

Multiple Sonogashira Reactions of Polychlorinated Molecules. Synthesis and Photophysical Properties of the First Pentaalkynylpyridines

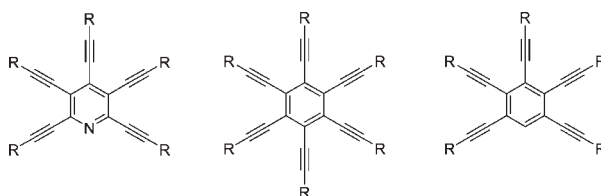
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ABSTRACT



Hitherto unknown pentaalkynylpyridines have been prepared in high yields by Sonogashira cross-coupling reactions of pentachloropyridine. Their photophysical properties were studied and compared to those of penta- and hexaalkynylbenzenes which were efficiently prepared by the first Sonogashira reactions of pentachlorobenzene and hexachlorobenzene. The pentaalkynylpyridines show promising fluorescence properties because of their high quantum yields.

In recent years, much attention has been devoted to polyethynylated carbon-rich molecules, because of their extended conjugated π -systems.¹ Especially polyethynylbenzenes (PEBs) have potential as liquid crystals,² core

structures for dendritic molecules,³ as nonlinear optical materials,⁴ or as building blocks for 2D carbon networks,⁵ which could have a high degree of hardness and thermal stability. Hexaalkynylbenzenes have been prepared by Diels–Alder reactions⁶ and by palladium catalyzed cross-coupling reactions of hexabromobenzene or hexaiodobenzene.⁷ These syntheses have the drawback of long

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reaction times, low yields, and/or undesirable side reactions.⁸

In contrast to benzene derivatives, the synthesis of polyalkynylated heterocycles has not been extensively studied so far,⁹ despite the fact that the heteroatoms can have a strong and interesting influence on the properties of the molecule. Herein, we report the synthesis of what are, to the best of our knowledge, the first pentaalkynylpyridines. To investigate the influence of the central pyridine core on the photophysical properties, we have compared the absorption and fluorescence of these molecules with a series of hexa- and pentaalkynylbenzene derivatives. Quantitative fluorescence studies (determination of quantum yields) had not been carried out for polyalkynylated benzene derivatives before.

In the context of our studies, we developed a new and general protocol for multiple Sonogashira reactions of hexa- and pentachlorobenzene. These polychlorinated arenes have, to our knowledge, not been used before in Sonogashira or Suzuki reactions. Using modern monodentate phosphine ligands, the Sonogashira reactions proceed in good yields and short reaction times and with low catalyst loadings. In fact, the conditions developed herein proved to be advantageous, in terms of yield, side reactions, and selectivity, compared to previous syntheses of hexa- and pentaalkynylbenzenes.⁸ Our starting point was the development of a general catalytic system for the pentafold Sonogashira coupling¹⁰ of pentachloropyridine (**1**) with phenylacetylene. The reaction of **1** with 7 equiv of phenylacetylene afforded the pentaalkynylpyridine **2a** in up to 95% yield.¹² During the optimization (Table 1), sterically demanding ligands, such as X-Phos (2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl) or HP(*t*Bu)₃BF₄, proved to be important. It is noteworthy that five C–C bonds are formed in only one step which refers to a nearly quantitative yield and less than 1 mol % of catalyst for each bond formation. Surprisingly, CuI as a cocatalyst proved to be necessary, while the groups of Buchwald and Beller independently showed that single Sonogashira reactions of different monochloroarenes is inhibited by CuI.¹¹

