Tetrahedron Letters 53 (2012) 123–126

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of new highly organosoluble metallophthalocyanines with 1,8-dioxo-octahydroxanthene substituents

Ali Reza Karimi *, Fahimeh Bayat

Department of Chemistry, Faculty of Science, Arak University, Arak 38156-8-8349, Iran

ARTICLE INFO

Article history:
Received 24 July 2011
Revised 27 September 2011
Accepted 21 October 2011
Available online 28 October 2011

Keywords:
Phthalocyanine
1,8-Dioxo-octahydroxanthene
Organosoluble
Microwave synthesis

ABSTRACT

New highly organosoluble metallophthalocyanines (M = Zn, Co, Ni and Cu) bearing four [4-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1*H*-xanthen-9-yl)phenoxy] substituents at peripheral positions have been prepared by tetramerization of 4-[4-(3,3,6,6-tetramethyl-1,8-dioxo-dodecahydro-1*H*-xanthen-9-yl)phenoxy]phthalonitrile in 2-(dimethylamino)ethanol using microwave irradiation or conventional heating. Ni(II), Co(II) and Cu(I) chloride were employed in order to synthesize the corresponding metal phthalocyanines and $Zn(OAc)_2$ was used for the preparation of the zinc phthalocyanines. 4-[4-(3,3,6,6-Tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1*H*-xanthen-9-yl)phenoxy]phthalonitrile was obtained by nucleophilic displacement of the nitro group in 4-nitrophthalonitrile with 9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2*H*-xanthene-1,8(5*H*,9*H*)-dione. 9-(4-Hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2*H*-xanthene-1,8(5*H*,9*H*)-dione was synthesized efficiently from dimedone and 4-hydroxybenzaldehyde. All the phthalocyanines are soluble in DMSO, DMF, $CHCl_3$, THF, CH_2Cl_2, and CH_3CN. The new compounds were characterized by IR, NMR, and UV–vis spectroscopy, elemental analysis and thermogravimetric analysis.

Significant interest has been focused on the synthesis of phthalocyanines (Pc) due to their applications as liquid crystals,[1,2] solar cells,[3,4] electrochromic displays,[5] in photodynamic therapy of cancer,[6,7] in semiconductor devices,[8] gas sensors,[9–11] non-linear optics,[12] laser dyes,[13] Langmuir–Blodgett films[14] and various catalytic processes.[15]

The solubility of phthalocyanines is very important for the investigation of their chemical and physical characteristics and is influenced by the nature of the substituents on the periphery of the Pc ring. The main limitation in the applications of metallophthalocyanine complexes is their low solubility in common organic solvents.[16]

Water-soluble phthalocyanines have received great attention with regard to photodynamic efficacy,[17a] but the purification of these compounds can be a problem. Furthermore, aggregation (especially in aqueous media) is a very common phenomenon in this family of compounds.[17b]

Organo-soluble phthalocyanines are, therefore, important and potentially useful materials. The insolubility of phthalocyanines in organic solvents can be overcome by the introduction of organo-solubilizing substituents into the ring system.[18]

A number of phthalocyanines bearing apolar groups, such as bulky substituents,[19] long-chain groups (e.g., alkyl and alkoxy),[20] *N*-tosyl derivatives[21] and crown ethers[22] have been reported.

Xanthenes have been of much interest due to the broad spectrum of their pharmaceutical and biological properties which include anti-inflammatory,[23] antibacterial,[24] and antiviral activities[25] as well as their efficiency in photodynamic therapy (PDT)[26] and as antagonists toward the paralyzing action of zoxazolamine.[27] Furthermore, xanthenes are employed in laser technology.[28] Among the xanthenes developed thus far, it is known that octahydroxanthene derivatives can be applied as fluorescent fuels[29] and as antispasmodics.[30]

The development of new systems that can target specific cells for PDT relies on a connection between biological subunits and the photosensitizer. We expect that the conjugation of phthalocyanines with xanthene moieties may improve their organosolubility, and PDT effects.

This information encouraged us to design highly organosoluble metal (Zn, Ni, Cu and Co) phthalocyanines **6–9** containing four 9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2*H*-xanthene-1,8(5*H*,9*H*)-dione moieties (Scheme 1).

