Expeditious Synthesis of Glycosylated Phthalocyanines

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Received 23 February 2007; revised 9 May 2007

Abstract: 3,4-Dicyanophenyl *O*- and *S*-glycosides in the gluco, galacto, lacto, and cellobiose series were prepared in virtually quantitative yield through nucleophilic aromatic substitution of 4-nitrophthalonitrile with acetyl-protected glycoses and 1-thio-glycoses. Similarly, 2-(3,4-dicyanophenoxy)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-gluco- and galacto-pyranosides were obtained by nucleophilic substitution of 2-(tosyloxy)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-gluco- and -galactopyranoside with 3,4-dicyanophenol in 82% and 94% yields, respectively. All glycosides were deacetylated and tetramerized to the corresponding glycosylated zinc(II) phthalocyanines without further purification using a template condensation in 42–54% yields.

Key words: carbohydrate, phthalocyanine, glycoside, cellular uptake

Carbohydrates habitually exist on cell surfaces as glycoproteins or glycolipids and are engaged in various important biological recognition processes, for example, cancer metastasis, inflammatory response, innate and adaptive immunity, viral and bacterial infection, and many other receptor-mediated signaling processes.[1] Moreover, a large number of natural products require glycosylation in order to exhibit biological activity.[2,3] However, the effect of glycosylation on the structure and function of glycosylated natural products is not well understood, mostly due to the lack of efficient synthetic methods to cover all the structural features.

Selective glycoside bond formation for the chemical synthesis of well-defined oligosaccharides based on highly reactive glycosyl donors, on versatile building block strategies, and on advanced protective-group design[4,5] is probably the most significant challenge of carbohydrate chemistry. Thus, a variety of useful methods have been developed over the last few decades, most noteworthy several efficient Koenigs–Knorr type glycosylation protocols, using various leaving groups at the anomeric center.[4–6]

In contrast, the anomeric O-alkylation or O-arylation has, as yet, been applied less widely for the synthesis of glycoconjugates.[7] Nevertheless, this methodology is superior to Koenigs–Knorr type glycosylations for the preparation of aryl glycosides.

Base-promoted direct anomeric O-arylation of protected sugars has been investigated by several authors,[8] by taking advantage of the excellent leaving group character of fluoride in substituted fluorinated nitro- or dinitrobenzenes. Mainly β-*O*-aryl glucosides are obtained in fairly good yields in this way. Recently, we reported a new method for the synthesis of *O*-aryl glycosides through nucleophilic substitution of nitrite in nitroarenes by anomeric glycosyl oxides.[9] The nucleophilic displacement of a nitro group from an activated aromatic substrate has been shown to proceed effectively for a variety of strong nucleophiles under dipolar aprotic solvent conditions. For example, at room temperature in *N*,*N*-dimethylformamide, dimethyl sulfoxide, or hexamethyphosphoramide, hydroxy or alkoxy anions,[10,11] the thiol anion,[10,12] and sulfinate anions[10] effect a synthetically practical displacement of a nitro group from carbonyl,[10–13] nitro,[10,13] cyano,[10–13] sulfone,[10] and aryl[12] activated substrates. In addition, as it has been previously demonstrated, nitrite is comparable to fluoride as leaving group in S_{NAr} reactions.[14] The cyano-substituted aryl glycosides prepared by this novel anomeric O-arylation strategy were used for the template synthesis of phthalocyanines.[9]

Phthalocyanines (Pcs) have been known for more than seven decades. These compounds have been widely investigated as advanced materials for diverse applications,[15] including photobiological and medical applications.[16] Phthalocyanines possess characteristic absorption spectra,[17] with a Soret band at approximately 350 nm and a usually narrow but very strong Q band around 675 nm, with a molar extinction coefficient in the range of 10^5 M^{-1} cm^{-1}. In addition to being red shifted compared to porphyrins, light absorption of phthalocyanines is approximately two orders of magnitude stronger than the highest Q band absorption of a porphyrin. The photophysical properties of the phthalocyanine dyes are strongly influenced by the presence and nature of the coordinated central metal. Closed shell, diamagnetic ions, such as Zn^{2+}, Al^{3+} and Ga^{3+}, give phthalocyanine complexes with both high triplet yields and long lifetimes of the excited triplet state.[18] Thus, these complexes are expected to exhibit strong photochemical and photodynamic activities, due to a higher efficiency in generating reactive oxygen species than porphyrins.[19] By possessing low dark toxicity,[20] these compounds appeared to be a very promising kind of second generation photosensitizer for biological purposes.

Phthalocyanine–carbohydrate conjugates are remarkably uncommon.[21] Recently, we reported for the first time the synthesis of peripherally substituted zinc(II) phthalocyanines linked anomerically to glucose moieties, which

SYNTHESIS 2007, No. 14, pp 2186–2192
Advanced online publication: 03.07.2007
DOI: 10.1055/s-2007-983753; Art ID: T04207SS

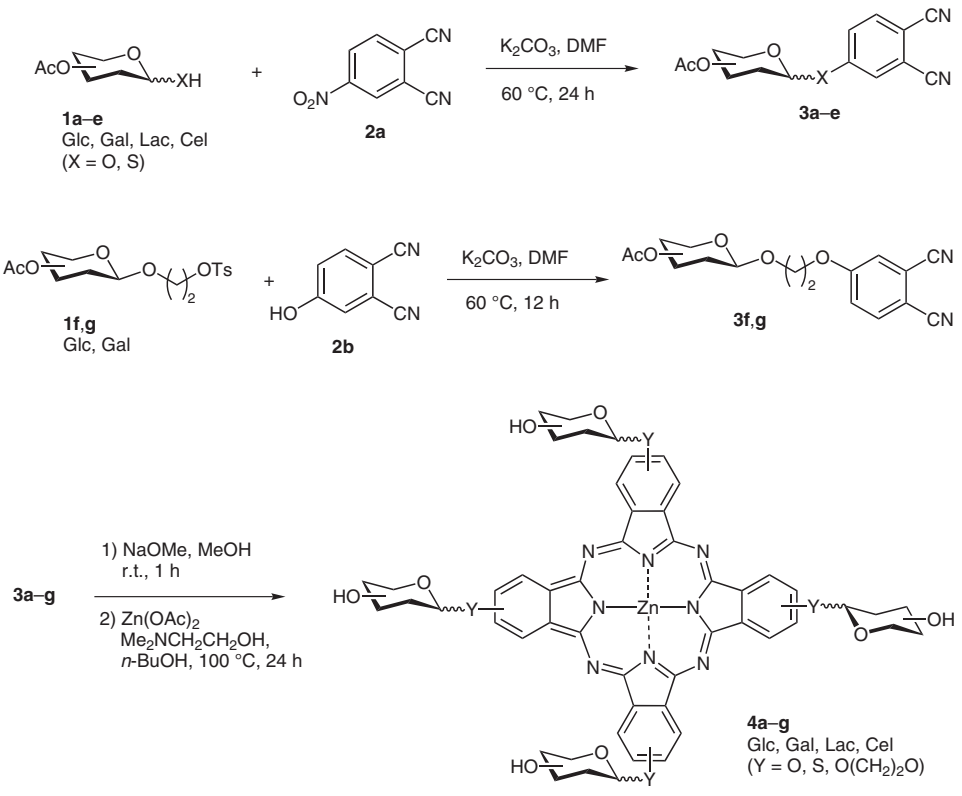
were thought to provide new biologically active photosensitizers.[22]

