Isopinocampheylhaloborane-Methyl Sulfide as Hydroborating and Stereoselective Reducing Agent

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Reactions of alkenes and alkynes with the recently discovered isopinocampheylhaloborane-methyl sulfide (IpcBHX·SMe_2, X=Cl, Br, I) were investigated in detail in order to establish their usefulness as hydroborating agents. The reagents readily hydroborated alkenes at 50 ℃ and alkynes at 25 ℃ with excellent regioselectivity in placing the boron atom exclusively at the less hindered carbon atom. Especially, the selectivity achieved by the iodo derivative reaches essentially 100%. In addition to that, IpcBHX·SMe_2 was applied to the reduction of cyclic ketones to examine its stereoselectivity. The halogen substituent in these reagents plays an important role in the stereoselective reduction. The stereoselectivity increased dramatically with increasing steric size of the substituent. Finally, the iodo derivative achieved highly stereoselective reduction, such selectivity being comparable to that previously achieved with trialkylborohydrides.

Introduction

Hydroboration of alkenes with borane (BH_3-THF or BH_3·SMe_2) produces trialkylboranes.[1] The dialkylhaloboranes are easily prepared by the hydroboration of alkenes.[2,3] Furthermore, dihaloboranes hydroborate olefins to provide alkyldihaloboranes.[4] Such boranes (R_3B, R_2BX, and RBX_2) have been found to be excellent intermediates for a wide variety of synthetic applications.[5,6] In addition to that, several hydroborating reagents[8,9] such as HBX_2·SMe_2[2,4a-b] 9-BBN,[7] and Sia_2-BH[8] were investigated to find a synthetic route to isomerically pure monoalkenylboranes from alkynes. Although these results indicate a pronounced directive effect placing the boron atom at the less hindered position, the results for 1-substituted propyne derivatives are not quite satisfactory.

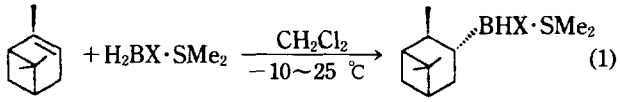
The isopinocampheyl (Ipc) group attached to boron is a particularly valuable chiral group in several reactions, especially asymmetric hydroboration of alkenes[5,6,10] and asymmetric reduction of prochiral ketones.[5,6,12] For example, mono- and diisopinocampheylboranes ($IpcBH_2$, Ipc_2BH) appear to be excellent chiral hydroborating agents for alkenes.[5,6,11] Quite recently, Brown and co-workers reported that (−)-diisopinocampheylchloroborane ((−)-Ipc_2BCl) reduces prochiral ketones to the corresponding alcohols in high optical purities.[5,6,12]

Such exceptional ability seems to arise from the structural fitness of Ipc group in the hydroboration and reduction reactions. Therefore, incorporation of the Ipc group and halogen atom into a borane is expected to afford quite different regioselectivity in the hydroboration and stereoselectivity in the reduction from those of alkylborane or haloborane itself. Accordingly, we prepared a series of isopinocampheylhaloborane-methyl sulfide (IpcBHX·SMe_2, X=Cl, Br, I), applied then to the hydroboration of alkenes and alkynes to examine the directive effect, and finally investigate their stereochemistry in the reduction of cyclic ketones, in the hope of better understanding the nature of reagents.

In this paper, we describe in full the results of our study on the hydroboration and reduction characteristics of isopinocampheylhaloborane-methyl sulfide.[13]

Results and Discussion

Preparation of IpcBHX·SMe_2. The reagents were prepared by the hydroboration of α-pinene with the corresponding H_2BX·SMe_2 (X=Cl, Br, I) in CH_2Cl_2 (Eq. 1). Both H_2BCl·SMe_2 and H_2BBr·SMe_2 are commercially available. H_2BI·SMe_2 was prepared from borane-methyl sulfide and iodine.[13]



(1)

X=Cl, IpcBHCl·SMe_2
X=Br, IpcBHBr·SMe_2
X=I, IpcBHI·SMe_2

The ^{11}B NMR spectra of the resulting IpcBHX·SMe_2 solution in CH_2Cl_2 showed a clean doublet centered at δ 6.8 ppm (J_{BH}=125 Hz) for IpcBHCl·SMe_2, δ 3.5 (J_{BH}=123 Hz) for IpcBHBr·SMe_2 and δ −1.7 (J_{BH}=123 Hz) for IpcBHI·SMe_2 relative to BF_3·OEt_2. All the reagents were stable when kept under a static pressure of dry nitrogen.

