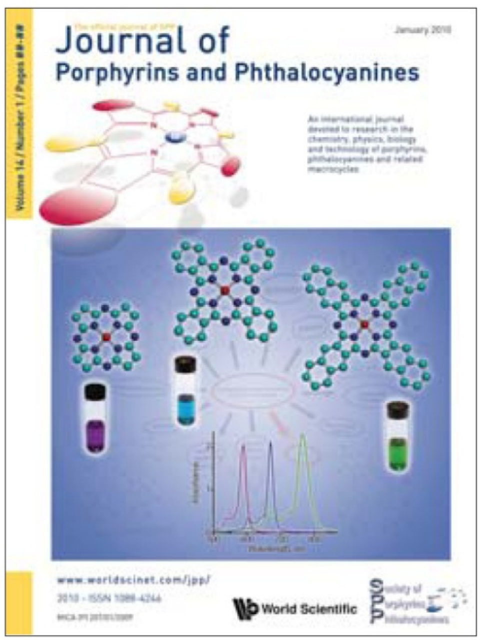
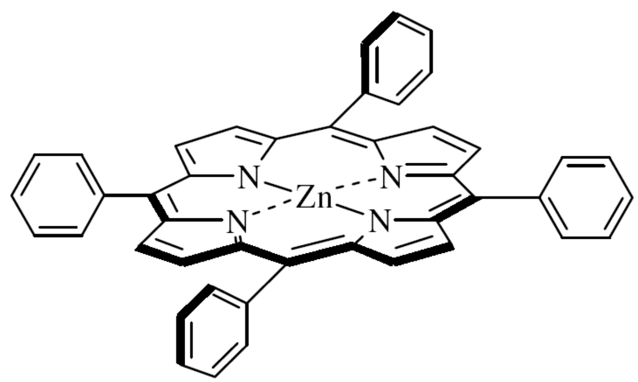
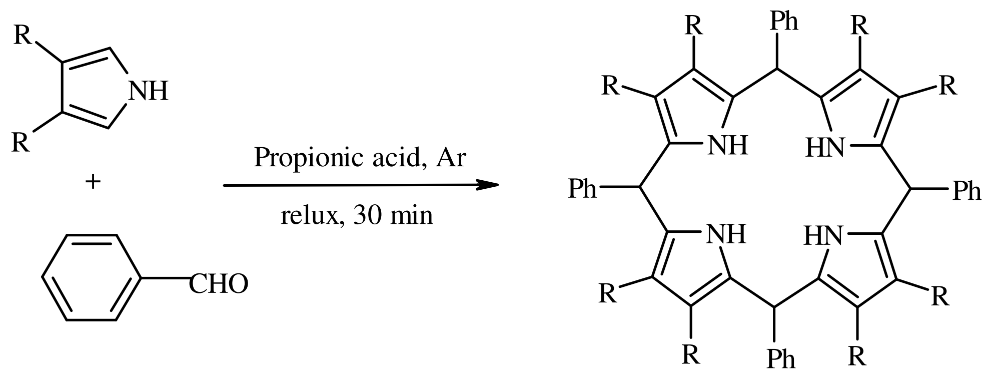
Microscale Synthesis of Porphyrin Complexes



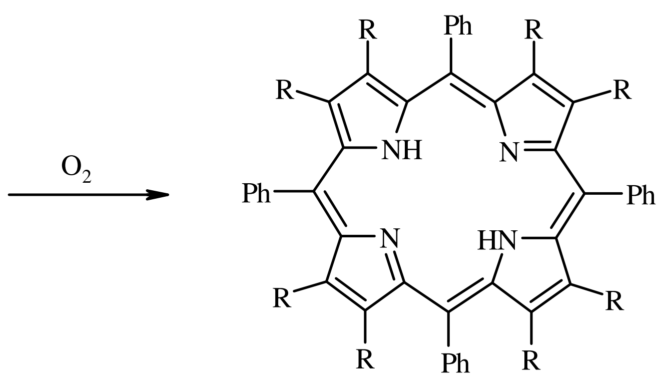


Synthetic Methods – Adler method



R = H, Me

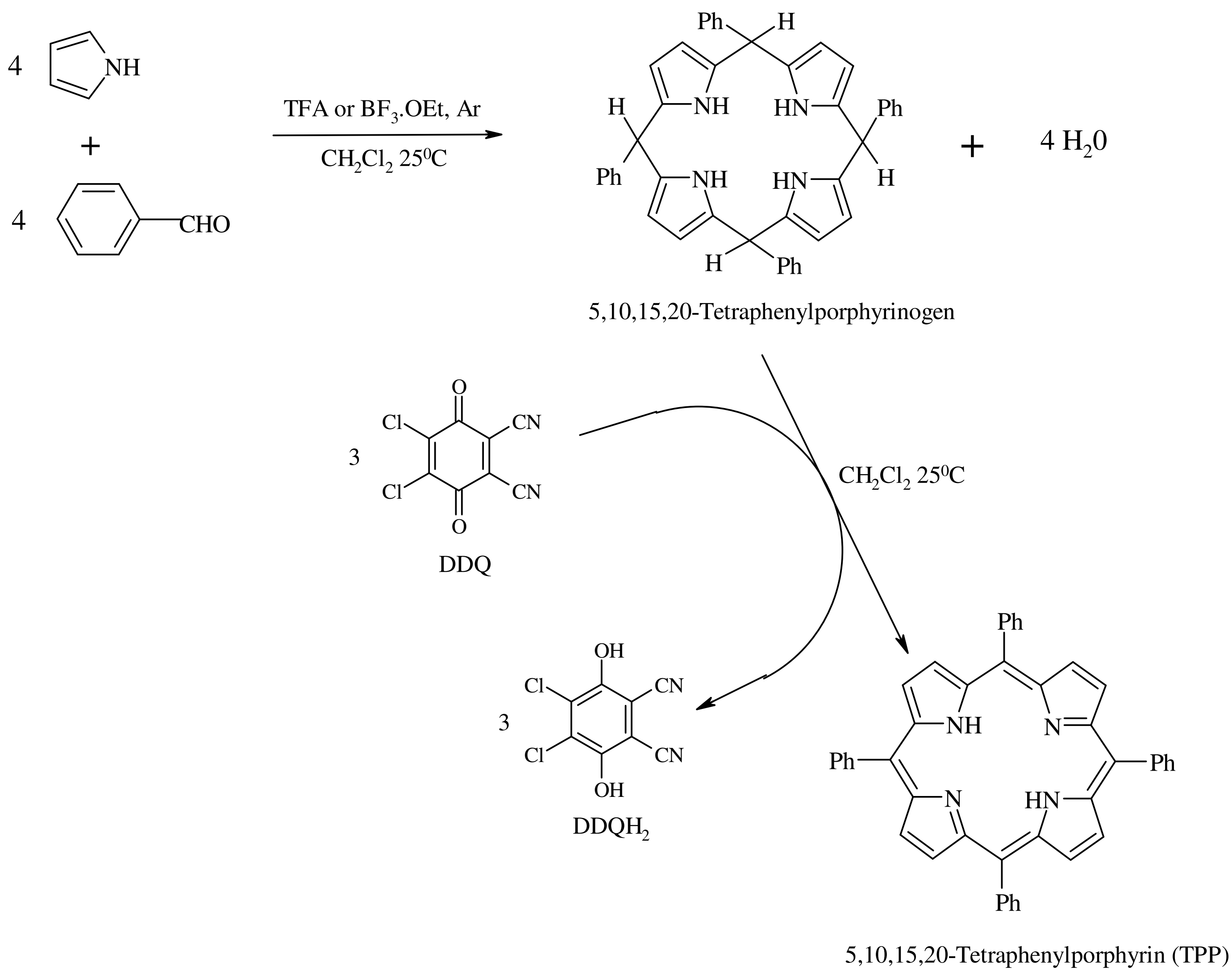
R = H - meso-Tetraphenylporphyrinogen
R = Me - β-octamethyl-meso-tetraphenylporphyrinogen