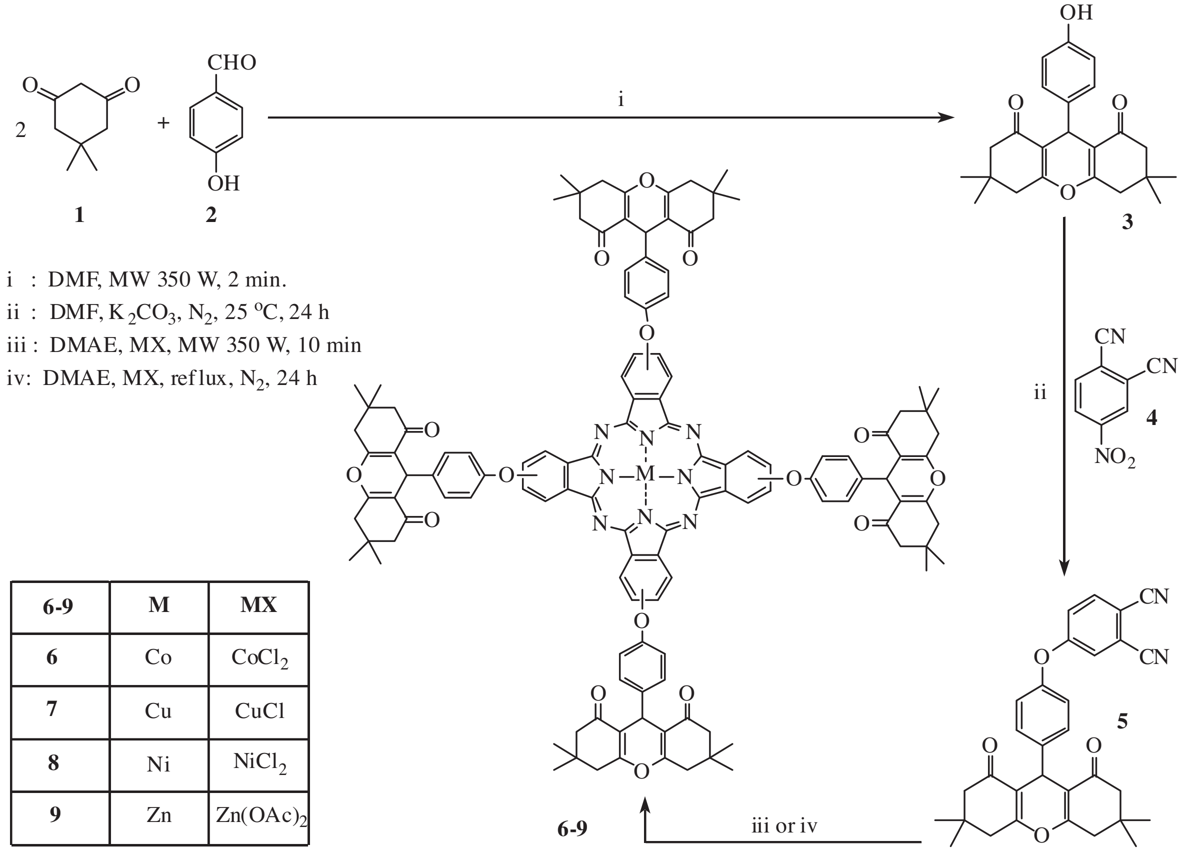
A number of methods have been developed for the preparation of MPcs. Microwave-assisted organic synthesis has attracted considerable attention, due to shorter reaction times, increased yields, and fewer side reactions.[31]

The present paper reports both the microwave-assisted and conventional synthesis of metal (Zn, Ni, Cu and Co) phthalocyanines **6–9**. These phthalocyanines display good solubility in common organic solvents such as DMSO, DMF, $CHCl_3$, THF, CH_2Cl_2 and CH_3CN.

---

* Corresponding author. Tel.: +98 861 4173400; fax: +98 861 4173406.
E-mail address: a-karimi@araku.ac.ir (A.R. Karimi).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.10.122



i : DMF, MW 350 W, 2 min.
ii : DMF, K_2CO_3, N_2, 25 °C, 24 h
iii : DMAE, MX, MW 350 W, 10 min
iv: DMAE, MX, reflux, N_2, 24 h

6-9	M	MX
6	Co	$CoCl_2$
7	Cu	CuCl
8	Ni	$NiCl_2$
9	Zn	$Zn(OAc)_2$

Scheme 1. Synthesis of metallophthalocyanines **6**–**9**.

