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"Furan Endwise Peeling" of Celluloses: Mechanistic Studies and Application Perspectives of a Novel Reaction

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The mechanism of a novel reaction type, the "furan endwise peeling" reaction, has been studied. Making extensive use of experiments on model compounds, the structural prerequisites to the reaction were found to be a 2-hydroxpyran β-glycosidically linked to a 2-(2-furyl)ethyl moiety. Proceeding from the reducing end of the celluloses, the reaction causes the one-by-one loss of anhydroglucose units (AGUs) which are concomitantly converted into 2-(tetrahydroxybutyl)furans (**4**) by co-reacting with 1,3-dicarbonyl compounds such as ethyl acetoacetate (**1**). The key step of the reaction is the formation of a furan at the reducing end followed by the attack of the 2-OH group of the last-but-one AGU at this terminal furan. The intermediate, unstable dioxepane fragments by cleavage of the glycosidic bond. The terminal AGU is released as a substituted furan, the "new" reducing end reacting immediately with the 1,3-dicarbonyl component to form a new terminal furan which, in turn, undergoes the same cycle. The "furan endwise peeling" reaction represents an interesting way to convert cellulosic biomass by an easy procedure into substituted furans that are valuable fine chemicals with multiple uses.

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Introduction

The degradation of cellulose can be affected in many ways. Acidic degradation, thermal degradation, aging processes, alkaline degradation starting from oxidized spots (oxo groups): All of these processes can affect a cleavage of the cellulose chain, that is, decrease the degree of polymerization (DP). Enzymatic degradation can either cleave the cellulose chain randomly (endoglucanases) or shorten the chain from the end (exoglucanases). Also, nonenzymatic processes are known that start selectively from the reducing end, the "endwise peeling" occurring in alkaline media at elevated temperatures during pulping being the most well-known process. The cellulose chain is shortened in a step-by-step manner by one anhydroglucose which is released as *meta*-saccharinic acid by a rearrangement/elimination mechanism. The shortening proceeds until the structural prerequisite (the aldehyde function of the reducing end) is no longer present: The "stopping reaction", for instance, causes the formation of a terminal carboxy group which prevents further peeling.

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In recent work, we have identified another mechanism that, in principle, proceeds similarly: The "endwise peeling" of cellulose in *N*,*N*-dimethylacetamide (DMAc) or DMAc/LiCl at elevated temperatures (80–120 °C).[1,2] We came across this reaction when studying procedures to activate cellulose for dissolution in DMAc/LiCl prior to GPC measurements.[3] Heating in DMAc or DMAc/LiCl had been proposed as a means of activation, but was shown to be unsuitable because of this type of degradation. The actual reagent promoting the degradation is *N*,*N*-dimethylacetoacetamide (DMAcAc), a product of the LiCl-catalyzed self-condensation of DMAc which converts the reducing end into a substituted tetrahydroxybutylfuran derivative. Once converted into such a derivative, the former terminal anhydroglucose unit is cleaved in this form, the new reducing end is liberated at the (n – 1) anhydroglucose unit which, in turn, will also be converted into a furan derivative and once more released as (tetrahydroxybutyl)furan. In the presence of excess DMAcAc, being added in addition to being formed in small amounts thermally from DMAc, the derivatization of the reducing end and the subsequent peeling process can be significantly accelerated. Finally, a cellulose chain of n anhydroglucose units was converted into n equiv. of (tetrahydroxybutyl)furan by consumption of n equiv. of DMAcAc (Scheme 1). A control experiment using cellotetraose as a model compound showed a conversion into 4 equiv. of (tetrahydroxybutyl)furan. The degradation proceeds under noncatalytic conditions; thus, the degradation cannot be attributed to acid-catalyzed hydrolysis

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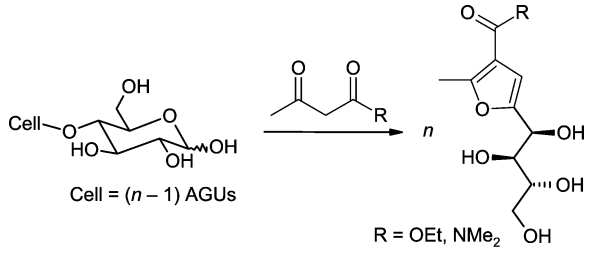
of the polysaccharide chain followed by furan formation from the fragments. In these degradation experiments, DMAcAc can be replaced with ethyl acetoacetate which gives the same results, the only difference being that the 4-substituent of the product furan is not an *N*,*N*-dimethylcarbamoyl ($CONMe_2$) but an ethoxycarbonyl (COOEt) group. In the experiments carried out in the present study, ethyl acetoacetate and other acetoacetates were used; these compounds, and not DMAcAc for which the reaction was first reported, are shown to be the co-reactants of the anhydroglucose units.



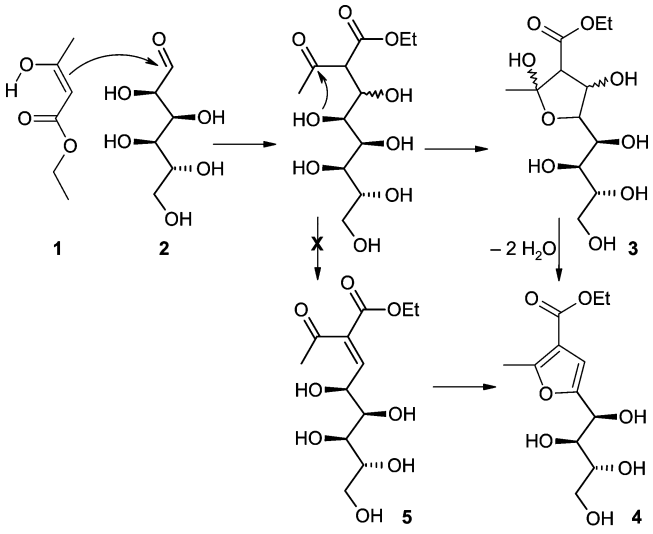
Scheme 1. Schematic representation of the "furan endwise peeling" reaction of cellulose with ethyl acetoacetate (**1**) or *N*,*N*-dimethylacetoacetamide.

The mechanism of the degradation process, for which we would like to introduce the short term "furan endwise peeling", remained unclear. Recently, we proposed a mechanism that includes a neighboring-group effect of the (n – 1) 2-OH group that reversibly adds to the furan moiety, thus facilitating cleavage of the terminal glycosidic bond.[1,2] At that time, experimental confirmation of the mechanism could not be provided. This problem has now been overcome, and we would like to communicate herein our studies regarding the mechanism of the "furan endwise peeling" process.

Results and Discussion

Furan formation by reaction of a 1,3-dicarbonyl component with a nonprotected aldose, sometimes referred to as the Garcia-Gonzalez reaction,[4,5] was reported in the late 1950s to proceed under relatively harsh conditions in fair yields (methanol, zinc chloride, 32%), but the reaction has not received much interest since then.[6–8] The mechanism of this process starts with a classical aldol addition with an aldose acting as the carbonyl component and a 1,3-dicarbonyl compound as the CH-acidic component [see ethyl acetoacetate (**1**) and glucose (**2**) in Scheme 2]. This is followed by nucleophilic attack of the 2-hydroxy moiety of the aldose on the oxo carbonyl carbon atom, establishing a tetrahydrofuran structure **3**.

Finally, 2 equiv. of water is eliminated to form the furan ring in **4**. It should be noted that the results of NMR studies and studies at lower reaction temperatures were in line with this mechanism. No indications were found for an alternative Knoevenagel-type condensation, establishing one double bond first to form the hypothetical intermediate **5** (Scheme 2) followed by ring closure to a dihydrofuran and



Scheme 2. Garcia-Gonzalez reaction of an aldose (glucose **2**) with a 1,3-dicarbonyl compound [ethyl acetoacetate (**1**)] to form a trisubstituted furan derivative [(tetrahydroxybutyl)furan (**4**)].

final elimination of water to establish the second double bond and provide furan **4**. At lower reaction temperatures, the tetrahydrofuran intermediate was detected, showing a characteristic NMR resonance of the hemiketal carbon atom at δ = 93.5 ppm, whereas evidence of an α,β-unsaturated Knoevenagel product such as **5** was absent.

