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3-Butyl-1-methylimidazolinium borohydride ([bmim][BH_4])—a novel reducing agent for the selective reduction of carbon–carbon double bonds in activated conjugated alkenes

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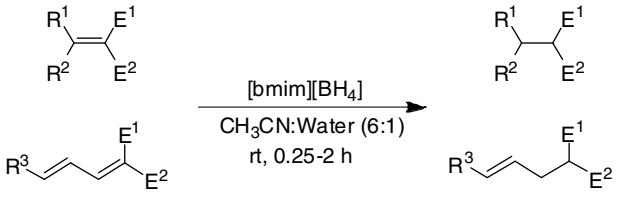
ABSTRACT

A novel ionic reducing reagent, 3-butyl-1-methylimidazolium borohydride ([bmim][BH_4]), was synthesized and successfully used for the selective reduction of carbon–carbon double bonds in conjugated alkenes as well as the α,β-carbon–carbon double bonds in highly activated α,β,γ,δ-unsaturated alkenes. The reagent can be regenerated and reused several times without losing its activity.

The selective reduction of carbon–carbon double bonds, especially conjugated double bonds, is a real challenge in organic synthesis. Typically, either a metal-containing catalyst or a complex reducing reagent is needed to obtain the target product in acceptable yield and selectivity. Examples of such reducing systems include resin supported formates-Pd catalyst,[1] combination of a formate reagent and palladium catalyst,[2] 1,4-dihydropyridine ester,[3] combination of sodium cyanoborohydride and acid,[4] indium metal,[5] combination of sodium borohydride and indium(III) chloride,[6] ruthenium complexes[7] and copper hydride complex.[8,9] Unfortunately, these methods are rather expensive and some may also have a negative environmental impact. Sodium borohydride has been traditionally used as a reducing agent for ketones,[10] aldehydes,[10] C–N double bonds,[11] alkenes,[12] esters,[13] carboxyls,[14] alkynes,[15] oximes[16] and nitryls.[17] It was reported that a few electron-deficient alkenes could also be reduced by sodium borohydride without any catalyst.[7d] But it required an extended reaction time (22 h) at 100 °C, which is obviously unsuitable for alkenes with sensitive groups. During our research on functionalized ionic liquids, a novel ionic reducing reagent, 3-butyl-1-methyl-imidazolium borohydride ([bmim][BH_4]), was synthesized and successfully applied to the reduction of carbon–carbon double bonds in conjugated alkenes as well as to the selective reduction of α,β-carbon–carbon double bonds in α,β,γ,δ-unsaturated dicyano compounds, cyanoesters and dicarboxylic esters at room temperature without any catalyst (Scheme 1). The reagent can be regenerated and recycled several times without losing its activity.

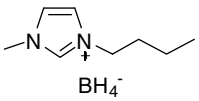
As shown in Scheme 2, 1-methylimidazole and 1-bromobutane were reacted at 80 °C for 3 h to form 3-butyl-1-methyl-imidazolium bromide. [bmim][BH_4] was then afforded by anion metathesis between 1-butyl-3-methylimidazolium bromide and sodium borohydride in anhydrous acetonitrile.[18] To avoid degradation, caution needs to be exercised to exclude moisture from [bmim][BH_4] in storage.

For the reduction of a conjugated alkene or an α,β,γ,δ-unsaturated alkene, 1.2 equiv [bmim][BH_4] was stirred with an alkene in the mixed solvent of acetonitrile and water (6:1) for a certain



R^1 = Ph, p-(MeO)-C_6H_4, m-(NO_2)-C_6H_4...
R^2 = H, alkyl.
R^3 = Ph, p-(MeO)-C_6H_4.
E^1 = CN, COOEt,$COOBu^n$
E^2 = H, CN, COOEt.

[bmim][BH_4]:



Scheme 1. Reduction of carbon–carbon bonds.

