Synthesis of Radialene-Shaped Pyrroles by Multiple-Anion-Capture Reactions of 1,3-Dianions

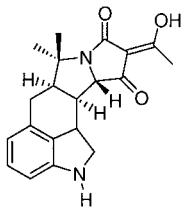
Peter Langer,*[a] Manfred Döring,[b] Peter R. Schreiner,[c] and Helmar Görls[b]

Abstract: A new multicomponent reaction (multiple-anion-capture reaction) of 1,3-dianions with nitriles and oxalic acid-bis(imidoyl)chlorides is reported. This process allows for an efficient and regioselective synthesis of a variety of radialene-shaped pyrroles which constitute structurally new and interesting heterocyclic systems. The cyclization products can be considered as aza-analogues of the pharmacologically relevant substance class of 3-acetyltetramic acids. A rationalization of the experimental results is given based on quantum chemical computations.

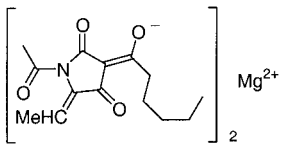
Keywords: anions · cyclization · multicomponent reactions · quantum chemical calculations · regioselectivity

Introduction

Radialenes and the related pseudooxocarbons are cyclic compounds containing only sp^2-hybridized ring atoms and exocyclic double bonds.[1, 2] Radialene-shaped substructures are not only of academic interest, but also occur in a variety of pharmacologically relevant natural products, which include the structurally mobile 3-acetyltetramic acids.[3] For example, the mycotoxin α-cyclopiazonic acid is produced by the fungus *Penicillium cyclopium*;[4a] it is very toxic[4b] and possesses neurological activity by changing the neurotransmitter levels.[4c] This compound, which suppresses the cytotoxic effects of patulin, can act as an antioxidant.[4d] In addition, α-cyclopiazonic acid is a potent inhibitor of calcium uptake and Ca^{2+}ATP-ase activity in the endoplasmatic reticulum.[4e] The antiprotozoal compound malonomycin was isolated from *Streptomyces rimosus var. paromomycinus* and has particularly potent activity against *Trypanosomes*.[5] Ikarugamycin shows strong specific antibiotic activity and has been used as an antiulcer agent.[6] The interesting radialene-shaped pyrrole magnesidin inhibits various Gram-positive bacteria.[7]



α–Cyclopiazonic Acid



Magnesidin

Multicomponent reactions have found widespread application in organic synthesis.[8] Carbanionic multicomponent reactions (multiple-anion-capture reactions) involve attack of a nucleophile on a suitable relais species to form a reactive intermediate which is subsequently trapped by an electrophile. Recent examples include the reaction of carbon nucleophiles with allenes and subsequent cyclization with acrylates[9] and reactions involving isocyanates[10] or allenyl isothiocyanates as the relais species.[11] Multiple-anion-capture reactions using nitriles as the relais species have been observed in the reaction of bislithiated 2,3-dimethylbutadiene with benzonitrile[12a] and in the 1,4-addition of nitriles to (butadiene)zirconocene.[12b, c] In the course of our program directed at the development of regio- and stereoselective cyclization reactions of dianions and dianion equivalents[13] we have recently studied nitriles,[14a, b, 15] esters,[14c–e] and ketones[14f, g] as relais species in multiple-anion-capture reactions of dianions. Herein, we wish to report a new and regioselective three-component reaction of 1,3-dianions with nitriles and oxalic acid-bis(imidoyl)chlorides.[15] This domino process allows for an efficient synthesis of a variety of radialene-shaped pyrroles. These compounds represent aza-analogues of pharmacologically relevant natural products and constitute structurally new heterocyclic systems. A rationalization of the experimental results is given based on quantum chemical computations.

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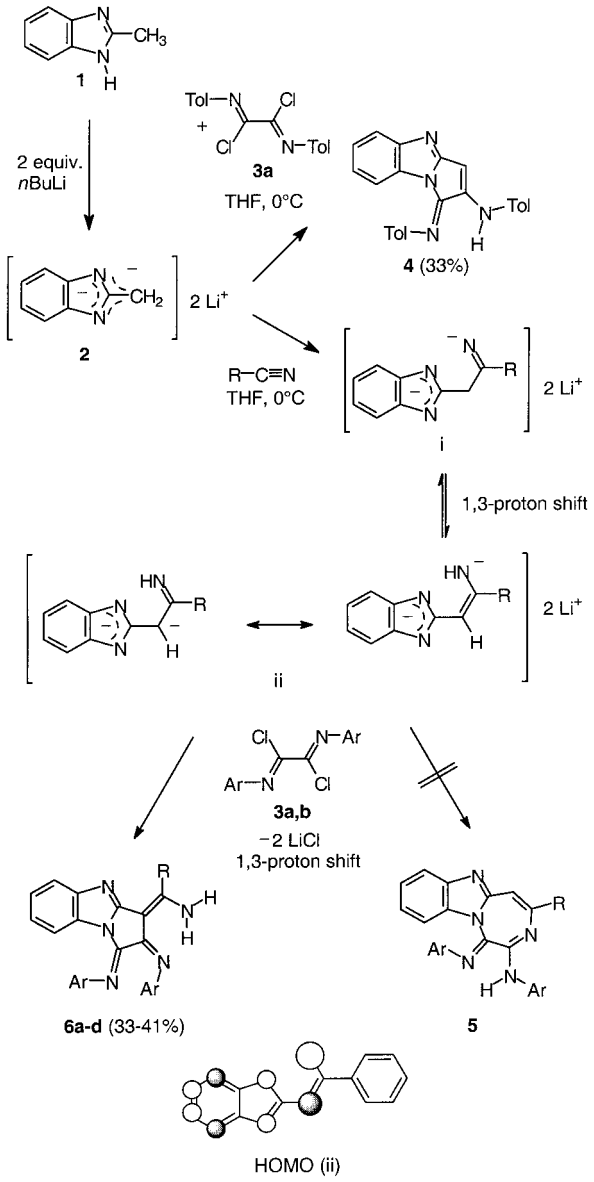
Results and Discussion

Benzimidazole-derived radialene-shaped pyrroles: Cyclization reactions of dianions[16] with oxalic acid dielectrophiles had not been reported until recently.[13a] These reactions are problematic since they can suffer from several drawbacks, such as polymerization or decarbonylation.[17] In fact, all attempts to induce a cyclization of the dianion **2** of 2-methylbenzimidazole **1** (generated by addition of two equivalents of *n*BuLi)[18] with oxalyl chloride or oxalic diethylester proved unsuccessful. However, we have recently shown[15, 13w] that the reaction of **2** with oxalic acid-bis(*p*-tolylimidoyl)chloride **3a**, which can be considered as an aza-analogue of oxalyl chloride,[19] resulted in regioselective cyclization and formation of the 1-arylimino-1*H*-pyrrolo[1,2-*a*]benzimidazol-2-amine **4** (Scheme 1). Heterocycles related to **4** have been shown to exhibit antitumor activity against a variety of cancer cell lines.[20]

Based on these initial results, multiple-anion-capture reactions of dianions with nitriles as relais species were studied. The reaction of the dianion **2** with nitriles and subsequent cyclization with oxalic acid-bis(imidoyl)chlorides regioselectively afforded the orange colored products **6a–d** containing a unique functionality (Scheme 1). Heterocycles **6** exhibit four neighboring exocyclic double bonds and thus represent radialene-shaped pyrroles (vide infra). The formation of **6a–d** can be explained as follows: the initial attack of the dianion on the nitrile regioselectively occurred at the carbon atom of the dianion to give the dianionic intermediate i. A subsequent 1,3-proton shift afforded the ambident intermediate ii, which, in principle, can give rise to formation of regioisomers on treatment with bis(imidoyl)chlorides **3**. In fact, regioselective *C*,*N*-cyclization rather than *N*,*N*-cyclization was observed, followed by a second 1,3 H-shift to give the final product. During the course of the reaction, the CH_3 group of 2-methylbenzimidazole was transformed into a sp^2-hybridized quaternary carbon atom.

Semiempirical calculations (AM1) show that the regioselectivity has to be explained by kinetic considerations, since the most stable tautomer of **6a** and the isomeric seven-membered ring **5** (R = Ph, Ar = Tol) are very similar energetically. The observed regioselectivity can be explained based on AM1 calculations: the carbon atom of dianion ii possesses a relatively high HOMO coefficient (compared with related systems), although the value is of course lower than that of the (more electronegative) nitrogen atom. Besides, HSAB effects presumably play an important role for the regioselectivity.



Scheme 1. Synthesis of radialene-shaped pyrroles **6**.

For comparison of the spectroscopic properties, the colorless enamine **7** was prepared by condensation of dianion **2** with benzonitrile (Scheme 2). At 20 °C, the ^{1}H NMR spectrum of **7** only shows a single N–H resonance assigned to the intramolecular hydrogen bond ([D_8]THF, $\delta = 11.49$). When the temperature is decreased, the signal becomes sharp, and at –60 °C two more N–H resonances appear ($\delta = 9.07$, 6.64)

Table 1. Yields for compounds **6a–d** with various substituents.

6	R	Ar[a]	%[b]
a	Ph	Tol	41
b	Tol	Tol	40
c	Ph	Ph	33
d	*t*Bu	Tol	40

[a] Tol = 4-$CH_3C_6H_4$. [b] Isolated yield.

