J. Org. Chem. 1992, 57, 1555–1559

A Molecular Dynamics Approach to the Study of Symmetrical and Unsymmetrical Quadruply Bridged, Closely Interspaced Cofacial Tetraphenylporphyrin Dimers

Rafik Karaman, Örn Almarsson, and Thomas C. Bruice*

Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106

Received August 21, 1991 (Revised Manuscript Received November 6, 1991)

Gas-phase structural parameters for a series of symmetrical and unsymmetrical quadruply three- and five-atom, aza-bridged closely interspaced cofacial bis(5,10,15,20-tetraphenylporphyrins) were calculated by the molecular mechanics method CHARMm. Reasonably good linear relationships exist between the calculated interplanar distances of the two porphyrin rings and (i) the ^{1}H NMR chemical shifts of the pyrrolic N–H as well as *o*-phenylic-H resonances and (ii) the width of the UV/vis Soret band. Moreover, it was found that the global minima of all the dimeric porphyrins studied are associated with the closest approach of the porphyrin planes reached by "screwed down" conformations. By semiempirical and molecular mechanics calculations, the "screwed down" conformations are reached because the legs (N-substituted dibenzylamine) which separate the two porphyrin rings have global energy minima with folded conformations. In order to establish credence to the reliability of this computational approach we have examined the closely interspaced cofacial dimers **4a**, **4b**, and **5b** whose X-ray structures are known. The structures reached by CHARMm calculations were found to be roughly the same as the corresponding crystal structures. Thus, the average change in interplanar distance between the gas-phase calculated structure and the solid-state X-ray structure is only 0.05 Å. This indicates that the gas-phase calculations of the dimeric porphyrins are indeed capable of providing geometries that are in harmony with that in the crystal structures. In the absence of crystallographic data, the relationship of ^{1}H NMR and UV/vis absorbance to the calculated distance between porphyrin planes could be fruitful in providing a rapid and fairly reliable way to predict geometries and interplanar distances of porphyrin dimers. This will provide a useful guiding tool for designing models of a number of important enzymes.

Metal-centered closely interspaced cofacial porphyrin dimers are of considerable interest to chemists and biochemists alike due to their intriguing nature.[1] For example, they have been offered as models for a number of enzymes such as cytochrome c_3,[2] cytochrome-c-oxidase,[3] and others.[4] It is of great importance to design dimeric porphyrins such that certain distances and angles between the planes of the two porphyrin cores are realized. It is especially useful to juxtapose two porphyrins in cofacial proximity, so as to have a possibility of binding molecules such as dioxygen[5] and dinitrogen[6] to the two metals in the centers of the dimeric species. Of continuing interest in our laboratory is the synthesis and study of the properties of covalently linked cofacial tetraphenylporphyrin dimers.[7,8] The ^{1}H NMR and UV/vis spectral properties of these dimers are indicative of cofacial juxtaposition of the two porphyrin rings. The ^{1}H-NMR displays resonances that are dramatically upfield shifted as a result of one porphyrin being in the shielding region of the other. The absorption spectra show bandwidth broadening and blue shifting of the Soret band and red shifting of the visible bands compared to that of the corresponding monomeric tetraphenyl porphyrins.[9] Moreover, it has been shown that the chemical shifts of the N–H resonances and the bandwidths of the Soret bands of the dimeric porphyrins are largely determined by the closeness of the two porphyrin cores.[8] It occurred to us that these physical properties along with theoretical calculations could be used to predict distances between the two porphyrin planes of the dimers. In the absence of crystallographic data, the correlation between solution physical properties and gas-phase calculated properties may serve as a rapid and fairly reliable way to estimate interplanar distances of porphyrin dimers which could aid in designing models of a number of important enzymes.

Results and Discussion

We have explored the geometries of the porphyrin dimers by molecular mechanics empirical force-field calculations (CHARMm)[10] since higher level calculations by ab initio self-consistent-field molecular orbital (SCF-MO) procedures and semiempirical methods are expected to become cumbersome for these relatively large molecules.[11] In order to establish credence to the reliability of the CHARMm molecular mechanics computational approach, results from CHARMm have been compared to results calculated by AM1[12] and MNDO[13] semiempirical methods. The dimeric porphyrins **1a** to **1e** are held in place by four linkers of the general structure m-$C_6H_4CH_2N(Y)CH_2$-m-C_6H_4. The geometries of the linkers calculated by CHARMm were found to be comparable to structures calculated by AM1[12] and MNDO[13] semiempirical methods. Both molecular mechanics and semiempirical calculations show that the geometry associated with the global minima involves the folding of the linkers such that the cofacial porphyrin dimers **1a** to **1e** would be in a screwed down conformation. Further, the interconversion barrier between folded and a possible extended form is very high.

