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Reactivity of polyhydroxyalkyl-heterocycles towards Lewis acids

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Abstract—We report the reactivity of different polyhydroxyalkyl-heterocycles towards ceric ammonium nitrate (CAN) and ferric chloride. The behaviour of 2-methyl-5-(tetritol-1-yl)-pyrroles and -furans is different towards CAN oxidation. Pyrroles afford 2,5-diformylheterocycles, while furans give access to 1,4-dicarbonyl compounds containing three stereogenic centres. Ferric chloride promotes an intramolecular *C*-arylation reaction on *O*-benzylated-polyhydroxyalkyl furans, yielding an isochroman moiety, which is the basic skeleton of a variety of natural products.

1. Introduction

Five-membered heteroaromatic rings are interesting intermediates in organic syntheses.[1] Among them, polyhydroxyalkyl-heterocycles—particularly tetritol-1-yl derivatives, a class of acyclic *C*-nucleoside that can be easily obtained from inexpensive starting materials, such as D-glucosamine, D-glucose, β-dicarbonyl compounds[2] and alkyl(aryl)isothiocyanates—have been transformed into different products. Thus, the corresponding transformations into *C*-erythrofuranosyl heterocycles,[3] into heterocycle monocarbaldehydes,[4] nitropyrroles,[5] α-furfurylamides[6] and benzimidazoles without a polyhydroxylic chain[7] have been studied. Many of these transformations involve a decrease in the number of stereogenic centres, but the yields and the low price of the starting materials give them synthetic interest. *O*-Benzyl substituted sugars can undergo intramolecular *C*-arylation reactions when activated with protic[8] or Lewis acids.[9] The bibliographic data on this *C*-arylation process in benzylated polyhydroxyalkyl-heterocycles are scarce.

At the same time, pyrrole 2,5-dicarbaldehydes are interesting precursors in the preparation of bioactive compounds having in many cases macrocyclic structures.[1,10,11] Of these compounds, the β-alkylsubstituted porphyrins are the most widely studied, because of their conformational[12] and therapeutic properties.[13] To date, only a few procedures for the preparation of 3,4-disubstituted pyrrole 2,5-dicarbaldehydes have been reported,[14] and in some cases long multistep sequences were necessary.[15] In 1988, the preparation of these compounds by oxidation of 2,5-dimethyl derivatives with $Pb(OAc)_4$–PbO_2, was reported[16] and recently, a one-step procedure starting from pyrrole-2-carboxylic acids has been described.[17]

Other five-membered hetaryl-dicarbaldehydes are also interesting. Thiophene derivatives, for example, are used in the synthesis of tetrathiafulvalene, an organic semi-conductor[18] and the preparation of many macrocycles containing 2,5-furylene rings in their structure has been described.[18,19] The oxidation of different furan derivatives by both chemical[1,20] and photocatalytic[20] methods has been studied. These oxidations, depending on the reagents, conditions and starting materials, effect either oxidation of benzylic positions or opening of the furan ring.[1,21,22]

Ceric ammonium nitrate (CAN) is a versatile reagent for the oxidation of numerous functional groups in organic synthesis.[22] This reagent has been applied to the oxidations of carbon atoms in benzylic positions of arenes.[22b] However, the use of CAN in heterocyclic chemistry is limited, and, as far as we are aware, only the oxidations of furoin[23] and polyhydroxyalkyltriazoles,[24] with formation of the corresponding carboxylic acids, have been described. More recently, Lightner et al.[25] and Moranta et al.[26] have reported the oxidation of α-benzyl and α-methylpyrroles to the corresponding hydroxy- and formyl-derivatives.

In a previous communication,[27] we have reported preliminary results on the oxidation of polyhydroxyalkyl-heterocycles, which, in the case of

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2-methyl-5-(tetritol-1-yl)pyrroles, gave access to pyrrole-2,5-dicarbaldehydes.

O-Benzyl protection is a standard strategy in syntheses of carbohydrate derivatives.[28] The *O*-benzyl groups can be removed in several ways, one of which is acetolysis in the presence of a protic or Lewis acid and mild conditions. Recently, it has been observed[8,9] that *O*-debenzylation in the mentioned conditions can produce internal electrophilic aromatic substitution.

Herein, we report on the oxidation of 2-methyl-5-(tetritol-1-yl)-pyrroles and -furans with CAN. These compounds exhibit a wide range of behaviours towards this reagent that strongly depend on the heterocycle, the substituents on the heterocyclic ring, the equivalents of the reagent and the form of its addition. We also report the behaviour of different furan tetra-*O*-benzyl derivatives in the acetolysis of *O*-benzyl groups in the presence of ferric chloride.

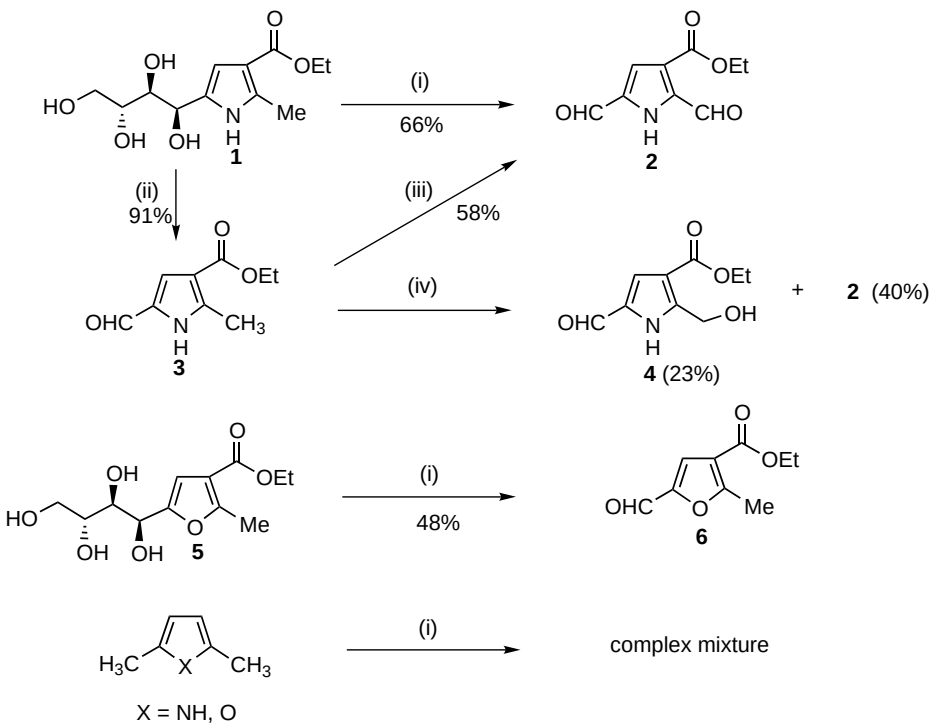
2. Results and discussion

The reactivity of 3-ethoxycarbonyl-2-methyl-5-D-*arabino*-tetritol-1-ylpyrrol **1**[4] towards CAN is depicted in Scheme 1. The slow addition of 11 equiv. of CAN over 165 min (1 equiv. each 15 min), gave dicarbaldehyde **2** in 66% isolated yield, whereas rapid addition of the reagent to compound **1**[4] gave a complex mixture of products from which **2** was isolated in only 10% yield. This different behaviour is probably due to the action of CAN as a Lewis acid in high initial concentration. Compound **2** was also obtained from aldehyde **3** after treatment with 6 equiv. of CAN. Alcohol **4**, an intermediate in the oxidation, was obtained after treatment of **3** with 4.2 equiv. of CAN, indicating that oxidative cleavage of the polyol chain takes place first, followed by oxidation of the 2-methyl group.