The mechanism shown in Scheme 3, which shall be critically inspected below, was proposed for the "furan endwise peeling" reaction in accord with the procedure described in the Exp. Sect. with the overall reaction given in Scheme 1. The overall process starts with the reaction of the reducing terminal AGU of cellulose with ethyl acetoacetate to form a "furan endwise" structure similar to **4** (compound **6** in Scheme 3). The two key steps, which certainly need confirmation as they are somewhat peculiar, are the attack by the 2-hydroxy moiety of the last-but-one AGU on the terminal furan ring in **6** to form a seven-membered ring, a 1,4-dioxepane derivative **7** spiro-annulated to the dihydrofuran derivative, and subsequent cleavage of the terminal glycosidic bond.

In contrast, the two subsequent steps, reaction of the resulting resonance-stabilized oxonium ion with the 1,3-dicarbonyl compound to dihydrofuran **8** and re-elimination to release trisubstituted furan **4** by regeneration of **6′** having one AGU less than **6**, are rather common reactions which evidently will readily proceed.

Isotopic labeling experiments using ethyl [1,3-$^{13}C_2$]acetoacetate (**1***) corroborated this mechanism. Owing to the isotopic enrichment of 99+% ^{13}C, the ^{13}C NMR intensity of the respective carbon signals are increased about 100-fold relative to material with a natural isotopic abundance. A ^{13}C NMR experiment with a small number of scans will reveal these two labeled carbon atoms in all types of compounds and intermediates involving **1*** with all the other carbon atoms present effectively blinded out. Before the reaction, only the two resonances due to C-1 and C-3 in **1***

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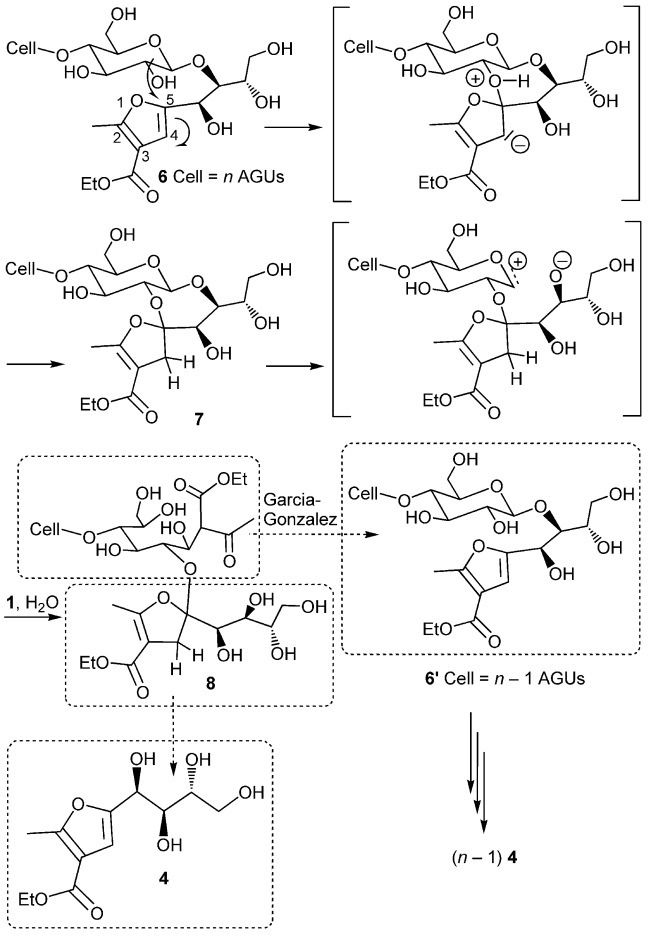


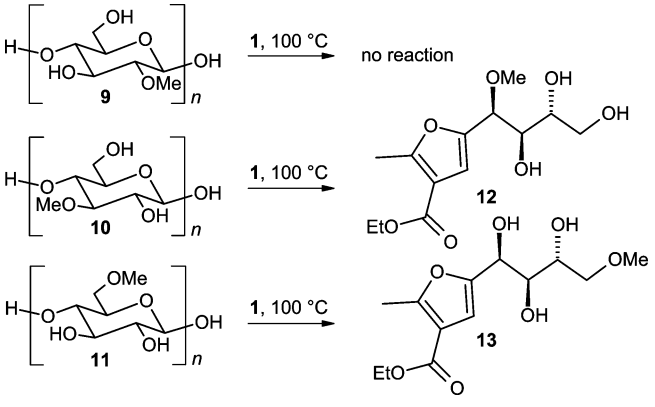
Scheme 3. Mechanism of the "furan endwise peeling" reaction (stereochemical designation omitted), converting cellulose built up of *n* anhydroglucose units (AGUs) and *n* equiv. of ethyl acetoacetate (**1**) into *n* equiv. of trisubstituted furan **4**.

were present. After a short reaction time of 1 h, two additional peaks at δ = 13 and 115 ppm appeared, assigned to the methyl group and C-3 of the furan moieties in **4**, **6**, and **6′** (Scheme 3). At longer reaction times, additional resonances at δ = 17 and 99 ppm and at 19 and 2 ppm appeared which were tentatively assigned to the intermediates **7** and **8**, respectively (see Scheme 3). This assignment is in complete agreement with resonances arising from similar structures (dihydrofurans and 3-alkylacetoacetates) reported in the literature.[9,10] With the progress of the reaction, the intensity of the product resonances (δ = 13 and 115 ppm) constantly increased while the signals of the starting material decreased. After completion of the reaction, the resonances of the starting material had completely disappeared and so had the peaks at δ = 17 and 99 ppm and at 19 and 62 ppm. The disappearance of the latter two pairs supported their assignment to intermediates **7** and **8** which per definitionem must be consumed at the end of the reaction. The only resonances persisting were those of the product furan **4** (δ = 13 and 115 ppm), while all other resonances had disappeared.

An ideal material to confirm the crucial role of the 2-hydroxy groups in the "furan endwise peeling" of cellulose would be a derivative in which this group is selectively blocked: 2-*O*-methylcellulose. This compound should not be able to undergo "furan endwise peeling" as the 2-methoxy group cannot add to furan in the way the 2-hydroxy group does. While methyl protection of the 2-hydroxy group should prevent the degradation reaction, methyl substitution of the 3-OH or 6-OH groups would be expected to have no such effect.

The cationic ring-opening polymerization of Nakatsubo et al. allowed the synthesis of cellulose derivatives in a completely regioselective manner. In this way, 2-*O*-methylcellulose (**9**), 3-*O*-methylcellulose (**10**), and 6-*O*-methylcellulose (**11**) were chemically synthesized.[11,12] Owing to the chemical build-up from monomeric units that already inherently carry the respective substitution pattern, complete regioselectivity in the product was assured which could not have been guaranteed by any alternative procedure starting from (already polymerized) cellulose.

When heated to 100 °C in the presence of ethyl acetoacetate (**1**), 2-*O*-methylcellulose (**9**) proved to be completely stable, even after prolonged reaction times of 48 h. In contrast, 3-*O*-methylcellulose (**10**) and 6-*O*-methylcellulose (**11**) were degraded into the [trihydroxy(methoxy)butyl]furans **12** and **13**, respectively (Scheme 4). The kinetics of these processes is shown in Figure 1. Apparently, an induction period of about 3 h was followed by a continuous release of the respective furans according to zero-order kinetics. The degradation of 3-*O*-methylcellulose (**10**) and 6-*O*-methylcellulose (**11**) thus proceeded in a way completely analogous to "normal", that is, nonsubstituted cellulose, as shown in Schemes 1 and 3. In the absence of **1**, both **10** and **11** were as stable as cellulose derivative **9**.



Scheme 4. Thermal "furan endwise peeling" reaction of regioselectively substituted celluloses. While 3-*O*-methylcellulose (**10**) and 6-*O*-methylcellulose (**11**) provided the [trihydroxy(methoxy)butyl]-furan derivatives **12** and **13**, respectively, 2-*O*-methylcellulose (**9**) showed no reaction at all as the crucial 2-hydroxy group was blocked by methylation.

