A Study of the Reaction between Nitrosobenzene and the Grignard Reagent

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Although the ionic mechanism has generally been assumed for most Grignard reactions, it has been shown, as will be described below, that free radicals can be observed during the course of the reaction between nitrosobenzene and a Grignard reagent by the electron-spin resonance (ESR) technique. The reaction between nitrosobenzene and phenylmagnesium bromide was the subject of an extensive investigation by Wieland and his co-workers about fifty years ago,1) and this reaction has been established as the usual synthetic method of diphenylhydroxylamine.

The present investigation is concerned mainly with reactions between nitrosobenzene and phenylmagnesium bromide, between *p*-nitrosotoluene and phenylmagnesium bromide and between nitrosobenzene and *p*-tolylmagnesium bromide. The free radical species produced during the reactions were determined from the hyperfine structures of their ESR spectra. The equilibrium among the reaction products will be discussed below.

Experimental

ESR Measurements.—An ESR spectrometer with an X-band and a 100 Kc. modulation was used in this work. The ESR measurement of the reaction

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1) H. Wieland and S. Gambarjan, *Ber.*, **36**, 1499 (1906); H. Wieland and A. Roseeu, ibid., **45**, 494 (1912); H. Wieland and M. Offenbächer, ibid., **47**, 2111 (1914); H. Wieland and K. Roth, ibid., **53**, 210 (1920); H. Wieland and F. Kögl, ibid., **55**, 1798 (1922).

between nitrosobenzene and a Grignard reagent was carried out as follows: prior to the sealing of part A of the reaction vessel, the ether used as a solvent was evaporated as completely as possible under a high vacuum (about 10^{-6} mmHg), and this part was connected with part B of the vessel (see Fig. 1). Thereafter, part B of the vessel which contained nitrosobenzene was evacuated under a high vacuum, a known amount of tetrahydrofuran was distilled into this vessel, and the vessel was sealed off from the vacuum line. Nitrosobenzene and a Grignard reagent which had been separated from each other by a break seal were mixed at the dry ice-acetone temperature in the absence of air and moisture. The reacting mixture was then inserted into the cavity, which had previously been cooled to the desired temperature with a stream of boiling liquid nitrogen. The reaction temperature in the cavity was controlled by regulating the boiling rate of liquid nitrogen. The reaction vessel is shown in Fig. 1.

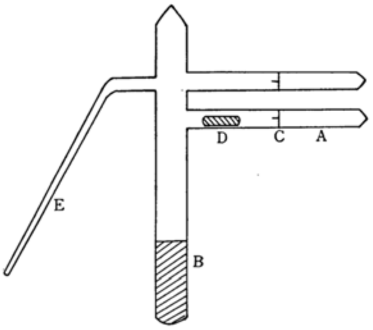


Fig. 1. Reaction vessel.

A : Grignard reagent
B : Nitrosobenzene in THF
C : Break seal
D : Hammer
E : Inserted into the cavity

Materials.—*Nitrosobenzene.*—Commercial Fulka special-grade reagent was twice recrystallized from ethanol. This sample did not show any ESR signal in tetrahydrofuran. M. p. 68°C.

p-Nitrosotoluene.—This was prepared by the oxidation of *p*-tolylhydroxylamine with an aqueous ferric chloride solution.[2] This sample did not show any ESR signal in tetrahydrofuran. M. p. 48.5°C.

Phenylmagnesium Bromide.—Phenylmagnesium bromide was prepared from bromobenzene and magnesium turnings of reagent grade suitable for the Grignard reagent in ether. This reagent was stored in a sealed bottle, and the upper transparent solution was used for the reaction. The concentration of this reagent was determined by the acid titration method.[3] This Grignard reagent did not show any ESR signal in tetrahydrofuran.

p-Tolylmagnesium Bromide. — *p*-Tolylmagnesium bromide was prepared from *p*-bromotoluene and reagent-grade magnesium turnings for the Grignard reagent in ether. The succeeding treatment was the same as in the case of phenylmagnesium bromide. This reagent did not show any ESR signal in tetrahydrofuran.

