119. New 2,2′-Bipyridine Derivatives and Their Luminescence Properties with Europium(III) and Terbium(III) Ions[1])

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Twenty differently substituted 2,2′,2″,2‴-[(2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic acids) **75–94** were synthesized with the purpose of developing new markers to be used in bioaffinity assays based on the unique luminescence properties of Eu^{III} and Tb^{III} ions. The relative luminescence yields, excitation maxima, and emission decay constants were determined for the corresponding Eu^{III} and Tb^{III} chelates. The substituents at the bipyridine moiety had a significant effect on the luminescence properties: the best relative luminescence yields *R* were obtained for ligands with electron-donating substituents (*e.g.* Me, Ph), electron-withdrawing substituents (*e.g.* NO_2, COOH) had a reverse effect. However, no clear correlation between the relative luminescence yields and the substituent parameters was found.

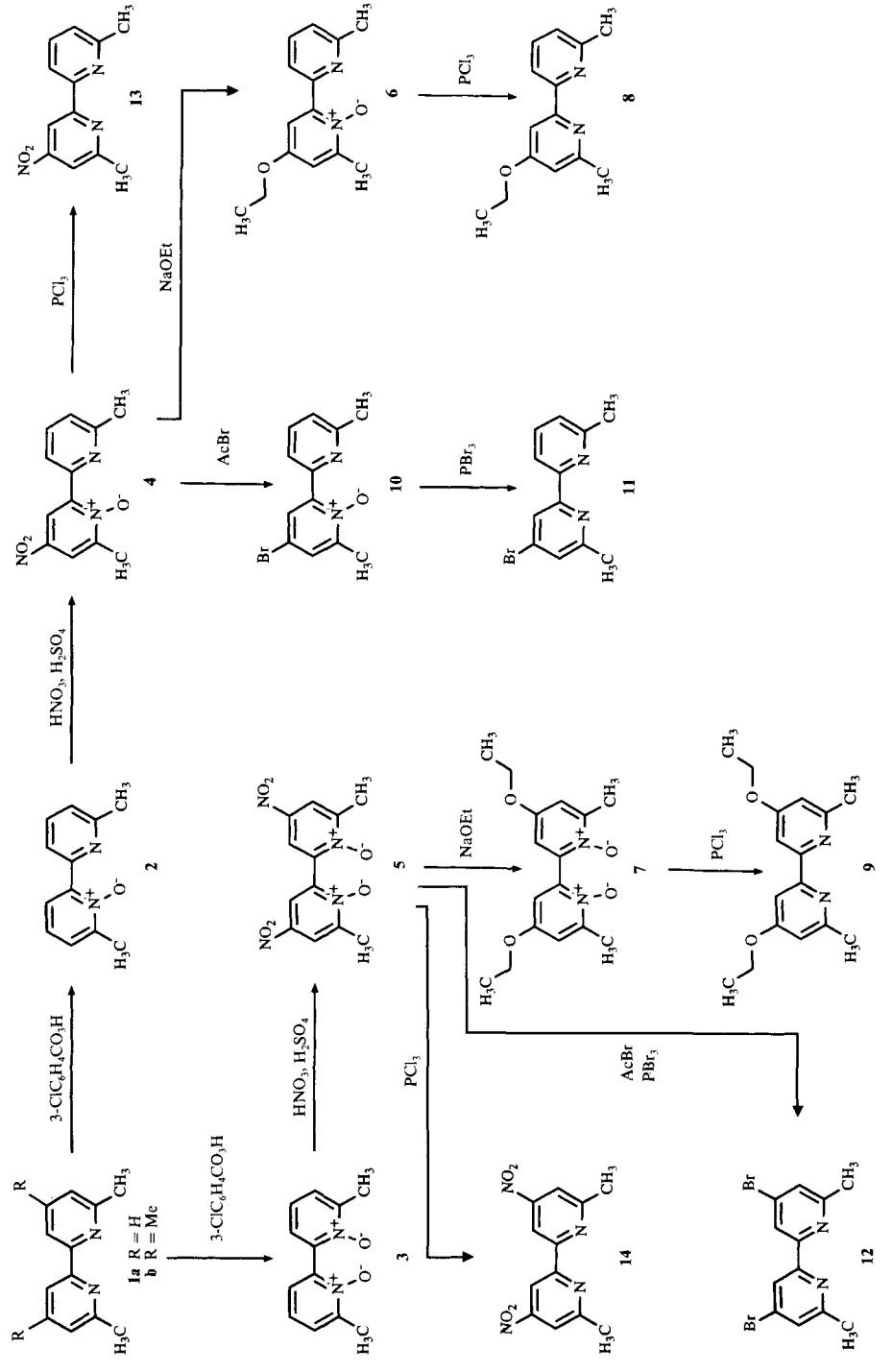
Introduction. – Lanthanide chelates have found extensive applications as labels in immunological and DNA hybridization assays due to their unique luminescence properties: high quantum efficiency, large *Stokes'* shift, narrow emission band, and long decay time [2]. In the most useful system, a non-luminescent chelate is used for the labelling of biologically active molecules, and the luminescence is enhanced after immunoreaction or hybridization with dissociative luminescence enhancement [3]. With stable luminescent chelates, no luminescence-enhancement step is needed [4].

As a very suitable energy-absorbing and energy-transferring moiety, 2,2′-bipyridine is widely used in the research of the luminescence properties of Ru^{II} and Os^{II} ions. It forms kinetically stable chelates with these ions in H_2O solution, even without the incorporation of additional chelating groups [5]. With Eu^{III} and Tb^{III}, however, these groups are needed. By introducing a (methylenenitrilo)bis(acetic acid) group in the 6- and 6′-positions of 2,2′-bipyridine, the stabilities of Eu^{III} and Tb^{III} chelates are sufficiently increased, and the chelates still possess good luminescent properties. The parent ligand having these substituents was prepared by *Ohm* and *Vögtle* [6], but the luminescence properties of its lanthanide chelates were not studied. On the other hand, the energy transfer in Eu^{III} and Tb^{III} cryptates having a 2,2′-bipyridine ligand as an energy-absorbing moiety were studied widely [7].

In this paper, we describe the syntheses and luminescent properties of 20 different 2,2′-bipyridine derivatives chelated with Eu^{III} or Tb^{III} ions. The purpose of this work was

[1]) A preliminary report was presented in [1] in connection with ICFE, Leuven, Belgium, 1990.

Scheme 1


1a R = H
b R = Me
3-ClC6H4CO3H
HNO3, H2SO4
PCl3
NaOEt
AcBr
PBr3
2
3
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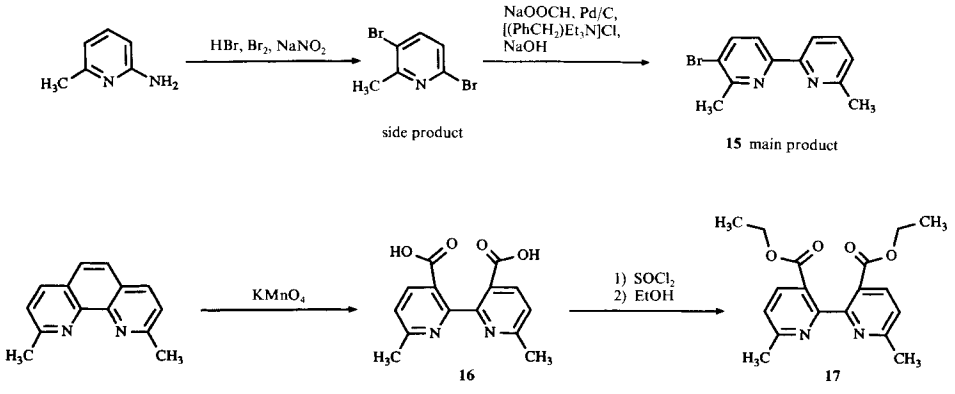
to study the influence of the substituents on the luminescence properties, with the aim to enhance the relative luminescence yield and to develop lanthanide chelates suitable for immunoassays. Results from an analogous study were published earlier for Eu^{III} chelates of differently substituted 2,6-bis{[*N*,*N*-bis(carboxymethyl)amino]methyl}-substituted 4-(phenylethynyl)pyridines = 2, 2′, 2″, 2‴-{[4-(phenylethynyl)pyridine-2, 6-diyl]bis(methylenenitrilo)}tetrakis(acetic acids) [8].

Results and Discussion. – *Syntheses.* The 6,6′-dimethyl-2,2′-bipyridine derivatives were prepared mainly using the procedures developed for the corresponding 2,2′-bipyridines lacking the Me groups in 6- and 6′-positions. The 6,6′-dimethyl-2,2′-bipyridine (**1a**) was a very versatile starting material in this respect (*Scheme 1*). It was oxidized to the corresponding *N*-oxide **2** and *N*,*N*′-dioxide **3** with 3-chloroperbenzoic acid [9]. The latter were nitrated to the nitro-*N*-oxides **4** and **5**, respectively, using HNO_3 and H_2SO_4 [10]. The NO_2 groups were then displaced in nucleophilic substitutions with NaOEt [10] to give the ethoxy-*N*-oxides **6** and **7** which were reduced with PCl_3 [10] to the EtO-substituted 6,6′-dimethyl-2,2′-dipyridines **8** and **9**, respectively. The reaction of nitro compounds **4** and **5** with acetyl bromide [11] yielded bromides (see, *e.g.*, **10**); on reduction with PBr_3, the Br-substituted 6,6′-dimethyl-2,2′-dipyridines **11** and **12**, respectively, were obtained. Finally, removal of the oxide functions of **4** and **5** with PCl_3 gave **13** and **14**, respectively.

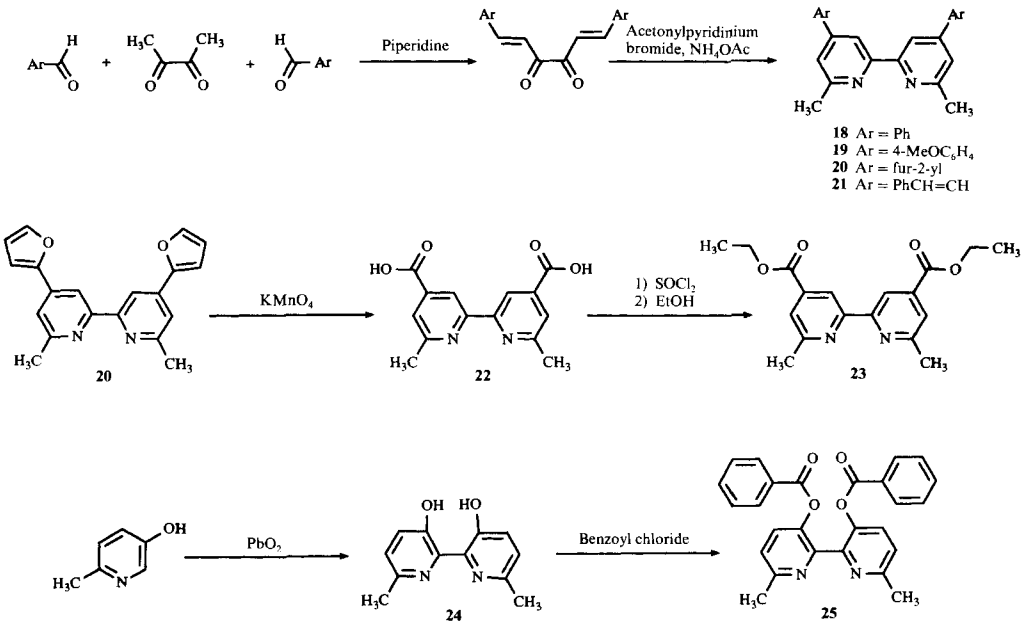
The 5-bromo-6,6′-dimethyl-2,2′-bipyridine (**15**) was prepared by coupling two 3,6-dibromo-2-methylpyridine molecules using the method developed by *Newkome et al.* [12] (*Scheme 2*); no 5,5′-dibromo derivative was found, probably because of the easy cleavage of Br-atoms under the reaction conditions. The oxidation of 2,9-dimethyl-1,10-phenanthroline with $KMnO_4$ [13] gave, among other products, 6,6′-dimethyl-2,2′-bipyridine-3,3′-dicarboxylic acid (**16**) which was converted to its ester **17** (*Scheme 2*).

