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FULL PAPER

Pyrones Synthesis from Renewable Sources: Easy Preparation of 3-Acetoxy-2-oxo-2*H*-pyran-6-carboxylic Salts and their Derivatives as 3-Hydroxy-2*H*-pyran-2-one from C6 Aldaric Acids

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Abstract: 2-Pyrones are compounds present in several natural products and represent interesting building blocks for the preparation of intermediates in organic syntheses. For these reasons, many different preparation protocols have been developed for the syntheses of pyrone moieties. In this work, a green approach toward the synthesis of those compounds starting from C6 aldaric acids has been investigated. These products are an interesting and versatile class of poly functional C6 units coming from renewable sources. In this paper, we report a green procedure based on a reaction with acetic anhydride under different pH conditions to convert mucic acid and glucaric acid salts into the 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid salts and their derivatives. The salts, in the presence of hydrochloric acid, are quantitatively converted to the corresponding 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid, which afforded 3-hydroxy-2*H*-pyran-2-one in very high yield by further thermal decarboxylation. Crystal structure of the five membered ring lactone intermediate is reported.

Introduction

Nowadays, in the quest for more sustainable chemical processes, as well as to reduce the fossil-based feedstock, the global community is moving towards the development of a green and sustainable economy based on natural and renewable resources. At the same time, the continuous population growth forces institutions and industries towards the valorisation of agrofood residues and waste.[1] In this context, the transformation of biomass into valuable building blocks has a key role in the sustainable bio-based green economy.[2] The major fraction of biomass is based on C5 and C6 sugars building blocks and structural polysaccharides, containing repeating units of D-glucose, D-galactose, D-mannose, D-xylose, D-arabinose, etc., that are economically suitable for using as chemical raw materials.

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Among the large variety of carbohydrate derivatives, in the last decades, aldaric acids have aroused great interest in the industry as precursor of several derivatives starting from natural feedstock. As hydroxyl acids, these compounds show a significant tendency, also in aqueous media, to give the corresponding lactones and dilactones[3] depending on the stereochemistry of the carbon atoms bearing the hydroxyl groups. They undergo dehydration reactions resulting in the corresponding unsaturated derivatives; therefore, these compounds are good candidates for the syntheses of 2-pyrones starting from natural sources. In particular, hexaric acids should be a suitable platform for substituted pyrones. Based on this, we report an easy preparation of 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid salts and their derivatives. In particular, the 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid, recently patented as precursor of terephthalic acid,[4] was prepared in very low yields starting from ethyl succinate and oxalate (Figure 1A).[5] In general, 2-pyrones are a class of six-membered unsaturated lactones present in several natural products[6] such as pheromones, solanopyrones, α-chymotrypsin. These compounds exhibit pharmacological activity as antifungal, antibiotic, neuro-, cyto- and phyto-toxic, HIV protease and selective COX-2 inhibitors.[7] Due to their peculiar structure in which conjugated diene and lactone functions are present, and at the same time aromatic like[8] character, they are important building blocks in organic, medicinal[9] and polymer chemistry.[10,11] As dienes they are widely utilized in cycloaddition reactions to obtain functionalized intermediates.[10,12] In the last decades, many synthetic procedures have been developed for the synthesis of pyrone scaffolds,[9a,13] including biosynthetic methods[7a] and protocols based on renewable resources.[10,11,14]

In this context, procedures for the synthesis of substituted 2-pyrones from aldo-derivatives as glucosaminic acid, gluconolactone and rhamnonolactone have been proposed.[15] However, to the best of our knowledge, only few examples on the use of C6 aldaric acids as precursor of 2-pyrones are reported. In 1956, a 2*H*-pyrone derivative was prepared from mucic acid diethyl ester; the authors claimed to have probably obtained 4-acetoxy-6-(ethoxycarbonyl)-*2H*-2-pyrone.[16] 3-Hydroxy-2-pyrone, synthesized in 1927 from arabinose,[17] is actually prepared from pyrolysis of mucic acid[18] with a loss of one carbon atom in low yield in the presence of potassium hydrogen sulfate or potassium dihydrogen phosphate at high temperature (Figure 1B).

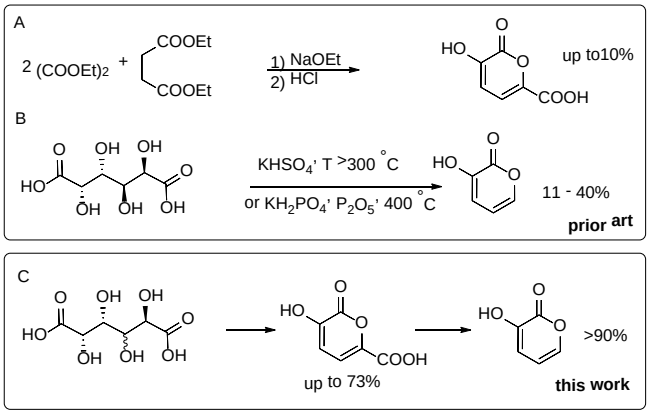


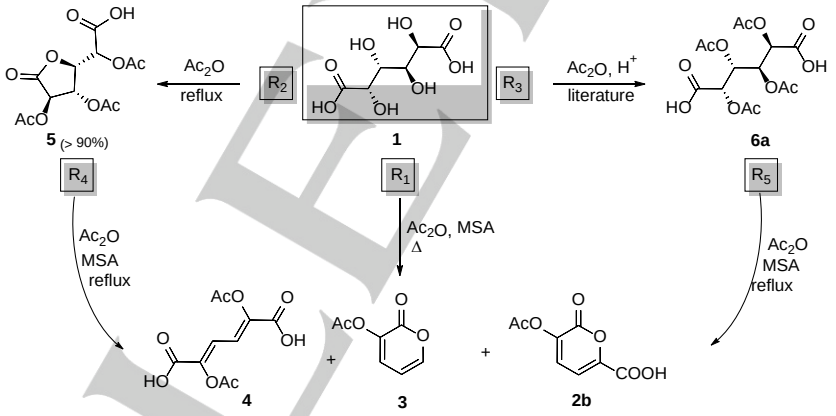
Figure 1. Prior syntheses of target 3-hydroxy-2-pyrones.

Our aim was therefore to find an efficient and low cost 2*H*-pyrone-6-carboxylic acid derivatives synthetic protocol, which would allow to preserve all the six carbon atoms present in the starting hexaric acid and to focus our attention on the overall mechanism and on the reaction intermediates as well. At the same time an easy procedure to obtain the corresponding decarboxylated 3-hydroxypyrone in high yield has been developed (Figure 1C).

Results and Discussion

The direct dehydration reaction of the aldaric acids is not a simple process: the most effective reaction is in fact based on oxorhenium-catalyzed deoxydehydration in alcohols,[19] performed under harsh conditions and limited to substrates where vicinal *syn* hydroxyl groups are present. Looking for a sustainable process, we investigated the dehydration reactions of the mucic acid, as representative model of the C6 aldaric acids, following an approach based on cheap and safe reactants potentially applicable to these classes of compounds. Then, we verified the possibility to extend the method starting from galactaric calcium and potassium salts, with comparable results.

Dehydration of alcohols is a reaction typically performed in the presence of a strong acid as catalyst but, in the case of aldaric acids, these reaction conditions lead to a complex mixture where also furane derivatives and their polymers are formed.[20] To minimize the formation of polymers derivatives we investigated mucic acid reactivity in the system acetic anhydride/ methane sulfonic acid (Ac_2O/MSA): Scheme 1 summarizes investigated reactions in acid medium.



Scheme 1. Investigated reactions in acid medium. Lactone **5**, was obtained as racemic mixtures.

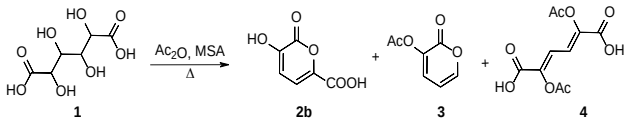
As indicated in R1 (Scheme 1), the main products obtained were the pyrones **2b** and **3**, and the diacetoxy muconic acid **4**. Target pyrone **2b** was fully characterized; product **4** was isolated in a very small amount, whereas structure of **3** was assigned on the basis of its ^{1}H NMR spectrum.

