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Oxidative Coupling of N,N- and 2,6-Disubstituted Aniline Derivatives Mediated by Cerium(IV) Ions in Aqueous Perchloric Acid

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Summary. N,N- and 2,6-disubstituted anilines were oxidized by cerium(IV) perchlorate in aqueous solutions of perchloric acid to the corresponding derivatives of 4,4′-diphenoquinonediimine and N-phenyl-*p*-phenylenediimine in high yields. The type of the products obtained was determined by the properties of the substituents, by steric hindrance, and by the concentration of protons in the reaction mixtures. On the basis of experimental data and quantum mechanical calculations, which were performed using the semi-empirical AM1 method, a reaction mechanism was suggested.

Keywords. N,N- and 2,6-Disubstituted anilines; Cerium(IV) perchlorate; Products of oxidation; Mechanism; Quantum mechanical AM1 calculations.

Cer(IV)-Ionen-vermittelte oxidative Kupplung von N,N- und 2,6-disubstituierten Anilinderivaten in wäßriger Perchlorsäure

Zusammenfassung. N,N- und 2,6-disubstituierte Aniline wurden durch Cer(IV)perchlorat in wäßrigen Lösungen von Perchlorsäure in hohen Ausbeuten zu den ensprechenden Diphenodiiminen und N-Phenyl-*p*-phenylendiiminen oxidiert. Die Art der Produkte wird dabei durch die Eigenschaften des Substituenten, die sterische Hinderung und die Protonenkonzentration im Reaktionsmedium bestimmt. Auf der Basis von experimentellen Daten und quantenchemischen Rechnungen mit Hilfe der semiempirischen AM1-Methode wurde ein Reaktionsmechanismus vorgeschlagen.

Introduction

Investigations on the chemical and electrochemical oxidation of 2,6-disubstituted anilines have shown that the products of these one-electron reactions are derivatives of benzidine (**I**), 4-aminodiphenyleneamine (**II**), and hydrazobenzene (**III**) [1–16].

Experimental data show that type and constitution of the products depend strongly on the concentration of protons in the reaction medium and on the basic

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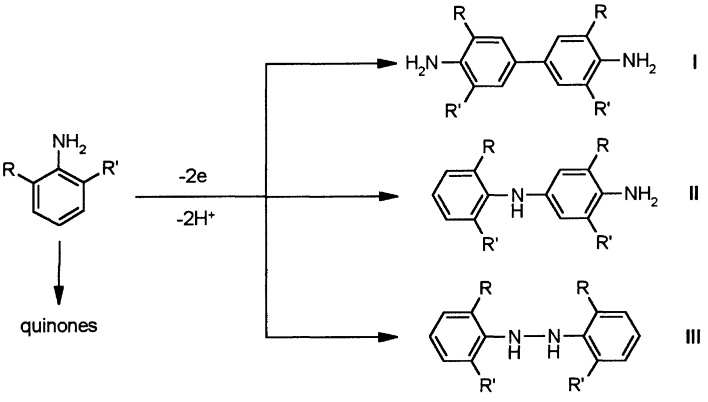
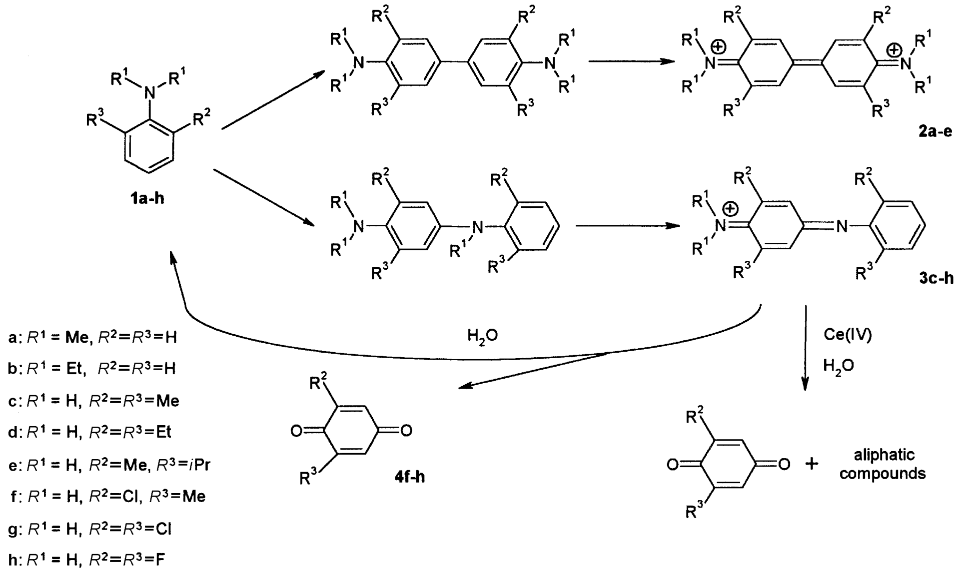


