Heteroatom Chemistry
Volume 1, Number 1, 1990

Organoboranes. 52. The Successful Ring Enlargement of Boracyclanes via Sequential One-Carbon Homologation: The First Synthesis of Boracyclanes in the Strained Medium-Ring Range

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Received 23 March 1989.

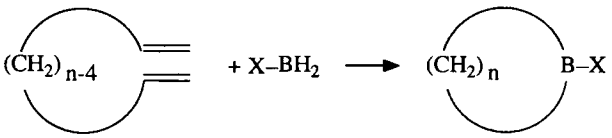
ABSTRACT

Previous attempts to synthesize boracyclanes in the medium-ring range (9-, 10-, 11-, and 12-ring members) via cyclic hydroboration of α,ω-dienes have failed. However, their synthesis via the sequential one-carbon homologation of B-methoxyboracyclanes has been achieved utilizing the successive reaction of B-methoxyboracyclanes with in situ generated (chloromethyl)lithium (LiCH₂Cl): MeOB(CH₂)₅ → MeOB(CH₂)₆ → MeOB(CH₂)₇ → MeOB(CH₂)₈ → MeOB(CH₂)₉ → MeOB(CH₂)₁₀ → MeOB(CH₂)₁₁. The yields achieved are in the range of 75–85%. In each case the products are identified by conversion via *the DCME reaction into the known cycloalkanones. This development provides the first entry into boracyclanes of the strained medium ring range.*

INTRODUCTION

Boracyclanes may be defined as those cyclic species that contain at least one boron atom in the ring structure. Although a number of boron-containing heterocycles have been known for a long time [1], the discovery of hydroboration and the recent developments in organoborane chemistry [2, 3] have remarkably widened this field.

Methods available for the preparation of boracyclanes include cyclic hydroboration of dienes and polyenes [3, 4], transmetallation [5], disproportionation [6], displacement reactions [6], substitution [6], and allylboration [7]. However, in cases where cyclic hydroboration (Eq. 1) is applicable, it is usually the method of choice, since it is simpler and more convenient than other methods. These approaches and their limitations have been discussed in detail elsewhere [3, 4]. In the past few years, the cyclic hydroboration of dienes with various hydroborating agents, such as diborane [8], thexylborane [9], BH_2Cl [10], and 9-BBN [11] have been actively investigated.



(1)

Where X = H, Cl,

One of the major difficulties with the synthesis of pure boracyclanes via the cyclic hydroboration of unsubstituted acyclic dienes arises from the attack of the borane at the internal positions of the diene. This leads to the formation of polymeric species, which, upon thermal depolymerization, undergo isomerization into isomeric boracyclanes. This difficulty was circumvented by applying 9-BBN and BH_2Cl to the hydroboration of α,ω-dienes

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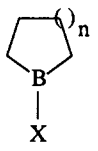
[10, 11]. The six-membered boracyclane, borinane (**2**, X = H), was prepared in excellent yield via the cyclic hydroboration of 1,4-pentadiene with 9-BBN, followed by redistribution with $BH_3 \cdot SMe_2$ [11b]. A derivative of the eight-membered boracyclane, borocane (**4**, X = OMe), was realized via the cyclic hydroboration of 1,6-heptadiene with $BH_2Cl \cdot OEt_2$ [10]. However, this method suffers from the contamination of the reaction product with isomeric boracyclanes and it fails in the attempted synthesis of higher membered boracyclanes.



Ring Size		
1	n = 1, X = H	5 borolane, boracyclopentane
2	n = 2, X = H	6 borinane, boracyclohexane
3	n = 3, X = H	7 borepane, boracycloheptane
4	n = 4, X = H	8 borocane, boracyclooctane
5	n = 5, X = H	9 boronane, boracyclononane
6	n = 6, X = H	10 borecane, boracyclodecane
7	n = 7, X = H	11 boracycloundecane
8	n = 8, X = H	12 boracyclododecane

Of these various boracycles prepared, only borinane (**2**, X = H), was found to be thermally stable. Borepane (**3**, X = H), and borocane (**4**, X = H), appeared to be thermally unstable. Indeed, attempted distillation under reduced pressure resulted in the deterioration of the compound, presumably because of polymerization [10] via ring opening. This problem of thermal instability was circumvented by converting the parent boracycles to the corresponding methoxy derivatives by treatment with MeOH; the resulting borinic esters could then be purified by fractional distillation [11].

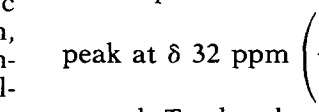
This long string of failures in the cyclic hydroboration of α,ω-dienes to synthesize medium-ring systems containing a boron heteroatom as a part of the ring implied that the strains in these medium-ring boracyclanes were too large for the relatively labile boron–carbon bonds [12]. Because of the considerable success we have achieved in applying the Matteson homologation procedure [13] in lengthening the chain of optically active derivatives [14], we decided to explore this procedure as a means of enlarging the size of the ring in *B*-methoxyboracyclanes while avoiding the undesired ring opening and polymerization.

