Oxidation of organic amide ions by dioxygen.
2*. Stable and intermediate products

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The products of base-catalyzed oxidation of secondary aromatic amines were identified by the GC-MS and EPR techniques as nitroxyls, quinone nitrones, quinone imines, and for diarylamines also as the products of C—N bond cleavage-substituted nitrobenzenes, anilines and phenols. It was shown that nitroxyl radicals are the primary paramagnetic products of the reaction and do not form by the interaction of aminyl radicals with dioxygen. A mechanism of the amide ion oxidation through the nonradical addition of dioxygen to the amide ion at the rate-limiting stage is suggested and discussed.

Key words: aromatic amines, amide ions, oxidation, dioxygen, mechanism, nitroxyl radicals, synthesis.

Analysis of the literature reveals that currently there are no generally accepted concepts of the mechanism of aromatic amine oxidation by molecular oxygen. Base-catalyzed oxidation of primary amines is studied most intensively. The oxidation of substituted anilines and naphthylamines is characterized by the formation of azobenzene or phenazine derivatives, respectively[2—4], as well as nitroso- and nitro compounds[3,4].

Secondary aromatic amines (SAA), which possess sufficiently reactive C—H bonds in the α-position with respect to the amino group, are oxidized in the presence of bases with cleavage of the C—H and C—N bonds[4]. In the suggested schemes and mechanisms of the organic amide ion oxidation, the majority of the intermediates were assumed to explain the observed set of reaction products[2—4]. Only one early work[5] showed by EPR, that during oxidation of diphenylamine and phenyl-2-naphthylamine in the mixture of toluene and alcohol alkali, several types of paramagnetic species were formed, nitroxyl radicals being the most stable ones.

The wide variety of products in the base-catalyzed oxidation of aromatic amine and, especially, the formation of the C—N- and N—N-condensation products[2—4] were explained by the aminyl radical formation during the interaction of amide ions with dioxygen. These radicals enter the reactions of disproportionation, oxidation and C—N- or N—N-recombination. However, the complicated set of oxidation products observed for the aromatic amines in the basic media can not be sufficient justification for a free-radical reaction mechanism. This is why, to establish the mechanism of the base-catalyzed oxidation of aromatic amines, we have investigated the nature of intermediates, as well as the consecutive order and kinetic patterns of the stable product formation.

Results and Discussion

Paramagnetic oxidation products of the secondary amines in strongly basic media

Oxidation of the majority of tested secondary aromatic amines** in strongly basic media is accompanied by the formation of paramagnetic species (Fig. 1, *a*—*c*). These species were identified by comparing their EPR spectra with the published data concerning hyperfine splitting (HFS) of the spectra of nitroxyl and aminyl radicals with the proposed or similar structures (see Table 1).

The comparison of EPR spectra of SAA oxidates measured at various depths of reaction revealed no differences between them, except the line broadening with an increase in nitroxyl radical concentration. This allows us to consider that nitroxyl radicals are the major paramagnetic products of the SAA oxidation both with deep amine conversions and at early reaction stages. The yield of nitroxyl radicals in the base-catalyzed oxidation of secondary amines (SA) depends largely on their stability and reaction conditions and varies from fractions

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* The previous report see Ref. 1.

** Structural formula of amines **1—12** and the main experimental techniques of the SAA oxidation in the strongly basic media see in Ref. 1.

