  Bull. Chem. Soc. Jpn., 56, 203—207 (1983)

Aryliminodimagnesium Reagents. IV. The Independent Preparation of Unsymmetrically Substituted Azoxyarene Isomers and Their Deoxygenation

Masao Ōkubo* and Kōji Koga

Department of Chemistry, Faculty of Science and Engineering, Saga University, Honjō-machi, Saga 840

(Received May 12, 1982)

By use of the condensation reaction of aryliminodimagnesium reagents ($ArN(MgBr)_2$) with nitroarenes, six symmetrical and eight unsymmetrical azoxyarenes including four pairs of isomers were prepared in 40—80% yields. The deoxygenation reaction of the azoxyarenes by treating with five molar equivalents of *p*-$MeOC_6H_4N(MgBr)_2$ at 55 °C in tetrahydrofuran was also studied, and the reactivity of deoxygenation was correlated to the shift of the electronic absorption maximum of azoxyarene.

So far, unsymmetrical azoxyarenes have been obtained by oxidation of unsymmetrical azoarenes,[1-3] by condensation of nitrosoarenes with *N*-arylhydroxylamines,[4,5] or by selective substitution on azoxybenzenes.[6] The first method often gives a mixture of isomers, their separation not always being easy.[5] The second method is more selective, but is ultimately limited by the instability of the starting materials. A method involving a Grignard reaction of substituted *N*-nitrosohydroxylamine derivatives[7] has also been reported, depending on the uncommon type of the starting material. These limitations have been an obstacle to the development of azoxyarene chemistry: The electronic effect of substituents on the deoxygenation by use of phosphorus(III) reagents, for instance, has not been studied enough.[8]

In the preceding paper,[9] the condensation of nitroarenes with aryliminodimagnesium reagents ($ArN(MgBr)_2$, aryl-IDMg) was reported. The reaction involves rapid deoxygenative condensation affording the azoxyarenes followed by much slower deoxygenation giving the azoarenes (Scheme 1). Since the intermediately formed azoxyarenes do not isomerize under the reaction conditions,[9] the IDMg method provides a novel route for preparing unsymmetrical azoxyarene isomers independently.

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

Scheme 1.

The authors first endeavored to find the optimum reaction conditions for preparing typical symmetrical and unsymmetrical azoxyarenes, and second to study their substituent effect on the deoxygenation by the treatment with an aryl-IDMg reagent. The results are reported in this paper.

Results and Discussion

Preparation of Azoxyarenes. On the basis of the reaction profiles given in the preceding paper,[9] the reaction conditions suitable for preparing unsymmetrical azoxyarenes (Scheme 1) are i) a less electron-donating reagent, ii) a less electron-accepting substrate, and iii) a lower molar ratio of reagent to substrate. However, the formation of the final products, unsymmetrical azoarenes, as well as that of the oxidative coupling products, symmetrical azoarenes, are unavoidable.

The molar ratio of the IDMg reagents to the nitroarenes used in Expts 1—6 (Table 1) were chosen in order to convert the substrates completely and also to minimize the subsequent deoxygenation of the primarily produced azoxyarenes. No substrate was recovered except in Expt 3 in which *ca.* 5% of the nitroarene was found in the product mixture. The facts that the most electron-donating *p*-methoxyphenyl-IDMg gave the highest combined yield of the azo products and that the least electron-donating *m*-methoxyphenyl-IDMg gave the lowest yield of the symmetrical azo product accord with the previous results.[9]

In the reactions carried out for preparing symmetrically substituted azoxyarenes (Scheme 2), the amount of the symmetrical azoarenes formed comes partly from the deoxygenation of azoxyarenes and partly from the oxidative coupling of the reagent molecules: The results are given in Table 2 (Expts 7—12).

$$RC_6H_4NO_2 + RC_6H_4N(MgBr)_2 \longrightarrow RC_6H_4\text{-}N(O)\text{=}NC_6H_4R + RC_6H_4\text{-}N\text{=}N\text{-}C_6H_4R$$

Scheme 2.

