CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201000468

From Furan to Molecular Stairs: Syntheses, Structural Properties, and Theoretical Investigations of Oligocyclic Oligoacetals

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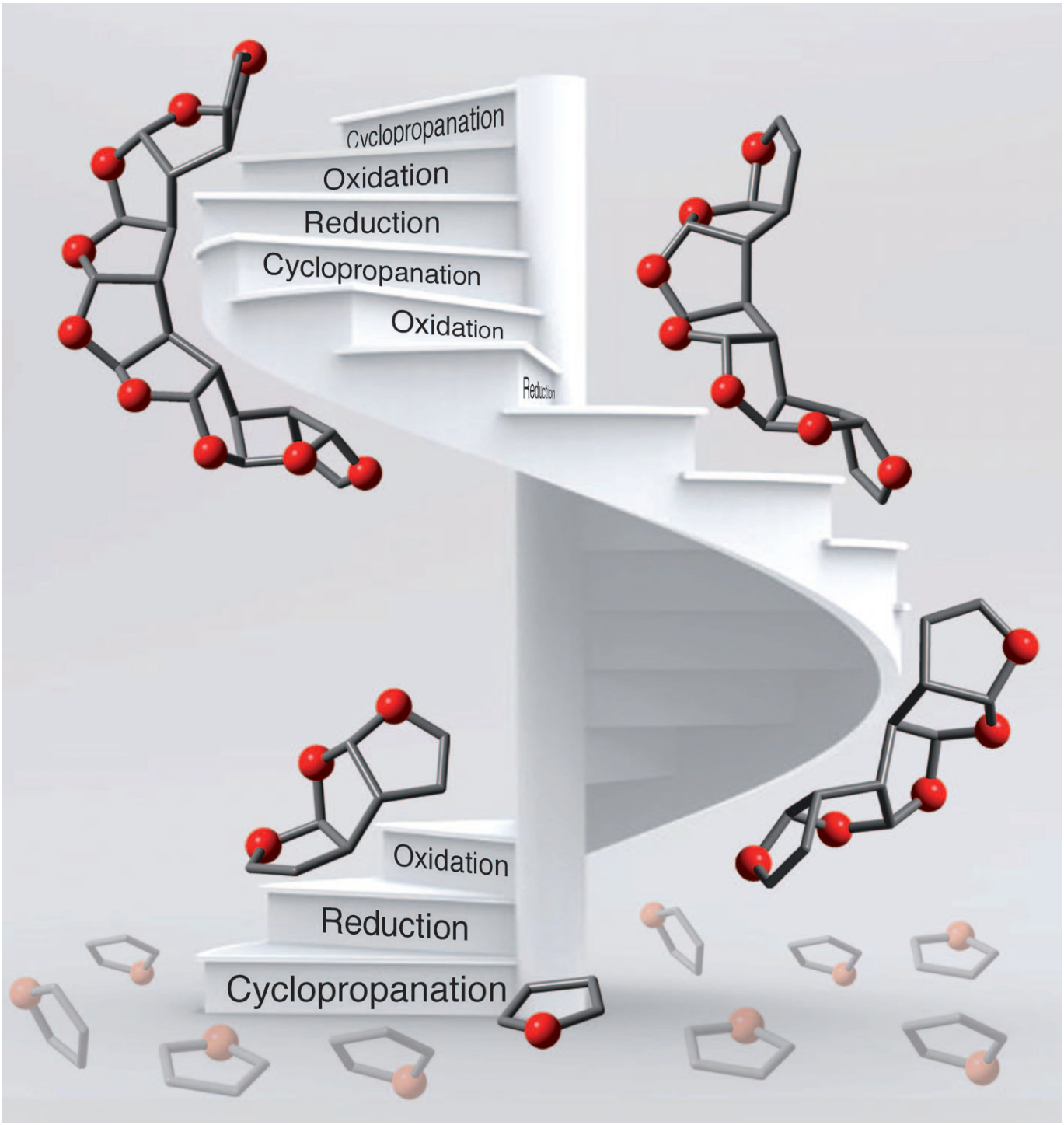
Dedicated to Professor Henning Hopf on the occasion of his 70th birthday



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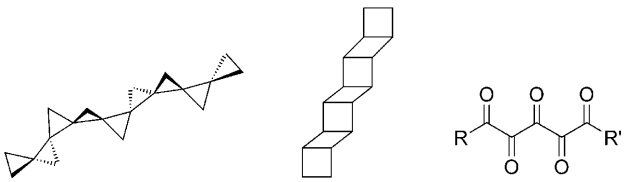
Abstract: The synthesis of oligocyclic oligoacetals using five-membered rings as repetitive unit is described. Furan was used as the starting material, which is converted by a three-step procedure consisting of twofold cyclopropanation, reduction, and oxidative ring enlargement into a tricyclic bis(enol ether). A repetition of this synthetic procedure leads to the formation of extended oligoacetal systems. Insights into the structures were gained by X-ray crystallographic investigations and revealed helical arrangements of the subunits in the solid-state. DFT (B3LYP) calculations have been carried out to elucidate the transition state of the ring enlargement and the flexibility of the annelated oligocyclic systems. Strain energies and topologies of potential cyclically condensed oligoacetals are predicted.

Keywords: acetals · cyclopropanes · ring expansion · structure elucidation

Introduction

Acetal and ketal moieties are ubiquitous in nature. The glycosidic bonds in oligosaccharides, the most abundant natural products, are acetal moieties, and ketal motives are found in a plethora of spiroketal metabolites.[1] However, the search for an extension of these structural units to the corresponding oligoacetals or oligoketals in natural products reveals almost no results.

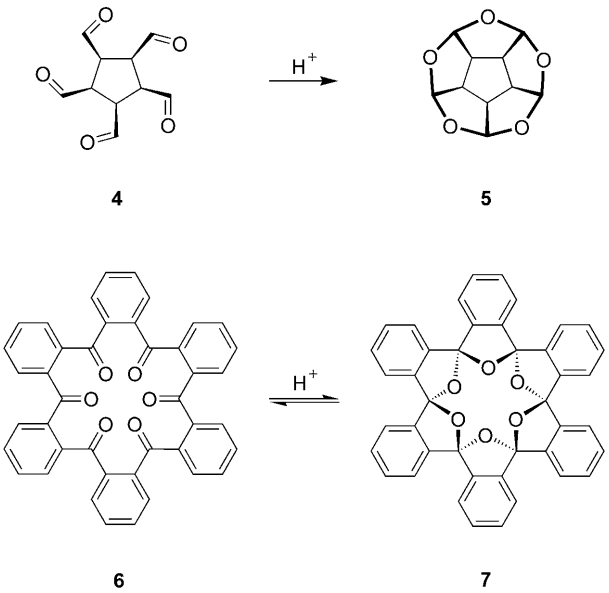
A repetition of structural units commonly leads to highly aesthetic molecules with often unusual properties. Prominent examples with repeating units arranged in a cyclic fashion are crown ethers,[2,3] cyclodextrins,[2,3] and cyclacenes.[4] Oligomers of defined length consisting of repeating units are also well-known, for example, the helical triangulanes of type **1** consisting of spiro-fused three-membered rings,[5] the ladderanes of type **2** consisting of annelated cyclobutane systems[6] or oligoketones such as **3** (Figure 1).[7] Very often repetitive strategies are applied in the synthesis of these compounds.[5–7]



1 2 3

Figure 1. Triangulane **1**, ladderane **2**, and pentaketone **3**.

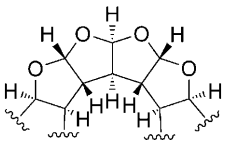
The challenge to synthesize distinct oligoacetals and oligoketals has been undertaken by several groups. For oligoacetals and oligoketals cyclically arranged, a domino cyclization approach was successfully carried out by the groups of Mehta[8] and Lee[9] using either aldehydes or ketones. In the presence of traces of acid starting materials **4** and **6** immediately led to the corresponding oligocyclic oligoacetal **5** and oligospiroketal **7**, respectively (Scheme 1).



4 5 6 7

Scheme 1. Syntheses of oligocyclic oligoacetal **5** and oligospiroketal **7** by Mehta[8] and Lee.[9]

Our approach to linear oligocyclic oligoacetals of type **8** uses a repetitive strategy to build up the acetal moieties. To reach this goal, we made use of the unique tendency of push–pull-substituted three-membered rings to open the bond between the electron-donating and electron-withdrawing substituents.[10] This property has been intensively investigated[10] and has led to remarkable syntheses of a variety of natural products.[11] It has been shown that donor–acceptor-substituted cyclopropanes can be used as 1,3-dipolar building



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blocks in acid-mediated rearrangement reactions,[12] and in ring-opening and ring-enlargement reactions[13] with electrophilic and nucleophilic double or triple bond systems. Ester groups have found wide use as acceptor substituents, whereas fewer reactions have been performed with aldehydes as acceptors.[14,15]

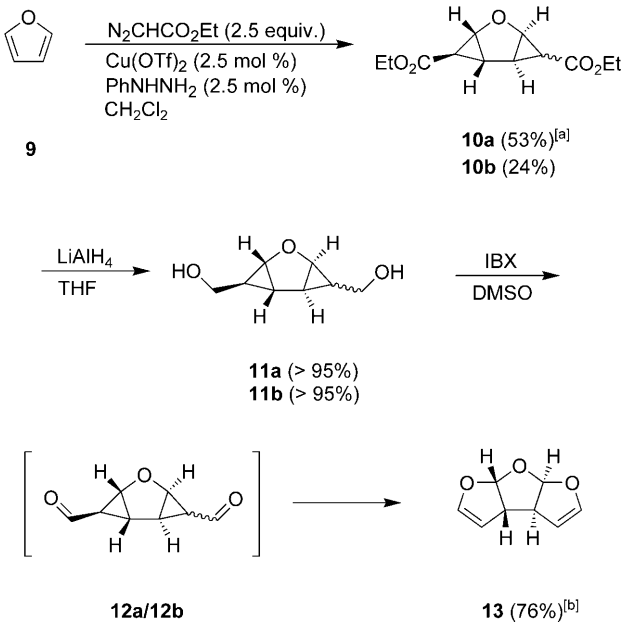
In this article we report full details of our recent communication[16] on the synthesis of *anti*-fused oligocyclic oligoacetals. Furthermore, we discuss their structural properties by means of X-ray investigations and DFT calculations.

