Tetrahedron Letters, Vol. 34, No. 43, pp. 6907-6910, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Incorporation of Molecular Nitrogen into Organic Compounds. Titanium Catalyzed Nitrogenation

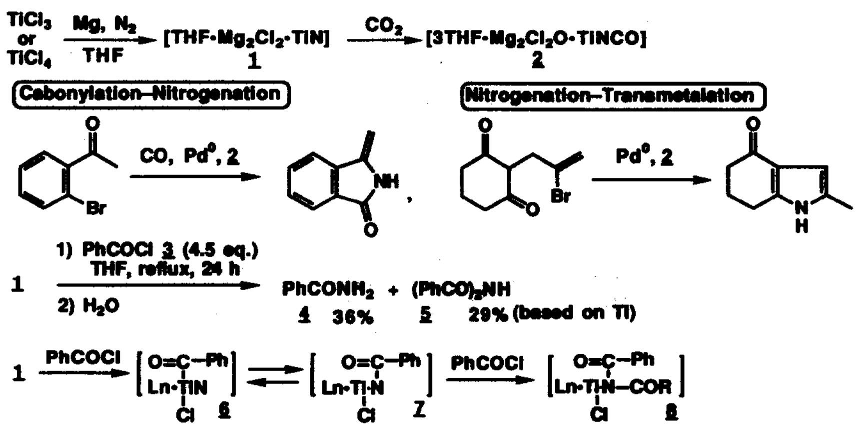
Mami Kawaguchi, Shin-ichi Hamaoka, and Miwako Mori*
Faculty of Pharmaceutical Sciences, Hokkaido University Sapporo 060, Japan

Key words: Molecular nitrogen; Titanium nitrogen complex; Nitrogen fixation; $TiCl_4$-N_2-Li; Heterocycles

Summary: Incorporation of molecular nitrogen into organic compounds was realized using a catalytic amount of $TiCl_4$ in the presence of excess TMSCl and Li under nitrogen.

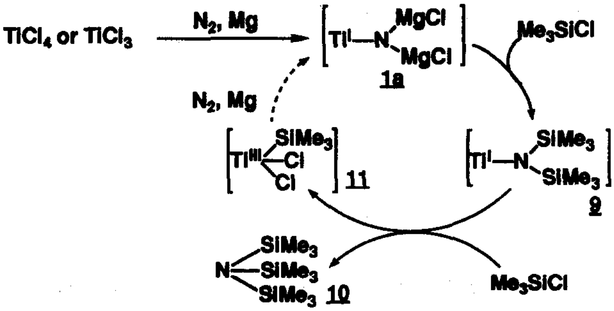
The incorporation of molecular nitrogen into organic compounds is very challenging work. We have already reported the incorporation of molecular nitrogen into organic compounds[1] using the titanium nitrogen complex[2] and titanium isocyanate complex[3] generated from molecular nitrogen, Mg, and $TiCl_4$. By the reaction, many heterocycles such as isoindolinone,[1b] quinazoline,[1b] indole,[1c] and quinoline derivatives[1c] were synthesized in good yields. These reactions are very interesting, however, an equimolar amount of the titanium isocyanate complex **2** is required for the preparation of the heterocycle (Scheme1). Thus, the next problem is to examine whether the reaction proceeds by a catalytic amount of the titanium nitrogen complex **1** or **2**. In the case of the reaction of the titanium nitrogen complex **1** with benzoyl chloride (**3**), we proposed the following reaction course: Oxidative addition of the low-valent titanium nitrogen complex(I) **1** occurs to produce the benzoyl titanium nitrogen complex(III) **6**. Migration of the benzoyl group from titanium to nitrogen provides the amide complex **7**. Benzoyl chloride further reacts with **7** to produce the imide complex **8**. Hydrolysis of these complexes, **7** and **8**, afforded the amide **4** and the imide **5**. Presumably the oxidation state of the amide complex would be same as that of the imide complex **8**. In order to make this reaction proceed using a catalytic amount of the titanium complex **1**, the amide **7** or imide complex **8** must be reduced to the low-valent titanium complex **1** with an appropriate reducing agent.

Scheme 1



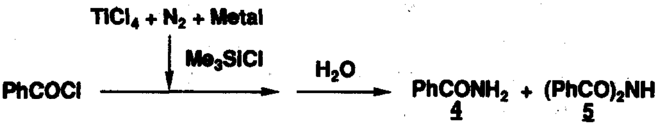
Our working hypothesis for the formation of the catalytic cyclè is as follows: The titanium nitrogen complex **1** can be considered to be **1a**. If trimethylsilyl chloride (TMSCl) is added to this reaction, **1a** would react with TMSCl to give the titanium silylamine complex **9**. The TMSCl would then oxidatively add to **9** followed by transmetalation to afford tris(trimethylsilyl)amine (**10**) and the titanium complex **11**. If excess Mg is present, the titanium complex **11** would be reduced under nitrogen to the titanium nitrogen complex **1a** (Scheme2).