Scheme 2



The 4,4′-diaryl-substituted 6,6′-dimethyl-2,2′-bipyridines **18**–**21** were prepared according to *Kröhnke* from the corresponding 1,6-diarylhexa-1,5-diene-3,4-dione derivatives by refluxing them with acetonylpyridinium bromide and NH_4OAc [16] (*Scheme 3*). The furyl-substituted compound **20** was then oxidized with $KMnO_4$ in *t*-BuOH [14] to dicarboxylic acid **22** which was esterified to **23** (*Scheme 3*). The 6,6′-dimethyl-2,2′-

Scheme 3



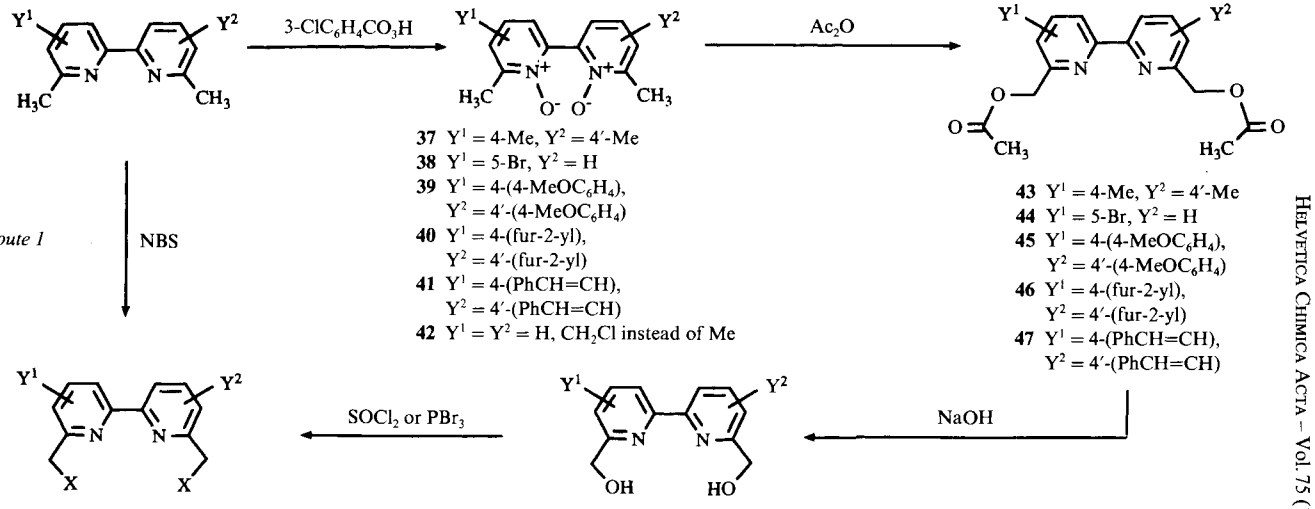
bipyridine-3,3′-diol (**24**) was synthesized by oxidative coupling of 6-methylpyridin-3-ol using PbO_2 as oxidant [15]; dibenzoylation of **24** yielded **25**.

Two different routes to prepare 6,6′-bis(halomethyl)-2,2′-bipyridine derivatives are presented in *Scheme 4*. The direct halogenation of 6,6′-dimethyl-2,2′-bipyridines with *N*-bromosuccinimide (NBS) or *N*-chlorosuccinimide (*Route 1*) usually gave the wanted product, but the yield of the 6,6′-bis(halomethyl)-2,2′-bipyridine derivative was low because of the many other halogenated compounds formed. Particularly large amounts of unwanted products were formed, if there was only one additional substituent in the starting 6,6′-dimethyl-2,2′-bipyridine. It was usually also difficult to separate pure 6,6′-bis(bromomethyl)-2,2′-bipyridines from the two isomeric, unsymmetrical (dibromomethyl)methyl derivatives using flash chromatography. This was, however, not a problem, because in the next step the reactivity of the dibromomethyl group was low, and the product was easy to purify. Thus, bis(bromomethyl) derivatives **26**–**36** were prepared by bromination with NBS of the corresponding dimethyl derivatives.

In some cases, direct halogenation could not be used because of the high reactivity of the substituents. *E.g.*, the furyl group in **20** had a higher affinity to halogenation than the Me groups. Also compound **1b** (see *Scheme 1*; prepared according to [12]) had a high risk for undesirable reactions. In these cases, the 6,6′-dimethyl-2,2′-bipyridines were oxidized to the corresponding 6,6′-dimethyl-2,2′-bipyridine *N*,*N*′-dioxides **37**–**41** using 3-chloroperbenzoic acid (*Route 2*). (Compound **42** was synthesized by oxidation of 6,6′-bis(chloromethyl)-2,2′-bipyridine [9] with 3-chloroperbenzoic acid.) Refluxing of **37**–**41** in Ac_2O gave the 2,2′-bipyridine-6,6′-dimethyl diacetates **43**–**47** [9]. The latter were hydrolyzed with base to the 6,6′-dimethanols **48**–**52** and further transformed to the 6,6′-bis(halomethyl)-2,2′-bipyridines **53**–**57** with $SOCl_2$ or PBr_3 using standard methods.

Scheme 4

Route 2



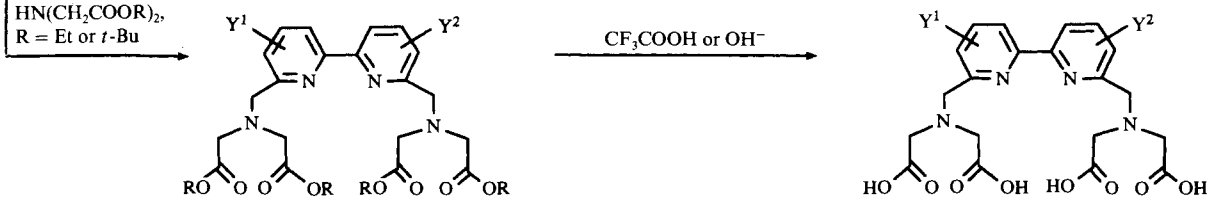
37 Y^1 = 4-Me, Y^2 = 4′-Me
38 Y^1 = 5-Br, Y^2 = H
39 Y^1 = 4-(4-$MeOC_6H_4$), Y^2 = 4′-(4-$MeOC_6H_4$)
40 Y^1 = 4-(fur-2-yl), Y^2 = 4′-(fur-2-yl)
41 Y^1 = 4-(PhCH=CH), Y^2 = 4′-(PhCH=CH)
42 Y^1 = Y^2 = H, CH_2Cl instead of Me

43 Y^1 = 4-Me, Y^2 = 4′-Me
44 Y^1 = 5-Br, Y^2 = H
45 Y^1 = 4-(4-$MeOC_6H_4$), Y^2 = 4′-(4-$MeOC_6H_4$)
46 Y^1 = 4-(fur-2-yl), Y^2 = 4′-(fur-2-yl)
47 Y^1 = 4-(PhCH=CH), Y^2 = 4′-(PhCH=CH)

48 Y^1 = 4-Me, Y^2 = 4′-Me
49 Y^1 = 5-Br, Y^2 = H
50 Y^1 = 4-(4-$MeOC_6H_4$), Y^2 = 4′-(4-$MeOC_6H_4$)
51 Y^1 = 4-(fur-2-yl), Y^2 = 4′-(fur-2-yl)
52 Y^1 = 4-(PhCH=CH), Y^2 = 4′-(PhCH=CH)

26 X = Br, Y^1 = Y^2 = H
27 X = Br, Y^1 = 4-NO_2, Y^2 = H
28 X = Br, Y^1 = 4-NO_2, Y^2 = 4′-NO_2
29 X = Br, Y^1 = 4-EtO, Y^2 = H
30 X = Br, Y^1 = 4-EtO, Y^2 = 4′-EtO
31 X = Br, Y^1 = 4-Br, Y^2 = H
32 X = Br, Y^1 = 4-Br, Y^2 = 4′-Br
33 X = Br, Y^1 = 3-COOEt, Y^2 = 3′-COOEt
34 X = Br, Y^1 = 4-COOEt, Y^2 = 4′-COOEt
35 X = Br, Y^1 = 3-PhCOO, Y^2 = 3′-PhCOO
36 X = Br, Y^1 = 4-Ph, Y^2 = 4′-Ph

53 X = Cl, Y^1 = 4-Me, Y^2 = 4′-Me
54 X = Cl, Y^1 = 4-(4-$MeOC_6H_4$), Y^2 = 4′-(4-$MeOC_6H_4$)
55 X = Cl, Y^1 = 4-(fur-2-yl), Y^2 = 4′-(fur-2-yl)
56 X = Cl, Y^1 = 4-(PhCH=CH), Y^2 = 4′-(PhCH=CH)
57 X = Br, Y^1 = 5-Br, Y^2 = H



58 $Y^1 = Y^2 = H$, R = *t*-Bu
59 Y^1 = 4-Me, Y^2 = 4′-Me, R = *t*-Bu
60 $Y^1 = 4\text{-}NO_2$, $Y^2 = H$, R = *t*-Bu
61 $Y^1 = 4\text{-}NO_2$, $Y^2 = 4'\text{-}NO_2$, R = *t*-Bu
62 Y^1 = 4-EtO, $Y^2 = H$, R = *t*-Bu
63 Y^1 = 4-EtO, Y^2 = 4′-EtO, R = *t*-Bu
64 Y^1 = 4-Br, $Y^2 = H$, R = *t*-Bu
65 Y^1 = 4-Br, Y^2 = 4′-Br, R = *t*-Bu
66 Y^1 = 5-Br, $Y^2 = H$, R = *t*-Bu
67 Y^1 = 3-COOEt, Y^2 = 3′-COOEt, R = *t*-Bu
68 Y^1 = 4-COOEt, Y^2 = 4′-COOEt, R = Et
69 Y^1 = 3-PhCOO, Y^2 = 3′-PhCOO, R = *t*-Bu
70 Y^1 = 4-Ph, Y^2 = 4′-Ph, R = Et
71 $Y^1 = 4\text{-}(4\text{-}MeOC_6H_4)$, $Y^2 = 4'\text{-}(4\text{-}MeOC_6H_4)$, R = Et
72 Y^1 = 4-(fur-2-yl), Y^2 = 4′-(fur-2-yl), R = Et
73 Y^1 = 4-(PhCH=CH), Y^2 = 4′-(PhCH=CH), R = *t*-Bu
74 $Y^1 = Y^2 = H$, *N*,*N*′-dioxide, R = *t*-Bu

75 $Y^1 = Y^2 = H$
76 Y^1 = 4-Me, Y^2 = 4′-Me
77 $Y^1 = 4\text{-}NO_2$, $Y^2 = H$
78 $Y^1 = 4\text{-}NO_2$, $Y^2 = 4'\text{-}NO_2$
79 Y^1 = 4-EtO, $Y^2 = H$
80 Y^1 = 4-EtO, Y^2 = 4′-EtO
81 Y^1 = 4-Br, $Y^2 = H$
82 Y^1 = 4-Br, Y^2 = 4′-Br
83 Y^1 = 5-Br, $Y^2 = H$
84 Y^1 = 3-COOEt, Y^2 = 3′-COOEt
85 Y^1 = 4-COOH, Y^2 = 4′-COOH
86 Y^1 = 3-PhCOO, Y^2 = 3′-PhCOO
87 Y^1 = 4-Ph, Y^2 = 4′-Ph
88 $Y^1 = 4\text{-}(4\text{-}MeOC_6H_4)$, $Y^2 = 4'\text{-}(4\text{-}MeOC_6H_4)$
89 Y^1 = 4-(fur-2-yl), Y^2 = 4′-(fur-2-yl)
90 Y^1 = 4-(PhCH=CH), Y^2 = 4′-(PhCH=CH)
91 $Y^1 = Y^2 = H$, *N*,*N*′-dioxide
92 $Y^1 = 4\text{-}NH_2$, $Y^2 = H$
93 Y^1 = 3-COOH, Y^2 = 3-COOH
94 Y^1 = 3-OH, Y^2 = 3′-OH

The 2,2′,2″,2‴-[(2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetates) **58–73** and *N*,*N*′-dioxide **74** were synthesized from the corresponding 6,6′-bis(halomethyl) compounds by refluxing them with di(*tert*-butyl) or diethyl iminobis(acetate) in dry MeCN. Hydrolysis of the di(*tert*-butyl) esters **58–67**, **69**, **73**, and **74** with CF_3COOH and of the diethyl esters **68** and **70–72** with NaOH gave the corresponding tetraacids **75–91**. The 4-amino-tetraacid **92**, hexaacid **93**, and 3,3′-dihydroxy-tetraacid **94** were obtained by reduction of 4-nitro-tetraacid **77**, by hydrolysis of 3,3′-bis(ethoxycarbonyl)-tetraacid **84**, and by hydrolysis of 3,3′-bis(benzoyloxy)-tetraacid **86**, respectively.

