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BENZAMIDINES, ALKAMIDINES AND FORMAMIDINES FORMED BY USE OF ARYL- AND ALKYLIMINODIMAGNESIUM: MOLAR RATIO AND STRUCTURE OF REAGENT GOVERNING THE REACTION*

MASAO OKUBO† AND YASUMASA OMOTE

Department of Chemistry, Faculty of Science and and Engineering. Saga University, Honjo-machi, Saga 840, Japan

In order to extend the the method for preparation of amidines using N–Mg reagents, aryl- and alkyliminodimagnesium [IDMg, $ArN(MgBr)_2$ and $RN(MgBr)_2$] were reacted with esters, amides, ortho- esters, acetals, aminoacetal and arene- and alkane carbonitriles. Among the compounds used, aminoacetal and carbonitriles were proved to be useful as starting materials for amidine preparation; alkyl-IDMgs were successfully used for the first time. It was noted that an excess molar amount of IDMg is needed in the reported reaction of $ArN(MgBr)_2$ with benzonitrile (aryl–aryl combination), whereas no excess is needed in aryl–alkyl, alkyl–aryl, and alkyl–alkyl combinations of reagent and substrate. From the viewpoint previously proposed in terms of relative efficiency of single electron transfer in the reactions of magnesium reagents, the most probable reason for the difference in the need for an excess molar amount of aryl and alkyl IDMg was ascribed to the difference in the electron-donating abilities of reagents. Additional minor reasons are discussed.

INTRODUCTION

Amidines ($R^1{}_2NCR{=}NR^2$) are useful synthetic intermediates,[1] and the conventional preparative method using Lewis acids is well known. Previously, methods using aryliminodimagnesium [$ArN(MgBr)_2$, IDMg] were proposed as novel synthetic procedures for amidines.[2] Benzo-, phenylaceto- and cinnamonitriles and/or *N,N*-dimethylformamide (DMF) were utilized as substrate, and the modification of IDMg + DMF reaction (by addition of benzoyl chloride to reaction mixture leading to binding of the three components) was reported. These results forced the authors to extend the IDMg procedure for amidine synthesis. In this study, using IDMg reagents derived from aryl-, benzyl- and alkylamines, the behaviours of esters, amides, ortho-esters, acetals, aminoacetal, and nitriles were compared. Using the last two substrates, giving amidines, the effects of molar ratio of reaction components, the substituents of aryl groups and the structures of alkyl groups were investigated. The effects of molar ratio depending on the aryl and alkyl structures of the reactants will be discussed in terms of general principles of reactions of magnesium reagents.[3]

RESULTS AND DISCUSSION

Unsymmetrical formamidines from aminoacetal and IDMg

The compounds used in the preliminary study of the abilities of condensation (with C=O) and replacement [of alkoxyl (OR) and/or amino (NMe_2)], and the results after the treatment with $ArN(MgBr)_2$ at 55 °C for 3 h in tetrahydrofuran (THF) are formulated in Figure 1 (combinations 1a, 1b, 2a, 2b, 3a, 3b, 4a, 4b, and 5). In combinations 1a and 1b, replacement of OEt and/or Cl took place, but no further condensation with C=O was observed. In combinations 2a and 2b, no reaction took place, indicating the weaker electron-donating ability (EDA) of IDMg than Grignard reagent (C-Mg).[3,4] Among combinations 3a, 3b, 4a and 4b, the orthofor-

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† Present address: Grand Forme Sumaura 401, Ichinotani, Suma-Ku, Kobe 654, Japan

