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Chemistry of Dimethylaminomethylporphyrins. New Synthesis of *meso*-Methylporphyrins *via* Triphenylporphyrinylmethylphosphonium Iodides

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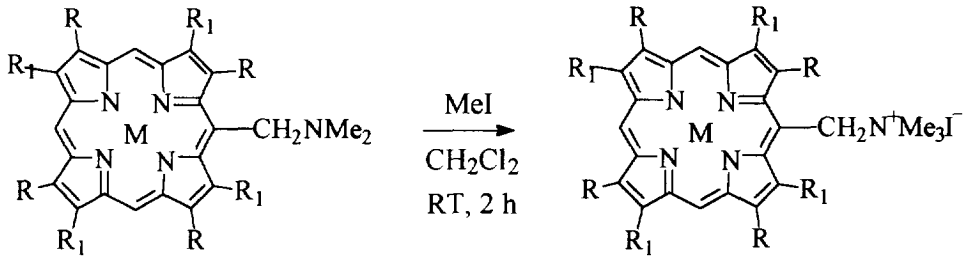
Abstract: Reaction of various trimethyl(porphyrinylmethyl) ammonium iodides (generated *in situ* from the corresponding *meso*-dimethylaminomethylporphyrins and iodomethane) with triphenylphosphine afforded triphenylporphyrinylmethylphosphonium iodides which, when subjected to mild basic hydrolysis, gave *meso*-methylporphyrins in high yields.

Recently we have reported the reactions *via* trimethylporphyrinylmethyl ammonium salts, of dimethylaminomethyl(DMAM)porphyrin derivatives (such as **1** - **3**) with different nucleophiles (alcohols[1], pyrroles[2]). In a new application of this research we report the reaction of the trimethylporphyrinylmethyl ammonium iodide derivatives (**4** - **6**) with triphenylphosphine.

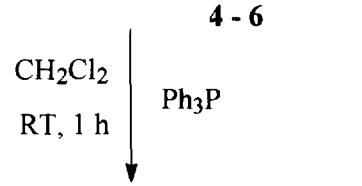
Thus, *in situ* generation of salts **4** - **6** using MeI in dichloromethane[2] followed by the addition of triphenylphosphine led to new *meso*-porphyrin derivatives **7** - **9**[3] which were purified by simple recrystallisation in high yields.[4] *meso*-Porphyrinylmethylphosphonium salts are previously unknown. Bonfantini and Officer reported β-tetraphenylporphyrinyl(TPP)methylphosphonium chloride, and its conversion to the corresponding ylide, *via* β-chloromethylTPP.[5] On the other hand, *meso*-halomethylporphyrins are inaccessible, and our new procedure circumvents the necessity to handle these unstable halides. The complexed metal ion is necessary, as the free base DMAM-porphyrins yield a complex mixture of products under the same conditions. The bis(phosphonium salt) **10**[3] was readily prepared by treating bis(diphenylphosphino)ethane with an excess of ammonium salt **4**.

Some chemistry of the products **7** - **9** has been studied. Thus treatment of **7** - **9** with methanol (water) in presence of excess of Et_3N (2% NaOHaq[6]) in CH_2Cl_2 at room temperature afforded very smooth formation of

meso-methylporphyrins **11**[7], **12**[3] and **13** (the latter was subjected to demetallation with conc. H_2SO_4 to give the desired **14**[8]). Alkaline hydrolysis of phosphonium salts is well known to give C–P cleavage , with loss of the group which forms the more stable carbanion.[9] The use of methanol-d_4 led to the formation of NiOEP-CH_2D, as shown by ^{13}C NMR.