Results and Discussion

Syntheses: Our synthetic endeavor towards the synthesis of *anti*-annelated five-membered ring acetals commenced with the use of furan as starting material. Furan (**9**) can be viewed as the simplest cyclic bis enol ether system and is prone to cyclopropanation reactions due to its reduced aromaticity.[17] The synthetic sequence for the formation of two acetal moieties and two new five-membered rings comprises of three steps and can be applied in a repetitive way leading to large (oligo)acetal structures consisting of annelated tetrahydrofuran units.

In the first step furan **9** was subjected to a Cu^{I}-mediated double cyclopropanation using ethyl diazoacetate in dichloromethane to afford a mixture of the tricyclic products **10a** and **10b** with two three-membered rings in an *anti*-arrangement (Scheme 2). The use of $LiAlH_4$ in THF yielded quantitatively the corresponding diols **11a** and **11b**. For the envisioned ring enlargement from the three-membered ring to the five-membered enol ether system an aldehyde functionality as substituent of cyclopropane is required. Therefore, several attempts were made to convert the hydroxymethyl unit into an aldehyde unit. Oxidizing agents such as pyridinium chlorochromate (PCC), tetra-*n*-propylammonium perruthenate (TPAP) or Dess–Martin periodinane only led to traces of the product. The Swern reaction also showed no product formation, but complete decomposition of the starting material. We assume that the oxidation reaction of the primary hydroxyl group to the corresponding aldehyde and also the subsequent ring enlargement take place in all cases. However, the newly formed enol ether system is also prone to oxidation and electrophilic addition. It seems natural that oxidizing agents and electrophiles may also attack the electron-rich double bond system. Finally, the only reagent suitable for the oxidative rearrangement of the diols **11** to the tricyclic bisacetal **13** proved to be 2-iodoxybenzoic acid (IBX) in DMSO.[18] Thus, compound **13** could be afforded in only three steps from furan in an overall yield of 56%.[16]

The tricyclic C_2-symmetric compound **13** can also be accessed in an enantioselective way by using a chiral catalyst for the cyclopropanation step. The best enantioselectivity that could be achieved was 86% *ee* by utilizing a C_2-symmetric bisoxazoline (box) ligand with phenyl substituents. Similar results and enantioselectivities were already



Scheme 2. Generation of the tricyclic bisacetal **13** from furan (**9**) by cyclopropanation, reduction, and oxidative rearrangement. [a] **a** designates always the C_2-, **b** the C_1-symmetrical product. [b] **11a** was used as starting material.

achieved for the monocyclopropanation of furans substituted by an electron-withdrawing group.[11b–d] However, due to a significantly reduced yield of the twofold cyclopropanation when using the chiral box ligand (35 vs. 77%) we abstained from pursuing our synthetic route with highly enantioenriched material.

To access larger oligoacetal structures the two electron-rich double bonds in the tricycle **13** are ideally suited for a repetition of the sequence described above. The twofold cyclopropanation of **13** proceeded with high *anti*-selectivity. In contrast to the very first cyclopropanation with furan as starting material our experiments have revealed that much better yields are obtained by using an almost stoichiometric amount (0.6–0.8 equiv) of elemental copper powder in hot toluene (Scheme 3). Ethyl diazoacetate was added in large excess to the reaction mixture over several hours via a syringe pump. Besides the C_2-symmetric compound **14a** the same amount of an asymmetric product **14b** was obtained; the latter differs from **14a** in the position of the ester group. One of the two ester units is oriented toward the adjacent five-membered ring. The two diastereomers could be separated by careful column chromatography. A separation is not really necessary to access the pentacyclic tetraacetal **18**, because both diastereomers **14a** and **14b** lead to the same product after reduction and oxidative rearrangement of the three-membered rings. Higher yields for the transformation were obtained when only the C_2-symmetric product was utilized. During the cyclopropanation at 100°C also traces of the diesters **15a/15b** with one three-membered ring being in *syn*-position to the adjacent THF moiety were found. Due to its very similar polarity a complete removal of this diaste-

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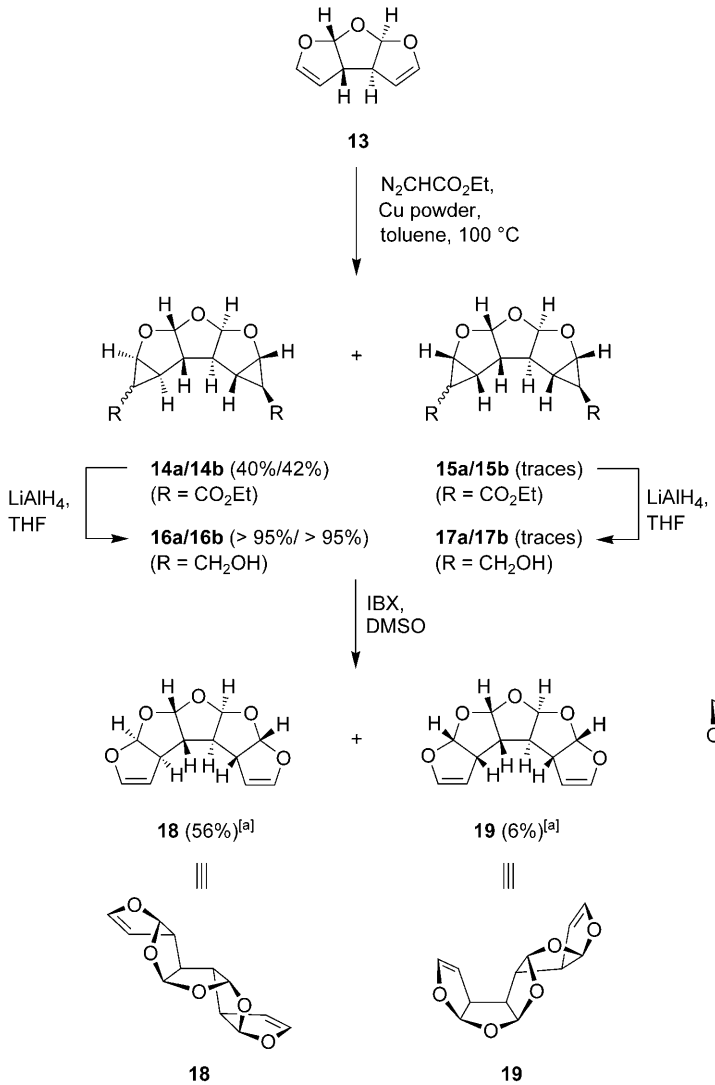
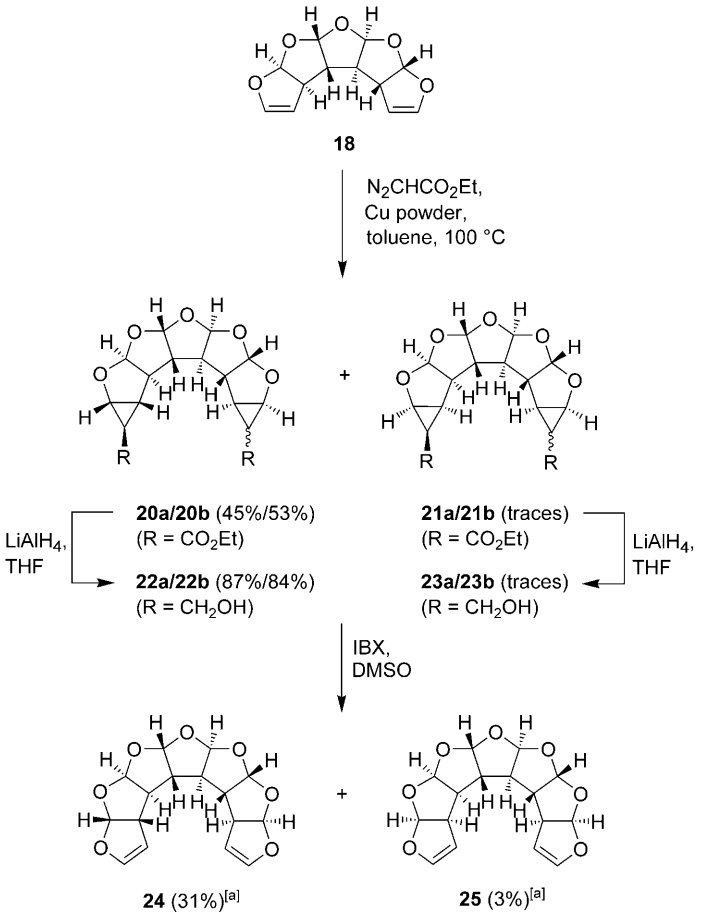
reomer proved to be almost impossible; the same holds true after the reduction to the diols **17a/17b**. However, after the oxidative rearrangement a separation of the two pentacyclic stereoisomers **18** and **19** did not cause any problems. Extensive 2D NMR spectroscopy analysis combined with NOE experiments as well as an X-ray crystallographic investigations have unambiguously proven the identity of compound **19**.

A further repetition of this sequence with the C_2-symmetric compound **18** led via the cyclopropyl diesters **20a/20b** and **21a/21b**, and the corresponding diols **22a/22b** and **23a/23b**, respectively, to the heptacyclic hexaacetals **24** and **25** (Scheme 4). Again, the cyclopropanation of **18** at 100 °C did not proceed with complete *anti*-selectivity giving rise to a minor amount of the asymmetric hexaacetal **25**.

