Oligomeric Cyclization of Dinitriles in the Synthesis of Phthalocyanines and Related Compounds: the Role of the Alkoxide Anion

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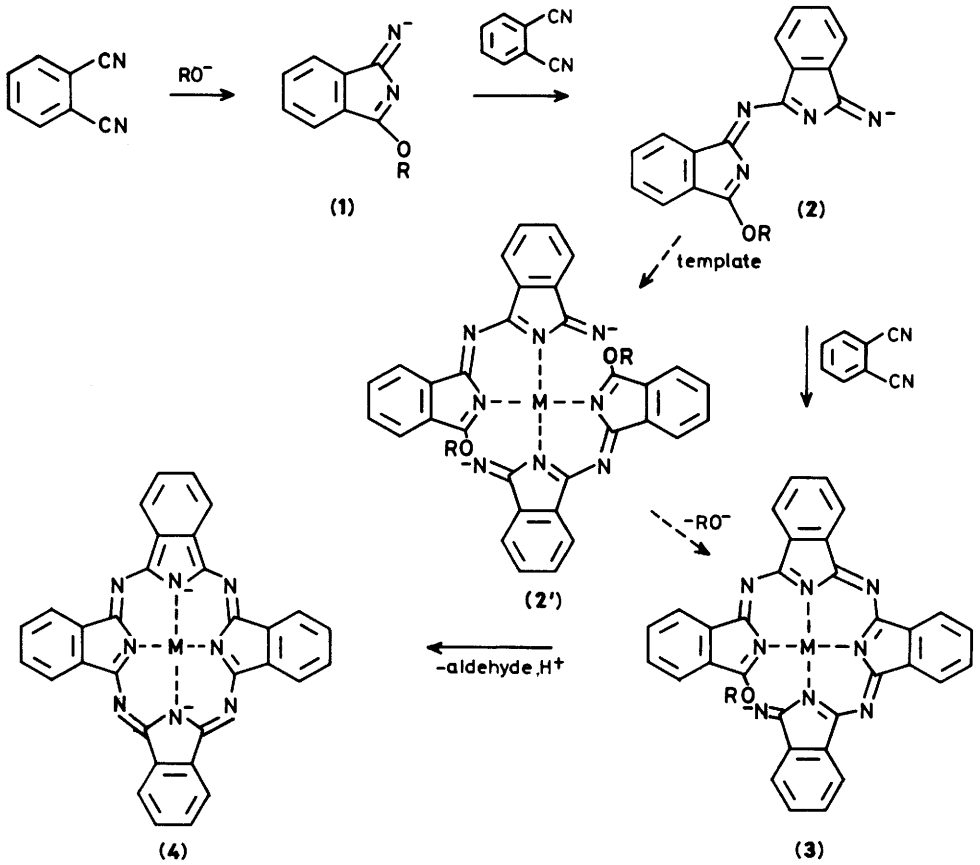
The formation of phthalocyanine from phthalonitrile has been shown to proceed through reactive precursors condensing to reactive oligomeric intermediates which, as a result of ring-closure reactions, cyclize to conjugated macrocyclic product. The roles of alkoxide anion in the reaction scheme leading to phthalocyanine has been illustrated by isolation of reactive precursor sodium 1-imido-3-methoxyisoindolene and reactive intermediate lithium 1-imido-3-(3-methoxy-5-nitroisoindolenin-1-ylideneamino)-5-nitroisoindole (**6**) while its role in the overall yield of desired conjugated macrocyclic product has been shown by comparing the yield of magnesium dibenzobarrelenoporphyrazine to that obtained when the alkoxide concentration was reduced during the synthesis.

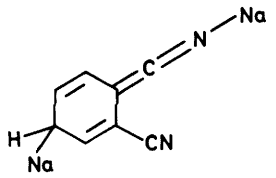
The synthesis of metallophthalophthalocyanines starting with phthalonitrile and related compounds has long been thought to proceed through complex reaction pathways which could involve the formation of reactive precursors, condensation to reactive intermediates, and ring-closure mechanisms leading to macrocyclic compounds. Such stages in the reaction pathways are shown in the Scheme which shows the essential role played by the alkoxide anion in bringing about various chemical changes. It is the purpose of this work to isolate compounds which play a role in the mechanism and to show the key roles played by the alkoxide anion.

Results and Discussion

In earlier investigations Linstead and co-workers[1] found that reaction of lithium amyloxide with phthalonitrile (in the mole ratio 1:4) in hot pentanol gave lithium hydrogen phthalocyanine. Other work[2] claimed that reaction of sodium n-butoxide with phthalonitrile in n-butanol gave product (**5**) which was thought to lead ultimately to formation of phthalocyanine. However, Borodkin[3] found that the initial reaction of sodium methoxide with phthalonitrile leads to a product formulated as the sodium salt of 1-imido-3-methoxyisoindoline (**1**). In the present work this formulation



Scheme.



