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Zirconium borohydride piperazine complex, an efficient, air and thermally stable reducing agent

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Abstract—A zirconium borohydride piperazine complex (Ppyz)$Zr(BH_4)_2Cl_2$, obtained by the reaction of an ethereal solution of $ZrCl_4$ and $LiBH_4$ with piperazine is a stable, selective and efficient reducing agent. (Ppyz)$Zr(BH_4)_2Cl_2$ reduces aldehydes, ketones, silylethers, α,β-unsaturated carbonyl compounds and esters. The reactions were performed in diethyl ether at room temperature or under reflux, and the yields of the corresponding alcohols were excellent. The selective reduction of aldehydes in the presence of ketones and complete regioselectivity in the reduction of α,β-unsaturated carbonyl groups were observed.

A number of covalent transition-metal borohydride complexes are known, which are volatile, unstable materials and which cannot be used as reducing agents,[1] without modification, in organic synthesis. There are only a few reports in the literature of the use of modified, stable forms of these compounds for reductive transformations including, $(Ph_3P)_2CuBH_4$,[2] $[(Ph_3P)_2CuBH_3CN]_2$,[3] $(C_5H_5)_2Zr(Cl)BH_4$,[4] $Zn(BH_4)_2$,[5] DABCO and (pyz)$Zn(BH_4)_2$,[6,7] $[Zr(BH_4)_2Cl_2(dabco)_2]$[8] and $Zr(BH_4)_2$-crown ethers.[9] Zirconium borohydride is a highly volatile solid, which decomposes around room temperature, inflames in air, and which hydrolyses explosively.[10]

Polymer supported zirconium borohydride complexes have received considerable attention in recent years and while exhibiting the advantages of polymeric reagents, have been used for the mild and selective reduction of organic compounds.[11]

Herein we report a coordination polymer of zirconium borohydride with a bidentate ligand, piperazine, as a new, air and thermally stable and efficient bench top reducing agent for the reduction of a variety of organic compounds. The zirconium borohydride piperazine complex was easily prepared by treatment of $ZrCl_4$ and an ethereal solution of $LiBH_4$ with piperazine at 0–5 °C. It is a white powder, which can be stored in a vacuum dessicator for months without significant change in its activity. Based on data obtained by atomic absorption spectroscopy and borohydride content by an iodometric titration,[12] together with elemental analysis, (Ppyz)$Zr(BH_4)_2Cl_2$ was confirmed as its empirical formula.

This reagent reduces both aliphatic and aromatic aldehydes readily at room temperature in diethyl ether and ketones at reflux (Tables 1 and 2). A comparison of these data showed that aldehydes are reduced rapidly and more conveniently than ketones. Therefore the chemoselective reduction of an aldehyde in the presence of a ketone was achieved at room temperature and the unreacted ketone was recovered (Table 3). Numerous methods exist for the chemoselective reduction of an aldehyde in the presence of a ketone,[13] but each has its limitations and therefore this new methodology should be of interest. Deprotection of aliphatic and phenolic trimethylsilyl ethers to the corresponding alcohols and phenols was achieved using (Ppyz)$Zr(BH_4)_2Cl_2$ in diethyl ether at ambient temperature (Table 4). α,β-Unsaturated carbonyl compounds undergo regioselective 1,2-reduction to the corresponding allylic alcohols at room temperature or under reflux conditions in diethyl ether in the presence of (Ppyz)$Zr(BH_4)_2Cl_2$ (Table 5).

An improved procedure for the reduction of the carbonyl group of α,β-unsaturated carbonyl compounds to

Keywords: Zirconium borohydride; Piperazine; Reducing agent.
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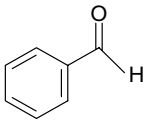
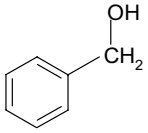
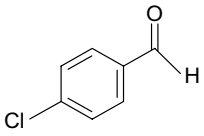
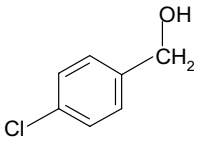
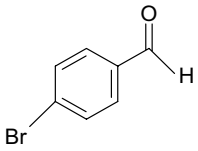
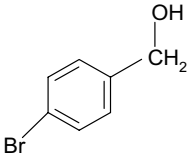
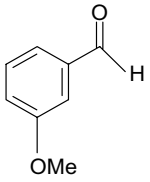
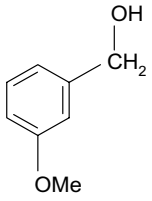
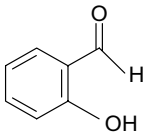
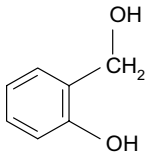
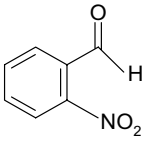
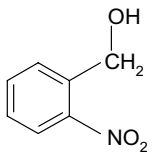
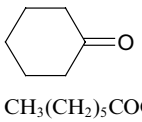
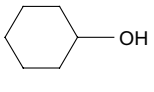
Table 1. Reduction of aldehydes with (Ppyz)$Zr(BH_4)_2Cl_2$ in diethyl ether[a]

