Synthesis of Novel Functionalized Bi- and Oligopyridines

Dirk Sielemann,[a] Ralf Keuper,[a] and Nikolaus Risch*[a]

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An annelation reaction is presented in which 1,3-cyclohexanedione (**1**) and Mannich bases **6a**,**b** are used for the preparation of functionalized bipyridines **12a**, **13a**, **14a** and dihydropyridine derivatives **10b**, **11b**. All these products possess a keto group which will allow further transformations. The same concept was applied for the synthesis of the S-shaped terpyridine **25**. The reaction of the Mannich base **21** with 1,3-cyclohexanedione yielded the heptacyclic terpyridine **22**, which is a key intermediate for the synthesis of torands and other tridentate clefts. The ketone **12a** was used for the synthesis of the quaterpyridine **26**.

Introduction

The design of oligopyridines and related compounds has recently been the subject of intensive investigation. Ligands bearing 2,2'-bipyridine, 2,2':6',2''-terpyridine, or 1,10-phenanthroline subunits are extremely versatile building blocks for the construction of metallo-supramolecular systems.[1,2] Interest has especially centered around ruthenium polypyridine complexes which can be used for the synthesis of luminescent and redox-active polynuclear complexes where energy- and/or electron-transfer processes can be induced by light.[3−6] Most systems described in the literature are based on ditopic ligands linked by polyene[7] or polyalkyne[8−10] chains. A variety of potential applications such as artificial photosynthesis,[11] photocatalysis,[12] molecular photovoltaic cells,[13] molecular informatics[14] and optoelectronic devices[15,16] are beginning to emerge from this new field of research. Moreover, fused polypyridine compounds constitute an effective route to preorganised clefts and cavities for the complexation of metals[17−19] and organic guests.[20,21] Several toroidal macrocycles with potentially useful metal-binding properties[22] and also polypyridine ligands which wrap around guest ions to form helical complexes have been designed previously.[23] The discovery of the anticancer drug *cis*-[$Pt(NH_3)_2Cl_2$] has fostered new interest in the field of metallodrugs. Studies on polypyridyl compounds of ruthenium, osmium, cobalt, nickel, rhodium, and platinum indicate that these complexes bind to DNA, often in an intercalative fashion.[24]

Most approaches to oligopyridines involve either coupling reactions of pyridine subunits,[25,26] condensation reactions[27,28] or pyrolysis.[29] Relatively little work has been done with substituted oligopyridine derivatives, due to synthetic limitations in their preparation. Our studies in the field of ternary iminium salts have led to the development of one-pot reactions yielding a wide range of functionalized pyridines, bipyridines, and terpyridines.[30−32] Such domino reactions offer many advantages over traditional syntheses; namely, minimization of waste, and less consumption of solvents, reagents, adsorbents, and energy.

Results and Discussion

In a recent paper we reported on a simple annelation reaction in which a pyridine nucleus can be fused to different cyclic ketones.[32] Herein we wish to elaborate on this new method. The utilization of diketones rather than simple carbonyl compounds results in keto-functionalized pyridines which again can serve as starting materials. Therefore, stepwise syntheses of polypyridines should be possible. In our first studies we were able to prepare the bipyridines **12a**, **13a,** and **14a** in reasonable to good yields by reacting ketones **3**, **4**, and **5** with the Mannich base **6a** in the presence of NH_4OAc (Scheme 1). All products are formed by a Michael addition mechanism. In the case of ketone **5**, the condensation resulted in a mixture of **13a** and dihydropyridine **8a**. Stirring that mixture for 8 days in CH_2Cl_2 under an oxygen atmosphere led to a complete conversion of **8a** into **13a**. Dihydropyridine intermediates have been isolated previously, but normally they are oxidized to the corresponding pyridine quite rapidly.[30] To our surprise, the Mannich reaction of **3** and **5** with **6b** in the presence of NH_4OAc yielded the stable dihydropyridines **10b** and **11b**, which could not be converted into the corresponding pyridines by simple oxidation with oxygen (Scheme 1). The stability of dihydropyridines with aryl substituents at C-4, in combination with electron-withdrawing groups at C-3 and C-5 is long known.[33,34] A great deal of attention has been focused on this class of compounds, because they play an important role as calcium antagonists.[35]

These results encouraged us to extend our methodology. Unfortunately, the reaction of **2c–e** with 1,3-cyclohexanedione did not succeed, presumably due to the equilibrium described in Scheme 2. In the course of these experiments, precipitates formed. The pathways presented in Scheme 2 account for the formation of these insoluble products. NMR studies showed that they mainly consist of the amine hydrochlorides **15c–e** and intermediates **17c–e**, **18c–e,** and

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[a] Fachbereich Chemie und Chemietechnik der Universität-GH Paderborn,
Warburger Strasse 100, D-33100 Paderborn, Germany
Fax: (internat.) +49-(0)5251/603245
E-mail: nr@chemie.uni-paderborn.de

