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Journal of Macromolecular Science, Part A

Publication details, including instructions for authors and subscription information:

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To cite this Article Domb, A. and Avny, Y.(1985) 'Reduction of Carbonyl Compounds by Cross-Linked Poly(4-vinylpyridine)-Borane in Acidic Media', *Journal of Macromolecular Science, Part A*, 22: 2, 183 – 201

To link to this Article: DOI: 10.1080/00222338508063305

URL: <http://dx.doi.org/10.1080/00222338508063305>

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Reduction of Carbonyl Compounds by Cross-Linked Poly(4-vinylpyridine)-Borane in Acidic Media

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ABSTRACT

Cross-linked poly(4-vinylpyridine)-borane was successfully used for the reduction of aldehydes and ketones to the corresponding alcohols. Reduction was carried out in protic and aprotic acidic media at room temperature. Polymer reactivity depends on solution pH. Due to the relative high hydrolytic stability of the borane-bound polymer, reduction can be carried out in pH 1 buffer solution and in acetic acid. A low degree of cross-linking did not affect the polymer reactivity. Complete reduction of carbonyl compounds can be reached in the presence of excess of borane-bound polymer at a 1:1 reactants molar ratio. Only two of the borane hydrides are available for reduction; the third one is consumed by hydrolysis of the partially reacted borane derivatives formed during and after reduction. The chemoselectivity in the competitive reduction of cyclohexanone and other ketones as well as acetophenone and benzaldehyde with cross-linked poly(4-vinylpyridine)-borane was investigated. The cross-linked polymer borane was found to be a much better chemoselective reduction agent than its low molecular weight analog pyridine-borane. Chemoselectivity of this polymer is as good as that of available low molecular weight chemoselective reduction agents.

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INTRODUCTION

Hydride-delivering polymers are of interest as polymeric reagents which can be used for reduction of carbonyl compounds. In these polymers hydride-containing functional groups are part of the polymer segment, or part of a molecule which is chemically bound to the polymer. When reacted, the reduction capability of these polymers can be regenerated. Such polymers are: anion-exchange resins having borohydride [1] and cyanoborohydride [2] counterions, polymers containing organotin dihydride groups [3], and borane-bound polymers in which borane is complexed by sulfide [4] and amine groups [5-9]. Special attention was given to the use of borane-bound polymers derived from 4-vinylpyridine and 2-vinylpyridine. Hallensleben [5] reported the use of linear and cross-linked copolymers of the 4-vinylpyridine-borane complex for reductions of aldehydes and ketones to the corresponding alcohols. These polymers gave low yields of reduction in refluxing benzene. Better results, under milder conditions, were reported by Menger et al. [6]. When poly(2-vinylpyridine)-borane reacted in benzene in the presence of a Lewis acid, boron trifluoride etherate, which facilitated reduction by complexing with the carbonyl oxygen, high reduction yields of aldehydes and ketones were obtained. Low yields were reported for the reduction of benzoic acid, methyl benzoate, and benzoyl chloride with this polymer. It was reported, too, that poly(4-vinylpyridine)-borane reacted sluggishly with carbonyl compounds. Only after partial alkylation of this polymer was good reduction yield obtained. An increase in polymer accessibility due to conformational changes caused by an enhanced positive charge on the alkylated polymer as well as structural changes resulted from the presence of the alkyl groups and were responsible for the increase in poly(4-vinylpyridine)-borane reactivity [6]. The use of homo and cross-linked poly(4-vinylpyridine)-borane for reduction of carbonyl compounds in water or polar organic solvents in the presence of strong mineral acid was not investigated. Acidic media does not prevent the use of pyridine-borane as a reduction reagent [10]. Thus, for example, oximes [11], heterocyclic compounds [12], and carbon-nitrogen double bond [13] were reduced by pyridine-borane in the presence of acid. It was also reported that this reagent reduced aldehydes and ketones in trifluoroacetic acid [14, 15].

The kinetics and mechanism of carbonyl reduction by low molecular weight amine borane in acidic aqueous media were investigated by Kelley et al. [16-19]. The reduction of carbonyl compound by transfer of hydrogen from boron to the carbonyl carbon can occur by two pathways, one independent of, and the other first-order in, hydrogen ion:

$$-\frac{d[\text{amine-borane}]}{dt} = [\text{amine-borane}][\text{RCOR}'] [k_1 + k_2 (\text{H}_3\text{O}^+)] \quad (1)$$

k_1 is an acid-independent reaction rate constant, and k_2 is an acid-dependent reaction rate constant.

In the acid-independent reaction path, attack of the amine-borane on the ketone is the rate determining step with concurrent or subsequent hydride transfer from boron to carbon. The carbonyl compound and the solvent compete on the remaining two hydrides. A four-center transition state has been proposed for that reaction path. In the acid-catalyzed reaction the attack of amine-borane on a protonated carbonyl is the rate determining step.

