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S. Narasimhan [a], K. Ganeshwar Prasad [a] & S. Madhavan [a]
[a] Centre for Agrochemical Research, SPIC Science Foundation, 110 Mount Road, Guindy, Madras, 600 032, India
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CALCIUM BOROHYDRIDE: A REAGENT FOR FACILE CONVERSION OF CARBOXYLIC ESTERS TO ALCOHOLS AND ALDEHYDES

S. Narasimhan, K. Ganeshwar Prasad and S. Madhavan

Centre for Agrochemical Research, SPIC Science Foundation,
110 Mount Road, Guindy, Madras 600 032, India.

ABSTRACT: Calcium borohydride reduces both aliphatic and aromatic esters to alcohols completely in the presence of alkene catalysts. The intermediate borates formed during the reduction of aromatic esters are converted to aldehydes with aqueous NaOCl in good yields.

Sodium borohydride (SBH) is unreactive towards esters and similar functional groups- with aldehydes and ketones being the exceptions. The reactivity of sodium borohydride can be modified by varying the cation. Substituting a more covalent cation like Li^+ for Na^+ increases the solubility of the borohydride in simple ether solvents like Et_2O and THF. Lithium borohydride (LBH) thus formed reduces esters in both refluxing Et_2O and THF. The reducing power of lithium borohydride is well documented in literature[1].

$$NaBH_4 + MX = MBH_4 + NaX \quad (1)$$

$M = Li^+, Ca^{2+}, Zn^{2+}$ etc. $\qquad$ $X = Cl, Br$

Since lithium halides are expensive, to develop a metal borohydride which is affordable and also as reactive as lithium borohydride, we selected $CaCl_2$. The advantages of $CaCl_2$ being cheap, easy availability as a laboratory reagent and

reasonably dry, in the fused state. Calcium borohydride (CBH) solution in THF was prepared by a metathetical reaction, as in equation 1, between $CaCl_2$ and SBH as a 1.0M (or 2.0M) solution [2]. The solution thus made was found to retain a stable active hydride concentration over a period of six months when kept at room temperature under nitrogen atmosphere. The solution is freely miscible in water without any reaction, but reacts with methanol and dilute mineral acids to liberate hydrogen. CBH in THF reduces carboxylic esters under reflux, but the reaction is incomplete (Table 1). In contrast to lithium borohydride which reduced esters to alcohols in 4-8h, CBH proved to be a sluggish reductant. With CBH we observed that methyl-10-undecenoate was 'reduced' in 1h, to 1,11-undecanediol. Both LBH[3] and CBH[4] show similar behavior by hydroborating the double bond present in the ester.

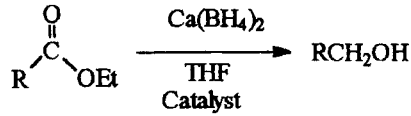
Table 1: Reduction of Representative Esters by $Ca(BH_4)_2$ in Refluxing THF.

Ester	Reaction (%)					
	0.25	0.5h	1.0h	2.0h	4.0h	6.0h
Methyl myristate	-	24	32	50	67[a]	85
Ethyl benzoate	4	11	14	43[b]	56[b]	
Methyl-10-undecenoate	-	-	100[c]			

[a] At 3h; [b] At 5h; [c] Gel formation; whole of the reaction mixture was quenched.

Previous studies on the reduction of esters with LBH revealed that addition of dilakyl borinates, such as B-methoxy-9-BBN, enhanced the rate of the reaction[5]. Since dialkyl borinates can be formed by hydroboration of alkene, we attempted to synthesize them *in situ* which would act as catalysts in the reduction of esters by CBH. Three different alkenes were investigated for their catalytic activity on the rate of reductions of methyl myristate and ethyl benzoate (Table 2).

Table 2: Rate and Stoichiometry data on the Reduction of Representative Esters by CBH



Ester R =	Catalyst (1mmol)	H^- consumed (mmol)/ mmol of ester						
		0.25h	0.5h	1.0h	2.0h	3.0h	4.0h	5.0h
$CH_3(CH_2)_{12}$-	No catalyst	0.32	0.48	0.69	1.07	1.2	1.42	1.51[b]
	1-Decene	0.66	0.98	1.22	1.49	1.70	1.73	2.05[b]
	Cyclohexene	0.69	0.78	1.25	1.41	1.65	1.74	1.82
	1,5-Cyclooctadiene	1.55	1.76	1.92	2.25	2.25		
C_6H_5-	No catalyst	0.08	0.22	0.27	0.48[a]	0.85	0.91	1.12
	1-Decene	0.5	0.74	0.83	1.46	1.66	1.82	1.95
	Cyclohexene	0.46	0.66	0.9	1.1	1.33	1.49	1.71
	1,5-Cyclooctadiene	0.38	0.75	0.9	1.38	1.79	2.25	2.25

[a]At 2.25h; [b] At 6h.