The remarkable recovery of the substrate in Expt 8 is ascribable to the weakest electron-donating ability of *p*-chlorophenyl-IDMg.

Summarizing the results given in Tables 1 and 2, the optimum molar ratio suitable for preparing azoxyarenes seems to depend mainly on the electron-donating ability of the aryl-IDMg reagents. The most, the medium, and the least electron-donating reagents require the lowest, the medium, and the highest molar ratio respectively (Table 3).

An unusual result was obtained when *p*-dimethylaminophenyl-IDMg, which was expected to be more electron-donating than the *p*-methoxyphenyl reagent, was allowed to react with *N*,*N*-dimethyl-*p*-nitroaniline (molar ratio=1.5). A 35% yield of the final product, the symmetrical azoarene, and a 38% of the unreacted substrate were isolated. The result, which is in conflict with all the preceding ones, is probably to be ascribed to the aggregation of the reagent molecules, due to the coordination ability of the nitrogen atom of the substituent.

The effectiveness of the aryl-IDMg method for pre-

Table 1. Yields of unsymmetrically substituted azoxybenzenes (Scheme 1)

Expt No.	Ar^1	Ar^2	Molar ratio	Yields/% Azoxy	Unsym. azo	Sym. azo
1	C_6H_5	p-MeC_6H_4	1.5	(60	: 40) [a]	
2	p-MeC_6H_4	C_6H_5	1.5	(70	: 30) [a]	
3	m-ClC_6H_4	p-$MeOC_6H_4$	1.5	48	21	15
4	p-MeC_6H_4	m-$MeOC_6H_4$	2.0	62	22	2.8
5	m-ClC_6H_4	C_6H_5	2.0	71	17	8.1
6	C_6H_5	m-ClC_6H_4	2.0	81	10—12	

a) The product ratio was estimated by NMR.

Table 2. Yields of symmetrically substituted azoxybenzenes (Scheme 2)

Expt No.	R	Molar ratio	Yields/% Azoxy	Azo
7	p-MeO	1.2	59	26
8	p-Cl	1.5	41 [a]	16 [a]
9	p-Cl	2.0	(71 :	29) [b]
10	p-Me	2.0	(64 :	36) [b]
11	m-Cl	2.5	78	17
12	meO	2.0	80	15

a) A 27% of p-$ClC_6H_4NO_2$ was recovered. b) The product ratio was estimated by NMR.

Table 3. Optimum molar ratio of reagents to substrates based on the electron-donating ability of the reagents

RC_6H_4-IDMg R	Molar ratio	Yields of azoxyarenes/%
p-MeO	1.2—1.5	50—60
p-Me, m-MeO, H	1.5—2.0	55—70
p-Cl, m-Cl	2.0—2.5	65—80

paring unsymmetrical azoxyarenes is demonstrated by the successful preparation of a new azoxy isomer derived from 1-phenylazonaphthalene (Scheme 3a).

a. 1-$NaphNO_2$ + $PhN(MgBr)_2$ ⟶ 1-Naph-N(O)=N-Ph (α-isomer)

b. $PhNO_2$ + 1-$NaphN(MgBr)_2$ ⟶ 1-Naph-N=N(O)-Ph (β-isomer)

Scheme 3.

The previous study on the peroxy acid oxidation of 1-phenylazonaphthalene[3] showed the exclusive formation of the sterically less hindered "β"-isomer (*cf.* Scheme 3b). By use of two molar equivalents of the respective reagents and the substrates as shown in the scheme, both the "α"- and "β"-isomers were prepared in yields of 43 and 63% respectively.

Deoxygenation of Azoxyarenes by the Aryl-IDMg Procedure. The deoxygenation of the substituted azoxyarenes by the IDMg method was studied. Since the deoxygenation is quite a mild reaction,[9] the azoxyarenes were treated with five molar equivalents of the most electron-donating p-methoxyphenyl-IDMg at 55 °C for 3 h (Scheme 4). The percentage of deoxygenation observed is given in Table 4.