Some low molecular weight amine-boranes show high chemoselectivity in the reduction of a variety of aldehydes and ketones under mild conditions in most organic and protic solvents. Amine boranes 9-borabicyclo[3.3.1]nonane-pyridine complex [20], di-n-butyl-9-borabicyclo[3.3.1]nonane "ate" complexes [21], ammonia-borane, and t-butylamine-borane [22, 23] are among the few reagents [20-27] capable of reducing an aldehyde from a reactive ketone such as cyclohexanone. An easily prepared borane-bound polymer such as cross-linked poly(4-vinylpyridine)-borane, which will show similar chemoselectivity, may be of interest as a reduction polymer transfer agent.

It is expected that the enhanced reactivity reported for positively charged alkylated poly(4-vinylpyridine)-borane will also be found for protonated cross-linked poly(4-vinylpyridine)-borane. In the present work the use of cross-linked poly(4-vinylpyridine)-borane for reduction of carbonyl compounds in protic and aprotic acidic media was investigated. The chemoselectivity of the borane-bound polymer and the influence of the cross-linking level on its reactivity were also studied.

EXPERIMENTAL

Materials

Cross-linked poly(4-vinylpyridine) was prepared by copolymerization of divinylbenzene with 4-vinylpyridine as previously described [28]. The corresponding borane complex was prepared by reaction of the polymer hydrochloride derivative with sodium borohydride in DMF [28]. 12.5% Cross-linked poly(4-vinylpyridine)-borane (7.2 mmol BH_3 /g), 22.5% cross-linked poly(4-vinylpyridine)-borane (4.8 mmol BH_3 /g), and 35.0% cross-linked poly(4-vinylpyridine)-borane (2.7 mmol BH_3 /g) were used. Pyridine-borane was prepared according to the literature [29]. Benzene, tetrahydrofuran (Frutarom), dimethylsulfoxide (Fluka), cyclohexanone, cyclopentanone, cycloheptanone, hexanoic acid, benzaldehyde, 2-octanone, 2-methyl cyclohexanone, and acetophenone (BDH) were redistilled before use. Acetic acid (Frutarom), benzoic acid (Mullinckrodt), d-camphor, and p-chlorobenzaldehyde (BDH) were used. Buffer solutions were prepared according to the literature [30], and were diluted with methanol (9:1) before use. Nonaqueous hydrochloric acid solutions were prepared by dissolving gaseous hydrochloric acid in the organic solvent.

Determination of Borane-Bound Polymer

Borane-bound polymer was determined volumetrically as previously described [28].

Determination of Boric Acid

Boric acid was determined according to a known procedure [31]. After the reacted polymer had been isolated by filtration, the filtrate was neutralized with 0.1 N NaOH solution, using phenolphthalein as indicator. Manitol (0.5 g) was added and the boric acid was titrated with 0.1 N NaOH solution. The isolated polymer was treated with concentrated hydrochloric acid (1 mL). When hydrolysis was completed, boric acid was determined similarly after neutralization of the hydrochloric acid.

Determination of Reduction Products

The reduction products were determined by GLC using a Packard gas chromatograph Model 7300/7400. Nitrogen was used as the carrier gas. Glass column of 1.80 m and 0.25 in. tubing with solid support chromosorb W and 5% butanediolsuccinate as the liquid phase was used. Benzyl alcohol and α -phenyl ethyl alcohol were determined at 130°C column temperature using biphenyl and dibenzyl as internal standards. Aliphatic alcohols were determined at 70°C column temperature using naphthalene as the internal standard. Cyclohexanol and cyclohexanone were determined similarly using n-octanol as the internal standard, or from the cyclohexanol/(cyclohexanol + cyclohexanone) peak area ratio using a calibration curve.

Reduction Reactions

The reduction reactions were carried out under constant magnetic stirring in a closed flask equipped with a self-sealing cap for the introduction of reagents by syringes.

Reduction of Cyclohexanone in Protic and Aprotic Solvents

In a typical procedure, cyclohexanone (0.2 mL, 2.0 mmol), dissolved in the reaction solvent (1 mL), was added to a suspension of 12.5% cross-linked poly(4-vinylpyridine)-borane (0.28 g, 2.0 mmol BH_3) in the reaction solvent (9 mL) containing n-octanol (0.05 mL) as the internal standard. The reaction was carried out under constant stirring at room

temperature. Aliquats (0.25 mL) were removed and analyzed by GLC. When reduction was carried out in aprotic organic solvent, a 2.0% methanolic hydrochloric acid solution (0.5 mL) was added prior to the gas chromatography determination of the reduction product.