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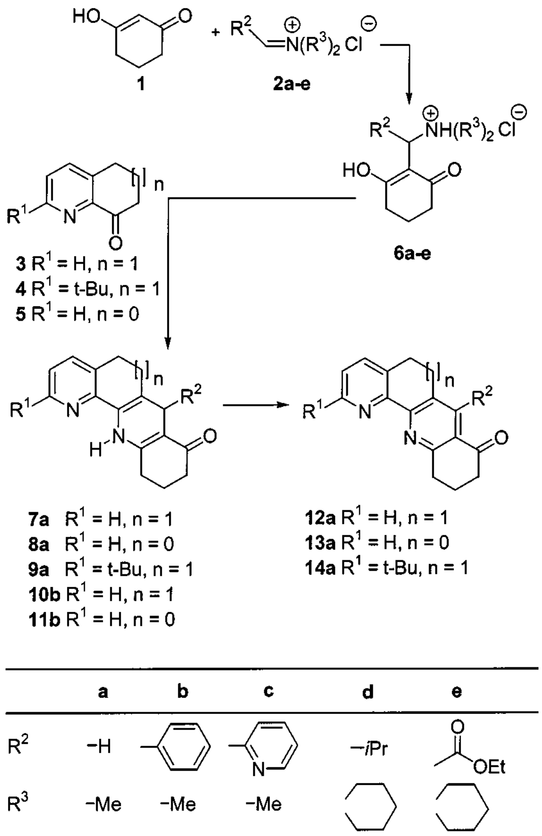
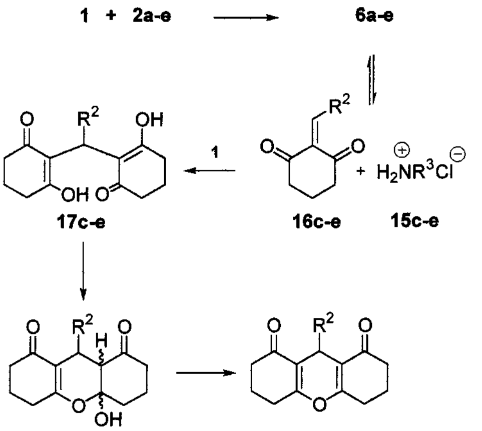


Scheme 1. Synthesis of functionalized bipyridines and dihydropyridines

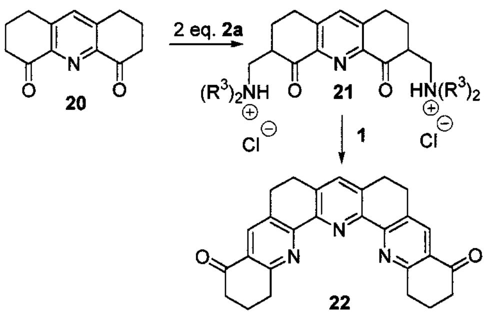


Scheme 2. Formation of xanthenes (substituents R^2 are listed in Scheme 1)

19c–e. We assumed that an α,β-unsaturated ketone **16c–e** is formed by amine elimination and reacts with 1,3-cyclohexanedione which is present in the reaction mixture, to yield **17c–e**. Elimination of water via **18c–e** should lead to the xanthenes **19c–e**.

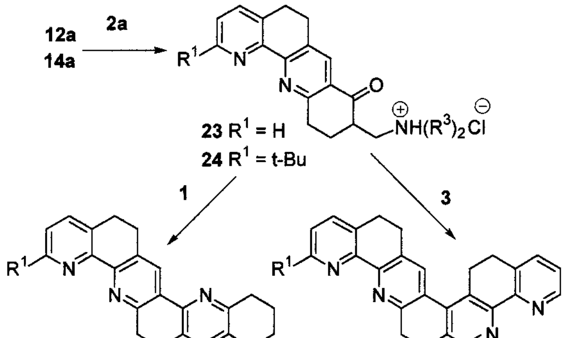
Similar observations were made by us[32] and Möhrle et al.,[36] previously. General methods for the synthesis of xanthenes are mentioned in the literature.[37] We prepared the unknown compounds **19c–e** by an alternative method, by heating a solution of two equiv. of **1** and one equiv. of iminium salt in the presence of NaOAc. The reaction of the iminium salt **2c** with **1** afforded the expected xanthene **19c**. In the case of **2d**, the reactions stopped after the Michael addition step and yielded **17d**. When the in situ generated iminium salt **2e** was reacted with **1**, the Michael addition product **17e** and the xanthene **19e** were isolated.

Pursuing our studies on this novel annelation reaction, we developed a second simple procedure. Instead of using **6a-b** as Mannich base components, we employed **21**, **23,** and **24** which are obtained easily by the reaction of **20**, **12a,** and **14a** with the iminium salt **2a**. All these salts are insoluble in most solvents and attempts to dissolve the Mannich bases lead to decomposition. Therefore **21**, **23,** and **24** were used directly, without characterization, in the next step. The two-fold condensation of **21** with 1,3-cyclohexanedione in the presence of NH_4OAc by the Michael addition pathway[30] produced the functionalized terpyridine **22** in a yield of 46%.



