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THE CONTRASTING BEHAVIOUR OF OXIRANE AND OXETANE IN CATIONIC CYCLOOLIGOMERIZATION AND POLYMERIZATION

JOHANNES DALE
Kjemisk Institutt, Universitetet i Oslo, N-0315 Oslo, Norway

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CONTENTS

1. INTRODUCTION

It has long been recognized by polymer chemists that ethylene oxide (oxirane) and trimethylene oxide (oxetane) respond very differently to catalysts of Lewis acid type (BF_3, PF_5, etc.) and to alkylation agents (triethyloxonium tetrafluoroborate, etc.). Thus, in 1957 Worsfold and Eastham[1] showed that oxirane in the presence of BF_3 with water as a cocatalyst gave a polymer with a molecular weight that hardly exceeded 700, together with a steadily increasing quantity of the cyclic dimer (1,4-dioxane). Polymers of molecular weight 4000–20,000, prepared by other methods, although stable in the *presence of* BF_3 *alone*, were degraded to the same low molecular weight in the *presence of* BF_3 *and oxirane*.[1] Furthermore, when the same polymers were treated with triethyloxonium tetrafluoroborate in the *absence of oxirane*, complete decomposition to dioxane took place.[2] It was concluded[1,2] that the low molecular weight polymer obtained from oxirane/BF_3 must be the result of a balance between the building-up of polymer chains from oxirane units, and the degradation of these polymer chains by the BF_3/oxirane catalyst to the thermodynamically most stable end product dioxane. Being the smallest strain-free ring, dioxane is favoured by entropy, and higher cyclic oligomers (crown-ethers) were not seen. Eastham *et al.*[2] made further important observations: When deuteriated oxirane was used with BF_3 to degrade the non-deuteriated polymer, the initially formed dioxane contained no detectable deuterium, but the rearranged byproduct methyldioxolane was always fully deuteriated. Similar observations are discussed below for the cyclooligomerization.

In striking contrast, it had already been reported by Rose[3] in 1956 that oxetane, as well as 3,3-dimethyloxetane, in the presence of BF_3 gave irreversibly a mixture of a polymer of molecular weight 20,000 and the crystalline cyclic tetramer. It might have been argued that in this system the 16-membered ring of the cyclic tetramer is again the smallest strain-free ring and therefore favoured by entropy, the 8- and 12-membered rings having medium-ring strain. However, it has been convincingly shown, using a variety of cationic catalysts, that cyclic oligomers and the polymer are formed directly from oxetane in concurrent irreversible reactions.[4] It is this contrast that will be discussed in the present report in the light of our results from detailed studies of the mechanism of the cyclooligomerization of oxirane and the concomitant degradation of the obtained crown ethers.

2. CROWN ETHER FORMATION

The familiar cation-complexing unsubstituted crown ethers, like 18-crown-6, were first prepared in 1967 by Pedersen in a Williamson ether synthesis from chlorohydrins of oligoethylene glycols.[5] In 1971 we,[6,7] and independently Greene,[8] worked out an improved synthesis from oligoethylene glycols and their ditosylates.

Since all these glycols are made commercially from oxirane, it was natural to consider the possibility of obtaining crown ethers directly from oxirane using cationic catalysts like BF_3. In the literature there was already an indication to the contrary by authors[9] who had obtained stereo- and regio-isomeric mixtures of cyclic dimers, tetramers, pentamers and polymers from methyloxirane using BF_3 as catalyst. From unsubstituted oxirane, on the other hand, only dioxane and polymer were obtained.[9] An early patent,[10] however, described the preparation of cyclic tetramer (12-crown-4) together with dioxane and polymer from oxirane by the use of triethylaluminium as catalyst.

This was the situation when we started our systematic investigations that led to a preparative synthesis of the most interesting crown ethers (12-crown-4, 15-crown-5, 18-crown-6) directly from oxirane. Careful studies of the mechanism involved when BF_3 was the catalyst, followed later.

On the other hand, the unfamiliar crown ethers obtained from oxetane (12-crown-3, 16-crown-4) turned out to be selective, although weak, complexers for the small Li^+ cation.[11,12] It therefore became important to study carefully also the formation of cyclic oligomers from oxetane and from its 3,3-dimethyl derivative.

3. OXIRANE

3.1. *Conditions for obtaining cyclic oligomers*

To ensure the formation of cyclic oligomers at the expense of open-chain oligomers and polymers it was considered necessary to use catalysts and solvents incapable of furnishing permanent end groups. In fact, it was soon found[13,14] that a mixture of all the possible cyclic oligomers, unaccompanied by open-chain oligomers and polymers, could be obtained from oxirane in the presence of BF_3 or similar acidic fluorine compounds (PF_5, SbF_5). A typical product mixture contained 40% dioxane, 1% 9-crown-3, 15% 12-crown-4, 5% 15-crown-5, 4% 18-crown-6, 3% 21-crown-7, 2% 24-crown-8, 2% 27-crown-9, 1% 30-crown-10, etc. The common practice of using BF_3 as its etherate led to a mixture of rings and open-chain compounds terminated by ethoxy groups. Another common practice, to add water as a cocatalyst,[1,2] led to hydroxyl-terminated open-chain compounds (polyethylene glycols). Only HF gas proved acceptable as a cocatalyst, but it was later found to be unnecessary. Suitable solvents were CH_2Cl_2 and benzene (no hydroxyethylation of benzene was observed!), and of course dioxane, being also a member of the product family. Dioxane was in fact the solvent chosen for the industrial process exploited for some years by Borregaard Industries, Ltd. In non-polar solvents like hexane, or in the gas phase, ethylene oxide is dehydrated, producing dark-coloured tars and polyethylene glycols. The only unavoidable byproducts were cyclic acetals, found in small quantities in the dimer and trimer fractions (2-methyl-1,3-dioxolane and 2-methyl-1,3,6-trioxocane, respectively).

Other Lewis acids were either ineffective as catalysts ($AlCl_3$, $FeCl_3$) or gave waxy polymers ($SnCl_4$, $SbCl_3$), while oxygen acids ($HClO_4$, *p*-toluenesulfonic acid) were rapidly transformed into half-esters of ethylene glycol.

In the Williamson ether synthesis of crown ethers a template effect by the counter cation present has been reported.[7,15] Because the reaction is irreversible, this template effect must act on the kinetics by inducing a folding of the chain around the cation, whereby the anionic end is brought closer to the point of attack. A similar kinetic effect would be inconceivable in a cationic cyclization reaction. However, when it was realized that the formed crown ethers, like the oxirane polymer, are continuously being degraded in the presence of BF_3/oxirane, the possibility was considered that the desired crown ethers could be selectively protected against degradation by the positive charge furnished by a complexed cation. This proved to be the case[16,17] when salts with non-nucleophilic anions were used, especially the anion that matches the catalyst (BF_4^- with BF_3, PF_6^- with PF_5, etc.). The salt dissolves as the reaction proceeds, whereafter the crown ether complexes start to precipitate. Only 12-crown-4, 15-crown-5 and 18-crown-6 could be trapped in this way as crystalline or liquid precipitates. After pyrolysis of the precipitate, the salt could be returned to the mother liquor and the process continued. The majority of the product was always dioxane, but this served as the solvent and was even reincorporated in the macrocycles (see below). Salts of alkali metals, alkaline earths and transition metals could be used. The highest selectivity in the precipitation was obtained with $CsBF_4$ and $RbBF_4$ (100% 18-crown-6). KBF_4 trapped also 15-crown-5, and $NaBF_4$ trapped all three crown ethers.