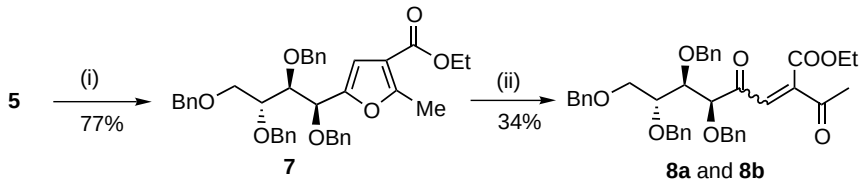
When the same reaction conditions were applied to furan **5**, different behaviour was observed. Thus, the reaction of **5** with 11 equiv. of CAN, in a slow addition (1 equiv. each 15 min), gave compound **6** that was isolated in 48% yield. Further addition of CAN, did not effect oxidation of the methyl group. Compound **6** is totally unreactive to further oxidation. Nevertheless, the rapid addition of all the reagent to compound **5** gave a complex mixture of decomposition products. The same treatment applied to commercially available compounds such as 2,5-dimethylpyrrole and 2,5-dimethylfuran gave a complex mixture of decomposition products.

The differing behaviour of furan **6** and pyrrole **3** indicates that the oxidation must be strongly dependent on the π-electron density of the heterocyclic ring; lower π-electron density of the heterocyclic ring makes oxidation of the 2-methyl group more difficult.

With the aim of avoiding the oxidative cleavage of the 5-polyolic chain to an electron-withdrawing group such as a formyl group, and thus favouring the oxidation of the 2-methyl furan in **5**, we envisaged the oxidation of the tetra-*O*-benzyl derivative **7** obtained after conventional benzylation of **5**. For compound **7** (Scheme 2)



Scheme 1. *Reaction conditions*: (i) 11 equiv. of CAN, MeCN–H_2O (5:1), 165 min; (ii) $NaIO_4$, MeOH–H_2O; (iii) 6.6 equiv. of CAN, MeCN–H_2O (9:1), 15 min; (iv) 4.2 equiv. of CAN, MeCN–H_2O (9:1), 15 min.



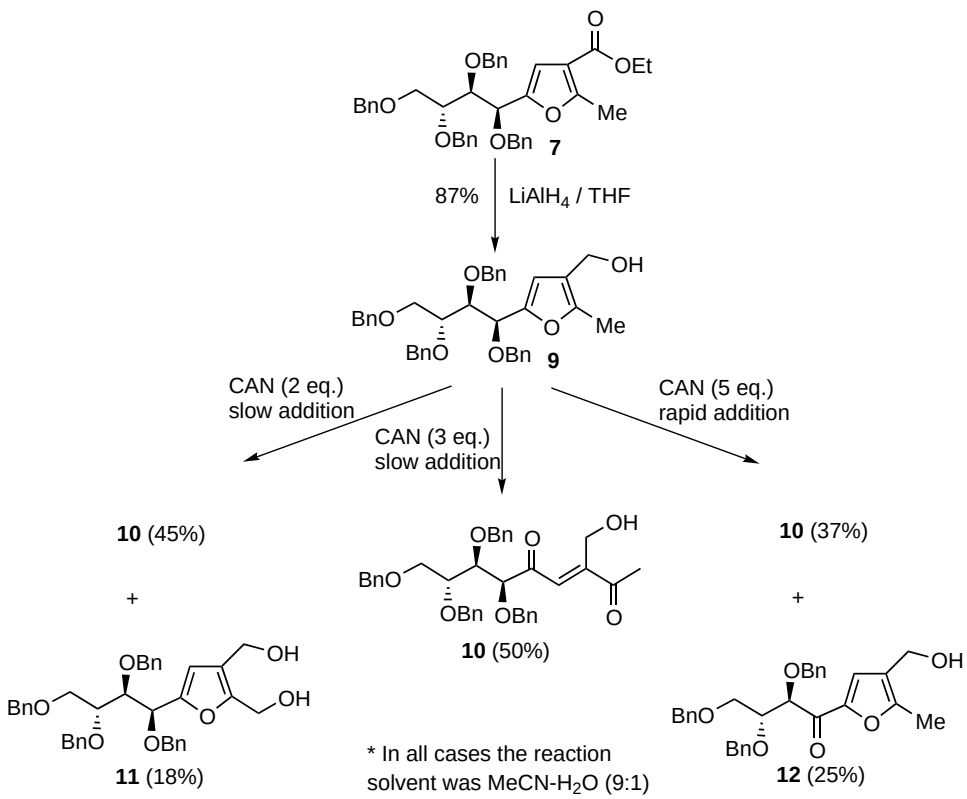
Scheme 2. *Reaction conditions*: (i) BnBr, NaH, DMF; (ii) 5 equiv. of CAN, MeCN–H_2O (9:1), 75 min.

with an ester group in position 3, both slow and rapid addition of 5 equiv. of CAN in MeCN–H_2O effected oxidative opening of the furan ring and a mixture of two compounds **8a** and **8b** in a 1:1.3 ratio was isolated in 34% yield. No formyl group was observed, and the exact configuration of each compound was not determined.

The opening of the furan ring is clearly demonstrated by the appearance of two IR bands at 1707 and 1732 cm^{-1} corresponding to ν_{max} of CO of ketone and ester, respectively. The ^1H NMR spectra indicate the deshielding of the C(4) proton of the furan ring from 6.54 ppm to 7.2–7.4 ppm. It is worth noting the appearance of signals at 201.1 (2C), 200.9 and 194.2 corresponding to C(2) and C(5) of each isomer.

The configuration of the C=C bond cannot be deduced from the spectroscopic data. Nevertheless, we tentatively assigned (*E*)-configuration to the major compound based on reported data[1,18b] as the oxidation reaction has previously been conducted in a slightly acidic medium and under such conditions, oxidative opening of the furan ring produces (*E*)-2-ene-1,4-diones.

In the case of compound **9** (Scheme 3) with a hydroxymethyl group at position 3, formed by the reduction of **7** with $LiAlH_4$/THF, the reaction with slow addition of 2 equiv. of CAN gave **10** in 45% yield as a result of oxidative ring opening, and compound **11** in 18% yield as a result of the oxidation of the 2-methyl group into a hydroxymethyl group. Compound **10**, presented IR bands at 3468 cm^{-1} (OH) and 1696 cm^{-1} (C=O). In the ^1H NMR spectrum the C(4)H signal appeared at 6.56 ppm as a triplet with two allylic coupling constants (1.9 Hz) with the methylene protons of the CH_2OH group. The CO groups (C(2) and C(5)) resonated at 205.5 and 200.6 ppm, as corresponds to α,β-unsaturated ketones. The presence of two hydroxymethyl groups in compound **11** was deduced from the IR band at 3420 cm^{-1} (OH), and from two ^1H NMR resonances at 4.50 and 4.54 ppm for the methylene protons. The resonance of the C(4) proton of the furan ring in **11**



Scheme 3.

appeared at 6.24 ppm, which is very close to the corresponding signal in **9**.

