Regioselective Anionic [3+2] Cyclizations of Imidazole Dinucleophiles with Oxaldiimidoyl Dichlorides − A Combined Experimental and Theoretical Study

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

Keywords: Cyclizations / Nitrogen heterocycles / Regioselectivity / Semiempirical calculations

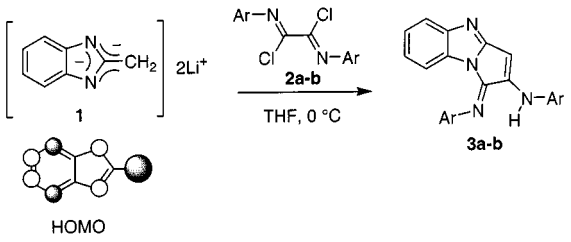
Regioselective cyclization reactions between oxaldiimidoyl dichlorides and imidazole-derived dinucleophiles provide convenient access to biologically relevant diazabicyclo[2.2.1]heptanones, 1*H*-pyrrolo[1,2-*a*]benzimidazoles, 3*H*-imidazo[1,2-*a*]benzimidazoles and 2,3-dihydrothiazolo[3,2-*a*]benzimidazoles. All cyclizations proceed with good regioselectivity, directed by the heteroatoms of the dinucleophile. The tautomeric forms of the structurally mobile benzimidazoles have been studied both in solution and in the solid state. The structural properties and the regioselectivities are explained by semiempirical calculations.

Introduction

Imidazoles and benzimidazoles represent important heterocyclic systems, thanks to their pharmacological activity.[1] Annulated imidazoles[2] and benzimidazoles[3] have been prepared stepwise by various methods. In this context, the synthesis of 1,2,3-trihydropyrrolo[1,2-*a*]benzimidazoles by cyclization of benzimidazoles with 1,2-dielectrophiles (1,2-dibromoethane or 1-bromo-2-chloroethane) proved to be relatively difficult, due to competing elimination reactions.[4a] Katritzky et al. reported an efficient approach to fused [1,2-*a*]indoles, based on the reaction between an indole-derived dianion and 1-bromo-2-chloroethane.[4b] In the course of our investigations towards the development of new anionic domino reactions, we have studied cyclizations between imidazole-derived dinucleophiles and oxalic acid derived 1,2-dielectrophiles. Anionic cyclization reactions between oxalyl dichloride and oxalic diesters are often unpredictable or give unsatisfactory yields, since various side reactions − such as extrusion of CO, polymerization or formation of open-chained products − can occur.[5] For example, treatment of oxalyl dichloride with heterocyclic nitrogen dinucleophiles, such as 2-aminopyridines or 2-aminoimidazoles, results in formation of open-chain oxalamides rather than in cyclization products. Until very recently, cyclization reactions of dianions[6,7] with oxalic acid dielectrophiles had not been described.[8] Here, we wish to report that base-mediated cyclizations can be induced for a variety of imidazole-derived and benzimidazole-derived dinucleophiles when oxaldiimidoyl dichlorides[9] are employed as dielectrophiles. Using this methodology, it was possible to prepare efficiently a variety of biologically relevant imidazole-derived heterocycles containing a 1,2-diimine substructure. In this context, the influence of the heteroatoms of the dinucleophiles on the regiochemistry of cyclization was systematically studied. This was also supported by semiempirical computations on some of the key structures, to explain the geometric preferences and the observed regioselectivities.

Results and Discussion

The reactions between dilithiated 2-methylbenzimidazole (**1**) and oxalyl dichloride or oxalic diesters resulted in formation of polymeric materials. However, it was possible to induce a cyclization when the dianion **1** was treated with the diimidoyl dichlorides **2a**,**b** to give the 1-arylimino-1*H*-pyrrolo[1,2-*a*]benzimidazol-2-amines **3a**,**b** (Scheme 1).[10] The cyclization proceeds regioselectively, through the carbon and a nitrogen atom of the dianion. This can be rationalised by the largest coefficient of the highest occupied molecular orbital (HOMO) of the dianion being on the *exo*-methylene carbon atom (Scheme 1). The reaction should start at this position first and then be directed further to one of the adjacent nitrogen atoms.

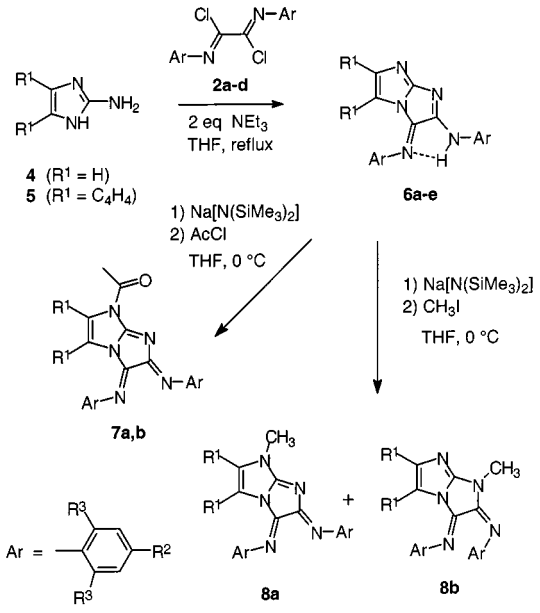


Scheme 1. Cyclizations between dilithiated 2-methylbenzimidazole and oxaldiimidoyl dichlorides: **3a**, Ar = Tol = 4-$CH_3C_6H_4$, 35%; **3b**, Ar = Ph, 28%

[a] Institut für Organische Chemie der Georg-August-Universität Göttingen,
Tammannstrasse 2, 37077 Göttingen, Germany
[b] Institut für Anorganische und Analytische Chemie der Universität Jena,
August-Bebel-Strasse 2, 07743 Jena, Germany
[c] Department of Chemistry, The University of Georgia,
1001 Cedar St., Athens, GA 30602-2556, USA

  1434−193X/01/0612−2245 $ 17.50+.50/0

Treatment of **2a**−**d** with 2-aminoimidazole (**4**) and 2-aminobenzimidazole (**5**) (Scheme 2, Table 1) gave the 3*H*-imidazo[1,2-*a*]imidazoles **6a**−**e**,[11] which are aza analogues of heterocycles **3**. Structures of these types have recently been shown to exhibit antitumor activity against a variety of cancer cell lines.[1c]



Scheme 2. Cyclizations between 2-aminoimidazoles and oxaldiimidoyl dichlorides

Several possible tautomers may exist in the structures under consideration (Figure 1). The spectroscopic data suggest that heterocycles **3** and **6** exist in solution as tautomers A (containing an intramolecular N−H···N hydrogen bond). The IR spectra of **6a**−**e** exhibit broad vibration bands (ν_{N-H} at ca. 3280−3200 cm^{-1}) characteristic of N−H···N hydrogen bonds. The absence of sharp heterocyclic ν_{N-H} vibration bands for **3a**−**c** and **6a**−**e** (as characteristic of 2-methylbenzimidazole, 2-aminoimidazole and 2-aminobenzimidazole) suggests that tautomers B are not present. As expected, the protected heterocycles **7** and **8** do not exhibit ν_{N-H} absorptions.

The ^{1}H NMR spectra of **3a**−**c** and **6a**−**e** feature broad singlets at low field (hydrogen bonds N−H···N). The protons 8-H (for **3**) and 5-H (for **6**) are positioned within the anisotropic cones of the arylimino groups attached to carbon atoms C-1 and C-3, respectively (note the different numberings in the heterocyclic systems **3** and **6**). The deshielding is therefore drastically decreased for these protons, relative to the corresponding protons in 2-methylbenzimidazole and 2-aminobenzimidazole. As expected, this effect is not observed for the hydrogen atoms located on the opposite side of the benzimidazole system. On increasing the temperature (−80 → 20 °C, [D_8]THF, 20 → 90 °C, [D_6]DMSO), the resonances are shifted downfield (by 0.30 and 0.22 ppm for **3a** and **3b**, respectively), presumably due to increased freedom of rotation of the arylimino group and, hence, decreased electronic influence of the latter on the benzimidazole unit. The imino group is forced into a (*Z*) geometry by the intramolecular N−H···N hydrogen bond. Therefore, (*E*)/(*Z*) isomerization can be responsible for the temperature effect only if a prototropic shift occurs at the same time. The chemical shift of 8-H (or 5-H) is a sensitive measure of the geometry of the imino group attached to C-1 (or C-3). The structure of the cyclization products **6** is fully supported by mass spectrometry, elemental analyses and ^{13}C NMR (APT) data. The presence of 19 signals for **6c** shows that (unlike in heterocycles **12**, vide infra) an asymmetrical structure is adopted. For **6c**, nine quaternary carbon atoms are detected [δ = 130.3, 134.9 (benzimidazole-C to N), 135.3, 136.7 (Tol-C to C), 140.0, 146.1 (Tol-C to N), 148.8 (C-3), 163.6 (C-2), 168.9 (C-9a)].

The structure of **6c** was independently confirmed by an X-ray structure analysis (Figure 2), which showed that tautomer A is present in the solid state. As expected, the heterocyclic system is planar. Whereas the arylamino group attached to C-2 is only twisted out of plane by 25.9°, the arylimino group attached to C-3 is twisted out of plane by 66.8°. The structure shows clearly that proton 5-H (IUPAC

Table 1. Synthesis of 3*H*-imidazo[1,2-*a*]imidazol-2-amines and 3*H*-imidazo[1,2-*a*]benzimidazol-2-amines

2	**3**, **6**−**8**	R^1	R^2	R^3	IR: ν_{N-H}, $\nu_{C=N}$, $\nu_{C=C}$ [cm^{-1}] (KBr or Nj = Nujol)	UV/Vis: λ_{max} (log ε) [nm]	^{1}H NMR: δ≅[a]	%[b]	M.p. [°C]
a	**3a**	H	CH_3	−	3444, 3055, 1666, 1618 (KBr)	356 (4.05), 436 (3.58)[c]	4.90[d]	35	168−170
b	**3b**	H	H	−	3348, 3056, 1692, 1620 (KBr)		4.86[d]	28	162−164
a	**6a**	H	CH_3	H	3279, 1696, 1639, 1612 (Nj)	387 (3.79), 418 (3.80)[c]	−	60	248−250
c	**6b**	H	NO_2	H	3409, 1717, 1640, 1611 (Nj)	428 (3.92)[e]	−	63	320−322
a	**6c**	C_4H_4	CH_3	H	3209, 1703, 1655, 1622 (Nj)	331 (3.91), 403 (3.99)[c]	5.08[f]	66	335−340
b	**6d**	C_4H_4	H	H	3206, 1702, 1653, 1618 (Nj)		5.00[f]	77	300 (dec.)
d	**6e**	C_4H_4	CH_3	CH_3	3248, 1698, 1653, 1616 (Nj)		5.13[g]	47	126−128
−	**7a**[h]	H	CH_3	H	1737, 1686, 1650, 1606 (Nj)		−	36	178−180
−	**7b**[i]	C_4H_4	CH_3	H	1732, 1681, 1644, 1606 (Nj)	401 (4.05)[c]	5.01[d]	53	215−216
−	**8a**[h]	H	CH_3	H	1674, 1652, 1608 (Nj)	429 (3.95)[c]	−	48[j]	208−210
−	**8b**[h]	H	CH_3	H	1693, 1669, 1622, 1613 (Nj)	344 (3.54), 397 (3.62)[c]	−	48[j]	162−164

[a] Chemical shift of the proton located in the anisotropic cone of the arylimino group. − [b] Isolated yields. − [c] CH_3CN. − [d] $CDCl_3$. − [e] Acetone. − [f] [D_7]DMF. − [g] CD_2Cl_2. − [h] Prepared from **6a**. − [i] Prepared from **6c**. − [j] Combined yield of **8a** and **8b**: 96%.

