Pergamon

Tetrahedron Vol. 50, No. 39, pp. 11339-11362, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)00698-9

Synthesis of a Spheroidal Bis-porphyrin: a Ligand Designed to Accept Two Catalytic Metal Ions in an Isolated Environment

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ABSTRACT: A spheroidal bis-porphyrin (dual capped quadruply cofacial dimeric tetraphenylporphyrin, **1**), designed to be employed as a ligand for a class of catalysts that mimic the combined enzyme activities of superoxide dismutase and catalase, has been synthesized in 9 steps. C-Alkylation of 2-(2'-lithio-5'-*tert*-butyldimethylsiloxy-methyl)phenyl-1,3-dioxolane (**D**) with tetra-bromide **6**, prepared from bicyclo[2.2.2]oct-7-ene-2,3,5,6-tetracarboxylic dianhydride by 5 steps, afforded the key intermediate, tetra-alkylated compound **3a**, in 68% yield. An alternative route to **3**, O-alkylations of tetrol **4** with aliphatic halides **5**, was also tested. Conversion of the four protected hydroxy groups to bromo substituents is crucial in the preparation of porphyrin **2**. Therefore, tetra-benzyl bromide **24b** was prepared and then treated with pyrrole in the presence of boron trifluoride etherate, followed by DDQ oxidation to obtain the capped porphyrin **2**. The coupling of two molecules of **2** to form a spheroidal porphyrin **1** was carried out in dilute DMF solution, using 0.8 equivalent of 2-trimethylsilylethane sulfonamide ($H_2NSO_2CH_2CH_2Si(CH_3)_3$, SES-$NH_2$) and cesium carbonate. The structure of **1** was confirmed by ^1H NMR, UV/VIS, FABMS and laser desorption high resolution MS. The two isomers of **1**, eclipsed and gauche, formed due to two possible modes of approach of the units of **2**, were observed in approximately 1 : 1 ratio by both ^1H NMR and HPLC techniques.

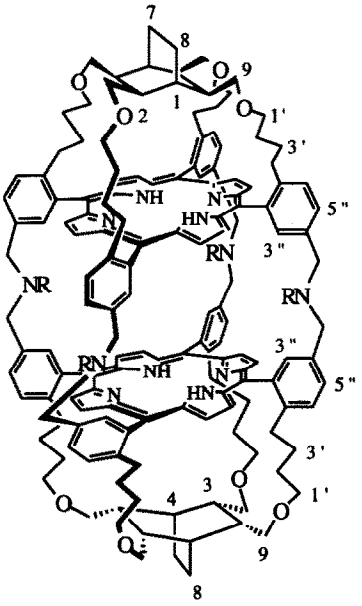
INTRODUCTION: Superoxide is a highly toxic chemical species which is generated in aerobic cells through many biological pathways[1] and contributes to the onset of atherosclerosis, cancer and aging by damaging critical biomolecules[2]. Oxygen reperfusion following a myocardial attack is accompanied by the generation of superoxide, and the resulting ischemic damage to the heart and brain is a major cause of death[2c]. The superoxide dismutase (SOD) enzymes which catalyze the dismutation of superoxide to oxygen and hydrogen peroxide (eq 1) are a defense against superoxide cell damage. The decomposition of the toxic hydrogen peroxide is then catalyzed by catalase (eq 2) or peroxidase. Attempts at combining the superoxide dismutase and catalase activities (eq 3) into a single synthetic molecule have not been reported[3]. Such a dual catalyst might be constructed from a synthetic ligand that consists of two closely spaced cofacial porphyrins whose

$$2\,O_2^{\cdot-} + 2\,H^+ \rightarrow O_2 + H_2O_2 \qquad (1)$$

$$2\,H_2O_2 \rightarrow O_2 + 2\,H_2O \qquad (2)$$

$$4\,O_2^{\cdot-} + 4\,H^+ \rightarrow 3\,O_2 + 2\,H_2O \qquad (3)$$

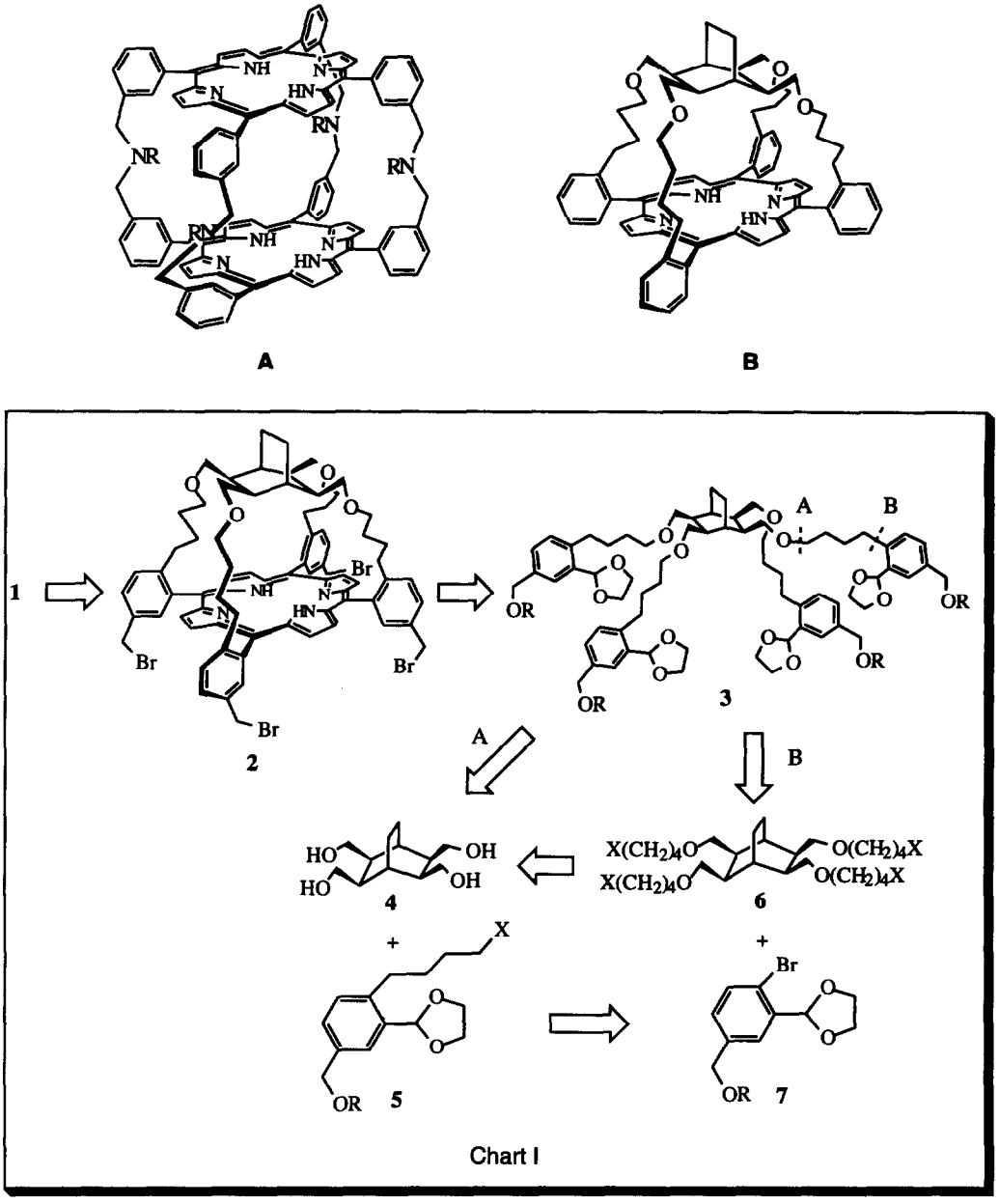
outer faces are protected from contact with molecules of the bio milieu. Since the reaction of $O_2^{\cdot-}$ with iron(III) porphyrins is diffusion controlled[4], the hydrogen peroxide product captured by the two metal species {under the reducing conditions obtained in the presence of $O_2^{\cdot-}$} would be reduced to water. We describe here the studies of synthesis of a spheroidal bis-porphyrin ligand (**1**, dual capped quadruply cofacial dimeric tetraphenylporphyrin) designed to be used in the preparation of model catalysts.



1 R = $SO_2CH_2CH_2Si(CH_3)_3$

Our designed putative catalyst will be obtained from **1** by insertion of metals and exchange of -$SO_2CH_2CH_2Si(CH_3)_3$ blocking groups for water solubilizing substitutes. Studies are in progress to this end.

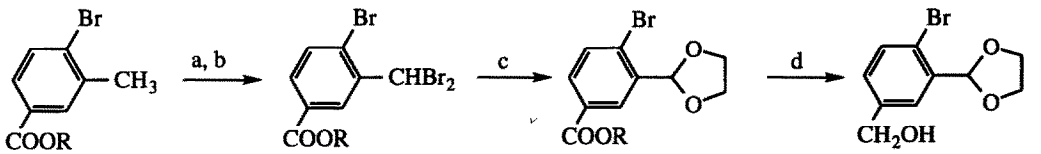
RESULTS AND DISCUSSION: Our strategy for synthesizing **1** is an integrated approach based on our synthesis of quadruply bridged dimeric porphyrins (**A**)[5] and bicyclo-capped porphyrins (**B**)[6]. Retrosynthetic analysis (Chart I) reveals that the spheroidal porphyrin **1** can be synthesized from two molecules of capped porphyrin **2** with four benzyl bromide groups[5]. The important precursor **2**, in turn, can be synthesized from the corresponding tetra-acetal **3**[6]. There are two convenient ways to synthesize this key intermediate **3**: Disconnection A will give precursors of bicyclo[2.2.2]octane cap **4** and an aliphalic halide **5**. This strategy has been used successfully in the capped porphyrin study[6]. Disconnection B, which is a convergent synthesis, will lead to precursors of a substituted bicyclo[2.2.2]octane cap **6** and a simpler aromatic bromide **7**. Both routines then give the same intermediates **7** and **4**.



Synthesis of alcohol 14 (Scheme I): Starting from 3-methyl-4-bromobenzoic acid (**8**), ethyl 3-methyl-4-bromobenzoate (**9**) was obtained in 85% yield by esterification of **8** with ethanol and sulfuric acid. Benzylic dibromination of **9** with NBS (2.2 equivalents) in carbon tetrachloride,

monitored by TLC, gave two *gem*-dibromo products: one is the desired compound ethyl 3-dibromomethyl-4-bromobenzoate (**10**, 85% after column chromatography) and the other is over-brominated 1-bromoethyl 3-dibromomethyl-4-bromobenzoate (**11**, in 15% yield).

It is well known that a *gem*-dihalide (as **10** or **11**) can be hydrolyzed to an aldehyde in either aqueous acidic or basic conditions. However, to our knowledge, no method has been reported for conversion of a *gem*-dihalide to a cyclic acetal, although there are a few examples of conversion of *gem*-dihalides to dimethyl acetals[7]. Therefore, we anticipated that the dibromomethyl group in either **10** and **11** could be converted into a cyclic acetal by reaction with ethylene glycol in the presence of base without the intermediate formation of the corresponding aldehyde. When a mixture of **10** and **11** (85 : 15) was treated with a slight excess of powdered calcium carbonate in anhydrous ethylene glycol at 160 °C for 15 h, two desired acetal compounds were obtained in 77% total yield after column chromatography: 2-[(2'-bromo-5'-ethoxycarbonyl)phenyl]-1,3-dioxolane (**12**, 48% yield) and 2-{[2'-bromo-5'-(2"-hydroxyethoxy)carbonyl]phenyl}-1,3-dioxolane (**13**, 29% yield). Hydroxyethyl ester **13** was formed partly by transesterification of **12** and partly by attacking of 1-bromoethyl ester in **11** with ethylene glycol. The corresponding 2-(2'-bromo-5'-hydroxymethyl)-phenyl-1,3-dioxolane (**14**) was afforded in 90% yield from either **12** or **13** through a standard reduction procedure with lithium aluminum hydride.



