Diels–Alder Reactions of Protoporphyrin Dimethyl Esters with Nitrosobenzenes: A Novel Degradation to Formyl Porphyrins

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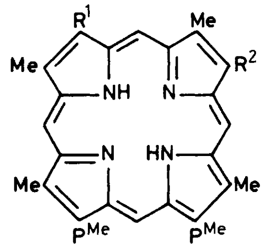
The reaction of the divinyl porphyrins, protoporphyrins-II and -IX dimethyl ester, with *p*-nitronitrosobenzene affords mono-vinyl mono-adducts, and with an excess of reagent mono-formyl mono-adducts.

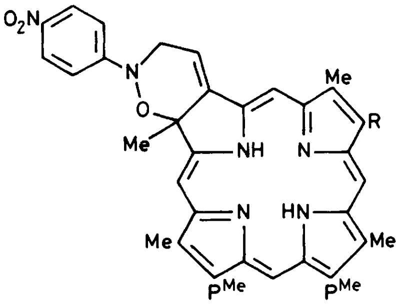
Protoporphyrin-IX dimethyl ester (**1a**) reacts with singlet oxygen in a Diels–Alder type reaction to form isomeric mono-adducts involving the vinyl groups and the neighbouring peripheral double bonds.[1] Tetracyanoethylene and dimethyl acetylenedicarboxylate were later reported[2] to form bis-adducts with protoporphyrin-IX dimethyl ester but subsequent reinvestigations[3,4] showed that the reactions were more complex: thus in the case of tetracyanoethylene both [2 + 2] and [2 + 4] mono-adducts were formed as well as small amounts of bis-adducts.[4]

We have recently explored the use of other dienophiles as an approach to the preparation of bis-adducts, which might lead to the synthesis of tetrahydroporphyrins of the isobacteriochlorin series. Preliminary studies with a range of substituted nitrosobenzenes[5] showed that those with electron withdrawing substituents readily reacted with protoporphyrin-IX dimethyl ester in chloroform, or dichloromethane, *e.g.* *p*-nitronitrosobenzene afforded the two isomeric green mono-adducts (**2a**) and (**3a**) within a few minutes at room temperature. H.p.l.c. analysis revealed that in addition to the major products, two other minor (green) by-products were also formed. Larger amounts of these by-products were formed if the original reactions were carried out with a large excess of *p*-nitronitrosobenzene and these were isolated by preparative h.p.l.c. The visible spectra of the new products showed that like the mono-adducts themselves they were chlorins (dihydroporphyrins) rather than the hoped for bis-adducts. Their n.m.r. spectra each exhibited five very low field peaks, four of which were in similar positions to the *meso*-proton resonances of the mono-adducts, and the lowest field peak in each case (*ca.* δ 10.9) was assigned to a formyl proton resonance. This evidence together with the absence of resonances due to a vinyl group, was consistent with the isomeric structures (**2b**) and (**3b**), and these were confirmed by the field desorption mass spectra which showed pseudomolecular ions at *m*/*z* 745 (*M* + 1). Thermolysis of both



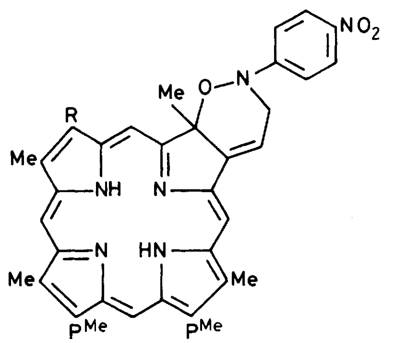
(**1**)

a; $R^1 = R^2 =$ vinyl
b; $R^1 =$ CHO, $R^2 =$ vinyl
c; $R^1 =$ vinyl, $R^2 =$ CHO
d; $R^1 =$ vinyl, $R^2 =$ H
e; $R^1 =$ CHO, $R^2 =$ H



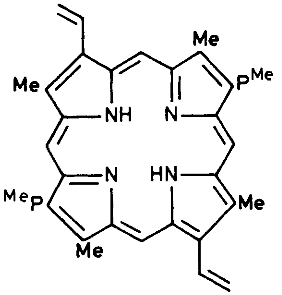
(**2**)

a; R = vinyl
b; R = CHO
c; R = H

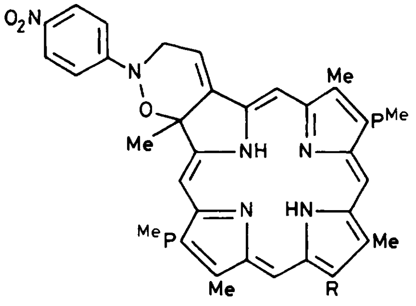


(**3**)

