

Reduction of acid chlorides using dichloro bis[(1,4-diaza bicyclo [2.2.2] octane) bis(tetrahydroborato)] zirconium (IV)

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Aliphatic and aromatic acid chlorides were efficiently reduced to give the corresponding alcohols when treated with $[\text{Zr}(\text{BH}_4)_2\text{Cl}_2(\text{dabco})_2]$, (ZrBDC).

Keywords: acid chloride, alcohol, reduction, ZrBDC

Lithium borohydride and sodium borohydride are two extremes of nucleophilic hydride transfer agents. Lithium borohydride is a very powerful reducing agent and can reduce most of the reducible functional groups. On the other hand, sodium borohydride is a mild reagent, used mostly for the reduction of aldehydes and ketones in protic solvents.¹ In spite of the great convenience of using NaBH_4 , certain limitations such as reduction of a few functional groups, long reaction times, and requirement for polar and protic solvents may be observed with this reagent. Modification of sodium borohydride, to increase or decrease its activity, has attracted a great deal of attention recently.²⁻⁷

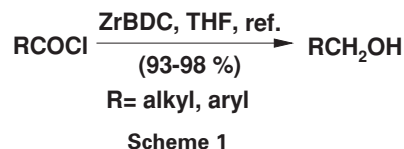
In general, modification of the usual reducing ability of sodium borohydride has led to selective reduction of several functional groups that are otherwise inert to sodium borohydride alone. For instance, the reduction of acid chlorides to aldehydes,^{3a} and alkenes to saturated hydrocarbons^{3b} can be achieved by use of the combination of sodium borohydride with Cu(I) and Co(II), respectively.

Transition metal tetrahydroborates such as $\text{Zn}(\text{BH}_4)_2$, $\text{Zr}(\text{BH}_4)_4$ and $\text{Ti}(\text{BH}_4)_3$ are very reactive, volatile, unstable, and difficult to handle and can not be easily used in organic synthesis as reducing agents without modification.⁸ The use of coligands can induce considerable stabilities in these transition metal borohydrides. Some of these modified reducing agents are: $[\text{Zn}(\text{BH}_4)_2(\text{dabco})]$,^{9a} $[\text{Zn}(\text{BH}_4)_2(\text{Ph}_3\text{P})]$,^{9b} $[\text{Zn}(\text{BH}_4)_2(\text{pyz})]_n$,¹⁰ $[\text{Cu}(\text{BH}_4)_2(\text{Ph}_3\text{P})_2]$ ¹¹ and $[\text{Zr}(\text{BH}_4)_2(\text{Cp})_2\text{Cl}]$.¹²

Recently, dichloro bis[(1,4-diazabicyclo [2.2.2] octane) bis(tetrahydroborato)] Zirconium(IV), $[\text{Zr}(\text{BH}_4)_2\text{Cl}_2(\text{dabco})_2]$, ZrBDC, has been reported for reduction of carbonyl compounds, reductive amination of aldehydes and ketones and reductive methylation of amines.¹³ Very recently, we have applied this reducing agent for preparation of alkanes from corresponding carbonyl compounds.¹⁴

Direct conversion of acid chlorides into the corresponding alcohols is one of the key functional group interconversions in organic chemistry and some hydride reagents have been introduced for this purpose.¹⁵ NaBH_4 involves vigorous conditions for achieving this transformation.¹⁶ However, this method is less effective for polyfunctional molecules and produces different reduced products. In order to eliminate these problems, several modified methods have been developed in the literature, such as $\text{Zn}(\text{BH}_4)_2 / \text{N,N,N',N'}$ -tetramethylene diamine (TMEDA),¹⁵ 1-Benzyl-4-aza-1-azoniabicyclo[2.2.2] octane tetrahydroborate (BAAOTB),^{7a} Tetrabutylammonium tetrahydroborate (TBATB),¹⁷ N-Methylpyrrolidine zinc borohydride ($\text{NMP-Zn}(\text{BH}_4)_2$).¹⁸

Now we report a safe and efficient method for preparation of alcohols from acid chlorides using ZrBDC in THF under reflux conditions (Scheme 1).



Result and discussion

In order to find the optimum conditions for reduction of acid chlorides with ZrBDC, we have chosen benzoyl chloride as a model compound. Reduction of benzoyl chloride was first investigated in different solvents such as THF, CH_2Cl_2 , hexane and CH_3CN . We observed that THF was best solvent for this purpose. The amount of ZrBDC in this reaction was also examined with different molar ratio of reductant to substrate in refluxing THF. The optimum ratio of reductant to benzoyl chloride (1.5:1) was found to be ideal for complete conversion to benzyl alcohol, while the reaction remains incomplete with lesser amounts, for example 1:1 and 1: 1.2.