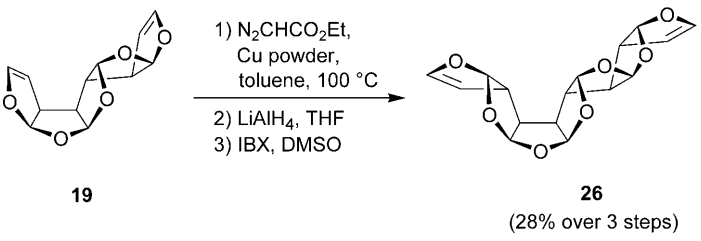
The asymmetric hexaacetal **19** was also subjected to the respective three-step procedure. The reduction was performed without further purification of the corresponding diastereomeric mixture of diesters, followed by subsequent oxidative ring enlargement. Thus, compound **26** being another asymmetric stereoisomer to **24** and **25** could be accessed (Scheme 5).



Scheme 3. Repetition of the three-step sequence to the pentacyclic tetraacetal **18** and its stereoisomer **19**. [a] **16a** (with traces of **17a**/**17b**) was used as starting material.



Scheme 4. Preparation of the heptacyclic hexaacetals **24** and **25**. [a] **22a** (with traces of **23a**/**23b**) was used as starting material.



Scheme 5. Formation of the asymmetric heptacyclic hexaacetal **26**.

The C_2-symmetric heptacyclic hexaacetal **24** was further transformed into the nonacyclic octaacetal **29** (Scheme 6). In comparison to the analogous transformations using the smaller congeners the yields in this sequence are significantly lower. We ascribe this to the dramatically reduced solubility of compounds **24** and **27**–**29**.

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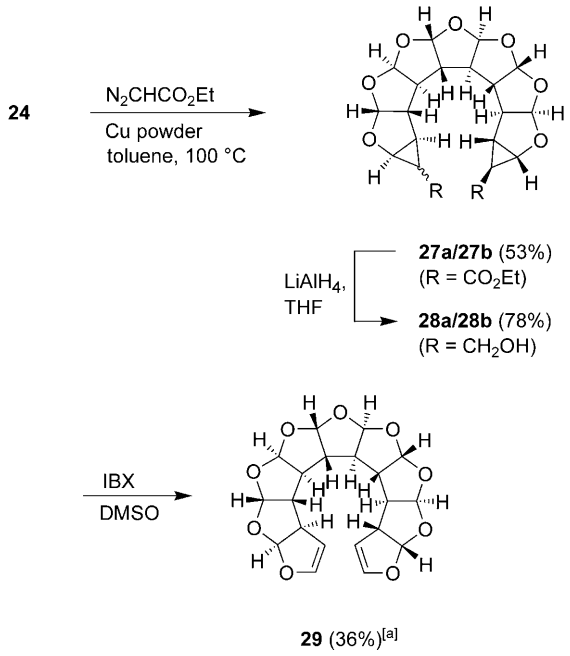


Scheme 6. Formation of the nonacyclic octaacetal **29**. [a] A mixture of **28a**/**28b** (2:1) was used as starting material.

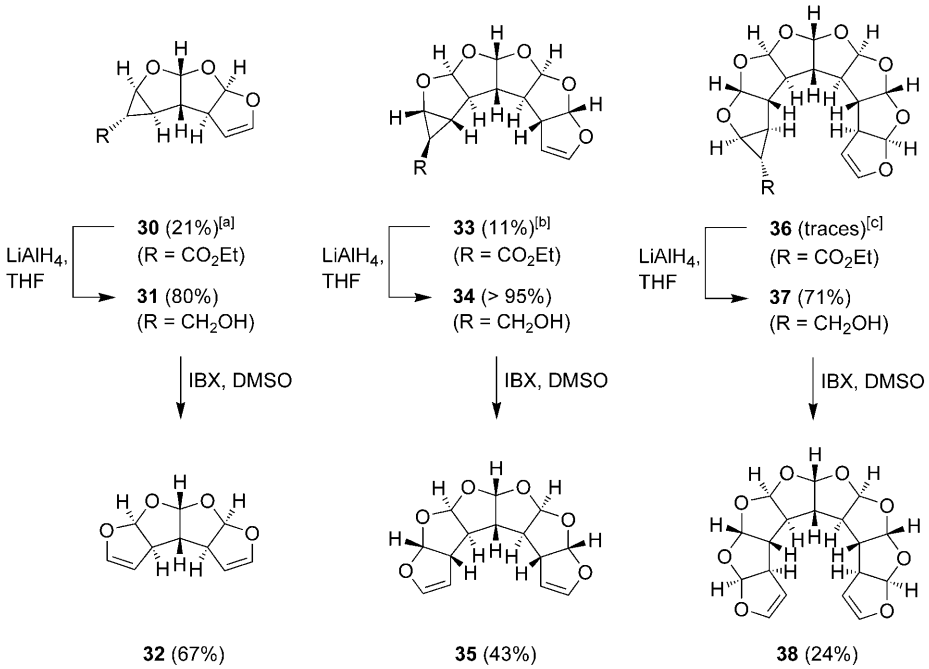
An entry to *anti*-annelated THF moieties with an even number of five-membered rings was possible by monocyclopropanation of oligoacetals with an odd number of corresponding rings. Such *anti*-annelated oligocyclic systems are achiral, C_s-symmetric compounds. Monocyclopropanated esters **30**, **33**, and **36** were achieved using less amounts of ethyl diazoacetate in the cyclopropanation reaction and are often also obtained as side products of the double cyclopropanation. Monoesters could easily be separated from the corresponding diesters by column chromatography due to their much lower polarity. Reduction and oxidative ring enlargement were performed as described above to afford the corresponding oligoacetals **32**, **35**, and **38** (Scheme 7).

Attempts to prepare the smallest congener of this series, the bicyclic bis(enol ether) **41**, were unsuccessful. The oxidation of the monocyclopropanated furan derivative **39** afforded a stereoisomeric mixture of the double unsaturated bisaldehydes **42** and **43** in low yields;[19] the desired bicycle could not be detected (Scheme 8).[20]

Structural investigations: For two systems with donor–acceptor-substituted three-membered rings (**10a** and **14a**) we were able to grow single crystals suitable for X-ray investigations. Crystallographic details of diesters **10a** and **14a** and further X-ray structure determinations are given in Tables 2 and 3 (see below). The molecular structures of the two diesters are depicted in Figure 2. As anticipated according to the Walsh model[21] of cyclopropane the plane of the ester moieties are almost perpendicular to the plane of the three-membered ring (87° (**10a**) und 85° (**14a**), respectively). A comparison of the bond lengths within the cyclopropane moiety, also in accord with the Walsh model, reveals the bond opposite to the electron-withdrawing group is the shortest (1.473/1.487 Å (**10a**) and 1.490 Å (**14a**)).

We were also able to grow single crystals of all oligocyclic oligoacetals (with exception of the octacyclic congener **38**). The structures with all-*anti*-annelated THF moieties are depicted in Figure 3. The structures with an odd number of five-membered rings (**13**, **18**, **24**, and **29**) also show a C_2 axis in the solid-state. However, the respective congeners with an even number of subunits (**32** and **35**) do not reveal a mirror plane in the solid-state. Due to the *anti*-annelation of five-membered rings all the molecular structures show the arrangement of corkscrew stairs (Figure 3). In contrast, analogous structures based on fused cyclobutane units show a ladder-type arrangement.

X-ray structural analyses were also obtained from the respective asymmetric oligoacetals **19**, **25**, and **26**. As already anticipated from extensive 2D NMR spectroscopic studies, one *syn*-arrangement of three adjacent THF moieties was confirmed by crystallographic analysis. Figure 4 depicts the



Scheme 7. Preparation of oligoacetals **32**, **35**, and **38** with an even number of five-membered rings. [a] Obtained as side product of the twofold cyclopropanation of **13** under Rh catalysis. [b] Obtained as side product of the twofold cyclopropanation of **18** under Rh catalysis. [c] Obtained as a mixture with **27a**/**27b**.

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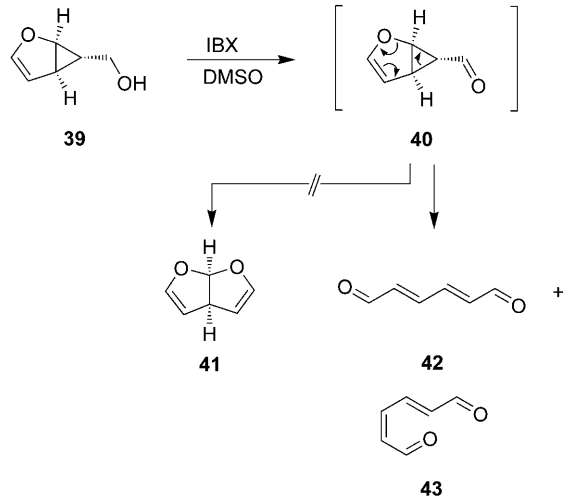


Scheme 8. Attempt to synthesize the bicyclic acetal **41**.