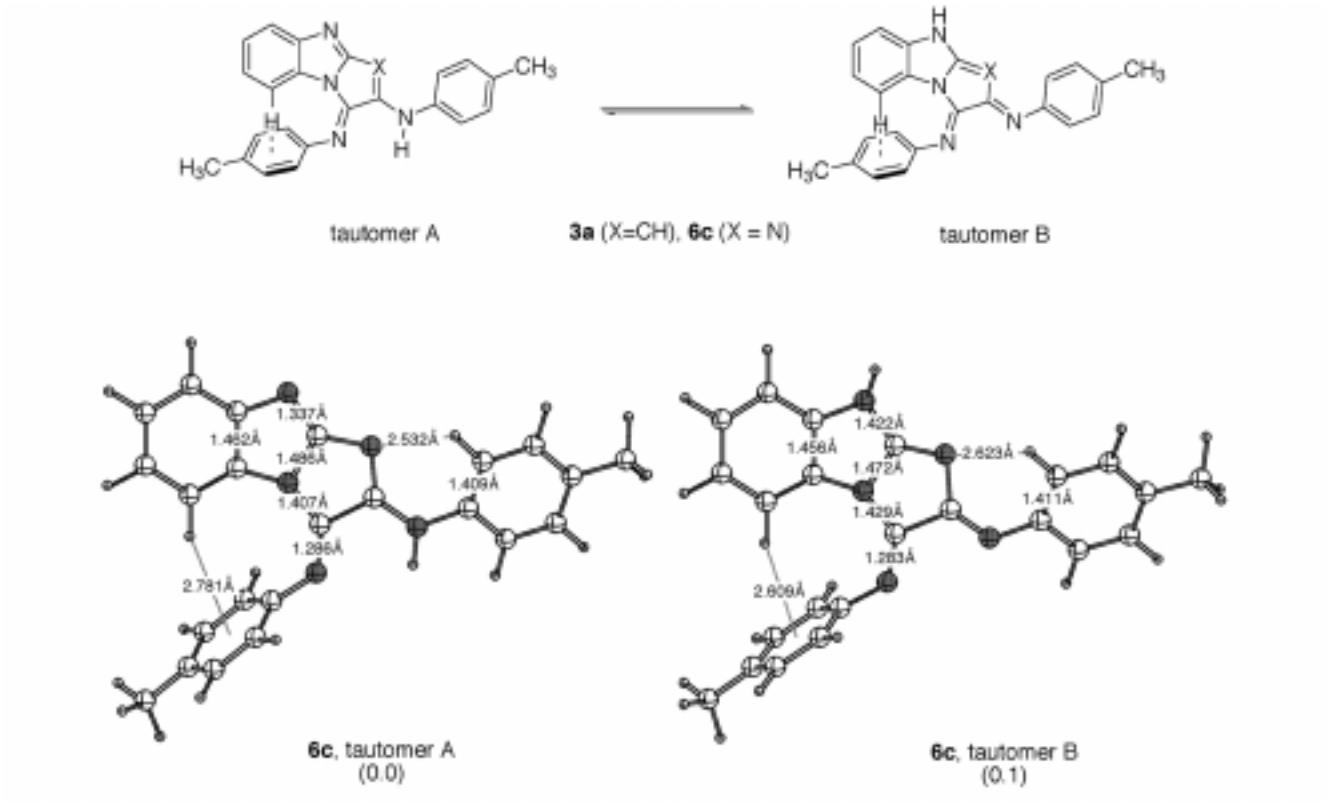


Figure 1. Calculations of the tautomeric structures of **6c**

numbering) is indeed located in the anisotropic cone of the arylimino group attached to C-3 (distance: 2.800 Å). Inspection of the bond lengths shows that the double bonds within the heterocyclic moiety are delocalized. For example, the bond lengths for N2−C2 (1.320 Å) and N4−C2 (1.336 Å) are very similar, although the structural formula of **6c** suggests that nitrogen atoms N-2 and N-4 are sp^2- and sp^3-hybridised, respectively. In the crystal lattice, an interaction between the N−H hydrogen and a heterocyclic nitrogen atom of a neighbouring molecule is observed (N···N distance: 3.028 Å).

These structural findings could be reproduced by semiempirical computations at the AM1 level (see Computational Methods below for details) which lends some support to using this level for analysing these types of structures qualitatively (Figure 2). The weak quadrupole C−H···π bond of H is also well reproduced; this feature is present in many of the compounds considered here and appears to be a structure-directing element.[12] A second such element is the weak in-plane C−H···N hydrogen bond between the other tolyl moiety and the basic imidazole nitrogen atom; this feature is also found in many of the other derivatives reported here. Although the computed energy ordering agrees with the conclusion that tautomer A is adopted for **3** and **6**, the 0.1 kcal/mol energy difference for **6c** is far too small to be decisive and suggests that those tautomers are likely to be of very similar thermodynamic stabilities. Solvents or crystal packing effects may favour one over the other.

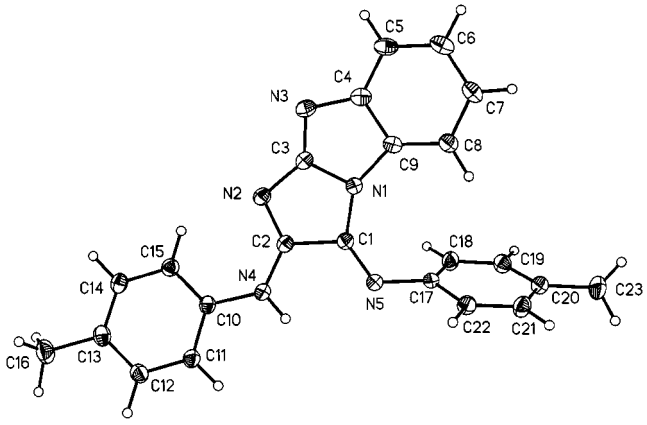


Figure 2. ORTEP plot of **6c**; 50% probability thermal ellipsoids are shown for the non-hydrogen atoms; selected bond lengths [Å] and angles [°]: N(1)-C(1) 1.400(2), N(1)−C(3) 1.403(2), N(1)−C(9) 1.410(2), N(2)−C(2) 1.320(2), N(2)−C(3) 1.387(2), N(3)−C(3) 1.300(2), N(3)−C(4) 1.417(2), N(4)−C(2) 1.336(2), N(4)−C(10) 1.420(2), N(5)−C(1) 1.268(2), C(1)−C(2) 1.518(2), C(4)−C(5) 1.393(2), C(4)−C(9) 1.422(2), C(5)−C(6) 1.392(3), C(6)−C(7) 1.393(2), C(7)−C(8) 1.398(2), C(8)−C(9) 1.384(2); C(1)−N(1)−C(3) 107.82(12), C(1)−N(1)−C(9) 145.93(12), C(3)−N(1)−C(9) 106.25(11), C(2)−N(2)−C(3) 104.35(11), C(2)−N(4)−C(10) 128.74(13), C(2)−N(4)−H(1N4) 113.9(11), C(1)−N(5)−C(17) 123.57(12), N(5)−C(1)−N(1) 135.96(13), N(1)−C(1)−C(2) 101.59(11), N(2)−C(2)−C(1) 113.28(12), N(3)−C(3)−N(2) 132.12(13), N(2)−C(3)−N(1) 112.96(12), C(5)−C(4)−C(9) 119.90(15)

Acetylation of the monoanions of **6a** and **6c** (generated with 1 equiv. of $Na[N(SiMe_3)_2]$) regioselectively afforded 3*H*-imidazo[1,2-*a*]imidazoles **7a** and **7b**, respectively

(Scheme 2). In contrast, methylation of the carbanion of **6a** with methyl iodide yielded a separable mixture of the regioisomers **8a** and **8b** (1:1). The structure of **7a** was independently confirmed by X-ray structure analysis (Figure 3). Compound **7a** has an oxalic amidine substructure, since the ring nitrogen atom of **6a** was acetylated in preference to the 1,2-diimine nitrogen atom. In the solid state, diimine **7a** adopts a (*Z*,*Z*) configuration, presumably for steric reasons. The geometry of **8b** was also independently confirmed by X-ray structure analysis (Figure 4). In contrast to **7a**, diimine **8b** adopts an (*E*,*Z*) configuration, due to the substitution of the nitrogen atom N-3 and the resulting steric interaction between the methyl and the *p*-tolyl groups.

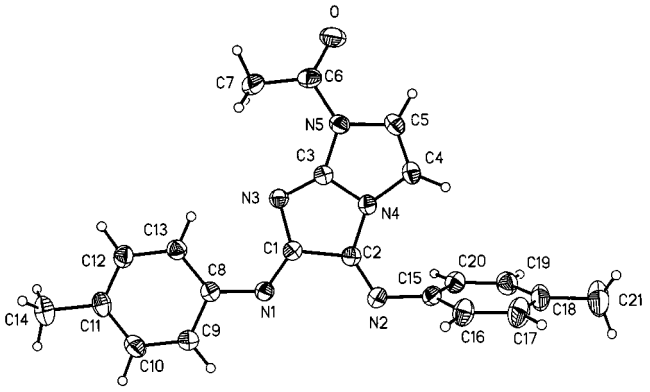


Figure 3. ORTEP plot of **7a**; 50% probability thermal ellipsoids are shown for the non-hydrogen atoms; selected bond lengths [Å] and angles [°]: O−C(6) 1.206(2), N(1)−C(1) 1.279(2), N(1)−C(8) 1.407(2), N(2)−C(2) 1.260(2), N(4)−C(3) 1.370(2), N(4)−C(2) 1.398(2), N(5)−C(3) 1.372(2), C(1)−C(2) 1.516(2); C(1)−N(1)−C(8) 124.8(2), C(3)−N(3)−C(1) 103.36(15), C(3)−N(4)−C(4) 109.6(2), C(5)−N(5)−C(6) 123.4(2), N(1)−C(1)−C(2) 119.2(2), N(2)−C(2)−N(4) 130.5(2), O−C(6)−N(5) 117.2(2)

The regioselectivity of the acylation can also be understood with the help of the computations (Figure 5). While the products acylated at the imino nitrogen atom are thermodynamically disfavoured by 9−29 kcal/mol, acylation at the ring nitrogen atoms results in structures rather similar in energy. Although these reactions formally proceed under kinetic control, under which the negative charges on the basic atoms should determine the regioselectivity, it turned out that the more remote ring nitrogen atom was acylated, despite carrying a less negative charge in the anion. We surmise that this is due to the internal hydrogen bond (vide supra), which is strengthened in the anion (the bond length shortens from 2.536 Å in the neutral state to 2.457 Å in the anion). Since this hydrogen bond must be broken for acylation to occur at this nitrogen atom, a higher barrier to this mode of attack results. This is also supported by the fact that methylation with the sterically less demanding methyl iodide occurred at both imidazole nitrogen atoms. Furthermore, as the internal hydrogen bond is no longer available in the methylated product **8b**, the tolyl group adopts a different configuration.

