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SYNTHESIS OF N-AMINOPORPHYRINS

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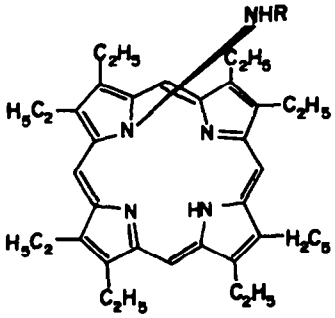
Abstract—Amination of octaethylporphyrin and *meso*-tetraphenylporphyrin using O-mesitylsulfonylhydroxylamine leads to N-aminooctaethylporphyrin and N-amino-*meso*-tetraphenylchlorin respectively.

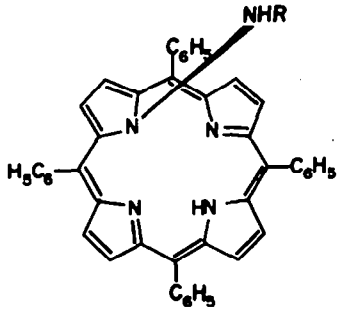
The preparation of N-substituted-N-aminoporphyrins **1** or **2** has been recently described by two groups, including ours.[1,2] Metalation of these bases led to a series of porphyrins like **3** bearing a nitrene moiety inserted between the metal and a pyrrolic nitrogen.[1-3] An oxygen analog, porphyrin N-oxide or its tautomer N-hydroxyporphyrin, has been isolated[4] and the existence of metal complexes showing an oxygen insertion postulated. These results prompted us to report the first isolation and characterization of N-aminoporphyrin **4** and N-aminochlorin **5**.

Treatment of octaethylporphyrin (OEP) with excess O-mesitylsulfonylhydroxylamine (OMSH)[5] gave stable N-amino-OEP **4** (41% based on transformed starting material). Both NMR and visible spectra were similar to those of N-Me-OEP[6] (strong shielding of two Et groups, 2:2 pattern for the *meso* protons). Tosylation of **4** gave **1** (R = tosyl), similar to the known tosylamino- and acylaminoporphyrins.[1,2] Also metalation of **1** (R = tosyl) gave a bridged compound **6**.

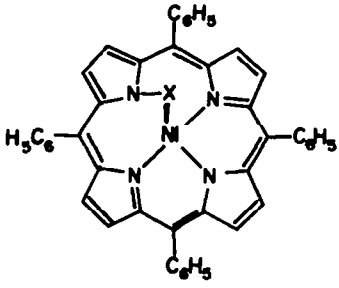
Surprisingly *meso*-tetraphenylporphyrin (TPP) did not react with OMSH to give N-amino-TPP but instead furnished the corresponding chlorin **5** (32% based on transformed starting material). This product could not



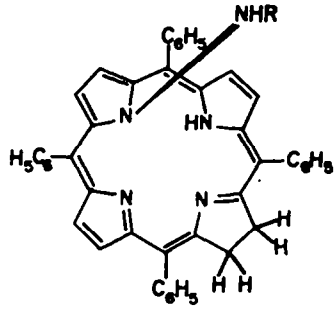
1: R = tosyl, COAryl
4: R = H



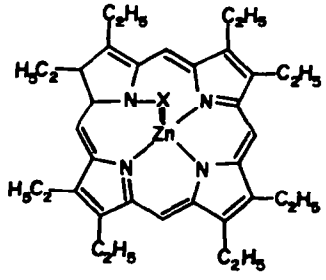
2: R = tosyl, COAryl



3: X = N-tosyl



5: R = H
7: R = tosyl



6: X = N-tosyl

originate from chlorin present as an impurity since the starting material was purified using DDQ.[7] The reaction gave similar results in the dark thus ruling out the known photoreduction of porphyrins.[8] We suggest (a) that the reactivity of H_2TPP is markedly lower than that of the more nucleophilic chlorin[9] and/or the nitrogen of a more distorted chlorin is less sterically hindered, (b) an initial reduction of H_2TPP by diimide generated according to:

$$2RSO_2ONH_2 + H_2TPP \rightarrow RSO_2ONHNH_2 + H_3TPP^+RSO_3^-$$

$$RSO_2ONHNH_2 + H_2TPP \rightarrow NH{=}NH + H_3TPP^+RSO_3^-.$$

Reaction of pure tetraphenylchlorin[10] gave the same product 5 at a higher rate.

