Synthesis of 3-Nitrophthalonitrile and Tetra-α-substituted Phthalocyanines

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An efficient synthesis of phthalocyanines prepared from *ortho*-substituted phthalonitriles is described. The precursor to these phthalocyanines, 3-nitrophthalonitrile, is a key reagent for syntheses of phthalonitriles substituted at the 3-position by means of nucleophilic aromatic substitutions. An example of this type of phthalocyanine, prepared from 3-(4-cumylphenoxy)phthalonitrile, is compared with the phthalocyanine derived from 4-(4-cumylphenoxy)phthalonitrile. Substitution of the phthalocyanine at this more sterically crowded site causes a 20 nm bathochromic shift of the Q-band (π-π* transition).

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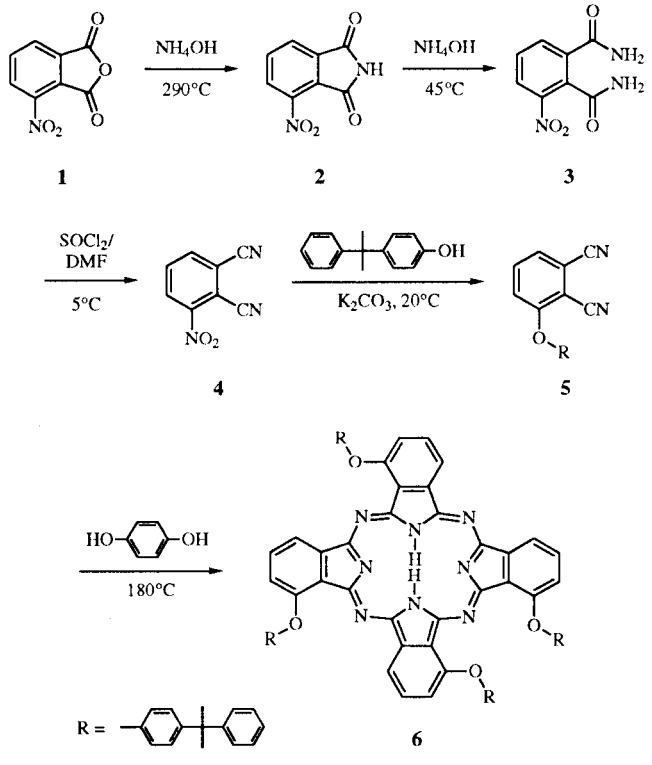
Phthalocyanines with peripheral substituents located on the inner, sterically crowded α-positions [1] of the benzo rings of the macrocycle exhibit more interesting electronic properties than phthalocyanines with substituents attached at the outer carbons of the benzo ring. However, the synthesis of precursors to α-substituted phthalocyanines (α-Pc's) is generally much more difficult and the corresponding phthalocyanine yields are lower than phthalocyanines substituted at the outer, less crowded positions of the benzo ring (β-Pc's) [2-4]. A significant bathochromic shift of the Q-band (π-π* transition) compared to β-Pc's has been observed [2,5] in studies of the few known α-Pc's. For the purpose of investigating the origin of this effect, efficient syntheses for α-Pc's with the appropriate peripheral substituents must be developed. In this communication, we present a general synthesis for tetra-substituted α-Pc's with alkyl- or aryl-ether substituents. This involves the synthesis of a key intermediate, 3-nitrophthalonitrile. A reliable synthesis of 3-nitrophthalonitrile and the corresponding α-Pc's is of importance for physiochemical studies of substituent effects on Pc electronic structure and for the subsequent control of these properties. The availability of 3-nitrophthalonitrile as a synthetic precursor of general utility provides a means by which many direct structure-property comparisons can be made with derivatives of 4-nitrophthalonitrile (commercially available). As an example, in this work we make a direct comparison of tetrakis(cumylphenoxy)-substituted α- and β-Pc's.

