# **Supporting information**

Calcium Hypophosphite Mediated Deiodination in Water: Mechanistic Insights and Applications in Large Scale Syntheses of D-Quinovose and D-Rhamnose

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# 1. General Comments

All reactions were monitored by thin-layer chromatography over silica-gel-coated TLC plates (Yantai Chemical Industry Research Institute). The spots on TLC were visualized by warming 10% H<sub>2</sub>SO<sub>4</sub> (10% H<sub>2</sub>SO<sub>4</sub> in ethanol) sprayed plates by heat gun. Column chromatography was performed on silica gel (Qingdao Marine Chemical Inc., China). NMR spectra were recorded on a Bruker AM-400 spectrometer (400 MHz), and the <sup>1</sup>H NMR chemical shifts were referenced to the solvent or solvent impurity peaks for CDCl<sub>3</sub> at  $\delta$ H 7.24. Proton-coupled <sup>31</sup>P NMR spectra were recorded on a Bruker AM-500 spectrometer (500 MHz), and all chemical shifts are relative to 85% phosphoric acid dissolved in an equal volume of D<sub>2</sub>O as external reference. High resolution mass spectra were recorded on a Bruker micrOTOF II spectrometer using electrospray ionization (ESI). X-Ray Photoelectron Spectroscopy spectra were recorded on a Shimadzu/Kratos AXIS-ULTRA DLD-600W, and all the narrow scan datum were calibrated with C 1s 285 eV. X-Ray Fluorescencespectra were recorded on the EDAX Inc. EAGLE III X-Ray fluorescence scanner

# 2. Materials

Organic solvents were purchased from Adamas and used without further purification. Unless otherwise stated, water was normal running water. Calcium hypophosphite,  $H_3PO_2$  (50% in  $H_2O$ ) and all other commercially available chemicals were purchased from Adamas and used without further purification.

### 3. Optimization of iodination reactions

#### Table S1. Iodination reaction of 2.<sup>[a]</sup>

	1) I <sub>2</sub> (1.3 equ imidaz 2) Ac <sub>2</sub> O (6.0 e DMe DMAP	tiv), PPh <sub>3</sub> (1.5 equiv). cole (2.0 equiv) quiv), Et <sub>3</sub> N (6.0 equiv) <sup>A</sup> (0.1 equiv), DCM	AcO OMe	AcO AcO AcO AcO AcO OMe S1	Ph <sub>3</sub> P <sup>©</sup> I <sup>©</sup> HO HO HO HO HO OMe Intermediate I
Entry	Solvent	Temperature	Time	Yield ( <b>4</b> ) <sup>[b]</sup>	Yield ( <b>S1</b> )
1	THF	70 °C	10 h	87%	6%
2	toluene	70 °C	10 h	86%	9%
3	CHCl <sub>3</sub>	70 °C	10 h	48%	46%
4	MeCN	70 °C	10 h	94%	-
5 <sup>[c]</sup>	MeCN	70 °C	24 h	66%	25%
6	MeCN	50 °C	24 h	95%	-
7	MeCN	R.T.	24 h	45%	53%

[a] All reactions were conducted in 500 mg scale. All yields were isolated yields by coloumn chromatography purification. [b] Isolated yield in two steps. [c] 1.5 equiv of imidazole was used.