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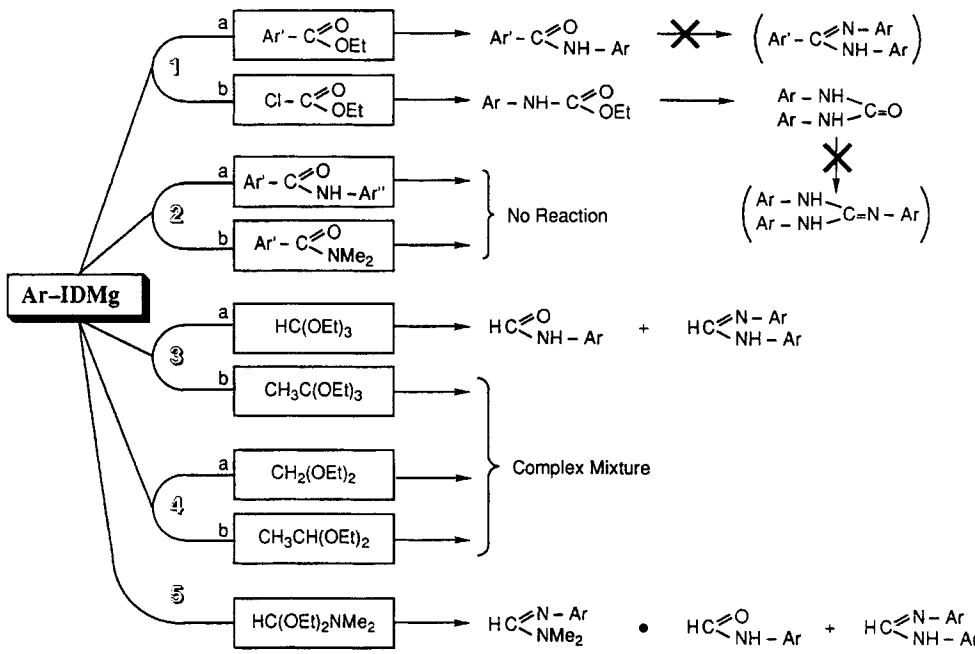


Figure 1

mate (3a) gave large amount of formanilide and a trace amount of formamidine whereas the other ortho-esters and acetals gave unidentifiable complex mixtures.

Only in combination 5 [with *N*,*N*-dimethylformamide diethylacetal (DMFE)], the OEt groups are removed leading efficiently to unsymmetrical formamidine accompanied by trace amounts of formanilide and symmetrical amidine. The reactions of DMFE with $ArN(MgBr)_2$ [reaction (1)], with $ArCH_2N(MgBr)_2$ [reaction (2)] and with alkyl-$N(MgBr)_2$ [reaction (3)], were carried out for examine the effects of molar ratio, substituents and reaction temperature and time. The yields of the products in reactions (1), (2) and (3) are summarized in Tables 1, 2 and 3, respectively.

Reaction (1) (Table 1)

The products are unsymmetrical formamidine (**1**), symmetrical formamidine (**2**) and anilide (**3**). A change of the *p*-substituent of phenyl-IDMg, from MeO via Me to Cl leads to decrease in yields of **2** and **3**, and exclusive formation of **1** arises from *p*-Cl-C_6H_4-IDMg (weaker EDA[4] accompanied by stronger $\delta+$ on Mg). The higher yield of **1** arises from the use of equimolar IDMg and/or the reaction at room temperature. These facts, implying milder conditions, suggest that **1** is formed via EtO removal.

In the reported IDMg reaction with *N*,*N*-dimethylformamide (DMF, parent amide of DMFE), the major product is **2** [formed via condensation (with C=O) and succeeding replacement (of NMe_2)] accompanied by minor product **1**.[2b,5] Alternation of major and minor products from the acetal and parent amide is interesting. The exclusive formation of **1** in run 3 using ArNHMgBr (anilinomagnesium having one Mg atom) seems to exclude the one-by-one pathway for the replacement of two OEt groups by IDMg.

Reaction (2) (Table 2)

p-$RC_6H_4CH_2$-IDMg (R = MeO, Me, Cl) was used similarly. The effect of the substituent is not great owing to the shielding by methylene, but the yield of amidine **4** decreases slightly by change in the substituent R (Me > MeO > Cl). The use of an equimolar amount of the IDMg led to sufficient yield of **4** accompanied by a small amount of formamide **5**. By use of equal molar amounts, the reactions at 55 °C for 3 h and at room temperature for 6 h led eventually to the same yields. The use of a three-fold molar amount always led to no amidine but, instead, to small amounts of amide and recovered DMFE (runs 3, 6 and 9). Owing to the poor results with the use of an excess, a possibility arising from the specific nature of the benzyl reagent is considered: the SET efficiency from *p*-Me-benzyl-IDMg may be comparable to that from *p*-Me-phenyl-IDMg (see E_{ox}: 1·02 and 0·99 V), but the benzylaminyl radical generated may aggregate with excess reagents and the

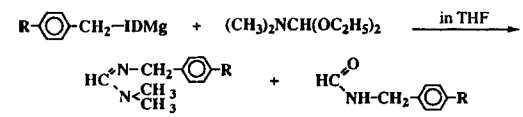
Table 1. Yields of products in reaction (1)