8 R = H
9 R = Et

10, R = CH_2CH_3, 85%
11, R = $CHBrCH_3$, 15%

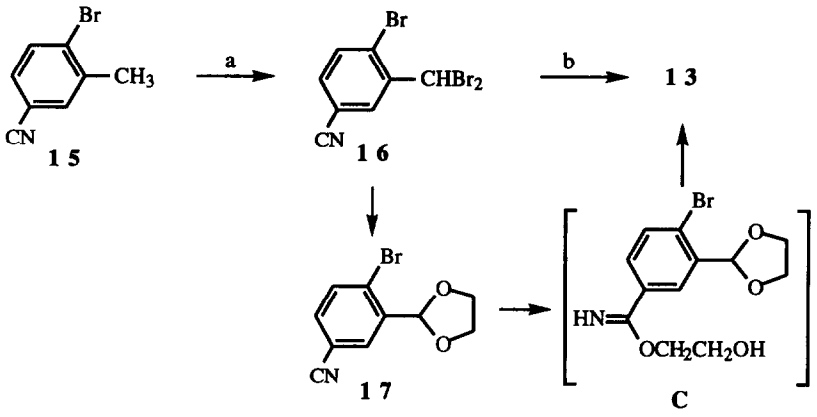
12, R = CH_2CH_3, 48%
13, R = CH_2CH_2OH, 29%

14

Conditions: a. EtOH, H_2SO_4, toluene, 85%; b. NBS, hυ, CCl_4, 100%; c. $CaCO_3$, ethylene glycol, 160 °C, 77%; d. $LiAlH_4$, THF, 90%.

Scheme I

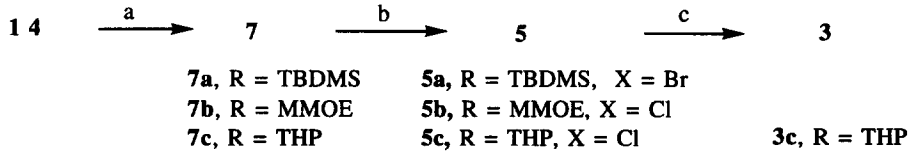
By an alternative procedure (Scheme II), compound **13** was obtained in 70% yield from 3-methyl-4-bromobenzonitrile (**15**) by benzylic dibromination with NBS (2.2 equivalents, quantitatively) and ethylene glycol alcoholysis of the dibromide at slightly higher temperature (165 °C). Here, the cyano group of 3-dibromomethyl-4-bromobenzonitrile (**16**) was also attacked by ethylene glycol via an isolable 2-(2'-bromo-5-cyanophenyl)-1,3-dioxolane (**17**)[8] and a possible intermediate **C**: when **17** was formed after the substitution of *gem*-dibromide by ethylene glycol, the cyano group was subsequently attacked by ethylene glycol to form an imino intermediate **C**, which then converted into **13** by hydrolysis with adventitious water.



Conditions: a. NBS, *hv*, CCl_4, 100%; b. $CaCO_3$, ethylene glycol, 165 °C, 70%.

Scheme II

Routine A: Preparation of 5a-c and attempts to prepare 3a-c. Alcohol **14** must be protected prior to alkylation. The protective group should be stable under conditions of C-alkylation and, later, O-alkylation. To meet this requirement, three different protective groups were studied: *tert*-butyldimethylsilyl (TBDMS), 1-methyl-1-methoxylethyl (MMOE) and tetrahydropyranyl (THP)[9]. Compounds 2-(2'-bromo-5'-*tert*-butyldimethylsiloxymethyl)phenyl-1,3-dioxolane (**7a**), 2-[2'-bromo-5'-(1"-methyl-1"-methoxyethoxy)methyl]phenyl-1,3-dioxolane (**7b**) and 2-[2'-bromo-5'-(2"-tetrahydro-2H-pyranyloxy)methyl]phenyl-1,3-dioxolane (**7c**) were prepared by a standard procedure[9] in 90 - 100% yields (Scheme III).



Conditions: a. i) TBDMS-Cl, EtN^iPr_2, DMAP, CH_2Cl_2, 100%; or ii) 2-methoxypropene, TsOH·Py, CH_2Cl_2, 90%; or iii) Dihydropyrane, TsOH·Py, CH_2Cl_2, 95%. b. i) Mg, MeI, THF, reflux; $Br(CH_2)_4Br$, CuBr, HMPA, THF, reflux; or ii) ^{t}BuLi, THF, -78 °C; $I(CH_2)_4Cl$, THF, -20 °C. c. i) **4**, NaH, HMPA, 50 °C; or ii) **4**, K, HMPA, 50 °C; or iii) **4**, KH, KI, HMPA, 50 °C.

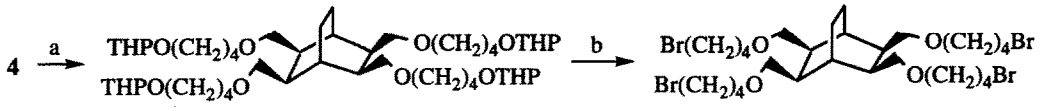
Scheme III

The preparative methods for the aliphalic halides **5a**, **5b** and **5c** were as follows: when TBDMS was used, the bromide **7a** was converted into 2-[2'-(4"-bromobutyl)-5'-*tert*-butyldimethylsiloxymethyl]phenyl-1,3-dioxolane (**5a**) in 80% yield by reacting **7a** with magnesium turnings, activated by methyl iodide[10], and then coupling with 1,4-dibromobutane in the presence of cupric bromide[6,11] in HMPA/THF under reflux. When MMOE and THP were used, **7b** and **7c** were

changed into the corresponding 2-[2'-(4"-chlorobutyl)-5'-(1"-methyl-1"-methoxyethoxy)-methyl]phenyl-1,3-dioxolane (**5b**) (80% yield) and 2-[2'-(4"-bromobutyl)-5'-(2"-tetrahydro-2H-pyranyloxy)methyl]-phenyl-1,3-dioxolane (**5c**) (80% yield) by adding *tert*-butyl lithium [Caution!] at -78 °C in THF and then condensed[12] with 1-iodo-4-chlorobutane at -20 °C.

Turning to the capping unit, 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrahydroxymethylbicyclo[2.2.2]octane (**4**)[6,13] was prepared from bicyclo[2.2.2]oct-7-ene-2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*--tetracarboxylic dianhydride via three steps[6]. O-alkylations of halides **5a-c** with **4** were attempted using strong bases (sodium hydride, potassium hydride [Caution!] or potassium metal [Caution!]) in dry polar aprotic solvents (DMF, DMSO or HMPA). However, the attempted alkylations were not successful. Only 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-(2"'-tetrahydro-2H-pyranyloxy)-methyl)phenyl]butoxymethyl)bicyclo[2.2.2]octane (**3c**) was obtained in poor yield (5%) on alkylation of **4** by **5c** in the presence of potassium hydride and potassium iodide in HMPA at 50 °C.

Routine B: Preparation of 6 and 3a (Scheme IV). The alternative disconnection, B in Chart I, was then studied. O-Alkylation of **4** with 4-(2'-tetrahydro-2H-pyranyloxy)butyl chloride[14] in the presence of sodium hydride and potassium iodide in HMPA at 55-60 °C provided 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*--tetrakis[4'-[2"-tetrahydro-2H-pyranyloxy)butoxy]methylbicyclo[2.2.2]-octane (**18**) in 20-60% yield. The yield depends upon the scale of the reaction, precise temperature control and the addition rate of the alkyl chloride. The best condition for this reaction is the addition of a HMPA solution of alkyl chloride at a rate of 0.5 mL/h into a suspension of 50% sodium hydride, **4** (1 g) and potassium iodide in dry HMPA at 60 °C (See experimental section for details). Attempts to alkylate **4** under other conditions (different bases with alkyl chloride or bromide[15] in different solvents and at different temperatures) gave poorer yields of **18**. The four THP groups in **18** were easily converted to bromide to give 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*--tetrakis(4'-bromobutoxy)methylbicyclo[2.2.2]octane (**6**) in 81% yield by treatment of **18** with bromotriphenylphosphonium bromide in methylene chloride[16].



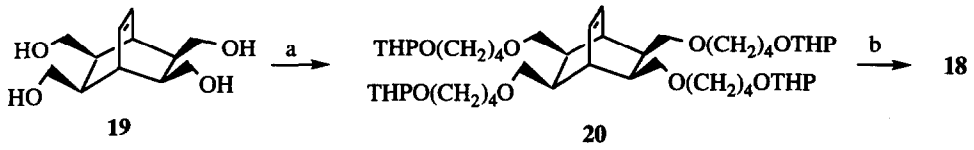
18 **6**, X = Br

Conditions: a. $Cl(CH_2)_4OTHP$, NaH, KI, HMPA, 60 °C, 60%; b. Br_2Ph_3P, CH_2Cl_2, 81%.

Scheme IV

Because O-alkylation of **4** is not easily reproduced, we have successfully developed another way (Scheme V) to make **18**: when 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrahydroxymethylbicylo[2.2.2]oct-7-ene (**19**)[17] was alkylated with 4-(2'-tetrahydro-2H-pyranyloxy)butyl chloride under conditions similar to those used with **4**, there was obtained 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis[4'-[2"-tetrahydro-2H-pyranyloxy)butoxy]methylbicyclo[2.2.2]oct-7-ene (**20**) in a reproducible 80% yield. Compared with

saturated tetrol **4**, **19** is much easier to alkylate, presumably due to less steric interactions of the ether moieties with unsaturated C7 and C8 bridge. This observation is in agreement with like observations in our synthesis of bicyclo-capped porphyrins[6]. Catalytic hydrogenation of **20** to form **18** was very slow under the normal catalytic hydrogenation conditions (Pd/C, 1 - 4 atm of hydrogen, 0 - 80 °C, ethyl acetate). In contrast, palladium catalyzed hydrogen transfer reduction[18] of **20** in methanol, using ammonium formate as a hydrogen donor, was found to be facile.

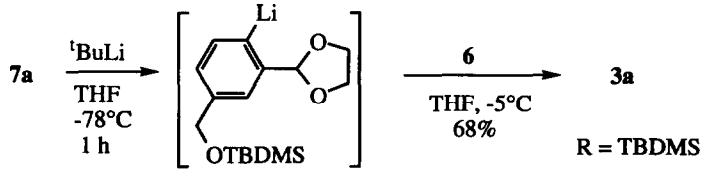


19 **20**

Conditions: a. $Cl(CH_2)_4OTHP$, NaH, KI, HMPA, 60 °C, 80%; b. Pd/C, $HCOONH_4$, MeOH, 95%

Scheme V

The aryl bromide **7a** was then treated with *t*-butyl lithium [Caution!] in THF at -78 °C to form a lithio compound **D**, followed by coupling with tetra-bromide **6** in THF at -5 °C for 1 h. The desired compound of 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-(*t*butyldimethylsiloxymethyl)phenyl]butoxymethyl}bicyclo[2.2.2]octane (**3a**) was obtained in 68% yield (Scheme VI). The identity of **3a** was established by C_{2v} symmetry in its ^1H and ^{13}C NMR and the molecular ion peak in its high resolution FAB mass spectroscopy (Calcd. for $C_{92}H_{150}O_{16}Si_4$: 1623.0001; found: 1622.9951).



D

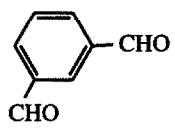
Scheme VI

Model studies on the formation of *meta*-substituted tetraphenylporphyrin (23). The conversion of **3** → **2** (Chart I) involves the formation of a porphyrin ring and the change of the blocked hydroxy groups to bromo substituents. The following experiments were carried out to determine the best order for their conversions.

