EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201402778

Modular Syntheses of Star-Shaped Pyridine, Bipyridine, and Terpyridine Derivatives by Employing Sonogashira Reactions

Daniel Trawny,[a] Valentin Kunz,[a] and Hans-Ulrich Reissig*[a]

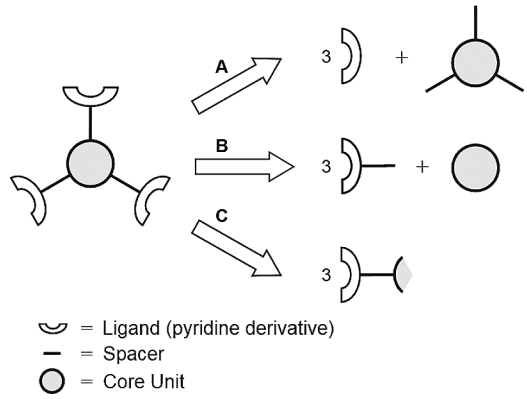
Dedicated to Professor Armin de Meijere on the occasion of his 75th birthday

Keywords: Nitrogen heterocycles / Alkynes / C–C coupling / UV/Vis spectroscopy / Fluorescence spectroscopy

A simple and flexible synthesis for a series of star-shaped pyridine, bipyridine, and terpyridine derivatives is reported by using a modular approach that combines the use of a ligand, spacer, and core unit. A fairly efficient method to prepare 4′-nonafloxy-functionalized terpyridine derivatives is described. The building blocks that contain the functionalized pyridine, bipyridine, or terpyridine derivatives were linked to different C_3-symmetrical core units. In most cases, Sonogashira reactions were employed in the crucial final steps of the synthesis. A star-shaped dodecafluorinated compound was also prepared in a straightforward fashion. A simple procedure for the preparation of partially silylated 1,3,5-triethynylbenzene derivatives is presented, which provides an approach to C_2-symmetrical star-shaped compounds that have only one terpyridine and two terphenyl units as "dummy" ligands. The absorption and emission spectra of the fully conjugated C_3-symmetrical pyridine derivatives were systematically investigated, and fairly large Stokes shifts were observed.

Introduction

Star-shaped multivalent pyridine derivatives are remarkable compounds because of their self-assembly behavior at the graphite surface.[1] The C_3-symmetric core unit plays a crucial role, as this molecular arrangement fits perfectly to the graphite lattice. However, the pyridine end groups are also important, if additional surface experiments are envisioned, such as complexation with metal ions. This type of compound can be prepared by employing three different synthetic routes (see Scheme 1).[1a] The star-shaped target compounds can be divided in the three moieties, that is, ligand, spacer and core unit. Pathways A and B are examples of two common approaches that use coupling reactions, such as the Sonogashira or Suzuki reactions.[2] Pathway C illustrates a third strategy by using a trimerization process to generate the central core unit from three functionalized ligand-spacer portions.[3] The syntheses of C_6-symmetrical star-shaped derivatives that contain six pyridine, bipyridine, and terpyridine moieties have also been reported.[4] In previous studies, we described a C_3-symmetrical tris(oxazole) derivative and its ability to form self-assembled monolayers.[5] We also showed the remarkable self-assembly behavior of star-shaped monopyridine derivatives that were efficiently prepared by employing pathway C.[1a] In the present report, we use pathway A and focus on the syntheses of a series of star-shaped pyridine, bipyridine, and terpyridine derivatives that have different substitution patterns. To increase the compound library for our self-assembly studies, we also present a simple and reliable synthetic route to C_2-symmetrical terpyridine derivatives by employing partially protected core units.



Scheme 1. Three routes to star-shaped C_3-symmetrical compounds with pyridine end groups.[1a]

Results and Discussion

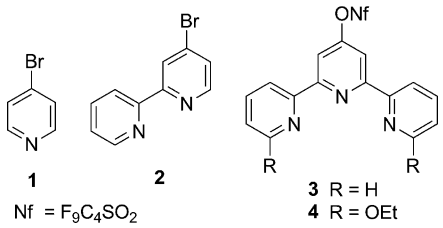
Synthesis of Terpyridine Building Blocks

We used mono-, bi-, and terpyridine ligands **1**–**4** as building blocks for the preparation of the desired star-shaped

[a] Institut für Chemie und Biochemie, Freie Universität Berlin, Takustraße 3, 14195 Berlin, Germany
E-mail: hans.reissig@chemie.fu-berlin.de
www.bcp.fu-berlin.de/en/chemie/chemie/forschung/OrgChem/reissig

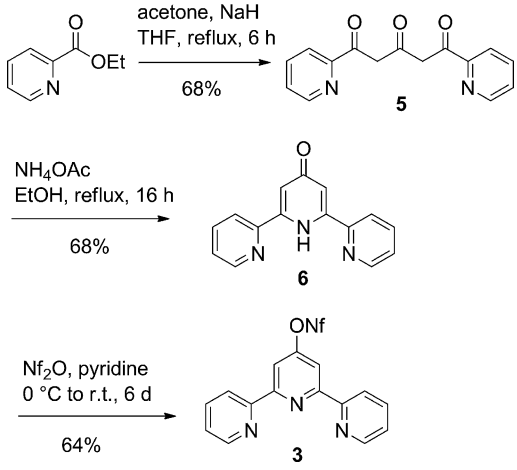
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402778.

pyridine derivatives (see Scheme 2). 4-Bromopyridine (**1**) could be purchased as its hydrochloride, whereas 4-bromo-2,2′-bipyridine (**2**) was synthesized by using the protocols of Woodward and Wade starting from commercially available 2,2′-bipyridine.[6,7]



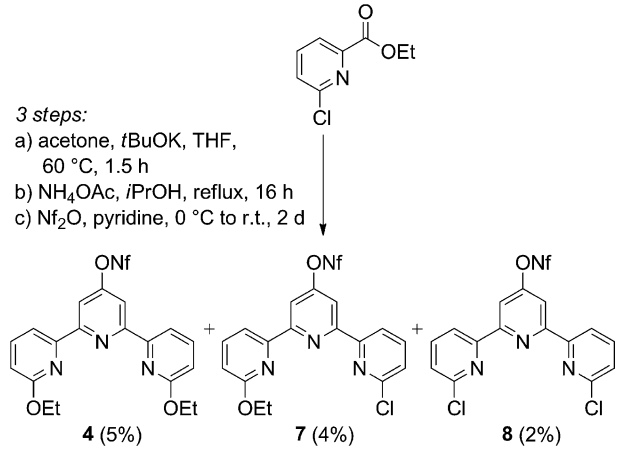
Scheme 2. Mono-, bi-, and terpyridine building blocks **1**–**4** required for the preparation of the star-shaped pyridine derivatives described herein.

