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First Synthesis and Electronic Properties of Ring-Alkynylated Phenothiazines

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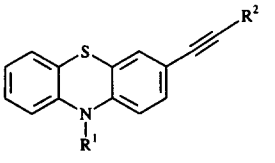
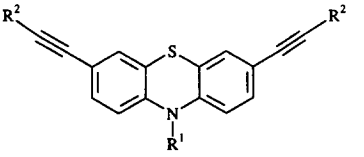
Summary: 3-mono- and 3,7-bis(alkynylated) phenothiazines **7** and **8** can be readily synthesized from the corresponding phenothiazinyl carbaldehydes. The monoalkynylated phenothiazines **7** are dimerized or cross-coupled to give highly fluorescent phenothiazinyl-terminated redox active dumbbells **9** and **10** that display large Stokes shifts. Compound **9** reveals a strong electronic coupling of the phenothiazinyl moieties according to cyclic voltammetry.

Phenothiazines are a pharmaceutically important class of tricyclic nitrogen-sulfur heterocycles. In particular, they are anti-histaminica with a strong effect on the central nervous system,[1] and due to their pharmacological efficacy they are applied as sedativa, tranquilizers, anti-epilectica, anti-tuberculotica, antipyretica, anti-tumor agents, bactericides and parasiticides.[2] Upon photoinduction phenothiazines are also able to cleave DNA.[3] Fairly early, it was found that the low oxidation potential of phenothiazines and the formation of stable radical cations play a key role in their physiological activities.[4] More recently, phenothiazine derivatives being attractive reversible redox systems[1,5] have become attractive supramolecular[6] and material scientific[7] motifs. Although, alkenylated phenothiazines have been synthesized in the context of electro-active donor-acceptor systems,[7c,d,e] ring-alkynylated phenothiazines, like **1** and **2**, representing interesting building blocks for redox active oligomers have been unknown so far. The standard approach to alkynylated heteroarenes by palladium-catalyzed cross-coupling reactions requires the corresponding halo heteroarenes. However, this straight forward approach to alkynylated phenothiazines was hampered since the preparation of 3-bromo or 3-iodo phenothiazines is either difficult or inefficient. Here, the first syntheses and electronic properties of 3-mono- and 3,7-dialkynylated phenothiazines **1** and **2** are described.



1



2

Retrosynthetically, an aldehyde-alkyne transformation represents a suitable alternative to cross-coupling methodologies, especially, since phenothiazine carbaldehydes are readily available by *Vilsmeier-Haack*-formylations. Thus, the synthesis of alkynylated phenothiazines commences with dibromo

