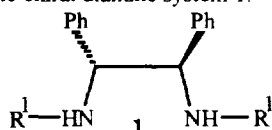


Low Valent Titanium Induced One Pot Syntheses of Imidazolines

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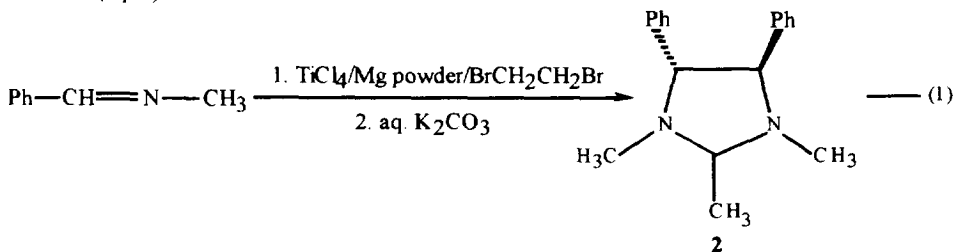
Abstract: Reaction of low valent titanium reagent, prepared in situ in THF by the reduction of $TiCl_4$ by Mg powder, with certain imines leads to the formation of imidazolidine derivatives in moderate to good yields. Copyright © 1996 Published by Elsevier Science Ltd

In connection with studies on the hydroborations and reductions using amine-boranes,¹⁻⁴ we were looking for a method of synthesis of the chiral diamine system 1.



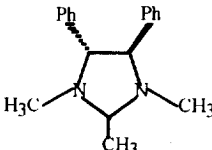
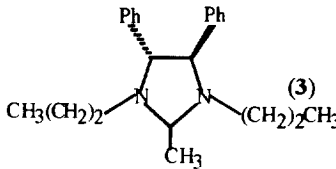
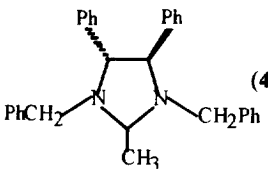
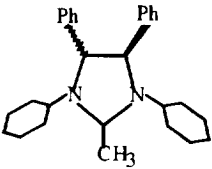
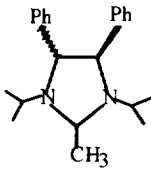
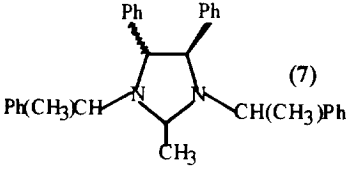
Alexakis and co-workers reported the synthesis of the symmetrical vicinal di-diamines 1 from the corresponding imines using low valent titanium species generated utilizing $TiCl_4$ and Mg-Hg reagent system.⁵ More recently, reductive coupling of aldimines into vicinal diamines has been reported in the action of Al/Bi powder/KOH in methanol.⁶ This prompted us to report the use of $TiCl_4$ /Mg powder/ $BrCH_2CH_2Br$ combination, which on reaction with certain imines leads to the formation of imidazolidines in 54-74% yield.

We have observed that the reaction of low valent titanium species generated by the $TiCl_4$ /Mg-powder/ $BrCH_2CH_2Br$ combination in THF with N-phenylbenzalimine gives dl-N,N-diphenyl-1,2-diphenylethylenediamine as reported by Alexakis and coworkers in the reaction using $TiCl_4$ /Mg-Hg.⁵ However, when the reaction was carried out using the N-methyl derivative, the imidazolidine 2 was obtained (eq. 1).



Clearly, the reagent combination used here is different compared to that prepared using Mg/Hg.⁵ In the present studies, the reagent was prepared using $TiCl_4$ (15 mmol), Mg powder (25 mmol) and 1,2-dibromoethane (10 mmol) in THF (60 ml) at 0°C. The reaction with N-methylbenzalimine (10 mmol) was carried out for 10h at 25°C. The formation of imidazolidines has been also observed in the transformations using certain other N-alkyl imines (Table 1).

Table 1: Conversion of imines to imidazolidines using TiCl_4/Mg powder/ $\text{BrCH}_2\text{CH}_2\text{Br}$ system.

Entry ^a	Substrate	Product ^b	Yield ^c (%)
1.	$\text{Ph}-\text{CH}=\text{N}-\text{CH}_3$	 (2)	54
2.	$\text{Ph}-\text{CH}=\text{N}-(\text{CH}_2)_2\text{CH}_3$	 (3)	63
3.	$\text{Ph}-\text{CH}=\text{N}-\text{CH}_2-\text{Ph}$	 (4)	70
4.	$\text{Ph}-\text{CH}=\text{N}-\text{C}_6\text{H}_{11}$	 (5)	74 ^d
5.	$\text{Ph}-\text{CH}=\text{N}-\text{C}_2\text{H}_5$	 (6)	66 ^d
6.	$\text{Ph}-\text{CH}=\text{N}-\text{CH}(\text{CH}_3)\text{Ph}$	 (7)	58 ^d

