

Thexylhaloborane-Methyl Sulfide as Hydroborating and Stereoselective Reducing Agent

Jin Soon Cha*, Soo Jin Min, and Jong Mi Kim

Department of Chemistry, Yeungnam University, Kyongsan 712-749

Received February 14, 1994

Reactions of alkenes and alkynes with thexylhaloborane-methyl sulfide ($\text{ThxBHX} \cdot \text{SMe}_2$, $X = \text{Cl, Br, I}$) were investigated in detail in order to elucidate the effect of halogen substituent in thexylborane and hence establish their usefulness as hydroborating agent. The reagents readily hydroborated alkenes at 50°C and alkynes at 25°C in exceptional regioselectivity. Especially, the selectivity achieved by the bromo and iodo derivative reaches essentially 100%. In addition to that, $\text{ThxBHX} \cdot \text{SMe}_2$ was applied to the reduction of cyclic ketones to examine its stereoselectivity. The halogen substituent in thexylborane 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

Thexylchloroborane-methyl sulfide ($\text{ThxBHCl} \cdot \text{SMe}_2$) is a useful reagent for the selective hydroboration of alkenes of different structural types to produce isomerically pure thexylalkylchloroboranes.¹⁻³ These versatile intermediates have been used effectively in organic synthesis.^{3,4}

$\text{ThxBHCl} \cdot \text{SMe}_2$ and the bromo derivative ($\text{ThxBHBr} \cdot \text{SMe}_2$) are also attractive selective reducing agent,^{5,6} especially for the conversion of carboxylic acids and their derivatives to the corresponding aldehydes.^{7,8} In the systematic study to investigate their general reducing characteristics,^{5,6} $\text{ThxBHBr} \cdot \text{SMe}_2$ proved to be weaker in reducing strength but much higher in stereoselectivity than $\text{ThxBHCl} \cdot \text{SMe}_2$. These results clearly suggest that the halogen substituent in the thexylboranes exerts an additional influence in rate and stereoselectivity in the reduction of organic compounds.

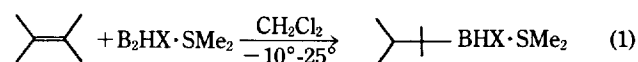
Accordingly, we decided to extend our investigation to the reaction of the iodo derivative ($\text{ThxBHI} \cdot \text{SMe}_2$). We prepared a series of thexylhaloborane-methyl sulfide ($\text{ThxBHX} \cdot \text{SMe}_2$, $X = \text{Cl, Br, I}$), applied them to the hydroboration of alkenes and alkynes 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 and of exploring their role in organic synthesis.

A portion of our results has appeared in the form of preliminary communications.⁹ We now describe in full the results of our study on the hydroboration and reduction characteristics of thexylhaloborane.

Results and Discussion

Preparation of $\text{ThxBHX} \cdot \text{SMe}_2$. The reagents were prepared by the monohydroboration of 2,3-dimethyl-2-butene with the corresponding $\text{H}_2\text{BX} \cdot \text{SMe}_2$ ($X = \text{Cl, Br, I}$) in CH_2Cl_2 Eq. (1). Both $\text{H}_2\text{BCl} \cdot \text{SMe}_2$ and $\text{H}_2\text{BBr} \cdot \text{SMe}_2$ are commercially available. $\text{H}_2\text{BI} \cdot \text{SMe}_2$ was prepared from borane-methyl sulfide and iodine.¹⁰

The ^{11}B -NMR spectra of the resulting $\text{ThxBHX} \cdot \text{SMe}_2$ solution in CH_2Cl_2 exhibited a clean doublet centered at δ 6.9 ppm ($J_{\text{BH}} = 128$ Hz) for $\text{ThxBHCl} \cdot \text{SMe}_2$, δ 5.2 ($J_{\text{BH}} = 132$ Hz)



$X = \text{Cl, ThxBHCl} \cdot \text{SMe}_2$

$X = \text{Br, ThxBHBr} \cdot \text{SMe}_2$

$X = \text{I, ThxBHI} \cdot \text{SMe}_2$

for $\text{ThxBHBr} \cdot \text{SMe}_2$ and $\delta -1.4$ ($J_{\text{BH}} = 123$ Hz) for $\text{ThxBHI} \cdot \text{SMe}_2$, relative to $\text{BF}_3 \cdot \text{OEt}_2$. In each case a small signal was observed (δ 20.6, ThxBHCl ; δ 18.9, ThxBHBr ; δ 13.2, ThxBHI), presumably due to the dimer or uncomplexed monomer of ThxBHX . All the reagents were quite stable when kept under a static pressure of dry nitrogen at 0° .

