

Some Recommended Procedures for Conversion of Carboxylic Acid and Its Derivatives to Aldehydes by Metal Hydride Reductions

Jin Soon Cha[†]

Abstract

Some recommended procedures for obtaining aldehydes from carboxylic acid itself and its derivatives, which have been developed in relatively recent years, are summarized. Such procedures should provide a new practical methodology to synthesize the desired aldehyde products in high yields.

Key word : Metal Hydride, Reduction, Aldehyde, Carboxylic Acid

1. Introduction

For more than fifty years, some hundreds chemists have been devoted their efforts to develop practical procedures for obtaining aldehydes. In this review the recommended procedures for synthesis of aldehydes from readily available carboxylic acids and their derivatives by reduction, developed by the author and collaborators, are summarized in item by carboxylic acid derivatives, such as carboxylic acid, carboxylic acid metal salt, acid chloride, ester, amide, and nitrile. As a result, these developments should provide a proper resolution to meet what chemists have been seeking for a long time.

The author has paid attention mainly to the developments published in the journals by the author and his collaborators.

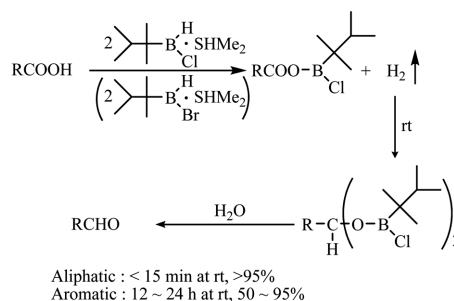
2. Conversion of Carboxylic Acid to Aldehyde

The most desirable method to get aldehydes must be the direct conversion of carboxylic acid itself, because they are abundant in nature. However, the reduction is quite resistant to usual reducing agents. The recommended procedures for the conversion of carboxylic acid itself to aldehyde are classified as follows: (i) a

direct partial reduction, (ii) a partial reduction through a reactive acyloxy-9-BBN, and (iii) a complete reduction to alkoxy moiety, and followed by partial oxidation.

The procedure for direct partial reduction involves the utilizing thexylhalo- or thexylalkoxyboranes-methyl sulfide (**ThxBHX·SMe₂**, X=Cl, Br, OR),^[1,2,5] as illustrated in Scheme 1 and 2. Generally, the yields of aromatic series are lower than those in the aliphatic series. Examining the results for the aromatic series more closely, a significant influence of substituents upon the yield appears to exist. However, in the case of aliphatic compounds, it appears that the yields of aldehydes are almost quantitative, with no observable dependence on the structure of the acid. Even the aliphatic dicarboxylic acids are reduced to the corresponding dialdehydes in essentially quantitative yields.

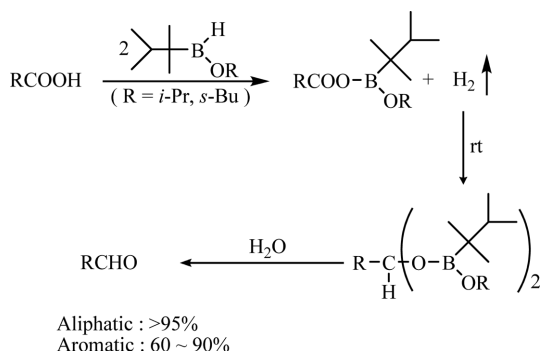
Especially, the ability for converting only aromatic carboxylic acids to the corresponding aldehydes selec-



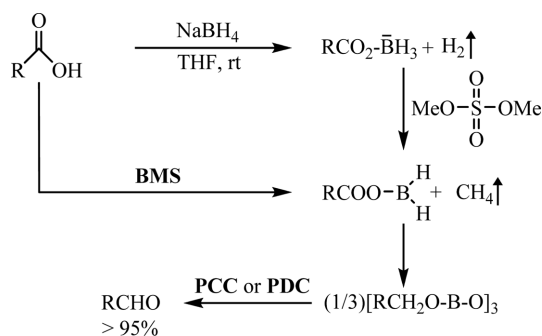
Scheme 1

Department of Chemistry, Yeungnam University, Gyongsan 712-749, Korea

[†]Corresponding author : jscha@yu.ac.kr
(Received : June 2, 2012, Revised : June 20, 2012,
Accepted : June 24, 2012)