To investigate the interactions between the two porphyrin moieties in the dimers, the van der Waals energy

---

[1] For a review of the literature up to 1980, see: Dolphin, D.; Hiom, J.; Paine, J. B., III. *Heterocycles* **1981**, *16*, 417.

[2] Yagi, T.; Aruyama, K. *Biochim. Biophys. Acta* **1971**, *243*, 214.

[3] (a) Chang, C. K. *Adv. Chem. Ser.* **1979**, *173*, 162. (b) Chang, C. K.; Abdalmuhdi, I. *J. Org. Chem.* **1983**, *48*, 5388.

[4] (a) Winter, H. C.; Burris, R. H. *Annu. Rev. Biochem.* **1976**, *45*, 409. (b) Cohen, I. A. *Struct. Bonding (Berlin)* **1980**, *40*, 1.

[5] Chang, C. K. *J. Chem. Soc., Chem. Commun.* **1977**, 800.

[6] Collman, J. P.; Hutchison, J. E.; Lopez, M. A.; Guilard, R.; Reed, R. A. *J. Am. Chem. Soc.* **1991**, *113*, 2794.

[7] (a) Karaman, R.; Bruice, T. C. *J. Org. Chem.* **1991**, *56*, 3470. (b) Bookser, B. C.; Bruice, T. C. *J. Am. Chem. Soc.* **1991**, *113*, 4208.

[8] Karaman, R.; Bruice, T. C. Manuscript in preparation.

[9] Kagan, N. E.; Mauzerall, D.; Merrifield, R. B. *J. Am. Chem. Soc.* **1977**, *99*, 5484. See also ref 8.

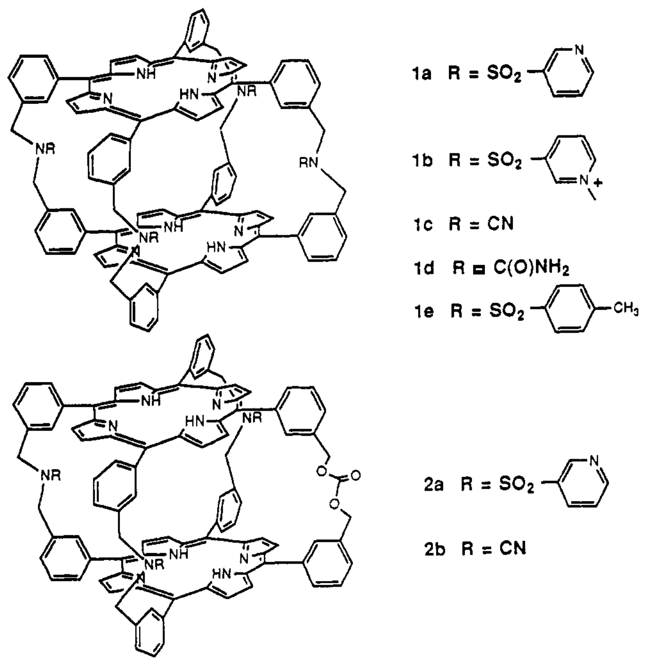
[10] Brooks, B. R.; Bruccoleri, R. E.; Olafson, B. D.; States, D. J.; Swaminathan, S.; Karplus, M. *J. Comput. Chem.* **1983**, *4*, 187.

[11] Clark, T. *A. Handbook of Computational Chemistry*; Wiley and Sons: New York, 1985.

[12] Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

[13] Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

0022-3263/92/1957-1555$03.00/0



of two 5,10,15,20-*meso*-tetraphenylporphyrin (TPP) molecules was calculated as a function of interplanar distance and dihedral angle (Φ = N1–Ct–Ct′–N1′ in Figure 1). The angle Φ was varied from 45° to 0° and the interplanar distances were varied from 7.5 to 3.6 Å (see Figure 1). Figure 2 shows the surface obtained by plotting the calculated energy values against interplanar distances and dihedral angles. The energy surface of the two TPP entities (Figure 2) reveals an energy minimum at 26° and 4.6 Å, amounting to 10.7 kcal/mol of van der Waals attraction. Similarly, calculations of two nonlinked porphine molecules (the basic porphyrin skeleton without phenyl rings) were done with interplanar distances ranging from 7.0 to 3.1 Å. In this case, no marked dependence of the angle was found and only a slight preference amounting to less than 1 kcal/mol exists for the eclipsed conformation (Φ = 0°). The optimal distance was found to be 3.5 Å, at a value close to two van der Waals radii of carbon as expected.[14] A comprehensive survey of the geometries of porphine dimers and aggreggates in the solid state reveals optimal interplanar distances around 3.5 Å on average, which supports our finding.[15] In the case of TPP, the slipping of the two planes relative to one another is impeded by the phenyl rings. Apparently, the presence of *meso*-phenyl rings incurs a considerable steric effect, resulting in an increase in optimal interplanar distance of 1.1 Å. In addition, angle dependence is greatly increased, as anticipated.

