Bimacrocyclic Pyridines and 1,8-Naphthyridines: Basicities and Application in Base Catalysis[1]

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Abstract: Di-α-substituted N-heterocycles such as 2,6-halogenopyridines or 2,7-dichloro-1,8-naphthyridines can be coupled with 2,6-bis(alkenyloxy) substituted areneboronic acids. The resulting tetraenes are then cyclized by ring-closing metathesis to give bimacrocyclic concave pyridines or concave 1,8-naphthyridines. The relative basicity of the concave N-heterocycles was measured and their activity and selectivity was tested in the base-catalyzed addition of alcohols to diphenylketene.

Key words: macrocycles, boronic acids, molecular recognition, basicity, base catalysis

Molecular recognition is the basis of many processes in chemistry and in biology, from transport to catalysis.[2,3] The high selectivity of enzymatic processes arises in a large part from the concave shielding of the active site.[4–6] Concave reagents[7,8] copy this geometry but are not restricted to the twenty or so naturally occurring amino acids. Based on artificial substructures, concave bases,[7,9–11] concave acids,[12] and even concave N-heterocyclic carbenes[13] have been prepared. Their overall shape resembles that of a light bulb in a lamp shade,[7] with the light bulb being the active center and the lamp shade being the concave shielding (see Figure 1).

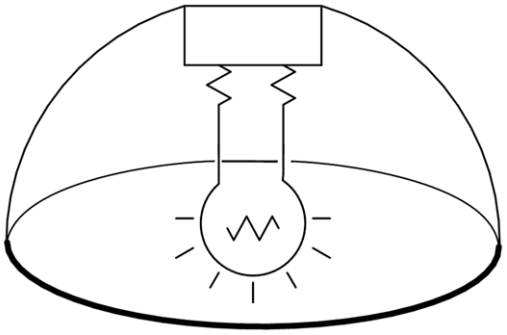
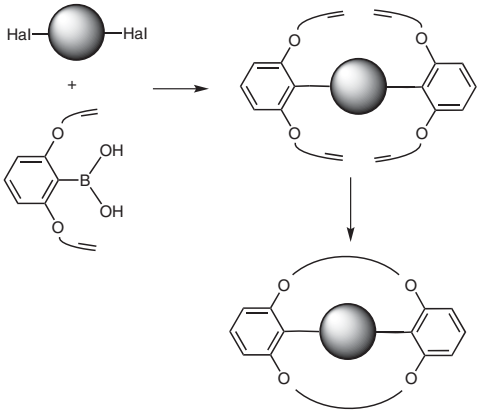


Figure 1 The 'light bulb in a lamp shade' model for concave reagents (see text)

In several applications, the necessity to tailor the active site of concave reagents has become apparent. As prognosticated by the blunt saying 'one enzyme – one substrate' (or vice versa), good selectivities have only been found when substrates and catalysts match. Slight variations in one or the other lead to more unselective reactions,[14,15] which is often observed with enzymes.

To enlarge the pool of concave bases, we have extended the family of concave pyridines[7,16,17] and have also synthesized and analyzed respective concave 1,8-naphthyridines.

Concave pyridines have been prepared by using a number of different synthetic routes,[7,16,17] and the same applies to related compounds such as concave 1,10-phenanthrolines.[9,18] The most efficient route involves the initial preparation of a diarylheterocycle that carries four alkenyl groups as substituents. Bimacrocyclization of the tetraene is then performed by ring-closing metathesis (Scheme 1).



Scheme 1 General synthetic strategy to bimacrocyclic concave reagents employing cross-coupling and ring-closing metathesis, optionally followed by hydrogenation; the sphere represents a dihalogeno-N-heterocycle in this work

The required building blocks are di-α-substituted heterocycles (Figure 2) and 2,6-dialkenyloxy substituted arylboronic acids (Scheme 1). For solubility and other reasons, in addition to di-α-substituted pyridines and 1,8-naphthyridines, heterocycles that were further substituted were also used. 2,6-Dibromopyridine (**1**) is commercially available, whereas 2,6-diiodo-3-methoxypyridine (**2**)[19] and the boronic acids[20] **8** were prepared as described.

Mangini and Colonna[21] developed a route to 4-substituted naphthyridines in 1942. Accordingly, 2,6-diaminopyridine (**4**) and ethyl benzoylacetate (**5**) were condensed in concentrated sulfuric acid to give 7-amino-2-hydroxy-4-phenyl-1,8-naphthyridine (**6**) as the hydrogensulfate in 75% yield (Scheme 2). Next, the amino group was substituted by a hydroxy group through diazotization and sub-

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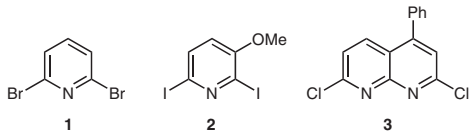
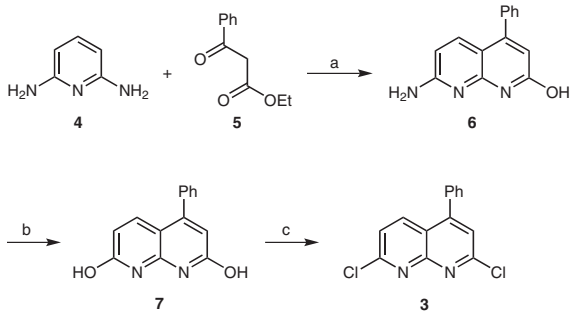


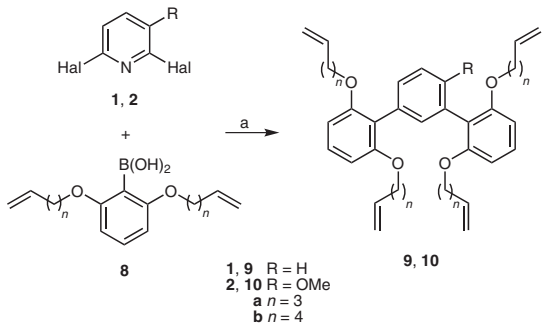
Figure 2 Di-α-substituted N-heterocycles **1**–**3** as coupling partners for Suzuki–Miyaura reactions (see Scheme 1)

sequent decomposition in water. Finally, two chlorine atoms were introduced by reaction of **7** with phosphorous pentachloride in phosphoryl chloride. The formally hydroxy-substituted naphthyridines **6** and **7** are able to form tautomers, therefore, intermediate **7** was not isolated and the yield of dichloride **3** was determined to be 38% over two steps. Although the yield was modest, the reaction can be carried out on a multigram scale.



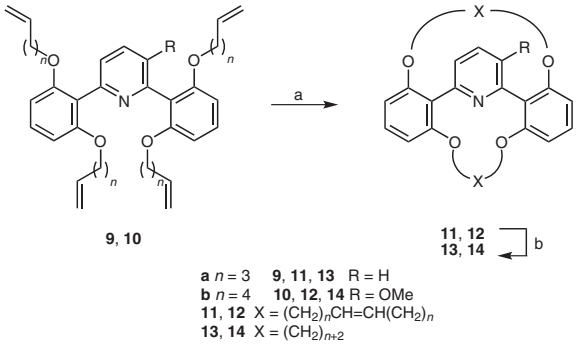
Scheme 2 Synthesis of 4-phenyl substituted dichloro-1,8-naphthyridine **3**. *Reagents and conditions*: (a) H_2SO_4, <40 °C, 16 h; (b) H_2SO_4, $NaNO_2$, 0 °C, 15 min; H_2O, 0–20 °C; (c) PCl_5, $POCl_3$, 0 °C; then reflux, 2.5 h.[21]

En route to the desired bimacrocyclic concave heterocycles, the next task was to introduce the bridgeheads. As described for a related system,[17] the Suzuki–Miyaura reaction was used to couple 2,6-dihalogenopyridines **1** and **2** with boronic acids **8a** and **8b**. The twofold coupling went well and tetraalkenes **9a**,**b** and **10a**,**b** were obtained in yields between 63 and 76% (Scheme 3).



Scheme 3 Suzuki–Miyaura cross coupling of 2,6-dihalogenopyridines **1** and **2** with dialkenyloxyboronic acids **8a**,**b**. *Reagents and conditions*: (a) $Pd(PPh_3)_4$, DME, H_2O, $Ba(OH)_2$, reflux, 16–48 h.