The only reported synthesis of 3-nitrophthalonitrile is described in a patent for a one-pot, multi-step synthesis [6]. That work described the conversion of 3-nitrophthalic anhydride to the diamide derivative followed by dehydration to 3-nitrophthalonitrile using phosphorous oxychloride. In our experience, this was a laborious procedure with only marginal yields (<20%). Furthermore, no characterization of this compound was reported, except for an irreproducible melting point. We have developed a stepwise method (described below) which consists of preparing the phthalimide, converting it to the phthalamide, and dehydrating to the phthalonitrile. Using this procedure, we have achieved an efficient yield (>80%) and are presenting a detailed characterization of 3-nitrophthalonitrile.

The general procedure for preparing α-phthalocyanines is shown in Scheme 1. Commercially available 3-nitrophthalic anhydride (**1**) is first reacted with ammonium hydroxide to yield 3-nitrophthalimide (**2**). This compound is isolated and reacted with ammonium hydroxide under mild conditions to produce the diamide derivative **3**. The amide is subsequently dehydrated, using the Vilsmeier reagent [7,8], to yield 3-nitrophthalonitrile (**4**). We have

Scheme 1. General Synthetic Scheme for the Preparation of α-Substituted Pc's. As an example, the synthesis of 1,8 (or 11), 15 (or 18), 22 (or 25)-(4-cumylphenoxy)phthalocyanine (abbreviated $H_2Pc(\alpha\text{-}CP)_4$) is shown.



