A New Generation of 6,6′-Disubstituted 2,2′-Bipyridines: Towards Novel *Oligo*(bipyridine) Building Blocks for Potential Applications in Materials Science and Supramolecular Chemistry

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The 6,6′-disubstituted 2,2′-bipyridines and *oligo*(bipyridines) are often used as ligands in supramolecular chemistry; however, their range of application has been limited due to the lack of unsymmetrically functionalized compounds and their poor solubility. We describe herein a new generation of specially designed unsymmetrical bipyridine building blocks possessing different protecting groups for the hydroxy functionality and reasonable solubility behavior. These molecules permit the synthesis of a wide range of functionalized *oligo*(bipyridines) with new potential applications in supramolecular chemistry and materials science. As initial examples, we present the synthesis of mono- and bis-functionalized bis- and tris-2,2′-biypridines.

Introduction

In the last two decades, many well-defined supramolecular architectures have been achieved by the self-assembly of organic components[1]. Possible applications are seen in catalysis[2], electrochemistry[3], photochemistry[4], or new materials[5]. However, only a few systems fulfill the requirements for practical applications such as formation of special architectures using recognition-directed self-assembly features, availability of the components in usable quantities, and the presence of end groups that can be covalently incorporated into networks and assemblies. The most prominent examples for self-organization systems are the 6,6′-disubstituted *oligo*(2,2′-bipyridine) copper(I) or silver(I) complexes with methyloxymethylene linkers between the bipyridine units[1a][1b][6] due to their ability to spontaneously form well-defined helical architectures, similar to the Watson and Crick double-helix in nucleic acids[7]. However, only the simple non-functionalized ligands and their complexes are known[6]. A different approach using a stepwise construction starting from different template units was recently described[8] by Siegel et al.

Transformations of such building blocks into other systems (like synthetic macromolecules) or combination with other supramolecular systems are rare[9][10]. This may be explained by the lack of a suitable synthetic route to unsymmetrically 6,6′-functionalized 2,2′-bipyridines or functionalized *oligo*(bipyridines), and by the relatively low solubility of methyl substituted *oligo*(bipyridines)[6f]. However, such systems should show novel properties due to the helicity, self-organization and cooperative features of the bipyridine units.

Results and Discussion

The syntheses of 6,6′-disubstituted-2,2′-bipyridine building blocks have been a major goal in organic and supramolecular chemistry[11][12]. Besides efforts towards metal-binding cryptands or spherands (see, for instance, the most prominent example in this field, the "sexipyridine"[13]), ligand systems for potential antitumor agents[14] or derivatives for protein labeling[15], the central interest in the last decade has been focused on the construction of *oligo*(bipyridine) strands as basic ligands for double helical architectures[1a][1b][6]. Non-functionalized *oligo*(bipyridines) containing two to five 2,2′-bipyridine units have been synthesized using chemistry based on such well-described com-

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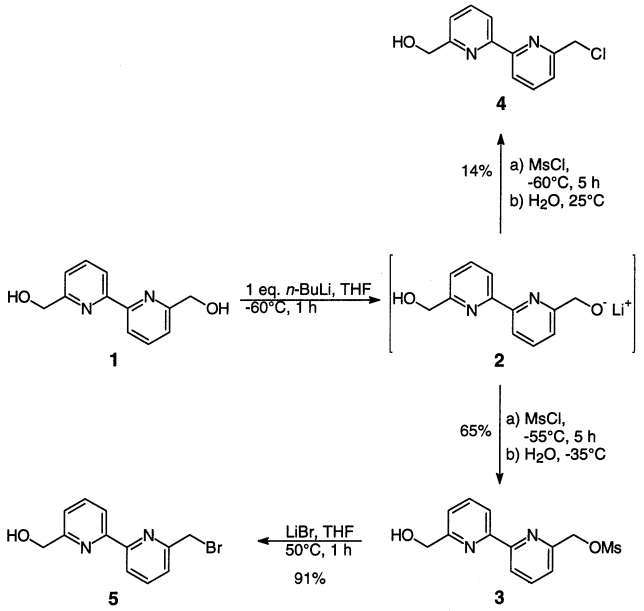
pounds as 6,6′-disubstituted-2,2′-bipyridine. Although notable efforts have been made in the last few years to develop large scale routes[9a][9e][9g][12a], to the best of our knowledge, there have been no directed strategies towards unsymmetrically functionalized bipyridines known prior to our first communication in 1995[9b]. Furthermore, there has been a complete lack of functionalized and soluble *oligo*(bipyridines). Two exceptions should, however, be mentioned: Lehn et al. described a method for the synthesis of terminated monobromo bis(bipyridine) and the corresponding hydroxy compound in small scale and medium yields[6f]. The bisfunctionalized 2,2′-bipyridine was obtained, as a side product in 8% yield, during the bromination of the bishydroxy compound with HBr[16].

We recently published preliminary results in the first directed strategy towards unsymmetrically functionalized bipyridines (Scheme 1)[9b]. Treatment of the 6,6′-bis(hydroxymethyl)-2,2′-bipyridine **1** (available in multigram quantities using the traditional *N*-oxidation and Boekelheide rearrangement strategy starting from 6,6′-dimethyl-2,2′-bipyridine[6b][9e][9g][12a]) with *n*-butyllithium in THF in a narrow temperature range of −50 to −60°C resulted in a white precipitate (the monolithium salt **2**)[17]. Subsequent treatment of **2** with methanesulfonyl chloride (MsCl) led to 6-methylsulfonyloxymethyl-6′-hydroxymethyl-2,2′-bipyridine (**3**) in 65% yield when the reaction was quenched at −35°C with water. The corresponding 6-chloromethyl-6′-hydroxymethyl-2,2′-bipyridine (**4**) was obtained in 17% yield if the reaction mixture was allowed to warm up to 25°C. Reaction of **3** with LiBr in THF gave (91%) the previously described 6-bromomethyl-6′-hydroxymethyl-2,2′-bipyridine (**5**).

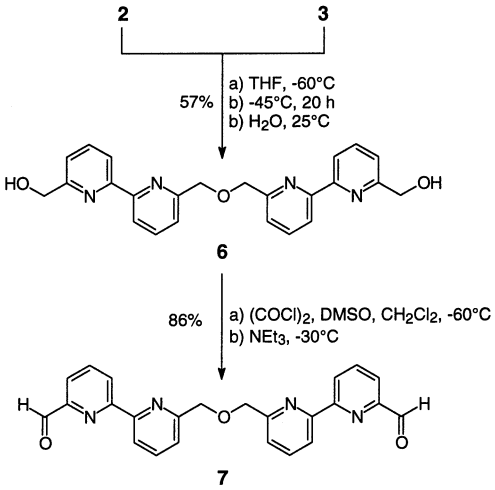
Scheme 1



The methodology using the low solubility of a non-functionalized intermediate represents, to the best of our knowledge, the most powerful strategy towards novel bipyridine building blocks[18]. Recently it was shown that symmetrically 5,5′-difunctionalized 2,2′-bipyridines can be also converted into unsymmetrically functionalized molecules with the same strategy[19].

As a first application towards functionalized *oligo*(bipyridines), we treated **3** with the monolithio compound **2** to obtain (57%) the bishydroxymethylbis(bipyridine) **6**, which is the first reported bisfunctionalized *oligo*(bipyridine)[9b][17][20] (Scheme 2). Treatment of **6** with oxalyl chloride in DMSO[21] in the prescence of NEt_3 resulted in the formation of the bis(aldehyde) **7**[17], an interesting intermediate towards hydrogen bonding supramolecular units (e.g., through oxime functionalities[22]). These compounds (especially **6**) show very low solubility in aprotic solvents; furthermore, the key methanesulfonyl intermediate could not be stored due to its rapid decomposition[23]. The synthesis of higher generations of functionalized *oligo*(bipyridines) by sequential Williamson condensation using this building block seemed not to be the best way.

