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Monoglycoconjugated water-soluble phthalocyanines. Design and synthesis of potential selectively targeting PDT photosensitisers

Yunus Zorlu [a], Fabienne Dumoulin [a], Denis Bouchu [b], Vefa Ahsen [a,*], Dominique Lafont [c,*]

[a] Gebze Institute of Technology, Department of Chemistry, PO Box 141, 41400 Kocaeli, Turkey
[b] Centre Commun de Spectrométrie de Masse UMR 5246, CNRS-Université Claude Bernard Lyon 1, Université de Lyon, Batiment Curien, 43 Bd du 11 Novembre 69622 Villeurbanne Cedex, France
[c] Laboratoire de Chimie Organique II-Glycochimie ICBMS-UMR 5246, CNRS-Université Claude Bernard Lyon 1, Université de Lyon, Batiment Curien, 43 Bd du 11 Novembre 69622 Villeurbanne Cedex, France

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ABSTRACT

A series of asymmetrically substituted phthalocyanines conjugated to four different carbohydrate units has been designed to be used as photosensitisers for potential selective recognition by targeted cells.

Photodynamic therapy (PDT) is a non-invasive powerful treatment of cancer, based on the tumour-localised generation of singlet oxygen by irradiation of photosensitisers.[1] Among the different types of photosensitisers, appropriately metallated and substituted phthalocyanines are gaining increasing interest, thanks to their absorption wavelength fitting the biological window.

In addition to suitable photophysical and photochemical properties,[2] preferential accumulation of the photosensitisers in the tumour is sought to increase efficiency, leading to the development of tumour-targeting phthalocyanines and other functionalized photosensitisers.[3] This strategy led to the development of the so-called third generation of PDT agents, in which the photosensitiser is covalently bioconjugated.[4] Grafting of antibodies, is a common strategy, recently applied to cationic water soluble porphyrins[5] and previously developed on organosoluble,[6] sulfonated[7] or carboxylated[8] water-soluble phthalocyanines. Water-solubility is indeed a challenging property to confer to phthalocyanines,[9] and carbohydrates, even if they are used widely as tumour markers and tumour promotors[10] for many types of molecules, have been mainly used as biocompatible water-solubilizing substituents of phthalocyanines.[11] Related, but more simple substitution by glycerol proved to be an even more efficient means to provide water-solubility to phthalocyanines with no dark cytotoxicity and good photoinactivation.[12] The recent work of Thiem has addressed, from a more biologically oriented point of view, the advantages of the phthalocyanine core as a support for several carbohydrate units, spatially close enough to each other to be likely to mimic their interactions with lectins.[13] The glycoconjugation was achieved on conveniently octafunctionalized phthalocyanines, either octahydroxylated undergoing coupling with glucopyranosyl isocyanate or bearing eight alkyne functions submitted to click reaction with glucopyranosyl azide.[14]

Two advantages can indeed arise from the use of carbohydrates as substituents of photosensitisers, in addition to water-solubility: a potential selective recognition by the targeting cancer cells and/or an increased uptake due to the high energy requirements of cancer cells that consume much more carbohydrate than other cells, as it is a readily available energy source.

Through a structure–activity relationship approach, we sought purpose to establish whether carbohydrate substitution of water-soluble phthalocyanines may lead to their selective recognition. Thus we designed water-soluble phthalocyanines bearing a single carbohydrate unit. Water-solubility is provided by three glycerol units, each attached to an isoindole subunit at the non-peripheral position, as in our previous work we described their powerful

* Corresponding authors. Tel.: +902626053103; fax: +902626053101 (V.A.); tel.: +33426237131 (D.L.).
E-mail addresses: ahsen@gyte.edu.tr (V. Ahsen), dominique.lafont@univ-lyon1.fr (D. Lafont).