Hydroboration of Representative Alkenes with IpcBHX·SMe_2. In all, seven representative alkenes bearing different steric environments were selected for this study. Each alkene was hydroborated with 10 mol% excess quantity of IpcBHCl·SMe_2 or IpcBHBr·SMe_2 (1.0 M in alkene and 1.1 M in IpcBHX·SMe_2) and with 100 mol% excess quantity of IpcBHI·SMe_2. The reaction was quite slow at 25°. Therefore, we examined the rate of hydroboration with the reagents at 50°. The rate of reaction was monitored by hydrolyzing aliquots with a mixture of glycerine-methanol-water, followed by measurement of hydrogen evolved. The relative rate of hydroboration with IpcBHX·SMe_2 toward alkenes depends on the steric and electronic nature of the reagents, as anticipated. Thus, the rate is in order of IpcBHCl·SMe_2 >IpcBHBr·SMe_2>IpcBHI·SMe_2. The reaction of the iodo derivative in a 10 mol% excess amount at 50° was so slow that 100 mol% excess amount of the reagent was utilized in this experiment to maintain a satisfactory rate. Consequently, all the alkenes examined undergo the hydroboration readily under the experimental conditions. The results are summarized in Table 1.

Table 1. Reaction of Representative Alkenes with Isopinocampheylhaloborane-Methyl Sulfide in Methylene Chloride at 50 ℃[a]

Alkene	Time, h	Hydride used for hydroboration[b]		
		IpcBHCl·SMe_2	IpcBHBr·SMe_2	IpcBHI·SMe_2[c]
1-pentene	1.0	0.88	0.72	0.84
	3.0	0.99	0.98	1.00
	6.0	1.00	1.00	1.00
1-octene	1.0	0.74	0.68	0.73
	3.0	0.96	0.93	0.94
	6.0	1.00	1.00	1.00
1-decene	1.0	0.66	0.60	0.65
	3.0	0.89	0.84	0.89
	6.0	1.00	1.00	1.00
3,3-dimethyl-1-butene	1.0	0.89	0.82	0.86
	3.0	1.00	1.00	1.00
	6.0	1.00	1.00	1.00
2,4,4-trimethyl-2-pentene	1.0	0.76	0.74	0.81
	3.0	0.92	0.90	0.94
	6.0	1.00	1.00	1.00
1-methylcyclohexene	1.0	0.84	0.84	0.82
	3.0	1.00	1.00	1.00
	6.0	1.00	1.00	1.00
α-methylstyrene	1.0	0.74	0.66	0.62
	3.0	1.00	0.92	0.93
	6.0	1.00	1.00	1.00

[a]Reagent : alkene = 1.1 : 1. [b]Rates determined gasometrically. [c]Regent : alkene = 2 : 1.

The directive effects in the hydroboration of alkenes with IpcBHX·SMe_2 were also investigated. After standard hydroboration with the reagents under the same conditions described above, the product in each case was oxidized with alkaline hydrogen peroxide, and the oxygenated products were identified by GC analysis. The results are summarized in Table 2. All the reagents show an excellent selectivity in placing the boron atom exclusively at the less hindered carbon atom. Especially, the selectivity achieved by the iodo derivative reaches essentially 100%. This exceptional regioselectivity obtained at such a high temperature (50°) is rather surprising. The selectivity matches that displayed by 9-BBN[7] and ThxBHCl·SMe_2,[15] the most selective hydroborating agents known. IpcBHI·SMe_2, therefore, represents a new, stable, selective hydroborating agent.

