Selective Reduction of Carbonyl Compounds with *B*-Trifluoromethanesulfonyldiisopinocampheylborane in Ethyl Ether

Jin Soon Cha[a]

Department of Chemistry, Yeungnam University, Gyongsan 712-749, Korea. E-mail: jscha@yu.ac.kr
Received March 11, 2009, Accepted June 4, 2009

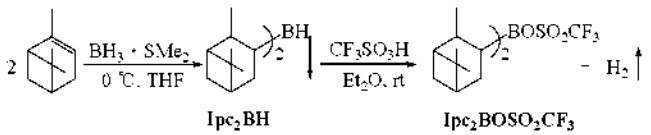
Key Words: *B*-Trifluoromethanesulfonyldiisopinocampheylborane, Reduction of aldehydes and ketones. **MPV**-type reduction, Selective reduction, $Ipc_2BOSO_2CF_3$

In the previous reports,[1-4] we showed that Lewis acidity of trisubstituted borane derivatives, a series of new Meerwein-Ponndorf-Verley (**MPV**) type borane reagents, plays a role in part on their reactivity toward the reduction of carbonyl compounds: for example, the strong electron-withdrawing effect of fluorine substituent of *B*-trifluoroacetoxydiisopinocampheylborane ($Ipc_2BO_2CF_3$) makes it much more reactive than Ipc_2BOAc itself. This phenomenon strongly indicates the reaction proceeds by the activation of carbonyl group through coordination of Lewis acidic boron atom followed by hydride transfer from β-hydrogen source to the carbonyl acceptor *via* the six-membered transition state, quite similar to the mechanism which is generally accepted in the original **MPV** reaction using aluminum isopropoxide.[5]

From such mechanistic point of view, we extended to design other derivative *B*-trifluoromethanesulfonyldiisopinocampheylborane ($Ipc_2BOSO_2CF_3$). Evidently, trifluoromethanesulfonyl group is one of the strongest electron-withdrawing ones. Accordingly, we examined the general reducing characteristics of the reagent in order to understand its nature and explore its role in organic synthesis.

Results and Discussion

$Ipc_2BOSO_2CF_3$ was prepared by hydroboration of α-pinene with borane-methyl sulfide followed by treatment with trifluoromethanesulfonic acid in Et_2O (Eq. 1).



(1)

The reactivity of $Ipc_2BOSO_2CF_3$ toward some representative aldehydes and ketones in Et_2O was examined, and the results are summarized and compared with those obtained by $Ipc_2BO_2CF_3$ in Table 1. As shown in the Table, $Ipc_2BOSO_2CF_3$ readily reduced a variety of aldehydes and ketones examined to the corresponding alcohols at 0 °C. The reactivity of the reagent toward carbonyl compounds is quite comparable to that of $Ipc_2BO_2CF_3$ reacted in Et_2O.[2] As in the reaction of $Ipc_2BO_2CF_3$, the reactivity of $Ipc_2BOSO_2CF_3$ in Et_2O appeared to be much stronger than that in THF. In general, the reduction of aldehydes by $Ipc_2BOSO_2CF_3$ is much faster than that of

Table 1. Reaction of Aldehydes, Ketones and other Functional Compounds with *B*-Trifluorodiisopinocampheylborane ($Ipc_2BOSO_2CF_3$) in Ethyl Ether at 0 °C[a]

Compound	Time (h)	Yield of alcohol (%)[b]	
		$Ipc_2BOSO_2CF_3$	$Ipc_2BO_2CCF_3$[c]
hexanal	0.5	100	99
	1	100	99,74[d]
benzaldehyde	0.5	99	99
	1	99	99
o-tolualdehyde	0.5	100	89
	1	100	95
	3		99
	6		99
p-chlorobenzaldehyde	0.5	99	96
	1	99	98
	3		99
p-methoxylbenzaldehyde	0.5	100	100
	1	100	100
2-naphthaldehyde	0.5	99	98
	1	98	99
	3		99
2-butanone	0.5	100	100
	0.5	79	61
2-heptanone	6	99	95
	24	99	95
	48		99
acetophenone	0.5	97	97
	6	98	97
	24	99	98
hexanoyl chloride	6	1	0
ethyl caproate	12	0	0
benzonitrile	24	0	0

[a]Ten % excess utilized. [b]GC yield with a suitable internal standard. [c]*B*-Trifluorodiisopinocampheylborane. The data cited from ref. 2. [d]Isolated yield on distillation.