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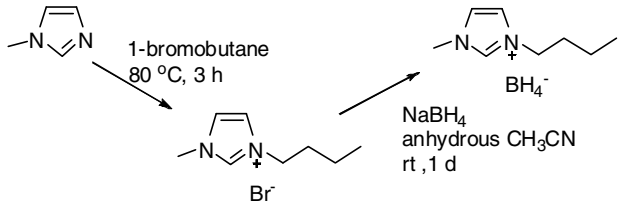
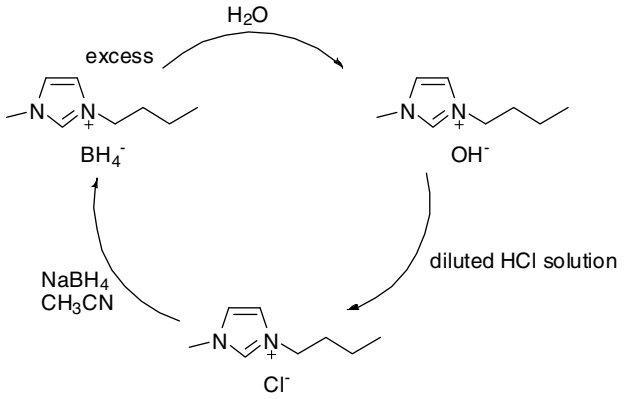


Scheme 2. Synthesis of ionic reducing reagent.

period of time (monitored by TLC) at room temperature. After removing the solvent in vacuo, the reaction mixture was quenched with water and the aqueous solution was extracted with ether. After removing the ether, the crude reduction product obtained was purified by column chromatography over silica gel.[19,20]

As shown in Table 1, a wide range of electron-deficient alkenes α-substituted by dicyano olefins, cyanoesters or dicarboxylic esters, could be reduced to their corresponding alkanes by [bmim][BH_4] in good yields (84–92%). While the carbon–carbon double bonds were efficiently reduced, sensitive groups such as NO_2 (entry 4), Cl (entry 5), MeO (entries 2, 8 and 9), methylenedioxy (entries 3 and 10) on phenyl, as well as the sensitive furan (entry 11) remained unaffected. Butyl acrylate (entry 18) can also be reduced to butyl propionate without any difficulty. [bmim][BH_4] was also applied to the reduction of highly activated α,β,γ,δ-unsaturated dienes (α-substituted by dicyano compounds, cyanoesters or dicarboxylic esters). Only the α,β-carbon–carbon double bond was reduced, and the corresponding γ,δ-unsaturated derivations were accessed in moderate to good yields (69–84%).

In a comparative study, butyl acrylate (entry 18) was treated with sodium borohydride in the mixed solvent of acetonitrile and water (6:1) at room temperature for 2 h. The yield of product was only 23%. 2-(3-phenylallylidene) malononitrile (entry 13) was treated with sodium borohydride in the solution of [bmim]Cl (2 mmol) in acetonitrile (1 ml) to demonstrate the possible activation of [bmim]Cl. The yield of product was only 42%. The high activity of [bmim][BH_4] may be due to its high solubility in organic solvents and good affinity for substrates.



Scheme 3. Regeneration of reducing reagent.

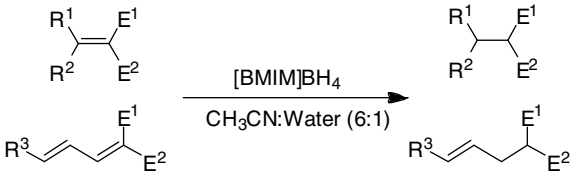
The reducing agent [bmim][BH_4] can be regenerated conveniently (Scheme 3). After extracting the reduction product from a quenched reaction mixture, the residue was neutralized with

Table 2
Reducing with regenerated [bmim][BH_4]

Cycle no.	1	2	3
Yield[a] (%)	86	84	85

[a] Isolated yields.

