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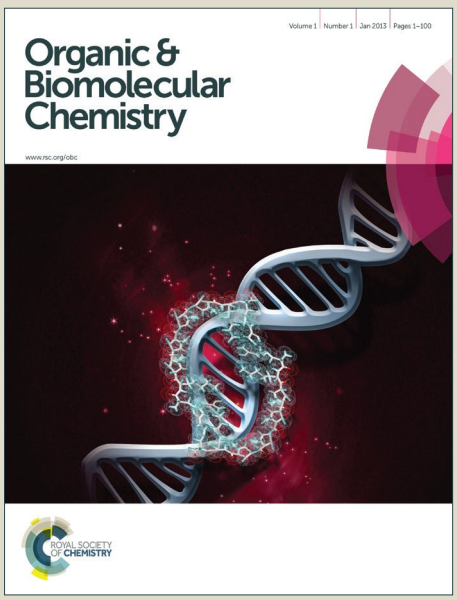





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# Straightforward Synthesis of Tetraalkynylpyrazines and Their Photophysical Properties

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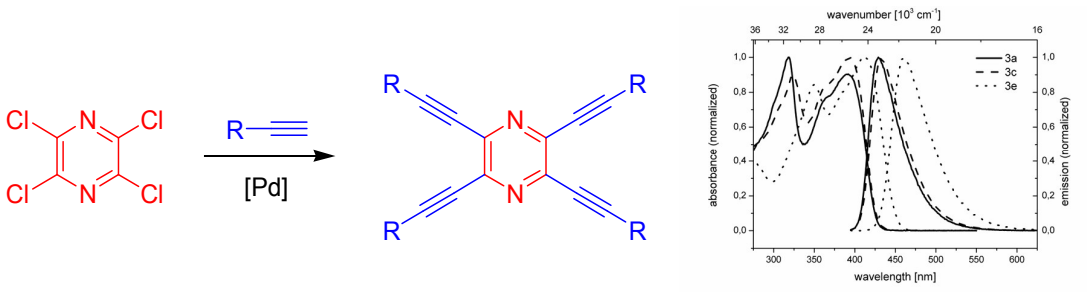
**Abstract:** Tetrafold Sonogashira reactions of tetrachloropyrazine were investigated to provide a one-step synthesis of various tetraalkynylpyrazines. The reaction conditions were thoroughly optimized using modern catalysts and ligands, and products were generally isolated in good to excellent yields. Furthermore, photophysical and electrochemical properties of selected compounds were studied and compared with those of previously reported tetraalkynylpyridines and –benzenes. As a matter of fact, tetraalkynylpyrazines proved to show very promising fluorescence properties due to very high quantum yields reaching up to 0.85.

**Key words:** pyrazines; heterocycles; cross-coupling reactions; palladium, quantum yield; fluorescence; catalysis; electrochemistry

## Graphical Abstract




## Introduction

In the last two decades palladium-catalysed cross-couplings have grown into an indispensable tool for the construction of $C_{sp}^2$-$C_{sp}^2$ or $C_{sp}^2$–$C_{sp}$ bonds in organic synthesis. The importance of this reaction was highlighted by awarding the Nobel price to Heck, Suzuki and Negishi in 2010.[1]

In particular, the Sonogashira reaction is undoubtedly the most prominent pathway for the alkynylation of $sp^2$-carbon atoms. Currently, the Sonogashira reaction is applied in all fields of organic synthesis ranging from natural product synthesis to material science.[2]

Pyrazines are found in several natural products.[3] Examples include the botrillazines A and B,[4] cephalostatines[5] or ritterazines,[6] which are alkaloids with strong cytotoxic and cancerostatic activity. Furthermore, several synthetic alkynylated pyrazines possess considerable activity against various tumor cell lines.[7]

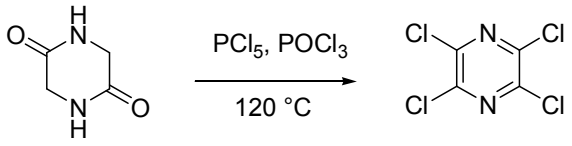
Alkynylated *N*-heterocycles such as pyridines and pyrazines are of interest in materials science due to their optical and electronic features.[8] Moreover, polyalkynylated carbon-rich molecules were found to serve as discotic liquid crystals,[9] nonlinear optical materials[10] and as scaffolds for dendritic molecules.[11]

Recently, we disclosed our studies on the synthesis of tetraarylpyrazines starting from tetrachloropyridine.[12] We also described the synthesis of polyalkynylated heterocycles and benzenes from the corresponding polyhalogenated starting materials using the Sonogashira reaction.[13] Polyalkynylated pyridines with corresponding benzene derivatives show greatly

improved optical properties (extinction coefficient, quantum yield) by substitution of one carbon atom by nitrogen in the central aryl ring.[13d]

Herein we disclose our results for the synthesis of tetraalkynylpyrazines starting from tetrachloropyrazine. Moreover, we studied the influence of an additional nitrogen atom in the central aryl moiety on the photophysical properties compared to corresponding pyridine and benzene derivatives.

Tetrachloropyrazine (**2**) was prepared according to a known procedure[14] by reaction of 2,5-dioxopiperazine (**1**) with $PCl_5$ and $POCl_3$ (Scheme 1).




**1** **2**

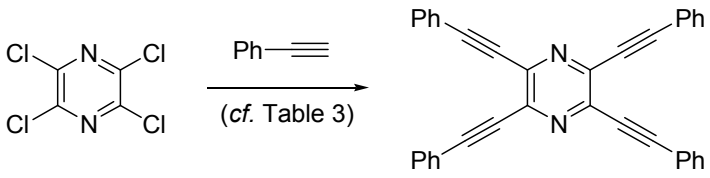
**Scheme 1.** Synthesis of tetrachloropyrazine **2**.