The preparation of substituted phthalonitrile derivatives is an important step in phthalocyanine synthesis. Nucleophilic aromatic substitution of the nitro group in 4-nitrophthalocyanine is a useful route to many tetrasubstituted phthalocyanines owing to the relative ease of this displacement. Using this method, suitable substituents can be introduced into the periphery of the final phthalocyanine to enhance solubility. The synthetic route to the compounds presented in this work is shown in Scheme 1.

Compound **3** was prepared via the one-pot pseudo three-component condensation of dimedone (**1**) and *p*-hydroxybenzaldehyde (**2**) using PPA–SiO_2 as the catalyst.[32] Dicyano compound **5** was obtained by base-catalyzed nucleophilic displacement of 4-nitrophthalonitrile **4** with 1,8-dioxo-octahydroxanthene **3**. The reaction was carried out at room temperature in anhydrous DMF with anhydrous K_2CO_3 as the base. Cyclotetramerization of dinitrile compound **5** in the presence of anhydrous metal salts [$CoCl_2$, CuCl, $NiCl_2$ and $Zn(OAc)_2$], gave the desired metallophthalocyanines **6–9** in 2-(dimethylamino)ethanol (DMAE) under microwave irradiation or via conventional heating. The products were precipitated by addition of ethanol and filtered. The residues were washed with ethanol and hot distilled water, respectively. Elemental analysis, IR, ^1H NMR, and UV–vis spectra confirmed the proposed structures of the synthesized componds.[33] Thermogravimetric analysis (TGA) was used for determining the thermal stability of these complexes.

In the IR spectrum, the formation of compound **3** was confirmed by the appearance of a new band at 3412 cm^{-1} related to the OH group. The disappearance of the OH band of 1,8-dioxo-octahydroxanthene **3** at 3412 cm^{-1} and the NO_2 band of 4-nitrophthalonitrile **4** at 1538 and 1355 cm^{-1}, and the appearance of a CN band at 2233 cm^{-1} indicated the formation of compound **5**. After conversion of **5** into phthalocyanines **6–9**, this sharp CN vibration was no longer present.

The ^1H NMR spectra were also in good agreement with the structures of the synthesized compounds. The spectrum of **5** exhibited aliphatic (–CH_3, –CH_3, –CH_2, –CH_2 and –CH) protons at δ 1.03, δ 1.14, δ 2.25, δ 2.51 and δ 4.81, as a singlet, singlet, ABq, broad singlet and singlet, respectively, and the aromatic protons in the low field region around δ 6.91–7.70 as doublets and doublet of doublets. ^1H NMR measurements **6** and **7** were precluded due to their paramagnetic nature. On the other hand, the ^1H NMR spectra were in good agreement with the structures of **8** and **9**. The aromatic protons appeared at δ 6.90–7.82 for **8** and at δ 7.01–9.10 for **9** while the aliphatic –CH signals were observed in the range δ 1.04–4.72 for **8** and at δ 0.90–4.67 for **9**.

The UV–vis spectral properties of Pcs have been of intrinsic interest since their inception. The spectra of MPc complexes consist of two strong absorption regions at 600–700 nm (Q band) and around 300–400 nm (Soret or B band). The UV–vis spectra of the phthalocyanines in chloroform are shown in Figure 1. The UV spectra of CoPc, NiPc, ZnPc and CuPc show single intense bands at 669, 670, 676, and 677 nm, respectively. There is also a shoulder at slightly higher energy for all the phthalocyanines. The weaker absorptions appear at 604, 604, 607, and 610 nm for CoPc, NiPc, ZnPc, and CuPc, respectively. This is typical of metal complexes of substituted and unsubstituted metallophthalocyanines with D_4h symmetry.[34] The B bands for CoPc, NiPc, ZnPc, and CuPc were observed at 238, 286; 238, 287; 237, 275, 348; 244 and 333 nm, respectively.

In this study, the aggregation behavior of the phthalocyanines (**8–9**) was investigated in different solvents (chloroform, dichloromethane, DMF, DMSO, and THF). While complex **9** did not show aggregation in these solvents, complex **8** showed aggregation in DMSO and minimal aggregation in DMF, as judged by the broadening of the Q band (Tables 1 and 2).

