Macrocyclic Oligolactones by Oligomerization of Simple Lactones

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The catalyst system K-t-butoxide/THF is useful not only for converting ε-caprolactone into the known cyclic oligomers (14-, 21-, 28-ring etc.) but also for preparing the unknown cyclic oligomers of δ-valerolactone (12-, 18-, 24-ring etc.) if large amounts of catalyst are used in the presence of t-butyl alcohol. With γ-butyrolactone, the acidity of the α-CH_2 leads instead to a bicyclic aldol type condensation product for which there is evidence of subsequent dimerization to a tricyclic 10-ring dilactone. β-Propiolactone undergoes eliminative ring-opening to acrylic acid which is in equilibrium with acyclic homologues. In contrast, the catalyst system BF_3/CH_2Cl_2 converts β-propiolactone (but not the other lactones) cleanly to cyclic oligomers (12-, 16-, 20-ring etc.). The driving force for these reactions is primarily the instability of the *cis* ester configuration in monolactones, the ester groups of the oligolactones adopting exclusively the *trans* ester configuration. Ring strain seems to contribute only in the case of β-propiolactone.

Open chain esters show a strong preference for the planar *trans* ester configuration over the *cis* ester configuration. Thus, *cis* methyl acetate has been shown by ultrasonic relaxation[1] to be higher in energy than *trans* methyl acetate by about 4.2 kcal/mol, corresponding to a population of only 0.1 % at 300 K. In lactones of small or normal ring size, the *cis* ester configuration is of course imposed, but as the ring size increases, the *trans* ester can again be accommodated without strain. In a classic investigation, Huisgen and Ott[2] showed that in 10-membered and larger rings, the *trans* ester again becomes dominant over *cis* by a factor estimated to be about 700, corresponding to an energy difference of 3.8 kcal/mol. A coexistence of *cis* and *trans* ester is observed for the 8- and 9-membered rings.

In the simple unsubstituted monolactones with from 3 to 7 ring members, as well as in the dilactone with 6 ring members (diglycolide), the high enthalpy of the *cis* ester configuration should constitute a considerable driving force for oligomerization to larger rings containing two or more *trans* ester groups, even though the entropy is in favour of the smaller rings. Furthermore, again based on the experience of Huisgen and Ott[1], such macrocycles with *trans* ester groups are expected to be chemically more stable than their parent monomer, for example, against hydrolysis. Until recently, only 6-hexanolide (ε-caprolactone) had been shown[3] to undergo dimerization to the dilactone (14-ring) under $SnCl_2$-catalysed pyrolytic conditions as used by Carothers[4] to prepare lactones from the polymer. In 1978, we managed to isolate very small quantities of the cyclic penta and hexamer (15- and 18-ring) of ethanolide (glycolide) from the crude dimer (diglycolide) obtained by pyrolysis of the polymer.[5] As expected, no trimer (9-ring) was observed; but, surprisingly, also no tetramer (12-ring). In 1981, Shanzer[6] prepared cyclic tri to heptamers from 3-propanolide (β-propiolactone) using a distannoxane catalyst, the smallest ring size being then the 12-ring. Thus, three but not four *trans* ester groups can be accommodated in a 12-ring.

No cyclic oligomers have ever been reported to form from 4-butanolide (γ-butyrolactone) or 5-pentanolide (δ-valerolactone) in spite of several attempts in this direction.[3] The former does not even polymerize[3] except at extremely high press-

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ure and temperature[7], the latter polymerizes spontaneously but reversibly.[3] There is, however, no reason to believe that cyclic dimers (and higher oligomers) of 4-butanolide and 5-pentanolide with *trans* ester groups should not be perfectly stable compounds.

Purpose and plan

The conviction that cyclic oligomers of 5- and 6-ring lactones should be stable compounds incited us to search for catalytic systems to effect their formation. The successful oligomerization of 6-hexanolide into dimer and larger rings had then been reported by Ito,[8,9] using K-t-butoxide in tetrahydrofuran. We therefore started a systematic study of this and other nucleophiles that would likewise provide no stable end groups for open chain oligomers but act reversibly as leaving groups in the final recyclization step (Fig. 1); and to test these also for cyclooligomerization of other simple lactones. Electrophilic catalysts were also considered.

One objective was to learn from the equilibrium composition which is the smallest ring that can accommodate a given number of *trans* ester groups without strain. For entropy reasons, the amount of strain-free oligomers at equilibrium must decrease with increasing ring size. If, therefore, the smallest ring present is found not to be the predominant one, it can only mean that it possesses some residual strain.

