Oligosaccharide Analogues of Polysaccharides

Part 18[1])

Synthesis of Cyclic Hybrids of 2,2′-Bipyridine and Acetylenosaccharides

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We report the efficient construction of cyclic hybrids of 2,2′-bipyridine and acetylenosaccharides from readily available building blocks involving a double *Castro-Stephens* coupling of an *O*-protected and an *O*-unprotected, mono-*C*-silylated 1,4-*cis*-diethynylated 1,5-anhydroglucitol (see **2** and **6**, resp.) to 6,6′-dibromo-2,2′-bipyridine (**1**) followed by oxidative cyclization of the resulting dialkynes (see *Scheme*). UV Spectra of the *C*-alkynylated linear and cyclized bipyridines **8** and **10** show that these ligands complex a range of metal ions (*Figs. 4* and *5*).

1. Introduction. – Cyclic host molecules, differing in geometric and physicochemical properties of their cavity, are efficiently constructed from appropriate building blocks [2]. Saccharides possess obvious advantages as enantiomerically pure, densely functionalised, and readily derivatised building blocks. Apart from cycloglucans [3–5], consisting exclusively of saccharide units, there is a range of hosts embodying building blocks derived from carbohydrate as well as non-carbohydrate sources, such as the 'glycophanes' [6] [7] and hosts obtained by combining saccharides with ethylenedioxy groups [8–12], butadiyne units [6] [13], and hydroxy acids [14]. In this context, the 2,2′-bipyridine-6,6′-diyl group is attractive [15], as it readily forms complexes with metal ions [16], and has proven useful in many applications [17]. We report the synthesis of a cyclic host combining bipyridine and acetylenosaccharides as building blocks by coupling 1,4-dialkynylated 1,6-anhydroglucitols with 6,6′-dibromo-2,2′-bipyridine (**1**).

2. Results and Discussion. – Coupling the dibromo-bipyridine **1** [18] to the dibenzylated dialkyne **2** [19] under conditions reported by *Kövári* and *Krämer* [20][2]) afforded the disubstituted bipyridine **3** in a yield of 78% (*Scheme*). Base-promoted deacetylation and desilylation of **3** yielded 92% of the diol **4**. Treatment of **4** with $Cu(OAc)_2$ in pyridine led to the macrocyclic bipyridine **5** in 59% yield.

The ^{1}H-NMR spectra (CD_2Cl_2) of the linear and cyclic bipyridines **4** and **5** show only one set of signals, in agreement with their C_2 symmetry. The temperature dependence of their spectra differs significantly. The signals of the macrocycle **5** show considerable broadening below $-40°$, while no line broadening was observed for **4**

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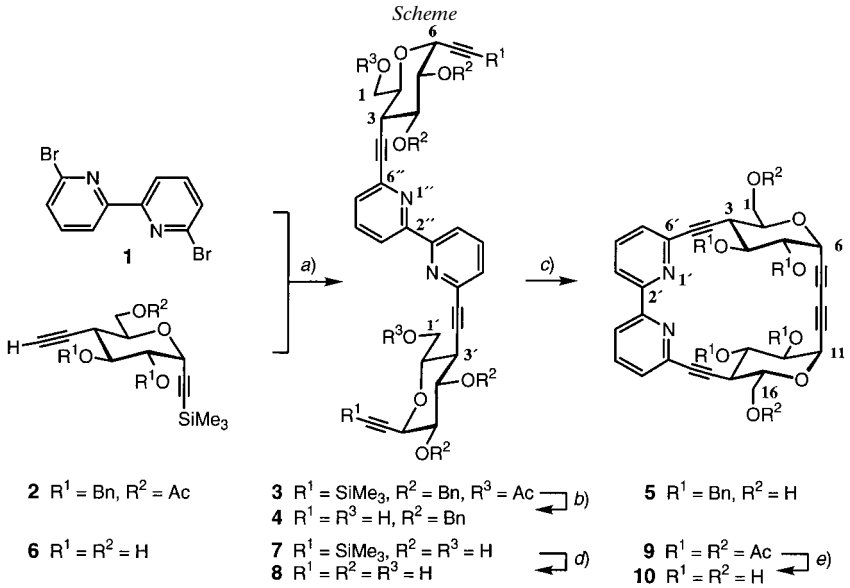
1) Part 17: [1].

2) *Kövári* and *Krämer* coupled **1** with 5.8 equiv. of *N*,*N*-dimethylpropargylamine in 64% yield to 3,3′-[(2,2′-bipyridine)-6,6′-diyl]bis[*N*,*N*-dimethylprop-2-ynamine]. By increasing the concentration of the coupling partners, we secured a higher yield of **3** while reducing the excess of the alkyne **1** to 2.2 equiv.

Scheme



a) $[PdCl_2(PPh_3)_2]$, CuI, PPh_3, Et_3N, [**1**] = 0.3M: **2** → **3**, 78%; **6** → **7**; 70%. *b*) NaOH, MeOH; 92%. *c*) $Cu(OAc)_2$, pyridine: **4** → **5**, [**4**] < 0.27 mM, 59%; **8** → **9**, [**8**] < 0.9 mM; Ac_2O, ca. 68%. *d*) NaOMe, MeOH, 93%. *e*) NaOMe, MeOH, 73%.

upon cooling to $-70°$ (*Figs. 1* and *2*). The specific rotation of **4** shows a strong and linear temperature dependence (*Fig. 3*), while that of **5** depends very little on temperature[3]).

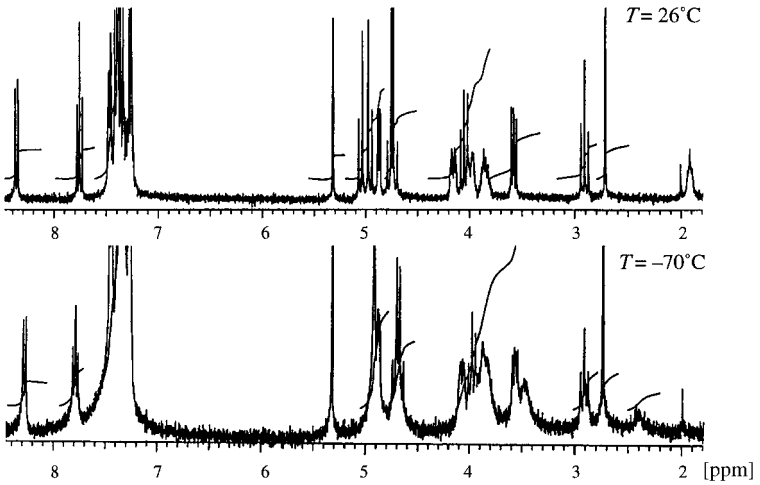


Fig. 1. *^{1}H-NMR Spectra* (300 MHz, CD_2Cl_2, 6.4 mM) *of* **4** *at 26 and* $-70°$

[3]) The specific rotation $[\alpha]_{405}$ of **5** ($CHCl_3$) at 25 and 50° is $-276.0°$ and $-276.6°$, respectively.

