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New synthetic applications of dialkylboron halide reagents

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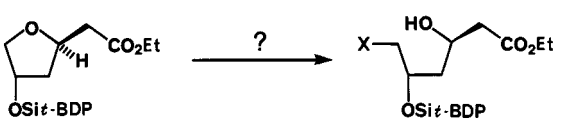
Abstract - An area of recent, active investigation in our laboratories has been the use of monofunctional boron halides as reagents for organic synthesis. We have found diaryl- and diakylboron bromides (Ph_2BBr and Me_2BBr) to be extremely useful for a variety of chemical transformations. The scope, synthetic utility and limitations of dimethylboron bromide and other dialkylboron halide reagents will be presented.

INTRODUCTION

The search for new synthetic methodology is a constant preoccupation of the organic chemist. New reagents which carry out chemical transformations in a predictable and controllable fashion are valuable contributions to the repertoire of tools available to the practitioner of organic chemistry. Recently, we have directed our efforts towards the development of a family of boron-based reagents primarily for application to chemical transformations involving the cleavage of a carbon-oxygen bond. We were particularly interested in solving the problem of regioselective cleavage of cyclic ethers at the least hindered carbon-oxygen bond (Scheme 1). We examined a number of known reagents for this transformation, including TMSI (ref. 1), $PhSSiMe_3/ZnI_2$ (ref. 2), BBr_3 (ref. 3) and $PhSH/AlCl_3$ (ref. 4) but obtained low yields or unsatisfactory product mixtures.

Scheme 1



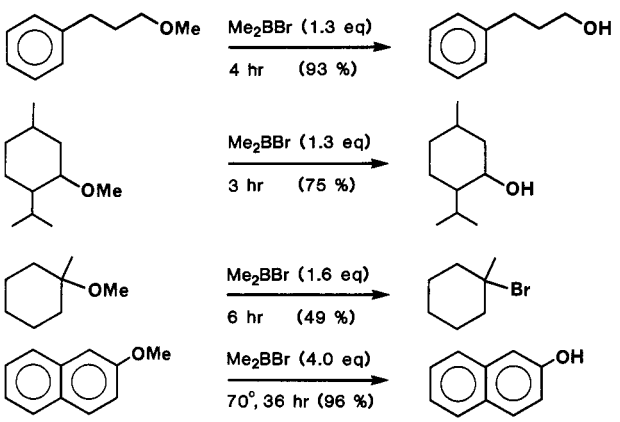
We therefore set about to find a new reagent which would carry out this transformation in a mild and regioselective fashion. From the outset we considered that mono-functional boron halides might be the reagents of choice. They would offer the advantage of a defined and unique reactive halide species present at any time during the course of the reaction. Furthermore, the reactivity of the Lewis acid could be controlled both sterically and electronically by modifying the remaining ligands on boron. Based on these considerations we examined dialkyl- and diarylboron halides, in particular dimethylboron bromide (Me_2BBr), diphenylboron bromide (Ph_2BBr) and 9-borabicyclo[3.3.1]nonyl bromide (9-BBN-Br). As a result of our investigations, we found dimethylboron bromide to be an excellent reagent for the cleavage of cyclic ethers (ref. 5,6). We then set about to explore other synthetic transformations to which this reagent could be applied. The following report describes the results of these studies and will illustrate three areas of potential application of monofunctional boron halide reagents (particularly Me_2BBr): 1. The transformation of functional groups; 2. a new synthetic sequence for acyclic asymmetric induction; and 3. as a probe for mechanistic studies.

I. TRANSFORMATION OF FUNCTIONAL GROUPS

We have studied the reactivity of disubstituted boron bromide reagents towards a variety of functional groups, in particular, ethers, acetals, ketals and sulfoxides. We first considered the regeneration of an alcohol from its methyl ether (ref. 5). In this context, it is of prime importance to increase the tendancy of the reagent to react via an S_N2 mechanism. Boron halide reagents such as BBr_3, Ph_2BBr, and 9-BBN-Br were found to be of little use in this respect because of their apparent tendancy to cleave ethers by an S_N1 process. In contrast, Me_2BBr reacts with primary, secondary and aryl methyl ethers as well as benzyl ethers to regenerate the parent alcohol in good to excellent yield (Scheme 2). Aryl methyl ethers, however, require elevated temperatures to react. The tertiary methyl ethers we examined generated the corresponding tertiary bromides. It is important to note that other functionality such as benzoates, acetates, alcohols, ethyl esters and tert-butyldiphenylsilyl ethers are recovered unchanged under the reaction conditions.

