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Iron-catalysed chemo-selective oxidation of unprotected sugars: application for the competitive oxidation of pentoses from a sugar mixture

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An iron-catalysed transfer hydrogenation methodology was developed to oxidise aldo-hexoses and -pentoses into sugar lactones using different acceptors. The transformation occurs on unprotected sugars with complete chemo-selectivity for the anomeric position. An application for the competitive oxidation of pentose from a mixture of C5 and C6 sugars is also reported. Finally, we managed to perform the oxidation of xylose with only an equimolar amount of a carefully chosen acceptor, improving drastically the sustainability of the transformation without compromising the equilibrium shift.

Introduction

Recent developments in lignocellulosic biomass treatments have improved the release of monosaccharides from natural polymers offering sustainable starting materials to prepare building blocks from renewable resources.[1–3] A fundamental challenge is to expand the range of eco-friendly, atom-efficient and selective methodologies to up-grade sugars. Particularly, *the selective and effective transformations of unprotected sugars* to develop platform molecules and more complex building blocks remain a crucial endeavour,[4] even though very innovative contributions have recently been reported.[5–9] In line with these objectives, our first goal is to develop more sustainable redox methodologies to selectively transform native (fully unprotected) sugars using cheap earth-abundant metal catalysis technologies.

Catalytic transfer hydrogenation (TH) is an attractive redox process alternative to direct hydrogenation involving high-pressured hydrogen,[10] as it (i) does not require any elaborate set-ups, (ii) can be efficient under milder conditions, and (iii) gives access to a wide range of building-blocks. Early reports of a transfer hydrogenation approach applied on unprotected monosaccharides involved platinum, rhodium and ruthenium catalysts.[11,12] More recently, sugars were reported as excellent hydrogen donors in a rhodium-catalysed reduction of alkenes, alkynes and ketones, in which hydride abstraction selectively occurred on the anomeric carbon.[13] To the best of our knowledge, earth-abundant metal complexes have not been investigated as transfer hydrogenation catalysts in unprotected carbohydrates oxidation.

In this context, we describe an iron catalysed selective oxidation of the anomeric position of unprotected hexoses and pentoses into sugars lactones. Importantly, our study relies on a transfer hydrogenation (TH) strategy where the sugar behaves as the formal hydrogen donor (reducing agent) and a ketone as the acceptor (oxidizing agent) and occurs without the need for a strong oxidant and/or halogenated derivatives in contrast to previous methodology.[14–19]

To achieve this transformation, we have selected as catalyst Knölker complex, known to oxidise alcohols using acetone as a hydrogen acceptor or catalyse ketones reduction via a TH using isopropanol as a formal hydrogen source.[20] Recently, this catalyst has been reported for the synthesis of lactones starting from simple diols occurring *via* a lactol intermediate (**Figure 1**).[21]

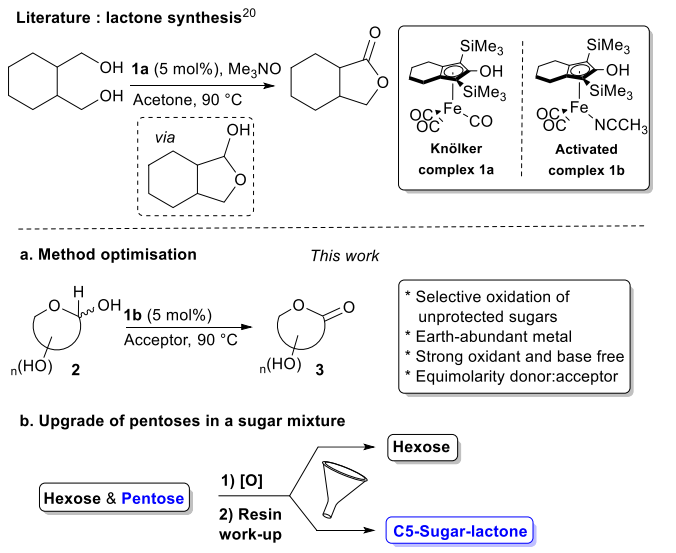

Figure 1: Context and overview of our study

Our selection of the Knolker catalyst was motivated by (i) its lower cost than the Shvo ruthenium catalyst and (ii) a similar mode of action to the latter, which is known to oxidise the anomeric carbon of several hexoses to afford sugar-lactones[22] through transfer hydrogenation reactions without the need of

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an exogenous base, thanks to the established cooperation of the ligand and metal centre during catalysis.[23]

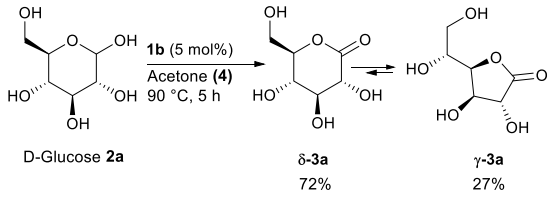
In this work, we detail the optimisation and scope of this seminal iron catalysed, strong-oxidant free, oxidation of unprotected sugars into sugar-lactones and a potential synthetic application for the direct upgrade of pentoses into furanolactones from sugar mixtures.

In the last section of this report, we focused to improve the sustainability of our transformation, by assessing the impact of the acceptor and its stoichiometry on the reaction efficiency. This has led to the identification of an optimal acceptor to perform a sustainable process enabling the oxidations in a stoichiometric carbohydrate to acceptor ratio.

Results and discussion

Catalytic system and substrate scope

Initial oxidation was performed on unprotected glucose **2a** as model substrate using acetone **4** as both acceptor and solvent. The reaction was carried out with activated Knölker catalyst **1b** (5 mol%) at 90 °C in a sealed tube. After 5 hours, complete conversion of the substrate was observed and a mixture of δ- and γ-gluconolactones **3a** (ratio 72:27 respectively) resulting from chemo-selective oxidation of the more reactive anomeric position was formed **(Scheme 1)**. Full conversion was also observed when the tricarbonyl precursor **1a** was employed and activated in situ in presence of trimethylamine N-oxide. Importantly, the glucose remained untouched when the reaction was performed without catalyst.

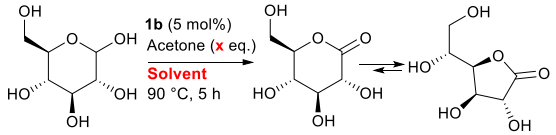


Scheme 1: Initial attempt on glucose oxidation with Knölker catalyst **1b**. Yields of **3** were determined by ^{1}H NMR of the crude mixture (DMSO-d6) using an internal standard.

The reaction proceeded cleanly to form the lactones **3** which were easily separated without chromatographic techniques as δ-**3a** selectively precipitated from cold acetone. In agreement with literature precedents (Shvo ruthenium catalyst),[22] kinetically formed δ-**3a** was fully isomerised to the thermodynamically more stable γ-**3a** in 24 hours with concomitant appearance of traces of acetal products resulting from the reaction of the lactone with acetone. Considering the formation of these side-products and in perspective to expand the range of acceptors tolerated while decreasing the amount required in the process, it was essential to find an eco-friendly, redox-stable solvent to run this oxidation. It was anticipated that the solvent was a crucial parameter as polar ones are playing an important role in improving the solvation of the sugars but also polarising the carbonyl acceptor and the catalyst to increase their reactivity. Thereby, polar solvents such as water, acetonitrile, *tert*-butanol and fluorinated solvents were tested with a set amount of acetone as acceptor **(Table 1)**. Water and acetonitrile seemed to inhibit the catalyst with complete recovery of the sugar despite the use of a higher amount of acceptor. The use of hexafluoroisopropanol (HFIP) resulted in a lot of decomposition while trifluoroethanol leads to the partial conversion of glucose. *Tert*-butanol proved to be the best solvent leading to high conversion with only 10 equivalents of acetone as acceptor. Noticeably, it was not possible to decrease further this amount without impacting the conversion likely due to the low boiling point of acetone. Several unprotected aldohexoses and pentoses were then tested in both acetone (**Condition A**, **Table 2)** and *tert*-butanol (**Condition B**, Table 2) with acetone as the acceptor. Under **Condition A**, D-glucose and D-mannose (**entry 1 & 2**) were quantitatively converted in 5 hours. The oxidation selectively occurred on the anomeric position for both substrates resulting in a mixture of **δ** and **γ** lactones **3a** et **3b.**

Oxidation under **Condition B** was equally efficient with the quantitative formation of the lactones **3a** and **3b** in 5 hours. It should be noted that full Isomerisation into the furanolactones was nearly complete under **Conditions A & B** by increasing the reaction time to 24 hours (see SI).

Table 1: Alternative solvent and amount of acceptor (acetone)



Solvent	Acetone (Eq.)	Yields 3a (%)
H_2O	10	0
CH_3CN	10	0
CH_3CN	100	0
HFIP	10	0
CF_3CH_2OH	10	40
***t*BuOH**	10	90
***t*BuOH**	9	58
***t*BuOH**	7	50

Yields of **3a** were determined by ^{1}H NMR of the crude mixture (DMSO-d6 or D_2O) using an internal standard

Noticeably, D-galactose **2c (entry 3)** required a longer reaction time to reach completion than other hexoses under the two sets of conditions. This discrepancy could potentially be due to low solubility (for solubility measurement, see SI). Solubility also appeared to be a critical parameter when evaluating glucuronic acid or disaccharides with an anomeric position accessible (e. g. D-maltose, D-cellobiose), with no conversion or very limited yields even in the presence of dimethylformamide as solubility-enhancing adjuvant (up to 20%, see SI for details).

Xylose **2e** oxidation was then tested on a preparative scale (500 mg) to establish the synthetic relevance of our procedure. Gluconolactones **3e** were successfully isolated via simple filtration in 82% yield under **Condition A** and 93% yield under **Condition B**.

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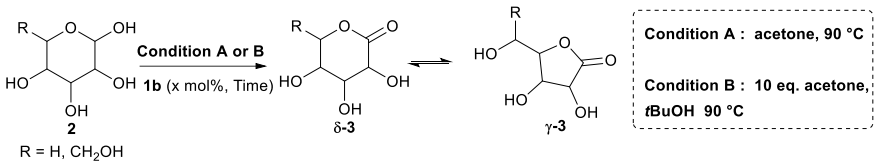
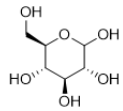
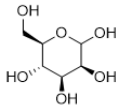
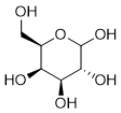
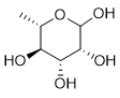
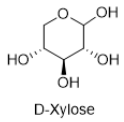
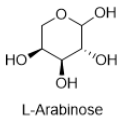
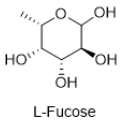
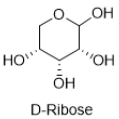
Table 2: Substrate scope



Entry	Sugar	Conditions (mol%, Time)	Yield 3 (%)	Ratio δ:γ
1	 D-glucose **2a**	**A** (5 mol%, 5 h)	>98	72:28
		(5 mol%, 5h, 500 mg)	95	nd
		(2.5 mol%, 3h)	22	66:34
		B (5 mol%, 5 h)	>98	57:43
		(5 mol%, 5h, 500 mg)	93	nd
		(2.5 mol%, 3h)	22	68:32
2	 D-Mannose **2b**	**A** (5 mol%, 5 h)	>98	53:47
		B (5 mol%, 5 h)	>98	58:42
3	 D-Galactose **2c**	**A** (5 mol%, 5 h)	54	n.d.
		(5 mol%, 24 h)	>98	0:100
		(2.5 mol%, 3h)	19	0:100
		B (5 mol%, 5 h)	35	0:100
		(5 mol%, 24 h)	85	0:100
		(2.5 mol%, 3h)	16	0:100
4	 L-Rhamnose **2d**	**A** (2.5 mol%, 5 h)	>98	77:23
		B (5 mol%, 5 h)	94	66:34

Entry	Sugar	Conditions (mol%, Time)	Yield 3 (%)	Ratio δ:γ
5	 D-Xylose **2e**	**A** (2.5 mol%, 5 h)	>98	34:66
		(2.5 mol%, 3 h)	98	43:57
		B (5 mol%, 2 h)	95	48:52
		(2.5 mol%, 5h)	96	44:56
		(2.5 mol%, 3 h)	95	45:55
6	 L-Arabinose **2f**	**A** (2.5 mol%, 5 h)	>98	25:75
		(2.5 mol%, 5 h)	100	
		B (2.5 mol%, 5h)	92	0:100
		(2.5 mol%, 3 h)	90	20:80
7	 L-Fucose **2g**	A (2.5 mol%, 5 h)	>98	43:57
		B (5 mol%, 5 h)	90	56:44
8	 D-Ribose **2h**	**B** (2.5 mol%, 5 h)	>98	13:87

Yields and ratios of lactones were determined by NMR (DMSO-d6) using an internal standard.

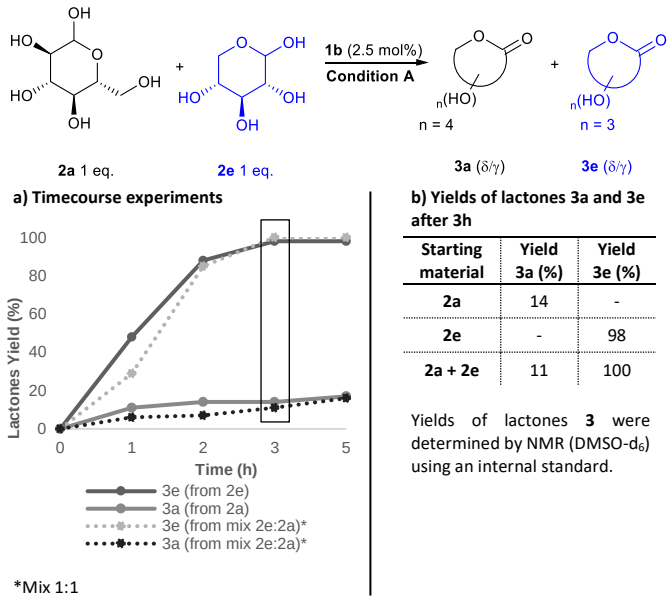
Pentoses (entries **5**,**6**,**8**) and deoxy-hexoses (entries **4**, **7**) proved to be more reactive than hexoses under both sets of conditions, with a remarkable reaction efficiency *when lowering the catalyst loading to 2.5 mol%* (full conversion into the lactones in 3-5 hours). Comparatively, after 3 hours under conditions **A** or **B** and with a reduced catalyst loading of 2.5 mol %, glucose **2a** and galactose **2c** were converted in poor yields (16-22%, entry 1 & 3). We envision that this rate discrepancy is an opportunity to devise a practical method to selectively upgrade pentoses into lactones from sugar mixtures.

Catalytic oxidation – application for the upgrade of pentoses in a sugar mixture

To substantiate our hypothesis while checking that the behaviour of the different sugars is not altered in mixtures, kinetic studies were performed on an equimolar mixture of xylose **2e** and glucose **2a** using **Condition A** and compared to

the oxidation of each sugar ran independently (same sugars concentration, **Figure 3a**, and see **SI** for details). The kinetic profiles of the 1:1 mixture were very similar to the results obtained from sugars run independently. In addition, these time-course experiments revealed the appropriate reaction time to reach the highest conversion of xylose **2e** while limiting the quantity of gluconolactones formed. Indeed, for the equimolar mixture **2a:2e**, complete oxidation of xylose **2e** was reached at 3 hours with only 11% of gluconolactone observed (**Figure 3a and 3b**).

Table 3 : Time course experiments : monosaccharide versus mixture (1:1)



b) Yields of lactones 3a and 3e after 3h

Starting material	Yield 3a (%)	Yield 3e (%)
2a	14	-
2e	-	98
2a + 2e	11	100

Yields of lactones **3** were determined by NMR (DMSO-d_6) using an internal standard.

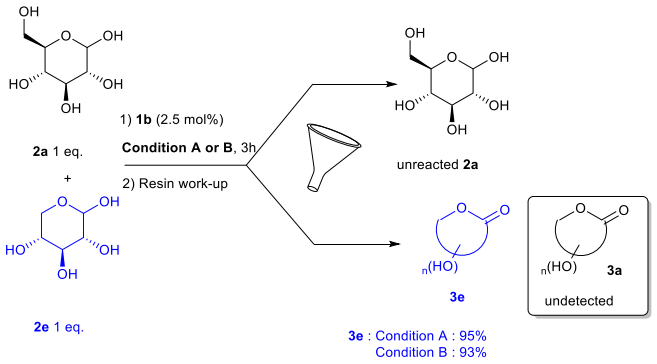
With these results in hand, a scale-up (≈ 500 mg of a 1:1 mix of **2a** and **2e**) was performed to prove the practicality of our procedure. **Conditions A & B** were both tested and the unreacted glucose **2a** was separated from the lactones **3e** with a simple solid phase work-up using an Ambersep®900(OH) resin (**Scheme 2**).[24] Remarkably, the application of these protocols allowed us to isolate the xylolactones **3e** in 95% (**Condition A)** and 93% (**Condition B)** with no traces of gluconolactones.

The practicality and efficiency of our oxidation procedure on mixture were also tested on a more challenging ternary mixture of glucose **2a**, galactose **2c** and xylose **2e** resulting in the selective isolation of the xylolactones in 62% yield without traces of gluconolactone **3a** and galactolactone **3c** (**see SI for details**).

Acceptor and equilibrium shift: toward an equimolar redox process

Our objective in this section is to decrease the stoichiometry of the acceptor to improve the sustainability of our procedure. **Condition B** developed in *tert*-butanol allowed us to compare different acceptors against acetone. Four acceptors were thus selected: (i) acetophenone **5** as a benchmark substrate in transfer hydrogenation, (ii) methyl pyruvate **6** and methyl levulinate **7** derived from biomass,[25] and finally (iii) isatin **8** a common core present in several biologically active molecules.

When glucose **2a** was used as the substrate, acetone proved to be by far the best candidate as the alternative acceptors only led to a limited amount of gluconolactones **3a** (≈30%) after 5 hours (**Figure 3**). Conversely and in agreement with our previous time course experiments, xylose **2e** was oxidised faster than glucose **2a** leading to a high yield of xylolactones **3e** in 5 hours with all the acceptors (96%, 98%, 78%, 90%, 75% with **4**, **5**, **6**, **7**, **8** respectively). Aware that a lower amount of acceptor could impair the equilibrium shift, the boundaries of our method were tested using the more reactive xylose **2e**.[26]



Scheme 2: Selective oxidation of xylose **2e** in an equimolar mixture of glucose (**2a**) and xylose (**2b**)

While developing **Condition B** (**Table 1)** we envisioned that employing less volatile acceptors would be better suited to decrease the quantity required (10 eq.) for the reaction to proceed efficiently and improve the sustainability of the process. We focused on isatin **8** for the reasons previously stated and for comparison, we also tested methyl levulinate **7** since it is reported to efficiently promote the oxidation of alcohols as its reduction leads to the formation of a stable lactone driving the equilibrium shift without the need for an excess of reagent.[27]

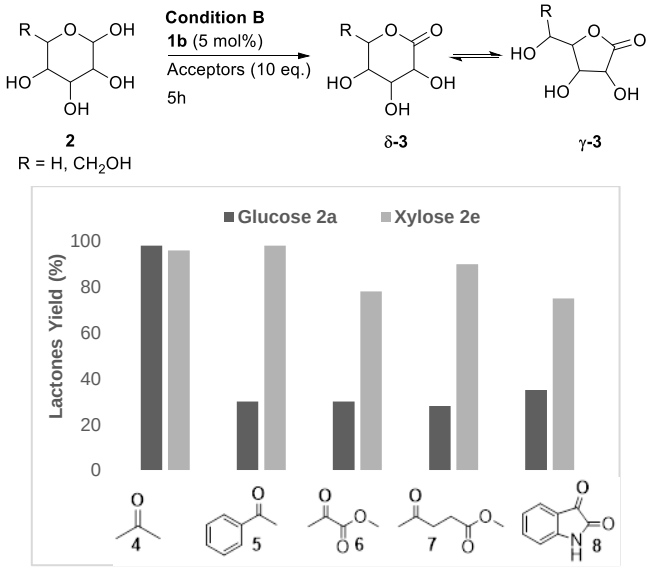
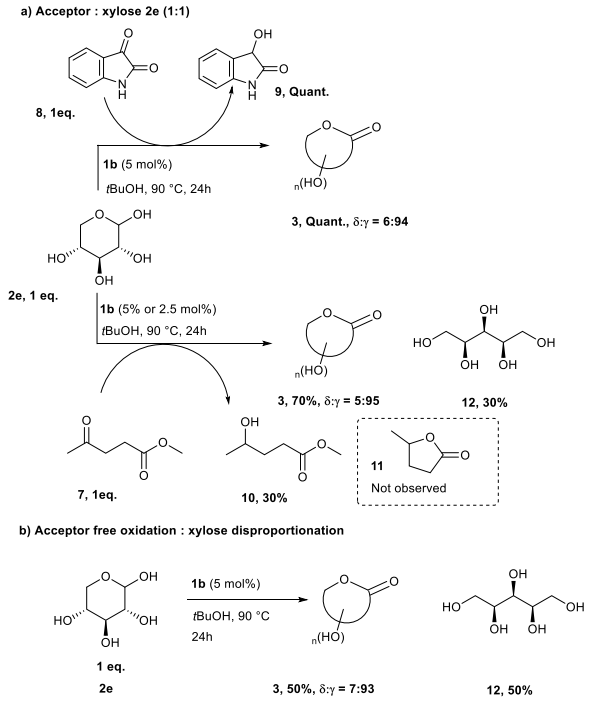


Figure 3: Oxidation of glucose and xylose under **Condition B** using different acceptors. Yields of lactones **3** were determined by NMR (DMSO-d6) using an internal standard.

Equimolar mixtures of xylose **2e** and acceptors were then heated in the presence of 5 mol% of catalyst in *tert*-butanol (**Scheme 3a**). As expected, the kinetic of the oxidation was strongly affected by lowering the quantity of acceptor resulting in longer reaction times. With isatin **8**, the xylolactone **2e** and 3-hydroxyoxindole **9** were quantitatively formed. Remarkably, it was also possible to decrease the catalyst loading to 2.5 mol% without impacting the yields of lactones **3e** obtained with both acceptors (see SI).

In contrast, when the methyl levulinate **7** was used, 70% of the lactones **3e** were obtained even though the xylose **2e** was fully consumed after 24 hours. Only 30% of methyl 4-hydroxypentanoate **10** was formed with no trace of valerolactone **11** highlighting the mildness of the process. In addition, NMR analyses revealed the formation of xylolactone (70%) with concomitant release of xylitol **12** (30%), likely due to the disproportionation of xylose **2e** when a low amount of acceptor was used. Indeed, when the reaction was carried out without acceptor, the xylose was fully consumed into lactone **3e** and xylitol **12** in 24 hours, highlighting the donor and acceptor capacity of the xylose in agreement with the data previously reported in the literature (**Scheme 3b**).[28,29] As expected, no disproportionation was observed when the xylose was heated without catalyst.

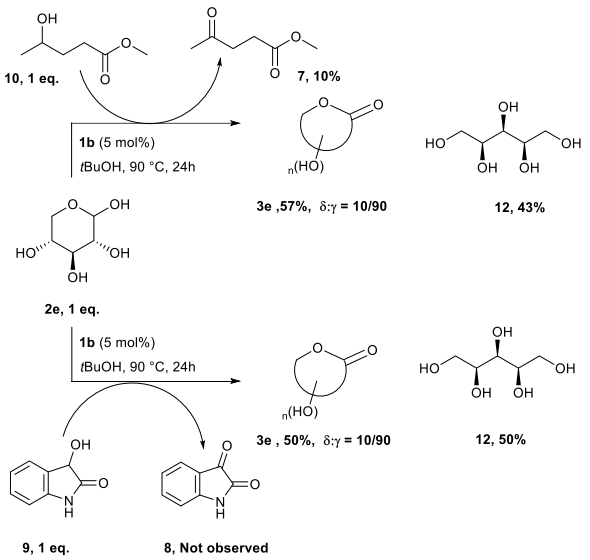
The formation of xylitol **12** could be rationalised by two competitive pathways: (i) the competitive rate of the disproportionation *versus* the oxidation of xylose **2e** as the low amount (1 eq.) of methyl levulinate **7** dramatically slowed down the formation of the xylolactone **3e** and (ii) the possibility of the methyl 4-hydroxypentanoate **10** to act as a hydrogen donor to reduce the xylose **2e** into xylitol **12**.



Scheme 3: Optimisation of the ratio acceptor/xylose a) Ratio = 1:1; b) Acceptor free oxidation of xylose. Yields of compounds were determined by NMR (DMSO-d6) using an internal standard.

To prove our hypotheses, 3-hydroxyoxindole **9** and methyl 4-hydroxypentanoate **10** were heated in presence of xylose and 5 mol% of iron catalyst to assess the donor properties of each alcohol in the reduction of xylose **2e** and determine the reversibility of the process (**Scheme 4**).

With methyl levulinate **7**, we observed competition between the disproportionation and the oxidation of methyl-4-hydroxypentanoate **10** with the formation of disproportionation products (lactones and xylitol) and methyl levulinate **7** (10%). The presence of methyl-levulinate proved the reversibility of the transfer hydrogenation process. The ratio of products suggested that the reaction conditions are not optimal to promote the oxidation of 4-hydroxypentanoate **10** and as a consequence favour the disproportionation. On the other hand, no traces of isatin **8** were detected from the reaction of 3-hydroxyoxindole **9**, confirming the irreversibility of the redox process involving the isatin and xylose **2e**. Those results help to rationalise the difference in performance between methyl levulinate **7** and isatin **8** as acceptors under these conditions and emphasize the superiority of isatin in the system studied.



Scheme 4: Study of the reversibility of the process under the reaction conditions

Conclusions

We report in this study an efficient and simple transformation for the upgrade of sugars from biomass, with an unprecedented iron-catalysed chemo-selective oxidation of fully unprotected monosaccharides into sugar lactones without the need for a strong oxidant and exogenous base. Two different procedures were developed using (i) conveniently acetone as solvent and acceptor (**Condition A**) or (ii) *tert*-butanol as solvent (**Condition B**) allowing the use of different acceptors. Under both conditions, several hexoses and pentoses were converted in

high yields and the lactones were isolated by simple filtration. Both procedures were successfully scaled-up on glucose. Time-course experiments revealed that hexoses were oxidised more slowly than pentoses under the same condition, a feature that we advantageously exploited for the selective oxidation of pentoses in a binary and ternary equimolar mixture of sugars.

In addition, we managed with **Condition B** to perform the oxidation using an equimolar amount of sugar and isatin as the acceptor without compromising the equilibrium shift in contrast to common transfer hydrogenation methodologies in which donor (e.g. isopropanol) or acceptors (e.g. acetone) are usually used in large excess or as solvent. Our results contribute to improve the sustainability of the transformation while simultaneously opening toward the exploitation of both reaction partners for synthetic applications.

The next step of our work is to investigate the development of the challenging stoichiometric hexose oxidation along with applications of selective oxidation on more complex mixtures from biomass waste.

