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Dioxane–Monochloroborane: A New and Highly Reactive Hydroborating Reagent with Exceptional Properties

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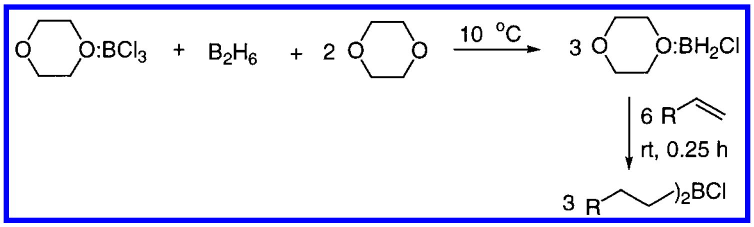
ABSTRACT



Dioxane–monochloroborane was prepared by the reaction of dioxane and dioxane–BCl$_3$ with diborane or NaBH$_4$ in 98% purity. The adduct thus obtained is a liquid, 6.2 M in BH$_2$Cl, stable indefinitely at either 0 or 25 °C. The adduct hydroborates simple unhindered olefins to the corresponding dialkylchloroboranes within 0.5 h, while moderately hindered olefins take 1–4 h at room temperature. Hindered tetrasubstituted olefins rapidly hydroborate to the monoalkylchloroborane stage with further hydroboration slow. Regioselectivity studies of representative olefins reveal that this new reagent possesses selectivities similar to those from the monochloroborane–diethyl ether adduct. Consequently, dioxane–monochloroborane can readily substitute for the older hydroborating agents, BH$_3$:THF and BH$_3$:DMS.

Hydroboration of alkenes using monochloroborane provides anti-Markovnikov hydroboration products in >99.5% isomeric purity,[1] unlike the simple borane reagents, such as BH$_3$:THF and BMS, which give a mixture of regioisomers.[2] These product dialkylchloroboranes are widely used for many synthetic transformations. For example, dicyclohexylchloroborane has been used as an enolizing agent for aldol type reactions,[3] while (+)- or (−)-Ipc$_2$BCl and Eap$_2$BCl reveal promising characteristics as chiral reducing agents.[4] The current monochloroborane adducts, such as dimethyl sulfide−monochloroborane and diethyl ether−monochloroborane, serve major needs in these applications. However, these reagents do suffer from some disadvantages. The dimethyl sulfide:BH$_2$Cl is a stable reactive adduct, but exists in equilibrium with dimethyl sulfide−BH$_3$ (12.5%) and dimethyl sulfide−BHCl$_2$ (12.5%). Also, the unpleasant odor of dimethyl sulfide poses significant environmental problems in large-scale operations. The diethyl ether:BH$_2$Cl adduct is free from these problems but can be obtained only in approximately 90% purity. Moreover, this reagent is unstable and must be freshly prepared before utilization.[5] The adduct, tetrahydrofuran−BH$_2$Cl, can be obtained in 98% purity; however, its slow reactivity and relatively rapid ring opening limits its applications.[5]

The increasing use of these monochloroborane reagents and the diverse applications of the product dialkylchloro-

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[1] (a) Brown, H. C.; Ravindran, N. *J. Org. Chem.* **1973**, *38*, 182. (b) Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1972**, *94*, 2112. (c) Brown, H. C.; Ravindran, N. *J. Org. Chem.* **1977**, *42*, 2533.

[2] (a) Brown, H. C.; Subba Rao, B. C. *J. Am. Chem. Soc.* **1959**, *81*, 6428. (b) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1960**, *82*, 4708. (c) Brown, H. C. *Organic Synthesis via Boranes*: Wiley: New York, 1975.

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[4] (a) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539. DIP chlorode is a trademark of Adrich Chemical Company, USA. (b) Brown, H. C.; Ramachandran, P. V.; Teodorovic, A. V.; Swaminathan, S. *Tetrahedron Lett.* **1991**, *32*, 6691. (c) Ramachandran, P. V.; Brown, H. C. In *Reductions in Organic Synthesis*; Abdel-Magid, A.F., Ed.; American Chemical Soceity: Washington, DC, 1996; Chapter 5.