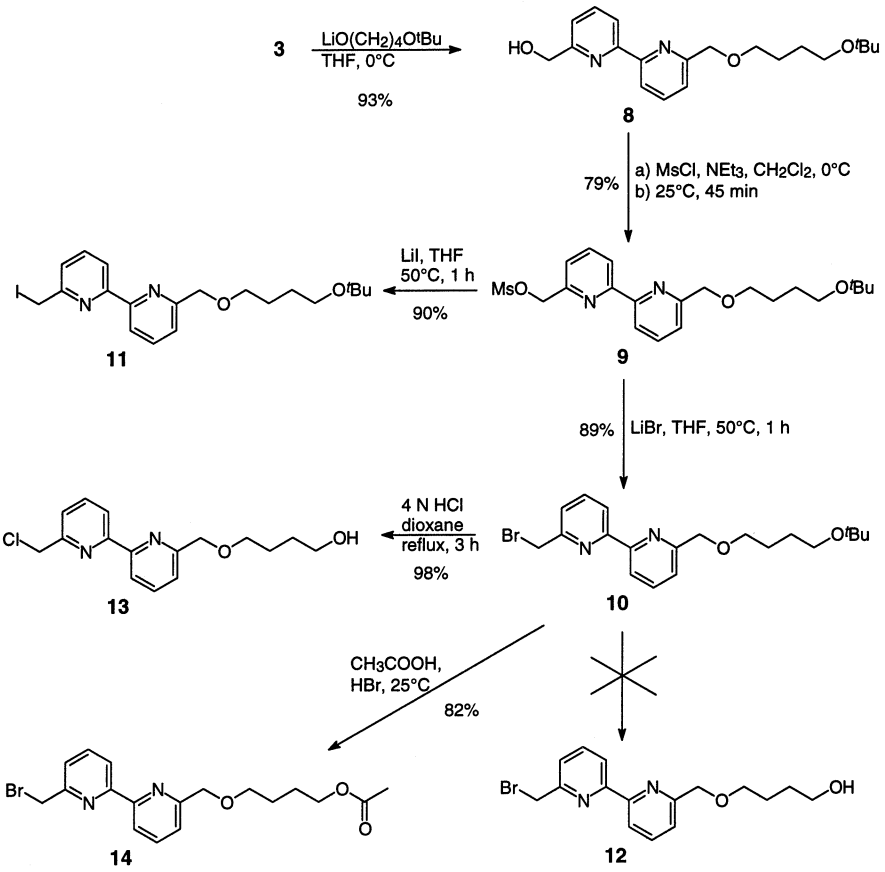
Scheme 2



A new strategy for the building blocks was devised to circumvent these problems. Reaction of mesylate **3** with a 10-fold excess of lithium 4-*tert*-butyloxybutoxide[24] afforded (93%) 6-(4′′-*tert*-butyloxytetramethylenoxymethyl)-6′-(hydroxymethyl)-2,2′-bipyridine (**8**)[25] (Scheme 3), which represents a very soluble, monoprotected bisfunctionalized bipyridine. Reaction of **8** with MsCl afforded (79%) the corresponding methylsulfonyl-terminated 2,2′-bipyridine (**9**) and, after reaction with LiBr in THF, the 6′-(bromomethyl)-6-(4′′-*tert*-butyloxytetramethylenoxymethyl)-2,2′-bipyridine (**10**) was obtained in 89% yield. Using LiI instead of LiBr resulted (90%) in the corresponding iodo-terminated product (**11**).

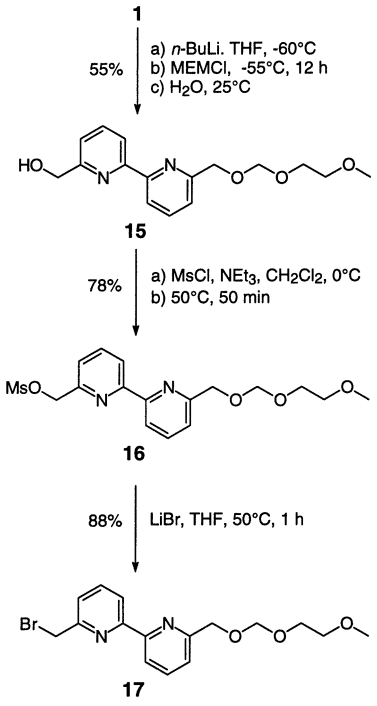
The standard deprotection procedures for such *tert*-butylalcohol protection groups (4 N HCl in dioxane[28b][9a][9e][9g][26]) gave, to our surprise, not the expected the compound (**12**), but the corresponding 6′-(chloromethyl)-6-(4′′-hydroxytetramethylenoxymethyl)-2,2′-bipyridine (**13**) in 98% yield. To circumvent this problem, we then utilized the acetyl group [bipyridine (**14**)], which could then be removed using mildly basic or acidic conditions[28b][27].

Scheme 3



Soluble, unsymmetrically functionalized bipyridines with a protecting group on the hydroxymethyl group could also be obtained using a slightly different approach (Scheme 4). The principle problem was to find a reagent that would react with the monolithium salt of **1** in a reasonable yield and time as well as in the required temperature range; methoxyethoxymethyl chloride (MEMCl) proved to be a suitable reagent. After 10 h of stirring at −60°C, followed by warming to 25°C, it was possible to isolate (55%) of the monoprotected bipyridine (**15**). Application of the transformation method (with methanesulfonyl chloride and LiBr) resulted in 6-(methoxyethoxymethyloxymethyl)-6′-(methylsulfonyloxymethyl)-2,2′-bipyridine (**16**) (78%) and 6′-(bromomethyl)-6-(methoxyethoxymethyloxymethyl)-2,2′-bipyridine (**17**) (88%), respectively. The MEM protecting group could be easily removed using the literature methods[28] to give the desired 6,6′-unsymmetrically bisfunctionalized 2,2′-bipyridines in high yields.

Scheme 4

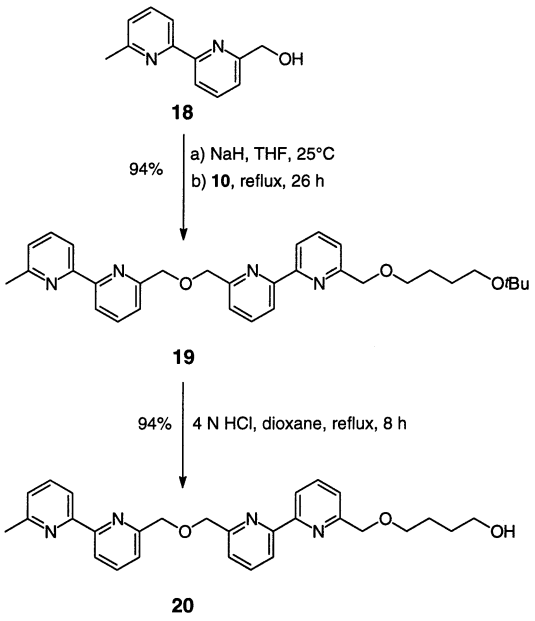


Reaction of **15**, **16**, or **17** with suitable coupling partners and subsequent removal of the MEM group allows the controlled building of supramolecular systems with bipyridine segments.

The specially designed building blocks described above were used to build larger functionalized *oligo*(bipyridines). The first examples are shown in Scheme 5. Reaction of the 6-(hydroxymethyl)-6′-methyl-2,2′-bipyridine (**18**) (available via *N*-oxidation route[9a][9e][9f][12a]) with the bromide **10** resulted in a 94% yield of the monofunctionalized bis(bipyri-

dine) **19**. Deprotection (4 N HCl, dioxane) resulted (94%) in the hydroxy terminated bis(bipyridine) **20**.

