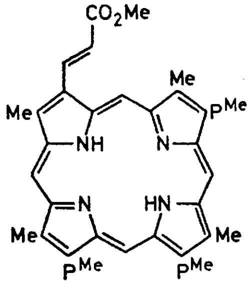
Protiodeacetylation of Porphyrins and Pyrroles: A New Partial Synthesis of Dehydrocoproporphyrin (S411-Porphyrin)

By KEVIN M. SMITH* and KEVIN C. LANGRY
(*Department of Chemistry, University of California, Davis, California* 95616)

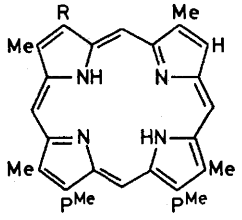
Summary Treatment of copper(II) complexes of acetylporphyrins with ethanedithiol and boron trifluoride–ether in acetic acid efficiently accomplishes deacetylation of the porphyrin system, and this reaction is demonstrated in a new partial synthesis of dehydrocoproporphyrin (S411-porphyrin); acetylpyrroles are also quantitatively deacetylated under these conditions.

PROTIODEVINYLATION[1] of hemins is one of the cornerstones of manipulative porphyrin chemistry.[2] In this surprising reaction the vinyl groups in hemins are replaced with hydrogens by fusion in resorcinol.[3] We now show that acetyl groups on porphyrin systems can also be efficiently removed, under somewhat milder conditions, and we demonstrate the effectiveness of this new transformation in a partial synthesis of the tetramethyl ester (**1**) of dehydrocoproporphyrin (S411-porphyrin). Dehydrocoproporphyrin is an important mono-acrylic porphyrin which is found in meconium and which was recently fully characterized by Jackson and his co-workers.[4]

During the course of studies on the protection of porphyrin acetyl groups[5] we showed that treatment of, for example, 2-acetyldeuteroporphyrin IX dimethyl ester (**2**) with ethanedithiol and boron trifluoride–ether in acetic acid at 60 °C for one hour gave a good yield of the expected dithio-

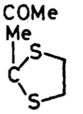


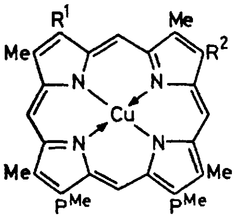
(1)

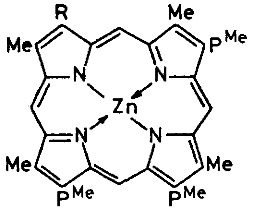


(2) R = COMe

(3) R =







$p^{Me} = CH_2CH_2CO_2Me$

(4) R^1 = COMe; R^2 = H

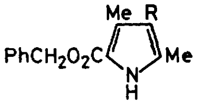
(5) $R^1 = R^2$ = H

(6) R^1 = COMe; $R^2 = p^{Me}$

(7) R^1 = H; $R^2 = p^{Me}$

(8) R = H

(9) R = HgCl



(10) R = COMe

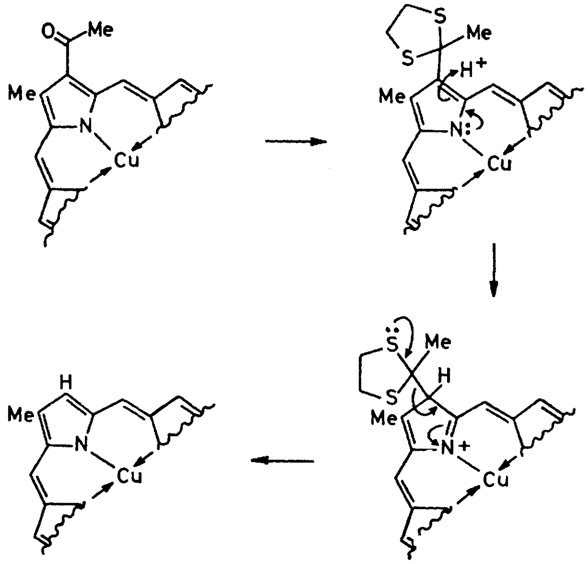
(11) R = H

(12) R = CO_2Bu^t

(13) R = CO_2H

acetal (**3**).† On the other hand, if the copper(II) complex (**4**) of compound (**2**) was subjected to the same conditions, a quantitative yield of copper(II) deuteroporphyrin IX dimethyl ester (**5**) was obtained. This novel deacetylation reaction, we surmise, proceeds by way of protonation of the copper(II) dithioacetal *in situ* (Scheme). The overall mechanism proposed in the Scheme is similar to that suggested[1,7] for protiodevinylation. Deacetylation of the metal-free porphyrin (**3**) presumably does not take place because it would be protonated on nitrogen under the reaction conditions and would therefore be resistant toward electrophilic substitution.

Treatment of the known[6] copper(II) 2-acetylporphyrin (**6**) likewise gave a very high yield of the copper(II) tripropionic porphyrin (**7**) which, after demetallation with CF_3CO_2H and H_2SO_4 and then reinsertion of zinc(II), gave (**8**). With mercury(II) acetate and chloride ions this gave[6] a high yield of the mercurichloride (**9**) which, with $LiPdCl_3$ and methyl acrylate, followed by demetallation, gave[6] a 35% overall yield [from (**6**)] of dehydrocoproporphyrin tetramethyl ester (**1**), m.p. 250—253 °C. This material was shown to be identical by n.m.r. and mixed m.p. comparison‡ with an authentic sample.[4]



SCHEME

The deacetylation procedure can also be efficiently applied to the monopyrrole series. For example, treatment of benzyl 3-acetyl-2,4-dimethylpyrrole-5-carboxylate (**10**) with ethanedithiol and boron trifluoride–ether in acetic acid gave a quantitative yield of the pyrrole (**11**); we had previously prepared this type of pyrrole from the Knorr's pyrrole mixed ester (**12**) by treatment with CF_3CO_2H [to give (**13**)] followed by copper–quinoline decarboxylation.[8]

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† With the exception of (**9**),[6] all new compounds gave satisfactory elemental analyses and mass and n.m.r. spectra compatible with the structures proposed.

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[1] R. Bonnett, I. H. Campion-Smith, and A. J. Page, *J. Chem. Soc., Perkin Trans.* 1, 1977, 68.
[2] J.-H. Fuhrhop and K. M. Smith in 'Porphyrins and Metalloporphyrins,' ed. K. M. Smith, Elsevier, Amsterdam, 1975, p. 757.
[3] H. Fischer and H. Orth, 'Die Chemie des Pyrrols,' Akademische Verlag, Leipzig, 1937, Vol. II, part 1, p. 407.
[4] P. W. Couch, D. E. Games, and A. H. Jackson, *J. Chem. Soc., Perkin Trans.* 1, 1976, 2492 and references therein.
[5] K. C. Langry, Ph.D. Thesis, University of California, 1981.
[6] K. M. Smith and K. C. Langry, *J. Chem. Soc., Chem. Commun.*, 1980, 217.
[7] G. W. Kenner, J. M. E. Quirke, and K. M. Smith, *Tetrahedron*, 1976, **32**, 2753.
[8] G. W. Kenner, J. Rimmer, K. M. Smith, and J. F. Unsworth, *J. Chem. Soc., Perkin Trans.* **1**, **1977**, **332**.