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# Functionalization of the Periphery of Calix[4]resorcinarenes with P(III)-Containing Substituents via Hydroxy, Trimethylsiloxy, and Ethoxy-Tethered Trimethylsiloxy Intermediates

Ion Neda,[1] Alexander Vollbrecht,[1] Jörg Grunenberg[2] and Reinhard Schmutzler[1]

[1]*Institut für Anorganische und Analytische Chemie der Technischen, Universität, Postfach 3329, D-38023 Braunschweig, Germany*

[2]*Institut für Organische Chemie der Technischen Universität, Postfach 3329, D-38023 Braunschweig, Germany*

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ABSTRACT: *Unlike C-undecylcalix[4]resorcinarene, C-methylcalix[4]resorcinarene* **1** *reacted with chlorodifluorophosphine in the absence of an auxiliary base to give the unstable octakis(difluorophosphite)-substituted derivative* **2**. *The existence of two conformational isomers of* **2** *in solution was observed by* $^{19}F$ *and* $^{31}P$ *NMR spectroscopy. Attempts to react the octakis(trimethylsilyl)calix[4]resorcinarene* **3** *and its tetrabromo derivative* **4** *with phosphorus trichloride and chlorodifluorophosphine were unsuccessful.*

*The ethoxy-tethered C-methyl-octakis(trimethylsilyl)calix[4]resorcinarene* **5** *was allowed to react with 2-chloro-1,3,5-trimethyl-1,3,5-triaza-2$\sigma^3\lambda^3$-phosphorin-4,6-dione and chlorodifluorophosphine. By substitution of all trimethylsilyl groups, the octakis(phosphorus(III))-substituted compounds* **6** *and* **7** *were formed. As for* **2**, *dynamic behavior in solution was observed for* **6** *and* **7**, *arising from the equilibrium between different conformational isomers.* © 1998 John Wiley & Sons, Inc. Heteroatom Chem 9:553–558, 1998

Dedicated to Prof. Günter Schmid on the occasion of his sixtieth birthday.

*Correspondence to:* R. Schmutzler.

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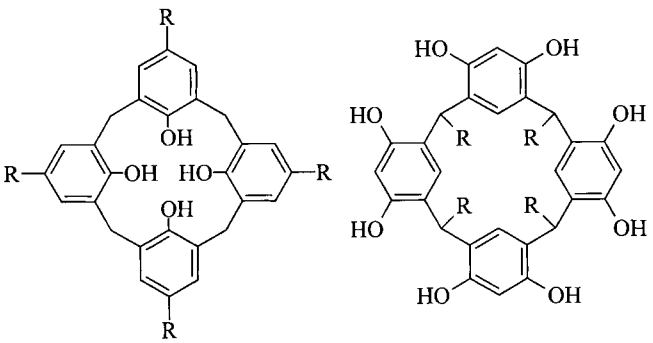
## *INTRODUCTION*

Calix[4]arenes (Figure 1, **A**) and calix[4]resorcinarenes (Figure 1, **B**) are an important class of oligocyclic compounds. Whereas calix[4]arenes have been extensively studied and have been used in industrial processes [1, 2], many areas of calix[4]resorcinarene chemistry remain unexplored.




**A** R = alkyl, aryl **B**

**FIGURE 1** Calix[4]arenes **A** and Calix[4]resorcinarenes **B**.

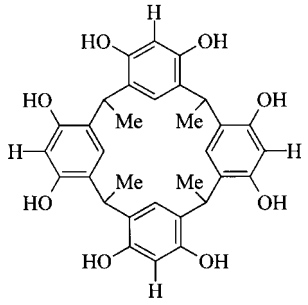
The reactivity of calix[4]resorcinarenes of type **B** (Figure 1) is often limited because of the proximity of the hydroxy groups to the bowl-shaped calixresorcinarene skeleton. For steric reasons, it is not always possible to substitute all eight oxygen-bonded hydrogen atoms of the molecule for bulky substituents. In addition, strong hydrogen bonds further lower the reactivity. Derivatives of calix[4]resorcinarenes with diethoxyphosphoryl or with diphenylphosphino groups show special properties, for example, the selective binding of metal ions as aggregates, or are employed as building blocks for the preparation of cation receptors [3, 4, 5a].

