Pergamon

Tetrahedron Letters 41 (2000) 7423–7426

TETRAHEDRON
LETTERS

The polymer-supported MacDonald-type porphyrin synthesis: coupling of two dissimilar dipyrromethanes

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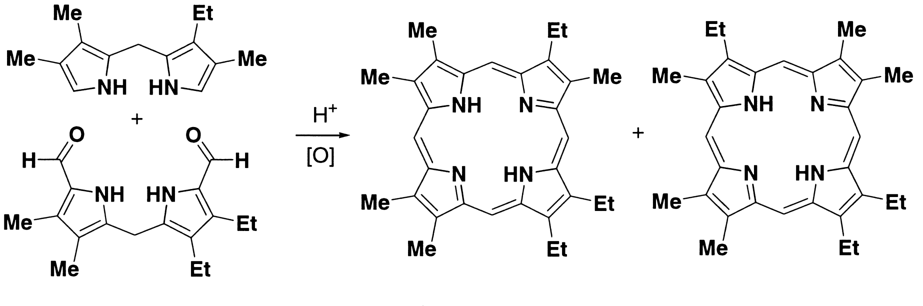
Received 13 July 2000; accepted 26 July 2000

Abstract

Syntheses of two completely unsymmetrical porphyrins have been achieved by MacDonald-type condensations of polymer-bound 9-formyldipyrromethanes with dissimilar solution-phase dipyrromethanes. The chemoselectivity of the process depends on the nature of the substituents at the α positions of the substrates. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: cyclization; dipyrromethanes; porphyrins; pyrroles; polymer support.

The MacDonald porphyrin synthesis[1,2] is a useful strategy for preparing porphyrins with C_2 or higher symmetry. In principle it can be applied to the synthesis of less symmetrical porphyrins by the condensation of dissimilar dipyrromethanes, but this method is rarely used because the components can couple in more than one way to give products which are typically difficult to separate, e.g. Scheme 1.



Scheme 1.

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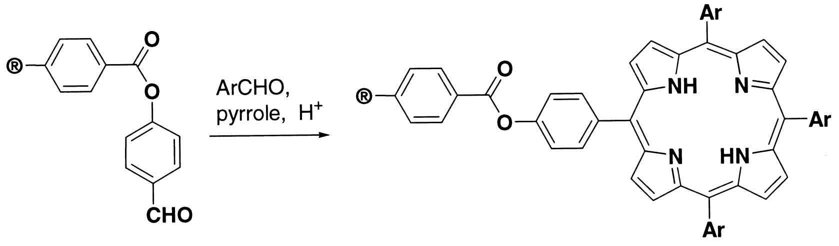
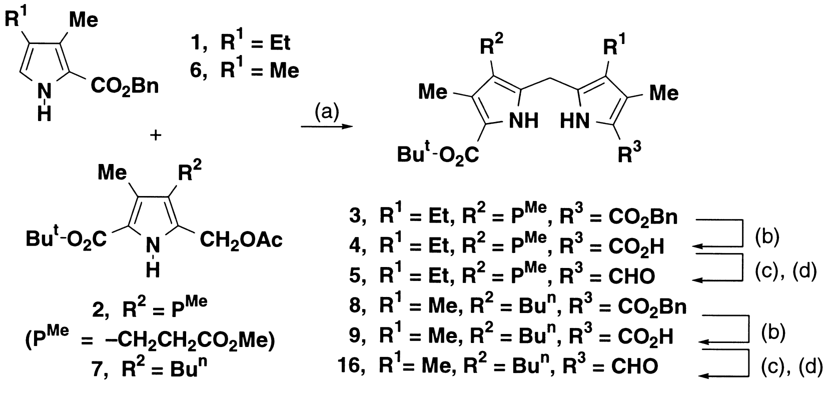
PII: S0040-4039(00)01269-7

By linking one of the dipyrromethanes to a solid support, however, the synthesis and purification of single completely unsymmetrical porphyrins should be possible.[3] In a very early study by Leznoff and Svirskaya,[4] a minor unsymmetrical porphyrin product was prepared on a polymer support (® in Scheme 2) in a reaction mixture in which the major symmetrical porphyrin product formed in solution and was easily washed away.



Scheme 2.

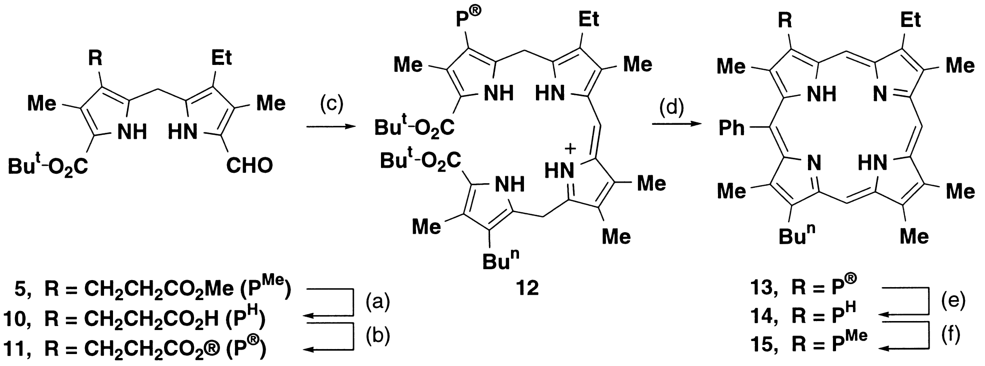
We chose to explore the potential chemoselectivity benefits of solid phase methodology on the MacDonald process. The α-free pyrrole **1**[5] was coupled with acetoxymethylpyrrole **2**[6], using Montmorillonite K10 clay as the acid catalyst, to yield dipyrromethane **3**. Cleavage of the benzyl ester gave acid **4**, which was decarboxylated and then formylated (Vilsmeier) to give formyldipyrromethane **5** (Scheme 3).