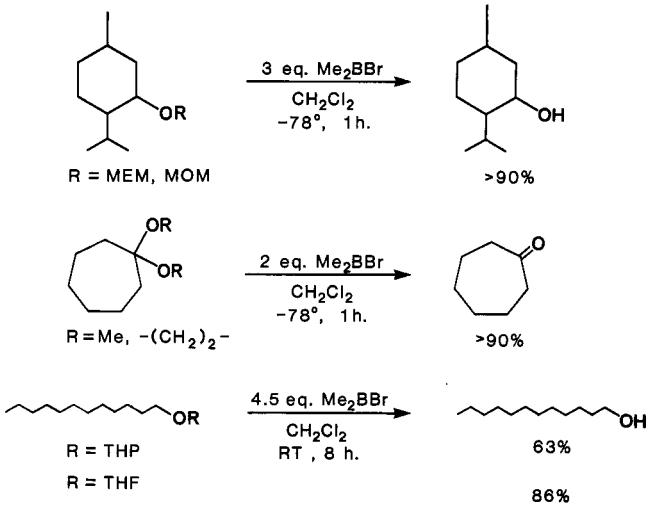
Note a: Present address for H.E.M.: Abbott Laboratories, Abbott Park, Illinois 60064

Scheme 2



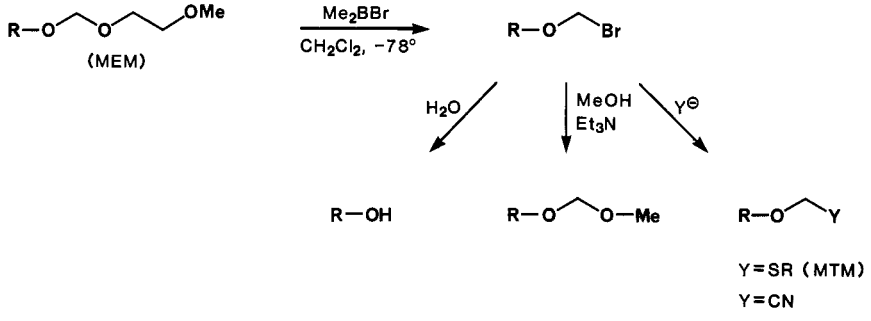
Acetals and ketals react with Me_2BBr and Ph_2BBr (Scheme 3). Cyclic and acylic acetals and ketals react with either reagent at -78°C to generate the parent aldehydes and ketones in excellent yield (ref. 7). Primary, secondary, and tertiary methoxymethyl (MOM), methoxyethoxymethyl (MEM), and methylthiomethyl(MTM) ethers react at -78°C within 1 h to give, after aqueous work-up, the corresponding alcohol (ref. 7,8). It is interesting to note that tertiary MOM ethers cleanly regenerate the parent alcohol without the formation of bromides or elimination products. This provides a striking demonstration of the mildness of the reagent. Tetrahydropyranyl (THP) and tetrahydrofuranyl (THF) ethers are converted to the corresponding alcohols by Me_2BBr at room temperature (ref. 7), although the acetal is cleaved at -78°C (see section III).

Scheme 3



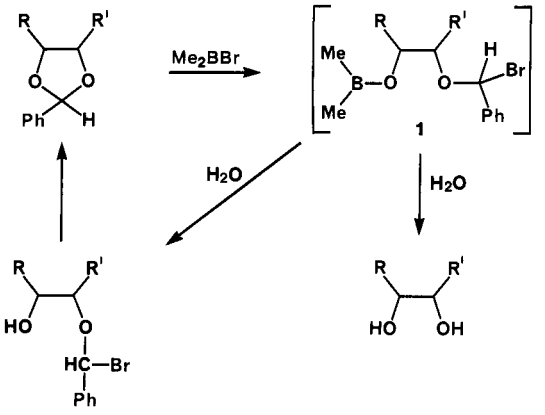
These reactions have been shown to proceed via α-bromo ether intermediates (Scheme 4). It is possible to trap these intermediates with nucleophiles such as thiol or cyanide (ref. 9). Thus the two step sequence of treatment with Me_2BBr followed by a nucleophile provides a means of interconverting functional groups. An example of the utility of this sequence is the conversion of a readily prepared MOM ether into a MTM ether.

Scheme 4



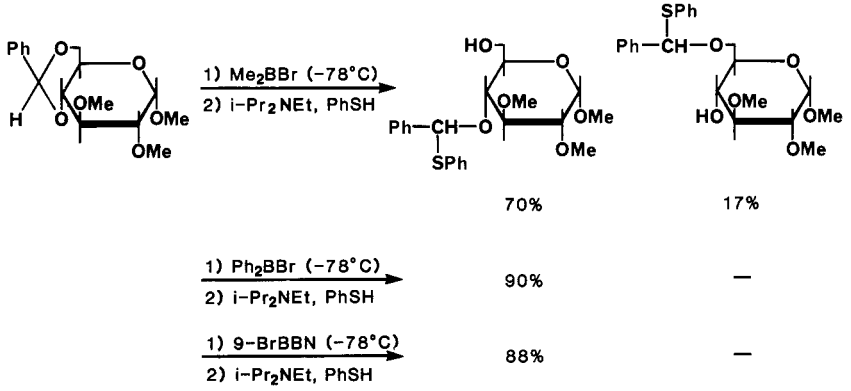
Treatment of an acetonide with Me_2BBr gives the parent diol in high yield (ref. 7). In contrast, under similar reaction conditions, benzylidene acetals are recovered unchanged. These reactions probably proceed via intermediates (1) where one of the hydroxyl groups is in the form of a borinate ester and the other, an α-bromo ether (Scheme 5).