Reduction of Carbonyl Compounds by Cross-Linked Poly(4-vinylpyridine)-Borane

Carbonyl compound (2.0 mmol), dissolved or suspended in pH 1 buffer solution or acetic acid (1 mL), was added to a suspension of 12.5% cross-linked poly(4-vinylpyridine)-borane (0.28 g, 2.0 mmol BH_3) in the reaction solvent (9 mL). The reaction was carried out for 1 or 24 h under constant stirring at room temperature. The polymer was removed by filtration. The filtrate was extracted with ethyl ether (10 mL), dried over magnesium sulfate, and removed in vacuum. The residue was dissolved in ether (2 mL). Biphenyl (0.1 g) or dibenzyl (0.1 g) was added and analyzed by gas chromatography. When the reaction was carried out in acetic acid, the filtrate was neutralized with saturated sodium bicarbonate solution before extraction. The competitive reduction of carbonyl compounds was carried out similarly.

Reduction by Pyridine-Borane

In a typical experiment cyclohexanone (0.20 mL, 2.0 mmol), dissolved in the reaction solvent (1 mL), was added to pyridine-borane (0.22 mL, 2.0 mmol) in the same solvent (9 mL). The reaction was carried out at room temperature. Aliquats (0.25 mL) were removed and extracted with ether (1 mL). The pyridine present was extracted with 0.5 N hydrochloric acid aqueous solution (0.5 mL). The reduction yield was determined by gas chromatography. The competitive reduction was carried out similarly.

Determination of Extent of Hydrolysis during Reduction Reaction

The extent of hydrolysis was determined volumetrically by measuring the volume of the hydrogen released during hydrolysis.

Reduction Rate of Cyclohexanone with Cross-Linked Poly(4-vinylpyridine)-Borane-pH Dependence

The reduction was carried out in the presence of a large molar excess of cyclohexanone, resulting in a "pseudo"-first-order (in borane-bound polymer) kinetic relationship. 12.5% Cross-linked poly(4-

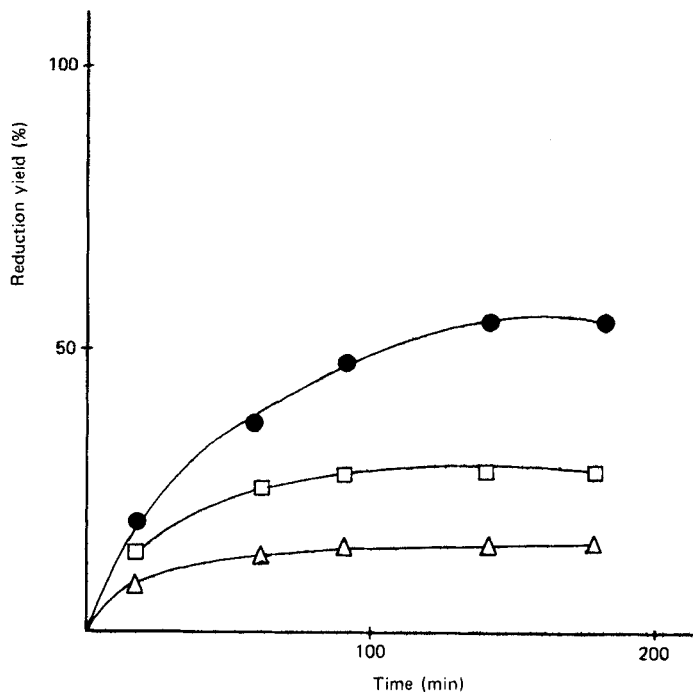


FIG. 1. Reduction of cyclohexanone with cross-linked poly(4-vinylpyridine)-borane in aprotic solvents: (Δ) 0.5 N HCl in benzene, (\square) 0.5 N HCl in THF, (\bullet) 0.5 N HCl in DMSO. 12.5% Cross-linked poly(4-vinylpyridine)-borane (0.28 g, 2.0 mmol BH_3) were reacted with cyclohexanone (0.20 mL, 2.0 mmol) in the corresponding solvent (10 mL) at 25°C.

was carried out in the presence of 10% methanol in order to increase the solubility of the carbonyl compound in the reaction media. An increase in reaction solvent polarity led to an increase in reduction rate and final yield. In protic solvents, too, the presence of acid is essential for obtaining high reduction yields in a reasonably short time. The best results were obtained when the reduction was carried out in pH 1 buffer solution and in acetic acid. The reduction in these solvents was completed after 30 and 120 min., respectively. At that time no hydrolysis of the borane-bound polymer took place, as determined in a separate experiment without cyclohexanone. In the absence of acid catalysis, a marked decrease in the borane-bound polymer reactivity was observed. In this case an increase in the reaction time and in the amount of borane-bound polymer led only to a moderate improvement in reduction yield. Thus, the reduction of cyclohexanone carried out

