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THE SYNTHESES OF A MONOSUBSTITUTED AND AN UNSYMMETRICAL TETRASUBSTITUTED PHTHALOCYANINE USING BINUCLEAR PHTHALOCYANINES

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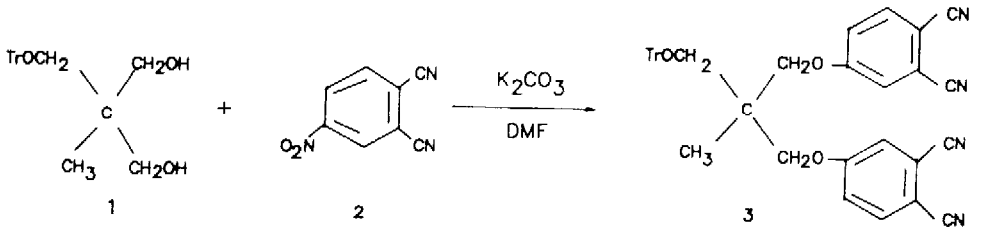
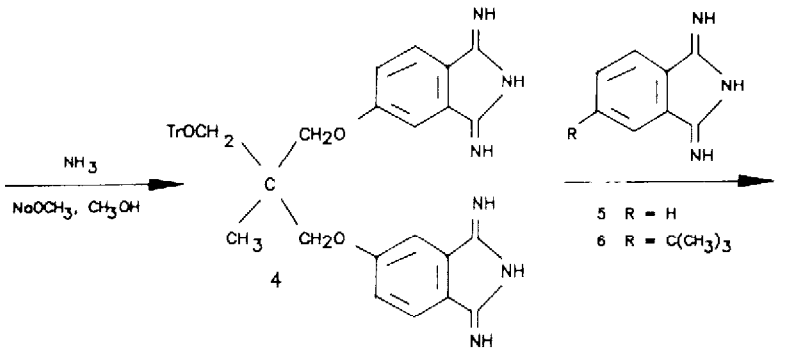
Summary. The syntheses of 2-hydroxyphthalocyanine and 2-hydroxy-9,16,23-tri-tert-butylphthalocyanine have been accomplished.

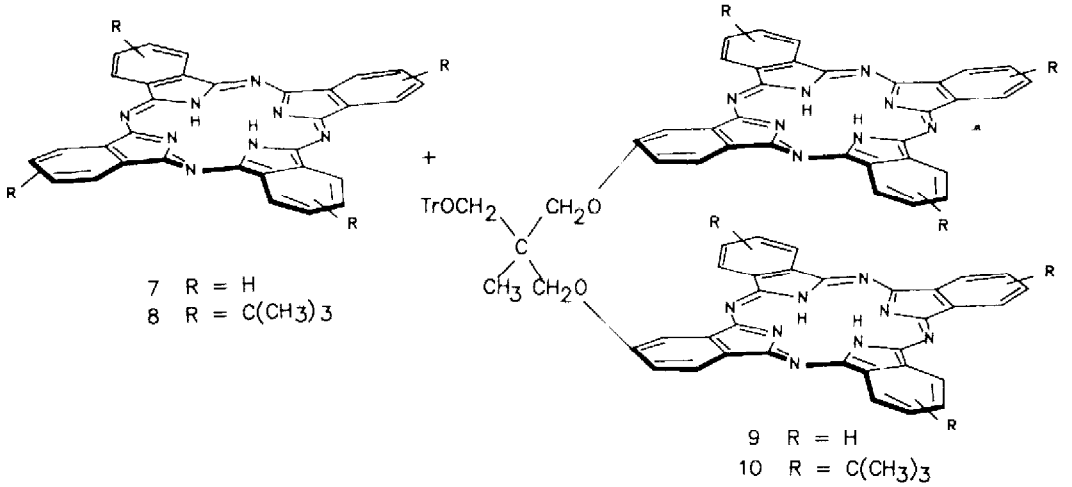
There has been much excitement recently concerning the use of phthalocyanines in a host of new applications such as chemical sensors[1] and photodynamic therapy[2] in addition to their traditional uses as dyes and in photocopying devices.[3] Although symmetrical tetra, octa and hexadecasubstitutedphthalocyanines are well documented,[3,4] the synthesis of unsymmetrical phthalocyanines[5] remains a challenging problem. Unsymmetrical phthalocyanines are often required for attachment to electrodes or for compatibility with biological membranes. As even simple mono[6,7] and disubstituted[7,8] phthalocyanines are extremely rare we now wish to describe a new method of preparing pure monosubstituted and unsymmetrical tetrasubstituted phthalocyanines.

