



HAL
open science

Peptoid-phthalocyanine architectures with different grafting positions: Synthetic strategy and photoproperties

Maha Rzeigui, Zeynel Şahin, Olivier Roy, Tuğba Küçük, Ömer Göler, Devrim Atilla, Jameleddine Khiari, Fabienne Dumoulin, Claude Taillefumier

► To cite this version:

Maha Rzeigui, Zeynel Şahin, Olivier Roy, Tuğba Küçük, Ömer Göler, et al.. Peptoid-phthalocyanine architectures with different grafting positions: Synthetic strategy and photoproperties. *Dyes and Pigments*, 2021, 189, pp.109095. 10.1016/j.dyepig.2020.109095 . hal-03166784

HAL Id: hal-03166784

<https://uca.hal.science/hal-03166784v1>

Submitted on 10 Mar 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1 Peptoid-phthalocyanine architectures with different grafting 2 positions: synthetic strategy and photoproperties

3
4 Maha Rzeigui,^{a,b} Zeynel Şahin^c Olivier Roy,^a Tuğba Küçük,^c Ömer Göler,^c Devrim Atilla,^c
5 Jameleddine Khiari,^b Fabienne Dumoulin^{*c,d} and Claude Taillefumier^{*a}

6
7 ^a *Université Clermont Auvergne, CNRS, SIGMA Clermont, ICCF, F-63000 Clermont-*
8 *Ferrand, France*

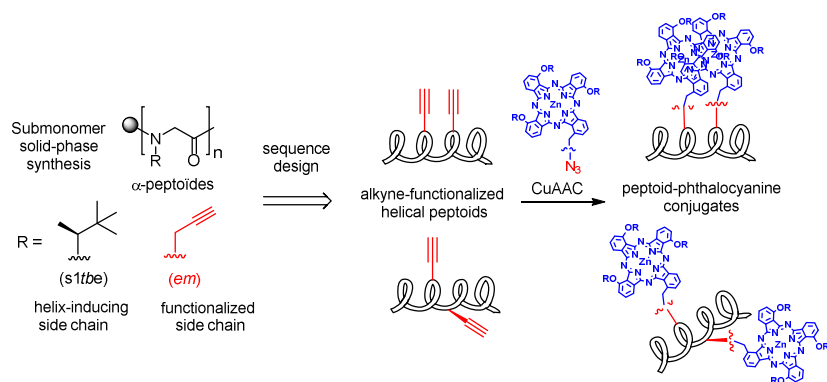
9 ^b *Université de Carthage, Faculté Des Sciences de Bizerte, Laboratoire de Chimie Organique*
10 *et Analytique, ISEFC, 2000, Bardo, Tunisie*

11 ^c *Gebze Technical University, Chemistry Department, Gebze, 41400 Kocaeli, Turkey (valid*
12 *until 31 December 2019 for F.D.)*

13 ^d *Acibadem Mehmet Ali Aydınlar University, Faculty of Engineering, Department of Medical*
14 *Engineering, Istanbul, Turkey*

15

16 Graphical abstract



17

18

19 Abstract

20 A monoazido Zn phthalocyanine has been grafted onto three different alkynyl-functionalized
21 peptoid helices using copper-catalyzed azide–alkyne cycloaddition, demonstrating the
22 feasibility of such conjugates. Their photoproperties have been examined relatively to the
23 spatial geometry induced by the peptoid helix.

24

25 Keywords

26 Peptoid, phthalocyanine, helix, conjugate.

27 **Highlights**

28

29 • Peptoid chains with one and two alkynyl moieties on different residues have been
30 prepared.

31 • A monoazido Zn phthalocyanine has been grafted using copper-catalyzed azide–
32 alkyne cycloaddition

33 • The absorption and fluorescence of these conjugates have been recorded

34

35 1. Introduction

36

37 Porphyrinoids are aromatic macrocycles with an extended electronic delocalization,
38 conferring sought-after electronic and spectroscopic properties, amongst others.¹ Many
39 biomolecules such as chlorophylls,² hemes³ and vitamin B12⁴ are natural porphyrinoid
40 derivatives. The most common porphyrinoids are porphyrins and phthalocyanines, used in
41 several applications fitting the preoccupations of our modern world, such as artificial
42 photosynthesis,⁵ catalysis⁶ and photocatalysis,⁷ photosensitisers for photodynamic therapy,⁸
43 conversion of light into electric current,⁹ amongst others. Many of these applications require
44 multi-porphyrinoids arrays, often to promote photoinduced electron¹⁰ or energy¹¹ transfers or
45 also mimic the antennas in the photosynthetic reaction center of photosystems.¹² Several
46 strategies have been developed to prepare multi-porphyrinoids arrays, either by using covalent
47 (possibly conjugated) bonds,^{13,14} self-assemblies^{15,16,17} or supramolecular edifices¹⁸. Peptoid
48 backbones have been used recently to prepare cofacial arrays of two porphyrins.¹⁹

49

50 Peptoids (*N*-substituted glycine oligomers)²⁰ are a special class of peptide mimics
51 with desirable pharmacokinetic characteristics,²¹ including resistance against enzymatic
52 degradation.²² They can be synthesized in a sequence-specific manner with hundreds of
53 different side chains, thanks to the submonomer method²³ which uses primary amines as a
54 source of side chains diversity.²⁴ For these reasons, they have been investigated for numerous
55 biological applications.²⁵ The supramolecular assembly properties of peptoids also lead
56 researchers to envisage their application as biomaterials.²⁶ The side chains of peptoids are
57 appended to the amide nitrogen atoms rather than to the α -carbons, resulting in tertiary amide
58 bonds. Unlike the peptide secondary amide bonds that are *trans*, with the exception of the
59 prolyl-amide bonds, the peptoid tertiary amide bonds can adopt both the *cis* and *trans*
60 conformations, one of the major cause of peptoid chain conformational flexibility.²⁷ Great
61 efforts have been devoted to controlling the *cis/trans* isomerization of peptoid amides.²⁸ This
62 allowed the identification of predictable discrete secondary structures, *i.e.* peptoid
63 foldamers.²⁹ Some foldamers are based on a defined combination of backbone *cis* and *trans*
64 amides,³⁰ whereas others comprise only *trans*³¹ or *cis*-amides.³² It is now well established that
65 peptoids with bulky α -chiral side chains adopt a helical conformation resembling the all-*cis*
66 polyproline I (PPI) helix, with a 3-fold periodicity and a pitch of approximately 6 Å. The
67 handedness of a peptoid PPI-type helix is governed by the side chains stereochemistries. (*S*)-
68 α -chiral side chains induce right-handed helices while the *R* configuration induces the left-

69 handed one. The most widely-used α -chiral side chains are aromatic, especially the
70 phenylethyl (*pe*)³³ and 1-naphthylethyl (*Inpe*) side chains.^{32a} Beside their bulkiness, it has
71 been reported that local $n \rightarrow \pi^*$ interactions between backbone carbonyls and the aromatic
72 groups might be operative for stabilizing the *cis*-amides required for peptoid helix
73 formation.^{28a-c} The presence of one or several aromatic helical faces may also contribute to the
74 conformational stability of peptoids.^{33a} By contrast, very few studies have so far been
75 undertaken to achieve conformationally stable peptoid PPI-type helices from non-aromatic
76 monomers.^{32b,34} Recently, we demonstrated that the very bulky *tert*-butyl (*tBu*) and α -*gem*-
77 dimethyl groups do provide exclusively the *cis*-amide geometry.³⁵ Another side chain
78 proposed by us with structure-inducing properties is the α -chiral 1-*tert*-butylethyl group
79 (1*tbe*). An octamer sequence consisting of *NtBu* and *Ns1tbe* monomers in equal proportion
80 provided a very stable PPI-type helix, the longest linear peptoid ever solved by X-ray
81 crystallography.^{32b}

82

83 So far, the insertion of one or several porphyrins on peptoid scaffolds has been
84 performed to optimize the cellular uptake efficiency of photosensitising porphyrins^{36,37} or
85 mimic the protein–chlorophyll ensemble found in photosynthetic antenna.³⁸ Jiwon Seo and his
86 team beautifully used peptoid scaffolds to control porphyrin interactions, in the case of pure
87 ^{19,39} or mixed^{40,41,42} porphyrinic arrays.

88

89 In this work, the construction of conformationally stable PPI-type helices is sought
90 after as topological templates to display phthalocyanine arrays. As such architectures are
91 entirely new, this exploratory work aims at demonstrating the synthetic feasibility of such
92 hybrids, at investigating the effect of the peptoid on the photoproperties of the phthalocyanine
93 core, and at assessing the efficiency of the peptoid backbone in controlling the topology of
94 dimeric phthalocyanine arrays.

95

96

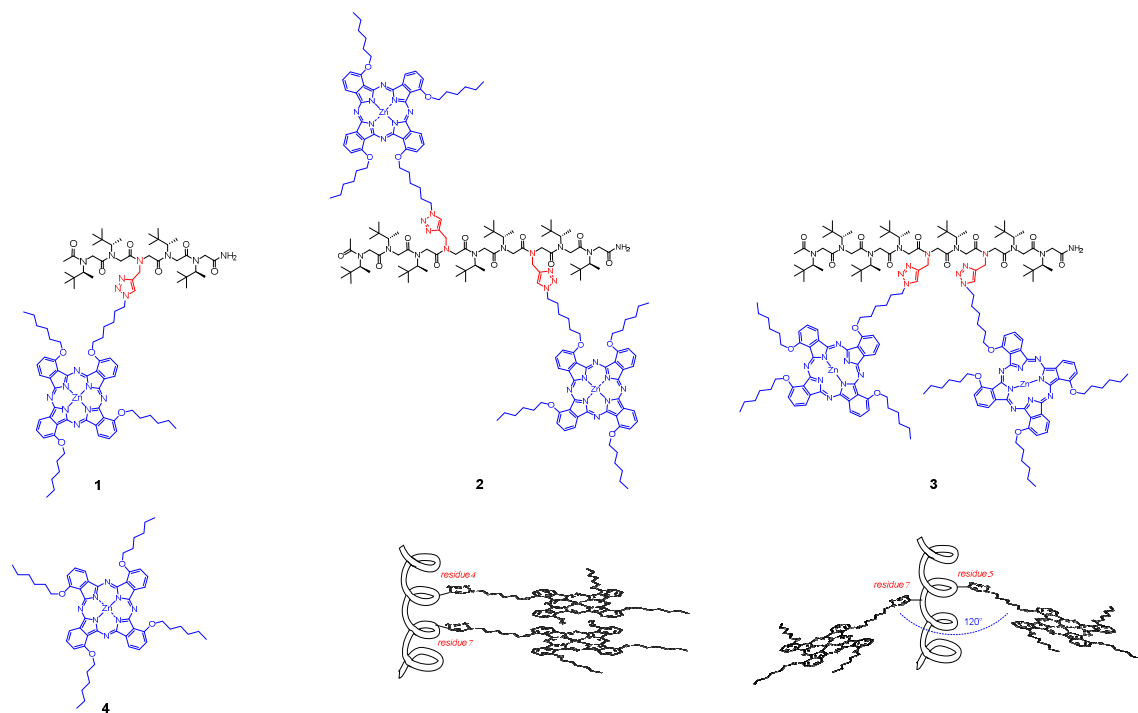
97 **2. Results and discussion**

98

99 **2.1. Molecular design.**

100 All the hybrid structures designed in the framework of these investigations are
101 represented in Fig. 1. The first conjugate **1** made of a single phthalocyanine on a pentapeptoid
102 scaffold was prepared to evaluate the effect of the presence of a peptoid scaffold on the

103 photoproperties of the phthalocyanine core. Hybrids **2** and **3** have each 2 phthalocyanines
 104 grafted on a nonameric peptoid scaffold, with two residues between the two phthalocyanines
 105 in hybrid **2**, and only residue between the two phthalocyanines in hybrid **3**. Phthalocyanine **4**
 106 will be used as the pristine reference phthalocyanine macrocycle.
 107



108
 109 **Fig. 1.** Structures of the peptoid-phthalocyanine architectures **1-3** (with their expected
 110 topology) and of reference phthalocyanine **4**. For each phthalocyanine, only one of the
 111 existing isomers is shown.

