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Formation of Amidines from Aryliminodimagnesium and N,N-Dimethylformamide.[1] Novel Catalytic Mediation by Single Electron Transfer with Use of Nitrobenzenes

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N,N'-Diarylformamidines were obtained in good yields by the reaction of aryliminodimagnesium ($ArN(MgBr)_2$) with N,N-dimethylformamide in the presence of nitrobenzene. Novel catalytic mediation by single electron transfer was disclosed.

The structure-reactivity relation study on the condensation of aryliminodimagnesium ($ArN(MgBr)_2$, IDMg) with nitrobenzenes[2] (Scheme 1) is related to the study on Grignard addition to ketones because the two reactions have comparable single electron transfer (SET) efficiency estimated by the difference (ΔE) between oxidation and reduction potentials (E_{ox} and E_{red}) of the respective reactants.[3b] During the course of this study regarding the effect of polar aprotic solvent added to the reagent solution in tetrahydrofuran (THF), it was disclosed that the IDMg reagent condenses with N,N-dimethylformamide (DMF) giving two types of formamidines (<u>1</u> and <u>2</u>, Scheme 2).

$$ArN(MgBr)_2 + Ar'NO_2 \longrightarrow ArN{=}N(O)Ar' + ArN{=}NAr' \quad (+ \ ArN{=}NAr)$$

Scheme 1.

$$p\text{-}RC_6H_4N(MgBr)_2 + Me_2N\text{-}CH{=}O \xrightarrow{Ar'NO_2}$$

$$\underset{<1>}{Me_2N\text{-}CH{=}N\text{-}C_6H_4R\text{-}p} + \underset{<2>}{p\text{-}RC_6H_4NH\text{-}CH{=}N\text{-}C_6H_4R\text{-}p}$$

$$+ \underset{<3>}{p\text{-}RC_6H_4\text{-}NH\text{-}CH{=}O} + \underset{<4>}{Ar'\text{-}N(O){=}N\text{-}Ar'}$$

Scheme 2.

Several attempts to obtain amidines with use of IDMg and acyl chlorides or ethyl carboxylates were unsuccessful due to inertness of the corresponding amides first formed. Benzonitrile was also unreacted even by the treatment with excess IDMg according to ordinary procedures in THF. The attempts failed rather reasonably from comparison of relative E_{ox} values,[3a-d] i.e., IDMg has weaker electron-donating ability (EDA) than that of ArMgBr, the latter being capable of converting the acyl and cyano derivatives by well-known mode of addition.[4] It is thus of mechanistic importance to give reasons for the success of reaction 2. It is also of significance to provide an alternative route having access to formamidines because they are utilized as synthetic intermediates having N-C-N components for ring formation and also as a -CH= synthon.[5]

By considering the fact that Grignard reagent is coordinated by two ether molecules as well as that four or more equivalent amount of IDMg has usually been used for reaction 1,[2] reaction 2 was carried out by addition of four molar equivalent amount of DMF to IDMg solution in THF followed by addition of a 1/4.2 equivalent amount of nitrobenzene. After stirring at 55 °C for 3 h followed by quick quenching with aqueous ammonium chloride, the products were chromatographically separated. The products obtained are N,N-dimethyl-N'-arylformamidine (**1**), N,N'-diarylformamidine (**2**), N-arylformamide (**3**), and symmetrical azoxybenzene (**4**) derived from nitrobenzene. As shown in Table 1, **2** formed via condensation-replacement is the main product.

Table 1. Yields of products **1**-**4** in the reaction of Scheme 2.

