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Organic LETTERS

Letter

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Synthesis and Reactivity of Triazaphenanthrenes

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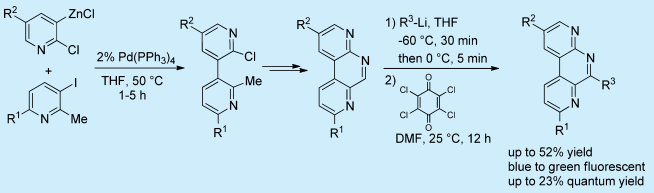
Supporting Information

ABSTRACT: Pyridonaphthyridines (triazaphenanthrenes) were prepared in 4 steps and in 13−52% overall yield using Negishi cross-couplings between iodopicolines and 2-chloropyridylzinc derivatives. After chlorination, Gabriel amination and spontaneous ring-closure, the final aromatization leading to the triazaphenanthrenes was achieved with chloranil. This heterocyclic scaffold underwent a nucleophilic addition at position 6 leading to further functionalized pyridonaphthyridines. The influence of these chemical modifications on the optical properties was studied by steady-state and time-resolved optical spectroscopy. While the thiophene-substituted heterocycles exhibited the most extended absorption, the phenyl- and furan-substituted compounds showed a stronger photoluminescence, reaching above 20% quantum yield and lifetimes of several nanoseconds.



Six-membered *N*-heterocyclic molecules have found numerous applications due to their biological or physical properties.[1] Especially a number of privileged ring systems have been extensively studied (e.g., pyridines,[2] quinolines,[3] isoquinolines,[4] acridines,[5] or diazines[6]). Annelated six-membered *N*-heteroaromatics bearing one nitrogen atom per ring (Figure 1), such as naphthyridines (**1**)[7] are much less studied, and the corresponding triazaanthracenes (**2**)[8] and triazaphenanthrenes (**3**)[9] are almost unknown.

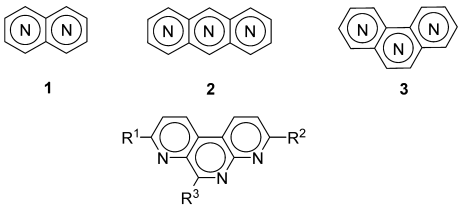
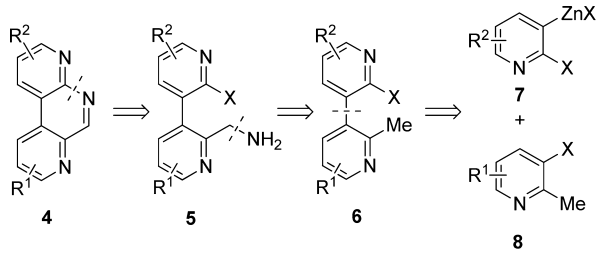


Figure 1. Fused six-membered *N*-heteroaromatics.

Due to the potential applications of triazaphenanthrenes derived from **3**, we became interested in a general synthesis of such heterocycles using a Negishi cross-coupling[10] with polyfunctional zinc intermediates. Herein, we report a straightforward synthesis of pyridonaphthyridines of type **4**, as well as further functionalizations of these new triazaphenanthrenes.

We have envisioned a retrosynthesis involving an intramolecular *N*-arylation of the bis-pyridine as final ring closure (**5**), possibly catalyzed by transition metals.[11] The aminopyridine (**5**) would be readily prepared from the bis-pyridine (**6**) by selective halogenation and amination of the methyl substituent. This polyfunctional bis-pyridine (**6**) would be available by a Negishi cross-coupling of the 3-zincated 2-chloropyridine (**7**) with the 3-halogenated 2-picoline (**8**; Scheme 1).

Scheme 1. Retrosynthetic Analysis



The polyfunctional zinc reagents of type **7** derived from the retrosynthetic analysis were prepared from the corresponding 3-bromo-2-chloropyridines (**9a−c**) by a bromine/magnesium exchange using *i*-PrMgCl·LiCl[12] followed by transmetalation with $ZnCl_2$. These pyridylzinc reagents underwent a Negishi cross-coupling with the iodopicolines (**8a−b**) in THF in the presence of 2% $Pd(PPh_3)_4$.[13,14] The cross-coupling reactions were usually complete within 1−5 h at 50 °C. As expected, the presence of electron-withdrawing substituents on the pyridylzinc reagents (**7**) significantly lowered the cross-coupling efficiency (Scheme 2).