Scheme 1

properties of the oxidized aniline derivatives. Accordingly, benzidine derivatives are obtained from aniline precursors with relatively strong basic properties in media with high proton concentrations. Hydrazobenzene derivatives are obtained from aniline derivatives with less basic properties in basic or less acidic media [3, 4, 6, 11]. The mechanisms suggested in previous papers do not explain such dependencies. In this paper, using experimental results regarding the oxidation of 2,6-disubstituted anilines by cerium(IV) perchlorate and quantum mechanical calculations performed using the AM1 method, we attempt to explain the influence of the concentration of the protons in the reaction medium and of the basic properties of anilines on the type and constitution of the products obtained. On the other hand, the experimental results regarding the oxidation of N,N- and 2,6-disubstituted anilines by cerium(IV) ions indicate that it is possible to develop simple and fast methods for the preparation of the corresponding derivatives of 4,4′-diphenoquinonediimine and/or N-phenyl-*p*-phenylenediimine in high yields [13, 14].

Results and Discussion

When oxidizing N,N-dimethyl- (**1a**) and N,N-diethylaniline (**1b**) by cerium(IV) ions in aqueous solutions of perchloric acid, we found that the only products of these processes (which involve reduction of 2.0 mmol of oxidizing agent per 1.0 mmol of aniline derivative) were the corresponding N,N,N′,N′-tetraalkyldiphenoquinone-4,4′-diammonium perchlorates (**2a**, **b**). Moreover, we observed that the reaction velocity decreased considerably with increasing proton concentration. However, in media with a perchloric acid concentration of 4.0 *M*, in which the reactions proceeded very slowly, we observed neither a lowering of the formal potential of the Ce(IV)/Ce(III) system nor a colour change of the solution during the addition of N,N-dialkylanilines. This indicates that under such conditions the formation of a donor-acceptor complex of the oxidizer-reducer takes place only to a very small degree. What plays a crucial role in the formation of these complexes is the electron pair of the amino nitrogen atom. Such an effect was not observed during the reaction of cerium(IV) ions with 2,6-dimethyl- (**1c**), 2,6-diethyl- (**1d**),



Scheme 2

and 2-isopropyl-6-methyl-aniline (**1e**) with protonation constants three orders of magnitude lower than those of N,N-dialkylanilines. The oxidation of these anilines occurred almost immediately. In 0.4 *M* aqueous solutions of perchloric acid, **1c** and **1d** were oxidized almost quantitatively to **3c** and **3d**, and with higher concentrations of perchloric acid, the additional formation of **2c** and **2d** was observed. In the case of **1e**, a mixture of **2e** and **3e** is obtained irrespective of the reaction conditions. When the 2,6-disubstituted aniline derivatives with protonation constants $\log K < 2.0$, *e.g.* as 2-chloro-6-methyl- (**1f**), 2,6-dichloro- (**1g**), or 2,6-difluoro-aniline (**1h**), are oxidized by cerium(IV) ions, the corresponding N-phenyl-*p*-phenylenediimine derivatives (**3f–h**) are obtained irrespective of the proton concentration in the reaction media. Products **3f–h** partially dissolved in the reaction medium and underwent hydrolysis to the corresponding *p*-benzoquinone derivatives (**4f–h**) and substrates (**1f–h**). This caused an increase in the amount of reduced cerium(IV) ions by 1.0 mmol of **1f–h**, and in the case of **1h** the amount even equalled 2.8 mmol. The results are summarized in Scheme 2 and Table 1.

