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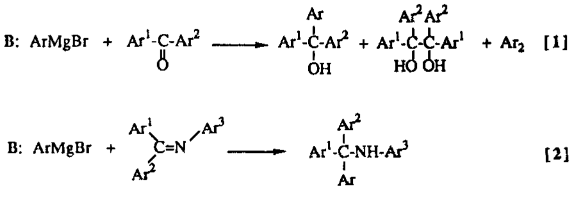
EFFICIENT FORMATION OF SOME AMIDINES BY THE REACTIONS OF ARYLIMINODIMAGNESIUM WITH WEAKLY ELECTRON-ACCEPTING BENZONITRILE, *N,N*-DIMETHYLFORMAMIDE AND RELATED COMPOUNDS. FEATURES OF REACTIONS GOVERNED BY σ-COMPLEXATION*

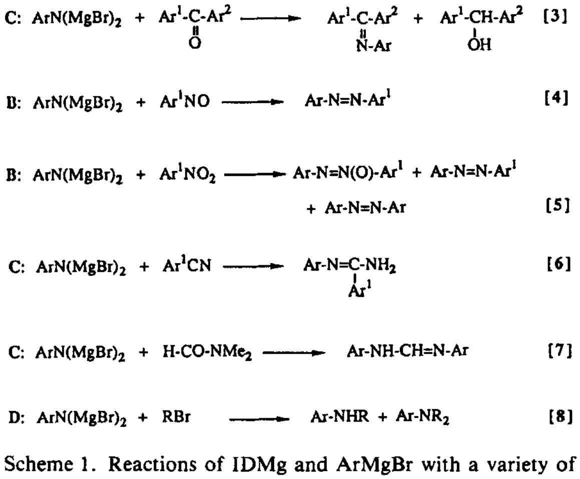
MASAO OKUBO,† KOJI MATSUO, NOBUYUKI TSURUSAKI, KEIJI NIWAKI AND MIKIO TANAKA
Department of Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi, Saga 840, Japan

In many reactions of magnesium reagents, including Grignard and aryliminodimagnesium [$ArN(MgBr)_2$, IDMg], the formation of abnormal products via reactions such as radical dimerization, hydrogen abstraction and conjugate 1,4-addition originating from efficient single electron transfer (SET) is not excluded. In IDMg reactions with benzonitrile and *N,N*-dimethylformamide in tetrahydrofuran, however, clean reactions took place affording *N*-arylbenzamidine and *N,N'*-diarylformamidine via exclusive 1,2-addition and condensation plus replacement, respectively. Some alkyl and arylvinyl cyanides gave the corresponding amidines without 1,4-addition or hydrogen abstraction. These results are the first observation of such reactions of magnesium reagents, and are attributed to a combination of the weak electron-donating ability (EDA) of IDMg with the weak electron-accepting ability (EAA) of nitriles. Although ESR is therefore inapplicable, factors governing the product yields were studied on the basis of effects caused by the addition of strongly coordinating hexamethylphosphoramide and pyridine to the reagent solution, and by addition of nitrobenzenes having a strong EAA. From the results, a large participation of σ-complexation followed by implicit SET in the inner sphere of the complex is proposed.

INTRODUCTION

As shown in Scheme 1, aryliminodimagnesium (IDMg) reacts with diaryl ketones [reaction (3)],[1c–e] nitrosoarenes [reaction (4)][2] and nitroarenes [reaction (5)][2a] via condensation, with benzonitrile [reaction (6)][3] via addition, with DMF [reaction (7)][3] via condensation plus replacement and with S_N1-inactive alkyl bromides [reaction (8)][4] via cross-coupling, the reactions having been precisely and/or preliminarily reported.





Scheme 1. Reactions of IDMg and ArMgBr with a variety of substrates

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[*] Aryliminodimagnesium Reagents, Part XXIII. For Part XXII, see Ref. 1.
† Author for correspondence.

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Including the Grignard reactions with ketones (reaction (1))[1a] and imines [reaction (2)][1b] via addition, all types of reactions with magnesium reagents have been classified and characterized from a unified view[5a] called the ΔE approach. The approach depends on the ΔE value derived from the difference between E_{ox} and E_{red}, indicating the 'single electron transfer (SET) efficiency' evaluated from the electron-accepting (EAA) and -donating abilities (EDA) of the reactants used. A smaller ΔE implies more efficient SET (Figure 1), the reactions being classified alphabetically (B–D; see Scheme 1).[6] The relative yields of products formed via normal modes (see above) versus those formed via abnormal modes [radical dimerization hydrogen (H) abstraction] are explained by ΔE irrespective of the difference in normal modes. It was proposed that, as ΔE varies from small (class A) via medium (class B) to large (class C) values, participation of the σ-complexation (via $=\mathrm{O}-\mathrm{Mg}<$ or $>\mathrm{N}-\mathrm{Mg}<$)[5b] in the initial stage becomes greater. Class D means the combination giving no reaction product because no SET takes place even by σ-complexation.

On the basis of the larger positive E_{ox} of $\mathrm{ArN(MgBr)_2}$(IDMg)[5a] than ArMgBr and the larger negative E_{red} of $\mathrm{Ar^1_2CO}$ than $\mathrm{Ar^1NO_2}$,[5b] the 'SET-controlled' characteristics (class B having medium ΔE) common to reactions (1) and (5) were reported.[1,7] The 'σ-complexation-controlled' nature of reaction (3) (an example of class C) was manifested by comparison with features of reaction (1).[1] The result of IDMg treatment of benzo-, naphtho- and anthraquinones illustrating the comprehensive effects of ΔE on the modes of reaction (including those of classes A, B and C) has been separately reported.[8] A novel method for activating the mild IDMg to make reaction (8) (class D combination) proceed will be reported elsewhere.[4]

This paper deals with the new class C reactions (6) and (7) leading to substituted amidines, and the related reaction with acetamides (7′).[3] The effects of added hexamethylphosphoramide (HMPA) and/or pyridine (Py), which strongly coordinate to the Mg of the reagent's, on the product yields in reactions (3), (5) and (6) and the effects of added nitrobenzenes (Adt) having small E_{red} on the yields in reactions (7) and (7′) were compared. No radical intermediate was detected by ESR owing to the large ΔE, but the results compared are recognized as indirect evidence clearly consistent with the characteristics expected from the proposed 'σ-complexation and SET in the inner sphere of the complex'.

