for a further 8 h at 25 °C, the reaction mixture was triturated with dry pentane (5 × 25 mL). The pentane extracts were combined, and the solvent was removed by distillation on a spinning-band column. The resulting benzyl fluoride was distilled under reduced pressure in a Kugelrohr apparatus to yield 2.07 g (66%) of pure product.

Acknowledgment. We are grateful to Professor R. A. Moss for helpful discussions, for the provision of laboratory space, and for financial support derived from NSF Grant CHE 8209007. We also acknowledge helpful discussion with Professor J. San Filippo. We are especially grateful to Professor D. B. Denney and Dr. Dorothy Z. Denney for the loan of polarimetry equipment and for ^{19}F NMR spectra.

Registry No. TBAF, 429-41-4; $CH_2{=}CHCH_2Br$, 106-95-6; $C_6H_5CH_2Br$, 100-39-0; $(C_6H_5)_3CCl$, 76-83-5; $Br(CH_2)_7CH_3$, 111-83-1; $TsO(CH_2)_7CH_3$, 3386-35-4; $CH_3CHBr(CH_2)_5CH_3$, 557-35-7; $CH_3CH(OTs)(CH_2)_5CH_3$, 1028-12-2; (−)-(*R*)-$CH_3CH(OTs)(CH_2)_5CH_3$, 27770-99-6; C_6H_5COCl, 98-88-4; $CH_2{=}CHCH_2F$, 818-92-8; $C_6H_5CH_2F$, 350-50-5; $(C_6H_5)_3CF$, 427-36-1; $F(CH_2)_7CH_3$, 463-11-6; $CH_3CHF(CH_2)_5CH_3$, 407-95-4; (+)-$CH_3CHF(CH_2)_5CH_3$, 56772-74-8; C_6H_5COF, 455-32-3.

Ring Opening of Epoxides with Morpholine–Borane

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Received December 28, 1983

The reductive ring opening of epoxides by borane is often both slow and complex.[1,2] However, Brown and co-workers have found the reaction to be accelerated by sodium and lithium borohydrides or by boron trifluoride etherate.[2,3] In the borohydride-catalyzed reduction of 1-methylcyclohexene oxide, the products were reported to be 74% *cis*-2-methylcyclohexanol and 26% 1-methylcyclohexanol.[3] In related examples the preferance for forming the less highly substituted alcohol was regularly evidenced.

The boron trifluoride catalyst also leads to the less substituted alcohol as the major product.[2] However, only epoxides substituted with one or more phenyl groups were reported to open with this Lewis acid catalyst. In contrast to the result reported above, 1-phenylcyclohexene oxide yields primarily *trans*-2-phenylcyclohexanol (82%) along with 18% of the cis isomer. It was conjectured that the function of the catalyst was to promote the rearrangement of the epoxide; the resulting carbonyl functional group then being reduced by the borane.

In the work described above, the solvent used was tetrahydrofuran, and borane was added in the form of its stable THF complex. However, this solvent system offers a practical difficulty in preparative applications in that THF forms an intractable polymer in the presence of boron trifluoride. In order to overcome the problem of product isolation posed by the polymer formation, it was decided to explore the utilization of other borane sources in solvent systems other than THF. In the course of this work it became evident that a number of exceptions existed to the previously published limitation of mandatory aryl substitution in the boron trifluoride catalyzed reaction. These results are reported here.

Results and Discussion

It has been known for some years that amine–borane complexes have the capability of reducing carbonyl compounds.[4] Consequently, it was desided to essay the epoxide reduction by using the morpholine–borane complex as a point of departure. When an ether solution of styrene oxide and an equivalent of morpholine–borane were treated at room temperature with an equivalent of boron trifluoride etherate, a quantitative yield of 2-phenylethanol was observed. Since only small amounts of material were being used in this study, no attempt was made to determine the stoichiometric requirements of the reaction. This result parallels the observations of Brown and Moon[2] with regard to the course of the reaction but avoids the undesireable formation of the THF polymer.

Subsequently, the same conditions were applied to the ring-opening of 1-methylcyclohexene oxide. The reaction product was analyzed by both C-13 and proton NMR. In contrast to the report for 1-phenylcyclohexene oxide above, the major product in this instance was the cis isomer of 2-methylcyclohexanol (84%). The minor product was 1-methylcyclohexanol (16%).

