Reaction of Aromatic Aldehydes with (Dialkylamino)magnesium Reagents. Formation of 1,2-Diaryl-1,2-ethenediamines

Kazuhiro Kobayashi,* Tomokazu Uneda, Masaharu Uchida, Yoshihisa Furuta, Miyuki Tanmatsu,
Osamu Morikawa, and Hisatoshi Konishi
Department of Materials Science, Faculty of Engineering, Tottori University, Koyama-minami, Tottori 680

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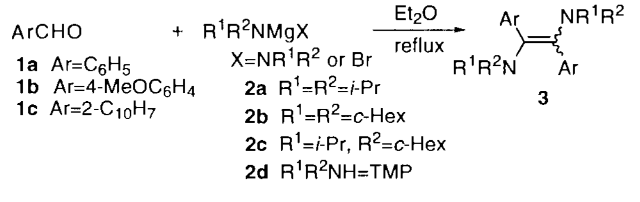
(Dialkylamino)magnesium reagents, derived from secondary amines and ethylmagnesium bromide, have been found to react with aromatic aldehydes to give 1,2-diaryl-1,2-bis(dialkylamino)ethenes in moderate to good isolated yields.

The two efficient syntheses of 1,2-enediamines by metal-induced coupling reactions of selenoamides[1a] and amides[1b] have been reported by Ogawa and Sonoda et al. A survey of the literature has revealed that there have been no other practical general methods for preparing this class of compounds.[2] We have found that 1,2-diaryl-1,2-bis(dialkylamino)ethenes **3** are conveniently available by reacting aromatic aldehydes **1** with (dialkylamino)magnesium reagents **2**,[3] derived from secondary amines and ethylmagnesium bromide, as shown in Scheme 1. We now wish to describe the results of our preliminary investigation.



Scheme 1.

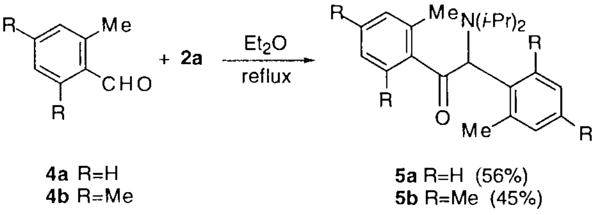
The aromatic aldehydes **1** were allowed to react with the magnesium amides **2**, generated *in situ* by treatment of secondary amines (8 molar amounts) with ethylmagnesium bromide (4 molar amounts), in refluxing diethyl ether to afford the enediamines **3** in moderate to good yields. The results using three aldehydes and four secondary amines are summarized in Table 1.[4] These products were obtained as inseparable mixtures of *E* and *Z* isomers, except for the exclusive production of **3d** with *E* configuration from benzaldehyde (**1a**) and the magnesium amide derived from 2,2,6,6-tetramethylpiperidine (TMP) (**2d**) (Entry 4), and each of them presented no stability problems during separation by preparative TLC on silica gel. The stereochemistries and *E/Z* ratios of the products were determined on the basis of ^{1}H NMR spectral analysis, including comparisons of the ^{1}H NMR spectral data with those of the related compounds reported by Ogawa and Sonoda et al.[1] Thus, the *E* isomers exhibit absorption signals assignable to the *N*-alkyl protons at much higher field than the *Z* isomers. For example, *E*-**3a** exhibits the signals at 0.78 (d, 19.2H) and 3.21 (sept, 3.2H) due to the four isopropyl groups, whereas the signals due to those of *Z*-**3a** are observed at δ 1.19 (d, 4.8H) and 3.88 (sept, 0.8H). It should be noted that we were unsuccessful in obtaining the corresponding enediamines from the reactions of benzaldehyde with diethylamine, pyrrolidine, and *N*-methylaniline. The use of a heterocyclic aldehyde, such as 2-furaldehyde, and an aliphatic aldehyde, such as 2,2-dimethylpropanal, was also found to fail to give the desired products.