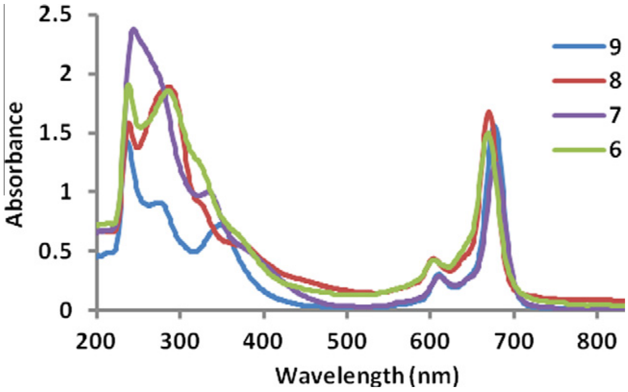


Figure 1. Absorption spectra of **6–9** in chloroform ($c = 2 \times 10^{-5}$).

Table 1
Absorption data for phthalocyanine **8** in different solvents ($c = 3 \times 10^{-5}$)

Solvent	λ_{max} (nm) ($\log\varepsilon$)
DMSO	673 (4.61), 622 (4.37), 282 (4.89)
DMF	670 (4.81), 606 (4.33), 281 (4.95)
CH_3Cl	669 (4.90), 604 (4.35), 287 (4.97), 241 (4.91)
THF	668 (4.85), 603 (4.32), 294 (4.89), 251 (4.83)
CH_2Cl_2	669 (4.85), 603 (4.31), 285 (4.93), 237 (4.91)

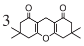
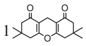
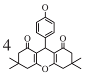
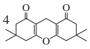
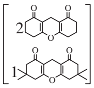
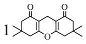
Table 2
Absorption data for phthalocyanines **9** in different solvents ($c = 3 \times 10^{-5}$)

Solvent	λ_{max} (nm) ($\log\varepsilon$)
DMSO	677 (4.76), 610 (4.17), 353 (4.52), 274 (4.69)
DMF	670 (4.81), 606 (4.33), 281 (4.95)
CH_3Cl	675 (4.96), 608 (4.33), 350 (4.73), 274 (4.81), 237 (4.85)
THF	671 (4.88), 606 (4.28), 374 (4.66), 289 (4.69), 250 (4.81)
CH_2Cl_2	679 (4.71), 611 (4.16), 351 (4.57), 237 (4.88)

The thermal properties of all the synthesized MPcs were analyzed by thermal gravimetric analysis (TGA) in the temperature range 30–900 °C under a nitrogen atmosphere with a heating rate of 10 °C/min. The initial weight loss up to 200 °C was related to the residual solvent which was typical of a TGA heating run. The ZnPc, CoPc and CuPc complexes exhibited some degradation steps whilst NiPc had one distinct degradation step. For all the complexes except CuPc, the xanthene moieties were sensitive to decomposition up to 900 °C and the aromatic rings were stable. CuPc from 240 up to 781 °C in two steps lost 70.77% of its mass which was attributed to the four xanthenes and four C_6H_4O groups. The groups which can be attributed to weight loss are listed in Table 3. The initial decomposition temperatures of the compounds are in the order: Ni > Cu > Co > Zn. No obvious correlation between the transition metal ions in the phthalocyanine rings and the initial decomposition temperature was observed.

In conclusion, the metallophthalocyanines **6–9** showed good solubility in common organic solvents (0.01 g in 5 mL of DMSO, DMF, $CHCl_3$, THF and CH_2Cl_2). Furthermore, for the conversion of dinitrile **5** into metallophthalocyanines microwave irradiation enhanced the yield and reduced the reaction times in comparison with conventional heating. While complex **9** did not show aggregation, complex **8** showed aggregation in DMSO and minimal aggregation in DMF. The Pcs reported in this work can be considered as efficient candidates for solution studies requiring the monomeric form of these materials as in the case of photosensitizers used in photodynamic therapy.

Table 3
Thermal analysis data for **6–9**

Pc	Temp of dec. °C	Mass loss (% found)	Probable (% calcd)	Nature of fragment lost
CoPc (**6**)	229–506	36	40.26	
	506–866	13.24	13.42	
CuPc (**7**)	240–781	70.77	71.87	
NiPc (**8**)	300–886	51	53.69	
ZnPc (**9**)	200–272	5.2	5.91	$8CH_3$
	288–540	33.90	34.53	
	540–869	13.81	13.38	

Acknowledgment

We gratefully acknowledge the financial support from the Research Council of Arak University.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.10.122.