1 2 3 (1)

Run No.	R	[IDMg]/[DMFE]	Reaction conditions		Yield[a] (%)		
			Temperature (°C)	Time (h)	**1**	**2**	**3**
1	MeO	1·0	55	3	89	1	0
2	MeO	1·0	r.t.	6	87	Trace	0
3	MeO	3·0	55	3	46	Trace	28
4	MeO	3·0	r.t.	6	64	2	23
5	MeO	6·0	55	3	44	2	38
6	MeO	6·0	r.t.	6	62	14	0
7	Me	1·0	r.t.	6	85	4	0
8[b]	Me	1·0	r.t.	5	93	Trace	0
9	Me	3·0	55	3	75	Trace	19
10	Me	3·0	r.t.	6	70	10	17
11	Cl	3·0	55	3	73	11	0
12	Cl	3·0	r.t.	6	99	0	0

[a] IDMg concentration 3–12 mmol in 40 ml of THF.
[b] Reaction with anilinomagnesium reagent.

Table 2. Yields of products in reaction (2)

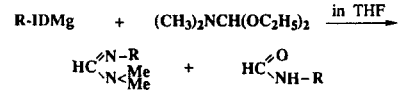


4 5 (2)

Run No.	R	[IDMg]/[DMFE]	Reaction conditions		Yield[a] (%)	
			Temperature (°C)	Time (h)	**4**	**5**
1	MeO	1·0	r.t.	6	83	5
2	MeO	1·0	55	3	83	2
3	MeO	3·0	55	3	—	9
4	Me	1·0	r.t.	6	91	3
5	Me	1·0	55	3	91	2
6	Me	3·0	55	3	—	27
7	Cl	1·0	r.t.	6	72	7
8	Cl	1·0	55	3	76	8
9	Cl	3·0	r.t.	6	—	25
10	Cl	3·0	55	3	—	27

[a] IDMg concentration 5–6 mmol in 30 ml of THF.

Table 3. Yields of products in reaction (3)



(3)

Run No.	R	Reaction conditions		Yield(%)	
		Temperature (°C)	Time (h)	**6**	**7**
1	Isobutyl	55	3	93	Trace
2	Isoamyl	55	3	92	4
3	*t*-butyl	55	3	64	Trace
4	*t*-butyl	55	6	84	Trace
5	*t*-butyl	r.t.	6	92	Trace
6	*n*-hexyl	55	3	92	4
7	Cyclohexyl	55	3	88	3
8	Benzyl	55	3	74	6
9	Benzyl	r.t.	6	89	5
10	2-Phenethyl	55	3	90	2
11	2-Phenethyl	r.t.	6	98	2

[a] Yield obtained by use of a 1 : 1 molar ratio. Nos 1–6, 9 and 10, 6 mmol of IDMg in 30 ml of THF; Nos 7 and 8 3 mmol of IDMg in 30 ml of THF.

radical transfer would thus be sluggish, leaving the anion radical to decompose by itself.

Reaction (3) (Table 3)

In reaction (3) using alkyl-IDMg [$RN(MgBr)_2$; R = isobutyl, isoamyl, *t*-butyl, *n*-hexyl, cyclohexyl, benzyl, 2-phenethyl], sufficient yields were obtained with the use of a 1:1 molar ratio. After treatment at 55 °C for 3 h, excellent yields of amidines (6) were obtained, except for treatment with benzyl reagent (see above). The sterically crowded *t*-butyl and cyclohexyl reagents gave slightly lower yields, but the yields were improved by treatment at room temperature for 6 h. The minor product, formamide (7), was formed in yields of less than 6%.

Although the commercial sample of DMFE is expensive and Reactions (1)–(3) are not perfectly recommendable, DMFE is a useful material for formamidine preparation using all kinds of IDMg-type reagents, except for the case of very weak EDA (e.g. *p*-ClC_6H_4-IDMg),[4] in a 1 : 1 molar ratio.