The assignment of structure 5 was unambiguous: the NMR spectrum showed the expected singlet (2H) and AB doublets (4H) for the 6 remaining pyrrolic protons. Correlation of 5 with a known compound was accomplished through the following reaction sequence: (a) tosylation to 7 (direct dehydrogenation did not yield N-amino-TPP), (b) dehydrogenation (DDQ) to the known 2 (R = tosyl).[1]

Both 4 and 5 are very stable crystalline compounds. They remained unchanged during chromatography and thus are more stable than the corresponding N-oxides.[4] Attempted metalation of 4 or 5, using Ni(II), Zn(II) or Cu(II) salts (acetates or acetylacetonates) led to polar mixtures which unfortunately transformed into the corresponding metalloporphyrins (MOEP or MTPP) before any definite compound could be isolated.

EXPERIMENTAL

Visible and NMR spectra were recorded on a Cary 118 spectrophotometer and a Cameca (250 MHz) respectively. The chemical shifts are expressed in δ values (ppm) relative to TMS internal standard and the coupling constants in Hz (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). Combustion analyses were performed at the Service Central de Microanalyse, Division de Strasbourg. We experienced difficulties in obtaining good analytical figures for N-substituted porphyrins.[11] Separation and purification of the products were obtained using Merck standardized alumina (II–III).

N-Amino-OEP 4. OMSH (0.5 g) and H_2OEP (0.5 g) were stirred for 16 hr at 20° in $CHCl_3$ (250 ml). Evaporation and chromatography (alumina, 100 g in CH_2Cl_2) gave H_2OEP (216 mg) and a green fraction. Crystallization from MeOH yielded 4 (120 mg; 41% based on transformed H_2OEP). NMR ($CDCl_3$) δ −3.1 (very broad, *ca.* 3H, NH), 1.55, 1.89, 1.92 (3t, 6:12:6, CH_3, J = 7 Hz), 3.77, 3.80, 3.97, 4.17 (4q, 2:2:8:4, CH_2, J = 7 Hz), 10.02 (s, 2, *meso*), 10.03 (s, 2, *meso*); visible (toluene) λ_{max} 408 nm (ϵ 141,000), 510 (9600), 545 (5700), 573 (6700), 628 (5900). (Found: C, 77.96; H, 8.13; N, 12.67. Calc. for $C_{36}H_{47}N_5$: C, 78.65; H, 8.62; N, 12.74%).

N-Tosylamino-OEP 1 (*R = tosyl*). A soln of 4 (30 mg), tosyl chloride (40 mg), Et_3N (0.1 ml) in CH_2Cl_2 (5 ml) was kept for 0.5 hr at 20°. Evaporation and filtration on a short alumina column (CH_2Cl_2) followed by crystallization (MeOH + 5% H_2O) gave 1 (32 mg; R = tosyl). NMR ($CDCl_3$) δ −0.94 (s, 2, NH), 1.48, 1.84, 1.90, 1.94 (4t, 6:6:6:6, J = 7 Hz), 2.21 (s, 3, tosyl CH_3), 3.79, 3.82 (2q, 2:2, CH_2, J = 7 Hz), 3.93–4.13 (m, 12, CH_2), 4.80, 6.39 (2d, 2:2, tosyl, AB J = 8 Hz), 10.01 (s, 2, *meso*), 10.25 (s, 2, *meso*); visible (toluene) λ_{max} 407 nm (ϵ 125,000), 532 (9100), 568 (14,800), 612 (2700). (Found: C, 72.36; H, 7.31; N, 10.02. Calc. for $C_{43}H_{53}N_5O_2S$: C, 73.36; H, 7.59; N, 9.95%).