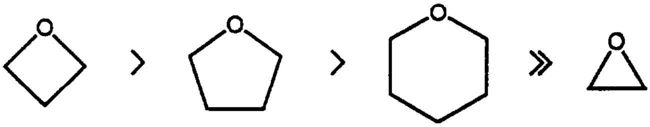
3.2. *Observations leading to a mechanistic hypothesis*

It was already clear that if there had been a direct path from oxirane to the thermodynamically stable end product dioxane, neither polymer nor crown ethers should have appeared. A number of observations helped to form a detailed picture of a very complex system of primary cyclization products, ring-expansion products and ring-contraction products, degradation to dioxane and reincorporation of dioxane.[18,19]

These observations were:

1. Like the polymer,[1,2] the crown ethers are perfectly stable in the presence of BF_3 alone at 160°C, but unstable even below 0°C when oxirane is also present.[19] The degradation, like the oligomerization, must therefore be initiated by O-alkylation, oxirane/BF_3 being the alkylating agent.
2. Oligomerization of oxirane alone in CH_2Cl_2 gives exclusively the cyclic tetramer in the very early phase of the reaction, while dioxane and higher oligomers appear only after a certain concentration of tetramer has been reached.[19]
3. When the reaction is carried out in CH_2Cl_2 in the presence of deuteriated dioxane,[18] the initially formed trimer and tetramer are largely non-deuteriated, whereas the pentamer and homologues are largely deuteriated in just two monomer units. This shows that the growing chain can be intercepted by one dioxane molecule before cyclization.
4. The two rearrangement products (acetals) contain no trace of deuterium even after long reaction times.[18] This is in accord with results from the degradation of the non-deuteriated polymer initiated by deuteriated oxirane; the 2-methyl-1,3-dioxolane was always fully deuteriated.[1,2]

A clue to understanding the mechanistic details, and also the contrasting behaviour of oxirane and oxetane, was found by comparing the basicity, hence nucleophilicity, of ether oxygen in the unstrained products (polymer and cyclic oligomers) with the basicities of the ring-strained starting materials (oxirane and oxetane). Thus, it had already been established[20] that the basicity sequence of the simple cyclic ethers is as follows:



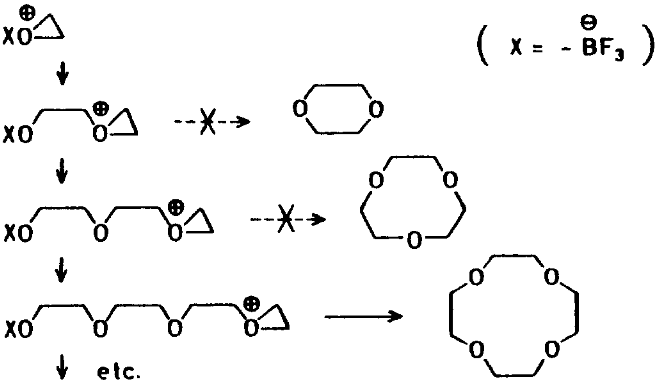
The basicity of ether oxygen in open chains and larger rings would be close to that of the six-membered ring. The polymeric or macrocyclic products formed from the *less basic oxirane monomer* will therefore tend to intercept the growing chain, whereby chain growth will stop, and other reactions, for example degradation to dioxane, become initiated. The products formed from oxetane will not be able to compete with the *more basic oxetane monomer*, and chain growth and/or cyclization will continue undisturbed and irreversibly.

A further assumption proved necessary to understand the details of the reaction in both series: The transition state in all reaction steps require an S_N2-like linear arrangement of the attacking ether oxygen and the leaving ether oxygen.[21]

With this background a mechanistic picture developed (see below) which could be tested experimentally by following the reaction in the presence of each of the crown ethers separately. For practical reasons, fully deuteriated oxirane was now oligomerized in the presence of non-deuteriated dioxane or crown ethers (trimer, tetramer, pentamer and hexamer) separately, observing the deuterium incorporation in each product quantitatively by GC–MS as a function of time.[19] The catalyst was gaseous BF_3 (no tetrafluoroborate salt added) and the solvent was CH_2Cl_2. It was of course particularly important to obtain data after very short reaction times before scrambling became troublesome.

3.3. *Postulated mechanism and predicted deuterium incorporation*[19]

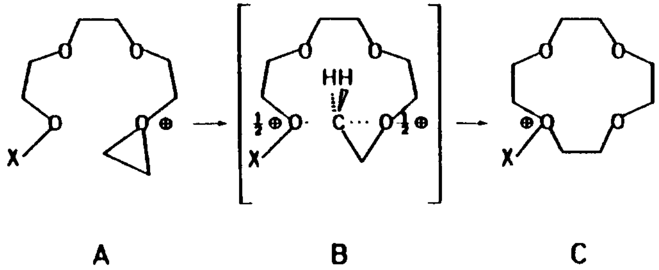
Initiation of a catalytic cycle. Only the BF_3 adduct of the strained 3-membered ring of the monomer can initiate oligomerization, that is, open its CO bond when attacked by a neutral monomer molecule (Scheme 1). The BF_3 adducts of unstrained cyclic (and acyclic) ethers are known to be stable against CO bond opening, and BF_3 can be transferred easily from one ether oxygen to another.



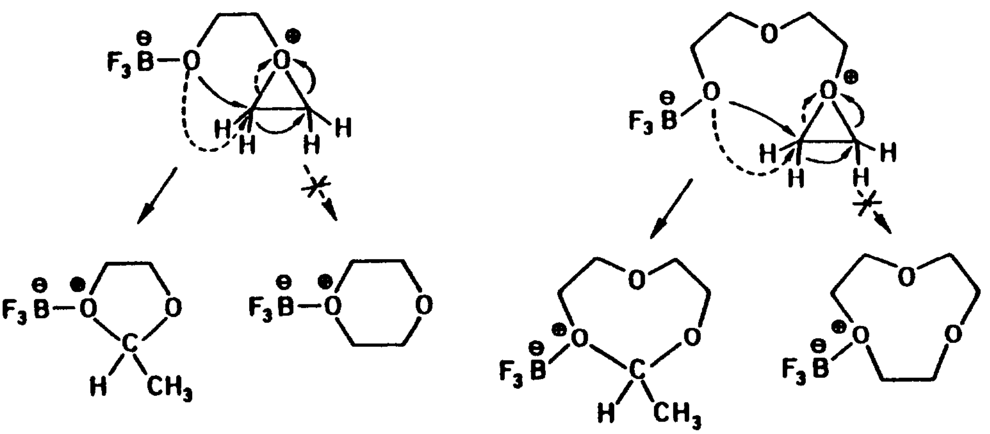
Scheme 1

Chain growth. An intermediate oxonium ion involving a strained 3-membered ring is non-discriminating against nucleophilic attack at a ring carbon, and reacts not only with the ether oxygen of normal basicity present in unstrained cyclic oligomers (as well as acyclic ethers) but also with the weakly basic[20] oxygen of the monomer and even with adjacent hydride by a 1,2-shift. The α-carbon of the unstrained side chain of such an oxonium intermediate is much less reactive. In the presence of a high concentration of monomer, the chain will therefore tend to grow in the 'normal' way shown in Scheme 1.

Chain termination. Since the solvent CH_2Cl_2 furnishes no permanent end groups, a growing chain can only be terminated by cyclization, whereby the reactive trialkyloxonium intermediate is converted to the unreactive BF_3 adduct of some unstrained cyclic product. To start a new catalytic cycle, BF_3 must be transferred to a new monomer molecule. Cyclization of the chain is favoured when little monomer is present to continue chain growth. The terminal oxygen carrying the negatively charged $-BF_3$ substituent is the strongest nucleophile present and should at any time stay very close to the oxonium charge at the other end as its counter-ion. However, as the attack must occur on the carbon of the strained ring, and the transition state is assumed to have an S_N2-like geometry,[21] direct cyclization requires a minimum chain length. This is illustrated in Scheme 2 where the chain linking the attacking and the leaving oxygen atoms contains three monomer units. The transition state thus contains a ring that can be defined as 11-membered and leads to a product with a 12-membered ring, the cyclic tetramer. Chains which have not reached this minimum length may instead undergo 1,2-hydride shift. The migrating hydride can then leave carbon collinear with and opposite to the attacking oxygen (Scheme 3). The product will be a cyclic 5- or 8-membered acetal, 2-methyl-1,3-dioxolane or 2-methyl-1,3,6-trioxocane.

