The Solid Phase, Room-Temperature Synthesis of Metal-free and Metallophthalocyanines, Particularly of 2,3,9,10,16,17,23,24-Octacyanophthalocyanines

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Room-temperature synthesis of phthalocyanines (pcs) by condensation of phthalonitriles in the presence of solid sodium methoxide in THF is proposed for the synthesis of metal-free pcs with temperature- and/or base-sensitive substituents. The addition of metal salts after metal-free pc formation in the same vessel produces metallopcs in moderate to high (ca. 30–90%) yields.

The most popular methods for the preparation of the phthalocyanines (pcs) and their metal complexes require either fusion of phthalic anhydride or its derivatives with urea at high temperature (200–300 °C), or tetramerization of phthalonitriles or the corresponding isoindolediimines in refluxing C3-C8 alcohol (roughly ca. 100-200 °C) or 2-*N,N*-dimethylaminoethanol (135 °C).[1] As discussed in previous reports,[2] it is possible, if the structure of the starting isoindolediimine is suitably modified, to decrease the reaction temperature for pc core formation, but the yields in this kind of synthesis are not particularly high. Recently, it was shown that the reaction of substituted phthalonitriles with lithium 2-*N,N*-dimethylaminoethoxide in 2-*N,N*-dimethylaminoethanol or lithium 1-octanolate in 1-octanol at room temperature leads to the formation of pcs in moderate yields.[3] However, even with this method, there remain limitations. The most important of these originates from the fact that there is almost a 10-fold excess of alkanolate (with respect to phthalonitrile) present in the solution. Thus, since the alkanolate anion is a very strong nucleophile, phthalonitriles or isoindolediimines containing groups sensitive to nucleophilic attack cannot be used. It would therefore be beneficial to find a method applicable to this type of pc precursor.

It is well known that strong bases in two- to ten-fold excess with respect to phthalonitriles are needed for the synthesis of pcs.[1] In general, there may be two ways to overcome this problem. The first is based on the use of strong bases with low nucleophilicity, such as DBU and DBN.[4] However, any attempts to prepare, for example, nucleophile-labile 2,3,9,10,16,17,23,24-octacyanophthalocyanine, pc(CN)$_8$H$_2$, in the presence of DBU and DBN in 2-(*N,N*-dimethylamino)ethanol, 1-octanol, THF, DMF, or DMSO, have failed. The second option is based on the use of solvents which have low or negligible solubility for strong bases. Non-polar organic solvents such as 1- or 2-chloronaphthalene and benzene, as well as organic ethers such as diethyl ether, THF, and dioxane are good candidates for this approach. From various combinations of bases and solvents, we have found that the use of dry THF as a solvent and sodium methoxide as an organic strong base is successful for metal-free pc formation reactions at room temperature. As exemplified below for the formation of pc(CN)$_8$H$_2$, this method is applicable to pcs having nucleophile-labile and/or high temperature-labile substituent groups. Furthermore, the addition of metal

salts after the pc formation reaction in the same vessel can produce metallopcs in moderate to high yields.

As shown in a typical procedure,[5] condensation of 1,2,4,5-tetracyanobenzene in THF in the presence of sodium methoxide at 20 °C readily took place to form, after a few days to one week, pc(CN)$_8$H$_2$. Addition of metal salts such as zinc acetate or cuprous chloride after formation of the metal-free pc leads to the corresponding metal complexes (Scheme 1).[6] Similarly,
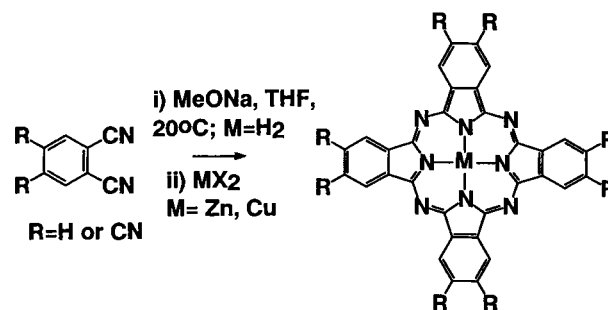
Scheme 1.