The key point for biological effectiveness in such materials is the balance between hydrophobicity and hydrophilicity in the cellular uptake, that is acknowledged as an important aspect for the design of new biological active photosensitizers,[23] A novel therapeutic antitumor approach termed photothermal therapy relies on the uptake of such type of chromophores by diseased tissues.[24] These chromophores can then be excited by laser pulses, thereby locally generating heat which eventually leads to the lysis of tumor cells. Several research groups synthesized a variety of new porphyrin–carbohydrate conjugates,[25] assuming that the presence of the carbohydrate moiety could improve the membrane interaction and thus, increasing their tumor selectivity. Moreover, since various types of glucose transporters are specific for different monosaccharides in cancer cells,[26] it is logical to expect a cellular uptake improvement of the complexes through glycoconjugation, which may increase the biological activity. Here we report on the expeditious synthesis of several novel phthalocyanine glycoconjugates linked anomerically to the glycoses, for which classical phthalocyanine template chemistry with the corresponding unprotected phthalonitrile glycosides was used.[9]

3,4-Dicyanophenyl-carbohydrate derivatives **3a**–**e** (see Scheme 1 and Table 1) were synthesized by nucleophilic displacement of the nitro group in 4-nitrophthalonitrile (**2a**), a method otherwise widely used for the synthesis of oxoaryl phthalonitriles.[27] Thus, treatment of glycosides **1a**–**e** and **2a** with potassium carbonate in *N*,*N*-dimethylformamide afforded phthalonitrile glycosides **2a**–**e** in virtually quantitative yield. As was observed previously,[9] glycosyl oxide **1a** gave predominantly the α-glycoside **3a** whereas all glycosyl thiolates **1b**–**e** afforded solely the corresponding β-thioglycosides **3b**–**e**. Therefore, it is recommended to use 1-thio-glycoses as nucleophiles for the preparation of 3,4-dicyanophenyl-carbohydrate derivatives since anomerically pure aryl 1-thio-glycosides are obtained in this case.

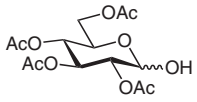
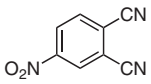
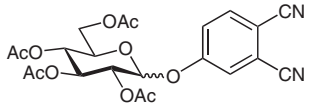
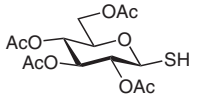
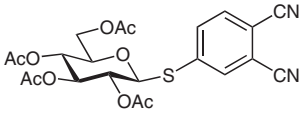
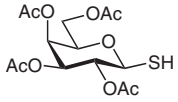
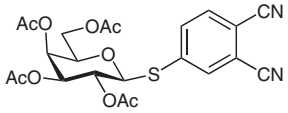
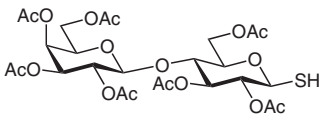
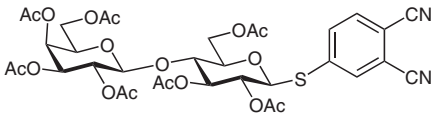
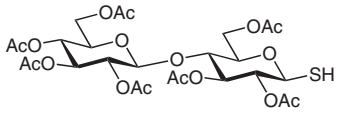
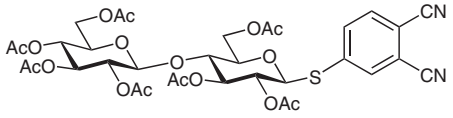
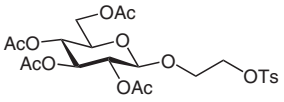
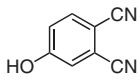
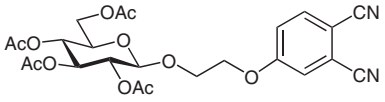
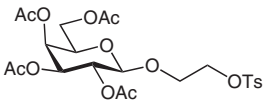
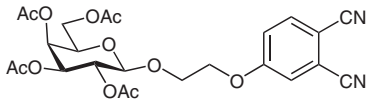
Phthalonitrile glycosides **3f** and **3g** were prepared by nucleophilic substitution of 2-(tosyloxy)ethyl glycosides **1f** and **1g**, respectively with 4-hydroxyphthalonitrile (**2b**) (Table 1). The latter procedure was chosen because peracetylated hydroxyethyl glycosides turned out to be insufficiently nucleophilic to induce nucleophilic substitution in the case of 4-nitrophthalonitrile (**2a**) (no further experimental details shown).

Synthesis of peripherally glycosylated zinc(II) phthalocyanines was performed according to the method described earlier.[22] Glycosides **3** were first Zemplén deacetylated,[28] and the resulting deprotected 3,4-dicyanophenyl glycosides and 1-thio-glycosides were directly cyclotetramerized by a template reaction without further purification, to afford phthalocyanines **4** (Scheme 1, Table 1). The choice of the solvent was crucial for this step because both substrates and products should be kept in solution during the cyclotetramerization in order to achieve good yields of phthalocyanines. As previously found,[22] a 2:1 mixture of 2-(dimethylamino)ethanol and butanol proved to be the best choice.



Scheme 1

Table 1 Yields of Phthalonitrile Glycosides **3** and Phthalocyanines **4**

Glycose **1**	Phthalonitrile **2**	Glycosylated phthalonitrile **3**	Yield (%)	
			3	**4**
 **1a**	 **2a**	 **3a**	99[a]	51
 **1b**	**2a**	 **3b**	99[a]	54
 **1c**	**2a**	 **3c**	98	48
 **1d**	**2a**	 **3d**	99	46
 **1e**	**2a**	 **3e**	99	42
 **1f**	 **2b**	 **3f**	82	48
 **1g**	**2b**	 **3g**	94	45

[a] See ref. 9.