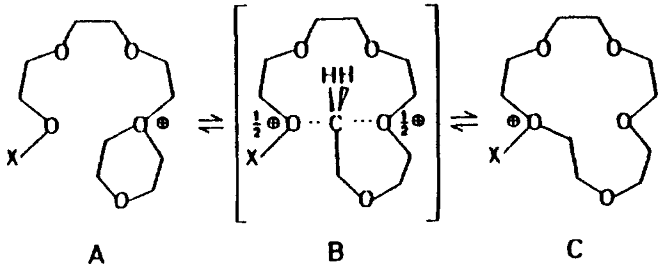


Scheme 2.



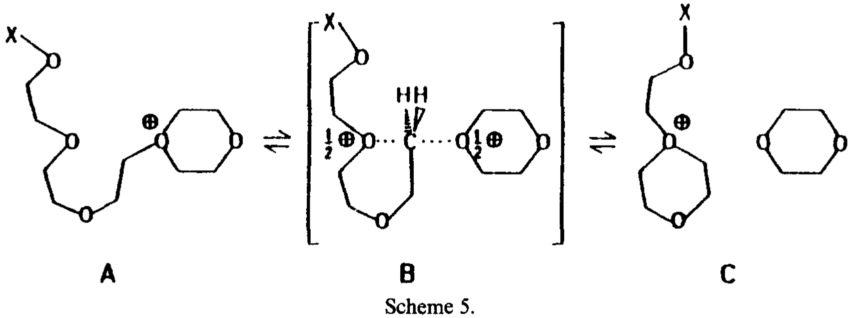
Scheme 3.

Product incorporation. When the cyclic oligomers start to accumulate as products, or are added deliberately, these stronger nucleophiles will, of course, compete effectively with the monomer and



Scheme 4.

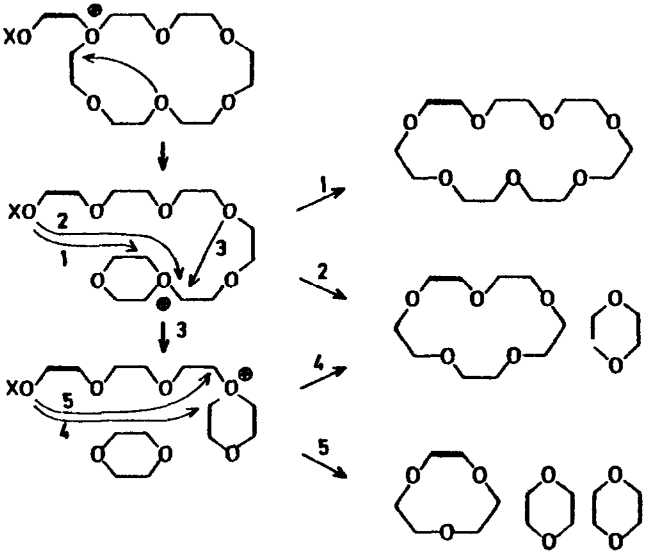
may enter the growing chain. The resulting oxonium intermediate, shown in Schemes 4 and 5 for the case of attack by dimer, is unstrained and becomes discriminating as to the next nucleophilic attack, excluding the less basic monomer. Further normal chain growth is thereby prevented, but additional product molecules may, in principle, enter the chain in a reaction similar to the reaction C → A in Scheme 5. Cyclization of the unstrained oxonium intermediate can occur in two different ways, since all three α-CH_2 groups are now equally vulnerable. Attack on ring carbon would lead to cyclization with net ring expansion (A → C in Scheme 4). Cyclization within the side chain (A → C in Scheme 5) leads to expulsion of the oligomer that terminated chain growth, so that its function has then only been that of a chain breaker. In the former cyclization the minimum ring size in the transition state is again 11-membered, although the product oligomer has a larger ring (in the example of Scheme 4 it is 15-membered). In the latter cyclization, the transition state geometry puts no restriction on ring size, since the departing oxygen is not part of the ring being formed. The ring size in the transition state is, therefore, the same as in the product and only influenced by conformational factors familiar from other cyclization reactions. Thus, the 6-membered ring is formed particularly easily and the 9-membered ring with more difficulty, although the overriding effect of the chemical reactivity of the terminal oxygen carrying the negatively charged $-BF_3$ substituent favours cyclization involving the full chain length. Even the cyclic trimer will be formed in preference to dimer if the chain contains just three units.



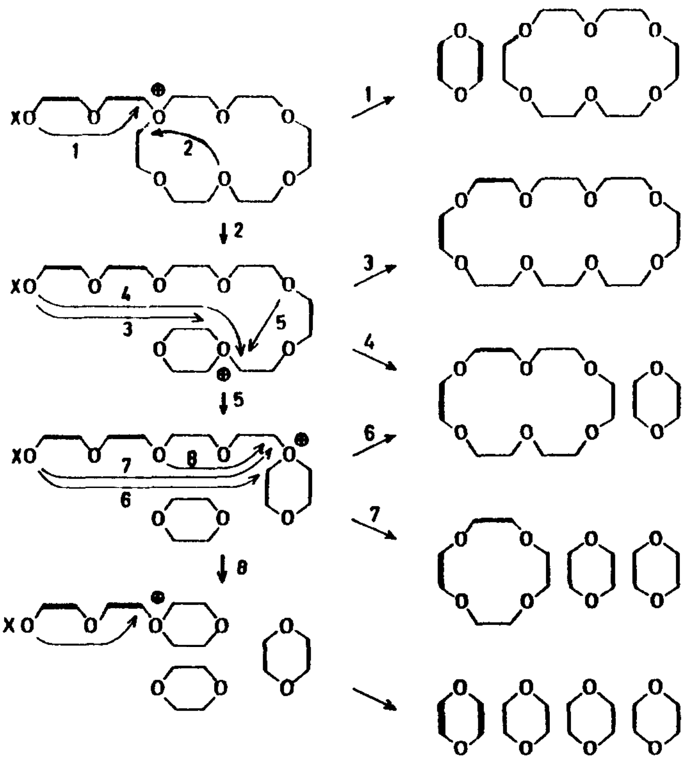
Scheme 5.

Degradation. Reactions of the type A → C shown in Scheme 5, when repeated, lead to a stepwise degradation of a linear chain to cyclic dimer molecules. If the chain is terminated initially by attack from a larger cyclic oligomer, the same type of oxonium intermediate can be formed by a transannular ring opening (or strictly ring contraction) as shown for the case of the cyclic pentamer in Scheme 4, C → A. This reversed ring expansion reaction is subject to the same restrictions with regard to the minimum length of the chain linking the attacking and the departing oxygen, so that the smallest ring for easy transannular opening is just the pentamer shown, and the cyclic dimer is the only possible product. Contraction to dimer is clearly favoured also in larger rings, although some competition from other modes of transannular attack may be expected in cyclic oligomers larger than the hexamer.

