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Organoboranes

LI *. Convenient procedures for the recovery of pinanediol in asymmetric synthesis via one-carbon homologation of boronic esters

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Abstract

Matteson's asymmetric synthesis via a one-carbon homologation of the pinanediol boronic esters with (dichloromethyl)lithium at $-100\,^{\circ}C$ results in the insertion of a chloromethyl group into the carbon–carbon bond with $> 99\%$ diastereoselectivity. This procedure makes possible the asymmetric synthesis of the chiral moiety, $RR'CH^{*}B(OR'')_2$, providing an alternative route to chiral hydroboration for these valuable chiral intermediates. Unfortunately, this method suffers from the remarkable difficulty encountered in the recovery of the pinanediol chiral auxiliary, making this asymmetric synthesis impractical. Fortunately, a systematic study of the problem has uncovered convenient procedures for the recovery of pinanediol from pinanediol boronate esters.

Introduction

Asymmetric synthesis in its broadest sense is, at best, a very effective method for the preparation of enantiomerically pure compounds. The discovery of asymmetric hydroboration in 1961 marked the beginning of an effective asymmetric synthesis [1]. Since then, intense interest has developed in efficient methods for asymmetric synthesis. Various chiral hydroborating agents from naturally abundant low cost terpenes of various steric requirements have been explored in our laboratory for the hydroboration of different classes of prochiral olefins [2]. Other examples of highly enantioselective synthesis utilize chiral auxiliary groups to direct the introduction of two adjacent chiral centers via chiral aldol condensation [3,4], chiral epoxidation of allylic alcohols [5], allylboration of aldehydes [6] and asymmetric reduction of ketones [7].

* For part L see ref. 29.

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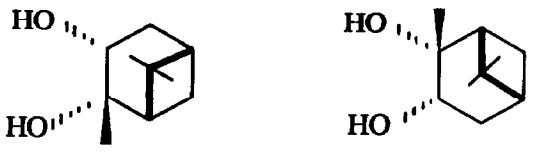
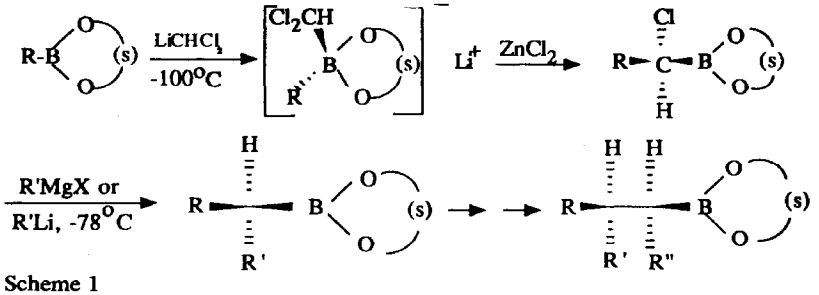
Matteson et al. recognized the possibilities for a new asymmetric synthesis during a study of the one-carbon homologation of cyclic boronate esters. After observing a modest asymmetric induction in the conversion of diacetonemannitol benzylboronate to the 1-chloro-2-phenylethylboronate [8], a more powerful chiral directing group was sought. The high chiral selectivities achieved in the hydroboration with α-pinene derivatives led Matteson et al. to an intuitive choice of pinanediol boronate esters. The pinanediol chiral auxiliary was prepared via the osmium tetroxide catalyzed oxidation of α-pinene [9]. As both enantiomers of α-pinene with > 99% ee are now readily available, both enantiomers of pinanediol can be prepared in very high optical purity. The diol derived from (+)-α-pinene will be designated as (*s*)-pinanediol (I) as it directs the reaction of the formation of (1*S*)-1-chloroalkylboronic esters, while (*r*)-pinanediol (II) is prepared from (−)-α-pinene.



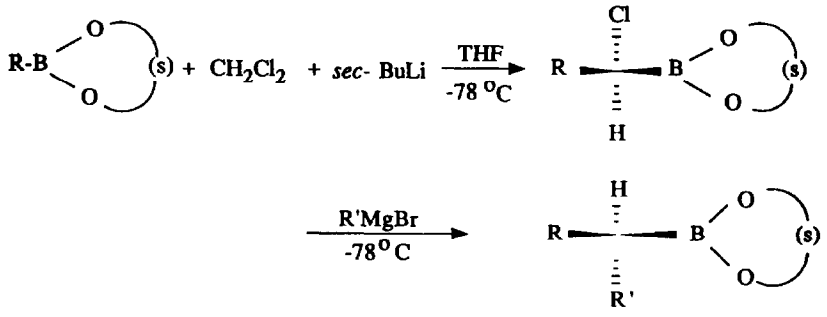
I II

(s)-pinanediol **(r)-pinanediol**

An elegant asymmetric synthesis via the successive one-carbon homologation of cyclic boronate esters derived from pinanediol with preformed (dichloromethyl)lithium, $LiCHCl_2$, at −100 °C, followed by transfer of the organic group from boron to carbon induced by anhydrous $ZnCl_2$, has been reported by Matteson [11]. Boronate esters derived from (*s*)-pinanediol furnish (1*S*)-I-(chloroalkyl)boronates and its enantiomer was prepared by the choice of (*r*)-pinanediol boronate ester. Nucleophilic displacement on (1-chloroalkyl)boronic esters yield new chiral boronic esters which can serve as the building block for successive one-carbon homologation. Adjacent chiral centers have been assembled with a high degree of stereo- and enantioselectivity (> 99% ee) independently of any chirality already existing. Both enantiomers of pinanediol are readily available in optically active form. In theory, one may be cleaved from boron and replaced by the other, which places the absolute configuration of each successive chiral center under the control of the chemist. This process of successive one-carbon homologation has been shown to be compatible with various functional groups and the significance of this chiral synthesis has been indicated by the synthesis of various insect pheromones, optically active *vic*-diol and chiral *vic*-amino alcohol, etc. [11].