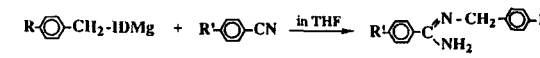
Arene- and alkanecarboamidines from nitriles and IDMg

The addition of weakly electron-donating aryl-IDMg to weakly electron-accepting benzonitriles, giving benzamidines, is a mild reaction involving 'σ-complexation' (—C≡N···Mg<) as the governing step followed by inner-sphere SET.[2,3]) On this basis, the study was extended to the use of alkyl-IDMg and/or alkyl-type nitriles. The combinations examined were benzyl-IDMg with benzonitriles [reaction (4)], alkyl-IDMg with a benzonitrile [reaction (5)] and alkyl-IDMg with alkanecarbonitriles [reaction (6)]. Almost all the reactions, carried out with the use of a 1 : 1 molar ratio, led to acceptable results, as shown in Tables 4, 5 and 6, respectively.

Reaction (4) (Table 4)

Equimolar amounts of benzyl-IDMg and benzonitrile, both having *p*-MeO, *p*-Me and *p*-Cl substituent, gave

Table 4. Yields of products in reaction (4)

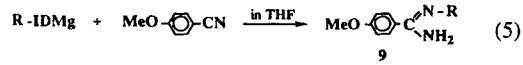


(4)

Run No.	R	R'	Yield[a] of **8** (%)
1	MeO	MeO	98
2	MeO	Me	72
3	MeO	Cl	96
4	Me	MeO	59
5	Me	Me	95
6	Me	Cl	71
7	Cl	MeO	73
8	Cl	Me	100
9	Cl	Cl	82

[a] Yields, based on the amount of substrates used, were obtained after heating at 55 °C for 3 h. Reagent: substrate = 1: 1; IDMg concentration 5 mmol in 30 ml of THF.

Table 5. Yields of products in reaction (5)



(5)

Run No.	R	Yield[a] of **9** (%)
1	Isobutyl	93
2	Isoamyl	94
3	*t*-butyl	77
4	*n*-hexyl	96
5	Cyclohexyl	100
6	2-Phenethyl	100

[a] Yields, based on the amount of substrates used, were obtained after heating at 55 °C for 3 h. Reagent: substrate = 1: 1; IDMg concentration, 5 mmol in 30 ml of THF.

the corresponding benzamidines (**8**) in sufficient or excellent yields.

When the substituent (R) of the reagent is fixed, the yield varies in interesting manners depending on R′ of the nitrile (see below). From the σ-complexation-controlled nature of the IDMg–CN reaction,[2c,3b] the manner of the variation implies the participation of electron-repelling resonance effects on the nitrile N atom; this participation will appreciably compensate for the weaker $\sigma+$ charge on Mg of the *p*-MeO reagent for σ-complexation, but will not need to operate with *p*-Me and *p*-Cl reagents having stronger $\sigma+$ charges.

	R	R′
Fix the reagent:	MeO	→ MeO, Cl > Me
	Me, Cl	→ MeO, Cl < Me

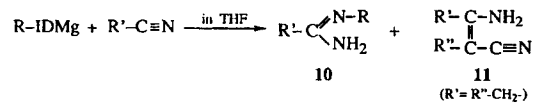
Reaction (5) (Table 5)

p-MeO-benzonitrile was treated with an equimolar amount of $RN(MgBr)_2$ (R = isobutyl, *t*-butyl, *n*-hexyl, cyclohexyl and 2-phenethyl). The yields of *N*-alkylbenzamidine (**9**) are excellent, except for that from the bulky *t*-butyl-IDMg.

Reaction (6) (Table 6)

The alkyl groups of IDMg used were phenethyl, *t*-butyl and isobutyl and the alkyl groups of cyanide used were ethyl, isobutyl, benzyl, *t*-butyl, and isopropyl. The results are classified into three groups. A (runs 1–6): no

Table 6. Yields of products in reaction (6)



(6)

Run No.	R[a]	R′[a]	R″[a]	Reaction condition: Temperature (°C) and Time (h)	Yield[b] (%) **10**	Yield[b] (%) **11**
1	Phe	Et	Me	rt, 0·5; refl., 1	—	91
2	Phe	Et	Me	55, 3	—	54
3	Phe	Et	Me	rt, 24	—	94
4	tBu	Et	Me	55, 3	—	73
5	iBu	Et	Me	rt, 0·5; refl., 1	—	94
6	Phe	iBu	iPr	rt, 0·5; refl., 1	—	72
7	iBu	Bzy		rt, 0·5; refl., 1	—	—
8	iBu	Bzy		rt, 24	—	—
9[c]	iBu	Bzy		rt, 0·5; refl., 1	—	—
10[d]	iBu	Bzy		rt, 0·5; refl., 1	9	—
11[e]	iBu	Bzy		rt, 0·5; refl., 1	4	—
12[f]	iBu	Bzy		rt, 0·5; refl., 1	6	—
13	Phe	tBu		45, 0·5; refl., 1	34	—
14	Phe	tBu		55, 3	57	—
15	Phe	iPr		rt, 0·5; refl. 1	93	—
16	Phe	iPr		rt, 0·5; refl., 1	89	—