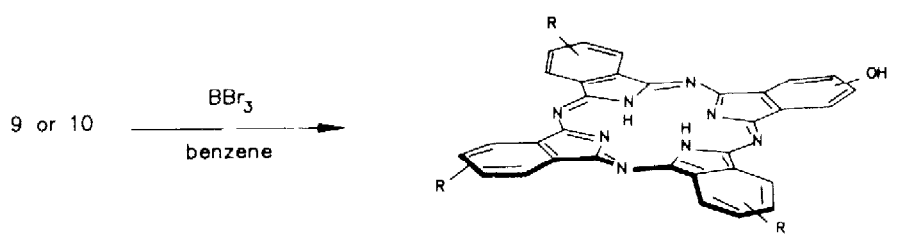
One difficulty encountered in most syntheses of unsymmetrical phthalocyanines, based on statistical methods, is that mixtures of phthalocyanines are obtained, which are difficult to separate by chromatography due to aggregation phenomena. In some cases polymer support methods[5] or specially designed directed synthesis[7] can overcome this problem. As binuclear phthalocyanines[4,9,10] can readily be separated from mononuclear phthalocyanine by-products, we planned to prepare pure unsymmetrical mononuclear phthalocyanines by cleaving pure binuclear phthalocyanines. Some early experiments[9] had shown that a trityloxy group in the bridge of a binuclear phthalocyanine imparted extra solubility to the binuclear phthalocyanine and aided in its purification. Thus, binuclear phthalocyanines, containing a trityloxy moiety in the bridge, were cleaved with boron tribromide to unsymmetrical mononuclear phthalocyanines as described below.

Treatment of 3.62 g of 2-methyl-2-trityloxymethyl-1,3-propanediol (**1**)[9] with more than two equivalents of 4-nitrophthalonitrile (3.80 g) (**2**) and K_2CO_3 in N,N-dimethylformamide for 48 h at room temperature[11] gave 5.01 g of 1,3-bis(3',4'-dicyanophenoxy)-2-methyl-2-trityloxymethylpropane (**3**),[9] m.p. 167-168°C in 82% yield. The purification of **3** was slightly modified from that previously described[9] and was accomplished by flash column chromatography[12] using acetonitrile/benzene (5:95) as the eluting solvent followed by recrystallization from ethyl acetate/methanol. Conversion of **3** with ammonia gave the bisdiiminoisoindoline **4**,[13] which was not purified but used directly in the subsequent condensation. The bisdiiminoisoindoline **4**, prepared from 0.66 g of **3**, was heated at 160°C with a large excess of 1,3-diiminoisoindoline (**5**), prepared from 5.00 g of phthalonitrile, in 2-N,N-dimethylaminoethanol for 60 h under argon and yielded 4.2 g of a dark blue solid.[13] The crude material was purified by Soxhlet extraction with acetonitrile to remove