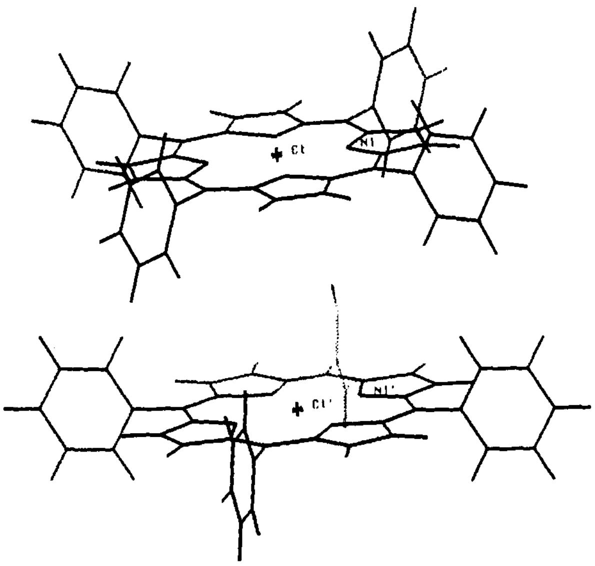


Figure 1. Two tetraphenylporphyrins (TPP's) in cofacial proximity. In D_{4h} symmetry (eclipsed form) the dihedral angle Φ (N1–Ct–Ct′–N1′) is 0°. If staggering is allowed the dihedral angle varies from Φ greater than 0 to 45°.

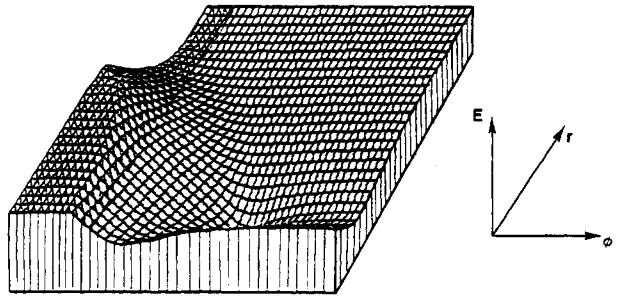


Figure 2. Three-dimensional energy surface for two TPP's interacting in cofacial juxtaposition. Φ is defined in Figure 1, *r* is the interplanar distance, and *E* is van der Waals interaction energy.

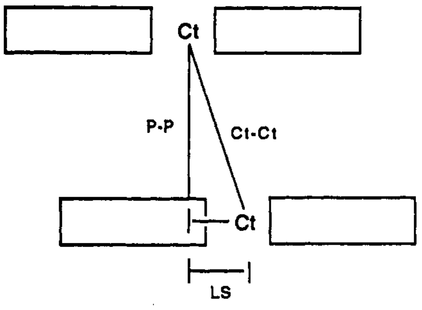


Figure 3. Schematic representation of the geometrical parameters used to describe the cofacial TPP dimers: Ct–Ct, center to center distance; P–P, interplanar separation; LS, lateral shift.

The final geometries for closely interspaced cofacial porphyrin dimers **1a–e** and **2a** and **2b** from molecular dynamics in CHARMm were analyzed in terms of the center to center distances (Ct–Ct), interplanar distances (P–P) and lateral shifts (LS) (see Figure 3 and Table I). The calculation results reveal that the size and the shape of the cavity between the two porphyrin rings are dependent on the nature of Y in the linker structure m-$C_6H_4CH_2N(Y)CH_2$-m-C_6H_4. Both the size and electronic environment of the group play dominant roles in determining the conformation of the dimer with global energy minimum. In the cases where Y represents large groups such as *p*-toluenesulfonamide or *m*-pyridinesulfonamide the interplanar distance of the porphyrin cores are shorter than in the case of a small groups such as cyanamide (see Table I). Moreover, the hybridization of the bridging nitrogen is also a determining factor. The more sp^3 character it displays, the more flexible the geometry and as a result the interplanar distance is shorter. In general, symmetrical dimers displayed approximate D_4 symmetry with a small lateral shift. An exception is the urea dimer (**1d**), in which the molecule assumed an offset geometry which allows the creation of two hydrogen bonding net-

---

[14] INDO semiempirical calculations show that the optimal distance between the planes of two porphines is 3.7 Å and that the planes are staggered but slipped relative to one another with a potential minimum of −5.6 kcal/mol. See: Surhindra, B. S.; Fuhrhop, J.-H. *Int. J. Quantum Chem.* 1981, *20*, 747.

