An Efficient Method for Phosphorylation of Alcohols: Preparation of Porphyrin-Derived Phosphates

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Abstract: An effective method for the phosphorylation of phenols and various alcohols including porphyrins bearing hydroxyl groups was developed. The reaction of 6,7-bis(3-hydroxypropyl)-1,3,5,8-tetramethyl-2,4-divinylporphyrin with dialkyl chlorophosphate in the presence of DABCO as both a catalyst and a proton scavenger gave the desired phosphate in 97% yield.

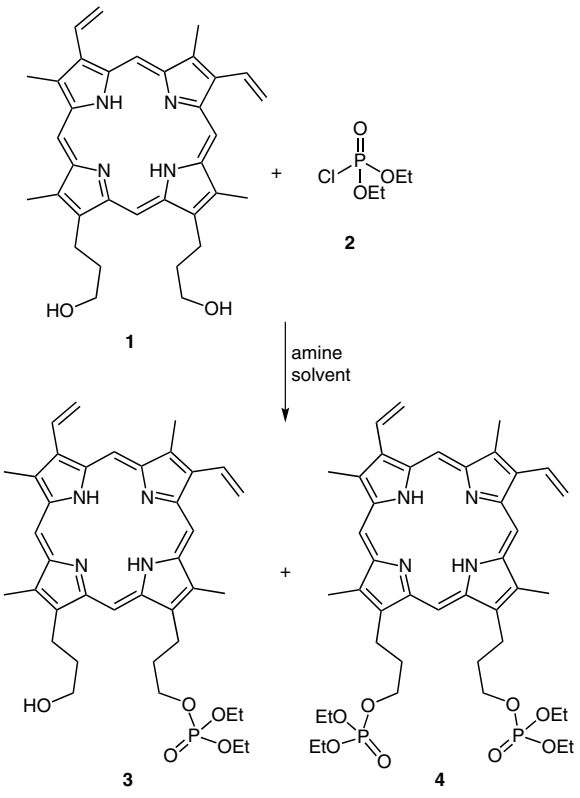
Key words: phosphorylation, dialkyl chlorophosphate, porphyrin, protoporphyrin IX

Phosphoric acid derivatives are commonly found in living organisms and play a key role in many vital processes such as photosynthesis, energy transfer, regulation of ions release, etc. They are also important components of nucleic acids and membrane building compounds.[1–3] Phosphates have also been employed, for example, in prodrug strategies to enhance the bioavailability of therapeutic agents; after passing through cell membranes they hydrolyze releasing bioactive molecules.[4,5]

Due to the importance of these compounds, various methods have already been developed for their preparation.[1,2,6] One of them is the reaction of alcohols with phosphoramidite followed by oxidation.[7–9] However, it is not suitable for substrates that do not tolerate oxidizing agents. Phosphorylation of alcohols can also be carried out through the formation of alkoxides and subsequent reaction with an appropriate dialkyl (or diaryl) chlorophosphate.[10,11] Alternatively, basic and acidic catalysts can be employed such as pyridine,[12] DMAP,[13,14] *N*-methylimidazole[15] or Ti(O*t*-Bu)$_4$, and Cu(OTf)$_2$.[16–18]

For life science applications mostly porphyrins bearing water-solubilizing moieties (e.g., *N*-methylpyridinium, 4-sulfophenyl, oligoethylene glycols, polyamine chains, etc.) were employed.[19] Only few of these groups are suitable for the preparation of hybrid molecules. Among them, the phosphate group occupies a special place assuring both water solubility and place for conjugation. For example, it was found that amphiphilic porphyrins bearing phosphorylcholine groups were prepared using 2-chloro-2-oxo-1,3,2-trioxaphospholane in the presence of triethylamine in dichloromethane.[20,21] Other porphyrin-derived phosphate esters were synthesized via a two-step procedure: phosphitylation followed by oxidation[22,23a,24] or via coupling with amines already bearing a phosphate moiety.[25] Recently, Lindsey has attempted direct phosphorylation of A_2B_2 porphyrin with an aliphatic chain bearing primary hydroxyl groups.[26,27] The reaction with dimethyl chlorophosphate in anhydrous pyridine gave very low yield of the desired product.