References and notes

1. Torre, G.; Bottari, G.; Hahn, U.; Torres, T. *Struct. Bond.* **2010**, *135*, 1.
2. Makhseed, S.; Bumajdad, A.; Ghanem, B.; Msayib, K.; McKeown, N. B. *Tetrahedron Lett.* **2004**, *45*, 4865.
3. Yang, F.; Forrest, S. R. *J. Am. Chem. Soc.* **2008**, *2*, 1022.
4. Fischer, M. K. R.; Lopez-Duarte, I.; Wienk, M. M.; Martinez-Diaz, M. V.; Janssen, R. A. J.; Bauerle, P.; Torres, T. *J. Am. Chem. Soc.* **2009**, *131*, 8669.
5. Somani, P. R.; Radhakrishnan, S. *Mater. Chem. Phys.* **2002**, *77*, 117.
6. Clarke, M. J. *Coord. Chem. Rev.* **2002**, *232*, 69.
7. Hu, Y. Y.; Lai, G. Q.; Shen, Y. J.; Li, Y. F. *Dyes Pigments* **2005**, *66*, 49.
8. Cai, X.; Zhang, Y.; Qi, D.; Jiang, J. *J. Phys. Chem. A* **2009**, *113*, 2500.
9. Schlettwein, D.; Wöhrle, D.; Jaeger, N. I. *J. Electrochem. Soc.* **1989**, *136*, 2882.
10. Ding, X.; Shen, S.; Zhou, Q.; Xu, H. *Dyes Pigments* **1999**, *40*, 187.
11. Basova, T.; Kol'tsov, E.; Ray, A. K.; Hassan, A. K.; Gürek, A. G.; Ahsen, V. *Sens. Actuators, B* **2006**, *113*, 127.
12. De La Torre, G.; Vazquez, P.; Agullo-Lopez, F.; Torres, T. *J. Mater. Chem.* **1998**, *8*, 1671.
13. Leznoff, C. C.; Lever, A. B. P. In *Phthalocyanines, Properties and Applications*; VCH: New York, 1996; Vol. 4,
14. Cook, M. J.; McKeown, N. B.; Simmons, J. M.; Thomson, A. J.; Daniel, M. F.; Harrison, K. J.; Richardson, R. M.; Roser, S. J. *J. Mater. Chem.* **1991**, *1*, 121.
15. Kaliya, O. L.; Lukyanets, E. A.; Vorozhtsov, G. N. *J. Porphyrins Phthalocyanines* **1999**, *3*, 592.
16. Beck, A.; Mangold, K. M.; Hanack, M. *Chem. Ber.* **1991**, *124*, 2315.
17. (a) Ogunsipe, A.; Nyokong, T. *J. Photochem. Photobiol., A: Chem.* **2005**, *173*, 211; (b) Sylvain, I.; Zerrouki, R.; Granet, R.; Huang, Y. M.; Lagorce, J.-F.; Guilloton, M.; Blais, J.-C.; Krausz, P. *Bioorg. Med. Chem.* **2002**, *10*, 57.
18. Sharon, N.; Lis, H. *Science* **1989**, *246*, 227.
19. Hanack, M.; Knecht, S.; Polley, R. *Chem. Ber.* **1995**, *128*, 929.
20. Biyiklioğlu, Z.; Kantekin, H. *Polyhedron* **2008**, *27*, 1650.
21. Biyiklioğlu, Z.; Kantekin, H. *J. Organomet. Chem.* **2008**, *693*, 505.
22. Biyiklioğlu, Z.; Koca, A.; Kantekin, H. *Polyhedron* **2009**, *28*, 2171.
23. Poupelin, J. P.; Saint-Rut, G.; Foussard-Blanpin, O.; Narcisse, G.; Uchida-Ernouf, G.; Lacroix, R. *Eur. J. Med. Chem.* **1978**, *13*, 67.
24. Hideo, T. Jpn Tokkyo Koho JP 56005480, 1981; *Chem. Abstr.* **1981**, *95*, 80922b.
25. Lambert, R. W.; Martin, J. A.; Merrett, J. H.; Parkes, K. E. B.; Thomas, G. J. PCT Int. Appl. WO 9706178, 1997; *Chem. Abstr.* **1997**, *126*, 212377y.
26. Ion, R. M. *Prog. Catal.* **1997**, *2*, 55.
27. Saint-Ruf, G.; De, A.; Hieu, H. T. *Bull. Chim. Ther.* **1972**, *7*, 83.
28. Sirkecioglu, O.; Tulinli, N.; Akar, A. *J. Chem. Res. (S)* **1995**, 502.
29. Zhao, T. F.; Zhao, D. F.; Sun, X. S.; Cheng, L. B. *Chem. Ind. Eng.* **1998**, *49*, 515.
30. Ji, X. S.; Liu, Y.; Miao, Y.; Jin, T. *Chin. J. Pharm. Sci.* **1998**, *7*, 221.
31. Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250.
32. Kantevari, S.; Bantu, R.; Nagarapu, L. *J. Mol. Catal. A: Chem.* **2007**, *269*, 53.