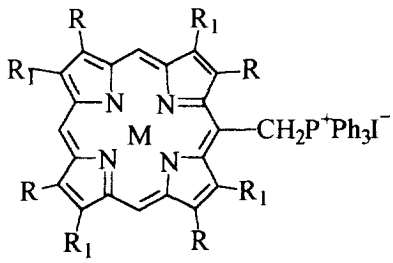
1 - 3 **4 - 6**



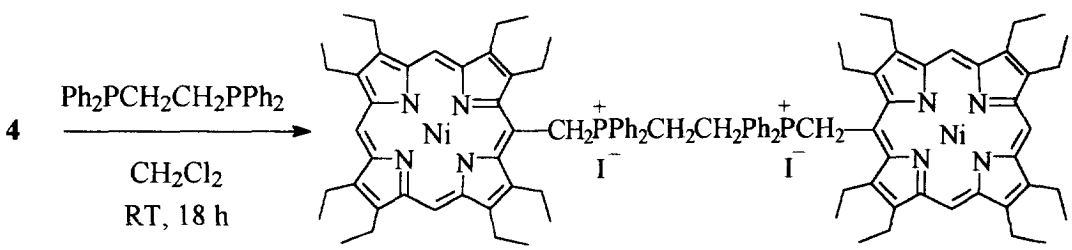
1,4,7: R = R_1 = Et (OEP), M = Ni

2,5,8: R = Me, R_1= $CH_2CH_2COOPr^i$, M = Ni

3,6,9: R = Me, R_1= Et, M = Cu



7 - 9



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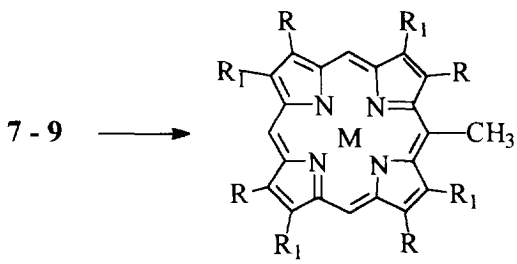
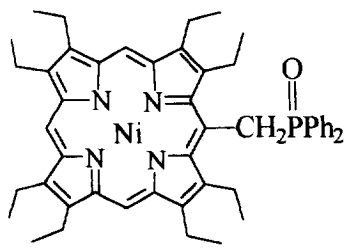
Although there are other methods of preparing *meso*-methylporphyrins,[7,8] our procedure is very mild and high-yielding, giving **11** from NiOEP in 85% overall yield.

Phosphonium salt 7 can also be used as a *meso*-porphyrinylmethyl cation (or cation radical) precursor (compare the use of DMAM-porphyrins[1]). Thus refluxing 7 in toluene in the presence of triethylamine gave the known dimer NiOEP-CH_2CH_2-NiOEP[10] in almost quantitative yield. In the absence of the base, heating in toluene produced the dimer, **11**, and NiOEP in the ratio 84:13:3.





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11: R = R_1 = Et (OEP), M = Ni (96%)

12: R = Me, R_1= $CH_2CH_2COOPr^i$, M = Ni (quant.)

13: R = Me, R_1= Et, M = Cu

14: R = Me, R_1= Et, M = 2 H (86% from **9**)

We naturally attempted to form the ylide from 7. However, the reaction of 7 with NaH in DMF smoothly led to the diphenylporphyrinylmethylphosphine oxide **15**[3] in 72% yield. In this case, the phenyl carbanion was preferentially cleaved, in contrast to the base reaction in protic solvents. This may be a specific effect of DMF, since NaH in THF on 7 gave a mixture of the above ethane dimer, NiOEP-CHO, and NiOEP-CH_2OH in ~1:1:1 ratio. Deviation from the normal leaving group abilities has been previously noted,[9] especially where one group is hindered, as in our case. Attempted reduction of oxide **15** with $LiAlH_4$ in THF or ether gave a complex mixture of products.

In conclusion, this chemistry has not only led to a simple method of preparing *meso*-methylporphyrins under gentle conditions, but has also initiated studies into *meso*-phosphoniummethyl derivatives of porphyrins.