Methylmagnesium Iodide and Ethylmagnesium Bromide.—Methylmagnesium iodide and ethylmagnesium bromide were prepared according to the method used for the above two reagents.

Results and Discussion

The Identification of Free Radicals.—The reaction between phenylmagnesium bromide and nitrosobenzene was carried out as follows: after the two reacting components (the mole ratio of the Grignard reagent to nitrosobenzene is 1/1∼5/1) had been mixed in a dry ice-acetone bath, the color of the mixture suddenly became brown, and at the same time strong ESR signals, which indicate the existence of free radical species, could be observed. This free radical was identified as diphenylnitric oxide by a comparison of the hyperfine structure of its ESR spectrum with that of pure diphenylnitric oxide, which was prepared by the oxidation of diphenylhydroxylamine with silver oxide[1] (see Fig. 2 and Eq. 1).

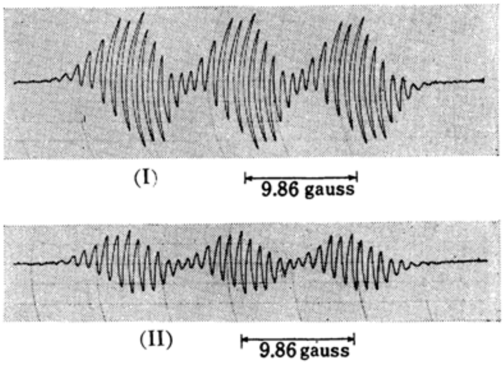
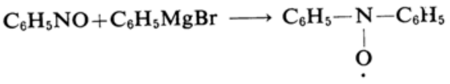


Fig. 2. A comparison of ESR spectra of the free radical produced with that of pure diphenylnitric oxide.
(I) ESR spectrum of the reaction mixture resulting from the reaction between nitrosobenzene and phenylmagnesium bromide.
(II) ESR spectrum of pure diphenylnitric oxide.



$$C_6H_5NO + C_6H_5MgBr \longrightarrow C_6H_5-\underset{\underset{\cdot}{O}}{\overset{}{\underset{|}{N}}}-C_6H_5 \tag{1}$$

The reaction between phenylmagnesium bromide and *p*-nitrosotoluene was carried out in just the same way as that between phenylmagnesium bromide and nitrosobenzene. A large amount of a free radical was also observed

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[2] E. Bamberger, ibid., **28**, 247 (1895).
[3] H. Gilman, E. A. Zoeller and J. B. Dickey, *J. Am. Chem. Soc.*, **51**, 1576 (1929).

in this reaction. This free radical was identified as *p*-methyldiphenylnitric oxide by a comparison of its hyperfine structure with a known sample.[1]

The reaction between *p*-tolylmagnesium bromide and nitrosobenzene was also examined, and the features of the reaction were quite the same as that of the above two. The ESR signals of the free radical produced were just the same as those of the free radical obtained in the reaction between phenylmagnesium bromide and *p*-nitrosotoluene (see Fig. 3 and Eq. 2).

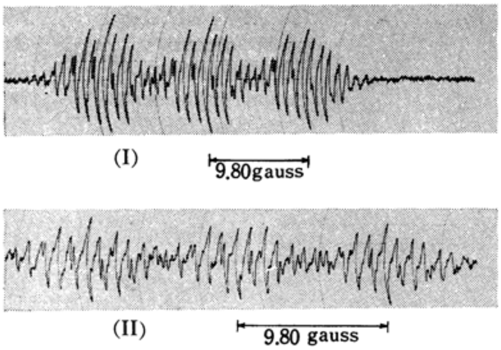
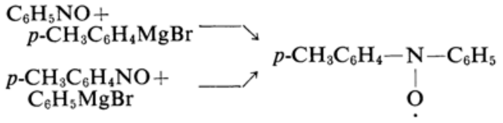


