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Benzoporphyrins and Acetylene-Substituted Porphyrins as Improved Photosensitizers in the Photodynamic Tumor Therapy with Porphyrin Platinum Conjugates

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Summary. A combination of a cisplatinum-like fragment and a porphyrin in the same molecule should not only result in the additivity of the dark toxicity of the platinum fragment and the phototoxicity of the porphyrin moiety, but also in the enrichment of the porphyrin platinum conjugates in tumor tissue, which cisplatinum alone does not show. To increase the penetration depth of the red light used in the photodynamic tumor therapy the conjugated system of the porphyrin components in porphyrin platinum conjugates had to be expanded. Sixteen new $(NH_3)_2Pt$ derivatives of benzoporphyrins and acetylene-substituted porphyrins were synthesized, characterized, and tested with respect to their antitumor activity on the mammary carcinoma cell line MDA-MB-231.

Keywords. Photodynamic tumor therapy; Porphyrin platinum conjugates; Benzoporphyrins; Acetylene-substituted porphyrins; MDA-MB-231 cell line.

Introduction

Two promising approaches in cancer chemotherapy are the 'cytostatic therapy' with platinum derivatives and the 'photodynamic therapy' with porphyrin compounds. We attempted to combine these two strategies by combining cisplatinum/carboplatinum fragments with porphyrin systems in the same molecule. These porphyrin platinum conjugates should show the cytostatic activity of the platinum part also in the dark. Upon irradiation, the photodynamic component of the porphyrin sensitizers should be added. In addition, porphyrin platinum conjugates should have an important advantage with respect to mixtures of platinum and porphyrin compounds. Whereas porphyrin derivatives enrich in cancer tissues, platinum complexes such as cisplatinum and carboplatinum penetrate unselectively into all fast growing tissues, giving rise to the known side-effects nausea, vomiting, myelosuppression, nephrotoxicity, *etc*. With porphyrin platinum conjugates we expect a selective enrichment of platinum compounds in tumors [1, 2]. First reports in this direction have been published [3–6]. In this paper we present a strategy to

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shift the absorption maxima of the porphyrin systems to longer wavelengths by expansion of the conjugated systems by using benzoporphyrins and porphyrins substituted with acetylenes [7].

In the photodynamic therapy (PDT), the irradiation of dye molecules gives cytotoxic effects in the tumor resulting in the death of the proliferating cells [8, 9]. The activation of the photosensitizers with long-wavelength light does not cause side-effects. As photosensitizers, hematoporphyrin derivative (HpD) and photofrin II, respectively, are used. HpD is a mixture of hematoporphyrin, hydroxyethyl-vinyl-deuteroporphyrin, and protoporphyrin as well as of dimers, trimers, and oligomers of these compounds [10]. Photofrin II is a fraction of HpD obtained by gel filtration [11–13]. The excited porphyrins react with biomolecules or, more frequently, with triplet oxygen. The highly reactive singlet oxygen which is formed oxidizes biomolecules leading to cell death [14–18]. The photodynamic tumor therapy with photofrin II and its congeners is accompanied by typical disadvantages. As a consequence of the long-wavelength absorption maximum at 623 nm common to all hematoporphyrin derivatives, the penetration depth of the light used for the therapy is at most 5 mm [19]. To treat tumors which are larger and located below the surface of the skin, a better penetration would be desirable. A prerequisite for this is a red-shift of the long-wavelength absorption maximum.

Results and Discussion

Benzoporphyrins in the photodynamic therapy

Benzoporphyrins are derivatives of protoporphyrin. They are formed in the $(4 + 2)$-cycloaddition of a dienophile to one of the vinylic double bonds and an adjacent double bond [20, 21]. 1967 described for the first time as oil constituents [22], benzoporphyrins have been investigated intensely since the end of the seventies [21, 23–25]. After *Diels-Alder* reactions with electron-poor dienes such as tetracyanoethylene had been carried out at the beginning of the eighties, *Dolphin* reported a $[4 + 2]$-cycloaddition of acetylene dicarboxylic acid esters to the vinyl groups in protoporphyrin dimethylester to give benzoporphyrins in 1986 [20]. It was only a few years later that their suitability as photosensitizers was recognized [26, 27]. The most active component is the isomer enlarged in porphyrin ring A, which has been widely studied in the photodynamic therapy [28, 29].

Benzoporphyrins have their long-wavelength absorption maximum at *ca.* 690 nm, affording almost a duplication of the penetration of the light compared to photosensitizers such as photofrin II. In addition, this absorption maximum has a higher extinction coefficient than the lowest energy maximum of hematoporphyrin, which increases the effectivity of the irradiation substantially [30–35]. Actually, a wavelength dependent antitumor activity has been observed *in vitro* as well as *in vivo* [36].

Benzoporphyrins have promising pharmacodynamic properties, showing up in a reduced incubation time (already after 3 hours the enrichment maximum is obtained) and in a drastically reduced retention time in the body. Different from photofrin II, which reaches its concentration maximum in the cell only after 24 hours, after this time the concentrations of the benzoporphyrins already have

dropped below the level causing irritations of the skin [37]. In addition, there is no appreciable photobleaching effect [38].

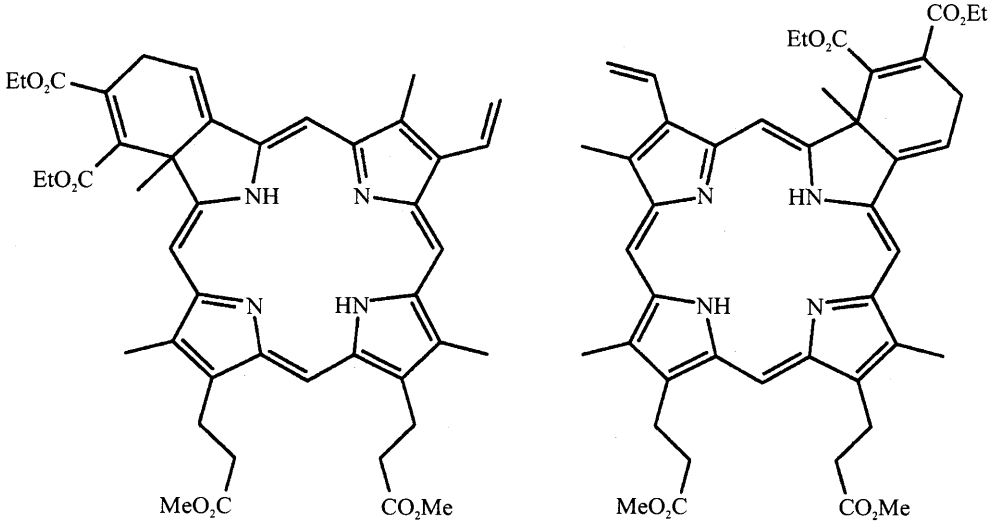
Synthesis of benzoporphyrin derivatives **1–12**

Protoporphyrin dimethylester was refluxed with a 20-fold excess of ethyl acetylenedicarboxylate for 6 days in toluene. After this time there was still some starting material left in the reaction mixture. However, the yield of the 1:1-mixture of the two cycloaddition products **1** and **2** was highest (Scheme 1). Longer reaction times increased the amount of by-products such as isobacteriochlorin. The double adduct did not form in measurable quantities, although a double cycloaddition is known in the reaction with the stronger dienophile tetracyanoethylene (*TCNE*). The crude product mixture was submitted to chromatography. First, the starting material eluted as a red zone, followed by the isomer mixture **1**/**2**.

The chromatographic separation of **1** and **2** was difficult, as only little material could be brought onto the columns and long elution times were necessary due to the unpolar solvent mixture which had to be used. Benzoporphyrin **2**, the more unpolar of the two compounds, was eluted first, followed by isomer **1**. The isomer mixture and the individual isomers have different phototoxic activities [30].

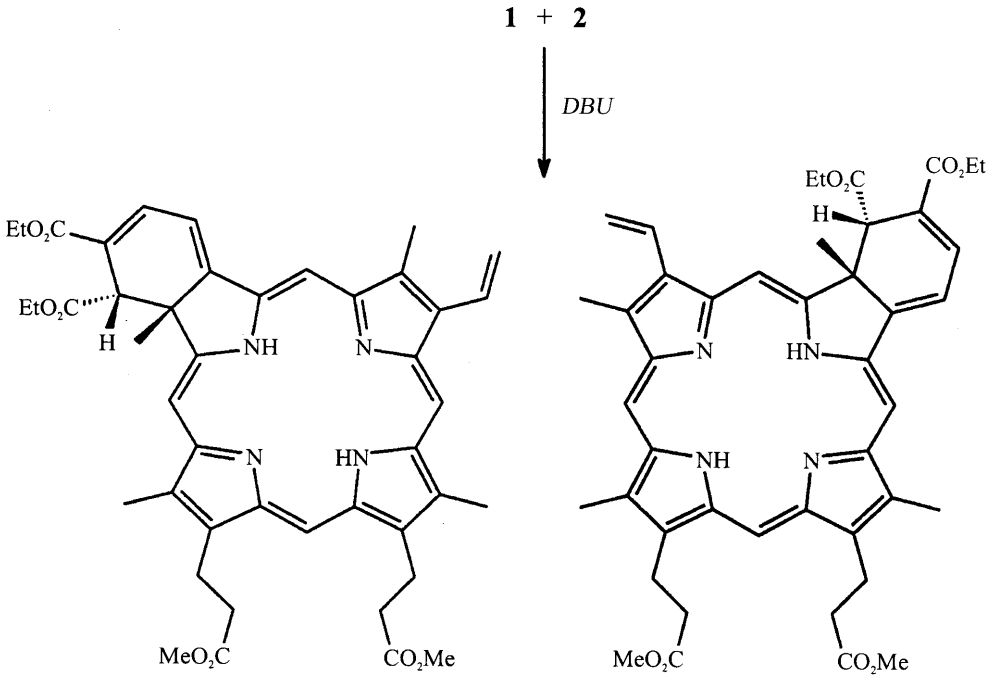
The intermediates **1** and **2** and the isomer mixture **1**/**2** were rearranged with 1,8-diazabicyclo[5.4.0]undec-5-ene (*DBU*) to give the *trans*-configurated products **3**, **4** and **3**/**4** which were obtained in the chromatography as the second zone (Scheme 2).

The final synthetic step to give the ligands **5** and **6** as well as **7** and **8** for the binding of the platinum fragment was the hydrolysis of the ester groups in **3** and **4**. As the alkaline hydrolysis was not successful [7], the partial saponification was carried out with 25% HCl at room temperature (TLC control). After *ca*. 5 hours the



1 **2**

Scheme 1



Scheme 2

two methyl ester groups were selectively hydrolyzed (Scheme 3). According to the mass spectra, in the products **5**, **6**, and **5**/**6** only a small part of the ethyl ester groups was hydrolyzed.

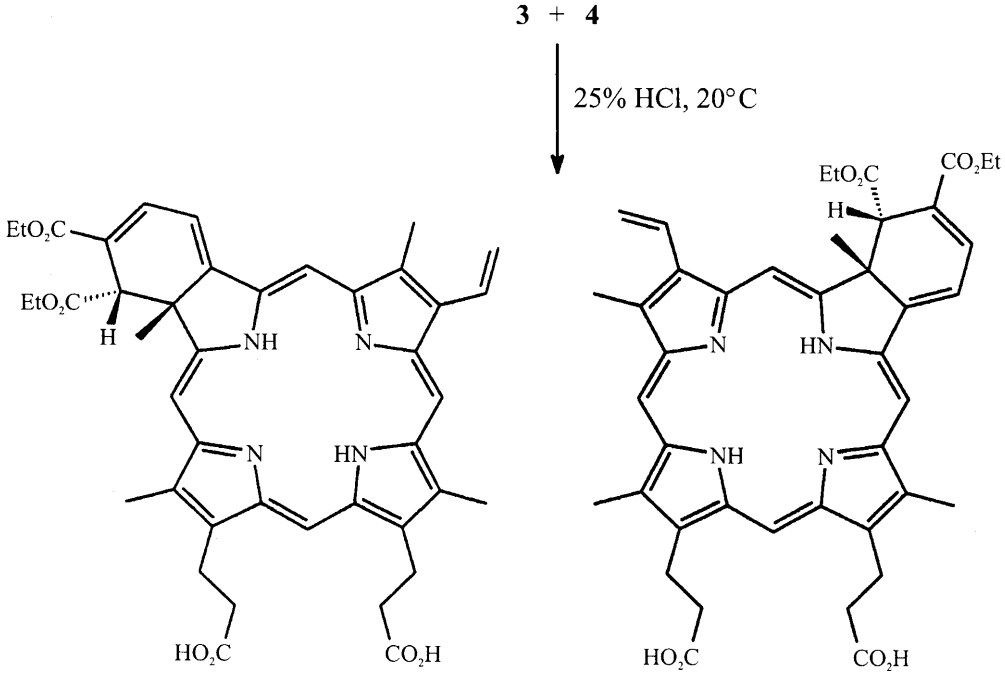
The ethyl ester groups in **3**/**4** were only attacked during longer reaction times. After reacting **3**/**4** with 25% HCl at 80°C for 20 hours, the hydrolysis to **7**/**8** was complete (Scheme 4).

With tetracyanoethylene, (4 + 2)- and (2 + 2)-cycloadditions to one as well as to both vinyl groups of protoporphyrin dimethylester are known [21]. The cycloadducts **9** and **10** are formed in the reaction of protoporphyrin dimethylester with equivalent amounts of *TCNE* at reflux (Scheme 5). In the chromatography, the narrow red zone of the starting material follows the two green zones of the products from which sufficient material of the isomers **9** and **10** for analytical measurements can be obtained. **9** elutes before **10** as assigned by NOE difference spectroscopy [7].

The preparative ester hydrolysis to give **11**/**12** was carried out with the isomer mixture **9**/**10** which was stirred with LiOH in *THF*/methanol according to Scheme 6 for one week at room temperature (conversion quantitative).