Conflicts of interests

No conflict of interest to declare.

Acknowledgements

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Iron-catalysed chemo-selective oxidation of unprotected sugars: application for the competitive oxidation of pentoses from a sugar mixture

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Table of contents

General Experimental Information

Catalytic reactions were carried out in sealed tube (7 and 15 mL) equipped with a screw-top cap. D-ribose and D-galactose were purchased from Acros Organics, L-arabinose, L-rhamnose and D-mannose were purchased from Sigma-Aldrich, D-glucose from Merck, L-fucose from C. Rother and D-xylose from TCI; and were used as received. Ion exchange resin Ambersep 900 (OH) was purchased from Thermo-Fischer Scientific. Reagent grade acetone and *tert*-butanol from Acros were degassed by argon bubbling. Reactions were monitored by Thin Layer Chromatography (TLC) on silica plates (0.20 mm silica gel 60 with UV_{254} indicator) and visualised using a combination of UV light and/or potassium permanganate (1.5 g $KMnO_4$, 10 g K_2CO_3, 1.25 mL 10% NaOH in 200 mL water) or vanillin (vanillin 15%, sulfuric acid 2.5% in ethanol) as staining solutions. Purifications were performed using an automated purification system Büchi C-815 puriflash, using 200-800 nm UV scan and ELSD as detector. Normal phase silica gel (50µm) were used as stationary phase for compounds **A, 1a** and **1b**. For carbohydrates purification, ion exchange resin ambersep 900 (OH) was used. (see page X for procedure)

NMR: ^{1}H NMR spectra were recorded at 300 MHz at 25°C on a Bruker 300 MHz FT-NMR spectrometer using the residual protic solvent defined as the internal standard. Chemical shifts are given in ppm, and are referenced to the internal solvent signal. Chemical shifts are quoted in ppm to the nearest 0.01 ppm using the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets), m (multiplet) defined as all multi-peak signals where overlap or complex coupling of signals make definitive descriptions of peaks difficult. $^{13}C\{^{1}H\}$ NMR spectra were recorded at 75 MHz at 25 °C using the stated solvent as standard. Chemical shifts are reported to the nearest 0.1 ppm. The coupling constants are defined as *J* and quoted in Hz. NMR yields where calculated using 1 equivalent of 1-bromo-4-nitrobenzene as internal standard.

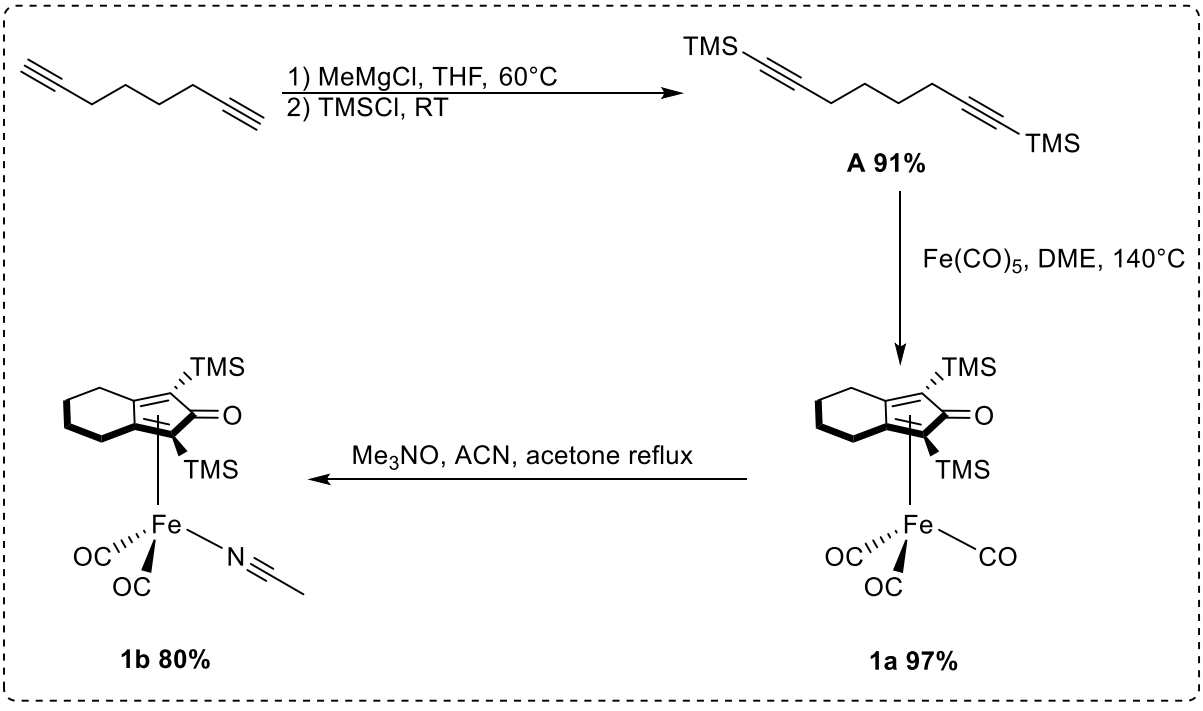
IR spectra were collected on a Perkin-Elmer Frontier operating in ATR mode.

Optical rotations were measured on a JASCO PTC-262 polarimeter at 568.6 nm with a path length of 10cm. [α] is expressed in $deg.cm^3.g^{-1}.dm^{-1}$, and c is expressed in $g/100cm^3$.

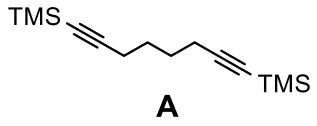
HRMS were measured on an Agilent 6530 QTOF-LC/MS mass-analyser in ESI+. LiCl dissolved in some samples to improve the ionization.

Solubility was estimated using a stability analyser Turbiscan™ Tower from Formulaction.

Synthesis of iron catalyst 1b



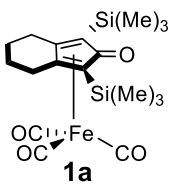
1,8-Bis(trimethylsilyl)-1,7-octadiyne A



A

A solution of 1,7-octadiyne (400 mg, 3.76 mmol, 1 equiv.) in THF (5.6 mL) was added dropwise over 1 hour to a solution of methyl magnesium chloride (5.3 mL, 3M in diethyl ether, 15.9 mmol, 4.2 equiv.) in THF (2 mL) at 60 °C. The solution was stirred at 65 °C for 3 hours and was allowed to cool down to room temperature. Trimethylsilyl chloride (2.22 g, 20.4 mmol, 5.4 equiv.) was then added slowly and the mixture was stirred at room temperature for 16 hours. The cloudy, white mixture was quenched with a saturated aqueous NH_4Cl solution (2 mL) and water was added until complete dissolution of the white precipitate. The organic layer was separated and the aqueous layer was extracted with cyclohexane (3 × 20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give a colorless oil. Purification of the crude material by flash chromatography using cyclohexane as eluent, afforded **A** (858 mg, 3.42 mmol, 91% yield) as a white low melting point solid. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.26 – 2.2 (m, 4H), 1.63 – 1.57 (m, 4H), 0.13 (s, 18H). **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$): δ 106.8, 84.5, 27.5, 19.2, 0.0. Spectral data are in agreement with the data previously reported in the literature.[1]

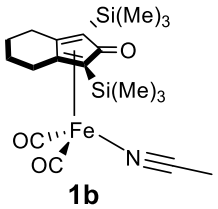
Tricarbonyl(1,3-bis(trimethylsilyl)-4,5,6,7-tetrahydro-2H-inden-2-one) iron 1a



1a

A solution of 1,8-bis(trimethylsilyl)-1,7-octadiyne **A** (350 mg, 1.39 mmol, 1 equiv.) and iron pentacarbonyl (363 µL, 544 mg, 2.78 mmol, 2 equiv.) in 1,2-dimethoxyethane (11.6 mL) was heated at 140 °C in a sealed tube for 24 hours. After cooling down, the mixture was evaporated under reduced pressure. Purification of the crude product was performed using flash chromatography using a gradient of cyclohexane:ethyl acetate (100:0 to 80:20) to afford **1a** (570 mg, 1.36 mmol, 97% yield) as a yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.49 – 2.62 (m, 4H), 1.76 – 1.87 (m, 4H), 0.26 (s, 18 H). **^{13}C{^{1}H} NMR** (75 MHz, $CDCl_3$): δ 209.3, 181.5, 111.3, 72.0, 25.1, 22.7, 0.0. Spectral data are in agreement with the data previously reported in the literature.[1]

Acetonitrile dicarbonyl(1,3-bis(trimethylsilyl)-4,5,6,7-tetrahydro-2H-inden-2-one) iron 1b

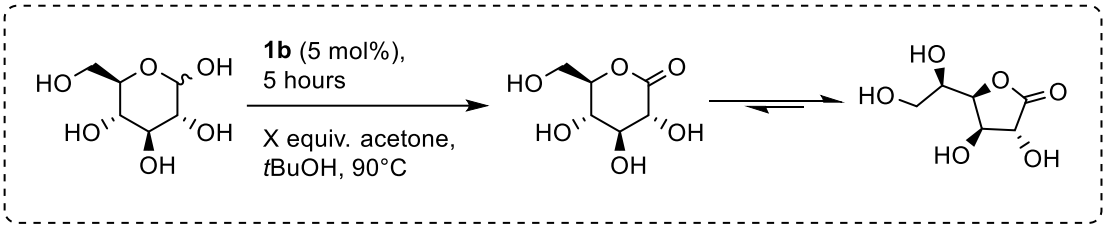


1b

A solution of iron compound **1a** (570 mg, 1.36 mmol, 1 equiv.), acetonitrile (144 µL, 113 mg, 2.75 mmol, 2 equiv.), and anhydrous trimethylamine *N*-oxide (123 mg, 1.63 mmol, 1.2 equiv.) in acetone (57 mL) was stirred at reflux for 24 hours. The orange/brown reaction was diluted with water (60mL) and was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the volatiles were removed under vacuum to afford a yellow/orange solid. Purification by flash chromatography on silica using a gradient of cyclohexane:ethyl acetate (100:0 to 0:100) afforded **1b** (479 mg, 1.11 mmol, 80 % yield. **^{1}H NMR** (300 MHz, $CDCl_3$): δ 2.30 (q, J = 5.9, 4H), 2.22 (s, 3H), 1.44 – 1.60 (m, 4H), 0.23 (s, 18H). **^{13}C{^{1}H} NMR** (75 MHz, CDCl3): δ 212.9, 180.2, 126.2, 106.7, 70.0, 24.9, 22.4, 4.6, 0.0. Spectral data matched the literatures values already reported.[1]

[1] **Plank, T. N.; Drake, J. L.; Kim, D. K.; Funk, T. W.** *Adv. Synth. Catal.* **2012**, *354* (4), 597–601.

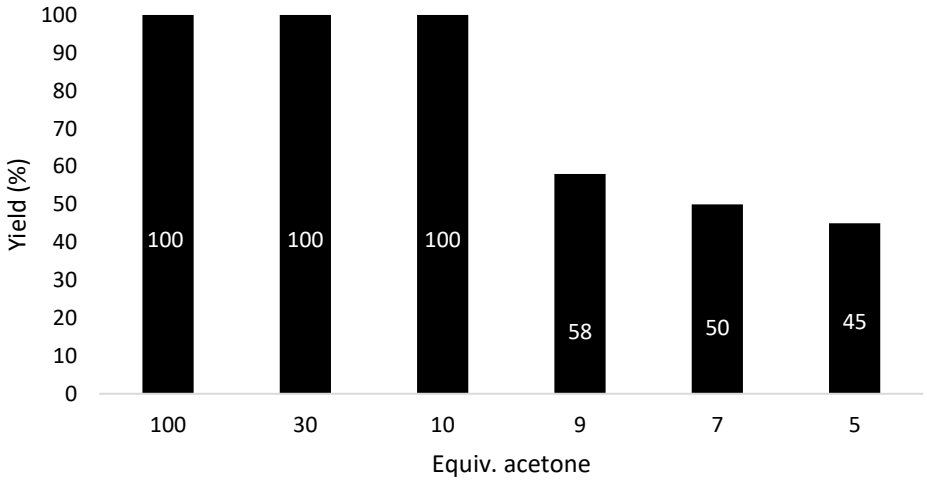
Optimization of acetone equivalence



Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-glucose (50 mg, 0.277 mmol) catalyst **1b** (6.0 mg, 5mol%) and acetone **4** (X mol, X equiv.). The reaction was stirred at 90 °C for 5 hours. 1-Bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Conversion of D-glucose (see table 1) was determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

Equiv. Acetone	NMR Yield (%)
100	100
30	100
10	100
9	58
7	50
5	45

Table 1: Gluconolactone yield in *t*-BuOH with acetone (X eq) as acceptor



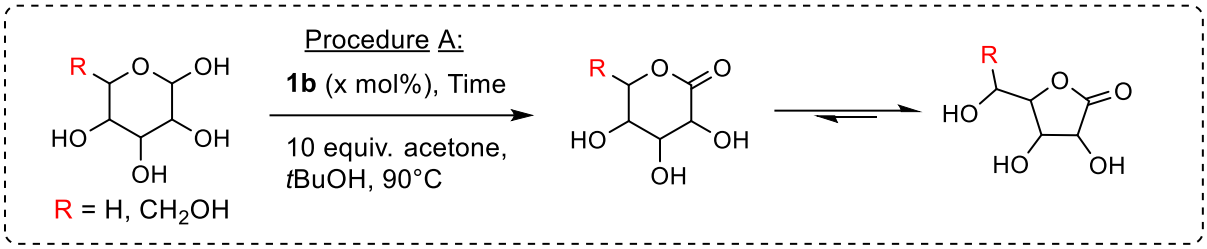
Solubility investigation

Various range of concentrations of carbohydrates were stirred vigorously during 1 hour in *tert*-butanol at 80°C in sealed vial. Solutions were immediately transferred into the stability analyser (Turbiscan Tower from Formulaction) at 80°C. The Turbiscan measures transmitted and backscattered intensities of an incident beam (λ = 880 nm) along the entire height of the sample (5 µm steps) every 2 minutes for 4 or 6 hours. Based on these parameters, the software calculates a Turbiscan Stability Index (TSI) which helps to detect flocculation/sedimentation.

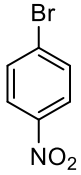
	galactose 2c	**galactose 2c + 1 eq xylose 2e**	**glucose 2a**	**glucose 2a + 1 eq xylose 2e**	**xylose 2e**
Solubility range (10^{-3} mmol/mL)	$0 < S < 5.31$	$4.31 < S < 6.31$	$29.809 < S < 32.309$	$29.809 < S < 32.309$	$87.31 < S < 107.107$

Table 2: Solubility range of monosaccharides in tert-butanol at 80°C

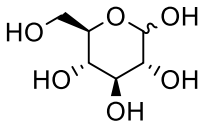
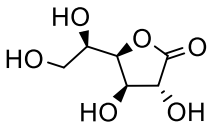
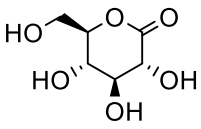
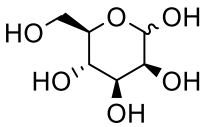
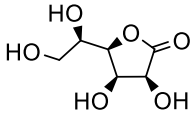
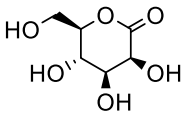
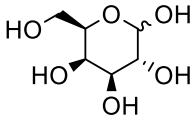
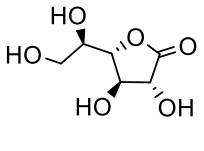
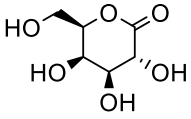
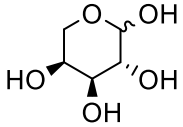
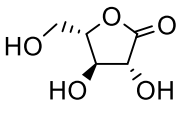
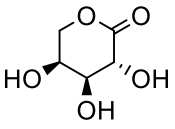
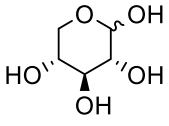
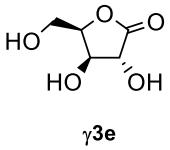
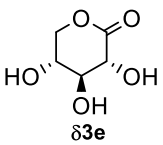
General Procedures of sugar C1-oxidation using catalyst 1b



Internal standard:
1-Bromo-4-nitrobenzene



Procedure A: *Tert*-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of sugar (50 mg, X mmol) catalyst **1b** (X mg, X mol%) and acetone **4** (X mol, 10 equiv.). The reaction was stirred at 90 °C for X hours. Upon completion of the reaction (TLC), 1-bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Yield of sugars lactones and ratios (see table 2) of 1,4-γ-, and 1,5-δ-lactones were determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

Substrate	Product (X) γ:δ	Catalyst loading (mol%)	Time (hours)	NMR Yield (%) Ratio γ:δ
 **2a**	 **γ3a**  **δ3a**	5	5	> 98 (43 :57)
 **2b**	 **γ3b**  **δ3b**	5	5	> 98 (42 :58)
 **2c**	 **γ3c**  **δ3c**	5 5	5 24	35 (100 :0) 85 (100 :0)
 **2d**	 **γ3d**  **δ3d**	2.5	2 5	60 (66 :34) > 98 (100 :0)
 **2e**	 **γ3e**  **δ3e**	2.5	2 2	96 (52 :48) 96 (56 :44)

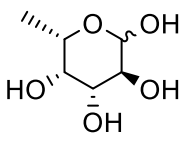
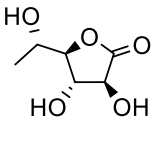
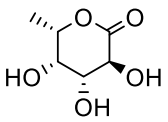
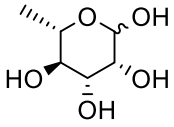
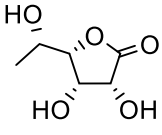
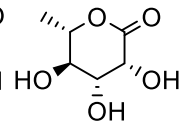
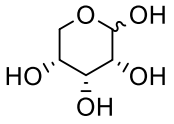
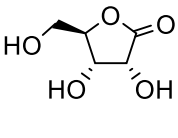
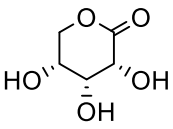
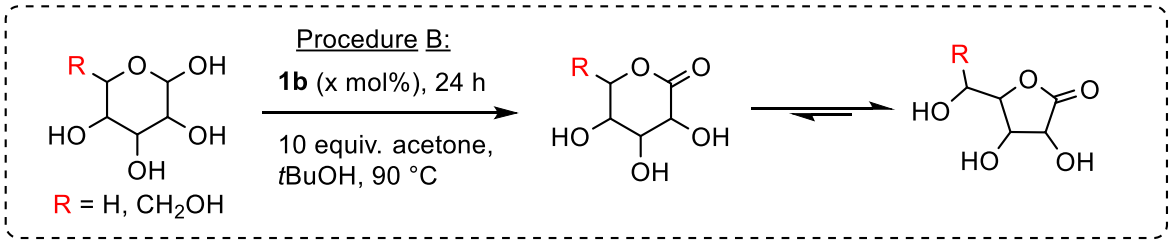
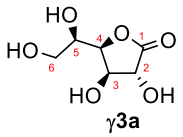
 **2f**	 **γ3f**  **δ3f**	2.5	5	> 98 (53 :47)
 **2g**	 **γ3g**  **δ3g**	2.5 5	5 5	85 (30 :70) 97 (34 :66)
 **2h**	 **γ3h**  **δ3h**	2.5	5	> 98 (87 :13)

Table 3: Scope on hexoses and pentoses using procedure A

Procedure B: A mixture of sugar (50mg) catalyst **1b** (2.5-5 mol%) and acetone **4** (X equiv.) in *tert*-butanol (0.8mL) in a sealed tube was degassed with argon for 15 min. The reaction was stirred at 90 °C for 24 hours, until total conversion of the monosaccharide and full isomerization of the resulting lactones. Purifications of the crude residue were carried out with successive diethyl ether sonication, or using flash chromatography on reverse phase (C18 Silica, 30 µm) as stationary phase; and a gradient of dichloromethane:methanol (100:0 to 60:40) as eluent.

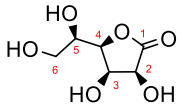


D-Glucono-1,4-lactone γ3a



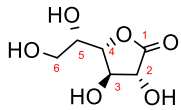
This product was prepared according to the general **procedure B**, using D-glucose (0.277mmol, 1 equiv.), catalyst **1b** (5.98mg, 0.013mmol, 5mol%) and acetone (205µL, 2.77mmol, 10 equiv.). $[\alpha]_D^{24}$ = +59 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3288, 1772, 1733 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 6.22 (d, *J* = 5.3 Hz, OH-2), 5.59 (d, *J* = 4.3 Hz, OH-3), 4.95 (d, *J* = 5.4 Hz, OH-5), 4.65 (t, *J* = 4.6 Hz, OH-6), 4.41 (dd, *J* = 6.9, 4.8 Hz, H-4), 4.17-4.12 (dd, *J* = 4.18 Hz, 8.28 Hz , H-3), 4.08-4.03 (dd, *J* = 3.9 Hz, 5.0 Hz, H-2), 3.82-3.73 (m, H-5), 3.61-3.52 (m, CH_2). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 176.0 (C-1), 80.5 (C-4), 73.6 (C-2), 73.1 (C-3), 69.7 (C-5), 63.2 (C-6). **HRMS** (ESI+): m/z calculated for $[M+H]^+$ 179.0555, found 179.0553.

D-Manno-1,4-lactone γ3b


γ3b

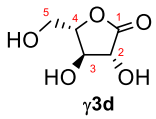
This product was prepared according to the general **procedure B**, using D-mannose (0.277mmol, 1 equiv.), catalyst **1b** (5.98mg, 0.013mmol, 5mol%) and acetone (205µL, 2.77mmol, 10 equiv.). $[\alpha]_D^{24}$ = +56 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3326, 1771 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 5.77 (d, *J* = 7.5 Hz, OH-2), 5.31 (d, *J* = 3.8 Hz, OH-3), 4.84 (d, *J* = 6.0 Hz, OH-5), 4.60 (t, *J* = 5.2 Hz, OH-6), 4.46 (dd, *J* = 7.2, 4.3 Hz, CH-2), 4.23 (q, *J* = 3.8 Hz, CH-3), 4.13 (m, CH-4), 3.73 (m, CH-5), 3.55 (m, CH_2). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 176.2 (C-1), 77.9 (C-4), 70.7 (C-2), 69.1 (C-3), 67.6 (C-5), 62.8 (C-6). **HRMS** (ESI+): m/z calculated for $[M+H]^+$ 179.0555, found 179.0552.

D-Galacto-1,4-lactone γ3c


γ3c

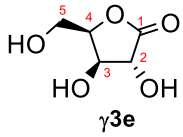
This product was prepared according to the general **procedure B**, using D-galactose (0.277mmol, 1 equiv.), catalyst **1b** (5.98mg, 0.013mmol, 5mol%) and acetone (205µL, 2.77mmol, 10 equiv.) $[\alpha]_D^{24}$ = -63 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3234, 1709 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 6.05 (d, *J* = 6.5 Hz, OH-2), 5.77 (d, *J* = 5.3 Hz, OH-3), 5.02 (d, *J* = 6.2 Hz, OH-5), 4.76 (t, *J* = 5.5 Hz, OH-6), 4.29-4.20 (dd, *J* = 6.5, 7.9 Hz, CH-2), 4.18-4.12 (m, CH-3), 4.10-4.07 (m, CH-4), 3.61 (ddd, *J* = 1.5 Hz, 6.2 Hz, 7.5 Hz, CH-5), 3.49-3.39 (m, CH_2). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 174.7 (C-1), 79.1 (C-4), 74.0 (C-2), 72.4 (C-3), 68.0 (C-5), 61.8 (C-6). **HRMS** (ESI+): m/z calculated for $[M+H]^+$ 179.0555, found 179.0547.

L-Arabino-1,4-lactone γ3d


γ3d

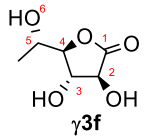
This product was prepared according to the general **procedure B**, using D-arabinose (0.333 mmol, 1 eq), catalyst **1b** (3.58mg, 0.0083mmol, 2.5mol%) and acetone (246µL, 3.33mmol, 10 equiv.). $[\alpha]_D^{24}$ = +46 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3282, 1772 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 6.05 (d, *J* = 6.6 Hz, OH-2), 5.81 (d, *J* = 5.1 Hz, OH-3), 5.04 (t, *J* = 5.6 Hz, OH-5), 4.23 (dd, *J* = 8.1, 6.5 Hz CH-2), 4.04-3.91 (m, CH-3, CH-4), 3.71 (ddd, *J* = 12.8, 5.2, 2 Hz, CH-5), 3.49 (ddd, *J* = 12.8, 5.9, 4.2 Hz, CH-5'). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 174.7 (C-1), 81.2 (C-4), 73.8 (C-2), 59.2 (C-5), 54.9 (C-3). **HRMS** (ESI+): m/z calculated for $[M+Li]^+$ 155.0531, found 155.0529.

D-Xylono-1,4-lactone γ3e


γ3e

This product was prepared according to the general **procedure B**, using D-xylose (0.333 mmol, 1 equiv.), catalyst **1b** (3.58mg, 0.0083mmol, 2.5mol%) and acetone (246µL, 3.33mmol, 10 equiv.). $[\alpha]_D^{24}$ = +78 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3251, 1755 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 6.03 (d, *J* = 5.7 Hz, OH-2), 5.71 (d, *J* = 3.5 Hz, OH-3), 4.90 (t, *J* = 4.8 Hz, OH-5), 4.42 – 4.36 (m, CH-4), 4.22 (m, CH-2,3), 3.68 – 3.60 (m, CH_2). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 175.6 (C-1), 80.0 (C-4), 73.2 (C-2), 72.4 (C-3), 58.6 (C-5). **HRMS** (ESI+): m/z calculated for $[M+Li]^+$ 155.0531, found 155.0530.

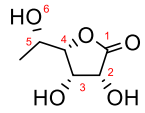
L-Fucono-1,4-lactone γ3f


γ3f

This product was prepared according to the general **procedure B**, using L-fucose (0.274 mmol, 1 equiv.), catalyst **1b** (2.96mg, 0.0068mmol, 2.5mol%) and acetone (203µL, 2.744mmol, 10 equiv.). $[\alpha]_D^{24}$ = +27 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3391, 3294, 1750 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 6.05 (d, *J* = 6.3 Hz, OH-2), 5.79 (d, *J* = 5.1 Hz, OH-3), 4.94 (d, *J* = 5.2 Hz, OH-5), 4.21 (dd, *J* = 7.4, 6.8 Hz, CH-2), 4.09 (d, *J* = 6.4 Hz, CH-3), 4.00 (q, *J* = 7.9 Hz, CH-5), 3.82-3.75 (m, CH-4), 1.15 (d, *J* = 6.4 Hz, CH_3) **^{13}C{^{1}H} NMR** (75 MHz, DMSO-

d_6) δ 174.7 (C-1), 83.5 (C-2), 74.1 (C-4), 73.12 (C-3), 64.12 (C-5), 19.6 (C-6). **HRMS** (ESI+): m/z calculated for $[M+Li]^+$ 169.0688, found 169.0684.

