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New Insights into Catechol Oxidation – Application of Ammonium Peroxydisulfate in the Presence of Arylhydrazines

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Dedicated to Prof. Dr. Cristian Silvestru on the occasion of his 65th birthday

The oxidative polymerisation of catechols in the presence of amino groups is an important reaction leading to polymers or oligomers of great practical importance. We present here, the oxidative polymerisation in the presence of nitro-substituted aryl hydrazines using ammonium peroxydisulfate (APS) as oxidizing reagent in the presence of Tris-buffer. Mixtures of deeply coloured oligomers are formed and analysed by FTIR-, NMR-, ESR-spectroscopy and, in particular, by HR-ESI MS. The results provided new insight into the oxidative depletion of azo dyes with APS in industrial waste water treatment.

1. Introduction

The oxidation of catechols is an important reaction that has found applications in several fields. Thus, the oxidation of Dopa results in eumelanines playing vital roles in living organisms.[1] Dopamine is an essential neurotransmitter and a cheap commercial compound that can be easily oxidized, e.g. by autoxidation, forming polydopamine, a polymer with excellent adhering properties. Polydopamine has been applied in various fields, such as surface coatings, molecular glue, stabilizer, catalyst and in electronics.[2] Dopa and dopamine contain in addition to a catechol unit a side chain amino group. This amino group plays an important role in the oxidation process, the reaction mechanism as well as in the properties of their polymers. In the course of oligomer/polymer formation C–C bonds are built up and cyclizations involving the amino groups to form indole rings by C–N bond formation can occur. The products contain catechol and o-quinone units as well as amino groups. All of them are responsible for the outstanding adhering properties. In addition, significant radical properties were detected.[3]

Many alterations of monomers containing catechol and amino groups were developed comprising the attachment of additional substituents, variation of the length of alkyl side chain and, hitherto less investigated, replacing C-atoms in the side chain by N-atoms.[6] Most of these compounds behave similarly to Dopa or dopamine, i.e. formation of black polymers upon oxidation. In a recent approach, we investigated the oxidation of 3,4-dihydroxybenzhydrazide that turned out to be more reluctant to the usual oxidation conditions. Finally, ammonium peroxydisulfate (APS) was successful applied, the product appeared as a mixture of black oligomers but lacked the adhering properties of PDA because of missing catechol groups.[5]

Another strategy to obtain catechol-containing polymers by oxidation is based on the idea to use starting materials wherein the two structural units of dopamine, i.e. the catechol and alkylamine are found in different molecules. In this way, catechol was oxidized with air in aqueous NaOH in the presence of n-propyl amine or dodecyl amine[6] and 4-methylcatechol was treated with sodium periodate in aqueous sodium carbonate in the presence of n-propyl amine.[7] In the former case, adhesive polymers were obtained. In the latter case, analysis of the reaction mechanism and product compo-
sition appeared to be very difficult. More than sixty different products with molecular masses ranging from 179 to 704 Da were formed within five minutes, which could not be isolated. Some of them were characterized by MS and hypothesized structures were provided. It was assumed that the products were formed by Michael addition of the amine to intermediate 4-methyl-o-benzoquinone and oxidative coupling of catechol rings by C–C or C–O bond formation.

We became interested to answer the question if catechol can be oxidized in the presence of hydrazines. Unlike simple alkyl amines, hydrazines can be oxidized to form azo or azoxy compounds in addition to a usual amine reactivity. As in our previous investigations with 3,4-dihydroxybenzhydrazide,[5] we used ammonium peroxydisulfate (APS) as oxidizing reagent.

2. Results and Discussion

Treatment of equimolecular quantities of 4-nitrophenylhydrazine 1a or 2,4-dinitrophenylhydrazine 1b and catechol 2 with two equivalents of APS in Tris-buffer resulted in sparingly soluble black precipitates, containing mixtures of products that could not be separated by HPLC. Therefore, the mixtures were investigated by NMR-spectroscopy, FTIR-spectroscopy, ESR-spectroscopy and, in particular, by HR-ESI-MS.

Attempts to get sufficiently resolved $^1$H-NMR spectra of products 3 in solution remained unsuccessful (for a ss $^1$H-NMR spectrum see Supporting Information), probably because of the presence of radical moieties (v. i.). We were able to record the solid state $^{13}$C-NMR spectrum of product 3a (Figure 1 bottom). It reveals signals in the aromatic region between 110 and 140 ppm (C=C) and 140–160 ppm (C=C-N, C=C-O). In addition, peaks at higher fields i.e. 66.1 ppm could be assigned to Tris-buffer derived species. The spectrum shows significant differences from those of the starting materials (Figure 1 middle and top). It is worth mentioning that o-benzoquinone moieties are not present in 3a as characteristic signals at lower fields (about 180 ppm) are missing.