Scheme 5



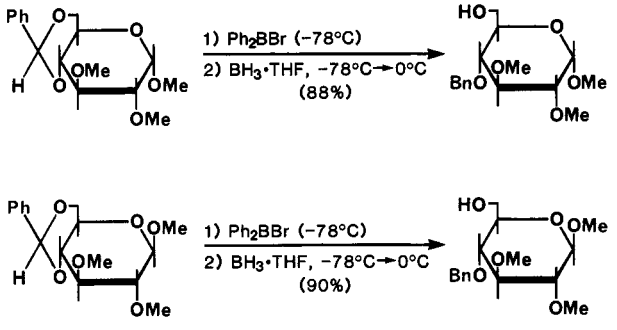
During aqueous workup, if hydrolysis of the borinate ester is faster than hydrolysis of the α-bromo ether, the intermediate hydroxy bromo ether can recyclise and regenerate starting material. This process would account for the apparent unreactivity of the benyzlidene acetals under the usual reaction conditions. Evidence for the presence of the putative intermediate (1) was obtained by quenching experiments using thiophenol as nucleophile (Scheme 6). Under these conditions benzylidene acetals are cleaved to generate hydroxy-O,S-acetals in excellent yield. These experiments demonstrate that benzylidene acetals do in fact react with disubstituted boron bromides at -78°C. In addition, these observations prompted us to explore the reductive cleavage of benzylidene acetals using R_2BBr reagents in conjunction with reducing agents. The widespread use of benzylidene acetals as protecting

Scheme 6



groups during the synthetic manipulation of carbohydrates makes this transformation of considerable potential utility. As is illustrated in Scheme 7, treatment of glycoside benzylidene acetals with a variety of disubstituted boron bromides followed by BH_3-THF generates 4-O-benzyl-6-hydroxypyranosides in excellent yield. Sterically encumbered boron halides optimize the regioselective complexation of boron to the least hindered oxygen atom and are therefore the reagents of choice for this process.

Scheme 7



The oxygenophilicity of these disubstituted boron bromide reagents can also be exploited for the mild reduction of sulfoxides. Dimethylboron bromide and 9-BBN-Br will rapidly and smoothly deoxygenate dialkyl, aryl alkyl, and diaryl sulfoxides, in the presence of propene (ref. 10).

In summary, a variety of synthetic transformations can be accomplished using mono-functional boron halide reagents. Most of our work has focussed on Me_2BBr because: a) our initial investigations into ether cleavage reactions indicated Me_2BBr to be superior to other boron halides because of its tendancy to react via an S_N2 process and b) the purification of products from reactions involving Me_2BBr is facilitated by the volatility of the Me_2B- containing bi-products. As a result of our studies, we can rank various oxygen containing functional groups according to their reactivity towards Me_2BBr (Table 1).

Table 1. Reactivity towards Me_2BBr

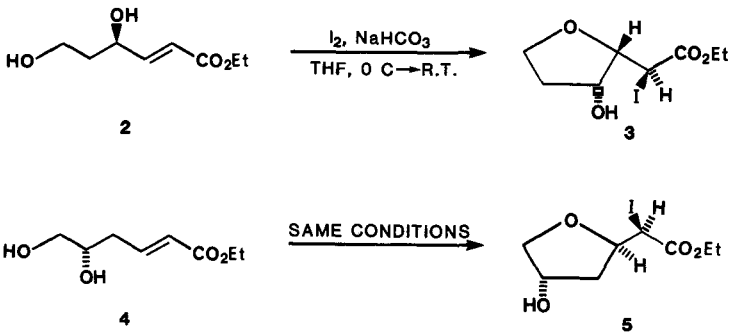
-78°C	-23°C	0-25°C
-EPOXIDES	-REDUCTION OF SULFOXIDES	R-OTHP
-ACETALS (DIMETHYL ACETALS)		R-OTHF
-ACETALS / KETALS		
-(CYCLIC / ACYCLIC)		-ALKYL-OMe
-MEM, MOM		-CYCLIC ETHERS
-ACETONIDES		ARYL-OMe
-BENZYLIDENES		

As the reactivity table suggests, Me_2BBr is indeed a chemoselective reagent. It is possible to manipulate the more reactive functionalities (dimethyl acetal, MOM ether) in the presence of less reactive groups (such as THP, methyl or benzyl ethers). The well characterized chemoselectivity of this reagent permits confident prediction of which functionality in a polyfunctional substrate will be affected at a given temperature. This property makes dimethylboron bromide an extremely valuable tool for the synthetic organic chemist.

II. A NEW SEQUENCE FOR ACYCLIC ASSYMETRIC INDUCTION

We have recently developed a synthetic sequence which results in the transformation of allylic or homoallylic chiral substrates into acylic products bearing two new stereogenic centers. Two key steps are involved in this process: 1. The preparation of optically active, unsymmetrical tetrahydrofurans using an iodoetherification reaction and 2. Selective cleavage of the resulting heterocycle to generate the desired acyclic product. Although the iodoetherification step will be discussed in detail elsewhere (ref. 11), two examples are shown in Scheme 8.