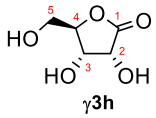
L-Rhamno-1,4-lactone γ3g



γ3g

This product was prepared according to the general **procedure B**, using L-rhamnose (0.274 mmol, 1 equiv.), catalyst **1b** (2.96mg, 0.0068mmol, 2.5mol%) and acetone (203µL, 2.744mmol, 10 equiv.). $[\alpha]_D^{24}$ = -17 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3377, 3319, 1722 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 5.59 (d, *J* = 5.7 Hz, OH-2), 5.35 (d, *J* = 6.4 Hz, OH-3), 5.30 (d, *J* = 3.6 Hz, OH-5), 4.47 (dd, *J* = 6.3, 3.5 Hz, CH-3), 4.20 – 4.08 (m, CH-4), 3.81 (t, *J* = 3.0 Hz, CH-5), 3.34 – 3.28 (m, CH-2), 1.29 (d, *J* = 6.2 Hz, CH_3). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 172.9 (C-1), 76.0 (C-4), 75.3 (C-2), 75.2 (C-3), 68.3 (C-5), 18.9 (C-6). **HRMS** (ESI+): m/z calculated for $[M+Li]^+$ 169.0688, found 169.0685.

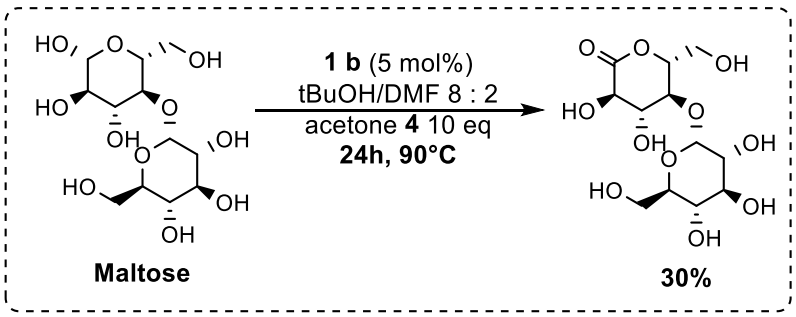
D-Ribono-1,4-lactone γ3h



γ3h

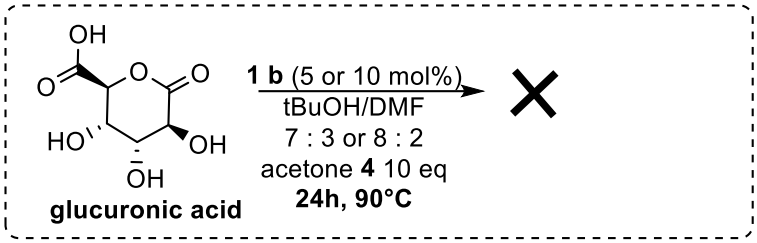
This product was prepared according to the general **procedure B**, using D-ribose (0.333 mmol, 1 equiv.), catalyst **1b** (3.58mg, 0.0083mmol, 2.5mol%) and acetone (246µL, 3.33mmol, 10 equiv.). $[\alpha]_D^{24}$ = +8 (c = 1.0g/100mL, H_2O). **IR** (neat): ν (cm^{-1}) 3276, 1769 (C=O). **^{1}H NMR** (300 MHz, DMSO-d_6) δ 5.75 (d, *J* = 7.5 Hz, OH-2), 5.37 (d, *J* = 3.5 Hz, OH-3), 5.16 (t, *J* = 5.2 Hz, OH-5), 4.42 (dd, *J* = 5.6, 1.9 Hz, CH-2), 4.22 (t, *J* = 3.5 Hz, CH-4), 4.13-4.09 (m, CH-3), 3.55-3.58 (m, CH_2). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 176.9 (C-1), 85.8 (C-4), 69.8 (C-3), 69.1 (C-2), 60.9 (C-5). **HRMS** (ESI+): m/z calculated for $[M+Li]^+$ 155.0531, found 155.0526.

Disaccharides oxidation



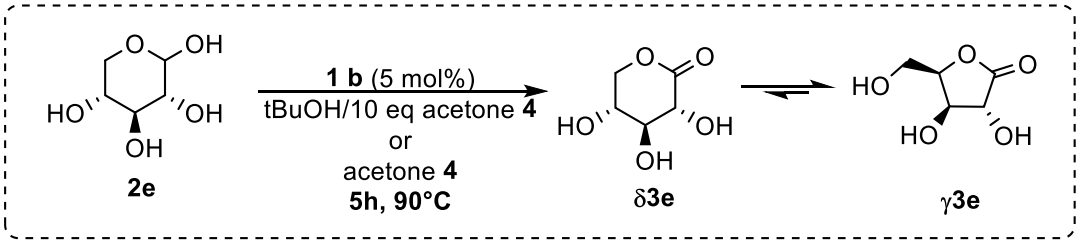
Tert-butanol-*N,N*-dimethylformamide mixture 8:2 (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of maltose (50 mg, 0.146 mmol) catalyst **1b** (3.1 mg, 5mol%) and acetone **4** (1.46 mol, 10 equiv.). The reaction was stirred at 90 °C for 24 hours. 1-bromo-4-nitrobenzene (1 equiv.) was added as an internal standard. Conversion of maltose was determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

Alduronic acids oxidation



Tert-butanol-*N,N*-dimethylformamide mixture 7:3 or 8:2 (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of glucuronic acid (50 mg, 0.257 mmol) catalyst **1b** (5.5 mg, 5mol%) and acetone **4** (2.57 mol, 10 equiv.). The reaction was stirred at 90 °C for 24 hours. 1-Bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Conversion of glucuronic acid was determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

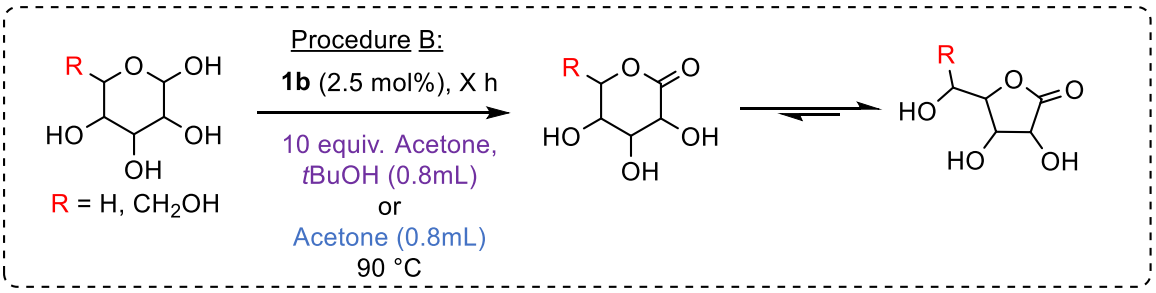
Scale-Up



A mixture of xylose **2e** (500 mg) catalyst **1b** (71 mg, 5 mol%) and acetone **4** (2.46 mL, 10 equiv.) in *tert*-butanol (8mL) in a sealed tube was degassed with argon for 30 min. The reaction was stirred at 90 °C for 5 hours, until total conversion of the monosaccharide. Purifications of the crude residue were carried out with successive diethyl ether sonication and filtration, to afford xylonolactones **δ3e** and **γ3e** as a white solid in **quantitative yield**.

A mixture of xylose **2e** (500 mg) catalyst **1b** (71 mg, 5 mol%) and acetone **4** (8 mL) in a sealed tube was degassed with argon for 30 min. The reaction was stirred at 90 °C for 5 hours, until total conversion of the monosaccharide. Purifications of the crude residue were carried out with successive diethyl ether sonication and filtration, to afford xylonolactones **δ3e** and **γ3e** as a white solid with **82% yield**.

Kinetics study:



A mixture of sugar (50 mg) catalyst **1b** (2.5 mol%), *tert*-butanol (0.8 mL) and acetone **4** (10eq) or only acetone **4** (0.8 mL) in a sealed tube was degassed with argon for 15 min. The reaction was stirred at 90 °C for X hours. 1-bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Yields of lactones were determined by ^{1}H NMR in DMSO-d_6, after filtration through a PTFE filter (0.2 µm).

Xylose 2e

Kinetics-xylose oxidation (2.5mol%) in acetone (0.8mL)

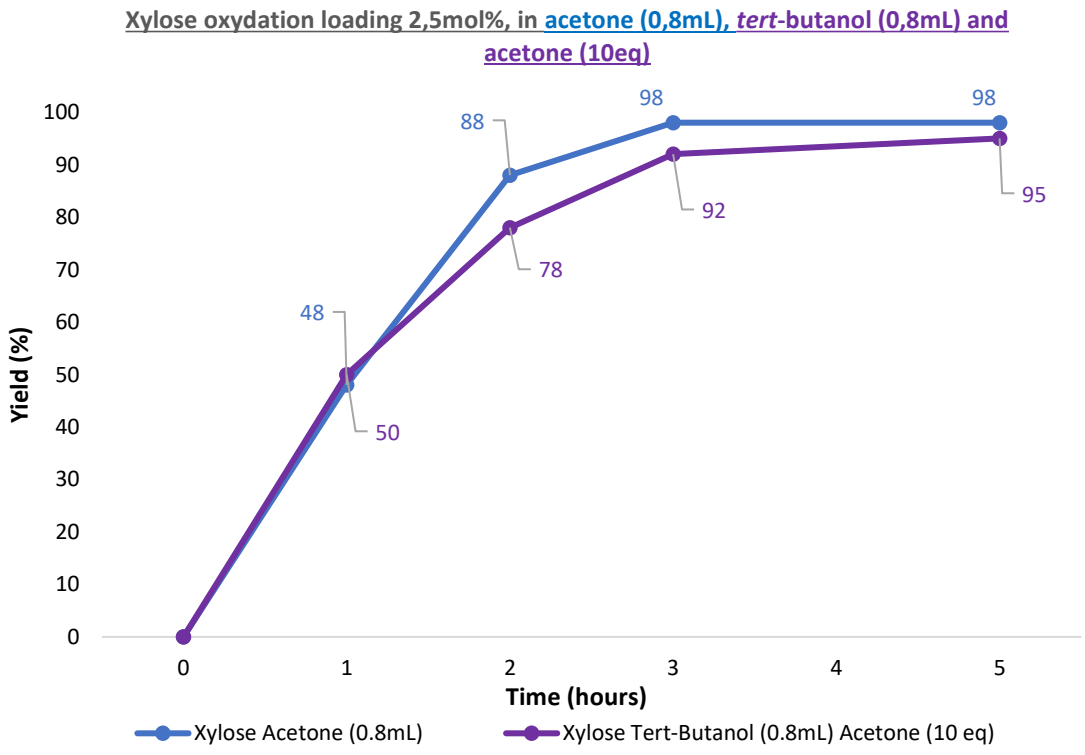
Time (hours)	Yield (%)
1	48
2	88
3	98
4	
5	98

Table 4: NMR yield of xylonolactones using procedure B in acetone

Kinetics-xylose oxidation (2.5mol%) in *tert*-butanol (0.8mL), and acetone (10 eq)

Time (hours)	Yield (%)
1	50
2	78
3	92
4	
5	95

Table 5: NMR yield of xylonolactones using procedure B in tert-butanol



Arabinose 2d

Kinetics-arabinose oxidation (2.5mol%) in acetone (0.8mL)

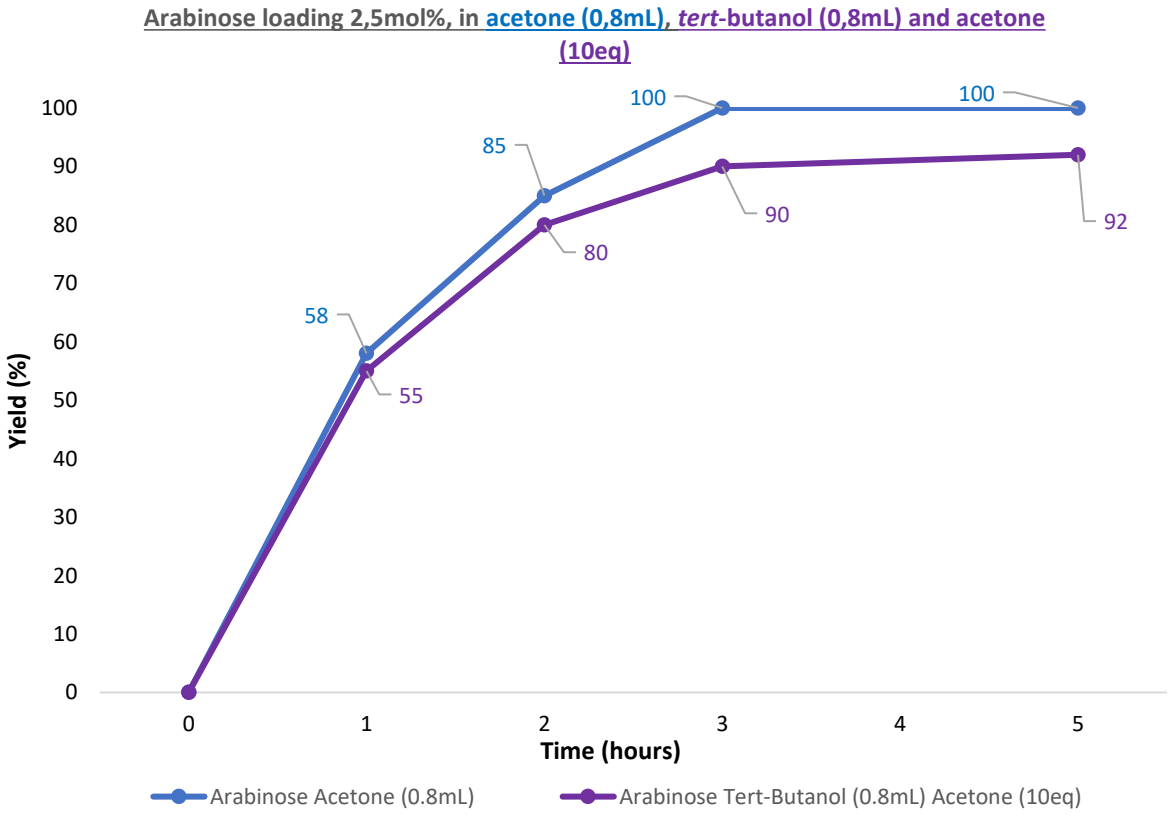
Time (hours)	Yield (%)
1	58
2	85
3	100
4	
5	100

Table 6: NMR yield of arabinolactones using procedure B in acetone

Kinetics-arabinose oxidation (2.5mol%) in *tert*-butanol (0.8mL), and acetone (10 eq)

Time (hours)	Yield (%)
1	55
2	80
3	90
4	
5	92

Table 7: NMR yield of arabinolactones using procedure B in tert-butanol



Glucose 2a

Kinetics-glucose oxidation (2.5mol%) in acetone (0.8mL)

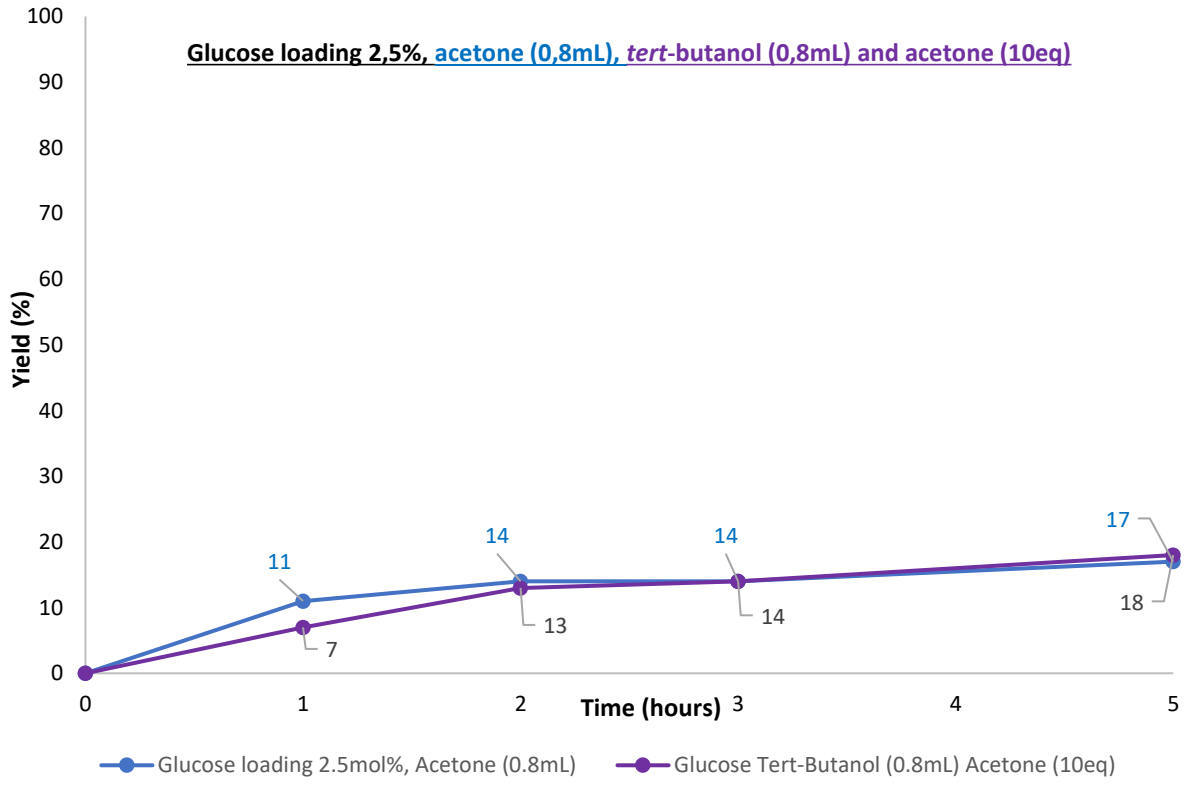
Time (hours)	Yield (%)
1	11
2	14
3	14
4	
5	17

Table 8: NMR yield of gluconolactones using procedure B in acetone

Kinetics-glucose oxidation (2.5mol%) in *tert*-butanol (0.8mL), and acetone (10 eq)

Time (hours)	Yield (%)
1	7
2	13
3	14
4	
5	18

Table 9: NMR yield of gluconolactones using procedure B in tert-butanol



Galactose 2c

Kinetics-galactose oxidation (2.5mol%) in acetone (0.8mL)

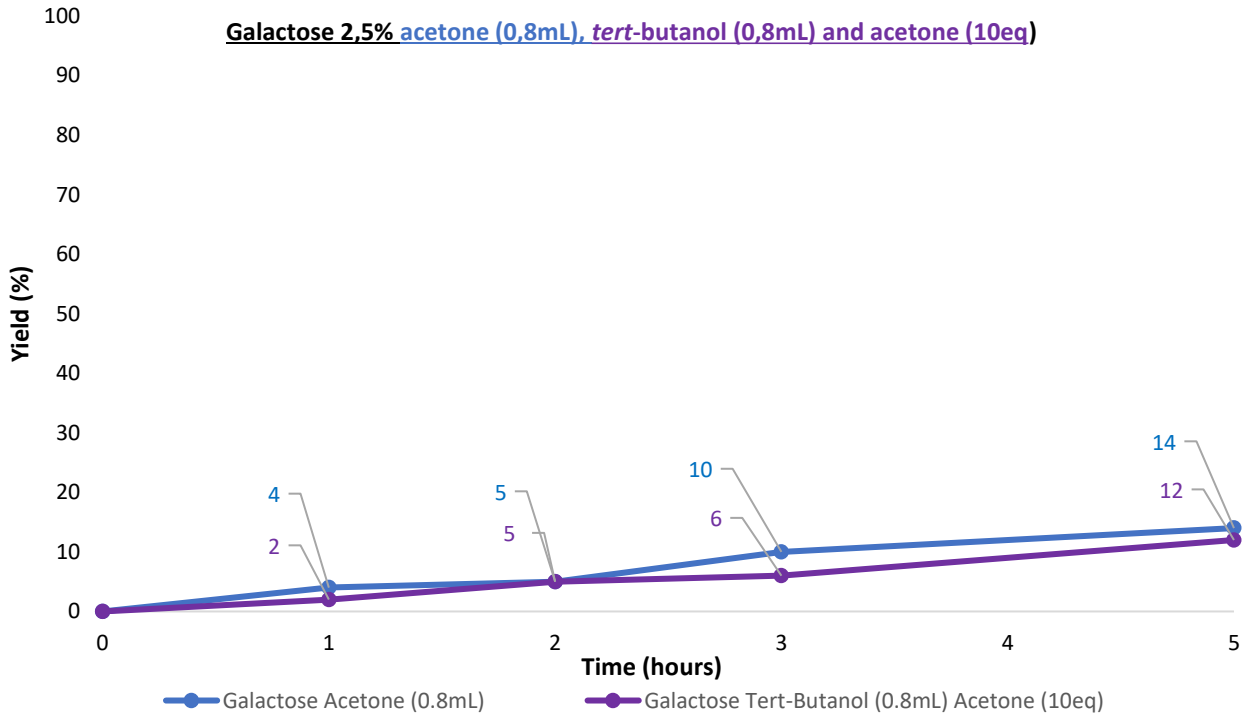
Time (hours)	Yield (%)
1	4
2	5
3	10
4	
5	14

Table 10: NMR yield of galactolactones using procedure B in acetone

Kinetics-Galactose oxidation (2.5mol%) in *tert*-butanol (0.8mL), and acetone (10 eq)

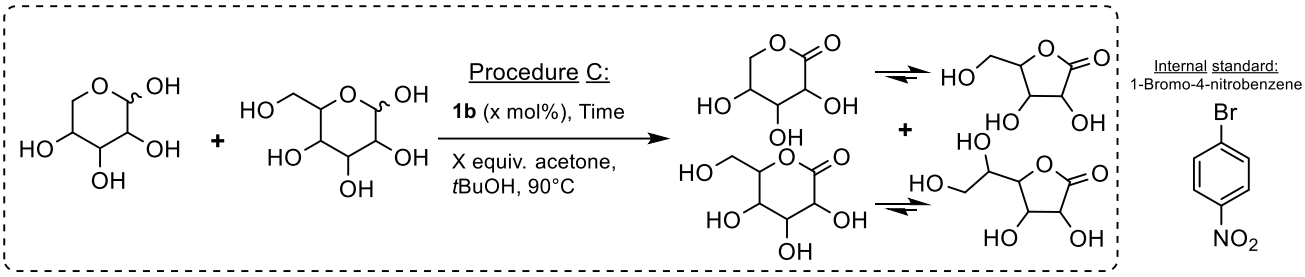
Time (hours)	Yield (%)
1	2
2	5
3	6
4	
5	12

Table 11: NMR yield of galactolactones using procedure B in tert-butanol

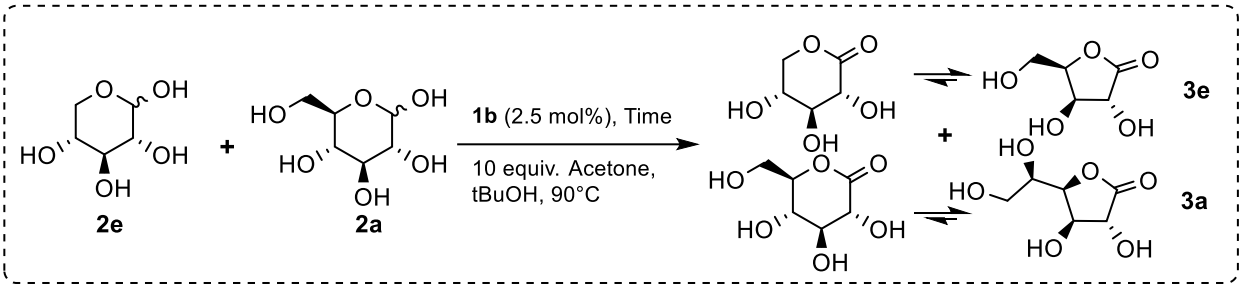


Mixtures-kinetics:

Procedure C: *Tert*-butanol (X mL) was degassed with argon for 15 min in a sealed tube after addition of sugars (X mg, X mmol, and X mg, X mmol; 1:1 mol or 1:1:1) catalyst **1b** (X mg, X mol%) and acceptor (X mol, X equiv.). The reaction was stirred at 90 °C for X hours. 1-bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Yield of sugars lactones was determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).



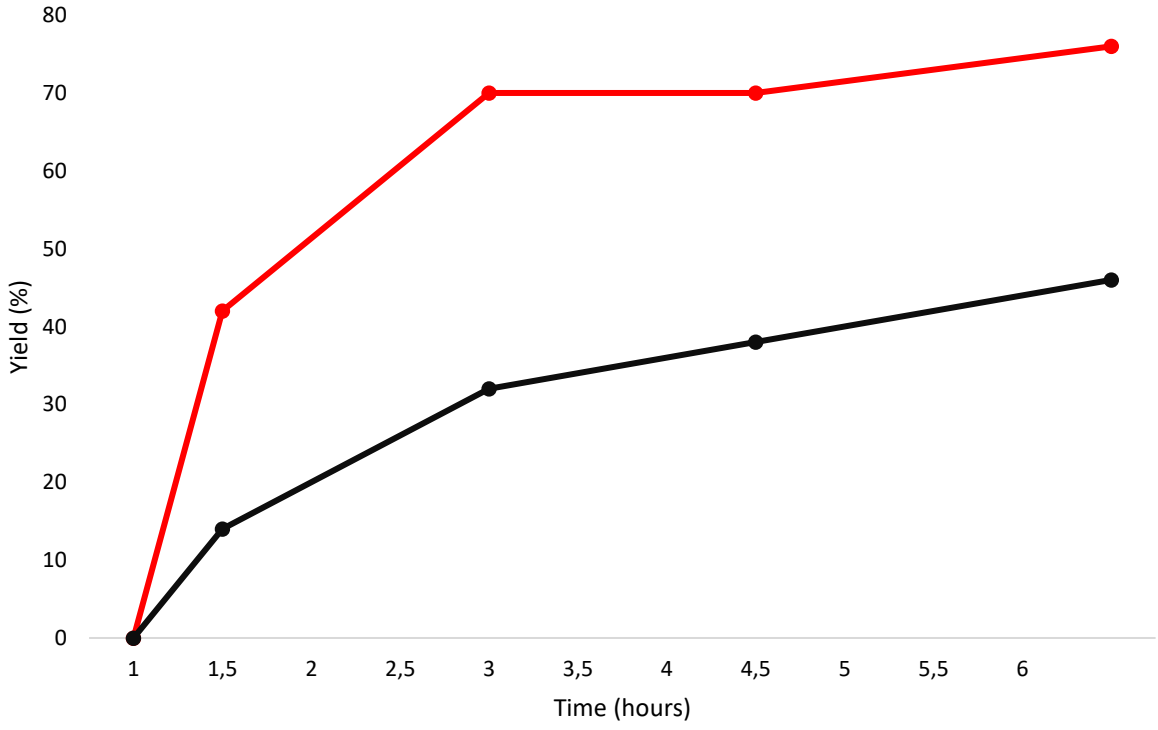
1 : 1 xylose/glucose mixture, acetone as acceptor



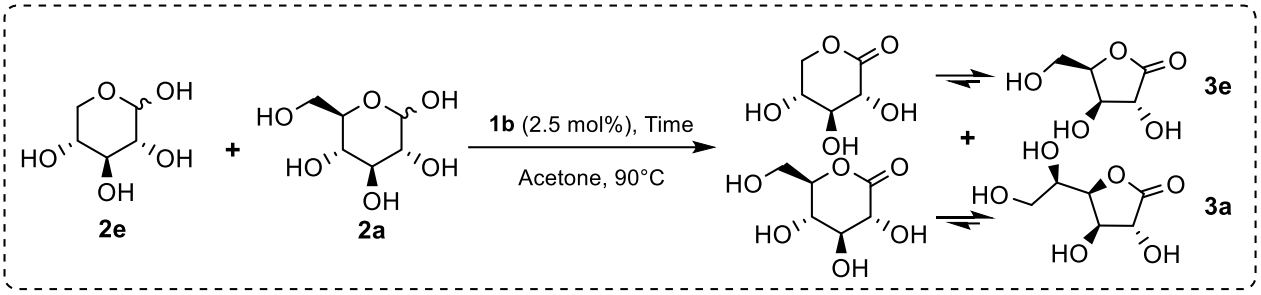
Reaction was carried out according to the general **procedure C**, using D-xylose **2e** (25 mg, 0.166 mmol, 1 equiv.) and D-glucose **2a** (30 mg, 0.166 mmol, 1 equiv.), catalyst **1b** (1.8 mg, 0.004 mmol, 2.5 mol%) and acetone **4** (246 µL, 3.333 mmol, 10 equiv.) as acceptor in *tert*-butanol (0.9 mL).