A further objective was to extend to smaller ring sizes a series of macrocyclic symmetrical dilactones[3], the smallest known member of which is the 14-ring already discussed. This series exhibits a fascinating alternation of dipole moments depending on the relative orientation of the *trans* ester groups, and an alternation of melting points. Both have been interpreted on a conformational basis.[3]

Still another objective was to provide a variety of crystalline compounds (most acyclic esters being liquid) to study the conformational details on either side of the *trans* ester group.

Catalytic studies

The chemical reactivity and/or the products obtained turned out to be strikingly different depending on the ring size of the monolactone. They are therefore discussed separately.

6-Hexanolide (Fig. 1). The K-t-butoxide catalyst as reported by Ito[8,9] was prepared in a very elaborate manner and produced initially and rapidly a high polymer which subsequently underwent degradation to macrocyclic oligomers. We obtained a satisfactory catalyst simply by dissolving potassium in t-butyl alcohol and displacing the excess of alcohol azeotropically with benzene. The solid K-t-butoxide was transferred to THF for the isomerization experiments.

The monomer *1* was consumed at room temperature in a few minutes producing a mixture of "living polymer" *3* and cyclic oligomers *4*. Gas chromatography showed the expected oligomers in quantities decreasing with molecular weight (at "equilibrium" 26 % dimer, 13 % trimer, 9 % tetramer, 52 % higher cyclics and polymer). This distribution was unchanged by oligomerizations at −70 °C, showing that the enthalpy per unit was very similar for all these ring sizes (14-, 21-, 28-ring, etc.). With very small quantities of catalyst, the conversion was slow; before the monomer had been fully converted, the trimer and not the dimer was the dominant oligomer. When the reaction mixture had not been treated with gaseous HCl before analysis, an additional small GLC peak due to the t-butyl ester of 6-hydroxyhexanoic acid was observed.

Although our catalyst was less active, no doubt

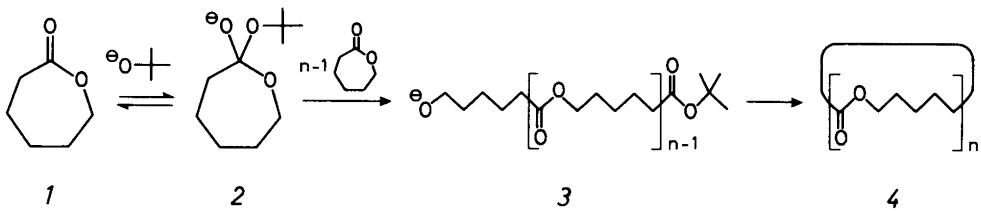

Fig. 1. Reactions of 6-hexanolide (ε-caprolactone).

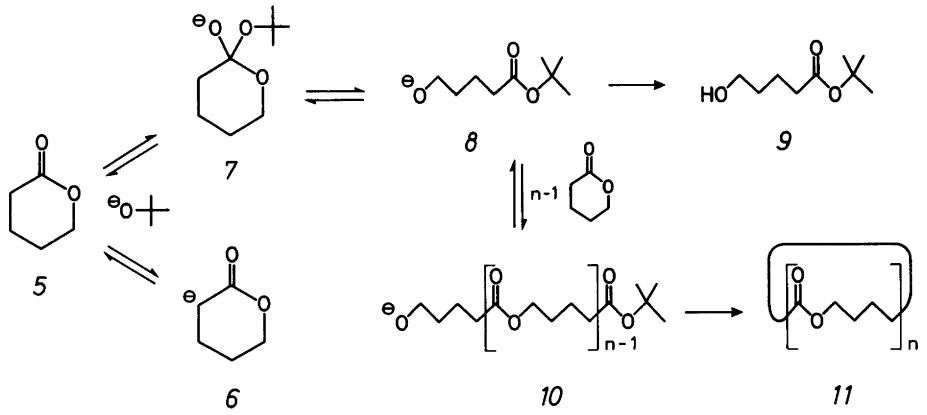

Fig. 2. Reactions of 5-pentanolide (δ-valerolactone).

the same type of intermediates, *2* and *3* proposed earlier,[8,9] were involved. Since more catalyst was needed and it contained traces of t-butyl alcohol, the intermediate polymer must have had shorter chains with mainly alkoxide groups as in *3*, or hydroxyl groups at the end when growth had stopped. The main difference is that the slower "back-biting" cyclization degradation can start in parallel in a larger number of shorter chains as soon as the more reactive monomer is used up.

Among other anionic catalysts tested, KI had no effect. With KOH, a very incomplete polymerization occurred, but no cyclic oligomers were detected. With BF_3 in CH_2Cl_2 also, the monomer was incompletely converted to polymer, and no cyclic oligomers were observed.

