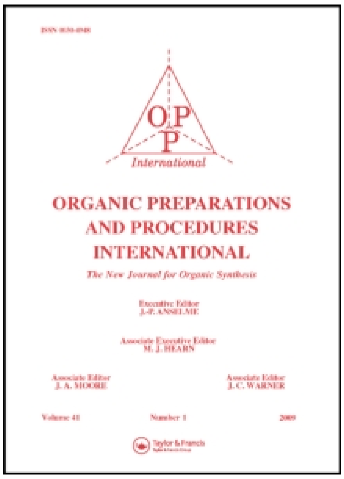


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

RECENT DEVELOPMENTS IN THE SYNTHESIS OF ALDEHYDES BY REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES WITH METAL HYDRIDES. A REVIEW

Jin Soon Cha[a]
[a] Department of Chemistry, Yeungnam University, Gyongsan, KOREA

To cite this Article Cha, Jin Soon(1989) 'RECENT DEVELOPMENTS IN THE SYNTHESIS OF ALDEHYDES BY REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES WITH METAL HYDRIDES. A REVIEW', Organic Preparations and Procedures International, 21: 4, 451 — 477

To link to this Article: DOI: 10.1080/00304948909356413

URL: http://dx.doi.org/10.1080/00304948909356413

ORGANIC PREPARATIONS AND PROCEDURES INT. 21(4), 451-477 (1989)

RECENT DEVELOPMENTS IN THE SYNTHESIS OF ALDEHYDES BY REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES WITH METAL HYDRIDES. A REVIEW

Jin Soon Cha

Department of Chemistry
Yeungnam University
Gyongsan 713-749, KOREA

RECENT DEVELOPMENTS IN THE SYNTHESIS OF ALDEHYDES BY REDUCTION OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES WITH METAL HYDRIDES. A REVIEW

Jin Soon Cha

Department of Chemistry
Yeungnam University
Gyongsan 713-749, KOREA

INTRODUCTION

The development of simple synthetic routes to aldehydes from readily available carboxylic acids and their derivatives is an important goal in organic chemistry. During the past 70 years, numerous efforts have been made to find simple and general synthetic routes to aldehydes.[1] Accordingly, many useful reducing agents have been developed and considerable success has been achieved in obtaining high transformations in this reduction process. This review attempts to cover all efforts paid to find reduction procedures from carboxylic acids and their derivatives to aldehydes. We have attempted to organize all the literature references in chronological order. Useful methods which have found widespread application in recent organic synthesis are emphasized.

I. REDUCTION OF CARBOXYLIC ACID DERIVATIVES TO ALDEHYDES

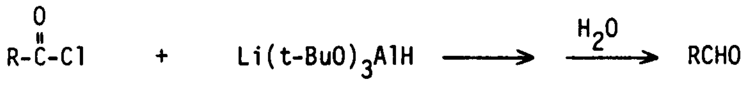
1. Brief Survey of the Older Methods

The oldest reduction method for preparation of aldehydes from carboxylic acid derivatives originated from Sonn and Müller in 1919.[2] This reaction involved the reduction of imido chlorides, derived themselves from acid anilides, with stannous chloride and the subsequent hydrolysis of the resultant imines to provide aldehydes. The Stephen reduction for the conversion of nitriles to aldehydes with stannous chloride[2,3] can be considered in the same class of reduction. Reductive desulfuration of thiol esters, prepared easily from acid chlorides, with Raney nickel[2,4] is also one of the ingeniously devised older methods. These reactions had been the recommended procedures until Friedman observed that the controlled reduction of nitriles and amides by lithium aluminum hydride (LAH) provides a convenient synthetic route.[2,5] Although he has not reported any detailed procedure of the LAH reduction, a number of authors have subsequently applied it with success to the partial reduction of various carboxylic acid derivatives using a limiting amount of LAH. However, in spite of its convenience LAH suffers from its own limitation due to its exceedingly powerful reducing characteristics. Consequently, it is quite difficult to apply this reagent for such transformation of a multifunctional molecule. Thereafter, extensive study on complex metal hydrides, involving the modification of parent complex hydrides and the exploration of new reducing systems, has proceeded for such transformations.

2. Acid Chlorides to Aldehydes

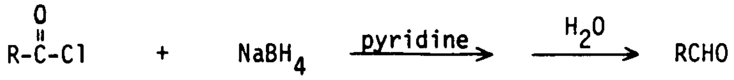
Until the 1950's, the Rosenmund reduction, which involves the hydrogenation of an acid chloride in the presence of a suitable catalyst, usually supported palladium, had been considered as the most useful method for transformation of acid chlorides into aldehydes.[6,7] The original Rosenmund reduction suffers from two series disadvantages: the difficulty of reproducing the precise poisoning of the catalyst to obtain good yields, and the sensitivity of some substituents to the hydrogenation conditions. However, several modified methods seem to overcome these difficulties to some extent.[7-20]

In the course of modifying the reducing characteristics of LAH, Brown and coworkers found lithium tri-t-butoxyaluminohydride (LTBA) provides a convenient synthetic route to aldehydes from acid chlorides in good yields.[21-24] Because of its simplicity and mildness, LTBA has been used



$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}Cl \quad + \quad Li(t\text{-}BuO)_3AlH \longrightarrow \xrightarrow{H_2O} RCHO$$

widely for such purposes. Sodium borohydride (SBH), which possesses advantages including ease of handling and low cost, has also been investigated extensively. SBH itself can not stop at the aldehyde stage in the reduction of acid chlorides under the usual conditions.[25] Several modified reaction conditions including the use of polar solvents such as N,N-dimethylformamide (DMF)[26] or the prevention of overreduction by pyridine as a borane scavenger,[27] have been introduced. A polymer-supported borohydride also



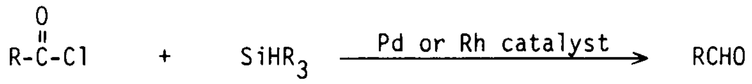
$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}Cl \quad + \quad NaBH_4 \xrightarrow{\text{pyridine}} \xrightarrow{H_2O} RCHO$$

effected such transformations.[28]

The application of several transition metal borohydrides for the partial reduction of acid chlorides has been studied. Especially complex copper borohydrides,[29,30] complex copper cyanoborohydrides,[31] and polymer-supported complex copper borohydrides[32] have been demonstrated to provide good yields of aldehydes. The Cu^+, Cu^{2+}, Cd^{2+}, or Zn^{2+}-moderated borohydride reduction of acid chlorides in suitable solvents, such as DMF, acetonitrile, or hexamethylphosphoramide (HMPA), have appeared to be effective for synthesis of the corresponding aldehydes.[33-35]

Anionic transition metal reductants, such as $Fe(CO)_4^{2-}$,[36-38] $HFe(CO)_4^-$,[39] $CpV(CO)_3H^-$,[40] $HCr(CO)_5^-$,[41] and $HW(CO)_5^-$,[41] have also been shown to be useful for such transformations. These methods employ relatively mild conditions and offer high yields (usually more than 80% both for aromatic and aliphatic derivatives). The attractive advantage of these methods is that the reagents can be regenerated from inexpensive starting materials. The polymer-supported $HFe(CO)_4^-$ anion can also reduce acid chlorides under mild conditions and the system provides a simple work-up procedure of the reduction product.[42]