[a]This article is dedicated to the memory of Professor Nung Min Yoon, a pioneer in the field of hydride reduction, who passed away in April 1, 2009. The author keeps in mind his warm-hearted guidance during the graduate school years.

Table 2. Reaction of α, β-Unsaturated Aldehydes and Ketoness with $Ipc_2BOSO_2CF_3$ in Ethyl Ether at 0 °C[a]

Compound	Time (h)	Yield of allylic alcohol (%)[b]
crotonaldehyde	0.5	100
2-hexenal	0.5	98
	1	100,75[c]
cinnamaldehyde	0.5	99
	1	100,93[d]
isophorone	1	85
	3	100
chalcone	3	69
	6	97
	24	99

[a]Ten % excess reagent utilized. [b]The purity of all allylic alcohol products is absolutely 100%, determined by GC. [c]Isolated yield on distillation. [d]Isolated yield by chromatography.

Table 3. Stereochemistry in the Reduction of Representative Cyclic Ketones with $Ipc_2BOSO_2CF_3$ in Ethyl Ether at 0 °C[a,b]

Compound	Time (h)	Total yield of alcohol (%)	Ratio of more stable isomer (%)[c]
2-methylcyclohexanone	0.5	98	46[d]
	1	100	46
3-methylcyclohexanone	0.5	98	48[e]
	1	100	48
4-methylcyclohexanone	0.5	100	49[d]
norcamphor	0.5	100	88[f]
camphor	1	71	92[g]
	24	92	93
	72	96	93
	120	100	93

[a]Ten % excess reagent utilized. [b]Determined by GC. [c]Normalized. [d]*Trans* isomer. [e]*Cis* isomer. [f]*Endo* isomer. [g]*Exo* isomer.

ketones : most aldehydes are reduced completely within 1 h at 0 °C, whereas ketones require a much longer reaction time under the same reaction conditions. However, $Ipc_2BOSO_2CF_3$ as well as $Ipc_2BO_2CF_3$[2] exhibited no reactivity toward acid chlorides, esters and nitriles, making possible the chemoselective reduction of carbonyl compounds in the presence of such inert compounds.

$Ipc_2BOSO_2CF_3$ can also convert α,β-unsaturated aldehydes and ketones cleanly to the corresponding allylic alcohols at 0 °C, the selectivity being absolutely perfect as summarized in Table 2.

Such a perfect regioselectivity in the reduction of α,β-unsaturated carbonyl compounds in one of the common and unique features achieved by diisobutylaluminum and diisopinocampheylboron derivatives,[3] apparently due to the unique reaction mechanism as proposed in the **MPV** type reactions.[3,5]

Finally, the reagent was applied to the reduction of representative cyclic ketones and its stereochemistry was examined (Table 3). The reagent readily reduced all the cyclic ketones examined at 0 °C. However, the stereoselectivity in the reduction appears to be insignificant, showing a quite simple result in similar to that obtained by $Ipc_2BO_2CF_3$.[2]

In conclusion, $Ipc_2BOSO_2CF_3$ appears to be one of the useful **MPV** type agents, showing a possibility for chemo- and regioselective reduction. The reagent shows a quite strong reactivity toward aldehydes and ketones, but no reactivity toward most other organic functional groups. In addition, the reagent nicely converts α,β-unsaturated aldehydes and ketones to the corresponding allylic alcohols with a perfect purity. Because of the easy preparation of the reagent using commercially available chemicals, it should find a role in organic syntheses.

Experimental Section

All glassware used in this study was predried at 140 °C for at least 9 hours, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reactions were performed under a dry N_2 atmosphere. All chemicals used were commercial products of the highest purity available, which were further purified by standard methods before use. THF and Et_2O were distilled from sodium-benzophenone ketyl prior to use. Gas chromatographic analyses were carried out with a varian 3300 chromatograph using a 10% Carbowax 20 M capillary column (30 m).