Table 4. Deoxygenation of symmetrical and unsymmetrical azoxybenzenes (Scheme 4)
$R^1C_6H_4$-N(O)=N-$C_6H_4R^2$

$R^1=R^2$	Deoxygn. (%)	$R^1 \neq R^2$		Deoxygn. (%)
p-MeO	16	p-Cl	p-MeO	18
		p-MeO	p-Cl	48
p-Me	41	p-MeO	p-Me	39
		p-Me	p-MeO	30
p-Cl	47	p-Me	m-MeO	59
		p-Me	H	63
H	75	H	p-Me	54
		m-Cl	H	80
m-Cl	>100	H	m-Cl	>100

$R^1C_6H_4$-N(O)=N-$C_6H_5R^2$ $\xrightarrow[55\,°C,\ 3\,h]{5\ p\text{-}MeOC_6H_4\text{-}IDMg}$ $R^1C_6H_4$-N=N-$C_6H_4R^2$

Scheme 4.

Among the results obtained in the deoxygenation of symmetrical azoxyarenes, the strongly retarding effect of the p-methoxyl substituent and the accelerating effect of the m-chloro substituent of the azoxyarenes should be noted first. The p-chloro substituent, which usually shows an electron-attracting character, exhibits a medium retarding effect: Retardation to a comparable extent was also shown by the p-methyl substituent which usually acts as a weak electron-donating group. These results suggest a remarkable enhacement of electron-repelling resonance operating in the deoxygenation reaction.

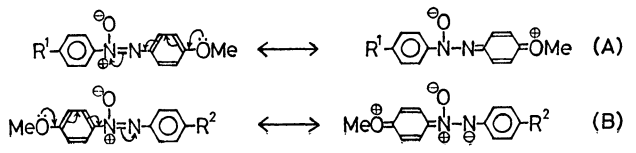
Table 4 also contains the results obtained in the deoxygenation reactions of unsymmetrically substituted azoxyarenes under the same conditions. The effect of the retardation by the p-methoxyl substituent as well as the acceleration by the m-chloro substituent is evidently enhanced when these groups are attached to the phenyl group opposite to the azoxy nitrogen atom. A qualitative explanation for the retardation by the p-methoxyl group opposite to the azoxy nitrogen can be given by the charge-separated resonance structure, A, which reduces the positive charge on the azoxy-nitrogen and prevents the attack of the anionic