First, the *meta*-hydroxymethyl benzaldehyde acetal **22a**[19] was prepared in 42% yield from isophthalic dicarboaldehyde (**21**) via two steps (mono-acetalization with 1.0 equivalent of ethylene glycol and pyridinium tosylate in hot benzene followed by sodium borohydride reduction in methanol). Protection of alcohol **22a** with either TBDMS and THP gave compounds **22b-c** in more than

95% yields. Attempts to prepare *meta*-substituted tetraphenylporphyrins **23a-c** (R = OH, OTBDMS or OTHP) by mixing **22a-c**, pyrrole and boron trifluoride etherate in chloroform followed by DDQ (2,3-dicyano-5,6-dichloroquinone) oxidation failed. This is because boron trifluoride etherate cleaves TBDMS or THP to give a corresponding hydroxy group and then coordinates with this hydroxy to form precipitates which prevent further reaction.

Since compounds with a hydroxy group or an acid sensitive protected hydroxy group cannot be used in the synthesis of porphyrin, one must convert the hydroxy group to some Lewis acid resistant moiety. We have found in our synthesis of quadruply bridged dimeric porphyrins (**I**)[5] that the benzylic bromide is stable to $BF_3{\cdot}Et_2O$. Therefore, bromide **22d**[19] was prepared in 90% yield from **22a** by using bromotriphenylphosphonium bromide and 2,6-lutidine[20] in methylene chloride. 5,10,15,20-Tetrakis(3-bromomethyl)phenylporphyrin[21] (**23d**, R = Br) was then formed from **22d** in 35% yield by reaction with pyrrole in the presence of boron trifluoride etherate in chloroform followed by DDQ oxidation.



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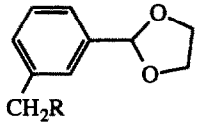
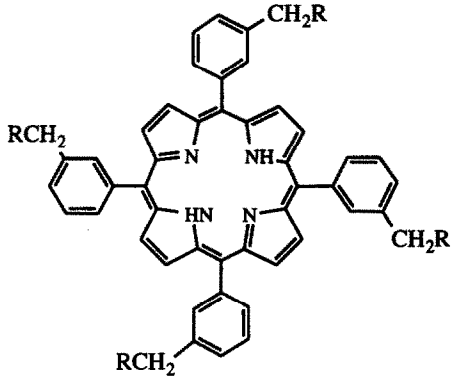


22a, R = OH
22b, R = OTBDMS
22c, R = OTHP
22d, R = Br

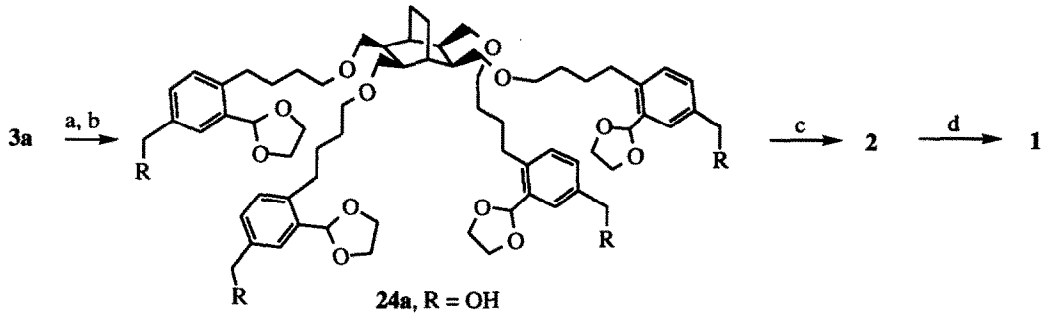


23d, R = Br

Synthesis of the quadruply cofacial dimeric tetraphenylporphyrin A (R = SES), a model study. We have synthesized an SES [$SO_2CH_2CH_2Si$-$(CH_3)_3$] dimeric porphyrin **A** (R = SES) as a model test. Tetrabromide porphyrin **23d** was treated with SES-NH_2[22,23] and cesium carbonate in diluted DMF solution at 50 °C to give tetrakis{*m,m*-[(methylene(2'-trimethylsilylethanesulfonyl)imino)methylene]}-*strati*-bis(5,10,15,20-tetraphenylporphyrin) (**A**, R = SES) in 10% yield.

Synthesis of spheroidal porphyrin 1. Treatment of **3a** with tetra^{n}butylammonium fluoride in THF at room temperature afforded 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-hydroxymethylphenyl]butoxymethyl}bicyclo[2.2.2]octane (**24a**) in 63% yield. The latter was subjected to bromination with bromotriphenylphosphonium bromide in the presence of 2,6-lutidine[20,24] in dichloromethane, 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-bromomethylphenyl]butoxymethyl}bicyclo[2.2.2]octane (**24b**) was afforded in 71% yield. Following a standard procedure[6] (pyrrole, boron trifluoride etherate, chloroform then DDQ oxidation) of porphyrin formation from a tetra-acetal moiety, the desired tetra-benzylbromide capped por-

phyrin **2** (Chart I) was obtained in 9.3% yield (Scheme VI). The coupling of two molecules of **2** with SES-NH_2 was carried out as in the synthesis of **A** (R = SES), by addition over 10 h of a DMF solution of **2** (20% excess) via a syringe pump into a suspension of SES-NH_2 and cesium carbonate in DMF at 60 °C. The desired spheroidal porphyrin **1** was obtained in 10% yield after purifications by column chromatography and preparative TLC. Normal HPLC shows only one peak on a silica gel column and using isopropanol/chloroform as a mobile phase.



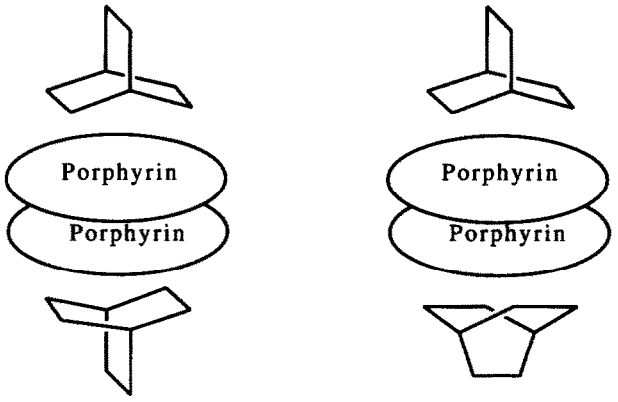
Conditions: a. ^{n}Bu_4NF, THF, 63%; b. $BrPh_3PBr$, 2,6-lutidine, CH_2Cl_2, 71%; c. i) Pyrrole, BF_3·Et_2O, $CHCl_3$, ii) DDQ, reflux, 9.3%; d. SES-NH_2, Cs_2CO_3, DMF, 60 °C, 10%.

Scheme VII

The UV/Vis spectrum of **1**, when compared to that of **2**, shows a broadened 5 nm blue-shifted Soret band at 417 nm and α,β-bands that are slightly red shifted. These shifts are characteristic of cofacial dimeric porphyrins[5]. The N-H protons in the ^{1}H NMR of **1** appear at -3.50 ppm, shifted upfield by 1.0 ppm from **2**. The 2-H protons and the 1-H protons in the bicyclo[2.2.2]octane caps appear at -2.9 ppm and -0.5 ppm, upfield shifted by 0.5 and 0.2 ppm, respectively, compared with **2**. These observations strongly support the structure having two porphyrin planes in close cofacial proximity. The porphyrin plane distal to the cap acts synergistically with the proximal porphyrin ring and the 2-H and 1-H in both caps are therefore shifted further upfield than the same protons in **B**[6] and **2**. FAB mass spectroscopy confirmed that the compound obtained has a molecular weight of 2944.1±0.3[25] which agrees with the formula of **1** (Calcd. for $C_{172}H_{212}N_{12}O_{16}S_4Si_4$: 2944.1). High resolution MS of **1**, using the matrix-assisted laser desorption/ionization (MALDI) method[26,27], gave the lowest isotopic peak at 2942.4172 [calcd. for $C_{172}H_{213}N_{12}O_{16}S_4Si_4$ (M + H): 2942.4177].

In the described synthesis there are two possible modes of approach of the two units of **2** to form isomers of **1** in which the capping units are either eclipsed or gauche (Chart II). Indeed, two isomers are observed by ^{1}H NMR, since there are two peaks of both 2-H and 1-H in 1 : 1 ratios. The slight difference in the magnetic environment of eclipsed and gauche isomers makes the 2-H and 1-H protons of the two isomers different. The isomers are separable by HPLC, eluted with 1.5% pyridine in toluene, and appear to be approximately 1 : 1 integration of peaks. The UV/Vis spectra of

those two peaks are identical[28] which indicates that both compounds are electronically similar. In other words, they both have dimeric bis-porphyrin structures.



eclipsed gauche

Chart II

EXPERIMENTAL: Melting points were obtained on a Baistolscope and are uncorrected. R_f values were obtained on E. M. Sciences 0.25 mm thick precoated glass-backed silica gel 60 F_{254} plates. NMR experiments were recorded on a General Electric GN-500 spectrometer or a Varian Gemini-200 spectrometer at 25 °C in $CDCl_3$. Chemical shifts were reported relative to the signal of $CHCl_3$ (^1H, 7.240 ppm, and ^{13}C, 77.000 ppm). IR spectra were recorded on a Perkin-Elmer 1330 spectrophotometer and FT-IR were on a Galaxy 2020 with MacFirst software. Mass Spectra were obtained by electron impact (EI) and fast atom bombardment (FAB) mass spectroscopy using *m*-nitrobenzyl alcohol as the matrix and a parallel run of cesium rubidium iodide for the reference. Exact mass spectra were obtained using PFK as a reference compound. High resolution MS were obtained from the Mass Spectrometry Laboratory of the University of California, Los Angeles. High resolution fast atom bombardment mass spectroscopy (HR FABMS) was performed by the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln. High resolution MS (MALDI) of **1** was performed at the University of California, Riverside. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee. HPLC was performed with a Hewlett Parkard 1050 pump and 1040 detector, Rheodyne injector along with HP HPLC^{3D} ChemStation software. UV/Vis spectra were obtained on an OLIS Cary-14 Spectrophotometer at 25 °C in chloroform. Column chromatography was performed with Fischer type 60A (200-425 mesh) silica gel. Preparative TLC was performed with E. M. Sciences Kieselgel 60 F_{254} glass-back plates. All reactions were carried out with purified reagents in dry, purified solvents[29] under an atmosphere of argon, unless noted otherwise, and followed by standard work up procedures[30].

Ethyl 3-methyl-4-bromobenzoate (9) A mixture of 3-methyl-4-bromobenzoic acid (**8**, 50 g, 0.232 mol., from Lancaster), ethanol (700 mL), toluene (700 mL) and sulfuric acid (5 mL) was heated under reflux for 1h. The solvents were removed by distillation. Additional solvents (ethanol 700 mL, and toluene 700 mL) were added and the process was repeated. The residue was dissolved in dichloromethane (500 mL) and washed with water (2 x 50 mL) and brine (50 mL). Standard work up and vacuum distillation of the crude product gave pure compound **9** (45 g, 80%). B.p. 76 - 78 °C/0.05 mm Hg. R_f = 0.55 (10% ethyl acetate/hexanes). ^{1}H NMR (500 MHz): δ 1.731 (t, 3H, J = 7.0 Hz, CH_3 in ester), 2.426 (s, 3H, 3-CH_3), 4.351 (q, 2H, J = 7.0 Hz, CH_2 in ester), 7.574 (d, 1H, J = 8.0 Hz, 5-H), 7.679 (dd, 1H, J = 8.0 and 2.0 Hz, 6-H), 7.878 (d, 1 H, J = 2.0 Hz, 2-H) ppm. ^{13}C NMR (50 MHz)[31a]: δ 13.99 (CH_3 in ester), 22.47 (3-CH_3), 60.73 (CH_2 in ester), 127.88 (6-C), 129.19 (4-C), 129.87 (1-C), 131.24 (2-C), 132.02 (5-C), 137.70 (3-C), 165.47 (carbonyl) ppm. IR: 2910, 1725, 1600, 1300, 1255, 1200, 1105, 1035, 760 cm^{-1}. MS: *m/z* 244 and 242 (M^+, 30%), 216 and 214 [(M-CH_2CH_2)$^+$, 35], 199 and 197 [(M-OCH_2CH_2)$^+$, 100]. Exact mass: 241.9935 (calcd. for $C_{10}H_{11}{}^{79}BrO_2$: 241.9943).

