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Synthesis and Electronic Properties of Sterically Demanding *N*-Arylphenothiazines and Unexpected Buchwald−Hartwig Aminations

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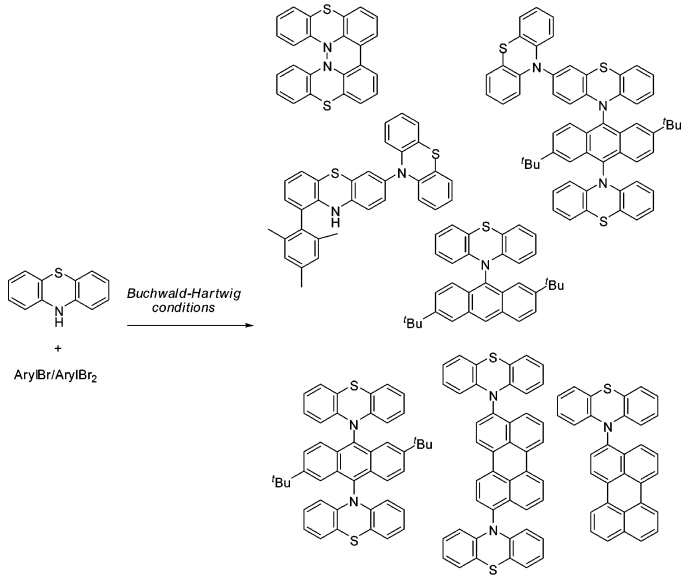

Phenothiazine is coupled under Buchwald−Hartwig conditions with bromo anthracenes and perylene as substrates to give phenothiazine−anthracene and phenothiazine−perylene dyads and triads. Investigation of the electronic properties of these sterically demanding *N*-aryl phenothiazines by absorption and emission spectroscopy, cyclic voltammetry, and DFT calculations revealed that the individual chromophores are decoupled in the electronic ground state but show unique electronic communication in the excited state. For the anthracenyl-bridged diphenothiazine an intense electronic coupling of the phenothiazinyl units is detected upon oxidation. Besides, attempts to synthesize phenothiazine compounds with even more sterically demanding aryl substituents in the 10-position under *N*-arylation conditions gave rise to the formation of quite unexpected products of arylation and/or oxidative coupling. The folding angle of the phenothiazine in a consanguineous series correlates well with the first oxidation potential.

Introduction

Phenothiazines belong to an important class of tricyclic nitrogen−sulfur heterocycles,[1] with a broad spectrum of pharmacological activity.[2] Most interestingly, phenothiazines are also able to cleave DNA upon photochemical induction.[3] As a consequence of a low oxidation potential, they readily form stable radical cations and some of their physiological activity can be attributed to this circumstance.[4] Furthermore, the radical cations give rise to a fingerprint of characteristic, deep-colored

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[§] X-ray structure analyses.

(1) Sainsbury, M. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, UK, 1984; Vol. 3, p 995.

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absorptions.[5] Thus, phenothiazine derivatives have become important spectroscopic probes in molecular and supramolecular arrangements for photoinduced electron transfer (PET) studies[6] and as motifs in organic materials.[7] The prospect of integrating strongly coupled redox fragments like phenothiazines into conjugated chains could constitute a so far unknown class of redox addressable molecular wires, in particular, for a redox manipulation of single molecules with nanoscopic scanning techniques.[8,9] As part of our program to synthesize and investigate phenothiazinyl based molecular wires,[10] we have communicated syntheses, structures, and first cyclic voltammetry measurements of directly linked phenothiazinyl dyads and triads[11] that can be regarded as models for polymer-based coupled electrophores. The oxidation potentials of phenothiazines can be influenced by electronic substituent effects in the 3- or 7-position[10−12] and by steric effects of substituents at the nitrogen atom. The latter directly affect the butterfly conformation as indicated by the folding angle.[13] Here, we report studies on the correlation of the folding angle of phenothiazines and the electronic properties by introducing several sterically demanding aromatic substituents in the 10-position. In some cases, although under standard conditions, rather unusual structures are formed that have been unambiguously assigned by X-ray structure analyses.

Results and Discussion

Computations. For several series of phenothiazines with extended π-conjugation the first reversible oxidation potential of phenothiazines can be sharply fine-tuned by introducing suitable substituents in the 3- or 7-position.[10−12] Since substituents in the 10-position can either adopt an extra (quasi-axial) or intra (quasi-equatorial) position[14] and, therefore, alter the folding angle in the butterfly structure[13] the oxidation potential can also be influenced to a large extent. Alkyl substituents, giving rise to lower oxidation potentials, rather prefer an extra configuration whereas hydrogen and aromatic substituents favor the intra orientation. Hence, the extra configuration shifts the oxidation potential anodically as a consequence of diminished interaction of the phenothiazine benzo π-electrons with the nitrogen lone pair. However, for planar phenothiazine structures, ensuring a coplanar orientation of all interacting orbitals, only few examples with highly electron withdrawing groups like fluorine or nitro have been reported.[15] As a consequence of the pronounced electron deficiency the desired oxidation to the phenothiazine radical cation is extremely hampered. Therefore, we decided first to explore the geometrical and electronic effects of sterically demanding *N*-aryl substituents on phenothiazines by DFT calculations on selected representatives **1** (Figure 1, Table 1).[16] The extent of the butterfly conformation is quantified by the folding angle θ of the intersecting planes of the benzo rings, or the tilt angle α which describes the deviation of these planes from coplanarity, i.e., $\alpha = 0°$.

The structures were optimized on the level of density functional theory with the B3LYP and the Becke−Perdew model, using increasing numbers of basis sets. In comparison to *N*-phenylphenothiazine[17] ($\alpha = 29.3°$) the computed tilt angles α of the model structures **1** are expectedly smaller, due to the increase in steric demand of the *N*-aryl substituents. Within the series of *N*-aryl phenothiazines **1** the steric interaction of the orthogonalized aryl fragment with their di-*o*-alkyl moieties with the *peri*-hydrogen atoms in the 1- and 9-benzo positions of the phenothiazine core gradually increases and causes a reduction

(2) (a) Mietzsch, F. *Angew. Chem.* **1954**, *66*, 363−371. (b) Ionescu, M.; Mantsch, H. *Adv. Heterocycl. Chem.* **1967**, *8*, 83−113. (c) Bodea, C.; Silberg, I. *Adv. Heterocycl. Chem.* **1968**, *9*, 321−460. (d) Valzelli, L.; Garattini, S. In *Principles of Psychopharmacology*; Clark, W. G., Ed.; Academic Press: New York, 1970; pp 255−258. (e) Okafor, C. O. *Heterocycles* **1977**, *7*, 391−427. (f) Eckstein, Z.; Urbanski, T. *Adv. Heterocycl. Chem.* **1978**, *23*, 1−53. (g) Szabo, J. *Chem. Heterocycl. Compd. USSR* (*Engl. Trans.*) **1979**, *15*, 291−308. (h) Albery, W. J.; Foulds, A. W.; Hall, K. J.; Hillman, A. R.; Edgell, R. G.; Orchard, A. F. *Nature* **1979**, *282*, 793−797.

