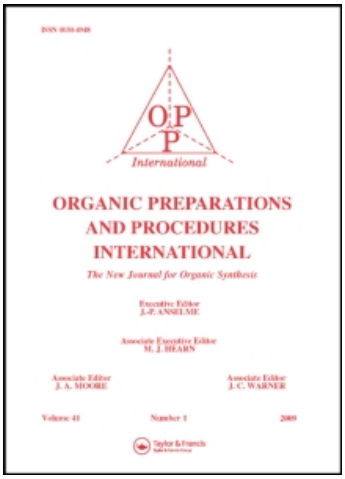

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REARRANGEMENTS OF EPOXY ALCOHOLS AND RELATED COMPOUNDS. A REVIEW

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INTRODUCTION

Epoxy alcohols and their derivatives are valuable synthons in organic chemistry. They undergo nucleophilic ring-opening reactions, epoxide migration, and rearrangements due to alkyl, aryl, and hydride migration. Rearrangement leading to ring-contracted products is the major topic of the present review although other examples will also be given.

Epoxy alcohols are generally synthesized via a rather limited selection of methods, mainly epoxidation of allylic alcohols (or ketones, followed by reduction) and base treatment of vicinal halohydrins and hydroxyalkylsulfonates. Excellent reviews[1,2] have appeared on various aspects of synthesis and reactivity of epoxy alcohols. The enantioselective syntheses recently developed by Sharpless and coworkers[2] are especially important because they allow the preparation of optically active epoxy alcohols from achiral allylic alcohols.

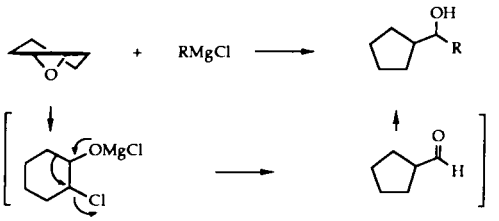
The bulk of the present review is concerned with ring-contractions of epoxy alcohols and related compounds. Hydride shifts, rearrangements in non-cyclic systems and ring-closure reactions are covered next. Finally, natural product

syntheses that take advantage of the rearrangement of epoxy alcohols are discussed in the last section of the review.

I. RING-CONTRACTION OF EPOXY ALCOHOLS AND RELATED COMPOUNDS

Examples of ring-contractions of epoxy alcohols are scarce in the literature. The few examples known emanate from the author's laboratory where it was *inter alia* shown that these reactions proceed *via* intermediate halohydrins formed by nucleophilic opening of the epoxide rings (see below). Ring-contractions of halohydrins and other alcohols carrying a vicinal leaving group are abundant and therefore review of such reactions seems to be a proper introduction to the present topic.

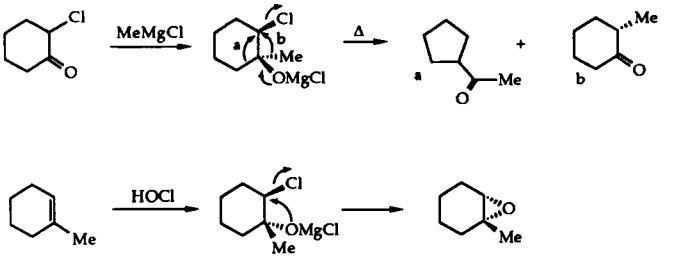
Gaylord and Becker[3] summarized the early examples concerning ring-contraction of 1,2-epoxycyclohexanes to cyclopentane derivatives. Vavon and Mitchovitch[4] and Godchot and Bedos[5] found in 1928 that treatment of 1,2-epoxycyclohexane with Grignard reagents gave 1-cyclopentylalkanols *via* the corresponding 2-chloro magnesiumalcoholates. Cyclopentanecarboxaldehyde was the postulated intermediate supposed to react further with the Grignard reagent.



In the following year, Bedos[6] showed that treatment of 1,2-epoxycyclohexane with magnesium bromide etherate gave cyclopentanecarboxaldehyde in 34% yield, thereby demonstrating for the first time the formation of an actual aldehyde by ring-contraction. Several research groups had previously suggested aldehydes to be present *en route* to cyclopentanyl alcohols. Furthermore, Bedos also observed a ring-contraction of 1,2-epoxycycloheptane to the corresponding cyclohexanecarboxaldehyde. The importance of magnesium halides in these reactions was further pointed out by Tiffeneau and Tchoubar[7] who found that,

in the cold, 1,2-epoxycyclohexane gave the corresponding halohydrins whereas upon heating, cyclopentanecarboxaldehyde was formed.

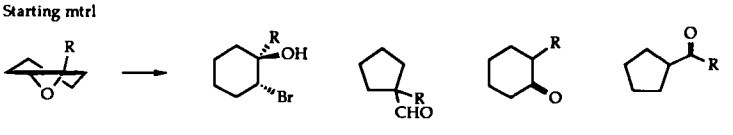
An early observation by Bouveault and Chereau[8] was followed by Tiffeneau and Tchoubar[9] and Bartlett and Rosenwald[10] who found that treatment of 2-chlorocyclohexanone with Grignard reagents, followed by heating of the resulting chlorohydrin salt, produced two isomeric ketones. Furthermore, Bartlett and Rosenwald prepared an isomeric chlorohydrin by adding hypochlorous acid to methylcyclohexene. The latter adduct gave 1-methyl-1,2-epoxycyclohexane under conditions similar to those used for the rearrangements. It was suggested that the different results depended upon the stereostructures of the intermediate halohydrins.



Bartlett[11] also investigated the stereochemical outcome of Grignard reduction (t-BuMgCl) of 2-chlorocyclohexanone as well as hypochlorous acid-addition to cyclohexene, thereby supporting the stereochemical interpretation of the scheme above.

Naqvi, Horwitz, and Filler[12] treated a series of 1,2-epoxycyclohexanes (Table 1)

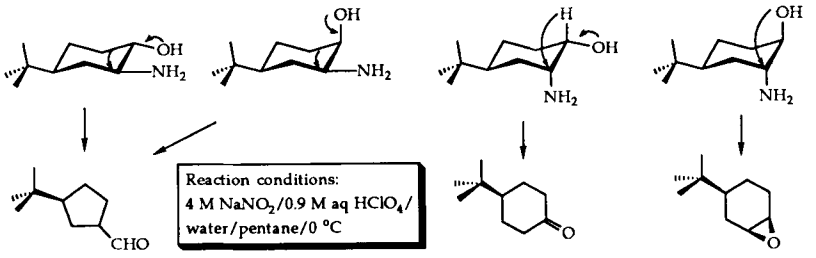
Table 1. Product distribution from treatment of 1,2-epoxycyclohexanes with $MgBr_2/Et_2O$ at different temperatures.[12]



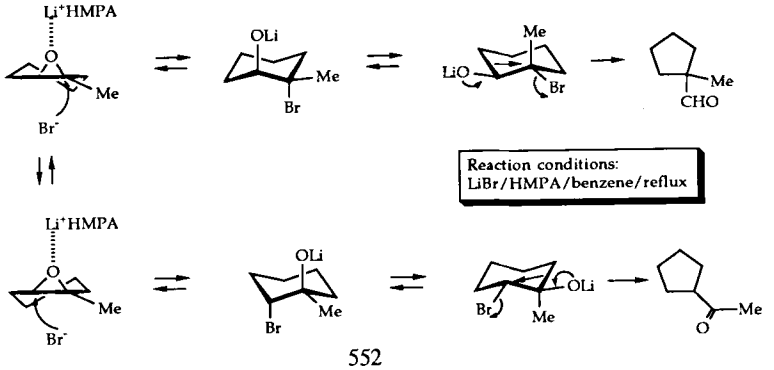
R = H	0°C	60			
	60°C	49	40		
R = Me	0°C		39		
	60°C			36	10
R = Et	0°C		20		
	60°C			35	

with magnesium bromide etherate at 0 and 60°C in an attempt to shed additional light on the mechanism of the rearrangements. It was suggested that the various products were formed via four different transition states, a conclusion that still seems to be valid (see below).

