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BUTYLTRIPHENYLPHOSPHONIUM TETRAHYDROBORATE (BTPPTB) AS A SELECTIVE REDUCING AGENT FOR REDUCTION OF ORGANIC COMPOUNDS

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ABSTRACT

Butyltriphenylphosphonium tetraborate (BTPPTB) (1) has been found to be a selective and versatile reducing agent. The reagent in dichloromethane solution or under solvent-free conditions is very useful for reduction of aldehydes, ketones, carboxylic acid chlorides, aryl azides, and aroyl azides to the corresponding alcohols, amines and amides, respectively.

Lithium borohydride and sodium borohydride are two extremes of nucleophilic hydride transfer agent. 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 may be observed with this reagent. Polar and protic solvents are needed. This reagent is able to reduce

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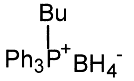
only a few functional groups, and a long reaction time is required. To increase or decrease the reactivity of $NaBH_4$, the modification of sodium borohydride has attracted a great deal of attention recently.[2–16]

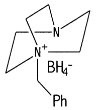
In general, modification of the usual reducing ability of the sodium borohydride has led to selective reduction of several functional groups that are otherwise inert to sodium borohydride alone. For instance, the reductions of acid chlorides to aldehydes,[4] and alkenes to saturated hydrocarbons[5] can be achieved by use of the combination of sodium borohydride with Cu (I) and Co (II), respectively, while such conversions cannot be achieved with sodium borohydride alone. Very recently, 1-benzyl-4-aza-1-azoniabiyclo[2.2.2]octane tetrahydroborate[2] has been reported for reduction of reducible organic compounds.[13–16]

We report the preparation of butyltriphenylphosphonium tetraborate (BTPPTB) (1) and reduction of reducible functional groups with this reagent. This reagent reduces reducible functional groups in CH_2Cl_2 at room temperature. It is quite soluble in CH_2Cl_2 and produces a clear solution that, on standing at room temperature, does not lose its reducing ability. This observation is in contrast to what is reported for tetrabutylammonium tetraborate. (Bu_4NBH_4), which decomposes to Bu_3N, BuH, and BH_3 on standing in solution.[17]. The stability of this reagent in comparison to Bu_4NBH_4 is the reflection of the presence of the phosphonium cation in the reagent that is more stable than ammonium cation. BTPPTB 1 reduces aldehydes, ketones, and carboxylic acids to their corresponding alcohols in high yield (Scheme 1 and Tab. 1). The reagent reduces benzylic and allylic aldehydes almost immediately. Reduction of saturated aldehydes and benzylic ketones with this reagent is much slower than benzylic and allylic aldehydes. $\alpha\beta$-Unsaturated carbonyl compounds are selectively reduced via 1,2-reduction.

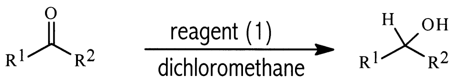


$$Ph_3\overset{\displaystyle Bu}{\overset{|}{P^+}}BH_4^-$$

(1)



(2)



Scheme 1.

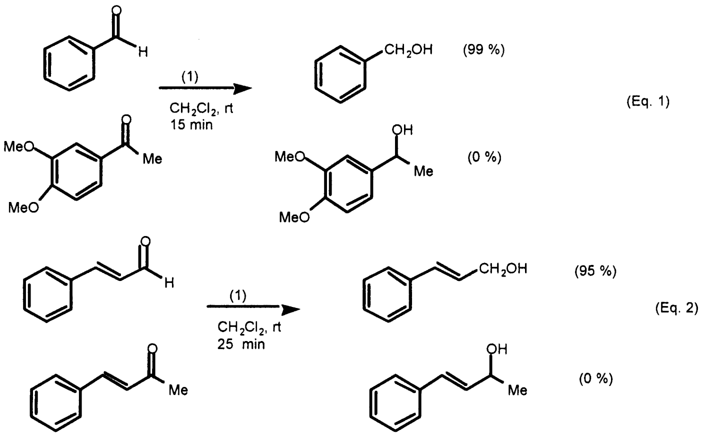
Another noteworthy advantage of this reaction lies in its selective reduction of aldehydes in the presence of other reducible functions such as ketones and double bonds. When we retreated an equimolar amount of aldehyde with **1** in the presence of ketone, only the aldehyde was selectively reduced (Eq. 1). The C=O groups of α,β-unsaturated aldehydes or α,β-unsaturated ketones were selectively reduced to the corresponding alcohols and the C=C double bonds remained intact (Tab. 1). To evaluate the