Abstract in German: *Eine neue Multikomponenten-Reaktion (Anionen-Einfang-Reaktion) von 1,3-Dianionen mit Nitrilen und Oxalsäure-bis(imidoyl)chloriden wird vorgestellt. Diese Umsetzungen erlauben einen effizienten und regioselektiven Zugang zu einer Reihe von Pyrrolen mit Radialen-artiger Topologie. Diese Verbindungen stellen die ersten Vertreter eines neuen heterocyclischen Systems dar und können als Azaanaloga der pharmakologisch relevanten Substanzklasse der 3-Acetyltetramsäuren aufgefaßt werden. Die experimentellen Befunde werden basierend auf quantenchemischen Rechnungen rationalisiert.*

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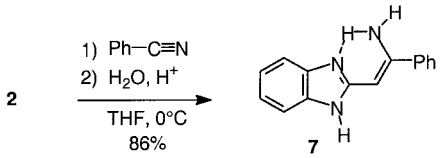
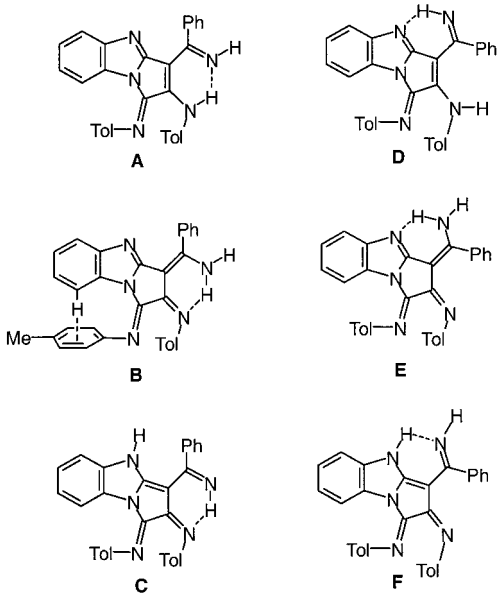


Scheme 2. Synthesis of enamine **7**.

which are assigned to the heterocyclic N–H group and to the nonchelating hydrogen atom of the NH_2 group, respectively. At 20 °C, a fast interchange between these hydrogen atoms takes place. The ^{13}C NMR spectrum shows the presence of six signals for the carbon atoms of the annelated benzene ring. This result indicates that the rotation around the N_2C–C single bond is slow on the NMR timescale, which is presumably due to strong intramolecular hydrogen bonding N–H···N. The vibration bands (IR) can be assigned to three N–H bonds with a sharp absorption at 3447 cm^{-1}, which is diagnostic for the presence of a heterocyclic N–H group.

The tautomeric forms of pyrroles **6a–d** were studied in solution and in the solid state.[21] Several structures are possible and they involve two sets of interchanging tautomers **A/B** and **E/F** that arise through proton transfer along the intramolecular hydrogen bond, together with three tautomeric pairs of *E*/*Z* isomers (**B**/**E**) and conformers (**A**/**D** and **C**/**F**) that arise from rotation of the C8 side chain (see structures **A–F** and Figure 1). Tautomers **A–C** and **D–F** exhibit different types of hydrogen bonds (N–H···N). Tautomers **A**/**D** and **C**/**F** are secondary enamines containing an amino group (–NHAr) or a heterocyclic N–H group, respectively. Tautomers **B**/**E** are primary enamines and exhibit a radialene-shaped pyrrole structure.

The ^1H NMR spectra of pyrroles **6a–d** exhibit two deuterium-exchangeable N–H protons. Drastic deshielding is observed for the low-field signal relative to the parent compound **4**, which indicates the presence of a significantly stronger hydrogen bond (located within a 6-membered rather



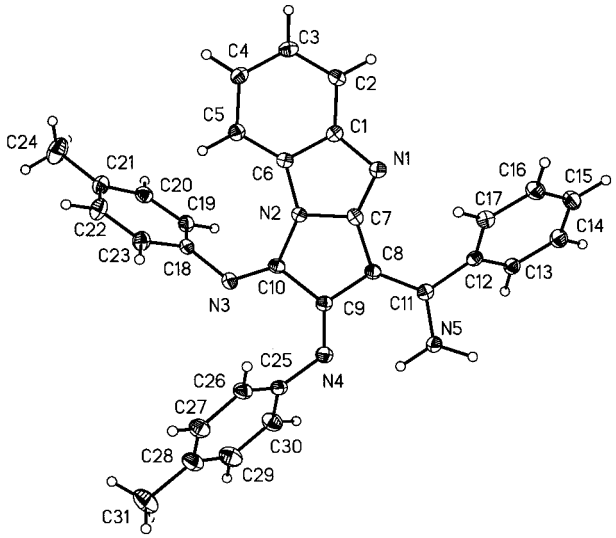


Figure 1. ORTEP plot of **6a**. The thermal ellipsoids of 50 % probability are shown for the non-hydrogen atoms. Selected bond lengths [Å] and angles [°]: N1–C7 1.318(4), N2–C7 1.393(4), C1–C2 1.387(4), C2–C3 1.388(5), C4–C5 1.397(5), C7–C8 1.432(4), C8–C9 1.451(4), N1–C1 1.393(4), N2–C6 1.407(4), N3–C10 1.259(4), N4–C9 1.292(4), N5–C11 1.331(4), C1–C6 1.410, C3–C4 1.384(5), C5–C6 1.384(4), C8–C11 1.392(4), C9–C10 1.509(4); C7–N1–C1 104.7(3), C7–N2–C10 111.4(2), C10–N3–C18 124.3(3), N1–C1–C6 111.6(3), C4–C3–C2 121.7(3), C5–C6–C1 121.6(3), N1–C7–N2 112.9(3), N2–C7–C8 109.9(3), C11–C8–C9 125.0(3), N4–C9–C8 123.6(3), C8–C9–C10 108.1(3), N3–C10–C9 123.9(3), N5–C11–C8 120.7(3), C8–C11–C12 123.9 3).

than a 5-membered ring). The high-field resonances ($CDCl_3$) of the free N–H groups of pyrroles **6** appear at lower frequencies than the N–H signal of **4**. The chemical shifts are in good agreement with those observed for the free N–H groups of the NH_2 group, but not with the heterocyclic N–H group of enamine **7**. The $^1H,^1H$-COSY spectra of **6a–d** ([D_6]DMSO) exhibit a significant $^2J(^1H,^1H)$ coupling of the N–H hydrogens which indicates the presence of a NH_2 group. In addition, the interchange of hydrogen atoms within the NH_2 group is slow on the NMR timescale as two separate N–H signals are detected. This is understandable since pyrroles **6** represent vinylogous amidines and two zwitterionic mesomeric structures of the type [N^-–C=C8–C11=NH_2^+] are possible (numbering: see Figure 1). Below 20 °C, both N–H signals split into doublets, as a result of the geminal $^2J(^1H,^1H) = 4.7$ Hz coupling (**6a**, [D_8]THF, –80 °C) within the NH_2 group. At elevated temperatures, the resonance lines become very broad.

Similar to the parent compound **4**, the ^1H NMR signal of proton 5-H of pyrroles **6a–d** is drastically shifted upfield, as a result of its location in the anisotropy cone of the arylimino group attached to carbon C10 (numbering: see Figure 1, Table 1). The resonance line is very broad at 20 °C (in contrast to the respective signal of **4**). At –30 °C, a sharp doublet is formed (**6a**, $\delta = 4.90$) and a second, smaller doublet appears ($\delta = 6.04$, integration: 1:6). The interconversion between tautomers **B/E** presumably accounts for the temperature effect observed. At 20 °C, the interchange between the tautomers **B**/**E** is fast on the NMR timescale ([D_6]DMSO), since the resonance of hydrogen 5-H is extremely broad. A ^{15}N INEPT (Insensitive Nucleus Enhancement by Polariza-

Table 2. Experimental results for compounds **4**, **6a–d**, **7**, and **13a**.

	IR (KBr) $\tilde{\nu}_{N-H}$, $\tilde{\nu}_{C=N}$, $\tilde{\nu}_{C=C}$	Solvent[a]	^{1}H NMR[a] δ (5-H)	^{1}H NMR[a] δ (NH)	^{13}C NMR[e] δ
4	3444, 1666, 1618	A	4.90 (d)	8.30	88.24
6a	3435, 3250	A	5.13 (brs)	10.72, 5.58	–
	1692, 1620	B	4.90 (brs)[c]	10.55, 7.70	92.90
		C	–[b]	10.43, 8.63	–
6b	3438, 3255	A	5.22 (brs)	10.65, 5.79	92.58
	1692, 1618	C	–[b]	10.45, 8.60	–
6c	3440, 3260	B	5.13 (brs)	10.47, 8.50	92.59
	1695, 1620		–[b]		
6d	3467, 1695, 1618	B	4.97 (brs)[c]	12.15, 7.95	90.82
7	3447 (sharp)	A	> 6.90[d]	11.20	–
	3420, 3279	B	> 6.90[d]	11.49, 9.07[c]	83.33
	1614			6.64[c]	
13a	3416, 3322	B	–	10.94, 7.89	93.51
	1730 (C=O)				

[a] Chemical shifts of 5-H and NH (numbering: see Figure 1); solvents: A = $CDCl_3$, B = [D_8]THF, C = [D_6]DMSO; d = doublet, br = broad. [b] Not detectable. [c] Detectable only below $-40\,^{\circ}C$. [d] Overlapped by aryl signals. [e] Chemical shifts of C-8 (for **6**, numbering: see Figure 1), C-3 (for **13a**, numbering: see Figure 5), and $N_2C-CH=$ (for **4** and **7**).

tion Transfer) experiment for **6b** was particularly helpful to prove the presence of radialene tautomers **B**/**E** in solution.[22] The detection of a triplet [$^1J(^{15}N,^1H) = 90$ Hz] indicated the presence of a NH_2 group. For the other nitrogen atoms singlets were observed, and no minor tautomer could be detected in the spectrum.