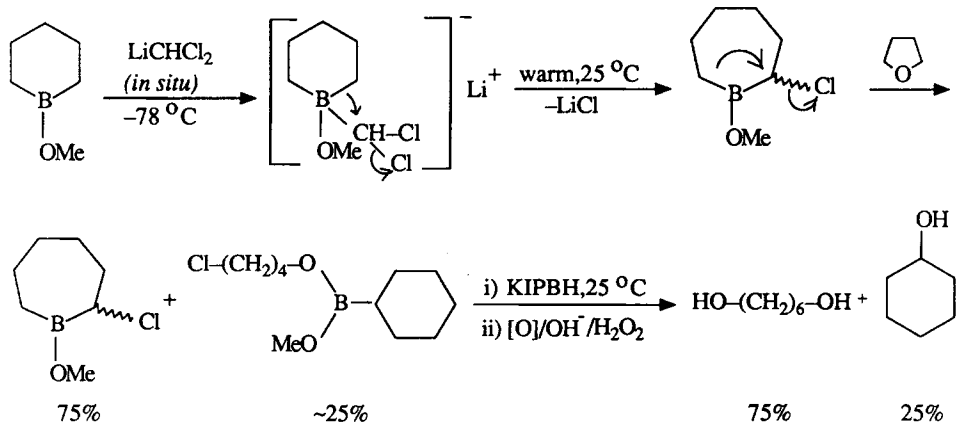
Although the one-carbon homologation of triorganylboranes and boronic esters has been thoroughly explored, very little is known regarding the homologation of borinic esters. Carbanionic reagents of the type (dichloromethyl)lithium, $LiCHCl_2$ [15]; [chloro(trimethylsilyl)methyl]lithium, $LiCHCl(SiMe_3)$ [16]; and [methoxy(phenylthio)methyl]lithium, LiCH(OMe)SPh [17] have been known to induce one-carbon homologation of all three classes of organoboranes viz. R_3B, R_2BOR', and $RB(OR')_2$. As far as the homologation of *B*-methoxyboracyclane is concerned, there has been only one report from our laboratory involving $LiCHCl(SiMe_3)$ [18].

We decided to forego all preconceived ideas in examining possible, convenient procedures for achieving one-carbon homologation of *B*-alkoxyboracyclanes. Sequential one-carbon homologation would then lead to the synthesis of medium-ring boracyclanes. We were particularly interested in the synthesis of boracyclanes in the medium-ring range (9 to 12 membered) since their existence is totally unknown, although they are potentially valuable intermediates for the preparation of medium-ring ketones via the DCME reaction [19]. The mild conditions and excellent yields in the DCME reaction of *B*-alkoxyboracyclanes are exceptionally promising when compared to the drastic conditions and low yields for the usual preparations of medium-ring ketones [20]. These considerations encouraged us to undertake the synthesis of these medium-ring boracyclanes via homologation [33].

RESULTS AND DISCUSSION

For the sequential one-carbon homologation of *B*-alkoxyboracyclanes, two procedures were explored: (dichloromethyl)lithium, $LiCHCl_2$, generated in situ, followed by potassium triisopropoxyborohydride (KIPBH) reduction of the α-chloro intermediae and (chloromethyl)lithium, $LiCH_2Cl$, generated in situ [21]. The six-membered boracycle, borinane, (**2**, X = H), was chosen as the starting boracyclane. Borinane was prepared via the cyclic hydroboration of 1,4-pentadiene with 9-BBN, following the reported procedure [11b], and then converted to *B*-methoxyborinane by treatment with an equivalent of methanol.

We first explored the utility of (dichloromethyl) lithium, $LiCHCl_2$, generated in situ by reacting dichloromethane and *sec*-BuLi in the presence of *B*-methoxyborinane. To a solution of *B*-methoxyborinane (10 mmol) in freshly distilled THF (20 mL) was added CH_2Cl_2 (11 mmol) and the solution was cooled to −78°C using a Dry-Ice–acetone bath. To this *sec*-BuLi was added dropwise by means of a syringe over a period of 15 min at −78°C. The reaction mixture was then slowly warmed to room temperature over a period of 14 h. Boron-11 NMR showed three peaks at δ 48 (major), 55 (trace), and 32 ppm (minor). The peak at δ 55 is that of the starting boracyclane, whereas the peak at δ 48 is that expected for the α-chloroborinate ester. The peak at δ 32 ppm  was unexpected. To the above solution, KIPBH (11 mmol) was added and the reaction mixture was stirred at room temperature for 3 h. Boron-11 NMR of an aliquot showed two peaks at δ 55 and 32 ppm. An aliquot was removed and subjected to oxidation using alkaline hydrogen peroxide. The oxidation product was then converted to the corresponding



SCHEME 1

bis(trimethylsilyl) ether using bis(trimethylsilyl) acetamide (BSA) [22]. Gas chromatographic analysis of the silyl ether indicated the oxidation product to be a mixture of the expected 1,6-hexanediol (major) and cyclohexanol (minor), with a trace contamination of 1,5-pentanediol. 1,6-Hexanediol arises from the oxidation of *B*-methoxyborepane (**3**, X = OMe), whereas 1,5-pentanediol is formed by the oxidation of starting *B*-methoxyborinane. The formation of cyclohexanol in ~25% yield was unexpected. Presumably it could have come as a result of the THF-assisted ionization of the C—Cl bond in the α-chloro-*B*-methoxyborepane. Ring contraction of this kind has been reported [23] in the homologation of *B*-methoxy-9-BBN with $LiCHCl_2$. The reaction sequence for the homologation of B-methoxyborinane is shown in Scheme 1.