For the introduction of an amino function, we chose to convert the 2-methyl substituent into a chloromethyl group, followed by a Gabriel reaction.[15] This chlorination was achieved by two methods. The most convenient procedure consisted of the treatment of the bis-pyridines (**6a−b**) with trichloroisocyanuric

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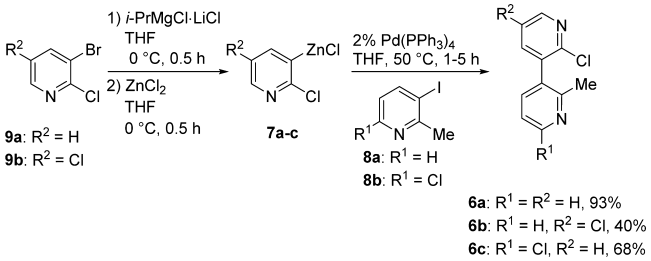
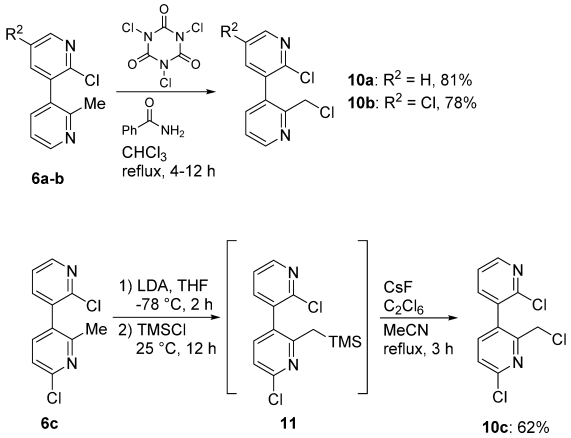
Scheme 2. Negishi Cross-Coupling Towards the Synthesis of the Bis-pyridines (6a–c)



acid in chloroform in the presence of 3% $PhCONH_2$ (60 °C, 4–12 h), leading to the chloromethyl bis-pyridines (**10a–b**) in 78–81% yield.[16] This electrophilic substitution did not proceed if the methyl substituent was attached to a pyridyl ring bearing an electron-withdrawing chlorine substituent. In this case, we prepared the intermediate trimethylsilylmethyl derivative (**11**) by deprotonation with LDA (1.2 equiv, −78 °C, 2 h), followed by trapping with TMSCl. This silyl intermediate (**11**) was smoothly chlorinated by the method of Fraser,[17] using C_2Cl_6 and CsF in acetonitrile (reflux, 3 h), affording the chloromethyl derivative (**10c**) in 62% yield (Scheme 3).

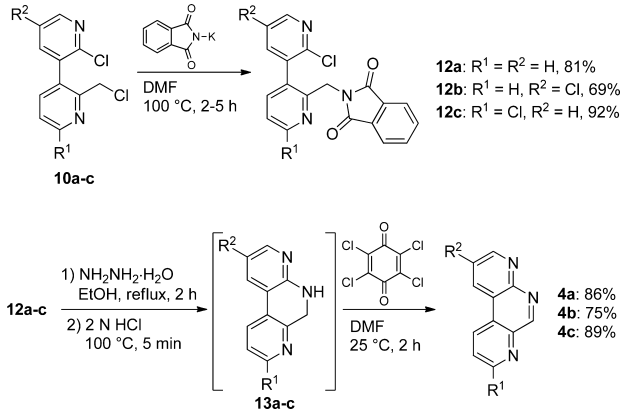
Scheme 3. Chlorination of the Picolyl Derivatives (6a–c)



Gabriel reaction using potassium phthalimide (DMF, 100 °C, 2–5 h) provided the phthalimides (**12a–c**) in 69–92% yield.[15] To our delight, deprotection of the phthalimides (**12a–c**) using hydrazine hydrate in ethanol gave aminomethyl intermediates of type **5**, which underwent a spontaneous ring closure under the reaction conditions, providing the dihydrotriazaphenanthrenes (**13a–c**). Treatment with chloranil in DMF (25 °C, 2 h) led to the aromatized target molecules (**4a–c**) in 75–89% yield; Scheme 4.