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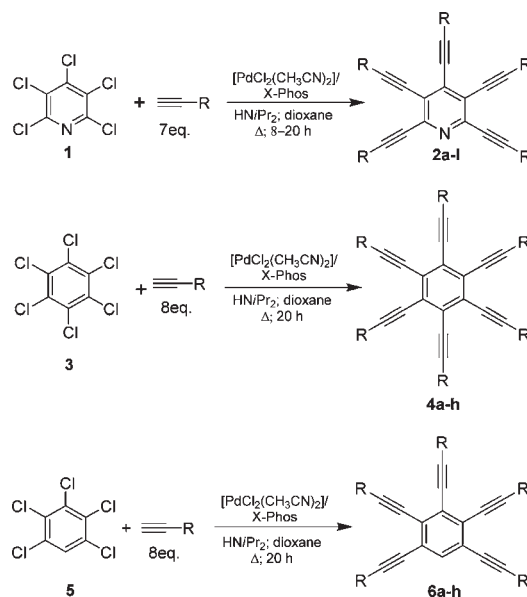
(12) Representative procedure: An argon flushed pressure tube was charged with [PdCl₂(CH₃CN)₂] (5.2 mg, 0.02 mmol, 4 mol %), X-Phos (19 mg, 0.04 mmol, 8 mol %), CuI (3 mg, 0.015 mmol, 3 mol %), and **1** (126 mg, 0.5 mmol), followed by 7 mL of anhydrous 1,4-dioxane and 4 mL of HN*i*Pr₂. The slightly yellow solution was stirred for 10 min, and then the appropriate alkyne (7 equiv) was added. The tube was sealed with a Teflon valve and stirred at the desired temperature. The reaction mixture was allowed to cool to room temperature, diluted with water, and extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, and the solvents were evaporated. The residue was dissolved in a 1:1 mixture of hexane and CH₂Cl₂. The CH₂Cl₂ was removed under reduced pressure. The precipitate formed was filtered off and washed with a 3:1 mixture of hexane and CH₂Cl₂. The solid was further purified by column chromatography (silica gel, hexane/CH₂Cl₂).

Table 1. Optimization of the Synthesis of **2a**

	catalyst	base	temp [°C]	CuI [mol]	time [h]	yield [%] ^a
1	5 mol % Pd(PPh ₃) ₄	HN(<i>i</i> Pr) ₂	20	5	20	Traces
2	5 mol % Pd(PPh ₃) ₄	HN(<i>i</i> Pr) ₂	80	5	20	Traces
3	5 mol % PdCl ₂ (CH ₃ CN) ₂	HN(<i>i</i> Pr) ₂	80	5	10	84
	10 mol % HP(<i>t</i> Bu) ₃ BF ₄					
4	5 mol % PdCl ₂ (CH ₃ CN) ₂	HN(<i>i</i> Pr) ₂	80	5	10	96
	10 mol % X-Phos					
5	5 mol % PdCl ₂ (CH ₃ CN) ₂	Cs ₂ CO ₃	80	-	10	12
	10 mol % X-Phos					
6	1 mol % PdCl ₂ (CH ₃ CN) ₂	HN(<i>i</i> Pr) ₂	80	1	20	6
	5 mol % X-Phos					
7	4 mol % PdCl ₂ (CH ₃ CN) ₂	HN(<i>i</i> Pr) ₂	80	3	10	95
	8 mol % X-Phos					
8	3 mol % PdCl ₂ (CH ₃ CN) ₂	HN(<i>i</i> Pr) ₂	80	2	10	91
	6 mol % X-Phos					




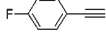




^a Yields of isolated products.

Scheme 1. Synthesis of Pentaalkynylpyridines **2a–k**, Hexaalkynylbenzenes **4a–h**, and Pentaalkynylbenzenes **6a–h**



The reaction of **1** with various alkynes, using our optimized procedure, afforded the desired pentaalkynylpyridines **2a–k** (Scheme 1, Table 2). The synthesis of alkyl-substituted derivative **2f** required a longer reaction time (20 h) compared to aryl-substituted derivatives (8–10 h). Electron-donating groups lead to a slight decrease in yield (product **2b**, **2e**) while electron-withdrawing groups resulted in high yield and a shorter reaction time (product **2d**).

Table 2. Synthesis of Pentaalkynylpyridines **2a–k**

product	alkyne	temp [°C]	time [h]	yield [%] ^a
2a		80	10	95
2b		80	10	66
2c		80	10	89
2d		80	8	88
2e		90	10	71
2f	C_4H_9	90	20	63
2g		80	10	79
2h		80	10	89
2i		90	10	80
2j	$C_8H_{11}O$	80	10	53
2k	C_7H_{15}	80	10	40

^a Yields of isolated products.