(3) (a) Nishiwaki, E.; Nakagawa, H.; Takasaki, M.; Matsumoto, T.; Sakurai, H.; Shibuya, M. *Heterocycles* **1990**, *31*, 1763−1767. (b) Decuyper, J.; Piette, J.; Lopez, M.; Merville, M. P.; Vorst, A. *Biochem. Pharmacol.* **1984**, *33*, 4025−4031. (c) Motten, A. G.; Buettner, G. R.; Chignell, C. F. *Photochem. Photobiol.* **1985**, *42*, 9−15. (d) Fujita, H.; Matsuo, I. *Chem. Biol. Interact.* **1988**, *66*, 27−36.

(4) (a) Forrest, I.; Forrest, F. *Biochim. Biophys. Acta* **1958**, *29*, 441−442. (b) Iida, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 663−667. (c) Moutet, J.-C.; Reverdy, G. *Nouv. J. Chim.* **1983**, *7*, 105−113.

(5) For UV/vis and EPR spectra of 10-methylphenothiazine, see e.g.: (a) Shine, H. J.; Mach, E. E. *J. Org. Chem.* **1965**, *30*, 2130−2139. (b) Shine, H. J.; Thompson, D. R.; Veneziani, C. *J. Heterocycl. Chem.* **1967**, *4*, 517−527. (c) For cyclovoltammetric and spectroscopic data of phenothiazine, see e.g.: Tinker, L. A.; Bard, A. J. *J. Am. Chem. Soc.* **1979**, *101*, 2316−2319. (d) Padusek, B.; Kalinowski, M. K. *Electrochim. Acta* **1983**, *28*, 639. (e) McIntyre, R.; Gerischer, H. *Ber. Bunsen-Ges. Phys. Chem.* **1984**, *88*, 963−969.

(6) (a) Duesing, R.; Tapolsky, G.; Meyer, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 5378−5379. (b) Jones, W. E., Jr.; Chen, P.; Meyer, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 387−388. (c) Brun, A. M.; Harriman, A.; Heitz, V.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8657−8663. (d) Burrows, H. D.; Kemp, T. J.; Welburn, M. J. *J. Chem. Soc., Perkin Trans. 2* **1973**, 969−974. (e) Collin, J.-P.; Guillerez, S.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1989**, 776−778. (f) Daub, J.; Engl, R.; Kurzawa, J.; Miller, S. E.; Schneider, S.; Stockmann, A.; Wasielewski, M. R. *J. Phys. Chem. A* **2001**, *105*, 5655−5665.

(7) (a) Wheland, R. C.; Gillson, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 3916−3925. (b) Berges, P.; Kudnig, J.; Klar, G.; Sanchez-Martinez, E.; Diaz-Calleja, R. *Synth. Met.* **1992**, *46*, 207−219. (c) Knorr, A.; Daub, J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2664−2666. (d) Spreitzer, H.; Scholz, M.; Gescheidt, G.; Daub, J. *Liebigs Ann. Chem.* **1996**, 2069−2077. (e) Spreitzer, H.; Daub, J. *Chem. Eur. J.* **1996**, *2*, 1150−1158.

(8) (a) For applications of AFM and STM in chemistry, see e.g. a special issue of Chemical Reviews: *Chem. Rev.* **1997**, *97*, Issue 4. (b) For applications in molecular electronics, see e.g.: Rabe, J. P. In *An Introduction to Molecular Electronics*; Petty, M. C., Bryce, M. R., Bloor, D., Eds.; Oxford University Press: New York, 1995; pp 261−278. (c) For nanoscale materials, see e.g. a special issue of Accounts of Chemical Reseach: *Acc. Chem. Res.* **1999**, *32*, Issue 5.

(9) For conductance of single molecules under STM conditions, see e.g.: (a) Bumm, L. A.; Arnold, J. J.; Cygan, M. T.; Dunbar, T. D.; Burgin, T. P.; Jones, L. I. I.; Allara, D. L.; Tour, J. M.; Weiss, P. S. *Science* **1996**, *271*, 1705−1707. (b) Davis, W. B.; Svec, W. A.; Ratner, M. A.; Wasielewski, M. R. *Nature* **1998**, *396*, 60−63. (c) Cygan, M. T.; Dunbar, T. D.; Arnold, J. J.; Bumm, L. A.; Shedlock, N. F.; Burgin, T. P.; Jones, L. I. I.; Allara, D. L.; Tour, J. M.; Weiss, P. S. *J. Am. Chem. Soc.* **1998**, *120*, 2721−2732. (d) Leatherman, G.; Durantini, E. N.; Gust, D.; Moore, T. A.; Moore, A. L.; Stone, S.; Zhou, Z.; Rez, P.; Liu, Y. Z.; Lindsay, S. M. *J. Phys. Chem. B* **1999**, *103*, 4006−4010.

(10) (a) Müller, T. J. J. *Tetrahedron Lett.* **1999**, *40*, 6563−6566. (b) Krämer, C. S.; Zeitler, K.; Müller, T. J. J. *Org. Lett.* **2000**, *2*, 3723−3726. (c) Krämer, C. S.; Müller, T. J. J. *Eur. J. Org. Chem.* **2003**, 3534−3548. (d) Hauck, M.; Schönhaber, J.; Zucchero, A. J.; Hardcastle, K. I.; Müller, T. J. J.; Bunz, U. H. F. *J. Org. Chem.* **2007**, *72*, 6714−6725.

(11) (a) Krämer, C. S.; Zeitler, K.; Müller, T. J. J. *Tetrahedron Lett.* **2001**, *42*, 8619−8624. (b) Krämer, C. S.; Zimmermann, T. J.; Sailer, M.; Müller, T. J. J. *Synthesis* **2002**, 1163−1170.

(12) Sailer, M.; Nonnenmacher, M.; Oeser, T.; Müller, T. J. J. *Eur. J. Org. Chem.* **2006**, 423−435.

(13) Jovanovic, M. V.; Biehl, E. R. *J. Heterocycl. Chem.* **1987**, *24*, 51−53.

(14) Malrieu, J.-P.; Pullman, B. *Theor. Chim. Acta* **1964**, *2*, 293−301.

(15) Brock, C. P.; DeLaLuz, P. J.; Golinski, M.; Lloyd, M. A.; Vanaman, T. C.; Watt, D. S. *Acta Crystallogr.* **1996**, *B52*, 713−719.

(16) Frisch, M. J.; et al. *Gaussian 03*, Revision C.03; Gaussian, Inc.: Wallingford, CT, 2004.

(17) Klein, C. L.; Conrad, J. M., III; Morris, S. A. *Acta Crystallogr.* **1985**, *C41*, 1202−1204.

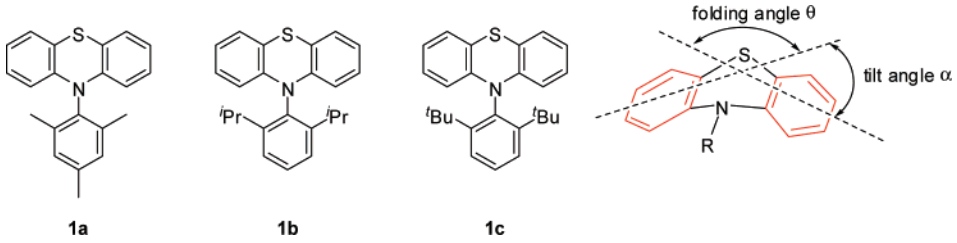


FIGURE 1. *N*-Mesitylphenothiazine (**1a**), *N*-2,6-bis(isopropyl)phenylphenothiazine (**1b**), and *N*-2,6-bis(*tert*-butyl)phenylphenothiazine (**1c**) and definition of the tilt angle.

