ACADEMIA ROMÂNĂ
Revue Roumaine de Chimie
http://web.icf.ro/rrch/

Rev. Roum. Chim.,
2014, *59*(11-12), 947-952

Dedicated to the memory of
Professor Candin Liteanu on his 100th anniversary

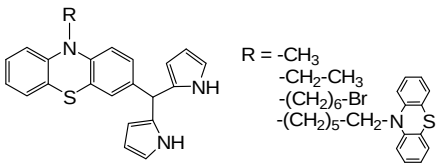
SYNTHESIS OF NOVEL (PHENOTHIAZINYL)DIPYRROLYLMETHANES

Balazs BREM, Emese GAL, Luiza GAINA, Castelia CRISTEA* and
Luminița SILAGHI-DUMITRESCU

Babeş-Bolyai University, Faculty of Chemistry and Chemical Engineering, RO-400028 Cluj-Napoca, Roumania

Received June 16, 2014

An optimized experimental protocol for the preparation of novel (hetero/aryl)dipyrrolylmethane derivatives is described and validated by the synthesis of a series of (phenothiazinyl)dipyrromethanes containing alkyl substituents of increasing bulk (methyl-, ethyl-, 6-bromohexyl- and phenothiazinyl-6-hexyl-) attached to the heterocyclic nitrogen atom of the phenothiazine unit. High yields of the title compounds were obtained by the condensation of N-alkyl-phenothiazin-3-carbaldehydes with pyrrole in the presence of a Lewis acid catalyst and their structural assignments were based on high resolution NMR spectroscopy and mass spectrometry. New *meso*-(N-methyl-phenothiazinyl-dipyrromethene and the corresponding N-methyl-phenothiazinyl-BODIPY dye were prepared and their UV-Vis absorption properties were compared. *Trans* A_2B_2 *meso*-phenothiazinyl-phenyl-porphyrin was prepared starting with N-methyl-phenothiazinyl-dipyrromethane.



INTRODUCTION

The *meso*-substituted porphyrins[1] and the borondifluorodipyrromethene[2] (BODIPY) are two types of versatile functional dyes characterized by intense light absorptions, high fluorescence quantum yields, excellent stability and for these reasons with consecrated as well as promising new applications in the field of analytical chemistry, material science, biology and medicine. Recent literature data reveal an increasing interest for (hetero/aryl)dipyrromethanes as important building blocks for both *meso*-substituted porphyrins and BODIPY fluorophores. The synthetic methodology for the preparation of dipyrromethane was initialy reported in 1994 by Lindsey's group and it was based on the acid catalyzed condensation of an aldehyde with pyrrole.[3] This methodology was further exploited in the preparation of a variety of 5-substituted dipyrromethanes bearing different functional groups. Several refinements were performed in order to improve the reactions performance according to the reactivity of the aldehydes such as: substituted benzaldehydes[4] or heteroaromatic aldehydes (furane-2-carbaldehyde,[5] tiofene-2-carbaldehyde,[6] tetrathiafulvalene-carbaldehyde,[7] pyridine-4-carbaldehyde,[8] pirimidin-5-carbaldehyde[9] and so forth.

The condensation of pyrrole with aldehydes was conducted in homogeneous catalysis conditions using organic acids in organic solvents (*e.g.* trifluoroacetic acid,[4] acetic acid,[10]) or various Lewis acids,[11] as well

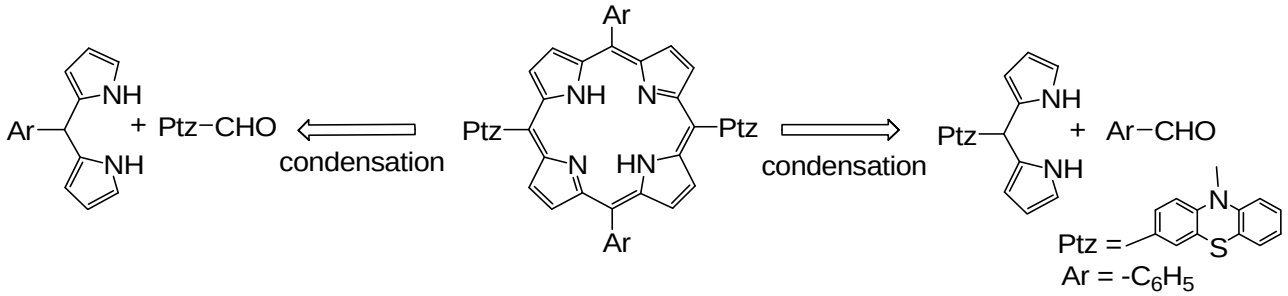
* Corresponding author: castelia@chem.ubbcluj.ro, tel: +40 264 593833

