The Synthesis of Carboxy- and Cyano-substituted 4*H*-Imidazoles: Redoxactive Ligands as Starting Materials for Metal-Metal Multiply Bonded Compounds and Heterobimetallic Complexes

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Dedicated to Professor Gerhard Maas on the occasion of his 60th birthday

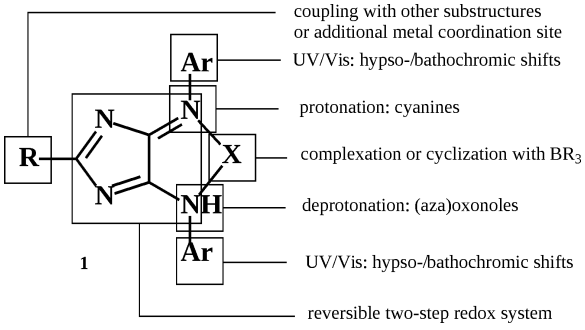
Cyanobenzoic acids proved to be suitable starting materials for the transformation into multifunctional products of the 4*H*-imidazole type. Employing two different pathways, the new derivatives **1b**–**d** which possess carboxy/cyano groups were synthesized. In addition, derivative **1d** formed the basis for the construction of novel *bis*-4*H*-imidazoles with two different complexation spheres. The structures of all new derivatives were confirmed by NMR spectroscopy, mass spectrometry, elemental analysis, UV/Vis-/fluorescence spectroscopy, and electrochemical measurements.

Key words: 4*H*-Imidazoles, Nitriles, Benzoic Acids, Ligands, Functional Dyes

Introduction

In the last decade, 4*H*-imidazoles **1** were developed in our group as a new class of functional dyes: depending on the nature of their substituents, they show absorptions in a wide range of the visible spectrum [1], are pH-switchable [2] reversible two-electron redox systems [3] and efficient chelating ligands for metals [4] (Scheme 1).

A further goal was to synthesize 4-carboxyphenyl-substituted 4*H*-imidazoles and in addition cyanoaryl-substituted derivatives (R = C_6H_4COOH, C_6H_4CN) with coordinating centers for the synthesis of special metal-containing chromophores. We are presently focussing on the synthesis of so called "paddlewheel" complexes by coordinating multiply bonded Mo_2, W_2 or Ru_2 entities to the carboxylate functions in 4-position of the 4*H*-imidazoles. Related Mo_2 tetracarboxylates have been shown to exhibit photochemical properties that are comparable to those of the well known $[Ru(bipy)_3]^{2+}$ complexes when the carboxylate functions are connected to electron-poor aromatic systems [5]. The intensity and range of the absorptions obtained make them interesting candidates for applications in the harvesting of photons. In addition, the

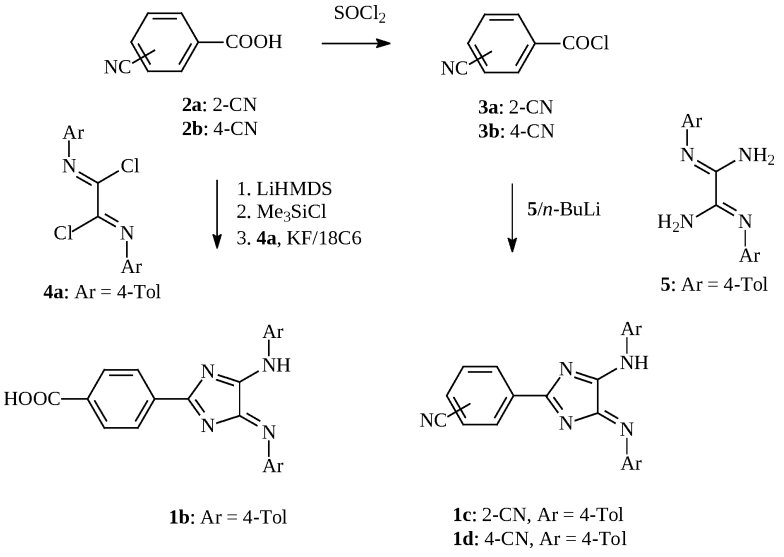


Scheme 1. 4*H*-Imidazoles as multi-functional molecules.

easy conversion of cyano groups into amidines opens the synthetic entry to *bis*-4*H*-imidazoles which possess two different arylic peripheries.