Hydroboration of Representative Alkynes with IpcBHX·SMe_2. The monohydroboration of representative terminal and internal alkynes with IpcBHX·SMe_2 in a stoichiometric ratio (1 : 1) was performed in CH_2Cl_2 at 25° and the results are summarized in Table 3. The rate data in Table 3 reveal that, in general, the terminal alkynes undergo hydroboration at a rate slightly faster than the internal alkynes. Again, the relative rate of hydroboration with IpcBHX·SMe_2 toward alkynes depends on the steric and electronic nature of the reagents: the rate is in order of IpcBHCl·SMe_2>IpcBHBr·SMe_2≫IpcBHI·SMe_2. Nonetheless, all the terminal and internal alkynes examined undergo the hydroboration readily with these reagents at 25° in a stoichiometric ratio. Especially noteworthy is the hydroboration of alkynes with excess reagents. IpcBHX·SMe_2 even in an excess amount undergo a clean monohydroboration with either internal or terminal alkynes under these conditions.

The directive effects of various unsymmetrically substituted acetylenes toward IpcBHX·SMe_2 was also examined[13] and the results are summarized in Table 4. The regioselectivity for the addition of >BH was determined by oxidation of the intermediate alkenylisopinocampheylhaloboranes with hydrogen peroxide. The distribution of carbonyl isomers was then quantified by GC analysis.

As is evident from the Table, the steric and electronic

Table 2. Directive Effects in the Hydroboration of Alkenes with Isopinocampheylhaloborane-Methyl Sulfide in Methylene Chloride at 50 ℃

Alkene	Products	Product distribution, %[a]		
		IpcBHCl·SMe_2	IpcBHBr·SMe_2	IpcBHI·SMe_2
1-pentene	1-pentanol	96.5	97.5	99
	2-pentanol	3.5	2.5	1
1-octene	1-octanol	97.5	99.5	99.5
	2-octanol	2.5	0.5	0.5
1-decene	1-decanol	99.5	99.5	>99.9
	2-decanol	0.5	0.5	trace
3,3-dimethyl-1-butene	3,3-dimethyl-1-butanol	99	99	99.5
	3,3-dimethyl-2-butanol	1	1	0.5
2,4,4-trimethyl-2-pentene	2,4,4-trimethyl-3-pentanol	97	98	99
	2,4,4-trimethyl-2-pentanol	3	2	1
1-methylcyclohexene	2-methylcyclohexanol	99.5	99.8	>99.9
	1-methylcyclohexanol	0.5	0.2	trace
α-methylstyrene	2-phenylpropanol	98	99.6	99.8
	2-phenyl-2-propanol	2	0.4	0.2

[a]Total yields are 94± 5%.

Table 3. Reaction of Representative Alkynes with Isopinocampheylhaloborane-Methyl Sulfide in Methylene Chloride at 25 ℃[a]

Alkyne	Time, h	Hydride used for hydroboration[b]		
		IpcBHCl·SMe_2	IpcBHBr·SMe_2	IpcBHI·SMe_2
1-hexyne	0.5	0.95	0.92	
	1.0	0.99	0.97	0.66
	3.0	1.00	1.00	0.89
	6.0	1.00	1.00	0.99
	12.0			1.00
1-heptyne	0.5	0.92	0.90	
	1.0	0.98	0.96	0.60
	3.0	1.00	1.00	0.79
	6.0	1.00	1.00	0.95
	12.0			1.00
2-hexyne	0.5	0.92	0.91	
	1.0	0.98	0.97	0.62
	3.0	1.00	1.00	0.86
	6.0	1.00	1.00	0.97
	12.0			1.00
3,3-dimethyl-1-butyne	0.5	0.98	0.95	
	1.0	1.00	1.00	0.70
	3.0	1.00	1.00	0.87
	6.0			1.00
4,4-dimethyl-2-pentyne	0.5	0.81	0.76	
	1.0	0.87	0.82	0.69
	3.0	0.92	0.90	0.77
	6.0	1.00	0.99	0.81
	12.0	1.00	1.00	0.95
	24.0			1.00
phenylethyne	0.5	0.80	0.80	
	1.0	0.93	0.92	0.74
	3.0	1.00	1.00	0.87
	6.0	1.00	1.00	0.93
	12.0			1.00
1-phenyl-1-propyne	0.5	0.77	0.72	
	1.0	0.84	0.80	0.70
	3.0	0.90	0.90	0.77
	6.0	1.00	1.00	0.80
	12.0	1.00	1.00	0.92
	24.0			1.00