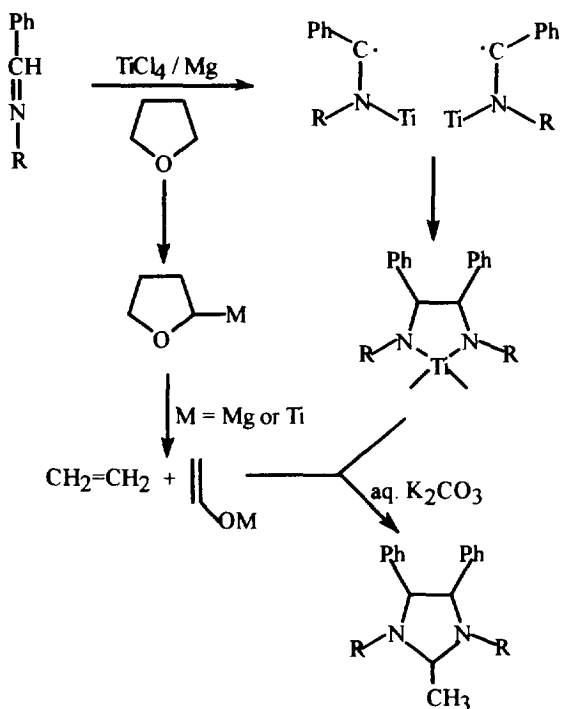
- a) In all entries, the low valent titanium reagent was prepared using TiCl_4 (15 mmol), Mg powder (50 mesh, 25mmol) and 1,2- dibromoethane (10 mmol) at 0°C in THF (60 ml) and the reaction with imines (10 mmol) was carried out at 25°C for 10h.
- b) All products were identified by spectral data (IR, ^1H , ^{13}C NMR)⁷. Mass spectral data (EI) was obtained for product 2. For products 4, 5 and 7 satisfactory elemental analyses ($\text{C} \pm 0.08\%$, $\text{H} \pm 0.20\%$, $\text{N} \pm 0.40\%$) were also obtained.
- c) Yields are of purified products based on the starting imine utilized.
- d) Isolated as a mixture of cis and trans isomers.

The following is the general procedure: Mg powder (50 mesh, 25 mmol) was added to TiCl_4 (15 mmol) in THF (60 ml) and activated with 1,2-dibromoethane (10 mmol) by dropwise addition (for 5 minutes) at 0°C under nitrogen atmosphere. The contents were stirred for 30 minutes at the same temperature and the imine (10 mmol) was added. The reaction mixture was brought to 25°C and stirred further for 10h. The black reaction mixture was quenched with saturated K_2CO_3 solution (5 ml). The resulting mixture was poured into H_2O (50 ml) and the organic phase was separated. The aqueous phase was saturated with NaCl and extracted with ether (2x40 ml). The combined organic extract was washed with brine (30 ml), dried over anhydrous MgSO_4 and concentrated. The residue was chromatographed on a silica gel column and the imidazolidine derivative was isolated using 5% ethyl acetate in hexane as an eluent.

The 1,2-dibromoethane was utilized in order to activate Mg .⁸ So, it was first thought that the CH_3CH -grouping in the product could have come from the dibromoethane. Later, it was found that this transformation takes place even without using 1,2-dibromoethane. However, the yields are somewhat less (by ~ 20%) in these experiments.

A possibility is that the TiCl_4/Mg system may generate certain reactive species of titanium and/or Mg-X species which might metallate THF leading to cleavage of THF. This type of cleavage of THF in reactions with organometallic reagents is not uncommon. For instance, *n*-BuLi abstracts proton from THF to give *n*-butane and the metallated THF undergoes further cleavage into ethylene and enolate moieties.^{9,10} Considering such a possibility, a tentative mechanism for this transformation may be visualized as shown in Scheme 1.

Scheme 1



The McMurry type low valent Ti- species are generally prepared in refluxing THF.¹¹ The Ti reagent utilised here is prepared under relatively mild conditions. It may be of interest to note that certain reactive nitrogen fixation complexes have been prepared from molecular nitrogen, TiCl₄ and Mg.¹² The nature of the reactive species formed under the present conditions is not understood. It is anticipated that further investigations on the utilization of this reagent system should be fruitful.

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- ¹³C NMR data of the compounds 2-7 in CDCl₃ are (2) δ ppm 15.3, 33.6, 36.6, 74.4, 76.1, 78.3, 125.8, 126.6, 138.5, 139.0. (3) 11.8, 11.9, 17.7, 21.3, 22.5, 48.0, 57.5, 74.2, 76.8, 78.0, 126.8, 127.2, 127.7, 128.0, 128.5, 140.4, 142.0. (4) 17.6, 50.2, 58.5, 73.9, 75.9, 77.3, 126.6, 126.8, 127.3, 127.7, 128.0, 128.3, 128.4, 128.5, 128.8, 129.2, 129.6, 137.4, 139.6, 139.9, 141.0. (5) 24.5, 24.9, 26.1, 32.3, 34.6, 53.0, 65.1, 126.4, 127.1, 127.8, 128.0, 128.3, 141.9. Additional signals seen at 24.6, 26.2, 32.6, 34.9, 53.8, 66.3, 127.6, 142.7, corresponding to the presence of ~30 % of cis isomer. (6) 12.0, 12.1, 22.1, 22.5, 25.2, 31.9, 54.5, 54.9, 65.8, 66.2, 126.7, 127.3, 127.9, 128.3, 141.7, 145.6. The signals due to ~25 % of cis isomer seen at 22.3, 25.3, 32.8, 54.7, 55.1, 66.1, 66.4, 127.1, 127.8, 128.0, 128.5, 141.5, 146.1. (7) 22.5, 24.6, 54.7, 64.1, 65.0, 66.1, 66.4, 126.5, 126.6, 127.0, 127.2, 127.7, 129.9, 128.5, 128.8, 141.0, 141.6, 146.3. Additional signals are seen at 22.1, 25.2, 54.9, 65.7, 66.2, 66.5, 126.7, 127.8, 128.2, 141.7, 146.4 corresponding to the presence of ~35 % of cis isomer.
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