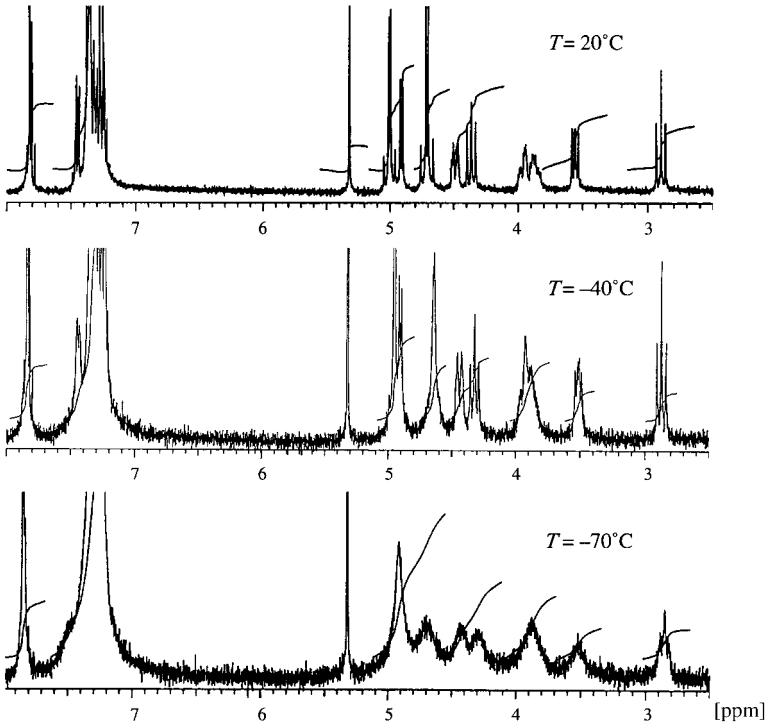


Fig. 2. *^{1}H-NMR Spectra* (300 MHz, CD_2Cl_2, 6.6 mM) *of* **5** *at 20, – 40, and – 70°*

Force-field calculations (MM3*) [21] suggest that **5** adopts the two conformers depicted in *Fig. 3*; line broadening suggests a slow transition between them. The absence of line broadening and the strong temperature dependence of the specific rotation of **4** suggest a rapid interconversion of conformers and a temperature-dependent shift of the position of the equilibrium between them.

To test the feasibility of the *Castro-Stephens* coupling with unprotected acetylenosaccharides, we exposed **1** and the readily available diethynylated triol **6** [19] to the same conditions that led to **4**, and obtained the diethynylated bipyridine **7** in a yield of 70%. The Me_3Si groups of **7** were removed with NaOMe in MeOH (93%), and the resulting dialkyne **8** was treated with $Cu(OAc)_2$ in pyridine. The crude product was acetylated *in situ* to facilitate the removal of copper salts. Chromatography yielded 68% of the hexaacetate **9** as a bright-yellow solid. According to the ^{1}H- and ^{13}C-NMR spectra, this material did not contain any organic impurity. However, deacetylation of **9** followed by selective precipitation from a solution in CH_2Cl_2/MeOH led to a colourless hexaol **10** (73%).

We compared the UV spectra (*Figs. 4* and *5*) of aqueous solutions of the unprotected bipyridines **8** and **10**, in the presence and absence of metal ions, as described by *Sone et al.* [22] for 2,2′-bipyridines.

Aqueous solutions of the ligands (**L**) **8** and **10** absorb strongly between λ 270 and 330 nm, whereas the pure metal (**M**) solutions absorb only weakly between 250 and

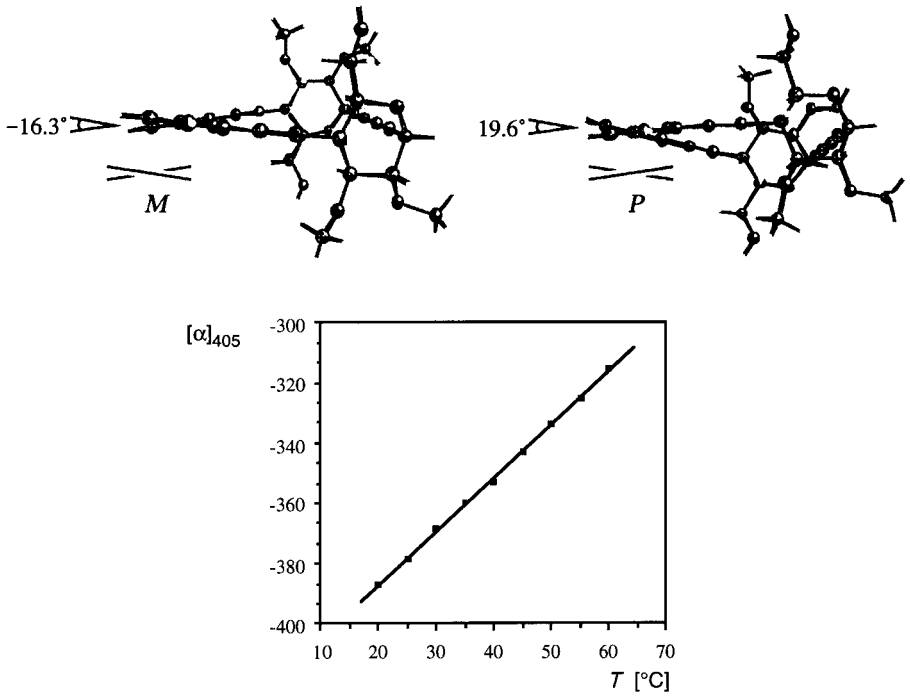


Fig. 3. Top: *Calculated conformations of the bipyridine* **5** (MM3*). The $PhCH_2$ groups were replaced by Me groups for clarity. The angles between the aromatic ring planes are −16.3 and 19.6°, respectively. Bottom: *Temperature dependence of the specific rotation* (at 405 nm in $CHCl_3$) *of the bipyridine* **4**.