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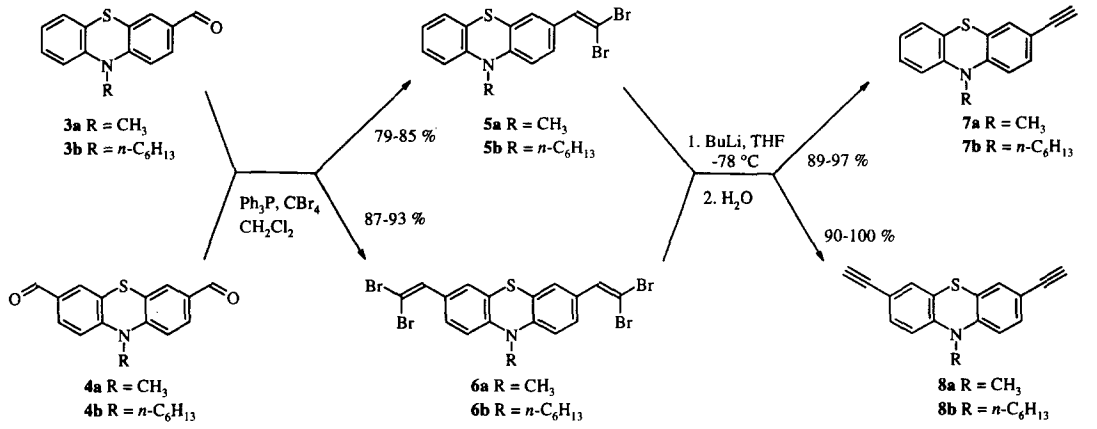
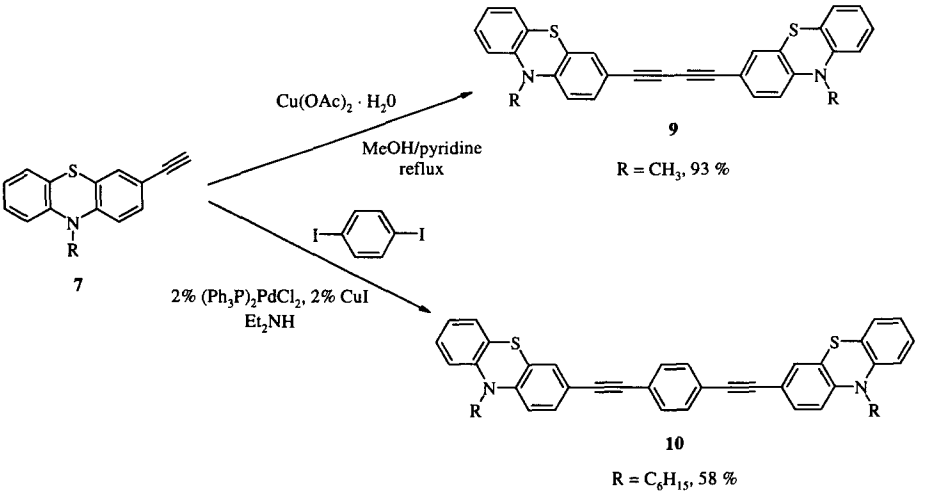
methylenations of the phenothiazine 3-carbaldehydes **3**[8] and phenothiazine 3,7-biscarbaldehydes **4**,[9] respectively, to give the mono- and bis(dibromo ethenylated) phenothiazines **5** and **6** and concludes with a dehydrobromination and halogen-metal exchange according to the Corey-Fuchs protocol[10] to give the 3-mono- and 3,7-bisalkynylated phenothiazines **7** and **8** and good to excellent yields (Scheme 1).[11]



Scheme 1

The monoethynylated compounds **7** are suitable building blocks for alkynyl-bridged phenothiazine based redox systems. Thus, the copper mediated *Eglinton* coupling[12] of **7a** and the palladium copper catalyzed *Sonogashira* coupling[13] of **7b** and 1,4-diiodo benzene give rise to the dumbbell-shaped alkynyl-bridged diphenothiazinyl compounds **9** and **10**, respectively (Scheme 2).



Scheme 2

Electronically, the novel alkynylated phenothiazines **7b**, **8a**, **9** and **10** reveal some interesting features (Table 1). Due to their rigid rod nature these systems fluoresce strongly, both in solution (λ_{max} (emission) =

450 to 500 nm) and in solid state (λ_{max} (emission) = 470 to 491 nm), and display large Stokes shifts ($\Delta\tilde{\nu}$ = 5020 to 9273 cm^{-1}). In the UV/Vis spectra of the ethynylated phenothiazines the longest wavelength absorption bands at 319 (**7b**) and 334 nm (**8a**) are significantly less intensive than the strong absorptions within the phenothiazine core[14] at 268 (**7b**) and 274 nm (**8a**), respectively. However, the diphenothiazinyl dumbbell-shaped compounds display fairly intense bands at 385 (**9**) and 390 nm (**10**) arising from π-π^* transitions within the extended π-system.[14] Already from the absorption and emission spectra a strong electronical coupling can be anticipated for the diphenothiazinyl dumbbells **9** and **10**.

Table 1. UV/Vis, fluorescence and electrochemical data of alkynylated *N*-methyl phenothiazines.