N-Tosylamino-OEPZn 6. Treatment of 1 (R = tosyl; 15 mg) with excess zinc acetate in CH_2Cl_2–MeOH and crystallization from MeOH gave 6 (12.5 mg). NMR ($CDCl_3$) δ 1.43, 1.86, 1.93, 1.94 (4t, 6:6:6:6, CH_3, J = 7 Hz), 2.38 (s, 3, tosyl CH_3), 3.68, 3.70, 3.92, 3.95, 4.06 (5q, 2:2:2:2:8, CH_2, J = 7 Hz), 5.56, 6.73 (2d, 2:2, tosyl, AB J = 7 Hz), 9.92 (s, 2, *meso*), 10.11 (s, 2, *meso*); visible (toluene) λ_{max} 413 nm (ϵ 186,000), 530 (9400), 565 (12,400), 610 (11,300). (Found: C, 67.50; H, 6.84; N, 9.32. Calc. for $C_{43}H_{51}N_5O_2SZn$: C, 67.30; H, 6.70; N, 9.13%).

N-Aminotetraphenylchlorin 5. A soln of H_2TPP (275 mg; DDQ purified) and OMSH (275 mg) in $CHCl_3$ (50 ml) was kept for 24 hr at 20°. Evaporation and chromatography (alumina, CH_2Cl_2) gave H_2TPP (189 mg) and chlorin 5 (28 mg), crystallized from CH_2Cl_2–MeOH. NMR ($CDCl_3$) δ 0.04 (broad, *ca.* 3H, NH), 3.80–4.30 (symetrical m, 4, CH_2–CH_2), 7.41 (s, 2, pyrrole), 7.60–7.79 and 7.96–8.25 (2m, 20, phenyl), 8.01 and 8.51 (2d, 4, AB J = 4.8 Hz, pyrrole); visible (toluene) λ_{max} 428 nm (ϵ 122,000), 447 (sh, 106,000), 545 (12,300), 610 (sh, 5800), 660 (8300). (Found: C, 82.58; H, 5.29; N, 11.27. Calc. for $C_{44}H_{33}N_5$: C, 83.65; H, 5.27; N, 11.08%).

The same product was obtained from tetraphenylchlorin[10] the rate of conversion being *ca.* 2–3 times higher. The most convenient preparation of 5 is obviously amination of crude H_2TPP.

N-Tosylaminotetraphenylchlorin 7. A soln of 5 (25 mg), tosyl chloride (40 mg) and Et_3N (0.1 ml) in CH_2Cl_2 (5 ml) was kept for 4 hr at 20°. Evaporation and crystallization of the residue from MeOH gave 7 (24.5 mg). NMR ($CDCl_3$) δ *ca.* 1.4 (very broad, *ca.* 2H, NH), 2.14 (s, 3, tosyl CH_3), 4.18–4.28 (symetrical m, 4, CH_2–CH_2), 5.27 and 6.52 (2d, 2:2, AB J = 8 Hz, tosyl), 7.54 (s, 2, pyrrole), 7.66–8.07 (m, 20, phenyl), 8.18 and 8.65 (2d, 2:2, AB J = 4.8 Hz, pyrrole), ; visible (toluene) λ_{max} 427 nm (ϵ 133,000), 442 (141,000), 550 (sh, 9200), 568 (12,200), 582 (14,000), 634 (12,500). (Found: C, 77.35; H, 4.83; N, 9.12. Calc. for $C_{51}H_{39}N_5O_2S$: C, 77.94; H, 5.00; N, 8.91%).

Dehydrogenation of 7 to 2 (*R = tosyl*). Chlorin 7 was quantitatively dehydrogenated in refluxing toluene (0.5 hr) using DDQ (3 equivs). The product was identified with the known 2 (R = tosyl).[1]

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