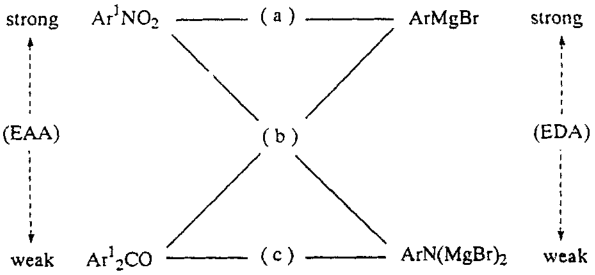


Figure 1. Illustration: combination of electron-donating and -accepting abilities of reactants: (a) small ΔE and highly efficient SET; (b) medium ΔE and fairly efficient SET; (c) large ΔE and mild SET

RESULTS AND DISCUSSION

Estimation of large E_{red} of nitriles

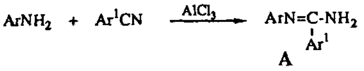
The E_{red} value of benzonitrile in the tetrahydrofuran (THF)–$\mathrm{Bu_4NClO_4}$ system is located far outside its potential window,[5c] and an approximate value was suggested in an indirect manner. The E_{red} value of benzophenone in the *N,N*-dimethylformamide (DMF)–$\mathrm{Bu_4NClO_4}$ system appears at smaller negative region (by *ca* 0·2 V) than the reported value in THF.[5c] The two values for benzophenone were compared with the E_{red} of *p*-chlorobenzonitrile (2·6 V) determined in DMF, and the E_{red} of the same nitrile in THF was suggested to be *ca* 2·8 V. The much larger value than that of the ketone, implying a mild electron-accepting ability (EAA), is supported by much smaller σ_π of the CN group ($\mathrm{NO_2} > \mathrm{CHO} > \mathrm{COC_6H_5} > \mathrm{COCH_3} > \mathrm{CN}$) reported for the effect of electron-attracting substituents.[9a] The small value for the CN group, implying its weak resonance demand and confirmed by slight stabilization of the benzonitrile anion radical,[9b] is consistent with the E_{red} value of phenylvinyl cyanide (see below).

Concerning IDMg reactions with nitriles, (i) the retarding effect of added HMPA and/or Py on reaction (6) in contrast to the accelerating effect on reaction (5), (ii) the normal 1,2-addition mode of arylvinyl and alkyl cyanides in contrast to the abnormal 1,4-addition and/or α-H abstraction modes of the corresponding carbonyl compounds and (iii) the need for an excess molar amount of reagent and its role in obtaining a good yield of product in reaction (6) will be described. Concerning the reactions with DMF and *N,N*-dimethylacetamide (DMA), (iv) the clear difference in the behaviour of DMF in reaction (7) from that of DMA in reaction (7′),[3] and (v) the novel mediation of implicitly involved inner-sphere SET by added nitrobenzenes (Adt) leading to an improvement in yield will be described.

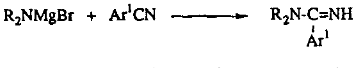
Reaction (6)

Amidine formation by IDMg addition to nitriles

According to the usual IDMg procedure, reaction (6) was examined in THF using *para-* and *ortho-*substituted IDMg and benzonitriles. Efficient binding of the components took place, affording *N*-arylbenzamidines (**A**) (Table 1). Owing to the excellent yield of **A** even under mild conditions (at 55 °C), reaction (6) is superior to the reaction of the same nitriles and anilines with the use of $AlCl_3$ [reaction (6′) at 200 °C].[11] A similar addition [reaction (6″)] of dialkylaminomagnesium to benzonitrile (in diethyl ether and/or benzene) was reported but not systematically studied.[12]



$$ArNH_2 + Ar^1CN \xrightarrow{AlCl_3} \underset{\textbf{A}}{ArN{=}\underset{Ar^1}{C}{-}NH_2} \qquad [6']$$



$$R_2NMgBr + Ar^1CN \longrightarrow R_2N{-}\underset{Ar^1}{C}{=}NH \qquad [6'']$$

Almost independent of substituents on the reactants, the yields of **A** from benzonitriles and a threefold molar amount of IDMg are excellent, as shown by runs 1–18 in Table 1. The poor yields obtained only from 2,6-$Me_2C_6H_3CN$ (runs 12, 15 and 18) indicate that reaction (6) is much less sterically hindered than reaction (3) by crowded reactants.[1,7] The mode of IDMg addition to the CN group in reaction (6) is distinct from that of IDMg condensation in reactions (3)[7] and (5).[2,13] Similar addition takes place on the alternative treatment of *p*-MeC_6H_4CN with *p*-$ClC_6H_4NHMgBr$ (anilinomagnesium) to afford **A** (92%).

Table 1. Yields in the reaction $ArN(MgBr)_2 + Ar^1CN \rightarrow Ar^1C(NH_2){=}NAr$[a]

Run no.	Ar = RC_6H_4 or $R_2C_6H_3$: R =	$Ar^1 = R^1C_6H_4$ or $R^1_2C_6H_3$: R^1 =	Yield (%)
1	4-MeO	4-MeO	62
2	4-Me	4-MeO	69
3	3-Me	4-MeO	81
4	4-Cl	4-MeO	83
5	4-MeO	4-Me	80
6	4-Me	4-Me	100
7	4-Cl	4-Me	95
8	4-MeO	4-Cl	98
9	4-Me	4-Cl	81
10	4-Cl	4-Cl	100
11	4-Me	2-Me	64
12	4-Me	2,6-Me_2	13
13	2-Me	4-Me	93
14	2-Me	2-Me	98
15	2-Me	2,6-Me_2	24
16	2,6-Me_2	2-Me	87
17	2,6-Me_2	4-MeO	86
18	2,6-Me_2	2,6-Me_2	8
19	3-MeO (NH)	4-MeO	7
20	3-MeO[b] (NH)	4-MeO	82
21	3-MeO	4-MeO	39
22	3-MeO[b]	4-MeO	86

[a] Concentration of IDMg = 100 mmol l^{-1}; [IDMg] : [nitrile] = 3 : 1.
[b] Molar ratio of IDMg (or ArNHMgBr) to nitrile = 6 : 1.

