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Design of Novel Binuclear Phthalocyanines formed by Dioxyphenyl Bridges: Synthesis and Investigation of Thermal and Antioxidant Properties

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Abstract. 4,4′-(1,4-Phenylenebis(oxy)diphthalonitrile was synthesized by reaction of hydroquinone with 4-nitrophthalonitrile. Binuclear metallophthalocyanines **2–4** were obtained by the reaction between 4,4′-(1,4-phenylenebis(oxy)diphthalonitrile and 4-(benzo [d] [1,3] dioxol-5-ylmethoxy)phthalonitrile in the presence of metal salts. These new compounds were characterized by using elemental analysis, FTIR, ^{1}H-NMR and UV/Vis spectroscopic data. Thermal properties of phthalocyanines **2-4** were investigated by TG and DTA. In addition, antioxidant properties of compounds **II**, **3** and **4** were investigated. Their radical-scavenging capacity and chelating effects was fully studied. The maximum 1,1-diphenyl-2-picrylhydrazyl radicals (DPPH) were obtained from compound **3**. Chelating effects on ferrous ions were 91.6 % at concentration of 100 mg L^{-1} with compound **II**.

1 Introduction

Phthalocyanines have been considered as synthetic porphyrin analogs. They possess a conjugated system of π-electrons and exhibit the ability to chelate metal ions in the center of the ring. Many of properties of phthalocyanines are highly dependent on the extent of intermolecular π-π stacking interactions between the planar faces of the macrocycles. Phthalocyanines and related derivatives have been widespread applications in various areas including chemical sensors,[1] non-linear optic devices,[2,3] optical recording media,[4] semi-conductors,[5] dyes and pigments,[6] catalysts,[7] electrochromic devices,[8] photo chromic materials,[9] photosensitizers for photodynamic therapy,[10–12] liquid crystals,[13] and promising H_2 adsorbents.[14,15]

Recently, attention has been attracted to phthalocyanines containing two metal atoms, due to their interesting properties. Binuclear and multi nuclear phthalocyanine derivatives have been reported in the literature.[16–20] It is well known that antioxidants reduce the risk for chronic diseases such as cancer and heart disease. Researches focused on the elucidation of the antioxidant and therapeutic properties of new phthalocyanine compounds have been continuously performed by research groups This is the reason that the search for selective methods of synthesizing binuclear phthalocyanines with various structures currently attracts special attention. The presence of binuclear metal in the same molecule may provide additional features such as increased solubility and reactivity. Herein, we reported the synthesis, thermal stability and antioxidant properties of binuclear phthalocyanines carrying six benzo [d] [1,3] dioxol-5-ylmethoxy groups.

2 Experimental Section

2.1 General

4-(benzo [d] [1,3] dioxol-5-ylmethoxy)phthalonitrile (**II**) was prepared according to the literature procedure.[21] All chemicals used were reagent grade. The solvents were purified according to standard procedure and stored over molecular sieves (4 Å).[22] All reactions were carried out under dry nitrogen atmosphere unless otherwise noted. Melting points were measured on an electrothermal apparatus. Electronic spectra were recorded with a Hitachi U-2900 Spectrophotometer. Routine IR spectra were recorded with a Thermo Scientific FTIR (ATR sampling accessory) spectrophotometer. Elemental analyses results were found in good agreement with calculated values. ^{1}H NMR spectra were recorded with a Bruker 300 MHz spectrometer in DMSO; chemical shifts were reported (δ) relative to Me_4Si as an internal standard. Thermal experimental was performed with a SETARAM TG/DTA/DSC-16 instrument.