The reaction essentially proceeds via the formation of an ate complex, which, upon warming to 25°C, undergoes the migration of a boron–carbon bond with the displacement of chloride to furnish α-chloro-*B*-methoxyborepane. Some of this then undergoes a partial ionization of the carbon–chlorine bond, assisted by the solvent (THF), to furnish ~25% of cyclohexylboronate ester, ^{11}B: (δ 32 ppm). Subsequent reduction with KIPBH, followed by oxidation, furnishes 1,6-hexanediol and cyclohexanol.

We then diverted our attention to suppressing the THF-assisted partial ionization of α-chloro-*B*-methoxyborepane to achieve the quantitative formation of homologated product. We thought the addition of KIPBH at −78°C should reduce the intermediate α-chloroboronate ester in situ, minimizing the side reaction arising from the partial ionization of carbon–chlorine bond. Indeed, this procedure suppressed the formation of the boronate ester side product and the desired one-carbon homologation of the *B*-alkoxyborinane was achieved in quantitative yield.

Alternatively, we thought that an increase in the steric bulk of the alkoxy group in *B*-alkoxyborinane might suppress the rate of ionization of the carbon–chlorine bond during the homologation sequence and thereby improve the yield of the homologated product. Accordingly, various representative *B*-alkoxyborinanes were prepared by reacting borinane with an equivalent of the corresponding alcohol. One-carbon homologation of these *B*-alkoxyborinanes was studied with (dichloromethyl)lithium ($LiCHCl_2$) generated in situ, followed by KIPBH reduction in situ. However, the increase in the bulk of the alkoxy group in the *B*-alkoxyborinanes did not show any improvement in the yield of the homologated product (Table 1). Therefore, we decided to standardize on the *B*-methoxyboracyclanes for our homologation study.

The procedure for the one-carbon homologation of *B*-methoxyborinane (**2**, X = OMe) with $LiCHCl_2$ generated in situ and KIPBH reduction in situ is representative. To a solution of *B*-methoxyborinane (10 mmol) in freshly distilled THF (20 mL) was added CH_2Cl_2 (11 mmol) and the solution cooled to −78°C using a Dry-Ice–acetone bath. To this was added *sec*-BuLi (11 mmol) dropwise by means of a syringe over a period of 15 min at −78°C. The reaction mixture was stirred at −78°C for 0.25 h. To this mixture was added (KIPBH (12 mmol) at −78°C (addition of KIPBH at −78°C was essential to minimize the side reaction leading to the formation of a boronate ester). The reaction mixture was then allowed to warm to room temperature over a period of 14 h. The ^{11}B NMR spectrum showed a single peak at δ 55 ppm, indicating the completion of the reaction. Tetrahydrofuran was removed in vacuo and the residue extracted with *n*-pentane (2 × 10 mL). Removal of the volatiles in vacuo furnished *B*-methoxyborepane (**3**, X = OMe), a seven-membered boracycle, in 73% yield. The reaction pathway is shown in Scheme 2. The structure of *B*-methoxyborepane (**3**, X = OMe) was further ascertained by GC analysis of its oxidation product [24].

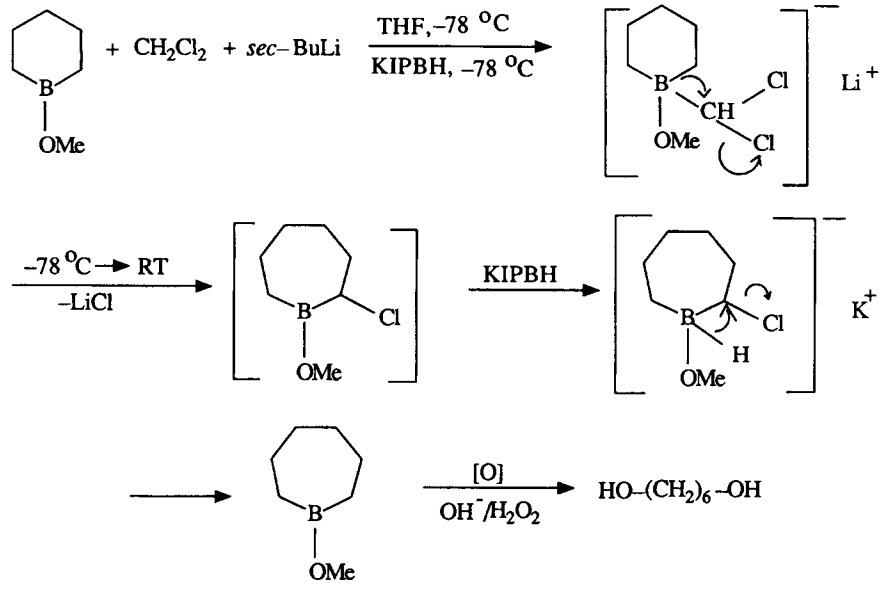
TABLE 1 One-Carbon Homologation[a] of *B*-Alkoxyborinane with (Dichloromethyl)lithium, $LiCHCl_2$, Generated in situ/KIPBH Reduction and (Chloromethyl)lithium, $LiCH_2Cl$, Generated in situ in THF at −78°C