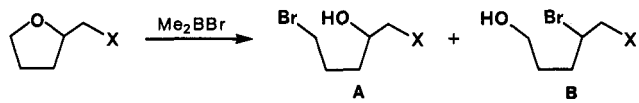
Scheme 8



Allylic alcohol 2 reacts under the indicated conditions to give exclusively the cis-2,3-disubstituted tetrahydrofuran 3 in excellent yield. Homoallylic alcohol 4 generates a mixture of 2,4-disubstituted products in a 4:1 ratio favouring the trans isomer. Compound 5 has been elaborated into the lactone portion of mevinolin or compactin (ref. 12) and the natural product (1R,3R,5S)-1,3-dimethyl-2,9-dioxabicyclo[3.3.1]nonane (ref. 13).

The second part of the process, namely the regioselective opening of tetrahydrofurans was made possible through the development of Me_2BBr. We have studied the regiocontrolled opening of unsymmetrical 2-substituted tetrahydrofuran derivatives by Me_2BBr and have established the relative importance of various factors which impact on the regioselectivity (ref. 6). Greater regioselectivity was seen in the cleavage of 2-substituted tetrahydrofurans from the least hindered side, when the substituent at position 2 increased in size. This is illustrated in Scheme 9. We have also noted that increased selectivity can be achieved through

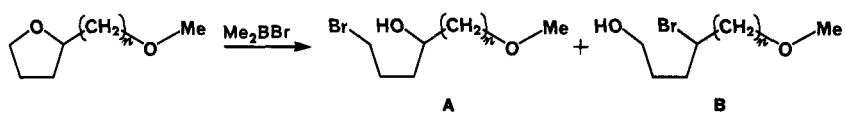
Scheme 9



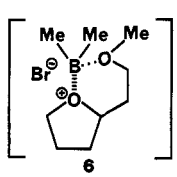
Entry	x	Ratio: A/B	Yield (%)
1	H	3.5/1	83
2	OMe	4/1	87
3	OSit-BDP	>25/1	88

the participation of remote functionality on the side chain (anchimeric effects). These results are summarized in Scheme 10. Complete regioselective opening was observed (entry 2) when the formation of a six membered ring complex involving the Lewis acid and functionality on the side chain (a methoxy group) was possible (Scheme 10, structure 6). The length of the chain bearing the methoxy group significantly affected the regioselectivity of the ring opening (entries 1 and 3). Thus the extent of regiocontrol observed in the opening of tetrahydrofurans is affected by both steric considerations and the participation of remote functionality (anchimeric effects).

Scheme 10

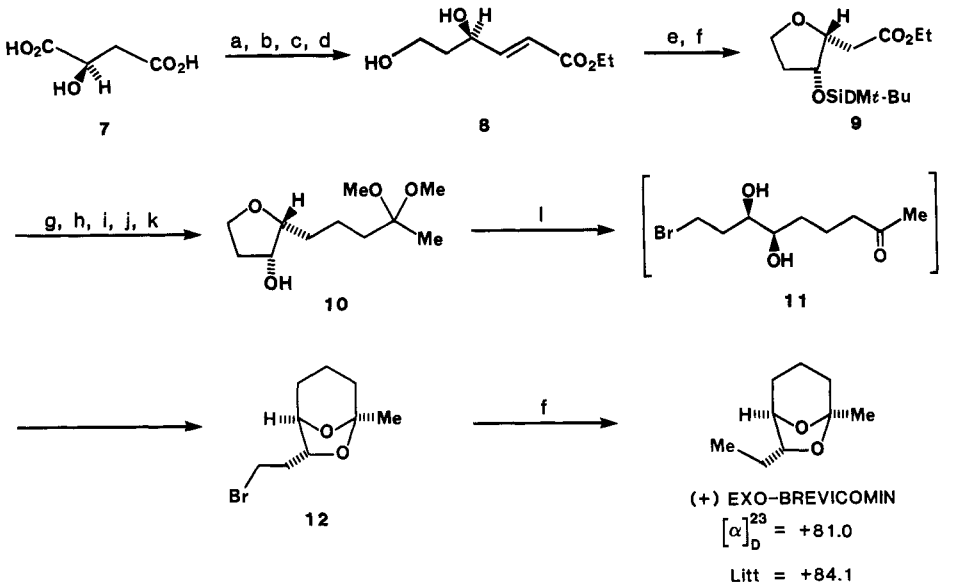


Entry	*n*	Ratio A/B	Yield (%)
1	1	79:21	85
2	2	100:0	84
3	3	79:21	68



We have applied this sequence to the synthesis of (+)-exo-brevicomin, a principal sex attractant in the female western pine beetle (ref. 14). The synthesis started with R-malic acid(7) which was converted by a straightforward series of reactions into allylic alcohol 8. Iodoetherification of 8 proceeded completely stereospecifically to give, after protection of the alcohol and reduction of the iodide, cis-tetrahydrofuran 9. Side chain elongation and functional group manipulation gave hydroxy-tetrahydrofuran 10. Treatment of 10 with Me_2BBr effected cleavage of both the dimethyl ketal and the cyclic ether to afford, after work-up, the volatile bromo-bicyclic ketal 12. This transformation presumably proceeds through keto-diol 11 (or a synthetic equivalent) which undergoes intramolecular ketalization during work-up. Tri-n-butyltin hydride reduction of the bromide 12 completed the synthesis (Scheme 11).

