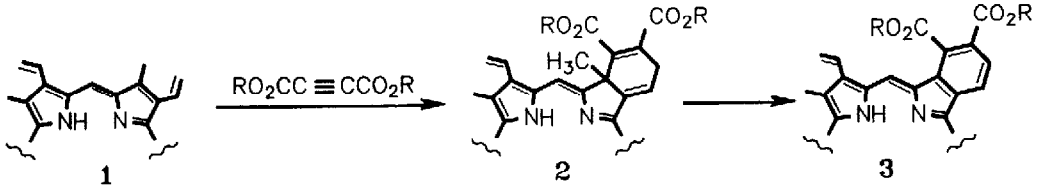
Tetrahedron Letters,Vol.30,No.45,pp 6135-6138,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

TRANSFORMATION OF A MONOVINYLPORPHYRIN TO BENZOPORPHYRINS VIA DIELS-ALDER ADDUCTS

Paul Yon-Hin, Tilak P. Wijesekera and David Dolphin*
Department of Chemistry
University of British Columbia
2036 Main Mall, Vancouver, B.C.
Canada V6T 1Y6

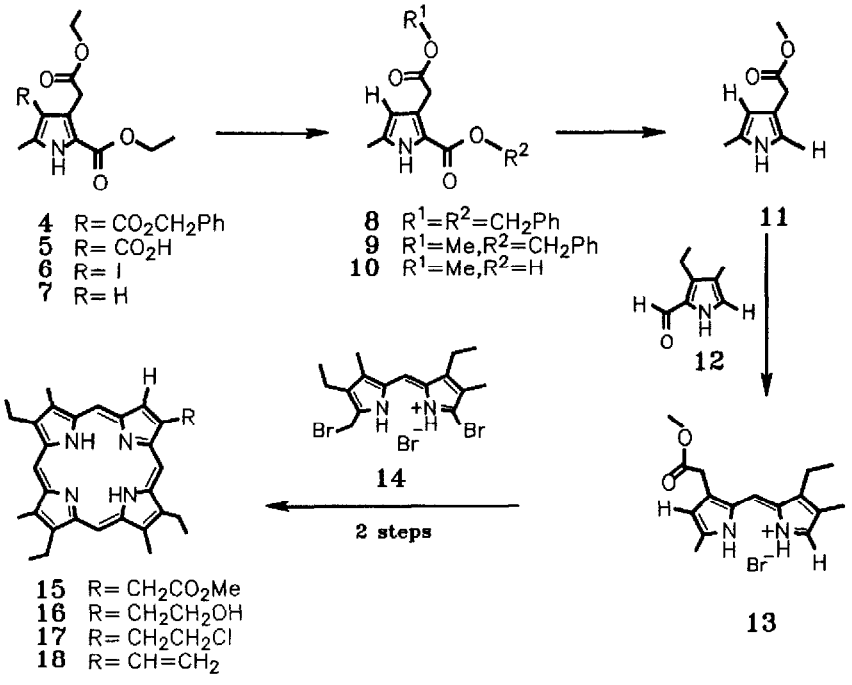
A β-unsubstituted-β'-vinylporphyrin has been synthesized which reacted with an excess of acetylenedicarboxylate ester to give monobenzoporphyrins in high yield. Evidence that suggests an isomerization of the initial adduct to a new porphyrin enroute to the benzoporphyrin is presented.

Activated dienophiles are known to undergo [2+4] cycloaddition reactions with the vinyl and cross-conjugated β,β'-double bond of protoporphyrin IX dimethyl ester (1) to give "chlorins" as stable products.[1,2] Recently, we have shown that the chlorin cycloadduct 2 formed with an acetylenedicarboxylate ester, undergoes aromatization (with the loss of the angular methyl group) in the presence of base and excess dienophile or other electron acceptors such as *p*-benzoquinone to give a benzoporphyrin 3 (Scheme 1).[3] In order to further explore the aromatization of the cycloadduct and also provide a more direct and facile approach to benzoporphyrins, the reaction of acetylenedicarboxylate esters with a β-unsubstituted-β'-monovinylporphyrin 18 was investigated.