A characteristic spectroscopic feature (^{13}C NMR) of pyrroles **6** is the resonance of carbon atom C8 (numbering: see Figure 1) which appears at relatively high field. This can be explained by the π-donor effect of four neighboring nitrogen atoms. The IR spectra (KBr) of **6a–d** exhibit diagnostic vibration bands at approximately 3435–3465 cm^{-1} (free N–H bond) and 3255 cm^{-1} (intramolecular hydrogen bond N–H···N, Table 2). The absence of sharp heterocyclic $\tilde{\nu}_{N-H}$ vibration bands (as characteristic for **7**) suggests that structures **C** and **F** are *not* adopted.

Differentiation between tautomers **B** and **E** was not possible by spectroscopic methods. However, as shown by the crystal structure analysis of **6a**, tautomer **B** is the structure present in the solid state (Figure 1). Inspection of the bond lengths and of the location of the hydrogen atoms clearly shows that pyrrole **6a** indeed possesses a radialene-shaped structure: the bond length of C8–C11 (numbering: see Figure 1) is significantly shorter than the bond lengths of C7–C8, C8–C9, and C9–C10. Thus, the double-bond character of C8–C11 is much greater than that of C8–C9. In addition, the double-bond character of N4–C9 (imino group) is much greater than that of N5–C11 (amino group). The same is true for N1–C7 relative to N1–C1 and N2–C10. In addition, the crystal structure of **6a** clearly shows that the *ortho* hydrogen atom of the benzimidazole unit is located in the anisotropy cone of the arylimino group which independently confirms the structural information obtained by the ^{1}H NMR data. Radialene-shaped pyrroles **6a–d** contain five nitrogen atoms and two N–H bonds and are thus well set up for recognition processes: inspection of the crystal lattice of **6a** (Figure 2) shows that the hydrogen atoms of the NH_2 group are not only involved in intramolecular hydrogen bonding (N···H distance: 1.906 Å), but also act as an intermolecular binding site for the nitrogen atom of a neighboring molecule (N···H distance: 1.987 Å).

The structure of **6a** was reproducible computationally (Figure 3), for which the experimentally isolated tautomer **B** is also the lowest-lying minimum structure at the B3LYP/3-21G//AM1 level of theory; all other tautomers are at minima and display the aforementioned internal hydrogen bonds (see Experimental Section for details of the computations). As it is difficult to chemically predict or rationalize the energetic ordering of these tautomers, we computed the nucleus-independent chemical shift (NICS) values to assess the differences in aromatic stabilization energies in the tricyclic core. Indeed, the aromaticity of the benzene moiety is not interrupted and is even slightly higher than that of benzene itself (NICS = –10) at this level of theory. Interestingly, **B** has the highest NICS value for the benzannelated part. The fused

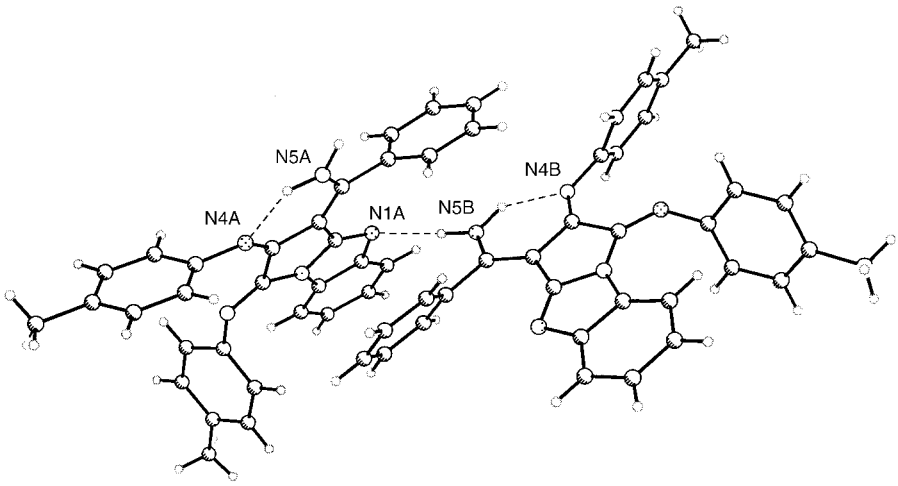


Figure 2. Dimer formation of **6a** in the solid state.

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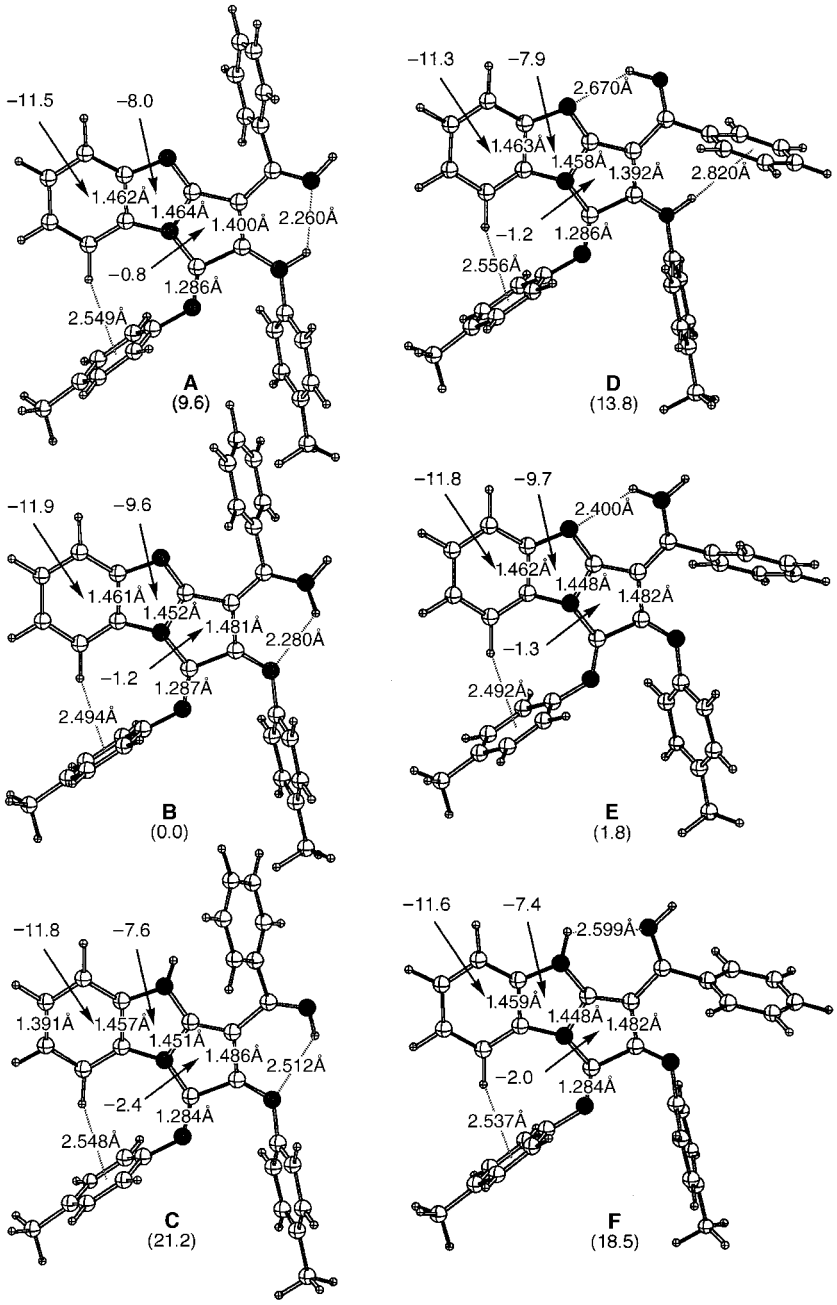


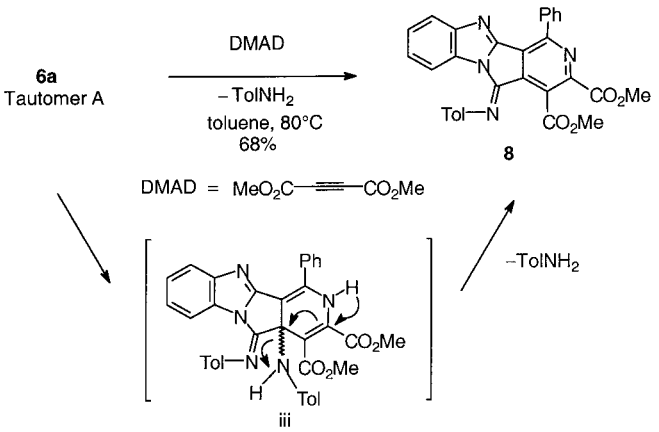
Figure 3. Geometry of **6a** computed at B3LYP/3-21G//AM1.

five-membered heterocycle also is clearly aromatic and again displays the largest NICS value for tautomers **B** and **E**, which are very similar in energy ($\Delta H = 1.8$ kcal mol^{-1}). The third fused heterocycle is marginally aromatic and apparently does not contribute much to the overall stability. Hence, **B** is favored energetically because it is able to maximize the aromaticity and the conjugation of the contiguous unsaturated ring system.