The different results in thermal "furan peeling" obtained with celluloses bearing methoxy groups in the 2-, 3-, or 6-position, or better the completely suppressed reaction in the case of 2-*O*-methylcellulose (**9**), confirmed the crucial role of the next-to-last 2-hydroxy group. As the "furan endwise peeling" continued until the polysaccharide was completely

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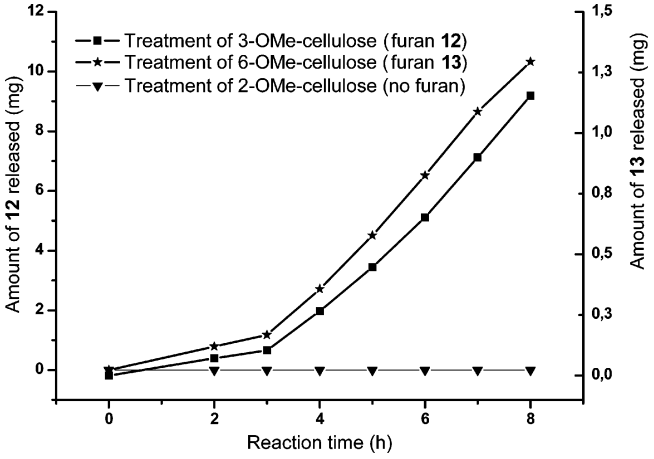
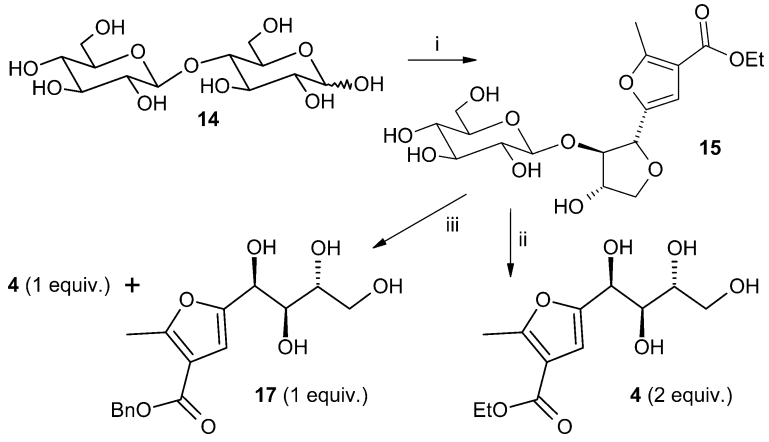


Figure 1. Kinetics of the thermal "furan endwise peeling" of 3-*O*-methylcellulose (**10**) and 6-*O*-methylcellulose (**11**) showing a linear increase of the released furan derivative after an initial induction period. 2-*O*-Methylcellulose (**9**) showed no reaction under otherwise identical conditions.

converted into furan monomers, there was evidently no influence of the chain length on the reaction: only the terminal and second to last AGU were involved in the respective reaction. To further support the mechanism we used the (glucosyltetrahydrofuranyl)furan **15** as the starting material which was readily obtained by $CeCl_3$-catalyzed condensation of cellobiose (**14**) with ethyl acetoacetate (**1**) (see Scheme 5).[13] This reaction corresponds to the furan formation proceeding thermally by a "furan endwise peeling" reaction, but additionally the trihydroxybutyl residue undergoes intramolecular etherification to a tetrahydrofuran due to the strong Lewis acidic action of the catalyst.[14]

Compound **15** appeared to exhibit all the structural prerequisites to undergo a reaction similar to the "furan endwise peeling" of cellulose as it represented the terminal cellobiose end of a furan-derivatized cellulose chain such as **6** or **6′** (cf. Scheme 3). Heating of **15** with ethyl acetoacetate (**1**) produced 2 equiv. of (tetrahydroxybutyl)furan **4**. The thermal "furan endwise peeling" reaction of this model compound proceeded in an analogous way to cellulose. The tetrahydrofuran ring (ether) present in **15** was opened during the reaction which thus afforded 2 equiv. of **4** from 1 equiv. of **15** (Scheme 5). To render the "equivalent one", coming from the furan already present in **15**, distinguishable from "equivalent two", that is, the furan which was formed by the actual "endwise peeling" process, we replaced the co-reacting ethyl acetoacetate (**1**) by benzyl acetoacetate (**16**) and obtained 1 equiv. of both ethyl ester **4** and benzyl ester **17** instead of 2 equiv. of the former (Scheme 5). This outcome, in combination with the results of the isotopic labeling experiments and those from thermal "furan endwise peeling" of the regioselectively substituted celluloses (cf. Scheme 4), provided sufficient evidence to regard the mechanism in Scheme 3 as confirmed.

Nevertheless, we were interested in what would be the minimum structural requirements for the reaction to proceed. Can we simplify the structural motifs in the substituted furan, the trihydroxybutyl link, and the next β-glucopyranosyl unit without interfering with the mechanism? To address this question we used 2-(2-furyl)ethyl β-glucopyranoside (**18**), (2-furyl)methyl β-glucopyranoside (furfuryl β-glucopyranoside, **19**), 3-(2-furyl)propyl β-glucopyranoside (**20**), 2-(tetrahydro-2-furyl)ethyl β-glucopyranoside (tetrahydrofurfuryl β-glucopyranoside, **21**), 2-phenylethyl β-glucopyranoside (**22**), and benzyl β-glucopyranoside (**23**) as the starting material (Scheme 6). Heating each of these compounds with ethyl acetoacetate (**1**) provided different results. In the presence of phenyl substituents, as in **22** and **23**, no reaction at all occurred. The same was the case with the tetrahydrofuran substituent in compound **21**. This is consistent with the notion that a furan ring to which the 2-hydroxy moiety can add is required for the reaction to proceed. 2-(2-Furyl)ethyl β-glucopyranoside (**18**) reacted readily to give (tetrahydroxybutyl)furan **4** and 2-(2-furyl)ethanol. At reaction times beyond the completion of the "furan endwise peeling", the latter was slowly consumed due to thermal condensation side-reactions, whereas **4** was quite



Scheme 5. $CeCl_3$-catalyzed synthesis and thermal "furan endwise peeling" of (glucosyltetrahydrofuranyl)furan **15**. i: **1** (1.5 equiv.), $CeCl_3$ (0.25 equiv.), H_2O, reflux, 5 h, 78%; ii: **1** (1.2 equiv.), H_2O/dioxane (1:1, v/v), reflux, 3 h, 82%; iii: benzyl acetoacetate (**16**; 5 equiv.), H_2O/dioxane (1:1, v/v), reflux, 3 h, 88%.

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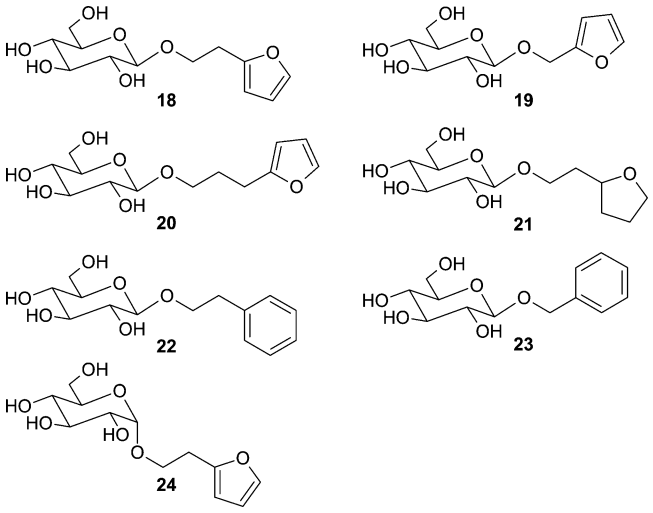
stable. In the case of (2-furyl)methyl β-glucopyranoside (**19**), the "lower C_1 homologue", and 3-(2-furyl)propyl β-glucopyranoside (**20**), the "higher C_3 homologue", the thermal reaction with **1** was much slower than in the case of **18**. Even though the steric conditions for the attack of the hydroxy group at the furan seem even better in the case of **19** than for **18**, since a six-membered ring is formed, the yield of (tetrahydroxybutyl)furan **4** was only 35%, and many byproducts were observed. These might mainly be due to side-reactions of the released furfuryl alcohol as the yield of this compound was below 10%, but still the reaction was far from being as quantitative as it was in the case of **18**. It can be speculated that the six-membered ring structure formed as an intermediate by attack of the 2-hydroxy moiety on the furan ring of **19** is favored, but subsequent cleavage of the glycosidic bond is disfavored by the inherent stability of this ring. In contrast, the seven-membered ring formed during the "furan endwise peeling" reaction of **18** might on one hand be less favored with regard to its formation, but on the other hand it could have a much higher tendency towards cleavage. Starting from propylfuran **20**, the yield of **4** was below 15%.



Scheme 6. Starting materials used to test the structural requirements for the thermal "furan endwise peeling" reaction.

2-(2-Furyl)ethyl α-glucopyranoside (**24**) showed no tendency to undergo "furan endwise peeling", in complete contrast to the β isomer, under otherwise identical conditions. Further increasing the reaction temperature caused uncontrolled thermal degradation of the product and polymerization of the furan moieties without formation of isolable products; the yield of **4** remained below 5%. In the absence of ethyl acetoacetate (**1**), all the compounds **18**–**23** were thermally stable, although at prolonged reaction times the furan residues tended towards polymerization and discoloration.

