ON THE DETERMINATION AND USE OF REDUCTION POTENTIALS OF SHORT-LIVED RADICALS. A REVIEW

Henning LUND[1,]*, Karen SKOV, Steen Uttrup PEDERSEN[2], Torben LUND[3] and Kim DAASBJERG[4]

Department of Organic Chemistry, University of Aarhus, DK-8000 Aarhus C, Denmark;
e-mail: [1] hlund@kemi.aau.dk, [2] sup@kemi.aau.dk, [3] tlund@virgil.ruc.dk, [4] kdaa@kemi.aau.dk

Received October 19, 1999
Accepted December 23, 1999

Presented at the 32nd Heyrovský Discussion on Organic Electrochemistry, Třešť, June 6–10, 1999.

A method, the "competition method", for the determination of reduction potentials and estimation of standard potentials for short-lived radicals is reviewed. Applications of the reduction potentials of radicals as arguments for reaction mechanisms are presented for the Grignard reaction, the photoreduction of ketones with alcohols, and the SRN1 reaction. Reductions induced by hydroxide ions are discussed in more detail, and the classic reaction between nitrosobenzene and hydroxide ion in aqueous solution is used as an example of such a reaction. A nucleophilic attack by hydroxide ion rather than an electron transfer initiates the reduction sequence. A review with 26 references.

Key words: Redox potentials; Reductions; Reaction mechanism; Grignard reaction; Ketones; Photoreductions**.**

Knowledge of redox potentials of radicals is useful for understanding of radical reactions and prediction of whether radicals or ionic species are involved in a reaction. Potentials of short-lived radicals may be determined in different ways and a review of such methods as well as a collection of potentials of radicals have recently been published[1].

A method for the estimation of redox potentials of short-lived radicals[2], the "competition method", will be reviewed herein along with a description of reactions that illustrate the applications of such potentials. New results on reductions initiated by hydroxide ions will be presented together with a review of the literature on the reaction between hydroxide/alkoxide ions and nitrosobenzene.

Competition Method

The "competition method" rests on the competition between coupling of a radical with a radical anion and reduction of the radical by the same radical anion as shown in Scheme 1.

In Scheme 1, A is an aromatic or heteroaromatic compound which, by electron uptake, forms a radical anion stable on the time scale of the experiment. RX is a derivative of the radical $R^{\bullet}$, usually an alkyl halide, which should be reduced in a dissociative electron transfer. The anions formed, R^- and AR^-, are finally protonated. Reaction (*3*) is regarded as an outer-sphere electron transfer and its rate assumed to follow the Marcus activation-driving force relationship, $\Delta G^{\#} = (\lambda / 4)\{1 + [F(E^0_A - E^0_{R^{\cdot}})] / \lambda\}^2$. Accordingly, the rate of the reaction is dependent on the redox potentials of the radical ($E^0_{R^{\cdot}}$) and A (E^0_A) and the reorganization energy associated with the electron transfer, λ.

The rate of the competing reaction (*2*) is close to diffusion-control. If the coupling reaction can be assumed to be constant for all the different radicals and radical anions employed, a competition parameter $q = k_3/(k_2 + k_3)$ can be introduced from which information on k_3 can be extracted. When q is plotted against E^0_A, an S-shaped curve is obtained and, at the mid-point of

$$A + e^- \rightleftarrows A^{\bullet-} \qquad (E^o_A)$$

$$A^{\bullet-} + RX \xrightarrow{k_1} A + R^{\bullet} + X^- \qquad (1)$$

$$R^{\bullet} + A^{\bullet-} \xrightarrow{k_2} RA^- \qquad (2)$$

$$R^{\bullet} + A^{\bullet-} \xrightarrow{k_3} R^- + A \qquad (3)$$

$$R^-,\ AR^- + H^+ \longrightarrow RH,\ ARH$$

SCHEME 1

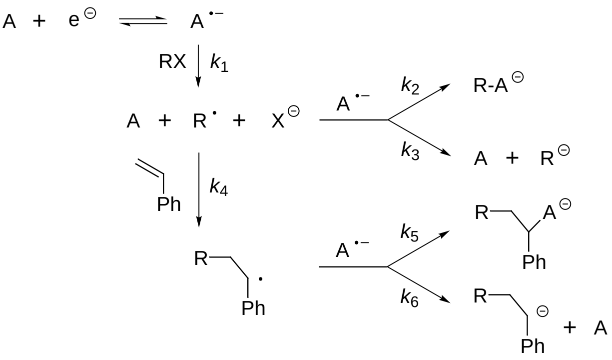
the curve, a reduction potential $E^q_{1/2}$ can be found. The uncertainty of $E^q_{1/2}$ is estimated to be about 50 mV.

