Nickel(II)-promoted Rearrangements of Some N-Substituted Porphyrins

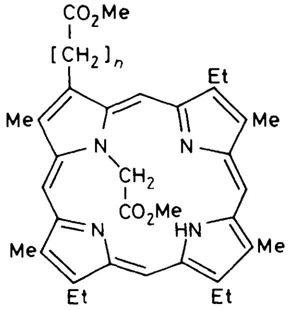
Kevin M. Smith,* Ravindra K. Pandey, and Kevin M. Snow
Department of Chemistry, University of California, Davis, California 95616, U.S.A.

Nickel(II)-promoted rearrangement of an (*N*-methoxycarbonylmethyl)-substituted porphyrin (**1**) affords the nickel(II) *meso*-methoxycarbonylmethylporphyrins, (**3**) and (**4**), produced by intramolecular migration of the N-substituent to carbon; when the pyrrole subunit containing the N-substituent also possesses a β-methoxycarbonylmethyl group, [*e.g.* compound (**5**)] a good yield of a nickel(II) chlorin (**7**) is obtained.

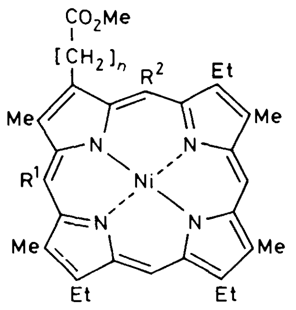
Several synthetically important precursors and degradation products of chlorophyll a possess *meso*-substituents, and the synthesis of such complex unsymmetrical porphyrins has been a recent aim in our laboratory. Such *meso*-functions can be introduced onto the porphyrin nucleus, either during porphyrin ring formation from *a*,*c*-biladienes,[1,2] or less regioselectively by *meso*-functionalization of intact metalloporphyrins using electrophilic reagents.[3]

Following the successful ring syntheses of isomerically pure unsymmetrically substituted *N*-methylporphyrins[4,5] we decided to adopt the approach of migration of N-substituents to carbon as a means of preparing unsymmetrically substituted *meso*-functionalized porphyrins. We show here that *N*-methoxycarbonylmethyl substituents can be successfully induced to migrate, *intramolecularly*, to give *meso*-substituted porphyrins, and that under certain circumstances, chlorin macrocycles which are otherwise difficult to synthesize, are obtained in good yield.

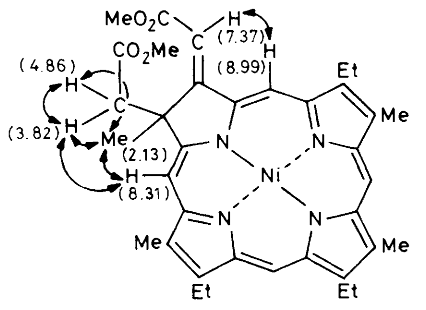
Some years ago, Callot and Tschamber[6] showed that symmetrically substituted *N*-ethoxycarbonylmethylporphyrins could be rearranged, using nickel(II) salts, to homoporphyrins or to *meso*-ethoxycarbonylmethylporphyrins (with a homoporphyrin as a suggested intermediate). The N-substituted porphyrins were prepared by treatment of octaethylporphyrin or tetraphenylporphyrin with carbenes. This work was an extension of earlier nitrene studies of Grigg[7] and



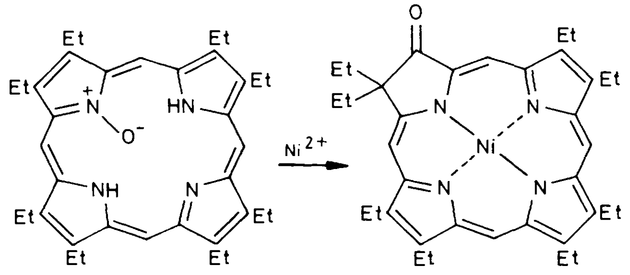
(**1**) n = 2
(**5**) n = 1



n = 2, (**2**) $R^1 = R^2 = H$
(**3**) $R^1 = CH_2CO_2Me$; $R^2 = H$
(**4**) $R^1 = H$; $R^2 = CH_2CO_2Me$
n = 1, (**6**) $R^1 = R^2 = H$



(**7**)



(**8**) (**9**)

carbene studies of Johnson and coworkers.[8] The N-methoxycarbonylmethylporphyrin (**1**)† was synthesized from monopyrroles using standard procedures.[4,5] Treatment with acetylacetonatonickel(II) [$Ni(acac)_2$] in refluxing benzene gave a minor amount of the N-unsubstituted nickel(II) complex (**2**), along with a 62% yield of the isomeric *meso*-substituted nickel(II) porphyrins (**3**) and (**4**), obtained in a 1 : 1 ratio. Use of the unsymmetrical substrate (**1**) made it possible to categorize the reaction as an intramolecular rearrangement because only two products were obtained, each of which was substituted at a *meso*-position adjacent to the originally N-substituted pyrrole subunit. This approach therefore represents a relatively facile method for preparation of porphyrins possessing adjacent β-propionic and *meso*-acetic side chains, as present in chloroporphyrin e_6 and chlorin e_6.