Scheme 5



Use of the 6′-(bromomethyl)-6′′′-methyl-6,6′′-[oxybis-(methylene)]bis[2,2′-bipyridine] (**22**) as starting material gave the corresponding monofunctionalized tris(bipyridine) **23** with a molecular mass of 724.90 g/mol in 90% yield by reaction with (**8**) (Scheme 6). The coupling of the 6-(hydroxymethyl)-6′-methyl-2,2′-bipyridine (**18**) with the 6,6′-dibromomethyl-2,2′-biypridine (**21**)[9e][29] was performed on a multigram scale yielding 55% of 6′-(bromomethyl)-6′′′-methyl-6,6′′-[oxybis(methylene)]bis[2,2′-bipyridine] (**22**) using a 1.7 fold excess of **21**[30] (the preparation of compound **22** has already been described in the literature on a smaller scale with 45% yield[6f]).

Scheme 6

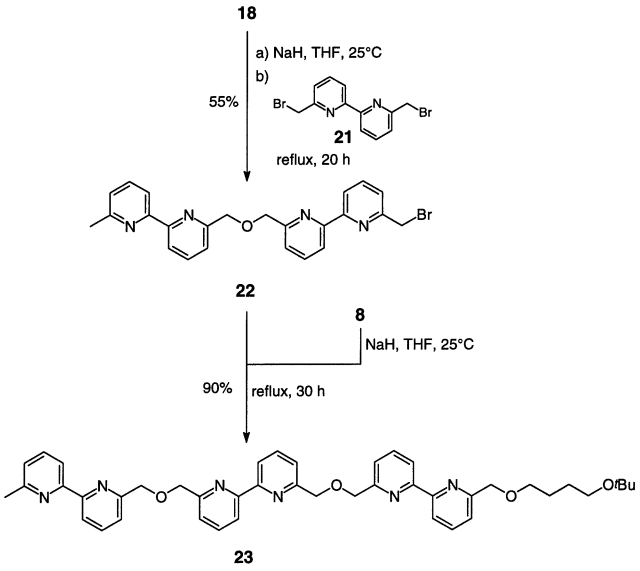
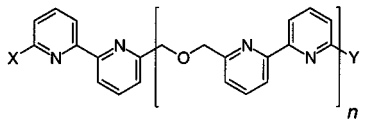


Table 1. Described functionalized *oligo*(bipyridines) including the molecular masses of the molecules and the functional groups[a]



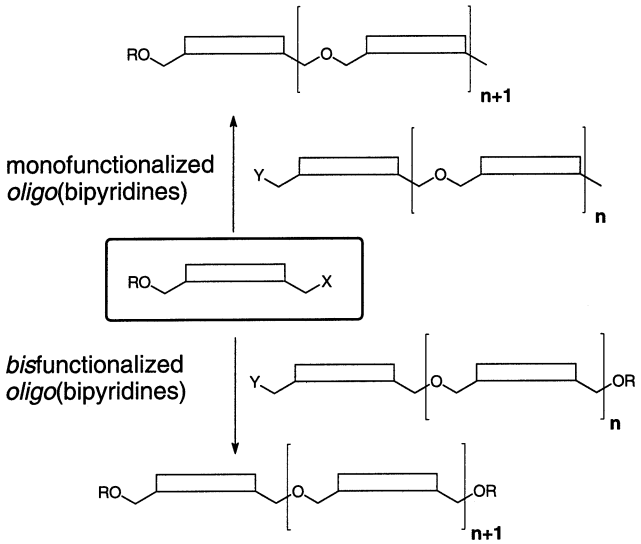
Compound	Yield [%]	Calculated molecular mass [g/mol]	*n*	X	Y
6	57	414.46	1	CH_2OH	CH_2OH
7	86	410.43	1	CHO	CHO
19	94	526.68	1	CH_3	$CH_2O(CH_2)_4OtBu$
20	94	470.57	1	CH_3	$CH_2O(CH_2)_4OH$
22	55	461.36	1	CH_3	CH_2Br
23	90	724.90	2	CH_3	$CH_2O(CH_2)_4OtBu$

[a] X, Y = substituents including functional groups; *n* = repeat units.

All *oligo*(bipyridine) compounds described are highly soluble in common organic solvents. Most resonance peaks and couplings of the compounds described here were confirmed taking cross-peaks and correlation peaks.

The functionalized *oligo*(bipyridines) are summarized in Table 1. Using the new building blocks and Williamson condensation reactions a wide range of functionalized ligands with 1 to 5 bipyridine units are accessible, opening new avenues for the use of such *oligo*(bipyridines) (Figure 1).

Figure 1. Schematic representation of the Williamson condensation strategy leading to functionalized *oligo*(bipyridines) [for non-functionalized *oligo*(bipyridines) see[6f]]



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Experimental Section

General Remarks: All solvents were dried and distilled before use. − Column chromatography: Merck silica gel 50, 0.0040−0.0063 mm (230−400 mesh). − NMR: Bruker AC 250 (250 and 62.9 MHz for ^{1}H and ^{13}C, respectively) and Bruker AMX 300 (300 and 75 MHz for ^{1}H and ^{13}C, respectively) and Bruker DRX 500 (500 and 125.8 MHz for ^{1}H and ^{13}C, respectively) spectrometers were used to record ^{1}H- and ^{13}C-NMR spectra in $CDCl_3$ (25°C) unless specified otherwise. ^{1}H- and ^{13}C chemical shifts are given in δ units relative to $CDCl_3$ or TMS as internal standard. − For kugelrohr distillations a Büchi kugelrohr was used.

6,6′-Bis(hydroxymethyl)-2,2′-bipyridine (**1**) was synthesized according to published procedures[12a][9g] with m.p. 145−146°C (146−147°C[12a]). − ^{1}H NMR (250 MHz): δ = 4.01 (t, 2 H, *J* = 4.7, OH-H), 4.84 (d, 2 H, *J* = 4.7, 7,7′-H), 7.26 (d, 2 H, *J* = 7.8, 5,5′-H), 7.83 (t, 2 H, *J* = 7.8, 4,4-H), 8.34 (d, 2 H, *J* = 7.8, 3,3′-H). − ^{13}C NMR (62.9 MHz): δ = 64.26 (7,7′-C), 119.73 (3,3′-C), 120.59 (5,5′-C), 137.60 (4,4′-C), 154.66 (6,6′-C), 158,64 (2,2′-C). − MS (EI, 70 eV); *m/z* (%): 215 (100) [$M^+ - 1$]. − $C_{12}H_{12}N_2O_2$ (216.2): calcd. C 66.65, H 5.61, N 12.96; found: C 66.66, H 5.51, N 12.86.

6′-(Hydroxymethyl)-6-(methylsulfonyloxymethyl)-2,2′-bipyridine (**3**): A solution of 5.0 g (23.1 mmol) of 6,6′-bis(hydroxymethyl)-2,2′-bipyridine (**1**) in 250 ml of dry THF was cooled to −60°C and treated dropwise under argon with 9.25 ml (23.1 mmol) of *n*-butyllithium (2.5 N solution in hexane). Immediately a white precipitate could be observed (the mono lithium salt **2**). The reaction mixture was stirred for 1 h at −55°C and then treated with 1.8 ml (23.1 mmol) of methanesulfonyl chloride (MsCl) in dry THF (30 ml). The color changed to light yellow. After 5 h at −50°C, the solution was warmed up to −35°C and quenched with 10 ml of water. The solvent was removed in vacuo (low temperature!). The solid was dissolved in 250 ml of CH_2Cl_2 and extracted with water (3 × 100 ml). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 3.5 g (65%) of **3**, as a white solid with m.p. 101−103°C. − ^{1}H NMR (250 MHz): δ = 3.11 (s, 3 H, 8-H), 4.83 (s, 2 H, 7′-H), 5.31 (s, 2 H, 7-H), 7.29 (d, *J* = 7.8, 1 H, 5′-H), 7.51 (dd, *J* = 7.9, 0.4, 1 H, 5-H), 7.85 (t, *J* = 7.8, 1 H, 4′-H), 7.91 (t, *J* = 7.9, 1 H, 4-H), 8.34 (d, *J* = 7.8, 1 H, 3′-H), 8.43 (dd, *J* = 7.9, 1 H, 3-H). − ^{13}C NMR (62.9 MHz): δ = 37.85 (8-C), 63.94 (7′-C), 71.55 (7-C), 119.53 (3′-C), 120.00 (3-C), 120.61 (5′-C), 122.18 (5-C), 137.48 (4′-C), 137.81 (4-C), 152.87 (2′-C), 153.91 (2-C), 155.27 (6-C), 58.53 (6′-C). − MS (EI, 70 eV); *m/z* (%): 294 (7) [M^+]. − $C_{13}H_{14}N_2O_4S$ (294.3): calcd. C 53.05, H 4.79, N 9.52; found: C 53.44, H 4.61, N 9.37.