Table 1 summarizes the most significant data collected while performing the reactions in acetic anhydride under different conditions, in terms of molar ratio MSA/mucic acid, temperature and reaction time. The molar ratio Ac_2O/mucic acid used was 8.

As expected, the products distribution depends mainly on the molar ratio MSA/mucic acid although temperature and reaction time have a role too: in fact, a higher molar ratio between MSA and mucic acid favours the formation of the open chain di-eliminated derivative **4** (entries 1-3); while high initial temperature (entry 1) or longer reaction time at 128 °C (entries 5, 8 and 9), lead to lower mass balance. In this temperature range decarboxylation of **2b** to give the pyrone **3** always occurs, and the ratio **3**/**2b** is substantially constant. In almost all the experiments, various acetylated derivatives of mucic acid and its lactone were found (entries 2-9). The best result was obtained when performing the reaction with a low ratio MSA/mucic acid and long reaction time (Table 1, entry 5). In any case, the isolation and the purification of **2b** from the crude reaction mixture was laborious

and time consuming mainly because of the presence of several by-products, which interfered in the isolation process steps.

Table 1. Reactivity of mucic acid **1** in the system Ac_2O/MSA [R1] at reflux



Entry[a]	MSA [Mr][b]	Ti[c] [°C]	t [h]	2b [Y_a%][d]	3 [Y_a%][d]	4 [Y_a%][d]
1	3	140	4	53	12	15
2	3	120	9	56	15	15
3	3	120	4	43	10	15
4	1[e]	120	8	46	11	4
5	1	128	9	52	16	8
6	0.8	128	9	66	14	4
7	0.8[e]	128	9	54	17	4
8	0.6	128	9	60	12	3
9	0.4	128	9	33	8	<1

[a] Reaction reported as R1 in the experimental part. [b] M_r= molar ratio. [c] T_i= initial temperature of the reaction. [d] Y_a= analytical yield. [e] MSA was added over 5 hours.

Furthermore, the two main side products **3** and **4** were unavoidable under these conditions. In particular, pyrone **2b** underwent decarboxylation at 90-100 °C in acidic medium giving pyrone **3.**

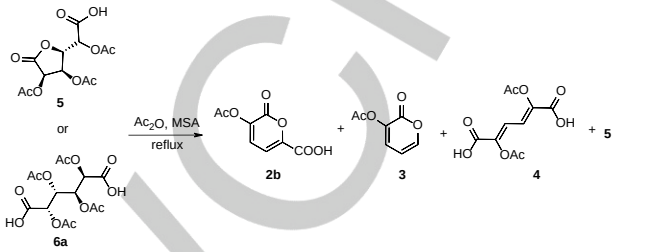
It is known that in the presence of a catalytic amount of strong acids, mucic acid reacts in acetic anhydride at 60-85 °C, achieving the corresponding tetra-acetylated derivative **6a**.[21] We found that in the presence of sulfuric acid at solvent reflux temperature, the carboxylic pyrone **2b** and the corresponding decarboxylated **3** were formed together with a small amount of diacetoxy muconic acid **4**. On the other hand, by refluxing mucic acid in acetic anhydride only the corresponding lactone **5** is formed in high yield.

However, even reactions of lactone **5** and mucic acid tetracetate **6a** in the Ac_2O/MSA system resulted in the same mixture made of **2b**, **3** and **4**. The results of the two reactions R4 and R5 are listed in Table 2**.** The presence of products **3** and **4** denotes how, even though the final products are identical, the pyrone synthesis from mucic acid can follow different paths in which **6a** and **5** can be considered as reaction intermediates.

The data show that formation of **2b** is faster starting from five membered ring lactone **5** than from the open chain *O*-peracetylated derivative **6a**, although significant amounts of the by-products **3** and **4** are still present. This different reactivity can be related to the fact that **6a** converts to **5**.

These results, combined with the work-up difficulties showed that the acid promoted reaction of acetylated mucic acid derivatives does not seem to be a convenient process for the synthesis of pyrones**.**

Table 2. Reaction of **5** and **6a** in the system Ac_2O/MSA (R4 and R5) at reflux for 5 hours. Molar ratio of MSA/reagent = 2 and Ac_2O/reagent = 3



Entry [Reaction]	Reag.	Conv. %	2b [Y_a%][a]	3 [Y_a%][a]	4 [Y_a%][a]	5 [Y_a%][a]
1 [R4]	5	98	68	13	16	2
2 [R5]	6a	99	46	10	13	30

[a] Y_a= analytical yield.

As a consequence, the reactivity of the C6 aldaric acids in buffered acido-base media was investigated.

As known, mucic acid presents a very low solubility in almost all solvents and shows marked propensity to cyclize, in several media, including water, to give a more soluble five membered lactone.[22]The latter can be a convenient substitute of mucic acid to perform such chemical reactions. Surprisingly, there are no methods described in literature where this derivative has been isolated as a pure solid and also our attempts to make it have failed. For this reason, the structural attribution of this lactone has been assigned only by NMR analysis. On the contrary, the corresponding pyridinium salt **7** can be easily synthetized and isolated by boiling mucic acid in pyridine (Scheme 2 [R6]). The single crystal structure analysis of the corresponding DABCO salt **7'** has definitely confirmed the structure of this lactone (Figure 2).

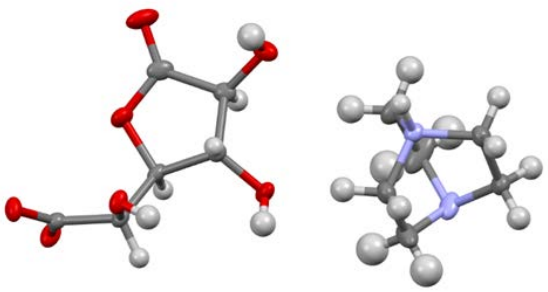
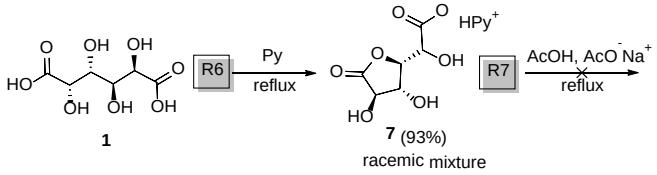


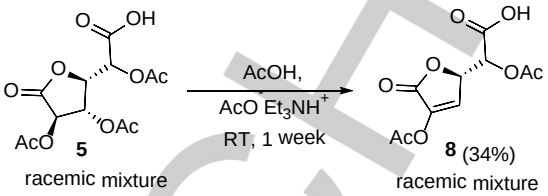
Figure 2. Crystallographic representation (ellipsoid 50% of probability) of compound 7'. Colour code: C, grey; O, red; N, blue; H, white.

However, attempts to perform the direct dehydrating reactions in moderate acid buffered media (AcOH/AcO$^-$Na$^+$ at reflux) on this substrate failed (Scheme 2 [R7]).



