# Preparative Syntheses of Bis(4-tert-butylphenyl)aminoxyl

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**Abstract**—Bis(4-*tert*-butylphenyl)aminoxyl was obtained in 80 and 95% yield by oxidation of the corresponding amine and hydroxylamine with  $H_2O_2/WO_4^{2-}$  in methanol at 65°C. The oxidation of bis(4-*tert*-butylphenyl)-hydroxylamine to bis(4-*tert*-butylphenyl)aminoxyl was catalyzed by Cu<sup>+</sup> and Ag<sup>+</sup> ions which also catalyzed disproportionation of the former to bis(4-*tert*-butylphenyl)aminoxyl. Mechanisms of the catalytic oxidation of the amine and hydroxylamine and disproportionation of the latter were proposed.

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Bis(4-*tert*-butylphenyl)aminoxyl (**I**) is one of the most stable diarylnitroxyl radicals. Nitroxyl radicals play the key role in the mechanism of stabilization of polymeric materials and lubricating oils by diphenyl-amine derivatives [1–4]. Nitroxyl **I** is generally prepared by oxidation of bis(4-*tert*-butylphenyl)amine (**II**) with *m*-chloroperoxybenzoic acid [1], hydrogen peroxide in combination with Na<sub>2</sub>WO<sub>4</sub> [5], and acetone peroxide [6], as well as by oxidation of bis(4-*tert*-butylphenyl)hydroxylamine (**III**) with silver oxide [1] (Scheme 1).

From the viewpoint of accessibility of reactants and their cost, the most promising is the oxidation of amine **II** with hydrogen peroxide in the presence of Na<sub>2</sub>WO<sub>4</sub>. However, in this case the oxidation process is very slow, and the yield of **I** attains 70% in 10 days. Moreover, the resulting radical contains impurities of the initial amine and by-products assumingly having quinoid structure. The latter are difficult to separate by crystallization, as follows from the low melting point of the target radical (96–98°C) [5]. The goal of the present work was to develop a more efficient preparative procedure for the synthesis of aminoxyl **I**. Amine II is almost insoluble in water; therefore, its oxidation with  $H_2O_2/WO_4^{2-}$  was carried out in methanol. The consumption of amine II and accumulation of radical I were monitored by HPLC, and the consumption of  $H_2O_2$  was determined by measuring the volume of liberated oxygen. When the evolution of oxygen was complete, an additional amount of hydrogen peroxide was added. The optimal conditions for the oxidation of amine II were as follows: initial concentration of II  $c_0 = 0.20-0.25$  M, reactant molar ratio  $H_2O_2-II$  2.5:3.0 and  $WO_4^2-II$  0.1, heating under reflux. The conversion of II was ~96% in 6–7 h, and the yield of I after recrystallization from methanol was ~80%.

Presumably, the oxidation of amine II to radical I follows a mechanism proposed by us previously for ditert-alkylamines [7]. The true oxidant is peroxotungstate ( $WO_5^{2-}$  to  $WO_8^{2-}$ ) generated by reaction of  $H_2O_2$ with  $WO_4^{2-}$  [8] [reaction (1) in Scheme 2]. Peroxotungstate oxidizes amine II to hydroxylamine III and then to hydroxylamine oxide  $R_2N^+(O^-)OH$  [reactions (2), (3)]. Nitroxyl radical I is formed via one-electron reduction of an equilibrium mixture of hydroxylamine oxide  $R_2N^+(O^-)OH$  and oxoammonium cation  $R_2N^+=O$ 



$$WO_4^{2-} + iH_2O_2 \longrightarrow iH_2O_2 + WO_n^{2-}$$
 (1)  
 $i = 1-4 \cdot n = 4 + i$ 

$$\begin{array}{c} \mathsf{R}_{\mathsf{N}} \mathsf{P}^{\mathsf{R}} + \mathsf{WO}_{n}^{2-} & \longrightarrow & \begin{array}{c} \mathsf{R}_{\mathsf{N}} \mathsf{P}^{\mathsf{R}} + \mathsf{WO}_{n-1}^{2-} \\ \mathsf{I} \\ \mathsf{OH} \end{array}$$
(2)

$$\begin{array}{c} R \\ N \\ R \\ N \\ OH \end{array} + WO_{n}^{2-} \longrightarrow \left[ \begin{array}{c} R \\ N \\ HO \end{array} \right] \left[ \begin{array}{c} R \\ N \\ O^{-} \end{array} \right] \left[ \begin{array}{c} R \\ N \\ O$$

$$2 \overset{R}{\underset{\substack{\downarrow \\ 0}}{}^{+}} \overset{R}{\underset{\substack{\downarrow \\ 0}}{}^{+}} + 20H^{-} + H_{2}O_{2} \longrightarrow 2 \overset{R}{\underset{\substack{\downarrow \\ 0}}{}^{R}} + O_{2} + 2H_{2}O \qquad (4)$$

$$2 \xrightarrow[H]{R} N \xrightarrow[H]{R} + 5H_2O_2 \longrightarrow 2 \xrightarrow[H]{R} N \xrightarrow[H]{R} + O_2 + 6H_2O$$
(5)