Scheme 1



Scheme 2

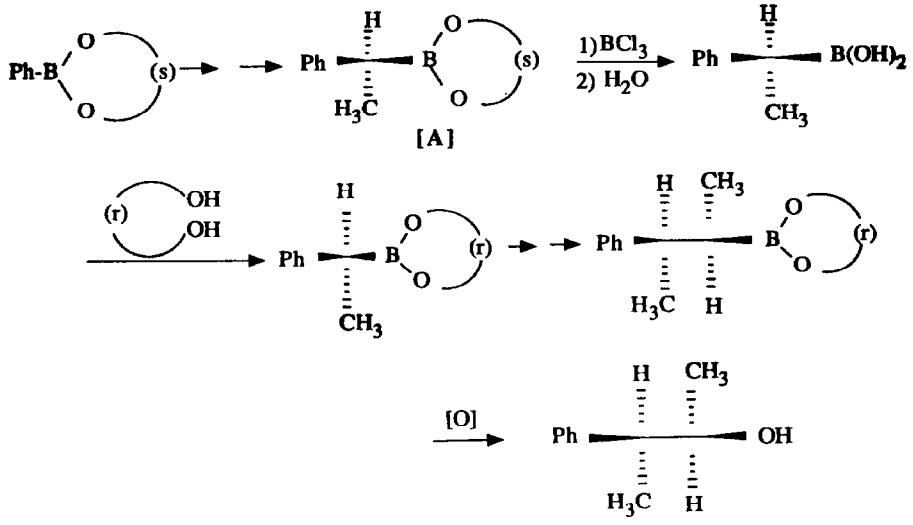
The most elegant feature of this asymmetric synthesis is the prediction of chirality at each chiral center and the possibility of immediate repetition of the cycle to introduce additional chiral centers without limit, except for the attrition of material inherent in the best of linear multistep syntheses.

Conciseness has always been a desirable goal in asymmetric synthesis. Apart from its many desirable features, Matteson's asymmetric synthesis suffers from certain demerits. Firstly, the above synthesis involves the generation of $LiCHCl_2$ at $-100\,°C$ in THF by reacting dichloromethane with n-BuLi. This method for the preformed generation of $LiCHCl_2$ at $-100\,°C$ is both impractical and inconvenient on a large scale. Secondly, and more importantly, the above asymmetric synthesis suffers from the remarkable difficulty encountered in the recovery of the pinanediol chiral auxiliary.

During the course of our investigation of one-carbon homologation of cyclic boronate esters, we have established the utility of $LiCHCl_2$, generated in situ by reacting CH_2Cl_2 and sec-BuLi in the presence of the boronate ester in THF at $-78\,°C$ [12]. We applied the same procedure to the one-carbon homologation of pinanediol boronate esters. Indeed, the reaction worked very well (Scheme 2) and enantioselectivities in the range of $> 99\%$ were achieved. This method for the in situ generation of $LiCHCl_2$ at $-78\,°C$ makes Matteson's asymmetric synthesis more practical and convenient.

Remarkable difficulty was experienced in recovering the pinanediol chiral auxiliary during the synthesis of [2*R*,3*S*]-3-phenyl-2-butanol. Conversion of the boronate ester **A** to the desired compound required the installation of a second chiral center in the opposite sense to the first one. Although a double inversion method is possible in principle, it failed and the alternative procedure of replacing (*s*)-pinanediol with (*r*)-pinanediol was undertaken. Unfortunately, an unusual resistance of pinanediol boronate esters toward hydrolysis, transesterification, or ligand exchange was encountered. Degradative cleavage to the boronic acid by the use of excess BCl_3 was finally adopted [8] (Scheme 3).

This procedure made possible the preparation of the desired boronic acid, at the cost of destroying the expensive pinanediol chiral auxiliary. Pinanediol boronate esters are too sterically hindered for some purposes, including the remarkable difficulties in the hydrolytic removal of the pinanediol group from the boron.



Scheme 3

Consequently, various other chiral directing groups with *C*-2 symmetry, such as [*R*,*R*]-2,3-butanediol, [*S*,*S*]-diisopropylethanediol (DIPED) and 1,2-dicyclohexyl-1,2-ethanediol, have been tried [13]. The boronate esters derived from these diols have equivalent diastereotopic faces for the nucleophilic attack, which makes dichloromethaneboronic esters useful for asymmetric synthesis. The diastereoselectivity achieved by the use of DIPED and 1,2-dicyclohexyl-1,2-ethanediol was comparable to that of pinanediol (> 99%), while [*R*,*R*]-2,3-butanediol afforded diastereoselectivity in the range of 90–95%. However, 2,3-butanediol boronate esters have the advantage of being readily hydrolyzed to the corresponding boronic acid and hence permits ready recovery of the chiral auxiliary. Boronate esters derived from [*S*,*S*]-DIPED and 1,2-dicyclohexyl-1,2-ethanediol resist hydrolysis [14], behaving like pinanediol boronate esters. However, these can be transesterified with pinanediol but their use in the asymmetric synthesis is restricted due to the restriction of a single replacement. In other words, once pinanediol had been introduced, it was not possible to replace it except by destruction with BCl_3. The ready availability of both enantiomers of pinanediol and the excellent diastereoselectivity achieved (> 99% ee) prompted us to use pinanediol as a chiral auxiliary in our asymmetric synthesis. The present project was undertaken in the hope of overcoming the problem of the recovery of pinanediol from the pinanediol boronate esters.

Results and discussion

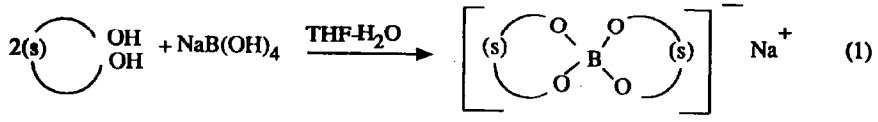
The present study has been divided into two parts: (a) recovery of pinanediol from sodium bis(pinanediol)borate and (b) recovery of pinanediol from the pinanediol boronate esters.