A greater amount of *m*-MeO-substituted IDMg and ArNHMgBr is required for satisfactory yields of **A** (compare runs 20 and 22 with runs 19 and 21). The yield from 2 mol of the IDMg and *p*-MeC_6H_4CN is also low, but is improved considerably by addition of an equimolar amount of pyridine (at room temperature for 0·5 h; at 70 °C for 1·5 h, see below).

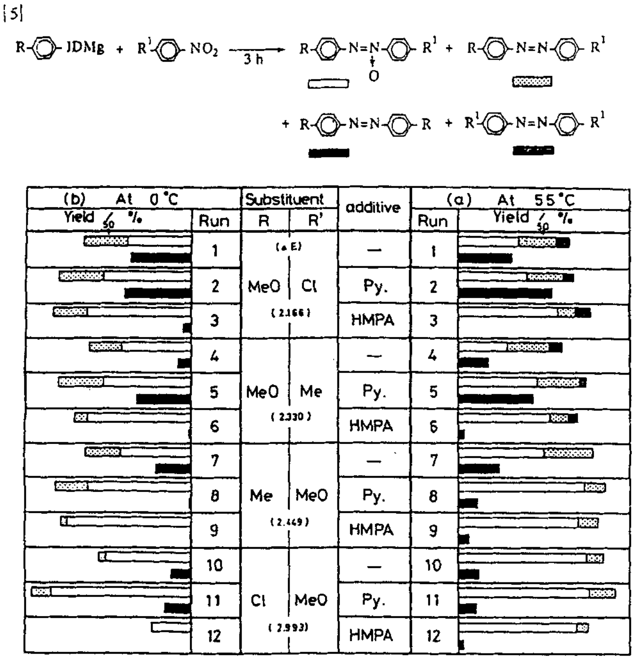
Effects of added polar solvents on reactions (6), (3) and (5)

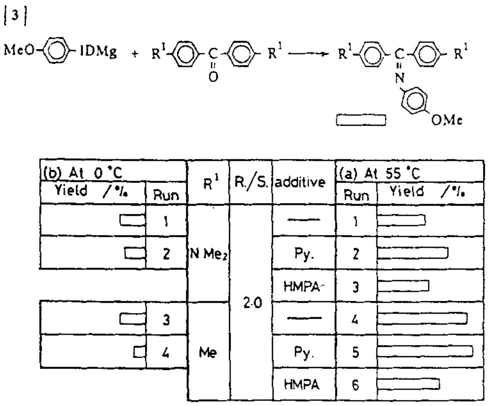
The formation of *sym.*-azoarenes (ArN=NAr) via oxidative coupling of IDMg is an indication of SET being involved in the reaction; the formation is frequently observed in reaction (5)[2] and rarely in reaction (6), reflecting the much milder SET. The difference in the nature of reactions (6) and (3) from that of reaction (5) is revealed, in a novel way, by comparison of the yield variations caused by added HMPA and Py.

The σ-complexation of IDMg with substrates involves exchange of solvent ligand. Owing to the strong coordinating abilities indicated by the relative values of Gutmann's donor numbers (*DN*) (HMPA 38·8; Py 33·1; THF 20·0),[14] four THF molecules (on Mg atoms of IDMg similarly to RMgBr[15]) must be replaced with the same molar amount of HMPA and Py. Thus the product yields in reactions (3), (5) and (6) with and without addition of HMPA and/or Py and (a) at 55 °C and (b) at 0 °C were compared with each other. The lower temperature (b) was selected because the σ-complexation is expected to be retarded by strongly bound HMPA or Py,[13] whereas the higher temperature (a) is same with that of previous experiments giving products in satisfactory yields.[1,2]

The results are summarized in Figure 2 [reactions (5), (3) and (6)]. As preliminarily reported,[13] the azoxy yield in reaction (5) is improved by HMPA (largest *DN*). In contrast, the yields of anil in reaction (3)[1a] and those of amidine in reaction (6) are suppressed. With Py (smaller *DN*), the yields are suppressed and/or improved to different extents.

The variation in the yields of the respective reactions is attributed to the effects on their essential steps affected by the relative EAA of the substrates, the relative *DN* values and the applied temperatures. Figure 2 indicates notable features of reaction (5) having a smaller ΔE: (i) at 55 °C and partly at 0 °C using HMPA and by Py, the azoxy plus unsymmetrical azo yield (condensation efficiency) is improved (see runs 1 → 3, 4 → 5, 7 → 8 and 10 → 11); (ii) the azoxy yield is improved by HMPA and Py in almost all runs; the exceptional suppression in run 12 is greater at 0 than at





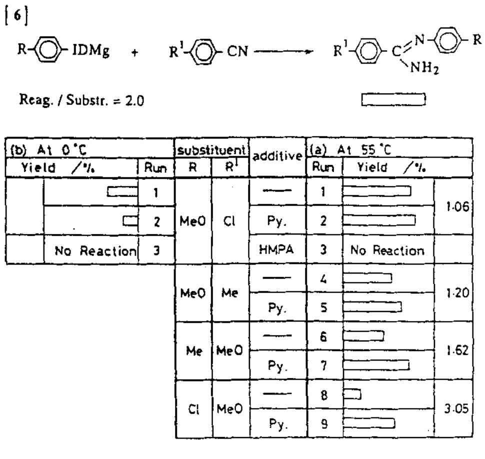


Figure 2. Effects of HMPA and Py on the yields of products in reactions (3), (5) and (6) in THF for 3 h, (a) at 55 °C and (b) at 0 °C.
Reaction (5): azoxy and azo products based on Ar^1NO_2. [IDMg] : [Ar^1NO_2] : [solvent] = 4·2 : 1·0 : 16·8.
Reaction (3): ketone anils based on Ar^1_2CO and recovery. [IDMg] : [Ar^1_2CO] : [solvent] = 2·0 : 1·0 : 4·0.
Reaction (6): *N*-arylbenzamidines based on Ar^1CN. [IDMg] : [Ar^1CN] : [solvent] = 2·0 : 1·0 : 4·0

55 °C; (iii) oxidative coupling of IDMg giving ArN=NAr is suppressed by HMPA throughout runs 1–12. The Cl–MeO combination (run 12) has the largest ΔE near 3·0 V and is hybridized with class C character, the participation of σ-complexation (ligand exchange) being prevented by strongly bound HMPA or Py. The suppression is exceptional but resembles that in reactions (3) and (6) (see below).

