Aryliminodimagnesium Reagents. XIV.[1] Reactions with Nitrobenzenes Having Electronegative *ortho*-Substituents. Effects of Reaction Conditions on Condensation, Replacement, and Substitution

Masao Ōkubo,* Yoshito Inatomi, Naoki Taniguchi, and Kaori Imamura
Department of Chemistry, Faculty of Science and Engineering, Saga University, Honjō-machi, Saga 840
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In reactions of $ArN(MgBr)_2$ with *o*-MeO- and *o*-halo-substituted nitrobenzenes, types and yields of products were different from those in its reactions with *m*- and *p*-substituted substrates. Condensation (leading to unsymmetrical azoxy- and azobenzenes), *o*-substituent replacement, and nuclear substitution took place. Relative yields of products were greatly affected by substituents and reaction conditions. *o*-MeO and *o*-F favor replacement, while *o*-Cl, *o*-Br, and *o*-I favor substitution. Replacement and/or substitution predominate when small molar excess of reagent and low concentration are used, while condensation predominates when large molar excess of reagent and high concentration are used, which phenomenon is mechanistically discussed.

The aryliminodimagnesium ($ArN(MgBr)_2$, aryl-IDMg) derived from aniline and EtMgBr condenses with *m*- and *p*-substituted nitrobenzenes (cf. Scheme 1),[2] and provides a convenient method for the independent preparation of *ONN* and *NNO* isomers of unsymmetrical (*unsym*-) azoxybenzenes (**1**).[3] **1** undergoes simple deoxygenation by molar excess of IDMg to give the corresponding *unsym*-azobenzene (**2**).[2] IDMg molecules are oxidatively dimerized, via single electron transfer (SET), to afford symmetrical (*sym*-) azobenzene (**3**).[2,4] The relative yield of **1**—**3** depends mainly on the relative efficiency of SET.[5,6]

The first purpose of the present study is to examine the formation of *o*-substituted azoxybenzene isomers which have so far been difficultly accessible. The second purpose is to examine the replacement of electronegative *o*-substituents on nitrobenzene via SET. 1-MeO and 1-Br substituents on the 9-fluorenylidene system are replaced by Grignard and IDMg reagents,[7] but no similar examples have been reported in reactions of nitroarenes with magnesium reagents. In IDMg reactions with *o*-MeO- and *o*-halo-nitrobenzenes, the expected azoxy formation and replacement as well as nuclear substitution took place, and relative yields of products depended greatly on reaction conditions. The results obtained will be summarized and discussed.

Results and Discussion

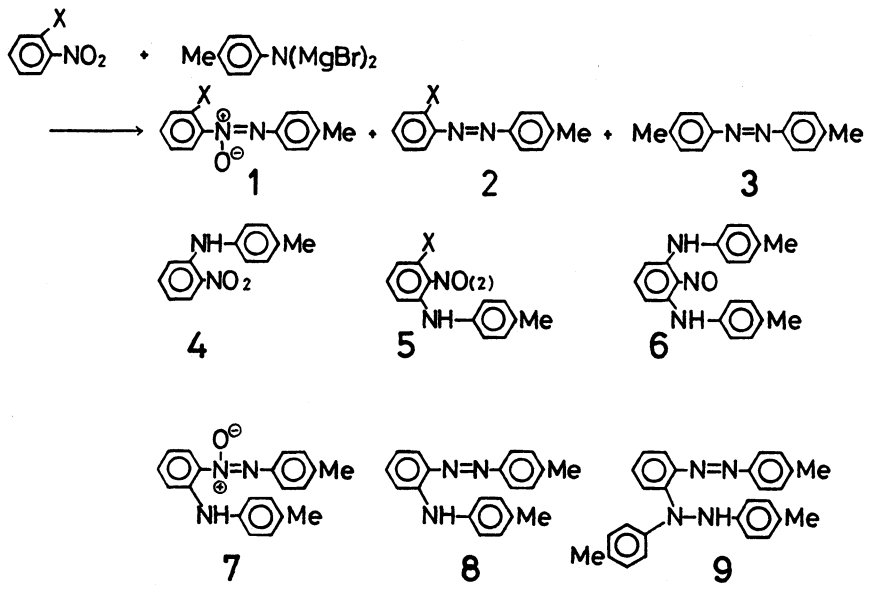
The results obtained by use of small and large molar excesses of IDMg will be separately described.