By using this reduction system a number of alkyl and aryl benzoyl chlorides were successfully reduced to their corresponding alcohols in excellent yields. The results are

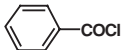

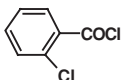
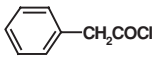
Table 1 Reduction of different acid chlorides (RCOCl) with ZrBDC.

Entry	Acid chlorides	Product ^b	Time/h	Yield% ^c
1			1.9	96
2			1.8	97
3			1.7	98
4			1.7	98
5			1.5	98
6			4.5	93
7			1.2	98
8			2.7	95
9			1.1	97

^aAll reactions were carried out under reflux conditions with ZrBDC/acid chloride (1.5/1) molar ratio; ^bAll of the products were characterised by comparing with known compounds and their IR and ¹H NMR showed physical and spectral data in accordance with their expected structure and by comparison with authentic samples; ^cYields refer to isolated products.

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Table 2 Comparison of the results obtained by ZrBDC with several other reducing agents for the reduction of acid chlorides to corresponding alcohols

Entry	Substrate	ZrBDC		TBATB ^a		Zn(BH ₄) ₂ / TMDE ^b		BAAOTB ^c	
		Molar ratio	Time/h Yield/%	Molar ratio	Time/h Yield/%	Molar ratio	Time/h Yield/%	Molar ratio	Time/h Yield/%
1		1.5	1.9 (96)	4	2 (90)	1.4	4.5 (95)	–	–
2		1.5	1.7 (98)	4	1 (85)	1.4	0.25 (93)	3	2 (95)
3		1.5	1.8 (97)	4	0.5 (95)	–	–	3	0.25 (95)
4		1.5	1.2 (98)	4	1.5 (85)	1.4	0.5 (95)	3	2 (85)

^aTetrabutylammonium tetrahydroborate (TBATB).¹⁷^bZn(BH₄)₂/N,N,N',N'-tetramethylene diamine (TMEDA).¹⁵^c1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane tetrahydroborate (BAAOTB).^{7a}

summarised in Table 1. The data indicated that reduction of different aromatic (entries 1–6) and aliphatic (entries 7–9) acid chlorides to their corresponding alcohols occurs in excellent yields using ZrBDC in THF. Chemoselective reduction with different substituted groups on the aromatic ring have been performed smoothly under similar reaction conditions (Table 1, entries 2–5, 9). Thus, chloro and nitro groups were not affected during the progress of the reaction. Interestingly, ortho-phthaloyl chloride gave an excellent yield of ortho-phthalyl alcohol (Table 1, entry 6).

In order to show the advantages and drawbacks of our method, we have compared reduction of benzoyl chloride with other reagents in Table 2.

As indicated in Table 2, our method in comparison with others gives excellent yields of the corresponding alcohols with a lower molar ratio of ZrBDC to substrate.

In conclusion, although there are several methods available for the reduction of acid chlorides to their corresponding alcohols, we believe that the present method offers considerable advantages in terms of simpleness, functional selectivity, readily available reagent, mild conditions, easy reaction work up, efficiency, excellent reaction yields, and lack of requirement of an inert atmosphere.

Experimental

ZrBDC used in this study was prepared according to the literature procedure.¹³ Acid chlorides were purchased from Merck companies. All the products are known compounds and were identified by comparison of their spectra and physical data with those of the authentic samples. Infrared (IR) spectra were recorded on Bruker VECTOR 22 spectrometer. ¹H NMR spectra were measured on a Bruker DRX500 AVANCE, GNM-Ex90A (90 MHz) spectrometers, using CDCl₃ as solvent. Reaction monitoring and purity determination of the products were accomplished by TLC.

General procedure for the reduction of acid chlorides with ZrBDC: To a solution of acid chloride (1.0 mmol) in dry THF (5 ml) the reagent (0.624 g, 1.5 mmol) was added and the mixture stirred under reflux conditions for the specified time (Table 2). The progress of the reaction was followed by TLC (eluent: n-hexane/EtOAc: 4/1). After addition of 5% HCl (10 ml), the mixture was extracted with diethyl ether (2 × 20 ml). The combined organic layers were dried on anhydrous MgSO₄ and evaporated. The crude product was purified by column chromatography on silica gel, and eluted with 2–5% solution of ethyl acetate in n-hexane to afford pure alcohols in 93–98% yields. The products were identified by comparison of their spectra and physical data with those of authentic samples.