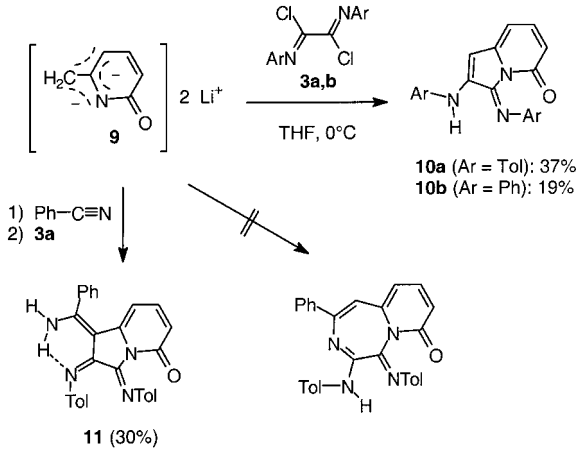
In order to elucidate the tautomerism **A**/**B** (which was expected to be fast on the NMR timescale), pyrrole **6a** was treated with dimethyl acetylenedicarboxylate (DMAD). This reaction afforded the imidazo[1′,2′:1,2]pyrrolo[3,4-*c*]pyridin-5-one **8**. Formation of **8** can be explained by cycloaddition of DMAD with the 1-azadiene system of **6a** (tautomer **A**) and subsequent elimination of *p*-aminotoluene and aromatization (Scheme 3). Compound **8** contains a new heterocyclic substructure, which has to our knowledge not yet been reported.

Pyridone-derived radialene-shaped pyrroles: Dilithiated 6-methylpyridone **9**[23] was treated with oxalic acid-bis(imidoyl)chlorides **3a**,**b** to give the deep red colored 2-arylamino-3-arylimino-5(3*H*)-indolizinones **10a**,**b** (Scheme 4).[24] The cyclization proceeded regioselectively through the carbon and the nitrogen atom of the dianion. Addition of one equivalent of benzonitrile to the dianion and subsequent addition of **3a** resulted in regioselective formation of the pyridone-derived heterocycle **11**. Formation of **11** can be explained by a mechanism similar to that discussed for the synthesis of pyrroles **6**. Although several tautomeric forms are possible for indolizinone **11**, only the radialene-shaped pyrrole tautomer is present in solution (as suggested by the spectroscopic data). An indolizinone system related to that of **10a**,**b** is present in the antitumor alkaloid *camptothecin*.[25]

The structure of **10a** was independently confirmed by a crystal structure analysis (Figure 4). In the solid state, a pyridone rather than a hydroxypyridine tautomer containing an intramolecular hydrogen bond N–H···N is present (N···H distance: 2.277 Å). The aromaticity of the indolizinone system is significantly disturbed as indicated by the alteration of the bond lengths within the heterocyclic substructure. For example, the bond length of C7–C8 is 1.488 Å, whereas the bond length of C6–C7 is only 1.348 Å (numbering: see Figure 4). The disturbed aromaticity of indolizinones **10a**,**b** and **11** is also reflected by their ^{1}H NMR data. In the case of **10a**, the resonances of 4-H and 6-H are significantly shifted to higher field ($\delta = 5.89$ and 6.08, respectively, numbering: see Figure 4). This effect can be explained by the *push-pull* substitution of the heterocyclic system and by the influence of zwitterionic mesomeric structures of **10a**,**b** and **11**, which can thus be regarded as heterocyclic merocyanines. Compounds **10a**,**b** exhibit strong UV/Vis absorption bands in the range of approximately 465–475 nm. For



Scheme 3. Hetero-Diels–Alder reaction of pyrrole **6a**.



Scheme 4. Synthesis of radialene-shaped pyrrole **11**.

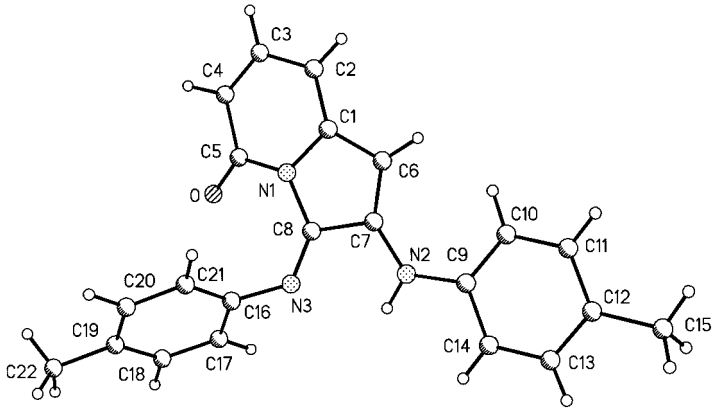
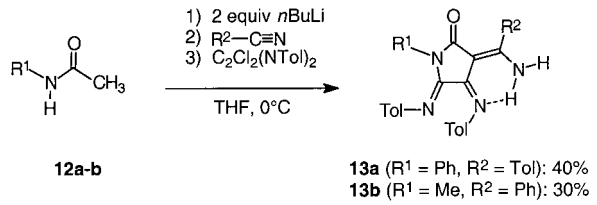


Figure 4. Crystal structure analysis of **10a**. Selected bond lengths [Å]: C1–C2 1.359(4), C2–C3 1.420(4), C3–C4 1.351(4), C4–C5 1.456(4), C5–N1 1.410(3), C1–N1 1.406(3), C1–C6 1.443(4), C6–C7 1.348(4), C7–C8 1.488(3), C8–N1 1.428(3).

radialene-shaped pyrrole **11**, containing a larger π-system than **10a**,**b**, a bathochromic shift is observed.

Amide-derived radialene-shaped pyrroles: We have recently reported the synthesis of pyrroles **13a**,**b** from dilithiated amides by a multiple-anion-capture reaction related to those described for the synthesis of radialene-shaped pyrroles **6** and **11** (Scheme 5).[14a] The four relevant tautomers of **13a** are

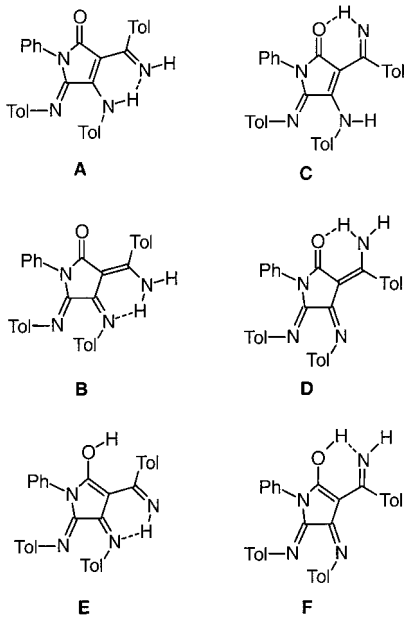


Scheme 5. Synthesis of radialene-shaped pyrroles **13**.

structures **A**–**D**, including the radialene-shaped structures **B** and **D** (see illustration of structures **A**–**F**). As a result of their enolic structure, tautomers **E** and **F** are less likely.

The spectroscopic data of pyrroles **13a**,**b** (COSY, ^{1}H NMR, IR) suggest that a radialene structure (**B** or **D**) is adopted in solution. As a result of the similarity of the spectroscopic features to those of benzimidazole-derived pyrroles **6**, only a brief discussion seems appropiate. The structural mobility of **13b** was detected by variable-temperature ^{1}H NMR: from 60 to 30 °C, a single sharp peak is present for the NCH_3 group ($\delta = 2.59$). Broadening of the signal and coalescence (10 °C) is observed upon cooling, and two singlets appear at low temperature with the integration ratio 1:5. The temperature effect can be explained by a (slow) interconversion of tautomers **B**/**D**. The free energy of activation of this process is $\Delta G\neq$ (**B** → **D**) = 59.0 ± 1.9 kJ mol^{-1}. The intramolecular hydrogen bond of tautomer **D** should result in deshielding of the CH_3 group relative to tautomer **B**. The NCH_3 signal of the major isomer appears at higher field than the respective signal of the minor one, which suggests that the major tautomer adopts structure **B** rather than **D**.

The crystal structure analysis of **13a** unambigiously showed that radialene-shaped structure **B** (rather than **D**) is present in the solid state (Figure 5). Single-bond character is observed for C6–N6, C3–C4, and C4–C5, whereas C3–C6, C4–N4, and C5–N5 possess double-bond character (numbering: see Figure 5).



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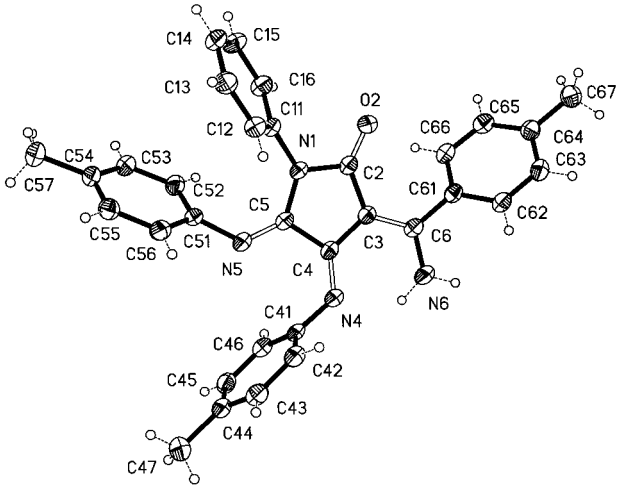
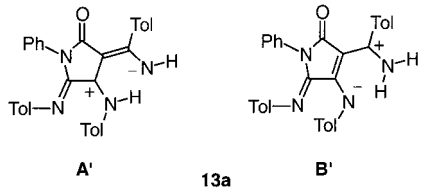


Figure 5. ORTEP plot of **13a**. The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms. Selected bond lengths [Å] and angles [°]: N1–C5 1.396(2), C2–C3 1.457(2), C3–C4 1.441(2), N5–C5 1.271(2), N6–C6 1.335(2), N1–C2 1.429(2), O2–C2 1.214(2), C3–C6 1.400(2), N4–C4 1.288(2), C4–C5 1.512(2); C5–N1–C2 122.08(13), O2–C2–C3 132.12(15), C6–C3–C4 124.27(15), N4–C4–C3 125.21(15), N1–C2–C3 106.70(13), N4–C4–C5 127.75(15), N6–C6–C3 118.3(2).



and **B′**). The positive charge of **B′** is stabilized by the *p*-tolyl group. A related energetically favorable resonance structure exists for tautomer **D**. In contrast, the mesomeric structure **A′**, which is derived from the non-radialene tautomer **A**, is not energetically favorable, since the positive charge resides in the α-position to the imino group. The same is true for the related resonance structure of tautomer **C**. The slightly higher stability of tautomer **B** relative to **D** can be explained by the higher stability of a hydrogen bond N–H···N relative to a hydrogen bond N–H···O as a result of the higher basicity of nitrogen relative to oxygen.