Spectroscopic data of all compounds are in full agreement with common substituted phthalocyanines. Although all phthalocyanines prepared here are mixtures of isomers,[29] they show typical chemical shifts in their ^{1}H and ^{13}C NMR spectra. However, the phthalocyanine protons appear usually at slightly lower fields when compared to other oxo-substituted phthalocyanines.[29] This low-field shift of the phthalocyanine protons is probably due to the deshielding effect caused by the carbohydrate moieties. The chemical shifts of the protons at the anomeric carbons are also affected by the electron-rich core of the phthalocyanine and, therefore, also appear at lower fields. All UV/Vis spectra are very similar to zinc-substituted phthalocyanines, showing the Q-band maxima at around 690 nm.

In conclusion, we have prepared by template condensation and fully characterized several novel peripherally glycosylated zinc(II) phthalocyanines, where the sugar moieties are linked glycosidically through O or S.

Our findings show that the aromatic nitro displacement is a very useful method to form phenyl glycosides owing to such important features as bearing electron-withdrawing groups, namely cyano or nitro, and using a dipolar aprotic solvent like *N*,*N*-dimethylformamide. Moreover, this type of carbohydrate is a very versatile building block for the preparation of anomerically linked carbohydrate-substituted phthalocyanines, which can have an important role in some biological processes, displaying very high solubility in water.

All reagents were commercially obtained at highest commercial quality and used without further purification. Air- and moisture-sensitive liquids and solns were transferred via syringe or stainless steel cannula. Organic solns were concentrated by rotary evaporation below 45 °C. Reactions were carried out under anhydrous conditions using flame-dried glassware within an argon atmosphere in anhydrous, freshly distilled solvents, unless otherwise noted. Yields refer to chromatographically and spectroscopically (^{1}H NMR,^{13}C NMR) homogeneous materials, unless otherwise stated. Analytical

TLC was performed on glass plates precoated with a 0.25 mm thickness of Macherey & Nagel Polygram SIL G/UV254 with UV light as the visualizing agent and 5% H_2SO_4 in EtOH soln and heat as detecting agents. Silica gel 60 (particle size 0.040–0.063 mm) was used for flash chromatography. NMR spectra were recorded on a Bruker Advance 250 (250 MHz) spectrometer and calibrated using the deuterated solvent as an internal reference. IR spectra were recorded on a Bruker Tensor 27; solid substances were ground with KBr and pressed to pellets, liquid compounds were measured directly. UV spectra were recorded on a Shimadzu UV 2102 PC using a 1 cm quartz cell. Melting points were recorded on a Büchi B-540 and are uncorrected. MS spectra were recorded on a MALDI-TOF Bruker Autoflex, the spectra were measured with a-cyano-*m*-hydroxycinnamic acid for phthalocyanines and 2-(4-hydroxyphenylazo)benzoic acid for other compounds as matrixes, a Finnigan MAT TSQ 70 with direct inlet, temperature of ion source 200 °C, electron energy 70 eV (EI) or a Finnigan MAT TSQ 70 using xenon atoms for the ionization and 3-nitrobenzyl alcohol as the matrix (FAB). Elemental analysis was performed on Hekatech GmbH Euro EA 3000 analyzer. Preparative RP-HPLC was performed on an aqueous system using a GROM SIL 120 ODS-4HE;10 mm; 250 × 20 mm (C-8 column); the eluents used were H_2O and MeCN.

3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranoside (**3a**), and 3,4-dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**3b**) were prepared as previously described.[9]

3,4-Dicyanophenyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (3c); Typical Procedure

K_2CO_3 (5.60 g, 40.2 mmol) was added at r.t. to a stirred soln of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose[30,31] (**1c**, 7.00 g, 19.2 mmol) and 4-nitrophthalonitrile (**2a**, 1.28 g, 7.4 mmol) in anhyd DMF (25 mL), and the mixture was stirred overnight. At the end of this period, the mixture was poured into H_2O (200 mL), and CH_2Cl_2 (100 mL) was added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (3 × 50 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the crude product (silica gel, toluene–acetone, 10:1) gave **3c** as an amorphous white powder; yield: 9.24 g (98%).

$[\alpha]_D^{20}$ –13.7 (*c* 1, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.96 (s), 2.06 (s), 2.09 (s), 2.17 (s) (12 H, H-CH_3), 4.01–4.06 (m, 1 H, H5), 4.14–4.18 (m, 2 H, H6), 4.80 (d, $J_{1\text{-}2}$ = 9.1 Hz, 1 H, H1), 5.05–5.11 (dd, $J_{3\text{-}2}$ = 9.9, $J_{3\text{-}4}$ = 3.2 Hz, 1 H, H3), 5.19–5.27 (dd, $J_{2\text{-}3}$ = 9.9, $J_{2\text{-}1}$ = 9.1 Hz, 1 H, H2), 5.47 (d, $J_{4\text{-}3}$ = 3.2 Hz, 1 H, H4), 7.68 (d, $J_{5'\text{-}6'}$ = 8.4 Hz, 1 H, H5′), 7.70–7.74 (dd, $J_{6'\text{-}5'}$ = 8.1, $J_{6'\text{-}2'}$ = 1.7 Hz, 1 H, H6′), 7.94 (d, $J_{2'\text{-}6'}$ = 1.7 Hz, 1 H, H2′).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.62, 20.64, 20.7 (CCH_3), 61.9 (C6), 66.3 (C2), 67.1 (C4), 71.5 (C3), 75.3 (C5), 83.9 (C1), 113.8 (C4′), 114.9 (C3′-CN), 115.0 (C4′-CN), 116.4 (C3′), 133.2 (C5′), 134.1 (C2′), 134.2(C6′), 141.7 (C1′), 169.3, 169.8, 169.9, 170.4 (C-CO).

MS-MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{22}N_2NaO_9S$: 513.47; found: 513.73.

Anal. Calcd for $C_{22}H_{22}N_2O_9S$: C, 53.87; H, 4.52; N, 5.71; S, 6.54. Found: C, 54.04; H, 4.55; N, 5.75; S, 6.34.

3,4-Dicyanophenyl 2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-1-thio-β-lactoside (3d)

Prepared from 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-1-thio-β-lactoside[30,31] (**1d**, 12.50 g, 19.15 mmol) as described for compound **3c**. Amorphous white powder; yield: 14.90 g (99%).