Recovery of pinanediol from bis[pinanediol]borate

Oxidation of the pinanediol boronate ester with $NaOH/H_2O_2$ in aqueous THF results in the formation of a precipitate of sodium bis(pinanediol)borate (III). Matteson et al. have attempted various methods for the recovery of pinanediol from

this bisborate salt III [8]. Acidification of III with aqueous HCl affords a 1/1 mixture of pinanediol and pinanediol boric acid IV, an unusually stable boric acid ester (eq. 2). Although this 1/1 mixture behaves much like pinanediol as a reagent for esterifying boronic acids, it would be more desirable to recover pure pinanediol free from IV for synthetic transformations.

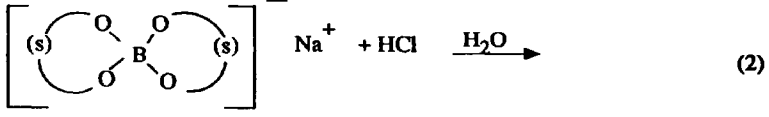
For our present study, sodium bis(pinanediol)borate (III) was prepared by reacting two equivalents of pinanediol with an equivalent of sodium tetraborate in alkaline aqueous THF solution [8] (eq. 1).



(1)

III

Acidification of III with aqueous HCl furnished a 1/1 mixture of pinanediol/pinanediol boric acid (IV). The reaction of this 1/1 mixture with refluxing methanol did not furnish the expected trimethylborate, as is evident by ^{11}B NMR. Hence, the only resort was to distill off pinanediol from the stable IV under reduced pressure. IV was then treated with an aqueous NaOH solution to obtain the bisborate salt and the cycle continued. However, this procedure is tedious.



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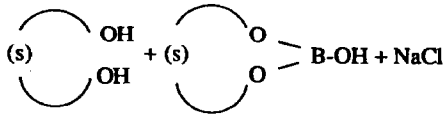
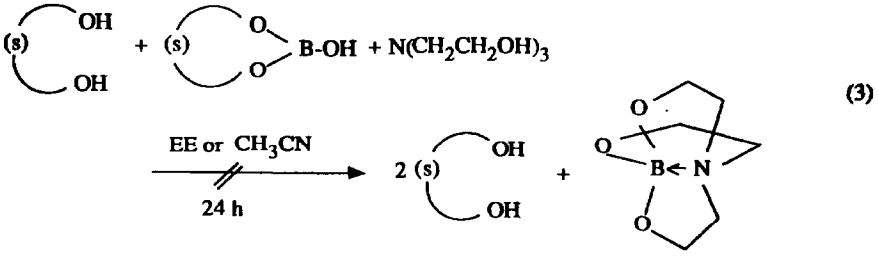


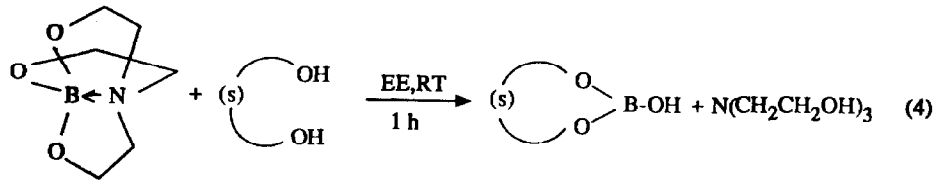
IV

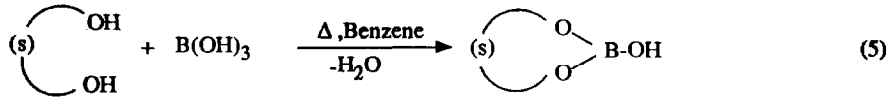
Boric acid is known to form a very stable complex with triethanolamine and a triptych structure for the borate has been well established [15]. Our efforts to form a complex of pinanediol boric acid (IV) with triethanolamine failed.The reaction of 1/1 mixture of pinanediol/IV with triethanolamine in ether or acetonitrile did not furnish any borate, as is evident by ^{11}B NMR, and the starting material was recovered (eq. 3).



(3)

This reaction was indicative of an unfavorable equilibrium. To confirm this conclusion, the reaction of triethanolamine borate with pinanediol was performed in





IV

ether/CH_3CN. The reaction readily furnished pinanediol boric acid IV, free from the separated triethanolamine (eq. 4). IV was characterized by ^{11}B NMR (δ 21 ppm) and ^1H NMR. An authentic sample of IV was prepared by reacting pinanediol with an equivalent of boric acid and removing water formed azeotropically using a Dean–Stark separator (eq. 5).

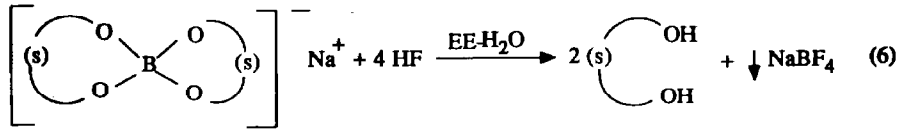
Use of amberlite IRA-743 resin

Amberlite IRA-743 resin is known to be a boron specific resin and has been used for the removal of boric acid from water. We tested the utility of this resin for the recovery of boric acid from a 1/1 mixture of pinanediol/IV. When this 1/1 mixture was eluted over a column of Amberlite IRA-743 resin at a rate of 60 drops/min, pinanediol was recovered quantitatively, free from the boric acid, in the ethanol eluate. *N*-Methyl-D-glucamine being the component of this resin, it was tested separately for our studies. Indeed, to our pleasant surprise, treatment of a 1/1 mixture of pinanediol/IV with a saturated solution of *N*-methyl-D-glucamine in ether/H_2O furnished a quantitative recovery of pinanediol in the ether phase.

Our efforts to achieve transesterification of the bisborate salt III with ethylene glycol at both 25 and 100 °C failed and no recovery of pinanediol via transesterification [16] could be achieved.