Compound **5** represents an important building block in supramolecular chemistry. It is possible to synthesize multidentate phosphorus(III)-containing calix[4]resorcinarenes, based on **5**, that may act as complexing ligands in transition metal chemistry. The reactivity of C-methyl-calix[4]resorcinarene (**B** in Figure 1; R = Me) is different from that of its ethoxy-tethered derivative because of the different reactivity of the phenolic and alcoholic OH groups [6].

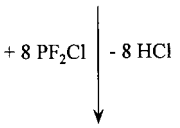
## *RESULTS AND DISCUSSION*

### *Preparation of* **2**

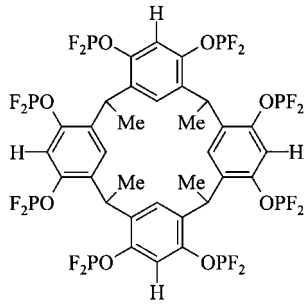
The functionalization of C-methylcalix[4]resorcinarene, **1**, with phosphorus-containing groups has been described [7] in a few cases, but the reaction of **1** with chlorodifluorophosphine ($PF_2Cl$) (cf. Equation 1) has not been investigated until now. Recently, we have reported the reaction of C-undecylcalix[4]resorcinarene, octakis(trimethylsilyl)C-undecylcalix[4]resorcinarene [8] and bis(trimethylsilyl)-*p-tert*-butylcalix[4]resorcinarene [9a] with $PF_2Cl$. In neither case could the corresponding octakis(difluorophosphite) derivatives be obtained. Only by lithiation of C-undecylcalix[4]resorcinarene, followed by reaction with $PF_2Cl$, could the desired octakis(difluorophosphito) derivative be synthesized. The reaction of bis(trimethylsilyl)-*p-tert*-butylcalix[4]arene with $PF_2Cl$, depending on the stoichiometry of the reactants, led to the mono- and disubstituted difluorophosphite derivatives [9]. In contrast, octakis(trimethylsilyl)-C-undecylcalix[4]resorcinarene was found to react with $PF_2Cl$ with exclusive formation of the tetrakis-(difluorophosphito)-tetrakis-(trimethylsilyl)-C-undecylcalix[4]resorcinarene. This compound is stable in solution at 25°C; no intramolecular elimination of fluorotrimethylsilane was observed [8]. The reaction of C-undecylcalix[4]resorcinarene with $PF_2Cl$ failed [8]. When C-methylcalix[4]resorcinarene **1** was allowed to react with $PF_2Cl$, the octakis(difluorophosphite) derivative, **2**, was formed in good yield. Both the octakis(difluorophosphito)-C-undecylcalix[4]resorcinarene [8] and compound **2** were found to undergo a transformation in solution after 1 day at −35°C and 25°C, respectively, with formation of $PF_3$ [9b] and a mixture of different products with -P(:O)F(O)- and $-P(:O)F_2$ structural elements. This was established by $^{31}P$ NMR spectroscopy [$\delta(^{31}P)$ = 120.05 [11] d, $^1J(PF)$ = 1357 Hz and $\delta(^{31}P)$ = −0.28 d, $^1J(PF)$ = 1328 Hz].




**1**

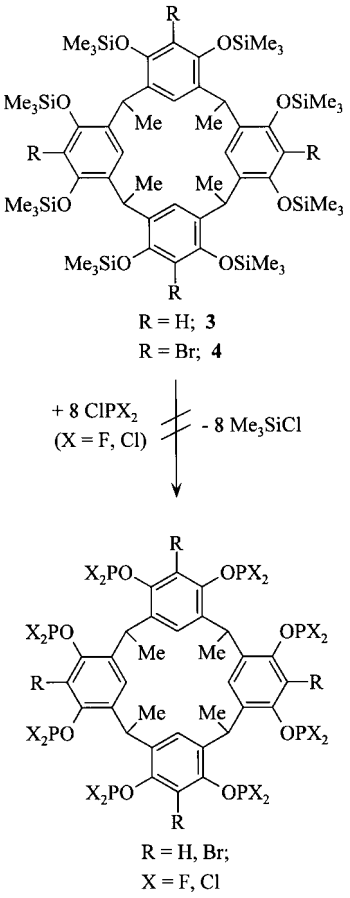



(1)




**2**

While $^1H$ and $^{13}C$ NMR spectra revealed clear-cut resonances for **2**, $^{19}F$ and $^{31}P$ NMR spectra, recorded at room temperature, exhibited two resonances, due to two types of magnetically different $PF_2$ groups in the molecule. It is suggested that this effect is due to the interconversion between two identical boat conformations (flexible $C_{2v}$ conformation) of **2** on the NMR timescale. No reaction was observed when **3** and **4** were treated with excess $PCl_3$ or $PF_2Cl$ in dichloromethane at room temperature (cf. Equation 2).