[a] Abbreviations: Phe, 2-phenethyl; tBu, *t*-buty; iBu, isobutyl; Et, ethyl; Bzy, benzyl; iPr, isopropyl; Me, methyl.
[b] Yields obtained by use of a 1 1 molar ratio. IDMg concentration 5 mmol in 30 ml of THF.
[c] Pyridine (Py) added; [IDMg]: substration: Py = 3: 1: 3.
[d] Pyridine (Py) added; [IDMg]: substration: Py = 1: 1: 1.
[e] Pyridine (Py) added; [IDMg]: substration: Py = 1: 1: 2.
[f] Substration added for 0·5 h under reflux, then conditions (d).

addition takes place and, instead, self-dimerization of nitrile takes place to give β-amino-α,β-enenitrile (**11**); B (runs 7–12): benzyl cyanide (phenylacetonitrile) undergoes addition or dimerization only with difficulty; and C (runs 13–16): the expected amidine (**10**) is obtained from pivalo- and isovaleronitriles. The mixture with sterically crowded pivalonitrile has to be heated for a longer time.

The dimerization of nitriles induced by α-proton abstraction with a Grignard reagent[6] and a similar process from carboxamides with IDMg and a Grignard reagent[2b,2c] have been reported. Although IDMg has a weaker basicity than Grignard reagents, a similar process arising from nitriles is expected. Table 6 indicates that (A) the alkyl group of nitriles having two α-protons (α-methylene) suffers hydrogen abstraction to give **11**, and (C) otherwise, two alkyl groups [(B) except for benzyl] are introduced into the *N*-alkylalkanecarboxamidines **10**.

The poor yield from alkyl-IDMg and phenylacetonitrile in runs 9–11 (very slight improvement by addition of pyridine to the solution of IDMg[2c,7]) is in contrast to the reported great improvement in the reaction of aryl-IDMg with the same nitrile.[2c] The reason remains for further study.

DISCUSSION

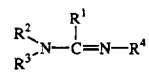
Almost all types of alkyl and aryl cyanides undergo addition of all types of reagents. In Table 7, all types of amidines prepared by the IDMg procedure are summarized.

The extensive success of reactions (4)–(6) reveals two important problems to be discussed from a generalized structure–reactivity viewpoint regarding the reactions of magnesium reagents.[3] First: why are an alkyl reagent and substrate successfully used only in IDMg-CN combinations? Second: why does the need for excess moles of reagent depends on the aryl or alkyl structure of the reaction components?

(1) Although nitroarenes and diaryl ketones react with aryl-IDMg in a condensation manner (—N(O)=N— and >C=N— formation), nitroalkanes[8] and alkyl ketones[9] do not undergo the expected condensation on the treatment with the same reagent, but instead decompose or dimerize via hydrogen abstraction induced by SET.[3b] (An attempted treatment of diaryl ketone with alkyl-IDMg to give a >C=N— product was not successful owing to hydrolysis of its precursor in the unavoidable operation of quenching.[9]) The different behaviours of aryl and alkyl substrates are ascribed, from a 'SET-efficiency' viewpoint, to the relative EAA of the functional groups ($NO_2 > CO > CN$) coinciding with their resonance electron demand.[2c,3b] The weak demand of nitrile is thus responsible for the first success of the IDMg procedure in binding of alkyl–alkyl combinations.

(2) In addition to the combination of RMgBr with $Ar^1{}_2CO$, the combinations of aryl-IDMg not only with $Ar^1{}_2CO$ and Ar^1NO_2[3b]) but also with Ar^1CN require excess amount of reagent. The 'general' need for an excess led to the proposal[2c,3b] that 'intermediate radicals form aggregates with excess reagent molecules, and the latter cooperate to assist the transfer of a reagent radical from the cation radical part. In comparison with the present IDMg-CN combinations given above, however,

Table 7. Types of amidines prepared by IDMg procedure.