5-Pentanolide (Fig. 2). With our simple K-t-butoxide/THF catalyst, containing only traces of t-butyl alcohol, the consumption of this 6-ring lactone *5* was much slower. In the favourable cases (1–3 mol % catalyst), it took about one hour. Mainly polymer was formed, and only traces of volatile products were sometimes observed by GLC. These were identified by MS as cyclic oligomers *11*, n = 2–5. Again, if the reaction mixture had not been neutralized before analysis, an additional GLC peak due to the t-butyl ester of 5-hydroxypentanoic acid *9* would be present. With higher concentrations of catalyst, a solid precipitate could be isolated. This was presumably the carbanion salt *6* obtained by abstraction of a 2-proton from the monomer, as was shown for 4-butanolide (see below). In the experiments where t-butyl alcohol was most carefully excluded, no traces of cyclic oligomers *11* or t-butyl 5-hydroxypentanoate *9* were formed. When some t-butyl alcohol was then deliberately added, the catalyst concentration could be increased without precipitation of the salt *6*. Using about 15 mol %, the yield of cyclic oligomers increased to the extent that isolation became possible. However, not only the t-butyl ester *9*, but a whole homologous series of t-butyl esters, corresponding to *10*, were now present, which pyrolysed on injection for gas chromatography to produce monolactone. These could be removed on alumina, the stable cyclic oligomers *11* being eluted with benzene. The yields achieved by preparative GLC were 1–3 % dimer, 4–6 % trimer, and 0.1–0.5 % tetramer. This indicates that some strain is present in the 12-ring dimer but absent in the 18-ring trimer.

To explain the different behaviour of the two monolactones, the much greater tendency of recyclization to 6- than to 7-membered rings must be invoked. Both monomers have the high reactivity of the *cis* ester group and should polymerize with comparable rates. During the slower "back-biting" degradation of the "living polymer" with only stable *trans* ester groups, there is a reasonable chance for the hexanolide chain *3* to produce also larger rings in competition with the 7-ring monomer. The 7-ring will be rapidly reincorporated in growing polymer chains, while the macrocycles *4* will accumulate. The pentanolide chain *10* will degrade faster and produce almost only the 6-ring monomer, so that it appears to be

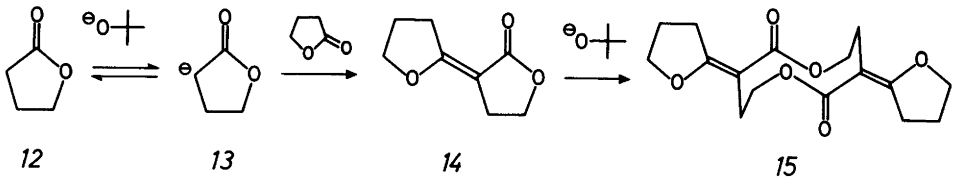

Fig. 3. Reactions of 4-butanolide (γ-butyrolactone).

consumed more slowly. Only when the "unzipping" reaches the end of a chain, does the higher reactivity of the terminal t-butyl ester group, as compared to the internal *trans* ester groups, lead to a certain competition from the cyclization to larger rings *11*. The effect of the higher percentage of catalyst and the presence of t-butyl alcohol is clearly to reduce the average mol wt. of the polymer chains, thereby increasing the probability for the alkoxide end to bypass a few chain ester groups and reach the more reactive t-butyl ester group.

Other nucleophilic catalysts (KOAc, KI, pyridine) in various solvents, as well as BF_3 in CH_2Cl_2, were tried but gave no conversion of 5-pentanolide.

4-Butanolide (Fig. 3). Using pure K-t-butoxide (3 %) in THF, no consumption of this 5-ring lactone *12* could be observed when analysed after neutralization. A precipitate was again found and in larger quantities than for the 6-ring lactone, suggesting the more acidic character of the 2-protons. To prove the structure *13*, the salt formed from equimolar quantities of 4-butanolide and K-t-butoxide was isolated and dissolved in D_2O containing an excess of deuterated TFA. The ^1H NMR spectrum showed, indeed, half intensity for the α protons and a different coupling pattern.

Only when the amount of K-t-butoxide was in the range 15–25 % and more, and the monomer concentration was 1 M or higher in THF/t-butyl alcohol or in t-butyl alcohol alone, could the conversion to products be observed. These were, however, neither cyclic oligomers nor open chain oligomeric acids or esters, but aldol type condensation products. The major product isolated by preparative GLC had ^1H and ^{13}C NMR spectra corresponding to the bicyclic compound *14*. A minor product had twice the mol wt. and was most likely the tricyclic dimeric lactone *15*.