R = H - meso-Tetraphenylporphyrin
R = Me - β-octamethyl-meso-tetraphenylporphyrin

A.D. Adler, F.R. Longo, J.D. Finarelli, J. Goldmacher, J. Assour, L. Korsakoff, *J. Org. Chem.* **1967**, 32, 476.

Synthetic Methods – Lindsey method



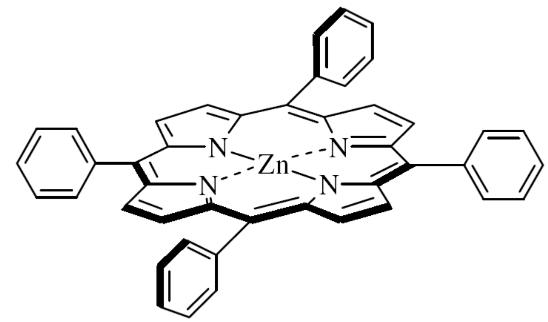
J. S. Lindsey, I. C. Schreiman, H.C. Hsu, P. Kearney, A. M. Marguerettaz, *J. Org. Chem.* **1987**, *52*, 827

The Porphyrin Chromophore

Porphyrins are particularly attractive for many applications due to their

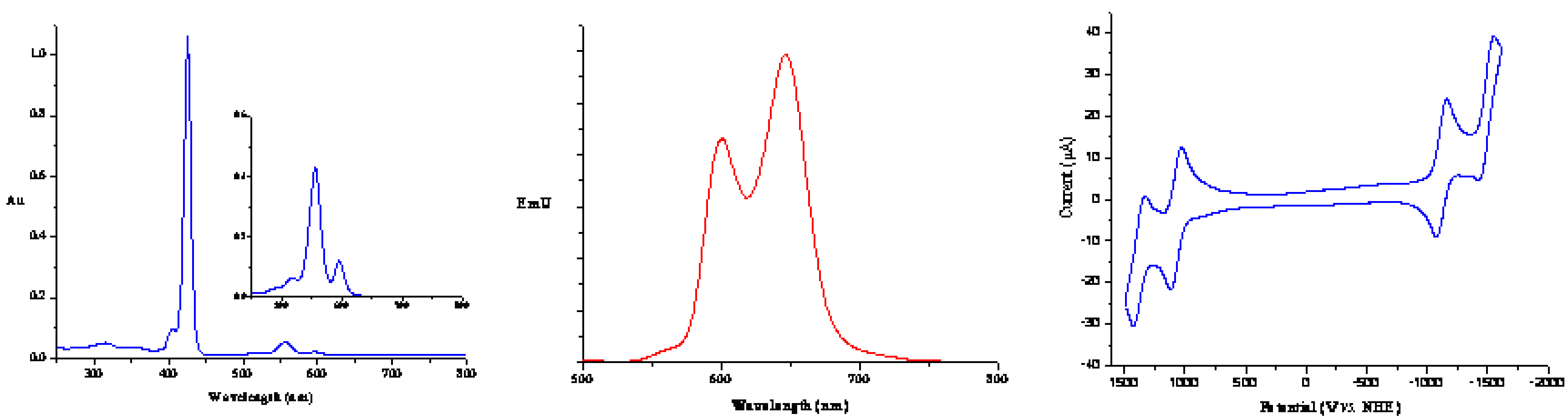
- rigid-planar geometry
- redox stability
- intense electronic absorption
- visible emission
- small HOMO-LUMO energy gap
- tunable optical and redox properties

Zinc-5,10,15,20-tetraphenylporphyrin



UV-Vis absorption			Fluorescence
Soret	Q(1,0)	Q(0,0)	Q(0,0)*, Q(1,0)*
λ_{max}, nm	λ_{max}, nm	λ_{max}, nm	λ_{max}, nm
(ε x10^5, $M^{-1}cm^{-1}$)	(ε x10^5, $M^{-1}cm^{-1}$)	(ε x10^5, $M^{-1}cm^{-1}$)	(Φ)
422 (2.55)	548 (9.72)	588 (1.90)	596, 647 (0.033)

Oxidation (V)		Reduction (V)		E_{0-0} (eV)	$E_{1/2}(P^+/P^*)$ (eV)
1st	2nd	1st	2nd		
1.10	1.46	-1.14	-1.49	2.07	**-0.97**



UV-Vis absorption, Fluorescencese Emission and Cyclic Voltammetry of ZnTPP

Introduction to Photophysics

- Upon irradiation, the a chromophore is excited from its (typically) singlet ground state (S_0) to a high energy Frank-Condon state.