33. *Preparation of 9-(4-hydroxyphenoxy)-3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8(5H,9H)-dione* (**3**): To a mixture of dimedone (**1**) (0.25 g, 1.7 mmol) and 4-hydroxybenzaldehyde (**2**) (0.11 g, 0.89 mmol) in DMF (2 mL), one drop of H_2SO_4 was added. The mixture was irradiated at 350 W for 2 min. After cooling to room temperature, EtOH (5 mL) and H_2O (2 mL) were added. The resulting precipitate was filtered and washed with hot H_2O. Yield: 87%. Mp: 250–252 °C. IR (KBr) (ν_{max}, cm^{-1}): 3412, 3024, 2962, 2931, 2899, 2872, 1662, 1614, 1514, 1450, 1359, 1246, 1201, 1003, 839. *Preparation of 4-[4-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)phenoxy] phthalonitrile* (**5**): 4-Nitrophthalonitrile (**4**) (0.11 g, 0.6 mmol) and compound **3** (0.22 g, 0.61 mmol) were dissolved in DMF (2 mL). Anhydrous K_2CO_3 (0.084 g, 0.61 mmol) was added and the mixture was stirred at room temperature for 24 h. Next, acetone (6 mL) and H_2O (2 mL) were added. The product was filtered and washed with hot H_2O. Yield: 80%, mp: 200–202 °C. IR (KBr) (ν_{max}, cm^{-1}): 3041, 2960, 2872, 2233, 1662, 1595, 1491, 1361, 1257, 1195, 1136, 1001, 841. ^{1}H NMR (DMSO-d_6, 300 MHz) δ_H: 1.03 (6H, s, $2CH_3$), 1.14 (6H, s, $2CH_3$), 2.19–2.32 (4H, ABq, $2CH_2$), 2.51 (4H, s, $2CH_2$), 4.81 (1H, s, CH), 6.91 (2H, d, J = 8.40 Hz, H_{arom}), 7.16 (1H, dd, J = 8.70 and 2.25 Hz, H_{arom}), 7.28 (1H, masked by the $CHCl_3$ signal), 7.40 (2H, d, J = 8.42 Hz, H_{arom}), 7.70 (1H, d, J = 8.70 Hz, H_{arom}). *Cobalt(II) phthalocyanine* (**6**): Method A: Compound **5** (0.10 g, 0.2 mmol) and anhydrous $CoCl_2$ (8.8 mg, 0.067 mmol) were added to 2-(dimethylamino)ethanol (DMAE) (2 mL). The mixture was irradiated at 350 W for 10 min and then cooled to room temperature. In the next step EtOH was added and the product was filtered under reduced pressure. Yield: 55%. IR (KBr) (ν_{max}, cm^{-1}): 2957, 2872, 1670, 1601, 1504, 1469, 1359, 1195, 1165, 1097, 856. UV/vis ($CHCl_3$): λ_{max}/nm: 669, 604, 285, 238. Anal. Calcd for $C_{124}H_{112}CoN_8O_{16}$: C, 73.40; H, 5.56; N, 5.52. Found: C, 73.00; H; 5.69; N; 5.80. Method B: A mixture of compound **5** (0.10 g, 0.2 mmol), anhydrous $CoCl_2$ (8.8 mg, 0.067 mmol) and DMAE (10 ml) was refluxed under a nitrogen atmosphere for 24 h. The above purification method was applied to this material. Yield: 45%.
34. Riesen, A.; Zehnder, M.; Kaden, T. A. *Helv. Chim. Acta* **1986**, *69*, 2074.