Oxidative Deamination of Benzylamine by Electrogenerated Quinonoid Systems as Mimics of Amine Oxidoreductases Cofactors

Martine Largeron and Maurice-Bernard Fleury*

Laboratoire de Chimie Analytique et Electrochimie, UMR 8638 CNRS - Université René Descartes, Faculté des Sciences Pharmaceutiques et Biologiques, 4 Avenue de l'Observatoire, 75270 Paris Cedex 06, France

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The reactions of a new type of quinonoid system with benzylamine have been investigated in methanol in order to mimic the reactions occurring in the course of the enzymatic oxidation of amines by quinone cofactors. Under strictly anaerobic conditions, unstable quinonoid species $\mathbf{1_{ox}}$−$\mathbf{4_{ox}}$ have been selectively electrogenerated using anodic-controlled potential electrolysis. Thus, we have demonstrated that 3,4-quinone $\mathbf{1_{ox}}$ is incapable of deaminating benzylamine, while 3,4-iminoquinone species $\mathbf{3_{ox}}$ and $\mathbf{4_{ox}}$ act as efficient catalysts for the autorecycling oxidation of benzylamine: the reaction efficiency reached 64 turnovers. Additional mechanistic investigations reveal that the oxidation of benzylamine by our quinonoid model cofactors proceeds unambiguously via a transamination mechanism, as suggested for many enzymatic systems.

Introduction

Copper amine oxidases and bacterial amine dehydrogenases are enzymes containing a covalently bound quinone cofactor. These enzymes catalyze the oxidative deamination of a primary amine to produce the corresponding aldehyde and ammonia, concomitant with a two-electron reduction of dioxygen to hydrogen peroxide.[1] For instance, the active carbonyl cofactor used by mammalian copper amine oxidases is the quinone form (TPQ) of an active site 2,4,5-trihydroxyphenylalanine (TOPA) residue.[2] Likewise, the bacterial methylamine dehydrogenase has been shown to contain an active site tryptophan tryptophylquinone (TTQ). It is also well-known that pyrroloquinoline quinone (PQQ) behaves as a catalyst of amine oxidation, although PQQ is now recognized not to be the cofactor of amine oxidases.[3]

The design of artificial catalysts that begin to approach the reactivity of amine oxidoreductases cofactors is a challenging problem that could provide further insight into the function of the quinonoid cofactors in amine oxidation. Several synthetic models of naturally occurring quinones have been developed, and model reactions of amine oxidoreductases were examined.[4−9] In particular, substantial information has been obtained through catalytic aerobic deamination of benzylamine mediated by model cofactors, providing relevant insight into the enzyme catalysis. All the ionic mechanisms proposed so far involve a carbinolamine intermediate (Scheme 1). The most popular pathway is akin to the transamination reaction of pyridoxal phosphate with amino acids. This involves a tautomerization of the benzyliminoquinone species to the product Schiff base, which is then hydrolyzed to yield the aldehyde product and the aminophenol. The latter is autoxidized to the iminoquinone species, which is in turn hydrolyzed to the quinone and ammonia. The alternative is an addition−elimination mechanism proposed first for PQQ, in which the carbinolamine is directly converted into the quinol and benzylimine without generating an aminophenol intermediate.[5] The quinol is then autoxidized to regenerate the quinone. The observation of catalytic turnover did not permit a distinction between transamination and addition−elimination mechanisms. Furthermore, attempts to distinguish under anaerobic single-turnover between these two mechanisms through product analysis (aminophenol from transamination or quinol from addition−elimination) were thwarted by the occurrence of redox interchange reactions that scrambled the initial cofactor reduction product.[7] Nonetheless, in the case of the TPQ- and TTQ-catalyzed amine oxidation reaction, solutions were found to circumvent these problems, allowing the demonstration of a preferred transamination mechanism.[10,11]

In the course of our search for new neuroprotective agents, we recently reported the one-pot electrochemical syntheses of two novel classes of derivatives exhibiting potent neuroprotective activities close to that of standard α-tocopherol.[12,13] The key step consisted of the reactivity of the highly electrophilic electrogenerated 3,4-quinone $\mathbf{1_{ox}}$ (Chart 1) with amino alcohols. Depending on the nature of the condensed amino alcohols, attack at the 2-position led to 3-substituted-1,4-benzoxazin-8-one derivatives, while attack at the 3-position gave substituted