No.	R^1	R^2	R^3	R^4	Substr.	R^4-IDMg	Substr./IDMg
1[a]	H	Ar	H	Ar	DMF	Ar	4:1
2	H	Me	Me	Ar	DMFE	Ar	1:1
3	H	Me	Me	ArCH2	DMFE	ArCH2	1:1
4	H	Me	Me	Alk	DMFE	Alk	1:1
5[b]	Ar^1	Me	Me	Ar^2	DMF + Ar^1COCl[d]	Ar^2	–[e]
6[c]	Ar^1	H	H	Ar^2	Ar^1CN	Ar^2	1:3
7[c]	Ar^1CH_2	H	H	Ar[f]	Ar^1CH_2CN	Ar^2	1:3
8[c]	$Ar^1CH{=}CH$	H	H	Ar^2	$Ar^1CH{=}CHCN$	Ar^2	1:2
9	Ar^1	H	H	Ar^2CH_2	Ar^1CN	Ar^2CH_2	1:1
10	Ar^1	H	H	Alk	Ar^1CN	Alk	1:1
11	Alk^1	H	H	Alk^2	Alk^1CN[f]	Alk^2	1:1

[a] See Refs 2 and 2d.
[b] See Ref. 2b.
[c] See Ref. 2c.
[d] Ar^1CoCl is added to the mixture of DMF + DMg.
[e] IDMg : DMF : Ar^1COCl = 3 : 12 : 1.
[f] Alk^1 must have no α-CH_2.

Table 8. Summary of the need for an excess of reagent

Substrate	Reagent	Excess reagent	(Optimum ratio)
(a) AR^1CN	Ar-IDMg	Needed	(3 : 1)
(b) RCN	Ar-IDMg	Not needed	(1 : 1)
(c) ArCN	R-IDMg	Not needed	(1 : 1)
(d) R'CN	R-IDMg	Not needed	(1 : 1)[a]

[a]Exception: α-H abstraction from R'.

the need for an excess is confined to aryl–aryl combinations (see below). Some related results concerning the amount of aryl-IDMg leading to the corresponding *N*-aryl-substituted amidine have been reported:[2c] The reaction with cinnamonitrile requires a molar ratio of 2·0, whereas that with acetonitrile requires equimolar amounts.[2c,10] The question is thus raised of the origin of the specific nature of aryl–aryl reactions. The need for an excess is summarized in Table 8.

Neither the E_{ox} values of alkyl reagents nor the E_{red} values of alkyl substrates have been determined (probably owing to the very rapid decomposition of cation and/or anion radicals), and no discussion in terms of ΔE values can be given. Nevertheless, it is reasonable to consider that, in case of (d) (Table 8), the stronger basicity of alkyl-IDMg due to localization of the lone pair of electrons on the amino N atom is responsible not only for the α-H abstraction but also for dimeric aggregation via $N: \rightarrow Mg^{\delta+}$ donation. Thus, even after a great part of the reagent has been consumed, the remaining part may still form an aggregate favourable for the cooperation. The specific requirement for an excess in aryl–aryl combination (a) is mainly ascribed to the weaker EDA of the aryl reagent which needs an excess for cooperation. From comparison with (b), a minor reason may be the spin density on the nitrile carbon, which is lowered owing to delocalization of unpaired electrons of the aryl substrate's anion radical. An additional possibility that (product's) precursor having two aryl groups is resonance stabilized and requires the assistance of an excess amount of weak reagent for the removal of ^+MgBr species is not excluded.

EXPERIMENTAL

Preparation of reagent. Prior to the preparation of IDMg, EtMgBr was prepared in tetrahydrofuran (THF).[4] An excess amount of EtBr is always used for complete conversion of metallic Mg. The unreacted amount of EtBr present in THF solution causes no interference in the reactions of aryl-IDMg with almost all types of aryl substrate, except for the reported *N*-alkylation.[11] In the present reactions, the unreacted EtBr was completely removed by way of precaution by refluxing the THF solution and distilling a small amount prior to addition of amines.