Results and Discussion

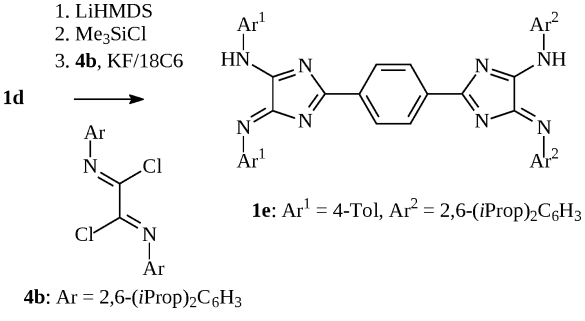
4*H*-Imidazoles **1** with a high variability of aryl substituents in 2-position were synthesized in the past [6], however the introduction of carboxy and cyano groups failed because of the difficult synthetic entry and low stability of the starting materials. Based on extended research activities in respect to synthetic pathways for 4*H*-imidazoles [1, 6], the easily accessible cyanobenz-



Scheme 2. Conversion of cyanobenzoic acids into 4*H*-imidazoles.

oic acids of type **2** were tested as building blocks for 4*H*-imidazoles. They are of interest for two reasons: the easy conversion of the cyano groups into amidine functions should allow a subsequent cycloacylation with *bis*-imidoyl chlorides of oxalic acid **4** to give finally carboxy-substituted 4*H*-imidazoles. On the other hand, the appropriate cyanobenzoylchlorides proved to be suitable reaction partners for oxalamidines **5** which can then be cyclized to 4*H*-imidazoles bearing a cyanoaryl substructure in 2/4-position. Thus, in a two-step one-pot reaction, 4-cyanobenzoic acid **2b** was first converted into the corresponding persilylated amidine using an excess of LiHMDS followed by quenching by chlorotrimethylsilane. As final step, the cyclization with *bis*-tolylimidoyl chloride **4a** yielded the 4-carboxy-substituted 4*H*-imidazole **1b**. Despite a broad variation of reaction conditions, all attempts to obtain the corresponding *ortho*-carboxyphenyl-substituted derivative were unsuccessful. In the meantime however, we developed another synthetic entry using the cyclization reaction of disubstituted oxalamidines with phthalic acid anhydride [2]. Nevertheless, the cyano derivatives **1c** and **1d** were synthesized by cyclization of cyanobenzoic acid chlorides **3a**, **b** with the oxalamidine **5** in the presence of *n*-BuLi in a smooth reaction (Scheme 2).

The newly synthesized 4*H*-imidazoles **1b–d** are soluble in polar aprotic solvents and have essentially the same properties as the phenyl-substituted derivatives [1]. Their longest wavelength absorption in the UV/Vis spectra is approximately 530 nm, with $\log(\varepsilon)$



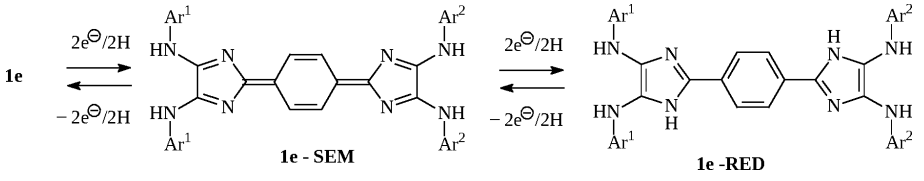
Scheme 3. Synthesis of the unsymmetrical 4*H*-imidazole **1e**.