Time (hours)	*3e Yield (%)*	*3a Yield (%)*
0	*0*	*0*
1	*42*	*14*
2.5	*70*	*32*
4	*70*	*38*
6	*76*	*46*
24	*80*	*66*

Table 12: NMR yield of xylono- and gluconolactones using procedure D in tert-butanol



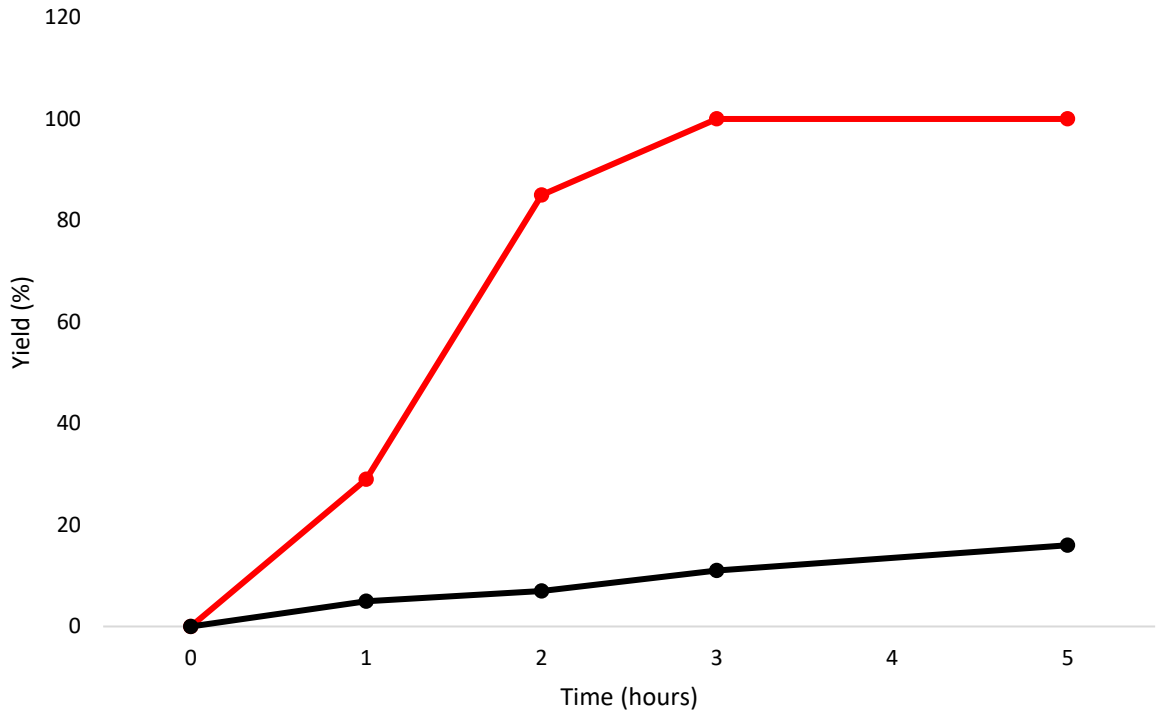
1 : 1 xylose/glucose mixture, acetone as acceptor/solvent



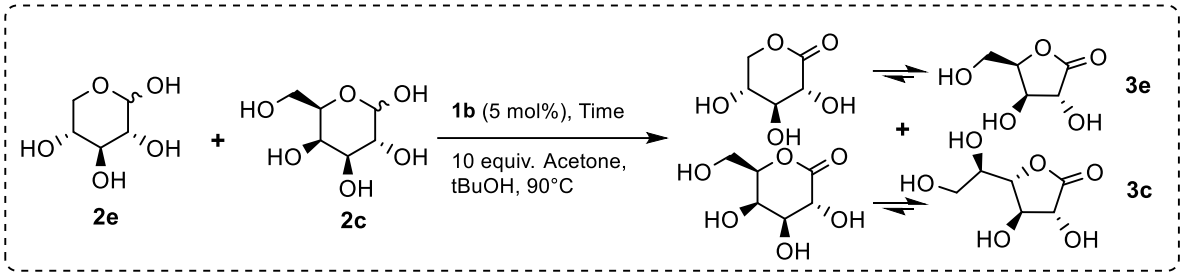
Reaction was carried out according to the general **procedure C**, using D-xylose **2e** (25 mg, 0.166 mmol, 1 equiv.) and D-glucose **2a** (30 mg, 0.166 mmol, 1 equiv.) catalyst **1b** (1.8 mg, 0.004 mmol, 2.5 mol%) in acetone **4** (0.9mL) as solvent and acceptor.

Time (hours)	*3e Yield (%)*	*3a Yield (%)*
0	*0*	*0*
1	*29*	*5*
2	*85*	*7*
3	*100*	*11*
5	*100*	*16*

Table 13: NMR yield of xylono- and gluconolactones using procedure D in acetone



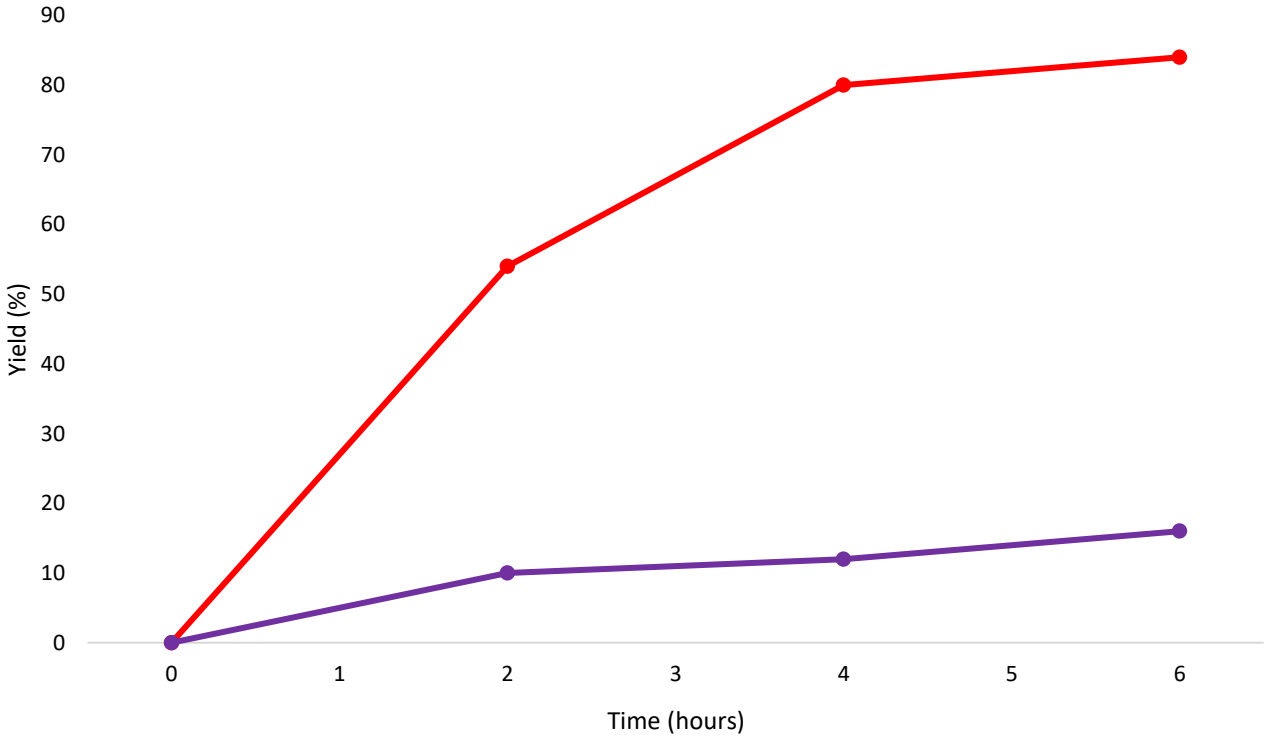
1 : 1 xylose/galactose mixture, acetone as acceptor



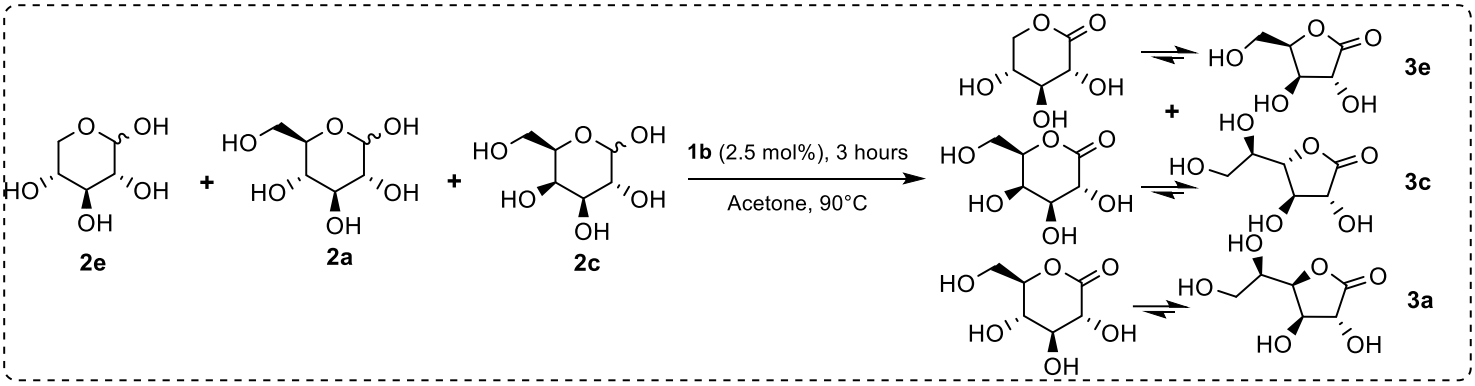
Reaction was carried out according to **procedure C**, using D-xylose **2e** (75 mg, 0.499 mmol, 1 equiv.) and D-galactose **2c** (90 mg, 0.499 mmol, 1 equiv.), catalyst **1b** (10.7 mg, 0.025 mmol, 5mol%) and acetone **4** (370 µL, 4.995 mmol, 10 equiv.) as acceptor in *tert*-butanol (2.6 mL).

Time (hours)	3e Yield (%)	3c Yield (%)
0	0	0
2	54	10
4	80	12
6	84	16

Table 14: NMR yield of xylono- and galactolactones using procedure D in tert-butanol



1 : 1 : 1 xylose/glucose/galactose mixture, acetone as acceptor



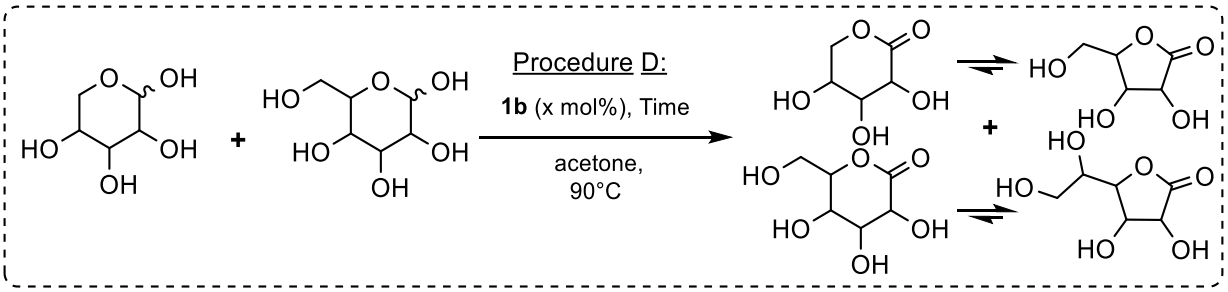
Reaction was carried out according to **procedure C**, using D-xylose **2e** (50 mg, 0.333 mmol, 1 equiv.) D-glucose **2a** (60 mg, 0.333 mmol, 1 equiv.) D-galactose **2c** (60 mg, 0.333 mmol, 1 equiv.) catalyst **1b** (3.6 mg, 0.008 mmol, 2.5 mol%) in acetone **4** (2.7 mL).

Time (hours)	3e Yield (%)	3a Yield (%)	3c Yield (%)
3	Quant.	16	8

Table 15: NMR yield of xylono-, glucono- and galactolactones using procedure D in acetone

Scale-up Mixtures:

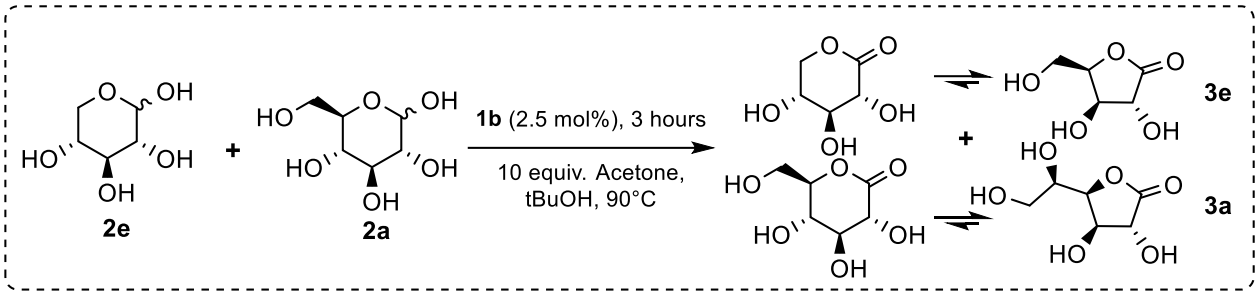
Procedure D: *Tert*-butanol (X mL) was degassed in a sealed tube after addition of sugars (X mg, X mmol, and X mg, X mmol, 1:1 mol) catalyst **1b** (X mg, X mol%) and acceptor (X mol, X equiv.). The reaction was stirred at 90 °C for X hours and the volatiles were evaporated under reduced pressure. The crude mixture was purified using the **resin procedure** detailed below.



Resin purification procedure II The ambersep 900 (OH) ion exchange resin was first washed with water, methanol, diethyl ether and dried. The volatiles from the crude were evaporated under reduced pressure, then the residue was washed three times with diethyl ether. The crude was then stirred overnight with the resin in water (20 mL). Then the first 20mL where removed and the resin was washed again 3 times for 5 min with 20mL distilled water. The resin was then extracted with 2/1 M HCl solution (10mL). The solution was then freeze dried several times (the residue was

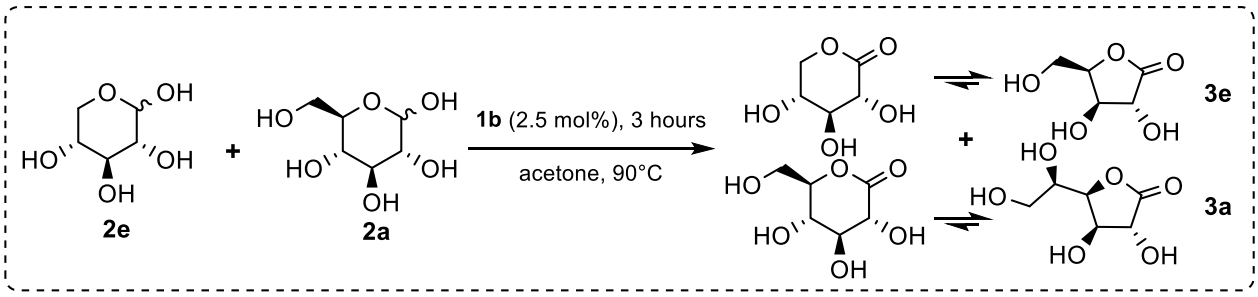
dissolved each time in distilled water prior to freeze drying) affording the product as a brown/white solid.

1:1 xylose/glucose mixture with acetone as acceptor



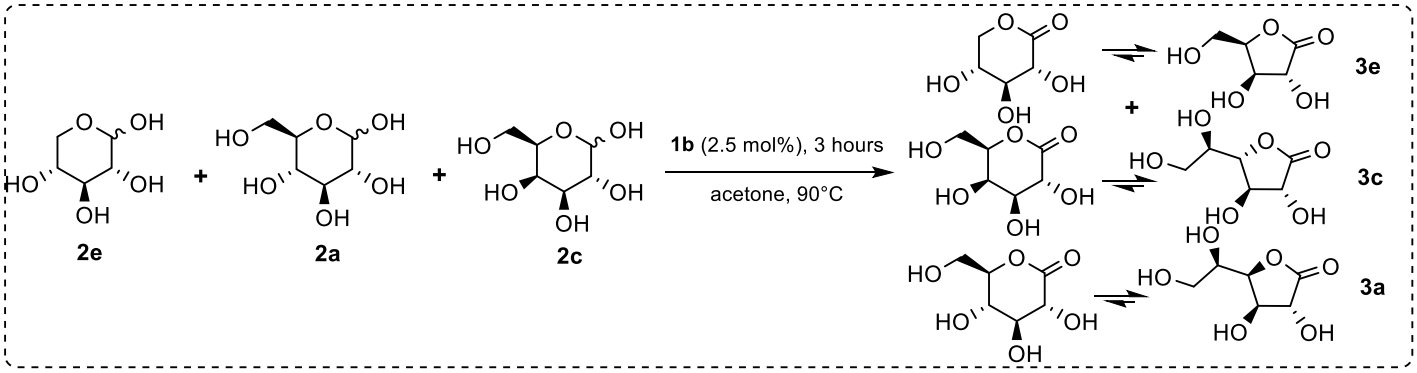
Reaction was carried out according to the general **procedure D**, using D-xylose **2e** (125 mg, 0.832 mmol, 1 equiv.), D-glucose **2a** (150 mg, 0.832 mmol, 1 equiv.), catalyst **1b** (8.9 mg, 0.020 mmol, 2.5 mol%) and acetone **4** (615 µL, 8.32 mmol, 10 equiv.) as acceptor in *tert*-butanol (4 mL). Purification using the ***resin procedure*** afforded xylonolactone **3e** (114 mg, 0.773 mmol, **93%** isolated yield).

1:1 xylose/glucose mixture with acetone as acceptor



Reaction was carried out according to the general **procedure D**, using D-xylose **2e** (125 mg, 0.832 mmol, 1 equiv.), D-glucose **2a** (150 mg, 0.832 mmol, 1 equiv.), catalyst **1b** (8.9 mg, 0.020 mmol, 2.5 mol%) and acetone **4** (4 mL) as acceptor and solvent. Purification using the ***resin procedure*** afforded xylonolactone **3e** (117 mg, 0.790 mmol, **95%** isolated yield).

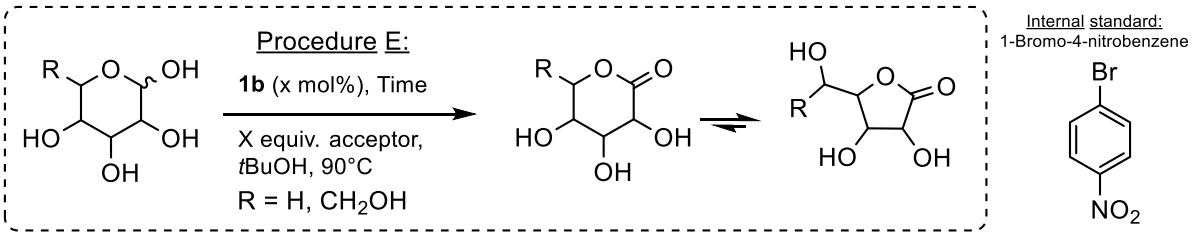
1:1:1 xylose/glucose/galactose mixture with acetone as acceptor



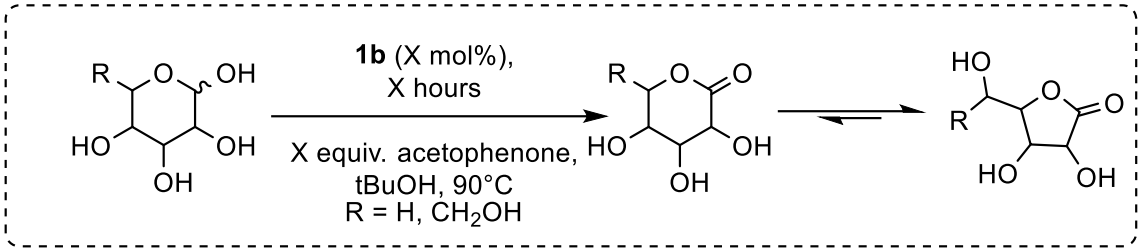
Reaction was carried out according to the general **procedure D**, using D-xylose **2e** (200 mg, 1.333 mmol, 1 equiv.), D-galactose **2c** (240 mg, 1.333 mmol, 1 equiv.) D-glucose **2a** (240 mg, 1.333 mol, 1 equiv.) catalyst **1b** (14 mg, 0.033 mmol, 2.5 mol%) and acetone (X mL) as acceptor and solvent. Purification using the ***resin procedure*** afforded xylonolactone **3e** (122 mg, 0.826 mmol, **62%** isolated yield).

Acceptor Screening

Procedure E: A mixture of sugar (50mg) catalyst **1b** (2.5-10 mol%) and acceptor (X equiv.) in *tert*-butanol (0.8mL) in a sealed tube was degassed with argon for 15 min. The reaction was stirred at 90 °C for X hours. 1-bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Yields of lactones were determined by ^{1}H NMR in DMSO-d_6, after filtration through a PTFE filter (0.2 µm).



Acetophenone as acceptor

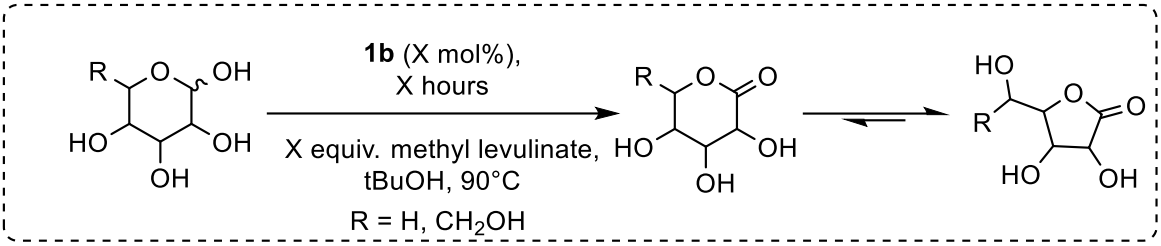


Reaction was carried out according to the general **procedure E**, using a mixture of sugar (50 mg) catalyst **1b** (X mg, X mol%), acetophenone (X mol, X equiv.) and *tert*-butanol (0.8 mL).

Substrat	Catalyst loading (mol%)	Equiv. acetophenone	Time (hours)	NMR Yield (%)
2a	5	10	5	30
2e	5	10	5	100

Table 16: NMR yield of xylono- and gluconolactones using procedure C and acetophenone as acceptor

Methyl Levulinate as acceptor

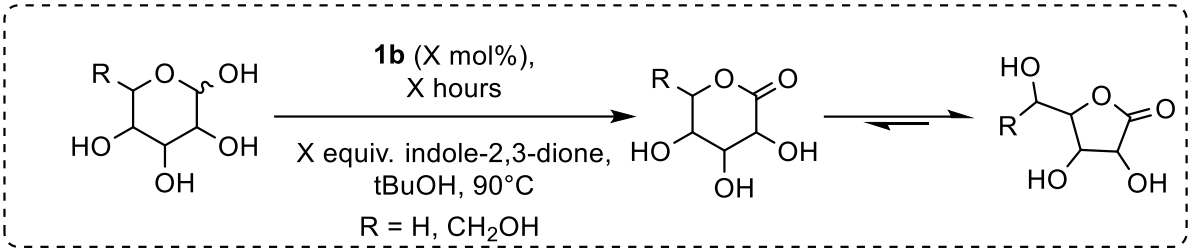


Reaction was carried out according to the general **procedure E** using a mixture of sugar (50 mg) catalyst **1b** (X mg, X mol%), methyl levulinate **7** (X mol, X equiv.) and *tert*-butanol (0.8 mL).

Substrate	Catalyst loading (mol%)	Equiv. Methyl Levulinate	Time (hours)	NMR Yield (%)
2a	5	10	5	40
2e	5	10	5	90
2e	2.5	1	24	80
2e	5	1	24	70

Table 17: NMR yield of xylono- and gluconolactones using procedure C and methyl levulinate as acceptor

Indole-2,3-dione as acceptor

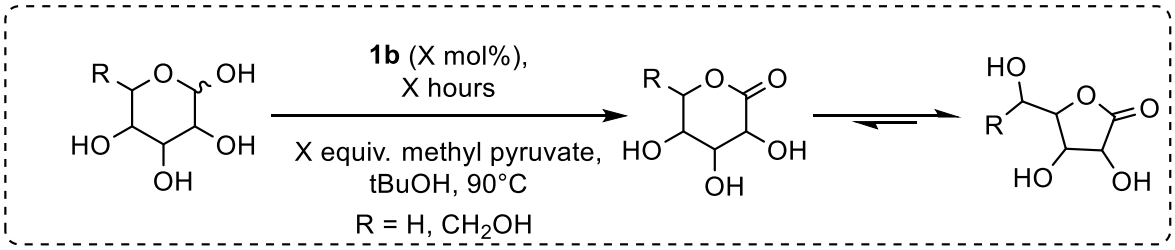


Reaction was carried out according to the general **procedure E** using a mixture of sugar (50 mg) catalyst **1b** (X mg, X mol%), Isatine **8** (X mol, X equiv.) and *tert*-butanol (0.8 mL).

