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meso-Tetraarylporphyrins as dipolarophiles in 1,3-dipolar cycloaddition reactions

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***meso*-Tetraarylporphyrins participate, as dipolarophiles, in 1,3-dipolar cycloaddition reactions with azomethine ylides to yield novel chlorins and isobacteriochlorins.**

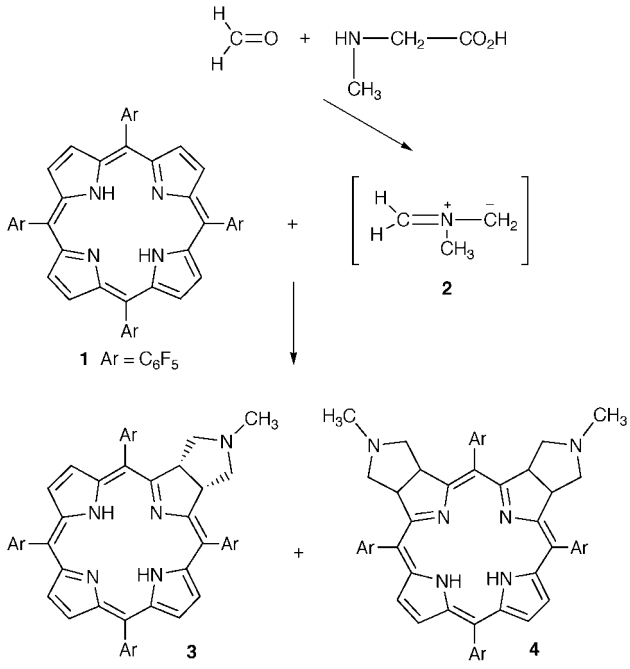
Recently we have shown that peripheral double bond(s) of the porphyrin nucleus can participate in Diels–Alder reactions.[1] The results of that work prompted us to investigate the behaviour of the porphyrins in other pericyclic reactions, namely in 1,3-dipolar cycloadditions with azomethine ylides.

A very simple approach to the generation of azomethine ylides involves the reaction of an aldehyde with an α-amino acid: the *in situ* thermal decarboxylation of the resulting imine gives the corresponding 1,3-dipole. Lately these transient species are being used extensively for the functionalization of fullerene C_{60}.[2]

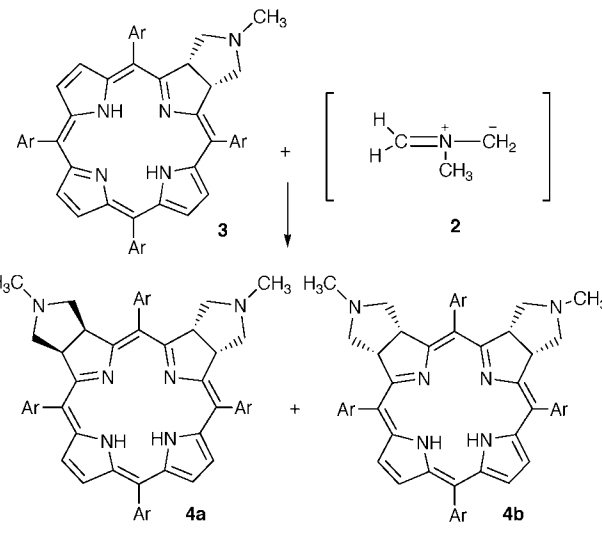
Here we report that azomethine ylides react with *meso*-tetraarylporphyrins to give, in good yields, pyrrolidine-fused chlorins and isobacteriochlorins.

Based on our previous results on the relative reactivities of the arylporphyrins in Diels–Alder reactions, we decided to use *meso*-tetrakis(pentafluorophenyl)porphyrin **1** as a dipolarophile in the reaction with azomethine ylide **2** (Scheme 1). A toluene (5 ml) solution of **1** (22 mg), *N*-methylglycine (4 mg, 2 equiv.) and paraformaldehyde (3.4 mg, 5 equiv.) was heated at reflux for 5 h under a nitrogen atmosphere. TLC of the reaction mixture showed that about half of the starting porphyrin was converted into two new products. Further portions of *N*-methylglycine (4 mg) and paraformaldehyde (3.4 mg) were then added and the resulting mixture was refluxed for another 5 h. The solvent was evaporated and the compounds were separated by column chromatography using a gradient of $CHCl_3$–light petroleum. The first fraction to be collected was the unchanged starting porphyrin (4.4 mg; 20%), then a chlorin (14.2 mg; 61%) and, finally, one isobacteriochlorin (2.8 mg; 11%) were eluted.

For the main product, the ^{1}H, ^{19}F and ^{13}C NMR and mass spectra, and its elemental analysis, are in agreement with structure **3**; also the UV-Vis spectrum of this compound is typical of a chlorin (λ_{max} = 652 nm).† The ^{1}H NMR spectrum of **3** shows, in the aliphatic region, a singlet at δ 2.21, corresponding to the N-CH_3 protons, and two multiplets at δ 2.52–2.56 and 3.11–3.16, corresponding to the methylene protons. Another multiplet at δ 5.24–5.27 was assigned to the resonance of the two β-pyrrolic protons of the reduced ring. In the aromatic region, four of the six β-pyrrolic protons appear as two doublets at δ 8.40 and 8.71 (*J* 4.9 Hz) and a singlet at δ 8.48 for the other two. The ^{19}F NMR spectrum of **3** shows two sets of equivalent pentafluorophenyl rings.‡ The mass spectrum of the minor product shows that it is a bis-adduct [$(M+H)^+$ = 1089]. On the basis of our previous results on the bis-addition of *o*-quinodimethanes to porphyrins we expected that this compound could be a bacteriochlorin. Surprisingly, its UV-Vis spectrum shows that it is an isobacteriochlorin (λ_{max} = 546 and 588 nm). In order to increase the amount of the bis-adduct, the chlorin **3** (21 mg) was treated with *N*-methylglycine and paraformaldehyde in refluxing toluene. After 40 h, and successive additions of small portions of the 1,3-dipole precursors, most of the chlorin was converted into bis-adducts (Scheme 2). Purification of the reaction mixture by preparative TLC gave several fractions. The one with higher R_f was the unchanged chlorin **3** (6.8 mg). The next two fractions (very small amounts) correspond to diasterioisomeric bacteriochlorins, on the basis of their mass [$(M+H)^+$ = 1089] and UV-Vis spectra (λ_{max} = 732 nm). The following fraction was the main product (8.3 mg); it is identical with the isobacteriochlorin previously obtained. The next fraction was also an isobacterio-