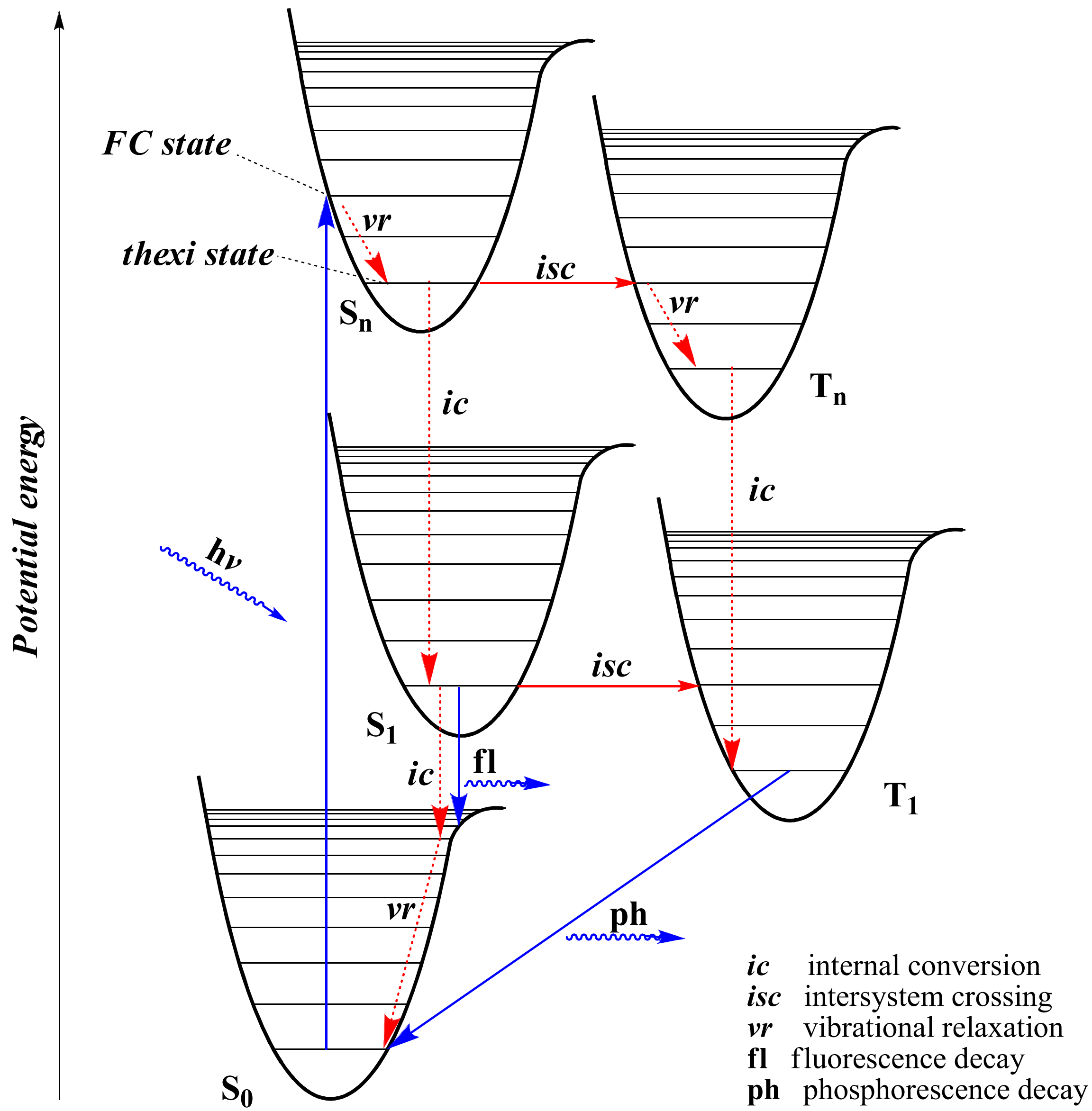
- The Frank-Condon state undergoes rapid internal conversion and vibrational relaxation (often referred to as radiationless decay) to the first singlet excited state (S_1) at lower energy [sometimes referred to as a **th**ermally-equilabrated **exci**ted (thexi) state].

- A number of energy loss mechanisms are possible from the S_1 state of the PS:

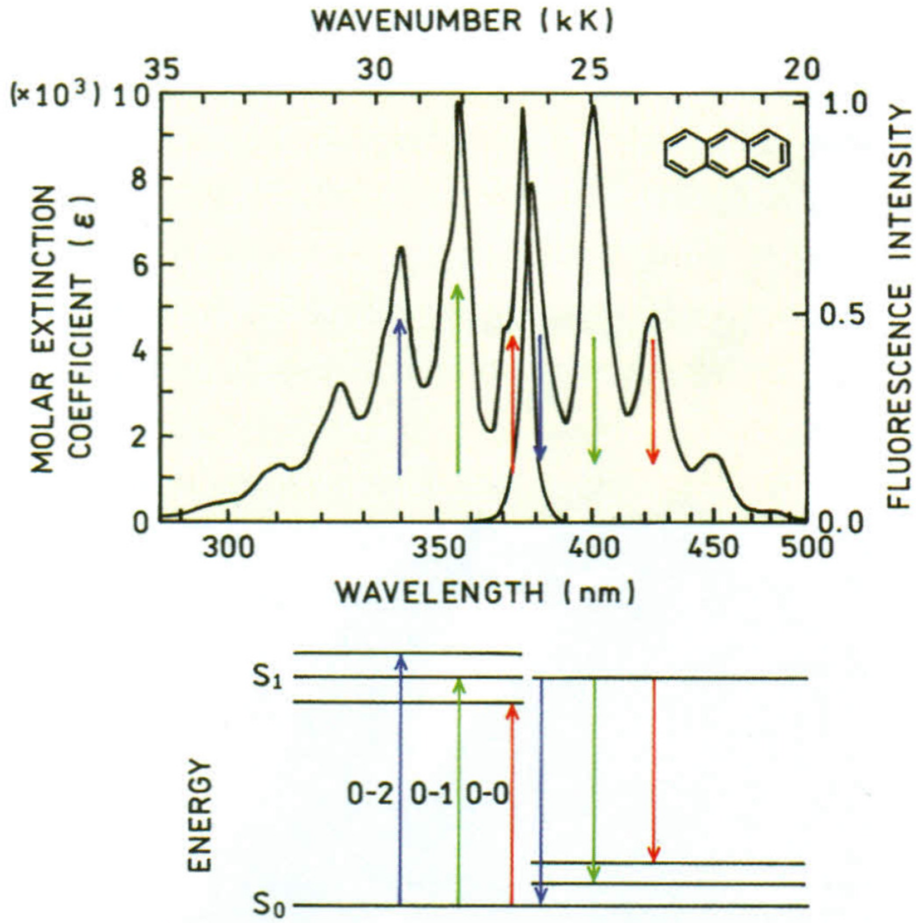
  - **Fluorescence emission *(nanosecond timescale)*.**
  - **Internal conversion (*ic*) and vibrational relaxation *(radiationless decay)*.**
  - **Intersystem crossing (*isc*) to the triplet excited state T_1.**

- From the T_1 state *phosphorescence emission* (micro- to millisecond timescale) occurs, or in the presence of O_2 reaction may occur via type 1 or type 2 mechanisms producing reactive oxygen species (re: photodynamic therapy).

