ORGANIC
LETTERS

2013
Vol. 15, No. 2
318–321

Per(2-thienyl)pyridines: Synthesis and Properties

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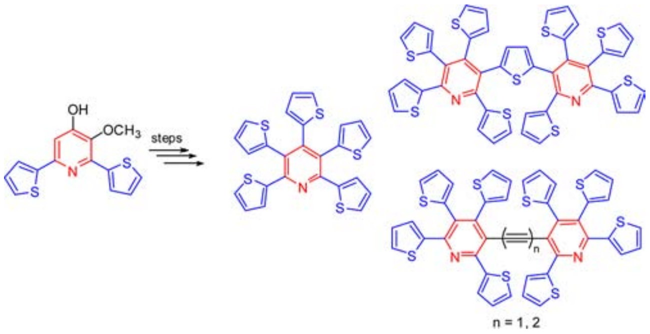
Received November 23, 2012

ABSTRACT



Starting from an easily available pyridinol derivative, a route to penta(2-thienyl)pyridine and related symmetrical compounds is reported. Key reactions are activation of the pyridine core and metal-catalyzed couplings proving the efficacy of these methods even in sterically highly encumbered systems. UV/vis and fluorescence spectra as well as first cyclovoltametric measurements of the synthesized novel thiophene–pyridine conjugates are reported.

Owing to their outstanding electronic, optical, and redox properties (oligo-)thiophene-based π-conjugated materials play a very important role as active components in organic electronic devices, e.g., organic light emitting diodes (OLEDs), field effect transistors (OFETs), and solar cells (OSCs), to name but a few. They usually exhibit high stabilities, unique arrangement, and stacking properties in the bulk or as films on surfaces. Thiophene moieties feature a high polarizability resulting in very efficient electronic conjugation and excellent charge transport properties.[1] The rich chemistry of thiophenes allows for a broad structural diversification and thus the possibility for a very flexible tuning of desired electronic properties: In addition to various chemical and electrochemical polymerization techniques,[1,2] numerous well established methods for the functionalization of the thiophene ring[3] are known, providing ideal building blocks for substitution reactions and for transition-metal-catalyzed cross-coupling reactions.[4]

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[1] (a) Fichou, D., Ed. *Handbook of Oligo- and Polythiophenes*; Wiley-VCH: Weinheim, 1999. (b) Müller, T. J. J., Bunz, U. H. F., Eds. *Functional Organic Materials*; Wiley-VCH: Weinheim, 2007. (c) Perepichka, I. F., Perepichka, D. F., Eds. *Handbook of Thiophene Based Materials*; J. Wiley & Sons: Hoboken, 2009. For selected reviews, see: (d) Roncali, J. *Chem. Rev.* **1997**, *97*, 173–206. (e) Perepichka, I. F.; Perepichka, D. F.; Meng, H.; Wudl, F. *Adv. Mater.* **2005**, *17*, 2281–2305. (f) Osaka, I.; McCullogh, R. D. *Acc. Chem. Res.* **2008**, *41*, 1202–1214. (g) Mishra, A.; Ma, C.-Q.; Bäuerle, P. *Chem. Rev.* **2009**, *109*, 1141–1276. (h) Zhang, F.; Wu, D.; Xua, Y.; Feng, X. *J. Mater. Chem.* **2011**, *21*, 17590–17600.

[2] (a) Leclerc, M., Morin, J.-F., Eds. *Design and Synthesis of Conjugated Polymers*; Wiley-VCH: Weinheim, 2007. (b) Chujo, Y., Ed. *Conjugated Polymer Synthesis: Methods and Reactions*; Wiley-VCH: Weinheim, 2007.

[3] (a) Gronowitz, S. *Thiophene and Its Derivatives*; Weissberger, A., Taylor, E. C., Eds.; *The Chemistry to Heterocyclic Compounds*; John Wiley & Sons: New York, 1985–1992; Vol. 44, Parts 1–5. (b) Schatz, J. *Sci. Synth.* **2000**, *9*, 287–422. (c) Gronowitz, S.; Hörnfeldt, A.-B. *Thiophenes*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; *Best Synthetic Methods*; Elsevier Academic Press: San Diego, CA, 2004.