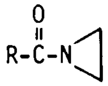
The transformation of acyl chlorides to aldehydes has also been achieved with tributyltin hydride catalyzed by zero- or divalent palladium complexes and the yields of aldehydes are satisfactory.[43-48] Organosilicon hydrides have been reported to react with acid chlorides in the presence of catalyst at elevated temperature to give aldehydes. However, in the case of the catalyzed reaction by rhodium complexes the product has been found to be usually a mixture of comparable amounts of aldehyde and ketone, the ratio being largely dependent upon the ligand of complexes and the nature of compounds.[49-51]



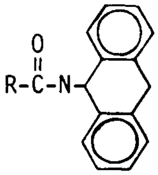
$$R\text{-}\overset{\overset{\large O}{\|}}{C}\text{-}Cl \quad + \quad SiHR_3 \xrightarrow{\text{Pd or Rh catalyst}} RCHO$$

3. Amides to Aldehydes

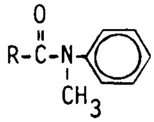
Since Friedman observed that LAH may be utilized for the partial reduction of amides to aldehydes in 1949,[5] a number of authors have subsequently applied it to the preparation of a variety of aldehydes. The most successful development has involved the selective reductions of N,N-disubstituted carboxamides such as 1-acylaziridines 1,[52] 1-acylcarbazoles 2,[53] N-methylanilides



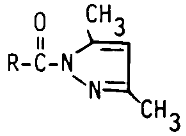
1



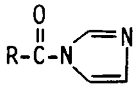
2



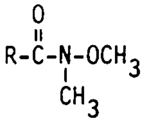
3



4



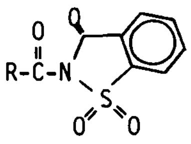
5



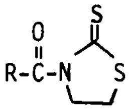
$$R\text{-}\overset{\overset{\large O}{\|}}{C}\text{-}\underset{\underset{\large CH_3}{|}}{N}\text{-}OCH_3$$

6

3,[54-58] 1-acyl-3,5-dimethylpyrazoles 4,[59,60] 1-acylimidazoles 5,[61] and N-methoxy-N-methylamides 6.[62] Such success seems due to the electronic effect of the substituent in reducing resonance interactions between the amide nitrogen and the carbonyl group. The reduction of N-methylanilides and N-acyl saccharins 7 with sodium bis(2-methoxyethoxy)aluminohydride (SDA),[63,64] and of 3-acylthiazolidine-2-thione 8 with diisobutylaluminum hydride (DIBAH)[65], SBH,[65a] or LTBA,[65c] have also been reported to be useful methods

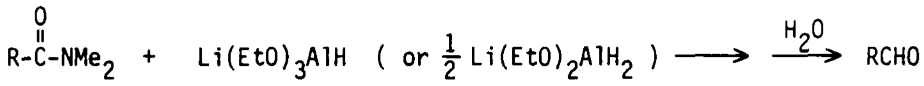


7



8

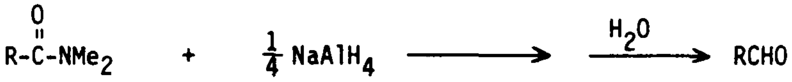
for preparation of aldehydes. Brown and Tsukamoto found that lithium triethoxyaluminohydride reduces N,N-dimethylamides to the corresponding aldehydes in ether solution at 0°C in yields of seventy to 90%.[66] The procedure appears to be equally satisfactory for aliphatic, alicyclic and aromatic derivatives, with the exception of conjugated ones. The diethoxyaluminohydride in a limiting amount has also been found to provide similar results.[66,67]



$$R\text{-}\overset{O}{\overset{\|}{C}}\text{-}NMe_2 \;+\; Li(EtO)_3AlH \;\left(\text{ or } \tfrac{1}{2}\,Li(EtO)_2AlH_2\right) \longrightarrow \xrightarrow{H_2O} RCHO$$

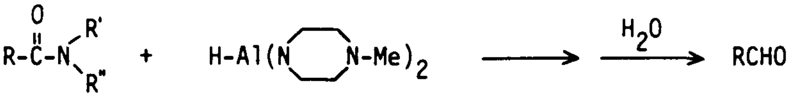
While DIBAH and sodium diisobutylaluminum hydride have proved to be useful reagents for transformation of nitriles[101] and esters[68b,71] into aldehydes, both have been appeared less than effective for conversion of amides to aldehydes.[68] However, the selective reduction of N,N-disubstituted amides by sodium aluminum hydride (SAH) and sodium alkoxyaluminohydrides has proved a useful route to the corresponding aldehydes.[69] Especially SAH has reduced dimethylamides of aliphatic, aromatic and heterocyclic acids of widely varying structural types to aldehydes in yields from

70-90%. Diaminoaluminum hydrides, especially bis(4-methyl-1-piperazinyl)



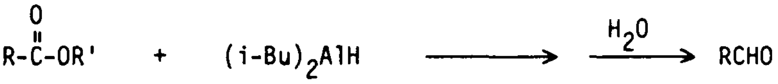
$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}NMe_2} \quad + \quad \frac{1}{4}\,\mathrm{NaAlH_4} \longrightarrow \xrightarrow{H_2O} \mathrm{RCHO}$$

aluminum hydride (BMPA), have also proved to be useful reagents in a new preparative method for aldehydes from the corresponding carboxamides.[70]



4. Esters to Aldehydes

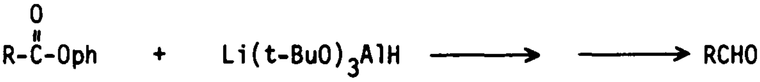
The conversion of carboxylic esters to aldehydes originated from Zakharkin and coworkers. They utilized commercially available DIBAH on the reduction of various aliphatic and aromatic esters at low temperature (about $-70^{o}C$).[71] The yields of aldehydes are very high. This procedure has found widespread application to the selective reduction of the ester function.



$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}OR'} \quad + \quad \mathrm{(i\text{-}Bu)_2AlH} \longrightarrow \xrightarrow{H_2O} \mathrm{RCHO}$$

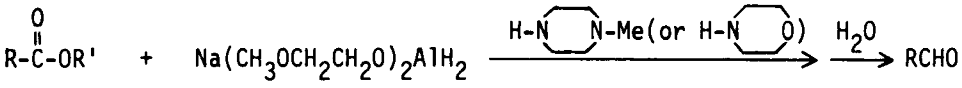
Sodium diisobutylaluminohydride as well has been successfully applied.[68b] Variation of cations in metal aluminum hydride using lithium, sodium, or potassium has also been examined.[72] Among these, the sodium derivative has achieved the most satisfactory result for such transformation at low temperature.

