A porphyrin chlorination reaction

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Treatment of nickel and palladium porphyrin complexes with thionyl chloride readily affords products of *meso*- and β-chlorination; further reaction leads to chlorination of macrocyclic methyl groups.

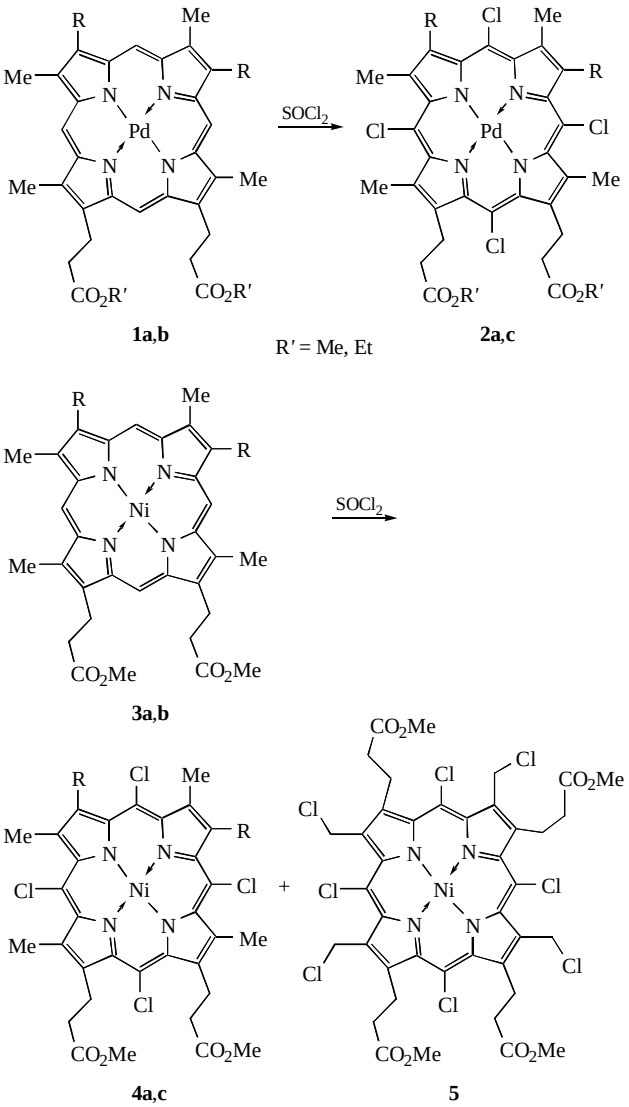
A reaction for the chlorination of porphyrin metal complexes has been found. In this study, instead of traditional chlorinating agents (*e.g.* HCl and hydrogen peroxide,[1,2] sulfuryl chloride[3] and chlorosulfonic acid[4]), we tried thionyl chloride, as used in the case of tetraazaporphyrin.[5] This reagent is known to readily replace the hydroxyl group in alcohols and carboxylic acids but has scarcely been used in reactions involving C–H linkages.[6] Thionyl chloride has been widely used in porphyrin chemistry for transforming carboxylic acids into the corresponding chlorides. However, on attempting the activation of the carboxylic acids in palladium coproporphyrin III with thionyl chloride, we noted an abrupt colour change from orange–red to deep green. The electron absorption spectrum of the product showed a significant bathochromic shift of both the Soret band and the α- and β-bands, with the intensity ratio of the α- and β-bands being considerably lower, evidencing disturbance of the porphyrin macrocycle. Unfortunately, full characterisation of the compound thus obtained was unsuccessful, presumably due to the formation of a highly reactive chloride.