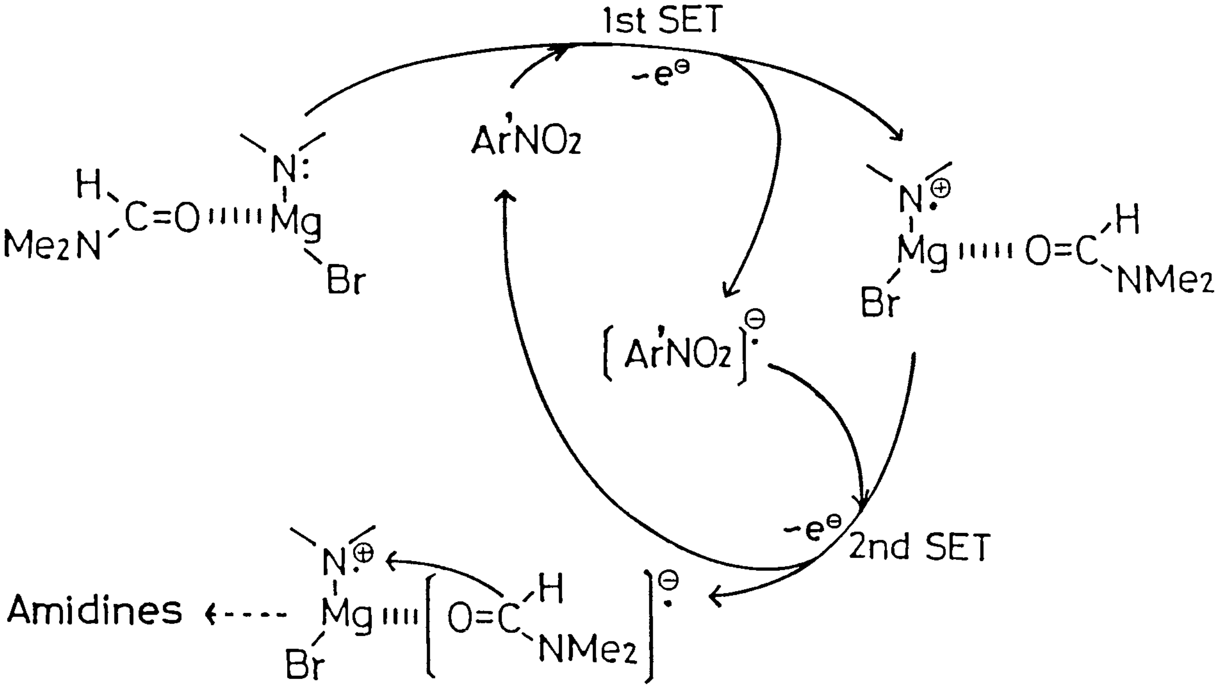
Run No.	R	Ar'= p-R'C_6H_4 R'	ΔE /V	Yield / %				Recov. of Ar'NO_2 /%
				1[1]	**2**[1]	**3**[1]	**4**[2]	
1	MeO	MeO	2.52	5	70	--	--	87
2		Me	2.33	8	56	--	25	75
3		Cl	2.17	8	58	--	45	27
4	Me	MeO	2.55	13	87	--	--	74
5		Me	2.36	16	84	--	10	68
6		Cl[3]	2.20	3	85	--	24	45
7	Cl	MeO	3.09	31	51	4	6	77
8		Me	2.90	17	59	2	12	63
9		Cl[4]	2.75	25	57	--	37	43

1) Yields of **1**-**3** are based on IDMg.
2) Yield of **4** is based on Ar'NO_2.
3) 4,4'-dichloro-2-dimethylaminoazoxybenzene[(O)NN](4%) was obtained.
4) 4,4'-dichloro-2-dimethylamino-azoxy[(O)NN]- (4%) and -azobenzene (2%) were obtained.

For convenience of discussion, Gutmann's donor numbers (DN) useful for estimating relative coordination abilities of solvents are cited:[6) DMF: 26.6, THF: 20.0. The reported E_{ox} and E_{red} values of substituted IDMg and nitrobenzenes, respectively, are also cited below,[3a,b) the positive and negative smaller values being responsible for more efficient SET due to smaller ΔE.

phenyl-IDMg: p-MeO: 0.912 V, p-Me: 0.941 V, p-Cl: 1.485 V
nitrobenzene: p-MeO: -1.608 V, p-Me; -1.418 V, p-Cl: -1.254 V

Since both IDMg and DMF were almost completely recovered in a control experiment without nitrobenzene, nearly complete recovery of the latter and absense of **4** in Runs 1 and 4 indicate that nitrobenzene behaves as a carrier of single electrons (SE) as illustrated in Scheme 3. It is suggested that IDMg HOMO level is elevated by coordination of DMF (DN is greater than that of THF), because a remarkable elevation of (free) Grignard HOMO level by coordination of two ether molecules was disclosed by ab initio SCF MO calculations using model compounds.[7) In the proximity of ligand sphere, SET from IDMg (coordinated by DMF) takes place first to generate Ar'NO_2 anion radical which undergoes second SET to DMF molecule, its (HOMO and) LUMO levels being somewhat lowered by coordination to Mg atom. The pathway leading to formation of amidines will thus be opened by attack of DMF (anion) radical on arylaminyl (cation) radical probably after the neutral Ar'NO_2 molecule leaves from the ligand sphere.



Scheme 3.

The catalytic cycle of Scheme 3 is based on the good combined yields of <u>1</u> and <u>2</u> even by use of 1/4.2 molar equivalent of Ar'NO_2 (Table 1). The combined yields of amidines are only slightly affected by ΔE values (estimated for the reactions in THF$^{3b)}$) irrespective of remarkable decrease and increase of the recovery of Ar'NO_2 and the yield of <u>4</u>, respectively (see Run 1-3, 4-6, and 7-9), the azoxy formation being reasonably favored by efficient generation of Ar'NO_2 anion radical due to more rapid SET (smaller ΔE). The SET catalysis was verified by use of 1/100 molar equivalent of crowded 2,4,6-Me_3-nitrobenzene, this being recovered due to sterically inhibited dimerization which, otherwise, leads to azoxy product.

The seemingly unusual replacement of stronger nucleophile (Me_2N) by weaker one (ArNH) is justified by the SET mechanism, which evokes the nucleophilic substitution on MeO-substituted electron-rich aromatics by use of salts and/or complexes of metal ions of high oxidation state (S_{ON} reaction).$^{8)}$ Possibility of further development with use of other kinds of SE carriers is expected.

References

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