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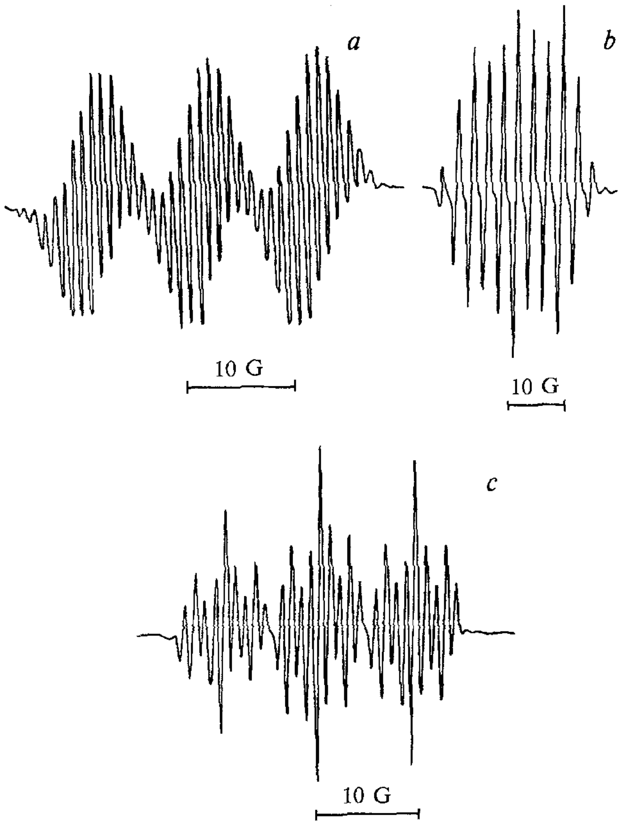


Fig. 1. EPR spectra of paramagnetic species observed during base-catalyzed oxidation of SA (DMSO; 25 °C; Ar): *a*, 4,4'-di-*tert*-butyl diphenylamine-*N*-oxyl; *b*, 4,4'-dimethoxydiphenylaminyl radical; *c*, anion radical of 4-*tert*-butyl nitrobenzene.

of a percent (amines **1**, **3**, **4**, **7**) to tens of percent (amines **2**, **5**, **6**, **9**).

Table 1. EPR spectral parameters of nitroxyl radicals ($R_2NO^{\cdot}$) in the base-catalyzed oxidation of SA (DMSO; 25 °C; Ar)

HFS constants/G	Amine*								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**9**	**11**
a^N	12.0	10.6	10.1	10.1	10.2	10.4	9.8	12.1	14.8
a^H_o	2.7	1.9	1.9	1.9	1.9	—	2.3	2.8	—
a^H_m	—	0.94	0.93	0.95	0.95	—	—	—	—

* In the oxidation of amines **8** and **10**, the formation of nitroxyle radicals was not detected.

Along with nitroxyl radicals, the other nitrogen-containing paramagnetic species can be observed during the base-catalyzed oxidation of SA under certain conditions. Thus, when the reaction is interrupted at an early stage of oxidation by discontinuing the oxygen supply (*e.g.*, by bubbling argon through the reaction mixture), the consumption of nitroxyl radicals is observed by EPR. The rate of the process depends on the solvent and is especially high in DMSO. In some cases (amines **4**, **5**, **6**), the consumption of nitroxyl radicals is partly or completely reversible: when oxygen is bubbled through the reaction mixture, the intensity of EPR signal increases sharply. A similar picture is observed in the oxidation of amines **1** and **2**: discontinuation of the oxygen supply also results in the disappearance of the EPR signal of the nitroxyl radical. However, in these cases, the signals of new paramagnetic species appear on a background of the nitroxyl signals. These particles were identified as the corresponding aminyl radicals by their HFS parameters and characteristic ratio of the isotropic (a^N) and anisotropic (b^N) HFS constants (see Table 2 and Fig. 1, *b*). According to the published data, the a^N/b^N values typical for aromatic nitroxyl radicals vary from 1.27 to 1.36[6], whereas for aminyl radicals the range is $a^N/b^N = 1.05 \pm 0.05$[7]. For the radicals formed from compounds **2**—**7** under aerobic conditions, we found $a^N/b^N = 1.33 \pm 0.05$. This confirms the validity of their classification as nitroxyls. At the same time, the value of a^N/b^N parameter for the new paramagnetic species, which appeared under anaerobic conditions, is close to those of aminyl radicals.