The intense orange colour and the high extinction coefficients of heterocycles **3a**−**c**, **6a**−**e**, **7a**, **7b**, **8a** and **8b** suggest

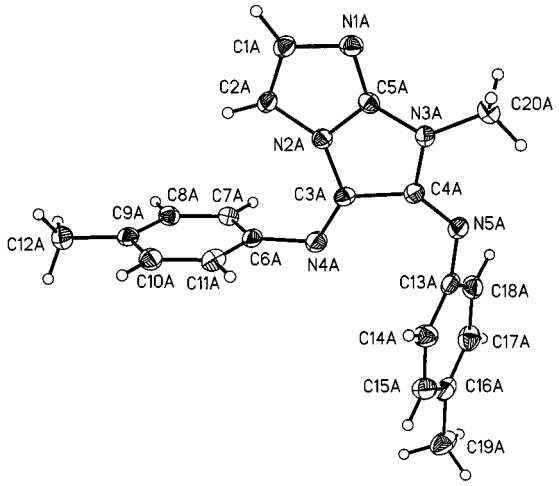


Figure 4. ORTEP plot of **8b**; 50% probability thermal ellipsoids are shown for the non-hydrogen atoms; selected bond lengths [Å] and angles [°]: N(1A)−C(5A) 1.308(4), N(1A)−C(1A) 1.427(4), C(1A)−C(2A) 1.355(4), N(2A)−C(3A) 1.403(4), N(2A)−C(2A) 1.417(4), N(3A)−C(5A) 1.377(4), N(3A)−C(20A) 1.449(4), C(3A)−N(4A) 1.272(4), C(4A)−N(5A) 1.268(4), N(4A)−C(6A) 1.438(4), N(1B)−C(5B) 1.313(4), N(1B)−C(1B) 1.412(4); C(5A)−N(1A)−C(1A) 101.9(2), C(3A)−N(2A)−C(2A) 143.5(3), C(1A)−C(2A)−N(2A) 104.8(3), C(4A)−N(3A)−C(20A) 124.4(2), N(4A)−C(3A)−N(2A) 130.0(3), N(4A)−C(3A)−C(4A) 126.0(3), C(4A)−N(5A)−C(13A) 124.3(3), N(1A)−C(5A)−N(2A) 115.4(3)

that some zwitterionic character is present in these compounds. This is supported by the computed ground state charges (computation of the excited state and simulation of the UV spectrum is beyond the scope of this paper) which, despite all being negative on the nitrogen atoms (nitrogen being the most electronegative element in these structures), display considerable polarisation across the heterocycles. Bathochromic shifts are observed for the $\pi\rightarrow\pi^*$ transitions of 1*H*-pyrrolo[1,2-*a*]benzimidazole **3a**, relative to those of its aza analogue **6c**. A bathochromic shift is also observed for the nitro derivative **6b**, relative to **6a**. The λ_3 transitions in **6c** and in acetylated derivative **7b** are again very similar. In contrast, a bathochromic shift is observed for **8a**, relative to **6a** and **8b**.

To study the regioselectivity of cyclization reactions of benzimidazole-derived dinucleophiles containing heteroatoms other than nitrogen, we turned our attention to reactions between oxaldiimidoyl dichlorides and 2-mercaptobenzimidazole (**9**) and 2-hydroxybenzimidazole (**11**). Refluxing of a THF solution of diimidoyl dichlorides **2a** or **2d** with 2-mercaptobenzimidazole (**9**) in the presence of Et_3N afforded the 2,3-dihydrothiazolo[3,2-*a*]benzimidazoles **10a**−**b** through *S*/*N*-cyclization of the dinucleophile (Scheme 3, Table 2).[13] These products were also formed by treatment of the dianion of **9** (generated by addition of 2 equiv. of *n*BuLi to **9** and stirring for 1 h at 0 °C) with the dielectrophile.

The structure of the cyclization products **10** is fully supported by mass spectrometry, elemental analyses and ^{13}C NMR (APT) data. The presence of 19 ^{13}C NMR signals in **10a** shows that (in contrast to heterocycles **12**, vide infra) an asymmetrical structure is present. Similarly to **6c**, nine

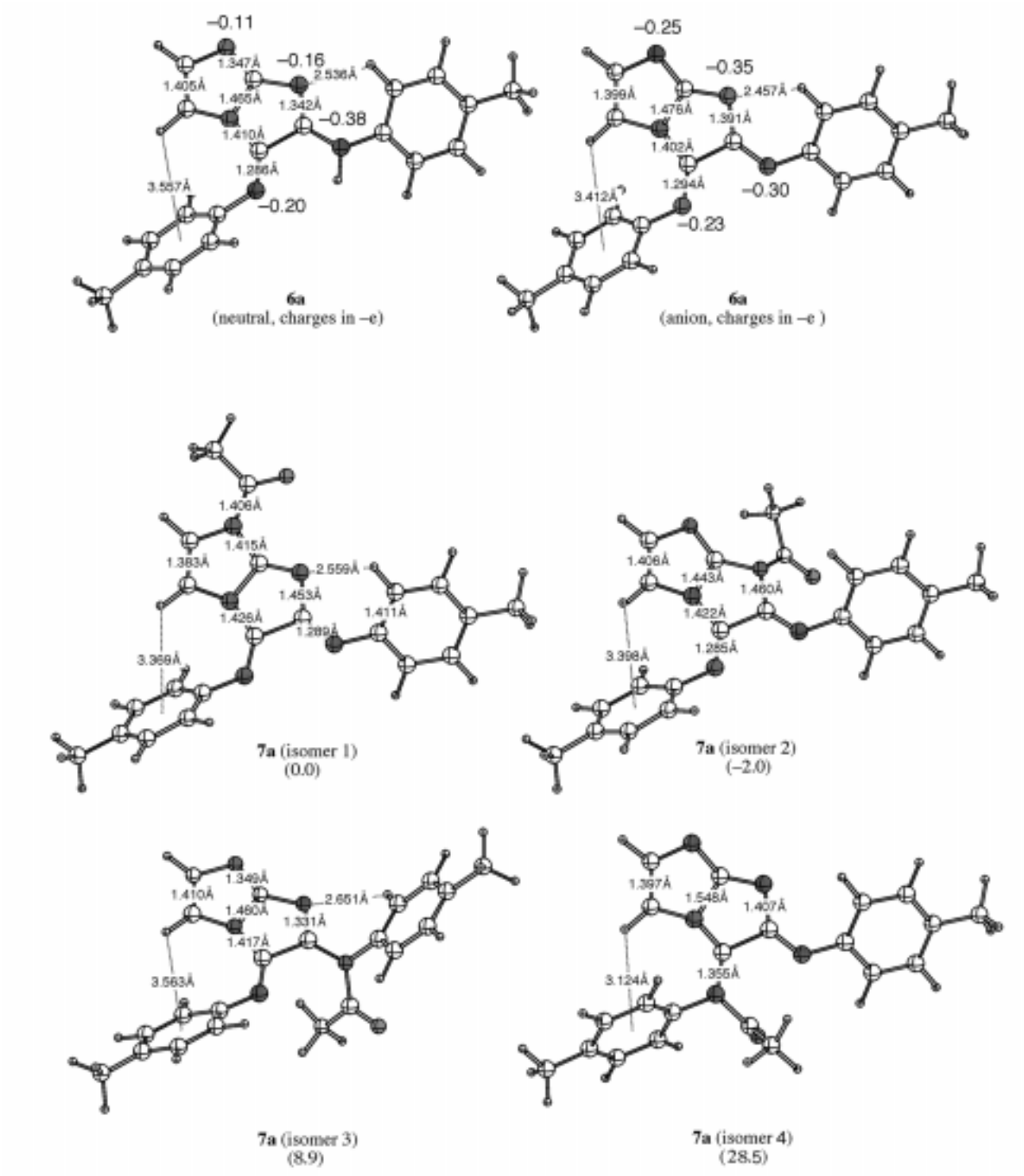
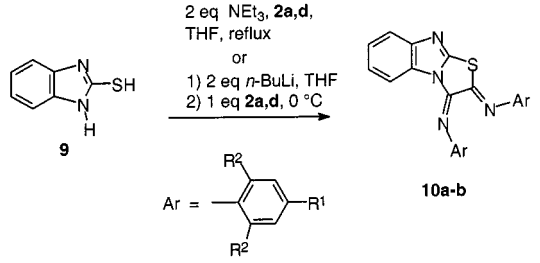


Figure 5. Calculations of the regioselective acetylation of **6a**

quaternary carbon atoms are detected for **10a** [δ = 131.0, 133.5 (benzimidazole-C to N), 137.9, 138.8 (Tol-C to C), 144.1, 144.8, 145.0, 146.7 (Tol-C to N, C-3, C-2), 149.2 (C-9a)]. Because of the presence of a sulfur in place of a nitrogen atom in **10a**, the signals of C-9a and C-2 appear at higher field than the respective signals in **6c**. Unlike in heterocycles **3**, **6** and **7b**, the benzimidazole signals of the protons 5-H in **10a**,**b** (**10a**, CD_2Cl_2, δ = 7.34) are not shifted upfield. This suggests either that the aforementioned C−H-quadrupole interaction is energetically much less favourable, or that there is no clear-cut preference for this orientation of the arylamino group. The computations show that the two configurations for this group around the imino nitrogen atom are virtually identical in energy (ΔH = 0.3

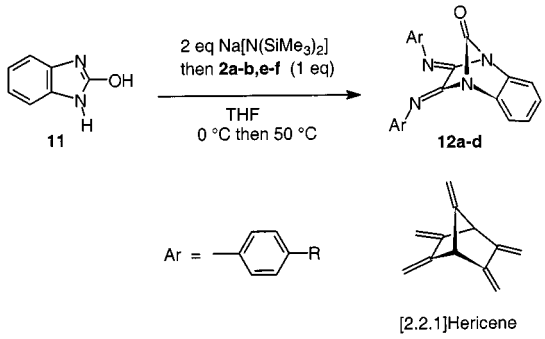


Scheme 3. Cyclizations between 2-mercaptobenzimidazole and oxaldiimidoyl dichlorides

Table 2. Synthesis of 2,3-dihydrothiazolo[3,2-*a*]benzimidazoles

2	10	R^1	R^2	%[a]	M.p. [°C]
a	**a**	CH_3	H	72	200−202
d	**b**	CH_3	CH_3	61	160−162

[a] Isolated yields.