Scheme 1

In the only previously reported synthesis of a β-unsubstituted-β'-monovinylporphyrin, Djerassi and coworkers[4] employed dipyrromethanes as intermediates with an acetyl function as the vinyl precursor. However, the inherent deactivating effect of the acetyl substituent towards nucleophilic reactions of α-unsubstituted pyrroles, resulted in structurally similar by-products (which required chromatographic separation) both at the dipyrromethane and porphyrin cyclization stages. We chose to construct the porphyrin macrocycle using Johnson's regioselective synthesis[5,6] via dipyrromethenes and biladienes-a,c with a less deactivating acetate ester as the vinyl precursor (Scheme 2).

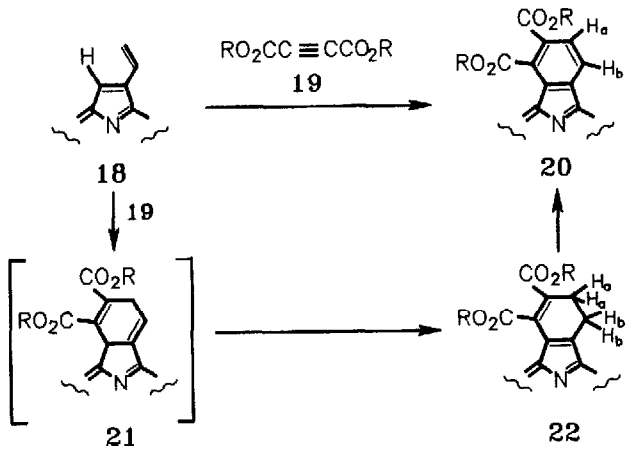


Scheme 2

The crucial monopyrrolic precursor **11**† was prepared in high yield from the pyrrole **4**[7] via the intermediates **5** through **10** using standard transformations described in the literature.[7,8] Condensation of **11** with the 5-unsubstituted 2-pyrrolecarboxaldehyde **12**[9] in the presence of aqueous hydrobromic acid gave a first crop yield of 65% for the crystalline 5'-unsubstituted-5-methyl-2,2'-dipyrromethene **13**. Coupling of **13** with 5'-bromomethyl-5-bromo-2,2'-dipyrromethene **14**[6] using anhydrous stannic chloride as the catalyst, produced the corresponding 1-bromo-19-methyl,5,15-biladiene (>85%) which was cyclized in dimethyl sulphoxide-pyridine to the porphyrin **15** in 75% yield. Metalation of **15** with zinc, reduction of the acetate substituent ($LiAlH_4$) followed by demetalation (trifluoroacetic acid) gave the hydroxyethylporphyrin **16** (90% overall) which was subsequently converted to the chloroethyl derivative **17** in near quantitative yield, using thionyl chloride. Treatment of **17** with sodium hydroxide in pyridine-water produced the desired monovinylporphyrin **18**[10] (85%).

† All new compounds have been characterized by high resolution mass and ^1H n.m.r. spectroscopy.

Heating **18** with a 50 fold molar excess of dimethyl acetylenedicarboxylate (**19**, R=Me) in toluene at 110°C in a degassed sealed tube gave, after 24 h, the benzoporphyrin **20** (R=Me) in 80% yield (Scheme 3). This exhibited a rhodo-type electronic spectrum‡ (λ_{max} CH_2Cl_2 - 402, 512, 548, 578 and 630 nm) characteristic of benzoporphyrins and its structure was confirmed by ^1H n.m.r. and mass spectroscopy (molecular ion m/z 602). With diethyl acetylenedicarboxylate (**19**, R=Et), under similar reaction conditions, the corresponding benzoporphyrin (**20**, R=Et) was obtained in equally high yield. However, when di-tert-butyl acetylenedicarboxylate (**19**, R=$(Me)_3C$-) was used, two porphyrin products (in 3:1 ratio) were isolated in 60% overall yield. The minor component corresponded to the benzoporphyrin **20** (R=$(Me)_3C$-) with a rhodo-type spectrum, an (M^+ + 1) peak at m/z 687 in the fast atom bombardment-mass spectrum and a ^1H n.m.r. consistent with its proposed structure, showing two doublets at δ 8.58 and δ 9.44 assigned to H_a and H_b respectively. The major component also exhibited a rhodo-type spectrum (λ_{max} CH_2Cl_2 - 408, 510, 550, 574 and 636 nm) and its mass spectrum (molecular ion m/z 688) and ^1H n.m.r. spectrum (two triplets at δ 3.30 and δ 4.25 assigned to H_a and H_b respectively, Scheme 3) were consistent with the structure **22** (R=$(Me)_3C$-).