The order of Pd mediated alkylation is directed by the electronic properties of the pyridine core. At first positions 2 and 6 are functionalized, followed by position 4. The last steps are the alkylation of positions 3 and 5.¹³

Addition of alkyne moieties to the pyridine leads to an activating effect due to the withdrawing nature of the alkyne. Thus using our developed condition with 2.4 equiv of alkyne gave the pentaethynylpyridine as a major product and 3,4,5-trichloro-2,6-bis(ethynyl)pyridine as one of the minor products.

The facile pentafold Sonogashira reactions of **1** are in striking difference to Suzuki–Miyaura (S–M) reactions which proved to be *not* possible (*vide infra*).¹⁴




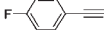



The molecular structure of **2g** was independently confirmed by X-ray crystal structure analysis (see Supporting Information). The phenyl groups and the pyridine moiety are nearly in plane. Layers are formed in the crystal lattice. A detailed discussion is provided in the Supporting Information.

The reaction of hexachlorobenzene (**3**) with 8 equiv of phenylacetylene, using the procedure developed for the synthesis of **2a–k**, proceeded sluggishly and gave the desired product **4a** in only 36% yield. This can be explained by the fact that the oxidative addition of the catalyst is faster for electron-poor pyridine **1** than for hexachlorobenzene (**3**). Nevertheless, the yield of product **4a** could be increased to 93% by increasing the temperature (100 °C), extending the reaction time (20 h) and using a slightly

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Table 3. Synthesis of Hexaalkynylbenzenes **4a–h**^a

product	alkyne	temp [°C]	time [h]	yield [%] ^b
4a		100	20	93
4b		100	20	54
4c		100	20	81
4d		100	20	89
4e		100	20	61
4f	C_4H_9	100	20	14
4g		100	20	73
4h		100	20	87

^a Conditions: 5 mol % PdCl₂(CH₃CN)₂, 10 mol % X-Phos, 3 mol % CuI, 3, 1–4 dioxane, HNiPr₂, 8 equiv of alkyne. ^b Yields of isolated products.




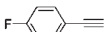




increased catalyst loading (Table 3). Using these conditions, products **4a–h** were prepared in good yields (except for alkyl derivative **4f**).

The structure of **4g** was independently confirmed by X-ray crystal structure analysis (see Supporting Information). Similar to **2g**, the phenyl groups and the central benzene unit are nearly in plane (see Supporting Information).

The reaction of pentachlorobenzene with various arylalkynes afforded the pentaalkynylbenzenes **6a–h** (Table 4). Good yields were obtained when 6 mol % of the catalyst were used and when the reaction was stirred at 100 °C for 20 h.

Steady-state absorption and fluorescence spectroscopic studies of compounds **2**, **4**, and **6** were carried out. Typical absorption and corrected fluorescence spectra are shown

Table 4. Synthesis of Pentaalkynylbenzenes **6a–h**

product	alkyne	temp [°C]	time [h]	yield [%] ^a
6a		100	20	75
6b		100	20	73
6c		100	20	89
6d		100	20	73
6e		100	20	68
6f		100	20	89
6g		100	20	69
6h		100	20	72

^a Yields of isolated products.

in Figure 1 for compounds **2a**, **4a**, and **6a** (in CH₂Cl₂). The absorption and fluorescence properties of all derivatives are summarized in Table 5.

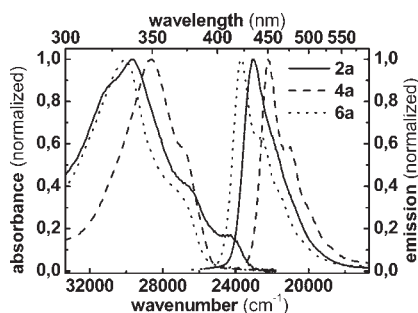


Figure 1. Normalized absorption and corrected emission spectra of compounds **2a**, **4a**, and **6a** in CH₂Cl₂.