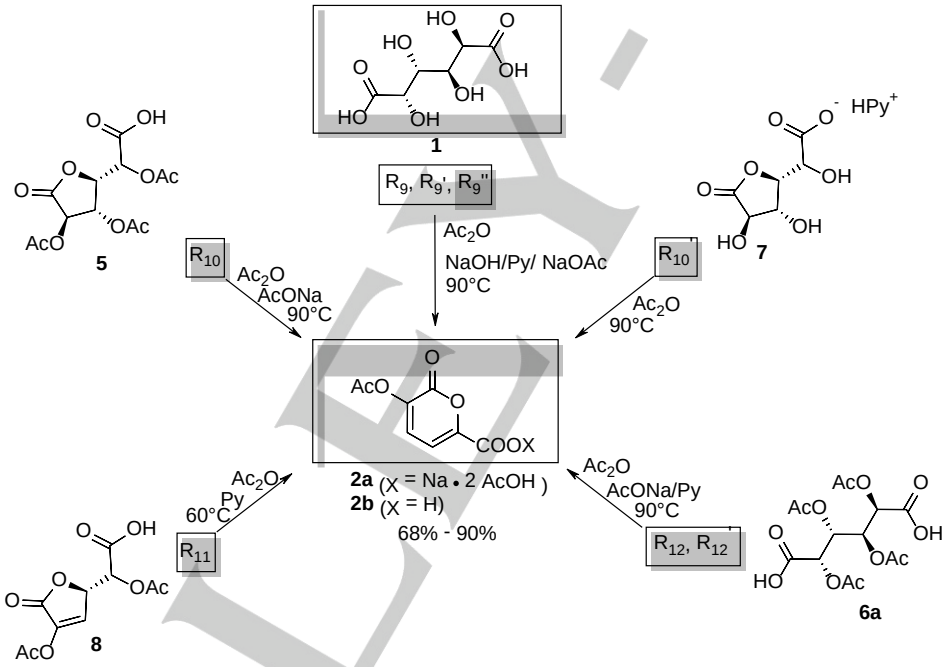
Scheme 2. Synthesis of mucic acid 1,4-lactone pyridiniun salt (**7**) [R6] and its reactivity in moderate acid buffered medium [R7] .

This result can be ascribed to the too weak acidity of the HOC-H bonds present in the molecule: therefore, we tested the reactivity of the per-acetylated lactone **5** in moderate acidic buffer AcOH/AcO$^-$Et$_3$NH$^+$; in this case the mono-eliminated five-membered ring lactone **8** was isolated (24% yield) without traces of the pyrone derivatives (Scheme 3). Lower yields were obtained using other bases such as NaOH, AcONa and 1,4-diazabicyclo[2.2.2]octane (DABCO).



Scheme 3. Synthesis of lactone **8** [R8]

At the light of this result, mucic acid was reacted with acetic anhydride in the presence of a base (NaOH, pyridine or NaOAc) (R9, R9' or R9''). Scheme 4 summarizes the reactions investigated in buffered medium.



Scheme 4. Investigated reactions in buffered medium. Lactones **5** and **8** were obtained as racemic mixtures

In these conditions the pyrone **2b** (or its sodium salt **2a**) was obtained in good yields (69-78%). The reaction can be performed with a stoichiometric (Table 3, entry 1 [R9] and entry 2 [R9']) or catalytic amount (entry 3 [R9'']) of base. When NaOH was used in stoichiometric quantity, the product crystalized directly from the crude mixture as sodium salt•2 AcOH while, when using pyridine or AcONa in catalytic amount the acid form of the pyrone **2c** could be advantageously isolated by treatment with hydrochloric acid.

As expected, when following the reactions through the time, the per-acetylated five membered ring lactone **5** was observed as intermediate. To better understand the mechanism of the reactions R9, R9' and R9'', lactone **5** was reacted in an Ac$_2$O/AcONa system (Table 3, entry 4 [R10]): the pyrone **2b** was obtained in short time and high yield (94%). This result clearly indicates that the lactone **5** is a key reaction intermediate. Thus, the conversion of the per-acetylated five membered ring lactone **5** to the six membered ring pyrone **2b** requires an open chain

intermediate. When following the reaction R10' (Table 3, entry 5) by ^{1}H-NMR analysis through time species **4** and **8** were identified.

In order to reduce the amount of acetic anhydride and, at the same time, use a cheaper base, we found that it was possible to obtain **2a** in good yield using NaOH in an equimolar amount in respect to mucic acid in the minimum amount of anhydride needed to have a stirrable mixture (Table 3, entry 1). This experiment was performed on 50 g scale obtaining the direct crystallization of the desired product **2a** in a 61% yield and another 8% of **2a** after work-up of the remaining solution.

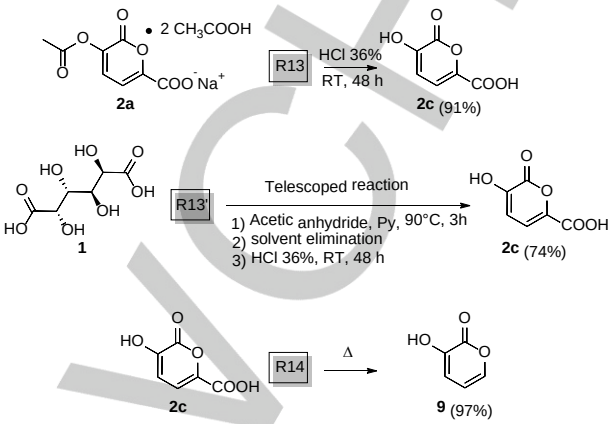
We also investigated the reactivity of the mucic acid tetracetate **6a** in the system B^-, $B:/Ac_2O$ (Table 3, entry 7 [R12] with AcONa as base and entry 8 [R12'] with Pyridine as base): also in those cases the pyrone **2a** (or **2b**) was formed fast and in high yield.

Table 3. Synthesis of Pyrones **2a**, **2b**, **2c, 2d and 2e**

Entry [Reaction]	R[a]	Ac_2O [M_f][b]	Base [M_f][b]	T [°C]	t [h]	P [Y_a%][c] *[Yi%]*[d]
1 [R9]	**1**	13	NaOH 1.04	90	4	**2a** *69*
2 [R9']	**1**	22	Py 1.00	90	3	**2b + 2c** *54 + 21*
3 [R9'']	**1**	53	AcONa 0.15	100	18	**2b** *78*
4 [R10]	**5**	20	AcONa 0.28	90	15	**2b** 94 *74*
5 [R10']	**7**	21	-	90	3	**2b + 2c** 64+30 =94 *36+26 =62*
6 [R11]	**8**	151	Py 0.23	60	2	**2b** 78
7 [R12]	**6a**	34	AcONa 1.13	reflux	4	**2a** *78*
8 [R12']	**6a**	71	Py 2.28	100	3	**2b + 2c** 94+3
9 [R15]	**10**	39	-	100	9	**2d** *45*[e]
10 [R15']	**11**	13	-	110	1	**2e** 90 *53*

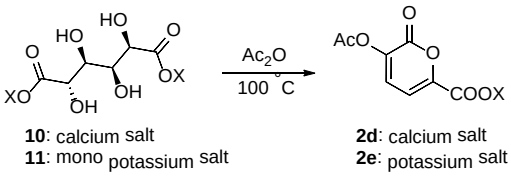
[a] R = Reagent. [b] M_r = molar ratio. [c] Y = analytical yield. [d] Y_i = isolated yield. [e] Precipitate from the reaction mixture.

Notice that **2a** and **2b** represent an easy access to 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid (**2c**). In fact, by stirring **2a** or **2b** in concentrated hydrochloric acid at room temperature for 48 hours, **2c** was obtained in high yield. Hydrolysis of **2a**, performed on 35 g scale afforded 91% yield. [R13]. We found also that **2c** can be obtained in high yield in a telescoped reaction using pyridine to convert mucic acid to the mixture of **2b** and **2c** and then HCl to complete the hydrolysis. [R13']. In addition, the pyrone **2c** can be easily decarboxylated to the 3-hydroxypyrone (**9**) in very high yield (97%) by heating under vacuum (170 °C and 0.3 mmHg) (Scheme 5 [R14]).



Scheme 5. Synthesis of **2c** from **2a** (R13) or from **1** (R14) and **9** from **2c** [R14].

As anticipated we also verified the reactivity of two glucaric acid salts. This C6 aldaric acid is a glucose derivative, the cheapest and the most abundant renewable feedstock. As expected, these salts showed a comparable reactivity in respect to mucic acid: the difference is mainly related to their different solubility in the reaction media. We tested calcium glucarate **10**, a cheap and commercially available derivative, very insoluble in the reaction conditions, as well as the corresponding pyrone calcium salt (Table 3, entry 9, Scheme 6 [R15]). The process allows to recover the reaction product **2d** by filtration. The co-precipitated product (5%) is compatible with 2.5-diacetoxymuconic salt in the unfavourable *trans-trans* conformation to cyclize to the pyrone derivative.