Conclusion

We have reported a new multiple-anion-capture reaction which is based on the regioselective condensation of 1,3-

These findings were reproducible computationally (Figure 6), for which the experimentally isolated tautomer **B** is also the lowest-lying minimum structure at the B3LYP/3-21G//AM1 level of theory; all other tautomers are at minima and display the aforementioned internal hydrogen bonds. We computed again the NICS values to assess the differences in aromatic stabilization energies in the heterocyclic core. Similar to the benzimidazole-derived pyrroles **6**, the radialene subunit is only marginally aromatic. Although the overall stability is reproducible computationally, the aromaticity is slightly lower for the radialene structures **B** and **D** than for the non-radialene tautomers **A** and **C**.

We suggest the following working hypothesis to explain the high, counterintuitive stability of the radialene structures of compounds **6**, **11**, and **13**: zwitterion **B′** represents a significant and nontrivial mesomeric structure of tautomer **B**, for which no charges are located at a nitrogen atom or next to a negative charge (structures **A′**

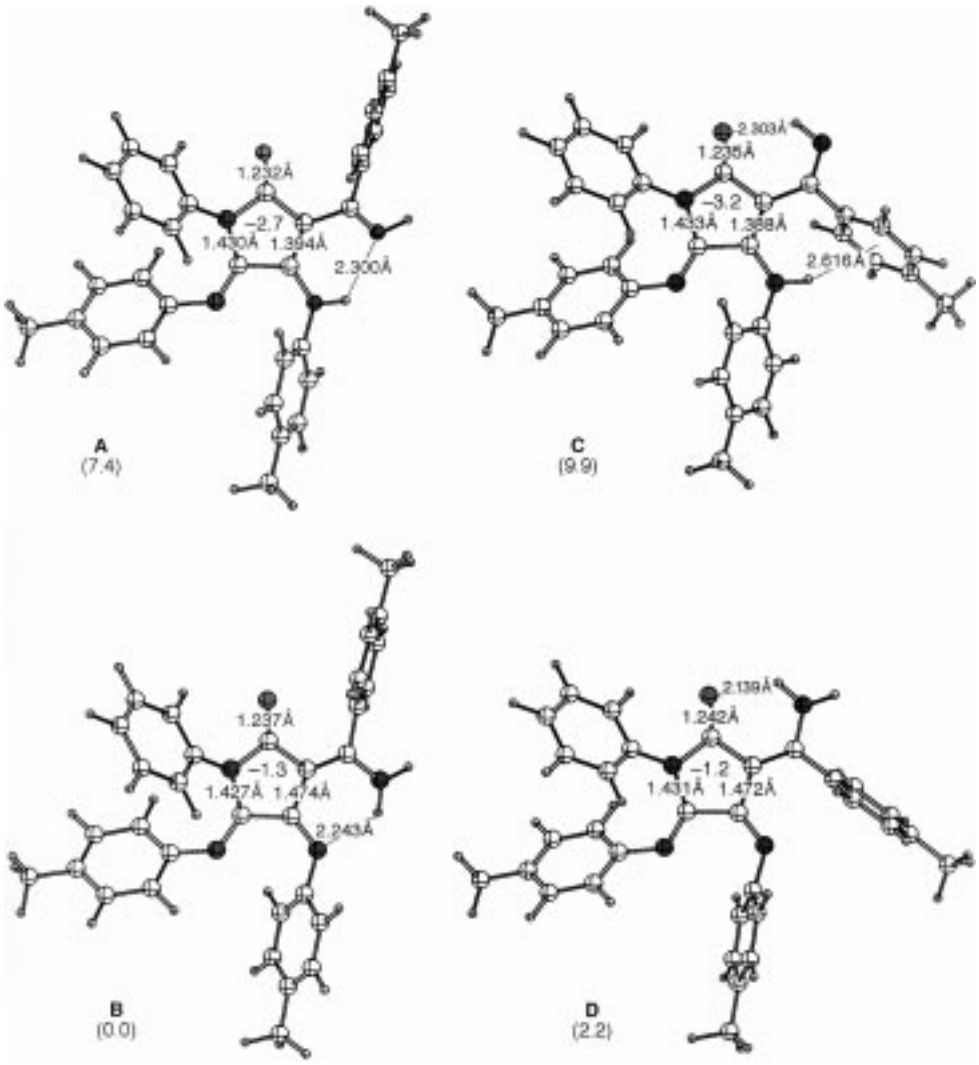


Figure 6. Geometry of **13a** computed at B3LYP/3-21G//AM1.

dianions with nitriles and subsequent regioselective cyclization with oxalic acid-bis(imidoyl)chlorides. Whereas the synthesis of [5]radialenes is generally very difficult, our methodology allows for an efficient one-pot synthesis of a variety of radialene-shaped pyrroles. The products prepared constitute structurally new and interesting heterocyclic systems, since they are aza-analogues of the pharmacologically relevant substance class of 3-acetyltetramic acids.

Experimental Section

General comments: All solvents were dried by standard methods, and all reactions were carried out under an inert atmosphere. The oxalic acid-bis(imidoyl)chlorides **3** were prepared according to a literature procedure.[19] For the ^{1}H and ^{13}C NMR spectra, the deuterated solvents indicated were used. The multiplicity of the ^{13}C NMR signals was determined with the DEPT 135 technique and quoted as: CH_3, CH_2, CH, and C for primary, secondary, tertiary, and quaternary carbon atoms. The atom numbering used for the assignment of the ^{1}H NMR and ^{13}C NMR signals refers to the IUPAC names of the respective compounds. Mass spectrometric data (MS) were obtained using the electron ionization (70 eV), the chemical ionization (CI, H_2O), or the FAB technique. For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected. Elemental analyses were performed at the microanalytical laboratories of the Universities of Hannover and Jena.

Crystal structure analyses:[26] For the data collection, a Nonius CAD4 diffractometer using graphite-monochromated $Mo_{K\alpha}$ radiation was used. Data were corrected for Lorentz and polarization effects.[27] No absorption corrections were made. The structures were solved by direct methods (SHELXS)[28] and refined by full-matrix least-squares techniques against F^2 (SHELXL-93).[29] For the amino group N5 of **6a**, the hydrogen atoms were located by difference Fourier synthesis and refined isotropically. For the other compounds, the hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-hydrogen atoms were refined anisotropically.

Crystal data for 6a: $C_{31}H_{25}N_5 \cdot 0.5\,C_4H_8O$, $M_r = 503.61\ g\,mol^{-1}$, orange cubes, size $0.40 \times 0.38 \times 0.36\ mm^3$, monoclinic, space group $P2_1/n$, $a = 18.160(4)$, $b = 7.785(2)$, $c = 21.972(4)$ Å, $\beta = 112.84(3)^\circ$, $V = 2663(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.171\ g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 0.072\ mm^{-1}$, $F(000) = 1064$, 6532 reflections in $\pm h$, $-k$, $-l$, measured in the range $2.43^\circ \le \Theta \le 27.55^\circ$, 6371 independent reflections, $R_{int} = 0.067$, 2972 reflections with $F_o > 4\sigma(F_o)$, 378 parameters, $R = 0.066$, $wR^2 = 0.169$, GOF = 1.07, largest difference peak: 0.39 e Å^{-3}.

Crystal data for 10a: $C_{47}H_{38}N_6O$, $M_r = 341.4\ g\,mol^{-1}$, deep red cubes, size $0.40 \times 0.38 \times 0.36\ mm^3$, orthorhombic, space group $Pbcn$, $a = 14.884(3)$, $b = 13.884(2)$, $c = 16.904(4)$ Å, $\alpha = 90$, $\beta = 90$, $\gamma = 90^\circ$, $V = 3493(1)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.30\ g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 0.82\ cm^{-1}$, $F(000) = 1440$, 3905 reflections in $\pm h$, $-k$, $-l$, measured in the range $1.92^\circ \le \Theta \le 20.9^\circ$, 3905 independent reflections, 229 parameters, GOF = 1.01, $R = 0.057$, $wR^2 = 0.172$, largest difference peak: 0.29 e Å^{-3}.

