124. New Heteroaromatic Complexing Agents and Luminescence of Their Europium(III) and Terbium(III) Chelates

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Twelve heteroaromatic complexing agents **9a–l** were synthesized with the purpose to develop suitable labels for time-resolved luminescence-based bioaffinity assays. The relative luminescence yields, excitation maxima, and emission decay constants of their europium(III) and terbium(III) chelates were determined. According to these results, 2,2′,2″,2‴-[(2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic acid) (**9e**) and 2,2′,2″,2‴-[(2,2′:6′,2″-terpyridine-6,6″-diyl)bis(methylenenitrilo)]tetrakis(acetic acid) (**9l**) are the most promising agents.

Introduction. – Luminescent and fluorescent probes were the subject of intensive research during the last years. The most used fluorescent probes have such a short decay time that it is difficult to separate their fluorescence from the background and the scatterings of the sample [1]. The long-lived luminescence characteristic of certain rare-earth chelates was known for a long time [2]. These rare-earth chelates possess narrow emission bands and a large difference between the excitation and emission wavelengths, which can be exploited to decrease the interference caused by the background and the scatterings [1].

General requirements for luminescent lanthanide chelates to be used as labels in immunoassays are the high quantum yield of the emission, high kinetic stability, good H_2O solubility, and the existence of a functional group for covalent coupling to an antigen or antibody. Moreover, the coupling process should neither decrease the immunoreactivity of the labeled substances nor increase its unspecific binding to plastics *etc.* The chelates generally comprise a central metal ion and a chromophore, playing numerous roles in the complex. The chromophore absorbs light and transfers the excitation energy to the lanthanide ion. Furthermore, it shields the lanthanide ion from the interaction with H_2O molecules, which would otherwise cause nonradiative deactivation of the excited state.

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The commonly used commercial system *Delfia*® utilizes nonluminescent europium-(III) chelates as immunolabels. The luminescence is developed with 4,4,4-trifluoro-1-(naphth-2-yl)butane-1,3-dione in the micellar environment after the dissociation of lanthanide ion from the nonfluorescent transporting chelate [1]. β-Diketones as such are not suitable as labels, because their chelates are kinetically too unstable in aqueous solutions. The requirement for marker release prohibits the application of typical *Delfia* labels in the areas where the fluorescence signal has to be localized, *e.g. in situ* immunostaining, *in situ* and Southern blot nucleic-acid hybridization, DNA sequencing, or cytofluorometry. Obviously, strongly and directly luminescent lanthanide chelates should be developed to avoid this problem.

Cryptates which can encapsulate lanthanide ions, thus forming stable luminescent complexes, were reported [3]. In these macrocycles, 2,2′-bipyridine and its *N*,*N*′-dioxide, 2,2′-bipyrimidine, 3,3′-biisoquinoline and its *N*,*N*′-dioxide, 2,2′-biimidazole, 2,2′-bithiazole, and 4-(phenylethynyl)pyridine were used as the chromophoric groups. These compounds were shown to be promising luminescent labels. Another important group of luminescent lanthanide chelates comprises compounds, in which the ligand is a polyaminopolycarboxylate [4]. These compounds are stable, H_2O-soluble, and often well suited as labels for biological applications.

Because relatively little is known about aromatic ligands which can transfer the excitation radiation to the rare-earth ion by an internal energy-transfer process, we synthesized different candidates containing six-membered N-heteroaromatic rings as an energy absorbing and transferring moiety. These ring systems alone form quite unstable chelates with rare earths in aqueous solutions, if no additional chelating groups are present. In this work, we used two (methylenenitrilo)bis(acetic acid) groups in suitable positions to increase the stability of the chelates.

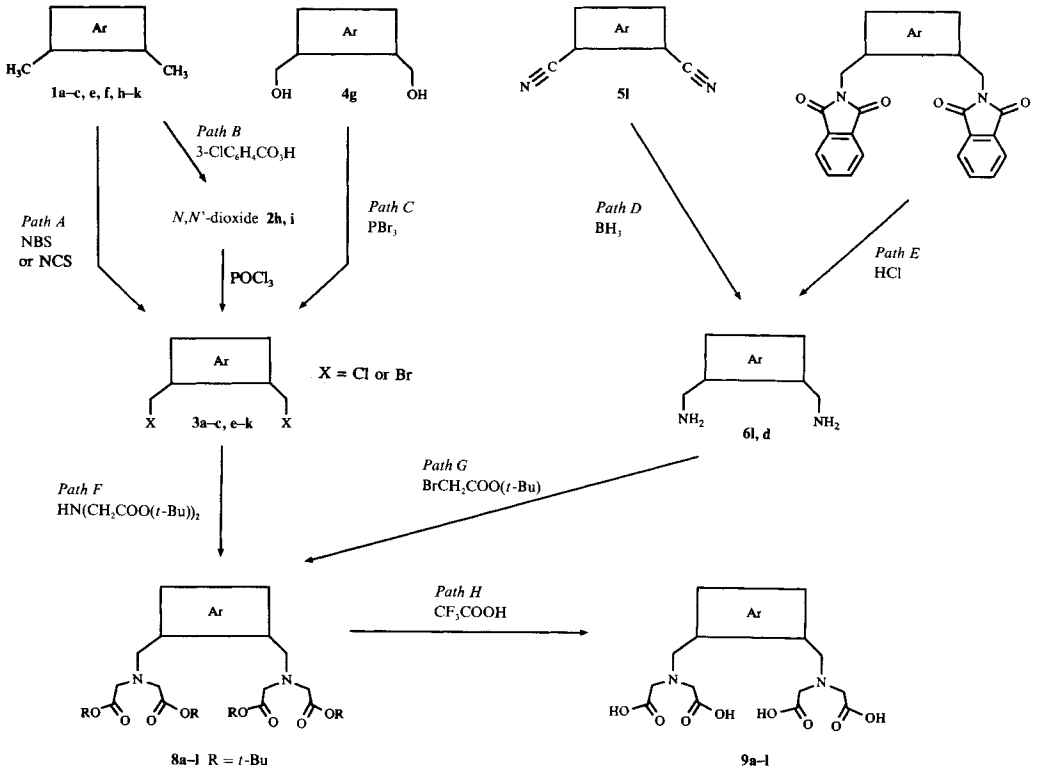
In this article, we report the synthesis of the twelve ligands (**9a–l**) and their spectral and luminescent properties with Eu^{III} and Tb^{III} ions.

Results and Discussion. – *Syntheses.* A number of different pathways were used for the preparation of ligands **9a–l** (see *Scheme*). The key intermediates were the bis(halogenomethyl) compounds **3** or the bis(methylamines) **6**. The former were prepared using three different routes (*Paths A–C*) starting either from the dimethyl precursors **1**, directly or *via* their *N*,*N*′-dioxides **2**, or, in one case, from a dimethanol, *i.e.* **4g**.

The 2,6-bis(bromomethyl)pyridine [5] (**3a**; from **1a**), 6,6′-bis(bromomethyl)-2,2′-bipyridine (**3e**; from **1e**) [6], 1,1′-bis(bromomethyl)-3,3′-biisoquinoline (**3f**; from **1f**) [7], 2,2′-dimethyl-4,4′-bipyrimidine (**1i**) [8], and 2,7-dimethyl-1,8-naphthyridine (**1j**) [9] were prepared as reported in the literature.