Use of HF

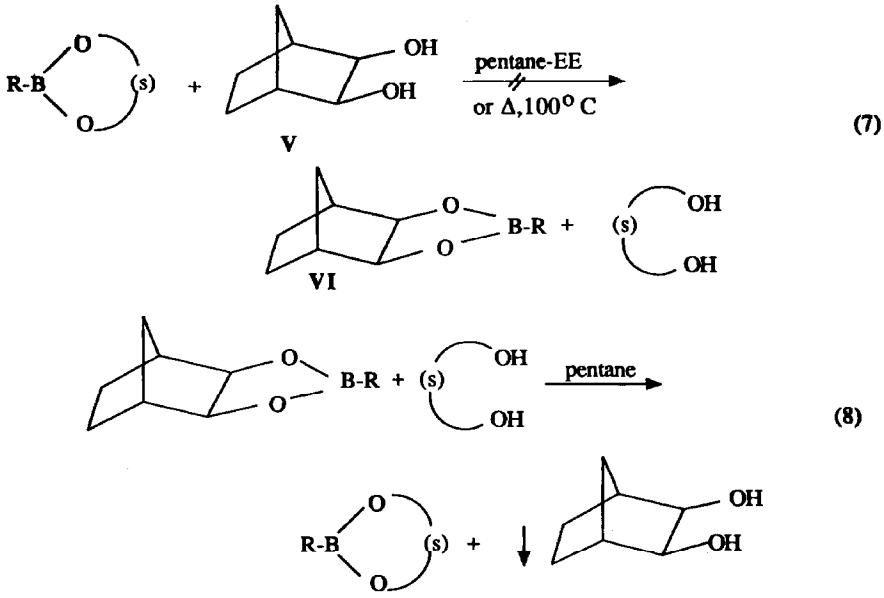
Reaction of the bisborate salt III with four equivalents of HF in ether/water furnished the recovery of pinanediol in 95% yield (eq. 6).



Presumably the formation of $NaBF_4$, which precipitated out of ether solution, accounts for shifting the equilibrium in the desired direction, making possible the recovery of pinanediol. This reaction was performed in a glass flask, but no significant etching was observed. We have also used triethylamine-tris-hydrofluoride as a source of HF for the recovery of pinanediol in quantitative yield from the bisborate salt III.

Recovery of pinanediol from pinanediol boronic esters

The formation of boronic acid from pinanediol boronate esters and the recovery



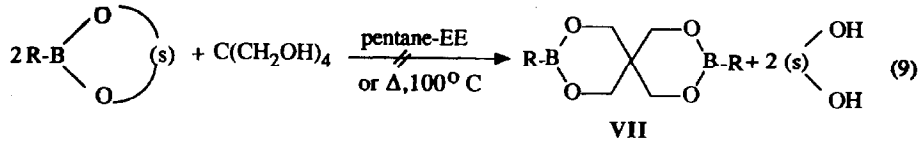
of pinanediol assumes importance when a second chiral center with an absolute configuration in opposite sense to that of the first is required in asymmetric synthesis of compounds in which successive chiral centers are to be introduced. Pinanediol boronate esters are thermodynamically stable towards hydrolysis, so much so that a solution of pinanediol in hexane will extract boric acid from pure water. Also, alkyl- or arylboronic acids can be esterified with pinanediol in the presence of boiling water, which clearly indicates the exceptional stability of pinanediol boronate esters towards hydrolysis. This stability is a convenience for purposes of chromatography and other purification procedures, but is a major obstacle when cleavage of the pinanediol group is desired in a synthesis.

Transesterification with diols and tetraols

Transesterification of the pinanediol boronate ester was then attempted with methaneboronic ester, but with no success. Transesterification was then attempted with *exo,exo*-2,3-norbornanediol (V) [17] in pentane/ether and heating under neat conditions at 100 °C (eq. 7). However, no transesterification could be achieved, indicating a possible unfavorable equilibrium. To test this conclusion, boronate ester VI was treated with an equivalent of pinanediol in pentane at 25 °C. There was an instantaneous displacement of norbornanediol, separating as a precipitate from the pentane solution, and pinanediol boronate ester was recovered from the pentane layer in quantitative yield (eq. 8).

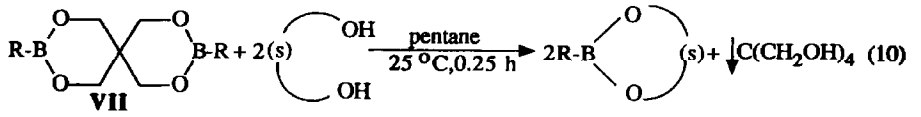
Alkyl- and arylboronic acids are known to form a boronate ester of the type VII with pentaerythritol [18]. However, our efforts to use a half equivalent of pentaerythritol for the transesterification of pinanediol boronic esters repeatedly failed. To test the probability of an unfavorable equilibrium, the boronate ester VII derived from pentaerythritol was treated with two equivalents of pinanediol in pentane/ether at 25 °C. Pentaerythritol precipitated out and pinanediol boronate ester was isolated from the pentane/ether phase (eq. 10). Even heating the pinanediol boronate ester with a half equivalent of pentaerythritol at 100 °C and distillation under reduced

pressure did not provide pinanediol. Only the starting pinanediol boronate ester was isolated in the distillate portion (eq. 9).



(9)

VII

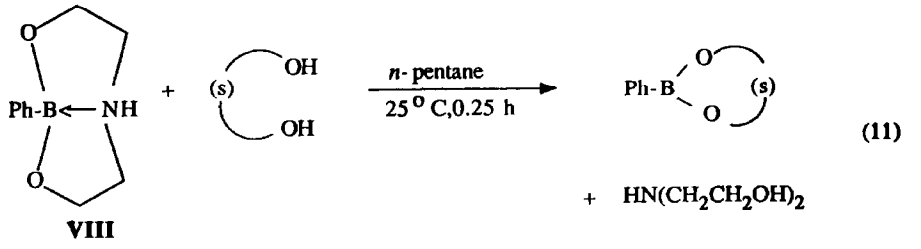


(10)