$[\alpha]_D^{20}$ –37.5 (*c* 1, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.93, 2.01, 2.02, 2.04, 2.11, 2.13 (21 H, CH_3), 3.72–3.75 (m, 2 H, H4, H5), 3.82–3.87 (m, 1 H, H5′), 4.04–4.13 (m, 3 H, H6a, H6′), 4.46 (d, $J_{1'\text{-}2'}$ = 7.8 Hz, 1 H, H1′), 4.52 (br d, $J_{6b\text{-}6a}$ = 11.8 Hz, 1 H, H6b), 4.79 (d, $J_{1\text{-}2}$ = 9.9 Hz, 1 H, H1), 4.85–4.97 (m, 2 H, H2, H3′), 5.04–5.11 (dd, $J_{2'\text{-}3'}$ = 10.6, $J_{2'\text{-}1'}$ = 7.8 Hz, 1 H, H2′), 5.18–5.25 (dd, *J* = 8.8, *J* = 8.6 Hz, 1 H, H3), 5.31–5.32 (m, 1 H, H4′), 7.68–7.69 (m, 2 H, H5″, H6″), 7.83–7.85 (m, 1 H, H2″).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.6, 20.7, 20.8 (CH_3), 60.7 (C6′), 62.0 (C6), 66.6 (C4′), 69.1 (C2′), 69.7 (C2), 70.8 (C3′), 70.9 (C5′), 73.3 (C3), 75.7 (C4), 77.2 (C5), 83.7 (C1), 101.1 (C1′), 114.2 (C4″), 114.9 (C3″-CN), 115.0 (C4″-CN), 116.4 (C3″), 133.3 (C5″), 134.6 (C2″), 134.8 (C6″), 141.2 (C1″), 169.0, 169.4, 169.5, 169.9, 170.0, 170.2, 170.3 (C-CO).

MS-MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{38}N_2NaO_{17}S$: 801.73; found: 801.38.

Anal. Calcd for $C_{34}H_{38}N_2O_{17}S$: C, 52.44; H, 4.92; N, 3.60; S, 4.12. Found: C, 52.82; H, 4.90; N, 3.60; S, 3.92.

3,4-Dicyanophenyl 2,3,6,2′,3′,4′,6′-Hepta-*O*-acetyl-1-thio-β-cellobiose (3e)

Prepared from 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-1-thio-β-cellobiose[30,31] (**1e**, 12.50 g, 19.18 mmol) as described for compound **3c**. Amorphous white powder; yield: 14.96 g (99%).

$[\alpha]_D^{20}$ –48.6 (*c* 1, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.95, 1.97, 1.98, 2.00, 2.03, 2.05, 2.14 (21 H, CH_3), 3.60–3.69 (m, 1 H, H5′), 3.70–3.73 (m, 2 H, H4, H5), 3.99–4.12 (m, 2 H, H6a, H6a′), 4.30–4.37 (dd, $J_{6b'\text{-}6a'}$ = 12.5, $J_{6b'\text{-}5'}$ = 4.1 Hz, 1 H, H3), 4.49 (d, $J_{1'\text{-}2'}$ = 7.8 Hz, 1 H, H1′), 4.49 (br d, $J_{6b\text{-}6a}$ = 12.1 Hz, 1 H, H6b), 4.78 (d, $J_{1\text{-}2}$ = 10.1 Hz, 1 H, H1), 4.86–4.93 (m, 2 H, H2, H2′), 4.99–5.24 (m, 3 H, H3, H3′, H4′), 7.66–7.68 (m, 2 H, H5″, H6″), 7.84–7.85 (m, 1 H, H2″).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.41, 20.49, 20.58, 20.61, 20.8 (CH_3), 61.5 (C6′), 61.9 (C6), 67.7 (C3′), 69.6 (C2′), 71.6 (C2), 72.1 (C5′), 72.8 (C4′), 73.1 (C3), 75.9 (C5), 77.3 (C4), 83.7 (C1), 100.8 (C1′), 114.1 (C4″), 114.9 (C3″-CN), 115.0 (C4″-CN), 116.4 (C3″), 133.3 (C5″), 134.6 (C2″), 134.8 (C6″), 141.2 (C1″), 169.0, 158.3, 169.4, 169.5, 170.1, 170.2, 170.4 (C-CO).

MS-MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{34}H_{38}N_2NaO_{17}S$: 801.73; found: 801.74.

Anal. Calcd for $C_{34}H_{38}N_2O_{17}S$: C, 52.44; H, 4.92; N, 3.60; S, 4.12. Found: C, 52.27; H, 4.82; N,3.45; S, 3.92.

2-Hydroxyethyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside

Powdered molecular sieves (3Å) and ethylene glycol (13.4 mL, 243 mmol) were added to α-D-acetobromogalactose[30] (10.00 g, 24.3 mmol) in anhyd CH_2Cl_2 (100 mL). After 15 min, $HgBr_2$ (8.75 g, 24.3 mmol) was added and the mixture was stirred overnight. The mixture was diluted with CH_2Cl_2 (300 mL) and filtered over a pad of Celite. The organic phase was washed with 5% aq soln of KI (3 × 50 mL) and H_2O (3 × 50 mL), dried (Na_2SO_4), and the solvent was evaporated to afford the product as a slightly yellowish oil (7.47 g, 78%) that was sufficiently pure for the next step. The spectroscopic data were in accordance with those in the literature.[32]

2-(Tosyloxy)ethyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside (1g)

TsCl (5.83 g, 30.6 mmol) was added at 0 °C in small portions to 2-hydroxyethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (6.00 g, 15.3 mmol) in CH_2Cl_2 (75 mL) and pyridine (6.75 mL) and the soln was stirred overnight at r.t. The mixture was diluted with CH_2Cl_2 to a volume of 300 mL and washed with aq 1 M HCl (3 × 50 mL), sat. aq $NaHCO_3$ (50 mL), and H_2O (50 mL). After drying (Na_2SO_4), filtration, and removal of the solvent in vacuo, the crude product was

purified by chromatography (silica gel, toluene–acetone, 10:1) to give compound **1g**; yield: 7.98 g (95%).