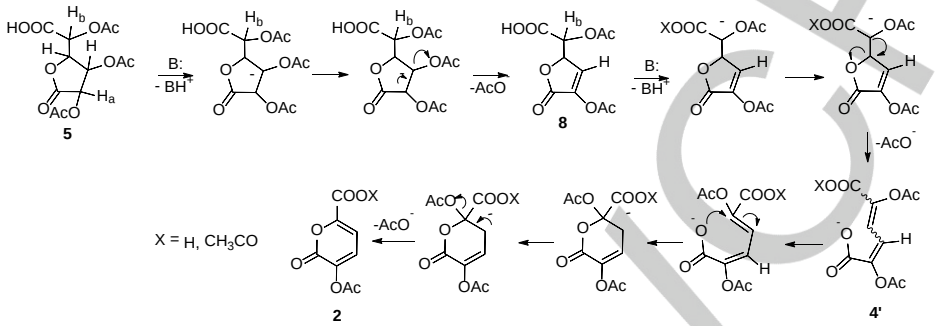
Scheme 6. Synthesis of **2d** and **2e** from D-glucaric acid calcium salt (**10**) [R15] and glucarate mono potassium salt (**11**) [R16] respectively.

We tested also a more soluble (and much more expensive) potassium glucarate mono acid **11**: in this case the reaction is faster and proceeded without significant formation of by-products to give the corresponding pyrone potassium salt **2e** in high yield and purity (Table 3, entry 10 [R15']).

It is worth mentioning that in both cases the reaction runs in acetic anhydride without catalysts, because the carboxylate anions (glucarate and acetate generated *in situ*) are able to promote the reaction themselves.

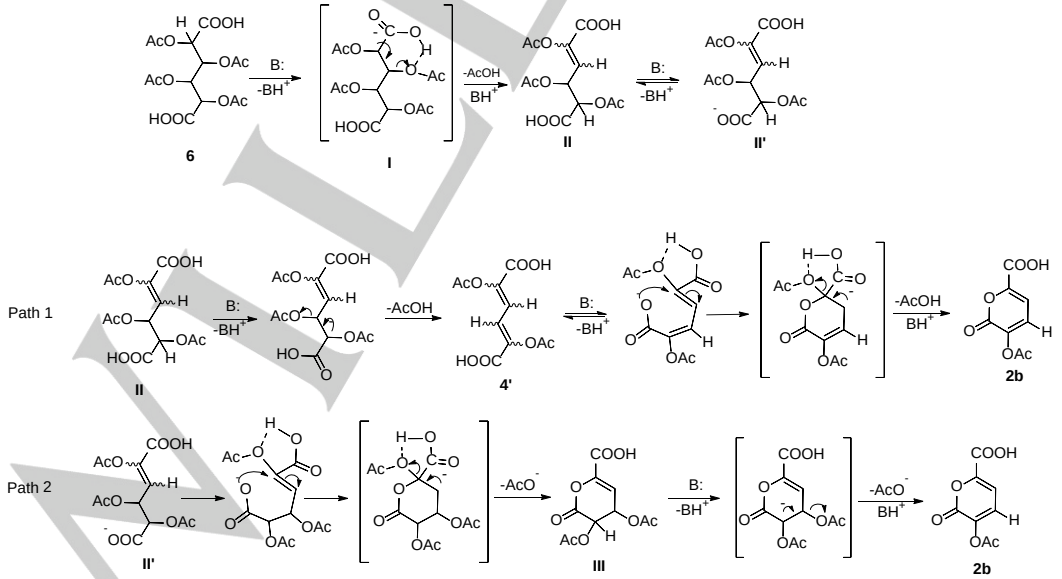
Reaction mechanism

Scheme 7 reports the mechanism proposed for the reactions R10 and R10' (Scheme 4). Although the lactone **5** has four C-H bonds, all in principle susceptible of deprotonation, the mechanism suggested involves the loss of the proton H_a as the first step: this hypothesis is supported by the reaction R8 (Scheme 3). In that case, in fact, by working in moderate acidic buffered conditions (AcO^-/AcOH) only the unsaturated five membered ring lactone **8** is formed: this result indicates that the most acidic hydrogen present in the molecule is H_a (Scheme 7).



Scheme 7. Suggested mechanism for the reactions R10 and R10'

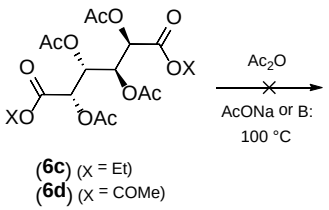
It is remarkable how it is possible to control the C-H deprotonation of the saturated lactone **5** in different solvents by modulating the strength of the base AcO^-: in acetic acid it is possible to stop the reaction to the mono eliminated derivative **8** while using acetic anhydride (Table 3, entry 4 [R10], entry 5 [R10'], entry 6 [R11]), also a second deprotonation occurs leading to dieliminated derivatives. The unsaturated lactone **8** is a second intermediate in the pyrone synthesis starting from mucic acid (the first intermediate is the lactone triacetate **5**). This hypothesis was confirmed by the reaction R11 where the unsaturated lactone **8**, in presence of AcO^-/Ac_2O (instead of AcO^-/AcOH) was easily converted to the pyrone **2**. A possible mechanism could involve the loss of H_b as proton from unsaturated lactone **8** giving the open chain derivative **4'** which evolves to the six membered pyrone **2** (Scheme 7). As anticipated, the synthesis of the pyrone can be also promoted by a typical organic Lewis's base like pyridine. Indeed, in reaction R10' (Table 3, entry 5) the pyridinium salt of the mucic acid lactone **7** is converted *in situ* to the corresponding per-acetylated lactone **5**, which is then deacetylated to the pyrone in high yields without addition of an external base thanks to the basic species present in solution: pyridine and $RCOO^-$.



Scheme 8. Suggested mechanism for the reactions R12 and R12'

We also investigated the reactivity of mucic acid tetracetate **6a**: in the moderate buffered media AcO^-/AcOH, in analogy with reaction R8, this substrate did not react. This result is coherent with the supposed acidic difference of H_a and H_b observed in the per-acetatylated lactone **5** by the reaction R8: in fact, in the open chain derivative **6a**, the reactive H_a is not present and, as already observed, H_b hydrogen does not react in that media. On the other hand, as expected, the derivative **6a** reacts well in the system B^-, B:/Ac_2O (Table 3, entry 7 [R12] and entry 8 [R12']): in these cases the pyrone **2a** (or **2b**) was formed faster and in higher yield if compared with the analogue reaction R10. Clearly now, in principle, the formation of the five membered ring lactone is not possible, and a different mechanism has to be taken into account (Scheme 8).

The first step of the process is compulsory: it is the deprotonation of the hydrogen in *α* to the carboxylic group to give the intermediate **I** in Scheme 8. It is worth noting that the next step of deacetylation is kinetically assisted by the hydrogen bond traced in the structure in square brackets. This deduction is supported by the experimental observation that the corresponding diethyl ester **6c** or the diacetyl mixed anhydride of mucic acid tetracetate **6d,** prepared by literature procedure,[21] did not react under the same reaction conditions (Scheme 9).



(**6c**) (X = Et)
(**6d**) (X = COMe)

Scheme 9. 6c and **6d** in moderate acid buffered medium.

The reactions starting from the substrate **6a** present less by-products if compared with the ones starting from the lactone derivatives and no intermediates were detected by ^{1}H NMR in the crude mixtures. In particular no trace of the compound **4'** (or its configurational isomers)**,** key intermediate of the Path 1, was observed in the analysed crude mixtures. On the contrary, this product was detected when starting from five membered ring lactones (lactone **5**, Table 3, entry 4 (R10) and lactone **8** entry 6 (R11)). This means that Path 2 should be the favourite one. The preference for this path is also supported by relative abundance of species **II'** compared with the species **II** due to the favourable acido-base equilibrium between them. Moreover, the species **II**, requires a C-H deprotonation step to evolve, which is not needed for the intermediate **II'**.