#### **Procedures of reaction in entry 4:**

To a solution of glucose **2** (500 mg, 2.56 mmol) in acetonitrile (5.1 mL) at room temperature was added triphenylphosphine (1.014 g, 3.86 mmol) followed by imidazole (349 mg, 5.12 mmol). Iodine (850 mg, 3.35 mmol) was then added slowly in batches (3 or 4 times). The reaction mixture was heated to 70 °C for 10 h. The reactions were monitored by TLC (DCM-methanol 5:1). (An alkoxyphosphonium intermediate **I** ( $R_f$  = 0.70) was directly detected by mass spectrum from the crude reaction mixture. HRMS: calcd. for C<sub>25</sub>H<sub>28</sub>O<sub>6</sub>P<sup>+</sup> [M]<sup>+</sup> 455.1618, found: 455.1634.) The reaction mixture was cooled to room tempertaure, quenched with Et<sub>3</sub>N (0.55 mL, 3.86 mmol), and stirred for another 0.5 h. The resulting solution was concentrated *in vacuo*. To a solution of the crude product in dry DCM (5.1 mL) was added additional of Et<sub>3</sub>N (2.1 mL, 15.44 mmol), 4-DMAP (31 mg, 0.26 mmol) and Ac<sub>2</sub>O (1.5 mL, 15.44 mmol) at 0 °C, the reaction mixture was stirred at room temperature for 2 h. Then the reaction mixture was quenched with H<sub>2</sub>O and extracted with EtOAc. The organic phase was washed with saturated aqueous NaHCO<sub>3</sub>, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and brine, dried with Na<sub>2</sub>SO<sub>4</sub>, concentrated, and purified by silica gel flash column chromatography to give **4** (1.042 g, 94%).

Methyl-2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (4)<sup>[1]</sup>



White solid.  $R_f = 0.40$  (petroleum ether-EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.42 (t, J = 10.0 Hz, 1H, H-3), 4.91 (d, J = 3.6 Hz, 1H, H-1), 4.88-4.78 (m, 2H, H-2 and H-4), 3.74 (td, J = 9.2, 2.4 Hz, 1H, H-5), 3.43 (s, 3H, -OMe), 3.26 (dd, J = 10.8, 2.4 Hz, 1H, H-6a), 3.09 (dd, J = 10.8, 8.4 Hz, 1H, H-6b), 2.03 (s, 3H, -OAc), 2.01

(s, 3H, -OAc), 1.96 (s, 3H, -OAc).

# Methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (S1)<sup>[2]</sup>



White solid.  $R_f = 0.25$  (petroleum ether-EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.43 (t, J = 10.0 Hz, 1H, H-4), 5.03 (t, J = 10.0 Hz, 1H, H-3), 4.91 (d, J = 3.6 Hz, 1H, H-1), 4.86 (dd, J = 10.0, 3.6 Hz, 1H, H-2), 4.22 (dd, J = 12.0, 4.4 Hz, 1H, H-6a), 4.07 (dd, J = 12.4, 2.0 Hz, 1H, H-6b), 3.94 (ddd, J = 10.0, 4.4, 2.0 Hz, 1H, H-5), 3.37

(s, 3H, -OMe), 2.06 (s, 3H, -OAc), 2.04 (s, 3H, -OAc), 1.99 (s, 3H, -OAc), 1.97 (s, 3H, -OAc).

# **Table S2. Iodination reaction of 7.**<sup>[a]</sup>

		1) l <sub>2</sub> (1.3 equiv), PPh <sub>3</sub> (1.5 e Imidazole (2.0 equiv)	equiv), I	OAc 0
	HO OMe 7	Ac <sub>2</sub> O (6.0 equiv), Et <sub>3</sub> N (6.0 d DMAP (0.1 equiv), DCM	equiv) AcO	OMe 10
Entry	Solvent	Temperature	Time	Yield (10) <sup>[b]</sup>
1	toluene	80 °C	2 h	89%
2	toluene	70 °C	5 h	93%
3	MeCN	70 °C	5 h	85%
4	MeCN	50 °C	20 h	95%

[a] All reactions were conducted in 500 mg scale. Isolated yields by coloumn chromatography purification. [b] Isolated yield in two steps.

# Methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-mannopyranoside (10)<sup>[3]</sup>



White solid.  $R_f = 0.40$  (petroleum ether-EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.22 (dd, J = 10.0, 3.2 Hz, 1H, H-3), 5.13 (dd, J = 3.2, 1.6 Hz, 1H, H-2), 5.02 (t, J = 10.0 Hz, 1H, H-4), 4.65 (d, J = 1.2 Hz, 1H, H-1), 3.72 (td, J = 9.2, 2.0 Hz, 1H, H-5), 3.39 (s, 3H, - OMe), 3.24 (dd, J = 10.8, 2.4 Hz, 1H, H-6a), 3.10 (dd, J = 10.8, 9.0

Hz, 1H, H-6b), 2.06 (s, 3H, -OAc), 1.99 (s, 3H, -OAc), 1.90 (s, 3H, -OAc).