A crucial point for the competition method is thus that the rate of the coupling reaction is reasonably constant. Three approaches have been employed to investigate the problem. In the first method, radical clocks have been used[3]; here the rate of the second-order reaction, the coupling, is compared with the rate of the first-order reaction, in general the internal addition of a radical to a double bond. Most radical clocks involve primary radicals, and the method showed that for the radicals tested, the rate constant, k_2, was about 10^9 mol^{-1} l s^{-1}.

Two other methods were developed for determination of k_2 not only for primary, but also for secondary and tertiary radicals[4]. In one of them, the competition was set up between the coupling reaction (*2*) and another second-order reaction, the addition of the radical to an olefin. Scheme 2 illustrates the competing reactions in the case of styrene. The outcome of the competition is found by GLC analysis of the products RAH and $PhCH_2CH_2R$. From the ratio of the products, $\xi = [PhCH_2CH_2R]/[RAH]$ (Eq. (*4*)), k_2 can be found when k_4, k_1, the applied current i and the volume V are known.

$$\xi = \frac{2FVk_1}{-ik_2}\left(k_4\,[\mathrm{PhCH_2CH_2R}][\mathrm{RX}]\right) \qquad (4)$$

The concentration of the radical anion $A^{\bullet-}$ can be controlled electrochemically, but to make certain that the ratio of the concentrations of $PhCH_2CH_2R$ and RAH reflects k_4/k_2, a number of experimental conditions should be met. It is also assumed that the coupling product is formed by



SCHEME 2

coupling of the radical with the radical anion and not in an SN2-like reaction between RX and the radical anion[5].

The addition of radicals to styrene is a relatively slow reaction; hence if this reaction should be able to compete significantly with the fast coupling reaction, a high concentration of styrene and a low concentration of radical anion should be used. A low concentration of radical anions is obtained simply by using a low, constant current in the reduction of A. This leads to a steady-state concentration of the radical anion when the rates of formation of $A^{\bullet-}$ and its consumption in the subsequent reaction become the same. The steady-state concentration of $A^{\bullet-}$ can be measured by UV-VIS spectroscopy using a fibre-optics spectrometer and a dip-in probe immersed directly into the cathodic compartment during the electrolysis. A high concentration of RX is used to ensure that the loss of RX during the experiment is insignificant. Furthermore, the aromatic compound A is chosen such that the electron transfer between $A^{\bullet-}$ and RX is slow. This means that the electron transfer takes place in the bulk of the solution and the radical reacts with styrene or the radical anion before it diffuses to the electrode where it would be reduced.

According to Scheme 2 (and 1) the reaction between a given radical and the radical anion could result in a coupling or reduction with the radical anion. The mediator A is chosen such that its radical anion is able to reduce the benzyl radical, formed on addition of $R^{\bullet}$ to styrene, to the benzyl anion ($k_6 >> k_5$) at a diffusion-controlled rate (*i.e.* $q_{\mathrm{benzyl}} = 1$), but not the alkyl radical ($k_3 << k_2$) formed in the initial step; here the coupling reaction dominates, $q_{\mathrm{alkyl}} = 0$. This is illustrated in Fig. 1. The redox potential of the compound A should be more positive than $E^q_{1/2}$ of the alkyl radical and less positive than $E^q_{1/2}$ of the benzyl radical and thus be between approximately –2.0 and –1.6 V *vs* SCE. The benzyl radical does not add to styrene since this reaction is slow. Having low concentrations of the radical $R^{\bullet}$ and the benzyl radical means that the rates of the different radical–radical couplings are low. The results of this method again show that k_2 is 10^9 mol^{-1} l s^{-1} within a factor of about 2.

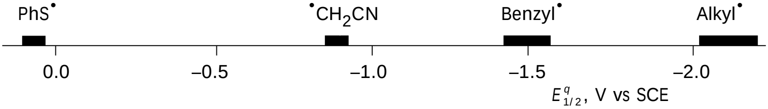


FIG. 1
Reduction potentials $E^q_{1/2}$ for alkyl and benzyl radicals in DMF

In the third method, a competition between the coupling reaction (*2*) and a reaction between the radical $R^{\bullet}$ and a hydrogen atom donor is used to determine k_2. Benzenethiol is a good hydrogen atom donor, and the rate of hydrogen abstraction from benzenethiol by an alkyl radical is of the order of 10^8 mol^{-1} l s^{-1}. This means that a useful competition between the coupling reaction and the hydrogen abstraction can be established when the concentration of benzenethiol is in the mmol l^{-1} range. The reactions may thus be described by Eqs (*1*) to (*3*) and (*5*) to (*9*) (Scheme 3) and the competition of interest is between reactions (*2*) and (*5*).