Table 1. Preparation of 1,2-diaryl-1,2-ethenediamines **3**

entry	1	2	3 (Yield/%;[a] *E/Z*)[b]
1	**1a**	**2a**	**3a** (72; 80/20)
2	**1a**	**2b**	**3b** (80; 60/40)
3	**1a**	**2c**	**3c** (73; 70/30)
4	**1a**	**2d**	**3d** (37; 100/0)
5	**1b**	**2a**	**3e** (56; 80/20)
6	**1c**	**2a**	**3f** (59; 80/20)

[a] Yield of product isolated by preparative TLC on silica gel.
[b] Determined by ^{1}H NMR spectrum.

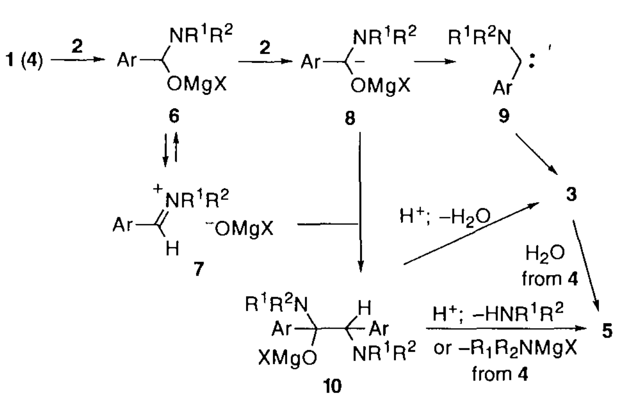
We next examined the reactions of *o*-substituted benzaldehydes, such as 2-methylbenzaldehyde (**4a**) and 2,4,6-trimethylbenzaldehyde (**4b**), with the (diisopropylamino)-magnesium reagent **2a** under the same conditions as described above. We found that the reactions gave 1,2-diphenyl-2-(diisopropylamino)ethanones[5] **5a** and **5b**, respectively, in moderate yields, and that no trace of the corresponding enediamine was obtained in each reaction (Scheme 2).



Scheme 2.

Typical experimental procedure is illustrated for the preparation of 1,2-bis(diisopropylamino)-1,2-diphenylethene (**3a**). Diisopropylamine (8.0 mmol, 0.81 g) was added to an ethereal solution (8 ml) of EtMgBr (4.0 mmol) at 0 °C, and the mixture was refluxed for 1 h under a positive pressure of argon. To the boiling turbid solution was added dropwise benzaldehyde (**1a**) (1.0 mmol, 0.11 g), and refluxing was continued for an additional 2.5 h.[6] After cooling, saturated aqueous NH_4Cl was added and the layers were separated. The aqueous layer was extracted twice with Et_2O, and the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a residue, which was subjected to preparative TLC on silica gel (EtOAc-hexane) to give **3a** (0.14 g, 72% yield) as a yellow oil.[7]

Although the mechanism for the present reaction is not yet clear, the production of the enediamines **3** may be interpreted as follows (Scheme 3). First, attack of the magnesium amide **2** to the aldehyde **1** or **4** yields the magnesium aminoalkoxide intermediate **6**, which is equilibrated with the immonium intermediate **7**. The intermediate **6** is deprotonated to give the anionic intermediate **8**, which is coupled with **7** to generate the magnesium diaminoalkoxide intermediate **10**. This is protonated and then is dehydrated to give rise to **3**. Alternatively, **8** may generate the α-aminocarbene intermediate **9**,[1,8] which dimerizes to give **3**. The failure with diethylamine, pyrrolidine, and *N*-methylaniline appears to indicate that the relatively strong basicity of magnesium amides is responsible for the success in the present reaction. The intermediate **10** derived from the *o*-substituted benzaldehydes **4** gives, on losing R^1R^2NMgX or R^1R^2NH after protonation, the α-amino ketone **5**, which may be formed *via* hydrolysis of the corresponding enediamine **3** during work-up and/or separation procedures. The formation of **5** may be ascribed to the steric crowding by the *o*-substituent in **10** or **3**.



