Reactions of an Indolinonic Nitroxide with Superoxide Radical Anion in the Presence of Alkylhalides. Unexpected Formation of a Reduced Transposed Product

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This study concerns the reactions of 2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl and 2,2,6,6-tetramethylpiperidine-1-oxyl with alkylperoxyls, generated from potassium superoxide and a series of alkylhalides, in order to evaluate possible differences in reactivity with primary, secondary and tertiary alkylperoxyls. To better understand the reactivity of the studied indolinonic aminoxyl in alkaline medium, the investigation was extended to its reactions with potassium hydroxide and potassium *tert*-butoxide in different solvents.

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Introduction.

The reactions of organic compounds with atmospheric oxygen are some of the most important of all chemical processes. In fact respiration and combustion are essential for human life, and autoxidation is becoming of great importance because of its implication in several pathologies and in deterioration of biological and organic substrates.

The phenomena proceeds mainly by a free-radical chain process which involves peroxy radicals. There is an accumulating body of evidence indicating that nitroxide radicals (aminoxyls) protect against these processes. In fact, aminoxyls are a particular group of antioxidants which selectively react with potentially toxic free radicals and to which a SOD (superoxide dismutase) mimic activity has been attributed [1-3]. Most of these studies have involved piperidine nitroxides such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO). However, in recent years, our group has focused its attention on a different class of nitroxides, namely indolinonic [4] and quinolinic [5,6]. These aminoxyls have been shown to react efficiently with all kinds of radicals. They couple with carbon-centered radicals affording alkylated hydroxylamines [7-10], and with all oxygen-centered radicals, such as hydroxyl (HO·) [10,11], alkoxyl (RO·) [7,10,12] and peroxyl (ROO·) [10,12] radicals, to form paramagnetic and non-paramagnetic compounds.

Because primary, secondary and tertiary alkyl radicals and their correponding peroxyls could be involved during polymer and biological autoxidation chain, and because aminoxyls may be used to inhibit this process, the aim of this work was to test different types of peroxyl radicals with an indolinonic and a piperidinic aminoxyl to understand if the different structure of the alkyl moiety of the peroxy radical may influence its reactivity and the path of the reaction. Up to date, due to their commercial availability, only *tert*-butyl and cumyl peroxyls [12] have been studied towards indolinonic and quinolinic aminoxyls [10,12]. The peroxyls studied in this work were generated by nucleophilic substitution of superoxide anion on alkyl halides [13-16]. The obtained results showed that superoxide reacts more rapidly with the indolinonic aminoxyl than with alkyl halides so that the formation of peroxyls and its reactions with the aminoxyl, even if it occurs, is not the main process of the reaction. 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO), studied for comparison with indolinonic aminoxyls does not react with peroxyls and cannot be reduced by superoxide.

Results and Discussion.

The ability of superoxide radical anion to react with alkylhalides by a nucleophilic reaction has been known since the seventies [17,18]. In aprotic solvents, primary alkylhalides react to produce the corresponding dialkylperoxide through the formation of the peroxy radical as shown in Eqs. 1-3 [14,16]. Several studies confirm that reaction (1) which produces peroxy radicals, is first order with respect to the substrate and that the rate constant for this reaction decreases on changing the halide in the order: primary > secondary >> tertiary [13].

$$O_2^{\bullet -} + RX \rightarrow RO_2^{\bullet} + X^- \quad (1)$$

$$O_2^{\bullet -} + RO_2^{\bullet} \rightarrow RO_2^- + O_2 \quad (2)$$

$$RO_2^- + RX \rightarrow ROOR + X^- \quad (3)$$

This reaction was therefore used to generate different kinds of peroxy radicals and to test their reactivity towards aminoxyls. As a source of superoxide radical, potassium superoxide was used, and to improve its dissolution in organic solvents, a 18-crown-6-ether (1,4,7,10,13,16-hexaoxacyclooctadecane) was added to the reaction mixture [19]. Dry benzene was chosen as solvent to avoid the problems connected with the use of high boiling solvents (such as dimethylsulfoxide) [14] and with the presence of traces of water that rapidly reacts with superoxide radical anion [16].