[15] Scheidt, W. R.; Lee, Y. J. In *Structure and Bonding 64*; Springer-Verlag: Heidelberg, 1987.

Table I. ^{1}H NMR and UV/vis Spectral Data and Calculated Properties[a] of Quadruply Linked Dimers from Dynamics Simulation

				^{1}H NMR[b]				UV/vis[d]	
compd	Ct–Ct[e]	P–P[e]	LS[e]	δ(N–H)	Δδ(N–H)	δ(H2′)	Δδ(H2′)	*w*	Δ*w*
1a	5.03	5.00	0.28	−4.34	−1.64	7.04	−1.21	18.9	6.9
1b[f]	5.60	5.54	0.27	−5.4[c]	−2.70[c]				
1c	5.75	5.73	0.20	−3.85	−1.15	7.31	−0.94	18.1	6.1
1d	5.15	4.39	2.69	−4.35[c]	−1.65[c]	6.95[c]	−1.30[c]	20.0	8.0
1e	5.03	4.99	0.67	−4.42	−1.72	7.14	−1.11	19.1	7.1
2a[f]	5.52	5.32	1.46	−3.95	−1.25			19.0	7.0
2b[f]	5.36	5.35	0.34	−3.80	−1.10			19.0	7.0

[a] All distances are in Å. [b] Chemical shifts in ppm relative to TMS. Solvent used is $CDCl_3$, unless otherwise indicated. [c] Solvent used is DMSO-d_6. [d] Soret bandwidth at half-maximum in nm. [e] For the definition see Figure 3. [f] These have more than one H2′ resonance.

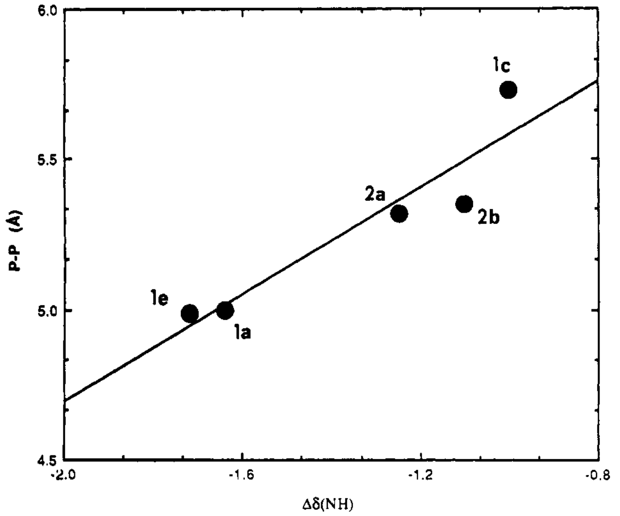


Figure 4. Interplanar distance in Å calculatd in CHARMm vs Δδ(NH) in ppm in $CDCl_3$.

works between adjacent amide sidechains. The cyanodimer (**1c**) was found to be quite extended in accord with the bridging nitrogens being almost complete sp^2 centers. The unsymmetrical dimers **2a** and **2b** were quite skewed, being perturbed by the relatively long and rigid carbonate linker.

The interplanar distances calculated from dynamics were plotted against ^{1}H-NMR chemical shifts of N–H in $CDCl_3$ and ortho phenylic-H (H2′) resonances to provide linear relationships with good correlation values, *r*, described by eqs 1 and 2, respectively. The correlation results of equations 1[16] and 2 are illustrated graphically in Figures 4 and 5, respectively.

$$\text{P–P} = 6.46 + 0.88\Delta\delta\text{NH} \qquad r = 0.96 \qquad (1)$$

$$\text{P–P} = 8.91 + 3.41\Delta\delta\text{H2}' \qquad r = 0.96 \qquad (2)$$

As anticipated, the gradual upfield shift of the N–H resonances in the series of the dimers studied (Table I) results from a decrease in separation between the two porphyrin rings; one porphyrin core experiences more of the shielding effect of the other as it comes closer to its shielding region. Comparison of the slopes of eqs 1 and 2 indicates that the H2′ resonances are affected more dramatically by the magnetic anisotropy of the two porphyrin rings than that of the pyrrolic N–H. This is confirmed by the calculated global minima structures which indicate that the ortho phenylic proton (H2′) is more directed into the shielding cone of the porphyrin moieties than N–H.