Scheme 3.

In summary, we have shown that the reaction of aromatic aldehydes with (dialkylamino)magnesium reagents gives 1,2-diaryl-1,2-bis(dialkylamino)ethenes. This preparation may find some value in synthesis because of the ready availability of the starting materials. Work on elaborations as well as mechanistic aspects of the present reaction is currently in progress in our laboratory. The results will be described in detail elsewhere.

References and Notes

1 a) M. Sekiguchi, A. Ogawa, N. Kambe, and N. Sonoda, *Chem. Lett.*, **1991**, 315. b) A. Ogawa, N. Takami, M. Sekiguchi, I. Ryu, N. Kambe, and N. Sonoda, *J. Am. Chem. Soc.*, **114**, 8729 (1992).

2 For earlier reports on the formation of this class of molecules, see: A. Halleux and H. G. Viehe, *J. Chem. Soc. (C)*, **1968**, 1726; H.-D. Becker, *J. Org. Chem.*, **35**, 2099 (1971); E. J. Macpherson and J. G. Smith, *J. Org. Chem.*, **36**, 2516 (1971); J. A. Deyrup and W. A. Szabo, *J. Org. Chem.*, **40**, 2048 (1975); R. S. Monson and A. Baraze, *Chem. Lett.*, **1976**, 535 and references therein.

3 We have recently reported the utilization of magnesium amides in syntheses of organosulfur compounds[4a-d] as well as heterocyclic compounds.[4e,f] a) K. Kobayashi, M. Kawakita, T. Mannami, O. Morikawa, and H. Konishi, *Chem. Lett.*, **1994**, 1551 ; b) K. Kobayashi, M. Kawakita, K. Yokota, T. Mannami, K. Yamamoto, O. Morikawa, and H. Konishi, *Bull. Chem. Soc. Jpn.*, **68**, 1401 (1995); c) K. Kobayashi, K. Yokota, H. Akamatsu, O. Morikawa, and H. Konishi, *Bull. Chem. Soc. Jpn.*, **68**, 441 (1996); d) K. Kobayashi, M. Kawakita, H. Akamatsu, O. Morikawa, and H. Konishi, *Bull. Chem. Soc. Jpn.*, **69**, 2645 (1996); e) K. Kobayashi, Y. Kanno, S. Seko, and H. Suginome, *J. Chem. Soc., Perkin Trans. 1*, **1992**, 3111; f) K. Kobayashi, H. Takabatake, T. Kitamura, O. Morikawa, and H. Konishi, *Bull. Chem. Soc. Jpn.*, **70**, 1697 (1997).

4 The reaction of **1a** with magnesium amides, derived from 2:2, 2:4, and 4:4 molar ratios of EtMgBr to i-Pr_2NH, gave the product **3a** in 28, 36, and 42% yields.

5 For syntheses and reactions of this class of molecules, see: L. Y. C. Lee, X. Ci, C. Giannotti, and D. G. Whitten, *J. Am. Chem. Soc.*, **108**, 175 (1986); F. A. Davis and A. C. Sheppard, *Tetrahedron Lett..*, **29**, 4365 (1988) and references therein.