Hydroboration of Representative Alkenes with $\text{ThxBHX} \cdot \text{SMe}_2$. We examined the reaction of $\text{ThxBHX} \cdot \text{SMe}_2$ with alkenes of different structural types under standard conditions in CH_2Cl_2 to determine the time required for complete hydroboration. The rate of hydroboration of alkenes with $\text{ThxBHCl} \cdot \text{SMe}_2$ and $\text{ThxBHBr} \cdot \text{SMe}_2$ at 25° was quite satisfactory, whereas the reaction with the iodo derivative was very sluggish. Therefore, a drastic reaction condition was required for a direct comparison: each alkene was hydroborated at 50° with 10% excess quantity of $\text{ThxBHCl} \cdot \text{SMe}_2$ or $\text{ThxBHBr} \cdot \text{SMe}_2$ (1.0 M in alkene and 1.1 M in reagent) and with 100% excess quantity of $\text{ThxBHI} \cdot \text{SMe}_2$. The rate of hydroboration was monitored by hydrolyzing aliquots with a mixture of methanol-glycerine-water (1 : 1 : 1), followed by measurement of hydrogen evolved.

The relative rate of hydroboration with $\text{ThxBHX} \cdot \text{SMe}_2$ toward alkenes is essentially dependent on steric and electronic nature of the reagents. Thus, the rate is in order of $\text{ThxBHCl} \cdot \text{SMe}_2 > \text{ThxBHBr} \cdot \text{SMe}_2 > \text{ThxBHI} \cdot \text{SMe}_2$. The reaction of the iodo derivative in a 100% excess amount at 50° proceeded at a satisfactory rate, showing a complete hydroboration in less than 6h. Consequently, all the alkenes examined undergo the hydroboration readily with these reagents under the experimental conditions. The results are summarized in Table 1.

The directive effects in the hydroboration of alkenes with $\text{ThxBHX} \cdot \text{SMe}_2$ were next investigated. After standard hydroboration with the reagents under the same conditions

Table 1. Reaction of Representative Alkenes with Thexylhaloborane-Methyl Sulfide in Methylene Chloride at 50°C^a

Alkene	Time, h	Hydride used for hydroboration ^b		
		ThxBHCl·SMe ₂	ThxBHBr·SMe ₂	ThxBHI·SMe ₂ ^c
1-pentene	1.0	0.98	0.94	0.89
	3.0	1.00	1.00	1.00
	6.0	1.00	1.00	1.00
1-octene	1.0	0.99	0.88	0.85
	3.0	1.00	1.00	1.00
	6.0	1.00	1.00	1.00
1-decene	1.0	0.97	0.74	0.72
	3.0	1.00	0.98	0.89
	6.0	1.00	1.00	1.00
3,3-dimethyl-1-butene	1.0	1.00	1.00	0.92
	3.0	1.00	1.00	1.00
	6.0			1.00
2,4,4-trimethyl-2-pentene	1.0	1.00	1.00	0.91
	3.0	1.00	1.00	1.00
	6.0			1.00
1-methylcyclohexene	1.0	0.94	0.72	0.98
	3.0	1.00	0.98	1.00
	6.0	1.00	1.00	1.00
α-methylstyrene	1.0	0.99	0.87	0.78
	3.0	1.00	1.00	0.96
	6.0	1.00	1.00	1.00

^aReagent : alkene = 1.1 : 1. ^bMolar equivalent determined gravimetrically. ^cReagent : alkene = 2 : 1.

described above, the product in each case was oxidized with alkaline hydrogen peroxide, and the oxygenated products were analyzed by GC. The results are summarized in Table 2.