as in water solvent using hydrogenchloride solution[12] assisted by sonication,[13] or tetramethyl-tetra-3,4-pyridinoporphyrazinato copper(II) methyl sulfate[Cu(3,4-tmtppa)](MeSO$_4$)$_4$] as a water soluble catalyst.[14] Solid–liquid heterogeneous catalysis experiments were also reported using sillica-supported sulfuric acid[15] or Amberlyst 15 ion exchange resin.[16] A simple route suitable for the large-scale synthesis of substituted dipyrromethanes was claimed to be the condensation of aldehyde (substituted benzaldehydes, pyridyl-, thienyl-, furyl-carbaldehydes) with pyrrole in water without catalyst at 80 °C,[17] but seems to require a long reaction time. A large excess of pyrrole was usually employed in each case in order to minimize the formation of higher homologues (tripyrromethanes and polymers).

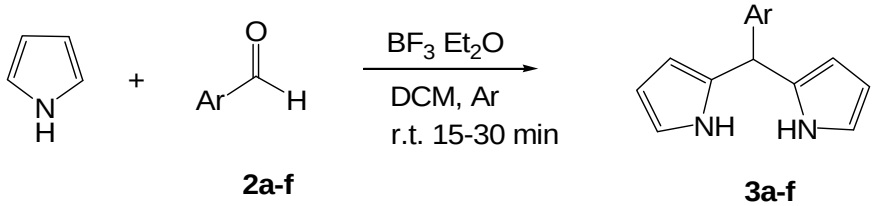
In one of our previous work we emphasized the optical and electron transfer properties of some *meso*-phenothiazinyl-porphyrins together with *in vitro* studies performed for their evaluation as suitable candidates for photodynamic therapy (PDT) of epidermoid carcinoma cell lines.[18] The synthetic strategy employed was based on the mixed condensation of 10-methyl-phenothiazin-3-carbaldehyde and *para*-substituted benzaldehyde derivatives with pyrrole and afforded mixtures of *meso*-phenothiazinyl-phenyl-porphyrins with statistical distribution of the aromatic substituents attached to the porphyne core; after separation by column chromatography A$_3$B and *trans*A$_2$B$_2$ substitution patterns were assigned for the main reaction products. Continuing our interest in this area we believe that a selective preparation of *meso*-phenothiazinyl-porphyrins with distinct *trans*A$_2$B$_2$ substitution pattern could be better achieved by a convergent synthetic methodology which include the phenothiazinyl-dipyrrolylmethanes precursors as illustrated in the retrosynthetic approach from Scheme 1. For this reason, in this work we described an optimized experimental protocol which afforded novel 5-(N-alkyl-phenothiazinyl)dipyrrolylmethane derivatives in high yields.

RESULTS AND DISCUSSION

A series of (hetero/aryl)dipyrrolylmethane **3a-f** containing phenyl or 10-alkyl-phenothiazin-3yl units with various alkyl chain lengths was successfully obtained by the modification of a previously reported procedure.[19] The condensation of the corresponding (hetero)aryl-carbaldehyde **2a-f** with pyrrole took place in dichloromethane solution using $BF_3.Et_2O$ catalyst, as shown in scheme 2. The reaction was performed at room temperature, in the dark and under inert atmosphere (Ar) in order to avoid any oxidative degradation of the product. The reaction progress was monitored by TLC which signaled the presence of dipyrromethane derivatives under UV light as spots dark brown in appearance. The excess pyrrole was removed under reduced pressure and the crude product was purified by column chromatography. Table 1 summarizes the reaction conditions and the results obtained.