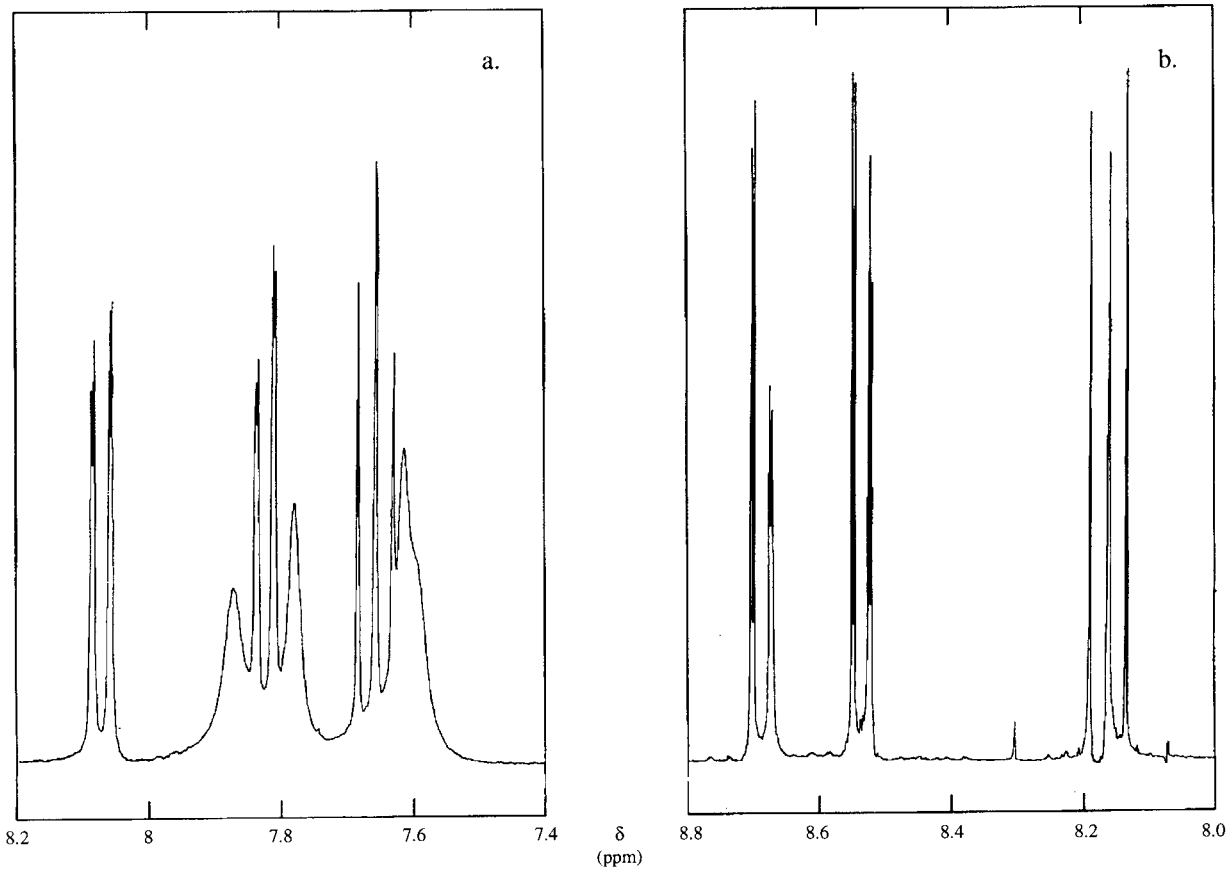


Figure 1. Comparison of ^1H nmr spectra for a) 3-nitrophthalamide (**3**) and b) 3-nitrophthalonitrile (**4**) in DMSO-d_6 in the aromatic proton resonance region as described in the text.

also obtained the same results starting with commercially available 3-nitrophthalic acid which is dehydrated easily and nearly quantitatively to 3-nitrophthalic anhydride (**1**) under acetic anhydride/sulfuric acid conditions [9]. The ^1H nmr spectra of 3-nitrophthalamide (**3**) and 3-nitrophthalonitrile (**4**) are shown in Figure 1. The observed aromatic proton splitting pattern is a triplet and two doublets which overlap the amide proton resonances in the case of **3**. Upon conversion of **3** to **4**, the aromatic proton pattern is retained but with an increased chemical shift. Further splitting is observed for protons which are *ortho* and *para* to the nitro group. This splitting behavior is consistent with spectra of 4-nitrophthalamide and 4-nitrophthalonitrile, collected in our laboratory for comparison purposes, which also show this additional splitting in the proton groups *ortho* to the nitro group.

The 3-nitrophthalonitrile intermediate **4** is a key reagent for synthesis of many alkoxy- and aryloxyphthalonitrile α-Pc precursors. Nitro-displacement [10] with an alcohol or phenol to give such a precursor which is then converted to the corresponding α-substituted phthalocyanine is shown in Scheme 1 using 4-cumylphenol as an example.

This aryl-ether phthalonitrile precursor **5** is subsequently cyclotetramerized [11] to the corresponding α-substituted phthalocyanine **6**. From statistical considerations, the product is a mixture of geometric isomers. Separation of α-Pc isomers by hplc has been recently reported [12]. The synthetic details for preparing **5**, 3-(4-cumylphenoxy)phthalonitrile and **6**, 1,8 (or 11), 15 (or 18), 22 (or 25)-(4-cumylphenoxy)-phthalocyanine (abbreviated $H_2PC(\alpha\text{-}CP)_4$) are described in the Experimental. The visible spectrum of **6** exhibits a Q-band with a red-shift of 20 nm compared to the corresponding 4-nitrophthalonitrile-derived phthalocyanine [11].

In summary, a high yield synthesis of 3-nitrophthalonitrile and its versatility as a synthetic precursor to a new class of phthalocyanines is demonstrated. The availability of 3-nitrophthalonitrile as a general synthetic reagent to polymeric and phthalocyanine-based materials (much like the well-studied reagent, 4-nitrophthalonitrile [10,11,13-21]), provides opportunities for alteration of physical properties through steric hinderance effects, and for perturbation of phthalocyanine electronic structure by the introduction of substituents at electronically influential peripheral sites.

EXPERIMENTAL

Unless otherwise stated, all reactions were performed under dry, oxygen-free nitrogen. All melting points were measured in open capillaries and are uncorrected.

3-Nitrophthalic Anhydride (**1**).

