

The Synthesis of Metal-Free Phthalocyanines from Phthalonitriles with Hexamethyldisilazane

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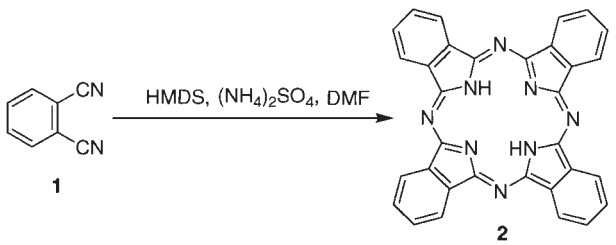
Metal-free phthalocyanines were prepared in good yields by heating phthalonitriles with hexamethyldisilazane, $(NH_4)_2SO_4$, and DMF. Good yields of metal-free phthalocyanines involving peripherally substituted phthalocyanines were attained with a catalytic amount of hexamethyldisilazane. Naphthalocyanine was also prepared. Additional additives were examined to accelerate the formation of the phthalocyanine framework.

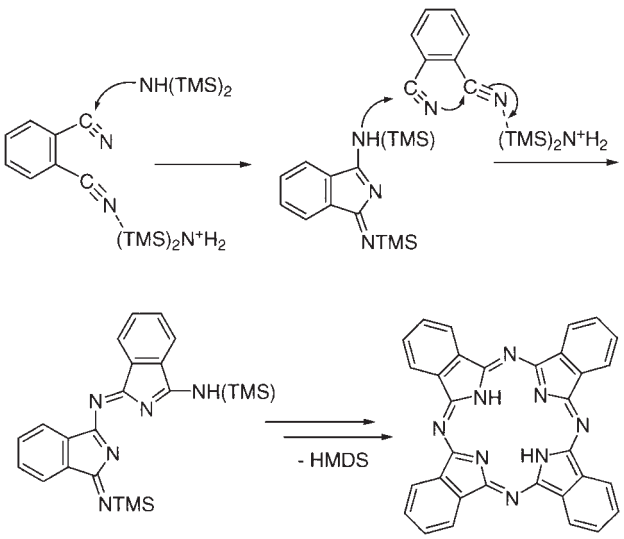
Metal-free phthalocyanines (H_2-Pcs) **2** are an important class of phthalocyanines. They often serve as precursors not only for normal metal–Pcs, but also for those not easily obtainable by direct synthesis from phthalic anhydrides, phthalimides, or phthalonitriles with metal salts.[1] H_2-Pcs are usually prepared from phthalonitriles in alcohols such as 1-pentanol or 2-dimethylaminoethanol.[2] The formation of H_2-Pcs is promoted by the addition of a basic catalyst such as DBN,[3] DBU,[3] tertiary amines,[3c] ammonia,[4] benzene tellurolate,[5] selenolate[5] or thiolate.[5] Recently, the cerium-promoted formation of H_2-Pcs in pentanol was reported.[6] When alkali metal[7] or alkali earth metal alkoxides[8] are used, H_2-Pcs are obtained after acidic treatment of the initial alkali (or alkali earth) metal–phthalocyanines. Heating phthalonitriles without a solvent in the presence of hydroquinone is another effective method.[9] In addition to these phthalonitrile-based syntheses, H_2-Pcs are also obtainable from diiminoisoindolines.[10] Recently, we found that hexamethyldisilazane (HMDS) is an excellent regent for use in the formation of metal–Pcs from phthalonitriles[11] or phthalimides.[12] Furthermore, we also reported the first synthesis of H_2-Pcs from phthalimides or phthalic anhydrides upon treatment with HMDS.[13] In continuation of our study to develop new methods for the preparation of phthalocyanines, we now report a new convenient route for the synthesis of H_2-Pcs from phthalonitriles with HMDS.

Results and Discussion

Phthalonitrile **1** was heated with HMDS and DMF[14] in a sealed tube to avoid the evaporation of volatile substances including HMDS (Scheme 1). The results obtained under various conditions are shown in Table 1. The reaction with **1** and HMDS in a molar ratio of 1.0:2.0 for 10 h at 100 °C gave no H_2-Pc **2** (entry 1), but heating for 24 h afforded **2** in a 59% yield (entry 2). Heating at 150 °C for 10 and 24 h gave **2** in 23% and 56% yields, respectively (entries 5 and 7). $(NH_4)_2SO_4$ was found to accelerate the formation of the phthalocyanine skeleton, giving **2** in 68% and 72% yields for 24 h at 100 °C and 150 °C, respectively (entries 4 and 8). In the preparation of metal–Pcs, a metal template effect would be expected to promote the formation of the phthalocyanine skeleton.



Scheme 1.



Scheme 2.