Essentially quantitative conversions of the alkenes to the

corresponding alcohols with an exceptional regioselectivity in placing the boron atom exclusively at the less hindered carbon atom were observed in every case.

The selectivity achieved by all these reagents appears exceptional. This exceptional regioselectivity obtained at such a high temperature (50°) is rather surprising. Inspection of the data for product distribution, however, reveals that the steric size of halogen substituent in the hydroboration of alkenes. The relative selectivity is in order of ThxBHCl·SMe₂ < ThxBHBr·SMe₂ < ThxBHI·SMe₂. Especially, the selectivity achieved by ThxBHBr·SMe₂ and ThxBHI·SMe₂ reaches essentially 100%. The selectivity matches that displayed by 9-BBN,¹¹ the most selective hydroborating agent known.

	CH ₃ (CH ₂) ₅ CH=CH ₂	(CH ₃) ₃ CCH=C(CH ₃) ₂	Ph(CH ₃)C=CH ₂
	↑	↑	↑
ThxBHCl·SMe ₂	0.5	99.5	2
ThxBHBr·SMe ₂	0.4	99.6	0.5
ThxBHI·SMe ₂	trace	>99.9	0.2

Hydroboration of Representative Alkynes with ThxBHX·SMe₂. The monohydroboration of representative terminal and internal alkynes with ThxBHX·SMe₂ in a stoichiometric ratio (1 : 1) was examined in CH₂Cl₂ at 25° and the results are summarized in Table 3.

Whereas each reagent is rather insensitive to the position of triple bond in alkynes in the hydroboration reaction, the relative reactivity of the reagents toward alkynes is influenced by the steric and electronic nature of halogen substituent. The rate is in order of ThxBHCl·SMe₂ > ThxBHBr·SMe₂ > ThxBHI·SMe₂. Nevertheless, thexylhaloboranes have all exhibited satisfactory reactivity toward both the internal and terminal alkynes at 25° in a stoichiometric ratio. Especially noteworthy is the hydroboration of alkynes with excess reagents : only the monohydroboration product was realized in every case under these reaction conditions.

The directive effects of various unsymmetrically substitu-

Table 2. Directive Effects in the Hydroboration of Alkenes with Thexylhaloborane-Methyl Sulfide in Methylene Chloride at 50°C

Alkene	Products	Product distribution, % ^a		
		ThxBHCl·SMe ₂ ^b	ThxBHBr·SMe ₂	ThxBHI·SMe ₂ ^c
1-pentene	1-pentanol	96	99.2	99.5
	2-pentanol	4	0.8	0.5
1-octene	1-octanol	99.5	99.6	>99.9
	2-octanol	0.5	0.4	trace
1-decene	1-decanol	99.5	99.8	>99.9
	2-decanol	0.5	0.2	trace
3,3-dimethyl-1-butene	3,3-dimethyl-1-butanol	99	99.2	99.5
	3,3-dimethyl-2-butanol	1	0.8	0.5
2,4,4-trimethyl-2-pentene	2,4,4-trimethyl-3-pentanol	98	99.5	99.8
	2,4,4-trimethyl-2-pentanol	2	0.5	0.2
1-methylcyclohexene	2-methylcyclohexanol	99.5	99.6	>99.9
	1-methylcyclohexanol	0.5	0.4	trace
α-methylstyrene	2-phenylpropanol	99.5	99.9	>99.9
	2-phenyl-2-propanol	0.5	0.1	trace

^aTotal yields are 94 ± 5%. ^bThe data listed in ref. (1) are performed at 25°.