Table 5. Physical constants of azoxyarenes
$R^1C_6H_4$-N(O)=N$C_6H_4R^2$

Expt No.[a]	R^1	R^2	Mp θ_m/°C	λ_{max}/nm	NMR data δ
11	*m*-Cl	*m*-Cl	98.5—100[11]	323.0	8.22—7.99(3H, m, ArH), 7.99—7.80(1H, m, ArH), 7.52—7.20(4H, m, ArH).
6	H	*m*-Cl	53.0—53.5	322.0	8.36—8.14(3H, m, ArH), 8.02—7.86(1H, m, ArH), 7.50—7.20(5H, m, ArH).
5	*m*-Cl	H	23.5—24	327.5	8.35—8.02(4H, m, ArH), 7.52—7.10(5H, m, ArH).
P1	H	H	35—35.5[8]	323.5	8.42—8.15(4H, m, ArH), 7.56—7.30(6H, m, ArH).
2	*p*-Me	H	62—64.5[12]	325.5	8.34—8.10(4H, m, ArH), 7.52—7.26(3H, m, ArH), 7.16—6.98(2H, m, ArH), 2.16(3H, s, Me).
4	*p*-Me	*m*-MeO	60—62	325.0	8.06(2H, d, ArH), 7.84—7.60(2H, m, ArH), 7.34—7.02(3H, m, ArH), 6.90—6.86(1H, m, ArH), 3.72(3H, s, Me), 3.22(3H, s, Me).
1	H	*p*-Me	50—51.5[12]	332.5	8.36—8.10(4H, m, ArH), 7.48—7.28(3H, m, ArH), 7.16(2H, d, ArH), 2.30(3H, s, Me).
P1	*p*-MeO	*p*-Cl	105.5—107[1]	340.0	8.27(8.15) and 7.42(4H, ABq, ArH), 8.15 (8.27) and 6.93(4H, ABq, ArH), 3.87(3H, s, Me).
9	*p*-Cl	*p*-Cl	154—156[13]	335.0	8.50—8.24(4H, m, ArH), 7.72—7.50(4H, m, ArH), 7.72—7.50(4H, ArH).
10	*p*-Me	*p*-Me	68—69[14]	333.0	8.24—8.04(4H, m, ArH), 7.18(4H, d, ArH), 2.34(6H, s, Me).
P1	*p*-MeO	*p*-Me	77—79[1]	339.5	8.28(8.13) and 7.28(4H, ABq, ArH), 8.13 (8.28) and 6.94(4H, ABq, ArH), 3.84(3H, s, Me).
P1	*p*-Me	*p*-MeO	108.5—110[1]	349.0	8.30(8.20) and 7.24(4H, ABq, ArH), 8.20 (8.30) and 6.92(4H, ABq, ArH), 3.86(3H, s, Me), 2.44(3H, s, Me).
P1	*p*-Cl	*p*-MeO	144—146.5[1]	359.0	8.56(8.46) and 7.65(4H, ABq, ArH), 8.46 (8.56) and 7.17(4H, ABq, ArH), 3.98(3H, s, Me).
7	*p*-MeO	*p*-MeO	120[15]	353.5	8.40—8.20(4H, m, ArH), 7.10—6.86(4H, m, ArH), 3.84(3H, s, Me), 3.82(3H, s, Me).
12	*m*-MeO	*m*-MeO	51—51.5[11]	325.0	7.96—7.64(4H, m, ArH), 7.44—7.16(2H, m, ArH), 7.04—6.80(2H, m, ArH), 3.78(6H, s, Me).
N	*p*-MeO	H	53—54	331.5	8.38—8.10(4H, m, ArH), 7.54—7.30(3H, m, ArH), 6.98—6.80(2H, m, ArH), 3.78(3H, s, Me).
3	*m*-Cl	*p*-MeO	97—99.5	359.0	8.40—8.10(4H, m, ArH), 7.48—7.38(2H, m, ArH), 6.98—6.80(2H, m, ArH), 3.82(3H, s, Me).
S3	1-Naph.	H	69.5—71	—	8.36—8.16(3H, m, ArH), 7.84—7.64(3H, m, ArH), 7.56(6H, m, ArH).
S3	H	1-Naph.	82.5—84[4]	—	9.10(1H, d, ArH), 8.66—8.56(1H, m, ArH), 8.46—8.30(2H, m, ArH), 7.82—7.72(2H, m, ArH), 7.68—7.36(6H, m, ArH).

a) The number indicates the Expt No. given in Tables 1 and 2. S3 means the products prepared according to Scheme 3, and P1 means the products obtained in the previous work: N indicates that neither the prepative yield nor the deoxygenation reactivity were determined.

part of the reagent molecule. Since the isomeric resonance structure, B, cannot reduce the positive charge, the dramatic retardation is unexpected in this case.