Godchot and Mousseron[13] and McCasland[14] found that cyclopentanecarboxaldehyde was formed in a high yield on treatment of *trans*-2-aminocyclohexanol with aqueous sodium nitrite in acetic acid. Under the same conditions, the *cis* compound gave a mixture of the aldehyde and cyclohexanone. Chérest et al.[15] found direct evidence for the importance of ring conformation in these rearrangements by deaminating the conformationally stable amino alcohols shown below. The migrating bond is always oriented antiperiplanar to the C-N bond, thereby forming either an aldehyde (by ring-contraction) or a ketone (by hydride migration). Epoxides are formed when the hydroxyl group is antiperiplanar to the C-N bond.

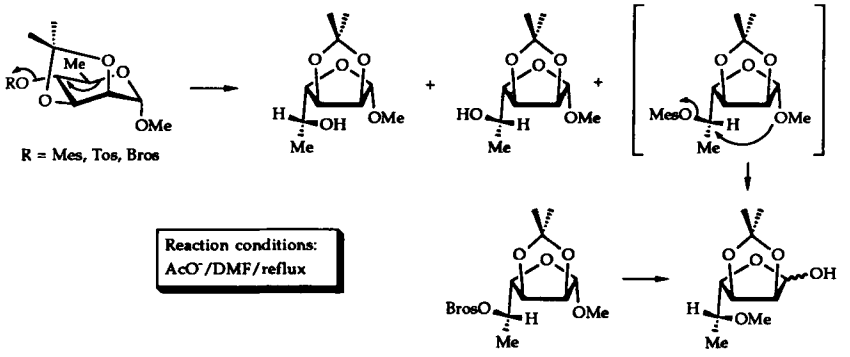


Rickborn and Gerkin[16] found that 1,2-epoxycyclohexanes rearranged to five-membered-ring aldehydes and ketones on treatment with lithium bromide/hexamethylphosphoric triamide (HMPA) in refluxing benzene. They postulated a mechanism involving the intermediacy of bromohydrin salts, which indicates that the reaction medium was strongly basic.



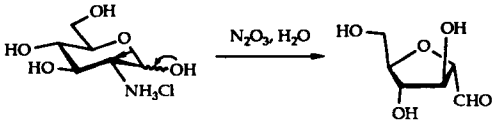
Later Suga and Miyake[17] devised two pyrolytic methods, suitable for large-scale preparation of cyclopentanecarboxaldehyde and Yamamoto et al.[18] used a bulky aluminum reagent (see below) as an efficient catalyst for the rearrangement of epoxides into carbonyl compounds.

In the carbohydrate field, Stevens et al.[19] showed that an attempted displacement of 4-O-sulfonate by acetate ion in a protected methyl α-D-mannopyranoside gave, instead of the expected talo derivative, ring-contracted products. Similarly, heating of the mannoside in aqueous dioxane in the presence of sodium bicarbonate or sodium hydroxide gave ring-contracted products, one of which was suggested to be formed by a novel 1→5 methoxyl migration. Confirmation was obtained by transformation of a brosylate into the 5-methoxy derivative. Kihlberg et al.[20] recently reported a 1→6 methoxyl migration on attempted fluorination of a protected methyl galabioside.

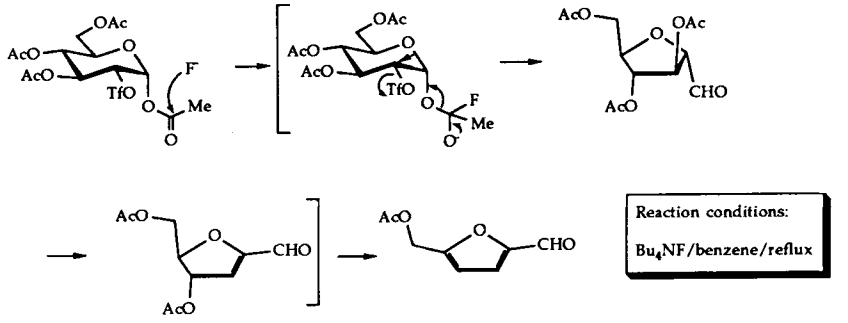


It should be noted that the ring-contraction is not a carbon skeleton-rearrangement but rather an example of migration of the pyranosidic ring oxygen atom.

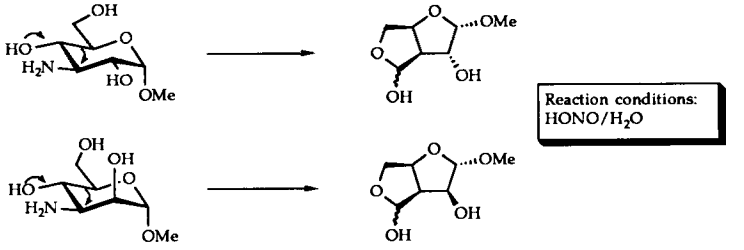
Intramolecular displacements of sulfonyloxy and amino groups by heteroatoms are well-known and leading references have been given by Austin, Buchanan, and Saunders.[21] For example, Chen and Joullié[22] found that deamination of D-glucosamine hydrochloride afforded 2,5-anhydro-D-mannose.



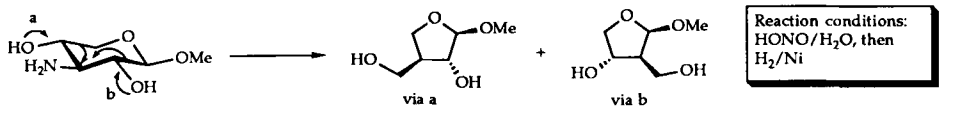
Binkley, Ambrose and Heheman[23] postulated acetylated 2,5-anhydro-D-mannose as intermediate in the fluoride-ion-induced formation of 5-acetoxy-2-formylfuran (unspecified yield) from a glucose acetate triflate.



Austin, Buchanan, and Saunders[21] observed a carbon-skeleton-rearrangement on treatment of methyl 3-amino-3-deoxy-manno- (and -gluco)-pyranoside with aqueous sodium nitrite/hydrochloric acid. The intermediacy of aldehydes was postulated and hemiacetals were isolated in moderate yields.



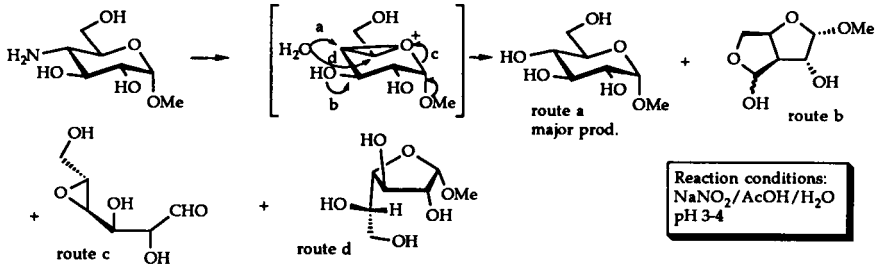
In a similar investigation, Reist, Calkins, and Goodman[24] treated methyl 3-amino-3-deoxy-β-D-xylopyranoside with nitrous acid, followed by hydrogenation of the crude product, to give a ring-contracted alcohol (route a). An isomeric alcohol (route b) was also suggested, but the structural evidence was limited to an additional methoxyl group singlet in the ^{1}H-NMR spectrum.



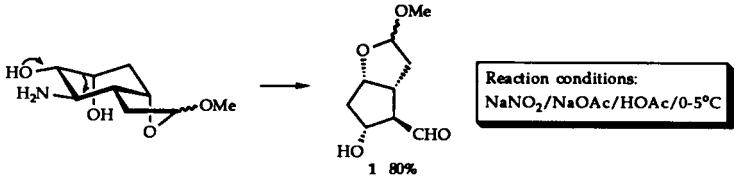
Further evidence is needed of skeletal rearrangement by migration of the anomeric carbon. Such rearrangements have not been observed at the author's laboratory, despite the investigation of numerous compounds (see below) and

further evidence against it is discussed in connection with reference 51 below.