## Results and Discussion

**Synthesis.** The synthesis of tetraalkynylpyrazines from tetrachloropyrazine has not been reported in the literature so far. Therefore, it was of special interest to study tetrafold Sonogashira coupling reactions of tetrachloropyrazine. Nonetheless, it has to be mentioned that a similar approach was applied by Haley and co-workers to provide different tetrakis(arylethynyl)benzenes. Along with that, a single example of tetraalkynylated pyrazine was synthesized using tetrabromopyrazine as starting material.[8d]

To identify the best conditions for the reaction of **2** with phenylacetylene a thorough optimization was carried out (Scheme 2, Table 1). The application of simple palladium catalysts like $Pd(PPh_3)_4$ and $PdCl_2(PPh_2)$ provided poor yields (Table 1, entry 1-2). The best yield (84%) of tetraalkynylpyrazine **3a** was obtained when $PdCl_2(CH_3CN)_2$ and X-Phos[15] was used as the catalyst and ligand and when diisopropylamine was used as the base (Table 1, entry 8, Figure 1). The optimal amounts of catalyst and ligand were found to be 3 mol% and 6 mol%, respectively. Further lowering of the catalyst loading led to a significant decrease of the yield. In all reactions, CuI (5 mol%) was used as the co-catalyst. Interestingly, a

reasonable yield was obtained when the reaction was carried out in the absence of CuI (entry 10). All reactions were carried out in 1,4-dioxane at 100 °C (20 h).



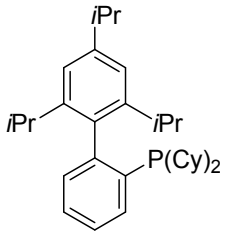

**2** **3a**

**Scheme 2.** Optimization of the synthesis of **3a**.

**Table 1.** Optimization of the synthesis of **3a**.

| Entry | Catalyst and ligand ([mol%]) | Co-catalyst ([mol%]) | Ph—≡ [equiv.] | Base | Yield [%] [a] |
|---|---|---|---|---|---|
| 1 | $Pd(PPh_3)_4$ (5) | CuI (5) | 8 | $HN(iPr)_2$ | 14 |
| 2 | $PdCl_2(PPh_3)_2$ (5) | CuI (5) | 8 | $HN(iPr)_2$ | 39 |
| 3 | $PdCl_2(CH_3CN)_2$ (5) X-Phos (10) | CuI (5) | 8 | $HN(iPr)_2$ | 75 |
| 4 | $PdCl_2(CH_3CN)_2$ (5) CataCXium A (10) | CuI (5) | 8 | $HN(iPr)_2$ | 64 |
| 5 | $PdCl_2(CH_3CN)_2$ (5) $[(t\text{-}Bu)_3PH]BF_4$ (10) | CuI (5) | 8 | $HN(iPr)_2$ | 68 |
| 6 | $PdCl_2(CH_3CN)_2$ (5) X-Phos (10) | CuI (5) | 6 | $HN(iPr)_2$ | 88 |
| 7 | $PdCl_2(CH_3CN)_2$ (5) X-Phos (10) | CuI (5) | 6 | $NEt_3$ | 74 |
| 8 | $PdCl_2(CH_3CN)_2$ (3) X-Phos (6) | CuI (5) | 6 | $HN(iPr)_2$ | 84 |
| 9 | $PdCl_2(CH_3CN)_2$ (1) X-Phos (2) | CuI (5) | 6 | $HN(iPr)_2$ | 44 |
| 10 | $PdCl_2(CH_3CN)_2$ (3) X-Phos (6) | - | 6 | $HN(iPr)_2$ | 65 |

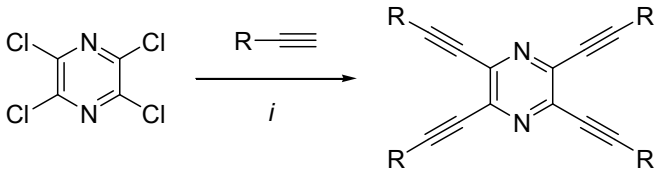
[a] Yields of isolated products.




X-Phos

**Figure 1.** Structure of X-Phos.

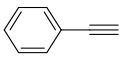
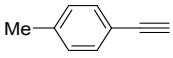
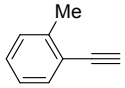
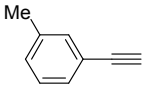
The reaction of **2** with various alkynes, using our optimized conditions, mainly afforded desired tetraalkynylpyrazines in good to very good yields (Scheme 3, Table 2). Products **3f** and **3k** were also formed but could not be isolated in pure form due to solubility problems. The moderate yield of **3d** can be explained by separation problems during the chromatographic purification.

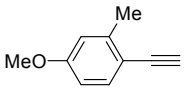
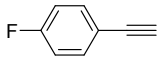
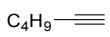
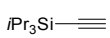
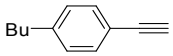
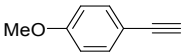
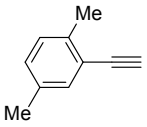
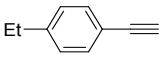
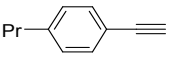



**2** **3a-n**

**Scheme 3.** Synthesis of **3a-n**; conditions: *i*: **2**, alkyne, $PdCl_2(CH_3CN)_2$ (3 mol%), X-Phos (6 mol%), CuI (5 mol%), $HN(iPr)_2$, 1,4-dioxane, 100 °C, 20 h.