400 nm. The UV spectra of both ligands show a significant bathochromic shift upon addition of $Cu(NO_3)_2$ or $AgNO_3$. A strong bathochromic shift is also observed for the mixtures **8**/$NiCl_2$ and **10**/$ZnCl_2$. Addition of $Pb(OAc)_2$, $Co(NO_3)_2$, $MnSO_4$, or $Mg(NO_3)_2$, however, had only a small effect. Although the extent of a bathochromic shift is not directly correlated to the stability of a complex, a qualitative comparison of the UV spectra suggests that the tendency to form complexes decreases for the acyclic bipyridine **8** in the order $Cu(NO_3)_2 > NiCl_2 \approx AgNO_3 > ZnCl_2 \approx Pb(OAc)_2 \approx Co(NO_3)_2 > MnSO_4 \approx Mg(NO_3)_2$ and for the macrocyclic bipyridine **10** in the order $Cu(NO_3)_2 \approx ZnCl_2 > AgNO_3 \approx Pb(OAc)_2 > NiCl_2 > Co(NO_3)_2 \approx MnSO_4 \approx Mg(NO_3)_2$. Unfortunately, none of these compounds crystallized in our hands, and the exact structure of the complexes in solution has not been determined.

The strongest difference between the two ligands is observed for the complexation of $ZnCl_2$ and $NiCl_2$. $ZnCl_2$ causes only a weak change of the UV spectrum of **8**, but strongly affects the UV spectrum of the macrocycle **10**, indicating that its complexation depends strongly upon the enforced *'cisoid'*-conformation of the bipyridine unit in **10**. In contradistinction, $NiCl_2$ causes a strong change of the UV spectrum of **8**, but not of **10**, indicating that $NiCl_2$ forms 1:2 or 1:3 complexes [16] with bipyridines.

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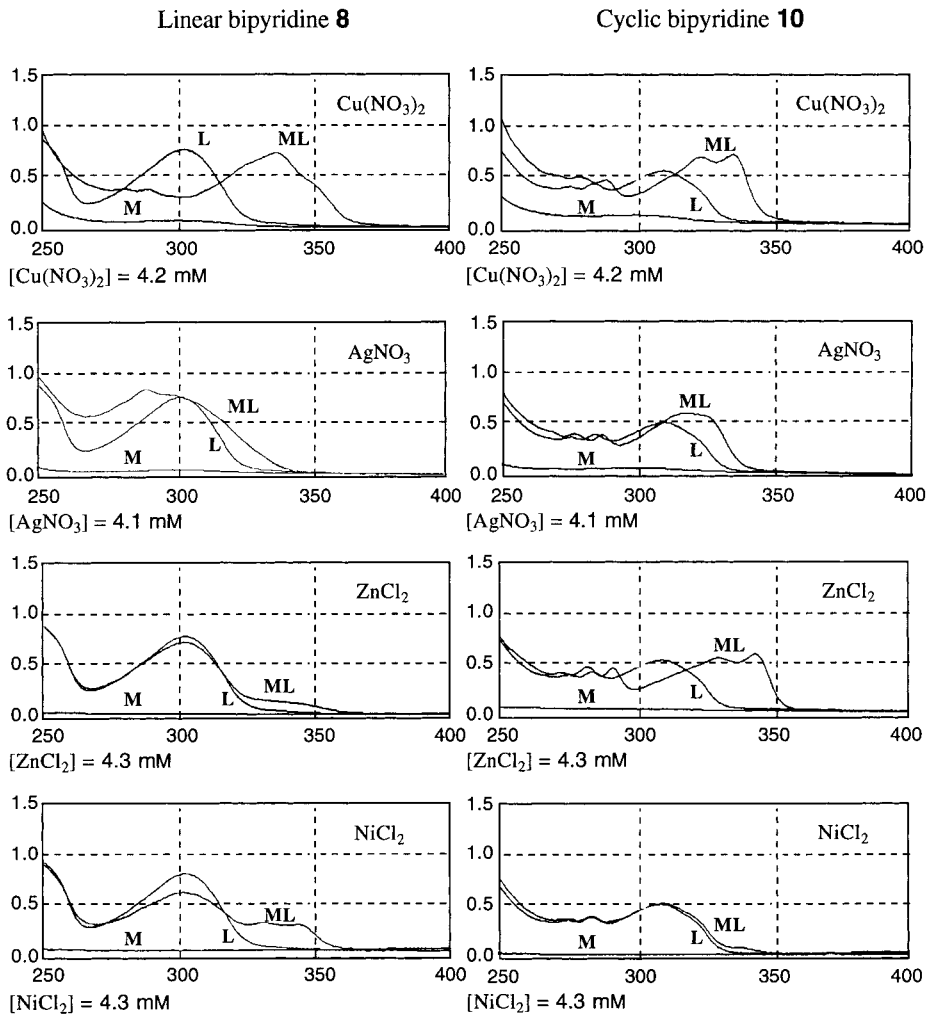

Fig. 4. *UV Spectra of the mixtures of the linear bipyridine* **8** (left) *and the cyclic bipyridine* **10** (right) *with* $Cu(NO_3)_2$, $AgNO_3$, $ZnCl_2$, *and* $NiCl_2$. Extinction *vs.* wavelengths [nm]; in H_2O at 24°. **L**: [ligand] = 0.04 mM; **M**: [metal salt] ≈ 4 mM; **ML**: [ligand] = 0.04 mM and [metal salt] ≈ 4 mM.

Experimental Part

General (*cf.* [13a]). Workup: The mixture was diluted with the indicated solvent and a sat. aq. NH_4Cl soln., the aq. layer extracted (3–5 times) with the indicated solvent, and the combined org. phase washed once with brine, dried ($MgSO_4$), and evaporated. UV spectra (*Figs. 4* and *5*): the samples were prepared with *SOCOREX-SWISS* (100–1000 µl) pipettes from aq. solns. of **8**, **10**, $AgNO_3$, $Co(NO_3)_2$, $Cu(NO_3)_2$, $Mg(NO_3)_2$, $MnSO_4$, $NiCl_2$, $Pb(OAc)_2$, and $ZnCl_2$; solns.: [ligand] = 0.08 mM; [metal salt] ≈ 8 mM; H_2O was not buffered and purified with a *Millipore* apparatus. UV Spectra: *UVIKON-931* spectrophotometer, quartz cell (1 cm) at *ca.* 24°.