Crystal data for 13a: $C_{32}H_{28}N_4O$, $M_r = 484.58\ g\,mol^{-1}$, orange cubes, size $0.60 \times 0.40 \times 0.40\ mm^3$, triclinic, space group $P\bar{1}$ (No. 2), $a = 6.5012(11)$, $b = 10.674(2)$, $c = 18.857(4)$ Å, $\alpha = 79.51(14)$, $\beta = 81.47(13)$, $\gamma = 85.83(13)^\circ$, $V = 1.2712(4)\ nm^3$, $Z = 2$, $\rho_{calcd} = 1.266\ g\,cm^{-3}$, $\mu(Mo_{K\alpha}) = 0.078\ mm^{-1}$, $F(000) = 512$, 6051 reflections in $\pm h$, $-k$, $-l$, measured in the range $3.55^\circ \le \Theta \le 25.06^\circ$, 4504 independent reflections, $R_{int} = 0.0624$, 345 parameters, GOF = 1.053, $R = 0.0456$, $wR^2 = 0.1102$ [$I > 2\sigma(I)$], $R = 0.0548$, $wR^2 = 0.1245$ (all data), largest difference peak: 0.23 e Å^{-3}.

***N*-(4-Methylphenyl)-1-[(4-methylphenyl)imino]-1*H*-pyrrolo[1,2-*a*]benzimidazol-2-amine (4)**:[13w] *n*BuLi (8.25 mL, 2.2 equiv, 1.6 M solution in hexane) was added to a solution of 2-methylbenzimidazole **1** (792 mg, 6.0 mmol) in THF (20 mL) at 0 °C. A colorless suspension was formed. After stirring for 60 min at 0 °C, the suspension was transferred to a solution of oxalic acid-bis(*p*-tolylimidoyl)chloride (6.0 mmol) in THF (80 mL) using a metal cannula at 0 °C. The color of the solution became deep red. The solution was stirred at 0 °C for 15 min and at room temperature for 2 h. THF was removed using a rotary evaporator, and the crude product obtained was purified by chromatography (silica gel, diethyl ether/petroleum ether = 1:3) to give an orange colored solid (762 mg, 35 %), m.p. 168 °C (dec). The preparation of **4** has been recently reported.[13w] For reasons of comparison, the spectroscopic data are listed below.

^{1}H NMR (200 MHz, $CDCl_3$, 20 °C): $\delta = 2.29, 2.38$ ($2 \times$ s, 2×3H; CH_3), 4.90 (d, $J = 8$ Hz, 1H; 8-H), 6.02 (s, 1H; 3-H), 6.60 (t, $J = 8$ Hz, 1H; 7-H), 6.80–7.50 (m, 10H; Ar), 8.30 (br s, 1H; NH); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C): $\delta = 20.77$, 21.00 (CH_3), 88.24 (C-3), 113.05 (C-8), 118.44, 118.45, 119.15, 120.93, 123.10, 129.89, 130.14 (Ar–CH), 130.86, 132.97 (Tol–C to CH_3), 134.75, 136.92 (C-4, C-9), 142.36 (C-2), 144.34, 144.99 (Tol–C to N), 149.29 (C-1), 164.02 (C-3a); IR (KBr): $\tilde{\nu} = 3444$ (w), 3055 (w), 1666 (m), 1618 (s), 1573 (s), 1525 (s), 1504 (s), 1448 (m), 1407 (m), 1273 (w), 1139 cm^{-1} (m); UV/Vis (CH_3CN): λ_{max} (logε) = 281 (4.33), 356 (4.05), 436 nm (3.58); MS (CI, H_2O): *m*/*z* (%): 365 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{24}H_{20}N_4$: C 79.10, H 5.53, N 15.37; found C 78.52, H 5.23, N 14.88.

Preparation of benzimidazole-derived pyrroles 6a–d: *n*BuLi (8.25 mL, 2.2 equiv, 1.6 M solution in hexane) was added to a solution of 2-methylbenzimidazole **1** (792 mg, 6.0 mmol) in THF (20 mL) at 0 °C. After stirring for 1 h, a solution (5 mL, 1.3 equiv) of the respective nitrile in THF was added by syringe at 0 °C. In the case of **6a** and **6c**, benzonitrile (0.8 mL) was added, in the case of **6d**, pivalonitrile (498 mg) was added, and in the case of **6b**, *p*-tolunitrile (702 mg) was added. After stirring for 2 h at 20 °C, the orange suspension (red color of the solution) was transferred to a solution of **3** in THF. The solution was stirred at 0 °C for 15 min and at room temperature for 4 h. THF was removed in vacuo, and the crude product was purified by chromatography (silica gel, diethyl ether/petroleum ether: 1:1) without previous filtration of LiCl formed in the reaction. Similar yields were obtained when an aqueous workup (0.1 M hydrochloric acid) was carried out before the chromatographic purification.

3-(Iminophenylmethyl)-*N*-(4-methylphenyl)-1-[(4-methylphenyl)imino]-1*H*-pyrrolo-[1,2-*a*]benzimidazol-2-amine (6a): Starting with **3a** (6.0 mmol), orange colored crystals (1.15 g, 41 %) were isolated, m.p. 165 °C.

^{1}H NMR (200 MHz, [D$_8$]THF, 20 °C): $\delta = 2.28, 2.30$ ($2 \times$ s, 2×3H; CH_3), 5.20 (very broad at 20 °C, doublet at $\delta = 4.90$ at -80 °C: $J = 8$ Hz, 1H; 8-H), 6.55 (d, $J = 8$ Hz, 2H; Ar), 6.80–7.20 (m, 12H; Ar), 7.40, 7.85 ($2 \times$ m, 2H; Ar), 7.70 (br s, 1H; NH, exchangeable with D_2O), 10.55 (br s, 1H; NH, exchangeable with D_2O); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): $\delta = 20.78$, 20.94 (CH_3), 92.90 (C, C-3), 115.02 (CH, C-8), 118.93, 120.74, 121.04, 121.89, 123.73, 128.49, 129.22, 129.66, 129.81, 130.80 (CH, Ar), 132.62, 132.63 (C, Tol–C to CH_3), 133.77 (C, Ph–C), 136.21, 137.55 (C, C-4a, C-8a), 146.57 (C, C-2), 148.40, 149.28 (C, Tol–C to N), 159.14, 159.15, 159.68 (C, C-1, C-3a, C=*C*PhNH$_2$); IR (KBr): $\tilde{\nu} = 3443$ (w), 3055 (w), 1620 (s), 1573 (s), 1533 (s), 1504 (s), 1448 (m), 1358 (w), 1273 (w), 1139 (m), 1016 cm^{-1} (m); MS (CI, H_2O): *m*/*z* (%): 468 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{31}H_{25}N_5$: C 79.64, H 5.39, N 14.97; found C 79.84, H 5.95, N 15.50.

3-[Imino(4-methylphenyl)methyl]-*N*-(4-methylphenyl)-1-[(4-methylphenyl)-imino]-1*H*-pyrrolo[1,2-*a*]benzimidazol-2-amine (6b): Starting with **3a** (6.0 mmol), orange colored crystals (1.15 g, 40 %) were isolated, m.p. 167 °C.

^{1}H NMR (200 MHz, $CDCl_3$, 20 °C): $\delta = 2.28, 2.33, 2.44$ ($2 \times$ s, 3×3H; CH_3), 5.22 (at 20 °C: very broad, 1H; 8-H), 5.79 (br s, 1H; NH), 6.57, 6.80 ($2 \times$ m, 2×2H; Ar), 6.90–7.10 (m, 2H; Ar), 7.30–7.65 (m, 9H; Ar), 10.65 (br s, 1H; NH); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C): $\delta = 20.84$, 20.90, 21.28 (CH_3), 92.58 (C, C-3), 113.72 (CH, C-8), 118.69, 119.94, 120.35, 121.71, 123.34, 128.47, 128.80, 129.07, 129.18 (CH, Ar), 129.76, 129.77, 131.90, 132.63, 133.41, 141.22 (C, Tol–C to C, C-4a, C-8a), 145.14 (C, C-2), 146.84, 147.80 (C, Tol–C to N), 157.91, 157.92, 158.49 (C, C-1, C-3a, C=*C*NH$_2$); IR (KBr): $\tilde{\nu} = 3438$(w), 3255 (br), 3021 (w), 2920 (w), 1692 (m), 1618 (s), 1605 (s), 1561 (s), 1540 (s), 1504 (s), 1448 (m), 1138 cm^{-1} (m); MS (CI, H_2O): *m*/*z* (%): 482 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{32}H_{27}N_5$: C 79.81, H 5.65, N 14.54; found C 80.42, H 5.52, N 15.16.

3-(Iminophenylmethyl)-*N*-(phenyl)-1-(phenylimino)-1*H*-pyrrolo[1,2-*a*]-benzimidazol-2-amine (6c): Starting with **3b** (6.0 mmol), orange colored crystals (870 mg, 33 %) were isolated, m.p. 163 °C.

^{1}H NMR (200 MHz, [D$_8$]THF, 20 °C): $\delta = 5.13$ (br s, 1H; 8-H), 6.50 (t, $J = 8$ Hz, 1H; 7-H), 6.67 (d, 2H; Ar), 6.80–7.80 (m, 15H; Ar), 8.50 (very broad, 1H; NH), 10.47 (br s, 1H; NH); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): $\delta =$ 92.59 (C, C-3), 118.65 (CH, C-8), 120.17, 120.41, 120.67, 121.68, 123.00,

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123.53, 123.91, 128.19, 128.38, 129.05, 129.33, 130.56 (CH, Ar), 130.75 (C, Ph–C), 136.07, 137.29 (C, C-4a, C-8a), 149.04, 149.28, 151.22 (C, C-2, Ph–C to N), 159.38, 159.47, 159.94 (C, C-1, C-3a, C=*C*NH$_2$); IR (KBr): $\tilde{\nu}$ = 3440 (br), 3060 (w), 1695 (m), 1620 (s), 1590 (s), 1568 (s), 1540 (s), 1490 (s), 1450 (m), 1332 (m), 1140 (m), 1078 cm^{-1} (m); MS (CI, H_2O): *m*/*z* (%): 440 (100) [*M*+H]$^+$; UV/Vis (CH_3CN): λ_{max} (logε) = 265 (4.45), 348 (4.28), 434 nm (3.67); elemental analysis calcd (%) for $C_{29}H_{21}N_5$: C 79.26, H 4.82, N 15.93; found C 78.90, H 4.88, N 15.41.