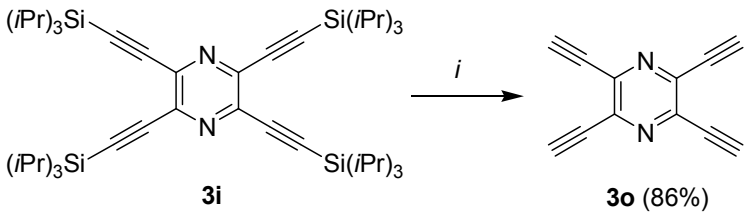
**Table 2.** Synthesis of **3a-n**.

| **3** | Alkyne | Yield[a] [%] |
|---|---|---|
| **a** |  | 84 |
| **b** |  | 83 |
| **c** |  | 82 |
| **d** |  | 60 |

| | | |
|---|---|---|
| **e** |  | 50 |
| **f** |  | 0 [b] |
| **g** |  | 88 |
| **h** |  | 44 |
| **i** |  | 78 |
| **j** |  | 60 |
| **k** |  | 0 [b] |
| **l** |  | 79 |
| **m** |  | 61 |
| **n** |  | 49 |

[a] Yields of isolated products; [b] product was formed but could not be isolated in pure form due to solubility problems.

Treatment of silylated derivative **3i** with TBAF afforded parent 2,3,5,6-tetraethynylpyrazine (**3o**) in 86% yield (Scheme 4). This product tends to be unstable in the air[16] but can be stored under argon atmosphere at low temperature.

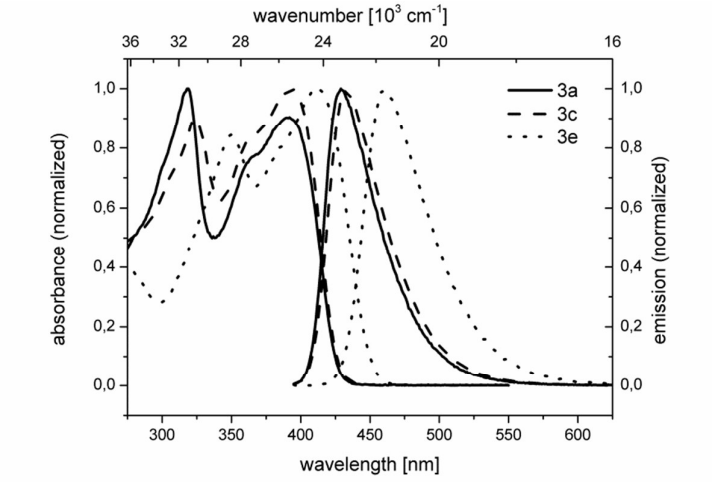



**Scheme 4.** Synthesis of **3o**; *conditions*: *i*: TBAF, THF, 0→20 °C, 2 h.

Initial attempts to introduce selectively one or two alkynyl substituents failed because of the fact that the reactivity of the molecule is increased in the course of the alkynylation. This

observation we already have made earlier in the case of the polyalkynylation of other heterocycles.[13d] Currently, we try to address this problem by the use of pyrazines containing different leaving groups.

**Photophysical properties.** As we observed strong blue fluorescence of our isolated products, we studied the steady-state absorbtion and fluorescence properties of selected alkynylpyrazines **3a-3e**. Normalized absorption and fluorescence spectra, meassured in $CH_2Cl_2$, are shown in Figure 2. All absorption spectra consist of two conspicuous transitions between 318 nm – 349 nm and 390 nm – 412 nm, respectively. Fluorescence spectra show one typical maximum in the range of 429 nm to 461 nm.



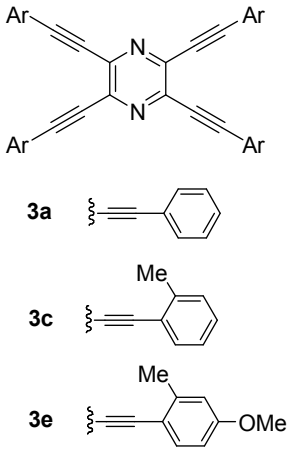




**Figure 2.** Normalized absorption and corrected emission spectra of compounds **3a**, **3c** and **3e** in $CH_2Cl_2$.

Functionalisation of the phenylethynyl moiety by a σ-donating methyl group led to a marginal bathochromic shift of the absorption- and fluorescence spectra. Compound **3e**, containing an additional π-donating methoxy substituent in *para*-position gave a more intense redshift in the absorption- and fluorescence spectrum compared to the unsubstituted derivative **3a** (Figure 2, Table 3).

To gain insights into the impact of an additional nitrogen atom in the central aryl ring, we compared the absorption and fluorescence spectra of pyrazine **3a** with its benzene- and pyridine[17] analogs **4** and **5** (Figure 3, Table 3). Whereas the first transitions in the absorption spectra of **3a**, **4** and **5** have approximatly the same $\lambda_{max}$ values, the second transition at higher wavelengths shifts with the number of nitrogen atoms in the central aryl ring to higher

wavelengths. However, the absorption coefficients of the first transition are almost half of that of its corresponding pyridine and benzene derivatives, while for the second transition they are roughly the same. The fluorescence spectra are bathochromically shifted with an increasing number of nitrogen atoms incorporated in the central aryl ring. The quantum yields of synthesized alkynylpyrazine **3a** is about 50 % higher compared to the analog pyridine **4** and benzene **5** derivatives. Moreover, the quantum yields are only slightly effected by the studied substitution pattern (Table 3).