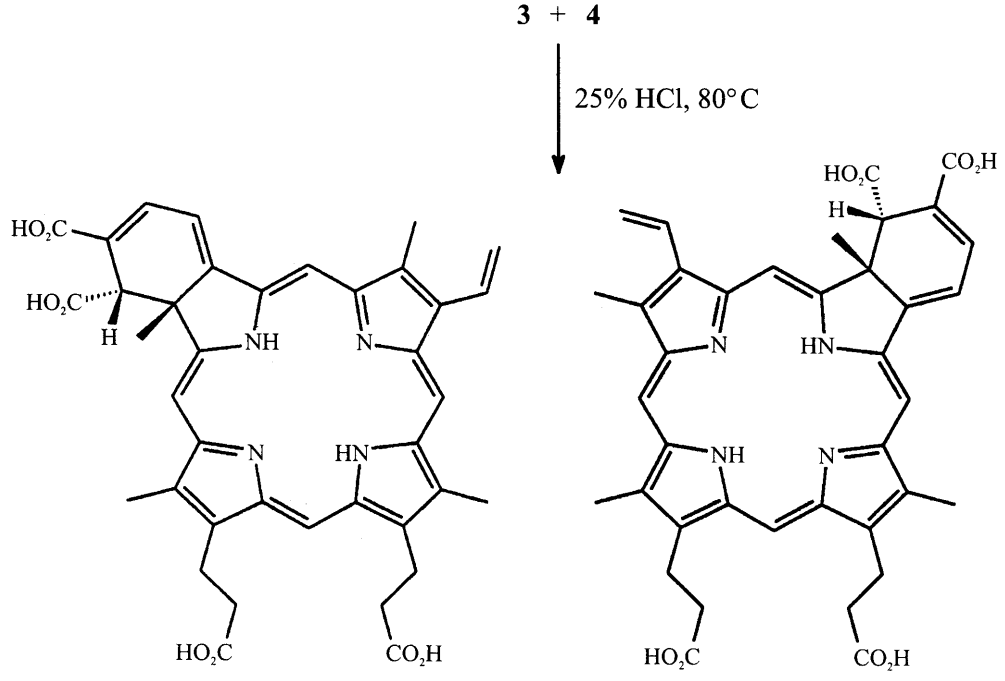
Porphyrins with acetylene substituents

As outlined in the introduction, the expansion of the π-system should lead to a red-shift of the porphyrin absorption spectrum. Therefore, we started to synthesize acetylene-substituted porphyrin ligands from halogeno-substituted porphyrins and monosubstituted acetylenes [7]. It turned out that the zinc complex of



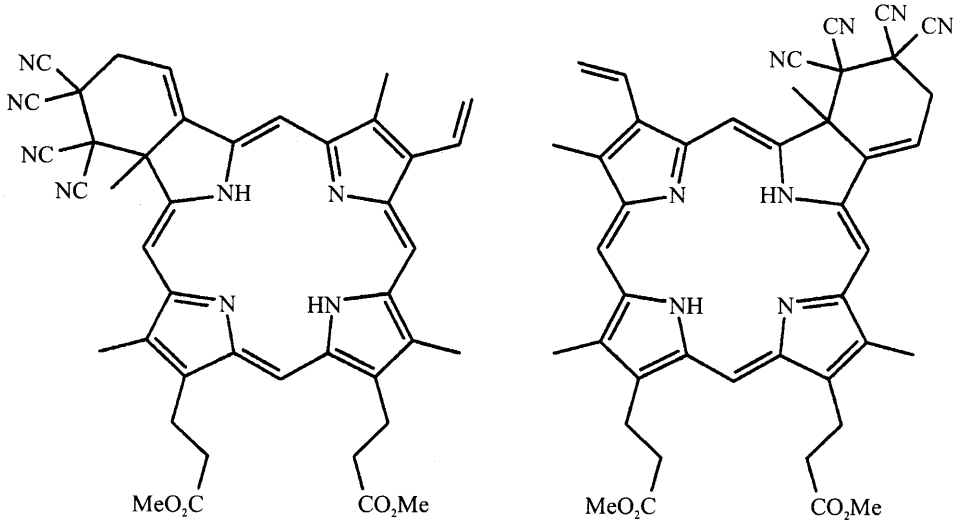
5 **6**

Scheme 3



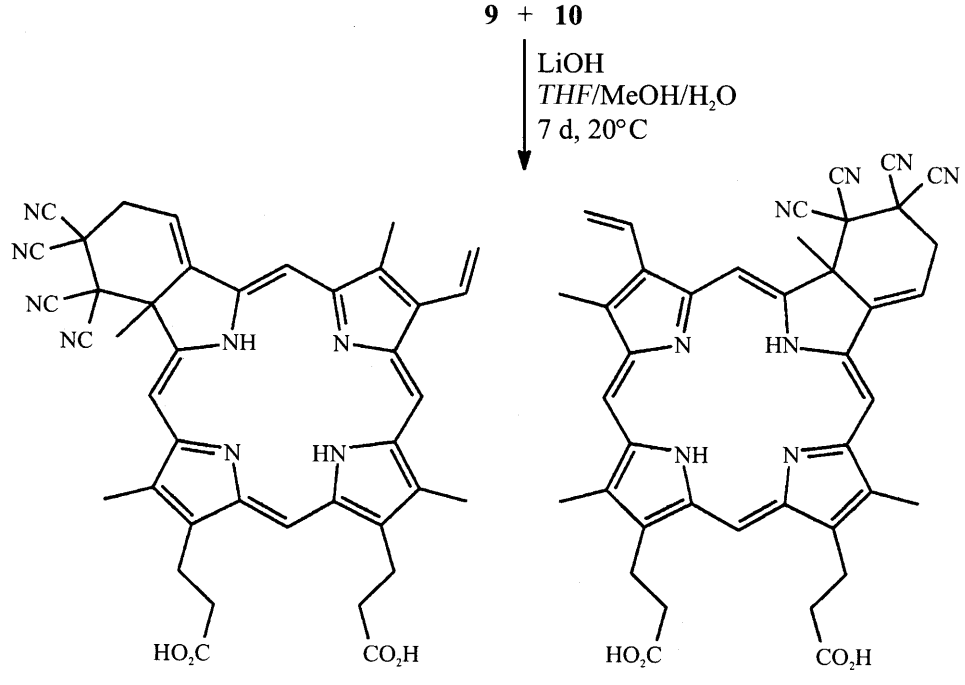
7 **8**

Scheme 4



9 **10**

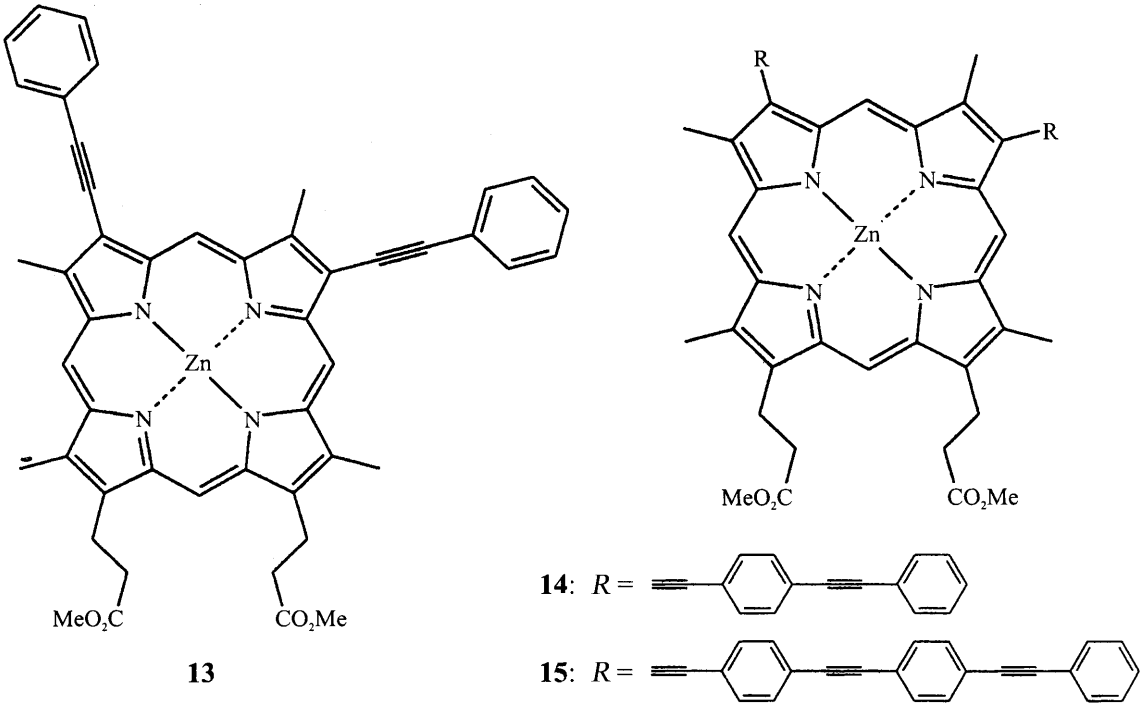
Scheme 5



11 **12**

Scheme 6

3,8-dibromodeuteroporphyrin [6] did not react with phenylacetylene, neither with the catalyst $Pd(PPh_3)_2Cl_2/CuI$ nor with other Pd catalysts [39–41]. However, employing the catalyst $Pd(PPh_3)_2Cl_2/CuI$ (5:2.5 mol%) reaction of the zinc

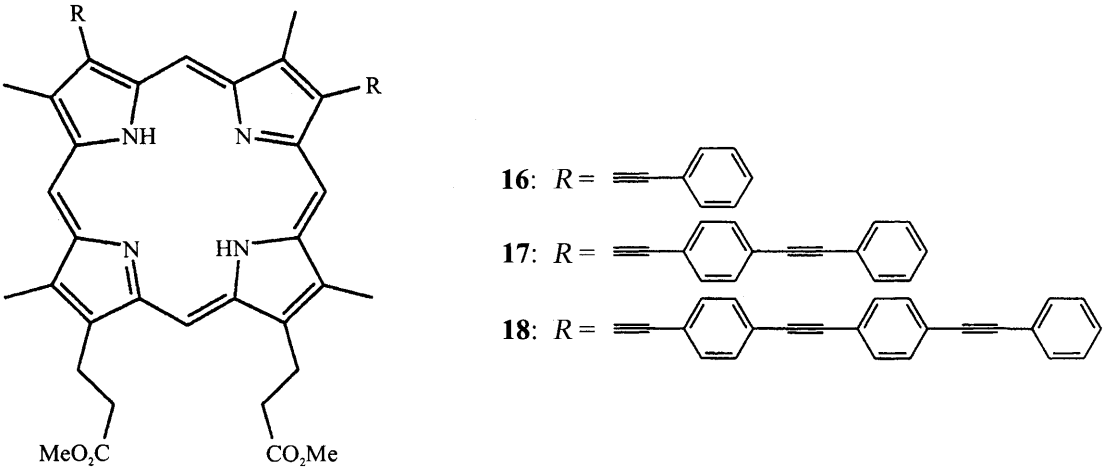


Scheme 7

complex of 3,8-diiododeuteroporphyrin [6] with phenylacetylene resulted in product **13** in *ca.* 90% yield after 20 hours reaction time in *THF*/NEt_3 (Scheme 7). The corresponding monosubstituted intermediates were formed in *ca.* 10% yield as shown by HPLC-MS [7].

Compounds with varying phenylethynyl units were intended to be synthesized, which subsequently should be coupled to porphyrins *via* the free ethyne end. The synthesis of the monofunctionalized ethynes from haloarenes and trimethylsilyl acetylene in the presence of Pd-catalysts was carried out such that the reaction only took place at the free ethyne position. After the coupling, the trimethylsilyl group was cleaved with K_2CO_3. For sequential reactions at the phenyl nucleus, *p*-bromoiodobenzene was used [42]. With phenylacetylene and employing a $Pd(PPh_3)_2Cl_2$/CuI catalyst in *THF*/NEt_3 it was transformed into (4-bromophenyl)-phenylethyne, which reacted with trimethylsilyl acetylene under similar conditions to give trimethylsilyl(4-(phenylethynyl)phenyl)ethyne and, after K_2CO_3/MeOH cleavage, (4-(phenylethynyl)phenyl)ethyne [7]. The (4-(phenylethynyl)phenyl) ethynyl group bound to porphyrin **14** is shown in Scheme 7.

To add another 4-phenylethynyl unit, (4-(phenylethynyl)phenyl)ethyne was reacted with bromoiodobenzene. The reaction of the resulting *p*-bromo derivatives with trimethylsilyl acetylene was so slow that the reaction mixture had to be treated several times with trimethylsilyl acetylene. After three runs, trimethylsilyl(4-(4-(phenylethynyl)phenylethynyl)phenyl)ethyne was obtained in acceptable yield and purity. The *TMS* protecting group could not be removed with K_2CO_3. However, the cleavage was possible with tetra-*n*-butylammoniumfluoride, which for a better separation was immobilized on silica gel. The isolation and purification of



Scheme 8

(4-(4-(phenylethynyl)phenylethynyl)phenyl)ethyne was carried out by elution with diethyl ether/petroleum ether [7]. The (4-(4-(phenylethynyl)phenylethynyl)-phenyl)ethyne group bound to porphyrin **15** is shown in Scheme 7.

The products **14** and **15** were synthesized by $Pd(PPh_3)_2Cl_2$/CuI-catalyzed coupling of (4-(phenylethynyl)phenyl)ethyne and (4-(4-(phenylethynyl)phenyl-ethynyl)phenyl)ethyne with the zinc complex of 3,8-diiododeuteroporphyrin (Scheme 7).