The standard potential of the phenylthiyl radical has been estimated to be +0.12 V *vs* SCE in DMF; hence, virtually all the radical anions employed will be able to reduce the radical to thiolate. It should thus be possible to change from a situation where $q = 0$ (only coupling occurs) in the absence of benzenethiol to a situation where a nearly full catalytic reaction takes place in the presence of benzenethiol with regeneration of the aromatic compound. Benzenethiol, besides being a good hydrogen atom donor, is also a relatively strong proton donor, and this must be taken into consideration when choosing a radical anion as electron donor. Only relatively weakly basic radical anions can be used.

$$R^{\bullet} + SH \xrightarrow{k_8} R\text{–}H + S^{\bullet} \tag{5}$$

$$A^{\bullet-} + S^{\bullet} \xrightarrow{k_9} A\text{–}S^{-} \tag{6}$$

$$A^{\bullet-} + S^{\bullet} \xrightarrow{k_{10}} A + S^{-} \tag{7}$$

$$AR^{-} + SH \xrightarrow{k_{11}} ARH + S^{-} \tag{8}$$

$$RX + S^{-} \xrightarrow{k_{12}} S\text{–}R + X^{-} \tag{9}$$

SCHEME 3

The competition between (*2*) and (*5*) can be measured by linear sweep voltammetry and, from a comparison with simulated curves, k_2 can be found if k_8 is known. As all three approaches for most radicals have given similar results for k_2 ($\approx 10^9$ mol^{-1} l s^{-1}) the "competition method" seems reliable for determination of the potential at which radical chemistry changes to ionic reactions for a carbon-centred radical, *i.e.* $E^q_{1/2}$.

To obtain the standard potential of the radical from $E^q_{1/2}$, knowledge of the value of λ is necessary. An estimate of λ can be obtained from the width of the q *vs* E^0_A curve, but the estimation of λ in this way is not precise enough to provide a value of the standard potential with precision approaching that of $E^q_{1/2}$. The standard potential $E^0_{R^\cdot}$ can be calculated from $E^q_{1/2}$ as shown in Eqs (*10*) and (*11*).

$$E^0_{R^\cdot} = E^0_{1/2} + H_{\text{corr}} \tag{10}$$

$$H_{\text{corr}} = \frac{\lambda}{F}\left\{1 - \sqrt{\frac{4RT}{\lambda}\ln\left[\frac{1}{A}\left(\frac{k_d}{k_2} - 1\right)\right]}\right\} \tag{11}$$

However, although the present estimation of $E^0_{R^\cdot}$ is not satisfactory, whenever a better determination of λ is available, a more precise estimation of the standard potential can be made.

Attempts to use the "competition method" for the determination of reduction potentials of oxygen-centred radicals in DMF did not meet with success. The oxygen-centred radicals abstracted a hydrogen atom from DMF with formation of the radical $Me_2NCO^\bullet$. A nice S-shaped curve pertaining to this radical was obtained in the plot of q *vs* E^0_A, and a preparative reduction using anthraquinone as mediator ($q = 0$) and di-*tert*-butyl peroxide as substrate yielded a coupling product between the DMF derived radical $Me_2NCO^\bullet$ and anthraquinone radical anion, 9-hydroxy-*N*,*N*-dimethyl-10-oxo-9,10-dihydroanthracene-9-carboxamide[6]. However, this failure inspired the use of electrochemical hydrogen abstraction for the formation of radicals from hydrocarbons RH for the coupling of the radical $R^\bullet$ with a radical anion without the need of preparing RX (ref.[7]).

Applications of Redox Potentials

To illustrate the application of the reduction potentials $E^q_{1/2}$, a few examples will briefly be discussed. The examples chosen are the Grignard reaction, the photochemical reduction of ketones with alcohols, and the SRN1 reaction.

Grignard reaction. The addition of Grignard reagents to ketones is generally described in textbooks as a polar reaction but in some cases the product distribution indicates a radical reaction. It is interesting that there is a good correspondence between the experimental results and the predictions made on the basis of the redox potentials of reactants, even if no steric and bonding interactions have been taken into account; furthermore, the potentials are measured in DMF and not in diethyl ether, and the radical reaction may or may not be an outer-sphere electron transfer. In the following examples, the oxidation potential of the carbanion and the reduction potential of the ketone have been helpful for prediction of the reaction path. The reaction of benzophenone (E^0_{A} = –1.72 V *vs* SCE) with *t*-BuMgCl ($E^0_{t\text{-Bu}^\bullet/t\text{-Bu}^-}$ = –1.77 V) and *s*-BuMgCl ($E^0_{s\text{-Bu}^\bullet/s\text{-Bu}^-}$ = –1.77 V) gives some radical products whereas reaction with CH_3MgI ($E^0_{\mathrm{Me}^\bullet/\mathrm{Me}^-}$ = –1.19 V) and BzMgCl ($E^0_{\mathrm{Bz}^\bullet/\mathrm{Bz}^-}$ = –1.40 V) gives no radical products. However, in the reaction with fluorenone (E^0 = –1.19 V), all of the Grignard reagents mentioned give the same sort of "radical products" as formed, when the radical anion of fluorenone reacts with the corresponding alkyl halides[8]. The potentials should, however, be taken only as an indication of possible involvement of radicals, as other variables, such as steric hindrance, may influence the competition between radical and polar reactions.