Further study of this reaction was performed using the palladium coproporphyrin III tetramethyl ester **1a**. This was dissolved in $SOCl_2$, kept for 2 h at 20 °C, poured into ice and the resulting precipitate was filtered to give almost pure products (TLC assay) in 92% yield. Prior to elemental analysis, the porphyrin obtained was passed through alumina and recrystallised from chloroform–methanol. Elemental analysis data showed that the product contained four additional chlorine atoms. The mass spectrum also provided evidence in favour of four chlorine atoms (*m*/*z* 952).† The ^{1}H NMR spectrum showed the disappearance of four *meso*-protons. Therefore, the structure **2a** was assigned to the new compound.‡

In the case of palladium deuterioporphyrin **1b**, not only the *meso*-protons, but also both β-positions were replaced to give the hexachloro-substituted porphyrin **2c**.§ This showed an even greater colour change and bathochromic shift of absorption bands.

Similar behaviour was observed for nickel porphyrins. In the case of coproporphyrin **3a**, the *meso*-tetrachloro-derivative **4a**¶ was obtained at 4 °C for 15 min in 93% yield. Deuterioporphyrin **3b** was transformed into the hexachloro-derivative **4c**.††

However, nickel porphyrins demonstrated higher reactivity. Prolonged treatment of **3a** led to substitution of not only the *meso*-protons, but also the methyl groups. Heating for 1 h resulted in chlorination of all four methyl group to produce the octachloroporphyrin **5**.‡‡ Shortening the reaction time makes it



1a,**b** **2a**,**c** **3a**,**b** **4a**,**c** **5**

a R = $CH_2CH_2CO_2Me$
b R = H
c R = Cl

Scheme 1

† Mass spectra were measured on a MSBKh instrument (SELMI, Sumy, Ukraine). Ionisation was effected by ^{252}Cf fission products and a time-of-flight monitoring ion analyser was employed.

‡ Data for **2a**, methyl ester: mp 199–202 °C. ^{1}H NMR ($CDCl_3$) δ: 4.08 (t, 8H, C*H*$_2$CH$_2$CO$_2$Me), 3.81 (s, 6H, COOMe), 3.78 (s, 6H, COOMe), 3.26 (s, 6H, Me), 3.24 (s, 6H, Me), 2.95 (m, 8H, CH$_2$C*H*$_2$CO$_2$Me). UV [$CHCl_3$, λ_{max}/nm ($\varepsilon\times10^{-3}$)]: 440 (146), 561 (9.6), 606 (6.4). MS, *m*/*z*: 952 (M^+). Found (%): C 50.23, H 4.18, Cl 15.41, N 5.81. Calc. for $C_{40}H_{40}Cl_4N_4O_8Pd$ (%): C 50.41, H 4.23, Cl 14.88, N 5.88.

§ Data for **2c**, ethyl ester: mp >300 °C. ^{1}H NMR ($CDCl_3$) δ: 4.22 (m, 8H, C*H*$_2$CH$_2$CO$_2$Me and C*H*$_2$Me), 3.30 (s, 12H, Me), 3.00 (t, 4H, CH$_2$C*H*$_2$CO$_2$Me), 1.30 (t, 6H, CH$_2$*Me*). UV ($CHCl_3$, λ_{max}/nm): 452, 561 (β), 618 (α) (α/β = 0.70). MS, *m*/*z*: 878 (M^+).

¶ Data for **4a**: mp 111–113 °C. ^{1}H NMR ($CDCl_3$) δ: 4.41 (m, 8H, C*H*$_2$CH$_2$CO$_2$Me), 3.78 (s, 12H, COOMe), 3.24 (s, 12H, Me), 2.92 (m, 8H, CH$_2$C*H*$_2$CO$_2$Me). UV [$CHCl_3$, λ_{max}/nm ($\varepsilon\times10^{-3}$)]: 442 (121), 577 (9.7), 621 (5.0). MS, *m*/*z*: 905 (M^+). Found (%): C 53.44, H 4.24, Cl 15.01, N 5.81. Calc. for $C_{40}H_{40}Cl_4N_4O_8Ni$ (%): C 53.07, H 4.45, Cl 15.67, N 6.19.