Since such an effect is not present in the formation of H_2-Pc, an additive such as $(NH_4)_2SO_4$ is necessary for the acceleration of the cyclization. HMDS, possibly coordinated with $(NH_4)_2SO_4$, activates the cyano group of phthalonitrile for intramolecular cyclization to give the diiminoisoindoline derivative. This activated HMDS also promotes further intermolecular reactions. HMDS is requisite for the formation of **2** (entry

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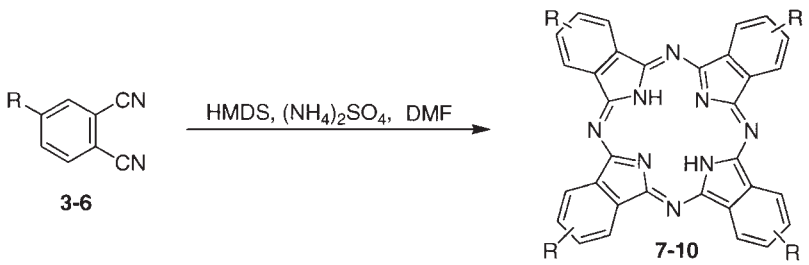
Table 1. Preparation of H_2-Pc **2** from **1** under Various Conditions[a)]

Entry	HMDS (molar ratio)[b)]	$(NH_4)_2SO_4$ (molar ratio)[b)]	Reaction time/h	Reaction temperature/°C	Yield /%
1	2.0	—	10	100	0
2	2.0	—	24	100	59
3	2.0	0.1	10	100	0
4	2.0	0.1	24	100	68
5	2.0	—	10	150	23
6	2.0	0.1	10	150	56
7	2.0	—	24	150	56
8	2.0	0.1	24	150	72
9	4.0	0.1	10	150	49
10	0	0.1	24	150	0
11	0.1	0.1	10	150	42
12	0.2	0.1	10	150	50
13	0.3	0.1	10	150	60
14	0.3	0.1	24	150	64
15	1.0	0.1	10	150	61
16	0.3	0.1	24	100	3

a) An equimolar amount of DMF to **1** was used. b) The molar ratio to **1**.

10), but excessive HMDS did not increase the yield of **2** (entry 9). We found that a catalytic amount of HMDS was also effective for the formation of the phthalocyanine framework. Thus, the reaction with **1** and HMDS in a molar ratio of 1.0:0.3 gave **2** in 64% yield by heating for 24 h at 150 °C (entry 14). It is reasonable that a catalytic amount of HMDS forms H_2-Pc according to the plausible reaction mechanism (Scheme 2): HMDS promotes cyclization of phthalonitriles not only by activation of the cyano group together with $(NH_4)_2SO_4$, but also by nucleophilic attack on the cyano carbon, and furthermore accelerates subsequent intermolecular reactions. HMDS is then reproduced at the intramolecular cyclization stage to form the phthalocyanine skeleton.

Various peripherally substituted H_2-Pcs such as tetra(*tert*-butyl)-, tetrapropoxy-, tetraphenoxy-, and tetrakis(octylthio)-phthalocyanines **7**–**10** were prepared from the corresponding 4-substituted phthalonitriles **3**–**6** (Scheme 3, Table 2). The reactions were performed with a catalytic amount (0.3 molar ratio) of HMDS for 24 h at 150 °C, giving **7**–**10** in good yields (entries 1, 4, and 6). The phthalocyanine derivatives **7**–**10** were obtained as a mixture of regioisomers that were not separated. The reaction of 4-*tert*-butylphthalonitrile **3** with an excess amount (2.0 molar ratio) of HMDS did not significantly increase the yield of **7** (entries 2 and 3). Tetraphenoxyphthalocyanine **9** was not formed in good yield (entry 5). Naphthalocyanine **12** was formed in 44% yield upon heating of a mixture of 2,3-naphthalonitrile **11** and HMDS in a molar ratio of 1.0:2.0 for 24 h at 150 °C (Scheme 4).

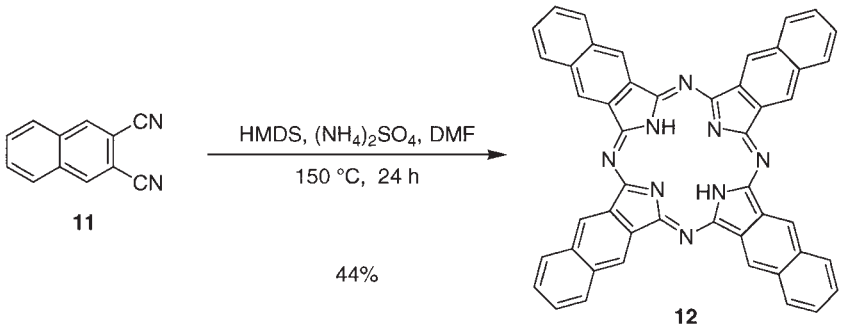


Scheme 3.