(2)

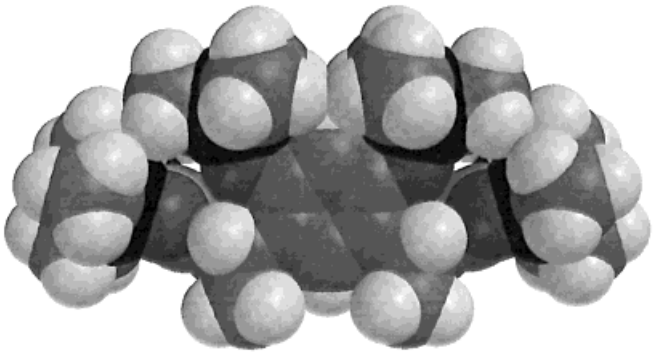


**FIGURE 2** Spacefilling diagram of the calix[4]resorcinarene **3** determined by SYBYL force field calculations.

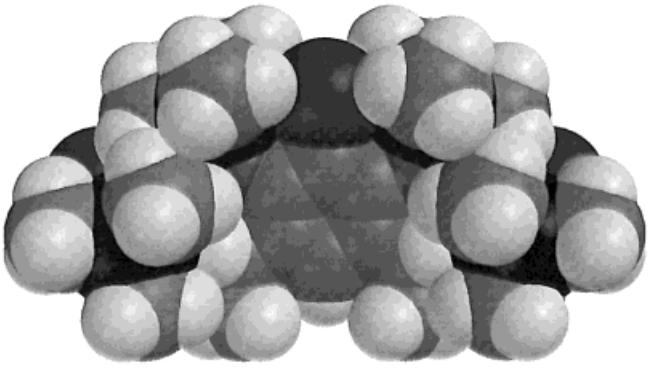


**FIGURE 3** Space-filling diagram of the calix[4]resorcinarene **4** determined by SYBYL force field calculations.

The lack of reactivity of **4** toward halophosphorus(III) compounds is probably due to steric and electronic effects, caused by the bromine atoms bonded to the aromatic rings of the molecule. In order to assess the influence of the nature of the substituents in the para position on the relative stabilities and the geometries of the conformers of the derivatives **3** and **4**, molecular mechanics calculations of the strain energy with the SYBYL force field [10] were performed (Figures 2 and 3).

The structure of **4**, with bromine substituents in the para position, avoids additional strain by an increase of the C-C-O-Si-dihedral angle (cf. relative conformations, **4a** and **4b**, Figure 4), accompanied by a decrease of the strain energy (6.54 kcal/mol$^{-1}$). The structure of **4a** shows that the oxygen sites of the molecule are no longer accessible to the $ClPF_2$ molecules. In contrast, for compound **3**, the conformation **3a** is more stable than **3b**. The conformation **3a** was confirmed by the X-ray structure determination [6] of **3**.

## *Preparation of* **6** *and* **7**

Because of the better solubility of **5** in common organic solvents, compared to that of its octakis(hydroxy) analog [6], compound **5** was allowed to react with two selected phosphorus(III) chlorides, in order to functionalize the rim of the molecule.

According to Scheme 1, compound **6** was synthesized by reaction of **5** with stoichiometric amounts of 2-chloro-1,3,5-trimethyl-1,3,5-triaza-2$\sigma^3\lambda^3$-phosphorin-4,6-dione in dichloromethane.

The $^1$H NMR spectrum of **6** at room temperature revealed only broad signals, probably due to a rapid pseudorotation process [11a], caused by site exchange of perpendicular and coplanar benzene rings. Thus, an $^1$H NMR spectrum at $-50$°C was recorded. The results were comparable to those described for compound **3** [flexible $C_{2v}$-symmetrical boat conformation, leading to four separate doublets (resonances split by coupling to $^{31}$P) for the $CH_3NC(:O)$ protons and four singlets for the aromatic protons] [6]. The decrease in temperature slowed down the pseudorotation process and froze out the energetically preferred boat conformation.