Table 3. Reaction of Representative Alkynes with Thexylhaloborane-Methyl Sulfide in Methylene Chloride at 25°C^a

Alkyne	Time, h	Hydride used for hydroboration ^b		
		ThxBHCl·SMe ₂ ^b	ThxBHBr·SMe ₂	ThxBHI·SMe ₂
1-hexyne	0.5	0.93	0.90	
	1.0	0.97	0.95	0.64
	3.0	1.00	1.00	0.84
	6.0	1.00	1.00	0.94
	12.0			1.00
1-heptyne	0.5	0.90	0.87	
	1.0	0.99	0.93	0.60
	3.0	1.00	1.00	0.84
	6.0	1.00	1.00	0.95
	12.0			1.00
2-hexyne	0.5	0.90	0.86	
	1.0	0.96	0.93	0.60
	3.0	1.00	1.00	0.78
	6.0	1.00	1.00	0.93
	12.0			1.00
3,3-dimethyl-1-butyne	0.5	0.95	0.93	0.77
	1.0	0.99	0.95	0.89
	3.0	1.00	1.00	0.89
	6.0	1.00	1.00	1.00
	12.0			1.00
4,4-dimethyl-2-pentyne	0.5	0.82	0.76	
	1.0	0.86	0.81	0.62
	3.0	0.94	0.89	0.71
	6.0	1.00	0.99	0.87
	12.0	1.00	1.00	0.93
phenylethyne	0.5	0.84	0.80	
	1.0	0.94	0.90	0.72

	3.0	1.00	1.00	0.85
	6.0	1.00	1.00	0.91
	12.0			1.00
1-phenyl-1-propyne	0.5	0.82	0.79	
	1.0	0.89	0.85	0.69
	3.0	0.95	0.91	0.75
	6.0	1.00	1.00	0.80
	12.0	1.00	1.00	0.90
	24.0			1.00

^aEquimolar amount of reagent and alkynes was utilized. ^bMolar equivalent determined gasometrically.

ted acetylenes toward ThxBHX·SMe₂ were next investigated. The regioselectivity for the addition of B-H bond was determined by oxidation of the intermediate alkenylthexylhaloboranes with hydrogen peroxide in a buffered solution. The distribution of carbonyl isomers was then quantified by GC analysis. The results are summarized in Table 4.

As is evident from the Table, all the thexylhaloboranes achieve the clean monohydroboration of alkynes examined at 25° with exceptional regioselectivity (>97% purity). Even in the hydroboration of internal alkynes the reagents show an exceptional selectivity. The selectivity is in order of ThxBHI·SMe₂ > ThxBHBr·SMe₂ > ThxBHCl·SMe₂, as the case of hydroboration of alkenes. Especially, the selectivity achieved by ThxBHI·SMe₂ and ThxBHBr·SMe₂ reaches essentially 100%. The selectivity is far superior to that displayed by various prominent hydroborating agents.^{11c,12-16} Therefore, regioselective hydroboration of ThxBHX·SMe₂ provides a valuable synthetic route to isomerically pure aldehydes and ketones from alkynes.

Table 4. Directive Effects in the Monohydroboration of Alkynes with Thexylhaloborane-Methyl Sulfide in Methylene Chloride at 25°C

Alkyne	Products	Product Distribution, % ^{a,b,c}		
		ThxBHCl·SMe ₂	ThxBHBr·SMe ₂	ThxBHI·SMe ₂
1-hexyne	hexanal	97	98	99
	2-hexanone	3	2	1
1-heptyne	heptanal	98	99	>99.9
	2-heptanone	2	1	trace
2-hexyne	2-hexanone	98	98.5	99
	3-hexanone	2	1.5	1
3,3-dimethyl-1-butyne	3,3-dimethylbutanal	99	>99.9	>99.9
	3,3-dimethyl-2-butanone	1	trace	trace
4,4-dimethyl-2-pentyne	4,4-dimethyl-2-pentanone	99	99.5	>99.9
	4,4-dimethyl-3-pentanone	1	0.5	trace
phenylethyne	phenylacetaldehyde	98	99	99
	acetophenone	2	1	1
1-phenyl-1-propyne	1-phenyl-2-propanone	97	99	99
	1-phenyl-1-propanone	3	1	1

^aThe distribution is deduced by GC analysis from the oxygenated products produced following oxidation of the alkenylalkylborane.

^bTotal yields are 90±5%, ^cRef. 9(b).