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3. **7**: ^{1}H NMR ($CDCl_3$, 300 MHz): 9.42 (s, 1 H, *meso*-10-H), 9.30 (s, 2 H, *meso*-5,15-H), 7.00-6.44 (m, 15 H, Ph), 6.43 (d, 2 H, J(PH) = 14 Hz, PorCH_2P), 3.92-3.56 (overlapping q, 16 H, CH_2 of peripheral Et), 1.92-1.58 (overlapping t, 24 H, CH_3 of peripheral Et); ^{31}P NMR ($CDCl_3$): 25.6 (*vs.* Ph_3P); UV/vis ($CHCl_3$) λ_{max} (ε x 10^{-3}) ($CHCl_3$) 421 (122), 559sh (8.7), 594 (13) nm; IR (KBr): 2961, 2927, 2867, 1432, 1367, 1312, 1269, 1221, 1106, 1017, 992, 956, 868, 838, 735, 717, 687 cm^{-1}; ESI-MS: 865.8 (2) $(M - I)^+$, 603.6 (100) $(NiOEPCH_2)^+$.
   10: ^{1}H NMR ($CDCl_3$, 300 MHz): 9.40 (s, 2 H, *meso*-10-H), 9.06 (s, 4 H, *meso*-5,15-H), 6.10-5.70 (m, 24 H, Ph and PorCH_2), 3.90-3.30 (overlapping q, 32 H, CH_2 of peripheral Et), 2.54 (m, 4 H, PCH_2CH_2P), 1.88-1.24 (overlapping t, 48 H, CH_3 of peripheral Et); UV/vis ($CHCl_3$) λ_{max} (ε x 10^{-3}) ($CHCl_3$) 417 (246.5), 550 (13.7), 591 (23.8) nm.
   12: ^{1}H NMR ($CDCl_3$, 300 MHz): 9.42, 9.41 and 9.40 (s, 3 H, *meso*-H), 5.20-5.00 (overlapping septets, 4 H, OCHMe$_2$), 4.22-4.08 (m, 8 H, PorCH_2CH_2COOR), 3.80 (s, 3 H, *meso*-CH_3), 3.42, 3.38 and 3.37 (s, 12 H, peripheral CH_3), 3.10-2.95 (m, 8 H, PorCH_2CH_2COOR), 1.35-1.15 (overlapping d, 24 H, OCHMe_2); UV/vis ($CHCl_3$) λ_{max} (ε x 10^{-3}) ($CHCl_3$) 407 (202), 532 (12), 567 (16) nm.
   15: ^{1}H NMR ($CDCl_3$, 300 MHz): 9.39 (s, 1 H, *meso*-10-H), 9.23 (s, 2 H, *meso*-5,15-H), 6.42-6.02 (m, 10 H, Ph), 5.56 (d, 2 H, J(PH) = 17 Hz, PorCH_2P), 3.90 - 3.55 (overlapping q, 16 H, CH_2 of peripheral Et), 1.90-1.55 (overlapping t, 24 H, CH_3 of peripheral Et); ^{31}P-NMR ($CDCl_3$): 35.6 (*vs.* Ph_3P); UV/vis ($CHCl_3$) λ_{max} (ε x 10^{-3}) ($CHCl_3$) 416 (128.5), 551 (8.8), 583 (12) nm; IR: 2963, 2928, 2868, 1447, 1373, 1270, 1225, 1205 (P=O), 1113, 1054, 1017, 956, 866, 836, 693 cm^{-1}; FAB-MS: 804.2 (45) (M^+), 603.2 (100) $(NiOEPCH_2)^+$.
4. *Typical procedure*: A mixture of **1** (20 mg, 30.8 μmol), MeI (50 μL) and methylene chloride (3 mL) was stirred at room temperature for 2 h. After evaporation under reduced pressure at room temperature the residue (**4**) was dissolved in methylene chloride (3 mL) followed by addition of Ph_3P (16 mg, 62 μmol, 2 eq.) and the resulting mixture was stirred at room temperature for 1 h. Methanol (0.5 mL) was added followed by addition of Et_3N (0.3 mL) and the mixture was stirred at room temperature for 15 min. After evaporation under reduced pressure the residue was purified on silica gel with hexane/methylene chloride (3 : 1) as eluent to give pure **11** (18 mg, 96%).
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