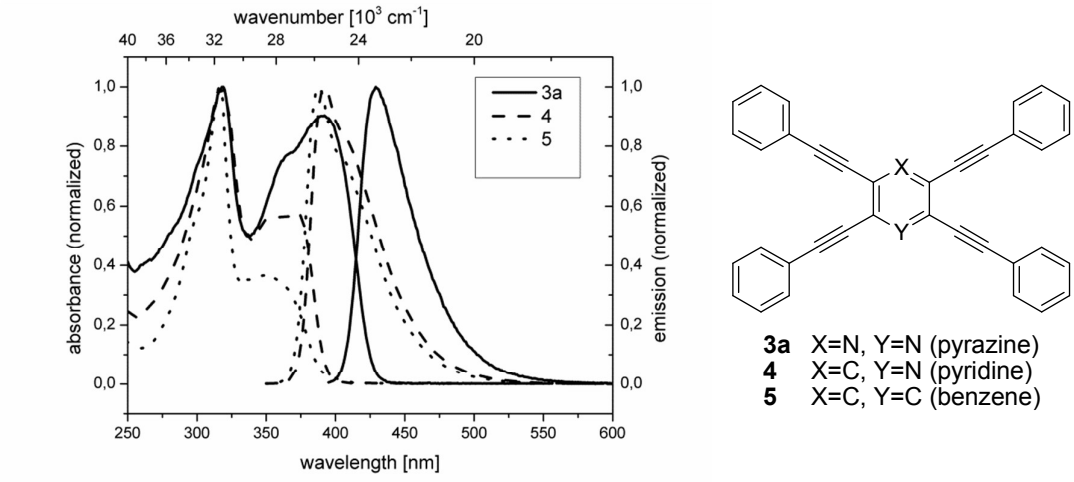


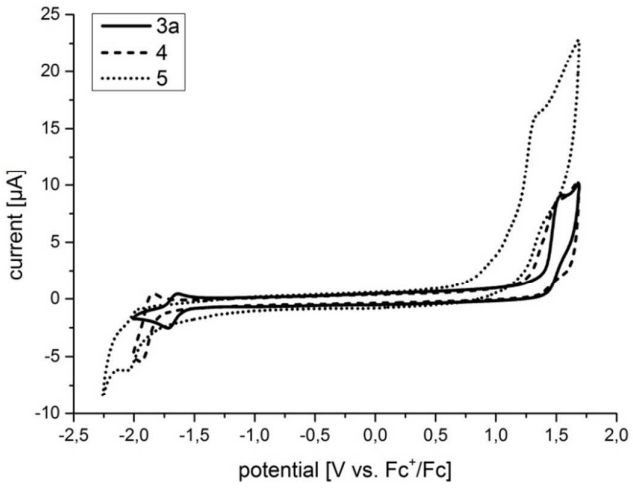

**Figure 3.** Comparison of absorption and fluorescence spectra of tetrakis(phenylethynyl)pyrazine **3a** with corresponding pyridine and benzene derivatives **4** and **5**, respectively.

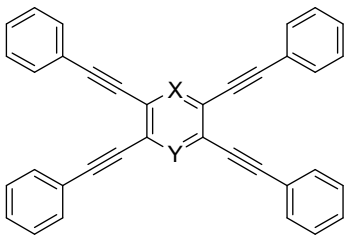
**Table 3.** Photophysical properties of compounds **3a-e**, **4** and **5** in $CH_2Cl_2$.

| Compd | $\lambda_{abs}(\varepsilon_{abs})$ [nm] ([$10^4$ $M^{-1}cm^{-1}$]) | $\tilde{\nu}_{Stokes}$ [$cm^{-1}$] | $\lambda_{max}^{fluo}$ [nm] | $\phi_{fluo}$ Quantum yield[18] | $\tilde{\nu}_{00}$ [$cm^{-1}$] | $E_{opt.}$ [eV] |
|---|---|---|---|---|---|---|
| **3a** | 318 (5.41)<br>390 (4.84) | 2330 | 429 | 0.81 | 24084 | 2.98 |
| **3b** | 328 (5.8)<br>398 (5.5) | 2350 | 439 | 0.83 | 23596 | 2.92 |
| **3c** | 324 (4.24)<br>393 (4.76) | 2350 | 433 | 0.77 | 24009 | 2.97 |
| **3d** | 323 (5.4)<br>394 (5.1) | 2290 | 433 | 0.85 | 23923 | 2.96 |
| **3e** | 349 (4.90)<br>412 (5.80) | 2580 | 461 | 0.79 | 22732 | 2.81 |
| **4** | 317 (10.0)<br>353 (5.7) | 1520 | 392 | 0.42 | 26116 | 3.23 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **5** | 370 (5.8)<br>317 (12.6)<br>347 (4.5) | 3050 | 388 | 0.45 | 26462 | 3.28 |