Although these methods gave the desired phosphate derivatives they posses several limitations: (1) direct phosphorylation usually is low yielding; (2) the use of dialkylphosphoroamidate is followed by oxidation thus the method is not suitable for compounds possessing easily oxidized groups; (3) coupling with amines, already bearing a phosphate moiety, introduces additional structural fragments (not necessarily needed in the final structure). Therefore, the development of a direct phosphorylation procedure for porphyrin-derived alcohols would be highly advantageous.



Scheme 1 Phosphorylation of diol **1**

The aim of our studies was to obtain phosphate derivatives of porphyrins. Initially, phosphorylation of proto-

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porphyrin IX derived diol **1** was attempted. The starting material was prepared from protoporphyrin IX via esterification with methanol followed by reduction with $LiAlH_4$.[28,29]

The reaction of diol **1** with diethyl chlorophosphate in anhydrous triethylamine or DIPEA as proton scavengers furnished monoproduct **3** (as a mixture of two isomers) in moderate yields (Scheme 1, Table 1, entries 1 and 2). Surprisingly, whereas the substrates examined by Lindsey's group did not undergo phosphorylation efficiently in anhydrous pyridine, the reaction of porphyrin **1** under the same conditions did afford the desired phosphorylated product **4** in 72% yield (Table 1, entry 3).[14] Extending the reaction time did not affect the outcome of the phosphorylation, while heating of the reaction mixture caused decomposition of the starting material. In our case porphyrin **1** dissolved in pyridine thus we believed that the solubility of the starting material was crucial. Although the phosphorylation gave satisfactory results, a further search for more general conditions was performed. In order to surpass both the solubility problem for other porphyrins and the use of a high excess of pyridine, reactions in various polar solvents were conducted. Unfortunately, when the amount of pyridine was reduced to 30 equivalents and dichloromethane was used as a solvent, the yield of product **4** decreased to 30% (Table 1, entry 4). Similar results were generated in anhydrous THF and dioxane (Table 1, entries 5 and 6). Interestingly, the reaction in DMF furnished only monoproduct **3** in 40% yield (Table 1, entry 7). Even the addition of a catalytic amount of DMAP did not improve the results (Table 1, entry 8).

Table 1 Solvent Screening for the Phosphorylation Reaction of Diol **1**[a]

Entry	Amine	Solvent	Yield of **3** (%)	Yield of **4** (%)
1	Et_3N	–	64	–
2	DIPEA	–	53	–
3	pyridine	–	–	72
4	pyridine	CH_2Cl_2	–	30
5	pyridine	THF	–	42
6	pyridine	dioxane	–	34
7	pyridine	DMF	40	–
8	pyridine[b]	THF	–	43

[a] Reactions performed with 30 equiv of $ClP(O)(OEt)_2$ and 30 equiv of amine at r.t. overnight.
[b] DMAP was used as a catalyst.

Having established that THF could be used as a solvent for this reaction, attempts were made to maximize the yield of product **4** by testing amines of various basicity (Table 2).[30] The use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, $pK_b = 1.1$) resulted mainly in decomposition of porphyrin **1** (Table 2, entry 3) while the reaction in the presence of imidazole furnished a mixture of porphyrin **3** and **4** (Table 2, entry 4). The best result was achieved when 1,4-diazabicyclo[2.2.2]octane (DABCO, $pK_b = 5.2$) in THF was used. Phosphate **4** was obtained in excellent yield (Table 2, entry 5).

Table 2 Optimization Studies[a]

Entry	Amine	Solvent	Yield of **3** (%)	Yield of **4** (%)
1	Et_3N	THF	–	55
2	DIPEA	THF	–	46
3	DBU	THF	–	7
4	imidazole	THF	33	48
5	DABCO	THF	–	97
6	DABCO	DMF	–	trace
7	DABCO	CH_2Cl_2	–	trace

[a] Reactions performed with 30 equiv of $ClP(O)(OEt)_2$ and 30 equiv of amine at r.t. overnight.