Scheme 1

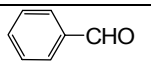
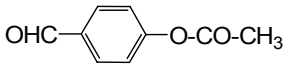
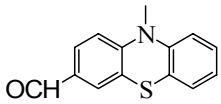
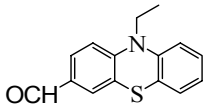
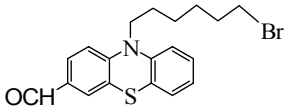
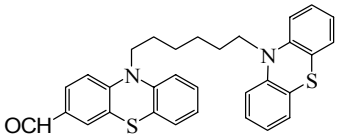


2a-f **3a-f**

Scheme 2

Table 1

Synthesis of (hetero/aryl)dipyrrolylmethane and chemical shifts of the *meso* proton

Entry	Aldehyde **2a-f**	(hetero/aryl)-dipyrrolylmethane	Yield[a] [%]	$\delta_{H\text{-}C(Ar)3}$[b] [ppm]
1		**3a**	67	5.50
2		**3b**	74	5.41
3		**3c**	82	5.37
4		**3d**	81	5.35
5		**3e**	89	5.35
6		**3f**	80	5.39

[a] Isolated after purification by column chromatography
[b] ^{1}H-NMR, 300 MHz, in $CDCl_3$

At room temperature the formation of tripyrrolylmethanes and other oligomeric compounds was observed to be minimized, while a raise in temperature increased the rate of the competitive reactions. As shown in Table 1, the substitution of pyrrole proceeded well under the effect of the mild electrophiles generated by the heteroaryl-carbaldehydes in the presence of catalytic amounts of BF_3; the results were mediocre when benzaldehyde was employed (entry 1), but in the presence of electron donor substituents attached to the aromatic carbaldehyde the reaction yields were slightly increased (entry 2). Phenothiazine-3-carbaldehyde derivatives **2c-f** gave the corresponding (N-alkylphenothiazinyl) dipyrrolylmethanes **3c-f** in 80-89% yields despite the length of the alkyl chain attached to the heterocyclic nitrogen atom (entry 3-6), thus indicating the absence of steric hindrance at the reaction site.

The structure of the (hetero/aryl)dipyrrolylmethane were unambiguously assigned based on recorded ^{1}H–, ^{13}C–NMR and MS spectra. The 300 MHz ^{1}H-NMR spectra appear as first order spectra giving the possibility of complete structural assignment. The symmetrical pyrrol units gave three distinct signals situated at chemical shift ranging in 5.9-6.7 ppm area, the phenothiazine units produced more deshielded signals ranging in the 6.8-7.2 ppm area, while the acidic NH protons gave downfield signals situated around 7.9 ppm. In Table 1 are presented the chemical shifts of the distinctive methyne proton (H-C(Ar)$_3$) which is subjected to a shielding effect induced by the magnetic anisotropy of the aromatic rings and completed by the electronic effects of the substituents; as expected, the phenothiazine units proved the most pronounced electron-donor tendency and thus, the recorded signals for the *meso* protons appeared slightly shielded (entry 3-6). In the EI-MS spectra of each product **3a-f** the molecular ion was recorded in high abundance. The main fragmentation pattern implies the loss of alkyl groups (attached to the phenothiazine core) and the loss of pyrrole units.

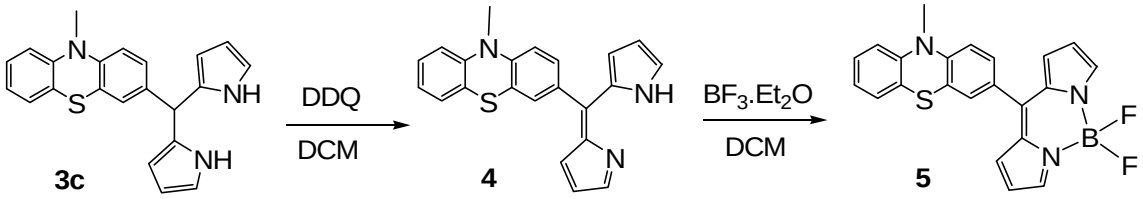
N-methyl-phenothiazinyl-dipyrromethene **4** was prepared by the oxidation of **3c** and further complexation with boron trifluoride generated N-methyl-phenothiazinyl-borontrifluoridedipyrromethene (phenothiazinyl-BODIPY) dye **5** as shown in Scheme 3.

The complete structural assignments of **4** and **5** were performed based on 2D NMR homonuclear correlation (H-H COSY) and heteronuclear (HMQC) experiments. The 2D NMR proton homonuclear correlation spectrum of **5** afforded the discrimination between the coupling patterns of dipyrromethene (δ= 6.5, 6.9 and 7.9 ppm) and

phenothiazine units (δ = 6.8-7.4 ppm). The recorded ^{11}B-NMR shows a shielded signal splitted by the direct coupling of the boron atom with the two fluorine atoms (^{1}J=90.2 Hz).

