

Novel Efficient Preparative Method for Phthalocyanines from Phthalimides and Phthalic Anhydride with HMDS

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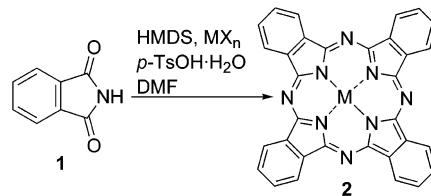
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Abstract: A convenient synthesis of peripherally substituted or unsubstituted phthalocyanines having a variety of metals is described. Phthalocyanines can be obtained by heating phthalimides or phthalic anhydride with metal salts, hexamethyldisilazane, a catalytic amount of *p*-TsOH, and DMF at 150 °C.

Phthalocyanines find versatile application in the area of material science because of their distinctive optical and electrical properties as well as their chemical and thermal stability.¹ Phthalocyanines are prepared from phthalonitriles² or phthalic acid analogues such as phthalimides, phthalic anhydrides, and phthalic acids.³ A number of studies for the application of phthalocyanines to functional dyes have been carried out,¹ generally adopting the preparation of these peripherally substituted phthalocyanines starting from substituted phthalonitriles; the preparative methods using phthalic acid analogues and urea generally need drastic conditions, which often cause undesired contamination with inseparable impurities such as halogenated phthalocyanine.⁴ The preparative methods for phthalocyanine derivatives with high purity starting from phthalimides or phthalic anhydrides have long been desired because these starting substrates are less expensive and more accessible than phthalonitrile or diiminoisoindoline derivatives. Such methods should be extremely attractive for the study of new functional dyes. Recently, we reported a convenient synthesis of

SCHEME 1



phthalocyanines from phthalonitriles with metal salts and hexamethyldisilazane (HMDS).⁵ We now report a novel convenient synthesis of phthalocyanines directly from phthalimides and phthalic anhydride by the action of HMDS under mild conditions.

We have recently reported⁶ the high-yield synthesis of N-substituted imides on treatment of amic acids with HMDS. In the case of transformation of phthalic anhydride to N-substituted phthalimides in the presence of ZnBr₂, we occasionally observed the formation of a trace amount of phthalocyanine-like blue material along with almost quantitative yield of phthalimide derivatives. We studied the reaction conditions using HMDS⁷ for the preferential transformation of phthalimides to phthalocyanines (Scheme 1). The results under various reaction conditions are summarized in Table 1.

As shown in the reaction with 0.25 equiv of CuCl₂, DMF should be present for the formation of the phthalocyanine framework and the amount of DMF was apparently crucial in the high-yield formation of phthalocyanine **Cu-2**, where 1.0 equiv with respect to phthalimide was an optimized amount (entries 1–4). DMAc could be used instead of DMF, but the yield of **Cu-2** was better in DMF and no formation of **Cu-2** was observed in DMSO or chloronaphthalene. At least a 4-fold excess of HMDS was found to be necessary for the good yield formation of **Cu-2** (entries 2, 6, 8, and 9). **Cu-2** was not yielded without *p*-TsOH⁸ (entry 5). Concentrated H₂SO₄ was also effective (entry 7). Although the formation of **Cu-2** was observed on heating at 100 °C, the reaction at 150 °C showed higher yield (entries 2 and 10). An excess amount of CuCl₂ did not improve the yield (entry 12). In addition, the reaction starting with 5.0 g of phthalimide under similar conditions produced **Cu-2** in 56% yield, showing that this procedure is compatible with large-scale production. Furthermore, HMDS is a reagent widely used as an adhesive agent for photoresists in the process of manufacturing silicon semiconductors.