It may be concluded that cyclic oligomers of 5-ring lactones should be stable compounds obtainable with the 5-butoxide catalyst if the α carbon is doubly substituted.

No other nucleophilic catalyst tried gave a detectable conversion of 4-butanolide. Also, there was no reaction with BF_3 in CH_2Cl_2 at room temperature. On the other hand, a derivative with a particular acetalic bicyclic structure, 6,8-dioxabicyclo[3.2.1]octan-7-one, has been successfully oligomerized with BF_3 etherate at low temperature to give the *meso* dimer and higher oligomers.[10,11]

3-Propanolide (Fig. 4). The reactivity of this 4-ring lactone *16* is so high that careful purification was necessary to distinguish between the effect of the catalyst and of the impurities. A marked difference between acidic and basic catalysts was observed. Only acidic catalysts (BF_3, $TiCl_4$, H_2SO_4) in CH_2Cl_2 gave cyclic oligomers in addition to polymer, presumably through intermediates like *21* and *22** activated for alkyl-oxygen cleavage.[12] No 8-ring dimer was ever observed, but all higher oligomers *23* up to the cyclic decamer (n=10) in decreasing quantities were identified by GC/MS. As expected, the ratio between cyclic oligomers and polymer increased with dilution. Thus, in 0.1 M solution, the weight distribution was 15 % trimer, 6 % tetramer, 3 % pentamer and 76 % higher cyclics + polymer, while in 0.05 M solution, the figures were 28, 10, 4 and 58 % respectively. That these are probably equilibrium values is supported by the observation that a mixture made up as an analytical standard containing equal quantities of tri, tetra, penta

* In these, for simplicity, the ring oxygen carries the BF_3 and acts as the nucleophile. The equivalent formulations, choosing the carbonyl oxygen, lead to exactly the same products.

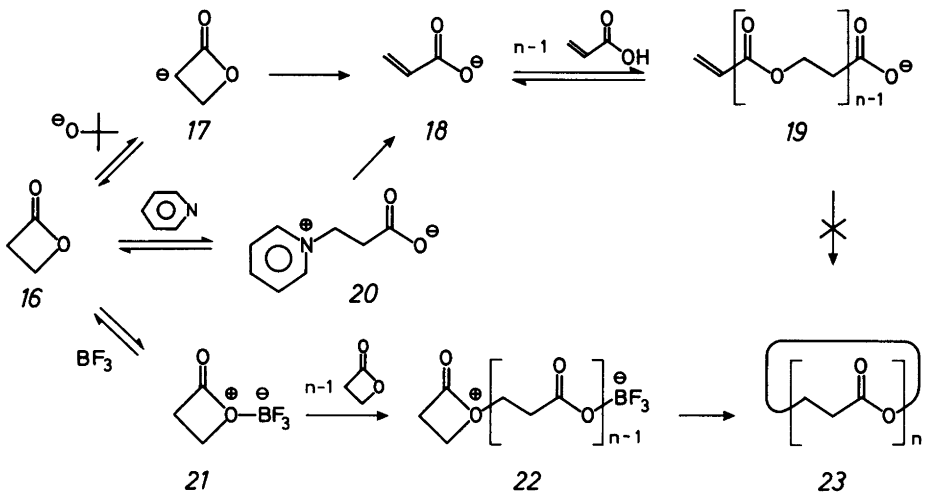

Fig. 4. Reactions of 3-propanolide (β-propiolactone).

and hexamer in CH_2Cl_2, without added catalyst, slowly changed its composition with time; hexamer decreased most, trimer increased most.

The anionic catalysts were surprisingly slow in converting the monomer, but more efficient in CH_2Cl_2 than in THF. With K-t-butoxide, not only were no cyclic oligomers *23* found, but also no acyclic t-butyl esters or ethers, as required if butoxide opens the ring by attack on the 1 carbon (acyl-oxygen cleavage[12]) as in *2* or *7*, or by S_N2 attack on the 3 carbon (alkyl-oxygen cleavage[12]). Instead, acrylic acid *18* and its homologues *19* (n=2 and 3), were isolated, as well as a polymer of presumably analogous structure. The fact that again the carbanionic salt *17* precipitated in THF, suggested that the initial proton abstraction by butoxide was followed by eliminative ring-opening to acrylate *18*, which, in its turn, acted as the base. Oligomerization to give the series of homologous olefinic acids *19*, including polymer, could occur by conjugate addition of acrylate ion on acrylic acid as the first step. An argument for this is the easy reversibility among these homologues. Thus, on concentration and cooling, the homologues "disappeared" and the product crystallized as acrylic acid.