Entry	Substrate	Product	Time (min)	Reagent/substrate	Yield (%)[b]
1			60	1	97
2			45	1	98
3			45	1	96
4			75	1	90
5			240	2	95
6			20	1	98
7	$PhCH_2CHO$	$PhCH_2CH_2OH$	45	1	95
8	$CH_3(CH_2)_4CHO$	$CH_3(CH_2)_4CH_2OH$	30	1	100[c]

[a] Reductions were performed at room temperature.
[b] The yields refer to isolated products.
[c] GC yield.

Table 2. Reduction of ketones with (Ppyz)$Zr(BH_4)_2Cl_2$[a]

Entry	Substrate	Product	Time (h)	Reagent/substrate	Yield (%)[b]
1	PhCOPh	PhCHOHPh	5	3	90
2	$PhCOCH_3$	$PhCHOHCH_3$	8	1	95
3	$(PhCH_2)_2CO$	$(PhCH_2)_2CHOH$	2.5	1	95
4			2.5	1	90[c]
5	$CH_3(CH_2)_5COCH_3$	$CH_3(CH_2)_5CHOHCH_3$	2.5	1	95[c]

[a] Reactions were performed in diethyl ether under reflux.
[b] Yields refer to isolated products.
[c] GC yields.

allylic alcohols has long been a desired synthetic transformation, since this reaction frequently results in undesired 1,4-reduction products.[14] Several methods are known to bring about such a conversion but these

Table 3. Reduction of aldehydes versus ketones with $(Ppyz)Zr(BH_4)_2Cl_2$ in diethyl ether[a]

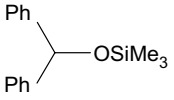
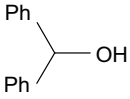
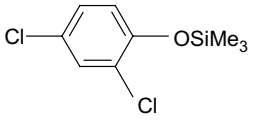
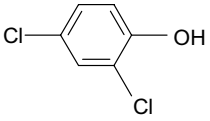
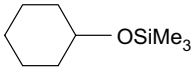
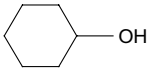
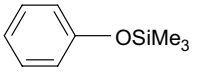
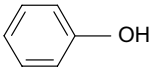
Entry	Starting mixture	Time (min)	Yield (%)[b]
1	2-Nitrobenzaldehyde	25	100
	Acetophenone		0
2	Hexanal	30	100
	Benzophenone		0
3	4-Bromobenzaldehyde	45	100
	Cyclohexanone		0

[a] Reactions were performed under room temperature using a 1:1 molar ratio of substrate to reducing agent.
[b] Yields refer to isolated product alcohols.

methods call for the use of an excess of the reagents and can result in over-reduction products.[15,16]

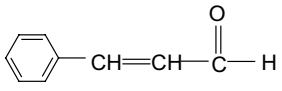
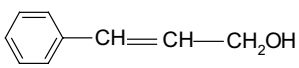
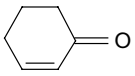
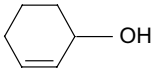
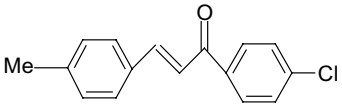
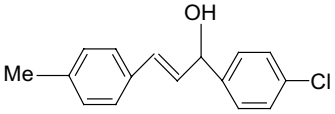
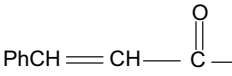
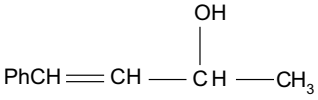
In addition, aliphatic and aromatic carboxylic acid esters are also reduced to the corresponding alcohols in excellent yields (Table 6). Nitriles, amides and nitro compounds are completely unaffected by this reagent. In order to show the advantages and the drawbacks of $(Ppyz)Zr(BH_4)_2Cl_2$ for the reduction of carbonyl groups, we compared our results with examples reported for other modified borohydride reagents (Table 7).

Table 4. Deprotection of trimethylsilyl ethers with $(Ppyz)Zr(BH_4)_2Cl_2$[a]

Entry	Substrate	Product	Time (h)	Yield (%)[b]
1	$PhCH_2CH_2OSiMe_3$	$PhCH_2CH_2OH$	3	93
2	$ClCH_2CH_2OSiMe_3$	$ClCH_2CH_2OH$	8	90
3			8	88
4			2	98[c]
5			9	98
6			4	95

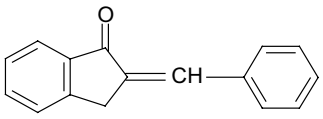
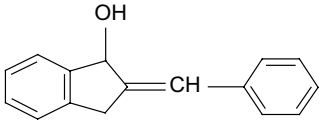
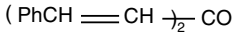
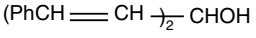
[a] Reactions were carried out at room temperature using a 1:1 molar ratio of substrate to reducing agent.
[b] Yields refer to isolated products.
[c] The reaction was conducted at reflux temperature.