Of the three alkenes, COD proved to be the best catalyst, by enhancing the rate of the reduction ten times relative to the uncatalysed reaction, presumably due to the formation of 9-BBN borinate species which can exchange quite rapidly because of the thermodynamic stability of the 9-BBN moiety compared to dicyclohexyl borinate (lesser solubility in THF) and didecyl borinate (steric factors)[6]. Several esters have been reduced with CBH in the presence of 0.1 equivalent of COD and the rate & stoichiometry data are presented in Table 3. Aliphatic esters were reduced in 1h; aliphatic α,ω-diesters formed a gel on refluxing under afore

Table 3: Rate and Stoichiometry of Reduction of Esters By Calcium Borohydride Catalyzed by *cis, cis*-1,5-Cyclooctadiene[a]

Ester	Catalyst (mmol)	H^- Consumed (mmol)/ mmol of Ester					
		0.25h	0.5h	1.0h	2.0h	3.0h	4.0h
Methyl myristate	1	1.97		2.25	2.25	2.25	-
	0	-	0.47	0.63	1.01[f]		1.69[h]
Methyl laurate	1	1.42	1.60	1.89	2.08	2.08	
Dimethyl azelate[b]	1	-	-	4.3[c,e]	-	-	
Dimethyl brassylate[b]	1	-	-	4.4[c,e]	-	-	
Ethyl benzoate	1	1.04	1.20	1.37	1.47	1.56	1.80
	0	0.08	0.22	0.27		0.85	1.12[i]
Methyl-2-hydroxy	1	3.17	3.28	3.25	3.28[d]		
benzoate	0	2.41	2.60	2.77	2.8	2.9[d,g]	
Methyl-2-chloro	1	1.73	2.02	1.97	2.03		
benzoate	0		1.41	1.70	1.90	1.92[h]	2.07
Dimethyl terephthalate[b]	1	2.46	3.55	-	-	3.60[e]	
Methyl-4-nitro benzoate	1	1.71	2.19	-	-	-	
	0		1.78	1.91	2.07	2.07	
Methyl phenyl acetate	1	1.44	1.74	2.08	2.06	-	
	0	0.47	0.6	0.92	1.2	1.89	2.1

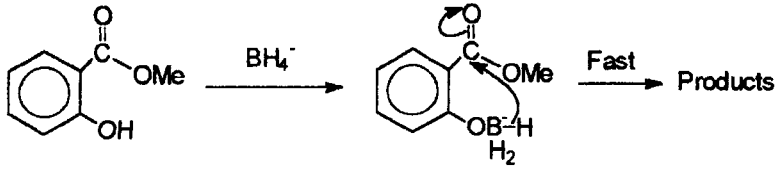
[a] $[BH_4^-]$ = 0.5M, [ESTER] = 0.25M, [COD] =0.05M;
[b] $[BH_4^-]$ = 0.5M, [ESTER] = 0.25M, [COD] =0.05M;
[c] Formation of white precipitate; [d] Includes hydride used for liberation of H_2;
[e] Whole of the reaction mixture was quenched with 2N H_2SO_4;
[f] At 1.75h; [g] At 3.5h; [h] At 2.5h.

mentioned conditions, yielding the diols after hydrolysis. The yield data is presented in Table 4. The aromatic esters with electron withdrawing groups were reduced faster due to the reduced electron density of the ester group which aids the hydride transfer from the BH_4^-. Electron donating groups like 4-hydroxy show very low reactivity towards reduction whereas 2-hydroxy group aid the reduction due to its close proximity to the ester functionality (Eqn. 2).

Table 4: Alcohols obtained from the Reduction of Esters by Calcium Borohydride Catalyzed by 1,5-Cyclooctadiene.

Compound	Reaction Time	Product	m.p.[a] °C	Yield [b] (%)
Methyl myristate	2h	Myristyl alcohol	38 (39)	80
Methyl laurate	2h	Lauryl alcohol	24 (24-6)	95 (100)
Dimethyl azelate	1h	1,9-Nonanediol	43 (46)	96 (100)
Dimethyl brassylate	1h	1,13-Tridecanediol	81 (81)	96 (100)
Ethyl Benzoate	4h	Benzaldehyde		(43)[c]
		Benzylalcohol		(57)[c]
Methyl-2-hydroxybenzoate	0.5h	2-Hydroxy benzylalcohol	(87)	95(100)
Methyl-2-chlorobenzoate	0.5h	2-Chlorobenzyl alcohol	72 (74)	98 (100)
Dimethyl terephthalate	2h	1,4-Benzenedimethanol	114(115)	75(81)
Methyl-4-nitro benzoate	3h	4-Nitrobenzyl alcohol	94(93)	76
Methyl-3-nitro benzoate	3h	3-Nitrobenzyl alcohol		75
Methylphenyl acetate	1h	2-Phenyl ethanol		96

[a] Literature melting points given in brackets; [b] Isolated yields; GC purity of crude product is given in brackets; [c] Yields based on HPLC analysis.