condensation using unsubstituted phthalonitrile also proceeded smoothly. The reaction conditions and yields of pcs are summarised in Table 1. Since pc(CN)$_8$H$_2$ contains eight cyano groups, the formation of pc dimers, trimers or polymers using cyano groups on the periphery might occur, as well as nucleophilic attack on the cyano groups. To examine such possibilities, the crude reaction mixture was tested by MALDI-TOF MS

Table 1. Low-temperature synthesis of phthalocyanines in THF

Complex	NaOMe[a]	T/°C	Time/day	Yield/%
pc(CN)$_8$H$_2$	3	20	5	50
pc(CN)$_8$H$_2$	5	20	5	28
pc(CN)$_8$H$_2$	3	50	1	52
pc(CN)$_8$Zn	3	20	7 + 3[b]	82
pc(CN)$_8$Cu	3	20	7 + 3[b]	91
pcH$_2$	3	20	8	19
pcH$_2$	5	20	8	34
pcH$_2$	10	20	8	32
pcH$_2$	5	50	1	38
pcZn	3	20	7 + 3[b]	37
pcZn	5	20	7 + 3[b]	46
pcZn	10	20	1 + 1[b]	39
pcCu	3	20	7 + 2[b]	33
pcCu	5	20	7 + 2[b]	44
pcCu	10	20	1 + 1[b]	41

[a]Equivalents of NaOMe used against the starting phthalonitriles.
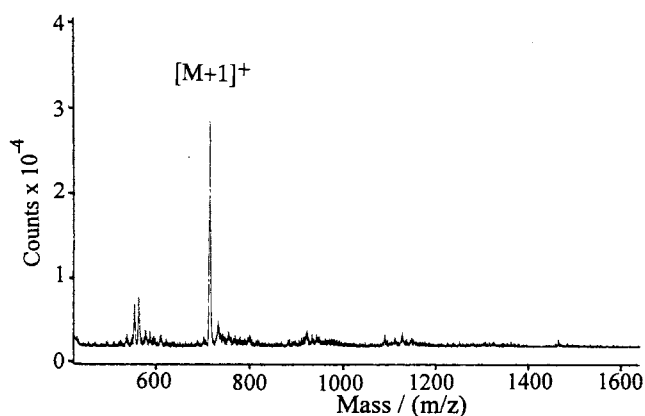[b]Second numbers reflect time after metal salt was added.

Figure 1. MALDI-TOF MS spectrum of crude pc(CN)$_8$H$_2$.

spectrometry, as well as gel permeation chromatography. The MALDI-TOF MS spectrum shown in Figure 1 clearly indicates that essentially only one macrocyclic product, i.e. pc(CN)$_8$H$_2$ is present. Signals of planar di-, tri-, or higher condensation products of pc(CN)$_8$H$_2$, as well as carboxylic acid-containing pcs, were absent or negligibly small.[6] The results of gel-permeation chromatography also support the MS data: only one blue-green pc band was observed on Bio-beads, SX-2 column (Bio-rad), which was pc(CN)$_8$H$_2$. This high selectivity for the formation of pc(CN)$_8$H$_2$ can be explained by taking into consideration the solubility of sodium methoxide in THF. Thus, in a separate experiment, we found that the solubility of sodium methoxide in dry THF was ca. 10^{-4} mol/L at 20 °C and therefore the ratio of 1,2,4,5-tetracyanobenzene : sodium methoxide in THF solution was ca. 1000:1 (mol/mol). Such a low concentration of the base is obviously not enough for nucleophilic attack on cyano groups not only in pc(CN)$_8$H$_2$, but also in 1,2,4,5-tetracyanobenzene. On the other hand, it is considered that the pc core formation is probably occurring on the surface of solid sodium methoxide, since the yields of pc formation decreased when the stirring speed was reduced.[7]