Table 1. Reduction of Carbonyl Compounds and Carboxylic Acid Chlorides to their Alcohols in CH_2Cl_2 at Room Temperature

Entry	R^1	R^2	Reaction Time (min)	Yield%[a,b]	M.p. or b.p.°C/mm Hg
1	C_6H_5	H	5	94	205
2	2-$MeOC_6H_4$	H	5	93	245–246/760
3	3-$MeOC_6H_4$	H	5	94	130–132/760
4	4-$MeOC_6H_4$	H	5	92	257–259/760
5	2-BrC_6H_4	H	7	90	78–80
6	4-BrC_6H_4	H	6	87	77–79
7	2-MeC_6H_4	H	5	89	35–36
8	4-MeC_6H_4	H	7	96	59–61
9	2-ClC_6H_4	H	5	91	69–71
10	3-ClC_6H_4	H	8	88	235
11	4-ClC_6H_4	H	5	90	70–71
12	2-$NO_2C_6H_4$	H	5	94	69–71
13	3-$NO_2C_6H_4$	H	7	91	30–32
14	4-$NO_2C_6H_4$	H	5	93	92–94
15	2,5-$(MeO)_2C_6H_3$	H	10	85	99–101/0.2
16	3,4-$(MeO)_2C_6H_3$	H	10	90	135–37/0.2
17	3,5-$(MeO)_2C_6H_3$	H	7	94	43–46
18	$(-CH_2-)_5$	—	50	95	22–24
19	$(-CH_2-)_4$	—	50	92	139–40/760
20	C_6H_5	CH_3	40	88	204/745
21	$(-CH_2-)_6$	H	55	90	82–85/10
22	$C_6H_5CH=CH$	H	5	90	33–35
23	$C_6H_5CH=CH$	Me	45	94	142–44/21
24	C_6H_5	Cl	5	94	202–205
25	$C_6H_5CH_2$	Cl	10	91	219–21/750
26	4-$NO_2C_6H_4$	Cl	5	93	92–93
27	$(-CH_2-)_6$	Cl	10	90	82–85/10

[a] All yields refer to pure isolated products; [b] All of the products were fully characterized by comparing with known compounds and by their IR and ^1H NMR spectra.

chemo- and regioselectivity of reagent **1**, another experiment was performed with equimolar amounts of α,β-unsaturated aldehyde or α,β-unsaturated ketone and reagent **1** (Eq. 2).



In recent years, organic reactions on solid supports[19,20] under solvent-free conditions have attracted attention.[21,22] The advantage of these methods over conventional homogenous reactions is that they provide greater selectivity, enhanced reaction rates, cleaner products, and manipulative simplicity.[23–29] Toda has reported the reduction of various ketones with $NaBH_4$ under solvent-free conditions. In those reports, a ten-fold molar ratio of $NaBH_4$ was mixed with ketone and kept in a dry box for 5 days.[30,31] This method does not show selectivity for the reduction of α,β-unsaturated carbonyl compounds, and also needs large excesses of the reducing agent and long reaction times. Very recently, Varma reported microwave-assisted reduction of carbonyl compounds under solid-state conditions using supported $NaBH_4$ on Al_2O_3. In that report, α,β-unsaturated carbonyl compounds were reduced to the corresponding saturated alcohols in 40% and allyl alcohol in 60% yields using 8 molar ratio of supported $NaBH_4$ on Al_2O_3 and microwave irradiation.[32]

In continuation of our ongoing program to develop environmentally benign methods using solid supports,[23–29] we tried the reduction of aldehydes, ketones, and carboxylic acid chlorides to the corresponding alcohols with reducing reagent **1** under solvent-free conditions. The reduction proceeded faster than in dichloromethane. The reaction was normally completed within 5–30 min grinding a mixture of aldehydes, ketones, or carboxylic acid chlorides with reagent **1**. The process in its entirety involves a simple mixing of aldehydes, ketones, or carboxylic acid chlorides with reagent **1**. The process in its entirety involves a simple mixing of aldehydes, ketones, or carboxylic acid chlorids with reagent **1**. The mixture was ground for the time specified in Table 2 at room temperature. The yields of the reactions are excellent (90–97%) and the reaction times are exceedingly short (1–20 min) (Tab. 2).