Luminescence. The relative luminescence yields (as logarithmic values, $\log R$; see *Exper. Part*), excitation maxima (λ_{exc}), and emission decay constants (k_{chel}) of the Eu^{III} and Tb^{III} chelates of the 20 different 2,2′-bipyridine derivatives **75–94** are shown in the *Table*.

Table. *Relative Luminescence Yields* ($\log R$), *Excitation Maxima* (λ_{exc}), *and Emission Decay Constants* (k_{chel}) *of the Europium(III) and Terbium(III) Chelates of 2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acids)* **75–94**

	Substitution at the bipyridine moiety	Eu^{3+}			Tb^{3+}		
		$\log R$	λ_{exc} [nm]	k_{chel} [ms^{-1}]	$\log R$	λ_{exc} [nm]	k_{chel} [ms^{-1}]
75	unsubstituted	5.50	307	1.70	5.27	307	0.82
76	4,4′-dimethyl	5.61	310	1.69	5.51	308	0.68
77	4-nitro	4.12	328	1.87	2.94	310	0.71
78	4,4′-dinitro	4.14	338	1.87	too weak		
79	4-ethoxy	5.33	298	1.72	5.31	299	0.62
80	4,4′-diethoxy	5.11	290	1.80	5.13	287	0.67
81	4-bromo	5.36	315	1.76	5.12	310	0.96
82	4,4′-dibromo	5.31	310	1.86	5.02	310	1.33
83	5-bromo	4.16	320	1.77	4.50	320	1.37, 9.71
84	3,3′-bis(ethoxycarbonyl)	4.31	275	1.80	too weak		
85	4,4′-dicarboxy	4.42	325	1.71	3.54	325	1.59
86	3,3′-bis(benzoyloxy)	5.36	292	1.84	2.83	290	1.59, 9.71
87	4,4′-diphenyl	5.52	325	1.73	5.18	325	1.12
88	4,4′-bis(4-methoxyphenyl)	5.57	325	1.78	4.84	325	3.07
89	4,4′-bis(fur-2-yl)	5.32	330	1.76	2.10	320	1.50
90	4,4′-distyryl	2.95	315	1.75	2.63	313	1.11
91	*N*,*N*-dioxide	4.72	280	1.35, 5.10	3.74	280	1.11, 4.72
92	4-amino	4.42	290	1.72	4.62	294	0.67
93	3,3′-dicarboxy	4.90	283	1.74	2.23	280	0.63, 5.53
94	3,3′-dihydroxy	3.91	340	2.62	too weak		

The decay constants k_{chel} of the chelates were measured only in borate buffer (pH 8.5). For the study of the H_2O coordination numbers, the measurements should be performed also in D_2O. Anyhow, the variation in the decay constants of different types of Eu^{III} chelates seems to be quite small with the average of *ca.* 0.5 ms^{-1} [17]. The emission decay constants of the studied Eu^{III} chelates range between 1.69 and 1.87 ms^{-1} (excluding the compounds having 3,3′-dihydroxy and *N*,*N*′-dioxide substituents, *i.e.* **94** and **91**, respectively), indicating that one H_2O molecule is coordinated to the Eu^{III} ion. This is in accordance with the structures of the anticipated chelates. The emission decay constant of the Eu^{III} chelate of ligand **94** is 2.62 ms^{-1}. According to this, two H_2O molecules are coordinated to the Eu^{III} ion. The Eu^{III} chelate of the *N*,*N*′-dioxide **91** shows two exponential decay times.

This either indicates the existence of two different chelates in the solution or two alternative energy-releasing processes. It is obvious that the geometry of this chelate is different from that of the others, because this ligand has two *N*-oxide groups near the coordinated lanthanide ion.

The decay constants of the Tb^{III} chelates vary between 0.62 and 1.59 ms^{-1}. Ligand **88** is, however, an exception, because the decay constant in this case is 3.07 ms^{-1}. The triplet state of ligand **88** might be so near the lowest excited level of the Tb^{III} ion that the energy goes also from the excited Tb^{III} back to the ligand [18].

The best relative luminescence yields *R* (see *Exper. Part*) for the Eu^{III} and Tb^{III} chelates are obtained with the 4,4′-dimethyl derivative **76** (see log*R* in the *Table*). Also the parent ligand **75**, the ethoxy (**79** and **80**), diphenyl (**87**), and 4,4′-bis(4-methoxyphenyl) (**88**) derivatives exhibit high log*R*'s, both with Eu^{III} and Tb^{III}. The 4,4′-distyryl derivative **90** has the lowest log*R* value with the Eu^{III} ion. This might be due to *trans-cis* isomerisation in styryl groups.

We have not been able to demonstrate a straightforward correlation between the relative luminescence yields *R* and the substituent parameters. This will need more detailed studies including the measurement of the triplet states of the ligands. However, the electron-donating substituents (*e.g.* Me and Ph) seem to enhance *R*, and the electron-withdrawing substituents (*e.g.* NO_2 and COOH) lower it.

Because of the considerable differences in *R* of the chelates, caused by the different substituents (*ca.* 500 times for Eu^{III} and over 3200 times for Tb^{III}), a careful optimization of the groups required for coupling of 2,2′-bipyridine chelates to immunoreagents is needed to preserve the good luminescence properties of the parent chelate. If this can be accomplished, 2,2′,2″,2‴-[(2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic acids) are well-suited for labels in time-resolved luminescence-based bioaffinity assays. A suitable linking group could be an alkyl or alkoxy substituent incorporating a reactive group for coupling to biologically active molecules.

Experimental Part

General. Commercially available chemicals were used without further purification. The syntheses are unoptimized. Flash chromatography = FC. M.p.: uncorrected. UV Spectra: *Beckman-DU8* spectrophotometer; λ_{max} in nm. Luminescence measurements: *Perkin-Elmer-LS5* spectrofluorometer connected to an *Apple II* computer; the use of the phosphorescence mode allowed the recording of emission curves. ^{1}H-NMR Spectra: 400-MHz *Jeol-GX-400* or, in some cases, 60-MHz *Hitachi-Perkin-Elmer-R-60* spectrometer; tetramethylsilane or sodium 3-(trimethylsilyl)propane-1-sulfonate as internal standards, chemical shifts δ in ppm, coupling constants *J* in Hz.

1. *Syntheses of 6,6′-Dimethyl-2,2′-bipyridine Derivatives* **1**, **4**, **8**, **9**, *and* **11**–**25**. *6,6′-Dimethyl-2,2′-bipyridine* (**1a**) was synthesized from 2-bromo-6-methylpyridine according to [12].

2-Bromo-4,6-dimethylpyridine was synthesized analogously to 2-bromo-6-methylpyridine [12] starting from 2-amino-4,6-dimethylpyridine. Yield 58%. B.p. 106°/11 Torr. UV (EtOH): 268. ^{1}H-NMR ($CDCl_3$): 2.27 (*s*, 3 H); 2.48 (*s*, 3 H); 6.92 (*s*, 1 H); 7.12 (*s*, 1 H).

4,4′,6,6′-Tetramethyl-2,2′-bipyridine (**1b**) was prepared from 2-bromo-4,6-dimethylpyridine (see above) analogously to **1a**. Yield 12%. UV (EtOH): 289, 241. ^{1}H-NMR ($CDCl_3$): 2.35 (*s*, 6 H); 2.56 (*s*, 6 H); 6.94 (*s*, 2 H); 8.00 (*s*, 2 H).

6,6′-Dimethyl-4-nitro-2,2′-bipyridine N-*Oxide* (**4**). To a soln. of 6,6′-dimethyl-2,2′-bipyridine *N*-oxide (**2**; 1.50 g, 7.49 mmol) [9] in conc. H_2SO_4 soln. (8.0 ml), fuming HNO_3 (6.0 ml) was added dropwise, and the mixture was warmed at 100° for 4 h. After pouring on ice, the pH was adjusted to 5.5 with 10% NaOH soln. The precipitated product was filtered: 0.98 g (53%). UV (EtOH): 337, 294, 233. ^{1}H-NMR ($CDCl_3$): 2.62 (*s*, 3 H); 2.65 (*s*, 3 H); 7.27 (*d*, *J* = 7.8, 1 H); 7.75 (*t*, *J* = 7.8, 1 H); 8.10 (*d*, *J* = 3.2, 1 H); 8.56 (*d*, *J* = 7.8, 1 H); 8.93 (*d*, *J* = 3.2).

6,6′-Dimethyl-4-nitro-2,2′-bipyridine (**13**). PCl_3 (0.5 ml) was added slowly to a cold soln. of **4** (0.49 g, 2.0 mmol) in $CHCl_3$ (7.0 ml). The mixture was refluxed overnight. The cooled soln. was poured on ice, the pH adjusted to 10 with 10% NaOH soln., and the product filtered and purified by FC (silica gel, CH_2Cl_2): 0.40 g (87%). UV (EtOH): 324, 287, 242. ^{1}H-NMR ($CDCl_3$): 2.62 (*s*, 3 H); 2.71 (*s*, 3 H); 7.18 (*d*, *J* = 7.6, 1 H); 7.68 (*t*, *J* = 7.6, 1 H); 7.76 (*d*, *J* = 2.1, 1 H); 8.19 (*d*, *J* = 7.6, 1 H); 8.88 (*d*, *J* = 2.1, 1 H).

6,6′-Dimethyl-4,4′-dinitro-2,2′-bipyridine N,N′-*Dioxide* (**5**) was prepared analogously to **4** starting from 6,6′-dimethyl-2,2′-bipyridine *N,N′*-dioxide (**3**) [9]. Yield 42%. UV (EtOH): 336, 250 (sh). ^{1}H-NMR ((D_6)DMSO): 2.48 (*s*, 6 H); 8.53 (*d*, *J* = 3.4, 2 H); 8.61 (*d*, *J* = 3.4, 2 H).

6,6′-Dimethyl-4,4′-dinitro-2,2′-bipyridine (**14**) was prepared analogously to **13** starting from **5**. Yield 27%. M.p. 215° (dec.). UV (EtOH): 318, 236. ^{1}H-NMR ($CDCl_3$): 2.84 (*s*, 6 H); 7.96 (*s*, 2 H); 8.96 (*s*, 2 H).