Relative Yields of Replacement, Substitution, and Condensation Products from *o*-MeO- and *o*-Halo-Nitrobenzenes in the Reaction with Small Molar Excess of Noncrowded IDMg. Effects of *o*-Substituted IDMg. The four products **4**—**7** in addition to **1**—**3** were obtained by the treatment of *o*-MeO- and *o*-halo-nitrobenzenes with small molar excess of *p*-MeC_6H_4-IDMg in tetrahydrofuran (THF, 50 ml). The product **4** is formed via replacement, **5** via substitution, **6** via

Table 1. Product Distribution in the Reaction with Small Excess of *p*-MeC_6H_4-IDMg

Run *o*-$XC_6H_4NO_2$ No.	X	Addn. manner[a]	Molar ratio	Yield/% 1	2	3	4	5	6	7	Recov.
S1	MeO	N	1.2	35	14	4	27	3	0	0	14
S2	MeO	R	1.5	29	10	3	50	3	0	0	3
S3	F	R	1.5	44	9	7	19	4	4	2	0
S4	F	R	2.0	66	18	6	2	0	3	4	0
S5	Cl	R	1.5	8	17	7	1	29	2	0	36
S6	Cl	R	2.0	17	21	11	Trace	36	2	0	13
S7	Br	R	1.5	15	10	10	Trace	31	2	0	20
S8	Br	R	2.0	41	21	12	0	27	2	0	0
S9	I	R	1.5	14	9	7	0	27	3	0	39
S10	Cl	N	2.0	38	28	16	0	14	3	0	0
S11	Cl	N	5.0	28	36	36	0	0	0	0	0
S12	Cl[b]	R	2.0	12	13	12	0	35	1	0	27
S13	Me(*p*)[c]	N	1.5	46	18	1	0	0	0	0	13
S14	Et	N	1.2	28	12	13	0	0	0	0	18
S15	Me(*p*)[d]	N	1.5	14	13	14	0	0	0	0	4

a) N: "Normal" addition of substrate to reagent at 0 °C, followed by heating at 55 °C for 3 h. R: "Reverse" addition of reagent to substrate at room temp (12—15 °C) for 0.5 h, followed by heating at 55 °C for 1.5 h. b) 250 ml of THF was used. c) *o*-$MeOC_6H_4$-IDMg was used. d) *o*-EtC_6H_4-IDMg was used.



Scheme 1.

substitution-replacement, and **7** via substitution-condensation (limited to *o*-F substrate). $\mathbf{5}^{MeO}$ and $\mathbf{5}^{F}$ are nitro compounds, while $\mathbf{5}^{Cl}$, $\mathbf{5}^{Br}$, and $\mathbf{5}^{I}$ are nitroso compounds. The yields of **1**—**7** are summarized in Table 1 (Runs S1—S12).

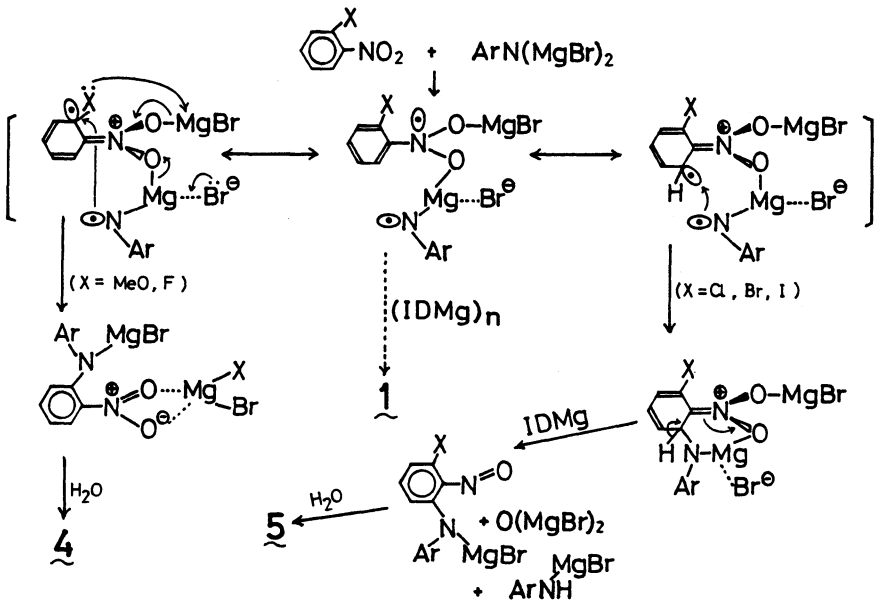
By the "reverse" addition of slight molar excess of IDMg to substrate at room temperature (12—15 °C) for 30 min (S2—S9), the products **4** and **5** become predominant, while **6** and **7** remain as minor. The replacement is almost completely limited to *o*-MeO and *o*-F (S2—S4), while the substitution is limited to *o*-Cl, *o*-Br, and *o*-I (S5—S9). This cannot be explained in terms of the redox potentials (MeO, −1.540; F, −1.324; Cl, −1.321; Br, −1.348; I, −1.377 V),[6] but is probably due to the different leaving abilities of these substituents as anions (as their Mg salts) from the radical anion of substrate.[8] The replacement requires 1.2—1.5 mol of reagent and the substitution requires 1.5—2.0 mol (S1—S4 and S5—S9). The reason for the almost no replacement of *o*-Br on nitrobenzene (S7 and S8), in contrast to the facile replacement of 1-Br on 9-fluorenylidene system,[7] is equivocal. The replacement and substitution solely at ortho positions arise from tight coordination of the nitro group to the Mg atom of reagent.