Scheme 3. Synthesis of heptacyclic terpyridine **22**

Considering the number of reaction steps involved in this transformation, the yield is quite high. Heptacyclic terpyridyl hosts such as **22** exhibit potent complexation abilities[19] which can be attributed to enforced orientation of relatively large ligand functional group dipoles towards the center of the molecular cleft. Reduction of **22** and subsequent introduction of two oxo groups at the α-positions with help of known procedures[38] should afford a compound that is



Scheme 4. Synthesis of terpyridine **25** and quaterpyridine **26**

an important precursor for the preparation of dodecahydrohexaazakekulene. The simplicity of our method makes it an alternative to known synthetic routes.[19]

The reaction of **24** with **1** was also accomplished, to afford **25**. All pyridine nuclei in hexacyclic **25** were synthesized in a similar fashion. One could describe **25** as a molecule of the third generation, since our concept was applied in every step of the synthesis. We also previously developed a different synthetic pathway to functionalized S-shaped terpyridines.[30]

It should be possible to construct oligopyridines by successive utilization of the reaction sequence presented in this paper, thereby providing a step towards creating molecular coils. Note that the oxo group determines the position of the pyridine nucleus to be introduced. Compounds with an oxo group in the α-position, for example, **3, 4, 5,** and **20** produce 3,3'-bridged 2,2'-bipyridines subunits, while δ-oxo compounds, for example, **24** give 3,2'-bridged 2,3'-bipyridines subunits. Since the position of the oxo group can be varied, we should be able to create oligopyridines with different fixed conformations, selectively.

Further experiments were conducted in which **3** was used as ketone component and **23** as Mannich base. Our goal was to prepare a quaterpyridine with two coordination sites. Upon condensation by an aldol-type mechanism, **26** was formed. An alternative mechanism via an α,β-amino enone was discussed by Bell[19] for a similar condensation reaction. The structure of **26** was elucidated by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. This structure can be distinguished from the possible Michael addition product by the number of protons adjacent to the nitrogen atoms.[39] Unsymmetrically fused quaterpyridines are quite unusual. Most systems described in the literature are symmetrical large cavities. In some cases binuclear complexes could be prepared, although congestion within the molecular cavity is large.[40] Other approaches towards ditopic ligands are based on Pd-catalyzed cross-coupling reactions involving bipyridines or terpyridines.[8,9,41,42]

Experimental Section

General: All reactions were conducted under argon unless otherwise indicated. Anhydrous solvents were distilled as follows: $CHCl_3$, CH_3CN were distilled from P_4O_{10}; EtOH was distilled from sodium . – Melting points are uncorrected. – ^{1}H and ^{13}C NMR: Bruker ARX-200 (200/50 MHz), chemical shifts are reported relative to Me_4Si; coupling constants are reported in Hz. – IR: FT-IR Nicolet 510 P, frequencies are reported in cm^{-1}. – EI MS: Finnigan MAT 8200, mass spectra were recorded at 70 eV; FAB MS (*m*-nitrobenzyl alcohol matrix): Finnigan MAT 8200 and VG Autospec. – Elemental analyses: Perkin–Elmer 2400. – Ketones **3,4,5** were prepared by known literature procedures.[43,44]

[(2-Hydroxy-6-oxocyclohex-1-enyl)methyl]dimethylammonium Chloride (6a): A solution of 1,3-cyclohexanedione (3.0 g, 26.8 mmol) in abs. $CHCl_3$ (60 mL) is cooled to –40 °C and iminium salt **2a** (2.4 g, 26.8 mmol) is added. The resulting mixture is stirred at this temperature under an argon atmosphere for 3 h during which Mannich base **6a** precipitates. The suspension is stored in a refrigerator (–10 °C) for ca. 12 h. The precipitate is collected by vacuum filtration and dried in vacuo. Yield: 4.12 g (76%), m.p. 134 °C. – IR (KBr): $\tilde{\nu}$ = 2944, 2892, 2862, 1624, 1482, 1414, 1399, 1357, 1335, 1296, 1159, 1148, 1053, 1013, 933, 729. – ^{1}H NMR (200 MHz, $CDCl_3$/MeOD, 5:1): δ = 1.92 (m_c, 2 H), 2.49 (t, ^{3}J = 6.32 Hz, 4 H), 2.69 (s, 6 H), 3.85 (s, 2 H). – $C_9H_{16}ClNO_2$ (205.7): calcd. C 52.56, H 7.84, N 6.81; found C 52.70, H 7.71, N 7.00.