The most important approaches to alkyl-substituted isoquinolines such as 1,3-dimethylisoquinoline (**1b**) are the *Bischler-Napieralski* reaction of (phenylethyl)amines [11] or the *Beckmann* rearrangement of α,β-unsaturated oximes [12] [13]. After comparative studies, however, we preferred a modification of a latter approach introduced by *Sato et al.* [14] to produce **1b** in 66% yield from allylbenzene and MeCN in the presence of I_2 and a *Lewis* acid, followed by KOH/MeOH treatment. It is noteworthy that this two-step synthesis from easily available starting materials allows a facile reaction of nonactivated phenyl species. The preparation of 1,3-dimethylbenz[*f*]isoquinoline (**1c**) *via* the oxime method [12] was chosen merely on the basis of the accessibility of starting materials and gave a product identical with that obtained by *Schleigh* [15] using the (phenylethyl)amine

Scheme[a])



[a]) For **a**–**l**, see aryl moieties in Formulae **9a**–**l**.

route. Although the yield was only modest, 4,4′-dimethyl-2,2′-bipyrimidine (**1h**) was prepared using the method described by *Tiecco et al.* [16].

In the most straightforward method, the dimethyl compounds **1** were halogenated to **3** with *N*-halogenosuccinimide, usually *N*-bromosuccinimide (= NBS; *Path A*). In the case of 2,7-dimethyl-1,8-naphthyridine (**1j**), NBS gave a complex mixture of unstable products, while *N*-chlorosuccinimide (NCS) yielded the desired bis(chloromethyl) derivative **3j** (X = Cl), although only in 18% yield. The direct bromination of 2,9-dimethyl-1,10-phenanthroline (**1k**) to **3k** (X = Br) was found to be much more convenient than the earlier approach through the dialdehyde and dimethanol route [17]. The NBS or NCS halogenation was unsuccessful in the case of dimethylbipyrimidines **1h** and **1i**. Thus, the latter were first oxidized with 3-chloroperbenzoic acid to the *N*,*N*′-dioxides **2h** (3 isomers) and **2i** (1 isomer) which reacted with $POCl_3$ [18] to the expected bis(chloromethyl) derivatives **3h** (X = Cl; from all isomers of **2h**) and **3h** (X = Cl), respectively (*Path B*). Di[6-(bromomethyl)pyrid-2-yl] ketone (**3g**) was previously prepared by bromination of the corresponding dimethyl derivative **1g** [19]. We synthesized it from dimethanol **4g** and PBr_3 (*Path C*). Dimethanol **4g** was obtained from 6-bromopyridine-2-carbaldehyde [20], after protection of the CHO group, *via* di(6-formylpyrid-2-yl) ketone using standard methods [21] followed by reduction with $NaBH_4$.

In the case of the terpyridine and acridine derivatives, the bis(methylamines) **6l** and **6d**, respectively, were the most convenient key intermediates. Indeed, the modified *Reissert-Henze* reaction [22] with 2,2′:6′,2″-terpyridine *N*,*N*″-dioxide [23] yielded 2,2′:6′,2″-terpyridine-6,6″-dicarbonitrile (**5l**) which was reduced with borane to **6l** (*Path D*), and acridine-4,5-bis(methylamine) (**6d**) was prepared by the known [10] hydrolysis of bis(phthalimide) **7d** with HCl (*Path E*).

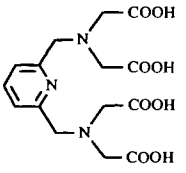
Finally, the tetra(*tert*-butyl) esters **8a–l** were synthesized from the bis(halogenomethyl) compounds **3a–c,e–k** and di(*tert*-butyl) iminobis(acetate) or from the bis(methylamines) **6l,d** and *tert*-butyl bromoacetate (*Paths F* and *G*, resp.) and hydrolyzed with CF_3COOH to the target tetraacetic acids **9a–l**.

Luminescence. The relative luminescence yields expressed in logarithmic values (log *R*), excitation maxima (λ_{exc}), and emission decay constants (k_{chel}) of the europium(III) and terbium(III) chelates of ligands **9a–l** were determined as described in [3b]; the results are shown in the *Table*.

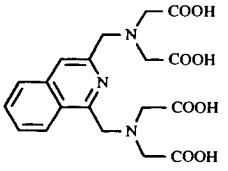
Table. *Relative Luminescence Yields* (as log *R*), *Excitation Maxima* (λ_{exc}), *and Emission Decay Constants* (k_{chel}) *of the Europium(III) and Terbium(III) Chelates of Ligands* **9a–l**

Ligand	Parent aromatic structure	Eu^{III}			Tb^{III}		
		log *R*	λ_{exc} [nm]	k_{chel} [ms^{-1}]	log *R*	λ_{exc} [nm]	k_{chel} [ms^{-1}]
9a	pyridine	4.83	265	2.48	4.87	267	0.80
9b	isoquinoline	4.44	324	2.63	too weak		
9c	benz[*f*]isoquinoline	4.41	355	2.65	2.35	355	45.5
9d	acridine	too weak			too weak		
9e	2,2′-bipyridine	5.50	307	1.70	5.27	307	0.82
9f	3,3′-biisoquinoline	5.33	330	2.75	too weak		
9g	di(pyrid-2-yl) ketone	4.61	272	1.02, 4.07	4.51	272	0.54, 4.10
9h	2,2′-bipyrimidine	5.17	250	1.96	too weak		
9i	4,4′-bipyrimidine	5.08	290	1.78	2.27	284	1.60, 5.72
9j	1,8-naphthyridine	4.65	312	3.09	4.50	312	1.02
9k	1,10-phenanthroline	5.26	272	1.98, 4.42	4.71	272	1.46
9l	2,2′: 6′,2″-terpyridine	5.94	333	0.73, 5.03	5.64	333	0.76

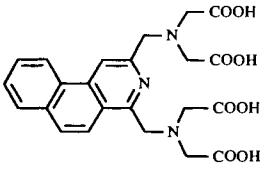
The excitation wavelengths λ_{exc} of chelates used in bioaffinity assays based on time-resolved luminescence should be as high as possible; a high excitation wavelength makes the selection of materials (strips, lenses, excitation sources, *etc.*) more flexible. On the other hand, the triplet state of compounds with a long absorption wavelength may lie below that of the lanthanide(III) ion. In that case, the energy is not transferred from the ligand to the lanthanide(III) ion. An example thereof is the acridine ligand **9d**, which has very low luminescence when complexed with Eu^{III} or Tb^{III} ions. Also the triplet states of the isoquinoline, 3,3′-biisoquinoline, and 2,2′-bipyrimidine ligands **9b,f,h** probably lie below the triplet state of the Tb^{III} ion. Since increased conjugation in the aromatic moiety shifts the excitation maximum to longer wavelength, the Eu^{III} chelate of the benz[*f*]isoquinoline ligand **9c** is excited at as high as 355 nm, while the Eu^{III} chelates of the less conjugated isoquinoline and pyridine ligands **9b** and **9a** have their λ_{exc} at 324 and 265 nm, respectively. The same tendency can be seen between the Eu^{III} chelates of the 3,3′-biisoquinoline and 2,2′-bipyridine ligands **9f** (330 nm) and **9e** (307 nm), respectively. The Eu^{III} chelate of the biisoquinoline ligand **9f** has almost the same λ_{exc} as that of the