Further optimization of reaction conditions with respect to amounts of phosphorylation reagent and DABCO demonstrated that 12 equivalents of both diethyl chlorophosphate (**2**) and amine were enough to achieve full conversion of diol **1**. Larger excess of reagent **2** caused problems with purification of the product. These established reaction conditions were also effective in phosphorylation of diol **1** using dimethyl chlorophosphate. Moreover, in all cases the formation of side products such as chlorides or ethers, which could be the result of nucleophilic substitution, were not observed while these were formed during reactions catalyzed by Lewis acids.[25]

Optimized reaction conditions for porphyrin-derived alcohols are as follow: 0.014 M of **1**, 12 equiv of phosphorylation reagent, 12 equiv of DABCO in anhydrous THF for 16 hours at room temperature. Under these conditions other porphyrins bearing alcohol or phenol moieties were found to generate the desired phosphates **Zn6** and **7** in satisfactory yields (Figure 1). For zinc-metalated porphyrin **Zn6** partial demetalation occurred hence the reaction mixture was treated with $Zn(OAc)_2$ and stirred for an additional four hours at room temperature. In comparison to the literature data for the known derivative our method provides a good mean for the synthesis of porphyrin-derived phosphates (30%[14] vs. 88%).

Subsequently, the wide utility of the developed procedure was demonstrated in the phosphorylation of a number of representative alcohols (Table 3). Gratifyingly, for all alcohols tested, shorter reaction times and a smaller amount of both diethyl chlorophosphate (1.5 equiv) and DABCO (1.5 equiv) was sufficient to gain satisfactory yields. Phosphoric esters from both primary and secondary alcohols were obtained over the course of four hours (Table 3, entries 1–5). The procedure worked nicely also for phenol (Table 3, entry 6).

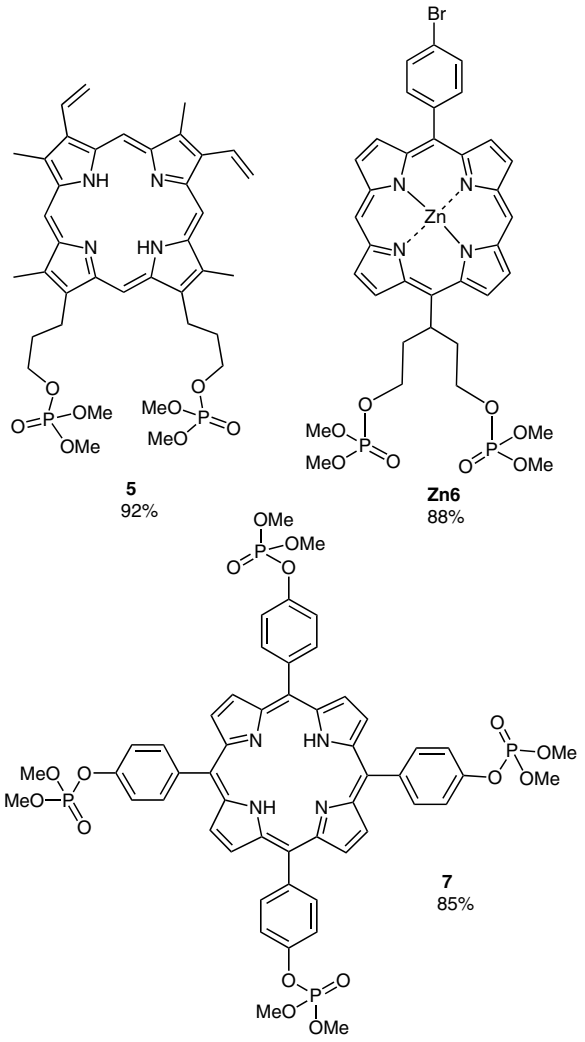


Figure 1 Porphyrin-derived phosphates

Again, established reaction conditions were also effective for the phosphorylation of alcohols using dimethyl chlorophosphate (Figure 2).

