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Aryliminodimagnesium Reagents. III. The Deoxygenative Condensation with Nitroso- and Nitroarenes: Electronic Effect of Substituents on Product Distribution

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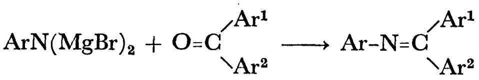
Aryliminodimagnesium reagents ($\mathrm{ArN(MgBr)_2}$) condense with nitrosoarenes and nitroarenes giving the corresponding azoarenes and azoxyarenes, respectively. Azoxyarenes were moderately deoxygenated by treatment with excessive amounts of the reagent giving the corresponding azoarenes. The reaction of nitroarenes with differently substituted reagents afforded unsymmetrically substituted azoxy- and azoarenes: Small amounts of symmetrically substituted azoarenes, which originated from the oxidative coupling of the reagent molecules, were also isolated. The distribution of the three types of condensation products are governed by the electronic effect of substituents of both the reagents and the substrates.

It has been reported very recently that aryliminodimagnesium reagents ($\mathrm{ArN(MgBr)_2}$, aryl-IDMg), derived from anilines and two molar equivalents of EtMgBr, condense with diaryl ketones giving the corresponding anils[1,2] (Scheme 1). According to the manner of deoxygenative condensation, aryl-IDMg are expected to react with a wide variety of substrates. Actually, the treatment of nitroso- and nitroarenes with the reagents afforded the corresponding azo- and azoxyarenes, respectively. In this paper, the electronic effect on the product distribution will be explained in comparison with those reported previously on the reaction of ArMgBr.[3,5,6]

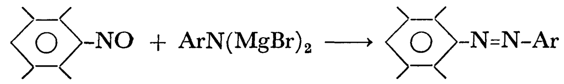


$$\mathrm{ArN(MgBr)_2 + O{=}C}\begin{smallmatrix}\nearrow \mathrm{Ar^1}\\ \searrow \mathrm{Ar^2}\end{smallmatrix} \longrightarrow \mathrm{Ar\text{-}N{=}C}\begin{smallmatrix}\nearrow \mathrm{Ar^1}\\ \searrow \mathrm{Ar^2}\end{smallmatrix}$$

Scheme 1.

Results and Discussion

The condensation ability of aryl-IDMg towards nitrosoarenes is exemplified by the reaction with highly hindered 2,3,5,6-tetramethylnitrosobenzene(nitrosodurene, Scheme 2 and Table 1). The comparison of the yields of the hindered azoarenes in Expt 1 with that in Expt 2 suggests that the deoxygenative condensation reaction with the nitrosoarene requires two molar equivalents of the reagent: This feature is in contrast with results obtained in the reactions with diaryl ketones which require usually an equimolar amount of the reagent.[1,2] The more strongly electron-donating *p*-methoxyphenyl-IDMg gave an excellent yield of the azo product (Expt 3), though a trace amount of an unidentifiable contaminant was eliminated with difficulty. The less strongly electron-donating *p*-chlorophenyl-IDMg reduced the yield (Expt 4), which, however, was improved by heating for more than 3 h and/or by use of three or more molar equivalents of the reagent.



Scheme 2.

The facts that the formation of a radical species in Expt 1 was detected by ESR and that the more strongly electron-donating reagent is more favorable to the reaction (*p*-MeO>*p*-Me>*p*-Cl) suggest that the condensation reaction is governed by the electron-transfer from the reagent to the substrate: The same order was observed for the formation of the nitroxide radical in the Grignard reaction of the same substrate.[3]

The condensation ability of the IDMg reagents with the nitroso functional group is confirmed. This reaction, however, is of no synthetic importance since the facile condensation of nitrosoarenes with arylamines in acetic acid has been well established.[4] The IDMg reaction with nitrosoarenes was not investigated further.