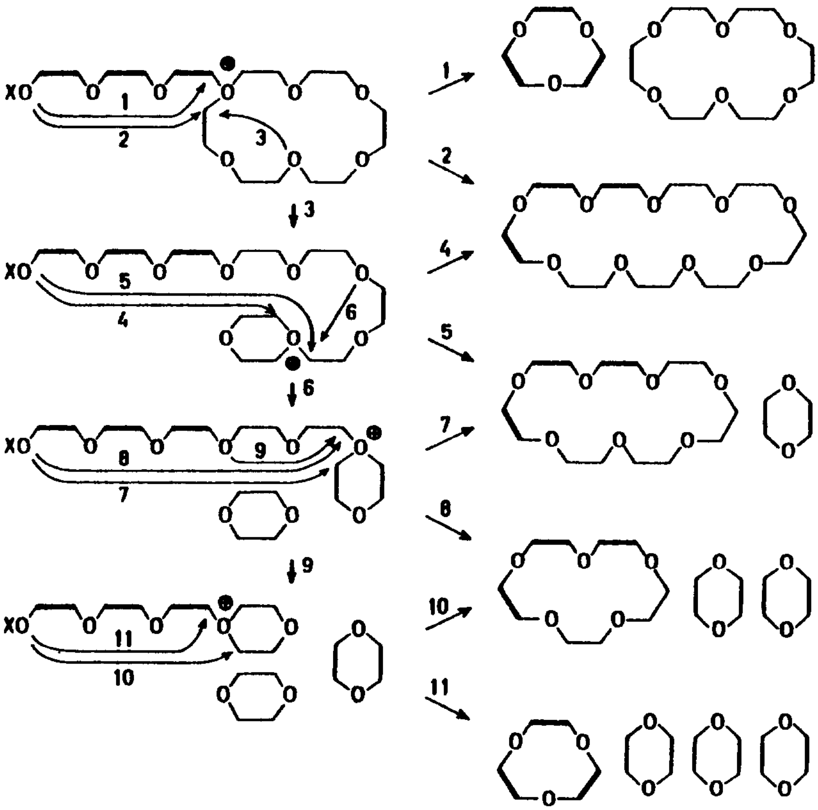
Detailed predictions of the likely paths are given as three reaction schemes for each non-deuteriated cyclic oligomer (Schemes 6, 7, 8, 9 and 10; a, b and c). Heavy lines symbolize



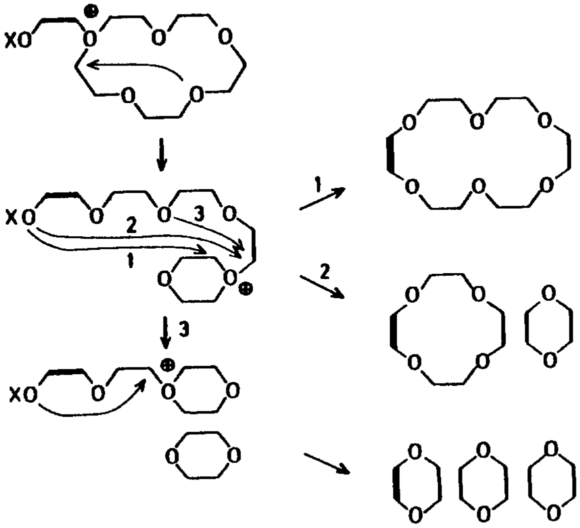
Scheme 6(a).



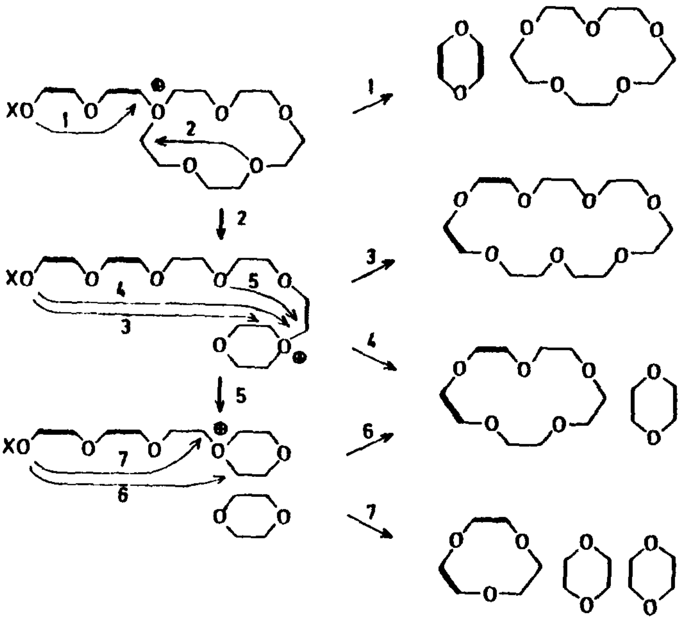
Scheme 6(b)



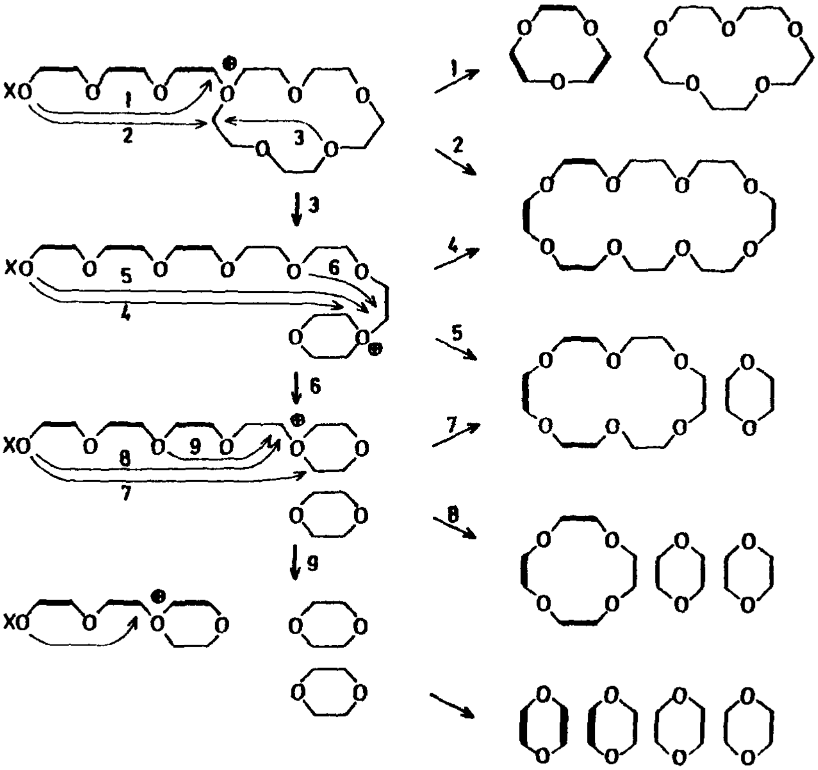
Scheme 6(c)



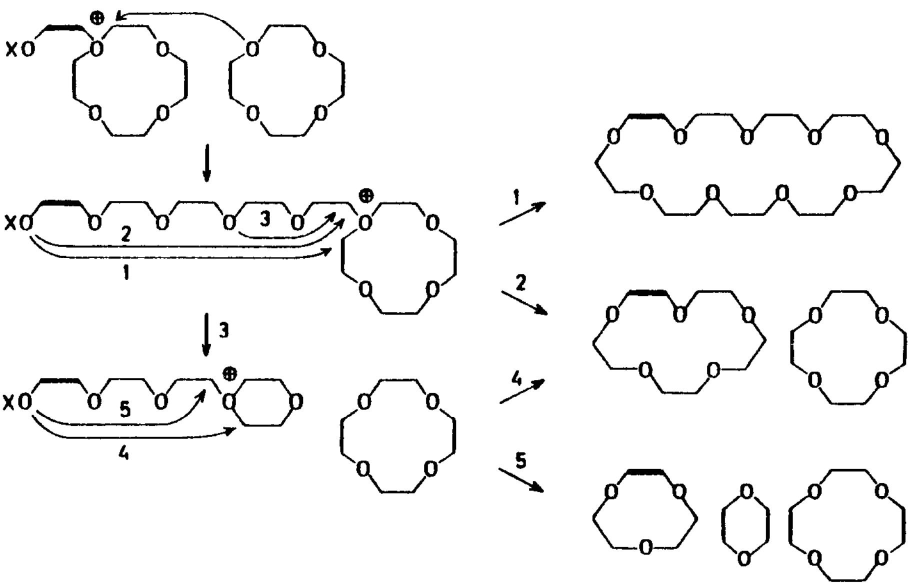
Scheme 7(a).