The results shown in Table 1 unequivocally indicate that the type and constitution of the products of the oxidation of anilines by one-electron oxidizing agents strongly depend on the proton concentration in the reaction medium, on the steric hindrance, and on the basic properties of the anilines – but in fact, the most crucial factors are the properties of the first products of their oxidation, *i.e.* cation radicals *CR*.

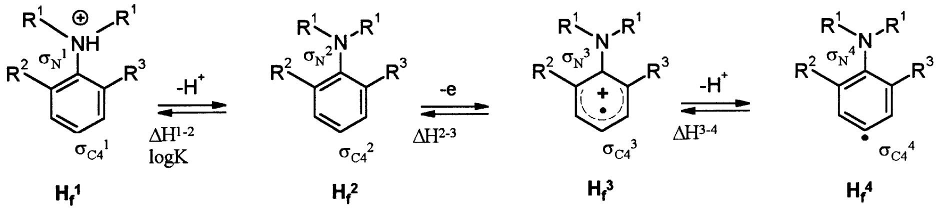
The cation radicals (*CR*) of 2,6-disubstituted anilines can undergo the reactions shown in Scheme 4.

According to the experimental results, the process $CR \rightarrow CR\mathrm{OH}$ does not take place. This is in agreement with the results obtained for the oxidation of 2,6-disubstituted phenols [17–19] which show that the hydroxylation process of the carbon atoms C4 of the cation radicals occurs only if charges on the C4 atoms are positive (>0.03). The process $R \rightarrow C$ is unlikely to occur either, because with the

Table 1. Oxidation of substituted anilines **1a–h** with Ce(IV) in H_2O or H_2O-acetonitrile (∗) solutions in room temperature; conversion rate: 100%

	Aniline	Molar ratio ox:red	Time (min)	$[HClO_4]$ $(mol \cdot dm^{-3})$	Product (%)[a]
1	**1a**	2.2±0.1	40	0.4	**2a** (>95)↓
2		2.1±0.1	140	4.0	**2a** (>95)[b]
3	**1b**	2.1±0.1	20	0.4	**2b** (>95)↓
4		2.2±0.1	50	4.0	**2b** (>95)[b]
5	**1c**	2.2±0.1	0	0.4	**3c** (>95)↓
6		2.1±0.1	0	4.0	**2c** (65)↓, **3c** (25)↓
7	**1d**	2.3±0.2	0	0.4	**3d** (>95)↓
8		2.1±0.1	0	4.0	**2d** (55)↓, **3d** (35)↓
9	**1e**	2.3±0.2	0	0.4	**2e** (40)↓, **3e** (50)↓
10		2.1±0.1	0	4.0	**2e** (60)↓, **3e** (30)↓
11	**1f**	2.3±0.1	0	0.4	**3f** (>95)↓
12		2.5±0.1	0	4.0	**3f** (70)↓, **4f** (20)
13*	**1g**	2.3±0.1	0	0.4	**3g** (80)↓, **4g** (10)
14		2.2±0.1	0	4.0	**3g** (85)↓, **4g** (5)
15	**1h**	2.4±0.2	0	0.4	**3h** (80)↓, **4h** (10)
16		2.8±0.2	0	4.0	**3h** (60)↓, **4h** (30)

[a] Yields based on the amount of aniline added; [b] from spectroscopic measurements; ↓: product precipitates during oxidation