Photochemistry. The photoreduction of benzophenone with propan-2-ol with formation of benzophenone pinacol (1,1,2,2-tetraphenylethane-1,2-diol) and acetone is a textbook reaction. After the transfer of a hydrogen atom, the radicals $Ph_2C^\bullet OH$ and $(CH_3)_2C^\bullet OH$ are formed (Eq. (*13*)). Question remains why these carbon-centred radicals do not couple to a mixed pinacol.

$$Ph_2C{=}O + h\nu \longrightarrow Ph_2C{=}O^* \qquad (12)$$

$$Ph_2C{=}O^* + (CH_3)_2CHOH \longrightarrow Ph_2C^\bullet OH + (CH_3)_2C^\bullet OH \qquad (13)$$

$$Ph_2C{=}O + (CH_3)_2C^\bullet OH \longrightarrow 1/2\ (Ph_2C(OH){-})_2 + (CH_3)_2C{=}O \qquad (14)$$

$$(CH_3)_2C{=}O + Ph_2CHOH + h\nu \longrightarrow ((CH_3)_2COH)_2 + \\ + (Ph_2C(OH){-})_2 + Ph_2COH{-}COH(CH_3)_2 \qquad (15)$$

However, when acetone and diphenylmethanol are photolyzed, a similar hydrogen atom transfer occurs, and the same radicals as in Eq. (*13*) are formed, but one obtains a product mixture with symmetric and crossed coupling products. If benzophenone is photolyzed in the presence of toluene, the product distribution of symmetrical and cross-coupled products is close to the statistical one.

If one calculates the energetics of the combined electron transfer and proton transfer from the redox potentials of the ketones and radicals involved, it turns out that in the former reaction (Eq. (*14*)) the 2-hydroxypropan-2-yl radical can reduce benzophenone whereas in the latter case (Eq. (*15*)) the hydroxydiphenylmethyl radical is not able to reduce acetone; the radicals then couple without subsequent redox reactions[9].

From these results and the relevant redox potentials one would predict that photolyzing a mixture of 4-methylacetophenone and phenylethan-1-ol would give the three different coupling products but also, in the course of the reaction, some acetophenone. The experiments are in accord with that.

SRN1 reaction. Electrochemical and photochemical induction of the nucleophilic substitution reaction, SRN1, give fair to good yield of substitution products when aromatic halides and suitable anions are used. Photostimulated SRN1 substitution of adamantyl halides in liquid ammonia with diphenylphosphide ion gives a good yield of the substitution product[10]. However, attempts to make direct electrolysis of 1-iodoadamantane (AdI) in the presence of arenethiolate ion gave no substitution products[11].

In the reduction of most aromatic halides, the radical anion has a certain lifetime and has time to diffuse away from the electrode before the cleavage to aryl radical and X^-. On the other hand, aliphatic halides, including adamantyl iodide, cleave immediately upon uptake of an electron. The aliphatic radical is thus formed at the electrode surface and if the potential used to reduce AdI is more negative than the standard potential of $Ad^•$ as is the case, the radical will immediately be reduced to the anion and an SRN1 reaction cannot be initiated[11].

Nucleophilic/electrophilic radicals. Radicals are often characterized as nucleophilic or electrophilic. Typical nucleophilic radicals are aliphatic radicals[12], while halogen or hydroxyl radicals are typical electrophilic radicals. The "nucleophilicity" or "electrophilicity" is for radicals much less pronounced than for polar reagents, and this might explain the lack of investigations on the relative nucleophilicity or electrophilicity of radicals. The degree to which the nucleophilicity/electrophilicity of a radical influences a reaction depends on the substrate. But could an important factor in determining the nucleophilicity/electrophilicity be the redox potential of the radical?

There is at least a qualitative confirmation of this assumption. Alkyl radicals are characterized as being "nucleophilic"; this is in accordance with the fact that they have the most negative potential. The halogen and hydroxyl radicals have a much more positive reduction potential. Further investigations are necessary to establish to what degree the potentials of the radicals can be used to predict the relative nucleophilicity of radicals.

Hydroxide Ion as Reductant

An interesting point in the above discussion is that, regardless of the fact that the hydroxide ion has an oxidation potential which should make it a very poor reducing agent, the addition of hydroxide or alkoxide ions in many cases induces a reduction. In an account: "Hydroxide Ion: An Effective One-Electron Reducing Agent?" Sawyers and Roberts[13] discuss several aspects of the problem. Another example is the report by Paradisi and Scorrano[14] on the isolation of reduction products in high yield from the reaction of 4-chloro-1-nitrobenzene with isopropoxide in propan-2-ol with no clear indication of the mechanism. A classic example is also the reaction of nitrosobenzene with hydroxide ion with formation of azoxybenzene, that was first published about hundred years ago; some new aspects of this reaction will be discussed below.