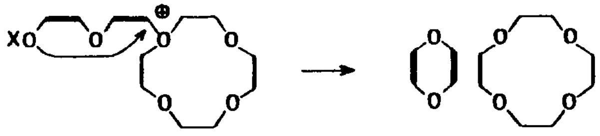
Scheme 7(b).



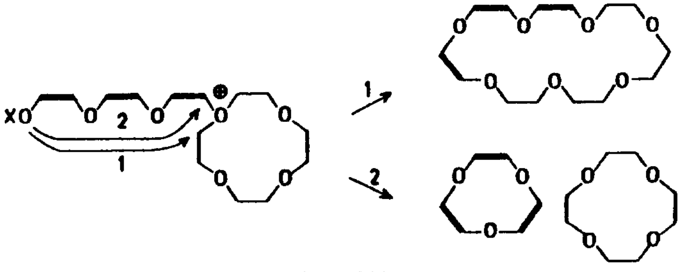
Scheme 7(c).



Scheme 8(a).



Scheme 8(b).

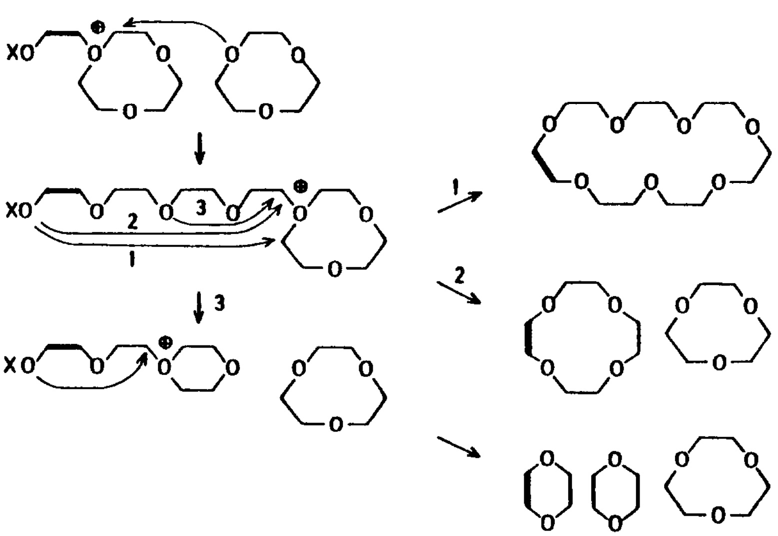


Scheme 8(c)

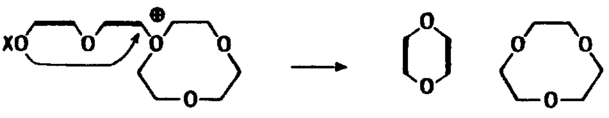
—CD_2—CD_2— units, thin lines —CH_2—CH_2— units, and —X = —BF_3^-. It is assumed that the non-deuteriated oligomer will attack either the activated monomer, the growing dimeric chain, or the growing trimeric chain (Scheme 1, left), all being deuteriated. If the chain should survive to become tetrameric, it would most likely cyclize immediately to produce the fully deuteriated cyclic tetramer.

3.4. *Comparison with the experimental results*

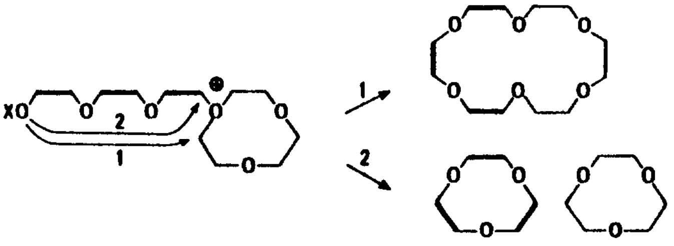
The deuteriation patterns observed experimentally by GC–MS analysis for each ring size were in striking agreement with our predictions.[19] It was also found that the two cyclic acetals accumulated with reaction time in all experiments and were always 100% deuteriated, even after 7 days. This



Scheme 9(a).



Scheme 9(b)

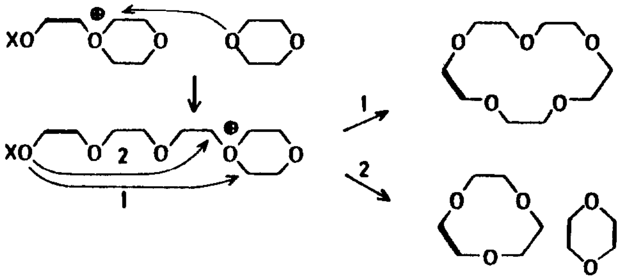


Scheme 9(c).

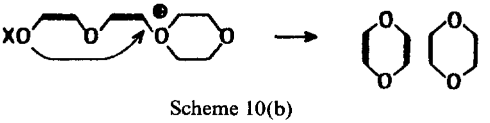
confirms that acetals are only formed by rearrangement in the growing chain (Scheme 3) and never as products of degradation. Furthermore, since the only observed acetals were isomeric with the dimer (2-methyl-1,3-dioxolane) and the trimer (2-methyl-1,3,6-trioxocane) and no trace of the higher ones were seen, it can be concluded that 1,2-hydride shift is an alternative reaction resorted to only when the chain grows slowly and is too short to cyclize in the normal way.

The experimental results further confirm that the thermodynamically stable end product 1,4-dioxane is not formed directly from oxirane, but after termination of a growing chain by an already formed cyclic oligomer with subsequent degradation. Each catalytic cycle must be initiated by the reactive BF_3 adduct of oxirane and is finished when cyclization yields the stable BF_3 adduct of any of the cyclic products. A new catalytic cycle can only be started by transfer of BF_3 to a molecule of oxirane.

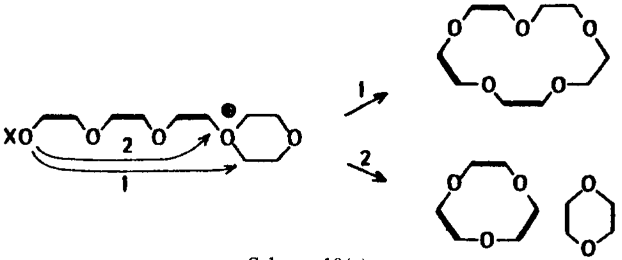
They also confirm that the smallest ring that can be formed directly from oxirane alone is the tetramer, due to the geometric restrictions in an S_N2-like transition state, but that a growing chain



Scheme 10(a)



Scheme 10(b)



Scheme 10(c).

terminated by a cyclic oligomer is able to cyclize within the chain to produce also cyclic trimer and dioxane.

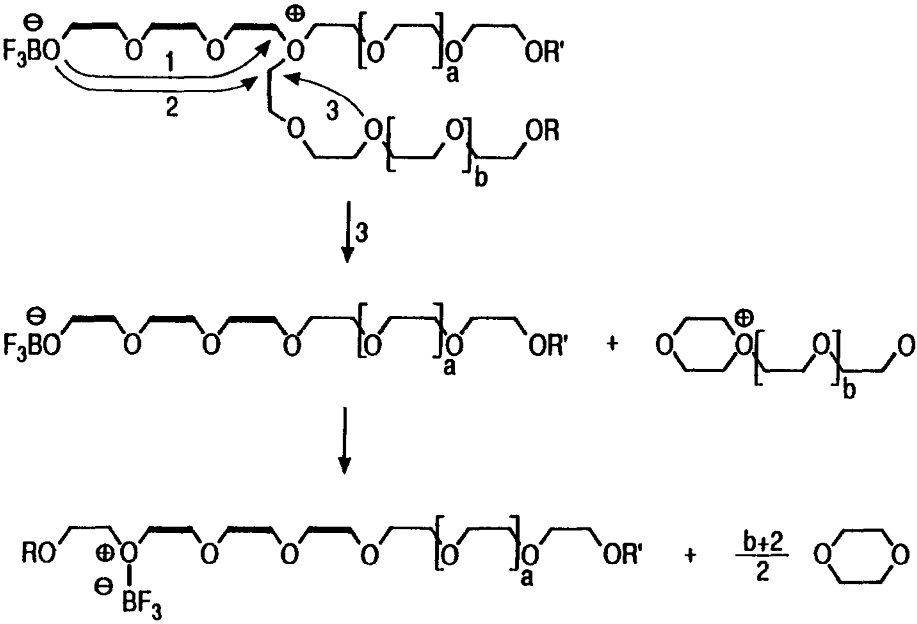
Unexpectedly, the GC analytical data revealed that degradation of penta- and hexamer is particularly fast. This is due to the possibility of rapid transannular ring opening of the oxonium-activated ring, which is impossible in the tri- and tetramer due to the same geometric restrictions of the transition state that are operative in cyclization. The resulting oxonium intermediate also recyclizes to a large extent to yield larger rings, which in their turn become activated and degraded.