Scheme 3

The above results suggest that the reaction of acetylenedicarboxylate esters with the vinylporphyrin **18** also proceeds via a (4+2) cycloaddition reaction to give, initially, a chlorin type adduct **21** (Scheme 3). However, unlike the case of the methyl-vinyl analogue (protoporphyrin IX),[3] the chlorin **21** undergoes a rapid rearrangement to give the thermodynamically more stable porphyrin **22** which is subsequently oxidized to the benzoporphyrin **20**. The fact that the yield of benzoporphyrin was significantly reduced and

‡ In rhodo-type porphyrin spectra the intensity of the four visible bands is III > IV > II > I.

that the porphyrin **22**, with the conjugated diene system, could be isolated when the dienophile **19** was changed to the sterically hindered tert-butyl ester is consistent with the suggestion that the dienophile acts as the electron acceptor in the oxidation of **22** to the benzoporphyrin **20**.

Acknowledgements

This work was supported by the U.S. National Institutes of Health (AM 17989) and the Canadian Natural Sciences and Engineering Research Council. A Killam Predoctoral Fellowship (to P.Y-H.) is gratefully acknowledged.

References

1. H.J. Callot, A.W. Johnson, and A. Sweeney, J. Chem. Soc., Perkin Trans. 1, 1973, 1424.
2. R.K. DiNello and D. Dolphin, J. Org. Chem., 1980, **45**, 5196; V. Scherrer Pangka, A.R. Morgan, and D. Dolphin, J. Org. Chem., 1986, **51**, 1094.
3. A.R. Morgan, V. Scherrer-Pangka, and D. Dolphin, J. Chem. Soc. Chem. Commun., 1984, 1047.
4. A.G.H. Wee, A.Y.L. Shu, E. Bunnenberg, and C. Djerassi, J. Org. Chem., 1984, **49**, 3327.
5. R.L.N. Harris, A.W. Johnson, and I.T. Kay, J. Chem. Soc. C, 1966, **22**; P. Bamfield, R.L.N. Harris, A.W. Johnson, I.T. Kay, and K.W. Shelton, J. Chem. Soc. C, 1966, 1436.
6. J.B. Paine, III, J. Hiom, and D. Dolphin, J. Org. Chem., 1988, **53**, 2796.
7. A.R. Battersby, E. Hunt, E. McDonald, J.B. Paine III, and J. Saunders, J. Chem. Soc., Perkin Trans. 1, 1976, 1008.
8. J.B. Paine, III, in The Porphyrins, Vol. 1, ed. D. Dolphin, Academic Press, New York, 1978, pp. 101-234.
9. J.B. Paine, III, and D. Dolphin, J. Org. Chem., 1988, **53**, 2787.
10. ^{1}H-NMR of **18** ($CDCl_3$, 400 MHz): δ -3.66 (s, 2H, NH), 1.90 (3t, 9H, 3 x $CH_2\underline{CH}_3$), 3.60 (3H), 3.64 (3H), and 3.66 (3H), (s, 3 x CH_3), 4.15 (3q, 6H, 3 x $\underline{CH}_2CH_3$), 6.40 (d, 1H, J = 12 Hz, CH=$\underline{CH}_2$), 6.63 (d, 1H, J = 17 Hz, CH=$\underline{CH}_2$), 8.47 (dd, 1H, $\underline{CH}$=CH_2), 9.44 (s, 1H, pyrrole-H), 10.06 (1H), 10.07 (1H), 10.10 (1H), and 10.26 (1H) (s, 4 x meso-H).

(Received in USA 22 June 1989)