[(2-Hydroxy-6-oxocyclohex-1-enyl)phenylmethyl]dimethylammonium Chloride (6b): A solution of 1,3-cyclohexanedione (0.5 g, 4.46 mmol) in abs. $CHCl_3$ (5 mL) is cooled to –10 °C, and iminium salt **2b** (0.75 g, 4.46 mmol) is added. The resulting mixture is stirred at this temperature under an argon atmosphere for 1 h and is then allowed to warm to room temperature. The suspension is stored in a refrigerator (–10 °C) for 12 h. The precipitate is collected by vacuum filtration and is dried in vacuo. Yield: 1.12 g (89%), m.p. 160 °C. – IR (KBr): $\tilde{\nu}$ = 3147, 2980, 2480, 1605, 1585, 1388, 1299, 1166, 1155, 1000, 700. – ^{1}H NMR (200 MHz, MeOD): δ = 2.00 (m_c, 2 H), 2.55 (t, ^{3}J = 6.4 Hz, 4 H), 2.71 (s, 3 H), 2.95 (s, 3 H), 5.36 (s, 1 H), 7.44 (m_c, 3 H), 7.60 (m_c, 2 H). – ^{13}C NMR (50 MHz, MeOD): δ = 20.4 (t), 32.8 (t), 42.0 (q), 42.8 (q), 68.2 (d), 110.5 (s), 128.3 (d), 129. 3 (2d), 136.1 (s). – $C_{15}H_{20}ClNO_2$ (281.7): calcd. C 63.94, H 7.14, N 4.97; found C 63.82, H 7.31, N 4.73.

General Procedure for the Preparation of Pyridine Derivatives: A suspension of 5 mmol of the appropriate carbonyl compound, 5 mmol of the β-amino ketone hydrochloride and 15 mmol of ammonium acetate (anhydrous) in 25–30 mL of abs. ethanol was refluxed for 3–4 h under argon. After the solution was cooled to room temperature, the ethanol was removed in vacuo. The crude product was dissolved in a mixture of 35–40 mL CH_2Cl_2, 15–20 mL of H_2O and 5 mL of 25% ammonia solution. The organic layer was separated and the residual aqueous layer was extracted, three times, with 15 mL of CH_2Cl_2. The combined organic layers were washed with H_2O and were dried with Na_2SO_4. After removal of the solvent, the residue was purified by chromatography. The initial quantities and possible variations are mentioned in the experimental part of the compound concerned.

7-Phenyl-5,6,7,10,11,12-hexahydro-9*H*-benzo[*b*][1,10]phenanthrolin-8-one (10b): 10b was synthesized from **3** (0.32 g, 2.1 mmol), β-amino ketone hydrochloride **6b** (0.52 g, 2.1 mmol), and NH_4OAc (0.47 g, 6.0 mmol). Yield: 456 mg (66%) after chromatography on Al_2O_3, CH_2Cl_2, m.p. 163–165 ° C. – IR (KBr): $\tilde{\nu}$ = 3317, 29945, 2872, 1615, 1615, 1585, 1496, 1434, 1382, 1264, 1135, 1031, 798, 695. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.12–1.94 (m, 2 H), 2.41–2.26 (m, 4 H), 2.69–2.52 (m, 2 H), 2.98–2.74 (m, 2 H), 4.69 (s, 1 H), 7.31–7.68 (m, 5 H), 7.43 (m_c, 2 H), 7.58 (s, 1 H, NH), 8.36 (dd, ^{3}J = 4.9 Hz; ^{4}J = 1.3 Hz, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.7 (t), 25.2 (t), 27.1 (t), 28.5 (t), 37.5 (t), 42.9 (d), 109.5 (s), 120.5 (s), 122.7 (d), 126.7 (d), 127.2 (s), 128.6 (d), 128.7 (d), 130.7 (s), 135.4 (d), 146.5 (d), 146.6 (s), 147.6 (s), 152.3 (s), 195.0 (s). – MS (FAB^+): *m*/*z* (%): 329 $[M + H]^+$ (100), 307 (20), 251 (46), 154 (100), 136 (59). – $C_{22}H_{20}N_2O$ (328.4): calcd. C 80.46, H 6.14, N 8.53; found C 80.27, H 6.35, N 8.38.