The formation of radical ions by reduction of a substrate on treatment with hydroxide ion requires the presence of a concomitant oxidation process. However, it is unlikely that a direct electron transfer from hydroxide ion to the substrate can take place even in aprotic solvents like acetonitrile[13] where the solvation energy is 20–25 kcal mol^{-1} (85–110 kJ mol^{-1}) less than that in water. It has therefore been suggested[13] that the hydroxide ion in some cases acts as a nucleophile, and that it is the adduct which reduces the substrate and thus gets oxidized.

The reaction of nitrosobenzene (**1**) with hydroxide or alkoxide ions in aqueous or aqueous alcoholic medium has been the subject of several investigations[15–21]. On treatment of **1** (800 g) with base for 3 1/2 months at ambient temperature or 4 h at 100 °C, Bamberger[15] obtained azoxybenzene (**2**; 400 g) as the main product (besides tar), but also isolated small amounts of nitrobenzene, aniline, 4-nitrosophenol, 2-aminophenol, 4-aminophenol, *N*-(4-nitrosophenyl)-*N*-phenylhydroxylamine (**3**), 2-hydroxyazoxybenzene, and the so-called iso-2-hydroxyazoxybenzene, $C_{12}H_{10}N_2O_2$. A good yield of azoxybenzene was also obtained by treatment of **1** with potassium ethoxide in diethyl ether[16] or with base in aqueous ethanol[17].

Azoxybenzene is generally assumed to be the result of a reaction between nitrosobenzene and phenylhydroxylamine (**4**). Russell *et al.*[18] observed with EPR spectroscopy rapid formation of nitrosobenzene radical anion $\mathbf{1}^{\bullet-}$ during the reaction between **1** and **4** in deoxygenated dimethyl sulfoxide, DMSO, containing potassium *tert*-butoxide; in this solvent $\mathbf{1}^{\bullet-}$ decays slowly over a period of days. In the absence of base, phenylaminoxyl ($PhNHO^{\bullet}$) is formed in the reaction between **1** and **4**. In ethanol containing sodium hydroxide, **2** is formed in a high yield; $\mathbf{1}^{\bullet-}$ can be detected, but it decays rapidly in a reaction which is second order in $\mathbf{1}^{\bullet-}$. Besides the EPR spectra of $\mathbf{1}^{\bullet-}$ and phenylaminoxyl, an EPR spectrum of another stable, third radical could be obtained from **1** on reduction with sodium dithionite in a slightly acidic medium; the general structure $PhN^{\bullet+}(O^-)OX$ was proposed for this stable radical. The radical is converted to $\mathbf{1}^{\bullet-}$ on treatment with base. In the presence of ethanol and hydroxide, azoxybenzene is formed from **1**, but this does not occur in DMSO (80%)/*t*-BuOH (20%). In pure DMSO half-saturated with potassium hydroxide, azoxybenzene slowly forms nitrosobenzene radical anion[18], whereas **2** is stable in DMSO/*t*-BuOH containing potassium hydroxide.

Waters *et al.*[19] concluded from a kinetic investigation that the formation of **2** from nitrosobenzene in aqueous alcoholic solution involved a hydride ion transfer, probably from the alkoxide ion, to **1** giving the anion of *N*-phenylhydroxylamine, $PhNHO^-$ ($\mathbf{4}^-$), which then combined with a second molecule of **1** to **2**. The reaction was assumed to involve the transfer of a single electron from $\mathbf{4}^-$ to **1**, thereby forming $\mathbf{1}^{\bullet-}$ which dimerized and lost a hydroxide ion to afford **2**.

When the reaction was performed under nitrogen[19], small amounts of azobenzene, 2-hydroxyazobenzene, and *N*-(4-nitrosophenyl)-*N*-phenylhydroxylamine (**3**) were isolated besides **2**. Schindler *et al.*[20] also detected **3** during a spectroelectrochemical investigation of the reduction of **1** in acetonitrile; at the same time an absorption band arose at 320 nm which they assigned to $\mathbf{1}^{\bullet-}$. It was concluded that **3** was formed by an attack of $\mathbf{1}^{\bullet-}$ on **1**, whereas **2** was formed through a dimerization of $\mathbf{1}^{\bullet-}$.