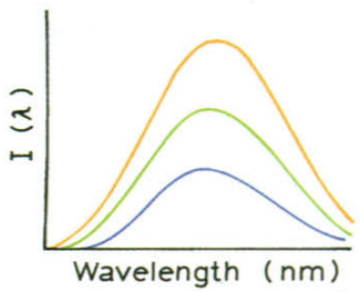
Jablonski diagram



Fluorescence Spectroscopy (e.g. anthracene)



- Mirror-image rule and Franck-Condon factors.
- The numbers 0, I, and 2 refer to vibrational energy levels.
- ***As phosphorescence is a spin forbidden $T_1 – S_0$ transition the mirror rule does not apply***.



Φ_f = no. of photons emitted / no. of photons absorbed

- Fluorescence quantum yields (Φ_f) are calculated using *steady state* methods by ***actinometry***:

  Typically, in de-aerated, optically dilute solutions fluorescence spectra of both the actinometer (ref) and sample (s) are recorded following *__identical monochromatic excitation__* of uniform intensity

$$\Phi_f = (A_{ref}/A_s)(I_s/I_{ref})(\eta_s/\eta_{ref})^2\Phi_{ref}$$

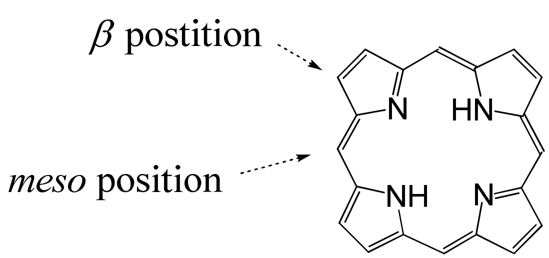
  where A is the absorbance at the excitation wavelength, I is the integrated emission area and η is the solvent refractive index.

- If an actinometer is used which allows use of the same solvent this equation reduces to

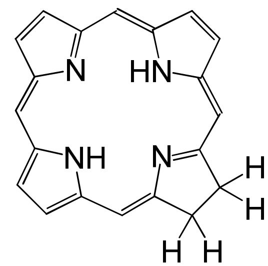
$$\Phi_f = (A_{ref}/A_s)(I_s/I_{ref})\Phi_{ref}$$

The Porphyrinoid Family

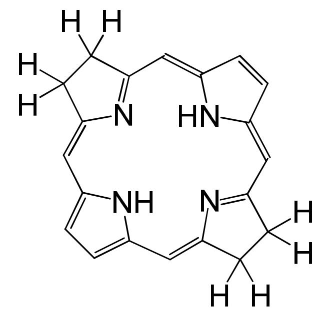
- The most extensively studied photosensitizers are *tetrapyrrole* chromophores, which includes porphyrins, chlorins, bacteriochlorins, benzoporphyrins, and phtalocyanines.