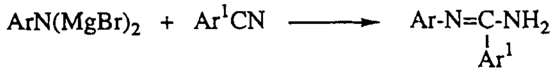
In reaction (3) (Figure 2), product formation is inhibited by HMPA at both 55 and 0 °C. With the less strong Py, product formation is suppressed at 0 °C but improved at 55 °C. The product yield in reaction (6) (Figure 2) is improved at 55 °C and suppressed at 0 °C by Py, and is inhibited at both 55 and 0 °C by HMPA. Although the CO group of benzophenone, crowded by two Ar^1, is less favourable for σ-complexation, the results for reactions (3) and (6) are apparently the same irrespective of the different reaction modes. By considering the smaller ΔE of reaction (3) than that of reaction (6), reaction (3) could be characterized as 'C hybridized slightly with B'. The results reflect the expected increase in participation of σ-complexation [reaction (5) < (3) < (6)], and also the effects of the first and second largest *DN*. The effects of *DN* values on class B and C reactions of uncrowded substrates of different EAAs (Figure 3) are recognized as those distinguishing their essential steps (Scheme 2).

Features (i) and (ii) in reaction (5) led us to propose that an enhanced reactivity of IDMg is responsible for the improvement in condensation efficiency. The enhancement of EDA, attributed to elevation of the IDMg HOMO level caused by the large *DN* of HMPA (supported by heat evolution on its addition[13]) is derived, by analogy, from the great elevation of the (free) Grignard HOMO level by coordination of two Et_2O molecules concluded by MO calculation.[16] The concurrent decrease in ArN=NAr yield by HMPA [feature (iii)] suggests that the bulky and heavy HMPA molecules bound to IDMg retard its self-association;[13] supply of the electronic field of the phosphorus 3d orbi-

[5]-B: $\mathrm{ArN(MgBr)_2 + Ar^1NO_2 \longrightarrow Ar\text{-}N{=}N(O)\text{-}Ar^1 + Ar\text{-}N{=}N\text{-}Ar^1}$

$\mathrm{+\ Ar\text{-}N{=}N\text{-}Ar}$

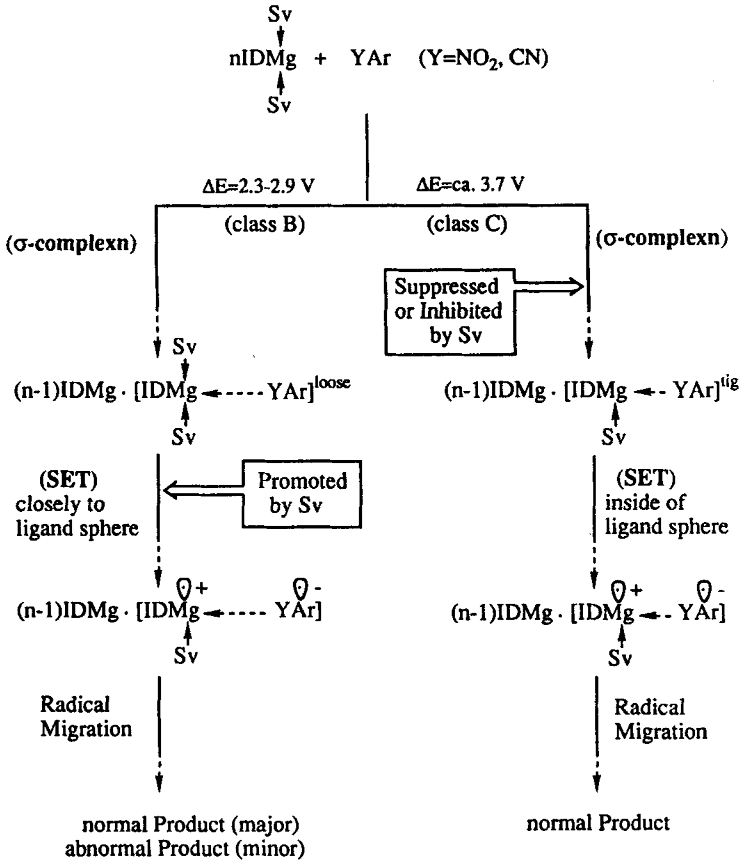
[6]-C:



$$\mathrm{ArN(MgBr)_2 + Ar^1CN \longrightarrow Ar\text{-}N{=}\underset{\substack{|\\ Ar^1}}{C}\text{-}NH_2}$$

	ΔE /V	Class	IDMg	Reacn. Condtn.	Product Yield affected by addn of	
			Substr.		HMPA(38.8)	Py(33.1)
Ar^1NO_2	2.17 | 2.99	SET -controlled type	4.2	55 °C 3 h	Improved Efficiency of Condensn. Increase of Azoxy	
				0 °C 3 h	Increase	Increase
Ar^1CN	> 3.7	σ-complexn. -controlled type	2.0	55 °C 3 h	Decrease	Increase
				0 °C 3 h	Inhibition	

Figure 3. Summary of effects of polar solvent addition on IDMg reactions (5) and (6) at 55 and 0 °C



Scheme 2. Illustration: distinction of class B and C reactions. Relative tightness of σ-complexation (see the lengths of dotted arrows) and principal effects of polar solvent molecules (Sv; see 'boxed arrows')

tals feasible for SET and/or radical migration is also possible, as indicated by the increase, in contrast, caused by Py.