Fig. 3. A comparison of the ESR spectra.
(I) ESR spectrum of the reaction mixture resulting from the reaction between nitrosobenzene and *p*-tolylmagnesium bromide.
(II) ESR spectrum of the reaction mixture resulting from the reaction between *p*-nitrosotoluene and phenylmagnesium bromide.



$$\left.\begin{array}{l} C_6H_5NO + p\text{-}CH_3C_6H_4MgBr \\ p\text{-}CH_3C_6H_4NO + C_6H_5MgBr \end{array}\right\} \longrightarrow p\text{-}CH_3C_6H_4\text{—}\underset{\underset{\cdot}{O}}{\overset{}{\underset{|}{N}}}\text{—}C_6H_5 \tag{2}$$

The above three reactions indicate that the production of free radical species is due solely to the reaction between nitrosobenzene and the Grignard reagent and not to any other cause, such as the decomposition of nitrosobenzene.

The reaction between nitrosobenzene and methylmagnesium iodide and the reaction between nitrosobenzene and ethylmagnesium bromide were also examined. A large amount of free radicals could be observed in these reactions by the ESR technique. The free radical species, however, could not be identified because of the complication of their hyperfine structures (see Fig. 4).

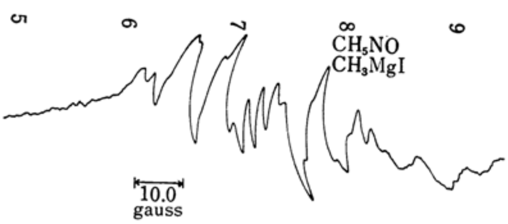


Fig. 4. The ESR spectra of free radicals produced by reaction between nitrosobenzene and methylmagnesium bromide.

The Equilibrium between the Free Radicals Produced and the Grignard Reagent.—In several preliminary reactions, it was found that the total amount of free radicals in the reaction mixture is considerably influenced by the mole ratio of the two reacting components. The quantitative determination of the free radicals in the reaction mixture was performed by the overmodulated modulation technique of ESR[4] (sweep range, about 200 gauss; modulation amplitude, 11.2 gauss; crystal current, 60 mamp.). A solution of diphenylpicrylhydrazyl in tetrahydrofuran whose concentration was known was used as the standard sample. The results obtained are shown in Table I.

The change in the concentration of free radicals on the successive addition of nitrosobenzene to the solution with a constant amount of the Grignard reagent (phenylmagnesium bromide) was examined by the successive breaking of break seals; thereby the reaction mixture and a known amount of nitrosobenzene in a vacuum tube (in this case, the Grignard reagent dissolved in 10 ml. of tetrahydrofuran is in part B of the reaction vessel and nitrosobenzene is in part A of the vessel) were separated. The results are shown in Table II.

Although the above two series of reactions suggest the existence of an equilibrium in the reaction mixture, the analysis of the reaction product was carried out when nitrosobenzene was mixed with a large excess of phenylmagnesium bromide in order to ascertain whether or not the disappearance of the free radicals is caused by a further reaction, such as a formation of diphenylamine. Thus, two vessels, containing phenylmagnesium bromide dissolved in tetrahydrofuran and nitrosobenzene dissolved in tetrahydrofuran respectively, were degassed and connected with each other by using a break seal; then they were cooled to −80°C and mixed by breaking the seal. The whole reaction vessel was kept at this temperature for thirty minutes after mixing. A rather large amount of a white crystalline precipitate was formed. Then the reaction

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[4] J. S. Hyde and H. W. Brown, *J. Chem. Phys.*, **37**, 368 (1962); K. Halbach, *Phys. Rev.*, **119**, 1230 (1960).