[4] Diedrich, F., Stang, P. J., Eds. *Metal Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 1998 and 2006.

[5] For selected recent examples, see: (a) Ortiz, R. P.; Casado, J.; Hernández, V.; Navarrete, J. T. L.; Letizia, J. A.; Ratner, M. A.; Facchetti, A.; Marks, T. J. *Chem.—Eur. J.* **2009**, *15*, 5023–5039 and references 25–27 cited therein. (b) Mastalerz, M.; Fischer, V.; Ma, C.-Q.; Janssen, R. A. J.; Bäuerle, P. *Org. Lett.* **2009**, *11*, 4500–4503. (c) Pasker, F. M.; Le Blanc, S. M.; Schnakenburg, G.; Höger, S. *Org. Lett.* **2011**, *13*, 2338–2341 and references 6 and 7 cited therein. (d) Potratz, S.; Mishra, A.; Bäuerle, P. *Beilstein J. Org. Chem.* **2012**, *8*, 683–692. (e) Hemgesberg, M.; Ohlmann, D. M.; Schmitt, Y.; Wolfe, M. R.; Müller, M. K.; Erb, B.; Sun, Y.; Gooßen, L. J.; Gerhards, M.; Thiel, W. R. *Eur. J. Org. Chem.* **2012**, 2142–2151. (f) Liu, Y.; Zhang, F.; He, C.; Wu, D.; Zhuang, X.; Xue, M.; Liu, Y.; Feng, X. *Chem. Commun.* **2012**, *48*, 4166–4168.

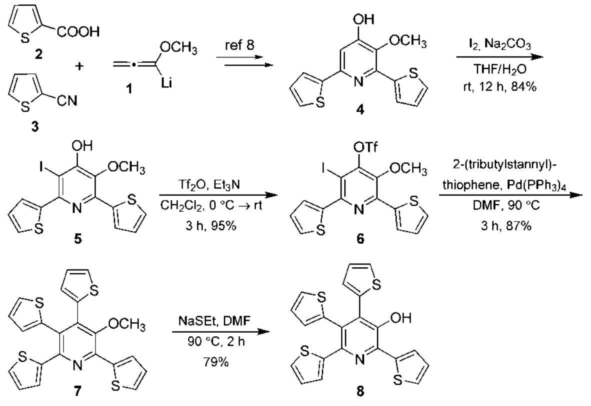
10.1021/ol303231c

Apart from oligomers and polymers containing (functionalized) thiophene moieties, a variety of donor-, acceptor-, and donor–acceptor-substituted thiophene conjugates[1c,h,5] have been investigated in the search for novel promising organic electronic materials. In this respect and also for other applications, many pyridyl-thienyl-substituted conjugates[6] have been reported.

Our group has discovered a remarkably flexible method for the synthesis of highly functionalized pyridine derivatives utilizing a three-component reaction of lithiated alkoxyallenes, nitriles, and carboxylic acids as precursors,[7] which allows the introduction of a broad range of different substituents in all five positions of the pyridine ring. We recently employed this methodology for the synthesis of a series of highly 2-thienyl-substituted pyridine derivatives showing interesting photophysical properties.[8] Unfortunately, all our attempts failed to transform key compound **5** into the ultimate goal penta(2-thienyl)pyridine **11**. Here we report now the successful synthesis of this compound and the use of intermediate **8** for the preparation of other per(2-thienyl) pyridines with extended π-systems (**13**, **16**, and **17**). Although we were mainly interested in the photophysical and redox properties of these new thiophene-pyridine conjugates, we also wanted to explore the scope of modern Pd-catalyzed cross coupling reactions in sterically highly encumbered aromatic systems.