VII

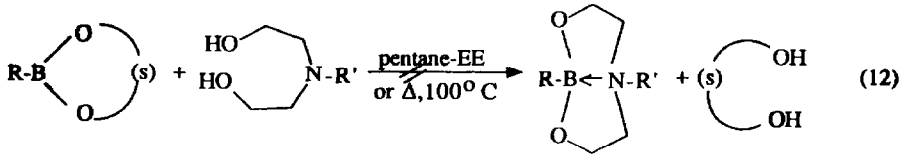
Use of diethanolamine and aminodiol derivatives

The formation of stable chelated complexes of boronic acids with diethanolamine have been well documented [19]. In an effort to test the utility of such aminodiol derivatives for the desired recovery, Matteson did report [8] the successful formation of such chelated diethanolamine boronate from pinanediol benzeneboronate in refluxing butanol. However, this method of chelation failed for the higher homologues of pinanediol boronate esters. Intrigued by these facts, we repeated the reaction of pinanediol benzeneboronate ester with diethanolamine in refluxing butanol under the identical conditions reported by Matteson. This reaction repeatedly failed in our hands and no chelation could be achieved, as is evident by ^{11}B NMR. To further confirm this conclusion, a diethanolamine complex VIII was prepared and treated with pinanediol in n-pentane. Diethanolamine was displaced, leading to the formation of the pinanediol boronate ester (eq. 11).



(11)

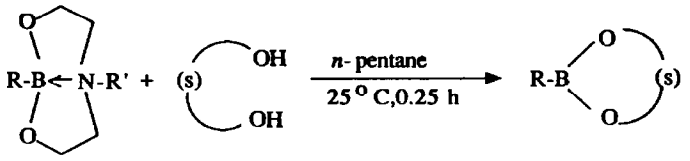
VIII



(12)

R' = -Me, IX; R' = -COONa, X

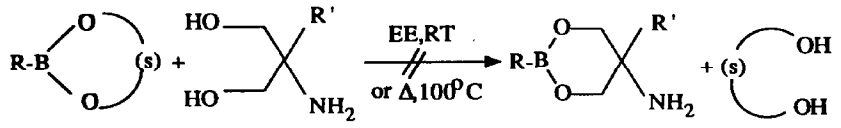
We hoped effective chelation might be achieved by increasing the basicity of the nitrogen. Hence *N*-methyldiethanolamine (IX) and the sodium salt of bicine (X) were tested. However, the reaction of pinanediol boronic esters with these diethanolamine derivatives did not furnish chelated boronate ester. Only the starting boronate ester was recovered (eq. 12). Alternately, the reaction of a chelated complex derived from a boronic acid and these diethanolamine derivatives, upon reaction with pinanediol in pentane, rapidly provided the pinanediol boronic esters (eq. 13).



(13)

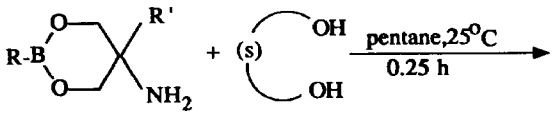
+ R'-N$(CH_2CH_2OH)_2$

R' = Me, -COONa

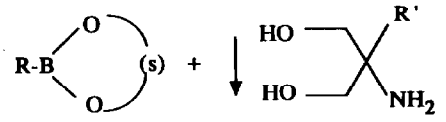


(14)

R' = -Me, XI; R' = -Et, **XII**



(15)

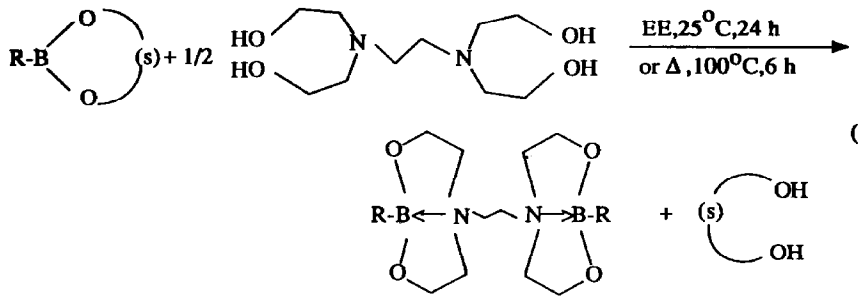


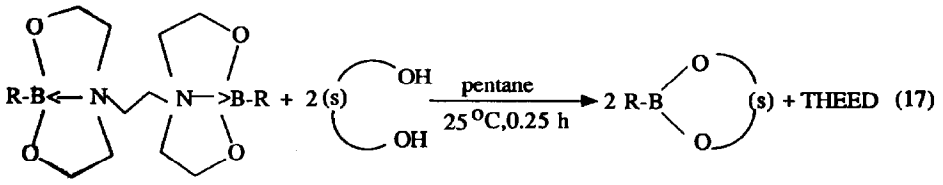
We also explored the utility of 2-amino-2-alkyl-1,3-propanediol (XI and XII) for achieving effective chelation. However, the reaction of pinanediol boronic esters with XI and XII did not displace pinanediol and the starting pinanediol boronic ester was recovered (eq. 14). Alternately, the reaction of a boronate ester XIII with an equivalent of pinanediol did not displace aminodiol from the boronate ester and pinanediol boronic ester was isolated (eq. 15). It is pertinent to mention that there was no coordination of nitrogen with boron in the boronate ester XIII, as is evident by its ^{11}B NMR (δ 31 ppm).

Tetrahydroxyethylethylenediamine (THEED) forms 1 : 2 complexes with boronic acids [20]. The reaction of the pinanediol boronate ester with a half equivalent of THEED in ether did not induce chelation, as is evident by ^{11}B NMR and the starting boronate ester was recovered (eq. 16). Alternately, the reaction of a chelated complex obtained by reacting boronic acid with a half equivalent of THEED, with an equivalent of pinanediol, furnished pinanediol boronate ester in quantitative yield (eq. 17). Evidently, the utility of THEED did not help in displacing pinanediol from the pinanediol boronate esters.