Scheme 11

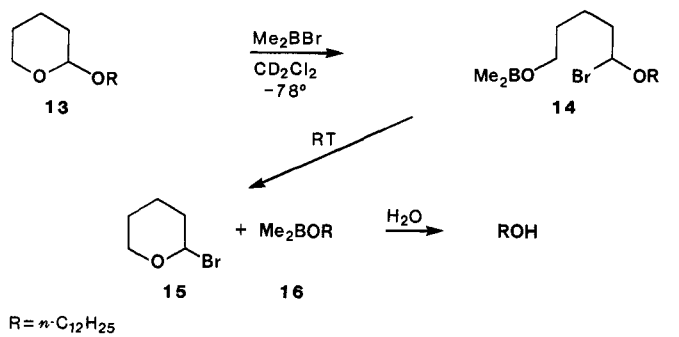


a)BH_3·THF,THF,0°C → R.T.; b)PhCH$(OMe)_2$,BF_3·Et_2O(81%); c)$(COCl)_2$,DMSO,CH_2Cl_2,-78°C, 45 min., $(iPr)_2$EtN R.T.,Ph_3PCHCO_2Et 0°C →R.T.,5 h (70%); d)HCl(1N),THF (94%); e)I_2, $NaHCO_3$,THF,6 h, (88%); t-BDMSiOTf,Lutidine,CH_2Cl_2,-10°C →R.T.(70%); f)AIBN,n-BuSnH,Hexane,R.T.→Δ,1 h (94%); g)DIBAL,THF (94%); h)$Ph_3PCHCOCH_3$(88%); i)H_2,(10%)Pd/C(90%); j)$(MeO)_3CH$,BF_3·Et_2O,Toluene(96%); k)n-Bu_4NF,THF(75%); l)Me_2BBr(2.1 eq.),Et_3N(0.1 eq.), -5°C→R.T.(67%).

III. DIMETHYLBORON BROMIDE AS A PROBE FOR MECHANISTIC STUDIES

Occasionally a new synthetic reagent provides new insight into a previously studied process. We found this to be the case during the course of our studies of the reaction of Me_2BBr with THP and THF ethers (ref. 15,16). We had previously noted that while most simple acetals and ketals (including MEM, MOM and MTM ethers) were cleaved efficiently at -78°C, tetrahydropyranyl (THP) and tetrahydrofuranyl (THF) ethers required more forcing conditions 8-24 h at room temperature) to regenerate the parent alcohol (ref. 7). The unexpected difference in reactivity between these classes of acetals led us to re-examine these reactions by ^1H NMR. When we treated a simple THP ether with Me_2BBr in CD_2Cl_2 at -78°C, we were surprised to observe instant and complete conversion to an α-bromo ether intermediate. The product, however, was that resulting from selective cleavage of the ring carbon-oxygen bond. This acyclic intermediate was relatively stable at low temperature, however, warming to room temperature resulted in the slow conversion to 2-bromotetrahydropyran (Scheme 12).

Scheme 12

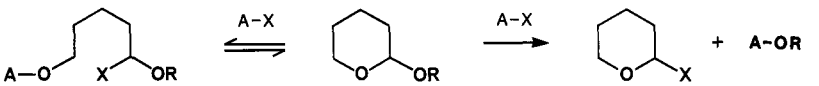


R=*n*-$C_{12}H_{25}$

These observations explained the anomalously slow cleavage of THP ethers as judged by production of the parent alcohol. In fact, Me_2BBr reacts very quickly with THP and THF ethers as it does with other acetals and ketals. The kinetic product, however, is that resulting from selective cleavage of the ring carbon-oxygen bond. Hydrolysis of 14, while giving some of the desired alcohol, also regenerates starting material by cleavage of the boron-oxygen bond and recyclisation. While there exist in the literature isolated examples of Lewis acids