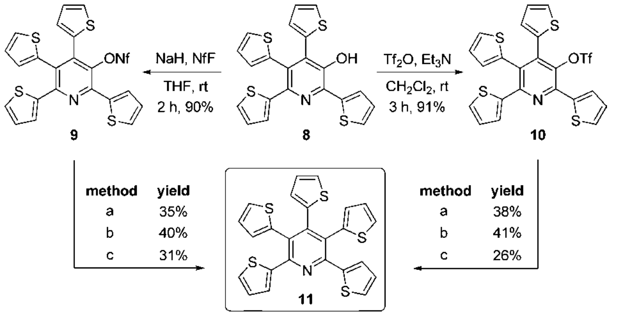
Our reaction sequence started with easily available tetrasubstituted pyridine derivative **4** which was converted into pyridinol **8**.[8] Activation of C-3 of compound **4** was achieved by iodination under basic conditions[9] to furnish 3-iodopyridinol **5** (Scheme 1). In order to introduce two 2-thienyl groups in one step, the free hydroxyl group was converted under standard conditions into triflate **6**. The palladium-catalyzed 2-fold Stille coupling of **6** with 2-(tributylstannyl)thiophene in DMF at 90 °C afforded the desired tetra(2-thienyl)-substituted pyridine derivative **7**. Dealkylation of the C-5 methoxy group with an excess of sodium ethanethiolate in hot DMF[10] furnished the desired pyridinol **8**. For all steps we could improve the reported yields considerably.[8]

Scheme 1. Improved Synthesis of 2,4,5,6-Tetra(2-thienyl)pyridin-3-ol (**8**)



Key compound **8** was subsequently converted into pyridyl nonaflate[11] **9** in excellent yield by treatment with sodium hydride and nonafluorobutanesulfonyl fluoride (NfF) in THF at room temperature (Scheme 2).

Scheme 2. Synthesis of Penta(2-thienyl)pyridine Derivative **11**[a]



[a] Reagents and conditions: (a) thiophene-2-boronic acid, Pd(PPh$_3$)$_4$, K$_2$CO$_3$, DMF, 80 °C, 3 h; (b) 2-(tributylstannyl)thiophene, Pd(PPh$_3$)$_4$, DMF, 90 °C, 3 h; (c) thiophene, *n*-BuLi, ZnBr$_2$, Pd(PPh$_3$)$_4$, THF, 60 °C, 3 h.

Alternatively, **8** and triflic anhydride/triethylamine afforded pyridyl triflate **10**. The crucial final palladium-catalyzed couplings of nonaflate **9** and triflate **10**, respectively, were challenging because of the steric hindrance exhibited by the neighboring substituents. Gratifyingly, the attempted Suzuki, Stille, or Negishi couplings with **9** or **10** and the corresponding 2-thienyl metal precursors delivered the targeted penta(2-thienyl)pyridine **11**, albeit all reactions provided only moderate yields in the range of 26 to 41%.

After successful synthesis of penta(2-thienyl)pyridine **11**, we subjected intermediate **10** to other coupling reactions to gain additional symmetric per(2-thienylated) compounds. The 2-fold Suzuki reaction of triflate **10** with thiophene-2,5-diboronic acid **12** furnished the expected product **13** with good efficacy (Scheme 3). This unique compound contains not less than nine thiophene rings! Surprisingly, the reaction of **10** with benzene-1,4-diboronic

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(6) For selected recent examples, see: (a) Chevallier, F.; Charlot, M.; Katan, C.; Mongin, F.; Blanchard-Desce, M. *Chem. Commun.* **2009**, 692–694 and references cited therein. (b) Rocha, S. V.; Finney, N. S. *Org. Lett.* **2010**, *12*, 2598–2601 and reference 7 cited therein. (c) Coluccini, C.; Manfredi, N.; Calderon, E. H.; Salamone, M. M.; Ruffo, R.; Roberto, D.; Lobello, M. G.; De Angelis, F.; Abbotto, A. *Eur. J. Org. Chem.* **2011**, 5587–5598. (d) Liu, B.; Bao, Y.; Du, F.; Wang, H.; Tian, J.; Bai, R. *Chem. Commun.* **2011**, *47*, 1731–1733. (e) De Giorgi, M.; Voisin-Chiret, A. S.; Sopková-de Oliveira Santos, J.; Corbo, F.; Franchini, C.; Rault, S. *Tetrahedron* **2011**, *67*, 6145–6154.