Table 1
Reduction of conjugated alkenes by [BMIM]BH_4



Entry	R^1	R^2	R^3	E^1	E^2	Time (min)	Yield[a] (%)
1	Ph	H		CN	CN	30	86 (0[b,6b])
2	*p*-(MeO)-Ph	H		CN	CN	20	92
3	3,4-Methylenedioxy-Ph	H		CN	CN	20	88
4	*m*-(NO_2)-Ph	H		CN	CN	15	85
5	2,4-Dichloro-Ph	H		CN	CN	15	84
6	Cyclohexylidene			CN	CN	50	88
7	Ph	H		CN	COOEt	40	85
8	*p*-(MeO)-Ph	H		CN	COOEt	30	90
9	3,4-Dimethyloxy-Ph	H		CN	COOEt	20	85
10	3,4-Methylenedioxy-Ph	H		CN	COOEt	30	87
11	α-Furanyl	H		CN	COOEt	30	86
12	2,4-Dichloro-Ph	H		COOEt	COOEt	60	85
13		H	Ph	CN	CN	50	82 (42,[c] 70[d])
14		H	*p*-(MeO)-Ph	CN	CN	45	84
15		H	Ph	CN	COOEt	70	75
16		H	*p*-(MeO)-Ph	CN	COOEt	70	78
17		H	Ph	COOEt	COOEt	90	69
18	H	H		H	COO-*n*-Butyl	120	88[e] (23[e,f])

[a] Isolated yields, all products were identified by ^{1}H NMR, ^{13}C NMR and GC–MS/HRMS.
[b] Reaction was conducted with sodium borohydride in acetonitrile.[6b]
[c] Reaction was conducted with sodium borohydride in the solution of [bmim]Cl (2 mmol) in acetonitrile (1 ml) for 50 min at room temperature.
[d] Reaction was conducted with [bmim]BH_4 in acetonitrile for 50 min at room temperature.
[e] Determined by GC.
[f] Reaction was conducted with sodium borohydride in CH_3CN/Water (6:1) for 2 h at room temperature.

diluted HCl solution to afford an aqueous solution of 3-butyl-1-methylimidazolinium chloride. The solution was then dehydrated in vacuo, followed by anion exchange with sodium borohydride in anhydrous acetonitrile to give the regenerated [bmim][BH_4]. In the demonstration reduction of 2-benzylidenemalono-nitrile, the regenerated [bmim][BH_4] can be reused at least three times without losing its activity (Table 2).

In conclusion, a new reducing reagent, 3-butyl-1-methylimidazolium borohydride ([bmim][BH_4]), has been synthesized and successfully applied to the chemoselective reduction of carbon–carbon double bonds in conjugated alkenes as well as to the selective reduction of the α,β-carbon–carbon double bonds in highly activated α,β,γ,δ-unsaturated alkenes. This method has the advantage of good reductive activity, room temperature reaction, no need for catalyst and easy reagent regeneration. Further work to apply this reducing reagent to other substrates is in progress.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.08.110.