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Scheme 1

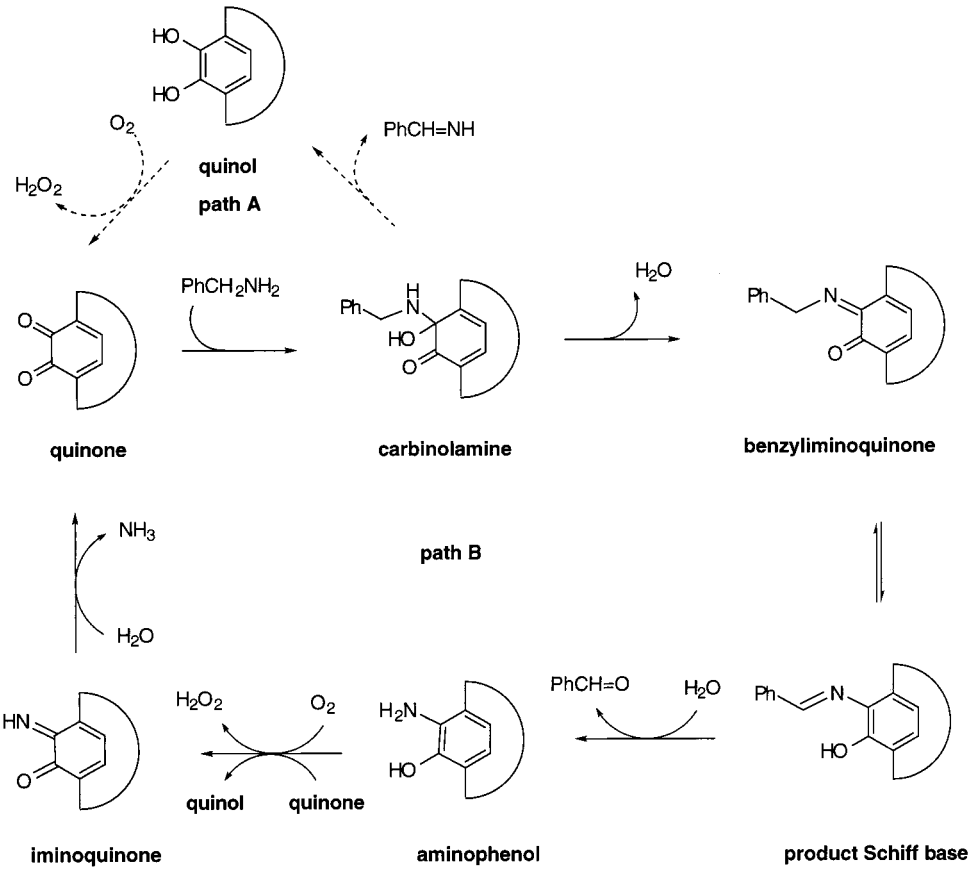
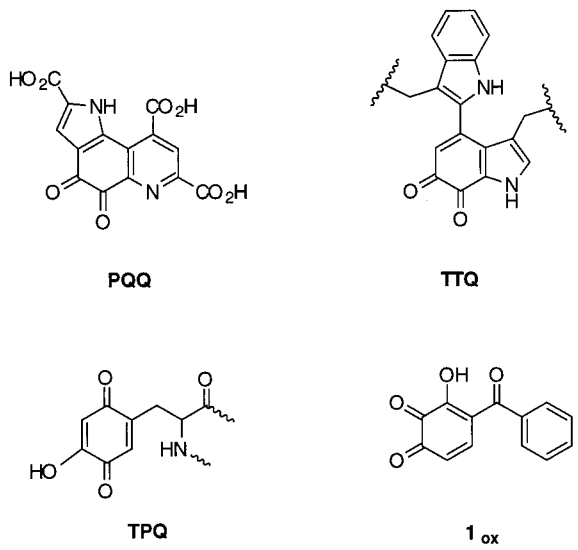


Chart 1



alkylaminophenols.[14,15] The C(3) reactivity of the electrogenerated 3,4-quinone $\mathbf{1_{ox}}$ was further extended to amines. At the outset, we believed that 3,4-quinone $\mathbf{1_{ox}}$ efficiently catalyzed the oxidative deamination of benzylamine, in deaerated CH_3OH, in a way reminiscent of that reported for PQQ, TTQ, and TPQ model cofactors.

This paper describes our efforts to provide an unambiguous conclusion based on an electrochemical approach. Through controlled potential electrolysis, whose advantages derive from the possibility of realizing selective oxidation by varying the potential applied to the working anode, we will endeavor to demonstrate that 3,4-quinone $\mathbf{1_{ox}}$ is incapable of deaminating benzylamine, while 3,4-iminoquinone species $\mathbf{3_{ox}}$ and $\mathbf{4_{ox}}$ act as a new type of efficient cofactor for the autorecycling oxidation of benzylamine.

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Results and Discussion

Reaction of the Electrogenerated 3,4-Quinone $\mathbf{1_{ox}}$ with Benzylamine. The cyclic voltammogram of compound $\mathbf{1_{red}}$ (2 mM), in deaerated CH_3OH containing $LiClO_4$ as the supporting electrolyte and an excess of benzylamine (100 mM) at a dropping mercury electrode, showed an oxidation peak Pa_1, due to a diffusion-controlled two-electron process, at − 140 mV vs SCE, the sweep rate v being 0.5 V s^{-1}. As can be seen in Figure 1 (curve a), a cathodic peak Pc_1 appeared on the reverse sweep, at − 190 mV vs SCE, illustrating the partial reversibility of the two-electron transfer that could be assigned to the 3,4-quinol $\mathbf{1_{red}}$/3,4-quinone $\mathbf{1_{ox}}$ redox couple. However, the redox potential E'^0 could not be accurately evaluated, under our experimental conditions, as the system (Pa_1, Pc_1) did not fulfill all the diagnostic criteria required for a reversible process, at least when v was ≤500 V s^{-1}: the ratio of the height of Pa_1 over that of Pc_1 never reached unity ($i_{Pc_1}/i_{Pa_1} \sim 0.8$) and the value of $E_{Pa_1} - E_{Pc_1}$ (E being the peak potential) was found to be higher than 30 mV. Note that, in the reverse sweep, a second reduction peak was recorded at a more negative potential (−1720 mV vs SCE), due to the irreversible two-electron reduction of the carbonyl group of the benzophen-