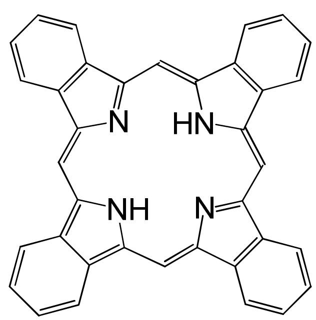
porphine



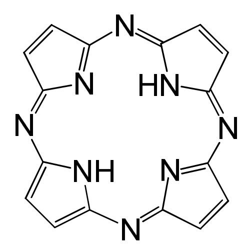
chlorin



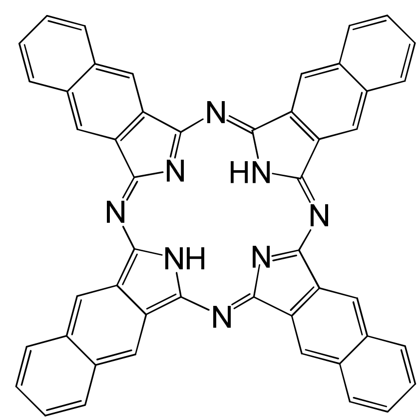
bacteriochlorin



benzoporphyrin



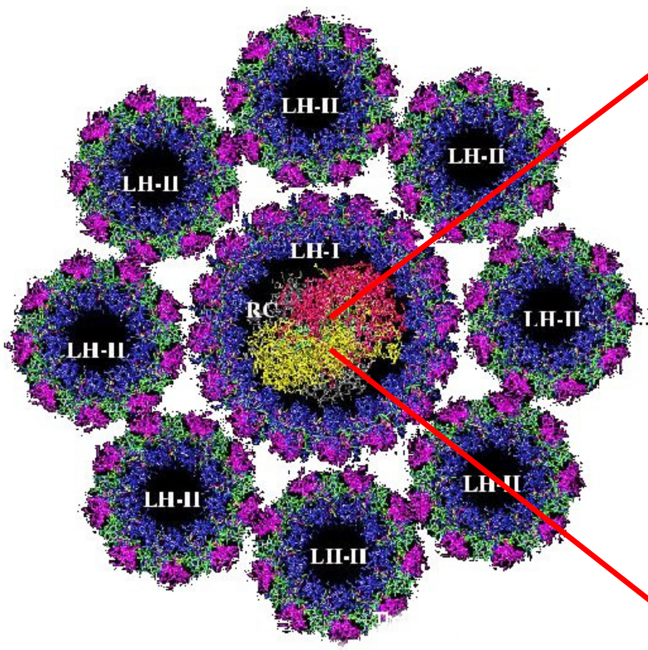
phtalocyanine



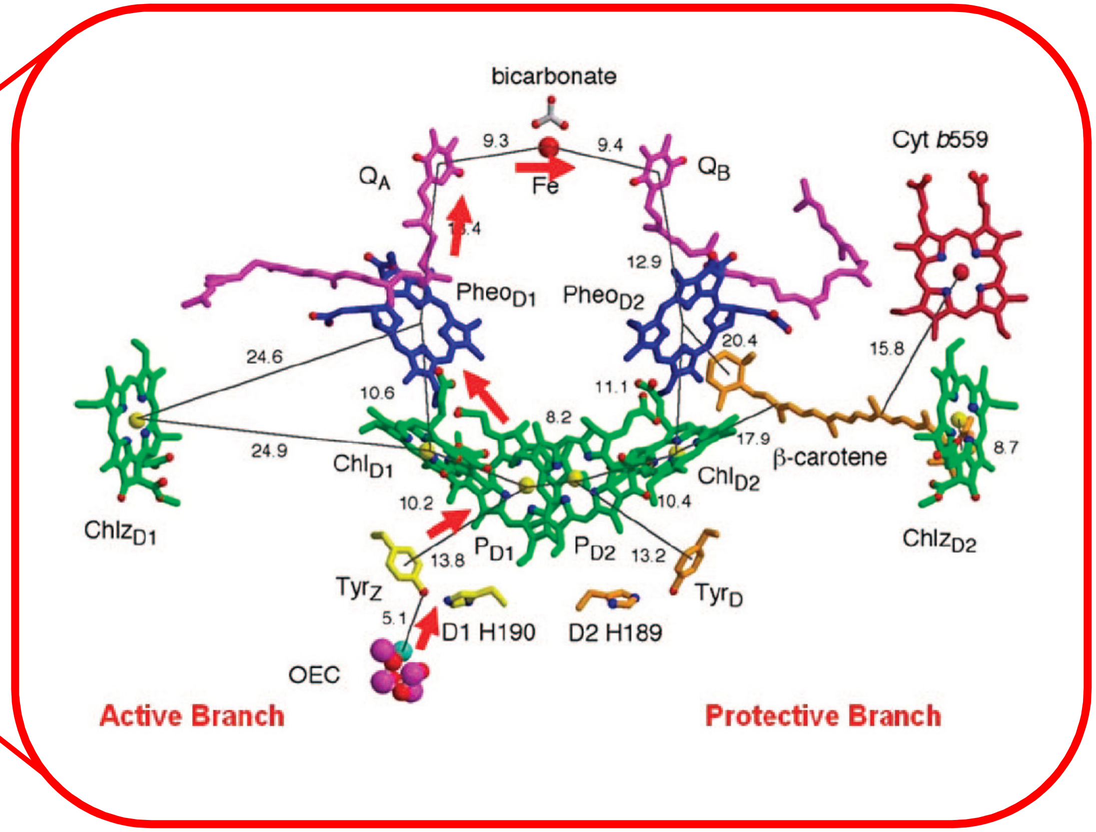
naphtalocyanine

Photosynthesis

$(6CO_2 + 6H_2O + h\nu \rightarrow (CH_2O)_6 + 6O_2)$



Light-Harvesting
(energy transfer)



Reaction Center

(charge-separation via e^- transfer)

Porphyrin Catalysts for CO_2 Reduction

- The metalloporphyrins and related metallo-macrocycles studied for CO_2 reduction reactivity include metalloporphyrins (MP), metallocorrins (MN), metallophthalocyanines (MPc), and metallocorroles (MC), Figure 4, where M = Fe or Co.

- The active catalytic states as identified by cyclic voltametry have the metal in the formal oxidation state of zero for porphyrins $[M^0P]^{2-}$ and corrins $[M^0N]^{2-}$, +1 for corroles $[M^IC]^{2-}$, and +1 with a reduced phthalocyanine ring $[M^IPc^{\bullet -}]^{2-}$.

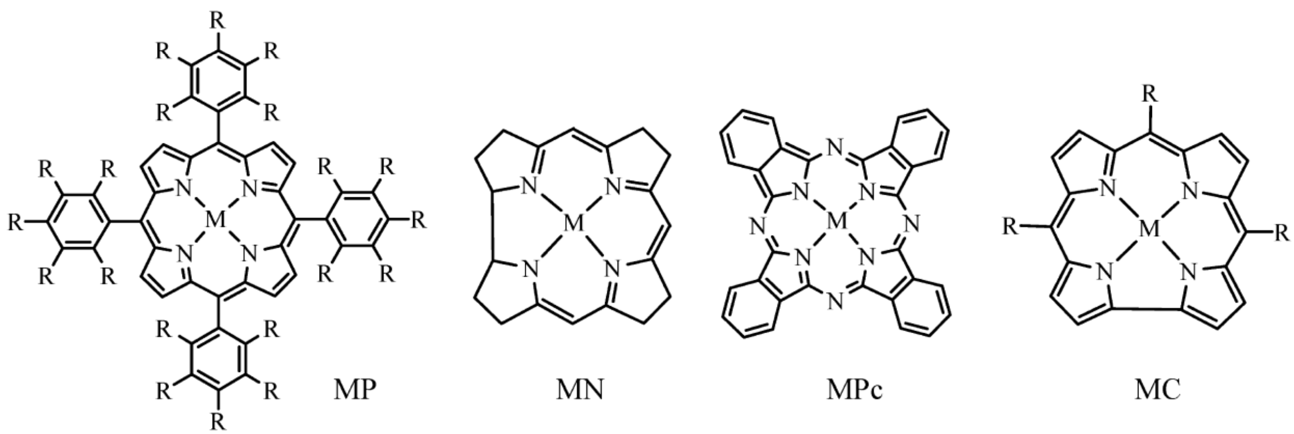
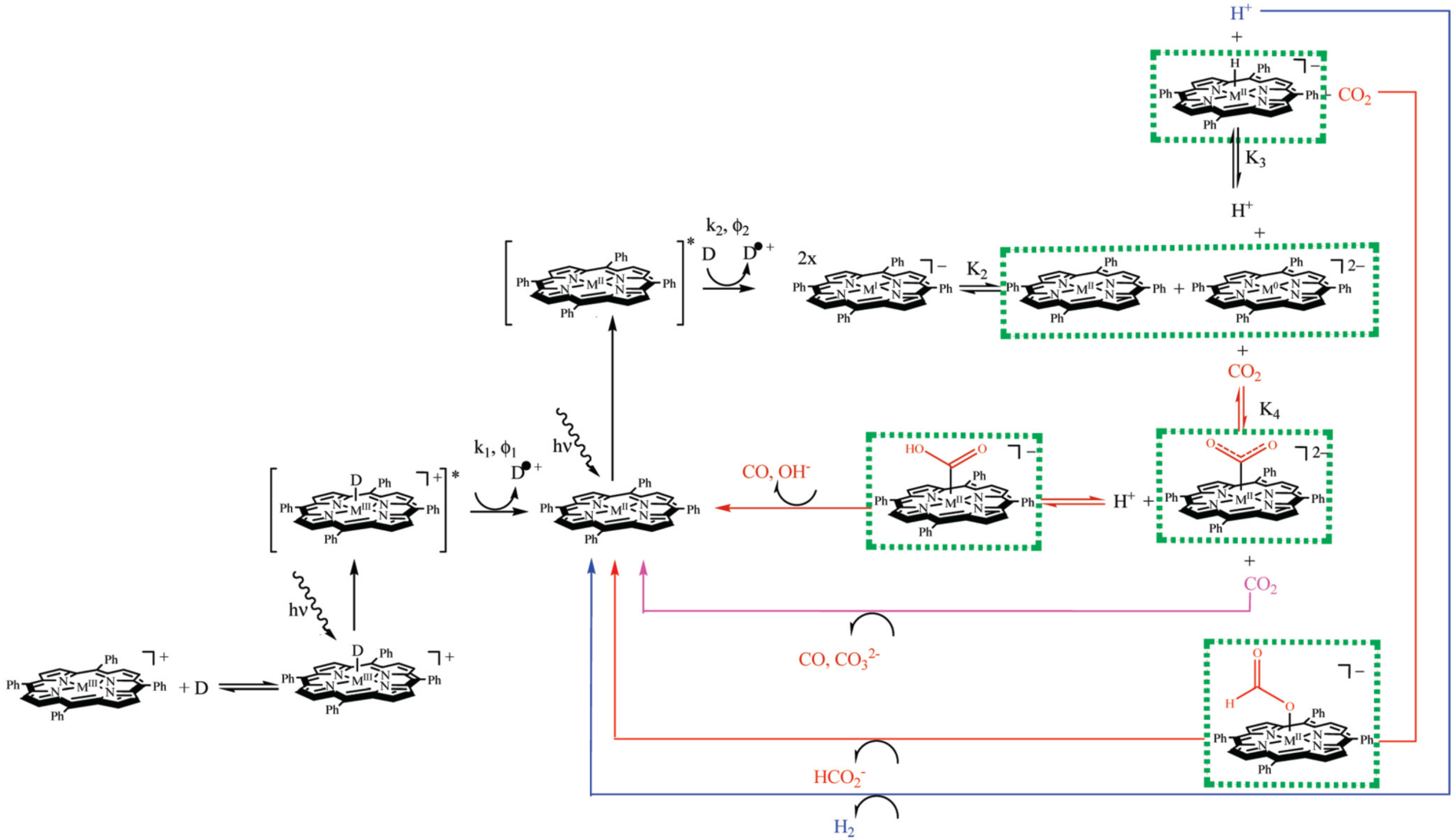