Terpyridine building blocks **3** and **4** were prepared by a modified procedure that was reported by Constable et al. (see Scheme 3).[8] By starting from ethyl 2-picolinate, triketone **5** was obtained in good yield through a twofold Claisen condensation of acetone in the presence of sodium hydride. In a glass pressure tube, the subsequent treatment of **5** with ammonium acetate led to the formation of pyridinone **6** in 68% yield. The nonaflyl group was introduced by the addition of nonafluorobutanesulfonic acid anhydride to a solution of pyridinone **6** in pyridine. The resulting terpyridyl nonaflate **3**, isolated in 64% yield, is an excellent precursor for further functionalization by using a palladium-catalyzed cross-coupling reaction.[9]



Scheme 3. Synthesis of terpyridyl nonaflate **3** based on a protocol by Constable et al.[8] (THF = tetrahydrofuran, ONf = nonaflate).

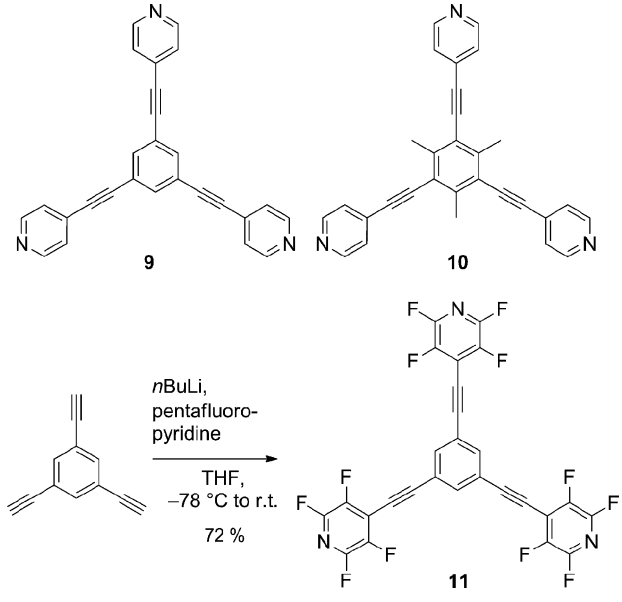
The preparation of the corresponding 6,6′′-disubstituted terpyridyl nonaflates **4**, **7**, and **8** was achieved analogously to the synthesis of compound **3**. This modifications at the 6,6′′-positions should be very useful for the intended studies, as the solubility of the resulting star-shaped compounds can be increased by further substitution at these (or other) positions (see Scheme 4). We therefore attempted the preparation of 6,6′′-dichloro-substituted terpyridyl nonaflate **8** by starting from ethyl 6-chloropicolinate and then planned to introduce different substituents by employing iron-catalyzed coupling reactions.[10] However, during the twofold Claisen condensation, the liberated potassium ethoxide caused the partial nucleophilic substitution at C-6 and C-6′′. Because separation of the obtained triketones was not simple, the mixture was directly treated with ammonium acetate and subsequently with nonafluorobutanesulfonic acid anhydride. Fortunately, the resulting mixture of terpyridyl nonaflates **4**, **7**, and **8** could be separated by column chromatography (three steps, 11% overall yield). Although the combined overall yield was fairly low, these easily available precursors were now ready to be used as versatile building blocks for the synthesis of various functionalized terpyridine derivatives.[8]



Scheme 4. Synthesis of 6,6′′-disubstituted terpyridyl nonaflates **4**, **7**, and **8**.

Synthesis of C_3-Symmetric Pyridine Derivatives

Almost all star-shaped multivalent pyridine derivatives were prepared by using a Sonogashira reaction as the final step (see Scheme 1, pathway A). For the syntheses of known tris(pyridylethynyl)-substituted derivatives **9** and **10**, the

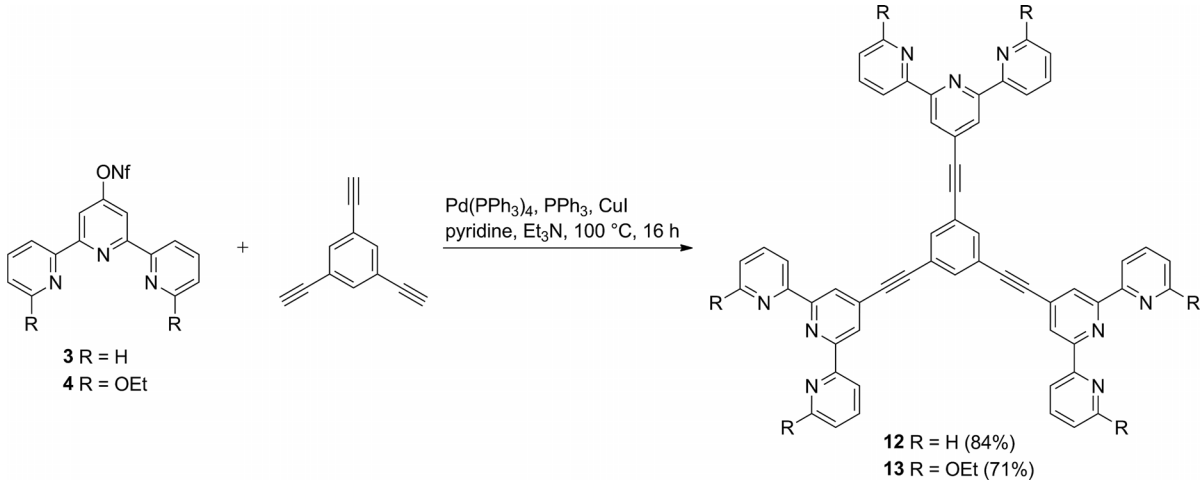


Scheme 5. Structures of star-shaped pyridine derivatives **9** and **10**[11] and synthesis of dodecafluorinated analogue **11**.

protocols of Hupp and Clays were followed by using 4-bromopyridine (**1**) and 1,3,5-triethynylbenzene or 1,3,5-triethynylmesitylene, respectively, to give the products in good yields (see Scheme 5).[11] As an extension of our compound library, dodecafluorinated compound **11** was also prepared by employing a simple nucleophilic aromatic substitution with pentafluoropyridine as the electrophile.[12] A threefold deprotonation of 1,3,5-triethynylbenzene by treatment with *n*BuLi followed by a reaction of the resulting species with pentafluoropyridine furnished target compound **11** in 72% yield.