Having these new *N*-heterocycles in hand, we studied their functionalization.[18] However, metalations using various TMP-bases (TMPLi, $TMP_2Mg·2LiCl$, TMPMgCl·LiCl, $TMP_2Zn·2LiCl$, TMPZnCl·LiCl)[19] or additions of organomagnesium compounds led to complex mixtures. In contrast, the treatment of **4a** with a range of organolithium reagents at −60 °C for 0.5 h led to smooth addition, and after rearomatization with chloranil (DMF, 25 °C), the functionalized triazaphenanthrenes (**4d–m**) were obtained in 34–93% yield (Table 1). A range of aryllithium reagents (**14a–d**) bearing electron-donating (**14b**) and withdrawing groups (**14c–d**) reacted well with **4a**, leading to the azaphenanthrenes (**4d–g**) in 62–93% yields after rearomatization (entries 1–4). Also, heterocyclic lithium derivatives smoothly added to the pyridonaphthyridine (**4a**). Thus, 2-lithiofuran (**14e**), 2-lithiothiophene (**14f**), as well as 2-lithiobenzofuran (**14g**) and 2-lithiobenzothiophene (**14h**) led to azaphenanthrenes (**4h–k**) in 32–80% yield (entries 5–8). Interestingly, 1-lithio-1-ethoxyethene[20] (**14i**) reacted well with **4a** under these reaction conditions, and the keto-azaphenanthrene derivative (**4l**) was produced in 90% yield (entry 9). Surprisingly, alkyllithium reagents such as *n*-BuLi (**14j**) underwent a similar addition on the azaphenanthrene core without concurrent metalation, affording the butyl-substituted azaphenanthrene (**4m**) in 76% yield (entry 10).

Scheme 4. Gabriel Substitution and Corresponding Deprotection Leading to the Azaphenanthrenes (4a–c)



We noted that depending on the substituent the color of the new pyridonaphthyridines ranges from almost colorless (**4a**, **4d**) to intense yellow (**4k**). As the observable optical transitions allow for insights into the electronic structure and are of key importance for a potential application of the newly synthesized materials as dyes or molecular semiconductors, we analyzed the optical properties using steady-state and time-resolved spectroscopic methods.

The UV–vis spectra of **4a**, **4d**, and **4h–k** exhibit a distinct vibrational fine structure with a double-peak close to the absorption edge (Figure 2a and SI, Figure S1). These spectral features are sharpest for the particularly rigid molecules **4a**, **4h**, and **4j** and appear more broadened for the thiophene-containing compounds **4i** and **4k**. The overall shape of the spectra close to the absorption edge, however, is very similar among all six compounds, indicating a similar electronic structure close to the frontier molecular orbitals. While the bare azaphenanthrene **4a** absorbs light only at wavelengths below 350 nm, the absorption onset of the substituted pyridonaphthyridines is red-shifted as the conjugated π-system is extended.

Upon photoexcitation with UV light the compounds emit strongly in the 400–450 nm range (Figure 2b and SI, Figure S2). While the emission maximum seems almost not affected by the selection of the substituent, the photoluminescence quantum yield (PLQY) reveals differences between the differently substituted compounds. The highest PLQY of 23% was observed for **4d** (SI, Table S1). Also, the furan-containing **4h** and **4j** exhibit decent quantum yields of above 10%, whereas the thiophene-based analogues **4i** and **4k** show only moderate PLQYs. Systematically lower quantum yields for sulfur-containing heterocycles compared to their oxygen analogues have also been observed for quinoxaline derivatives.[21] These differences might result from a competing nonradiative deactivation