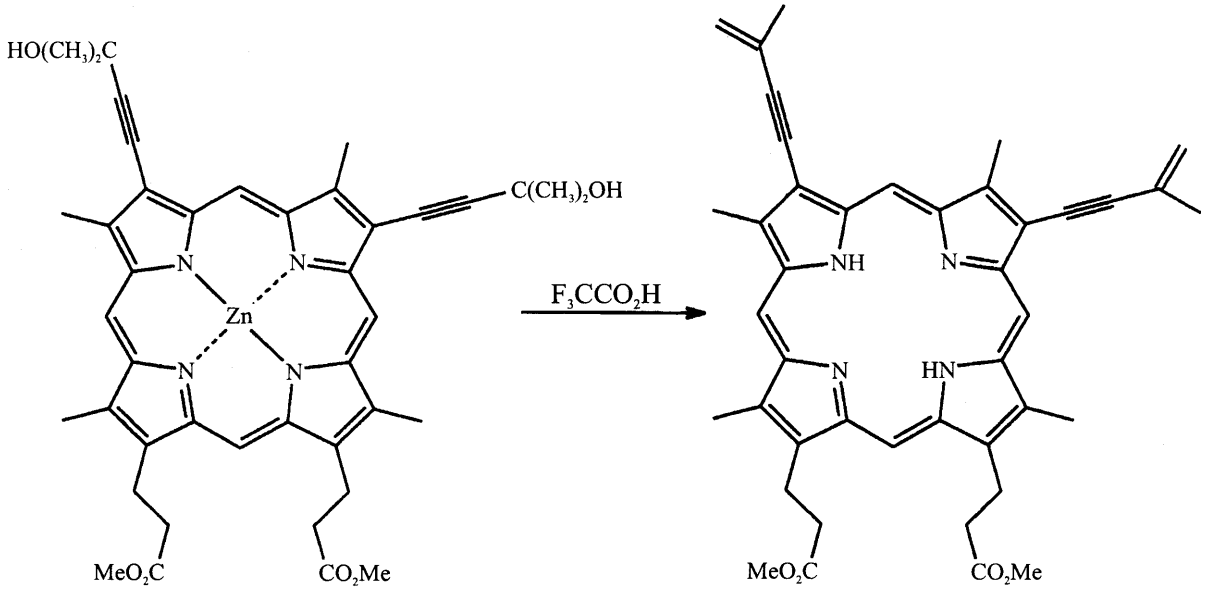
As the longest-wavelength absorption maximum of the zinc complexes **13**–**15** is only at 580 nm, they were transformed to the metal-free porphyrins **16**–**18** with trifluoroacetic acid (Scheme 8).

The zinc complex **19** was accessible from 2-methyl-3-butyn-2-ol and 3,8-diiododeuteroporphyrin with a $Pd(PPh_3)_2Cl_2$/CuI catalyst (Scheme 9). During removal of the metal from **19** with trifluoroacetic acid, a loss of water to give product **20** was observed which contains an ene-yne structure conjugated with the porphyrin system (Scheme 9).

The catalytic reaction of diiododeuteroporphyrin with trimethylsilylacetylene gave the product **21** in high yield. To avoid the loss of the *TMS* group, work-up (filtration over SiO_2 to remove the quaternary ammonium salts and chromatography on SiO_2 with CH_2Cl_2:MeOH = 100:1) was carried out under anhydrous conditions (Scheme 10).

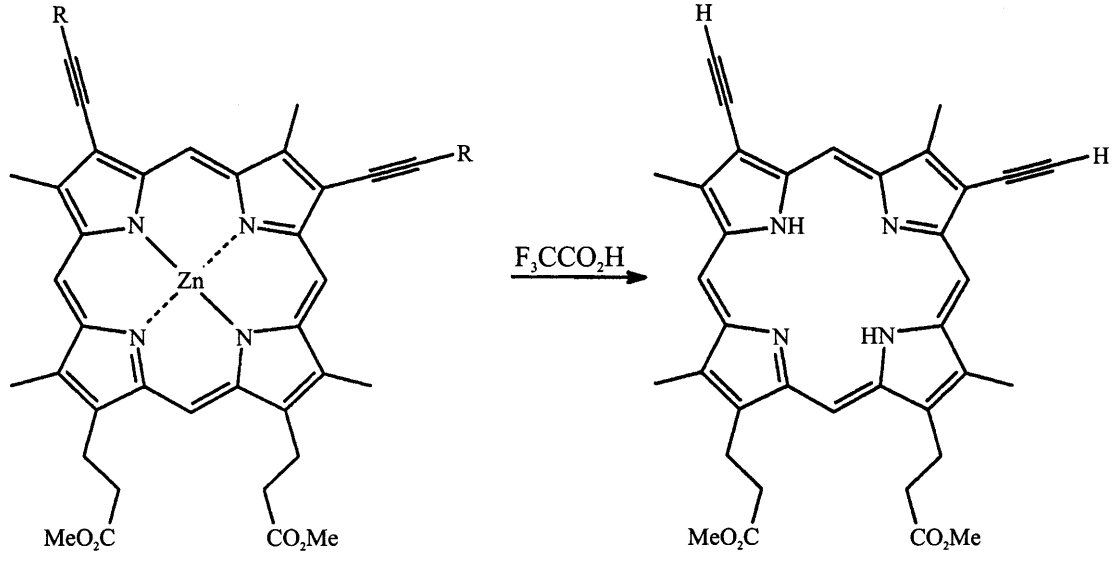
The attempt to remove the *TMS* groups from **21** with K_2CO_3/MeOH led to appreciable hydrolysis of the ester functions [7]. However, the ethyne groups could be liberated to give compound **22** with tetra-*n*-butylammoniumfluoride in absolute *THF* (Scheme 10). The demetalation of **22** with trifluoroacetic acid gave the metal-free porphyrin ester **23** in good yield (Scheme 10).

Hydrolysis of the methyl ester groups in the porphyrins **13**–**20**, **22**, and **23** was accomplished with 20% KOH in methanol. The porphyrin esters **13**–**18**, **20**, and **22** were refluxed, whereas compounds **19** and **23** were stirred at room temperature for 1 d to guarantee milder reaction conditions. The hydrolysis products were the free carboxylic acids **24**–**33** (Scheme 11).



19 **20**

Scheme 9



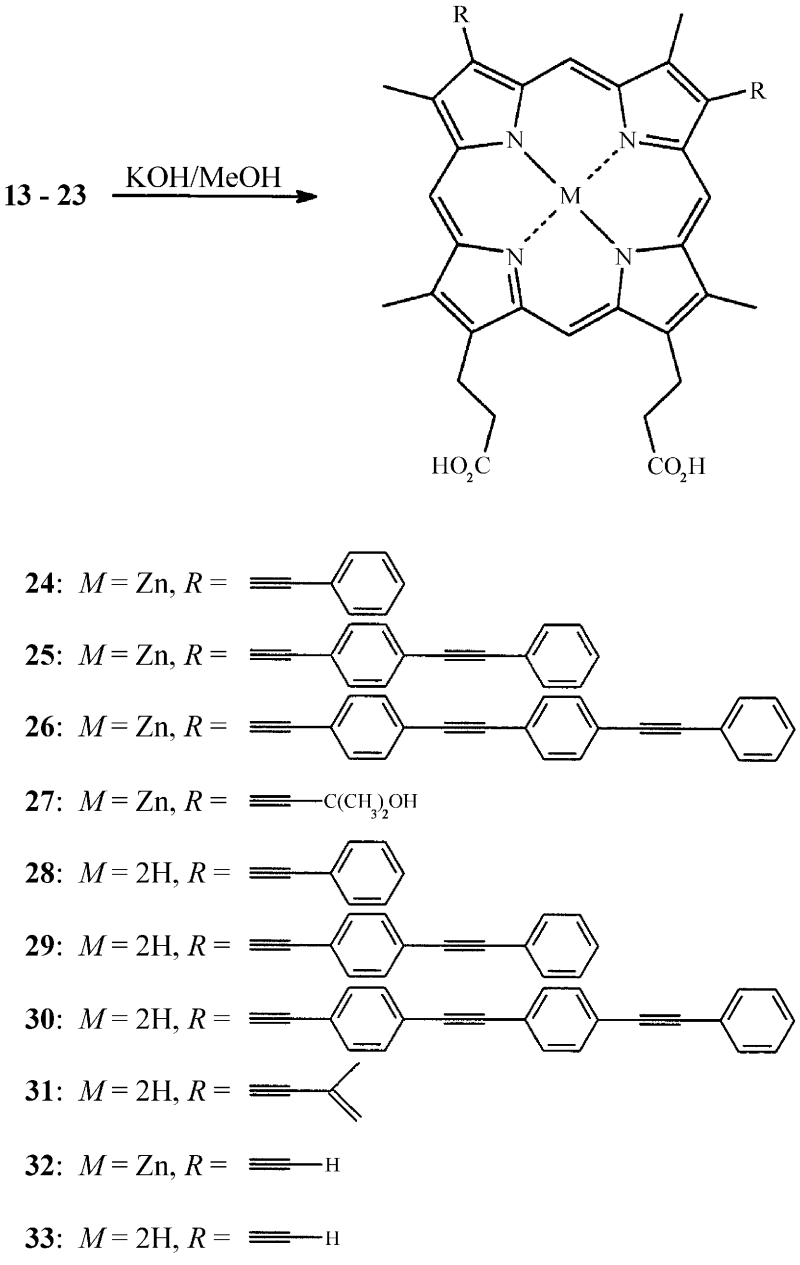
21: $R = Si(CH_3)_3$
22: $R = H$

23

Scheme 10

Synthesis of the platinum complexes

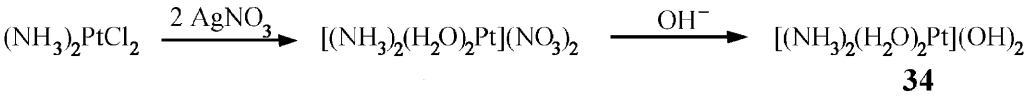
The last step in the synthesis of the porphyrin platinum conjugates was the complexation of the porphyrin ligands with the platinum fragments. To this end it was necessary to transform cisplatinum into a reactive hydrolysis product [43].



Scheme 11

Cisplatinum was stirred with two mol equivalents of silver nitrate in aqueous solution under exclusion of light for one week. The two chloro ligands were replaced by aqua ligands, and AgCl was precipitated. Subsequently, the nitrate counter ions were exchanged for hydroxide ions by chromatography on a strongly basic ion exchanger. Diammine(diaqua)platinum(II)-dihydroxide **34** was formed (Scheme 12).

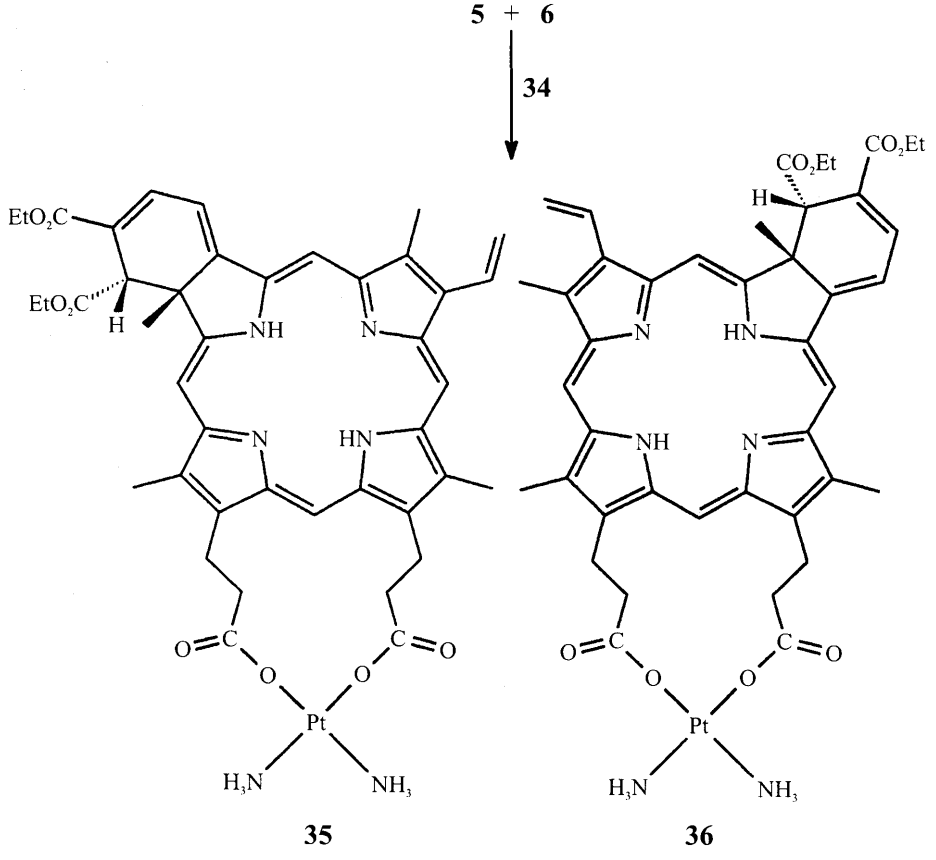
The complexation starts by dissolving the porphyrin ligand in a solvent miscible with water, *e.g.* methanol, ethanol, or *THF*. Subsequently, **34** is added



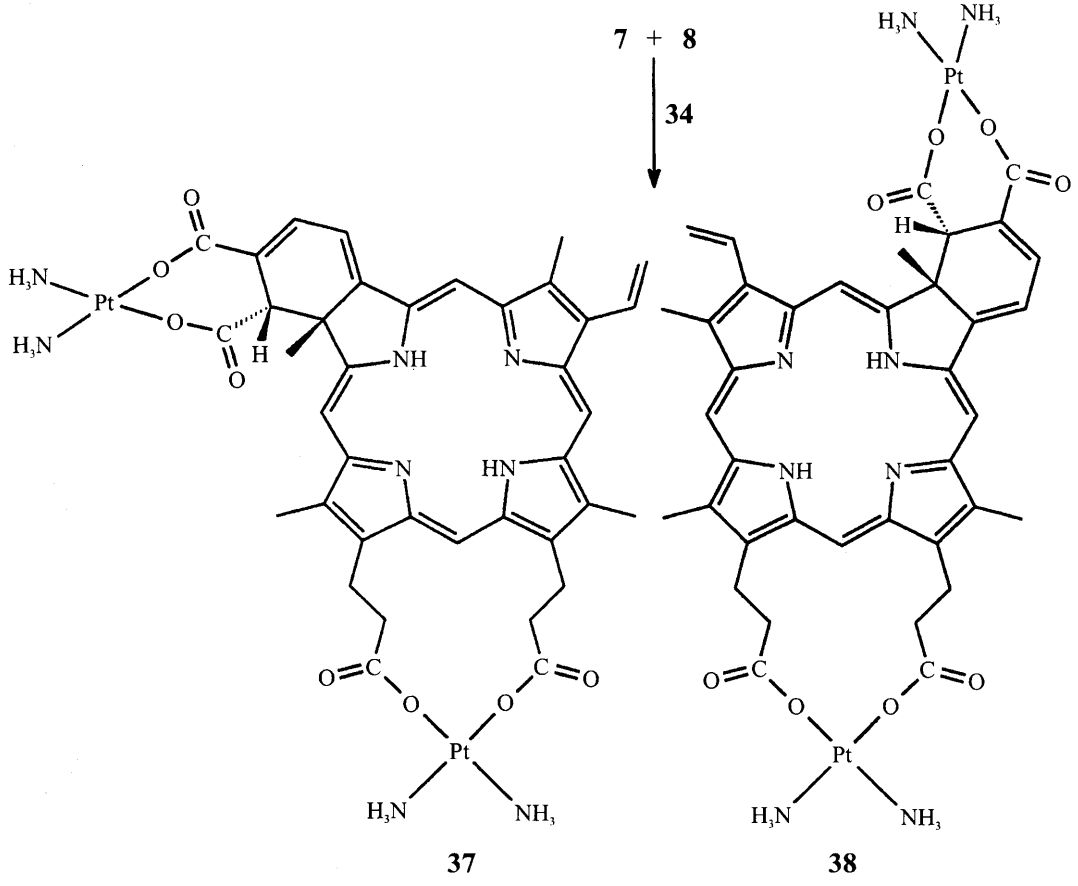
Scheme 12

as a 50% water/ethanol solution (equimolar or a small excess) and stirred at room temperature for several hours. The porphyrin platinum conjugates precipitate. To obtain a high product yield it is important to take care that the solvent mixture used has the right composition, as the complexes are slightly soluble, particularly in *THF*. On the other hand, enough solvent should be used, as otherwise upon addition of the aqueous platinum solution the ligands, which are not water-soluble, precipitate. To complete the precipitation, it is recommended to leave the reaction mixture at −25°C. For purification the products are washed with water to remove excess platinum compounds and then with solvents in which the ligands are soluble.