In Runs S6 and S10—S12, the effect of reaction conditions on the conversion of *o*-Cl substrate is made disclosed. By the "normal" addition of substrate to 2.0 mol of IDMg (S10), the yields of **1** and **2** increase, while that of **5** decreases (cf. S6). By use of 5.0 mol of IDMg (S11), **1**—**3** become predominant at the expense of **5**. The use of 250 ml of THF (S12) causes a decrease in yield of **1** and **2**, but almost no effect on that of **5** (cf. S6).

The results of S1—S12 indicate that, under an ideal condition,[9] the replacement requires one molecule of IDMg, whereas the substitution requires two molecules; the second one may be consumed for eliminating the nitro-oxygen and ortho-hydrogen (Scheme 2). For the condensation, two or more IDMg molecules may cooperate via a complicated pathway and not via a simple addition-elimination. Since larger moles and/or higher concentrations of reagent favor also the deoxygenation of **1** (S11),[2,3] the optimum condition for the preparation of *o*-substituted **1** must be carefully explored.

The comparably bulky *o*-Et and *o*-MeO groups "on reagent" affect noticeably the yield of **1** and **2** in comparison with the same groups "on substrate" (S1 and S13—S15). In the "on substrate" cases (S1 and S14), the two groups lead to comparable yields of **1** and **2** lower than those in S13 (**4** is also formed in S1). In the "on reagent" cases, the *o*-MeO group (S13) favors the condensation, while the *o*-Et group (S15) leads to a poor combined amount of **1** and **2** and a poor recovery. The *o*-MeO group on reagent, probably chelating with its Mg atom, assists the IDMg nitrogen to access to the nitro group. The *o*-Et group on reagent causes interference with the access, resulting in self-decomposition of substrate via SET.[10]

Relative Yields of Condensation Products in the Reaction with Large Molar Excess of IDMg. By use of 8.0 mol of *p*-Me-C_6H_4-IDMg (L1—L7, Table 2), the other minor products **7**—**9** appeared at the expense of **4**—**6**. The products **7** and **8** are formed from **4** via condensation and deoxygenation, and **9** having a hydrazino group via replacement, probably by a dimeric salt ((ArN(MgBr)-)$_2$). Their formation in yields lower than 10% only in the case of *o*-MeO and *o*-F substrates (L1, L5, and L6) is in accord with the results of S1—S4. The products **1**—**3** are major ones (L1—L6), and the yields differ from those in the case of the *p*-substituted substrates (L8—L12), as specified by the following two features.



Scheme 2.

Table 2. Product Distribution in the Reaction with Large Excess (8.0 mol) of p-MeC_6H_4-IDMg

Run No.	$XC_6H_4NO_2$ X	Yields/%					
		1	**2**	**3**	**7**	**8**	**9**
L1	*o*-F	7	48	38	8	0	0
L2	*o*-Cl	16	35	40	0	0	0
L3	*o*-Br	7	36	39	0	0	0
L4	*o*-I	16	25	59	0	0	0
L5	*o*-MeO	0	57	33	6	0	3
L6	2,5-$(MeO)_2$	0	62	25	3	7	3
L7	*o*-Me	28	48	24	0	0	0
L8	*p*-F	27	39	22	0	0	0
L9	*p*-Cl	28	45	12	0	0	0
L10	*p*-Br	33	42	19	0	0	0
L11	*p*-I	36	39	19	0	0	0
L12	*p*-MeO	24	52	14	0	0	0
L13	2,4,6-Me_3	0[a] 16[b]	39	23	0	0	0
L14[c]	2,4,6-Me_3	36[a] 16[b]	23	20	0	0	0
L15[d]	2,4,6-Me_3	11[a] 2[b]	18	5	0	0	0

a) *ONN*-Isomer. b) *NNO*-Isomer. c) 4.0 mol of p-MeC_6H_4-IDMg was used. d) 1.2 mol of p-MeC_6H_4-IDMg was used. Product **4** was isolated in 29% yield.

