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Novel dodecaarylporphyrins: synthesis and dynamic properties

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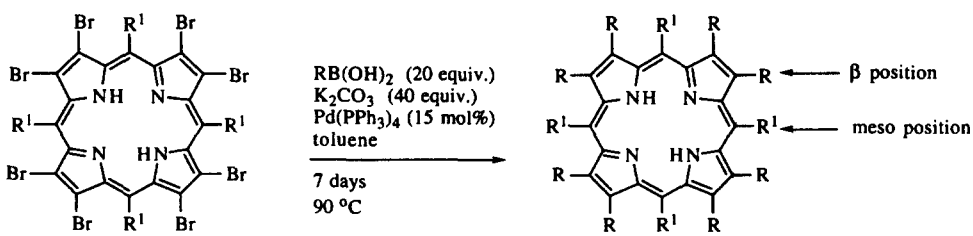
Abstract

An investigation of the synthesis of dodecaarylporphyrins using the Suzuki coupling reaction of arylboronic acids with octabromotetraarylporphyrins is reported. Variable temperature ^{1}H NMR studies of these new porphyrins reveal several dynamic processes including the first examples of β-aryl rotation.

For the past several years, interest has been expressed in the possible functional role of the nonplanar conformational distortions observed for some tetrapyrroles in biological systems.[1] One way the effect of these deformations has been investigated is by studying sterically crowded dodecasubstituted porphyrins such as octaethyltetraphenylporphyrin[2,3] (**2**) (Scheme 1, R=ethyl, R^1=phenyl) and dodecaphenylporphyrin[4] (**3a**) (Scheme 1, R=R^1=phenyl). These studies have demonstrated that nonplanar distortions can produce alterations in some biologically relevant features of porphyrins such as redox potentials and excited state properties.[1]



1 **porphyrins 2-8**

Scheme 1.

Despite major progress in the study of porphyrin nonplanarity, relatively little is known about the conformational flexibility and dynamic behavior of nonplanar porphyrins or whether these properties

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Table 1
Percent yields (unoptimized) for Suzuki coupling reactions

Porphyrin	R	R_1	%Yield
3a	phenyl	phenyl	58
3b	3-methoxyphenyl	phenyl	43
3c	2-methoxyphenyl	phenyl	14
3d	2,4,6-trimethylphenyl	phenyl	0[b]
4a	2-fluorophenyl	phenyl	0[a]
4b	2,6-difluorophenyl	phenyl	0[b]
4c	4-chlorophenyl	phenyl	48
4d	3,5-dichlorophenyl	phenyl	30
4e	2,4-dichlorophenyl	phenyl	0[a]
5a	phenyl	2,4,6-trimethylphenyl	31
5b	2-methoxyphenyl	2,4,6-trimethylphenyl	27
6a (nickel complex)	phenyl	phenyl	48
6b (nickel complex)	phenyl	2,3,4,5,6-pentafluorophenyl	52
7a	2-thienyl	phenyl	0[b]
7b	2-furanyl	phenyl	0[b]
7c	4-pyridyl	phenyl	0[b]
7d	3-thienyl	phenyl	19

[a]Mass spectral analysis revealed that some of the fully substituted porphyrin was obtained in this case; however, the reaction did not proceed to completion and separation of the target molecule proved to be impractical.
[b]None of the fully substituted porphyrin was observed by mass spectral analysis.