The UV-Vis absorption properties of the parent phenothiazinyl-dipyrrolylmethane **3c**, phenothiazinyl-dipyrrolylmethene **4** and phenothiazinyl-BODIPY dye **5** are very distinct as shown in Fig. 1. While the parent **3c** had no absorbance in the visible range, the phenothiazinyl-dipyrrolylmethene **4** was characterized by a broad absorption band situated around 430 nm and a bathochromic shift of about 70 nm was achieved by complexation in **5**.

(Phenothiazinyl)dipyrromethane **3c** was also subjected to the condensation with benzaldehyde in the presence of catalytic amounts of trifluoroacetic acid. *Trans* A_2B_2 *meso*-phenothiazinyl-phenyl-porphyrin **6** was thus obtained in 12% yield after the oxidation of the intermediate with *p*-chloranil (Scheme 4).



Scheme 3

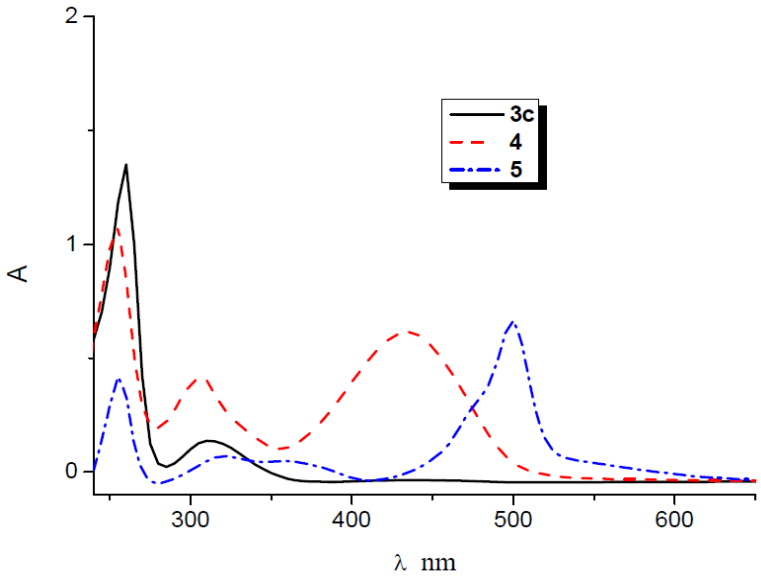
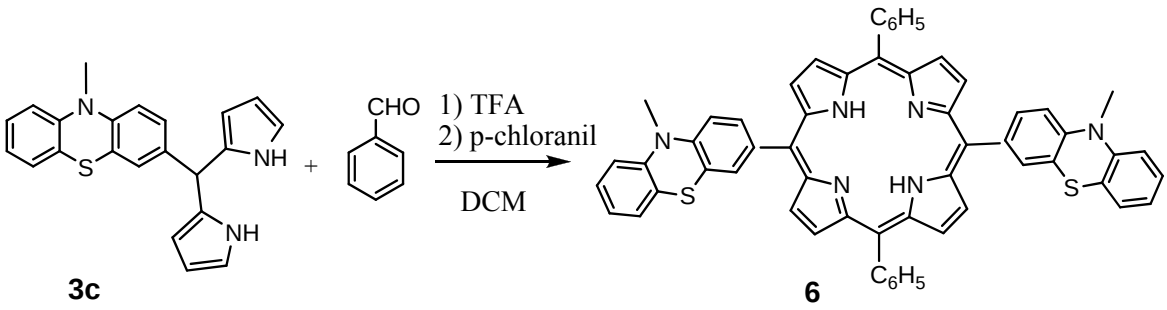


Fig. 1 – UV-Vis absorption spectra of phenothiazinyl-dipyrromethane derivatives in 10^{-4} M DCM solution.



Scheme 4

EXPERIMENTAL

^{1}H and ^{13}CNMR spectra were recorded on Bruker Advance 300 MHz or 400 MHz instruments. The mass spectra were recorded on a GS-MS QP 2010 Shimadzu mass spectrometer and HRMS Thermo LTQ Orbitrap XL**.** The infrared spectra were recorded on a Bruker Vector 22 FT-IR spectrometer with scanning between 4000 and 600 cm^{-1}. Thin layer chromatography was performed on Merck DC Alufolien, silica gel 60 F_{254} and components were visualised by UV VL-

4LC. The melting points were determined in capillaries with an Electrothermal 9100 instrument.