Scheme 2

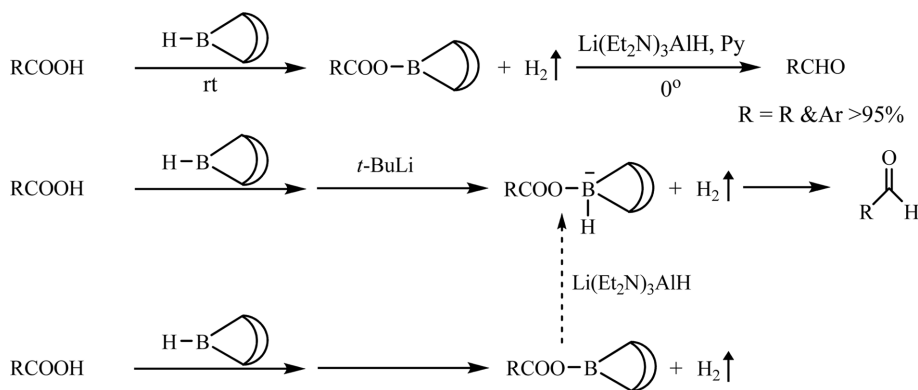


Scheme 5

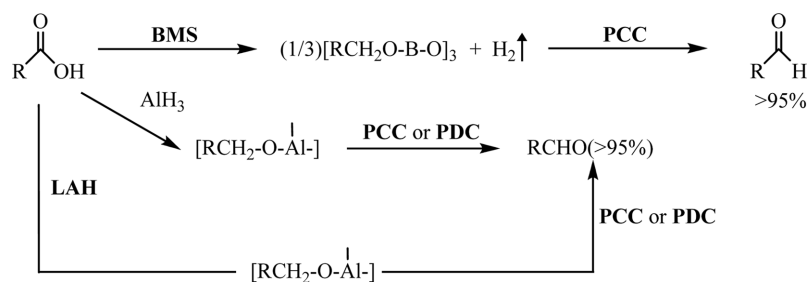
tively in the presence of aliphatic acids intact with hexylhalo- and hexylalkoxyboranes is noteworthy.

The recommended procedure for conversion of acyloxy group of acyloxy-9-BBN, a reactive intermediate, to aldehyde involves the partial reduction with lithium tri(diethylamino)aluminum hydride (LTDEA) in the presence of two equivalent of pyridine.^[15] In this case, when no pyridine is added, the yields decrease significantly to 60-70% (Scheme 3).

The stepwise reduction-oxidation procedure, involved the complete reduction of carboxylic acid to alkoxy moieties utilizing borane-methyl sulfide (BMS)^[16], aluminum hydride^[17] or lithium aluminum hydride (LAH)^[18] and oxidation with PCC or PDC, is also recommended (Scheme 4). Especially, the procedure utilizing sodium borohydride and dimethyl sulfate appears to be the best one, because of its mildness, easy handling and its low cost^[19] (Scheme 5).