Using this procedure, the conjugates **35** and **36** were obtained from benzoporphyrins **5** and **6** (Scheme 13). In the case of the complexation of the benzoporphyrin mixture **7**/**8** attention had to be paid to the fact that two binding sites are available in each molecule. Therefore, 2 mol of **34** were reacted with 1 mol of the isomer mixture **7**/**8** to give the conjugates **37**/**38** (Scheme 14).



Scheme 13



Scheme 14

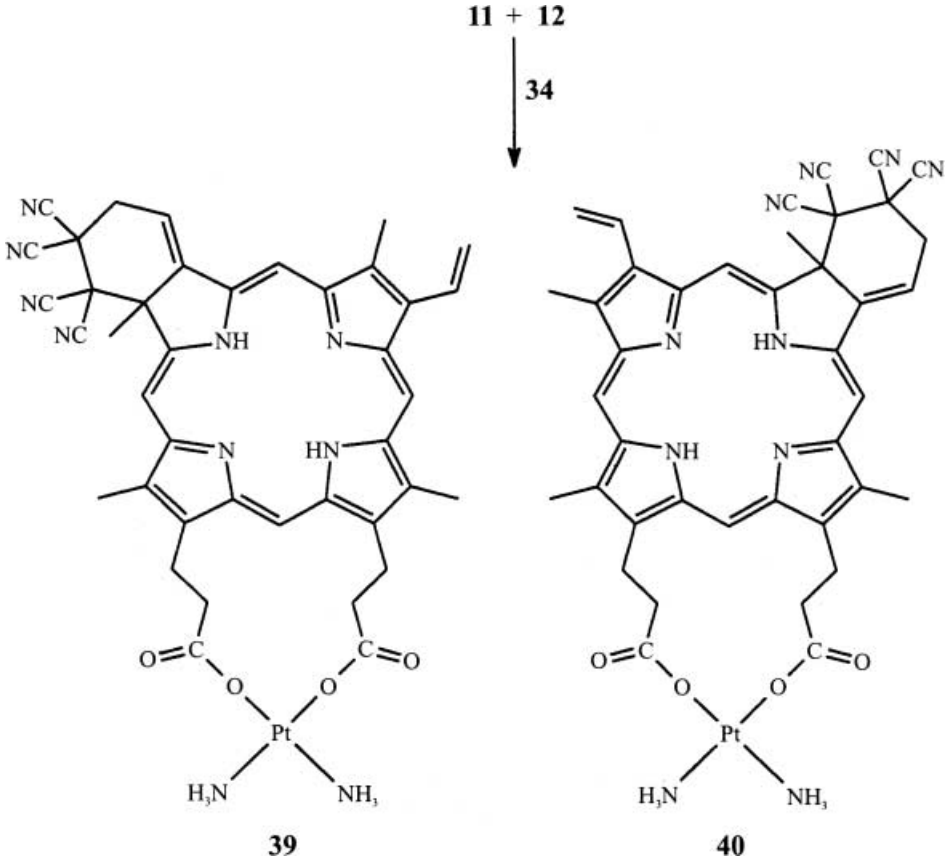
Similarly, the *TCNE* adducts **11**/**12** yielded the complex mixture **39**/**40** (Scheme 15).

The acetylene-substituted porphyrin platinum conjugates **41**–**50** are shown in Scheme 16.

Spectroscopy

IR spectroscopy is a suitable method to monitor the course of the reactions described. The porphyrins show the characteristic, sharp NH absorption of pyrrole at 3300 cm^{-1}, which is useful to check whether metal insertion into the porphyrin center or metal removal is complete. The shift of the CO absorption of the esters (1740–1725 cm^{-1}) during hydrolysis to the porphyrindicarboxylic acids ($\sim$ 1700 cm^{-1}) can be used to check the completion of hydrolysis. The complexation of the porphyrindicarboxylates with the platinum fragments results in compounds with CO absorptions around 1600 cm^{-1}. Another diagnostic IR tool is the weak Pt–O band around 375 cm^{-1} in the dicarboxylato complexes.

All porphyrins exhibit the characteristic *Soret* band at about 400 nm (molar extinction coefficient up to 400 000 $dm^3 \cdot mol^{-1} \cdot cm^{-1}$). The hematoporphyrin derivatives show absorption spectra of the etio type. The sequence of the satellite

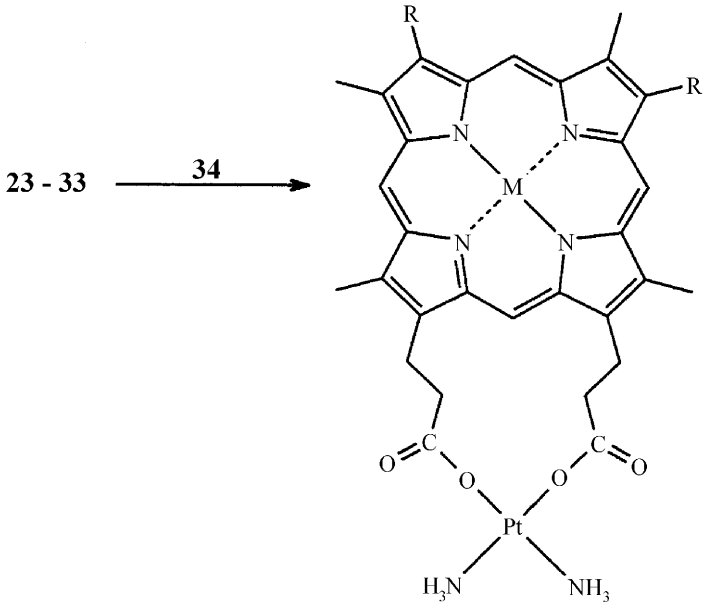


Scheme 15

band intensity is IV > III > II > I. The satellite band I appears at 620 nm, II at 570 nm, III at 530 nm, and IV at 500 nm. In contrast to the free porphyrins with their 4 typical satellite bands the metalloporphyrins, *e.g.* the Zn complexes, exhibit only two more intense satellite bands. This demonstrates that in the platination reaction the platinum does not coordinate in the center of the porphyrin but at the peripheral carboxylato groups.

The magnetic anisotropy of the macrocyclic porphyrins expands the ^{1}H NMR spectra up to 15 ppm. The signals of the 4 methine bridges of the hematoporphyrin derivatives appear at about 10 ppm. The 2 NH protons show a broad signal at about −4 ppm due to fast exchange. The methyl groups of the hematoporphyrin derivatives in the positions 2, 7, 12, and 18 are strongly affected by the anisotropy and appear at 3.6 ppm. The signals of the α-methylene groups in the positions 13 and 17 show up at 4.2 ppm, those of the β-methylene groups at 3.2 ppm. The ^{1}H NMR signals of the platinum complexes tend to broaden.

All synthesized compounds were examined by mass spectrometry, mostly with the LISIMS technique. The porphyrin platinum compounds were embedded in a matrix consisting of glycerol and *DMSO*. The more soluble porphyrins were measured in a matrix of 3-nitrobenzylalcohol and CH_2Cl_2. Interestingly, for most of the porphyrin platinum compounds the molecular ion was observed, albeit in low intensity, establishing their composition.



41: M = Zn, R =

42: M = Zn, R =

43: M = Zn, R =

44: M = Zn, R = $C(CH_3)_2OH$

45: M = 2H, R =

46: M = 2H, R =

47: M = 2H, R =

48: M = 2H, R =

49: M = Zn, R = H

50: M = 2H, R = H

Scheme 16

Cell tests

All complexes were tested with the MDA-MB-231 mammary carcinoma cell line in three different concentrations with and without irradiation in *DMF* solution as described in Ref. [44] and, in particular, in Ref. [6]. The T/C values, which express

Table 1. Antitumor activity of the porphyrin platinum(II) complexes **35–50** measured at 1×10^{-5}, 5×10^{-6}, and 1×10^{-6} mol/dm^3 *in vitro* on the MDA-MB-231 mammary carcinoma cell line (solvent: *DMF*)

c	Without irradiation			With irradiation		
(μmol/dm^3)	1	5	10	1	5	10
35	102.1±6.9	94.1±8.5	85.0±6.6	83.2±9.8	79.2±12.8	−14.8±2.0
35/**36**	69.3±5.3	34.2±5.2	7.3±3.4	53.4±8.8	9.1±3.3	−7.7±1.9
37/**38**	99.4±12.3	92.2±12.9	77.1±7.5	93.4±12.9	96.8±9.0	84.4±8.4
39/**40**	107.1±8.9	77.6±8.8	43.2±3.8	99.2±11.6	42.0±6.0	15.1±4.1
41	108.3±9.4	94.4±9.4	72.4±7.2	101.8±9.8	51.8±5.3	33.6±5.7
42	114.2±8.9	108.2±9.3	83.1±7.8	112.1±8.8	103.1±8.5	87.9±7.5
43	106.5±8.6	112.7±9.9	107.4±8.8	113.6±8.7	115.9±9.6	105.9±9.2
44	114.3±7.8	101.6±6.7	80.4±5.9	104.8±9.3	67.6±6.1	48.5±3.9
45	104.7±8.8	90.7±7.1	70.0±6.5	101.1±9.3	67.0±6.5	52.7±6.0
46	109.1±9.3	101.6±8.1	88.4±7.5	113.8±8.9	93.7±7.4	77.3±6.8
47	106.5±8.2	79.6±7.9	59.4±5.1	106.0±9.9	70.6±7.4	37.1±6.0
48	103.3±9.1	85.0±7.3	73.8±6.8	96.6±10.5	57.8±6.3	44.4±4.2
49	102.1±9.7	88.1±8.1	86.0±7.2	105.9±8.3	78.5±7.9	68.1±5.1
50	106.2±7.3	84.6±7.5	77.7±7.5	105.1±8.2	38.0±4.3	21.0±2.8
Cisplatinum	91.5±5.0	46.1±9.2	24.5±4.4	87.3±6.1	41.3±7.0	21.9±3.3

the relative inhibition of the solution of a compound on the cell growth compared to the solvent reference, are given in Table 1. T/C is defined by Eq. (1) in which T is the mean absorbance of the treated cells, C the mean absorbance of the solvent control, and C_0 the mean absorbance of the cells at the time when the drug was added ($t = 0$). A T/C value of 100% indicates a cell growth identical to the untreated control containing only the solvent used. A T/C value of 0% means that cell proliferation has come to a complete stop.

$$T/C = \frac{T - C_0}{C - C_0} \cdot 100\% \tag{1}$$

To classify the values obtained above, the clinically used compound cisplatinum was included in the tests. The T/C values show that cisplatinum lacks phototoxicity. Upon irradiation, some of the porphyrin platinum complexes come up to the values of cisplatinum and even exceed them, in particular **35** and **50** and the isomer mixtures **35**/**36** and **39**/**40**. Lack of solubility might be the reason for the unsatisfactory values of the benzoporphyrins **37**/**38**, which are twofold platinated. Probably, the reason for the low efficiency of some of the complexes is their limited solubility. Even treatment with ultrasound for hours did not give homogeneous solutions. Therefore, it is not sure that some of the solutions really had the concentrations indicated. Maybe part of the complexes remained insoluble and, thus, inactive.

In conclusion, the tests of the porphyrin platinum conjugates show a combination of a cytostatic and a phototoxic effect, some of which being more effective than cisplatinum.

Experimental

IR: Beckman spectrometer 4240, Perkin-Elmer-FT-IR spectrometer Paragon 1000 PC; ^{1}H NMR: Bruker WM 250 (250 MHz) and ARX 400 (400 MHz); *TMS* was used as internal standard; MS: Finnigan MAT 95 and MAT 112S; M.p.: Büchi SMP 20; the melting points are not corrected; UV/Vis: Kontron Instruments spectrophotometer Uvikon 930 and Uvikon 922.

Hemin (Fluka) was used without further purification. Protoporphyrin dimethylester was synthesized according to Ref. [45].

The nomenclature of the porphyrins and their complexes was based on the recommendation of IUPAC and the International Union of Biochemistry (IUB) [46]. The priority in the enumeration was given to the derivatized groups, which were defined as 3 and 8. This led to numbers 13 and 17 for the propionic acid groups. Correct elemental analyses were obtained for most of the compounds described [7].

Benzoporphyrin isomers **1** *and* **2** ($C_{44}H_{48}N_4O_8$)

Under N_2 protection, protoporphyrin dimethylester (1.00 g, 1.70 mmol) was dissolved in 100 cm^3 of toluene, and diethyl acetylenedicarboxylate (1.06 g, 1.00 cm^3, 6.30 mmol) was added. After 6 d of reflux the solvent was removed and the residue chromatographed on SiO_2 (120 × 2.5 cm) with CH_2Cl_2:Et_2O = 50:1. First, the red zone of unreacted starting material eluted, followed by the product mixture **1**/**2** as a long brown-green zone.

1/**2**: Yield: 260 mg (20%); green solid; m.p.: 130–150°C; IR (KBr): ν = 3300 (NH), 1720, 1700 (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): 761 (100%) MH^+.

Separation of the isomers **1** and **2**: 30 mg (0.04 mmol) of the isomer mixture **1**/**2** were dissolved in 10 cm^3 of CH_2Cl_2 and chromatographed on SiO_2 (120 × 4 cm) with CH_2Cl_2:Et_2O = 50:1. **2** eluted before **1**.