Table 18: NMR yield of xylono- and gluconolactones using procedure C and indole-2,3-dione as acceptor

Substrate	Catalyst loading (mol%)	Equiv. Indole-2,3-dione	Time (hours)	NMR Yield (%)
2a	5	10	5	35
2e	5	1	24	100
2e	2.5	1	24	100

Methyl pyruvate as acceptor

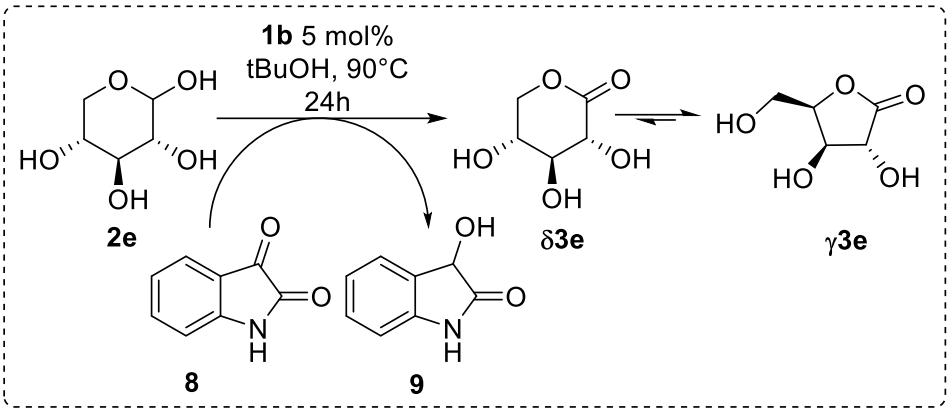


Reaction was carried out according to the general **procedure E** using a mixture of sugar (50 mg) catalyst **1b** (X mg, X mol%), methyl pyruvate **6** (X mol, X equiv.) and *tert*-butanol (0.8 mL).

Table 19: NMR yield of xylono- and gluconolactones using procedure C and methyl pyruvate as acceptor

Substrate	Catalyst loading (mol%)	Equiv. Methyl Pyruvate	Time (hours)	NMR Yield (%)
2a	5	10	5	30
2e	5	10	5	78

1:1 Donnor : Acceptor experiment

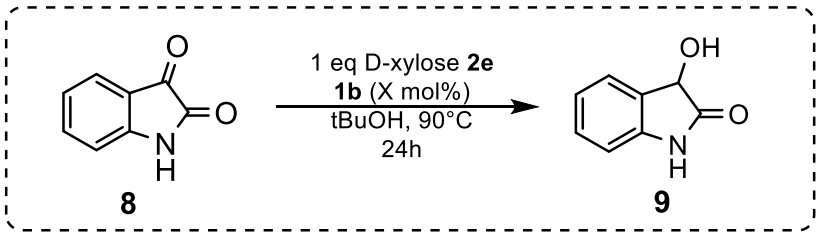


Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-xylose **2e** (50 mg, 0.333 mmol, 1 equiv.) catalyst **1b** (7.8 mg, 0.016 mmol, 5 mol%) and isatin **8** (49 mg, 0.333 mmol, 1 equiv.). The reaction was stirred at 90 °C for 24 hours. Yields of xylonolactones **3e** were determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

3e Yield (%)	**9 Yield (%)**
>98	>98

Table 20: NMR yield of xylonolactones and 3-hydroxyindolin-2-one using indol-2,3-dione in a 1:1 ratio as acceptor

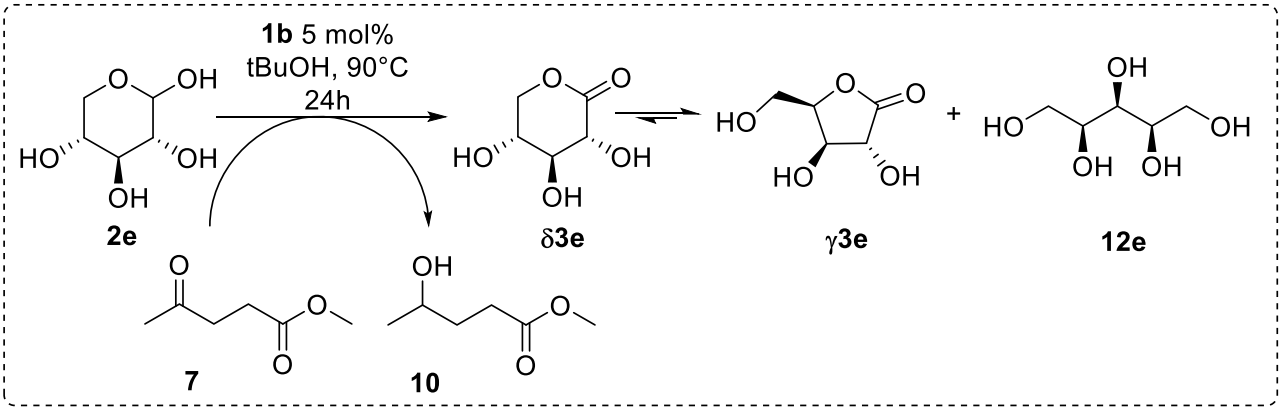
Acceptor reduction:



Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of isatin **8** (100 mg, 0.679 mmol) catalyst **1b** (X mg, X mol%) and D-xylose **2e** as donor (0.679 mol, 1 equiv.). The reaction was stirred at 90 °C for 24 hours. 1-Bromo-4-nitrobenzene (1 equiv.) was added as an internal standard and the crude mixture was evaporated under reduced pressure. Yield of 3-hydroxyindolin-2-one was determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm). The purification was performed on silica gel using a cyclohexane/ethyl acetate gradient starting from 100:0 to 33:67 affording 3-hydroxyindolin-2-one **9** (85.8 mg, 0.579 mmol, **85%**) as a light-yellow solid. **^{1}H NMR** (300 MHz, DMSO-d_6) δ 10.23 (s, 1H), 7.27 (d, *J* = 7.3 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.16 (d, *J* = 7.6 Hz, 1H), 4.82 (d, *J* = 7.6 Hz, 1H). **^{13}C{^{1}H} NMR** (75 MHz, DMSO-d_6) δ 177.9, 142.1, 129.3, 128.9, 124.7, 121.5, 109.4, 69.1, 40.3, 40.0, 39.8, 39.5, 39.2, 38.9, 38.6. Spectral data are in agreement with the data previously reported in literature.[2]

Loading (mol%)	Time (hours)	NMR Yield (%)	Isolated Yield (%)
5	24	100	/
2.5	24	100	85

Table 20: NMR and isolated yields of 3-hydroxyindolin-2-one using D-xylose in a 1:1 ratio as donor

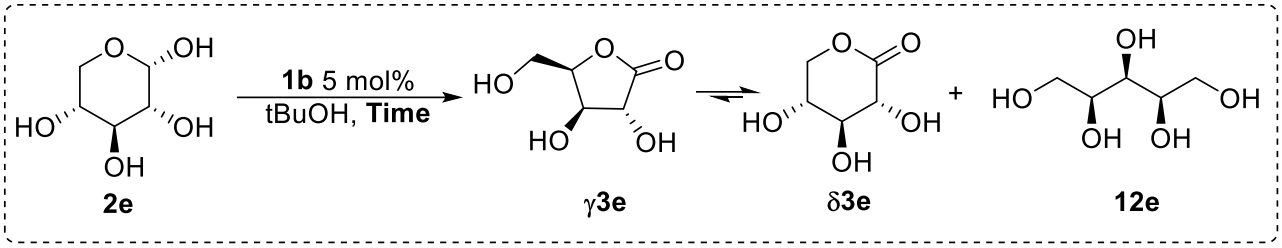


Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-xylose **2e** (50 mg, 0.333 mmol, 1 equiv.) catalyst **1b** (7.8 mg, 0.016 mmol, 5 mol%) and methyl levulinate **7** (43 mg, 0.333 mmol, 1 equiv.). The reaction was stirred at 90 °C for 24 hours. Yields of xylonolactones **3e**, xylitol **12e** and methyl 4-hydroxypentanoate **10** were determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

3e Yield (%)	12e Yield (%)	10 Yield (%)
70	30	30

Table 21: NMR yield of xylonolactones, xylitol and 4-hydroxypentanoate using methyl levulinate in a 1:1 ratio as acceptor

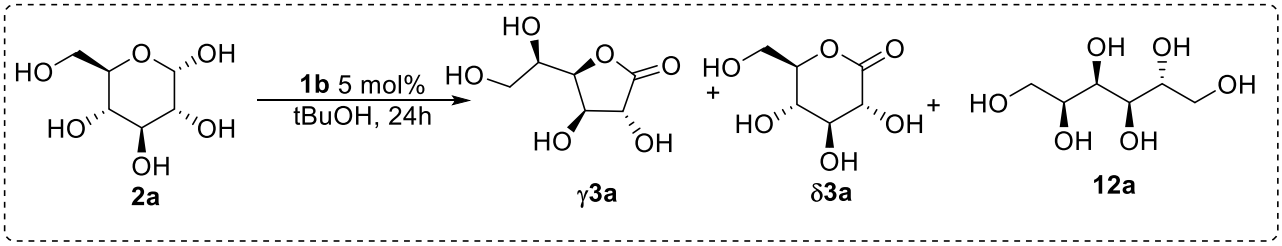
Disproportionation experiment



Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-xylose **2e** (50 mg, 0.333 mmol, 1 equiv.) catalyst **1b** (7.8 mg, 0.016 mmol, 5 mol%) with no acceptor. The reaction was stirred at 90 °C for X hours. Yield and ratios of xylonolactones **3e** and xylitol **12e** were determined by ^{1}H NMR in DMSO-d_6 using an internal standard (1,4-bromonitrobenzene) after filtration trough a PTFE filter (0.2 µm).

Time (hours)	3e Yield (%)	γ-δ ratio	12 Yield (%)
5	55	90:10	45
24	55	95:5	45

Table 22: NMR yield of xylonolactones and xylitol in acceptor free conditions

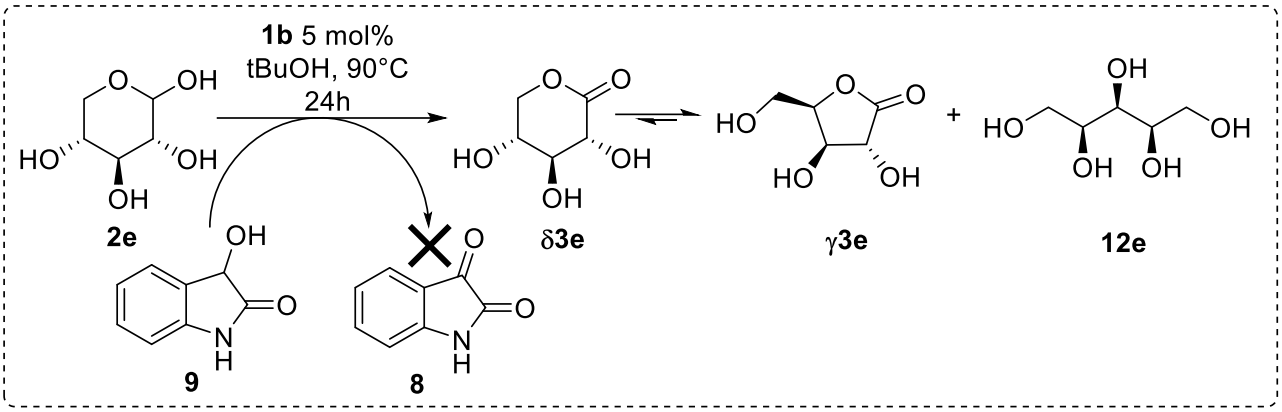


Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-glucose (50 mg, 0.277 mmol, 1 equiv.) catalyst **1b** (5.9 mg, 0.014 mmol, 5 mol%) with no acceptor. The reaction was stirred at 90 °C for 24 hours. Yield and ratios of gluconolactones **3a** and sorbitol **12a** were determined by ^{1}H NMR in DMSO-d_6 using an internal standard (1,4-bromonitrobenzene) after filtration trough a PTFE filter (0.2 µm).

3a Yield (%)	γ-δ ratio	12a Yield (%)
25	80:20	~30

Table 23: NMR yield of gluconolactones and sorbitol in acceptor free conditions

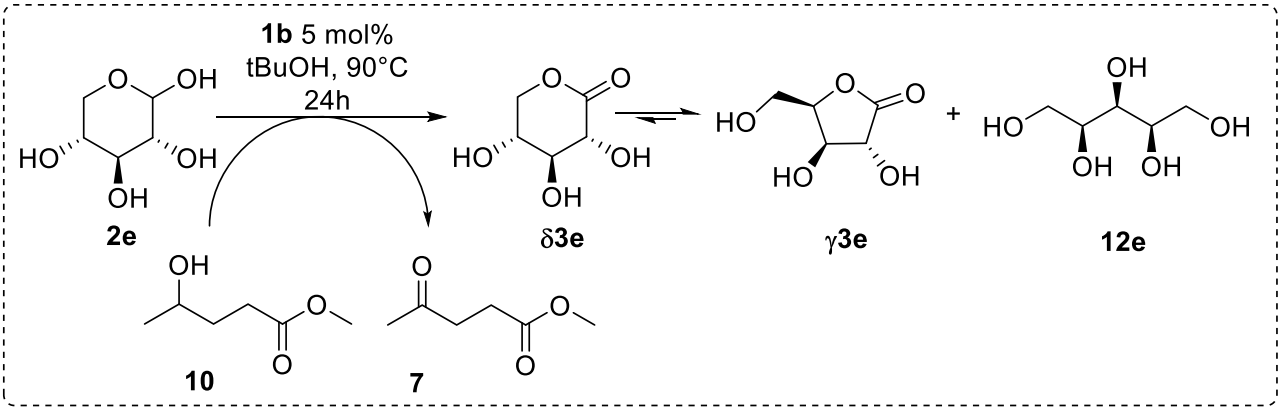
Reversibility experiments



Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-xylose **2e** (50 mg, 0.333 mmol, 1 equiv.) catalyst **1b** (7.8 mg, 0.016 mmol, 5 mol%) and 3 hydroxyindolin-2-one **9** (49 mg, 0.333 mmol, 1 equiv.). The reaction was stirred at 90 °C for 24 hours. Yields and ratios of xylonolactones **3e**, xylitol **12e** and isatin **8** were determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

3e Yield (%)	γ-δ ratio	12e Yield (%)	8 Yield (%)
50	90:10	50	/

Table 23: NMR yield of xylonolactones and xylitol using 3-hydroxyindolin-2-one



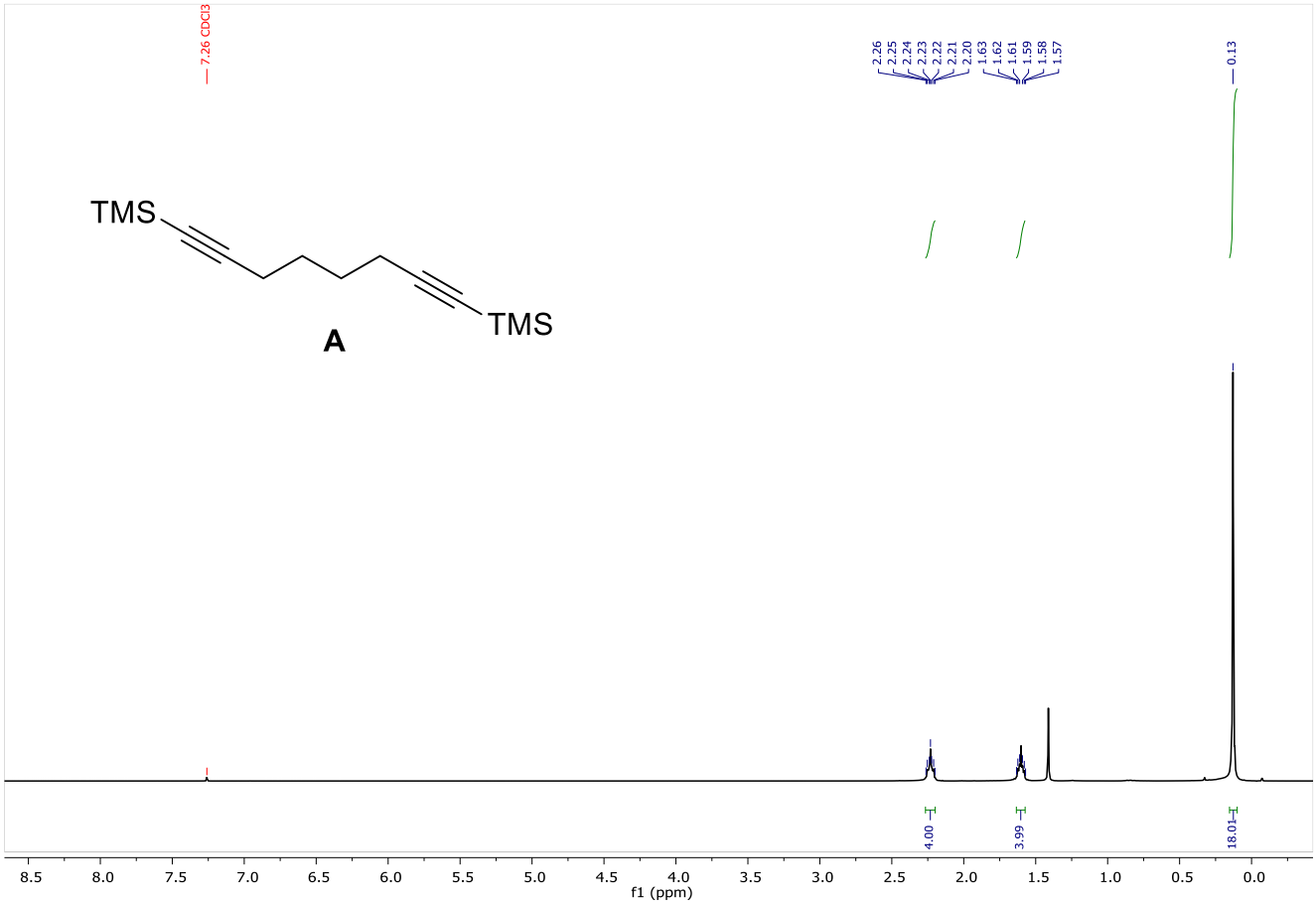
Tert-butanol (0.8 mL) was degassed with argon for 15 min in a sealed tube after addition of D-xylose **2e** (50 mg, 0.333 mmol, 1 equiv.) catalyst **1b** (7.8 mg, 0.016 mmol, 5 mol%) and methyl 4-hydroxypentanoate **10** (44 mg, 0.333 mmol, 1 equiv.). The reaction was stirred at 90 °C for 24 hours. Yields and ratios of xylonolactones **3e**, xylitol **12e** and methyl levulinate **7** were determined by ^{1}H NMR in DMSO-d_6, after filtration trough a PTFE filter (0.2 µm).

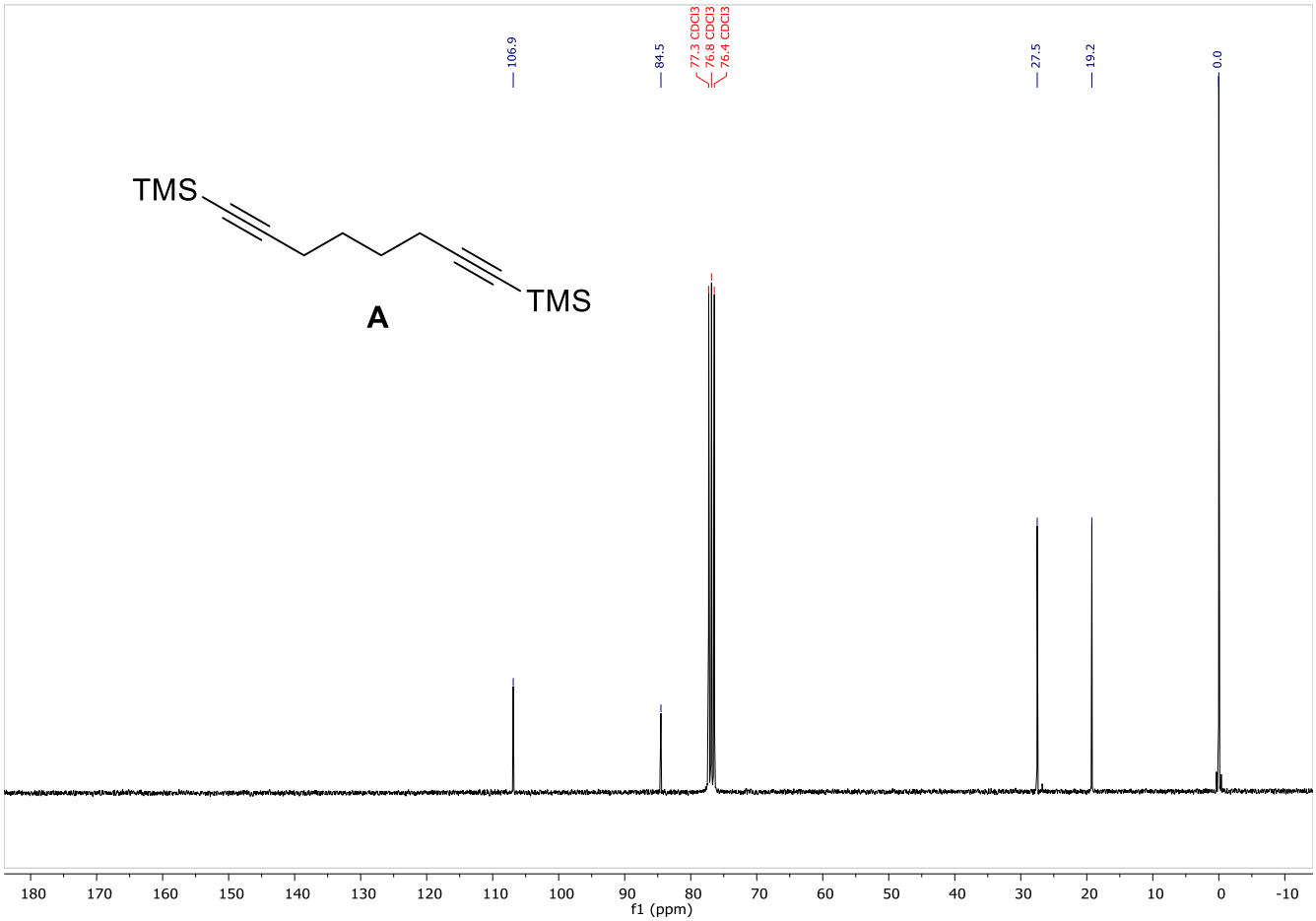
3e Yield (%)	γ-δ ratio	12e Yield (%)	7 Yield (%)
57	9:1	43	10

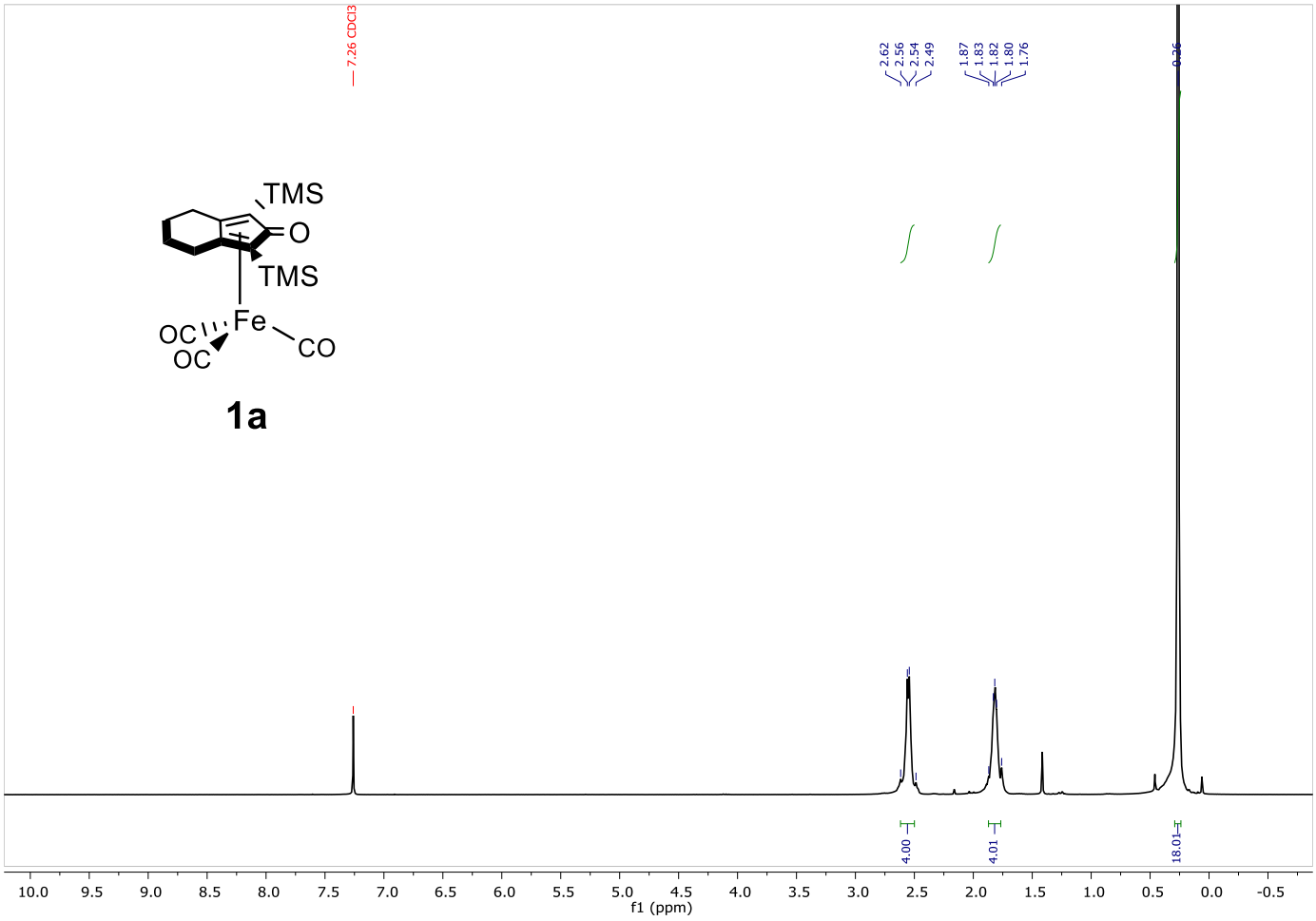
Table 24: NMR yield of xylonolactones and xylitol using 4-hydroxypentanoate