Work-up and isolation of amidines. In order to avoid hydrolysis of products on quenching, quick treatment with the minimum amount of saturated NH_4Cl aqueous solution is recommended. The product mixture was taken up with Et_20 and/or CH_2Cl_2, dried with $MgS0_4$,

Table 9. Melting points and ^1H NMR data for formamidines **1**, **4** and **6**

Product			
No.	R	M.p. (°C)	δ (ppm)
1	MeO	Oil	2·91 (6H, s), 3·70 (3H, s), 6·79 and 6·85 (4H, ABq, J = 2·4 Hz), 7·42 (1H, s)
1	Me	Oil	2·28 (3H, s), 2·97 (6H? s), 6·84 and 7·03 (4H, ABq, J = 7·8 Hz), 8·46 (1H, s)
1	Cl	Oil	2·96 (6H, s), 6·84 and 7·15 (4H, ABq, J = 11·2 Hz), 7·42 (1H, s)
4	MeO	Oil	3·24 (3H, s), 3·27 (3H, s), 3·75 (3H, s), 4·60 (2H, s), 6·82 and 7·46 (4H, ABq, J = 8·1 Hz), 8·60 (1H, s)
4	Me	Oil	2·34 (3H, s), 3·20 (3H, s), 3·25 (3H, s), 4·60 (2H, s), 7·10 and 7·39 (4H, ABq, J = 6·8 Hz), 8·63 (1H, s)
4	Cl	Oil	3·29 (6H, s), 4·63 (2H, s), 7·34 and 7·46 (4H, ABq, J = 5·4 Hz), 8·67 (1H, s)
6	Isobutyl	Oil	0·97 (6H, d), 2·05–2·20 (1H, m), 3·32 (2H, d), 3·37 (6H, s), 8·35 (1H, b)
6	Isoamyl	Oil	0·98 (6H, d), 1·60–1·80 (1H, m), 1·60–1·80 (2H, q), 3·35 (3H, s), 3·40 (3H, s), 3·53 (2H, t), 8·43 (1H, s)
6	*t*-buty	182·0–182·5	1·55 (9H, s), 3·40 (3H, s), 3·50 (3H, s), 7·86 (1H, d)
6	*n*-hexyl	Oil	0·92 (3H, t), 1·20–1·40 (6H, m), 1·60–1·90 (2H, m), 3·30 (3H, s), 3·35 (3H, s), 3·48 (2H, t), 8·32 (1H, s)
6	Cyclohexyl	180·5–181·5	1·10–1·40 (2H, m), 1·60–1·70 (2H, m), 1·70–1·90 (4H, m), 1·90–2·05 (2H, m), 3·30–3·40 (6H, b), 3·40–3·60 (1H, m), 8·05 (1H, s)
6	Benzyl	Oil	3·20 (3H, s), 3·30 (3H, s), 4·65 (2H, s), 7·20–7·35 (3H, m), 7·45–7·52 (2H, q), 8·70 (1H, s)
6	2-Phenethyl	Oil	3·10 (2H, t), 3·14 (3H, s), 3·25 (3H, s), 3·70 (2H, t), 7·15–7·25 (SH, m), 7·72 (1H, s)

Table 10 Melting points and ^{1}H NMR data for benzamidines and alkamidines **8**, **9** and **10**