In this instance it was possible to test the hypothesis that rearrangement of the epoxide to the ketone precedes the reduction step. It was found, not unexpectedly, that boron trifluoride does cause such a rearrangement of the epoxide. The reduction of 2-methylcyclohexanone with borane in THF gave a mixture comprised of 83% *trans*-2-methylcyclohexanol along with 17% of the cis isomer. The same result was obtained in ether solutions of morpholine–borane and with morpholine–borane plus boron trifluoride. The fact that each of these various forms of borane leads mainly to the trans isomer while the epoxide reduction yields primarily the cis isomer rules out the prior rearrangement of the epoxide in this case.

As a comparison to the above result, the reduction of the epoxide from 2-ethyl-1-hexene was also carried out. The yield of crude product was 92%, and NMR analysis indicated that only 2-ethyl-1-hexanol was formed.

In contrast to the results above, the application of the above reduction to 2,3-epoxypropyl *p*-methoxyphenyl ether and to epichlorohydrin, respectively, led to the formation of the appropriate secondary alcohols, 1-(*p*-methoxyphenoxy)-2-propanol and 1-chloro-2-propanol. The latter was isolated only in 80% yield due to its water solubility.

Four cases were found in which reduction did not follow the desired course. The reduction of norbornene epoxide gave a very complex mixture in which neither the exo nor endo norbornol were evident. The ^{13}C NMR of this product suggested that the morpholine had become involved in the reduction process. It is also true that this very reactive epoxide polymerizes when reacted with boron trifluoride. Consequently, the matter was not further pursued. The epoxide from 1-butene also gave a complex mixture of products. There was a suggestion of 2-butanol in the proton NMR, but only products of low volatility were present. Since a green flame was produced on combustion, it seems likely that borate esters were produced. At the other extreme, the reduction of the syn epoxide of 5,8-diacetoxy-1,4-dihydro-1,4-ethanonaphthalene[5] was

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0022-3263/84/1949-3219$01.50/0

attempted under a variety of conditions without evidence of any of the desired ring opening. This molecule is highly sterically hindered, and nucleophilic ring-opening reactions (methyl Grignards, methyllithium, dimethylcopper lithium) have all been found to fail. A similar failure was found for the ring-opening of tetraphenylethylene oxide.

With this additional background one can now postulate a reasonable sequence of events for the reductive ring-opening reactions of epoxides with morpholine–borane and boron trifluoride. The boron trifluoride is clearly required to complex with the epoxide oxygen as well as to tie up the morpholine in the borane complex. If the epoxide can ring open to give a relatively stable carbocation, then reduction may give the less substituted alcohol with attack of the reducing agent occurring from the side of the incipient hydroxyl function as reported for 1-phenylcyclohexene oxide.[2] If the carbocation has less stability, as in the case of 1-methylcyclohexene oxide, the borane attacks not the free ion but the complexed epoxide with inversion of configuration at the tertiary center. Styrene oxide can form a relatively stable cation and 2-phenylethanol results. Epichlorohydrin and 2,3-epoxypropyl *p*-methoxyphenyl ether have electronegative groups on the methylene attached to the epoxide ring. These destabilize the system for carbocation formation at the more highly substituted ring carbon. Consequently, the hydride is delivered to the least sterically hindered terminal position in these molecules.

Experimental Section

All chemicals were obtained from Aldrich and used as received. The oxide from 1-methylcyclohexene was made in the usual fashion from the olefin and *m*-chloroperbenzoic acid. The same reaction was utilized to produce the epoxide from 2-ethyl-1-hexene.[6] Proton NMR spectra were taken on a Varian EM 390 instrument in deuteriochloroform solution by using Me_4Si as an internal standard. Carbon-13 NMR were taken on a JEOL FX-60 instrument operating at 15 MHz and using 8K transforms. Identification of all compounds was by a combination of TLC and proton and carbon-13 NMR using comparisons with a variety of standard compounds. Whenever possible quantification was by means of integrating of the proton NMR spectrum. However, it was often best to use the peak intensities of selected lines in the carbon spectrum. Since the product molecules were all of the same size by using methylene carbons, differences in relaxation effects are small or nil. From standard mixes it is estimated that analyses carried out in this fashion are good to 5% to 10% which was considered good enough for this study.