2.2 Synthesis of Compound 1

A mixture of hydroquinone (0.55 g, 5 mmol) and 4-nitrophthalonitrile (1.73 g, 10 mmol) in dimethylformamide (DMF) (20 mL) was stirred under nitrogen. K_2CO_3 (5 g, 36 mmol) was added into the mixture over a period of 2 h. The reaction mixture was stirred under nitrogen at room temperature for 24 h. Afterwards, the reaction mixture was poured into water (200 mL) and stirred. The precipitate was filtered and washed with water. Yield: 1.5 g (83 %). The compound is soluble in DMF, dimethyl sulfoxide, hot ethyl acetate and butanol. Mp: 260 °C. **^{1}H NMR** (300 MHz, [D6]DMSO): δ = 8.15 (2H, d, Ar-H), 7.80 (2H, d, Ar-H), 7.54 (2H, dd, Ar-H), 7.40 (4H, s, Ar-H) ppm. **IR:**

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υ = 3076, 2232, 1595, 1500, 1481, 1284, 1 243, 1191 cm^{-1}. Anal calculated for $C_{22}H_{10}N_4O_2$: C, 72.92; H, 2.78; N, 15.46 %, found C, 72.83; H, 2.81; N, 15.35 %.

2.3 Synthesis of Compound 2

Compound **1** (0.091 g, 0.25 mmol), 4-(benzo [d] [1,3] dioxol-5-ylmethoxy)phthalonitrile (0.209 g, 0.75 mmol), $ZnCl_2$ (0.020 g) and dry DMF (1.5 mL) were placed in a standard tube in the presence of DBU (0.05 mL) under nitrogen and held at 160 °C for 20 h. After cooling to room temperature, the reaction mixture was precipitated by adding water. The product was washed with water, EtOH, acetone, and $CHCl_3$. DMF was added to the residue in order to dissolve the product. The reaction mixture was precipitated by water in the presence of $NaHCO_3$. The precipitate was filtered and washed with EtOH, butanol, and $CHCl_3$. The purity was analyzed by thin-layer chromatography. This compound is soluble in THF, DMF, and DMSO. Yield: 0.139 g (25 %). Calcd. for $C_{118}H_{70}N_{16}O_{20}Zn_2$: C, 65.53; H, 3.26; N, 10.36 %, found C, 65.66; H, 3.33; N, 10.41 %. **^{1}H NMR** (300 MHz, [D6]DMSO): δ = 8.05–6.95 broad (Ar-H), and aliphatic protons at 6.04 (OCH_2O) and 5.15 (CH_2O) ppm. **IR:** υ = 3066, 2884, 1604, 1485, 1442, 1216, 1035 cm^{-1}. **UV/Vis** (DMF): λ_{max} (log ε): 684 (5.23), 618 (4.71), 352 (5.13) nm.

2.4 Synthesis of Compound 3

Compound **1** (0.091 g, 0.25 mmol), 4-(benzo [d] [1,3] dioxol-5-ylmethoxy)phthalonitrile (0.209 g, 0.75 mmol), $Co(CH_3COO)_2$ (0.020 g) and dry DMF (1.5 mL) were placed in a standard tube in the presence of DBU (0.05 mL) under nitrogen and held at 160 °C for 20 h. After cooling to room temperature, the reaction mixture was precipitated by adding water. The product was washed with water, EtOH, acetone, and $CHCl_3$. The purity was analyzed by thin-layer chromatography. Compound **3** is soluble in THF, DMF, and DMSO. Yield: 0.125 g (23 %). Calcd. for $C_{118}H_{70}N_{16}O_{20}Co_2$: C, 65.93; H, 3.28; N, 10.42 %, found C, 65.81; H, 3.35; N, 10. 38 %. **IR:** υ = 3063, 2956, 1607, 1499, 1488 1441, 1405, 1362, 1242, 1222, 1190, 1096, 1036, 928, 811, 753 cm^{-1}. **UV/Vis** (DMF): λ_{max} (log ε): 670 (5.04), 340 (5.09) nm.

2.5 Synthesis of Compound 4

Compound **1** (0.091 g, 0.25 mmol), 4-(benzo [d] [1,3] dioxol-5-ylmethoxy)phthalonitrile (0.209 g, 0.75 mmol), $Cu(CH_3COO)_2$ (0.020 g) and dry DMF (1.5 mL) were placed in a standard tube in the presence of DBU (0.05 mL) under nitrogen and held at 160 °C for 20 h. After cooling to room temperature, the reaction mixture was precipitated by adding water. The product was washed with water, EtOH, acetone, and $CHCl_3$. The purity was analyzed by thin-layer chromatography. The compound is soluble in THF, DMF, and DMSO. Yield: 0.119 g (21 %). Calcd. for $C_{118}H_{70}N_{16}O_{20}Cu_2$: C, 65.64; H, 3.27; N, 10.38 %, found C, 65.73; H, 3.24; N, 10.43 %. **IR:** υ = 3069, 2954, 1606, 1486, 1441, 1230, 1190, 1156, 1036, 929, 810, 746 cm^{-1}. **UV/Vis** (DMF): λ_{max} (log ε): 683 (5.07), 618 (4.39), 350 (4.92) nm.