Preparation of *B*-Trifluoromethanesulfonyldiisopinocampheylborane ($Ipc_2BOSO_2CF_3$). To an oven-dried, 100-mL flask with a sidearm and a reflux condenser leading to mercury bubbler were added 2.5 mL of BMS (10 M, 25 mmol) and 2 mL of THF. It was cooled to 0 °C, and 8.5 mL (52.5 mmol) of α-pinene was added dropwise with stirring. After the complete addition of α-pinene, the stirring was stoped and the flask was stored at 0 °C for 6 hrs. The supernatant solution was decanted by using a double-ended needle. The crystalline lumps of Ipc2BH was suspended in Et_2O (10 mL), and to this was added 5.5 mL of a 5.0 M solution of trifluorometanesulfonic acid (27.5 mmol) dropwise with stirring. An equivalent of hydrogen gas was evolved immediately. Then the solution was diluted with Et_2O to be 1.0 M.

General Reduction of Carbonyl Compounds with $Ipc_2BOSO_2CF_3$. The reaction of hexanal with $Ipc_2BOSO_2CF_3$ is illustrative. An oven-dried, 50-mL flask, fitted with a sidearm and a bent adapter connected to a mercury bubbler, was charged with 2.5 mL of a 2.0 M solution of hexanal (5 mmol) in Et_2O and dodecane as an internal standard. The solution was maintained in a circulating bath at 0 °C. To this was added 5.5 mL of a stock solution of $Ipc_2BOSO_2CF_3$ (5.5 mmol) in Et_2O with stirring. At the appropriate time intervals, an aliquot (*ca.* 1 mL) was withdrawn, and the mixture was quenched by addition of NaOH (3 N, 2 mL). The organoborane was then oxidized by addition of 30% H_2O_2 (1 mL). The aqueous layer was saturated with K_2CO_3 and the organic layer was dried over anhydrous $MgSO_4$. The organic layer was then subjected to gas chromatographic analysis.

Isolation of Alcohol Products. The following procedure is illustrative for isolation of product alcohols on distillation. In the assembly previously described was placed 30 mmol of carbonyl compound to be reduced in 15 mL of Et_2O and the solution was maintained in a circulating bath at 0 °C. Into the silution was injected 33 mL of a stock solution of $Ipc_2BOSO_2CF_3$

(33 mmol) in Et_2O with stirring, and the reaction mixturewas stirred for the appropriate time of interval. The mixture was then quenched with 3 *N* NaOH (16 mL) and the organoborane derivative was oxidized by addition of 30% H_2O_2 (8 mL). The aqueous layer was saturated with NaCl. The separated organic layer was dried over anhydrous K_2CO_3. The solvent was evaporated under reduced pressure and a careful fractional distillation gave a desired product. The purity of the product was further confirmed by GC.

The following procedure is representative for isolation of product alcohols by column chromatography. In the assembly was placed 0.61 g of cinnamaldehyde (5 mmol) in 2 mL of Et_2O and the flask was maintained in a circulating bath at 0 °C. Into the flask was injected 5.5 mL of a stock solution of $Ipc_2BOSO_2CF_3$ (5.5 mmol) in Et_2O with stirring, and the reaction mixture was stirred for 1 h. The mixture was then quenched with 3 *N* NaOH (2 mL) and the organborane was oxidized by addition of 30% H_2O_2 (1.5 mL). The solvent was removed under reduced pressure and the impure product was chromatographed on a column of silica gel using a mixture of hexane : ethyl acetate (10 : 1) as eluent to afford 0.62 g (93%). The purity of product was confirmed by GC.

References

1. Cha, J. S.; Nam, H. T.; Jang, S. H.; Kwon, S. Y.; Park, S. J.; Kwon, O. O. *Bull. Korean Chem. Soc.* **2004**, *25*, 1948.
2. Cha, J. S.; Nam, H. T.; Park, S. J.; Kwon, S. Y.; Kwon, O. O. *Ibid.* **2006**, *27*, 667.
3. Reviews for **MPV** reduction, see: (a) Cha, J. S. *Org. Process & Devel.* **2006**, *10*, 1032. (b) Cha, J. S. *Bull. Korean Chem. Soc.* **2007**, *28*, 2162.
4. Cha, J. S.; Yu, S. J.; Roh, M. Y.; Park, S. J.; Yi, J. E.; Kwon, O. O. *Bull. Korean Chem. Soc.* **2008**, *29*, 885.
5. Cohen, R.; Graves, C. R.; Nguyen, S. T.; Martin, J. M. L.; Ratner, M. A. *J. Am. Chem. Soc.* **2004**, *126*, 14796.