl_3$): δ = −91.1 [dd, ^2J(F,F) = 38.2 Hz, ^3J(F,H) = 19.1 Hz], −102.6 [d, ^2J(F,F) = 38.1 Hz] ppm. MS (EI, 70 eV): m/z (%) = 339 (100) [M^+], 220 (23), 167 (80), 166 (86) [$PhCNCHCF_2^+$], 158 (40), 127 (73), 104 (34) [$PhCNH^+$], 103 (25) [$PhCN^+$], 84 (60), 77 (31) [Ph^+], 70 (35) [$(CH_2)_4N^+$]. $C_{20}H_{19}F_2N_3$ (339.38): calcd. C 70.78, H 5.64, N 12.38; found C 70.60, H 5.45, N 12.33.

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