With 3 equiv. of CAN and slow addition of the reagent, only **10** was isolated in 50% yield. Using 5 equiv. of CAN and a rapid addition, the oxidation of the 1′-benzylic position was observed and compound **12** was isolated in 25% yield together with the ring-opened compound **10** in 37% yield. In neither of these experiments was any aldehyde detected. Compound **12** had IR bands at 3420 cm^{-1} (OH) and 1704 cm^{-1} (CO). The ^1H and ^{13}C NMR spectra showed the disappearance of the signal of C(1′) and a signal at 186.8 ppm for C(1′) indicates a carbonyl group. The signal of C(2′)H is deshielded to 4.6 ppm and appears as a doublet with $J_{2',3'}=6.6$ Hz. The resonances for only one hydroxymethyl group (4.41 ppm for CH_2OH and 55.9 for CH_2OH), the methyl group (2.36 ppm for CH_3 and 12.2 ppm for CH_3), and the deshielded signal for C(4)H (7.44–7.12 ppm) and C(4) (121.6 ppm) also confirmed the proposed structure.

Treatment of **7** and **9** with CAN under the above conditions gives access to 1,4-dicarbonyl compounds bearing three stereogenic centres.

It is worth pointing out the formation of (*Z*)- and (*E*)-geometric isomers of **8**, in almost equimolar ratio from the oxidation of **7** and the appearance of only one (*E*)-isomer for **10** as the major product in all of the CAN oxidations of **9** (Scheme 3). Taking into account steric and electronic effects, the most probable structures for isomers **8** and **10** are indicated in Fig. 1.

In order to confirm a possible intramolecular hydrogen bond in compound **10** (structures 10 (*I*) and 10 (*II*)), we have performed the CAN oxidation of **13** where the hydroxymethyl group is protected as *tert*-butyldiphenylsilyl ether (Scheme 4). The rapid addition

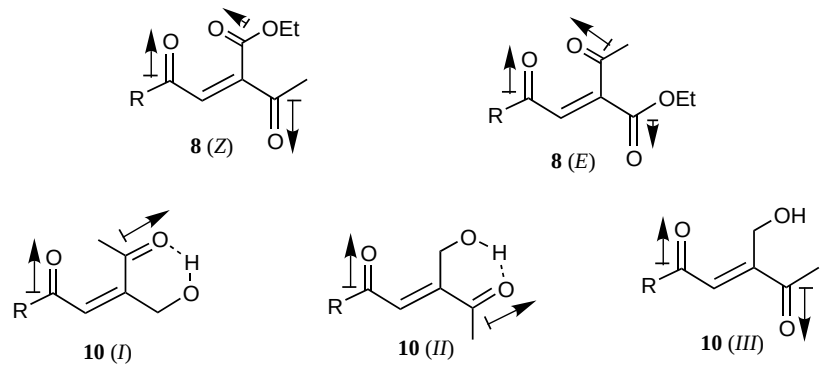
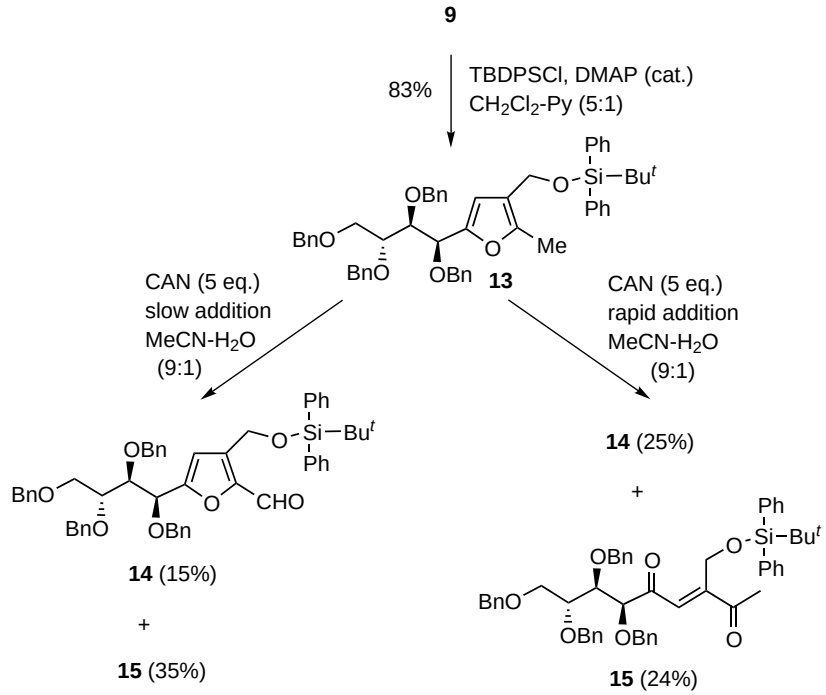


Figure 1.



Scheme 4.

of 5 equiv. of CAN yielded a 1:1 mixture of the aldehyde **14** and the ring-opened compound **15** in 25 and 24% yield, respectively. However, with a slow addition of 5 equiv. of CAN, the ring-opened compound **15** was isolated in 35% yield, and only 15% of the aldehyde (^{1}H and ^{13}C NMR of CHO at 9.60 ppm, 178.4 ppm) was formed. The spectroscopic data for **15** were very close to that for **10**. C(4) resonated as a triplet (^4J=1.8 Hz) and the resonances of the CO groups appeared at 205.5 and 200.6 ppm.

The existence of an intramolecular hydrogen bond in **10** must produce a deshielding of 3–4 ppm in the chemical shift of C(2) due to the local diamagnetic effect.[29] The similarity between the ^{1}H and ^{13}C NMR spectra of compounds **10** and **15** (see Section 4) rules out the intramolecular hydrogen bonding and hence the (*E*)-configuration (*III*, Fig. 1) is proposed for **10** and **15**. The absence of any NOE in **10** for C(4)H/-CH_2O- or CH_3 (Fig. 2) confirms the assignment which is also in accordance with published data.[20c]

Ferric chloride is a reagent that has been successfully used[30] in natural product chemistry, in particular oligosaccharide chemistry, showing itself to be a highly efficient reagent for debenzylation both at room temperature and at 0°C. Reaction of alcohol **9** with ferric chloride in acetic anhydride and dichloromethane at room temperature and at 0°C effected decomposition of the products. However, when the reaction was carried out on the ester **7**, a mixture of the two 4-furyl-3,4-dihydro-1*H*-benzo[*c*]pyrans **16** and **17** was formed. The reaction takes place by intramolecular alkylation of the benzyl group at C(2′) and leads to isochromane, the basic skeleton of a variety of natural products.[31] The easily formed carbocation at C(1′) reacts with the benzyl group at C(2′) through Friedel–Crafts-type reaction in a poorly stereoselective process giving the mixture of epimers **16** and **17**. The results are summarised in Scheme 5. A mixture of **16** and **17** was isolated in each case (same R_f in chromatography) and the ratio determined by ^{1}H NMR. It is observed that with 2, 4 and 10 equiv., the ratio is the same, although the optimal yield is obtained with 2 equiv. of ferric chloride. With 1 equiv. of reagent, compound **18** that still has a benzyl group at position 1″, was easily isolated by chromatography in 11% yield.