Replacement of the propionic side chain in compound (**1**) with an acetic side chain [*i.e.* compound (**5**)] resulted in dramatically different results upon treatment with acetylacetonatonickel(II). This time, along with a minor quantity of the nickel(II) N-unsubstituted product (**6**), a 61% yield of the chlorin (**7**) was obtained. The structure of this nickel(II) chlorin was established principally by proton n.m.r. nuclear Overhauser enhancement studies and the connectivities established and important chemical shifts (in parentheses) are indicated in structure (**7**). A similar chlorin, obtained from photochemical ring opening of a cyclopropanochlorin, has previously been characterized by Johnson and coworkers.[8] Such chlorins, bearing a geminally substituted carbon and an exocyclic carbon–carbon double bond on one of the pyrrole subunits are of some current interest owing to the presence of this type of structural feature in bacteriochlorophylls,[9] and the suggested presence of it in haem d_1[10] and in sulphhaems.[11] Reduction of the exocyclic double bond also provides a synthetic route to a structural feature present in sirohydrochlorin.[12]

At this time it is not clear whether the original N-substituent is that which appears in the product on the same carbon as the methyl group (the product being formed as a result of the thermodynamic sink, or low energy point in the reaction profile, provided by the α,β-unsaturated system), or whether it appears as a result of a double migration of the original β-acetic side chain to the β-carbon bearing the methyl group and the N-substituent to the vacated β-position. A model for the latter transformation is the rearrangement of a porphyrin N-oxide (**8**) to the β-oxochlorin (**9**).[13] This latter mechanism appears less likely because migratory aptitudes (at least in porphyrin pinacol/pinacolone reactions)[14] for propionate are greater than for acetate, so one might have expected compound (**1**) to form chlorin even more readily than porphyrin (**5**), and this is not the case. What is clear, however, is that the migration from nitrogen to carbon is *intramolecular*, and this work represents the first definitive demonstration of this fact in the porphyrin series. The finer mechanistic points outlined above can be solved by planned labelling studies, and a detailed discussion of mechanism and of successful attempts to use steric bulk to influence the relative proportions of isomeric *meso*-substituted products [*e.g.* (**3**) and (**4**)] will be reported elsewhere.

This research was supported by grants from the National Science Foundation and the National Institutes of Health.

Received, 20th May 1986; Com. 683

References

1 K. M. Smith and R. K. Pandey, *J. Chem. Soc., Perkin Trans. 1*, in the press.
2 K. M. Smith and O. M. Minnetian, *J. Org. Chem.*, 1985, **50**, 2073.
3 J.-H. Fuhrhop, in 'Porphyrins and Metalloporphyrins,' ed. K. M. Smith, Elsevier, Amsterdam, 1975, ch. 15.
4 A. H. Jackson, R. K. Pandey, and E. Roberts, *J. Chem. Soc., Chem. Commun.*, 1985, 470.
5 K. M. Smith and R. K. Pandey, *Tetrahedron Lett.*, 1986, **27**, 2717.
6 H. J. Callot and T. Tschamber, *J. Am. Chem. Soc.*, 1975, **97**, 6175.
7 R. Grigg, *J. Chem. Soc.*, (*C*), 1971, 3664.
8 H. J. Callot, A. W. Johnson, and A. Sweeney, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1424.
9 H. Scheer, W. A. Svec, B. T. Cope, M. H. Studier, R. G. Scott, and J. J. Katz *J. Am. Chem. Soc.*, 1974, **96**, 3714.
10 C. K. Chang, *J. Biol. Chem.*, 1985, **260**, 9520.
11 M. J. Chatfield, G. N. La Mar, J. T. J. Lecomte, A. L. Balch, K. M. Smith, and K. C. Langry, *J. Am. Chem. Soc.*, in the press.
12 L. M. Siegel, M. J. Murphy, and H. Kamin, *J. Biol. Chem.*, 1973, **248**, 251.
13 A. L. Balch and Y. W. Chan, *Inorg. Chim. Acta*, in the press.
14 C. K. Chang and C. Sotiriou, *J. Heterocycl. Chem.*, 1985, 1739.

---

† New compounds were characterized by n.m.r. spectra, high resolution mass spectra, and/or elemental combustion analysis.