The Mechanism of Azoxybenzene Formation[1]

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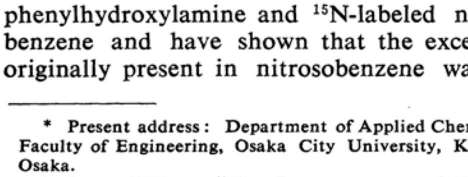
It has been well known for many years[2] that nitrobenzene is readily reduced to azoxybenzene by refluxing it with sodium alkoxide in alcohol, and the formation of azoxybenzene is generally believed to involve the condensation of phenylhydroxylamine and nitrosobenzene, both of which are produced in the reduction of nitrobenzene. Recently the condensation of phenylhydroxylamine and nitrobenzene has been studied and the formation of azoxy compounds discussed by Ogata, Tsuchida and Takagi[3]. More recently, Ogata and Mibae[4] have studied the kinetics and mechanism of azoxybenzene formation in the reduction of nitrobenzene by sodium methoxide and have suggested that the condensation of phenylhydroxylamine with nitrosobenzene to form azoxybenzene (4) is very fast compared with the reduction step of nitrobenzene with sodium methoxide and that the reduction step ((1) and (2)) is rate-determining. They have also indicated that nitrosobenzene and phenylhydroxylamine can be readily interconverted.

$$\mathrm{PhNO_2+2CH_3ONa \rightarrow PhNO+HCHO+NaOH+CH_3ONa} \quad (1)$$

$$\mathrm{PhNO_2+2CH_3ONa \rightarrow PhNHOH+HCOONa+CH_3ONa} \quad (2)$$

$$\mathrm{PhNHOH+PhNO_2 \rightarrow 2PhNO+H_2O} \quad (3)$$



$$\mathrm{PhNHOH+PhNO \rightarrow Ph\underset{\underset{O}{\downarrow}}{N}{=}NPh+H_2O} \quad (4)$$

Shemyakin, Maimind and Vaichunaite[5] have studied the azoxy coupling reaction between phenylhydroxylamine and ^{15}N-labeled nitrosobenzene and have shown that the excess ^{15}N originally present in nitrosobenzene was distributed equally in both nitrogens of the azoxybenzene, suggesting the formation of an intermediate compound with an equivalent location of the N atom such as (Ph ^{15}NOH)$_2$.

During the course of our study of the Wallach rearrangement, we have also come to be interested in this azoxy-coupling reaction. Here again, our approach to this problem is through ^{18}O. When ^{18}O-labeled nitrobenzene was reacted with sodium methoxide in refluxing aqueous methanol, the resulting azoxybenzene was found to retain 0.69 atom % of ^{18}O; that is, about 22% of the excess ^{18}O was lost during the reaction, and the azoxybenzene retained 77% of the excess ^{18}O originally present in nitrobenzene. This means that a small portion of oxygen exchange is taking place at some stage, either at the reduction or at the azoxy coupling of the reaction.

We then examined the reaction of nitrosobenzene with ^{18}O-labeled phenylhydroxylamine in boiling ethanol containing potassium hydroxide and found that the amount of excess ^{18}O in the resulting azoxybenzene was almost exactly a half of that of the phenylhydroxylamine employed. This is excellent supporting evidence both for Ogata's idea that the azoxy-coupling reaction is a very fast step and for the Russians' mechanism of the prior formation of a symmetrical N, N'-diol intermediate in the coupling reaction. However, since we found that the reaction of phenylhydroxylamine alone with sodium methoxide gave azobenzene in a good yield and that of nitrosobenzene alone with sodium methoxide gave azoxybenzene in a superb yield, there remain the other possibility that nitrosobenzene was exchanging oxygen with ^{18}O-enriched water formed from the azoxy coupling of hydroxylamine before self-condensing to form azoxybenzene.

This, however, was not the case, because the reaction of nitrosobenzene alone with ^{18}O-labeled sodium methoxide was found to give azoxybenzene incorporated with no excess ^{18}O. The most likely path for the azoxy-coupling reaction appears to be via an intermediate, N, N'-diol before dehydration to give azoxybenzene in a rapid process, regardless of whether one uses both phenylhydroxylamine and nitrosobenzene or nitrosobenzene alone.