FIGURE 4. Metal porphyrin derivates investigated for CO_2 reduction: (left to right) metalloporphyrin (MP), metallocorrin (MN), metallophthalocyanine (MPc), and metallocorrole (MC, where R = C_6F_5 or 2,6-$C_6H_3Cl_2$).

Morris et. al *Acc. Chem. Res.*, 2009, 42 (12), pp 1983–1994

Mechanism for CO_2 Reduction

SCHEME 2. Proposed Mechanistic Steps in the Reduction of CO_2 by Metal Porphyrin Derivatives (M = Fe or Co) via a Type II Mechanism[a]



[a] Hydrogen production (blue), formate production (red), CO formation (brown and pink), and putative intermediates (green); as a representative compound, metalloporphyrin is illustrated.

Porphyrin Catalysts for O_2 Activation

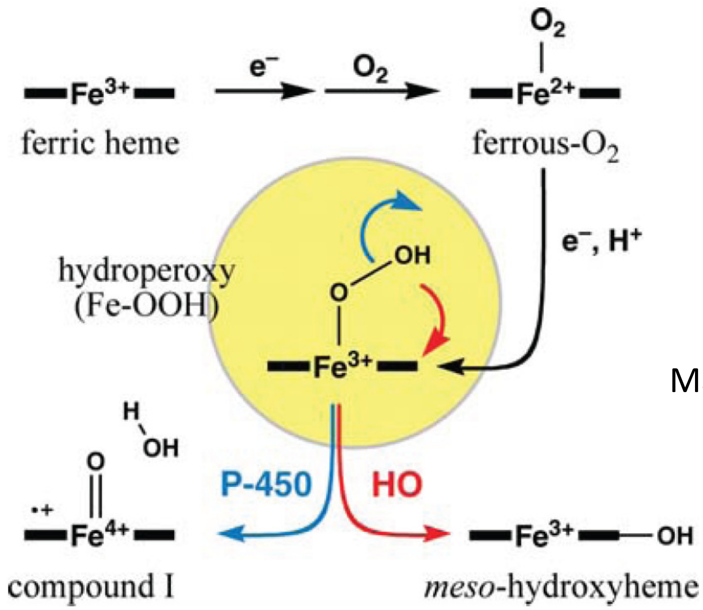
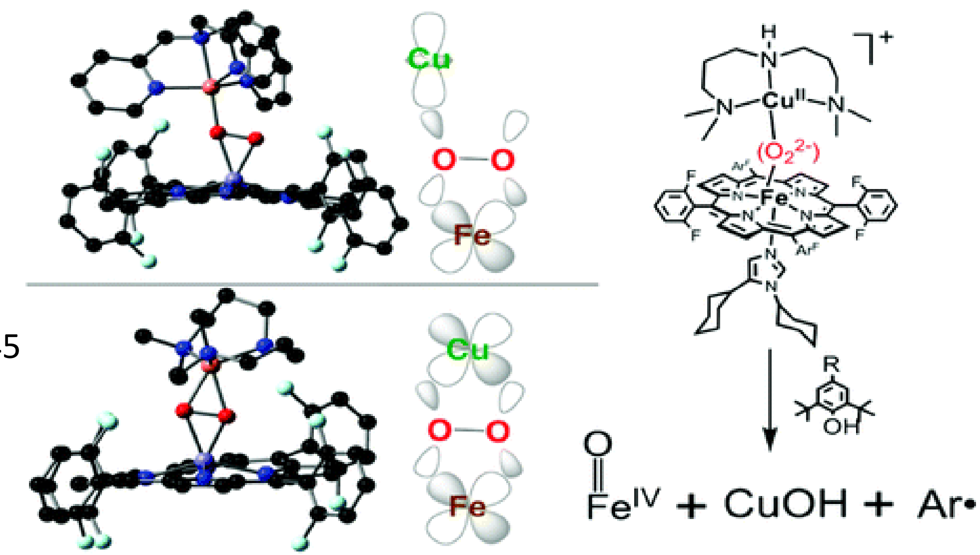


Figure 2. Comparison of O_2 activation by HO and cytochrome P450.