[a] Equimolar amount of reagent and alkynes was utilized. [b] Rates determined gasometrically.

natures of the substituents play major roles in affecting the direction of addition of the B-H bond. All the isopinocampheylhaloboranes achieve the clean monohydroboration of both internal and terminal alkynes with high regioselectivity. Especially, IpcBHI·SMe_2 shows almost perfect regioselectivity in these hydroboration reactions at 25°. Even in the hydroboration of internal alkynes the reagent shows an exceptional regioselectivity. Comparision with other disubstituted boranes such as $HBBr_2$·SMe_2,[4b] catecholborane,[9a] 2,2'-biphenoxyborane,[9b] 9-BBN,[7] Sia_2BH,[8] and Mes_2BH[10] reveals a superior regioselectivity for IpcBHX·SMe_2. For 1-phenyl-1-propyne, IpcBHX·SMe_2 shows rather better results, even in comparison with ThxBHX·SMe_2,[13,15] known as one of the most selective hydroborating agent. However, the reagent provides a slightly lower regioselectivity for 2-hexyne. In particular, regioselective hydroboration with the iodo derivative provides a valuable synthetic route to isomerically pure aldehydes and ketones from alkynes.

Stereochemistry in the Reduction of Cyclic Ketones with IpcBHX·SMe_2. The stereochemistry in the reduction of cyclic ketones with IpcBHX·SMe_2 was next investigated so as to elucidate the halogen effect and hence pro-

Table 4. Directive Effects in the Monohydroboration of Alkynes with Isopinocampheylhaloborane-Methyl Sulfide in Methylene Chloride at 25 ℃

Alkyne	Products	Product distribution, %[a,b]		
		IpcBHCl·SMe_2	IpcBHBr·SMe_2	IpcBHI·SMe_2
1-hexyne	hexanal	92	96	98
	2-hexanone	8	4	2
1-heptyne	heptanal	95(96)[c]	97(98)	99
	2-heptanone	5(4)	3(2)	1
2-hexyne	2-hexanone	87	90	95
	3-hexanone	13	10	5
3,3-dimethyl-1-butyne	trimethylacetaldehyde	97	98.5	>99.9
	3,3-dimethyl-2-butanone	3	1.5	trace
4,4-dimethyl-2-pentyne	4,4-dimethyl-2-pentanone	93	96	99
	4,4-dimethyl-3-pentanone	7	4	1
phenylethyne	phenylacetaldehyde	99	99.5	>99.9
	acetophenone	1	0.5	trace
1-phenyl-1-propyne	1-phenyl-2-propanone	99.5	99.5	>99.9
	1-phenyl-1-propanone	0.5	0.5	trace

[a] The distribution is deduced by GC analysis from the oxygenated products produced following oxidation of the B-alkylborane product. [b] Total yields are 90± 5%. [c] The figures in parenthesis are yields at 0°.

Table 5. Stereoselective Reduction of Cyclic Ketones with Isopinocampheylhaloborane-Methyl Sulfide in Methylene Chloride 0 °C[a-c]

Ketone	IpcBHCl·SMe_2	IpcBHBr·SMe_2	IpcBHI·SMe_2
cyclohexanone			
2-methyl-	79	91	98
3-methyl-	77	82	96
4-methyl-	69	73	90
4-*tert*-butyl-	85	95.5	99.9
3,3,5-trimethyl-	70	92.5	99.5
norcamphor	88	99	99.7
camphor	85	94	98

[a]A 2 : 1 ratio for reagent : ketone was utilized. [b]The yields of alcohols were more than 95%. [c]The figures are percentage of the less stable isomers.

vide a new class of stereoselective reducing agents. The results are summarized in Table 5.