LTBA readily reacts with phenyl esters of aliphatic carboxylic acids at $0^{o}C$, forming the corresponding aldehydes in yields of approximately 70%.[73] Brown and Weissman noted that the mildness of the reagent is particularly

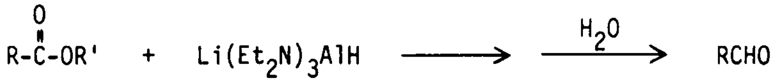


$$\mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}Oph} \quad + \quad \mathrm{Li(t\text{-}BuO)_3AlH} \longrightarrow \longrightarrow \mathrm{RCHO}$$

advantageous in cases where the molecule contains other readily reducible functional groups. Muraki and Mukaiyama have successfully applied various diaminoaluminum hydrides to the partial reduction of carboxylic esters.[74] BMPA was found to be the most effective in the series of aluminum reagents. Kanazawa and Tokoroyama modified the SDA solution by the addition of one equivalent of N-methylpiperazine or morpholine, which affords an excellent reagent for the partial reduction of esters to aldehydes in even better yields than diaminoaluminum hydrides.[75] Very recently, Cha and coworkers



developed a new class of reducing agents, lithium tris(dialkylamino)aluminum hydrides, prepared from the reaction of LAH with three equivalents of the corresponding dialkylamines. Preliminary experiments on the reducing characteristics of lithium tris(diethylamino)aluminum hydride (LTDEA), one of the class of reducing agents, revealed that the reagent effects the desired transformation, showing sixty to 90% yields at -78°C.[76] The extensive investigation of this kind of reagent for such purposes is progressing.



$$R\overset{O}{\overset{\|}{C}}OR' + Li(Et_2N)_3AlH \longrightarrow \xrightarrow{H_2O} RCHO$$

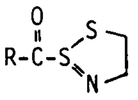
Hydrogenation of carboxylic esters using yttrium oxide or zirconium oxide catalyst seems to provide a highly effective transformation into aldehydes, although full experimental details are lacking.[77]

5. Lactones to Lactols

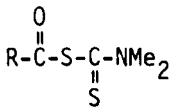
Sodium amalgam[78] was the sole reagent for the partial reduction of lactones until Wolfrom and Wood used SBH to replace it in the classical partial reduction of sugar lactones.[79] Arth first utilized LAH successfully to reduce lactones to aldehydes.[80] SAH also reduces δ-valerolactone to ω-hydroxyvareraldehyde at -45°C in a yield of 75%.[72] Although the systematic study of such partial reductions with DIBAH has not yet been carried out, some successful applications of the reagent for the selective reduction of lactone function in the course of total syntheses of natural products have been found.[81-85] Bis-3-methyl-2-butylborane (disiamylborane, Sia_2BH) also have proved to be a useful reagent.[86,87] The relatively rapid reaction of Sia_2BH with lactones provides a convenient entry to the corresponding hydroxyaldehydes. A considerable number of interesting applications of the reagent for this purpose have been described.[88] SDA in the presence of one equivalent of absolute ethanol has effected such purpose; it smoothly reduces lactones selectively at 0°C to afford the corresponding lactols in good yields.[75]

6. Thioesters to Aldehydes

Thioesters derived from carboxylic acids have proved to be facile derivatives being satisfactorily converted to aldehydes by simple reduction procedures. Wolfrom and Karabinos initiated this reductive desulfurization method using Raney nickel.[1,3,89] The yields are generally in the range of fifty to 80%. 2-Thiazoline-2-thiol esters 9[90] or carboxylic dimethyldithiocarbamic anhydrides 10[91] have also been converted to aldehydes by treatment with DIBAH in yields of sixty to 90%. The thioacid salt function in an N-acylated 6-aminothiopenicillanic acid salt has been subjected to reductive desulfurization with Raney nickel in a homogeneous combination of THF, acetic acid, and N,N'-diphenylethylenediamine, which served to trap the nascent aldehyde through formation of the imidazolidine derivative.[92] The yields of the corresponding penicillin aldehydes, produced upon the con-



9



$R-\overset{O}{\overset{\|}{C}}-S-\underset{\underset{S}{\|}}{C}-NMe_2$

10

trolled hydrolysis, are approximately 50%.

7. Anhydrides to Aldehydes

One of two acyl groups in anhydrides has been converted selectively to the aldehyde stage. Selective hydrogenation has been applied to this conversion; however, the reaction has appeared synthetically of no practical use because of low yields and drastic conditions.[93] The first successful example achieved using disodium tetracarbonylferrate.[94] The reagent has converted acid anhydrides to aldehydes and carboxylic acids, or aldehydic acids in the case of cyclic anhydrides, in good yields. Thexylchloroborane-dimethyl sulfide ($ThxBHCl{\cdot}SMe_2$) has also revealed the possibility of producing aldehydes or aldehydic alcohols from acid anhydrides.[95] Preliminary experiments confirmed the formation of acetaldehyde from the reaction of acetic anhydride with the reagent in a yield of more than 80%. However, any systematic study has not been carried out yet.

8. Nitriles to Aldehydes

Transformation from organic nitriles to aldehydes generally takes the form of partial reduction of the nitrile to an aldimine 11 followed by hydrolysis to give the aldehyde.[1,96] One of the oldest variations of this attractive synthetic route is the Stephen reaction reported in 1925.[2,3] While it is usually satisfactory for aromatic nitriles, it has proved less than satisfactory and undependable for aliphatic derivatives.[2,97]

$$R\text{-}C{\equiv}N \longrightarrow \underset{\underline{11}}{RCH{=}NR'} \longrightarrow RCHO$$

LAH has generally not been applicable to the partial reduction of nitriles even under controlled conditions with a limiting amount of hydride at low temperature.[98] However, several modified aluminum hydrides have been used successfully. Sodium triethoxyaluminohydride converts various aromatic nitriles to aldehydes, but this procedure is not applicable to the selective reduction of aliphatic nitriles.[99] Lithium triethoxyaluminohydride, however, has appeared to be an excellent reagent both for aliphatic and aromatic nitriles.[100] DIBAH also can be used successfully for such conversion.[101] Although sodium dialkylaluminohydrides such as sodium diisobutylaluminohydride[68b] and sodium diethylaluminohydride[102] have not been applied satisfactorily for the partial reduction, the addition of a bulky Lewis acid seems to control the overreduction by means of adduct formation with the nitrile. For example, sodium diethylaluminohydride in the presence of 2,6-di-t-butylphenoxydiethylaluminum reduces various aliphatic and aromatic derivatives to aldehydes in high yields.[102]

Hydrogenation procedures with Raney nickel in an acidic medium are complicated with further reduction.[103] Improved yields have been reported by conducting the reduction in the presence of hydrazine,[104] phenylhydrazine,[105] or semicarbazide,[106,107] which removes the aldehyde from further reaction, but subsequent liberation of the aldehyde from the product presents difficulties. However, the recent developments for regeneration of aldehyde products from oximes and hydrazones using thallium(III) nitrate[108] or cetyltrimethylammonium permanganate[109] may overcome this drawback. A procedure involving the liberation of hydrogen with Raney nickel in the presence of sodium hypophosphite in aqueous acetec acid has conducted the conversion of aromatic nitriles to aldehydes in good yields; however, the yields for hindered nitriles such as o- and p-toluonitriles and α-naphthonitrile are less than 40%.[110] Finally, a modified method involving Raney alloy in 75% aqueous formic acid in reflux has succeeded in converting nitriles, including hindered ones, to the corresponding aldehydes in good yields.[111] However, the yields of aldehydes are largely dependent upon the reaction conditions.