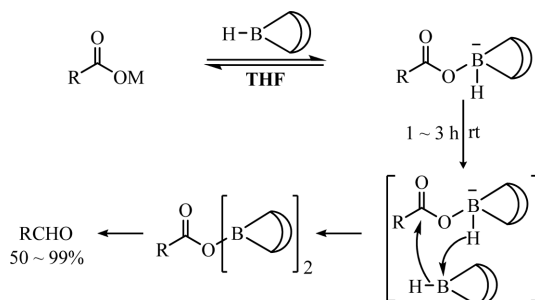
Scheme 3



Scheme 4

3. Conversion of Carboxylic Acid Metal Salts to Aldehyde

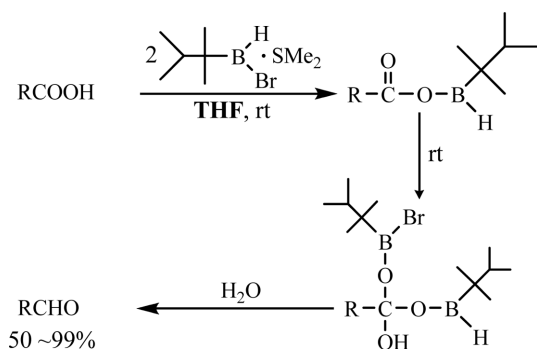
Depending on the structure of compounds applied, users can choose any one among the procedures developed: the procedures utilizing thexylbromoborane-methyl sulfide (**ThxBHBr·SMe₂**)^[3,4] (Scheme 6), **9-BBN**,^[20,21] (Scheme 7), or **BH₃** in **THF**^[22] (Scheme 8 and 9). However, the procedure depicted in Scheme 9 seems to be the most practical. The direct conversion of carboxylic acid metal salts to aldehydes illustrated in the following Schemes are the first examples appeared in the journals.



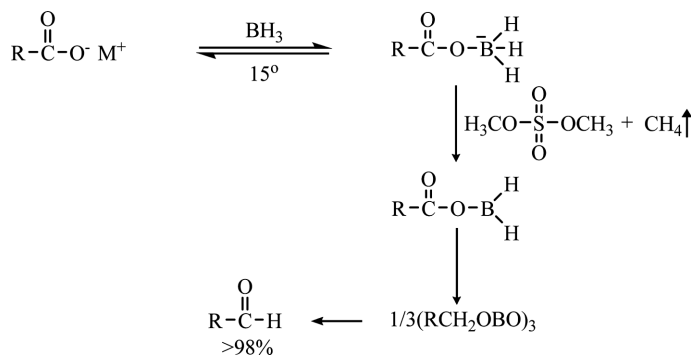
Scheme 7

4. Conversion of Acid Chloride to Aldehyde

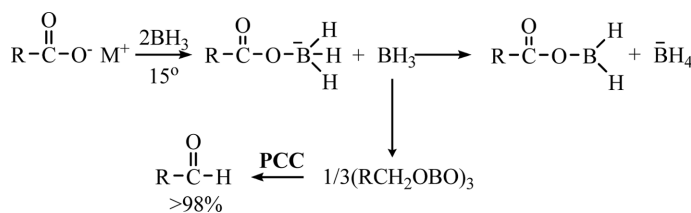
The recommended procedure for conversion of acid chloride to aldehyde is the direct reduction with sodium tri-*tert*-butoxyaluminumhydride (**STBA**)^[7] and thexylalkoxyborane (**ThxBHOR**, **R=*i*-Pr, *s*-Bu**)^[5] as depicted in Scheme 10. It is noteworthy that **STBA** is much useful than the lithium derivative, **LTBA** in terms of the easiness in handling of sodium aluminum hydride (**SAH**) than **LAH** and the much higher yield of aldehyde products. In addition to these, the stepwise reduction-oxidation procedures^[23,24] (particularly, utilizing sodium borohydride^[24]) are recommended (Scheme 11).