2.6 Biological Assay

1,1-Diphenyl-2-picryl-hydrazyl (DPPH), ferrous chloride, 3-(2-pyridyl)-5,6-bis(4-phenyl-sulfonic acid)-1,2,4-triazine (Ferrozine), butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and Dimethylformamide (DMF) were purchased from Sigma (Sigma-Aldrich GmbH, Sternheim, Germany).

2.7 1, 1-Diphenyl-2-picrylhydrazyl (DPPH) Radical-Scavenging Activity

In this experiment, the scavenging ability of the free and metal bounded compounds on 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical was performed according to an earlier reported method[23] with some modifications. Different concentrations (5-100 mg/L) of the compounds (0.5 mL) were mixed with a DMF solution (2 mL) of DPPH radicals. The mixture was shaken vigorously and then left to stand in the dark for 30 min. The inhibition of the DPPH radical was determined by spectrophotometer at 517 nm. The DPPH radical scavenging activity (%) was calculated by the following equation:

Radical scavenging activity (%) = $(1 - A_{sample}/A_{control}) \times 100$,

Where A_{sample} is the absorbance in the presence of sample and $A_{control}$ is the absorbance in the absence of sample, respectively. BHA and BHT were used as standards.[23]

2.8 Chelating Effects on Ferrous Ions

Chelating effects of DMF solution of compounds was determined according to an earlier reported method.[24] Briefly, an amount (0.5 mL) of a DMF solution of the compounds with varied concentrations (5–100 $mg\,L^{-1}$) was incubated with a $FeCl_2$ solution (25 µL, 2 mM). Afterwards, the reaction was initiated by addition of ferrozine (100 µL, 5 mM) and was left standing for 10 min at room temperature. Metal chelating activity was determined by spectrophotometer at 562 nm. The percentage inhibition of the ferrozine–Fe^{2+} complex formation was calculated as follows:

Chelating ability (%) = $(A_{blank} - A_{sample})/A_{blank} \times 100$;

Where A_{blank} is the absorbance of the control reaction (containing only $FeCl_2$ and ferrozine), and A_{sample} is the absorbance of the compounds/reference. EDTA was used as a positive control.[24]

3 Results and Discussion

3.1 Synthesis and Characterization

4,4′-(1,4-Phenylenebis(oxy)diphthalonitrile **1** was obtained by the reaction between hydroquinone and 4-nitrophthalonitrile in dry DMF in the presence of dry K_2CO_3 and at room temperature. Binuclear metallophthalocyanines **2–4** were obtained from 4,4′-(1,4-Phenylenebis(oxy)diphthalonitrile **1** and 4-(benzo [d] [1,3] dioxol-5-ylmethoxy)phthalonitrile (1:3) and corresponding anhydrous metal salts $ZnCl_2$, Co $(CH_3COO)_2$, Cu $(CH_3COO)_2$ in the presence of N_2 atmosphere. The route for synthesis of compounds **1–4** was shown in Scheme 1. Characterization of the compounds contain a combination of methods, including elemental analysis, IR, ^{1}H NMR and UV/Vis spectra confirmed the proposed structures of the compounds. The thermal properties of phthalocyanines **2–4** were investigated by thermo gravimetric analysis.