6 Longer reaction times did not improve the yield of **3a**.

7 All new compounds gave satisfactory IR (neat or KBr), ^1H NMR (270 MHz, $CDCl_3$), and LR-MS spectra, and were further characterized by HR-MS and/or elemental analyses. Selected IR, ^1H NMR, and LR-MS properties of the products follow. **3a**: *E*:*Z*=~80:20; ν/cm^{-1} 1596, 701; δ_H 0.78 (19.2 H, d, *J*=6.9 Hz), 1.19 (4.8 H, d, *J*=6.9 Hz), 3.21 (3.2 H, sept, *J*=6.9 Hz), 3.88 (0.8 H, sept, *J*=6.9 Hz), 6.8-6.95 (1.2H, m), 7.08 (0.8 H, dd, *J*=7.9, 1.6 Hz), 7.10 (1.6H. t, *J*=7.9 Hz), 7.18 (3.2H, t, *J*=7.9 Hz), 7.49 (3.2 H, dd, *J*=7.9, 1.6 Hz); *m/z* 379 (M+1, 6.2), 378 (M^+, 13), 104 (100). **3b**: *E*:*Z*=~60:40; ν/cm^{-1} 1596, 703; δ_H 2.6-2.8 (2.4 H, m), 3.4-3.55 (1.6 H, m); *m/z* 539 (M+1, 3.8), 538 (M^+, 1.8), 104 (100). **3c**: *E*:*Z*=~70:30; ν/cm^{-1} 1596, 701; δ_H 2.65-2.8 (1.4 H, m), 3.22 (1.4 H, sept, *J*=6.9 Hz), 3.55-3.6 (0.6 H, m), 3.90 (0.6 H, sept, *J*=6.9 Hz); *m/z* 459 (M+1, 5.3), 458 (M^+, 5.3), 104 (100). **3d**: ν/cm^{-1} 1603, 1260, 700; δ_H 0.99 (24 H, s), 1.3-1.6 (12 H, m), 7.12 (2 H, t, *J*=7.3 Hz), 7.25 (4 H, t, *J*=7.3 Hz), 7.44 (2 H, d, *J*=7.3 Hz), 7.53 (2 H, d, *J*=7.3 Hz); *m/z* 459 (M+1, 13), 458 (M^+, 8.5)), 209 (100). **3e**: *E*:*Z*=~80:20; ν/cm^{-1} 1604, 764; δ_H 0.82 (19.2H, d, *J*=6.8 Hz), 1.20 (4.8H, d, *J*=6.8 Hz), 3.26 (3.2H, sept, *J*=6.8 Hz), 3.66 (1.2H, s), 3.81 (4.8H, s), 3.91 (0.8H, sept, *J*=6.8 Hz), 6.52 (0.8H, d, *J*=7.9 Hz), 6.88 (3.2H, d, *J*=7.9 Hz), 7.02 (0.8H, d, *J*=7.9 Hz), 7.43 (3.2H, d, *J*=7.9 Hz); *m/z* 439 (M+1, 3.1), 438 (M^+, 2.2), 134 (100). **3f**: *E*:*Z*=~80:20; ν/cm^{-1} 1626, 1596, 820, 806; δ_H 0.83 (19.2H, d, *J*=6.9 Hz), 1.24 (4.8H, d, *J*=6.9 Hz), 3.32 (3.2H, sept, *J*=6.9 Hz), 3.95 (0.8H, sept, *J*=6.9 Hz); *m/z* 479 (M+1, 12), 478 (M^+, 12), 154 (100). **5a**: ν/cm^{-1} 1694, 1600; δ_H 0.95 (6H, d, *J*=6.9 Hz), 1.17 (6H, d, *J*=6.9 Hz), 2.39 (3H, s), 2.42 (3H, s), 3.35 (2H, sept, *J*=6.9 Hz), 5.64 (1H, s), 7.0-7.3 (7H, m), 7.43 (1H, d, *J*=7.9 Hz); *m/z* 323 (M^+, 4.0), 280 (100). **5b**: ν/cm^{-1} 1694, 1610; δ_H 1.05 (6H, d, *J*=6.9 Hz), 1.12 (6H, d, *J*=6.9 Hz), 1.73 (3H, s), 1,84 (6H, s), 2.19 (6H, s), 2.66 (3H, s), 3.36 (2H, sept, *J*=6.9 Hz), 5.57 (1H, s), 6.60 (1H, s), 6.62 (2H, s), 6.71 (1H, s); *m/z* 379 (M^+, 0.11), 232 (100).

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