The FTIR spectrum of 3a confirms the presence of several structural elements, such as aryl-H (3000-3100 cm$^{-1}$), OH and NH (3100 – 3600 cm$^{-1}$) and, C=O 1705 cm$^{-1}$. NO$_2$ groups (1550-1560 and 1240–1350 cm$^{-1}$), C=N and C=C (aromatic) species (1630 – 1690 cm$^{-1}$), N=N 1509 cm$^{-1}$ or aromatic C–N 1106 cm$^{-1}$, C–O-C 852 cm$^{-1}$ (Figure 2).

Further structural information could be obtained from HR-ESI-MS. The HR-ESI(-)MS spectrum of the product 3a shows significant peaks in the mass range of m/z=180 – 800 (Figure 3, Scheme 3). The base peak was found at m/z=499.1004. This corresponds to a calculated chemical formula C$_{24}$H$_{15}$N$_6$O$_7$ (499.1002), i.e. it contains two units derived from 4-nitrophenylhydrazine (4 x N and 12 x C) and two units derived from catechol (12 x C), while one O-atom is missing. Thus, it is likely that two catechol units are connected by a C–O–C bridge while one OH group is lost, as in structure 3a–499. A related structure 3a–515 wherein the C–O–C bridge is formed without the elimination of an O-atom from a catechol unit is confirmed by an intensive MS-peak at 515.0952 (calcd. 515.0951 for C$_{24}$H$_{15}$N$_6$O$_8$). The number of H-atoms in both ion peaks is reduced by 6 due to the C–O–C bond formation and transformation of the hydrazine moieties into azo structures. Azo-formation is also confirmed by the peak at 258.0519 (calcd. 258.0519 for C$_{12}$H$_7$N$_2$O$_2$).

Figure 1. Solid state $^{13}$C-NMR spectrum of product 3a (bottom), catechol (middle) and 4-nitrophenylhydrazine (top).

Figure 2. FTIR-spectrum of product 3a.

Figure 3. HR-ESI(-)MS of product 3a.
Remarkably, mass peaks, e.g. in 3a-379 and 3a-620, are found where a 4-nitrophenylhydrazine unit lose the N-N fragment, thus connecting the 4-nitrophenyl unit directly to the catechol moiety. The peak at 394.0789 counting for a composition of C_{18}H_{12}N_{5}O_{6} (calcd. 394.0789) gives evidence for products formed without the involvement of catechol, while aryl moieties are connected to the hydrazine N-atoms. Related triarylhydrazines were reported in the literature, but were obtained in different ways.\(^{[8]}\) The peak at 137.0359 can be ascribed to 4-nitrophenylamine. Since its formation is unlikely under oxidation conditions, it is probably formed as a fragment peak of a 4-nitrophenylhydrazine/one unit. Considering all these structures shown in Scheme 3 and also isomers not shown (different connectivity or tautomers, such as hydroxyl-azo versus o-quinone hydrazone as shown in 3a-379), it is understandable that the material does not have adhering properties to solid surfaces, unlike PDA, because of missing catechol moieties and basic aliphatic amino groups. Furthermore, the structures are much different from products obtained by the reported oxidation of catechol in the presence of aliphatic amines (see Scheme 1).\(^{[7]}\)

In general, the formation of the structures 3a shown in Scheme 3 can be understood by combining three major pathways, wherein either the catechol or the arylhydrazine or both are oxidized (see Scheme 4). Transformation of catechol \(\mathbf{2}\) into the o-benzoquinone \(\mathbf{5}\) is a typical reaction. The latter represents a Michael system that can react with amino groups in a 1,4-addition (Way A) as known in polyDopa and polydopamine chemistry resulting in the hydrazinocatechol \(\mathbf{7}\). Subsequent formal dehydrogenation results in azo compounds \(\mathbf{8}\) similar to the structure of known azo dyes. Such compounds are conventionally synthesized by azo coupling.\(^{[9]}\) As an alternative, the radical \(\mathbf{4}\) formed by oxidation of catechol can be expected to react with o-benzoquinone \(\mathbf{5}\) (way C) to form a C–O–C bridged fragment \(\mathbf{15}\) via intermediates \(\mathbf{13\text{ and 14}}\). Similar dimerizations of catechol were reported in oxidation reactions of dihydroxynaphthalenes\(^{[10]}\) or pyrogallols.\(^{[11]}\) The
oxidation/dehydrogenation product of arylhydrazine such as aryldiazenes 9 can form aryl radicals 10 in the further course of oxidation. These are able to undergo C−C-coupling with catechol or catechol containing species in a Sandmeyer-type reaction[12] (way B) forming diaryl structures such as 12. Arylation of electron rich aromatic compounds by aryl hydrazines with the elimination of dinitrogen was observed in air-oxidation in DMSO/K2CO3.[13] Aryl radicals 10 may also be involved in the formation of triaryldiazines 16.