As a consequence of these experiments we can state that a β-glycosidically linked 2-(2-furyl)ethyl moiety is a minimum structural prerequisite for the "furan endwise peeling" reaction as far as the "furan half" is concerned. A β-configured glycosidic linkage, the C_2 tether, and the 2-furyl moiety seem to be indispensable requirements. A complementary experiment was now needed to show whether the structure of the "glucopyranoside half" could also be simplified. For this purpose we used model compound **25** which had an α-hydroxy acetal structure as a minimum substitute for the glucopyranose moiety, besides the required 2-(2-furyl)ethyl moiety (Scheme 7). Its synthesis started from dihydropyran which was dibrominated. The two bromine atoms show significantly different reactivities in nucleophilic substitutions,[15,16] the 2-Br atom being replaced under mild conditions by 2-(2-furyl)ethanol in the presence of DMAP. The second bromine atom required refluxing ethanol for exchange with OH^-. The *cis* compound **26** and the *trans*-configured product (**25**), resembling α-glucoside **24** and β-glucoside **18**, were formed in an approximate 2:5 ratio. Heating of *trans*-2-hydroxy acetal **25** in the presence of ethyl acetoacetate (**1**) provided 2-(2-furyl)ethanol in addition to furan **27** in nearly quantitative yields. Thus, this simplified model structure also smoothly underwent the "furan peeling"-type reaction. The *cis*-2-hydroxy acetal **26** also gave the peeling product, although in rather low yields (17%) in addition to unreacted starting material (34%) under otherwise identical conditions. This result corresponds fully to the observed reactivity differences of α-glucopyranoside **24** and β-glucopyranoside **18**, with the former compound giving very low yields of the "furan endwise peeling" product in contrast to the latter which reacted quantitatively.

To further corroborate the importance of the 2-hydroxy group, an analogous reaction was carried out with acetal **28**, which was completely stable under the conditions that caused complete conversion of **25** into **27** in nearly quantitative yields (Scheme 7). Consequently, a 2-hydroxypyran structure, preferably with a *trans* configuration with respect to the 2-(2-furyl)ethoxy moiety in the 2-position of the pyran was the second structural prerequisite for the "furan endwise peeling" reaction to proceed.

The reaction was not only a good candidate for mechanistic studies, it is first of all an interesting way to convert cellulosic biomass by an easy procedure into substituted furans that are valuable fine chemicals with multiple uses. This is especially interesting with regard to the current need to convert renewable resources into high-value chemicals by facile processes that can readily be scaled up. Direct utilization of cellulose as the starting material is possible, but due to the inherent stepwise mechanism, completion of the reaction requires comparatively long reaction times. It is more straightforward instead to hydrolyze (or enzymatically degrade) the cellulose to oligosaccharides (or even glucose) first and subsequently treat the formed fragments with ethyl acetoacetate to give the functionalized furan **4**. In a preliminary experiment using energy-economic microwave heating it was shown that an 8 h reaction of cotton linters at 120 °C afforded 70% yield of furan **4** at 12% conversion. When the same overall reaction time was divided into an acidic hydrolysis step (4 h) followed by the reaction with ethyl acetoacetate (**1**) (4 h) the conversion was increased to 72% at 75% yield.

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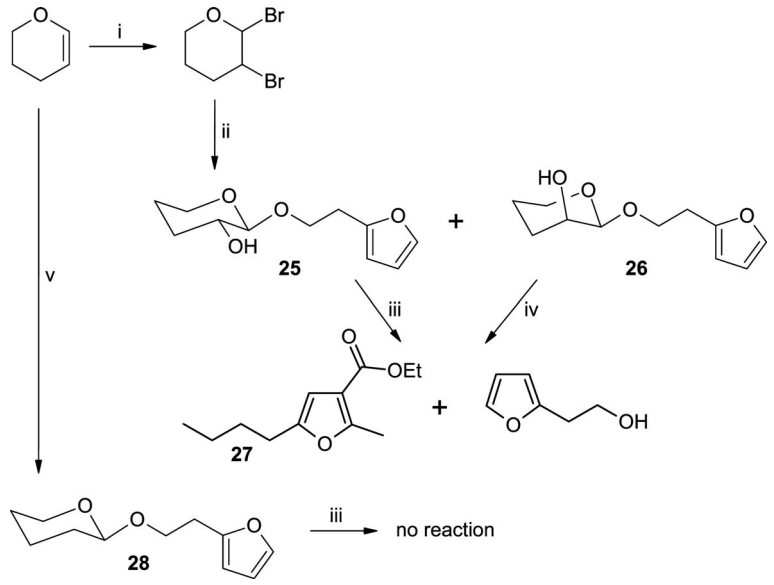

Scheme 7. Synthesis and "furan endwise peeling"-type reaction of model compounds **25**, **26**, and **28**. i: Br_2, CH_2Cl_2, 5 min, –20 °C to r.t., quant.; ii: (1) 2-(fur-2-yl)ethanol, $PhNMe_2$, r.t., 15 min; (2) $EtOH/K_2CO_3$ aq., reflux, 1 h, 74%; iii: **1**, 100 °C, 2 h, 94% **27**; iv: **1**, 100 °C, 2 h, 17% **27**; v: 2-(fur-2-yl)ethanol, $BF_3{\cdot}Et_2O$ (cat.), 78%.

Conclusions

The "furan endwise peeling" reaction is a novel type of reaction hitherto not reported in the pertinent literature. Reacting with acetoacetic acid derivatives, cellulose or cellooligosaccharides are shortened from the reducing end by stepwise release of single anhydroglucose units which are converted into trisubstituted furan derivatives. The reaction starts with the reducing end reacting with the β-oxocarbonyl compound to yield a terminal furan in a Garcia-Gonzalez-type reaction. In the actual "peeling" steps, the 2-OH group of the last-but-one anhydroglucose unit, that is, the unit neighboring the terminal furan moiety, plays a crucial role. It reversibly adds to this furan, thus weakening the terminal glycosidic bond and preparing it for cleavage to occur. This cleavage releases the terminal furan into the reaction medium, the new reducing end reacts with the acetoacetate and starts a new cycle of this process.

Mechanistic studies involving selectively substituted celluloses and low-molecular-weight model compounds have shown that a β-glycosidically linked 2-(2-furyl)ethyl moiety is a minimum structural prerequisite for the "furan endwise peeling" reaction as far as the "furan side" or "aglycon" is concerned. Each of the three features, the β-configured glycosidic linkage, the C_2 tether, and the 2-furyl moiety, seems to be an indispensable requirement. For the "glucose side", a *trans*-configured α-hydroxy acetal structure is the minimum structure required for the "furan endwise peeling" reaction to proceed.

The reaction has been shown to be a facile and scaleable approach to the conversion of natural cellulosic biomass by a simple reaction into trisubstituted furans that are valuable chemicals of high complexity and which offer ample opportunities for further chemical manipulation. Combined with microwave heating and hydrolytic or enzymatic prehydrolysis, the "furan endwise peeling" reaction is a prime example of green chemistry principles, with regard to both the materials involved and the reaction conditions. Of course, these conversion processes require further optimization with regard to optimum conversion, yields, and reaction conditions, such topics being the subject of current and future studies in our group.

Experimental Section

General: Commercial chemicals were of the highest grade available and were used without further purification. Reagent-grade solvents were used for all extractions and workup procedures. Distilled water was used for all aqueous extractions and for all aqueous solutions. *n*-Hexane, diethyl ether, ethyl acetate, and petroleum ether used in chromatography were distilled before use. All reactions involving nonaqueous conditions were conducted in oven- (140 °C, overnight) or flame-dried glassware under argon or nitrogen. TLC was performed using Merck silica gel 60 F_{254} precoated plates. Flash chromatography was performed using Baker silica gel (40 μm particle size). All products were purified to homogeneity by TLC/GC-MS analysis. The use of brine refers to saturated NaCl(aq). All the yields given refer to isolated pure products. Melting points, determined with a Kofler-type micro-hot stage with a Reichert–Biovar microscope, are uncorrected. Elemental analyses were performed at the Microanalytical Laboratory of the Institute of Physical Chemistry at the University of Vienna. NMR spectra were recorded with Bruker Avance 300 and Avance II-400 spectrometers operating at 300.13 MHz and 400.13 MHz, respectively, for ^1H and at 75.47 MHz and 100 MHz, respectively, for ^{13}C NMR in $CDCl_3$ unless otherwise stated. Chemical shifts, relative to TMS as internal standard, are given in ppm, coupling constants in Hz. ^{13}C NMR peaks were assigned by means of APT, HMQC, and HMBC experiments. The abbreviations "Fu", "THF", "Bu", "Bn", and "Py" used in the NMR assignments designate furan, tetrahydrofuran, butyl, benzyl, and pyran moieties, respectively.