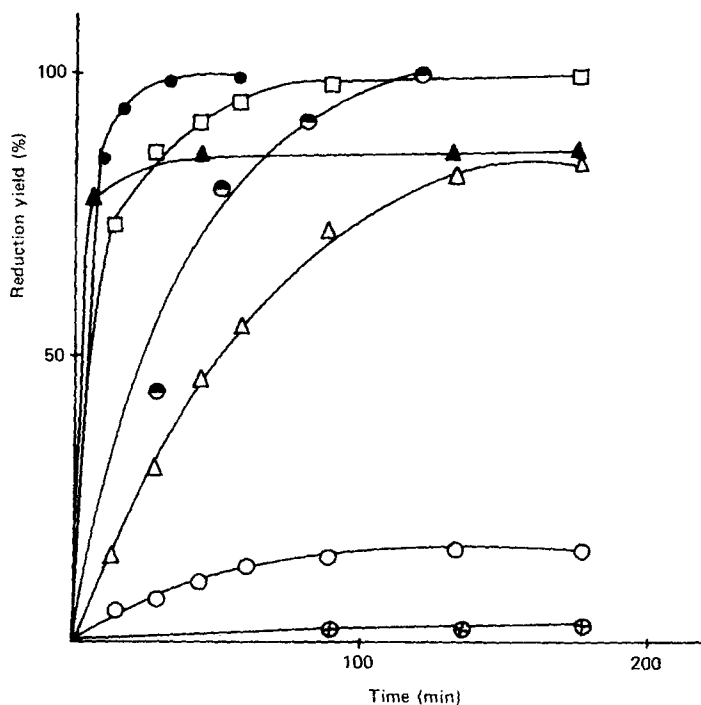


FIG. 2. Reduction of cyclohexanone in protic solvents. Reduction by cross-linked poly(4-vinylpyridine)-borane in (○) water, (●) pH 1 buffer solution, (△) 0.5 N HCl in methanol, (⊕) methanol, (□) acetic acid; reduction by pyridine borane in (⊙) water, (▲) pH 1 buffer solution. 12.5% Cross-linked poly(4-vinylpyridine)-borane (0.28 g, 2.0 mmol BH_3) was reacted with cyclohexanone (0.20 mL, 2.0 mmol) in the corresponding solvent (10 mL) at 25°C. Pyridine-borane (0.11 mL, 0.10 mmol) was reacted similarly with cyclohexanone (0.10 mL, 0.10 mmol) in the corresponding solvent (5 mL).

in water for 24 h led to 17% conversion. When a large excess (eight-fold) of borane-bound polymer was used, only 46.1% reduction yield was reached.

The enhanced reactivity of the borane-bound polymer in acidic media should be attributed to protonation of both carbonyl compound and polymer. Protonation of oxygen carbonyl enhances its reactivity toward the borane hydrides. Protonation of the polymer increases its swelling in the reaction media and causes conformation changes [32] which may improve its accessibility and enhances its reactivity. Similar activation of poly(4-vinylpyridine)-borane by the introduction

of a positive charge on the polymer as a result of partial alkylation was reported in the literature [6].

The reactivity of cross-linked poly(4-vinylpyridine)-borane may differ from that of its low molecular weight analog pyridine-borane. Reduction of cyclohexanone in aqueous media by this reduction agent was carried out with and without acid catalysis (Fig. 2). In the absence of acid catalysis the polymer-borane is much less reactive than its low molecular weight analog. Reduction in the absence of acid was completed after 2 h. At that time a final reduction yield of 16% was reached with cross-linked poly(4-vinylpyridine)-borane. On the other hand, when the reduction was carried out in acidic media, the borane-bound polymer was practically as reactive as pyridine-borane. Complete reduction was achieved with the polymer-borane while an 86% reduction yield was reached with pyridine-borane. The lower reduction yield obtained with pyridine-borane is due to its lower hydrolytic stability. Under these experimental conditions the borane-bound polymer does not hydrolyze during the time required for reduction. Pyridine-borane is less stable. In a separate experiment carried out in the absence of cyclohexanone, 40% of the pyridine-borane were hydrolyzed after 10 min. It can be seen that complete reduction can be reached with smaller amounts of borane when its polymer complex is used. The high reactivity of the borane-bound polymer in acidic media, combined with its hydrolytic stability, makes it a very potent reduction agent.

Cross-linking of poly(4-vinylpyridine) is essential when the polymer is used in aqueous acidic media in which the polymer is soluble. Cross-linking may decrease the polymer reactivity. The influence of cross-linking level on reduction of cyclohexanone in pH 1 buffer solution is described in Fig. 3. A low cross-linking level does not affect the polymer reactivity. 12.5% Cross-linked polymer-borane was as reactive as uncross-linked poly(4-vinylpyridine)-borane. A decrease in borane-bound polymer reactivity was found at higher cross-linking levels.

All reduction reactions of cyclohexanone by cross-linked poly(4-vinylpyridine)-borane reported so far were carried out using borane-bound polymer:ketone in a 1:1 molar ratio. If all borane hydrides are reactive and participate in the reduction of cyclohexanone, a third of the borane-bound polymer used should be sufficient for complete reduction of the ketone. Reduction of cyclohexanone and benzaldehyde at different borane bound polymer:carbonyl compound molar ratios in pH 1 buffer solution and in acetic acid is described in Table 1 and its time dependence in Fig. 4. The reaction carried out at a 1:3 molar ratio led to moderate reduction yield. Full conversion of the carbonyl compound to the corresponding alcohol was reached at a 1:1 molar ratio. Reduction was always accompanied by hydrolysis. The extent of hydrolysis was determined by measuring the hydrogen evolved during reduction. The borane-bound polymer does not hydrolyze in pH 1 buffer solution or in acetic acid under these experimental conditions.