TABLE I. YIELDS OF FREE RADICALS IN THE REACTION MIXTURE OF C_6H_5MgBr AND C_6H_5NO

	C_6H_5NO* mol.	C_6H_5MgBr* mol.	Mol. ratio C_6H_5NO/C_6H_5MgBr	Yields of radicals based on C_6H_5NO used, %
i	7.5×10^{-4}	7.5×10^{-4}	1	76.6
ii	2.5×10^{-4}	7.5×10^{-4}	1/3	36.4
iii	1.5×10^{-4}	7.5×10^{-4}	1/5	13.5
iv	7.5×10^{-5}	7.5×10^{-4}	1/10	0

* These two reagents react in 10 ml. of tetrahydrofuran.

TABLE II. CHANGES IN THE CONCENTRATION OF FREE RADICALS ON SUCCESSIVE ADDITIONS OF C_6H_5NO TO A CONSTANT AMOUNT OF C_6H_5MgBr

	Components of the reaction mixture	Yieds of free radicals based on the total C_6H_5NO, %
Solution 1	C_6H_5MgBr*: 7.5×10^{-4} mol. + C_6H_5NO: 7.5×10^{-5} mol.	0
Solution 2	Solution 1 + C_5H_5NO: 7.5×10^{-5} mol.	12.8
Solution 3	Solution 2 + C_6H_5NO: 7.5×10^{-5} mol.	37.0

* This was dissolved in 10 ml. of tetrahydrofuran.

TABLE III. ANALYSIS OF THE REACTION PRODUCT OF C_6H_5NO WITH C_6H_5MgBr

	C_6H_5NO (I)	C_5H_5MgBr (II)	Mol. ratio I/II	Yield of DPHA based upon C_6H_5NO mg. (%)
1	45×10^{-4} mol. in 20 ml. THF	450×10^{-4} mol. in 20 ml. THF	1/10	810 (93)
2	45×10^{-4} mol. in 20 ml. THF	450×10^{-4} mol. in 20 ml. THF	1/10	845 (98)

DPHA: Diphenylhydroxylamine

mixture was allowed to stand until its temperature reached 0°C. The reaction mixture was hydrolyzed by a usual method under a stream of nitrogen. After the evaporation of tetrahydrofuran, an almost colorless crystalline mass was obtained. This was nearly pure diphenylhydroxylamine. Recrystallization of this sample from ligroin gave pure diphenylhydroxylamine (m. p. 59~60°C) (see Table III). The results of this reaction indicate unambiguously that the disappearance of free radicals which occurs when a large excess of phenylmagnesium bromide to nitrosobenzene is used is not brought about by a further reaction.

Furthermore, the dependency of the concentration of free radicals in the reaction mixture on the temperature was examined by the ESR technique. The results are shown in Fig. 5. The plots in Fig. 5 were completely reproducible at each temperature.

Reaction Mechanism.—It was described above that free radical species could not be observed

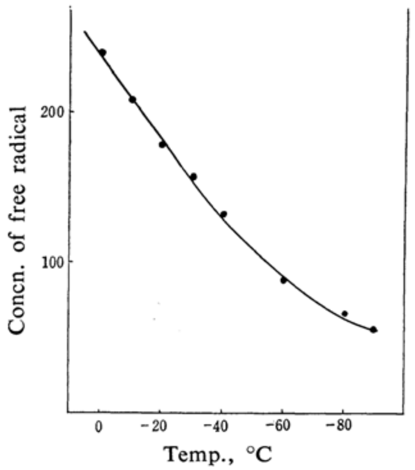
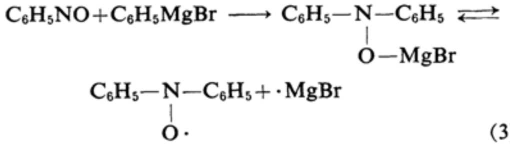


Fig. 5. Change in free radical concentration with temperature.