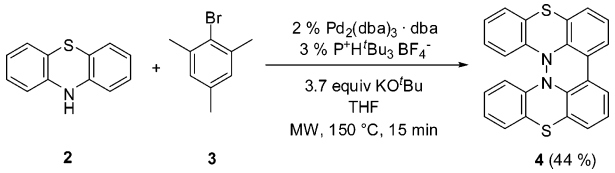
TABLE 1. Computed Tilt Angles and HOMO Energies [eV] of the Phenothiazine Derivatives 1a−c

	1a		1b		1c	
DFT basis set	tilt angle α [deg]	HOMO [eV]	tilt angle α [deg]	HOMO [eV]	tilt angle α [deg]	HOMO [eV]
B3LYP/3-21G	22.5	−4.8980	16.5	−4.8436	8.7	−4.8164
B3LYP/6-31G	22.7	−4.8708	16.1	−4.8436	10.4	−4.7892
B3LYP/6-311G	23.6	−5.0885	20.3	−5.1157	12.3	−5.0341
B3LYP/6-311+G	27.4	−5.1974	19.1	−5.1702	10.7	−5.0613
BP86/3-21G	22.8	−4.2722	18.6	−4.2722	12.4	−4.2178
BP86/6-31G	21.9	−4.2178	17.9	−4.2178	11.3	−4.1633
BP86/6-311G	23.0	−4.4627	21.0	−4.4899	11.4	−4.4627
BP86/6-311+G	21.7	−4.4899	18.6	−4.5171	11.4	−4.4627

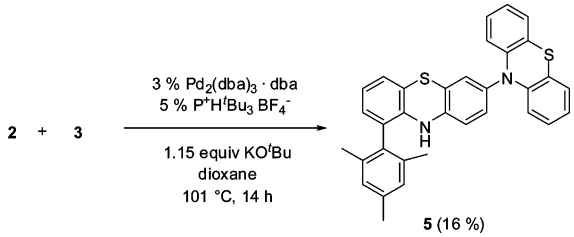
of the tilt angle α. Although both computational models are reproducing the same trend for α, the more rapid and cheaper Becke−Perdew formalism only very poorly mimics the development of the energy of the HOMO. The position of the HOMO represents, to some extent, the ease of oxidation. Upon reducing the tilt angle α from **1a** (2,4,6-trimethylphenyl) over **1b** (2,6-bis(isopropyl)phenyl) to **1c** (2,6-bis(*tert*-butyl)phenyl) in the B3LYP based computations over a range of 11° to 16°, the HOMO energies increase by 0.05 to 0.13 eV. This range should be detectable with cyclic voltammetry. Therefore, the conclusion of the computations suggests synthesizing *N*-aryl-substituted phenothiazines and to establish experimentally based correlations between the tilt angle α and the oxidation potential.

Syntheses. Retrosynthetic analysis of *N*-aryl phenothiazines suggests an Ullmann-type coupling[18] of phenothiazine and suitable aryl halides. The contemporary methodology to achieve this goal is the Buchwald−Hartwig arylation.[19] Although syntheses of phenothiazines bearing sterically demanding substituents in the 10-position according to a modified Ullmann arylation protocol are known,[20] these conditions could not be successfully applied to the synthesis of *N*-mesitylphenothiazine (**1a**). Upon applying Buchwald−Hartwig conditions[19] in the ventured synthesis of **1a**, which was met with failure under conventional heating, we observed, both by conventional and dielectric heating, a rather unusual outcome of the attempted cross-coupling reaction. Upon heating a THF solution of phenothiazine (**2**), 2-bromomesitylene (**3**), and potassium *tert*-butoxide in the presence of catalytic amounts of $Pd_2(dba)_3$dba and tris(*tert*-butyl)phosphonium tetrafluoroborate in a microwave cavity at 150 °C for 15 min the desired *N*-arylation product **1a** was not obtained, but the unexpected product 7,16-dithia-11b,11c-diazadibenzo[*a*,*o*]perylene (**4**) was isolated in 44% yield (Scheme 1).

SCHEME 1. Unexpected Synthesis of 7,16-Dithia-11b,11c-diazadibenzo[*a*,*o*]perylene (4)



SCHEME 2. Unexpected Synthesis of 9-(2,4,6-Trimethylphenyl)-10*H*-[3,10′]biphenothiazinyl (5)



Reacting **2** and **3** according to the Buchwald−Hartwig protocol in dioxane as a solvent and under conductive heating for an extended time gave rise to the formation of 9-(2,4,6-trimethylphenyl)-10*H*-[3,10′]biphenothiazinyl (**5**) as the only isolable product besides recovered, unreacted phenothiazine (**2**) (Scheme 2).

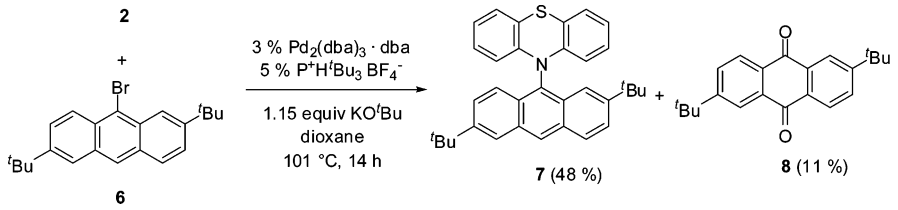
The structures of **4** and **5** were unambiguously assigned by ^{1}H and ^{13}C NMR, UV/vis, and IR spectroscopy, by mass spectrometry, by combustion analyses, and later by X-ray structure analyses.[21] To the best of our knowledge, compounds containing a dithia-diazo perylene core as in structure **4** have not been reported in the literature before. Interestingly, three unusual dimers of phenothiazine with N-N-, C^3-N-, and C^1-N-

(18) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382−2384.

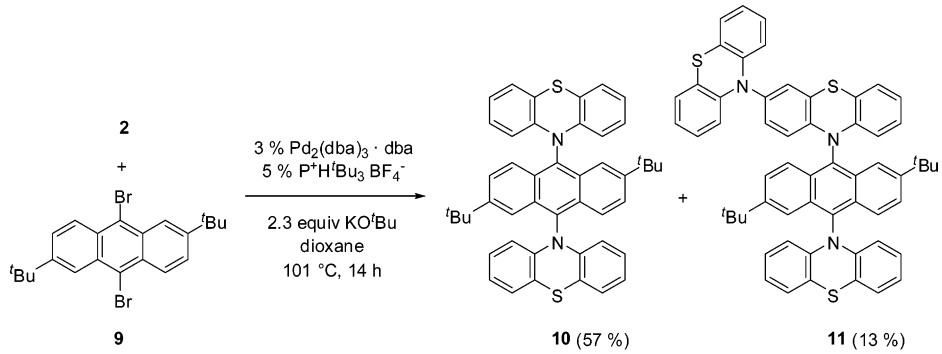
(19) (a) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1995**, *34*, 1348−1350. (b) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609−3612. (c) For reviews see: Hartwig, J. F. in *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley-Interscience: New York, 2002; pp 1051−1096. (d) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131−209. (e) For an excellent overview of modern aromatic carbon−nitrogen cross-coupling reactions see: Jiang, L.; Buchwald, S. L. In *Metal-Catalyzed Cross-Coupling Reactions*, end ed.; De Meijere, A., Diederich, F., Eds.; Wiley-VCH: New York, 2004; pp 699−760 and references cited therein.