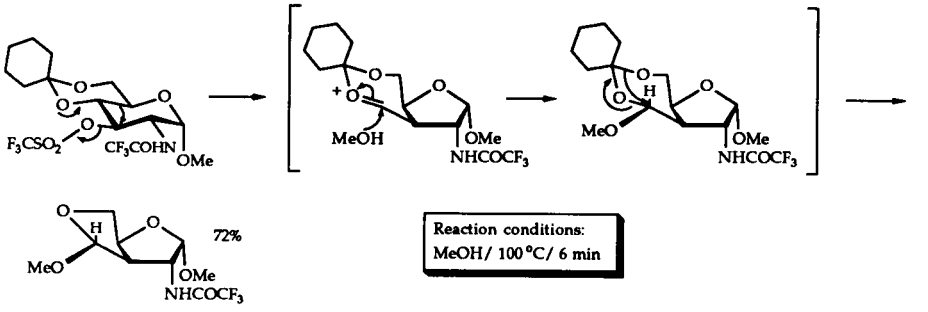
In yet another diazotization-induced rearrangement, now with methyl 4-amino-4-deoxy-α-D-glucopyranoside, Ng Ying Kin, Williams, and Horsington[25] obtained at least six products (four shown below). They suggested that the initial cation should be stabilized by the ring oxygen atom and that the resulting epoxonium ion was then rearranged (b) or attacked by water in positions 4 (a), 5 (d), and 1(c), thereby giving rise to the products shown. The hemiacetal should be formed via migration of C-2 (route b) in the initial cation, followed by epimerization of the formyl group and ring-closure.



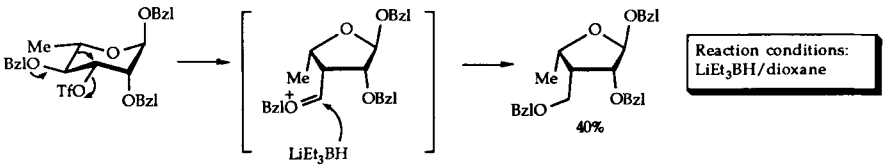
Woodward et al.[26] rearranged a bicyclic aminoalcohol to obtain aldehyde **1**, a starting material for prostaglandin synthesis[27] (see below).



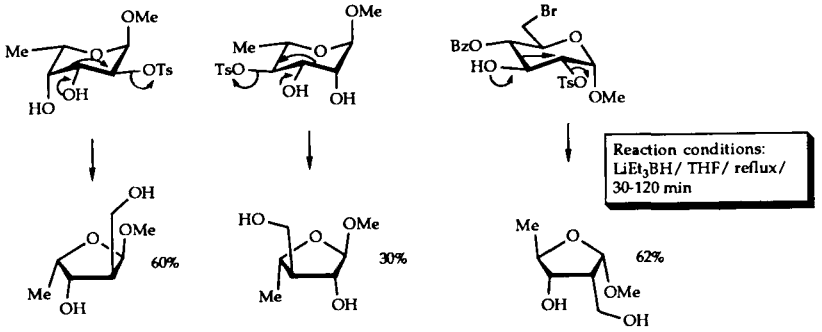
During attempts to manipulate the 3´´-position of kanamycin and other aminoglycoside antibiotics, Tsuchiya et al.[28] treated a protected glucosamine triflate with hot methanol, which resulted in the formation of a ring-contracted compound in 72% yield. The authors refer to several similar ring-contractions.



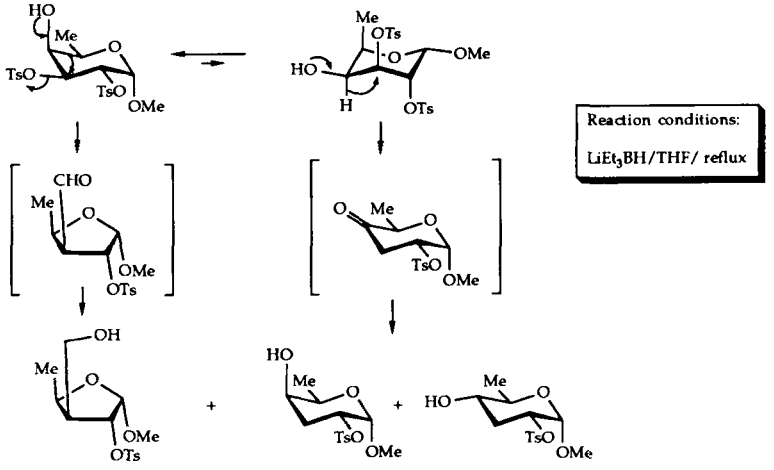
Pozsgay and Neszméli[29] found that a rhamnoside triflate rearranged to a furanoside on treatment with lithium triethylborohydride.



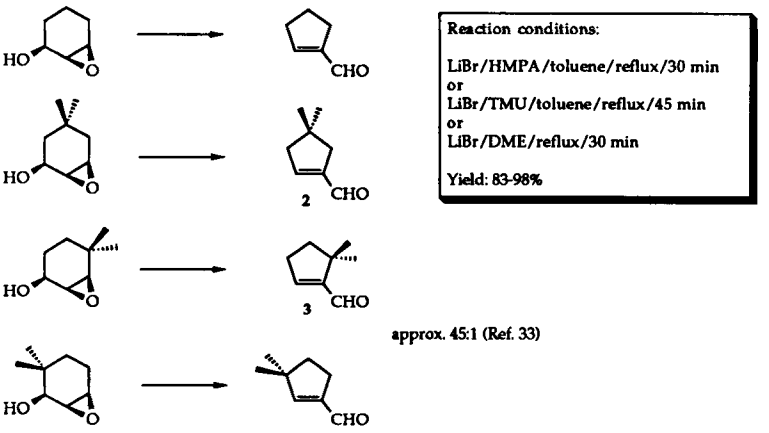
Baer et al.[30] observed that mono- and ditosylated pyranosides on heating with $LiEt_3BH$ also underwent ring-contraction to yield branched furanosides. The presumed aldehydes formed initially were reduced *in situ* to the corresponding alcohols. It should be noticed that both the bromine atom and the benzoyl group of the glucose derivative were reductively removed.



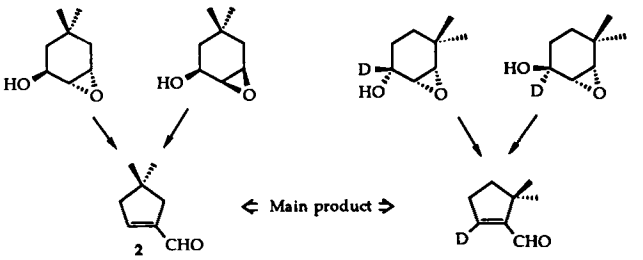
Binkley[31] observed the formation of three major products on treatment of a D-fucoside ditosylate with $LiEt_3BH$ and rationalized the reactions according to the scheme shown below.



At the author's laboratory, Magnusson and Thorén[32] performed the first skeletal rearrangement of epoxy alcohols, leading directly to α,β-unsaturated cyclopentenals, by employing essentially the LiBr/HMPA-procedure of Rickborn and Gerkin[16] (see above) from their synthesis of cyclopentanals. It was proposed[32] that β-hydroxycyclopentanals were formed as intermediates and that water was eliminated during the process. The yields of cyclopentenals were in the range 83-98%.



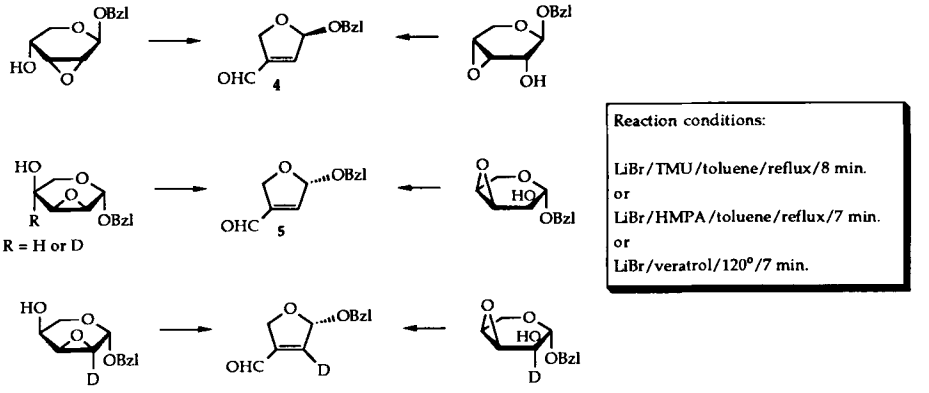
Later, Bergman and Magnusson[33] found that *trans* epoxy alcohols were at least as effective as the originally used *cis* epoxy alcohols, thereby simplifying the preparation of starting materials, and that tetramethylurea (TMU) or dimethoxyethane (DME) could be used to advantage to solvolyze the lithium bromide instead of the suspect carcinogenic compound HMPA. Insight into the mechanism of the ring-contraction reaction was gained by analyzing in detail the distribution and deuteration pattern of the products obtained by reacting pure deuterated *cis* and *trans* epoxy alcohols.