may also be relevant to biological function. Recent crystallographic[5,6] and excited state[7,8] studies of dodecaarylporphyrins (DAPs) (Scheme 1, R=aryl, R^1=aryl) have indicated that these molecules appear to access a wider range of nonplanar structures than other dodecasubstituted porphyrins. DAPs may therefore be interesting model compounds in which to investigate conformational and dynamic effects in nonplanar porphyrins. Unfortunately, DAPs can be difficult to prepare by the standard acid-catalyzed condensation of 3,4-diarylpyrroles and substituted benzaldehydes,[9,10] partly because of problems in preparing appropriately substituted pyrroles. Recently, Chan et al.[11] reported the application of the Suzuki coupling reaction[12] to the synthesis of DAPs from phenyl or *para*-substituted phenyl boronic acids coupled with octabromotetraarylporphyrins (Scheme 1), opening up the possibility of accessing a wider range of β-aryl substitutents. We now describe further studies of this reaction in which the steric and electronic features of both the boronic acid and the porphyrin macrocycle are varied and the limitations of the Suzuki reaction for incorporating β-aryl substituents are investigated. We also report preliminary variable temperature (VT) ^{1}H NMR studies of the new DAPs which reveal an unusually large number of dynamic processes.

The DAPs targeted for synthesis are listed in Table 1. To examine the usefulness of the Suzuki coupling, a series of reactions were carried out in which steric and electronic effects in the boronic acid were varied (entries **3a–d**, **4a–e**, **7a–d**). Steric (**3a** vs **5a**, **3c** vs **5b**), electronic (**6a** vs **6b**), and metalation effects (**3a** vs **6a**) in the octabromotetraarylporphyrin were also examined. Some of the β-aryl substituents were selected with the aim of manipulating the β-aryl rotational barrier so that this process, which has not previously been observed in porphyrins using VT NMR spectroscopy,[13] could be characterized. To this end, porphyrins were synthesized where the β-aryl rotational barrier should be raised by the presence of an *ortho*-substituent (**3c**), or lowered by incorporating smaller aryl groups (**7d**). In one porphyrin (**3b**), the β-aryl group was chosen to facilitate detection of β-aryl rotation with a minimal steric perturbation compared to an unsubstituted phenyl ring.

As can be seen in Table 1, the coupling reaction was successfully used to prepare porphyrins with a wide range of aryl substituents. It was found that the reaction tolerated some steric effects in the boronic acid (e.g. an *ortho*-methoxy group **3c**) as well as electron-withdrawing groups at the *meta* and *para* positions (**3b**, **4c**, **4d**). Difficulties were encountered when electron-withdrawing groups were placed at the *ortho* position of the boronic acid (**4a**, **e**) and when two *ortho* substituents were present (**3d** and **4b**). In two of these cases, **4a** and **4e**, the fully substituted porphyrin was observed via mass spectral analysis of the crude reaction mixture, although the mixture also contained substantial quantitites of intermediates with fewer β-aryl substituents. No fully aryl substituted porphyrin was observed when the boronic acid contained two *ortho* substituents. Problems were also seen during attempts to synthesize porphyrins with heteroatoms at the *ortho* position of the aryl ring (**7a,b**) or with strongly electron-withdrawing heterocycles (**7c**), but in the absence of these effects the heterocyclic DAP **7d** was successfully prepared. The reaction yields were not as dramatically affected by steric (**3a** vs **5a**, **3c** vs **5b**), electronic (**6a** vs **6b**), or metalation effects (**3a** vs **6a**) in the octabromotetraarylporphyrin. It even proved possible to make porphyrin **5b** which had no fewer than 16 *ortho* substituents.

The reason for the poor coupling seen in some of the reactions is not clear, but may be a result of competitive side-reactions such as hydrolytic deboronation of the boronic acid due to the presence of trace amounts of water (it is known that *ortho*-substituted boronic acids, especially 2,6-disubstituted acids containing either electron-donating or -withdrawing groups, are quite sensitive to hydrolytic deboronation under aqueous conditions).[12] However, given that the detailed mechanism of the Suzuki reaction in anhydrous conditions has not been elucidated, many other factors could also be contributing to the reduced yields.[12] Potentially, several of the DAPs that could not be synthesized and/or isolated may be accessible by varying the reaction parameters (e.g. increasing the boronic acid/porphyrin ratio, using borate esters, or changing the catalyst, base, or solvent). We are currently exploring some of these possibilities.