**Electrochemical studies.** Electrochemistry was used to validate the photophysical results and to confirm the substituent effects. The cyclic voltammograms of the compounds **3a**, **4** and **5** are depicted in Figure 4. Table 4 summarizes all determinable peak potentials for all investigated substrates. In every case we found two redox events. An oxidation of the compounds occured at positive potentials higher than 1.5 V [vs. Ag/AgCl/$LiCl_{sat.}$ in EtOH] and is electrochemically non-reversible. Therefore the corresponding reduction potentials are missing in Table 4. The second redox event, an electrochemically reversible process, was observed at negative potentials below -0.5 V [vs. Ag/AgCl/$LiCl_{sat.}$ in EtOH]. With the knowledge of these potentials it was possible to calculate the HOMO and LUMO levels of the respective compound[19] (Table 4). Instead of the standard electrode potentials or onset potentials the peak potentials of the oxidation event 1 ($E_{peak}^{1-ox}$) and the reduction event 2 ($E_{peak}^{2-red}$) have been used for the calculation of the HOMO level (ionization potential; IP) and the LUMO level (electron affinity, EA) by application applying the equations $IP = E_{peak}^{1-ox} + 4.4$ eV and $EA = E_{peak}^{2-red} + 4.4$ eV,[20] respectively. The electrochemical band gaps could be estimated with the formula $E_{EC} = IP - EA$.[19] These are somewhat larger than the band gaps obtained by optical spectroscopy which correspond to the point of intersection of the normalized absorption and fluorescence spectra. Nevertheless, we found a similar relationship between the structure and the band gap.




**3a** X=N, Y=N (pyrazine)
**4** X=C, Y=N (pyridine)
**5** X=C, Y=C (benzene)

**Figure 4.** Cyclic voltammograms of tetrakis(phenylethynyl)pyrazine **3a** with corresponding pyridine and benzene derivatives **4** and **5**, respectively.

**Table 4.** Redox properties of compounds **3a-e**, **4** and **5** in acetonitrile.

| Compd | $E_{opt.}$ [eV] | $E_{peak}^{1-ox}$ [V vs. Ag/AgCl] | $E_{peak}^{1-ox}$ [V vs. NHE] | IP [eV] | $E_{peak}^{2-red}$ [V vs. Ag/AgCl] | $E_{peak}^{2-red}$ [V vs. NHE] | $E_{peak}^{2-ox}$ [V vs. Ag/AgCl] | $E_{peak}^{2-ox}$ [V vs. NHE] | EA [eV] | $E_{EC}$ [eV] |
|---|---|---|---|---|---|---|---|---|---|---|
| **3a** | 2.98 | 2.05 | 2.19 | 6.63 | -1.21 | -1.06 | -1.13 | -0,99 | 3.38 | 3.25 |
| **3b** | 2.92 | 2.04 | 2.18 | 6.62 | -1.21 | -1.06 | -1.14 | -1.00 | 3.38 | 3.24 |
| **3c** | 2.97 | 1.98 | 2.13 | 6.57 | -1.25 | -1.10 | -1.17 | -1.03 | 3.34 | 3.23 |
| **3d** | 2.96 | 1.97 | 2.12 | 6.56 | -1.19 | -1.05 | -1.11 | -0.97 | 3.39 | 3.17 |
| **3e** | 2.81 | 2.02 | 2.16 | 6.60 | -0.82 | -0.68 | -0.72 | -0.58 | 3.76 | 2.84 |
| **4** | 3.23 | 2.03 | 2.17 | 6.61 | -1.43 | -1.29 | -1.33 | -1.19 | 3.15 | 3.46 |
| **5** | 3.28 | 1.84 | 1.98 | 6.42 | -1.53 | -1.39 | -1.47 | -1.33 | 3.05 | 3.37 |

In conclusion, we have elaborated a facile and efficient procedure for the synthesis of tetraalkynylpyrazines by multiple Sonogashira reactions. The tetra-fold coupling reaction requires only 3 mol% of palladium catalyst which represents less than 1 mol% for each coupling step. Furthermore, photophysical and electrochemical properties of tetraalkynylpyrazines were studied and compared with their appropriate pyridine and benzene counterparts. The synthesized alkynylpyrazines possess high quantum yields which make them interesting building blocks for optoelectronic applications. The emission wavelength (fluorescence) can be finetuned by the choice of substituents as the central pyrazine core communicates electronically with the aryl groups in the periphery via the alkynyl groups. It was shown that introduction of a nitrogen atom into the central aromatic ring of the tetraalkynylated arene dramatically increases the quantum yield of the molecule. In fact, the quantum yields of the tetraalkynylpyrazines are considerably higher than those of all tetraalkynylated pyridines and benzens studied previously. This can be explained by the push-pull character of the molecules. A similar structure-activity relationship was also found with electrochemical methods. HOMO and LUMO levels as well as the electrochemical band gaps could be calculated from CV measurements. The band gaps have been found to be comparable to those obtained by optical spectroscopy. The electrochemically reversible reduction event is related to the nitrogen atom in the central aromatic ring. An increasing number of nitrogen atoms leads to more positive reduction potentials and thus to higher LUMO levels.