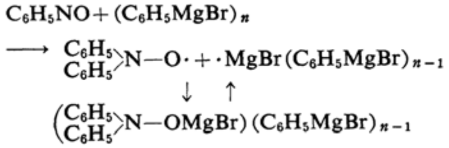
Sample: reaction mixture between 2.5×10^{-4} mol. of nitrosobenzene and 7.5×10^{-4} mol. of phenylmagnesium bromide.

in the reaction mixture at the equilibrium state in which the mole ratio of the reacting components (C_6H_5NO/C_6H_5MgBr) was 1/10. However, even in this reaction mixture, free radicals could be detected shortly after the mixing of the reacting components (2∼3 min. at $-50°C$) by ESR and until its equilibrium was attained. This fact excludes the possibility (of Eq. 3) that a Grignard-type complex is formed at first through an ionic mechanism, and that then this complex dissociates into free radicals:



$$C_6H_5NO+C_6H_5MgBr \longrightarrow \underset{\displaystyle O-MgBr}{C_6H_5-\underset{|}{N}-C_6H_5} \rightleftarrows \underset{\displaystyle O\cdot}{C_6H_5-\underset{|}{N}-C_6H_5}+\cdot MgBr \qquad (3)$$

From the discussion so far, it seems resonable to conclude that the reaction between nitrosobenzene and a Grignard reagent proceeds through the free radical mechanism and that the following equilibrium exist between the free radicals formed and the mixture of Grignard reagents:



$$\begin{aligned}&C_6H_5NO+(C_6H_5MgBr)_n\\ &\longrightarrow {C_6H_5 \atop C_6H_5}\!\!>\!N-O\cdot+\cdot MgBr(C_6H_5MgBr)_{n-1}\\ &\qquad\qquad\downarrow\ \uparrow\\ &\left({C_6H_5 \atop C_6H_5}\!\!>\!N-OMgBr\right)(C_6H_5MgBr)_{n-1}\end{aligned} \qquad (4)$$

Although the Grignard reagent is one of the most familiar reagents to organic chemists, its structure is still the subject of great controversy.5) It has been accepted, in general, that the reagent is an equilibrium mixture, that is:

$$2\ RMgX \rightleftarrows RMgR+MgX_2 \qquad (5)$$

However, a simple mixture of one mole of RMgR and one mole of MgX_2 is less reactive than the reagent prepare from Mg and RX.6) On the other hand, it was confirmed that a large excess of the Grignard reagent ($C_6H_5\cdot MgBr$) can combine with pure diphenylnitric oxide to result in the disappearance of this free radical (see Fig. 6).

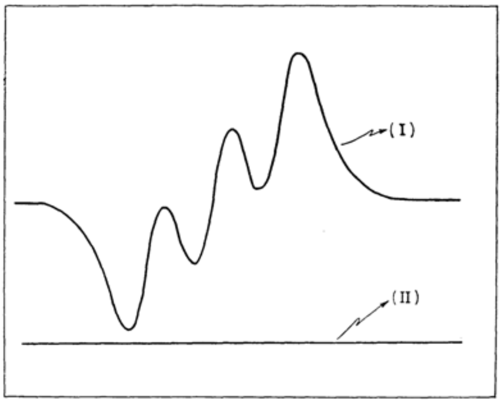


Fig. 6. Reaction of diphenylnitric oxide with phenylmagnesium bromide, ESR spectra of solutions.
(I) 1.25×10^{-4} mol. solution of diphenylnitric oxide in 10 ml. THF.
(II) After addition of 7.5×10^{-4} mol. of phenylmagnesium bromide to solution I.

These facts seem to suggest that the Grignard reagent contains some sort of $(MgBr)_2\cdot(RMgBr)_n$-type complex.7) Therefore, the existence of an equilibrium between diphenylnitric oxide and an excess of the Grignard reagent seems not surprising.

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5) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963); A. D. Vreugdenhill and C. Blomberg, *Rec. trav. chim.*, **28**, 453 (1963).

6) H. Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, New York (1949), p. 489.

7) The Grignard reagent can produce ketyl-like free radicals from the ketones, which can be easily reduced to the corresponding metal ketyls. This investigation will be reported on later.