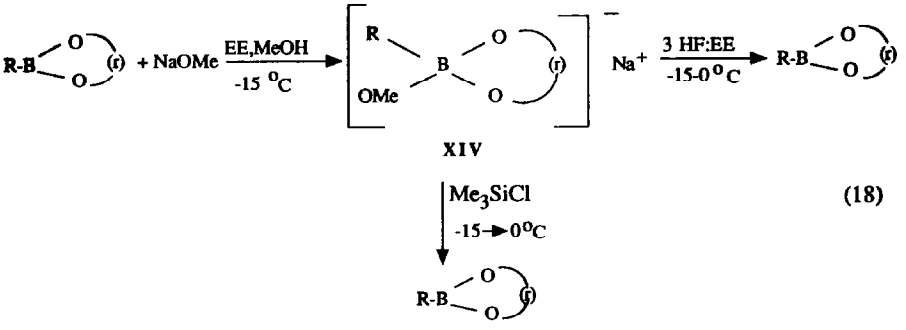
Reaction with metal alkoxides

Because of the significant success achieved in the recovery of pinanediol from the bis borate salt III by the use of HF, we were encouraged to test the utility of HF with pinanediol boronate esters. Unfortunately, no reaction was observed. We then treated an ate complex XIV with three equivalents of HF. However, this reaction



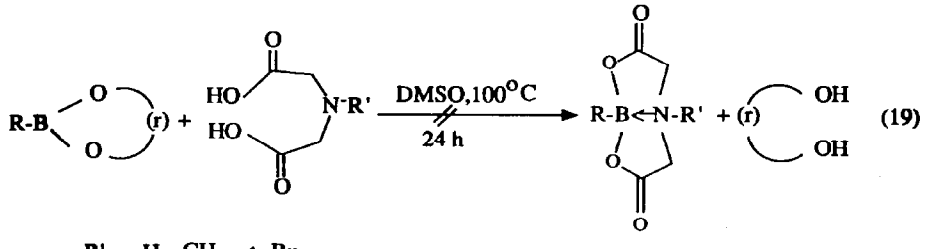


did not furnish the desired sodium alkyltrifluoroborate. Only the starting pinanediol boronate ester was recovered. Evidently, the cleavage of the *B*-alkoxy bond occurs. Reaction of the ate complex XIV with Me_3SiCl also induces cleavage of the *B*-alkoxy bond and the starting pinanediol boronate ester was recovered (eq. 18).



Reaction with iminodiacetic acid derivatives

The formation of stable chelated complexes of boronic acids with iminodiacetic acid and its derivatives has been reported from our laboratory [21]. Accordingly, we tested their utility for the recovery of pinanediol. The reaction of pinanediol boronate ester with an equivalent of iminodiacetic acid in DMSO at 140 °C for 24 h did not furnish any chelated derivative, as is evident by ^{11}B NMR. After the removal of DMSO in vacuo, the starting boronate ester was recovered (eq. 19).



R' = -H, $-CH_3$, *t*- Bu

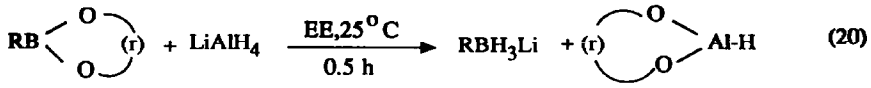
Even the increase of the basicity of nitrogen by the use of the *N*-methyl- and *N*-t-butyl iminodiacetic acid, and the use of a half equivalent of EDTA, did not show any measurable displacement.

Successful recovery of pinanediols from boronic esters

After this string of failures to achieve the displacement and recovery of pinanediol from their boronic esters, it was a delight to achieve two successful procedures for recovery.

Reaction with $LiAlH_4$

An elegant reaction of $LiAlH_4$ with a cyclic boronate ester in ether to furnish lithium monoalkylborohydride and a precipitate of dialkoxyalane has been reported from our laboratory [22]. As this method makes possible the isolation of $LiRBH_3$ cleanly from precipitated dialkoxyalane, we undertook to study the reaction of the pinanediol boronate ester with $LiAlH_4$. Indeed, the reaction of pinanediol boronate ester with $LiAlH_4$ in ether proceeded readily to provide the corresponding borohydride and pinanediol alane XV (eq. 20).

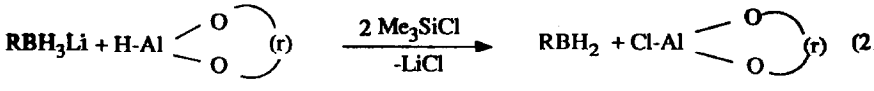


(20)

XV

Unfortunately, unlike other dialkoxyalanes, XV was soluble in pentane, ether and THF, making the isolation of the borohydride free from the alane derivative XV rather difficult.

Treatment of a mixture of borohydride and XV with two equivalents of Me_3SiCl furnished a mixture of the monoalkylborane and pinanediolchloroalane (XVI). Unfortunately, unlike the chloroalane derivatives of other cyclic diols, XVI proved to be highly soluble in pentane and ether, making difficult the isolation of monoalkylborane free of the aluminium species (eq. 21).

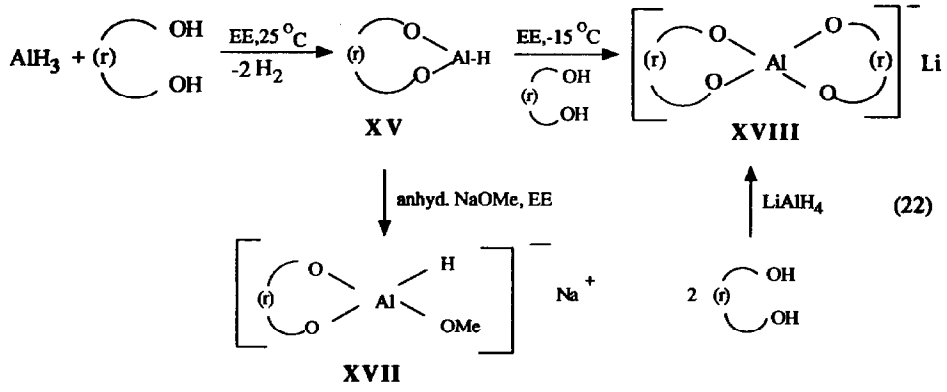


(21)

XV XVI

Our efforts to precipitate XV selectively using ethylenediamine, TMEDA, TED and piperidine failed.