The structure of compounds **16**, **17** and **18** is supported on ^{1}H and ^{13}C NMR data. In the case of compounds **16** and **17**, the appearance of two acetyl groups (2.04 and 1.97 ppm) and the deshielding of the corresponding protons of the polyol chain (H(1″), H(2″a) and H(2″b), Scheme 5, see Section 4) is observed. Resonances for two benzyl-type methylenic protons (H-1a, H-1b) appeared for each compound. The configuration of the newly-formed stereogenic centre C(4) is based on the coupling constant $J_{3,4}$, that indicates an *anti*-relationship ($J_{3,4}$=7.2 Hz) in **16** and a *syn*-relationship ($J_{3,4}$=2.9 Hz) in **17**. Additionally, NOEs between pairs H-4/H-3 (2%) in **17** confirm the assignment. It is worth

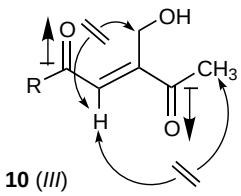
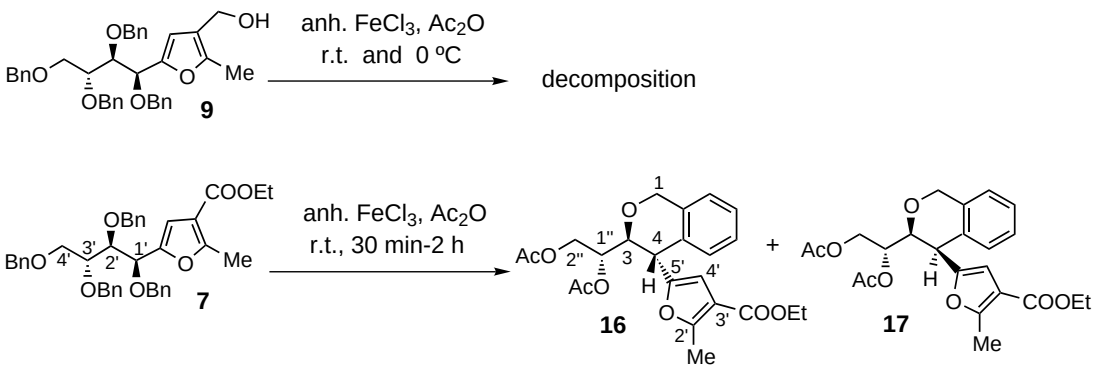
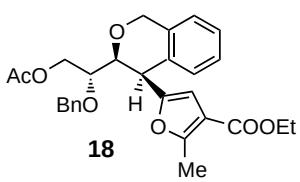


Figure 2.



$FeCl_3$ (equiv.)	yield **16** + **17**	yield **18**	ratio **16** : **17**
1	44%	11%	1.8 : 1
2	63%	---	1.1 : 1
4	52%	---	1.1 : 1
10	47%	---	1.1 : 1



Scheme 5.

noting the chemical shifts of C(4) at 38.3 and 39.4 ppm for **16** and **17**, respectively, that are consistent with the absence of oxygen at this carbon and with carbon attached to two aromatic moieties [C-*C*H(Ar)$_2$], which is in accordance with bibliographic data.[9] The presence of one acetyl group signal and $J_{3,4}=2.5$ Hz in **18** confirms the assigned structure.

3. Conclusion

In conclusion, the different behaviour of polyhydroxyalkyl-pyrroles and furans towards CAN oxidation is demonstrated. With an unprotected polyolic chain, oxidative degradation is observed in both cases. The oxidation of the 2-methyl moiety to a formyl group only takes place on pyrroles bearing electron-withdrawing groups. For (tetra-*O*-benzylated-tetritol-1-yl)-3-ethoxycarbonylfurans, oxidative opening of the furan ring is observed, giving access to 1,4-dicarbonyl compounds that bear three stereogenic centres. Finally, an intramolecular *C*-arylation reaction of benzylated polyhydroxyalkyl-furans is carried out leading to new compounds containing the isochroman moiety, which is the basic skeleton of a variety of natural products.[32]

4. Experimental

Melting points are uncorrected. Optical rotations were measured at 25±1°C for solutions in dichloromethane. ^{1}H NMR spectra (300 and 500 MHz) were obtained for solutions in $CDCl_3$, *J* values are given in Hz and δ in ppm. The FABMS spectra were measured with a KRATOS MS-80RFA instrument. Ions were produced by a beam of xenon atoms (6–7 keV) using a matrix consisting of glycerol or thioglycerol and NaI as salt, $(CsI)_{37}Cs$ was used as reference. TLC was performed on Silica Gel HF_{254} (Merck), with detection by UV light or charring with H_2SO_4. Silica Gel 60 (Merck, 230 mesh) was used for preparative chromatography.

4.1. 3-Ethoxycarbonyl-2,5-diformylpyrrole 2

4.1.1. Procedure a. To a stirred solution of 3-ethoxycarbonyl-2-methyl-5-(D-*arabino*-tetritol-1-yl)pyrrole[4] **1** (50 mg, 0.18 mmol) in MeCN–H_2O, 5:1 (6 mL) at rt, CAN (1.10 g, 1.98 mmol, 11.0 equiv.) was added over 165 min (by adding 100 mg, 0.18 mmol, each 15 min). After 3 h (total reaction time) the reaction mixture was diluted with ether, washed with water (3×20 mL), dried (Na_2SO_4) and evaporated to give **2** as a solid (23 mg, 66%).

4.1.2. Procedure b. To a stirred solution of **3** (142 mg, 0.78 mmol) in MeCN–H_2O, 9:1 (6 mL) at rt, CAN (2.8 g, 5.13 mmol, 6.6 equiv.) was added and the mixture was stirred for 15 min at rt. Work-up of the residue as described above gave **2** as a solid (86 mg, 58%) that crystallised from EtOH–H_2O, 1:1; mp 130–132°C, lit.[4] 128–129°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.17 (s, 1H, N*H*), 10.40, 9.76 (2s, 2H, 2C*H*O), 7.40 (s, 1H, H-4), 4.41 (q, 2H, $J_{H,H}=7.1$, CH_2CH$_3$), 1.41 (t, 3H, $J_{H,H}=7.1$, CH$_2$CH_3); ^{13}C NMR (75.4 MHz): δ 183.9, 180.7 (2*C*HO), 162.5 (*C*OOEt), 135.1, 133.3 (C-2, C-5), 120.9 (C-4), 112.6 (C-3), 61.2 (*C*H$_2$CH$_3$), 14.2 (CH$_2$*C*H$_3$).

4.2. 3-Ethoxycarbonyl-5-formyl-2-hydroxymethylpyrrole 4

To a stirred solution of 3-ethoxycarbonyl-5-formyl-2-methylpyrrole[4] **3** (150 mg, 0.83 mmol) in MeCN–H_2O, 9:1 (6 mL) at rt, CAN (1.9 g, 3.48 mmol, 4.2 mol equiv.) was added and the mixture was stirred for 15 min at rt. The reaction mixture was diluted with dichloromethane, washed with water (3×50 mL), dried (Na_2SO_4), evaporated and the residue was purified by column chromatography (dichloromethane–acetone, 40:1→10:1). Eluted first **2** (64 mg, 40%). Eluted second **3** (37 mg, 23%) that crystallised from EtOH–H_2O, 1:8; mp 136–138°C, lit.[4] 138–139.5°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.22 (bs, 1H, N*H*), 9.49 (s, 1H, C*H*O), 7.37 (d, 1H, $J_{4,CHO}=2.7$, H-4), 5.03 (d, 2H, $J_{H,OH}=5.3$, CH_2), 4.33 (q, 2H, $J_{H,H}=7.1$, CH_2CH$_3$), 3.73 (bs, 1H, OH), 1.37 (t, 3H, $J_{H,H}=7.1$, CH$_2$CH_3); ^{13}C NMR (75.4 MHz): δ 179.5 (*C*HO), 164.2 (*C*OOEt), 145.3 (C-5), 130.5 (C-2), 123.5 (C-4), 114.4 (C-3), 60.4 (*C*H$_2$CH$_3$), 14.3 (CH$_2$*C*H$_3$).