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Capillary Electrophoresis (CE): An Agilent Technologies 3D-CE instrument equipped with a UV-DAD detector was employed. The operation of the CE system, data acquisition, and peak area integrations were performed using the software 3D-CE ChemStation for Windows NT 4.0. A roll of fused silica capillary having an internal diameter (ID) of 30 μm was supplied by Skandinaviska Genetec (Göteborg, Sweden). A 48.5 cm piece was cut using a CE(C) Column Cutter (Hewlett-Packard) and a 2–4 mm length detection window was created by removing the polyimide coating by burning, its center being located 8.5 cm from the outlet end. The capillary was fitted into the cassette and the temperature control was set to 20 °C. For the setup see also refs.[17–19] As the running electrolyte a solution of 0.001% (w/v) 1,5-dimethyl-1,5-diazaundecamethylene polymethobromide (hexadimethrine bromide, HDB), 550 mM boric acid, 5% methanol, and 5% 1-propanol in purified water was used. The pH was adjusted to 10.7 with 3 M KOH. For CE measurements, an HPCE-3D instrument (Agilent Technology) equipped with a capillary column (64 cm × 50 μm) and DAD-UV detector were used. The capillary was kept at 15 °C. The run current was set to –100 μA. The resulting voltage was about 28 kV. Conditioning of the column was performed by flushing with 1.0 M aqueous NaOH for 10 min. Between the runs the capillary was preconditioned by flushing with the running electrolyte for 8 min. Absorption of the furan derivatives (**4**, **12**, **13**, **15**, **17**, **27**) was determined at 200 nm (detector response time = 0.1 s; data collection rate = 20.8 Hz), with the detector being placed 8 cm from the anodic end of the column. Hydrostatic injection was performed by applying 50 mbar pressure for 8 s. To achieve optimum reproducibility, an internal standard was used for the quantification of the furan derivatives. Benzoic acid proved to be advantageous as its peak was clearly separated from the signal of the analytes. A benzoic acid stock solution was prepared by dissolving benzoic acid (50 mg) in water (10 mL). A 15 μL aliquot of this solution was added to each analyte sample.

General Procedure for the Thermal "Furan Endwise Peeling" of Cellulose: Oven-dried cellulose (100 mg) was suspended in 1,4-dioxane (50 mL, b.p. 100–102 °C) and ethyl acetoacetate (**1**, 1.2 equiv. rel. to AGU) was added. The mixture was heated at reflux. At certain intervals, aliquots (100 μL) were withdrawn, diluted with methanol (900 μL), and directly analyzed by CE. The hot mixture was filtered and cooled to room temp., and a white precipitate separated. Toluene (20 mL) was added and the mixture was kept at –20 °C in the refrigerator overnight. The precipitate, in the form of white needles, was filtered off, washed with petroleum ether, and dried. Yields depended on the reaction time. In the case of complete consumption of the starting cellulose, readily visible by complete disappearance of solids in the refluxing mixture, yields generally were above 80%, being 96% for cotton linters, 87% for a beech sulfite pulp, and 88% for a eucalyptus prehydrolysis kraft pulp. The reaction can be scaled up without any problems (tested up to 10 g of starting cellulose).

Ethyl 2-Methyl-5-(1,2,3,4-tetrahydroxybutyl)furan-3-carboxylate (4): $[\alpha]_D^{20}$ = –5.3 (*c* = 1.00, MeOH), m.p. 118–120 °C (ethanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 1.32 (t, ^3J = 6.8 Hz, 3 H, CH_3 in Et), 2.54 (s, 3 H, C*H*$_3$-Fu), 3.55–3.85 (m, 4 H), 4.26 (q, ^3J = 6.8 Hz, 2 H, CH_2 in Et), 4.75 (d, 1 H, 1-H in Bu), 6.57 (s, 1 H, C*H* in Fu) ppm. ^{13}C NMR (CD_3OD): δ = 13.4 (CH_3 in Fu), 14.2 (CH_3 in Et), 61.25 (CH_2 in Et), 64.8 (C-4 in Bu), 67.9 (C-1 in Bu), 70.6 (C-3 in Bu), 74.2 (C-2 in Bu), 108.5 (C-4), 115.1 (C-3), 155.5 (C-2), 159.6 (C-5), 165.7 (COO) ppm. $C_{12}H_{18}O_7$ (274.27): calcd. C 52.55, H 6.62; found C 52.43, H 6.71.

Thermal "Furan Endwise Peeling" of Cellotriose in the Presence of Isotopically Labeled Ethyl Acetoacetate: Cellotriose (50.4 mg, 0.1 mmol) was placed in an NMR tube. [D_8]Dioxane (0.8 mL) and ethyl [1,3-$^{13}C_2$]acetoacetate (**1***, 40.0 mg, 0.3 mmol, 1 equiv. rel. to AGU) was added. The tube was closed and a ^{13}C NMR spectrum (4 scans) was recorded. The tube was heated to 110 °C and spectra were recorded in 1 h intervals (16 scans each) at 110 °C. After 9 h, the starting material had been completely consumed. The reaction could be suspended by cooling to room temp. and resumed by heating to 110 °C. The higher temperature during the measurement thus was not required from the viewpoint of the reaction mechanism, but was advantageous due to the high viscosity of the reaction mixture at room temp. and the resulting decreased resolution.

Thermal "Furan Endwise Peeling" of Regioselectively Substituted Celluloses 9–11: The respective cellulose derivative (5 mg) was suspended in 1,4-dioxane (10 mL, b.p. 100–102 °C) and ethyl acetoacetate (**1**, 8.0 mg, 7.8 μL, 2 equiv. rel. to AGU) was added. The mixture was heated at reflux. At certain intervals, aliquots (10 μL) were withdrawn, diluted with methanol (90 μL), and directly analyzed by GC-MS or CE. After 48 h, the reaction mixture was cooled to room temp., concentrated in vacuo to a volume of about 0.5 mL, and purified by chromatography on silica gel (toluene/ethyl acetate, 5:1, v/v) to provide the furan derivative (82% of **12**, 94% of **13**) as white solids after evaporation of the eluent.

Ethyl 2-Methyl-5-(2,3,4-trihydroxy-1-methoxybutyl)furan-3-carboxylate (12): $[\alpha]_D^{20}$ = –12.4 (*c* = 1.00, MeOH), m.p. 86–88 °C (ethanol). ^{1}H NMR (300 MHz, DMSO): δ = 1.26 (t, 3 H, CH_3 in Et), 2.50 (s, 3 H, C*H*$_3$-Fu), 3.24 (s, 3 H, OMe), 3.38–3.54 (m, 3 H), 3.84 (m, 1 H), 4.21 (q, 2 H, CH_2 in Et), 4.48 (d, 1 H, 1-H in Bu), 6.45 (s, 1 H, C*H* in Fu) ppm. ^{13}C NMR (CD_3OD): δ = 13.4 (CH_3 in Et), 14.4 (CH_3 in Fu), 51.3 (OMe), 59.4 (CH_2 in Et), 63.4 (C-4 in Bu), 68.4 (C-3 in Bu), 70.5 (C-1 in Bu), 72.8 (C-2 in Bu), 106.5 (C-4), 113.3 (C-3), 155.2 (C-2), 156.9 (C-5), 163.5 (COO) ppm. $C_{13}H_{20}O_7$ (288.30): calcd. C 54.16, H 6.99; found C 54.23, H 7.08.

Ethyl 2-Methyl-5-(1,2,3-trihydroxy-4-methoxybutyl)furan-3-carboxylate (13): $[\alpha]_D^{20}$ = 8.7 (*c* = 1.00, MeOH), m.p. 132–133 °C (ethanol). ^{1}H NMR (300 MHz, DMSO): δ = 1.26 (t, 3 H, CH_3 in Et), 2.51 (s, 3 H, C*H*$_3$-Fu), 3.26 (s, 3 H, OMe), 3.42–3.58 (m, 4 H), 4.21 (q, 2 H, CH_2 in Et), 4.77 (d, 1 H, 1-H in Bu), 6.48 (s, 1 H, C*H* in Fu) ppm. ^{13}C NMR (CD_3OD): δ = 13.4 (CH_3 in Et), 14.4 (CH_3-Fu), 54.5 (OMe), 59.6 (CH_2 in Et), 65.6 (C-1 in Bu), 70.0 (C-2 in Bu), 71.2 (C-3 in Bu), 72.1 (C-4 in Bu), 106.8 (C-4), 113.3 (C-3), 155.9 (C-2), 157.2 (C-5), 162.9 (COO) ppm. $C_{13}H_{20}O_7$ (288.30): calcd. C 54.16, H 6.99; found C 53.96, H 7.28.