With pyridine, on the other hand, there was evidence of initial nucleophilic ring-opening by attack on the 3 carbon followed by elimination to acrylic acid. Thus, the crystalline 1-(2-carboxyethyl)pyridinium betaine, prepared from 3-propanolide and pyridine[13], underwent slow decomposition in water to produce acrylic acid and not 3-hydroxypropanoic acid. Pyrolysis of the betaine gave first pyridine, then a mixture of mainly acrylic acid with some monolactone, but no cyclic oligomers. Clearly, the carboxylate end of the betaine is not a strong enough nucleophilic to propagate the reaction by ring-opening of new monomer molecules. Used as catalyst in THF or CH_2Cl_2, pyridine gave the same mixture of acrylic acid *18* and its homologues *19*, including polymer, as obtained with K-t-butoxide.

Summary of chemical properties

The only nucleophilic catalyst useful for the cyclooligomerization of lactones is K-t-butoxide. It is capable of ring-opening, and the relative instability of the t-butyl ester formed permits recyclization after chain growth. Ring-opening by attack on the ω-CH_2 carbon does not occur, since only t-butyl esters and not ethers are observed as intermediates. After ring-opening, chain growth will occur until the supply of the reactive monomer is exhausted. The slower back-biting degradation produces a fair amount of macrocyclic oligomers along the whole chain of the 6-hexanolide polymer since cyclization to reform the 7-ring monomer is not particularly favoured. In the 5-pentanolide polymer, cyclization to reform the 6-ring monomer is strongly favoured. Macrocycles

are formed only towards the end of the chain and involves the more reactive t-butyl ester as leaving group. To increase the yield of macrocycles, it is therefore necessary to reduce the average polymer chain length by using larger amounts of catalyst and t-butyl alcohol to maintain catalyst solubility. As ring size decreases, the increasingly acidic CH_2 proton ties up the catalyst more completely. In 4-butanolide, no ring-opening occurs, not even in t-butyl alcohol, but the carbanion ultimately effects an aldol type condensation to give a bicyclic lactone that has no α-CH_2 protons and therefore can undergo ring-opening by acyl cleavage. In 3-propanolide, eliminative ring-opening of the carbanion leads to acrylic acid, and only acyclic oligomers of this are produced, but reversibly.

No other anionic catalysts gave cyclooligomerization. Tertiary amines like pyridine give betaine by attack on the ω-CH_2 carbon when the ring is strained as in 3-propanolide, but this undergoes subsequent elimination to acrylic acid rather than initiating chain growth.

Electrophilic catalysts, like BF_3 in CH_2Cl_2, are remarkably ineffective, except in the case of 3-propanolide where macrocyclic oligomers are formed corresponding closely to those obtained with the distannoxane catalysts.[6] Presumably, ring-opening occurs here by alkyl-oxygen cleavage to relieve the strain of this small ring, quite analogous to the cyclooligomerization of oxetanes with BF_3.[14]

The lactone oligomers obtained showed the chemical stability expected of macrocyclic lactones with all ester groups in *trans* configuration. They resist hydrolysis under mild conditions and can be distilled, sublimed, and gas chromatographed unchanged.

Physical properties

The macrocyclic lactones, except some higher members, are crystalline solids at room temperature, in contrast to most acyclic esters of similar molecular size and structure. In several cases, their crystal structures have been determined, and in all reported cases the *trans* ester configuration has indeed been confirmed. The crystal structures will be discussed in detail in the following paper.

If one asks the question what is the smallest ring size that can accommodate without strain the *trans* ester group, the answer is not a simple one; our results show that it depends on how many (when symmetrically placed). For a monolactone it is known to be the 10-ring.[2] For a dilactone, so far, it is the 14-ring. The 12-ring reported here must have some strain, but it may still turn out that the unknown simple 10-ring dilactone is strain-free. For a trilactone, it is the 12-ring; for tetralactone, it is the 16-ring; for a pentalactone, the 15-ring.[5] Clearly, these variations must be due to more subtle conformational factors to be discussed in the following paper.