4.3. 3-Ethoxycarbonyl-5-formyl-2-methylfuran 6

4.3.1. Procedure a. To a stirred solution of 3-ethoxycarbonyl-2-methyl-5-(D-*arabino*-tetritol-1-yl)furan[4] **5** (57.5 mg, 0.21 mmol) in MeCN–H_2O, 9:1 (5 mL) at rt, CAN (575 mg, 1.05 mmol, 5 equiv.) was added over 1 h (by adding 115 mg, 0.21 mmol, each 15 min). After 75 min (total reaction time) the reaction mixture was diluted with ether, washed with water (3×20 mL), dried (Na_2SO_4) and evaporated to give **6** as a solid (15 mg, 38%) which crystallised from EtOH–H_2O, 1:1; mp 56–58°C, lit.[4] mp 57°C; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 176.9 (*C*HO), 164.5 (*C*OOEt), 162.4, 150.2 (C-2, C-5), 122.3 (C-4), 116.4 (C-3), 60.7 (*C*H$_2$CH$_3$), 14.1 (2C, CH$_2$*C*H$_3$, *C*H$_3$).

4.3.2. Procedure b. To a stirred solution of **5** (57.5 mg, 0.21 mmol) in MeCN–H_2O, 9:1 (5 mL) at rt, CAN (1.27 g, 2.31 mmol, 11.0 mol equiv.) was added over 165 min (by adding 115 mg, 0.21 mmol, each 15 min). After stirring the mixture for 3 h (total reaction time), the reaction mixture was elaborated as described above to give **6** (18.5 mg, 48%).

4.4. 3-Ethoxycarbonyl-2-methyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan 7

To a stirred solution of 3-ethoxycarbonyl-2-methyl-5-(D-*arabino*-tetritol-1-yl)furan **1a** (1.28 g, 4.7 mmol) in dry DMF (6 mL), NaH (1.8 g, 74.74 mmol) and benzyl bromide (9 mL, 74.7 mmol) were added at 0°C. The reaction mixture was stirred for 2 h at rt. Excess NaH and benzyl bromide were removed by addition of methanol and Et_3N. The reaction mixture was evaporated, diluted with dichloromethane, washed with water (3×100 mL), dried (Na_2SO_4) and evaporated. Column

chromatography (ether–petroleum ether, 1:3→1:1) gave **7** as a syrup (2.28 g, 77%); $[\alpha]_D$ −30.9 (*c* 1.0, CH_2Cl_2); IR: 1717 cm^{-1} (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.20–7.34 (m, 20H, arom.), 6.54 (s, 1H, H-4), 4.64 (d, 1H, $J_{1',2'}=5.3$, H-1′), 4.59, 4.52 (2d, 1H each, $^2J_{H,H}=11.2$, CH_2Ph),), 4.57, 4.32 (2d, 1H each, $^2J_{H,H}=11.8$ Hz, CH_2Ph),), 4.53, 4.35 (2d, 1H each, $^2J_{H,H}=11.7$, CH_2Ph),), 4.49, 4.42 (2d, 1H each, $^2J_{H,H}=12.1$ Hz, CH_2Ph), 4.29 (q, 2H, $J_{H,H}=7.1$, CH_2CH$_3$), 4.02 (t, 1H, $J_{2',3'}=5.30$, H-2′), 3.58–3.70 (m, 3H, H-3′, H-4′a, H-4′b), 2.50 (s, 3H, CH_3), 1.35 (t, 3H, $J_{H,H}=7.1$, CH$_2$CH_3); ^{13}C NMR (75.4 MHz): δ 163.9 (*C*OOEt), 159.0, 149.8 (C-2, C-5), 138.3, 138.3, 138.2, 137.7 (C-1 of Ph), 128.2–127.4 (20C, Ph), 114.1 (C-3), 109.9 (C-4), 80.5 (C-2′), 78.0 (C-3′), 74.5 (C-1′), 74.8, 73.2, 71.8, 71.1 (*C*H$_2$Ph), 68.9 (C-4′), 60.0 (*C*H$_2$CH$_3$), 14.3 (*C*H$_3$), 13.8 (CH$_2$*C*H$_3$); FABMS: *m*/*z* 657 [100%, (M+Na)$^+$]; HRFABMS: Found (M+Na)$^+$ 657.2865. $C_{40}H_{42}NaO_7$ requires 657.2828. Anal. calcd for $C_{40}H_{42}O_7$: C, 75.68; H, 6.67. Found: C, 75.99; H, 6.35%.

4.5. (*Z*,*E*)-(6*S*,7*R*,8*R*)-6,7,8,9-Tetrabenzyloxy-3-ethoxycarbonylnon-3-ene-2,5-dione 8

To a stirred solution of **7** (81 mg, 0.127 mmol) in MeCN–H_2O, 9:1 (7.5 mL) at rt, CAN (348 mg, 0.638 mmol, 5 mol equiv.) was added and the resulting mixture was stirred for 15 min at rt. Work-up of the residue as described above and purification by column chromatography (ether–petroleum ether, 1:5→1:1) gave, as syrups, a mixture of two compounds **8** in a ratio of 1:1.3 (28 mg, 34%); $[\alpha]_D$ −31.8 (*c* 1.0, CH_2Cl_2); IR: 1732, 1704 cm^{-1} (C=O); ^{13}C NMR (125.7 MHz, $CDCl_3$), 201.1 (2C), 200.9, 194.7 (4C=O), 165.7, 163.0 (2*C*OOEt), 144.0, 141.1 (2C-3), 138.1 (2C), 138.0, 138.0, 137.5, 137.4, 136.8, 136.7 (8C-1 of Ph), 132.2, 131.9 (2C-3), 128.4–127.5 (40C, Ph), 85.5, 85.1 (2C-6), 80.1, 79.8 (2C-7), 77.6, 77.4 (2C-8), 74.7, 74.5, 73.5 (2C), 73.3 (2C), 71.7, 71.6 (8*C*H$_2$Ph), 68.1, 67.9 (2C-9), 61.9, 61.7 (2*C*H$_2$CH$_3$), 29.8, 27.3 (2C-1), 13.9, 13.8 (2CH$_2$*C*H$_3$); FABMS: *m*/*z* 673 [100%, (M+Na)$^+$]; HRFABMS: Found (M+Na)$^+$ 673.2781. $C_{40}H_{42}NaO_8$ requires 673.2777.

4.6. 3-Hydroxymethyl-2-methyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan 9

To a stirred solution of lithium aluminium hydride (46 mg, 1.15 mmol) in dry THF (2 mL), a solution of compound **7** (371 mg, 0.6 mmol) in dry THF (4 mL) was added. After 30 min, aqueous sodium sulphate was added to destroy excess sodium hydride. The reaction mixture was diluted with ether, filtered and the solvents removed in vacuo. The residue was diluted with dichloromethane, washed with water (50 mL), dried and evaporated to give pure **9** as a syrup (281 mg, 81%); $[\alpha]_D$ −26.1 (*c* 12.8, CH_2Cl_2); IR: 3452 cm^{-1} (OH); ^1H NMR (300 MHz, $CDCl_3$): δ 7.37–7.23 (m, 20H, Ph), 6.24 (s, 1H, H-4), 4.63 (d, 1H, $J_{1',2'}=5.8$, H-1′), 4.64, 4.60 (2d, 1H each, $^2J_{H,H}=11.2$, CH_2Ph), 4.50, 4.44 (2d, 1H each, $^2J_{H,H}=11.9$ Hz, CH_2Ph),), 4.57, 4.42 (2d, 1H each, $^2J_{H,H}=11.6$, CH_2Ph), 4.41 (s, 2H, CH_2OH), 4.60, 4.38 (2d, 1H each, $^2J_{H,H}=12.0$, CH_2Ph), 4.09 (dd, 1H, $J_{1',2'}=5.8$, $J_{2',3'}=4.8$, H-2′), 3.72–3.60 (m, 3H, H-3′, H-4′a, H-4′b), 2.25 (s, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 149.7, 149.0 (C-2, C-5), 138.5, 138.5, 138.2, 138.0 (C-1 of Ph), 127.3–128.2 (20C, Ph), 119.4 (C-3), 110.4 (C-4), 80.8 (C-2′), 78.2 (C-3′), 75.0, 74.7 (C-1′, *C*H$_2$Ph), 73.1, 71.8, 71.0 (*C*H$_2$Ph), 69.3 (C-4′), 56.5 (*C*H$_2$CH$_3$), 11.6 (*C*H$_3$); FABMS: *m*/*z* 615 [100%, (M+Na)$^+$]. Anal. calcd for $C_{38}H_{40}O_6$: C, 77.00; H, 6.80. Found: C, 76.75; H, 6.46%.