*3,3′-[(2,2′-Bipyridine-6,6′-diyl)diethyne-2,1-diyl]bis[1-*O*-acetyl-2,6-anhydro-4,5-di-*O*-benzyl-3-deoxy-1-*C*-(trimethylsilyl)-*D*-glycero-*L*-gulo-oct-7-ynitol]* (**3**). A degassed suspension of **1** (116 mg, 0.37 mmol), $[PdCl_2(PPh_3)_2]$ (7.44 mg, 10.6 µmol), CuI (9.6 mg, 50.4 µmol), and PPh_3 (7.68 mg, 29.2 µmol) in Et_3N (1.2 ml)

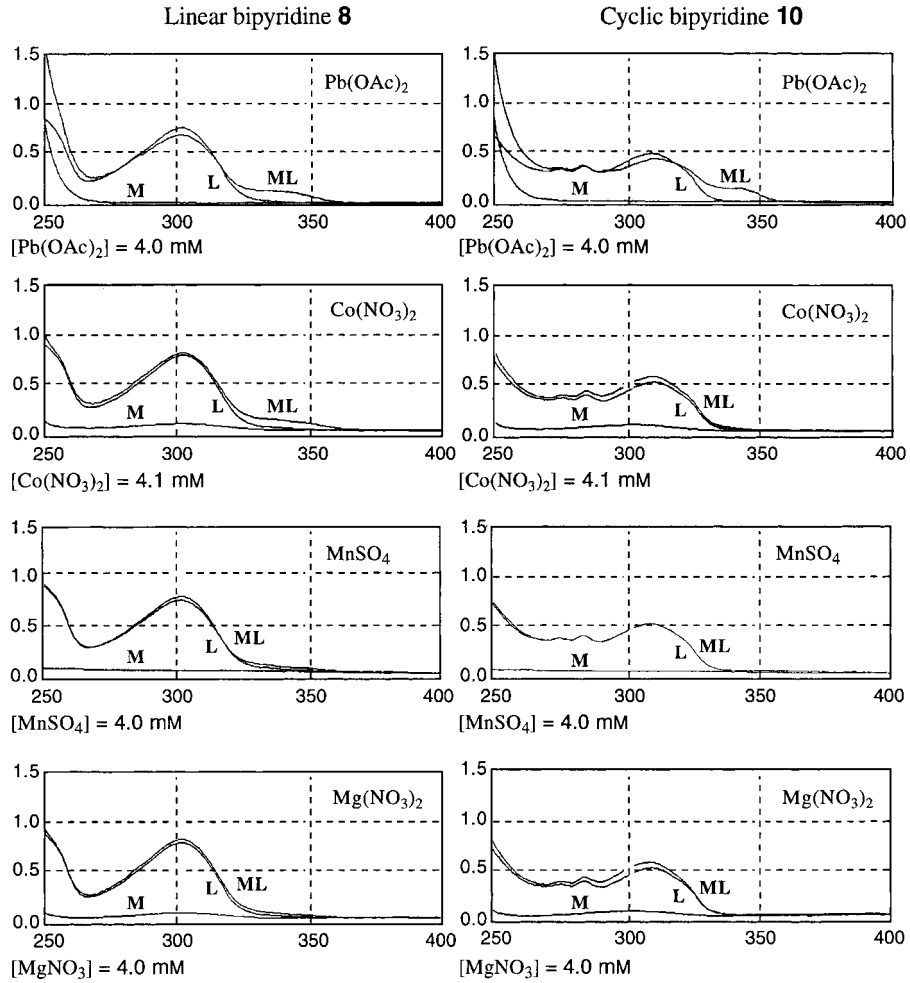

Fig. 5. *UV Spectra of the mixtures of the linear bipyridine* **8** (left) *and the cyclic bipyridine* **10** (right) *with* $Pb(OAc)_2$, $Co(NO_3)_2$, $MnSO_4$ *and* $Mg(NO_3)_2$. Extinction *vs.* wavelengths [nm]; in H_2O at 24°. **L**: [ligand] = 0.04 mM; **M**: [metal salt] ≈4 mM; **ML**: [ligand] = 0.04 mM and [metal salt] ≈4 mM.

was stirred under N_2 at r.t. for 5 min and treated with a soln. of **2** (400 mg, 0.81 mmol) in Et_3N (1.2 ml). The mixture was heated to 70°, stirred for 2 h, cooled to 0°, and diluted with a 5% aq. soln. of H_2SO_4 and CH_2Cl_2. Workup (CH_2Cl_2) and FC (hexane/Et_2O 7:3 → 1:1) gave **3** (327 mg, 78%). Colourless oil. R_f (hexane/Et_2O 2:3) 0.15. IR: 3089*w*, 3066*w*, 3007*m*, 2960*w*, 2903*w*, 2234*w*, 2170*w*, 1739*s* (br.), 1569*m*, 1436*s*, 1367*m*, 1119*s* (br.), 1037*m*, 908*m* (br.), 846*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.39 (*dd*, *J* = 1.0, 8.0, H–C(3″)); 7.73 (*t*, *J* = 7.8, H–C(4″)); 7.50–7.47 (*m*, H–C(5″), 1 arom. H); 7.43–7.24 (*m*, 9 arom. H); 5.06 (*d*, *J* = 10.6, PhC*H*); 4.98 (*d*, *J* = 10.6, PhC*H*); 4.86 (*d*, *J* = 5.6, H–C(6)); 4.78 (*d*, *J* = 11.9, PhC*H*); 4.72 (*d*, *J* = 12.0, PhC*H*); 4.48 (br. *d*, *J* ≈ 11.2, H–C(1)); 4.47 (br. *d*, *J* ≈ 11.2, H′–C(1)); 4.32 (*td*, *J* ≈ 3.7, 10.5, H–C(2)); 4.03 (*dd*, *J* = 9.3, 10.3, H–C(4)); 3.58 (*dd*, *J* = 5.7, 9.2, H–C(5)); 2.95 (br. *t*, *J* ≈ 10.5, H–C(3)); 2.11 (*s*, Ac); 0.26 (*s*, Me_3Si). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.83 (*s*, C=O); 155.68 (*s*, C(2″)); 142.36 (*s*, C(6″))[4]; 138.31, 138.17 (2*s*);

[4]) The assignment of the signals of C(2″) and C(6″) is based on a comparison with similar bipyridines [23].

137.06 (*d*, C(4″)); 128.54 (*d*, 2 C); 128.40 (*d*, 2 C); 128.33 (*d*, 2 C); 127.79 (*d*); 127.74 (*d*); 127.68 (*d*, 2 C); 127.57 (*d*); 120.71 (*d*); 99.64 (*s*, C(7)); 95.58 (*s*, C(8)); 85.99, 83.90 (2*s*, 2 *C*≡C); 79.60, 78.71 (2*d*, C(4), C(5)); 75.90, 72.55 (2*t*, 2 PhCH$_2$); 71.93 (*d*, C(2)); 67.53 (*d*, C(6)); 64.52 (*t*, C(1)); 37.69 (*d*, C(3)); 20.93 (*q*, Me); −0.03 (*q*, Me$_3$Si). MS-FAB: 1133 (100, $[M+H]^+$), 915 (11).