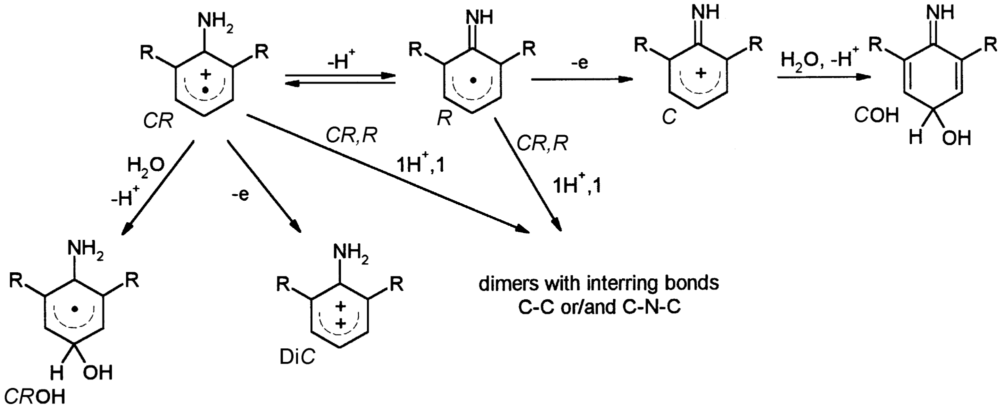
Scheme 3

charges on the carbon atoms C4, which are 0.14–0.16 for the corresponding cations *C*, it is difficult to explain the lack of the corresponding *p*-iminobenzoquinones among the reaction products.

The quantum mechanical calculations show that the process *CR*→Di*C* is not probable either. Some authors try to connect this process with the second peak observed only on CVA curves (at potentials about 0.2 V higher than the formation potential of *CR*) of N,N-dialkylanilines [11]. It seems that this peak is associated with one of the stages of the oxidation of one of the intermediate dimers, *e.g.* a cation radical dimer, to **2a**, **b**. This leads to the conclusion (Scheme 3, Table 3) that in the case of N,N-dialkylanilines one of the possible processes which the cation

Table 2. Calculated data for reaction presented in Scheme 3; H_f: heat of formation ($\mathrm{kJ \cdot mol^{-1}}$), ΔH: heat of reaction ($\mathrm{kJ \cdot mol^{-1}}$), σ_x^y: partial charge of atom x in form y

Substituents	σ_{N}^1	σ_{C4}^1	ΔH^{1-2}	σ_{N}^2	σ_{C4}^2	ΔH^{2-3}	σ_{N}^3	σ_{C4}^3	ΔH^{3-4}	σ_{N}^4	σ_{C4}^4
	H_{f}^1		$\log K$	H_{f}^2			H_{f}^3			H_{f}^4	
$R^1 = \mathrm{Me}$,	0.06	−0.07	212.9	−0.26	−0.17	732.2	−0.08	0.00	357.9	−0.25	−0.13
$R^2 = R^3 = \mathrm{H}$	764.4		5.03	130.0			862.2			372.8	
$R^1 = \mathrm{Et}$,	0.05	−0.07	209.8	−0.26	−0.17	726.3	−0.08	0.00	363.9	−0.25	−0.13
$R^2 = R^3 = \mathrm{H}$	719.9		6.53	82.4			808.7			325.3	
$R^1 = \mathrm{H}$,	0.00	−0.06	207.5	−0.32	−0.17	737.2	−0.21	0.01	285.7	−0.23	−0.11
$R^2 = R^3 = \mathrm{Me}$	664.9		3.70	25.1			762.3			200.7	
$R^1 = \mathrm{H}$,	0.00	−0.06	211.1	−0.33	−0.17	731.1	−0.22	0.01	289.5	−0.23	−0.11
$R^2 = R^3 = \mathrm{Et}$	621.3		3.80	−14.9			716.2			158.4	
$R^1 = \mathrm{H}$,	−0.01	−0.06	214.0	−0.33	−0.17	731.9	−0.21	0.01	290.3	−0.23	−0.11
$R^2 = \mathrm{Me}$, $R^3 = i\mathrm{Pr}$	625.6		3.75	−7.7			724.2			167.2	
$R^1 = \mathrm{H}$,	0.00	−0.05	192.5	−0.33	−0.17	759.9	−0.20	0.01	264.0	−0.21	−0.10
$R^2 = \mathrm{Cl}$, $R^3 = \mathrm{Me}$	679.3		1.97	24.5			784.4			201.1	
$R^1 = \mathrm{H}$,	0.00	−0.05	177.6	−0.34	−0.17	781.8	−0.20	0.01	247.8	−0.19	−0.10
$R^2 = R^3 = \mathrm{Cl}$	696.1		<2	26.4			808.2			208.7	
$R^1 = \mathrm{H}$,	0.01	−0.02	173.1	−0.32	−0.13	787.3	−0.18	0.03	235.2	−0.18	−0.08
$R^2 = R^3 = \mathrm{F}$	383.4		1.13	−290.8			496.5			−115.6	