4.7. Oxidation of 3-hydroxymethyl-2-methyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan 9

4.7.1. Procedure a. To a stirred solution of **9** (64 mg, 0.108 mmol) in MeCN–H_2O, 9:1 (5 mL) at rt, CAN (128 mg, 0.218 mmol, 2 equiv.) was added over 30 min (by adding 64 mg, 0.108 mmol, each 15 min). After the first addition, the initial red–orange colour had faded to colourless. Further CAN was added and the mixture was stirred for 15 min. The reaction mixture was diluted with dichloromethane and washed successively with brine and water (3×25 mL), dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (ether–petroleum ether, 1:3→1:1). Eluted first (*E*)-(6*S*,7*R*,8*R*)-6,7,8,9-tetrabenzyloxy-3-hydroxymethylnon-3-ene-2,5-dione **10** (30 mg, 45%) as a colourless oil; $[\alpha]_D$ −34.6 (*c* 1, CH_2Cl_2); IR: 3468 cm^{-1} (OH), 1696 (C=O), 1625 (C=C); ^1H NMR (500 MHz, $CDCl_3$): δ 7.32–7.24 (m, 20H, arom.), 6.56 (t, 1H, $^4J_{4,CHOH}=1.9$, H-4), 4.62, 4.34 (2d, 1H each, $^2J_{H,H}=11.6$, CH_2Ph), 4.56, 4.41 (2d, 1H each, $^2J_{H,H}=11.6$, CH_2Ph),), 4.55, 4.40 (2d, 1H each, $^2J_{H,H}=11.1$, CH_2Ph), 4.52 (s, 2H, CH_2Ph), 4.22 (d, 1H, $J_{6,7}=3.4$, H-6), 4.12 (bs, 2H, CH_2OH), 4.06 (dd, 1H, $J_{7,8}=8.2$, H-7), 3.84 (m, 1H, H-8), 3.80 (dd, 1H, $J_{8,9a}=2.4$, $J_{9a,9b}=10.7$ Hz, H-9a), 3.68 (dd, 1H, $J_{8,9b}=3.9$, H-9b), 2.21 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 205.5 (C-2), 200.6 (C-5), 157.9 (C-3), 138.2, 138.0, 137.7, 137.1 (C-1 of Ph), 128.3–127.5 (20C of Ph), 120.1 (C-4), 84.8 (C-6), 79.8 (C-7), 77.5 (C-8), 74.4, 73.4, 71.3, 71.7 (*C*H$_2$Ph), 68.1 (C-9), 63.0 (*C*H$_2$OH), 29.5 (C-1). FABMS: *m*/*z* 631 [100%, (M+Na)$^+$]; HRFABMS: Found (M+Na)$^+$ 631.2644. $C_{38}H_{40}NaO_7$ requires 631.2671. Anal. calcd for $C_{38}H_{40}O_7$: C, 75.00; H, 6.62. Found: C, 75.53; H, 6.55%.

Eluted second 2,3-dihydroxymethyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan **11** (12 mg, 18%) as a colourless oil; $[\alpha]_D$ −28.3 (*c* 1, CH_2Cl_2); IR: 3420 cm^{-1} (OH); ^1H NMR (500 MHz, $CDCl_3$): δ 7.23–7.29 (m, 20H, Ph), 6.24 (s, 1H, H-4), 4.67 (d, 1H, $J_{1',2'}=5.4$, H-1′), 4.60, 4.53 (2d, 1H each, $^2J_{H,H}=11.3$, CH_2Ph),), 4.58, 4.36 (2d, 1H each, $^2J_{H,H}=11.8$, CH_2Ph),), 4.57, 4.40 (2d, 1H each, $^2J_{H,H}=11.9$, CH_2Ph), 4.54, 4.50 (2s, 2H each, CH_2OH), 4.49, 4.44 (2d, 1H each, $^2J_{H,H}=12.1$, CH_2Ph), 4.04 (t, 1H, $J_{2',3'}=5.44$, H-2′), 3.71 (td, 1H, $J_{3',4'a}=3.1$, $J_{3',4'b}=5.4$, H-3′), 3.66 (dd, 1H, $J_{4'a,4'b}=10.6$, H-4′a), 3.61 (dd, 1H, H-4′b); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 151.3, 150.8 (C-2, C-5), 138.6, 138.5, 138.2, 138.0 (4C-1 of Ph), 128.2–127.3 (20C, Ph), 122.5 (C-3), 110.4 (C-4), 80.9 (C-2′), 78.3 (C-3′), 75.1 (C-1′), 74.6, 73.3, 71.9, 71.4 (*C*H$_2$Ph), 69.4 (C-4′), 56.6, 55.9 (*C*H$_2$OH); FABMS: *m*/*z* 631 [100%, (M+Na)$^+$];

HRFABMS: Found $(M+Na)^+$ 631.2671. $C_{38}H_{40}NaO_7$ requires 631.2672.

4.7.2. Procedure b. As described above but by adding CAN (180 mg, 0.327 mmol, 3 mol equiv.) over 45 min (by adding 64 mg, 0.108 mmol, each 15 min). Work-up of the residue and column chromatography (ether–petroleum ether, 1:3→1:1) gave **10** (50 mg, 50%).

4.7.3. Procedure c. To a stirred solution of **9** (98 mg, 0.16 mmol) in MeCN–H_2O, 9:1 (10 mL) at rt, CAN (438 mg, 0.80 mmol, 5 mol equiv.) was added and the mixture was stirred for 15 min until TLC indicated total consumption of the starting material (ether–petroleum ether 3:1). The residue was diluted with ether, treated as described above, and purified by column chromatography (ether–petroleum ether, 1:3→1:1). Eluted first **10** (36 mg, 37%). Eluted second 3-hydroxymethyl-2-methyl-5-(2′,3′,4′-tri-*O*-benzyl-D-*erythro*-butanoyl)furan **12** (20 mg, 20%) as a colourless oil; IR: 3420 cm^{-1} (OH), 1704 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.12 (m, 21H, Ph and H-4), 4.66, 4.49 (2d, 1H each, $^2J_{H,H}=11.8$, CH_2Ph), 4.64, 4.45 (2d, 1H each, $^2J_{H,H}=11.7$, CH_2Ph), 4.62 (d, 1H, $J_{2',3'}=6.6$, H-2′), 4.55, 4.50 (2d, 1H each, $^2J_{H,H}=12.1$, CH_2Ph), 4.41 (s, 2H, CH_2OH), 4.06–4.00 (m, 1H, H-3′), 3.83–3.68 (m, 2H, H-4′a, H-4′b), 2.36 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 186.8 (C-1′), 155.5, 149.8 (C-2, C-5), 138.1, 137.9, 137.2 (C-1 of Ph), 128.2–127.0 (15C, Ph), 122.2 (C-3), 121.6 (C-4), 80.1 (C-2′), 79.0 (C-3′), 73.2, 72.5, 72.4 (*C*H_2Ph), 69.3 (C-4′), 55.9 (*C*H_2OH), 12.2 (*C*H_3); FABMS: m/z 523 [100%, $(M+Na)^+$].