6-(Chloromethyl)-6′-(hydroxymethyl)-2,2′-bipyridine (**4**): A suspension of 9.3 mmol of 6′-(hydroxymethyl)-6-(lithiooxymethyl)-2,2′-bipyridine (**2**) in 100 ml of THF under argon was treated dropwise at −60°C with 1.06 g (9.3 mmol) of MsCl in dry THF (10 ml). The reaction mixture was warmed up to 25°C and quenched with 5 ml of water. The solvent was removed in vacuo, the remaining solid was dissolved in 150 ml of CH_2Cl_2 and extracted with water (3 × 50 ml). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 300 mg (14%) of **4**, as a white solid with m.p. 98−100°C. − ^{1}H NMR (250 MHz): δ = 4.76 (s, 2 H, 7-H), 4.84 (s, 2 H, 7′-H), 7.26 (d, *J* = 7.6, 1 H, 5-H), 7.51 (d, *J* = 7.6, 1 H, 5′-H), 7.82 (t, *J* = 7.6, 1 H, 4-H), 7.86 (t, *J* = 7.6, 1 H, 4′-H), 8.37 (d, *J* = 7.6, 2 H, 3,3′-H). − ^{13}C NMR (62.9 MHz): δ = 46.85 (7-C), 63.93 (7′-C), 119.93 (3-C), 120.15 (3′-C), 120.57 (5-C), 122.82 (5′-C), 137.64 (4-C), 137.89 (4′-C), 154.41 (2-C), 155.19 (2′-C), 156.16 (6-C), 158.20 (6′-C). − MS (EI, 70 eV); *m/z* (%): 234 (41) [M^+].

6-(Bromomethyl)-6′-(hydroxymethyl)-2,2′-bipyridine (**5**): To a solution of 1.0 g (7.9 mmol) of 6′-(hydroxymethyl)-6-(methylsulfonyloxymethyl)-2,2′-bipyridine (**3**) in 100 ml of THF was added 6.5 g (75.7 mmol) of lithium bromide. The mixture was heated at 50°C for 1 h and then concentrated in vacuo. The crude product was partitioned between $CHCl_3$ and saturated ammonium chloride solution (1:1; each 100 ml). The aqueous solution was extracted with $CHCl_3$ (3 × 150 ml), the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 99:1) to yield 920 mg (91%) of **5**, as a white solid with m.p. 129−131°C (130−131°C[16]). − ^{1}H NMR (250 MHz, ^{1}H-^{1}H COSY): δ = 3.99 (s, 1 H, OH-H), 4.63 (s, 2 H, 7-H), 4.71 (s, 2 H, 7′-H), 7.25 (d, 1 H, *J* = 7.6, 5′-H), 7.48 (d, 1 H, *J* = 7.6, 5-H), 7.81 (t, 1 H, *J* = 7.6, 4-H or 4′-H), 7.82 (t, 1 H, *J* = 7.6, 4-H or 4′-H), 8.33 (d, 1 H, *J* = 7.6, 3-H or 3′-H), 8.39 (d, 1 H, *J* = 7.6, 3-H or 3′-H). − ^{13}C NMR (62.9 MHz): δ = 34.01 (7-C), 63.93 (7′-C), 120.00 (3′-C), 120.13 (3-C), 120.58 (5′-C), 123.51 (5-C), 137.66 (4′-C), 137.89 (4-C), 154.40 (2′-C), 155.34 (2-C), 156.33 (6-C), 158.17 (6′-C). − MS (EI, 70 eV); *m/z* (%): 279/279 (81/83) [M^+]. − $C_{12}H_{11}BrN_2O$ (279.1): calcd. C 51.63, H 3.97, N 10.04; found: C 51.67, H 4.13, N 9.90.

6′,6′′′-Bis(hydroxymethyl)-6,6′-[oxybis(methylene)]bis[2,2′-bipyridine] (**6**): A suspension of 9.3 mmol of 6′-(hydroxymethyl)-6-(lithiooxymethyl)-2,2′-bipyridine (**2**) in 100 ml of THF was treated dropwise at −60°C with 2.54 g of (9.3 mmol) 6′-(hydroxymethyl)-6-(methylsulfonyloxymethyl)-2,2′-bipyridine (**3**) in dry THF. The mixture was stirred for 20 h at −45°C, then warmed slowly to 25°C and quenched with 5 ml water. The solvent was evaporated in vacuo and the residue washed with $CHCl_3$ to yield 2.19 g (57%) of **6**, as a white solid with m.p. 187−189°C (188−190°C[17]). − ^{1}H NMR ([D$_6$]DMSO, 250 MHz): δ = 4.65 (s, 3 H, 7′,7′′′-H), 4.85 (s, 2 H, 7,7′′-H), 7.53 (d, *J* = 7.6, 1 H, 5′,5′′′-H), 7.61 (d, *J* = 7.6, 1 H, 5,5′′-H), 7.93 (t, *J* = 7.6, 1 H, 4′,4′′′-H), 7.97 (t, *J* = 7.6, 1 H, 4,4′′-H), 8.23 (d, *J* = 7.6, 1 H, 3′,3′′′-H), 8.30 (d, *J* = 7.6, 1 H, 3,3′′-H). − MS (EI, 70 eV); *m/z* (%): 414 (7) [M^+]. − $C_{24}H_{22}N_4O_3$ (414.5): calcd. C 69.55, H 5.36, N 13.52; found: 69.19, H 5.64, N 13.72.

6′,6′′′-Bis(formyl)-6,6′′-[oxybis(methylene)]bis[2,2′-bipyridine] (**7**): A solution of 1.1 ml (12 mmol) of oxalyl chloride in dry CH_2Cl_2 (30 ml) was cooled down to −60°C under argon and treated with 1.9 ml (25 mmol) of DMSO in 5 ml of CH_2Cl_2. After 10 min 0.50 g (3.8 mmol) of 6′,6′′′-bis(hydroxymethyl)-6,6′′-[oxybis(methylene)]bis[2,2′-bipyridine] (**6**) in 5 ml of DMSO was added dropwise. The temperature was raised slowly to −30°C, the mixture stirred for 2 h and quenched with 10 ml of NEt_3. The

solution was warmed to 20°C, treated with 40 ml of H_2O and extracted with CH_2Cl_2 (2 × 100 ml). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product was washed with Et_2O and recrystallized from MeOH to yield 400 mg (86%) of **7**, as a white solid with m.p. 200−202°C (ref.[17] 201−203°C). − ^{1}H NMR (250 MHz): δ = 4.94 (s, 4 H), 7.64 (d, *J* = 7.8, 2 H), 7.92 (t, *J* = 7.8, 2 H), 7.97 (d, *J* = 4.5, 4 H), 8.48 (d, *J* = 7.8, 2 H), 8.68 (q, *J* = 7.8, 2 H), 10.18 (s, 2 H). − ^{13}C NMR (62.9 MHz): δ = 73.93, 120.00, 121.40, 122.01, 125.24, 137.76, 137.84, 152.32, 154.37, 156.63, 158.05, 193.68. − MS (EI, 70 eV); *m/z* (%): 345 (100) [M^+]. − $C_{24}H_{18}N_4O_3$ (410.4): calcd. C 70.23, H 4.42, N 13.65; found: C 69.89, H 4.18, N 13.77.