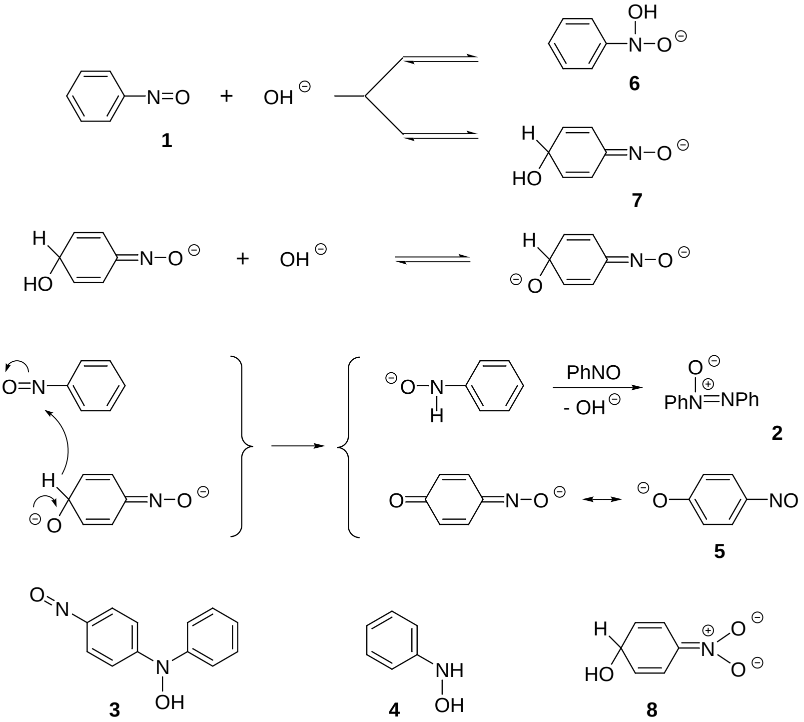
Zuman *et al.*[21] investigated by polarography the reaction of **1** with hydroxide ion in 10% aqueous ethanol at a high pH. In this reaction **1** was found to add a hydroxide ion to the nitroso group analogously to the addition of a hydroxide ion to an aldehyde group. The equilibrium constant of the equilibrium $ArNO + OH^- \rightleftharpoons ArN(OH)O^-$ was found to be 1.58. The concentration of **1** was followed by polarography[21] and, in the absence of oxygen and light, two linear segments were found on the log $i = f(t)$ curve; the reaction corresponding to the first segment was virtually independent of pH, whereas the second reaction was virtually independent of the initial concentration of **1** and first order in $[OH^-]$. Further, irreversible reaction of the addition product of **1** with hydroxide ion, $PhN(OH)O^-$, involved a second hydroxide ion, and led in the absence of oxygen to **2**. The kinetics indicated that the formation of an intermediate, such as $ArN(O^-)_2$, was the rate-determining step both in the absence and the presence of dioxygen. It was also found that the yield of **2** was only 50–60% of the converted **1**. Accordingly, accumulation of a nonreducible intermediate or a nonreducible product may have taken place. An adduct of hydroxide ion with **1** was also proposed by Russell *et al.*[18]. They, however, suggested that the hydroxide did not add to the nitrogen, as no nitrobenzene was detected in the absence of oxygen and one would expect the electron-donating adduct to form nitrobenzene.

Hawley *et al.*[22] investigated the reduction of **1** in acetonitrile (MeCN) and observed an influence of the electrogenerated base on the reduction. They found that addition of tetraethylammonium hydroxide to **1** in MeCN gave **2** and an unidentified compound **10** which showed in the cyclic voltammogram of the exhaustively reduced solution of **1** reversible reduction at –0.2 V *vs* SCE; the yields of **2** and **10** were similar to those obtained by electrolysis of **1**. The properties of **10** were not inconsistent with those of a compound formed on attack of hydroxide ion on the aromatic ring of **1** as suggested by Russell *et al.*[18].

In the reaction between **1** and RO^- in aqueous-alcoholic solution with formation of **2**, some **1** is reduced but, in the absence of dioxygen, the nature of the simultaneously oxidized compound has not been proved. In some cases small amounts of nitrobenzene were detected, but never enough to explain the reduction of **1**. In most cases it was assumed that the alcohol was oxidized, and that the aldehyde or ketone subsequently underwent aldol condensation or another secondary reaction and thus avoided detection. In the presence of dioxygen it has been found[18,21] that a decrease in nitrosobenzene concentration was virtually equal to an increase in the nitrobenzene concentration.

The reaction between nitrosobenzene and sodium hydroxide was investigated in water and aqueous acetonitrile rather than in alcoholic solution to avoid complications of a possible oxidation of the solvent.

