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Hydroxylation of aromatic amines with dioxygen in photooxidation sensitized by substituted phthalocyanines

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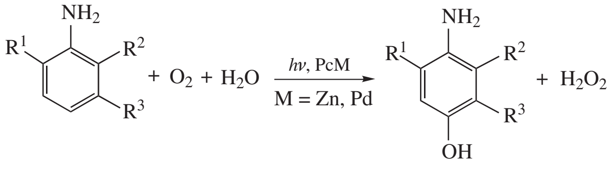
Photooxidation of aniline and its methyl and chloro derivatives with dioxygen sensitized by substituted zinc (PcZn) and palladium (PcPd) phthalocyanines in solution and on the carrier surface upon visible light irradiation affords selectively the corresponding *p*-aminophenols. Active and the most stable PcPd derivative adsorbed on Amberlite XAD 7HP provides conversion of 2,6-dimethylaniline with selectivity over 90% without the loss of sensitizer activity at least in 8 repeated cycles, the overall turnover number of the sensitizer being greater than 25,000.



5 examples

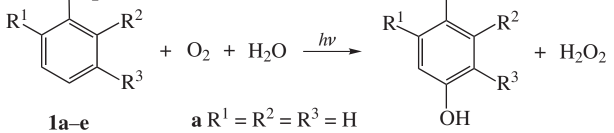
Keywords: photooxidation, singlet oxygen, arylamines, sensitizers, photocatalysis, hydroxylation, *p*-aminophenols, phthalocyanines.

p-Aminophenols are valuable compounds for fine organic synthesis in the interests of pharmaceutics, agricultural chemistry and dye technology. Modern methods for their preparation from chlorobenzene, phenol[1] or nitrobenzene[2] comprise several steps that require high temperatures, pressure and expensive Pt/Pd-catalysts. In particular, 4-amino-3,5-dimethylphenol is prepared from 3,5-dimethylphenol *via* nitration and reduction of thus obtained nitro intermediate.[3] The traditional stoichiometric oxidation of aniline with oxidants ($KHSO_5$, $K_2Cr_2O_7$, KIO_3) produces polyaniline. Catalytic oxidation of aniline and other arylamines using hydrogen peroxide and hydroperoxides occurs at the amino-group with the formation of nitroso, azoxy, nitro and azobenzenes.[4] The use of the Fenton reagent [hydrogen peroxide and iron(II) salts] and photo-Fenton process causes degradation of aniline[5] and *o*-toluidine.[6] Destruction of aniline molecules up to CO_2 occurs under sunlight irradiation of TiO_2 with formation of trace quantities of *p*-aminophenol[7] as intermediate product.

The oxidation of organic substrates with singlet oxygen is comprehensively reviewed.[8–12] However, its interaction with aromatic amines has not been systematically studied. In works where it is nevertheless mentioned,[13–15] the purposeful production of *p*-aminophenol is not even discussed. *p*-Aminophenol and 3,5-dimethylphenol[16] are formed in living organisms under the action of enzymes (a series of cytochrome P450) as metabolites of aniline and 2,6-dimethylaniline, respectively. In addition, 3,5-dimethylphenol is formed in liver as a metabolite of lidocaine, and it can serve as a marker of the liver function.[17] This allowed us to hope that in the absence of radical-forming (one-electron) oxidation systems, selective hydroxylation of aromatic amines with oxygen can become possible. These expectations have been accomplished in the present study.

Herein, we report an unusual hydroxylation of benzene ring of some anilines into the corresponding *p*-aminophenols under visible light irradiation of substrate solutions containing substituted PcM in both homogeneous and heterogenized forms (Scheme 1). These results were previously patented[18] and in part were presented at the conferences on catalysis.[19,20]

Under the assumption that singlet oxygen $^1O_2$ can be an effective oxidant in the photooxidation of aromatic amines, substituted phthalocyanines PcM (M = Zn, Pd) known as effective sensitizers of $^1O_2$ formation under the action of visible-range radiation were tested. Halogen 300 W lamp with a filter that cuts off light with $\lambda < 450$ nm or laser MRL 250 ($\lambda = 671$ nm) with output power of 150 mW or four 0.2 W LEDs ($\lambda = 664$ nm) were used as a light sources. The participation of $^1O_2$ in the photooxidation of amines with these sensitizers was confirmed by special experiments confirming acceleration of the process in D_2O compared to H_2O (since $^1O_2$ lifetime is 20 times longer in D_2O) and retardation upon NaN_3 ($^1O_2$ physical quencher) addition.