The studied aminoxyls were 2-methyl-2-phenyl-3-phenylimino-2,3-dihydro-indol-1-oxyl (indolinonic aminoxyl) **1** and the commercial 2,2,6,6-tetramethyl-piperidine-1-oxyl (TEMPO). The reactions were performed using the following reagents ratio: aminoxyl (1 mmole), potassium superoxide (10 mmoles), alkylhalide (100 mmoles).

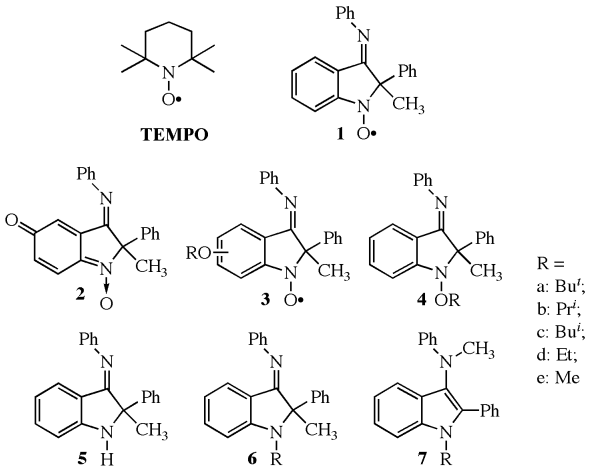


Figure 1

In the case of indolinonic aminoxyl **1** with all the alkylhalides used (2-iodo-2-methypropane, 2-chloropropane, 2-iodopropane, 2-iodobutane, iodoethane, iodomethane) the conversion is not very high and many products are formed. The isolated products are reported in Figure 1 while their yields are reported in Table 1.

Table 1

Reaction products yields for the reaction of indolinonic aminoxyl **1** in benzene, with potassium superoxide in the presence of different alkyl halide and 18-crown-6 ether.

Products	**a**= Bu^{t}I	**b**= Pr^{i}Cl	**b'**= Pr^{i}I	**c**= Bu^{i}I	**d**= EtI	**e**= MeI	/
1	50	38	22	29	13	15	11
2	8	2	3	11	3	2	8
3	/	/	3	5	3	3	/
3'	/	/	3	/	3	/	/
4	12	9	23	8	48	53	/
5	12	53	8	21	11	18	52
6	/	/	/	/	3	7	/
7	/	/	/	/	6	7	/

Only the quinoneimine-*N*-oxide **2** (3-phenylimino-2-methyl-1-oxy-2-phenyl-2,3-dihydroindol-5-one) and the alkoxy substituted aminoxyls **3** and **3'** (5- or 7-alkoxy-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl) isolated in very low yields can prove the formation of peroxyradicals [10,12], whereas the formation of the alkoxyamine **4** [(1-alkoxy-2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine] and of the amines **5** [(2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine], **6** [(1-alkyl-2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine] and **7** ((1-alkyl-2-methyl-1*H*-indol-3-yl)-methyl-phenylamine) could be attributed to the interaction of the superoxide with the starting indolinonic aminoxyl **1** and to the basicity of the medium.

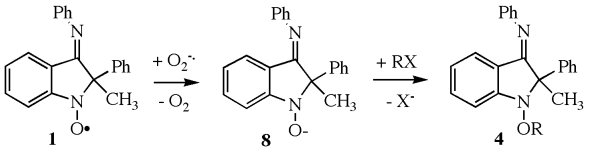
In fact, quinoneimine-*N*-oxide **2** and alkoxy substituted aminoxyls like **3** or **3'** are formed when *tert*-butyl or cumyl peroxyl were reacted with indolinonic aminoxyl **1** [10,12]. The detection of these compounds is therefore evidence for the formation of peroxyl and alkoxyl radicals (the latter generated from the coupling of two peroxyradicals and the decomposition of the formed tetroxide [20]).