6-Phenyl-6,9,10,11-tetrahydro-5*H*,8*H*-pyrido[3',2':4,5]cyclopenta-[1,2-*b*]quinolin-7-one (11b): Compound **11b** was synthesized from **5** (0.35 g, 2.6 mmol), β-amino ketone hydrochloride **6b** (0.65 g, 2.6 mmol), and NH_4OAc (0.60 g, 7.8 mmol). Yield: 356 mg (44%) after chromatography on Al_2O_3, CH_2Cl_2, m.p. 217 °C (dec.). – IR (KBr): $\tilde{\nu}$ = 3214, 3147, 3074, 2934, 2862, 1621, 1579, 1507, 1466, 1435, 1363, 1259, 1181, 793, 700. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.10–1.97 (m, 2 H), 2.45–2.38 (m, 2 H), 2.58 (m_c, 2 H), 3.15 (s, 2 H), 5.32 (s, 1 H), 7.38–7.06 (m, 6 H), 7.44 (s, 1 H, NH), 7.60 (dd, ^{3}J = 7.4 Hz, ^{4}J = 0.7 Hz, 1 H), 8.40 (dd, ^{3}J = 5.1 Hz, ^{4}J = 1.1 Hz, 1 H). – ^{13}C NMR(50 MHz, $CDCl_3$): δ = 21.7 (t), 28.7 (t), 34.3 (t), 37.7 (t), 40.5 (d), 110.5 (s), 120.2 (d), 126.6 (d), 127.8 (s), 128.3 (d), 128.7 (d), 131.4 (d), 133.8 (s), 137.0 (s), 146.6 (s), 147.1 (d), 152.8 (s), 156.6 (s), 196.5 (s). – MS (FAB$^+$); *m/z* (%): 315 [M + H]$^+$ (100), 237 (68), 154 (63), 136 (44), 91 (26). – $C_{21}H_{18}N_2O$ (314.4): calcd. C 80.23, H 5.77, N 8.91; found C 80.57, H 5.52, N 8.99.

5,6,7,10,11,12-hexahydro-9*H*-benzo[*b*][1,10]phenanthrolin-8-one (12a): Compound **12a** was synthesized from **3** (0.6 g, 4.1 mmol), β-amino ketone hydrochloride **6a** (0.85 g, 4.2 mmol), and NH_4OAc (0.97 g, 12.6 mmol). Yield: 510 mg (75%) after chromatography on SiO_2, CH_2Cl_2/petroleum ether (1:1), CH_2Cl_2, CH_2Cl_2/acetone (3:1), CH_2Cl_2, CH_2Cl_2/MeOH; m.p. 192 °C. – IR (KBr): ṽ = 2949, 2878, 1671, 1595, 1454, 1438, 1421, 1347, 1224, 1197, 1595, 1454, 1438, 1421, 1347, 1224, 1197, 1160, 1092, 907, 760. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.19 (m$_c$, 2 H), 2.73 (m$_c$, 2 H), 3.04 Hz (s, 4 H), 3.34 (t, ^3J = 6.16 Hz, 2 H), 7.30 (m$_c$, 1 H), 7.62 (dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, 1 H), 8.18 (s, 1 H), 8.77 (dd, ^3J = 4.7 Hz, ^4J = 1.6 Hz, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ =22.4 (t) 27.3 (t), 27.7 (t), 33.0 (t), 39.0 (t), 124.8 (d), 128.0 (s), 132.7 (s), 135.0 (d), 135.6 (s), 136.7 (d), 149.6 (d), 155.1 (s), 163.3 (s), 198.6 (s). – MS (70 eV); *m/z* (%): 251 (30), 250 [M$^+$] (100), 222 (79), 194 (27), 166 (7), 97 (9), 72 (20). – $C_{16}H_{14}N_2O$ (250.3): calcd. C 76.78, H 5.64, N 11.19; found C 76.96, H 5.81, N 11.43.

9,10-Dihydro-5*H*,8*H*-pyrido[3',2':4,5]cyclopenta[1,2-*b*]quinolin-7-one (13a): Compound **13a** was synthesized from **5** (1.0 g, 7.5 mmol), **6a** (1.43 g, 7.5 mmol), and NH_4OAc (1.73 g, 22.5 mmol). After workup according to the general procedure described, the residue was chromatographed on Al_2O_3, eluting with CH_2Cl_2/methanol (125:1), to yield a pale brown solid. This solid consisted of **13a** and **8a** (ratio **13a**/**8a** = 1.6:1). Stirring a solution of the mixture in 10 mL of CH_2Cl_2 under an oxygen atmosphere led to complete conversion of **8a** to **13a**. Removal of the solvent yielded 510 mg (29%) of **13a**, m.p. 181–183 °C. – IR (KBr): ṽ = 2955, 2867, 1677, 1600, 1455, 1403, 1359, 1171, 788. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.68 (t, ^3J = 6.1 Hz, 2 H), 3.28 (t, ^3J = 6.1 Hz, 2 H), 3.83 (s, 2 H), 7.29 (dd, ^3J = 7.7 Hz, ^4J = 4.8 Hz, 1 H), 7.86 (d, ^{3}J = 7.7 Hz, 1 H), 8.33 (s, 1 H), 8.69 (d, ^3J = 4.8 Hz, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.3 (t), 32.5 (t), 33.2 (t), 39.1 (t), 124.0 (d), 127.4 (s), 131.8 (d), 133.6 (d), 135.0 (s), 139.9 (s), 150.2 (d), 162.4 (s), 164.7 (s), 198.5 (s). – MS (70 eV); *m/z* (%): 236 (99), 208 (100), 179 (37), 154 (7), 103 (10), 76 (8), 63 (8).