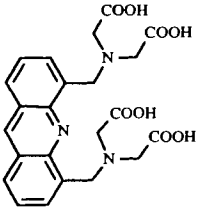
9a



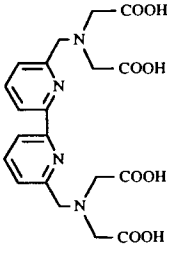
9b



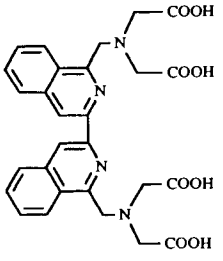
9c



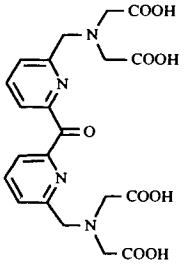
9d



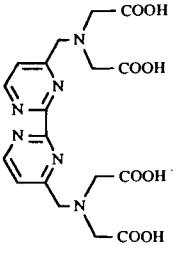
9e



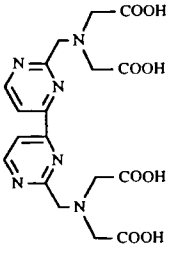
9f



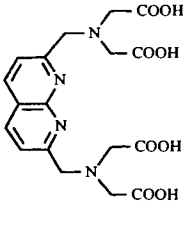
9g



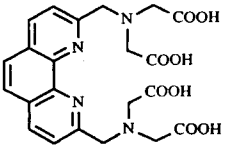
9h



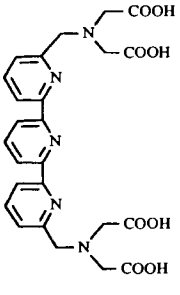
9i



9j



9k



9l

isoquinoline ligand **9b**. When two aromatic C-atoms of the 2,2′-bipyridine ligand **9e** are replaced by N-atoms, such as in the bipyrimidine ligands **9h** and **9i**, the λ_{exc} of the Eu^{III} chelate is considerably shifted to shorter wavelength. Especially the Eu^{III} chelate of the 2,2′-bipyrimidine ligand **9h** has a very low ε in λ_{exc} corresponding to the $n \rightarrow \pi^*$ transition, and it is practically excited only at 250 nm due to the $\pi \rightarrow \pi^*$ transition. The same phenomenon might also be the reason for the low λ_{exc} of the Eu^{III} chelates of the ligands **9g** and **9k**. Complexation of the lanthanide ion shifts λ_{max} to longer wavelengths in ligands, in which the coplanarity of the aromatic rings can be destroyed by torsional rotation (see **9e,f,h,i,l**), the only exception being ligand **9h** (for the UV spectrum of ligand **9l** and its Eu^{III} chelate, see *Fig.*). Eu^{III} and Tb^{III} chelates have almost the same excitation maxima.

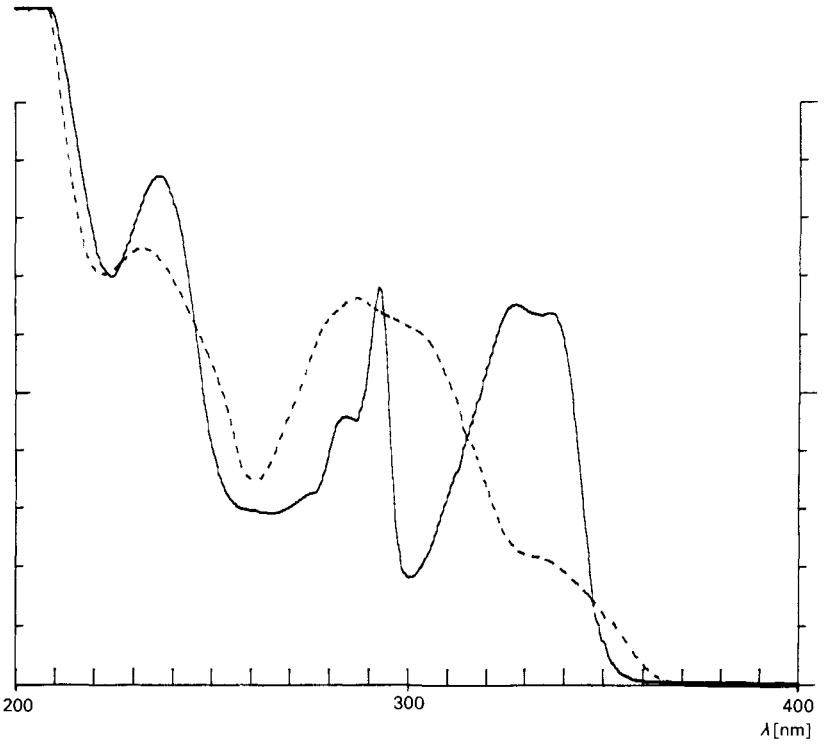


Figure. *UV Spectra of 2,2′,2″,2‴-[(2,2′:6′,2″-terpyridine-6,6″-diyl)bis(methylenenitrilo)]tetrakis(acetic acid)* (**9l**; – – –) *and of its europium(III) chelate* (——)

The decay constants k_{chel} of the chelates shown in the *Table* were measured only in borate buffer. For the study of the H_2O coordination numbers, the measurements should be performed also in D_2O. Anyhow, the variation in the decay times seems to be quite small with the average *ca.* 0.5 ms^{-1} [24]. Using this value, the decay constants of the studied Eu^{III} chelates are in accordance with anticipated values, with the exception of the Eu^{III} chelates of the ligands **9f,g,j**. The first decay constant of the Eu^{III} chelate of **9g** is 1.02 ms^{-1} indicating that only one H_2O molecule is coordinated to the Eu^{III} ion in the excited state. The carbonyl group between the pyridyl moieties of ligand **9g** appears to participate

in chelating the Eu^{III} ion or in some other way prevents more than one H_2O molecule from coordinating to the Eu^{III} ion. Probably, the aromatic N-atoms of the 1,8-naphthyridine ligand **9j** do not both participate in the chelation of Eu^{III} as indicated by the decay constant (3.09 ms^{-1}). The decay constants of Tb^{III} chelates are usually smaller than that of the corresponding Eu^{III} chelates, with the exception of ligands **9c** and **9l**. Contrary to the other chelates, the luminescence of the Tb^{III} chelate of ligand **9c** decreases very fast. The presence of two decay constants for some chelates indicates either the formation of two different chelates in solution or the effect of two alternative energy-releasing processes.

The relative luminescence yields are generally higher for Eu^{III} than for Tb^{III} chelates of the ligands **9a–l**. In spite of the higher conjugation of benz[*f*]isoquinoline compared to isoquinoline, ligand **9c** has almost the same log *R* value with Eu^{III} ion as **9b**, while the Eu^{III} chelate of the 3,3′-biisoquinoline derivative **9f** luminesces nearly ten times stronger than the Eu^{III} chelate of the isoquinoline ligand **9b**. Since k_{chel} of the chelates of **9b** and **9f** are almost the same, the difference in their relative luminescence yield is due to the aromatic part of the complexes. All the above mentioned ligands as well as both bipyrimidine derivatives **9h** and **9i** have a low relative luminescence yield with Tb^{III}. The high relative luminescence yields of the Eu^{III} and Tb^{III} chelates of 2,2′-bipyridine and 2,2′:6′,2″-terpyridine ligands **9e** and **9l**, respectively, are partly due to long decay times and the suitable energy level of the triplet states. The ligands **9a**, **g**, **k** have moderate luminescence with Eu^{III} and Tb^{III} ions, but the λ_{exc} are below 300 nm.

The results show that the Eu^{III} and Tb^{III} chelates of 2,2′,2″,2‴-[(2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic acid) (**9e**; see also [4b]) and of 2,2′,2″,2‴-[(2,2′:6′,2″-terpyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic acid) (**9l**) are potential alternatives for luminescent probes in time-resolved luminescence-based bioaffinity assays. Modifications suitable for labelling of biomolecules will be reported elsewhere.

