CHEMCOMM
Communication
www.rsc.org/chemcomm

Comment on 'Self-assembled multiporphyrin arrays mediated by self-complementary quadrupole hydrogen bond motifs'†‡

Gianfranco Ercolani*

Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata, Via della Ricerca Scientifica, 00133 Roma, Italy. E-mail: ercolani@uniroma2.it

Received (in Cambridge, UK) 20th February 2001, Accepted 4th June 2001
First published as an Advance Article on the web 12th July 2001

The self-assembly of discrete linear tapes claimed by the title communication is questioned on the basis of a rigorous thermodynamic analysis; moreover the reported thermodynamic data are not consistent with self-assembly of the square.

There is currently much interest in the preparation and isolation of monodisperse oligomers because of their technological applications.[1] In a recent communication in this journal,[2] Drain, Shi, Milic and Nifiatis (DSMN) reported ^{1}H NMR experiments aimed at supporting a strong bias in favour of well defined linear oligomers in solution simply by changing the stoichiometric ratio between monofunctional and bifunctional reactants capable of reacting with each other in a reversible addition reaction. In particular they claimed that mixing 5-[2,6-bis(acetylamino)-pyridin-4-yl]-10,15,20-tris(4-*tert*-butylphenyl)porphyrin and 5,15-bis[2,6-bis(acetylamino)pyridin-4-yl]-10,20-bis(4-*tert*-butylphenyl)porphyrin in a 2 : 1 stoichiometry leads essentially to a linear trimer (Scheme 1, $i = 1$) whereas using a 2:2 ratio a linear tetramer ($i = 2$) is formed in prevalence.

This approach which seems to be self-evident, would have a profound influence on the preparation of monodisperse linear oligomers, also in view of the fact that end-terminated oligomers would inhibit the competitive formation of cyclic species.[3] Owing to the importance of the observation, I believe that a warrant based on rigorous thermodynamic grounds is required.

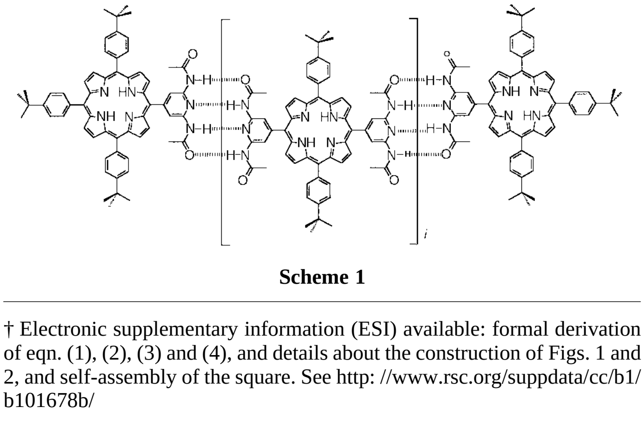
At first consider a monomer A–A (L_1) bearing two identical functional groups, capable of reacting with each other in a reversible addition reaction. If rings are assumed to be completely absent, a system initially composed of monomer units L_1, after equilibration, contains in principle an infinite number of linear oligomers L_i, i being the polymerisation degree. Let K be the equilibrium constant for the dimerisation of a monofunctional reactant R–A, if the association between end groups is independent of the length of the chain, then the oligomer distribution can be expressed as follows:†

$$[L_i] = (\sigma K)^{-1} x^i \qquad (1)$$

where σ is a symmetry number, that in the present case is equal to 4,§ and x is the fraction of reacted end-groups. Eqn. (1) is of course equivalent to the classical Flory distribution valid in the case of polycondensation.[4] The mass balance equation is given by eqn. (2)†

$$[L_1]_0 = (\sigma K)^{-1} x\,(1 - x)^{-2} \qquad (2)$$

where $[L_1]_0$ is the initial monomer concentration. Solving eqn. (2) for x, the weight fraction w_i of the oligomer L_i, can be easily evaluated.† In Fig. 1 are reported plots of the weight fraction of the first five oligomers as a function of $\sigma K[L_1]_0$. Extensive polymerisation occurs at high values of the product $K[L_1]_0$, whereas for the highest yield of a specific oligomer a specific $K[L_1]_0$ value is required. By inspection of Fig. 1, it results that with simple oligomerisation the yield of the dimer can be 30% at best, that of the trimer 19%, that of the tetramer 14% and that of the pentamer 11%. It would be very useful if by addition of appropriate amounts of a chain terminator R–A one could selectively increase the yield of a specific oligomer as suggested by DSMN.