Synthesis of (Glucosyltetrahydrofuranyl)furan 15: D-Cellobiose (3.42 g, 10.0 mmol), ethyl acetoacetate (**1**, 1.95 g, 15.0 mmol), and $CeCl_3 \cdot 7H_2O$ (930 mg, 2.50 mmol) were dissolved in distilled water. The reaction mixture was refluxed for 5 h. After completion of the reaction (TLC control; toluene/ethyl acetate, 1:1, v/v), the reaction mixture was cooled to room temp., and the solvents were evaporated to dryness in vacuo. The crude remainder was directly purified by chromatography on silica gel (toluene/ethyl acetate, 3:1, v/v) to afford pure **15** (78%) as a white solid. $[\alpha]_D^{20}$ = –43.2 (*c* = 1.00, MeOH), m.p. 108–110 °C (ethanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 1.33 (t, 3 H, CH_3 in Et), 2.55 (s, 3 H, Me), 3.19–3.37 (m, 4 H, 2′′-H, 3′′-H, 4′′-H, 5′′-H), 3.64 (dd, ^2J = 12.0, ^3J = 5.5 Hz, 1 H, 6′′-H_{2A}), 3.74 (dd, ^2J = 12.4, ^3J = 2.8 Hz, 1 H, 6′′-H_{2B}), 3.81 (dd, ^2J = 9.6, ^3J = 3.6 Hz, 1 H, 4′-H_{2A}), 4.11 (dd, ^2J = 9.6, ^3J = 4.4 Hz, 1 H, 4′-H_{2B}), 4.26 (q, 2 H, CH_2 in Et), 4.44 (d, ^3J = 8.0 Hz, 1 H, 1′′-H), 4.45–4.49 (m, 1 H, 3′-H), 4.50–4.54 (m, 1 H, 2′-H), 4.91 (d, ^3J = 6.4 Hz, 1 H, 1′-H), 6.67 (s, 1 H, 3-H) ppm. ^{13}C NMR (DMSO): δ = 13.9 (Me), 14.6 (CH_3 in Et), 61.4

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(CH_2 in Et), 62.3 (C-6′′), 71.1 (C-3′), 71.5 (C-4′′), 73.3 (C-4′), 75.1 (C-2′′), 77.0 (C-1′), 77.8/77.9 (C-3′′ /C-5′′), 83.1 (C-2′), 104.2 (C-1′′), 110.3 (C-3), 115.2 (C-2), 152.1 (C-4), 160.7 (C-1), 165.4 (COO) ppm. $C_{18}H_{26}O_{11}$ (418.40): calcd. C 51.67, H 6.26; found C 51.62, H 6.31.

Synthesis of β-Glucopyranosides 18–23 and α-Glucopyranoside 24: The glucosides **18**–**24** were prepared according to standard procedures, starting from commercially available pentaacetylbromo-D-glucose as the glycosyl donor and the free alcohols as the respective glycosyl acceptors.

2-(2-Furyl)ethyl β-Glucopyranoside (18): $[\alpha]_D^{20}$ = –45.2 (*c* = 1.0, MeOH), m.p. 95–98 °C (methanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 2.75 (m, 2 H, Fu-CH_2), 3.20–3.37 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 3.71 (m, 1 H, Fu-CH_2-CH_{2A}), 3.65 (dd, ^2J = 12.0, ^3J = 5.5 Hz, 1 H, 6-H_{2A}), 3.84 (dd, ^2J = 12.0, ^3J = 2.0 Hz, 1 H, 6-H_{2B}), 3.89 (m, 1 H, Fu-CH_2-CH_{2B}), 4.34 (d, ^3J = 7.7 Hz, 1 H, 1-H), 6.25 (d, ^3J = 2.7 Hz, 1 H, Fu), 6.40 (m, 1 H, Fu), 7.45 (d, ^3J = 1.3 Hz, 1 H, Fu) ppm. ^{13}C NMR (DMSO): δ = 32.1 (Fu-CH_2), 62.6 (C-6), 71.6 (C-4), 70.0 (Fu-CH_2-*C*H_2), 75.0 (C-2), 77.9/78.0 (C-3/C-5), 104.1 (C-1), 110.7, 111.3, 142.5, 153.6 (Fu) ppm. $C_{12}H_{18}O_7$ (274.27): calcd. C 52.55, H 6.62; found C 52.63, H 6.68.

2-(2-Furyl)methyl β-Glucopyranoside (Furfuryl β-Glucopyranoside, 19): $[\alpha]_D^{20}$ = –35.5 (*c* = 1.00, MeOH), colorless wax. ^{1}H NMR (300 MHz, CD_3OD): δ = 3.16–3.38 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 3.67 (dd, ^2J = 12.0, ^3J = 5.5 Hz, 1 H, 6-H_{2A}), 3.88 (dd, ^2J = 12.0, ^3J = 2.0 Hz, 1 H, 6-H_{2B}), 4.33 (d, ^3J = 7.7 Hz, 1 H, 1-H), 4.63 (d, ^2J = 12.7 Hz, 1 H, Fu-CH_{2A}), 4.80 (d, ^2J = 12.7 Hz, 1 H, Fu-CH_{2B}), 6.37 (m, 1 H, Fu), 6.41 (m, 1 H, Fu), 7.47 (m, 1 H, Fu) ppm. ^{13}C NMR (DMSO): δ = 62.8 (C-6), 63.4 (Fu-CH_2), 71.6 (C-4), 75.0 (C-2), 78.01/78.04 (C-3/C-5), 102.8 (C-1), 110.9, 111.4, 144.1, 152.6 (Fu) ppm. $C_{11}H_{16}O_7$ (260.25): calcd. C 50.77, H 6.20; found C 50.91, H 6.05.

3-(2-Furyl)propyl β-Glucopyranoside (20): $[\alpha]_D^{20}$ = –5.0 (*c* = 1.00, MeOH), m.p. 88–90 °C (methanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 1.82 (m, 2 H, CH_2-C*H*$_2$-CH_2), 2.58 (t, 2 H, Fu-CH_2), 3.20–3.37 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 3.39 (m, 1 H, CH_2-CH_{2A}-O), 3.65 (dd, ^2J = 12.0, ^3J = 5.5 Hz, 1 H, 6-H_{2A}), 3.84 (dd, ^2J = 12.0, ^3J = 2.0 Hz, 1 H, 6-H_{2B}), 3.56 (m, 1 H, CH_2-CH_{2B}-O), 4.34 (d, ^3J = 7.5 Hz, 1 H, 1-H), 6.36 (m, 1 H, Fu), 6.42 (m, 1 H, Fu), 7.47 (m, 1 H, Fu) ppm. ^{13}C NMR (DMSO): δ = 27.8 (Fu-CH_2), 32.0 (Fu-CH_2-*C*H_2) 62.5 (C-6), 63.1 (Glc-O-CH_2), 71.5 (C-4), 75.3 (C-2), 77.9/78.1 (C-3/C-5), 103.1 (C-1), 109.9, 111.3, 144.6, 152.7 (Fu) ppm. $C_{13}H_{20}O_7$ (288.30): calcd. C 54.16, H 6.99; found C 54.01, H 7.09.

2-(Tetrahydro-2-furyl)ethyl β-Glucopyranoside (21): $[\alpha]_D^{20}$ = –12.1 (*c* = 1.00, MeOH), m.p. 35–36 °C (methanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 1.59 (m, 2 H, THF-CH_2), 1.78–2.14 (m, 4 H, THF), 3.23–3.40 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 3.42 (m, 1 H, CH_2-CH_{2A}-O), 3.50–3.61 (m, 1 H, CH_2-CH_{2B}-O), 3.67 (dd, ^2J = 11.8, ^3J = 5.8 Hz, 1 H, 6-H_{2A}), 3.78–3.92 (m, 2 H, THF), 3.87 (dd, ^2J = 11.8, ^3J = 2.4 Hz, 1 H, 6-H_{2B}), 4.12–4.20 (m, 1 H, THF), 4.36 (d, ^3J = 7.0 Hz, 1 H, 1-H) ppm. ^{13}C NMR (DMSO): δ = 25.2, 31.6, 66,4, 78.2 (THF), 36.4 (THF-CH_2), 59.0 (THF-CH_2-*C*H_2) 62.5 (C-6), 71.4 (C-4), 75.3 (C-2), 77.9/78.0 (C-3/C-5), 104.0 (C-1) ppm. $C_{12}H_{22}O_7$ (278.30): calcd. C 51.79, H 7.97; found C 52.01, H 7.89.