		Yield of the homologated product[b] (%)	
Starting boracyclane	*Product boracyclane*	*With $LiCHCl_2$ generated in situ at −78°C/KIPBH reduction*	*With $LiCH_2Cl$ generated in situ at −78°C*
B-methoxyborinane	*B*-methoxyborepane	73	85
B-ethoxyborinane	*B*-ethoxyborepane	66	75
B-isopropoxyborinane	*B*-isopropoxyborepane	68	71
B-*t*-butyloxyborinane	*B*-*t*-butyloxyborepane	61	74
B-neopentyloxyborinane	*B*-neopentyloxyborepane	71	88
B-phenoxyborinane	*B*-phenoxyborepane	62	70
B-benzyloxyborinane	*B*-benzyloxyborepane	64	72
B-(diethylbenzyloxy)borinane	*B*-(diethylbenzyloxy)borepane	64	74

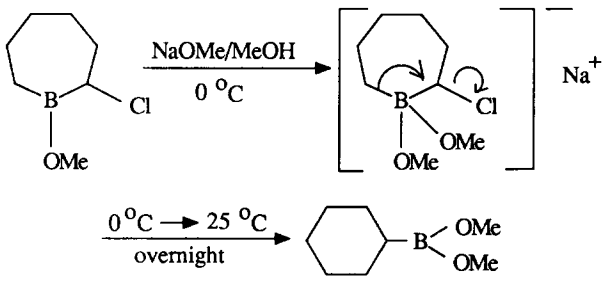
[a] All of these reactions were run on a 10 mmol scale.
[b] Determined by oxidizing the boracycle to the corresponding 1,6-hexanediol and analyzing the diol by GC [24] as its bis(trimethylsilyl)ether with *n*-hexadecane as an internal standard.

These observations suggested the possibility for preparing the higher cycloalkylboronic esters from the intermediate α-chloro-*B*-methoxyboracyclane by a slight modification of the present procedure. Indeed, treatment of the intermediate α-chloro-*B*-methoxyborepane with an equivalent of NaOMe in methanol at 0°C facilitated the ionization of carbon–chlorine bond to furnish cyclohexylboronate ester in 70% isolated yield. The reaction sequence is shown in Scheme 3.

The reaction essentially proceeds via the formation of an ate complex, followed by the ring contraction to furnish the carbocyclic boronate ester. The structure of the carbocyclic boronate ester was ascertained by direct comparison of its spectral data (IR, ^1H NMR, ^{11}B NMR) with an authentic sample [25] and, also, by oxidizing with alkaline hydrogen peroxide and analyzing the product alcohol, cyclohexanol, by GC. By following this procedure, various cycloalkylboronic acids that are otherwise difficult to prepare via hydroboration could be prepared in good yields. We have demonstrated the utility of this reaction procedure by converting *B*-methoxyborecane (**6**, X = OMe) to cyclodecyl



SCHEME 2



SCHEME 3

boronate ester in 70% isolated yield. The importance of such boronic esters in asymmetric synthesis is well recognized [26].

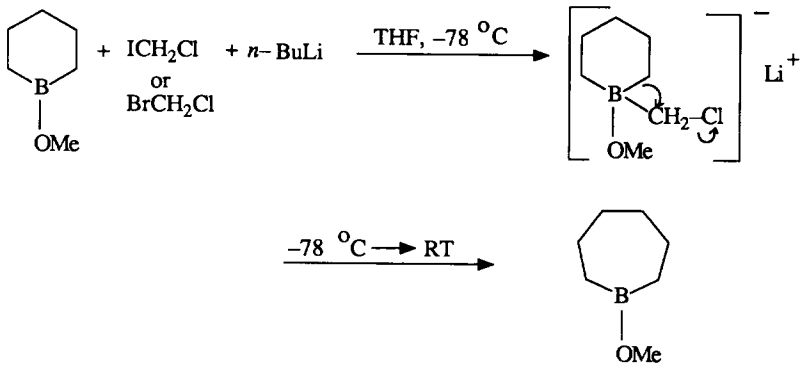
Next, we decided to explore the utility of (chloromethyl)lithium, $LiCH_2Cl$, generated in situ by reacting either iodochloromethane [27] and/or bromochloromethane [21] with *n*-BuLi in THF at −78°C in the presence of *B*-alkoxyborinane. The procedure for the one-carbon homologation of *B*-methoxyborinane (**2**, X = OMe) with $LiCH_2Cl$ generated in situ is representative. To a solution of *B*-methoxyborinane (10 mmol) in THF (20 mL) was added chloroiodomethane and/or bromochloromethane (11 mmol) and the solution was cooled to −78°C. To this was slowly added *n*-BuLi (11 mmol) from the side of the flask over a period of 0.25 h. The reaction mixture was allowed to stir at −78°C for 1 h and then warmed to room temperature over a period of 14 h. The completion of the reaction was monitored by ^{11}B NMR (δ 55 ppm). *B*-Methoxyborepane (**3**, X = OMe) was then purified by fractional distillation under reduced pressure (bp 70–71°C at 35 mm Hg); yield, 85%. Oxidation of a small aliquot furnished 1,6-hexanediol identified by GC analysis [24] of its bis(trimethylsilyl) derivative. The reaction proceeds via the formation of an ate complex and the reaction sequence is shown in Scheme 4.