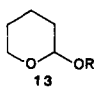
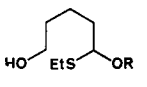
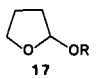
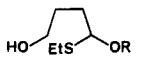
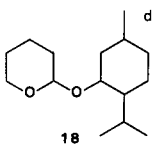
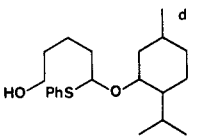
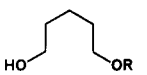
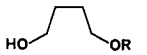
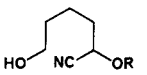
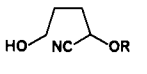
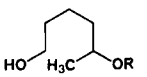
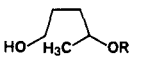
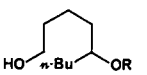
generating ring-opened products from THP ethers (ref. 17), many more examples exist where cleavage of the exocyclic bond is the favoured pathway. The acid-catalysed hydrolysis and anomerization of pyranosides, in particular glycopyranosides has been studied extensively and the evidence suggests that these reactions proceed via cleavage of the exocyclic carbon-oxygen bond (ref. 18). Cleavage of the endocyclic bond is not observed. While more data will have to be collected before the unusual regioselectivity of this Me_2BBr reaction can be fully explained, we would like to propose that in non-participating solvents, cleavage of the ring carbon-oxygen bond is the kinetically favoured process. The fact that ring-opened products are not observed with many other Lewis or Bronstead acids may reflect the instability of the ring-opened intermediates (Scheme 13). With an acid reagent represented by the formula A-X, where A is, for example, a proton or TMS group, recyclisation of the ring-opened intermediate might be fast, so that only the thermodynamic (cyclic) product is observed. When A is Me_2B, the deactivating nature of the boron-oxygen bond slows the recyclisation down considerably so that the kinetic (ring-opened) product can be observed.

Scheme 13



We have exploited this observation synthetically, by trapping these ring-opened α-bromo ether intermediates with various nucleophiles to generate stable ring-opened products (Table 2)(ref. 15). A wide variety of nucleophiles may be used including thiols sterically hindered alcohols, cyanide, hydride reagents and a number of organometallic species (alkyllithium, Grignard and cuprate reagents).

Table 2 Ring opening of THP and THF ethers using Me_2BBr

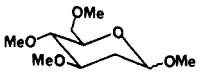
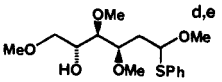
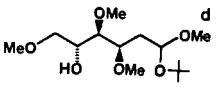
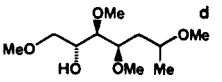
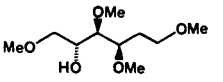
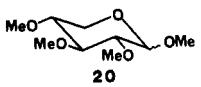
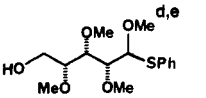
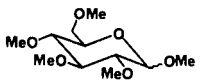
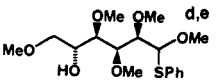
ENTRY	SUBSTRATE	NUCLEOPHILE	PRODUCT[b]	YIELD[c]
1)	 13	EtSH		90%
2)	 17	EtSH		62%
3)	 18	PhSH		90%
4)	17			87%
5)	17	$LiEt_3BH$		86%
6)	17	$LiEt_3BH$[e]		67%
7)	13	AgCN[e,f]		87%
8)	17	AgCN[e,f]		39%
9)	13	CH_3MgBr[e,g]		92%
10)	17	CH_3MgBr[e,g]		94%
11)	13	$n\text{-}Bu_2CuLi$[e,g]		89%

R = $n\text{-}C_{12}H_{25}$

a) UNLESS STATED OTHERWISE, ALL REACTIONS WERE CARRIED OUT IN CH_2Cl_2 USING A CONCENTRATION OF 0.1 M IN SUBSTRATE AND 2.0 eq. OF Me_2BBr AT -78°C FOR 30 MIN. N,N-DIISOPROPYLETHYLAMINE (2.5 eq.) AND NUCLEOPHILE (3.0 eq.) WERE THEN ADDED b) ALL NEW PRODUCTS HAD SATISFACTORY SPECTRAL (NMR,IR AND MASS SPECTRA) AND ANALYTICAL (COMBUSTION ANALYSIS OR HIGH RESOLUTION MASS SPECTRUM) DATA. c) ISOLATED YIELDS OF PURIFIED PRODUCTS. d) DIASTEREOMER MIXTURE. e) NO N,N-DIISOPROPYLETHYLAMINE WAS USED. f) THE REACTION WAS WARMED TO -25°C AFTER ADDITION OF THE NUCLEOPHILE. g) ADDED AS A SOLUTION IN ETHER.

We have extended this reaction to more complex substrates including glycosides (Table 3) (ref. 16). With the more reactive 2-deoxyglucopyranosides good yields of ring-opened products can be obtained with a variety of nucleophiles when the reaction is performed at -78°C (Table 3, entries 1-4). The corresponding glucopyranoside and xylopyranoside derivatives (Table 3, entries 5,6) were less reactive and gave low yields at -78°C but synthetically useful yields when the reaction was performed at -45°C. With these less reactive substrates, we also noted differences in reactivity between the α- and β- anomers. Generally the β-anomers were more reactive than the corresponding α-anomers.