From the given explanation, the reactivity of deoxygenation should be correlated with the shift of the electronic absorption maximum, λ_{max} for $\pi \rightarrow \pi^*$ transition.[10] Since the deoxygenation is generally slow even on treatment with five molar equivalents of the reagent, the percentage of the deoxygenation given in Table 4 can be substituted, as a rough approximation, for the relative reaction rate constant. The λ_{max}'s of

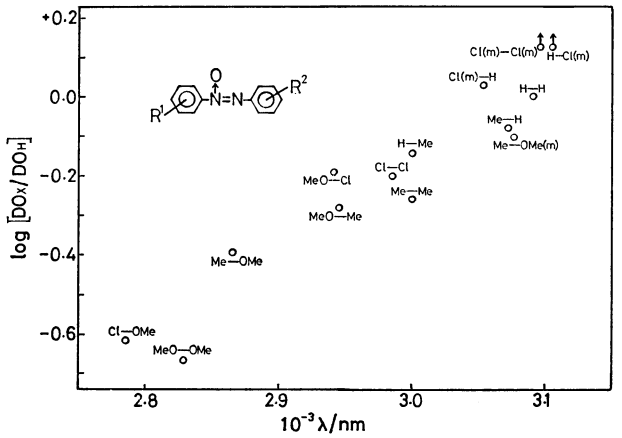


Fig. 1. Correlation between the relative deoxygenation reactivity and $\pi \rightarrow \pi^*$ transition energy.

azoxyarenes are listed in Table 5 together with the other physical constants observed. The expectation is verified as shown in Fig. 1: The logarithm of the relative deoxygenation, $\log[DO_X/DO_H]$ (the value for the unsubstituted substrate was taken as the standard), is less satisfactorily but nevertheless still correlated with the reciprocal of the λ_{max}'s.

Explicit evidence for the attack of the reagent's anionic nitrogen on the substrate's positive nitrogen is provided by the identification of the by-product formed in the reaction. The formation of a trace amount of by-product containing a methoxyl group was detected by NMR in the reaction (Scheme 4) of an azoxyarene which has no methoxyl group; the formation is usually negligible and the structure of the by-product is unidentifiable. The formation, however, becomes notable when a reactive azoxyarene is treated with *p*-methoxyphenyl-IDMg. The most reactive, 3,3'-dichloroazoxybenzene, which was consumed completely under the conditions given in Scheme 4, gave the corresponding azoarene and a 20% yield of 3-chloro-4'-methoxyazobenzene. The same by-product was obtained in a 21% yield in the reaction of 3-chloro-*NNO*-azoxybenzene, *m*-$ClC_6H_4N(O)=NC_6H_5$. In the reaction of the isomeric 3-chloro-*ONN*-azoxybenzene, *m*-$ClC_6H_4N=N(O)C_6H_5$, 4-methoxyazobenzene was isolated in a 17% yield. The other possible by-products were not detected. The results show that, in the reaction with $ArN(MgBr)_2$, an unsymmetrical azoxyarene, $Ar^1N(O)=NAr^2$, gives $Ar^1N=NAr$ but not $ArN=NAr^2$ as the by-product.

The mechanism of both the major and minor reaction is still equivocal. Undoubtedly, however, the existence of such an exchange reaction is evidence for the attack of the anionic nitrogen on the positive azoxy nitrogen. In order to reduce the by-product formation in the deoxygenation of the very reactive azoxyarenes, the less electron-donating *p*-methylphenyl-IDMg is recommended.

Experimental

The melting points are uncorrected. All the nitroarenes and the arylamines were commercially available, and were purified by distillation before use.

Procedures. To an aryliminodimagnesium reagent (15.9 mmol) prepared under N_2 atmosphere in THF (35 ml) according to the reported method,[9] a THF solution (15 ml) of nitroarenes was added at once at 0 °C. The deeply colored[9] reaction mixture was stirred gently at 55 °C for 3 h. The mixture was quenched at 0 °C with aqueous ammonium chloride, and worked up as reported previously.[9] The yields of the individual products were obtained by column chromatographic separation as well as estimation by measuring the fractions by NMR.[9]

The experiments for the deoxygenation of azoxyarenes were carried out similarly: The color change of the reaction mixture was slow at 0 °C but a reddish brown color developed on heating.

The electronic spectra of azoxyarenes were recorded on an Hitachi 323 Spectrophotometer using 1.0×10^{-4} mol dm^{-3} solution in 1,4-dioxane (spectrograde).