2-Phenylethyl β-Glucopyranoside (22): $[\alpha]_D^{20}$ = –30.3 (*c* = 1.00, MeOH), m.p. 122–123 °C (methanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 2.93 ("t", 2 H, Ph-CH_2), 3.16–3.39 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 3.59–3.79 (m, 1 H, Ph-CH_2-CH_{2A}), 3.65 (dd, ^2J = 12.0, ^3J = 5.5 Hz, 1 H, 6-H_{2A}), 3.86 (dd, ^2J = 12.0, ^3J = 2.0 Hz, 1 H, 6-H_{2B}), 4.05–4.13 (m, 1 H, Ph-CH_2-CH_{2B}), 4.30 (d, ^3J = 7.7 Hz, 1 H, 1-H), 7.15–7.26 (m, 5 H, Ph) ppm. ^{13}C NMR (DMSO): δ = 37.2 (Ph-CH_2), 62.7 (C-6), 71.6 (C-4), 71.7 (Ph-CH_2-*C*H_2), 75.0 (C-2), 77.9/78.0 (C-3/C-5), 104.3 (C-1), 127.1 (Ph-4), 129.3/130.0 (Ph-2/6, Ph-3/5), 140.0 (Ph-1) ppm. $C_{14}H_{20}O_6$ (284.31): calcd. C 59.14, H 7.09; found C 59.14, H 7.14.

Benzyl β-Glucopyranoside (23): $[\alpha]_D^{20}$ = –58.4 (*c* = 1.00, MeOH), m.p. 121–122 °C (methanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 3.22–3.38 (m, 4 H, 2-H, 3-H, 4-H, 5-H), 3.69 (dd, ^2J = 12.0, ^3J = 5.5 Hz, 1 H, 6-H_{2A}), 3.89 (dd, ^2J = 12.0, ^3J = 2.1 Hz, 1 H, 6-H_{2B}), 4.35 (d, ^3J = 7.6 Hz, 1 H, 1-H), 4.65 (d, ^2J = 11.8 Hz, 1 H, Ph-CH_{2A}), 4.93 (d, ^2J = 11.8 Hz, 1 H, Ph-CH_{2B}), 7.23–7.43 (m, 5 H, Ph) ppm. ^{13}C NMR (DMSO): δ = 62.8 (C-6), 71.6 (C-4), 71.7 (Ph-CH_2), 75.1 (C-2), 78.0/78.05 (C-3/C-5), 103.2 (C-1), 128.7 (Ph-4), 129.2/129.25 (Ph-2/6, Ph-3/5), 139.0 (Ph-1) ppm. $C_{13}H_{18}O_6$ (270.28): calcd. C 57.77, H 6.71; found C 58.05, H 6.88.

2-(2-Furyl)ethyl α-Glucopyranoside (24): $[\alpha]_D^{20}$ = 2.6 (*c* = 1.00, MeOH), colorless wax. ^{1}H NMR (300 MHz, CD_3OD): δ = 2.74 (m, 2 H, Fu-CH_2), 3.22–3.30 (m, 1 H, 4-H), 3.37 (dd, ^3J = 9.1, 3.8 Hz, 1 H, 2-H), 3.52 (ddd, ^3J = 9.8, 6.7, 1.5 Hz, 1 H, 5-H), 3.60 (t, ^3J = 9.1 Hz, 1 H, 3-H), 3.72 (m, 1 H, Fu-CH_2-CH_{2A}), 3.65 (dd, ^2J = 11.8, ^3J = 6.7 Hz, 1 H, 6-H_{2A}), 3.79 (dd, ^2J = 11.8, ^3J = 1.5 Hz, 1 H, 6-H_{2B}), 3.90 (m, 1 H, Fu-CH_2-CH_{2B}), 4.65 (d, ^3J = 3.7 Hz, 1 H, 1-H), 6.29 (m, 1 H, Fu), 6.39 (m, 1 H, Fu), 7.37 (m, 1 H, Fu) ppm. ^{13}C NMR (DMSO): δ = 32.6 (Fu-CH_2), 62.4 (C-6), 71.6 (C-4), 68.1 (Fu-CH_2-*C*H_2), 73.1 (C-2), 73.7 (C-5), 75.2 (C-3), 100.3 (C-1), 108.9, 111.0, 144.0, 153.1 (Fu) ppm. $C_{12}H_{18}O_7$ (274.27): calcd. C 52.55, H 6.62; found C 52.70, H 6.89.

Thermal "Endwise Peeling" of Model Compounds 15 and 18–24: The respective model compound (1 mmol) was dissolved in a mixture of 1,4-dioxane and water (1:1, v/v, 50 mL), ethyl acetoacetate (**1**, 156 mg, 0.15 mL, 1.2 mmol) was added, and the mixture was heated at reflux. After consumption of the model compound (TLC control) or after 6 h, respectively, the mixture was cooled to room temp. An aliquot (100 μL) was withdrawn for CE and GC-MS analysis, and the reaction mixture was three times co-evaporated with toluene (3 × 20 mL), finally concentrated to a volume of about 0.5 mL, and purified by chromatography on silica gel (toluene/ethyl acetate, 5:1, v/v). Tetrahydroxybutylfuran **4** was recovered from **15** in 82% yield, from 2-(2-furyl)ethyl β-glucopyranoside (**18**) in 96% yield, from furfuryl β-glucopyranoside (**19**) in 35% yield, from 3-(2-furyl)propyl β-glucopyranoside (**20**) in 15% yield, and from 2-(2-furyl)ethyl α-glucopyranoside (**24**) in 3% yield. Model compounds **21**–**23** did not produce any furan **4**, nor showed any conversion of the starting material. The recovery of the starting material was 96% in the case of **21** and **23**, 95% from **22**, and 37% from **24**. According to the above procedure, (tetrahydrofuranyl)furan **15** also reacted with benzyl acetoacetate (**16**, 0.23 g, 1.2 mmol) instead of ethyl acetoacetate (**1**). Chromatography on silica gel (toluene/ethyl acetate, 7:1, v/v) provided furan **17** as a white solid (296 mg, 88%).

Benzyl 2-Methyl-5-(1,2,3,4-tetrahydroxybutyl)furan-3-carboxylate (17): $[\alpha]_D^{20}$ = –5.0 (*c* = 1.00, MeOH), m.p. 140–141 °C (ethanol). ^{1}H NMR (300 MHz, CD_3OD): δ = 2.53 (s, 3 H, CH_3-Fu), 3.50–3.82 (m, 4 H), 4.88 (d, 1 H, 1-H in Bu), 5.25 (s, 2 H, Bn), 6.61 (s, 1 H, CH in Fu), 7.30–7.41 (m, 5 H, Bn) ppm. ^{13}C NMR (CD_3OD): δ = 13.9 (CH_3 in Fu), 64.9 (C-4 in Bu), 66.9 (CH_2, Bn), 68.0 (C-1 in Bu), 70.4 (C-3 in Bu), 74.2 (C-2 in Bu), 108.4 (C-4), 115.1 (C-3), 129.1 (C-2/6, Bn), 129.2 (C-4, Bn), 129.6 (C-3/5, Bn), 137.8 (C-1, Bn), 155.4 (C-2), 158.9 (C-5), 165.5 (COO) ppm. $C_{17}H_{20}O_7$ (336.34): calcd. C 60.71, H 5.99; found C 60.89, H 6.02.