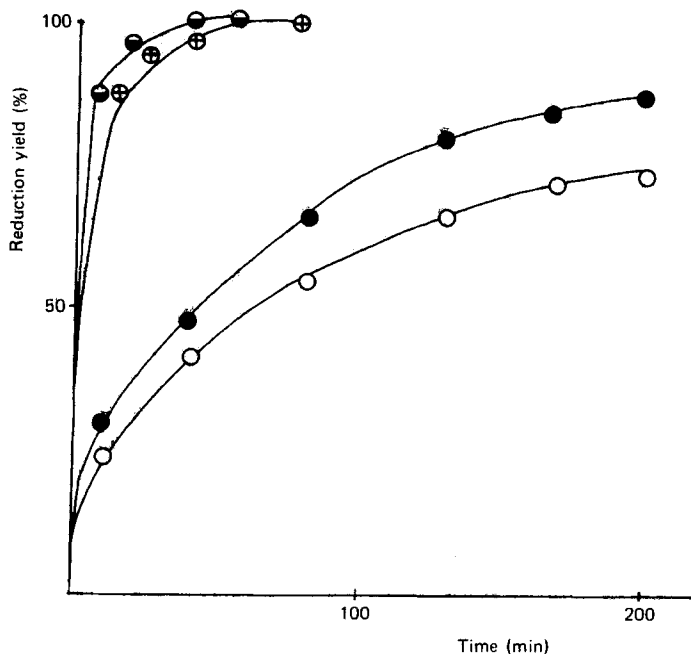


FIG. 3. Reduction of cyclohexanone with poly(4-vinylpyridine)-borane of different degrees of cross-linking: (⊕) poly(4-vinylpyridine), (⊖) 12.5% cross-linking, (●) 22.5% cross-linking, (○) 35.0% cross-linking. Polymer-borane (1.0 mmol BH_3) was reacted with cyclohexanone (0.10 mL, 1.0 mmol) in pH 1 buffer solution (5 mL) at 25°C.

Hydrolysis started upon addition of the carbonyl compound. The hydrolysis observed is that of hydride-containing intermediates formed after the first of the three borane-bound polymer hydrides had been reacted. Such intermediates may be the esters H_2BOR and $\text{BH}(\text{OR})_2$ formed upon reduction of the carbonyl compound and the corresponding hydroxy boranes H_2BOH and $\text{HB}(\text{OH})_2$ formed after hydrolysis of these esters. These hydride-containing intermediates are more reactive than the borane-bound polymer hydrides and react with the reaction solvent, too. The unreacted carbonyl compound competes with the reaction solvent on these hydrides. Therefore, it was found that an increase in carbonyl compound concentration led to a decrease in the extent of hydrolysis. In the reduction experiments carried out at a 1:3 molar ratio of borane-bound polymer to cyclohexanone or benzaldehyde in pH 1 buffer solution, almost two-thirds of the reacted hydrides were consumed in the reduction reaction. Similar results were obtained in reduction experiments carried out with a lower and a higher reactants molar ratio. Some improvement in the extent of hydride participation in the reduction was found when the reaction was carried out in acetic acid.

TABLE 1. Reduction of Cyclohexanone and Benzaldehyde by Cross-Linked Poly(4-vinylpyridine)-Borane

Carbonyl compound	$\text{BH}_3 : \begin{array}{c} \text{O} \\ \\ \text{C} \end{array}$ BH ₃ : C	Reaction media	Reaction time (min)	Reduction yield (%)	Reacted			Unreacted (%) ^{b, d}
					% ^b	% ^c	Hydrolysis (%) ^b	
Cyclohexanone	1:1	Buffer pH 1	60	97.2	32.4	50.5	31.7	44.0
"	1:2	"	60	71.6	47.7	67.7	22.6	28.2
"	1:3	"	60	60.8	60.8	67.0	30.0	14.2
"	1:6	"	60	35.1	70.2	72.0	27.3	3.0
"	1:1	Acetic acid	130	75.6	25.2	71.2	10.3	55.6
Benzaldehyde	1:1	Buffer pH 1	60	100	33.3	54.7	27.6	37.0
"	1:2	"	60	92.9	61.9	67.9	29.3	8.1
"	1:3	"	60	66.1	66.1	67.0	32.5	3.3
"	1:1	Acetic acid	180	93.9	31.3	70.0	13.7	48.9
"	1:2	"	180	87.0	58.0	71.6	23.0	16.6
"	1:3	"	180	70.7	70.7	75.4	23.1	13.0

^a12.5% Cross-linked poly(4-vinylpyridine)-borane (0.14 g, 1.0 mmol BH₃) was allowed to react with the carbonyl compound at 21°C. Hydrolysis was followed volumetrically.