Table 5. Stereoselective Reduction of Cyclic Ketones with Thexylhaloborane-Methyl Sulfide in Methylene Chloride at 0°C^{a-d}

Ketone	ThxBH ₂ ^e	ThxBHCl·SMe ₂ ^f	ThxBHBr·SMe ₂ ^g	ThxBHI·SMe ₂
Cyclohexanone				
2-methyl-	47-50	94.5	97.5	99
3-methyl-		68.5	81	93
4-methyl		56.5	77	89
4- <i>tert</i> -butyl-	11	65.5	78.5	99
3,3,5-trimethyl-		97	98	99
Norcamphor	92	98.5	99	99.9
Camphor	80	95	97	99

^aA 2:1 ratio for reagent:ketone was utilized. ^bThe yields of alcohols were more than 95%. ^cThe figures are percentage of the less stable isomers. ^dRef. 9(a). ^eData taken from ref. 12-13. ^fRef. 5 ^gRef. 6.

	CH ₃ (CH ₂) ₄ C≡CH	CH ₃ (CH ₂) ₂ C≡CCH ₃	Ph-C≡CCH ₃
	↑	↑	↑
ThxBHCl·SMe ₂	2	98	2
ThxBHBr·SMe ₂	1	99	1.5
ThxBHI·SMe ₂	trace	>99.9	1

Stereoselective Reduction of Cyclic Ketones with ThxBHX·SMe₂. The stereoselectivity in the reduction of mono- and bicyclic ketones with ThxBHX·SMe₂ was also examined in order to elucidate the halogen effect and hence provide a new class of stereoselective reducing agents. The results are summarized in Table 5.

As Table 5 shows, the halogen substituent in hexylborane plays an important role in the stereoselective reduction of typical cyclic ketones as anticipated. The stereoselectivity increased dramatically with increasing steric size of the substituent. For example, in the reduction of 4-*tert*-butylcyclohexanone thexylborane affords only 11% *cis*-4-*tert*-butylcyclohexanol, the less stable isomer. However, the substitution of a chlorine atom for hydrogen in thexylborane exerts a tremendous stereoselectivity enhancement (to 66%). Furthermore, the stereoselectivity increases consistently with increasing size of the halogen substituent, approaching 99%. Finally, the iodo derivative, ThxBHI·SMe₂ achieved highly stereoselective reductions with representative cyclic ketones. Such stereoselectivities are comparable to the results previously achieved at 0° with trialkyl- and alkylalkoxyborohydrides.¹⁷

Conclusion

It is evident from this study that ThxBHX·SMe₂ (X=Cl, Br, I) is a class of highly selective hydroborating and reducing agents. The reagents monohydroborate alkenes and alkynes in exceptional regioselectivity. The exceptional selectivity in the hydroboration of 1-substituted propynes is extraordinary. Furthermore, the reagents reduce cyclic ketones in exceptional stereoselectivity. The selectivity increases consistently with increasing steric size of halogen substituent. Especially, the selectivity achieved by the bromo and iodo derivatives reaches essentially 100%. With alkenes and alky-

nes, these reagents result in the clean and essentially quantitative formation of isomerically pure alkyl- and alkenylthexylhaloboranes. The rich chemistry associated with the dialkyl- and alkenylalkylhaloboranes must utilize these reagents in organic synthesis.

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 dry nitrogen. Syringes were assembled and fitted with needles while hot and then 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.¹⁸

Materials

Commercial grade CH₂Cl₂ was pretreated by stirring over concentrated H₂SO₄ and distilling from P₂O₅. All chemicals were commercial products of the highest purity, which were carefully purified by standard methods before use. Monochloroborane-methyl sulfide (H₂BCl·SMe₂) and monobromoborane-methyl sulfide (H₂BBr·SMe₂) were used as received from Aldrich. Monoiodoborane-methyl sulfide (H₂BI·SMe₂) was prepared from iodine and borane-methyl sulfide (Aldrich), as described previously. Alkenes were distilled from LiAlH₄ and stored under nitrogen at ambient temperatures. Alkynes were distilled under nitrogen from a small amount of NaBH₄.