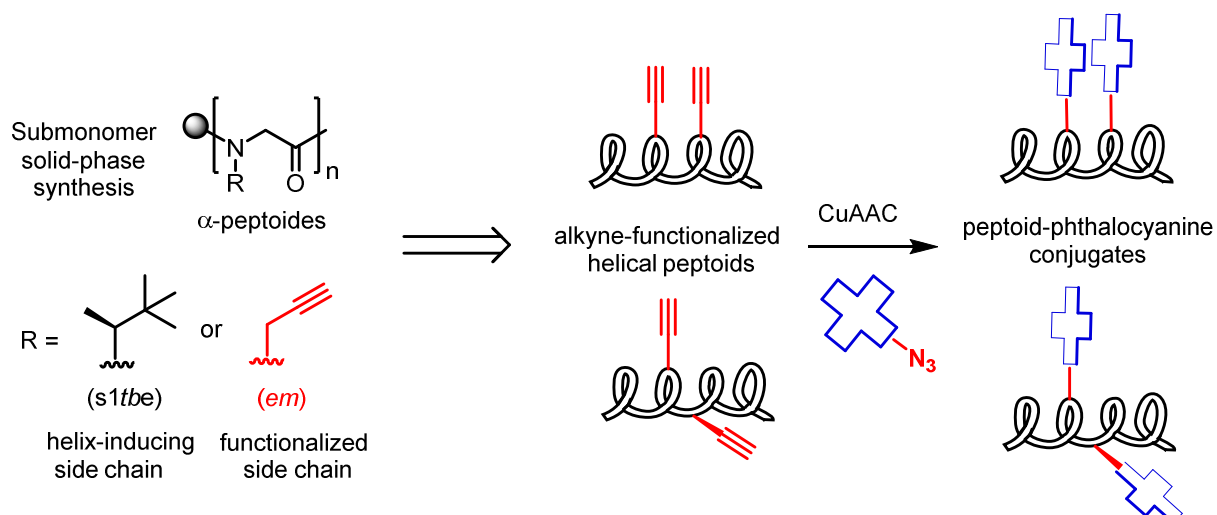
112
 113 The phthalocyanine core was chosen taking into account several considerations: Zn
 114 phthalocyanines have interesting photophysical and photochemical properties which can be
 115 tailored by their substitution pattern,⁴³ and *O*-hexyl non-peripheral substitution is known to
 116 ensure of a satisfying solubility in common organic solvents.⁴⁴

117
 118 The sequence design of the oligomers lies on the 3-fold periodicity of the PPI-like
 119 helix. The aliphatic *Ns1tbe* monomers have been chosen as helical structure inducers (Fig. 2).
 120 Rather than aromatic side chains likely to interact with the phthalocyanine moieties, aliphatic
 121 side chains have been chosen, also because among all the aliphatic side chains tested so far
 122 the chiral bulky *s1tbe* side chain have achieved the best performance as helical structure
 123 inducer. Three peptoid oligomers have been selected: one pentamer (**5**) and two nonamers (**6**

124 and **7**), each with an acetamide and a carboxamide group at the *N*- and *C*-termini (Table 1).
 125 The pentamer **5** comprises a (propargyl side chain as the central residue, flanked on each side
 126 by two *Ns1tbe* residues. Both nonamers are composed of seven *Ns1tbe* and two *Nem* (*N*-
 127 ethynylmethyl glycine) residues. In the sequence of **6**, the propargyl side chains are appended
 128 on residues 4 and 7 (*i* and *i*+3), thus the two functional side chains are expected to be on the
 129 same face of the helix. For the nonamer **7**, the two *Nem* residues correspond to the residues 5
 130 and 7 of the sequence. Consequently, based on the three-fold periodicity, the propargyl side
 131 chains are expected to form a 120° degree angle.

132 The synthetic strategy was conceived as detailed on Fig. 2. To anchor the
 133 phthalocyanines onto the peptoid scaffold, the copper(I)-catalyzed alkyne-azide cycloaddition
 134 (CuAAC) was chosen for its great versatility^{45,46,47} and the easy access to azide-functionalized
 135 phthalocyanines. This implied the introduction of peptoid side chains containing an alkyne
 136 function, which we have demonstrated to be achievable.⁴⁸ Another expected advantage is that
 137 the formed 1,2,3-triazole linker is also, at least to some extent, a *cis*-amide inducer,^{28c} which
 138 may help folding the peptoid chain of the conjugate compounds.

139
 140



141
 142 **Fig. 2.** Retrosynthetic strategy for the preparation of the targeted peptoid-phthalocyanine
 143 conjugates

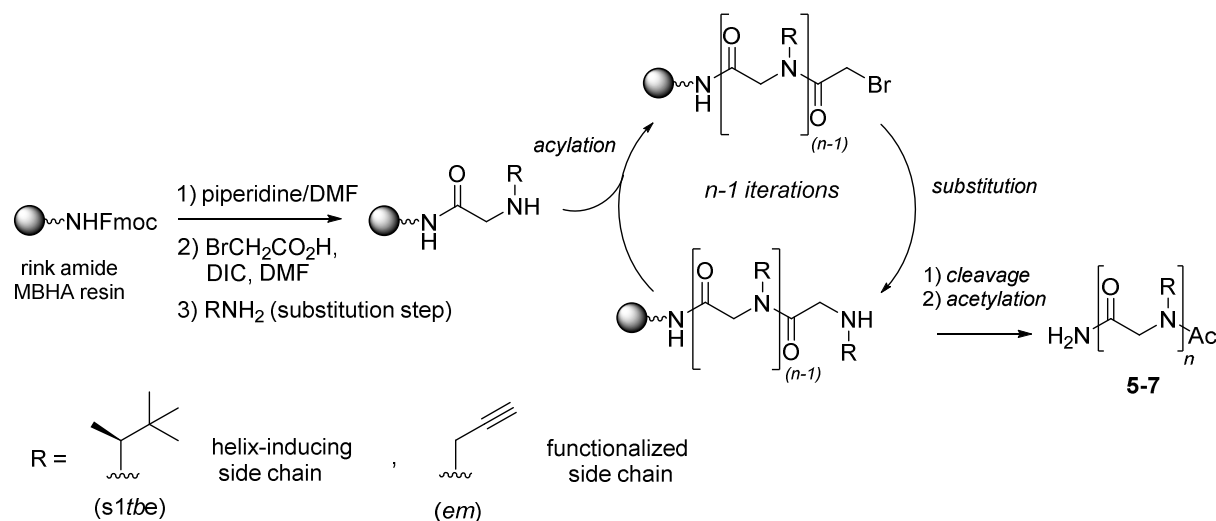
144
 145
 146
 147
 148

2.2. Synthesis and characterization.

149

150 **2.2.1. Propargyl-functionalized peptoid scaffold.** Peptoids are commonly synthesized on
151 solid support by the submonomer method pioneered by Zuckermann.²³ In this method, each
152 new monomer is constructed in two iterative steps: (1) bromoacetylation of the *N*-terminus of
153 the growing chain, (2) introduction of the side chain by bromine atom displacement of the
154 formed bromoacetamide by a primary amine. This process is most often very efficient,
155 yielding to pure peptoids in high yields. The major limitation may originate from the steric
156 hindrance of the formed *N*-terminus secondary amine which may impair chain elongation
157 efficiency. In this work, the solid-phase synthesis of peptoid oligomers comprising *Ns1tbe*
158 monomers was evaluated for the first time. The optimized conditions for the synthesis of
159 peptoids **5-7** are depicted in Scheme 1.

160



169 **Scheme 1.** Solid-phase submonomer synthesis of peptoids **5-7** (optimized conditions).
170 Acylation step: BrCH₂CO₂H (6 equiv., 0.4 M/DMF), diisopropylcarbodiimide (DIC, 8 equiv.,
171 2 M/DMF), 2 x 5 min at 40 °C. Substitution step: 25 equiv. of HC≡CCH₂NH₂, 2M/DMF, 1h
172 at 40 °C or 15 equiv. of *t*BuCH(CH₃)NH₂, 2 M/DMF, 2 x 1h at 40 °C. Cleavage: TFA/DCM
173 (95/5), RT, 10 min. Acetylation: Ac₂O (4 equiv.), Et₃N (2 equiv.), EtOAc (0.2 M), 18h, RT.

167

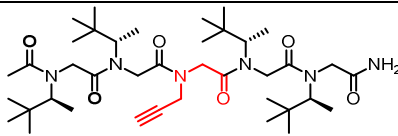
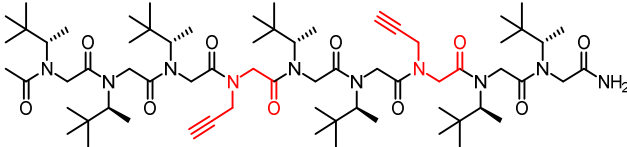
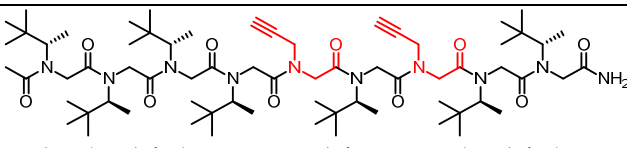
168

169 The syntheses were performed manually using a Fmoc-protected Rink amide MBHA resin as
170 the support, leading to *C*-terminus carboxamides upon cleavage. After several round of
171 optimizations, we found that conducting the two steps of the submonomer protocol under
172 gentle warming (40 °C) had a beneficial effect on the purity of the peptoids. Other important
173 improvements concern the acylation step and the substitution reactions with the bulky (*2S*-

174 3,3-dimethylbutan-2-amine (*sItbe* amine) which were systematically repeated with new
 175 amount of reagents. The final acetylation of the peptoids was carried out in solution (Ac₂O,
 176 Et₃N), after cleavage from the resin, and the compounds were purified by flash
 177 chromatography on silica gel. We have indeed observed that the cleavage of the acetylated
 178 resin-bound peptoids under acidic conditions led to the loss of one residue at the *N*-extremity
 179 of the oligomers (Table 1).

180
 181

182 **Table 1.** Sequence, purity, and mass spectra data of the peptoids **5-7**

peptoid	monomer sequence ^a	overall yield ^b	% purity ^c	expected mass	observed mass
5	 Ac-Ns1tbe-Ns1tbe-Nem-Ns1tbe-Ns1tbe-NH ₂	57	96	718.54	719.54 [M+H] ⁺
6	 Ac-(Ns1tbe) ₃ -Nem-(Ns1tbe) ₂ -Nem-(Ns1tbe) ₂ -NH ₂	46	94	1236.92	1237.92 [M+H] ⁺
7	 Ac-(Ns1tbe) ₄ -Nem-Ns1tbe-Nem-(Ns1tbe) ₂ -NH ₂	56	94	1236.92	1237.92 [M+H] ⁺

183 ^aThe peptoids were drawn with amides in the *trans* conformation by ease of drawing.

184 ^bBased on the resin loading (0.52 mmol.g⁻¹), include all the solid-phase steps and the final
 185 acetylation in solution.