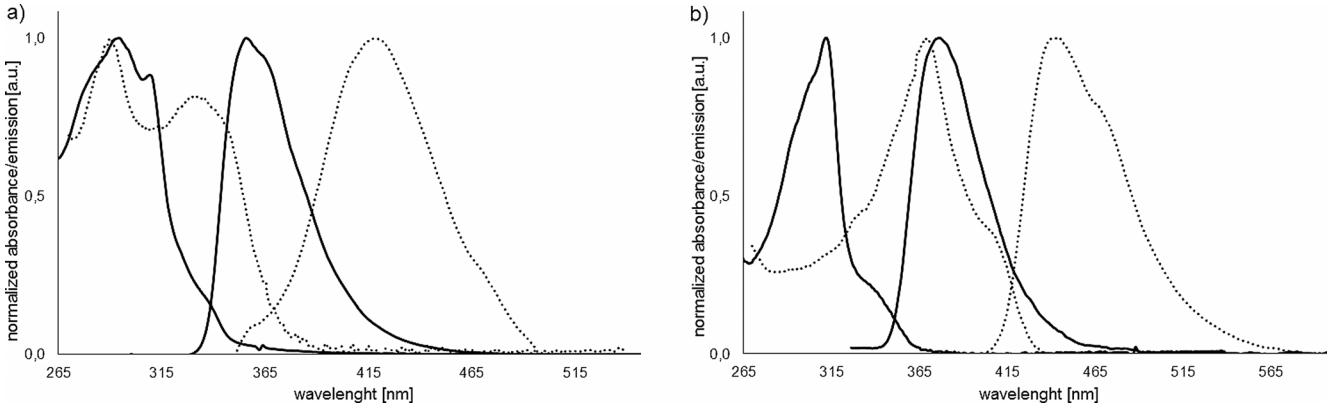
Surprisingly, the UV/Vis absorption of star-shaped compound **9** and its dodecafluorinated analogue **11** are only slightly different in chloroform compared to a mixture of chloroform and trifluoroacetic acid (99:1). The absorption maxima of nonprotonated and protonated **9** and **11** are almost identical (around 290 nm). The emission maxima of **9** (354 nm) was redshifted to 372 nm in its protonated form, whereas the emission spectra of nonprotonated and protonated **11** are identical, which indicates that the trifluoroacetic acid (TFA) is not able to protonate the electron-deficient nitrogen atom (for details, see Supporting Information).

The new star-shaped terpyridine derivatives **12** and **13** were synthesized in an analogous manner to the synthesis of **9** by using terpyridyl nonaflates **3** and **4** as precursors (see Scheme 6). Because of the expected low solubility of the desired products, pyridine was used as the solvent along with the employment of higher temperatures. Although three subsequent coupling steps were required to produce the target compounds, the C_3-symmetrical products **12** and



Scheme 6. Synthesis of the star-shaped terpyridine derivatives **12** and **13**.

Table 1. UV and fluorescence spectra of **12** (a) and **13** (b) in $CHCl_3$ (solid lines) and $CHCl_3$/TFA (99:1, dashed lines) as well as the corresponding absorption and emission data.



	$CHCl_3$			$CHCl_3$/TFA (99:1)		
	Absorption[a] λ_{max} [nm], ($\log\varepsilon$)	Emission[b] λ_{max} [nm]	Stokes shift [cm^{-1}]	Absorption[a] λ_{max} [nm], ($\log\varepsilon$)	Emission[b] λ_{max} [nm]	Stokes shift [cm^{-1}]
12	294, 309 sh[c]	356	5900	290, 331[c]	417	10500, 6200[d]
13	311 (4.87)	377	5600	368 (4.59)	444	4700

[a] Absorption: recorded at $c = 10^{-5}$ mol L^{-1} in 1 cm cuvettes. [b] Emission after excitation at the maximum absorption wavelength, recorded at $c = 10^{-6}$–10^{-5} mol L^{-1} in 1 cm cuvettes. [c] Qualitative spectrum, $\log\varepsilon$ could not be calculated because of solubility problems. [d] Stokes shifts were calculated by using both absorption maxima.

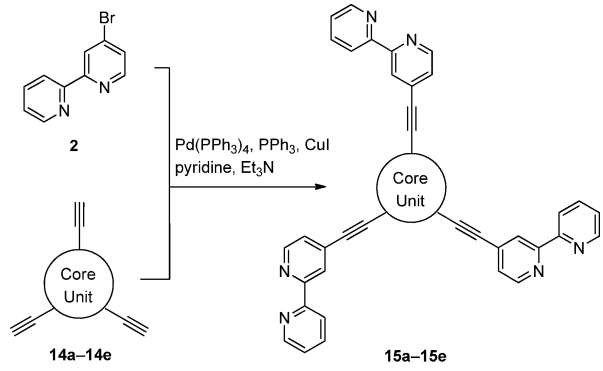
13 were isolated in good yields. Nishihara and co-workers used a different strategy and prepared compound **12** by using Stille reactions.[13] The laborious preparation of 4-[(tributylstannyl)ethynyl]terpyridine and its toxicity as well as the obtained lower yield of 65% make their synthesis less attractive in comparison to our protocol.

The fully conjugated terpyridine derivatives **12** and **13** show remarkable photophysical properties. Their UV/Vis absorption and fluorescence spectra were recorded in chloroform or a mixture of chloroform and trifluoroacetic acid (99:1) and are presented in Table 1. The introduction of the electron-donating ethoxy group in compound **13** led to a redshift for the absorption and the emission of approximately 20 nm in comparison to those of **12**. The Stokes shifts are 5900 cm^{-1} for **12** and 5600 cm^{-1} for **13**, respectively. Although the absorption maximum of protonated **12** is similar to that of the nonprotonated compound, a considerable redshift of 61 nm was observed for the emission of protonated **12**. Furthermore, the absorption shoulder at 309 nm for **12** became a distinct second maximum at 331 nm after protonation. The absorption and emission maxima of **13** are also strongly influenced by protonation (see Table 1).

By using different core units and 4-bromobipyridine as a ligand, five new star-shaped bipyridine derivatives were prepared in a similar manner to the synthesis of **12** (see Table 2). The building blocks **14a**–**14e** were used as the central core units, and they were either commercially available (e.g., **14a**; see Table 2, Entry 1) or prepared by following modified literature procedures (e.g., **14b**–**14e**, see Supporting Information for detailed experimental data; see Table 2, Entries 2–5).[14] The reaction of 1,3,5-triethynylbenzene with 4-bromobipyridine **2** afforded the corresponding star-shaped compound **15a** in 74% yield (see Table 2, Entry 1). In comparison, the sterically more demanding **15b** was obtained in 61% yield. However, to obtain full conversion, the reaction time had to be extended from 16 h to 2 d (see Table 2, Entry 2). A longer reaction time was also needed for the syntheses of the enlarged, fully conjugated star-shaped derivatives **15c** and **15d**, which were obtained in 62% and 47% yield, respectively (see Table 2, Entries 3 and 4). For the preparation of **15d**, the reaction temperature was decreased to 40 °C to avoid the formation of unknown side products that were produced when the reaction was conducted at 70 °C. We were also able to prepare unconjugated derivative **15e**, which contains an adamantane core unit. With respect to the bonding distances, this compound could be compared to planar bipyridine derivative **15a**. However, in adamantane derivative **15e**, the three side arms were obviously forced out-of-plane.