Ethyl 3-dibromomethyl-4-bromobenzoate (10) and **1'-Bromoethyl 3-dibromomethyl-4-bromobenzoate (11)** A mixture of **9** (6.00 g, 24.68 mmol) and N-bromosuccinimide (11.0 g, 61.8 mmol) in carbon tetrachloride (270 mL) was heated under reflux while exposed to irradiation with a 200 W lamp for 3 h. TLC indicated that starting material had been consumed and no monobromination product remained (TLC was developed three times in carbon tetrachloride). Succinimide was removed by filtration with silica gel (22 g) and the solid was washed with carbon tetrachloride (75 mL). After concentration of the filtrates there was obtained a quantitative yield of a mixture of **10** and **11** (85 : 15 from ^{1}H NMR) which was used in the next step without purification. Analytical samples were afforded by column chromatography on silica gel, eluted by toluene/hexanes (2 : 3), followed by recrystallization (hexanes and ether): **10** (8.33 g, 84%): R_f = 0.29 (carbon tetrachloride). M.p.: 56.5 - 58.0 °C. ^{1}H NMR (500 MHz): δ 1.392 (t, 3H, J = 7.0 Hz, CH_3), 4.386 (q, 2H, J = 7.0 Hz, OCH_2), 7.038 (s, 1H, Ar$CHBr_2$), 7.546 (d, 1H, J = 8.5 Hz, 5-H), 7.782 (dd, 1H, J = 8.5 and 2.0 Hz, 6-H), 8.627 (d, 1 H, J = 2.0 Hz, 2-H) ppm. ^{13}C NMR (50 MHz)[31a]: δ 14.26 (CH_3), 38.76 ($CHBr_2$), 61.60 (OCH_2), 124.65 (4-C), 131.06 (1-C), 131.53 (6-C), 132.05 (2-C), 132.81 (5-C), 140.68 (3-C), 164.95 (carbonyl) ppm. IR: 2980, 1725, 1596, 1465, 1400, 1370, 1300, 1260, 1210, 1180, 1150, 1110, 1020, 840, 760, 730 cm^{-1}. MS: *m/z* 357, 355 [(M-EtO)$^+$, 6%], 321 [(M-Br)$^+$, 100]. $C_{10}H_9Br_3O_2$: Calcd. C 29.96, H 2.26, Found C 29.84, H 2.24.

11 (2.1 g, 16%): R_f = 0.37 (carbon tetrachloride). M.p.: 66 - 68 °C. ^{1}H NMR (500 MHz): δ 2.144 (d, 3H, J = 6.0 Hz, CH_3), 6.937 (q, 1H, J = 6.0 Hz, OCHBr), 7.047 (s, 1H, Ar$CHBr_2$), 7.616 (d, 1H, J = 8.5 Hz, 5-H), 7.819 (dd, 1H, J = 8.5 and 2.0 Hz, 6-H), 8.654 (d, 1 H, J = 2.0 Hz, 2-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 26.78 (CH_3), 38.41 ($CHBr_2$), 72.21 (OCHBr), 125.94 (4-C), 129.37 (1-C), 131.73 (6-C), 132.46 (2-C), 133.17 (5-C), 141.12 (3-C), 162.54 (carbonyl) ppm. IR: 3000, 1745, 1596, 1465 cm^{-1}. MS: *m/z* 396.8 [(M-Br)$^+$, 7%], 352.8 [(M-OCHBrCH_3)$^+$, 36], 273.8 [(M-Br-OCHBr-CH_3)$^+$, 21]. $C_{10}H_8Br_4O_2$: Calcd. C 25.03, H 1.68; Found C 25.08, H 1.75.

2-[(2'-Bromo-5'-ethoxycarbonyl)phenyl]-1,3-dioxolane (12) and **2-{[2'-bromo-5'-(2"-hydroxyethoxy)carbonyl]phenyl}-1,3-dioxolane (13)** A mixture of **10** and **11** (27.3 g at a ratio 85 : 15, 66.3 mmol) and calcium carbonate powder (7.5 g, 75 mmol) in anhydrous ethylene glycol (120 mL) was heated under argon at 160 °C for 3 h. After cooling, the glycol was removed via vacuum distillation and the residue was subjected to standard work up. Column chromatography on silica gel (25% ethyl acetate in hexanes to 50% ethyl acetate in hexanes) gave **12** (9.6 g, 48%) as a oil and **13** (6.1 g, 29%) as solid. **12**: R_f = 0.51 (25% ethyl acetate in hexane). ^{1}H NMR (500 MHz): δ 1.371 (t, 3H, J = 7.5 Hz, CH_3), 4.05 - 4.20 (m, 4H, 4-H and 5-H), 4.359 (q, 2H, J = 7.5 Hz, OCH_2), 6.089 (s, 1H, 2-H), 7.622 (d, 1H, J = 8.5 Hz, 3'-H), 7.856 (dd, 1H, J = 8.5 and 2.5 Hz, 4'-H), 8.213 (d, 1 H, J = 2.5 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 13.96 (CH_3), 60.91 (ester), 65.19 (4-C and 5-C), 101.77 (2-C), 127.78 (2'-C), 128.61 (6'-C), 129.55 (5'-C), 130.94 (4'-C), 132.83 (3'-C), 136.89 (1'-C), 165.19 (carbonyl) ppm. FT-IR: 1720 cm^{-1}. MS: *m/z* 301, 299 [(M-H)$^+$, 18%], 273, 271 [(M-Et)$^+$, 4], 257, 255 [(M-OEt), 15], 229, 227 [(M-COOEt), 9], 73 (dioxolanyl, 100%). Exact mass: 298.9924 [calcd. for $C_{12}H_{12}{}^{79}BrO_4$ (M-H): 298.9919].

13: M.p.: 83 - 84 °C. R_f = 0.24 (25% ethyl acetate in hexane). ^{1}H NMR (300 MHz on NT-300): δ 2.531 (br, 1H, OH), 3.889 (t, 2H, J = 4.5 Hz, 2"-H), 4.00 - 4.20 (m, 4H, 4-H and 5-H), 4.401 (t, 2H, J = 4.5 Hz, 1"-H), 6.038 (s, 1H, 2-H), 7.592 (d, 1H, J = 8.4 Hz, 3'-H), 7.827 (dd, 1H, J = 8.4, ~ 2 Hz, 4'-H), 8.185 (d, 1H, J = ~ 2 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 60.74 (2"-C), 65.36 (4-C and 5-C), 66.70 (1"-C), 101.87 (2-C), 128.37 (2'-C), 128.85 (6'-C), 129.08 (5'-C), 131.26 (4'-C), 133.13 (3'-C), 136.98 (1'-C), 165.80 (carbonyl) ppm. FT-IR: 3427 - 3332, 2954, 2885, 1712, 1600, 1284 cm^{-1}. MS: *m/z* 317, 315 [(M-H)$^+$, 18%], 273, 271 [(M-CH_2CH_2OH)$^+$, 10], 257, 255 [(M-OCH_2-CH_2OH), 15], 229, 227 [(M-$COOCH_2CH_2OH$), 14], 73 (dioxolanyl, 100%). $C_{12}H_{13}BrO_5$: Calcd. C 45.45, H 4.13, Found C 45.62, H 4.31.

2-(2'-Bromo-5'-hydroxymethyl)phenyl-1,3-dioxolane (14). From **12**: To a solution of **12** (10.6 g, 35.2 mmol) in dry THF (150 mL) was added a solution of lithium aluminum hydride (26.4 mL of 1.0 M in THF, 26.4 mmol) under argon at 0 °C. The reaction was stirred at 0 °C for 30 min. Ethanol (10 mL) was added and a saturated aqueous solution of potassium sodium tartrate (20 mL) was added at 0 °C and the mixture was stirred at room temperature for 1 h. The mixture was filtered through silica gel (30 g) and washed with ethyl acetate (125 mL x 4). The filtrates were combined and concentrated. After column chromatography on silica gel, the pure product **14** was obtained (7.86 g, 86.2%) as an oil: R_f = 0.36 (50% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 1.98 (br, 1H, OH), 4.00 - 4.20 (m, 4H, 4-H and 5-H), 4.616 (s, 2H, $ArCH_2O$), 6.053 (s, 1H, 2-H), 7.197 (dd, 1H, J = 8.0 and 1.0 Hz, 4'-H), 7.512 (d, 1H, J = 8.0 Hz, 3'-H), 7.556 (d, 1 H, J = 1.0 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 63.54 ($ArCH_2O$), 65.11 (4-C and 5-C), 102.12 (2-C), 121.15 (2'-C), 125.76 (6'-C), 128.70 (4'-C), 132.61 (3'-C), 135.84 (5'-C), 140.40 (1'-C) ppm. IR: 3400, 2890, 1600, 1465, 1395 cm^{-1}. MS: *m/z* 260, 258 [M$^+$, 11%], 259, 257 [(M-1)$^+$, 21], 229, 227 [(M-CH_2OH)$^+$, 20], 179 [(M-Br)$^+$, 19], 73 [(dioxolanyl, 100]. HRMS: 258.9812 (calcd. for $C_{10}H_{10}{}^{81}BrO_3$: 258.9793).

From **13**: Similar conditions were used with **13** (14.5 g, 45.8 mmol), lithium aluminum hydride (50.0 mL of 1.0 M in THF, 50.0 mmol) to give 10.7 g product (90% yield) with identical spectra.

3-Dibromomethyl-4-bromobenzonitrile (16) A mixture of 3-methyl-4-bromobenzonitrile (**15**, 5.00 g, 25.5 mmol) and N-bromosuccinimide (10.4 g) in carbon tetrachloride (160 mL) was heated under reflux while exposed to irradiation with a 200 W lamp for 3 h. TLC indicated that no starting material nor monobromination product remained (the TLC was developed three times in carbon tetrachloride). The succinimide was removed by filtration with silica gel (22 g) and the solid was washed with carbon tetrachloride (75 mL). After concentration, **16** was obtained quantitatively (9.03 g) and used in the next step without purification. Analytical samples were afforded as needles by recrystallization (hexanes and ether): R_f = 0.49 (10% ethyl acetate in hexanes). M.P.: 75.5 - 76.5 °C. ^{1}H NMR (500 MHz): δ 6.980 (s, 1H, $ArCHBr_2$), 7.420 (dd, 1H, J = 8.0 and 2.0 Hz, 6-H), 7.637 (d, 1H, J = 8.0 Hz, 5-H), 8.284 (d, 1 H, J = 2.0 Hz, 2-H) ppm. ^{13}C NMR (50 MHz): δ 37.35 ($CHBr_2$), 117.12 (CN), 112.90, 124.91, 133.45, 133.77, 134.65, 142.02 (phenyl carbons) ppm. IR (KBr): 3000, 2230, 1592, 1456, 1396, 1290, 1154, 1025, 896, 820, 736, 718, 680 cm^{-1}. MS: *m/z* 357 (15%), 355 (45%), 353 (46%), 351 (16%) (M^+), 273 [$(M-Br)^+$, 100]. $C_8H_4Br_3N$: Calcd. C 27.16, H 1.14, N 3.96, Br 67.75, Found C 26.62, H 1.10, N 3.93, Br 67.49.