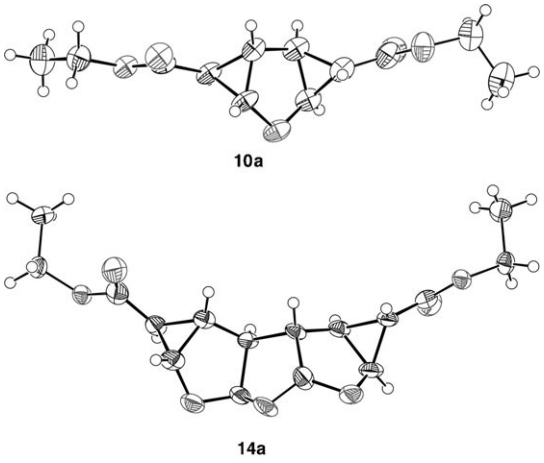
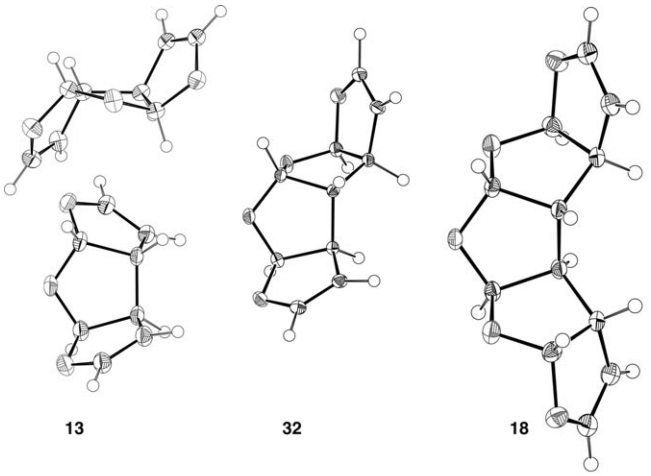


Figure 2. ORTEP plots of the molecular structures of diesters **10a** (top) and **14a**[16] (bottom) with donor-acceptor-substituted three-membered rings. Ellipsoids represent 50% probability level. Oxygen atoms are shown in light gray.



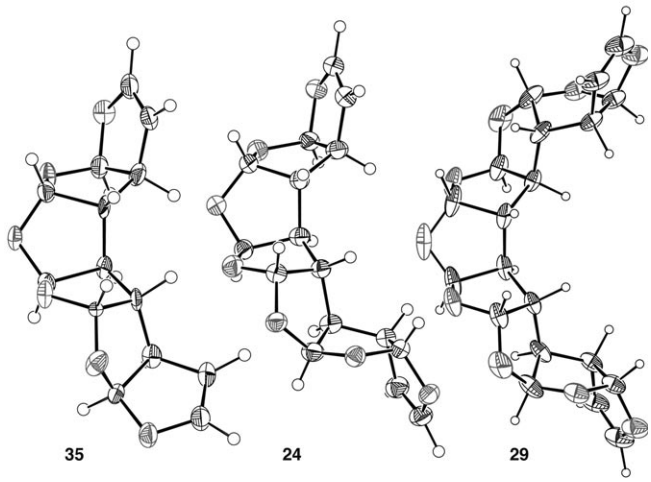


Figure 3. ORTEP plots of the molecular structures of linear *anti*-annelated oligoacetals with three (**13**, side and top view), four (**32**), five (**18**),[16] six (**35**), seven (**24**),[16] and nine (**29**) five-membered rings. Ellipsoids represent 50% probability level. Oxygen atoms are shown in light gray.

molecular structures of the two asymmetric heptacyclic hexaacetal isomers **25** and **26**.

A careful inspection of the C–O bond lengths in all oligoacetal structures reveals an interesting feature. The C–O distances vary between 1.385 and 1.443 Å with a mean value of about 1.42 Å. In almost all cases, two neighboring C–O bonds differ strongly in length. A long C–O bond is always located next to a relatively short one. Due to symmetry reasons (C_2 axis) the only exception are the C–O bonds of the middle THF unit of the oligoacetals with an odd number of subunits. We ascribe the phenomenon of the long–short alternance to the anomeric effect[22] resulting in a contraction and elongation of two adjacent

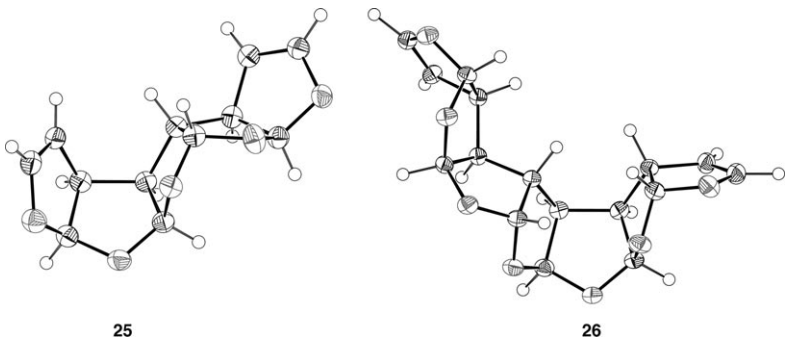


Figure 4. ORTEP plots of the molecular structures of the asymmetric linear annelated oligoacetals **25** (left) and **26** (right) with seven five-membered rings. Ellipsoids represent 50% probability level. Oxygen atoms are shown in light gray.

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Table 1. Most distinct differences of adjacent C–O bonds in (oligo)cyclic oligoacetals. Given are the pairs with the most significant differences of the bond lengths. The respective compound numbers are also given.

Compound	O–C [Å]	C–O [Å]
13	1.414	1.424
32	1.394	1.441
18	1.417	1.440
35	1.391	1.430
24[a]	1.414	1.432
29	1.385	1.434
19	1.394	1.431
25	1.394	1.443
26	1.392	1.431

[a] Refined with IAM scattering factor: comparison of bond lengths with other structures has to be taken with a grain of salt.

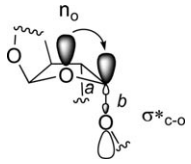
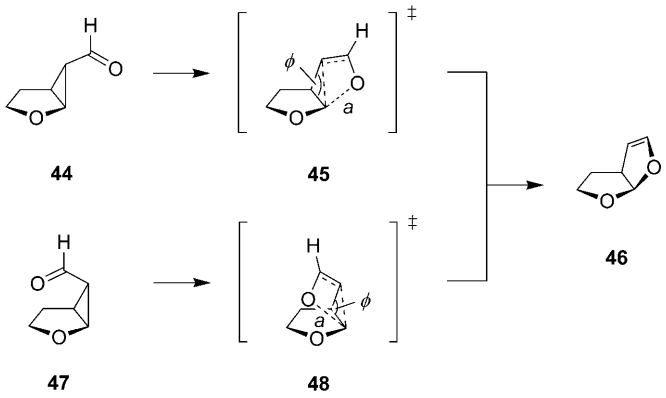


Figure 5. Schematic representation for the reason of the bond length alternance showing the interaction of the oxygen lone pair with the σ^*_{C-O} orbital of the adjacent C–O bond. The bond length of *a* is decreased whereas the bond length of *b* is increased.

bonds. The most distinct differences of vicinal C–O bond lengths are compiled in Table 1 for each oligoacetal. In these cases the five-membered ring is screwed in such a way that one lone pair of the oxygen donor in this subunit is situated in an exact parallel fashion to the adjacent C–O bond. As a result, one bond (*a*) is shortened, the other bond (*b*) is elongated (Figure 5).

DFT calculations: The key reaction for the synthesis of the acetal unit is the oxidative ring enlargement of the donor–acceptor-substituted three-membered ring into the five-membered enol ether system. Although a variety of experimental reports using ring opening and ring enlargements of push–pull-substituted cyclopropanes are known, a theoretical study for oxygen donors and aldehyde acceptors has not been carried out.[23] For the reaction of interest we used a simple model system consisting of a five- and a three-membered ring (**44** and **47**) as starting material. By means of density functional theory using the three-parameter hybrid functional by Becke (B3)[24] and the correlation functional suggested by Lee, Yang, and Parr (LYP)[25] we followed the course of the ring enlargement via **45** (and **48**, respectively) to the bicycle **46**. In order to allow biradicaloid transition structures we used the unrestricted open-shell (U)DFT procedure. As basis set we used 6-311G(d) as recommended by Pople et al., implemented in Gaussian 03.[26] All stationary points were characterized by harmonic vibrational frequency calculations, and all energies were corrected by zero-point vibrational energies. To gain insight into the respective potential hypersurface, we carried out a relaxed two-dimensional scan using two relevant parameters: the angle ϕ and the distance *a*. The angle ϕ was varied in steps of 5° (from 61 to 131°) whereas the distance *a* was varied in steps of 0.1 Å (from 3.66 to 1.46 Å). In addition, the area around the transition state **45** (compare Scheme 9) was further scanned by a smaller grid. In total 460 points were computed. The results are summarized in Figure 6. Further investigations have re-



Scheme 9. Ring enlargement investigated by UB3LYP/6-311G(d).

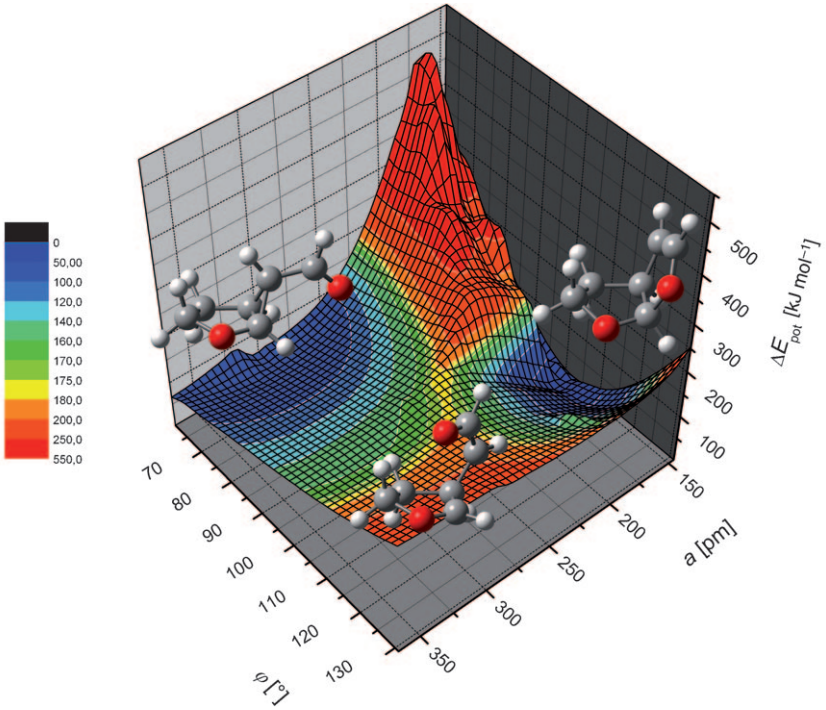


Figure 6. Potential surface according to UB3LYP/6-311G(d) for the reaction depicted in Scheme 9.

