New chemistry of porphyrin β-ketoesters: synthesis of a novel covalently-linked dimer

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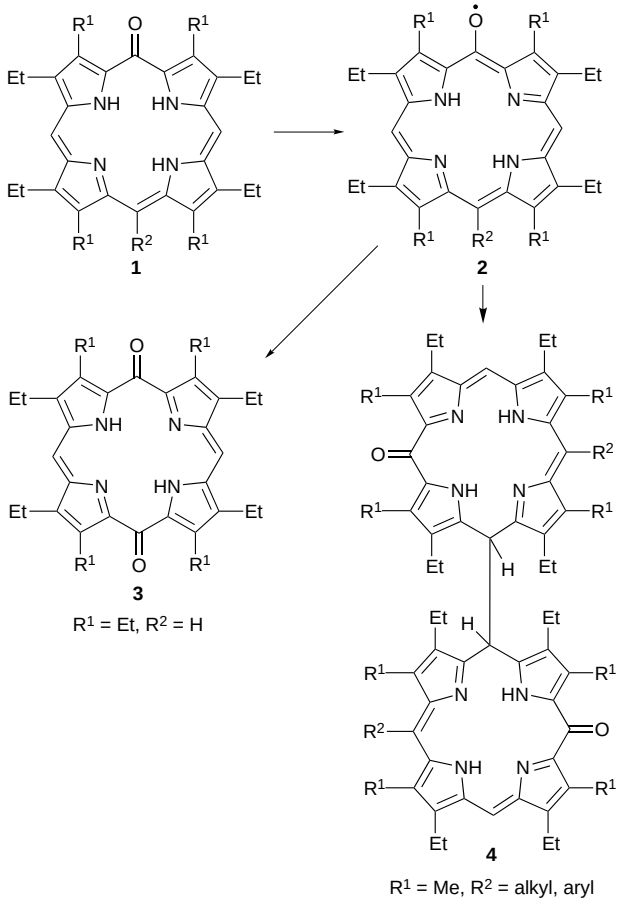
Porphyrinyl β-ketoesters dimerize to afford novel bistetrapyrrole systems by way of a radical process; the X-ray structure of one such bistetrapyrrole 14 is reported.

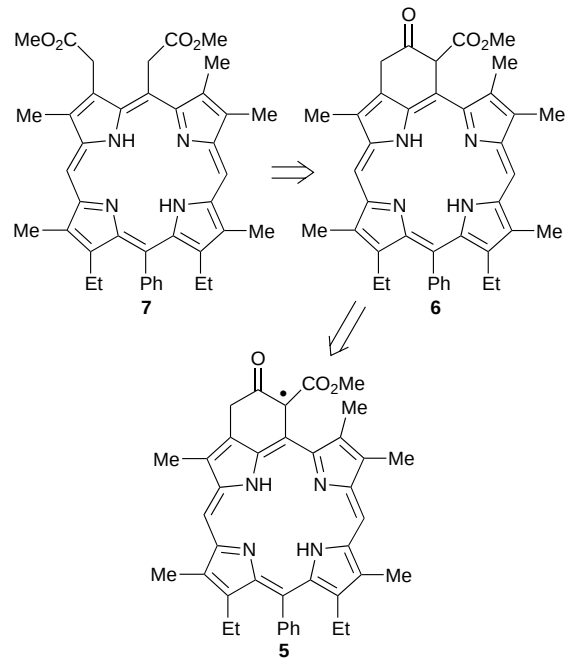
Oxophlorins **1** can be readily oxidized by dioxygen to form π-stabilized radicals **2**,[1] oxo derivatives **3**,[2] or covalently linked dimers **4**,[3] by mechanisms similar to those established in phenolic chemistry (Scheme 1).[4] An example of a very stable (sterically encumbered) oxophlorin π-radical was recently reported,[5] and although porphyrins can readily undergo one-electron oxidation (to give π-cation radicals) these transient species usually decompose to the parent porphyrin.[6] Based on knowledge of phenolic chemistry and its analogies with oxophlorin chemistry,[7] one might anticipate that any porphyrin system which could efficiently form a radical at a *meso*-benzylic atom (*e.g*. the carbonyl oxygen in oxophlorins, or a *meso*-benzylic methylene carbon) should undergo chemistry similar to that of oxophlorins (*e.g*. carbon–carbon dimerization, reaction with dioxygen). Literature precedent suggests[8] that benzylic porphyrin radicals (*e.g*. **5**) should, in principle, be accessible through porphyrins (*e.g*. **6**) suitably substituted with β-ketoester substituents (Scheme 2).