$[\alpha]_D^{20}$ –9.1 (*c* 1, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.95 (s), 2.01 (s), 2.04 (s), 2.11 (s) (12 H, CH_3), 2.42 (s, 3 H, H-CH_3), 3.72–3.82 (m, 1 H, H7a), 3.83–3.90 (m, 1 H, H5), 3.93–4.15 (m, 5 H, H6, H7b, H8), 4.46 (d, $J_{1\text{-}2}$ = 7.9 Hz, 1 H, H1), 4.94–5.00 (dd, $J_{3\text{-}2}$ = 10.6, $J_{3\text{-}4}$ = 2.8 Hz, 1 H, H3), 5.12–5.20 (dd, $J_{2\text{-}3}$ = 10.6, $J_{2\text{-}1}$ = 7.9 Hz, 1 H, H2), 5.05–5.11 (dd, $J_{4\text{-}3}$ = 2.8, $J_{4\text{-}5}$ = 1 Hz, 1 H, H4), 7.33 (d, $J_{2'\text{-}3'/6'\text{-}5'}$ = 8.4 Hz, 2 H, H2′, H6′), 7.75 (d, $J_{3'\text{-}2'/5'\text{-}6'}$ = 8.4 Hz, 2 H, H3′, H5′).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.59, 20.61, 20.7 (CH_3), 21.6 (CCH_3), 61.2 (C6), 66.9 (C4), 67.1 (C7), 68.4 (C2), 68.5 (C8), 70.7 (C3), 70.8 (C5), 101.4 (C1), 127.9 (C2′, C6′), 129.9 (C3′, C5′), 132.8 (C1′), 145.0 (C4′), 169.6, 170.0, 171.1, 170.3 (C-CO).

MS-MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{30}NaO_{13}S$: 569.53; found: 569.64.

Anal. Calcd for $C_{23}H_{30}O_{13}S$: C, 50.54; H, 5.53. Found: C, 50.24; H, 5.59.

3,4-Dicyanophenol (2b)

K_2CO_3 (41.00 g, 300 mmol) was added to a soln of benzyl alcohol (6.20 mL, 60 mmol) and 4-nitrophthalonitrile (7.00 g, 40 mmol) in DMF (100 mL). The mixture was heated and stirred at 80 °C for 6 h. At the end of this period, the mixture was cooled to r.t. and poured into ice-water (1 L). The product, 4-(benzyloxy)phthalonitrile, was filtered off and recrystallized (EtOH). A soln of 4-(benzyloxy)phthalonitrile (8.9 g, 38 mmol) in EtOAc (200 mL) was added to a suspension of 10% Pd/C (300 mg) in EtOAc (100 mL) and the resulting slurry was stirred in an atmosphere of H_2 for 6 h. The catalyst was removed from the soln by filtration over Celite and the solvent was evaporated in vacuo. The residue was dissolved in 5% aq NaOH, the soln was filtered, and the filtrate was neutralized with concentrated HCl whereupon **2b** crystallized. Filtration and drying afforded of **2b**; yield: 4.6 g (85%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.16–7.22 (dd, $J_{5\text{-}3}$ = 2.5, $J_{5\text{-}6}$ = 8.6 Hz, 1 H, H5), 7.37 (d, 1 H, $J_{3\text{-}5}$ = 2.5 Hz, 1 H, H3), 7.89 (d, 1 H, $J_{6\text{-}5}$ = 8.6 Hz, 1 H, H6).

^{13}C NMR (62.9 MHz, CD_3OD): δ = 107.74 (C4), 118.17 (C6), 118.82 (C3, C5), 119.64 (C2), 123.38 (C1-CN), 128.11 (C2-CN), 164.57 (C1).

EI-MS: *m*/*z* [M]$^+$ calcd for $C_8H_4N_2O$: 144.1; found: 143.9.

2-(3,4-Dicyanophenoxy)ethyl 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranoside (3f); Typical Procedure

Glucopyranoside **1f**[33] (4.00 g, 7.3 mmol), K_2CO_3 (2.00 g, 15 mmol), and 3,4-dicyanophenol (**2b**, 1.44 g, 10 mmol) in DMF (25 mL) were heated overnight at 60 °C. After cooling, the mixture was diluted with H_2O (500 mL), extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic extracts were dried (Na_2SO_4). After evaporation of the solvent, the crude product was purified by chromatography (silica gel, toluene–acetone, 10:1); yield: 3.12 g (82%).

$[\alpha]_D^{20}$ –22.0 (*c* 1, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.93 (s), 1.98 (s), 2.00 (s), 2.06 (s) (12 H, CH_3), 3.65–3.74 (m, 1 H, H5), 3.86–3.97 (m, 1 H, H8), 4.10–4.27 (m, 5 H, H6, H7, H8), 4.59 (d, $J_{1\text{-}2}$ = 7 9 Hz, 1 H, H1), 4.94–5.01 (dd, $J_{2\text{-}1}$ = 7.9, $J_{2\text{-}3}$ = 9.3 Hz, 1 H, H2), 5.02–5.11(dd, $J_{4\text{-}3}$ = 9.4, $J_{4\text{-}5}$ = 9.8 Hz, 1 H, H4), 5.14–5.24 (dd, $J_{4\text{-}5}$ = 9.3, $J_{3\text{-}4}$ = 9.4 Hz, 1 H, H3), 7.15–7.22 (dd, $J_{6'\text{-}2'}$ = 2.5, $J_{6'\text{-}5'}$ = 8.6 Hz, 1 H, H6′), 7.25 (d, $J_{2'\text{-}6'}$ = 2.6 Hz, 1 H, H2′), 7.69 (d, $J_{5'\text{-}6'}$ = 8.6 Hz, 1 H, H5′).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.7 (CH_3), 61.7 (C6), 67.4 (C8), 68.1 (C7), 68.3 (C4), 71.1 (C2), 72.1 (C5), 72.6 (C3), 100.8 (C1), 107.7 (C4′), 115.1 (C3′-CN), 115.5 (C4′-CN), 117.5 (C3′), 119.4 (C6′), 119.8 (C2′), 135.3 (C5′), 161.8 (C1′), 169.2, 169.3, 170.2, 170.5 (C-CO).

MS-MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{26}N_2NaO_{11}$: 541.5; found: 541.4.

Anal. Calcd for $C_{24}H_{26}N_2O_{11}$: C, 55.60; H, 5.05; N, 5.40. Found: C, 56.50; H, 5.11; N, 5.33.

2-(3,4-Dicyanophenoxy)ethyl 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranoside (3g)

Treatment of **1g** (7.5 g, 13.7 mmol), 3,4-dicyanophenol (**2b**, 2.37 g, 16.4 mmol), and K_2CO_3 (5.68 g, 41.1 mmol) in DMF (75 mL) as described for the preparation of compound **3f** gave **3g**; yield: 6.71 g (94%).