6-(4-tert-Butyloxytetramethylenoxymethyl)-6′-(hydroxymethyl)-2,2′-bipyridine (**8**): A solution of 14 g of 4-*tert*-butoxybutane-1-ol (mixture with 1,4-bis-*tert*-butoxybutane, 45% 4-*tert*-butoxybutane-1-ol[24]) in 100 ml of THF was treated at 25°C with 4.1 ml (10.1 mmol) of *n*-butyllithium (2.5 M in hexane). The solution was then warmed to 50°C for 15 min and then cooled to 0°C. A solution of 1.0 g (3.4 mmol) of 6′-(hydroxymethyl)-6-(methylsulfonyloxymethyl)-2,2′-bipyridine (**3**) in 100 ml of THF was added dropwise followed by stirring for 2 h at 25°C. The reaction was quenched with 10 ml of water and concentrated in vacuo. The crude product was dissolved in 100 ml of $CHCl_3$, extracted with saturated ammonium chloride solution (3 × 100 ml) and water (3 × 100 ml), dried (Na_2SO_4), and concentrated in vacuo. The excess of butane spacer was removed by kugelrohr distillation to yield 1.09 g (93%) of **8**, as a light colored oil. − ^{1}H NMR (300 MHz, ^{1}H-^{1}H COSY): δ = 1.16 (s, 9 H, 6′′-H), 1.62 (m, 2 H, 3′′-H), 1.75 (m, 2 H, 2′′-H), 3.36 (t, 2 H, *J* = 6.3, 4′′-H), 3.60 (t, 2 H, *J* = 6.3, 1′′-H), 4.03 (t, 1 H, *J* = 4.0, OH-H), 4.64 (s, 2 H, 7-H), 4.79 (t, 2 H, *J* = 4.0, 7′-H), 7.46 (d, 1 H, *J* = 7.7, 5-H), 7.50 (d, 1 H, *J* = 7.7, 5′-H), 7.74 (t, 1 H, *J* = 7.7, 4′-H), 7.77 (t, 1 H, *J* = 7.7, 4-H), 8.27 (d, 2 H, *J* = 7.7, 3-H), 8.31 (d, 2 H, *J* = 7.7, 3′-H). − ^{13}C NMR (75 MHz, ^{1}H-^{13}C COSY, SEFT, HMBC): δ = 26.68 (2′′-C), 27.33 (3′′-C), 27.50 (6′′-C), 61.30 (4′′-C), 63.90 (7′-C), 71.00 (1′′-C), 72.48 (5′′-C), 73.90 (7-C), 119.40 (3-C), 119.80 (3′-C), 120.28 (5′-C), 121.32 (5′-C), 137.40 (4-C), 137.90 (4′-C), 154.80 (2′-C), 154.90 (2-C), 158.10 (6′-C), 158.70 (6-C). − MS (EI, 70 eV); *m/z* (%): 345 (100) [M^+]. − $C_{20}H_{28}N_2O_3$ (344.5): calcd. C 69.73, H 8.21, N 8.13; found: C 69.61, H 8.11, N 8.00.

6-(4-tert-Butyloxytetramethylenoxymethyl)-6′-(methylsulfonyloxymethyl)-2,2′-bipyridine (**9**): At 0°C 0.5 ml (6 mmol) of MsCl and 1.6 ml (11 mmol) of NEt_3 were added sequentially to a solution of 0.50 g (1.5 mmol) of 6-(4-*tert*-butyloxytetramethylenoxymethyl)-6′-(hydroxymethyl)-2,2′-bipyridine (**8**) in 50 ml of CH_2Cl_2. After 15 min the solution was warmed to 25°C and stirred for 45 min. The solution was washed with saturated ammonium chloride solution (3 × 100 ml), dried ($MgSO_4$) and concentrated in vacuo at 30°C. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 99:1) to yield 480 mg (79%) of **9**, as a white, easily decomposable solid with m.p. 41−43°C. − ^{1}H NMR (300 MHz, ^{1}H-^{1}H COSY): δ = 1.18 (s, 9 H, 6′′-H), 1.66 (m, 2 H, 3′′-H), 1.74 (m, 2 H, 2′′-H), 3.10 (s, 3 H, CH_3S-H), 3.40 (t, 2 H, *J* = 6.3, 4′′-H), 3.63 (t, 2 H, *J* = 6.3, 1′′-H), 4.71 (s, 2 H, 7′-H), 5.41 (s, 2 H, 7-H), 7.47 (d, 1 H, *J* = 7.7, 5-H), 7.50 (d, 1 H, *J* = 7.7, 5′-H), 7.82 (t, 1 H, *J* = 7.7, 4′-H), 7.86 (t, 1 H, *J* = 7.7, 4-H), 8.28 (d, 2 H, *J* = 7.7, 3′-H), 8.42 (d, 2 H, *J* = 7.7, 3-H). − ^{13}C NMR (75 MHz, ^{1}H-^{13}C COSY, SEFT, HMBC): δ = 26.6 (2′′-C), 27.3 (3′′-C), 27.5 (6′′-C), 38.1 (CH_3S), 61.2 (4′′-C), 71.0 (1′′-C), 71.8 (7-C), 72.4 (5′′-C), 73.8 (7-C), 119.6 (3-C), 121.0 (3-C), 121.5 (5′-C), 122.2 (5-C), 137.5 (4′-C), 137.9 (4-C), 152.9 (2-C), 154.6 (2′-C), 158.1 (6-C), 158.6 (6′-C). − MS (EI, 70 eV); *m/z* (%): 423 (100) [M^+]. − $C_{21}H_{30}N_2O_5S$ (422.5): calcd. C 59.72, H 7.17, N 6.63; found: C 59.67, H 7.12, N 6.58.

6-(4′′-tert-Butyloxytetramethylen-1′′-oxymethyl)-6′-(bromomethyl)-2,2′-bipyridine (**10**): To a solution of 400 mg (1.0 mmol) of 6-(4′′-*tert*-butyloxytetramethylenoxymethyl)-6′-(methylsulfonyloxymethyl)-2,2′-bipyridine (**9**) in 30 ml of THF was added 1.84 g (21 mmol) of lithium bromide. The mixture was heated at 50°C for 1 h and then concentrated in vacuo. The crude product was partitioned between $CHCl_3$ and saturated ammonium chloride solution (1:1; each 100 ml). The aqueous solution was extracted with $CHCl_3$ (3 × 50 ml), and the combined organic layers dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 0.34 g (89%) of **10**, as a white solid with m.p. 71−73°C. − ^{1}H NMR (300 MHz, ^{1}H-^{1}H COSY): δ = 1.18 (s, 9 H, 6′′-H), 1.63 (m, 2 H, 3′′-H), 1.72 (m, 2 H, 2′′-H), 3.38 (t, 2 H, *J* = 6.3, 4′′-H), 3.62 (t, 2 H, *J* = 6.3, 1′′-H), 4.68 (s, 2 H, 7-H), 4.71 (s, 2 H, 7′-H), 7.44 (d, 1 H, *J* = 7.7, 5-H), 7.48 (d, 1 H, *J* = 7.7, 5′-H), 7.79 (t, 1 H, *J* = 7.7, 4-H), 7.81 (t, 1 H, *J* = 7.7, 4′-H), 8.31 (d, 2 H, *J* = 7.7, 3,3′-H). − ^{13}C NMR (75 MHz, ^{1}H-^{13}C COSY, SEFT, HMBC): δ = 26.64 (2′′-C), 27.29 (3′′-C), 27.52 (6′′-C), 34.11 (7-C), 61.22 (4′′-C), 70.97 (1′′-C), 72.43 (5′′-C), 73.85 (7′-C), 119.75 (3′-C), 120.28 (3-C), 21.29 (5′-C), 123.21 (5-C), 137.37 (4′-C), 137.73 (4-C), 154.90 (2′-C), 156.11 (2,6-C), 158.60 (6′-C). − MS (EI, 70 eV); *m/z* (%): 408 (43%) [M^+]. − $C_{20}H_{27}BrN_2O_2$ (407.4): calcd. C. 58.96, H. 6.69, N. 6.99; found: C 59.03, H 6.76, N 6.80.