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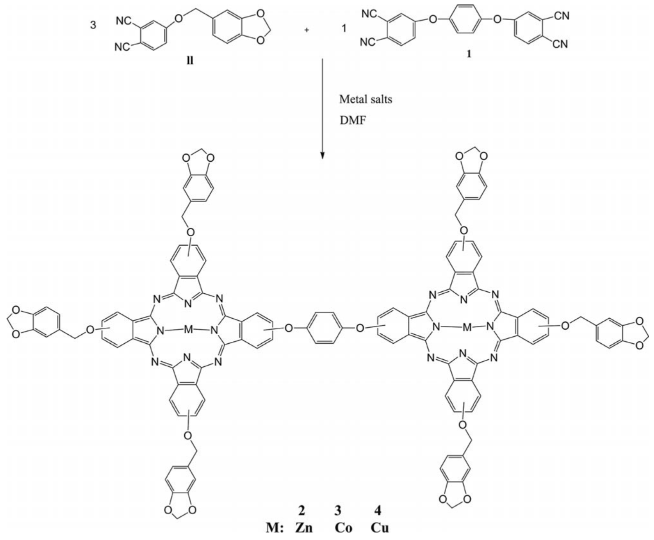

Scheme 1. Synthesis of compounds **1–4**.

In the IR spectrum of **1** the disappearance of NO_2 and OH stretching, along with the appearance of new bands at 2232, 1595 and 1243 cm^{-1} arising from $C\equiv N$, $C=C$ and Ar–O–Ar groups, respectively. They are in agreement with the proposed structure. After conversion of the 4-(benzo [d] [1,3] dioxol–5-ylmethoxy)phthalonitrile and tetranitrile compound **1** into phthalocyanine **2** the band of the characteristic vibration of $C\equiv N$ at 2232 cm^{-1} disappeared. For phthalocyanines **3** and **4** similar bands were observed (Ar at 3066 cm^{-1}, CH_2 at 2884 cm^{-1}, Ar–O–Ar bands at 1216 cm^{-1}, $C=C$ (in phenyl rings) bands at 1604 cm^{-1} and disappeared $C\equiv N$ bands at 2232).

In the ^{1}H NMR spectrum of compound **1** in [D$_6$]DMSO the signal of the aromatic protons appears at 8.15–7.40 (Ar–H) (Figure 1). In the ^{1}H NMR spectrum of compound **2** in [D$_6$]DMSO, the aromatic proton signals appear at 8.05–6.95 ppm (Ar–H) and aliphatic proton peaks at 6.04 (OCH_2O) and 5.15 (CH_2O). A common feature of the ^{1}H NMR spectrum of the compound **2** are the broad absorptions probably caused by aggregation of the phthalocyanine, which is frequently encountered at the concentrations used for NMR spectroscopic measurements. All the analytical and spectral data are consistent with the predicted structures. Elemental analyses corresponded closely with the values calculated for **1–4**.

The UV/Vis spectra of the phthalocyanines **2–4** in DMF showed characteristic Q band absorptions between 684–670 nm, which were attributed to the π-π^* transition from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) of the Pc ring. The other bands (B) in UV region at 340–352 nm were observed due to transition from the deeper π levels to the LUMO.The absorption spectra of **2–4** in DMF is shown in Figure 2. Indeed *Bayo* et al have reported that in the binuclear species the π system is not delocalized on the whole of both phthalocyanine cycles, which explain the nil movement of the Q band toward red.[25]

Thermogravimetric (TG) analyses of the phthalocyanine complexes were carried out in air and nitrogen atmosphere.

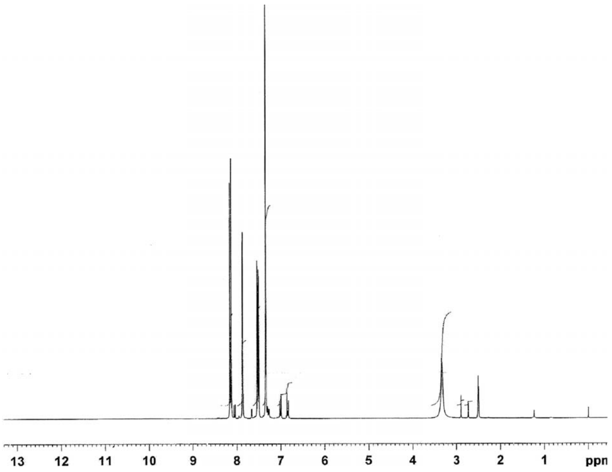

Figure 1. The ^{1}H NMR spectrum of compound **1**.