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Since no oxygen exchange was observed in the azoxy-coupling stage, the loss of some of the excess ^{18}O found in the reduction of nitrobenzene to azoxybenzene must be taking place in the slow stage, where nitrobenzene is being reduced to nitrosobenzene. A similar loss of excess ^{18}O was observed in the reduction of ^{18}O-labeled nitrobenzene to phenylhydroxylamine with zinc and ammonium chloride. Here also about 22% of the excess ^{18}O was lost during the reduction. Probably, in both reductions, there is a common step where an incipient intermediate exchanges its oxygen with that of the solvent medium.

Experimental

^{18}O-Labeled Azoxybenzene was prepared by heating ^{18}O-labeled nitrobenzene[6] (8 g., 0.84 atom % of ^{18}O) with sodium hydroxide (8 g.) in methanol (8 g.); m. p., 35~36°C, 0.69 atom % of ^{18}O.

Found: C, 72.60; H, 4.99. Calcd. for $C_{12}H_{10}N_2O$: C, 72.73; H, 5.05%.

^{18}O-Labeled Phenylhydroxylamine.—In a 50 ml., three-necked flask fitted with a stirrer were placed 2.5 g. of ammonium chloride, 5 g. of nitrobenzene (0.66 atom % of ^{18}O) and 50 ml. of water; the mixture was then cooled to 5°C and 7 g. of zinc powder was stirred in over a period of 40 min., keeping the temperature between 5 and 10°C. Stirring was continued for 10 min. The zinc hydroxide formed was removed by filtration and washed with 40 ml. of hot water three times. The filtrate and washing were combined 25 g. of sodium chloride was added, and the mixture was allowed to stand overnight in a refrigerator. The precipitate formed was collected and recrystallized from a mixture of petroleum ether and benzene. Phenylhydroxylamine (m. p., 81°C) (lit.[7] 81°C), 0.56 atom % of ^{18}O) was thus obtained. The yield was 3 g. (70%).

The Condensation Reaction of ^{18}O-Labeled Phenylhydroxylamine and Nitrosobenzene Using Potassium Hydroxide.—In a three-necked flask was placed a mixture of 0.4 g. of ^{18}O-labeled phenylhydroxylamine (0.56 atom % of ^{18}O), 0.4 g. of nitrosobenzene and 10 ml. of ethanol; an ethanol solution which had been saturated with 0.45 g. of potassium hydroxide was stirred in and then allowed to react for 1 hr. at 75~80°C. After ethanol had been removed by evaporation under reduced pressure, the residue was poured into 100 ml. cold water. The yellow solid formed was collected and recrystallized from methanol. Azoxybenzene (m. p., 36°C, 0.38 atom % of ^{18}O) was thus obtained. The yield was 0.5 g. (80%).

The Condensation Reaction of Phenylhydroxylamine and Nitrosobenzene Using ^{18}O-Labeled Potassium Hydroxide.—^{18}O-Labeled potassium hydroxide was prepared by exchange reaction between potassium hydroxide and ^{18}O-enriched water. A mixture of 0.4 g. of phenylhydroxylamine, 0.4 g. of nitrosobenzene and ^{18}O-labeled potassium hydroxide (0.54 atom % of ^{18}O) was allowed to react similarly. The main product, azoxybenzene (m. p., 35°C) contained 0.22 atom % of ^{18}O. The yield was 0.5 g. (80%).

The Condensation Reaction of Phenylhydroxylamine alone with Potassium Hydroxide.—A mixture of 0.8 g. of phenylhydroxylamine and 0.45 g. of potassium hydroxide in 10 ml. of ethanol was allowed to react for 1 hr. at 75~80°C and was then treated similarly. The main product was red crystals (m. p., 66~67°C). The yield was 0.5 g. (75%). It did not depress the melting point of an authentic sample, azobenzene (m. p., 66~67.5°C) on admixture.

The Condensation Reaction of Nitrosobenzene alone with ^{18}O-Labeled Potassium Hydroxide.—A mixture of 0.8 g. of nitrosobenzene and 0.45 g. of ^{18}O-labeled potassium hydroxide (0.54 atom % of ^{18}O) in 10 ml. of ethanol was allowed to react for 1 hr. at 75~80°C and was then treated similarly. Azoxybenzene (m. p., 35~36°C) was the main product obtained, but unreacted nitrosobenzene was not recovered. This azoxybenzene contained 0.21 atom % of ^{18}O. The yield was 0.48 g. (66%).

The Determination of ^{18}O is described elsewhere[8].

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