Conclusions

The more the valorization of renewable biomass will progress toward not only production of fuel but also toward production of useful chemicals, the more lignocellulosic biomass or bio-waste could really replace oil. The main challenge of our work was to use an oxidized pectine-based and polysaccharides-based feedstock, such as mucic and glucaric acid, to obtain pyrones by an easy synthesis of 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid salts and their derivatives in good yields. This approach preserves all the six carbon atoms present in the starting C6 aldaric acids, and allows a green isolation procedure of the products. 3-Acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid sodium salt can be seen as a protected form of 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid which is obtainable in very high yield by a simple hydrolysis reaction. These syntheses have been performed on several grams scale, and the good results achieved suggest the possibility of an easy further scale-up. At the same time, a simple procedure to obtain the corresponding decarboxylated 3-hydroxypyrone in high yield has been reported; in this case, the synthesis was performed only on a gram scale due to the limitation of the sublimation apparatus utilized. A complete characterization of the two most important pyrones here synthesized is provided by crystallographic studies.

A reaction mechanism has been proposed on the base of the identified intermediates, starting from mucic 1,4-lactone salt isolated for the first time during this work. A second reaction mechanism has been proposed starting from the open chain mucic acid tetracetate.

As underlined in the introduction, pyrones are interesting intermediates for the synthesis of several classes of compounds including polymers. The synthesis here reported represents a convenient green method for the production of these derivatives from removable sources and can favour a further development of compounds and materials based on them.

Experimental Section

Reagents and solvents, commercially available, were purchased from Sigma-Aldrich except acetic anhydride (Carlo Erba), mucic and methanesulfonic acid (Acros, Organics) and were used as received.

^{1}H NMR (400 MHz) and ^{13}C NMR (100.5 MHz) spectra were recorded at 302 K on a Bruker Avance 400 instrument. Chemical shifts were reported in ppm respect to the solvent residual peak as internal standard (DMSO-d_6: δ_H= 2.50 ppm, $CDCl_3$: δ_H= 7.26 ppm, Acetone-d_6: δ_H= 2.05 ppm). Analytical yields were calculated using terephtalic acid as standard. Infrared spectra were recorded with FTIR Varian 640 instrument acquired in KBr disks. Mass spectra were recorded by using Electrospray Ionization (ESI) with a Bruker Esquire 3000 plus ion-trap mass spectrometer instrument equipped with an ESI Ion Trap LC/MSn System. Melting points were determined by using a Büchi 535 apparatus and were not corrected. Direct phase silica gel TLC plates were used for thin layer chromatography. Single crystals X-ray diffraction data were collected on a Bruker KAPPA-APEX II CCD diffractometer using Mo-Kα radiation (λ = 0.71073 Å), see Supporting information for specific crystallographic details (Table S1 and Figure S1-S6).

Synthesis of 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid (2b) from 1 with methanesulfonic acid [R1]. Mucic acid (**1**) (5.0 g, 24 mmol), acetic anhydride (18.0 mL, 190 mmol) and methanesulfonic acid (1.24 mL, 19.0 mmol) were loaded in a round bottom flask. The reaction was refluxed under stirring for 9 hours; after this time the mixture was cooled to room temperature. A sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yields of **2b** (66%), **3** (14%) and **4** (4%) in the presence of an internal standard. The reaction mixture was then cooled down and kept overnight at 4 °C. The solid was filtered and washed with 6

mL of a mixture of acetic acid-acetic anhydride 5:1 obtaining **2b** as a beige solid (1.1 g, purity 91%, 5.0 mmol, yield 21%,); Rf: 0.3 (5% acetic acid in ethyl acetate); ^{1}H NMR (DMSO-d6,): δ 7.47 (d, 1H, *J* = 7.2 Hz), 7.02 (d, 1H, *J* = 7.2 Hz), 2.26 (s, 3H); ^{13}C NMR (DMSO-d6): δ 168.1, 160.2, 156.4, 147.2, 140.1, 131.6, 110.6, 20.6; FT-IR (($\nu_{max\ max}$, cm^{-1})**:** 3560, 3444, 3141, 3102, 3065, 2893, 2831, 2763, 2598, 2654, 2598, 2511, 2485, 2189, 1978, 1950, 1781, 1735, 1708, 1644, 1619, 1438, 1377, 1268, 1232, 1194, 1141, 1121, 1070, 1007, 980, 902, 877, 796, 774, 759, 671, 597, 529, 458; -MS/MS (ESI): m/z 197 (14) $[M - H]^-$, 153 (100) $[M - H - CO_2]^-$, 111(86) $[153 - CH_2CO]^-$, 81 (3). **2,5-Diacetoxymuconic acid (4)** ^{1}H NMR (400 MHz, DMSO-d6): δ 6.99 (s, 2H), 2.28 (s, 6H); FT-IR (ν_{max}, cm^{-1}): 3466, 3082, 2991, 2866, 2674, 2592, 2530, 1779, 1713, 1695, 1614, 1431, 1376, 1319, 1261, 1182, 1107, 1048, 1007, 921, 896, 833, 767, 665, 657, 585. +MS (ESI) (methanol):m/z 281 $[M + Na]^+$, 539 $[2{\cdot}M + Na]^+$, 561 $[2M – H + 2{\cdot}Na]^+$. **3-Acetoxy-2H-pyran-2-one (3):** ^{1}H NMR (400 MHz, DMSO-d6): δ 7.69 (dd, 1H, *J* = 1.8 Hz; *J* = 5.1 Hz), 7.38 (dd, 1H, *J* = 1.8 Hz; *J* = 7.1 Hz), 6.43 (dd, 1H, *J* = 5.1 Hz; *J* = 7.1 Hz), 2.24 (s, 3H).

Synthesis of 2-acetoxy-2-(-3,4-diacetoxy-5-oxotetrahydrofuran-2-yl)acetic acid (5) (mucic acid 1,4-lactone triacetate) [R2]. Mucic acid (**1**) (5.0 g, 23.8 mmol) and acetic anhydride (22.5 mL, 214 mmol) were charged in a three-neck bottom flask equipped with a thermometer and a condenser. The reaction mixture was refluxed under stirring for 6 hours. A sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yield of **5** (94%) in the presence of an internal standard. The solvent and the formed acetic acid were removed in vacuo at 60 °C and a green/brown oil was obtained. The oil was stirred with 250 mL of diethyl ether overnight to give **5** as a white precipitate (4.85 g, purity 97%, 14.79 mmol, yield 62%,); ^{1}H NMR (DMSO) δ: 5.89 (d, 1H, *J* = 7.7 Hz), 5.49 (dd, 1H, *J* = 7.7 Hz, *J* = 7.3 Hz), 5.26 (d, 1H, *J* = 2.8 Hz), 5.01 (dd, 1H, *J* = 2.8 Hz, *J* = 7.3 Hz), 2.14 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (DMSO-d6): δ 170.4, 169.8, 169.7, 168.7, 167.9, 77.5, 72.4, 72.0, 70.0 , 20.9, 20.7, 20.6; FT-IR (ν_{max}, cm^{-1}): 3487, 2947, 1852, 1817, 1758, 1645, 1432, 1375, 1323, 1226, 1171, 1118, 1047, 959, 926, 894, 782, 741, 708, 605; -MS (ESI) (CH_3CN): m/z 634 (100) $[2{\cdot}M - H]^-$, 575 (4) $[2{\cdot}M – CH_3COOH – H]^-$, 317 (7) $[M - H]^-$.