The data revealed in addition that the slower degradation of the tri- and tetramer occurs by a different mechanism. The oxonium-activated ring is opened by attack of a second molecule of the same ring. Such intermediates may also recyclize to larger rings, whereby effectively one or two product molecules become incorporated. It is particularly noteworthy that 1,4-dioxane molecules are similarly incorporated. Thus, cyclic pentamer is produced from two molecules of the thermodynamically stable end product dioxane and only one molecule of the energy-supplying monomer!

3.5. *Relevance to the mechanism of polymer degradation*

The detailed mechanistic insight gained from the cyclooligomerization studies should be directly applicable to the interpretation of the reported observations on polymer degradation by the BF_3/oxirane catalyst.[1,2] One has to explain why crown-ethers are not formed as intermediates that subsequently become ring-expanded or ring-contracted, and why, when using deuteriated oxirane, the initially formed dioxane contains no detectable deuterium,[2] while the rearranged byproduct methyldioxolane is 100% deuteriated at all times.[2]

A mechanism is proposed in Scheme 11. A polymer chain containing $a+b+5$ non-deuteriated monomer units, where a and b are on an average large numbers, intercepts the growing chain containing one, two or at most three deuteriated units (three shown in the Scheme). The resulting oxonium-ion intermediate must choose between three possible reaction paths. Cyclization within the shorter branch (1) will produce just one molecule of deuteriated 9-crown-3 and the unchanged polymer chain is split off, having thus functioned only as a chain breaker. Rearrangement before interception will of course produce the fully deuteriated acetals. Attack by the activated oxygen on CH_2 in either of the two longer branches (2) will simply lead to insertion of the three deuteriated units into the original polymer chain. This process corresponds to ring expansion in the case of macrocycles. Finally, cyclization within either of the longer branches, as outlined in Scheme 11 (3), will split off one polymer fragment carrying the deuteriated units together with the anionic charge, leaving the other fragment as a dioxane-terminated oxonium cation. The latter will undergo successive degradation steps to produce a large number of deuterium-free dioxane molecules. The central point is that the degrading cationic chain carries no anionic charge in the opposite end to favour macrocycle formation, the other polymer fragment playing the role of a counter ion. Thus, the natural preference for six-ring formation can manifest itself without restriction.

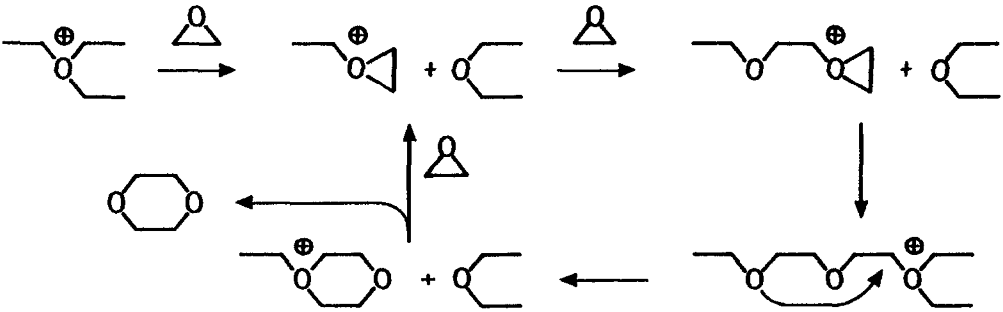


Scheme 11.

Final transfer of RO—CH_2CH_2 (or R) from the last oxonium intermediate to the anionic polymer fragment produces the unreactive BF_3 adduct of a stable partly deuteriated polymer chain, from which BF_3 can be transferred to a new molecule of oxirane, if still present, to start a new catalytic cycle. In their turn, such polymer fragments with incorporated deuteriated units will become degraded to give dioxane molecules, of which at first only very few will contain deuterium, the number increasing with time.

Some further observations by Eastham *et al.*[2] also merit comment. Using triethyloxonium tetrafluoroborate as the catalyst in the absence of oxirane, complete decomposition of the polymer took place with dioxane as the exclusive product. The reason would be that now we have not to do with a series of closed catalytic cycles each ending up dead, but an essentially everlasting oxonium cation. After ethyl transfer to the polymer chain, with production of one molecule of diethyl ether, the degradation can proceed from the point of attack to one end of the chain. The last fragment will be transferred to a new polymer chain to give a new oxonium ion initiating degradation, and so on.

Not surprisingly, it was also observed[2] that the same oxonium catalyst brings about nearly quantitative conversion of oxirane apparently directly to dioxane. The shortest conceivable route, however, for such a process is depicted in Scheme 12. After ethyl transfer from the catalyst, the growing chain is intercepted at the dimeric stage by the diethyl ether molecule, which is set free again after cyclization. Ethyl transfer from the dioxane cation to a new molecule of oxirane starts a new cycle, while BF_4^- plays only the passive role of a counter ion.



Scheme 12.

4. OXETANE

4.1. *Conditions for obtaining cyclic oligomers*

This monomer, having a four-membered ring, has also got sufficient ring strain to secure complete conversion to polymer or cyclic oligomers. Aiming at the polymer, Rose[3] observed that, with BF_3 as a catalyst, up to 68% of the product was the cyclic tetramer (16-crown-4), and even with water as a cocatalyst a small amount (0.5%) was formed. In later work aiming at cyclic oligomers, Dreyfuss and Dreyfuss[4] found that the use of either BF_3 or triethyloxonium tetrafluoroborate as catalyst led to cyclic oligomers in yields of 35%. These consisted mainly of tetramer with a little trimer, as identified by GC–MS. Using ethyl trifluoromethanesulfonate as the catalyst, the yield of cyclic oligomers was 15%, and surprisingly the trimer predominated. In both cases the cyclic oligomer yield and trimer/tetramer ratio increased with temperature. However, in the hands of Bucquoye and Goethals[22] the triethyloxonium tetrafluoroborate catalyst produced also higher cyclic oligomers up to and including the octamer (as seen by GC–MS). The major product was the tetramer, and only very little trimer was present. Both research groups agreed that the cyclic oligomers are not formed from the polymer by degradation, but concurrently with the polymer, and that once formed, the products do not change.

When we discovered the lithium-complexing ability of the cyclic trimer (12-crown-3)[12] it became of interest to increase its yield in the cyclooligomerization. The obvious way to attack this problem was to work at high dilution.[23] By dropping CH_2Cl_2 solutions of oxetane and BF_3 in parallel to a large volume of solvent, it was possible to obtain the cyclic trimer in an isolated yield of 50% at the expense of the cyclic tetramer (12%), higher volatile oligomers (10%) and polymer. Among other catalysts, PF_5 in CH_2Cl_2 gave a 60% yield of volatile products: 23% trimer, 30% tetramer, 7% pentamer. $AlEt_3$ and CF_3SO_3H gave mainly polymers.