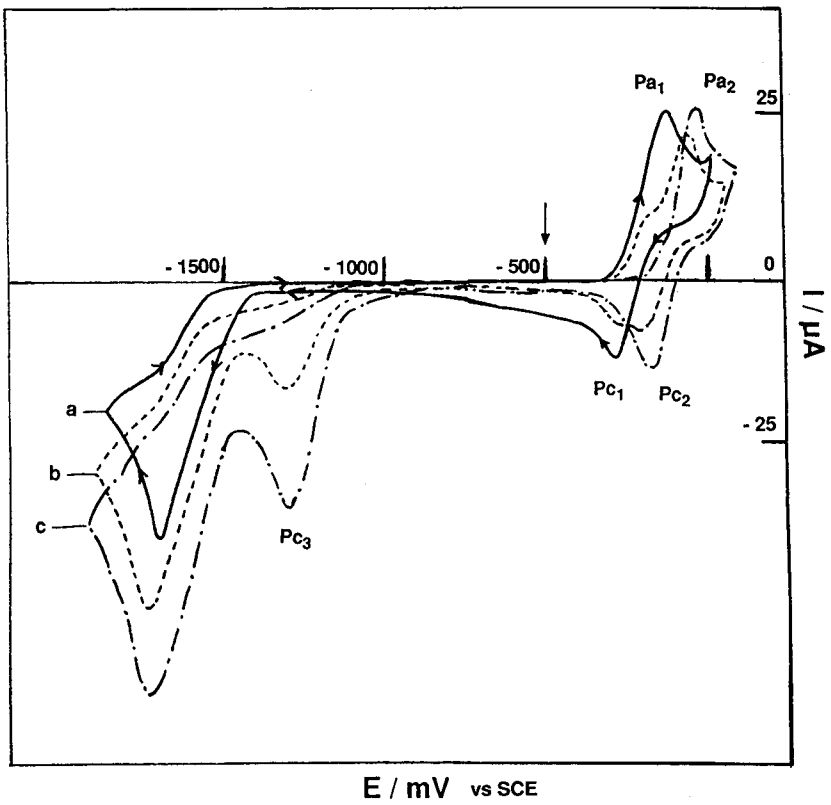
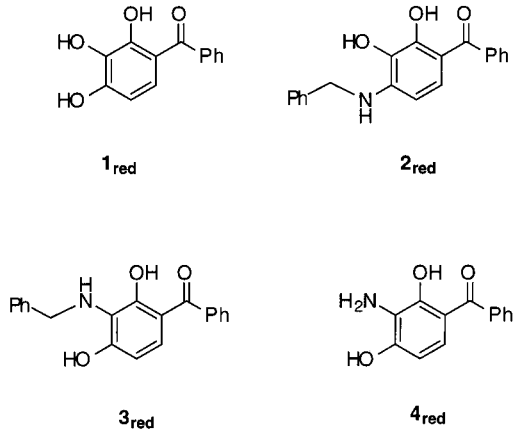


Figure 1. Progress of the cyclic voltammogram in the course of anodic controlled potential electrolysis of $\mathbf{1_{red}}$ (2 mM) at a mercury working electrode ($E = -180$ mV vs SCE), in deaerated CH_3OH containing $LiClO_4$ (200 mM) and benzylamine (100 mM). Curve a (—), before electrolysis; curve b (---), after consumption of 1 F mol^{-1} of substrate; curve c (-·-), after exhaustive electrolysis (2.1 F mol^{-1}). Arrowheads indicate the direction of the potential sweep; $v = 0.5$ V s^{-1}. The vertical arrow indicates the initial potential point.

Chart 2



one skeleton.[16] From the results of preparative electrolyses, two different anodic behaviors could be distinguished, depending on the selected potential.

When the controlled potential *E* of the mercury pool was fixed at −180 mV vs SCE, i.e., at a potential for which the quinol $\mathbf{1_{red}}$ could be oxidized exclusive of the reaction products $\mathbf{2_{red}}$-$\mathbf{4_{red}}$ (Chart 2), a coulometric value of 2.1 ± 0.1 was found for the number of electrons (n) involved in the oxidation of one molecule of $\mathbf{1_{red}}$. As the electrolysis proceeded, a decrease in the Pa_1 and Pc_1 intensities was observed, while a new system of peaks (Pa_2, Pc_2) developed at a 100 mV more positive potential, due to a partially reversible two-electron transfer. The lack of peak Pc_1 in the voltammogram of the oxidized solution clearly indicated that the electrochemical oxidation of $\mathbf{1_{red}}$ was followed by a chemical reaction involving the produced 3,4-quinone $\mathbf{1_{ox}}$. The height of Pa_2 was found to be roughly identical to that of the initial peak Pa_1, and the voltammogram of the oxidized solution exhibited a well-defined cathodic peak Pc_3 at −1300 mV vs SCE (Figure 1, curve c). This corresponded to the reduction of *N*-benzylidenebenzylamine ($PhCH{=}NCH_2$-Ph), as further confirmed after recording the cyclic voltammogram of an authentical sample. The progress of the electrolysis was simultaneously followed by monitoring the UV−vis absorption spectrum. After applying the potential E, no spectral changes were observed: the UV−vis spectrum shown by the oxidized solution was nearly identical with that of the monoanionic form of the quinol $\mathbf{1_{red}}$ with λ_{max} at 348 nm, suggesting a similarity in their chromophoric groups. The preparative electrolysis was stopped after consumption of 2.1 faraday (F) mol^{-1}, when a negligible value of the current was recorded, allowing the isolation of two benzylaminophenols, $\mathbf{2_{red}}$ (16% yield) and $\mathbf{3_{red}}$ (5% yield), as the minor products, along with aminophenol $\mathbf{4_{red}}$ (62% yield) as the major product (see Experimental Section). The structure of products $\mathbf{2_{red}}$−$\mathbf{4_{red}}$ justified, in the cyclic voltammogram of the oxidized solution, the presence of the system of peaks (Pa_2, Pc_2) that could be assigned to the oxidation/reduction of the aminophenol/iminoquinone redox couples. These structures were also consistent with the analogy existing between the UV−vis absorption spectrum of the oxidized solution and that of the starting quinol $\mathbf{1_{red}}$.

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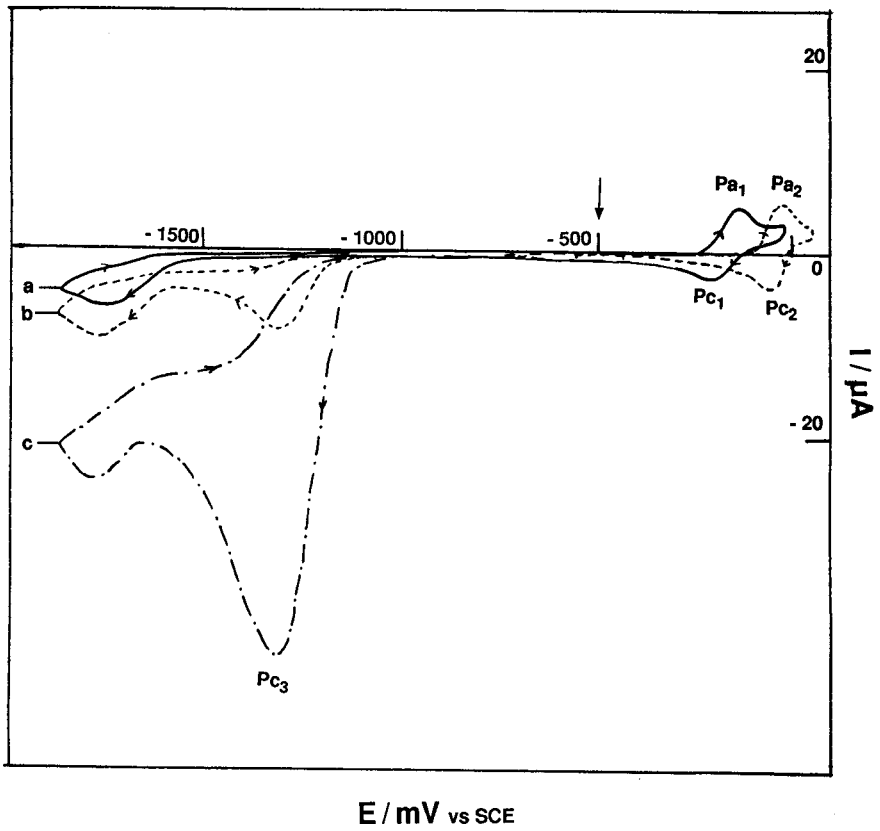