Table 5. Regioselective reduction of α,β-aldehydes and ketones with $(Ppyz)Zr(BH_4)_2Cl_2$[a]

Entry	Substrate	Product	Time (h)	Yield (%)[b]
1			0.25	93[c]
2	Citral	$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2OH$	2	95[c]
3			3	90[c]
4			4	85
5			5	86

(*continued on next page*)

Table 5. (*continued*)

Entry	Substrate	Product	Time (h)	Yield (%)[b]
6			5	82
7			3	80

[a] Reactions were conducted in diethyl ether under reflux using a 1:1 molar ratio of substrate to reducing agent.
[b] Yields refer to isolated products.
[c] Room temperature.

Table 6. Reduction of esters with $(Ppyz)Zr(BH_4)_2Cl_2$[a]

Entry	Ester	Product	Time (h)	Yield (%)[b]
1	$CH_3COO(CH_2)_3CH_3$	CH_3CH_2OH	4	95
2	$CH_3COOC_2H_5$	CH_3CH_2OH	4	94
3	$PhCH_2COOC_2H_5$	$PhCH_2CH_2OH$	8	90
4	$PhCH_2COOCH_2Ph$	$PhCH_2CH_2OH$	8	92
5	$PhCH(COOC_2H_5)_2$	$PhCH(CH_2OH)_2$	9	90[c]
6	PhCOOPh	$PhCH_2OH$	8	50
7	$CH_3CH_2COOCH_3$	$CH_3CH_2CH_2OH$	4	90
8	$CH_3CH{=}CHCOOCH_3$	$CH_3CH{=}CHCH_2OH$	5	92

[a] Reactions were conducted in diethyl ether under reflux using a 1:1 molar ratio of substrate to reducing agent.
[b] Yields refer to isolated products.
[c] Using a 1:2 mole ratio.

Table 7. Comparison of $(Ppyz)Zr(BH_4)_2Cl_2$ with other zirconium borohydride reagents for the reduction of aldehydes and ketones to the corresponding alcohols

Entry	Substrate	$(Ppyz)Zr(BH_4)_2Cl_2$		ZrBDC[a]		$Cp_2Zr(BH_4)Cl$[b]		$[XP_4–Zr(BH_4)_4]$[c]	
		Time (h)/ yield (%)	Conditions	Time (h)/ yield (%)	Conditions	Time (h)/ yield (%)	Conditions	Time (h)/ yield (%)	Conditions
1	Benzaldehyde	1/97	Et_2O, rt	3.5/80 2/79	i-C_3H_7OH (Ref. 8) H_2O (Ref. 8)	—	—	4/96	THF, rt
2	4-Chlorobenzaldehyde	0.75/98	Et_2O, rt	2.2/92	i-C_3H_7OH (Ref. 8)	–/96	C_6H_6, rt	—	—
3	Cyclohexanone	2.5/90	Et_2O, reflux	2.8/86	i-C_3H_7OH (Ref. 8)	—	—	15/80	THF, rt
4	Phenylcinnamaldehyde	0.75/90	Et_2O, rt	2.7/92 0.7/90	i-C_3H_7OH (Ref. 8) H_2O (Ref. 8)	–/49	C_6H_6, rt	6/95	THF, rt
5	Acetophenone	8/95	Et_2O, reflux	8/90	H_2O (Ref. 8)	0.2/98	C_6H_6, rt	12/80	THF, rt

[a] Dichlorobis[1,4-diazabicyclo(2,2,2)octane]-(tetrahydroborato)zirconium.[8]
[b] Bis(cyclopentadienyl)chlorotetrahydroborato zirconium(IV).[4]
[c] Polyvinylpyridinium supported zirconium borohydride.[11]

In conclusion, $(Ppyz)Zr(BH_4)_2Cl_2$, unlike its unmodified form, zirconium borohydride, is a stable bench top reducing agent. Its mildness, chemo- and regio-selectivity and high reaction yields make this new reagent useful for organic synthesis.