Paramagnetic species of the third type, which were identified as the anion radicals of 4-nitro-*tert*-butyl benzene (Fig. 1, *c*), were observed during base-catalyzed oxidation of amine **5** in DMSO in the presence of catalytic amounts of Co^{2+} stearate. The HFS parameters of EPR spectrum of this particle are listed in Table 2. It is noteworthy that the value $a^N/b^N = 1.20$ appears to be

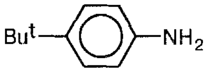
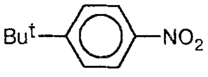
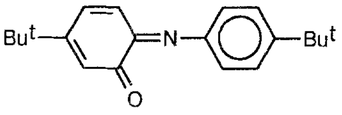
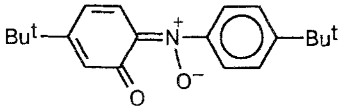
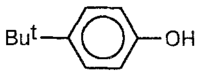
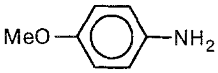
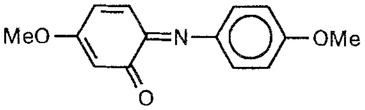
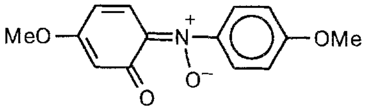
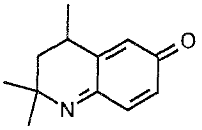
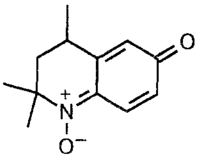
Table 2. EPR spectral parameters of paramagnetic particles observed in the oxidation of SA (DMSO; 25 °C; Ar)

Amine	HFS constants/G			a^N/b^N	Radical identified
	a^N	a^H_o (= a^H_p)	a^H_m		
1	12.0	2.7		1.33±0.05	$>NO^{\cdot}$
	7.0	2.7		—	$>N^{\cdot}$ *
2	10.6	1.9	0.94	1.33±0.05	$>NO^{\cdot}$
	7.8	2.6		0.87±0.07	$>N^{\cdot}$ *
5	10.2	1.9	0.95	1.33±0.05	$>NO^{\cdot}$
	10.15	3.15	1.05	1.19±0.07	$>NO^{\overset{-}{\cdot}}$ **

* Observed upon bubbling of argon through the oxidate at the initial stages of the reaction.

** Observed when the reaction is conducted in the presence of $2 \cdot 10^{-4}$ mol L^{-1} $CoCl_2$.

Table 3. Products of base-catalyzed oxidation of SA in DMSO, identified by GC-MS (electron impact, 70 eV)

Amine	Major ions, *m/z* (*I* (%))	Compound identified	Molecular mass
5	149(25), 134(100), 118(13), 106(22), 91(12), 78(12)		149
	179(12), 164(100), 136(11), 134(13), 115(24), 91(30), 78(31), 62(30)		179
	295(80), 280(100), 264(32), 249(45), 134(28)		295
	311(75), 296(100), 280(15), 266(12), 141(25)		311
	150(50), 136(98), 119(14), 95(36), 91(68), 77(100)		150
2	123(80), 107(100), 80(16), 65(5), 62(9)		123
	243(74), 228(100), 213(18), 198(20), 81(25)		243
	259(75), 244(100), 229(20), 228(22), 213(15)		259
3	189(31), 174(100), 160(9), 158(7), 144(22), 132(12), 130(11)		189
	205(27), 190(100), 175(9), 174(6), 60(14)		205

sufficiently characteristic for the anion radicals of aromatic nitro derivatives, because we obtained the same value for the anion radical of nitrobenzene as well.