Figure 2. Progress of the cyclic voltammogram in the course of anodic controlled potential electrolysis of $\mathbf{1}_{red}$ (0.4mM) at a mercury working electrode ($E = +100$ mV vs SCE), in deaerated CH_3OH containing $LiClO_4$ (40 mM) and benzylamine (20 mM). Curve a (—), before electrolysis; curve b (---), after consumption of 2 F mol^{-1} of substrate; curve c (-·-), after consumption of 10 F mol^{-1}; curve c is superimposed on curve b in the anodic domain. Arrowheads indicate the direction of the potential sweep; $v = 0.5$ V s^{-1}. The vertical arrow indicates the initial potential point.

At that point it could be deduced that, when the controlled potential E of the mercury working electrode was fixed at −180 mV vs SCE, i.e. at a potential for which the quinol $\mathbf{1}_{red}$ could be electrochemically oxidized but the reaction products $\mathbf{2}_{red}$−$\mathbf{4}_{red}$ remained nonoxidizable, no catalytic behavior was observed. Accordingly, PhCH=NCH_2Ph (quantified in terms of benzaldehyde phenylhydrazone obtained upon workup of the oxidized solution with phenylhydrazine) was isolated in equimolar amount based on the initial concentration of $\mathbf{1}_{red}$.

These results demonstrated that, under our experimental conditions, the electrogenerated quinone $\mathbf{1}_{ox}$ was incapable of deaminating benzylamine, whatever the nature of the mechanism (path A or path B in Scheme 1). Consequently, the primary identification of $\mathbf{1}_{ox}$ as an efficient catalyst for benzylamine oxidation proved to be unfounded.

In contrast, **when E was fixed at +100 mV vs SCE,** i.e. at a potential following the peak Pa_2 for which the reaction products $\mathbf{2}_{red}$−$\mathbf{4}_{red}$ could be oxidized to the iminoquinone forms $\mathbf{2}_{ox}$−$\mathbf{4}_{ox}$, a different anodic behavior was observed. After the consumption of 2 F mol^{-1}, the system of peaks (Pa_2, Pc_2) remained unchanged over a long time, a result in agreement with a steady-state catalytic behavior, while a significant increase in the cathodic peak Pc_3 intensity was observed (Figure 2). At the same time, a new absorption band at 250 nm markedly increased, its height being much higher than the absorption band at 348 nm. The electrolysis proceeded further until a coulometric value of 55 ± 1 was found for n. It could be noted that (a) during the last part of the anodic electrolysis ($n > 40$) a new cathodic peak Pc_4 developed at a more negative potential (−1550 mV vs SCE), which could be assigned to the reduction of PhCHO, as corroborated after recording the cyclic voltammogram of an authentical sample; (b) the voltammogram given by the exhaustively oxidized solution no longer exhibited the pair of peaks (Pa_2, Pc_2).

As benzylamine was present in large amounts compared with the quinonoid forms, these results supported the suggestion that benzylamine suffered catalytic oxidation. The turnover yield was first determined in terms of the benzaldehyde phenylhydrazone, which was isolated in 2600% turnover yield, based on $\mathbf{1}_{red}$ initial concentration (Table 1). To quantify more accurately the products of benzylamine anodic oxidation, these were isolated after subsequent electrochemical reduction of the exhaustively oxidized solution conducted at a potential fixed at −1600 mV vs SCE, i.e. at a potential immediately following the peak Pc_4. The results of the exhaustive cathodic electrolyses are summarized in Table 2. They indicated that the main product of benzylamine oxidation was PhCH=NCH_2Ph, whereas PhCHO was present as a minor product. As earlier reported,[17] dibenzylamine **5** resulted from a two-electron reduction process, while dimers **6** and **7**, isolated as meso and (D,L) forms, arose from a one-electron reduction mechanism. The formation of imidazolidine **8** could be reasonably regarded as proceeding through a tandem two-electron oxidation−cyclization

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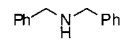
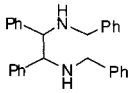
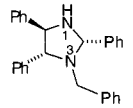
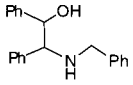
Table 1. Yields of Catalytic Deamination of Benzylamine Mediated by Electrogenerated Model Quinonoid Cofactors in Deaerated CH_3OH[a]

	yield (%)	
substrate	(a)	(b)
$\mathbf{1_{red}}$	2600	53
$\mathbf{2_{red}}$	800	16
$\mathbf{3_{red}}$	3200	64
$\mathbf{4_{red}}$	3200	64

[a] Electrochemical oxidation of the substrate was performed at a mercury pool (E = +100 mV vs SCE), [substrate] = 2 mM, [$PhCH_2NH_2$] = 100 mM, under N_2, in CH_3OH. Control studies indicated that the amount of PhCHO produced either from simple autoxidation or from electrochemical oxidation of benzylamine in the absence of catalyst was negligible. Yields represent mol % of isolated benzaldehyde phenylhydrazone based on the initial concentration of substrate (a) and on the initial concentration of $PhCH_2NH_2$ (b).