Again, we studied the photophysical properties of the fully conjugated bipyridine derivatives **15a**–**15d** and the unconjugated adamantane derivative **15e**. Table 3 presents their UV/Vis absorption and emission maxima as well as the calculated Stokes shifts. As expected, the λ_{max} values increase as the π-systems are extended, with a maximum redshift of 40 nm from **15a** to **15d**. Although the π-systems of **15b** are not extended (in comparison to **15a**), its λ_{max} value did slightly increase. We assume that the methyl groups slightly enhance the electron density of the central benzene ring and lead to the observed redshift. Interest-

Table 2. Synthesis of the star-shaped bipyridine derivatives **15a**–**15e** with five different core units.



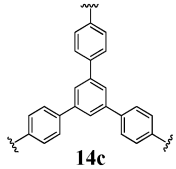
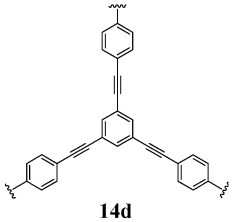
Entry	Core unit	Conditions	Product	Yield
1	 **14a**	70 °C, 16 h	**15a**	74%
2	 **14b**	70 °C, 2 d	**15b**	61%
3	 **14c**	70 °C, 5 d	**15c**	62%
4	 **14d**	40 °C, 16 h	**15d**	47%
5	 **14e**	70 °C, 16 h	**15e**	46%

Table 3. Absorption and emission data of star-shaped bipyridine derivatives **15a**–**15d**.

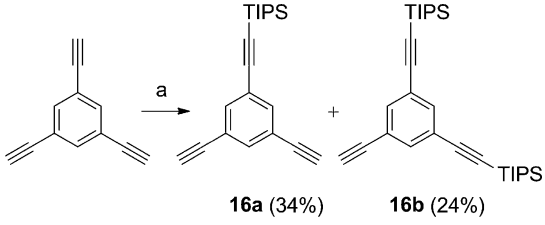
Entry		Absorption[a] λ_{max} [nm] (log ε)	Emission[b] λ_{max} [nm]	Stokes shift [cm^{-1}]
1	**15a**	290 (4.43)	354, 368 sh	6200
2	**15b**	304 (4.63), 324 sh	368	7000
3	**15c**	311 (4.66)	360	4400
4	**15d**	330 (5.65)	368, 377 sh	3100

[a] Absorption: recorded at $c = 10^{-5}$ mol L^{-1} in 1 cm cuvettes. [b] Emission after excitation at maximum absorption wavelength, recorded at $c = 10^{-6}$–10^{-5} mol L^{-1} in 1 cm cuvettes.

ingly, the emission values do not vary significantly, which results in decreasing Stokes shifts of 6200 to 3100 cm^{-1} going from **15a** to **15d**. As expected the unconjugated adamantane derivative **15e** shows only a weak absorption around 280 nm and no emission after excitation at this absorption wavelength.

Synthesis of C_2-Symmetric Terpyridine Derivatives

In addition to the described synthesis of C_3-symmetrical terpyridine derivatives, we also developed straightforward methods for the preparation of new C_2-symmetrical analogues that have one of the pyridine ligands substituted by a terphenyl unit as a "dummy" ligand. For this purpose, 1,3,5-triethynylbenzene was treated with *n*BuLi (1.5 equiv.) following by quenching with triisopropylsilyl chloride (TIPSCl) to give the partially protected core units **16a** and **16b** in 34 and 24% yield, respectively, after separation by simple column chromatography (see Scheme 7). In addition, the trisilylated compound was isolated in 8% yield. Although, the syntheses of **16a** and **16b** were described in the literature by using three steps for each of these compounds,[15] our direct approach provides both compounds in only one step. This simple method should also be applicable to other trialkynes (core units). The partial protection of 1,3,5-triethynylbenzene was also examined by using other chorosilanes, however, TIPSCl gave the best total yield when compared to other chlorosilanes.[16]

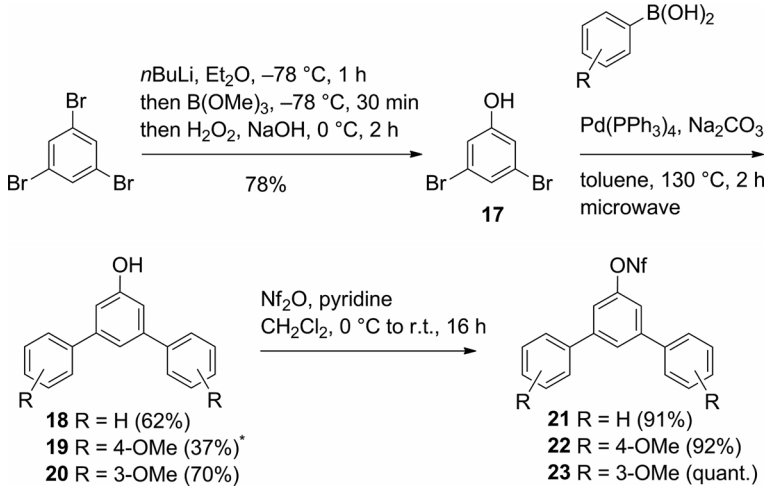


Scheme 7. Direct synthesis of partially protected 1,3,5-triethynylbenzene core units **16a** and **16b** by using TIPSCl.

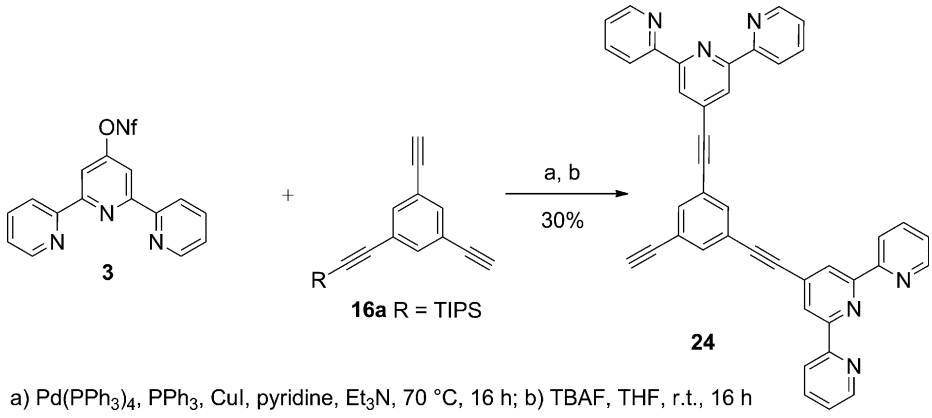
A series of terphenyl ligands were prepared to test their influence on the solubility of the desired C_2-symmetrical star-shaped derivatives and determine their effect on the self-assembly of these compounds (see Scheme 8). By starting from 1,3,5-tribromobenzene, the corresponding phenol **17** was prepared under a standard protocol that involved a bromine-lithium exchange, borate formation, and oxidation by treatment with hydrogen peroxide.[17] Microwave-assisted Suzuki reactions of **17** with three commercially available phenylboronic acid derivatives afforded phenols **18**–**20** in moderate to good yields. A final nonaflation with nonafluorobutanesulfonic acid anhydride furnished terphenyl nonaflates **21**–**23** in excellent yields.