Table 2. Reduction of Carbonyl Compounds and Carboxylic Acid Chlorides to Their Alcohols Under Solvent-Free Conditions

Entry	R^1	R^2	Reaction Time (min)	Yield%[a,b]
1	C_6H_5	H	1	99
2	2-$MeOC_6H_4$	H	1	90
3	3-$MeOC_6H_4$	H	1	96
4	4-$MeOC_6H_4$	H	1	90
5	2-BrC_6H_4	H	1	95
6	4-BrC_6H_4	H	1	93
7	2-MeC_6H_4	H	1	94
8	4-MeC_6H_4	H	1	92
9	2-ClC_6H_4	H	1	90
10	3-ClC_6H_4	H	2	94
11	4-ClC_6H_4	H	1	90
12	2-$NO_2C_6H_4$	H	1	98
13	3-$NO_2C_6H_4$	H	1	92
14	4-$NO_2C_6H_4$	H	2	98
15	2,5-$(MeO)_2C_6H_3$	H	1	98
16	3,4-$(MeO)_2C_6H_3$	H	1	93
17	3,5-$(MeO)_2C_6H_3$	H	3	98
18	$(-CH_2-)_5$	—	10	90
19	$(-CH_2-)_4$	—	10	94
20	C_6H_5	CH_3	3	98
21	$(-CH_2-)_6$	H	5	93
22	$C_6H_5CH{=}CH$	H	1	92
23	$C_6H_5CH{=}CH$	Me	4	90
24	C_6H_5	Cl	1	93
25	$C_6H_5CH_2$	Cl	2	95
26	4-$NO_2C_6H_4$	Cl	1	90
27	$(-CH_2-)_6$	Cl	2	96

[a] All yields refer to pure isolated products; [b] All of the products were fully characterized by comparing with known compounds and by their IR and ^1H NMR spectra.

BTPPTB **1** is a highly selective reagent for the reduction of aryl azides and aroyl azides in CH_2Cl_2 at room temperature to the corresponding amines and amides, respectively (Scheme 2, Tab. 3). Quaternary ammonium tetraborates do not show such selectivity, e.g., benzyl azide is reduced with 1-benzyl-4-aza-1-azoniabiyclo[2.2.2]octane tetrahydroborate **2** and Bu_4NBH_4 in 10 and 5 h, respectively, with excellent yields.[13–18]

$$ArN_3 \xrightarrow[\text{dichloromethane}]{\text{reagent (1)}} ArNH_2$$

Scheme 2.

In conclusion, we have discovered a new and useful method for the reduction of aldehydes, ketones, and carboxylic acid chloride to their corresponding alcohols with reducing reagent **1** in high yield. The reaction proceeds in dichloromethane or under solvent-free conditions. Under solvent-free conditions, the yield of the reactions is higher and the reactions are faster. The reagent also reduces aryl azides and aroyl azides to their corresponding amines and amides, respectively, in high yields.

Table 3. Reduction of Aryl and Aroyl Azides to the in Corresponding Amines and Amides in CH_2CL_2 AT Room Temperature

Entry	Ar	Reaction Time (min)	Yield(%)[a,b]	M.p.°C
1	$4\text{-}NO_2C_6H_4$	1	97	147–149
2	$2\text{-}ClC_6H_4$	5	99	69–71
3	$4\text{-}NO_2\text{-}2\text{-}Cl\text{-}C_6H_3$	2	98	107–109
4	$4\text{-}EtO_2CC_6H_4$	10	92	88–90
5	$4\text{-}MeC_6H_4$	16	98	42–46
6	$C_6H_4CH_2$	—	no reaction	—
7	$C_6H_4CH(OH)CH_2$	—	no reaction	—
8	$2\text{-}ClC_6H_4CO$	20	97	167–170
9	$4\text{-}MeC_6H_4CO$	10	91	180–182
10	$4\text{-}NO_2C_6H_4CO$	8	81	165–67
11	$3,4(MeO)_2C_6H_3CH_2CO$	—	no reaction	—
12	$C_6H_4CH_2CO$	—	no reaction	—

[a] All yields refer to pure isolated products; [b] All of the products were fully characterized by comparing with known compounds and by their IR and ^1H NMR spectra.