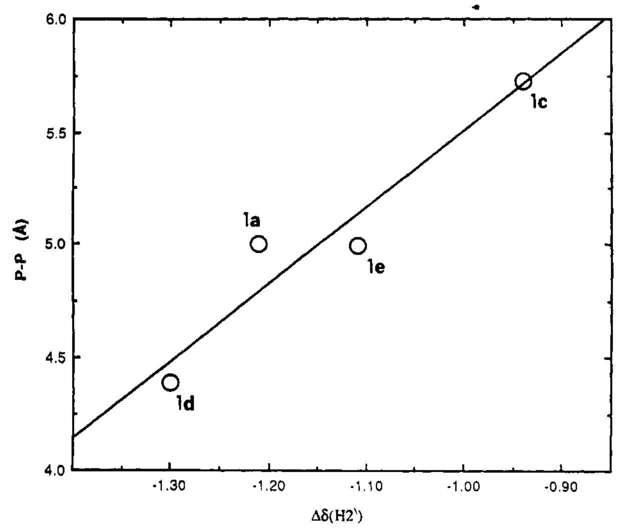


Figure 5. Interplanar distance in Å calculated in CHARMm vs Δδ(H2′) in ppm.

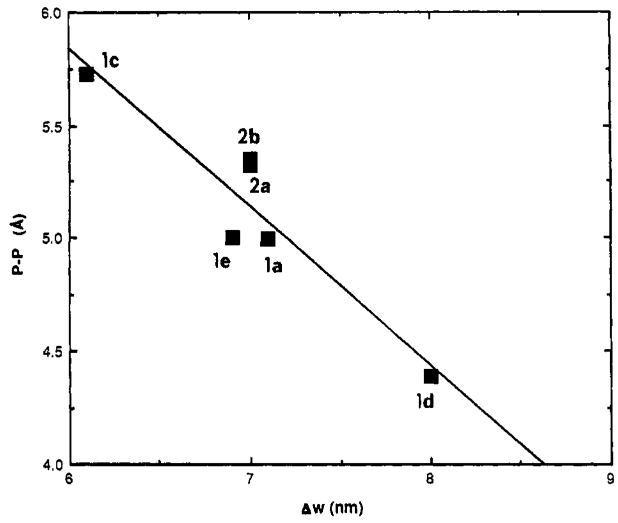


Figure 6. Interplanar distances in Å calculated in CHARMm vs Δ*w*(Soret) in nm.

The phenomenon of exciton coupling has been shown to become important when two porphyrins are brought together into cofacial proximity.[17] The increased band-

---

[16] The tetracationic bis-porphyrin **1b** was seemingly anomalous and was excluded from the correlation analysis. Apparently its geometry in the gas phase exhibits a larger interplanar separation than the solution structure in order to disperse the positive charges more effectively. Additional parameters for **1c** were taken from: Li, Y. S.; Durig, J. R. *J. Mol. Struct.* **1973**, *16*, 433. Force constants were chosen by comparison with those of similar functional groups already existing in the parameter set (e.g., C≡N was chosen to be the same as C≡C). If **1c** is excluded in the correlation analysis of equation 1, the equation obtained is P–P = 6.09 + 0.65ΔδNH (*r* = 0.99).

[17] Chang, C. K. *J. Heterocycl. Chem.* **1977**, *14*, 1285. See also ref 1.

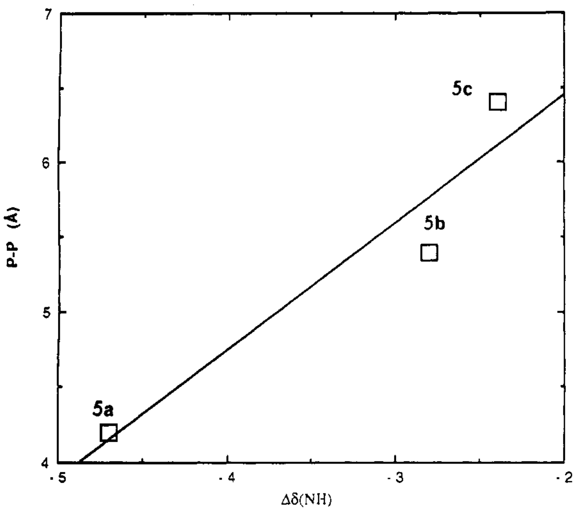
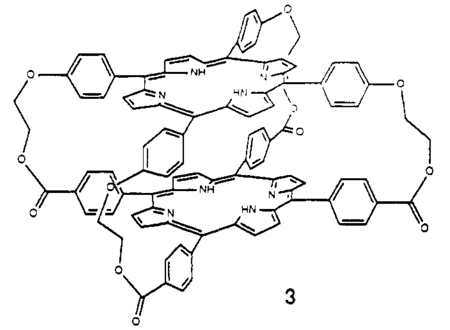


Figure 7. Interplanar distances of dimers **5a–c** in Å vs Δδ(NH) in ppm (data from ref 3a).