values higher than 4.0; the infrared spectra show characteristic bands at 2237 cm^{-1} for the cyano-groups in **1c**, **d**. As demonstrated before, 4*H*-imidazoles **1b–d** behave as electrophores which can easily be switched between oxidized and reduced forms [3]. In the first step, the corresponding radical anion is generated. By a subsequent electron transfer step the dianion of the respective leuco-form is then produced. Both consecutive single-electron transfer processes could be recorded by electrochemical measurements. Employing difference pulse polarographic measurements, two peaks can clearly be ascribed to two different single-electron transfer steps. The quasi-reversibility of the reduction was confirmed by cyclovoltammetric measurements ($\Delta E_{RED,OX}{}^{1,2} > 0.059$ V). The redox potentials of 4*H*-imidazoles **1b–d** are listed in Table 1. Chemically induced reduction could be achieved by treating a solution of the 4*H*-imidazoles with sodium dithionite in THF. The color of the reaction mixture

Compound	E^1_{Red}	E^2_{Red}	λ_{max} (log ε)[a]	λ_{max} (log ε)[b]	λ_{max} (log ε)[c]	$\lambda_{max,em.}$ ($\lambda_{exc.}$)[c]
1b	−0.87	−0.99	532 (4.1)	638 (4.1)	398 (4.0)	570 (402)
1c	−0.81	−1.25	528 (4.0)	649 (4.0)	410 (4.0)	566 (408)
1d	−0.92	−1.05	532 (4.0)	651 (4.0)	406 (4.0)	558 (409)

Table 1. Redox potentials (in V), and UV/Vis- and fluorescence data (λ in nm) for the cyano derivatives **1b**–**1c**.

[a] In THF; [b] protonated form; [c] reduced form.



Scheme 4. Redox behavior of *bis*-4*H*-imidazole **1e**.

changed from red to light-yellow, indicating the formation of 1*H*-imidazoles. These nearly colorless, but fluorescent products (see Table 1) are immediately reoxidized when exposed to air.

A further interesting feature of 4*H*-imidazoles **1b–d** is the protonation-deprotonation reaction with acids or bases. While the neutral species is based on a merocyanine system, the formation of the protonated or deprotonated 4*H*-imidazole causes an alteration of their chromophoric systems and consequently of their long wavelength absorption in the UV/Vis spectra [1d]. Compared to the neutral species, both the protonated (cyanine, Table 1) and the deprotonated 4*H*-imidazole (azaoxonole) display a bathochromic shift in their UV/Vis spectra.

The cyano-/carboxy-phenyl-substituted 4*H*-imidazoles are not only novel examples in the series of these switchable heterocycles, but also offer a way to synthesize unsymmetrical *bis*-4*H*-imidazoles. The latter have attracted considerable interest due to the fact that Pd and Ru complexes of 4*H*-imidazoles display intense long-wavelength absorptions in their UV/Vis spectra, and in addition, are electrochemically switchable [4]. Therefore, the synthesis of unsymmetrical *bis*-4*H*-imidazoles could be the decisive step in the synthesis of heterobimetallic complexes. Different peripheric groups permit a differentiation of the ligand sphere and consequently a selective complexation.

In order to build up a second 4*H*-imidazole substructure in the same molecule, both functional groups in **1b–d** may serve as electrophilic (carboxylic acid chloride from **1b**) or nucleophilic (amidines from **1c**, **d**) building blocks as described above. Unfortunately, all attempts to convert the 4*H*-imidazoles **1b** into the acid chlorides failed, and only decomposition took place. Starting from derivative **1d** *via* its silylated amidine and subsequent cycloacylation with *bis*-imidoyl chloride **4b**, however, turned out to a be successful pathway to obtain the first unsymmetrical *bis*-4*H*-imidazole **1e** (Scheme 3). The new bifunctional derivative **1e** was isolated as dark red microcrystals and was fully characterized by elemental analysis, MS and NMR spectroscopy. It showed the same reduction behavior as other *bis*-4*H*-imidazoles [1c, e], exemplified by the formation of a deep blue quinomethide-like SEM-form **1e-SEM** (λ_{max} = 635 nm; log ε = 4.3). The latter can be reduced to finally yield the yellowish *bis*-1*H*-imidazole (**1e-RED**) which immediately was reoxidized to **1e** upon contact with air (Scheme 4).