Scheme 3. (a) Montmorillonite K10 clay, CH_2Cl_2, 25°C; (b) H_2, Et_3N, THF, Pd–C, 25°C; (c) *p*TsOH, CH_2Cl_2, 25°C; (d) $POCl_3$, DMF, K_2CO_3, CH_2Cl_2, 0–25°C; **5**, 35% from **1**; **16**, 46% from **6**

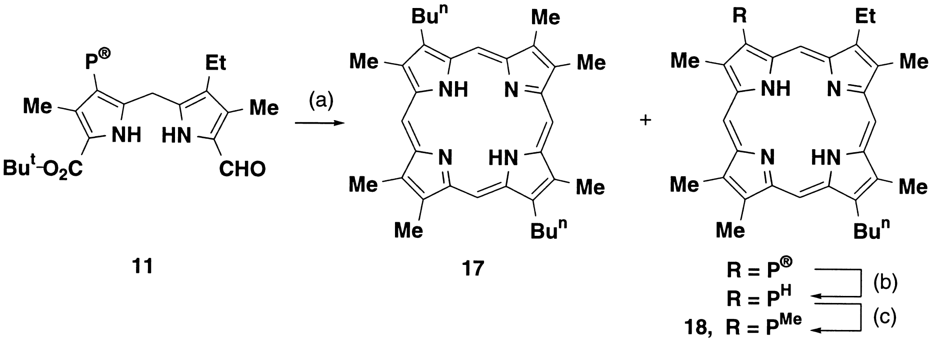
Similarly, α-free pyrrole **6**[7] was coupled with pyrrole **7**[8] to give benzyl ester **8**, which upon hydrogenolysis gave protected dipyrromethane **9**.

Saponification of the side-chain methyl ester of **5** yielded acid **10**, whose sodium salt was attached to Merrifield polymer as **11** in loadings as high as 0.87 meq g^{-1}. Coupling of polymer-supported **11** with solution-phase **9** yielded polymer-bound tetrapyrrole **12**. An initial ring closure attempt using trimethyl orthoformate failed, but treatment of **12** with TFA, *p*TsOH, and benzaldehyde gave polymer-supported porphyrin **13**. Saponification of **13** followed by esterification of the crude acid **14** gave methyl ester **15** completely free of isomers, confirming the complete chemoselectivity of the sequence (Scheme 4).



Scheme 4. (a) LiOH, THF, H_2O, 25°C, 18 h, 100%; (b) NaOH, H_2O, then 2% crosslinked Merrifield's resin, THF, 65°C, 48 h; (c) **9**, *p*TsOH, MeOH, CH_2Cl_2, 65°C, 48 h; (d) PhCHO, *p*TsOH, CH_2Cl_2, 45°C, 120 h, then O_2, CH_2Cl_2, 72 h; (e) *n*Bu_4NBr, KOH, THF, H_2O, 65°C, 48 h; (f) MeOH, H_2SO_4, 25°C, 18 h, 2.4% from **11**

As a control we then allowed the same polymer-supported formyldipyrromethane **11** to couple with a second, solution-phase *formyl*dipyrromethane, to determine the competition between formation of the polymer-supported unsymmetrical porphyrin and self-condensation of two molecules of solution-phase component. Decarboxylation of **9** followed by Vilsmeier reaction gave an appropriate formyldipyrromethane **16** (Scheme 3). Condensation between **11** and **16** followed by hydrolysis and esterification gave rise to pure, unsymmetrical **18** (Scheme 5). The symmetrical porphyrin **17** was readily washed away from the resin prior to liberation of **18**.



Scheme 5. (a) **16**, CH_2Cl_2, 25°C, 0.5 h; then, *p*TsOH, CF_3CO_2H, O_2, 48 h, filter; (b) *n*Bu_4NBr, KOH, THF, H_2O, 65°C, 48 h; (c) MeOH, H_2SO_4, 25°C, 18 h, 15% from **11**

Although the condensation between **11** and **16** was carried out using 1, 2, and 4 equivalents of the latter, the yield of unsymmetrical porphyrin **18** was found to vary very little, remaining in the 15–20% range. Not surprisingly, the yield of the easily separated symmetrical porphyrin **17** was the greatest with the largest excess of **16**. Thus, in addition to demonstrating the compatibility of polymer-support strategies with the standard methodologies of pyrrole manipulation and porphyrin synthesis, this system represents another case where the polymer-supported reaction affords significant practical benefits for the preparation and isolation of a cross-coupled product for which no inherent selectivity exists with respect to symmetrical byproduct formation.[9]

Acknowledgements

Acknowledgment is made to the National Science Foundation by N.E.S. for support of research in polymer-supported synthesis (CHE-97-10286) and by K.M.S. for support of research in porphyrin synthesis (CHE-99-04076). We also acknowledge a research fellowship to A.G.D. from the MURPPS (Minority Undergraduate Research Participation in the Physical and Mathematical Sciences) program at UC Davis.

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