Upon reaction of **5** with excess $PF_2Cl$ in dichloromethane, the octakis (difluorophosphite) deriva-

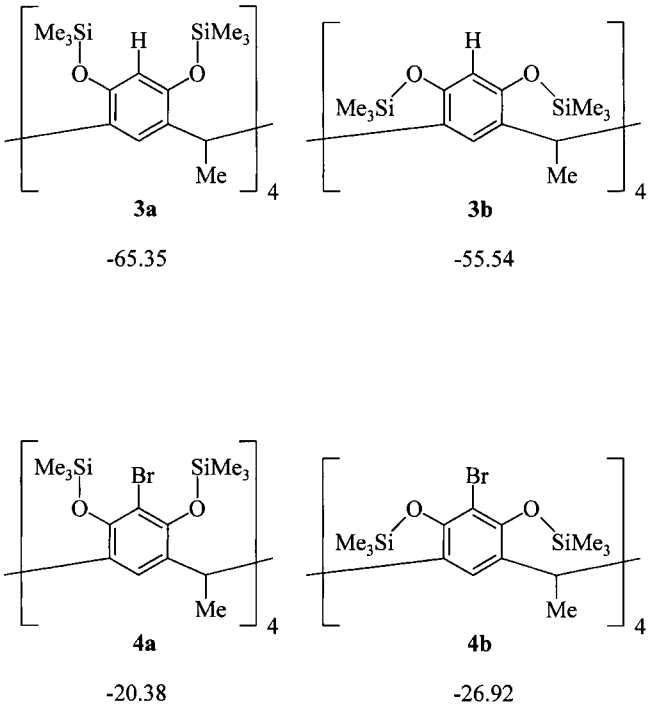



**FIGURE 4** Fragments of the two selected conformers of compounds **3** and **4** in their highest and lowest energy conformations, as determined by SYBYL force field calculations and their calculated energies [kcal/mol$^{-1}$].

tive **7** was formed (Scheme 1). In contrast to observations made for octakis(difluorophosphito)-C-undecylcalix[4]resorcinarene [8] and **2**, no intramolecular elimination of phosphorus trifluoride was observed. In order to determine its stability in solution, 100 mg of **7** was dissolved in 0.5 mL of toluene-$d_8$ and heated to 115°C for 5 hours. Derivative **7** was recovered unchanged: $^1$H, $^{19}$F, and $^{31}$P NMR spectra recorded after the above-mentioned heating period were identical to those recorded before heating **7**. The unusual stability of **7** compared to that of **2** or of 1-O-(difluorophosphito)-2-O-(trimethylsilyl)catechol [11b,c] is caused, apparently, by the fact that all $PF_2$ groups are sufficiently removed from each other and because of the different reactivity of the $PF_2$ groups bonded to the phenolic and alcoholic oxygen atoms. NMR spectra ($^1$H, $^{13}$C, $^{19}$F, and $^{31}$P) at room temperature and $-50$°C were recorded and confirmed the dynamic behavior of **7** in solution, as observed previously for compounds **3** [6], **4** [6], **3** [6], **4** [6], **5**, and **6**. In contrast to the room-temperature spectrum (one broad resonance), sharp signals for the aromatic protons of **7** (four singlets at $\delta = 5.74$, 6.06, 6.33, and 7.21) were observed at low temperature in its $^1$H NMR spectrum. None of the further $^1$H NMR resonances showed any temperature dependence. The room-temperature $^{13}$C NMR investigation revealed doubling of all resonances for the aromatic carbon atoms. Likewise, the $^{19}$F NMR spectrum showed two doublets in the expected range with values of $\delta = -48.28$ and $-48.77$. The $^{31}$P NMR spectrum of **7**, recorded at room temperature, showed only a broad triplet at $\delta = 112$. By lowering the temperature to $-50$°C, the resonance was split into two sharp triplets, due to the presence of only two different aromatic rings, as described for **3** in Ref. [6].