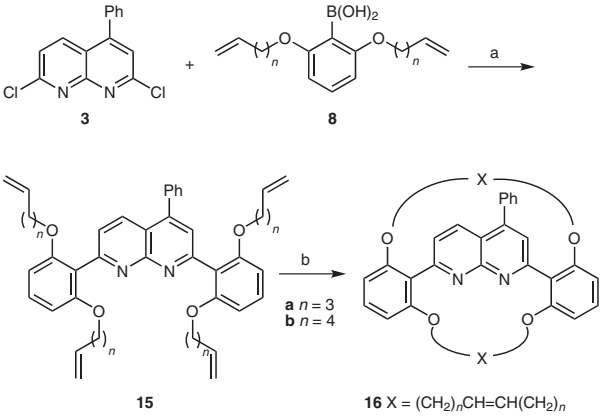
Using Grubbs' catalyst, tetraalkenes **9** and **10** were cyclized to form doubly unsaturated bimacrocycles **11** and **12** (Scheme 4). As found for related systems, the ring-closing metatheses proceeded in good yields of up to 92%. Products **11** and **12** were obtained as mixtures of *E*,*E*-, *E*,*Z*-, and *Z*,*Z*-diastereoisomers.



Scheme 4 (a) Ring-closing metatheses of tetraalkenyloxy-pyridines **9** and **10**: *Reagents and conditions*: (a) Grubbs' 1st generation catalyst, CH_2Cl_2, 16–48 h, r.t.; (b) Hydrogenation of *E*,*E*-, *E*,*Z*-, and *Z*,*Z*-mixtures of bimacrocyclic concave pyridines **11** and **12** to give concave pyridines **13** and **14** with saturated chains.

To transform the diastereoisomeric mixtures into a single compound, the double bonds of the bimacrocycles **11** and **12** were hydrogenated, and bimacrocycles **13** and **14** with saturated chains were obtained in yields of 88 to 97%.

An analogous route was chosen for the synthesis of concave bimacrocyclic 1,8-naphthyridines. Suzuki–Miyaura cross-coupling reactions have been reported for unsubstituted dichloronaphthyridine.[22] Not surprisingly, the cross coupling between boronic acids **8** and 2,7-dichloro-4-phenyl-1,8-naphthyridine (**3**) also went well. Tetrapentenyl (**15a**) and tetrahexenyl (**15b**) derivatives could be isolated in yields of 68 and 44%, respectively (Scheme 5). These yields correspond to yields of up 67 to 83% per coupling.



Scheme 5 Synthesis of concave 1,8-naphthyridines **16** by Suzuki–Miyaura cross-coupling between dichloronaphthyridine **3** and boronic acids **8**, followed by ring-closing metatheses of the resulting tetraenes **15**. *Reagents and conditions*: (a) $[Pd(PPh_3)_4]$, DME, H_2O, $Ba(OH)_2$, reflux, 16–48 h; (b) Grubbs' 1st generation catalyst, CH_2Cl_2, r.t., 16–48 h.

Tetraalkenes **15** were then subjected to ring-closing metathesis using Grubbs' 1st generation catalyst. In contrast to some other dimacrocyclizations in which monomacrocycles were also obtained,[23] the twofold metatheses proceeded smoothly with **15a** and **15b**, and the resulting bimacrocyclic dienes **16** were isolated in 87 and 83%, respectively.

One application of concave N-heterocycles is in base catalysis. In a bimacrocyclic system, the concave shielding has a distinct influence on the performance of the base. In general, the nature of the basic center determines the approximate basicity, but the shielding can generate distinct differences.[24,25] When the base reacts as a Brønsted base, it has to pick up a proton. In this process, the shielding will have a small but not negligible influence. The main difference compared with a nonshielded parent system originate from differences in solvation.[26–28]

In contrast, in reactions in which the base reacts as a nucleophile or a Lewis base, the shielding has an enormous influence on the performance of the base. In experiments with concave pyridines, for instance, the different shieldings were responsible for the selectivities of base-catalyzed reactions such as alcohol additions to ketenes.[24,25]

The basicity constant K_b describes the basicity of a Brønsted base quantitatively. To be able to compare all acids and bases, it is more convenient to discuss the acidity of the conjugate acids of the bases in the form of their pK_a values. By definition, pK_a values are based on water as solvent with pK_a + pK_b = 14 at 25 °C.[29] However, not all organic acids and bases are completely soluble in water. Therefore, related acidity constants have also been determined in several organic solvents.[30] In any case, each acidity constant reflects a relative acidity. In water, the reference point is the acidity of water (pK_a 15.5).

To investigate the Brønsted basicity of the new bimacrocyclic bases in ethanol, they were titrated with an acid/base indicator (thymol blue[31]) and the equilibrium constants were determined as described.[32] The resulting log *K* values can be discussed as the basicities of the bases, or as the acidities of the corresponding acids, with the first deprotonation of thymol blue being the reference point. Table 1 compiles these relative basicities log *K* for concave naphthyridines **16a** and **16b**, for concave pyridines **11**–**14** and other pyridines.

2,6-Lutidine (2,6-dimethylpyridine) and 2,4,6-collidine (2,4,6-trimethylpyridine) were included for comparison. These compounds are both 2,6-disubstituted, and the difference in basicity arises from the +I effect of the additional methyl substituent in the 4-position of collidine.

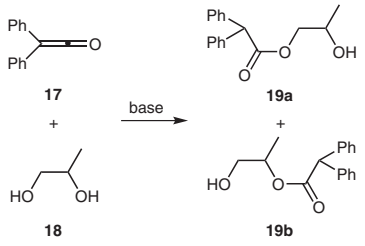
All concave pyridines **11**–**14** proved to be much more basic than the methylated pyridine analogues. One may speculate whether the oxygen atoms of the bridgeheads may stabilize the protonated form by hydrogen bonds. When compared with the concave 1,8-naphthyridines **16**, the pyridines are approximately two orders of magnitude more basic. This reflects the difference in basicity of the parent compounds [pK_a (pyridine): 5.25; pK_a (1,8-naphthyridine): 3.36].[33]

Table 1 The log *K* Values for Concave Naphthyridines **16a** and **16b**, Concave **11**–**14**, and Other Pyridines[a]

Base	log *K*
2,6-dimethylpyridine	1.3
2,4,6-trimethylpyridine	2.1
11a (*n* = 3)	3.2
11b (*n* = 4)	3.1
12a (*n* = 3)	3.5
12b (*n* = 4)	3.3
13b (*n* = 4)	3.5
14b (*n* = 4)	3.3
16a (*n* = 3)	0.9
16b (*n* = 4)	1.4

[a] The log *K* values are referenced to the first deprotonation of thymol blue in ethanol. Larger log *K* values correspond to stronger bases.

Finally, some of the pyridines were tested as catalysts in the base-catalyzed addition of alcohols to ketenes.[24] 1,2-Propanediol (**18**) was chosen as substrate and the regioselectivity of the mono-acylation by diphenylketene (**17**) was measured (Scheme 6). The addition of different alcohols to ketenes has been studied with a variety of shielded pyridines. The catalysis occurs by hydrogen-bond formation between the pyridine nitrogen atom and the OH groups thus enhancing the nucleophilicity of the alcohol.[24] To study the influence of the bimacrocyclic structure of a concave pyridine on the selectivity, the smallest bimacrocycle **11a**[34] and a respective non-bimacrocyclic pyridine **20** (which can be considered a bimacrocycle with infinitely long chains) were first compared (Table 2).



Scheme 6 Regioselective acylation of 1,2-propanediol (**18**) with diphenylketene (**17**) catalyzed by bases.