The manner of the variation in the yield of **A** in reaction (6) by Py is similarly explicable. With four combinations of substituents (runs 8, 5, 2, and 4 in Table 1), the yield in the absence of Py from 2 mol of IDMg at 55 °C is poor when ΔE is larger but is greatly improved by Py [see ratios given in Figure 2 for reaction (6a)].[5] The ΔE dependence of the yield decrease implies 'HOMO–LUMO interaction' of the reactants, and the increase results in comparable yields because 'more reactive reagent is less selective'.

The present results also provide guidelines for the preparative use of the large *DN* compounds in calculated small amounts: HMPA for azoxy preparation by reaction (5) and Py for benzamidine preparation by reaction (6), avoiding the use of an unnecessarily large excess IDMg. The effect of Py and HMPA has been studied only concerning the composition of or radical generation from Grignard reagents.[17,18]

Exclusive 'normal addition' to alkyl and arylvinyl cyanides

On IDMg treatment of phenylacetonitrile and cinnamonitrile, the expected amidines are formed only via the normal 1,2-addition mode (Table 2; some cases favoured by added Py), although the conditions are unoptimized. Abnormal 'α-H abstraction or conjugate 1,4-addition' modes are absent, in contrast to the abnormal modes on Grignard treatment of nitriles[19] and on IDMg treatment of acetophenone (enolized).[1b] With IDMg, some α-benzylideneacetophenones undergo 1,4-addition[20] and β-nitrostyrene reacts vigorously to give several products,[21] including those of C=C bond breaking. The results, observed for the first time throughout reactions of C—Mg and N—Mg, reflect the EAAs of $C_6H_5CH{=}CHY$ (E_{red}: Y = NO_2, −1·18 V, COC_6H_5, −1·59 V; CN, −1·72 V). The value for Y = CN is smaller than that for C_6H_5CN by more than 1·0 V, and the weak EAA of nitriles is attributed to that of cyano group itself.

Remarks on reaction (6) from the unified view

Although no direct evidence for SET in reaction (6) and related reactions has been obtained, all the results given above are attributed to a combination of the weak EAA of the CN group and the weak EDA of IDMg. Two comments are made below from the unified view.

1. The ΔE approach is based on the simple relationship between ΔE and the final distribution of the products in spite of the 'multi-step' nature and the difference in reaction modes. For validity of the simplicity, the role of an excess amount of reagent must be considered. As concluded from reaction (1)[10] by a detailed ESR study of the long-lived dimeric pair of ketyl and reagent radicals generated from a 1 : 1 molar ratio and from reaction (5)[13] from need for excess of IDMg related to the effects of its structure and concentration, an excess of reagent 'assists the radical

Table 2. Amidine formation from phenylacetonitrile and cinnamonitrile[a]

Nitrile	R	Temperature (°C)	Time (h)	Py present	Yield (%)
$PhCH_2CN$[b]	MeO	55	3	−	27
	Me	55	3	−	84
	Cl	55	3	−	72
	MeO	55	3	+	86
	Me	55	3	+	52
	Cl	55	3	+	14
	MeO	r.t.[c]	16	−	0
	Me	r.t.	8	−	30
	Me	r.t.	8 + reflux 1	−	57
	Me	r.t.	8	+	0
	Cl	r.t.	6	+	0
PhCH=CHCN[d]	MeO	55	3	−	3
	Me	55	3	−	26
	Cl	55	3	−	55
	MeO	55	2 + reflux 1	−	79
	Me	55	2 + reflux 1	−	93
	Cl	55	2 + reflux 1	−	70

[a] Concentration of IDMg = 100 mmol l^{-1} in THF.

[b] [IDMg]/[nitrile] = 3·0.

[c] Room temperature.

[d] [IDMg]/[nitrile] = 2·0.

migration' in a later stage. The stage proceeds inside the assembly composed of intermediate radicals and reagent aggregate.

In class B, the assembly formation may be favoured by association of reagent molecules caused by a dynamic 'pre-interaction' with the substrate, owing to the smaller ΔE, responsible for a dimeric type of abnormal products.[13] In reaction (6) of class C, excess of IDMg (see above) may be needed, owing to the larger ΔE, to assist the 'inner-sphere SET via σ-complexation in an $n:1$ (not $1:1$) ratio'. The manner of radical generation in the initial stage is governed by ΔE, whereas later stages proceed in a closed environment of the assembly. This feature gives a clue to the validity of the simple ΔE approach.

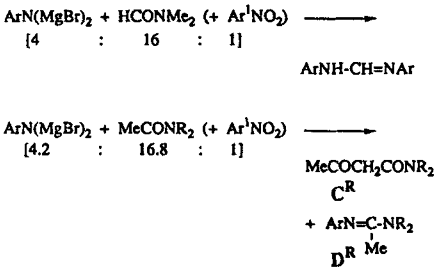
2. The different effects of HMPA (or Py) on reactions (6) and (5) evokes the different effects of 2,4,6-trimethylbenzophenone on reactions (3) and (1).[7a] Whereas weak IDMg gives no σ-complex with the crowded ketone, strong ArMgBr is capable of SET. The ketyl radical generated in reaction (1) accumulates to a high concentration, because the radical migration in later stages is hindered. If the ketone is uncrowded, reaction (3) proceeds via fairly tight σ-complexation and inner-sphere SET, whereas reaction (1) proceeds via SET with little assistance from σ-complexation. Owing to the crowdedness, the σ-complexation step in reaction (3) is hindered whereas the SET step in reaction (1) is not. Among the two initial steps, that essential to each class of reaction is affected by both the polar solvent and the substrate's crowdedness.

In the present experiments on reaction (6) with Ar^1CN, the IDMg concentration was fixed at $100\ \mathrm{mmol\,l^{-1}}$ in THF. The detailed results of inter- and intramolecular competition experiments, the applicability of reaction (6) to alkyl substrates and reagents and the effects of concentrations on reaction (6) will be reported in future papers.

