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Aryliminodimagnesium Reagents. XII. The Distribution of Products in the Condensation with Nitrobenzothiazoles. Reduction of Electron-Donating Ability of Reagent by the Interaction with Thiazolyl Group

Masao Ōkubo,* Keiko Asao, and Hiroyuki Hyakutake
Department of Chemistry, Faculty of Science and Engineering, Saga University, Honjō-machi, Saga 840
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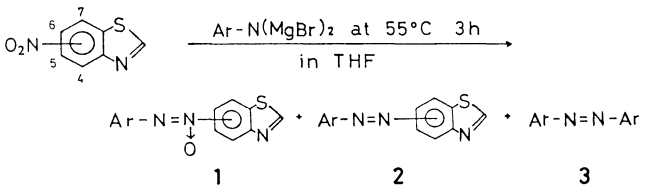
The 4-, 5-, 6-, and 7-nitro derivatives of benzothiazole condense with $ArN(MgBr)_2$ giving unsym-azoxy and -azo products. The product distribution indicated the mild nature of the reaction, and could be explained in terms of a reduced electron-donating ability of the reagent due to an interaction with thiazolyl group.

The electron transfer initiated condensation of aryliminodimagnesium reagent($ArN(MgBr)_2$, aryl-IDMg) with nitroarenes[1] and diaryl ketones[2] has been developed in our laboratory. Independently of the manners of reactions of IDMg (condensation) and ArMgBr (addition) as well as those of other magnesium reagents, the principal factor governing the distribution of normal and abnormal (radical) products is a combination of electron-donating and -accepting abilities (EDA and EAA) of reactants:[3,4] The combination represents the relative efficiency of an electron transfer. The efficiency is generally estimated (as the first approximation in fifteen reactions of various magnesium reagents with aromatic substrates) by the value of the difference between the oxidation and reduction potentials of reactants.[4]

A Grignard reaction with nitroarenes had attracted no attention until 1977, since the formation of a large amount of radical product was unavoidable.[5] However, during the past decade, Bartoli and his coworkers have investigated the reaction at lower temperatures, and have established the deoxygenative conjugate addition mechanism involving an electron transfer.[6] Among a lot of nitroarenes, nitrobenzothiazoles, which were first used by the Italian authors,[7] attracted our attention from the EDA-EAA viewpoint since these substrates seemed to be favorable for affording "normal" conjugate addition product as the result of a moderate electron transfer.

The IDMg reagent has a weaker EDA than that of ArMgBr.[8] If IDMg condense with nitrobenzothiazoles in the usual manner,[1] the product distribution is expected to be similarly explainable by a much milder



Scheme 1.

Table 1. Product Distribution in IDMg Reaction with Nitrobenzothiazoles

Run No.	Substr.	*p*-RC_6H_4-IDMg (R)	[IDMg]/[Substr.]	Yield[c]/% *unsym*-azoxy **1**	*unsym*-azoxy **2**	*sym*-azoxy **3**	Recov. %
1	4-NBT[a]	MeO	2.0	27	6	27	13
2	4-NBT	Me	2.0	28	3	24	10
3	4-NBT	Cl	2.0	17	0	16	72
4	5-NBT	MeO	2.0	46	15	31	7
5	5-NBT	Me	2.0	36	7	5	31
6	5-NBT	Me	5.0	62	8	12	0
7	5-NBT	Cl	2.0	21	6	4	29
8	5-NBT	Cl	7.0	74	7	5	0
9	6-NBT	MeO	2.0	50	11	28	trace
10	6-NBT	Me	2.0	45	8	10	13
11	6-NBT	Me	5.0	49	0	20	13
12	6-NBT	Cl	2.0	22	0	10	54
13	6-NBT	Cl	7.0	73	6	11	0
14	7-NBT	MeO	2.0	47	3	12	3
15	7-NBT	Me	2.0	40	6	7	—
01	4-MeNB[b]	MeO	2.0	39	34	10	0
02	4-MeNB	Me	2.0	64	[36]		0
03	4-ClNB	MeO	2.0	50	12	9	0
04	4-ClNB	Cl	2.0	71	[24]		0

a) NBT=nitrobenzothiazole. b) NB=nitrobenzene. c) Yields, based on the amount of NBT used, are obtained after stirring at 55 °C for 3 h.

electron transfer. This expectation was verified. The effect of the thiazolyl group on the reaction is discussed in this paper.