The observed low melting point of the 12-ring dilactone *11* (n=2) extrapolates well from the alternating melting points of the higher symmetric dilactones:[3] 96, 57, 92, 45, 112 and *43 °C* for 22, 20, 18, 16, 14 and *12* ring members respectively. Also, the measured high molecular dipole moment of the 12-ring dilactone extrapolates well from the alternating dipole moments of the higher dilactones:[3] 2.2, 2.7, 2.0, 2.8, 1.6 and *2.8 D* for 22, 20, 18, 16, 14 and *12* ring members respectively. Thus, the earlier interpretation[3] that the higher dipole moments were due to conformationally imposed parallel orientation of the two ester dipoles, and the lower moments to antiparallel orientation, receives support from the present extension of the series. Still stronger support comes from the crystal structures of the two lowest members (12- and 14-ring) which confirm the perfect parallel and antiparallel orientation (following paper).

Such agreement was not found between measured molecular dipole moments in benzene and crystal structures[6,15] for the series of 3-propanolide oligomers. For the 12-ring trilactone, the 16-ring tetralactone and the 24-ring hexalactone, the values calculated from crystal structures were 5.5, 0 and 0 *D* respectively, whereas the measured values were 1.9, 2.1 and 3.5 *D*. The explanation is, of course, that there must be different or additional conformers present in solution, and this was convincingly demonstrated by the observation of marked differences in the far infrared spectra of the trilactone in the solid state and in benzene solution. The ^1H and ^{13}C NMR spectra were fast exchange down to $-150\,°C$.

Experimental

Potassium-t-butoxide catalyst. To t-butyl alcohol (14 ml), previously dried by azeotropic distilla-

tion with benzene, were added at 60 °C pieces of freshly cut potassium (~ 1 g). After vigorous stirring for 2 h, the reaction was finished. Benzene was added and the excess of alcohol removed by azeotropic distillation. The catalyst precipitated and was kept under benzene and nitrogen until used. To neutralize the catalyst after an experiment, gaseous HCl was bubbled in; a slight excess not influencing the oligomer composition.

Boron trifluoride catalyst. Dry CH_2Cl_2 under nitrogen was saturated with gaseous BF_3 (polyethylene tubing!) and then kept until used. The concentration was determined by titration (phenolphthalein) with 0.1 M KOH in water (3HF + $B(OH)_3$) as 0.004 M. After an experiment, the catalyst was neutralized with solid KF or $KHCO_3$.

General procedure for lactone oligomerization. Solutions of lactone in stabilizer-free redistilled THF, or in ethanol-free redistilled CH_2Cl_2, were prepared (30 ml, ~ 0.1 M). Catalyst was added in quantities ranging normally from 1 to 3 mol % of the quantity of lactone present, and the solution stirred under nitrogen. Withdrawn samples were neutralized and analysed by GLC (SP 2100, 10 %, 8 feet or 3 %, 2 feet, 100–300 °C) or by TLC (neutral Al_2O_3, DC-Alufolien, Typ E, Merck) using THF/benzene or THF/hexane 3:2. The spots were made visible by spraying first with a solution of hydroxylamine in ethanol and, after 10 min., with a solution of $FeCl_3$ and HCl in ether.[16] Quantitative GLC analyses were made using naphthalene as an internal standard and the same response factor for oligomers as for the parent monomer. Samples for identification by NMR spectroscopy and MS (CI, isobutane) were obtained by preparative GLC.

6-Hexanolide. Commercial 6-hexanolide was redistilled in vacuum, b.p. 39–41 °C/0.7 mmHg. Authentic oligomers for identification and calibration purposes were first prepared by depolymerization of the polymer using tetrabutyl titanate as catalyst.[17] Solutions of the monomer (0.1 M) in CH_2Cl_2 containing 3 mol % BF_3 at 25 °C for 2 days gave <20 % polymerization and no cyclic oligomer. Solutions (0.1 M) in THF containing 3 mol % K-t-butoxide gave complete conversion to polymer and oligomers in 2 min. at 25 °C and in 6 h at −70 °C. A small GLC peak just in front of the dimer peak, identified as the t-butyl ester of 6-hexanoic acid, MS 189 (M+1), disappeared after neutralization. The ratio monomer/dimer/trimer/tetramer/pentamer was unchanged, 0:10:7:4:3. In an experiment with much less catalyst, it was 10:1:2:1:0.5. Benzene (10 %) in the THF hindered the reaction. No conversion was observed with KI in THF, with or without 18-crown-6, nor with conc. HCl in THF.