Diamagnetic products of oxidation of secondary amines in strongly basic media

The main data about qualitative composition of the low-molecular-weight reaction products have been obtained by GC-MS. The oxidation products of amine **5** are studied in greatest detail; their qualitative composition is listed in Table 3. A similar product set was observed during base-catalyzed oxidation of amines **2** and **9**, although in the latter case there were no products of C—N cleavage (see Table 3).

In the electron absorption spectra of the amine **9** oxidation products in DMSO, absorption bands (AB) were observed at λ = 295, 375 and 520 nm. The AB at 295 and 375 nm agree with the absorption spectra of quinone imines (λ_{max} = 290 nm)[8] and quinone nitrons (λ_{max} = 371 nm)[9], which were also identified by GC-MS. The broad weak band at λ_{max} = 520 nm we can tentatively assign to the absorption of the oligomeric products of the amine N—N and C—N condensation.

Base-catalyzed oxidation of SAA in DMSO is characterized by an intense green color of the solution. The color appears a few minutes after the reaction beginns and lasts throughout the oxidation (amine **2**) or for a prolonged time (amines **3**, **4**), or quickly turns red-brown (amines **5**, **6**). In all cases, the green color results from the formation of oxidation products, which possess a broad AB near 640 nm. These species can tentatively be assigned to the products of diarylamine N—N and C—N condensation.

Thus, base-catalyzed oxidation of SA yields a wide variety of products and intermediate species. To elucidate the pathways of their formation and role in the oxidation process, a number of kinetic studies were undertaken.

Kinetic patterns of formation and consumption of nitroxyl radicals

During the base-catalyzed oxidation of secondary amines, the EPR method demonstrates either continuous growth of the nitroxyl radical concentration, or its variation through an extremum. The first pattern of kinetic behavior is typical for amines **2**, **5**, and **6**, which produce stable nitroxyl radicals. The second pattern is typical for amines **1**, **3**, **4**, **7** and **9**, oxidation of which leads to the formation of radicals with lesser stability.

We have used the oxidation of amine **5** as a model reaction for studying kinetic patterns of the nitroxyl radical formation. When **5** is oxidized in DMSO at room temperature, the rate of nitroxyl radical accumulation increases with an increase in the initial concentrations of base and amine as well as in oxygen pressure. The formation of nitroxyl radicals exhibits the following reaction orders with respect to the system components: $n_{O_2} = 0.9$, $n_{R_2NH} = 1.2$, $n_{KOH} = 0.7$.

The yield of the nitroxyl radical is strongly affected by the solvent. In the series of solvents tested (except DMSO), the rate of nitroxyl radical accumulation and its yield change in the same general order as the rate of amine oxidation (the yield of nitroxyl radical after 24 h is given in parentheses): chlorobenzene (65—70 %) > toluene (45—50 %) > THF (30—35 %). In DMSO, the yield of the nitroxyl radical is only 10—12 %, although the rate of amine oxidation measured by oxygen consumption is maximal.

The reaction stoichiometry (the ratio of the amount of oxygen consumed to the amount of the nitroxyl radical formed) varies from 1 in chlorobenzene (at the amine conversion < 50 %) to 10 in DMSO. Note the relation between the high yield of the radical and the low stoichiometry of oxygen consumption. This relation is grounds for believing that there exists a reaction pathway such that the consumption of 1 mole O_2 per 1 mole of amine produces 1 mole of nitroxyl radical.

As indicated above, when SA oxidation is interrupted at an early stage by purging the reaction mixture with argon, one can observe the disappearance of the accumulated nitroxyl radicals by EPR. We have suggested that an electron transfer takes place under these conditions:

$$R_2NO^{\cdot} + R_2N^- \longrightarrow R_2NO^- + R_2N^{\cdot}\ .$$

The aminyl radicals thus formed generally disappear rapidly, but if they are relatively stable and actively generated, the radicals are directly detectable by EPR (*e.g.*, during oxidation of **1** and **2**).