Experimental Part

General. See [4b]. Moreover: MeCN and decaline were dried with CaH_2 and tetrahydrofuran with Na. Flash chromatography (FC): silica gel *Merck 7731*.

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(Pyridine-2,6-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8a**). A mixture of 2,6-bis(bromomethyl)pyridine [5] (**3a**; 106 mg, 0.40 mmol), di(*tert*-butyl) iminobis(acetate) [25] (196 mg, 0.80 mmol), dry Na_2CO_3 (210 mg, 2.0 mmol) and dry MeCN (10 ml) was refluxed overnight. Filtration and evaporation gave pure **8a** (233 mg, 98%). UV (EtOH): 265. ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 36 H); 3.61 (*s*, 8 H); 4.51 (*s*, 4 H); 8.03 (*d*, *J* = 7.9, 2 H); 8.43 (*t*, *J* = 7.9, 1 H).

2,2′,2″,2‴-[(Pyridine-2,6-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9a**). A soln. of **8a** (202 mg, 0.34 mmol) in CF_3COOH (5 ml) was stirred for 2 h at r.t. [25]. After evaporation, the mixture was triturated with Et_2O and filtered: **9a** (100%). UV (H_2O): 262. UV ([Eu^{III} (**9a**)], H_2O): 268. ^{1}H-NMR ((D$_6$)DMSO): 3.61 (*s*, 8 H); 4.22 (*s*, 4 H); 7.72 (*d*, *J* = 7.9, 2 H); 8.19 (*t*, *J* = 7.9, 1 H).

1,3-Dimethylisoquinoline (**1b**). Allylbenzene (5.9 g, 50 mmol) in MeCN (100 ml) was added to a soln. of $Ag(CF_3SO_3)$ (12.8 g, 50 mmol) in MeCN (100 ml) at r.t. The stirred soln. was cooled to 0°, and I_2 (12.7 g, 50 mmol) in MeCN (100 ml) was added dropwise. The mixture was allowed to warm up to r.t. and stirred overnight. The precipitate was filtered off and KOH (14.0 g, 250 mmol) in MeOH (150 ml) added. After stirring at 40° for 1 h, the mixture was evaporated and the residue dissolved in H_2O (250 ml) and extracted with CH_2Cl_2 (3 × 100 ml). The combined extracts were stirred with $Na_2S_2O_3$ (15.8 g, 100 mmol) for 1 h and dried (K_2CO_3). Evaporation followed by vacuum distillation yielded **1b** (5.2 g, 66%). Yellowish oil. B.p. 134–136°/15 Torr ([13]: 134–135°/15 Torr). UV (EtOH): 329, 316, 281, 272, 262, 220. ^{1}H-NMR ($CDCl_3$): 2.63 (*s*, 3 H); 2.89 (*s*, 3 H); 7.26 (*s*, 1 H); 7.44 (*dd*, *J* = 7.0, 8.2, 1 H); 7.56 (*dd*, *J* = 7.0, 7.9, 1 H); 7.62 (*d*, *J* = 8.2, 1 H); 7.99 (*d*, *J* = 7.9, 1 H).

1,3-Bis(bromomethyl)isoquinoline (**3b**). A mixture of **1b** (1.57 g, 10 mmol), NBS (3.92 g, 22 mmol), dibenzoyl peroxide (0.10 g, 0.41 mmol), and CCl_4 (150 ml) was refluxed under UV light for 6 h. After cooling, the mixture was filtered, the filtrate evaporated, and the residue treated with Et_2O (3 × 75 ml) to give **3b** (1.42 g, 45%). White powder. M.p. 163–165°. UV (EtOH): 331, 320, 295, 280, 233. ^{1}H-NMR ($CDCl_3$): 4.72 (*s*, 2 H); 5.03 (*s*, 2 H); 7.69 (*dd*, *J* = 7.0, 7.9, 1 H); 7.73 (*dd*, *J* = 7.0, 8.2, 1 H); 7.77 (*s*, 1 H); 7.86 (*d*, *J* = 7.9, 1 H); 8.25 (*d*, *J* = 8.2, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(Isoquinoline-1,3-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8b**). As described for **8a**, from **3b** (24 h at r.t.): 96% of **8b**. UV (EtOH): 325, 315, 285, 275, 222, ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 18 H); 1.46 (*s*, 18 H); 3.46 (*s*, 4 H); 3.55 (*s*, 4 H); 4.20 (*s*, 2 H); 4.52 (*s*, 2 H); 7.58 (*dd*, *J* = 7.0, 8.2, 1 H); 7.65 (*dd*, *J* = 7.0, 7.9, 1 H); 7.79 (*d*, *J* = 7.9, 1 H); 7.86 (*s*, 1 H); 8.78 (*d*, *J* = 8.2, 1 H).

2,2′,2″,2‴-[(Isoquinoline-1,3-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9b**). As described for **9a**, from **8b**: 100%, of **9b**. UV (H_2O): 320, 315, 285, 275, 225. UV ([Eu^{III} (**9b**)], H_2O): 330, 320, 285, 275, 225. ^{1}H-NMR ((D$_6$)DMSO): 3.62 (*s*, 4 H); 3.65 (*s*, 4 H); 4.24 (*s*, 2 H); 4.75 (*s*, 2 H); 7.79 (*dd*, *J* = 7, 8, 1 H); 7.96 (*dd*, *J* = 7, 8, 1 H); 8.07 (*s*, 1 H); 8.08 (*d*, *J* = 7, 1 H); 8.56 (*d*, *J* = 8, 1 H).

3-Methyl-4-(naphth-1-yl)but-3-en-2-one. A stream of dry HCl was passed through a mixture of redistilled naphthalene-1-carbaldehyde (62.5 g, 0.40 mol) and butan-2-one (57.7 g, 0.80 mol) at −10° for 4 h. The resulting black mixture was left at 0° for 24 h. After dissolving in toluene (500 ml), the mixture was washed with sat. Na_2CO_3 soln. (3 × 150 ml) and H_2O (2 × 50 ml), dried (Na_2SO_4), and evaporated the crude material dissolved in EtOH (95%), the undissolved polymeric material discarded by decantation, and the EtOH soln. evaporated: oily product (72.6 g, 86%). ^{1}H-NMR ($CDCl_3$): 1.90 (*s*, 3 H); 2.50 (*s*, 3 H); 7.3–8.0 (*m*, 8 H).

3-Methyl-4-(naphth-1-yl)but-3-en-2-one Oxime. A mixture of the butenone (see above; 31.7 g, 0.15 mol), $NH_2OH \cdot HCl$ (20.9 g, 0.30 mol), NaOH (6.0 g, 0.15 mol), EtOH (250 ml), and H_2O (100 ml) was refluxed for 30 min. The mixture was poured into cold H_2O (1000 ml) and left at 0° for 2 days. The white precipitate was filtered and crystallized from EtOH: 19.0 g (56%). M.p. 133–135°. UV (EtOH): 295, 256 (sh), 224. ^{1}H-NMR ($CDCl_3$): 1.95 (*d*, *J* = 1.0, 3 H); 2.30 (*s*, 3 H); 7.35–7.37 (*m*, 2 H); 7.47–7.53 (*m*, 3 H); 7.81 (*d*, *J* = 8.3, 1 H); 7.87–7.92 (*m*, 2 H); 8.50 (*s*, 1 H).