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vealed that a concerted mechanism takes place; neither hypothetical zwitterionic structures nor radical intermediates are accessible in energy.

For the vacuum the computations revealed that the product **46** is about 46 and 62 kJ mol^{-1} more stable than the starting materials **44** and **47**, respectively. The analogous calculations in DMSO using the PCM model[27] have shown that the energy gain is slightly smaller (41 and 58 kJ mol^{-1}). The transition states **45** and **48** are 133 and 103 kJ mol^{-1} higher in energy than the cyclopropane derivatives. However, in DMSO as solvent these activation barriers are decreased to 98 and 82 kJ mol^{-1}.

To test the conformational flexibility of *anti*-oligoannelated THF structures we carried out further quantum chemical calculations. Two systems, the synthesized nonacyclic octaacetal **29** and a hypothetical 13-mer **49** were studied in detail. For both compounds the distance *d* between the two outer oxygen atoms was varied stepwise by 1 Å. Small values of *d* force the molecule in a circular arrangement whereas large values of *d* result in a expanded array of fused tetrahydrofuran units. According to our computational investigations both compounds show a high conformational flexibility. For the 13-mer these results are illustrated in Figure 7. This behavior—somehow unusual for oligoannelated systems of normal rings—can be rationalized by the unique conformational properties of five-membered rings. For the parent compounds, cyclopentane and tetrahydrofuran, respectively, two low energy conformations (envelope and half-chair) exist being only separated by a rather small energy barrier. Due to the incorporation into five-membered rings anomeric effects operating at the acetal moieties do not really play a crucial role for the fixation of distinct conformations in solution. Small alterations of the bond angles at the tetrahedral carbon atoms are only associated with tiny changes of the potential energy. All in all, these facts can lead to dramatic conformational changes of the oligocyclic system. Such a behavior stands in sharp contrast to the conformational flexibility of annelated π-systems or fused saturated six-membered rings.

In order to get an impression how many *anti*-annelated THF subunits are required to form a macrocyclic oligoacetal we performed systematic theoretical calculations within this series. All geometrical parameters of the macrocyclic congeners **50**–**56** were optimized (without any symmetry restriction) using the same method and basis as employed for the calculation of the potential hypersurface, with the exception of a closed shell rather than a unrestricted B3LYP calculation. Starting

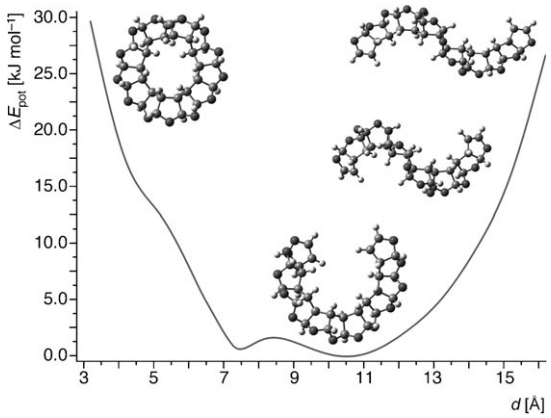

Figure 7. Calculated potential energy relative to the minimum structure of a potential 13-mer **49** dependent on the distance *d* between the two outer oxygen atoms at the B3LYP/6-311G(d) level of theory. Oxygen atoms are shown in dark gray.

point for our calculations was a hypothetical macrocyclic structure **50** consisting of eight THF subunits. Due to the *all-anti* annelation only macrocycles with even numbers of THF moieties were considered. Therefore, we investigated next to **50** the higher congeners with ten (**51**), twelve (**52**), fourteen (**53**), sixteen (**54**), eighteen (**55**), and twenty (**56**) subunits (see Figure 8). With the exception of cyclic 8-mer **50** all structures were identified as minima on the potential surface ($N_{Imag}=0$). According to our calculations, the macrocyclic system consisting of 16 subunits is almost strain-free and was used as reference. Figure 8 summarizes the calculated relative strain energy per THF subunit. Starting from **51** the strain decreases significantly until **54**, proceeding from **54** to the larger members of this family (**55**, **56**) the strain rises slightly. It is noteworthy that the smaller macrocycles **52** and **53** do not show any bowl-like topography. A similar behavior was recently investigated for annelated π-systems

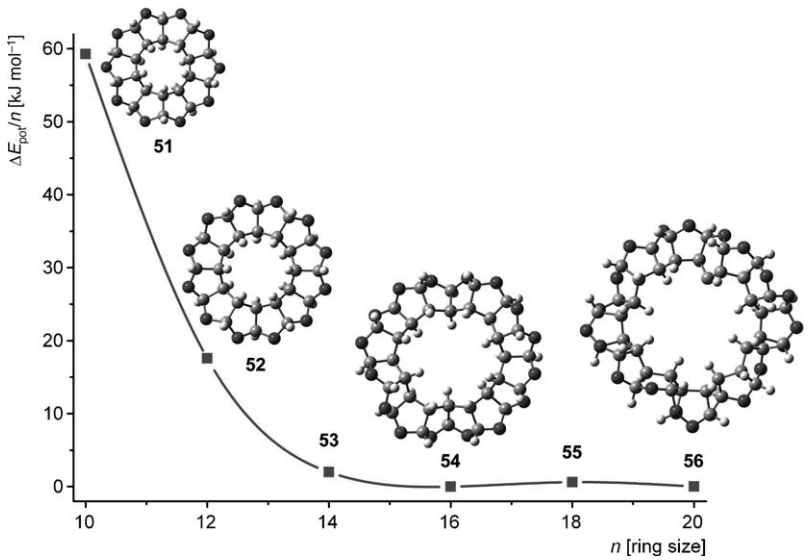

Figure 8. Calculated strain energies (relative to the most stable cyclic 16-mer **54**) per THF subunit at the B3LYP/6-311G(d) level of theory. Oxygen atoms are shown in dark gray.

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such as coronene and [4]circulene.[28] In order to accommodate the further THF subunits the macrocycles larger than the 16-mer (**54**) evade to a saddle-like topography.

Conclusion

Our investigations demonstrate that oligoacetals with *anti*-annelated THF moieties can be prepared by a repetitive strategy starting from furan. By applying a three-step procedure consisting of twofold cyclopropanation using ethyl diazoacetate, reduction of the corresponding esters and subsequent oxidative ring enlargement of the push–pull-substituted three-membered rings the tricyclic bisacetal **13** could be obtained. A repetition of the sequence allowed access to the corresponding oligoacetals **18**, **24**, and **29** with an odd number of subunits. An entry to the congeners with an even number of subunits is the monocyclopropanation, followed by reduction and oxidative rearrangement.

Structural investigations of the larger oligoacetals by means of X-ray crystallography revealed arrangements of annelated five-membered rings in a corkscrew stairs-like fashion. Due to anomeric stabilization pronounced differences between the bond lengths of two adjacent C–O bonds were found in the solid state.

DFT calculations were carried out in order to elucidate the transition states of the ring enlargement. For this concerted mechanism activation barriers in DMSO of 82 kJ mol^{-1} (for *cis* substituents) and 98 kJ mol^{-1} (for *trans* substituents) were found. Additional computational studies have shown that the products of the sequence—the oligoannelated oligoacetals—are conformationally rather flexible compounds. Even larger analogues are not expected to be separated in helical enantiomers. Furthermore, we studied the optimal size of a hypothetical macrocyclic system consisting of *all-anti*-annelated THF moieties. These computations revealed that a cyclic arrangement of 16 THF units shows the least strain energy.

Our synthetic investigations may serve as a useful starting point for the synthesis of fused furans which are—in sharp contrast to fused thiophenes—hitherto still unknown for more than two subunits. Such structures would be of high interest in terms of materials science and should be accessible by dehydrogenation of *anti*-annelated THF scaffolds.

Experimental Section

General methods: All solvents were distilled before use unless otherwise stated. Tetrahydrofuran (THF) was distilled from sodium/benzophenone under a nitrogen atmosphere. CH_2Cl_2 and toluene were distilled from $CaCl_2$ under a nitrogen atmosphere. Air- and moisture-sensitive reactions were carried out in flame-dried glassware, septum-capped under atmospheric pressure of argon. Commercially available compounds were used without further purification unless otherwise stated. Melting points (m.p.) are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 300, 400, 500 or 600 MHz instrument using the residual signals from $CHCl_3$, δ 7.26 ppm and δ 77.0 ppm, and methanol, δ 4.87 ppm and δ 49.2 ppm, as internal references for ^{1}H and ^{13}C, respectively. Assignments of the respective signals were made by the combination of H,H-COSY, HSQC, HMBC, and NOESY experiments. ESI-HRMS mass spectrometry was carried out on a FTICR instrument. IR spectra were measured on Vector 22 spectrometer (Bruker). UV spectra were measured with a Lambda 2 photometer (Perkin–Elmer). IBX was synthesized according to literature methods.[18] Analytical data of compounds not described in this section have been reported previously.[16]

Preparation of 19: The C_2-symmetric diol **16a** (202 mg, 841 μmol, 1.0 equiv) with impurities of **17a/17b** was dissolved in DMSO (15 mL). IBX (518 mg, 1.85 mmol, 2.2 equiv) was added and the reaction mixture was stirred for 9 h at RT. After addition of water (10 mL) the solution was extracted with EtOAc (5×15 mL). The combined organic phases were washed with water (20 mL) and dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue was purified by silica gel column chromatography (pentane/EtOAc 3:1 → 2:1) to afford **18** (111 mg, 56%) and **19** (11.8 mg, 6%) as colorless solids.