Table 2. Products and Yields of Cathodic Controlled Potential Electrolysis Consecutive to Catalytic Electrochemical Oxidation of Benzylamine in Deaerated CH_3OH[a]

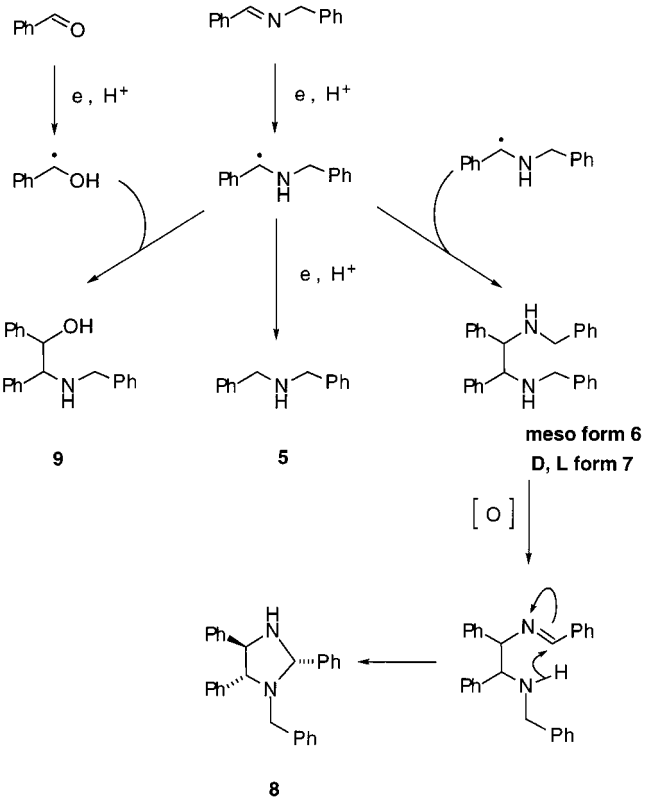
Product		Yield %	
		(a)	(b)
	**5**	11	13
	**6** (meso form)	12	12
	7 (D, L form)	10	10
	**8**	5	4
	**9**	2	2

[a] E_{an} = 100 mV vs SCE; E_{cath} = 1600 mV vs SCE. Yields represent mol % of isolated product based on the initial concentration of $PhCH_2NH_2$; [substrate] = 2 mM, [$PhCH_2NH_2$] = 100 mM, under N_2, in CH_3OH. (a) 1_{red} was used as the substrate; (b) $\mathbf{4_{red}}$ was used as the substrate.

reaction of a dimer form, during isolation or upon column chromatography (Scheme 2). Interesting enough, the isolation of mixed dimer **9** constituted a proof of the presence, in the exhaustively oxidized solution, of benzaldehyde as the minor product. Mixed dimer **9** resulted obviously from the condensation reaction of radicals formed consecutively to the one-electron reduction of both PhCHO and PhCH=NCH_2Ph.[17]

Therefore, we were encouraged to think that one of the iminoquinone systems $\mathbf{2_{ox}}$−$\mathbf{4_{ox}}$ could be effective in benzylamine oxidative deamination. Consequently, to clarify the substantial role of each iminoquinone form in supporting the catalytic efficiency, the electrochemical oxidation of compounds $\mathbf{2_{red}}$−$\mathbf{4_{red}}$ was separately performed, in deaerated CH_3OH, in the presence of benzylamine excess. With $\mathbf{2_{red}}$ as the starting material, the catalytic process ceased after 16 turnovers, and the yield of benzaldehyde phenylhydrazone did not exceed 800% (Table 1). As a consequence, $\mathbf{2_{ox}}$ could not be considered as responsible for the potent catalytic efficiency (2600% turnover yield) in deaminating benzylamine. So, we focused our attention on the catalytic potential of iminoquinone derivatives $\mathbf{3_{ox}}$ and $\mathbf{4_{ox}}$, which proved to be equivalent.

Scheme 2



Reaction of the Electrogenerated 3,4-Benzyliminoquinone $\mathbf{3_{ox}}$ with Benzylamine. The cyclic voltammogram of $\mathbf{3_{red}}$ (2 mM), in deaerated CH_3OH containing $LiClO_4$ as the supporting electrolyte and an excess of benzylamine (100 mM), at a dropping mercury electrode, exhibited an oxidation peak Pa_1 at −70 mV vs SCE, in agreement with the two-electron oxidation of $\mathbf{3_{red}}$ to $\mathbf{3_{ox}}$. The partial reversibility of the two-electron transfer was illustrated by the appearance of a cathodic peak Pc_1, on the reverse sweep, at −120 mV vs SCE.

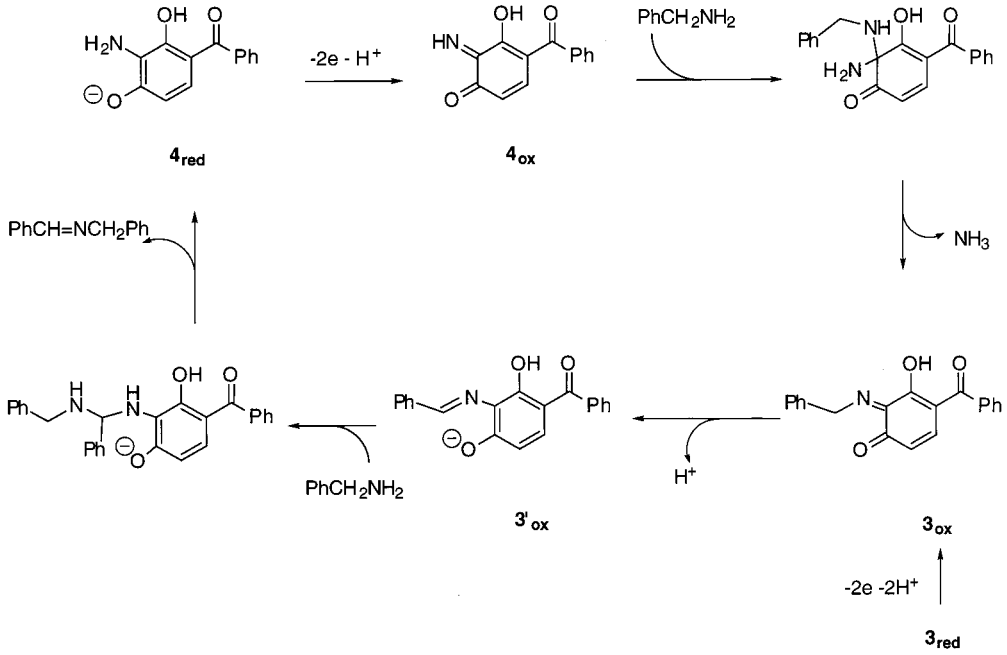
When E was fixed at +100 mV vs SCE, a decrease in the Pa_1 and Pc_1 intensities was observed simultaneously, while a new system of peaks (Pa_2, Pc_2) developed at a 30 mV more positive potential, due to a partially reversible two-electron transfer. Simultaneously, the cathodic peak Pc_3, characteristic of the reduction of PhCH=NCH_2Ph, developed at −1300 mV vs SCE.