(2)

Synthesis of aldehydes from organoborates using PCC was reported by Brown *et al*[7]. In our search for cheaper and non-carcinogenic oxidant for the synthesis of aldehydes from organoborates, we tried aqueous solution of NaOCl -commercial bleach. Literature reports[8] on the use of this reagent suggested that it can be

Table 5: Oxidation of Aryloxy Borates by Sodium Hypochlorite.

Ester	Product	Yield (%)
Methyl Benzoate	Benzaldehyde	88
Methyl-2-chloro benzoate	2-Chloro benzaldehyde	88
Methyl-4-nitro benzoate	4-Nitro benzaldehyde	70
Dimethyl terephthalate	Benzene-1,4-dicarboxaldehyde	70
Methyl phenacetate	Phenethyl phenacetate	70

applied for the syntheses of aromatic aldehydes which do not contain any hydroxy substituents. After the reduction of the esters with calcium borohydride, the aryloxy borate formed was oxidized with a 10% aqueous solution of NaOCl in the presence of 10mol% of tetra butyl ammonium bromide. The reactions were complete in 2h at room temperature (Table 5). Oxidation of phenethyl borate yielded phenethyl phenacetate in 70% yield, probably by the auto-oxidation of the aldehyde formed.

Experimental Section:

Tetrahydrofuran was distilled from sodium under nitrogen, stored over sodium under nitrogen. Commercial sodium borohydride of 90% purity and laboratory grade fused $CaCl_2$ were used. All the esters were purified by conventional methods before use. The products were characterized by ^{1}H-NMR (HITACHI 60 MHz), MS (SHIMADZU GCMS QP-1000A; direct inlet) and IR (BRUKER FTIR IFS-85). The melting points are uncorrected. GLC analyses were performed on SHIMADZU GC-15A with 3% OV-17 on Supelcoport, 2metres SS column using FID and nitrogen as carrier gas. All glassware was flame dried after assembly or alternatively dried in an oven at 120 °C, assembled hot and cooled under a stream of nitrogen. All materials, sensitive to air and moisture were handled with hypodermic syringe following the reported procedures[9].

Preparation of Calcium Borohydride:

A pre-dried 500 ml sidearm flask fitted with a reflux condenser, connected to a mercury bubbler was charged with 11g (0.1mol) of freshly fused $CaCl_2$, followed by 200ml of THF using a double-ended needle. 7.6g (0.2 mol) of $NaBH_4$ was added under nitrogen blanket in one lot to the magnetically stirred suspension in the flask. The reaction mixture was refluxed for 24h with vigorous magnetic stirring. The rate of conversion was followed by quenching aliquots with 2N H_2SO_4 and estimating the hydrogen evolved using a gas burette. Active hydride concentration of the supernatant solution was found to be 3.5M (90% conversion). The clear supernatant solution was used for further reactions.

Procedure for rate study :

Reduction of methyl myristate is representative for the rate study.

A pre-dried 50ml side-armed flask fitted with reflux condenser was charged with 2.4g (0.010mol) of methyl myristate, 11.4 ml (0.01mol BH_4^-, 0.875M solution in THF) of $Ca(BH_4)_2$. The volume of the solution was adjusted to 40ml with dry THF. 0.123ml (0.001 mol) of cyclooctadiene was added and the reaction mixture was refluxed on an oil-bath . Aliquots were with drawn at suitable time intervals with a hypodermic syringe, residual hydride was quenched with 2N H_2SO_4, hydrogen liberated was estimated using a gas burette. From the value of the residual hydride, mmoles of hydride consumed per mmole of ester was calculated. The data is presented in Table 3. In a parallel reaction, after the reaction was complete MeOH was added to quench the residual hydride, anhydrous K_2CO_3 was added and the organic layer was decanted, residue extracted with THF (2x10ml). The combined extracts were dried over Na_2SO_4 and concentrated to yield the alcohol. The data is presented in Table 4.

Rate study without the added catalyst was performed under similar conditions. The data is presented in Table 3.

Preparation of Aldehydes:

Preparation of 2-chlorobenzaldehyde is representative.

0.78g (0.005mol) of methyl 2-chlorobenzoate was reduced with 2.3ml (0.00275mol of BH_4^-, 1.2M solution in THF) of $Ca(BH_4)_2$ and 0.06ml (0.0005mol) of cyclooctadiene at the reflux temperature of THF. The residual hydride was quenched with MeOH (0.5ml) and the solvent was stripped off at pump (40mm Hg). The residue was dissolved in 5ml $CHCl_3$ and 10ml of 10% aqueous solution of NaOCl (0.0134mol) containing 100 mg (0.0005mol) of $nBu_4N^+Br^-$ was added and stirred at room temperature. The reaction was followed by tlc. When the reaction was complete (ca. 2h), the organic layer was separated and the aqueous layer was extracted with 2x10ml of $CHCl_3$. The combined organic extracts were dried over Na_2SO_4 and the solvent was removed under reduced pressure to yield 0.6g (85%) of the pure 2-chlorobenzaldehyde.

The results with other esters are presented in Table 5.

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