[2] ***Rui, H.; Shanchao, W.; Haoming, T.; Xiaohang, H.; Zhenliang, S.; Waubin, Z.;*** *Org. Lett.* **2018**, 20, 19, 6183–6187

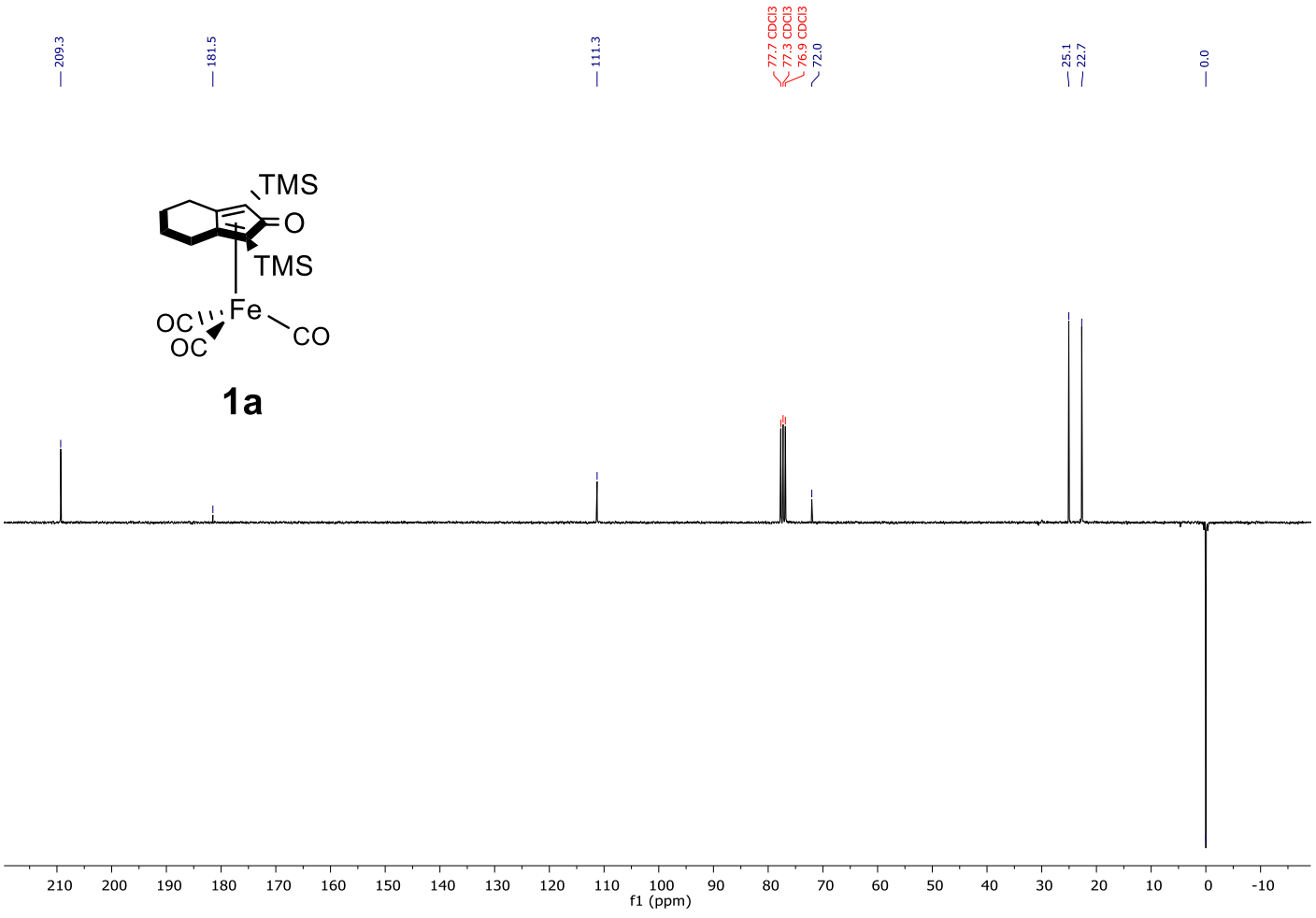
NMR Spectra


7.26 CDCl3
2.26
2.25
2.24
2.23
2.22
2.21
2.20
1.63
1.62
1.61
1.59
1.58
1.57
0.13
TMS
TMS
A
4.00
3.99
18.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

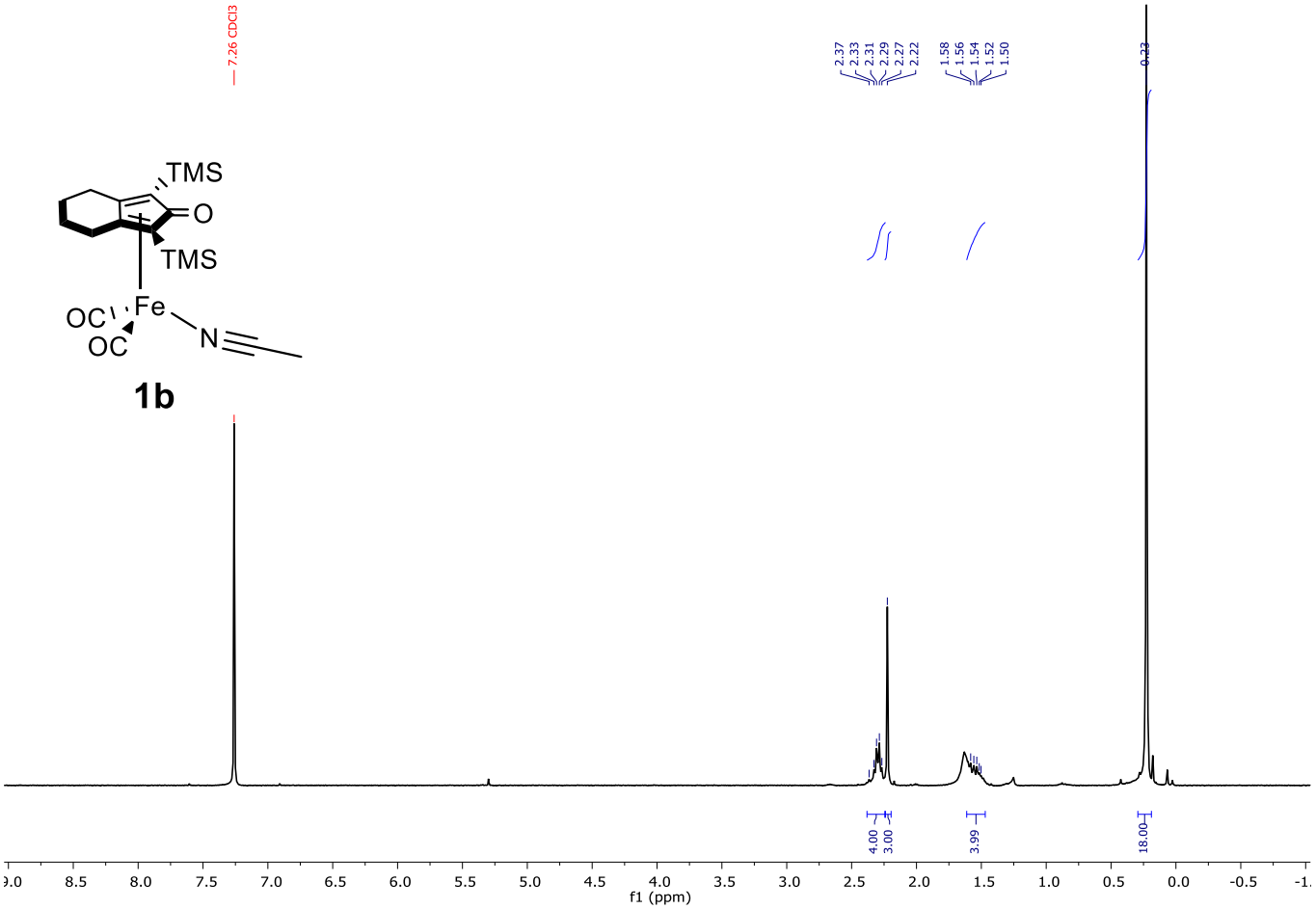

106.9
84.5
77.3 CDCl3
76.8 CDCl3
76.4 CDCl3
27.5
19.2
0.0
TMS
TMS
A
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.26 CDCl3
2.62
2.56
2.54
2.49
1.87
1.83
1.82
1.80
1.76
0.36
TMS
O
TMS
Fe
OC
OC
CO
4.00
4.01
18.01
f1 (ppm)

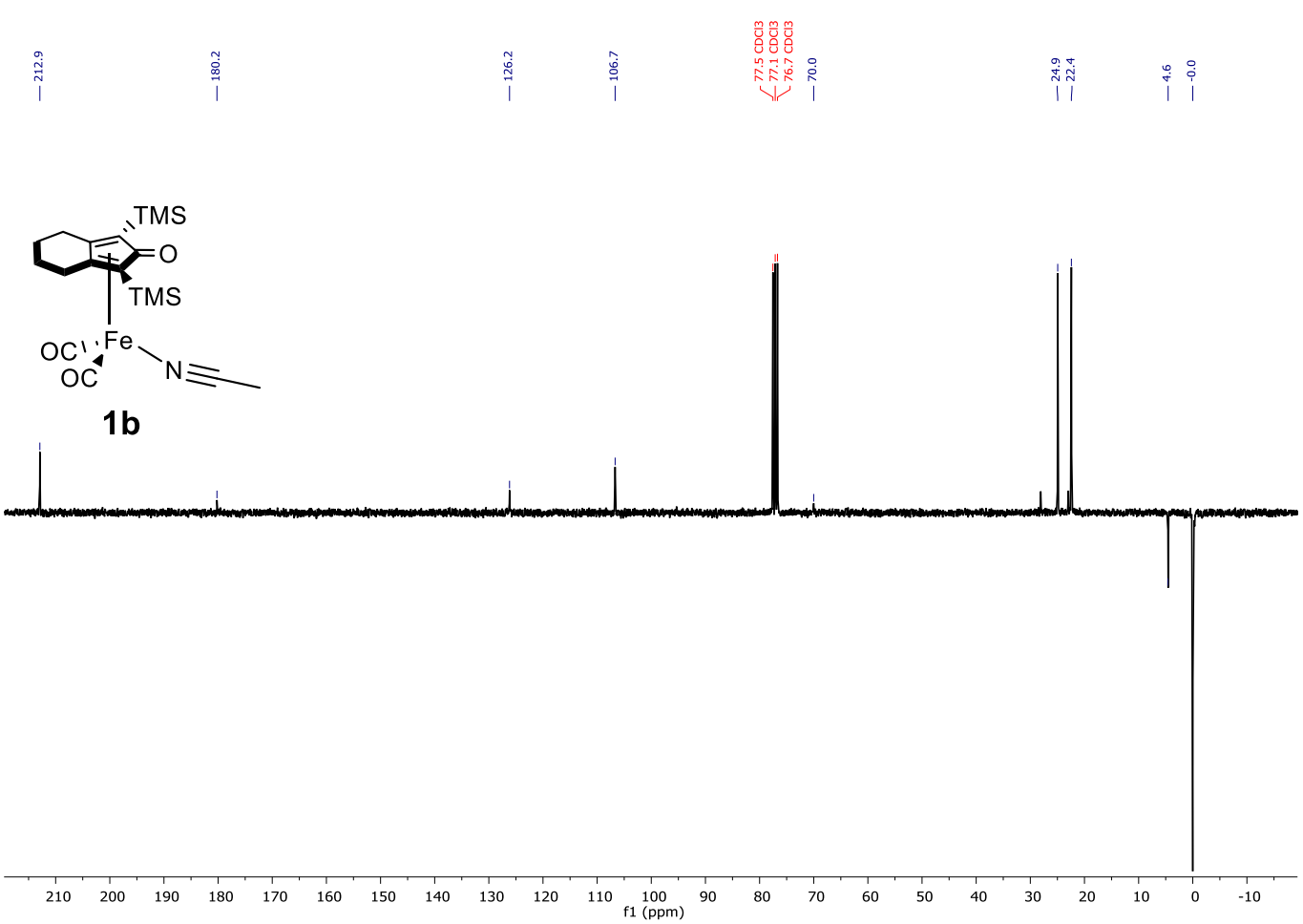
1a


209.3
181.5
111.3
77.7 CDCl3
77.3 CDCl3
76.9 CDCl3
72.0
25.1
22.7
0.0
TMS
O
TMS
Fe
OC
OC
CO
f1 (ppm)

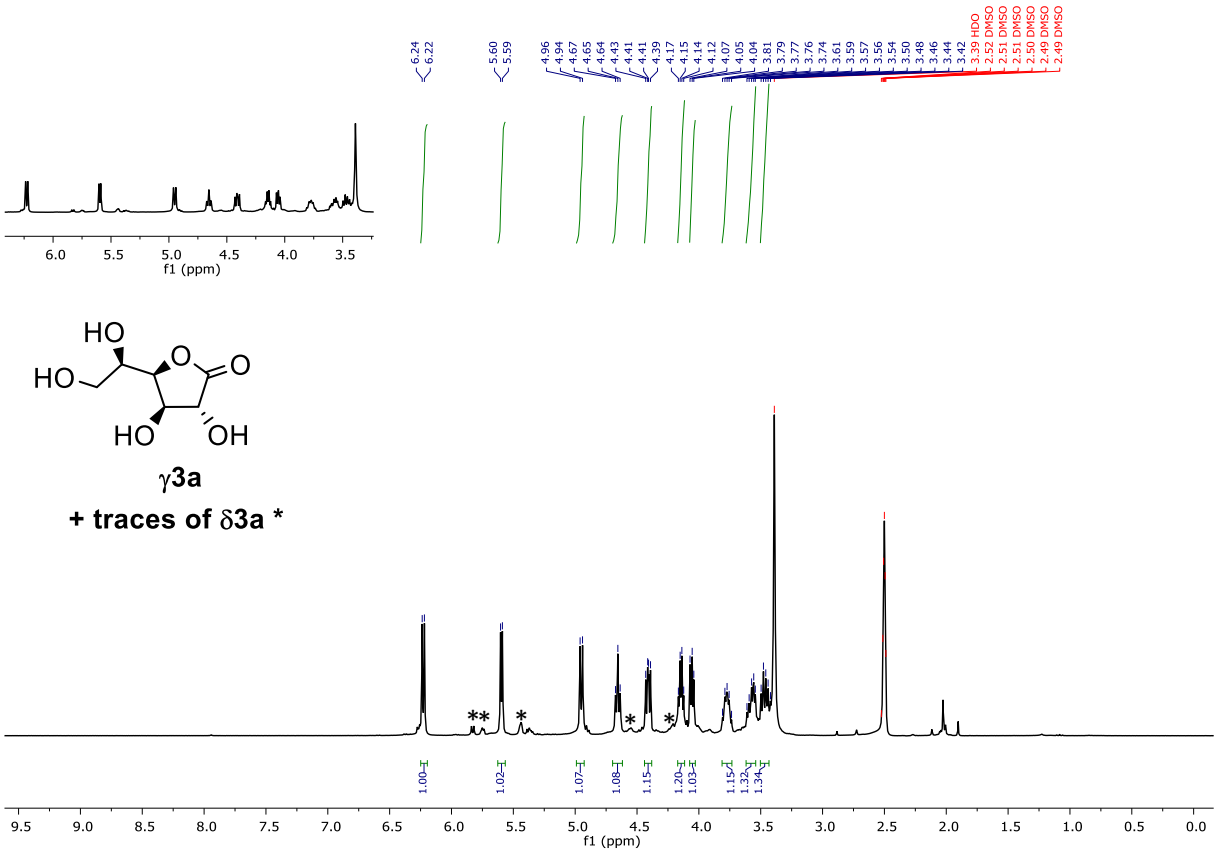
1a

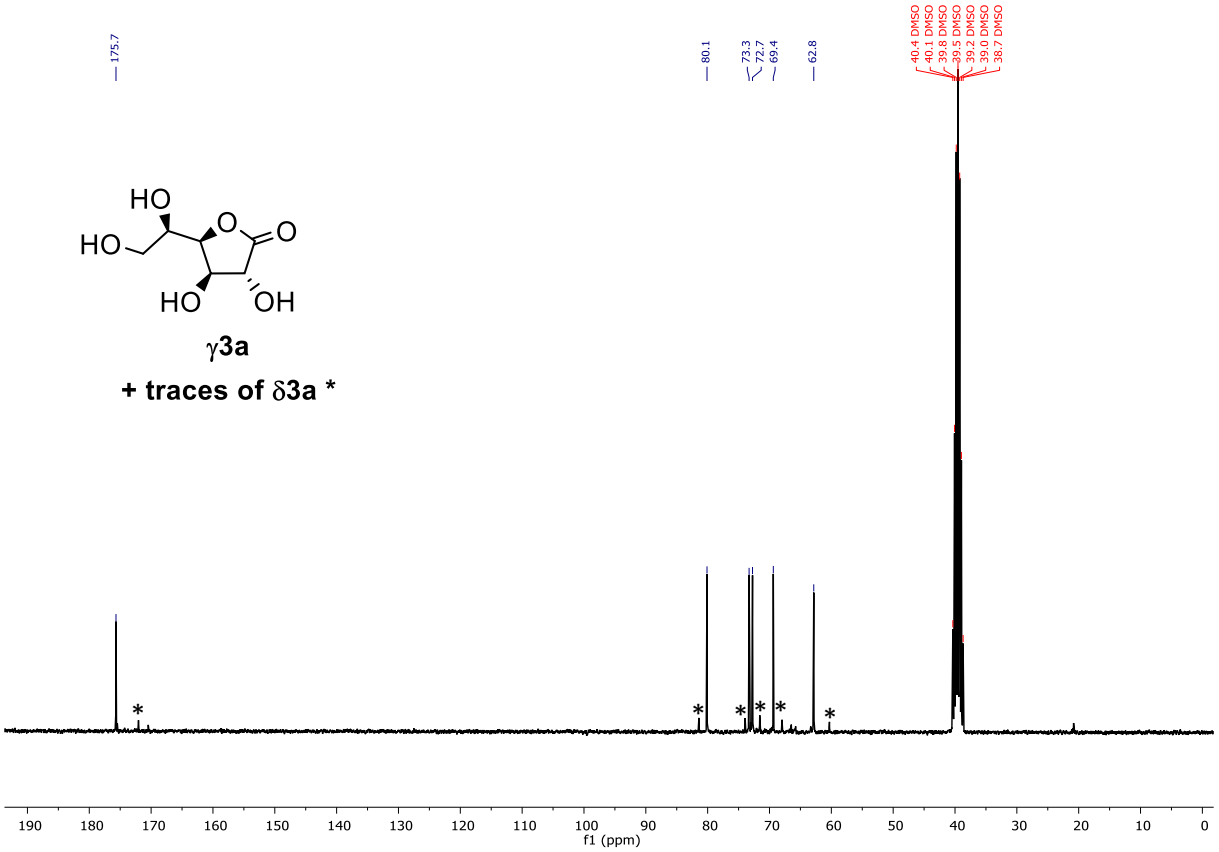

7.26 CDCl3
2.37
2.33
2.31
2.29
2.27
2.22
1.58
1.56
1.54
1.52
1.50
0.33
TMS
O
TMS
OC
Fe
OC
N
4.00
3.00
3.99
18.00
f1 (ppm)

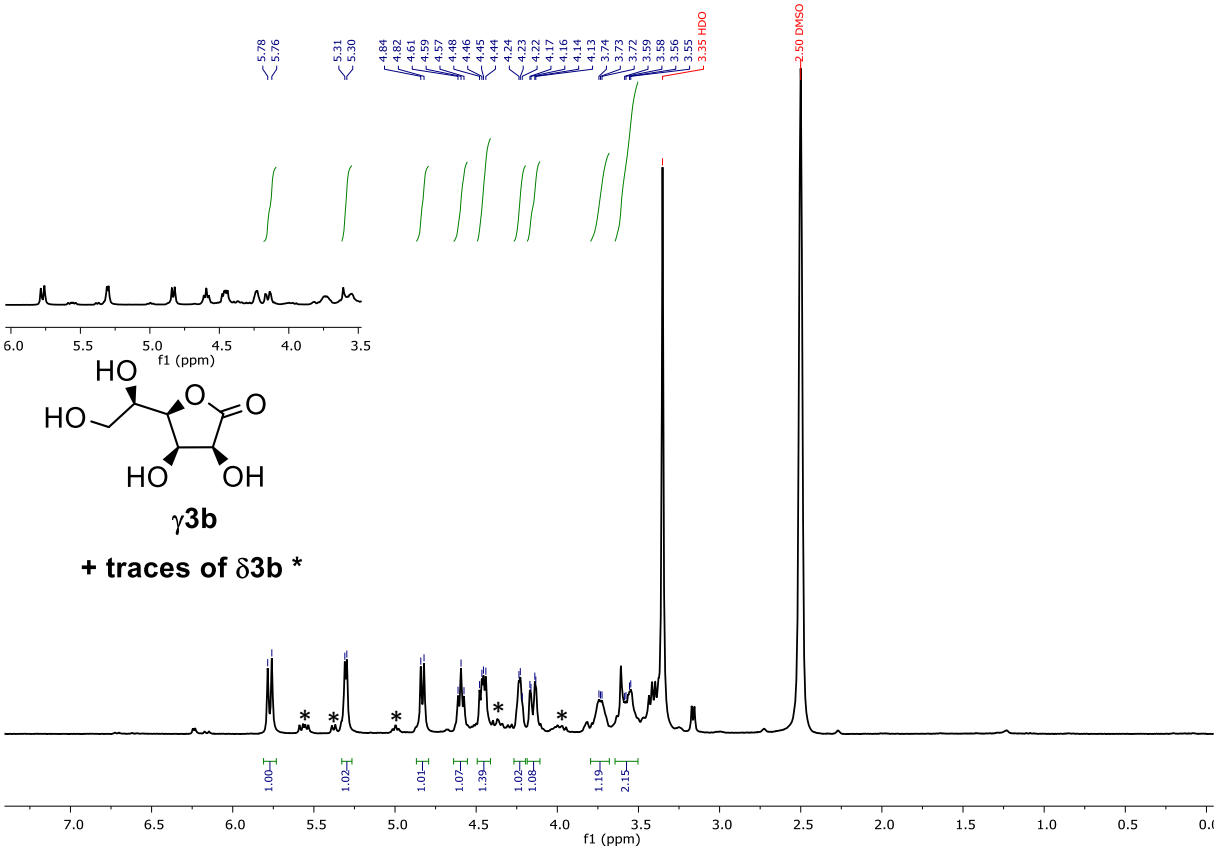
1b

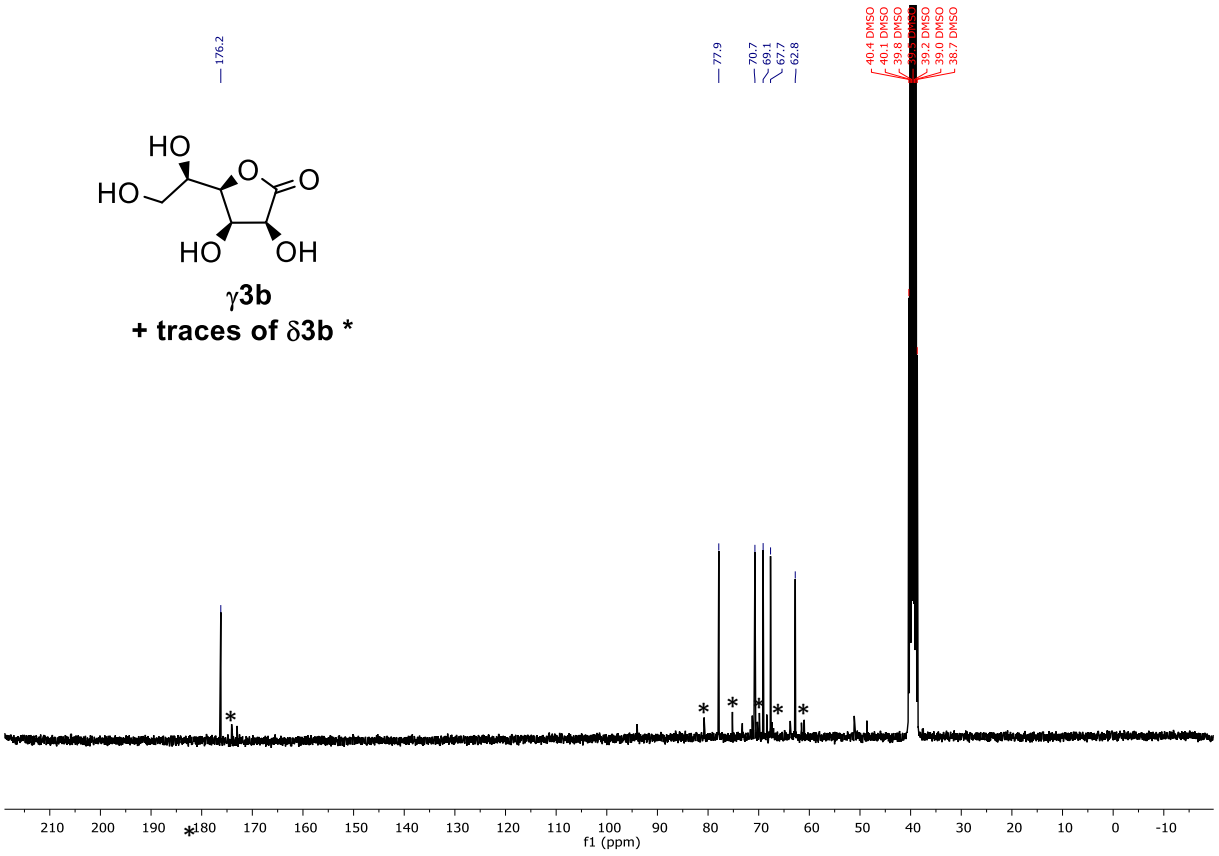

212.9
180.2
126.2
106.7
77.5 CDCl3
77.1 CDCl3
76.7 CDCl3
70.0
24.9
22.4
4.6
-0.0
TMS
O
TMS
OC
Fe
OC
N
f1 (ppm)