This compound is commercially available and, alternatively, can be prepared in nearly quantitative yield by dehydration of 3-nitrophthalic acid by acetic anhydride, catalyzed by sulfuric acid [9].

3-Nitrophthalimide (**2**).

This compound was prepared using a modification of the method reported for unsubstituted phthalimide [22]. A minimum of concentrated (~29%) aqueous ammonium hydroxide (35 ml) was added to **1** (25.0 g, 1.30 x 10^{-1} mole). The flask was fitted with a 6 inch glass tube open to air and the mixture was heated strongly to boiling (~85°) and then slowly to 290° over a 4 hour period. During this time, a yellow solid formed (~220°) which subsequently melted as the temperature increased to 290°. Care was taken to ensure that any material which sublimed into the air condenser was returned to the reaction mixture with a spatula. The resulting solid was used directly in the formation of **3**, yield 23.70 g (95%), mp 203°; ir (neat/sodium chloride): 3231 m (br), 3093 w, 1785 m, 1774 ms, 1736 s, 1729 s, 1705 s, 1615 w, 1540 s, 1368 ms, 1356 s, 1311 w, 1248 w, 1155 w, 1071 ms, 842 w, 801 w, 780 w, 755 vw, 721 ms cm^{-1}.

3-Nitrophthalamide (**3**).

Product **2** (23.7 g, 1.23 x 10^{-1} mole) was pulverized and concentrated (29%) aqueous ammonium hydroxide (60 ml) at room temperature was added with stirring, to form a yellow-brown suspension. The reaction mixture was heated slightly to 45° and stirred for 5 hours. The resulting solid was filtered from the reaction mixture and rinsed with cold water. This product was air dried to a constant weight, yield 22.2 g (82%), mp 219° with gas evolution, dec (lit 201°, no dec noted [23]); ir (potassium bromide pellet): 3425 vs, 3338 m, 3301 m, 3203 s, 3104 w, 1670 vs, 1621 m, 1607 s, 1569 m, 1537 s, 1474 w, 1396 m, 1350 s, 1172 w, 1101 w, 907 m, 752 m, 674 w, 631 w, 552 m cm^{-1}; ^1H nmr (DMSO-d_6): (see Figure 1) δ 7.62 (broad unresolved doublet, 2H), 7.66 (triplet, J = 8.0 Hz, 1H), 7.83 (broad doublet, J = 27.3 Hz, 2H), 7.83 (doublet, J = 7.7 Hz, 1H), 8.07 (doublet, J = 8.2 Hz, 1H); ^{13}C nmr (DMSO-d_6): δ 124.9 (C_4), 129.4 (C_2), 131.4 (C_5), 132.4 (C_6), 137.1 (C_1), 146.9 (C_3), 165.8 (C_{Cl}), 167.7 (C_{C2}).

3-Nitrophthalonitrile (**4**).

In an ice bath, thionyl chloride (25 ml) was added (dropwise, keeping the temperature between 5 and 7°) to DMF (38 ml), cooled to 5°, and then stirred for 3 hours at this temperature. 3-Nitrophthalamide (**3**) (7.014 g, 3.354 x 10^{-2} mole) was then added slowly to this reagent mixture, at such a rate as to keep the temperature below 10°. This mixture was stirred for 6 hours at 0-5° and then 1-2 days at room temperature, stopping the reaction immediately if there was any evidence of sulfur formation (reagent decomposition). The reaction mixture was then poured slowly onto 160 g of ice, at which point, the product began crystallizing. When the ice had entirely melted, the aqueous mixture with crystallized product was vacuum filtered cold, and rinsed three times with cold water (5°). The pale yellow crystalline product was air dried to a constant weight. This product was sufficiently pure for use directly in the preparation of **5** or could be further purified by recrystallization in ethanol, yield 4.837 g (83%), mp 160° (lit 141° [6]); ir (neat/sodium chloride): 3132 vw, 3086 m, 3045 w, 2239 m, 1608 m, 1539 vs, 1354 vs, 1206 w, 1071 w, 916 m, 828 s, 803 ms, 768 ms, 748 s cm^{-1}; ^1H nmr (DMSO-d_6): (see Figure 1) δ 8.16 (triplet, J = 8.3 Hz), 8.54 (doublet, J = 7.7 Hz), 8.69 (doublet, J = 8.3 Hz); ^{13}C nmr (DMSO-d_6): δ 110.9 (C_2), 113.1 (C_{C2}), 114.9 (C_{Cl}), 117.8 (C_1), 129.7 (C_4), 135.0 (C_5), 138.6 (C_6), 148.9 (C_3).