Analytical data of **19**: R_f = 0.29 (pentane/EtOAc 1:1); m.p. 167 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.71–2.77 (m, 1H), 2.88 (dd, J = 9.8, 4.7 Hz, 1H), 3.31 (m, 1H), 3.53–3.63 (m, 1H), 4.95 (dd, J = 2.8, 2.8 Hz, 1H), 5.00 (dd, J = 2.6, 2.5 Hz, 1H), 5.77 (d, J = 4.9 Hz, 1H), 5.85 (d, J = 4.7 Hz, 1H), 6.06 (d, J = 6.1 Hz, 1H), 6.19 (d, J = 6.8 Hz, 1H), 6.28 (dd, J = 2.5, 2.5 Hz, 1H), 6.37 ppm (dd, J = 2.6, 2.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.0, 49.9, 52.7, 53.9, 99.5, 103.5, 108.3, 108.6, 109.1, 112.9, 144.6, 146.7 ppm; IR (KBr): $\tilde{\nu}$ = 3099, 2981, 1620, 1383, 1315, 1235, 1126 cm^{-1}; UV (CH_3CN): λ_{max} (log ε) = 201 (4.017), 251 nm (2.875); MS (ESI): m/z (%): 259.1 (100) $[M+Na]^+$, 495.1 (55) $[2M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{12}H_{12}O_5Na$: 259.05769; found: 259.05782.

Preparation of 25: Diol **22a** (172 mg, 530 μmol, 1.0 equiv) with impurities of the asymmetric diols **23a/23b** and IBX (327 mg, 1.17 mmol, 2.2 equiv) were dissolved in DMSO (25 mL). The reaction mixture was stirred for 8 h at RT. After addition of water (15 mL) the solution was extracted with EtOAc (5×20 mL). The combined organic phases were washed with water (20 mL) and dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH 150:1 → 120:1) to afford **24** (52.0 mg, 31%) and **25** (4.7 mg, 3%) as colorless solids.

Analytical data of **25**: R_f = 0.37 (CH_2Cl_2/MeOH 25:1); ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.60–2.67 (m, 1H), 2.76 (dd, J = 6.0, 4.5 Hz, 1H), 2.88 (pt, J = 4.6 Hz, 1H), 2.99 (dd, J = 9.8, 4.6 Hz, 1H), 3.49 (m, 1H), 3.55–3.59 (m, 1H), 5.09 (pt, J = 2.6 Hz, 1H), 5.14 (pt, J = 2.7 Hz, 1H), 5.54 (d, J = 5.0 Hz, 1H), 5.71 (d, J = 4.7 Hz, 1H), 5.74 (2d, J = 4.6, 4.6 Hz, 2H), 6.03 (d, J = 5.9 Hz, 1H), 6.11 (d, J = 6.8 Hz, 1H), 6.43–6.46 ppm (m, 2H); ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 47.4, 48.9, 51.4, 52.8, 53.0, 53.1, 100.4, 103.8, 107.7, 107.7, 108.0, 108.4, 108.5, 112.0, 144.0, 145.0 ppm; IR (KBr): $\tilde{\nu}$ = 3098, 2962, 2935, 1728, 1615, 1376 cm^{-1}; UV (CH_3CN): λ_{max} (log ε) = no absorption between 190–350 nm; MS (EI): m/z (%): 343.1 (100) $[M+Na]^+$, 663.2 (20) $[2M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{16}H_{16}O_7Na$: 343.0788; found: 343.0791.

Preparation of 26: A solution of **19** (88.0 mg, 373 μmol, 1.0 equiv) and copper powder (14.0 mg, 224 μmol, 0.6 equiv) in toluene (8 mL) was heated to 100 °C. A solution of ethyl diazoacetate (213 mg, 1.86 mmol, 5.0 equiv) in toluene (8 mL) was slowly added via a syringe pump (1 mL h^{-1}). The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (CH_2Cl_2/MeOH 50:1) to afford a diastereomeric mixture of esters **21a** and **21b**. The esters were dissolved in THF (25 mL), slowly dropped into a solution of $LiAlH_4$ (38.0 mg, 949 μmol, 2.5 equiv) in THF (30 mL) and stirred for 2 h at RT. Methanol (50 mL) was added dropwise to destroy excess lithium aluminum hydride. The solvents were removed in vacuo. After purification via silica gel column chromatography (CH_2Cl_2/MeOH 10:1) a diastereomeric mixture of the two diols **23a** and **23b** was obtained. The two diols were dissolved in DMSO (25 mL), IBX (181 mg, 646 μmol, 1.7 equiv) was added and the solution was stirred for 8 h at RT. After addition of water (20 mL) the solution was extracted with EtOAc (5×25 mL). The combined organic phases were washed with water (50 mL) and dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH 20:1)

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to afford **26** (34.0 mg, 28% over 3 steps) as a colorless solid. R_f = 0.55 (CH_2Cl_2/MeOH 20:1); m.p. 174°C; ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 2.64 (dd, J = 4.8, 4.8 Hz, 1H), 2.67–2.70 (m, 1H), 2.88–2.95 (m, 2H), 3.56–3.59 (m, 1H), 3.60–3.63 (m, 1H), 5.03 (dd, J = 2.5, 2.5 Hz, 1H), 5.06 (dd, J = 2.6, 2.6 Hz, 1H), 5.67 (d, J = 4.6 Hz, 1H), 5.71–5.73 (m, 2H), 5.83 (d, J = 4.9 Hz, 1H), 6.04 (d, J = 6.0 Hz, 1H), 6.09 (d, J = 5.8 Hz, 1H), 6.45 (dd, J = 2.5, 2.5 Hz, 1H), 6.50 ppm (dd, J = 2.6, 2.6 Hz, 1H); ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 47.4, 48.6, 49.4, 49.7, 51.1, 53.9, 103.5, 103.6, 107.6, 107.7, 108.0, 109.0, 109.5, 110.7, 144.2, 144.5 ppm; IR (KBr): $\tilde{\nu}$ = 3111, 2964, 1616, 1370, 1319, 1210, 1035 cm^{-1}; UV (CH_3CN): λ_{max} (log ε) = 200.5 nm (4.061); MS (ESI): m/z (%): 343.1 (38) $[M+Na]^+$, 663.2 (100) $[2s+Na]^+$; HRMS (ESI): m/z: calcd for $C_{16}H_{16}O_7Na$: 343.0788; found: 343.0789.

Preparation of 30: To a solution of the unsaturated tricyclic compound **13** (1.35 g, 8.87 mmol, 1.0 equiv) and dirhodium tetraacetate (39.2 mg, 88.7 μmol, 3.0 mol%) in CH_2Cl_2 (200 mL) a solution of ethyl diazoacetate (2.53 g, 22.2 mmol, 2.5 equiv) in CH_2Cl_2 (50 mL) was slowly added via a syringe pump (5 mL h^{-1}). After evaporation of the solvent the crude product was purified by silica gel column chromatography (pentane/EtOAc 5:1 → 3:1) to afford **14a** and **14b** (1.562 g, 54%) and **30** (435 mg, 21%) as yellow oils. Better yields of **14a/14b** were obtained using a copper-mediated cyclopropanation in toluene as solvent at 100°C. In the latter case compound **30** was not obtained.

Analytical data of **30**: R_f = 0.25 (pentane/EtOAc 5:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, J = 7.1 Hz, 3H), 1.53 (dd, J = 4.0, 1.0 Hz, 1H), 2.03 (m, 1H), 2.83 (d, J = 4.4 Hz, 1H), 3.54 (m, 1H), 4.05 (q, J = 7.1 Hz, 2H), 4.29 (dd, J = 5.6, 1.0 Hz, 1H), 4.91 (dd, J = 2.6, 2.5 Hz, 1H), 5.59 (d, J = 4.4 Hz, 1H), 6.19 (d, J = 5.8 Hz, 1H), 6.27 ppm (dd, J = 2.6, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 29.5, 31.1, 52.0, 52.4, 60.7, 65.2, 102.8, 108.4, 112.6, 145.0, 169.9 ppm; MS (ESI): m/z (%): 261.07 (55) $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{12}H_{14}O_5Na$: 261.07334; found 261.07347.

Preparation of 31: A solution of **30** (378 mg, 1.59 mmol, 1.0 equiv) in THF (15 mL) was added slowly to a solution of $LiAlH_4$ (144 mg, 3.81 mmol, 1.4 equiv) in THF (35 mL). The reaction was stirred for 2 h at RT. TLC control showed the completion of the reaction. Methanol was added dropwise to destroy excess lithium aluminum hydride. The reaction mixture was concentrated by rotary evaporation. The crude product was purified by silica gel column chromatography (CH_2Cl_2/MeOH 30:1 → 20:1) to afford **31** (251 mg, 80%) as a colorless solid. R_f = 0.15 (CH_2Cl_2/MeOH 20:1); m.p. 118°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (m, 1H), 1.38 (d, J = 5.1, 4.9 Hz, 1H), 1.79 (br s, 1H), 2.75 (d, J = 4.2 Hz, 1H), 3.23–3.33 (m, 1H), 3.37–3.46 (m, 1H), 3.51 (d, J = 6.0 Hz, 1H), 3.97 (dd, J = 5.9,1.3 Hz, 1H), 4.92 (dd, J = 2.6, 2.6 Hz, 1H), 5.62 (d, J = 4.2 Hz, 1H), 6.20 (d, J = 5.9 Hz, 1H), 6.28 ppm (dd, J = 2.6, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 25.1, 32.7, 52.2, 52.9, 61.7, 63.2, 103.1, 108.2, 114.1, 144.8 ppm; IR (KBr): $\tilde{\nu}$ = 3328, 3102, 2961, 1615, 1415, 1211, 1030 cm^{-1}; UV (CH_3CN): λ_{max} (log ε) = 200.5 nm (3.762); MS (ESI): m/z (%): 197.1 (4) $[M+H]^+$, 219.1 (2) $[M+Na]^+$, 415.4 (68) $[2M+Na]^+$, 807.0 $[4M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{10}H_{12}O_4Na$: 219.06278; found 261.06289.