The possibility of the reaction under discussion occuring was tested under the model conditions: amine **5** and the corresponding nitroxyl radical were dissolved in certain proportion in DMSO under inert gas and the reaction was initiated by adding the alkali. The R_2N^- concentration was monitored spectrophotometrically and the $R_2NO^{\cdot}$ concentration was measured by EPR. Under such conditions, the kinetics of $R_2NO^{\cdot}$ disappearance is described by the equation

$$W = k[R_2NO^{\cdot}]\cdot[R_2N^-]$$

with the rate constant $k = 7.5\pm0.4$ L mol^{-1} s^{-1}.

When **5** was replaced with **2**, we observed the appearance of the EPR signal of aminyl radicals, which were generated from **2** under similar conditions. The fact that $R_2NO^{\cdot}$ regenerates after the system is supplied with oxygen is evidence that the interaction between $R_2NO^{\cdot}$ and R_2N^- leads to an electron transfer from the amide ion to the radical. Such regeneration, which takes place at rates two orders of magnitude higher than that of radical accumulation during base-catalyzed oxidation of SA, evidently takes place due to rapid oxidation of diarylhydroxylamine anions by oxygen:

$$R_2NO^- + O_2 \longrightarrow R_2NO\cdot + O_2^{\overline{\cdot}}$$

$$R_2NO^- + O_2^{\overline{\cdot}} \longrightarrow R_2NO\cdot + O_2^{2-}$$

Provided a large excess of the amine to maintain nearly constant concentration of the amide ions, the cycle {$R_2NO^{\cdot}$ consumption under inert gas — $R_2NO^{\cdot}$ regeneration after a brief purging of the system with oxygen} can be repeated many times (Fig. 2).

Thus, a high concentration of amide ion may lead to a decrease in the yield of stable nitroxyl radicals, and this is the probable cause of the abnormally low yield of the nitroxyl radicals during the oxidation of **5** in DMSO as compared to less polar solvents (less basic media).

It seems likely that relatively stable aminyl radicals generated from amines **1** and **2** not only recombine but

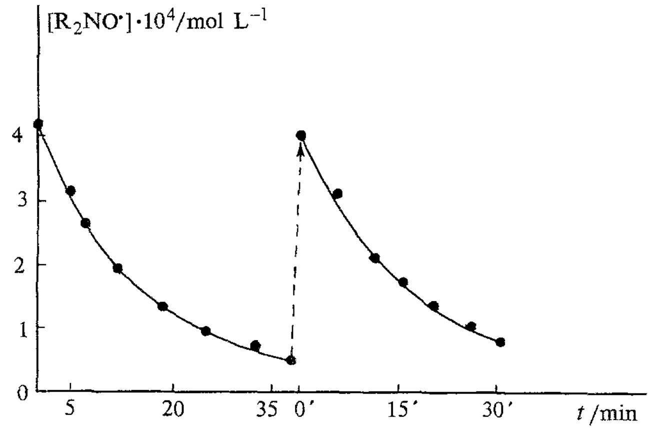


Fig. 2. Variation of the nitroxyl radical concentration during amine **5** oxidation in the system DMSO+KOH+18-crown-6 upon consecutive bubbling of argon and oxygen through the oxidate. DMSO; 25 °C; $[R_2NH]_0 = 8 \cdot 10^{-4}$ mol L^{-1}, $[KOH]_0 = 1.6 \cdot 10^{-2}$ mol L^{-1}. The broken line denotes the points where oxygen is bubbled through the system.

also enter the reaction of cross-disproportionation with nitroxyl radicals. This is evident from the appearance of an EPR signal of aminyl radicals only after virtually complete disappearance of the EPR signal of the nitroxyl radicals. The amount of aminyl radicals therewith corresponds to no more than a few percent of the initial nitroxyl concentration. EPR signals of aminyl radicals, generated from amines **1** and **2**, can be observed in the solution for several hours. They are retained when oxygen is introduced into the system (in the case of amine **2**) or disappear without formation of an EPR signal of nitroxyl radicals (in the case of amine **1**).