3-(4-Cumylphenoxy)phthalonitrile (**5**).

This procedure is a modification of a reported synthesis and characterization of 4-(4-cumylphenoxy)phthalonitrile [11]. 3-Nitrophthalonitrile (**4**) (1.116 g, 6.454 x 10^{-3} mole) was added to a stirred solution of 4-cumylphenol (1.444 g, 6.803 x 10^{-3} mole, Aldrich Chemical Co.) dissolved in DMSO (10 ml, purified by recrystallization). Pulverized, anhydrous potassium carbonate (1.643 g, 1.189 x 10^{-3} mole) was added to this mixture in 12 equal additions over a 4 hour period. The reaction mixture was stirred for 20.5 hours at room temperature and then poured into water (60 ml), forming a gum-like material which was dissolved by addition of dichloromethane (100 ml). The aqueous layer was further extracted (3x) with 100 ml portions of dichloromethane. The total crude dichloromethane extract was rotary evaporated to dryness (40°) resulting in an oily solid with some crystalline platelets present. This crude solid was recrystallized from methanol and dried in air (50°) to a constant weight, yield 1.939 g (89%), mp 113°; ir (neat/sodium chloride): 3086 w, 3057 w, 3032 w, 2970 m, 2872 w, 2234 m, 1576 ms, 1503 s, 1463 s, 1275 vs, 1209 ms, 1165 ms, 1016 m, 986 m, 851 m, 799 m, 765 m, 701 s cm^{-1}.

1,8 (or 11), 15 (or 18), 22 (or 25)-(4-Cumylphenoxy)phthalocyanine (abbreviated $H_2Pc(\alpha\text{-}CP)_4$ (**6**).

This procedure is a modification of a reported preparation of $H_2Pc(\beta\text{-}CP)_4$ [11]. Hydroquinone (0.164 g, 1.49 x 10^{-3} mole, sublimed) and 3-(4-cumylphenoxy)phthalonitrile (**5**) (1.791 g, 5.295 x 10^{-3} mole) were weighed into a 10 x 70 mm tube. The tube was sealed in air and placed in a 150° oven to melt the mixture, and subsequently heated at 180° for 21.5 hours. The crude product, a glassy blue-green solid, was then taken up into a minimum of chloroform and precipitated into 400 ml of rapidly stirred methanol. The precipitate was isolated by centrifugation, washed with methanol, and vacuum dried at 50°/55 mm Hg. Attempts to purify the crude product by chromatography on neutral alumina (as for $H_2Pc(\beta\text{-}CP)_4$ [11]) succeeded in purifying the product but resulted in a significant decrease in product solubility accompanied by partial separation of the structural isomers. The high solubility of mixed isomer Pc's is thought to be related to a lower degree of order in the solid state as noted in other studies [12]. (If separation of isomers occurred during chromatography and each of the isomers selectively crystallized, a lower solubility would result, as observed here. In such a scenario, the solubility would be a function of the degree of isomer separation.) The yield was 1.563 g (87%); uv/vis (chloroform): λ_{max} 722, 689, 658, 624, 333, 241 nm; ir (neat/sodium chloride): 3290 w (br), 3084 w, 3057 w, 3032 w, 2966 m, 2934 w, 2870 w, 1584 m, 1503 vs, 1445 m, 1334 m, 1254 vs, 1175 m, 1107 m, 1028 ms, 945 m,

829 m, 750 s, 700 s cm^{-1}.