We decided to undertake a detailed study of the alane derivative XV in order to establish a convenient procedure for its removal. Accordingly, a pure sample of AlH_3 in ether was prepared by adapting the published procedure [23]. The AlH_3 was converted into XV by treating with an equivalent of pinanediol. Treatment of the intermediate XV with a suspension of NaOMe in ether provided a white crystalline precipitate XVII. Removal of this precipitate gave a solution free of any aluminum species. Alternately, the solution of XV in ether was treated with a solution of the monolithio-derivative of pinanediol. There was an almost instantaneous formation and precipitation of XVIII. Again the solution was free of any aluminum species. An authentic sample of XVIII was prepared for comparison by



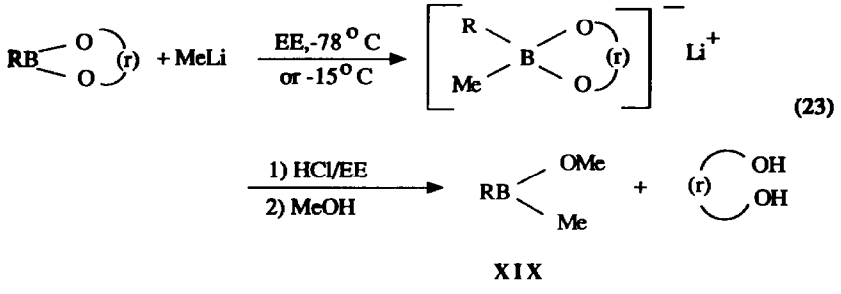
the direct treatment of $LiAlH_4$ in ether with two molar equivalents of pinanediol (eq. 22).

Pinanediol could be quantitatively recovered from both XVII and XVIII by treating them with a strong aqueous solution of sodium hydroxide with ether extraction.

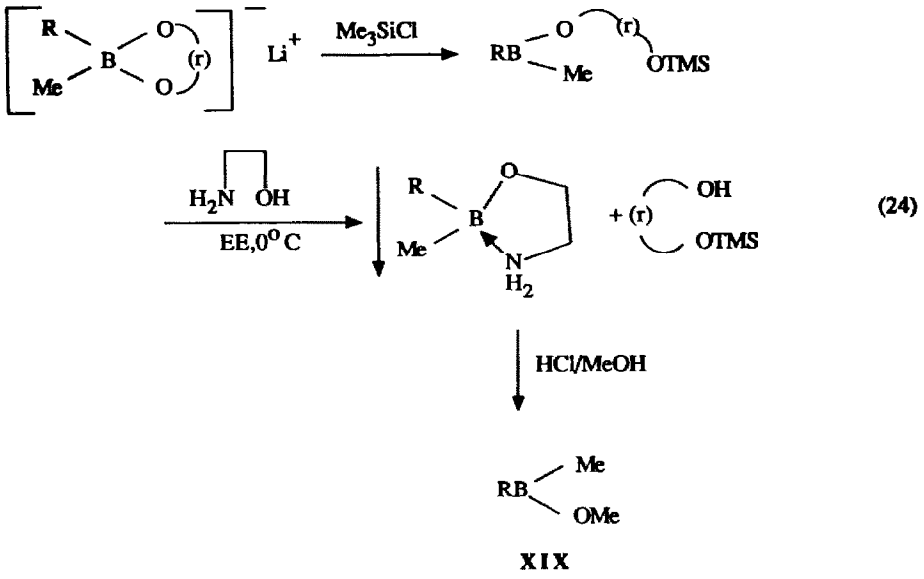
We then tested these procedures for the separation of the desired monoalkylborohydride from XV by carrying out the formation and precipitation of XVII and XVIII in the presence of the borohydride. In each case, a quantitative precipitation of the aluminum by-product was achieved, providing a pure solution of the borohydride in ethyl ether. Simple methods for the ready generation of such monoalkylborohydride into monoalkylboranes and boronic acids have been established [22].

Reaction with alkyllithium

An elegant reaction for the quantitative preparation of borinate esters from the boronate ester by the use of MeLi has been reported from our laboratory [24]. Indeed, the reaction of pinanediol boronate ester with an equivalent of MeLi in ether at $-78\,°C$ or at $-15\,°C$ furnished the desired ate complex, which upon treatment with anhydrous HCl/ether, followed by methanol, afforded the borinate ester XIX (eq. 23).



The borinate ester was then easily separated from the pinanediol either by fractional distillation or by extraction with pentane. We have also demonstrated the utility of either Me_3SiCl or CH_3COCl for the opening of the ate complex. Purification of the borinate ester was also achieved via chelation using ethanolamine (eq. 24).

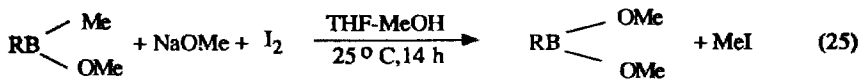


(24)

XIX

This procedure provides a quantitative recovery of pinanediol. Borinate ester was then readily obtained by treatment of the chelated complex with an equivalent of HCl in methanol, precipitating the hydrochloride of the ethanolamine. The use of such borinate esters as potential intermediates for the preparation of ketones via the DCME reaction has been examined [25].

We then explored the possibility of converting the borinate ester XIX back to the desired boronate ester by treating with $NaOMe/I_2$. Our early study of the base induced reaction of iodine with R_3B had indicated that methyl should be the most reactive group in this reaction [26]. Indeed, the reaction of XIX with $NaOMe/I_2$ in THF/MeOH provided a quantitative formation of the boronic ester and methyl iodide. There was no evidence of any attack on the R groups (eq. 25).



(25)

XIX XX

This appears to be the first report for the conversion of borinic esters into boronic esters.