With terphenyl nonaflates **21**–**23** in hand, we started to prepare the C_2-symmetrical derivatives. The Sonogashira reaction between terpyridyl nonaflate **3** and the monoprotected core unit **16a** followed by deprotection with tetra-*n*-butylammonium fluoride (TBAF) provided the desired bis(terpyridine) derivative **24** in 30% yield (see Scheme 9). The low yield is probably a result of purification difficulties that arose from the scarcely soluble product. Subsequent attempts to couple the terminal alkyne moiety of compound **24** with terphenyl nonaflates **21**–**23** were unsuccessful. Most likely, the low solubility of **24** and the generated compounds caused these failures.

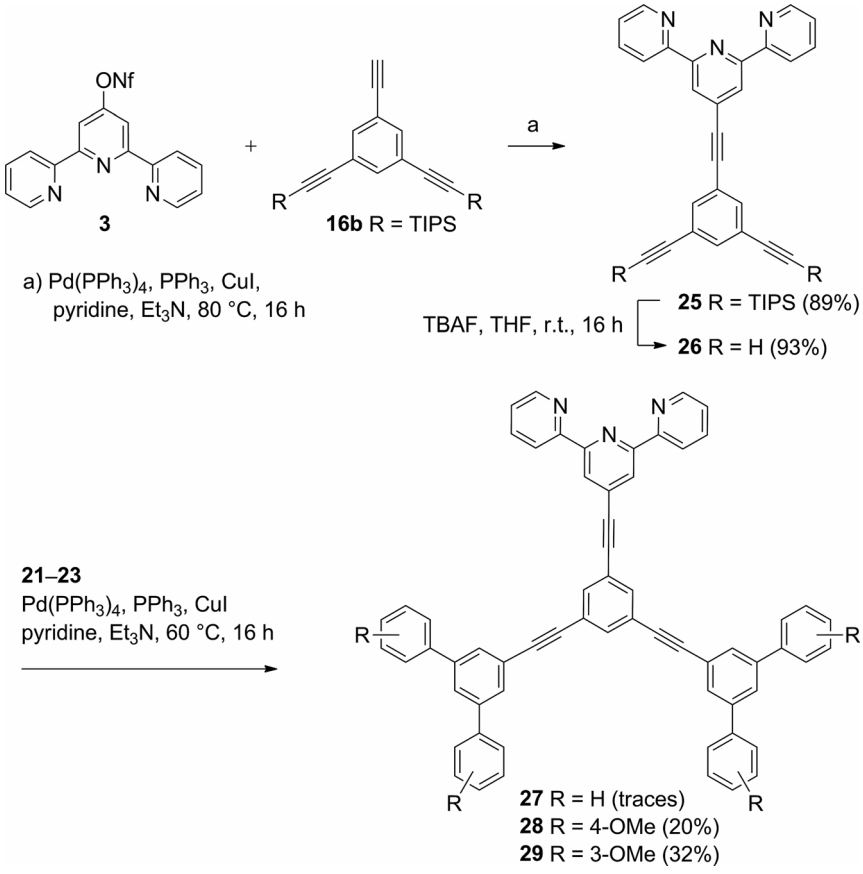
On the other hand, the Sonogashira reaction of terpyridyl nonaflate **3** and diprotected core unit **16b** led to the formation of precursor **25** in 89% yield (see Scheme 10). The subsequent deprotection of **25** by treatment with TBAF furnished terminal dialkyne **26** in 93% yield. This was coupled in the final step with terphenyl nonaflates **22** and **23** to furnish the desired star-shaped compounds **28** and **29** in moderate yields. Their UV/Vis absorption and fluorescence spectra are very similar to that obtained for **12**. Unfortunately, the coupling of **26** with terphenyl derivative **21** did not provide unsubstituted derivative **27**, again probably because of solubility problems. The prepared C_2-symmetrical terpyridines **28** and **29** are good candidates for the generation and investigation of new supramolecular architectures at the surface or in solution.



Scheme 8. Synthesis of 4,4′′-disubstituted terphenyl nonaflates **21**–**23** [*$Pd(PPh_3)_2Cl_2$ was used as catalyst].



Scheme 9. Synthesis of bis(terpyridine) derivative **24**.



Scheme 10. Synthesis of C_2-symmetrical star-shaped terpyridine derivatives **28** and **29**.

Conclusions

We were able to generate a library of star-shaped pyridine, bipyridine, and terpyridine derivatives by employing a Sonogashira reaction in the crucial final step of their preparation. The employed methods are simple and flexible. Because our synthetic strategy is based on a modular construction principle that includes a ligand, spacer, and core unit, quite a number of compounds were easily prepared. By using partially protected core units, we also presented the syntheses of two C_2-symmetrical star-shaped terpyridine derivatives that contain two terphenyl groups as "dummy" ligands, instead of the terpyridine units. This method should be applicable to other compounds of this type. Other bipyridine or terpyridine derivatives that are of interest as ligands in catalytic processes[18] can certainly be prepared by employing the building blocks and reactions presented herein. We also studied the photophysical properties of the fully conjugated pyridine derivatives and show their remarkable absorption and fluorescence spectra. In the future, we will report our studies of the self-assembly processes of the star-shaped compounds by using scanning tunneling microscopy experiments and compare the results with the behavior of related compounds.[1,5]

Experimental Section

General Methods: See Supporting Information.

Typical Procedure 1: (2,2′:6′,2′′-Terpyridin)-4′-yl Nonafluorobutanesulfonate (3): Pyridinone **6**[8] (1.26 g, 5.05 mmol) was dissolved in dry pyridine (60 mL), and the solution was cooled to 0 °C. Nonafluorobutanesulfonic acid anhydride (4.56 g, 7.58 mmol) was added dropwise, and the mixture was warmed to room temperature and stirred for 6 d. Ice was added, and after the mixture was stirred for 30 min, a precipitate formed. This was collected by filtration. Purification of this crude solid by recrystallization (hot hexane) afforded nonaflate **3** (1.71 g, 64%) as colorless crystals; m.p. 94–96 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (ddd, J = 1.8, 4.8, 7.7 Hz, 2 H, 5-H), 7.86 (dt, J = 1.8, 7.7 Hz, 2 H, 4-H), 8.42 (s, 2 H, 3′-H), 8.59 (ddd, J = 0.8, 1.1, 7.7 Hz, 2 H, 3-H), 8.70 (ddd, J = 0.8, 1.8, 4.8 Hz, 2 H, 6-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 113.1, 121.4, 124.8, 137.1, 149.5 (5 d, C-3′, C-3, C-5, C-4, C-6), 154.3, 158.8, 158.9 (3 s, 3 Ar) ppm. IR [attenuated total reflectance (ATR)]: $\tilde{\nu}$ = 3100–3060 (=C–H), 1420 (S=O) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{10}F_9N_3O_3S$ [M + H]$^+$ 532.0372; found 532.0394. $C_{19}H_{10}F_9N_3O_3S$ (531.4): calcd. C 42.95, H 1.90, N 7.91; found C 43.00, H 1.71, N 7.88.

