Synthesis of *N,N'*-Phenyleneporphyrins. Models for Cytochrome P-450–1-Aminobenzotriazole Inactivation Products

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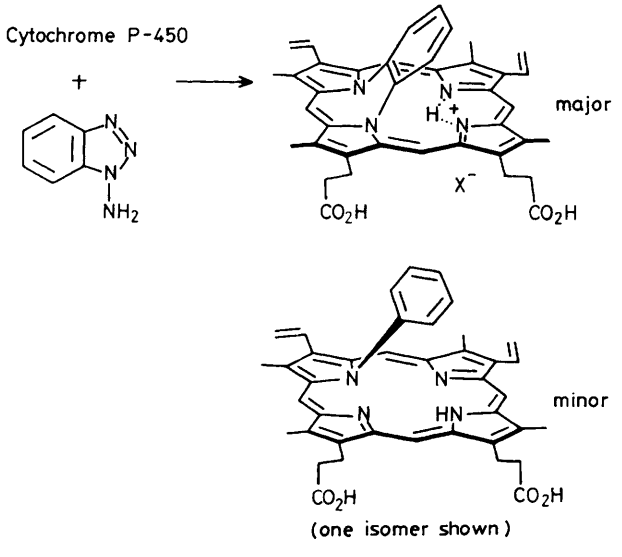
N,N'-Phenyleneporphyrins were prepared either by oxidative cyclisation of cobalt(II)-*N*-phenylporphyrins or by direct interaction of a cobalt(III)-porphyrin and 1-aminobenzotriazole in the presence of dioxygen.

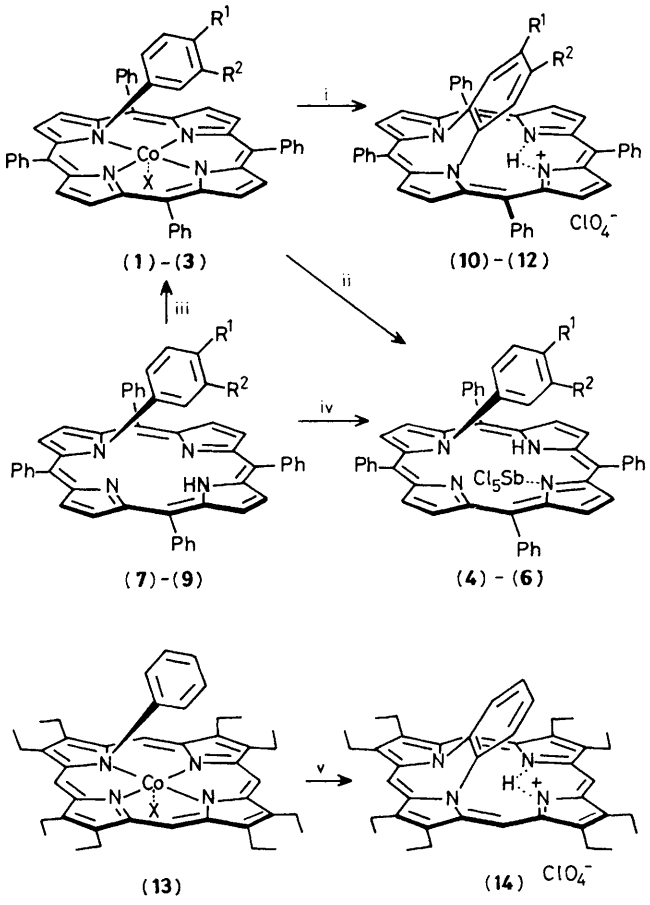
Deactivation of haemoproteins in the presence of various substrates was explained by the formation of N-substituted porphyrins[1] whose geometrical, electronic, and co-ordinating properties differ significantly from those of 'normal' porphyrins. In particular 1-aminobenzotriazole (ABT), an insecticide and herbicide synergist,[2] modifies the protohaeme of cytochrome P-450 into a mixture of inactive *N,N'*-phenyleneprotoporphyrins and *N*-phenylprotoporphyrins[3] (Scheme 1).