N-[1-Methyl-2-(naphth-1-yl)ethenyl]acetimidoyl Chloride. PCl_5 (10.4 g, 50 mmol) in dry decaline (100 ml) was added dropwise to a cooled (0°) and stirred soln. of the dried oxime (see above; 11.3 g, 50 mmol) in decaline (250 ml) under N_2. Stirring was continued at 0° for 6 h. The soln. as such was used in the next step.

1,3-Dimethylbenz[f]isoquinoline (**1c**). P_2O_5 (52.0 g, 0.25 mol) was added to the decaline soln. of the acetimidoyl chloride (see above) and the mixture refluxed for 45 min. After cooling to r.t., the decaline layer was separated from the precipitate by decantation. The solid residue was cautiously stirred with cold H_2O (1000 ml) and the undissolved material filtered off. The decaline layer was extracted with dil. HCl soln. (2 × 100 ml). The combined aq. fractions were washed with Et_2O (2 × 100 ml), brought to pH 8–9 with 10M NaOH, and extracted with Et_2O (3 × 300 ml). The Et_2O extract was dried (Na_2SO_4) and evaporated and the black resinous material purified by FC (silica gel, petroleum ether (b.p. 50–70°)/AcOEt 10:1): **1c**. M.p. 130°. UV (EtOH): 355, 338, 323, 300, 288, 275, 249. ^{1}H-NMR ($CDCl_3$): 2.75 (*s*, 3 H); 2.96 (*s*, 3 H); 7.62–7.68 (*m*, 2 H); 7.72 (*d*, *J* = 9, 1 H); 7.85–7.88 (*m*, 1 H); 7.89 (*d*, *J* = 9, 1 H); 8.11 (*s*, 1 H); 8.58–8.64 (*m*, 1 H).

1,3-Bis(bromomethyl)benz[f]isoquinoline (**3c**). A mixture of **1c** (0.41 g, 2.0 mmol), NBS (0.71 g, 4.0 mmol), α,α′-azobis[isobutyronitrile] (= 2,2′-dimethyl-2,2′-azobis[propanenitrile]; 33 mg, 0.2 mmol), and CCl_4 (50 ml) was refluxed for 6.5 h. After 4 h, an additional amount of the catalyst (33 mg) was added. The cold mixture was filtered and the filtrate evaporated. The residue was purified by FC (silica gel, petroleum ether (B.p. 50–70°)/AcOEt 10:1): 0.13 g (18%) of **3c**. UV (EtOH): 358, 341, 309, 300, 258. ^{1}H-NMR ($CDCl_3$): 4.82 (*s*, 2 H); 5.08 (*s*, 2 H); 7.74–7.78 (*m*, 2 H); 7.95 (*d*, *J* = 9, 1 H); 7.90–8.02 (*m*, 1 H); 8.09 (*d*, *J* = 9, 1 H); 8.58 (*s*, 1 H); 8.67–8.72 (*m*, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(Benz[f]isoquinoline-1,3-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8c**). As described for **8a**, from **3c** (3 h). FC (silica gel, $CHCl_3$, then $CHCl_3$/MeOH 95:5) gave 80% of **8c**. UV (EtOH): 354, 338, 332, 301, 288, 254. ^{1}H-NMR ($CDCl_3$): 1.47 (*s*, 36 H); 3.47 (*s*, 4 H); 3.60 (*s*, 4 H); 4.29 (*s*, 2 H); 4.55 (*s*, 2 H); 7.65–7.71 (*m*, 2 H); 7.84 (*d*, *J* = 9, 1 H); 7.89–7.94 (*m*, 1 H); 8.66 (*d*, *J* = 9, 1 H); 8.75–8.82 (*m*, 2 H).

2,2′,2″,2‴-[(Benz[f]isoquinoline-1,3-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9c**). As described for **9a**, from **8c**: 100% of **9c**. UV (H_2O): 353, 337, 302, 256, 213. UV ([Eu^{III} (**9c**)], H_2O): 361, 343, 301, 259. ^{1}H-NMR ((D$_6$)DMSO): 3.69 (*s*, 4 H); 3.71 (*s*, 4 H); 4.42 (*s*, 2 H); 4.84 (*s*, 2 H); 7.86–7.94 (*m*, 2 H); 8.14–8.19 (*m*, 2 H); 8.35 (*d*, *J* = 9, 1 H); 8.96 (*d*, *J* = 9, 1 H); 9.11 (*s*, 1 H).

*Tetra(*tert*-Butyl) 2,2′,2″,2‴-[(Acridine-4,5-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8d**). A mixture of acridine-4,5-bis(methylamine) dihydrochloride [10] (**6d** · 2 HCl; 1.50 g, 4.8 mmol), *tert*-butyl bromoacetate (3.75 g, 19.2 mmol), dry (i-Pr)$_2$EtN (5.62 g, 43.5 mmol), and dry MeCN (50 ml) was refluxed for 20 h. After evaporation, the residue was dissolved in $CHCl_3$ (80 ml), the soln. washed with H_2O (3 × 40 ml), dried (Na_2SO_4) and evaporated, and the product purified by FC (silica gel, petroleum ether (b.p. 50–70°)/AcOEt 5:1): 0.96 g (29%) of **8d**. M.p. 86°.

UV (EtOH): 358, 254, 214. ^{1}H-NMR ($CDCl_3$): 1.41 (*s*, 36 H); 3.63 (*s*, 8 H); 4.77 (*s*, 4 H); 7.53 (*dd*, *J* = 6.1, 8.2, 2 H); 7.88 (*d*, *J* = 8.2, 2 H); 8.04 (*d*, *J* = 6.1, 2 H); 8.71 (*s*, 1 H).

2,2′,2″,2‴-[(Acridine-4,5-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9d**). As described for **9a** from **8d**: 100% of **9d**. M.p. 240–245° (dec.). UV (H_2O): 356, 255, 215. UV ([Eu^{III} (**9d**)], H_2O): 360, 258, 210. ^{1}H-NMR ((D_6)DMSO): 4.01 (*s*, 8 H); 5.08 (*s*, 4 H); 7.73 (*dd*, *J* = 6.7, 7.9, 2 H); 8.15 (*d*, *J* = 6.7, 2 H); 8.28 (*d*, *J* = 7.9, 2 H); 9.31 (*s*, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* **8e** *and Acid* **9e**. See [4b].

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(3,3′-Biisoquinoline-1,1′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8f**). As described for **8a**, from 1,1′-bis(bromomethyl)-3,3′-biisoquinoline [7] (**3f**): 31% of **8f**. UV (EtOH): 330, 312, 252. ^{1}H-NMR ($CDCl_3$): 1.47 (*s*, 36 H); 3.55 (*s*, 8 H); 4.68 (*s*, 4 H); 7.62–7.71 (*m*, 4 H); 7.91 (*d*, *J* = 7.6, 2 H); 8.88–8.94 (*m*, 4 H).

2,2′,2″,2‴-[(3,3′-Biisoquinoline-1,1′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9f**). As described for **9a**, from **8f**: 100% of **9f**. UV (H_2O): 331, 311, 254, 216. UV ([Eu^{III} (**9f**)], H_2O): 361, 324, 260, 217. ^{1}H-NMR ((D_6)DMSO): 3.71 (*s*, 8 H); 4.69 (*s*, 4 H); 7.71 (*t*, *J* = 7.6, 2 H); 7.84 (*t*, *J* = 7.6, 2 H); 8.13 (*d*, *J* = 7.6, 2 H); 8.74 (*d*, *J* = 7.6, 2 H); 8.83 (*s*, 2 H).