To explore the scope and limitations of the present method, we performed the reaction using other metal salts such as CuCl, CuBr₂, CuBr, Cu(OTf)₂, ZnCl₂, ZnBr₂, Zn(OTf)₂, CoCl₂, CoBr₂, NiCl₂, NiBr₂, MgCl₂, and MgBr₂. Various metallophthalocyanines were obtained in moder-

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(1) (a) Moser, F. H. *The Phthalocyanines: Properties*; Thomas, A. L., Ed.; CRC Press: Boca Raton, FL, 1983; Vols. 1 and 2. (b) *Phthalocyanines: Properties and Applications*; Leznoff, C. C., Lever, A. B. P., Eds.; VCH: Weinheim, 1989; Vol. 1, 1993; Vols. 2 and 3, and 1996; Vol. 4. (c) Thomas, A. L. *The Phthalocyanines: Research and Applications*; CRC Press: Boston, 1990. (d) McKeown, N. B. *Phthalocyanine Materials, Synthesis, Structure and Function*; Cambridge University Press: Cambridge, 1998. (e) Hanack, M.; Heckmann, H.; Polley, R. In *Methods of Organic Chemistry*; Schumann, E., Ed.; Georg Thieme Verlag: Stuttgart, 1998; Vol. E9d, pp 717–846. (f) Torre, G.; Claesenssens, C. G.; Torres, T. *Eur. J. Org. Chem.* **2000**, 2821.

(2) Linstead, R. P. *J. Chem. Soc.* **1934**, 1016.

(3) Wyler, M. U.S. Pat. Appl. 2197458 and 2197459, 1940; *Chem. Abstr.* **1940**, 34, 37564. For a number of improved preparative methods reported thereafter, see ref 1. For more recent reports of microwave irradiation methods, see: (a) Shaabani, A. *J. Chem. Res., Synop.* **1998**, 672. (b) Ungurensau, C. *Synthesis* **1999**, 10, 1729. (c) Jung, K. S.; Ro, J. Y.; Lee, J. Y.; Park, S. S. *J. Mater. Sci. Lett.* **2001**, 20, 2203. (d) Shaabani, A.; Bahadoran, F.; Bazgir, A.; Safari, N. *Indian J. Chem. Sec. A* **2001**, 40A, 195 and references therein. (e) Villemin, D.; Hammadi, M.; Hachemi, M.; Bar, N. *Molecules* **2001**, 6, 831.

(4) Yao, J.; Yonehara, H.; Pac, C. *Bull. Chem. Soc. Jpn.* **1995**, 68, 1001.

(5) Uchida, H.; Tanaka, H.; Yoshiyama, H.; Reddy, P. Y.; Nakamura, S.; Toru, T. *Synlett* **2002**, 1649.

(6) (a) Reddy, P. Y.; Kondo, S.; Toru, T.; Ueno, Y. *J. Org. Chem.* **1997**, 62, 2652. (b) Reddy, P. Y.; Kondo, S.; Fujita, S.; Toru, T. *Synthesis* **1998**, 999.

(7) For a review of HMDS in syntheses, see: Vorbrüggen, H. *Acc. Chem. Res.* **1995**, 28, 509.

(8) Reaction of phthalonitrile with HMDS gave **2** without *p*-TsOH; see ref 5.

TABLE 1. Preparation of Metallophthalocyanines 2 by Treatment of Phthalimides 1 with Metal Salts, HMDS, *p*-TsOH, and DMF

entry	MX _n	HMDS (equiv)	<i>p</i> -TsOH·H ₂ O (equiv)	DMF (equiv)	reaction temp (°C)	reaction time (h)	product	yield (%)
1	CuCl ₂	4	0.1	0	150	10	Cu-2	0
2	CuCl ₂	4	0.1	1.0	150	10	Cu-2	63
3	CuCl ₂	4	0.1	2.0	150	10	Cu-2	45
4	CuCl ₂	4	0.1	4.0	150	10	Cu-2	10
5	CuCl ₂	6	0	1.0	150	12	Cu-2	0
6	CuCl ₂	6	0.2	1.0	150	10	Cu-2	66
7	CuCl ₂	4	0.2 ^a	1.0	150	10	Cu-2	60
8	CuCl ₂	3	0.1	1.0	150	12	Cu-2	38
9	CuCl ₂	5	0.1	1.0	150	12	Cu-2	64
10	CuCl ₂	6	0.1	1.0	100	48	Cu-2	45
11	CuCl ₂	6	0.1	1.0	130	48	Cu-2	65
12	CuCl ₂ ^b	4	0.1	1.0	150	48	Cu-2	64
13	CuCl	4	0.1	1.0	150	4	Cu-2	63
14	CuBr ₂	4	0.1	1.0	150	10	Cu-2	72
15	CuBr	4	0.1	1.0	150	10	Cu-2	60
16	Cu(OTf) ₂	4	0	1.0	150	10	Cu-2	71
17	ZnCl ₂	4	0.1	1.0	150	10	Zn-2	47
18	ZnBr ₂	4	0.1	1.0	150	10	Zn-2	42
19	Zn(OTf) ₂	4	0	1.0	150	10	Zn-2	61
20	CoCl ₂	4	0.1	1.0	150	10	Co-2	51
21	CoBr ₂	4	0.1	1.0	150	4	Co-2	44
22	NiCl ₂	4	0.1	1.0	150	4	Ni-2	53
23	NiBr ₂	4	0.1	1.0	150	10	Ni-2	45
24	MgCl ₂	4	0.1	1.0	150	10	H₂-2	22
25	MgBr ₂	4	0.1	1.0	150	4	H₂-2	34