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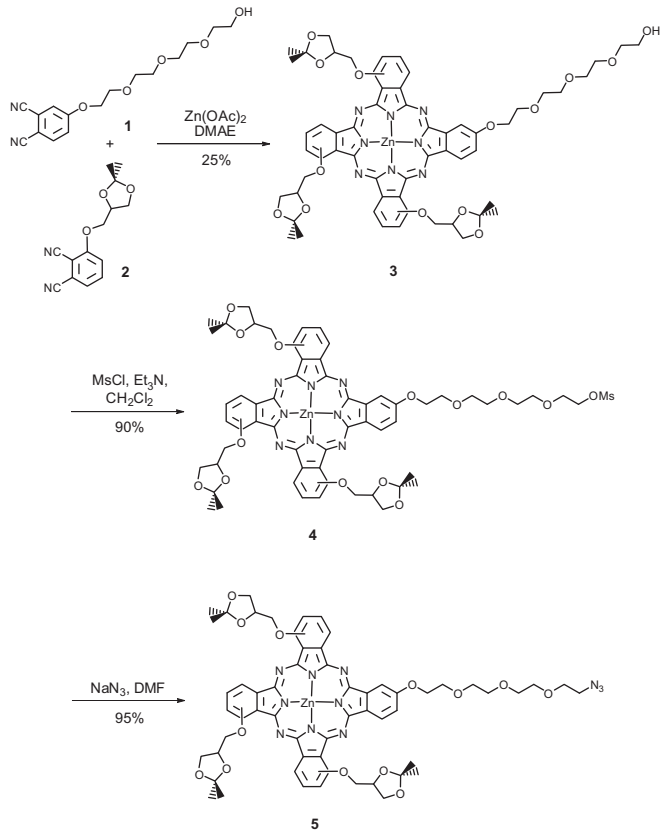
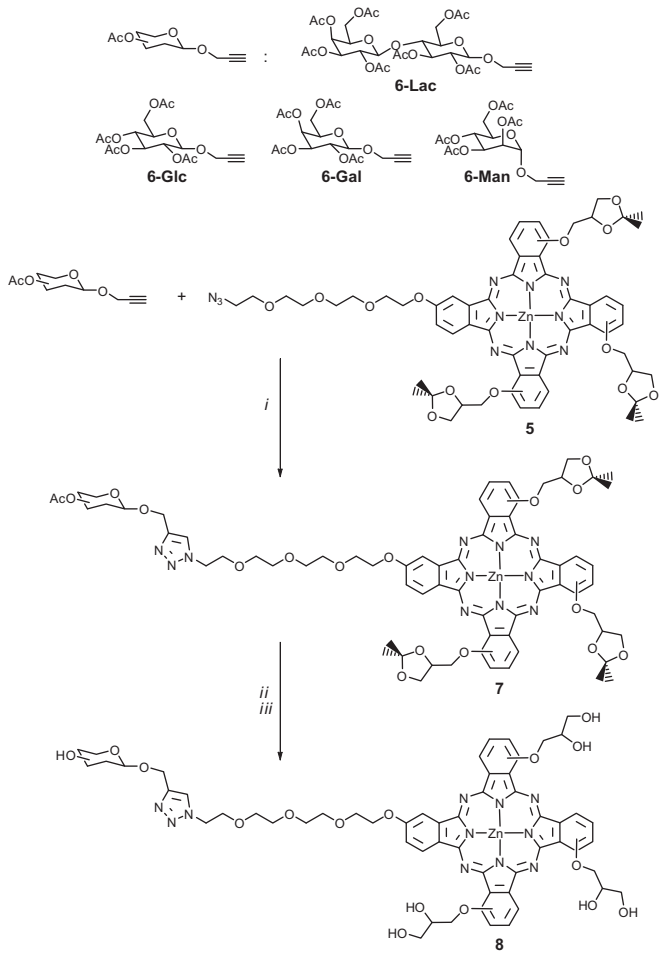


Scheme 1.