6-(4′′-tert-Butyloxytetramethylen-1′′-oxymethyl)-6′-(iodomethyl)-2,2′-bipyridine (**11**): To a solution of 300 mg (0.71 mmol) of 6-(4′′-*tert*-butyloxy-tetramethylene-1′′-oxymethyl)-6′-(methylsulfonyloxymethyl)-2,2′-bipyridine (**10**) in 30 ml of THF was added 1.9 g (14.2 mmol) of lithium iodide. The mixture was heated at 50°C for 1 h and then concentrated in vacuo. The crude product was partitioned between $CHCl_3$ and saturated ammonium chloride solution (1:1; each 100 ml). The aqueous solution was extracted with $CHCl_3$ (3 × 100 ml), the combined organic layers dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, $CHCl_3$/acetone/25% NH_3, 10:1:0.012) to yield 290 mg (90%) of **11**, as a white solid. − ^{1}H NMR (500 MHz): δ = 1.18 (s, 9 H, 6′′-H), 1.60−1.75 (m, 2 H, 2′′,3′′-H), 3.38 (t, 2 H, *J* = 6.4, 4′′-H), 3.62 (t, 2 H, *J* = 6.4, 1′′-H), 4.58 (s, 2 H, 7′-H), 4.70 (s, 2 H, 7-H), 7.40 (d, 1 H, *J* = 7.8, 5-H), 7.48 (d, 1 H, *J* = 7.8, 5′-H), 7.73 (t, 1 H, *J* = 7.8, 4-H), 7.82 (t, 1 H, *J* = 7.8, 4′-H), 8.26 (d, 1 H, *J* = 7.8, 3-H), 8.33 (d, 1 H, *J* = 7.8, 3′-H). − ^{13}C NMR (125.8 MHz): δ = 6.7 (7′-C), 26.7 (2′′-C), 27.4 (3′′-C), 27.6 (6′′-C), 61.3 (4′′-C), 71.0 (1′′-C), 72.5 (5′′-C), 73.9 (7-C), 119.8 (3′-C), 119.9 (3-C), 121.3 (5′-C), 122.7 (5-C), 137.4 (4′-C), 137. 7 (4-C), 155.0 (6′-C), 156.0 (6-C), 157.6 (2′-C), 158.5 (2-C). MS (EI, 70 eV); *m/z* (%): 455.1 (77) [M^+ + H]. − $C_{20}H_{27}N_2O_2I$ (454.4): calcd. C 52.86, H 6.00, N 6.17; found: C 52.92, H 6.06, N 6.30.

6′-(Chloromethyl)-6-(hydroxytetramethylen-oxymethyl)-2,2′-bipyridine (**13**): To a mixture of 60 ml of dioxane and 10 ml of 4 N HCl was added 740 mg (1.82 mmol) of 6′-(bromomethyl)-6-(4′′-*tert*-butoxytetramethylen-1′′-oxymethyl)-2,2′-bipyridine (**10**) and the mixture was refluxed for 3 h. The solvent was removed in vacuo, the residue was neutralized with 1 M $NaHCO_3$ solution and extracted with CH_2Cl_2 (3 × 50 ml). The combined layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, $CHCl_3$/acetone/25% NH_3, 10:1:0.025) to yield 550 mg (98%) of **13**, as an oil. − ^{1}H NMR (250 MHz): δ = 1.69−1.80 (m, 4 H, 2′′,3′′-H), 2.21 (s, 1 H, OH-H), 3.63−3.69 (m, 4 H, 1′′,2′′-H), 4.72 (s, 2 H, 7-H), 4.75 (s, 2 H, 7′-

H), 7.46 (d, 1 H, *J* = 7.7, 5-H or 5′-H), 7.48 (d, 1 H, *J* = 7.7, 5-H or 5′-H), 7.82 (t, 1 H, *J* = 7.7, 4-H or 4′-H), 7.83 (t, 1 H, *J* = 7.7, 4-H or 4′-H), 8.34 (d, 1 H, *J* = 7.7, 3-H or 3′-H), 8.35 (d, 1 H, *J* = 7.7, 3-H or 3′-H). − ^{13}C NMR (62.9 MHz): δ = 26.8 (2′′-C), 30.0 (3′′-C), 46.9 (7′-C), 62.7 (4′′-C), 71.0 (1′′-C), 73.9 (7-C), 119.9 (3′-C), 120.4 (3-C), 121.4 (5′-C), 122.6 (5-C), 137.5 (4′-C), 137.8, (4-C), 155.1 (6′-C), 155.7 (6-C), 156.0 (2′-C), 158.0 (2′-C).− MS (EI, 70 eV); *m/z* (%): 305 (43) [M$^+$]. − $C_{16}H_{19}ClN_2O_2$ (306.8): calcd. C 62.63, H 6.25, N 9.13; found: C 62.47, H 6.23, N 9.18.

6-(4′′-Acetoxytetramethylen-1′′-oxymethyl)-6′-(bromomethyl)-2,2′-bipyridine (**14**): To a solution of 120 ml of acetic acid and 8 ml of HBr (48%) was added 700 mg (1.7 mmol) of 6′-(bromomethyl)-6-(4′′-*tert*-butoxytetramethylen-1′′-oxymethyl)-2,2′-bipyridine (**10**), and the mixture was stirred for 30 min at 25°C. The mixture was concentrated in vacuo and the liquid residue was neutralized with 1 M $NaHCO_3$ solution. The aqueous solution was extracted with $CHCl_3$ (3 × 100 ml), the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, $CHCl_3$/acetone/25% NH_3, 25:1:0.012) to yield 550 mg (82%) of **14**. − ^{1}H NMR (250 MHz,): δ = 1.73−1.79 (m, 4 H, 2′′,3′′-H), 2.04 (s, 3 H, 6-H), 3.63 (t, 2 H, *J* = 6.3, 1′′-H), 4.11 (t, 2 H, *J* = 6.3, 4′′-H), 4.63 (s, 2 H, 7′-H), 4.74 (s, 2 H, 7-H), 7.46 (d, 1 H, *J* = 7.8, 5-H or 5′-H), 7.49 (d, 1 H, *J* = 7.8, 5-H or 5′-H), 7.81 (t, 1 H, *J* = 7.8, 4′-H or 4-H), 7.86 (t, 1 H, *J* = 7.8, 4′-H or 4-H), 8.35 (d, 2 H, *J* = 7.8, 3,3′-H). − ^{13}C NMR (62.9 MHz): δ = 20.96 (6′′-C), 25.50 (3′′-C), 26.27 (2′′-C), 34.05 (7′-C), 64.26 (4′′-C), 70.46 (1′′-C), 73.70 (7-C), 120.03 (3′-C), 120.46 (3-C), 121.42 (5′-C), 123.42 (5-C), 137.79 (4′-C), 137.86 (4-C), 154.69 (6′-C), 155.50 (2-C), 156.22 (6′-C), 158.17 (2′-C), 171.12 (5′′-C). − MS (EI, 70 eV); *m/z* (%): 390 (5) [M$^+$ + H]. − $C_{18}H_{21}BrN_2O_3$ (393.3): calcd. C 54.94, H 5.39, N 7.12; found: C 54.84, H 5.30, N 7.16.