The reaction of nitrobenzene with more than five molar equivalents of phenyl-IDMg was studied first, the results being given in Table 2. High overall yields of azoxy- and azobenzenes were obtained (Expts 5 and 6). An authentic sample of azoxybenzene was

Table 1. Reaction of nitrosodurene with aryl-IDMg reagents

Expt No.	Nitrosodurene (mmol)	$p\text{-RC}_6\text{H}_4\text{N(MgBr)}_2$ R	(mmol)	$p\text{-RC}_6\text{H}_4\text{-N=N-Dur}$[a] yield/%
1	4.9	H	4.9	15[b]
2	6.1	Me	12.6	84[c]
3	3.0	MeO	6.1	93[c]
4	3.0	Cl	6.1	31[c]

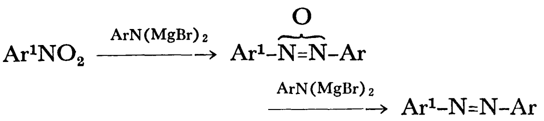
a) Dur=2,3,5,6-$\mathrm{Me_4C_6H}$. b, c) Yields, based on the amounts of nitrosodurene used, were obtained after heating at 55 °C b) for 2 h, and c) for 3 h.

Table 2. Reaction of aryl-IDMg for converting nitro- and azoxybenzene into azobenzene

Expt No.	Substates	(mmol)	$\mathrm{ArN(MgBr)_2}$ Ar	$\mathrm{ArN(MgBr)_2}$ (mmol)	Molar ratio [IDMg]/[Substr.]	Yields[a)]/% Overall	Yields[a)]/% $\underset{\overset{\downarrow}{\mathrm{O}}}{\mathrm{PhN{=}NAr}}$	Yields[a)]/% $\mathrm{PhN{=}NAr}$
5	$\mathrm{PhNO_2}$	(4.1)	$\mathrm{C_6H_5}$	(20.5)	5.0	85.1	53.4	31.7
6	$\mathrm{PhNO_2}$	(2.6)	$\mathrm{C_6H_5}$	(20.3)	8.0	82.8	21.5	61.3
7	$\underset{\overset{\downarrow}{\mathrm{O}}}{\mathrm{PhN{=}NPh}}$	(5.5)	*p*-$\mathrm{MeC_6H_4}$	(11.0)	2.0	97.7	75.0[b),c)]	22.7[b)]

a) Yields, based on the amount of substrates used, were obtained after heating at 55 °C for 3 h. b) Ar=Ph. c) Recovered amount.

deoxygenated at a moderate rate on treatment with two molar equivalents of *p*-methylphenyl-IDMg (Expt 7). Thus, the formation of azobenzene *via* the intermediate formation of azoxybenzene followed by its deoxygenation (Scheme 3) is confirmed.



$$\mathrm{Ar^1NO_2} \xrightarrow{\mathrm{ArN(MgBr)_2}} \mathrm{Ar^1\text{-}\overset{O}{N}{=}N\text{-}Ar} \xrightarrow{\mathrm{ArN(MgBr)_2}} \mathrm{Ar^1\text{-}N{=}N\text{-}Ar}$$

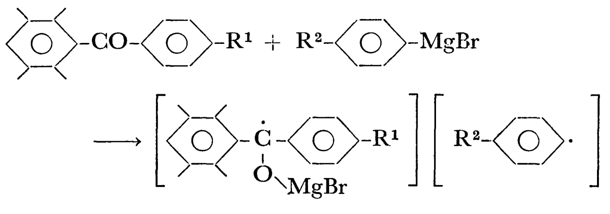
Scheme 3.

Three types of condensation products were obtained in the reaction of a substituted nitroarene with a differently substituted aryl-IDMg (Scheme 4 and Table 3).

$$\mathrm{Ar^1NO_2} + \mathrm{Ar^2N(MgBr)_2} \longrightarrow$$
$$\mathrm{Ar^1\text{-}N(O){=}N\text{-}Ar^2} + \mathrm{Ar^1\text{-}N{=}N\text{-}Ar^2} + \mathrm{Ar^2\text{-}N{=}N\text{-}Ar^2}$$

Scheme 4.

In the reaction with nitroarenes carried out using a fixed molar ratio of reagent to substrate (Expts 8—11), the distribution of the yields of the unsymmetrically substituted azoxy- and azoarenes varies remarkably with the electronic effect of the substituents of both the substrates and the reagents. The variation can be explained in terms of the electron-accepting and -donating ability of the reactants;[5)] the explanation given below is similar to that given previously for the Grignard reaction involving initial electron-transfer process.[6)] The process for the Grignard reaction with hindered benzophenones (Scheme 5), as estimated by ESR, is governed by the effect of the substituents R^1 and R^2 as shown in the following:



Scheme 5.

faster ← electron-transfer → slower

$R^2 = H$: $R^1 = F$, $Cl > H > OMe$[6)]

(← electron-accepting ability of substrates)

$R^1 = H$: $R^2 = OMe > H > F$[7)]

(← electron-donating ability of reagents).