4.2. *Proposed mechanism*

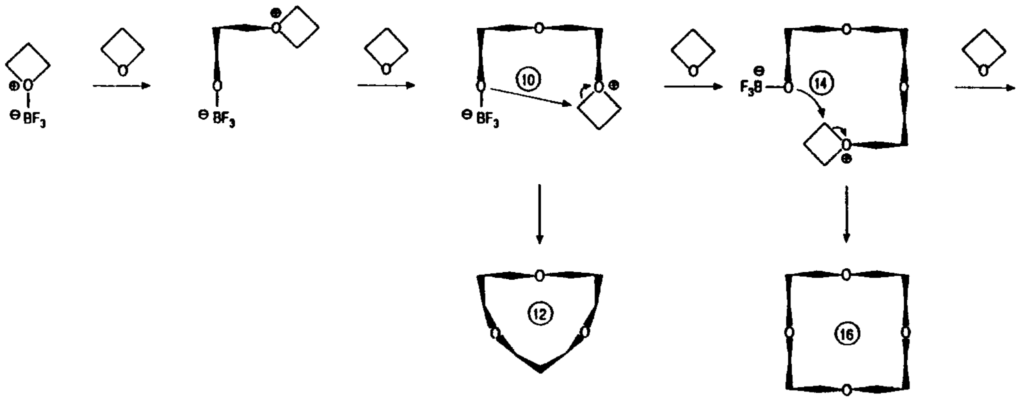
Two striking features of the oxirane reaction are not found with oxetane, and any mechanistic scheme should account for these.

The first is that product incorporation and degradation ('ring expansion' and 'ring contraction') does not occur. An answer has already been suggested: The growing oxetane chain will be attacked only by the more basic oxetane monomer as long as this is present, and when this is consumed, there will also be no growing chain. The equivalent statement is that the products cannot become 'alkylated' to give the oxonium ion that is required to initiate degradation.

The second feature is that macrocycle formation from oxetane does not require that anionic charge resides at one end of the growing chain to increase the nucleophilic reactivity of the terminal ether oxygen and to bring it close to the cationic charge of the oxonium cation at the other end. This conclusion is based on the finding[4] that alkylating agents like triethyloxonium tetrafluoroborate and ethyl trifluoromethanesulfonate, which initiate chain growth by transferring an ethyl cation to oxetane oxygen, leaving the negative charge on a separated counter-anion, are nevertheless good catalysts for producing macrocycles.

It seems likely that the well-established conformational 'folding pattern' of this kind of polyether chains,[22,24,25] closely related to the unique conformation of the cyclic tetramer,[26] is responsible for bringing the two reaction centres together, thereby facilitating cyclization if the oxetane concentration is sufficiently low.

In Scheme 13 a reaction sequence is proposed for the case when BF_3 is the catalyst. It will be remembered that the smallest macrocycle that could be formed by direct cyclization in the oxirane series was 12-crown-4 via an 11-membered cyclic transition state (linear S_N2 geometry). The smallest macrocycle from oxetane is 12-crown-3, formed through a 10-membered cyclic transition state, and accordingly with more difficulty. The very easy formation of 16-crown-4 through a 14-membered transition state can immediately be understood from Scheme 13. Also the reported[3,4] increasing yield of these macrocycles, particularly of 12-crown-3, with temperature can be rationalized, since some deviations from perfect *gauche* and *anti* torsion angles (60 and 180°) are required to adjust to the structure of the transition state with its linear S_N2 like geometry.

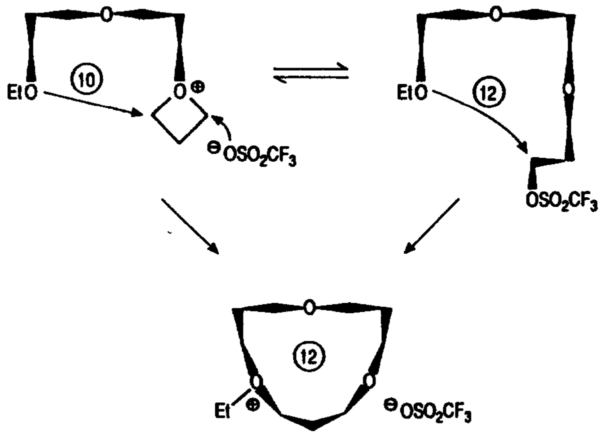


Scheme 13.

There is still the question why the superacid ester catalyst should favour the formation of cyclic trimer over that of tetramer.[4] A possible answer may be found in the work by Saegusa and coworkers[27] on the propagating species in the polymerization of 3,3-bis(chloromethyl)oxetane. Using large amounts of the ester 'catalyst', they established by ^1H NMR spectroscopy the presence of oligomeric intermediates terminated by ethoxy in one end and trifluoromethanesulfonate in the other. If such a species were formed from the normal oxonium intermediate and retained the necessary S_N2 reactivity, the high-energy 10-membered cyclic transition state of the trimeric intermediate (*cf.* Scheme 13) would be replaced by a 12-membered cyclic transition state of lower energy

(Scheme 14). In the case of a similar tetrameric ester-type intermediate, the same natural chain-folding tendency would bring the ester group either out of reach of, or too close to, the ethoxy group, for it to form a 16-membered cyclic transition state. The alternative attack by a new monomer molecule would be more likely, leading to further chain growth.

This may all be taken as support for the view that the observed cyclization tendency is closely connected with the unique conformational folding pattern of such polyether chains.[24,25]



Scheme 14

5. 3,3-DIMETHYLOXETANE

5.1. *Conditions for obtaining cyclic oligomers*

In the early work by Rose,[3] only a BF_3-dihydrate catalyst was used with this monomer. Mostly polymer was obtained, and the cyclic tetramer was isolated in $<10\%$ yield. In later work by Bucquoye and Goethals,[22] using triethyloxonium tetrafluoroborate in CH_2Cl_2, it was demonstrated by GC–MS that cyclic oligomers from tetramer to nonamer were formed in decreasing concentrations, but no trimer was detected. Polymer was the main product, the oligomer fraction constituting only $\sim 15\%$, with the tetramer as the main component (92%). Similar results were obtained with other catalysts, including BF_3 diethyletherate.

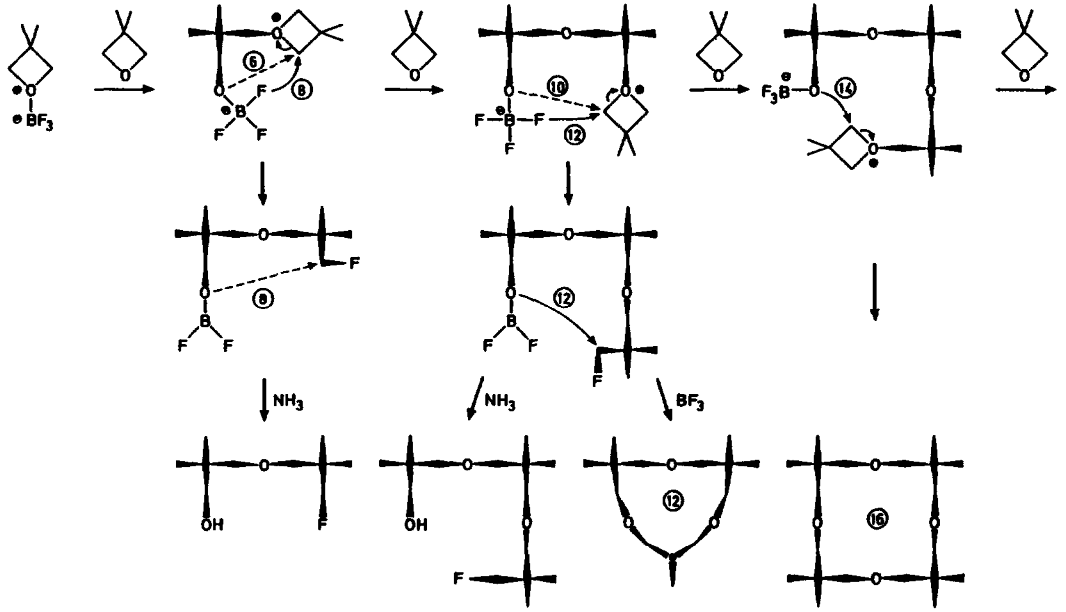
Working with dilute CH_2Cl_2 solutions we found that the outcome depended very much on the catalyst.[23] With PF_5 the cyclic tetramer was isolated in 73% yield, by also some pentamer and very little trimer were present. Using BF_3, however, this catalyst was slowly consumed, and BF_3 had to be refurnished repeatedly to complete the reaction of the monomer. When worked up directly, the cyclic trimer and tetramer could be isolated in yields of 10 and 3%, respectively, and also higher cyclic oligomers were present. Most surprisingly, however, each fraction, in particular the trimer fraction, was accompanied by the corresponding fluorohydrin. A final treatment with BF_3 after all monomer had been consumed converted each fluorohydrin, except the dimeric, to the desired cyclic oligomer, thus boosting the isolated yields of trimer and tetramer to 20 and 8%, respectively. The ratio of trimer to tetramer increased even further at higher temperatures.