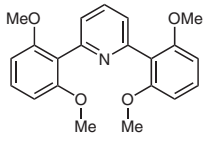
Even without any catalyst, the primary alcohol function is acylated fastest but only slightly less than three times as fast as the secondary function. The strongly shielded and less basic 2,6-di-*tert*-butylpyridine showed the same selectivity. Presumably, only the background reaction is detected in this case. The other pyridines, however, speed up the reaction and lead to the preferred formation of 1-(di-

Table 2 Regioselectivities of the Monoacylation of 1,2-Propanediol with Diphenylketene (**17**) Catalyzed by Concave and Nonconcave Pyridines

Base	**19a**/**19b**[a]
–	2.8[b]
pyridine	6.5[b]
2-methylpyridine	9.6[b]
2,6-dimethylpyridine	6.9[b]
2,6-di-*tert*-butylpyridine	2.7
20	10.3
11a (n = 3)	10.0

[a] The selectivities are reported as the ratio of 1- to 2-acylated products.
[b] Selectivities comparable to reported values.[25a]

phenylacetoxy)-2-propanol (**19a**). By comparison to 2,6-dimethylpyridine, introduction of aryl rings in the α-position in the pyridine enhances the selectivity (**11a** and **20**). In this base-catalyzed reaction, however, it does not make a difference whether a bimacrocyclic structure is used as in **11a** or the 'open' tetramethoxy analogue **20** is employed (Figure 3).



20

Figure 3 2,6-Diarylpyridine **20**[35] as an 'open' comparison to concave pyridines

In conclusion, starting from di-α-halogeno-N-heterocycles (pyridines **1** or **2**, or 1,8-naphthyridine **3**) and 2,6-dialkenyloxyboronic acids **8**, concave N-heterocycles **11**–**14** and **16** can easily be synthesized by a reaction sequence involving Suzuki–Miyaura cross-coupling and ring-closing metathesis. The basicity of the nitrogen atoms in the concave structures is conserved and they may be used as catalysts in base catalysis.

Commercially available chemicals were used without further purification. 2,6-Bis(pent-4-enyloxy)phenylboronic acid (**8a**),[20] 2,6-bis(hex-5-enyloxy)phenylboronic acid (**8b**),[20] 2,7-dichloro-4-phenyl-1,8-naphthyridine (**3**),[21] and 2,6-diiodo-3-methoxypyridine (**2**)[19] were prepared according to literature procedures. Anhydrous solvents were obtained with suitable desiccants. Column chromatography was carried out on silica gel (0.04–0.063 mm, Macherey–Nagel). ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC 200, ARX 300, DRX 500, or AV 600 instruments. Assignments were supported by COSY, HSQC, and HMBC experiments. Even when obtained by DEPT, the type of ^{13}C signal is always listed as singlet, doublet, etc. All chemical shifts are referenced to TMS or to the residual proton or carbon signal of the solvent. If not stated otherwise, coupling constants are ^3J. Mass spectra were recorded with a Finnigan MAT 8200 or MAT 8230. ESI mass spectra were recorded with an Applied Biosystems Mariner Spectrometry Workstation. IR spectra were recorded with a Perkin–Elmer 1600 Series spectrometer. Elemental analyses were carried out with a Euro EA 3000 Elemental Analyzer from Euro Vector.

Miyaura-Suzuki Cross-Coupling; General Procedure A
In DME and H_2O (ca. 4:1), dihalogeno-N-heterocycle **1**, **2**, or **3** was mixed with boronic acid **8** (2.5 equiv), barium hydroxide (1.5 equiv, based on the amount of boronic acid **8**), and $Pd(PPh_3)_4$ (5–10 mol%, based on the amount of N-heterocycle **1**, **2** or **3**). The mixture was heated to reflux for 16–48 h, then H_2O (20–30 mL) and $CHCl_3$ (20–30 mL) were added and the layers were separated. The aqueous layer was extracted with $CHCl_3$ (3 × 20–30 mL) and brine (20 mL). After drying with $MgSO_4$, the solvent was evaporated in vacuo and the product was purified by chromatography.

Ring-Closing Metathesis; General Procedure B
Excluding oxygen, the tetraalkene precursor was dissolved in anhydrous CH_2Cl_2 (c = 0.01 mmol/l). After addition of benzylidenebis(tricyclohexylphosphine)-dichlororuthenium (Grubbs' 1st generation cat.; 5–10 mol-%), the mixture was stirred at r.t. for 16–48 h. Diisopropylamine (5–10 mL) was then added and stirring was continued for 45 min. The mixture was filtered through basic aluminum oxide using a mixture of CH_2Cl_2 and diisopropylamine as eluent. No fractions were taken so that all *E*/*Z* isomers could be collected. The crude product mixture was purified by chromatography.

Hydrogenation; General Procedure C
The product of the ring-closing metathesis was dissolved in MeOH. In case of low solubility, some $CHCl_3$ was added. As catalyst, for every 100 mmol of substrate, 10.0 mg of palladium on charcoal (10%) was used. The catalyst was mixed with MeOH (5.0 mL) and hydrogen was bubbled through the resulting suspension for 30 min to activate the catalyst. The solution of the substrate was then added and the resulting mixture was stirred under hydrogen at r.t. for 16–24 h. The solvents were evaporated and the crude product was purified by chromatography.

2,7-Dichloro-4-phenyl-1,8-naphthyridine (3)
While cooling with ice, crude 2,7-dihydroxy-4-phenyl-1,8-naphthyridine (**7**; 13.8 g, max. 57.9 mmol) and phosphorous pentachloride (10.5 g, 50.4 mmol) were added to phosphoryl chloride (50.0 mL, 536 mmol). The mixture was heated to reflux for 2.5 h. After cooling to r.t., the mixture was poured on ice. A beige solid precipitated, which was purified by chromatography (silica gel, CH_2Cl_2).

Yield: 6.13 g (38%); mp 157–159 °C (Lit.[21] 158 °C).

IR (KBr): 2928, 1654, 1116 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.7 Hz, 1 H, H-5), 7.47 (s, 1 H, H-3), 7.45 (d, J = 8.7 Hz, 1 H, H-6), 7.62–7.40 (m, 5 H, Ph-H).

MS (EI, 70 eV): m/z (%) = 276, 274 (60, 100) $[M]^+$, 241, 239 (51, 54) $[M - Cl]^+$, 203 (60) $[M - 2Cl]^+$.

MS (CI, isobutane): m/z (%) = 277, 275 (69, 100) $[M]^+$.

2-Hydroxy-4-phenyl-1,8-naphthyridin-7-yl-ammonium Hydrogensulfate (6·H_2SO_4)
2,6-Diaminopyridine (**4**; 10.9 g, 83.5 mmol) was added to ethyl benzoylacetate (**5**; 24.7 g, 123 mmol) and the mixture was warmed to 120 °C to give a homogeneous mixture. After cooling to –10 °C, concd H_2SO_4 (25 mL) was added dropwise to the solid mass in such a way that the temperature remained below 40 °C. The mixture was stirred for 16 h at 35–40 °C and then poured on ice (100 g). The mixture was made basic with concd ammonia (ca. 50 mL) and stirred at r.t. for 1 h. The resulting solid was filtered off and washed with hot EtOH to give the product.

Yield: 16.9 g (max. 85%); green solid.

IR (KBr): 3325, 3135, 1619, 1369 cm^{-1}.

2,7-Dihydroxy-4-phenyl-1,8-naphthyridine (7)
Compound **6**·H_2SO_4 (16.9 g, 71.4 mmol) was added to concd H_2SO_4 (140 mL). While cooling with ice, sodium nitrite (8.05 g, 116 mmol) was added and the solution was stirred for 15 min at 0 °C and at r.t. for 10 min. Carefully, the mixture was poured on ice (300 mL) and the mixture was stirred for 10 min. To neutralize, (a large amount of) sodium carbonate solution was added. The resulting solid was separated, washed with deionized water, and dried in vacuo. The crude product was poorly soluble and was therefore used without further purification.

Crude yield: 13.8 g (ca. 81%).

IR (KBr): 3426, 1654, 1116 cm^{-1}.

MS (ESI+, DMSO): *m/z* (%) = 239 (27) $[M + H]^+$.

2,6-Bis[2,6-bis(pent-4-enyloxy)phenyl]pyridine (9a)
Synthesized according to General Procedure A with 2,6-dibromopyridine (**1**; 360 mg, 1.52 mmol), 2,6-bis(pent-4-enyloxy)phenylboronic acid (**8a**; 1.11 g, 3.79 mmol) and $Pd(PPh_3)_4$ (178 mg, 150 μmol) in DME (95 mL) and H_2O (15 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 6:1) gave **9a** as almost colorless flakes.