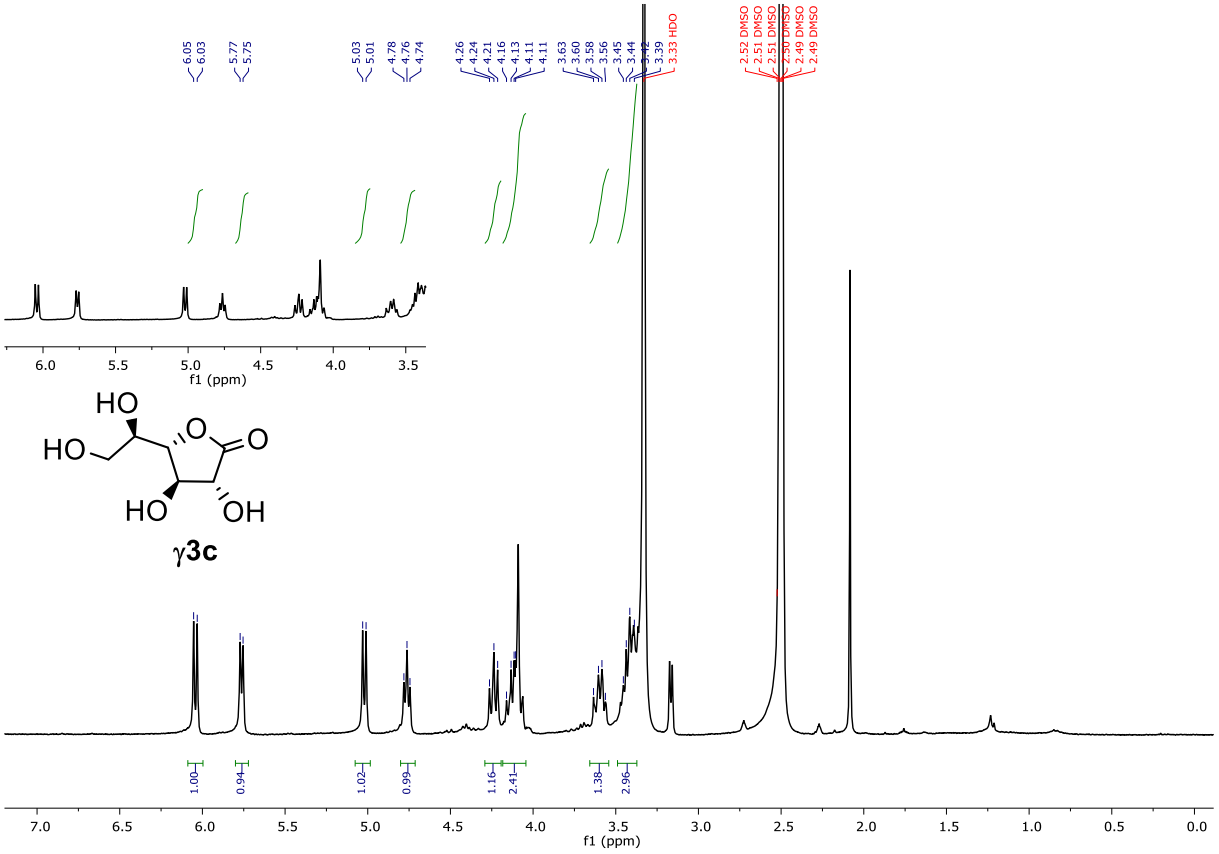
1b

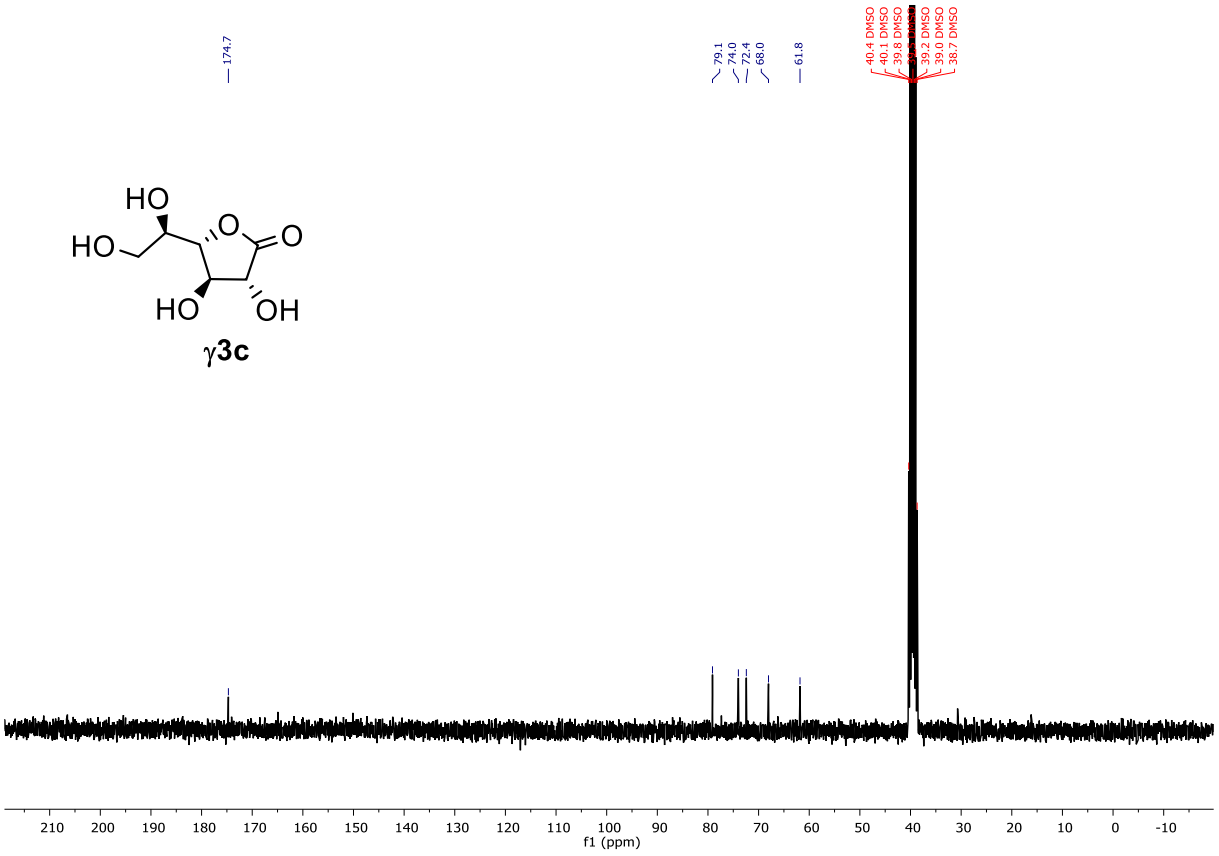

6.24
6.22
5.60
5.59
4.96
4.94
4.67
4.65
4.64
4.43
4.41
4.41
4.39
4.17
4.15
4.14
4.12
4.07
4.05
4.04
3.81
3.79
3.77
3.76
3.74
3.61
3.59
3.57
3.56
3.54
3.50
3.48
3.46
3.44
3.42
3.39 HDO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.49 DMSO
2.49 DMSO
f1 (ppm)
HO
HO
O
O
HO
OH
γ3a
+ traces of δ3a *
1.00
1.02
1.07
1.08
1.15
1.20
1.03
1.15
1.32
1.34
f1 (ppm)

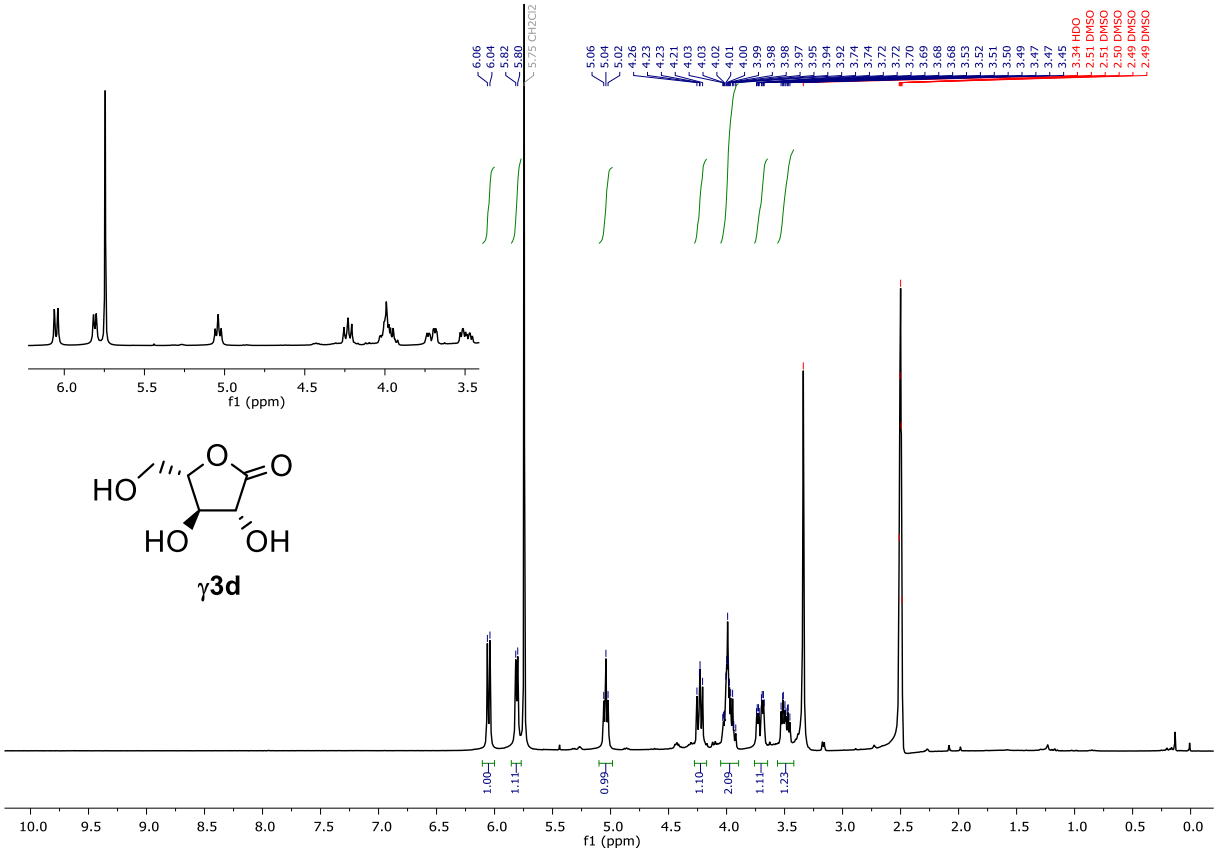

175.7
80.1
73.3
72.7
69.4
62.8
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.5 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
HO
HO
O
O
HO
OH
γ3a
+ traces of δ3a *
f1 (ppm)

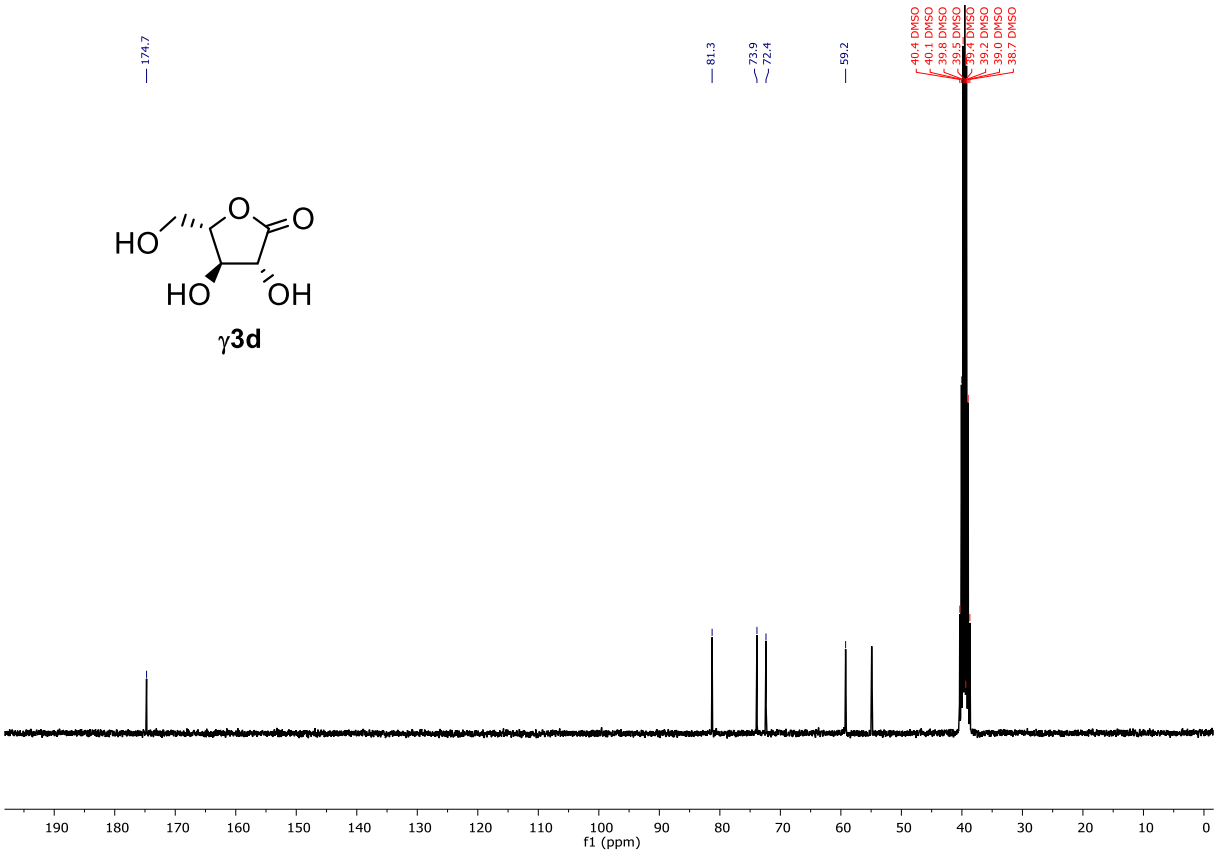

5.78
5.76
5.31
5.30
4.84
4.82
4.61
4.59
4.57
4.48
4.46
4.45
4.44
4.24
4.23
4.22
4.17
4.16
4.14
4.13
3.74
3.73
3.72
3.59
3.58
3.56
3.55
3.35 HDO
2.50 DMSO
f1 (ppm)
HO
HO
O
O
HO
OH
γ3b
+ traces of δ3b *
1.00
1.02
1.01
1.07
1.39
1.02
1.08
1.19
2.15
f1 (ppm)

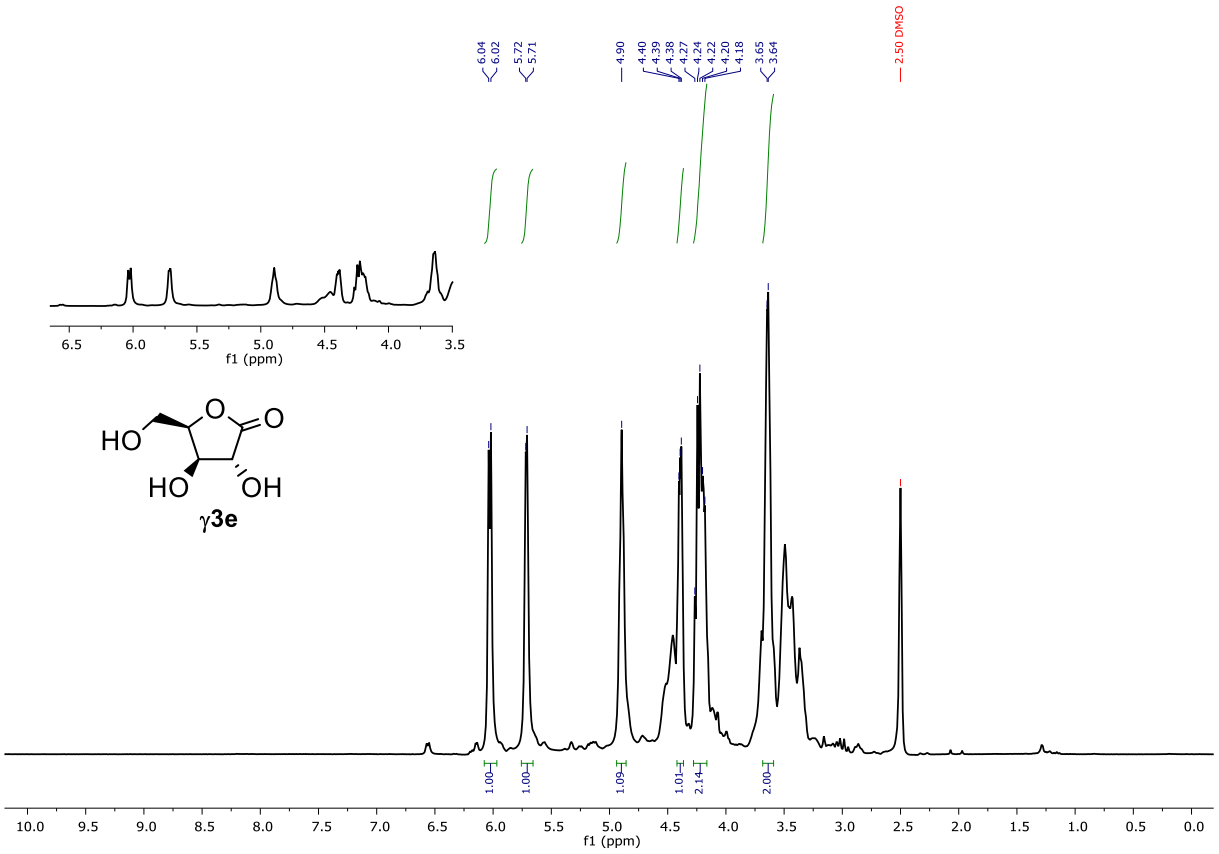

176.2
77.9
70.7
69.1
67.7
62.8
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
HO
HO
O
O
HO
OH
γ3b
+ traces of δ3b *
f1 (ppm)

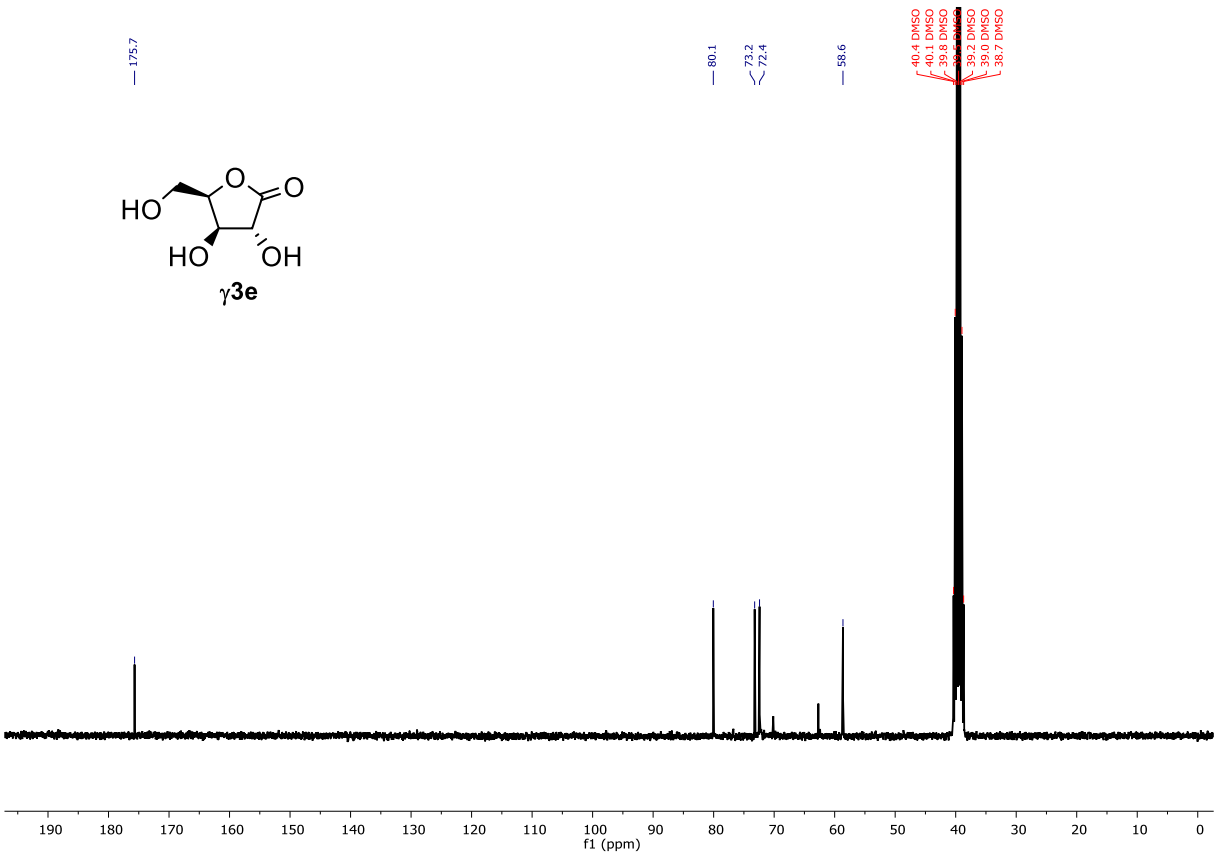

6.05
6.03
5.77
5.75
5.03
5.01
4.78
4.76
4.74
4.26
4.24
4.21
4.16
4.13
4.11
4.11
3.63
3.60
3.58
3.56
3.45
3.44
3.42
3.39
3.33 HDO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.49 DMSO
2.49 DMSO
f1 (ppm)
HO
HO
O
O
HO
OH
γ3c
1.00
0.94
1.02
0.99
1.16
2.41
1.38
2.96
f1 (ppm)

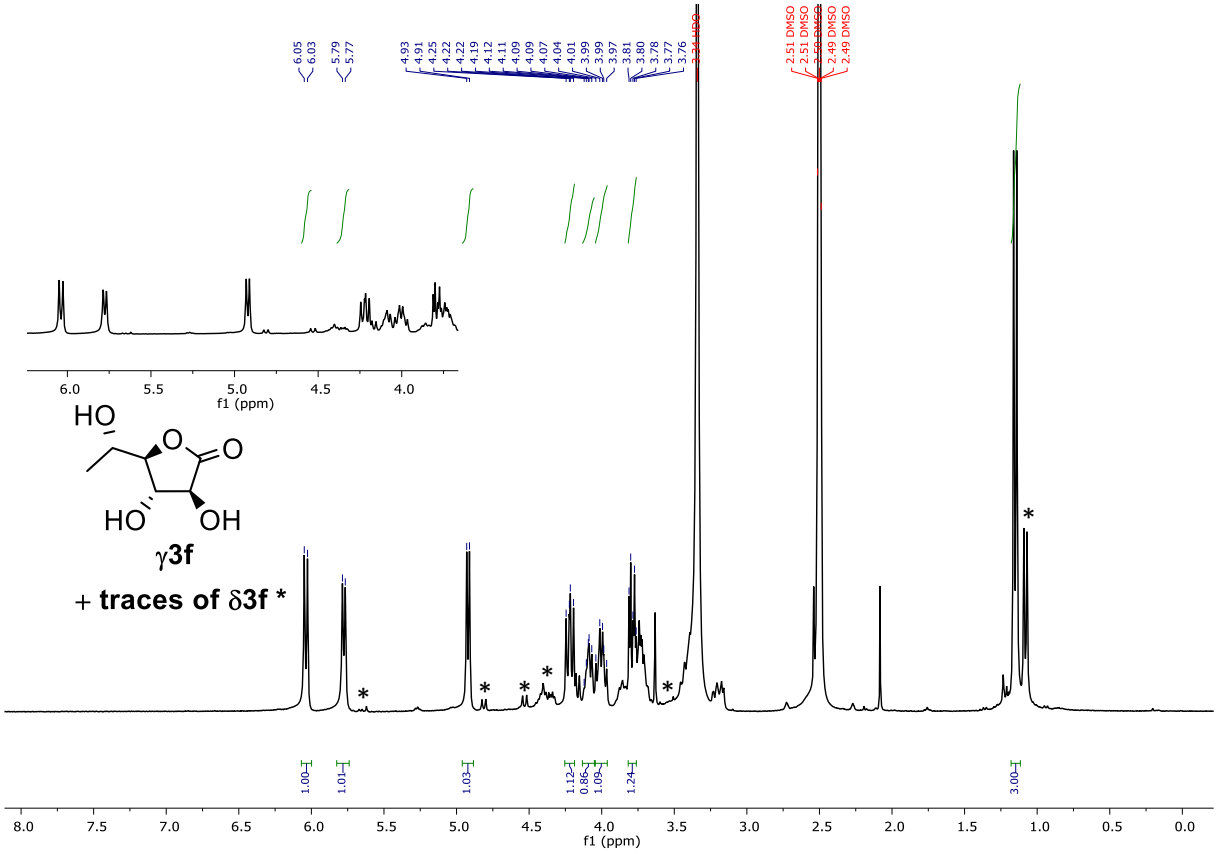

174.7
79.1
74.0
72.4
68.0
61.8
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
HO
HO
O
O
HO
OH
γ3c
f1 (ppm)

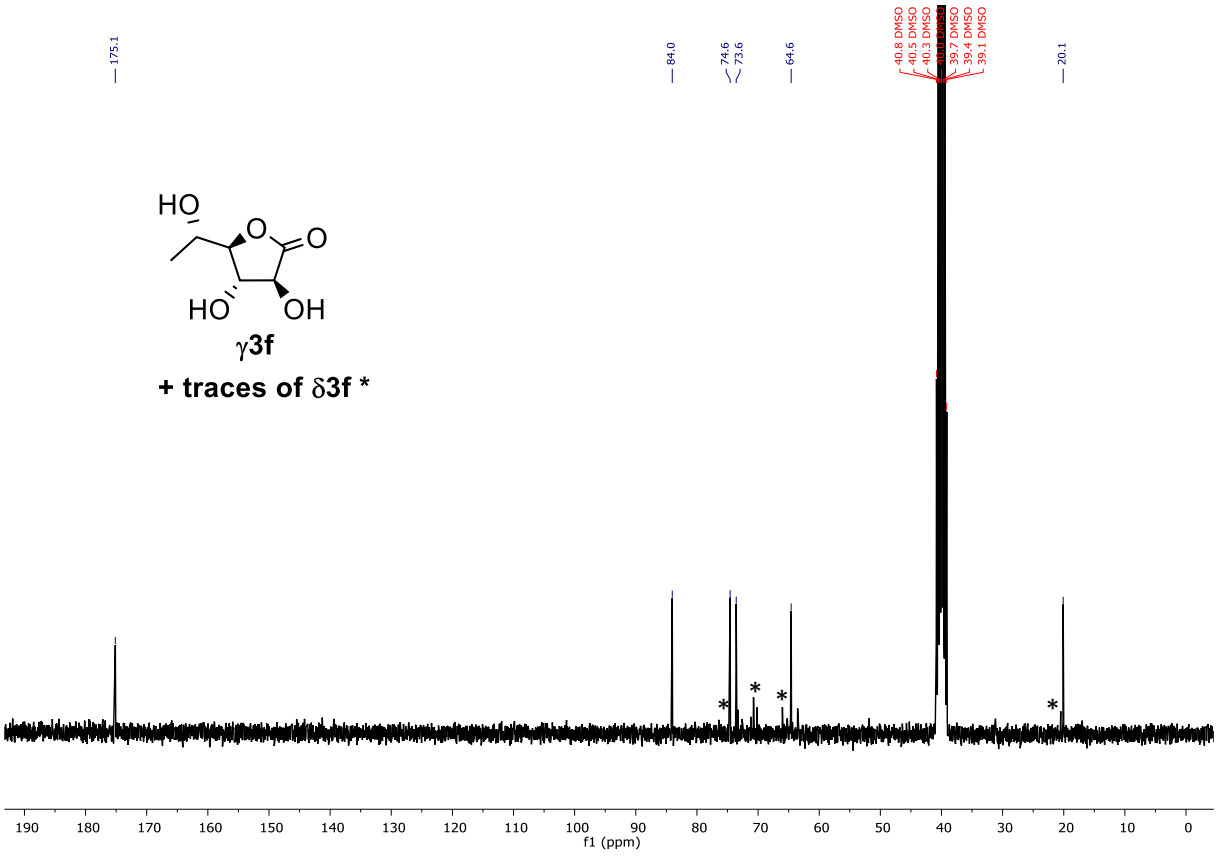

6.06
6.04
5.82
5.80
5.75 CH2Cl2
5.06
5.04
5.02
4.26
4.23
4.23
4.21
4.03
4.03
4.02
4.01
4.00
3.99
3.98
3.98
3.97
3.95
3.94
3.92
3.74
3.74
3.72
3.72
3.70
3.69
3.68
3.68
3.53
3.52
3.51
3.50
3.49
3.47
3.47
3.45
3.34 HDO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.49 DMSO
2.49 DMSO
f1 (ppm)
HO
O
O
HO
OH
γ3d
1.00
1.11
0.99
1.10
2.09
1.11
1.23
f1 (ppm)