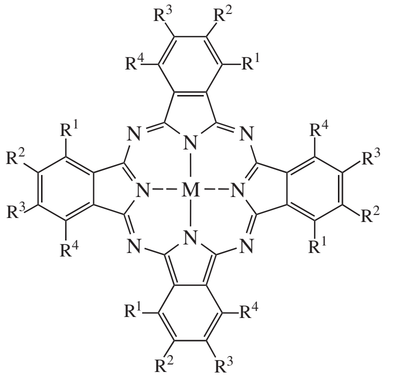


1a–e

2a–e

a $R^1 = R^2 = R^3 = H$
b $R^1 = Me, R^2 = R^3 = H$
c $R^1 = R^2 = H, R^3 = Me$
d $R^1 = R^2 = Me, R^3 = H$
e $R^1 = Cl, R^2 = R^3 = H$

Scheme 1 *Reagents and conditions*: PcM, MeCN–H_2O, 25 °C, visible light irradiation.



3a–h

a M = Zn, R^1 = $PhSO_2$, R^2 = R^4 = H, R^3 = Bu^t
b M = Zn, R^1 = $PhSO_2$, R^2 = R^3 = R^4 = H
c M = Zn, R^1 = R^3 = R^4 = H, R^2 = $PhSO_2$
d M = Zn, R^1 = PhS, R^2 = R^3 = R^4 = H
e M = Zn, R^1 = PhS, R^2 = R^4 = H, R^3 = Bu^t
f M = Zn, R^1 = R^3 = R^4 = H, R^2 = Bu^t
g M = Zn, R^1 = R^4 = H, R^2 = R^3 = C(O)NBu_2
h M = Pd, R^1 = R^4 = H, R^2 = R^3 = C(O)NBu_2

Synthesis of zinc phthalocyanines **3a**–**f**[21]and palladium ones **3g**,**h**[22] was reported previously.

Photooxidation of anilines **1a**–**e** in water-organic mixtures (H_2O–MeCN, H_2O–MeOH) was carried out in a glass reactor (35 mm in diameter) at continuous stirring and saturation with dioxygen. The reaction did not occur in anhydrous MeOH or MeCN. The reaction progress was monitored by seeding of sample aliquots at the certain time intervals. Conversion of substrate and yield of the products were measured by HPLC.[†]

Photooxidation products **2a**–**e** were identified by coincidence of their retention volumes and retention times with those of authentic samples purchased from Sigma-Aldrich. Compounds **2** were mostly the only products of the photooxidation. The structure of product **2d** was additionally confirmed by GC/MS.[‡] The mass spectrum of isolated compound **2d** contained a molecular ion peaks with *m/z* 136 $[M-H]^+$ and 107 $[M-2Me]^+$.

The influence of substituent (R) nature in R_4-PcZn on the sensitizer effectiveness was investigated on the example of photooxidation of substrate **1d** (Table 1). The selectivity of **2d** formation in the presence of **3a** exceeded 90%.

The substrate conversion was determined based on the sensitizer stability and was higher at greater electron-withdrawing properties of the substituents. In full compliance with these data, the highest conversions were achieved in the case of **3a**,**b** and the lowest ones with sensitizers containing donor substituents.

The effect of the nature of the central metal atom in PcM was defined by comparing the efficiencies of **3g** and **3h** bearing the same substituents under the same conditions ([**1d**] = 0.01 mol dm^{-3}, [PcM] = 0.25×10^{-5} mol dm^{-3}, MeCN–H_2O, 9 : 1, LEDs). The conversions of substrate **1d** upon 90 min irradiation with **3g** and **3h** were 56.8 and 96.3%, respectively. The higher activity of **3h** compared to its Zn analogue **3g** is determined not only by higher stability of **3h** (absence of degradation) but also, probably, by the higher quantum yield of $^1O_2$ for carbamoyl derivatives of PcPd than those of PcZn, 0.78±0.08[23] and 0.56,[24] respectively.