Yield: 540 mg (63%).

IR (KBr): 2940, 2866, 1641, 1598, 1456, 1246, 1101 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.72 (t, *J* = 7.7 Hz, 1 H, H-4), 7.21 (t, *J* = 8.3 Hz, 2 H, H-4′, H-4″), 7.20 (d, *J* = 7.7 Hz, 2 H, H-3, H-5), 6.55 (d, *J* = 8.4 Hz, 4 H, H-3′, H-3″, H-5′, H-5″), 5.72 (tdd, *J* = 6.7, 10.2, 17.2 Hz, 4 H, C*H*=CH_2), 4.98–4.87 (m, 8 H, CH=CH_2), 3.98 (t, *J* = 6.5 Hz, 8 H, OCH_2), 2.01–1.91 (m, 8 H, CH_2CH=CH_2), 1.69–1.59 (m, 8 H, OCH_2CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.7 (s, C-2′, C-2″, C-6′, C-6″), 154.1 (s, C-2, C-6), 138.1 (d, *C*H=CH_2), 134.7 (d, C-4), 128.9 (d, C-4′, C-4″), 123.7 (d, C-3, C-5), 121.1 (s, C-1′, C-1″), 114.1 (t, CH=CH_2), 105.6 (d, C-3′, C-3″, C-5′, C-5″), 67.8 (t, OCH_2), 29.9 (t, $OCH_2CH_2CH_2$), 28.3 (t, OCH_2CH_2).

MS (CI, isobutane): *m/z* (%) = 568 (100) $[M + H]^+$.

Anal. Calcd for $C_{37}H_{45}NO_4$: C, 78.27; H, 7.99; N, 2.47. Found: C, 77.97; H, 8.27; N, 2.55.

2,6-Bis[2,6-bis(hex-5-enyloxy)phenyl]pyridine (9b)
Synthesized according to General Procedure A with 2,6-dibromopyridine (**1**; 300 mg, 1.26 mmol), 2,6-bis(hex-5-enyloxy)phenylboronic acid (**8b**; 1.01 g, 3.14 mmol), $Pd(PPh_3)_4$ (145 mg, 125 μmol) in DME (75 mL) and H_2O (10 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 7:1) gave **9b** as an almost colorless powder.

Yield: 589 mg (75%).

IR (KBr): 2938, 2869, 1640, 1598, 1455, 1244, 1101 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.66 (t, *J* = 7.7 Hz, 1 H, H-4), 7.21 (t, *J* = 8.3 Hz, 2 H, H-4′, H-4″), 7.18 (d, *J* = 7.7 Hz, 2 H, H-3, H-5), 6.58 (d, *J* = 8.4 Hz, 4 H, H-3′, H-3″, H-5′, H-5″), 5.72 (tdd, *J* = 6.7, 10.2, 17.2 Hz, 4 H, C*H*=CH_2), 5.01–4.87 (m, 8 H, CH=CH_2), 3.88 (t, *J* = 6.5 Hz, 8 H, OCH_2), 2.01–1.91 (m, 8 H, CH_2CH=), 1.62–1.52 (m, 8 H, OCH_2CH_2), 1.38–1.30 (m, 8 H, $OCH_2CH_2CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.8 (s, C-2′, C-2″, C-6′, C-6″), 154.1 (s, C-2, C-6), 138.7 (d, *C*H=CH_2), 134.6 (d, C-4), 128.9 (d, C-4′, C-4″), 123.7 (d, C-3, C-5), 121.3 (s, C-1′, C-1″), 114.4 (t, CH=CH_2), 105.7 (d, C-3′, C-3″, C-5′, C-5″), 68.5 (t, OCH_2), 33.2 (t, CH_2CH=CH_2), 28.5 (t, OCH_2CH_2), 25.1 (t, $OCH_2CH_2CH_2$).

MS (ESI+, MeOH): *m/z* (%) = 624 (100) $[M + H]^+$.

2,6-Bis[2,6-bis(pent-4-enyloxy)phenyl]-3-methoxypyridine (10a)
Synthesized according to General Procedure A with 2,6-diiodo-3-methoxypyridine (**2**; 274 mg, 760 μmol), 2,6-bis(pent-4-enyloxy)phenylboronic acid (**8a**; 560 mg, 1.93 mmol) and $Pd(PPh_3)_4$ (90 mg, 78 μmol) in DME (50 mL) and H_2O (6 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 6:1) gave **10a** as almost colorless flakes.

Yield: 310 mg (68%).

IR (KBr): = 2931, 2865, 1641, 1596, 1452, 1252, 1100 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.9 Hz, 1 H, H-4), 7.21 (d, *J* = 7.9 Hz, 1 H, H-5), 7.19 (t, *J* = 8.3 Hz, 1 H, H-4′), 7.17 (t, *J* = 8.3 Hz, 1 H, H-4″), 6.56 (d, *J* = 8.3 Hz, 2 H, H-3′, H-5′), 6.55 (d, *J* = 8.3 Hz, 2 H, H-3″, H-5″), 5.72 (tdd, *J* = 6.7, 10.3, 17.0 Hz, 2 H, C*H*′=CH_2), 5.69 (tdd, *J* = 6.7, 10.3, 17.0 Hz, 2 H, C*H*″=CH_2), 4.96–4.85 (m, 8 H, CH=CH_2), ca. 3.88 (t, *J* = 6.5 Hz, 4 H, OCH_2′), ca. 3.86 (t, *J* = 6.5 Hz, 4 H, OCH_2″), 3.76 (s, 3 H, OCH_3), 2.04–1.94 (m, 8 H, CH_2CH=), 1.69–1.59 (m, 8 H, OCH_2CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.1 (s, C-2″, C-6″), 157.7 (s, C-2′, C-6′), 152.7 (s, C-3), 145.6 (s, C-2), 144.4 (s, C-6), 138.1 (d, *C*H=CH_2), 129.1 (t, C-4′), 128.7 (d, C-4″), 124.8 (d, C-5), 120.9 (s, C-1″), 117.8 (s, C-1′), 116.8 (d, C-4), 114.8 (t, CH=CH_2′), 114.7 (t, CH=CH_2″), 105.9 (d, C-3″, C-5″), 105.6 (d, C-3′, C-5′), 68.1 (t, OCH_2″), 67.7 (t, OCH_2′), 55.5 (q, OCH_3), 29.9 (t, $OCH_2CH_2CH_2$′), 29.8 (t, $OCH_2CH_2CH_2$″), 28.4 (t, OCH_2CH_2″), 28.3 (t, OCH_2CH_2′).

MS (CI, isobutane): *m/z* (%) = 598 (100) $[M + H]^+$.

Anal. Calcd for $C_{38}H_{47}NO_5$: C, 76.34; H, 7.93; N, 2.34. Found: C, 76.36; H, 8.12; N, 2.33.

2,6-Bis[2,6-bis(hex-5-enyloxy)phenyl]-3-methoxypyridine (10b)
Synthesized according to General Procedure A with 2,6-diiodo-3-methoxypyridine (**2**; 180 mg, 500 μmol), 2,6-bis(hex-5-enyloxy)phenylboronic acid (**8b**; 400 mg, 1.25 mmol) and $Pd(PPh_3)_4$ (58 mg, 50 μmol) in DME (30 mL) and H_2O (4 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 7:1) gave **10b** as an almost colorless powder.

Yield: 250 mg (76%).