Conclusion

Two methods for the recovery of pinanediol from sodium bis(pinanediol)borate dihydrate via the use of HF and Amberlite IRA-743 resin have been developed in our laboratory. Two methods for the recovery of pinanediol from the pinanediol boronate ester using $LiAlH_4$ and alkyllithium have been developed. The present study provides practical procedures for the recovery of pinanediol from their boronate esters, markedly extending the applicability of the elegant Matteson asymmetric synthesis.

Experimental

General remarks

All glassware was dried in an oven at 140 °C, assembled hot, and allowed to cool under nitrogen [27]. Both enantiomers of pinanediol (> 99% ee) were purchased from Aldrich Chemical Company. *Exo-exo* norbornanediol was obtained by the OsO_4 oxidation of norbornene [9]. *N*-t-butyliminodiacetic acid was prepared in accordance with the reported procedure [28].

Analysis

^1H NMR spectra were recorded on a Varian T-60 spectrometer. ^{11}B NMR spectra were scanned on a Varian FT-80A spectrometer and ^{11}B NMR chemical shifts are expressed in δ (ppm) upfield from $BF_3 \cdot OEt_2$ as a reference standard. GC analyses were performed on a Hewlett-Packard 5850 Chromatograph using 12′ × 0.125″, 10% SP-2100 on Chromosorb W (100–120) column.

Preparation of sodium bis(pinanediol)borate dihydrate (III)

III was prepared in 60% yield by following the reported procedure [8].

Recovery of pinanediol from III; reaction with HF

Sodium bis(pinanediol)borate(III), 1.53 g (5 mmol) was suspended in anhydrous ether (15 ml) and cooled to 0 °C. To this was added an aqueous solution of HF, 1.67 ml (48% soln., 20 mmol) or triethylamine-tris-hydrofluoride, 1.34 ml (20 mmol) and the reaction mixture stirred at 25 °C for 0.5 h. A white precipitate of $NaBF_4$ separated out. The ether portion was separated from $NaBF_4$, washed with water (2 × 5 ml) and dried over anhydrous $MgSO_4$. Removal of ether in vacuo furnished 1.6 g of pinanediol (96% yield). The absence of any residual boron containing species was ascertained by ^{11}B NMR. ^1H NMR analysis of the sample obtained was identical to that of an authentic sample of pinanediol.

Reaction of the pinanediol boronate ester with $LiAlH_4$

(*r*)-Pinanediolcyclohexylboronate, 2.62 g (10 mmol), was dissolved in anhydrous ether (15 ml) and to this was added a solution of $LiAlH_4$ in ether (10 ml, 10 mmol) dropwise and the reaction mixture stirred at 25 °C for 1 h. ^{11}B NMR of an aliquot indicated the formation of lithium cyclohexylborohydride (δ −22 ppm). Two procedures were developed for the isolation of the borohydride free from aluminum species. In one experiment, anhydrous NaOMe, 0.54 g (10 mmol) was added to the solution of a mixture of borohydride and pinanediolalane XV and the reaction mixture stirred at 25 °C for 2 h. A precipitate of aluminate XVI separated out. ^{11}B NMR of an ether aliquot showed the presence of borohydride free from any residual aluminum species (ascertained by ^{27}Al NMR). In another experiment, a mixture of the borohydride and XV was treated with preformed monolithio derivative of pinanediol (prepared by reacting pinanediol with an equivalent of n-BuLi in ether/hexane at −15 °C, 10 mmol) and stirred at 25 °C for 3 h. A precipitate of lithium bis(pinanediol)aluminate (XVII) precipitated out. An aliquot from the ether portion was taken out and checked by ^{11}B NMR, which indicated the borohydride free from any residual aluminum species. Cyclohexylboronic acid was then prepared from lithium cyclohexylborohydride via hydrolysis following a reported procedure [22]; 1.10 g (85% yield).

Reaction of (r)-pinanediol cyclohexylboronate with MeLi; preparation of borinate ester XIX

(*r*)-Pinanediol cyclohexylboronate, 2.62 g (10 mmol), was dissolved in anhydrous ethyl ether (10 ml) and to this cooled solution at −15 °C was added methyllithium, 7.14 ml (10 mmol, 1.4 *M* in ether) and stirred at −15 °C for 0.5 h. To this was added anhydrous HCl in ether, 3.45 ml (10 mmol) at 0 °C and the reaction mixture was warmed to 25 °C and stirred at 25 °C for 3 h. ^{11}B NMR of an aliquot indicated the formation of borinate ester (δ 54 ppm). Ether was pumped off in vacuo and the residue extracted with pentane (2 × 20 ml). The pentane portion was separated from precipitated LiCl and treated with excess methanol (at 25 °C for 14 h). The pentane phase was separated and dried over anhydrous $MgSO_4$. Removal of pentane in vacuo furnished 1.18 g of the borinate ester XIX (84% yield). The pinanediol was recovered from the methanol (1.50 g, 88% yield) as a viscous oil, which was induced to crystallization. The borinate ester XIX was characterized by ^{11}B NMR (δ 54 ppm) and ^1H NMR ($CDCl_3$) δ 3.60 (s, 3H, $-OCH_3$), 1.76–1.11 (m, 11H) and 0.33 (s, 3H, $-B-CH_3$).

Reaction of the borinate ester XIX with I_2 / NaOMe: preparation of the boronate ester XX

Borinate ester XIX, 0.7 g (5 mmol) was dissolved in anhydrous THF (10 ml) and to this was added iodine, 1.40 g (5.5 mmol) and NaOMe, 1.22 ml (5.5 mmol in MeOH) and the reaction mixture stirred at 25 °C for 14 h. An aliquot was taken out and its ^{11}B NMR spectrum was recorded, which showed a peak at δ 32 ppm. THF was pumped off in vacuo and the residue was extracted with pentane (2 × 10 ml). The pentane layer was separated and dried over anhydrous $MgSO_4$. Removal of pentane in vacuo furnished 0.741 g of the boronate ester XX; ^{11}B NMR δ 32 ppm.

Acknowledgement

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