Scheme 4

radicals *CR* can undergo is their recombination along with the formation of a C–C bond between the aromatic rings.

This process is determined by the steric effects. In some media, especially at low concentration of perchloric acid, the process with definitely the lowest enthalpy is possible: *CR*+**1a**, **b** → cation radical of the dimer with a C–C bond between the aromatic rings. The oxidation reaction enthalpies of the cation radicals

Table 3. Enthalpies of reactions leading to the formation of dimeric forms with inter-ring bonds (C–C or C–N–C) for anilines **1a–h** (kJ · mol^{-1})

Reaction	N,N-*DMA* (**1a**)		N,N-*DEA* (**1b**)		2,6-*DMA* (**1c**)		2,6-*DEA* (**1d**)		2-*i*P-6-*MA* (**1e**)		2-Cl-6-*MA* (**1f**)		2,6-*DClA* (**1g**)		2,6-*DFA* (**1h**)	
	C–C	C–N–C	C–C	C–N–C	C–C	C–N–C	C–C	C–N–C	C–C	C–N–C	C–C	C–N–C	C–C	C–N–C	C–C	C–N–C
CR+**1**H$^+$	232.8	324.9	209.5	314.0	236.4	298.5	232.3	298.5	234.3	293.9	245.2	301.1	254.4	305.1	284.9	317.7
CR+**1**	16.1	26.6	15.1	49.6	19.7	−18.1	20.9	−17.4	20.3	−18.7	23.1	−16.2	27.4	−12.7	43.4	−14.6
CR+*CR*	102.6	220.1	91.4	225.9	121.7	201.5	116.9	197.7	114.9	192.0	130.5	203.0	142.6	207.5	182.9	229.4
CR+*R*	–	–	–	–	−109.3	−159.4	−111.6	−157.3	−113.1	−162.3	−98.4	−158.4	−96.0	−162.8	−71.4	−143.2
R+**1**H$^+$	–	–	–	–	33.5	−17.3	30.4	−15.8	31.8	−19.8	37.7	−19.7	42.1	−24.5	59.2	−12.8
R+**1**	–	–	–	–	34.2	−22.0	31.3	−20.2	32.5	−24.4	32.9	−23.0	32.5	−27.4	40.8	−25.9
R+*R*	–	–	–	–	−104.2	−158.7	−108.6	−158.5	−110.9	−162.6	−97.6	−158.0	−99.6	−160.0	−81.2	−148.7

of the dimers are higher by about 81.0±5.0 kJ/mol than the enthalpies of the reactions **1a**, **b** → *CR*, and they can explain the presence of the second peaks on the voltammograms of the N,N-dialkylanilines. In the case when there is no steric hindrance (**1c**–**h**), the processes *CR*+**1** lead to the formation of the cation radical of the dimers with C–N–C bonding between the rings (Table 3). The reaction enthalpies of their oxidation to dications are higher by about 220.0 (**1c**) to 245.0 kJ/mol (**1h**) than the oxidation reaction enthalpies of the aniline molecules **1c**–**h**.