The low yields of quinoneimine-N-oxide **2** and alkoxy substituted aminoxyls **3** and **3'** suggest that peroxy radicals may undergo other competitive reactions. In fact, they could be reduced by the superoxide to their corresponding anions (Eqn. 2), which react with excess alkyl halide affording dialkylperoxides (Eqn. 3) [14,16]. Peroxy radicals are rather good oxidants and it may be assumed that their reduction rate constant by superoxide is $\geq 10^7$ $M^{-1}s^{-1}$ [15]; the redox process is thus in competition with the attack on the indolinonic ring ($k \approx 10^6$ $M^{-1}s^{-1}$) [12] which leads to the formation of the quinoineimine *N*-oxide **2**.

Moreover, the distribution of the reaction products indicates that superoxide can also reduce indolinonic aminoxyl **1**. This supposition is supported by the redox potential of the aminoxyl ($E_{1/2}$= -0.10 V *vs.* NHE) [21] which suggests a high rate constant (7 x 10^5 $M^{-1}s^{-1}$) [21] for this reaction.

On the bases of these suggestions, it may be hypothesized that indolinonic aminoxyl **1** is reduced to 2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-ol anion **8**, which reacts with the alkyl halide through a S_N2 mechanism affording alkoxyamine **4** as shown in Scheme 1.

Scheme 1



The formation of amine **5** could be explained by the well known disproportionation reaction of the starting indolinonic aminoxyl **1** [22], but this process may be excluded on the basis of the yields of compounds **5** and **2**, which are higher for **5** in all cases, instead of the 1:1 ratio observed in disproportionation reactions. These data suggest that the mechanism concerning the formation of **5** is completely different.

In order to obtain more information on the formation of amine **5**, and supposing that the basicity of the reaction

medium can influence the mechanism of the reaction, indolinonic aminoxyl **1** was reacted in the presence of iodomethane with potassium superoxide, potassium *tert*-butoxide and potassium hydroxide in dimethylsufoxide at room temperature. In all cases, compound **5** was isolated and identified. In addition, amine **5** treated with the above alkali in dimethylsulfoxide gave rise to a pink-red solution which gives a well resolved epr signal, stable for hours (Figure 2) and attributed to radical anion **9** or to the corresponding deprotonated radical anion **10** (Scheme 2) on the basis of its hyperfine coupling constants (Figure 2) which are in agreement with other similar anions [23].

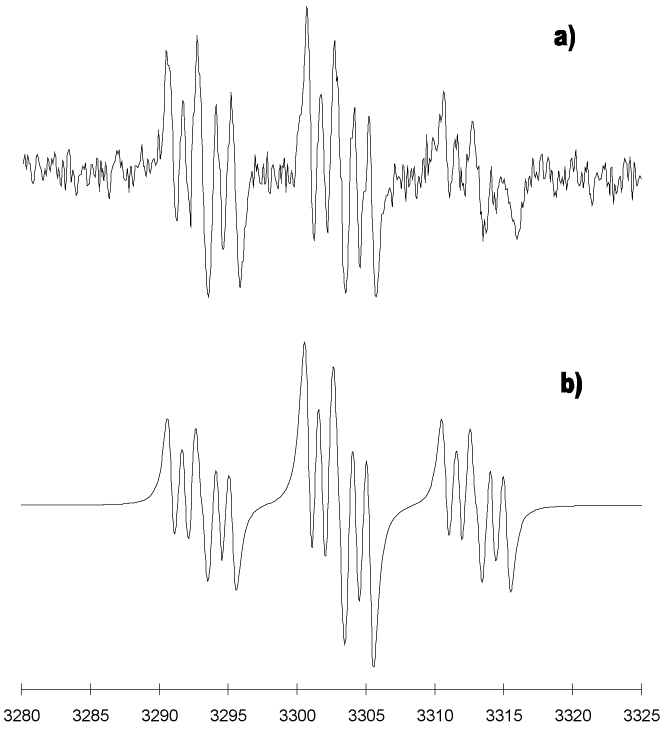
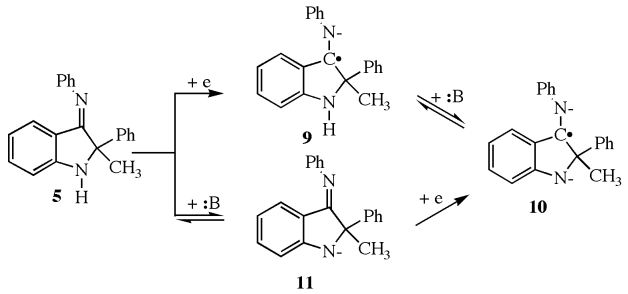