5-Pentanolide. Commercial 5-pentanolide (Fluka) was redistilled in vacuum, b.p. 36 °C/0.02 mmHg. Solutions of this monomer (0.1 M) in CH_2Cl_2 containing 3 mol % BF at 25 °C for 2 days gave no conversion, nor did pyridine, KI (with or without 18-crown-6) or KOAc (with or without 18-crown-6) at 25 °C for 2 days in CH_2Cl_2, acetonitrile, or THF. Only with K-t-butoxide (3 mol %) in THF was the oligomer (>90 %) to give mainly polymer. Weak GLC peaks were then sometimes observed and identified by GC/MS (M+1): 175 (t-butyl ester), 201 (dimer), 301 (trimer), 401 (tetramer), 501 (pentamer). With larger amounts of catalyst, a precipitate formed, but not when some t-butyl alcohol was present.

In a preparative experiment, dry t-butyl alcohol (30 ml) was kept at 60 °C. Potassium (0.3 g) was dissolved, then dry THF (970 ml) and the monolactone (4.0 g) were added. After stirring for 2 days at 25 °C, dry HCl gas was introduced until weakly acidic. The solvents were evaporated and acetone (50 ml) and water (1 ml) added. The suspension was well stirred and the solids filtered off. Benzene was added and the solvents evaporated. The MS spectrum showed peaks not only for cyclic oligomers (101, 201, 301, 401,501), but also weaker peaks for acyclic t-butyl esters (175, 275, 375, 475). The residue was therefore taken up in benzene, filtered through a column of neutral alumina, then evaporated. Preparative GLC gave the individual cyclic oligomers *11*; recrystallization from hexane.

Dimer (115 mg, 2.9 %), m.p. 42–43 °C, MS 201 (M+1). ^{1}H NMR ($CDCl_3$): δ 1.73 (*quint*, βCH_2), 1.90 (*quint*, γCH_2), 2.42 (*t*, αCH_2), 4.13 (*t*, δCH_2). ^{13}C NMR ($CDCl_3$): δ 22.5, 27.2, 34.1, 64.5, 173.4.

Trimer (175 mg, 4.4 %), m.p. 45–46 °C, MS 301 (M+1). ^{1}H NMR ($CDCl_3$): δ 1.73 (*m*), 2.37 (*t*), 4.12 (*t*). ^{13}C NMR ($CDCl_3$): δ 22.5, 28.1, 34.6,

63.8, 173.0. In $CHCl_2F/CHClF_2$, the ^{13}C signals started to broaden at −130 °C, but did not split at −140 °C.

Tetramer (5 mg, 0.1 %), liquid, MS 401 (*M*+1). ^1H NMR ($CDCl_3$): δ 1.70 (*m*), 2.36 (*t*), 4.11 (*t*). ^{13}C NMR ($CDCl_3$): δ 21.7, 28.0, 33.9, 63.9, 173.2.

An analogous experiment with higher concentration of monolactone (0.08 M instead of 0.04 M) and less catalyst (11 mol % instead of 15 mol %) gave 1.2 % dimer, 6.0 % trimer and 0.5 % tetramer.

4-Butanolide. Commercial 4-butanolide was redistilled in vacuum, b.p. 80 °C/8 mmHg. Solutions of this lactone (0.1 M) in CH_2Cl_2 with 3 mol % of BF_3 gave no conversion at 25 °C for 2 days. Also in THF with pyridine, KI or K-t-butoxide, there was no conversion. In the last case, a white precipitate formed, more copious than with 5-pentanolide. In a separate experiment, equimolar quantities of 4-butanolide and K-t-butoxide were mixed, and the precipitate washed with CH_2Cl_2 and dried. A sample was dissolved in D_2O containing excess of TFA d_1. The ^1H NMR spectra showed that one α proton had been replaced by deuterium.

Detectable conversion of monolactone was achieved after 2 days when its concentration was 1 M or higher and the amount of catalyst was 12 mol % or higher. To keep the catalyst in solution, t-butyl alcohol was used alone or mixed with THF. GC/MS showed that none of the expected simple cyclic oligomers or acyclic t-butyl esters had formed. The two main volatile products had MW 154 and 308 indicating that condensation had occurred. The former could be isolated by preparative GLC and proved to be *2-(2-tetrahydro-furanylidene)4-butanolide 14*,[18] m.p. 85°, MS 155 (*M*+1). ^1H NMR ($CDCl_3$): δ 2.1 (2H, *quint*), 2.9 (2H, *t*), 3.1 (2H, *t*), 4.3 (4H, *t*). ^{13}C NMR ($CDCl_3$): δ 24.2, 25.1, 29.0, 65.3, 72.5, 93.2, 169.5, 173.2. The second product could not be isolated in sufficient quantity for NMR, but was most likely the tricyclic dimer *15*, MS 309 (*M*+1).