Table 1 Conversion of **1d** and selectivity towards **2d** in homogeneous photooxidation in the presence of some zinc phthalocyanines.[a]

Reaction characteristics	PcZn complex				
	3a	**3c**	**3d**	**3e**	**3f**
Conversion (%)	95	78	75	25[b]	20[b]
Selectivity (%)	> 90	70	50	-	-

[a] [**1d**] = 0.01 mol dm^{-3}, [PcZn] = 0.25×10^{-5} mol dm^{-3}, MeCN–H_2O (9:1), irradiation time 4 h, laser. [b] The reaction was complete after full solution bleaching (~50 min irradiation).

Taking into account the advantages of the use of heterogeneous sensitizers on homogeneous systems, the possibility of arylamine photooxidation has been studied in the presence of heterogenized PcM on a carrier. This possibility was not obvious because *a priori* the loss of immobilized phthalocyanine activity in the $^1O_2$ generation due to intermolecular interaction (aggregation) and the inevitable quenching of PcM excited triplet states seemed probable.

Heterogenization of phthalocyanines **3a**,**b**,**d**,**f**–**h** was carried out in two ways. First, equilibrium adsorption onto amino-modified silica gel (NH_2-SiO_2) or Amberlite XAD7HP (Amb) provided adsorbed heterogeneous sensitizers (AHSs). Second, covalently grafting of compounds **3b**,**d**,**e** to the NH_2 groups of the carrier afforded covalently grafted heterogenized sensitizers (GHSs). Heterogeneous sensitizers are characterized by the number of PcM moles per 1 g of the carrier (a, mol g^{-1}), while the substrate/PcM molar ratio (α) is used for characterization of the photooxidation process.

In fact, the heterogeneous process occurred with specific (per mole PcM) rate and selectivity very close to those in homogeneous systems. The regularities of the influence of both the nature of R in R_4-PcZn and the central metal atom in the PcM (M = Zn, Pd) on the efficiency of arylamine photooxidation also retained.

However, PcM aggregation in heterogeneous sensitizer surface layer occurs, and the part of active in $^1O_2$ generation monomeric and inactive aggregated PcM forms can be clearly monitored by the ratio between absorption band intensities of monomeric (Q-band at λ_{max} = 668–720 nm, A_1) and dimeric (609–654 nm, A_2) PcZn forms (Table 2) in UV-VIS spectra[§] of AHS (on NH_2-SiO_2) and GHS suspensions in glycerol.

The introduction of electron-withdrawing substituents, such as $PhSO_2$, into the PcZn molecule leads to decrease in the aggregation of the complexes on the NH_2-SiO_2 surface and, consequently, to their higher photoactivity in the oxidation (see Table 2). The higher values of **1a** conversion with GHS compared to that with AHS with the use of the same PcZn are also consistent with UV-VIS spectral data (see Table 2). Selectivity towards **2a** being 90% in the initial reaction period (up to 45 min) further reduces to 60–70% due to insufficient stability of the product under the reaction conditions.

Table 2 Characteristics of the AHS and GHS absorption spectra and conversion of **1a** in the presence of heterogeneous sensitizers.[a]

PcZn	AHS			GHS		
	λ_1/λ_2	A_1/A_2	Conversion (%)	λ_1/λ_2	A_1/A_2	Conversion (%)
3a	671/609	5.5	90	-	-	-
3b	668/630	2.4	45	669/620	3.6	76
3d	711/654	1.4	15	720/654	2.7	38
3f	677/635	2.1	14	684/640	3.0	59

[a] [**1a**] = 0.4 mmol dm^{-3}, 10% aq. MeOH (35 ml), irradiation time 2 h, α = 40, halogen lamp.

[†] An HP 1100 Agilent series chromatograph equipped with Zorbax EclipseXDB-C8 column (4.6 x 150 mm, 5 μm) and UV-detector (at 250 nm) was used [the mobile phase was H_2O–MeCN (40 : 60), a flow rate was 1 ml min^{-1}, internal standard was naphthalene].

[‡] GC/MS spectra were measured on a GC-MS Varian Saturn 2100 instrument.

[§] UV-visible absorption spectra were recorded on an HP-8453 UV-Vis spectrophotometer.