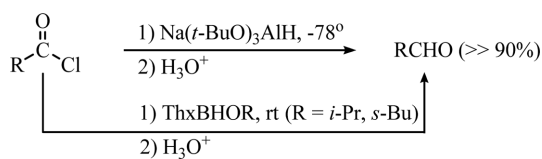
Scheme 6



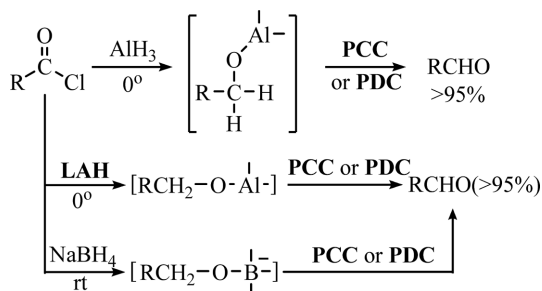
Scheme 8



Scheme 9



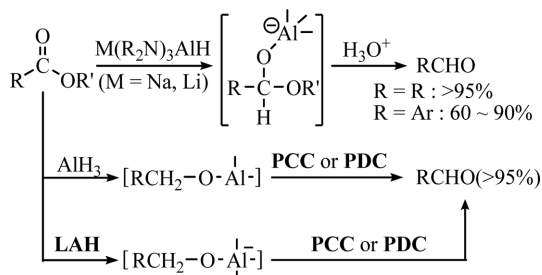
Scheme 10



Scheme 11

5. Conversion of Ester to Aldehyde

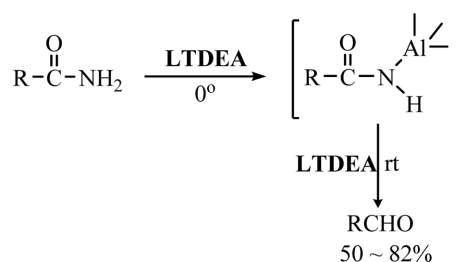
The direct reduction of esters with sodium^[12] and lithium^[13] tri(diethylamino)aluminum hydride (**STDEA** and **LTDEA**) produces aldehydes in good yields. Moreover, the stepwise reduction-oxidation procedures afford the corresponding aldehydes in higher than 95%^[25,26] (Scheme 12). There is no structural dependence of esters in yields of aldehydes.



Scheme 12.

6. Conversion of Primary Carboxamide to Aldehyde

There have appeared a number of reduction methods to convert tertiary amides to aldehydes in literature. However, the direct conversion of primary amides to aldehydes by reduction with **LTDEA** seems to be the

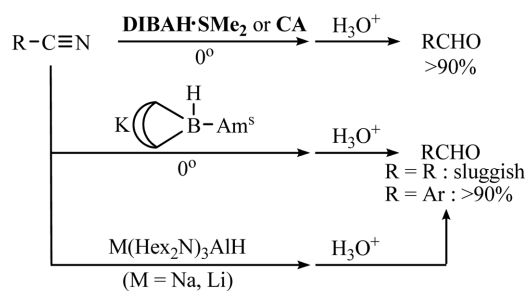


Scheme 13

first example.^[27] The yields are satisfactory (Scheme 13).