In the *first procedure*, the anodic electrolysis was allowed to go to completion. As the electrolysis proceeded, the system of peaks (Pa_2, Pc_2) remained unchanged for a long time, consistent with a steady-state catalytic behavior, while the cathodic peak Pc_3 continuously increased. Finally, a coulometric value of 70 ± 1 was found for n, and benzaldehyde phenylhydrazone was isolated in 3200% turnover yield (Table 1).

In the *second procedure*, the anodic electrolysis was spontaneously stopped after consumption of 2 F mol^{-1}. Then, 3,4-aminophenol $\mathbf{4_{red}}$ was isolated in 70% yield along with 6% of the recovered starting material $\mathbf{3_{red}}$, a result in agreement with a transamination mechanism, which implied the 3,4-iminoquinone species $\mathbf{4_{ox}}$ as the efficient catalyst in deaminating benzylamine.

The hypothesis that $\mathbf{4_{ox}}$ might play a crucial role in the oxidative deamination of benzylamine was further

Scheme 3



substantiated when considering the specific behavior of $\mathbf{4}_{red}$, under the same experimental conditions.

Reaction of the Electrogenerated 3,4-Iminoquinone 4_{ox} with Benzylamine. The cyclic voltammogram of $\mathbf{4}_{red}$ (2 mM), in deaerated CH_3OH containing $LiClO_4$ as the supporting electrolyte and an excess of benzylamine (100 mM) at a dropping mercury electrode, showed an oxidation peak Pa at − 40 mV vs SCE, characteristic of the two-electron oxidation of $\mathbf{4}_{red}$ to $\mathbf{4}_{ox}$.When *E* was fixed at +100 mV vs SCE, the intensity of the anodic peak at −40 mV vs SCE remained unchanged, in agreement with steady-state catalytic behavior. When the electrolysis was stopped after consumption of 2 F mol^{-1}, 76% of the starting material $\mathbf{4}_{red}$ was recovered without evidence of other products. When the controlled potential electrolysis was pursued beyond 2 F mol^{-1}, the catalytic efficiency was identical to that previously described from $\mathbf{3}_{red}$. The results of these experiments are collected in Tables 1 and 2.

Mechanism of Benzylamine Oxidation. On the basis of the results given by the controlled potential electrolyses, we can formulate the following assumptions about the mechanism of benzylamine oxidative deamination. Electrogenerated 3,4-iminoquinone species $\mathbf{3}_{ox}$ and $\mathbf{4}_{ox}$ turned out to be efficient catalysts in deaminating benzylamine, producing 3200% turnover yield. The fact that, starting from $\mathbf{3}_{red}$, $\mathbf{4}_{red}$ was isolated in 70% yield after a single turnover (2 F mol^{-1}) clearly demonstrated that the oxidative catalytic deamination of benzylamine proceeded via a transamination mechanism. This involved α-proton abstraction and the subsequent electron flow from the α-carbon to the quinone moiety, to produce the Schiff base intermediate $\mathbf{3'}_{ox}$, the driving force being the tendency to restore aromaticity within the 3,4-iminoquinone ring. The proposed mechanism (Scheme 3) is the analogue of path B in Scheme 1, which is the accepted mechanism for catalytic deamination by quinonoid cofactors.

Although the structure of our model compounds markedly differs from that of naturally occurring quinones, the reaction displays two features that are most often associated with enzymatic systems: (a) the reaction seems to be enhanced through the participation of neighboring substituents, here, the benzoyl and 2-hydroxyl substituents, as they prevented the competing formation of Michael adducts and (b) the presence of an active hydroxyl proton at the 2-position very probably is an essential component of the catalytic activity. It can be remembered that similar active hydrogens (pyrrole proton 1-NH of PQQ and hydroxyl proton 2-OH of TPQ) were found to be essential for optimal catalytic activity.[5,7] In this connection, further analogues development would be useful to confirm the substantial role of both the benzoyl and 2-hydroxyl groups in enhancing the reactivity of the iminoquinone ring.

Concluding Remarks

In this paper, the catalytic efficiency of a new type of quinonoid cofactor was investigated toward the oxidation of benzylamine. Contrary to previous studies on related redox cofactors, in our work the unstable quinonoid species were electrogenerated. Under strictly anaerobic conditions, the use of controlled potential electrolysis enabled us to modulate the oxidative strength by a simple variation of the potential applied to the working anode. On this basis, we have established that electrogenerated 3,4-quinone $\mathbf{1}_{ox}$ was incapable of deaminating benzylamine, while electrogenerated 3,4-iminoquinone species $\mathbf{3}_{ox}$ and $\mathbf{4}_{ox}$ behaved as effective catalysts. Under our experimental conditions, the reaction efficiency reached 64 turnovers.

Finally, using $\mathbf{3}_{red}$ as the starting material, we were led to conclude that the deamination mechanism of benzylamine was akin to the transamination reaction reported earlier for quinone cofactors of amine oxidoreductases. We are currently conducting experiments to explore the ability of our model system $\mathbf{4}_{ox}$ to catalyze the oxidative deamination of unactivated aliphatic primary amines.