4-Ethoxy-6,6′-dimethyl-2,2′-bipyridine N-*Oxide* (**6**). Na (0.19 g, 8.3 mol) was added to dry EtOH (25 ml). After the Na had reacted, **4** (1.00 g, 4.08 mmol) was added and the soln. warmed at 70° for 30 min. The mixture was neutralized with conc. HCl soln., the salts were filtered, and the soln. was evaporated. The product was purified by FC (silica gel, 0–20% MeOH/$CHCl_3$): 0.96 g (96%). UV (EtOH): 272, 239. ^{1}H-NMR ($CDCl_3$): 1.45 (*t*, *J* = 7.0, 3 H); 2.58 (*s*, 3 H); 2.61 (*s*, 3 H); 4.14 (*q*, *J* = 7.0, 2 H); 6.84 (*d*, *J* = 3.4, 1 H); 7.20 (*d*, *J* = 7.7, 1 H); 7.54 (*d*, *J* = 3.4, 1 H); 7.70 (*t*, *J* = 7.7, 1 H); 8.65 (*d*, *J* = 7.7, 1 H).

4-Ethoxy-6,6′-dimethyl-2,2′-bipyridine (**8**) was prepared analogously to **13** starting from **6**. Yield 69%. M.p. 90–91°. UV (EtOH): 286, 243. ^{1}H-NMR ($CDCl_3$): 1.45 (*t*, *J* = 7.0, 3 H); 2.56 (*s*, 3 H); 2.62 (*s*, 3 H); 4.18 (*q*, *J* = 7.0, 2 H); 6.67 (*d*, *J* = 2.1, 1 H); 7.14 (*d*, *J* = 7.6, 1 H); 7.67 (*t*, *J* = 7.6, 1 H); 7.75 (*d*, *J* = 2.1, 1 H); 8.16 (*d*, *J* = 7.6, 1 H).

4,4′-Diethoxy-6,6′-dimethyl-2,2′-bipyridine N,N′-*Dioxide* (**7**) was prepared analogously to **6** starting from **5**. Yield 73%. M.p. 230–233°. UV (EtOH): 268, 222. ^{1}H-NMR ($CDCl_3$): 1.42 (*t*, *J* = 7.0, 6 H); 2.55 (*s*, 6 H); 4.06 (*q*, *J* = 7.0, 4 H); 6.87 (*d*, *J* = 3.5, 2 H); 6.93 (*d*, *J* = 3.5, 2 H).

4,4′-Diethoxy-6,6′-dimethyl-2,2′-bipyridine (**9**) was prepared analogously to **13** starting from **7**. Yield 77%. M.p. 157–158°. UV (EtOH): 281, 257. ^{1}H-NMR ($CDCl_3$): 1.45 (*t*, *J* = 7.0, 6 H); 2.55 (*s*, 6 H); 4.18 (*q*, *J* = 7.0, 4 H); 6.66 (*d*, *J* = 2.4, 2 H); 7.33 (*d*, *J* = 2.4, 2 H).

4-Bromo-6,6′-dimethyl-2,2′-bipyridine N-*Oxide* (**10**). A mixture of **4** (1.0 g, 4.1 mmol), AcOH (15 ml), and AcBr (7.8 ml) was refluxed for 2 h. The cooled soln. was poured on ice and neutralized with 10% NaOH soln. The product was filtered and purified by FC (silica gel, 10% MeOH/$CHCl_3$). UV (EtOH): 275, 247. ^{1}H-NMR ($CDCl_3$): 2.55 (*s*, 3 H); 2.62 (*s*, 3 H); 7.21 (*d*, *J* = 7.8, 1 H); 7.41 (*d*, *J* = 2.9, 1 H); 7.70 (*t*, *J* = 7.8, 1 H); 8.23 (*d*, *J* = 2.9, 1 H); 8.65 (*d*, *J* = 7.8, 1 H).

4-Bromo-6,6′-dimethyl-2,2′-bipyridine (**11**) was prepared analogously to **13** starting from **10**. UV (EtOH): 291, 242, 217. ^{1}H-NMR ($CDCl_3$): 2.59 (*s*, 3 H); 2.62 (*s*, 3 H); 7.17 (*d*, *J* = 7.6, 1 H); 7.33 (*d*, *J* = 1.5, 1 H); 7.68 (*t*, *J* = 7.6, 1 H); 8.17 (*d*, *J* = 7.6, 1 H); 8.41 (*d*, *J* = 1.5, 1 H).

4,4′-Dibromo-6,6′-dimethyl-2,2′-bipyridine (**12**). Compound **5** (5.00 g, 16.3 mmol) was added slowly to a cold mixture of AcBr (10.0 ml, 135 mmol), PBr_3 (16 ml, 49 mmol), and AcOH (10 ml). After refluxing the soln. for 2 h, it was poured on ice, and the pH was adjusted to 7 with 30% NaOH soln. The product was extracted with $CHCl_3$ and purified by FC (silica gel, CH_2Cl_2). Yield 12%. UV (EtOH): 289, 248. ^{1}H-NMR ($CDCl_3$): 2.60 (*s*, 6 H); 7.36 (*d*, *J* = 1.7, 2 H); 8.40 (*d*, *J* = 1.7, 2 H).

3,6-Dibromo-2-methylpyridine (see *Scheme 2*) was formed as a side product (*ca.* 1%) in the synthesis of 2-bromo-6-methylpyridine [12]. M.p. 37°. UV (EtOH): 278, 229. ^{1}H-NMR ($CDCl_3$): 2.60 (*s*, 3 H); 7.17 (*d*, *J* = 8.2, 1 H); 7.60 (*d*, *J* = 8.2, 1 H).

5-Bromo-6,6′-dimethyl-2,2′-bipyridine (**15**). When trying to prepare 5,5′-dibromo-6,6′-dimethyl-2,2′-bipyridine analogously to **1a** starting from 3,6-dibromo-2-methylpyridine (1.25 g, 5.0 mmol), only **15** was isolated: 0.20 g (31%). UV (EtOH): 296, 251, 245. ^{1}H-NMR ($CDCl_3$): 2.61 (*s*, 3 H); 2.73 (*s*, 3 H); 7.16 (*d*, *J* = 7.6, 1 H); 7.67 (*t*, *J* = 7.6, 1 H); 7.88 (*d*, *J* = 8.5, 1 H); 8.12 (*d*, *J* = 8.5, 1 H); 8.19 (*d*, *J* = 7.6, 1 H).

6,6′-Dimethyl-2,2′-bipyridine-3,3′-dicarboxylic Acid (**16**). A mixture of 2,9-dimethyl-1,10-phenanthroline (2.50 g, 12.1 mmol), NaOH (0.76 g, 19 mmol), $KMnO_4$ (4.51 g, 28.5 mmol), and H_2O (60 ml) was refluxed for 24 h. The mixture was filtered and evaporated to ½ volume, the pH adjusted to 2 with conc. HCl, and the precipitated product filtered: 0.74 g (22%). UV (EtOH): 270, 226. ^{1}H-NMR ((D_6)DMSO): 2.60 (*s*, 6 H); 7.58 (*d*, *J* = 8.1, 2 H); 8.38 (*d*, *J* = 8.1, 2 H).

Diethyl 6,6′-Dimethyl-2,2′-bipyridine-3,3′-dicarboxylate (**17**). A soln. of $SOCl_2$ (0.5 ml) and EtOH (10 ml) was stirred for 15 min, **16** (180 mg, 0.66 mmol) added, and the mixture refluxed overnight. After pouring the soln. on ice, it was neutralized with solid Na_2CO_3 and extracted with AcOEt. Evaporation gave **17** (140 mg, 65%). UV (EtOH): 270, 227. ^{1}H-NMR ($CDCl_3$): 1.01 (*t*, *J* = 7.0, 6 H); 2.63 (*s*, 6 H); 4.08 (*q*, *J* = 7.0, 4 H); 7.28 (*d*, *J* = 8.1, 2 H); 8.28 (*d*, *J* = 8.1, 2 H).

6,6'-Dimethyl-2,2'-bipyridine-4,4'-dicarboxylic Acid (**22**). $KMnO_4$ (34.04 g, 215 mmol) was added to a warm mixture of **20** (5.24 g, 16.6 mmol), *t*-BuOH (1000 ml), and H_2O (210 ml). After refluxing overnight, the mixture was filtered through *Celite*. The soln. was evaporated to 200 ml, the pH adjusted to 2 with 2N HCl, and the precipitated product filtered: 1.36 g (30%). UV (EtOH): 304, 235 (sh). ^{1}H-NMR ((D_6)DMSO): 2.67 (*s*, 6 H); 7.77 (*s*, 2 H); 8.64 (*s*, 2 H).

Diethyl 6,6'-Dimethyl-2,2'-bipyridine-4,4'-dicarboxylate (**23**) was prepared analogously to **17** starting from **22**. Yield 75%. UV (EtOH): 308, 241. ^{1}H-NMR ($CDCl_3$): 1.43 (*t*, *J* = 7.2, 6 H); 2.63 (*s*, 6 H); 4.45 (*q*, *J* = 7.2, 4 H); 7.76 (*s*, 2 H); 8.75 (*s*, 2 H).

6,6'-Dimethyl-2,2'-bipyridine-3,3'-diol (**24**). A mixture of 6-methylpyridin-3-ol (24.0 g, 219 mmol), PbO_2 (98.2 g, 411 mmol), and toluene (1.0 l) was refluxed overnight. The hot mixture was filtered, the soln. evaporated, the residue extracted with boiling petroleum ether (b.p. 40–60°), and the product crystallized on cooling: 4.4 g (9.3%). UV (EtOH): 350, 246. ^{1}H-NMR ($CDCl_3$): 2.52 (*s*, 6 H); 7.10 (*d*, *J* = 8.2, 2 H); 7.31 (*d*, *J* = 8.2, 2 H).

6,6'-Dimethyl-2,2'-bipyridine-3,3'-diyl Dibenzoate (**25**). A soln. of **24** (0.22 g, 1.0 mmol), benzoyl chloride (0.30 g, 2.1 mmol), and pyridine (12 ml) was stirred at r.t. for 1.5 h. $CHCl_3$ (60 ml) was added, the soln. extracted with sat. $NaHCO_3$ soln. (80 ml), the org. phase evaporated, and the residue triturated with cyclohexane: 0.22 g (51%). UV (EtOH): 276, 232. ^{1}H-NMR ($CDCl_3$): 2.33 (*s*, 6 H); 7.17 (*d*, *J* = 8.5, 2 H); 7.40–7.45 (*m*, 4 H); 7.56–7.62 (*m*, 2 H); 7.60 (*d*, *J* = 8.5, 2 H); 7.99–8.03 (*m*, 4 H).

Compounds **18–21** were prepared according to [15].

6,6'-Dimethyl-4,4'-diphenyl-2,2'-bipyridine (**18**). UV (EtOH): 302, 246. ^{1}H-NMR ($CDCl_3$): 2.71 (*s*, 6 H); 7.40 (*s*, 2 H); 7.44 (*t*, *J* = 7.3, 2 H); 7.50 (*t*, *J* = 7.3, 4 H); 7.76 (*d*, *J* = 7.3, 4 H); 8.48 (*s*, 2 H).

4,4'-Bis(4-methoxyphenyl)-6,6'-dimethyl-2,2'-bipyridine (**19**). UV (EtOH): 285, 267. ^{1}H-NMR ($CDCl_3$): 2.68 (*s*, 6 H); 3.87 (*s*, 6 H); 7.01 (*d*, *J* = 8.7, 4 H); 7.36 (*d*, *J* = 1.2, 2 H); 7.72 (*d*, *J* = 8.7, 4 H); 8.44 (*d*, *J* = 1.2, 2 H).

4,4'-Bis(fur-2-yl)-6,6'-dimethyl-2,2'-bipyridine (**20**). UV (EtOH): 293, 268. ^{1}H-NMR ($CDCl_3$): 2.68 (*s*, 6 H); 6.49–6.58 (*m*, 2 H); 6.98 (*d*, *J* = 3.3, 2 H); 7.44 (*d*, *J* = 1.2, 2 H); 7.56 (*d*, *J* = 1.2, 2 H); 8.46 (*d*, *J* = 1.2, 2 H).