1,3,5-Tris(perfluoropyridin-4-ylethynyl)benzene (11): A solution of 1,3,5-triethynylbenzene (60 mg, 400 µmol) in THF (10 mL) was stirred at –78 °C under argon and then treated dropwise with *n*-butyllithium (2.5 M in hexanes, 0.7 mL, 1.60 mmol). The resulting mixture was stirred at –78 °C for 45 min, and pentafluoropyridine (338 mg, 2.00 mmol) in THF (2 mL) was added dropwise. The mixture was stirred at –78 °C for 30 min, and the solution was warmed to room temperature overnight. The volatile components were removed under reduced pressure. To the residue were added CH_2Cl_2 (10 mL) and hexane (3 mL), and the solution was cooled with an ice bath. The resulting precipitate was removed by filtration, washed with a small amount of cold CH_2Cl_2, and dried in vacuo to provide **11** (239 mg, 72%) as a pale yellow solid; m.p. 148–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 3 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 75.6 (t, $J_{C,F}$ = 4.2 Hz, C≡C), 102.6 (t, $J_{C,F}$ = 3.4 Hz, C≡C), 122.6 (s, C-1′), 136.9 (d, C-2′), 140.4–145.1 (3 m, 3 C-F) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –89.3 (s, 6 F, 2-F), –137.3 (s, 6 F, 3-F) ppm. IR (ATR): $\tilde{\nu}$ = 3080 (=C–H), 2225 (C≡C) cm^{-1}. UV/Vis ($CHCl_3$): λ [log(ε/M^{-1} cm^{-1})] = 296 [3.32] nm. HRMS (EI): calcd. for $C_{27}H_3F_{12}N_3$ [M]$^{+\cdot}$ 597.0136; found 597.0103.

Typical Procedure 2: 1,3,5-Tris[(2,2′:6′,2′′-terpyridin)-4′-ylethynyl]-benzene (12): A mixture of 1,3,5-triethynylbenzene (25 mg, 166 µmol), nonaflate **3** (310 mg, 583 µmol), $Pd(PPh_3)_4$ (19 mg, 17 µmol), triphenylphosphine (5 mg, 19 µmol), and CuI (3 mg, 16 µmol) in pyridine (5 mL) and triethylamine (0.2 mL) was heated to 100 °C for 16 h under argon. The mixture was cooled to 0 °C, and a precipitate formed. The solid was removed by filtration and washed with CH_2Cl_2. Purification by recrystallization (hot pyridine) afforded **12** (118 mg, 84%) as a pale brown solid; m.p. >235 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.42 (m, 6 H, 5-H), 7.79 (s, 3 H, 2′′-H), 7.89 (t, J = 7.4 Hz, 6 H, 4-H), 8.56–8.70 (m, 12 H, 3-H, 3′-H), 8.72–8.79 (m, 6 H, 6-H) ppm. Because of poor solubility, a satisfactory ^{13}C NMR spectrum was not obtained. IR (ATR): $\tilde{\nu}$ = 3060 (=C–H), 2220 (C≡C) cm^{-1}. UV/Vis ($CHCl_3$, qualitative because of the low solubility): λ = 294 nm. HRMS (ESI-TOF): calcd. for $C_{57}H_{33}N_9$ [M + H]$^+$ 844.2932; found 844.2933.

Typical Procedure 3: 3,5-Diethynyl-1-[(triisopropylsilyl)ethynyl]-benzene (16a) and 5-Ethynyl-1,3-bis[(triisopropylsilyl)ethynyl]benzene (16b): 1,3,5-Triethynylbenzene (100 mg, 666 µmol) was dissolved in THF (8 mL), and *n*-butyllithium (2.5 M in hexanes, 0.4 mL, 1.00 mmol) was added at –78 °C. After 45 min, triisopropylsilyl chloride (330 µL, 1.99 mmol) was added, and the solution was warmed to room temperature overnight. The mixture was quenched with water, and the aqueous phase was extracted with THF. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated to dryness. The residue was purified by chromatography on a silica gel column (hexane) to give **16a** (70 mg, 34%), **16b** (75 mg, 24%), and the trisilylated derivative (32 mg, 8%) as pale yellow gluey oils. Data of **16a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (br. s, 21 H, TIPS), 3.09 (s, 2 H, C≡CH), 7.52 (t, J = 1.4 Hz, 1 H, 4-H), 7.55 (d, J = 1.4 Hz, 2 H, 2-H) ppm. This compound was previously reported,[14a] but a different method was employed for its synthesis. The observed analytical data agree with those reported. Data of **16b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.09–1.14 (m, 42 H, TIPS), 3.08 (s, 1 H, C≡CH), 7.51 (t, J = 1.4 Hz, 1 H, 2-H), 7.52 (d, J = 1.4 Hz, 2 H, 4-H) ppm. This compound was previously reported,[14b] but a different method was employed for its synthesis. The observed analytical data agree with those reported. Data of trisilylated derivative: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07–1.17 (m, 63 H, TIPS), 7.46 (s, 3 H, Ar) ppm. IR (ATR): $\tilde{\nu}$ = 2940, 2865 (C–H), 2160 (C≡C), 1460 (C–Si) cm^{-1}. HRMS (EI, 270 °C, 80 eV): calcd. for $C_{39}H_{66}Si_3$ [M]$^{+\cdot}$ 618.4472; found 618.4459.