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Synthesis of Hydroxy Acetals 25 and 26: A solution of bromine (320 mg, 102 μL) in CH_2Cl_2 (20 mL) was added dropwise to a cooled (–78 °C), stirred solution of 3,4-dihydro-2*H*-pyran (168 mg, 156 μL, 2 mmol) in CH_2Cl_2 (20 mL). The yellow mixture was stirred for 15 min, and one drop of 3,4-dihydro-2*H*-pyran was added to consume excess bromine, turning the mixture colorless. A solution of *N*,*N*-dimethylaniline (250 mg, 2.06 mmol) in CH_2Cl_2 (5 mL) was added followed by a solution of 2-(2-furyl)ethanol (250 mg, 2.23 mmol) in CH_2Cl_2 (5 mL). The mixture was warmed to room temp. and stirred for 6 h. The solvent was removed in vacuo at room temp., and the remainder was dissolved in ethanol (50 mL). A concentrated aqueous solution of K_2CO_3 (15 mL) was added, and the mixture was refluxed whilst stirring for 1 h. After cooling to room temp., the mixture was co-evaporated three times with toluene (150 mL). The solvents were removed, the remainder, a green semi-solid, was triturated with dichloromethane, and filtered through a layer of active charcoal. Removal of the solvent in vacuo at room temp. afforded α-hydroxy acetals **25** and **26** as a diastereomeric mixture (white solid, 314 mg, 74%). Separation by column chromatography on silica gel (*n*-hexane/toluene, 1:1, v/v) provided compounds **25** (white solid, 224 mg, 53%) and **26** (white solid, 90 mg, 21%) in pure form.

***trans*-2-[2-(Furan-2-yl)ethoxy]tetrahydropyran-3-ol (25):** M.p. 96–98 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56–1.60 (m, 2 H, 5-H, Py), 1.68–1.76 (m, 2 H, 4-H, Py), 2.75 (t, 2 H, Fu-CH_2), 3.48 (m, 1 H, 6-H_{2A}, Py), 3.64–3.89 (m, 4 H, Fu-CH_2-CH_{2A}, Fu-CH_2-CH_{2B}, 3-H Py, 6-H_{2B} Py), 4.43 (d, ^3J = 8.4 Hz, 1 H, 2-H, Py), 5.96 (d, ^3J = 2.7 Hz, 1 H, 3-H, Fu), 6.32 (m, 1 H, 4-H, Fu), 7.34 (d, ^3J = 1.3 Hz, 1 H, 5-H, Fu) ppm. ^{13}C NMR (CD_3OD): δ = 20.2 (C-5, Py), 25.8 (C-4, Py), 32.0 (Fu-CH_2), 62.7 (C-6, Py), 68.2 (Fu-CH_2-CH_2), 70.9 (C-3, Py), 103.5 (C-2, Py), 105.2 (C-2, Fu), 110.2 (C-3, Fu), 140.8 (C-4, Fu), 156.3 (C-1, Fu) ppm. $C_{11}H_{16}O_4$ (212.25): calcd. C 62.25, H 7.60; found C 62.05, H 7.89.

***cis*-2-[2-(Furan-2-yl)ethoxy]tetrahydropyran-3-ol (26):** M.p. 44–49 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56–1.62 (m, 2 H, 5-H, Py), 1.66–1.76 (m, 2 H, 4-H, Py), 2.75 (t, 2 H, Fu-CH_2), 3.46 (m, 1 H, 6-H_{2A}, Py), 3.62–3.84 (m, 4 H, Fu-CH_2-CH_{2A}, Fu-CH_2-CH_{2B}, 3-H Py, 6-H_{2B} Py), 4.43 (d, ^3J = 8.4 Hz, 1 H, 2-H, Py), 5.96 (d, ^3J = 2.7 Hz, 1 H, 3-H, Fu), 6.32 (m, 1 H, 4-H, Fu), 7.33 (d, ^3J = 1.3 Hz, 1 H, 5-H, Fu) ppm. ^{13}C NMR (CD_3OD): δ = 20.2 (C-5, Py), 23.0 (C-4, Py), 32.1 (Fu-CH_2), 61.5 (C-6, Py), 67.5 (Fu-CH_2-CH_2), 70.2 (C-3, Py), 100.3 (C-2, Py), 104.9 (C-2, Fu), 110.0 (C-3, Fu), 141.0 (C-4, Fu), 156.8 (C-1, Fu) ppm. $C_{11}H_{16}O_4$ (212.25): calcd. C 62.25, H 7.60; found C 62.22, H 7.72.

Synthesis of Model Compound 28: Pyridine (16 mg, 16.1 μL, 0.2 mmol) and *p*-toluenesulfonic acid monohydrate (TsOH, 19 mg, 0.1 mmol) were dissolved in dry dichloromethane (20 mL). 3,4-Dihydro-2*H*-pyran (84 mg, 78 μL, 1 mmol) and 2-(2-furyl)ethanol (112 mg, 1 mmol) were added, and the mixture was stirred at room temp. for 5 h. Evaporation of the solvent and chromatography on silica gel (*n*-hexane/toluene, 3:1, v/v) afforded acetal **28** as a colorless, viscous oil (153 mg, 78%), solidifying at 0 °C. It should be noted that TsOH causes a pronounced side-reaction of the 2-(2-furyl)ethanol, whereas pyridinium *p*-toluenesulfonate, formed in situ from pyridine and TsOH, is of sufficiently low acidity to catalyze the acetalization without affecting the integrity of the readily polymerizable furan moieties.

2-[2-(Furan-2-yl)ethoxy]tetrahydropyran (28): Yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50–1.62 (m, 4 H, 4-H, 5-H, Py), 1.64–1.95 (m, 2 H, 3-H, Py), 2.76 (t, 2 H, Fu-CH_2), 3.46–3.55 (m, 1 H, 6-H_{2A}, Py), 3.68 (t, 2 H, Fu-CH_2-CH_2-O), 3.81–3.89 (m, 1 H, 6-H_{2B}, Py), 4.51 (m, 1 H, 2-H, Py), 5.96 (d, ^3J = 2.8 Hz, 1 H, 3-H, Fu), 6.29 (m, 1 H, 4-H, Fu), 7.32 (d, ^3J = 1.2 Hz, 1 H, 5-H, Fu) ppm. ^{13}C NMR (CD_3OD): δ = 19.2 (C-4, Py), 25.3 (C-5, Py), 32.2 (Fu-CH_2), 32.3 (C-3, Py), 61.9 (C-6, Py), 68.8 (Fu-CH_2-CH_2), 99.1 (C-2, Py), 105.4 (C-3, Fu), 110.0 (C-4, Fu), 140.6 (C-5, Fu), 156.3 (C-2, Fu) ppm. $C_{11}H_{16}O_3$ (196.25): calcd. C 67.32, H 8.22; found C 67.34, H 8.30.

Thermal "Endwise Peeling" of Model Compounds 25, 26, and 28: *trans*-2-Hydroxy acetal **25** (212 mg, 1 mmol) was dissolved in a mixture of 1,4-dioxane and water (1:1, v/v, 50 mL), and ethyl acetoacetate (**1**, 156 mg, 0.15 mL, 1.2 mmol) was added, and the mixture was heated at reflux. After consumption of the model compound (TLC control), the mixture was cooled to room temp. An aliquot (100 μL) was withdrawn for CE and GC-MS analysis, and the solvents were evaporated in vacuo. The oily remainder was purified by chromatography on silica gel (*n*-hexane/toluene, 3:1, v/v) to afford butylfuran **27** as a colorless wax (199 mg, 94%). According to the same procedure, *cis*-2-hydroxy acetal **26** (30 mg, 0.14 mmol) was treated with ethyl acetoacetate, providing 34% (10 mg) of the starting material and 17% (7 mg) of the "peeling" product **27** after chromatography and workup. According to the same procedure, acetal **28** (196 mg, 1 mmol) and ethyl acetoacetate afforded no furan "peeling" product, and 92% (180 mg) of the starting material was recovered.

Ethyl 2-Methyl-5-butylfuran-3-carboxylate (27): M.p. 118–120 °C (ethanol). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, 3 H, CH_3 in Bu), 1.26 (t, 3 H, CH_3 in Et), 1.32 (sext, 2 H, 3-H in Bu), 1.55 (quint, 2 H, 2-H in Bu), 2.50 (s, 3 H, CH_3-Fu), 2.66 (t, 2 H, 1-H in Bu), 4.23 (q, 2 H, CH_2 in Et), 6.44 (s, 1 H, CH in Fu) ppm. ^{13}C NMR (CD_3OD): δ = 11.8 (CH_3 in Bu), 13.4 (CH_3 in Et), 14.2 (CH_3 in Fu), 20.8 (3-CH_2 in Bu), 30.4 and 31. 9 (C-1 and C-2 in Bu), 59.4 (CH_2 in Et), 106.4 (C-4), 113.2 (C-3), 155.6 (C-2), 156.3 (C-5), 163.0 (COO) ppm. $C_{12}H_{18}O_3$ (210.27): calcd. C 68.55, H 8.63; found C 68.61, H 8.69.

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