Scheme 4. Cyclizations between 2-hydroxybenzimidazole and oxaldiimidoyl dichlorides

Table 3. Synthesis of 1,2,3,4-tetrahydro-1,4-methanoquinoxalin-9-ones

2	12	R	%[a]	M.p. [°C]
a	**a**	CH_3	57	> 400
b	**b**	H	56	> 400
e	**c**	*t*Bu	42	> 400
f	**d**	MeO	38	> 400

[a] Isolated yields.

kcal/mol) and we ascribe this to the absence of the intramolecular N−H···N hydrogen bond (Figure 6).

Treatment of 2-hydroxybenzimidazole (**11**) with **2a**, **2b**, **2e** and **2f** proceeded regioselectively, through *N*/*N*-cyclization rather than *O*/*N*-cyclization, to afford the novel diazabicyclo[2.2.1]heptanones **12a**−**d** in good yields (Scheme 4, Table 3).[14a] The formation of a cyclization product rather than an open-chain one was indicated by mass spectrometry and elemental analyses. Nine signals were detected in the ^{13}C NMR spectrum of **12a**, which suggests that a symmetrical structure is present. Comparison of the ^{13}C NMR spectroscopic data of **12a** [CD_2Cl_2, δ = 114.7, 121.1, 125.1, 125.6, 127.3 (CH), 129.2 (quinoxaline-C to N), 140.8 (Ph-C to N), 146.4 (C=N), 151.9 (C=O)] with those of 1,3-dihydro-1,3-dimethyl-2*H*-benzimidazol-2-one [$CDCl_3$, δ = 27.1 (Me), 107.4, 121.2 (CH), 130.0 (C), 154.6 (C=O)][14b] further supports the proposed bicyclic structure. Chemical ionization mass spectrometry (CI) ruled out the formation of a macrocyclic product. The high value of the carbonyl absorption (IR, $\tilde{\nu}$ = 1748−1752 cm^{-1}) can be explained by the low double bond character of the urea moiety (Bredt rule).

The regioselectivity can be explained in several ways. First of all, the enol form of **11** is higher in energy; that is, the keto form is clearly the major equilibrium component under basic conditions (this structure is favoured by 13.2 kcal/mol at AM1, Figure 6). However, since it is likely that the dianion is produced under the reaction conditions, this point is moot as a single structure would result from either tautomer upon double deprotonation. The existence of the dianion is supported further by the fact that the formation of the hericene-type product **12a** (*N*/*N*-product) must be kinetically controlled; the analogous *O*/*N*-product is thermodynamically favoured by 22.2 kcal/mol but is not formed. Secondly, the HOMO of the dianion of **11** has the largest coefficients on the two nitrogen atoms; reaction should thus occur at these positions first. This contrasts nicely with the analogous sulfur-containing dianion, which bears the largest HOMO contribution on the sulfur atom. Hence, the hericene-type structure is even more unfavourable, which is evident from the relative product energies (**10a** is 55.0 kcal/mol more stable than the corresponding bridged *N*/*N*-product).

In contrast to all the other (yellow to red) 1,4-diazadiene derivatives presented here, diazabicyclo[2.2.1]heptanones **12a**−**d** are colourless. According to the Bredt rule, heterocycles **12** should not exhibit zwitterionic character. Diazabicyclo[2.2.1]heptanones **12a**−**d** represent hetero analogues of [2.2.1]hericenes[14c] and are of biological relevance since the related quinuclidine substructure is present in a variety of pharmacologically active compounds. Quinuclidines act as agonists of muscarine receptors[15] and have therefore proved active against Alzheimer's disease. Additionally, quinuclidines play an important role as peptide mimetics and are used clinically against arthritis and as painkillers, or to lower cholesterol levels.[16,17] Modified diazabicyclo[2.2.1]heptanes may be used in DABCO-type coupling reactions.[18]

Conclusions

To the best of our knowledge, we report here the first cyclization reactions between imidazole-derived dinucleophiles and oxalic acid dielectrophiles, together with a systematic investigation of the parameters controlling the regioselectivity of these reactions. In order to induce cyclization, the use of the moderately electrophilic oxaldiimidoyl dichlorides **2** was essential. This methodology provides convenient access to a variety of biologically relevant heterocycles, including the novel 1*H*-pyrrolo[1,2-*a*]benzimidazoles

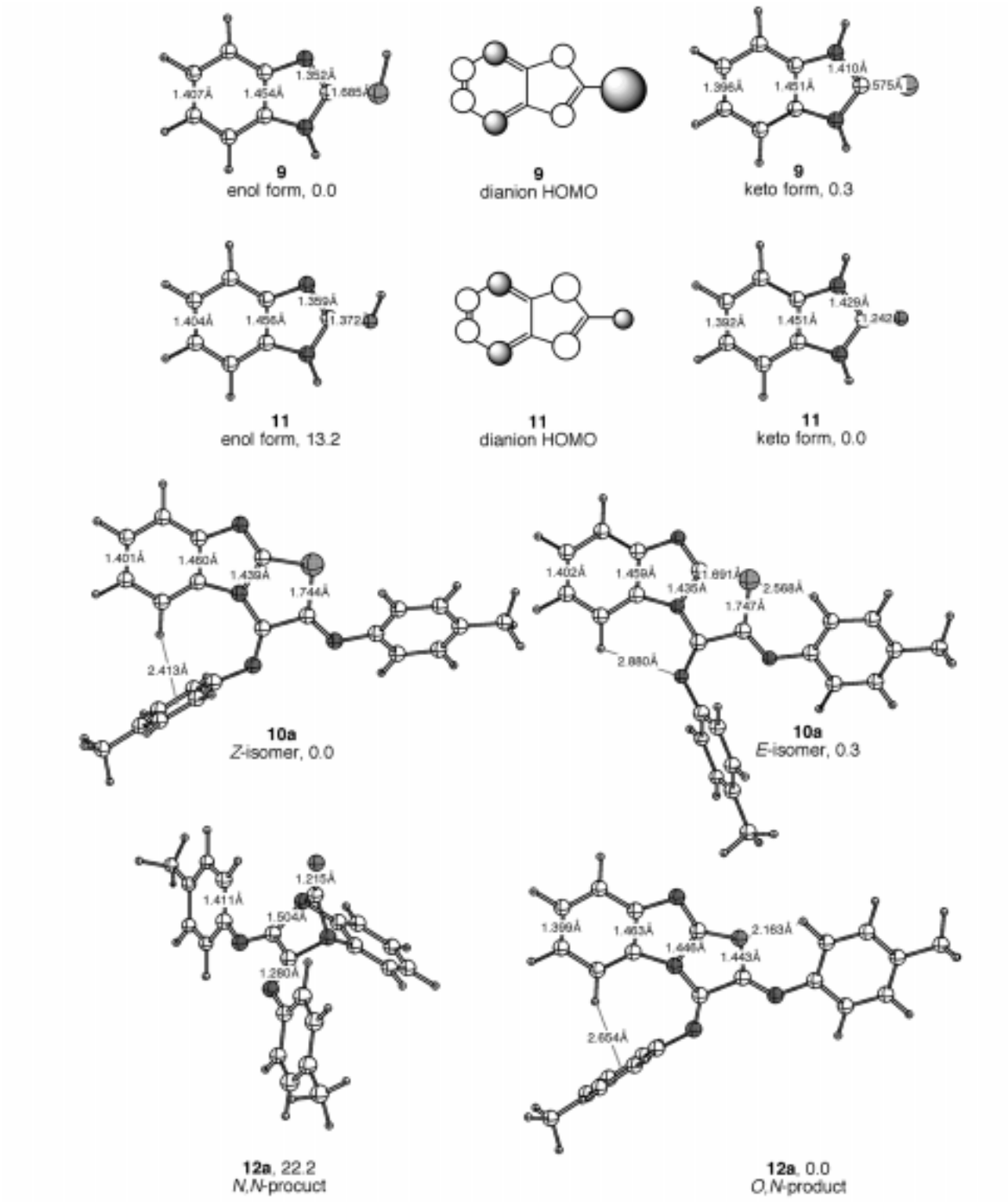


Figure 6. Calculations of the regioselective formation of **10a** and **12a**

3, 3*H*-imidazo[1,2-*a*]benzimidazoles **6** and diazabicyclo[2.2.1]heptanones **12**. All the compounds reported here (except for **12a**−**d**) constitute heterocyclic merocyanines, which are of interest as NIR dyes.[19] The cyclization regiochemistry is controlled by the heteroatoms in the nucleophile. In the case of the dianion of 2-methylbenzimidazole, regioselective *C*/*N*-cyclization was observed. *N*/*N*-Cyclization involving the amino group of the dinucleophile was found for amino-substituted imidazoles, pyrazoles and triazoles. Whereas *S*/*N*-cyclization was observed for the reaction between diimidoyl dichlorides and 2-mercaptobenzimidazoles, regioselective *N*/*N*-cyclization was surprisingly ob-

served for 2-hydroxybenzimidazole, giving the novel diazabicyclo[2.2.1]heptanones **12**.