## *CONCLUSIONS*

The reaction of the C-methylcalix[4]resorcinarene, **1**, with $PF_2Cl$ led to the expected compound **2**, unstable at room temperature (due to a scrambling process by elimination of phosphorus trifluoride). The octakis(trimethylsilyl)-substituted derivative of C-undecylcalix[4]resorcinarene reacted with $PF_2Cl$ [8], while its C-methyl derivative, bearing one bromo substituent on each of its aromatic rings, did not.

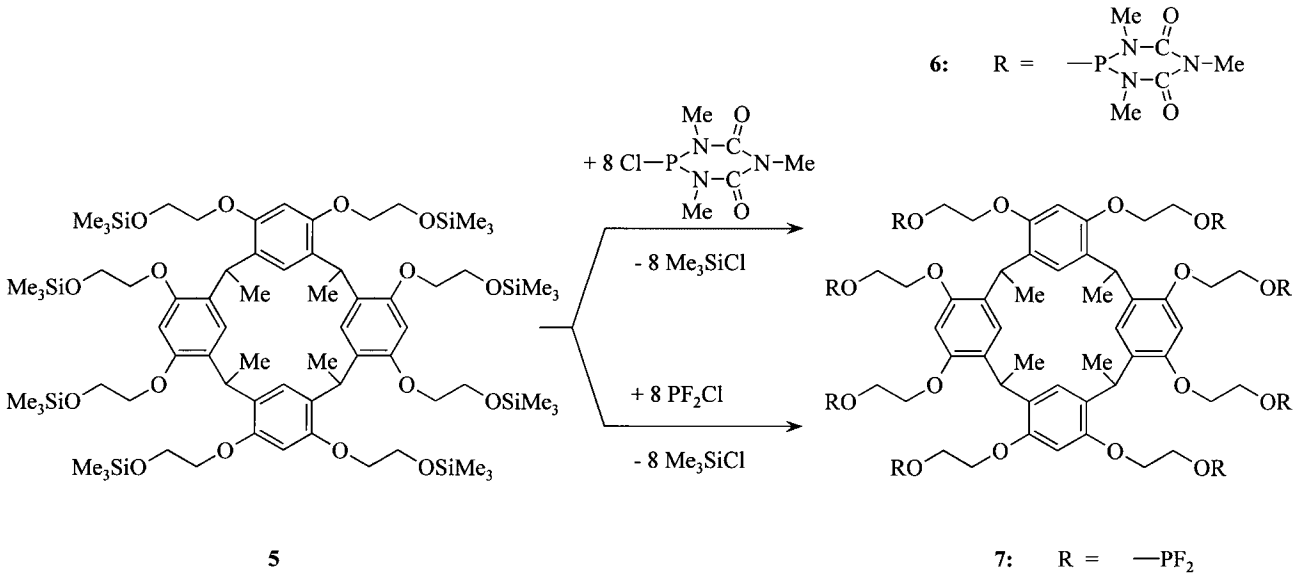
By introducing spacers (ethoxy groups) into the O–Si bonds of the trimethylsiloxy groups bonded to the upper rim of the molecule (compound **5**), the steric hindrance is reduced, and the stable octakis(phosphorus(III))-substituted derivatives **6** and **7** are formed in good yield. Compounds corresponding to **5** (*without* spacer) in their reaction with phosphorus(III) halides [8] only undergo incomplete substitution due to, presumably, steric effects.

The ethoxy-tethered octakis(trimethylsilyl)calix-[4]resorcinarene **5**, as one example for many other compounds of this kind, offers many possibilities for the functionalization of the periphery of calix[4]resorcinarenes. It is possible now to design multidentate, phosphorus(III)-containing calix[4]-resorcinarenes as potentially important complexing ligands useful, for example, in transition metal chemistry and catalysis.

## *EXPERIMENTAL*

Experimental conditions and instruments used for the NMR spectroscopic and mass spectrometric investigations were identical to those mentioned in Ref. [12]. The expression "in vacuo" (i.v.) relates to a pressure of ca. 0.1 mm Hg.

2-Chloro-1,3,5-trimethyl-1,3,5-triaza-2$\sigma^3\lambda^3$-phosphorin-4,6-dione [13], chlorodifluorophosphine [14], C-methylcalix[4]resorcinarene **1** [15], C-methyl- octakis(trimethylsilyl)calix[4]resorcinarene **3** [6], and C-methyl-tetrakis(monobromo)-octakis(trimethylsilyl)calix[4]resorcinarene **4** [6] were synthe-




**SCHEME 1**

sized according to methods described in the literature. All the other starting compounds were commercially available.