Scheme 2. Reagents and conditions: (i) Sodium ascorbate–H_2O–$CuSO_4{\cdot}5H_2O$, rt, 16 h; (ii) 80% AcOH, 70 °C, 6 h; (iii) 2:1:1 MeOH–H_2O–Et_3N, 2 d, rt.

ability to confer water-solubility to phthalocyanines.[12] The carbohydrate unit is linked to a long spacer, avoiding any steric disturbance of the macrocycle during the recognition process and is flexible enough to allow simultaneous multiple carbohydrate recognition. In this preliminary work, four different carbohydrate units were grafted: glucose, galactose, lactose and mannose, as they are among the most commonly encountered. These carbohydrates bearing a propargyl moiety on their anomeric position were grafted onto the azido phthalocyanine **5** via click reaction.

We recently described the successful use of the click reaction on organosoluble Ni(II) phthalocyanines to introduce carbohydrate units on phthalocyanines bearing an azido group.[15] This synthetic strategy was adopted to prepare the azido phthalocyanine **5** as the key intermediate for attaching the carbohydrate moieties via the click reaction.

Formation of the AB3-type asymmetric monohydroxylated phthalocyanine **3** was the starting point for the synthesis. Compound **3** is prepared by cyclotetramerization of a statistical mixture of phthalonitriles **1**[16] and **2**,[12] with a 10-fold excess of **2** in order to limit the number of possible resulting phthalocyanines (Scheme 1). These conditions led to a mixture of the symmetric tetrasolketal-substituted phthalocyanine and the desired asymmetric **3** in a very satisfactory yield (25%),[17] the formation of other statistical products being negligible, as was observed by us during previous work.[15,18]

Mesylation of the hydroxy group of **3** gave **4** which was followed by nucleophilic substitution by sodium azide in DMF at 100 °C, leading to the azido phthalocyanine **5**.[19] Compound **5** underwent click reactions with the four selected peracetylated propargyl carbohydrates **6** (the β-glycosides **6-Glc**,[20] **6-Gal**[20] and **6-Lac**[20] and the α-glycoside **6-Man**[21]), in yields of around 95%.[22] The resulting phthalocyanines **7-Glc**, **7-Gal**, **7-Lac** and **7-Man** were deprotected in two steps:[23] firstly acidic hydrolysis of the acetal (80% acetic acid at 70 °C over 6 h), then removal of the acetyl groups in a 2:1:1 methanol–water–triethylamine mixture (Scheme 2).

The solubility of the four deprotected phthalocyanines **8** in water was evidenced by their UV–vis spectra. Each of the four phthalocyanines exhibited similar UV–vis spectra in water and

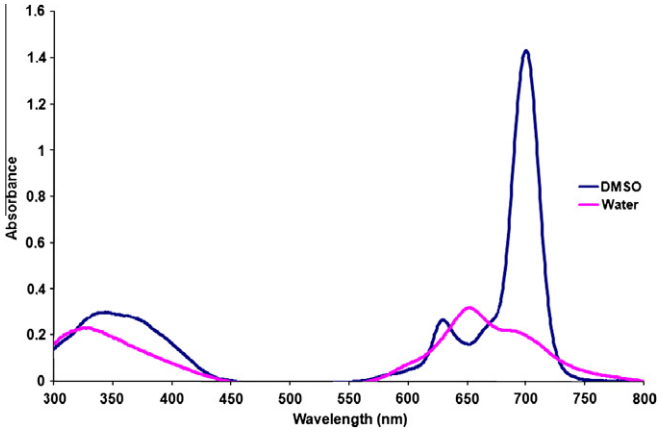


Figure 1. UV–vis spectra of **8-Glc** recorded at 10 μM concentrations (blue: DMSO, pink: H_2O).