Conclusions

Cyanobenzoic acids proved to be useful building blocks for 4*H*-imidazoles **1c–d** possessing carboxyaryl/cyanoaryl substructures. Furthermore, the first unsymmetrical *bis*-4*H*-imidazole **1e** was obtained, starting from the *para*-cyanophenyl-substituted 4*H*-imidazole **1d**. This transformation allows the build-up of two different chelation spheres and thus could be the decisive step for the synthesis of heterobimetallic complexes.

Experimental Section

The reagents described in the following section were purchased from commercial sources and were used directly unless stated otherwise in the text. All solvents were of reagent grade and were dried according to common practice and distilled prior to use. Reactions were monitored by TLC using aluminium plates coated with Al_2O_3 or SiO_2 from Fluka. Melting points were measured with a digital detector system KSPS 1000 from Krüss and with a B-545 (Boetius system) from Büchi and are uncorrected. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 250 (250 MHz) or a Bruker DRC-400 (400 MHz) spectrometer; shifts are relative to the signals of the solvent. Mass spectra were measured on a spectrometer Trio 2000 from Fisons. UV/Vis spectra were recorded on a Perkin-Elmer Lambda 19 spec-

trophotometer. The fluorescence spectra were recorded with a JASCO P-6500 instrument. Elemental analyses were carried out with an automatic analyzer Varion EL III from Elementar Analysensysteme GmbH. Electrochemical measurements were carried out with a Metrohm 663VA Stand using mercury or platinum electrodes and tetrabutylammonium hexafluoro-phosphate as conductive salt.

The *N*,*N*'-*bis*-aryloxaldiimidoyl chloride **4b** [7] and the oxalamidine **5** [6] were synthesized according to literature. The cyano-substituted benzoyl chlorides **3a**, **b** were synthesized by heating of the appropriate cyanobenzoic acid with an excess of thionyl chloride and a catalytic amount of DMF under reflux for 3 h.

*4-{5-p-Tolylamino-4-[p-tolylimino]-4H-imidazol-2-yl}-benzoic acid (**1b**)*

To a suspension of 1 mmol (147 mg) of 4-cyanobenzoic acid **2b** in 20 mL of THF in a Schlenk tube, 2 mmol of Li-hexamethyldisilazide (1 M solution in THF) was added dropwise. The reaction mixture was then stirred for 1 d at r. t. The solution was evaporated to dryness, and the residue was suspended in toluene. 2 mmol (0.26 mL) of chlorotrimethylsilane was added, and the reaction mixture was heated under reflux for 12 h. The mixture was again evaporated to dryness, and the remaining residue was reacted with 1 mmol (305 mg) of *bis*-imidoylchloride **4a** in the presence of 4 mmol (232 mg) of KF and a catalytic amount of 18-crown-6 ether in THF. For the completion of the reaction the mixture was stirred for 24 h at r. t. Recrystallization from acetonitrile gave **1b** as dark red microcrystals (80 mg, 20 % yield), m. p. > 200 °C (decomp.). – ^{1}H NMR (250 MHz, [D$_8$]THF): δ = 2.37 (s, 6H), 7.25 (d, ^3J = 8.5 Hz, 4H), 7.78 (d, ^3J = 8.5 Hz, 2H), 7.99 (d, ^3J = 8.5 Hz, 4H), 8.56 (d, ^3J = 8.5 Hz, 2H). – ^{13}C NMR (62 MHz, [D$_8$]THF): δ = 18.4, 122.0, 125.5, 126.2, 127.3, 127.9, 130.0, 131.5, 132.9, 134.2, 163.0, 164.9, 176.2. – MS (DEI): *m/z* = 397 [M+1]$^+$, 396 [M]$^+$, 394, 234, 146, 130, 106. – IR (ATR): ν = 1726, 3303 cm^{-1}. – UV/Vis (THF): λ_{max} (log ε) = 281 nm (4.4), 337 (4.3), 397 (4.2), 410 (4.1), 496 (4.2), 523 (4.1). – $C_{24}H_{20}N_4O_2$ (396.4): calcd. C 72.71, H 5.08, N 14.13; found C 72.60, H 5.15, N 14.29.