2-(2'-Bromo-5'-*t*-butyldimethylsiloxymethyl)phenyl-1,3-dioxolane (7a) To a solution of **14** (6.30 g, 24.3 mmol), catalytic amount of DMAP (0.4 g) and N-ethyl-diisopropylamine (8.5 mL, 48.6 mmol) in dry methylene chloride (80 mL) was added a solution of ^{t}butyldimethylsilyl chloride (5.50 g, 36.5 mmol) in methylene chloride (20 mL) via a cannula at 0 °C. The mixture was allowed to warm to room temperature slowly during 1 h and stirred for an additional 1 h. Hexanes (120 mL) were added followed by the standard work up. After column chromatography on silica gel, pure **7a** was obtained (9.08 g, 100%) as an oil: R_f = 0.50 (10% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 0.067 (s, 6H, 2 x $SiMe_2$), 0.916 (s, 9H, t-Bu), 4.03 - 4.15 (m, 4H, 4-H and 5-H), 4.680 (s, 2H, $ArCH_2O$), 6.081 (s, 1H, 2-H), 7.194 (dd, 1H, J = 8.5 and 2.0 Hz, 4'-H), 7.497 (d, 1H, J = 8.5 Hz, 3'-H), 7.514 (d, 1 H, J = 2.0 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31a]: δ -5.38 (Si-Me) 18.23 (quaternary C in t-Bu), 25.79 (Me in ^{t}Bu), 64.04 ($ArCH_2O$), 65.34 (4-C and 5-C), 102.48 (2-C), 120.79 (2'-C), 125.20 (6'-C), 128.01 (4'-C), 132.64 (3'-C), 136.18 (5'-C), 140.94 (1'-C) ppm. IR: 2850 - 2950, 1460, 1390, 1360, 1250, 1190 cm^{-1}. MS: *m/z* 373,371 [$(M-1)^+$, 2%], 359, 357 [$(M-Me-1)^+$, 2], 317, 315 [$(M-^tBu)$]. HRMS: Calcd. for $C_{16}H_{24}{}^{79}BrO_3Si$ (M-H): 371.0678. Found: 371.0597.

2-[2'-Bromo-5'-(2"-methyl-2"-methoxylethoxyl)methyl]phenyl-1,3-dioxolane (7b) To a solution of **14** (5.15 g, 19.9 mmol) and catalytic amount of pyridinium tosylate (50 mg) in dry methylene chloride (30 mL) was added 2-methoxypropene (4 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min before washing the solution with 5% sodium bicarbonate (10 mL) and brine (10 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated. After column chromatography on silica gel, eluted first with 1% Et_3N in 10% ethyl acetate in hexanes and then

with 1% Et_3N in 25% ethyl acetate in hexanes, pure **7c** was obtained (5.95 g, 90%) as an oil: R_f = 0.50 (25% ethyl acetate in hexanes). ^1H NMR (500 MHz): δ 1.391 (s, 6H, Me_2), 3.209 (s, 3H, OMe), 4.02 - 4.17 (m, 4H, 4-H and 5-H), 4.432 (s, 2H, $ArCH_2O$), 6.063 (s, 1H, 2-H), 7.230 (dd, 1H, J = 8.0 and 1.5 Hz, 4'-H), 7.508 (d, 1H, J = 8.0 Hz, 3'-H), 7.532 (d, 1 H, J = 1.5 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 24.37 (2"-Me), 48.52 (2"-OMe), 61.97 ($ArCH_2O$), 65.28 (4,5-C), 100.29 (2"-C), 102.35 (2-C), 121.23 (2'-C), 126.52 (6'-C), 129.34 (4'-C), 132.75 (3'-C), 136.17 (5'-C), 138.54 (1'-C) ppm. FT-IR: 2885 - 2990, 1600, 1469, 1379, 1211, 1150, 1083, 1030 cm^{-1}. MS: *m/z* 331, 329 [$(M - 1)^+$, 10%, 28%], 300, 298 [$(M - MeOH)^+$, 37%], 241 [$(M - OMMOE)^+$, base]. HRMS: Calcd. for $C_{13}H_{15}{}^{79}BrO_3$ (M - MeOH) 298.0205; Found 298.0185.

2-[2'-Bromo-5'-(tetrahydropyran-2"-yloxy)methyl]phenyl-1,3-dioxolane (7c) Dihydropyran (6.2 mL) was added to a solution of **14** (6.70 g, 25.9 mmol) and catalytic amount of pyridinium tosylate (0.4 g) in dry methylene chloride (100 mL) at 0 °C. The mixture was allowed to warm to room temperature slowly during 1 h and stirred for an additional 4 h before the solution was washed with 5% sodium bicarbonate (30 mL), water (30 mL) and brine (20 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated. After column chromatography on silica gel, pure **7c** was obtained (8.43 g, 95%) as an oil: R_f = 0.50 (25% ethyl acetate in hexanes). ^1H NMR (500 MHz): δ 1.46 - 1.87 (m, 6H), 3.48 - 3.54 (m, 1H, 6"a-H), 3.84 - 3.90 (m, 1H, 6"b-H), 4.00 - 4.18 (m, 4H, 4-H and 5-H), 4.458 (d, 1H, J = 12.5 Hz, Ha on $ArCH_2O$), 4.658 (t, 1H, J = 3.5 Hz, 2"-H), 4.714 (d, 1H, J = 12.5 Hz, Hb on $ArCH_2O$), 6.053 (s, 1H, 2-H), 7.232 (dd, 1H, J = 8.0 and 2.0 Hz, 4'-H), 7.515 (d, 1H, J = 8.0 Hz, 3'-H), 7.550 (d, 1 H, J = 2.0 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 19.06 (4"-C), 25.20 (5"-C), 30.27 (3"-C), 61.87 (6"-C), 65.24 (4,5-C), 67.71 ($ArCH_2O$), 97.50 (2"-C), 102.28 (2-C), 121.51 (2'-C), 126.89 (6'-C), 129.72 (4'-C), 132.71 (3'-C), 136.22 (5'-C), 137.41 (1'-C) ppm. FT-IR: 2850 - 2950, 1460, 1390, 1360, 1250, 1190 cm^{-1}. MS: *m/z* 343 ,341 [$(M-1)^+$]. HRMS: Calcd. for $C_{15}H_{18}{}^{79}BrO_4$ (M-H) 341.0389; Found 341.0394.

2-[2'-(4"-Bromobutyl)-5'-(*t*-butyldimethylsiloxymethyl)]phenyl-1,3-dioxolane (5a) Magnesium turnings (310 mg, 12.88 mmol) were placed in a 100 mL of three-neck flask with a condenser. The flask was dried with flame under vacuum and argon was introduced. Dry THF (10 mL) was added into the flask and the flask was heated under reflux. Bromide **7a** (1.00 mL first) was added through a syringe in one portion and 0.1 mL of MeI (1.60 mmol) was added to initiate the reaction. The other portion of **7a** (1.00 mL; total 2.00 mL, 2.40 g, 6.44 mmol) was added at such a rate that the reaction proceeded smoothly over a period of 10 min. After addition, the mixture was refluxed for an additional 2 h.

To a solution of cuprous bromide (100 mg, 0.64 mmol), dry hexamethylphosphoramide (HMPA, 2.0 mL), dry THF (5 mL) and 1,4-dibromobutane (1.50 mL, 2.70 g, 12.5 mmol) was added quickly a solution of the reagent prepared above under argon with reflux and the reaction mixture was kept under reflux for 3 h before cooling down to room temperature. Water (10 mL) and aqueous saturated ammonium chloride solution (10 mL) were added, the mixture was extracted with ether (50 mL) Standard work up procedure gave **5a** (2.2 g, 80%) as an oil: R_f = 0.50 (25%

ethyl acetate in hexanes). ^{1}H NMR (300 MHz): δ 0.085 (s, 6H, Si-Me_2), 0.930 (s, 9H, ^{t}Bu), 1.68 - 1.82 (m, 2H, 2"-H), 1.85 - 1.98 (m, 2H, 3"-H), 2.732 (t, 2H, J = 7.8 Hz, 1"-H), 3.419 (t, 2H, J = 6.6 Hz, 4"-H), 3.95 - 4.25 (m, 4H, 4-H and 5-H), 4.710 (s, 2H, $ArCH_2O$), 5.974 (s, 1H, 2-H), 7.141 (d, 1H, J = 7.8 Hz, 3'-H), 7.271 (d, 1H, J = 7.8 Hz, 4'-H), 7.410 (s, 1 H, 6'-H) ppm. IR: 2850 - 2930, 1450, 1250, 1100 cm^{-1}. MS: 429 and 427 [(M-H)$^+$, 10%), 373 and 371 [(M-^{t}Bu)$^+$, 3%], 293 {[M-$(CH_2)_4Br$]$^+$, 15%}, 73 (base).

2-[2'-(4"-Chlorobutyl)-5'-(2"'-methyl-2"'-methoxylethoxyl)methyl]phenyl-1,3-dioxolane (5b) A solution of *t*-butyl lithium (17.6 mL of 0.97 M[32] in pentane, 17.07 mmol) was added dropwise into a cold solution of **7b** (4.93 g, 14.9 mmol) in dry THF (50 mL) at -78 °C under argon. The solution was kept at -78 °C for 1 h before adding 4-chloro-1-iodobutane (2.75 mL, 4.88 g, 22.4 mmol, redistilled). The reaction solution was stirred for 1 h at -78 °C and then warmed to room temperature and atirred overnight. The reaction was diluted with diethyl ether (150 mL) and washed with water (70 mL) and brine (70mL). After drying over anhydrous sodium sulfate and concentrating, column chromatography on silica gel, eluted first with 1% Et_3N in 10% ethyl acetate in hexanes and then with 1% Et_3N in 25% ethyl acetate in hexanes, gave **5b** (4.12 g, 80%) as an oil: R_f = 0.42 (25% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 1.396 (s, 6H, Me_2), 1.70 - 1.90 (m, 4H, 3'- and 2'-CH_2), 2.70 - 2.76 (m, 2H, 1"-CH_2), 3.233 (s, 3H, OMe), 3.536 (t, 2H, J = 7.5 Hz, 4"-CH_2), 3.98 - 4.15 (m, 4H, 4-H and 5-H), 4.436 (s, 2H, $ArCH_2O$), 5.950 (s, 1H, 2-H), 7.145 (d, 1H, J = 8.0 Hz, 3'-H), 7.292 (dd, 1H, J = 8.0 and 1.0 Hz, 4'-H), 7.503 (d, 1 H, J = 1.0 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 24.45 (2"'-Me), 28.49 (2"-C), 30.93 (1"-C), 32.22 (3"-C), 44.70 (4"-C), 48.51 (2"'-OMe), 62.61 ($ArCH_2O$), 65.09 (4,5-C), 100.19 (2"'-C), 101.39 (2-C), 125.40 (6'-C), 128.14 (4'-C), 129.59 (3'-C), 134.73 (2'-C), 136.61 (5'-C), 139.44 (1'-C) ppm. IR: 2880 - 2990, 1460, 1380, 1210, 1150, 1070 cm^{-1}. MS: 344 and 342 (M$^+$, 2% and 5%), 312 and 310 [(M - MeOH)$^+$, 25%], 270 [(M - methoxypro-pene)$^+$, 10%], 253 [(M - OMMOE)$^+$, base]. HRMS: 342.1604 [calcd. for $C_{18}H_{27}{}^{35}ClO_4$ (M) 342.1598].