As the Table shows, the halogen substituent in the monoalkylboranes plays an important role in the stereoselective reduction of typical cyclic ketones as expected. The stereoselectivity increased dramatically with increasing steric size of the substituent. For example, in the reduction of 2-methylcyclohexanone IpcBHCl·SMe_2 affords 79% *cis*-2-methylcyclohexanol, the less stable isomer. However, the substitution of a bromine atom for chlorine in IpcBHCl·SMe_2 exerts a tremendous stereoselectivity enhancement (to 91%). Furthermore, the stereoselectivity increases consistently with increasing size of the halogen substituent, approaching 98%. The iodo derivative achieved highly stereoselective reductions with representative cyclic ketones. Such stereoselectivities are comparable to the results previously achieved at 0° with trialkyl- and alkylalkoxyborohydrides.[16]

Conclusion

This study has shown that IpcBHX·SMe_2, readily available from the monohydroboration of α-pinene with $H_2BX·SMe_2$ in CH_2Cl_2, is a new, stable hydroborating and reducing agent with exceptional regio- and stereoselectivity. The selectivities increase consistently with increasing steric size of the halogen substituent. Especially, the iodo derivative monohydroborates of alkenes and alkynes in essentially 100% regioselectivity, and reduces cyclic ketones in exceptional stereoselectivity. In addition to that, chiral IpcBHX·SMe_2 possesses a potential for asymmetric hydroboration of olefins and asymmetric reduction of prochiral ketones. A detailed study for this possibility is in progress.

Experimental Section

The reaction flasks and other glassware required for the experiments were predried at 140° for several hours, assembled hot, and cooled under a stream of purified nitrogen. Syringes were assembled and fitted with needles while hot and cooled. All reactions were carried out under a static pressure of nitrogen in flasks fitted with septum-covered sidearms, using standard techniques for handling air-sensitive materials.[5]

Materials

Commercial grade CH_2Cl_2 was pretreated by stirring over concentrated H_2SO_4 and distilling from P_2O_5. All chemicals were commercial products of the highest purity, which were carefully purified by standard methods before use. Monochlorohorane-methyl sulfide ($H_2BCl·SMe_2$) and monobromoborane-methyl sulfide ($H_2BBr·SMe_2$) were used as received from Aldrich. Monoiodoborane-methyl sulfide ($H_2BI·SMe_2$) was prepared from iodine and borane-methyl sulfide (Aldrich), according to the literature.[14] Alkenes were distilled from $LiAlH_4$ and stored under nitrogen at ambient temperatures. Alkynes were distilled under nitrogen from a small amount of $NaBH_4$.

Analyses

Yields reported in all cases are of analytically pure compounds. ^{11}B NMR spectra were recorded on a Bruker WP 80 SY spectrometer. Chemical shifts are with reference to $BF_3·OEt_2$. GC analyses were carried out on a Varian 3300 FID chromatograph equipped with a Varian 4400 integrator/plotter using Carbowax 20 M capillary column (15 m).

Preparation of Isopinocampheylhaloborane-Methyl Sulfide (IpcBHX·SMe_2) in CH_2Cl_2

The following reaction is typical of the procedure adopted in the preparation of IpcBHX·SMe_2. A 100-mL round-bottomed flask equipped with magnetic stirring bar, septum-covered sidearm, and connector tube leading to a mercury bubbler was charged with 16.1 mL of 6.2 M neat $BH_2I·SMe_2$[14] (100 mmol) and 16.9 mL of CH_2Cl_2. Then 14.6 g of α-pinene (105 mmol) was added slowly while stirring at room temperature. The reaction mixture was stirred at room temperature for 48 hrs. The usual analysis for active hydride by hydrolysis showed this solution to be 2.50 M in IpcBHI·SMe_2 : ^{11}B NMR δ −1.7 ppm (d, J_{BH}=123 Hz).

General Procedure for the Determination of the Rate of Reaction of Alkenes and alkynes

The general procedure was to add 10 mmol of compound to 11 mmol of the reagent (in the reaction of alkynes 10 mmol of the reagent was added) taken in sufficient quantity of the solvent containing a known quantity of a saturated hydrocarbon (generally 5 mmol of *n*-dodecane to serve as internal standard for GC analyses), so that the concentrations were 1 M in the reagent and compound. The reaction mixture was stirred at 50° for alkenes or at 25° for alkynes. The reaction temperature was maintained in a water bath. Aliquots of the reaction mixtures were withdrawn at specific intervals and hydrolyzed with a mixture of glycerine-water-methanol (1 : 1 : 1) to measure the residual hydride content. From the amount of hydride remaining, the extent of reaction was calculated.