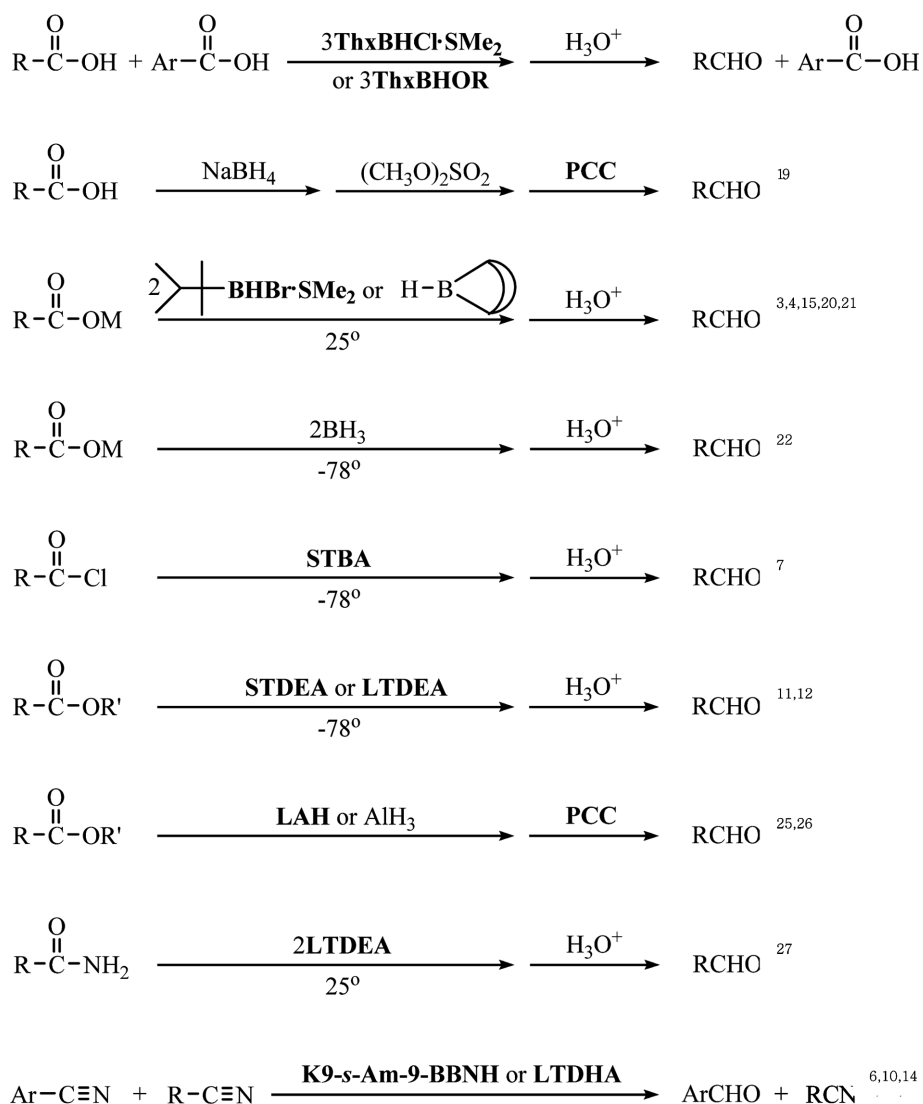
7. Conversion of Nitrile to Aldehyde

Diisobutylaluminum hydride-methyl sulfide (**DIBAH·SMe₂**)^[8] and catecholalane (**CA**)^[9] can convert both aliphatic and aromatic nitriles to the corresponding aldehydes in very high yields. Especially noteworthy is that a simple addition of dimethyl sulfate to the THF solution of diisobutylaluminum hydride changes dramatically the reducing characteristics of the original one of **DIBAH**. However, it is worthwhile to note that potassium 9-*sec*-amyl-9-**BBNH** (**K9-*s*-Am-9-BBNH**),^[6] sodium^[14] and lithium^[10] tri(diethylamino)aluminum hydrides (**STDEA** and **LTDEA**) achieve the selective conversion of aromatic nitriles to aldehydes in the presence of aliphatic nitriles unattacked (Scheme 14).



Scheme 14.

In Scheme 15, all the recommended procedures for conversion of carboxylic acids and their derivatives to aldehydes are summarized. Because each procedure possesses its own usefulness and limitation, users



Scheme 15.

should refer the original references before utilizing each procedure.

8. Concluding Remarks

It is evident that one of the most desirable goal of the chemists working in the field of conversion of organic functional groups is to develop a full scope of selective reducing agents which can transform selectively a particular functional group of concern while other functional groups being intact in a polyfunctionalized

complex molecule.

There have appeared a variety of reducing systems, which can possibly achieve a selective reduction of any organic functional group. However, it should be pointed out that in spite of their abundant choice in literature one should consider carefully which reagent satisfies one's purpose, because each reagent possesses its own limitation.

Besides, as growing the complexity of molecules which chemists are concerning, continuous efforts to develop new methods and new reagents providing a

very clean and selective conversion of particular organic functional group are demanding. In this respect, this review summarizing the recommended procedures for the conversion of carboxylic acid and its derivatives to the corresponding aldehydes should provide a valuable tool which will meet the users's purpose.