For both absorption and fluorescence maxima of compounds **2**, **4**, and **6**, electron-donor groups (derivatives **b**, **c**, and **e**) led to a slight red shift, while electron-acceptor groups (derivatives **d**) led to a slight blue shift (compared to phenyl-substituted derivatives **a**) (Table 5). The absorption spectra of pentaalkynylpyridines **2** extend to lower energies compared to benzene derivatives **4** and **6**. The lowest absorption bands S₁←S₀ appear in the range of 410 to 420 nm (exemplarily shown for **2a** in Figure 1). The fluorescence quantum yields of donor substituted pentaalkynylpyridines are about 50% higher compared to the corresponding pentaalkynylbenzenes (Table 5).

In conclusion, we have reported a facile synthesis of pentaalkynylpyridines, hexaalkynylbenzenes, and pentaalkynylbenzenes from readily available arylchlorides. The synthesis of pentaalkynylpyridines had not been reported before. Polyalkynylated benzene derivatives had been previously prepared, but in lower yields. Penta-fold S–M reactions of pentachloropyridine (**1**) proved to be unsuccessful. The reactions only occurred, under harsh conditions, at positions 2 and 6.¹⁴ The facile penta-fold Sonogashira reactions of **1** are in striking difference to the S–M reactions and can be explained by the activating (electron-withdrawing) effect of the alkynyl groups. In fact, the activating effect of the alkynyl groups is so strong that regioselective Sonogashira reactions of **1** at positions 2 and 6 could not be realized because the pentaalkynylated pyridines are rapidly formed.

The absorption and fluorescence properties of the products were studied and compared to each other. In this context, the quantum yields were determined for the first time. The results show that donor substituted pentaalkynylpyridines (especially derivative **2b**) represent promising light emitting organic materials, due to their high quantum yields compared to the corresponding

Table 5. Photophysical Properties of Compounds **2a–e**, **4a–e**, and **6a–e** in Dichloromethane: Molar Absorption Coefficients at Absorption Maxima (and Shoulders), Fluorescence Band Maxima, and Quantum Yields

compd	λ_{abs} (λ_{abs}) [nm] ($[10^4 \text{ M}^{-1} \text{ cm}^{-1}]$)	λ_{max}^{flu} [nm]	ϕ_{flu} quantum yield
2a	338 (11.0)	438	0.55 ± 0.08
	376 (4.6)		
	421 (1.4)		
2b	356 (26.6)	459	0.81 ± 0.12
	396 (12.4)		
	421 (6.2)		
2c	347 (20.1)	444	0.63 ± 0.09
	384 (9.3)		
	421 (3.9)		
2d	337 (6.4)	436	0.47 ± 0.07
	372 (2.7)		
	407 (1.5)		
2e	342 (17.9)	441	0.48 ± 0.07
	379 (8.0)		
	411 (3.6)		
4a	349 (20.0)	452	0.43 ± 0.07
	371 (11.9)		
4b	366 (22.2)	466	0.55 ± 0.08
	386 (12.6)		
4c	357 (19.3)	459	0.44 ± 0.07
	379 (10.9)		
4d	347 (16.6)	450	0.25 ± 0.04
	368 (9.6)		
4e	351 (16.5)	453	0.27 ± 0.04
	371 (10.5)		
6a	332 (11.9)	424	0.26 ± 0.04
	364 (7.3)		
6b	349 (14.1)	437	0.53 ± 0.08
	380 (7.0)		
6c	343 (11.6)	429	0.41 ± 0.06
	373 (5.5)		
6d	330 (15.5)	421	0.43 ± 0.06
	371 (5.3)		
6e	334 (11.2)	425	0.32 ± 0.05
	372 (4.3)		

benzene derivatives. The photophysical data suggest that a strong electronic interaction between the pyridine core and the phenyl group is present. This is supported by the X-ray crystal structure analysis of **2g** (see Supporting Information) which shows that the pyridine and phenyl moieties are nearly in plane.

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Supporting Information Available. Experimental procedures, full spectroscopic data, details of crystal structure analyses, CIF information, and copies of NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.