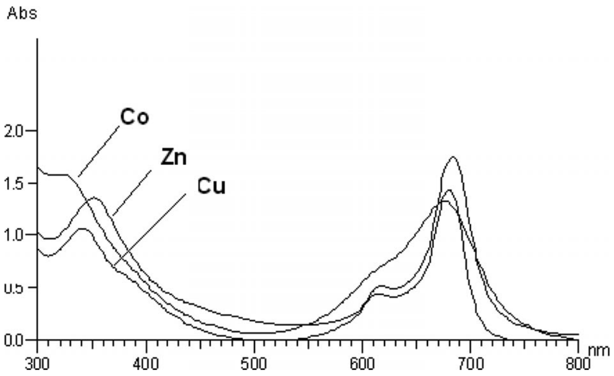

Figure 2. UV/Vis spectra of **2–4** in DMF.

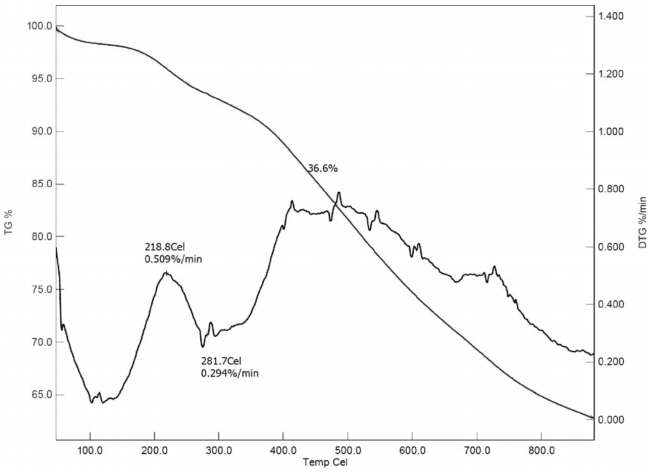

Figure 3. TG/DTA curves of compound **2**.

After initial loss of moisture at 100–130 °C, the loss of weight at major decomposition temperature was 36 % for **2**, 53 % for **3** and 54 % for **4** (Figure 3, Figure 4, Figure 5). The residues remaining after thermal decomposition correspond to the metal oxides. The observed thermal stability of metallo phthalocyanines in air was in the order of $2>3>4$. This study revealed that these new phthalocyanines **2–4** can serve good thermal stability.

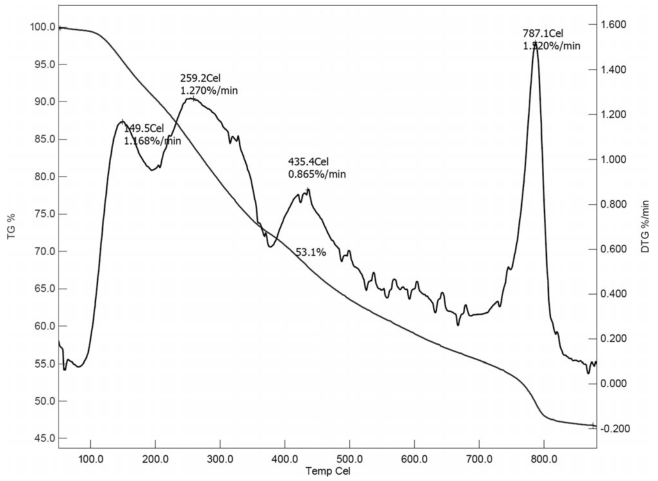

Figure 4. TG/DTA curves of compound **3**.

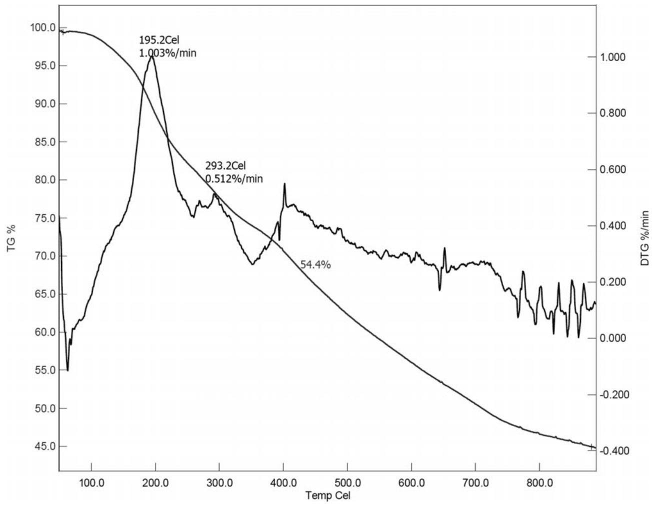

Figure 5. TG/DTA curves of compound **4**.