Anal. Calcd. for $C_{92}H_{74}N_8O_4$: C, 81.4; H, 5.5; N, 8.3. Found: C, 81.0; H, 5.5; N, 8.1.

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REFERENCES AND NOTES

[1] A convention designating the phthalocyanine inner benzo position as "α" and the outer benzo position as "β" was originally concieved by R. P. Linstead, *et al.*, *J. Chem, Soc.*, 1820 (1939) and further defined in ref [3].

[2] M. J. Cook, A. J. Dunn, S. D. Howe, A. J. Thomson, and K. J. Harrison, *J. Chem. Soc., Perkin Trans. I*, 2453 (1988).

[3] M. J. Chen, J. W. Rathke, S. Sinclair, and D. W. Slocum, *J. Macromol. Sci. Chem.*, **A27**, 1415 (1990).

[4] C. C. Leznoff, in Phthalocyanines. Properties and Applications, Vol **1**, C. C. Leznoff and A. B. P. Lever, eds, VCH Publisher's, Inc., New York, 1989, pp 1-54.

[5] B. D. Rihter, M. E. Kenney, W. E. Ford, and M. A. J. Rodgers, *J. Am. Chem. Soc.*, **112**, 8064 (1990).

[6] M. Scalera and R. E. Brouillard, US Patent 2,525,620, 1950.

[7] W. Ziegenbein, *Angew. Chem., Int. Ed. Engl.*, **4**, 358 (1965).

[8] J. C. Thurman, *Chem. Ind. (London)*, 752 (1964).

[9] B. H. Nicolet and J. A. Bender, in Organic Syntheses, 2nd Ed, Vol **1**, H. Gilman, ed, John Wiley & Sons, Inc., New York, 1941, pp 410-411.

[10] T. M. Keller, T. R. Price, and J. R. Griffith, *Synthesis*, **8**, 613 (1980).

[11] A. W. Snow and N. L. Jarvis, *J. Am. Chem. Soc.*, **106**, 4706 (1984).

[12] M. Hanack, G. Schmid, and M. Sommerauer, *Angew. Chem., Int. Ed. Engl.*, **32**, 1422 (1993).

[13] D. Wöhrle and B. Schulte, *Makromol. Chem.*, **189**, 1167 (1988).

[14] J. G. Young and W. Onyebuagu, *J. Org. Chem.*, **55**, 2155 (1990).

[15] W. O. Siegel, *J. Heterocyclic Chem.*, **18**, 1613 (1981).

[16] C. C. Leznoff and T. W. Hall, *Tetrahedron Letters*, **23**, 3023 (1982).

[17] C. C. Leznoff, S. M. Marcuccio, S. Greenberg, A. P. B. Lever, and K. B. Tomer, *Can. J. Chem.*, **63**, 623 (1985).

[18] R. D. George, A. W. Snow, P. F. McMillan, and V. A. Burrows, *J. Am. Chem. Soc.*, **114**, 8286 (1992).

[19] R. D. George and A. W. Snow, *Chem. Mater.*, **6**, 1587 (1994).

[20] T. R. Walton, J. R. Griffith, and J. P. Reardon, *J. Appl. Polym. Sci.*, **30**, 2921 (1985).

[21] J. R. Griffith, J. G. O'Rear, and T. R. Walton, in Copolymers, Polyblends & Composites, Vol **142**, N. A. J. Platzer, ed, American Chemical Society, Washington, DC, 1975, pp 458-464.

[22] W. A. Noyes and P. K. Porter, in Organic Syntheses, Vol **1**, Wiley, New York, 1941, pp 457-459.

[23] R. A. McClelland, N. E. Seaman, J. M. Duff, and R. E. Branston, *Can. J. Chem.*, **63**, 121 (1985).