It was deduced that the actual rearrangement step is preceeded by a rapid

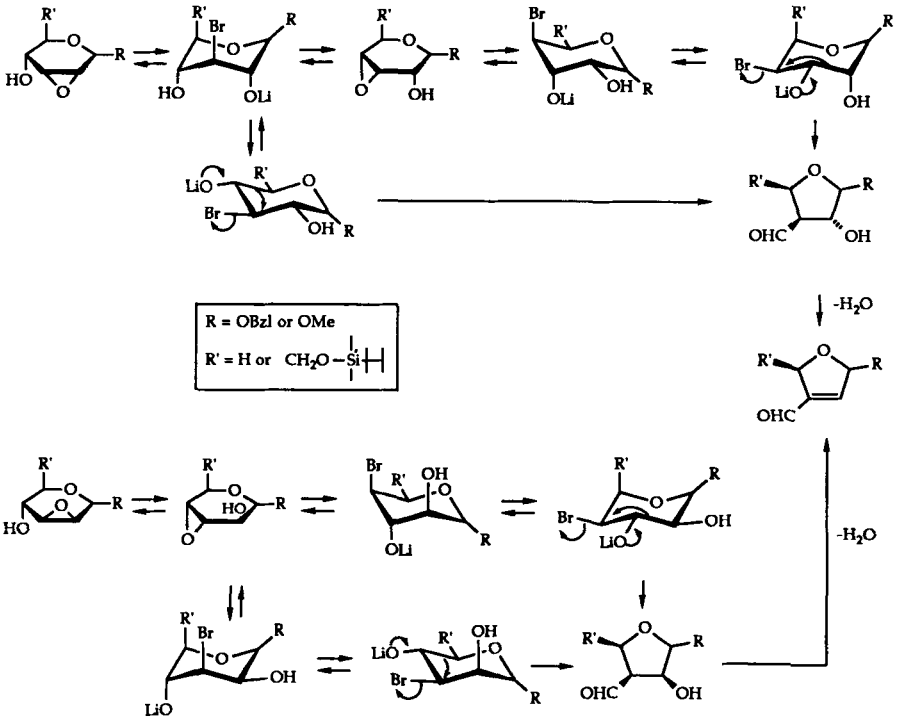
equilibrium between all reasonable intermediary bromohydrins and epoxy alcohols formed by bromide-ion attack, epoxide migration and epoxide ring-formation; detailed mechanistic schemes were put forward. In addition, it was found that excess lithium bromide in refluxing dimethoxyethane effected the ring-contraction and a practical procedure was reported for the large-scale (75 g) preparation of the valuable 4,4-dimethylcyclopentene-1-carboxaldehyde (**2**), starting from an 86:14 *trans/cis*-mixture of epoxy alcohols. It should be noted that **2** was the only aldehyde formed, thus simplifying the purification as compared with the aldol condensation[34] procedure that gave **3** in addition to **2**. It was also found that **3** and its isomer were formed in a more favorable ratio (approx. 45:1) when *trans* epoxy alcohols were used as starting materials.[33]

Sundin, Frejd, and Magnusson[35] introduced epoxy alcohol rearrangements to the field of carbohydrate chemistry by reacting benzyl 2,3- and 3,4-anhydro-β-D- and L-ribopyranoside with LiBr/TMU in refluxing toluene, thereby providing the enantiomeric aldehydes **4** and **5**.

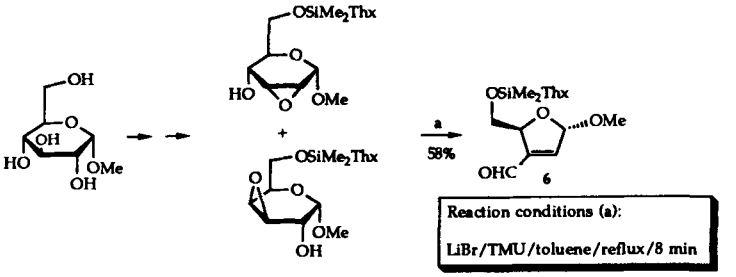


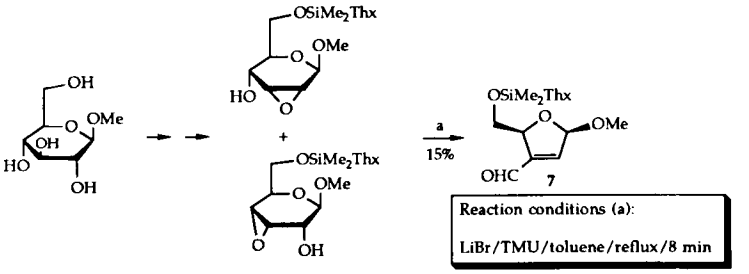
Despite the quite modest yield (approx. 30%), the procedure has merit because **4** and **5** are chiral isoprenoids with unique structural features of use in the synthesis of enantiomerically pure natural products (see below). Simple filtration of the reaction mixtures through silica gel permitted an easy isolation of the fast-moving aldehydes. Furthermore, the starting anhydroribosides are easily prepared from arabinose in approx. 60% over-all yield via crystalline intermediates.

As in the epoxy cyclohexanol case described above, specifically deuterated anhydroribosides were rearranged and analysis of the products gave insight into the mechanism of the reaction.[35] Here also, a complex equilibrium between epoxy alcohols and bromohydrins preceeded the actual rearrangement step.



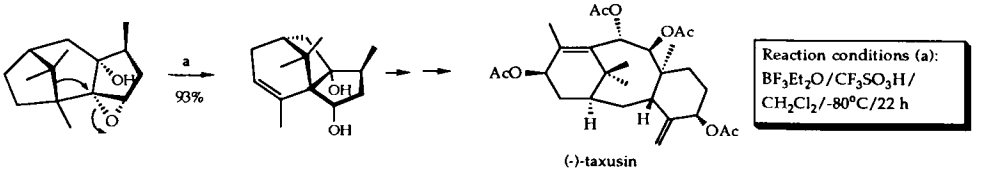
Recently, Rehnberg and Magnusson[36] expanded these reactions into the anhydrohexosides by preparing the aldehydes **6** and **7** from α- and β-glycoside epoxides in 58% and 15% yield, respectively. The latter were prepared in two steps (62% and 55% over-all yield, respectively) from commercially available methyl α- and β-D-glucopyranoside. The fact that the new aldehyde **6** is available in few steps and fair yield from inexpensive starting material makes **6** an attractive synthon in enantioselective synthesis.





Marshall and Kerschen[37] found that on ring-contraction of a 1,2-epoxy-9-*cis*-decalol, a bridged ketone was formed in 84% yield instead of the desired hydroazulene. They concluded that these hydroxyl-assisted epoxide pinacol-rearrangements are not useful for pseudoguaianolide-type hydroazulene synthesis. The migrating carbon atom is situated virtually antiperiplanar to the carbon-oxygen-bond of the epoxide ring, as evidenced from a low-energy conformation (author's results) obtained with the MM2 program[38]. This is similar to the hydride migration (see below) observed as a side reaction in the ring-contraction of epoxycyclohexanols.[33]

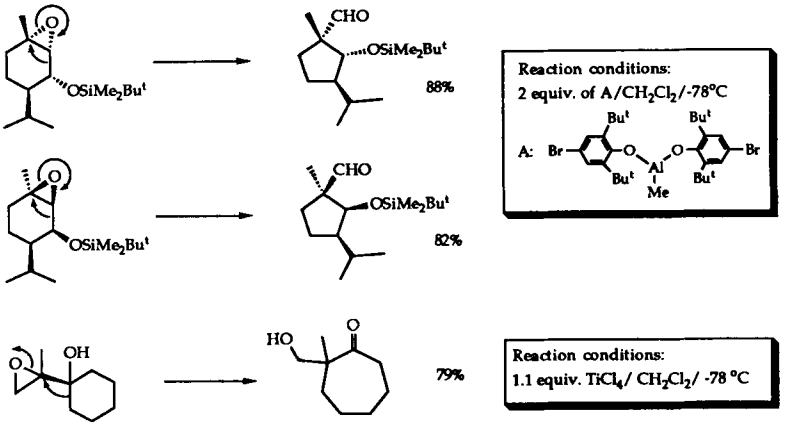
Holton et al.[39] utilized a rearrangement of an epoxy alcohol, obtained in two steps from commercially available β-patchoulene oxide, as a key step in their synthesis of (-)-taxusin. It should be noticed that also here the migrating carbon is situated virtually antiperiplanar to the plane of the epoxide ring in contrast to the carbons bound to the hydroxyl-bearing carbon.