10-Alkyl-10*H*-phenothiazine-3-carbaldehydes **2c-f** were prepared by the Vilsmeyer formylation of the corresponding 10-alkyl-10*H*-phenothiazine.

General procedure for the preparation of (hetero/ aryl)dipyppolylmethanes **3a-f**

A solution of aldehyde **2a-f**(20 mmol) and 20-fold excess pyrrole (28 mL, 400 mmol) in 20 ml dichloromethane were combined in a three neck round bottom flask. The mixture was stirred in the dark at room temperature, degassed with argon for 10 min followed by dropwise addition of $BF_3{\cdot}Et_2O$ (0.2 mmol, 0.1 eq.). Completion of reaction was monitored by TLC; after 15-30 min stirring at room temperature the excess pyrrole was removed under reduced pressure to yield a black/brown oil. The crude product was purified by column chromatography using silica gel support and dichloromethane and *n*-heptane eluent.

2,2'-(phenylmethylene)bis(1H-pyrrole) **(3a)**

Column chromatography (DCM/n-heptane: 2/1, v/v) afforded the product as a yellow solid, 67% yield, m.p. 102-104^{o}C (lit.[14]109-111^{o}C)

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.50 (s, 1H, *meso*H), 5.97 (br s, 2H, Pyrrole $H_{3,3'}$), 6.23 (dd, ^{3}J=2.79, ^{3}J=1.14 Hz, Pyrrole 2H, $H_{4,4'}$), 6.72 (d ^{3}J=1.14 Hz, Pyrrole 2H, $H_{5,5'}$), 7.25-7.41 (m, 5H, ArH), 7.89 (br s, 2H, NH). ^{13}C NMR (75 Hz, $CDCl_3$) δ (ppm): 44.0, 107.3, 108.5, 117.3, 127.0, 128.5, 128.7, 132.6, 142.1.

IR (*KBr*) ν: 3421, 3375, 2960, 1598, 1510, 1492, 1261, 1029, 919, 880, 865, 764, 724, 700 cm^{-1}; EI-MS *m/z* 222 ($M^{+\cdot}$), 156, 146.

4-(di(1H-pyrrol-2-yl)methyl)phenyl acetate[19] **(3b)**

Column chromatography (DCM/n-heptane: 2/1, v/v) afforded the product as a pale yellow solid 74% yields, m.p. 71—73^{o}C

^{1}H NMR (*300 MHz, $CDCl_3$*) δ (ppm): 2.36 (s, 1H, $COCH_3$), 5.41 ppm (s, 1H, *meso*H), 5.96 ppm (br s, 2H, Pyrrole$H_{3,3'}$), 6.25 ppm (dd, ^{3}J=2.82, ^{3}J=1.5 Hz, 2H, Pyrrole$H_{4,4'}$), 6.65 ppm (d^{3}J= 1.5 Hz, 2H, Pyrrole$H_{5,5'}$), 7.07 ppm (d, ^{3}J= 8.52 Hz 2H, Ph $H_{2,6}$), 7.21 ppm (d, ^{3}J= 8.52 Hz, 2H, Ph$H_{3,5}$), 8.04 ppm (br s, 2H, NH). ^{13}C NMR (*75 Hz, $CDCl_3$*) δ (ppm): 20.9, 43.0,107.1, 107.9, 117.3, 121.4, 129.3, 132.3, 139.9, 149.1, 169.9. IR (*KBr*) ν: 3431, 3376, 1727, 1560, 1501, 1430, 1370, 1228, 1200, 1162, 1114, 1084, 919, 882, 862, 768, 719, 630, 597, 569 cm^{-1}. EI-MS*m/z*: 280 ($M^{+\cdot}$), 237, 214, 172, 145, 117, 43.