†† Data for **4c**: mp 164–166 °C. ^{1}H NMR ($CDCl_3$) δ: 4.14 (m, 4H, C*H*$_2$CH$_2$CO$_2$Me), 3.77 (s, 6H, COOMe), 3.23 (s, 3H, Me), 3.18 (s, 3H, Me), 3.14 (s, 3H, Me), 3.12 (s, 3H, Me), 2.83 (m, 4H, CH$_2$C*H*$_2$CO$_2$Me). UV [$CHCl_3$, λ_{max}/nm ($\varepsilon\times10^{-3}$)]: 442 (156), 585 (7.0), 632 (4.9). MS, *m*/*z*: 802 (M^+). Found (%): C 47.53, H 3.75, N 6.63. Calc. for $C_{32}H_{26}Cl_6N_4O_4Ni$ (%): C 47.92, H 3.27, N 6.99.

‡‡ Data for **5**: mp 120–122 °C. ^{1}H NMR ($CDCl_3$) δ: 5.75 (s, 4H, CH_2Cl), 5.71 (s, 4H, CH_2Cl), 4.12 (m, 8H, C*H*$_2$CH$_2$CO$_2$Me), 3.76 (s, 12H, COOMe), 3.05 (m, 8H, CH$_2$C*H*$_2$CO$_2$Me). UV [$CHCl_3$, λ_{max}/nm ($\varepsilon\times10^{-3}$)]: 459 (130), 593 (10.4), 641 (6.6). MS, *m*/*z*: 1042 (M^+). Found (%): C 45.64, H 3.39, Cl 26.91, N 5.12. Calc. for $C_{40}H_{36}Cl_8N_4O_8Ni$ (%): C 46.06, H 3.48, Cl 27.19, N 5.37.

possible to obtain products with partially chlorinated methyl groups: we succeeded in isolating heptachloro-substituted nickel coproporphyrin III tetramethyl ester **6**.§§ The number of chlorine atoms in **4a**, **4c**, **5** and **6** was proved by mass spectrometry, ^{1}H NMR spectroscopy and elemental analysis data.

The presence of a transition metal ion in the porphyrin molecule presumably plays the determining role in this reaction. On treatment of deuterioporphyrin dimethyl ester and coproporphyrin tetramethyl ester with thionyl chloride under similar conditions, no chlorination was observed. It seems likely that coordination of thionyl chloride with a central metal atom followed by a chain of redox reactions leads to the reduction of sulfur and to the formation of a highly reactive chlorine species (possibly, the chlorine radical), which attacks the macrocycle. Finding crystalline sulfur in the reaction mixture obtained during the synthesis of **2c** provides evidence in favour of this assumption.

§§ Data for **6**: mp 190–192 °C. ^{1}H NMR ($CDCl_3$) δ: 5.76 (s, 6H, CH_2Cl), 4.18 (m, 8H, $CH_2CH_2CO_2Me$), 3.77 (s, 12H, COOMe), 3.25 (s, 3H, Me), 3.00 (m, 8H, $CH_2CH_2CO_2Me$). UV [$CHCl_3$, λ_{max}/nm ($\varepsilon\times10^{-3}$)]: 448 (157), 582 (13.1), 627 (8.5). MS, *m*/*z*: 1007 (M^+). Found (%): C 47.31, H 3.93, Cl 24.31, N 5.93. Calc. for $C_{40}H_{37}Cl_7N_4O_8Ni$ (%): C 47.63, H 3.70, Cl 24.60, N 5.56.

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References

1 H. Fischer and W. Klendauer, *Ann. Chem.*, 1941, **547**, 123.
2 R. Bonnett, P. Brewer, K. Noro and T. Noro, *Tetrahedron*, 1978, **34**, 379.
3 D. Dolphin, *The Porphyrins*, Academic Press, New York, 1978, vol. 2, p. 153.
4 E. Samuels, R. Shuttleworth and T. S. Stevens, *J. Chem. Soc. C*, 1968, 145.
5 O. G. Khelevina, S. V. Timofeeva and B. D. Berezin, *Zh. Org. Khim.*, 1994, **30**, 295 (*Russ. J. Org. Chem.*, 1994, **30**, 312).
6 L. Fieser and M. Fieser, *Reagents for Organic Synthesis*, Wiley, New York, 1968.

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