However, the fact that the $LiCH_2Cl$ procedure involved only a single step, as compared to the two steps involved in the $LiCHCl_2$ procedure, persuaded us to adopt this route. We also examined the utility of the $LiCH_2Cl$ procedure with representative *B*-alkoxyborinane derivatives (Table 1). However, there was no significant improvement in the yield of the homologated product accompanying the increase in the steric bulk of the alkoxy group in the *B*-alkoxyborinane.

For the present study we chose as the starting material *B*-methoxyborepane (**3**, X = OMe) prepared either via homologation of *B*-methoxyborinane (**2**, X = OMe) or by methanolysis of borepane prepared via hydroboration of 1,5-hexadiene with 9-BBN [11c]. One-carbon homologation of *B*-methoxyborepane with $LiCH_2Cl$ furnished the eight-membered boracycle (**4**, X = OMe) in 82% yield. Oxidation of **4** with alkaline H_2O_2 furnished 1,7-heptanediol, which was analyzed by GC as its bis(trimethylsilyl)ether. *B*-Methoxyborocane was purified by fractional distillation under reduced pressure. By following similar successive one-carbon homologation with $LiCH_2Cl$, generated in situ, all *B*-methoxyboracycles through the 12-membered derivatives have been prepared (Table 2). In each case the product boracyclane was purified by fractional distillation. The fact that no significant deterioration or isomerization was observed clearly shows the thermal stability of these medium-ring boracyclanes.

The formation of these medium-ring boracycles was confirmed by converting them to the corresponding diols via oxidation and analyzing the product diols by GC as their bis(trimethylsilyl) ethers prepared by treating the product diols with BSA [24].

These boracycles from 5- to 12-membered rings were converted to the corresponding crystalline ethanolamine adducts [32] and characterized by ^{11}B NMR, ^1H NMR, and mass spectra (Table 2). These ethanolamine adducts gave satisfactory ele-



SCHEME 4

TABLE 2 Physical Constants and Spectra Data for the Medium-Ring Boracycles Prepared by One-Carbon Homologation of *B*-Methoxyboracycles[a]

Starting boracyclane	*Yield of the homologated product,*[b] (%)	*Product boracyclane*	*bp of boracyclane* (°C/mmHg)	*Monoethanolamine adduct*[c] *mp* (°C), *mass ion*		*DCME reaction product*	*DCME reaction product* (%)
B-Methoxyborinane				154–155	142	Cyclohexanone	73
B-Methoxyborinane	85	*B*-Methoxyborepane	70–71/35	140–141	156	Cycloheptanone	70
B-Methoxyborepane	82	*B*-Methoxyborocane	89–90/30	140–141	170	Cyclooctanone	74
B-Methoxyborocane	80	*B*-Methoxyboronane	34–35/3	95–96	184	Cyclononanone	75
B-Methoxyboronane	80	*B*-Methoxyborecane	60–61/2	127	198	Cyclodecanone	79
B-Methoxyborecane	75	*B*-Methoxyboracycloundecane	80–81/3	139	212	Cycloundecanone	77
B-Methoxyboracycloundecane	82	*B*-Methoxyboracyclododecane	80–81/1	165	226	Cyclododecanone	75

[a] All of these reactions were run on a 50-mmol scale.
[b] Determined by oxidizing the boracycle to the corresponding diol a*nd analyzing the diol by GC [24] as its bis(trimethylsilyl)ether with a proper choice of an internal standard.*
[c] Gave correct elemental analysis for C, H, N, and B.

mental analyses. This crystalline ethanolamine adduct is a convenient means for storing these medium-ring boracyclanes over a prolonged period of time. Also, these adducts can be conveniently handled in air as they are air stable. When needed, the medium-ring *B*-alkoxyboracyclanes can be regenerated by treatment with an equivalent of anhydrous HCl–ether in the presence of an equivalent of the corresponding alcohol.

The difficulties encountered in synthesizing medium-ring cycloalkanones prompted us to test the utility of these boracyclanes in the medium-ring range toward the synthesis of the corresponding medium-ring cycloalkanones. A practical and convenient procedure for the conversion of a borinic ester into a ketone via the DCME reaction has been established in our laboratory [19]. We applied this methodology to the medium-ring boracycles to obtain cycloalkanones in good yields (Table 2). The structure of these cycloalkanones was ascertained by IR, PMR, mass spectral data, and direct comparison with an authentic sample by GC. The ease of preparation of cycloalkanones in the medium-ring range in good yields via the DCME reaction under mild conditions indicates the versatility of these boracyclanes.