a; R = vinyl
b; R = CHO

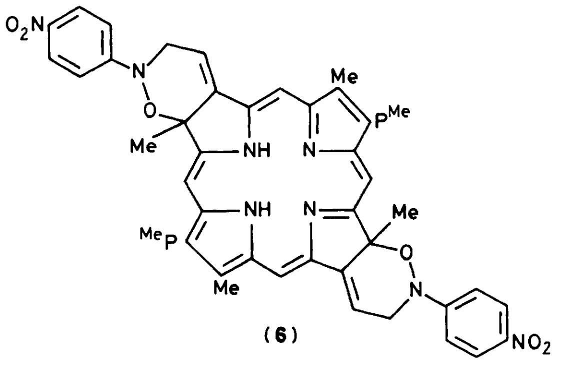


(**4**)



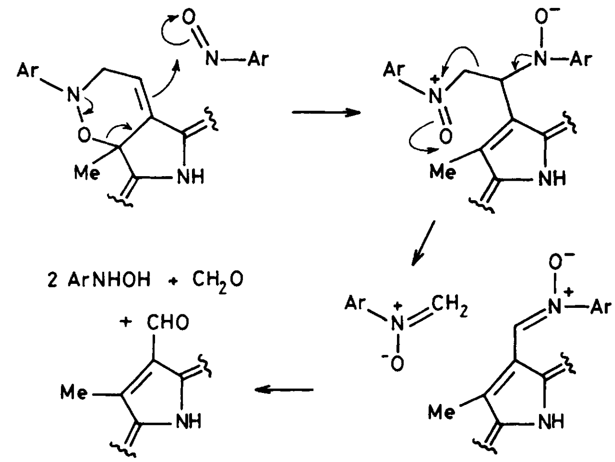
(**5**)

a; R = vinyl
b; R = CHO



(**6**)

$P^{Me} = CH_2CH_2CO_2Me$



Scheme 1

compounds afforded the well-known chlorocruoro- and isochlorocruoro-porphyrins (**1b**) and (**1c**) respectively; conversely reaction of the latter two porphyrins with *p*-nitronitrosobenzene at 20 °C gave the two new mono-adducts (**2b**) and (**3b**) in quantitative yield, thus firmly establishing their structures.

The failure to form bis-adducts of protoporphyrin-IX with the nitrosobenzenes (in contrast to the relative stability of the *mono*-adducts) was attributed to the lower aromatic stability of isobacteriochlorins (unsymmetrical tetrahydroporphyrins) relative to chlorins (dihydroporphyrins) or porphyrins. It seemed possible that the more symmetrical bacteriochlorins (with the opposite pyrrole rings reduced) might be more stable and more readily formed, and for this reason we synthesised protoporphyrin-II dimethyl ester (**4**)[6] and studied its reactions with *p*-nitronitrosobenzene. The expected mono-adduct (**5a**) ($\lambda_{max.}$ 406, 590, and 650 nm) was formed in good yield together with some (15—20%) of a green chlorin-like by-product ($\lambda_{max.}$ 430, 530, 560, 590, and 645 nm) which was readily identified by its visible, n.m.r., and mass spectra as the formyl mono-adduct (**5b**).

When this reaction was followed by h.p.l.c. and visible spectroscopy an unstable intermediate ($\lambda_{max.}$ 410, 640, 690, and 728 nm) was observed. This was also formed when the mono-adduct (**5a**) was treated with an excess of *p*-nitronitrosobenzene and after isolation by careful h.p.l.c. the field desorption mass spectrum showed a molecular ion (*m/z* 894) consistent with that expected for the bis-adduct (**6**). The 360 MHz n.m.r. spectrum confirmed that the product was a mixture of diastereoisomers of the bacteriochlorin structure (**6**). These proved to be too unstable to separate chromatographically but on further treatment with *p*-nitronitrosobenzene afforded the mono-formyl mono-adduct (**5b**), thus suggesting that the bis-adduct (**6**) was an intermediate in formation of the latter. On the other hand the mono-vinyl porphyrin, isopemptoporphyrin dimethyl ester (**1d**) with an excess of *p*-nitronitrosobenzene readily formed the mono-adduct (**2c**) ($\lambda_{max.}$ 406, 495, 500, 597, 624, and 654 nm), and this was then further transformed into the related formyl porphyrin (**1e**) showing that direct conversion of a mono-adduct into a mono-formyl porphyrin was also possible.

A possible mechanism for the conversion of the nitrosobenzene adducts into formyl derivatives is shown in Scheme 1; the overall process involves an oxidation of the original vinyl group, and the oxidant must be the additional nitrosobenzene.

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