Regioselectivity of Hydroboration of Alkenes with IpcBHX·SMe_2

The regioselectivity of hydroboration was determined by oxidizing the intermediate alkylboranes to the corresponding alcohols with hydrogen peroxide, followed by GC analysis.

The following reaction is typical of the procedure utilized

for determining the directive effect. A dry 100-mL round-bottom flask, equipped with a sidearm capped with a rubber septum, a magnetic stirring bar, and a connecting tube attached to a mercury bubbler, was flushed with nitrogen. The flask was immersed in a water bath at 50° and 3.4 mL of CH_2Cl_2 was injected into the flask, followed by 1.12 g of 1-octene (10 mmol) and 1.70 g of *n*-dodecane (10 mmol). The mixture was stirred, and 4.4 mL of a 2.50 M solution of IpcBHBr·SMe_2 (11 mmol) in CH_2Cl_2 was injected into the flask all at once. Stirring was continued keeping the flask in the water bath for reaction at 50°. The total volume of the mixture was 10 mL (1 M in alkene and 1.1 M in IpcBHBr·SMe_2). The reaction mixture was stirred for 6 hrs at 50° to complete the hydroboration. The dialkylbromoborane formed in the reaction was oxidized at 0° by adding 6 mL of 3 N aqueous NaOH and 3 mL of 30% H_2O_2. After 2 h of stirring at 25°, the mixture was saturated with K_2CO_3. The organic layer was separated, dried with anhydrous $MgSO_4$, and then analyzed by GC for the amounts of 1-octanol and 2-octanol formed in the reaction. The total yield of alcohols was 98%, of which 99.5% was 1-octanol and 0.5% was 2-octanol. The experiment was repeated for other representative alkenes listed in Table 2, and the alcohols produced following oxidation were determined.

Regioselectivity of Hydroboration of Unsymmetrically Substituted Alkynes with IpcBHX·SMe_2

The regioselectivity of hydroboration was determined by oxidizing the intermediate alkenylboranes to the corresponding carbonyl compounds with hydrogen peroxide, followed by GC analysis.

Analysis for 1-Alkynes. To a 25° solution of 0.58 m*l* of 1-hexyne (0.415 g, 5.05 mmol), 0.85 g of dodecane (5.0 mmol) and 1.7 mL of CH_2Cl_2 were added, and finally 2.0 m*l* of a 2.50 M IpcBHI·SMe_2 solution in CH_2Cl_2 was injected into this mixture at 25°. After 12 h, the reaction mixture was cooled to 0°, neutralized with 2 mL of 2.5 N NaOH, followed by addition of 5 mL of buffer solution (pH 7). Then the mixture was oxidized by addint 1.5 mL of 30% H_2O_2 dropwise at 0°. The mixture was stirred for 2 h at 0°. Then the aqueous layer was saturated with K_2CO_3 and the organic layer was separated. Analysis of the organic layer by GC on a Carbowax 20 M capillary column revealed the presence of 98% hexanal and 2% 2-hexanone in a total yield of 92%.

Analysis for 2-Alkynes. To a 25° solution of 0.62 mL of 1-phenyl-1-propyne (0.581 g, 5.0 mmol), 0.85 g of dodecane (5.0 mmol) and 1.7 mL of CH_2Cl_2 was added 2.0 mL of a 2.50 M IpcBHI·SMe_2 solution in CH_2Cl_2. After 12 h at 0°, the reaction mixture was cooled to 0°, quenched with 5 mL of 3 N NaOH, and oxidized by adding 2.5 mL of 30% H_2O_2. The aqueous layer was saturated with K_2CO_3 and the organic layer was separated. Analysis of the organic layer by GC on a Carbowax 20 M capillary column revealed the presence of more than 99.9% 1-phenyl-2-propanone and only a trace of 1-phenyl-1-propanone in a total yield of 93%.