Experimental Section

Chemicals were commercial products of the highest available purity and were used as supplied. All apparatus, cells, and electrodes were identical with those described previously.[18]

Preparation of 4-Benzylamino-2,3-dihydroxybenzophenone (2_{red}), 3-Benzylamino-2,4-dihydroxybenzophenone (3_{red}), and 3-Amino-2,4-dihydroxybenzophenone (4_{red}) from Electrochemical Oxidation of 1_{red} in the Presence of Benzylamine. Method A. A solution of 2,3,4-trihydroxybenzophenone ($\mathbf{1_{red}}$) (115 mg, 0.5 mmol), $LiClO_4$ (5.30 g, 50 mmol), and benzylamine (2.67 g, 25 mmol) in CH_3OH (250 mL) was oxidized under N_2, at room temperature, at a mercury pool working electrode ($E = -180$ mV vs SCE). After exhaustive oxidation (2 F mol^{-1}), i.e., when a negligible value of the current was recorded, the methanolic solution was poured into a molar citric acid buffered aqueous solution of pH ~ 3 (100 mL). The resulting hydroalcoholic solution was concentrated to remove CH_3OH and extracted with ether (100 mL). After the extract was dried over $MgSO_4$, evaporation of the solvent gave a dark yellow residue from which aminophenols $\mathbf{2_{red}}$, $\mathbf{3_{red}}$, and $\mathbf{4_{red}}$ were isolated in 16%, 5%, and 62% yields, respectively, by flash column chromatography (SiO_2, toluene−acetone gradient from 100:0 to 95:5).

$\mathbf{2_{red}}$ (recrystallized from ether): mp 124−126 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.45 (d, 2H, $J = 5$ Hz), 6.10 (d, 1H, $J = 9$ Hz), 6.85 (d, 1H, $J = 9$ Hz), 6.90 (t, 1H, $J = 5$ Hz), 7.20−7.35 (m, 5H), 7.40−7.55 (m, 5H), 8.95 (s, br, 1H), 12.70 (s, br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 46.2, 103.1, 110.0, 127.8, 128.0, 128.3, 129.3, 129.5, 131.9, 130.4, 139.2, 140.8, 146.0, 151.5, 197.0; MS DCI m/z 320 (MH^+). Anal. Calcd for $C_{20}H_{17}NO_3$ C, 75.23; H, 5.33; N, 4.39. Found: C, 74.97; H, 5.37; N, 4.36.

$\mathbf{3_{red}}$ (recrystallized from ether): mp 149−151 °C dec; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.50 (d, 2H, $J = 5$ Hz), 6.40 (d, 1H, $J = 9$ Hz), 6.85 (d, 1H, $J = 9$ Hz), 7.20−7.35 (m, 5H), 7.50−7.65 (m, 5H), 12.80 (s, br, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 50.1, 108.8, 113.1, 125.1, 126.9, 127.6, 128.5, 129.2, 129.4, 129.7, 132.4, 139.2 and 142.6, 155.3, 155.7, 201.0; MS DCI m/z 320 (MH^+). Anal. Calcd for $C_{20}H_{17}NO_3$ C, 75.23; H, 5.33; N, 4.39. Found: C, 74.93; H, 5.35; N, 4.37.

$\mathbf{4_{red}}$ (recrystallized from CH_2Cl_2): mp 186−188 °C dec; Spectroscopic data for product $\mathbf{4_{red}}$ have been reported earlier.[15]

Catalytic Oxidation of Benzylamine from Electrogenerated 3,4-Quinone 1_{ox}. Method B. A solution of 2,3,4-trihydroxybenzophenone ($\mathbf{1_{red}}$) (115 mg, 0.5 mmol), $LiClO_4$ (5.30 g, 50 mmol), and benzylamine (2.67 g, 25 mmol) in CH_3OH (250 mL) was oxidized under N_2, at room temperature, at a mercury pool working electrode ($E = +100$ mV vs SCE). After exhaustive oxidation (55 F mol^{-1}), phenylhydrazine (2.70 g, 25 mmol) and 100 mL of a molar acetic buffered aqueous solution of pH ~ 4.5 were added to the reaction mixture. The resulting hydroalcoholic solution was concentrated to remove CH_3OH and allowed to come to room temperature. The solid was collected by filtration, washed with H_2O, and dried in a vacuum desiccator. Benzaldehyde phenylhydrazone was then isolated as a colorless solid in 53% yield, based on $PhCH_2NH_2$ initial concentration, mp 156−158 °C (recrystallized from toluene). Spectroscopic data of benzaldehyde phenylhydrazone have been reported earlier.[19,20]

Method C. A solution of 2,3,4-trihydroxybenzophenone ($\mathbf{1_{red}}$) (115 mg, 0.5 mmol), $LiClO_4$ (5.3 g, 50 mmol), and benzylamine (2.67 g, 25 mmol) in CH_3OH (250 mL) was oxidized using method B. After exhaustive oxidation (55 F mol^{-1}), the resulting methanolic solution was immediately reduced after the potential of the mercury pool was switched to −1600 mV vs SCE. After exhaustive cathodic electrolysis, the solution was poured into H_2O (100 mL). The resulting hydroalcoholic solution was concentrated to remove CH_3OH and extracted with CH_2Cl_2 (100 mL). After the extract was dried over $MgSO_4$, evaporation of the solvent gave a pale yellow oil from which pure dimer product **6** (meso form) was isolated after washing with ethanol in 12% yield, based on the initial concentration of $PhCH_2NH_2$. The resulting ethanolic layer was concentrated to remove ethanol, leading to a crude product which was purified by flash column chromatography (SiO_2, toluene−acetone gradient of 100:0 for 200 mL, 95:5 for 200 mL, and 90:10 for 200 mL. Dibenzylamine **5**, dimer **7** (D,L form), imidazolidine **8**, and mixed dimer **9** were then isolated in 11%, 10%, 5%, and 2% yields, respectively.