Figure 2. Epr spectra of radical anion **9** or **10** in dimethylsulphoxide, (a) experimental, (b) simulated. H.f.c.cs: a_H(C4)=10.03; a_H(C6)=9.85; a_H(C5)=2.45; $a_{N\text{-}exo}$=0.99 Gauss.

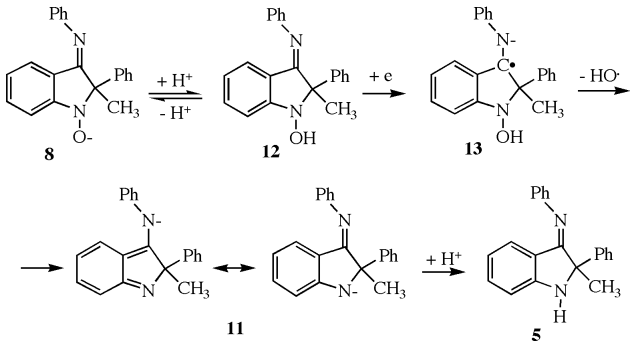
Scheme 2



Since amine **5** in alkali gives rise to an acid-base equilibrium, it remains difficult to state with certainty if the radical anion observed is **9** or **10** and if the reduction of the amine occurs before or after deprotonation (see Scheme 2).

On the basis of these results the following mechanism can be put forward for the main reaction. Anion **8** in the reaction mixture gives rise to an acid-base equilibrium forming hydroxylamine **12** (2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-ol) (it cannot be excluded that in these conditions alkyl halides undergo elimination to give an alkene thus acting as a proton source). This in turn may react with superoxide radical anion affording radical anion **13**, which then generates anion **11** [(2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine anion] by elimination of an hydroxy radical (Scheme 3). Protonation of this anion leads to the formation of amine **5**.

Scheme 3



Concerning with the formation of amine **6**, it can be reasonably formed by nucleophilic substitution of anion **11** on the alkylhalide. In fact, the reaction of amine **5** with potassium hydroxide in the presence of iodomethane in dimethylsulphoxide leads to the formation of amine **6** (see Experimental). The formation of this compound, observed only when the alkyl halides used were iodomethane and iodoethane, suggests that nucleophilic substitution in this case takes place only with primary alkyl halides.

It is worth noting that in the reaction with iodomethane and iodoethane, amine **7** (see Table 1) was also obtained. This involves migration of the methyl group from C-2 to the exocyclic nitrogen and alkylation of the endocyclic nitrogen. 1,2-Migrations involving anions are rare; 1,3 migrations seem to be impossible. Nevertheless, based on the assumption that anion **11** could be a suitable intermediate for rearrangement, the reaction of amine **5** with potassium superoxide or potassium hydroxide which could afford anion **11**, was carefully performed with the aim of obtaining a rearranged compound; however only the starting amine was quantitatively recovered. The same reaction carried out in the presence of iodomethane affords mainly amine **6**, as previously described. Since this compound does not undergo any change under alkaline treatment, we

are unable to suggest a likely mechanism for the formation of amines **7d** and **7e**.

In the reaction of TEMPO with potassium superoxide in the presence of all the alkyl halides used, the starting aminoxyl was totally recovered after reaction workup. To confirm that this aminoxyl does not react with the peroxy radicals which could be formed, further experiments were carried out. *tert*-Butylperoxyradicals were generated by hydrogen abstraction of lead dioxide on *tert*-butylhydroperoxide [10,12], but also in this case, only unreacted TEMPO was recovered when the reaction was carried out in benzene. However when acetone was used as solvent, 1-(2,2,6,6-tetramethylpiperidin-1-yloxy)-propan-2-one was isolated. The formation of this product can be ascribed to the coupling of the nitroxide function with the acetonyl radical formed by hydrogen abstraction of the *tert*-butoxyradicals (generated from the decomposition of *tert*-butylperoxy radical [20]) on the solvent [10,11]. Experimental results confirm that the lower oxidation power of TEMPO ($E_{1/2}$= -0.58 V *vs.* NHE) [21], with respect to indolinonic aminoxyl **1**, does not permit electron transfer with superoxide [21].