^a Concentrated H₂SO₄ (0.2 equiv) was used instead of *p*-TsOH·H₂O. ^b CuCl₂ (0.375 equiv) was used.

ate to good yields (entries 13–25). In all cases, the reaction mixture was poured into concentrated H₂SO₄ to remove the side products, after the reaction was completed. As has been already observed in the reaction with urea,³ the reaction also proceeded with cuprous chloride or bromide, giving Cu(II)-phthalocyanine⁹ **Cu-2** (entries 13 and 15). Notably, when Cu(OTf)₂ or Zn(OTf)₂ was used as a metal salt, the reaction proceeded without *p*-TsOH giving **Cu-2** or **Zn-2**¹⁰ in high yields, respectively (entries 16 and 19). This is probably because trifluoromethanesulfonic acid is formed during the course of the reaction and acts as a catalyst in place of *p*-TsOH or because Cu(OTf)₂ and Zn(OTf)₂ accelerate the reaction. In the reaction with magnesium salts, the first formed **Mg-2** was hydrolyzed on treatment with concentrated H₂SO₄ to give H₂-phthalocyanine **H₂-2**¹¹ (entries 24 and 25). Since the reaction with HMDS could be performed at lower temperature than those with ammonia or urea, isolated phthalocyanines were free from contamination with halogenated phthalocyanines or other inseparable side products.¹² No contamination with such halogenated phthalocyanines was confirmed by EI MS and MALDI TOF MS spectra.

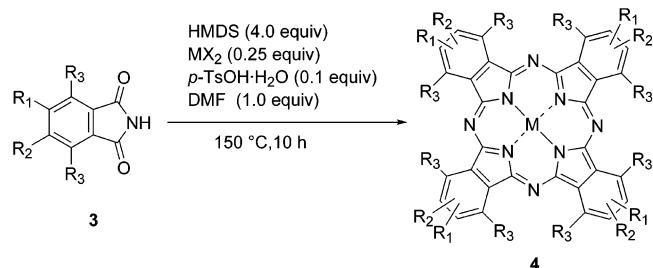
The present procedure was compatible with phthalimides having a variety of substituents such as 4-*tert*-butyl-**3a**, 4,5-dichloro-**3b**, and 3,4,5,6-tetrachlorophthalimide **3c**, giving the corresponding peripherally substituted Cu- and Zn-phthalocyanines **Cu-4a**,¹³ **Cu-4b**,¹⁴ **Cu-4c**,¹⁵ **Zn-4a**,¹³ and **Zn-4c**¹⁶ in good yields (Scheme 2, Table 2).

(9) Dent, C. E.; Linstead, R. P. *J. Chem. Soc.* **1934**, 1027.

(10) Barrett, P. A.; Dent, C. E.; Linstead, R. P. *J. Chem. Soc.* **1936**, 1719.

(11) Byrne, G. T.; Linstead, R. P.; Lowe, A. R. *J. Chem. Soc.* **1934**, 1017.

(12) In the reaction with CoCl₂, CoBr₂, NiCl₂, or NiBr₂, formation of a small amount of **H₂-2** was observed in MALDI-TOF-Ms spectra of the products.