Matsui et. al *Inorg. Chem.*, 2010, 49 (8), pp 3602–3609



Halime et. al *Inorg. Chem.*, 2010, 49 (8), pp 3629–3645

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doi:10.1038/nrc1894

Photodynamic therapy and anti-tumour immunity

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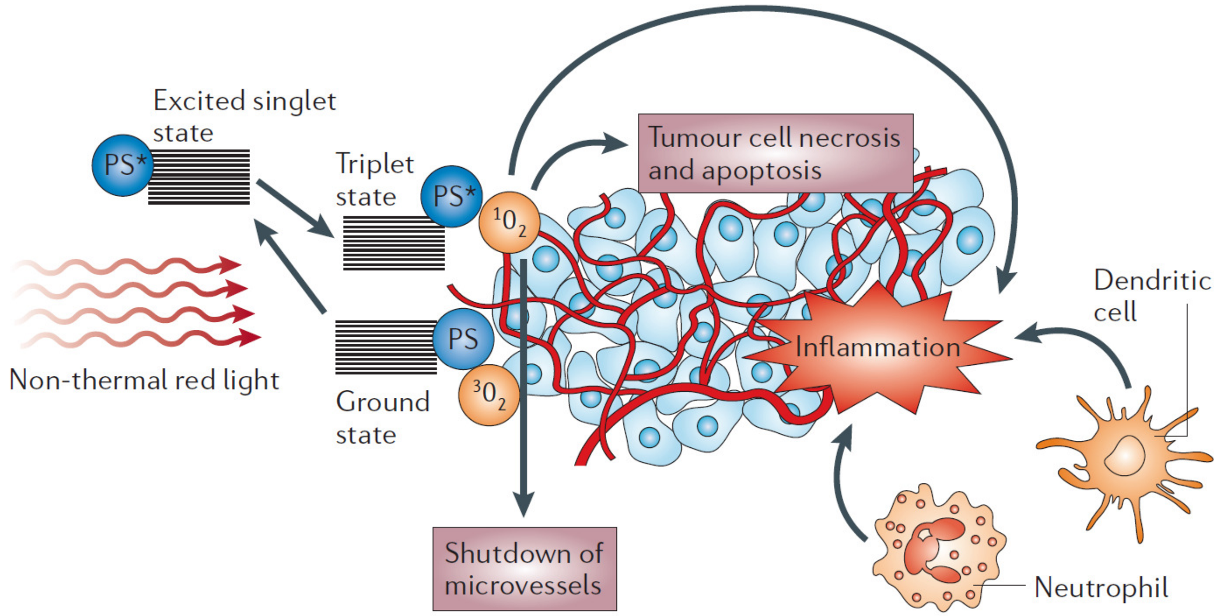
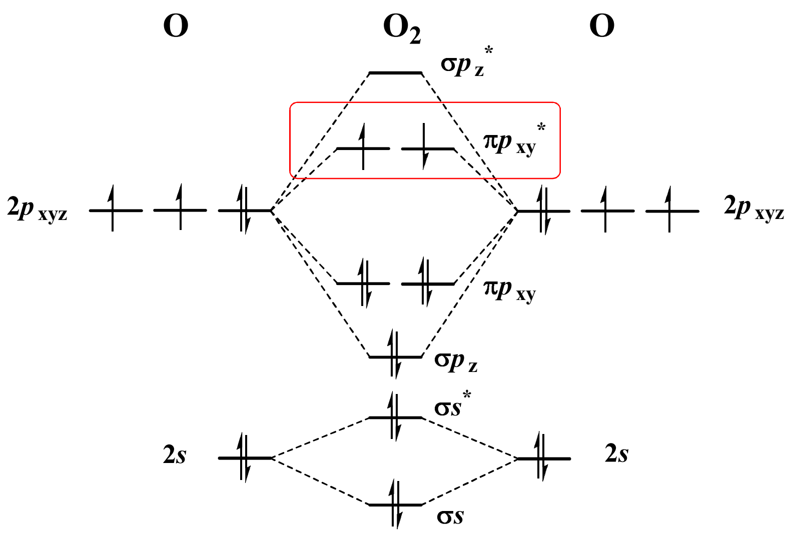
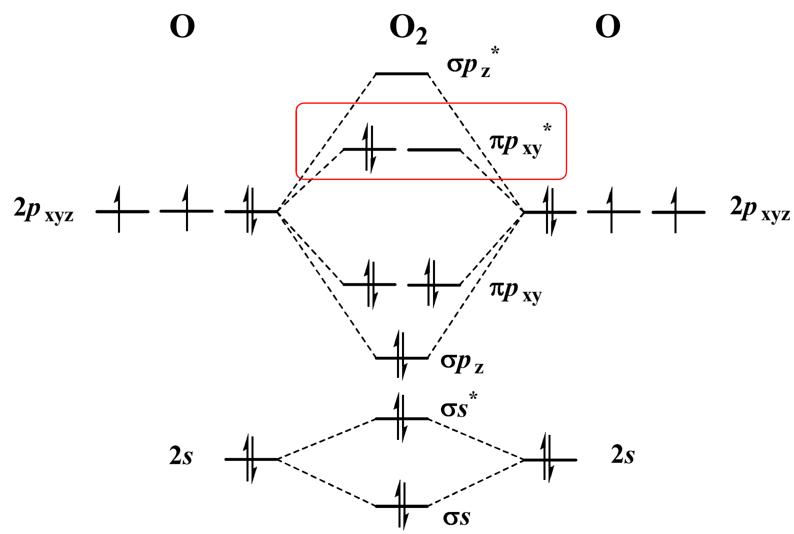


Figure 1 | **The mechanism of action on tumours in photodynamic therapy.** The photosensitizer (PS) absorbs light and an electron moves to the first short-lived excited singlet state. This is followed by intersystem crossing, in which the excited electron changes its spin and produces a longer-lived triplet state. The PS triplet transfers energy to ground-state triplet oxygen, which produces reactive singlet oxygen ($^1O_2$). $^1O_2$ can directly kill tumour cells by the induction of necrosis and/or apoptosis, can cause destruction of tumour vasculature and produces an acute inflammatory response that attracts leukocytes such as dendritic cells and neutrophils.



$^{1}\Sigma_g^{+}$



$^{1}\Delta_g$

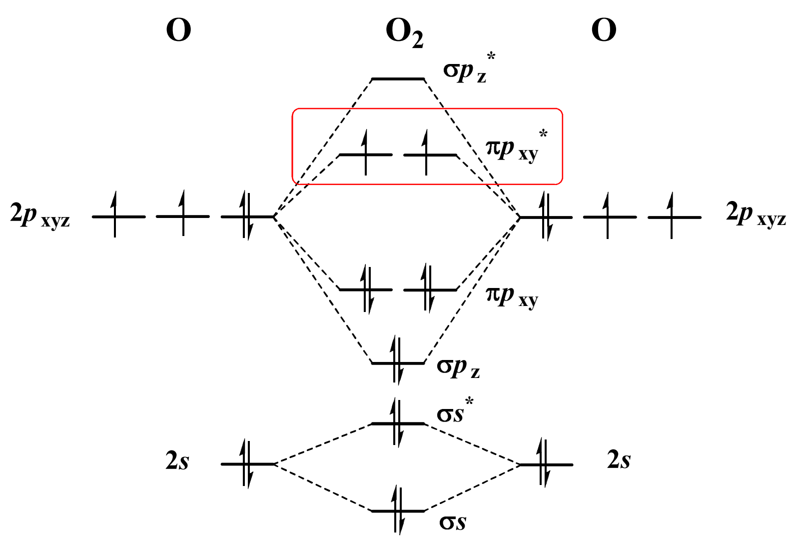
Molecular orbital diagrams for the three electronic configurations of O_2.