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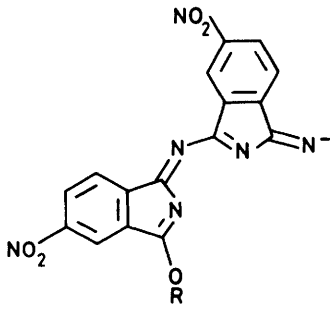

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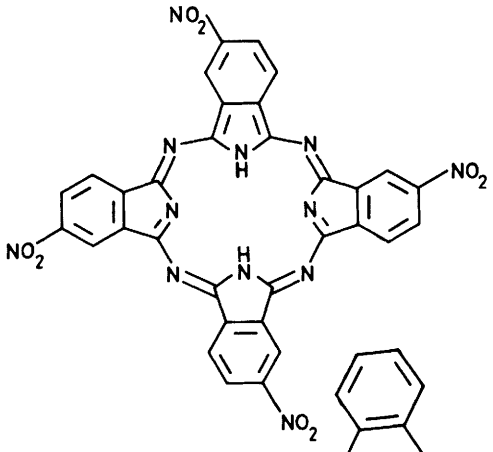

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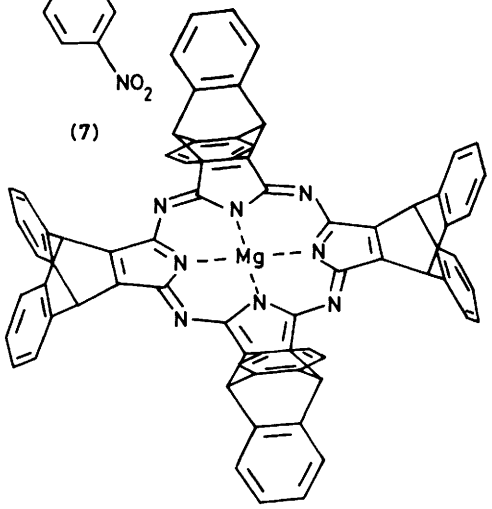

(8)

has been confirmed (a) by the observation using mass spectroscopy of a parent molecular ion peak due to the protonated base which is expected to form the sodium salt, (b) by the presence of i.r. absorptions due to imine and methyl ether groups, and (c) by the appearance in the ^1H n.m.r. spectrum of peaks attributable to four aromatic protons and a further resonance consistent with a methyl ether group (three protons).

The next step in the reaction sequence is thought to be cyclization of phthalonitrile by 1-imido-3-methoxyisoindoline (**1**) to form product (**2**). It has proved impossible to isolate such a product starting from phthalonitrile. However, the reaction of lithium methoxide with 4-nitrophthalonitrile gives lithium 1-imido-3-(3-methoxy-5-nitroisoindolenin-1-ylideneamino)-5-nitroisoindole (**6**) which, when heated in n-butanol, leads to the formation of dilithium 3,10,17,24-tetranitrophthalocyanine (**7**). Product (**6**) is similar to 1-imido-3-(3-pentoxyisoindolin-3-ylideneamino)isoindole which, prepared as the nickel(II) chelate, was found to be a key intermediate[4] in the preparation of nickel(II) phthalocyanine starting from di-iminoisoindolene. As outlined in the Scheme, further reaction of (**2**) with phthalonitrile or condensation of (**2**) could lead to product (**3**) which, after ring closure, leads to phthalocyanine (**4**). While the final conjugated macrocyclic structure (**4**) is essentially planar, a similar planar representation of (**3**) requires an unacceptable opening of the aza bridge bond angle opposite the ring closure region. Thus space-filling molecular graphical representations of (**3**) in planar forms which allow the ring closure groups to just touch show that the aza bridge C=N–O bond has to be increased from 126 to *ca.* 156° so that structure (**3**) must deviate considerably from planarity.

Besides initiating oligomerization of the phthalonitrile groups, the alkoxide group is important in the reaction sequence resulting in ring closure. This may be regarded as involving two important steps, namely initial nucleophilic attack by the imide group on the aryl ether, and subsequent loss of the ether not as the alkoxide but as its oxidation product, the aldehyde [reaction (1)[4,5] where in the case of the formation of

$$-OC_4H_9 + {}^-N= \longrightarrow C_3H_7{\cdot}CHO + H^+ + -N= + 2e^- \quad (1)$$

the dilithium chelate the hydrogen ion is taken up by alkoxide to form the alcohol]. The transfer of two electrons endows $4n + 2$ character on the conjugated macrocyclic system, thus providing a driving force for the reaction. [Ring closure would be assisted by the presence of a metal cation co-ordinated by the nitrogen donor atoms of structure (**3**) or (**4**) as a result of positioning the terminal functional groups for reaction.]