SCHEME 2**TABLE 2. Preparation of Peripherally Substituted Phthalocyanines 4 from Phthalimide Derivatives 3**

entry	phthalimide			MX _n	<i>p</i> -TsOH·H ₂ O (equiv)	product	yield (%)
	R ₁	R ₂	R ₃				
1	<i>tert</i> -Bu	H	H	3a	CuCl ₂	0.1	Cu-4a 52
2	Cl	Cl	H	3b	CuCl ₂	0.1	Cu-4b 43
3	Cl	Cl	Cl	3c	CuCl ₂	0.1	Cu-4c 24
4	<i>tert</i> -Bu	H	H	3a	ZnCl ₂	0.1	Zn-4a 62
5	Cl	Cl	Cl	3c	Zn(OTf) ₂	0	Zn-4c 34

These phthalocyanine derivatives **Cu-4a** and **Zn-4a** were obtained as a mixture of regioisomers, which were not separated. Naphthalocyanines **Cu-6**¹⁷ and **Zn-6**¹⁸ could also be prepared in moderate yields in the reaction of 2,3-naphthalimide **5** (Scheme 3).

(13) Mikhaleko, S. A.; Barkanova, S. V.; Lebedev, O. L.; Luk'yanets, E. A. *Zh. Obshch. Khim.* **1971**, 41, 2735.

(14) Barrett, P. A.; Bradbrook, E. F.; Dent, C. E.; Linstead, R. P. *J. Chem. Soc.* **1939**, 1820.

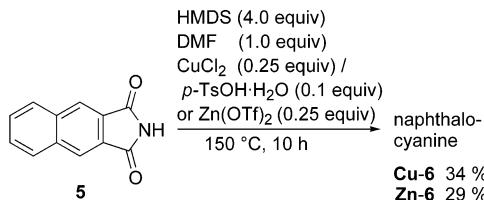
(15) Shigemitsu, M. *Bull. Chem. Soc. Jpn.* **1959**, 32, 607.

(16) Birchall, J. M.; Haszeldine, R. N.; Morley, J. O. *J. Chem. Soc. C* **1970**, 2667.

(17) Lebedev, O. L.; Luk'yanets, E. A.; Puchnova, V. A. *Opt. Spektrosk.* **1971**, 30, 640.

(18) Mikhaleko, S. A.; Luk'yanets, E. A. *Zh. Obshch. Khim.* **1969**, 39, 2554.

SCHEME 3



SCHEME 4

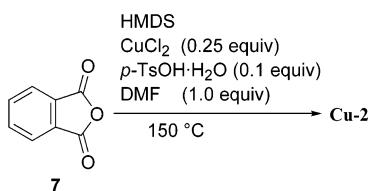
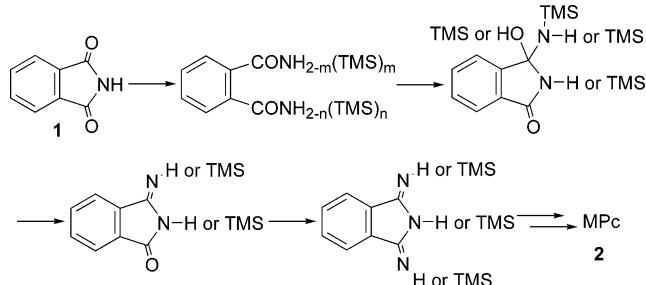


TABLE 3. Yields of Cu-Phthalocyanine Cu-2 by Treatment of Phthalic Anhydride with HMDS

entry	HMDS (equiv)	reaction time (h)	product	yield (%)
1	4	10	Cu-2	33
2	5	4	Cu-2	33
3	5	10	Cu-2	61
4	6	10	Cu-2	62

SCHEME 5. Plausible Reaction Mechanism



Furthermore, this procedure was able to extend the substrate to phthalic anhydride. We examined the reaction of phthalic anhydride with HMDS under reaction conditions similar to those described above and found that it indeed gave **Cu-2** (Scheme 4). This reaction proceeds possibly through the formation of phthalimides, showing that another nitrogen source from HMDS is requisite, and the reaction with a 5- to 6-fold excess of HMDS resulted in the best yield of **2** as shown in Table 3.