When 2,6-disubstituted anilines (**1f**–**h**), whose cation radicals should most readily undergo the process of deprotonation, are oxidized by cerium(IV) ions, the stages $CR \leftrightarrow R$, $\mathbf{1}H^+ \leftrightarrow \mathbf{1}$, and $R+CR$, $R+\mathbf{1}H^+$, $R+\mathbf{1}$ or $R+R$ lead to the formation of dimers with C–N–C bonds between the aromatic rings. The same situation is observed for anilines **1c**–**e** whose cation radicals have stronger basic properties (Scheme 3, Table 2) in media with lower proton concentrations. Such conclusions result from the analysis of the quantum mechanical calculations (Table 2 and 3). It follows that the enthalpies of reactions with participation of the radical, which lead to the formation of dimers with a C–N–C bond between aromatic rings, are lower than those of the C–C dimer formation; this is in agreement with the experiment.

Although the quantum mechanical calculations were performed for the gas phase, they are in very good agreement with the experimental data, suggesting that they can be used in this kind of experimental modelling.

The presented experimental results show that the use of cerium(IV) ions as a mediator of the oxidative coupling of aniline derivatives seems to provide a simple and economical method for the synthesis of **2a**–**e** or/and **3c**–**h**; methods for the electrochemical regeneration of the oxidizing agent in purified post-reaction solutions (filtration through active carbon) have been described [20].

Experimental

Melting points were determined with a melting points apparatus (Veb Nagema). UV/Vis spectra of the reaction mixtures with various molar concentration ratios of the reagents and the compounds obtained were recorded on a Philips PU9630 spectrophotometer. IR spectra were recorded on a Specord IR M-80, and NMR spectra on a Tesla BS 487 NMR spectrometer (60 MHz). The quantum mechanical calculations (AM1 [21], MOPAC 6 package) were carried out on a 486DX/50 computer with 16 MB RAM. The geometries of all analyzed structures were calculated using the PRECISE option. All internal coordinates were taken into account, and no assumptions as to the symmetry were made during the geometry optimization.

General procedure for the oxidation of N,N- and 2,6-disubstituted anilines **1a–h** *on the example of 2,6-dimethylaniline* (**1c**)

In 25 cm^3 of an aqueous solution of 0.8 *M* $HClO_4$ containing 0.3 *M* cerium(III) perchlorate, 2.5 mmol **1c** are dissolved. An aqueous solution of 0.8 *M* $HClO_4$ containing 0.24 *M* cerium(IV) perchlorate and 0.06 *M* cerium(III) perchlorate is added dropwise within 5 min at room temperature. The oxidation process occurs immediately. The moment when an excess of cerium(IV) ions appears (which indicates completeness of the reaction) is detected potentiometrically. The precipitate (almost ~ 100% yield) is filtrated, washed with aqueous 0.1 *M* $HClO_4$ and H_2O, and dried at 80°C to a solid mass.

Yield: 0.378 g N-(2,6-dimethylphenyl)-2′,6′-dimethyl-*p*-phenyleneimineamonium perchlorate (95%); m.p.: >600 K, UV (acetonitrile): $\lambda_{\max} = 292$ nm ($\varepsilon = 1.7 \times 10^4$); IR (KBr): $\nu = 2900$, 2880, 1660, 1600, 1590, 1210, 880, 785 cm^{-1}.

In the case of oxidation of **1a**,**b** which occurs more slowly, the amount of cerium(IV) ions necessary for a 100% conversion of the reducing agent was assessed experimentally, and those processes were followed until the cerium(IV) ions disappeared in the reaction mixture. In the case of **1c**, the mixture of the products was separated chromatographically on an Al_2O_3 column with CH_2Cl_2 as eluent. The remaining quinones in the post-reaction solutions (**4g–h**) were extracted with CCl_4.

The general procedure for the conversion of the anilines **1a–h** to 4,4′-diiminediphenoquinone and/or to N-phenyl-*p*-phenylenediimine derivatives in 4.0 *M* perchloric acid solution is similar; **2a**,**b** are dissolved in the reaction medium, and in the case of **1c–e**, the product mixtures are separated chromatographically on an Al_2O_3 column using CH_2Cl_2 as eluent. Quinones **4f–h** remaining in the solution are extracted with CCl_4.

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