Typical Procedure 4: 1-[(2,2′:6′,2′′-Terpyridin)-4′-ylethynyl]-3,5-bis-[(triisopropylsilyl)ethynyl]benzene (25): A mixture of alkyne **16b** (30 mg, 65 µmol), nonaflate **3** (41 mg, 77 µmol), $Pd(PPh_3)_4$ (7.5 mg, 6.5 µmol), triphenylphosphine (2 mg, 8 µmol), and CuI (1 mg, 5 µmol) in pyridine (2 mL) and triethylamine (420 µL) was heated to 80 °C for 16 h under argon. The volatile components were removed under reduced pressure, and the residue was purified by chromatography on an aluminum oxide column (hexane/ethyl acetate, 20:1) to give **25** (40 mg, 89%) as a pale yellow solid; m.p. 199–201 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (br. s, 42 H, TIPS), 7.34 (dd, J = 4.8, 7.7 Hz, 2 H, 5-H), 7.54 (t, J = 1.4 Hz, 1 H, 4′′-H), 7.61 (d, J = 1.4 Hz, 2 H, 2′′-H), 7.85 (dt, J = 1.7, 7.7 Hz, 2 H, 4-H), 8.56 (s, 2 H, 3′-H), 8.60 (d, J = 7.7 Hz, 2 H, 3-H), 8.71 (br. d, J = 4.8 Hz, 2 H, 6-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 11.4 [d, Si*C*H(CH_3)$_2$], 18.8 (q, CH_3), 88.5, 92.0, 92.6, 105.2 (4 s, 4 C≡C), 121.3, 122.9 (2 d, C-3, C-3′), 123.0 (s, Ar), 124.1 (d, C-5), 124.4, 132.9 (2 s, 2 Ar), 135.1, 135.2, 136.9, 149.3 (4 d, C-2′′, C-4′′, C-4, C-6), 155.6, 155.7 (2 s, 2 Ar) ppm. IR (ATR): $\tilde{\nu}$ = 3060–3010 (=C–H), 2945, 2865 (C–H), 2145 (C≡C), 1465 (C–Si) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{45}H_{55}N_3Si_2$ [M + Na]$^+$ 716.3827; found 716.3860.

Typical Procedure 5: 1-[(2,2′:6′,2′′-Terpyridin)-4′-ylethynyl]-3,5-bis-(ethynyl)benzene (26): A solution of **25** (82 mg, 118 µmol) and TBAF (1 M in THF, 320 µL, 320 µmol) in THF (4 mL) was stirred at room temperature for 16 h. The volatile components were removed under reduced pressure, and the residue was diluted with CH_2Cl_2 (10 mL). Water (20 mL) was added, and the phases were separated. The organic phase was washed with water (3× 10 mL). The organic layer was dried with Na_2SO_4 and then concentrated to dryness. The residue was purified by chromatography on an aluminum oxide column (hexane/ethyl acetate, 10:1) to give **26** (42 mg, 93%) as a colorless solid; m.p. 189 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.14 (s, 2 H, C≡CH), 7.35 (ddd, J = 1.0, 4.8, 7.7 Hz, 2 H, 5-H), 7.59 (t, J = 1.5 Hz, 1 H, 4′′-H), 7.64 (d, J = 1.5 Hz, 2 H, 2′′-H), 7.87 (dt, J = 1.7, 7.7 Hz, 1 H, 4-H), 8.56 (s, 2 H, 3′-H), 8.61 (br. d, J = 7.7 Hz, 2 H, 3-H), 8.71 (dd, J = 1.7, 4.8 Hz, 2 H, 6-H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 78.9, 88.8, 91.5 (3 s, 3 C≡C), 81.7, 121.3, 123.0 (3 d, C≡*C*H, C-3, C-3′), 123.2, 123.4,

(2 s, 2 Ar), 124.3 (d, C-5), 132.8, (s, Ar), 135.5, 135.9, 137.0, 149.3 (4 d, C-2′′, C-4′′, C-4, C-6), 155.6, 155.7 (2 s, 2 Ar) ppm. IR (ATR): $\tilde{\nu}$ = 3290 (≡C–H), 3070–2860 (=C–H), 2220 (C≡C) cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{27}H_{15}N_3$ $[M + H]^+$ 382.1339; found 382.1340.

Typical Procedure 6: 1-[(2,2′:6′,2′′-Terpyridin)-4′-ylethynyl]-3,5-bis[5′-ethynyl-3,3′′-dimethoxy-(1,1′:3′,1′′-terphenyl)]benzene (29): A mixture of **26** (25 mg, 66 µmol), nonaflate **3** (51 mg, 87 µmol), $Pd(PPh_3)_4$ (4.5 mg, 4.0 µmol), triphenylphosphine (1 mg, 4 µmol), and CuI (0.5 mg, 2.6 µmol) in pyridine (2 mL) and triethylamine (230 µL) was heated to 60 °C for 16 h under argon. The volatile components were removed under reduced pressure, and the residue was purified by chromatography on an aluminum oxide column (hexane/ethyl acetate, 10:1) to give **29** (12 mg, 32%) as a colorless solid; m.p. 68–71 °C. ^{1}H NMR (700 MHz, $CDCl_3$): δ = 3.92 (s, 12 H, CH_3), 6.98 (ddd, J = 0.9, 2.1, 7.9 Hz, 4 H, 4′′′′-H), 7.23 (t, J = 2.1 Hz, 4 H, 2′′′′-H), 7.29 (ddd, J = 0.9, 2.1, 7.9 Hz, 4 H, 6′′′′-H), 7.39 (ddd, J = 1.1, 4.7, 7.7 Hz, 2 H, 5-H), 7.42 (t, J = 7.9 Hz, 4 H, 5′′′′-H), 7.78 (d, J = 1.6 Hz, 2 H, 2′′-H), 7.80 (d, J = 1.6 Hz, 4 H, 4′′′-H), 7.81–7.82 (m, 3 H, 4′′-H, 2′′′-H), 7.90 (dt, J = 1.8, 7.7 Hz, 2 H, 4-H), 8.63 (s, 2 H, 3′-H), 8.65 (br. d, J = 7.7 Hz, 2 H, 3-H), 8.76 (dd, J = 1.8, 4.7 Hz, 2 H, 6-H) ppm. ^{13}C NMR (176 MHz, $CDCl_3$): δ = 55.4 (q, CH_3), 87.9, 88.7, 90.8, 91.9 (4 s, 4 C≡C), 112.9, 113.4, 119.8, 121.2, 122.9 (5 d, C-2′′′′, C-4′′′′, C-6′′′′, C-3, C-3′), 123.4, 123.6 (2 s, 2 Ar), 124.1 (d, C-5), 124.2 (s, Ar), 126.6, 129.5, 129.9 (3 d, C-2′′′, C-4′′′, C-5′′′′), 132.9 (s, Ar), 134.5, 134.9, 136.9 (3 d, C-2′′, C-4′′, C-4), 141.8, 142.0 (2 s, 2 Ar), 149.3 (d, C-6), 155.65, 155.70, 160.1 (3 s, 3 Ar) ppm. IR (ATR): $\tilde{\nu}$ = 3060–2915 (=C–H), 2830 (C–H), 2215 (C≡C) cm^{-1}. UV/Vis ($CHCl_3$): λ [log(ε/M^{-1} cm^{-1})] = 294 [4.04] nm. HRMS (ESI-TOF): calcd. for $C_{67}H_{47}N_3O_4$ $[M + H]^+$ 958.3639; found 958.3694.