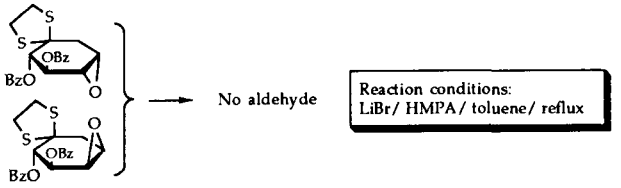
Sepulveda et al.[40] observed that epoxycyclohexanolates (formed *in situ* by reacting epoxycyclohexanone with Grignard reagent) under certain conditions rearranged to give cyclopentane derivatives.

Many examples are known of rearrangements of epoxy alcohol *derivatives*. Santelli and Viala[41] treated a series of epoxytosylates with aqueous calcium carbonate and obtained β-ketols. With 2,3-epoxycyclohexanol tosylate, the expected β-hydroxyaldehyde underwent elimination of water and cyclopentene-carboxaldehyde was formed in an unspecified yield. A peculiar rearrangement comprising breakage of the oxirane carbon-carbon bond was suggested as the reaction route. However, alternative routes via isomeric epoxy alcohols seem more reasonable.

Following work on titanium tetrachloride-induced rearrangement of silylated epoxy alcohols to give β-hydroxyketones, Yamamoto et al.[42] found that their bulky aluminum reagent effected rearrangement, thus furnishing β-silyloxy aldehydes in high yields. The reactions are highly stereoselective and some representative examples are shown below.



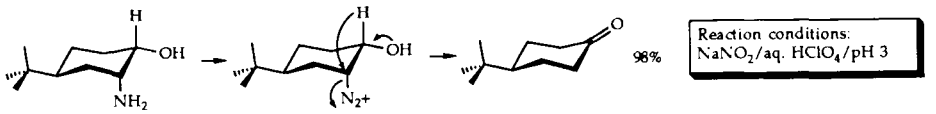
In connection with their work on the synthesis of chiral cyclopentanes, Ferrier and Haines[43] attempted a ring-contraction of an epoxy benzoate, using the LiBr/HMPA-reagent mentioned above[32]. However, no aldehyde was formed, which might be due to relative conformational stability of the initially formed bromohydrins; the necessary ring-flip[33] into the alternative chair conformations may not occur. An additional factor might be that internal and external[44] activation of epoxides by e.g. hydroxyl groups increase the reactivity towards nucleophiles; in the present case the hydroxyl groups are protected as benzoates.



Although it is outside the scope of this review, it should be mentioned that epoxy ketones rearrange into β-ketoaldehydes on Lewis-acid-treatment. Following the original discovery by House and coworkers,[45] Klix and Bach and Kunisch, Hobert and Weizel[46] reported additional examples of this useful reaction.

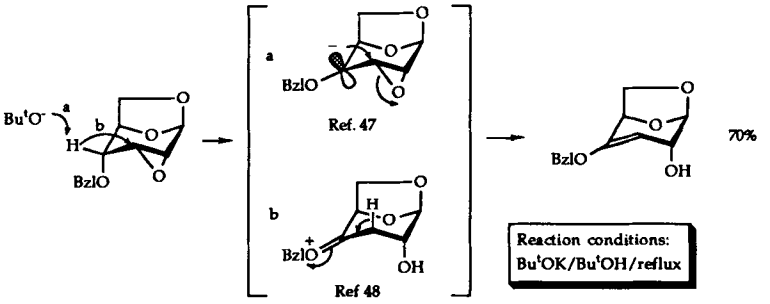
II. HYDRIDE SHIFTS

As mentioned earlier, Chérest, Felkin and coworkers[15] found that on treatment of a conformationally stable amino alcohol (axial NH_2) with nitrous acid, a hydride shift occurred, thereby giving 4-t-butylcyclohexanone in virtually quantitative yield. This is in complete agreement with the demand for antiperiplanarity between the migrating- and the leaving group. As discussed above, compounds with equatorial amino groups rearrange by migration of a ring carbon-atom.[15]

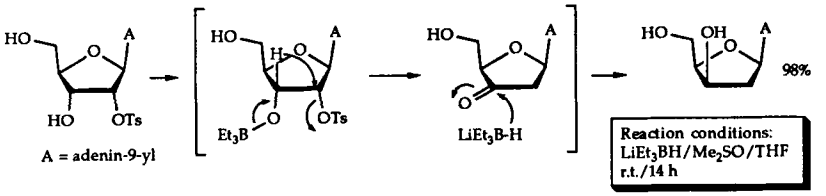


Trnka and Cerny[47] suggested that epoxide ring opening in 4-O-benzyl-1,6:2,3-dianhydro-β-D-allopyranose was initiated by proton abstraction by the strongly basic potassium t-butoxide to give the benzyl enol ether shown below. The structure elucidation was based on the transformation, by hydrogenation, into 1,6-anhydro-3-deoxy-β-D-*ribo*- and *xylo*-hexopyranose and on IR and ^{1}H-NMR data; however, no vinylic proton signal was reported. In a review on displacement, elimination and rearrangement reactions in carbohydrates, Buchanan[48] suggested that the enol ether was instead formed *via* an intramolecular hydride shift, followed by loss of the migrating proton. Such

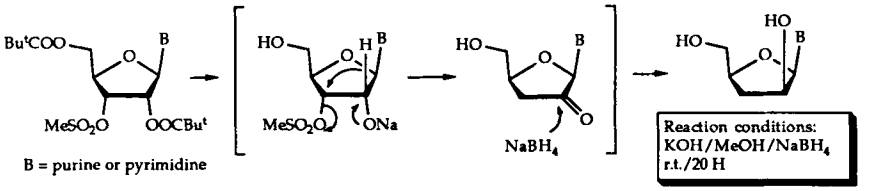
hydride shifts are however normally observed on treatment of epoxy *alcohols* with base, where the alcoholate anion provides an electron push for the migration of the hydride. Alternatives include addition/elimination of ^{t}BuOH, with and without participation of the benzyloxy group. Further investigation is needed in order to clarify the mechanism of this reaction.



A hydride shift was observed by Hansske and Robins[49] on an attempted direct reductive displacement of tosylate in a furanoside with lithium triethylborohydride. The initially formed ketone was immediately reduced from the less hindered side of the furanose ring to give the 2-deoxy sugar with inverted configuration at the 3-position in an impressive yield of 98%.

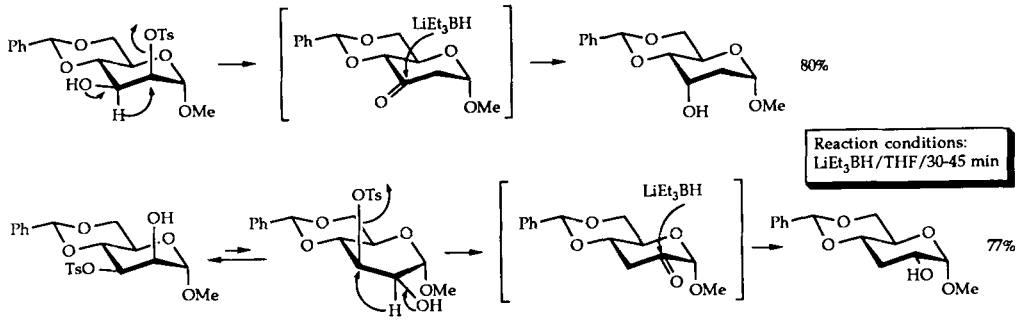


A similar reaction was recently reported by Kawana et al.[50] for the synthesis of 3′-deoxy nucleosides. It should be noticed that the reaction sequence was performed with two one-pot reactions (pivaloylation/mesylation and depivaloylation/hydride shift/reduction).