Conclusions.

The yields reported in Table 1 for compounds **2** and **3**, ascribed to the interaction of peroxyls or its derivatives with indolinonic aminoxyl **1**, clearly show that all alkylperoxyls (primary, secondary and tertiary) behave in a similar way and that the decomposition of peroxyls with hydrogens in α position to the peroxy group gives rise to alkoxy radicals in accordance with the last literature reports [24]. Moreover, aromatic aminoxyls such as **1** in alkaline medium undergo reduction with subsequent deoxygenation to the corresponding amines while aliphatic aminoxyls such as TEMPO do not react with peroxyls and cannot be reduced by superoxide.

EXPERIMENTAL

Ir spectra were recorded on a Nicolet Fourier Transform Infrared 20-SX spectrophotometer equipped with a Spectra Tech "Collector" for DRIFT measurements or on a Perkin Elmer 298 Infrared Spectrometer. ^{1}H nmr and ^{13}C nmr spectra were recorded at room temperature in deuterochloroform on a Varian Gemini 200 spectrometer (δ in ppm referred to tetramethylsilane). Mass spectra were recorded on a Carlo Erba QMD 1000 spectrometer in EI$^+$ mode and high resolution mass spectra on a VG7070-E 5000 spectrometer with PFK as the resolution and calibration standard. Epr spectra were recorded on a Varian E4 spectrometer interfaced with a computer. Elemental analyses of the new compounds were performed with a Carlo Erba CHNSO E.A. 1108 elemental analyser.

1,2-Dihydro-2-methyl-2-phenyl-3-phenylimino-3*H*-indole-1-oxyl **1** was prepared according to literature methods [4]. 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO), potassium superoxide, potassium *tert*-butoxide, *tert*-butylhydroperoxide, potassium hydroxide and all the alkylhalides were Aldrich commercial reagent grade products and used as purchased. Lead dioxide was a Janssen Chimica commercial reagent grade product and used as purchased. 18-Crown-6 ether (1,4,7,10,13,16-hexaoxacyclooctadecane), was an Aldrich commercial reagent grade product and was crystallized according to the literature [25]. 1-Alkoxy-2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine **4a**, **4b**, **4d** and **4e** [8], amines **5** [(2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine] [26,27] and **7e** [methyl-phenyl-(1,2-dimethyl-1*H*-indol-3-yl)-amine] [26], and 3-phenylimino-2-methyl-1-oxy-2-phenyl-2,3-dihydroindol-5-one **2** [12], were characterised by comparison with authentic samples.

General Procedure for the Reaction of Aminoxyl with Potassium Superoxide and Alkyl Halide in Benzene.

Potassium superoxide (227 mg, 3.2 mmol) was added to a solution of 169 mg (0.64 mmol) of 18-crown-6 ether in 20 ml of benzene; to the mixture, 32 mmol of alkyl halide followed by 0.32 mmol of aminoxyl were added. The reaction mixture was stirred for 24 hrs; then 10 ml of distilled water were added and the mixture was neutralized with 10% hydrochloric acid. The reaction was extracted with methylene chloride, dried over sodium sulphate and concentrated to a small volume. The residue was chromatographed on preparative plates eluting with cyclohexane/ethyl acetate 9:1. In the case of indolinonic aminoxyl **1**, the products were isolated in the following order: amine **6** ((1-alkyl-2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine), alkoxyamine **4**, amine **7** ((1-alkyl-2-methyl-1*H*-indol-3-yl)-methylphenylamine), indolinonic aminoxyl **1**, 5-alkoxy substituted aminoxyl **3** (5-alkoxy-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl), 7-alkoxy substituted aminoxyl **3'** (7-alkoxy-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl), amine **5** and quinoneimine *N*-oxide **2**; yields are reported in Table 1. With TEMPO only the starting aminoxyl was recovered in all cases.