5.2. *Proposed mechanism*

The observation[23] that, with the stable catalyst PF_5, it is much more difficult to achieve cyclization at the trimeric stage for 3,3-dimethyloxetane than for unsubstituted oxetane, supports our hypothesis that this cyclization requires deviations from normal torsion angle values in *gauche* and *anti* bonds to adjust to the required geometry of the transition state. Methyl substituents would substantially increase the torsional barriers, and this conformational restriction makes the formation of 10-

membered cyclic transition state, as in Scheme 13 for oxetane, too difficult for the 3,3-dimethyl derivative. At the tetrameric stage much less adjustment is needed, and the yield of cyclic tetramer is high.

In the case of BF_3 catalysis the better yield of trimer and the formation of fluorohydrins must obviously be connected with the catalyst consumption. Our rationalization[23] is presented in Scheme 15. A low concentration of monomer, as used here, gives the trimeric chain intermediate a lifetime long enough to ring-open the oxonium cation by transfer of fluoride in a less strained 12-membered cyclic transition state producing an intermediate which by ammonolysis gives the fluorohydrin. The dimeric and higher chain intermediates also undergo this type of reaction, but not to the same extent. The function of BF_3 to induce cyclization of the fluorohydrin precursors is probably to activate the primary fluoride as leaving group. Particularly in the case of the trimeric precursor this final cyclization has now become easy, going through a 12-membered cyclic transition state.



Scheme 15.

This kind of alkyl fluoride activation to give a BF_4^- leaving group is not unknown. It has been reported for the alkylation of aromatic compounds,[27] and alkyl fluoride complexes have even been isolated.[28] Activation of other alkyl halides is less efficient.[29]

An important question is of course: Why is catalyst consumption and fluoride transfer not observed with PF_5? There are numerous data in the literature on relative fluoride affinities in the gas phase, but more relevant here are the ^{19}F NMR studies of CH_2Cl_2 solutions by Brownstein.[30] He showed that fluoride anion is not transferred from PF_6^- to BF_3, whereas the transfer is complete from BF_4^- to PF_5.

Support for the explanation proposed here, that fluoride transfer is an escape reaction when the 'normal' cyclization of the growing chain is conformationally hindered by methyl substituents, can be found in an observation by Kern during cyclooligomerization of methyloxirane.[9] Short bursts of BF_3 gas were needed when additional BF_3 failed to cause heat evolution. Clearly, the catalyst was consumed, and the intermediacy of fluorohydrins would not be noted if extra BF_3 was added after full consumption of monomer. Thus, as far as fluoride transfer is concerned, there is no contrasting behaviour of oxiranes and oxetanes.

6. SUMMARY, WITH COMMENTS ON OXOLANE AND FORMALDEHYDE

The present report has been limited to a comparison of the chemistry of two types of simple cyclic ethers, one of which (oxirane) is less basic than the cyclic oligomers and the polymer produced from it, while the other (oxetane) is more basic than its cyclic oligomers and polymer.

There are two reasons for this limitation in scope. The first is our interest in crown-ether chemistry. The macrocyclic oxirane oligomers are identical with the familiar crown ethers used for complexation of 'normal' cations, while the macrocyclic oxetane oligomers form a less familiar crown-ether series that complex 'small' cations. The second reason is that these are the only simple cyclic ethers that have sufficient ring strain to ensure complete reaction of the monomer and to prevent depolymerization of products back to the monomer.

Cyclic oligomers and polymers can nevertheless be obtained also from the nearest higher homologue, tetramethylene oxide (oxolane, THF), and from the nearest lower homologue, formaldehyde (methanal). Some comments about these systems may therefore be appropriate.

Oxolane. Until 1977 only the linear polymer had been observed in the product obtained from oxolane in the presence of cationic catalysts. Above a ceiling temperature the polymer is degraded back to the monomer, since its marginal ring strain is then insufficient to compensate for the entropy gain on depolymerization.[31,32] The basicity of oxolane being near that of oxetane[20] (in the gas phase even higher[33]), it can function effectively both in the role of initiator in its adduct with the catalyst, and as the propagating nucleophile. Pruckmayr and collaborators[34–36] were able to observe analytically the formation in small amounts of a series of volatile macrocyclic oligomers. Using trimethyloxonium tetrafluoroborate as the catalyst, macrocycles from trimer to octamer were obtained in a total yield of 3%.[34] Interestingly, the tetramer, although it is a 20-membered ring, was formed in highest yield. With ethyl trifluoromethanesulfonate similar amounts of volatile macrocycles were observed, the best yields being now obtained for the tetra-, penta- and hexamer.[35] Using finally the free trifluoromethanesulfonic acid,[35,36] somewhat higher yields were obtained from oxolane monomer alone, and from oxirane monomer alone, as well as from mixtures of both monomers. Again, the tetrameric rings were formed in highest concentration. Mechanistically, the situation seems unclear; most likely the cyclic oligomers and the polymer are formed in concurrent reactions, as in the oxetane case, but macrocycles could also be formed along with monomer by degradation of the polymer.

Formaldehyde. The existence of a linear polymer of formaldehyde (paraformaldehyde) and its easy thermal depolymerization above the ceiling temperature (~120°C) to produce gaseous formaldehyde is textbook knowledge. Acid-catalysed depolymerization below this temperature produces instead the stable cyclic trimer (1,3,5-trioxane). Other stable macrocyclic oligomers have also been isolated: the tetramer (1,3,5,7-tetraoxocane), the pentamer (1,3,5,7,9-pentaoxecane), the hexamer, and the pentadecamer.[37]

In the present context it is interesting to note that the driving force for polymerization of formaldehyde[38] is very small compared with that of oxirane.[32] Thus, any expected strain in a 'two-membered ring' is largely relieved by the change in hybridization to form the double bond. Also related to hybridization is the low basicity of formaldehyde, actually much lower in the gas phase than for oxirane.[33] The conclusion may therefore be drawn that formaldehyde should function well in its role as initiator in its adduct with the acidic catalyst, but less well as the propagating nucleophile. In fact, polyformaldehyde is often prepared by BF_3-catalysed ring-opening polymerization of the cyclic trimer,[39] and it has been found that there is an induction period until a sufficient concentration of formaldehyde is formed, or is added, before polymerization of the trimer can start.[40] It is of particular interest that the cyclic tetramer appears as the main initially formed byproduct,[41] suggesting that just one molecule of formaldehyde is necessary to form the initiator, whereafter the cyclic trimer takes over as the nucleophile. This can be illustrated by a scheme analogous to Scheme 9a, Path 2, for the oligomerization of oxirane in the presence of 9-crown-3. Similarly, when the formaldehyde tetramer in its turn plays the role as nucleophile, the cyclic pentamer would be the expected byproduct, as is also observed.[41] The analogy is now found in Scheme 8a, Path 2, for the oligomerization of oxirane in the presence of 12-crown-4.

Thus, there seems to be a closer chemical relationship between formaldehyde and oxirane than one would perhaps expect.

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