Dibenzylamine 5: colorless oil. Spectroscopic data of dibenzylamine have been reported earlier.[21]

***N,N′*-Dibenzyl-1,2-diphenyl-1,2-diaminoethane 6 (meso form)**: white solid recrystallized from ethanol, mp 149−151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (s, br, 2H), 3.30 (d, 2H, $J = 14$ Hz), 3.55 (d, 2H, $J = 14$ Hz), 3.75 (s, 2H), 7.00−7.35 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.9, 67.1, 126.6, 127.6, 127.8, 128.1, 128.3, 128.5, 140.2, 140.7; MS DCI m/z 393 (MH^+). Anal. Calcd for $C_{28}H_{28}N_2$ C, 85.71; H, 7.14; N, 7.14. Found: C, 85.77; H, 7.19; N, 7.11.

***N,N′*-Dibenzyl-1,2-diphenyl-1,2-diaminoethane 7 (D,L form)**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, br, 2H), 3.50 (d, 2H, $J = 13$ Hz), 3.75 (d, 2H, $J = 13$ Hz), 3.80 (s, 2H), 7.10−7.40 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.3, 68.3, 126.7, 126.9, 127.9, 128.0, 128.3, 140.6, 141.1; MS DCI m/z 393 (MH^+).

3-Benzyl-2,4,5-triphenylimidazolidine 8: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.05 (1H, broad s, NH, D_2O exchanged), 3.65 (2H, AB, $J = 16$ Hz, CH_2–N), 3.80 (1H, d, $J = 8$ Hz, H-4), 4.42 (1H, d, $J = 8$ Hz, H-5), 4.88 (1H, s, H-2), 6.95 (2H, broad d, $J = 8$ Hz, ortho Ph-3), 7.20 (2H, broad d, $J = 8$ Hz, ortho Ph-5), 7.25−7.40 (12H, m, aromatic proton), 7.45 (2H, broad d, $J = 8$ Hz, ortho Ph-4), 7.70 (2H, broad d, $J = 8$ Hz, ortho Ph-2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 53.5 (CH_2–N), 69.8 (C-5), 75.6 (C-4), 81.3 (C-2), 127.2−130.4 (CH, aromatic carbon), 136.3, 140.5 and 142.7 (C_Q, aromatic); HRMS (LC TOF, reserpine as the lock mass) m/z 391.2185 (MH^+) calcd for $C_{28}H_{27}N_2$ 391.2174.

The relative stereochemistry of the three asymmetric centers was determined through a 2D NOESY experiment (mixing time = 250 ms). NOE cross-peaks were observed between H-2 and H-4, ortho Ph-5, on one hand, while correlations were obtained between H-5 and ortho Ph-4, ortho Ph-2, on the other. The carbon type (methyl, methylene, methide, or quaternary) was determined by DEPT experiments.

***N*-Benzyl-1,2-diphenyl-aminoethanol 9:** white solid recrystallized from ethanol, mp 156−158 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (s, 1H), 3.00 (s, 1H), 3.55 (d, 1H, $J = 13$ Hz), 3.75 (d, 1H, $J = 13$ Hz), 3.95 (d, 1H, $J = 13$ Hz), 4.85 (d, 1H, $J = 6$ Hz), 7.10−7.35 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.0, 67.8, 76.7, 126.8, 126.9, 127.6, 127.7, 127.8, 128.0, 128.2, 128.3, 128.4, 139.1 139.8 and 140.3; MS DCI m/z 304 (MH^+). Anal. Calcd for $C_{21}H_{21}NO$ C, 83.17; H, 6.93; N, 4.62. Found: C, 82.87; H, 6.97; N, 4.60.

Catalytic Oxidation of Benzylamine by Electrogenerated 4,3-Benzyliminoquinone 2_{ox}. The above-described method A, replacing $\mathbf{1_{red}}$ by $\mathbf{2_{red}}$, with $E = +100$ mV vs SCE and $n = 2$, led, after flash column chromatography (SiO_2, toluene−acetone 98:2), to the recovered starting material in 75% yield.

The above-described method B, replacing $\mathbf{1_{red}}$ by $\mathbf{2_{red}}$, allowed, after consumption of 18 F mol^{-1}, the isolation of benzaldehyde phenylhydrazone in 16% yield, based on the initial concentration of $PhCH_2NH_2$.

Catalytic Oxidation of Benzylamine by Electrogenerated 3,4-Benzyliminoquinone 3_{ox}. The above-described method A, replacing $\mathbf{1_{red}}$ by $\mathbf{3_{red}}$, with $E = +100$ mV vs SCE

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and $n = 2$ afforded, after flash column chromatography (SiO_2, toluene−acetone 90:10), compound $\mathbf{4_{red}}$ in 70% yield, along with 6% of the recovered starting material $\mathbf{3_{red}}$.

The above-described method B, replacing $\mathbf{1_{red}}$ by $\mathbf{3_{red}}$, allowed, after consumption of 70 F mol^{-1}, the isolation of benzaldehyde phenylhydrazone in 64% yield, based on the initial concentration of $PhCH_2NH_2$.

Catalytic Oxidation of Benzylamine by Electrogenerated 3,4-Iminoquinone $\mathbf{4_{ox}}$. The above-described method A, replacing $\mathbf{1_{red}}$ by $\mathbf{4_{red}}$, with $E = +100$ mV vs SCE and $n = 2$, led, after flash column chromatography (SiO_2, toluene−acetone 90:10), to the recovered starting material $\mathbf{4_{red}}$ in 76% yield.

The above-described method B, replacing $\mathbf{1_{red}}$ by $\mathbf{3_{red}}$, allowed, after consumption of 70 F mol^{-1}, the isolation of benzaldehyde phenylhydrazone in 64% yield, based on the initial concentration of $PhCH_2NH_2$.

The above-described method C, replacing $\mathbf{1_{red}}$ by $\mathbf{4_{red}}$, afforded dibenzylamine **5** (13% yield), dimer compounds **6** (12% yield, meso form) and **7** (10% yield, D,L form), imidazolidine **8** (4% yield), and mixed dimer **9** (2% yield).

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