Scheme 2 Working Hypothesis



For the preliminary experiment, the reaction was carried out in the presence of TMSCl using the previously reported[1a] reaction conditions (Table 1, runs 1 and 2). Namely, a mixture of $TiCl_4$, TMSCl, and Mg in THF was stirred under nitrogen at room temperature overnight, and then benzoyl chloride (**3**) was added to the mixture. The whole mixture was refluxed overnight. After the usual work up, the desired benzamide **4** and benzimide **5** were obtained. The total yields of the amide **4** and the imide **5** were same as that of the previous work and the reaction proceeded even at room temperature (run 3). When the reaction was carried out in excess Mg (50 eq.) and TMSCl (50 eq.) at room temperature, the yields were improved. On the other hand, the use of Li as a reducing agent afforded the same effect and the reaction conditions are moderate (runs 5, 6 and 7). In these cases, the yields of the desired product were improved, but the reaction did not proceed by a catalytic amount of $TiCl_4$ in each case.

Table 1 Effect of Metals

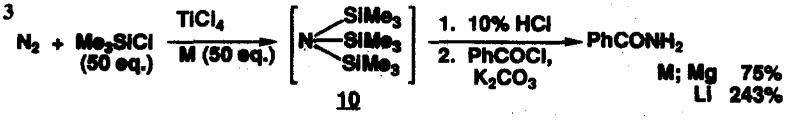


run	Metal (eq.)	Me₃SiCl	Temp	Yields (%)*		
				4	**5**	Total
1	Mg (4)	none	reflux	27	1	28
2	Mg (4)	5 eq.	reflux	23	6	29
3	Mg (4)	5 eq.	rt	13	9	22
4	Mg (50)	50 eq.	rt	36	20	56
5	Li (50)	50 eq.	rt	42	17	59
6	Li (50)	50 eq.	0 °C	21	11	32
7	Li (50)	50 eq.	reflux	33	6	39

* based on Ti

It is considered that tris(trimethylsilyl)amine (**10**) can not react with benzoyl chloride. In order to get all of the incorporated nitrogen, hydrolysis of the reaction products with 10% HCl was tried. The aqueous solution was made basic with K_2CO_3 and the benzene solution of benzoyl chloride was added. As a result, we obtained benzamide in 75% yield when Mg was used as a reducing agent. On the other hand, when Li was used as a reducing agent, benzamide was obtained in 243% yield based on the titanium (Scheme3).

Scheme 3



Using Li as a reducing agent, we examined the various forms of Li. Each form of Li [wire (243%), granular (250%), and powder (147%)] was an effective reducing agent. The reaction mechanism is not clear at present. Thus, the change in the amount of Li and TMSCl was examined. The results are shown in Table 2. In the absence of TMSCl, the desired product was not obtained and the use of 4 eq. of Li and 5 eq. of TMSCl did not afford the product (Table 2, runs 1 and 2). When 10 eq. of Li was used for this reaction, the desired product was obtained in 79% yield, and increasing the amount of Li raised the yield of the desired product.

Table 2 The effect of Li and Me_3SiCl

run	Li (eq.)	Me_3SiCl (eq.)	Yield (%)
1	4	–	–
2	4	5	–
3	10	10	79
4	10	50	83
5	20	20	142
6	30	30	202
7	50	50	250

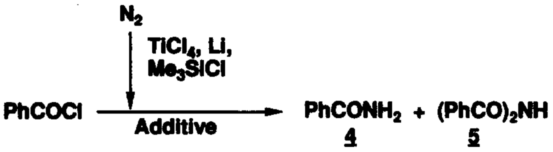
$Cl{-}Ti{=}N{-}SiMe_3$ **12a**

$Ti{=}N{-}SiMe_3$ **12b**

Shiina reported[4] the reductive silylation of molecular nitrogen *via* fixation to tris(trimethylsilyl)amine. He described that using $CrCl_3$ for the metal afforded 5.4 eq. mol. of tris(trimethylsilyl)amine (**10**) but $TiCl_4$ afforded only 0.8 eq. mol. of **10**. In our reaction, we obtained 250% of benzamide. Thus, other nitrogen sources, such as the titanium nitrogen complex **12a** or **12b**, should be produced.[5]

Next, in order to remove the silyl group from the product, various reagents were added. The results are shown in Table 3. The yield of the desired product was increased (Table 3, run 2) when CsF was used. However, other additives such as KF, KF•HF, and Me_3SiOTf were not effective for this reaction.