$[\alpha]_D^{20}$ –5.8 (*c* 0.25, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.94 (s), 1.96 (s), 2.02 (s), 2.13 (s) (12 H, CH_3), 3.88–3.96 (m, 2 H, H5, H7a), 4.06–4.25 (m, 5 H, H6, H7b, H8), 4.55 (d, $J_{1\text{-}2}$ = 7.9 Hz, 1 H, H1), 4.98–5.03 (dd, $J_{3\text{-}2}$ = 10.6, $J_{3\text{-}4}$ = 3.4 Hz, 1 H, H3), 5.15–5.22 (dd, $J_{2\text{-}3}$ = 10.6, $J_{2\text{-}1}$ = 7.9 Hz, 1 H, H2), 5.37–5.39 (dd, $J_{4\text{-}3}$ = 3.4, $J_{4\text{-}5}$ = 1 Hz, 1 H, H4), 7.15–7.25 (m, 2 H, H2′,H6′), 7.69 (d, $J_{5'\text{-}6'}$ = 8.6 Hz, 1 H, H5′).

^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 20.5, 20.61, 20.64 (CH_3), 61.2 (C8), 66.9 (C4), 67.4 (C7), 68.2 (C6), 68.5 (C2), 70.7 (C3), 70.9 (C5), 101.3 (C1), 107.7 (C4′), 115.1 (C3′-CN), 115.6 (C4′-CN), 117.5 (C3′), 119.5 (C2′), 119.8 (C6′), 135.3 (C5′), 161.8 (C1′), 169.3, 170.0, 170.1, 170.3 (C-CO).

MS-MALDI-TOF: *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{26}N_2NaO_{11}$: 541.5; found: 541.9.

Anal. C, 55.60; H, 5.05; N, 5.40. Found: C, 55.43; H, 4.92; N, 5.41.

[2(3),9(10),16(17),23(24)-Tetrakis(α/β-D-glucopyranosyloxy)phthalocyaninato]zinc (4a); Typical Procedure

An α/β mixture (10:1) of 3,4-dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranoside (**3a**, 1.0 g, 2.0 mmol) was suspended in anhyd MeOH (25 mL). NaOMe (100 μmol) was added and the soln was stirred for 1 h. Dowex 50WX8-400 ion-exchange resin was added to neutralize the soln. The resin was filtered off and the solvent evaporated in vacuo. To the deprotected phthalonitrile dissolved in a mixture of 2-(dimethylamino)ethanol (1 mL) and BuOH (0.5 mL), $Zn(OAc)_2$ (183 mg, 1 mmol) was added. The mixture was stirred under argon for 24 h at 100 °C. After cooling, the residue was dissolved in a minimal amount of H_2O and crude **4a** was precipitated from the resulting soln by adding acetone. The solid was filtered off, redissolved in a minimal amount of H_2O, precipitated again by adding acetone, and collected by filtration. Purification was achieved by preparative RP-HPLC chromatography (H_2O–MeCN, 10:1) to afford **4a** as a green solid; yield: 320 mg (51%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 6.05 (br, 4 H, H1′), 7.95 (br, 4 H, H6), 9.08 (br, 4 H, H3), 9.35 (s, 4 H, H5).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.3 (C6′), 70.5 (C5′), 72.3 (C4′), 73.8 (C2′), 74.8 (C3′), 98.9 (C1′), 109.8 (C3), 120.2 (C5), 124.2 (C6), 132.5 (C7), 140.1 (C2), 153 (C1, C8), 159 (C4).

MS-MALDI-TOF: *m*/*z* [M + H]$^+$ calcd for $C_{56}H_{57}N_8O_{24}Zn$: 1289.2777; found: 1289.2690.

UV-Vis (DMSO): λ (% rel. int.) = 354 (41, B band), 613 (17, sh), 681 nm (100, Q band).

[2(3),9(10),16(17),23(24)-Tetrakis(β-D-glucopyranosylsulfanyl)phthalocyaninato]zinc (4b)

3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (**3b**, 1.5 g, 3.1 mmol) was deacetylated with a catalytic amount of NaOMe in MeOH and condensed with $ZnCl_2$ as described for the preparation of compound **4a**. RP-HPLC chromatography (H_2O–MeCN, 10:1) afforded **4b** as a green solid; yield: 565 mg (54%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.3 (br, 4 H, H6), 9.3 (br, 4 H, H5), 9.5 (br, 4 H, H3).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.6 (C6′), 70.3 (C4′), 73.1 (C2′), 78.8 (C5′), 81.7 (C3′), 88.0 (C1′), 123.0 (C3), 123.6 (C6), 130.9 (C4), 136.5 (C7), 137.8 (C2), 139 (C4), 153 (C1, C8).

MS-MALDI-TOF: *m/z* [M + H]$^+$ calcd for $C_{56}H_{57}N_8O_{20}S_4Zn$: 1353.18634; found: 1353.14486.

UV-Vis (DMSO): λ (% rel. int.) = 362 (33, B band), 622 (16, sh), 691 nm (100, Q band).

[2(3),9(10),16(17),23(24)-Tetrakis(β-D-galactopyranosylsulfanyl)phthalocyaninato]zinc (4c)

3,4-Dicyanophenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranoside (**3c**, 1.0 g, 2.0 mmol) was deacetylated with a catalytic amount of NaOMe in MeOH and condensed with $ZnCl_2$ as described for the preparation of compound **4a**. RP-HPLC chromatography (H_2O–MeCN, 10:1) afforded **4c** as a green solid; yield: 325 mg (48%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.3 (br, 4 H, H6), 9.2 (br, 4 H, H5), 9.4 (br, 4 H, H3).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.3 (C6′), 69.1 (C4′), 70.2 (C2′), 75.3 (C5′), 79.9 (C3′), 88.6 (C1′), 123.3 (C3), 123.7 (C6), 130.8 (C4), 136.1 (C7), 138.4 (C2), 138.8 (C4), 153 (C1, C8).

MS-MALDI-TOF: *m/z* [M]$^+$ calcd for $C_{56}H_{57}N_8O_{20}S_4Zn$: 1352.178; found: 1352.157.

UV-Vis (DMSO): λ (% rel. int.) = 363 (33, B band), 623 (16, sh), 692 nm (100, Q band).

[2(3),9(10),16(17),23(24)-Tetrakis(β-D-lactosylsulfanyl)phthalocyaninato]zinc (4d)

3,4-Dicyanophenyl 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-1-thio-β-lactoside (**3d**, 1.95 g, 2.5 mmol) was deacetylated with a catalytic amount of NaOMe in MeOH and condensed with $ZnCl_2$ as described for the preparation of compound **4a**. RP-HPLC chromatography (H_2O–MeCN, 10:1) afforded **4d** as a green solid; yield: 576 mg (46%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.3 (br, 4 H, H6), 9.1 (br, 4 H, H5), 9.3 (br, 4 H, H3).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 60.9 (C6′, C6″), 68.6 (C4″), 71.0 (C2″), 73.2 (C2′), 73.7 (C5′), 76.0 (C3′), 76.9 (C3″), 79.6 (C5″), 80.6 (C4′), 87.6 (C1′), 104.3 (C1″).