Conversion of a borinate ester to the corresponding lithium dialkylborohydride by treatment with $LiAlH_4$ in ether is reported from our laboratory [28]. These borohydrides are very stable and can be stored over a prolonged period of time without significant disproportionation or redistribution [28]. Methods for the generation of the dialkylborane from lithium dialkylborohydride have been reported from our laboratory [29]. This method was extended to the five-membered boracycle, *B*-methoxyborolane (**1**, X = OMe) and the stable borohydride was isolated. Because of the elusive behavior of borolane, treatment of methanesulfonic acid with the borohydride was performed in the presence of an olefin, such as 1-octene, and the corresponding trialkylborane was isolated in excellent yield [28]. By following the same methodology, the medium-ring boracyclanes represented in Table 2 could be converted to the corresponding B—H derivatives. This method should make possible an entry into such boracyclanes for the first time.

CONCLUSION

This is the first report in the literature for the preparation of medium-ring boracyclane structures without any contamination of isomeric boracycles. Cycloalkanones that are otherwise difficult to prepare via known synthetic transformations can be prepared conveniently in good yields via the DCME reaction of these boracycles. Intermediate α-chloroboracyclanes are versatile intermediates for the synthesis of α-substituted cycloalkanones via treatment with the appropriate alkyl- or aryllithium, as well as for the synthesis of cycloalkylboronic esters, which are otherwise difficult to prepare via hydroboration because of the unavailability of the necessary cycloalkene.

The versatility of the *B*-alkoxyborinane (**2**, X = OMe) has been demonstrated in our laboratory by a one-pot synthesis of alkyn-1-ol [30]. The same methodology could be extended for the synthesis of higher homolgs of these alkyn-1-ols using these medium-ringed *B*-alkoxyboracyclanes.

It is evident that considerable progress has been made in developing a simple and convenient method for the synthesis of strained medium-ring boracycles. This development has revealed a number of fascinating theoretical questions worthy of exploration.

EXPERIMENTAL

All operations were carried out under a nitrogen atmosphere with oven-dried glassware [31]. Boron-11 NMR spectra were recorded on a Varian FT-80A instrument and the chemical shifts are in δ relative to $EE \cdot BF_3$, with chemical shifts downfield from $EE \cdot BF_3$ as positive. Proton NMR spectra were recorded on a Varian T-60 (60 MHz) spectrometer and the chemical shifts are in δ relative to Me_4Si. Infrared spectra were recorded on a Perkin-Elmer 1420 ratio recording spectrophotometer. The GC analyses were carried out on a Hewlett-Packard 5890 gas chromatograph equipped with a flame ionization detector (columns 12 ft × 1/8 in. packed with 5% Carbowax 20M on Chromosorb W, AW, DMCS and 5% SP-2100 on Chromosorb W, AW, DMCS).

MATERIALS

Tetrahydrofuran was freshly distilled from sodium benzophenone ketyl prior to use. Anhydrous diethyl ether was purchased from Mallinckrodt, Inc., and was used directly. Dichloromethane, bromochloromethane, and chloroiodomethane were distilled over P_2O_5 and stored over 4-Å molecular sieves. *n*-Butyllithium (Aldrich) in hexane was estimated (2.3 *M*). *sec*-Butyllithium was purchased from the Aldrich Chemical Company and estimated prior to use. Potassium triisopropoxyborohydride (KIPBH, 1.0 *M*) in THF was purchased from the Aldrich Chemical Company.

The six-membered boracyclane, borinane (**2**, X = H), was prepared via the cyclic hydroboration of 1,4-pentadiene with 9-BBN, followed by redistribution with BMS in accordance with the literature procedure [11]. The seven-membered boracyclane, borepane (**3**, X = H), was prepared via the cyclic hydroboration of 1,5-hexadiene with 9-BBN, followed by redistribution with BMS [11c]. These boracyclanes were converted into the correspond-

ing *B*-alkoxy derivatives by treatment with R-OH [11].

One-Carbon Homologation of B-*Methoxyborinane* (**2**, *X = OMe*) to B-*Methoxyborepane* (**3**, *X = OMe*)

The following procedure using ICH_2Cl and/or $BrCH_2Cl$ and *n*-BuLi at −78°C is representative. A solution of *B*-methoxyborinane (**2**, X = OMe) (1.12 g, 10 mmol) and chloroiodomethane (0.8 mL, 11 mmol) in THF (20 mL) was cooled to −78°C (Dry-Ice–acetone bath). To this was added *n*-BuLi (4.5 mL, 11 mmol) dropwise from the side of the flask, maintaining the temperature at −78°C in an atmosphere of nitrogen. The reaction mixture was allowed to warm to room temperature over a period of 14 h. The completion of the reaction was monitored by ^{11}B NMR (δ 55 ppm). Tetrahydrofuran was removed under nitrogen and the residue was extracted with *n*-pentane (2 × 20 mL). The pentane portion was separated from the precipitated LiCl. Removal of the volatiles followed by fractional distillation under reduced pressure furnished *B*-methoxyborepane (**3**, X = OMe) (bp 70–71°C at 35 mmHg), yield, 0.95 g, 85%.