Reaction (7) and related reaction (7')

Different condensation modes of DMF and DMA on IDMg treatment

As preliminarily reported,[3] reactions (7) with DMF and (7') with DMA were revealed as an extension of a study of the effects of large *DN* compounds on IDMg reaction (5) with Ar^1NO_2.[13] The mode of reaction (7) is mutual condensation plus replacement giving *N*,*N'*-diarylformamidine (**B**), whereas that of reaction (7') is Claisen-like self-condensation giving *N*,*N*-dimethylacetoacetamide ($\mathbf{C}^R$, R = Me). An IDMg : DMF (or DMA) : Adt = 4 : 16 : 1 or 4·2 : 16·8 : 1·0 was used considering the fact that a fourfold molar amount of IDMg is required for effective condensation in reaction (5),[11] and for the purpose of replacing four THF molecules on Mg atoms.[14]



$$\underset{[4\quad:\quad16\quad:\quad1]}{ArN(MgBr)_2 + HCONMe_2\ (+\ Ar^1NO_2)} \longrightarrow ArNH\text{-}CH{=}NAr \qquad [7]$$

$$\underset{[4.2\quad:\quad16.8\quad:\quad1]}{ArN(MgBr)_2 + MeCONR_2\ (+\ Ar^1NO_2)} \longrightarrow \underset{\mathbf{C}^R}{MeCOCH_2CONR_2} + \underset{\mathbf{D}^R}{ArN{=}\underset{Me}{C}\text{-}NR_2} \qquad [7']$$

$R_2 = Me_2, Et_2, \text{-}(CH_2)_4\text{-}, \text{-}(CH_2)_2O(CH_2)_2\text{-}$
$Ar^1NO_2 : Ar^1 =$ (a) 2, 4, 6,-$Me_3C_6H_2$, (b) p-$MeOC_6H_4$, (c) p-ClC_6H_4

A mixture of DMF or DMA with Ar^1NO_2 dissolved in THF was added to IDMg solution. The product yields in reactions (7) and (7') were compared in the absence and presence of Ar^1NO_2 additives (**a**, **b**, **c**) at 0 and 55 °C. The yields were calculated based on the amount of nitro additives, irrespective of their presence or absence, for the purpose of evaluating their effects.

From the fairly weak EAA of DMF ($E_{red} = -2{\cdot}1$ V) resembling that of Ar^1_2CO and the larger *DN* values of DMA (27·8) and DMF (26·6) than that of THF (20·0),[14] class C characteristics of reactions (7) and (7'), i.e. the σ-complexation-controlled nature involving exchange of the THF ligand with the amides as an essential step (followed by SET in the inner sphere of the complex) is proposed. The highest yield of **B** in reaction (7) at 10 °C among those at higher and lower temperatures (with a rapid treatment with IDMg),[3b] suggesting an equilibrium between reactants, is consistent with class C character. The reasons for the differences in the reaction modes and the effects caused by nitro additives are discussed separately.

The relative tightness of the σ-complex of IDMg with the substrate is reflected in the features of class C reactions. The crowded CO group in reaction (3) sometimes leads to benzohydrol[7] via a ketyl radical leaving the σ-complex after SET. The least crowded CO of DMF responsible for tight σ-complexation leads to efficient formation of **B** in reaction (7). A lower yield of **B** from *N*,*N*-diethylformamide[3b] implies a decreased favouring of the bulkier amino group for σ-complexation. The bulkier acetyl group of DMA is responsible in reaction (7') for loose σ-complexation followed by dissociation of radicals and leads to $\mathbf{C}^R$ via self-condensation (see below).

The tightness of the σ-complex proposed for reaction (7) is reflected in the yield of **B** being unaffected by Ar^1NO_2.[3] In contrast, the looseness of the σ-complex proposed for reaction (7') is reflected in the yield of $\mathbf{C}^{Me}$ being greatly affected by the Ar^1NO_2 additive. The effect of the additive on reaction (7') was examined in detail using *N*,*N*-diethylacetamide (DEA) and some amides having different amino groups. The resulting yields of $\mathbf{C}^R$ summarized in Figures 4 and 5 are discussed in the following section. The difference in azoxy + azo formation via reaction (5) accompanying reactions (7) and (7′) is described in footnotes of Figure 4.

SET catalysis of reaction (7′) mediated by added Ar^1NO_2

The possible sequence of steps of reaction (7′) is given in Scheme 3: initial exchange of THF with DMA, SET inside a loose σ-complex, dissociation of radical cation and anion, leaving of dimethylamide anion, abstraction of acetyl hydrogen by arylaminyl radical and final coupling of acetyl and *N,N′*-dimethylcarbamoylmethyl radicals leading to $\mathbf{C^{Me}}$. It is certain that σ-complexation with amides precedes the SET to Ar^1NO_2 (strong EAA), even with simultaneous addition, and the steps must proceed in the close proximity of the ligand sphere. The given sequence explains features i–iii of reaction (7′) derived from Figures 4 and 5, as shown below.

Feature i is 'eight- to tenfold improvement of $\mathbf{C^{R}}$ yield (from 25–30% to 200–280%) by Ar^1NO_2 additive'. This is attributed to catalysis of implicit SET caused by access of Ar^1NO_2 to the ligand sphere: 'SET mediation' is shown by the dashed arrows in Scheme 3. The great improvement in $\mathbf{C^{Me}}$ yield at 0 °C by additive **a** [Figure 4(b)] indicates that even the crowded **a** is accessible at 0 °C. The improvement by **b** at 55 °C [Figure 4(a)] implies that access of the nitro oxygen to Mg is favoured by the *p*-MeO group of uncrowded **b** even at 55 °C. The $\mathbf{C^{Me}}$ yield at 0 °C is slightly improved by the use of *p*-Me-IDMg and **b** (Figure 4). The great improvement in $\mathbf{C^{Et}}$ yield from DEA by **a** (Figure 5) may be due to steric contraction of the DEA molecule caused by access of **a**, or to bond lengthening in the DEA anion radical generated via SET mediation.