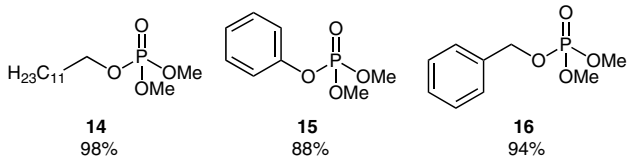
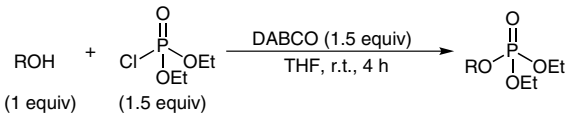


Figure 2 Phosphorylation of various alcohols by dimethyl chlorophosphate

In summary, we have developed an efficient procedure for the phosphorylation of various alcohols and phenols with dialkyl chlorophosphates in the presence of DABCO. The base acts as both a catalyst and a proton scavenger, which eliminates the necessity for an additional catalyst. Dimethyl and diethyl chlorophosphates furnished phosphates in excellent yield, and a large excess of these reagents is not required. Representative alcohols and phenols were phosphorylated showing broad application of the developed procedure. Notably, the optimized reaction conditions are particularly effective for the direct synthesis of porphyrin-derived phosphates.

Table 3 Phosphorylation of Various Alcohols with Diethyl Chlorophosphate[a]



Entry	Phosphate product	Yield (%)
1	**8**	98
2	**9**	94
3	**10**	94
4	**11**	94
5	**12**	96
6	**13**	95

[a] Reactions performed with 1.5 equiv of $ClP(O)(OEt)_2$ and 1.5 equiv of DABCO at r.t. for 4h.

Analytical-grade solvents were used as received. All solvents used for a reaction were dried prior to use. ^1H NMR and ^{13}C NMR spectra were recorded at r.t. on either 400 or 500 MHz instrument. Dry column vacuum chromatography (DCVC) was performed using silica gel (200–300 mesh). Flash column chromatography was performed using silica gel (60 mesh). Thin-layer chromatography (TLC) was performed using silica gel GF254, 0.20 mm thickness. UV/vis absorption spectra were recorded in CH_2Cl_2 at r.t.

General Procedure for the Phosphorylation of Porphyrin Alcohols

To a solution of diol (0.056 mmol, *c* 0.014 M) and DABCO (12.0 equiv, 0.67 mmol, 75 mg) in anhyd THF (4 mL), at r.t., dialkyl chlorophosphate (12.0 equiv, 0.672 mmol, 97 μL) was added dropwise via syringe. The resulting mixture was stirred overnight at r.t. It was then poured into CH_2Cl_2 and washed with aq HCl (5%), sat. aq $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude solid was purified using DCVC.

6-[3-(Diethoxyphosphoryloxy)propyl]-7-(3-hydroxypropyl)-1,3,5,8-tetramethyl-2,4-divinyl-porphyrin (3)

Diol **1** (30 mg, 0.056 mmol) was dissolved in anhyd Et_3N (1.5 mL) at r.t., dialkyl chlorophosphate (30.0 equiv, 1.68 mmol, 243 μL) was added dropwise via syringe. The resulting mixture was stirred overnight at r.t. It was then poured into CH_2Cl_2 and washed with aq HCl (5%), sat. aq $NaHCO_3$, and brine. The crude product was purified by DCVC (20% acetone in toluene). It was then dissolved in the

minimum amount of CH_2Cl_2. Hexane was added to the solution till a precipitate appeared, compound **3** was isolated as a red solid (24 mg, 64%); mp 251 °C. R_f = 0.95 (Al_2O_3, 3% MeOH in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.12–9.96 (m, 4 H), 8.29–8.29 (m, 2 H), 6.38–6.14 (m, 4 H), 4.39–4.34 (m, 2 H), 4.16–3.98 (m, 10 H), 3.86–3.84 (m, 1 H), 3.67–3.65 (m, 6 H), 3.58–3.54 (m, 6 H), 2.61 (pent, J = 2.5 Hz, 2 H), 2.49 (pent, J = 2.6 Hz, 2 H), 1.21 (t, J = 7.1 Hz, 12 H), –3.87 (br s, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 130.4, 130.3, 120.7, 120.5, 97.8, 97.7, 97.2, 96.8, 96.7, 96.5, 67.6 (d, J_{CP} = 5.9 Hz), 63.8 (d, J_{CP} = 5.7 Hz), 62.1, 35.9, 33.4 (d, J_{CP} = 6.4 Hz), 31.9, 22.7, 22.1, 16.1 (d, J_{CP} = 6.7 Hz), 12.7, 12.6, 11.7, 11.5 ppm. ESI-HRMS: *m/z* calcd for $C_{38}H_{47}N_4O_5P$ $[M + H]^+$: 671.3359; found: 671.3357. UV/vis (CH_2Cl_2) λ_{max} (ε) = 669 ($1.23\cdot10^3$), 629 ($4.95\cdot10^3$), 574 ($6.81\cdot10^3$), 540 ($1.09\cdot10^4$), 505 ($1.28\cdot10^4$), 406 ($1.51\cdot10^5$) ($L\cdot mol^{-1}\cdot cm^{-1}$).