Preparation of the zirconium borohydride–piperazine complex: A 500 mL round bottomed flask equipped with a magnetic pellet and fitted with a reflux condenser was flame dried under a stream of nitrogen. To this cooled assembly, a solution of zirconium tetrachloride (2.5 g, 8.91 mmol) in diethyl ether (15 mL) was added followed by a solution of lithium borohydride (1.2 g, 44.8 mmol) in diethyl ether (30 mL). The resulting mixture was stirred for 1 h at 0–5 °C and then centrifuged to give a clear ethereal solution. To this clear solution piperazine (0.6 g, 6.6 mmol) in dichloromethane (10 mL) was added dropwise. The white precipitate, which formed imme-

diately was filtered and washed several times with diethyl ether and dried to give a white stable powder in 96% yield.

General procedure for reduction of various organic compounds: To a solution of the substrate (1.0 mmol) in diethyl ether (10 mL) the reagent (1.0 mmol) was added and the mixture stirred at room temperature or under reflux for the specified time (Tables 1, 2, 4, 5 and 6).[6] The progress of the reaction was followed by TLC (eluent: CCl_4/diethyl ether). On completion of the reaction, the mixture was filtered and evaporated to obtain the pure product.

In a few cases, the crude products were purified by chromatography. The products were identified by comparison of their spectra and physical data with those of authentic samples.

Reduction of aldehydes versus ketones: To an equimolar amount of aldehydes and ketones (4.0 mmol) in diethyl ether (10 mL), the reagent (1.0 g, 4 mmol) was added and the reaction mixture was stirred at room temperature for the specified time (Table 3). The progress of the reaction was monitored by TLC or GC. On completion of the reaction, the mixture was purified on a silica gel plate.

References and notes

1. Marks, T. J.; Kolb, J. R. *Chem. Rev.* **1977**, *77*, 263–293.
2. Fleet, G. W. J.; Harding, P. J. C. *Tetrahedron Lett.* **1981**, *22*, 675–678.
3. Hutchins, R. O.; Marcowitz, M. *Tetrahedron Lett.* **1980**, *21*, 83–86.
4. Sorrell, T. N. *Tetrahedron Lett.* **1978**, *50*, 4985–4986.
5. Ranu, B. C.; Basu, M. K. *Tetrahedron Lett.* **1991**, *32*, 3243–3246.
6. Firouzabadi, H.; Adibi, N.; Zeynizadeh, B. *Synth. Commun.* **1998**, *28*, 1257–1273.
7. Tamami, B.; Mansour Lakouraj, M. *Synth. Commun.* **1995**, *25*, 3089–3096.
8. Firouzabadi, H.; Iranpoor, N.; Alinejad, H. *Synth. Commun.* **2002**, *32*, 3575–3586.
9. Maltseva, N. N.; Kedrova, N. S.; Gorobiskii, L. V.; Kuznetzof, N. T. *Russ. J. Coord. Chem.* **2000**, *26*, 232–234.
10. Narasimhan, S.; Balakumar, R. *Synth. Commun.* **2000**, *30*, 941–946.
11. Tamami, B.; Goudarzian, N. *J. Chem. Soc., Chem. Commun.* **1994**, 1079.
12. Lattle, D. A.; Jensen, E. H.; Sturck, W. A. *Anal. Chem.* **1952**, *24*, 1843.
13. (a) Rao, C. S.; Deshmuleh, A. A.; Patel, B. J. *Ind. J. Chem.* **1986**, *25B*, 626; (b) Bordaruah, M.; Barua, N. C.; Sharma, R. P. *Tetrahedron Lett.* **1987**, *28*, 5741–5742; (c) Ranu, B. C.; Chakraborty, R. *Tetrahedron Lett.* **1990**, *31*, 7663–7664; (d) Nakano, T.; Umano, S.; Kino, Y.; Ishii, Y.; Ogawa, M. *J. Org. Chem.* **1988**, *53*, 3752–3757.
14. (a) Ashbi, E. C.; Lin, J. J. *Tetrahedron Lett.* **1976**, *17*, 3865–3868; (b) Kim, S.; Moon, Y. C.; Ahn, K. H. *J. Org. Chem.* **1984**, *49*, 17–20.
15. (a) Krishnamurthy, S.; Brown, H. C. *J. Am. Chem. Soc.* **1976**, *94*, 7159–7162; (b) Fortunato, J. M.; Ganem, B. *J. Org. Chem.* **1976**, *41*, 2194–2200; (c) Luche, L. *J. Am. Chem. Soc.* **1981**, *103*, 5454–5459.
16. (a) Ranu, B. C.; Das, A. R. *J. Org. Chem.* **1991**, *56*, 4796–4798; (b) Mittakanty, M.; Peters, J. L.; Morse, K. W. *J. Org. Chem.* **1990**, *55*, 4464–4468; (c) Nutaitis, C. F.; Bernardo, J. E. *J. Org. Chem.* **1989**, *54*, 5629–5630; (d) Kaspar, J.; Trovanelli, A.; Lenarda, M.; Graziani, M. *Tetrahedron Lett.* **1989**, *30*, 2705–2706.