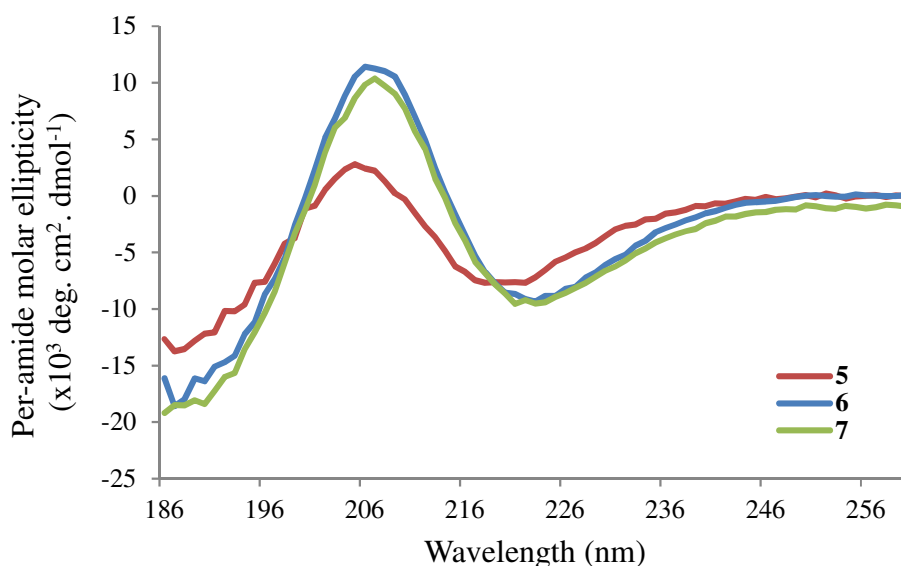
186 ^cDetermined by integration of the high-performance liquid chromatography (HPLC) UV trace
 187 at 214 nm.

188
 189

190 **2.2.2. Conformational studies.** The helical character of the three peptoids **5-7** was assessed by
 191 Circular Dichroism (CD) in methanol (Fig. 3). The three peptoids display the typical signature
 192 associated with the PPI-type helical conformation of peptoid oligomers bearing aliphatic side

193 chains. It is worth noting that peptoids with α -chiral aromatic side chains exhibit a completely
194 different profile resembling that of the peptide α -helix. In our case, the *S* configuration of the
195 *sItbe* side chains produces CD curves with the same right-handed helicity as those of poly-(L-
196 prolines) in alcohol solvents. The curves are characterized by a positive maximum at around
197 210 nm and two minima at 190 and 225 nm. The strong intensities of ellipticity on a per-
198 residue molar basis, at 210 nm for the two nonamers, as compared to literature data, are
199 indicative of well-structured compounds and likely also reflect a cooperative folding process.
200 Unsurprisingly, the short length pentamer is less structurally stable; protohelical structures are
201 generally observed from the tetramer length. Measurements at the Q band wavelength were
202 not expected to be meaningful due to the high concentrations used to record CD and the
203 subsequent aggregation affecting their absorption at this wavelength, unlike porphyrins that
204 are much less prone to aggregation¹⁹.

205



206

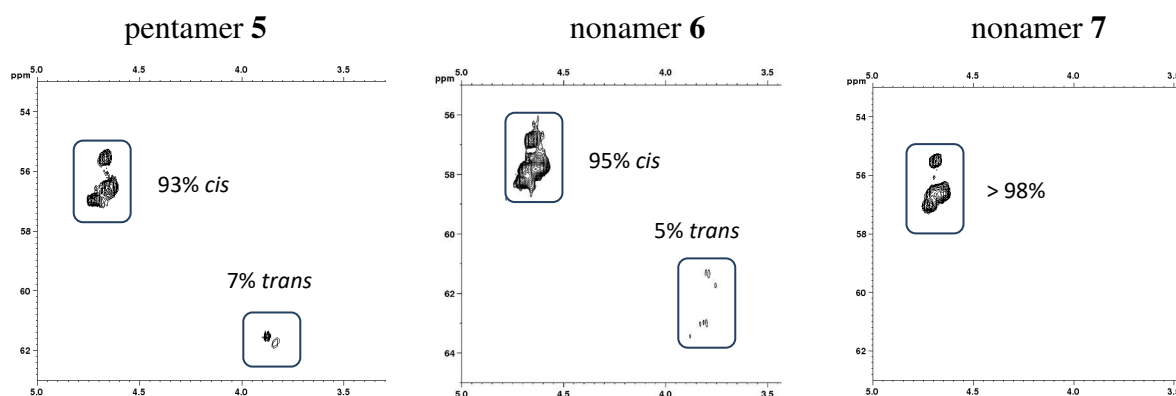
207 **Fig. 3.** CD spectra of peptoid oligomers **5-7** in MeOH at 500 μ M

208

209

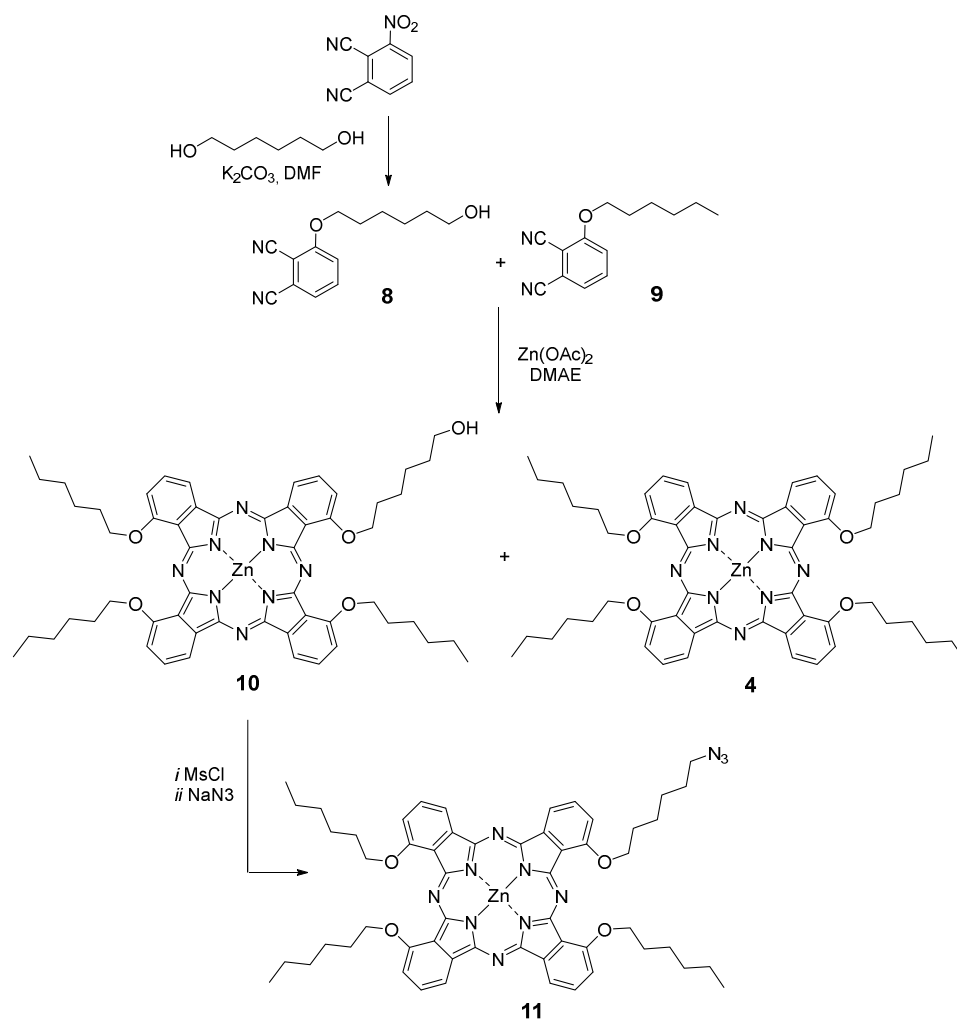
210 As the degree of PPI helical conformational order depends on the population of *cis*-amide
211 bonds, we also estimated overall backbone amide $K_{cis/trans}$ values. As recently described by us,
212 the calculations were made on the basis of the NMR integration (2D-HSQCAD experiments,
213 Fig. 4) of the methyne protons of the *sItbe* side chains, which show distinct resonances
214 depending on the *cis* or *trans* conformation of the amides (Supporting information). This
215 calculation does not take into account the amide bonds connecting the *Nem* residues with their

216 preceding residues, which corresponds to one in five amide bonds in the case of the pentamer
 217 **5**, and two in nine amides in the case of the nonamers **6** and **7**. The overall proportion of *cis*-
 218 amide determined for the amide bonds connecting the *Ns1*be residues with their preceding
 219 residu was found to be 93% for the pentamer **5** ($K_{cis/trans} = 13.2$), and 95% for the nonamer **6**
 220 ($K_{cis/trans} = 21.5$). The *trans*-amide rotamers were no longer detectable in the case of nonamer
 221 **7**, it can be confidently considered that the proportion of *cis*-amides >98% ($K_{cis/trans} > 49.0$) in
 222 this case. These results confirm the high helical character of the nonamer peptoids, the lower
 223 degree of structuration of the pentamer, as seen from CD, appears to be correlated to a
 224 substantial conformational heterogeneity arising from *cis/trans* amide bond isomerization.
 225
 226



227
 228 **Fig. 4.** ^1H - ^{13}C HSQCAD NMR spectra of peptoids **5-7**. Panels display side chains *Ns1*be
 229 methyne protons. Peptoid concentration was ~ 10 mM in CD_3OD .

230
 231
 232
 233 **2.2.3. Synthesis of azidophthalocyanine.** Azidophthalocyanines, especially when an
 234 asymmetric substitution pattern, are often prepared from corresponding hydroxylated
 235 phthalocyanines, via successive mesylation then azidation. Hence monohydroxylated
 236 phthalocyanine **10** was first prepared from phthalonitriles **8** and **9**, reference phthalocyanine **4**
 237 being produced concomitantly. The significant difference in polarity of both phthalocyanines
 238 allowed the quite easy separation by silica gel chromatography. Monohydroxylated
 239 phthalocyanine **10** was first mesylated, and the crude product was immediately reengaged
 240 without further purification in the nucleophilic substitution by sodium azide, yielding
 241 phthalocyanine **11** (Scheme 2).



242

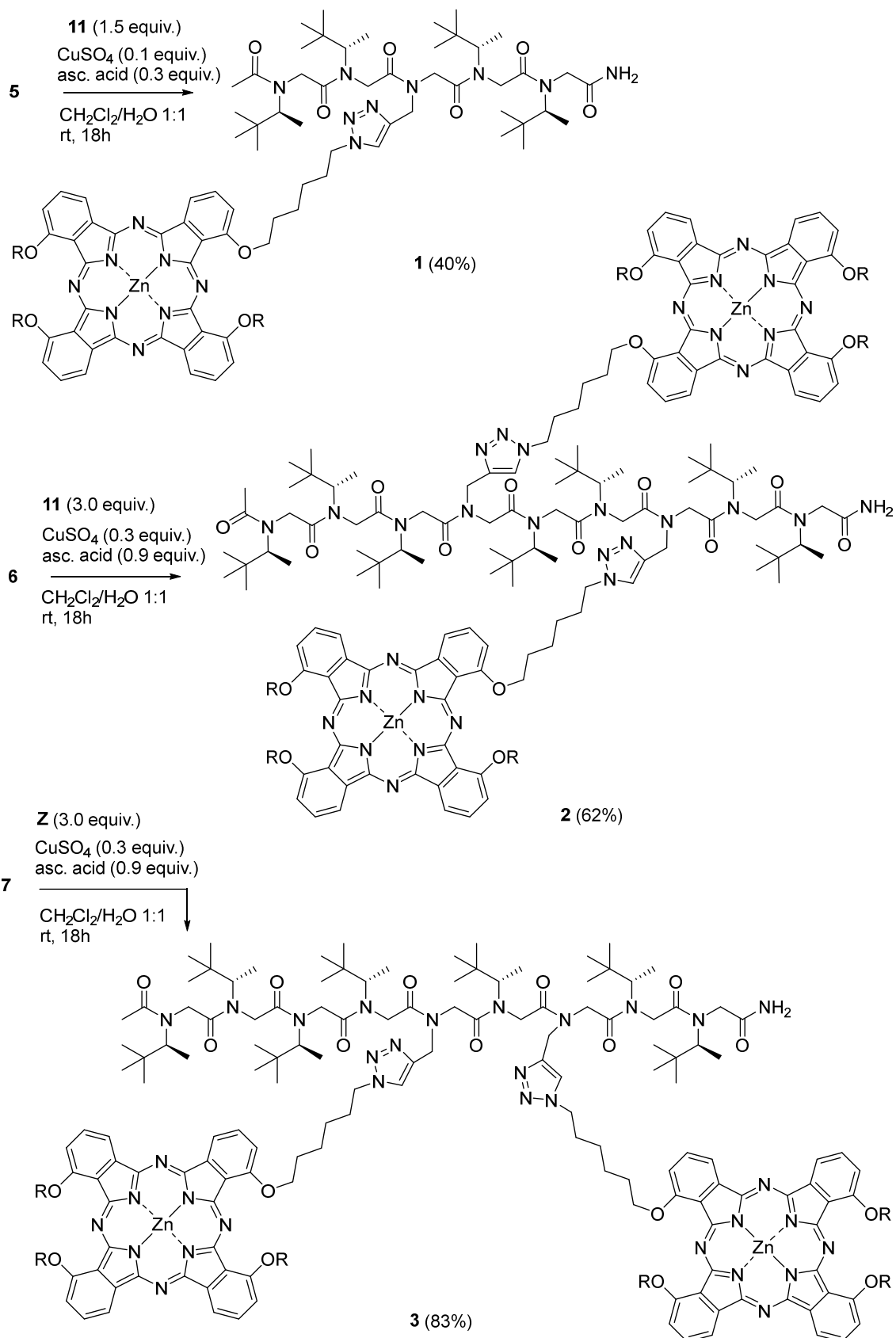
243 **Scheme 2.** Synthesis of azidophthalocyanine **11** and of the reference phthalocyanine **4**. For
 244 each phthalocyanine, only one of the existing isomers is shown.