3-(di(1H-pyrrol-2-yl)methyl)-10-methyl-10H-phenothiazine **(3c)**

Column chromatography (DCM/n-heptane: 1/1, v/v) afforded the product as a pale yellow solid 82% yields, m.p. 77-80^{o}C;

^{1}H NMR (*300 MHz, $CDCl_3$*) δ (ppm): 3.38 (s, 3H, CH_3), 5.37 (s, 1H, *meso*H), 5.96 (br s, 2H, Pyrrole$H_{3,3'}$), 6.21 ppm (m, 2H, Pyrrole$H_{4,4'}$), 6.69 (d, ^{3}J=1.26Hz, 2H, Pyrrole$H_{5,5'}$), 6.99 (d,^{3}J= 8.8Hz 1H, Ptz H_1), 7.01 (d, ^{3}J= 8.0Hz 1H, Ptz H_9), 7.02-7.04(m, 2H, Ptz $H_{2,4}$), 7.16-7.25 (m, 3H, Ptz $H_{6,7,8}$), 7.90 (br s, 2H, NH).

^{13}C NMR (*75 Hz, $CDCl_3$*) δ (ppm): 35.3, 43.0, 107.2, 108.4, 114.1, 117.3, 122.5, 123.1, 123.6, 127, 127.2, 127.5, 127.6, 132.4, 136.4, 144.7, 145.7. IR (*KBr*) ν: 3423, 3358, 1601, 1576, 1557, 1496, 1464, 1400, 1330, 1288, 1257, 1140, 1110, 1089, 1027, 970, 882, 852, 771, 748, 722 cm^{-1}.EI-MS*m/z*: 357 ($M^{+\cdot}$), 291, 275, 145.

3-(di(1H-pyrrol-2-yl)methyl)-10-ethyl-10H-phenothiazine **(3d)**

Column chromatography (DCM/n-heptane:1/1, v/v) afforded the product as a pale yellow solid 81% yields, m.p. 70-73^{o}C;

^{1}H NMR (*300 MHz, $CDCl_3$*) δ (ppm): 1.42 (t, 3H, CH_3) 3.91 (q, 2H, CH_2), 5.35 (s, 1H, *meso*H), 5.94 (br s 2H, Pyrrole $H_{3,3'}$), 6.18 (m, 2H, Pyrrole $H_{4,4'}$), 6.67(dd,^{3}J=2.5 Hz, 2H, Pyrrole $H_{5,5'}$), 6.82 (d, ^{3}J= 8.9Hz, 1H, Ptz H_1), 6.88 (d, ^{3}J= 8.2Hz 1H, Ptz H_9), 6.93-6.99 (m, 3H, Ptz $H_{2,4,6}$), 7.11-7.19 (m, 2H, Ptz $H_{7,8}$), 7.86 (br s, 2H, NH). ^{13}C NMR (*75 Hz, $CDCl_3$*) δ (ppm): 13.0, 41.7, 43.0, 107.2, 108.4, 115.0117.3, 122.4, 124.1, 124.6, 127.1, 127.31, 127.36, 127.4, 132.4, 136.2, 143.8, 144.8. IR (*KBr*) ν: 3420, 3340, 1599, 1555, 1494, 1464, 1363, 1332, 1285, 1251, 1135, 1110, 1090, 1027, 970, 882, 768, 748, 719 cm^{-1}. EI-MS*m/z*: 371 ($M^{+\cdot}$), 342, 305, 275, 145, 29.

10-(6-bromohexyl)-3-(di(1H-pyrrol-2-yl)methyl)-10H-phenothiazine **(3e)**

Column chromatography (DCM/n-heptane: 1/1, v/v) afforded the product as a yellow solid 89% yields, m.p. 57-60^{o}C;