A two-step procedure for the partial reduction of nitriles, in which the nitrile function is activated with a Lewis acid or through N-alkylation of the nitrile to N-alkylnitrium ion 12 followed by reduction with organosilicon hydride, has been reported by Fry.[112] This approach has proved to be effective, especially for the selective reduction of the nitrile function in polyfunctional substrates.

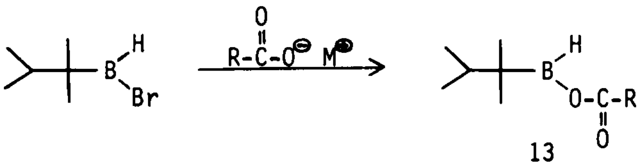
$$\text{R-C}{\equiv}\text{N} \longrightarrow \text{RCH}\overset{+}{\equiv}\text{NR}'\ \text{X}^- \xrightarrow{\text{Et}_3\text{SiH}} \text{RCH=NR}' \longrightarrow \text{RCHO}$$

12

Very recently, a systematic study on the partial reduction of nitriles to aldehydes with thexylbromoborane-dimethyl sulfide (2,3-dimethyl-2-butylbromoborane-dimethyl sulfide, ThxBHBr•SMe_2) under practical conditions has been carried out.[113] The yields of aldehydes are good in the aliphatic series, while the yields of aromatic series vary with the substituents. Grignard reaction of nitriles in the presence of titanocene dichloride also provides aldehydes in fifty-two to 68% yields.[114]

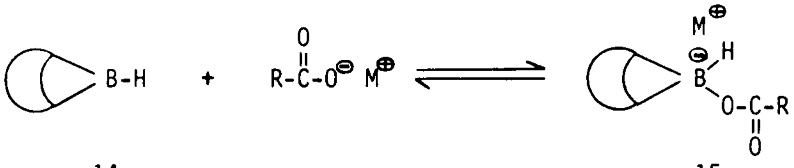
9. Acid Salts to Aldehydes

The first development for conversion of sodium and lithium carboxylates to aldehydes has been achieved by using ThxBHBr•SMe_2 at room temperature in high yields.[115] The facile reduction is due to the simple substitution for bromine by carboxylate to form thexyl(acyloxy)borane 13, the acyloxy group



13

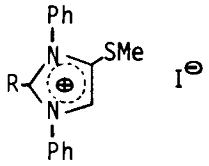
of which is then readily reduced to an aldehyde by another equivalent of the reagent. The carboxylates have also been readily converted to aldehydes by treatment with two equivalents of 9-borabicyclo[3.3.1]nonane (9-BBN, 14).[116] The reaction is believed to form an addition compound 15, the acyloxy moiety of which is subsequently reduced to the aldehyde stage in the presence of another equivalent of 14.



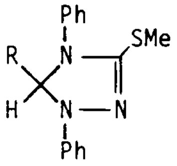
14 15

10. Miscellaneous

A number of miscellaneous useful methods for preparation of aldehydes from carboxylic acid derivatives, through formation of suitable intermediates followed by reduction, have been published. Daleschall has converted various acid chlorides to aldehydes via s-triazolium salts 16, which are reduced with SBH or LAH to the corresponding s-triazolines 17 followed by hydrolysis.[117] Carboxylic acids have been converted to aldehydes through formation

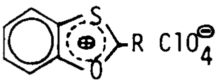


16

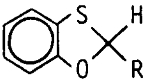


17

of 2-substituted 1,3-benzoxathiolium perchlorates 18. The intermediates are reduced with LAH to the corresponding 2-substituted 1,3-benzoxathiole derivatives 19, which then produce aldehydes upon hydrolysis. Although this method is effective both for a variety of aliphatic and aromatic carboxylic acids in over-all yields of sixty to 90%, it suffers from the multi-step proce-

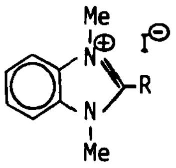


18

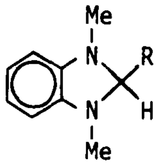


19

dure.[118] Similarly, Craig and coworker have achieved such transformation through formation of the quaternary 1,3-dimethylbenzimidazolium salts 20 and subsequent reduction to 21 with SBH or LAH, followed by hydrolysis.[119]

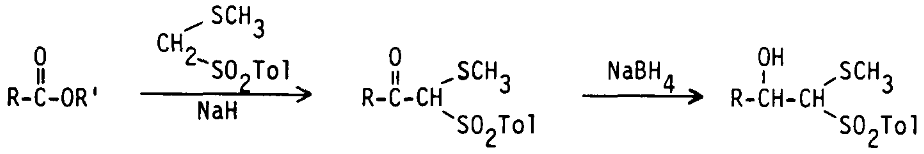


20



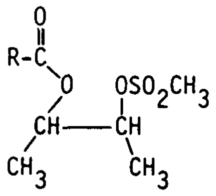
21

Ogura and coworkers have devised a method utilizing formation and dissociation of a C-C bond at the acyl carbon by employment of methylthiomethyl p-tolyl sulfone to form the acylated derivatives 22. The intermediates are then reduced to the corresponding alcohols 23 by SBH, followed by base catalyzed degradation to aldehydes.[120] Acyldiethylphosphonates, prepared from

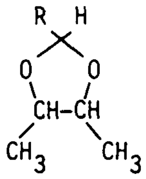


22 23

the corresponding acid chlorides and triethylphosphate, have proved to be converted readily to aldehydes by SBH.[121] The yields of aldehydes are high. The reduction of ester-mesylate intermediates 24 with SBH simply leads to formation of the acetal 25, which then readily provides aldehydes upon hydrolysis.[122] The reductive desulfuration of thiobenzanilides with Raney nickel is one of the classical methods.[123]



24



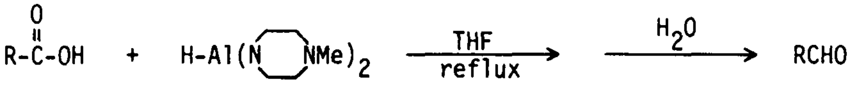
25

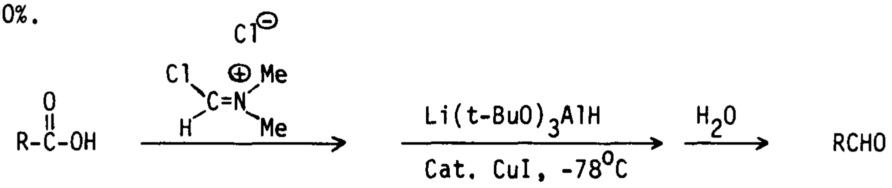
II. DIRECT REDUCTION OF CARBOXYLIC ACIDS TO ALDEHYDES

Although a number of methods have appeared to be widely applicable method to get aldehydes from carboxylic acid derivatives, the most desirable method seems to be a direct conversion of free carboxylic acids to aldehydes because of their abundance in nature.