## Experimental Section

**General.** All reactions were carried out under argon atmosphere. All chemicals are commercially available and were used without further purification. Column chromatography was performed using Merck Silicagel 60 (0.043 - 0.06 mm). NMR data were recorded on Bruker ARX 300, Bruker ARX 400 and Fourier 300 spectrometers. $^{13}C$ and $^{1}H$ NMR spectra were referenced to signals of deuterated solvent and residual protonated solvent, respectively. Peak characterization: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, bs = broad singlet, dd = doublet of doublet. Infrared Spectra were recorded on a Nicolet 550 FT – IR spectrometer with ATR sampling technique for solids as well as liquids. Signal characterization: w = weak, m = medium, s = strong. Gas chromatography-mass analyses were carried out on an Agilent HP-5890 instrument with an Agilent HP-5973 Mass Selective Detector (EI) and a HP-5 capillary column using helium carrier gas. ESI HR-MS measurements were performed on an Agilent 1969A TOF mass spectrometer. For high resolution MS (HRMS) a Finnigan MAT 95 XP was used. Only the measurements with an average deviation from the theoretical mass of ± 2mDa were accounted as correct. Elemental analyses (EA) were performed with a LecoMikroanalysator - TrueSpec CHNS Micro. Melting points were determined on a Micro-Hot-Stage GalenTM III Cambridge Instruments, and are not corrected. X-ray crystal structure data were collected on a STOE IPDS II diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares procedures on $F^2$ with the SHELXTL software package.[21] Absorption spectra were measured on an Analytik Jena Specord 50 or Perkin-Elmer UV/Vis spectrometer Lambda2. The fluorescence spectra were recorded with a Fluoromax-4 Spectrofluorometer (Horiba Scientific). For the absorption spectra dichloromethane was used as solvent and a concentration of $5 \times 10^{-6}$ M was applied for the quantitative determination of molar extinction coefficients. A solution of quinine sulphate in 0.05 M sulphuric acid was applied as standard for the measurement of the fluorescence quantum yields ($\phi_f = 0.52$). Air-equilibrated solutions of the sample and standard with an absorbance of ~ 0.1 at the excitation wavelength were used in the fluorescence measurements. All electrochemical studies were performed at room temperature in dried acetonitrile p.A. (VWR) under an Argon atmosphere with 0.1 M tetrabutylammonium hexafluorophosphate (Fluka) as conducting salt using an Autolab

(PGSTAT 302N, Metrohm). A glassy carbon disk electrode (d=2 mm) was used as working electrode, a Pt-electrode as the counter electrode and an Ag/ AgCl/ $LiCl_{sat.}$ in EtOH-system as the reference electrode (all electrodes: Metrohm). All potentials mentioned in this paper were measured with respect to this reference system and were checked by using the ferrocenium/ ferrocene-internal reference system (potential of $Fc^+/Fc$: 0.51 V [vs. Ag/AgCl/$LiCl_{sat.}$ in EtOH]. The CV scans were done three times at a scan rate of 40 $mVs^{-1}$. The measurements were performed with 2 mM compound dissolved in the electrolyte.

**Synthesis of tetraalkynylpyrazines 3a-n.**

An argon-flushed glass pressure tube was charged with 2.3 mg of $PdCl_2(CH_3CN)_2$ (0.009 mmol, 3 mol%), 8.6 mg of X-Phos (0.018mmol, 6 mol%), 2.8 mg of CuI (0.015 mmol, 5mol%) and **2** (65.4 mg, 0.3mmol), followed by the addition of anhydrous 1,4-dioxane (4 mL), 0.5 mL of $HN(iPr)_2$ and appropriate alkyne (1.8 mmol, 6 equiv.). The tube was sealed with a teflon cap and the reaction mixture was stirred at 100 °C for 20 hours. The resulting mixture was cooled down to room temperature, diluted with water and extracted with dichloromethane. The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was evaporated. The crude residue was purified by column chromatography on silica gel using mixture of hexane and dichloromethane as eluent. Obtained solid compounds were additionally washed with cold hexane to give pure products

**2,3,5,6-Tetrakis(phenylethynyl)pyrazine (3a):**

According to the general procedure, compound **3a** was isolated as a dark yellow solid (121 mg, 84 %); mp. = 221 – 223 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 7.34 - 7.45 (m, 12H), 7.62 - 7.67 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 86.0 (C≡C), 97.7, 121.6 (C), 128.5, 129.8, 132.2 (CH), 139.0 (C). MS (EI, 70 eV): m/z (%) = 480 ($M^+$, 100), 226 (47), 127 (3). HRMS (EI, 70 eV): calcd. for $C_{36}H_{20}N_2$: 480.16210; found: 480.16222. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 3052 (w), 2208 (m), 1489 (m), 1385 (m), 1164 (m), 1138 (m), 746 (s), 680 (s), 529 (s), 486 (m).

**2,3,5,6-Tetrakis(*p*-tolylethynyl)pyrazine (3b):**

According to the general procedure, compound **3b** was isolated as a dark yellow solid (134 mg, 83 %); mp. = 296 – 298 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 12H, $CH_3$), 7.16 - 7.19 (m, 8H), 7.51 - 7.55 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 21.6 ($CH_3$), 85.8,

97.9 (C≡C), 118.6 (C), 129.3, 132.1 (CH), 138.9, 140.2 (C). MS (EI, 70 eV): m/z (%) = 536 ($M^+$, 100), 268 (3), 254 (26), 239 (3), 44 (6). HRMS (EI, 70 eV): calcd. for $C_{40}H_{28}N_2$: 536.22470; found: 536.22606. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2910 (w), 2195 (m), 1508 (m), 1374 (m), 1157 (m), 807 (s), 527 (s), 417 (m).

**2,3,5,6-Tetrakis(*o*-tolylethynyl)pyrazine (3c):**

According to the general procedure, compound **3c** was isolated as a yellow solid (132 mg, 82 %); mp. = 214 – 216 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 2.49 (s, 12H, $CH_3$), 7.13 - 7.31 (m, 12H), 7.57 (dd, 4H, $^3J$ = 7.7 Hz, $^4J$ = 1.3 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 20.8 ($CH_3$), 89.7, 96.4 (C≡C), 121.4 (C), 125.6, 129.6, 129.7, 132.7 (CH), 138.9, 141.2 (C). MS (EI, 70 eV): m/z (%) = 536 ($M^+$, 100), 521 (7), 268 (8), 252 (93), 239 (11), 140 (8), 115 (11). HRMS (EI, 70 eV): calcd. for $C_{40}H_{28}N_2$: 536.22470; found: 536.22429. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2943 (w), 2200 (m), 1485 (m), 1454 (m), 1375 (m), 1147 (m), 755 (s), 713 (m), 491 (m).