6,6'-Dimethyl-4,4'-distyryl-2,2'-bipyridine (**21**). UV (EtOH): 311, 227. ^{1}H-NMR ($CDCl_3$): 2.69 (*s*, 6 H); 7.12 (*d*, *J* = 16.3, 2 H); 7.28 (*s*, 2 H); 7.32 (*t*, *J* = 7.3, 2 H); 7.40 (*t*, *J* = 7.3, 4 H); 7.43 (*d*, *J* = 16.3, 2 H); 7.58 (*d*, *J* = 7.3, 4 H); 8.33 (*s*, 2 H).

2. *General Method for the Synthesis of 6,6'-Bis(bromomethyl)-2,2'-bipyridines* (**26–36**) *Using* N-*Bromosuccinimide* (*Route 1*). A mixture of 6,6'-dimethyl-2,2'-bipyridine derivative (1.0 mmol), NBS (0.39 g, 2.2 mmol), dibenzoyl peroxide (25 mg, 0.10 mmol), and CCl_4 (25 ml) was refluxed for 2 h to overnight, usually without UV light. The cooled mixture was filtered and evaporated and the 6,6'-bis(bromomethyl)-2,2'-bipyridine derivative purified by FC (silica gel, MeOH/$CHCl_3$).

6,6'-Bis(bromomethyl)-2,2'-bipyridine (**26**) was prepared according to [19].

6,6'-Bis(bromomethyl)-4-nitro-2,2'-bipyridine (**27**). UV (EtOH): 322, 288. ^{1}H-NMR ($CDCl_3$): 4.65 (*s*, 2 H); 4.71 (*s*, 2 H); 7.56 (*dd*, *J* = 0.9, 7.8, 1 H); 7.88 (*t*, *J* = 7.8, 1 H); 8.15 (*d*, *J* = 2.0, 1 H); 8.41 (*dd*, *J* = 0.9, 7.8, 1 H); 9.07 (*d*, *J* = 2.0, 1 H).

6,6'-Bis(bromomethyl)-4,4'-dinitro-2,2'-bipyridine (**28**). UV (EtOH): 319, 236 (sh). ^{1}H-NMR ($CDCl_3$): 4.77 (*s*, 4 H); 8.29 (*s*, 2 H); 9.12 (*s*, 2 H).

6,6'-Bis(bromomethyl)-4-ethoxy-2,2'-bipyridine (**29**). UV (EtOH): 286, 225. ^{1}H-NMR ($CDCl_3$): 1.45 (*t*, *J* = 7.0, 3 H); 4.19 (*q*, *J* = 7.0, 2 H); 4.55 (*s*, 2 H); 4.60 (*s*, 2 H); 6.95 (*d*, *J* = 2.3, 1 H); 7.43 (*dd*, *J* = 0.9, 7.6, 1 H); 7.77 (*t*, *J* = 7.6, 1 H); 7.90 (*d*, *J* = 2.3, 1 H); 8.35 (*dd*, *J* = 0.9, 7.6, 1 H).

6,6'-Bis(bromomethyl)-4,4'-diethoxy-2,2'-bipyridine (**30**). UV (EtOH): 281. ^{1}H-NMR ($CDCl_3$): 1.47 (*t*, *J* = 7.0, 6 H); 4.21 (*q*, *J* = 7.0, 4 H); 4.55 (*s*, 4 H); 6.97 (*d*, *J* = 2.3, 2 H); 7.90 (*d*, *J* = 2.3, 2 H).

4-Bromo-6,6'-bis(bromomethyl)-2,2'-bipyridine (**31**). UV (EtOH): 290. ^{1}H-NMR ($CDCl_3$): 4.56 (*s*, 2 H); 4.62 (*s*, 2 H); 7.49 (*dd*, *J* = 1.0, 7.8, 1 H); 7.63 (*d*, *J* = 1.7, 1 H); 7.82 (*t*, *J* = 7.8, 1 H); 8.35 (*dd*, *J* = 1.0, 7.8, 1 H); 8.57 (*d*, *J* = 1.7, 1 H).

4,4'-Dibromo-6,6'-bis(bromomethyl)-2,2'-bipyridine (**32**). UV (EtOH): 290, 248. ^{1}H-NMR ($CDCl_3$): 4.57 (*s*, 4 H); 7.67 (*d*, *J* = 1.7, 2 H); 8.56 (*d*, *J* = 1.7, 2 H).

Diethyl 6,6'-Bis(bromomethyl)-2,2'-bipyridine-3,3'-dicarboxylate (**33**). UV (EtOH): 274, 230. ^{1}H-NMR ($CDCl_3$): 1.03 (*t*, *J* = 7.2, 6 H); 4.11 (*q*, *J* = 7.2, 4 H); 4.57 (*s*, 4 H); 7.62 (*d*, *J* = 8.1, 2 H); 8.39 (*d*, *J* = 8.1, 2 H).

Diethyl 6,6'-Bis(bromomethyl)-2,2'-bipyridine-4,4'-dicarboxylate (**34**). UV (EtOH): 318, 308, 246. ^{1}H-NMR ($CDCl_3$): 1.46 (*t*, *J* = 7.2, 6 H); 4.49 (*q*, *J* = 7.2, 4 H); 4.70 (*s*, 4 H); 8.06 (*d*, *J* = 1.5, 2 H); 8.90 (*d*, *J* = 1.5, 2 H).

6,6'-Bis(bromomethyl)-2,2'-bipyridine-3,3'-diyl Dibenzoate (**35**). UV (EtOH): 278, 233. ^{1}H-NMR ($CDCl_3$): 4.27 (*s*, 4 H); 7.43–7.48 (*m*, 4 H); 7.53 (*d*, *J* = 8.8, 2 H); 7.57–7.63 (*m*, 2 H); 7.75 (*d*, *J* = 8.8, 2 H); 8.02–8.05 (*m*, 4 H).

6,6′-Bis(bromomethyl)-4,4′-diphenyl-2,2′-bipyridine (**36**). UV (EtOH): 299, 252. ^{1}H-NMR ($CDCl_3$): 4.71 (*s*, 4 H); 7.46–7.55 (*m*, 6 H); 7.71 (*d*, *J* = 1.5, 2 H); 7.75–7.83 (*m*, 4 H); 8.67 (*d*, *J* = 1.5, 2 H).

3. *General Method for the Synthesis of 2,2′-Bipyridine* N,N′*-Oxides* (**37–42**) (*Route 2*). A mixture of 6,6′-dimethyl-2,2′-bipyridine derivative (or 6,6′-bis(chloromethyl)-2,2′-bipyridine [9]; 4.0 mmol), 3-chloroperbenzoic acid (50–60%; 3.0 g, 8.8 mmol), and $CHCl_3$ (90 ml) was stirred for 3 h. The soln. was washed with sat. $NaHCO_3$ soln. (2 × 100 ml), dried (Na_2SO_4), and evaporated. The product was purified by FC (silica gel, $CHCl_3$ or 5% MeOH/$CHCl_3$).

4,4′,6,6′-Tetramethyl-2,2′-bipyridine N,N′*-Dioxide* (**37**). Yield 46%. UV (EtOH): 265, 226. ^{1}H-NMR ($CDCl_3$): 2.33 (*s*, 6 H); 2.54 (*s*, 6 H); 7.15 (br. *s*, 2 H); 7.17 (br. *s*, 2 H).

5-Bromo-6,6′-dimethyl-2,2′-bipyridine N,N′*-Dioxide* (**38**). Yield 71%. UV (EtOH): 264, 235. ^{1}H-NMR ((D$_6$)DMSO): 2.38 (*s*, 3 H); 2.56 (*s*, 3 H); 7.33 (*t*, *J* = 7.8, 1 H); 7.44 (*d*, *J* = 8.5, 1 H); 7.47 (*dd*, *J* = 2.0, 7.8, 1 H); 7.60 (*dd*, *J* = 2.0, 7.8, 1 H); 7.70 (*d*, *J* = 8.5, 1 H).

4,4′-Bis(4-methoxyphenyl)-6,6′-dimethyl-2,2′-bipyridine N,N′*-Dioxide* (**39**). Yield 21%. UV (EtOH): 313, 226. ^{1}H-NMR ($CDCl_3$): 2.64 (*s*, 6 H); 3.84 (*s*, 6 H); 6.95 (*d*, *J* = 8.7, 4 H); 7.55 (*s*, 2 H); 7.56 (*d*, *J* = 8.7, 4 H); 7.59 (*s*, 2 H).

4,4′-Bis(fur-2-yl)-6,6′-dimethyl-2,2′-bipyridine N,N′*-Dioxide* (**40**). Yield 47%. UV (EtOH): 336, 321, 244. ^{1}H-NMR ($CDCl_3$): 2.61 (*s*, 6 H); 6.46–6.56 (*m*, 2 H); 6.74 (*d*, *J* = 3.6, 2 H); 7.51 (*d*, *J* = 1.2, 2 H); 7.61 (br. *s*, 4 H).

6,6′-Dimethyl-4,4′-distyryl-2,2′-bipyridine N,N′*-Dioxide* (**41**). Yield 67%. UV (EtOH): 341, 241. ^{1}H-NMR ($CDCl_3$): 2.61 (*s*, 6 H); 6.98 (*d*, *J* = 16.3, 2 H); 7.16 (*d*, *J* = 16.3, 2 H); 7.31 (*t*, *J* = 7.3, 2 H); 7.38 (*t*, *J* = 7.3, 4 H); 7.45 (*d*, *J* = 2.5, 2 H); 7.50 (*d*, *J* = 7.3, 4 H); 7.53 (*d*, *J* = 2.5, 2 H).

6,6′-Bis(chloromethyl)-2,2′-bipyridine N,N′*-Dioxide* (**42**). Yield 27%. UV (EtOH): 261, 233. ^{1}H-NMR ((D$_6$)DMSO): 4.90 (*s*, 4 H); 7.47 (*t*, *J* = 7.8, 2 H); 7.70 (*dd*, *J* = 2.1, 7.8, 2 H); 7.86 (*dd*, *J* = 2.1, 7.8, 2 H).

4. *General Method for the Synthesis of 2,2′-Bipyridine-6,6′-dimethyl Diacetates* (**43–47**) (*Route 2*). A soln. of 6,6′-dimethyl-2,2′-bipyridine *N,N′*-dioxide derivative (0.90 mmol) in Ac_2O (2 ml) was refluxed for 15 min. The mixture was evaporated and the product purified by FC (silica gel, 2–5% MeOH/$CHCl_3$).

4,4′-Dimethyl-2,2′-bipyridine-6,6′-dimethyl Diacetate (**43**). Yield 71%. UV (EtOH): 286, 243. ^{1}H-NMR ($CDCl_3$): 2.17 (*s*, 6 H); 2.43 (*s*, 6 H); 5.10 (*s*, 4 H); 7.15 (*s*, 2 H); 8.17 (*s*, 2 H).

5-Bromo-2,2′-bipyridine-6,6′-dimethyl Diacetate (**44**). Yield 52%. UV (EtOH): 293, 251, 246. ^{1}H-NMR ($CDCl_3$): 2.19 (*s*, 3 H); 2.22 (*s*, 3 H); 5.29 (*s*, 2 H); 5.39 (*s*, 2 H); 7.37 (*d*, *J* = 7.8, 1 H); 7.82 (*t*, *J* = 7.8, 1 H); 7.96 (*d*, *J* = 8.4, 1 H); 8.29 (*d*, *J* = 8.4, 1 H); 8.31 (*d*, *J* = 7.8, 1 H).

4,4′-Bis(4-methoxyphenyl)-2,2′-bipyridine-6,6′-dimethyl Diacetate (**45**). Yield 74%. UV (EtOH): 291, 268. ^{1}H-NMR ($CDCl_3$): 2.20 (*s*, 6 H); 3.87 (*s*, 6 H); 5.37 (*s*, 4 H); 7.01 (*d*, *J* = 9.0, 4 H); 7.54 (*d*, *J* = 1.5, 2 H); 7.73 (*d*, *J* = 9.0, 4 H); 8.60 (*d*, *J* = 1.5, 2 H).