245

246

247 **2.2.4. Peptoid-phthalocyanine conjugates 1-3.** Access to the three conjugates **1-3** by copper-
 248 catalysed azide-alkyne cycloadditions (CuAAC) was successfully achieved using ligand-free
 249 conditions. The azidophthalocyanine **11** and alkyne-functionalized peptoids were simply
 250 combined in presence of CuSO₄ and ascorbic acid in a biphasic CH₂Cl₂/H₂O solvent system
 251 known to increase CuAAC reaction rates (Scheme 3).⁴⁹ The azidophthalocyanine **11** was used
 252 in a 1.5-fold excess per alkyne functional group to facilitate peptoid conversion. The three
 253 conjugates were first purified on silica gel to remove excess azidophthalocyanine **11**, and then
 254 by size-exclusion chromatography, using THF or dichloromethane as eluent, to eliminate
 255 residual amount of starting peptoids.

256



257

258 **Scheme 3.** Synthesis of the peptoid-phthalocyanine conjugates **1-3**. For each phthalocyanine,

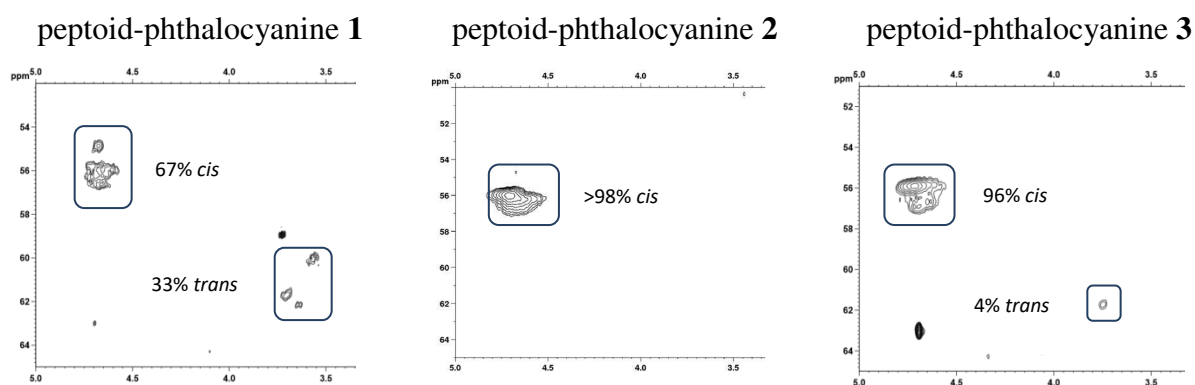
259 only one of the existing isomers is shown.

260

261 CD analysis of peptoid backbone is based on the amide chromophore in the far UV region
262 (240-180 nm), which necessitates the use of UV-transparent solvents, typically, acetonitrile,
263 methanol and water. Unfortunately, the poor solubility of peptoid-phthalocyanine conjugates
264 **1-3** in these solvents prevented their CD analysis.

265 Interestingly, we were able to determine the peptoid amide $K_{cis/trans}$ for the three conjugates,
266 from ^1H - ^{13}C -HSQCAD experiments in deuterated dichloromethane (Fig. 5). As previously,
267 the methyne *cis* and *trans* peaks of the sltbe side chains were integrated for $K_{cis/trans}$
268 determination. We observed a dramatic decrease (84%) in average $^{N_{sltbe}}K_{cis/trans}$ value for the
269 shorter peptoid oligomer conjugate **1** (*cis/trans* ratio ~2:1), relative to its parent peptoid **5**
270 (>13:1). By contrast, peptoid amide isomerism was not significantly affected in the conjugates
271 **2** and **3** relative to peptoid nonamers **6** and **7**, respectively. Interestingly, the conformational
272 homogeneity is even increased for the conjugate **2**, for which the *trans* rotamers are no longer
273 detectable. The opposite is observed for the conjugate **3** relative to **7**. A small proportion of
274 *trans*-amide rotamers (4%) are observed for **3**, while the parent nonamer **7** was completely
275 homogeneous in term of amide rotamerism. Overall, the conformational homogeneity of the
276 two peptoid-phthalocyanine conjugates **2** and **3** is remarkable, especially considering the size
277 of the phthalocyanine moieties relative to the peptoid templates, and also, the potential intra-
278 and inter-molecular interactions they can establish. The unique conformation known for
279 peptoids displaying all-*cis* amides is the PPI helix, the most likely outcome for the two
280 nonameric conjugates.

281
282



283 **Fig. 5.** ^1H - ^{13}C HSQCAD NMR spectra of peptoids **1-3**. Panels display side chains N_{sltbe}
284 methyne protons. Peptoid concentration was ~ 5 mM in deuterated dichloromethane.

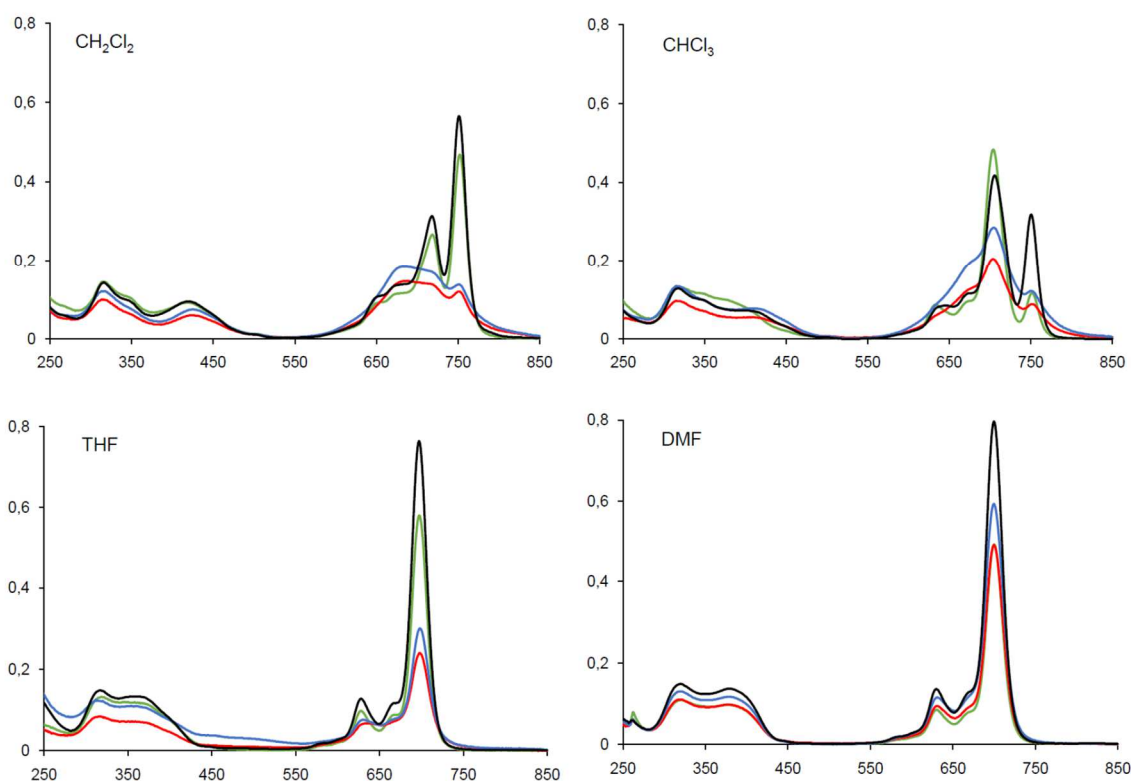
285

286 **2.3. UV-vis spectroscopy.**

287 The photoproperties of phthalocyanines are depending on structural factors (metal,
288 nature, number and position of substituents) as well as on external parameters such as the
289 solvent, concentration and temperature. As all compounds **1-4** have the same phthalocyanine
290 core, and for the sake of comparisons, UV-vis spectra of **1-4** have been first recorded in
291 different solvents. As derivatives **2** and **3** have twice the amount of phthalocyanines, 2 μM
292 concentrations were used for **2** and **3** whereas 4 μM concentrations were used for **1** and **4**
293 (Fig. 6). The maximum absorption for the Q band in each solvent is summarized in Table 2,
294 together with the extinction coefficient values. Spectra used to determine these values are
295 displayed in the supplementary material (Figs S1-16).

296

297



298

299 **Figure 6.** Superimposed UV-vis spectra of **1** (green, 4 μM), **2** (red, 2 μM), **3** (blue, 2 μM) and
300 **4** (black, 4 μM) in dichloromethane (top left), chloroforme (top right), tetrahydrofurane
301 (bottom left) and dimethylformamide (bottom right)

302

303 The first observation is that the presence of a peptoid helix and of the triazole ring does not
304 affect by itself the photoproperties of the phthalocyanine macrocycle, as can be deduced when
305 comparing spectra of **1** and **4**, whose spectra have roughly the same shape and intensity in all
306 solvents, with the presence of H-aggregates in chlorinated solvents characterised by the

307 apparition of a red-shifted second Q band in THF and DMF. Conjugates **2** and **3** are very
 308 aggregated in dichloromethane and in chloroform, as evidenced by their large and potato-
 309 shaped Q band. In THF and DMF, their Q band is sharper but the absorption is much less
 310 intense than for **1** and **4**. As the overall concentration of phthalocyanines is the same in all the
 311 samples, one can infer that it is due to their spatial proximity induced by the grafting of two
 312 phthalocyanine units on a same peptoid backbone, who therefore interact with each other. The
 313 position of the phthalocyanine on the peptoid backbone does not affect significantly this
 314 phenomenon. Even though the helix retains its conformation after the grafting, the flexibility
 315 of the C6 spacer between the peptoid backbone and the phthalocyanine core provide enough
 316 freedom of movement to the two macrocycles whose π - π stacking occurs similarly for both
 317 conjugates **2** and **3** in dichloromethane and chloroforme. Tetrahydrofuran and *N,N*-
 318 dimethylformamide both appear to inhibit this intramolecular aggregation, in line with
 319 previous general observations on phthalocyanines.