Feature ii is 'high yields of $\mathbf{C^{R}}$ in the absence of Ar^1NO_2'. The very high $\mathbf{C^{R}}$ yield from acetopyrrolidide (Figure 5) implies the favouring of the less crowded amino nitrogen in the five-membered ring for σ-complexation. The fair $\mathbf{C^{Me}}$ yield obtained with the use of *p*-MeO-IDMg (Figure 4) is also notable.

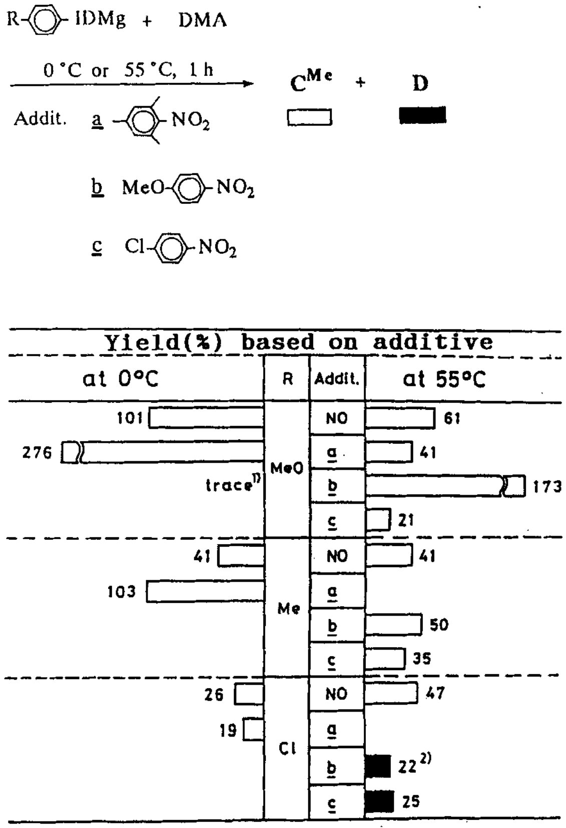


Figure 4. Effects of nitro additive and temperature on the yields of acetoacetamide ($\mathbf{C^{Me}}$; white boxes) and acetamidine (**D**; black boxes) in reaction (7′) for 1 h.

Footnotes: (1) Azoxy (77%) and azo (15%) products (see Scheme 3) were obtained only in this case. (2) Except for this case, addition of **b** and **c** led to overall azoxy + azo yields of 78–93%

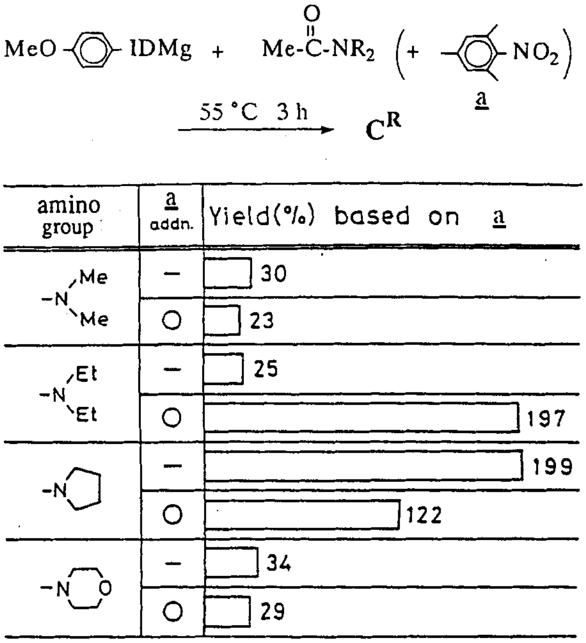
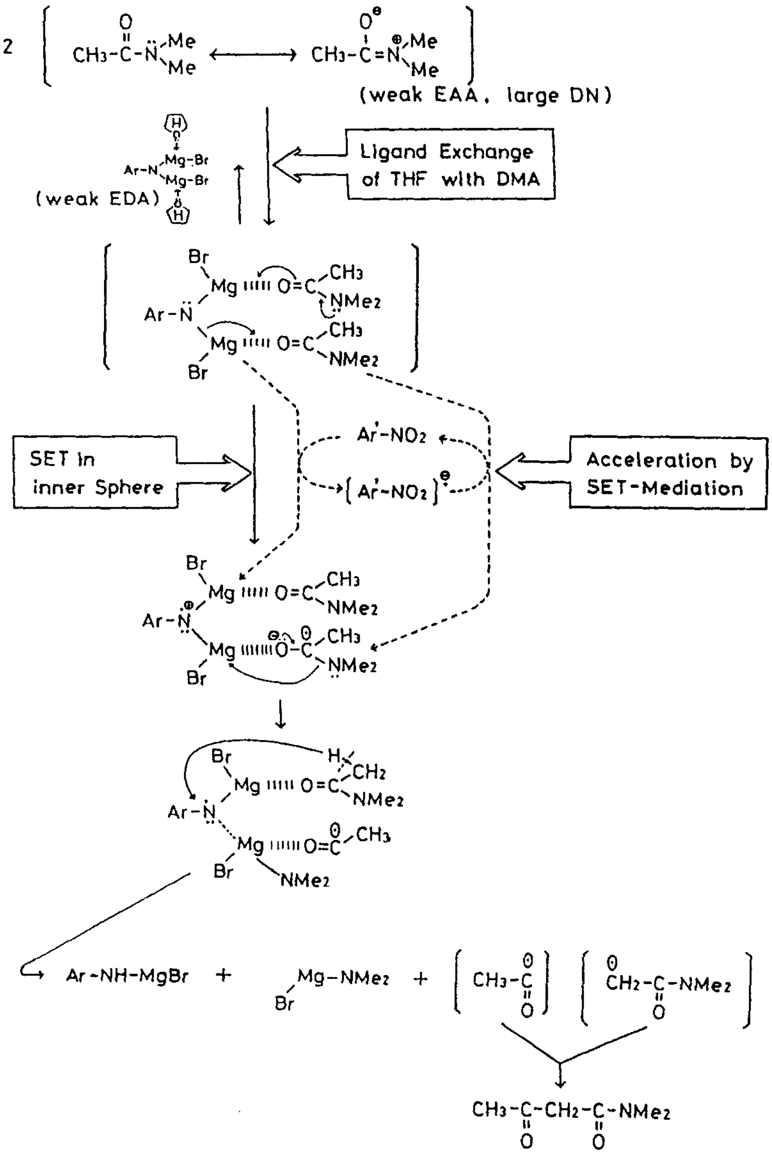