#### 4. Optimization of deiodination reactions

### 4.1 Preparation of crude substrates 3 and 9



To a solution of **2** (500 mg, 2.57 mmol) in acetonitrile (5.1 mL) at room temperature was added triphenylphosphine (1.014 g, 3.86 mmol) followed by imidazole (349 mg, 5.12 mmol). Then iodine (850 mg, 3.35 mmol) was added slowly in batches (3 or 4 times), the reaction mixture was heated to 70 °C for 10 h. Then the reaction mixture was cooled to room tempertaure, quenched with Et<sub>3</sub>N (0.55 mL, 3.86 mmol), and stirred for another 0.5 h. The resulting solution was then concentrated to dryness *in vacuo*. The residue was dissovled in 5 mL of DCM and transferred to a seperating funnel, then 20 mL of petroleum ether was added. The organic layer was extracted with water three times and the aqueous layers (total 24 mL, 0.1M) was combined and used for the next step directely. Alternatively, for 5-20 grams synthesis, the residue from the first step could be dissovled in appropriate amount of toluene and then transferred to a seperating funne. The organic layer was extracted with water 5-6 times and the aqueous layers (0.05M) was combined and used for the next step directely.



Following the same procedure as preapration of **3**, except the reaction temperature decreased to 50  $^{\circ}$ C.

#### 4.2 Optimization of the deiodination reaction





Entry	Reductants (equiv)	Time	Yield ( <b>5</b> ) <sup>[b]</sup>	Precipitate
1	H <sub>3</sub> PO <sub>2</sub> /TEA (5.0/5.0) <sup>[c]</sup>	2 h	87%	-
2	$H_3PO_2/TEA(3.0/3.0)^{[d]}$	2 h	85%	-
3	H <sub>3</sub> PO <sub>2</sub> (3.0) <sup>[e]</sup>	2 h	81%	-
4	Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> (1.0)	1.5 h	89%	0.25 g <sup>[f]</sup>
5	NaH <sub>2</sub> PO <sub>2</sub> ·H <sub>2</sub> O (1.4) <sup>[g]</sup>	2 h	26% <sup>[h]</sup>	-
6	NaH <sub>2</sub> PO <sub>2</sub> ·H <sub>2</sub> O (1.4) <sup>[g]</sup>	12 h	82%	-
7	Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> /CaO (0.7/0.55)	1.5 h	87%	0.36 g
8	Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> (0.7) <sup>[i]</sup>	1.5 h	85% <sup>[j]</sup>	_ [k]

[a] Unless otherwise stated, the equivalents of additives were calculated based on the starting material **2** (500 mg); acetylation conditions: Ac<sub>2</sub>O (6.0 equiv.), TEA (6.0 equiv.), DMAP (0.1 equiv.). [b] Isolated yield in three steps after one flash column chromatography purification. [c] 0.3 equiv of VA-044. [d] 0.2 equiv. of VA-044. [e] The acetylation reaction required 15 equiv of Ac<sub>2</sub>O and TEA. [f] After reaction was completed (pH  $\approx$  5.0), TEA was added (pH  $\approx$  7.0) and another 85 mg of precipitates were obtained, the total precipitates were 335 mg. [g] reaction was carried out at 40 °C. [h] Determined by <sup>1</sup>H NMR. [i] 0.55 equiv. of Ca(OH)<sub>2</sub> was added after the reaction was completed. [j] Water taken directly from the Yangtze river at Wuhan. [k] Unfiltered.