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18. *General procedure for synthesis of [bmim][BH_4]*: A mixture of 1-methylimidazole (4.1 g, 0.05 mol) and 1-bromobutane (6.85 g, 0.05 mol) in absence of solvent was heated with stirring at 80 °C for 3 h. Then, the product was washed with dimethyl ether and dried in vacuum to afford [bmim]Br. On completion, 50 ml of CH_3CN and 2.28 g $NaBH_4$ (0.06 mol) were added in sequence. The mixture was stirred for 24 h at room temperature under nitrogen. After filtrating, the filtrate was evaporated in vacuo to get [bmim][BH_4] (7.39 g, 0.048 mol, yield 96%) as a viscous liquid: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.85 (s, 1H), 7.46 (s, 1H), 7.38 (s. 1H), 4.27 (t, J = 7.2 Hz, 2H), 4.05 (s, 3H), 1.85–1.92 (m, 2H), 1.32–1.41 (m, 2H), 0.94 (t, J = 7.6 Hz, 3H), −0.21–0.41 (4H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 137.29, 123.60, 122.12, 49.73, 36.52, 32.08, 19.36, 13.36; HRMS (ESI) calcd for $C_{16}H_{34}BN_4^+$ (2 M-BH_4^-) 293.2871, found 293.2897.
19. *General procedure for reduction*: (a) Representative procedure for the reduction of 2-benzylidenemalononitrile (Table 1, entry 1): To a stirred solution of 2-benzylidenemalononitrile (154 mg, 1 mmol) in acetonitrile (3 ml) and water (0.5 ml), [bmim][BH_4] (185 mg, 1.2 mmol) was added at room temperature. Stirring was continued for another 0.5 h (monitored by TLC), and the solvent was evaporated to leave water. Then, 10 ml water was added to the residue to quench the remaining [bmim][BH_4], and 10 ml diethyl ether was added to extract the organic compound for three times. The combined ether extract was washed with brine, dried (Na_2SO_4) and evaporated to leave the crude products which were purified by column chromatography over silica gel to furnish the pure 2-benzylmalononitrile (0.137 mg, 88%) as a white solid: ^{1}H NMR($CDCl_3$, 400 MHz): δ 7.33–7.43 (m, 5H), 3.92 (t, J = 7.0 Hz, 1H), 3.31 (d, J = 3.6 Hz, 2H); ^{13}C NMR ($CDCl_3$,100 MHz): δ 132.91, 129.31 (2C), 129.11 (2C), 128.84, 112.11 (2C), 36.78, 24.99; MS (GC/MS) m/z: 156(M^+), 91. This procedure was followed for the reduction of all the substrates listed in Table 1. (b) Procedure for the reduction of butyl acrylate (Table 1, entry 18,): To a stirred solution of butyl acrylate (0.128 mg, 1 mmol) and water (0.2 ml), [bmim][BH_4] (185 mg, 1.2 mmol) was added at room temperature. Stirring was continued for another 2 h. Then 5 ml water was added to quench the reaction, and 5 ml diethyl ether was added to extract the organic compound for three times. The combined ether extract was washed with brine, dried (Na_2SO_4) and evaporated to leave the crude products as a colourless liquid. The yield of product was 88% (GC).
20. *Characterization of the products*. Entry 14: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34 (d, J = 4.4 Hz, 2H), 6.88 (d, J = 4.4 Hz, 2H), 6.65 (d, J = 7.8 Hz, 1H), 6.01–6.08 (m, 1H), 3.79–3.83 (m, 4H), 2.89–2.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.95, 136.71, 128.29, 127.95, 127.88 (2C), 117.30, 114.14 (2C), 112.19, 55.33, 34.41, 23.55; MS (GC/MS) m/z: 212(M+), 147, 132, 115, 103, 91; HRMS (EI) calcd for $C_{13}H_{12}N_2O$ (M) 212.0950, found 212.0950. Entry 16: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.3 (d, J = 4.2 Hz, 2H), 6.86 (d, J = 4.2 Hz, 2H), 6.53 (d, J = 7.6 Hz, 1H), 6.00–6.08 (m, 1H), 4.28 (q, J_1 = 7.1 Hz, J_2 = 3.6 Hz, 2H), 3.82 (s, 3H), 3.61 (t, J = 6.4 Hz, 1H), 2.84 (t, J = 3.2 Hz, 2H), 1.32 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.57, 159.49, 134.42, 129.11, 127.63 (2C), 120.15, 116.19, 114.02 (2C), 62.88, 55.29, 38.06, 33.39, 14.03; MS (GC/MS) m/z: 259(M+), 147, 115, 91; HRMS (EI) calcd for $C_{15}H_{17}NO_3$ (M) 259.1208, found 259.1208.