DMSO, with no influence due to the nature of the carbohydrate head. They are slightly aggregated in water and monomeric in DMSO, for example as shown for **8-Glc** (Fig. 1). Their solubility in water is similar to those of the symmetric tetra non-peripheral glycerol-substituted Zn(II) phthalocyanine as we previously reported.[12a]

In conclusion, we have developed an efficient method to produce monoglycoconjugated water-soluble phthalocyanines containing one of four different carbohydrate moieties. The next step involves testing these phthalocyanines against different cancer cell lines to determine their potential selective targeting efficiency, and to produce other molecules with more complex carbohydrates which are likely to be more selective.

Acknowledgements

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References and notes

1. (a) Pandey, R. K. *J. Porphyrins Phthalocyanines* **2000**, *4*, 368–373; (b) Macdonald, I. J.; Dougherty, T. J. *J. Porphyrins Phthalocyanines* **2001**, *5*, 105–129; (c) Josefsen, L. B.; Boyle, R. W. *Met.-Based Drugs* **2008**, 1–24; (d) Ali, H.; Van Lier, J. E. *Chem. Rev.* **1999**, *99*, 2379–2450.
2. Tedesco, A. C.; Rotta, J. C. G.; Lunardi, C. N. *Curr. Org. Chem.* **2003**, *7*, 187–196.
3. (a) Taquet, J.-P.; Frochot, C.; Manneville, V.; Barberi-Heyob, M. *Curr. Med. Chem.* **2007**, *14*, 1673–1687; (b) Hudson, R.; Boyle, R. W. *J. Porphyrins Phthalocyanines* **2004**, *8*, 954–975; (c) Sutton, J. M.; Clarke, O. J.; Fernandez, N.; Boyle, R. W. *Bioconjugate Chem.* **2002**, *13*, 249–263; (d) Sibrian-Vazquez, M.; Jensen, T. J.; Vicente, M. G. H. *Org. Biomol. Chem.* **2010**, *8*, 1160–1172.
4. Alonso, C.; Boyle, R. W. In *Handbook of Porphyrin Science*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; World Scientific, 2010; Vol. 4, pp 121–190.
5. Alonso, C.; Palumbo, A.; Bullous, A. J.; Pretto, F.; Neri, D.; Boyle, R. W. *Bioconjugate Chem.* **2010**, *21*, 302–313.
6. Duan, W.; Smith, K.; Savoie, H.; Greenman, J.; Boyle, R. W. *Org. Biomol. Chem.* **2005**, *3*, 2384–2386.
7. Dubuc, C.; Langlois, R.; Bénard, F.; Cauchon, N.; Klarskov, K.; Tone, P.; van Lier, J. E. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 2424–2427.
8. Drechsler, U.; Pfaff, M.; Hanack, M. *Eur. J. Org. Chem.* **1999**, 3441–3453.
9. Dumoulin, F.; Durmuş, M.; Ahsen, V.; Nyokong, T. *Coord. Chem. Rev.* **2010**, *254*, 2792–2847.
10. Kannagi, R.; Sakuma, K.; Miyazaki, K.; Lim, K.-T.; Yusa, A.; Yin, J.; Izawa, M. *Cancer Sci.* **2010**, *101*, 586–593.