R = 4-tert-butylphenyl.

with hydrogen peroxide [reaction (4)]. The overall process is represented by stoichiometric equation (5). Thus the oxidation of 1 mol of amine **II** to radical **I** requires ~6 mol of  $H_2O_2$ . The greater consumption of hydrogen peroxide than it follows from Eq. (5) may be rationalized by its catalytic decomposition in the presence of  $WO_4^{2-}[9]$ .

Intermediate hydroxylamine III was detected by HPLC. Its current concentration was lower by about two orders of magnitude than the concentration of amine II. As follows from Eqs. (1)–(4) (Scheme 2),  $[R_2NOH]/[R_2NH] = k_2/k_3$ . Therefore, the rate constant  $k_3$  is higher than  $k_2$  by two orders of magnitude, and the rate of the overall process is determined by the rate of oxidation of amine II to hydroxylamine III according to reaction (2).

Radical I can also be obtained from hydroxylamine III by oxidation with  $H_2O_2/WO_4^{2-}$  under the same conditions as in the oxidation of II. The complete conversion of III is attained in ~30 min, and the yield of I (isolated product) is ~95%. This procedure ensures preparation of purest radical I with mp 137°C. The physical constants and spectral parameters of pure radical I considerably differed from those reported for samples of I prepared by other methods [1, 5, 6]. In particular, the three long-wave absorption bands at  $\lambda_{max}$  539, 406, and 319 nm in the UV spectrum of I displayed vibrational structure (see Experimental). The weakest absorption band in the spectrum ( $\lambda_{max}$  539 nm) appreciably shifted to shorter wavelengths in going from hexane as solvent to ethanol; presumably, it originates from the  $n \rightarrow \pi^*$  transition in the nitroxyl group. The IR band at 1420 cm<sup>-1</sup> was assigned to

stretching vibrations of the nitroxyl group, for no such band was observed in the spectra of amine **II** and hydroxylamine **III**.

The <sup>1</sup>H NMR spectrum of **I** contained only a signal at  $\delta$  6.01 ppm from protons in the *tert*-butyl groups. This signal appeared by 4.71 ppm downfield relative to the corresponding signal of amine **II** due to interaction with the unpaired electron with a hyperfine coupling constant  $a_{\rm H}$  of 0.0063 mT. Signals from aromatic protons were not observed in the <sup>1</sup>H NMR spectrum of **I** owing to paramagnetic broadening. The ESR spectrum of **I** consisted of 33 lines and showed couplings of the unpaired electron with the nitrogen atom ( $a_{\rm N} =$ 0.99 mT) and *ortho-* and *meta*-protons in the benzene rings ( $a_{\rm H} = 0.186$  and 0.09 mT).

We also studied oxidation of hydroxylamine **III** with atmospheric oxygen. If no catalyst was added, hydroxylamine **III** was oxidized according to Scheme 3 with a half-conversion period of 2.5 days. Copper(II) sulfate pentahydrate effectively catalyzed the oxidation of **III**. The conversion of **III** in methanol at 20°C ([**III**]<sub>0</sub> =  $4 \times 10^{-3}$  M, [Cu<sup>2+</sup>]<sub>0</sub>/[**III**]<sub>0</sub> = 0.1) was complete in ~6 min. The oxidation of **III** to radical **I** was accompanied by its reduction to amine **II**. The fraction of amine **II** in the final product increased in parallel with the initial concentration of hydroxylamine **III**. At [**III**]<sub>0</sub> =  $4 \times 10^{-3}$  and 0.2 M, the fraction of **II** in the oxidation product was 1.6 and 21%, respectively.



The reduction of **III** to amine **II** is the result of its disproportionation. The disproportionation of **III** at room temperature in the absence of a catalyst is very slow, whereas on heating at the melting point (115°C) the conversion of **III** is complete in ~30 s (Scheme 4). In the first step, two molecules of **III** give rise to radical **I** and aminyl radical  $R_2N$ ; the latter abstracts hydrogen atom from the third hydroxylamine **III** molecule to produce amine **II** (Scheme 5).