Water used in entry 8 (taken from Yangtze river)

#### Procedures for the reaction in Table 1, entry 9

Argon was bubbled through the solution (obtained in **4.1**) of crude **3** for at least 30 min.  $Ca(H_2PO_2)_2$  (306 mg, 1.80 mmol) and VA-044 (83 mg, 0.26 mmol) were added immediately and degassed with argon for another 10 min. The reaction mixture was heated to 70 °C under argon for 1.5 h and monitored by TLC (DCM-methanol 5:1). After the reaction was completed, it was cooled to rt and  $Ca(OH)_2$  (105 mg, 1.42 mmol) was added. The mixture was stirred for another 0.5 h and filtrated. The filter cake was collected and washed with water until the pH close to seven. The filtrate was combined and concentrated *in vacuo* (water bath below 60 °C) and dried to afford crude **6**. To the solution of above crude product **6** in dry DCM (5.1 mL) was added Et<sub>3</sub>N (2.1 mL, 15.44 mmol), 4-DMAP (31 mg, 0.26 mmol) and Ac<sub>2</sub>O (1.5 mL, 15.44 mmol) at 0 °C, the mixture was stirred at room temperature for 2 h, then the reaction mixture was extracted with EtOAc. The organic phase was washed with saturated aqueous NaHCO<sub>3</sub>, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>

and brine, then dried with  $Na_2SO_4$ , concentrated and purified by silica gel flash column chromatography to give 5 (674 mg, 86%).

# Methyl 2,3,4-Tri-O-acetyl-6-deoxy-α-D-glucopyranoside (5)<sup>[4]</sup>



White solid.  $R_f = 0.40$  (petroleum ether-EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.41 (t, J = 9.6 Hz, 1H, H-3), 4.88 – 4.81 (m, 2H, H-1, H-2), 4.77 (t, J = 9.6 Hz, 1H, H-4), 3.86 (dq, J = 12.4, 6.4 Hz, 1H, H-5), 3.37 (s, 3H, -OMe), 2.05 (s, 3H, -OAc), 2.01 (s, 3H, -OAc), 1.98 (s, 3H, -OAc), 1.17 (d, J = 6.4 Hz, 3H, H-6).

# **Deiodination reaction of 9**



The reaction from crude **9** afforded **11** in 87% yield. (84% yield when using water taken from Yangtze River).

# Methyl 2,3,4-Tri-O-acetyl-6-deoxy-α-D-mannopyranoside (11)<sup>[5]</sup>



Colorless syrup.  $R_f = 0.40$  (Petroleum ether-EtOAc 5:1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.25 (dd, J = 10.0, 3.6 Hz, 1H, H-3), 5.20 (dd, J = 3.2, 1.6 Hz, 1H, H-2), 5.03 (t, J = 9.6 Hz, 1H, H-4), 4.60 (s, 1H, H-1), 3.83 (dq, J = 12.4, 6.4 Hz, 1H, H-5), 3.36 (s, 3H, -OCH<sub>3</sub>), 2.12 (s, 3H, -OAc), 2.01 (s, 3H, -OAc), 1.95 (s, 3H, -OAc), 1.20 (d,

J = 6.4 Hz, 3H, H-6).

# 4.3 Recycling of unreacted Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub>



# Recovery of unreacted Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub>:

After the deiodination step was completed, the mixed water solution containing **6** was concentrated and dried *in vacuo*. Then ethanol (25 mL/g) was added with vigorously stirring for 15 min at 45 °C. The mixture was filtrated, the filter cake was washed with ethanol and acetonitrile, dried *in vacuo* to afford crude Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub> as a pale-yellow solid. <sup>31</sup>P NMR (202 MHz, D<sub>2</sub>O)  $\delta$  6.96 (t, *J* = 520 Hz).

# Table S4: Reuse of unreacted Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub>:

+ (	HO HO OMe 3 Crude in water	1) Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> , VA-044 (0.1 equiv), 70 °C, H <sub>2</sub> O, 1.5 h 2) Ac <sub>2</sub> O (6.0 equiv), Et <sub>3</sub> N (6.0 equiv) DMAP (0.1 equiv), DCM,2 h	AcO AcO OMe
•	Entry	Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> (equiv)	Yield ( <b>5</b> ) <sup>[a]</sup>
	1	$0.7^{[b]}$	68% <sup>[d]</sup>
	2	1.2 <sup>[b]</sup>	84%
	3	$0.7^{[c]}$	85%

[a] Isolated yield in two steps with one flash column chromatography purification. [b] recovered Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub>. [c] Commercially available Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub>. [d] Determined by <sup>1</sup>H NMR.