6,9,10,11-Tetrahydro-5*H*,8*H*-pyrido[3',2':4,5]cyclopenta[1,2-*b*]-quinolin-7-one (8a): Compound **8a** was not isolated from the mixture of **13a** and **8a**, but it could be identified. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.1–1.91 (m, 2 H), 3.18 (s, 2 H), 3.42 (m$_c$, 4 H), 3.45 (s, 2 H), 7.06 (dd, ^3J = 7.4 Hz, ^4J = 5.2 Hz, 1 H), 7.50 (s, 1 H, NH), 7.64 (dd, ^3J = 7.4 Hz, ^4J = 0.5 Hz, 1 H), 8.27 (d, ^3J = 5.2 Hz, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.8 (t) 24.2 (t), 28.5 (t), 36.0 (t) 37.2 (t), 105.9 (s), 119.9 (d), 126.0 (s), 131.5 (d), 134.2 (s), 137.0 (s), 146.2 (d), 154.5 (s), 156.4 (s), 197.1 (s).

2-*tert*-Butyl-5,6,10,11-tetrahydro-9*H*-benzo[*b*][1,10]phenanthrolin-8-one (14a): Compound **14a** was synthesized from **4** (0.83 g, 4.1 mmol), β-amino ketone hydrochloride **6a** (0.85 g, 4.2 mmol), and NH_4OAc (0.97 g, 12.6 mmol). Yield: 982 mg (75%) after chromatography on Al_2O_3, CH_2Cl_2, CH_2Cl_2,/acetone (5:1); m.p. 168 °C. – IR (KBr): ṽ = 2940, 1672, 1605, 1481, 1460, 1419, 1335, 1233. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.48 (s, 9 H), 2.21 (m, 2 H), 2.71 (t, ^3J = 6.1 Hz, 2 H), 2.96 (s, 4 H), 3.30 (t, ^3J = 6.1 Hz, 2 H), 7.39 (d, ^3J = 8.1 Hz, 1 H), 7.53 (d, ^3J = 8.1 Hz, 1 H), 8.12 (s, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.4 (d), 27.5 (d), 27.7 (d), 30.7 (q), 33.2 (d), 38.2 (s), 39.1 (t), 121.1 (d), 127.6 (s), 132.8 (s), 133.0 (s), 134.7 (d), 136.7 (d), 149.5 (s), 155.9 (s), 163.3 (s), 169.2 (s), 198.7 (s). – $C_{20}H_{22}N_2O$ (306.4): calcd. C 78.40, H 7.24, N 9.14; found C 78.64, H 7.13, N 9.35.

General Procedure for the Preparation of Xanthene Derivatives 17 and 19: A suspension of 1,3-cyclohexanedione (8.92 mmol), the iminium salt (4.46 mmol), and ammonium acetate (anhydrous) (5 mmol) in abs. chloroform (5 mL) was refluxed for 4 h under argon. After it was cooled to room temperature, a mixture of 20 mL CH_2Cl_2 and 20 mL of H_2O was added to it. The organic layer was separated and the residual aqueous layer was extracted three times with 15 mL of CH_2Cl_2. The combined organic layers were washed with H_2O and dried with Na_2SO_4. After removal of the solvent, the residue was purified by chromatography. The initial quantities and possible variations are mentioned in the experimental part of the compound concerned.

9-Pyridin-2-yl-3,4,5,6,7,9-hexahydro-2*H*-xanthene-1,8-dione (19c): Compound **19c** was prepared from 1,3-cyclohexanedione (1.0 g, 8.92 mmol), iminium salt **2c** (0.77 g, 4.46 mmol), and sodium acetate (0.41 g , 5.0 mmol) in abs. chloroform (5 mL). Yield: 0.68 g (52% after crystallization from CH_2Cl_2) of an orange solid, m.p. 192–193 °C. – IR (KBr): ṽ = 2985, 2835, 1683, 1652, 1429, 1352, 1207, 1186, 1129, 958, 757. – ^{1}H NMR (200 MHz, $CDCl_3$/MeOD, 20:1): δ = 2.11–1.88 (m, 4 H), 2.44–2.20 (m, 4 H), 2.76–2.47 (m, 4 H), 4.88 (s, 1 H), 7.07–7.00 (m, 1 H), 7.68–7.53 (m, 2 H), 8.37 (dd, ^3J = 4.9 Hz, ^4J = 0.9 Hz, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$/MeOD, 20:1): δ = 20.6 (t), 27.6 (t), 35.1 (d), 37.2 (t), 115.6 (s), 122.0 (d), 126.0 (d), 136.4 (d), 149.0 (d), 162.2 (d), 165.4 (s), 197.5 (s). – MS (70 eV); *m/z* (%): 295 (66), 233 (19), 217 (100), 198 (8), 154 (9), 91 (8). – $C_{18}H_{17}NO_3$ (295.3): calcd. C 73.20, H 5.80, N 4.74; found C 73.01, H 5.62, N 4.95.