Synthesis of (2*R*,3*S*,4*R*,5*S*)-2,3,4,5-tetraacetoxyhexanedioic acid (6a) (mucic acid tetracetate) [R3]. Mucic acid (**1**) (10.0 g, 47.6 mmol), acetic anhydride (45.0 mL, 476 mmol) and trifluoroacetic acid (20.0 mL, 260 mmol) were charged in this order in a round bottom flask equipped with a condenser. The mixture was heated and stirred at 80 °C for 9 hours; then the heterogeneous reaction mixture was cooled to room temperature. The solid was filtered, washed twice 4 mL of ethyl acetate and filtered to give **6a** as a white solid (12.5 g, purity 88%, 29.1 mmol, yield 61%); m.p.: 243-248 °C; ^{1}H NMR (acetone-d6): δ 5.75 (s, 2H), 5.17 (s, 2H), 2.13 (s, 6H), 2.05 (s, 6H); ^{1}H NMR (DMSO-d6): δ 5.57 (s, 2H), 5.03 (s, 2H), 2.10 (s, 6H), 2.01 (s, 6H); ^{13}C NMR (DMSO-d6): δ 170.0, 169.2, 168.3, 69.9, 68.3, 21.5, 20.7; FT-IR (ν_{max}, cm^{-1}): 3406, 3058, 2916, 1757, 1737, 1420, 1376, 1328, 1230, 1107, 1058, 948, 898, 846, 769, 675, 634, 593, 561; -MS/MS (ESI) (methanol):m/z 377 (100) $[M - H]^-$, 317 (57) $[M - H - CH_3COOH]^-$, 273 (40) $[M - H - CH_3COOH - CO_2]^-$, 213 (14), 171 (11), 141 (11). Spectroscopic data in accordance with what stated in literature.[21]

Synthesis of mucic acid 1,4-lactone pyridinium salt (7) [R6]. Mucic acid (**1**) (5.0 g, 2.4 mmol) and pyridine (50 mL, 0.62 mol) were charged in a round bottom flask equipped with a condenser. The mixture was refluxed under stirring for 4 hours. The solvent of the reaction mixture was removed in vacuo at 60 °C to obtain a sticky solid. The solid was dispersed in 30 mL of CH_3CN and stirred overnight; then was filtered to give **7** as a light-yellow solid (6.0 g, purity 93%, 2.1 mmol, yield 88%); m.p.: 123-132 °C**;** (DMSO-d6): δ 8.58 (m, 2H), 7.79 (m, 1H), 7.39 (m, 2H), 4.34 (dd, *J* =1.7, *J* =9.1 Hz, 1H), 4.32 (d, *J* =9.1 Hz, 1H), 4.21 (d, *J* =1.8 Hz, 1H), 4.17 (7, *J* =8.7, 1H); ^{13}C NMR (DMSO-d6): 174.5, 173.43, 150.0, 136.7, 124.4, 80.9, 74.0, 72.3, 67.4; FT-IR (KBr, ν_{max}, cm^{-1}): 3423, 3364, 3137, 3103, 2946, 2922, 2883, 2697, 2520, 2168, 2041, 1785, 1760, 1638, 1596, 1546, 1487, 1384, 1328, 1286, 1225, 1204, 1172, 1149, 1133, 1105, 1016, 990, 956, 921, 879, 830, 762, 734, 686, 642, 599, 517, 479; – MS (ESI) (methanol): m/z 619 (10) $[(3{\cdot}M - H) + 2{\cdot}Na]^-$, 405 (11) $[2(M - H) + Na]^-$, 383 (76) $[2(M - H) + H]^-$,191 (100) $[M - H]^-$.

Synthesis of mucic acid 1,4-lactone DABCO salt (7') [R6']. Pyridinium mucic acid 1,4-lactone salt (**7**) (1.0 g, purity 93%, 3.4 mmol) and ethanol (25 mL) were charged in a two-neck round bottom flask equipped with a condenser. The mixture was refluxed under stirring until the mixture turned homogeneous. Then, DABCO (0.82 mg, 7.2 mmol) was added to the hot solution obtaining initially a sticky solid which in 20 minutes turned into a fine powder. The reaction mixture was then cooled to room temperature and filtered obtaining **7'** as a white solid (907 mg, purity 99%, 2.94 mmol, yield 87%); m.p.: 203-212 °C ; ^{1}H NMR (DMSO-d6, ppm): δ 4.24 (d, *J* =9.1 Hz, 1H), 4.21 (dd, *J* =2.7, *J* =8.3 Hz, 1H), 4.07 (t, *J* =8.8 Hz, 1H), 3.79 (d, *J* =2.7 Hz, 1H), 2.96 (s, 12H) ; ^{13}C NMR (DMSO-d6): δ 175.0, 174.2, 81.5, 74.1, 73.9, 68.9.

Synthesis of 2b from 5 with methanesulfonic acid [R4]. Mucic acid tetraacetate (**6a**) (1.13 g, 88% purity, 2.63 mmol), acetic anhydride (750 µL, 7.92 mmol) and methanesulfonic acid (507 mg, 5.28 mmol) were charged in a round bottom flask equipped with a condenser. The mixture was refluxed under stirring for 5 hours and then cooled to room temperature. A sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yields of **2b** (46%), **3** (10%), **4** (13%) and **5** (30%) in the presence of an internal standard.

Synthesis of 2b from 6a with methanesulfonic acid [R5]. Mucic acid 1,4-lactone triacetate (**5**) (0.26 g, 97% purity, 0.79 mmol), acetic anhydride (225 µL, 2.37 mmol) and methanesulfonic acid (151 mg, 1.57 mmol) were charged in a round bottom flask equipped with a condenser. The mixture was refluxed under stirring for 5 hours and then cooled to room temperature. A sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yields of **2b** (68%), **3** (13%), **4** (16%) and **5** (2%) in the presence of an internal standard.

Synthesis of 2-acetoxy-2-(-4-acetoxy-5-oxo-2,5-dihydrofuran-2-yl)acetic acid (8) from 5 [R8]. Mucic acid 1,4-lactone triacetate (**5**) (0.23 g, purity 97%, 0.70 mmol), acetic acid (4.30 mL, 45.5 mmol) and triethylamine (30 µL, 0.22 mmol) were loaded in a round bottom flask. The reaction was stirred at room temperature for one week. After this time, a sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yields of **8** (34%). The solvent was removed in vacuo at 60 °C and product **8** was recovered by flash chromatography (eluent 1.25% of CH_3COOH in AcOEt) as a white solid (41 mg, 24% yield); ^{1}H NMR (DMSO-d6): δ 7.37 (d, 1H, *J* =2.0 Hz); 5.69 (dd, 1H, *J* = 2.0 Hz, *J* =3.2 Hz); 5.19 (d, 1H, *J* =3.2 Hz); 2.28 (s, 3H); 2.00 (s, 3H); ^{13}C NMR (DMSO-d6): δ 169.8, 167.8, 167.6, 166.7, 137.8, 134.3, 79.1, 71.4, 20.9, 20.8; IR (ν_{max}, cm^{-1}): 3528.9, 3467.3, 3272.2, 3148.7, 2951.4, 1782.9, 1739.9, 1642.9, 1562.7, 1433.5, 1376.7, 1347.5, 1303.1, 1237.9, 1187.7,1120.9, 1073.3, 1016.0, 922.6, 867.0, 828.2, 793.4,760.3,704.3, 682.6, 640.6, 609.7, 567.1, 512.9, 444.9; +MS(ESI) m/z: 303 $[M - H + 2{\cdot}Na]^+$.