There are a number of plausible reaction pathways to form the phthalocyanine framework, and Scheme 5 illustrates one of these pathways. HMDS attacks the activated carbonyl carbon to give the phthalimide, which is cyclized to form 1,3-diiminoisoindoline through 3-iminoisoindolinone. The diiminoisoindoline is known to give the phthalocyanine framework under mild conditions.¹⁹ It should be noted that HMDS acts as a nitrogen source; besides, it accelerates the dehydration steps forming the

C≡N double bonds by easy removal of trimethylsilyl alcohol and ether. In addition, HMDS has sufficient nucleophilicity toward carbonyl groups of the imide and the anhydride when activated with a strong protic acid. These characteristic reaction features of HMDS realized a novel, convenient synthetic method for peripherally substituted or unsubstituted phthalocyanines having various metals from phthalimides and phthalic anhydride.

Experimental Section

Phthalimide was recrystallized from ethyl acetate. HMDS was distilled under an argon atmosphere. *p*-TsOH·H₂O was dried under high vacuum. Metal salts were heated under vacuum before use. DMF was dried over P₂O₅ and distilled under vacuum. All solvents for extraction and other reagents were used as obtained without additional purification.

Preparation of Cu-Phthalocyanine Cu-2.⁹ A glass tube was charged with phthalimide (100 mg, 0.68 mmol), CuCl₂ (23 mg, 0.25 mmol), *p*-toluenesulfonic acid monohydrate (13 mg, 0.07 mmol), and HMDS (560 μ L, 438 mg, 2.7 mmol), and the mixture was stirred at 100 °C for 1 h under an argon atmosphere. The mixture was cooled, and DMF (50 μ L, 0.68 mmol) was added. Then, the tube was sealed and the mixture was heated at 150 °C. A dark purple solid immediately appeared. After being heated for 10 h, the mixture was cooled and filtered. The solid was washed with methanol and then dissolved in concentrated H₂SO₄ (5 mL). The solution was poured into water (100 mL). The resulting blue precipitates were filtered and washed successively with dilute H₂SO₄, water, and methanol. The solid was further purified by extraction with methanol by Soxhlet's extractor to give 62 mg (63%) of **Cu-2** as a blue solid.

The reaction starting with 5.0 g of phthalimide was performed in a SUS 316 pressure bottle (100 mL Taiatsu Techno Co., Ltd.) under identical conditions. After separation and purification, 2.7 g (56%) of **Cu-2** was obtained.

Phthalocyanines **Zn-2**,¹⁰ **Co-2**,¹⁰ **Ni-2**,¹⁰ **H₂-2**,¹¹ **Cu-4b**,¹⁴ **Cu-4c**,¹⁵ and **Zn-4c**¹⁶ and naphthalocyanines **Cu-6**¹⁷ and **Zn-6**¹⁸ were prepared as above.

Preparation of Tetra-*tert*-butyl-Cu-Phthalocyanine Cu-4a.¹³ The reaction was carried out as described in the preparation of **Cu-2** except that 4-*tert*-butylphthalimide (138 mg, 0.68 mmol) was used. After completion of the reaction, the precipitates were filtered, washed with methanol, and dissolved in concentrated H₂SO₄. The H₂SO₄ solution was poured into water, and the resulting blue precipitates were filtered. The solid was further purified by silica gel column chromatography using benzene/THF (99:1) as an eluent to give 70 mg (52%) of **Cu-4a** as a blue solid.

Tetra-*tert*-butyl-Zn-phthalocyanine **Zn-4a**¹³ was prepared as above.

Typical Procedure for Cu-Phthalocyanine Cu-2 from Phthalic Anhydride. The reaction was performed as described in the preparation of **Cu-2** except that phthalic anhydride (100 mg, 0.68 mmol), CuCl₂ (23 mg, 0.17 mmol), *p*-toluenesulfonic acid monohydrate (13 mg, 0.07 mmol), and HMDS (700 μ L, 548 mg, 3.4 mmol) were used, giving 60 mg (61%) of **Cu-2**.

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(19) Timokhin, G. A.; Kissin, B. I.; Faeshkina, N. N. *Appl. Chem. USSR* **1969**, 42, 2187.