3,3′-[(2,2′-Bipyridine-6,6′-diyl)diethyne-2,1-diyl]bis[2,6-anhydro-4,5-di-O-*benzyl-3-deoxy*-D-glycero-D-gulo-*oct-7-ynitol]* (**4**). A soln. of **3** (322 mg, 0.28 mmol) in MeOH (30 ml) was treated at 0° under N_2 with a 0.1M NaOH soln. in MeOH (6 ml), warmed to r.t., stirred for 1 h, and treated with *Dowex* (H^+ form). The solids were filtered off and washed (MeOH). Evaporation of the filtrate and FC (hexane/AcOEt 1:1) of the residue left **4** (238 mg, 92%). White foam. R_f (hexane/AcOEt 1:1) 0.16. $[\alpha]_D^{25} = -108.0$ ($c = 0.68$, $CHCl_3$). UV (CH_2Cl_2, 12.3 μM): 302 (15870), 272 (5450), 228 (29200). IR: 3597*w*, 3450*w* (br.), 3304*m*, 3007*m*, 2930*w*, 2876*w*, 2234*w*, 2120*w*, 1570*m*, 1496*w*, 1436*s*, 1364*w*, 1078*s* (br.), 1027*m* (br.). ^{1}H-NMR (500 MHz, $CDCl_3$): 8.35 (*dd*, $J = 1.1, 8.0$, H−C(3″)); 7.70 (*t*, $J = 7.8$, H−C(4″)); 7.48–7.45 (*m*, H−C(5″), 1 arom. H); 7.39–7.22 (*m*, 9 arom. H); 5.08 (*d*, $J = 10.6$, PhC*H*); 4.97 (*d*, $J = 10.6$, PhC*H*); 4.80 (*d*, $J = 11.9$, PhC*H*); 4.77 (*dd*, $J = 2.3, 5.7$, H−C(6)); 4.72 (*d*, $J = 11.9$, PhC*H*); 4.18 (*ddd*, $J = 2.5, 5.1, 10.6$, H−C(2)); 4.07 (*dd*, $J = 9.2, 10.3$, H−C(4)); 4.01 (*ddd*, $J = 2.5, 6.5, 12.0$, H−C(1)); 3.87 (*ddd*, $J = 5.1, 6.5, 11.9$, H′−C(1)); 3.55 (*dd*, $J = 5.7, 9.2$, H−C(5)); 2.92 (br. *t*, $J \approx 10.5$, H−C(3)); 2.65 (*d*, $J = 2.3$, H−C(8)); 1.99 (*t*, $J = 6.5$, OH). ^{13}C-NMR (125 MHz, $CDCl_3$): 155.67 (*s*, C(2″)); 142.32 (*s*, C(6″)); 138.41, 137.82 (2*s*); 137.02 (*d*, C(4″)); 128.50 (*d*, 2 C); 128.31 (*d*, 2 C); 128.28 (*d*, 2 C); 127.98 (*d*); 127.93 (*d*, 2 C); 127.69 (*d*); 127.34 (*d*); 120.69 (*d*); 86.25, 83.82 (2*s*, C≡C); 80.06, 78.49 (2*d*, C(4), C(5)); 78.31 (*d*, C(8)); 77.80 (*s*, C(7)); 76.01 (*t*, PhCH$_2$); 74.27 (*d*, C(2)); 73.19 (*t*, PhCH$_2$); 67.02 (*d*, C(6)); 63.48 (*t*, C(1)); 37.55 (*d*, C(3)). FAB-MS: 1810 (13, $[2M+H]^+$), 905 (100, $[M+H]^+$). Anal. calc. for $C_{58}H_{52}N_2O_8 \cdot 0.5\ H_2O$ (914.06): C 76.21, H 5.84, N 3.06; found: C 76.20, H 5.84, N 2.95.

2,6:11,15-Dianhydro-4,5,12,13-tetra-O-*benzyl-3,14*-C-*[(2,2′-bipyridine-6,6′-diyl)diethyne-2,1-diyl]-3,7,8,9,10,14-hexadeoxy*-D-erythro-L-ido-L-gulo-*hexadeca-7,9-diynitol* (**5**). A degassed soln. of $Cu(OAc)_2$ (449 mg, 2.47 mmol) in pyridine (450 ml) was treated at 50° under N_2 with a soln. of **4** (112 mg, 0.12 mmol) in pyridine (1 ml) within 10 h, stirred for 20 h, and evaporated. The residue was dissolved in CH_2Cl_2 (20 ml) and a sat. aq. KCN soln. (7 ml) and stirred for *ca.* 12 h. Workup (CH_2Cl_2) and FC (twice: 1. CH_2Cl_2/MeOH 49:1; 2. $CHCl_3$/AcOEt 4:1) gave **5** (66 mg, 59%). White solid. R_f (AcOEt) *ca.* 0.26. M.p. 189–191° (dec.). IR: 3602*m*, 3444*w* (br.), 3007*m*, 2924*m*, 2232*w*, 2150*w*, 1601*m*, 1581*m*, 1564*m*, 1496*m*, 1149*s*, 1364*m*, 1332*m*, 1117*s* (br.), 1077*s*, 1016*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.83–7.79 (*m*, H−C(3′), H−C(4′)); 7.44 (*dd*, $J = 2.5, 6.1$, H−C(5′)); 7.36–7.23 (*m*, 10 arom. H); 5.10 (*d*, $J = 11.5$, PhC*H*); 4.98 (*d*, $J = 11.4$, PhC*H*); 4.85 (*d*, $J = 5.5$, H−C(6)); 4.72 (*d*, $J = 12.1$, PhC*H*); 4.65 (*d*, $J = 12.1$, PhC*H*); 4.40 (*ddd*, $J = 2.1, 4.2, 10.5$, H−C(2)); 4.28 (*t*, $J = 9.7$, H−C(4)); 3.98 (br. *ddd*, $J \approx 2.1, 5.0, 11.9$, H−C(1)); 3.89 (br. *ddd*, $J \approx 4.2, 6.2, 11.9$, H′−C(1)); 3.53 (*dd*, $J = 5.5, 9.5$, H−C(5)); 2.93 (br. *t*, $J \approx 10.4$, H−C(3)); 2.02 (br. *t*, $J \approx 6.0$, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 154.75 (*s*, C(2′)); 144.25 (*s*, C(6′)); 139.03, 137.84 (2*s*); 137.52 (*d*, C(4′)); 128.54 (*d*, 2 C); 128.21 (*d*, 2 C); 127.97 (*d*, 2 C); 127.59 (*d*, 2 C); 127.52 (*d*); 127.35 (*d*); 126.39 (*d*); 120.61 (*d*); 88.14, 82.99 (2 *s*, C≡C); 80.42, 79.02 (2*d*, C(4), C(5)); 75.77 (*t*, PhCH$_2$); 74.62 (*d*, C(2)); 74.51, 73.14 (2*s*, C(7), C(8)); 73.06 (*t*, PhCH$_2$); 67.45 (*d*, C(6)); 63.38 (*t*, C(1)); 37.00 (*d*, C(3)). MS-FAB: 903 (100, $[M+H]^+$).