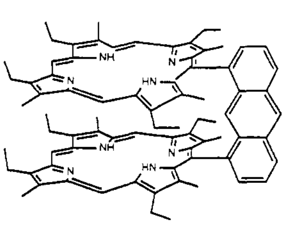
width of the Soret band is a good indication for the closeness of the two porphyrin cores. The magnitude of the Soret bandwidth is dependent on the interplanar distance similar to that seen with ^{1}H-NMR chemical shifts of the N–H resonances. The correlation results of eq 3, shown in Figure 6, indicate clearly the linear relationship between the width (Δw) of the Soret band and the calculated interplanar distances in the dimeric porphyrins.

$$\text{P-P} = 10.04 - 0.70\Delta w \qquad r = 0.94 \qquad (3)$$

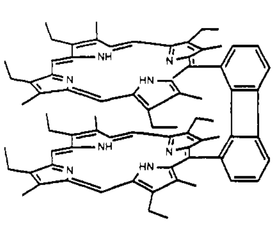
In order to further support our approach, five synthesized cofacial porphyrin dimers with known X-ray structures,[17] **4a**, **4b**, and **5a–c**, have been studied. A linear relationship between interplanar distance and chemical shift of the pyrrolic N–H resonances of **5a–c** was found (see eq 4 and Figure 7). The linearity is fairly good, and the slope of the line is quite comparable to that obtained for dimers **1a–e** and **2a,b** (see eq 1).



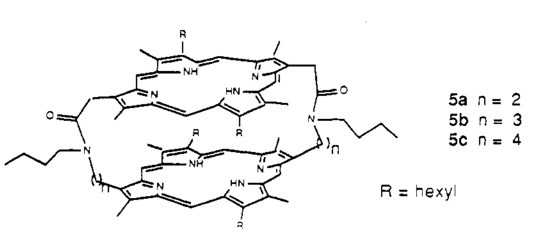
3



4a Anthracene linker



4b Biphenylene linker



$$\text{P-P} = 8.15 + 0.85\Delta\delta\text{N-H} \qquad r = 0.95 \qquad (4)$$

The uncertainty whether X-ray structures reflect the solution structure is of continuing concern. To test the extent to which the crystal packing determines the structures of the porphyrin dimers, the structures of compounds **4a**, **4b**, and **5b** were calculated by CHARMm. It was found that the calculated minimum structures are roughly the same as the crystal structures[18] and the average change in interplanar distance between the gas-phase calculated structure and the solid-phase X-ray structure is only 0.05 Å. This indicates that the effect of packing forces on the interplanar distances of the dimers is minimal and, therefore, calculations in the gas phase are indeed capable of providing geometries that are in harmony with that in the crystal structures. Further work is underway to explore the effects of different solvents on the conformations of the dimeric porphyrins.

Methods

The AM1 and MNDO calculations were done using the AMPAC package[19a] running on a VAX station 6100 computer. The starting geometries were obtained from the program Quanta (Polygen Corp.). The calculations were carried out by the standard AM1[12] and MNDO[13] programs based on the restricted Hartree–Fock (RHF) method. Geometries were optimized in internal coordinates and were terminated when Herberts test was satisfied in the Broyden–Fletcher–Goldfarb–Shanno method (BFGS).[19b] All optimizations were terminated when the change in energy on successive iterations was less than 0.00001 kcal/mol and the change in density matrix elements on two successive iterations was less than 0.001. All the calculations have been performed with full optimization of all geometrical variables (bond lengths, bond angles, and dihedral angles) without any symmetry constraint.