4,4′-Bis(fur-2-yl)-2,2′-bipyridine-6,6′-dimethyl Diacetate (**46**). Yield 41%. UV (EtOH): 300, 276, 229. ^{1}H-NMR ($CDCl_3$): 2.23 (*s*, 6 H); 5.36 (*s*, 4 H); 6.52–6.60 (*m*, 2 H); 7.02 (*d*, *J* = 3, 2 H); 7.61 (*d*, *J* = 1, 2 H); 8.61 (*d*, *J* = 1, 2 H).

4,4′-Distyryl-2,2′-bipyridine-6,6′-dimethyl Diacetate (**47**). Yield 29%. UV (EtOH): 313, 227. ^{1}H-NMR ($CDCl_3$): 2.24 (*s*, 6 H); 5.37 (*s*, 4 H); 7.16 (*d*, *J* = 16.4, 2 H); 7.34 (*t*, *J* = 7.4, 2 H); 7.42 (*t*, *J* = 7.4, 4 H); 7.47 (*d*, *J* = 1.2, 2 H); 7.48 (*d*, *J* = 16.4, 2 H); 7.60 (*d*, *J* = 7.4, 4 H); 8.49 (*d*, *J* = 1.2, 2 H).

5. *General Method for the Synthesis of 2,2′-Bipyridine-6,6′-dimethanols* (**48–52**) (*Route 2*). To a soln. of 2,2′-bipyridine-6,6′-dimethyl diacetate derivative (0.50 mmol) in acetone (2.5 ml), 1N NaOH (1 ml) was added and the mixture stirred for 30 min. After addition of H_2O (10 ml), the mixture was extracted with $CHCl_3$ (2 × 10 ml) and the org. phase dried with molecular sieves and evaporated.

4,4′-Dimethyl-2,2′-bipyridine-6,6′-dimethanol (**48**). Yield 45%. UV (EtOH): 288, 242. ^{1}H-NMR ($CDCl_3$): 2.42 (*s*, 6 H); 4.73 (*s*, 4 H); 7.00 (*s*, 2 H); 8.05 (*s*, 2 H).

5-Bromo-2,2′-bipyridine-6,6′-dimethanol (**49**). Yield 76%. UV (EtOH): 296, 252, 245. ^{1}H-NMR ($CDCl_3$): 4.82 (*s*, 2 H); 4.84 (*s*, 2 H); 7.37 (*d*, *J* = 7.7, 1 H); 7.85 (*t*, *J* = 7.7, 1 H); 7.99 (*d*, *J* = 8.2, 1 H); 8.29 (*d*, *J* = 8.2, 1 H); 8.31 (*d*, *J* = 7.7, 1 H).

4,4′-Bis(4-methoxyphenyl)-2,2′-bipyridine-6,6′-dimethanol (**50**). Yield 50%. UV (EtOH): 289, 275. ^{1}H-NMR ($CDCl_3$): 3.89 (*s*, 6 H); 4.90 (*s*, 4 H); 7.04 (*d*, *J* = 8.3, 4 H); 7.44 (*s*, 2 H); 7.71 (*d*, *J* = 8.3, 4 H); 8.56 (*s*, 2 H).

4,4′-Bis(fur-2-yl)-2,2′-bipyridine-6,6′-dimethanol (**51**). Yield 86%. UV (EtOH): 298, 275. ^{1}H-NMR ((D$_6$)DMSO): 4.74 (*s*, 2 H); 6.66–6.77 (*m*, 2 H); 7.34 (*d*, *J* = 2.7, 2 H); 7.82 (*d*, *J* = 1.2, 2 H); 7.94 (*d*, *J* = 1.6, 2 H); 8.51 (*d*, *J* = 1.6, 2 H).

4,4′-Distyryl-2,2′-bipyridine-6,6′-dimethanol (**52**). Yield 81%. UV (EtOH): 311, 228. ^{1}H-NMR ((D$_6$)DMSO): 4.73 (*d*, *J* = 5.9, 4 H); 5.56 (*t*, *J* = 5.9, 2 H); 7.35 (*t*, *J* = 7.3, 2 H); 7.44 (*t*, *J* = 7.3, 4 H); 7.47 (*d*, *J* = 16.4, 2 H); 7.60 (*d*, *J* = 16.4, 2 H); 7.76 (*d*, *J* = 7.3, 4 H); 7.76 (*s*, 2 H); 8.40 (*s*, 2 H).

6. *General Method for the Synthesis of 6,6′-Bis(chloromethyl)-2,2′-bipyridines* (**53–56**) (*Route 2*). The 2,2′-bipyridine-6,6′-dimethanol (1.2 mmol) was dissolved in $SOCl_2$ (2 ml) and stirred at r.t. for 1.5 h. After evaporation, the residue was dissolved in $CHCl_3$ and washed with 10% $NaHCO_3$ soln. The $CHCl_3$ phase was dried (Na_2SO_4) and evaporated and the product purified by FC (silica gel, CH_2Cl_2).

6,6′-Bis(chloromethyl)-4,4′-dimethyl-2,2′-bipyridine (**53**). Yield 47%. UV (EtOH): 286, 244. ^{1}H-NMR ($CDCl_3$): 2.43 (*s*, 6 H); 4.68 (*s*, 4 H); 7.23 (*s*, 2 H); 8.12 (*s*, 2 H).

6,6′-Bis(chloromethyl)-4,4′-bis(4-methoxyphenyl)-2,2′-bipyridine (**54**). Yield 74%. UV (EtOH): 292, 265. ^{1}H-NMR ($CDCl_3$): 3.88 (*s*, 6 H); 4.85 (*s*, 4 H); 7.03 (*d*, *J* = 8.4, 4 H); 7.71 (*d*, *J* = 1, 2 H); 7.77 (*d*, *J* = 8.4, 4 H); 8.66 (*d*, *J* = 1, 2 H).

6,6′-Bis(chloromethyl)-4,4′-bis(fur-2-yl)-2,2′-bipyridine (**55**). Yield 86%. UV (EtOH): 300, 275. ^{1}H-NMR ($CDCl_3$): 4.81 (*s*, 4 H); 6.52–6.62 (*m*, 2 H); 7.05 (*d*, *J* = 3.3, 2 H); 7.61 (*d*, *J* = 1.5, 2 H); 7.78 (*d*, *J* = 1.3, 2 H); 8.62 (*d*, *J* = 1.3, 2 H).

6,6′-Bis(chloromethyl)-4,4′-distyryl-2,2′-bipyridine (**56**). Yield 82%. UV (EtOH): 313. ^{1}H-NMR ($CDCl_3$): 4.82 (*s*, 4 H); 7.17 (*d*, *J* = 16.5, 2 H); 7.35 (*t*, *J* = 7.3, 2 H); 7.42 (*t*, *J* = 7.3, 4 H); 7.48 (*d*, *J* = 16.5, 2 H); 7.60 (*d*, *J* = 7.3, 4 H); 7.62 (*s*, 2 H); 8.50 (*s*, 2 H).

7. *5-Bromo-6,6′-bis(bromomethyl)-2,2′-bipyridine* (**57**). A mixture of **49** (0.53 g, 1.8 mmol), PBr_3 (0.73 g, 2.7 mmol), and $CHCl_3$ (5 ml) was refluxed for 1 h. The soln. was evaporated, the residue dissolved in $CHCl_3$ and washed with sat. $NaHCO_3$ soln., the $CHCl_3$ phase evaporated, and the product purified by FC (silica gel, CH_2Cl_2). Yield 12%. UV (EtOH): 293, 256. ^{1}H-NMR ($CDCl_3$): 4.61 (*s*, 2 H); 4.78 (*s*, 2 H); 7.48 (*d*, *J* = 7.8, 1 H); 7.83 (*t*, *J* = 7.8, 1 H); 7.98 (*d*, *J* = 8.4, 1 H); 8.28 (*d*, *J* = 8.4, 1 H); 8.37 (*d*, *J* = 7.8, 1 H).

8. *General Method for the Synthesis of Tetra(*tert*-butyl) or Tetraethyl 2,2′,2″,2‴-[2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetates)* **58–74**. A mixture of 6,6′-bis(halomethyl)-2,2′-bipyridine derivative (0.40 mmol), di(*tert*-butyl) iminobis(acetate) or diethyl iminobis(acetate) (0.88 mmol), Na_2CO_3 (0.21 g, 2.0 mmol), and dry MeCN (10 ml) was refluxed overnight. The cooled mixture was filtered and evaporated. Purification by FC (silica gel, $CHCl_3$ or MeOH/$CHCl_3$) gave the viscous tetraester.

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**58**). UV (EtOH): 290, 238. ^{1}H-NMR ($CDCl_3$): 1.53 (*s*, 36 H); 3.53 (*s*, 8 H); 4.12 (*s*, 4 H); 7.57 (*d*, *J* = 7.5, 2 H); 7.77 (*t*, *J* = 7.5, 2 H); 8.30 (*d*, *J* = 7.5, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4,4′-Dimethyl-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**59**). UV (EtOH): 288, 243. ^{1}H-NMR ($CDCl_3$): 1.47 (*s*, 36 H); 2.41 (*s*, 6 H); 3.52 (*s*, 8 H); 4.09 (*s*, 4 H); 7.45 (*s*, 2 H); 8.12 (*s*, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4-Nitro-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**60**). UV (EtOH): 323, 286, 236. ^{1}H-NMR ($CDCl_3$): 1.48 (*s*, 36 H); 3.53 (*s*, 4 H); 3.55 (*s*, 4 H); 4.14 (*s*, 2 H); 4.25 (*s*, 2 H); 7.76 (*dd*, *J* = 1.0, 7.7, 1 H); 7.83 (*t*, *J* = 7.7, 1 H); 8.34 (*dd*, *J* = 1.0, 7.7, 1 H); 8.38 (*d*, *J* = 2.2, 1 H); 9.00 (*d*, *J* = 2.2, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4,4′-Dinitro-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**61**). UV (EtOH): 315. ^{1}H-NMR ($CDCl_3$): 1.49 (*s*, 36 H); 3.55 (*s*, 8 H); 4.28 (*s*, 4 H); 8.53 (*d*, *J* = 2.1, 2 H); 9.01 (*d*, *J* = 2.1, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4-Ethoxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**62**). UV (EtOH): 286, 218. ^{1}H-NMR ($CDCl_3$): 1.44 (*t*, *J* = 7.0, 3 H); 1.47 (*s*, 36 H); 3.53 (*s*, 8 H); 4.07 (*s*, 2 H); 4.11 (*s*, 2 H); 4.19 (*q*, *J* = 7.0, 2 H); 7.18 (*d*, *J* = 2.1, 1 H); 7.62 (*d*, *J* = 7.4, 1 H); 7.76 (*t*, *J* = 7.4, 1 H); 7.86 (*d*, *J* = 2.1, 1 H); 8.28 (*d*, *J* = 7.4, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4,4′-Diethoxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**63**). UV (EtOH): 281, 255, 215. ^{1}H-NMR ($CDCl_3$): 1.43 (*t*, *J* = 6.4, 6 H); 1.47 (*s*, 36 H); 3.52 (*s*, 8 H); 4.05 (*s*, 4 H); 4.18 (*q*, *J* = 6.4, 4 H); 7.17 (br. *s*, 2 H); 7.82 (br. *s*, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4-Bromo-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**64**). UV (EtOH): 291, 242. ^{1}H-NMR ($CDCl_3$): 1.47 (*s*, 36 H); 3.52 (*s*, 8 H); 4.10 (*s*, 2 H); 4.11 (*s*, 2 H); 7.66 (*d*, *J* = 7.6, 1 H); 7.78 (*t*, *J* = 7.6, 1 H); 7.83 (*s*, 1 H); 8.27 (*d*, *J* = 7.6, 1 H); 8.49 (*s*, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4,4′-Dibromo-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**65**). UV (EtOH): 290, 247, 221. ^{1}H-NMR ($CDCl_3$): 1.48 (*s*, 36 H); 3.51 (*s*, 8 H); 4.18 (*s*, 4 H); 7.89 (*d*, *J* = 1.7, 2 H); 8.47 (*d*, *J* = 1.7, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(5-Bromo-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**66**). UV (EtOH): 305, 296, 252. ^{1}H-NMR ($CDCl_3$): 1.47 (*s*, 36 H); 3.52 (*s*, 4 H); 3.68 (*s*, 4 H); 4.11 (*s*, 2 H); 4.30 (*s*, 2 H); 7.67 (*t*, *J* = 6.7, 1 H); 7.69 (*dd*, *J* = 2.0, 6.7, 1 H); 7.90 (*d*, *J* = 8.3, 1 H); 8.25 (*d*, *J* = 8.3, 1 H); 8.34 (*dd*, *J* = 2.0, 6.7, 1 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-{[3,3′-Bis(ethoxycarbonyl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}-tetrakis(acetate)* (**67**). UV (EtOH): 270, 225. ^{1}H-NMR ($CDCl_3$): 1.02 (*t*, *J* = 7.0, 6 H); 1.45 (*s*, 36 H); 3.49 (*s*, 8 H); 4.07 (*q*, *J* = 7.0, 4 H); 4.10 (*s*, 4 H); 7.88 (*d*, *J* = 7.9, 2 H); 8.35 (*d*, *J* = 7.9, 2 H).

