

THE SYNTHESSES 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 sensors¹ and photodynamic therapy² in addition to their traditional uses as dyes and in photocopying devices.³ Although symmetrical tetra, octa and hexadecasubstituted phthalocyanines are well documented,^{3,4} the synthesis of unsymmetrical phthalocyanines⁵ 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 methods⁵ or specially designed directed synthesis⁷ 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 experiments⁹ 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 K₂CO₃ in N,N-dimethylformamide for 48 h at room temperature¹¹ gave 5.01 g of 1,3-bis(3',4'-dicyanophenoxy)-2-methyl-2-trityloxy-methylpropane (3),⁹ m.p. 167-168°C in 82% yield. The purification of 3 was slightly modified from that previously described⁹ and was accomplished by flash column chromatography¹² 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

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 bisdiiminoisindoline 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 BBr₃ 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 data¹⁸ 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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References and Notes

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18. **9** IR(KBr) 3240(NH), 1600, 1105, 1000(NH), 865, 730cm⁻¹; ¹Hnmr (300MHz, C₆D₆) δ 9.42(d), 7.29(q), 6.79(t), -5.00(NH); UV(CH₂Cl₂) 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; ¹Hnmr (300MHz, C₆D₆) δ 9.57, 7.83, 7.36, -3.14(NH); UV(CH₂Cl₂) 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; ¹Hnmr (300MHz, pyridine-d₅) 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; ¹Hnmr (300MHz, C₆D₆) δ 9.47, 8.16, 8.02, 7.86, 1.74, 1.72, 1.71, 1.69, 1.68, -1.90(NH); UV(CH₂Cl₂) 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.