(20) (a) Sasaki, S.; Murakami, F.; Yoshifuji, M. *Organometallics* **2006**, *25*, 140−147. (b) Sasaki, S.; Murakami, F.; Yoshifuji, M. *Tetrahedron Lett.* **1997**, *38*, 7095−7098.

SCHEME 3. Synthesis of an *N*-Anthracenylphenothiazine 7



SCHEME 4. Synthesis of Anthracenyl-Bridged Diphenothiazine 10 and Triphenothiazine 11



connectivity have been reported by Diudea and Silberg[22] formed upon mild oxidation of phenothiazine with copper(II) chloride, i.e., under very mild oxidizing conditions and obviously in the coordination sphere of a transition metal. These peculiar dimerizations can be obviously accounted for by the ease of oxidation and the relative stability of the phenothiazinyl radical cation. In our case palladium complexes might rationalize a related mechanistic scenario. Presumably, compound **4** is formed through a palladium-catalyzed redox pathway giving rise to an N-N-diphenothiazine. Here, 2-bromomesitylene (**3**) might serve as a stoichiometric sacrificing oxidant. Recently, some examples of oxidative CC- and NN-homocouplings,[23] of oxidative NN-homocouplings,[24] and of oxidative CC-homocouplings under microwave irradiation in the synthesis of carbazoles have been reported.[25] However, many attempts to expand the scope of these two unusual reactions to other nitrogen heterocycles, such as indole, carbazole, phenoxazine, 3-bromophenothiazine, and 2-acetylphenothiazine, met with failure. It was not even possible to replace 2-bromomesitylene (**3**) by 1,2-dibromoethane as an oxidizing agent. Obviously, the mesityl substituent is too bulky as a substituent to be applied in Buchwald−Hartwig reactions.

However, 2,6-di-*tert*-butyl-9-bromoanthracene (**6**) can be successfully reacted with **2** under Buchwald−Hartwig conditions and conductive heating to give the expected *N*-anthracenylphenothiazine **7** in good yield as the major product (Scheme 3). Interestingly, 2,6-di-*tert*-butylanthracene-9,10(4a*H*,9a*H*)-dione (**8**)[26] was isolated as the sole byproduct, obviously also as a consequence of Pd-catalyzed oxidative side reactions.

Besides spectroscopy, mass spectrometry, and combustion analyses, the structures of **7** and **8** were unambiguously corroborated by X-ray structure analyses.

Likewise, the *N*-arylation of **2** with 2,6-di-*tert*-butyl-9,10-dibromoanthracene (**9**) under standard conditions furnishes the anthracenyl-bridged diphenothiazine **10** in 57% yield as the major product and the unusual anthracenyl-bridged terphenothiazine **11** in 13% yield (Scheme 4). In comparison with 9,10-dibromoanthracene, where an oxidative coupling is not observed,[27] the steric bias and the electron density in the anthracenyl moiety of **9** is even increased. Again, an oxidative Pd-catalyzed pathway seems to be responsible for the unexpected formation of **11**.

Finally, inspired by the synthesis of phenothiazine−pyrene dyads under modified Ullmann conditions[28] the Buchwald−Hartwig reaction of **2** and 3,10-dibromoperylene **12** gave rise to the selective formation of the biscoupling product **13** and the monocoupling product **14** in moderate yields (Scheme 5). The structure of the perylenyl-bridged diphenothiazine **13** was additionally supported by an X-ray structure analysis (Figure

(21) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 664654 (**4**), CCDC 664655 (**5**), CCDC 664656 (**8**), CCDC 664657 (**7**), and CCDC 664658 (**13**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax + 44-1223/336-033; E-mail deposit@ccdc.cam.ac.uk).

(22) Diudea, M. V.; Silberg, I. A. *J. Prakt. Chem.* **1982**, *324*, 769−776.

(23) Shiraishi, K.; Rajca, A.; Pink, M.; Rajca, S. *J. Am. Chem. Soc.* **2005**, *127*, 9312−9313.

(24) Wu, W.; Grimsdale, A. C.; Müllen, K. *Chem. Commun.* **2003**, 1044−1045.

(25) Sridharan, V.; Martín, M. A.; Menédez, J. C. *Synlett* **2006**, 2375−2378.

(26) Compound **8** can be independently obtained by CAN oxidation of 2,6-di-*tert*-butylanthracene as reported by: Müller, U.; Enkelmann, V.; Adam, M.; Müllen, K. *Chem. Ber.* **1993**, *126*, 1217−1225.

(27) Kim, S.-K.; Lee, C.-J.; Kang, I.-N.; Park, J.-W.; Lee, J.-H.; Kim, K.-S.; Choi, C.-K.; Lee, S.-D. *Mol. Cryst. Liq. Cryst.* **2007**, *462*, 135−142.

(28) Daub, J.; Engl, R.; Kurzawa, J.; Miller, S. E.; Schneider, S.; Stockmann, A.; Wasielewski, M. R. *J. Phys. Chem. A* **2001**, *105*, 5655−5665.

(29) Sun, D.; Rosokha, S. V.; Kochi, J. K. *J. Am. Chem. Soc.* **2004**, *126*, 1388−1401.

(30) Parkanyi, C.; Boniface, C.; Aaron, J. J.; Maafi, M. *Spectrochim. Acta Part A* **1993**, *49*, 1715−1726.

(31) Freed, D. J.; Faulkner, L. R. *J. Am. Chem. Soc.* **1972**, *94*, 4790−4792.

(32) Du, H.; Fuh, R. A.; Li, J.; Corkan, A.; Lindsey, J. S. *Photochem. Photobiol.* **1998**, *68*, 141−142.

(33) Magdesieva, T. V.; Kukhareva, I. I.; Shaposhnikova, E. N.; Artamkina, G. A.; Beletskaya, I. P.; Butin, K. P. *J. Organomet. Chem.* **1996**, *526*, 51−58.

(34) Fukuzumi, S.; Ohkubo, K.; Imahori, H.; Guldi, D. M. *Chem. Eur. J.* **2003**, *9*, 1585−1593.

(35) Donkers, R. L.; Maran, F.; Wayner, D. D. M.; Workentin, M. S. *J. Am. Chem. Soc.* **1999**, *121*, 7239−7248.

(36) Dietrich, M.; Heinze, J. *J. Am. Chem. Soc.* **1990**, *112*, 5142−5145.

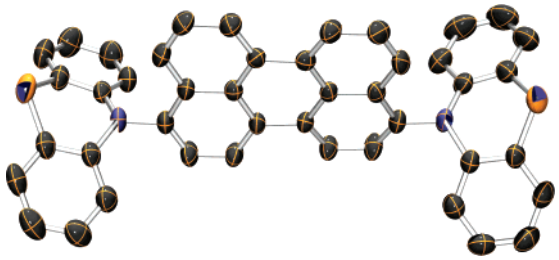


FIGURE 2. Molecular structure of the perylene-bridged diphenothiazine **13** (hydrogen atoms were omitted for clarity).