Figure 5. Effects of additive **a** and structure of amino moiety on $\mathbf{C^{R}}$ yields in reaction (7′) at 55 °C for 1 h

Feature iii is 'limited cases of mutual condensation of DMA with IDMg affording *N,N*-dimethyl-*N*′-arylacetamidine (**D**) [in low yield, but similar to reaction (7)] by use of *p*-Cl-IDMg combined with **b** or **c** at 55 °C (Figure 4)'. To the ligand sphere of the tight σ-complex formed via the 'strongly positive Mg of weak *p*-Cl-IDMg',[5b] the uncrowded **b** or **c** has access to mediate SET leading to **D**.

A summary is illustrated in Figure 6. For the SET catalysis of reaction (7′), the effect of the nitro additive is related to the 'extent of access of its oxygen to Mg' shown by the lengths of the broken bars; the length is arbitrarily given by considering the relative ΔE in reaction (5) (affected by substituents[5b]) and applied temperature. The requisite for mediation of SET catalysis is 'appropriately close access of nitro oxygen to Mg': insufficient access causes no mediation and too close access leads to mutual condensation and/or azoxy



Scheme 3. Possible sequence of steps of reaction (7′)

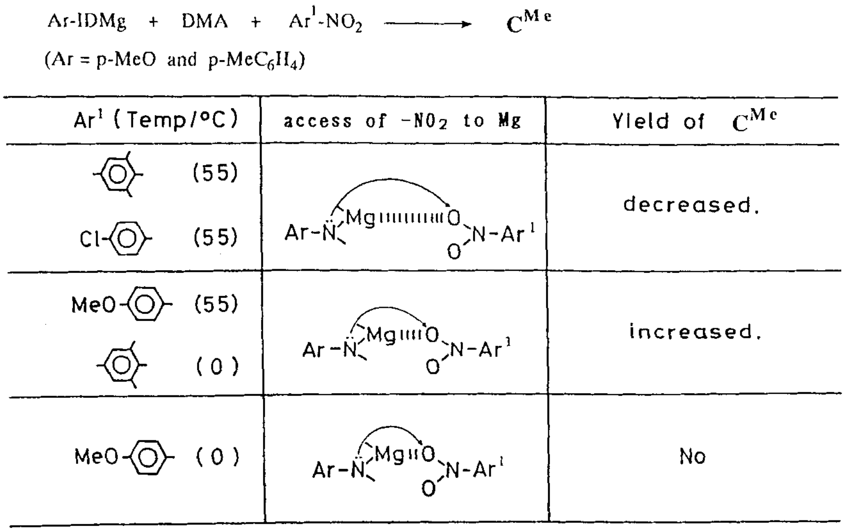


Figure 6. Summary of effects of structure of Ar^1NO_2 and temperature on efficiency of SET and σ-complexation in reaction (7′)

formation. Consistent with the very tight σ-complex with DMF being unaffected by Ar^1NO_2, implicit SET in reaction (7) is not revealed.

Remarks on reactions (7) and (7′) from the unified view

Reaction (7′) leading to C^R is also possible by use of anilinomagnesium, diisopropylaminomagnesium and Grignard reagent, although time and temperature are not unified. Very efficient C^R formation using RMgBr has been reported;[22] neither acyl nor amino bulkiness retarded the reaction and no possibility other than an ionic mechanism (probably ester condensation using ethoxide ion) was considered. The absence of a bulkiness effect with the use of strong RMgBr is reasonable because a small ΔE reaction requires no tight σ-complexation. The present result is of significance for the manifestation of inner-sphere SET based on acceleration by an Ar^1NO_2 additive. Its early use for the manifestation of a similar possibility in S_{RN} reactions based on retardation[23] is noted.

CONCLUSION

It should be stressed that the proposed characteristics of class C reactions of magnesium reagents have been confirmed, in an indirect manner, by (a) the complete absence of an 'abnormal mode' in high ΔE reactions according to 'less reactive, more selective' principle, (b) the distinction of essential steps of low and high ΔE reactions by use of large *DN* compounds and (c) the revealing of implicit SET by use of additives having strong EAA.

This study was based on product analysis and not on a kinetic treatment, and the term 'essential' is used in place of 'rate-determining'. The mechanism of the proposed inner-sphere SET, probably depending on the relative tightness in σ-complexation causing perturbation of the HOMO and LUMO levels of the reactants, remains to be studied theoretically.

EXPERIMENTAL

Procedures and products. The THF solutions of IDMg were prepared according to the reported procedure using the corresponding anilines and a twofold molar amount of EtMgBr. The reaction mixture was stirred at given temperatures for a definite time and quenched with aqueous ammonium chloride. The products were separated chromatographically on silica gel (Wako Gel FC-40) and the structures were determined from ^1H NMR spectra.

Reaction (6). All the reactions were carried out using 4·0 mmol of IDMg in 40 ml of THF. The molar ratio of reagent, substrate and polar solvents and the reaction time and temperature are given in the figure captions. Spectra of the products of reactions (3) and (5) have been published[8,11] and those of **A**, including some anomalies, will be reported elsewhere.

Reaction (7). A 10 ml volume of a THF solution containing calculated amounts of DMA and Ar^1NO_2 was added to IDMg solution (4·20 mmol in 35 ml of THF) and the mixture was stirred at a definite temperature for 1 h. Spectral data for azoxy and azo products have been published[2] and the precise data for **B**–**D** will be reported elsewhere.

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