The precursor **7** of **6** was synthesized using established pyrrole chemistry; it was initially anticipated that Dieckmann cyclization of **7** would give **6**. The Michael acceptor pyrrole **8** was obtained from the formylpyrrole **9** by way of a Horner–Wadsworth–Emmons reaction (Scheme 3). Treatment of **8** with the 2-unsubstituted pyrrole **10** in refluxing acetic acid containing TFA gave the unsymmetrical dihydrodipyrrin **11**,[9] which upon catalytic bisdebenzylation gave **12**. MacDonald ('2 + 2') condensation between **13**[10] and the unsymmetrical dihydrodipyrrin dicarboxylic acid **12** in the presence of acid and zinc acetate, followed by removal of zinc with acid and then a basic work-up, did not yield the expected porphyrin **7**. Instead, a green compound was isolated (λ_{max} 424, 606 nm). ^{1}H NMR spectroscopy indicated a non-conjugated macrocycle had been formed [δ 12.67, 11.51 (each s, 1 H, NH)]. X-Ray crystallographic analysis‡ (Fig. 1) confirmed the structure of the compound to be the novel 10, 10′-bismacrocycle **14**. The linking 10,10′ carbon–carbon bond length is 1.58 Å. Along with dimer **14**, porphyrins **15** and **16** and the hydroxy-substituted chlorin **17** [λ_{max} 424, 606 nm; δ 11.50, 8.93 (each br s, 1 H, OH)] were isolated. The structural assignment of **17** is based on spectroscopic similarities between **17** and the analogue in the 15-unsubstituted series, for which an X-ray crystal structure (not shown) has been obtained.

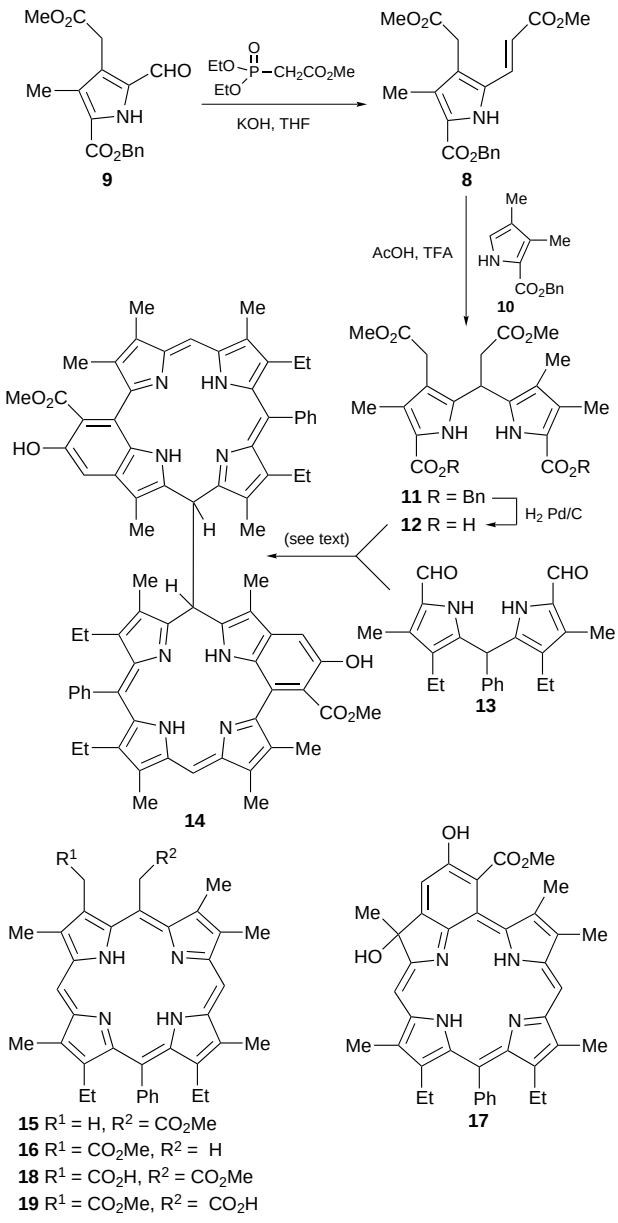
It was possible to isolate the target dimethyl ester porphyrin **7** in good yield by purifying the crude reaction mixture on neutral alumina instead of silica gel. Based on observations of the reactivity of **7** it became clear that the β-ketoester function