The detection of any radical species by ESR at room temperature in Expts 5—11 was unsuccessful, probably due to the unhindered structure[6,7)] of the nitroarenes used.

Symmetrical azoarenes (Expts 8—11), which were not observed in the reaction with diaryl ketones,[1,2)] should be formed as the result of oxidative coupling of the reagent molecules due to the much higher electron-accepting ability of nitroarenes than that of ketones.[8,9)] Yields of the symmetrical azoarenes increase in the reaction of strongly electron-donating reagent (*p*-MeO>*p*-Me>*p*-Cl) with strongly electron-accepting nitroarene (*p*-Cl>*p*-Me>*p*-MeO).

Typical extremes of the product distribution are demonstrated by the results of Expts 10 and 11. The combination of the highly electron-accepting *p*-chloronitrobenzene with the highly electron-donating *p*-methoxyphenyl-IDMg gave a high combined yield of the azo products, but no azoxy product. The other combination of *p*-methoxynitrobenzene with *p*-chlorophenyl-IDMg gave the highest yield of the azoxy product together with the lowest combined yield of the azo products.

The effect of the molar ratio of reagent to substrate is another factor governing the distribution of the products especially when the highly electron-donating reagent is used. The highest yield of the azoxyarene in Expt 11 is due to the use of the less electron-donating *p*-chlorophenyl-IDMg: Even the treatment with ten molar equivalents of the reagent for 10 h reduced the yield only slightly (Expts 12 and 13). In contrast, the use of only two molar equivalents of the more electron-donating *p*-methoxyphenyl-IDMg reduced the yield of the azoxy product (Expts 14 and 15).

It is important to note that the azoxy products obtained in Expts 14 and 15 are isomeric with those obtained in Expts 9 and 11, respectively. Since any isomerization of an azoxy compound was not detected under the reaction conditions, this method provides a new route for preparing isomeric pairs of azoxyarenes, $\mathrm{Ar^1\text{-}N(O){=}N\text{-}Ar^2}$ and $\mathrm{Ar^1\text{-}N{=}N(O)\text{-}Ar^2}$, independently.[10)] A more detailed study on the preparation and the deoxygenation of azoxyarenes will be described in the subsequent paper.

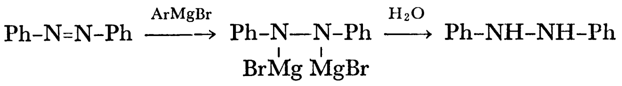
All the aryl-IDMg reagents used in this study are

Table 3. Effect of substituents and molar ratio on product distribution in the reaction of p-$R^1C_6H_4NO_2$ with p-$R^2C_6H_4$-IDMg

Expt No.	Substituents		Molar ratio [IDMg]/[$ArNO_2$]	Yields[a)]/%			
	R^1	R^2		Overall	Unsym. azoxy.	Unsym. azo.	Sym. azo.
8	Me	MeO	6.2[b)]	90.1	0	73.0	17.1
9	MeO	Me	6.2[b)]	89.7	24.3	51.7	13.7
10	Cl	MeO	6.2[b)]	84.4	0	57.7	26.7
11	MeO	Cl	6.2[b)]	93.1	73.4	14.8	4.9
12	MeO	Cl	5.0[c)]	97.7	77	15	5.7
13	MeO	Cl	10.0[d)]	89.5	60	22	7.5
14	Me	MeO	2.0[b)]	83	39	34	10
15	Cl	MeO	2.0[b)]	71.3	50	12	9.3

a) Yields are based on the amount of $ArNO_2$ used. b, c, d) The reaction mixtures were heated at 55 °C for b) 3 h, c) 5 h, and d) 10 h, respectively.