3,3′-[(2,2′-Bipyridine-6,6′-diyl)diethyne-2,1-diyl]bis[2,6-anhydro-3-deoxy-1-C-*(trimethylsilyl)*-D-glycero-L-gulo-*oct-7-ynitol]* (**7**). A degassed suspension of **1** (1.17 g, 3.73 mmol), $[PdCl_2(PPh_3)_2]$ (47 mg, 67.1 μmol), CuI (44 mg, 0.23 mmol), and PPh_3 (43 mg, 0.16 mmol) in Et_3N (12 ml) was stirred for 10 min at r.t. under N_2, treated within 10 min with a soln. of **6** (2.20 g, 8.20 mmol) in Et_3N (12 ml), heated to 70°, stirred for 9 h, and evaporated. FC (supported on SiO_2 as a solid; $CHCl_3$/MeOH 20:1) of the residue gave **7** (1.80 g, 70%). White solid. R_f (AcOEt/MeOH 7:3) 0.65. M.p. 147–148°. $[\alpha]_D^{25} = 67.3$ ($c = 1.08$, MeOH). IR (KBr): 3680–3000*s* (br., max. at 3380), 2957*m*, 2232*m*, 2169*m*, 1636*m*, 1571*s*, 1436*s*, 1334*m*, 1250*s*, 1124*m*, 1076*s* (br.), 901*m*, 844*s* (br.), 802*m*, 761*m*, 710*w*, 639*w*, 577*w*. ^{1}H-NMR (300 MHz, CD_3OD): 8.25 (*dd*, $J = 0.9$, 8.0, H−C(3″)); 7.92 (*t*, $J = 7.8$, H−C(4″)); 7.57 (*dd*, $J = 0.9, 7.8$, H−C(5″)); 4.76 (*d*, $J = 5.6$, H−C(6)); 4.08 (*ddd*, $J = 2.2, 4.7, 10.4$, H−C(2)); 3.93 (*dd*, $J \approx 2.2, 12.1$, H−C(1)); 3.92 (br. *t*, $J \approx 10.0$, H−C(4)); 3.85 (*dd*, $J = 4.7, 12.1$, H′−C(1)); 3.50 (*dd*, $J = 5.9, 9.3$, H−C(5)); 2.77 (br. *t*, $J \approx 10.3$, H−C(3)); 0.20 (*s*, Me$_3$Si). ^{13}C-NMR (75 MHz, CD_3OD): 157.37 (*s*, C(2″)); 144.43 (*s*, C(6″)); 139.29 (*d*, C(4″)); 129.08, 122.30 (2*d*, C(3″), C(5″)); 102.06 (*s*, C(7)); 95.62 (*s*, C(8)); 88.96, 84.25 (2*s*, C≡C); 76.31 (*d*, C(2)); 73.86, 72.80 (2*d*, C(4), C(5)); 70.76 (*d*, C(6)); 64.04 (*t*, C(1)); 39.71 (*d*, C(3)); −0.02 (*q*, Me$_3$Si). MALDI-MS: 689 ($[M+H]^+$). Anal. calc. for $C_{36}H_{44}N_2O_8Si_2 \cdot H_2O$ (706.93): C 61.16, H 6.56, N 3.96; found: C 60.94, H 6.53, N 4.06.

3,3′-[(2,2′-Bipyridine-6,6′diyl)diethyne-2,1-diyl]bis[2,6-anhydro-3-deoxy-D-glycero-L-gulo-*oct-7-ynitol]* (**8**). A soln. of **7** (1.80 g, 2.61 mmol) in MeOH (10 ml) was treated at 0° under N_2 with a 2% NaOMe soln. in MeOH (3.5 ml), stirred for 3 h, and neutralized with *Dowex* (H^+ form). The solids were filtered off and washed (MeOH). Evaporation of the filtrate left **8** (1.32 g, 93%). White solid. R_f (AcOEt/MeOH 7:3) 0.44. M.p. 215–

216°. $[\alpha]_D^{25} = 43.3$ ($c = 0.78$, DMSO). UV (MeOH, 51 μM): 301 (19166). IR: 3620–3000*s* (br., max. at 3350), 3289*w*, 2921*m*, 2231*m*, 2113*w*, 1640*w*, 1568*s*, 1438*s*, 1363*m*, 1274*w*, 1123*s*, 1076*s* (br.), 918*w*, 881*m*, 833*w*, 801*s*, 680*m* (br.). ^{1}H-NMR (300 MHz, CD_3OD): 8.25 (*dd*, $J = 1.3$, 8.1, H–C(3″)); 7.91 (br. *t*, $J \approx 7.8$, H–C(4″)); 7.57 (*dd*, $J = 1.0$, 7.6, H–C(5″)); 4.78 (*dd*, $J = 2.2$, 5.6, H–C(6)); 4.10 (*ddd*, $J = 2.2$, 4.4, 10.3, H–C(2)); 3.94 (br. *t*, $J \approx 9.7$, H–C(4)); 3.92 (*dd*, $J = 2.2$, 12.1, H–C(1)); 3.85 (*dd*, $J = 4.6$, 12.1, H′–C(1)); 3.52 (*dd*, $J = 5.6$, 9.3, H–C(5)); 3.04 (*d*, $J = 2.4$, H–C(8)); 2.77 (br. *t*, $J \approx 10.3$, H–C(3)). ^{13}C-NMR (75 MHz, (D_6)DMSO): 155.03 (*s*, C(2″)); 142.51 (*s*, C(6″)); 138.14 (*d*, C(4″)); 127.97, 120.23 (2*d*, C(3″), C(5″)); 88.86, 82.49, 79.87 (3*s*, C(7), C≡C); 79.43 (*d*, C(8)); 74.95 (*d*, C(2)); 71.65, 71.12 (2*d*, C(4), C(5)); 68.32 (*d*, C(6)); 62.01 (*t*, C(1)); 37.82 (*d*, C(3)). CI-MS: 545 (40, $[M+H]^+$), 459 (100), 373 (63), 279 (24). FAB-MS: 545 (40, $[M+H]^+$), 459 (100), 373 (63), 345 (27), 279 (24), 97 (20). Anal. calc. for $C_{30}H_{28}N_2O_8 \cdot H_2O$ (562.57): C 64.05, H 5.37, N 4.98; found: C 63.75, H 5.67, N 4.80.