Scheme 1



Scheme 2



Scheme 3

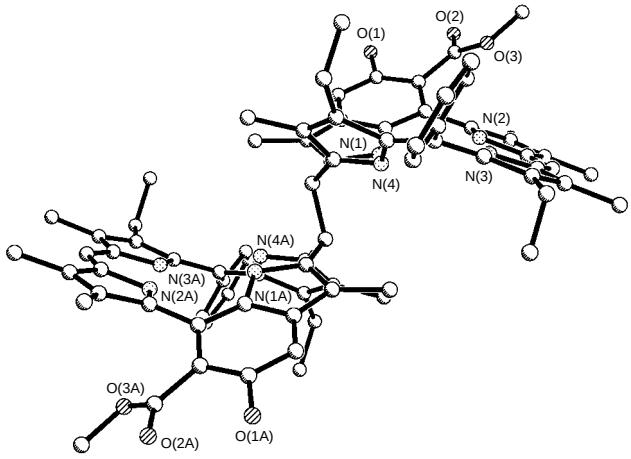


Fig. 1 Molecular structure of dimer **14**

was not being formed by way of a base-catalysed Dieckmann process upon **7**. Subsequently, non-basic methods were developed to permit the controlled synthesis of covalent dimer **14** (by way of **6**), and the side products, simply by adsorbing porphyrin **7** on silica gel under CH_2Cl_2 for 14 h. Presumably, water present on the silica gel makes it possible for small amounts of the bis(methoxycarbonylmethyl)porphyrin **7** to hydrolyse and form monocarboxylic acid by-products such as **18** and **19**. At this point, decarboxylation would form porphyrin **15** (or **16**, depending upon which ester has been hydrolysed) or it could follow a mechanism to form the corresponding 'anhydro' derivative. The so-called anhydro-reaction[12,13] proceeds reversibly by way of an acid catalysed equilibrium which, in this case, would be driven by formation of the β-ketoester moiety on the periphery of the porphyrin **6** *via* attack by the methylene adjacent to the remaining ester in **18** upon a putative acylium species formed from its acetic acid substituent.

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Footnotes

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‡ *Crystal data* for **14**. Crystals were grown from CH_2Cl_2–cyclohexane. A parallelepiped single crystal was selected with dimensions 0.18 × 0.13 × 0.05 mm. The unit cell was triclinic $P\bar{1}$ with cell dimensions a = 11.208(2), b = 12.474(3), c = 14.368(3) Å, α = 78.35(3), β = 76.86(3), γ = 83.98(3)°, V = 1912.2(7) Å^3, and Z = 2 (FW = 748.7). X-ray diffraction data were collected on a Siemens $P2_1$ diffractometer with a fine-focus sealed tube [λ(Cu-Kα) = 1.54178 Å] at 130(2) K in θ–2θ scan mode to $2\theta_{max}$ = 112°. Of 5278 reflections measured ($\pm h,\pm k,\pm l$) 3283 were independent and 1932 had $I > 2\sigma$ (R_{int} = 0.039). The structure was solved by direct methods and refined (based on F^2 using all independent data) by full-matrix least-squares methods (Siemens SHELXTL V. 5.02); number of parameters = 441. Hydrogen atom positions were located by their idealized geometry and refined using a riding model. An absorption correction was applied using XABS2.[11] Final R factors were $R1$ = 0.083 (based on observed data) and $wR2$ = 0.1998 (based on all data). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/406.

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