less electron-donating than arylmagnesium bromides since the formers do not affect azoarenes whereas the latters convert azobenzene into hydrazobenzene[11)] (Scheme 6). The vigorous reaction of the highly electron-accepting nitrobenzene with the highly electron-donating Grignard reagent (PhMgBr) affords comparable amounts of the products due to the addition-reduction (Ph_2NH), the deoxygenation (PhOH), and the oxidative coupling (Ph–Ph).[12)] The reaction has been little studied and attracted no attention until the interesting Grignard reaction of nitrobenzothiazoles was reported.[13)] The deoxygenative condensation reaction presented here owes its success to the moderate electron-donating ability of the aryl-IDMg reagents,[1–3)] though the detailed structure and the mechanism remain to be investigated.



$$\mathrm{Ph\text{-}N{=}N\text{-}Ph} \xrightarrow{\mathrm{ArMgBr}} \underset{\mathrm{BrMg}\quad\mathrm{MgBr}}{\mathrm{Ph\text{-}N{-}N\text{-}Ph}} \xrightarrow{\mathrm{H_2O}} \mathrm{Ph\text{-}NH\text{-}NH\text{-}Ph}$$

Scheme 6.

The overall yield was somewhat lower when the yield of the symmetrical azoarene was higher, and *vice versa* (Table 3): In Expt 10, a recognizable amount of an unidentifiable and poorly soluble black material was formed, probably due to a free radical reaction initiated by the quick electron-transfer from the reagent to the substrate.[14)] Some attempts, *i.e.*, the dilution of the reagent and/or the substrate solution, the addition of the reagent solution in the reverse manner, and the addition at −78 °C, were not effective in reducing the formation of the black material as well as the symmetrical azoarene.

The unimportant limitations given are difficult to overcome; nevertheless, the IDMg process provides a general method for preparing unsymmetrical azoxy- and azoarenes.

Experimental

The melting points of azo- and azoxyarenes are uncorrected.

Materials. Nitrosodurene was prepared according to the reported method.[3)] All the nitroarenes and the anilines used in this study were commercially available, and were purified by distillation before use.

Procedures. The typical procedure is given as follows. Ethylmagnesium bromide (30.8 mmol) was prepared under N_2 atmosphere as usual in THF (20 ml), and a 2—3% excess amount of the aniline (15.8 mmol) dissolved in THF (15 ml) was added at 0 °C to the Grignard solution. The mixture was stirred gently at 55 °C for 40 min to complete the evolution of ethane.[1)] The nitroarene (3.08 mmol) dissolved in THF (15 ml) was added to the IDMg solution at 0 °C; the color of the mixture turned deep reddish brown, The colored mixture was stirred at 55 °C for 3 h, quenched with aqueous NH_4Cl, extracted with diethyl ether followed by washing with dilute HCl (0.5—1.0 mol dm^{-3}) for removing the unreacted aniline. After washing with water, the colored solution was dried on $MgSO_4$ and concentrated under reduced pressure; the product mixture was chromatographed on silica gel (Wako-Gel C-200).

Products. The chromatographic separation of the three types of the products was sometimes incomplete. The yields of the products in individual experiments, however, were estimated easily by ^{1}H-NMR since the signals of the four *ortho*-protons around the –N(O)=N– group appear at lower field than 8.0 ppm while those of the protons around the –N=N– group appear at higher field.

The melting points and ^{1}H-NMR data of azo- and azoxyarenes are given in Tables 4 and 5, respectively. Among the ^{1}H-NMR data, some aromatic proton signals which consist of two AB-quartets are not assigned and the figures are given in parentheses.

The molecular weight of the product was recorded on a Denshi Kagaku EMD-05A Mass Spectrometer. Results of the elemental analyses of the new azo- and azoxyarenes, which are represented by the Expt Nos. as shown in Tables 4 and 5, are given in the following.

(1): Found: C, 81.77; H, 7.51; N, 11.65%. Calcd for $C_{16}H_{18}N_2$: C, 80.67; H, 7.56; N, 11.76%.

(2): Found: C, 81.02; H, 7.85; N, 11.06%. Calcd for $C_{17}H_{20}N_2$: C, 80.95; H, 7.93; N, 11.11%.

(3): Found: C, 76.21; H, 7.40; N, 10.55%. Calcd for $C_{17}H_{22}N_2O$: C, 76.12; H, 7.46; N, 10.44%.

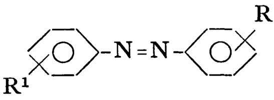
(4): Found: C, 70.31; H, 6.50; N, 10.30%. Calcd for $C_{16}H_{18}ClN_2$: C, 70.20; H, 6.58; N, 10.24%.