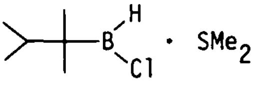
Apparently the first achievement in the direct transformation of carboxylic acid into aldehydes was reported by Burgstahler and Worden in 1961, in which dehydroabietic acid was reduced by lithium metal in ethylamine followed by hydrolysis to provide Δ^8-abietanal in a yield of 80%.[124] They promptly applied this interesting result to a number of other aliphatic carboxylic acids.[125] However, the yields of aldehydes were much lower. A decade later, Bedenbaugh, Bergin and Adkins developed this reaction as a general synthetic route to aliphatic aldehydes; they utilized methylamine instead of ethylamine and isolated imines to afford aldehydes upon hydrolysis.[126] The yields of aldehydes from saturated acids are approximately 60%. In 1964, Zakharkin and Khorlina utilized DIBAH, which had been successfully applied for the reduction of esters[71] and nitriles[101] to aldehydes, in the conversion of free acids to aldehydes at -70 to -75°C. The yields of aldehydes obtained were forty to 70% at that temperature; however, on raising the reaction temperature to -60°C the yields droped to less than 30%, showing the strong dependence on reaction temperature.[127]

Brown, Heim and Yoon initiated the use of substituted boranes on the partial reduction of free carboxylic acids.[128] Excess thexylborane ($ThxBH_2$), a monoalkylborane, reduced caproic acid and benzoic acid in refluxing THF to the corresponding aldehydes in yields of 98% and 82%, respectively. However, in view of the fact that $ThxBH_2$ requires such refluxing of the THF solution and a considerable excess of the reagent (three equivalents excess), the reagent seems not to be recommended for practical purposes. Similarly, Muraki and Mukaiyama have utilized BMPA for the straightforward conversion with excess reagent in refluxing THF.[129] Seventy to 86% yields of aldehydes were observed. Recently, an easy and inexpensive way to prepare this reagent from LAH has been reported and the excellence of this reagent has been demonstrated.[130] Brown and coworkers devised a valuable new methodology which involves the rapid reduction of carboxylic acid with borane-dimethyl sulfide (BMS), followed by oxidation of the resultant trialkoxyboroxine with pyridinium chlorochromate (PCC) in refluxing methylene chloride.[131] This reaction is broadly applicable, tolerating many reducible substituents with high yields of aldehydes. Attempts to convert carboxylic acids to aldehydes using Grignard reagent in the presence of dichlorobis[π-cyclopetadienyl]-titanium have been reported by Sato and Jinbo.[132] The yields are fifty to 73%. Fujisawa and coworkers proposed a simple and chemoselective method to convert carboxylic acids to aldehydes using N,N-dimethylchloromethyleniminium chloride, which activates the carboxylic group, and LTBA, which is a mild, selective reducing agent, in a one-pot operation.[133] This method has afforded a means for chemoselective reduction without attack on various reducible substituents, such as bromo, cyano and ester groups, in yields of sixty to 90%.

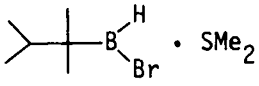




Recently, Brown, Cha, Nazer and Yoon have developed an effective procedure using thexylchloroborane-dimethyl sulfide (ThxBHCl•SMe_2, 26) to convert acyclic and alicyclic carboxylic acids to aldehydes in almost quantitative yields, with no observable dependence on the structure of the acid, in a matter of minutes at 25°C.[134] The reaction is quite general. Furthermore, many other readily reducible functional groups so long as alkene function are not present, tolerated these reaction conditions. However, the reduction of aromatic acids with this reagent was much more sluggish and the yields varied with the substituent. The remarkable difference in rates in the reduction of aliphatic and aromatic carboxylic acids has provided a means for the selective conversion of a carboxylic acid group attached to an aliphatic or alicyclic moiety in the presence of a carboxylic acid group attached to an aromatic moiety. Furthermore, the systematic study of the reducing characteristics of 26 toward the representative organic functional groups has been carried out.[135] A practical method has been developed to isolate the aldehyde products in a pure form by forming the sodium bisulfite adduct, followed by regeneration with formaldehyde, or by using steam distillation to remove the byproduct. An analogous reagent, ThxBHBr•SMe_2 (27), has also proved to work equally well.[115] The reagent tolerates more organic functionalities. However, the most useful feature of this reagent is its reluctance to hydroborate carbon-carbon double bonds, an advantage of this reagent over 26 which readily adds to alkenes. The reducing power of this reagent has also been fully characterized.[115c]

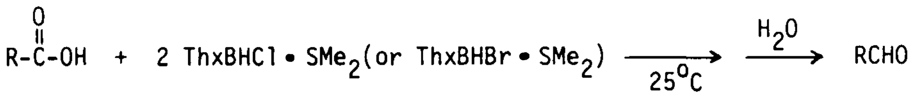


26



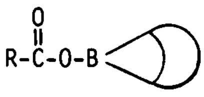
27

Very recently, Cha and coworkers have centered their efforts to uti-

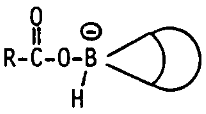


$$R\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}OH \;+\; 2\ ThxBHCl\bullet SMe_2(\text{or } ThxBHBr\bullet SMe_2) \xrightarrow[25^{\circ}C]{} \xrightarrow{H_2O} RCHO$$

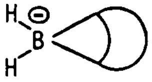
lize the commercially avialble 9-BBN in the direct reduction of free acids to aldehydes. The acyloxy-9-BBN 28 seems to possess adequate structural and electronic features for the acyloxy group being converted to the aldehyde stage readily. The acyloxy moiety of 28 was readily reduced by lithium 9-boratabicyclo[3.3.1]nonane (Li 9-BBNH, 30) and the reduction stops at the aldehyde stage.[136] The yields of aldehydes are 80-100%. The acyloxy group of 28 was also readily converted to the aldehyde stage through stepwise treatment with t-butyllithium and 9-BBN.[137] This interesting reaction seems to be rationalized by the consecutive hydride-transfer pathway in which the hydride from 29 migrates to 9-BBN (i.e., formation of 30) and then again the hydride from 30 species attacks the carbonyl carbon of the acyloxy moiety.[138] Furthermore, the acyloxy group of 28 can also be reduced to the aldehyde stage even by one equivalent of LAH or LTDEA in the presence of excess pyridine in high yields.[139] The role of pyridine in this reaction is under investigation in detail.



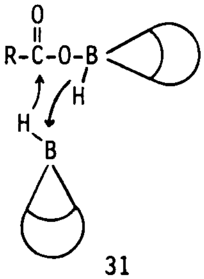
28



29



30



31

A report has appeared that the hydrogenation of carboxylic acids in the presence of an inorganic catalyst provides the corresponding aldehydes efficiently,[140] but details are lacking.

CONCLUDING REMARKS

A number of useful methods for transformation of carboxylic acids themselves or their derivatives to the corresponding aldehydes using various reducing systems have been developed. However, none of these methods really offers a simple, general, direct procedure both for the reduction and the isolation of aldehyde products processes. Every system has its own limitation.

There are two approaches of devising new methodology for such a transformation: development of the new reducing agents or of reactive intermediates of carboxylic acids. At the present time, the systematic modification of reducing characteristics of the parent aluminum and boron hydrides is under extensive investigation. In addition, the reactive intermediates, with adequate structural and electronic features for the acyloxy group being converted to the aldehyde stage, is being examined systematically with various metal hydride systems.