The first feature is that shift of substituents from the para to ortho position causes decrease in combined yield of **1** and **2** from 66—76% (L8—L12) to 41—57% (L1—L5) and increase in that of **3** from 12—22% to 33—59%. The feature arises from the effect of lone-pair electrons of *o*-substituents favorable for the dimerization and not from that of steric repulsion against condensation, as indicated by the comparable yields caused by *o*-Me- (L7) and *p*-substituents (L8—L12). The formation of **3** is observed in IDMg reaction with ortho-quinones, but not with para-quinones.[11] According to the mechanism of two-electron oxidation of IDMg molecules,[4] all the adjacent halogeno, methoxyl, carbonyl, and nitro groups may coordinate to the Mg atoms of IDMg molecules to assist the arylaminyl radicals ($Ar(MgBr)N\cdot$) to be produced in the proximity of each other in favor of the dimerization.

The second feature is the evidently lower yields of **1** in L1—L6 (0—16%) than those in L7—L12 (24—36%). The feature arises also from the effect of lone-pair electrons of *o*-substituents of **1** favoring its deoxygenation. The reciprocal of λ_{max}'s of *m*- and *p*-substituted azoxybenzenes are correlated with their reactivity in IDNg deoxygenation.[3] Thus the reduced electron-repelling resonance effect of *o*-substituent by steric hindrance causes the enhancement of positive charge on azoxy nitrogen to facilitate the attack of anionic IDMg nitrogen.[3]

Determination of *ONN* and *NNO* Structures of Azoxybenzenes, and Unique *ONN-NNO* Isomerization Caused by 2,6-Me_2 Groups. The *ONN*-structure of *o*-substituted *unsym*-azoxyarenes, having azoxy oxygen combined to the original "nitro" nitrogen, was confirmed by means of ^1H NMR spectra different from those of the known *NNO*-isomer obtained by the reaction of *o*-substituted phenyl-IDMg with *p*-Me-nitrobenzene. Comparison of photo-Wallach rearrangement products with authentic *o*-hydroxyazobenzenes[12,13] was also useful. X-Ray crystallography was not used because almost all the azoxyarenes are oil. A solid one having 2,6-Me_2 groups tends to form fluffy needles, and no single crystals of sufficient size with clean surface were obtained.

Similarly to *p*- and *m*-substituted azoxybenzenes,[3] the *o*-monosubstituted ones undergo no *ONN-NNO* isomerization even by being heated with large molar excess of IDMg. A unique *ONN-NNO* isomerization under the same conditions was observed in the case of the most crowded 2,4,6-Me_3-nitrobenzene (L13, Table 2). The less crowded azoxy product $\mathbf{1}^{3Me}_{NNO}$ is formed via isomerization of the much crowded "normal" isomer $\mathbf{1}^{3Me}_{ONN}$ by an interaction with IDMg. Even by use of 4.0 or 1.2 mol of IDMg (L14 and L15), both $\mathbf{1}^{3Me}_{ONN}$ and $\mathbf{1}^{3Me}_{NNO}$ were isolated.

Conclusion

The various effects of coordination proposed are in line with those given for modifying relative efficiency of SET estimated by oxidation and reduction potentials.[6] The reasons given for yield variations with leaving abilities and positional change of substituents are still equivocal, but the cooperation of reagent molecules for condensation is possibly an important clue to the mechanism of the essential reaction pathway of Scheme 1. Though optimum conditions remain to be studied, the IDMg method has proved to be useful for the preparation of crowded azoxyarenes available for studying the photoinduced[12,13] and acid-catalyzed[14] rearrangements as well as the deoxygenation by PX_3-type reagents.[15]

Table 3. Melting Points and ^1H NMR Data of Products Including Some Crowded Azoxybenzenes