# 5. Acetylation and Acetolysis

#### Failed one-pot acetylation and acetolysis 5.1



### Table S5. Investigation of the components inhibited the acetylation reaction

	Additives HO $HO$ $HO$ $HO$ $HO$ $HO$ $HO$ $HO$ $H$	
Entry	Additives (equiv)	Yield ( <b>S3</b> )
1	H <sub>2</sub> O / NaH <sub>2</sub> PO <sub>4</sub> ·2H <sub>2</sub> O (3.0 /1.0)	96%
2	Na <sub>2</sub> HPO <sub>3</sub> ·5H <sub>2</sub> O (1.0)	89%
3	H <sub>2</sub> O / Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> (5.0 /0.5)	83%
4	H <sub>2</sub> O (5.0)	93%
5	Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> /VA-044 (0.1 /0.1)	91%
6	Ca(H <sub>2</sub> PO <sub>2</sub> ) <sub>2</sub> /VA-044 /KI (0.1 /0.1 /2.6)	trace

These reactions revealed that iodine anion inhibited the one-pot acetylation and acetolysis, thus it must be removed before the one-pot reaction.

#### 5.2 Acetylation and Acetolysis in two steps



After obtaining crude **6**, it was dissovled in DCM and added Et<sub>3</sub>N (2.1 mL, 15.44 mmol), 4-DMAP (31 mg, 0.26 mmol) and Ac<sub>2</sub>O (1.5 mL, 15.44 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h, and then concentrated and extracted with EtOAc. The organic phase was washed with saturated aqueous NaHCO<sub>3</sub>, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and brine; dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated to give crude **5**. Then concentrated H<sub>2</sub>SO<sub>4</sub> (83 uL) was added dropwise into a solution of crude **5** in Ac<sub>2</sub>O-AcOH (2.5 mL/2.5 mL) at 0 °C, the resulting solution was stirred at room temperature for 2 h. The reaction mixture was slowly added to the chilled saturated aqueous NaHCO<sub>3</sub>, extracted with EtOAc for three times.The combined organic phases were washed with brine, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give **1** as a white solid. (642 mg, 75%).

# 1,2,3,4-tetra-O-acetyl-6-deoxy-α/β-D-glucopyranose (1)<sup>[1]</sup>



Anomeric mixture,  $\alpha:\beta = 5:1$ ,  $R_f = 0.35$  (petroleum ether-EtOAc 5:1). Analytical data for  $\alpha$  anomer : <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.21 (d, J = 3.6 Hz, 1H, H-1), 5.37 (t, J = 10.0 Hz, 1H, H-3), 5.01 (dd, J = 10.4, 3.6 Hz, 1H, H-2), 4.80 (t, J = 10.0 Hz, 1H, H-4), 3.96 (dq, J = 12.4, 6.4 Hz, 1H, H-5), 2.12 (s, 3H, -OAc), 2.01 (s, 3H, -

OAc), 1.97 (s, 3H, -OAc), 1.96 (s, 3H, -OAc), 1.15 (d, J = 6.4 Hz, 3H, H-6). Analytical data for  $\beta$  anomer : <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.66 (d, J = 8.0 Hz, 1H, H-1), 5.17 (t, J = 9.6 Hz, 1H, H-3), 5.08 (dd, J = 9.6, 8.4 Hz, 1H, H-2), 4.82 (t, J = 9.6 Hz, 1H, H-4), 3.68 (dq, J = 12.4, 6.0 Hz, 1H, H-5), 2.08 (s, 3H, -OAc), 2.02 (s, 3H, -OAc), 1.99 (s, 3H, -OAc), 1.98 (s, 3H, -OAc), 1.21 (d, J = 6.0 Hz, 3H, H-6).