Analyses

Yields reported in all cases are of analytically pure compounds. ¹¹B-NMR spectra were recorded on a Bruker WP 80 SY spectrometer. Chemical shifts are with reference to BF₃OEt₂. GC analyses were carried out on a Varian 3300 FID chromatograph equipped with a Varian 4400 integrator/plotter using Carbowax 20 M capillary column (50 m).

Preparation of Thexylhaloborane-Methyl Sulfide (ThxBHX·SMe₂) in CH₂Cl₂^{1-3,19}

The following reaction is typical of the procedure utilized in the preparation of ThxBHX·SMe₂. A 100 ml round-bottom flask equipped with a magnetic stirring bar, septum-covered sidearm, and connector tube leading to a mercury bubbler was charged at room temperature with 16.1 ml of 6.2 M neat BH₂I·SMe₂¹³ (100 mmol) and 16.9 ml of CH₂Cl₂. Then 8.8 g of 2,3-dimethyl-2-butene (105 mmol) was added slowly while stirring at room temperature. The reaction mixture was stirred at room temperature for 48 h. The usual analysis for active hydride showed this solution to be 2.50 M in ThxBHI·SMe₂: ¹¹B-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 ThxBHX·SMe₂

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 10 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 CH₂Cl₂ 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 ThxBHBr·SMe₂ (11 mmol) in CH₂Cl₂ 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 ThxBHBr·SMe₂). The reaction mixture was stirred for 3 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% H₂O₂. After 2 h of stirring at 25°, the mixture was saturated with K₂CO₃. The organic layer was separated, dried with anhydrous MgSO₄, 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 ThxBHX·SMe₂

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°C solution of 0.58 ml of 1-hexyne (0.415 g, 5.05 mmol), 0.85 g, of dodecane (5.0 mmol) and 1.7 ml of CH₂Cl₂ were added 2.0 ml of 2.50 M ThxBHI·SMe₂ solution in CH₂Cl₂. After 12 h at 25°C, the reaction mixture was cooled to 0°C, 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 adding 1.5 ml of 30% H₂O₂ dropwise at 0°C. The mixture was stirred for 2h at 0°C. Then the aqueous layer was saturated with K₂CO₃ and the organic layer was separated. Analysis of the organic layer by GC on a Carbowax 20 M capillary column (15 m) revealed the presence of 99% hexanal and 1% 2-hexanone in a total yield of 91%.

Analysis for 2-Alkynes. To a 25°C 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 CH₂Cl₂ was added 2.0 ml of a 2.50 M ThxBHI·SMe₂ solution in CH₂Cl₂. After 12 h at 25°C, the reaction mixture was cooled to 0°C, quenched with 5 ml of 3 N NaOH, and oxidized by adding 2.5 ml of 30% H₂O₂. The aqueous layer was saturated with K₂CO₃ and the organic layer separated. Analysis of the organic layer by GC

on a Carbowax 20 M capillary column (15 m) revealed the presence of 99% 1-phenyl-2-propanone and 1% 1-phenyl-1-propanone in a total yield of 93%.

Conversion of 1-Heptyne to Heptanal with ThxBHI·SMe₂. To a 25°C solution of 4.81 g of 1-heptyne (50 mmol) in 23 ml in CH₂Cl₂. After 12 h at 25°C, the reaction mixture was cooled to 0°C, neutralized with 10 ml of 3 N NaOH, and followed by addition of 25 ml of buffer solution (pH 7). Then the mixture was oxidized by adding 15 ml of 30% H₂O₂ dropwise. The mixture was stirred for 2 h at 0°C. Then the aqueous layer was saturated with NaCl and the organic layer separated. The aqueous layer was extracted with ether (3×20 ml). The combined organic layer was dried over anhydrous MgSO₄, followed by removal of the volatile components. Distillation afforded 4.7 g of heptanal; bp. 152-153°C (lit.¹² 152.8°C), *n*_D²² 1.4120 (lit.¹² *n*_D²⁰ 1.4113). GC analysis showed >99.9% purity and the ¹H-NMR spectrum agreed with that of an authentic sample.

