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Colorful Friedel–Crafts Chemistry of *meso*-Tetraarylporphyrins. An Unexpected Route to Porphyrinic Spiro Dimers

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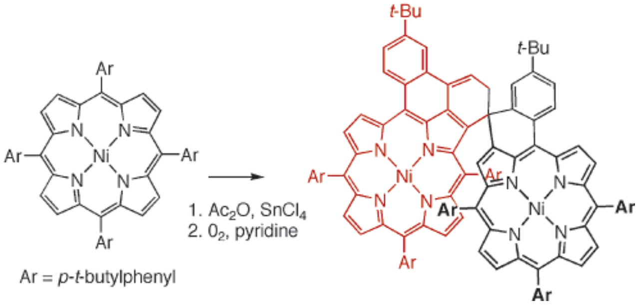
ABSTRACT



Under Friedel–Crafts conditions, *meso*-tetraarylporphyrins give porphyrin spiro dimers in good yield. This reaction involves acylation, acid-catalyzed cyclization, and dimerization. A stable dimer possessing three additional six-membered rings could be isolated and its structure determined. By modifying the substrate and reagents, intermediates could be isolated and characterized. The reactivity of the substrates, the side-reactions, and the concentration requirements to form the dimers, all explain why this reaction remained apparently unexplored in the widely used *meso*-tetraarylporphyrin series.

meso-Tetraarylporphyrins are the most accessible synthetic porphyrins, and thousands of articles describe their use as models for natural porphyrins. In addition to the easy variation of the *meso*-substituents, functionalization of their β-positions (halogenation, nitration, cyanation, etc.) allows the preparation of a variety of monomeric and oligomeric pigments.[1−3] Surprisingly, within this large number of synthetic reactions, the acylation of the β-pyrrolic positions is almost exclusively represented by the Vilsmeier−Haack formylation, while the classical Friedel−Crafts acylation is virtually unknown. This is in contrast with the β-alkylated porphyrins, whose Friedel−Crafts acylation at the free β-positions, if any, and in a few occurrences at the *meso* bridges, is well documented.[2,4]

Herein, we report the versatility of the Friedel−Crafts reaction applied to *meso*-tetraarylporphyrins, the variety of reactions following the initial acylation, the isolation of all reaction intermediates using hindered substrates and reagents, and the highly unexpected production of porphyrin dimers.

Reaction of nickel *meso*-tetraphenylporphyrin **1** (Ar = phenyl) with acetic anhydride and SnCl$_4$ as a Lewis acid

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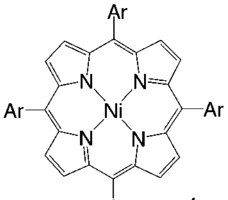
proceeded slowly, due to the insolubility of the substrate, and gave a complex mixture, even at low conversion. To improve the solubility, nickel *meso*-tetraphenylporphyrin **1** was replaced by nickel tetra-*p*-*tert*-butyl-phenylporphyrin **1** (Ar = *p*-*tert*-butyl-phenyl), which under the same conditions, gave green compound **2** (Ar = *p*-*tert*-butylphenyl) as the major product (19% after chromatographic purification; 100% conversion of **1**). This low yield is best explained by the air sensitivity of **2**, and we observed that, when exposed to air in solution, **2** gave brown compound **3** in high yield. This reaction proceeded faster in pyridine and could be run on the crude product from the acylation step to give **3** in 45−58% yield. We also noticed that both the conversion and the yield in dimers are a function of the initial concentration of starting material, the high concentration of porphyrin being a beneficial factor (for experimental details see, Supporting Information).



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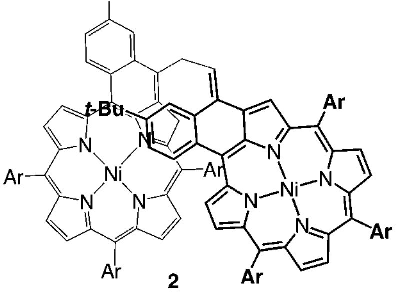

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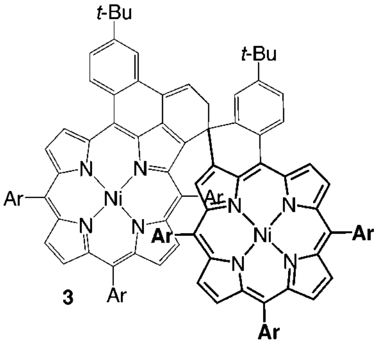
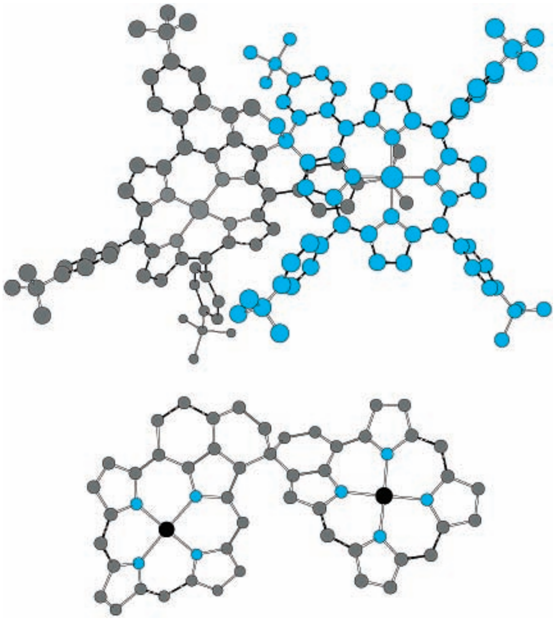


3

2,**3** Ar = *p*-*t*-butylphenyl

The structure of **3** was determined by X-ray diffraction. Compound **3** is a dimer whose two porphyrin units are connected by a spiro carbon common to two of the three new six-membered rings (Scheme 1). The two porphyrin rings are strongly distorted and saddle-shaped, and the angle between the two N4 planes is ca. 30°. It should be noted that one aryl group of one porphyrin points to the center of the other (central *tert*-butyl carbon-Ni = 4.26 Å). The NMR spectra of **3** (COSY + ROESY) showed signals and correlations that could be assigned to the two “northern” halves of the porphyrins and the spiro connection. As expected, the *tert*-butyl group close to a nickel atom is strongly shielded ($\delta = -0.69$ ppm).