References

- [1] H. C. Brown, J. S. Cha, N. M. Yoon, and B. Nazer, "Selective reductions. 39. Partial reduction of carboxylic acids with thexylchloroborane-methyl sulfide. A direct and simple aldehyde synthesis", *J. Org. Chem.*, Vol. 52, p. 5400, 1987.
- [2] H. C. Brown, B. Nazer, J. S. Cha and J. A. Sikorski, "Selective reductions. 38. Reaction of thexylchloroborane-methyl sulfide complex in methylene chloride with selected organic compounds containing representative functional groups. Comparison of the reducing characteristics of thexylchloroborane, thexylborane, and diborane" *J. Org. Chem.*, Vol. 51, p. 5264, 1986.
- [3] J. S. Cha, J. E. Kim and K. W. Lee, "Facile reduction of saturated and unsaturated carboxylic acids and their salts to aldehydes by thexylbromoborane-dimethyl sulfide" *J. Org. Chem.*, Vol. 52, p. 5030, 1987.
- [4] J. S. Cha, K. W. Lee, M. S. Yoon and J. C. Lee, "Facile Reduction of Carboxylic Acid Salts to Aldehydes by Boron Hydrides Thexylbromoborane-Dimethyl Sulfide and 9-Borabicyclo [3.3.1]nonane", *Bull. Korean Chem. Soc.*, Vol. 9, p. 384, 1988.
- [5] J. S. Cha, S. W. Chang, J. M. Kim, O. O. Kwon and J. C. Lee, "Transformation of Carboxylic Esters to Aldehydes with Sodium Tris(diethylamino)aluminum Hydride", *Org. Prep. Proced. Int.*, Vol. 29, p. 665, 1997.
- [6] J. S. Cha, M. S. Yoon, Y. S. Kim and K. W. Lee, "A new class of stereoselective reducing agents, potassium 9-alkyl-9-boratabicyclo [3.3.1]nonanes", *Tetrahedron Lett.*, Vol. 29, p. 1069, 1988.
- [7] J. S. Cha and H. C. Brown, "Exceptionally facile reduction of acid chlorides to aldehydes by sodium tri-tert-butoxyaluminumhydride" *J. Org. Chem.*, Vol. 58, p. 4732, 1993.
- [8] J. S. Cha, O. O. Kwon, M. K. Jeoung and E. J. Kim, "Conversion of Nitriles into Aldehydes by Diisobutylaluminum Hydride-Dimethyl Sulfide Complex", *Bull. Korean Chem. Soc.*, Vol. 15, p. 1021, 1994.
- [9] J. S. Cha, S. W. Chang, O. O. Kwon and J. M. Kim, "Partial reduction of nitriles of aldehydes by catecholalane(1,3,2-Benzodioxaluminole)", *Synlett*, Vol. 165, 1996.
- [10] J. S. Cha, S. E. Lee and H. S. Lee, "Transformation of Carboxylic Esters to Aldehydes by Lithium Tris(diethylamino)aluminum Hydride", *Org. Prep. Proced. Int.*, Vol. 24, p. 331, 1992.
- [11] J. S. Cha, M. K. Jeoung, J. M. Kim, O. O. Kwon, K. D. Lee and E. J. Kim, "Reaction of Sodium Tris(diethylamino)aluminum Hydride with Selected Organic Compounds Containing Representative Functional Groups", *Bull. Korean Chem. Soc.*, Vol. 15, p. 881, 1994.
- [12] J. S. Cha, J. M. Kim, M. K. Jeoung, O. O. Kwon and E. J. Kim, "Transformation of Carboxylic Esters to Aldehydes with Sodium Tris(diethylamino)aluminum Hydride", *Org. Prep. Proced. Int.*, Vol. 27, p. 95, 1995.
- [13] J. S. Cha, J. M. Kim and M. K. Jeoung, "Transformation of Primary Carboxamides to Aldehydes by Sodium Tris(dialkylamino)aluminum Hydrides", *Bull. Korean Chem. Soc.*, Vol. 15, p. 708, 1994.
- [14] J. S. Cha, M. K. Jeoung, J. M. Kim, O. O. Kwon and J. C. Lee, "Conversion of Aromatic Nitriles to Aldehydes by Sodium Tris(dialkylamino)aluminum Hydrides", *Org. Prep. Proced. Int.*, Vol. 26, p. 583, 1994.
- [15] J. S. Cha, J. C. Lee, H. S. Lee and S. E. Lee, "Transformation of Carboxylic Esters to Aldehydes by Lithium Tris(diethylamino)aluminum Hydride", *Org. Prep. Proced. Int.*, Vol. 24, p. 285, 1992.
- [16] H. C. Brown, S. V. Kulkarni and C. G. Rao, "Facile Oxidation of Trialkyl Borates to Aldehydes and Ketones with Pyridinium Chlorochromate. A Remarkable Oxidizability of Such Borate Esters as Compared to Acetates", *Synthesis*, Vol. 702, 1979.
- [17] J. S. Cha, M. G. Kim, J. M. Kim, O. O. Kwon, J. H. Chun and S. D. Cho, "Conversion of Alcohols to Aldehydes and Ketones by Oxidation of Trialkoxyaluminum with Pyridinium Chlorochromate", *Bull. Korean Chem. Soc.*, Vol. 19, p. 724, 1998.
- [18] J. S. Cha, J. M. Kim, J. H. Chun, O. O. Kwon and J. C. Lee, "Conversion of Carboxylic Acids into Aldehydes by Oxidation of Alkoxyaluminum Intermediate with Pyridinium Chlorochromate or Pyridinium Dichromate", *Bull. Korean Chem. Soc.*, Vol. 19, p. 730, 1998.
- [19] J. S. Cha, D. Y. Lee and J. M. Kim, "Reductive Oxidation of Carboxylic Acids to Aldehydes with Sodium Borohydride and Pyridinium Chlorochromate"