Reduction of benzoyl chloride with ZrBDC as a typical procedure: To a solution of benzoyl chloride (0.140 g, 1.0 mmol) in dry THF (5 ml), was added ZrBDC (0.624 g, 1.5 mmol). The mixture was then stirred under reflux conditions until completion of the reaction, as monitored by TLC. After addition of 5% HCl (10 ml), the mixture extracted with diethyl ether (2 × 20 ml). The combined organic layers

were dried on MgSO₄ and evaporated. The crude resulting material was purified by column chromatography on silica gel, and eluted with 2% solution of ethyl acetate in n-hexane. Pure benzyl alcohol was obtained (0.103 g, 96%) and identified by comparison of its spectra and physical data with those of authentic sample.

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References

- F.A. Carey and R.J. Sundberg, *Advanced Organic Chemistry*, Plenum Press, New York, 1993, pp. 219–270.
- (a) E.J. Corey, N.H. Anderson, R.M. Carlson, J. Paust, E. Vedjs, I. Vlattas and R.E.K. Winter, *J. Am. Chem. Soc.*, 1968, **90**, 3245; (b) T. Nakata and T. Oishi, *Tetrahedron Lett.*, 1980, **21**, 1641.
- (a) G.W.J. Fleet and P.J.C. Harding, *Tetrahedron Lett.*, 1979, **20**, 975; (b) S.-K. Chung, *J. Org. Chem.*, 1979, **44**, 1014.
- (a) Y. Tsuda, T. Sano and H. Watanabe, *Synthesis*, 1977, 602; (b) T. Satoh, N. Mitsud, M. Nishiki, Y. Inoue and Y. Ooi, *Chem. Pharm. Bull.*, 1981, **29**, 1443.
- (a) R.A.W. Johnstone and R.P. Telford, *J. Chem. Soc., Chem Commun.*, 1978, 354; (b) J.L. Luche, *J. Am. Chem. Soc.*, 1978, **100**, 2226.
- (a) M. Nishiki, H. Miyataka, Y. Niiono, N. Mitsuo and T. Satoh, *Tetrahedron Lett.*, 1982, **23**, 193; (b) S.T. Lin and J.A. Roth, *J. Org. Chem.*, 1979, **44**, 309; (c) R. A. Egli, *Helv. Chem. Acta*, 1968, **51**, 2090.
- (a) H. Firouzabadi and G.R. Afsharifar, *Synth. Commun.*, 1992, **22**, 497; (b) H. Firouzabadi, and G.R. Afsharifar, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 2595; (c) A.R. Hajipour, *Tetrahedron*, 1997, **53**, 16883; (d) A. R. Hajipour, I. Mohammadpoor-Baltork and A. Rahi, *Indian. J. Chem.*, 2000, **39B**, 239.
- T.J. Marks and J.R. Kolb, *Chem. Rev.*, 1977, **77**, 263.
- (a) H. Firouzabadi and B. Zeynizadeh, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 155; (b) H. Firouzabadi and M. Ghadami, *Phosphorous, Sulfur Silicon*, 1998, **142**, 191.
- B. Tamami and M.M. Lakouraj, *Synth. Commun.*, 1995, **25**, 3089.
- (a) G.W.J. Fleet and P.J.C. Harding, *Tetrahedron Lett.*, 1981, **22**, 675; (b) T.N. Sorrell and R.J. Spillane, *Tetrahedron Lett.*, 1978, **19**, 2473.
- T.N. Sorrell, *Tetrahedron Lett.*, 1978, **19**, 4985.
- (a) H. Firouzabadi, N. Iranpoor and H. Alinezhad, *Synth. Commun.*, 2002, **32**, 3575; (b) H. Firouzabadi, N. Iranpoor, and H. Alinezhad, *Bull. Chem. Soc. Jpn.*, 2003, **76**, 143.
- H. Alinezhad, M. Tajbakhsh and F. Salehian, *Synlett*, 2005, 170.
- H. Kotsuki, Y. Ushio, N. Yoshimura, M. Ochi, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 2684.
- S.W. Chaikin and W.G. Brown, *J. Am. Chem. Soc.*, 1949, **71**, 122.
- D.J. Raber and W.C. Guida, *J. Org. Chem.*, 1976, **41**, 690.
- M. Tajbakhsh, M.M. Lakouraj, F. Mohanazadeh and A. Ahmadi-nejhad, *Synth. Commun*, 2003, **33**, 229.