**2,3,5,6-Tetrakis(*m*-tolylethynyl)pyrazine (3d):**

According to the general procedure, compound **3d** was isolated as a dark yellow solid (96 mg, 60 %); mp. = 201 – 203 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 12H, $CH_3$), 7.20 - 7.29 (m, 8H), 7.44 - 7.48 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 21.1 ($CH_3$), 85.9, 98.0 (C≡C), 121.4 (C), 128.4, 129.3, 130.7, 132.8 (CH), 138.2, 139.1 (C). MS (EI, 70 eV): m/z (%) = 536 ($M^+$, 100), 254 (28), 69 (5), 44 (13). HRMS (ESI): calcd. for $C_{48}H_{28}N_2$ ($[M+H]^+$): 537.23253; found: 537.23248. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2917 (w), 2197 (m), 1483 (m), 1380 (m), 1153 (m), 773 (s), 682 (s), 496 (s).

**2,3,5,6-Tetrakis((4-methoxy-2-methylphenyl)ethynyl)pyrazine (3e):**

According to the general procedure, compound **3e** was isolated as a dark yellow solid (116 mg, 60 %); mp. = 220 – 221 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 2.46 (s, 12H, $CH_3$), 3.80 (s, 12H, $OCH_3$), 6.68 - 6.74 (m, 8H), 7.49 (d, 4H, $^3J$ = 8.4 Hz). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 21.1 ($CH_3$), 55.2 ($OCH_3$), 89.1, 96.5 (C≡C), 111.4 (CH), 113.8 (C), 115.1, 134.2 (CH), 138.7, 143.2, 160.5 (C). MS (EI, 70 eV): m/z (%) = 656 ($M^+$, 100), 641 (4), 569 (3), 328 (3), 226 (3), 84 (3), 66 (3), 44 (6). HRMS (EI, 70 eV): calcd. for

$C_{44}H_{36}N_2O_4$: 656.26696; found: 656.26471. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2931 (w), 2837 (w), 2195 (m), 1602 (m), 1565 (m), 1494 (m), 1280 (m), 1242 (m), 1115 (m), 1040 (m), 865 (s), 807 (s), 500 (s).

**2,3,5,6-Tetrakis((4-(*tert*-butyl)phenyl)ethynyl)pyrazine (3g):**

According to the general procedure, compound **3g** was isolated as a dark yellow solid (186 mg, 88 %); mp. = 282 – 284 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 36H, $CH_3$), 7.38 - 7.42 (m, 8H), 7.57 - 7.61 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 31.0 ($CH_3$), 34.9 ($C_{t\text{-Bu}}$), 85.8, 97.9 (C≡C), 118.6 (C), 125.5, 132.0 (CH), 138.9, 153.2 (C).MS (EI, 70 eV): m/z (%) = 704 ($M^+$, 100), 690 (4), 456 (6), 337 (8). HRMS (ESI): calcd. for $C_{52}H_{53}N_2$ ($[M+H]^+$): 705.42033; found: 705.4202. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2956 (m), 2863 (w), 2206 (m), 1503 (m), 1386 (m), 1162 (m), 1104 (m), 828 (s), 557 (s).

**2,3,5,6-Tetra(hex-1-yn-1-yl)pyrazine (3h):**

According to the general procedure, compound **3h** was isolated as a brown oil (53 mg, 44 %). $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, $^3J$ = 7.1 Hz, 12H, $CH_3$), 1.40 - 1.63 (m, 16H, $CH_2$), 2.46 (t, $^3J$ = 6.9 Hz, 8H, $CH_2$). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 13.5 ($CH_3$), 19.3, 21.9, 30.1 ($CH_2$), 77.8, 98.8 (C≡C), 138.6 (C).MS (EI, 70 eV): m/z (%) = 400 ($M^+$, 100), 371 (10), 357 (18), 125 (12), 111 (22), 83 (26), 71 (28), 57 (44). HRMS (EI, 70 eV): calcd. for $C_{28}H_{36}N_2$: 400.28730; found: 400.28703. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2956 (m), 2927 (m), 2961 (w), 2228 (m), 1380 (s), 1160 (m), 496 (m).

**2,3,5,6-Tetrakis((triisopropylsilyl)ethynyl)pyrazine (3i):**

According to the general procedure, compound **3i** was isolated as a light yellow solid (188 mg, 78 %); mp. = 234 – 236 °C. $^1$H NMR (300 MHz, $CDCl_3$): δ = 1.08 - 1.17 (m, 84H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 11.3 (CH), 18.6 ($CH_3$), 101.1, 102.5 (C≡C), 138.0 (C). MS (EI, 70 eV): m/z (%) = 800 ($M^+$, 11), 757 (33), 715 (100), 611 (8), 569 (16). HRMS (EI, 70 eV): calcd. for $C_{48}H_{84}N_2Si_4$: 800.57061; found: 800.57168. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2941 (m), 2864 (m), 1460 (m), 1350 (s), 1157 (m), 997 (m), 881 (s), 767 (m), 678 (s), 655 (s), 580 (m).