1: Yield: 11.4 mg (38%); green-black crystals; m.p.: 111°C; ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 9.85, 9.75, 9.39, 9.15 (4s, 4H, =CH), 8.18 (dd, $^3J_{cis}$ = 11.5, $^3J_{trans}$ = 17.8, 1H, vinyl H-8), 7.41 (m, 1H, H-2^4), 6.37 (m, 1H, vinyl H-8), 6.15 (m, 1H, vinyl H-8), 4.53 (q, ^3J = 7.2, 2H, CH_2OOC-2^1), 4.43–4.29 (m, 4 H, =CCH_2, CH_2OOC-2^2), 4.19 (t, ^3J = 7.6, 2H, =CCH_2), 4.02 (dd, ^3J = 22.2, ^2J = 6.7, 1H, H-2^3), 3.69–3.58 (dd, ^3J = 20.0, ^2J = 2.5, 1H, H-2^3), 3.67, 3.66, 3.59, 3.50, 3.41 (5s, 15H, CH_3, $COOCH_3$), 3.21 (t, ^3J = 7.6, 2H, CH_2COO), 3.17 (t, ^3J = 7.6, 2H, CH_2COO), 2.11 (s, 3H, CH_3-2), 1.41, 1.05 (2t, ^3J = 7.2, 6H, C*H*$_3$$CH_2$OOC-2^2, C*H*$_3$$CH_2$OOC-2^1), −2.57 (s, 2H, =NH) ppm.

2: Yield: 17 mg (57%); dark-green crystals; m.p.: 208°C; ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 9.82, 9.68, 9.32, 9.25 (4s, 4H, =CH), 8.17 (dd, $^3J_{cis}$ = 11.5, $^3J_{trans}$ = 17.7, 1H, vinyl H-3), 7.40 (dd, ^3J = 6.7, ^2J = 2.1, 1H, H-7^4), 6.33 (m, ^3J = 17.7, 1H, vinyl H-3), 6.15 (d, ^3J = 11.5, 1H, vinyl H-3), 4.53 (q, ^3J = 7.3, 2H, CH_2OOC-7^1), 4.42–4.36 (m, 2H, CH_2OOC-7^2), 4.33 (t, ^3J = 7.8, 2H, =CCH_2), 4.19 (t, ^3J = 7.8, 2H, =CCH_2), 3.96 (dd, ^3J = 19.8, ^2J = 6.7, 1H, H-7^3), 3.74–3.54 (m, 1H, H-7^3), 3.67, 3.65, 3.50 (int. 2), 3.44 (4s, 15H, CH_3, $COOCH_3$), 3.21 (t, ^3J = 7.8, 2H, CH_2COO), 3.17 (t, ^3J = 7.8, 2H, CH_2COO), 2.11 (s, 3H, CH_3-7), 1.40, 0.99 (2t, ^3J = 7.1, 6H, C*H*$_3$$CH_2$OOC-7^2, C*H*$_3$$CH_2$OOC-7^1), −2.46 (s, 2H, =NH) ppm.

Benzoporphyrin isomers **3** *and* **4** ($C_{44}H_{48}N_4O_8$)

100 mg (0.13 mmol) of **1** or **2** were reacted under N_2 protection in 30 cm^3 CH_2Cl_2 with 5 cm^3 of 1,8-diazabicyclo[5.4.0]undec-7-ene (*DBU*) for 24 h at 20°C. The reaction mixture was poured onto 100 cm^3 of 2 *N* HCl and extracted with 200 cm^3 of CH_2Cl_2. The organic phase was washed three times with 200 cm^3 of H_2O and once with 150 cm^3 of brine. After drying over $MgSO_4$ the solvent was removed, and the residue was chromatographed on SiO_2 (120 × 5 cm) with CH_2Cl_2:MeOH = 50:1. The product **3** or **4** eluted as an olive-green zone after a narrow red zone.

3: Yield: 75 mg (75%); black-green crystals; m.p.: 180°C; IR (KBr): $\nu = 3300$ (NH), 1740, 1710 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.78$, 9.63, 9.36, 8.97 (4s, 4H, $=CH$), 8.16 (dd, $^3J_{cis} = 11.9$, $^3J_{trans} = 17.7$, 1H, vinyl H-8), 7.77, 7.40 (2d, $^3J = 5.8$, 2H, H-2^3, H-2^4), 6.31 (dd, $^3J = 17.7$, $^2J = 1.5$, 1H, vinyl H-8), 6.13 (dd, $^3J = 11.9$, $^2J = 1.5$, 1H, vinyl H-8), 4.99 (s, 1H, H-2^1), 4.50–4.35 (m, 2H, CH_3CH_2OOC-2^2), 4.30, 4.15 (2t, 4H, $^3J = 7.7$, $=CCH_2$), 3.66, 3.65, 3.54, 3.48, 3.38 (5s, 15H, CH_3, $COOCH_3$), 3.51–3.27 (m, 2H, CH_3CH_2OOC-2^1), 3.20, 3.15 (2t, $^3J = 7.7$, 4H, CH_2COO), 1.82, (s, 3H, CH_3-2), 1.47, 0.31 (2t, $^3J = 7.0$, 6H, CH_3CH_2OOC-2^2, CH_3CH_2OOC-2^1), −2.28 (s, 2H, $=NH$) ppm.

4: Yield: 81 mg (81%); black-green crystals; m.p.: >250°C; IR (KBr): $\nu = 3300$ (NH), 1740, 1720 (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 761$ (100) MH^+; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 412 (4.70), 504 (3.71), 547 (3.70), 572 (3.83), 625 (3.58), 692 (4.05) nm; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.76$, 9.69, 9.36, 9.17 (4s, 4H, $=CH$), 8.14 (dd, $^3J_{cis} = 11.7$, $^3J_{trans} = 17.8$, 1H, vinyl H-3), 7.82, 7.45 (2d, $^3J = 5.8$, 2H, H-7^3, H-7^4), 6.37 (dd, $^3J = 17.7$, $^2J = 1.5$, 1H, vinyl H-3), 6.15 (dd, $^3J = 11.9$, $^2J = 1.5$, 1H, vinyl H-3), 5.01 (s, 1H, H-7^1), 4.49–4.37 (m, 2H, CH_3CH_2OOC-7^2), 4.33, 4.19 (2t, 4H, $^3J = 7.7$, $=CCH_2$), 3.67, 3.65, 3.64, 3.49, 3.42 (5s, 15H, CH_3, $COOCH_3$), 3.54–3.28 (m, 2H, CH_3CH_2OOC-7^1), 3.21, 3.17 (2t, $^3J = 7.7$, 4H, CH_2COO), 1.80 (s, 3H, CH_3-7), 1.48, 0.29 (2t, $^3J = 7.1$, 6H, CH_3CH_2OOC-7^2, CH_3CH_2OOC-7^1), −2.28 (s, 2H, $=NH$) ppm.

Benzoporphyrin diacids **5** *and* **6** ($C_{42}H_{44}N_4O_8$)

75 mg (0.10 mmol) **3** (or **4**, **3**/**4**) were stirred with 50 cm^3 of 25% HCl for 5 h at 20°C. Then, the solvent was removed by freeze-drying under high vacuum to give **5** (or **6**, **5**/**6**).

5: Yield: 58 mg (82%); green-black solid; m.p.: >250°C; IR (KBr): $\nu = 3600$–2800 (OH, NH), 1730 (CO, ester), 1690 (CO, acid) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 733$ (100) MH^+; ^1H NMR (CF_3COOD, 250 MHz): $\delta = 9.93$, 9.35, 9.26, 9.03 (4s, 4H, $=CH$), 8.21 (m, 1H, vinyl H-8), 8.01, 7.82 (2m, 2H, H-2^3, H-2^4), 6.54, 6.30 (2m, 2H, vinyl H-8), 5.00 (s, 1H, H-2^1), 4.43 (m, 2H, CH_3CH_2OOC-2^2), 4.15 (m, 4H, $=CCH_2$), 3.68, 3.60, 3.55 (3s, 9H, CH_3), 3.26 (m, 2H, CH_3CH_2OOC-2^1), 2.80 (m, 4H, CH_2OOC), 1.82 (s, 3H, CH_3-2), 1.55 (m, 3H, CH_3CH_2OOC-2^2), 0.33 (m, 3H, CH_3CH_2OOC-2^1), −2.11 (s, 2H, $=NH$) ppm.

6: Yield: 55 mg (78%); green-black solid; m.p.: >250°C; IR (KBr): $\nu = 3600$–2800 (OH, NH), 1730 (CO, ester), 1700 (CO, acid) cm^{-1}; ^1H NMR (CF_3COOD, 250 MHz): $\delta = 9.89$, 9.31, 9.29, 9.09 (4s, 4H, $=CH$), 8.15 (m, 1H, vinyl H-3) 7.91, 7.76 (2m, 2H, H-7^3, H-7^4) 6.52, 6.27 (m, 2H, vinyl H-3), 5.01 (s, 1H, H-7^1), 4.46 (m, 2H, CH_3CH_2OOC-7^2), 4.12 (m, 4H, $=CCH_2$), 3.67, 3.61, 3.53 (3s, 9H, CH_3), 3.23 (m, 2H, CH_3CH_2OOC-7^1), 2.80, 2.74 (m, 4H, CH_2OOC), 1.76 (s, 3H, CH_3-7), 1.50 (m, 3H, CH_3CH_2OOC-7^2), 0.31 (m, 3H, CH_3CH_2OOC-7^1), −2.08 (s, 2H, $=NH$) ppm.

Benzoporphyrin tetraacid isomer mixture **7**/**8** ($C_{38}H_{36}N_4O_8 \cdot 3HCl$)

121 mg (0.16 mmol) of **3**/**4** were stirred in 100 cm^3 of 25% HCl for 20 h at 80°C. Then, the solvent was removed by freeze-drying under high vacuum.

7/**8**: Yield: quantitative; m.p.: >250°C; IR (KBr): $\nu = 1705$, 1675 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 679$ (100%) MH^+; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 407 (4.25), 502 (4.01), 547 (3.99), 572 (3.99), 625 (3.96), 688 (3.95) nm.

TCNE adducts **9**/**10** ($C_{42}H_{38}N_8O_4$)

Under N_2 protection, protoporphyrin dimethylester (349 mg, 0.59 mmol) and 76 mg (0.59 mmol) of tetracyanoethylene (*TCNE*) were refluxed in 30 cm^3 of $CHCl_3$. After 30 min, another 7 mg (0.05 mmol) of *TCNE* were added, and heating was continued for 90 min. After removal of the solvent the residue was chromatographed on SiO_2 (120 × 2.5 cm) with CH_2Cl_2:Et_2O = 50:1. At first,

a red band of the starting material eluted. Then, the two green product zones followed, first **9** and then **10**.

9: M.p.: >250°C; IR (KBr): $\nu = 3300$ (NH), 1725 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 9.69$ (s, 1H, H-10), 9.57 (s, 1H, H-15), 9.36 (s, 1H, H-20), 9.27 (s, 1H, H-5), 8.03 (dd, $^3J_{cis} = 11.5$, $^3J_{trans} = 17.8$, 1H, H-8^1), 7.00 (t, $^3J = 4.0$, 1H, H-3^1), 6.28 (dd, $^2J = 1.2$, $^3J_{trans} = 17.8$, 1H, H-8^2_{trans}), 6.13 (dd, $^2J = 1.2$, $^3J_{cis} = 11.5$, 1H, H-8^2_{cis}), 4.26 (t, $^3J = 7.7$, 2H, H-17^1), 3.99 (dd, $^2J = 3.3$, $^3J = 12.1$, 2H, H-3^2), 3.92 (t, $^3J = 7.7$, 2H, H-13^1), 3.66, 3.63 (2s, 6H, $COOCH_3$), 3.54 (s, 6H, CH_3-7, CH_3-18), 3.26 (s, 3H, CH_3-12), 3.19 (t, $^3J = 7.7$, 2H, H-17^2), 3.08 (t, $^3J = 7.7$, 2H, H-13^2), 2.36 (s, 3H, CH_3-2), −2.80 (s, 2H, =NH) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 173.6$, 173.5, 158.4, 152.4, 151.2, 150.4, 146.2, 140.5, 138.8, 138.1, 137.2, 136.9, 134.7, 133.6, 133.2, 131.4, 130.1, 129.2 (C-8^2), 122.2 (C-8^3), 113.2 (d, $^2J = 7.0$, C-3^2), 112.6, 111.9, 109.7, 100.6 (C-10), 100.2 (C-15), 90.5 (C-20), 90.4 (C-5), 51.8, 51.7 (2s, $COOCH_3$), 46.8, 37.3, 36.7 (C-13^2), 36.4 (C-17^2), 34.9 (C-3^2), 24.5 (C-22), 21.5 (C-13^1), 21.4 (C-17^1), 12.6 (C-7^1), 12.2 (C-12^1), 11.4 (C-18^1) ppm.

10: M.p.: >250°C; IR (KBr): $\nu = 3305$ (NH), 1730 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 9.69$ (s, 1H, H-20), 9.57 (s, 1H, H-15), 9.36 (s, 1H, H-5), 9.27 (s, 1H, H-10), 8.08 (dd, $^3J_{cis} = 11.5$, $^3J_{trans} = 17.6$, 1H, H-3^1), 7.01 (t, $^3J = 4.8$, 1H, H-3^1), 6.40 (d, $^3J_{trans} = 17.6$, 1H, H-3^2_{trans}), 6.23 (d, $^3J_{cis} = 11.5$, 1H, H-3^2_{cis}), 4.25 (t, $^3J = 7.5$, 2H, H-13^1), 4.06 (t, $^3J = 7.5$, 2H, H-17^1), 4.01 (dd, $^2J = 3.0$, $^3J = 10.0$, 2H, H-3^2), 3.64, 3.63 (2s, 6H, $COOCH_3$), 3.60 (s, 3H, CH_3-2), 3.46 (s, 3H, CH_3-12), 3.36 (s, 3H, CH_3-18), 3.17 (t, $^3J = 7.5$, 2H, H-13^2), 3.12 (t, $^3J = 7.5$, 2H, H-17^2), 2.31 (s, 3H, CH_3-7), −2.72, −2.75 (2s, 2H, =NH) ppm.