Table 2. Preparation of Peripherally Substituted H_2-Pcs **7**–**10**[a)]

Entry	Phthalonitrile R		HMDS (molar ratio)[b)]	Reaction temperature/°C	Phthalocyanine	Yield /%
1	*t*-Bu	**3**	0.3	150	**7**	49
2	*t*-Bu	**3**	2.0	100	**7**	53
3	*t*-Bu	**3**	2.0	150	**7**	52
4	PrO	**4**	0.3	150	**8**	56
5	PhO	**5**	2.0	150	**9**	21
6	OctS	**6**	0.3	150	**10**	62

a) The molar ratio of $(NH_4)_2SO_4$ to **1** was 0.1. The mixture was heated for 10 h. b) The molar ratio to **1**.



Scheme 4.

Table 3. Preparation of H_2-Pc **2** in the Presence of Various Additives[a)]

Entry	Additive	Reaction time/h	Yield /%
1	—	10	17
2	—	24	62
3	*p*-TsOH·H_2O	10	61
4	*p*-TsOH·H_2O	24	56
5	*p*-TsOH·H_2O	48	48
6	TfOH	10	52
7	TfOH	24	49
8	TMSCl	10	54
9	TMSCl	24	47
10	imidazole	10	62
11	imidazole	24	57
12	pyridine	10	37
13	pyridine	24	64
14	*i*-Pr_2NH	10	39
15	Et_3N[b)]	10	27
16	DBU	10	34
17	Bu_3SnH	10	56
18	hydroquinone	10	65
19	hydroquinone	24	51
20	hydroquinone/$(NH_4)_2SO_4$[c)]	24	62
21	1,4-$(TMSO)_2C_6H_4$/$(NH_4)_2SO_4$[d)]	10	60
22	1,4-$(TMSO)_2C_6H_4$	10	0

a) A mixture of **1**, HMDS, an additive, and DMF in a molar ratio of 1.0:0.3:0.1:1.0 was heated at 150 °C unless otherwise noted. b) A mixture of **1**, HMDS, Et_3N, and DMF in a molar ratio of 1.0:2.0:0.1:1.0 was heated at 150 °C. c) A mixture of **1**, HMDS, hydroquinone, $(NH_4)_2SO_4$, and DMF in a molar ratio of 1.0:0.6:0.3:0.1:1.0 was heated. d) A mixture of **1**, HMDS, 1,4-$(TMSO)_2C_6H_4$, $(NH_4)_2SO_4$, and DMF in a molar ratio of 1.0:0.3:0.1:0.1:1.0 was heated.

We examined some other additives in place of $(NH_4)_2SO_4$. We reported earlier that the formation of metal–Pcs with HMDS was promoted by *p*-TsOH and H_2SO_4.[12] The reaction was performed by using **1** and HMDS in a molar ratio of 1.0:0.3 (Table 3). *p*-TsOH and TfOH were effective in the formation of H_2-Pc as compared with the yields in the reaction without an additive for 10 h at 150 °C (entry 1 vs entries 3 and 6), but heating for a longer time decreased the yield (entries 4, 5, and 7). Chlorotrimethylsilane increased the yield of **1** for 10 h at 150 °C (entry 8). The weakly basic imidazole also accelerated the formation of H_2-Pc (entry 10), whereas pyridine, diisopropylamine, triethylamine, and DBU had no significant effect (entries 12, 14–16). Chlorotrimethylsilane and imidazole are known to effectively catalyze the trimethylsilylation of alcohols, enols, and thiols with HMDS.[15] This is probably the reason why these additives promoted the formation of H_2-Pc. Hydroquinone is also sometimes effective in the preparation of H_2-Pcs.[9] Bu_3SnH and hydroquinone were examined, and good yields of **2** were obtained in the reaction without $(NH_4)_2SO_4$ (entries 17, 18, and 19) and also in the presence of $(NH_4)_2SO_4$ (entry 20). Since hydroquinone was supposed to be silylated by the action of HMDS during the reaction, 1,4-bis(trimethylsiloxy)benzene[16] was examined and found to be effective as well in the presence of $(NH_4)_2SO_4$ (entry 21), but not effective without $(NH_4)_2SO_4$ (entry 22). When the reaction was performed with HMDS for 24 h at 150 °C, H_2-Pc **2** was obtained in good yield even without an additive (entry 2). Unfortunately, the yields obtained by heating for 24 h at 150 °C with any additives did not significantly exceed those without an additive. Most of the additives listed in Table 3, whether they are acidic or basic, increased the yield of H_2-Pc **2** when compared with those obtained by heating for 10 h at 150 °C without an additive.

Conclusion

We have developed a new and efficient protocol for the production of unsubstituted and substituted H_2-phthalocyanines that can be performed under substantially neutral and mild conditions. Some additives were effective in the preparation of H_2-Pcs with HMDS.