Catalytic disproportionation of III is likely to follow Scheme 6. The first step of the catalytic process is addition of III to CuSO<sub>4</sub> with formation of complex **A**. Copper(II) ion in aqueous solution exists as octahedral complex [Cu(H<sub>2</sub>O)<sub>6</sub>]<sup>2+</sup>. In going to methanol as solvent, a part of water molecules is replaced by MeOH. Complex **A** is formed by replacement of one ligand (H<sub>2</sub>O or MeOH) by hydroxylamine III. The reaction of **A** with the second molecule III leads to disproportionation of the latter with formation of radical **I**, H<sub>2</sub>O, and complex **B** containing aminyl radical R<sub>2</sub>N' as ligand. In the final step, complex **B** reacts with the third hydroxylamine molecule, yielding radical **I**, amine **II**, and CuSO<sub>4</sub>. Silver nitrate catalyzed the disproportionation of hydroxylamine **III** considerably



more effectively than did CuSO<sub>4</sub>. The reaction in methanol at  $[III]_0 = 0.2$  and  $[AgNO_3] = 0.02$  M occurred almost instantaneously (during reactant mixing). The mechanisms of catalysis by Cu<sup>2+</sup> and Ag<sup>+</sup> ions are likely to be similar.

Scheme 7 illustrates the catalytic oxidation of hydroxylamine III with atmospheric oxygen. As in the catalytic disproportionation, the first step is addition of III to  $CuSO_4$  with formation of complex **A**. The latter reacts with oxygen to give radical I and intermediate complex **C** containing HO<sub>2</sub><sup>-</sup> radical as ligand. The reaction of **C** with hydroxylamine III leads to radical I and H<sub>2</sub>O<sub>2</sub> and regenerates CuSO<sub>4</sub>.



The oxidation and disproportionation of hydroxylamine III in the presence of CuSO<sub>4</sub> are competing processes. The ratio of the average oxidation and disproportionation rates can be calculated from the ratio of radical I and amine II in the final product by the equation  $V_{\text{ox}}/V_{\text{dis}} = ([\mathbf{I}] - 2[\mathbf{II}])/3[\mathbf{II}]$  which takes into account stoichiometry of the reaction. The reaction in dilute methanol solution ([III]<sub>0</sub> =  $4 \times 10^{-3}$  M,  $c_{O_2} \approx 2 \times 10^{-3}$  M) gave a product consisting of 98.4% of radical I and 1.6% of amine II. This means that the rate of oxidation of III to radical I is higher by a factor of  $\sim 20$  than the rate of its disproportionation. The contribution of disproportionation increases as the initial concentration of hydroxylamine rises. At  $[III]_0 \approx$ 0.2 M (the concentration of oxygen dissolved in methanol is lower by a factor of  $\sim 100$ ), the fractions of radical I and amine II are 79 and 21%, respectively. Therefore, the rate of disproportionation is approximately twice as high as the rate of oxidation. We can conclude that preparative oxidation of hydroxylamine III in the presence of CuSO<sub>4</sub> should be carried out under an oxygen pressure of higher than 10 atm to minimize formation of amine II.

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Thus the most efficient procedure for the synthesis of radical I is oxidation of amine II and hydroxylamine III with  $H_2O_2/WO_4^{2-}$  in boiling methanol. These conditions ensure short reaction time and high selectivity.

#### **EXPERIMENTAL**

Bis(4-*tert*-butylphenyl)amine (II) was synthesized according to the procedure reported in [10] and was purified by recrystallization from methanol, mp 108°C. Bis(4-*tert*-butylphenyl)hydroxylamine (III) was prepared from 4-*tert*-butyl-1-nitrosobenzene and 4-*tert*butylphenylmagnesium bromide according Wieland and Rosseu [1, 11] and was recrystallized from hexane, mp 113–115°C. HPLC analyses were performed on a Milikhrom chromatograph equipped with a 2×64mm column packed with Separon C18 (5 µm) and a UV detector ( $\lambda$  210 nm); eluent 80% acetonitrile; retention volumes, µl: 570 (III), 785 (I), 900 (II).

Bis(4-tert-butylphenyl)aminoxyl (I). a. A solution of 28.1 g (0.1 mol) of amine II in 450 ml of methanol was heated to the boiling point, 34 ml (0.3 mol) of 30% hydrogen peroxide and a solution of 3.3 g (10 mmol) of Na<sub>2</sub>WO<sub>4</sub>·2H<sub>2</sub>O in 7 ml of water were added in succession, and the mixture was heated under reflux on a water bath, the consumption of H<sub>2</sub>O<sub>2</sub> being monitored by the evolution of oxygen. When oxygen no longer evolved (after ~3 h), a solution of 34 ml (0.3 mol) of 30% hydrogen peroxide in 200 ml of methanol was added, and the mixture was again heated under reflux until evolution of oxygen ceased (~3.5 h). Most part of methanol (420 ml) was distilled off, the residue was cooled, and the precipitate was filtered off, washed with 50% methanol, dried in air, and recrystallized from methanol. Yield 23.8 g (80%), red crystals, mp 134–135°C; published data: mp 134–135°C [1], 96-98°C [5]. According to the HPLC data, the product contained 99% of I and 1% of amine II.