TCNE adduct diacid isomer mixture **11**/**12** ($C_{40}H_{34}N_8O_4$)

Under N_2 protection, 85 mg (0.12 mmol) of **9**/**10** were dissolved in 60 cm^3 of *THF*/15 cm^3 MeOH. LiOH (15 mg, 0.63 mmol) was added, and the mixture was stirred for 7 d at 20°C. After each 24 h period another 10 mg (0.42 mmol) of LiOH were added. The solvent was removed, and the residue was dissolved in 25 cm^3 of H_2O. Acidification with 7% HCl gave a precipitate of **11**/**12** which was filtered and washed with H_2O and *THF*.

11/**12**: Yield: 70 mg (86%); brown-black solid; m.p.: >250°C; IR (KBr): $\nu = 3305$ (NH), 1705 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 691$ (100%) MH^+; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 409 (4.78), 503 (4.14), 539 (4.02), 572 (4.00), 625 (3.97), 690 (3.85) nm; ^1H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.25$ (sb, 4H, COOH), 10.08 (int. 2), 10.05 (int. 2), 10.00 (int. 2), 9.94 (int. 2) (4s, 8H, =CH), 8.35 (m, 2H, H-8^1, H-3^1), 6.87, 6.64 (2t, $^3J = 4.8$, 2H, H-3^1, H-8^1), 6.41 (d, $^3J_{trans} = 16.3$, H-8^2_{trans}, 2H, H-3^2_{trans}), 6.17 (d, $^3J_{cis} = 10.8$, 2H, H-3^2_{cis}, H-8^2_{cis}), 4.28, 4.25 (2m, 8H, $=CCH_2$), 4.08 (m, 4H, H-3^2, H-8^2), 3.65–3.08 (m, 26H, CH_3, CH_2COO), 2.18 (s, 6H, CH_3-7, CH_3-2), −2.75 (int. 2), −4.20, −4.24 (3s, 4H, =NH) ppm.

General procedures A–C for the synthesis of the acetylene-substituted porphyrins **13–33**

Procedure A: Under N_2 protection, diiododeuteroporphyrin (200 mg, 0.23 mmol) was dissolved in 50 cm^3 of absolute NEt_3. [$PdCl_2(PPh_3)_2$] (30 mg, 0.04 mmol) and CuI (10 mg, 0.05 mmol) were added. After stirring for 10 min, a solution of the 2.2-fold amount of the respective ethyne in 30 cm^3 of *THF* was added and refluxed for 18 h. After removal of the solvent the residue was dissolved in 150 cm^3 of CH_2Cl_2 and extracted twice with 150 cm^3 of H_2O. After drying over Na_2SO_4 the organic phase was chromatographed on SiO_2. With CH_2Cl_2 a yellow zone and with CH_2Cl_2/MeOH mixtures the respective products were eluted which were recrystallized from CH_2Cl_2/pentane.

Procedure B: 0.15 mmol of the respective Zn-porphyrin were treated with 15 cm^3 of trifluoroacetic acid without solvent. After stirring for 25 min, 150 cm^3 of CH_2Cl_2 were added. The organic phase was extracted twice with 200 cm^3 of H_2O and once with 200 cm^3 of 5% $NaHCO_3$ solution. After drying over Na_2SO_4 the solvent was removed. The residue was purified by SiO_2 chromatography, if possible, and recrystallized from CH_2Cl_2/pentane.

Procedure C: 0.30 mmol of the porphyrin ester were refluxed with 70 cm^3 of 20% methanolic KOH for 1 h. The progress of the reaction was monitored with TLC (Al_2O_3). As long as spots developed with CH_2Cl_2:MeOH = 100:1, hydrolysis of the ester groups was incomplete. The reaction mixture was concentrated to 20 cm^3. 7% HCl was added until $pH = 4$. The product was extracted with CH_2Cl_2. After drying over Na_2SO_4 the solvent was removed.

3,8-Bis(phenylethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**13**; $C_{48}H_{40}N_4O_4Zn$)

Proc. A; 200 mg (0.23 mmol) of 13,17-bis(2-methoxycarbonylethyl)-3,8-diiodo-2,7,12,18-tetramethylporphinatozinc(II), 230 mg (2.25 mmol) of phenylacetylene; SiO_2 chromatography (20 × 3 cm): first yellow zone, then red-brown product **13** with CH_2Cl_2:MeOH = 100:1; yield: 140 mg (75%); red-brown solid; m.p.: >250°C; IR (KBr): $\nu = 1730$ (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 801$ (100%) MH^+; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.05$, 8.72, 8.57, 8.37 (4s, 4H, =CH), 8.08–8.01, 7.69–7.57 (2m, 10H, C_6H_5), 3.91 (t, $^3J = 7.5$, 4H, $=CCH_2$), 3.61, 3.59 (2s, 6H, $COOCH_3$), 3.26, 3.15, 3.14, 3.05 (4s, 12H, $=CCH_3$), 2.95 (t, $^3J = 7.5$, 4H, CH_2COO) ppm.

3,8-Bis[4-(phenylethynyl)phenylethynyl]-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**14**; $C_{64}H_{48}N_4O_4Zn$)

Proc. A; 221 mg (0.26 mmol) of 13,17-bis(2-methoxycarbonylethyl)-3,8-diiodo-2,7,12,18-tetramethylporphinatozinc(II), 31 mg (0.04 mmol) of [$PdCl_2(PPh_3)_2$], 31 mg (0.16 mmol) of CuI, 156 mg (0.77 mmol) of (4-(phenylethynyl)phenyl)ethyne; 60 cm^3 of NEt_3, 130 cm^3 of THF; SiO_2 chromatography: first narrow, yellow zone, then product with CH_2Cl_2:MeOH = 100:1; recrystallization from 5 cm^3 of CH_2Cl_2 and 20 cm^3 of pentane at −18°C; yield: 190 mg (75%); red solid; m.p.: >260°C; IR (KBr): $\nu = 2180$ (C≡C), 1730 (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 1003$ (100%) MH^+; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 8.98$, 8.84, 8.43 (int. 2) (3s, 4H, =CH), 7.95, 7.82 (2d, $^3J = 7.5$, 8H, C_6H_4), 7.67, 7.41 (2m, 10H, C_6H_5), 4.00 (m, 4H, $=CCH_2$), 3.65, 3.62, 3.59 (int. 2), 3.27, 3.10 (5s, 18H, $=CCH_3$, $COOCH_3$), 2.99 (m, 4H, CH_2COO), 2.45, 2.44 (2s, 6H, $H_2C=CCH_3$), −3.88 (s, 2H, =NH) ppm.

3,8-Bis(4-(4-(phenylethynyl)phenylethynyl)phenylethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**15**; $C_{80}H_{46}N_4O_4Zn$)

Proc. A; 322 mg (1.07 mmol) of (4-(4-phenylethynyl)phenylethynyl)phenyl)ethyne, 303 mg (0.36 mmol) of 13,17-bis(2-methoxycarbonylethyl)-3,8-diiodo-2,7,12,18-tetramethylporphinatozinc(II), 30 mg (0.04 mmol) of [$PdCl_2(PPh_3)_2$], 15 mg (0.08 mmol) of CuI (2 d reflux); SiO_2 chromatography (25 × 4 cm): first yellow zone, then intense red product zone with CH_2Cl_2:MeOH = 50:1; yield: 320 mg (69%); red-brown solid; m.p.: >250°C; IR (KBr): $\nu = 2170$ (C≡C) 1730 (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 1191$ (100%) MH^+, 1045 (28%); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.89$, 9.80, 9.53, 9.45 (4s, 4H, =CH), 7.90–6.95 (m, 26H, arom. H), 4.17 (t, $^3J = 7.6$, 4H, $=CCH_2$), 3.60 (s, 6H, $COOCH_3$), 3.57, 3.54, 3.49, 3.48 (4s, 12H, $=CCH_3$), 3.10 (t, $^3J = 7.6$, 4H, CH_2COO) ppm.

3,8-Bis(phenylethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphin (**16**; $C_{48}H_{42}N_4O_4$)

Proc. B; 120 mg (0.15 mmol) of **13**, 12 cm^3 of CF_3CO_2H; recrystallization from 9 cm^3 of CH_2Cl_2 and 6 cm^3 of pentane; yield: 83 mg (0.11 mmol, 75%); brown-black solid; m.p.: >250°C; IR (KBr): $\nu = 1735$, 1725 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.88$, 9.72, 9.65, 9.52 (4s, 4H, =CH), 8.04–7.99, 7.65–7.55 (2m, 10H, C_6H_5), 4.27 (t, $^3J = 7.6$, 4H, $=CCH_2$), 3.63 (s, 6H, $COOCH_3$), 3.58, 3.56, 3.50, 3.15 (4s, 12H, $=CCH_3$), 3.18 (t, $^3J = 7.6$, 4H, CH_2COO), −4.78 (s, 2H, =NH) ppm.

3,8-Bis(4-(phenylethynyl)phenylethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphin (**17**; $C_{64}H_{50}N_4O_4 \cdot 3H_2O$)

Proc. B; 120 mg (0.12 mmol) of **14**; SiO_2 chromatography under N_2 with CH_2Cl_2:MeOH = 100:1: long red band; recrystallization from 10 cm^3 of CH_2Cl_2 and 25 cm^3 of pentane; yield: 97 mg (0.10 mmol, 86%); red-brown solid; m.p.: >250°C; IR (KBr): $\nu = 2170$ (C≡C), 1725 (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 939$ (100%) MH^+, 866 (40%); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.95$, 9.80, 9.68 (int. 2) (3s, 4H, =CH), 7.94 (m, 4H, *o*-C_6H_5), 7.75, 7.65 (2d, $^3J = 7.2$, 8H, C_6H_4), 7.40 (m, 6H, *m*- and *p*-C_6H_5), 4.31 (t, $^3J = 7.5$, 4H, $=CCH_2$), 3.65 (s, 6H, $COOCH_3$), 3.57, 3.54, 3.49 (int. 2) (3s, 12H, $=CCH_3$), 3.22 (t, $^3J = 7.5$, 4H, CH_2COO), −4.40 (s, 2H, =NH) ppm.

3,8-Bis(4-(4-(phenylethynyl)phenylethynyl)phenylethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphin (**18**, $C_{80}H_{48}N_4O_4$)

Proc. B; 150 mg (0.13 mmol) of **15**, 12 cm^3 of CF_3CO_2H; SiO_2 chromatography with CH_2Cl_2:MeOH = 100:1; yield: 70 mg (46%); red-brown solid; m.p.: >250°C; IR (KBr): $\nu = 2170$ (C≡C), 1730 (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $mz = 1129$ (100%) MH^+, 983 (28%); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.91$, 9.83, 9.60, 9.51 (4s, 4H, =CH), 7.93–7.10 (m, 26H, arom. H), 4.24 (t, $^3J = 7.6$, 4H, $=CCH_2$), 3.60, 3.59 (2s, 6H, $COOCH_3$), 3.57, 3.53, 3.48 (int. 2) (3s, 12H, $=CCH_3$), 3.13 (t, $^3J = 7.6$, 4H, CH_2COO), −4.15 (s, 2H, =NH) ppm.

3,8-Bis(3-hydroxy-3-methylbutyn-1-yl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**19**; $C_{42}H_{44}N_4O_6Zn$)

Proc. A; 200 mg (0.23 mmol) of 13,17-bis(2-methoxycarbonylethyl)-3,8-diiodo-2,7,12,18-tetramethylporphinatozinc(II), 200 mg (2.38 mmol) of 2-methyl-3-butyn-2-ol; SiO_2 chromatography with CH_2Cl_2:MeOH = 50:1; yield: 137 mg (78%); red solid; m.p.: 229°C; IR (KBr): $\nu = 1730$ (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 765$ (100%) MH^+, 748 (20%); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.13$, 9.12, 8.33, 8.22 (4s, 4H, =CH), 4.31 (t, $^3J = 7.7$, 4H, $=CCH_2$), 3.66, 3.64 (2s, 6H, $COOCH_3$), 3.48, 3.31, 3.22, 2.93 (4s, 12H, $=CCH_3$), 2.79 (t, $^3J = 7.7$, 4H, CH_2COO), 2.18 (s, 12H, $C(CH_3)_2$) ppm.

3,8-Bis(2-methylbut-1-en-3-yn-4-yl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphin (**20**; $C_{42}H_{42}N_4O_6$)

Proc. B; 100 mg (0.13 mmol) of **19**, 12 cm^3 of CF_3CO_2H; SiO_2 chromatography with CH_2Cl_2:MeOH = 100:1, the desired elimination product **20** eluted as a first, rapidly migrating zone; recrystallization from CH_2Cl_2:pentane = 10:12; yield: 31 mg (36%); brown solid; m.p.: >250°C; IR (KBr): $\nu = 1750$ (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z = 668$ (100%) MH^+; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.88$, 9.83, 9.67, 9.61 (4s, 4H, =CH), 5.89, 5.64 (2s, 4H, $=CH_2$), 4.34 (t, $^3J = 7.1$, 4H, $=CCH_2$), 3.68, 3.67, 3.57, 3.53 (4s, 12H, $=CCH_3$), 3.64 (s, 6H, $COOCH_3$), 3.22 (t, $^3J = 7.1$, 4H, CH_2COO), 2.45, 2.44 (2s, 6H, $H_2C=CCH_3$), −3.88 (s, 2H, =NH) ppm.

3,8-Bis(trimethylsilylethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**21**; $C_{36}H_{48}N_4O_4Si_2Zn$)

Proc. A; 500 mg (0.59 mmol) of 13,17-bis(2-methoxycarbonylethyl)-3,8-diiodo-2,7,12,18-tetramethylporphinatozinc(II), 232 mg (2.36 mmol) of trimethylsilylacetylene, 50 mg (0.07 mmol) of $[PdCl_2(PPh_3)_2]$, 30 mg (0.15 mmol) of CuI; SiO_2 chromatography (30 × 5 cm): first a yellow, rapidly migrating zone, then **21** as a red zone with CH_2Cl_2:MeOH = 100:1; yield: 400 mg (0.57 mmol, 97%); red-brown solid; m.p.: >250°C; ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 9.34$, 9.25, 8.73, 8.66 (4s, 4H,

$=CH$), 4.11 (t, $^3J=7.6$, 4H, $=CCH_2$), 3.59, 3.57 (2s, 6H, $COOCH_3$), 3.56, 3.43, 3.41, 3.18 (4s, 12H, $=CCH_3$), 2.98, 2.89 (2t, $^3J=7.6$, 4H, CH_2COO), 0.76 (s, 18H, $Si(CH_3)_3$) ppm.