(7) (a) Flögel, O.; Dash, J.; Brüdgam, I.; Hartl, H.; Reissig, H.-U. *Chem.—Eur. J.* **2004**, *10*, 4283–4290. (b) Dash, J.; Lechel, T.; Reissig, H.-U. *Org. Lett.* **2007**, *9*, 5541–5544. (c) Review: Lechel, T.; Reissig, H.-U. *Pure Appl. Chem.* **2010**, *82*, 1835–1845. (d) For an interesting alternative three-component-synthesis of substituted pyridines, see: Micalizio, G. C.; Chen, M. Z. *J. Am. Chem. Soc.* **2012**, *134*, 1352-1356.

(8) Bera, M. K.; Hommes, P.; Reissig, H.-U. *Chem.—Eur. J.* **2011**, *17*, 11838–11843.

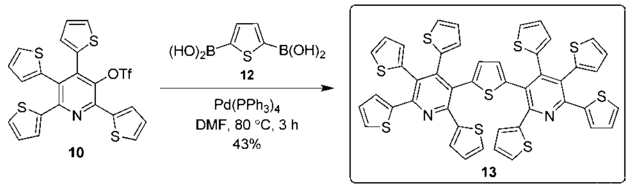
(9) Meketa, M. L.; Weinreb, S. M. *Org. Lett.* **2007**, *9*, 853–855.

(10) Feutrill, G. I.; Mirrington, R. N. *Tetrahedron Lett.* **1970**, *11*, 1327–1328.

(11) For a review summarizing the advantages of alkenyl and aryl nonaflates in transition-metal-catalyzed reactions, see: Högermeier, J.; Reissig, H.-U. *Adv. Synth. Catal.* **2009**, *351*, 2747–2763.

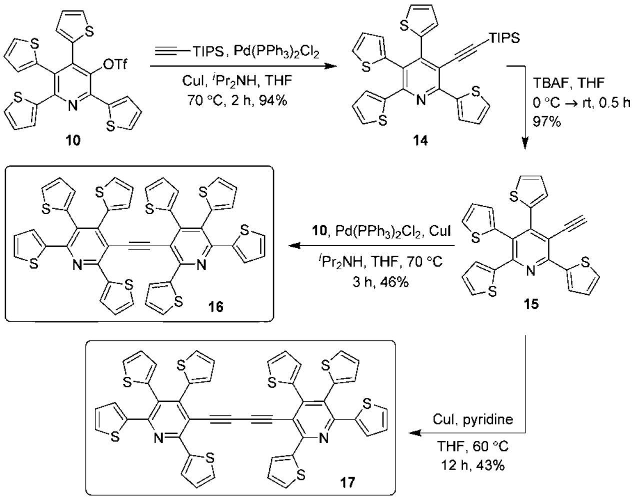
acid under similar conditions failed to give the related product with a central benzene unit.

Scheme 3. Twofold Suzuki Coupling of **10** Leading to Thiophene Derivative **13**



Next, we examined metal-catalyzed coupling reactions with alkynes (Scheme 4). We were very pleased to observe that the coupling of pyridyl triflate **10** with (triisopropylsilyl)acetylene under standard Sonogashira conditions[12] afforded alkyne **14** in excellent yield. Deprotection with tetra-*n*-butylammonium fluoride (TBAF) gave monosubstituted alkyne **15** in 97% yield, which on reaction with pyridyl triflate **10** under similar Sonogashira conditions furnished bis[penta-2-(thienyl)pyridyl]-substituted alkyne **16**. Alkyne **15** was also subjected to Glaser coupling conditions, hence providing the expected bis[penta-2-(thienyl)pyridyl]substituted butadiyne **17** in good yield. All these successful reactions show that metal-catalyzed couplings of highly substituted compounds such as **10** occur with surprising efficacies.