No.	Run No.	Mp θ_m/°C	^1H NMR Data δ
$\mathbf{1}^{F}$	S3, S4, L1	Oil	8.12 and 7.22 (4H, ABq, J=15Hz), 7.96—7.78 (1H, m), 7.50—7.10 (3H, m), 2.42 (3H, s).
$\mathbf{1}^{Cl}$	S10, S11, L2	Oil	8.12 and 7.24 (4H, ABq, J=20Hz), 7.72—7.24 (4H, m), 2.40 (3H, s).
$\mathbf{1}^{Br}$	S7, S8, L3	Oil	8.12 and 7.24 (4H, ABq, J=20Hz), 7.84—7.20 (4H, m), 2.40 (3H, s).
$\mathbf{1}^{I}$	S9, L4	Oil	8.24 and 7.36 (4H, ABq, J=15Hz), 8.10 (1H, d), 7.80—7.15 (3H, m), 2.45 (3H, s).
$\mathbf{1}^{Me}$	L7	Oil	8.12 (2H, d), 7.77—7.58 (1H, m), 7.37—7.04 (5H, m), 2.44 (3H, s), 2.38 (3H, s).
$\mathbf{1}^{MeO}_{ONN}$	S1, S2, L5	Oil	8.00 and 7.17 (4H, ABq, J=27Hz), 7.66—6.76 (6H, m), 3.87 (3H, s), 2.40 (3H, s).
$\mathbf{1}^{MeO}_{NNO}$	S13	54.5—55	8.10 and 7.10 (4H, ABq, J=25Hz), 7.95—7.73 (1H, m), 7.73—6.66 (3H, m), 3.80 (3H, s), 2.43 (3H, s).
$\mathbf{1}^{3Me}_{ONN}$	L14	121—123	7.00 and 6.67 (4H, ABq, J=27Hz), 6.73 (2H, s), 2.27 (6H, s), 2.17 (6H, s).
$\mathbf{1}^{3Me}_{NNO}$	L13, L14	74.5—76.5	8.00 and 7.23 (4H, ABq, J=27Hz), 6.76 (2H, s), 2.44 (3H, s), 2.33 (3H, s), 2.23 (6H, s).
$\mathbf{1}^{Et}$	S14	Oil	8.00 and 7.13 (4H, ABq, J=27Hz), 8.16—7.87 (1H, m), 7.66—6.76 (3H, m), 2.66 (2H, q), 2.40 (3H, s), 1.26 (3H, t).
4	S1—S3	66.5—67	9.47 (1H, s), 8.22—6.71 (8H, m), 2.38 (3H, s).
$\mathbf{5}^{F}$	S3, S4	Oil	7.41—6.79 (8H, m), 2.25 (3H, s).
$\mathbf{5}^{Cl}$	S5, S6	Oil	7.33—6.82 (8H, m), 2.22 (3H, s).
$\mathbf{5}^{Br}$	S7, S8	Oil	7.67—6.93 (8H, m), 2.19 (3H, s).
$\mathbf{5}^{I}$	S9	Oil	7.70—6.76 (8H, m), 2.19 (3H, s).
$\mathbf{5}^{MeO}$	S1, S2	Oil	7.30—6.76 (8H, m), 3.67 (3H, s), 2.22 (3H, s).
6	S3—S10	147—149	13.39 (1H, s), 8.95 (1H, s), 7.29—6.20 (11H, m), 2.37 (6H, s).
7	S3, S4, L1, L5	Oil	9.50 (1H, s), 8.20—8.00 (3H, m), 7.79 (1H, d), 7.36—7.04 (7H, m), 6.86—6.64 (1H, m), 2.40 (3H, s), 2.24 (3H, s).
$\mathbf{7}^{MeO}$	L6	Oil	9.50 (1H, s), 8.38 (2H, d), 8.10—7.98 (1H, m), 7.64—7.00 (8H, m), 4.00 (3H, s), 2.50 (3H, s) 2.40 (3H, s).
$\mathbf{8}^{MeO}$	L6	Oil	9.42 (1H, s), 8.10—7.95 (2H, m), 7.64—7.00 (9H, m), 3.98 (3H, s), 2.46 (3H, s), 2.38 (3H, s).
9	L5	Oil	7.80—7.62 (3H, m), 7.34—7.02 (10H, m), 6.70—6.40 (3H, m), 5.76 (1H, s), 2.40 (3H, s), 2.36 (3H, s), 2.32 (3H, s).
$\mathbf{9}^{MeO}$	L6	Oil	9.50 (1H, s), 7.60—7.20 (2H, m), 7.08—6.80 (12H, m), 6.28 (1H, s), 3.80 (3H, s), 2.32 (3H, s), 2.22 (6H, s).

Experimental

Materials and Procedures. The reactions of Scheme 1 were carried out using 3—5 mmol of nitroarenes and calculated amounts of IDMg reagent in 50 ml of THF,[2,3] except in Run S12 where 250 ml of THF was used. The reaction conditions applied to the individual runs are given in Tables 1 and 2. Products were separated by column and preparative thin-layer chromatographies on silica gel and then recrystallized. Physical data of products **1** and **4—9** are summarized in Table 3, melting points being uncorrected. Elemental analyses gave satisfactory results. An identification of *ONN* and *NNO* structures of azoxyarenes by indirect means using photoreactions was carried out by comparison with authentic samples of *o*-hydroxyazoarenes.[13]

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