MS-MALDI-TOF: *m/z* [M + Na]$^+$ calcd for $C_{80}H_{96}N_8NaO_{40}S_4Zn$: 2023.403; found: 2023.378.

UV-Vis (DMSO): λ (% rel. int.) = 363 (55, B band), 622 (22, sh), 689 nm (100, Q band).

[2(3),9(10),16(17),23(24)-Tetrakis(β-D-cellobiosylsulfanyl)phthalocyaninato]zinc (4e)

3,4-Dicyanophenyl 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-1-thio-β-cellobioside (**3e**, 1.56 g, 2.0 mmol) was deacetylated with a catalytic amount of NaOMe in MeOH and condensed with $ZnCl_2$ as described for the preparation of compound **4a**. RP-HPLC chromatography (H_2O–MeCN, 10:1) afforded **4e** as a green solid; yield: 421 mg (42%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 8.3 (br, 4 H, H6), 9.2 (br, 4 H, H5), 9.3 (br, 4 H, H3).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 60.9 (C6′), 61.5 (C6″), 70.5 (C3″), 73.1 (C2″), 73.8 (C2′), 76.9 (C5″,C4″), 77.3 (C3′), 79.6 (C5′), 80.3 (C4′), 87.6 (C1′), 103.6 (C1″), 123.3 (C3), 123.5 (C6), 131.5 (C4), 136.3 (C7), 137.4 (C2), 138.7 (C4), 153 (C1, C8).

MS-MALDI-TOF: *m/z* [M]$^+$ calcd for $C_{80}H_{96}N_8O_{40}S_4Zn$: 2000.389; found: 2000.134.

UV-Vis (DMSO): λ (% rel. int.) = 360 (32, B band), 621 (17, sh), 690 nm (100, Q band).

{2(3),9(10),16(17),23(24)-Tetrakis[2-(β-D-glucopyranosyloxy)ethoxy]phthalocyaninato}zinc (4f)

2-(3,4-Dicyanophenoxy)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**3f**, 1.08 g, 2 mmol) was deacetylated with a catalytic amount of NaOMe in MeOH and condensed with $ZnCl_2$ as described for the preparation of compound **4a**. RP-HPLC chromatography (H_2O–MeCN, 10:1) afforded **4f** as a green solid; yield: 367 mg (48%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.8 (br, 4 H, H6), 8.9 (br, 4 H, H5), 9.2 (br, 4 H, H3).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.6 (C6′), 67.8 (C8′), 68.7 (C7′), 70.6 (C4′), 74.0 (C2′), 77.3 (C5′), 77.5 (C3′), 103.8 (C1′) 106.3 (C3), 118.7 (C5), 124.1 (C6), 131.6 (C7), 140.5 (C2), 153 (C1, C8), 160.9 (C4).

MS-MALDI-TOF: *m/z* [M]$^+$ calcd for $C_{64}H_{72}N_8O_{28}Zn$: 1464.375; found: 1464.347.

UV-Vis (DMSO): λ (% rel. int.) = 357 (46, B band), 613 (17, sh), 682 nm (100, Q band).

{2(3),9(10),16(17),23(24)-Tetrakis[2-(β-D-galactopyranosyloxy)ethoxy]phthalocyaninato}zinc (4g)

2-(3,4-Dicyanophenoxy)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (**3g**, 1.08 g, 2 mmol) was deacetylated with a catalytic amount of NaOMe in MeOH and condensed with $ZnCl_2$ as described for the preparation of compound **4a**. RP-HPLC chromatography (H_2O–MeCN, 10:1) afforded **4g** as a green solid; yield: 343 mg (45%).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 7.7 (br, 4 H, H6), 8.7 (br, 4 H, H5), 9.1 (br, 4 H, H3).

^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 61.1 (C6′), 67.7 (C8′), 68.7 (C7′, C4′), 71.1 (C2′), 74.0 (C3′), 75.9 (C5′), 104.4 (C1′) 106.3 (C3), 118.7 (C5), 124.0 (C6), 131.4 (C7), 140.3 (C2), 153 (C1, C8), 160.9 (C4).

MS-MALDI-TOF: *m/z* [M]$^+$ calcd for $C_{64}H_{72}N_8O_{28}Zn$: 1464.375; found: 1464.138.

UV-Vis (DMSO): λ (% rel. int.) = 355 (40, B band), 614 (21, sh), 684 nm (100, Q band).

Acknowledgment

This work was financially supported by the Fonds der Chemischen Industrie. We thank Dr. B. Kammerer, Clinical Pharmacology, University of Tübingen for performing the MALDI-TOF MS.

References

(1) (a) Varki, A. *Glycobiology* **1993**, *3*, 97. (b) Sears, P.; Wong, C.-H. *Cell. Mol. Life Sci.* **1998**, *54*, 223.
(2) Gabius, H. J.; Gabius, S. *Glycosciences: Status and Perspectives*; Chapman & Hall: Weinheim, **1997**.
(3) (a) Paulson, J. C. *Trends Biochem. Sci.* **1989**, *14*, 272. (b) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683.
(4) (a) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212; *Angew. Chem.*, **1986**, *98*, 213. (b) Schmidt, R. R.; Kinzy, W. *Adv. Carbohydr. Chem. Biochem.* **1994**, *50*, 21. (c) Schmidt, R. R. *Pure Appl. Chem.* **1989**, *61*, 1257.
(5) Schmidt, R. R. *Pure Appl. Chem.* **1998**, *70*, 397.
(6) (a) Kazunoho, T.; Tatsuta, K. *Chem. Rev.* **1993**, *93*, 1503. (b) Jung, K.-H.; Müller, M.; Schmidt, R. R. *Chem. Rev.* **2000**, *100*, 4423.