IR (KBr): 2932, 2865, 1642, 1595, 1456, 1250, 1100 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 8.0 Hz, 1 H, H-4), 7.19 (d, *J* = 8.0 Hz, 1 H, H-3, H-5), 7.17 (t, *J* = 8.2 Hz, 2 H, H-4′, H-4″), 6.56 (d, *J* = 8.4 Hz, 4 H, H-3′, H-3″, H-5′, H-5″), 5.74 (tdd, *J* = 6.7, 10.3, 17.0 Hz, 2 H, C*H*′=CH_2), 5.69 (tdd, *J* = 6.7, 10.3, 17.0 Hz, 2 H, C*H*″=CH_2), 4.98–4.86 (m, 8 H, CH=CH_2), ca. 3.88 (t, *J* = 6.5 Hz, 4 H, OCH_2′), ca. 3.86 (t, *J* = 6.5 Hz, 4 H, OCH_2″), 3.74 (s, 3 H, OCH_3), 2.01–1.91 (m, 8 H, CH_2CH=CH_2), 1.64–1.51 (m, 8 H, OCH_2CH_2), 1.40–1.26 (m, 8 H, $OCH_2CH_2CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.1 (s, C-2″, C-6″), 157.9 (s, C-2′, C-6′), 152.7 (s, C-3), 145.5 (s, C-2), 144.3 (s, C-6), 138.8 (d, CH_2CH=CH_2), 138.7 (d, CH_2CH=CH_2), 129.1 (d, C-4′), 128.7 (d, C-4″), 124.8 (d, C-5), 120.9 (s, C-1″), 117.7 (s, C-1′), 116.9 (d, C-4), 114.4 (t, CH=CH_2′), 114.3 (t, CH=CH_2″), 105.9 (d, C-3″, C-5″), 105.5 (d, C-3′, C-5′), 68.6 (t, OCH_2″), 68.3 (t, OCH_2′), 55.5 (t, OCH_3), 33.3 (t, CH_2′CH=CH_2), 33.2 (t, CH_2″CH=CH_2), 28.6 (t, OCH_2CH_2″), 28.5 (t, OCH_2CH_2′), 25.1 (t, $OCH_2CH_2CH_2$′), 25.0 (t, $OCH_2CH_2CH_2$″).

MS (EI, 70 eV): *m/z* (%) = 653 (81) $[M]^+$, 622 (59) $[M - OCH_3]^+$, 570 (100) $[M - C_6H_{11}]^+$.

MS (CI, isobutane): *m/z* (%) = 654 (100) $[M + H]^+$.

2,11,13,22-Tetraoxa-1,12(1,3,2)-dibenzena-23(2,6)-pyridinabicyclo[10.10.1]tricosaphan-6,17-diene (11a)
Synthesized according to General Procedure B with **9a** (540 mg, 951 μmol) and benzylidenebis(tricyclohexylphosphine)dichlororuthenium (70 mg, 85 μmol, 9 mol%) in CH_2Cl_2 (210 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 6:1) gave **11a** as an almost colorless solidifying oil.

Yield: 320 mg (66%).

IR (KBr): 2934, 1593, 1458, 1246, 1101 cm^{-1}.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.75, 7.74 (2 × t, *J* = 7.7, 7.7 Hz, 1 H, H-4), 7.26, 7.22 (2 × d, *J* = 7.7, 7.7 Hz, 2 H, H-3, H-5), 7.21, 7.20 (2 × t, *J* = 8.3, 8.3 Hz, 2 H, H-4′, H-4″), 6.55, 6.54 (2 × d, *J* = 8.4, 8.4 Hz, 4 H, H-3′, H-3″, H-5′, H-5″), 5.34–5.30, 4.98–4.95 (2 × m, 2 H, *E*- and *Z*-CH=CH), 4.04–3.97, 3.91–3.81 (2 × m, 8 H, OCH_2), 2.01–1.81 (m, 8 H, $CH_2CH=CH_2$), 1.67–1.43 (m, 8 H, OCH_2CH_2).

^{13}C NMR (125 MHz, CD_2Cl_2): δ = 157.8, 157.6, 157.1 (3 × s, C-2′, C-2″, C-6′, C-6″), 154.3, 154.1 (2 × s, C-2, C-6), 134.6 (d, C-4), 130.6, 129.9 (2 × d, *Z*- and *E*-CH=CH), 128.9 (2 × d, C-4′, C-4″), 123.9, 123.6 (2 × d, C-3, C-5), 120.9, 120.3 (2 × s, C-1′,C-1″), 105.5, 104.5, 104.2 (3 × d, C-3′, C-3″, C-5′, C-5″), 67.2, 66.5 (2 × t, OCH_2), 29.4, 29.3, 29.2, 28.2, 23.2, 23.1 (6 × t, CH_2).

MS (ESI+, MeOH): *m*/*z* (%) = 534 (100) $[M + Na]^+$, 512 (52) $[M + H]^+$.

Anal. Calcd for $C_{33}H_{37}NO_4$: C, 77.47; H, 7.29; N 2.74; Calcd for $C_{33}H_{37}NO_4 \cdot 0.2CH_2Cl_2$: C, 75.43; H, 7.13; N, 2.65. Found: C, 75.50; H, 7.33; N, 2.73.

2,13,15,26-Tetraoxa-1,14(1,3,2)-dibenzena-27(2,6)-pyridinabicyclo[12.12.1]heptacosaphan-7,20-diene (11b)

Synthesized according to General Procedure B with **9b** (300 mg, 480 μmol), benzylidenebis(tricyclohexylphosphine)-dichlororuthenium (21 mg, 18 μmol, 9 mol%) in CH_2Cl_2 (120 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 6:1) gave **11b** as an almost colorless solid.

Yield: 250 mg (92%).

IR (KBr): 2935, 1593, 1458, 1246, 1102 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68, 7.66 (2 × d, *J* = 7.7, 7.7 Hz, 1 H, H-4), 7.19, 7.18 (2 × t, *J* = 8.3, 8.3 Hz, 2 H, H-4′, H-4″), 7.15, 7.13 (2 × d, *J* = 7.7, 7.7 Hz, 2 H, H-3, H-5), 6.53 (d, *J* = 8.3 Hz, 4 H, H-3′, H-3″, H-5′, H-5″), 5.29–5.26, 5.21–5.17 (2 × m, 2 H, *Z* and *E*-CH=CH), 3.94–3.84, 3.80–3.70 (2 × m, 8 H, OCH_2), 2.12–1.90 (m, 8 H, $CH_2CH=CH_2$), 1.64–1.46 (m, 8 H, OCH_2CH_2), 1.44–1.22 (m, 8 H, CH_2).

^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ = 157.9, 157.8 (2 × s, C-2′, C-2″, C-6′, C-6″), 154.4 (s, C-2, C-6), 134.6 (d, C-4), 130.7, 130.2 (2 × d, *Z*- and *E*-CH=CH), 128.8 (d, C-4′, C-4″), 123.5 (d, C-3, C-5), 120.6 (s, C-1′, C-1″), 104.8, 104.7, 104.6 (3 × d, C-3′, C-3″, C-5′, C-5″), 68.7, 68.6, 68.5 (3 × t, OCH_2CH_2), 31.5 (t, $CH_2CH=CH_2$), 27.6, 26.9, 26.6, 25.0, 24.9, 24.8 (6 × t, CH_2).

MS (ESI+, $CHCl_3$–MeOH): *m*/*z* (%) = 564 (10) $[M + Na]^+$, 542 (100) $[M + H]^+$.

Anal. Calcd for $C_{37}H_{45}NO_4$: C, 78.27; H, 7.99; N, 2.47. Found: C, 78.08; H, 7.72; N, 2.36.

23^3-Methoxy-2,11,13,22-tetraoxa-1,12(1,3,2)-dibenzena-23(2,6)-pyridinabicyclo[10.10.1]tricosaphan-6,17-diene (12a)

Synthesized according to General Procedure B with **10a** (120 mg, 200 μmol), benzylidenebis(tricyclohexylphosphine)dichlororuthenium (16 mg, 19 μmol, 9 mol%) in CH_2Cl_2 (50 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 6:1) gave **12a** as an almost colorless solidifying oil.

Yield: 97 mg (90%).

IR (KBr): 2930, 2865, 1593, 1456, 1253, 1100 cm^{-1}.