TrOCH2
CH2OH
C
CH3
CH2OH
1
+
CN
O2N
CN
2
K2CO3
DMF
TrOCH2
CH2O
C
CH3
CH2O
CN
CN
CN
CN
3


NH3
NaOCH3, CH3OH
TrOCH2
CH2O
C
CH3
CH2O
NH
NH
NH
NH
NH
NH
4
R
5 R = H
6 R = C(CH3)3


R
R
R
+
TrOCH2
CH2O
C
CH3
CH2O
7 R = H
8 R = C(CH3)3
9 R = H
10 R = C(CH3)3


9 or 10
BBr3
benzene
R
OH
R
R
11 R = H
12 R = C(CH3)3

brown impurities followed by extraction with tetrahydrofuran (THF) to yield 0.29 g of **9** admixed with trace amounts of **7** and brown impurities which were detected by tlc using THF as eluant. The latter were removed by Soxhlet extraction with acetonitrile leaving 0.20 g of **9** (11% based on **1**). A sample of 91 mg of **9** was chromatographed as above. Elution with THF yielded 26 mg of **9** free of **7**, (29% recovery). Binuclear **9** was moderately soluble in THF, benzene and toluene.

Similarly the bisdiiminoisoindoline **4**, prepared from 0.62 g of **3**, reacted with a large excess of **6**, prepared from 5.90 g of 4-tert-butylphthalonitrile,[14] to give 3.61 g of a dark blue solid. Flash chromatography of the product, using hexane/toluene (1:3) as solvents, yielded 2.04 g (40%) of 2,9,16,23-tetra-tert-butylphthalocyanine (**8**).[15] Continued elution with toluene yielded a mixed fraction consisting of **8** and **10**. This fraction was further purified as above to give 0.32 g of **10** (16% based on **1**). Binuclear **10** was extremely soluble in a variety of organic solvents.

The monohydroxyphthalocyanine (3.0 mg) (**11**) and the 2-hydroxy-9,16,23-tri-tert-butylphthalocyanine (19.4 mg) (**12**) were prepared in 22% and 30% yield respectively by cleavage of the ether linkage of 18 mg of **9** and 79 mg of **10** with boron tribromide in refluxing benzene[16,17] for 20 h. Thus the overall yields of **11** and **12** are 0.7% and 4.8% respectively based on **1**. Compound **11** was soluble in DMSO and pyridine but not in common organic solvents and therefore it was purified by washing with water and acetonitrile to remove the impurities generated during the BBr_3 cleavage. On the other hand the soluble unsymmetrical phthalocyanine **12**, was purified by column chromatography as above using 2-methoxyethanol/toluene (1:9) as eluant. The characterization of **9-12** were based on spectroscopic data[18] and elemental analysis. Most importantly the mass spectra of **9-12** only gave parent ions in the molecular ion region for the given compounds with no evidence of contamination.

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18. **9** IR(KBr) 3240(NH), 1600, 1105, 1000(NH), 865, 730cm^{-1}; ^{1}Hnmr (300MHz, C_6D_6) δ 9.42(d), 7.29(q), 6.79(t), -5.00(NH); UV(CH_2Cl_2) 694(log ϵ, 4.71), 656(4.66), 602(4.22), 338(4.66), 278(4.75); Mass spectrum (FAB): m/z 1386.5. **10** IR(KBr) 3280(NH), 1610, 1090, 1005(NH), 750cm^{-1}; ^{1}Hnmr (300MHz, C_6D_6) δ 9.57, 7.83, 7.36, -3.14(NH); UV(CH_2Cl_2) 640(log ϵ, 4.99), 338(5.07), 290(4.99); Mass spectrum (FAB): m/z 1724. **11** IR(KBr) 3290(NH), 1610, 1110, 1005(NH), 740cm^{-1}; ^{1}Hnmr (300MHz, pyridine-d_5) δ -4.47(NH); UV(50% DMF in methanol) 692(log ϵ, 4.25), 664(4.18), 348(4.17). Mass spectrum (EI): m/z 530. **12** IR(KBr) 3290(NH), 1610, 1090, 1010(NH), 750cm^{-1}; ^{1}Hnmr (300MHz, C_6D_6) δ 9.47, 8.16, 8.02, 7.86, 1.74, 1.72, 1.71, 1.69, 1.68, -1.90(NH); UV(CH_2Cl_2) 698(log ϵ, 5.16), 664(5.09), 644(4.74), 604(4.50), 342(4.94), 290(4.66); Mass spectrum (FAB): m/z 698.

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