Product				
No.	R	R′	M.P. (°C)	δ (ppm)
8	MeO	MeO	152·0–152·8	3·80(3H, s), 3·85 (3H, s), 4·77 (2H, d), 6·89 and 7·45 (4H, ABq, J = 5·4 Hz), 6·99 and 7·90 (4H, ABq, J = 9·0 Hz), 8·80–9·80 (3H, b)
8	MeO	Me	150·5–151·0	2·21(3H, s), 3·80 (3H, s), 4·78 (2H, d), 6·87 and 7·42 (4H, ABq, J = 8·6 Hz), 7·29 and 7·97 (4H, ABq, J = 9·0 Hz), 9·05–9·80 (3H, b)
8	MeO	Cl	171·5–172·0	3·82(3H, s), 4·78 (2H, d), 6·87 and 7·51 (4H, ABq, J = 8·4 Hz), 7·49 and 7·90 (4H, ABq, J = 8·2 Hz), 9·20–10·20 (3H, b)
8	Me	MeO	209·0–209·4	2·37(3H, s), 3·88 (3H, s), 4·77 (2H, d), 6·99 and 7·38 (4H, ABq, J = 5·4 Hz), 7·15 and 7·18 (4H, ABq, J = 10·8 Hz), 8·60–9·80 (3H, b)
8	Me	Me	111·0–112·2	2·33(3H, s), 2·40 (3H, s), 4·79 (2H, d), 7·16 and 7·37 (4H, ABq, J = 5·4 Hz), 7·28 and 7·81 (4H, ABq, J = 9·2 Hz), 8·70–10·00 (3H, b)
8	Me	Cl	169·5–169·9	2·33(3H, s), 2·80 (2H, d), 7·18 and 7·39 (4H, ABq, J = 5·4 Hz), 7·47 and 7·91 (4H, ABq, J = 13·5 Hz), 9·20–10·15 (3H, b)
8	Cl	MeO	220·0–221·0	3·85(3H, s), 4·83 (2H, d), 7·01 and 7·49 (4H, ABq, J = 5·5 Hz), 7·10 and 7·88 (4H, ABq, J = 8·8 Hz), 9·00–10·00 (3H, b)
8	Cl	Me	98·3–99·0	2·42(3H, s), 4·86 (2H, d), 7·32 and 7·52 (4H, ABq, J = 5·4 Hz), 7·32 and 7·79 (4H, ABq, J = 7·2 Hz), 8·70–9·80 (3H, b)
8	Cl	Cl	171·0–173·0	4·84(2H,d), 7·36 and 7·50 (4H, ABq, J = 12·5 Hz), 7·48 and 7·88 (4H, ABs, J = 16·5 Hz) 9·35–10·10 (3H, b)
9	isobutyl	—	195·3–195·8	1·00(6H, d), 2·00–2·22 (1H, m), 3·40 (2H, t), 3·88 (3H, s), 7·00 and 7·90 (4H, ABq, J = 4·0 Hz), 8·80–9·40 (3H, b)
9	isoamyl	—	179·0–179·5	0·89(3H, d), 1·50–1·80 (1H, m), 1·50–1·80 (2H, m), 3·47 (2H, q)· 377 (3H, s), 6·89 and 7·76 (4H, ABq, J = 9·2 Hz), 8·75–9·10 (3H, b)
9	*t*-butyl	—	166·5–167·51·59	(9H, s), 3·88 (3H, s), 7·00 and 7·77 (4H, ABq, J = 8·3 Hz), 8·20–9·40 (3H, b)
9	n-hexyl	—	128·0–128·80·89	(3H, t), 1·30–1·50 (6H, m), 1·70–1·81 (2H, m), 3·59 (2H, q), 3·86 (3H, s), 7·02 and 7·88 (4H, ABq, J = 9·5 Hz), 8·80–9·35 (3H, b)
9	cyclohexyl	—	208·0–208·5	1·10–2·15(9H, m), 3·88 (3H, s), 7·01 and 7·79 (4H, ABq, J = 5·4 Hz), 8·60–9·20 (3H, b)
9	2-phenetyl	—	241·5–241·8	3·13(1H, q), 3·85 (3H, s), 3·85 (2H, q), 6·99 and 7·79 (4H, ABq, J = 6·8 Hz), 7·20–7·38 (SH, m), 8·95–9·40 (3H, b)
10	2-phenetlyl	Isopropyl	143·0–144·0	1·26(6H, d), 3·03 (2H, t), 3·10–3·20 (1H, m), 3·72 (2H, t), 7·18–7·30 (SH, m), 8·30–9·10 (3H, b)
10	2-phenethyl	*t*-butyl	Oil	1·28 (9H, s), 3·03 (2H, t), 3·82 (2H, t), 7·20–7·35 (SH, m), 8·20–8·50 (3H, b)

rotary evaporated, and the mixture obtained was separated by flash chromatography on silica gel (Wako Gel FC-40). Considering the poor solubility of amidines formed in the reaction, the chromatographic procedure was omitted as described below.

For the isolation of unsymmetrical *N*,*N*-dimethyl-*N*′-alkylformamidines [poorly soluble in Et_20; reactions (2) and (3)], the quenched mixture was triturated with an amount of Et_2O sufficient to dissolve the starting materials, decanted, dissolved in CH_2Cl_2, dried with $MgS0_4$, and evaporated. The residue is amidine (**4** or **6**) pure enough to omit recrystallization.

For the isolation of *N*-alkylbenzamidines [**8** and **9**, reactions (4) and (5)] and *N*-alkylalkanecarboxamidines (**10**), which are soluble in CH_2Cl_2 and $CHCl_3$, the quenched mixture was triturated successively with Et_2O and CH_2Cl_2 and decanted. The residue was repeatedly triturated with mixed solvent [$CHCl_3$–EtOH (10 : 1)] and the combined mixture was evaporated to give pure amidines.

The melting points and ^{1}H NMR spectra of amidines prepared in this present study are summarized in Tables 9 and 10.

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