2-Bromo-6-(dimethoxymethyl)pyridine. A soln. of 6-bromopyridine-2-carbaldehyde [20] (11.4 g, 61.2 mmol) dry in MeOH (200 ml) and trimethyl orthoformate (26.5 g, 250 mmol) was treated with $TsOH \cdot H_2O$ (250 mg, 1.3 mmol), refluxed for 1 h, cooled, and neutralized by addition of pyridine (5 ml). Evaporation and distillation of the residue under reduced pressure yielded pure product (13.6 g, 96%). Colorless liquid. UV (EtOH): 266, 216. ^{1}H-NMR ($CDCl_3$): 3.41 (*s*, 6 H); 5.31 (*s*, 1 H); 7.46 (*d*, *J* = 7.8, 1 H); 7.53 (*d*, *J* = 7.8, 1 H); 7.61 (*t*, *J* = 7.8, 1 H).

Di[6-(dimethoxymethyl)pyrid-2-yl] Ketone. A soln. of 2.6M BuLi (65 mmol) in hexane was added dropwise to the mixture of bromo(dimethoxymethyl)pyridine (see above; 14.2 g, 61.2 mmol) and dry Et_2O (200 ml) at $< -60°$. After stirring for 1 h, ethyl chloroformate (4.52 g, 41.7 mmol) in dry Et_2O was added and the yellow suspension stirred for 45 min at −60° and then for 15 min at −40°. After quenching with MeOH (20 ml), the mixture was poured into sat. $NaHCO_3$ soln. (300 ml), the Et_2O phase separated, the aq. phase extracted with CH_2Cl_2 (2 × 100 ml) and the combined org. phase evaporated and co-evaporated with toluene to yield the crude product. UV (EtOH): 275, 241. ^{1}H-NMR ($CDCl_3$): 3.42 (*s*, 12 H); 5.34 (*s*, 2 H); 7.76 (*dd*, *J* = 1.1, 7.8, 2 H); 7.92 (*t*, *J* = 7.8, 2 H); 8.08 (*dd*, *J* = 1.1, 7.8, 2 H).

6,6′-Carbonylbis(pyridine)-2,2′-dicarbaldehyde. Crude di[(dimethoxymethyl)pyridyl] ketone (see above) was dissolved in 1,4-dioxane (40 ml), H_2O (25 ml), and conc. HCl soln. (3 ml) and the stirred mixture refluxed for 15 min. The dark soln. was poured into sat. $NaHCO_3$ soln. (100 ml) and extracted with $CHCl_3$ (3 × 100 ml). After evaporation of the combined extracts, the residue was purified by FC (silica gel, $CHCl_3$/EtOH 96:4). The product was crystallized from toluene (100 ml): 4.78 g (65%, based on bromo(dimethoxymethyl)pyridine). UV (EtOH): 278, 240. ^{1}H-NMR ($CDCl_3$): 8.15 (*t*, *J* = 7.6, 2 H); 8.20 (*dd*, *J* = 1.5, 7.6, 2 H); 8.39 (*dd*, *J* = 1.5, 7.6, 2 H); 10.07 (*s*, 2 H).

Di[6-(hydroxymethyl)pyrid-2-yl] Ketone (**4g**). $NaBH_4$ (270 mg, 7.14 mmol) in dry EtOH (20 ml) was added dropwise within 15 min to a soln. of the dicarbaldehyde (see above; 10.4 mmol) in dry EtOH (50 ml) at 0°. The mixture was stirred for 10 min, the unreacted reducing agent destroyed with acetone (20 ml), the mixture evaporated, and the residue dissolved in $CHCl_3$/EtOH 1:1 and extracted with $NaHCO_3$ soln. The org. phase was evaporated and co-evaporated with toluene and the residue purified by FC (silica gel, $CHCl_3$/EtOH 9:1): 1.22 g (48%) of **4g**. ^{1}H-NMR ($CDCl_3$/CD_3OD): 4.77 (*s*, 4 H); 7.40–7.98 (*m*, 6 H).

Di[6-(bromomethyl)pyrid-2-yl] Ketone (**3g**). PBr_3 (1.82 g, 6.7 mmol) was added to a mixture of **4g** (410 mg, 1.68 mmol) and CH_2Cl_2 (15 ml) and the mixture refluxed for 5 min. $CHCl_3$ (100 ml) was added and the soln. washed with $NaHCO_3$. The org. phase was evaporated, co-evaporated with toluene, and purified by FC (silica gel, $CHCl_3$): 0.54 g (87%) of **3g**. UV (EtOH): 282, 245. ^{1}H-NMR ($CDCl_3$): 4.63 (*s*, 4 H); 7.69 (*dd*, *J* = 0.9, 7.6, 2 H); 7.93 (*t*, *J* = 7.6, 2 H); 8.07 (*dd*, *J* = 0.9, 7.6, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-{[6,6′-Carbonylbis(pyridine)-2,2′-diyl]bis(methylenenitrilo)}tetrakis(acetate)* (**8g**). As described for **8a**, from **3g**. The product was purified by FC (silica gel, $CDCl_3$/MeOH 95:5): 82% of **8g**. UV (EtOH): 278, 243. ^{1}H-NMR ($CDCl_3$): 1.44 (*s*, 36 H); 3.49 (*s*, 8 H); 4.10 (*s*, 4 H); 7.85 (*t*, *J* = 7.3, 2 H); 7.93 (*d*, *J* = 7.3, 2 H); 7.99 (*d*, *J* = 7.3, 2 H).

2,2′,2″,2‴-{[6,6′-Carbonylbis(pyridine)-2,2′-diyl]bis(methylenenitrilo)}tetrakis(acetic Acid) (**9g**). As described for **9a**, from **8g**. UV (H_2O): 284, 277, 244. UV ([Eu^{III} (**9g**)], H_2O); 278, 272, 262. ^{1}H-NMR ((D_6)DMSO): 3.65 (*s*, 8 H); 4.15 (*s*, 4 H); 7.82 (*d*, *J* = 7.6, 2 H); 7.93 (*d*, *J* = 7.6, 2 H); 8.06 (*t*, *J* = 7.6, 2 H).

2-Bromo-4-methylpyrimidine. Conc. HBr soln. (48%; 100 ml) was added slowly to a mixutre of 2-amino-4-methylpyrimidine (40.0 g, 0.367 mol), NaBr (180 g, 1.75 mol), $NaNO_2$ (60.0 g, 0.870 mol), and H_2O (160 ml) while the temp. was kept below 0° [26]. Then the mixture was stirred for 4 h at −5 to +5° and neutralized with conc.

NaOH soln. The product was extracted from the aq. phase with $CHCl_3$ (3 × 200 ml). After evaporation, the product was distilled, b.p. 69–70°/0.6 Torr: 14.6 g (23%). UV (EtOH): 255. ^{1}H-NMR ($CDCl_3$): 2.55 (*s*, 3 H); 7.17 (*d*, *J* = 4.9, 1 H); 8.42 (*d*, *J* = 4.9, 1 H).