The CHARMm (Polygen Corp.) calculations and structure manipulations in the Quanta program were performed on a Silicon Graphics Iris 4D/220GTX workstation. Single leg linkers were created in the Quanta 2D modeling facility (Chemnote), and the topology file PORPHYRINH.RTF supplied by Polygen was used as a basis for the porphyrin moieties. Starting geometries for all dimers were intentionally selected as screwed down forms. Following extensive CHARMm minimization of the initial structures, dynamics simulations were performed in vacuo at 600 K for 110 ps to avoid possible local minima. A 3-ps heating phase was followed by 7 ps of equilibration and finally 100 ps of acquisition (collection phase). Molecular dynamics were performed using Verlet integration and the SHAKE algorithm to fix C–H bonds. The maximum allowable fluctuation in temperature was fixed at 25 °C. Nonbonded interaction and hydrogen bonding interaction lists were updated every 0.001 ps. Coordinates were written out every 50 steps (0.05 ps), resulting in 2000 structures in the collection phase. In each case, the collection phase results were divided into two parts and from each part a minimum was sought out. The resulting lowest energy conformations were minimized, and the lower of the two was taken as the global minimum. Minimizations were performed using steepest descent algorithm, followed by adopted basis Newton–Raphson algorithm until the energy change tolerance was less than 10^{-9} kcal/mol. Nonbonded interaction cutoff distance and hydrogen bonding cutoff distance were chosen to be 11.5 to 7.5 Å, respectively. The crystal structures of metalloderivatives of dimers **4a**, **4b**, and **5b** were obtained from the Cambridge structural data base (Refcodes DILSIA, DILSOG and CUHXPY10, respectively). These were modified by removing the metals and adding hydrogens to the

---

(18) (a) Fillers, J. P.; Ravichandran, K. G.; Abdalmuhdi, I.; Tulinsky, A.; Chang, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 417. (b) Kim, K.; Collman, J. P.; Ibers, J. A. *J. Am. Chem. Soc.* **1988**, *110*, 4242.

(19) (a) Dewar, M. J. S. *QCPE* 506, 15. (b) Cioslowski, J.; Kertesz, M. *QCPE Bull.* 1987, *7*, 159.

entire framework. Hydrogen atom minimization was performed to alleviate any unreasonable contacts resulting from the hydrogen adding process. The resulting structures were subjected to molecular dynamics in CHARMm and the minimum energy conformation compared to the initial structures obtained from hydrogen addition to the crystal structures.

Acknowledgment. This work was supported by the National Institutes of Health.

Registry No. **1a**, 138312-87-5; **1b**, 138312-88-6; **1c**, 138333-42-3; **1d**, 138312-89-7; **1e**, 138312-90-0; **2a**, 138312-91-1; **2b**, 138312-92-2; **4a**, 87597-38-4; **4b**, 88549-97-7; **5a**, 65599-38-4; **5b**, 65540-90-1; **5c**, 138312-93-3.

Supplementary Material Available: Cartesian coordinates for the CHARMm calculated minimum structures for dimers **1a–e**, **2a**, **2b**, **4a**, **4b**, and **5b** (38 pages). Ordering information is given on any current masthead page.

An Iterative and Convergent Synthesis of Syn Polyols

Scott D. Rychnovsky*[1] and George Griesgraber

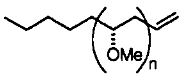
Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received November 20, 1991

We have developed a new iterative and convergent synthesis of alternating (1,3,5...) polyol chains based on enantiomerically enriched (94% ee) chloro nitrile 1. Chloro nitrile 1 is both a potential nucleophile and a potential electrophile; orthogonal nucleophilic or electrophilic activation leads to a highly efficient synthetic strategy for alternating polyol chains. As an illustration permethylated polyol 2 ($n = 10$), a natural product with 10 stereogenic centers isolated from the blue green alga *Tolypothrix conglutinata* var. *chlorata*, was prepared in 10 steps from 1.

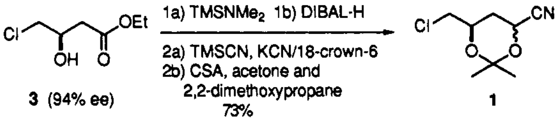
Numerous methods have been developed for the stereoselective synthesis of alternating polyol chains,[2] including several convergent approaches.[3] Our new strategy is based on the stereoselective reduction of cyanohydrin acetonides to give *syn*-1,3-diol acetonides.[4] The key synthon, cyanohydrin acetonide 1, is the precursor for both the nucleophilic and electrophilic components of a convergent coupling (Figure 1). Orthogonal nucleophilic or electrophilic activation of chloro nitrile 1 allows polyols to be synthesized in an iterative strategy reminiscent of solution peptide synthesis.

We have prepared a permethylated isotactic alternating polyol first isolated from the blue-green alga *Tolypothrix conglutinata* var. *chlorata*.[5] This alga produces numerous permethylated polyols of the general formula **2**, where $n = 8–10$. These permethylated polyols also have been isolated from blue-green algae belonging to the family scytonemataceae, along with homologues where $n = 5$ and 6.[6] Compound **2** ($n = 9$) has been prepared by two different groups,[3g,3e] and syntheses of permethylated polyols **2** ($n = 5$, 6, and 8) have been reported recently.[6] We report herein the first synthesis of permethylated polyol **2** ($n = 10$).