2-[2'-(4"-Chlorobutyl)-5'-(tetrahydropyran-2"'-yloxy)methyl]phenyl-1,3-dioxolane (5c) A solution of *t*-butyl lithium (19.2 mL of 1.7 M[32] in pentane, 32.7 mmol) was added dropwise into a solution of **7c** (8.30 g, 24.1 mmol) in dry THF (150 mL) at -78 °C under argon. The solution was kept at -78 °C for 1 h before warming to -20 °C. 4-Chloro-1-iodobutane (4.38 mL, 7.90 g, 36.2 mmol, redistilled) was added at -20 °C and the solution was stirred for 2 h, warmed to room temperature and stirred overnight. The reaction was diluted with diethyl ether (250 mL) and washed with water (100 mL) and brine (100 mL). After drying over anhydrous sodium sulfate and concentrating, column chromatography on silica gel gave pure **5c** (7.00 g, 82%) as an oil: R_f = 0.50 (25% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 1.45 - 1.90 (m, 10H), 2.734 (t, 2H, J = 8.0 Hz, 1"-H), 3.50 - 3.55 (m, 1H, 6"'a-H), 3.541 (t, 2H, J = 6.5 Hz, 4"-H), 3.86 - 3.92 (m, 1H, 6"'b-H), 3.98 - 4.15 (m, 4H, 4-H and 5-H), 4.607 (d, 1H, J = 12.0 Hz, Ha on $ArCH_2O$), 4.65 - 4.70 (m, 1H, 2"'-H), 4.734 (d, 1H, J = 12.0 Hz, Hb on $ArCH_2O$), 5.956 (s, 1H, 2-H), 7.154 (d, 1H, J = 8.0 Hz, 3'-H), 7.300 (dd, 1H, J = 8.0 and 1.0 Hz, 4'-H), 7.520 (d, 1 H, J = 1.0 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31a]: δ

19.18 (4"'-C), 25.26 (5"'-C), 28.47 (2"-C), 30.39 (3"'-C), 30.94 (1"-C), 32.21 (3"-C), 44.66 (4"-C), 61.87 (6"'-C), 65.08 (4,5-C), 68.37 ($ArCH_2O$), 97.42 (2"'-C), 101.34 (2-C), 125.74 (6'-C), 128.49 (4'-C), 129.55 (3'-C), 134.77 (2'-C), 135.91 (5'-C), 139.69 (1'-C) ppm. FT-IR: 2870 - 2940, 1500, 1440, 1120, 1075, 1033 cm^{-1}. MS: 356 and 354 (M^+, 20% and 60%), 355 and 353 [$(M - H)^+$, 10% and 30%], 272 and 270 [$(M - THP)^+$, 5% and 15%], 263 {$(M - (CH_2)_4Cl]$, 12%}, 255 and 253 [$(M - OTHP)^+$, 35% and 100%]. HRMS: 354.1588 [calcd. for $C_{19}H_{27}{}^{35}ClO_4$ (M) 354.1598].

O-Alkylation of 5c and 2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrahydroxymethylbicyclo-[2.2.2]octane (4) A mixture of sodium hydride (60% in oil, 156 mg, 3.83 mmol), tetrol **4**[6,13] (54.65 mg, 0.238 mmol) and potassium iodide (106 mg) was dried under high vacuum and then argon was introduced. Dry HMPA (15 mL) was charged under argon and the mixture was stirred for 20 min. The temperature was raised to 50 °C (oil bath) at which point the chloride **5c** (1.0 g, 2.8 mmol) was added dropwise by syringe during the course of a week (one drop per hour in average during daytime; continuous addition via a syringe driver failed to yield the product). After addition, the reaction mixture was stirred at 50 °C for an additional 12 h. The mixture was diluted with 25% methylene chloride in diethyl ether (10 mL) and washed with water (5 mL) and brine (5 mL). Standard work-up (silica gel, 50% ethyl acetate in hexanes) gave tetra-substituted **3c** (15 mg, 4.4%) as well as tri- and di-substituted products as oils. **3c**: R_f: 0.23 (50% ethyl acetate in hexanes). ^1H NMR (200 Mhz on Gemini 200): δ 1.40 - 1.90 (m, 46H), 2.112 (s, 4H, 2,3,5,6-H), 2.60 - 2.80 (m, 8H, benzylic), 3.30 - 3.70 (m, 20H), 3.85 - 4.00 (m, 4H, 9, 11-H), 4.00 - 4.20 (m, 16H, dioxolanyl groups), 4.40 - 4.80 (m, 12H, benzylic-CH_2O and acetal-H in THP groups), 5,978 (s, 4H, acetal-H in dioxolanyl groups), 7.10 - 7.30 (m, 8H), 7.538 (s, 4H).

2-*Syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis[4'-[2"-tetrahydro-2H-pyranyloxy)butoxy]-methylbicyclo[2.2.2]octane (18). Method A: A mixture of sodium hydride (60% in oil, 2.3 g, 57.5 mmol), **4** (1.00 g, 4.35 mmol) and potassium iodide (1.0 g) was dried under high vacuum and then argon was introduced. Dry HMPA (15 mL) was added under argon and the mixture was stirred for 20 min. The temperature was raised to 60 °C (oil bath) when the 4-(2'-tetrahydro-2H-pyranyl-oxy)butyl chloride[14] (7.0 mL) was introduced by syringe driver at a rate of 0.5 mL/h and stirred overnight. A second portion of chloride (4 mL, total 11.0 mL, 11.55 g, 60.0 mmol) was added at a rate of 0.2 mL/h and then again stirred overnight. Total reaction time was 48 h. The mixture was diluted with 25% methylene chloride in diethyl ether (100 mL) and washed with water (50 mL) and brine (50 mL). After drying and concentrating, column chromatography on silica gel (60 g) gave pure **18** (2.38 g, 60%) as an oil: R_f = 0.42 (50% ethyl acetate in hexanes). ^1H NMR (500 MHz): δ 1.396 (s, 4H, 7,8-H), 1.45 - 1.72 (m, 38H), 1.75 - 1.85(m, 4H), 2.086 (s, 4H, 2,3,5,6-H), 3.38 - 3.45 (m, 16H), 3.45 - 3.52 (m, 4H), 3.55 - 3.62 (m, 4H), 3.70 - 3.77 (m, 4H), 3.80 - 3.87 (m, 4H), 4.554 (t, 4H, J = 2.5 Hz, 2"-H) ppm. ^{13}C NMR (50 MHz): δ 16.09 (7-C and 8-C), 19.50, 25.38, 26.44, 26.51, 29.09 (1,4-C), 30.63, 38.41 (2,3,5,6-C), 62.10, 67.18, 70.11. 70.57, 98.63 (2"-C) ppm. IR: 2920 - 2850, 1440, 1370, 1350, 1200, 1120, 1030, 905, 865, 810 cm^{-1}. FABMS: *m/z* 687.4 {[(M+1)-2 x DHP]$^+$}, 603.6 {[(M+1)-3 x DHP]$^+$}, 519.4 {[(M+1)-4 x DHP]$^+$}.

Formation of 18 via hydrogenation of 20 (see below), **method B** To a mixture of **20** (1.88 g, 2.20 mmol) and 5% Pd/C (200 mg, 8.6% based on Pd) in methanol (20 mL) was added solid ammonium formate (0.70 g, 10.9 mmol) in one portion at room temperature. The reaction mixture was stirred for 16 h before addition of another portion of Pd/C (100 mg) and ammonium formate (350 mg). After stirring for 10 h, the mixture was filtered through silica gel (5 g) and washed with ethyl acetate. Standard workup gave **18** quantitatively and spectrally identical with the sample previously prepared.

2-*Syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis[4'-[2"-tetrahydro-2H-pyranyloxy)butoxy]-methylbicyclo[2.2.2]oct-7-ene (20) the same procedure was used as in the synthesis of **18**, method A [2-*syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrahydroxymethylbicyclo[2.2.2]oct-7-ene (**19**, 3.0 g)[17], potassium iodide (3.0 g), sodium hydride (60% in oil, 7 g), and 4-(2'-tetrahydro-2H-pyranyloxy)butyl chloride (33 mL)]. The product **20** was obtained in 80% yield as an oil: R_f = 0.42 (50% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 1.45 - 1.72 (m, 36H), 1.76 - 1.85(m, 4H), 2.167 (m, 4H, 2,3,5,6-H), 2.743 (s, 2H, 1,4-H), 3.05 - 3.12 (m, 4H), 3.25 - 3.32 (m, 8H), 3.32 - 3.40 (m, 8H), 3.55 - 3.62 (m, 4H), 3.70 - 3.77 (m, 4H), 3.80 - 3.87 (m, 4H), 4.557 (t, 4H, J = 3.5 Hz, 2"-H), 6.118 (t, 2H, J = 3.5 Hz, 7,8-H) ppm. ^{13}C NMR (50 MHz): δ 19.22, 25.15, 26.22, 30.36, 36.13 (1,4-C), 41.01 (2,3,5,6-C), 61.74, 66.85, 70.18. 70.82, 98.30 (2"-C), 132.21 (7,8-C) ppm. FT-IR: 2945, 2874, 1458, 1370, 1263, 1210, 1139, 1122, 1078, 1033, 989, 918, 874, 821 cm^{-1}. FABMS: *m/z* 876 $(M+Na)^+$ (sample in 3-NBA/Na_2CO_3 matrix). HR FABMS: Calcd. for $C_{48}H_{84}O_{12}Na$: 875.5860; Found: 875.5847.

2-*Syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis(4'-bromobutoxy)methylbicyclo[2.2.2]-octane (6, R = Br) To a solution of bromotriphenylphosphonium bromide (8.56 mmol, Aldrich) in dry methylene chloride (40 mL, Aldrich) was added a solution of **18** (1.22 g, 1.43 mmol). The mixture was stirred at room temperature for 16 h before diluting with pentane (150 mL) to precipitate the triphenylphosphine oxide. The mixture was filtered through silica gel (10 g) and washed with ether (25 mL x 2). The filtrates were combined, concentrated and chromatographied on silica gel (50 g) to give a pale yellow oil **6** (0.89 g, 81% yield): R_f = 0.47 (25% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 1.400 (s, 4H, 7,8-H), 1.680 (s, 2H, 1,4-H), 1.65 - 1.75 (m, 8H, 2'-H), 1.88 - 1.95 (m, 8H, 3'-H), 2.078 (s, 4H, 2,3,5,6-H), 3.35 - 3.45 (m, 20H, 9,11-H, 4'-H and 1'-H), 3.55 - 3.60 (m, 4H, 10, 12-H) ppm. ^{13}C NMR (50 MHz): δ 15.85 (7,8-C), 28.10 (3'-C), 28.75 (1,4-C), 29.55 (2'-C), 33.63 (4'-C), 38.24 (2,3,5,6-C), 69.54 and 69.88 (9,10,11,12-C and 1'-C) ppm. IR: 2920 - 2850, 1440, 1370, 1250, 1100 cm^{-1}. FABMS: *m/z* 767 $[(M+1)^+]$, 615 $[(M-BrC_4H_8O]^+$.