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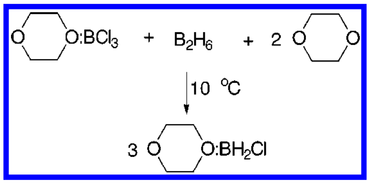
boranes in organic synthesis prompted us to investigate the possibilities of providing a more convenient reagent for these applications. Herein we report a new, highly pure, reactive monochloroborane:dioxane adduct for such applications. Moreover, dioxane−monochloroborane can readily substitute for the older hydroborating agents BH_3:THF and BMS.

Dioxane−BCl_3 was prepared by passing BCl_3 gas slowly into dioxane at 0 °C. The adduct thus obtained is a solid which melts at 56 °C (with decomposition), but is stable at 0 °C for several weeks. Reaction of this adduct with diborane in dioxane produces dioxane−BH_2Cl, as outlined in Scheme 1.

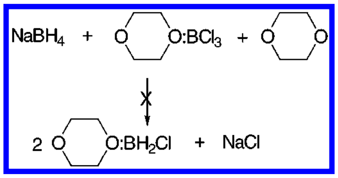
Scheme 1



The dioxane−BH_2Cl adduct thus obtained was 98% pure by ^{11}B NMR (+7.9, triplet). The adduct is a liquid, 6.2 M in BH_2Cl, with a hydrogen-to-chlorine ratio of 2.00:1.00. The stability of this adduct at 0 °C and room temperature (25 °C) was monitored using ^{11}B NMR examination of a sealed sample (2 M dioxane−BH_2Cl in dioxane) in an NMR tube, recording the ^{11}B NMR at intervals. It was also checked using active hydride analysis. Both of these studies did not show any detectable change over a period of one year.

To make the synthesis more convenient, the possibility was explored of synthesizing the dioxane−BH_2Cl complex using $NaBH_4$ and dioxane:BCl_3. However, the formation of dioxane−BH_2Cl was not achieved, as indicated by ^{11}B NMR, even after 3 days of stirring at room temperature (Scheme 2).

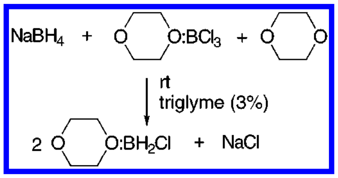
Scheme 2



Fortunately, addition of small catalytic amounts of triglyme changed the course of reaction dramatically, so that dioxane:BH_2Cl was conveniently prepared by taking appropriate amounts of $NaBH_4$ (10% excess), dioxane, dioxane:BCl_3, and 3 mol % of triglyme (Scheme 3).

Decantation of the clear supernatant layer provided dioxane:BH_2Cl of 98% purity. Interestingly, the ^{1}H NMR spectrum in $CDCl_3$ of dioxane:BH_2Cl thus obtained did not show the presence of triglyme. It is apparently absorbed by the precipitated sodium chloride. The adduct thus obtained is 6.3 M in BH_2Cl and is stable indefinitely both at 0 °C and at room temperature.

Scheme 3



Hydroboration of Representative Olefins with Dioxane−BH_2Cl. To examine the reactivity of this new adduct toward representative olefins, hydroboration studies using dioxane:BH_2Cl were carried out in dioxane and in dichloromethane solvents. The hydroborations were carried out by the addition of an olefin in dioxane or dichloromethane to dioxane:BH_2Cl at 0 °C, followed by further stirring as the reaction mixture was brought to room temperature. The final solution was 0.5 M in BH_2Cl and 1 M in the olefin. Representative olefins such as 1-decene, 2-methyl-1-pentene, *cis*-4-methyl-2-pentene, 2-methyl-2-butene, β-pinene, cyclohexene, α-pinene, 3-carene, 1-phenyl-2-methyl-1-propene, 2,3-dimethyl-2-butene, and 1,2-dimethylcyclopentene were utilized. The progress of these hydroboration reactions was monitored by ^{11}B NMR and hydride analysis of the residual active hydride present by removing aliquots at intervals and measuring the hydrogen evolved by injecting them into a