2-Methyl-2-phenyl-3-phenylimino-5-(2-propyloxy)-2,3-dihydroindol-1-oxyl (**3b**).

This compound was obtained as dark green solid; ir: 1644, 1581, 1469, 1417, 1331, 1258 cm^{-1}; epr: a^N (NO·) = 10.1, a^H (H4, H6) = 1.0, a^H (H7) = 3.1, a^N (NPh) = 0.95 gauss; ms: m/z 371 (M$^+$, 91 %); 356 (70); 329 (72); 313 (81); 77 (100); hrms calcd for $C_{24}H_{23}N_2O_2$ 371.4612, found 371.4615.

5-(2-Butoxy)-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl (**3c**).

This compound was obtained as brown solid; ir: 1644, 1581, 1469, 1420, 1331, 1258 cm^{-1}; epr: a^N (NO·) = 10.1, a^H (H4, H6) = 1.1, a^H (H7) = 2.9, a^N (NPh) = 0.9 gauss; ms: m/z 385 (M$^+$, 12 %); 370 (28); 329 (25); 313 (42); 77 (100); hrms calcd for $C_{25}H_{25}N_2O_2$ 385.4882, found 385.4883.

5-Ethoxy-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl (**3d**).

This compound was obtained as dark green solid; ir: 1644, 1581, 1469, 1417, 1329, 1258 cm^{-1}; epr: a^N (NO·) = 10.0, a^H (H4, H6) = 1.0, a^H (H5 or H7) = 3.0, a^N (N Ph) = 0.85 gauss; ms: m/z 357 (M$^+$, 71 %); 341 (42); 329 (7); 313 (18); 77 (100); hrms calcd for $C_{23}H_{21}N_2O_2$ 357.4342, found 357.4340.

5-Methoxy-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl (**3e**).

This compound was obtained as dark green solid; ir: 1645, 1581, 1470, 1417, 1331, 1258 cm^{-1}; epr: a^N (NO·) = 10.1, a^H

(H4, H6) = 1.1, a^H (H7) = 2.9, a^N (NPh) = 0.9 gauss; ms: m/z 343 (M^+, 100 %); 328 (77); 313 (48); hrms calcd for $C_{22}H_{19}N_2O_2$ 343.4073, found 343.4070.

2-Methyl-2-phenyl-3-phenylimino-7-iso-propyloxy-2,3-dihydro-indol-1-oxyl (**3'b**).

This compound was obtained as dark red solid; ir: 1644, 1581, 1465, 1417, 1331, 1260 cm^{-1}; epr: a^N (NO·) = 9.6, a^H (H4, H6) = 1.0, a^H (H5) = 3.3, a^N (NPh) = 0.82 gauss; ms: m/z 371 (M^+, 10 %); 356 (67); 329 (12); 313 (100); hrms calcd for $C_{24}H_{23}N_2O_2$ 371.4612, found 371.4610.

7-Ethoxy-2-methyl-2-phenyl-3-phenylimino-2,3-dihydroindol-1-oxyl (**3'd**).

This compound was obtained as dark red solid; ir: 1644, 1583, 1469, 1417, 1331, 1258 cm^{-1}; epr: a^N (NO·) = 10.0, a^H (H4, H6) = 1.0, a^H (H5 or H7) = 3.0, a^N (NPh) = 0.85 gauss; ms: m/z 357 (M^+, 71 %); 341 (42); 329 (7); 313 (18); 77 (100); hrms calcd for $C_{23}H_{21}N_2O_2$ 357.4342, found 357.4343.

1-(2-Butoxy)-2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine (**4c**).