Results and Discussion

Product Distribution in IDMg Reaction with Nitrobenzothiazoles. In a reaction of aryl-IDMg with 4-, 5-, 6-, and 7-nitrobenzothiazoles (Scheme 1), unsymmetrical(*unsym*-) azoxy- and azobenzothiazoles (**1** and **2**) and symmetrical (*sym*-) azobenzenes (**3**) were obtained. The product **1** was formed via condensation with IDMg, **2** via a subsequent deoxygenation of **1** with excess IDMg, and **3** via an oxidative coupling of reagent molecules. The types of products are same with those obtained in reactions with nitrobenzenes.[1] The yields of **1**—**3** obtained under fixed reaction conditions are summarized in Table 1 (Runs 1—15); four previous results (Runs 01—04)[1] are also listed for a comparison. As described in the following, the notable features of product distribution meet the expectation given above.

The first feature is that the recovery of the substrate was observed in all cases using two molar equuivalents of reagents. Two molar equivalents of *p*-ClC_6H_4-IDMg, having the weakest EDA,[8] leads to a large amount of recovery (Runs 7 and 12), and seven molar equivalents are needed for a complete conversion (Runs 8 and 13). In the case of *p*-MeC_6H_4-IDMg, having a stronger EDA,[8] five molar equivalents are needed (Run 6). In contrast, in cases of nitrobenzenes (Runs 01—04), no recovery was observed, even upon using two molar equivalents of *p*-ClC_6H_4-IDMg (Run 04).

The second feature is that, even in Runs 6, 8, 11, and 13 using a large excess of IDMg, the yield of *unsym*-azoxy product **1** was always much higher than those of the corresponding *unsym*-azo product **2**. This indicates that **1** was quite sluggishly deoxygenated by IDMg, as compared to the previous results (Runs 01—03).[1] As previously reported, the IDMg deoxygenation of azoxyarenes is accelerated and/or retarded, depending on their EAA's.[1,9]

Table 2. Melting Points and ^1H NMR Data of Azoxy- and Azobenzothiazoles

No.	Mp θ_m/°C	^1H NMR data[b] δ
$\mathbf{1}_4^{MeO}$	137—138	9.18(1H, s), 8.44 & 7.03(4H, ABq), 8.12(1H, d), 8.01(1H, d), 3.91(3H, s).
$\mathbf{2}_4^{MeO}$	101—105	9.28(1H, s), 8.23—8.09(3H, m), 7.89(1H, d), 7.63(1H, t), 7.12(2H, d), 3.94(3H, s).
$\mathbf{1}_4^{Me}$	105—105.5	9.24(1H, s), 8.28 & 7.36(4H, ABq), 8.16(1H, d), 8.04(1H, d), 7.60(1H, t), 2.24(3H, s).
$\mathbf{2}_4^{Me}$	135—136	9.45(1H, s), 8.11(1H, d), 8.05 & 7.38(4H, ABq), 7.90(1H, d), 7.61(1H, t), 2.46(3H, s).
$\mathbf{1}_4^{Cl}$	127.5—129	9.20(1H, s), 8.29 & 7.49(4H, ABq), 8.17(1H, d), 8.03(1H, d), 7.60(1H, t).
$\mathbf{2}_4^{Cl}$	—[a]	9.26(1H, s), 8.20—8.04(4H, m), 7.60—7.51(3H, m).
$\mathbf{1}_5^{MeO}$	162—163	9.07(1H, s), 8.49 & 7.98(2H, ABq), 8.34 & 6.97(4H, ABq), 3.87(3H, s).
$\mathbf{2}_5^{MeO}$	122.5—123	9.06(1H, s), 8.65(1H, d), 8.05(2H, s), 7.96 & 7.02(4H, ABq), 3.90(3H, s).
$\mathbf{1}_5^{Me}$	192—192.5	9.09(1H, s), 9.06(1H, d), 8.44 & 8.18(2H, ABq), 7.97 & 7.31(4H, ABq), 2.45(3H, s).
$\mathbf{2}_5^{Me}$	174—175	9.06(1H, s), 8.67(1H, d), 8.06(2H, s), 7.90(2H, s), 7.90 & 7.33 (4H, ABq), 2.49(3H, s).
$\mathbf{1}_5^{Cl}$	201—202	9.12(1H, s), 9.05(2H, d), 8.44 & 8.05(2H, ABq), 8.21 & 7.45(4H, ABq).
$\mathbf{2}_5^{Cl}$	212—213	9.06(1H, s), 8.65(1H, d), 8.059(2H, s), 7.92 & 7.48(4H, ABq).
$\mathbf{1}_6^{MeO}$	153—153.5	9.17(1H, s), 8.96(1H, d), 8.54 & 8.22(2H, ABq), 8.40 & 7.04(4H, ABq), 3.90(3H, s).
$\mathbf{2}_6^{MeO}$	143—144	9.08(1H, s), 8.51(1H, d), 8.28 & 8.09(2H, ABq), 7.98 & 7.03(4H, ABq), 3.90(3H, s).
$\mathbf{1}_6^{Me}$	122—124	9.15(1H, s), 8.97(1H, d), 8.54 & 8.22(2H, ABq), 8.20 & 7.33(4H, ABq), 2.43(3H, s).
$\mathbf{2}_6^{Me}$	132—134	9.05(1H, s), 8.50(1H, d), 8.23 & 8.10(2H, ABq), 7.87 & 7.31(4H, ABq), 2.43(3H, s).
$\mathbf{1}_6^{Cl}$	146—147	9.18(1H, s), 8.95(1H, d), 8.53 & 8.22(2H, ABq), 8.20 & 7.48(4H, ABq).
$\mathbf{2}_6^{Cl}$	130—132	9.15(1H, s), 8.57(1H, d), 8.30 & 8.16(2H, ABq), 7.96 & 7.55(4H, ABq).
$\mathbf{1}_7^{Me}$	125—126.5	9.10(1H, s), 8.51(1H, d), 8.29(1H, d), 8.24 & 7.30(4H, ABq), 7.62(1H, t), 2.42(3H, s).
$\mathbf{2}_7^{Me}$	147—148	9.18(1H, s), 8.31(2H, d), 8.00 & 7.39(4H, ABq), 7.79 (1H, t), 2.49(3H, s).
$\mathbf{1}_7^{MeO}$	—[a]	9.11(1H, s), 8.52(1H, d), 8.29(1H, d), 8.41 & 7.00(4H, ABq), 7.65(1H, t), 3.91(3H, s).
$\mathbf{2}_7^{MeO}$	—[a]	9.13(1H, s), 8.32(2H, d), 8.07 & 7.05(4H, ABq), 7.76 (1H, t), 7.62(1H, t), 3.92(3H, s).