^bPercent of original borane content of the polymer.

^cPercent of reacted borane.

^dDetermined after completion of reduction.

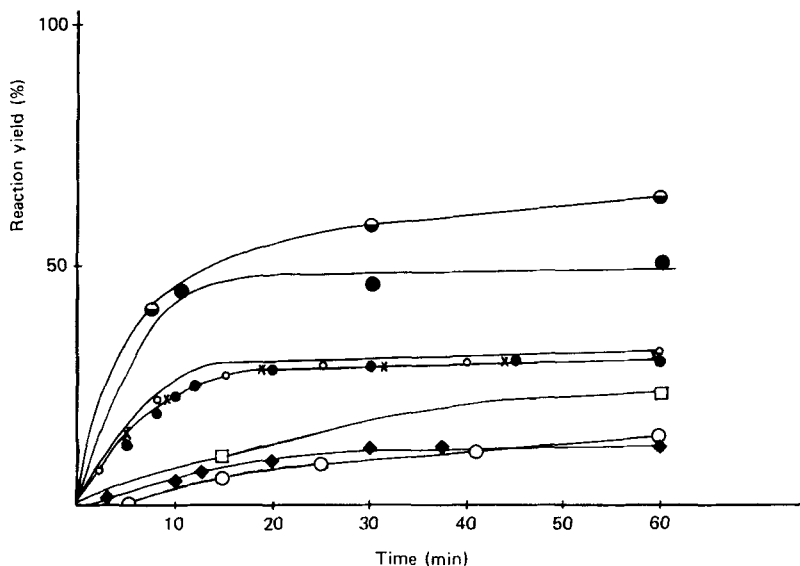


FIG. 4. Reduction and hydrolysis during reaction of cross-linked poly(4-vinylpyridine)-borane with cyclohexanone at different borane/ketone molar ratios. Reaction in pH 1 buffer solution, reduction: (○) 1:1, (●) 1:2, (⊖) 1:3; hydrolysis: (●) 1:1, (◆) 1:2, (×) 1:3. Reaction in acetic acid: reduction (□) 1:1, hydrolysis (○) 1:1. 12.5% Cross-linked poly(4-vinylpyridine) (0.14 g, 1.0 mmol BH_3) was reacted with cyclohexanone in the corresponding solvent (5 mL) at 21°C.

It seems that only two of the borane hydrides are available for reduction while the third one preferably hydrolyzes. It is reasonable to assume that the mono hydride derivatives are those that are more susceptible to hydrolysis. The nitrogen-boron bond of these derivatives, in which the boron is substituted by two oxygen atoms, should be weakened to such an extent that a fast hydrolysis of these derivatives takes place. The difference in the extent of participation of the hydrides in reduction reactions carried out in pH 1 buffer solution and in acetic acid should be attributed to the difference in hydrolytic stability of the mono hydride derivatives in these solvents. Pyridine-borane hydrides reacted similarly. Only 69.2% of the borane hydrides participated in the reduction of cyclohexanone in a reaction carried out at a 1:3 molar ratio in pH 4 buffer solution in which the borane does not hydrolyze.

After the final reduction yield had been reached, the polymer contained unreacted hydrides. These hydrides should belong only to unreacted borane-bound polymer. The amount of reacted borane-bound polymer can also be determined by titration of the boric acid formed in solution after reduction and hydrolysis. The unreacted borane-bound

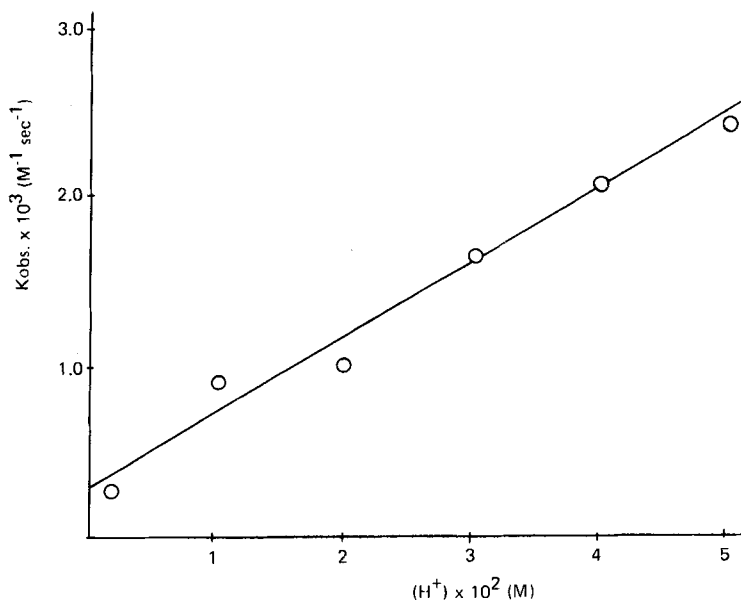









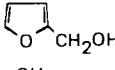



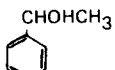
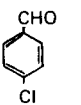
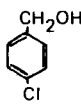