4,4'-Dimethyl-2,2'-bipyrimidine (**1h**). $NiCl_2 \cdot 6\ H_2O$ (8.48 g, 35.7 mmol) and Ph_3P (37.4 g, 143 mmol) were dissolved in DMF (180 ml) at 50°. After bubbling N_2 through the soln. for 20 min, Zn powder (2.30 g, 0.0352 mol) was added and the mixture stirred for 1 h. Then, 2-bromo-4-methylpyrimidine (see above; 6.25 g, 36.1 mmol) was added and the mixture kept at 50° for 3.5 h. After pouring the mixture into dil. NH_3 soln. (500 ml), the org. material was extracted with $CHCl_3$ (3 × 150 ml). The product was extracted from $CHCl_3$ with 1M HCl (3 × 50 ml). The HCl soln. was made alkaline with 5M NaOH and extracted with $CHCl_3$ (3 × 50 ml), the solvent evaporated, and the product purified by FC (silica gel, $CHCl_3$/MeOH 95:5): 0.41 g (12%) of **1h**. UV (EtOH): 248. ^{1}H-NMR ($CDCl_3$): 2.72 (*s*, 6 H); 7.28 (*d*, *J* = 4.8, 2 H); 8.86 (*d*, *J* = 4.8, 2 H).

4,4'-Dimethyl-2,2'-bipyrimidine N,N'-*Dioxides* (**2h**). A soln. of **1h** (210 mg, 1.13 mmol) and 3-$ClC_6H_4CO_3H$ (50%; 1.40 g, *ca.* 6.5 mmol) in $CHCl_3$ (15 ml) was refluxed for 5 h. Insoluble material was filtered off, and the products (three different *N,N*-dioxides) were purified by FC (silica gel, $CHCl_3$ with MeOH gradient).

Isomer 1 *of* **2h**: 29 mg (12%). UV (EtOH): 312 (sh), 274. ^{1}H-NMR ($CDCl_3$): 2.61 (*s*, 6 H); 7.42 (*d*, *J* = 5.0, 2 H); 8.26 (*d*, *J* = 5.0, 2 H).

Isomer 2 *of* **2h**: 50 mg (20%). UV (EtOH): 316 (sh), 272. ^{1}H-NMR ($CDCl_3$): 2.59 (*s*, 6 H); 7.44 (*d*, *J* = 5.0, 1 H); 7.44 (*d*, *J* = 7.0, 1 H); 8.28 (*d*, *J* = 5.0, 1 H); 8.49 (*d*, *J* = 7.0, 1 H).

Isomer 3 *of* **2h**: 32 mg (13%). UV (EtOH): 320 (sh), 273. ^{1}H-NMR ($CDCl_3$): 2.59 (*s*, 6 H); 7.29 (*d*, *J* = 7.0, 2 H); 8.47 (*d*, *J* = 7.0, 2 H).

4,4'-Bis(chloromethyl)-2,2'-bipyrimidine (**3h**). A mixture of isomer *2* of **2h** (50 mg, 0.23 mmol), 1,4-dioxane (4 ml), and $POCl_3$ (0.40 ml, 4.3 mmol) was refluxed for 2 h and then evaporated. Some EtOH was added and the mixture evaporated again. The product was purified by FC (silica gel, $CHCl_3$ with MeOH gradient): 16 mg (27%) of **3h**. UV (EtOH): 245. ^{1}H-NMR ($CDCl_3$): 4.85 (*s*, 4 H); 7.76 (*d*, *J* = 5.0, 2 H); 9.09 (*d*, *J* = 5.0, 2 H).

Isomers *2* and *3* of **2h** gave the same product **3h** under identical conditions, according to TLC and ^{1}H-NMR.

*Tetra(*tert*-butyl) 2,2',2'',2'''-[(2,2'-Bipyrimidine-4,4'-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8h**). As described for **8a**, from **3h**. FC (silica gel, $CHCl_3$ with MeOH gradient) gave 47% of **8h**. UV (EtOH): 244. ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 36 H); 3.50 (*s*, 8 H); 4.23 (*s*, 4 H); 7.97 (*d*, *J* = 4.9, 2 H); 8.97 (*d*, *J* = 4.9, 2 H).

2,2',2'',2'''-[(2,2'-Bipyrimidine-4,4'-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9h**). As described for **9a**, from **8h**: 100% of **9h**. UV (H_2O): 247. UV ([Eu^{III} (**9h**)], H_2O): 248. ^{1}H-NMR ((D_6)DMSO): 3.54 (*s*, 8 H); 4.09 (*s*, 4 H); 7.80 (*d*, *J* = 5.1, 2 H); 8.95 (*d*, *J* = 5.1, 2 H).

2,2'-Dimethyl-4,4'-bipyrimidine [8] (**1i**). UV (EtOH): 286, 277. ^{1}H-NMR ($CDCl_3$): 2.83 (*s*, 6 H); 8.21 (*d*, *J* = 5.2, 2 H); 8.84 (*d*, *J* = 5.2, 2 H).

2,2'-Dimethyl-4,4'-bipyrimidine N,N'-*Dioxide* (**2i**). A mixture of **1i** (150 mg, 0.81 mmol), 3-$ClC_6H_4CO_3H$ (50%; 420 mg, *ca.* 1.9 mmol) and $CHCl_3$ (7.0 ml) was stirred overnight. The solvent was evaporated and the product purified by FC (silica gel, $CHCl_3$ with MeOH gradient): 100 mg (57%) of **2i**. UV (EtOH): 368, 295. ^{1}H-NMR ($CDCl_3$/CD_3OD): 2.81 (*s*, 6 H); 8.29 (*d*, *J* = 7.0, 2 H); 8.51 (*d*, *J* = 7.0, 2 H).

2,2'-Bis(chloromethyl)-4,4'-bipyrimidine (**3i**). As described for **3h**, from **2i**. Prep. TLC (silica gel, $CHCl_3$/MeOH 95:5) gave 13% of **3i**. UV (EtOH): 285, 276. ^{1}H-NMR ($CDCl_3$): 4.85 (*s*, 4 H); 8.41 (*d*, *J* = 5.2, 2 H); 9.00 (*d*, *J* = 5.2, 2 H).

*Tetra(*tert*-butyl) 2,2',2'',2'''-[(4,4'-Bipyrimidine-2,2'-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8i**). As described for **8a**, from **3i**. TLC (silica gel, $CHCl_3$/MeOH 9:1) gave 33% of **8i**. UV (EtOH): 285 (sh), 276. ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 36 H); 3.68 (*s*, 8 H); 4.34 (*s*, 4 H); 8.34 (*d*, *J* = 5.1, 2 H); 8.91 (*d*, *J* = 5.1 Hz, 2 H).

2,2',2'',2'''-[(4,4'-Bipyrimidine-2,2'-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9i**). As described for **9a**, from **8i**. UV (H_2O): 280. UV ([Eu^{III} (**9i**)], H_2O): 293. ^{1}H-NMR ((D_6)DMSO): 3.79 (*s*, 8 H); 4.37 (*s*, 4 H); 8.31 (*d*, *J* = 5.0, 2 H); 9.07 (*d*, *J* = 5.0, 2 H).

2,7-Dimethyl-1,8-naphthyridine [9] (**1i**). UV (EtOH): 316, 308, 303, 251. ^{1}H-NMR ($CDCl_3$): 2.76 (*s*, 6 H); 7.28 (*d*, *J* = 8.4, 2 H); 7.99 (*d*, *J* = 8.4, 2 H).

2,7-Bis(chloromethyl)-1,8-naphthyridine (**3j**). A mixture of **1j** (330 mg, 2.1 mmol), NCS (560 mg, 4.2 mmol), CCl_4 (10 ml), $CHCl_3$ (1.0 ml), and dibenzoyl peroxide (10 mg, 0.04 mmol) was refluxed for 30 min. After filtration and evaporation, the product was purified by FC (silica gel, $CHCl_3$ with MeOH gradient): 87 mg (18%) of **3j**. The product contained *ca.* 20% of unsymmetrical dichloro compound. UV (EtOH): 318, 309, 306, 254. ^{1}H-NMR ($CDCl_3$): 4.90 (*s*, 4 H); 7.77 (*d*, *J* = 8.4, 2 H); 8.27 (*d*, *J* = 8.4, 2 H).