SCHEME 5: Synthesis of Perylenyl-Bridged Diphenothiazine 13 and Phenothiazine−Perylene Dyad 14

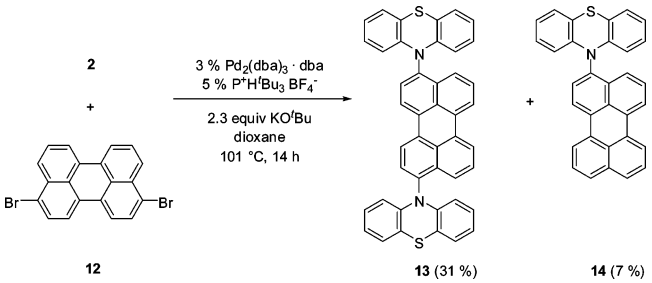


TABLE 2. Tilt Angles α of the Phenothiazine Derivatives 4, 5, 7, and 13 (Extracted from X-ray Analyses)

	4	5	7	13
tilt angle α [deg]	44[a]	26.3[a]	20	45.6/37.5

[a] Both phenothiazine moieties show the same tilt angle α.

2). From the X-ray analyses of the phenothiazine derivatives **4**, **5**, **7**, and **13** the tilt angles α could be extracted (Table 2).

Electronic Properties. The electronic structure and properties of (hetero)aryl-substituted and -bridged phenothiazines have been investigated by experimental (absorption and emission spectra, cyclic voltammetry) and computational methods (DFT calculations)[16] (Table 3). Optical spectroscopy (UV/vis and fluorescence spectra) reveals all systems display considerable fluorescence with emission of blue to blue-green light (Figures 3 and 4) and large Stokes shifts ($\Delta\tilde{\nu} = 1700-9100$ cm^{-1}).

Most remarkable is the enormous separation of the two anodic oxidations of dimer **4** by 700 mV. The perfect Nernstian behavior of the former at 786 mV excludes a subsequent chemical transformation of the radical cation $\mathbf{4}^{+}$, e.g., an N−N-bond scission. Furthermore, a full planarization upon oxidation to the dication is not only hampered as a consequence of *peri*-interactions and appears therefore at 1485 mV, but as an irreversible oxidation wave. This indicates that a subsequent chemical reaction instantaneously follows the oxidation to the dication. The systems **4**, **5**, and **11** represent unusual oligophenothiazines with an intriguing connectivity pattern, yet their electronic properties are difficult to interpret. Therefore, the following discussion predominantly focuses on the anthracenyl- and perylenyl-substituted and -bridged phenothiazines **7**, **10**, **13**, and **14**. The electronic ground state as reflected by UV/vis spectroscopy supports an additive superposition of the phenothiazinyl and the anthracenyl or perylenyl moieties, respectively. As shown by comparison with the spectra of phenothiazine (**1**), *N*-phenylphenothiazine, anthracene, and perylene, the same absorption maxima appear in the spectra of the dyads and triads (Table 3), indicating that the donor (phenothiazine) and acceptor (anthracene or perylene) π-systems are essentially electronically decoupled in the electronic ground state. This conclusion is also supported by the crystal structure analyses where donor and acceptor moieties are arranged in an almost orthogonal orientation. Furthermore, DFT calculations (B3LYP/6-31G+(d,p))[16] for **7** reveal a clear spatial separation of HOMO and LUMO (Figure 5). While the HOMO is almost completely phenothiazine centered (**7**), the LUMO is localized in the anthracenyl moiety, a favorable property for PET (photoinduced electron transfer) systems.

Most remarkably, the dyad **7** and the triad **10** show intense blue fluorescence at wavelengths that are significantly red-shifted with respect to the individual components. Concomitantly, the Stokes shift is significantly increased in comparison to anthracene. Hence, an electronic communication in the excited state is responsible for the coupling of donor and acceptor. A similar behavior has previously been reported for dimethylaminoanthracene,[37] carbazolylanthracene,[38] bis(dimethylamino)-anthracene,[39] and bisphenothiazinylanthracene.[27] In several studies we also have observed substantial Stokes shifts for phenothiazine derivatives[10,12] which can be attributed to significant geometrical changes upon excitation from a highly nonplanar ground state to a largely planarized excited state.[40]

Likewise, the electronic spectra of the phenothiazine perylene triad **13** and the dyad **14** behave accordingly. The more extended π-conjugation of the perylene unit gives rise to an overall red shift of the absorption bands, yet reflecting an overall additive superposition of the individual constituents. This can be attributed to a low intramolecular electronic communication in the electronic ground state. The same holds true for the computed electronic properties as illustrated by the distinct separation of HOMO and LUMO (Figure 6). While the HOMO is localized on the electron-rich phenothiazinyl moieties the LUMO resides on the perylene bridge. However, the emission properties again show, as in the case of the anthracenyl systems, that in the excited state an electronic communication might occur that is responsible for the pronounced bathochromic shift of the shortest wavelength emission maxima and the accompanying large Stokes shifts. Again, all this renders the phenothiazine perylene dyad and triad intriguing for intramolecular PET systems.

Additionally, for the novel phenothiazine systems cyclic voltammetry was performed to identify the redox behavior and to establish correlations in the case of sterically demanding *N*-aryl substituents. The cyclovoltammogram of **4** only shows a single reversible process with perfect Nernstian behavior at lower voltages that can be accounted for by one-electron oxidation. As a consequence of planarization upon oxidation to phenothiazine radical cations,[5] it is reasonable to assume that only one of the two identical phenothiazine moieties will be oxidized to minimize van der Waals repulsions in a fully planar dicationic specimen. Therefore, at a considerably anodically shifted potential of 1485 mV, a second, irreversible oxidation step, responsible for the oxidation to a

(37) Dey, J.; Warner, I. M. *J. Phys. Chem. A* **1997**, *101*, 4872−4878.
(38) Catalan, J.; Diaz, C.; Lopez, V.; Perez, P.; Claramunt, R. M. *J. Phys. Chem.* **1996**, *100*, 18392−18398.
(39) Hasegawa, E.; Takizawa, S.; Seida, T.; Yamaguchi, A.; Yamaguchi, N.; Chiba, N.; Takahashi, T.; Ikeda, H.; Akiyama, K. *Tetrahedron* **2006**, *62*, 6581−6588.
(40) Yang, L.;Feng, J.-K.; Ren, A.-M. *J. Org. Chem.* **2005**, *70*, 5987−5996.

TABLE 3. Selected Electronic Properties of Sterically Hindered *N*-Aryl Phenothiazines, Anthracene, and Perylene (Absorption[a] and Emission Spectra[a] and Cyclic Voltammetry[b])

compd	absorption $\lambda_{max,abs}$ [nm]	emission $\lambda_{max,em}$ [nm]	stokes shift $\Delta\tilde{\nu}$ [cm^{-1}]	quantum yield[c]	$E_0^{0/-1}$ [mV]	$E_0^{0/+1}$ [mV]	$E_0^{+1/+2}$ [mV]	$E_0^{+2/+3}$ [mV]
1	255, **316**[29]	**447**[30,d]	9300	*e*		610[30]		
N-phenyl-phenothiazine	255, **315**[29]	**446**[31,f]	9300			740[30]		
anthracene	312, 323, 339, 356, **376**[32,g]	**376**, 397, 420, 446, 475, 508[32,g]	0	0.36[32,g]	−1980[33,d]	940[34]		
perylene	253, 386, 408, **436**[34,g]	**436**, 463, 496, 528, 594[34,g]	0	0.94[34,g]	−1645[35,f]	940[36]	1640[36]	
4	252, 276, 320, **396**	513	5800	*e*		786	1485[h]	
5	260, **320**	451	9100	*e*		608	1030	
7	264, 286, 336, 352, 368, **386**	**439**, 470 (sh)	3100	0.14		755	1266	
10	260, 322, 360, 376, **396**	**484**, 518 (sh)	4600	*e*		574	804	
11	259, 267, 324, 358, 375, **395**	448	3000	*e*		719	831	982
13	258, 323, 403, 424, **449**	**486**, 521 (sh)	1700	0.68	−1386	758		
14	257, 328, 398, 419, **445**	**484**, 518 (sh)	1800	0.31	−1507	722		

[a] Recorded in CH_2Cl_2. [b] Recorded in CH_2Cl_2, 20 °C, ν = 100 mV/s, electrolyte: $^nBu_4N^+$ PF_6^-, Pt working electrode, Pt counter electrode, Ag/AgCl reference electrode. [c] Determined in ethanol with coumarine 1 as a standard (Φ_f = 0.73). [d] Recorded in acetonitrile. [e] The quantum yield was below 0.001. [f] Recorded in DMF. [g] Recorded in cyclohexane. [h] Anodic peak potential of an irreversible oxidation.