EXPERIMENTAL

All products were identified by comparison with an authentic sample (IR, NMR, m.p. and b.p.). All m.p. were taken on a Gallenkamp melting apparatus and are uncorrected. Elemental analyses were performed by the Research Institute of Petroleum Industry, Tehran, I. R. Iran. ^{1}H NMR spectra were recorded on a Varian EM-390 NMR Spectrometer operating at 90 MHz, or a Varian Unity 250 Fourier Transform NMR Spectrometer operating at 250 MHz. ^{13}C NMR spectra were recorded on a Varian Unity 400 Fourier Transform NMR Spectrometer operating at 100 MHz. The spectra were measured in $CDCl_3$ unless otherwise stated, relative to TMS (0.00 ppm) Mass spectra were recorded on a Shimadzu GC-MS-QP 1000PX.

Synthesis of Reducing Agent (1)

To a solution of butyltriphenylphosphonium bromide (19.97 g, 50 mmol, 50 mL H_2O), was added sodium borohydride (1.89 g, 50 mmol) in one portion. The reaction mixture was stirred at room temperature for 90 m. The resulting white solid product was collected, washed with water (10 mL) and dried in a desiccator under vacuum over calcium chloride to yield 16.38 g (98%) of white solid product m.p. 270°–72°C. ^{1}H NMR: δ 7.90–7.50 (m, 15 H), 3.5 (d, **J** = 25.6 Hz, CH_2-P), 1.8 (m, 4 H), 0.98 (t, 3 H). ^{13}C NMR: δ 133.50, 133.20, 130.20, 129.60, 129.40, 128.10, 127.70, 127.2, 108.30 (d, **J** = 85.5 Hz, P-CH_2). IR (KBr): 1298, 1269, 1098, 1060, 700, 658, 590, 546 cm^{-1}. MS (CI) *m/z* 334 (100, M^+). Anal calc. for $C_{22}H_{28}BP$: C, 79.06; H, 8.44%. Found; C, 78.80; H, 8.80%.

Reduction of Aldeydes, Ketones, and Carboxylic Acid Chlorides to Their Corresponding Alcohols with Reducing Reagent (1) in Dichloromethane at Room Temperature

Aldehyde, ketone, or carboxylic acid chloride (1 mmol) was added to a stirred solution of reducing agent (**1**) (**1** mmol, 0.33 g) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature until TLC showed complete disappearance of the starting material, which required 5–60 min, depending on the substrate, and then the reaction mixture was washed with water (2×15 mL). The dichloromethane layer was dried over $MgSO_4$. Evaporation of the solvent gave the corresponding alcohols. The product was purified by column chromatography on silica gel using a mixture of ethyl acetate/n-hexane (10/90) as eluent.

Reduction of Aryl Azides and Aroyl Azides with Reducing Reagent (1) in Dichloromethane at Room Temperature

Azide (**1** mmol) was added to a stirred solution of reducing agent (**1**) (1 mmol, 0.33 g) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature until TLC showed complete disappearence of the starting material, which required 5–60 m depending on the substrate, and then the reaction mixture was washed with water (2×15 mL). The dichloromethane layer was dried over $MgSO_4$. Evaporation of the solvent gave the corresponding amines or azides. The product was purified by column chromatography on natural alumina using a mixture of ethyl acetate/n-hexane (30/70) as eluent.

Reduction of Aldehydes, Ketones, and Carboxylic Acid Chlorides to Their Corresponding Alcohols with Reducing Reagent (1) Under Solvent-Free Conditions

A mortar was charged with aldehyde, ketone, or carboxylic acid chloride and reducing reagent (**1**) (1 mmol, 0.33 g). The mixture was ground at room temperature with a pestle until TLC showed complete disappearance of the starting material. The mixture was then extracted with CCl_4 (2×10 mL). Evaporation of the solvent gave the corresponding alcohols. The product was purified by column chromatography on silica gel using a mixture of ethyl acetate/n-hexane (10:90) as eluent.

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