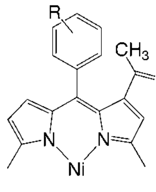
Scheme 1. X-ray Structure of Dimer **3**[a] (Hydrogen Atoms Ommitted for Clarity) and View of the Core of the Molecule



Although crystals suitable for X-ray study could not be obtained, the structure of **2** could be deduced from its NMR data (COSY + ROESY). As for **3**, these data allowed the full assignment of the signals of the cyclized *meso* aryl groups and the connecting carbon chain. The folding of dimer **2** in solution is illustrated by the high-field shift observed for two *tert*-butyl groups at δ 0.03 and −0.80 ppm. At variance with that of **3**, the UV−visible spectrum of **2** shows a strong long-wavelength absorption (674 nm), typical for a chlorin chromophore.

In the view of these surprising results, it is clear that we are dealing with a reaction sequence whose key steps are an acylation, an intramolecular cyclization involving the *meso*-aryl group, and a dimerization. To understand these transformations, we modified the nature of both the reagent and the starting porphyrin in the hope to block this reaction sequence at various stages. The *p*-*tert*-butylphenyl group was replaced by mesityl and 3,5-di-*tert*-butylphenyl in order to introduce either a substituent or a significant steric hindrance at the aromatic carbon involved in the cyclization. Acetic anhydride was in turn replaced by a hindered reagent, pivalic anhydride. In all cases, we used $SnCl_4$ as a catalyst and stirred the crude hydrolysis product in pyridine under an air atmosphere to isolate a stable dimer if any.

Nickel *meso*-tetramesitylporphyrin (**1**, Ar = 2,4,6-trimethylphenyl) reacted slowly with acetic anhydride to give as the only product the expected acetyl derivative **4** (R = 2,4,6,-trimethyl) (35 + 65% recovered starting material). When we turned to 3,5-di-*tert*-butylphenyl as the *meso* substituent, the reaction went further: acetylporphyrin **4** (R = 3,5-di-*tert*-butyl) was produced rapidly, but diene **6** (up to 63%) (R = 3,5-di-*tert*-butyl) formed at the expense of **4**.[5] However, alcohol **5** (R = 3,5-di-*tert*-butyl) was not among the products. These experiments confirmed that the Friedel−Crafts reaction occurred in high yield but also that the cyclization, similar to that of the β-formylporphyrins,[6−9] followed by an elimination, operated at an even faster rate when not inhibited.



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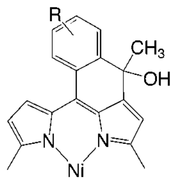

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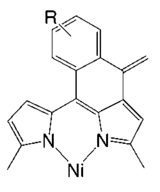

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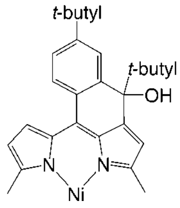

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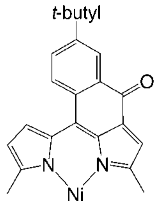

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When, in order to inhibit the elimination step, we replaced acetic anhydride by pivalic anhydride in the acylation of **1** (Ar = *p*-*tert*-butylphenyl), tertiary alcohol **7** analogous to **5** (methyl replaced by *tert*-butyl) was isolated (15%), in addition to ketone **8** (5%; synthesized independently using a known procedure[7]) and recovered starting material (13%). The loss of a *tert*-butyl group under oxidative conditions has precedents and explains the formation of ketone **8**.

The last steps, viz. the dimerization to **2** and the oxidation of **2** to **3** with concomitant formation of the spiro structure, may be viewed as (a) an acid-catalyzed C−C bond formation starting with two molecules of **6** to give **2** and (b) an allylic oxidation at one of the available sp^3 carbons (pyrrole or bridge) followed by an elimination of an oxygenated fragment from the product to give a triene, whose electrocyclization gives **3**.

The Friedel−Crafts acylation is a straightforward and efficient synthetic method, provided that the initial product does not have simple and intramolecular pathways for side reactions. This is obviously realized if one considers the *peri* positions of the acyl and *meso*-aryl groups. This neighboring group effect has already been illustrated in the porphyrin series by formyl[6−9] and vinyl group cyclizations,[10] electrocyclic ring formation,[11] or hydride transfer.[12]

Our results go further and show that a multistep sequence of reactions gives unexpected products such as porphyrin dimers. They also explain why the Friedel−Crafts acylation applied to simple *meso*-tetraarylporphyrins may have discouraged chemists earlier: not only does the reaction take an unexpected course, but, for substrates of low solubility, overreaction of the few porphyrins present in solution may hide the simple composition observed in favorable cases. These results also provide, in a one-pot and high yield reaction, an additional entry to unsymmetrical macrocyclic dimers, a porphyrin-chlorin like **2**, and a porphyrin-modified porphyrin like **3**. The study of the coordination chemistry and physical properties of these dimers is currently being investigated.

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Supporting Information Available: X-ray data for dimer **3**, NMR and UV−visible data for selected new compounds, and selected experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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