^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.33, 7.31 (2 × d, *J* = 8.5, 8.5 Hz, 1 H, H-4), 7.25, 7.24 (2 × t, *J* = 8.3, 8.3 Hz, 2 H, H-4′, H-4″), 7.20, 7.19 (2 × d, *J* = 8.5, 8.5 Hz, 1 H, H-5), 6.59 (d, *J* = 8.4 Hz, 2 H, H-3′, H-5′), 6.57 (d, *J* = 8.4 Hz, 2 H, H-3″, H-5″), 5.39–5.34, 5.03–4.96 (2 × m, 2 H, *Z*- and *E*-CH=CH), 4.04–3.90, 3.89–3.80 (2 × m, 8 H, OCH_2), 3.79 (s, 3 H, OCH_3), 2.01–1.73 (m, 8 H, $CH_2CH=$), 1.67–1.45 (m, 8 H, OCH_2CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.0, 157.8 (2 × s, C-2′, C-2″, C-6′, C-6″), 152.8 (s, C-3), 146.1 (s, C-2), 144.7 (s, C-6), 130.9, 130.7 (2 × d, *Z*- and *E*-CH=CH), 129.9 (d, C-4′), 129.1 (d, C-4″), 125 (d, C-5), 120.9 (s, C-1″), 117.3 (s, C-1′), 117.1 (C-4), 105.7, 104.7 (2 × d, C-3″, C-5″), 104.6, 104.2 (2 × d, C-3′, C-5′), 67.0, 66.6 (2 × t, OCH_2CH_2), 29.5, 29.0, 28.9, 28.5, 23.3, 23.2 (6 × t, CH_2).

MS (ESI+, $CHCl_3$–MeOH): *m*/*z* (%) = 564 (10) $[M + Na]^+$, 542 (100) $[M + H]^+$.

Anal. Calcd for: $C_{34}H_{39}NO_5$: C, 75.39; H, 7.26; N, 2.59. Found: C, 75.09; H, 7.14; N, 2.48.

27^3-Methoxy-2,13,15,26-tetraoxa-1,14(1,3,2)-dibenzena-27(2,6)-pyridinabicyclo[12.12.1]heptacosaphan-7,20-diene (12b)

Synthesized according to General Procedure B with **10b** (250 mg, 382 μmol), benzylidenebis(tricyclohexylphosphine)dichlororuthenium (15 mg, 18 μmol, 5 mol%) in CH_2Cl_2 (100 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 7:1) gave **12b** as an almost colorless solid.

Yield: 196 mg (86%).

IR (KBr): 2930, 1592, 1454, 1252, 1101 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.24, 7.23 (2 × d, 8.5 Hz, 1 H, H-4), 7.19, 7.18 (2 × t, *J* = 8.3, 8.3 Hz, 2 H, H-4′, H-4″), 7.16, 7.15 (2 × d, *J* = 8.5, 8.5 Hz, 1 H, H-5), 6.53 (d, *J* = 8.4 Hz, 2 H, H-3′, H-5′), 6.52 (d, *J* = 8.4 Hz, 2 H, H-3″, H-5″), 5.30–5.26, 5.21–5.17 (2 × m, 2 H, *Z*- and *E*-CH=CH), 3.94–3.84, 3.80–3.70 (2 × m, 8 H, OCH_2), 3.75 (s, 3 H, OCH_3), 2.12–1.90 (m, 8 H, $CH_2CH=CH_2$), 1.64–1.46 (m, 8 H, OCH_2CH_2), 1.44–1.22 (m, 8 H, CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.2, 158.0 (2 × s, C-2′, C-2″, C-6′, C-6″), 152.9 (s, C-3), 146.0 (s, C-2), 144.8 (s, C-6), 130.7, 130.2 (2 × d, *Z*- and *E*-CH=CH), 128.9 (d, C-4′), 128.6 (d, C-4″), 124.5 (d, C-5), 117.1 (d, C-4), 104.9, 104.8 (2 × d, C-3′, C-5′), 104.7, 104.6 (2 × d, C-3″, C-5″), 68.8, 68.7 (2 × t, OCH_2CH_2), 55.7 (q, OCH_3), 31.5 (t, $CH_2CH=CH_2$), 28.5, 28.3, 27.6, 27.5, 26.9, 26.7 (6 × t, OCH_2CH_2), 25.1, 25.0, 24.9 (3 × t, CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 597 (53) $[M]^+$, 566 (100) $[M - OCH_3]^+$.

MS (CI, isobutane): *m*/*z* (%) = 598 (100) $[M + H]^+$.

Anal. Calcd for $C_{38}H_{47}NO_5$: C, 76.35; H, 7.92; N, 2.34. Found: C, 76.11; H, 7.78; N, 2.24.

2,11,13,22-Tetraoxa-1,12(1,3,2)-dibenzena-23(2,6)-pyridinabicyclo[10.10.1]tricosaphan (13a)

Synthesized according to General Procedure C with **11a** (130 mg, 254 μmol), palladium (10%) on charcoal (42 mg) in MeOH (15 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 1:1) gave **13a** as almost colorless crystals.

Yield: 115 mg (88%).

IR (KBr): 2931, 2860, 1591, 1459, 1250, 1101 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68 (t, *J* = 7.7 Hz, 1 H, H-4), 7.21 (t, *J* = 8.3 Hz, 2 H, H-4′, H-4″), 7.18 (d, *J* = 7.7 Hz, 2 H, H-3, H-5), 6.54 (d, *J* = 8.3 Hz, 4 H, H-3′, H-5′, H-3″, H-5″), 3.98–3.95, 3.86–3.80 (2 × m, 8 H, OCH_2CH_2), 1.66–1.48 (m, 8 H, OCH_2CH_2), 1.32–1.08 (m, 16 H, CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9 (s, C-2′, C-6′, C-2″, C-6″), 154.1 (s, C-2, C-6), 134.2 (d, C-4), 128.8 (d, C-4′, C-4″), 123.8 (d, C-3, C-5), 120.2 (s, C-1′,C-1″), 104.3 (d, C-3′, C-3″, C-5′, C-5″), 67.7 (t, OCH_2CH_2), 28.1, 26.7, 24.4 (3 × t, CH_2).

MS (ESI+, MeOH): *m*/*z* (%) = 538 (60) $[M + Na]^+$, 516 (100) $[M + H]^+$.

HRMS (ESI+, MeOH): *m*/*z* $[M + H]^+$ calcd for $C_{33}H_{41}NO_4$: 515.30359; found: 515.30329; *m*/*z* $[M + H]^+$ calcd for $C_{32}{}^{13}CH_{41}NO_4$: 516.30688; found: 516.30616.

2,13,15,26-Tetraoxa-1,14(1,3,2)-dibenzena-27(2,6)-pyridinabicyclo[12.12.1]heptacosaphan (13b)
Synthesized according to General Procedure C with **11b** (48.0 mg, 84.6 μmol), palladium (10%) on charcoal (20 mg) in MeOH (10 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 1:1) gave **13b** as an almost colorless solidifying oil.

Yield: 47 mg (97%).

IR (KBr): 2931, 2860, 1591, 1459, 1250, 1101 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.69 (t, *J* = 7.7 Hz, H-4), 7.21 (d, *J* = 7.7 Hz, 2 H, H-3, H-5), 7.20 (t, *J* = 8.3 Hz, 2 H, H-4′, H-4″), 6.57 (d, *J* = 8.3 Hz, 4 H, H-3′, H-5′, H-3″, H-5″), 4.03–3.95, 3.89–3.82 (2 × m, 8 H, OCH_2CH_2), 1.60–1.49 (m, 8 H, OCH_2CH_2), 1.35–1.10 (m, 24 H, CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9 (s, C-2′, C-6′, C-2″, C-6″), 154.2 (s, C-2, C-6), 134.4 (d, C-4), 128.8 (d, C-4′, C-4″), 123.8 (d, C-3, C-5), 120.9 (s, C-1′,C-1″), 104.9 (d, C-3′, C-3″, C-5′, C-5″), 68.5 (t, OCH_2CH_2), 28.1, 26.7, 25.7, 24.4 (4 × t, CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 571 (100) $[M]^+$, 458 (56) $[M - C_8H_{16}]^+$.

MS (CI, isobutane): *m*/*z* (%) = 572 (100) $[M + H]^+$.

HRMS (ESI+, MeOH): *m*/*z* $[M]^+$ calcd for $C_{37}H_{49}NO_4$: 571.36615; found: 571.36605; *m*/*z* $[M]^+$ calcd for $C_{36}{}^{13}CH_{49}NO_4$: 572.36951; found: 572.36958.