11. (a) Maillard, P.; Guerquin-Kern, J.-L.; Momenteau, M. *J. Am. Chem. Soc.* **1989**, *111*, 9125–9127; (b) Alvarez-Mico, X.; Calvete, M. J. F.; Hanack, M.; Ziegler, T. *Tetrahedron Lett.* **2006**, *47*, 3283–3286; (c) Ribeiro, A. O.; Tomé, J. P. C.; Neves, M. G. P. M. S.; Tomé, A. C.; Cavaleiro, J. A. S.; Iamamoto, Y.; Torres, T. *Tetrahedron Lett.* **2006**, *47*, 9177–9180; (d) Ribeiro, A. O.; Tome, J. P. C.; Neves, M. G. P. M. S.; Tome, A. C.; Cavaleiro, J. A. S.; Serra, O. A.; Torres, T. *Tetrahedron Lett.* **2006**, *47*, 6129–6132; (e) Ramesh Reddy, M.; Shibata, N.; Yoshiyama, H.; Nakamura, S.; Toru, T. *Synlett* **2007**, 628–632; (f) Alvarez-Mico, X.; Calvete, M. J. F.; Hanack, M.; Ziegler, T. *Synthesis* **2007**, 2186–2192; (g) Iqbal, Z.; Hanack, M.; Ziegler, T. *Tetrahedron Lett.* **2009**, *50*, 873–875; (h) Iqbal, Z.; Lyubimtsev, A.; Hanack, M.; Ziegler, T. *Tetrahedron Lett.* **2009**, *50*, 5681–5685; (i) Liu, J.-Y.; Lo, P.-C.; Fong, W.-P.; Ng, D. K. P. *Org. Biomol. Chem.* **2009**, *7*, 1583–1591; (j) Soares, A. R. M.; Tomé, J. P. C.; Neves, M. G. P. M. S.; Tomé, A. C.; Cavaleiro, J. A. S.; Torres, T. *Carbohydr. Res.* **2009**, *344*, 507–510.
12. (a) Zorlu, Y.; Ermeydan, M. A.; Dumoulin, F.; Ahsen, V.; Savoie, H.; Boyle, R. W. *Photochem. Photobiol. Sci.* **2009**, *8*, 312–318; (b) Pashkovskaya, A.; Kotova, E.; Zorlu, Y.; Dumoulin, F.; Ahsen, V.; Agapov, I.; Antonenko, Y. *Langmuir* **2010**, *26*, 5726–5733.
13. Berthold, H. J.; Franke, S.; Thiem, J.; Schotten, T. *J. Org. Chem.* **2010**, *75*, 3859–3862.
14. Berthold, H. J.; Schotten, T.; Hoffmann, F.; Thiem, J. *Synthesis* **2010**, 741–748.
15. Ermeydan, M. A.; Dumoulin, F.; Basova, T. V.; Bouchu, D.; Gürek, A. G.; Ahsen, V.; Lafont, D. *New J. Chem.* **2010**, *34*, 1153–1162.
16. Karabörk, M.; Serin, S. *Synth. React. Inorg. Met.-Org. Chem.* **2002**, *32*, 1635–1647.
17. *Synthesis of [1(4),8(11),15(18)-tri-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy-23-(12-hydroxy-1,4,7,10-tetraoxadodecyl)]phthalocyaninato Zn(II)* (**3**). 4-[12-Hydroxy-(1,4,7,10-tetraoxadodecyl)] phthalonitrile (**1**) (0.50 g, 1.56 mmol), 3-[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy] phthalonitrile (**2**) (4.02 g, 15.60 mmol) and $Zn(CH_3COO)_2$ were stirred under argon for 10 h in refluxing *N*,*N*-dimethylaminoethanol (35 mL). The blue reaction mixture was then poured into hexane (500 mL) and the resulting precipitate filtered. The resulting blue solid was dissolved in a minimum amount of CH_2Cl_2 and precipitated several times from hot hexane. The crude product was loaded on a silica gel column, and first eluted by EtOAc to obtain the symmetric phthalocyanine, then by a mixture of CH_2Cl_2–THF (2:1) to obtain the desired asymmetric phthalocyanine **3** as a blue solid. 450 mg, 25%. $C_{58}H_{62}N_8O_{14}Zn$, MW: 1160.57. ^{1}H NMR (DMSO-d_6) δ: 9.15–7.14 (m, 12H, Ar), 5.31–4.23 (m, 15H, $3CH_2CHCH_2$), 4.09–3.49 (m, 16H, $4OCH_2CH_2O$), 1.63–1.44 (m, 18H, $6CH_3$). ^{13}C NMR (DMSO-d_6) δ: (overlapping signals) 160.78, 158.63, 155.92, 152.63, 140.86, 130.92, 126.93, 125.38, 123.72, 116.95, 115.51, 113.59, 109.67, 106.03, 75.07, 74.39, 73.12, 72.59, 70.71, 69.94, 68.55, 67.15, 27.52, 26.20. UV–vis, λ_{max} (log ε): DMSO 698 (5.29), 628 (4.56), 343 (4.65). MALDI-TOF-MS (2,5-dihydroxybenzoic acid) *m*/*z*: 1159.28 [M+H]. HRMS (ESI) *m*/*z* calcd for $C_{58}H_{63}N_8O_{14}Zn$ $[M+H]^+$: 1159.3750; found 1159.3695.