The $^{13}C$ NMR resonances of the carbon atoms in **2**, **6**, and **7** were assigned using the following numbering scheme. (See Figure 5.)

*Compound* **2**. In a heavy-walled glass tube fitted with a TEFLON® stopcock, a solution of 0.62 g (1.14 mmol) of **1** in 20 mL of tetrahydrofuran and 30 mL of diethyl ether was cooled to −196°C. At this temperature, 1.9 g (18.2 mmol) of chlorodifluorophosphine was condensed onto the solution. The reaction mixture was allowed to warm to room temperature (1 h) and was stirred for 3 days. Subsequently, excess $PF_2Cl$, solvent, and all volatile components were removed i.v. The remaining colorless solid was washed with 2 × 5 mL of diethyl ether and dried i.v. for 1 day. Compound **2** was obtained as a THF adduct (ca. 1.4:1, based on the integration of the $^1H$ NMR spectra). Yield: 1.44 g (72%); dec. 400°C.

$^1H$ NMR: $\delta$ = 1.52 [d, $^3J$(HH) = 7.0 Hz, 12H, CHC$H_3$], 1.98 and 4.02 [2m, 11H, $C_4H_8O$], 4.53 [q, $^3J$(HH) = 7.0 Hz, 4H, C$H$CH$_3$], 6.74 and 6.81 [2s, 8H, $C_6H_2$]. -$^{13}C$ NMR: $\delta$ = 19.96 [s, 4C, CH$C$H$_3$], 31.74 [s, 4C, $C$HCH$_3$], 26.8 and 68.6 [2s, C, $C_4H_8O$], 113.79 [s, 4C, *C*5, 11, 17, 23], 126.57 [s, 4C, *C*25, 26, 27, 28], 133.34 [s, 8C, *C*1, 3, 7, 9, 13, 15, 19, 21], 145.16 [s, 8C, *C*4, 6, 10, 12, 16, 18, 22, 24]. -$^{19}F$ NMR: $\delta$ = −43.34* and −44.30* [2d, $^1J$(PF) = 1332 and 1338 Hz]. -$^{31}P$ NMR: $\delta$ = 111.38* and 112.54* [2t, $^1J$(PF) = 1336 and 1338 Hz]. −MS (70 eV): *m/z* (%): 1088 (84) [$M^+$], 1073 (100) [$M^+ - CH_3$], 1003 (16) [$M^+ - OPF_2$], 69 (90) [$PF_2^+$].

$C_{32}H_{24}F_{16}O_8P_8$ (1088.30): Satisfactory elemental analyses could not be obtained because the THF molecules in the cavity of **2** could not be removed.

*Compound* **6**. A solution of 0.53 g (0.36 mmol) of **5** and 0.6 g (2.88 mmol) of 2-chloro-1,3,5-trimethyl-1,3,5-triaza-2$\sigma^3\lambda^3$-phosphorin-4,6-dione in 20 mL of dichloromethane was stirred for 10 hours at room temperature. Subsequently, the solvent and volatile components were removed i.v. The residue was washed with 3 × 30 mL of diethyl ether. The organic phases were combined, and the solvent was removed i.v. The remaining colorless solid was dried i.v. Yield: 0.74 g (90%); m.p. 134°C (dec.).

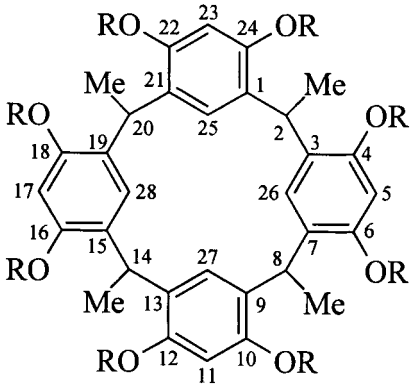



**FIGURE 5** Atom numbering in the calix [4] resorcinarene system.

*Two magnetically nonequivalent $PF_2$ groups.