Stereoselective Reductions. The following procedure was used to explore the stereoselectivity of these reagents. In a 25-mL, round-bottom flask was placed 1.6 mL of a 2.50 M solution of IpcBHI·SMe_2 (4.0 mmol) in CH_2Cl_2. The flask was maintained at 0° by immersion in an ice-water bath. To this flask was added 0.23 g of 2-methylcyclohexanone (2 mmol) dissolved in 1 mL of CH_2Cl_2 and the mixture was stirred for 24 hrs at 0°. The reaction mixture was then quenched by addition of water. The organoborane was oxidized by treatment with 4 mL of 3 M NaOH followed by the dropwise addition of 0.5 mL of 30% H_2O_2. The aqueous layer was saturated with anhydrous K_2CO_3, and the organic layer was separated and dried. GC analysis revealed the presence of 98% 2-methylcyclohexanol containing 98% of the *cis* isomer and 2% of the *trans* isomer.

In a larger-scale reaction, 5.6 g of 2-methylcyclohexanone (50 mmol) was added dropwise as a neat liquid to 30 mL of a 2.50 M solution of the reagent (75 mmol) in CH_2Cl_2 at 0°. The reaction mixture was stirred for 6 hrs and hydrolyzed with 10 mL of cold water. The mixture was treated with 30 mL of 6 M NaOH followed by the dropwise addition of 10 mL of 30% H_2O_2. The aqueous layer was saturated with NaCl, and the organic layer was separated. Fractional distillation of the solution gave 4.6 g (80% yield) of essentially pure 2-methylcyclohexanol, bp 166-168° (757 mm). GC examination revealed the presence of 98% *cis*- and 2% *trans*-2-methylcyclohexanol.

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Molecular Conformation-Dependent Complexation between Acidic- and Basic-Polypeptides *via* Hydrogen Bonding in Solution

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Interpolymer complex formation between basic polypeptide poly(L-proline) Form II (PLP(II)) and acidic polypeptides poly(L-glutamic acid) (PLGA) and poly(L-aspartic acid)(PLAA) has been studied in water-methanol (1 : 2 v/v) mixed-solvent by viscometry, potentiometry, light scattering and circular dichroism (CD) measurements. It has been found that polymer complexes between PLP(II) and PLGA (or PLAA) are formed *via* hydrogen bonding with a stoichiometric ratio of PLP(II)/PLGA (or PLAA)=1 : 2 (in unit mole ratio) and that PLP(II) forms polymer complex more favorably with PLGA than with PLAA. In addition, the minimum (for pH 5.0) and the maximum (for pH 3.2) in reduced viscosity of dilute PLP(II)-PLGA mixed solutions are observed at 0.67 unit mole fraction of PLGA (*i.e.*, [PLP(II)]/[PLGA]=1/2). These findings could be explained in terms of molecular structure (or conformation) of the complementary polymers associated with the complex formation.

Introduction

Polymer complexes are formed, almost stoichiometrically, by the association of two or more complementary polymers *via* electrostatic forces, hydrophobic interactions, hydrogen (H) bonding, van der Waals forces or combinations of these interactions.[1-3] Due to the long-chain character of the polymers, the complex formation process is usually cooperative. Especially, the formation of polymer complexes between a proton-accepting (or Lewis base) polymer [*e.g.*, poly(ethylene oxide) (PEO), poly(N-vinyl pyrrolidone) (PVP), poly(L-proline) (PLP), etc.] and a proton-donating (or Lewis acid) polymer [*e.g.*, poly(methacrylic acid) (PMAA), poly(glutamic acid) (PGA), poly(aspartic acid) (PAA), etc.] *via* H-bonding in organic or aqueous media has attracted a continuing interest as a model of biological systems.[4-10] The interpolymer complexation *via* H-bonding in solution is highly sensitive to such factors as pH, ionic strength, temperature, solvent, concentration, structure and molecular weight of the component polymers, hydrophobic interaction, etc.[11] Hence, most studies have been performed on the polymer complex systems based on H-bonding, mainly focusing on the effects of these factors on complexation.

However, only a few studies[12-14] have been reported so far on the H bonding complexation between acidic- and basic- biopolymers with different conformations (*e.g.*, one with a helical structure and the other with a coiled structure) and on the conformational change of the complementary polymer upon complexation. Hence, for a model study on the interpolymer complexation *via* H bonding between acidic- and basic- biopolymers we have chosen PLP Form II (PLP (II)) as a basic polypeptide and L-forms of PGA and PAA