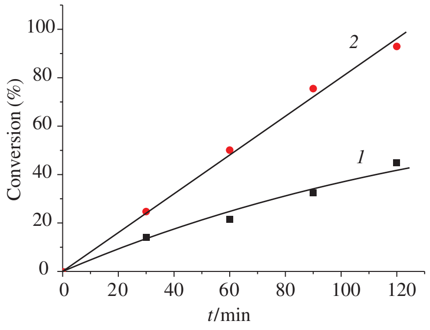


Figure 1 Conversion of **1d** in the presence of AHSs (*1*) **3g**/Amb and (*2*) **3h**/Amb. [**1d**] = 0.01 mol dm^{-3}, LEDs, MeCN–H_2O (1:1), α = 3950, selectivity towards **2d** > 90%.

Despite the more ordered structure of GHS-**3b** surface layer compared with AHS-**3b**, these Bu^t-containing materials are two times more active than their heterogenized analogues based on **3a**. Degradation of the active layer in AHS-**3a**/NH_2-SiO_2 is about 15%. AHS-**3a**/Amb obtained by equilibrium adsorption of **3a** on Amberlite is more stable.

The GHS–**3b** efficiency in photooxidation of **1d** (0.01 M, MeCN–H_2O, 9 : 1) was compared with the same performance of **3b** in the homogeneous process. In both cases, the conversion and selectivity amounted to 90% after 120 min irradiation by LEDs at α = 4000. This example confirms the aforesaid, namely, that the heterogenization of substituted PcZn does cause a noticeable decrease in its efficiency.

Complex **3h** adsorbed on Amb as well as in solution is more active and stable in **1d** photooxidation than its analogue **3g** (Figure 1).

The effect of solvent on **1a** photooxidation is mainly determined by the lifetimes of $^1O_2$, the main oxidizing particles, which in MeCN, MeOH and H_2O are 30, 7 and 3 μs,[25,26] respectively. Therefore, conversions of **1d** (0.01 M) in 5% mixtures of MeOH–H_2O and MeCN–H_2O after 60 min irradiation with LEDs in the presence of GHS-2 (substrate/**3b** molar ratio of 3800) are 43 and 95%, respectively, while the selectivities in all cases are 80–95%. The increase in the water fraction in MeCN–H_2O leads to a significant retardation of the reaction, while (as it was mentioned above) in anhydrous organic solvent the reaction does not occur. The similar effect of solvents is observed during the aniline photooxidation. In this case, the increase in water content in MeCN–H_2O from 50 to 90% leads not only to reaction deceleration, but also to a significant (4–5 times) drop in the selectivity for **2a** due to its further transformation (likely by the radical way) with the formation of colored compounds deposited on the heterogeneous sensitizer.

The prepared AHS-**3a**/Amb and GHS-**3b** sensitizers were used at least in three sequential reactions of **1a** and **1d** photooxidation, however heterogeneous sensitizer activity gradually decreased due to their insufficient stability. Sensitizer AHS-**3h**8/Amb showed significantly higher stability in cyclic and quasi continuous experiments, and it was used in eight repeated cycles of **1d** photooxidation without losing its activity.

Table 3 The k_{obs} values in photooxidation of substituted anilines.[a]

Substrate	$k_{\text{obs}}/10^2$ min^{-1}	Hammett σ-constants
1a	2.11	0
1b	3.70	$\sigma_p = -0.14$
1c	6.04	$\sigma_m = -0.06$
1d	5.05	
1e	0.411	$\sigma_p = 0.24$

[a] [**1a–e**] = 1 mmol dm^{-3}, AHS-**3a**/Amb, $a = 0.8\times10^{-6}$ mol g^{-1}, α = 1795, MeCN–H_2O (1:1), LEDs, product selectivity > 80%.

The overall turnover number exceeded 25,000 at the selectivity for **2d** being higher than 90%.

The effect of substituents in the substrate molecule was investigated for the series of *ortho*- and *meta*-methyl-substituted anilines, the observed rate constants of pseudo first order reaction are given in Table 3.

The effect of electronic properties of substituents in aniline molecules on k_{obs} values is consistent with the electrophilic nature of the oxidant, $^1O_2$.

In conclusion, substituted PcZn and PcPd in both homogeneous and heterogenized versions are effective sensitizers for photooxidation of anilines, the best sensitizers providing selective formation of *p*-aminophenols.

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