a) Melting points are undetermined because the trace amounts of samples were not purified completely.
b) For AB-quartets of aromatic protons, all the ΔJ values are 8—9 Hz.

The third feature is that the yields of **1** and **2** in reactions of the 4-nitro isomer (Runs 1—3) having neighboring nitrogen atom are lower than those in cases of other isomers (Runs 4, 5, 7, 9, 12, 14, and 15). Even the 7-nitro isomer, having a neighboring sulfur atom, gave **1** and **2** in yields comparable to those in cases of 5- and 6-nitro isomers. Thus, the anomaly indicates that 4-nitro group is less favorable for the condensation with IDMg, probably due to a steric repulsion caused by the neighboring nitrogen atom, whereas the "normal" yields in cases of the 7-isomer may be ascribed to the long C_{Ar}–S bond causing no appreciable repulsion. The retardation of IDMg condensation by some ortho substituents of nitrobenzene was observed.[10] In this connection, the Grignard reagent[7] converts the 4-nitro isomer into a non-deoxygenative product(*vide supra*) different from the deoxygenative ones obtained in cases involving the other isomers.

Reduction of EDA of Reagent Caused by Coordination of Thiazolyl Group to Mg Atom. The first and second features of the product distribution seem to indicate that the electron transfer involved in the reaction of Scheme 1 is milder than those in the IDMg reaction with nitro- and azoxybenzenes.[1,9] However, the normalized reduction potentials of the nitro- and azoxybenzothiazoles are lower than or comparable to those of the corresponding benzene derivatives, as shown below(BT=benzothiazolyl).

Nitroarenes ($ArNO_2$):

Ar	V (redox)
p-$MeOC_6H_4$	−1.508
p-MeC_6H_4	−1.418
p-ClC_6H_4	−1.254
4-BT	−1.314
5-BT	−1.299
6-BT	−1.220
7-BT	−1.142

Azoxyarenes (Ar^1-N(O)=N-Ar^2):

Ar^1	Ar^2	V (redox)
p-$MeOC_6H_4$	*p*-$MeOC_6H_4$	−1.748
p-$MeOC_6H_4$	C_6H_5	−1.642
C_6H_5	C_6H_5	−1.596
p-$MeOC_6H_4$	*p*-ClC_6H_4	−1.574
p-MeC_6H_4	*p*-ClC_6H_4	−1.524
C_6H_5	*m*-ClC_6H_4	−1.423
5-BT	*p*-$MeOC_6H_4$	−1.608
5-BT	*p*-ClC_6H_4	−1.443
6-BT	*p*-$MeOC_6H_4$	−1.732
6-BT	*p*-ClC_6H_4	−1.359