320

321 **Table 2**

Compound	Solvent	λ_{\max} Q band (nm)	log ϵ
1	CH ₂ Cl ₂	752	5.1
	CHCl ₃	704	5.1
	THF	698	5.2
	DMF	700	5.1
2	CH ₂ Cl ₂	683	4.9
	CHCl ₃	704	5.0
	THF	698	5.0
	DMF	700	5.4
3	CH ₂ Cl ₂	682	5.0
	CHCl ₃	704	5.1
	THF	698	5.2
	DMF	698	5.5
4	CH ₂ Cl ₂	751	5.2
	CHCl ₃	705	5.1
	THF	697	5.3
	DMF	700	5.3

322

323 **2.3. Fluorescence**

324 Fluorescence has been recorded in THF to explore more in detail the behaviour of the set of
325 compounds, as it known to be a more sensitive technique. Spectra are displayed on Fig. 7 and
326 data are gathered in Table 3.

327

328

329 **Table 3.**

	Excitation λ_{Ex} (nm)	Emission λ_{Em} (nm)	Stokes shift Δ_{Stokes} (nm)	Φ_{F}
1	698	705	7	0.168
2	698	705	7	0.098
3	698	705	7	0.074
4	700	707	10	0.270

330

331

332 At the working concentrations (normalized at absorption 0.2), a significant effect of the sole
333 presence of the peptoid helix is observed when comparing **1** and **2**. The fluorescence quantum
334 yield (Φ_{F}) of **1** is indeed only 2/3 of those of the reference phthalocyanine **4**. When comparing
335 the data for **3** and **4**, Φ_{F} value is significantly lower than for the monomeric derivatives, and is
336 interestingly slightly higher for **2** than for **3**, even though the helix of conjugate **2** is more
337 likely to promote intramolecular interactions as it would promote co-facial geometry. It
338 confirms the fact the phthalocyanines have enough freedom of movement and hence that their
339 relative configuration is not much affected by the helix configuration but rather by being
340 maintained close to each other by the grafting on the same peptoid backbone.

341

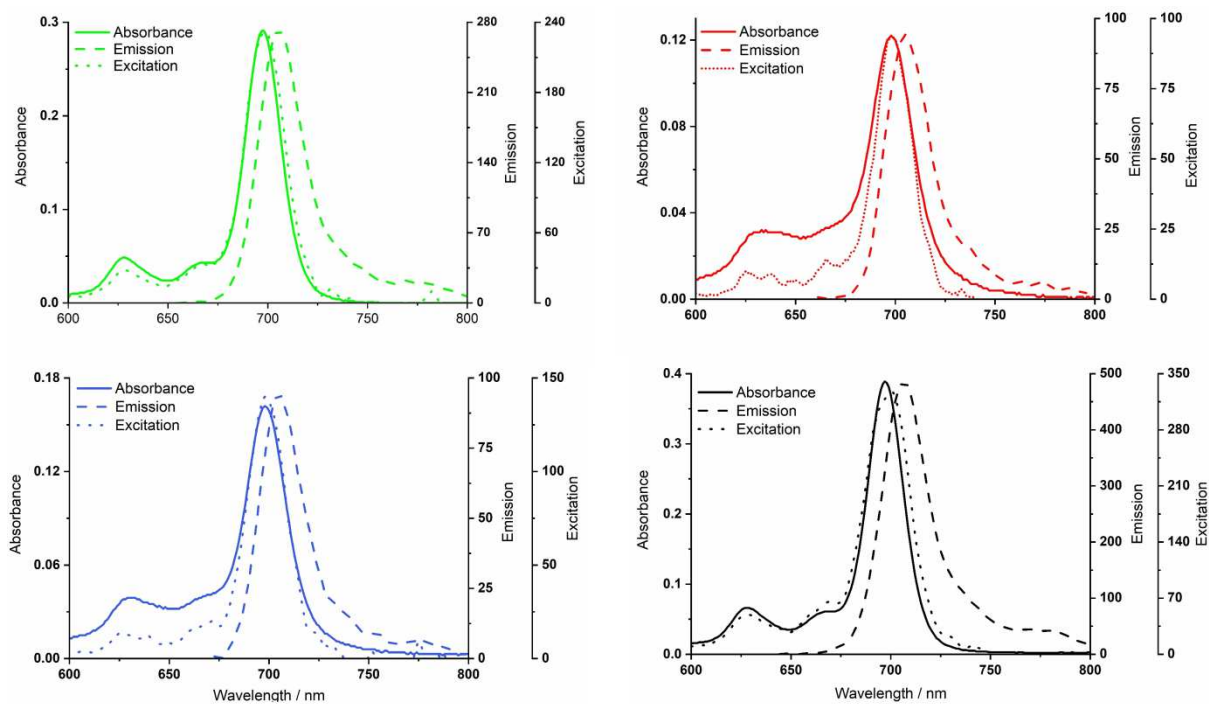


Fig. 7 Normalized fluorescence spectra of compounds **1** (green), **2** (red), **3** (blue) and **4** (black) in tetrahydrofuran

3. Experimental

3.1. Materials and methods.

Synthesis and analysis of compounds 1-3 and 5-7: THF, CH₂Cl₂ were dried over aluminum oxide via a solvent purification system. EtOAc, CH₂Cl₂, cyclohexane, and MeOH for column chromatography were obtained from commercial sources and were used as received. All other solvents and chemicals obtained from commercial sources were used as received. NMR spectra were recorded on a 400 MHz Bruker Avance III HD spectrometer. Chemical shifts are referenced to the residual solvent peak and *J* values are given in Hertz. The following multiplicity abbreviations are used: (s) singlet, (bs) broad singlet, (d) doublet, (t) triplet, (q) quartet, (m) massif, and (br) broad. TLC was performed on Merck TLC aluminum sheets, silica gel 60, F254. Visualizing of spots was effected with UV-light and vanillin in EtOH/H₂SO₄, or ninhidrin or phosphomolybdic acid in EtOH. Flash chromatography was performed with Merck silica gel 60, 40–63 μm. HRMS was recorded on a Micromass Q-ToF Micro (3000 V) apparatus or a Q Exactive Quadrupole-Orbitrap Mass Spectrometer. LC–MS was recorded a Q Exactive Quadrupole-Orbitrap mass spectrometer coupled to a UPLC

363 Ultimate 3000 (Kinetex EVO C18; 1.7 μm ; 100 mm \times 2.1 mm column with a flow rate of
364 0.45 mL min⁻¹ with the following gradient: a linear gradient of solvent B from 5% to 95%
365 over 7.5 min (solvent A = H₂O + 0.1% formic acid, solvent B = acetonitrile + 0.1% formic
366 acid) equipped with a DAD UV/vis 3000 RS detector.

367 *Synthesis of compounds 4 and 8-11*: All solvents and reagents were of reagent grade quality
368 and obtained commercially from Aldrich, Fluka or Merck. Phthalonitrile **9**⁴⁴ and 3-
369 nitrophthalonitrile⁵⁰ were prepared as previously reported. Previously reported procedure for
370 phthalonitrile **8** was slightly modified⁵¹. IR spectra were recorded between 4000 and 650 cm⁻¹
371 using a PerkinElmer Spectrum 100 FT-IR spectrometer. Mass spectra were recorded on a
372 MALDI (matrix assisted laser desorption ionization) BRUKER Microflex LT using dithranol
373 (DIT) or 2,5-dihydroxybenzoic acid (DHB) as the matrix. High resolution mass spectra were
374 measured on an Agilent 6530 Accurate-Mass Q-TOF LC/MS spectrometer equipped with
375 electrospray ionization (ESI) source. NMR spectra of **4**, **8**, **10** and **11** were recorded in
376 deuterated solvents (CDCl₃) on a Varian 500 MHz spectrometer at 298 K. Electronic
377 absorption spectra were measured with a Shimadzu UV-2600 UV-vis spectrophotometer, and
378 a Varian Cary Eclipse spectrofluorometer is used to record steady-state fluorescence emission
379 spectra were recorded by using at room temperature, using 10 mm path length cuvettes.
380 Details about the determination of the fluorescence quantum yields are provided in the
381 supplementary material.

382

383 **3.2. Synthesis of peptoid oligomers.**

384 Peptoid oligomers **5-7** were prepared by solid-phase submonomer synthesis. All steps were
385 carried out manually in 5 mL plastic fritted syringes fitted with a stopcock. The syringes were
386 placed on a benchtop orbital shaker for reaction incubations. Peptoids were synthesized on
387 polystyrene resin with an Fmoc-protected Rink amide MBHA linker (Novabiochem 100-200
388 mesh; 0.52 mmol g⁻¹). The Fmoc-protected resin (0.150 g, 0.078 mmol) was swollen in DMF
389 (2 mL) for 10 min. The swelling was repeated (2x). The Fmoc group was removed by soaking
390 the resin in a 20% piperidine/DMF solution for 15 min at rt after which time the resin was
391 washed with DMF (5 \times 2 ml) and drained. The deprotection reaction was repeated (1x). A
392 solution of bromoacetic acid (65 mg, 0.46 mmol, 6 equiv) in DMF (1.2 mL) was added to the
393 deprotected resin, followed by a solution of diisopropylcarbodiimide (DIC) (0.1 mL, 0.63
394 mmol, 8 equiv) in DMF (0.3 mL). The reaction was heated at 40 °C under stirring for 10 min.
395 This acylation step was repeated (1x) when the growing chain was ended by a bulky *N*-
396 *tert*butylethyl group. The resin was filtered, washed with DMF (5 \times 2 ml) and drained. A

397 solution of amine (for s1tbe 0.16 mL / 0.6 mL DMF 1.17 mmol, 15 equiv; for em 0.124 mL/
398 0.6 mL DMF, 1.95 mmol, 25 equiv) added to the resin, and the reaction mixture was agitated
399 at 40 °C for 1 h.. This step was repeated (1x) in the case of a substitution by the (2S)-3,3-
400 dimethylbutan-2-amine. The resin was filtered, washed with DMF (5x2 mL) and drained. This
401 2-steps sequence of acylation and substitution was repeated until the target oligomer was
402 obtained. After the elongation steps, the resin was washed with CH₂Cl₂ (5 x 2 mL) and
403 drained. The peptoid was cleaved from the resin by stirring in 95% trifluoroacetic
404 acid/CH₂Cl₂ (2 mL) for 10 min at rt. This cleavage procedure was repeated (1x). The resin
405 was washed with CH₂Cl₂ (2 x 2 mL) and the filtrate evaporated under reduced pressure. The
406 residual TFA was eliminated by adding CH₂Cl₂ (5 mL) and evaporation. Identity of the
407 peptoids was controlled by LC-MS (UV detection at 220 nm). The crude oligomers were
408 acetylated in solution. The peptoid was dissolved in EtOAc (0.2 M) and cooled to 0 °C under
409 Ar. Et₃N (2.0 equiv) was added to the stirring solution of amine, followed by addition of
410 acetic anhydride (4 equiv) under Ar. After 2 h at 0 °C, the mixture was allowed to stand
411 overnight at room temperature. The mixture was filtered, and the solids washed with EtOAc.
412 The filtrate was then concentrated in vacuo, yielding the crude *N*-acetylated compound which
413 was purified by flash column chromatography on silica gel. Purity was determined by HPLC
414 (UV detection at 220 nm), and the product identity was confirmed by HRMS before CD and
415 NMR analyses.

416 **Peptoid 5** (*Ac-NsItbe-NsItbe-Nem-NsItbe-NsItbe-NH₂*). Pentamer **5** was isolated as a white
417 solid after purification by flash column chromatography on silica gel. 32.8 mg (0.045 mmol)
418 were obtained. *R_f* = 0.63 (9:1 CH₂Cl₂/MeOH). ¹H NMR (400 MHz, CDCl₃) δ (ppm): 0.76-
419 1.41 (m, 48 H, CH(CH₃)C(CH₃)₃), 1.92-2.26 (m, 4 H, COCH₃ and C≡CH), 3.33-5.10 (m, 16
420 H, 5xNCH₂CO, NCH₂C≡C and 4xCH(CH₃)C(CH₃)₃), 5.52-7.95 (m, 2 H, CONH₂). HRMS
421 (TOF MS ES+) *m/z* calcd for C₃₉H₇₁N₆O₆⁺ [M+H]⁺ 719.5429; found 719.5417.