Experimental Section

General Comments: All solvents were dried by standard methods and all reactions were carried out under an inert gas. The oxaldiimidoyl dichlorides **2** were prepared according to literature procedures.[9] − For the ^{1}H and ^{13}C NMR spectra (^{1}H NMR: 200 MHz, ^{13}C NMR: 50.288 MHz), tetramethylsilane was used as internal standard and the indicated deuterated solvents were employed. − MS data were obtained using the electron ionization (70 eV) or the chemical ionization techniques (CI, H_2O). 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:[20] A Nonius CAD4 diffractometer (compound **7a**) and a Nonius Kappa CCD (compounds **6c** and **8b**) using graphite-monochromated Mo-K_α radiation were used for data collection. Data were corrected for Lorentz and polarisation effects.[21] No absorption correction were made. The structures were solved by direct methods (SHELXS)[22] and refined by full-matrix, least-squares techniques against F^2 (SHELXL-93).[23] For **6c**, 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 6c: $C_{23}H_{19}N_5$, M = 365.43 gmol^{-1}, red prisms, size 0.30 × 0.28 × 0.24 mm, monoclinic, space group $P2_1/c$, a = 13.5975(4), b = 16.2198(5), c = 8.6860(2) Å, β = 99.861(2)°, V = 1887.38(9) Å^3, T = −90 °C, Z = 4, $\rho_{calcd.}$ = 1.286 gcm^{-3}, μ(Mo-K_α) = 0.79 cm^{-1}, F(000) = 768, 5003 reflections in h (−14/15), k (−17/18), l (−9/0), measured in the range 2.51° ≤ Θ ≤ 23.25°, completeness Θ_{max} = 96%, 2698 independent reflections, R_{int} = 0.018, 2395 reflections with $F_o > 4\sigma(F_o)$, 330 parameters, 0 restraints, $R1_{obs}$ = 0.035, wR^2_{obs} = 0.103, $R1_{all}$ = 0.0519, wR^2_{all} = 0.144, GOOF = 1.019, largest difference peak and hole: 0.170/−0.175 eÅ^{-3}.

Crystal Data for 7a: $C_{21}H_{19}N_5O$, M = 357.41 gmol^{-1}, yellow prisms, size 0.40 × 0.38 × 0.36 mm, monoclinic, space group $C2/c$, a = 30.357(6), b = 7.676(2), c = 16.879(3) Å, β = 106.13(3) °, V = 3778.3(14) Å^3, T = 20 °C, Z = 8, $\rho_{calcd.}$ = 1.257 gcm^{-3}, μ(Mo-K_α) = 0.81 cm^{-1}, F(000) = 1504, 8219 reflections in h (−39/37), k (−9/9), l (0/18), measured in the range 1.40° ≤ Θ ≤ 27.40°, 4123 independent reflections, R_{int} = 0.024, 3112 reflections with $F_o > 4\sigma(F_o)$, 296 parameters, 0 restraints, $R1_{obs}$ = 0.057, wR^2_{obs} = 0.137, $R1_{all}$ = 0.077, wR^2_{all} = 0.147, GOOF = 1.380, largest difference peak and hole: 0.233/−0.225 eÅ^{-3}.

Crystal Data for 8b: $C_{20}H_{19}N_5$, M = 329.40 gmol^{-1}, red prisms, size 0.32 × 0.30 × 0.28 mm, monoclinic, space group $C2/c$, a = 28.6757(7), b = 13.0809(3), c = 18.3931(6) Å, β = 91.141(2)°, V = 6898.0(3) Å^3, T = −90 °C, Z = 16, $\rho_{calcd.}$ = 1.269 gcm^{-3}, μ(Mo-K_α) = 0.79 cm^{-1}, F(000) = 2784, 9116 reflections in h (−31/31), k (−14/0), l (−20/20), completeness Θ_{max} = 98%, measured in the range 2.05° ≤ Θ ≤ 23.25°, 4940 independent reflections, R_{int} = 0.048, 3287 reflections with $F_o > 4\sigma(F_o)$, 452 parameters, 0 restraints, $R1_{obs}$ = 0.058, wR^2_{obs} = 0.165, $R1_{all}$ = 0.104, wR^2_{all} = 0.222, GOOF = 1.139, largest difference peak and hole: 0.424/−0.267 eÅ^{-3}.

Preparation of 1*H*-Pyrrolo[1,2-*a*]benzimidazol-2-amines 3a,b: *n*BuLi (8.25 mL, 2.2 equiv., 1.6 M solution in hexane) was added at 0 °C to a THF solution (20 mL) of 2-methylbenzimidazole (792 mg, 6.0 mmol). A colourless suspension was formed. After stirring for 60 min at 0 °C, the suspension was added at 0 °C to a THF solution (80 mL) of oxaldiimidoyl dichlorides **2a** or **2b** (6.0 mmol), using a metal cannula. The colour 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; ether/petroleum ether, 1:3). Similar yields were obtained when an aqueous workup (dilute aqueous solution of HCl) was carried out before the chromatographic purification.

***N*-(4-Methylphenyl)-1-[(4-methylphenyl)imino]-1*H*-pyrrolo[1,2-*a*]-benzimidazol-2-amine (3a):** This compound was prepared from 2-methylbenzimidazole (792 mg, 6.0 mmol) and oxalbis(4-tolylimidoyl) dichloride (**2a**) (6.0 mmol). An orange solid (762 mg, 35%) was isolated, m.p. 168 °C (dec.). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.29, 2.38 (2 × s, 2 × 3 H, CH_3), 4.90 (d, J = 8 Hz, 1 H, H-8), 6.02 (s, 1 H, H-3), 6.60 (t, J = 8 Hz, 1 H, H-7), 6.80−7.50 (m, 10 H, Ar), 8.30 (br, 1 H, NH). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 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) cm^{-1}, 3055 (w), 1666 (m), 1618 (s), 1573 (s), 1525 (s), 1504 (s), 1448 (m), 1407 (m), 1273 (w), 1139 (m). − MS (CI, H_2O): m/z (%) = 365 [M^+ + 1]. − UV/Vis (CH_3CN): λ_{max} (log ε) = 281 nm (4.33), 356 (4.05), 436 (3.58). − $C_{24}H_{20}N_4$ (364.4): C 79.10, H 5.53, N 15.37; found C 78.52, H 5.23, N 14.88.

***N*-(Phenyl)-1-(phenylimino)-1*H*-pyrrolo[1,2-*a*]benzimidazol-2-amine (3b):** This compound was prepared from 2-methylbenzimidazole (792 mg, 6.0 mmol) and oxalbis(phenylimidoyl) dichloride (**2b**) (6.0 mmol). Orange crystals (565 mg, 28%) were isolated, m.p. 162 °C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.86 (d, J = 8 Hz, 1 H, H-8), 6.19 (s, 1 H, H-3), 6.55 (t, J = 8 Hz, 1 H, H-7), 6.88 (t, 1 H, H-6), 7.05 (m, 3 H, Ar), 7.20−7.60 (m, 8 H, Ar), 8.39 (br, 1 H, NH). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 89.81 (C-3), 112.83 (C-8), 119.54, 119.75, 120.75, 121.69, 123.39, 125.29, 129.39, 1129.96, 130.03 (Ar-CH), 131.87, 131.88 (C-4, C-9), 143.37 (C-2), 145.53, 149.39 (Ph-C to N), 150.75 (C-1), 164.43 (C-3a). − IR (KBr): $\tilde{\nu}$ = 3348 (w) cm^{-1}, 3056 (w), 1692 (m), 1620 (s), 1596 (s), 1560 (s), 1532 (s), 1496 (m), 1444 (m), 1368 (m), 1332 (m), 1296 (m), 1204 (m). − MS (CI, H_2O): m/z (%) = 337 [M^+ + 1], 233 [M^+ − 103, − PhNC]. − $C_{22}H_{16}N_4$: C 78.56, H 4.79, N 16.65; found C 78.42, H 5.03, N 16.31.

Preparation of 3*H*-Imidazo[1,2-*a*]imidazol-2-amines 6a and 6b and 3*H*-Imidazo[1,2-*a*]benzimidazol-2-amines 6c−e: A THF solution of 2-aminoimidazole or 2-aminobenzimidazole (5.0 mmol) was added to a solution of **2** (5.0 mmol) and Et_3N (1.4 mL, 10.0 mmol) in THF (50 mL) and the mixture was refluxed for 4 h. The precipitated Et_3NHCl was removed by filtration and the filtrate solvent was removed in vacuo. Methanol was added to the orange residue and the precipitated orange product was isolated, dried in vacuo and recrystallized from ethanol or DMF.

***N*-(4-Methylphenyl)-3-[(4-methylphenyl)imino]-3*H*-imidazo[1,2-*a*]-imidazol-2-amine (6a):** Treatment of 2-aminoimidazole (415 mg, 5.0 mmol) with oxalbis(4-tolylimidoyl) dichloride (**2a**) (5.0 mmol) gave 0.95 g (60%) of an orange solid, which was recrystallized from ethanol, m.p. 320−321 °C. − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 2.36, 2.39 (2 × s, 2 × 3 H, Tol-CH_3), 6.31, 6.59 (2 × d, 2 × 1 H,

J = 1.9 Hz, Hetar), 7.00, 7.23, 7.26, 7.73 (4 × d, 4 × 2 H, Ar, J = 6.5 Hz), 8.14 (s, 1 H, NH). − ^{13}C NMR (50 MHz, CD_2Cl_2): δ_C = 20.4, 20.5 (Tol-CH_3), 111.8, 119.7, 120.4, 129.2, 130.0, 131.4, 133.3, 134.9, 135.8, 140.7, 143.2, 160.6, 164.9. − IR (Nujol): $\tilde{\nu}$ = 3279 (m, ν_{NH}) cm^{-1}, 1696, 1639 (s, $\nu_{C=N}$), 1612 (m), 1547 (s), 1534 (s), 1511 (s), 1495 (s). − MS (EI): *m*/*z* (%) = 315 [M$^+$], 224, 198 (100), 117, 91, 65. − UV/Vis (CH_3CN): λ_{max} (log ε) = 387 nm (3.79), 418 (3.80). − $C_{19}H_{17}N_5$ (315.38): C 72.36, H 5.43, N 22.21; found C 72.09, H 5.41, N 21.85.

***N*-(4-Nitrophenyl)-3-[(4-nitrophenyl)imino]-3*H*-imidazo[1,2-*a*]-imidazol-2-amine (6b):** Treatment of 2-aminoimidazole (415 mg, 5.0 mmol) with oxalbis(4-nitrophenylimidoyl) dichloride **2c** (5.0 mmol) gave 1.19 g (63%) of a red to violet solid, which was recrystallized from DMF, m.p. 321−323 °C. − ^{1}H NMR (200 MHz, [D$_7$]DMF): δ = 6.34, 6.67 (2 × d, 2 × 1 H, J = 2.0 Hz, Hetar-CH), 7.48, 8.41 (2 × d, 2 × 4 H, J = 8.9 Hz, Ar), 11.15 (br, 1 H, NH). − ^{13}C NMR (50 MHz, [D$_7$]DMF): δ_C = 113.6, 121.1, 121.5, 125.5, 126.3, 133.1, 143.9, 146.0, 165.3 (4 overlapping signals). − IR (Nujol): $\tilde{\nu}$ = 3409 (w, ν_{NH}) cm^{-1}, 1717, 1640 (s, $\nu_{C=N}$), 1611 (s), 1588 (s), 1554 (s), 1508 (s). − MS (EI): *m*/*z* (%) = 377 [M$^+$], 229 (100), 183, 75. − UV/Vis (CH_3CN): λ_{max} (log ε) = 428 nm (3.92). − $C_{17}H_{11}N_7O_4$ (377.32): C 54.12, H 2.94, N 25.99; found C 53.61, H 2.99, N 25.73.