#### 1,2,3,4-tetra-*O*-acetyl-6-deoxy-α/β-D-mannopyranose (8)



Prepared as described for the preparation of **1**. Anomeric mixture,  $\alpha:\beta = 10:1$ , colorless oil.  $R_f = 0.35$  (petroleum ether-EtOAc 5:1). Analytical data for  $\alpha$  anomer<sup>[5]</sup>: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.98 (d, J = 1.6 Hz, 1H, H-1), 5.27 (dd, J = 10.0, 3.6 Hz, 1H, H-3), 5.22 (dd, J = 3.3, 2.0 Hz, 1H, H-2), 5.09 (t, J = 10.0 Hz, 1H, H-4), 3.90

(dq, J = 12.4, 6.0 Hz, 1H, H-5), 2.14 (s, 3H, -OAc), 2.12 (s, 3H, -OAc), 2.03 (s, 3H, -OAc), 1.97 (s, 3H, -OAc), 1.20 (d, J = 6.4 Hz, 3H, -CH<sub>3</sub>). Analytical data for  $\beta$  anomer <sup>[6]</sup>: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.81 (brs, 1H, H-1), 5.45 (s, 1H, H-2), 5.07 - 5.05 (m, 2H, H-3 and H-4), 3.64 (dq, J = 12.4, 6.4 Hz, 1H, H-5), 2.19 (s, 3H, -OAc), 2.08 (s, 3H, -OAc), 2.04 (s, 3H, -OAc), 1.98 (s, 3H, -OAc), 1.27 (d, J = 6.2 Hz, 1H, H-6).

#### 6. Large-scales syntheses of 6-deoxy rare sugars



#### 6.1 110 gram-scales (400 mmol) preparation of D-quinovose

#### Step 1:

To a solution of 2 (80.0 g, 412 mmol) in acetonitrile (820 mL) at 0 °C was added triphenylphosphine (162.1 g, 618 mmol) followed by imidazole (56.1 g, 824 mmol). Then iodine (130.7 g, 515 mmol) was added slowly in batches (7 or 8 times). The reaction mixture was heated at 70 °C for 10 h. Then the reaction mixture was cooled to room tempertaure, quenched with Et<sub>3</sub>N (85 mL, 616 mmol) and stirred for another 0.5 h. The resulting solution was concentrated in vacuo, the evaporeted MeCN was collected. 160 mL of water was added to above residues and stirred vigorously for 15 min at 45 °C. Then 4  $\times$  160 mL of water was added slowly and stirring for another 1 h. The mixture was cooled to room tempertaure under stirring then filtered through Buchner funnel. The precipitate was collected and 160 mL of water was added under stirring. After stiring for another 15 min, it was filtrared and washed again with water  $(2 \times 80 \text{ mL})$  untill all of the sugar was removed. The aqueous layers containinf crude 3 (total 1.12 L, 0.37 M) were combined and used into the next step directely. The filter cake was collected and recrystallized with EtOH and petroleum ether to afford TPPO (132.7 g, 78% of total organophosphorus) as a white solid, <sup>31</sup>P NMR (202 MHz, CDCl<sub>3</sub>)  $\delta$  29.06 (s), The remaining mother liquor was concentrated to afford crude organophosphorus (34.1 g, 20% of total organophosphorus). Step 2:

Argon was bubbled through above aqueous solution of crude **3** for at least 30 min. Then Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub> (49.0 g, 288 mmol) and VA-044 (13.3 g, 41mmol) were added immediately and degassed with argon for 10 min. The reaction mixture was heated to 70 °C for 1 h under argon. After the reaction was completed, it was cooled to rt and Ca(OH)<sub>2</sub> (16.7 g, 226 mmol) was added, then vigorously stirred for another 1 h. The mixture was filtrared, washed with water. The combined aqueous layer was concentrated *in vacuo* to affored crude **6**. The precipitate was washed with water until the pH was near seven, then washed with ethanol. The precipitate was dried to afford calcium phosphite monohydrate as a white powder (54.9 g, 97%).