Table 3 Ring opening of methyl D-glycopyranosides using Me_2BBr

ENTRY	SUBSTRATE	ANOMERIC CONFIGURATION	TEMPERATURE	NUCLEOPHILE	PRODUCT[b]	YIELD[c]
1)	 **19**	β	-78°	PhSH	 d,e	95%
		α				95%
2)	**19**	β[f]	-78°		 d	85%
3)	**19**	β[f]	-78°	Me_2CuLi[g]	 d	80%
4)	**19**	β[f]	-78°	$LiEt_3BH$[g]		45%
5)	 **20**	β	-78°	PhSH	 d,e	75%
		α	-78°			21%
			-45°			69%
6)	 **21**	β	-78°	PhSH	 d,e	11%
			-45°			82%
		α	-45°			15%

a) UNLESS OTHERWISE STATED, ALL REACTIONS WERE CARRIED OUT IN CH_2Cl_2 USING A CONCENTRATION OF 0.1 M IN SUBSTRATE AND 2.0 eq. OF Me_2BBr AT THE SPECIFIED TEMPERATURE FOR 30 MIN. N,N-DIISOPROPYLETHYLAMINE (2.5 eq.) AND NUCLEOPHILE (3.0 eq.) WERE THEN ADDED. b) ALL NEW PRODUCTS HAD SATISFACTORY SPECTRAL (NMR, IR AND MS) AND ANALYTICAL (COMBUSTION ANALYSIS OR HIGH RESOLUTION MASS SPECTRUM) DATA. c) ISOLATED YIELDS OF PURIFIED PRODUCTS. d) THE PRODUCT WAS A MIXTURE OF DIASTEREOMERS. e) IDENTICAL PRODUCT MIXTURES WERE OBTAINED FROM BOTH ANOMERS f) THE SUBSTRATE (1β) CONTAINED 17% OF THE α-ANOMER (1α). g) NO N,N-DIISOPROPYL-ETHYLAMINE WAS USED.

We previously suggested that our observations on the selective endocyclic carbon-oxygen bond cleavage and the differences in reactivity between α- and β- anomers could best be rationalised based on stereoelectronic considerations (ref. 16). Since complexation of Me_2BBr to one of the acetal oxygen atoms activates the corresponding carbon-oxygen bond to cleavage, the relative basicities of the oxygen atoms should affect both the rate and regioselectivity of the cleavage process. The relative basicities of the ring vs exocyclic oxygen atoms are affected by their participation in the endo- and exo-anomeric effects respectively (ref. 19). Consideration of these effects (Fig. 1) shows that of the four acetal oxygen atoms, only the ring oxygen of the β-anomer does not participate in an anomeric effect. The greater reactivity we observe for the β-anomer could therefore be a consequence of its greater basicity.

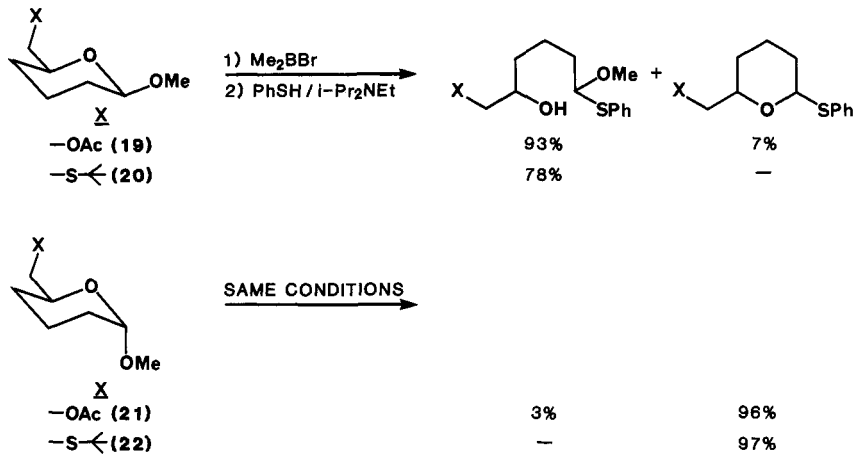
α Figure 1 β

Stereoelectronic factors could also be responsible for our observation that the only isolated products were those resulting from selective cleavage of the ring carbon-oxygen bond. In the case of the β-anomer, not only should the ring oxygen be the most basic, but also, cleavage of the ring carbon-oxygen bond can occur with stereoelectronic assistance from the exocyclic oxygen atom. If stereoelectronic assistance is an important factor in this process, then endocyclic bond cleavage is the only pathway favoured for the β-anomer reacting out of its ground-state conformation. In the α-anomer, on the other hand, both carbon-oxygen bonds can be cleaved with stereoelectronic assistance so we expected to observe products resulting from cleavage of both bonds. Even with the α-anomer, however, selective cleavage

of the endocyclic bond was observed. We propose three possible explanations for this. One possibility is that the exocyclic oxygen of the α-anomer being axially orientated, may be more sterically hindered than the ring oxygen. As a result, complexation of Me_2BBr at the ring oxygen followed by cleavage of the ring carbon-oxygen bond may be favoured for steric reasons. A second possibility is that the α-anomer might be reacting out of a non-ground-state conformation such as twist boat where, like the β-anomer, stereoelectronic assistance in the cleavage of the exocyclic bond is not possible. A third possibility is that the exo-anomeric effect is in fact stronger than the endo-anomeric effect and thereby favours formation of the ring-opened product.