REFERENCES

1. I. T. Harrison, H. Harrison, I. S. Hegedus, L. Wade and L. G. Wade, Jr., "Compendium of Organic Synthetic Methods", Wiley-Interscience, N.Y., Vol. I-V (1971-1984).

2. E. Mosettig, Org. React., 8, 218 (1954).

3. H. Stephen, J. Chem. Soc., 127, 1874 (1925).

4. M. L. Wolfrom and J. V. Karabinos, J. Am. Chem. Soc., 66, 909 (1944); 68, 724, 1455 (1946).

5. L. Friedman, Abstracts of Papers, 116th National Meeting of the American Chemical Society, Atlantic City, N.J., Sept, 1949, p. 5-M.

6. K. W. Rosenmund, Ber., 51, 585 (1918); K. W. Rosenmund and F. Zetzsche, ibid., 54, 425 (1921); K. W. Rosenmund, F. Zetzsche and F. Heise, ibid., 54, 638, 2038 (1921).

7. E. Mosettig and R. Mozingo, Org. React., 4, 362 (1948).

8. F. Wayne and K. Adkins, Org. Syn., 21, 39 (1941).

9. Y. Sakurai and Y. Tanabe, J. Pharm. Soc. Jpn., 64, 25 (1944).

10. E. B. Hershberg and J. Cason, Org. Syn., 21, 84 (1941).

11. W. P. Campbell and D. Todd, J. Am. Chem. Soc., 64, 928 (1942).

12. J. English, Jr. and S. F. Velick, ibid., 67, 1413 (1945).

13. S. Affrosmann and S. J. Thomson, J. Chem. Soc., 2024 (1962).

14. E. B. Hershberg and J. Cason, Org. Syn. Coll. Vol. III, 627 (1955).

15. D. C. Ayres, B. G. Carpenter and R. C. Denney, J. Chem. Soc., 3578 (1965).

16. G. B. Calleja and P. Rogers, J. Labelled Compd., 6, 135 (1970).

17. J. A. Peters and H. van Bekkum, Rec. Trav. Chim. Pays-Bas, 90, 1323 (1971); 100, 21 (9181).

18. A. I. Rachlin, H. Gurien and D. P. Wagner, Org. Syn., 51, 8 (1971).

19. A. W. Burgstahler, L. O. Weigel and C. G. Shaefer, Synthesis, 767 (1976).

20. K. R. Jethani, P. H. Mehta and S. B. Chandalia, Indian J. Tech., 19, 349 (1981).

21. H. C. Brown and R. F. McFarlin, J. Am. Chem. Soc., 78, 252 (1956).

22. H. C. Brown and R. F. McFarlin, ibid., 80, 5372 (1958).

23. H. C. Brown and B. C. Subba Rao, ibid., 80, 5377 (1958).

24. For a summary of the developments in this area, see H. C. Brown and S. Krishnamurthy, Tetrahedron, 35, 567 (1979).

25. D. J. Raber and W. C. Guida, J. Org. Chem., 41, 690 (1976).

26. J. H. Babler and B. J. Invergo, Tetrahedron Lett., 22, 11 (1981).

27. J. H. Babler, Synth. Comm., 12, 839 (1982).

28. K. Y. Gordeev, G. A. Serebrennikova and R. P. Evstigneeva, Zh. Org. Khim., 21, 2615 (1985); Chem. Abstr., 106, 17845 (1978).

29. (a) T. N. Sorrell and R. J. Spillane, Tetrahedron Lett., 2473 (1978). (b) G. W. J. Fleet, C. J. Fuller and P. J. C. Harding, ibid., 1437 (1978). (c) G. W. J. Fleet and P. J. C. Harding, ibid., 975 (1979).

30. T. N. Sorrell and P. S. Pearlman, J. Org. Chem., 45, 3449 (1980).

31. R. O. Hutchins and M. Markowitz, Tetrahedron Lett., 21, 813 (1980).

32. W. Amaratunga and J. M. J. Frechet, Am. Chem. Soc. Polym. Preprints, 22, 151 (1981).

33. R. A. W. Johnstone and R. P. Telford, Chem. Comm., 354 (1978).

34. I. D. Entwistle and R. A. W. Johnstone, U. S. Patent, US 4,211,727 (1980); Chem. Abstr., 93, 203410 (1980).

35. I. D. Entwistle, P. Boehm, R. A. W. Johnstone and R. P. Telford, J. Chem. Soc. Perkin Transaction I, 27 (1980).

36. M. P. Cooke, J. Am. Chem. Soc., 92, 6080 (1970).

37. Y. Watanabe, T. Mitsudo, M. Tanaka, K. Yamamoto, T. Okajima and Y. Takegami, Bull, Chem. Soc. Jpn., 44, 2569 (1971).

38. W. O. Siegl and J. P. Collman, J. Am. Chem. Soc., 94, 2516 (1972).

39. T. E. Cole and R. Pettit, Tetrahedron Lett., 781 (1977).

40. R. J. Kinney, W. D. Jones and R. Bergman, J. Am. Chem. Soc., 100, 7902 (1978).

41. S. C. Kao, P. L. Gaus, K. Youngdahl and M. Y. Darensbourg, Organometallics, 3, 1601 (1984).

42. G. Cainelli, F. Manescalchi and A. Umani-Ronchi, J. Organomet. Chem., 276, 205 (1984).

43. G. J. M. van der Kerk, J. G. Noltes and J. G. A. Luijiten, J. Appl. Chem., 7, 356 (1957).

44. H. G. Kuivila, Advan. Organomet. Chem., 1, 47 (1964).

45. H. G. Kuivila and E. J. Walsh, Jr., J. Am. Chem. Soc., 88, 571 (1966).

46. F. Guibe, P. Four and H. Riviere, Chem. Comm., 432 (1980).

47. P. Four and F. Guibe, J. Org. Chem., 46, 4439 (1981).

48. J. Lusztyk, E. Lusztyk, B. Maillard, L. Lunazzi and K. U. Ingold, J. Am. Chem. Soc., 105, 4475 (1983).

49. J. W. Jenkins and H. W. Post, J. Org. Chem., 15, 556 (1950).

50. J. D. Citron, ibid., 34, 1977 (1969).

51. B. Courtis, S. P. Dent, C. Eaborn and A. Pidcock, J. Chem. Soc. Dalton, 2460 (1975).

52. H. C. Brown and A. Tsukamoto, J. Am. Chem. Soc., 83, 4549 (1961).

53. G. Wittig and P. Hornberger, Ann., 577, 11 (1952).

54. F. Weygand and G. Eberhardt, Angew. Chem., 64, 458 (1952).

55. F. Weygand, G. Eberhardt, H. Linden, F. Schäfer and I. Eigen, Angew. Chem., 65, 525 (1953).

56. F. Weygand and H. Linden, Angew. Chem., 66, 174 (1954).

57. F. Weygand and R. Mitgau, Ber., 88, 301 (1955).

58. F. Weygand and H. J. Bestmann, Chem. Ber., 92, 528 (1959).

59. W. Ried and F. J. Königstein, Angew. Chem., 70, 165 (1958).

60. W. Ried and P. Pfaender, Ann., 640, 111 (1961).

61. H. A. Staab and H. Bräunling, ibid., 654, 119 (1962).

62. J. -A. Fehrentz and B. Castro, Synthesis, 676 (1983).

63. V. Bazant, M. Capka, M. Cerny, V. Chavalovsky, K. Kochloefl, M. Kraus and J. Malek, Tetrahedron Lett., 3303 (1968).

64. N. S. Ramegowda, M. N. Modi, A. K. Koul, J. M. Bora, C. K. Narang and N. K. Mathur, Tetrahedron, 29, 3985 (1973).

65. (a) Y. Nagao, K. Kwabata, K. Seno and E. Fujita, J. Chem. Soc. Perkin Transaction I, 2470 (1980). (b) T. Izawa and T. Mukaiyama, Chemistry Lett., 1443 (1977). (c) T. Izawa and T. Mukaiyama, Bull. Chem. Soc. Jpn., 52, 555 (1979).