#### Step 3:

To a solution of above crude product **6** in recycled MeCN obtained from iodination reaction step was added Et<sub>3</sub>N (350 mL, 2500 mmol), 4-DMAP (2.0 g, 16.3 mmol) and Ac<sub>2</sub>O (235 mL, 2500 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h, then 50 mL of water was added slowly at 0 °C. The mixture was concentrated *in vacuo* (no more than 60 °C) then extracted with EtOAc. The organic phase was washed with saturated aqueous NaHCO<sub>3</sub>, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and brine, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated to afford crude **5**.

### Step 4:

Concentrated H<sub>2</sub>SO<sub>4</sub> (10 mL) was added dropwise into a solution of above crude 5 in Ac<sub>2</sub>O-AcOH (300 mL/300 mL) at 0 °C, the resulting solution was stirred at room temperature. After completion of the reaction (confirmed by TLC), 130 mL of methanol was added slowly at 0 °C and kept the temperature below room temperature. Then water (50 mL) and AcONa (15.6 g, 190 mmol) were added and the mixture was stirred for 15 min. The resulting solution was concentrated in vacuo, the residue was neutralized with chilled saturated aqueous NaHCO3, extracted with EtOAc for three times. The combined organic phases were washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and brine, dried with Na<sub>2</sub>SO<sub>4</sub> and concentrated to 400 mL in vacuo. Then 100 g of activated carbon were added to decolorize at 50 °C. the supportion was filtered through Celite and washed with ethyl acetate. The organic phase was concentrated to 80 mL (slurry) at 40 °C. The residue was slowly cooled to about 10 °C, and kept for about half an hour. Then appropriate amount of petroleum ether (about 200-300 mL) was added dropwise over 2 h and kept for about 4 h at 0 °C. The precipitate was filtered and washed with petroleum ether, the mother liquor was concentrated and recrystalizaed again with ethyl acetate / petroleum ether. Collected all the precipitates to afford 1 as a white solid (112.0 g, 82% over four steps).

#### 6.2 30 gram-scales (100 mmol) preparation for D-rhamnose



#### Step 1:

To a solution of substrate 7 (25.0 g, 129 mmol) in acetonitrile (260 mL) at 0 °C was added triphenylphosphine (50.7 g, 193 mmol) followed by imidazole (17.5 g, 257 mmol), and then iodine (40.8 g, 161 mmol) was added slowly in batches (5 or 6 times).

The reaction mixture was heated at 50 °C for 20 h. Then the reaction mixture was cooled to room tempertaure, quenched with Et<sub>3</sub>N (26 mL, 193 mmol), and stirred for another 0.5 h. The resulting solution was concentrated *in vacuo*, the evaporeted MeCN was collected. 50 mL of water was added to the above residues and stirred vigorously for 15 min at 45 °C. Then  $4\times50$  mL of water was added slowly and stirring for another 1 h. The mixture was cooled to room tempertaure under stirring. The mixture was filtered through Buchner funnel. The precipitate was collected and 50 mL of water was added with stirring. After being stirred for another 15 min, it was filtrared andwashed again with water ( $2\times25$  mL) untill all of the sugar was removed. The aqueous layers containing **9** (total 350 mL, 0.37 M) were combined and used into the next step directely. The filter cake was collected and recrystallized with EtOH and petroleum ether to afford TPPO (37.94 g, 72% of total organophosphorus) as a white solid. The remaining mother liquor was concentrated to afford crude organophosphorus (12.38 g, 23% of total organophosphorus).

#### Step 2:

Argon was bubbled through above aqueous solution of curde **9** for at least 30 min. Then Ca(H<sub>2</sub>PO<sub>2</sub>)<sub>2</sub> (15.3 g, 90.1 mmol) and VA-044 (4.0 g, 13 mmol) were added immediately, and degassed with argon for 10 min. The reaction mixture was heated to 70 °C for 1 h under argon. After the reaction was completed, it was cooled to rt and Ca(OH)<sub>2</sub> (5.2 g, 70.8 mmol) was added, then vigorously stirred for another 1 h. The mixture was filtrared, washed with water. The combined aqueous layer was concentrated *in vacuo* to afforede crude **12**. The precipitate was washed with water until the pH was near seven, then washed with ethanol. The precipitate was dried to afford calcium phosphite monohydrate as white powder (17.0 g, 96%).