For convenience, the physical constants of nineteen azoxyarenes prepared in this and the preceding[9] works are summarized in Table 5. The fourteen among the nineteen azoxyarenes are listed in decreasing order of the deoxygenation reactivity (*cf.* Table 4). Among the NMR data, some aromatic proton signals which consist of two AB-quartets are not assigned and the figures are given in parentheses.

Molecular weight of the product was recorded on a Denshi Kagaku EMD-05A Mass Spectrometer. The result of the elemental analyses of the new azoxyarenes, which are represented by the Expt Nos. given in Table 5, are given below.

(6): Found: C, 62.01; H, 3.90; N, 12.00%. Calcd for $C_{12}H_9ClN_2O$: C, 61.93; H, 3.87; N, 12.04%.
(5): Found: C, 62.08; H, 3.82; N, 11.93%. Calcd for $C_{12}H_9ClN_2O$: C, 61.93; H, 3.87; N, 12.04%.
(4): Found: C, 70.01; H, 5.71; N, 11.60%. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.42; H, 5.78; N, 11.57%.
(N): Found: C, 68.50; H, 5.32; N, 12.21%. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.42; H, 5.26; N, 12.28%.
(3): Found: C, 60.01; H, 4.21; N, 10.60%. Calcd for $C_{13}H_{11}ClN_2O_2$: C, 59.43; H, 4.19; N, 10.67%.
(S3): Found: C, 77.49; H, 4.91; N, 11.32%. Calcd for $C_{16}H_{12}N_2O$: C, 77.42; H, 4.83; N, 11.29%.

The support of this work by the research grant from the Ministry of Education, Science and Culture (C-56540307) is gratefully acknowledged. The authors wish to thank Mr. Kōichirō Hirata for the measurement of UV-Vis absorption spectra.

References

1) C. S. Hahn and H. H. Jaffe, *J. Am. Chem. Soc.*, **84**, 949 (1962).
2) B. T. Gillis and K. F. Schimmel, *J. Org. Chem.*, **27**, 413 (1962).
3) G. M. Badger, R. G. Butterby, and G. E. Lewis, *J. Chem. Soc.*, **1953**, 2143; G. M. Badger and G. E. Lewis, *ibid.*, **1953**, 2147, 2151.
4) Y. Ogata, M. Tsuchida, and Y. Takagi, *J. Am. Chem. Soc.*, **79**, 3397 (1957).
5) S. Oae, T. Fukumoto, and M. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **36**, 728 (1963).
6) L. C. Behr, *J. Am. Chem. Soc.*, **76**, 3672 (1954); L. C. Behr, E. G. Alley, and O. Levand, *J. Org. Chem.*, **27**, 65 (1962).
7) T. E. Stevens, *J. Org. Chem.*, **29**, 311 (1964).
8) "Organophosphorus Reagents in Organic Synthesis," ed by J. I. G. Cadogan, Academic Press, London (1979),

Chaps. 6 and 7.
9) Part III: M. Ōkubo, T. Takahashi, and K. Koga, *Bull. Chem. Soc. Jpn.*, **56**, 199 (1983).
10) H. H. Jaffe and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy," John Wiley & Sons Inc., New York (1962), p. 282.
11) N. S. Kozlow and V. A. Soshin, *Uch. Zap. Permsk. Gos. Ped. Inst.*, **32**, 84 (1965); *Chem. Abstr.*, **66**, 2290k (1967).
12) D. Bigiavi and V. Sabatelli, *Gazz. Chim. Ital.*, **57**, 557 (1927).
13) B. T. Newbold and R. P. Leblanc, *J. Org. Chem.*, **27**, 312 (1962).
14) B. T. Newbold and R. P. Leblanc, *J. Chem. Soc.*, **1965**, 1547.
15) M. J. S. Dewar and R. S. Goldberg, *Tetrahedron Lett.*, **1966**, 2717.