*General procedure for the synthesis of cyano-substituted 4H-imidazoles **1c**, **d***

In a Schlenk tube equipped with a magnetic stirrer, 1 mmol (182 mg) of the corresponding cyanobenzoic acid chloride **3a**, **b** was added to a THF solution containing the deprotonated oxalamidine, produced by deprotonation of 1 mmol (266 mg) of **5** with 0.8 mL of *n*-BuLi (2.5 M solution in *n*-hexane). For the completion of the reaction the mixture was stirred for 20 h at r. t. The reaction mixture was evaporated to dryness, and the red residue was purified by column chromatography (SiO_2, toluene/acetone = 10/1). Recrystallization from acetonitrile gave pure products **1c** and **1d**.

*2-(2-Cyanophenyl)-5-p-tolylamino-4-p-tolylimino-4H-imidazole (**1c**)*

The compound was obtained as a dark red solid (106 mg, 28 % yield), m. p. > 130 °C (decomp.). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 6H), 6.89 (d, ^3J = 8.2 Hz, 1H), 7.25 (d, ^3J = 8.3 Hz, 4H), 7.38 (d, ^3J = 8.2 Hz, 1H), 7.70 – 7.80 (m, 2H), 7.97 (d, ^3J = 8.3 Hz, 4H). – ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.3, 112.9, 118.7, 121.5, 127.9, 131.9, 132.5, 135.3, 135.5, 136.5, 146.8, 162.7, 168.6, 176.5. – MS (DEI): *m/z* = 377 [M]$^+$, 376 [M–1]$^+$, 274, 265, 248, 147, 130, 106, 91. – IR (ATR): ν = 2237, 3309 cm^{-1}. – UV/Vis (THF): λ_{max} (log ε) = 285 nm (4.3), 412 (3.8), 500 (4.2), 528 (4.0). – $C_{24}H_{19}N_5$ (377.4): calcd. C 76.37, H 5.07, N 18.55; found C 76.50, H 5.18, N 18.38.

*2-(4-Cyanophenyl)-5-p-tolylamino-4-p-tolylimino-4H-imidazole (**1d**)*

The compound was obtained as a dark red solid (196 mg, 52 % yield), m. p. 252 – 254 °C. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.33 (s, 6H), 7.20 (d, ^3J = 8.3 Hz, 4H), 7.71 (d, ^3J = 8.3 Hz, 2H), 7.81 (d, ^3J = 8.3 Hz, 4H), 8.53 (d, ^3J = 8.3 Hz, 2H). – ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.7, 116.4, 118.9, 124.3, 130.3, 130.9, 132.5, 136.6, 137.8, 139.6, 163.6, 180.0. – MS (DEI): *m/z* = 377 [M]$^+$, 362, 268, 248, 234, 132, 117, 107, 91. – IR (ATR): ν = 2237, 3304 cm^{-1}. – UV/Vis ($CHCl_3$): λ_{max} (log ε) = 287 nm (4.3), 390 (3.9), 415 (3.9), 504 (4.1), 530 (4.0). – $C_{24}H_{19}N_5$ (377.4): calcd. C 76.37, H 5.07, N 18.55, found C 76.39, H 5.11, N 18.40.

*Bis-4H-imidazole **1e***

In a Schlenk tube equipped with a magnetic stirrer, to a solution of 0.5 mmol (189 mg) of 4*H*-imidazole **1d** in 15 mL of dry THF was added dropwise 1 mmol of Li-hexamethyldisilazide (1 M solution in THF). The reaction mixture was then stirred for 2 d at r. t. The solution was evaporated to dryness, and the residue was suspended in toluene. 1 mmol (0.13 mL) of chlorotrimethylsilane was added, and the reaction mixture was heated under reflux for 12 h. The mixture was again evaporated to dryness, and the residue was reacted with 0.5 mmol (223 mg) of *bis*-imidoylchloride **4b** in the presence of 2 mmol (116 mg) of KF and a catalytic amount of 18-crown-6 ether in 15 mL of THF by heating under reflux for 5 h. The dark red product was purified by column chromatography (SiO_2, toluene/acetone = 100/1). The *bis*-4*H*-imidazole **1e** was obtained as a red solid (66 mg, 17 %, yield), m. p. > 240 °C (decomp.). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28 (d, ^3J = 7.0 Hz, 24H), 2.38