Homologation of B-*Methoxyborinane* (**2**, *X = OMe*) *with Dichloromethane and* sec-*BuLi* (*$LiCHCl_2$, Generated in situ*) *Followed by Reduction with KIPBH*

A solution of *B*-methoxyborinane (**2**, X = OMe) (1.12 g, 10 mmol) and CH_2Cl_2 (0.7 mL, 11 mmol) in THF (20 mL) was cooled to −78°C (Dry-Ice–acetone bath). To this was added *sec*-BuLi (8.5 mL, 11 mmol, 1.3 *M* solution in cyclohexane) dropwise by means of a syringe. The reaction was allowed to stir at −78°C for 0.25 h and to this was added KIPBH (11 mL, 11 mmol) and the reaction mixture was allowed to warm to room temperature over a period of 14 h (addition of KIPBH at −78°C was essential to prevent the ionization of the C—Cl bond in the resulting α-chloroborinate ester). The completion of the reaction was monitored by ^{11}B NMR (δ 55 ppm). Solvent THF was removed under nitrogen and the residue extracted with *n*-pentane (2 × 20 mL). The pentane extract was separated and subjected to fractional distillation to obtain *B*-methoxyborepane (**3**, X = OMe) (bp 70–71°C at 35 mmHg), yield, 0.82 g, 73%.

B-*Methoxyborepane* (**3**, *X = OMe*). Yield, 85%; bp 70–71°C (35 mm Hg); ^{11}B NMR ($CDCl_3$), δ 55 ppm; ^1H NMR ($CDCl_3$), δ 0.96 (*m*, 4*H*), 1.56 (*bm*, 8*H*), 3.63 (*s*, 3*H*, —OCH_3).

B-*Methoxyborocane* (**4**, *X = OMe*). Yield, 82%; bp 89–90°C (30 mmHg); ^{11}B NMR ($CDCl_3$), δ 56 ppm; ^1H NMR ($CDCl_3$), δ 0.86 (m, 4H), 1.5 (bm, 10H), 3.66 (s, 3H, —OCH_3).

B-*Methoxyboronane* (**5**, *X = OMe*). Yield, 80%; bp 34–35°C (3 mmHg); ^{11}B NMR ($CDCl_3$), δ 54 ppm; ^1H NMR ($CDCl_3$), δ 0.9 (m, 4H), 1.4 (m, 12H), 3.66 (s, 3H, —OCH_3).

B-*Methoxyborecane* (**6**, *X = OMe*). Yield, 80%; bp 60–61°C (2 mmHg); ^{11}B NMR ($CDCl_3$), δ 55 ppm; ^1H NMR ($CDCl_3$), δ 0.93 (m, 4H), 1.36 (bm, 14H), 3.7 (s, 3H, —OCH_3).

B-*Methoxyboracycloundecane* (**7**, *X = OMe*). Yield, 75%; bp 80–81°C (3 mmHg); ^{11}B NMR ($CDCl_3$), δ 55 ppm; ^1H NMR ($CDCl_3$), δ 0.9 (m, 4H), 1.3 (bm, 16H), 3.7 (s, 3H, —OCH_3).

B-*Methoxyboracyclododecane* (**8**, *X = OMe*). Yield, 82%; bp 80–81°C (1 mmHg); ^{11}B NMR ($CDCl_3$), δ 55 ppm; ^1H NMR ($CDCl_3$), δ 0.9 (m, 4H), 1.33 (bm, 18H), 3.7 (s, 3H, —OCH_3).

Characterization of the Homologated Products by Oxidation

The homologated *B*-methoxyboracyclanes (Tables 1 and 2) were characterized by oxidation with alkaline hydrogen peroxide. The diols produced were converted to the corresponding bis(trimethylsilyl) ether by treating with BSA [24] and were analyzed by GC using an internal standard.

General Procedure for the Preparation of the Ethanolamine Adducts [32] of B-*Methoxyboracyclanes*

The preparation of an ethanolamine adduct of *B*-methoxyborinane is representative. To a solution of *B*-methoxyborinane in *n*-pentane was added an equivalent quantity of ethanolamine while stirring. A white crystalline adduct precipitated out, which was filtered under nitrogen. The adduct was recrystallized (THF : pentane) and characterized by mass spectral data and elemental analysis. Boron-11 NMR, δ 5 ppm; mp 154–155°C; mass spectrum, 142 (M^+ + H). Analysis, calculated, for $C_7H_{16}BNO$, C, 59.57; H, 11.35; N, 9.93; B, 7.66; found, C, 59.87; H, 11.34; N, 9.66; B, 7.36.

Ethanolamine Adduct of B-*Methoxyborepane.* Boron-11 NMR, δ 7.9 ppm; mp 140–141°C; mass spectrum, 156 (M^+ + H). Analysis, calculated for $C_8H_{18}BNO$, C, 61.94; H, 11.61; N, 9.03; B, 6.97; found, C, 61.93; H, 11.93; N, 9.40; B, 7.26.

Ethanolamine Adduct of B-*Methoxyborecane.* Boron-11 NMR, δ 7.7 ppm; mp 140–141°C; mass spectrum, 170 (M^+ + H). Analysis, calculated for $C_9H_{20}BNO$, C, 63.90; H, 11.83; N, 8.28; B, 6.39; found, C, 63.85; H, 11.81; N, 8.40; B, 6.36.