*Tetra(*tert*-butyl) 2,2',2'',2'''-[(1,8-Naphthyridine-2,7-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8j**). As described for **8a**, from **3j**. FC (silica gel, $CHCl_3$ with MeOH gradient) gave 36% of **8j**. UV (EtOH): 318, 310, 255 (sh). ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 36 H); 3.52 (*s*, 8 H); 4.25 (*s*, 4 H); 8.01 (*d*, *J* = 8.6, 2 H); 8.19 (*d*, *J* = 8.6, 2 H).

2,2′,2″,2‴-[(1,8-Naphthyridine-2,7-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9j**). As described for **9a**, from **8j**: 100% of **9j**. UV (H_2O): 315, 307, 256. UV ([Eu^{III} (**9j**)], H_2O): 316, 308, 303, 260. ^{1}H-NMR ((D_6)DMSO): 3.67 (*s*, 8 H); 4.37 (*s*, 4 H); 8.02 (*d*, *J* = 8.4, 2 H); 8.69 (*d*, *J* = 8.4, 2 H).

2,9-Bis(bromomethyl)-1,10-phenanthroline (**3k**). A mixture of 2,9-dimethyl-1,10-phenanthroline (**1k**; 2.26 g, 10 mmol), NBS (3.92 g, 22 mmol), dibenzoyl peroxide (200 mg, 0.83 mmol), and CCl_4 (100 ml) was refluxed under UV light for 1.5 h. The cold mixture was filtered and the filtrate evaporated. The resultant brown oil was dissolved in acetone, and Et_2O was added until the soln. appeared cloudy. After standing overnight at 0°, the precipitate was filtered, washed with Et_2O, and recrystallized from EtOH: 0.77 g (21%) of **1k**. M.p. 111–112° ([17]: 110–111°). UV (EtOH): 330, 310, 275, 235. ^{1}H-NMR ($CDCl_3$): 4.97 (*s*, 4 H); 7.83 (*s*, 2 H); 7.92 (*d*, *J* = 8.4, 2 H); 8.30 (*d*, *J* = 8.4, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(1,10-Phenanthroline-2,9-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8k**). As described for **8a**, from **3k**: 98% of **8k**. UV (EtOH): 330, 272, 233. ^{1}H-NMR ($CDCl_3$): 1.47 (*s*, 36 H); 3.56 (*s*, 8 H); 4.46 (*s*, 4 H); 7.78 (*s*, 2 H); 7.83 (*d*, *J* = 8.4, 2 H); 8.26 (*d*, *J* = 8.4, 2 H).

2,2′,2″,2‴-[(1,10-Phenanthroline-2,9-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9k**). As described for **9a**, from **8k**. UV (H_2O): 295 (sh), 275, 230. UV ([Eu^{III} (**9k**)], H_2O): 300 (sh), 279, 231. ^{1}H-NMR ((D_6)DMSO): 3.64 (*s*, 8 H); 4.40 (*s*, 4 H); 8.02 (*d*, *J* = 8.4, 2 H); 8.12 (*s*, 2 H); 8.61 (*d*, *J* = 8.4, 2 H).

2,2′:6′,2″-Terpyridine-6,6″-dicarbonitrile (**5l**). Me_3SiCN (12.9 g, 82 mmol) was added to a suspension of 2,2′:6′,2″-terpyridine *N*,*N*″-dioxide [23] (2.17 g, 8.2 mmol) and CH_2Cl_2 (80 ml). After stirring for 5 min, PhCOCl (3.66 g, 32.8 mmol) was added during 15 min and the mixture stirred overnight at r.t. The mixture was neutralized with 10% K_2CO_3 soln., the aq. phase extracted with $CHCl_3$, the combined org. phase evaporated, and the residue crystallized from MeCN/THF: 2.32 g (72%) of **5l**. UV (EtOH): 291, 250, 215. M.p. 230–232°. ^{1}H-NMR ($CDCl_3$): 7.75 (*d*, *J* = 8, 2 H); 8.01 (*t*, *J* = 8, 2 H); 8.05 (*t*, *J* = 8, 1 H); 8.58 (*d*, *J* = 8, 2 H); 8.82 (*d*, *J* = 8, 2 H).

2,2′:6′,2″-Terpyridine-6,6″-bis(methylamine) Pentahydrochloride (**6l**·5 HCl). The suspension of **5l** (0.55 g, 1.9 mmol) in dry THF (15 ml) was deaerated with N_2. Borane-THF complex (1M; 25 ml, 25 mmol) was added and the mixture stirred overnight. After complete reaction, the excess borane was destroyed by adding MeOH. The mixture was evaporated and the residue dissolved in EtOH saturated with HCl (30 ml). After refluxing for 1 h, the soln. was cooled and the product filtered: 0.50 g (54%) of **6l**·5 HCl. UV (H_2O): 293, 232. ^{1}H-NMR (D_2O): 4.68 (*s*, 4 H); 7.89 (*d*, *J* = 8, 2 H); 8.31 (*t*, *J* = 8, 2 H); 8.51 (*d*, *J* = 8, 2 H); 8.82 (*d*, *J* = 8, 2 H); 8.90 (*t*, *J* = 8, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(2,2′:6′,2″-Terpyridine-6,6″-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**8l**). A mixture of **6l**·5 HCl (0.43 g, 0.91 mmol), dry MeCN (15 ml), dry Na_2CO_3 (2.00 g, 18.9 mmol), and *tert*-butyl bromoacetate (1.44 g, 7.38 mmol) was refluxed for 2 h, and the salts were filtered. The filtrate was evaporated and purified by FC (silica gel, $CHCl_3$): 0.26 g (38%) of **8l**. UV (EtOH): 288, 235. ^{1}H-NMR ($CDCl_3$): 1.48 (*s*, 36 H); 3.56 (*s*, 8 H); 4.15 (*s*, 4 H); 7.66 (*d*, *J* = 8, 2 H); 7.84 (*t*, *J* = 8, 2 H); 7.90 (*t*, *J* = 8, 1 H); 8.47 (*d*, *J* = 8, 2 H); 8.50 (*d*, *J* = 8, 2 H).

2,2′,2″,2‴-[(2,2′:6′,2″-Terpyridine-6,6″-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**9l**). As described for **9a**, from **8l**: 87% of **9l**. UV (H_2O): 305 (sh), 288, 233. UV ([Eu^{III} (**9l**)], H_2O): 337, 329, 294, 285, 237. ^{1}H-NMR ((D_6)DMSO): 3.84 (*s*, 8 H); 4.33 (*s*, 4 H); 7.67 (*d*, *J* = 7.8, 2 H); 8.08 (*t*, *J* = 7.8, 2 H); 8.13 (*t*, *J* = 7.8, 1 H); 8.47 (*d*, *J* = 7.8, 2 H); 8.58 (*d*, *J* = 7.8, 2 H).

Luminescence Measurements. For general considerations and the definition of *R*, see [4b]. The luminescence properties of Eu^{III} and Tb^{III} chelates were measured using equimolar mixtures of the ligands **9a–l** and Eu^{III} or Tb^{III} chloride in a borate buffer (pH 8.5). The concentrations used were 10^{-5} or 10^{-6} M. Results: see *Table*.

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