1,4,5,12,13,16-Hexa-O-*acetyl-2,6 : 11,15-dianhydro-3,14*-C-*[(2,2′-bipyridine-6,6′-diyl)diethyne-2,1-diyl]-3,7,-8,9,10,14-hexadeoxy*-D-erythro-L-ido-L-gulo-*hexadeca-7,9-diynitol* (**9**). At 50° under N_2, a degassed soln. of $Cu(OAc)_2$ (3.33 g, 18.36 mmol) in pyridine (1.00 l) was treated dropwise with a soln. of **8** (0.50 g, 0.92 mmol) in pyridine (10 ml) within 12 h. The mixture was stirred for 14 h and evaporated slowly within 6 h. The residue was dissolved in pyridine (40 ml) and Ac_2O (20 ml), stirred for *ca.* 12 h at r.t. under N_2, and evaporated. The residue was dissolved in AcOEt and a sat. aq. KCN soln. The layers were separated, and the aq. layer was extracted (7 × with AcOEt). Workup (AcOEt) of the combined org. phases and FC (twice: 1. CH_2Cl_2/EtOH 99 : 1; CH_2Cl_2/AcOEt 9 : 1) gave **9** (499 mg, *ca.* 68%). Intensly yellow solid. R_f (AcOEt/MeOH 9 : 1) 0.27. M.p. >177° (dec.). IR: 2965*w*, 2237*w*, 2135*w*, 1747*s* (br.), 1581*w*, 1565*m*, 1463*w*, 1441*m*, 1370*m*, 1069*m* (br.), 1051*m*, 908*m*. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.81 (*dd*, $J = 1.1$, 7.9, H–C(3′)); 7.77 (br. *t*, $J = 7.5$, H–C(4′)); 7.41 (*dd*, $J = 1.2$, 7.5, H–C(5′)); 5.62 (br. *t*, $J \approx 10.1$, H–C(4)); 5.05 (*d*, $J = 5.7$, H–C(6)); 4.95 (*dd*, $J = 5.7$, 9.8, H–C(5)); 4.67 (*ddd*, $J = 2.2$, 4.1, 10.6, H–C(2)); 4.50 (*dd*, $J = 2.4$, 12.4, H–C(1)); 4.45 (*dd*, $J = 4.2$, 12.4, H′–C(1)); 3.07 (br. *t*, $J \approx 10.5$, H–C(3)); 2.14, 2.11, 2.05 (3*s*, 3 Ac). ^{13}C-NMR (125 MHz, $CDCl_3$): 170.76, 170.38, 168.98 (3*s*, 3 C=O); 154.71 (*s*, C(2′)); 143.45 (*s*, C(6′)); 137.27 (*d*, C(4′)); 126.45, 120.70 (2*d*, C(3′), C(5′)); 84.26, 84.00, 73.58, 73.36 (4*s*, 2 C≡C); 72.50, 71.62, 70.35 (3*d*, C(2), C(4), C(5)); 66.46 (*d*, C(6)); 64.21 (*t*, C(1)); 35.80 (*d*, C(3)); 20.95, 20.86, 20.82 (3*q*, 3 Me). FAB-MS: 1589 (1, $[2M+H]^+$), 795 (100, $[M+H]^+$).

2,6 : 11,15-Dianhydro-3,14-C-*[(2,2′-bipyridine-6,6′-diyl)diethyne-2,1-diyl]-3,7,8,9,10,14-hexadeoxy*-D-erythro-L-ido-L-gulo-*hexadeca-7,9-diynitol* (**10**). A soln. of **9** (440 mg, 0.55 mmol) in MeOH (20 ml) was treated at 4° under Ar with a 2% NaOMe soln. in MeOH, stirred at r.t. for 17 h, and neutralized with *Dowex* (H^+ form). The solids were filtered off and washed (MeOH). The filtrate was concentrated to *ca.* 4 ml, treated with CH_2Cl_2, and left for *ca.* 12 h. The precipitated solids were filtered off and washed (CH_2Cl_2: → **10**, 206 mg, 69%). The mother liquor was evaporated und the residue dissolved in MeOH and treated with CH_2Cl_2 (→ **10**, 13 mg, 4%). White solid. R_f (AcOEt/MeOH 7 : 3) *ca.* 0.11. M.p. >287° (dec.). $[\alpha]_D^{25} = 15$ ($c = 0.41$, DMSO). IR (KBr): 3600–3044*s* (br., max. at 3344), 2917*w*, 2229*m*, 2130*w*, 1582*m*, 1562*m*, 1461*m*, 1326*w*, 1137*m*, 1087*s*, 1068*s*, 1043*s*, 990*w*, 802*m*. UV (MeOH, 0.1 mM): 310 (12136), 286 (8607). ^{1}H-NMR (400 MHz, (D_6)DMSO): 8.12 (br. *dd*, $J \approx 0.5$, 7.8, H–C(3′)); 7.95 (*t*, $J = 7.8$, H–C(4′)); 7.55 (*dd*, $J = 0.5$, 7.8, H–C(5′)); 5.64 (*d*, $J = 4.6$, exchange with D_2O, HO–C(5)); 5.58 (*d*, $J = 6.1$, exchange with D_2O, HO–C(4)); 4.85 (br. *dd*, $J \approx 5.5$, 7.0, exchange with D_2O, HO–C(1)); 4.89 (*d*, $J = 5.6$, H–C(6)); 3.98 (*ddd*, $J = 1.6$, 5.2, 10.6, H–C(2)); 3.79–3.72 (*m*, addn. of D_2O → change of signal, H–C(4), H–C(1)); 3.57 (br. *ddd*, $J \approx 5.5$, 6.3, 12.1, addn. of D_2O → br. *dd*, $J \approx 5.5$, 12.4, H′–C(1)); 3.37 (br. *td*, $J \approx 5.3$, 9.6, addn. of D_2O → *dd*, $J = 5.6$, 9.3, H–C(5)); 2.57 (br. *t*, $J \approx 10.4$, H–C(3)). ^{13}C-NMR (100 MHz, (D_6)DMSO): 154.41 (*s*, C(2′)); 142.51 (*s*, C(6′)); 137.85 (*d*, C(4′)); 125.86, 120.95 (2*d*, C(3′), C(5′)); 88.55, 82.28, 76.02, 71.55 (4*s*, 2 C≡C); 75.99 (*d*, C(2)); 72.10, 70.85 (2*d*, C(4), C(5)); 69.01 (*d*, C(6)); 62.07 (*t*, C(1)); 37.70 (*d*, C(3)). MALDI-MS: 543 ($[M+H]^+$). Anal. calc. for $C_{30}H_{26}N_2O_8 \cdot 2.5\ H_2O$ (587.57): C 61.32, H 5.32, N 4.77; found: C 61.14, H 5.04, N 4.84.