2-*Syn*, 3-*syn*, 5-*syn*, 6-*syn*-Tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-(*t*-butyldimethylsiloxymethyl)phenyl]butoxymethyl}bicyclo[2.2.2]octane (3a) A solution of *t*-butyl lithium (2.8 mL of 1.8 M[32] in pentane, 5.04 mmol) was added dropwise into a solution of **7a** (1.60 g, 4.28 mmol) in dry THF (13 mL) at -78 °C under argon. The solution was kept at -78 °C for 1 h before warming to -5 °C. A solution of **28** (332 mg, 0.431 mmol) in THF (2 mL) was added. The mixture was stirred at -5 °C for 1h and then warmed to 0 °C slowly and allowed to reach room tem-

perature overnight. The reaction mixture was diluted with 25% methylene chloride in diethyl ether (75 mL) and washed successively with an aqueous solution of ammonium chloride (1 : 1 mixture of saturated ammonium chloride and water, 20 mL), water (20 mL) and brine (20 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated. Column chromatography on silica gel (70 g) eluted successively with 10% ethyl acetate in hexane (100 mL) and 7.7% diethyl ether in benzene (50 mL) and 25% diethyl ether in benzene (150 mL) to give pure product **3a** as an oil (478 mg, 68%): R_f = 0.21 (25% diethyl ether in benzene). ^{1}H NMR (500 MHz): δ 0.060 (s, 24H, Si-Me), 0.913 (s, 36H, ^{t}Bu), 1.396 (s, 4H, 7,8-H), 1.55-1.68 (m, 16H, 2'-H and 3'-H), 1.691 (s, 2H, 1,4-H), 2.096 (s, 4H, 2,3,5,6-H), 2.700 (t, 8H, J = 7.0 Hz, 4'-H), 3.32-3.44 (m, 12H, 9,11-H and 1'-H), 3.55-3.62 (m, 4H, 10,12-H), 3.95-4.12 (m, 16H, 4"'-H and 5"'-H), 4.688 (s, 8H, $ArCH_2O$), 5.966 (s, 4 H, 2"'-H), 7.124 (d, 4H, J = 8.0 Hz, 6"-H), 7.233 (dd, 4H, J = 8.0 and 1.0 Hz, 5"-H), 7.457 (d, 4 H, J = 1.0 Hz, 3"-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ -5.34 (Si-Me), 16.12 (7,8-C), 18.27 (quaternary C in t-Bu), 25.84 (Me in t-Bu), 28.07 (3'-C), 29.15 (1,4-C), 29.59 (3'-C), 31.54 (4'-C), 38.43 (2,3,5,6-C), 64.60 ($ArCH_2O$), 65.09 (4"'-C and 5"'-C), 70.13 (9,10,11,12-C), 70.61 (1'-C), 101.37 (2"'-C), 123.67 (3"-C), 126.52 (5"-C), 129.42 (6"-C), 134.62 (1"-C), 138.83 (4"-C), 139.54 (2"-C) ppm. FT-IR: 2930, 2850, 1600, 1580, 1450, 1390, 1215, 1100, 940, 750 cm^{-1}. FABMS: *m/z* 1622.4 $(M)^+$, 1492.2 $(M\text{-}OTBDMS)^+$. HR FABMS: 1622.9951 (calcd. for $C_{92}H_{150}O_{16}Si_4$: 1623.0001).

2-(3'-*t*-Butyldimethylsiloxymethyl)phenyl-1,3-dioxolane (22b) To a solution of 2-(3'-hydroxymethyl)phenyl-1,3-dioxolane (**22a**)[19] (1.60 g, 8.89 mmol), a catalytic amount of DMAP (100 mg) and N-ethyldiisopropylamine (3.00 mL, 17.2 mmol) in dry methylene chloride (30 mL) were added a solution of t-butyldimethylsilyl chloride (2.00 g, 13.3 mmol) in methylene chloride (10 mL) via a cannula at 0 °C under argon. The mixture was allowed to warm to room temperature slowly during 1 h and stirred for an additional 1 h. Hexanes (40 mL) were added and the whole solution was washed with water (10 mL x 2) and brine (10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated. After column chromatography on silica gel, pure **22b** was obtained (2.41 g, 92%) as an oil: R_f = 0.50 (10% ethyl acetate in hexanes). ^{1}H NMR (500 MHz): δ 0.079 (s, 6H, $SiMe_2$), 0.926 (s, 9H, ^{t}Bu), 4.00 - 4.12 (m, 4H, 4-H and 5-H), 4.740 (s, 2H, $ArCH_2O$), 5.804 (s, 1H, 2-H), 7.32 - 7.35 (m, 3H, aromatic), 7.407 (s, 1H, 2'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ -5.37 (Si-Me) 18.30 (quaternary C in ^{t}Bu), 25.85 (Me in t-Bu), 64.62 ($ArCH_2O$), 65.14 (4-C and 5-C), 103.64 (2-C), 123.91, 124.88, 126.68, 128.18, 137.71, 141.52 (aromatic) ppm. IR: 2860 - 2930, 1460, 1390, 1365, 1255, 1175, 1100, 1075, 840, 775 cm^{-1}. MS: *m/z* 293 $[(M\text{-}1)^+]$, 237 $[(M\text{-}^t\text{Bu})^+]$. HRMS: 293.1580 [calcd. for $C_{16}H_{25}O_3Si$ (M-H): 293.1573].

2-[3'-(tetrahydropyran-2"-yloxy)methyl]phenyl-1,3-dioxolane (22c) To a solution of **22a**[19] (1.18 g, 6.65 mmol) and a catalytic amount of pyridinium tosylate (100 mg) in dry methylene chloride (30 mL) was added dihydropyran (1.5 mL) at 0 °C. The mixture was allowed to warm to room temperature slowly during 1 h and stirred for an additional 4 h before the solution was washed with 5% sodium bicarbonate (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous sodium sulfate and concentrated. After column chromatography on silica

gel, pure **22c** was obtained (1.47 g, 85%) as an oil: R_f = 0.50 (25% ethyl acetate in hexanes). ^1H NMR (500 MHz): δ 1.48 - 1.88 (m, 6H), 3.50 - 3.55 (m, 1H, 6"a-H), 3.85 - 3.95 (m, 1H, 6"b-H), 4.00 - 4.15 (m, 4H, 4-H and 5-H), 4.493 (d, 1H, J = 12.5 Hz, Ha on $ArCH_2O$), 4.669 (t, 1H, J = 3.5 Hz, 2"-H), 4.776 (d, 1H, J = 12.5 Hz, Hb on $ArCH_2O$), 5.801 (s, 1H, 2-H), 7.32 - 7.40 (m, 3H, aromatic), 7.455 (s, 1H, 2'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 19.16 (4"-C), 25.32 (5"-C), 30.38 (3"-C), 61.90 (6"-C), 65.14 (4,5-C), 68.41 ($ArCH_2O$), 97.52 (2"-C), 103.50 (2-C), 121.17, 125.70, 128.29, 128.46, 137.84, 138.37 (aromatic) ppm. FT-IR: 2875 - 2950, 1452, 1384, 1322, 1078, 1030 cm^{-1}. MS: *m/z* 263 [(M-1)$^+$, 12%], 207 (10%), 180 [(M - DHP)$^+$, 11%], 163 [(M - OTHP)$^+$, base], 149 [(M - CH_2OTHP)$^+$]. HRMS: 263.1280 [calcd. for $C_{15}H_{19}O_4$ (M - H): 263.1283].

Tetrakis{*m,m*-[(methylene(2'-(trimethylsilyl)ethyl)imino)methylene]}-*strati*-bis(5,10,15,20-tetraphenylporphyrin) (A, R = SES) A 100-mL round bottom flask was dried by flame under high vacuum and argon was introduced. Cesium carbonate (540 mg, 1.65 mmol, Aldrich) was weighted into the flask and dried again. SES-NH2 (73.3 mg, 0.4043 mmol) was placed into the flask. The flask was dried by heat-gun for 30 min and argon was charged. Dry DMF (predried over molecular sieves overnight and distillated at reduced pressure under argon) (28.0 mL) was charged into the flask and the mixture was stirred at 50 °C for 10 min. To this suspension was added slowly a solution of 5,10,15,20-tetrakis(α-bromo-*m*-tolyl)porphyrin (**23d**)[5a] (240 mg, 0.243 mmol) in dry DMF (20.5 mL) via a syringe driver during 10 h. The solution was stirred overnight when the most solvent was removed by rotary evaporator at a reduced pressure and the residue dissolved in dichloromethane. Column chromatography on silica gel (2% methanol in chloroform), followed by preparative thin layer chromatography (100 x 200 x 0.50 mm, 1% methanol in chloroform) gave the mono-zinc bis-porphyrin[5a] [FAB MS: 2111 (M)$^+$] as a crude product. The crude product was subjected to trifluoroacetic acid for 20 min, and the resulting green solution was diluted with chloroform and washed with 5% ammonium hydroxide. Standard workup then gave pure **A** (R = SES) as a purple solid (23.9 mg, 9.6% based on **23d**): M.p. > 300 °C, R_f = 0.31 (2% methanol in chloroform). ^1H NMR (500 MHz)[31b]: δ -4.035 (s, 4H, NH), 0.110 (s, 36H, 4 x $SiMe_3$), 1.10 - 1.15 (m, 8H, 4 x $SiCH_2$), 3.12 - 3.18 (m, 8H, 4 x CH_2SO_2), 4.613 (s, 16H, $ArCH_2N$), 7.022 (s, 8H, 2-H), 7.732 (t, 8H, J = 8.0 Hz, 5-H), 7.980 (d, 8H, J = 8.0 Hz, 6-H), 8.113 (d, 8H, J = 8.0 Hz, 4-H), 8.271 (s, 16H, β-pyrrolic) ppm. FAB MS: 2050.8 (M$^+$) (Calcd. for $C_{116}H_{120}N_{12}O_8S_4Si_4$: 2050.9). UV/VIS: λ_{max} (log ε) 417.5 (5.81), 515.5 (4.40), 525.5 (4.02), 593 (3.91), 650 (3.68).

2-*Syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-hydroxymethylphenyl]butoxymethyl}bicyclo[2.2.2]octane (24a) To a solution of **3a** (7.00 g, 4.31 mmol) in dry THF (100 mL) was added a solution of tetra^{n}butylammonium fluoride (20 mL of 1 M solution in THF, 20 mmol) at room temperature. The reaction was stirred at room temperature for 10 h. Concentration and column chromatography on silica gel (400 g) eluted with 6.67% methanol in dichloromethane gave the desired product **24a** as an oil (3.7 g, 73%): R_f = 0.27 (6.67% methanol in dichloromethane). ^1H NMR (500 MHz): δ 1.387 (s, 4H, 7,8-H), 1.55-1.70 (m, 16H, 2'-H and 3'-H), 1.684 (s, 2H, 1,4-H), 2.074 (s, 4H, 2,3,5,6-H), 2.688 (t, 8H, J = 7.0 Hz, 4'-H), 3.30-3.42 (m, 12H, 9,11-

H and 1'-H), 3.55-3.60 (m, 4H, 10,12-H), 3.95-4.15 (m, 16H, 4"'-H and 5"'-H), 4.576 (s, 8H, $ArCH_2$-O), 5.936 (s, 4 H, 2"'-H), 7.130 (d, 4H, J = 8.0 Hz, 6"-H), 7.220 (d, 4H, J = 8.0 Hz, 5"-H), 7.508 (s, 4 H, 3"-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 16.00 (7,8-C), 27.98 (3'-C), 28.93 (1,4-C), 29.44 (2'-C), 31.42 (4'-C), 38.26 (2,3,5,6-C), 64.41 ($ArCH_2OH$), 65.02 (4"'-C and 5"'-C), 70.01 (9,10,11,12-C), 70.45 (1'-C), 101.04 (2"'-C), 124.52 (3"-C), 127.46 (5"-C), 129.53 (6"-C), 134.59 (1"-C), 138.61 (4"-C), 140.08 (2"-C) ppm. FT-IR: 3417, 2935, 2873, 1466, 1394, 1078 cm^{-1}. FAB MS: *m/z* 1166 $(M-1)^+$.