2,2'-(Isopropylmethylene)bis(1-hydroxy)cyclohexyl-1-en-3-one (17d): Compound **17d** was prepared from 1,3-cyclohexanedione (1.0 g, 8.92 mmol), iminium salt **2d** (0.73 g, 4.46 mmol), and sodium acetate (0.41 g, 5.0 mmol) in abs. chloroform (5 mL). Yield: 1.22 g (98%) of a yellow powder, m.p. 189 °C. – IR (KBr): ṽ = 2965, 2925, 2857, 1597, 1353, 1201, 1135, 902, 850, 839, 585. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.78 (d, ^3J = 6.4 Hz, 6 H), 1.92 (m$_c$, 4 H), 2.57–2.22 (m, 8 H), 2.84 (m$_c$, 1 H), 3.37 (d, ^3J = 11.2 Hz, 1 H). – ^{13}C NMR (50 Hz, $CDCl_3$): δ = 20.4 (t), 22.2 (t), 25.7 (t), 33.2 (q), 33.8 (q), 38.8 (t), 48.0 (d), 117.5 (s), 191.2 (s), 192.3 (s). – MS (70 eV); *m/z* (%): 278 (15), 235 (100), 166 (17), 151 (20). – $C_{16}H_{22}O_4$ (278.4): calcd. C 69.04, H 7.97; found C 69.41, H 8.03.

2,2'-(Ethoxycarbonylmethylene)bis(1-hydroxycyclohexyl-1-en-3-one) (17e) and Ethyl 1,8-Dioxo-2,3,4,5,6,7,8-octahydro-1*H*-xanthene-9-carboxylate (19e): Compound **19e** was prepared from 1,3-cyclohexanedione (1.0 g, 8.92 mmol), in situ generated iminium salt **2e** (4.46 mmol) [aminal (1.13 g, 4.46 mmol)[45] and CH_3COCl (0.32 mL, 4.46 mmol)], and sodium acetate (0.41 g, 5.0 mmol) in abs. chloroform (5 mL). Yield: 275 mg of **17e** as a white precipitate (19.9%, collected from the reaction solution) and 450 mg of **19e** as a yellow oil (54.8%, after chromatography on silica gel/CH_2Cl_2). **17e**: m.p. 143 °C. – IR (KBr): ṽ = 2993, 2972, 2958, 1725, 1658, 1622, 1357, 1321, 1206, 1177, 1132, 1116, 1027, 960. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28 (t, ^3J = 7.1 Hz, 3 H), 2.07 (m$_c$, 4 H), 2.74–2.28 (m, 8 H), 4.15 (q, ^3J = 7.1 Hz, 2 H), 4.45 (s, 1 H). – ^{13}C NMR (50 Hz, $CDCl_3$): δ = 14.4 (q), 20.4 (t), 27.5 (t), 33.6 (d), 37.0 (t), 61.5 (t), 112.4 (s), 165.9 (s), 172.7 (s), 196.7 (s). **19e**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.1 Hz, 3 H), 1.98 (m$_c$, 4 H), 2.47 (m$_c$, 8 H), 4.16 (q, ^3J = 7.1 Hz, 2 H), 4.83 (s, 1 H). – ^{13}C NMR (50 MHz): δ = 14.5 (q), 20.3 (t), 33.1 (t), 35.7 (d), 61.8 (t), 114.8 (s), 170.2 (s), 191.7 (s). – MS (70 eV); *m/z* (%): 290 (12), 262 (100), 245 25), 217 (31), 178 (78), 127 (34), 84 (65).

3,6-Bis(dimethylaminomethyl)-2,3,7,8-tetrahydro-1*H*,6*H*-acridine-4,5-dione Bishydrochloride (21): A solution of **20** (1.0 g, 4.66 mmol) and iminium salt **2a** (0.87 g, 9.32 mmol) in abs. CH_3CN (10 mL) is stirred under an argon atmosphere at room temperature for 12 h. The reaction mixture is kept in a refrigerator overnight and the resulting precipitate is collected by vacuum filtration and dried in vacuo. Yield 1.53 g (82%).

1,2,3,5,6,7,9,10,11,13,14,15-Decahydroacridino[4,3-*b*]benzo-[*j*][1,10]phenanthroline-4,12-dione (22): Compound **22** was synthesized from **1** (1.25 g, 3.12 mmol), β-amino ketone hydrochloride **21** (699 mg, 6.24 mmol), and NH_4OAc (1.44 g, 18.7 mmol). Yield: 598 mg (46% after chromatography on Al_2O_3; CH_2Cl_2/methanol, 100:1), m.p. >250 °C. – IR (KBr): $\tilde{\nu}$ = 2934, 2887, 1683, 1585, 1435, 1347, 1222, 1160, 897. – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.21 (m, 4 H), 2.70 (m, 4 H), 3.03 (s, 8 H), 3.37 (t, ^3J = 6.0 Hz, 4 H), 7.52 (s, 1 H), 8.16 (s, 2 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.3 (t), 27.3 (t), 32.3 (t), 39.1 (t), 128.1 (s), 132.7 (d), 135.1 (d), 136.6 (d), 136.9 (s), 150.3 (s), 154.9 (s), 163.3 (s),198.4 (s). – MS (70 eV), *m/z* (%):421 (100 M^+), 393 (32), 365 (10), 334 (2), 197 (11), 168 3), 140 (2). – $C_{27}H_{23}N_3O_2$ (421.5): calcd. C 76.94, H 5.50, N 9.97; found: C 76.63, H 5.31, N 10.15.