# Step 3:

To a solution of above crude product 12 in recycled MeCN obtained from iodination reaction step was added Et<sub>3</sub>N (110 mL, 780 mmol), 4-DMAP (0.6 g, 5.0 mmol) and Ac<sub>2</sub>O (74 mL, 781 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h, then 15 mL of water was added slowly at 0 °C, the reaction mixture was concentrated *in vacuo* (no more than 60 °C) then extracted with EtOAc. The organic phase was washed with saturated aqueous NaHCO<sub>3</sub>, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), concentrated to afford crude 11.

#### Step 4:

Concentrated H<sub>2</sub>SO<sub>4</sub> (3.2 mL) was added dropwise into a solution of above crude **11** in Ac<sub>2</sub>O-AcOH (95 mL/95 mL) at 0 °C, the resulting solution was stirred at room temperature. After completion of the reaction (confirmed by TLC), 40 mL of methanol was added slowly at 0 °C and kept the temperature below room temperature. Then water (15 mL) and AcONa (4.9 g, 59 mmol) were added and the mixture was stirred for 15 min. The result solution was concentrated *in vacuo*, the residue was neutralized with chilled saturated aqueous NaHCO<sub>3</sub>, extracted with EtOAc for three times. The combined organic phases were washed with Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated *in vacuo*. The residue was passed through a short pat of silica gel and eluted with petroleum ether-EtOAc 5:1 to afford **8** (35.2 g, 83% over four steps) as a colorless liquid.

#### Products and co-products in large-scales preparation



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# <sup>31</sup>P NMR Spectra





Figure S2. <sup>31</sup>P NMR (202 MHz, D<sub>2</sub>O) spectrum of Deiodination for 20 min (Figure 2b)



Figure S4. <sup>31</sup>P NMR (202 MHz, D<sub>2</sub>O) spectrum of Deiodination after Ca(OH)<sub>2</sub> added (Figure 2d)





20

15

10

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Figure S6. <sup>31</sup>P NMR (202 MHz, D<sub>6</sub>-DMSO) spectrum of Authentic CaHPO<sub>3</sub> (Figure 2f)



Figure S8. <sup>31</sup>P NMR (202 MHz, CD<sub>3</sub>Cl) spectrum of Recovered organophosphorus

![](_page_18_Figure_0.jpeg)

Figure S9. <sup>31</sup>P NMR (202 MHz, CD<sub>3</sub>Cl) spectrum of Recovered TPPO

**XRF Spectra** 

![](_page_18_Figure_3.jpeg)

Figure S10. XRF analysis spectrum of Deiodination precipitate (Figure 3a)

# **XPS Spectra**

![](_page_19_Figure_1.jpeg)

Figure S11. XPS survey spectrum of Authentic CaHPO<sub>3</sub>

![](_page_19_Figure_3.jpeg)

Figure S12. XPS survey spectrum of Deiodination precipitate (Figure 3b)

![](_page_20_Figure_0.jpeg)

Figure S13. P 2p spectrum of Authentic CaHPO<sub>3</sub>

![](_page_20_Figure_2.jpeg)

(Figure 3c)

![](_page_21_Figure_0.jpeg)

Figure S15. Powder XRD spectrum (reported data came from *Phosphorus, Sulfur Silicon Relat. Elem.*, 2001, 176, 83-94)

![](_page_22_Figure_0.jpeg)

Figure S17. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of 5

![](_page_23_Figure_0.jpeg)

![](_page_23_Figure_1.jpeg)

Figure S19. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of 8 ( $\beta$  anomer)

![](_page_24_Figure_0.jpeg)

Figure S20. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) spectrum of 11