Tetraethyl 2,2′,2″,2‴-{[4,4′-Bis(ethoxycarbonyl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis(acetate) (**68**). UV (EtOH): 307, 241. ^{1}H-NMR ($CDCl_3$): 1.26 (*t*, *J* = 7.2, 12 H); 1.44 (*t*, *J* = 7.2, 6 H); 3.69 (*s*, 8 H); 4.19 (*q*, *J* = 7.2, 8 H); 4.25 (*s*, 4 H); 4.46 (*q*, *J* = 7.2, 4 H); 8.16 (*d*, *J* = 1, 2 H); 8.82 (*d*, *J* = 1, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-{[3,3′-Bis(benzoyloxy)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis-(acetate)* (**69**). UV (EtOH): 276, 232. ^{1}H-NMR ($CDCl_3$): 1.45 (*s*, 36 H); 3.29 (*s*, 8 H); 3.74 (*s*, 4 H); 7.43 (*t*, *J* = 7.9, 4 H); 7.58 (*t*, *J* = 7.9, 2 H); 7.70 (*d*, *J* = 8.6, 2 H); 7.79 (*d*, *J* = 8.6, 2 H); 8.00 (*d*, *J* = 7.9, 4 H).

Tetraethyl 2,2′,2″,2‴-[(4,4′-Diphenyl-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate) (**70**). UV (EtOH): 300, 251. ^{1}H-NMR ($CDCl_3$): 1.21 (*t*, *J* = 7.2, 12 H); 3.71 (*s*, 8 H); 4.16 (*q*, *J* = 7.2, 8 H); 4.23 (*s*, 4 H); 7.42–7.59 (*m*, 6 H); 7.74 (*m*, 4 H); 7.86 (*d*, *J* = 1.5, 2 H); 8.62 (*d*, *J* = 1.5, 2 H).

Tetraethyl 2,2′,2″,2‴-{[4,4′-Bis(4-methoxyphenyl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis-(acetate) (**71**). UV (EtOH): 289, 268. ^{1}H-NMR ($CDCl_3$): 1.22 (*t*, *J* = 7.2, 12 H); 3.71 (*s*, 8 H); 3.88 (*s*, 6 H); 4.16 (*q*, *J* = 7.2, 8 H); 4.22 (*s*, 4 H); 7.01 (*d*, *J* = 8.4, 4 H); 7.77 (*d*, *J* = 8.4, 4 H); 7.83 (*d*, *J* = 1.6, 2 H); 8.57 (*d*, *J* = 1.6, 2 H).

Tetraethyl 2,2′,2″,2‴-{[4,4′-Bis(fur-2-yl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis(acetate) (**72**). UV (EtOH): 297. ^{1}H-NMR ($CDCl_3$): 1.25 (*t*, *J* = 7.2, 12 H); 3.72 (*s*, 8 H); 4.20 (*q*, *J* = 7.2, 8 H); 4.21 (*s*, 4 H); 6.51–6.59 (*m*, 2 H); 7.05 (*d*, *J* = 3.3, 2 H); 7.58 (*d*, *J* = 1.5, 2 H); 7.86 (*d*, *J* = 1.3, 2 H); 8.57 (*d*, *J* = 1.3, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(4,4′-Distyryl-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* (**73**). UV (EtOH): 313, 228. ^{1}H-NMR ($CDCl_3$): 1.48 (*s*, 36 H); 3.59 (*s*, 8 H); 4.20 (*s*, 4 H); 7.16 (*d*, *J* = 16.4, 2 H); 7.32 (*t*, *J* = 7.4, 2 H); 7.40 (*t*, *J* = 7.4, 4 H); 7.48 (*d*, *J* = 16.4, 2 H); 7.58 (*d*, *J* = 7.4, 4 H); 7.76 (*s*, 2 H); 8.44 (*s*, 2 H).

*Tetra(*tert*-butyl) 2,2′,2″,2‴-[(2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetate)* N,N′*-Dioxide* (**74**). UV (EtOH): 261, 225. ^{1}H-NMR ($CDCl_3$): 1.46 (*s*, 36 H); 3.53 (*s*, 8 H); 4.22 (*s*, 4 H); 7.34–7.36 (*m*, 4 H); 7.98 (*d*, *J* = 6.4, 2 H).

9. *General Method for the Hydrolysis of Tetra(*tert*-butyl) Esters to 2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis-(methylenenitrilo)]tetrakis(acetic Acids)* **75**–**84**, **86**, **90**, *and* **91**. A soln. of tetra(*tert*-butyl) ester (0.30 mmol) in CF_3COOH (5 ml) was stirred for 2 h at r.t. After evaporation, the mixture was triturated with Et_2O and filtered. The yield was usually *ca.* 100%.

2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**75**). UV (H_2O): 299, 287, 237. UV ([Eu^{III} (**75**)], H_2O): 314, 306, 246. ^{1}H-NMR ((D_6)DMSO): 3.77 (*s*, 8 H); 4.26 (*s*, 4 H); 7.62 (*d*, *J* = 7.7, 2 H); 8.00 (*t*, *J* = 7.7, 2 H); 8.32 (*d*, *J* = 7.7, 2 H).

2,2′,2″,2‴-[(4,4′-Dimethyl-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**76**). UV (H_2O): 295, 286, 242. UV ([Eu^{III} (**76**)], H_2O): 313, 304, 253. ^{1}H-NMR ((D_6)DMSO): 2.45 (*s*, 6 H); 3.75 (*s*, 8 H); 4.24 (*s*, 4 H); 7.50 (*s*, 2 H); 8.19 (*s*, 2 H).

2,2′,2″,2‴-[(4-Nitro-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**77**). UV (H_2O): 322, 282, 234. UV ([Eu^{III} (**77**)], H_2O): 330, 278. ^{1}H-NMR ((D_6)DMSO): 3.52 (*s*, 8 H); 4.07 (*s*, 2 H); 4.18 (*s*, 2 H); 7.62 (*d*, *J* = 7.7, 1 H); 7.99 (*t*, *J* = 7.7, 1 H); 8.24 (*d*, *J* = 2.1, 1 H); 8.29 (*d*, *J* = 7.7, 1 H); 8.80 (*d*, *J* = 2.1, 1 H).

2,2′,2″,2‴-[(4,4′-Dinitro-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**78**). UV (H_2O): 316, 234. UV ([Eu^{III} (**78**)], H_2O): 337, 235. ^{1}H-NMR ((D_6)DMSO): 3.59 (*s*, 8 H); 4.26 (*s*, 4 H); 8.48 (*d*, *J* = 2.0, 2 H); 8.82 (*d*, *J* = 2.0, 2 H).

2,2′,2″,2‴-[(4-Ethoxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**79**). UV (H_2O): 295, 286, 225. UV ([Eu^{III} (**79**)], H_2O): 308, 289, 231. ^{1}H-NMR ((D_6)DMSO): 1.42 (*t*, *J* = 7.0, 3 H); 3.70 (*s*, 8 H); 4.20 (*s*, 2 H); 4.22 (*s*, 2 H); 4.31 (*q*, *J* = 7.0, 2 H); 7.38 (*d*, *J* = 1.8, 1 H); 7.69 (*d*, *J* = 8.0, 1 H); 7.97 (*d*, *J* = 1.8, 1 H); 8.04 (*t*, *J* = 8.0, 1 H); 8.34 (*d*, *J* = 8.0, 1 H).

2,2′,2″,2‴-[(4,4′-Diethoxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**80**). UV (H_2O): 292, 281, 218. UV ([Eu^{III} (**80**)], H_2O): 305, 294, 229. ^{1}H-NMR ((D_6)DMSO): 1.39 (*t*, *J* = 6.6, 6 H); 3.57 (*s*, 8 H); 4.05 (*s*, 4 H); 4.22 (*q*, *J* = 6.6, 4 H); 7.23 (br. *s*, 2 H); 7.83 (br. *s*, 2 H).

2,2′,2″,2‴-[(4-Bromo-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**81**). UV (H_2O): 299, 288. UV ([Eu^{III} (**81**)], H_2O): 316, 305. ^{1}H-NMR ((D_6)DMSO): 3.66 (*s*, 8 H); 4.16 (*s*, 2 H); 4.31 (*s*, 2 H); 7.64 (*d*, *J* = 7.6, 1 H); 7.91 (*d*, *J* = 1.8, 1 H); 8.01 (*t*, *J* = 7.6, 1 H); 8.30 (*d*, *J* = 7.6, 1 H); 8.46 (*d*, *J* = 1.8, 1 H).

2,2′,2″,2‴-[(4,4′-Dibromo-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**82**). UV (H_2O): 288, 220. UV ([Eu^{III} (**82**)], H_2O): 315, 305, 220. ^{1}H-NMR ((D_6)DMSO): 3.53 (*s*, 8 H); 4.05 (*s*, 4 H); 7.91 (*d*, *J* = 1, 2 H); 8.36 (*d*, *J* = 1, 2 H).

2,2′,2″,2‴-[(5-Bromo-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**83**). UV (H_2O): 305, 294, 249. UV ([Eu^{III} (**83**)], H_2O): 322, 314, 258. ^{1}H-NMR ((D_6)DMSO): 3.52 (*s*, 4 H); 3.64 (*s*, 4 H); 4.05 (*s*, 4 H); 7.61 (*d*, *J* = 7.6, 1 H); 7.95 (*t*, *J* = 7.6, 1 H); 8.18 (br. *s*, 2 H); 8.25 (*d*, *J* = 7.6, 1 H).

2,2′,2″,2‴-{[3,3′-Bis(ethoxycarbonyl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis(acetic Acid) (**84**). UV (H_2O): 270. UV ([Eu^{III} (**84**)], H_2O): 285. ^{1}H-NMR ((D_6)DMSO): 0.93 (*t*, *J* = 7.0, 6 H); 3.69 (*s*, 8 H); 3.99 (*s*, 4 H); 4.01 (*q*, *J* = 7.0, 4 H); 7.76 (*d*, *J* = 7.9, 2 H); 8.27 (*d*, *J* = 7.9, 2 H).

2,2′,2″,2‴-{[3,3′-Bis(benzoyloxy)-2,2′-bipyridine]bis(methylenenitrilo)}tetrakis(acetic Acid) (**86**). UV (H_2O): 276, 237. UV ([Eu^{III} (**86**)], H_2O): 276, 237. ^{1}H-NMR ((D_6)DMSO): 3.35 (*s*, 8 H); 3.64 (*s*, 4 H); 7.53 (*t*, *J* = 7.5, 4 H); 7.70 (*t*, *J* = 7.5, 2 H); 7.70 (*d*, *J* = 8.5, 2 H); 7.89 (*d*, *J* = 7.5, 4 H); 7.93 (*d*, *J* = 8.5, 2 H).