Experimental

General. HMDS was distilled before use. DMF was distilled from P_2O_5 and stored over MS 4A. Phthalonitrile and naphthalonitrile were purchased from TCI. 4-Substituted phthalonitriles were synthesized according to the methods reported in the literature.[17] Additives were dried under vacuum before use. All solvents for extraction and other reagents were used without additional purification. UV–vis spectra were measured with a JASCO V-530 spectrometer. ^{1}H NMR spectra were taken on a Varian Gemini-200 spectrometer using tetramethylsilane as an internal standard. MALDI-TOF MS were recorded on a Perseptive Biosystems Voyager RN spectrometer without a matrix via external calibration using commercially available metal-free phthalocyanine and zinc naphthalocyanine as calibrants. Microanalyses were performed with a Perkin Elmer-240.

Preparation of Phthalocyanine (2).[8] **Method A:** A glass tube was charged with phthalonitrile (300 mg, 2.34 mmol), $(NH_4)_2SO_4$

(31 mg, 0.234 mmol), HMDS (0.99 mL, 4.69 mmol), and DMF (0.18 mL, 2.33 mmol) under an argon atmosphere. The tube was sealed and heated to 150 °C. A dark purple solid immediately appeared. After heating for 24 h, the mixture was cooled and filtered. The solid was washed with methanol and then dissolved in conc. H_2SO_4 (10 mL). The resulting solution was poured into water (200 mL) to give a blue precipitate. The precipitate was filtered and washed thoroughly with water. The solid was further purified by a soxhlet extractor with methanol to give 217 mg (72%) of **2**.

Method B: The reaction was performed as described in Method A except for the use of phthalonitrile (300 mg, 2.34 mmol), $(NH_4)_2SO_4$ (31 mg, 0.234 mmol), HMDS (0.15 mL, 0.71 mmol), and DMF (0.18 mL, 2.33 mmol) to give 192.5 mg (64%) of **2**.

Preparation of Tetra(*tert*-butyl)phthalocyanine (7).[18] A mixture of 4-*tert*-butylphthalonitrile (300 mg, 1.63 mmol), $(NH_4)_2SO_4$ (21 mg, 0.158 mmol), HMDS (0.69 mL, 3.27 mmol), and DMF (0.13 mL, 1.68 mmol) was heated as above. Then the mixture was cooled, filtered, and washed with methanol. The solid was purified by silica gel column chromatography (toluene/AcOEt = 99.5:0.5) to give 157 mg (52%) of **7**.

Preparation of Tetrapropoxyphthalocyanine (8).[3c] The reaction was the same as described for **7** except for the use of a mixture of 4-propoxyphthalonitrile (300 mg, 1.61 mmol), $(NH_4)_2SO_4$ (21 mg, 0.158 mmol), HMDS (0.10 mL, 0.47 mmol), and DMF (0.12 mL, 1.55 mmol) giving 168 mg (56%) of **8**.

Preparation of Tetraphenoxyphthalocyanine (9).[19] The reaction was the same as described for **7** except for the use of a mixture of 4-phenoxyphthalonitrile (280 mg, 1.27 mmol), $(NH_4)_2SO_4$ (17 mg, 0.126 mmol), HMDS (0.54 mL, 2.56 mmol), and DMF (0.10 mL, 1.29 mmol) giving 58 mg (21%) of **9**.

Preparation of Tetrakis(octylthio)phthalocyanine (10). The reaction was the same as described for **7** except for the use of a mixture of 4-octylthiophthalonitrile (300 mg, 1.10 mmol), $(NH_4)_2SO_4$ (15 mg, 0.111 mmol), HMDS (0.07 mL, 0.33 mmol), and DMF (0.09 mL, 1.16 mmol) giving 186 mg (62%) of **10**. UV–vis ($CHCl_3$) λ_{max} 716, 683, 355 nm; ^{1}H NMR ($CDCl_3$) δ 8.05–7.36 (m, 12H), 3.31–3.21 (brm, 8H), 2.01–1.25 (brm, 48H), 1.01–0.99 (br, 12H); MS (MALDI): m/z 1091.4 [M + H$^+$]; Anal. Calcd for $C_{64}H_{82}N_8S_4$: C, 70.41; H, 7.57; N, 10.26%. Found: C, 70.35; H, 7.48; N 10.13%.

Preparation of Naphthalocyanine (12).[20] The reaction was the same as described for **2** except for using a mixture of 2,3-naphthalonitrile (121 mg, 0.680 mmol), $(NH_4)_2SO_4$ (9 mg, 0.070 mmol), HMDS (0.29 mL, 1.37 mmol), and DMF (0.05 mL, 0.65 mmol) affording 54 mg (44%) of **12**.

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