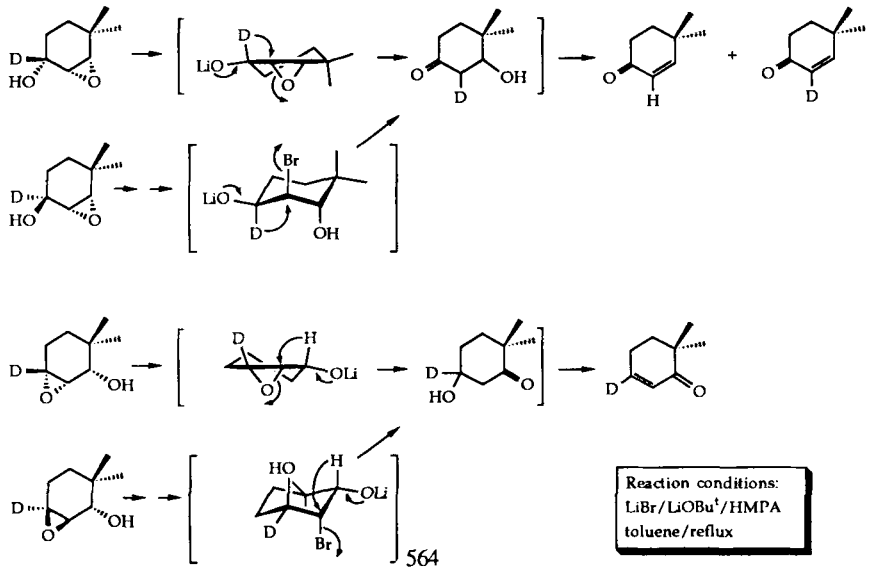


Baer and Mekarska-Falicki[51] observed hydride shifts in two mannoside tosylates. While the reaction route of the 2-tosylate is highly plausible, the 3-

tosylate needs to obtain a skew conformation for an easy hydride shift to occur. That the 3-tosylate prefers the rather awkward hydride-shift-route instead of the alternative ring-contraction into a furanosidic aldehyde is an indication that the anomeric carbon has a low migratory aptitude. As a matter of fact, the author is not aware of any example of such a ring-contraction.

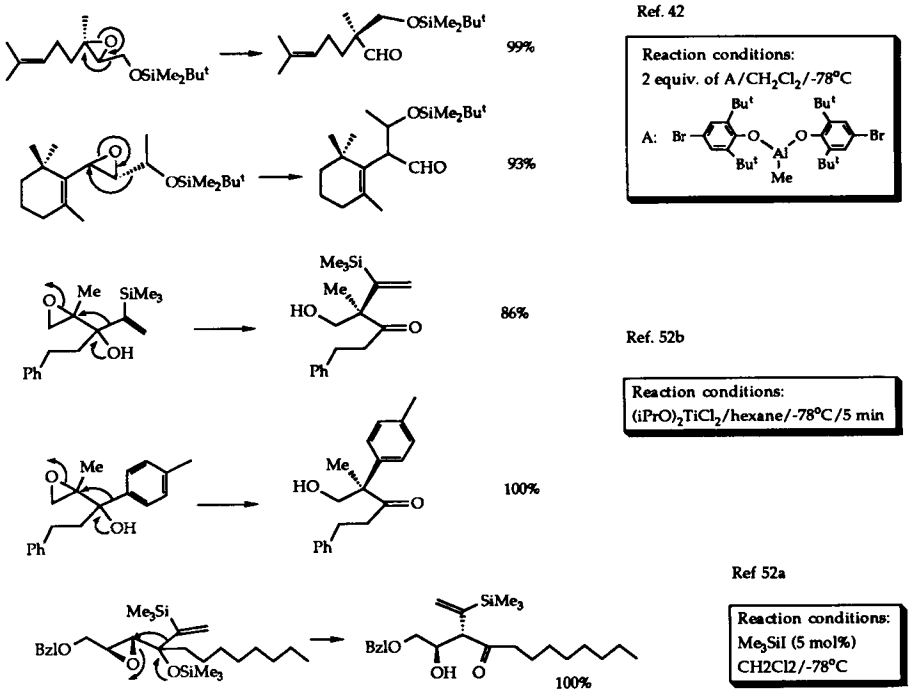


Bergman and Magnusson[33] observed the formation of several byproduct ketones when they treated specifically deuterated (and carefully purified) *cis* and *trans* epoxy alcohols with lithium bromide in cation-complexing solvents. It was suggested that the ketones were formed via hydride shifts as shown below. Hydride shifts were also reported by Ilyukhina, Kamernitzkii, and Voznesenskaya[52] and recently by Morrison and Wilkinson[53] in connection with an investigation of neighbouring group participation in the cleavage of steroidal epoxy alcohols.

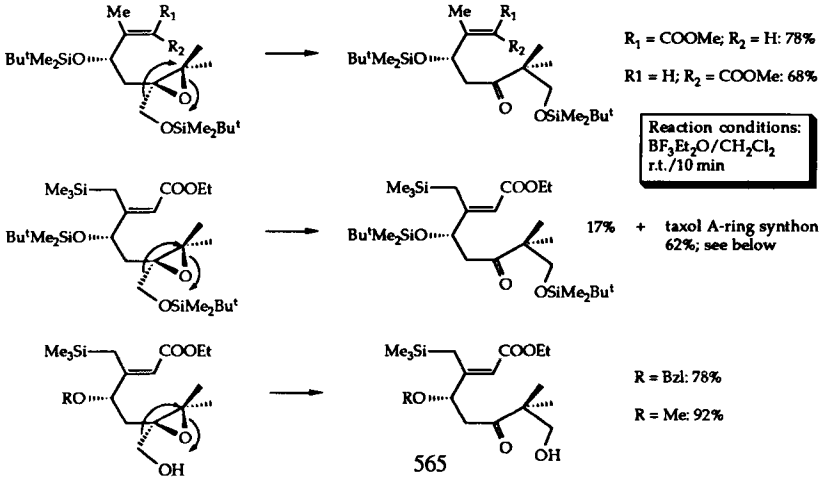


III. REARRANGEMENTS IN NON-CYCLIC SYSTEMS

Yamamoto[42] and Suzuki[54] and their coworkers reported high-yielding Lewis acid-promoted rearrangements of epoxy alcohols and silylether derivatives. A catalytic rearrangement is possible when the catalyst (e.g. Me_3SiI) can be re-created through the attack of iodide ion on the silicon atom of the protecting group.

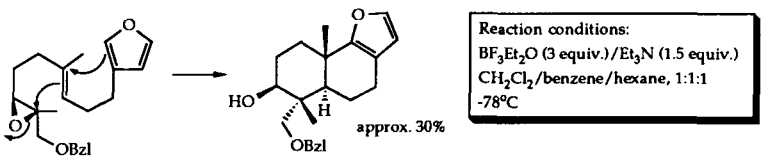


During the synthesis of the A-ring fragment of taxol, Pettersson, Frejd, and Magnusson[55] observed several examples of rearrangements of tetra-substituted epoxy ethers.