Synthesis of sodium 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylate (2a) from 1 with sodium hydroxide [R9]. Mucic acid (**1**) (50.0 g, 0.24 mol) and acetic anhydride (300.0 mL, 3.17 mol) were placed in a round bottom flask equipped with a condenser, stirred and heated at 90 °C. To this suspension, sodium hydroxide (10.0 g, 0.25 mol) was added over a period of 2 hours keeping the temperature between 90-95 °C and then mixture was left at this temperature for other 2 hours. The reaction was cooled to room temperature turning in a viscous brown solution. After one night the formed precipitate was filtered, washed twice with 10 mL of a mixture of 5% acetic anhydride in acetic acid and dried under vacuum, giving **2a** as a light brown solid (48.0 g, purity 98%, 13.8 mmol, yield 58%). The filtered solution was concentrated down to 100 mL at reduced pressure heating at 45 °C. At room temperature a solid was formed, then it was filtered, washed twice with the same mixture of acetic anhydride/ acetic acid and dried under vacuum obtaining another crop of **2a** (11.1 g, purity 81%, 2.70 mmol, yield 11%, impurity consists of sodium acetate and acetic acid). Overall yields of **2a** 69% ; ^{1}H NMR (DMSO-d6): δ 7.44 (d, 1H, *J* = 7.2 Hz), 6.87 (d, 1H, *J* = 7.2 Hz), 2.27 (s, 3H), 1.91 (s, 6H); ^{13}C NMR (DMSO-d6): δ 173.4, 168.4, 161.9, 157.9, 155.8, 137.3, 132.9, 105.9; 22.2, 20.6; FT-

IR (ν_{max}, cm^{-1}): 3416, 3104, 3076, 3022, 2941, 2900, 2840, 2774, 2667, 2607, 2539, 2365, 2165, 1772, 1727, 1651, 1619, 1412, 1372, 1332, 1289, 1200, 1135, 1100, 1062, 1007, 972, 150 , 887, 855, 811, 784, 747, 675, 654, 599, 577, 565, 529, 468, 429, 408; -MS/MS (ESI) (methanol): m/z 197 (6) $[M - H]^-$, 153 (29) $[M - H - CO_2]^-$, 111 (100) $[153 - CH_2CO]^-$, 81 (3).

Synthesis of 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid (2b) from 1 with pyridine [R9']. Mucic acid (**1**) (5.00 g, 23.8 mmol), pyridine (1.90 mL, 23.6 mmol) and acetic anhydride (50.0 mL, 529 mmol) were mixed together in a three-neck round bottom flask, equipped with a thermometer and a condenser, stirred and heated at 90 °C for 3 hours. After this time, the hot mixture was filtered to remove the small amount of mucic acid still present. The solution was concentrated to half of its volume obtaining a light violet solid (4.1 g). The solid was filtered and analysed by ^{1}H NMR revealing to be composed by **2b** (54%), **2c** (21%), acetic acid and pyridine in the presence of an internal standard.

Synthesis of 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid (2b) from 1 with sodium acetate [R9'']. Mucic acid (**1**) (5.00 g, 23.8 mmol), sodium acetate (500 mg, 3.67 mmol) and acetic anhydride (120 mL, 1.27 mol) were mixed together in a two-neck round bottom flask, equipped with a thermometer and a condenser, and were stirred and heated at 100 °C for 18 hours. After this time, the reaction was cooled down to 0 °C, 1 mL of HCl 36% was added and the mixture was stirred for two hours at room temperature. The solution was concentrated until a white solid precipitated (5.78 g). The solid was dispersed in 15 mL of acetic acid and the resulting suspension was refluxed obtaining a solution. This latter was then cooled to room temperature obtaining **2b** as white crystals (3.70 g, purity 85% yield 67%, the impurity consists of sodium acetate and acetic acid). From the filtered solution a second crop of **2b** was recovered as a white solid (800 mg, purity 67%, yield 11%, the impurity consists of sodium acetate and acetic acid).Overall yield of **2b** 78%.

Synthesis of 2b from 5 with sodium acetate [R10]. Mucic acid-1,4-lactone-triacetate (**5**) (520 mg, 97% purity, 1.59 mmol) and acetic anhydride (3.0 mL, 32 mmol) were charged in a round bottom flask equipped with a condenser. Sodium acetate ($AcONa \cdot 3H_2O$ 60 mg, 0.44 mmol) was added and, then, the system was heated and stirred at 90 °C for 15 hours. A sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yield of **2b** (97%) in the presence of an internal standard. The solvent was removed under reduced pressure, and the resulting brown viscous oil was dissolved in acetic anhydride (4.0 mL). To this solution, 0.5 mL of HCl 37% were added and the formed precipitate was filtered off obtaining a homogeneous solution. The solvent was removed under reduced pressure to obtain 324 mg of a sticky solid. The solid was dispersed in 3.0 mL of THF, stirred overnight and then filtered obtaining **2b** as a beige solid (250 mg, purity 93% 1.17 mmol, yield 74%,).

Synthesis of 2b + 2c from 7 [R10']. Mucic acid 1,4-lactone pyridinium salt (**7**) (200 mg, purity 98%, 0.71 mmol) and acetic anhydride (1.4 mL, 15 mmol) were charged in a three-neck round bottom flask, equipped with a condenser. The mixture was stirred and heated at 90 °C for 3 hours and then cooled to room temperature obtaining a viscous brown liquid. A sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yield of **2b** (64%) and **2c** (30%) (overall yield 94%, molar ratio **2c**/**2b** = 0.47).in the presence of an internal standard. To the crude, 10 mL of CH_3CN were added and the mixture was stirred overnight at room temperature giving a precipitate. The solid was filtered, washed twice with CH_3CN and dried under vacuum obtaining 107 mg of a mixture of **2b** + **2c** (overall yield 62%, molar ratio **2c**/**2b** = 0.42).

Synthesis of 2b from 8 with pyridine [R11]. 2-acetoxy-2-(-4-acetoxy-5-oxo-2,5-dihydrofuran-2-yl)acetic acid (**8**) (23.3 mg , purity 77%, 0.07 mmol), 1.00 mL (151 mmol) of acetic anhydride and pyridine (13 μL, 16 μmol) in were loaded in a round bottom flask. The reaction was stirred and heated at 60 °C for 2 hours. After this time, a sample was withdrawn and analysed by ^{1}H NMR to calculate conversion of **8** (100%) and analytical yields of **2b** (78%) in the presence of an internal standard.

Synthesis of 2a starting from 6a with sodium acetate [R12]. Mucic acid tetraacetate (**6a**) (2.00 g, 88% purity, 4.66 mmol) and acetic anhydride (15.0 mL, 159 mmol) were charged in a round bottom flask equipped with a condenser. The mixture was stirred and heated. When the reaction turned homogeneus (about 110 °C), sodium acetate ($AcONa \cdot 3H_2O$, 719 mg, 5.28 mmol) was added to the hot solution. The heterogeneous reaction mixture was refluxed for 4 hours until it became a yellow solution. The solution was then cooled to room temperature, concentrated to half of its volume obtaining the formation of **2a** as a white solid (0.60 g, %, purity: 98%, 1.73 mmol, yield: 37%). The mother liquors were concentrated to obtain a brown solid (**2a**, 0.69 g, purity 93%, 1.89 mmol, yield: 41%). Overall yield of **2a** (78).

Synthesis of 2b starting from 6a with pyridine [R12']. Mucic acid tetraacetate (**6a**) (255 mg, 88% purity, 0.59 mmol), pyridine (107 mg, 1.35 mmol) and acetic anhydride (4.0 mL, 42 mmol) were charged in a round bottom flask equipped with a condenser. The mixture was heated at 100 °C and stirred for 3 hours. After this time, a sample was withdrawn, concentrated and analysed by ^{1}H NMR to calculate the analytical yield of **2b** (94%) and **2c** (3%) in the presence of an internal standard.