18. Kumru, U.; Ermeydan, M. A.; Dumoulin, F.; Ahsen, V. *J. Porphyrins Phthalocyanines* **2008**, *12*, 1090–1095.
19. *Synthesis of [1(4),8(11),15(18)-tri-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy-23-(12-azido-(1,4,7,10 tetraoxadodecyl)]phthalocyaninato Zn(II)* (**5**). To a cold mixture (4 °C) of **3** (0.40 g, 0.35 mmol) and Et_3N (10 mL) in CH_2Cl_2 (25 mL) was added dropwise MsCl (4 equiv, 1.40 mmol, 160 mg, 110 μL). Following completion the reaction mixture was then allowed to reach room temperature, stirred for a further 20 min until completion, then diluted with H_2O (50 mL) and extracted with CH_2Cl_2 (3×50 mL). After drying over Na_2SO_4 and concentration, the obtained mesylated phthalocyanine **4** was used in the following reaction without further purification (380 mg, 90%). MALDI-TOF-MS (2,5-dihydroxybenzoic acid) *m*/*z*: calcd for $C_{59}H_{64}N_8O_{16}SZn$ 1236.35; found 1237.45 [M+H]). Compound **4** (0.30 g, 0.24 mmol) and NaN_3 (4 equiv, 0.96 mmol) were stirred in DMF (10 mL) at 100 °C for 18 h. After completion, the reaction mixture was poured into H_2O (50 mL) and the green precipitate filtered, dissolved in CH_2Cl_2 (50 mL) and washed with H_2O (3×50 mL). After drying over Na_2SO_4 and concentration, the crude product was purified by silica gel column chromatography, eluent CH_2Cl_2/THF 3:1, leading to 270 mg of **5** (95%). $C_{58}H_{61}N_{11}O_{13}Zn$, MW: 1185.58. ^{1}H NMR (DMSO-d_6) δ: 9.15–7.14 (m, 12H, Ar), 5.23–4.44 (m, 15H, $3CH_2CHCH_2$), 4.38–3.60 (m, 16H, $4OCH_2CH_2O$), 1.65–1.39 (m, 18H, $6CH_3$). ^{13}C NMR (DMSO-d_6) δ: (overlapping signals) 159.93, 158.46, 156.12, 153.02, 141.34, 131.16, 126.81, 125.79, 124.22, 116.91, 115.81, 113.87, 109.84, 106.46, 75.37, 74.38, 73.12, 72.44, 70.50, 70.02, 68.24, 67.02, 50.7, 27.45, 26, 46. UV–vis, λ_{max} (log ε): DMSO 698 (5.29), 627 (4.56), 343 (4.63). MALDI-TOF-MS (2,5-dihydroxybenzoic acid) *m*/*z*: 1186.83 [M+H]. HRMS (ESI) *m*/*z* calcd for $C_{58}H_{62}N_{11}O_{13}Zn$ [M+H]: 1184.3815; found 1184.3817
20. Mereyala, H. B.; Gurrala, S. R. *Carbohydr. Res.* **1998**, *307*, 351–354.
21. Wardrop, D. J.; Zhang, W.; Fritz, J. *Org. Lett.* **2002**, *4*, 489–492.
22. *General method for the click reaction*. To a mixture of the azido phthalocyanine **5** (60 mg, 0.0506 mmol) and propargyl glycoside **6** (0.1012 mmol, 2 equiv, 40 mg for monosaccharides, 68 mg for the disaccharide) in CH_2Cl_2 (0.70 mL) were successively added H_2O (0.70 mL), sodium ascorbate (3.0 mg, 15×10^{-3} mmol) and $CuSO_4{\cdot}5H_2O$ (1.25 mg, 5×10^{-3} mmol). The mixture was stirred vigorously for 16 h, diluted with CH_2Cl_2 (30 mL) and washed with H_2O (5 mL). The organic phase was dried (Na_2SO_4), concentrated and the crude residue purified by column chromatography first using pure EtOAc to remove the excess of reagent and then with 20:1 