(s, 6H), 2.84 (m, 4H) 6.92 (d, ^3J = 7.5 Hz, 2H), 7.2 – 7.4 (m, 4H), 7.58 (d, ^3J = 8.0 Hz, 4H), 7.82 (d, ^3J = 8.3 Hz, 4H), 8.65 (d, ^3J = 8.0 Hz, 4H), 9.34 (s, br, 2H). – ^{13}C NMR (62 MHz, $CDCl_3$): δ = 21.3, 22.9, 28.9, 116.0, 119.8, 123.3, 125.8, 129.7, 129.9, 130.2, 130.5, 135.3, 135.8, 142.2, 157.5, 163.2. – MS (DEI): m/z = 766 $[M]^+$, 664, 376, 362, 268, 186, 133, 116, 106, 91. – UV/Vis (THF): λ_{max} ($\log \varepsilon$) = 418 nm (3.7), 474 (3.9), 503 (4.1), 535 (4.0). – $C_{50}H_{54}N_8$ (767.0): calcd. C 78.30, H 7.10, N 14.61; found C 78.39, H 7.21, N 14.80.

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[1] a) J. Atzrodt, J. Brandenburg, C. Käpplinger, R. Beckert, W. Günther, H. Görls, J. Fabian, *J. Prakt. Chem./Chemiker-Ztg*. **1997**, *339*, 729 – 734; b) J. Fabian, H. Görls, R. Beckert, J. Atzrodt, *J. Prakt. Chem./Chemiker-Ztg*. **1997**, *339*, 735 – 741; c) R. Beckert, C. Hippius, T. Gebauer, F. Stöckner, C. Lüdigk, D. Weiß, D. Raabe, W. Günther, H. Görls, *Z. Naturforsch.* **2006**, *61b*, 437 – 447; d) M. Matschke, R. Beckert, *Molecules* **2007**, *12*, 723 – 734; e) M. Matschke, J. Blumhoff, R. Beckert, *Tetrahedron* **2008**, 7815 – 7821.

[2] M. Matschke, R. Beckert, L. Kubicova, C. Biskup, *Synthesis* **2008**, 2957 – 2962.

[3] a) M. Matschke, C. Käpplinger, R. Beckert, *Tetrahedron* **2006**, *62*, 8586 – 8590; b) T. Gebauer, R. Beckert, D. Weiß, K. Knop, C. Käpplinger, H. Görls, *Chem. Commun*. **2004**, 1860 – 1861.

[4] a) J. Blumhoff, R. Beckert, D. Walther, S. Rau, M. Rudolph, H. Görls, W. Plass, *Eur. J. Inorg. Chem*. **2007**, 481 – 486; b) J. Blumhoff, R. Beckert, S. Rau, S. Losse, M. Matschke, W. Günther, H. Görls, *Eur. J. Inorg. Chem*. **2009**, 2161 – 2169.

[5] a) M. J. Byrnes, M. H. Chisholm, J. A. Gallucci, Y. Liu, R. Ramnauth, C. Turro, *J. Am. Chem. Soc*. **2005**, *127*, 17343 – 17352; b) G. T. Burdzinski, R. Ramnauth, M. H. Chisholm, T. L. Gustafson, *J. Am. Chem. Soc*. **2006**, *128*, 6776 – 6777.

[6] D. Müller, R. Beckert, H. Görls, *Synthesis* **2001**, 601 – 606.

[7] D. Lindauer, R. Beckert, H. Görls, P. Fehling, M. Döring, *J. prakt. Chem./Chemiker-Ztg*. **1995**, *337*, 143 – 152.