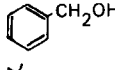




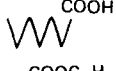
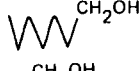
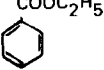



FIG. 5. Reduction rate of cyclohexanone with cross-linked poly(4-vinylpyridine)-borane, pH dependence: 12.5% cross-linked poly(4-vinylpyridine)-borane (0.14 g, 1.0 mmol BH_3) was reacted with cyclohexanone (0.52 mL, 5.0 mmol) in buffer solution (10 mL) at 20°C.

polymer can be determined similarly after hydrolysis. In the reduction of cyclohexanone at a 1:1 molar ratio (Table 1), it was found that 60.0% of the initial borane-bound polymer was converted to boric acid while 41.0% remained intact and was titrated as boric acid after hydrolysis. Good agreement between the amount of reacted (64.1%) and unreacted (44.0%) borane, as determined from reduction yield, volumetric determination of hydrolyzed and unreacted borane, and the amount of reacted and unreacted borane which was determined as boric acid indicates that partially reacted borane-bound polymer does not remain attached to the polymer. IR spectra of polymer isolated during and after reaction supports this finding. The B-H stretching frequency at 2340 cm^{-1} was always present while no B-O absorption frequencies [33] were found. The extent of borane-bound polymer participation in the reduction reaction increased with an increase in carbonyl compound concentration. The limited accessibility, which may vary with the carbonyl compound and the solvent used, should be responsible for the remaining intact borane-bound polymer at the end of the reaction.

The reduction rate of carbonyl compounds by low molecular weight amine-borane in acidic media is pH dependent [16]. A similar dependence was observed in the reduction of cyclohexanone with cross-linked poly(4-vinylpyridine)-borane (Fig. 5) which was carried out in the pres-

TABLE 2. Reduction of Carbonyl Compounds by Cross-Linked Poly(4-vinylpyridine)-Borane in Acidic Media^a

Carbonyl compound	Reduction product	Reduction yield (%)		
		pH 1 buffer solution		Acetic acid, 24 h
		1 h	24 h	
		100		100
		100		100
		49	50	61
		44	51	44
		89	100	100
		100		100
		65	90	100
		-	-	75
		100		100
		2 (47% endo)	5 (47% endo)	5 (46% endo)
		8	12	12
		8	14	15
		8	11	-


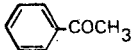





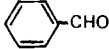
^a 12.5% Cross-linked poly(4-vinylpyridine)-borane (0.28 g, 2.0 mmol BH_3) was allowed to react with the carbonyl compound (2.0 mmol) in pH 1 buffer solution and in acetic acid (10 mL) at 25 °C.

ence of a large excess of the ketone. The rate equation proposed for the reduction of ketones by low molecular weight amine borane [16] is valid here, too. The reduction of cyclohexanone by cross-linked poly(4-vinylpyridine)-borane was first order in hydrogen ion. Rate constants characterizing the acid independent $k_1 = 3.0 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ and acid catalyzed $k_2 = 4.3 \times 10^{-2} \text{ M}^{-2} \text{ s}^{-1}$ pathways were found at 20°C.

The reduction of different aldehydes, ketones, carboxylic acids, and methyl benzoate by 12.5% cross-linked poly(4-vinylpyridine)-borane is reported in Table 2. Reduction was carried out at room temperature in water at pH 1 and in acetic acid. The reduction yield was determined after 1 and 24 h. It can be seen that cross-linked poly(4-vinylpyridine)-borane can be successfully used for the reduction of aldehydes and ketones. The carboxylic acids and the ester used are reduced to only a small extent by this reagent. A different reactivity of the borane-bound polymer toward ketones was observed. Full conversion of cyclohexanone took place while d-camphor was reduced only in very low yield.

The difference in reactivity of cross-linked poly(4-vinylpyridine)-borane toward carbonyl compounds and its pH dependence suggests its use as a chemoselective reduction agent. Competitive reduction of several ketones and benzaldehyde in the presence of cyclohexanone is reported in Table 3. Reaction was carried out in pH 1 buffer solution

TABLE 3. The Relative Reactivity of Ketones and Benzaldehyde to Cross-Linked Poly(4-vinylpyridine)-Borane via Competitive Reductions versus Cyclohexanone^a

Carbonyl compound	R ^b	Carbonyl compound	R ^b
	1.00		0.07
	0.09		0.02
	0.09		1.50
	0.00		3.90

^a12.5% Cross-linked poly(4-vinylpyridine)-borane (0.14 g, 1.0 mmol BH₃) was allowed to react with a mixture of the carbonyl compound (2.0 mmol) and cyclohexanone (2.0 mmol) in pH 1 buffer solution (10 mL) for 1 h at 25°C.

^bRatio of alcohol produced to cyclohexanol.