(10): Found: C, 63.21; H, 4.52; N, 11.50%. Calcd for $C_{13}H_{11}ClN_2O$: C, 63.28; H, 4.46; N, 11.36%.

(11): Found: C, 60.01; H, 4.09; N, 10.74%. Calcd for $C_{13}H_{11}ClN_2O_2$: C, 59.43; H, 4.19; N, 10.67%.

(14): Found: C, 69.60; H, 5.81; N, 74.30%. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.42; H, 5.78; N, 74.38%.

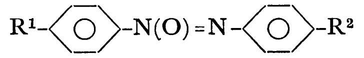
Table 4. Melting points and NMR data of azoarenes



Expt No.	R^1	R^2	Mp θ_m/°C		^{1}H-NMR data
			Obsd	Lit	δ
5	H	H	68.5	68.5	8.00—7.80(4H, m, Ar); 7.58—7.35(6H, m, Ar).
1	Dur.[a]	H	90—92	—	7.90—7.70(2H, m, Ar); 7.46—7.00(3H, m, Ar); 6.80 (1H, s, Ar); 2.22(6H, s, Me); 2.05(6H, s, Me).
2	Dur.	*p*-Me	99—101.5	—	7.72 and 7.22(4H, ABq, Ar); 6.84(1H, s, Ar); 2.41 (3H, s, Me); 2.24(6H, s, Me); 2.04(6H, s, Me).
3	Dur.	*p*-MeO	123—125	—	7.80 and 6.92(4H, ABq, Ar); 6.83(1H, s, Ar); 3.83 (3H, s, Me); 2.24(6H, s, Me); 2.04(6H, s, Me),
4	Dur.	*p*-Cl	89.5—91	—	7.84 and 7.44(4H, ABq, Ar); 6.92(1H, s, Ar); 2.24 (6H, s, Me); 2.08 (6H, s, Me).
8	*p*-Me	*p*-MeO	110—113	109—110[15]	7.98(7.90) and 7.32(4H, ABq, Ar); 7.90(7.98) and 7.00(4H, ABq, Ar); 3.80(3H, s, Me).
10	*p*-Cl	*p*-MeO	123—123.5	—	7.90(7.86) and 7.46(4H, ABq, Ar); 7.86(7.90) and 6.98(4H, ABq, Ar); 3.86(3H, s, Me).
	p-Cl	*p*-Cl	175—178	183—184[16]	7.90 and 7.52(8H, ABq, Ar).
	p-MeO	*p*-MeO	165—167	163[17]	7.92 and 7.02(8H, ABq, Ar); 3.86(6H, s, Me).
	p-Me	*p*-Me	139—142	142—143[16]	7.86 and 7.33(8H, ABq, Ar); 2.43(6H, s, Me).

a) Dur.=2,3,5,6-Me_4C_6H-.

Table 5. Melting points and NMR data of azoxyarenes



Expt No.	R^1	R^2	Mp θ_m/°C		^{1}H-NMR data
			Obsd	Lit	δ
6	H	H	35—35.5	35.5	8.40—8.16(4H, m, Ar); 8.52—8.32(6H, m, Ar).
	p-Cl	*p*-MeO	142—146.5	145[18]	8.56(8.46) and 7.65(4H, ABq, Ar); 8.46(8.56) and 7.17(4H, ABq, Ar); 3.98(3H, s, Me).
11	*p*-MeO	*p*-Cl	105.5—107	—	8.28(8.15) and 7.42(4H, ABq, Ar); 8.15(8.28) and 6.93 (4H, ABq, Ar); 3.87(3H, s, Me).
14	*p*-Me	*p*-MeO	108.5—110	—	8.30(8.20) and 7.24(4H, ABq, Ar); 8.20(8.30) and 6.92 (4H, ABq, Ar); 3.86(3H, s, Me); 2.44(3H, s, Me).
9	*p*-MeO	*p*-Me	77—78.5	—	8.28(8.13) and 7.65(4H, ABq, Ar); 8.13(8.28) and 6.94 (4H, ABq, Ar); 3.84(3H, s, Me); 2.39(3H, s, Me).

(9): Found: C, 69.52; H, 5.69; N, 74.51%. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.42; H, 5.78; N, 74.38%.

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