6,7-Bis[3-(diethoxyphosphoryloxy)propyl]-1,3,5,8-tetramethyl-2,4-divinylporphyrin (4)

Compound **4** was prepared from diol **1** (30 mg, 0.056 mmol) according to the general procedure. The crude product was purified by DCVC (25% acetone in toluene). It was then dissolved in the minimum amount of CH_2Cl_2. Hexane was added to the solution till a precipitate appeared, compound **4** was isolated as a red solid (42 mg, 97%); mp 128 °C. R_f = 0.85 (Al_2O_3, 3% MeOH in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.00 (s, 1 H), 9.96 (s, 1 H), 9.87 (s, 1 H), 9.85 (s, 1 H), 8.19–8.08 (m, 2 H), 6.32–6.26 (dd, J = 17.7, 12.2 Hz, 2 H), 6.14–6.10 (dd, J = 11.4, 10.7 Hz, 2 H), 4.34–4.31 (m, 4 H), 4.16–4.10 (m, 12 H), 3.58–3.54 (m, 12 H), 2.66–2.61 (m, 4 H), 1.30 (t, J = 7.1 Hz, 12 H), –3.99 (br s, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 130.2, 130.2, 120.6, 97.9, 97.2, 96.9, 96.9, 95.8, 67.0 (d, J_{CP} = 6.3 Hz), 63.7 (d, J_{CP} = 4.8 Hz), 33.4, 33.3, 22.2, 16.1 (d, J_{CP} = 6.3 Hz), 12.6, 11.7, 11.6 ppm. ESI-HRMS: *m/z* calcd for $C_{42}H_{56}N_4O_8P_2$ $[M + Na]^+$: 829.3470; found: 829.3466. UV/vis (CH_2Cl_2) λ_{max} (ε) = 821 ($4.63\cdot10^2$), 775 ($2.60\cdot10^2$), 669 ($1.72\cdot10^3$), 629 ($4.8\cdot10^3$), 575 ($6.34\cdot10^3$), 540 ($1.03\cdot10^4$), 505 ($1.22\cdot10^4$), 406 ($1.49\cdot10^5$) ($L\cdot mol^{-1}\cdot cm^{-1}$). Anal. Calcd for $C_{42}H_{56}N_4O_8P_2$: C, 62.52; H, 7.00; N, 6.94. Found: C, 62.41; H, 7.03; N, 7.04.

6,7-Bis[3-(dimethoxyphosphoryloxy)propyl]-1,3, 5,8-tetramethyl-2,4-divinylporphyrin (5)

Compound **5** was prepared from diol **1** (30 mg, 0.056 mmol) according to the general procedure using dimethyl chlorophosphate. The crude product was purified by DCVC (25% acetone in toluene). It was then dissolved in the minimum amount of CH_2Cl_2. Hexane was added to the solution till a precipitate appeared, compound **5** was isolated as a red solid (39 mg, 92%); mp 243 °C. R_f = 0.80 (Al_2O_3, 3% MeOH in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.18 (s, 1 H), 10.15 (s, 1 H), 10.05 (s, 1 H), 9.95 (s, 1 H), 8.31–8.23 (m, 2 H), 6.37 (dd, J = 17.8, 1.4 Hz, 2 H), 6.18 (dd, J = 11.5, 1.3 Hz, 2 H), 4.38–4.33 (m, 4 H), 4.19 (t, J = 7.4 Hz, 4 H), 3.8 (d, J_{HP} = 11.1 Hz, 12 H), 3.70 (s, 3 H), 3.69 (s, 3 H), 3.62 (s, 3 H), 3.61 (s, 3 H), 2.66 (tt, J = 6.6, 6.9 Hz, 4 H), –3,77 (br s, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 130.2, 120.8, 98.1, 97.4, 97.1, 95.8, 67.3 (d, J_{CP} = 5.8 Hz), 53.3 (d, J_{CP} = 5.9 Hz), 33.4, 33.3, 22.1, 12.6, 11.7 ppm. ESI-HRMS: *m/z* calcd for $C_{38}H_{48}N_4O_8P_2$ $[M + Na]^+$: 773.2839; found: 773.2875. UV/vis (CH_2Cl_2): λ_{max} (ε) = 669 ($5.22\cdot10^2$), 630 ($4.78\cdot10^3$), 576 ($6.82\cdot10^3$), 541 ($1.10\cdot10^4$), 506 ($1.22\cdot10^4$), 408 ($1.50\cdot10^5$) ($L\cdot mol^{-1}\cdot cm^{-1}$). Anal. Calcd for $C_{38}H_{48}N_4O_8P_2 + H_2O$: C, 59.37; H, 6.56; N, 7.29. Found: C, 59.64; H, 6.54; N, 7.50.