TABLE 4. Competitive Reduction of Benzaldehyde and Acetophenone with Cross-Linking Poly(4-vinylpyridine)-Borane, pH Dependence^a

pH	Reaction time (h)	Reduction yield (%)	
		Benzaldehyde	Acetophenone
1.0	1	91.4	2.6
1.6	3	71.0	1.3
3.0	5	66.8	0.7
4.0	5	63.6	0.4
7.0	24	48.3	0.0

^a 12.5% Cross-linked poly(4-vinylpyridine)-borane (0.14 g, 1.0 mmol BH_3) was allowed to react with a mixture of acetophenone (0.23 mL, 2.0 mmol) and benzaldehyde (0.20 mL, 0.20 mmol) in the corresponding buffer solution (5 mL) at 25°C.

in the presence of a molar excess of carbonyl compound using a 2:2:1 molar ratio of cyclohexanone:carbonyl compound:borane-bound polymer. The ratio of alcohol produced to cyclohexanol (R) was determined after 1 h when all borane-bound polymer available for reduction was consumed. It can be seen that benzaldehyde can be reduced in the presence of cyclohexanone, and the latter can be reduced in the presence of less active ketones.

The pH dependence of the polymer-borane chemoselectivity was determined in the competitive reduction of benzaldehyde and acetophenone (Table 4). The reaction was carried out using a 2:2:1 molar ratio of benzaldehyde:acetophenone:borane-bound polymer. The reduction yield was determined at the end of the reaction. The reaction was carried out in pH 1.0 to 7.0 buffer solutions. Very good chemoselectivity was found at pH 1. An increase in solution pH led to a further improvement in the polymer chemoselectivity. The time dependence of chemoselectivity of cross-linked poly(4-vinylpyridine)-borane in the competitive reduction of benzaldehyde and acetophenone using a 1:1:1 molar ratio in pH 1 buffer solution, acetic acid, and 1 N HCl solution is reported in Table 5. The reaction was carried out until all available borane-bound polymer was consumed. Moderate to good reduction yields of benzaldehyde in pH 1 buffer solution and in acetic acid can be reached before acetophenone is reduced.

A drastic decrease in the chemoselectivity of the polymer was found when the competitive reduction was carried out in a much lower pH value of 1 N hydrochloric acid solution. In this acidic media, relatively low chemoselectivity was observed from the beginning of the reaction.

Cross-linked poly(4-vinylpyridine)-borane is a much better chemo-

TABLE 5. Competitive Reduction of Benzaldehyde and Acetophenone with Cross-Linked Poly(4-vinylpyridine)-Borane^a

Reaction media	Reaction time (min)	Reduction yield (%)	
		Benzaldehyde	Acetophenone
Buffer pH 1	10	61.2	0.0
	20	65.0	0.0
	40	72.3	0.2
	60	79.5	0.6
	90	89.5	2.2
	150	93.5	3.4
	1140	97.0	5.2
Acetic acid	10	61.0	0.0
	25	73.1	0.0
	40	78.6	0.0
	60	83.0	0.0
	90	87.3	0.3
	140	89.0	2.4
	1140	96.2	5.4
1 N HCl	2	48.0	22.0
	10	53.0	24.4
	20	62.6	28.8
	40	66.4	30.0
	115	70.6	32.5
	230	85.8	34.1

^a 12.5% Cross-linked poly(4-vinylpyridine)-borane (0.14 g, 1.0 mmol BH₃) was reacted with a mixture of acetophenone (0.12 mL, 1.0 mmol) and benzaldehyde (0.10 mL, 1.0 mmol) in the corresponding solvent (5 mL) at 19°C.

selective reduction agent than its low molecular weight analog pyridine-borane. The competitive reduction of benzaldehyde and acetophenone with pyridine-borane at a 1:1:1 reactants molar ratio is reported in Table 6. Reduction was carried out in pH 4 buffer solution, in which

TABLE 6. Competitive Reduction of Benzaldehyde and Acetophenone with Pyridine-Borane^a

Reaction media	Reaction time (min)	Reduction yield (%)	
		Benzaldehyde	Acetophenone
Buffer pH 4	5	37.5	6.1
	20	48.0	8.2
	30	64.0	9.8
	60	70.3	16.9
Buffer pH 1	5	44.4	7.2
	30	68.0	12.1
	60	78.1	20.2

^aPyridine-borane (0.11 g, 1.0 mmol BH₃) was reacted with a mixture of benzaldehyde (0.10 mL, 1.0 mmol) and acetophenone (0.12 mL, 1.0 mmol) in buffer solution (5 mL) at 21° C.

pyridine-borane does not hydrolyze, and in pH 1 buffer solution. It can be seen that pyridine-borane is much less selective in the reduction of carbonyl compounds than its polymer analog.

The borane-bound cross-linked poly(4-vinylpyridine) shows chemoselectivity similar to that of *t*-butylamine-borane, which was reported [23] to be as good or better than other available chemoselective reducing agents.

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Accepted by editor March 26, 1984

Received for publication April 27, 1984