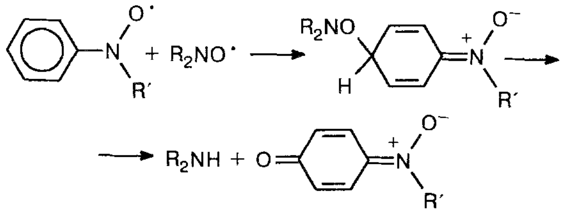
The presence of quinone imines and quinone nitrons among the oxidation products of **2** (unlike oxidation of amine **5**) prompts the hypothesis that the following reaction sequence occurs under the conditions described above:

$$R_2NO^{\cdot} + R_2N^- \longrightarrow R_2NO^- + R_2N^{\cdot}$$

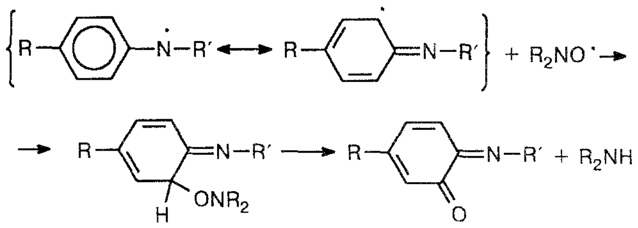
$$2\ R_2N^{\cdot} \rightleftharpoons (R_2N)_2$$

$$R_2NO^{\cdot} + R_2N^{\cdot} \longrightarrow R_2NH + \text{quinone imine}$$

Disproportionation of aminyl and nitroxyl radicals may proceed according to a mechanism similar to that reported for the disproportionation of aromatic nitroxyl radicals[10] and involving the formation of quinone nitrons:



This disproportionation may be the main source of quinone imines during the oxidation of secondary aromatic amines:



Although nitroxyl radicals were not detected in the $R_2N^{\cdot}$-containing solutions even upon their saturation with oxygen, the question of the possibility of $R_2NO^{\cdot}$ formation by direct interaction between $R_2N^{\cdot}$ and O_2 remains open, because the newly formed nitroxyl radicals can rapidly be eliminated according to the scheme reported above.

The mechanism of secondary aromatic amine oxidation in strong basic media

Based on the above discussion as well as previously obtained[1] data concerning the set of products and kinetics of base-catalyzed oxidation of SAA, which contain no C—H bonds in the α-position with respect to the amino group, the following reaction mechanism can be suggested:

$$R_2NH + OH^- \rightleftharpoons R_2N^- + H_2O \tag{1}$$

$$R_2NH + OH^- \longrightarrow RNH_2 + RO^- \tag{2}$$

$$R_2N^- + O_2 \longrightarrow R_2NO_2^- \tag{3}$$

$$R_2NH + R_2NO_2^- \longrightarrow R_2NOH + R_2NO^- \tag{4}$$

$$R_2NO_2^- \longrightarrow RNO_2 + R^- \tag{5}$$

$$2\,R^- + O_2 \longrightarrow 2\,RO^- \tag{6}$$

$$R_2NO^- + O_2 \longrightarrow R_2NO^{\cdot} + O_2^{\cdot -} \tag{7}$$

$$R_2NOH + O_2^{\cdot -} \longrightarrow R_2NO^{\cdot} + HO_2^- \tag{8}$$

$$R_2NO^{\cdot} + R_2N^- \longrightarrow R_2NO^- + R_2N^{\cdot} \tag{9}$$

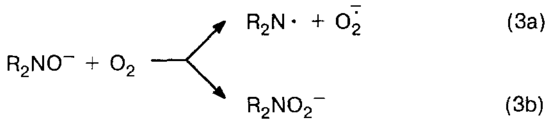
$$R_2N^{\cdot} + R_2N^{\cdot} \longrightarrow \text{recombination products} \tag{10}$$

$$R_2NO^{\cdot} + R_2N^{\cdot} \longrightarrow R_2NH + \text{quinoine imine} \tag{11}$$

$$R_2NO^{\cdot} + R_2NO^{\cdot} \longrightarrow R_2NH + \text{quinoine nitron} \tag{12}$$