2,2′,2″,2‴-[(4,4′-Distyryl-2,2′-bipyridine)bis(methylenenitrilo)]tetrakis(acetic Acid) (**90**). UV (H_2O): 315. UV ([Eu^{III} (**90**)], H_2O): 324, 236. ^{1}H-NMR ((D_6)DMSO): 3.76 (*s*, 8 H); 4.26 (*s*, 4 H); 7.38 (*t*, *J* = 7.3, 2 H); 7.42 (*d*, *J* = 16.5, 2 H); 7.45 (*t*, *J* = 7.3, 4 H); 7.65 (*d*, *J* = 16.5, 2 H); 7.75 (*d*, *J* = 7.3, 4 H); 7.85 (*s*, 2 H); 8.50 (*s*, 2 H).

2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) N,N′-*Dioxide* (**91**). UV (H_2O): 262, 223. UV ([Eu^{III} (**91**)], H_2O): 285, 225. ^{1}H-NMR ((D_6)DMSO): 3.56 (*s*, 8 H); 4.04 (*s*, 4 H); 7.48 (*t*, *J* = 7.6, 2 H); 7.55 (*dd*, *J* = 2.1, 7.6, 2 H); 7.79 (*dd*, *J* = 2.1, 7.6, 2 H).

10. *General Method for the Hydrolysis of Tetraethyl Esters to 2,2′,2″,2‴-[(2,2′-Bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acids)* **85** *and* **87**–**89**. To a soln. of tetraethyl ester (0.080 mmol) in acetone (1 ml), 1N NaOH (0.5 ml) was added. The mixture was stirred for 2 h at r.t. After neutralization with HCl, the soln. was evaporated and the product precipitated by adding more acetone.

2,2′,2″,2‴-[(4,4′-Dicarboxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**85**). UV (H_2O): 301, 240 (sh). UV ([Eu^{III} (**85**)], H_2O): 325, 245 (sh). ^{1}H-NMR (D_2O): 3.69 (*s*, 8 H); 4.45 (*s*, 4 H); 7.87 (*s*, 2 H); 8.58 (*s*, 2 H).

2,2′,2″,2‴-[(4,4′-Diphenyl-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid) (**87**). UV (H_2O): 305, 251. UV ([Eu^{III} (**87**)], H_2O): 326, 318, 256. ^{1}H-NMR ((D_6)DMSO): 3.61 (*s*, 8 H); 4.17 (*s*, 4 H); 7.54 (*t*, *J* = 7.2, 2 H); 7.60 (*t*, *J* = 7.2, 4 H); 7.91 (*d*, *J* = 7.2, 4 H); 7.94 (*d*, *J* = 1.5, 2 H); 8.60 (*d*, *J* = 1.5, 2 H).

2,2′,2″,2‴-{[4,4′-Bis(4-methoxyphenyl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis(acetic Acid) (**88**). UV (H_2O): 290, 267. UV ([Eu^{III} (**88**)], H_2O): 313, 278. ^{1}H-NMR ((D_6)DMSO): 3.85 (*s*, 6 H); 3.86 (*s*, 8 H); 4.37 (*s*, 4 H); 7.16 (*d*, *J* = 8.7, 4 H); 7.94 (*d*, *J* = 8.7, 4 H); 8.05 (*s*, 2 H); 8.71 (*s*, 2 H).

2,2′,2″,2‴-{[4,4′-Bis(fur-2-yl)-2,2′-bipyridine-6,6′-diyl]bis(methylenenitrilo)}tetrakis(acetic Acid) (**89**). UV (H_2O): 300, 225. UV ([Eu^{III} (**89**)], H_2O): 310, 291. ^{1}H-NMR ((D_6)DMSO): 4.19 (*s*, 8 H); 4.66 (*s*, 4 H); 6.78–6.79 (*m*, 2 H); 7.52 (*d*, *J* = 3.4, 2 H); 8.00–8.01 (*m*, 2 H); 8.01 (*s*, 2 H); 8.74 (*s*, 2 H).

11. *2,2′,2″,2‴-[(4-Amino-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid)* (**92**). Compound **77** (40 mg, 0.081 mmol) was dissolved in H_2O (10 ml) by adding $NaHCO_3$. Pd/C (5%; 10 mg) was added and H_2 bubbled through the soln., until the NO_2 group was reduced. The mixture was filtered and evaporated. UV (H_2O): 283, 239. UV ([Eu^{III} (**92**)], H_2O): 298, 244. ^{1}H-NMR (D_2O): 3.28 (*s*, 4 H); 3.36 (*s*, 4 H); 3.80 (*s*, 2 H); 3.99 (*s*, 2 H); 6.64 (*s*, 1 H); 7.18 (*s*, 1 H); 7.39 (*d*, *J* = 7.0, 2 H); 7.83–7.91 (*m*, 2 H).

12. *2,2′,2″,2‴-[(3,3′-Dicarboxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid)* (**93**) was prepared from **84** by hydrolysis with NaOH. UV (H_2O): 275. UV ([Eu^{III} (**93**)], H_2O): 296. ^{1}H-NMR (D_2O): 3.10 (*s*, 8 H); 3.77 (*s*, 4 H); 7.50 (*d*, *J* = 7.9, 2 H); 7.97 (*d*, *J* = 7.9, 2 H).

13. *2,2′,2″,2‴-[(3,3′-Dihydroxy-2,2′-bipyridine-6,6′-diyl)bis(methylenenitrilo)]tetrakis(acetic Acid)* (**94**) was prepared from **86** by hydrolysis with NaOH. UV (H_2O): 353, 253, 220 (sh). UV ([Eu^{III} (**94**)], H_2O): 372, 263, 225. ^{1}H-NMR ((D_6)DMSO): 3.51 (*s*, 8 H); 4.01 (*s*, 4 H); 7.52 (*d*, *J* = 8.6, 2 H); 7.57 (*d*, *J* = 8.6, 2 H).

14. *Luminescence Measurements.* For the purpose of characterizing the luminescence properties of the prepared ligands, a simple parameter, which can be rapidly determined, was needed. When used as a luminescent probe, the lanthanide chelate is subjected to a short excitation light pulse, and the decaying emission is measured taking advantage of the considerably longer decay time compared to the natural luminescence of biological samples. Hence the parameter was to describe the integrated intensity of emission. Let the luminescent system be described as the superposition of *N* exponential decay processes (*Eqn. 1*). Then the total integrated intensity is given by *Eqn. 2*.

$$I = \sum_{i=1}^{N} I_i \exp(-k_i t) \tag{1}$$

$$I_{tot} = \int_0^{\infty} I \, dt = \sum_{I=1}^{N} \frac{I_i}{k_i} \tag{2}$$

The basis of the parameter used in this work is I_{tot} divided by the concentration of the chelate c_{chel}. To get reliable results irrespective of the type of instrument used, the integrated emission intensity of an uncomplexed lanthanide ion was used as a standard. Hence the parameter used in this work, called 'relative luminescence yield' is defined by *Eqn. 3* where c_{Ln}, I_{Ln}, and k_{Ln} are the concentration, pre-exponential term of the emission intensity, and the emission decay constant of the uncomplexed lanthanide ion, respectively. The range of R for different chelates is relatively wide, and the parameter is more conveniently reported in a logarithmic scale.

$$R = \frac{c_{Ln} k_{Ln}}{c_{chel} I_{Ln}} \sum_{i=1}^{N} \frac{I_i}{k_i} \tag{3}$$

The luminescent values of uncomplexed lanthanides were measured using the excitation wavelength 395 nm for Eu^{III} and 370 nm for Tb^{III}. The excitation source of the fluorometer used was photon-corrected and, consequently, the different excitation wavelengths for the uncomplexed lanthanide and its chelate should not introduce appreciable dependency on the instrument. The emission intensities of the uncomplexed and complexed lanthanides were always measured at the same wavelength, 544 nm for Tb^{III} and 615 nm for Eu^{III}. The luminescence properties of Eu^{III} and Tb^{III} chelates were measured using equimolar mixtures of the ligands **75–94**, and Eu^{III} or Tb^{III} in a borate buffer (pH 8.5). The concentrations used were 10^{-5} or 10^{-6} M. Results: see the *Table*.

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REFERENCES

[1] V.-M. Mukkala, J.J. Kankare, *Eur. J. Solid State Inorg. Chem.* **1992,** *29,* 53.
[2] E. Soini, I. Hemmilä, P. Dahlén, *Ann. Biol. Clin.* **1990,** *48,* 567.
[3] I. Hemmilä, *Scand. J. Clin. Lab. Invest.* **1988,** *48,* 389.
[4] M.P. Bailey, B.F. Rocks, C. Riley, *Analyst* **1984,** *109,* 1449; S. Dakubu, R. Hale, A. Lu, J. Quick, D. Solas, J. Weinberg, *Clin. Chem.* **1988,** *34,* 2337; B. Alpha, V. Balzani, J.-M. Lehn, S. Perathoner, N. Sabbatini, *Angew. Chem.* **1987,** *99,* 1310; I. Hemmilä, O. Malminen, H. Mikola, T. Lövgren, *Clin. Chem.* **1988,** *34,* 2320; B. Alpha, Academic Dissertation, Université Louis Pasteur, Strasbourg, 1987; T.K. Christopoulos, E.P. Diamandis, *Analyst* **1991,** *116,* 627.
[5] M.J. Cook, A.P. Lewis, G.S.G. McAuliffe, V. Skarda, A.J. Thomson, J.L. Glasper, D.J. Robbins, *J. Chem. Soc., Perkin Trans. 2* **1984,** 1303; J. Telser, K.A. Cruickshank, K.S. Schanze, T.L. Netzel, *J. Am. Chem. Soc.* **1989,** *111,* 7221.
[6] C. Ohm, F. Vögtle, *Chem. Ber.* **1985,** *118,* 22.
[7] B. Alpha, J.-M. Lehn, G. Mathis, *Angew. Chem. Int. Ed.* **1987,** *26,* 266; G. Blasse, G.J. Dirksen, D. Van Der Voort, N. Sabbatini, S. Perathoner, J.-M. Lehn, B. Alpha, *Chem. Phys. Lett.* **1988,** *146,* 347.
[8] J. Kankare, M. Latva, H. Takalo, *Eur. J. Solid State Inorg. Chem.* **1991,** *28,* 183.
[9] G.R. Newkome, W.E. Puckett, G.E. Kiefer, V.K. Gupta, Y. Xia, M. Coreil, M.A. Hackney, *J. Org. Chem.* **1982,** *47,* 4116.
[10] R.A. Jones, B.D. Roney, W.H.F. Sasse, K.O. Wade, *J. Chem. Soc. (B)* **1967,** 106.
[11] G. Maerker, F.H. Case, *J. Am. Chem. Soc.* **1958,** *80,* 2745.
[12] G.R. Newkome, D.C. Pantaleo, W.E. Puckett, P.L. Ziefle, W.A. Deutsch, *J. Inorg. Nucl. Chem.* **1981,** *43,* 1529.
[13] F.L. Wimmer, S. Wimmer, *OPPI Briefs* **1983,** *15,* 368.
[14] D.D. Weller, G.R. Luellen, D.L. Weller, *J. Org. Chem.* **1982,** *47,* 4803.
[15] J. Rebek, Jr., R.V. Wattley, *J. Heterocycl. Chem.* **1980,** *17,* 749.
[16] F. Kröhnke, *Synthesis* **1976,** 1; P. Karrer, C. Cochand, *Helv. Chim. Acta* **1945,** *28,* 1181.
[17] W. DeW. Horrocks, Jr., D.R. Sudnick, *Acc. Chem. Res.* **1981,** *14,* 384. C.C. Bryden, C.N. Reilley, *Anal. Chem.* **1982,** *54,* 610.
[18] B. Alpha, R. Ballardini, V. Balzani, J.-M. Lehn, S. Perathoner, N. Sabbatini, *Photochem. Photobiol.* **1990,** *52,* 299.
[19] J.-C. Rodriguez, B. Alpha, D. Plancherel, J.-M. Lehn, *Helv. Chim. Acta* **1984,** *76,* 2264.