REFERENCES

[1] T. V. Bohner, O.-S. Becker, A. Vasella, *Helv. Chim. Acta*, **1999**, *82*, 198.
[2] I. Higler, P. Timmerman, W. Verboom, D. N. Reinhouldt, *Eur. J. Org. Chem.* **1998**, 2689.
[3] T. Ogawa, *Chem. Soc. Rev.* **1994**, 397.
[4] G. Wenz, *Angew. Chem.* **1994**, *106*, 851.
[5] P. R. Ashton, C. L. Brown, S. Mezner, S. A. Nepogodiev, J. F. Stoddart, D. J. Williams, *Chem. Eur. J.* **1996**, *2*, 580.
[6] R. R. Bukownik, C. S. Wilkox, *J. Org. Chem.* **1988**, *53*, 463.

[7] S. Penadés, J. M. Coteron, *J. Chem. Soc., Chem. Commun.* **1992**, 683.
[8] J. A. Haslegrave, J. F. Stoddart, D. J. Thompson, *Tetrahedron Lett.* **1979**, 2279.
[9] M. Pietraszkiewicz, J. Jurczak, *J. Chem. Soc., Chem. Commun.* **1983**, 132.
[10] R. Ellinghaus, G. Schröder, *Liebigs Ann. Chem.* **1985**, 418.
[11] B. Dumont, J.-P. Joly, Y. Chapleur, *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1123.
[12] P. P. Kanakamma, N. S. Mani, V. Nair, *Synth. Commun.* **1995**, *25*, 3777.
[13] a) R. Bürli, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 2215; b) R. Bürli, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 1027; c) R. Bürli, A. Vasella, *Angew. Chem.* **1997**, *109*, 1945.
[14] M. Uyeda, K. Yokomizo, Y. Miyamoto, E.-S. E. Habib, *J. Antib.* **1998**, *51*, 823.
[15] J. Nitschke, T. D. Tilley, *J. Org. Chem*. **1998**, *63*, 3673.
[16] E. C. Constable, *Adv. Inorg. Chem.* **1989**, *34*, 1; J. P. Sauvage, *Acc. Chem. Res.* **1990**, *23*, 319; H. Sleiman, P. Baxter, J.-M. Lehn, K. Rissanen, *J. Chem. Soc., Chem. Commun.* **1995**, 715.
[17] J.-M. Lehn, 'Supramolecular Chemistry', VCH, Weinheim, 1995; T. M. Garrett, U. Koert, J.-M. Lehn, *J. Phys. Org. Chem.* **1992**, *5*, 529; A. Pfeil, J.-M. Lehn, *J. Chem. Soc., Chem. Commun.* **1992**, 838; E. C. Constable, S. M. Elder, J. Healy, M. D. Ward, *J. Am. Chem. Soc.* **1990**, *112*, 4590; C. J. Cathey, E. C. Constable, M. J. Hannon, D. A. Tocher, M. D. Ward, *J. Chem. Soc., Chem. Commun.* **1990**, 621; H. Mürner, P. Belser, A. v. Zelewsky, *J. Am. Chem. Soc.* **1996**, *118*, 7989; Y. Habata, J. S. Bradshaw, X. X. Zhang, R. M. Izatt, *J. Am. Chem. Soc.* **1997**, *119*, 7145; F. Renaud, C. Piguet, G. Bernardinelli, J.-C. G. Bünzli, G. Hopfgartner, *Chem. Eur. J.* **1997**, *3*, 1646; F. Renaud, C. Piguet, G. Bernardinelli, J.-C. G. Bünzli, G. Hopfgartner, *Chem. Eur. J.* **1997**, *3*, 1660; A. C. Try, M. M. Harding, D. G. Hamilton, J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.* **1998**, 723; J.-B. Regnouf-de-Vains, R. Lamartine, B. Fenet, *Helv. Chim. Acta* **1998**, *81*, 661; H. Brunner, I. Poleschak, *Z. Naturforsch.* **1997**, *52b*, 839; C. Botteghi, A. Schionato, G. Chelucci, H. Brunner, A. Kürzinger, U. Obermann, *J. Organomet. Chem.* **1989**, *370*, 17; C. Botteghi, G. Chelucci, G. Chessa, G. Delogu, S. Gladiali, F. Soccolini, *J. Organomet. Chem.* **1986**, *304*, 217; H. Nishiyama, S. Yamaguchi, S.-B. Park, K. Itoh, *Tetrahedron Asymmetry* **1993**, *4*, 143; C. Bolm, M. Zehnder, D. Bur, *Angew. Chem.* **1990**, *102*, 206; C. Bolm, M. Ewald, M. Felder, *Chem. Ber.* **1992**, *125*, 1205; K. Ito, T. Katsuki, *Chem. Lett.* **1994**, 1857; K. Ito, M. Yoshitake, T. Katsuki, *Tetrahedron* **1996**, *52*, 3905; C. Chen, K. Tagami, Y. Kishi, *J. Org. Chem.* **1995**, *60*, 5386; C. Duboc-Toia, S. Ménage, C. Lambeaux, M. Fontecave, *Tetrahedron Lett.* **1997**, *38*, 3727; A. C. Benniston, P. R. Mackie, A. Harriman, *Tetrahedron Lett.* **1997**, *38*, 3577; S. Ohawa, T. Uchida, T. Uchiya, T. Hirano, M. Saburi, Y. Uchida, *J. Chem. Soc., Perkin Trans.1* **1990**, 1649; N. Sabbatini, M. Guardigli, F. Bolletta, I. Manet, R. Ziessel, *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1501; P. D. Beer, F. Szemes, *J. Chem. Soc., Chem. Commun.* **1995**, 2245; O. Kocian, R. J. Mortimer, P. D. Beer, *Tetrahedron Lett*. **1990**, *31*, 5069; F. Vögtle, I. Luer, V. Balzani, N. Armaroli, *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1333; C. Kaes, M. W. Hosseini, A. D. Cian, J. Fischer, *Tetrahedron Lett*. **1997**, *38*, 3901.
[18] J. E. Parks, B. E. Wagner, R. H. Holm, *J. Organomet. Chem.* **1973**, *56*, 53.
[19] R. Bürli, A. Vasella, *Helv. Chim. Acta* **1996**, *79*, 1159.
[20] E. Kövári, R. Krämer, *Chem. Ber.* **1994**, *127*, 2151.
[21] F. Mohamadi, N. H. J. Richards, W. C. Guida, R. Liskamp, C. Caufield, M. Lipton, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440.
[22] K. Sone, P. Krumholz, H. Stammreich, *J. Am. Chem. Soc.* **1955**, *77*, 777.
[23] R. Ziessel, J.-M. Lehn, *Helv. Chim. Acta* **1990**, *73*, 1149.

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