Scheme 4. Synthesis of Dipyridylalkyne **16** and Butadiyne **17**



With the symmetric per(2-thienyl)-substituted pyridine derivatives **11**, **13**, **16**, and **17** and alkyne **15** in hand, we studied their photophysical properties as neutral and protonated species (Table 1 and Figure 1). In chloroform solution, all compounds show UV absorptions with maxima between 307 and 329 nm with shoulders ranging up to 434 nm for **17**. After excitation at wavelengths corresponding to the absorption maxima, the compounds show fluorescence with maximum emission wavelengths between 430 nm (**11** and **15**) and 520 nm (**13** and **16**) resulting in Stokes shifts of 120−210 nm. As expected, the maximum absorption and emission wavelengths are significantly red-shifted for the corresponding pyridinium salts, measured in a 99:1 mixture of chloroform and trifluoroacetic acid.[13,14] Here, maximum emission wavelengths range from about 510 to 530 nm.

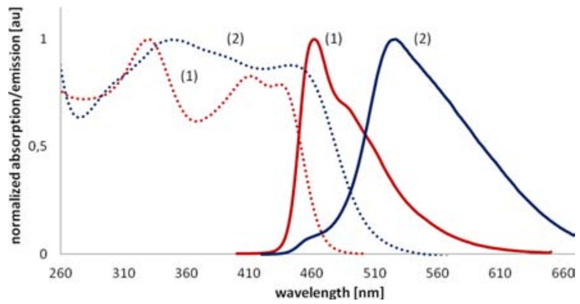


Figure 1. UV/vis spectra (dashed lines) and emission spectra (solid lines) of compound **17** in $CHCl_3$ (1) and $CHCl_3$/TFA (99:1) (2).

The electrochemical properties of our new compounds were investigated and compared with 2,4,6-tris(2-thienyl)-pyridine (**18**).[8] Cyclic voltammetry of **18** in acetonitrile showed irreversible oxidations at potentials of 1.36 and 1.86 V. Penta(2-thienyl)pyridine (**11**) gave very similar values of 1.33 and 1.76 V, indicating that the two additional thienyl group do not strongly contribute to the π-system due to nonplanarity. Figure 2 shows the cyclic voltammogram of **11** running 30 scans.

Compounds **13**, **16**, and **17** are not sufficiently soluble in acetonitrile; in chloroform solution they undergo irreversible oxidations at potentials of ca. 1.4 V. In all cases investigated, precipitation of a film was observed at the anode.[15] Not surprisingly, the electrochemical oxidation induced polymerization of the compounds, a behavior well-known from related compounds such as 1,3,5-trisarylbenzenes.[16]

In conclusion, we demonstrated the versatility of intermediates such as **4** for the syntheses of symmetrical per-(2-thienyl) pyridine derivatives. We also gave proof of the

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(12) Selected reviews: (a) Sonogashira, K. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., de Meijere, A., Eds.; Wiley: New York, 2002; pp 493−529. (b) Negishi, E.-i.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979–2017. (c) Doucet, H.; Hierso, J.-C. *Angew. Chem.* **2007**, *119*, 850–888. *Angew. Chem., Int. Ed.* **2007**, *46*, 834–871. (d) Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874–922.

(13) For related pH-sensitive fluorescence phenomena, see: (a) Monkman, A. P.; Palsson, L.-O.; Higgins, R. W. T.; Wang, C.; Bryce, M. R.; Batsanov, A. S.; Howard, J. A. K. *J. Am. Chem. Soc.* **2002**, *124*, 6049–6055. (b) Baxter, P. N. W. *J. Org. Chem.* **2004**, *69*, 1813–1821 and reference 19 cited therein. (c) References 5f and 6b.