Compound	λ_{max} [nm] absorption in solution	λ_{max} [nm] emission in solution	λ_{max} [nm] emission in solid state	Stokes shift[a] $\Delta\tilde{\nu}$ [cm^{-1}]	Oxidation potentials[b] $E^{0/+}$ [V]	Oxidation potentials[b] $E^{+1/+2}$ [V]	Reduction potentials[b] $E^{0/-1}$ [V]
7b[c]	267				0.805[f]	–	-1.144[h]
	319	453	471[e]	9273			
8a[d]	243				0.758[f]	–	-1.338[h]
	274						
	334	450	471	7718			
9[d]	289				0.350[f]	0.782[f]	-1.095[h]
	314						
	390	485	487	5022			
10[c]	271				0.674[g]	–	-1.197[i]
	318		414				
	385	499	491	5934			

[a]Difference of the longest wavelength maxima [cm^{-1}] in solution. [b]Determined by cyclic voltammetry at different scan rates in CH_2Cl_2, tetrabutylammonium hexafluorophosphate as electrolyte, gold working electrode, platinum wire counter electrode, Ag/AgCl/aqueous KCl reference electrode; ferrocene as internal standard with $E^{0/+}$ = 0.401 V. [c]Recorded in $CHCl_3$. [d]Recorded in CH_2Cl_2. [e]Compound **7a**. [f]Reversible one-electron oxidation. [g]Reversible two-electron oxidation. [h]Irreversible one-electron reduction. [i]Irreversible two-electron reduction.

According to cyclic voltammetry (Table 1) reversible oxidations and irreversible reductions can be found for all investigated compounds. Expectedly, the ethynyl substituents withdraw electron density from the phenothiazinyl core resulting in an anodic shift of the one-electron oxidations at 0.805 V (**7b**) and 0.758 V (**8a**) compared to *N*-methyl phenothiazine ($E^{0/+1}$ = 0.673 V). However, the butadiynyl-bridged system **9** can be oxidized in a one-electron oxidation at a significantly lower potential ($E^{0/+1}$ = 0.350 V) to give a radical cation that is oxidized in an other one-electron oxidation at 0.782 V to give the dication. For this two-step redox system the stability of the radical cation can be described by a semiquinone formation constant of $K_{SEM} = 1.9 \times 10^6$, indicating a strong electronical coupling of the phenothiazinyl moieties (ΔE = 0.432 V) through the diynyl bridge. In the case of the diethynyl phenylene bridged system **10** the phenothiazinyl substituents are electronically decoupled as indicated by the intense two-electron oxidation potential $E^{0/+2}$ = 0.674 V.

Thus, redox dumbbells like **9** and **10** could be an interesting new class of π-donors as hole transporters and emitters in organic electroluminescent devices.[15] Further studies directed to polymer and oligomer syntheses with the novel ethynylated phenothiazines **7** and **8** are currently underway.

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10. Typical experimental procedure for the synthesis of **8** from **6**. To a solution of 0.60 g (1.03 mmol) of **6a** in 15 ml of dry THF and cooled -78 °C 2.7 ml (4.3 mmol) of 1.6 *M* *n*-butyllithium in hexanes was added dropwise under nitrogen. The reaction mixture was stirred for 2 h at -78 °C and was then allowed to come to room temperature. After aqueous workup, extraction with diethyl ether and adsorptive filtration on silica gel (diethyl ether) 0.27 g (100 %) of **8a** was isolated as pale yellow crystals. Analytical data of **8a**: mp = 141 °C (ethanol), ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.98 (s, 2 H), 3.27 (s, 3 H), 6.64 (d, *J* = 8.4 Hz, 2 H), 7.15 (d, *J* = 1.9 Hz, 2 H), 7.21 (dd, *J* = 1.9, 8.4 Hz, 2 H), anal. calcd. for $C_{17}H_{11}NS$: C 78.13, H 4.24, N 5.36; found: C 77.94, H 4.13, N 5.10.
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