2-*Syn*, 3-*syn*, 5-*syn*, 6-*syn*-tetrakis{4'-[2"-(1"',3"'-dioxolan-2"'-yl)-4"-bromomethylphenyl]butoxymethyl}bicyclo[2.2.2]octane (24b)[33] To a solution of **24a** (670 mg, 0.574 mmol) and dry 2,6-lutidine (0.28 mL, 2.53 mmol, Aldrich) in dry methylene chloride (20 mL) was added a solution of dibromotriphenylphosphorane (1.56 g, 3.70 mmol) in dry methylene chloride (20 mL) at 0 °C under argon. The reaction mixture was stirred at 0 °C for 1 h when methylene chloride was removed by rotary evaporator. The residue was chromatographied on a silica gel (60 g) column, eluting with 20% diethyl ether in methylene chloride. The product **24b** was obtained in 70% yield (576 mg) as an oil: R_f = 0.59 (20% diethyl ether in dichloromethane). ^1H NMR (500 MHz): δ 1.394 (s, 4H, 7,8-H), 1.55-1.65 (m, 16H, 2'-H and 3'-H), 1.691 (s, 2H, 1,4-H), 2.089 (s, 4H, 2,3,5,6-H), 2.698 (t, 8H, J = 7.0 Hz, 4'-H), 3.30-3.42 (m, 12H, 9,11-H and 1'-H), 3.55-3.60 (m, 4H, 10,12-H), 3.95-4.15 (m, 16H, 4"'-H and 5"'-H), 4.447 (s, 8H, $ArCH_2Br$), 5.933 (s, 4 H, 2"'-H), 7.133 (d, 4H, J = 8.0 Hz, 6"-H), 7.279 (dd, 4H, J = 8.0 and 2.0 Hz, 5"-H), 7.556 (d, 4 H, J = 2.0 Hz, 3"-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 16.08 (7,8-C), 27.85 (3'-C), 29.04 (1,4-C), 29.53 (2'-C), 31.53 (4'-C), 33.44 ($ArCH_2Br$), 38.38 (2,3,5,6-C), 65.12 (4"'-C and 5"'-C), 70.09 (9,10,11,12-C), 70.50 (1'-C), 100.83 (2"'-C), 126.58, 129.49, 129.93, 135.14, 135.34, 141.41 (aromatic-C) ppm. FT-IR: 2947, 2876, 1490, 1400, 1221, 1117, 1114, 1087, 980, 917 cm^{-1}. FAB MS: *m/z* 1419 (M^+), 1339.5 [$(M-Br)^+$].

Capped porphyrin 2[33] To a solution of **24b** (140 mg, 0.0987 mmol) in chloroform (commercial, 99 mL) was added pyrrole (0.028 mL, 0.404 mmol) and boron trifluoride etherate (0.073 mL, 0.592 mmol) under argon. The reaction was stirred for 17 h at room temperature in the dark. DDQ (50 mg) was added and the solution was refluxed for 10 min when another portion of DDQ (50 mg) was added. The solution was refluxed for an additional 20 min. The appearance of porphyrin was monitored by UV/Vis at 420 nm. The solvent was removed by rotary evaporator, and the residue was dissolved in dichloromethane (4 mL) and then silica gel (2 g) was added. After drying, the silica gel was loaded on the top of a column of silica gel (30 g) and chromatographied by eluting with 25% ethyl acetate/hexanes. The porphyrin **2** was obtained in 9.3% yield (13.2 mg). M.p. > 300 °C. R_f = 0.33 (25% ethyl acetate/hexanes.). ^1H NMR (500 MHz)[31b,c]: δ -2.484 (s, 2H, NH), -2.468 (s, 4H, 2,3,5,6-H), -0.288 (s, 2H, 1,4-H), 0.270 (s, 4H, 7,8-H), 1.410 (m, 4H, 2'b-H), 1.464 (m, 4H, 2'a-H), 1.830 (m, 8H, 1'b-H and 3'b-H), 1.895 (m, 4H, 3'a-H), 2.109 (m, 4H, 9b-H), 2.222 (m, 4H, 9a-H), 2.304 (m, 4H, 1'a-H), 2.571 (m, 4H, 4'b-H), 2.910 (m, 4H, 4'a-H), 4.611 (m, 8H, $ArCH_2Br$), 7.72 - 7.78 (m, 12H, aromatic-H), 8.614 (s, 8H, β-pyrrolic-H) ppm. ^{13}C NMR (125 Hmz)[31b,c]: δ 13.47 (7,8-C), 26.05 (2'-C), 26.43 (1,4-C), 26.50 (3'-C), 30.73 (4'-C), 33.54 ($ArCH_2Br$), 33.68 (2,3,5,6-C), 66.83 (9,10,11,12-C), 68.69 (1'-C), 118.42 (*meso*), 128.11 (5"-C), 129.27 (3"-C), 130 (br, β-pyrrolic

carbons), 133.33 (4"-C), 134.95 (6"-C), 142.04 (1"-C), 143.54 (2"-C) ppm. FABMS: *m/z* 1434 $(M+1)^+$, 1433 $(M)^+$, 1353 $(M-HBr)^+$. UV/Vis: λ_{max} (logε): 368 (4.07), 421.5 (5.17), 483 (3.27), 515.5 (3.83), 549.0 (3.34), 591 (3.35), 647.5 (3.10) nm.

Spheroidal bis-porphyrin (1) A 10-mL round bottom flask was dried by flame under high vacuum and argon was introduced. Cesium carbonate (about 15 mg, Aldrich) was placed into the flask and dried again. After introducing argon, the cesium carbonate was weighed as 14.60 mg (44.8 μmol). SES-NH_2 (1.687 mg, 9.305 μmol) was weighed by microscale and placed into the flask. The flask was dried by heat-gun for 30 min and argon was charged. Dry DMF (predried over molecular sieves overnight and distillated at reduced pressure under argon) (0.63 mL) was charged and the mixture was stirred at 60 °C for 10 min. To this suspension was added slowly a solution of freshly prepared capped porphyrin **2** (8.10 mg, 5.65 μmol) in dry DMF (0.50 mL) by a syringe driver during 3 h at 60 °C under argon. The solution was stirred overnight when the most solvent was removed by rotary evaporator and the residue dissolved in dichloromethane. Column chromatography on silica gel (2 g, 2% methanol in chloroform), followed by preparative thin layer chromatography (100 x 200 x 0.25 mm, 1% methanol in chloroform) gave pure **1** as a purple solid (0.9 mg, 10% based on **2**): M.p. > 300 °C, R_f = 0.32 (one spot, 2% methanol in chloroform). ^1H NMR (500 MHz)[31b,c]: δ -3.480 and -3.473 (a pair of singlets, 4H, NH), -2.949 and -2.901 (a pair of singlets, 8H, 2,3,5,6-H), -0.575 and -0.512 (a pair of singlets, 4H, 1,4-H), 0.040 and 0.074 (a pair of singlets, TMS), 0.070 and 0.130 (a pair of singlets, 7,8-H), 0.86 (t, 8H, CH_2Si), 1.70 (m, 16H), 1.88 (m, 8H), 1.95 (m, 8H), 2.10 (m, 8H), 2.42 (m, 8H), 2.67 (m, 8H), 3.05 (t, 8H, CH_2SO_2), 3.30 - 3.60 (m, 16H), 4.35 and 4.65 (m, 8H, $ArCH_2N$), 6.843 (s, 8H, 3"-H), 7.698 (d, 8H, J = 8 Hz, 6"-H), 7.938 (d, 8H, J = 8 Hz, 5"-H), 8.084, 8.119 and 8.129 (s, 16H, β-pyrrolic-H) ppm. FAB MS: *m/z* 2943.8 $(M)^+$ (University of Nebraska-Lincoln); 2944.4 (UCSB) [calcd for $C_{172}H_{212}N_{12}O_{16}S_4Si_4$: 2944.2]. UV/Vis: λ_{max} (logε) 417 (5.77), 482.5 (3.79), 516 (4.47), 549.5 (3.96), 592.5 (3.96), 649 (3.68) nm. HPLC: (a) one peak, R_t = 2.90 min (2% isopropanol in chloroform, 1.0 mL/min); (b) two peaks, R_{t1} = 7.35min, R_{t2} = 7.92 min (1.5% pyridine in toluene, 0.50 mL/min). HR MS (MALDI)[27]: 2942.4272 (calcd. for M+H: 2942.4177).

ACKNOWLEDGMENT: This work was supported by the National Institutes of Health and Chiron Inc. of Emeryville, CA. The high resolution fast atom bombardment mass spectral determinations were performed by the Midwest Center for Mass Spectrometry with partial support by the National Science Foundation, Biology Division (Grant No. DIR9017262). We are grateful for the high resolution MS of **1** which was performed by Dr. John A. Castoro of Professor C. L. Wilkins' Laboratory at the University of California, Riverside.

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8 2-(2'-Bromo-5'-cyano)phenyl-1,3-dioxolane (**17**) R_f = 0.15 (10% ethyl acetate in hexanes). M.p.: 99 - 100 °C. ^{1}H NMR (500 MHz): δ 4.03 - 4.17 (m, 4H, 4,5-H), 6.044 (s, 1H, 2-H), 7.474 (dd, 1H, J = 8.5 and 2.0 Hz, 4'-H), 7.676 (d, 1H, J = 8.5 Hz, 3'-H), 7.870 (d, 1H, J = 2.0 Hz, 6'-H) ppm. ^{13}C NMR (50 MHz)[31b]: δ 65.57 (4,5-C), 101.45 (2-C), 117.82 (CN), 111.54 128.21, 131.44, 133.31, 133.95, 138.62 (aromatic) ppm. IR (KBr): 2979, 2908, 2229, 1593, 1467, 1388, 1090, 980 cm^{-1}. MS: *m/z* 254 (85%), 252 [(M - H)$^+$, (85%)]. $C_{10}H_8BrNO_2$: Calcd. C 47.27, H 3.17, N 5.51, Found C 47.05, H 3.22, N 5.32.
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23. SES-NH_2 was prepared from SES-Cl[22] and NH_4OH. We thank Professor Steven. M. Weinreb for providing the procedure for the preparation of SES-NH_2.
24. 2-Syn, 3-syn, 5-syn, 6-syn-Tetrakis[4'-(2"-formyl-4"-bromomethylphenyl)butoxymethyl]bicyclo[2.2.2]octane[33] was obtained in 90% yield from **24a** if no 2,6-lutidine present: R_f = 0.37 (9% diethyl ether in dichloromethane). ^1H NMR (500 MHz): δ 1.377 (s, 4H, 7,8-H), 1.55-1.65 (m, 16H, 2'-H and 3'-H), 1.667 (s, 2H, 1,4-H), 2.069 (s, 4H, 2,3,5,6-H), 2.983 (t, 8H, J = 7.0 Hz, 4'-H), 3.30-3.40 (m, 12H, 9,11-H and 1'-H), 3.53-3.58 (m, 4H, 10,12-H), 4.467 (s, 8H, $ArCH_2Br$), 7.220 (d, 4H, J = 8.0 Hz, 6"-H), 7.489 (dd, 4H, J = 8.0 and 2.0 Hz, 5"-H), 7.800 (d, 4 H, J = 2.0 Hz, 3"-H), 10.219 (s, 4H, CHO) ppm. ^{13}C NMR (50 MHz)[31b]: δ 15.96 (7,8-C), 28.73 (3'-C), 28.91 (1,4-C), 29.29 (2'-C), 31.71 (4'-C), 32.17 ($ArCH_2Br$), 38.28 (2,3,5,6-C), 70.03 (9,10,11,12-C), 70.30 (1'-C), 131.38 and 131.47 (3"-C and 6"-C), 133.68 (4"-C), 134.01 (5"-C), 136.04 (2"-C), 145.42 (1"-C), 191.32 (CHO) ppm. IR: 2900, 2850, 1680, 1600, 1560, 1208, 1155, 1100, 970 cm^{-1}.
25. Two different FAB MS facilities (UCSB and University of Nebraska-Lincoln) performed FAB MS of **1**.
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27. We are grateful for the high resolution MS of **1** which was performed by Dr. John A. Castoro of Professor C. L. Wilkins' Laboratory at the University of California, Riverside.

28. Hewlett Packard 1040 HPLC system with HPLC^{3D} ChemStation software were used. Seperation conditions: silica gel column, 1.5% pyridine in toluene, 1.0 mL/min. RT = 7.35 and 7.93 min.
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31 (a) Assignments are based on APT, ^{13}C - ^{1}H and ^{1}H - ^{1}H 2D NMR on Gemini-200. (b) Assignments are based on comparison with similar compounds. (c) 100% of deuterium chloroform was used after passing through a short column of anhydrous potassium carbonate to neutrilize trace amounts of acids.
32. *Tert*-butyllithium was titrated before use. See: Kofron, W. G. *J. Chem. Soc.*, **1976**, *41*, 1879
33. Benzyl bromide compounds **22d, 24b** and **2** are only stable at -20 °C for a few weeks. It is best to prepare them immediately prior to use.

(*Received in USA* 6 *May* 1994; *accepted* 1 *August* 1994)