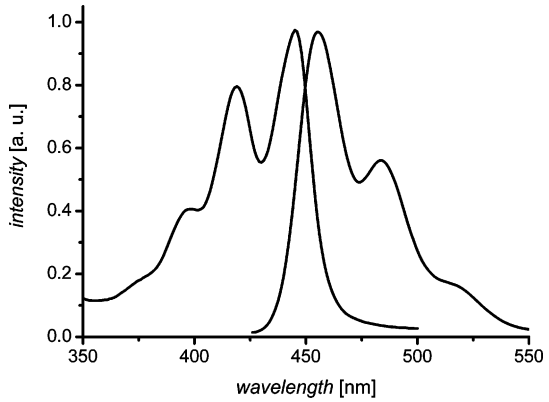


FIGURE 3. Normalized absorption and emission spectra of the perylene-substituted phenothiazine **14** (recorded in dichlormethane, T = 298 K).

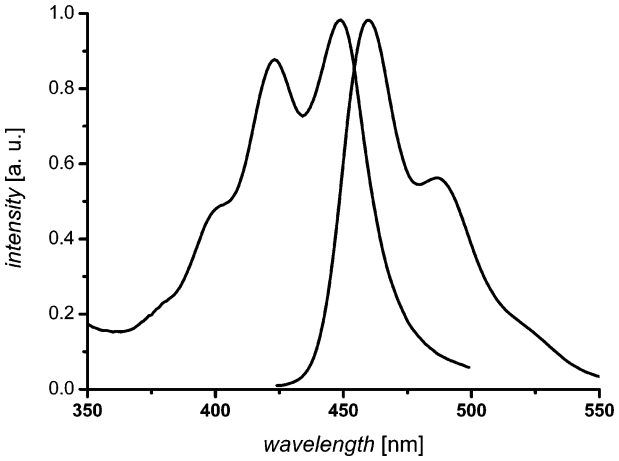


FIGURE 4. Normalized absorption and emission spectra of the perylene-substituted phenothiazine **13** (recorded in dichlormethane, T = 298 K).

highly reactive fully planar dication, can be observed. As expected for 3,10-bridged phenothiazines,[41] diphenothiazine **5** oxidizes at two well-separated, reversible oxidation potentials

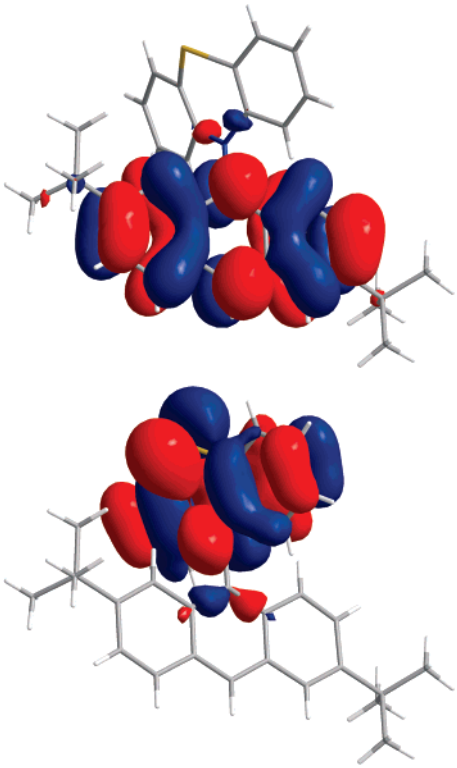


FIGURE 5. DFT calculated frontier orbitals, HOMO (bottom) and LUMO (top), of the phenothiazine anthracene dyad **7**.

as a consequence of the unsymmetrical substitution and electronic nature of both phenothiazinyl moieties. Analogously, terphenothiazine **11** displays three clearly distinguishable oxidation events.

In the case of the phenothiazine anthracene dyad **7**, two separated reversible one-electron oxidations can be observed in the cyclic voltammograms. The first oxidation at E_0 = 755 mV can be assigned to the phenothiazinyl unit and the second oxidation at E_0 = 1266 mV can be attributed to the anthracenyl

(41) Chu, S. S. C.; Van der Helm, D. *Acta Crystallogr.* **1974**, *B30*, 2489−2490.

(42) Bell, J. D.; Blount, J. F.; Briscoe, O. V.; Freeman, H. C. *Chem. Commun.* **1968**, 1656−1657.

(43) Okamato, T.; Kuratsu, M.; Kozaki, M.; Hirotsu, K.; Ichimura, A.; Matsushita, T.; Okada, K. *Org. Lett.* **2004**, *6*, 3493−3496.

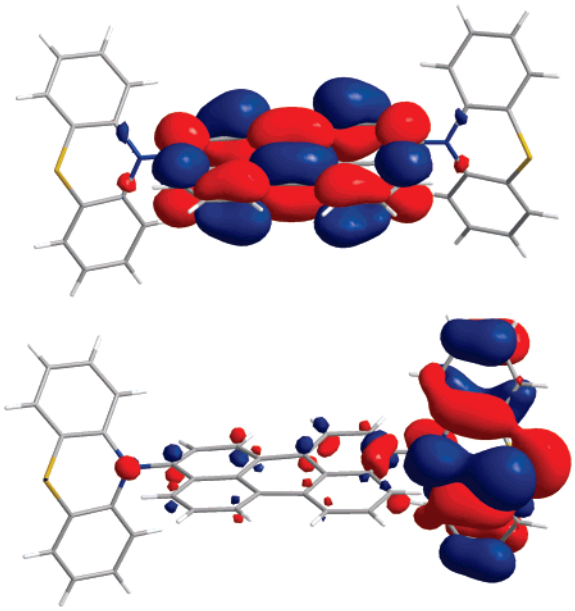


FIGURE 6. DFT calculated frontier orbitals, HOMO (bottom) and LUMO (top), of the phenothiazine perylene triad **13**.