This compound was obtained as yellow solid; ir: 1660, 1600, 755, 695 cm^{-1}; ^1H NMR: δ 0.84 (2H, m, CH_3-CH(O)-CH_2-CH_3); 0.85 (3H, t, CH_3-CH(O)-CH_2-CH_3, *J* = 7.3 Hz); 1.24 (3H, d, CH_3-CH(O)-CH_2-CH_3, *J* = 6.1 Hz); 1.93 (s, 3H, Ind-CH_3); 3.55 (1H, m, CH_3-C*H*(O)-CH_2-CH_3); 6.38 (1H, d, H7, *J* = 7.7 Hz); 6.64 (1H, t, H6, *J* = 7.2 Hz); 6.78 (2H, bd, arom.); 7.1 (2H, m, arom.); 7.35 (6H, m, arom.); 7.54 (2H, m, arom.) ppm; ms: m/z 370 (M^+, 41 %); 298 (100).

Anal. Calcd. For $C_{25}H_{26}N_2O$: C, 81.05; H, 7.07; N, 7.56. Found: C, 81.03; H, 7.09; N, 7.48.

1-Ethyl-2-methyl-2-phenyl-1,2-dihydroindol-3-ylidene)-phenylamine (**6d**).

This compound was obtained as yellow solid, mp 85-87 °C; ir: 1653, 1601, 1481, 1317 cm^{-1}; ^1H NMR: δ 1.16 (3H, t, -NCH_2CH_3, *J* = 7.1 Hz); 1.92 (3H, s, Ind-CH_3); 3.18 (1H, dq, -NCH_2CH_3, *J* = 14.2 and 7.2 Hz); 3.39 (1H, dq, -NCH_2CH_3, *J* = 14.2 and 7.2 Hz); 6.34 (2H, m, arom.); 6.71 (1H, m, arom.); 7.07 (1H, tt, arom., *J* = 7.4 and 1.2 Hz); 7.3 (8H, m, arom.) ppm; ms: m/z 326 (M^+, 76 %); 311 (36); 297 (100); 282 (54).

Anal. Calcd. For $C_{23}H_{22}N_2$: C, 84,63; H, 6,79; N, 8,58. Found: C, 84,62; H, 6,81; N, 8,50.

1,2-Dimethyl-2-phenyl-1,2-dihydro-indol-3-ylidene)-phenylamine (**6e**).

This compound was obtained as yellow solid, mp 89-91 °C; ir: 1653, 1601, 1481, 1317 cm^{-1}; ^1H NMR: δ 1.89 (3H, s, Ind-CH_3); 2.84 (3H, s, -NCH_3); 6.35 (2H, m, arom.); 6.66 (1H, d, arom., *J* = 8.1 Hz); 6.76 (2H, m, arom.); 7.08 (1H, tt, arom., *J* = 7.4 and 1.2 Hz); 7.31 (8H, m, arom.) ppm; ms: m/z 312 (M^+, 59 %); 297 (100); 282 (53).

Anal. Calcd. For $C_{22}H_{20}N_2$: C, 84,58; H, 6,45; N, 8,97. Found: C, 84,59; H, 6,47; N, 8,93.

(1-Ethyl-2-methyl-1*H*-indol-3-yl)-methylphenylamine (**7d**).

This compound was obtained as white solid, mp 145-7 °C; ir: 1597, 1496, 1456, 1368, 1339, 1229 cm^{-1}; ^1H NMR: δ 1.34 (3H, t,-NCH_2CH_3, *J* = 7.2 Hz); 3.09 (3H, s,Ph-N-CH_3); 4.19 (2H, q, -NCH_2CH_3, *J* = 7.2 Hz); 6.68 (2H, m, arom.); 7.28 (12H, m, arom.) ppm; ms: m/z 326 (M^+, 100 %); 311 (32); 297 (39); 282 (61).

Anal. Calcd. For $C_{23}H_{22}N_2$: C, 84,63; H, 6,79; N, 8,58. Found: C, 84,64; H, 6,77; N, 8,49.

Reaction of Indolinonic Aminoxyl **1** with Potassium Superoxide in Benzene.

The reaction was carried out as previously described above omitting the alkyl halide. Products **1**, **5** and **2** were isolated in the described order and yields are reported in Table 1.

Reaction of Indolinonic Aminoxyl **1** with Potassium Superoxide, or Potassium *tert*-Butoxide or Potassium Hydroxide in Dimethylsulfoxide in the Presence of 2-Iodopropane.