$^1$H NMR ($-50$°C): $\delta$ = 1.33 [s, br, 12H, C$H_3$CH], 3.03†, 3.07†, 3.08†, and 3.11† [4d, $^3J$(PH) = 7.7, 7.3, 7.9, and 8.8 Hz, ($H_3$N)$_2$P], 3.20 [s, 24H, C$H_3$N(C(:O))$_2$], 3.84 [m, 32H, C$H_2$C$H_2$], 4.40 [s, br, 4H, CH$_3$C$H$], 5.30, 5.54, 6.33, and 7.61 [4s, 8H, C$_6H_2$]. $-^{13}$C NMR: $\delta$ = 19.62 [s, 4C, CHC$H_3$], 30.17 [s, 4C, C$H$CH$_3$], 30.72† and 33.35† [2d, $^2J$(PC) = 33.42 and 36.27 Hz, 8 × 2 C, ($H_3$N)$_2$P], 30.94 [s, 8C, C$H_3$N(C(:O))$_2$], 62.60 [s, 8C, C$H_2$CH$_2$OP], 68.54 [d, $^2J$(PC) = 25.37 Hz, 8C, C$H_2$OP], 95.17 [s, 4C, C5, 11, 17, 23], 122.13 [s, 4C, C25, 26, 27, 28], 126.78 [s, 8C, C1, 3, 7, 9, 13, 15, 19, 21], 155.04 [s, 8C, C4, 6, 10, 12, 16, 18, 22, 24], 160.70 [s, 16C, C(:O)]. $-^{31}$P NMR: $\delta$ = 92.87 [s, br]. −FAB-MS (70 eV): *m/z* (%): 2282 (100) [M$^+$], 2109 (50) [M$^+$ − MeN(C(:O)NMe)$_2$P], 2065 (10) [M$^+$ − MeN(C(:O)NMe)$_2$P − OCH$_2$CH$_2$], 1935 (25) [M$^+$ − 2 MeN(C(:O)NMe)$_2$P]. $C_{88}H_{128}N_{24}O_{32}P_8$ (2281.91) C, 45.15 (calcd 46.32); H, 5.64 (5.65); N, 14.50 (14.73)%.

*Compound* **7**. In a heavy-walled glass tube, fitted with a TEFLON stopcock, a solution of 1.0 g (0.68 mmol) of **5** in 20 mL of dichloromethane was cooled to −196°C. Chlorodifluorophosphine (0.7 g; 6.8 mmol) was condensed onto this solution. The reaction mixture was allowed to warm to room temperature and was stirred for 2 days. Subsequently, excess chlorodifluorophosphine and the solvent were removed i.v. The remaining colorless solid was washed with 5 mL of hexane and dried i.v. Yield: 0.73 g (75%); mp 142–144°C.

$^1$H NMR (CD$_2$Cl$_2$): $\delta$ = 1.41 [d, 12H, $^3J$(HH) = 7.11 Hz, C$H_3$CH], 4.18 [m, br, 32H, C$H_2$C$H_2$], 4.61 [q, 4H, $^3J$(HH) = 7.08 Hz, CH$_3$C$H$], 6.22 [m, 8H, C$_6H_2$]. $-^{13}$C NMR: $\delta$ = 19.20 [s, 4C, CHC$H_3$], 62.21 [s, 8C, F$_2$POCH$_2$C$H_2$], 68.50 [d, $^2J$(PC) = 47.40 Hz, 8C, F$_2$POC$H_2$], 97.35† and 101.96† [2s, 4C, C5, 11, 17, 23], 126.68† and 126.91† [2s, 4C, C25, 26, 27, 28], 130.32† and 130.47† [2s, 8C, C1, 3, 7, 9, 13, 15, 19, 21], 154.05 and 155.42 [s, 8C, C4, 6, 10, 12, 16, 18, 22, 24]. $-^{19}$F NMR: $\delta$ = −48.77† and −48.28† [2d, $^1J$(PF) = 1276.15 and 1295.59 Hz]. $-^{31}$P NMR ($-50$°C): $\delta$ = 112.02† and 112.29† [2t, $^1J$(PF) = 1270.49 and 1267.15 Hz]. −MS (70 eV): *m/z* (%): 1440 (100) [M$^+$], 1425 (40) [M$^+$ − Me], 1395 [M$^+$ − 3 Me], 1380 [M$^+$ − 4 Me]. $C_{48}H_{56}F_{16}O_{16}P_8$ (1440.73) C 40.08 (calcd. 40.02); H 3.88 (3.92)%.

†Two conformational isomers.

## *ACKNOWLEDGMENTS*

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