We recently found[4] that a series of cobalt(II)-*N*-vinylporphyrins could be cyclised to give *N,N'*-vinylideneporphyrins. We now show that, under modified conditions, cyclisation of *N*-phenylporphyrins to *N,N'*-phenyleneporphyrins can be achieved. In addition direct formation of the phenylene bridge under biomimetic conditions, *viz* ABT + metalloporphyrin, is described.

Oxidation of chloro- or perchlorato-cobalt(II)-*N*-aryl-TPP derivatives[5] (**1**)—(**3**) (TPP = *meso*-tetraphenylporphyrin) by $(p\text{-}BrC_6H_4)_3N^{\bullet+}SbCl_6^-$ invariably led to transmetallation (although under these conditions the corresponding *N*-vinylporphyrins cyclised) and the $SbCl_5$ complexes (**4**)—(**6**) were isolated. They were independently prepared from the corre-



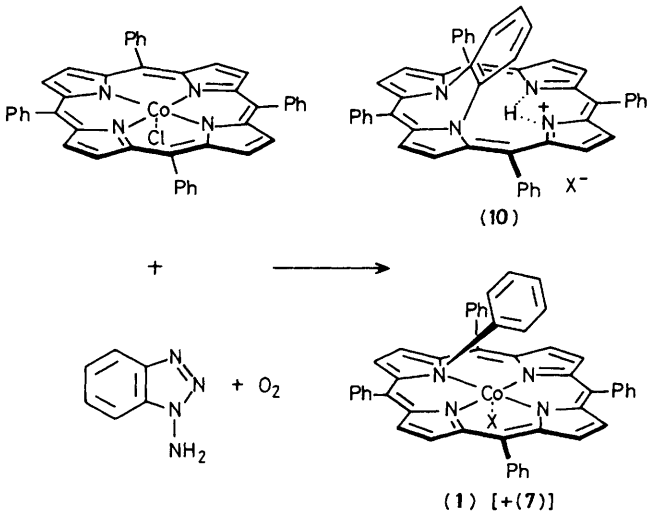
Scheme 1



Scheme 2. *Reagents:* i, $(p\text{-}BrC_6H_4)_3N^{\cdot+}ClO_4^-$; ii, $(p\text{-}BrC_6H_4)_3N^{\cdot+}SbCl_6^-$; iii, $Co(OAc)_2$, MeOH then NaX–H_2O (X = Cl or ClO_4); iv, $SbCl_5$, CH_2Cl_2; v, 0.85 V *vs.* S.C.E., 74 h, 120 °C. (**1**), (**4**), (**7**), and (**10**): $R^1 = R^2 = H$; (**2**), (**5**), (**8**), and (**111**): $R^2 = H$, $R^1 = OMe$; (**3**), (**6**), (**9**), and (**12**): $R^1 = R^2 = OMe$.

sponding bases (**7**)—(**9**) and $SbCl_5$ (Scheme 2). However, use of $(p\text{-}BrC_6H_4)_3N^{\cdot+}ClO_4^-$ produced the cyclised porphyrins (**10**)—(**12**) in refluxing 1,2-dichloroethane [(**11**) and (**12**)] or tetrachloroethane [(**10**)] in acceptable yields [up to 60% for (**10**)]. The porphyrins (**10**)—(**12**) show typical *N,N'*-bridged porphyrin spectra† with high-field phenyl signals [δ 2.37 and 1.82 for H next to N in (**10**) and (**12**) respectively, whose spectra also indicate a plane of symmetry owing to rapid NH exchange].