Acknowledgements. This research was supported by the Yeungnam University research grants in 1993.

References

- Brown, H. C.; Sikorski, J. A.; Kulkarni, S. V.; Lee, H. D. *J. Org. Chem.* **1982**, *47*, 863.
- Sikorski, J. A.; Brown, H. C. *J. Org. Chem.* **1982**, *47*, 872.
- Zweifel, G.; Person, N. R. *J. Am. Chem. Soc.* **1980**, *102*, 5919.
- (a) Kulkarni, S. V.; Lee, H. D.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 4542; (b) Kulkarni, S. V.; Lee, H. D.; Brown, H. C. *Synthesis* **1982**, 193; (c) Kulkarni, S. V.; Lee, H. D.; Brown, H. C. *Synthesis* **1982**, 195.
- Brown, H. C.; Nazer, B.; Cha, J. S.; Sikorski, J. A. *J. Org. Chem.* **1986**, *51*, 5264.
- Cha, J. S.; Kim, J. E.; Oh, S. Y. *Bull. Korean Chem. Soc.* **1987**, *8*, 313.
- (a) Brown, H. C.; Cha, J. S.; Nazer, B.; Yoon, N. M. *J. Am. Chem. Soc.* **1984**, *106*, 8001; (b) Brown, H. C.; Cha, J. S.; Nazer, B.; Yoon, N. M. *J. Org. Chem.* **1987**, *52*, 5400.
- (a) Cha, J. S.; Kim, J. E.; Lee, K. W. *J. Org. Chem.* **1987**, *52*, 5030; (b) Cha, J. S.; Oh, S. Y.; Kim, J. E. *Bull. Korean Chem. Soc.* **1987**, *8*, 301; (c) Cha, J. S.; Lee, K. W.; Yoon, M. S.; Lee, J. C. *Bull. Korean Chem. Soc.* **1988**, *9*, 384; (d) Cha, J. S. *Org. Prep. Proced. Int.* **1989**, *21*, 451.
- (a) Cha, J. S.; Min, S. J.; Kim, J. M.; Kwon, O. O.; Jeoung, M. K. *Org. Prep. Proced. Int.* **1993**, *25*, 469; (b) Cha, J. S.; Min, S. J.; Kim, J. M.; Kwon, O. O. *Tetrahedron. Lett.* **1993**, *34*, 5116.
- Kinberger, K.; Siebert, W. *Z. Naturforsch. Teil B* **1975**, *30*, 55.
- (a) Scouten, C. G.; Brown, H. C. *J. Org. Chem.* **1973**, *38*, 4092; (b) Brown, H. C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, *96*, 7765; (c) Brown, H. C.; Scouten, C. G.; Liotta, R. *J. Am. Chem. Soc.* **1979**, *101*, 96.
- Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 3834.
- Plamondon, J.; Snow, J. T.; Zweifel, G. *Organomet. Chem. Synth.* **1971**, 249.
- Brown, H. C.; Campbell, J. B. Jr. *J. Am. Chem. Soc.* **1980**, *45*, 389.

15. Cha, J. S.; Seo, J. B.; Lee, J. C.; Kim, J. M.; Lee, H. S.; Park, Y. B.; Uhm, J. K.; Shim, S. C.; Kim, H. S.; Kim, T. J.; Kwak, Y. W.; Lee, D. H. *Heterocycles* **1991**, *32*, 425.
16. Pelter, A.; Singaram, S.; Brown, H. C. *Tetrahedron Lett.* **1983**, *24*, 1433.
17. (a) Brown, H. C.; Cha, J. S.; Nazer, B. *J. Org. Chem.* **1984**, *49*, 2073; (b) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159; (c) Cha, J. S.; Yoon, M. S.; Kim, Y. S.; Lee, K. W. *Tetrahedron Lett.* **1988**, *29*, 1069; (d) Brown, H. C.; Cha, J. S.; Nazer, B. *J. Org. Chem.* **1985**, *50*, 549.
18. Brown, H. C. *Organic Synthesis via Boranes*; John Wiley and Sons: New York, 1975.
19. (a) Cha, J. S.; Kim, J. E.; Oh, S. Y.; Lee, J. C.; Lee, K. W. *Tetrahedron Lett.* **1987**, *28*, 2389; (b) Cha, J. S.; Kim, J. E.; Lee, K. W. *J. Org. Chem.* **1987**, *52*, 5030; (c) Cha, J. S.; Oh, S. Y.; Kim, J. E. *Bull. Korean Chem. Soc.* **1987**, *8*, 301.