It can be seen, therefore, that only one alkoxide per macrocycle is necessary for initiation and reduction: the other reagent necessary is a base to react with hydrogen ions resulting from the formation of aldehyde. Usually two moles of alkoxide per macrocycle are added, which satisfies both requirements. Presumably this also facilitates the reaction by initial formation of an intermediate such as (**2′**) which then displaces an alkoxide in a template-assisted reaction leading to (**3**).

However, alkoxides are quite reactive; they are, for instance, used to reduce ketones in the Meerwein–Ponndorf–Verley reaction,[6a,b] and have also been used to attack the imino links in a related conjugated ligand.[7] Thus, in addition to playing a vital role in reactive intermediate formation and also neutralizing hydrogen ion, it is possible that the alkoxide anions may react with the intermediate condensation products so as to diminish the yield of conjugated macrocyclic product. Therefore, substitution of alkoxide by hydroxide (after the initial reactions have taken place) may increase the yield. Since the reactions occurring after the reaction of lithium alkoxide with phthalonitrile proceed rapidly, the influence of alkoxide anion on reaction steps beyond that required to form the initial reactive intermediate is difficult to measure. However, the synthesis of magnesium(II) barrelenoporphyrazine (**8**) {systematic name [5,9,14,18,23,27,32,36-octahydro-5,36[1′,2′]:9,14[1″,2″]:-18,23[1‴,2‴]:27,32[1⁗,2⁗]-tetrabenzeno-6,35:17,24-di-imino-8,15:33,26-dinitrolotetranaphtho[2,3-*c*:2′,3′-*h*:2″,3″-*m*:2‴,3a-*r*]-[1,6,11,16]tetra-azacycloeicosinato(2−)-$N^{43}N^{44}N^{51}N^{58}$]-magnesium(II)}, a structurally related material, has been outlined and shown to proceed slowly. The yield has been reported to be as high as 50% starting from magnesium n-butoxide and 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonitrile with chromatographic purification of the product. In the present work the yield of chromatographically purified material was much smaller when using dried solvents (5%) though obtained quite reproducibly. The yield of crude product prior to chromatographic purification was much higher (*ca.* 23%). The synthesis of this material, carried out over *ca.* 6 h, although

obtained in small yield, lends itself more readily to an investigation of the influence of the alkoxide anion on the overall yield of the desired macrocyclic product.

The synthesis of the magnesium(II) chelate of barrelenoporphyrazine was carried out using magnesium n-butoxide and 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonitrile using scrupulously dried solvents and reaction conditions. The yield of macrocyclic product in crude form was *ca.* 23% which was reduced to 5% after chromatographic purification and found to be remarkably consistent in several preparations. Then, starting with the original components, the reaction was carried out as before for the first 10 min, after which time the mixture acquired a just discernible blue colour. At this point water was added in the mole ratio 1:1 with respect to the expected amount of alkoxide, and the reaction allowed to continue as before. The yield of chromatographically purified material more than doubled to 11%, and reproducibly so, with commensurate increase in the amount of crude product, as a result of addition of water. Thus, at the commencement of the reaction sequence, alkoxide present forms the reactive intermediate similar to the first step in the phthalocyanine process and which reacts further as outlined. The purpose of water addition when the initial process is judged to have finished is to quench the alkoxide anion concentration resulting from ring closure. The increased yield of desired macrocyclic material results from the lower incidence of attack by the alkoxide anion on the condensed reactive intermediates required for conjugated macrocyclic compound formation.

Experimental

Alcohols were distilled from magnesium alkoxide twice and stored over molecular sieves. Spectrophotometric measurements were made with a Varian G35 spectrophotometer at room temperature using 1 cm glass cells. Mass spectral measurements were made using a Micromass VF7070 mass spectrometer. Microanalyses were carried out by the Australian Mineral Development Laboratories, Melbourne.

Sodium 1-imido-3-methoxyisoindoline (**1**) was prepared by the method outlined by Borodkin.[3] The product was washed with methanol and dried at diminished pressure (0.1 mmHg), m.p. 122—123 °C (decomp.); *m/z* 160 (90%), 129 (82), 103 (100), and 76 (30); ν(Nujol) 1 680(m), 1 250(m), and 755(s) cm^{-1}; δ_H 7.7 (1 H), 7.4 (2 H, 7.25 (1 H), and 3.22 (3 H).