At the first step of the reaction, the amine is ionized yielding an amide ion, which undergoes subsequent oxidation. At a low rate of amine ionization (*e.g.*, during oxidation of amines with a $pK_a > 25$, or when the reaction is conducted in aprotic solvents of low polarity), this step may limit the oxidation rate.

In most cases, the rate-limiting step in the oxidation of secondary aromatic amines manifests itself as the interaction of the amide ion with oxygen (step 3). The published data concerning the mechanisms of interaction between anionic forms of substrates and O_2 are grounds for suggesting two possible routes for this step.



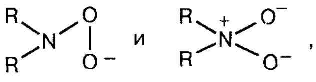
During alkaline oxidation of C—H acids, alcohols, ketones, and sulfides, the key step of the reaction is the interaction of carbanions (or sulfide ions) with O_2 that proceeds according to a single-electron mechanism with the formation of free radicals (route 3a). As this takes place, the reaction is markedly accelerated in the presence of catalytic amounts of strong electron acceptors[11].

For the oxidation of SAA, special experiments have shown that introduction of such electron acceptors as $PhNO_2$, $R_2NO^{\cdot}$, Co^{3+}, Cu^{2+}, Fe^{3+} virtually does not affect the oxidation rate. This prompts the suggestion that, during the oxidation of amide ions, unlike carbanions, the interaction with oxygen occurs according to the nonradical route (3b). This suggestion is also supported by the following arguments:

— aminyl radicals are not detectable by EPR during the oxidation;

— aminyl radicals are clearly not the precursors of nitroxyl radicals. During the interaction of anaerobically generated $R_2N^{\cdot}$ radicals with O_2, no formation of $R_2NO^{\cdot}$ is observed even in those cases when base-catalyzed oxidation leads to accumulation of large amounts of nitroxyl radicals.

Two isomeric forms can be proposed for the intermediate anion $R_2NO_2^-$:



but now it is impossible to decide between them. The nitroxyl radicals therewith may be formed according to the reaction sequence (4, 7, 8); where step 4 involves the anion $R_2NO_2^-$ (in one of the possible forms) as the donor of an oxygen atom.

The aminyl radicals are most likely the secondary products of the reaction and form in step (9), whose possibility was proved above.

As can be seen from Table 3, the products of the C—N bond cleavage (substituted anilines, nitrobenzenes, and phenols) are also obtained in the oxidation. We believe that these products are formed according to overall reactions (2, 5, 6). Reaction (2) occurs appreciably only in the system DMSO+KOH+18-crown-6, especially at elevated temperatures. This reaction does not involve an oxidant, because it takes place both under oxygen and under inert gas. The phenolate anions formed thereby are relatively resistant to base-catalyzed oxidation and do not affect the rate of SA oxidation.

Splitting of the intermediate species $R_2NO_2^-$ (reaction 5) may be the source of substituted nitrobenzenes, which were found in small amounts among the products of diarylamine oxidation. This reaction can probably be catalyzed by transition metal compounds, because in their presence, the yield of nitro compounds (detected in the form of corresponding anion radicals) increases substantially, while the yield of nitroxyl radicals decreases. The carbanions formed in reaction (5) are probably rapidly oxidized to substituted phenols according to the overall reaction (6).

The scheme proposed here provides a qualitatively adequate description of the set of products and the kinetic patterns of the SAA oxidation in strongly basic media. At the same time, the stages involving the assumed products of dioxygen attachment to the amide ions — the $R_2NO_2^-$ species — require further theoretical and experimental investigations.

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