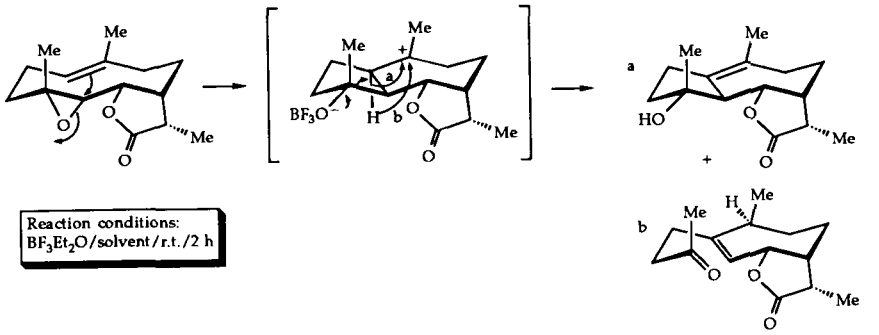


IV. RING-CLOSURE REACTIONS

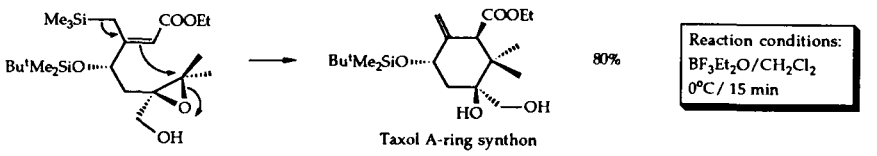
Tanis, Chuang, and Head[56] obtained a ring-closed furan on treatment of a benzyl-protected epoxyalcohol with BF_3Et_2O/Et_3N. Interestingly, when the epoxy alcohol was protected with a Bu^tMe_2Si-group, the bulk of the product consisted of acyclic ketones, probably formed via rearrangements similar to those described above.



Parodi and Fisher[57] used a similar BF_3Et_2O-initiated ring-closure of the germacrolide-4-epoxide dihydroparthenolide to obtain a guaianolide as the major product (route a). A minor xanthanolide product (2%; route b) was formed, presumably by fragmentation of the intermediate cation via a hydride shift similar to those described above.



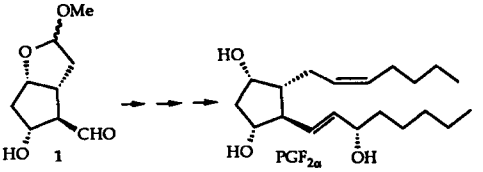
Pettersson, Frejd, and Magnusson[55] obtained an enantiomerically pure taxol A-ring synthon by ring-closure of a tetrasubstituted epoxy alcohol with BF_3Et_2O. The outcome of the reaction depends on the presence of suitable protecting groups (here Bu^tMe_2Si), even at positions remote from the reaction center. The reaction seems to be the first example of a successful ring-closure with a tetrasubstituted epoxide.



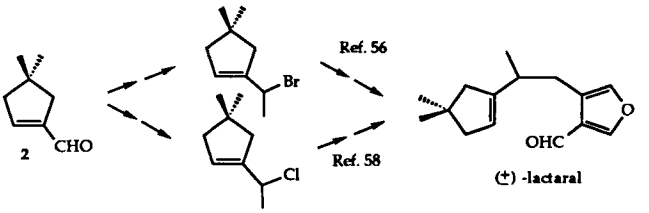
V. EPOXY ALCOHOL REARRANGEMENTS IN NATURAL PRODUCT SYNTHESIS

A number of natural products have been synthesized via synthons obtained by rearrangement of epoxy alcohols as described above. The aldehyde **2** is by far the most popular of these synthons and it has *inter alia* been used for the preparation of several sesquiterpenes.

Woodward et al.[26] used the aldehyde **1** (obtained by ring-contraction of an aminoalcohol; see above) as starting material for a synthesis of prostaglandin F2α, both in racemic and natural form.

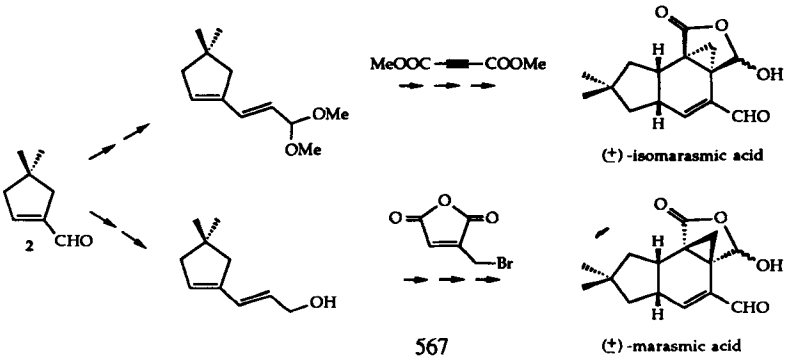


Froborg, Magnusson, and Thorén[58] used the aldehyde **2** as starting material in their low-yield synthesis of racemic lactaral[59], a furanoid sesquiterpene aldehyde isolated from *Lactarius* fungi. An improved synthesis was reported by Tanis and Head.[60]

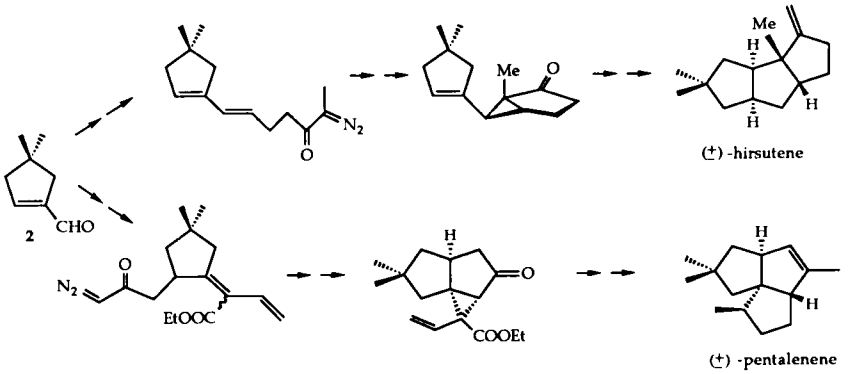


Wilson and Turner[34] employed **2** (prepared via aldol condensation of 3,3-dimethyladipic aldehyde) in an attempt to synthesize marasmic acid[61], a fungal metabolite of the Basidiomycetes.

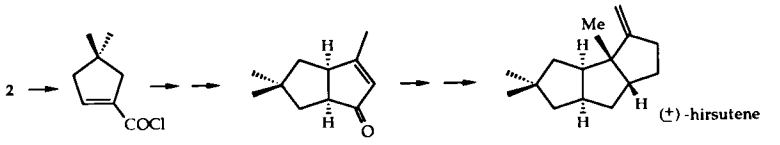
Greenlee and Woodward[62] accomplished the first synthesis of racemic marasmic acid and isomarasmic acid *via* a Diels-Alder reaction between bromomethylmaleic anhydride and a diene obtained from aldehyde **2**.



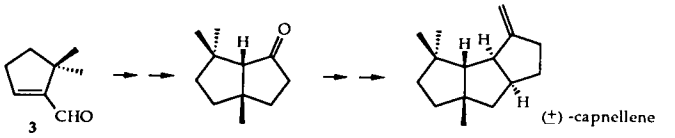
In a series of papers, Hudlicky and coworkers reported the synthesis of triquinane sesquiterpenes via integration of aldehyde **2** into the terpene skeletons, thereby completing syntheses of hirsutene and pentalenene.[63]



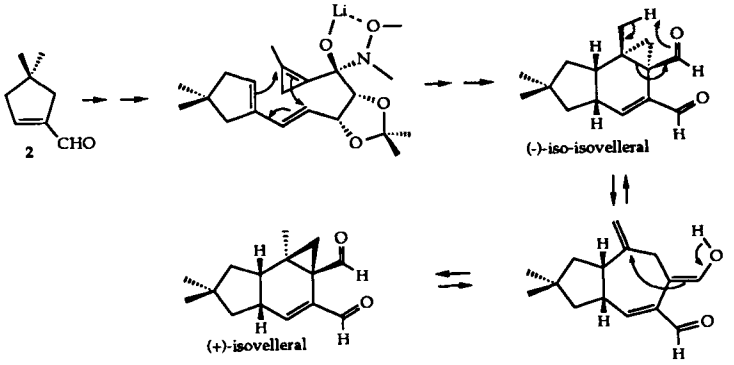
Magnus and Quagliato[64] prepared racemic hirsutene by a short route where every key step utilized organosilicon chemistry.



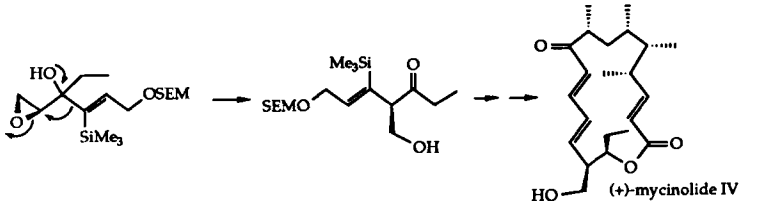
Stevens and Paquette[65] used aldehyde **3** in their synthesis of racemic capnellene. Key reaction steps were a Nazarov cyclization and conjugate addition of $LiMe_2Cu$ to an intermediate bicyclo-[3.3.0]-octenone.