Anal. Calcd for $C_{37}H_{49}NO_4$: C, 77.72; H, 8.64; N, 2.45. Found: C, 77.53; H, 8.73; N, 2.37.

23^3-Methoxy-2,11,13,22-tetraoxa-1,12(1,3,2)-dibenzena-23(2,6)-pyridinabicyclo[10.10.1]tricosaphan (14a)
Synthesized according to General Procedure C with **12a** (140 mg, 258 μmol), palladium (10%) on charcoal (65 mg) in MeOH (20 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 1:1) gave **14a** as an almost colorless solidifying oil.

Yield: 128 mg (92%).

IR (KBr): 2934, 2858, 1593, 1456, 1250, 1102 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.4 Hz, 1 H, H-4), 7.21 (t, *J* = 8.3 Hz, 1 H, H-4′), 7.19 (t, *J* = 8.3 Hz, 1 H, H-4″), 7.18 (d, *J* = 8.4 Hz, 1 H, H-5), 6.54 (d, *J* = 8.3 Hz, 2 H, H-3′, H-5′), 6.53 (d, *J* = 8.3 Hz, 2 H, H-3″, H-5″), 4.02–3.94 (m, 4 H, OCH'_2CH_2), 3.85–3.78 (m, 4 H, OCH''_2CH_2), 3.77 (s, OCH_3), 1.67–1.44 (m, 8 H, OCH_2CH_2), 1.34–1.04 (m, 16 H, CH_2).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 158.2 (s, C-2″, C-6″), 158.1 (s, C-2′, C-6′), 152.8 (s, C-3), 145.9 (s, C-2), 144.6 (s, C-6), 129.0 (d, C-4′), 128.6 (d, C-4″), 124.8 (d, C-5), 119.9 (s, C-1″), 117.1 (d, C-4), 117.0 (s, C-1′), 104.8 (d, C-3″, C-5″), 104.3 (d, C-3′, C-5′), 67.8 (t, OCH''_2CH_2), 67.7 (t, OCH'_2CH_2), 55.9 (q, OCH_3), 28.8 (t, OCH''_2CH_2), 28.5 (t, OCH'_2CH_2), 26.7, 26.6, 23.8, 23.6 (4 × t, CH_2).

MS (ESI+, MeOH): *m*/*z* (%) = 568 (56) $[M + Na]^+$, 546 (100) $[M + H]^+$.

Anal. Calcd for $C_{34}H_{43}NO_5$: C, 74.83; H, 7.94; N, 2.57. Found: C, 74.81; H, 8.02; N, 2.55.

27^3-Methoxy-2,13,15,26-tetraoxa-1,14(1,3,2)-dibenzena-27(2,6)-pyridinabicyclo[12.12.1]heptacosaphan (14b)
Synthesized according to General Procedure C with **12b** (90.0 mg, 150 μmol), palladium (10%) on charcoal (35 mg) in MeOH (15 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 1:1) gave **14b** as an almost colorless solidifying oil.

Yield: 87 mg (96%).

IR (KBr): 2934, 2858, 1593, 1456, 1250, 1102 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 8.4 Hz, 1 H, H-4), 7.21 (d, *J* = 8.4 Hz, 1 H, H-5), 7.19 (t, *J* = 8.3 Hz, 1 H, H-4′), 7.17 (t, *J* = 8.3 Hz, 1 H, H-4″), 6.55 (d, *J* = 8.3 Hz, 2 H, H-3′, H-5′), 6.54 (d, *J* = 8.3 Hz, 2 H, H-3″, H-5″), 4.04–3.97 (m, 4 H, OCH'_2CH_2), 3.87–3.80 (m, 4 H, OCH''_2CH_2), 3.74 (s, 3 H, OCH_3), 1.60–1.46 (m, 8 H, OCH_2CH_2), 1.38–1.08 (m, 24 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2 (s, C-3″, C-5″), 158.1 (s, C-3′, C-5′), 152.6 (s, C-3), 145.7 (s, C-2), 144.6 (s, C-6), 129.0 (d, C-4′), 128.6 (d, C-4″), 124.9 (d, C-5), 119.9 (s, C-1″), 117.4 (d, C-4), 116.4 (s, C-1′), 105.2 (d, C-3″, C-5″), 105.0 (d, C-3′, C-5′), 68.6 (t, OCH''_2), 68.5 (t, OCH'_2), 55.1 (q, OCH_3), 28.0 (t, OCH_2CH_2), 26.9, 26.8, 25.7, 25.6, 24.4, 24.2 (6 × t, CH_2).

MS (ESI+, MeOH): *m*/*z* (%) = 624 (44) $[M + Na]^+$, 602 (100) $[M + H]^+$.

HRMS (ESI+, MeOH): *m*/*z* $[M]^+$ calcd for $C_{38}H_{51}NO_5$: 601.37671; found: 601.37669; *m*/*z* $[M]^+$ calcd for $C_{37}{}^{13}CH_{51}NO_5$: 602.38007; found: 602.38007.

Anal. Calcd for $C_{38}H_{51}NO_5$: C, 75.84; H, 8.54; N, 2.33. Found: C, 75.98; H, 8.63; N, 2.32.

2,7-Bis[2,6-bis(pent-4-enyloxy)phenyl]-4-phenyl-1,8-naphthyridine (15a)
Synthesized according to General Procedure A with **3** (591 mg, 2.15 mmol), **8a** (1.50 g, 5.16 mmol) and $Pd(PPh_3)_4$ (250 mg, 216 μmol) in DME (120 mL) and H_2O (6 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 2:1) gave **15a** as an almost colorless solidifying oil.

Yield: 310 mg (68%).

IR (KBr): 2926, 1596, 1458, 1252, 1100 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 8.5 Hz, 1 H, H-5), 7.59–7.47 (m, 5 H, PhH), 7.57 (d, *J* = 8.5 Hz, 1 H, H-6), 7.53 (s, 1 H, H-3), 7.29, 7.28 (2 × t, *J* = 8.4 Hz, 2 H, H-4′, H-4″), 6.63 (d, *J* = 8.4 Hz, 4 H, H-3′, H-5′, H-3″, H-5″), 5.66, 5.61 (2 × tdd, *J* = 6.6, 10.3, 16.9 Hz, 2 H, $CH{=}CH_2$), 4.88–4.77 (m, 8 H, $CH{=}CH_2$), ca. 3.95, 3.94 (2 × t, *J* = 6.4 Hz, 8 H, OCH_2CH_2), 1.98–1.90 (m, 8 H, $CH_2CH{=}$), 1.71–1.62 (m, 8 H, OCH_2CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9 (s, C-7), 157.6 (s, C-2′, C-6′, C-2″, C-6″), 157.5 (s, C-2), 156.2 (s, C-8a), 147.5 (s, C-4), 137.7, 137.6 (2 × d, $CH_2CH{=}$), 137.5 (s, 4a), 133.1 (d, C-5), 129.5 (d, Ph-C-2, Ph-C-6), 129.4 (s, Ph-C-1), 129.3, 129.2 (2 × d, C-4′, C-4″), 128.3 (d, Ph-C-3, Ph-C-5), 128.0 (d, C-3), 124.8 (d, Ph-C-4), 124.7 (d, C-6), 120.4 (s, C-1′), 117.9 (s, C-1″), 114.5, 114.4 (2 × t, $CH{=}CH_2$), 105.4 (d, C-3′, C-5′, C-3″, C-5″), 67.9, 67.8 (2 × t, OCH_2), 29.8 (2 × t, $CH_2CH{=}$), 28.0 (2 × t, OCH_2CH_2).

MS (CI, isobutane): *m*/*z* (%) = 598 (100) $[M + H]^+$.

Anal. Calcd for $C_{46}H_{50}N_2O_4 \cdot 0.1CHCl_3$: C, 78.33; H, 7.14; N, 3.96. Found: C, 78.13; H, 7.27; N, 3.94.

2,7-Bis[2,6-bis(hex-5-enyloxy)phenyl]-4-phenyl-1,8-naphthyridine (15b)
Synthesized according to General Procedure A with **3** (362 mg, 1.32 mmol), **8b** (1.01 g, 3.14 mmol) and $Pd(PPh_3)_4$ (145 mg, 125 μmol) in DME (75 mL) and H_2O (10 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 7:1 to 1:1) gave **15b** as an almost colorless solidifying oil.