Ethanolamine Adduct of B-*Methoxyboronane.* Boron-11 NMR, δ 8.1 ppm; mp 95–96°C; mass spec-

trum, 184 (M^+ + H). Analysis, calculated for $C_{10}H_{22}BNO$, C, 65.57; H, 12.02; N, 7.65; B, 6.01; found, C, 65.19; H, 12.42; N, 7.94; B, 5.88.

Ethanolamine Adduct of B-*Methoxyborecane.* Boron-11 NMR, δ 8.9 ppm; mp 127–128°C; mass spectrum, 198 (M^+ + H). Analysis, calculated for $C_{11}H_{24}BNO$, C, 67.0; H, 12.18; N, 7.11; B, 5.48; found, C, 67.01; H, 12.53; N, 7.42; B, 5.38.

Ethanolamine Adduct of B-*Methoxyboracycloundecane.* Boron-11 NMR, δ 9.6 ppm; mp 139–140°C; mass spectrum, 212 (M^+ + H). Analysis, calculated for $C_{12}H_{26}BNO$, C, 68.25; H, 12.32; N, 6.63: B, 5.12; found, C, 68.30; H, 12.73; N, 6.78; B, 5.01.

Ethanolamine Adduct of B-*Methoxyboracyclododecane.* Boron-11 NMR, δ 9.8 ppm; mp 165–166°C; mass spectrum, 226 (M^+ + H). Analysis, calculated for $C_{13}H_{28}BNO$, C, 69.33; H, 12.44; N, 6.22; B, 4.80; found, C, 69.43; H, 12.83; N, 6.39; B, 4.49.

General Procedure for the Preparation of Cycloalkanones via the DCME Reaction

Preparation of cyclohexanone via the DCME reaction of *B*-methoxyborinane, (**2**, X = OMe), is representative [19]. To an ice-cold solution of *B*-methoxyborinane (1.12 g, 10 mmol) and α,α-dichloromethyl methyl ether, DCME (0.9 mL, 12 mmol) in THF (20 mL) was added lithium *tert*-butoxide (1.92 g, 24 mmol, freshly prepared by reacting *t*-BuOH with *n*-BuLi). The ice bath was removed and the mixture stirred at room temperature for 1 h, during which time a slightly exothermic reaction developed and a white precipitate formed. Then 4 mL of 95% ethanol was added, followed by 3 mL of 6 *N* sodium hydroxide solution and 4 mL of 30% hydrogen peroxide solution. The oxidation mixture was carefully heated to 50–60°C for 1 h to ensure the completion of oxidation. The aqueous phase was separated by saturation with sodium chloride. Distillation of the dry THF phase afforded 0.72 g of cyclohexanone, bp 153–155°C (752 mm); yield, 73%.

Various cycloalkanones (Table 2) were prepared via the DCME reaction of *B*-methoxyboracyclanes. These ketones were purified by fractional distillation and their structure was ascertained by IR, ^{1}H NMR, and mass spectral data. The purity of these cycloalkanones was ascertained by GC (5% SP-2100 on Chromosorb W 100–120 mesh) by direct comparison with an authentic sample (Aldrich Chemical Company).

General Procedure for the Preparation of Cycloalkylboronic Esters From B-*Methoxyboracyclanes*

The procedure for the preparation of cyclohexyldimethoxyborane from α-chloro-*B*-methoxyborepane is representative. A solution of *B*-methoxyborinane (**2**, X = OMe) (1.12 g, 10 mmol) and CH_2Cl_2 (0.7 mL, 11 mmol) in THF (20 mL) was cooled to −78°C (Dry-Ice–acetone bath). To this was added *sec*-BuLi (8.5 mL, 11 mmol, 1.3 *M* solution in cyclohexane) dropwise by means of a syringe. The reaction was allowed to stir at −78°C for 0.25 h and then warmed to 0°C. Sodium methoxide in methanol (2.3 mL, 10 mmol, 4.4 *M* solution in methanol) was then added at 0°C and stirred at 0°C for 2 h. Tetrahydrofuran was pumped off in vacuo and the residue was extracted with *n*-pentane (2 × 10 mL). The pentane portion was separated. Removal of the pentane, followed by fractional distillation, furnished 1.1 g of cyclohexyldimethylboronate ester, bp 79–80°C (16 mmHg); yield, 70%. The structure of this boronate ester was ascertained by ^{11}B and ^{1}H NMR spectra and by hydrolyzing to the cyclohexylboronic acid [25]. Oxidation of an aliquot with alkaline hydrogen peroxide afforded cyclohexanol in quantitative yield.

The same procedure should be applicable to preparing various boronate esters and cycloalkylboronic acids that are otherwise difficult to prepare via hydroboration. Indeed, by following the above procedure, *B*-methoxyborecane was converted to cyclodecylmethylboronate ester in 70% isolated yield.

Acknowledgment

ASP and MVR are postdoctoral research associates under grant CHE-8706102 from the National Science Foundation, for whose support they tender thanks.

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