3.2 DPPH Radical-Scavenging Activity

The model of scavenging the stable DPPH$^{\cdot}$ radical is a method to interpret antioxidant activities in short time to compare with the other methods. The impact of antioxidants on DPPH radical scavenging was showed as a result of their hydrogen donating ability.[26] Figure 6 shows the effects of the scavenging ability of the free and metal bounded compounds on DPPH radical. From those compounds a maximum DPPH radical-scavenging activity was obtained from **3**. The DPPH radical-scavenging activity of **3** was 76.7 % and 77.7 % at concentrations of 25 and 50 mg L^{-1}, respectively. Compounds **II** and **4** did not show significant DPPH radical-scavenging activity. BHA and BHT showed higher DPPH scavenging activity than all studied compounds and the maximum DPPH radical scavenging activities were found to be 93.4 % and 92.8 at a concentration of 100 mg mL^{-1}, respectively.

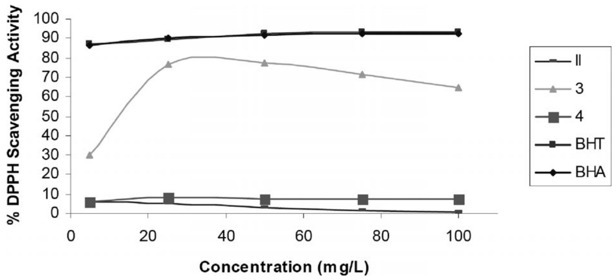

Figure 6. Radical-scavenging activity on DPPH radicals (%) of the compounds.

3.3 Chelating Effects on Ferrous Ions

To examine the effect of the chelating activity of the compounds against Fe^{2+}, the chelating experiments were carried out at different concentrations (5, 25, 50, 75 and 100 mg L^{-1}). Results are shown in Figure 7. The chelating activity of **II** increased from 55.8 to 91.6 % with increasing concentration from 5 to 100 mg L^{-1}. whereas the chelating activities of the **3** and **4** decreased when the concentrations increased. The results revealed that the maximum chelating activities of **II**, **3** and **4** were 91.6, 78.5 and 75.8 %, at concentrations of 100, 5 and 25 mg L^{-1} respectively. EDTA showed the maximum chelating activity at all concentrations. As a result, at a concentration of **II** of 100 mg L^{-1} may be used instead of EDTA for chelating activity.

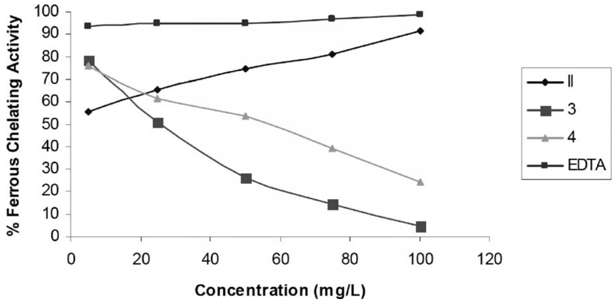

Figure 7. Chelating effect of compounds on ferrous ion.

4 Conclusion

A series of binuclear phthalocyanines carrying six benzo [d] [1,3] dioxol-5-ylmethoxy groups was synthesized. The compounds were characterized by elemental analyses, FTIR, ^{1}H-NMR and UV/Vis spectroscopy. The new metallo phthalocyanines were studied by thermogravimetry and differential thermal analysis. All of the three metallophthalocyanines have higher thermal stability, compared to the phthalocyanines substituted with different organic groups. With regard to the scavenging effect on hydroxy free radicals, compound **3** has the highest at concentration of 100 mg L^{-1}. On the other hand, compound **II** has shown a higher chelating activity on ferrous ions than compounds **3** and **4**. As a result, compounds **3** and **ll** show DPPH-scavenging activity and chelating activity.

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