3-(Imino-*tert*-butylmethyl)-*N*-(4-methylphenyl)-1-[(4-methylphenyl)imino]-1*H*-pyrrolo[1,2-*a*]benzimidazol-2-amine (6d): Starting with **3a** (6.0 mmol), orange colored crystals (1.07 g, 40%) were isolated, m.p. 170 °C.

^{1}H NMR (200 MHz, [D$_8$]THF, 20 °C): δ = 1.66 (s, 9H; *t*Bu), 2.28, 2.32 (2 × s, 2 × 3H; CH_3), 5.15 (br s at 20 °C, doublet at δ = 4.97 at −80 °C, *J* = 8 Hz, 1H; 8-H), 6.40–7.40 (m, 13H; Ar), 7.95 (br s, 1H; NH), 12.15 (br s, 1H; NH); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): δ = 20.80, 20.93 (CH_3), 27.03 (CH_3, *t*Bu), 38.81 (C, *t*Bu), 90.82 (C, C-3), 114.41 (CH, C-8), 118.71, 120.77, 120.97, 122.02, 123.74, 129.27, 129.80 (CH, Ar), 130.31, 132.11 (C, Tol–C to CH_3), 133.71, 137.27 (C, C-4a, C-8a), 146.57 (C, C-2), 148.16, 148.94 (C, Tol–C to N), 160.19, 160.55 (C, C-1, C-3a), 172.48 (C, C=*C*NH$_2$); IR (KBr): $\tilde{\nu}$ = 3467 (w), 2919 (w), 1614 (s), 1553 (s), 1504 (s), 1448 (m), 1364 (m), 1240 (w), 1145 (m), 1046 cm^{-1} (w); MS (CI, H_2O): *m*/*z* (%): 448 (100) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{29}H_{29}N_5$: C 77.83, H 6.53, N 15.64; found C 77.50, H 6.80, N 15.20.

Preparation of (*Z*)-[(1*H*-Benzimidazol-2-yl)methylene]benzenemethanamine (7): *n*BuLi (16.5 mL, 2.2 equiv, 1.6 M solution in hexane) was added to a solution (40 mL) of 2-methylbenzimidazole (1.58 g, 12.0 mmol) in THF at 0 °C. After stirring for 60 min at 0 °C, benzonitrile (1.5 mL, 1.2 equiv) was added at 0 °C. The color of the suspension turned yellow. After stirring for 4 h at 20 °C, the solution was poured into an aqueous solution of hydrochloric acid (0.1 M, 0 °C). After extraction with a mixture of THF and diethyl ether (1:1), the combined organic layers were dried ($MgSO_4$) and filtered. The filtrate was concentrated in vacuo. Addition of diethyl ether to the crude product resulted in precipitation of **7** (2.53 g, 86%) as a white solid, m.p. 95 °C.

^{1}H NMR (200 MHz, [D$_8$]THF, −80 °C): δ = 5.39 (s, 1H; =CH–), 6.64 (br s, 1H, not detectable at 20 °C; NH), 6.90–7.75 (m, 9H; Ar), 9.07 (br s, 1H, not detectable at 20 °C; NH), 11.49 (br s, 1H; NH); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): δ = 83.33 (=CH–), 109.92, 117.90, 121.31, 121.34, 126.70, 129.08, 129.40 (CH, Ar), 134.27 (C, Ph), 140.02, 145.43 (C, benzimidazole), 153.27, 155.61 (CN_2, *C*CNH$_2$); IR (KBr): $\tilde{\nu}$ = 3447 (m), 3279 (m), 3056 (w), 1614 (s), 1573 (s), 1523 (m), 1497 (m), 1406 (m), 1275 (m), 1015 (w), 753 (m), 766 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 236 [*M*+H]$^+$, 235 [*M*]$^+$, 234 [*M* − H]$^+$; elemental analysis calcd (%) for $C_{15}H_{13}N_3$: C 76.58, H 5.57, N 17.85; found C 76.32, H 5.73, N 17.93.

Preparation of imidazo[1′,2′:1,2]pyrrolo[3,4-*c*]pyridin-5-one (8): A solution of pyrrole **6a** (467 mg, 1.0 mmol) in toluene (5 mL) and dimethyl acetylenedicarboxylate (0.19 mL, 1.5 mmol) was stirred for 12 h at 80 °C. The solvent was removed in vacuo, and the residue was purified by chromatography (petroleum ether/diethyl ether 1:1) to give **8** as deep yellow crystals (340 mg, 68%), m.p. 166 °C.

^{1}H NMR (200 MHz, CD_2Cl_2, 20 °C): δ = 2.46 (s, 3H; CH_3), 3.98, 4.03 (s, 2 × 3H; CO_2CH_3), 6.91 (m, 3H; Ar), 7.15 (t, *J* = 8 Hz, 2H; Ar), 7.30 (d, 2H; Ar), 7.61 (m, 4H; Ar), 8.34 (m, 2H; Ar); ^{13}C NMR (50 MHz, CD_2Cl_2, 20 °C): δ = 21.15 (CH_3), 53.22, 53.67 (CO_2CH_3), 120.86, 121.79 (C, Pyr), 115.23, 120.85, 121.79, 125.02, 125.82, 128.68, 130.34, 130.39, 131.13 (CH, Ar), 135.95, 135.96, 136.10, 139.20, 139.22 (C, Ar), 145.70, 145.71, 145.80, 146.25, 148.99 (C, Pyridine–C to Ph, CN_2, Ph to N, Tol to N, N*C*COOCH$_3$), 164.60, 165.85 (C, CO); MS (CI, H_2O): *m*/*z* (%): 503 (100) [*M*+H]$^+$; elemental analysis calcd (%) for $C_{30}H_{22}N_4O_4$: C 71.71, H 4.41, N 11.14; found C 71.28, H 4.58, N 11.52.

Procedure for the preparation of 3-arylimino-5(3*H*)-indolizinones (10a,b and 11): A solution of 6-methylpyridone (654 mg, 6.0 mmol) in THF (5 mL) was added to a solution (20 mL) of LDA (prepared by addition of *n*BuLi (8.25 mL), 1.6 M solution in hexane, to a solution of diisopropylamine (1.8 mL) in THF). After stirring for 1 h at 0 °C, the orange colored solution was transferred to a solution of **3a,b** (6.0 mmol) in THF (70 mL) at 0 °C. After stirring for 15 min at 0 °C and for 4 h at 20 °C, the solvent was removed in vacuo, and the residue was purified by chromatography (silica gel, diethyl ether/petroleum ether, 1:1) without prior filtration of the LiCl formed in the reaction. Similar yields were obtained when an aqueous workup was carried out before the chromatographic purification. For the preparation of **11**, benzonitrile (1.1 equiv) was added to the dianion solution at 0 °C. After stirring for 2 h at 0 °C, the red colored solution was added by cannula to a solution of **3a** (70 mL) in THF.

2-[(4-Methylphenyl)amino]-3-[(4-methylphenyl)imino]-5(3*H*)-indolizinone (10a): Starting with **3a**, deep red crystals (755 mg, 37%) were isolated, m.p. 150 °C (dec).

^{1}H NMR (200 MHz, $CDCl_3$, 20 °C): δ = 2.31, 2.35 (2 × s, 2 × 3H; CH_3), 5.89 (d, *J* = 6.5 Hz, 1H; 6-H), 6.08 (s, 1H; 1-H), 6.76 (br s, 1H; 8-H), 7.05–7.20 (m, 8H; Ar), 7.53 (d, *J* = 8.5 Hz, 1H; Ar), 9.27 (br s, 1H; NH); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C): δ = 20.74, 21.15 (CH_3), 99.70 (CH, C-1), 118.41, 119.74 (CH, C-6, C-8), 120.97, 128.31, 129.74, 130.00 (CH, Ar), 132.52, 134.21 (C, Tol–C to CH_3), 137.48 (C, C-2), 139.36 (CH, C-7), 144.48, 145.10 (C, Tol–C to N), 157.34, 158.86 (C, C-3, C-8a), 172.30 (C, C-5); IR (KBr): $\tilde{\nu}$ = 3300 (m), 3024 (w), 2916 (w), 1680 (s), 1604 (s), 1524 (s), 1408 (m), 1280 (m), 1156 (m), 796 cm^{-1} (m); MS (FAB): *m*/*z* (%): 342 (100) [*M*+H]$^+$; UV/Vis (CH_3CN): λ_{max} (logε) = 468 nm (3.95); elemental analysis calcd (%) for $C_{22}H_{19}N_3O$: C 77.40, H 5.61, N 12.30; found C 77.50, H 5.54, N 12.48.

2-(Phenylamino)-3-(phenylimino)-5(3*H*)-indolizinone (10b): Starting with **3b**, red crystals (355 mg, 19%) were isolated, m.p. 143 °C (dec).