422 **Peptoid 6** (*Ac-NsItbe-NsItbe-NsItbe-Nem-NsItbe-NsItbe-Nem-NsItbe-NsItbe-NH₂*).
423 Peptoid **6** was isolated as a white solid after purification by flash column chromatography on
424 silica gel. 25.17 mg (0.020 mmol) were obtained. *R_f* = 0.65 (9:1 CH₂Cl₂/MeOH). ¹H NMR
425 (400 MHz, CDCl₃) δ (ppm): ¹H NMR (400 MHz, CDCl₃) δ (ppm): 0.71-1.36 (m, 84 H,
426 CH(CH₃)C(CH₃)₃), 1.92-2.17 (m, 3 H, COCH₃), 2.26-2.49 (m, 2 H, C≡CH), 3.47-4.88 (m, 29
427 H, 9xNCH₂CO, 2xNCH₂C≡C and 7xCH(CH₃)C(CH₃)₃), 5.97-7.92 (m, 2 H, CONH₂). HRMS
428 (TOF MS ES+) *m/z* calcd for C₆₈H₁₂₁N₁₀O₁₀⁺ [M+H]⁺ 1237.9262; found 1237.9267.

429 **Peptoid 7** (*Ac-NsItbe-NsItbe-NsItbe-NsItbe-Nem-NsItbe-Nem-NsItbe-NsItbe-NH₂*).
430 Peptoid **7** was isolated as a white solid after purification by flash column chromatography on

431 silica gel. 54.2 mg (0.043 mmol) were obtained. $R_f = 0.65$ (9:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$). ^1H NMR
432 (400 MHz, CDCl_3) δ (ppm): 0.62-1.37 (m, 84 H, $\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$), 2.00-2.07 (m, 3 H,
433 COCH_3), 2.26-2.39 (m, 2 H, $\text{C}\equiv\text{CH}$), 3.39-4.88 (m, 29 H, $9\times\text{NCH}_2\text{CO}$, $2\times\text{NCH}_2\text{C}\equiv\text{C}$ and
434 $7\times\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$), 5.97-7.92 (m, 2 H, CONH_2). HRMS (TOF MS ES+) m/z calcd for
435 $\text{C}_{68}\text{H}_{121}\text{N}_{10}\text{O}_{10}^+$ $[\text{M}+\text{H}]^+$ 1237.9262; found 1237.9247.

436

437 **3.3. Synthesis of azidophthalocyanine 11**

438 **Phthalonitrile 8.** 3-nitrophthalonitrile (3.46 g, 20 mmol), 1,6 hexanediol (100 mmol, 12.0 g)
439 and K_2CO_3 (500 mmol, 69 g) were stirred overnight at 60 °C in DMF (150 mL), then the
440 reaction mixture was poured into water. The resulting white precipitate was filtrated and
441 purified by column chromatography (silica gel) using $\text{CH}_2\text{Cl}_2/\text{EtOH}$ (50/1) as the eluent.
442 Yield: 53% (2.6 g). $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2$, MW: 244.29 g/mol. FT-IR (ν , cm^{-1}): 3315, 3088, 2935,
443 2861, 2238, 2226, 1978, 1580, 1473, 1453, 1399, 1291, 1177, 1033, 923, 844, 795, 729, 684.
444 ^1H NMR (500 MHz, CDCl_3) δ (ppm): 1.47 (2 H), 1.56 (m, 3 H), 1.90 (2 H), 3.67 (t, 2 H),
445 4.14 (t, 2 H), 7.21 (d, 1 H), 7.33 (d, 1 H), 7.62 (t, 1 H). ^{13}C NMR (125 MHz, CDCl_3), δ
446 (ppm): 25.58, 25.84, 28.81, 32.68, 62.91, 70.03, 110.01, 116.69, 117.37, 125.02, 134.57,
447 161.63.

448 **Hydroxyphthalocyanine 10 and phthalocyanine 4.** Phthalonitrile **8** (300 mg, 1.23 mmol),
449 phthalonitrile **9** (1.4 g, 6.15 mmol), and zinc acetate (0.13 g, 0.61 mmol) were stirred at 140
450 °C for 18 h under argon atmosphere in dry dimethylaminoethanol (6 mL). After evaporation
451 of the solvent, the residue was dissolved in dichloromethane and purified by column
452 chromatography (silica gel) using $\text{CH}_2\text{Cl}_2/\text{EtOH}$ (20/1) as the eluent. Symmetrically
453 substituted phthalocyanine **4** was first eluted, followed by the monohydroxylated AB_3
454 derivative **10**.

455 **Symmetric phthalocyanine 4.** Dark-blue waxy solid. 50 mg. $\text{C}_{56}\text{H}_{64}\text{N}_8\text{O}_4\text{Zn}$, MW 978.56.
456 ATR-IR: ν_{max} (cm^{-1}) 2924, 2853 (aliph. C-H), 1594 (C=N). ^1H NMR (500 MHz, CDCl_3) δ
457 ppm: 0.89-1.06 (m, 12 H, CH_3), 1.25-2.58 (m, 32 H, CH_2), 3.95-4.89 (m, 8 H, CH_2), 6.71-
458 9.04 (m, 12 H, ArCH). ^{13}C NMR (125 MHz, CDCl_3) δ ppm: 14.36, 22.98-32.44, 68.73-69.56,
459 68.55, 70.59, 110.31-157.47. Anal. calc. for $\text{C}_{56}\text{H}_{64}\text{N}_8\text{O}_4\text{Zn}$: 68.74 C, 6.59; H, 11.45; N %,
460 Found: C, 68.50; H, 6.40; N, 11.20. MALDI-TOF: m/z 979.12 $[\text{MH}]^+$. HR-ESI-MS m/z :
461 Calcd for $\text{C}_{56}\text{H}_{65}\text{N}_8\text{O}_5\text{Zn}$: 977.4420, Found 977.4331.

462 **Monohydroxyphthalocyanine 10.** Dark-blue waxy solid. 20 mg. $\text{C}_{56}\text{H}_{64}\text{N}_8\text{O}_5\text{Zn}$, MW 994.56.
463 ATR-IR: ν_{max} (cm^{-1}) 3410 (OH), 2924, 2853 (aliph. C-H), 1594 (C=N). ^1H NMR (500 MHz,
464 $\text{DMSO}-d_6$) δ ppm: 0.81-1.01 (m, 9 H, CH_3), 1.26-1.78 (m, 24 H, CH_2), 1.85-2.31 (m, 10 H,

465 CH₂), 3.50-3.58 (m, 1 H, OH), 4.07-4.94 (m, 8H, CH₂O), 7.27-8.25 (m, 12 H, ArCH). ¹³C
466 NMR (125 MHz, DMSO-*d*₆) δ ppm: 14.65, 22.73-33.40, 61.12, 61.44, 68.55, 70.59, 113.16-
467 156.50. Anal. calc. for C₅₆H₆₄N₈O₅Zn: 67.63 C, 6.49; H, 11.27; N %, Found: C, 67.50; H,
468 6.55; N, 11.35. MALDI-TOF: *m/z* 992.52 [M]⁺. HR-ESI-MS *m/z*: Calcd for C₅₆H₆₅N₈O₅Zn:
469 993.4369, Found 993.4282.

470 **Azido-phthalocyanine (II)**. Monohydroxlated **10** (50 mg, 0.05 mmol) and triethylamine (0.50
471 mL) were stirred in dichloromethane (2 mL) in an ice bath, then mesyl chloride (0.20 mL)
472 was added drop by drop over 10 min. The stirring continues overnight at room temperature,
473 then the reaction mixture was washed by a dilute solution of potassium carbonate then by
474 water. The organic phase was dried on sodium sulfate. The resulting crude mesylated
475 derivative and NaN₃ (0.5 mmol) are stirred in DMF at 80 °C overnight. CAUTION: NaN₃
476 must be kept away from acid medium and be handled with care. Water is then added to the
477 cooled reaction mixture and the resulting precipitate is filtrated, recovered in dichloromethane
478 and purified by column chromatography (silica gel) using CH₂Cl₂:EtOH (20:1) as the mobile
479 phase. Yield 90% (46 mg). C₅₆H₆₃N₁₁O₄Zn, MW 1019.57. ATR-IR: ν_{max} (cm⁻¹) 2924, 2854
480 (aliph. C-H), 2092 (N₃), 1590 (C=N). ¹H NMR (500 MHz, DMSO-*d*₆) δ ppm: 0.77-1.05 (m,
481 9H, CH₃), 1.20-2.37 (m, 34H, CH₂), 4.65, 4.90 (b, 8H, CH₂-O), 7.62-9.08 (m, 12H, ArCH).
482 ¹³C NMR (125 MHz, DMSO-*d*₆) δ ppm: 14.21, 22.52-32.21, 51.29, 55.44, 68.83, 70.76,
483 113.30-156.38. Anal. calc. for C₅₆H₆₃N₁₁O₄Zn: 65.97 C, 6.23; H, 15.11; N %, Found: C,
484 65.40; H, 6.35; N, 15.45. MALDI-TOF: *m/z* 1020.50 [MH]⁺. HR-ESI-MS *m/z*: Calcd for
485 C₅₆H₆₄N₁₁O₄Zn: 1018.4434, Found 1018.4331.

486

487 **3.4. Synthesis of peptoid-phthalocyanine conjugate**

488 **Synthesis of peptoid-phthalocyanine conjugate 1**. To a solution of peptoid **5** (13 mg, 0.0180
489 mmol) and phthalocyanine **11** (20 mg, 0.0216 mmol, 1.2 equiv) dissolved in a biphasic
490 CH₂Cl₂/H₂O (1:1) solvent system (0.5 mL) were added freshly prepared 0.1 M aq. ascorbic
491 acid (0.3 equiv.), and 0.1 M aq. CuSO₄ (0.1 equiv.). After vigorous stirring for 24 h, the
492 mixture was diluted with CH₂Cl₂ (6 mL), washed with water (2 x1 mL), dried over Na₂SO₄,
493 and concentrated in vacuo. The crude residue was purified first by flash column
494 chromatography (SiO₂, 0.1 % EtOH in CH₂Cl₂) and then on Bio-Beads S3 stationary phase
495 (CH₂Cl₂), to yield the peptoid-phthalocyanine conjugates **1** (12.4 mg, 40%) as a green
496 powder. TLC : R_f = 0.63 (9:1 CH₂Cl₂/MeOH). ¹H NMR (400 MHz, DMF-*d*₇) δ (ppm): 0.56-
497 2.32 (m, 91 H, 4×CH(CH₃)C(CH₃)₃, 3×OCH₂(CH₂)₄CH₃, and OCH₂(CH₂)₅), 2.40 (bs, 3 H,
498 COCH₃), 3.63-4.86 (m, 20 H, 4×OCH₂, 5×NCH₂CO, and NCH₂-triazole), 4.88-5.19 (m, 4 H,

499 $4\times\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$, 7.09-9.24 (m, 13 H, $4\times\text{Ar}(\text{CH})_3$, and $\text{C}=\text{CHN}$ -triazole). HRMS (TOF
500 MS ES+) m/z calcd for $\text{C}_{95}\text{H}_{134}\text{N}_{17}\text{O}_{10}^{64}\text{Zn}$ $[\text{M}+\text{H}]^+$ 1736.9785; found 1736.9771. MALDI-
501 TOF: m/z 1735.9712 (calcd. for $\text{C}_{95}\text{H}_{133}\text{N}_{17}\text{O}_{10}^{64}\text{Zn}$; $[\text{M}]^+$; found 1735.171).