Lithium 1-*Imido*-3-(3-*methoxy*-5-*nitroisoindolenin*-1-*ylidene-amino*)-5-*nitroisoindole* (**6**; R = Me).—4-Nitrophthalonitrile (15.0 g) was added to methanol (300 ml) in which cleaned lithium metal (0.29 g) had been dissolved. The mixture was heated (116 °C) with stirring for 5 h in a glass-lined autoclave. After cooling, the dark-green product was precipitated by addition of benzene (500 ml), filtered, and extracted into acetone solution from which it was removed by addition of benzene (500 ml). The product was finally washed with benzene and held at reduced pressure (0.1 mmHg) for 60 min, yield 11 g (72%) (Found: C, 53.65; H, 2.2; N, 21.3. Calc. for $C_{17}H_9LiN_6O_5 \cdot 0.25C_3H_6O$: C, 53.5; H, 2.7; N, 21.1%); *m/z* 376 (2%, $M^+ + I; -Li$), 292 (2), 271 (3), 256 (4), 238 (16), 237 (12), 223 (41), 194 (9), 169 (12), and 149 (46); δ_H 7.4 (6 H) and 3.8 (3 H); ν(Nujol) 1 650(m), 1 610(m), 1 520(s), and 1 380 cm^{-1}.

4,10,17,24-*Tetranitrophthalocyanine* (**7**).—An n-butanol solution (20 ml) of 4-nitrophthalonitrile (2.0 g) was added to a refluxing solution of lithium (40 mg) in n-butanol (20 ml) and the solution heated to reflux. After cooling, the green solution was decanted from the dark brown solid residue. Acetone (20 ml) and water (20 ml) were added and the solution acidified with concentrated hydrochloric acid (*ca.* 5 × 0.05 ml). The resultant dark green precipitate was isolated by filtration with ethanol and stored over silica gel, yield 0.4 g (20%) (Found: C, 55.15; H, 2.0; N, 24.3; O, 18.5. Calc for $C_{32}H_{14}N_{12}O_8$: C, 55.4; H, 2.1; N, 24.2; O, 18.4%).

9,10-*Dihydro*-9,10-*ethenoanthracene*-11,12-*diamide*.—Finely ground 9,10-dihydroanthracene-9,10-*endo*-α,β-maleate (11.0 g), prepared as described,[8] was added to dioxane (25% v/v)–methanol (25% v/v) and concentrated aqueous ammonium hydroxide (50% v/v) (300 ml). Further addition of liquid ammonia (70 ml) was made and the slurry stirred for two days. The solid product was collected and recrystallized from acetonitrile, yield 6.7 g (67%), m.p. 295 °C (decomp.) (lit.,[8] 285 °C); *m/z* 290 (M^+, 12%), 272 (22), 254 (12), 247 (65), 230 (38), 218 (17), 202 (160), and 178 (60).

11,12-*Dicyano*-9,10-*dihydro*-9,10-*ethenoanthracene*.—A chilled (−15 °C) slurry of 9,10-dihydro-9,10-ethenoanthracene-11,12-diamide (6.7 g) in dimethylformamide (50 ml) was added slowly to a chilled (−15 °C) solution of thionyl chloride (5.5 g) in dimethylformamide (50 ml), while keeping the temperature below −10 °C. The stirred mixture was allowed to come to room temperature and stirred for a further 24 h. The product was isolated by pouring the mixture onto crushed ice and filtering, and purified by recrystallization from acetonitrile, yield 5.3 g (89%), m.p. 267—268 °C (Found: C, 85.4; H, 4.2; N, 10.7. Calc. for $C_{18}H_{10}N_2$: C, 85.0; H, 4.0; N, 11.0%); *m/z* 254 (M^+, 100%), 227 (38), 203 (12), and 178 (38). The crystal structure of this compound has been determined.[9]

Magnesium Dibenzobarrelenoporphyrazine (**8**).—The procedure was similar to that described in the literature.[10] Magnesium n-butoxide was prepared under dinitrogen from the decomposition of methylmagnesium iodide as follows. Dry magnesium turnings (0.29 g) were added to dried diethyl ether (20 ml) containing methyl iodide (1.75 g) and the reaction started by addition of a small crystal of iodine. After dissolution of the magnesium turnings, dried n-butanol (5 ml) was added and most of the ether removed at diminished pressure (0.1 mmHg). 9,10-Dihydro-9,10-ethenoanthracene-11,12-dicarbonitrile (1.39 g) was added and the stirred mixture heated (125 °C) for 6 h. The solvent was removed at diminished pressure (1 mmHg) and the remaining green material washed (3 × 50 ml) with ethanol–water (50% v/v). The green solid product (0.8 g) was dissolved in chloroform, loaded on a silica column, and eluted with methanol (5% v/v)–chloroform. The coloured bands were in the order red, yellow, and blue, the desired product being last. The yield of magnesium chelate (log ε 4.94 at $\lambda_{max.}$) (lit.,[10] 4.92) was 70 mg. In experiments designed to show the effect of added water on the yield of purified product, the initial stirred mixture of alkoxide and dinitrile was heated for 10 min and water added. The remaining experimental procedure was as before, giving a yield of purified magnesium chelate of 170 mg (11%).

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