9-Dimethylaminomethyl-5,6,10,11-tetrahydro-9*H*-benzo[*b*][1,10]-phenanthroline Hydrochloride (23): A solution of **12a** (529 mg, 2.07 mmol) and iminium salt **2a** (192 mg, 2.07 mmol) in abs. CH_3CN (3 mL) is refluxed under an argon atmosphere for 2 h. The reaction mixture is kept in a refrigerator overnight. The resulting precipitate is collected by vacuum filtration. Yield: 369 mg (51%).

9-Dimethylaminomethyl-2-*tert*-butyl-5,6,10,11-tetrahydro-9*H*-benzo[*b*][1,10]phenanthrolin-8-one (24): A solution of **14a** (895 mg, 2.96 mmol) and iminium salt **2a** (276 mg, 2.96 mmol) in abs. CH_3CN (9 mL) is refluxed under an argon atmosphere for 2 h. The reaction mixture is kept in a refrigerator overnight. The resulting precipitate is collected by vacuum filtration. Yield: 752 mg (64%).

Terpyridine 25: Compound **25** was synthesized from **1** (752 mg, 1.90 mmol), β-amino ketone hydrochloride **24** (213 mg, 1.90 mmol), and NH_4OAc (438 mg, 5.7 mmol). Yield: 427 mg (55% after chromatography on Al_2O_3; CH_2Cl_2/methanol, 150:1), m.p. >250 °C. – IR (KBr): $\tilde{\nu}$ = 2955, 1683, 1590, 1460, 1347, 1228, 1166, 912, 845. – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.50 (s, 9 H), 2.25 (m_c, 2 H), 2.73 (m_c, 2 H), 3.36–2.99 (m, 10 H), 7.37 (d, ^3J = 8.0 Hz, 1 H), 7.54 (d, ^3J = 8.0 Hz, 1 H), 8.14 (s, 1 H), 8.50 (s, 1 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.6 (t), 27.7 (t), 27.9 (t), 28.2 (t), 30.7 (q), 33.1 (t), 38.4 (s), 39.2 (t), 120.8 (d), 127.7 (s), 129.5 (s), 131.4 (s), 132.4 (s), 133.7 (d), 134.0 (s), 135.0 (d), 136.9 (d), 150.3 (s), 153.6 (s), 155.5 (s), 159.0 (s), 163.0 (s), 169.4 (s), 199.2 (s). – MS (FAB^+); *m/z* (%): 409 $[M + H]^+$ (80), 394 (100), 353 (30), 191 (9), 169 (11), 155(3). – $C_{27}H_{27}N_3O$ (409.5): C 79.19, H 6.65, N 10.26; found C 78.89, H 6.84, N 10.13.

Quaterpyridine 26: Compound **26** was synthesized from **3** (132 mg, 0.88 mmol), β-amino ketone hydrochloride **23** (299 mg, 0.88 mmol), and NH_4OAc (182 mg, 2.36 mmol). Yield: 154 mg (45% after chromatography on Al_2O_3; CH_2Cl_2/methanol, 100:1), m.p. 236–238 °C. – IR (KBr): $\tilde{\nu}$ = 3038, 2935, 2883, 2829, 1564, 1440, 1403, 1222, 1176, 819, 788, 767, 700. – ^1H NMR (200 MHz, $CDCl_3$): δ = 3.03 (s, 6 H), 3.17–3.09 (m, 4 H), 3.38 (m_c, 2 H), 7.48 (s, 1 H), 7.68–7.56 (m, 2 H), 8.75 (m_c, 3 H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = 27.5 (t), 27.9 (t), 27.0 (t), 28.1 (2 t), 31.2 (t), 123.7 (d),. 130.5 (s), 133.0 (s), 133.2 (d), 133.2 (d), 134.0 (s), 134.2 (s), 134.6 (s),157.7 (s), 136.2 (2 d), 149.4 (d), 150.7 (s), 150.8 (s), 151.5 (s), 152.3 (s) 152.4 (s), 157.7 (s). – MS (FAB^+); *m/z* (%): 389 $[M + H]^+$ (100), 307 (4), 197 (17), 178 (8), 136 (9). – $C_{26}H_{20}N_4$ (388.5): C 80.39, H 5.19, N 14.42; found C 80.01, H 5.49, N 14.33.

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