Zn(II) 5-(4-Bromophenyl)-15-[1,5-bis(dimethoxyphosphoryloxy)pent-3-yl]porphyrin (Zn6)

Compound **Zn6** was prepared from Zn(II) 5-(4-bromophenyl)-15-(1,5-dihydroxypent-3-yl)porphyrin[26] (30 mg, 0.048 mmol) according to the general procedure, the reaction was performed with 12 equiv of both dimethyl chlorophosphate and DABCO. After reaction a partial demetalation was observed, so to the reaction mixture $Zn(OAc)_2$ dihydrate (0.053, 0.24 mmol) was added and stirred at r.t. for an additional 2 h. The crude product was purified by DCVC (25% acetone in toluene). It was then dissolved in the minimum amount of CH_2Cl_2. Hexane was added to the solution till a precipitate appeared, compound **Zn6** was isolated as a red solid (36 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.18 (s, 1 H), 10.05 (s, 1 H), 9.57 (d, J = 4.5 Hz, 1 H), 9.45 (t, J = 4.4 Hz, 2 H), 9.34 (d, J = 4.5 Hz, 1 H), 9.28 (d, J = 4.5 Hz, 1 H), 9.22 (d, J = 4.6 Hz, 1 H), 9.00 (t, J = 4.2 Hz, 2 H), 8.06 (d, J = 8.2 Hz, 2 H), 7.89 (d, J = 8.1 Hz, 2 H), 5.35 (s, 1 H), 3.05 (m, 6 H), 2.70 (m, 14 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 149.8, 149.7, 149.7, 149.4, 148.9, 148.4, 147.1, 141.9, 135.9, 132.0, 131.8, 131.7, 129.7, 129.5, 121.9, 118.4, 117.7, 105.9, 105.4, 65.9, 65.9, 53.3, 53.3, 53.2, 41.6, 41.5, 37.9 ppm.

5-(4-Bromophenyl)-15-[1,5-bis(dimethoxyphosphoryloxy)pent-3-yl]porphyrin (6)

Compound **6** was prepared from **Zn6** (25 mg, 0.029 mmol) according to the literature[26] (21 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (d, J = 7.8 Hz, 2 H), 9.85 (d, J = 4.8 Hz, 1 H), 9.67 (d, J = 4.7 Hz, 1 H), 9.50 (m, 2 H), 9.40 (m, 2 H), 9.11–8.98 (m, 2 H), 8.18–8.07 (m, 2 H), 8.02–7.89 (m, 2 H), 5.90–5.73 (m, 1 H), 4.13–4.06 (m, 2 H), 4.00–3.85 (m, 2 H), 3.66–3.35 (m, 14 H), 3.28–3.17 (m, 2 H), –2.88 (d, J = 25.9 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 147.8, 147.08, 146.3, 145.9, 144.5, 143.7, 143.6, 139.9, 136.1, 133.1, 132.6, 132.1, 131.8, 131.1, 130.3, 130.0, 128.6, 128.4, 122.6, 118.6, 117.3, 105.6, 105.0, 66.46, 66.4, 54.1, 54.0, 53.9, 41.8, 41.7, 37.8 ppm.