3-Propanolide. Commercial 3-propanolide was not obtained pure by redistillation. It had to be filtered through a column of neutral alumina to remove acrylic acid, eluting with CH_2Cl_2, and the solvent evaporated. Solutions of this lactone (0.1 M) in CH_2Cl_2 with 3 mol % of BF_3 gave full conversion in a few minutes at 25 °C, and even at −70 °C. Oligolactones *23* from trimer to decamer were identified by TLC using authentic samples,[6] and no other products were seen. Oligomers up to heptamer could be analysed by GLC. The main products, trimer, tetramer and pentamer, were formed in the ratio 3:2:1 (total yield of these 24 %). Using a lactone concentration of 0.05 M, the total yield of these three oligomers was raised to 42 %. With $TiCl_4$ or H_2SO_4 in CH_2Cl_2, similar results were obtained.

With K-t-butoxide (3 mol %) at 25 °C for 2–5 days, there was no conversion of lactone (0.1 M solution) in acetonitrile; some in THF; extensive in CH_2Cl_2. In the latter two cases, precipitation of carbanion salt was observed initially. The final reaction product was partly polymeric. The soluble part was neutralized with HCl, and GC/MS showed a series of peaks with the same molecular weights as the cyclic oligomers (*M*+1 = 73, 145, 217 etc.). Retention times were, however, different. The three first were isolated by preparative GLC and shown by ^1H NMR in $CDCl_3$ to be acrylic acid and its first two homologues corresponding to *19*, n=1, 2 and 3. The latter two had the same COOH and $-CH=CH_2$ signals at δ ~ 9 and between 5.7 and 6.7 as acrylic acid, but additional equal intensity triplets for αCH_2 and βCH_2 (δ 2.7 and 4.4 for dimer, 2.6 and 4.3 for trimer). These latter acids were, however, unstable. If the solution was concentrated before GLC injection, the trimeric acid was absent. On cooling to 0 °C, the mixture crystallized as acrylic acid. Similar products were obtained with KI, KOAc and pyridine catalysts in acetonitrile (incomplete conversion) and in THF (extensive conversion). In CH_2Cl_2, the pyridine catalyst gave the best conversion.

Formation and pyrolysis of 1-(2-carboxyethyl)pyridinium betaine. This betaine *20* was prepared in an exothermic reaction at 0 °C from 3-propanolide and a great excess of pyridine with a trace of water as catalyst.[13] ^1H NMR (D_2O): δ 2.9 (2H, *t*, αCH_2), 4.8 (2H, *t*, βCH_2), 8.0 (2H, *t*, *m*CH), 8.4 (1H, *t*, *p*CH), 8.8 (2H, *d*, *o*CH). This spectrum was surprisingly stable over time. Essentially the same spectrum was also obtained by dissolving equimolar quantities of the components directly in D_2O. Only after two weeks at 25 °C

could small quantities of acrylic acid be detected. No trace of pyridinium 3-hydroxypropanoate was formed, as concluded by comparison with an authentic sample: ^{1}H NMR (D_2O): δ 2.5 (2H, *t*, αCH_2), 3.8 (2H, *t*, βCH_2), 7.9 (2H, *t*, *m*CH), 8.3 (1H, *t*, *p*CH), 8.5 (2H, *d*, *o*CH), ~8.7 (very broad, NH).

During pyrolysis of the betaine at 200 °C/10 mmHg, pyridine distilled first, then a mixture of mainly acrylic acid with some monolactone. No cyclic oligomers were formed.

Dipole moment determinations. Dielectric constants were measured at 20 °C in a Weilheim Dipolmeter DM O1 on four different solutions of each compound. Refractive indices were measured on the same solutions in a Brice-Phoenix differential refractometer. Calculations of dipole moments were performed according to Hedestrand,[19] using no correction for atomic polarization.

Spectra of trimeric 3-propanolide. In the normal IR region 600–5000 cm^{-1}, no characteristic differences between solid phase and solution spectra were found. A Bruker 114 C Interferometer was therefore used to cover the region 50–650 cm^{-1}. The solid, a polyethylene pellet, had abs. max. at 59, 60, 125, 140, *164*, 206, 244, *261, 301, 332, 335*, 383, 405, *453*, 487, 529, *603, 621* cm^{-1}. The solution in benzene had abs. max. at *71*, 139, 161, 211, 237, 257, *306, 356, 382*, 406, 434, *456*, 526 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.99 (*t*), 4.41 (*t*). ^{13}C NMR ($CDCl_3$): δ 34.4, 60.8, 170.3. Low temperature spectra were measured in $CHCl_2F$/$CHClF_2$ (3:1) down to −150 °C on a Bruker WM 400 HMz instrument, but no splitting into slow exchange spectra was observed.

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