CH_2Cl_2–EtOH. *{1(4),8(11),15(18)-Tri-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl 2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside)]} phthalocyaninato Zn(II)* (**7-Glc**). Obtained as described above from propargyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**6-Glc**) and **5**. Yield 93%. Deep blue powder. R_f 0.40–0.44 (20:1 CH_2Cl_2–EtOH); R_f 0.64 (2:1 CH_2Cl_2–THF) and R_f 0.94 for the starting material **5**. ^{13}C NMR ($CDCl_3$) δ: 170.57, 170.07, 169.46, 169.19 (CH_3COO), 160.43–105.79 (aromatic C), 99.86 (C-1), 61.17, 60.13 (C-6, OCH_2=), 49.79 (CH_2N). HRMS (ESI) calcd for $C_{75}H_{84}N_{11}O_{23}Zn$ [M+H], 1570.5028; found 1570.4973. *{1(4),8(11),15(18)-Tri-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside)]}phthalocyaninato Zn(II)* (**7-Gal**). Obtained as described above from propargyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**6-Gal**) and phthalocyanine **5**. Yield 95%. Deep blue powder. R_f 0.40–0.44 (20:1 CH_2Cl_2–EtOH); R_f 0.64 (2:1 CH_2Cl_2–THF) and R_f 0.94 for the starting material **5**. ^{13}C NMR ($CDCl_3$) δ: 170.29, 170.21, 169.99, 169.35 (CH_3COO), 160.39–105.74 (aromatic C), 100.33 (C-1), 60.51, 60.21 (C-6, OCH_2=), 49.79 (CH_2N). HRMS (ESI) calcd for $C_{75}H_{84}N_{11}O_{23}Zn$ [M+H], 1570.5028; found 1570.5013. *{1(4),8(11),15(18)-Tri-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl 4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-β-D-glucopyranoside)]} phthalocyaninato Zn(II)* (**7-Lac**). Obtained as described above from propargyl 4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2,4,6-tri-*O*-acetyl-β-D-glucopyranoside (**6-Lac**) and phthalocyanine **5**. Yield 83%. Deep blue powder. R_f 0.43–0.45 (20:1 CH_2Cl_2–EtOH); R_f 0.64 (2:1 CH_2Cl_2–THF) and R_f 0.94 for the starting material **5**. ^{13}C NMR ($CDCl_3$) δ: 170.43, 170.43, 170.30, 170.22, 170.15, 169.90, 169.78, 169.64 (CH_3COO), 160.44–105.70 (aromatic C), 101.22 (C-1′), 99.72 (C-1), 61.46, 60.84 (C-6, C-6′, OCH_2=), 49.75 (CH_2N). HRMS (ESI) calcd for $C_{87}H_{100}N_{11}O_{31}Zn$ [M+H], 1858.5873; found 1858.5840. *{1(4),8(11),15(18)-Tri-(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl 2,3,4,6-tetra-O-acetyl-α-D-mannopyranoside)]}phthalocyaninato Zn(II)* (**7-Man**). Obtained as described above from propargyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**6-Man**) and phthalocyanine **5**. Yield 95%. Deep blue powder. R_f 0.43–0.45 (20:1 CH_2Cl_2–EtOH); R_f 0.64 (2:1 CH_2Cl_2–THF) and R_f 0.94 for the starting material **1**. ^{13}C NMR ($CDCl_3$) δ: 170.69, 169.90, 169.78, 169.64 (CH_3COO), 160.64–109.93 (aromatic C), 96.57 (C-1), 61.89, 59.19 (C-6, OCH_2=), 50.05 (CH_2N). HRMS (ESI) calcd for $C_{75}H_{84}N_{11}O_{23}Zn$ [M+H], 1570.5028; found 1570.5013.
23. *General method for phthalocyanine deprotection*. A solution of phthalocyanine **7** (0.040 mmol, 63 mg for **7-Glc**, **7-Gal** and **7-Man**, 74 mg for **7-Lac**) in 80% AcOH