**2,3,5,6-Tetrakis((4-butylphenyl)ethynyl)pyrazine (3j):**

According to the general procedure, compound **3j** was isolated as a yellow solid (128 mg, 60 %); mp. = 140 – 142 °C. $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 12H, $^{3}J$ = 7.3 Hz, $CH_3$), 1.29 - 1.41 (m, 8H, $CH_2$), 1.55 - 1.65 (m, 8H, $CH_2$), 2.63 (t, 8H, $^{3}J$ = 7.6 Hz, $CH_2$), 7.16 - 7.20 (m, 8H), 7.53 - 7.57 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 13.8 ($CH_3$), 22.2, 33.2, 35.7 ($CH_2$), 85.8, 97.9 (C≡C), 118.8 (C), 128.6, 132.2 (CH), 138.9, 145.1 (C). MS (EI, 70 eV): m/z (%) = 704 ($M^+$, 100), 619 (14), 352 (7), 295 (13), 267 (17), 252 (12). HRMS (EI, 70 eV): calcd. for $C_{52}H_{52}N_2$: 704.41250; found: 704.41019. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2951 (w), 2926 (m), 2860 (w), 2201 (m), 1509 (m), 1377 (s), 1156 (s), 823 (s), 539 (s). EA: calcd. for $C_{52}H_{52}N_2$ (704.98): C, 88.59; H, 7.43; N, 3.97; found: C, 88.56; H, 7.81; N, 3.90.

**2,3,5,6-Tetrakis((2,5-dimethylphenyl)ethynyl)pyrazine (3l):**

According to the general procedure, compound **3l** was isolated as a yellow solid (140 mg, 79 %); mp. = 237 – 239 °C. $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 12H, $CH_3$), 2.45 (s, 12H, $CH_3$), 7.06 - 7.12 (m, 8H), 7.39 (bs, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 20.3, 20.6 ($CH_3$), 89.5, 96.8 (C≡C), 121.2 (C), 129.4, 130.6, 133.2 (CH), 135.0, 138.1, 139.0 (C). MS (EI, 70 eV): m/z (%) = 592 ($M^+$, 100), 281 (6), 266 (9), 252 (6). HRMS (EI, 70 eV): calcd. for $C_{44}H_{36}N_2$: 592.28730; found: 592.28697. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2916 (w), 2201 (m), 1496 (m), 1367 (m), 1154 (m), 828 (m), 809 (s), 496 (s), 460 (m).

**2,3,5,6-Tetrakis((4-ethylphenyl)ethynyl)pyrazine (3m):**

According to the general procedure, compound **3m** was isolated as yellow solid (108 mg, 61 %); mp. = 206 – 208 °C. $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, 12H, $^{3}J$ = 7.6 Hz, $CH_3$), 2.67 (q, 8H, $^{3}J$ = 7.6 Hz, $CH_2$), 7.18 - 7.22 (m, 8H), 7.54 - 7.58 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 15.2 ($CH_3$), 28.9 ($CH_2$), 85.8, 97.9 (C≡C), 118.8 (C), 128.1, 132.2 (CH), 138.9, 146.4 (C). MS (EI, 70 eV): m/z (%) = 592 ($M^+$, 100), 267 (12), 133 (9), 71 (9), 57 (15), 44 (45). HRMS (EI, 70 eV): calcd. for $C_{44}H_{36}N_2$: 592.28730; found: 592.28613. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2963 (w), 2929 (w), 2870 (w), 2199 (m), 1508 (m), 1379 (m), 1157 (m), 828 (s), 530 (m).

**2,3,5,6-Tetrakis((4-propylphenyl)ethynyl)pyrazine (3n):**

According to the general procedure, compound **3n** was isolated as a yellow solid (95 mg, 49 %); mp. = 189 – 191 °C. $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 0.93 (t, 12H, $^{3}J$ = 7.3 Hz, $CH_3$), 1.58 - 1.71 (m, 8H, $CH_2$), 2.58 - 2.63 (m, 8H, $CH_2$), 7.16 - 7.20 (m, 8H), 7.53 - 7.57 (m, 8H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 13.7 ($CH_3$), 24.2, 38.0 ($CH_2$), 85.8, 97.9 (C≡C), 118.9 (C), 128.7, 132.2 (CH), 138.9, 144.9 (C). MS (EI, 70 eV): m/z (%) = 648 ($M^+$, 100), 281 (11), 252 (6), 66 (6), 44 (17). HRMS (EI, 70 eV): calcd. for $C_{48}H_{44}N_2$: 648.34990; found: 648.34993. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 2956 (w), 2930 (w), 2860 (w), 2201 (m), 1506 (m), 1378 (m), 1157 (m), 839 (m), 797 (m), 541 (s), 492 (m).

**Synthesis of 2,3,5,6-tetrakis(phenylethynyl)pyrazine (3o):**

To a dissolved pyrazine **3i** (200 mg, 0.25 mmol in 6 mL of THF), 2.2 mL of TBAF (1 M in THF, 2.2 mmol) was added at 0°C and stirred for 2h. Afterwards, water was added and the aqueous phase was three times extracted with $Et_2O$. Combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was evaporated. The crude material was purified by column chromatography on silica gel using mixture of hexane and dichloromethane as eluent. Compound **3o** was isolated as a brown solid (38 mg, 86 %). $^{1}$H NMR (300 MHz, $CDCl_3$): δ = 3.60 (s, 4H, C≡CH). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 78.6, 86.0 (C≡C), 139.0 (C). MS (EI, 70 eV): m/z (%) = 176 ($M^+$, 62), 74 (100), 61 (5), 51 (10), 37 (9). HRMS (ESI): calcd. for $C_{12}H_5N_2$ ($[M+H]^+$): 177.04472; found: 177.04475. IR (ATR, $cm^{-1}$): $\tilde{\nu}$ = 3284 (m), 3201 (m), 2105 (m), 1356 (s), 1162 (s), 680 (s), 660 (s), 503 (s).

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