Supporting Information (see footnote on the first page of this article): General experimental methods, all experimental procedures and characterization data.

Acknowledgments

The generous support of the Deutsche Forschungsgemeinschaft (DFG) (SFB 765), the Evonik Foundation (Ph.D. fellowship to D. T.), and Bayer HealthCare is gratefully acknowledged. The authors thank Dr. Boris Brusilowskij (research group of Prof. Dr. Christoph A. Schalley) for donating compounds **9**, **10**, and **14e** and Dr. Reinhold Zimmer for help during preparation of this manuscript.

[1] a) D. Trawny, L. Vandromme, J. P. Rabe, H.-U. Reissig, *Eur. J. Org. Chem.* **2014**, 4985–4992; b) A. Ciesielski, P. J. Szabelski, W. Rżysko, A. Cadeddu, T. R. Cook, P. J. Stang, P. Samorì, *J. Am. Chem. Soc.* **2013**, *135*, 6942–6950.

[2] a) H. L. Anderson, C. J. Walter, A. Vidal-Ferran, R. A. Hay, P. A. Lowden, J. K. M. Sanders, *J. Chem. Soc. Perkin Trans. 1* **1995**, 2275–2279; b) N. Kobayashi, M. Kijima, *J. Mater. Chem.* **2008**, *18*, 1037–1045; c) S. Winter, E. Weber, L. Eriksson, I. Csoregh, *New J. Chem.* **2006**, *30*, 1808–1819.

[3] C. Engler, H. E. Berthold, *Ber. Dtsch. Chem. Ges.* **1874**, *7*, 1123–1125.

[4] V. Marvaud, D. Astruc, *Chem. Commun.* **1997**, 773–774.

[5] T. Lechel, M. Gerhard, D. Trawny, B. Brusilowskij, L. Schefzig, R. Zimmer, J. P. Rabe, D. Lentz, C. A. Schalley, H.-U. Reissig, *Chem. Eur. J.* **2011**, *17*, 7480–7491.

[6] D. Wenkert, R. B. Woodward, *J. Org. Chem.* **1983**, *48*, 283–289.

[7] R. A. Jones, B. D. Roney, W. H. F. Sasse, K. O. Wade, *J. Chem. Soc. B* **1967**, 106–111.

[8] E. C. Constable, M. D. Ward, *J. Chem. Soc., Dalton Trans.* **1990**, 1405–1409.

[9] a) M. Rottländer, P. Knochel, *J. Org. Chem.* **1998**, *63*, 203–208; b) review: J. Högermeier, H.-U. Reissig, *Adv. Synth. Catal.* **2009**, *351*, 2747–2763; c) T. Ikawa, K. Saito, S. Akai, *Synlett* **2012**, *23*, 2241–2246.

[10] O. M. Kuzmina, A. K. Steib, D. Flubacher, P. Knochel, *Org. Lett.* **2012**, *14*, 4818–4821.

[11] a) S. J. Lee, K. L. Mulfort, J. L. O'Donnell, X. Zuo, A. J. Goshe, P. J. Wesson, S. T. Nguyen, J. T. Hupp, D. M. Tiede, *Chem. Commun.* **2006**, 4581–4583; b) I. Asselberghs, G. Hennrich, K. Clays, *J. Phys. Chem. A* **2006**, *110*, 6271–6275.

[12] T. M. Fasina, J. C. Collings, D. P. Lydon, D. Albesa-Jove, A. S. Batsanov, J. A. K. Howard, P. Nguyen, M. Bruce, A. J. Scott, W. Clegg, S. W. Watt, C. Viney, T. B. Marder, *J. Mater. Chem.* **2004**, *14*, 2395–2404.

[13] Y. Nishimori, K. Kanaizuka, M. Murata, H. Nishihara, *Chem. Asian J.* **2007**, *2*, 367–376.

[14] a) N. Ohshiro, F. Takei, K. Onitsuka, S. Takahashi, *J. Organomet. Chem.* **1998**, *569*, 195–202; b) S. Sirilaksanapong, M. Sukwattanasinitt, P. Rashatasakhon, *Chem. Commun.* **2012**, *48*, 293–295; c) N. Kobayashi, M. Kijima, *J. Mater. Chem.* **2008**, *18*, 1037–1045; d) W. Maison, J. V. Frangioni, N. Pannier, *Org. Lett.* **2004**, *6*, 4567–4569.

[15] a) K. Onitsuka, M. Fujimoto, H. Kitajima, N. Ohshiro, F. Takei, S. Takahashi, *Chem. Eur. J.* **2004**, *10*, 6433–6446; b) E. C. Constable, O. Eich, C. E. Housecroft, *J. Chem. Soc., Dalton Trans.* **1999**, 1363–1364.

[16] The employed chlorosilanes are *tert*-butyldimethylsilyl chloride, *tert*-butyldiphenylsilyl chloride, trimethylsilyl chloride, and tris(trimethylsilyl)silyl chloride. In the case of trimethylsilyl chloride and tris(trimethylsilyl)silyl chloride, the resulting mixtures could not be separated by column chromatography.

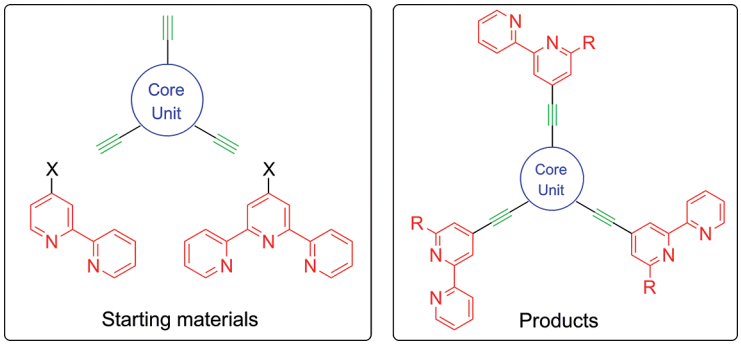
[17] D. Laliberté, T. Maris, J. D. Wuest, *J. Org. Chem.* **2004**, *69*, 1776–1787.

[18] P. Hommes, C. Fischer, C. Lindner, H. Zipse, H.-U. Reissig, *Angew. Chem. Int. Ed.* **2014**, *53*, 7647–7651; *Angew. Chem.* **2014**, *126*, 7778–7782, and references cited therein.

Received: June 19, 2014
Published Online: ■

EurJOC European Journal of Organic Chemistry

Star-Shaped Compounds



Modular, simple, and efficient! A library of C_3-symmetrical compounds with benzene cores and pyridine, bipyridine, and terpyridine end groups were prepared from simple precursors.

Keywords: Nitrogen heterocycles / Alkynes / C–C coupling / UV/Vis spectroscopy / Fluorescence spectroscopy