3,8-Bis(ethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**22**; $C_{36}H_{32}N_4O_4Zn$)

To 400 mg (0.58 mmol) of **21** dissolved in 125 cm^3 of abs. *THF* under N_2, 500 mg (0.60 mmol) of *n*-tetrabutylammoniumfluoride on silica gel were added, and the mixture was stirred for 20 h at 20°C. SiO_2 chromatography with CH_2Cl_2: red zone of **22**; yield: 310 mg (82%); red solid; m.p.: >250°C; IR (KBr): $\nu=2170$ (C≡C), 1730 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): $\delta=9.26$, 9.09, 8.83, 7.67 (4s, 4H, $=CH$), 4.24, 4.19 (2s, 2H, ≡CH), 4.10 (t, $^3J=7.6$, 4H, $=CCH_2$), 3.62, 3.59 (2s, 6H, $COOCH_3$), 3.34, 3.40 (int. 2), 3.10 (3s, 12H, $=CCH_3$), 2.98 (t, $^3J=7.6$, 4H, CH_2COO) ppm.

3,8-Bis(ethynyl)-13,17-bis(2-methoxycarbonylethyl)-2,7,12,18-tetramethylporphin (**23**; $C_{34}H_{34}N_4O_4$)

Proc. B; 150 mg (0.23 mmol) of **22**, 12 cm^3 of CF_3CO_2H; SiO_2 chromatography (15 × 2.5 cm) with CH_2Cl_2:MeOH = 100:1; yield: 100 mg (74%); brown-black solid; m.p.: >250°C; IR (KBr): $\nu=1730$ (CO) cm^{-1}; PI-LISIMS (*MNBA*/CH_2Cl_2): $m/z=587$ (100%) MH^+; ^1H NMR ($CDCl_3$, 250 MHz): $\delta=9.83$, 9.76, 9.61, 9.51 (s, 4H, $=CH$), 4.28, 4.27 (2t, $^3J=7.3$, 4H, $=CCH_2$), 4.21, 4.19 (2s, 2H, ≡CH), 3.64, 3.63 (2s, 6H, $COOCH_3$), 3.58, 3.53, 3.44 (int. 2) (3s, 12H, $=CCH_3$), 3.18, 3.17 (2t, $^3J=7.3$, 4H, CH_2COO), −4.90 (s, 2H, $=NH$) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(phenylethynyl)-2,7,12,18-tetramethylporphinatozinc(II) (**24**; $C_{46}H_{36}N_4O_4Zn$)

Proc. C; 140 mg (0.17 mmol) of **13**, 120 cm^3 of 20% methanolic KOH, 4 cm^3 of H_2O; filtration and washing with H_2O and CH_2Cl_2; yield: 125 mg (95%) brown-black solid; m.p.: >260°C; IR (KBr): $\nu=1710$ (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z=774$ (100%) MH^+, 730 (28%), 716 (50%), 702 (22%), 674 (20%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 433 (5.25), 554 (4.24), 592 (4.23) nm; ^1H NMR (*DMSO*-d_6, 250 MHz): $\delta=12.24$ (s, 2H, COOH), 10.17 (sb, 4H, $=CH$), 8.77, 7.67 (2m, 10H, arom. H), 4.32 (t, $^3J=6.6$, 4H, $=CCH_2$), 3.83, 3.61, 3.35 (int. 2) (3s, 12H, $=CCH_3$), 3.19 (t, $^3J=6.6$, 4H, CH_2COO), −3.13 (s, 2H, $=NH$) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(4-(phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphinatozinc(II) (**25**; $C_{62}H_{44}N_4O_4Zn$)

Proc. C; 85 mg (0.09 mmol) of **14**, 120 cm^3 of 20% methanolic KOH, 2 cm^3 of H_2O; washing with CH_2Cl_2 and H_2O; yield: 78 mg (94%); black solid; m.p.: >260°C; IR (KBr): $\nu=2160$ (C≡C), 1700 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z=973$ (100%) MH^+, 929 (30%), 914 (35%), 901 (25%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 442 (5.20), 557 (4.29), 595 (4.35) nm; ^1H NMR (*DMSO*-d_6, 250 MHz): $\delta=12.24$ (s, 2H, COOH), 10.15, 10.14, 10.08, 9.93 (4s, 4H, $=CH$), 8.08, 7.84 (2d, $^3J=$ 7.4, 8H, C_6H_4), 7.66–7.50 (m, 10H, arom. H), 4.25 (m, 4H, $=CCH_2$), 3.64, 3.50, 3.16 (int. 2) (3s, 12, $=CCH_3$), 3.16 (m, 4H, CH_2COO), −4.11 (s, 2H, $=NH$) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(4-(4-(phenylethynyl)phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphinatozinc(II) (**26**; $C_{78}H_{42}N_4O_4Zn \cdot 2H_2O$)

Proc. C; 100 mg (0.08 mmol) of **15**, 100 cm^3 of 20% methanolic KOH, 70 cm^3 of *THF*, 5 cm^3 of H_2O for 4 d at 20°C; washing with H_2O and *THF*; yield: 80 mg (81%); black solid; m.p.: >250°C; IR

(KBr): $\nu = 1700$ (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 1163$ (100%) MH^+; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 437 (5.03), 556 (4.14), 596 (4.20) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.24$ (s, 2H, COOH), 10.10, 10.08, 9.73, 9.66 (4s, 4H, $=CH$), 8.09–7.42 (m, 26H, arom. H), 4.12 (t, $^3J = 7.2$, 4H, $=CCH_2$), 3.67, 3.59, 3.50 (int. 2) (3s, 12H, $=CCH_3$), 3.09 (t, $^3J =$ 7.2, 4H, CH_2COO) ppm.

3,8-Bis(3-hydroxy-3-methylbutyn-1-yl)-13,17-bis(2-carboxyethyl)-2,7,12,18-tetramethylporphinatozinc(II) (**27**; $C_{40}H_{40}N_4O_6$)

Proc. C; 80 mg (0.10 mmol) of **19**, 50 cm^3 of 20% methanolic KOH, 2 cm^3 of H_2O at 20°C; washing with CH_2Cl_2 and H_2O; yield: 65 mg (85%); red solid; m.p.: >260°C; IR (KBr): $\nu = 1700$ (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 738$ (100%) MH^+, 720 (40%), 676 (50%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 426 (5.42), 551 (4.30), 589 (4.25) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.24$ (s, 2H, COOH), 10.11 (sb, 4H, $=CH$), 4.30 (t, $^3J = 7.2$, 4H, $=CCH_2$), 3.79, 3.78 (2s, 2H, OH), 3.73, 3.70, 3.59, 3.56 (4s, 12H, $=CCH_3$), 3.18 (t, $^3J = 7.2$, 4H, CH_2COO), 1.92 (s, 12H, $C(CH_3)_2$) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(phenylethynyl)-2,7,12,18-tetramethylporphin (**28**; $C_{40}H_{38}N_4O_4$)

Proc. C; 85 mg (0.12 mmol) of **16**, 80 cm^3 of 20% methanolic KOH, 3 cm^3 of H_2O for 60 h at 20°C; washing with H_2O and a little EtOH; yield: 69 mg (84%); brown solid; m.p.: >260°C; IR (KBr): $\nu = 1710$, 1695 (CO) cm^{-1}; NI-LISIMS (glycerol/*DMSO*): $m/z = 709$ (100%) $(M\text{-}H)^-$, 606 (55%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 418 (4.96), 514 (4.00), 550 (4.08), 579 (3.81), 635 (3.63) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.24$ (s, 2H, COOH), 10.00, 9.86, 9.72 (int. 2) (3s, 4H, $=CH$), 8.09–8.07, 7.71–7.67 (2m, 10H, C_6H_5), 4.30 (m, 4H, $=CCH_2$), 3.68, 3.59, 3.54, 3.53 (4s, 12H, $=CCH_3$), 3.15 (t, $^3J = 6.3$, 4H, CH_2COO), −4.81 (s, 2H, $=NH$) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(4-(phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphin (**29**; $C_{62}H_{46}N_4O_4$)

Proc. C; 120 mg (0.12 mmol) of **17**, 100 cm^3 of 20% methanolic KOH; washing with H_2O, Et_2O, and *PE* (40/60); yield: 93 mg (83%); brown-black solid; m.p.: >260°C; IR (KBr): $\nu = 2190$ (C≡C), 1710 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 911$ (100%) MH^+, 791 (35%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 412 (5.12), 513 (4.15), 552 (4.21), 579 (3.98), 636 (3.63) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.24$ (s, 2H, COOH), 10.15, 10.08, 9.93, 9.66 (4s, 4H, $=CH$), 8.07, 7.84 (2d, $^3J = 7.4$, 8H, C_6H_4), 7.66–7.50 (m, 18H, arom. H), 4.25 (t, $^3J = 7.4$, 4H, $=CCH_2$), 3.64 (int. 2), 3.50 (int. 2) (2s, 12H, $=CCH_3$), 3.16 (t, $^3J = 7.4$, 4H, CH_2COO), −4.11 (s, 2H, $=NH$) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(4-(4-(phenylethynyl)phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphin (**30**; $C_{78}H_{44}N_4O_4$)

Proc. C; 80 mg (0.07 mmol) of **18**, 60 cm^3 of 20% methanolic KOH, 40 cm^3 of *THF*, 3 cm^3 of H_2O, 2 h reflux; washing with H_2O and *THF*; yield: 60 mg (78%); black solid; m.p.: >250°C; IR (KBr): $\nu = 1700$, 1680 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 1101$ (100%) MH^+; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 415 (4.96), 512 (4.27), 553 (4.29), 580 (4.19), 637 (4.08) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.36$ (s, 2H, COOH), 10.10 (int. 2), 9.69 (int. 2) (2s, 4H, $=CH$), 8.15–7.55 (m, 26H, arom. H), 4.12 (m, 4H, $=CCH_2$), 3.56 (int. 2), 3.51 (int. 2) (2s, 12H, $=CCH_3$), 3.13 (m, 4H, CH_2COO), −4.10 (s, 2H, $=NH$) ppm.

3,8-Bis(2-methylbut-1-en-3-yn-4-yl)-13,17-bis(2-carboxyethyl)-2,7,12,18-tetramethylporphin (**31**; $C_{40}H_{38}N_4O_4Zn$)

Proc. C; 75 mg (0.11 mmol) of **20**, 100 cm^3 of 20% methanolic KOH, 3 cm^3 of H_2O; washing with H_2O and Et_2O; yield: 55 mg (78%); red-brown solid; m.p.: >250°C; IR (KBr): $\nu = 1715$, 1700 (CO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} (logε) = 415 (4.98), 513 (3.96), 549 (3.96), 579 (3.72), 605 (3.23), 635 (3.52) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.20$ (s, 2H, COOH), 9.83, 9.67, 9.56, 9.39 (4s, 4H, =CH), 5.94, 5.79 (2s, 4H, $=CH_2$), 4.26 (m, 4H, $=CCH_2$), 3.55 (int. 2), 3.50 (int. 2) (2s, 12H, $=CCH_3$), 3.17, 3.12 (2m, 4H, CH_2COO), 1.22 (s, 6H, $H_2C=CCH_3$), −5.38 (s, 2H, =NH) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(ethynyl)-2,7,12,18-tetramethylporphinatozinc(II) (**32**; $C_{34}H_{28}N_4O_4Zn$)

Proc. C; 100 mg (0.15 mmol) of **22**, 100 cm^3 of 20% methanolic KOH, 3 cm^3 of H_2O; washing with H_2O and CH_2Cl_2; yield: 80 mg (86%); red solid; m.p.: >250°C; IR (KBr): $\nu = 2090$ (C≡C), 1700 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 621$ (100%) MH^+; UV/Vis (*DMSO*): λ_{max} (logε) = 425 (5.40), 550 (4.23), 588 (4.10) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.21$ (s, 2H, COOH), 9.87, 9.76, 9.61, 9.50 (4s, 4H, =CH), 4.27 (t, $^3J = 7.2$, 4 H, $=CCH_2$), 4.22, 4.17 (2s, 2H, ≡CH), 3.56 (int. 2), 3.53, 3.44 (3s, 12H, $=CCH_3$), 3.18, 3.17 (2t, $^3J = 7.2$, 4H, CH_2COO) ppm.

13,17-Bis(2-carboxyethyl)-3,8-bis(ethynyl)-2,7,12,18-tetramethylporphin (**33**; $C_{34}H_{30}N_4O_4$)

Proc. C; 100 mg (0.17 mmol) of **23**, 100 cm^3 of 20% methanolic KOH, 40 cm^3 of *THF* for 24 h at 24°C; after evaporation of the solvent the residue was dissolved in 40 cm^3 of H_2O; precipitation with 7% HCl at 0°C; washing with H_2O and *THF* and drying in high vacuum; yield: 80 mg (84%); red solid; m.p.: >250°C; IR (KBr): 2100 (C≡C), 1690 (CO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z =$ 559 (100%) MH^+; UV/Vis (*DMSO*): λ_{max} (logε) = 411 (5.12), 507 (4.05), 543 (3.92), 575 (3.74), 631 (3.55) nm; ^{1}H NMR (*DMSO*-d_6, 250 MHz): $\delta = 12.10$ (s, 2H, COOH), 9.80 (int. 2), 9.50 (int. 2) (2s, 4H, =CH), 4.15 (t, $^3J = 7.3$, 4H, $=CCH_2$), 4.03 (s, 2H, ≡CH), 3.61, 3.58, 3.51, 3.44 (4s, 12H, $=CCH_3$), 3.18 (t, $^3J = 7.3$, 4H, CH_2COO), −4.83 (s, 2H, =NH) ppm.

Diammine(diaqua)platinum(II)-dihydroxide **34**, *the precursor for the synthesis of the platinum(II) complexes* **35**–**50**

300 mg (1.00 mmol) of cisplatinum were suspended with ultrasound in 50 cm^3 of H_2O. A solution of 340 mg (2.00 mmol) of $AgNO_3$ in 10 cm^3 of H_2O was added, and the mixture was stirred for 7 d under exclusion of light. The precipitated AgCl was filtered off. The colorless filtrate was brought onto an activated, strongly basic ion exchanger (Fa. Merck, ion exchanger III) and eluted with water. Activation was accomplished by flushing the ion exchanger first with 2 *N* NaOH and then by eluting with H_2O to *pH* 9. After drying the eluate a glassy, light-sensitive residue was obtained which can be stored in the dark at −20°C. Before use in the following procedures the product was dissolved in 50 cm^3 of H_2O:EtOH = 1:1.