6′-(Hydroxymethyl)-6-(methoxyethoxymethyloxymethyl)-2,2′-bipyridine (**15**): A solution of 2.0 g (9.3 mmol) of 6,6′-bis(hydroxymethyl)-2,2′-bipyridine (**1**) in 100 ml of THF was cooled to −60°C and treated dropwise with 3.7 ml *n*-butyllithium (2.5 M in hexane). After stirring for 1 h at −55°C, 1.06 ml (9.3 mmol) of methoxyethoxymethyl chloride (MEMCl) was added dropwise. The mixture was warmed to 25°C during 12 h, quenched with water (5 ml) and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (150 ml), washed with water (3 × 50 ml), and dried ($MgSO_4$). After concentration in vacuo, the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 1.55 g (55%) of **15**, as a light colored oil. − ^{1}H NMR (250 MHz): δ = 3.40 (s, 3 H, 4′′-H), 3.60 (m, 2 H, 3′′-H), 3.80 (m, 2 H, 2′′-H), 4.14 (s, b, 1 H, OH-H), 4.83 (d, 2 H, 7-H), 4.93 (s, 2 H, 7′-H), 4.94 (s, 2 H, 1′′-H), 7.24 (d, 1 H, *J* = 7.8, 5-H), 7.47 (d, 1 H, *J* = 7.8, 5′-H), 7.79 (t, 1 H, *J* = 7.8, 4-H), 7.82 (t, 1 H, *J* = 7.8, 4′-H), 8.13 (d, 1 H, *J* = 7.8, 3-H), 8.34 (d, 1 H, *J* = 7.8, 3′-H). − ^{13}C NMR (62.9 MHz): δ = 58.93 (4′′-C), 63.94 (7-C), 67.05 (3′′-C), 70.46 (2′′-C), 71.71 (7′-C), 95.38 (1′′-C), 119.54 (5′-C), 119.75 (5-C), 120.31 (3′-C), 121.49 (3′-C), 137.37 (4′-C), 137.49 (4′-C), 154.74 (6′-C), 154.93 (2′-C), 157.73 (2-C), 158.17 (6′-C). − MS (EI, 70 eV); *m/z* (%): 305.1 (100) [M$^+$ + 1]. − $C_{16}H_{20}N_2O_4$ (304.3): calcd. C 63.14, H 6.64, N 9.21; found: C 63.01, H 6.66, N 8.91.

6-(Methoxyethoxymethyloxymethyl)-6′-(methylsulfonyloxymethyl)-2,2′-bipyridine (**16**): At 0°C 1.1 ml (13 mmol) of MsCl and 3.7 ml (26 mmol) of NEt_3 were added sequentially to a solution of 1.00 g (3.3 mmol) of 6′-(hydroxymethyl)-6-(methoxyethoxymethyloxymethyl)-2,2′-bipyridine (**15**) in 100 ml of CH_2Cl_2. After 30 min the solution was warmed to 25°C and stirred for 50 min. The solution was washed with saturated ammonium chloride solution (3 × 150 ml), dried ($MgSO_4$), and concentrated in vacuo at 30°C. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 980 mg (78%) of **16**, as a viscous oil. − ^{1}H NMR (250 MHz): δ = 3.05 (s, 3 H, SCH_3-H), 3.36 (s, 3 H, 4′′-H), 3.54 (m, 2 H, 3′′-H), 3.75 (m, 2 H, 2′′-H), 4.78 (s, 2 H, 7′-H), 4.88 (s, 2 H, 1′′-H), 5.36 (s, 3 H, 7-H), 7.43 (dd, 1 H, *J* = 7.8, 0.5, 5-H), 7.44 (dd, 1 H, *J* = 7.8, 0.5, 5′-H), 7.79 (t, 1 H, *J* = 7.8, 4-H), 7.82 (t, 1 H, *J* = 7.8, 4′-H), 8.27 (dd, 1 H, *J* = 7.8, 0.5, 3-H), 8.44 (dd, 1 H, *J* = 7.8, 0.5, 3′-H). − ^{13}C NMR (62.9 MHz): δ = 37.96 (SCH_3-C), 58.83 (4′′-C), 66.95 (3′′-C), 70.31 (2′′-C), 71.60 (7-C), 71.70 (7′-C), 95.27 (1′′-C), 119.59 (5′-C), 120.89 (5-C), 121.59 (3′-C), 122.13 (3-C), 137.36 (4′-C), 137.78 (4-C), 152.79 (6′-C), 154.62 (2′-C), 155.86 (2-C), 157.66 (6-C). − MS (EI, 70 eV); *m/z* (%): 383 (100%) [M$^+$ + 1]. − $C_{17}H_{22}N_2O_6S$ (382.4): calcd. C 53.39, H 5.80, N 7.33; found: C 52.99, H 5.89, N 7.64.

6′-(Bromomethyl)-6-(methoxyethoxymethyloxymethyl)-2,2′-bipyridine (**17**): To a solution of 500 mg (1.3 mmol) of 6-(methoxyethoxymethyloxymethyl)-6′-(methylsulfonyloxymethyl)-2,2′-bipyridine (**16**) in 40 ml of THF was added 2.52 g (29 mmol) of lithium bromide. The mixture was heated at 50°C for 1 h, concentrated in vacuo and the crude product partitioned between $CHCl_3$ and saturated ammonium chloride solution (1:1; each 100 ml). The aqueous solution was extracted with $CHCl_3$ (3 × 100 ml), the combined organic layers were dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 420 mg (88%) of **17** as an oil. − ^{1}H NMR (250 MHz): δ = 3.40 (s, 3 H, 4′′-H), 3.59 (m, 2 H, 3′′-H), 3.79 (m, 2 H, 2′′-H), 4.62 (s, 2 H, 7′-H), 4.82 (s, 2 H, 7-H_7), 4.92 (s, 2 H, 1′-H), 7.43 (d, 1 H, *J* = 7.8, 5-H), 7.46 (d, 1 H, *J* = 7.8, 0.5, 5′-H), 7.79 (t, 1 H, *J* = 7.8, 4-H), 7.82 (t, 1 H, *J* = 7.8, 4′-H), 8.35 (d, 1 H, *J* = 7.8, 3-H), 8.36 (d, 1 H, *J* = 7.8, 3′-H). − ^{13}C NMR (62.9 MHz): δ = 34.09 (7′-C), 58.96 (4′′-C), 67.06 (3′′-C), 70.49 (2′′-C), 71.73 (7′-C), 95.39 (1′′-C), 119.87 (5′-C), 120.31 (5-C), 121.51 (3′-C), 123.27 (3-C), 137.39 (4′-C), 137.74 (4-C), 155.01 (6′-C), 155.81 (2′-C), 156.09 (2-C), 157.63 (6-C). − MS (EI, 70 eV); *m/z* (%): 367 (55%) [M$^+$]. − $C_{16}H_{19}BrN_2O_3$ (367.2): calcd. C 52.33, H 5.32, N 7.63; found: C 52.16, H 5.22, N 7.44.

6′-(4′′′′-tert-Butoxytetramethylen-1′′′′-oxymethyl)-6′′′-methyl-6,6′′-[oxybis(methylene)]bis[2,2′-bipyridine] (**19**): A solution of 638 mg (3.19 mmol) of 6-(hydroxymethyl)-6′-methyl-2,2′-bipyridine (**18**) in 100 ml of THF was treated under argon with 135.9 mg (3.40 mmol) of NaH (60%). After stirring for 1 h, 1.18 g (2.90 mmol) of 6′-(bromomethyl)-6-(4′′-*tert*-butoxytetramethylenoxymethyl)-2,2′-bipyridine (**10**) was added and the mixture refluxed for 26 h. The solvent was removed in vacuo, the residue was dissolved in $CHCl_3$ (200 ml), washed with water (3 × 150 ml), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 1.44 g (94%) of **19**, as a white solid. − ^{1}H NMR (300 MHz): δ = 1.18 (s, 9 H, 6′′′′-H), 1.67 (m, 2 H, 3′′′′-H), 1.75 (m, 2 H, 2′′′′-H), 2.63 (s, 3 H, 7′′′-H), 3.38 (t, 2 H, *J* = 6.3, 4′′′′-H), 3.62 (t, 2 H, *J* = 6.3, 1′′′′-H), 4.72 (s, 2 H, 7-H), 4.91 (s, 4 H, 7′,7′′′-H), 7.15 (d, 1 H, *J* = 7.7, 5′′′-H), 7.47 (d, 1 H, *J* = 7.7, 5-H), 7.57 (m, 2 H, 5′,5′′′-H), 7.67 (t, 1 H, *J* = 7.7, 4′′′-H), 7.78 (t, 1 H, *J* = 7.7, 4-H), 7.83 (m, 2 H, 4′,4′′′-H), 8.19 (d, 1 H, *J* = 7.7, 3′′′-H), 8.29 (d, 1 H, *J* = 7.7, 3-H), 8.31 (m, 2 H, 3′,3′′′-H). − ^{13}C NMR (75 MHz): δ = 24.66, 26.69, 27.35, 27.57, 61.29, 71.03, 72.48, 73.97, 74.00, 118.21, 119.68, 119.84, 121.12, 121.24, 123.20, 137.00, 137.36, 137.45, 155.39, 155.58, 155.63, 157.87, 157.90, 158.55. − MS (FAB); *m/z* (%): 527 (100) [M$^+$]. − $C_{32}H_{38}N_4O_3$ (526.7): calcd. C 72.96, H 7.29, N 10.64; found: C 73.01, H 7.08, N 10.31.