Conformations of the Acyl Esters of *p*-Tert-butylcalix[4]arene and Calix[4]arene

Kwanghyun No* and Hee Jung Koo

Department of Chemistry, Sookmyung Women's University Seoul 140-742

Received February 17, 1994

Tetra acyl esters of *p*-tert-butylcalix[4]arene and calix[4]arene, including acetyl, propionyl, butyryl and isobutyryl, are synthesized and their conformations are inferred from $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra. The conformer distribution is affected by the presence of *t*-butyl group, whereas the acylation products of *p*-*t*-butylcalix[4]arene are the cone conformers, those of calix[4]arene are mostly partial cone and/or 1,3-alternate conformers. The conformational outcome is also affected by the method of preparation, the NaH-induced reaction is preferred to the acid-induced reaction for cone and partial cone. Interestingly, 1,2-alternate conformer was isolated in 14% yield from the butyrylation of calix[4]arene.

Introduction

Calixarenes are cavity containing macrocyclic compound made up of phenol and formaldehyde building blocks, and have received a great deal of attention in recent years because of their basket shape and their ability to be functionalized in various ways^{1,2}. The cavity of calixarene is conformationally mobile³ and exists four possible conformational isomers; cone, partial cone, 1,2-alternate and 1,3-alternate as shown on Figure 1.

Shaping the cavity plays a potentially vital role in the design of calixarenes as enzyme mimics, for host-guest interactions depend on complementarity in shape as well as functionality. Upon replacement of the phenolic hydrogens with larger than ethyl group, the calix[4]arenes become conformationally inflexible, existing as discrete entities in one or another of the conformations^{4,5}. However, considerable confusion still exists in the conformer distribution on the alkylation or acylation of calixarene. In a study of the arylation of calix[4]arenes, Gutsche⁶ reported that the products partition principally between the cone and 1,3-alternate conformers and the particular conformation in which a calix[4]arene is fixed upon derivatization is dependent on the temperature, the solvent, the para substituent of the calix[4]arene, and the reactivity of the arylation agent. He also reported that the products of arylmethylation partition principally between the cone and partial cone conformers⁷. The conformation of

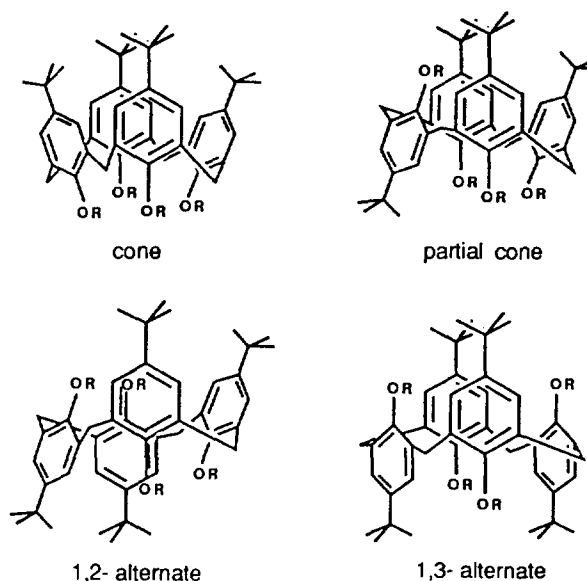


Figure 1. Conformations of calix[4]arene.

a derivatized calix[4]arene can be readily established on the bases of its $^1\text{H-NMR}$ spectrum, particularly from the patterns arising from the methylene protons joining the aromatic rings of the cyclic array, the cone conformer shows