Base (potassium superoxide, potassium *tert*-butoxide or 1 pellet of potassium hydroxide) (1.6 mmol) was added to a solution of 16 mmol of 2-iodopropane and 0.16 mmol of aminoxyl **1** in 2.5 ml of dimethylsulfoxide. The reaction mixture was stirred for 24 hrs; then 5 ml of distilled water were added and the mixture was neutralized with 10% hydrochloric acid. The reaction was extracted with ethylacetate, dried over sodium sulphate and concentrated to a small volume. The residue was chromatographed on preparative plates eluting with cyclohexane/ethyl acetate 9:1.

In all cases amine **5** was isolated in 70-80% yield.

Reaction of Amine **5** with Potassium Hydroxide and Iodomethane in Dimethylsulfoxide.

Potassium hydroxide (1 pellet) was added to a solution of 16 mmol of iodomethane and 0.16 mmol of amine **5** in 2.5 ml of dimethylsulfoxide. The reaction mixture was stirred for 24 hrs; then 5 ml of distilled water were added and the mixture was neutralized with 10% hydrochloric acid. The reaction was extracted with ethylacetate, dried over sodium sulphate and concentrated to a small volume. The residue was chromatographed on preparative plates eluting with cyclohexane/ethyl acetate 9:1 and product **6e** was isolated in 63% yield.

Reaction of Amine **5** with Potassium Superoxide or Potassium Hydroxide in Dimethylsulfoxide.

Potassium superoxide (1.6 mmol) or 1 pellet of potassium hydroxide was added to a solution of 0.16 mmol of amine **5** in 2.5 ml of dimethylsulfoxide. The reaction mixture was stirred for 24 hrs; then 5 ml of distilled water were added and the mixture was neutralized with 10% hydrochloric acid. The reaction was extracted with ethylacetate, dried over sodium sulphate and concentrated to a small volume. In all cases only the starting amine was recovered.

Reaction of Amine **6** with Potassium Hydroxide in Dimethylsulfoxide.

Potassium hydroxide (1 pellet) was added to a solution of 0.16 mmol of amine **6e** in 2.5 ml of dimethylsulfoxide. The reaction mixture was stirred for 24 hrs; then 5 ml of distilled water were added and the mixture was neutralized with 10% hydrochloric acid. The reaction was extracted with ethylacetate, dried over sodium sulphate and concentrated to a small volume, where only the starting amine was recovered.

Reaction of 2,2,6,6-Tetramethylpiperidine-1-oxyl (TEMPO) with *tert*-Butylhydroperoxide and Lead Dioxide in Different Solvents.

General Procedure.

Lead dioxide (155 mg, 0.64 mmol) was added to a solution of 100 mg (0.64 mmol) of 2,2,6,6-tetramethylpiperidin-1-oxide

(TEMPO) in 10 ml of solvent (benzene or acetone); to the mixture, a solution of 0.82 ml (6.4 mmol) of *tert*-butylhydroperoxide (70% in water) in 5 ml of solvent was added dropwise. The reaction mixture was stirred for 1 hr; then 10 ml of distilled water were added and the reaction was extracted with methylene chloride, dried over sodium sulphate and concentrated to a small volume. The residue was chromatographed on preparative plates eluting with cyclohexane/ethyl acetate 9:1. When the solvent used was acetone, besides the starting aminoxyl, 1-(2,2,6,6-tetramethylpiperidin-1-yloxy)-propan-2-one (29 %) was recovered.

1-(2,2,6,6-Tetramethylpiperidin-1-yloxy)-propan-2-one.

This compound was obtained as colourless oil; ir: 2900; 1710 (C=O); 1455; 1365; 1350; 1125; 1075 cm^{-1}; ^1H NMR: δ 1.13 (12H, d, CH_3); 1.45 (6H, d, CH_2); 2.19 (3H, s, -NOCH$_2$C(O)CH_3); 4.36 (2H, s, -NOCH_2C(O)CH$_3$) ppm; ^{13}C NMR: δ 17.43, 20.61, 27,74, 33.34, 40.07, 60.53, 83.76, 207.4 ppm; ms: m/z 213 (M^+, 4 %); 198 (52); 156 (23).

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