Scheme 1



Scheme 2

chlorin, but in a much smaller amount (1.2 mg) than the previous one. The last fraction (the one with lower R_f) was also obtained in small amount and was shown by MS (parent ion at *m/z* 1146) to be a 'tris-adduct'.

The formation of two isomeric isobacteriochlorins and two bacteriochlorins is not surprising since in the bis-adducts the two pyrrolidine rings can be in a '*cis*' or '*trans*' configuration. It is evident from the results of this experiment that the formation of the bis-adducts is regio- and stereo-selective, yielding mainly one of the four possible isomers. By analysis of the ^{1}H, ^{19}F, ^{13}C and 2D COSY and HETCOR NMR spectra of the two isobacteriochlorins we were able to establish their structures and configurations: the main product has structure **4a** and the minor one has structure **4b**. In the ^{1}H NMR spectra of these compounds, in addition to the expected aliphatic and aromatic proton resonances, a broad singlet appears at δ 4.12 for **4a** and at δ 4.08 for **4b**, corresponding to two protons in each case. These signals disappear after shaking with deuterium oxide and thus were assigned to the N*H* proton resonances.§ The ^{19}F NMR spectra of compounds **4a** and **4b** gave us important information for the establishment of the structure of these compounds as isobacteriochlorins. If the products were bacteriochlorins, then, due to the symmetry of the two possible diastereomers, all the pentafluorophenyl rings should be equivalent and only two signals would be expected for each group of *o*- and *m*-fluorine atoms, which is not the case. However, for the two possible diastereomers of isobacteriochlorin **4** three sets of non-equivalent pentafluorophenyl rings were expected, in the proportion 1:2:1, which is the case observed for compounds **4a** and **4b**. This fact is confirmed, in both isomers, by the integral values of the *p*-fluorine atoms (1F:2F:1F) in their ^{19}F NMR spectra. From the spectrum of compound **4b** we can conclude that: (i) the resonances attributed to the two *o*-fluorine atoms of the 5-phenyl ring are very different from each other (δ −133.32 and −137.62, 1F each), and the former have a quite different environment relative to all of the other fluorine atoms in the molecule; (ii) the phenyl rings at positions 10 and 20 are equivalent but again, in each ring, the two *o*-fluorine atoms are not equivalent (δ −136.66 and −139.73, 2F each); and (iii) the two *o*-fluorine atoms in the 15-phenyl ring are also not equivalent but have a similar environment (δ −139.26 and −139.53, 1F each). These results are only compatible with the structure of an isobacteriochlorin having a '*cis*' configuration. The ^{19}F NMR spectrum of compound **4a** shows that its structure must be more symmetrical than **4b**, since only four signals (δ−136.98, −137.16, −139.27 and −139.67) are observed for the *o*-fluorine atoms: one signal for the two *o*-F atoms in the 5-phenyl ring, two signals for the two non-equivalent *o*-F atoms in the equivalent 10- and 20-phenyl rings, and one signal for the two *o*-F atoms in the 15-phenyl ring. This spectrum is only compatible with the structure of an isobacteriochlorin having a '*trans*' configuration.

Table 1 Comparative reactivity and product yields of *meso*-tetraarylporphyrins with azomethine ylides

		Yield (%)	
meso-Aryl group	*t*/h	Monoadduct	Bis-adducts
C_6F_5	10	61	11
2,6-$C_6H_3Cl_2$	35	26	6
Ph	50	12	not observed

In order to find the effect of the substituents in the *meso*-aryl groups, we performed the same type of reaction (porphyrin, *N*-methylglycine and paraformaldehyde in refluxing toluene) with two other porphyrins. The results are presented in Table 1. It is evident from the results that the presence of electron-withdrawing atoms in the aryl groups increase the reactivity of the porphyrin towards azomethine ylides.

Work is in progress in our laboratory to extend these studies to other azomethine ylides and to other families of 1,3-dipoles.

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Notes and references

†*Selected data* for **3**: $\lambda_{max}(CHCl_3)$/nm [log (ε/10^3 dm^3 mol^{-1} cm^{-1})] 405 (5.29), 505 (4.26), 598 (3.77), 652 (4.72); *m/z* (LSIMS) 1032 $(M + H)^+$ (calc. for $C_{47}N_{17}N_5F_{20}$: C, 54.72; N, 6.79; H, 1.66; found: C, 54.69; N, 6.49; H, 2.10%).

‡ It is important to note that, for each pentafluorophenyl group, the two *o*-F and the two *m*-F are non-equivalent (they are coupled to each other, $^4J \sim 8$ Hz). This may result from the lack of free rotation of the pentafluorophenyl groups.

§ Similar chemical shift values (δ 2.98–3.65 ppm) were reported for N*H* protons of other isobacteriochlorins (ref. 3).

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