Scheme 1

A mixture of a monofunctional reactant R–A (A) and of a bifunctional reactant A–A (L_1) will generate in solution the dimer of R–A (N_0) and three families of oligomers, namely L_i having both ends free, M_i having only one end free, and N_i having both ends terminated as the species shown in Scheme 1.¶ The oligomer distribution of L_i is still given by eqn. (1) whereas those of M_i and N_i are given by eqn. (3) and (4), respectively.†

$$[M_i] = [A]\, x^i \qquad (3)$$

$$[N_i] = K\,[A]^2\, x^i \qquad (4)$$

It is useful to consider the total concentration of the oligomers with the same polymerisation degree, $[R_i]$, obtained by summing eqn. (1), (3), and (4)

$$[R_i] = \{(\sigma K)^{-1} + [A] + K[A]^2\}\, x^i \qquad (5)$$

Let us define the term in parentheses as $(\sigma K_{app})^{-1}$, where K_{app} is an apparent constant at a given concentration of $[L_1]_0$ and $[A]_0$, then eqn. (5) can be rewritten as eqn. (6)

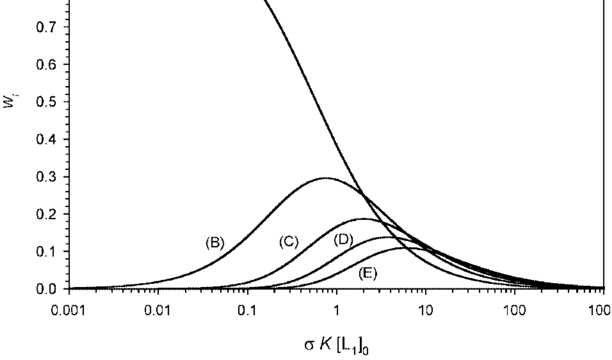


Fig. 1 Weight fraction of monomer, dimer, trimer, tetramer, and pentamer (curves from A to E, respectively) *vs.* $\sigma K[L_1]_0$.

---

† Electronic supplementary information (ESI) available: formal derivation of eqn. (1), (2), (3) and (4), and details about the construction of Figs. 1 and 2, and self-assembly of the square. See http: //www.rsc.org/suppdata/cc/b1/b101678b/

This journal is © The Royal Society of Chemistry 2001

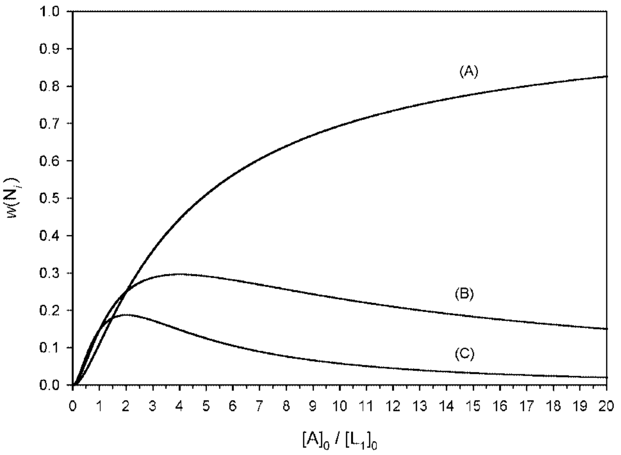


Fig. 2 Weighted fraction of N_0, N_1, and N_2 (curves A, B and C, respectively) *vs.* $[A]_0/[L_1]_0$ with K set very high.

$$[R_i] = (\sigma K_{app})^{-1}\, x^i \qquad (6)$$

which has the same form as eqn. (1). It is easy to show that now the mass balance equation has the same form as eqn. (2) with K replaced by K_{app}, therefore Fig. 1 can now be used to predict the weight fraction of R_i. Of course in no case can the weight fraction of the end terminated oligomer N_i, which is a part of R_i, be greater than the weight fraction of R_i, thus disproving the idea that specific stoichiometric ratios between $[L_1]_0$ and $[A]_0$ can drive the reaction toward a certain oligomer, as suggested by DSMN. An increase of $[A]_0$, of course, will cause an increase of [A], and consequently a decrease of the K_{app} value. This involves a shift to the left in the abscissa of Fig. 1, *i.e.* depolymerisation. An increase of [A] will also cause a change of the relative weight of each oligomer type within R_i disfavouring the L_i type; thus in the limit of $[A]_0$ tending to infinity only N_1 will be present in solution, apart of course from A and N_0. To further illustrate the extent of polydispersity, in Fig. 2 is reported the fraction of N_0, N_1, and N_2, weighted according to the content of functional groups, against the ratio $[A]_0/[L_1]_0$, with K set very high so that $[L_i] = [M_i] = 0$ and $[R_i] = [N_i]$.† It is evident from Fig. 2 that, although DSMN realised that linear self-assembly does not give pure N_1 and N_2, they certainly undervalued the extent of polydispersity. It also appears that the best $[A]_0/[L_1]_0$ value to obtain N_i is not $2/i$ but $4/i$.