It is known from polydopamine chemistry that Tris (2-amino-2-(hydroxymethyl)propane-1,3-diol) used as buffer can be incorporated into the product by Michael addition or azomethine formation.[14] In fact, in our case, species (e.g. 3a-757) containing Tris moieties can be detected in the HR-ESI-MS (Scheme 5). Interestingly, this species also contains a sulphate unit. Such a process finds its analogy in the well-known Boyland-Sims oxidation of anilines with APS where sulphate enters into ortho position to the amino group in an early step.[15]

The HR-MS detection of the 4-nitro-3',4'-dihydroxyazo benzene 2a-258 in the course of the APS-oxidation of 4-nitrophenylhydrazine in the presence of catechol raised another interesting question. Can this species act as an intermediate in the formation of other species detected in the HR-MS spectrum of 3a? Thus, we synthesized 4-nitro-3',4'-dihydroxyazo benzene by azo coupling of 4-nitrophenyl diazonium salt with catecho[16] and submitted it to oxidation with APS in Tris buffer. A black product 17 was formed sparingly soluble in DMSO/methanol, which could not be purified by chromatography.

Its FTIR spectrum (Figure 4) is very similar to that of 3a. Significant differences are found in the CH region between 2800 and 3000 cm−1.

HR-ESI(−)-MS revealed that 17 is a mixture of products. The comparison with the HR-ESI(−)-MS spectrum of the APS-mediated oxidation mixture 3a obtained from 4-nitrophenylhydrazine and catechol revealed both differences and similarities.

Figure 4. FTIR spectrum of product 17 in comparison with product 3a.
Remarkably, all significant peaks observed with 17 were also found with 3a. This fact supports the assumption that 3–258 can act as intermediate in the formation of 3a. It further implies that other processes are involved, accompanied by the loss of nitrogen atoms and C–C-aryl coupling as shown in Scheme 4. The loss of nitrogen in the course of the transformation of 3–258 (C12H12N4O4 calcd. C 55.60%, H 3.50%, N 16.21%) into product 17 mixture (found C 53.58%, H 3.28%, N 11.58%) was confirmed by elemental analysis. This decrease of the N-content corresponds to a loss of almost one N-atom per one molecule of starting material 1. Interestingly, APS has been considered as reagent to purify waste water appearing in the production of azo dyestuffs.\textsuperscript{[17]} Respective investigations sometimes focus only on the disappearance of the dyestuff without thorough analysis of the decomposition products.\textsuperscript{[18]} Our results show that oligoaryl compounds can be formed by the loss of both nitrogen atoms of the azo group whose environmental issue might be questionable. It is worth mentioning that investigations of the enzyme-catalyzed autoxidation of phenolic azo dyes showed that aryl radicals are formed being transferred into aryl hydroperoxides.\textsuperscript{[19]}

The ss $^{13}$C-NMR of the product mixture 17 showed some similarities to that of 3a. However the ratio of intensities of the signals in the range of 110–130 ppm compared with 140–160 ppm is reversed, i.e. more aromatic carbon atoms are present connected to N- or O-atoms. Furthermore weak broad signals were observed between 170 and 180 ppm that could count for carbonyl carbon atoms such as in o-benzoquinone moieties or imine carbon atoms.

The APS oxidation of a mixture of 2,4-dinitrophenylhydrazine, catechol and Tris buffer resulted in a black solid material 3b (see Scheme 2). Its FTIR spectrum resembles that of 3a (see Figure 7 and 2).

As compared with the product 3a obtained from 4-nitrophenylhydrazine 2a and catechol the ss $^{13}$C-NMR spectrum of the 2, 4-dinitrophenyl product 3b shows much more intense signals in the region 135–150 ppm due to the higher number of aromatic C-atoms substituted by N-atoms as found in nitro groups. Low intensity broad signals at around 176 ppm could be interpreted as C=N carbon atoms.

The HR-(-)-ESI-MS revealed peaks (Figure 9, Scheme 7) that were similar to the case of 4-nitrophenylhydrazine/catechol oxidation. Again, azo species could be assigned and, more abundant, C–C-coupling products wherein the 2,4-dinitrophenyl moiety was introduced into the catechol by the loss of the azo group. This elimination of N-atoms was confirmed by elemental analysis (starting materials 1b + 2: C12H12N4O4 calcd. C 46.76%, H 3.92%, N 18.18%) of the product 3b (found C 50.10%, H 2.76%, N 14.44%). The base peak at 182.0202 in the HR-(-)-ESI-MS of 3b is assigned to 2,4-dinitroaniline. The formation of aryl amines in the Fe-catalyzed oxidation of diazo dyes with persulfate was reported.\textsuperscript{[17a]} Eventually, this peak could also be a fragment peak.
The failure of obtaining well resolved solution NMR-spectra of compounds 3 and 17 led us to the conclusion that paramagnetism is responsible for this phenomenon. Therefore, we performed EPR spectroscopy of the samples 3a, 3b and 17 (Figure 10). All samples show similar behaviour. The spectra display a symmetric and relatively large line. The EPR spectral parameters: linewidth ($\Delta H$) and g-value evaluated from spectra are presented in Table 2. Slight variation of g factor and linewidth could be observed.