† Selected spectral data: (**10**): ^{1}H n.m.r. ($CDCl_3$; δ from Me_4Si) 9.09 and 9.01 (AB, pyrrole), 8.93 and 8.85 (AB, pyrrole), 8.2—7.8 (m, lateral Ph), 4.50 and 2.37 (AA'BB', bridge phenyl), and −3.73 (NH); visible spectrum (CH_2Cl_2): $\lambda_{max.}$ 442 (ε 91 200), 566 (7600), 604 (11 700), and 656 nm (6200). (**14**): ^{1}H n.m.r. ($CDCl_3$): 10.89, 10.85, and 10.06 (3s, 2:1:1, *meso*), 4.55—3.9 (m, CH_2), 4.25 and 1.96 (AA'BB', bridge Ph), 1.98, 1.88, 1.85, and 1.72 (4t, 1:1:1:1, Me), and *ca.* −4 (NH); visible spectrum (CH_2Cl_2): $\lambda_{max.}$ 410 (ε 77 600), 542 (6700), 576 (8700), and 624 nm (2500). (**5**): ^{1}H n.m.r. ($CDCl_3$): 8.86 and 8.82 (AB, pyrrole 4H), 8.74 (s, pyrrole 2H), 8.22 (s, pyrrole 2H), 8.55—8.35 and 8.1—7.8 (m, lateral Ph), 4.48 and 2.16 (2d, N–C_6H_4–OMe), 2.70 (s, OMe), and *ca.* −2.9 (br., NH); the plane of symmetry indicated by these data indicates a rapid H exchange (inverted positions for H and rapidly exchanging $SbCl_5$ cannot be excluded); visible spectrum (CH_2Cl_2): $\lambda_{max.}$ 444 (ε 181 000), 602 (9100), and 664 nm (18 000).



Scheme 3. Direct reaction of $ClCo^{III}TPP$ and ABT (excess) in aerated tetrachloroethane (90—147 °C). $Co(OAc)_2$ metallation of the crude mixture gave (**10**) and (**1**) [from (**1**) + (**7**)] both characterised as perchlorates.

As an approach to the natural series similar conditions were applied to compound (**13**) but led only to extensive decomposition. Cyclisation could only be performed under drastic thermal and electrochemical conditions, and only in low yield (3%).†

Electrochemical and e.s.r. measurements supported the mechanism earlier proposed[4] for the cyclisation reaction. Electrolysis of (**1**) [X = ClO_4; 1 V *vs.* standard calomel electrode (S.C.E.); tetrachloroethane, 0.1 M tetrapropylammonium perchlorate; 25 °C] above its first oxidation wave (0.93 V *vs.* S.C.E.) led to the disappearance of the Co^{II} e.s.r. signal which is expected if the diamagnetic Co^{III} is produced [electrolysis at 1.5 V (second oxidation wave) was accompanied by the increase in an e.s.r. signal which we assign to the porphyrin cation-radical]. Electron transfer from the group attached to the nitrogen to cobalt followed by nucleophilic attack of a neighbouring N will then lead to the observed products.

The phenyl group cyclisation is not limited to cobalt complexes; chloromanganese(II)-*N*-phenyl-TPP also produces a low yield of *N,N'*-phenylene-TPP upon oxidation by $(p\text{-}BrC_6H_4)_3N^{\cdot+}ClO_4^-$. The corresponding Fe^{II}, Ni^{II}, Cu^{II}, and Zn^{II} complexes however do not show the same behaviour and either starting material (Cu, Zn), demetallated (Fe), or *N*-dephenylated porphyrin (Ni) were recovered. This suggests that only a powerful 'localised' oxidant (Co^{III}, Mn^{III}), rather than a delocalised (porphyrin π-cation radical of Cu and Zn complexes) or weak (Fe^{III}) oxidant, can initiate the electron transfer from the *N*-phenyl group.

The ability of cobalt(III)-porphyrins to oxidise hydrazines suggested a more 'biomimetic' approach to the synthesis of *N,N'*-phenyleneporphyrins. Although at 25 °C no reaction occurred between ABT and chlorocobalt(III)-TPP, under more vigorous conditions (90—147 °C, air, tetrachloroethane, 1—3 days) (**10**) (10—15%, isolated as perchlorate) and (**1**) + (**7**) (together 20%) formed slowly (Scheme 3). This model suicide reaction parallels the formation of N-substituted porphyrins during the ClFe(TPP)–PhIO oxidation of terminal alkenes.[6]

Ortiz de Montellano[3] suggested that benzyne might be formed on reaction of ABT with the oxo form of cytochrome

P-450, in a way similar to the $Pb(OAc)_4$ oxidation of ABT from which benzyne adducts could be isolated in high yield.[7] We studied the ABT–$ClCo^{III}TPP$ reaction in the presence of a large excess of tetraphenylcyclopentadienone, an efficient benzyne trap, without being able to detect the expected adduct, tetraphenylnaphthalene. This suggests that if any benzyne is formed under our conditions it is trapped by the porphyrins before being able to escape the reaction site, or that a pathway not involving benzyne is responsible for the bridge formation.

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