66. H. C. Brown and A. Tsukamoto, J. Am. Chem. Soc., 86, 1089 (1964).

67. H. C. Brown and A. Tsukamoto, ibid., 81, 502 (1959).

68. (a) L. I. Zakharkin and I. M. Khorlina, Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk, 2146 (1959); Chem. Abstr., 54, 109326 (1960). (b) L. I. Zakharkin and I. M. Khorlina, Izv. Akad. Nauk SSSR, Ser. Khim., 465 (1964).

69. L. I. Zakharkin, D. N. Maslin and V. V. Gavrilenko, Tetrahedron, 25, 5555 (1969).

70. M. Muraki and T. Mukaiyama, Chemistry. Lett., 875 (1975).

71. L. I. Zakharkin and I. M. Khorlina, Izv. Akad. Nauk SSSR, 316 (1963).

72. L. I. Zakharkin, I. M. Khorlina, V. V. Gavrilenko, D. N. Maslin and I. M. Khorlina, Tetrahedron Lett., 2087 (1963).

73. P. M. Weissman and H. C. Brown, J. Org. Chem., 31, 283 (1966).

74. M. Muraki and T. Mukaiyama, Chemistry Lett., 215 (1975).

75. R. Kanazawa and T. Tokoroyama, Synthesis, 526 (1976).

76. Unpublished result.

77. (a) N. L. Holy, A. P. Gelbein and R. Hansen, U. S. Patent, US 4,585,900 (1986); Chem. Abstr., 105, 42333 (1986). (b) T. Maki and T. Tokoyama, Eur. Patent App. Ep 150,961 (1986); Chem. Abstr., 104, 50663 (1986).

78. (a) E. Fischer, Ber., 22, 2204 (1889). (b) N. Sperber, H. Zaugg and W. Sandstrom, J. Am. Chem. Soc., 69, 915 (1947).

79. M. L. Wolfrom and H. B. Wood, J. Am. Chem. Soc., 73, 2933 (1951).

80. G. E. Arth, ibid., 75, 2413 (1953).

81. J. Schmidlin and A. Wettstein, Helv. Chim. Acta, 46, 2799 (1963).

82. H. Minato and T. Nagasaki, J. Chem. Soc.(C), 621 (1968).

83. E. J. Corey, N. M. Weinshenker, T. K. Schaaf and W. Huber, J. Am. Chem. Soc., 91, 5675 (1969).

84. E. J. Corey and R. Noyori, Tetrahedron Lett., 311 (1970).

85. G. Saucy, R. Borer and A. Fürst, Helv. Chim. Acta, 54, 2034 (1971).

86. H. C. Brown and D. B. Bigley, J. Am. Chem. Soc., 83, 468 (1961).

87. H. C. Brown, D. B. Bigley, S. K. Arora and N. M. Yoon, ibid., 92, 7161 (1970).

88. W. R. Vaughan, C. T. Goetschel, M. H. Goodrow and C. L. Warren, J. Am. Chem. Soc., 85, 2282 (1963); F. J. McQuillin and R. B. Yeats, J. Chem. Soc., 4273 (1965); P. Kohn, R. H. Samaritano and L. M. Lerner, J. Am. Chem. Soc., 87, 5475 (1965); G. Buchi, D. M. Foulkes, M. Kurono and G. F. Mitchell, ibid., 88, 4534 (1966); R. W. Kierstead and A. Faraone, J. Org. Chem., 32, 704 (1967); T. A. Giudici and A. L. Fluharty, ibid., 32, 2043 (1967); P. Kohn, L. M. Lerner, A. Chan, Jr., S. D. Ginocchio and C. A. Zitrin, Carbohyd. Res., 7, 21 (1968).

89. G. B. Spero, A. V. McIntosh, Jr. and R. H. Levin, J. Am. Chem. Soc., 70, 1907 (1948); A. V. McIntosh, Jr., E. M. Meinzer and R. H. Levin, ibid., 70, 2955 (1948); A. V. McIntosh, Jr., A. M. Searcy, E. M. Meinzer and R. H. Levin, ibid., 71, 3317 (1949); F. Weygand and H. J. Bestmann, Chem. Ber., 92, 528 (1959); Y. Kitahara, A. Yoshikoshi and S. Oida, Tetrahedron Lett., 1763 (1964).

90. Y. Nagao, K. Kawabata and E. Fujita, Chem. Comm., 330 (1978).

91. H. Takaku and S. Watanabe, Chiba Kogyo Daigaku Kenkyu Hokoku, Riko-hen, 26, 93 (1981).

92. W. J. Gottstein, G. E. Bocian, L. B. Crast, K. Dadabo, J. M. Essery, J. C. Godfrey and L. C. Cheney, J. Org. Chem., 31, 1922 (1966).

93. H. Wakamatsu, J. Furukawa and N. Yamakami, Bull. Chem. Soc. Jpn., 44, 288 (1971); H. Musso and K. Figge, Chem. Ber., 95, 1844 (1962).

94. Y. Watanabe, M. Yamashita, T. Mitsudo, M. Tanaka and Y. Takegami, Tetrahedron Lett., 3535 (1973).

95. H. C. Brown, B. Nazer, J. S. Cha and J. A. Sikorski, J. Org. Chem., 51, 5264 (1986).

96. Z. Rappoport, "The Chemistry of the Cyano Group", Interscience, N.Y.,

PP. 307-340 (1970).

97. F. E. King and R. Robinson, J. Chem. Soc., 273 (1933); C. R. Harrington and R. C. G. Moggridge, ibid., 443 (1939); F. E. King, P. L'Ecuyer and H. T. Openshaw, ibid., 352 (1936); F. E. King, J. W. Clifton and H. T. Openshaw, ibid., 424 (1942); J. W. Williams, J. Am. Chem. Soc., 61, 2248 (1939); G. Wittig, R. Kethur, A. Klein and R. Wietbrock, Ber., 69B, 2078 (1936); G. Wittig and H. Hartmann, ibid., 72B, 1387 (1939); E. Lieber, J. Am. Chem. Soc., 71, 2862 (1949); C. J. Claus and J. L. Morgenthau, Jr., ibid., 73, 5005 (1951); J. A. Knight and H. D. Zook, ibid., 74, 4560 (1952); C. F. H. Allen, M. R. Gillbert and D. M. Young, J. Org. Chem., 2, 231 (1937); T. L. Tolbert and B. Houston, ibid., 28, 695 (1970).