***N*-(4-Methylphenyl)-3-[(4-methylphenyl)imino]-3*H*-imidazo[1,2-*a*]-benzimidazol-2-amine (6c):** Treatment of 2-aminobenzimidazole (675 mg, 5.0 mmol) with oxalbis(4-tolylimidoyl) dichloride (**2a**) (5.0 mmol) gave 1.20 g (66%) of an orange solid, which was recrystallized from ethanol, m.p. 340−342 °C. − ^{1}H NMR (200 MHz, [D$_7$]DMF): δ = 2.34, 2.42 (2 × s, 2 × 3 H, Tol-CH_3), 5.08 (d, J = 8.0 Hz, 1 H, H-5), 6.72, 7.01 (2 × t, 2 × 1 H, J = 7.8 Hz, Hetar), 7.10, 7.30, 7.36 (3 × d, 8 H, J = 8.2 Hz, Ar), 8.15 (d, J = 8.5 Hz, Hetar), 10.5 (br, 1 H, NH). − ^{13}C NMR (50 MHz, [D$_7$]DMF): δ = 20.7, 20.8 (Tol-CH_3), 113.3, 119.5, 121.3, 121.4, 123.0, 124.1, 129.8, 130.0, 130.3, 134.9, 135.3, 136.7, 140.0, 146.1, 148.8, 163.6, 168.9. − IR (Nujol): $\tilde{\nu}$ = 3209, 3165, 3108 (s, ν_{NH}) cm^{-1}, 1703, 1655 (s, $\nu_{C=N}$), 1622 (s), 1608 (s), 1540 (s), 1506 (s). − MS (EI): *m*/*z* (%) = 365 (100) [M$^+$], 350, 248, 117, 91. − UV/Vis (CH_3CN): λ_{max} (log ε) = 277 nm (4.30), 331 (3.91), 403 (3.99). − $C_{23}H_{19}N_5$ (365.44): C 75.60, H 5.24, N 19.16; found C 74.98, H 5.43, N 18.72.

***N*-Phenyl-3-(phenylimino)-3*H*-imidazo[1,2-*a*]benzimidazol-2-amine (6d):** Treatment of 2-aminobenzimidazole (675 mg, 5.0 mmol) with oxalbis(phenylimidoyl) dichloride (**2b**) (5.0 mmol) gave 1.21 g (72%) of an orange solid, which was recrystallized from DMF, m.p. 308−310 °C. − ^{1}H NMR (200 MHz, [D$_7$]DMF): δ = 5.00 (d, J = 7.8 Hz, 1 H, H-5), 6.72, 7.04 (2 × t, J = 7.8 Hz, Hetar), 7.23−7.61 (m, 10 H, Ar), 8.30 (d, J = 7.8 Hz, 1 H, Hetar), 10.82 (s, 1 H, NH). − ^{13}C NMR (50 MHz, [D$_7$]DMF): δ = 113.1, 119.7, 121.4, 121.6, 123.3, 124.3, 125.4, 125.8, 129.6, 130.0, 130.4, 139.2, 140.0, 148.7, 148.9, 163.9, 168.9. − IR (Nujol): $\tilde{\nu}$ = 3206, 3162, 3116 (s, ν_{NH}) cm^{-1}, 1715, 1702, 1653 (s, $\nu_{C=N}$), 1618 (s), 1597 (s), 1551 (s), 1498 (s). − MS (EI): *m*/*z* (%) = 337 (95) [M$^+$], 234 (100), 208, 169, 118, 77. − $C_{21}H_{15}N_5$ (337.38): C 74.76, H 4.48, N 20.76; found C 74.43, H 4.82, N 20.51.

***N*-(2,4,6-Trimethylphenyl)-3-[(2,4,6-trimethylphenyl)imino]-3*H*-imidazo[1,2-*a*]imidazol-2-amine (6e):** Treatment of 2-aminobenzimidazole (675 mg, 5.0 mmol) with oxalbis(2,4,6-trimethylphenylimidoyl) dichloride **2d** (5.0 mmol) gave 991 mg (47%) of an orange solid, which was recrystallized from methanol, m.p. 126−128 °C. − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 2.10, 2.37, 2.40 (3 × s, 18 H, CH_3), 5.13 (d, J = 7.9 Hz, 1 H, H-5), 6.74, 7.02 (2 × t, 2 × 1 H, J = 7.9 Hz, Hetar), 7.02 (s, 4 H, Ar), 7.37 (d, J = 7.7 Hz, 1 H, Hetar), 8.24 (s, 1 H, NH). − ^{13}C NMR (50 MHz, CD_2Cl_2): δ_C = 18.0, 18.5, 20.9, 21.1 (CH_3), 112.0, 119.8, 123.8, 124.3, 128.5, 129.0, 129.6, 129.9, 131.0, 135.2, 135.3, 138.7, 139.6, 142.9, 138.4, 165.1, 168.3. − IR (Nujol): $\tilde{\nu}$ = 3248 (s, ν_{NH}) cm^{-1}, 1698, 1653 (s, $\nu_{C=N}$), 1616 (s), 1543 (s), 1507 (s). − MS (CI, H_2O): *m*/*z* (%) = 422 (100) [M$^+$ + 1], 289, 211, 134. − $C_{27}H_{27}N_5$ (421.54): C 76.93, H 6.46, N 16.61; found C 76.79, H 6.40, N 16.56.

Acetylation of 6a and 6c: A solution of $NaN(SiMe_3)_2$ (1 M in THF, 1.1 mL) was added to a solution of **6a** or **6c** in THF (20 mL). The deep red solution was cooled to − 20 °C and acetyl chloride (126 μL, 1.1 mmol) was added. The mixture was warmed to 20 °C and stirred for 1.5 h. Precipitated NaCl was removed by filtration and the filtrate solvent was removed in vacuo. The residue was recrystallized from methanol or acetone.

7-Acetyl-*N*-(4-methylphenyl)-3-[(4-methylphenyl)imino]-3*H*-imidazo[1,2-*a*]imidazol-2-amine (7a): Treatment of **6a** (315 mg, 1.0 mmol) with acetyl chloride gave 0.129 g (36%) of a yellow solid, which was recrystallized from acetone, m.p. 178−180 °C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.35 (s, 6 H, Tol-CH_3), 2.73 (s, 3 H, $COCH_3$), 5.79, 6.87 (2 × d, 2 × 1 H, J = 2.9 Hz, Hetar), 6.93, 7.69 (2 × d, 2 × 2 H, J = 8.1 Hz, Ar), 7.17 (m, 4 H, Ar). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.9, 21.1 (Tol-CH_3), 24.1 (acetyl-CH_3), 112.4, 121.3, 126.1, 129.5, 129.9, 133.7, 136.2, 144.3, 156.8, 159.8, 162.6, 166.2 (2 overlapping signals). − IR (Nujol): $\tilde{\nu}$ = 1737 (s, $\nu_{C=O}$) cm^{-1}, 1686, 1650 (s, $\nu_{C=N}$), 1606 (s), 1581 (s), 1555 (s), 1500 (s). − MS (CI, H_2O): *m*/*z* (%) = 358 (100) [M$^+$ + 1], 314. − $C_{21}H_{19}N_5O$ (357.41): C 70.57, H 5.36, N 19.59; found C 70.50, H 5.36, N 19.22.

9-Acetyl-*N*-(4-methylphenyl)-3-[(4-methylphenyl)imino]-3*H*-imidazo[1,2-*a*]benzimidazol-2-amine (7b): Treatment of **6c** (365 mg, 1.0 mmol) with acetyl chloride gave 0.216 g (53%) of a yellow solid, which was recrystallized from methanol, m.p. 215 (dec.). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.29, 2.40 (2 × s, 2 × 3 H, Tol-CH_3), 2.81 (s, 3 H, $COCH_3$), 5.01 (d, J = 7.8 Hz, 1 H, H-5), 7.07−7.35 (m, 8 H, Ar), 7.61, 8.23 (2 × t, 2 × 1 H, J = 8.1 Hz, Hetar), 7.81 (d, J = 7.9 Hz, 1 H, Hetar). − ^{13}C NMR (50 MHz): δ = 21.2, 21.3 (Tol-CH_3), 25.9 (acetyl-CH_3), 111.8, 117.3, 212.9, 125.0, 126.2, 129.2, 129.5, 132.0, 134.9, 136.9, 144.2, 169.1 (6 overlapping signals). − IR (Nujol): $\tilde{\nu}$ = 1732 (s, $\nu_{C=O}$) cm^{-1}, 1681, 1644 (s, $\nu_{C=N}$), 1606 (s), 1554 (s), 1507 (s). − MS (EI): *m*/*z* (%) = 407 [M$^+$], 364, 290, 277, 248 (100), 133, 118, 107, 91, 42. − UV/Vis (CH_3CN): λ_{max} (log ε) = 273 nm (4.41), 401 (4.05). − $C_{25}H_{21}N_5O$ (407.51): C 73.69, H 5.19, N 17.19; found C 73.18, H 5.10, N 17.40.

Methylation of 6a: A solution of $NaN(SiMe_3)_2$ (1 M in THF, 1.1 mL) was added to a THF (20 mL) solution of **6a** (0.315 g, 1.0 mmol). The deep red solution was cooled to −20 °C and methyl iodide (75 μL, 1.2 mmol) was added. The temperature was allowed to rise to 20 °C. After stirring for 30 min, the precipitated NaCl was removed by filtration (Celite). The filtrate solvent was removed in vacuo. Chromatography (silica gel; toluene/acetone, 1:5) gave 150 mg (48%) of **8a** and 150 mg (48%) of **8b** (combined yield 96%).

7-Methyl-*N*-(4-methylphenyl)-3-[(4-methylphenyl)imino]-3*H*-imidazo[1,2-*a*]imidazol-2-amine (8a): M.p. 208−210 °C. − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 2.29, 2.32 (2 × s, 2 × 3 H, Tol-CH_3), 3.38 (s, 3 H, NCH_3), 5.70, 6.33 (2 × d, 2 × 1 H, J = 2.7 Hz, Hetar), 6.56, 7.31 (2 × d, 2 × 2 H, J = 8.2 Hz, Ar), 7.00−7.09 (m, 4 H, Ar). − ^{13}C NMR (50 MHz, CD_2Cl_2): δ = 21.0, 21.1 (Tol-CH_3), 31.8 (NCH_3), 110.5, 120.5, 125.1, 129.2, 130.1, 134.9, 135.7, 144.1, 145.7, 145.9, 160.7, 165.1 (1 overlapping signal). − IR (Nujol): $\tilde{\nu}$ = 1674, 1652 (s, $\nu_{C=N}$) cm^{-1}, 1608 (s), 1559 (s), 1501 (s). − MS (EI): *m*/*z* (%) = 329 [M$^+$], 314, 212 (100), 164, 116, 91. − UV/

Vis (CH_3CN): λ_{max} (log ε) = 429 nm (3.95). − $C_{20}H_{19}N_5$ (329.40): C 72.93, H 5.81, N 21.26; found C 73.16, H 5.63, N 21.15.