Synthesis of 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid 2c from 2a [R13]. In a 50 mL round bottom flask, 33 mL of HCl 37% were placed and then sodium 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylate (**2a**) (35.1 g, purity 98%, 101 mmol) was added. The heterogeneous mixture was stirred for 48 hours at room temperature. After this time, the solid was filtered, suspended in water (50 mL) and stirred at room temperature for 12 hours to remove NaCl. After this time the solid was filtered obtaining **2c** as a white solid (15.3 g, purity 94%, 92.2 mmol, yield 91%); m.p.: 209-212 °C with decomposition); ^{1}H NMR (DMSO-d6): δ 7.12 (d, 1H, *J* = 7.4 Hz); 6.69 (d, 1H, *J* = 7.4 Hz); ^{13}C NMR (DMSO-d6): δ 161.1, 158.8, 147.7, 141.2, 115.0, 113.8; IR (KBr, ν_{max}, cm-1): 3308, 3116, 3080, 2921, 2781, 2643, 2589, 2486, 2898, 1715, 1659, 1554, 1437, 1350, 1267, 1227, 1161, 1074, 972, 868, 756, 705, 634, 600, 535, 466; - MS((-)-ESI): m/z 155 (33) $[M - H]^-$, 127 (36) $[M - CHO]^-$, 111 (100) $[M - H - CO_2]^-$, 83 (11) $[M - CO_2 - CHO]^-$. Spectroscopic data are consistent with those reported in literature.[5]

Synthesis of 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid 2c from mucic acid 1. Mucic acid (**1**) (5.00 g, 23.8 mmol), pyridine (1.90 mL, 23.6 mmol) and acetic anhydride (50.0 mL, 529 mmol) were mixed together in a three-neck round bottom flask equipped with a thermometer and a condenser. The reaction was stirred and heated at 90 °C for 3 hours. Then, the hot mixture was filtered to remove the residual solid and the solution was evaporated to obtain 5.25 g of a brown solid. The solid was dispersed in 6 mL of HCl 37% and the resulting suspension was stirred for 48 hours at room temperature. The solid was filtered and washed with 3 x 1 mL of water recovering **2c** as a beige solid (3.14 g, purity 87%, 17.5 mmol yield 73.5%).

Synthesis of 3-hydroxy-2*H*-pyran-2-one (9) by decarboxylation of 2c [R14]. Pyrone **2c** (1.10 g, purity 94%, 6.62 mmol) was introduced in a sublimation apparatus and this latter was placed in an oil bath at 170 °C. At 140 °C and 0.3 torr the sublimation took place and the product started to deposit on the surface of the cold finger cooled by circulating tap water. At the end of the reaction, 3-hydroxy-2*H*-pyran-2-one (**9**) was recovered as a white solid (730 mg, purity 99%, 6.52 mmol, yield 98%); m.p.: 90-91 °C (sublimation);[23] ^{1}H NMR ($CDCl_3$, ppm): δ 7.09 (dd, 1H, *J* = 1.7 Hz, *J* = 5.2 Hz); 6.61 (dd, 1H, *J* = 1.7 Hz, *J* = 7.1 Hz); 6.14 (dd, 1H, *J* = 5.2 Hz, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$): δ 161.6, 142.4, 142.2, 114.5, 107.1. Spectroscopic data are consistent with those reported in literature.[24]

Synthesis of 3-hydroxy-2-oxo-2*H*-pyran-6-carboxylic acid (2c) from calcium D-glucarate (10) [R15]. Calcium D-glucarate tetrahydrate (**10**) (5.60 g, 17.5 mmol) and acetic anhydride (65.0 mL, 688 mmol) were mixed together in a three-neck round bottom flask, equipped with a thermometer and a condenser. The resulting mixture was stirred and heated at 100 °C for 9 hours. Then, the brown heterogeneous mixture was cooled to room temperature and filtered. The solid was washed twice with 3.0 mL of a mixture of 5% acetic anhydride in acetic acid and dried under vacuum obtaining a light brown solid (4.18 g). The ^{1}H NMR analysis in D_2O (trioxane as internal standard) revealed the presence of a product

compatible with 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylic acid calcium salt **2d** (analytical yield 45%) and a secondary product compatible with 2,5-diacetoxymuconic calcium salt (analytical yield 4.5%). ^{1}H NMR (D_2O), signals ascribed to pyrone **2d**: δ 7.55 (d, 1H, *J* = 7.4 Hz), 7.14 (d, 1H, *J* = 7.4 Hz), and 2.37 (s, 3H); signals ascribed to 2,5-diacetoxymuconic calcium salt: δ 6.93 (s, 2H) and 2.35 (s, 6H). In a round bottom flask, the light brown solid (4.0 g) was added to 6 mL of HCl 37% and the heterogeneous mixture was stirred for 48 hours at room temperature. Then, the solid was filtered, washed with water recovering 1.10 g of **2c** (purity 90%, 6.35 mmol, yield 80 % based on **2d**. The impurity mainly consists of product **4**).

Synthesis of potassium 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylate (2e) from D-glucaric acid potassium salt (11) [R15']. D-glucaric acid potassium salt (**11**) (0.41 g, 1.63 mmol) and acetic anhydride (2.0 mL, 21 mmol) were mixed together in a three-neck bottom round flask, equipped with a thermometer and condenser. The resulting mixture was stirred and heated at 110 °C. After 1 hour the mixture turned homogeneous and a sample was withdrawn and analysed by ^{1}H NMR to calculate the analytical yield of **2e** (90%) in the presence of an internal standard. The reaction mixture was cooled to room temperature, 5 mL of ethyl acetate were added obtaining the formation of a grey solid. The mixture was filtered and the solid was washed with 5 mL of ethyl acetate obtaining **2e** (0.22 g, purity: >95%, 0.89 mmol, yield: 55%); ^{1}H NMR (DMSO-d6): δ 7.41 (d, 1H, *J* = 7.2 Hz), 6.11 (d, 1H, *J* = 7.2 Hz), and 2.26 (s, 3H); ^{13}C NMR (DMSO-d6): δ 168.5, 160.7, 158.1, 157.3, 136.7, 133.1, 105.1, 20.7.

Synthesis of diethyl 2,3,4,5-tetraacetoxyhexanedioate (6c) from diethylmucate (6b). Diethylmucate, prepared according to a reported method[25] (1.00 g, purity 94%, 3.53 mmol) was dispersed in 10 mL of acetic anhydride. H_2SO_4 (0.7 mL, 13.1 mmol) was added dropwise into the mixture at room temperature under stirring. After few minutes the mixture turned homogenous and within one hour **6c** precipitated as a white solid that was recovered by filtration (1.30 g, purity 90%, 2.69 mmol, yield 76%,); ^{1}H NMR (DMSO-d6): δ 5.55 (d, 2H, *J* = 0.9 Hz), 5.17 (d, 2H, *J* = 0.9 Hz), 4.11 (dd, 4H, d, 2H, *J* = 7,1 Hz), 2.12 (s, 3H), 2.02 (s, 3H), 1.17 (t, 6H, *J* = 7,1 Hz); ^{13}C NMR (DMSO-d6): δ 170.0, 169.3, 166.8, 69.8, 67.9, 62.2, 20.6, 20.6, 14.2.

Keywords: 2-pyrones • mucic acid • aldaric acids • mucic acid lactone • renewable biomass

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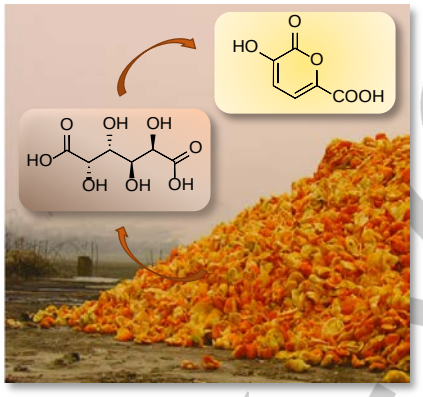
Entry for the Table of Contents

FULL PAPER

A green approach to the synthesis of 3-acetoxy-2-oxo-2*H*-pyran-6-carboxylated derivatives from bio-derived C6 aldaric acids has been investigated. All the six carbon atoms present in the aldaric acid are preserved. For the first time mucic acid lactone salt has been isolated and fully characterized.



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Page No. – Page No.

Pyrones Synthesis from Renewable Sources: Easy Preparation of 3-Acetoxy-2-oxo-2*H*-pyran-6-carboxylic Salts and their Derivatives as 3-Hydroxy-2*H*-pyran-2-one from C6 Aldaric Acids