It should be noted that the equilibrium constants reported by DSMN for the formation of the trimer and the tetramer (Scheme 1, $i = 1$ and 2, respectively), 110 $dm^6\ mol^{-2}$ and 70 $dm^9\ mol^{-3}$, respectively, are certainly wrong. Considering the value of the equilibrium constant for the dimerisation given by DSMN (K = 160 $dm^3\ mol^{-1}$) as a *bona fide* value, the constant for the formation of the trimer should be equal to $4K^2$, *i.e.* of the order of $10^5\ dm^6\ mol^{-2}$, and that of the tetramer $16K^3$, *i.e.* of the order of $10^8\ dm^9\ mol^{-3}$. In fact ^{1}H NMR cannot be used to assess the distribution of linear oligomer ; ^{1}H NMR records the average chemical shift of bound and unbound end groups, and since all the associations between end groups have the same probability of occuring, any experiment in which the total concentration of end groups is identical, no matter if they come from monofunctional or bifunctional reactants, will give the same chemical shift even if the distribution of the species actually present in solution are very different. This is demonstrated by the fact that DSMN found very similar $C_{1/2}$ values (the concentration at the half maximum increase in the chemical shift) for different linear self-assembly experiments. DSMN also reported that 5,10-bis[2,6-bis(acetylamino)pyridin-4-yl]-15,20-bis(4-*tert*-butylphenyl)porphyrin undergoes self-assembly to form a cyclic tetramer (a square), however the equilibrium constant they reported for the formation of the square (K_{square} = 2400 $dm^9\ mol^{-3}$) is not consistent with the reported $C_{1/2}$ value (0.8 mM). By assuming that the square and the monomer are the only species present in solution, a K_{square} value of $3.9 \times 10^9\ dm^9\ mol^{-3}$ can be estimated.† It appears therefore that DSMN made some serious computational error in the evaluation of K_{square}. If the value of K_{square} were that indicated by DSMN, self-assembly of the square would not occur.

I have reported a treatment for self-assembly macrocyclisations of a monomer of the type A–B.[5] One of the principal results of my treatment is that in order for self-assembly to be virtually complete in a certain range of initial monomer concentration the following condition must be verified [eqn. (7)], where EM is the effective molarity[6] of the self-assembled

$$\mathrm{EM}\ \sigma K \geqslant 185\ n \qquad (7)$$

ring, K is the equilibrium constant for the intermolecular model reaction, and n is the number of monomer units constituting the ring. Since $K_{square} = \mathrm{EM}(\sigma K)^4$, from a K_{square} value of $3.9 \times 10^9\ dm^9$, an EM of $\approx 0.02\ mol\ dm^{-3}$ can be calculated. According to eqn. (7) this value is too low to be compatible with complete self-assembly of the square. An approximate calculation indicates that the maximum molar fraction that can be reached by the square is about 67%.†

Another point regards the claimed quadruple hydrogen bonding. There is a general consensus that the most stable conformation of the amide linkage in 2,6-bis(acylamino)pyridines is *anti* and not *syn*,[7] as reported by DSMN; thus the subunits are probably just double hydrogen bonded. An example of a reversible polymer formed by a genuine quadruple hydrogen bond shows that such a bond can be very strong indeed ($K > 10^6\ dm^3\ mol^{-1}$).[8]

In conclusion the formation of discrete linear tapes by changing the stoichiometric ratio between monofunctional and bifunctional reactants is not supported by a rigorous thermodynamic analysis; the self-assembly of the cyclic tetramer should be re-examined in the light of actual knowledge in order to provide consistent thermodynamic data.

I thank both the referees for their helpful suggestions.

Notes and references

‡ Part 3 of the series Physical Basis of Self-Assembly. Part 2: G. Ercolani, D. Monti and M. Ioele, *New J. Chem.*, 2001, **25**, 783.

§ For the oligomerisation of a monomer A–B bearing two different functional groups the same equations hold but with $\sigma = 1$.

¶ Note that the species that DSMN call the dimer, the trimer and the tetramer are here defined as N_0, N_1, and N_2, respectively.

1 *Reactive Oligomers, (ACS Symposium Series, 282)*, ed. F. W. Harris and H. J. Spinelli, ACS, Washington, DC, 1985; C. V. Uglea and I. I. Negulescu, *Synthesis and Characterization of Oligomers*, CRC Press LLC, Boca Raton, FL, 1991; C. V. Uglea, *Oligomers Technology and Applications*, Marcel Dekker, New York, 1998; *Electronic Materials: The Oligomer Approach*, ed. K. Müllen and G. Wegner, Wiley-VCH, Weinheim, 1998.
2 C. M. Drain, X. Shi, T. Milic and F. Nifiatis, *Chem. Commun.*, 2001, 287.
3 G. Ercolani, L. Mandolini, P. Mencarelli and S. Roelens, *J. Am. Chem. Soc.*, 1993, **115**, 3901 and references therein.
4 P. J. Flory, *Principles of Polymer Chemistry*, Cornell University Press, Ithaca, 1953.
5 G. Ercolani, *J. Phys. Chem. B*, 1998, **102**, 5699.
6 A. J. Kirby, *Adv. Phys. Org. Chem.*, 1980, **17**, 183; L. Mandolini, *Adv. Phys. Org. Chem.*, 1986, **22**, 1.
7 F. H. Beijer, R. P. Sijbesma, J. A. J. M. Vekemans, E. W. Meijer, H. Kooijman and A. L. Spek, *J. Org. Chem.*, 1996, **61**, 6371.
8 R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lange, J. K. L. Lowe and E. W. Meijer, *Science*, 1997, **278**, 1601.

Typeset and printed by Black Bear Press Limited, Cambridge, England