2 ($n = 5,6,8,9$ and 10)

Cyanohydrin acetonide **1** was prepared from ethyl (3*R*)-4-chloro-3-hydroxybutyrate (**3**), which is available in 94% ee from ethyl 4-chloroacetoacetate by Noyori's enantioselective reduction.[7] The single stereocenter in hydroxy ester **3** controls eight of the 10 stereogenic centers in the final product. Hydroxy ester **3** was silylated with $TMSNMe_2$ and reduced with DIBAL-H in Et_2O at −78 °C. The resulting aldehyde was treated with trimethylsilyl cyanide (TMSCN) and potassium cyanide/18-crown-6 complex[8] followed by protection with acetone, 2,2-dimethoxypropane, and catalytic camphorsulphonic acid. Cyanohydrin acetonide **1** was isolated as a 1.7:1 mixture of syn- and anti-isomers which were used without separation.[9] The overall yield from hydroxy ester **3** was 73%.



(1)

Electrophilic activation of chloro nitrile **1** requires displacement of the chloride with an iodide, and that is very difficult when an α-alkoxy substituent is present.[10c] After many unsuccessful attempts,[10] we found that iodide **4** could be prepared by treatment of chloride **1** with 20 equiv of powdered potassium iodide and 1 equiv of 18-crown-6 in refluxing xylenes for 36 h. Nucleophilic activation of nitrile

---

[1] Camille and Henry Dreyfus Teacher–Scholar, 1990–1995.

[2] Oishi, T.; Nakata, T. *Synthesis* **1990**, 635–645.

[3] (a) Mori, Y.; Kuhara, M.; Takeuchi, A.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5419–5422. (b) Mori, Y.; Takeuchi, A.; Kageyama, H.; Suzuki, M. *Tetrahedron Lett.* **1988**, *29*, 5423–5426. (c) Mori, Y.; Suzuki, M. *Tetrahedron Lett.* **1989**, *30*, 4383–4386. (d) Mori, Y.; Suzuki, M. *Tetrahedron Lett.* **1989**, *30*, 4387–4388. (e) Mori, Y.; Kohchi, Y.; Ota, T.; Suzuki, M. *Tetrahedron Lett.* **1990**, *31*, 2915–2916. (f) Nakata, T.; Suenaga, T.; Oishi, T. *Tetrahedron Lett.* **1989**, *30*, 6525–6528. (g) Nakata, T.; Suenaga, T.; Nakashima, K.; Oishi, T. *Tetrahedron Lett.* **1989**, *30*, 6529–6532. (h) Rychnovsky, S. D. *J. Org. Chem.* **1989**, *54*, 4982–4984.

[4] Rychnovsky, S. D.; Zeller, S.; Skalitzky, D. J.; Griesgraber, G. *J. Org. Chem.* **1990**, *55*, 5550–5551.

[5] Mynderse, J. S.; Moore, R. E. *Phytochemistry* **1979**, *18*, 1181–1183.

[6] Mori, Y.; Kohchi, Y.; Suzuki, M.; Carmeli, S.; Moore, R. E.; Patterson, G. M. L. *J. Org. Chem.* **1991**, *56*, 631–637.

[7] Kitamura, M.; Ohkuma, T.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1988**, *29*, 1555–1556.

[8] Evans, D. A.; Truesdale, L. K.; Carroll, G. L. *J. Chem. Soc., Chem. Commun.* **1973**, 55.

[9] All new compounds were characterized by ^1H and ^{13}C NMR, IR, analysis, and where appropriate MS.

[10] (a) Schurink, H. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, pp 476–478. (b) Landini, D.; Maia, A. M.; Montanari, F.; Pirisi, F. M. *Gazz. Chim. Ital.* **1975**, *105*, 863–874. (c) Willy, W. E.; McKean, D. R.; Garcia, B. A. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1989–1995. (d) Weiss, M.; Sasson, Y. *Synthesis* **1984**, 34–35. (e) Sasson, Y.; Weiss, M.; Loupy, A.; Bram, G.; Pardo, C. J. *Chem. Soc., Chem. Commun.* **1986**, 1250–1252. (f) Hahn, R. C. *J. Org. Chem.* **1988**, *53*, 1331–1333. (g) Hahn, R. C.; Tompkins, J. *J. Org. Chem.* **1988**, *53*, 5783–5785. (h) Clark, J. H.; Jones, C. W. *J. Chem. Res. Synop.* **1989**, 39.

0022-3263/92/1957-1559$03.00/0 © 1992 American Chemical Society