*b*. A solution of 1.49 g (5 mmol) of hydroxylamine III in 25 ml of methanol was heated to the boiling point, 1.7 ml (15 mmol) of 30% hydrogen peroxide and a solution of 0.165 g (0.5 mmol) of Na<sub>2</sub>WO<sub>4</sub>· 2H<sub>2</sub>O in 0.5 ml of water were added in succession, and the mixture was heated under reflux on a water bath until complete consumption of initial hydroxylamine III (~30 min) and treated with 5 ml of water. The mixture was cooled, and the precipitate was filtered off, washed with 80% methanol, and dried under reduced pressure. Yield 1.41 g (95%), red crystals, mp 137°C. UV spectrum,  $\lambda_{max}$ , nm ( $\varepsilon$ , 1 mol<sup>-1</sup> cm<sup>-1</sup>): in EtOH: 495 (1020), 467 sh (1040), 456 (1130), 433 sh (1140), 407 (1340), 321 (21800), 294 sh (14300), 252 (3000); in hexane: 572 sh (102), 539 sh (172), 510 sh (196), 480 sh (450), 442 sh (926), 428 sh (1030), 406 (1230), 319 (25000), 309 sh (21400), 300 sh (16200), 292 sh (14400), 284 sh (12300), 254 (3100). IR spectrum (CCl<sub>4</sub>), v, cm<sup>-1</sup>: 3060 and 3040 (C–H<sub>arom</sub>), 2960, 2904, 2866 [C(CH<sub>3</sub>)<sub>3</sub>], 1590 and 1492 (C=C<sub>arom</sub>), 1420 (NO). <sup>1</sup>H NMR spectrum (500 MHz, CDCl<sub>3</sub>),  $\delta$ , ppm: 6.01 s (18H, CH<sub>3</sub>); signals from aromatic protons were not observed because of paramagnetic broadening. ESR spectrum (toluene): 33 lines,  $a_{\rm N} = 0.99$ ,  $a_{o-{\rm H}} = 0.186$ ,  $a_{m-{\rm H}} = 0.09$  mT.

c. A solution of 0.025 g (0.1 mmol) of CuSO<sub>4</sub>·  $5H_2O$  in 0.5 ml of water was added to a solution of 0.3 g (1 mmol) of hydroxylamine III in 5 ml of methanol. The mixture was vigorously stirred (so that a vortex cavity appeared) until complete consumption of hydroxylamine III (~30 min), and 5 ml of water was added. The precipitate was filtered off, washed with 80% methanol, and dried under reduced pressure. Yield 0.28 g (95%), red crystals, mp 105–125°C. According to the HPLC data, the product contained 79% of I and 21% of II.

## REFERENCES

- 1. Holt B. and Randel, D.R., FRG Patent Appl. no. 2110627, 1971.
- Kasaikina, O.T., Lobanova, T.V., Ivanov, Yu.A., Pokrovskaya, I.E., and Gagarina, A.B., *Neftekhimiya*, 1988, vol. 28, p. 552.
- Jensen, R.K., Korcek, S., Zinbo, M., and Gerlock, J.L., J. Org. Chem., 1995, vol. 60, p. 5396.
- 4. Denisov, E.T., Usp. Khim., 1996, vol. 65, p. 547.
- Ivanov, Yu.A., Kokorin, A.I., Shapiro, A.B., and Rozantsev, E.G., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1976, p. 2217.
- Rajka, A., Vale, M., and Rajka, S., J. Am. Chem. Soc., 2008, vol. 130, p. 9099.
- 7. Sen', V.D., Golubev, V.A., and Efremova, N.N., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1982, p. 61.
- Kamata, K., Kuzuya, S., Uehara, K., Yamaguchi, S., and Mizuno, N., *Inorg. Chem.*, 2007, vol. 46, p. 3768.
- Bogdanov, G.A., Korotchenko, L.A., and Kozlova, L.I., *Zh. Fiz. Khim.*, 1977, vol. 51, p. 1881.
- 10. Kostrab, G., Lovič, M., Janotka, I., Bajus, M., and Mravec, D., *Appl. Catal.*, *A*, 2008, vol. 335, p. 74.
- 11. Wieland, H. and Rosseu, A., *Ber.*, 1912, vol. 45, p. 494; *ibid.*, 1915, vol. 48, p. 1117.