Diammine(BPD-A-O,O′)platinum(II) (**35**; $C_{42}H_{49}N_6O_8Pt$)

A solution of 40 mg (0.06 mmol) of **5** in 40 cm^3 of EtOH and 0.07 mmol of **34** was stirred for 24 h. The precipitate was washed with EtOH and H_2O.

Yield: 37 mg (67%); green-black powder; m.p.: >250°C; IR (KBr): $\nu = 1550$ (C=C), 1380 (CO), 375 (PtO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 1023$ (52%) $(M\text{-}NH_3 + DMSO + H)^+$; 961

(25%) MH^+, 927 (77%), 733 (100%); UV/Vis (*DMSO*): λ_{max} (logε) = 416 (4.82), 505 (3.85), 549 (3.83), 579 (3.87), 630 (3.64), 690 (4.08) nm.

Diammine(BPD-B-O,O′)platinum(II) (**36**; $C_{42}H_{49}N_6O_8Pt$)

Analogous to **35** with ligand **6**; yield: 31 mg (55%); green-black powder; m.p.: >250°C; IR (KBr): ν = 1550 (C=C), 1370 (CO), 375 (PtO) cm^{-1}.

Tetrammine(BPD-O,O′)diplatinum(II) (isomer mixture) (**37**/**38**; $C_{38}H_{44}N_8O_8Pt_2$)

53 mg (0.08 mmol) of **7**/**8** were reacted in 40 cm^3 of *THF* with 0.16 mmol of **34**. The precipitate was washed with H_2O and *THF*.

Yield: 80 mg (91%); black solid; m.p.: >250°C; IR (KBr): ν = 1540, 1360 (CO), 375 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} (logε) = 407 (4.25), 499 (4.01), 572 (3.99), 603 (3.97), 625 (3.96), 688 (3.95) nm.

Diammine(TCNE-O,O′)platinum(II) (isomer mixture) (**39**/**40**; $C_{40}H_{38}N_{10}O_4Pt$)

53 mg (0.08 mmol) of **11**/**12** were reacted in 30 cm^3 of EtOH with an equimolar amount of **34** at 20°C. The precipitate was washed with H_2O and EtOH.

Yield: 40 mg (57%); black solid; m.p.: >250°C; IR (KBr): ν = 1540, 1360 (CO), 375 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} (logε) = 408 (4.92), 503 (4.24), 539 (4.17), 573 (4.12), 627 (4.06), 689 (3.98) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(phenylethynyl)-2,7,12,18-tetramethylporphinatozinc(II)-O,O′)platinum(II) (**41**; $C_{46}H_{40}N_6O_4PtZn$)

103 mg (0.13 mmol) of **24** were reacted in 25 cm^3 of *THF* with an equimolar amount of **34**. The resulting precipitate was washed with H_2O and MeOH.

Yield: 75 mg (58%); black solid; m.p.: >260°C; IR (KBr): ν = 1570, 1550, 1385 (CO), 375 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} (logε) = 434 (5.45), 555 (4.48), 593 (4.48) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(4-(phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphinatozinc(II)-O,O′)platinum(II) (**42**; $C_{62}H_{46}N_6O_4PtZn$)

50 mg (0.05 mmol) of **25** were dissolved in 35 cm^3 of *THF* and reacted with **34**. The precipitate was washed with H_2O and *THF*.

Yield: 38 mg (61%); black solid; m.p.: >250°C; IR (KBr): ν = 1540, 1375 (CO), 375 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} (logε) = 442 (5.19), 558 (4.29), 597 (4.34) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(4-(4-(phenylethynyl)phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphinatozinc(II)-O,O′)platinum(II) (**43**; $C_{78}H_{46}N_6O_4PtZn$)

62 mg (0.05 mmol) of **26** were stirred in 20 cm^3 of *THF* with an equimolar amount of **34**. The precipitate was washed with H_2O and *THF*.

Yield: 52 mg (70%); red solid; m.p.: >250°C; IR (KBr): ν = 1545, 1375 (CO), 370 (PtO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): m/z = 1389 (35%) MH^+, 1163 (100%); UV/Vis (*DMSO*): λ_{max} (logε) = 438 (4.94), 557 (4.29), 596 (4.32) nm.

Diammine(3,8-bis(3-hydroxy-3-methylbutyn-1-yl)-13,17-bis(2-carboxylatoethyl)-2,7,12,18-tetramethylporphinatozinc(II)-O,O′)platinum(II) (**44**; $C_{40}H_{44}N_6O_6PtZn$)

41 mg (0.06 mmol) of **27** were reacted in 30 cm^3 EtOH with **34**. The precipitate was washed with H_2O and EtOH.

Yield: 27 mg (50%); deep violet solid; m.p.: >260°C; IR (KBr): $\nu = 1540$, 1370 (CO), 370 (PtO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 963$ (20%) MH^+, 927 (20%), 925 (35%), 735 (100%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 427 (5.27), 552 (4.17), 589 (4.12) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(phenylethynyl)-2,7,12,18-tetramethylporphin-O,O′)platinum(II) (**45**; $C_{46}H_{42}N_6O_4Pt$)

45 mg (0.06 mmol) of **28** were dissolved in 45 cm^3 of *THF* and reacted with **34**. The precipitate was washed with H_2O and *THF*.

Yield: 47 mg (80%); black solid; m.p.: >260°C; IR (KBr): $\nu = 1530$, 1365 (CO), 370 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 417 (5.18), 515 (4.14), 550 (4.17), 580 (3.90), 636 (3.73) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(4-(phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphin-O,O′)platinum(II) (**46**; $C_{62}H_{50}N_6O_4Pt$)

66 mg (0.06 mmol) of **29** in 10 cm^3 of *THF* and 10 cm^3 of EtOH were reacted with an equimolar amount of **34**. The precipitate was washed with H_2O, *THF*, and EtOH.

Yield: 67 mg (95%); black solid; m.p.: >260°C; IR (KBr): 1580, 1365 (CO), 375 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 410 (4.78), 502 (4.02), 551 (4.00), 579 (3.89), 636 (3.51) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(4-(4-(phenylethynyl)phenylethynyl)phenylethynyl)-2,7,12,18-tetramethylporphin-O,O′)platinum(II) (**47**; $C_{78}H_{48}N_4O_4Pt$)

A solution of 52 mg (0.05 mmol) of **30** was stirred in 10 cm^3 of MeOH and 20 cm^3 of *THF* with an equimolar amount of **34**. The precipitate was washed with H_2O, *THF*, and MeOH.

Yield: 44 mg (72%); black solid; m.p.: >250°C; IR (KBr): $\nu = 1545$, 1380 (CO), 370 (PtO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 1299$ (48%) MH^+, 1101 (100%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 414 (5.01), 512 (4.28), 553 (4.31), 580 (4.20), 636 (4.07) nm.

Diammine(3,8-bis(2-methylbut-1-en-3-yn-4-yl)-13,17-bis(2-carboxylatoethyl)-2,7,12,18-tetramethylporphin-O,O′)platinum(II) (**48**; $C_{40}H_{42}N_6O_4Pt$)

68 mg (0.11 mmol) of **31** were reacted in 20 cm^3 of EtOH with **34**. The precipitate was washed with H_2O and EtOH and dried.

Yield: 86 mg (93%); black-brown solid; m.p.: >250°C; IR (KBr): $\nu = 1580$, 1365 (CO), 370 (PtO) cm^{-1}; PI-LISIMS (glycerol/*DMSO*): $m/z = 943$ (45%) $(M + DMSO + H)^+$, 865 (32%) MH^+, 639 (100%); UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 414 (4.97), 513 (3.98), 549 (3.98), 579 (3.75), 635 (3.56) nm; fluorescence (*DMSO*): λ_{max} (rel. units) = 513 (136.5), 638 (46.7) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(ethynyl)-2,7,12,18-tetramethylporphinatozinc(II)-O,O′)platinum(II) (**49**; $C_{34}H_{32}N_6O_4PtZn$)

61 mg (0.10 mmol) of **32** were reacted in 30 cm^3 of *THF* with an equimolar amount of **34**. The precipitate was washed with H_2O and *THF*.

Yield: 18 mg (22%); red solid; m.p.: >250°C; IR (KBr): $\nu = 1550$, 1370 (CO), 370 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 425 (5.22), 551 (4.07), 588 (3.92) nm.

Diammine(13,17-bis(2-carboxylatoethyl)-3,8-bis(ethynyl)-2,7,12,18-tetramethylporphin-O,O′)platinum(II) (**50**; $C_{34}H_{34}N_6O_4Pt$)

61 mg (0.11 mmol) of **33** were dissolved in 70 cm^3 of *THF* and suspended in an equimolar amount of **76** dissolved in $EtOH/H_2O$. The precipitate was washed with H_2O and *THF*.

Yield: 53 mg (62%); red solid; m.p.: >250°C; IR (KBr): $\nu = 1545$, 1375 (CO), 375 (PtO) cm^{-1}; UV/Vis (*DMSO*): λ_{max} ($\log\varepsilon$) = 410 (5.12), 506 (4.31), 542 (4.24), 576 (4.18), 631 (4.10) nm.

References

[1] Gomer CJ (1989) Sem Hematol **26**: 27
[2] Chan WS, Marshall JF, Lam GYF, Hart IR (1988) Cancer Res **48**: 3040
[3] Brunner H, Maiterth F, Treittinger B (1994) Chem Ber **127**: 2141
[4] Brunner H, Obermeier H, Szeimies R-M (1995) Chem Ber **128**: 173
[5] Brunner H, Obermeier H (1994) Angew Chem **106**: 2305; Angew Chem Int Ed Engl **33**: 2214
[6] Brunner H, Schellerer K-M, Treittinger B (1997) Inorg Chim Acta **264**: 67
[7] Schellerer K-M (1996) Dissertation, Universität Regensburg, Germany
[8] Kessel D, Dougherty TJ, Chang CK (1991) Photochem Photobiol **53**: 475
[9] Emtestam L, Berglund L, Angelin B, Drummond GS, Kappas A (1989) Lancet (I) 1231
[10] Brown SB, Truscott TG (1993) Chem Br 955
[11] Dougherty TJ (1987) Photochem Photobiol **46**: 569
[12] Kessel D, Thompson P (1987) Photochem Photobiol **46**: 1023
[13] Lipson RL, Blades FJ, Olsen AM (1961) J Natl Cancer Inst **26**: 1
[14] Smith K (1989) The Science of Photobiology. Plenum Press, New York
[15] Foote CS (1991) Photochem Photobiol **54**: 659
[16] Gomer CJ, Ferrario A, Naganobu H, Rucker N, Szirth BC, Murphee AL (1989) Lasers Surg Med **8**: 450
[17] Foote CS (1987) Photochem Photobiol **46**: 591
[18] Dougherty TJ (1995) In: Foye WO (ed) Cancer Chemotherapeutic Agents. American Chemical Society, Washington, DC
[19] Mang TS, Dougherty TJ, Potter WR, Boyle DG, Sommer S, Moan J (1989) Photochem Photobiol **50**: 221
[20] Pangka VS, Morgan AR, Dolphin D (1986) J Org Chem **51**: 1094
[21] DiNello RK, Dolphin D (1980) J Org Chem **45**: 5196
[22] Baker EW, Yen TF, Dickie JP, Rhodes RE, Clark LF (1967) J Am Chem Soc **89**: 3631
[23] Clezy PS, Fookes CJR, Mizra AH (1977) Aust J Chem **30**: 1337
[24] Clezy PS, Mizra AH (1982) Aust J Chem **35**: 197
[25] Morgan AR, Scherrer Pangka V, Dolphin D (1984) J Chem Soc Chem Commun 1047
[26] Richter A, Kelley B, Chow J, Liu D, Towers G, Dolphin D (1987) J Natl Cancer Inst **79**: 1327
[27] North J, Neyndorff H, King D, Levy JG (1992) Blood Cells **18**: 129
[28] Pandey RK, Potter WR, Meunier I, Sumlin AB, Smith KM (1995) Photochem Photobiol **62**: 764
[29] Kessel D (1989) Photochem Photobiol **49**: 579
[30] Richter AM, Waterfield E, Jain AK, Allison B, Sternberg ED, Dolphin D, Levy JG (1991) Br J Cancer **63**: 87
[31] Allison BA, Pritchard PH, Levy JG (1994) Br J Cancer **69**: 833
[32] Richter AM, Jain AK, Obochi M, Meadows H, Canaan AJ, Levy JG (1994) Photochem Photobiol **59**: 350
[33] Hunt DWC, Jiang H-J, Levy JG, Chan AH (1995) Photochem Photobiol **61**: 417
[34] Cincotta L, Szeto D, Lampros E, Hasan T, Cincotta AH (1996) Photochem Photobiol **63**: 229
[35] Glück S, Chadderton A, Ho AD (1996) Photochem Photobiol **63**: 846
[36] Waterfield EM, Renke ME, Smits CB, Gervais MD, Bower RD, Stonefield MS, Levy JG (1994) Photochem Photobiol **60**: 383

[37] Richter AM, Yip S, Waterfield E, Logan PM, Slonecker CE, Levy JG (1991) Photochem Photobiol **53**: 281
[38] Aveline B, Hasan T, Redmond RW (1994) Photochem Photobiol **59**: 328
[39] McMurry JE (1989) Chem Rev **89**: 1513
[40] Herrmann WA, Broßmer C, Öfele K, Reisinger C-P, Priermeier T, Beller M, Fischer H (1995) Angew Chem **107**: 1989; Angew Chem Int Ed Engl **34**: 1844
[41] Beller M, Fischer H, Herrmann WA, Öfele K, Broßmer C (1995) Angew Chem **107**: 1992; Angew Chem Int Ed Engl **34**: 1848
[42] Tao W, Nesbitt S, Heck RF (1990) J Org Chem **55**: 63
[43] Holler E (1993) In: Keppler BK (ed) Metal Complexes in Cancer Chemotherapy. VCH, Weinheim, p 41
[44] Brunner H, Maiterth F, Treittinger B (1992) Z Naturforsch **47b**: 942
[45] Caughey WS, Alben JO, Fujimoto WY, York JL (1966) J Org Chem **31**: 2631
[46] Moss GP (1987) Pure Appl Chem **59**: 779

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