(20 mL) was stirred for 6 h at 70 °C and then overnight at room temperature. After concentration, and coevaporation twice from EtOH (2 × 20 mL), the residue was treated for 2 d at rt in a 2:1:1 MeOH–H_2O–Et_3N mixture (20 mL). The solution was evaporated to dryness and coevaporated twice from H_2O. *{1(4),8(11),15(18)-Tri-(2,3-dihydroxypropyloxy)-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl β-D-glucopyranoside)]}phthalocyaninato Zn(II)* (**8-Glc**). Obtained quantitatively as described above from compound **7-Glc**. Deep blue powder. UV–vis, λ_{max} (log ε): DMSO 700 (5.14), 629 (4.41), 345 (4.50); H_2O 650 (4.45), 330 (4.32). HRMS (ESI) calcd for $C_{58}H_{64}N_{11}O_{19}Zn$ [M+H], 1282.3666; found 1282.3663. *{1(4),8(11),15(18)-Tri-(2,3-dihydroxypropyloxy)-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl β-D-galactopyranoside)]}phthalocyaninato Zn(II)* (**8-Gal**). Obtained quantitatively as described above from compound **7-Gal**. Deep blue powder. UV–vis, λ_{max} (log ε): DMSO 700 (5.00), 629 (4.27), 345 (4.35); H_2O 650 (4.66), 330 (4.52). HRMS (ESI) calcd for $C_{58}H_{64}N_{11}O_{19}Zn$ [M+H], 1282.3666; found 1282.3657. *{1(4),8(11),15(18)-Tri-(2,3-dihydroxypropyloxy)-23-[12-((1,4,7,10-tetraoxadodecyl)-1H-1,2,3-triazol-4-yl)methyl) 4-O-β-D-galactopyranosyl-β-D-glucopyranoside)]}-phthalocyaninato Zn(II)* (**8-Lac**). Obtained quantitatively as described above from compound **7-Lac**. Deep blue powder. UV–vis, λ_{max} (log ε): DMSO 700 (5.18), 629 (4.45), 345 (4.54); H_2O 650 (4.57), 330 (4.39). HRMS (ESI) calcd for $C_{64}H_{74}N_{11}O_{24}Zn$ [M+H], 1444.4194; found 1444.4119. *{1(4),8(11),15(18)-Tri-(2,3-dihydroxypropyloxy)-23-[12-((1,4,7,10-tetraoxadode-cyl)-1H-1,2,3-triazol-4-yl)methyl α-D-mannopyranoside)]} phthalocyaninato Zn(II)* (**8-Man**). Obtained quantitatively as described above from compound **7-Man**. Deep blue powder. UV–vis, λ_{max} (log ε): DMSO 700 (5.18), 629 (4.45), 345 (4.53); H_2O 650 (4.48), 330 (4.35). HRMS (ESI) calcd for $C_{58}H_{64}N_{11}O_{19}Zn$ [M+H], 1282.3666; found 1282.3673.