5,10,15,20-Tetrakis(4-dimethoxyphosphonoxyphenyl)porphyrin (7)

Compound **7** was prepared from 5,10,15,20-tetrakis(4-hydroxyphenyl)porphyrin[23b] (25 mg, 0.037 mmol) according to the general procedure, the reaction was performed with 24 equiv of both dimethyl chlorophosphate and DABCO. Chromatography (2% MeOH in CH_2Cl_2) of the crude product and subsequent recrystallization from hexane–CH_2Cl_2 yielded a red solid (35 mg, 85%); mp dec >280 °C. R_f = 0.70 (Al_2O_3, 2% MeOH in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (s, 8 H), 8.19 (d, J = 8.2 Hz, 8 H), 7.73 (dd, J = 8.6 Hz, J_{CP} = 1.0 Hz, 8 H), 4.08 (d, J_{CP} = 11.3 Hz, 24 H), –2.84 (br s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.7 (d, J_{CP} = 6.7 Hz), 138.9, 135.6, 119.1, 118.2 (d, J_{CP} = 5 Hz), 55.2 (d, J_{CP} = 6,2) ppm. UV/vis (CH_2Cl_2): λ_{max} (ε) = 645 ($5.32\cdot10^3$), 590 ($6.88\cdot10^3$), 549 ($1.00\cdot10^4$), 514 ($2.32\cdot10^4$), 447 ($1.40\cdot10^4$), 418 ($5.97\cdot10^5$), 292 ($1.87\cdot10^4$), 253 ($1.89\cdot10^4$) ($L\cdot mol^{-1}\cdot cm^{-1}$). ESI-HRMS: *m/z* calcd for $C_{52}H_{50}N_4O_{16}P_4$ $[M + Na]^+$: 1133.2041; found: 1133.2065. Anal. Calcd for $C_{52}H_{50}N_4O_{16}P_4 + H_2O$: C, 55.33; H, 4.64; N, 4.96. Found: C, 55.33; H, 4.76; N, 5.14.

General Procedure for the Phosphorylation of Alcohols

To a solution of an alcohol (0.65 mmol) and DABCO (1.5 equiv, 0.98 mmol) in anhyd THF (2 mL), at r.t., dialkyl chlorophosphate (1.5 equiv, 0.98 mmol) was added dropwise via syringe. The resulting mixture was stirred for 4 h at r.t. It was then poured into CH_2Cl_2 and washed with aq HCl (5%), sat. aq $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography.

Diethyl[2-(4-methylphenylsulfonamido)propyl]phosphate (9)

Compound **9** was prepared from *N*-tosyl alaninol (150 mg, 0.65 mmol) according to the general procedure using diethyl chlorophosphate (**2**). The crude product was chromatographed (10% EtOAc in hexanes) to afford phosphate **9** (225 mg, 94%) as a colorless oil. R_f = 0.6 (SiO_2, 3% MeOH in CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.77 (d, J = 8.3 Hz, 2 H), 7.30 (dd, J = 8.5, 0.6 Hz, 2 H), 5.28 (d, J = 7.7 Hz, 1 H), 4.09 (q, J = 7.1 Hz, 4 H), 3.91–3.88 (m, 2 H), 3.61–3.31 (m, 1 H), 2.42 (s, 3 H), 1.35–1.31 (m, 6 H), 1.13 (d, J = 6.8 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.4, 137.9, 129.7, 127.1, 127.0, 70.1 (d, J_{CP} = 5.8 Hz), 64.1 (d, J_{CP} = 5.7 Hz), 64.0 (d, J_{CP} = 5.7 Hz), 49.5, 49.4, 21.5, 17.9, 16.1, 16.0 ppm. ESI-HRMS: *m/z* calcd for $C_{14}H_{24}NO_6PS$ $[M + Na]^+$: 388.0954;

found: 388.0936. Anal. Calcd for $C_{14}H_{24}NO_6PS$: C, 46.02; H, 6.62; N, 3.83. Found: C, 46.25; H, 6.43; N, 3.73.

For compounds **8**,[31] **10**,[32] **11**,[31] **12**,[33] **13**,[31] **14**,[31] **15**,[34] and **16**[35] all analytical data are consistent with the literature.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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