502 **Synthesis of peptoid-phthalocyanine conjugate 2.** To a solution of peptoid **6** (10.5 mg,
503 0.0084 mmol) and phthalocyanine **11** (25.1 mg, 0.025 mmol, 3 equiv) dissolved in a biphasic
504 $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ (1:1) solvent system (0.66 mL) were added freshly prepared 0.1 M aq. ascorbic
505 acid (0.9 equiv.), and 0.1 M aq. CuSO_4 (0.3 equiv.). After vigorous stirring for 24 h, the
506 mixture was diluted with CH_2Cl_2 (10 mL), washed with water (2 x2 mL), dried over Na_2SO_4 ,
507 and concentrated in vacuo. The crude residue was purified first by column chromatography
508 (SiO_2 , 0.1 % EtOH in CH_2Cl_2) and then by Bio-Beads S3 (THF), to yield the peptoid-
509 phthalocyanine conjugates **2** (17.2 mg, 62 %) as a green powder. TLC: R_f = 0.65 (9:1
510 $\text{CH}_2\text{Cl}_2/\text{MeOH}$). ^1H NMR (400 MHz, $\text{DMF-}d_7$) δ (ppm): 0.64-2.62 (m, 173 H,
511 $7\times\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$, $6\times\text{OCH}_2(\text{CH}_2)_4\text{CH}_3$, $2\times\text{OCH}_2(\text{CH}_2)_5$ and COCH_3), 3.53-5.33 (m, 45 H,
512 $8\times\text{OCH}_2$, $9\times\text{NCH}_2\text{CO}$, $2\times\text{NCH}_2$ -triazole and $7\times\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$), 6.34-9.30 (m, 26 H,
513 $8\times\text{Ar}(\text{CH})_3$, and $2\times\text{C}=\text{CHN}$ -triazole). HRMS (TOF MS ES+) m/z calcd for
514 $\text{C}_{180}\text{H}_{248}\text{N}_{32}\text{O}_{18}^{64}\text{Zn}_2$ $[\text{M}+2\text{H}]^{2+}$ 1636.9023; found 1636.9044. MALDI-TOF: m/z 3271.790
515 (calcd. for $\text{C}_{180}\text{H}_{246}\text{N}_{32}\text{O}_{18}^{64}\text{Zn}_2$; $[\text{M}]^+$ 3271.7901).

516 **Synthesis of peptoid-phthalocyanine conjugate 3.** The same protocol as for the synthesis of
517 compound **2** was applied to the synthesis of conjugate **3**, which was isolated in 83% yield (22
518 mg), starting from 10 mg of peptoid **7**. TLC: R_f = 0.65 (9:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$). ^1H NMR (400
519 MHz, $\text{DMF-}d_7$) δ (ppm): 0.56-2.65 (m, 173 H, $7\times\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$, $6\times\text{OCH}_2(\text{CH}_2)_4\text{CH}_3$,
520 $2\times\text{OCH}_2(\text{CH}_2)_5$ and COCH_3), 3.54-5.39 (m, 45 H, $8\times\text{OCH}_2$, $9\times\text{NCH}_2\text{CO}$, $2\times\text{NCH}_2$ -triazole
521 and $7\times\text{CH}(\text{CH}_3)\text{C}(\text{CH}_3)_3$), 6.82-9.30 (m, 26 H, $8\times\text{Ar}(\text{CH})_3$, and $2\times\text{C}=\text{CHN}$ -triazole). HRMS
522 (TOF MS ES+) m/z calcd. for $\text{C}_{180}\text{H}_{249}\text{N}_{32}\text{O}_{18}^{64}\text{Zn}_2$ $[\text{M}+3\text{H}]^{3+}$ 1091.6039; found 1091.6047.
523 MALDI-TOF: m/z 3271.790 (calcd. for $\text{C}_{180}\text{H}_{246}\text{N}_{32}\text{O}_{18}^{64}\text{Zn}_2$; $[\text{M}]^+$ 3271.7901).

524

525 4. Conclusions

526 In this work, peptoid oligomers have been used as scaffolds to display phthalocyanines dyes.
527 In this way, the first synthesis and analysis of the photoproperties of peptoid-phthalocyanine
528 conjugates has been achieved. The peptoid oligomers with aliphatic side chains to prevent
529 aromatic interactions were designed to adopt the PolyProline type I conformation
530 characterized by *cis*-amide bonds and the phthalocyanines were grafted by CuAAC reactions.
531 Very importantly, the helix content of the peptoids is conserved upon phthalocyanine grafting,
532 allowing for an accurate comparison of the photoproperties of the conjugates. Measurements

533 of the electronic absorption and fluorescence spectra of the conjugates and of a monomeric
534 reference phthalocyanine showed that the presence of the peptoid backbone has no effect on
535 the photoproperties of the phthalocyanines. Conjugates in which two phthalocyanine units are
536 grafted on a same peptoid backbone exhibit intramolecular aggregation behaviour, due to the
537 fact that the two phthalocyanines are kept close to each other, quite independently of their
538 relative position on the peptoid backbone, probably due to the important flexibility of the
539 spacer used. Further works with more rigid spacers between the phthalocyanine and the helix
540 backbone should allow to better control the interactions between the macrocycles.

541

542 **Acknowledgments**

543 We thank Aurélie Job for HPLC measurements and Martin Lereboure (UCA Partner) for
544 LCMS. M.R. was supported by a grant from the Ministry for Higher Education and Scientific
545 Research of Tunisia. We acknowledge use of the UMS2008-IBSLor Biophysics and
546 Structural Biology core facility at Université de Lorraine for CD measurements.

547

548

549 **References**

[1] Rio Y, Rodríguez-Morgade MS, Torres T. Modulating the electronic properties of porphyrinoids: a voyage from the violet to the infrared regions of the electromagnetic spectrum. *Org Biomol Chem* 2008;6: 1877-1894.

[2] Senge MO, Ryan AA, Letchford KA, MacGowan SA, Mielke T. Chlorophylls, Symmetry, Chirality, and Photosynthesis. *Symmetry* 2014;6:781-843.

[3] a) Poulos TL. Heme Enzyme Structure and Function. *Chem Rev* 2014;114:3919-3962. b) Erdogan H. One small step for cytochrome P450 in its catalytic cycle, one giant leap for enzymology. *J. Porphyrins Phthalocyanines* 2019;23:358-366.

[4] Craig GW. Total synthesis of vitamin B12 - a fellowship of the ring. *J Porphyrins Phthalocyanines* 2015;20:1-20.

[5] Zhang B, Sun L. Artificial photosynthesis: opportunities and challenges of molecular catalysts. *Chem Soc Rev* 2019;48:2216-2264.

[6] a) Sorokin AB. Phthalocyanine Metal Complexes in Catalysis. *Chem Rev* 2013;113:8152-8191. b) Costentin C, Robert M, Savéant JM. Current Issues in Molecular Catalysis Illustrated by Iron Porphyrins as Catalysts of the CO₂-to-CO Electrochemical Conversion. *Acc Chem Res* 2015;48:2996-3006. c) Kariyawasam K, Ricoux R, Mahy J-P. Recent advances in the

field of artificial hemoproteins: New efficient eco-compatible biocatalysts for nitrene-, oxene- and carbene-transfer reactions. *J. Porphyrins Phthalocyanines* 2019;23:1273-1285.

[7] Fukuzumi S, Lee Y-M, Nam W. Photocatalytic redox reactions with metalloporphyrins. *J. Porphyrins Phthalocyanines* 2020;2:21-32.

[8] a) Lo PC, Rodríguez-Morgade MS, Pandey RK, Ng DKP, Torres T, Dumoulin F. The unique features and promises of phthalocyanines as advanced photosensitisers for photodynamic therapy of cancer. *Chem Soc Rev* 2020;49:1041-1056. b) Frochot C, Mordon S. Update of the situation of clinical photodynamic therapy in Europe in the 2003–2018 period. *J. Porphyrins Phthalocyanines* 2019;23:347-357. c) Li X, Zheng B-D, Peng X-H, Li S-Z, Ying J-W, Zhao Y, Huang J-D, Yoon J. Phthalocyanines as medicinal photosensitizers: Developments in the last five years. *Coord. Chem. Rev.* 2019;379:147-160.

[9] Urbani M, Ragoussi ME, Nazeeruddin MK, Torres T. Phthalocyanines for dye-sensitized solar cells. *Coord Chem Rev* 2019;381:1-64.

[10] El-Khouly ME, Ito O, Smith PM, D'Souza F. Intermolecular and supramolecular photoinduced electron transfer processes of fullerene-porphyrin/phthalocyanine systems. *J Photochem Photobiol C: Photochemistry Reviews* 2004;5:79-104.

[11] González-Rodríguez D, Giovanni Bottari G. Phthalocyanines, subphthalocyanines and porphyrins for energy and electron transfer applications. *J. Porphyrins Phthalocyanines* 2009;13:624-636.

[12] Llansola-Portoles MJ, Gust D, Moore TA, Moore AL. Artificial photosynthetic antennas and reaction centers. *C R Chim* 2017;20:296-313.

[13] Ryan A, Gehrold A, Perusitti R, Pinteá M, Fazekas M, Locos OB, Blaikie F, Senge MO. Porphyrin Dimers and Arrays. *Eur J Org Chem* 2011;2011:5817-5844.

[14] Tanaka T, Osuka A: Conjugated porphyrin arrays. synthesis, properties and applications for functional materials. *Chem Soc Rev* 2015;44:943-969.

[15] Medforth CJ, Wang Z, Martin KE, Song Y, Jacobsen JL, Shelnutt JA. Self-assembled porphyrin nanostructures. *Chem Commun* 2009;7261-7277.

[16] Drain CM, Varotto A, Radivojevic I. Self-Organized Porphyrinic Materials. *Chem Rev* 2009;109:1630-1658.

[17] Imahori H, Umeyama T, Kurotobi K, Takano Y. Self-assembling porphyrins and phthalocyanines for photoinduced charge separation and charge transport. *Chem Commun* 2012;48:4032-4045.

-
- [18] a) Fathalla M, Neuberger A, Li SC, Schmehl R, Diebold U, Jayawickramarajah J. Straightforward Self-Assembly of Porphyrin Nanowires in Water: Harnessing Adamantane/ β -Cyclodextrin Interactions. *J Am Chem Soc* 2010;132:9966-9967. b) Prigorchenko E, Ustrnul L, Borovkov V, Aav R. Heterocomponent ternary supramolecular complexes of porphyrins: A review. *J. Porphyrins Phthalocyanines* 2019;23:1308-1325.
- [19] Kang B, Chung S, Ahn YD, Lee J, Seo J. Porphyrin-Peptoid Conjugates: Face-to-Face Display of Porphyrins on Peptoid Helices. *Org Lett* 2013;15:1670-1673.
- [20] Zuckermann RN. Peptoid Origins. *Biopolymers* 2011;96:545-555.
- [21] (a) Kwon YU, Kodadek T. Quantitative Evaluation of the Relative Cell Permeability of Peptoids and Peptides. *Journal of the American Chemical Society* 2007;129:1508-1509. (b) Vollrath SBL, Furniss D, Schepers U, Brase S. Amphiphilic peptoid transporters - synthesis and evaluation. *Org Biomol Chem* 2013;11:8197-8201.
- [22] Miller SM, Simon RJ, Ng S, Zuckermann RN, Kerr JM, Moos WH. Comparison of the Proteolytic Susceptibilities of Homologous L-Amino-Acid, D-Amino-Acid, and N-Substituted Glycine Peptide and Peptoid Oligomers. *Drug Dev Res* 1995;35:20-32
- [23] Zuckermann RN, Kerr JM, Kent SBH, Moos WH. Efficient method for the preparation of peptoids [oligo(N-substituted glycines)] by submonomer solid-phase synthesis. *J Am Chem Soc* 1992;114:10646-10647.
- [24] Culf AS, Ouellette RJ. Solid-Phase Synthesis of N-Substituted Glycine Oligomers (alpha-Peptoids) and Derivatives. *Molecules* 2010;15:5282-5335.
- [25] (a) Patch JA, Kirshenbaum K, Seuryneck SL, Zuckermann RN, Barron AE: Versatile Oligo(N-Substituted) Glycines: The Many Roles of Peptoids in Drug Discovery. ed In *Pseudo-peptides in drug development*; Nielson, P. E., Ed., Wiley-VCH Weinheim, Germany, 2004. (b) Zuckermann RN, Kodadek T. Peptoids as potential therapeutics. *Curr Opin Mol Ther* 2009;11:299-307.
- [26] (a) Knight AS, Zhou EY, Francis MB, Zuckermann RN. Sequence Programmable Peptoid Polymers for Diverse Materials Applications. *Adv Mater* 2015;27:5665-5691. (b) Gangloff N, Ulbricht J, Lorson T, Schlaad H, Luxenhofer R. Peptoids and Polypeptoids at the Frontier of Supra- and Macromolecular Engineering. *Chem Rev* 2016;116:1753-1802.
- [27] Sui Q, Borchardt D, Rabenstein DL. Kinetics and Equilibria of Cis/Trans Isomerization of Backbone Amide Bonds in Peptoids. *J Am Chem Soc* 2007;129:12042-12048.
- [28] (a) Gorske BC, Bastian BL, Geske GD, Blackwell HE. Local and tunable n \rightarrow pi* interactions regulate amide isomerism in the peptoid backbone. *J Am Chem Soc*