The two-day reaction at ambient temperature of a deaerated suspension of finely powdered nitrosobenzene in potassium hydroxide solution (0.4–1 mol l^{-1}) in water or 30% aqueous acetonitrile under vacuum (to avoid any interference of dioxygen) gave azoxybenzene and 1,4-benzoquinone monoxime (**5**), as shown in Scheme 4. However, compared to the yield of **2**, the yield of **5** was variable and often lower than about 60% of that expected from Scheme 4. At hydroxide concentrations lower than 0.4 mol l^{-1}, the yield of **5** diminished and became insignificant at KOH concentrations smaller than 0.1 mol l^{-1}. Compound **5** slowly decomposed under the experimental conditions; one of the decomposition routes is probably an attack by hydroxide ion on the ring of **5** similar to the attack of nucleophiles on benzoquinone with formation of unidentified, coloured compounds. The anion (or dianion) obtained on the attack of hydroxide on the benzo-



SCHEME 4

quinone derivative **5** might be a sufficiently good electron donor to transfer an electron to **1**.

Other oxidation products were considered; the pressure was monitored during the reaction and no change in the pressure was observed in 1 M KOH, indicating that no gas (dioxygen) was evolved. Photochemical reactions were excluded as the reaction was shielded from light. No hydrogen peroxide was observed by polarography in the aqueous phase after extraction of organic compounds.

In Scheme 4 a direct electron transfer from the hydroxide to **1** is excluded as the oxidation potential of OH^- is much higher than the reduction potential of nitrosobenzene. The reaction is therefore formulated as an addition of hydroxide ion to nitrosobenzene. Such an addition may take place at the nitrogen of the nitroso group or at the benzene ring. Zuman[21] has shown from polarographic evidence that hydroxide adds reversibly to the nitroso group in much the same way as it may add to a carbonyl group; a second hydroxide ion slowly deprotonates the adduct **6** to the dianion which is supposed to react with the adduct **6** to azoxybenzene.

The addition could also take place at position 4 in the benzene ring with formation of adduct **7**, the anion of 4-hydroxycyclohexa-2,5-dien-1-one oxime. Adduct **7** is probably deprotonated to the dianion which then transfers the equivalent of a hydride ion to nitrosobenzene with formation of phenylhydroxylamine anion. Phenylhydroxylamine in alkaline solution reacts with nitrosobenzene through a radical anion to azoxybenzene, whereas the adduct **7**, by losing a hydride ion (or two electrons and a proton), is oxidized to 4-nitrosophenol/1,4-benzoquinone monoxime.

The finding of Waters[19] that on reaction of *tert*-butoxide with nitrosobenzene no products were isolated resulting from an attack of *tert*-butoxide on position 4 of nitrosobenzene suggests that formation of the dianion of 4-hydroxycyclohexa-2,5-dien-1-one oxime is necessary to induce the transfer of a hydride ion or its equivalent to nitrosobenzene. This is also consistent with the finding that in 1 M KOH a good yield of 4-nitrosobenzene is obtained whereas a low yield is observed in 0.1 M KOH. The oxidation potential of the dianion is unknown; hence, an electron transfer from the latter to **1** rather than a hydride transfer cannot be excluded.

Attack of hydroxide or alkoxide ions on aromatic rings having electron attracting groups is well known[13]. Thus in acetonitrile or dimethyl sulfoxide, hydroxide ions react rapidly and reversibly with 9,10-anthraquinone to form an adduct which subsequently reacts with a second molecule of anthraquinone to form near-stoichiometric amounts of the semiquinone radical anion[23]. In deaerated acetonitrile, 1,4-benzoquinone reacts with hydroxide ion to an adduct which reduces 1,4-benzoquinone. A nearly quantitative formation of the semiquinone is observed; the oxidized adduct reacts again with hydroxide ion and ends as the tetrahydroxy-1,4-benzoquinone dianion with all hydrogens substituted with oxygens[24].

Other electron-withdrawing groups could be expected to behave similar to nitrosobenzene. However, when nitrobenzene is treated with aqueous base (0.1–0.4 M sodium hydroxide) as described for nitrosobenzene, no 4-nitrophenol is observed on a similar time scale; the organic layer turns violet and later brown. The lack of reactivity could be explained by at least three facts: (i) it is known that the nitroso group is more electron-withdrawing than the nitro group and that the benzene ring in nitrosobenzene should be thus more easily attacked by nucleophiles than nitrobenzene; (ii) the reduction potential of nitrobenzene is more negative than that of nitrosobenzene; hence, an electron transfer from adduct **8** corresponding to adduct **7** to nitrobenzene, should be slower than that from adduct **7** to nitrosobenzene; (iii) hydride ion transfer from adduct **8** to nitrobenzene is slower than that from adduct **7** to nitrosobenzene.

The nitroso group has been estimated to activate the benzene ring as much as two nitro groups[25]; 1,3-dinitrobenzene gives only traces of dinitrophenol on treatment with aqueous KOH, whereas an old patent claims that heating with solid potassium hydroxide produces 2,4-dinitrophenol[26].

Benzylviologen adds a hydroxide ion in position 2, and the adduct reduces another benzylviologen to the radical cation; the oxidized adduct loses (formally) a hydroxyl radical which is suggested to form hydrogen peroxide[13].