- mate”, *Org. Prep. Proced. Int.*, Vol. 31, p. 694, 1999.
- [20] J. S. Cha, S. Y. Oh, K. W. Lee, M. S. Yoon and J. C. Lee, “Exceptionally Facile Reduction of Carboxylic Acid Salts to Aldehydes by 9-Borabicyclo[3.3.1]nonane”, *Heterocycles*, Vol. 27, p. 1595, 1988.
- [21] J. S. Cha, K. W. Lee, M. S. Yoon and J. C. Lee, “Facile Reduction of Carboxylic Acid Salts to Aldehydes by Boron Hydrides Thexylbromoborane-Dimethyl Sulfide and 9-Borabicyclo [3.3.1]nonane”, *Bull. Korean Chem. Soc.*, Vol. 9, p. 384, 1988.
- [22] J. S. Cha, J. H. Park and S. J. Moon, “Transformation of Carboxylic Acid Salts to Aldehydes by Stepwise Reduction with Borane and Oxidation with Pyridinium Chlorochromate”, *Bull. Korean Chem. Soc.*, Vol. 22, p. 1089, 2001.
- [23] J. S. Cha, J. M. Kim, J. H. Chun, O. O. Kwon, S. Y. Kwon and S. W. Han, “Conversion of Acid Chlorides to Aldehydes by Oxidation of Alkoxyaluminum Intermediate with Pyridinium Chlorochromate and Pyridinium Dichromate”, *Org. Prep. Proced. Int.*, Vol.31, p.204, 1999.
- [24] J. S. Cha and D. Y. Lee, “Reductive Oxidation of Acid Chlorides to Aldehydes with Sodium Borohydride and Pyridinium Chlorochromate”, *Bull. Korean Chem. Soc.*, Vol.21, p.1260, 2000.
- [25] J. S. Cha, J. M. Kim, J. H. Chun, O. O. Kwon, S. Y. Kwon and S. D. Cho, “Convenient Conversion of Carboxylic Esters to Aldehydes by Oxidation of Alkoxyaluminum Intermediate with Pyridinium Chlorochromate or Pyridinium Dichromate”, *Bull. Korean Chem. Soc.*, Vol. 19, p. 1301, 1998.
- [26] J. S. Cha, J. H. Chun, J. M. Kim, D. Y. Lee and S. D. Cho, “Preparation of Aldehydes from Carboxylic Esters by Reductive Oxidation”, *Bull. Korean Chem. Soc.*, Vol. 20, p. 1373, 1999.
- [27] J. S. Cha, S. E. Lee, H. S. Lee, J. C. Lee, J. M. Kim, O. O. Kwon and S. J. Min, “Selective Reduction by Lithium Bis- or Tris(dialkylamino)aluminum Hydrides. VI. One-Pot Conversion of Primary Carboxamides into Aldehydes via Stepwise Treatment with Diisobutylaluminum Hydride and Lithium Tris(diethylamino)aluminum Hydride”, *Bull. Korean Chem. Soc.*, Vol. 13, p. 338, 1992.