The triplet ground state $^{3}\Sigma_g^{-}$

The singlet oxygen a$^{1}\Delta_g$ excited state

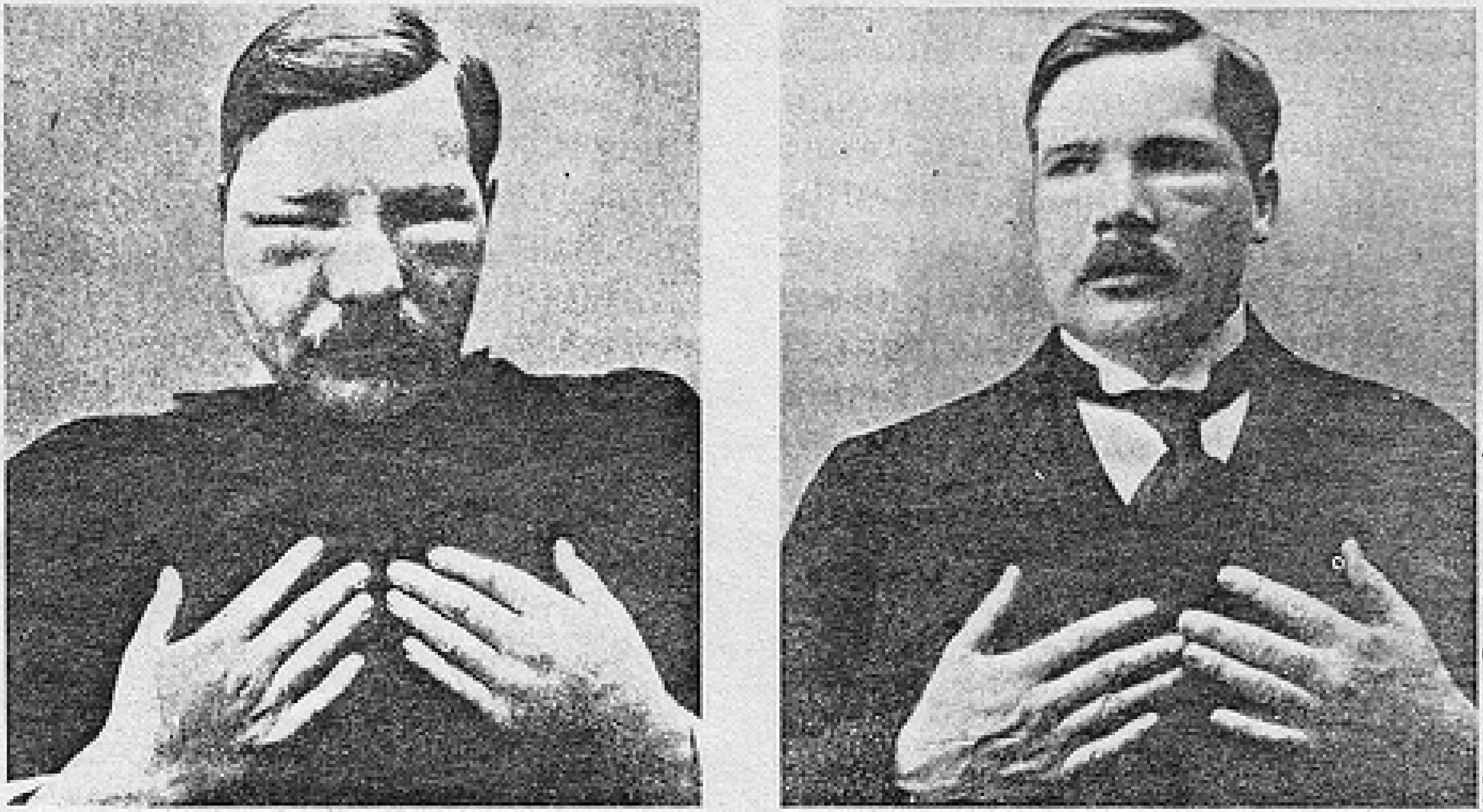
The singlet oxygen b$^{1}\Sigma_g^{+}$ excited state.

Note that the states only differ in the spin and the occupancy of two degenerate anti-bonding π_g^{*} orbitals.



$^{3}\Sigma_g^{-}$

Friedrich Meyer-Betz, a German physician, injected himself with porphyrin in 1912 to test whether it made humans sensitive to light. The first photograph shows him four days later, after he took a walk on a sunny day. Most of the swelling subsided by the sixth day, second photograph, but he remained light-sensitive for several months.



courtesy A. M. McDonagh, UCSF (2)

Porphyria

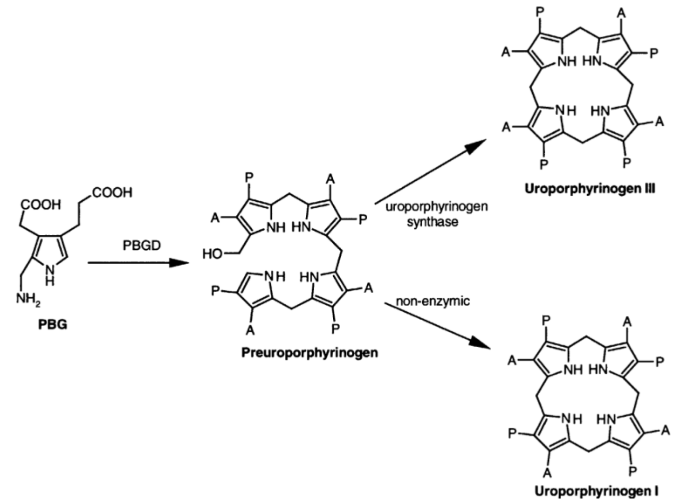
- Overproduction and accumulation of the porphyrins (or their chemical precursors).

- Decreased production of heme leads to increased production of precursors, PBG being one of the first substances in the porphyrin synthesis pathway.

- The principal problem of porphyria is the accumulation of porphyrins, which are toxic to tissue in high concentrations.

- The chemical properties of these intermediates determine the location of accumulation, whether they induce photosensitivity.

- Porphyria has been suggested as an explanation for the ***origin of vampire and werewolf legends***, based upon certain perceived similarities between the condition and the folklore.



- L. Illis' 1963 paper, "On Porphyria and the Aetiology of Werwolves", was published in *Proceedings of the Royal Society of Medicine*. In 1985, biochemist David Dolphin's paper for the American Association for the Advancement of Science, "Porphyria, Vampires, and Werewolves: The Aetiology of European Metamorphosis Legends", gained widespread media coverage, thus popularizing the connection.

- The theory has since faced heavy criticism, especially for the stigma it has placed on its sufferers. Norine Dresser's *American Vampires: Fans, Victims, Practitioners* (1989) treats the matter with more depth.