^{1}H NMR (*300 MHz, $CDCl_3$*)δ (ppm): 1.47 (m, 4H,-CH_2-), 1.73-1.81 (m, 4H, -CH_2-), 3.53 (t,^{3}J= 6.6Hz 2H, >N-CH_2-) 3.84 (t, ^{3}J= 6.8Hz2H, Br-CH_2-), 5.35 (s, 1H, *meso*H), 5.94 (br s, 2H, Pyrrol $H_{3,3'}$), 6.18 (m, 2H, Pyrrol $H_{4,4'}$), 6.68 (d, ^{3}J=1.5Hz, 2H, Pyrrol $H_{5,5'}$), 6.87 (d, ^{3}J=8.1 Hz,1H, Ptz H_9), 6.95(d, ^{3}J=7.53Hz1H, Ptz H_1), 6.96-7.02 (m, 3H, Ptz $H_{2,4,6}$), 7.13-7.18 (m, 2H, Ptz $H_{7,8}$), 7.91 (br s, 2H, NH).^{13}C NMR (*75 Hz, $CDCl_3$*) δ(ppm): 26.2, 26.5, 26.7, 32.5 43.1 45.1 47.2, 107.2, 108.5, 115.4, 117.3, 122.5, 124.8, 125.3, 127.25, 127.29, 127.31, 127.52, 127.55, 132.4, 136.4, 144.2, 145.2.IR (*KBr*) ν: 3417, 3390, 2932, 2855, 1599, 1555, 1573, 1557, 1494, 1464, 1461, 1363, 1332, 1286, 1251, 1152, 1110, 1088, 1027, 969, 882, 770, 748, 710, 644 cm^{-1}. HRMS (*ESI$^+$/MeCN*) m/z calculated: 507.1294, found: 507.1099 [(M+1)]$^+$EI-MS: 507 ($M^{+\cdot}$) less than 1%, 461, 275, 277, 145, 67.

10-(6-(10H-phenothiazin-10-yl)hexyl)-3-(di(1H-pyrrol-2-yl)methyl)-10H-phenothiazine **(3f)**

Column chromatography (DCM/n-heptane: 2/1, v/v) afforded the product as a yellow solid 80%, m.p. 62-65^{0}C

^{1}H NMR (*300 MHz, $CDCl_3$*) δ (ppm): 1.49 (s, 4H, -CH_2-), 1.81-1.83 (m, 4H, -CH_2-), 3.80-3.88 (m, 4H,>N-CH_2-), 5.39 (s, 1H, *meso*H), 5.97 (s, 2H, Pyrrole $H_{3,3'}$), 6.19-6.22 (m, 2H,Pyrrole $H_{4,4'}$), 6.71 (d, ^{3}J=1.5Hz, 2H, Pyrrole $H_{5,5'}$), 6.79 (d, 1H, H_1), 6.85-6.93 (m, 8H, Ptz), 7.14-7.22 (m, 6H, Ptz), 7.92 (br s, 2H, NH).

^{13}C NMR (*75 Hz, $CDCl_3$*) δ (ppm): 26.55, 26.57, 26.7, 32.5, 43.1, 47.14, 47.19, 107.2, 108.5, 115.4, 115.5 , 117.3, 124.7, 125, 125.2, 125.4, 127.3, 127.5, 128.3, 129.1, 132.4, 136.3, 144.2, 145.2, 145.3.

IR (*KBr*) ν: 3415, 3362, 2929, 2851, 1568, 1493, 1461, 1366, 1333, 1285, 1247, 1161, 1086, 1028, 881, 749, 718 cm^{-1}. HRMS (*ESI$^+$/MeCN*) m/z calculated: 625.2454, found: 625.2435[(M+1)]$^+$

3-((1Z)-(1H-pyrrol-2-yl)(2H-pyrrol-2ylidene)methyl)-10-methyl-10H- phenothiazine **(4)**

3c (500 mg, 1.4 mmol) was dissolved in DCM (30 mL), DDQ (320 mg, 1.5 mmol) was added and the mixture was stirred at room temperature for 1 hour. The solvent was evaporated under vacuum and the crude product was purified by column chromatography on silica gel support using eluent DCM/n-heptane (1/1, v/v).

^{1}H NMR (400 MHz, $CDCl_3$)δ (ppm):6.44 (d, ^{3}J=1.6 Hz, 1H, Py), 6.45 (d, ^{3}J=1.48 Hz, 1H, Py), 6.72 (s,1H, Py), 6.73 (s, 1H, Py), 6.84-6.88 (m, 2H, Ptz), 6.98 (m, 1H, Ptz), 7.15-7.19 (m, 2H, Ptz), 7.24-7.29 (m, 3H, Py+Ptz), 7.70 (s, 1H, NH)^{13}C-NMR (100 MHz, $CDCl_3$)δ (ppm): 35.6, 101.5, 113.3, 113.4, 114.5, 117.5, 123.2, 127.4, 127.8, 129.9, 130.0, 143. 5, 144.7.