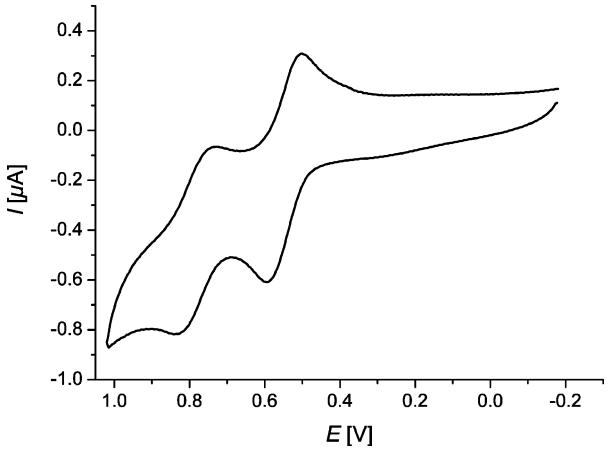


FIGURE 7. Cyclic voltammogram of **10** (recorded in dichloromethane, T = 293 K, v = 100 mV/s, electrolyte: $^{n}Bu_4N^+$ PF_6^-, Pt working electrode, Pt counter electrode, Ag/AgCl reference electrode).

part. The strongly electron-withdrawing nature of the phenothiazinyl radical cation hampers the oxidation of the anthracene, which is considerably shifted to higher potentials. Most interestingly, in the cyclic voltammogram of the highly symmetrical phenothiazine anthracene triad **10** two well-separated reversible one-electron oxidations are found at E_0 = 574 and 804 mV (Figure 7). According to the position of these two potentials it becomes obvious that these oxidations are phenothiazine centered and appear separated as a consequence of an intramolecular electronic coupling, i.e., the first oxidation imposes its influence on the second phenothiazinyl unit. This phenomenon is also found in related diphenothiazines,[11,12] yet it is still remarkable since the electronic communication occurs through an anthracenyl bridge. The anthracenyl bridge is not oxidized within the window of the cyclic voltammetry experiment.

The cyclic voltammetry of the phenothiazine perylene triad **13** and dyad **14** shows similarities but also distinct differences. Whereas the phenothiazinyl units are oxidized at a comparable potential and for the triad without intramolecular electronic

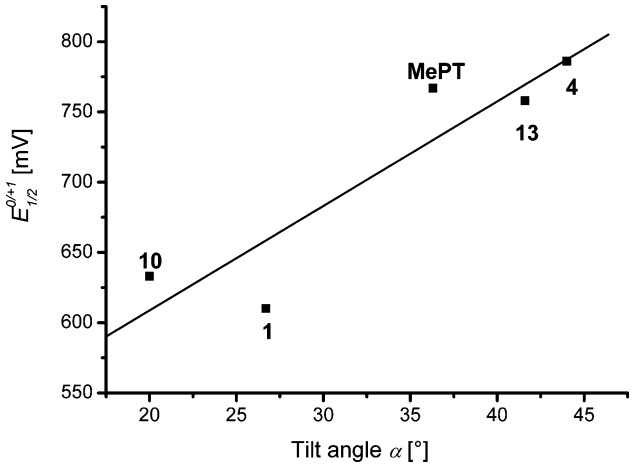


FIGURE 8. Linear fit of the tilt angles α vs first oxidation potentials $E_0^{0/+1}$ = 459.91 + 7.440α [mV] (r^2 = 0.915).

TABLE 4. Tilt Angles α (Extracted from X-ray Analyses) and Oxidation Potentials $E_0^{0/+1}$ (Recorded in CH_2Cl_2, 20 °C, v = 100 mV/s; Electrolyte: $^{n}Bu_4N^+$ PF_6^-, Pt Working Electrode, Pt Counter Electrode, Ag/AgCl Reference Electrode) for a Consanguineous Series of Phenothiazines

	4	**13**	10-methylphenothiazine (MePT)	10*H*-phenothiazine (**1**)	**10**
tilt angle α [deg]	44.0	41.6[a]	36.3[41]	26.7[42]	20.0
$E_0^{0/+1}$ [mV]	786	758	767[11]	610[42]	574

[a] Average of both tilt angles.

communication the reversible one-electron reductions are shifted anodically with respect to perylene ($E_0^{0/-1}$ = −1645 mV) and appear at −1386 (**13**) and −1507 mV (**14**). This is quite remarkable, since the electron donor phenothiazine obviously does not exert a strong electron donation into the perylenyl system. On the basis of the mutual orthogonalization of the substituents it becomes apparent that only the electron withdrawing −I substituent is effective and even causes an anodic shift of the reduction potential of the diphenothiazinyl triad **13**.

Finally, with X-ray structure analyses and oxidation potentials of *N*-aryl-substituted phenothiazines in hand we established a correlation between the tilt angle α and the first oxidation potential for a consanguineous series of phenothiazines (Table 4, Figure 8). The reversible oxidation potentials $E_0^{0/+1}$ and the corresponding tilt angles α correlate reasonably well (r^2 = 0.915) as already supported by theoretical considerations and computations (vide supra). Hence, by extrapolation for a completely planar phenothiazine an oxidation potential of E_0 = 460 mV can be expected. Therefore, on a theoretical and experimental basis the stage has been set for developing planarized phenothiazines with low oxidation potentials for PET applications.

Conclusion

In conclusion, the attempt to synthesize phenothiazine compounds with sterically demanding aryl substituents in the 10-position under *N*-arylation conditions gave rise to the formation of quite unexpected products of arylation and/or oxidative coupling. A unique phenothiazine dimer is formed by an unusual reaction sequence, which cannot be transposed to other related nitrogen-containing heterocycles. However, under Buchwald−Hartwig conditions with bromo anthracenes

and perylene as substrates the expected phenothiazine anthracene or perylene dyads and triads were formed. Investigation of the electronic properties of the sterically demanding *N*-arylphenothiazines by absorption and emission spectroscopy, cyclic voltammetry, and DFT calculations revealed that the individual chromophores are decoupled in the electronic ground state but show unique electronic communication in the excited state. The anthracenyl-bridged diphenothiazine displays an intense electronic coupling of the phenothiazinyl units upon oxidation. All this makes the systems **7**, **10**, **13**, and **14** interesting candidates for photoinduced electron transfer (PET) systems. In a consanguineous series of phenothiazines the folding angle correlates well with the first oxidation potential.

Experimental Sectiojn

General Considerations. Reagents, catalysts, ligands, and solvents were purchased reagent grade and used without further purification. THF and 1,4-dioxane were dried and distilled according to standard procedures.[44] 9-Bromo-2,6-di-*tert*-butylanthracene,[45] 9,10-dibromo-2,6-di-*tert*-butylanthracene,[45] and 3,10-dibromoperylene[46] were prepared in analogy or according to literature procedures. Column chromatography: silica gel 60, mesh 70−230. TLC: silica gel plates. ^{1}H and ^{13}C NMR spectra: CD_2Cl_2, $CDCl_3$, and [D_6]-acetone (locked to Me_4Si).[47] The assignments of quaternary C, CH, CH_2, and CH_3 have been made by using DEPT spectra. Elemental analyses were carried out in the Microanalytical Laboratories of the Organisch-Chemisches Institut, Ruprecht-Karls-Universität, Heidelberg, Germany.