2007;129:8928-8929. (b) Gorske BC, Stringer JR, Bastian BL, Fowler SA, Blackwell HE. New Strategies for the Design of Folded Peptoids Revealed by a Survey of Noncovalent Interactions in Model Systems. *J Am Chem Soc* 2009;131:16555-16567. (c) Caumes C, Roy O, Faure S, Taillefumier C. The Click Triazolium Peptoid Side Chain. A Strong cis-Amide Inducer Enabling Chemical Diversity. *J Am Chem Soc* 2012;134:9553-9556. (d) Roy O, Caumes C, Esvan Y, Didierjean C, Faure S, Taillefumier C. The tert-Butyl Side Chain: A Powerful Means to Lock Peptoid Amide Bonds in the Cis Conformation. *Org Lett* 2013;15:2246-2249. (e) Angelici G, Bhattacharjee N, Roy O, Faure S, Didierjean C, Jouffret L, Jolibois F, Perrin L, Taillefumier C. Weak backbone CH \cdots O=C and side chain tBu \cdots tBu London interactions help promote helix folding of achiral NtBu peptoids. *Chem Commun* 2016;52:4573-4576. Gimenez D, Aguilar JA, Bromley EH, Cobb SL. (f) Stabilising Peptoid Helices Using Non-Chiral Fluoroalkyl Monomers. *Angew Chem Int Ed* 2018;57:10549-10553. (g) Wijaya AW, Nguyen AI, Roe LT, Butterfoss GL, Spencer RK, Li NK, Zuckermann RN. Cooperative Intramolecular Hydrogen Bonding Strongly Enforces cis-Peptoid Folding. *J Am Chem Soc* 2019;141:19436-19447.

[29] (a) Horne WS. Peptide and peptoid foldamers in medicinal chemistry. *Expert Opinion on Drug Discovery* 2011;6:1247-1262. (b) Mandity IM, Fulop F. An overview of peptide and peptoid foldamers in medicinal chemistry. *Expert Opin Drug Discov* 2015;10:1163-1177.

[30] (a) Huang K, Wu CW, Sanborn TJ, Patch JA, Kirshenbaum K, Zuckermann RN, Barron AE, Radhakrishnan I. A Threaded Loop Conformation Adopted by a Family of Peptoid Nonamers. *J Am Chem Soc* 2006;128:1733-1738. (b) Crapster JA, Guzei IA, Blackwell HE. A Peptoid Ribbon Secondary Structure. *Angew Chem Int Ed* 2013;52:5079-5084. (c) Gorske BC, Mumford EM, Conry RR. Tandem Incorporation of Enantiomeric Residues Engenders Discrete Peptoid Structures. *Org Lett* 2016;18:2780-2783. (d) Gorske BC, Mumford EM, Gerrity CG, Ko I: A Peptoid Square Helix via Synergistic Control of Backbone Dihedral Angles. *J Am Chem Soc* 2017;139:8070-8073. (e) Dumonteil G, Bhattacharjee N, Angelici G, Roy O, Faure S, Jouffret L, Jolibois F, Perrin L, Taillefumier C. Exploring the Conformation of Mixed Cis-Trans α,β -Oligopeptoids: A Joint Experimental and Computational Study. *J Org Chem* 2018;83:6382-6396.

[31] Shah NH, Butterfoss GL, Nguyen K, Yoo B, Bonneau R, Rabenstein DL, Kirshenbaum K: Oligo(N-aryl glycines). A New Twist on Structured Peptoids. *J Am Chem Soc* 2008;130:16622-16632. Stringer JR, Crapster JA, Guzei IA, Blackwell HE. Construction of Peptoids with All Trans-Amide Backbones and Peptoid Reverse Turns via the Tactical

Incorporation of N-Aryl Side Chains Capable of Hydrogen Bonding. *J Org Chem* 2010;75:6068-6078. Mannige RV, Haxton TK, Proulx C, Robertson EJ, Battigelli A, Butterfoss GL, Zuckermann RN, Whitelam S. Peptoid nanosheets exhibit a new secondary-structure motif. *Nature* 2015;526:415-420.

[32] (a) Stringer JR, Crapster JA, Guzei IA, Blackwell HE. Extraordinarily Robust Polyproline Type I Peptoid Helices Generated via the Incorporation of α -Chiral Aromatic N-1-Naphthylethyl Side Chains. *J Am Chem Soc* 2011;133:15559-15567. (b) Roy O, Dumonteil G, Faure S, Jouffret L, Kriznik A, Taillefumier C. Homogeneous and Robust Polyproline Type I Helices from Peptoids with Nonaromatic α -Chiral Side Chains. *J Am Chem Soc* 2017;139:13533-13540. (c) Zborovsky L, Smolyakova A, Baskin M, Maayan G. A Pure Polyproline Type I-like Peptoid Helix by Metal Coordination. *Chem Eur J* 2018;24:1159-1167.

[33] (a) Wu CW, Sanborn TJ, Huang K, Zuckermann RN, Barron AE. Peptoid oligomers with α -chiral, aromatic side chains. Sequence requirements for the formation of stable peptoid helices. *J Am Chem Soc* 2001;123:6778-6784. (b) Wu CW, Sanborn TJ, Zuckermann RN, Barron AE. Peptoid Oligomers with α -Chiral, Aromatic Side Chains. Effects of Chain Length on Secondary Structure. *J Am Chem Soc* 2001;123:2958-2963.

[34] (a) Wu CW, Kirshenbaum K, Sanborn TJ, Patch JA, Huang K, Dill KA, Zuckermann RN, Barron AE. Structural and spectroscopic studies of peptoid oligomers with α -chiral aliphatic side chains. *J Am Chem Soc* 2003;125:13525-13530. (b) Rzeigui M, Traikia M, Jouffret L, Kriznik A, Khiari J, Roy O, Taillefumier C. Strengthening Peptoid Helicity through Sequence Site-Specific Positioning of Amide cis-Inducing NtBu Monomers. *J Org Chem* 2020;85:2190-2201.

[35] Shyam R, Nauton L, Angelici G, Roy O, Taillefumier C, Faure S. *NC* α -gem-dimethylated peptoid side chains: A novel approach for structural control and peptide sequence mimetics. *Biopolymers* 2019;e23273.

[36] Luo Y, Song Y, Wang M, Jian T, Ding S, Mu P, Liao Z, Shi Q, Cai X, Jin H, Du D, Dong WJ, Chen CL, Lin Y: Bioinspired Peptoid Nanotubes for Targeted Tumor Cell Imaging and Chemo-Photodynamic Therapy. *Small* 2019;15:1902485.

[37] Schröder T, Schmitz K, Niemeier N, Balaban TS, Krug HF, Schepers U, Bräse S: Solid-Phase Synthesis, Bioconjugation, and Toxicology of Novel Cationic Oligopeptoids for Cellular Drug Delivery. *Bioconjugate Chem* 2007;18:342-354.

-
- [38] Kim Y, Kang B, Ahn HY, Seo J, Nam KT: Plasmon Enhanced Fluorescence Based on Porphyrin-Peptoid Hybridized Gold Nanoparticle Platform. *Small* 2017;13:1700071.
- [39] Yang W, Kang B, Voelz VA, Seo J: Control of porphyrin interactions via structural changes of a peptoid scaffold. *Org Biomol Chem* 2017;15:9670-9679.
- [40] Lee YJ, Kang B, Seo J: Metalloporphyrin Dimers Bridged by a Peptoid Helix: Host-Guest Interaction and Chiral Recognition. *Molecules* 2018;23:2741
- [41] Yang W, Jo J, Oh H, Lee H, Chung Wj, Seo J: Peptoid Helix Displaying Flavone and Porphyrin: Synthesis and Intramolecular Energy Transfer. *J Org Chem* 2020;85:1392-1400.
- [42] Kang B, Yang W, Lee S, Mukherjee S, Forstater J, Kim H, Goh B, Kim TY, Voelz VA, Pang Y, Seo J. Precisely tuneable energy transfer system using peptoid helix-based molecular scaffold. *Sci Rep* 2017;7:4786.
- [43] Topal SZ, Işci Ü, Kumru U, Atilla D, Gürek AG, Hırel C, Durmuş M, Tommasino JB, Luneau D, Berber S, Dumoulin F, Ahsen V: Modulation of the electronic and spectroscopic properties of Zn(II) phthalocyanines by their substitution pattern. *Dalton Trans* 2014;43:6897-6908.
- [44] Kobayashi N, Narita F, Ishii K, Muranaka A: Optically Active Oxo(phthalocyaninato)vanadium(IV) with Geometric Asymmetry: Synthesis and Correlation between the Circular Dichroism Sign and Conformation. *Chem Eur J* 2009;15:10173-10181.
- [45] Kolb HC, Finn MG, Sharpless KB. Click Chemistry: Diverse Chemical Function from a Few Good Reactions *Angew. Chem. Int. Ed.* 2001;40:2004-2021.
- [46] Acherar S, Colombeau L, Frochot C, Vanderesse R. Synthesis of Porphyrin, Chlorin and Phthalocyanine Derivatives by Azide-Alkyne Click Chemistry. *Curr. Med. Chem.* 2015;22:3217–3254.
- [47] Dumoulin F, Ahsen V. Click chemistry: The emerging role of the azide-alkyne Huisgen dipolar addition in the preparation of substituted tetrapyrrolic derivatives. *J. Porphyrins Phthalocyanines* 2011;15:481-504
- [48] Aliouat H, Caumes C, Roy O, Zouikri M, Taillefumier C, Faure S. 1,2,3-Triazolium-Based Peptoid Oligomers. *J. Org. Chem.* 2017;82:2386-2398
- [49] Lee BY, Park SR, Jeon HB, Kim KS. A new solvent system for efficient synthesis of 1,2,3-triazoles. *Tetrahedron Lett* 2006;47:5105-5109.
- [50] George RD and Snow AW. Synthesis of 3-nitrophthalonitrile and tetra- α -substituted phthalocyanines. *J. Heterocycl. Chem.*,1995; 32: 495-498.

[51] Wang Z, Gai S, Wang C, Yang G, Zhong C, Dai Y, He F, Yan D and Yang P. Self-assembled zinc phthalocyanine nanoparticles as excellent photothermal/photodynamic synergistic agent for antitumor treatment. *Chem. Engin J* 2019;361:117-128.