The reductions initiated on addition of hydroxide ions thus involve in many cases a nucleophilic attack by the hydroxide ion on the substrate rather than an electron transfer. However, the reactions are often complex and not fully understood, and electron transfer may occur from compounds formed after the initial attack of hydroxide ions. One of the problems in understanding the reactions is that the oxidized products are not always identified.

REFERENCES

1. Daasbjerg K., Pedersen S. U., Lund H. in: *General Aspects of the Chemistry of Radicals* (Z. B. Alfassi, Ed.), p. 385. Wiley, Chichester 1999.
2. a) Lund H., Daasbjerg K., Occhialini D., Pedersen S. U.: *Russ. J. Electrochem. (Transl. of Elektrokhimiya)* **1995**, *31*, 865; b) Fuhlendorff R., Occhialini D., Pedersen S. U., Lund H.: *Acta Chem. Scand.* **1989**, *43*, 803; c) Occhialini D., Pedersen S. U., Lund H.: *Acta Chem. Scand.* **1990**, *44*, 715; d) Occhialini D., Kristensen J. S., Daasbjerg K., Lund H.: *Acta*

Chem. Scand. **1992**, *46*, 474; e) Occhialini D., Daasbjerg K., Lund H.: *Acta Chem. Scand.* **1993**, *47*, 1100.
3. Pedersen S. U., Lund T.: *Acta Chem. Scand.* **1991**, *45*, 397.
4. Pedersen S. U., Lund T., Daasbjerg K., Pop M., Fussing I., Lund H.: *Acta Chem. Scand.* **1998**, *52*, 657.
5. a) Daasbjerg K., Christensen T. B.: *Acta Chem. Scand.* **1995**, *49*, 128; b) Sorensen H. S., Daasbjerg K.: *Acta Chem. Scand.* **1998**, *52*, 51.
6. Kjær N. T., Lund H.: *Acta Chem. Scand.* **1995**, *49*, 848.
7. Kjær N. T., Lund H.: *Electrochim. Acta* **1997**, *42*, 2041.
8. a) Lund T., Pedersen M. L., Frandsen L. A.: *Tetrahedron Lett.* **1994**, *35*, 9225; b) Lund T., Ohlrich D., Borling P.: *Acta Chem. Scand.* **1999**, *53*, 932.
9. Lund T., Lundgren B., Lund H.: *Acta Chem. Scand.* **1995**, *49*, 755.
10. Palacios S. M., Santiago A. N., Rossi R. A.: *J. Org. Chem.* **1984**, *49*, 4609.
11. Ahbala M., Hapiot P., Houmam A., Jouini M., Pinson J., Savéant J.-M.: *J. Am. Chem. Soc.* **1995**, *117*, 11488.
12. Minisci F.: *Top. Curr. Chem.* **1976**, *62*, 1.
13. Sawyer D. T., Roberts J. L., Jr.: *Acc. Chem. Res.* **1988**, *21*, 469.
14. Paradisi C., Scorrano G.: *Adv. Chem. Ser.* **1985**, *125*, 339.
15. Bamberger E.: *Ber. Dtsch. Chem. Ges.* **1900**, *33*, 1939.
16. Hantzsch A., Lehmann M.: *Ber. Dtsch. Chem. Ges.* **1902**, *35*, 897.
17. Reissert A.: *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 1364.
18. a) Russell G. A., Geels E. J.: *J. Am. Chem. Soc.* **1965**, *87*, 122; b) Russell G. A., Geels E. J., Smentowski F. J., Chang K.-Y., Reynolds J., Kaupp G.: *J. Am. Chem. Soc.* **1967**, *89*, 3821.
19. Hutton J., Waters W. A.: *J. Chem. Soc. B* **1968**, 191.
20. Steudel E., Posdorfer J., Schindler R. N.: *Electrochim. Acta* **1995**, *40*, 1587.
21. a) Zuman P., Fijalek Z.: *J. Org. Chem.* **1991**, *56*, 5486; b) Zuman P., Shah B.: *Chem. Rev.* **1994**, *94*, 1621.
22. Asirvatham M. R., Hawley M. D.: *J. Electroanal. Chem.* **1974**, *57*, 179.
23. Roberts J. L., Jr., Sugimoto H., Barrette W. C., Jr., Sawyer D. T.: *J. Am. Chem. Soc.* **1985**, *107*, 4556.
24. Fukuzumi S., Nakanishi I., Maruta J., Yorisue T., Suenobu T., Itoh S., Arakawa R., Kadish K. M.: *J. Am. Chem. Soc.* **1998**, *120*, 6673.
25. LeFevre R. J. W.: *J. Chem. Soc.* **1931**, 810.
26. Wohl A.: *Chem. Zentralbl.* **1901**, *I*, 149.