A detailed study of the conformational and the dynamic properties of the DAPs prepared in this work, as well as more conventional DAPs synthesized using acid-catalyzed condensations (e.g. **8** where R=phenyl, R^1=3-methoxyphenyl), was undertaken using X-ray crystallography, molecular mechanics calculations, and VT ^{1}H NMR spectroscopy.[14] As suggested by the earlier crystallographic[5,6] and excited state[7,8] studies, the DAPs were found to display complex conformational and dynamic landscapes. A total of four dynamic processes (NH tautomerism, macrocyclic inversion, β-aryl rotation, and *meso*-aryl rotation) were observed during VT ^{1}H NMR studies. This is the first time that β-aryl rotation in a porphyrin system has been studied using VT NMR spectroscopy.[13]

An unusual feature of the new DAPs is the strong dependence of the aryl rotational barriers on the substituents in the porphyrin core. For example, the activation energies ($\Delta G^{\ddagger}$) for rotation of the 3-methoxyphenyl groups in the dications of **3b** and **8** were quite different: 42 kJ mol^{-1} for β 3-methoxyphenyl rotation in **3b** and 91 kJ mol^{-1} for *meso* 3-methoxyphenyl rotation in **8**. In contrast, the barriers in the corresponding nickel complexes were almost the same: 54 kJ mol^{-1} for β 3-methoxyphenyl rotation in **3b** and 55 kJ mol^{-1} for *meso* 3-methoxyphenyl rotation in **8**. Interestingly, the activation energy for rotation of the β 3-methoxyphenyl groups in the dication of the sterically crowded porphyrin **3b**, is actually lower than that found for rotation of unsubstituted or *para* substituted aryl groups in metal complexes of *meso*-tetraarylporphyrins, where $\Delta G^{\ddagger}$ is typically 70±10 kJ mol^{-1}.[13] Further investigation revealed that the rotational barriers were strongly correlated with the conformation of the porphyrin macrocycle and whether the aryl groups were moved out of the porphyrin plane to facilitate rotation. In the case of the dications, crystal structures and molecular mechanics calculations showed a saddle conformation where the β-aryl groups were moved out of the porphyrin plane but the *meso*-phenyl groups remained in the porphyrin plane. The nickel complexes, however, were found to adopt saddle or ruffled structures with almost equal ease, allowing the β- or *meso*-aryl groups to move out of plane.

Molecular mechanics calculations gave barriers that agreed well with the observed activation energies for 3-methoxyphenyl rotation: 64 and 103 kJ mol^{-1} for β and *meso* 3-methoxyphenyl rotation in the dications of **3b** and **8**, and 58 kJ mol^{-1} for *meso* 3-methoxyphenyl rotation in the nickel complex of **8** (see Shelnutt et al.[15] and Song et al.[16] for a description of the force field used in the calculations).

This new information concerning β-aryl rotation in DAPs indicated that a process previously[4] observed for the dication of dodecaphenylporphyrin (**3a**) was β-aryl rotation rather than macrocyclic inversion. An estimate of the true barrier for macrocyclic inversion ($\Delta G^{\ddagger} \geq 84$ kJ mol^{-1}) was obtained from the dication of porphyrin **3c**, where macrocyclic inversion could be more readily studied because the *ortho*-methoxy groups substantially increased the barrier for β-aryl rotation. The inversion barriers in the free base porphyrins and dications of DAPs are now consistent with those seen for other dodecasubstituted porphyrins, where the dications have much higher inversion barriers than the free base porphyrins.[13]

The results reported here illustrate the utility of the Suzuki coupling reaction for the synthesis of dodecaarylporphyrins and show that a wide range of porphyrins can be prepared using this method. NMR studies of the DAPs also reveal an unusually large number of dynamic processes, suggesting that the conformational and dynamic properties of nonplanar porphyrins are worthy of further study. In this regard, dodecaarylporphyrins appear to be especially complex and challenging systems against which to evaluate current techniques and models for investigating porphyrin nonplanarity.

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