1-Methyl-*N*-(4-methylphenyl)-3-[(4-methylphenyl)imino]-3*H*-imidazo[1,2-*a*]imidazol-2-amine (8b): M.p. 162−164 °C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.28, 2.33 (2 × s, 2 × 3 H, Tol-CH_3), 2.98 (s, 3 H, NCH_3), 5.91, 6.01 (2 × d, 2 × 1 H, *J* = 3.1 Hz, Hetar), 6.50, 7.34 (2 × d, 2 × 2 H, *J* = 8.4 Hz, Ar), 6.93−7.18 (m, 4 H, Ar). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.8, 20.9 (Tol-CH_3), 30.3 (NCH_3), 112.4, 117.5, 120.2, 126.9, 128.8, 129.8, 134.1, 135.5, 143.3, 145.5, 148.2, 160.1 (1 overlapping signal). − IR (Nujol): $\tilde{\nu}$ = 1693, 1669 (s, $\nu_{C=N}$) cm^{-1}, 1622 (s), 1613 (s), 1573 (s), 1504 (s). − MS (EI): *m*/*z* (%) = 329 (92) [M$^+$], 328 (100), 314, 211, 196, 183, 170, 117, 91, 65. − UV/Vis (CH_3CN): λ_{max} (log ε) = 344 nm (3.54), 397 (3.62). − $C_{20}H_{19}N_5$ (329.40): C 72.93, H 5.81, N 21.26; found C 72.76, H 5.93, N 21.55.

Preparation of 2,3-Dihydrothiazolo[3,2-*a*]benzimidazoles 10a,b: Heterocycles **10a**,**b** were prepared according to the procedures for the preparation of **6a**−**e** or **3a**,**b**. Both methods were equally efficient in terms of isolated product yields.

2,3-Bis(4-tolylimino)-2,3-dihydrothiazolo[3,2-*a*]benzimidazole (10a): This compound was prepared from 2-mercaptobenzimidazole (752 mg, 5.0 mmol) and 1.52 g of oxalbis(4-tolylimidoyl) dichloride (**2a**) (5.0 mmol). Yellow crystals (1.38 g, 72%) were obtained, m.p. 200−202 °C (toluene/hexane). − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 2.35 (s, 6 H, Tol-CH_3), 6.83, 6.98, 7.16, 7.22 (4 × d, 4 × 2 H, *J* = 8.2 Hz, Ar), 7.34 (d, *J* = 4.0 Hz, 1 H, Hetar), 7.37 (t, *J* = 4.5 Hz, 1 H, Hetar), 7.68 (t, *J* = 4.5 Hz, 1 H, Hetar), 8.19 (d, *J* = 4.0 Hz, 1 H, Hetar). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.0, 21.2 (Tol-CH_3), 112.9, 119.3, 119.6, 120.4, 124.2, 125.0, 129.1, 130.1 (CH), 131.0, 133.5, 137.9, 138.8, 144.1, 144.8, 145.0, 146.7, 149.2 (C). − IR (Nujol): $\tilde{\nu}$ = 1664, 1631 (s, $\nu_{C=N}$) cm^{-1}, 1611 (s), 1593 (s), 1568 (m), 1508 (s). − MS (CI, H_2O): *m*/*z* (%) = 383 (100) [M$^+$ + 1], 367, 265, 232, 136, 108. − $C_{23}H_{18}N_4S$ (382.48): C 72.23, H 4.74, N 14.65, S 8.38; found C 72.41, H 7.78, N 14.07, S 8.20.

2,3-Bis(2,4,6-trimethylphenylimino)-2,3-dihydrothiazolo[3,2-*a*]-benzimidazole (10b): This compound was prepared from 2-mercaptobenzimidazole (752 mg, 5.0 mmol) and 1.80 g of oxalbis(2,4,6-trimethylphenylimidoyl) dichloride (**2d**). Yellow crystals (1.34 g, 61%) were obtained, m.p. 160−162 °C (from *n*-hexane). − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 1.95, 2.19, 2.29 (3 × s, 3 × 6 H, CH_3), 6.89, 6.93 (2 × s, 2 × 2 H, Ar), 7.37−7.47, 7.74, 8.27 (3 × m, 4 H, Hetar). − ^{13}C NMR (50 MHz, CD_2Cl_2): δ = 17.8, 18.5, 20.9, 21.1 (CH_3), 113.3, 119.8, 124.8, 125.2, 125.5, 125.8, 129.1, 129.6, 131.8, 133.0, 136.0, 139.5, 143.3, 146.3, 147.4, 151.3, 151.6. − IR (Nujol): $\tilde{\nu}$ = 1660, 1645 (s, $\nu_{C=N}$) cm^{-1}, 1608 (s), 1512 (s). − MS (CI, H_2O): *m*/*z* (%) = 439 (100) [M$^+$ + 1], 423, 325, 294, 93. − $C_{27}H_{26}N_4S$ (438.59): C 73.94, H 5.98, N 12.77, S 7.31; found C 73.81, H 5.99, N 12.52, S 7.32.

General Procedure for the Preparation of Diazabicyclo[2.2.1]heptanones (12a−d): A THF solution of $NaN(SiMe_3)_2$ (1.0 M, 11 mL) was added to a suspension of 2-hydroxybenzimidazole (**11**) (670 mg, 5.0 mmol) in 50 mL of THF. After stirring for 30 min, the mixture was cooled to 0 °C and a THF solution of **2** (5.0 mmol) was added. The mixture was stirred at 50 °C until the starting material **2** had been completely consumed (ca. 2 h). Sodium chloride was removed by filtration (Celite) and the filtrate solvent was removed in vacuo. The crude product was precipitated by addition of 1 mL of methanol to the residue. The crude product was recrystallized from ether.

2,3-Bis(phenylimino)-1,2,3,4-tetrahydro-1,4-methanoquinoxalin-9-one (12a): This compound was prepared from oxalbis(phenylimidoyl) dichloride (**2b**) (5.0 mmol). Compound **12a** (0.947 g, 56%) was isolated as a colourless solid, m.p. > 400 °C. − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 6.65 (d, *J* = 7.0 Hz, 4 H, Ar), 6.92 (m, 2 H, Hetar), 7.20 (m, 6 H, Ar), 7.66 (m, 2 H, Hetar). − ^{13}C NMR (50 MHz, CD_2Cl_2): δ_C = 114.7, 121.1, 125.1, 125.6, 127.3 (CH), 129.2 (quinoxaline-C to N), 140.8 (Ph-C to N), 146.4 (C=N), 151.9 (C=O). − IR (Nujol): $\tilde{\nu}$ = 1748 (s, $\nu_{C=O}$) cm^{-1}, 1648 (s, $\nu_{C=N}$), 1594 (s). − MS (CI, H_2O): *m*/*z* (%) = 339 (16) [M$^+$ + 1], 236, 207, 195, 123, 120, 104 (100). − $C_{21}H_{14}N_4O$ (338.37): C 74.54, H 4.17, N 16.56; found C 74.79, H 4.57, N 16.46.

2,3-Bis(4-tolylimino)-1,2,3,4-tetrahydro-1,4-methanoquinoxalin-9-one (12b): This compound was prepared from oxalbis(4-tolylimidoyl) dichloride (**2a**) (5.0 mmol), Compound **12b** (1.044 g, 57%) was isolated as a colourless solid, m.p. > 400 °C. − ^{1}H NMR (200 MHz, CD_2Cl_2): δ = 2.34 (s, 6 H, Tol-CH_3), 6.46, 6.99 (2 × d, 2 × 4 H, *J* = 8.1 Hz, Ar), 6.89, 7.62 (2 × m, 2 × 2 H, Hetar). − ^{13}C NMR (50 MHz, CD_2Cl_2): δ_C = 21.1 (Tol-CH_3), 114.7, 121.0, 124.9, 127.4 (CH), 129.7 (quinoxaline-C to N), 135.4 (Ph-C to C), 140.8 (Ph-C to N), 144.0 (C=N), 151.8 (C=O). − IR (Nujol): $\tilde{\nu}$ = 1751 (s, $\nu_{C=O}$) cm^{-1}, 1651 (s, $\nu_{C=N}$), 1600 (s), 1505 (m). − MS (EI): *m*/*z* (%) = 366 (6) [M$^+$], 249, 234, 220, 117 (100), 104, 90, 77, 63, 51, 39. − $C_{23}H_{18}N_4O$ (366.42): C 75.39, H 4.95, N 15.29; found C 75.48, H 5.46, N 14.96.

2,3-Bis(4-*tert*-butylphenylimino)-1,2,3,4-tetrahydro-1,4-methanoquinoxalin-9-one (12c): This compound was prepared from oxalbis(4-*tert*-butylphenylimidoyl) dichloride (**2e**) (5.0 mmol). Compound **12c** (0.946 g 42%) was isolated as a colourless solid, m.p. > 400 °C. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (m, 18 H, *t*Bu), 6.50, 7.15 (2 × d, 2 × 4 H, *J* = 8.4 Hz, Ar), 6.83, 7.59 (2 × m, 2 × 2 H, Hetar). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 31.4 [C(CH_3)$_3$], 34.3 [*C*(CH_3)$_3$], 114.3, 120.2, 124.3, 125.4, 127.0, 140.1, 143.5, 147.8, 151.3. − IR (Nujol): $\tilde{\nu}$ = 1751 (s, $\nu_{C=O}$) cm^{-1}, 1650 (s, $\nu_{C=N}$), 1602 (s), 1505 (m). − MS (CI, H_2O): *m*/*z* (%) = 451 (8) [M$^+$ + 1], 319, 292, 276, 236, 160 (100), 144. − $C_{29}H_{30}N_4O$ (450.58): C 77.30, H 6.71, N 12.43; found C 76.95, H 6.43, N 12.71.