Yield: 440 mg (44%).

IR (KBr): 2940, 1596, 1458, 1250, 1102 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 8.51 Hz, 1 H, H-5), 7.57–7.42 (m, 5 H, PhH), 7.49 (s, 1 H, H-3), 7.47 (d, *J* = 8.5 Hz, 1 H, H-6), 7.25, 7.24 (2 × t, *J* = 8.4 Hz, 2 H, H-4′, H-4″), 6.62 (d, *J* = 8.4 Hz, 4 H, H-3′, H-5′, H-3″, H-5″), 5.61, 5.57 (2 × tdd, *J* = 6.6, 10.3, 16.9 Hz, 2 H, $CH{=}CH_2$), 4.84–4.74 (m, 8 H, $CH{=}CH_2$), ca. 3.94, 3.92 (2 × t, *J* = 6.4 Hz, 8 H, OCH_2CH_2), 1.90–1.84 (m, 8 H, $CH_2CH{=}$), 1.62–1.54 (m, 8 H, OCH_2CH_2), 1.34–1.26 (m, 8 H, $OCH_2CH_2CH_2$).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9 (s, C-7), 157.6 (s, C-2′, C-6′, C-2″, C-6″), 157.5 (s, C-2), 156.3 (s, C-8a), 147.6 (s, C-4), 138.4, 138.3 (2 × d, $CH_2CH{=}$), 137.6 (s, C-4a), 133.2 (d, C-5), 129.5 (d,

Ph-C-2, Ph-C-6), 129.4 (s, Ph-C-1), 129.3, 129.2 (2 × d, C-4′, C-4″), 128.3 (d, Ph-C-3, Ph-C-5), 128.0 (d, C-3), 124.8 (d, Ph-C-4), 124.7 (d, C-6), 120.4 (s, C-1′), 118.1 (s, C-1″), 114.1, 114.0 (2 × t, *C*H=CH_2), 105.2 (d, C-3′, C-5′, C-3″, C-5″), 68.5, 68.4 (2 × t, O*C*H_2), 32.9, 32.8 (2 × t, *C*H_2CH=), 28.3, 28.2 (2 × t, OCH_2*C*H_2), 25.0, 24.9 (2 × t, OCH_2CH_2*C*H_2).

MS (ESI+, MeOH): *m*/*z* (%) = 624 (100) $[M + H]^+$.

Anal. Calcd for $C_{50}H_{58}N_2O_4$: C, 79.96; H, 7.78; N, 3.73. Found: C, 79.87; H, 7.87; N, 3.72.

23⁴-Phenyl-2,11,13,22-tetraoxa-1,12(1,3,2)-dibenzena-23(2,7)-1,8-naphthyridinabicyclo[10.10.1]tricosaphan-6,17-diene (16a)

Synthesized according to General Procedure B with **15a** (310 mg, 446 µmol), benzylidenebis(tricyclohexylphosphine)dichlororuthenium (37 mg, 45 µmol, 10 mol%) in CH_2Cl_2 (300 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 1:1) gave **16a** as an almost colorless solidifying oil.

Yield: 248 mg (87%).

IR (KBr): 2925, 1599, 1456, 1249, 1101 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.33, 8.31 (2 × d, *J* = 8.4 Hz, 1 H, H-5), 7.61–7.43 (m, 5 H, PhH), 7.47 (s, 1 H, H-3), 7.45 (d, *J* = 8.4 Hz, 1 H, H-6), 7.28, 7.27 (2 × t, *J* = 8.3 Hz, 2 H, H-4′, H-4″), 6.67, 6.66 (2 × d, *J* = 8.3 Hz, 4 H, H-3′, H-5′, H-3″, H-5″), 5.13–5.02, 4.88–4.83 (2 × m in ratio 5:1, 4 H, CH_2C*H*=), 4.09–3.75 (m, 8 H, OCH_2CH_2), 1.91–1.44 [m, 16 H, OCH_2(CH_2)$_2$].

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.3, 158.2 (2 × s, C-7), 157.9, 157.8 (2 × s, C-2), 157.7, 157.6 (2 × s, C-8a), 157.7, 157.6 (2 × s, C-2′, C-6′, C-2″, C-6″), 148.3, 148.2 (2 × s, C-4), 137.7, 137.6 (2 × s, C-4a), 133.9, 133.8 (2 × d, C-5), 129.9 (s, Ph-C-1), 129.9, 129.8 (2 × d, Ph-C-2, Ph-C-6, C-4′, C-4″), 129.7, 129.6 (2 × d, CH_2*C*H=CH_2), 128.6, 128.4 (2 × d, C-3), 124.9, 124.8 (2 × d, C-6), 124.7 (d, C-4), 122.5 (s, C-1′), 118.2 (s, C-1″), 107.7, 107.5, 107.3, 107.1 (4 × d, C-3′, C-5′, C-3″, C-5″), 69.7, 69.5 (2 × d, O*C*H_2CH_2), 29.6, 29.5, 29.4, 24.2, 24.1, 24.0 (6 × t, CH_2).

MS (ESI+, MeOH): *m*/*z* (%) = 661 (15) $[M + Na]^+$, 639 (100) $[M + H]^+$.

Anal. Calcd for $C_{42}H_{42}N_2O_4$: C, 78.97; H, 6.63; N, 4.39. Found: C, 79.01; H, 6.81; N, 4.32.

27⁴-Phenyl-2,13,15,26-tetraoxa-1,14(1,3,2)-dibenzena-27(2,7)-1,8-naphthyridinabicyclo[12.12.1]heptacosaphan-7,20-diene (16b)

Synthesized according to General Procedure B with **15b** (400 mg, 532 µmol), benzylidenebis(tricyclohexylphosphine)dichlororuthenium (45 mg, 54 µmol, 10 mol%) in CH_2Cl_2 (210 mL). Purification by chromatography on silica gel (cyclohexane–EtOAc, 2:1) gave **16b** as an almost colorless solidifying oil.

Yield: 307 mg (83%).

IR (KBr): 2927, 1597, 1457, 1248, 1101 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 8.5 Hz, 1 H, H-5), 7.58–7.44 (m, 5 H, PhH), 7.48 (s, 1 H, H-3), 7.46 (d, *J* = 8.5 Hz, 1 H, H-6), 7.26, 7.24 (2 × t, *J* = 8.3 Hz, 2 H, H-4′, H-4″), 6.61, 6.60 (2 × d, *J* = 8.4 Hz, 4 H, H-3′, H-5′, H-3″, H-5″), 5.08–5.02, 4.92–4.86 (2 × m in ratio of 1:2, 4 H, CH_2C*H*=), 3.96–3.86 (m, 8 H, OCH_2CH_2), 1.74–1.64 (m, 8 H, CH_2CH=), 1.62–1.46 (m, 8 H, OCH_2CH_2), 1.22–1.08 (m, 8 H, CH_2).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.4 (s, C-7), 157.9 (s, C-2), 157.8 (s, C-2′, C-6′, C-2″, C-6″), 156.5 (s, C-8a), 147.7 (s, C-4), 138.0 (s, C-4a), 133.3 (d, C-5), 129.8, 129.7 (2 × d, CH_2*C*H=CH_2), 129.6 (s, Ph-C-1, 2 × d, Ph-C-2, Ph-C-6), 129.5 (2 × d, C-4′, C-4″), 128.6 (d, Ph-C-3, Ph-C-5), 128.2 (d, C-3), 125.0 (d, Ph-C-4), 124.8 (d, C-6), 120.5, 118.1 (2 × s, C-1′, C-1″), 105.0 (d, C-3′, C-5′, C-3″, C-5″), 68.9 (t, OCH_2), 31.8 (2 × t, *C*H_2CH=), 28.2 (2 × t, OCH_2*C*H_2), 26.1 (2 × t, CH_2).

MS (ESI+, MeOH): *m*/*z* (%) = 717 (33) $[M + Na]^+$, 695 (100) $[M + H]^+$.

Anal. Calcd for $C_{46}H_{50}N_2O_4$: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.67; H, 7.42; N, 4.17.

Supporting Information for this article is available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000084.

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