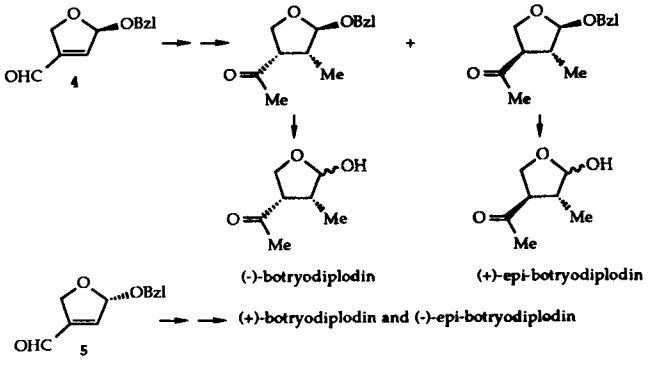
Wickberg et al.[66] employed aldehyde **2** in their enantioselective synthesis of isovelleral[67], a fungal metabolite from *Lactarius* fungi, suggested to be involved in the mushroom's chemical defense against predators.[68] The key step of the synthesis was an intramolecular Diels-Alder reaction, where the ribonolactone-derived portion was the chiral inductor. However, (-)-iso-isovelleral was formed, which underwent a remarkable equilibrium-epimerization on heating, thereby furnishing a separable 1:1 mixture of the desired (+)-isovelleral and (-)-iso-isovelleral.



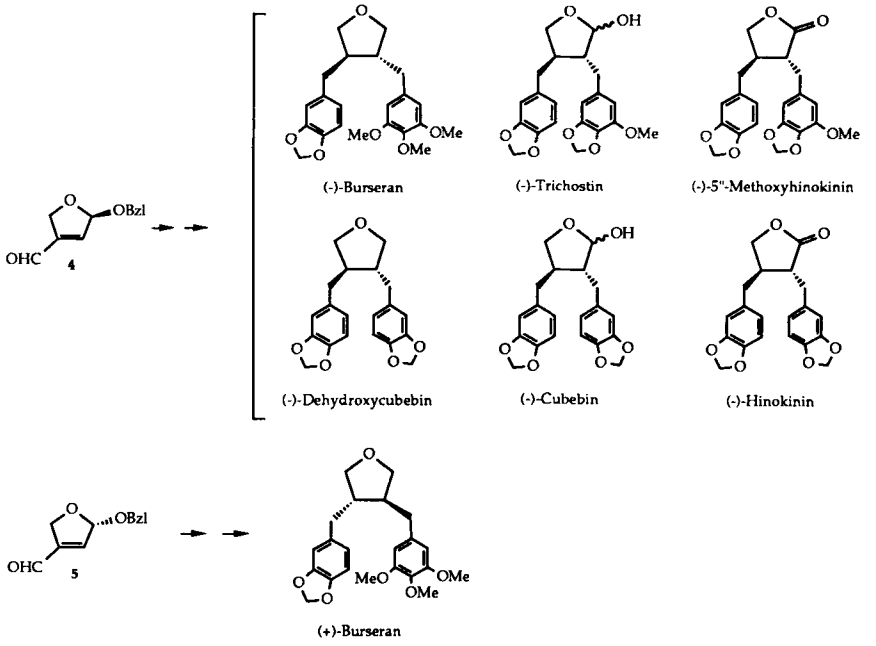
Suzuki et al.[69] used their epoxy alcohol rearrangement in the synthesis of optically active mycinolide IV, the aglycon of the macrolide glycoside antibiotic mycinamicin IV.[70] These rearrangements were discussed above.



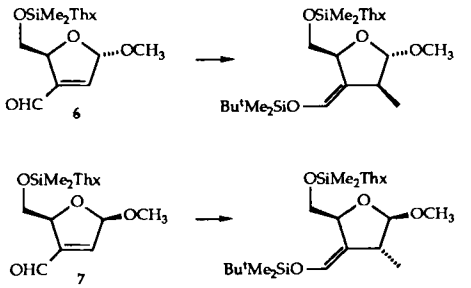
Rehnberg and Magnusson[71] used the chiral aldehydes **4** and **5** for the synthesis of both enantiomers of the fungal metabolites botryodiplodin and epi-botryodiplodin.[72]



Furthermore, aldehydes **4** and **5** turned out to be very useful synthons for the preparation of enantiomerically pure lignans, as exemplified below.[73]

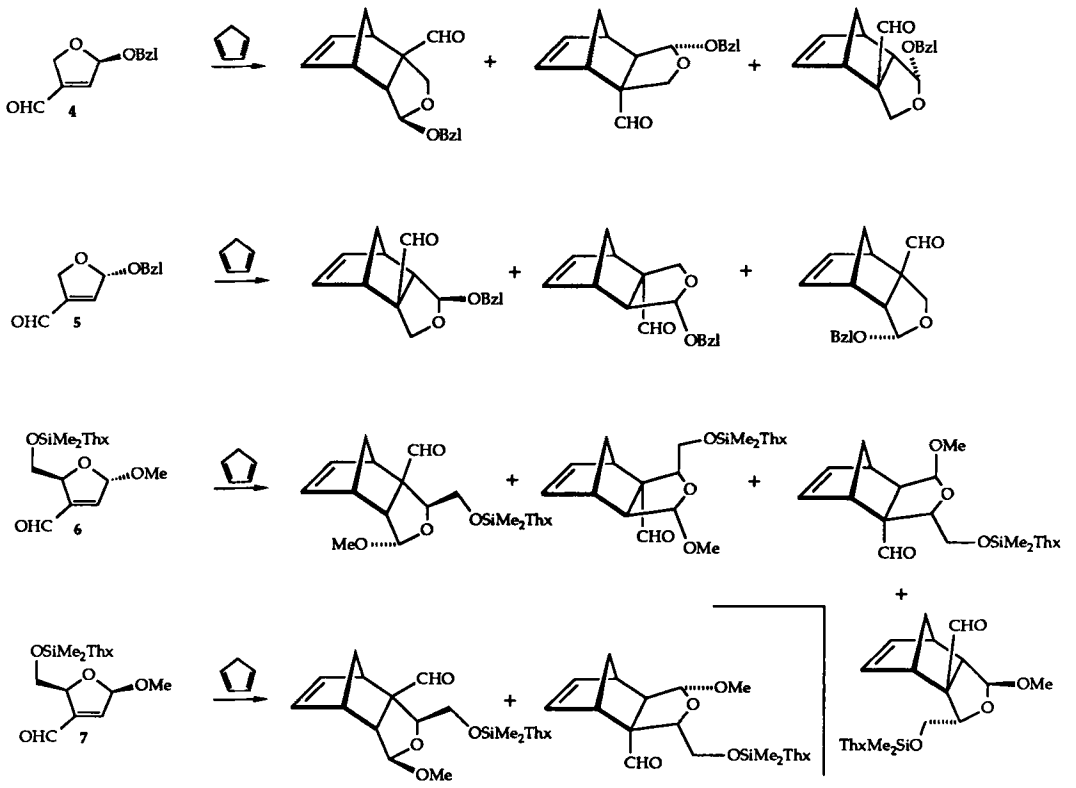


Recently, Rehnberg, Sundin, and Magnusson[74] investigated the stereochemical outcome of conjugate additions with aldehydes **4** and **5**, as well as with the novel aldehydes **6** and **7**. It turned out that the alkoxy group of the acetal function effectively guides the attacking nucleophile to the less hindered side of the ring, thereby giving virtually complete diastereoselectivity in the addition.



Finally, aldehydes **4-7** were submitted to Diels-Alder addition with cyclopentadiene, thereby furnishing a series of norbornenes of potential use in the synthesis of enantiomerically pure natural products.[75]

A detailed analysis of the NMR data for the norbornanes (where all four carbons of the furanosidic rings should be held in a rigid conformation), supported by molecular mechanics-calculated (MM2-program[38]) conformations, gave evidence for the existence of an anomeric effect in furanosides.[76]



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