2,3-Bis(4-methoxyphenylimino)-1,2,3,4-tetrahydro-1,4-methanoquinoxalin-9-one (12d): This compound was prepared from oxalbis(4-methoxyphenylimidoyl) dichloride (**2f**) (5.0 mmol). Compound **12d** (0.757 g, 38%) was isolated as a colourless solid, m.p. > 400 °C. − ^{1}H NMR (200 MHz, [D$_8$]THF): δ = 3.59 (s, 6 H, OCH_3), 6.55, 6.98 (2 × d, 2 × 4 H, *J* = 8.9 Hz, Ar), 6.76, 8.02 (2 × m, 2 × 2 H, Hetar). − ^{13}C NMR (50 MHz, [D$_8$]THF): δ = 55.4 (OCH_3), 109.0, 114.4, 121.9, 122.8, 123.6, 129.1, 140.3, 154.4, 159.1. − IR (Nujol): $\tilde{\nu}$ = 1752 (s, $\nu_{C=O}$) cm^{-1}, 1655 (s, $\nu_{C=N}$), 1606 (s), 1582 (m), 1504 (m). − MS (CI, H_2O): *m*/*z* (%) = 399 (17) [M$^+$ + 1], 267, 240, 150, 134 (100), 124. − $C_{23}H_{18}N_4O_3$ (398.42): C 69.34, H 4.55, N 14.06; found C 68.90, H 4.71, N 14.19.

Computational Methods: Geometries were fully optimized at the semiempirical AM1[24] level of theory, using analytical gradients as implemented in the Gaussian 98[25] program package. Harmonic vibrational frequencies were computed to ascertain the nature of all stationary points; the number of the imaginary modes is 0 for minima and 1 for the transition structures. All computed energies and geometries are available as supplementary materials from the authors upon request.

Acknowledgments

We thank Professor A. de Meijere for his support and Prof. R. Beckert for helpful discussions. Financial support came from the

Fonds der Chemischen Industrie (Liebig-scholarship and funds for P. L.) and the Deutsche Forschungsgemeinschaft.

[1] [1a] A. J. Charlson, J. S. Harrington, *Carbohydr. Res.* **1972**, *43*, 383. – [1b] H. G. Alpermann, *Arzneim.-Forsch.* **1966**, *16*, 1641. – [1c] R. Zhou, E. B. Skibo, *J. Med. Chem.* **1996**, *39*, 4321.

[2] [2a] P. Beak, J. L. Miesel, *J. Am. Chem. Soc.* **1967**, *84*, 2375. – [2b] G. P. Claxton, J. M. Grisar, N. L. Wiech, *J. Med. Chem.* **1974**, *17*, 364. – [2c] J. H. M. Hill, T. R. Fogg, H. J. Guttmann, *J. Org. Chem.* **1975**, *40*, 2562.

[3] [3a] M. D. Nair, R. Adams, *J. Am. Chem. Soc.* **1961**, *83*, 3518. – [3b] R. Huisgen, H. Rist, *Justus Liebigs Ann. Chem.* **1955**, *594*, 159.

[4] For literature related to imidazoles and benzimidazoles, see: [4a] J. R. McClure, J. H. Custer, H. D. Schwarz, D. A. Lill, *Synlett* **2000**, 710. – [4b] A. R. Katritzky, C. N. Fali, J. Li, *J. Org. Chem.* **1997**, *62*, 4148.

[5] For the extrusion of CO in the reaction between glycols and oxalyl dichloride, see: T. Iida, T. Itaya, *Tetrahedron* **1993**, *49*, 10511.

[6] For cyclization reactions of dianions, see, for example: [6a] K. G. Bilyard, P. J. Garratt, R. Hunter, E. Lete, *J. Org. Chem.* **1982**, *47*, 4731. – [6b] R. B. Bates, B. Gordon, T. K. Highsmith, J. J. White, *J. Org. Chem.* **1984**, *49*, 2981. – [6c] K. Tanaka, H. Horiuchi, H. Yoda, *J. Org. Chem.* **1989**, *54*, 63. – [6d] D. Seebach, M. Pohmakotr, *Tetrahedron* **1981**, *37*, 4047. – [6e] A. Maercker, A. Groos, *Angew. Chem.* **1996**, *108*, 216; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 210. – [6f] A. Maercker, M. Theis, *Top. Curr. Chem.* **1987**, *138*, 1. – [6g] J. Vollhardt, H.-J. Gais, L. Lukas, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 608. By "dianions" we refer to systems bearing two delocalized negative charges, the generation of which involves at least one abstraction of a proton attached to a carbon atom.

[7] For recent cyclization reactions between dianion equivalents and 1,2-dielectrophiles from our laboratory, see: [7a] P. Langer, E. Holtz, *Angew. Chem.* **2000**, *112*, 3208; *Angew. Chem. Int. Ed.* **2000**, *39*, 3086. – [7b] P. Langer, T. Eckardt, *Angew. Chem.* **2000**, *112*, 4503; *Angew. Chem. Int. Ed.* **2000**, *39*, 4343. – [7c] P. Langer, T. Krummel, *Chem. Commun.* **2000**, 967. – [7d] P. Langer, I. Freifeld, E. Holtz, *Synlett* **2000**, 501. – [7e] P. Langer, I. Freifeld, *Chem. Eur. J.* **2001**, *7*, 565. – [7f] P. Langer, T. Schneider, *Synlett* **2000**, 497. – [7g] P. Langer, J. Wuckelt, M. Döring, *J. Org. Chem.* **2000**, *65*, 729. – [7h] P. Langer, J. Wuckelt, M. Döring, H. Görls, *J. Org. Chem.* **2000**, *65*, 3603. – [7i] P. Langer, I. Karimé, *Synlett* **2000**, 743. – [7j] P. Langer, V. Köhler, *Org. Lett.* **2000**, 1597. – [7k] P. Langer, B. Kracke, *Tetrahedron Lett.* **2000**, 4545. – [7l] P. Langer, M. Döring, D. Seyferth, *Synlett* **1999**, 135. – [7m] P. Langer, M. Döring, *Chem. Commun.* **1999**, 2439. – [7n] P. Langer, *Chem. Commun.* **1999**, 1217. – [7o] P. Langer, J. Wuckelt, M. Döring, R. Beckert, *Eur. J. Org. Chem.* **1998**, 1467. – [7p] P. Langer, M. Döring, D. Seyferth, *Chem. Commun.* **1998**, 1927. – [7q] P. Langer, M. Döring, *Synlett* **1998**, 396. – [7r] P. Langer, M. Döring, *Synlett* **1998**, 399.

[8] [8a] P. Langer, M. Stoll, *Angew. Chem.* **1999**, *111*, 1919; *Angew. Chem. Int. Ed.* **1999**, *38*, 1803. – [8b] P. Langer, T. Schneider, M. Stoll, *Chem. Eur. J.* **2000**, 6, 3204. – [8c] P. Langer, T. Eckardt, *Synlett* **2000**, 844. – [8d] P. Langer, N. N. R. Saleh, *Org. Lett.* **2000**, 3333.

[9] D. Lindauer, R. Beckert, M. Döring, P. Fehling, H. Görls, *J. Prakt. Chem.* **1995**, *337*, 143.

[10] 1*H*-Pyrrolo[1,2-*a*]benzimidazol-1-ones have previously been prepared by a different approach: W. Ried, H. Knorr, *Justus Liebigs Ann. Chem.* **1976**, 284.

[11] [11a] For the preparation of a 2-hydroxy-1*H*-imidazo[1,2-*a*]imidazol-1-one, see: M. Smionar, *Chem. Heterocycl. Compd. (Engl. Transl.)* **1976**, *12*, 115. – [11b] For 1*H*-imidazo[1,2-*a*]indoles: I. T. Forbes, H. K. A. Morgan, M. Thompson, *Synth. Commun.* **1996**, *26*, 745. See also ref.[13b]

[12] S. Tsuzuki, K. Honda, T. Uchimaru, M. Mikami, K. Tanabe, *J. Am. Chem. Soc.* **2000**, 3746.

[13] For related compounds, see: [13a] R. Beckert, M. Gruner, *J. Prakt. Chem.* **1992**, *334*, 611. – [13b] A. K. El-Shafei, H. S. Kashef, A.-B. A. G. Ghattas, *Gazz. Chim. Ital.* **1981**, *111*, 409.

[14] Only a very few bicyclic systems related to **12a–d** have been reported previously: [14a] C. K. Ingold, S. D. Weaver, *J. Chem. Soc.* **1925**, *127*, 378. – For the spectroscopic data of 1,3-dihydro-1,3-dimethyl-2*H*-benzimidazol-2-one, see: [14b] H. Quast, S. Ivanova, E.-M. Peters, K. Peters, H. G. von Schnering, *Liebigs Ann.* **1996**, 1541. – [14c] For hericenes, see: P. Vogel, in *Theoretically interesting Molecules*, vol. 1 (Ed.: R. P. Thummel), JAI Press, Greenwich, CT, USA, **1989**, p. 201.

[15] M. S. Ashwood, A. W. Gibson, P. G. Houghton, G. R. Humphrey, D. C. Roberts, S. H. B. Wright, *J. Chem. Soc., Perkin Trans. 1* **1995**, 641.

[16] M. Kato, S. Nishino, K. Ito, H. Yamakuni, H. Takasugi, *Chem. Pharm. Bull.* **1995**, *43*, 1358.

[17] R. M. Snider, *Science* **1991**, *251*, 435.

[18] H. M. R. Hoffmann, J. Rabe, *Angew. Chem.* **1983**, *95*, 795; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 795.

[19] [19a] R. Gompper, H.-U. Wagner, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1437. – [19b] F. Effenberger, H. Schlosser, P. Bäuerle, S. Maier, H. Port, H. C. Wolf, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 281. – [19c] J. Fabian, H. Nakazumi, M. Matsuoka, *Chem. Rev.* **1992**, *92*, 1197. – [19d] Z. Riedl, G. Hajós, A. Messmer, A. Rockenbauer, L. Korecz, G. Kollenz, W. M. F. Fabian, K. Peters, E.-M. Peters, *Chem. Commun.* **1997**, 757.

[20] Further details of the crystal structure investigations are available on requests from the Cambridge Crystallographic Data Centre CCDC (12 Union Road, Cambridge CB2 1EZ, UK), on quoting the depository numbers CSD-132364 (**6c**), -132365 (**7a**), -132366 (**8b**), the names of the authors, and the journal citation.

[21] *MOLEN, An Interactive Structure Solution Procedure*, Enraf–Nonius, Delft, The Netherlands, **1990**.

[22] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467.

[23] G. M. Sheldrick, University of Göttingen, Germany, **1993**.

[24] J. J. P. Stewart, "AM1", in *The Encyclopedia of Computational Chemistry* (Eds.: P. v. R. Schleyer, N. L. Allinger, T. Clark, J. Gasteiger, P. Kollman, H. F. Schaefer III, P. R. Schreiner), John Wiley & Sons, Chichester, **1998**, pp. 2574.

[25] J. A. Pople et al., *Gaussian 98, Revision A.5*, Gaussian, Inc., Pittsburgh PA, **1998**.

Received July 25, 2000
[O00383]