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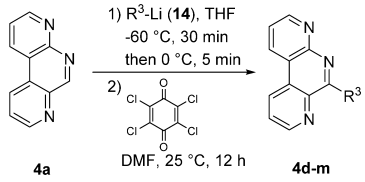
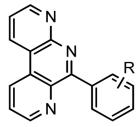
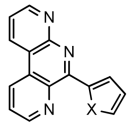
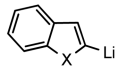
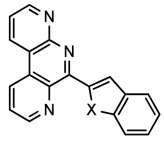
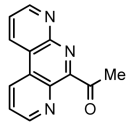
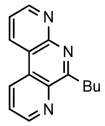
Table 1. Functionalization of Azaphenanthrene (4a) with Organolithium Reagents of Type 14 Leading to Substituted Pyridonaphthyridines (4d–m)



entry	organolithium reagent	product[a]
		
1	**14a**: R = H	**4d**: R = H, 93%
2	**14b**: R = *p*-OMe	**4e**: R = *p*-OMe, 87%
3	**14c**: R = *p*-CF_3	**4f**: R = *p*-CF_3, 68%
4	**14d**: R = *m*-F	**4g**: R = *m*-F, 62%
		
5	**14e**: X = O	**4h**: 80%
6	**14f**: X = S	**4i**: 46%
		
7	**14g**: X = O	**4j**: 32%
8	**14h**: X = S	**4k**: 51%
		
9	14i	**4l**: 90%
	BuLi	
10	14j	**4m**: 76%

[a]Isolated yields after purification by flash column chromatography.

mechanism that is more pronounced for the sulfur-containing heterocycles.

In order to analyze these differences in more detail, we studied the PL decay of the furan- and thiophene-containing compounds via time-correlated single photon counting (TCSPC) experiments. All four materials exhibit biexponential decay curves with the lifetimes being significantly longer for the furan compounds (Figure 2c,d and SI, Figure S3). In particular, the shorter-lived decay component τ_1 was found to be about double compared to the thiophene analogues. This observation further supports the existence of a competing decay mechanism that is more dominant for the thiophene compounds.

In conclusion, we have developed a short 4-step synthesis of triazaphenanthrenes and have shown that these heterocycles

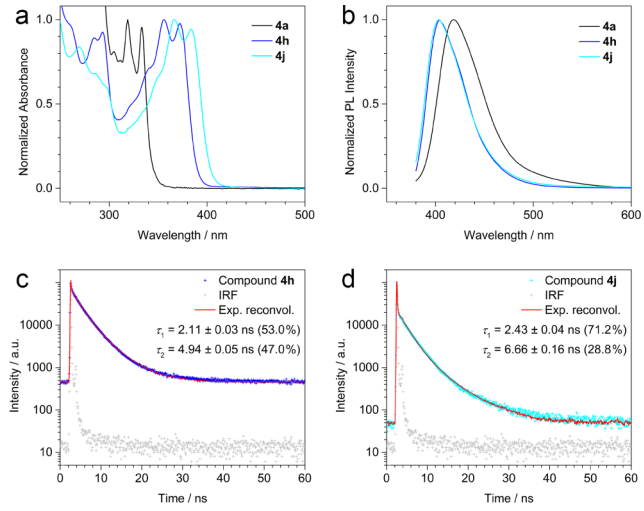


Figure 2. (a) Optical absorption spectra of the parent azaphenanthrene **4a** and the furan- and benzofuran-substituted compounds **4h** and **4j**. For clarity the spectra were normalized to the low-energy double peak absorption feature. (b) The corresponding photoluminescence (PL) spectra measured with 300 nm (**4a**) and 365 nm excitation (**4h, j**). (c,d) Time-correlated single photon counting (TCSPC) traces of **4h** and **4j**, respectively. The instrument response function is displayed in gray.

undergo smooth addition-rearomatization at position 6 with various lithium reagents. The optical properties of these molecules can be tuned via the selection of the substituent. Strongly fluorescent molecules with long excited state lifetimes were obtained for furan-substituted derivatives, whereas the incorporation of a thienyl moiety resulted in an extended absorption range.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01373.

Detailed experimental procedures and characterization data for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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