Preparation of 32: The tetracyclic alcohol **31** (186 mg, 948 μmol, 1.0 equiv) was dissolved in DMSO (25 mL). IBX (319 mg, 1.14 mmol, 1.2 equiv) was added to the solution and the mixture was stirred for 8 h at RT. After addition of water (20 mL) the solution was extracted with EtOAc (5×20 mL). The combined organic phases were washed with water (20 mL) and dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue was purified by silica gel column chromatography (pentane/EtOAc 7:1) to afford **32** (123 mg, 67%) as a colorless solid. R_f = 0.39 (pentane/EtOAc 5:1); m.p. 117°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.60 (m, 1H), 3.37 (m, 2H), 4.99 (dd, J = 2.6, 2.5 Hz, 2H), 5.89 (d, J = 4.6 Hz, 1H), 6.09 (d, J = 6.2 Hz, 2H), 6.28 ppm (dd, J = 2.6, 2.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 52.3, 54.4, 103.3, 107.9, 108.6, 144.8 ppm; IR (KBr): $\tilde{\nu}$ = 3113, 2977, 2924, 1617, 1365, 1308, 1272, 1139 cm^{-1}; UV (CH_3CN): λ_{max} (log ε) = 200.5 nm (4.039); MS (ESI): m/z (%): 217.1 (100) $[M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{10}H_{10}O_4Na$: 217.04713; found: 217.04716.

Preparation of 33: To a solution of **18** (345 mg, 1.46 mmol, 1.0 equiv) and dirhodium tetraacetate (6.5 mg, 14.6 μmol, 3.0 mol%) in CH_2Cl_2 (25 mL) a solution of ethyl diazoacetate (500 mg, 4.38 mmol, 3.0 equiv) in CH_2Cl_2 (10 mL) was slowly added via a syringe pump (1 mL h^{-1}). After evaporation of the solvent the crude product was purified by silica gel column chromatography (pentane/EtOAc 4:1 → 3:1) to afford **20a** and **20b** (207 mg, 52%) and **33** (51 mg, 11%) as a yellow oil.

Analytical data of **33**: R_f = 0.52 (pentane/EtOAc 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, J = 7.1 Hz, 3H), 1.53 (dd, J = 4.0, 1.1 Hz,

Table 2. Crystal data and structure refinement for compounds **10a**, **13**, **14a**, **18**, **19**, and **24**.

Compound	**10a**[a]	**13**	**14a**[a]	**18**	**19**	**24**[a]
CCDC	764648	764650	725973[16]	720562[16]	764652	720971[16]
empirical formula	$C_{12}H_{16}O_5$	$C_8H_8O_3$	$C_{16}H_{20}O_7$	$C_{12}H_{12}O_5$	$C_{12}H_{12}O_5$	$C_{16}H_{16}O_7$
formula weight	240.25	152.14	324.32	236.22	236.22	320.29
wavelength [Å]	0.71073	0.71073	0.71073	0.71073	1.54178	1.54178
crystal system	monoclinic	orthorhombic	monoclinic	orthorhombic	orthorhombic	orthorhombic
space group	$P2_1/c$	$Pbca$	$P2/c$	$C222$	$P2_12_12_1$	$Fdd2$
unit cell dimensions						
a [Å]	14.589(4)	8.9224(11)	11.269(3)	6.1208(7)	6.3179(3)	42.329(8)
b [Å]	8.569(3)	10.1536(14)	5.3090(16)	9.984(2)	9.4245(3)	5.8139(13)
c [Å]	10.423(3)	15.218(2)	12.835(4)	17.437(2)	16.7351(6)	11.242(2)
α [°]	90	90	90	90	90	90
β [°]	109.333(4)	90	90.832(5)	90	90	90
g [°]	90	90	90	90	90	90
Z	4	8	2	8	4	8
V [Å^3]	1229.5(6)	1378.7(3)	767.8(4)	1065.5(4)	996.46(7)	2766.6(9)
ρ_{calcd} [g cm^{-3}]	1.298	1.446	1.403	1.472	1.574	1.538
μ [mm]	0.101	0.113	0.110	0.116	1.046	1.034
θ range for data coll. [°]	2.96–25.80	2.50–26.41	3.20–25.74	3.90–26.93	5.29–71.65	4.18–70.54
index ranges	$-17 \le h \le 16$ $0 \le k \le 10$ $0 \le l \le 12$	$-7 \le h \le 11$ $0 \le k \le 12$ $0 \le l \le 19$	$-13 \le h \le 13$ $0 \le k \le 6$ $0 \le l \le 15$	$-8 \le h \le 8$ $0 \le k \le 13$ $0 \le l \le 24$	$0 \le h \le 7$ $0 \le k \le 11$ $0 \le l \le 20$	$0 \le h \le 51$ $0 \le k \le 6$ $0 \le l \le 13$
reflns collected	15806	30212	7439	15165	14064	6881
independent reflns	1646	1409	1435	1507	1150	677
reflns observed	1646	1169	1049	1284	1117	643
observ. data/parameters	1646/203	1169/100	1049/139	1284/96	1117/154	643/105
goodness-of-fit[b]	1.12[c]	3.52	1.08	1.69	2.64	1.19
$R(F)$	0.0864	0.0354	0.0556	0.0293	0.0157	0.0612
$R_w(F^2)$	0.2293	0.0423	0.1256	0.0379	0.0186	0.1711
$(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ [e Å^{-3}]	0.648, −0.301	0.216, −0.251	0.400, −0.345	0.245, −0.172	0.077, −0.101	0.362, −0.289

[a] Structure was refined with IAM scattering factors. [b] A weighting Scheme of $w = 1/\sigma^2$ was used as common for aspherical atom refinements. In case the experimental σ values are underestimated, the goodness-of-fit with this weighting scheme can deviate substantially from unity. [c] On F^2 using all reflections.

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1H), 2.07 (dd, $J=5.5$, 4.1 Hz, 1H), 2.53 (dd, $J=5.3$, 5.0 Hz, 1H), 2.63 (dd, $J=5.4$, 5.2 Hz, 1H), 2.89 (dd, $J=4.6$, 2.7 Hz, 1H), 3.49 (m, 1H), 4.08 (q, $J=7.1$ Hz, 2H), 4.33 (d, $J=4.4$ Hz, 1H), 4.95 (dd, $J=2.8$, 2.4 Hz, 1H), 5.62 (d, $J=4.6$ Hz, 1H), 5.87 (d, $J=4.4$ Hz, 1H), 6.03 (d, $J=4.6$ Hz, 1H), 6.13 (d, $J=5.9$ Hz, 1H), 6.34 ppm (dd, $J=2.6$, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=14.3$, 29.4, 30.7, 51.9, 52.3, 54.0, 54.3, 60.9, 65.2, 102.6, 108.1, 108.9, 109.5, 111.9, 145.4, 169.7 ppm.

Preparation of 34: A solution of **33** (51.0 mg, 158 μmol, 1.0 equiv) in THF (10 mL) was slowly dropped into a solution of $LiAlH_4$ (8.5 mg, 221 μmol, 1.4 equiv) in THF (15 mL). The reaction was stirred 2 h at RT and methanol was added dropwise to destroy excess lithium aluminum hydride. The solvents were removed in vacuo and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH 30:1 → 20:1) to afford **34** (44.0 mg, 99%) as a colorless solid. $R_f=0.18$ (CH_2Cl_2/MeOH 20:1); ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta=0.86$ (m, 1H), 1.39 (dd, $J=4.9$, 4.9 Hz, 1H), 2.61 (dd, $J=5.0$, 5.0 Hz, 1H), 2.74 (dd, $J=5.8$, 4.4 Hz, 1H), 2.78 (d, $J=4.4$ Hz, 1H), 3.03–3.16 (m, 1H), 3.17–3.25 (m, 1H), 3.55 (m, 1H), 3.85 (dd, $J=5.8$, 1.3 Hz, 1H), 4.49 (t, $J=5.5$ Hz, 1H), 5.07 (dd, $J=2.6$, 2.5 Hz, 1H), 5.53 (d, $J=4.3$ Hz, 1H), 5.68 (d, $J=4.6$ Hz, 1H), 5.86 (d, $J=4.7$ Hz, 1H), 6.05 (d, $J=5.8$ Hz, 1H), 6.44 ppm (dd, $J=2.6$, 2.5 Hz, 1H); ^{13}C NMR (125 MHz, [D$_6$]DMSO): $\delta=24.1$, 31.8, 51.2, 52.0, 53.0, 53.0, 59.7, 62.8, 103.8, 107.6, 108.0, 108.7, 112.9, 144.3 ppm; IR (KBr): $\tilde{\nu}=3410$, 2965, 1614, 1336, 1302, 1215 cm^{-1}; UV (MeOH): λ_{max} (log ε) = 201.5 (3.896), 203.0 nm (3.781); MS (ESI): m/z (%): 303.1 (85) $[M+Na]^+$, 583.2 (100) $[2M+Na]^+$, 863.3 (30) $[3M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{14}H_{16}O_6Na$: 303.08391; found: 303.08402.