6′-(Hydroxytetramethylenoxymethyl)-6′′′-methyl-6,6′′-[oxybis(methylene)]bis[2,2′′-bipyridine] (**20**): To a mixture of 100 ml of

dioxane and 20 ml of 4 N HCl was added 1.0 g (1.9 mmol) of 6′-(4′′′′-*tert*-butoxytetramethylen-1′′′′-oxymethyl)-6′′′-methyl-6,6′′-[oxybis(methylene)]bis[2,2′-bipyridine] (**19**) and the mixture refluxed for 8 h. The solvent was removed in vacuo, the residue was dissolved in $CHCl_3$ (200 ml) and washed with water (3 × 100 ml), dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 99:1) to yield 840 mg (94%) of **20**, as a white solid. – ^{1}H NMR (250 MHz): δ = 1.66–1.83 (m, 4 H, 2′′′′-H), 2.63 (s, 3 H, 7′′′-H), 3.35–3.69 (m, 4 H, 1′′′′,4′′′′-H), 4.72 (s, 2 H, 7-H), 4.91 (s, 4 H, 7′,7′′-H), 7.15 (d, *J* = 7.7, 1 H, 5′′′-H), 7.43 (d, *J* = 7.7, 1 H, 5-H), 7.52 (m, 2 H, 5′,5′′-H), 7.67 (t, *J* = 7.7, 1 H, 4′′′-H), 7.79 (t, *J* = 7.7, 1 H, 4-H), 7.83 (m, 2 H, 4′,4′′-H), 8.19 (d, *J* = 7.7, 1 H, 3′′′-H), 8.29–8.37 (m, 3 H, 3,3′,3′′-H). – ^{13}C NMR (62.9 MHz): δ = 24.56, 26.56, 29.98, 62.56, 70.97, 73.97, 118.16, 119.60, 121.08, 121.25, 123.16, 136.95, 137.40, 155.46, 155.81, 157.82, 157.93. – MS (FAB); *m/z* (%): 471 (12) [M^+ + 1]. – $C_{28}H_{30}N_4O_3$ (470.6): calcd. C 71.46, H 6.64, N 11.91; found: C 71.38, H 6.35, N 11.85.

6′-(Bromomethyl)-6′′′-methyl-6,6′′-[oxybis(methylene)]-bis[2,2′-bipyridine] (**22**): To a solution of 3.0 g (14.9 mmol) of 6-(hydroxymethyl)-6′-methyl-2,2′-bipyridine (**18**) in 200 ml of THF was added 400 mg (16.2 mmol) of NaH (97%) under argon. After stirring for 1 h at 25°C, 9.22 g (27.0 mmol) of 6,6′-bis(bromomethyl)-2,2′-bipyridine (**21**) was added and the mixture refluxed for 20 h. The solvent was removed in vacuo, the residue was dissolved in $CHCl_3$ (100 ml) and washed with water (3 × 100 ml), dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 99:1) to yield 3.80 g (55%, Lit.[6f]: 45%) of **20**, as a white solid with m.p. 143–145°C (Lit.[6f]: 142–144°C). – ^{1}H NMR (250 MHz): δ = 2.65 (s, 3 H, 7′′′-H), 4.62 (s, 2 H, 7-H), 4.90 (s, 2 H, 7′′-H), 4.91 (s, 2 H, 7′-H), 7.17 (d, *J* = 7.7, 1 H, 5′′′′-H), 7.44 (dd, *J* = 7.8, 0.8, 1 H, 5-H), 7.57 (d, *J* = 7.8, 1 H, 5′-H), 7.58 (d, *J* = 7.8, 1 H, 5′′-H), 7.69 (t, *J* = 7.7, 1 H, 4′′′-H), 7.78 (t, *J* = 7.8, 1 H, 4-H), 7.85 (t, *J* = 7.8, 2 H, 4′,4′′-H), 8.20 (d, *J* = 7.7, 1 H, 3,3′′-H), 8.34 (dd, *J* = 7.8, 0.8, 1 H, 4′,4′′′-H), 8.35 (d, *J* = 7.8, 1 H, 4,4′′-H), 8.37 (d, *J* = 7.8, 1 H, 3′,3′′′-H). – ^{13}C NMR (62.9 MHz): δ = 24.45, 34.12, 73.89, 73.93, 118.37, 119.97, 120.32, 121.21, 121.50, 123.27, 123.31, 137.23, 137.48, 137.76, 155.00, 155.33, 155.86, 156.12, 157.75, 157.86. – MS (FAB); *m/z* (%): 461 (9) [M^+]. – $C_{24}H_{21}BrN_4O$ (461.4): calcd. C 62.48, H 4.60, N 12.12; found: C 62.41, H 4.50, N 12.17.

6′-(4′′′′-tert-Butoxytetramethylen-1′′′′-oxymethyl)-6′′′-methyl-bis[2,2′-bipyridine]-6,6′′-[(2,2′-bipyridine-6,6′-diyl)bis-(methylenoxymethylene)] (**23**): A solution of 500 mg (1.45 mmol) of 6-(4′′-*tert*-butoxytetramethylenoxymethyl)-6′-(hydroxymethyl)-2,2′-bipyridine (**10**) in THF (100 ml) was treated with 67.95 mg (1.70 mmol) of NaH (60%). After stirring for 1 h at 25°C 738 mg (1.60 mmol) of 6′-(bromomethyl)-6′′′-methyl-6,6′′-[oxybis(methylene)]bis[2,2′-bipyridine] (**22**) was added and the mixture heated for 30 min under reflux and then concentrated in vacuo. The residue was dissolved in $CHCl_3$ (100 ml), washed with water (3 × 100 ml), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH, 98:2) to yield 946 mg (90%) of **23**, as a white solid. – ^{1}H NMR (300 MHz): δ = 1.18 (s, 9 H, 6′′′′-H), 1.67 (m, 2 H, 3′′′′-H), 1.72 (m, 2 H, 2′′′′-H), 2.63 (s, 3 H, 7′′′-H), 3.38 (t, 2 H, *J* = 6.2, 4′′′′-H), 3.62 (t, 2 H, *J* = 6.2, 1′′′′-H), 4.71 (s, 2 H, 7′′-H), 4.91 (s, 4 H, 7,7′-H), 7.16 (d, 1 H, *J* = 7.7), 7.47 (dd, 1 H, *J* = 7.7, 0.5), 7.57 (d, 2 H, *J* = 7.7), 7.68 (t, 1 H, *J* = 7.7), 7.78 (d, 1 H, *J* = 7.7), 7.83 (t, 2 H, *J* = 7.7), 7.84 (t, 2 H, *J* = 7.7), 8.19 (d, 1 H, *J* = 7.7), 8.28 (d, 1 H, H,H*J* = 7.7), 8.31 (d, 2 H, *J* = 7.7), 8.32 (d, 2 H, *J* = 7.7). – ^{13}C NMR (75 MHz): δ = 24.63, 26.68, 27.34, 27.55, 61.27, 71.01, 73.95, 118.20, 119.68, 119.85, 121.10, 121.23, 121.29, 123.17, 136.96, 137.34, 137.43, 155.36, 155.52, 157.86, 158.54. – MS (FD) *m/z* (%): 725 (100) [M^+]. – $C_{44}H_{48}N_6O_4$ (724.9): calcd. C 72.90, H 6.67, N 11.59; found: C 73.23, H 6.51, N 11.40.

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[O98259]