The EPR spectra of eumelanins, obtained by air oxidation of Dopa, wherein catechol and amino groups are covalently linked, presented in the literature was interpreted by Mostert et al. as a coexistence between two type of radicals: C-centred radical characterized by a g factor of 2.0036 and semiquinone radical with a $g \sim 2.0045$. The g-factor of samples 3a and 3b are closed to the g-value specific for C-centred radicals (Table 2), which might suggest that this radical is preponderant in these samples in contrast with sample 17, which has a g-factor closed to a semiquinone radical.

**Figure 9.** HR-ESI(-)-MS of product 3b.

**Scheme 7.** Assignment of some peaks in the HR-ESI(-) mass spectrum of product 3b.

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**Figure 10.** X-band EPR spectra of (a) 3a, (b) 3b and (c) 17 measured at room temperature.

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>Identical mass peaks (HR-ESI(-) MS) found in the APS-oxidation products 17 and 3a obtained from 4-nitro-3',4'-dihydroxy azobenzene 3–258 or 4-nitrophenylhydrazine 2a and catechol, respectively.</th>
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<tr>
<td><strong>m/z</strong></td>
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<td>8.0%</td>
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</table>

[a] relative peak intensity

<table>
<thead>
<tr>
<th>Table 2.</th>
<th>EPR spectral parameters of products 3a, 3b and 17.</th>
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<tbody>
<tr>
<td>Sample</td>
<td>$\Delta H$ (G)</td>
</tr>
<tr>
<td>3a</td>
<td>10</td>
</tr>
<tr>
<td>3b</td>
<td>8</td>
</tr>
<tr>
<td>17</td>
<td>9</td>
</tr>
</tbody>
</table>
To highlight the presence of these radicals in our samples, deconvolution of the absorption spectra of 3a, 3b and 17 obtained by integration of the EPR spectra was performed (see Figure 11). A pseudo-Voight function was used for deconvolution. We considered an isotropic g-value for the two radicals to avoid to over-parametrize the deconvolution. But usually both the carbon and the semiquinone radical are characterized by an anisotropic g-factor due to the coexistence of several species.[21]

Because of this limitation, only an approximate deconvolution could be achieved. It can be observed that C-centred radicals and semiquinone radicals are present in all samples.

Since the area under the integrated absorption curves (l) is proportional with the number of spins of each free radical,[22] the value of these areas corresponding to each radical was calculated and is provided in Table 2. Interestingly, it can be observed that the C-centred radical is predominant for sample 3a and 3b and the semiquinone radical for sample 17.

3. Conclusion

The oxidation of catechol with ammonium peroxydisulfate (APS) in the presence of nitro-substituted arylhydrazines leads to black, solid, inseparable product mixtures. Their analytical investigation by HR-ESI-MS, FTIR-, $^{13}$C-NMR- and ESR-spectroscopy showed that oligomers are built by C–C, C–O, and C–N bond formation, in some cases by the loss of the hydrazine N-atoms. These oligomers contain aryl-aryl, aryl-O-aryl and aryl-N=N structural elements, amongst them radical species and diaryl azo compounds as known in dye stuffs. Such a dihydroxydiaryl-azo compound was synthesized separately and oxidized with APS leading to a number of products also found in the oxidation of the catechol arylhydrazine mixture. This suggests that this azo dye acts as an intermediate in the APS-oxidation of arylhydrazine/catechol. On the other hand, this result provides new insight into the waste water treatment with APS in azo dye industries. EPR investigations revealed that C-centered radicals and semiquinone radicals are present in the oxidation products obtained by APS-oxidation of arylhydrazines/catechol or of the azo dye. New insight into the oxidation chemistry of catechol are provided, since the structures of the products obtained here, differ much from known cases where the oxidation was performed in the presence of aliphatic amines.

Figure 11. Deconvolution of the integrated EPR spectrum corresponding to samples: (a) 3 a, (b) 3 b and (c) 17. Two radicals were used for deconvolution: C-centred radical - R1 (g ∼ 2.0036) and semiquinone radical- R2 (g ∼ 2.0045).
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Conflict of Interest

The authors declare no conflict of interest.

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