Preparation of 35: Alcohol **34** (44.0 mg, 157 μmol, 1.0 equiv) was dissolved in DMSO (20 mL). IBX (52.6 mg, 188 μmol, 1.2 equiv) was added to the solution and the mixture was stirred for 8 h at RT. After addition of water (15 mL) the solution was extracted with EtOAc (5×15 mL). The combined organic phases were washed with water (20 mL) and dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue was purified by silica gel column chromatography (pentane/EtOAc 2:1 → 1:1) to afford **35** (19 mg, 43%) as a colorless solid. $R_f=0.27$ (pentane/EtOAc 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=2.49$–2.55 (m, 1H), 2.61 (dt, $J=4.4$, 1.8 Hz, 2H), 3.43 (m, 2H), 4.99 (dd, $J=2.6$, 2.5 Hz, 2H), 5.88–5.93 (m, 3H), 6.10 (d, $J=6.0$ Hz, 2H), 6.32 ppm (dd, $J=2.6$, 2.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=$ 52.3, 54.2, 54.4, 102.8, 108.3, 108.7, 109.2, 145.3 ppm; IR (KBr): $\tilde{\nu}=3106$, 2955, 1615, 1143, 955 cm^{-1}; UV (MeOH): λ_{max} (log ε) = 201.0 nm (4.071); MS (EI, 70 eV): m/z (%): 278.2 (100) $[M]^+$; HRMS (ESI): m/z: calcd for $C_{14}H_{14}O_6Na$: 301.06826; found: 301.06843.

Preparation of 38: Hexaacetal **24** (42.0 mg, 131 μmol, 1.0 equiv) and copper powder (12.5 mg, 197 μmol, 3.0 equiv) were mixed in toluene (10 mL) and heated to 100 °C. A solution of ethyl diazoacetate (748 mg, 656 μmol, 10.0 equiv) in toluene (8 mL) was slowly added via a syringe pump (1 mL h^{-1}). The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (CH_2Cl_2/MeOH 200:1 → 150:1) to afford of a diastereomeric mixture (34 mg, 53%) of **27a** and **27b** and a mixture (18 mg, 34%) of **36** and **27a/27b**. The mixture with compound **36** (12 mg, 29.5 μmol, 1.0 equiv) was dissolved in THF (5 mL), slowly dropped into a solution of $LiAlH_4$ (3.4 mg, 88.6 μmol, 3.0 equiv) in THF (5 mL) and stirred for 2 h at RT. Methanol (5 mL) was added dropwise to destroy excess lithium aluminum hydride, then the solvents were removed in vacuo. After purification via silica gel column chromatography (CH_2Cl_2/MeOH 10:1), **37** was obtained (7.6 mg, 71%). Compound **37** (7.6 mg, 20.9 μmol, 1.0 equiv) was dissolved in DMSO (5 mL) and IBX (8.8 mg, 31.3 μmol, 1.5 equiv) was added. The mixture was stirred for 8 h at RT. After addition of water (10 mL) the solution was extracted with EtOAc (5×25 mL). The combined organic phases were washed with water (50 mL) and dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH 20:1) to afford **38** as a colorless solid (2.0 mg, 24%). $R_f=0.63$ (CH_2Cl_2/MeOH 20:1); m.p. 183 °C (decomp); ^{1}H NMR (600 MHz, [D$_6$]DMSO): $\delta=2.66$–2.72 (m, 4H), 2.76–2.79 (m, 1H), 3.54–3.57 (m, 2H), 5.08 (dd, $J=2.5$, 2.5 Hz, 2H), 5.73 (d, $J=4.5$ Hz, 2H), 5.75 (d, $J=4.6$ Hz, 2H), 5.80 (d, $J=4.6$ Hz, 1H), 6.04 (d, $J=5.9$ Hz, 2H), 6.45 ppm (dd, $J=2.5$, 2.5 Hz, 2H); ^{13}C NMR (125 MHz, [D$_6$]DMSO): $\delta=51.2$, 52.5, 52.7, 52.7, 103.7, 107.6, 107.9, 108.2, 108.4, 144.1 ppm; IR (KBr): $\tilde{\nu}=2958$, 2925, 1617, 1351, 1288, 1196, 1037 cm^{-1}; UV (MeOH): λ_{max} (log ε) = 200.0 nm (4.079); MS (ESI): m/z (%): 385.1 (100) $[M+Na]^+$, 747.2 (58) $[2M+Na]^+$, 1109.3 (15) $[3M+Na]^+$; HRMS (ESI): m/z: calcd for $C_{18}H_{18}O_8Na$: 385.0894; found: 385.0891.

X-ray diffraction analyses: When $Cu_{K\alpha}$ (1.54178 Å) is indicated in Tables 2 and 3 measurements were carried out on a BRUKER Smart 6000 diffractometer with a rotating anode source, while intense $Mo_{K\alpha}$ (0.71073 Å) radiation for data collection was generated with an INCOATEC Microsource in the remaining cases. Both diffractometer systems are additionally equipped with mirror optics, allowing small specimen to be investigated with a high intensity to background ratio. In all cases diffractometer control for data collection, scaling, and an empirical absorption correction employed software from Bruker AXS, namely the programs APEX2, SAINT 7.61A and SADABS.[29] Space group assignments with XPREP[29] were verified with PLATON[30] after having established a

Table 3. Crystal data and structure refinement for compounds **25**, **26**, **29**, **30**, **32**, and **35**.

Compound	**25**	**26**	**29**	**30**	**32**	**35**
CCDC	764655	764654	764656	764649	764651	764653
empirical formula	$C_{16}H_{16}O_7$	$C_{16}H_{16}O_7$	$C_{20}H_{20}O_9$	$C_{10}H_{12}O_4$	$C_{10}H_{10}O_4$	$C_{14}H_{14}O_6$
formula weight	320.29	320.29	404.36	196.20	194.18	278.25
wavelength [Å]	1.54178	1.54178	1.54178	0.71073	1.54178	0.71073
crystal system	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	orthorhombic
space group	$P2_1/c$	$P2_1/c$	$C2/c$	$P2_1/c$	$P2_1/c$	$C222_1$
unit cell dimensions						
a [Å]	5.7956(3)	6.0974(4)	10.5058(5)	18.789(4)	9.6575(4)	6.511(3)
b [Å]	10.2641(6)	15.489(2)	6.8918(3)	4.6846(9)	8.2423(4)	9.657(4)
c [Å]	22.4943(12)	14.717(2)	24.0444(13)	10.0495(19)	11.1676(5)	39.243(17)
α [°]	90	90	90	90	90	90
β [°]	93.946(3)	100.044(4)	92.643(3)	90.432(3)	106.41(1)	90
γ [°]	90	90	90	90	90	90
Z	4	4	2	4	4	8
V [Å^3]	1334.94(13)	1368.6(4)	1739.06(15)	884.5(3)	852.73(9)	2467.5(19)
ρ_{calcd} [g cm^{-3}]	1.594	1.554	1.514	1.473	1.513	1.488
μ [mm]	1.072	1.045	1.011	0.114	0.995	0.118
θ range for data coll. [°]	4.18–70.54	8.36–71.16	3.68–71.74	2.17–29.23	4.77–71.45	3.11–26.99
index ranges	$-7\le h\le 7$ $0\le k\le 12$ $0\le l\le 27$	$-7\le h\le 6$ $0\le k\le 18$ $0\le l\le 18$	$-12\le h\le 12$ $0\le k$ k≤ 8 $0\le l\le 29$	$-25\le h\le 25$ $0\le k\le 6$ $0\le l\le 13$	$-11\le h\le 11$ $0\le k\le 10$ $0\le l\le 13$	$0\le h\le 8$ $0\le k\le 12$ $0\le l\le 49$
reflns collected	14487	28299	15655	14110	15630	14989
independent reflns	2538	2567	1687	2392	1660	1542
reflns observed	2343	2316	1396	1790	1650	1240
observ. data/parameters	2343/224	2316/272	1396/142	1790/175	1650/272	1240/181
goodness-of-fit[a]	5.77	5.21	4.59	2.42	4.17	5.30
$R(F)$	0.0472	0.0276	0.0464	0.0360	0.0184	0.0954
$R_w(F^2)$	0.0611	0.0422	0.0521	0.0339	0.0241	0.0844
$(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ [e Å^{-3}]	0.338, −0.289	0.224, −0.180	0.251, −0.160	0.450, −0.331	0.177, −0.152	0.617, −0.521

[a] See footnote [b] in Table 2.

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structural model. After structure solution with the program SHELXS independent atom model (IAM) refinements were carried out with SHELXL, providing starting values for subsequent invariom refinements with the charge-density least-squares refinement program XDLSM from the XD suite (2003). With the exception of **10a**, **14a**, and **24** that were refined with SHELXL due to noisy data or occurrence of disorder, all other structures benefited from higher accuracy and precision as can be achieved when non-spherical scattering factors (invariom)[31] are used. In invariom refinement scattering factors of the Hansen & Coppens multipole model[32] are predicted from theoretical calculations and are kept fixed, thereby not increasing the number of refinable parameters. A weighting scheme of $1/\sigma^2$ and a cut-off of 3σ (F) in refinements on F was chosen, whereas in SHELXL the refinement was carried out against F^2 using all reflections with adjusted weighting schemes. Input files for invariom refinement were generated with the program INVARIOMTOOL.[33] Entries in the invariom database[34] also cover the series of compounds studied here. All crystallographic data, details of the structure refinement, and the corresponding CCDC numbers are given in Tables 2 and 3 and can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

We are grateful to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and the Dr. Otto Röhm Gedächtnisstiftung for financial support (Emmy Noether Fellowship to D.B.W. (WE 2932/2-1) and B.D. (DI 921/3-1) as well as a Liebig Fellowship to D.B.W.). S.I.A. thanks the Higher Education Commission of Pakistan and the DAAD for a Ph.D. Fellowship. We thank Michele Zanoni and several research students for preparative assistance. We are grateful to Prof. Lutz F. Tietze for helpful discussions, an excellent working environment and generous support of our work.

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Received: February 22, 2010
Revised: July 20, 2010
Published online: September 9, 2010

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