(14) In comparison to the corresponding neutral compounds, a strong decrease in the fluorescence intensity was observed for the protonated species of **13**, **15**, **16**, and **17**.

(15) See the Supporting Information for further details.

(16) See Idzik, K. R.; Ledwon, P.; Beckert, R.; Golba, S.; Frydel, J.; Lapkowski, M. *Electrochim. Acta* **2010**, *55*, 7419–7426 and references cited therein.

Table 1. Absorption and Emission Data of the Oligo 2-Thienyl-Substituted Pyridine Derivatives

compd	λ_{abs} (nm)[a] in $CHCl_3$	log ε[b] in $CHCl_3$	λ_{em} (nm)[c] in $CHCl_3$	Stokes shift (nm)	λ_{abs} (nm)[a] in $CHCl_3$/TFA (99:1)	log ε[b] in $CHCl_3$/TFA (99:1)	λ_{em} (nm)[c] in $CHCl_3$/TFA (99:1)	Stokes shift (nm)
11	307	4.38	429	122	322	4.20	516	184
	348 (sh)	4.13			290 (sh)	4.12		
					404 (sh)	4.14		
13	307	4.75	516	209	390	4.60	517	127
	363 (sh)	4.63	430 (sh)		329 (sh)	4.57		
15	315	4.43	435	120	335	4.26	508	173
					390 (sh)	4.17		
16	324	4.67	519	195	335	4.54	523	188
	314 (sh)	4.67	468 (sh)		310 (sh)	4.49		
	364 (sh)	4.49			410 (sh)	4.45		
17	329	4.62	462	133	349	4.56	527	178
	411 (sh)	4.54			442 (sh)	4.49		
	434 (sh)	4.52						

[a] UV/vis absorption; measured at $c = 10^{-5}$–10^{-6} mol L^{-1} in 1 cm cuvettes; sh = shoulder. [b] Extinction coefficient. [c] Photoluminescence after excitation at maximum absorption wavelength; measured at $c = 10^{-5}$–10^{-6} mol L^{-1} in 1 cm cuvettes.

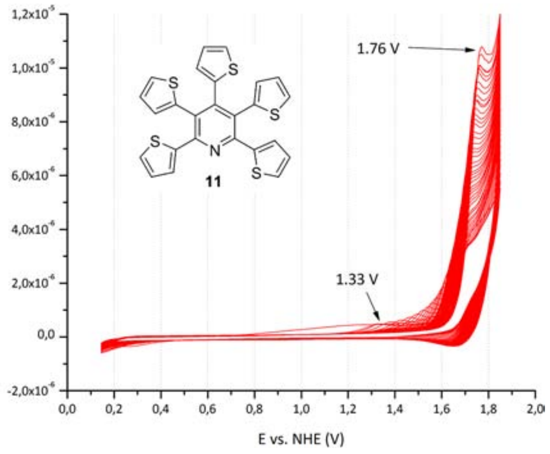

Figure 2. Cyclic voltammogram of **11** obtained in the range of 0.1–1.9 V on platinum electrodes; potential sweep rate ν = 100 mV/s; 0.030 mM solution in 0.1 M Bu_4NPF_6 in acetonitrile.

power of Pd-catalyzed processes in sterically highly encumbered systems. The resulting per(2-thienyl) pyridines showed interesting photophysical properties revealing fairly large Stokes shifts. The electrochemistry of these compounds has been investigated showing irreversible oxidation.

Acknowledgment. Generous support of this work by the Alexander von Humboldt Foundation (fellowship for S.L.G.) and the Center for Supramolecular Interaction of the Freie Universität Berlin (fellowship for P.H.) is most gratefully acknowledged. We thank Prof. Dr. Biprajit Sarkar and Dr. Reinhold Zimmer (both Freie Universität Berlin) for very helpful discussions.

Supporting Information Available. Experimental procedures, spectroscopic data (^1H and ^{13}C NMR for all new compounds, UV/vis and emission for **11**, **13**, **15**, and **16**), and details concerning the electrochemistry. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.