Reactions of Epoxides with Morpholine–Borane. A mixture of 5 mmol of the epoxide and 5 mmol of morpholine–borane in 30 mL of anhydrous ether was stirred at room temperature while 5 mmol of boron trifluoride etherate in 20 mL of ether were added dropwise. The reaction was stirred for 2 h and then poured into 50 mL of dilute hydrochloric acid. The ether layer was drawn off, and the acid layer was extracted with two small portions of methylene chloride. The combined organic layers were dried (anhydrous sodium sulfate) and filtered, and the solvent was removed on a rotary evaporator. Except where mentioned in the text, the yields of crude product weighed from 100% to 110% of the expected weight for 100% theoretical yield. In those cases where the weight was high, it was invariably found that the balance was due to unreacted morpholine–borane. The one exception to these statements was epichlorohydrin where the recovered material was only 80% of the expected. It was presumed that this was due to the water solubility of the propylene chlorohydrin product.

The following epoxides gave results discussed in the text: styrene oxide, 1-methylcyclohexene oxide, 2-ethyl-1-hexene oxide, epichlorohydrin, and 2,3-epoxypropyl *p*-methoxyphenyl ether. Norbornene oxide gave a very complex set of products which did not include the expected norbornols but appeared to indicate incorporation of morpholine in the product. As mentioned in the text, the epoxide of 1-butene gave a mixture which appeared to contain borate esters. The syn epoxide of 5,8-diacetoxy-1,4-dihydro-1,4-ethanonaphthalene did not react at all nor did tetraphenylethylene epoxide.

Ancillary Experiments. (a) A solution of 0.56 g (5 mmol) of 1-methylcyclohexene oxide in 10 mL of ether was treated with 0.63 g of boron trifluoride etherate at room temperature for 2 h. The solution was poured into water and the ether layer separated. The aqueous layer was extracted twice with small portions of ether. The combined ether extracts were evaporated to yield 0.43 g of oil with the proton and carbon-13 spectra of standard pure samples of 2-methylcyclohexanone. (b) In a series of three experiments, 0.56 g (5 mmol) of 2-methylcyclohexanone in 30 mL of ether was treated with (1) 0.53 g of morpholine–borane; (2) 0.53 g of morpholine–borane and then 0.63 g of boron trifluoride etherate; and (3) 5 mL of 1 M boron hydride in THF. Each of the experiments was allowed to stand for 2 h and then worked up as above. Yields and percent of *trans*-2-methylcyclohexanol were as follows (the balance of the product was *cis*-2-methylcyclohexanol): (1) 0.67 g, 83%; (2) 0.60 g, 86%; and (3) 0.69 g, 83%.

Acknowledgment. Grateful acknowledgment is hereby extended to the Robert A. Welch Foundation for their support of this work.

Registry No. $Ph(CH_2)_2OH$, 60-12-8; $CH_3CH(OH)CH_2Cl$, 127-00-4; styrene oxide, 96-09-3; 1-methylcyclohexene oxide, 1713-33-3; 2-ethyl-1-hexene oxide, 1436-35-7; epichlorohydrin, 106-89-8; 2,3-epoxypropyl *p*-methoxyphenol ether, 2211-94-1; norbornene oxide, 278-74-0; 1,2-epoxybutane, 106-88-7; 5,8-diacetoxy-1,4-dihydro-1,4-ethanonaphthylene syn epoxide, 86557-37-1; tetraphenylethylene epoxide, 470-35-9; morpholine–borane, 4856-95-5; *cis*-2-methylcyclohexanol, 7443-70-1; *trans*-2-methylcyclohexanol, 7443-52-9; 1-methylcyclohexanol, 590-67-0; 2-methylcyclohexanone, 583-60-8; 2-ethyl-1-hexanol, 104-76-7; 1-(*p*-methoxyphenoxy)-2-propanol, 42900-54-9; boron trifluoride etherate, 109-63-7; boron hydride, 11129-13-8.

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Total Synthesis of Leucoxylonine

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Received November 29, 1983

Leucoxylonine was first isolated[1] in 1960 from *Ocotea leucoxylon* (Lauraceae), but its structure was not determined until 1977 when it was reisolated and assigned structure **1** essentially on the basis of spectral data.[2] Leucoxylonine was the first known nonphenolic hexaoxygenated aporphine. Herein we describe a total synthesis of leucoxylonine which unambiguously confirms the assigned structure **1** for the alkaloid.

The scheme formulated for the synthesis of **1** (Scheme I) required the initial synthesis of 2-methoxy-3,4-(methylenedioxy)benzaldehyde (**2**). The usual method[3] for the preparation of this aldehyde involves a two-step conversion of *o*-vanillin to 1-methoxy-2,3-(methylenedioxy)benzene which, on formylation, gives the aldehyde **2** (in 46% yield) together with its isomer, 4-methoxy-2,3-(methylenedioxy)benzaldehyde (**3**) in comparable yield. The following new procedure was devised for the synthesis of **2** in order

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