Recently, we have studied the Me_2BBr reaction with a number of substituted THP ether substrates which generate either ring-opened or ring-closed products depending on the configuration of the anomeric center. Two examples are shown in Scheme 14. We find that substituted THP ethers with bulky groups adjacent to the ring oxygen generate the expected ring-opened products from the β-anomer, but ring-closed products from the α-anomer.

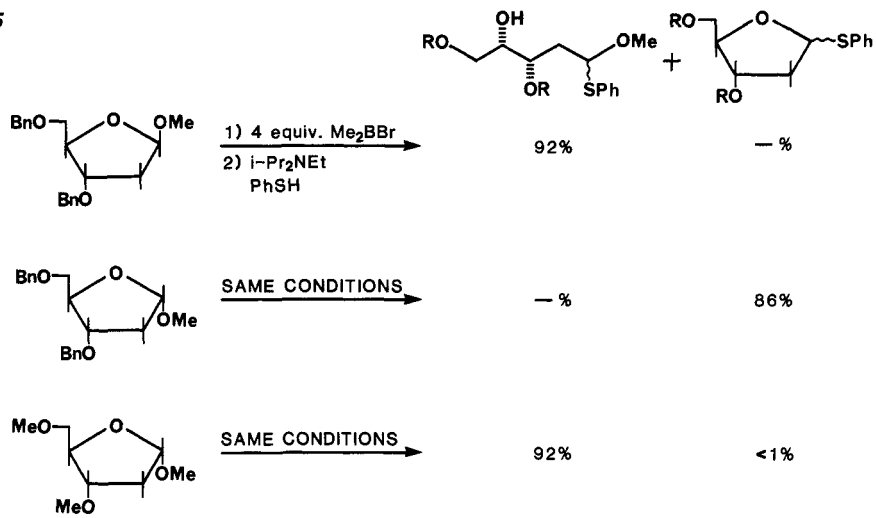
Scheme 14



We feel that these results strongly support our suggestion that stereoelectronic assistance is indeed an important factor in the carbon-oxygen bond cleavage process. In the α-anomer, either the endo- or exocyclic carbon-oxygen bond can be cleaved with stereoelectronic assistance (Fig. 1). When the side chain X-group is small (e.g. OMe, see Table 3), complexation of the Me_2BBr occurs at the ring oxygen and results in selective cleavage of the ring carbon-oxygen bond (for reasons described previously). When X is a large group such as acetate or S-tert-butyl, complexation of the Lewis acid at the ring oxygen appears to be disfavoured, possibly for steric reasons. Consequently, complexation of Me_2BBr occurs at the exocyclic oxygen to generate cyclic products. In contrast, for the β-anomer, only cleavage of the endocyclic carbon-oxygen bond can occur with stereoelectronic assistance. Even when the side chain X-group is large and complexation of Me_2BBr at the ring oxygen is disfavoured, endocyclic carbon-oxygen bond cleavage is observed because only this pathway can proceed with stereoelectronic assistance.

We have recently studied furanoside substrates in the Me_2BBr reaction and our preliminary observations suggest that they react in a fashion analogous to the pyranosides (Scheme 15).

Scheme 15



In summary, Me_2BBr reacts with THP and THF ethers (including glycosides) to generate α-bromo ether intermediates resulting from selective cleavage of the ring carbon-oxygen bond. These intermediates can be trapped with a variety of nucleophiles to generate stable ring-opened products. Mechanistically, our results suggest: a) that stereoelectronic factors are indeed important in the cleavage of THP ethers; and b) that cleavage of the endocyclic carbon-oxygen bond may be the kinetically favoured process. This is in striking contrast with the accepted mechanism for the acid-catalysed hydrolysis of pyranosides (ref. 18). Our results may find some support, however, in a recent publication by Gupta and Franck (ref. 20). These authors reported direct experimental evidence for the cleavage of both endo- and exocyclic carbon-oxygen bonds in the acid-catalyzed cleavage of THP ethers.

CONCLUSION

The preparation of monofunctional derivatives of classical Lewis acids offers an interesting approach to the development of new reagents with a more defined reactivity profile. We have taken this approach in our use of dialkyl- and diarylboron bromides (in particular Me_2BBr) as reagents for organic synthesis. Dimethylboron bromide is an excellent reagent for a variety of chemical transformations. We have shown here three areas where we have applied the reagent: 1. The transformation of functional groups, particularly, the cleavage of oxygen-based protecting groups; 2. as part of a new sequence for acyclic asymmetric induction and; 3. as a probe for stereoelectronic control in the cleavage of THP ethers.

Dimethylboron bromide can be purchased as a neat liquid from the Alpha Division of Ventron Corporation or from Aldrich Chemical Company. Alternatively, it can be prepared very simply from tetramethyltin and boron tribomide using the procedure of Noth and Vahrenkamp (ref. 21). It should be noted that neat dimethylboron bromide is pyrophoric when exposed to moist air, so appropriate care should be taken in its handling. We have found it convenient to make up solutions of the reagent in dry CH_2Cl_2 or $ClCH_2CH_2Cl$. These solutions can be stored at -15°C for several months without noticeable decomposition and can be handled safely and conveniently using standard syringe techniques.

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