Electrochemistry. Cyclic voltammetry experiments were performed under argon in dry and degassed CH_2Cl_2 at room temperature and at scan rates of 100, 250, 500, and 1000 mV s^{-1}. The electrolyte was Bu_4NPF_6 (0.025 M). The working electrode was a 1 mm platinum disk, the counter electrode was a platinum wire, and the reference electrode was an Ag/AgCl electrode. The potentials were corrected to the internal standard of Fc/Fc$^+$ in CH_2Cl_2 ($E_0^{0/+1}$= 450 mV).[48]

7,16-Dithia-11b,11c-diazadibenzo[*a*,*o*]perylene (4). 10*H*-phenothiazine (200 mg, 1 mmol), 415 mg (3.70 mmol, 3.7 equiv) of potassium *tert*-butoxide, 0.17 mL (1.1 mmol, 1.1 equiv) of bromo mesityl, 9.0 mg (3 mol %) of tri-*tert*-butylphosphine tetrafluoroborate, and 18 mg (2 mol %) of $Pd_2(dba)_3$·dba were dissolved in 5 mL of dry THF, which had been degassed previously with argon. The sealed microwave vessel was stirred for 15 min at 150 °C under dielectric heating (microwave irradiation). (MW: The step under dielectric heating was performed in a SmithCreator (Personal Chemistry AB, Uppsala, Sweden), sealed reaction vessel, ramp time 2 min, temperature measured by infrared sensor, 11.4 bar.) After cooling to rt, the solution was poured into 20 mL of a diluted Na_2SO_3 solution and the aqueous phase was extracted several times with small portions of methylene chloride. The combined organic phases were dried with magnesium sulfate and the solvents were removed in vacuo. The residue was chromatographed on silica gel (hexane/acetone 100:1) to give 86 mg (44%) of **4** as light yellow crystals; mp 108 °C. R_f 0.56(hexane/acetone 5:1). ^{1}H NMR (CD_2Cl_2, 250 MHz) δ 6.90 (d, J = 7.5 Hz, 2 H), 7.02 (d, J = 8.3 Hz, 2 H), 7.10 (t, J = 7.5 Hz, 4 H), 7.19 (d, J = 8.0 Hz, 2 H), 7.41 (d, J = 7.8 Hz, 2 H), 7.48 (d, J = 7.5 Hz, 2 H). ^{13}C NMR (75 MHz, CD_2Cl_2) δ 115.5 (CH), 118.7 ($C_{quat.}$), 120.1 ($C_{quat.}$), 122.3 ($C_{quat.}$), 123.2 (CH), 123.3 (CH), 126.9 (CH), 127.5 (CH), 127.8 (CH), 129.6 (CH), 140.1 ($C_{quat.}$), 141.5 ($C_{quat.}$). UV/vis (CH_2Cl_2) λ_{max} (ϵ) 252 (13500), 276 (15200), 320 (2600), 396 nm (900). IR (film) $\tilde{\nu}$ 2955, 2925, 2854, 1726, 1634, 1465, 1444, 1416, 1241, 1030, 766, 747 cm^{-1}. MS (EI$^+$) *m*/*z* (%) 396.1 (^{34}S − M$^+$, 30), 394.1 (^{32}S − M$^+$, 100), 362.1 (M$^+$ − S, 48), 330.1 (M$^+$ − 2S, 10), 197.0 (M$^+$ − $C_{12}H_{10}NS$). HRMS (EI$^+$) calcd for $C_{24}H_{14}N_2S_2$: 394.0598. Found: 394.0613. Anal. Calcd for $C_{24}H_{14}N_2S_2$·0.5$C_4H_{10}O$ (394.5 + 37.0): C, 72.36; H, 4.44; N, 6.49. Found: C, 72.47, H, 4.52, N, 6.62.

General Procedure for the Buchwald−Hartwig Cross-Coupling Reaction (GP). Under argon atmosphere, 1.0 equiv of the bromo arene, 1.1 equiv of 10*H*-phenothiazine (2.2 equiv in case of dibromo arenes), 3 mol % of $Pd_2(dba)_3$·dba, and 5 mol % of tri-*tert*-butylphosphine tetrafluoroborate were dissolved in 5 mL of dry 1,4-dioxane. The solution was degassed with argon for 5 min. Then, 1.15 equiv of potassium *tert*-butoxide (2.3 equiv in case of dibromo arenes) were added and the reaction mixture was stirred at 101 °C (oil bath temperature) for 14 h. After cooling to rt, the solution was diluted with deionized water, saturated Na_2SO_3 solution, and methylene chloride. The aqueous phase was extracted several times with small portions of methylene chloride, the combined organic phases were dried with magnesium sulfate, and the solvents were removed in vacuo. The residue was chromatographed on silica gel to give the products **5**, **7**, **10**, **11**, **13**, and **14** as solids.

9-(2,4,6-Trimethylphenyl)-10*H*-[3,10′]biphenothiazinyl (5). According to the GP and flash chromatography (hexane/acetone 50:1) on silica gel 125 mg (16%) of **5** were obtained as colorless needles; mp 114−115 °C. ^{1}H NMR (300 MHz, CD_2Cl_2) δ 2.05 (s, 6 H), 2.36 (s, 3 H), 5.68 (br, 1 H), 6.28 (d, J = 9.0 Hz, 2 H), 6.50 (d, J = 9.6 Hz, 1 H), 6.76−7.05 (m, 14 H). ^{13}C NMR (75 MHz, CD_2Cl_2) δ 20.5 (CH_3), 21.2 (CH_3), 113.9 (CH), 116.2 (CH), 116.4 (CH), 118.0 ($C_{quat.}$), 120.1 ($C_{quat.}$), 121.4 ($C_{quat.}$), 121.5 (CH), 122.6 ($C_{quat.}$), 122.7 (CH), 123.3 ($C_{quat.}$), 124.3 ($C_{quat.}$), 125.3 (CH), 126.0 (CH), 126.8 (CH), 127.2 (CH), 127.6 (CH), 127.8 (CH), 128.2 (CH), 129.1 (CH), 129.2 (CH), 129.3 (CH), 130.3 (CH), 132.6 ($C_{quat.}$), 135.5 ($C_{quat.}$), 137.2 ($C_{quat.}$), 137.5 ($C_{quat.}$), 138.5 ($C_{quat.}$), 139.0 ($C_{quat.}$), 142.1 ($C_{quat.}$), 144.7 ($C_{quat.}$). UV/vis (CH_2Cl_2) λ_{max} (ϵ) 260 (69192), 320 nm (5931). IR (KBr) $\tilde{\nu}$ 1635, 1571, 1486, 1461, 1438, 1307, 1285, 1264, 1239, 1129, 1042, 744 cm^{-1}. MS (EI$^+$) *m*/*z* (%) 514.2 (M$^+$, 100), 316.1 (M$^+$ − $C_{12}H_8NS$, 5), 257.1 (60), 242.1 (37), 225.2 (15), 198.1 (66, M$^+$ − $C_{12}H_8NS$ − Mes). Anal. Calcd for $C_{33}H_{26}N_2S_2$ (514.7): C, 77.01, H, 5.09, N, 5.44. Found: C, 76.90, H, 5.28, N, 5.36.

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Supporting Information Available: Spectroscopic and analytical data of compounds **7**, **8**, **10**, **11**, **13**, and **14**, ^{1}H and ^{13}C NMR spectra, crystallographic data, and molecular modeling coordinates. This material is available free of charge via the Internet at http://pubs.acs.org.

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(44) Becker, H. G. O., Beckert, R., Domschke, G., Fanghänel, E., Habicher, W. D., Metz, P., Pavel, D., Schwetlick, K. *Organikum*, 21st ed.; Wiley-VCH: New York, 2001.

(45) Müller, U.; Adam, M.; Müllen, K. *Chem. Ber.* **1994**, *127*, 437−444.

(46) Zinke, A.; Linner, F.; Wolfbauer, O. *Chem. Ber.* **1925**, *58*, 323−329.

(47) Hesse, M.; Meier, H.; Zeeh, B. *Spektroskopische Methoden in der organischen Chemie*; Georg Thieme Verlag: New York, 1991; p 69.

(48) Zanello, P. In *Ferrocenes*; Togni, A., Hayashi, T., Eds.; VCH: New York, 1995; pp 317−430.