98. Benzonitrile, however, has been reduced to benzaldehyde with a limiting amount of LAH in a yield of 92%; see H. C. Brown and C. J. Shoaf, J. Am. Chem. Soc., 86, 1079 (1964).

99. G. Hesse and R. Schrödel, Angew. Chem., 68, 438 (1956); Ann., 607, 24 (1957).

100. H. C. Brown, C. J. Shoaf and C. P. Garg, Tetrahedron Lett., 9 (1959); H. C. Brown, J. Chem. Educ., 38, 173 (1961); H. C. Brown and C. P. Garg, J. Am. Chem. Soc., 86, 1079, 1085 (1964); D. de Peretti, T. Strzalko-Bottin and J. Seyden-Penne, Bull. Soc. Chim. Fr., 12, 2925 (1974).

101. L. I. Zakharkin and I. M. Khorlina, Dokl. Akad. Nauk SSSR, 116, 422 (1957); J. A. Marshall, N. H. Andersen and P. C. Johnson, J. Org. Chem., 35, 186 (1970); R. V. Stevens, L. E. DuPree, Jr. and P. L. Loewenstein, ibid., 37, 977 (1972); M. P. L. Caton, E. C. J. Coffee and G. L. Watkins, Tetrahedron Lett., 585 (1974).

102. N. M. Yoon, S. K. Kim and Y. S. Gyong, Bull. Korean Chem. Soc., 7, 323 (1986).

103. F. E. Gould, G. S. Johnson and A. F. Ferris, J. Org. Chem., 25, 1658 (1960).

104. S. Peitra and C. Trinchera, Gazz. Chim. Ital., 85, 1705 (1955).

105. A. Gaiffe and R. Pallaud, Compt. Rend., 252, 1339 (1961); 254, 496 (1962).

106. H. Plieninger and G. Werst, Angew. Chem., 67, 156 (1955); Chem. Ber., 88, 1956 (1955).

107. J. N. Coker, W. L. Kohlhase, M. Fields, A. O. Rogers and M. A. Stevens, J. Org. Chem., 27, 850 (1962).

108. A. McKillop, J. D. Hunt, R. D. Naylor and E. C. Toylor, J. Am. Chem. Soc., 93, 4918 (1971).

109. P. Vankar, R. Rathore and S. Chandrasekaran, J. Org. Chem., 51, 3063 (1986).

110. O. G. Backeberg and B. Staskun, J. Chem. Soc., 3961 (1962).

111. B. Staskun and O. G. Backeberg, J. Chem. Soc., 5880 (1964); T. van Es and B. Staskun, ibid., 5775 (1965); T. van Es and B. Staskun, Org. Syn., 51, 20 (1971).

112. J. L. Fry, Chem. Comm., 45 (1974); J. L. Fry and R. A. Ott, J. Org. Chem., 46, 602 (1981).

113. J. S. Cha, S. Y. Oh and J. E. Kim, Bull. Korean Chem. Soc., 8, 301 (1987).

114. Z. Huang and Y. He, Youji Huaxue, 3, 204 (1986).

115. (a) J. S. Cha, J. E. Kim and K. W. Lee, J. Org. Chem., 52, 5030 (1987). (b) J. S. Cha, J. E. Kim, S. Y. Oh, J. C. Lee and K. W. Lee, Tetrahedron Lett., 28, 2389 (1987). (c) J. S. Cha, J. E. Kim and S. Y. Oh, Bull. Korean Chem. Soc., 8, 313 (1987).

116. J. S. Cha, S. Y. Oh, K. W. Lee, M. S. Yoon, J. C. Lee and J. E. Kim, Heterocycles, 27, 1595 (1988).

117. G. Doleschall, Tetrahedron Lett., 30, 2649 (1974); ibid., 32, 2549 (1976).

118. I. Degani, R. Fochi and P. Tundo, J. Heterocyclic Chem., 11, 507 (1974); L. Costa, I. Degani, R. Fochi and P. Tundo, ibid., 11, 943 (1974).

119. J. C. Craig, N. N. Ekwuribe, C. C. Fu and K. A. M. Walker, Synthesis, 303 (1981).

120. K. Pgura, N. Yahata, K. Takahashi and H. Iida, Tetrahedron Lett., 24, 5761 (1983).

121. L. Horner and H. Röder, Chem. Ber., 103, 2984 (1970).

122. M. Johnson and B. Rickborn, Org. Syn., 51, 11 (1971).

123. M. W. Cronyn and J. E. Goodrich, J. Am. Chem. Soc., 74, 3936 (1952).

124. A. W. Burgstahler and L. R. Worden, ibid., 83, 2587 (1961); 86, 96 (1964).

125. A. W. Burgstahler, L. R. Worden and T. B. Lewis, J. Org. Chem., 28, 2918 (1963).

126. A. O. Bedenbaugh, J. H. Bedenbaugh, W. A. Bergin and J. D. Adkins, J. Am. Chem. Soc., 92, 5774 (1970).

127. L. I. Zakharkin and I. M. Khorlina, Zh. Obshch. Khim., 34, 1029 (1964).

128. H. C. Brown, P. Heim and N. M. Yoon, J. Org. Chem., 37, 2942 (1972).

129. M. Muraki and T. Mukaiyama, Chemistry Lett., 1447 (1974).

130. T. D. Hubert, D. P. Eyman and D. F. Wiemer, J. Org. Chem., 49, 2279

(1984).

131. H. C. Brown, C. G. Rao and S. U. Kulkarni, Synthesis, 704 (1979).

132. F. Sato, T. Jinbo and M. Sato, ibid., 871 (1981).

133. T. Fujisawa, T. Mori, S. Tsuge and T. Sato, Tetrahedron Lett., 1543 (1983).

134. H. C. Brown, J. S. Cha, B. Nazer and N. M. Yoon, J. Am. Chem. Soc., 106, 8001 (1984); J. Org. Chem., 52, 5400 (1987).

135. H. C. Brown, B. Nazer, J. S. Cha and J. A. Sikorski, J. Org. Chem., 51, 5264 (1986).

136. J. S. Cha, J. E. Kim, S. Y. Oh and J. D. Kim, Tetrahedron Lett., 28, 4575 (1987).

137. J. S. Cha, J. E. Kim, M. S. Yoon and Y. S. Kim, ibid., 28, 6231 (1987).

138. J. S. Cha, S. Y. Oh, K. W. Lee, M. S. Yoon, J. C. Lee and J. E. Kim, Bull. Korean Chem. Soc., 9, 48 (1988).

139. Manuscripts in preparation.

140. (a) T. Maki and T. Yokoyama, Eur. Pat. Appl. Ep 150,961 (1985); Chem. Abstr., 104, 50663 (1986). (b) C. S. John, Eur. Pat. Appl. EP 178, 718 (1986); Chem. Abstr., 105, 45253 (1986). (c) N. L. Holy, A. P. Gelbein and R. Hansen, U. S. Pat. US 4,585,900 (1986); Chem. Abstr., 105, 42333 (1986); T. Maki and T. Yokoyama, Jpn. Pat. Koki Tokyl Koho JP 61,115,042 (1986); Chem. Abstr., 106, 4655 (1987).

(Received June 29, 1988; in revised form April 29, 1989)