Now we may need to explain why the sodium methoxide surface is much more selective for the activation of cyano groups in 1,2,4,5-tetracyanobenzene than those in pc(CN)$_8$H$_2$ (present in the reaction solution as a dianion). This kind of activation can be explained as a multistep process which consists, at least, of the adsorption of 1,2,4,5-tetracyanobenzene or pc(CN)$_8$H$_2$ onto the negatively charged surface of a methoxide anion and the nucleophilic attack of the methoxide anion on the cyano groups. The adsorption energy between the negatively charged surface (in this case sodium methoxide) and polar organic molecules depends predominantly on coulombic attractive interaction, which is roughly proportional to the positive values of the molecular electrostatic potential (V_{MEP}) of organic molecues. The V_{MEP} values for 1,2,4,5-tetracyanobenzene and the pc(CN)$_8$H$_2$ dianion calculated at the PM3 semi-empirical level,[8] are 16.95 and 10.23 eV, respectively, indicating that the adsorption energy of the pc(CN)$_8$H$_2$ dianion is probably less than that for 1,2,4,5-tetracyanobenzene.

The room-temperature pc synthesis in THF has several advantages over previously known methods. i) This method is applicable to precursors containing nucleophile-labile and/or high temperature-labile substituent groups. ii) We can spare

time to prepare alkoxides such as lithium 1-hexanolate. iii) If the resulting pcs are soluble in THF, they can be separated easily from sodium methoxide and/or metal salts present in solution by filtration. Conversely, if the pcs are insoluble in THF, they can be collected by filtration and the residual sodium methoxide and/or metal salts can be easily washed out with water.

References and Notes
1   C. C. Leznoff, in "Phthalocyanines: Properties and Applications," ed. by C. C. Leznoff and A. B. P. Lever, VCH, NY (1989), Vol. 1, Chap. 1.
2   H. Tomoda, S. Saito, and E. Hibiya, *Chem. Lett.*, **1976**, 1003; S. Greenberg, A. B. P. Lever, and C. C. Leznoff, *Can. J. Chem.*, **66**, 1059 (1988); J. G. Young and W. Onyebuagu, *J. Org. Chem.*, **55**, 2155 (1990).
3   C. C. Leznoff, M. Hu, and J. M. Nolan, *Chem. Commun.*, **1996**, 1245; C. C. Leznoff, A. M. D'ascanio, and S. Z. Yildiz, *J. Porphyrins Phthalocyanines*, **4**, 103 (2000).
4   H. Tomoda, S. Saito, S. Ogawa, and S. Shiraishi, *Chem. Lett.*, **1980**, 1277; T. G. Linssen, K. Dürr, M. Hanack, and A. Hirsch, *J. Chem. Soc., Chem. Commun.*, **1995**, 103.
5   Typical procedure: To a solution of 100 mg (5.62 x 10^{-4} mol) of 1,2,4,5-tetracyanobenzene in 5 mL of dry THF, was added 90 mg (1.66 x 10^{-3} mol) of sodium methoxide. The resulting suspension was stirred for 5 days at room temperature, and then the solution was acidified by acetic acid to neutral. The residue of pc(CN)$_8$H$_2$ was filtered, washed with 2-propanol and precipitated from DMF solution by adding water. Yield 51 mg (50%). UV-VIS (λ, nm, only peak positions are given because of the strong aggregation of pc(CN)$_8$H$_2$ in solution): 712, 662, 428sh, 406 (acetone); 696, 648, 629, 426, 406 (DMF); IR (KBr, cm^{-1}): 2210 (ν_{CN}); *m/z*: (MALDI-TOF$^+$, dithranol): 715 ([M+1]$^+$, 100%).
6   In Figure 1, small mass peaks are observed at ca. *m/z* = 580, 950, and 1100. These are corresponding to the fragmentation of pc(CN)$_8$H$_2$, M$^+$ + dithranol (matrix), and M$^+$ + 2 x dithranol. The degree of metallation may depend on the amount of metal salt present in solution. When ca. 25–30 mg of cuprous chloride or zinc acetate was added to the above pc(CN)$_8$H$_2$ solution in ref. 5, no metal-free species was detected from the solution after a 3-day reaction by mass spectroscopy.
7   One referee pointed out that the solubility of NaOMe may increase during the reaction, since the reaction time is long. We recovered, however, almost all NaOMe used for the reaction when the reaction solution was filtered through a membrane filter. Since the pore size of this filter was 3 μm, it may be said that most NaOMe was present as solid in the reaction.
8   All calculations were performed using the HyperChem 5.1 program (HyperCube Inc.).