Table 1. Hydroboration of Representative Olefins Using Dioxane−BH_2Cl in Dioxane and Dichloromethane at Room Temperature[a]

olefin	reaction time (h) in dioxane	hydride used[b] (equiv)	reaction time (h) in CH_2Cl_2	hydride used[b] (equiv)
1-decene	0.25	2.00	0.25	2.00
2-methyl-1-pentene	0.25	2.00	0.25	2.00
cis-4-methyl-2-pentene	0.25	2.00	0.25	2.00
2-methyl-2-butene	0.50	2.00	0.50	2.00
β-pinene	0.25	2.00	0.25	2.00
cyclohexene	0.50	2.00	0.50	2.00
3-carene	0.50	2.00	1.0	2.00
α-pinene	0.50	1.92	0.50	1.82
	1.0	2.00	1.50	2.00
2-methyl-1-phenyl-1-propene	0.25	1.00	0.50	1.00
	4.0	1.82	4.0	1.76
2,3-dimethyl-2-butene	0.25	1.18	0.50	1.18
	48.0	1.76	48.0	1.68
1,2-dimethylcyclopentene	0.50	1.00	0.50	1.00
	48.0	1.62	48.0	1.54

[a] All reactions were carried out in solutions of dioxane or dichloromethane which were 1.00 M in olefin and 0.50 M in BH_2Cl (the olefin was used in small excess (5%)). [b] Hydride analysis was carried out by hydrolyzing an aliquot with a 1:1 mixture of glycerol−water and measuring the hydrogen evolved.

Table 2. Products from Hydroboration−Oxidation of Representative Olefins with Dioxane−BH_2Cl in Dioxane

olefin	products[a]	relative yield (%) of products with dioxane:BH_2Cl[b]	relative yield (%) of products with $(C_2H_5)_2O$: BH_2Cl
1-octene	1-octanol	100	99.5
	2-octanol	0.0	0.5
2-methyl-1-butene	2-methyl-1-butanol	99.5	99.9
	2-methyl-2-butanol	0.5	0.1
2-methyl-2-butene	3-methyl-2-butanol	99.1	99.7
	2-methyl-2-butanol	0.9	0.3
styrene	2-phenyl-ethanol	95.0	96.0
	1-phenyl-ethanol	5.0	4.0
α-methylstyrene	2-phenyl-1-propanol	99.6	100
	2-phenyl-2-propanol	0.4	0.0
cis-4-methyl-2-pentene	4-methyl-2-pentanol	59.0	60.0
	2-methyl-3-pentanol	41.0	40.0

[a] The combined yields of the alcohol products were quantitative (≥99%) by GC analysis. [b] The relative yields of the product alcohols were obtained by GC analysis (Varian-3300) using a Carbowax column with an internal standard.

glycerin−water mixture. The mono-, di-, and some trisubstituted olefins were hydroborated rapidly to the corresponding dialkylchloroborane stage within 0.5 h. The more hindered olefins were rapidly hydroborated to the monoalkyl stage, with further hydroboration proceeding slowly. The results are presented in Table 1.

In the hydroboration of less hindered olefins using dioxane: BH_2Cl, only the corresponding dialkylchloroboranes[6] were obtained as observed by the ^{11}B NMR value (∼+75 ppm). These product dialkylboranes, being bulkier than BH_2Cl, do not complex with dioxane. Consequently, they can be used for further synthetic applications without any problem. Methanolysis of these products gave *B*-methoxydialkylboranes cleanly (∼+54 ppm). However, in the hydroboration of hindered olefins such as 2,3-dimethyl-2-butene and 1,2-dimethylcyclopentene, considerable amounts of the monoalkylchloroboranes were also formed.

Regioselectivity Studies in the Hydroboration of Representative Olefins Using Dioxane−Monochloroborane. In continuation of the hydroboration studies with dioxane−BH_2Cl, regioselectivity studies in hydroboration of some representative olefins were carried out. Hydroborations were carried out using dioxane−BH_2Cl (3 mmol) and an olefin (6 mmol) in dioxane. The olefin was added at 0 °C and the reaction mixture further stirred at room temperature. At the reaction time indicated (Table 1), the reaction mixture was oxidized using alkaline hydrogen peroxide. The ratio of the product alcohols was established by GC analysis using a Carbowax column with an internal standard. Table 2 summarizes the results. Earlier results obtained in a similar study using monochloroborane−ethyl etherate are included for comparison.[1a]

The present study clearly demonstrates that the new dioxane:BH_2Cl adduct is free of the problems that are associated with the reagents currently used and that clean hydroborations can be readily achieved with selectivities similar to those reported for the earlier reagents. Thus this new reagent should serve as an eco-friendly substitute for the reagents currently available.

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(6) The synthesis and applications of such dialkylboranes are under investigation and will be reported subsequently.