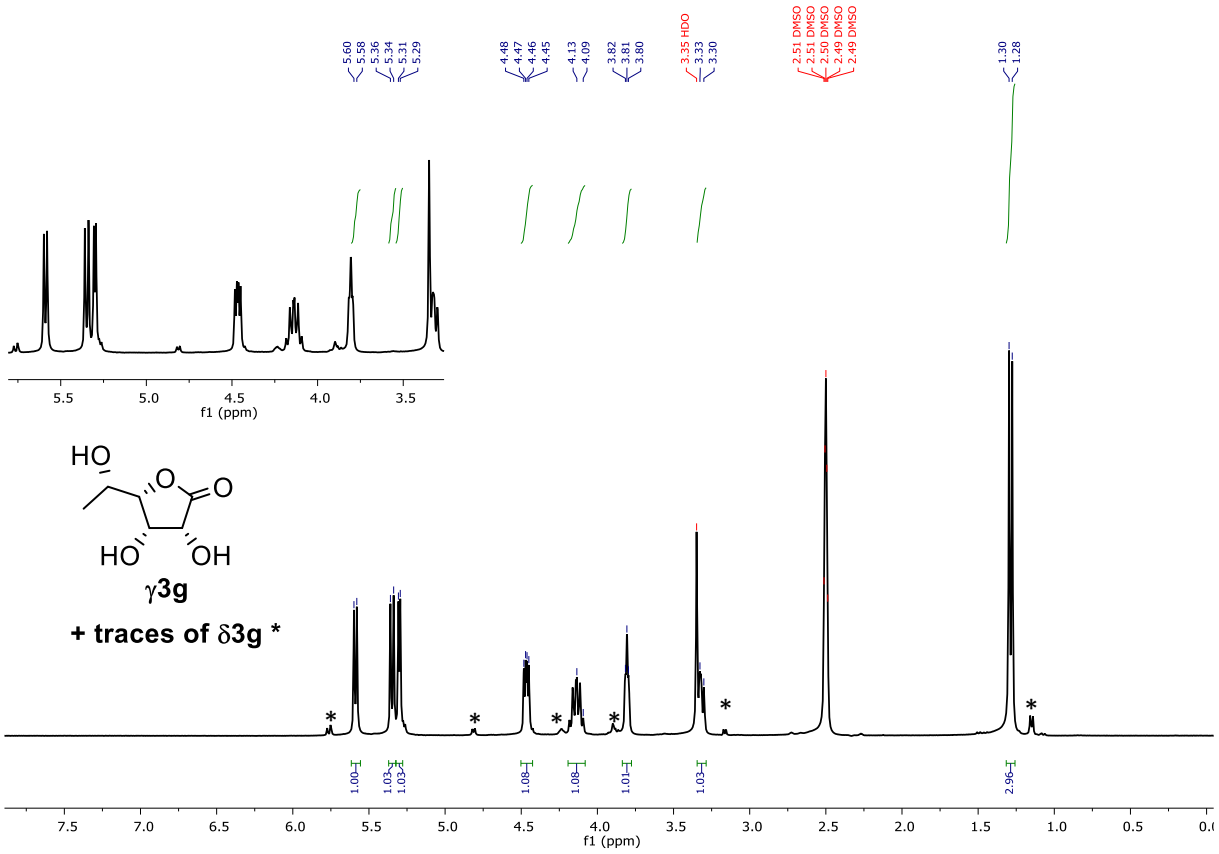

174.7
81.3
73.9
72.4
59.2
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.5 DMSO
39.4 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
HO
O
O
HO
OH
γ3d
f1 (ppm)

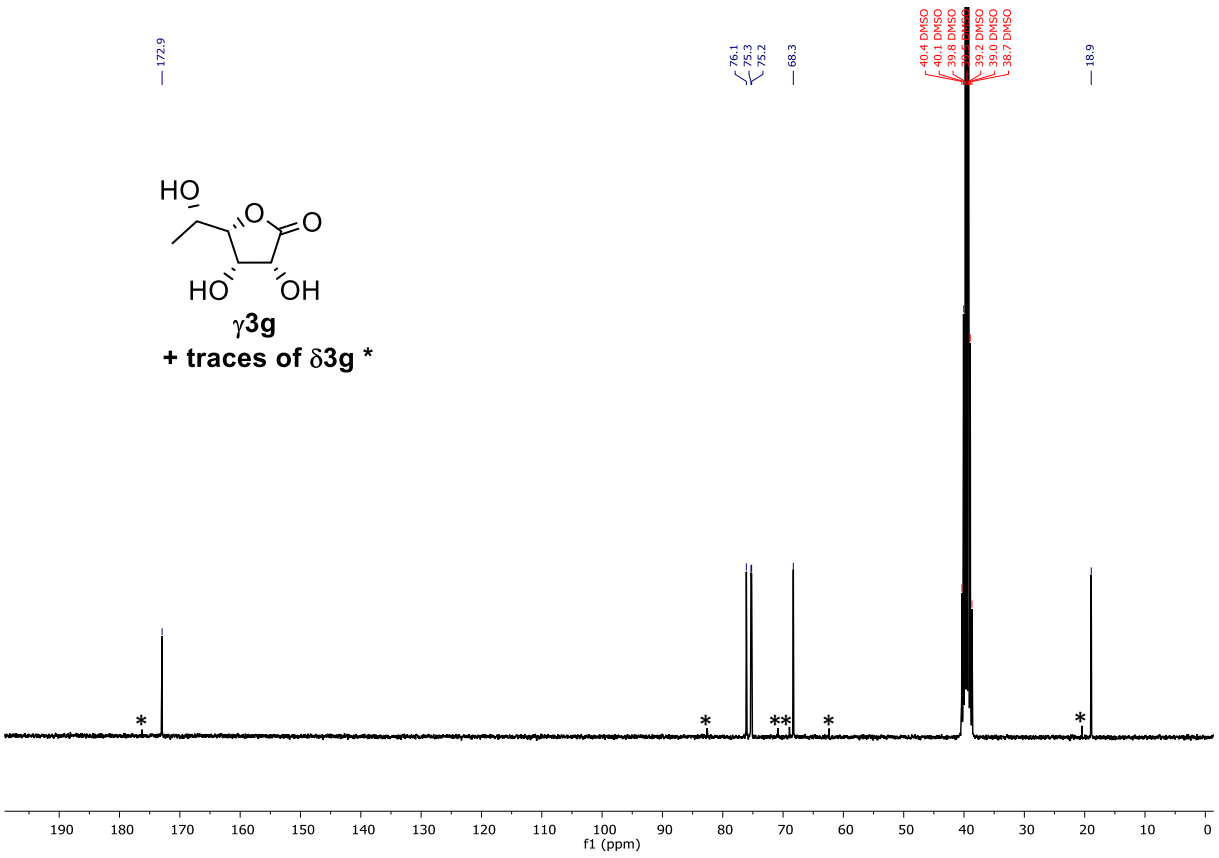

6.04
6.02
5.72
5.71
4.90
4.40
4.39
4.38
4.27
4.24
4.22
4.20
4.18
3.65
3.64
2.50 DMSO
f1 (ppm)
HO
O
O
HO
OH
γ3e
1.00
1.00
1.09
1.01
2.14
2.00
f1 (ppm)

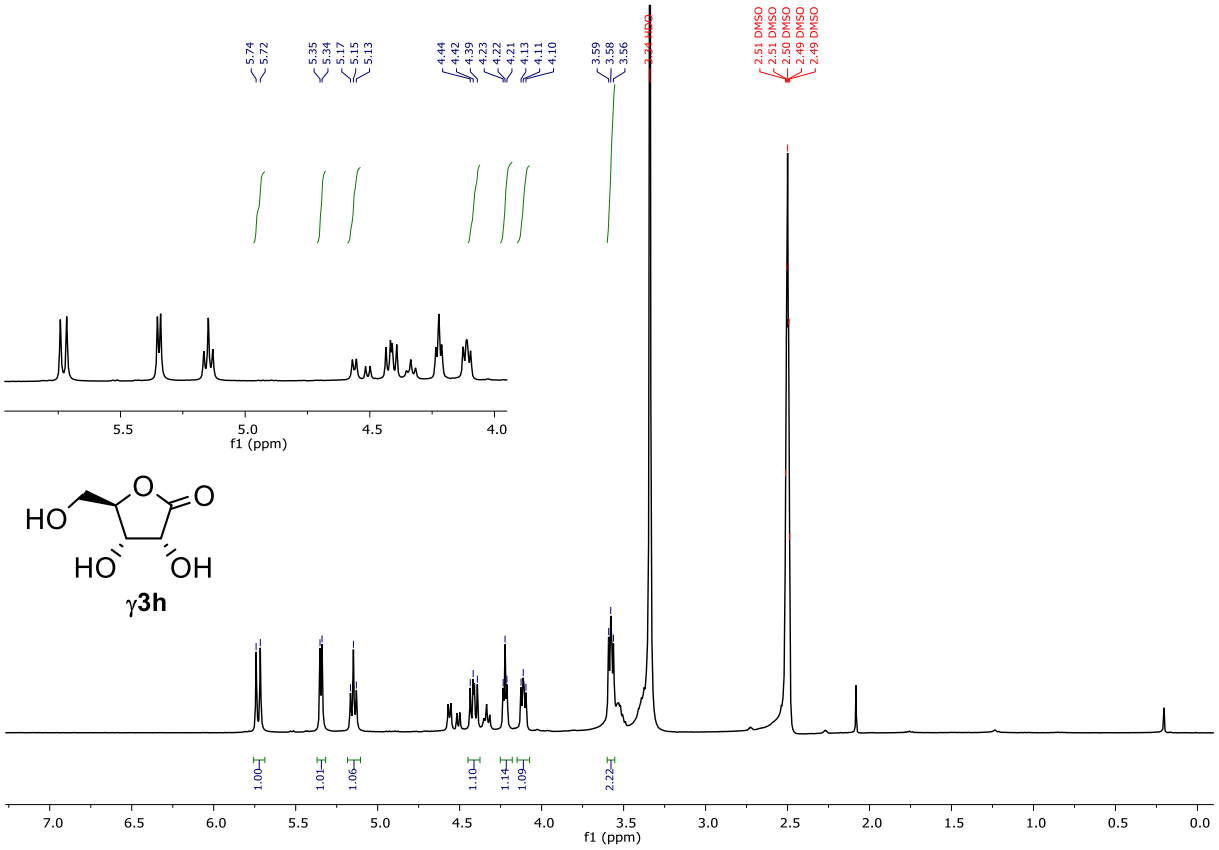

175.7
80.1
73.2
72.4
58.6
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
HO
O
O
HO
OH
γ3e
f1 (ppm)

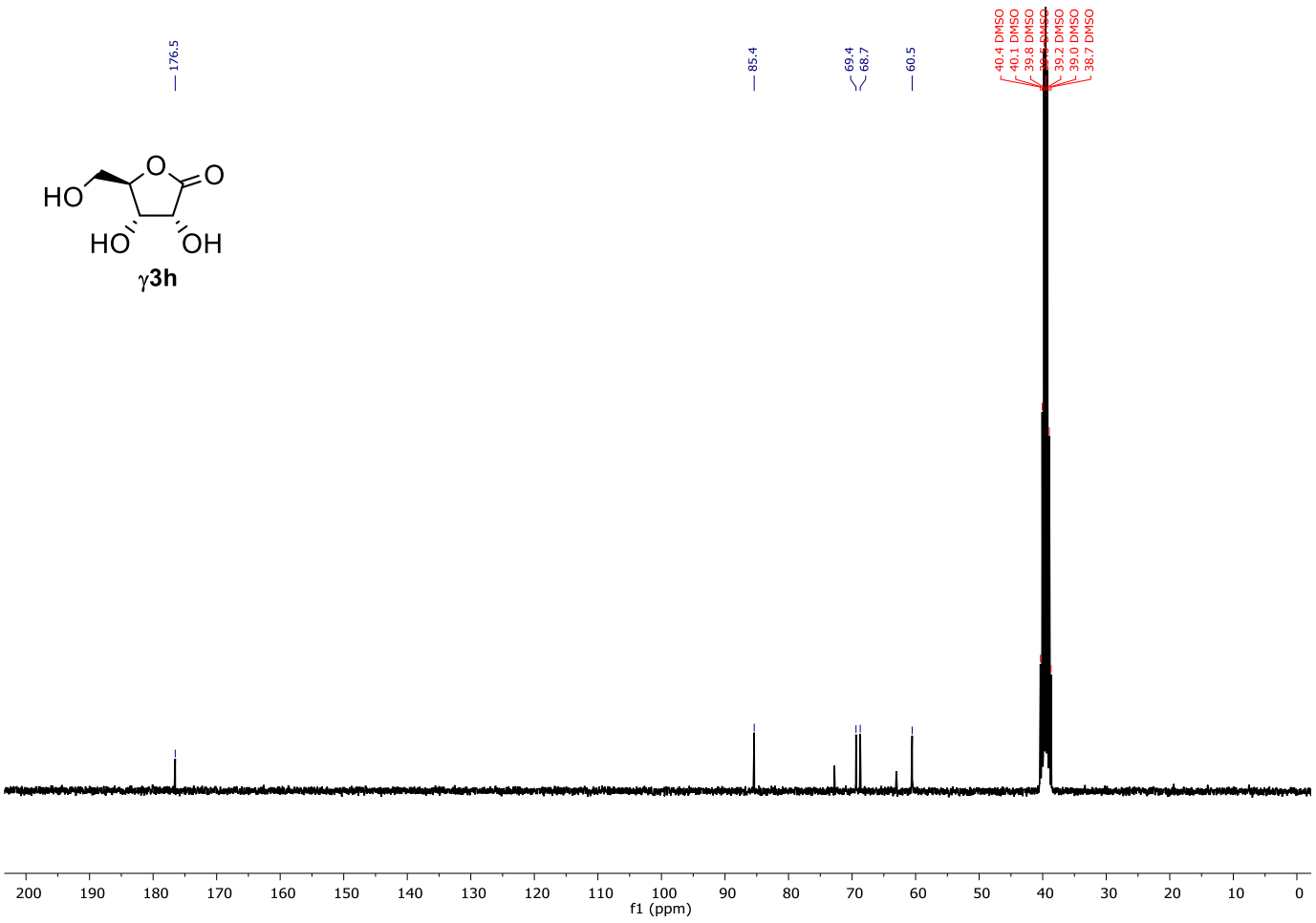

HO
O
O
HO
OH
γ3f
+ traces of δ3f *
f1 (ppm)

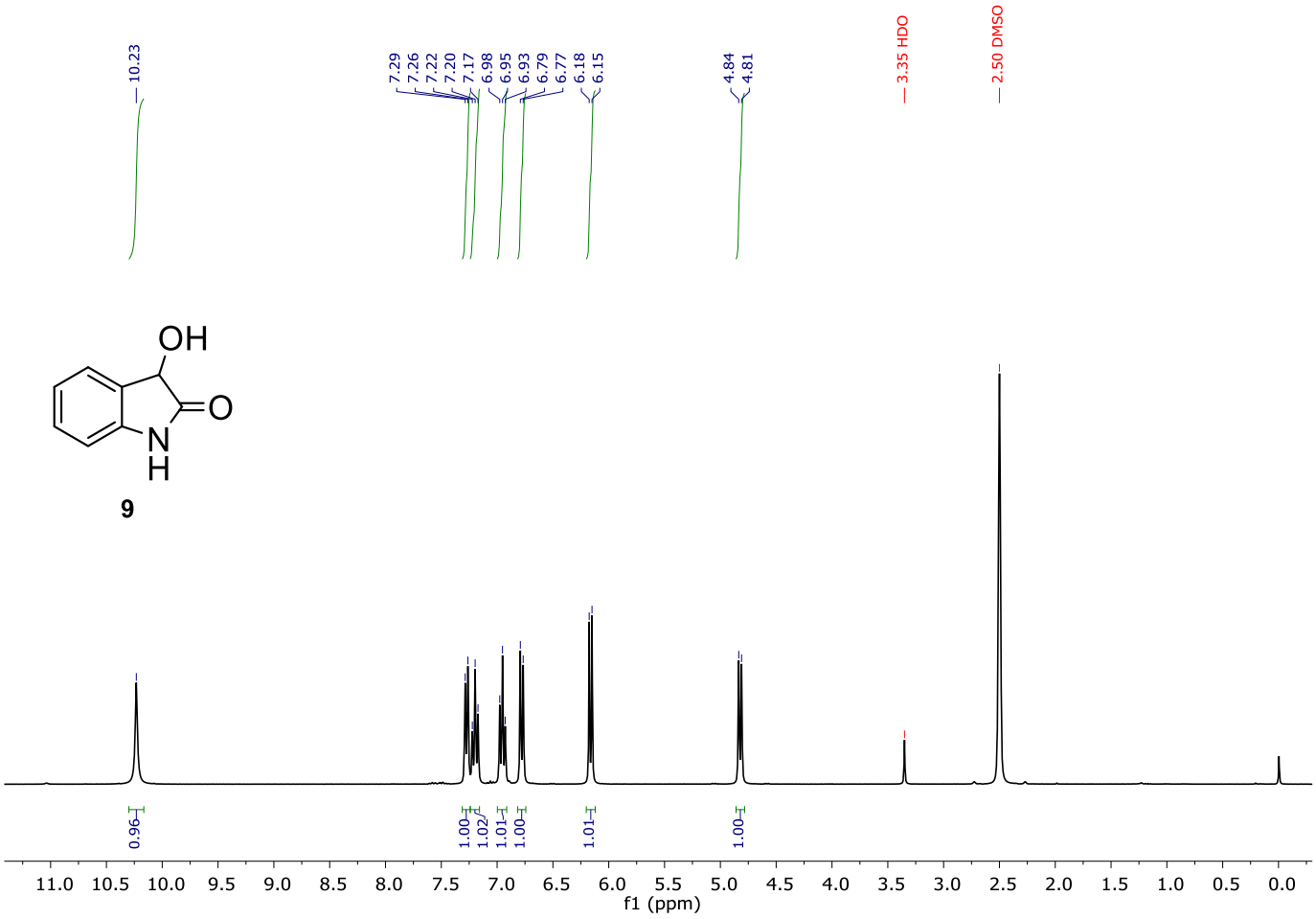

HO
O
O
HO
OH
γ3f
+ traces of δ3f *
f1 (ppm)

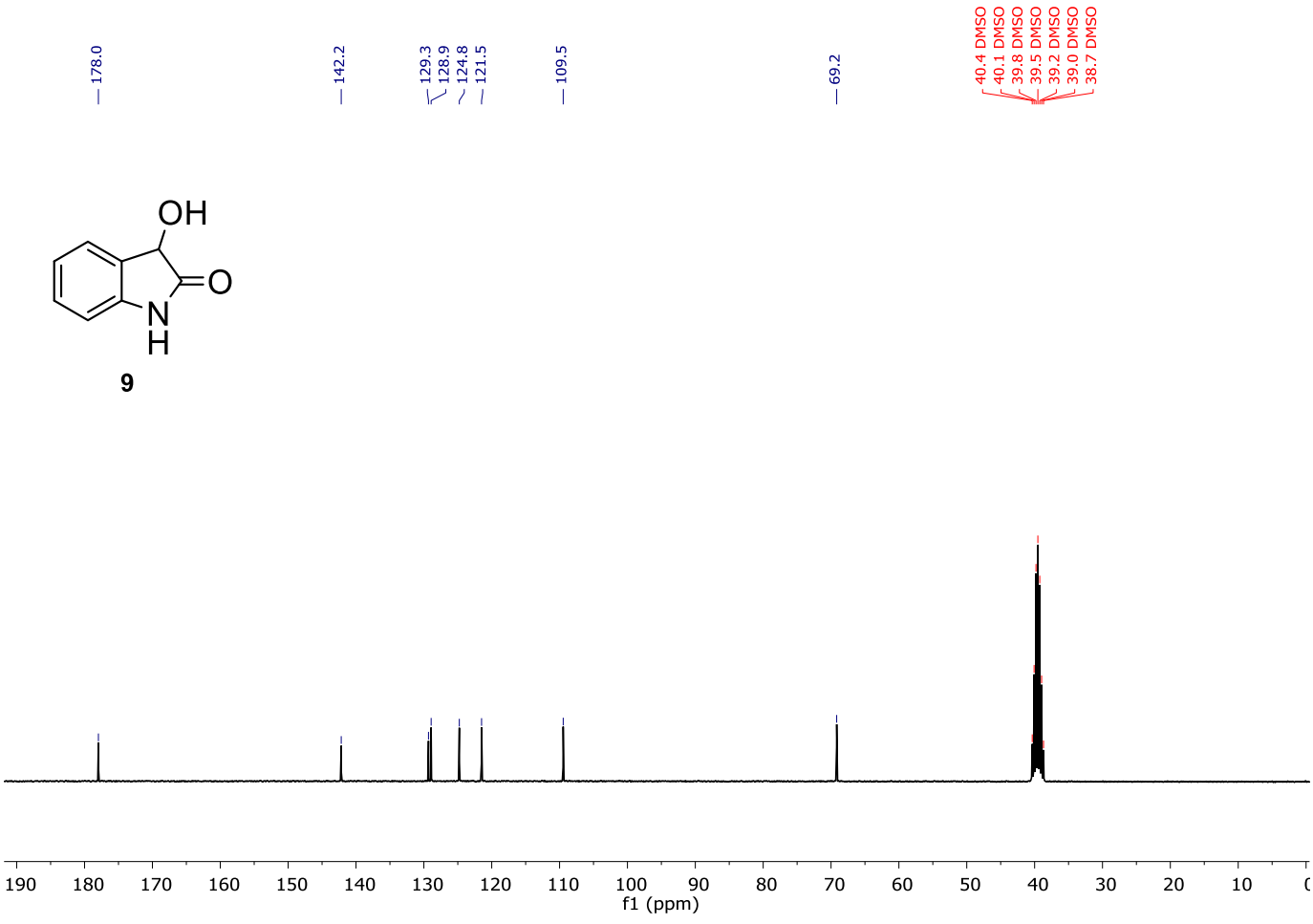

5.60
5.58
5.36
5.34
5.31
5.29
4.48
4.47
4.46
4.45
4.13
4.09
3.82
3.81
3.80
3.35 HDO
3.33
3.30
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.49 DMSO
2.49 DMSO
1.30
1.28
f1 (ppm)
HO
O
O
HO
OH
γ3g
+ traces of δ3g *
1.00
1.03
1.03
1.08
1.08
1.01
1.03
2.96
f1 (ppm)


172.9
76.1
75.3
75.2
68.3
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.5 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
18.9
HO
O
O
HO
OH
γ3g
+ traces of δ3g *
f1 (ppm)


5.74
5.72
5.35
5.34
5.17
5.15
5.13
4.44
4.42
4.39
4.23
4.22
4.21
4.13
4.11
4.10
3.59
3.58
3.56
3.34 H2O
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.49 DMSO
2.49 DMSO
f1 (ppm)
HO
O
O
HO
OH
γ3h
1.00
1.01
1.06
1.10
1.14
1.09
2.22
f1 (ppm)


176.5
85.4
69.4
68.7
60.5
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.5 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
HO
O
O
HO
OH
γ3h
f1 (ppm)


10.23
7.29
7.26
7.22
7.20
7.17
6.98
6.95
6.93
6.79
6.77
6.18
6.15
4.84
4.81
3.35 HDO
2.50 DMSO
OH
O
N
H
9
0.96
1.00
1.02
1.01
1.00
1.01
1.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


178.0
142.2
129.3
128.9
124.8
121.5
109.5
69.2
40.4 DMSO
40.1 DMSO
39.8 DMSO
39.5 DMSO
39.2 DMSO
39.0 DMSO
38.7 DMSO
OH
O
N
H
9
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

Dr Laure Benhamou

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Normandie Univ, UNILEHAVRE, FR 3038 CNRS, URCOM,
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Le Havre, July 2022

Dear Editor,

Please find enclosed our manuscript entitled: ***'Iron-catalysed chemo-selective oxidation of unprotected sugars: application for the competitive oxidation of pentoses from a sugar mixture.'*** This work is original and has not been previously reported. Moreover, all the authors have read the manuscript and agreed to its submission for publication.

In this work, we propose, in agreement with several Green Chemistry principles, an innovative and ***efficient iron-catalysed transfer hydrogenation*** transformation of ***unprotected sugars***, ***excluding the use of auxiliaries*** for better ***waste control***. Acetone was initially exploited as a benchmark solvent and formal hydrogen acceptor in transfer hydrogenation. The process was successfully scaled up and the lactones were isolated ***without requiring chromatography technics***.

The conversion of these ***renewable resources*** into lactones was optimised to selectively oxidise ***pentoses from a mixture*** of C6 and C5 sugars thanks to the difference in reactivity of hexoses and pentoses.

We, finally, devised an alternative procedure in *tert*-butanol to ***extend the range of acceptors tolerated*** and ***reduce the stoichiometry of the acceptor (down to 1 equivalent) required in the process without compromising the efficiency*** and allowing the ***upgrade of both reaction partners*** for future synthetic application.

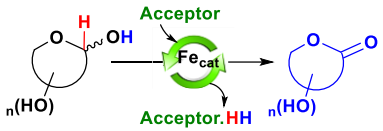
Consequently, we believe our contribution, which provides an innovative and eco-friendly approach to sugars chemistry, is perfectly suited for publication in Green Chemistry and will attract a large readership to your journal.

I am looking forward to hearing from you at your earliest convenience.

Sincerely,

Dr Laure Benhamou

Iron catalysed oxidation of UNPROTECTED SUGARS



- Chemo-selective of the anomeric position
- Strong oxidant free
- Equimolarity sugar : acceptor
- Scale-up