(7) Schmidt, R. R. *Modern Methods in Carbohydrate Synthesis*; Khan, S. H.; O'Neill, R. A., Eds.; Harwood Academic Publishers GmbH: Amsterdam, **1996**.
(8) (a) Berven, L. A.; Dolphin, D.; Withers, S. G. *Can. J. Chem.* **1990**, *68*, 1859. (b) Lindberg, B. *Acta Chem. Scand.* **1950**, *4*, 49. (c) Ferrier, R. J. *Fortschr. Chem. Forsch.* **1970**, *14*, 389. (d) Huchel, U.; Schmidt, C.; Schmidt, R. R. *Tetrahedron Lett.* **1995**, *36*, 9457.
(9) Alvarez-Mico, X.; Calvete, M. J. F.; Hanack, M.; Ziegler, T. h. *Carbohydrate Res.* **2006**, *324*, 440.
(10) Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A. *J. Org. Chem.* **1976**, *41*, 1560.
(11) (a) Rodimann, E.; Schmidt, W.; Nischk, G. E. *Makromol. Chem.* **1969**, *130*, 45. (b) Mauleon, D.; Granados, R.; Minguillon, C. *J. Org. Chem.* **1983**, *48*, 3105.
(12) Beck, J. R. *J. Org. Chem.* **1972**, *37*, 3224.
(13) Knudsen, R. D.; Snyder, H. R. *J. Org. Chem.* **1974**, *39*, 3343.
(14) (a) Idoux, J. P.; Gupton, M. T.; McCurry, C. K.; Crews, A. D.; Jurss, C. D.; Colon, C.; Rampi, R. *J. Org. Chem.* **1983**, *48*, 3771. (b) March, J. *Advanced Organic Chemistry*; McGraw-Hill: New York, **1977**, 2nd Ed..
(15) (a) Dini, D.; Hanack, M. *The Porphyrin Handbook*, Vol. 17; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 1. (b) Cook, M.; Chambrier, I. *The Porphyrin Handbook*, Vol. 17; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 37. (c) Wöhrle, D.; Schnurpfeil, G. *The Porphyrin Handbook*, Vol. 17; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 177. (d) Wark, M. *The Porphyrin Handbook*, Vol. 17; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 247. (e) Erk, P.; Hengelsberg, H. *The Porphyrin Handbook*, Vol. 19; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 105. (f) Bouvet, M. *The Porphyrin Handbook*, Vol. 19; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 37.
(16) Ben-Hur, E.; Chan, W.-S. *The Porphyrin Handbook*, Vol. 19; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: New York, **2003**, 1; and references cited therein.
(17) *Phthalocyanines, Properties and Applications*, Vols. 1-4; Leznoff, C. C.; Lever, A. B. P., Eds.; VCH: New York, **1989-1996**.
(18) van Lier, J. E.; Spikes, J. D. *Photosensitizing Compounds: Their Chemistry, Biology and Clinical Use (CIBA Foundation Symposium 146)*; Dougherty, T. J.; Bock, G.; Harnett, S., Eds.; Wiley: Chichester, **1989**, 17.
(19) Roeder, B.; Naether, D.; Lewald, T.; Braune, M.; Nowak, C.; Freyer, W. *Biophys. Chem.* **1990**, *35*, 303.
(20) Komatsu, K. *Jpn. J. Cancer Res.* **1991**, *82*, 599.
(21) (a) Maillard, P.; Guerquin-Kern, J.-L.; Momenteau, M.; Gaspard, S. *J. Am. Chem. Soc.* **1989**, *111*, 9125. (b) Lee, P.; Lo, P.-C.; Chan, E.; Fong, W.-P.; Ko, W.-H.; Ng, D. *Tetrahedron Lett.* **2005**, *46*, 1551. (c) Ribeiro, A. O.; Tomé, J. P. C.; Neves, M. G. P. M. S.; Tomé, A. C.; Cavaleiro, J. A. S.; Iammoto, Y.; Torres, T. *Tetrahedron Lett.* **2006**, *47*, 9177.
(22) Alvarez-Mico, X.; Calvete, M. J. F.; Hanack, M.; Ziegler, T. h. *Tetrahedron Lett.* **2006**, *47*, 3283.
(23) MacDonald, I.; Dougherty, T. *J. Porphyrins Phthalocyanines* **2001**, *5*, 105.
(24) Camerin, M.; Rello, S.; Villanueva, A.; Ping, X.; Kenney, M.; Rodgers, M.; Jori, G. *Eur. J. Cancer* **2005**, *8*, 1203.
(25) (a) Ono, N.; Bougauchi, M.; Maruyama, K. *Tetrahedron Lett.* **1992**, *33*, 1629. (b) Maillard, P.; Guerquin-Kern, J.-L.; Huel, C.; Momenteau, M. *J. Org. Chem.* **1993**, *58*, 2774. (c) Fujimoto, K.; Miyata, T.; Aoyama, Y. *J. Am. Chem. Soc.* **2000**, *122*, 3558. (d) Chen, X.; Hui, L.; Foster, D.; Drain, C. *Biochemistry* **2004**, *43*, 10918. (e) Li, G.; Pandey, S.; Graham, A.; Dobhal, M.; Ricky, M.; Chen, Y.; Gryshuk, A.; Rittenhouse-Olson, K.; Oseroff, A.; Pandey, R. *J. Org. Chem.* **2004**, *69*, 158. (f) Chen, X.; Drain, C. *Drug Design Rev. – Online* **2004**, *1*, 215; www.ingentaconnect.com/content/ben/ddro.
(26) (a) Chandler, J.; Williams, E.; Slavin, J.; Best, J.; Rogers, S. *Cancer* **2003**, *97*, 2035. (b) Kumamoto, K.; Goto, Y.; Sekikawa, K.; Takenoshita, S.; Ishida, N.; Kawakita, M.; Kannagi, R. *Cancer Res.* **2001**, *61*, 4620.
(27) Wöhrle, D.; Schnurpfeil, G.; Knothe, G. *Dyes Pigments* **1992**, *18*, 91.
(28) Zemplén, G. *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 1555.
(29) Sommerauer, M.; Rager, C.; Hanack, M. *J. Am. Chem. Soc.* **1996**, *118*, 10085.
(30) (a) Wolfrom, M. L.; Thompson, A. *Methods in Carbohydrate Chemistry*, Vol. 2; Whistler, R. L.; Wolfrom, M. L., Eds.; Academic Press: New York, **1963**, 211. (b) Mikamo, M. *Carbohydr. Res.* **1989**, *191*, 150.
(31) (a) Scheurer, P. G.; Smith, F. *J. Am. Chem. Soc.* **1954**, *76*, 3224. (b) Matta, K. L.; Girotra, R. N.; Barlow, J. *J. Carbohydr. Res.* **1975**, *43*, 101.
(32) Sorg, B. L.; Hull, W. I.; Kleim, H. C.; Mier, W.; Wiessler, M. *Carbohydr. Res.* **2005**, *340*, 181.
(33) Petrig, J.; Schibli, R.; Dumas, C.; Alberto, R.; Schubiger, P. A. *Chem. Eur. J.* **2001**, *7*, 1868.