Table 3 Effect of additive



run	Additive (eq.)		Yields (%) **4**	**5**	Total
1	none		42	17	59
2	CsF	(10)	77	11	88
3	KF	(10)	37	17	54
4	KF•HF	(10)	39	–	39
5	Me_3SiOTf	(0.1)	22	15	37

On the basis of these results, the synthesis of the heterocycles using titanium catalyzed nitrogenation was tried (Scheme4). To a solution of the nitrogen fixation products prepared from TMSCl (10 eq.), $TiCl_4$ (1 eq.), and Li (10 eq.) in THF, phthalic anhydride (13) (3 eq.) was added and the solution was stirred at room temperature overnight. Hydrolysis with H_2O followed by the usual work up gave the desired phthalimide **14** in 23% yield (Table4, Run 1). When the reaction was carried out in the presence of 50 eq. of Li and TMSCl, the yield of **14** raised to 51%. It was very surprising that when the THF solution was refluxed overnight in the presence of CsF, the desired phthalimide (**14**) was obtained in 204% yield(Run 3). These results suggest that incorporation of molecular nitrogen into phthalic anhydride (**13**) can be achieved by titanium catalyzed nitrogenation.

Scheme 4

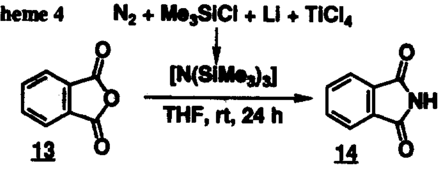


Table 4 Incorporation of N_2 into 13

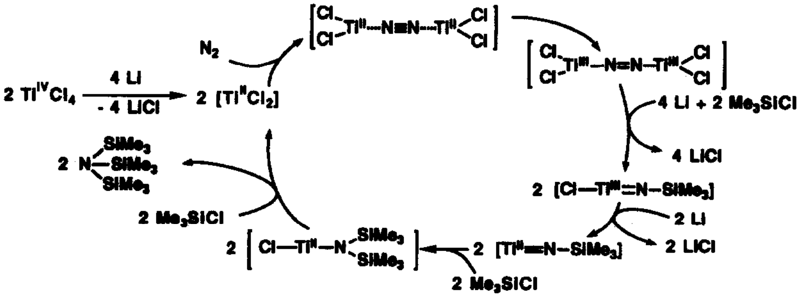
run	Li	Me_3SiCl	Additive	Yield
1	10 eq.	10 eq.	–	23%
2	50 eq.	50 eq.	–	51%
3	50 eq.	50 eq.	CsF	204%

The important characteristic of this reaction is as follows: The incorporation of molecular nitrogen proceeds using a catalytic amount of titanium in the presence of excess Li and TMSCl.[6] The procedure for the preparation of nitrogen fixation products [$(Me_3Si)_3N$, $Ti{=}NSiMe_3$ or others] from molecular nitrogen is easy. The incorporation of molecular nitrogen into an organic compound is realized by a catalytic amount of titanium in the presence of CsF in one pot. Further studies for the incorporation of molecular nitrogen into organic compounds are now in progress.

Acknowledgement: This work was supported by the Grant-in-Aid for Scientific Research on Priority Areas "Activation and Chemical Utilization of Molecular Nitrogen" (No. 04241101) from the Ministry of Education, Science and Culture, Japan.

REFERENCES AND NOTES

1. a) M. Mori, Y. Uozumi, and M. Shibasaki, *Tetrahedron Lett.*, **28**, 6187 (1987). M. Mori, Y. Uozumi, and M. Shibasaki, *J. Organometal. Chem.*, **395**, 255 (1990). b) Y. Uozumi, N. Kawasaki, E. Mori, M. Mori, and M. Shibasaki, *J. Am. Chem. Soc.*, **111**, 3725 (1989). Y. Uozumi, E. Mori, M. Mori, and M. Shibasaki, *J. Organometal. Chem.*, **399**, 93 (1990). c) Y. Uozumi, M. Mori, and M. Shibasaki, *J. Chem. Soc., Chem. Commun.*, **1991**, 81. M. Mori, Y. Uozumi, and M. Shibasaki, *Heterocycles*, **33**, 819 (1992).
2. A. Yamamoto, M. Ookawa, and S. Ikeda, *J. Chem.Soc., Chem. Commun.*, **1969**, 841. A. Yamamoto, S. Go, M. Ookawa, M. Takahashi, S. Ikeda, and T. Keii., *Bull. Chem. Soc. Jpn.*, **45**, 3110 (1972).
3. P. Sobota, B. Jezowska-Trzebiatowska and Z. Janas, *J. Organometal. Chem.*, **118**, 253 (1976).
4. K. Shiina, *J. Am. Chem. Soc.*, **94**, 9266 (1972).
5. The reaction mechanism was not clear. However, we considered the reaction course as follows.



6. Recently, Prof. Hidai reported the catalytic conversion of molecular nitrogen into silylamines using molybdenum and tungsten dinitrogen complexes in the presence of Na and TMSCl. K. Komori, H. Oshita, Y. Mizobe, and M. Hidai, *J. Am. Chem. Soc.*, **111**, 1939 (1989).

(Received in Japan 26 March 1993; accepted 12 July 1993)