^{1}H NMR (200 MHz, $CDCl_3$, 20 °C): δ = 5.92 (d, *J* = 6.5 Hz, 1H; 6-H), 6.17 (s, 1H; 1-H), 6.87 (br s, 1H; 8-H), 7.00–7.35 (m, 11H; Ar); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C): δ = 100.13 (CH, C-1), 118.17, 120.30 (CH, C-6, C-8), 120.32, 122.78, 124.55, 124.56, 127.73, 129.52 (CH, Ar), 139.40 (CH, C-7), 139.94 (C, C-2), 146.20, 146.28 (C, Ph–C to N), 156.50, 158.55 (C, C-3, C-8a), 172.45 (C, C-5); IR (KBr): $\tilde{\nu}$ = 3300 (m), 3026 (w), 2914 (w), 1680 (s), 1623 (s), 1605 (s), 1524 (s), 1407 (w), 1277 (m), 1157 cm^{-1} (m); MS (FAB): *m*/*z* (%): 314 (100) [*M*+H]$^+$; UV/Vis (CH_3CN): λ_{max} (logε) = 467 nm (3.89); elemental analysis calcd (%) for $C_{20}H_{15}N_3O$: C 76.66, H 4.83, N 13.40; found C 77.02, H 5.12, N 13.16.

1-(Iminophenylmethyl)-2-[(4-methylphenyl)amino]-3-[(4-methylphenyl)-imino]-5(3*H*)-indolizinone (11): Starting with **3a**, deep red crystals (796 mg, 30%) were isolated, m.p. 144 °C (dec).

^{1}H NMR (200 MHz, [D$_8$]THF, 20 °C): δ = 2.23, 2.30 (2 × s, 2 × 3H; CH_3), 5.72 (d, *J* = 6.5 Hz, 1H; 6-H), 6.38 (br s, 1H; 8-H), 6.70–7.70 (m, 14H; Ar), 8.23 (br s, 1H; NH), 10.80 (br s, 1H; NH); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): δ = 20.90, 21.02 (CH_3), 96.60 (C, C-1), 115.80, 120.70 (CH, C-6, C-8), 121.20, 121.90, 128.52, 128.60, 129.20, 129.80, 131.13 (CH, Ar), 129.60 (C, Ph–C), 133.20, 134.11 (C, Tol–C to CH_3), 137.80 (C, C-2), 139.60 (CH, C-7), 146.11, 147.00, 148.11 (C, Tol–C to N, C-3), 159.02 (C, C-8a), 162.10 (C, Imino–C), 172.10 (C, C-5); IR (KBr): $\tilde{\nu}$ = 3248 (br), 3024 (w), 2916 (w), 1684 (s), 1588 (s), 1516 (s), 1444 (m), 1396 (w), 1240 (w), 1160 (m), 1116 (m), 820 cm^{-1} (m); MS (FAB): *m*/*z* (%): 445 (100) [*M*+H]$^+$; UV/Vis (CH_3CN): λ_{max} (logε) = 381 (4.14), 475 nm (3.93); elemental analysis calcd (%) for $C_{29}H_{24}N_4O$: C 78.36, H 5.44, N 12.60; found C 78.14, H 5.54, N 12.28.

Preparation of amide-derived pyrroles (13a,b): Pyrroles **13** have been previously prepared according to the procedure as given for the preparation of pyrroles **6**.[14a] Similar yields were obtained for pyrroles **13** when an aqueous workup was carried out before the chromatographic purification, or when the reaction mixture was concentrated in vacuo and directly purified by chromatography. The spectroscopic data of **13a,b** are listed below for reasons of comparison.

1,5-Dihydro-3-[imino(4-methylphenyl)methyl]-4-[(4-methylphenyl)amino]-5-[(4-methylphenyl)imino]-1-phenyl-2*H*-pyrrol-2-one (13a):[14a] Starting with acetanilide (810 mg), *p*-tolunitrile (702 mg), and oxalic acid-bis(*p*-tolyl)imidoylchloride (1.80 g), **13a** (1.16 g, 40%) was isolated as a yellow solid, m.p. 194 °C.

^{1}H NMR (200 MHz, [D$_8$]THF, 20 °C): δ = 2.00, 2.27, 2.37 (s, 3 × 3H; CH_3), 6.05 (d, *J* = 8 Hz, 2H; Ar), 6.49 (d, *J* = 8 Hz, 2H; Ar), 6.75–7.50 (m, 13H; Ar), 7.89 (br s, 1H; NH), 10.94 (br s, 1H; NH); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): δ = 20.63, 20.96, 21.40 (CH_3), 93.51 (C, C-3), 120.71, 120.91, 126.46, 127.98, 128.32, 128.45, 128.83, 128.98, 129.34 (CH, Ar), 131.79, 132.00, 132.98 (C, Tol–C to CH_3), 135.79, 135.80 (C, Ph–C, Tol–C), 140.76 (C, C-4), 144.77, 149.11 (C, Tol–C to N), 157.60 (C, C-5), 164.76 (C, C(NH)Tol), 167.19 (C, C-2); IR (KBr): $\tilde{\nu}$ = 3416 (br), 3322 (w), 3021 (w), 2920 (w), 1730 (m), 1668 (m), 1615 (s), 1502 (s), 1358 (m), 1201 (m), 1090 cm^{-1} (m); UV/Vis (CH_3CN): λ_{max} (logε) = 239 (4.58), 318 (4.33), 425 nm (3.71); MS (CI, H_2O): *m*/*z* (%): 485 (100) [*M*+H]$^+$; elemental

analysis calcd (%) for $C_{32}H_{28}N_4O$ (484.6): C 79.32, H 5.82, N 11.56; found C 79.40, H 5.89, N 11.25.

1,5-Dihydro-3-(iminophenylmethyl)-4-[(4-methylphenyl)amino]-5-[(4-methylphenyl)imino]-1-methyl-2*H*-pyrrol-2-one (13b):[14a] Starting with $CH_3NHCOCH_3$ (438 mg), benzonitrile (0.8 mL), and oxalic acid-bis(*p*-tolyl)imidoylchloride (1.80 g), **13b** (735 mg, 30%) was isolated as a yellow solid, m.p. 202 °C.

^{1}H NMR (200 MHz, [D$_8$]THF, 20 °C): $\delta = 2.21$, 2.23 (s, 2×3H; Tol−CH_3), 2.59 (s, 3H; CH_3 to N), 6.31, 6.65 (d, $J = 8$ Hz, 4H; Tol), 6.80, 7.50 (m, 9H; Ar), 7.82 (brs, 1H; NH), 10.63 (brs, 1H; NH); ^{1}H NMR (200 MHz, [D$_8$]THF, −40 °C): The first values of the sets of signals (a/b) are those of the major isomer (a/b = 5:1): $\delta = 2.21$, 2.23/2.17, 2.18 (s, 3H; Tol−CH_3), 2.44/2.98 (s, 3H; CH_3 to N), 6.51, 6.81/6.08, 6.18 (d, $J = 8$ Hz, 4H; Tol), 6.65 (t, $J = 6$ Hz, 1H; Ar), 7.00, 7.51 (m, 8H; Ar), 8.32 (brs, 1H; NH), 10.70 (brs, 1H; NH); ^{13}C NMR (50 MHz, [D$_8$]THF, 20 °C): $\delta = 20.72$, 20.91 (CH_3, Tol−CH_3), 27.53 (CH_3, CH_3 to N), 94.17 (C, C-3), 120.45, 120.82, 128.21, 129.03, 129.13, 129.31, 130.71 (CH, Ar), 131.99, 132.17 (C, Tol−C to CH_3), 136.03 (C, Ph−C), 143.20 (C, C-4), 146.36, 148.76 (C, Tol−C to N), 156.87 (C, C-5), 163.42 (C, *C*(NH)Ph), 167.18 (C, C-2); IR (KBr): $\tilde{\nu} = 3420$ (br), 3320 (w), 3020 (w), 2920 (w), 1710 (m), 1670 (m), 1620 (s), 1503 (s), 1491 (m), 1360 (m), 1360 (m), 1203 (m), 1070 (m), 981 cm^{-1} (m); UV/Vis (CH_3CN): λ_{max} (logε) = 237 (4.55), 295 (4.25), 407 nm (3.74); MS (CI, H_2O): *m*/*z* (%): 409 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{26}H_{24}N_4O$ (408.5): C 76.45, H 5.92, N 13.71; found C 76.49, H 5.97, N 13.52.

Computational methods: Geometries of all stationary points were optimized using analytical energy gradients of AM1 semiempirical and Hartree–Fock self-consistent-field theory,[30] as implemented in the Gaussian 94 program package.[31] Final energies refer to the B3LYP/3-21G//AM1 level of theory, unless noted otherwise. For comparative purposes, we also computed the absolute magnetic shieldings, termed the "nucleus independent chemical shifts" (NICS)[32] at selected points in space as a function of the electron density using the GIAO (Gauge Invariant Atomic Orbitals) approach.[33] The geometrical center of the ring's heavy atoms served as the most easily defined reference point.[32] These isotropic chemical shifts yielded information about ring currents and aromatic properties of molecules.[32] Following the convention, aromatic molecules have negative isotropic NICS, while antiaromatic molecules have positive values. The absolute magnitude of a negative NICS is approximately proportional to the aromatic stabilization energy.

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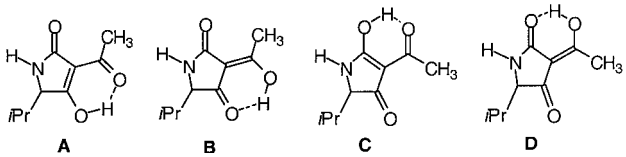

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