4,4-difluoro-8(10-methyl-10H-phenothiazin-3-yl)-4-bora-3a,4a-diaza-2-indacene **(5)**

4 (355 mg 1mmol) was dissoved in DCM (25 mL) then triethylamine (6 mL, 41 mmol) was added and the mixture was treated with $BF_3.Et_2O$ (6.3 mL, 50 mmol) and further stirred at room temperature for 30 minutes. The solvent was evaporated under vacuum and the crude product was purified by column chromatography on silica gel support using eluent petroleum ether/ethylacetate (9/1, v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.53 (d, ^{3}J=2.6 Hz, 2H, Py), 6.89 (t, ^{3}J=9.4 Hz, 2H, Ptz), 6.97-7.00 (m, 3H, Py+Ptz), 7.17 (d, ^{3}J=7.6 Hz, 1H, Ptz), 7.22 (d, ^{3}J=7.6 Hz, 1H, Ptz), 7.34 (s, 1H, Ptz), 7.38 (d, ^{3}J=8.4 Hz 1H, Ptz) 7.9 (s, 2H, Py). ^{13}C-NMR (100 MHz, $CDCl_3$)δ (ppm): 35.7, 113.8, 114. 7, 118.4, 122.5, 123.5, 124.1, 127.5, 128.0, 128.1, 129.1, 130.8, 131.2, 134.6, 143. 5, 144.7, 146.4, 148.6.

^{11}B-NMR (128.3 MHz, $CDCl_3$)δ (ppm): 0.27 (t, ^{1}J=90.2 Hz).

5,15-Bis-(10-methyl-10H-phenothiazin-3-yl)-10,20-diphenyl-21H,23H-porphyrin **(6)**

3c (780 mg, 3.8 mmol) and benzaldehyde (330 mg, 3.2 mmol) were dissolved in dichloromethane (500 mL) in 1L two neck round-bottom flask. The reaction mixture was stirred in the dark, under a slow stream of nitrogen for 30 min and then trifluoroacetic acid (150 μL) was added in one portion.The reaction mixture was stirred for 24h at room temperature. To the resulted dark red solution a solution of *p*-Chloranil (1.10 g, 4 mmol) indichloromethane (50 mL) was then added in one portion and the mixture was stirred for additional 2h. Triethylamine (0.3 mL) was added to the end of the reaction. The solvent was evaporated to dryness and the crude mixture was purified by column chromatography using toluene/hexane (1/1, v/v).

^{1}H NMR **(**300 MHz, $CDCl_3$) δ (ppm):-2.75 (s, 2H, NH), 3.62 (s, 6H, $-CH_3$), 7.00 (d, ^3J=8Hz, 2H), 7.04 (t, ^3J=7.6Hz,2H), 7.26 (d, ^3J=7.4Hz,2H), 7.3 (t, ^3J=8Hz,2H), 7.4 (d, ^3J=8Hz 2H,), 7.76 (m, 6H), 7.98 (dd, ^4J=1.2Hz, ^3J=8Hz,2H,), 8.02 (d, ^4J=1.2Hz,2H,), 8.22 (d, ^3J= 6Hz 4H), 8.85 (d, ^3J=4.6Hz,4H), 8.9 (d, ^3J=4.6Hz 4H)**^{13}C**-NMRδ (ppm): 35.3,112.3, 114.1, 119.9, 120.2, 122.6, 123.0, 123.5, 127.2, 127.5, 131, 132.8, 133.6, 134.4, 136.3, 142.1, 145.3, 145.6. HRMS:Calcd for: $C_{58}H_{40}N_6S_2$ $[M+H]^+$ 885.2829, Found: 885.2834.

CONCLUSIONS

In conclusion, we reported here the first synthesis of (N-alkylphenothiazine-3-yl)dipyrrolylmethanes **3c-f** based on an optimized experimental protocol which provides a simple and robust route for generating high yields of the target compounds.

The new (phenothiazinyl)dipyrromethene **4** and phenothiazinyl-BODIPY dye **5** were obtained by oxidation of (N-methylphenothiazine-3-yl)dipyrrolylmethane **3c** followed by complexation with $BF_3.Et_2O$.

Trans A_2B_2 *meso*-phenothiazinyl-phenyl-porphyrin **6** was prepared by the acid catalyzed condensation of **3c** with benzaldehyde.

Acknowledgments: This paper is a result of a doctoral research made possible by the financial support of the Sectoral Operational Programme for Human Resources Development 2007-2013, co-financed by the European Social Fund, under the project POSDRU/159/1.5/S/132400 "Young successful researchers – professional development in an international and interdisciplinary environment" (B. Brem).

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