4.8. 3-(*tert*-Butyldiphenylsilyloxymethyl)-2-methyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan 13

To a stirred solution of **9** (80 mg, 0.304 mmol) and 2,6-dimethylaminopyridine (15 mg) in CH_2Cl_2–pyridine, 5:1 (3 mL), TBDPSCl (0.155 mL, 0.608 mmol) at 0°C was added. The mixture was stirred for 2 h at rt and then evaporated in vacuo. Column chromatography (ether–petroleum ether, 1:30→1:20) gave **13** as a syrup (208 mg, 82%); $[\alpha]_D$ −25.8 (*c* 1.2, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$): δ 7.89–7.24 (m, 30H, Ph), 6.25 (s, 1H, H-4), 4.62 (d, 1H, $J_{1',2'}=5.5$, H-1′), 4.60, 4.56 (2d, 1H each, $^2J_{H,H}=11.3$, CH_2Ph), 4.60, 4.35 (2d, 1H each, $^2J_{H,H}=12.1$, CH_2Ph), 4.55, 4.41 (2d, 1H each, $^2J_{H,H}=11.8$, CH_2Ph), 4.50 (s, 2H, CH_2OSi), 4.48, 4.40 (2d, 1H each, $^2J_{H,H}=12.1$, CH_2Ph), 4.06 (t, 1H, $J_{2',3'}=5.5$, H-2′), 3.70 (m, 1H, H-3′), 3.67 (dd, 1H, $J_{3',4'a}=3.0$, $J_{4'a,4'b}=10.5$, H-4′a), 3.61 (dd, 1H, $J_{3',4'b}=5.8$, H-4′b), 2.04 (s, 3H, CH_3), 1.05 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 149.2, 148.0 (C-2, C-5), 138.6 (2C), 138.3, 138.1, 135.5, 133.5 (4C-1 of Ph), 129.5, 128.1–127.2 (30C, Ph), 119.5 (C-3), 110.7 (C-4), 80.8 (C-2′), 78.3 (C-3′), 74.8. 74.7 (C-1′, *C*H_2Ph), 73.2, 71.9, 70.8 (*C*H_2Ph), 69.4 (C-4′), 57.9 (*C*H_2OSi), 29.6 ($(CH_3)_3C$), 26.7 (3C, $(CH_3)_3$C), 11.6 (*C*H_3); FABMS: m/z 853 [100%, $(M+Na)^+$]; HRFABMS: Found $(M+Na)^+$ 853.3933. $C_{54}H_{58}NaO_6Si$ requires 853.3900.

4.9. Oxidation of 3-(*tert*-butyldiphenylsilyloxymethyl)-2-methyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan 13

4.9.1. Procedure a. To a stirred solution of **13** (122 mg, 0.147 mmol) in MeCN–H_2O, 9:1 (15 mL) at rt, CAN (403 mg, 0.73 mmol) was added and the mixture was stirred for 15 min until TLC (ether–petroleum ether, 2:1) indicated total consumption of the starting material. The reaction mixture was evaporated, diluted with CH_2Cl_2 and washed successively with brine (30 mL) and water (2×30 mL), dried (Na_2SO_4), and evaporated. Column chromatography of the residue (ether–petroleum ether, 1:3→1:1) eluted first 3-(*tert*-butyldiphenylsilyloxymethyl)-2-formyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan **14** (31 mg, 25%) as a colourless oil; $[\alpha]_D$ −26.4 (*c* 2.5, CH_2Cl_2); IR: 2936, 2864 cm^{-1} (CH), 1680 cm^{-1} (CHO); ^1H NMR (300 MHz, $CDCl_3$): δ 9.60 (s, 1H, CHO), 7.69–7.19 (m, 30H, Ph), 6.66 (s, 1H, H-4), 4.90 (s, 2H, CH_2OSi), 4.88 (d, 1H, $J_{1',2'}=3.7$, H-1′), 4.61, 4.36 (2d, 1H each, $^2J_{H,H}=11.6$, CH_2Ph), 4.60, 4.32 (2d, 1H each, $^2J_{H,H}=11.7$ Hz, CH_2Ph), 4.53, 4.48 (2d, 1H each, $^2J_{H,H}=12.1$, CH_2Ph), 4.52, 4.48 (2d, 1H each, $^2J_{H,H}=12.1$, CH_2Ph), 4.07 (dd, 1H, $J_{2',3'}=7.2$, H-2′), 3.82 (m, 1H, H-3′), 3.78 (dd, 1H, $J_{3',4'a}=2.8$, $J_{4'a,4'b}=11.7$, H-4′a), 3.66 (dd, 1H, $J_{3',4'b}=4.2$ Hz, H-4′b), 1.10 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 178.4 (C=O), 158.9, 146.6 (C-2, C-5), 138.2 (3C), 138.0, 137.6, 137.2 (C-1 of Ph), 135.4, 132.7, 129.8, 128.2–127.4 (31C, Ph and C-3), 111.3 (C-4), 79.6 (C-2′), 77.5 (C-3′), 74.9 (C-1′), 74.5, 73.2, 72.2, 71.7 (*C*H_2Ph), 69.2 (C-4′), 58.3 (*C*H_2OSi), 29.6 ($(CH_3)_3C$), 26.7 (3C, $(CH_3)_3$C); FABMS: m/z 867 [100%, $(M+Na)^+$]; HRFABMS: Found $(M+Na)^+$ 867.3742. $C_{54}H_{56}NaO_7Si$ requires 867.3693. Eluted second (*E*)-(6*S*,7*R*,8*R*)-6,7,8,9-tetrabenzyloxy-3-(*tert*-butyldiphenylsilyloxymethylnon)-3-ene-2,5-dione (**15**) (30 mg, 24%) as a colourless oil; $[\alpha]_D$ −14.1 (*c* 2.2, CH_2Cl_2); IR: 1704 cm^{-1} (C=O), 1625 cm^{-1} (C=C); ^1H NMR (300 MHz, $CDCl_3$): δ 7.63–7.18 (m, 30H, Ph), 6.78 (t, 1H, $^4J_{4,H}=1.8$, H-4), 4.66, 4.40 (2d, 1H each, $^2J_{H,H}=11.6$, CH_2Ph), 4.62, 4.34 (2d, 1H each, $^2J_{H,H}=11.7$, CH_2Ph), 4.52 (s, 2H, CH_2Ph), 4.27 (d, 1H, $J_{6,7}=3.2$, H-6), 4.26 (d, 2H, CH_2OSi), 4.52, 4.47 (2d, 1H each, $^2J_{H,H}=11.1$, CH_2Ph), 4.09 (dd, 1H, $J_{7,8}=8.1$, H-7), 3.84 (m, 1H, H-8), 3.78 (dd, 1H, $J_{8,9a}=2.5$, $J_{9a,9b}=10.6$, H-9a), 3.67 (dd, 1H, $J_{8,9b}=4.1$, H-9b), 2.23 (s, 3H, CH_3), 1.04 (s, 9H, $((CH_3)_3C$-); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 205.2, 200.9 (C-2, C-5), 158.3 (C-3), 138.2, 138.0, 137.6, 137.1 (C-1 of Ph), 135.3, 132.2, 129.9, 128.3–127.3 (32C, Ph), 119.2 (C-4), 84.6 (C-6), 79.6 (C-7), 77.4 (C-8), 74.4, 73.4 (2C), 71.7 (*C*H_2Ph), 68.2 (C-9), 64.3 (*C*H_2OSi), 29.7 (C-1), 29.6 ($(CH_3)_3C$-), 26.5 (3C, $(CH_3)_3$C-); FABMS: m/z 869 [100%, $(M+Na)^+$]; HRFABMS: Found $(M+Na)^+$ 869.3884. $C_{54}H_{58}NaO_7Si$ requires 869.3849. Anal. calcd for $C_{54}H_{58}O_7Si$: C, 76.56; H, 6.90. Found: C, 76.33; H, 7.05%.