The lower values of the reduction potentials indicate a stronger EAA; this seems to be in conflict with the suggestion of a mild electron transfer. However, when the oxidation peak potential of *p*-MeC_6H_4-IDMg in THF was measured in the presence of an equimolar amount of unsubstituted benzothiazole, the normalized potential value (1.055 V) was reproducible and was found to be higher than that (0.941 V) obtained in its absence.[8] This indicates that (in the reaction of Scheme 1) the actual EDA is much weaker, due to an interaction with the thiazolyl group, and gives rise to a mild electron transfer.

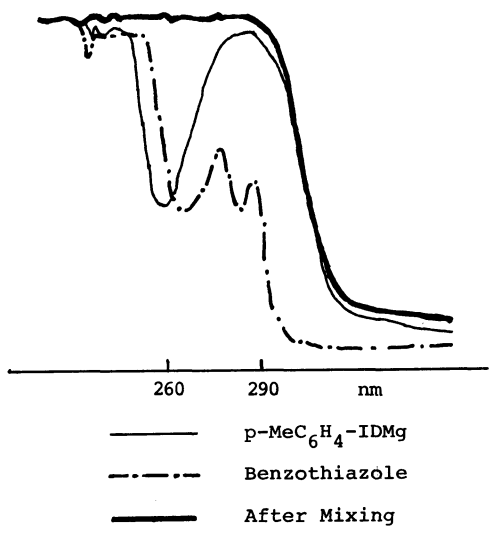


Fig. 1. Shift of n→π* transition band of benzothiazole by mixing with *p*-MeC_6H_4-IDMg.

The interaction arises from a coordination of the thiazolyl group to Mg atom of IDMg, as shown by the electronic absorption spectra measured in degassed THF solutions (Fig. 1). The λ_{max} of n→π* transition of *p*-MeC_6H_4-IDMg is observed at 290 nm and that of benzothiazole at 275 nm. By mixing two equimolar solutions through breaking the seal, the dip between the n→π* and π→π* bands of the reagent disappeared. The spectrum change is attributed to an overlap of the n→π* band of benzothiazole, shifted by 20—30 nm toward blue, due to coordination of the thiazolyl group (probably via nitrogen atom) to Mg atom of IDMg. Undoubtedly, the coodination gives rise to the first and second features of product distribution, i.e., an appreciable recovery and a sluggish deoxygenation. Among the two reagent molecules, tentatively depicted in Fig. 2, the one is coordinated and deactivated while the other is responsible for the condensation with the nitro group.

According to the discussion given above, Bartoli's Grignard reaction[7] owes its first success (as at least one of the reasons) to the reduction of EAA arising from a similar interaction of the thiazolyl group with the reagent. The EDA-EAA concept is useful for characterizing the reactions of aromatic substrates and magnesium reagents of simple molecular structures,[3,4]

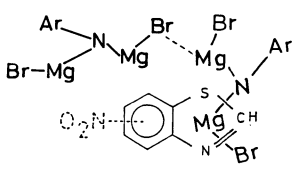


Fig. 2. Schematic depiction for coordination of thiazolyl group to Mg atom of reagent.

however, the modification of the concept on the basis of special molecular structures of substrates must be taken into account.

Experimental

Melting points are uncorrected.

Materials and Procedures. Four isomeric nitrobenzothiazoles were prepared by the nitration of benzothiazole, and separated by recrystallization, steam distillation, and repeated column chromatography on silica gel.[11]

The IDMg reactions were carried out according to the reported procedures; the reaction mixtures of substrates (3.0 or 5.0 mmol) with the given molar amounts of IDMg in THF (30 or 50 ml) were stirred at 55 °C for 3 h. The products were separated by column and thin-layer chromatographies on silica gel(Wako Gel C-200, C-300, and Merck's Kiesel Gel 60G).

Elemental analyses of the products gave satisfactory results. The melting points and ^{1}H NMR data of azoxy- and azobenzothiazoles (**1** and **2**) are summarized in Table 2.

The measurement of reduction potentials of nitro and azoxy compounds using bis(biphenyl)chromium(I) tetraphenylborate (BCTB) as internal reference was carried out according to the reported procedures.[4,9]

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