4.9.2. Procedure b. To a stirred solution of **13** (96 mg, 0.115 mmol) in MeCN–H_2O, 9:1 (12 mL) at rt, CAN (320 mg, 0.583 mmol, 5 equiv.) was added over 75 min (by adding 64 mg, 0.116 mmol, each 15 min). After 90 min (total reaction time) the reaction mixture was elaborated as described above to yield **14** (15 mg, 15%) and **15** (34 mg, 35%).

4.10. Treatment with $FeCl_3$ of 3-ethoxycarbonyl-2-methyl-5-(1′,2′,3′,4′-tetra-*O*-benzyl-D-*arabino*-tetritol-1-yl)furan 7

To a suspension of anhydrous $FeCl_3$ (x equiv., see Scheme 5) in freshly distilled Ac_2O (1 mL/mmol), a solution of **1a** (y mmol, see Scheme 5) in Ac_2O (3 mL/mmol) was added under an argon atmosphere. The reaction mixture was stirred at rt for 30 min to 2 h, then diluted with dichloromethane and washed successively with saturated solution of $NaHCO_3$ and water. The organic layer was dried (Na_2SO_4), evaporated and the residue was purified by column chromatography (ether–petroleum ether, 1:20→1:5). Eluted first (4*R*,3*S*,1″*R*)-3-(2-acetoxy-1-benzyloxyethyl)-4-(3-ethoxycarbonyl-2-methylfur-5-yl)-3,4-dihydro-1*H*-benzo[*c*]-pyran **18** as a colourless oil; $[\alpha]_D$ −84 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43–7.04 (m, 9H, arom.), 6.17 (s, 1H, H-4′), 5.00, 4.87 (2d, 1H each, $^2J_{H,H}$ = 15.2, H-1a, H-1b), 4.72, 4.37 (2d, 1H each, $^2J_{H,H}$ = 15.2, CH_2Ph), 4.72 (dd, 1H, $J_{1'',2''a}$ = 2.6, $J_{2''a,2''b}$ = 12.0, H-2″a), 4.33 (d, 1H, $J_{3,4}$ = 2.5, H-4), 4.24 (q, 2H, $^3J_{H,H}$ = 7.1, CH_2CH$_3$), 4.26 (dd, 1H, $J_{1'',2''b}$ = 3.8, H-2″b), 3.94 (dd, 1H, $J_{1'',3}$ = 9.5, H-3), 3.47 (ddd, 1H, H-1″), 2.54 (s, 3H, CH_3), 2.07 (s, 3H, CH_3CO), 1.31 (t, 3H, CH_2CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.8 (CH_3CO), 164.0 (*C*OOEt), 157.7, 153.0 (C-2′, C-5′), 137.8, 134.0, 133.7, 130.3–125.9 (12C, arom.), 114.2 (C-3′), 109.1 (C-4′), 77.0 (C-1″), 75.3 (C-3), 72.1 (CH_2Ph), 68.4 (C-1), 62.2 (CH_2CH_3), 59.9 (C-2″), 38.4 (C-4), 20.8 (CH_3CO), 14.2 (CH_2CH_3), 13.7 (CH_3); FABMS: m/z 501 [100%, (M+Na)$^+$]; CIMS: m/z 479 [100%, (M+H)$^+$]; HRCIMS: Found (M+H)$^+$ 479.2043, $C_{28}H_{30}O_7$+H requires 479.2069. Eluted second a mixture of (4*R* and 4*S*,3*S*,1″*R*)-3-(1,2-diacetoxyethyl)-4-(3-ethoxycarbonyl-2-methylfur-5-yl)-3,4-dihydro-1*H*-benzo[*c*]pyran **16** and **17** as a colourless oil.

Data for **16**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92–7.25 (m, 4H, arom.), 6.47 (s, 1H, H-4′), 5.20 (ddd, 1H, $J_{1'',3}$ = 7.1, $J_{1'',2''a}$ = 3.2, $J_{1'',2''b}$ = 4.5, H-1″), 4.88 (s, 2H, H-1a, H-1b), 4.48 (dd, 1H, $J_{2''a,2''b}$ = 12.2, H-2″a), 4.27 (q, 2H, $^3J_{H,H}$ = 7.1, CH_2CH$_3$), 4.22–4.15 (m, 3H, H-3, H-4, H-2″b), 4.21 (d, 1H, $J_{3,4}$ = 7.2, H-4), 2.52 (s, 3H, CH_3), 2.04, 1.97 (2s, 3H each, 2CH_3CO), 1.33 (t, 3H, CH_2CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.6, 169.9 (2CH_3CO), 163.8 (*C*OOEt), 158.8, 151.2 (C-2′, C-5′), 133.8, 133.4, 129.9–124.0 (6C, arom.), 114.0 (C-3′), 109.4 (C-4′), 74.0 (C-3), 71.9 (C-1″), 67.8 (C-1), 62.3 (CH_2CH_3), 60.0 (C-2″), 38.3 (C-4), 20.9, 20.6 (2CH_3CO), 14.2 (CH_2CH_3), 13.6 (CH_3).

Data for **17**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92–7.25 (m, 4H, arom.), 5.99 (s, 1H, H-4′), 4.98, 4.84 (2d, 1H each, $^2J_{H,H}$ = 15.2, H-1a, H-1b), 4.67 (ddd, 1H, $J_{1'',3}$ = 9.6, $J_{1'',2''a}$ = 2.4, $J_{1'',2''b}$ = 3.9, H-1″), 4.47 (dd, 1H, $J_{2''a,2''b}$ = 12.3, H-2″a), 4.26 (dd, 1H, H-2″b), 4.22–4.15 (m, 2H, CH_2CH$_3$), 4.14 (d, 1H, $J_{3,4}$ = 2.9, H-4), 4.05 (dd, 1H, H-3), 2.49 (s, 3H, CH_3), 2.16, 2.05 (2s, 3H each, 2CH_3CO), 1.27 (t, 3H, $^3J_{H,H}$ = 7.1, CH_2CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 170.6, 169.4 (2CH_3CO), 163.8 (*C*OOEt), 158.0, 152.1 (C-2′, C-5′), 133.0, 132.7, 129.9–124.0 (6C, arom.), 114.2 (C-3′), 109.8 (C-4′), 76.4 (C-3), 70.8 (C-1″), 68.3 (C-1), 62.1 (CH_2CH_3), 59.8 (C-2″), 39.4 (C-4), 20.9, 20.6 (2CH_3CO), 14.2 (CH_2CH_3), 13.4 (CH_3).

Data for **16** and **17**: FABMS: m/z 453 [100%, (M+Na)$^{+\bullet}$]; HRFABMS: Found (M+Na)$^+$ 453.1539, $C_{23}H_{26}O_8$+Na requires 453.1525. Anal. calcd for $C_{38}H_{40}O_6$: C, 64.17; H, 6.09. Found: C, 63.68; H, 6.07%.

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