新型天麻素中间体类似物的高效合成

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摘要　在葡萄糖酸的催化作用下，以 4-甲酰基苯基-2,3,4,6-O-四乙酰基-β-D-葡萄糖苷和 1,3-二噁烷-4,6-二酮为原料，发生 Knoevenagel 缩合反应合成了 10 种新型天麻素中间体类似物. 该反应具有收率高(78%～92%)、反应温和、操作简单及环境友好等优点. 此外，葡萄糖酸还可重复使用.

关键词　葡萄糖酸; Knoevenagel 反应; 4-甲酰基苯基-2,3,4,6-O-四乙酰基-β-D-葡萄糖苷; 天麻素中间体类似物

Highly Efficent Synthesis of Novel Gastrodine Intermediate Analogues

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Abstract　Ten gastrodine intermediate analogues were synthesized by the Knoevenagel reaction of 4-formylphenyl(2,3,4,6-tetra-O-acetyl)-β-D-glucoside and 1,3-dioxane-4,6-dione with gluconic acid as a catalyst. In this reaction there are many advantages with good to excellent yields (78%～92%), mild conditions, simple operations and environmental friendliness. Additionally, gluconic acid could be recycled and reused many times without lossing its efficiency.

Keywords　gluconic acid; Knoevenagel reaction; 4-formylphenyl(2,3,4,6-tetra-O-acetyl)-β-D-glucoside; gastrodine intermediate analogues

1　Introduction

Natural gastrodine (4-(hydroxymethyl)phenyl-β-D-glucopyranoside), one major active ingredient of Chinese herbal medicine, has been clinical as antalgic and hypnotic for a long time in China and no obvious side effects have been reported.[1,2] 4-Formylphenyl-(2,3,4,6-tetra-O-acetyl)-D-lucopyranoside as gastrodine intermediate, has exhibited a variety of biological effects, such as gantioxidative activity,[3] antiobesity,[4] antiinflammation,[5] anticonvulsant activity,[6] memory improvement[7] and acetylcholinesterase inhibitors.[8] However, such gastrodine intermediates exist many limitations, for example, long onset time, low bioavailability and poor lipophilicity, which prompted us to search for new derivatives of gastrodine intermediate through structure modifications.[9~11]

The Knoevenagel reaction of aromatic aldehydes and 1,3-dioxane-4,6-dione is a simple and effective strategy for C—C bond formation. 5-Arylmethylene-1,3-dioxane-4,6-dione and its bis-adducts have been attracted great interest because versatile substrates were used in various types of reactions.[12] They often act as acceptors in the 1,4-addition of organometallic reagents[13] and as dienophiles in Dielslder and tandem Knoevenagel-Michael additions.[14,15] They were commonly synthesized employing a variety of catalysts such as piperidine,[16] Et$_3$N,[17] anhydrous ZnCl$_2$,[18] and [bmim]BF$_4$.[19] However, many of these methodologies have not been entirely satisfactory, involving harsh reaction conditions, low yields, high catalyst loading, environmentally unfavorable solvents or tedious work-up to obtain the products. Hence, the development of a simple, green and efficient procedure is highly desirable.
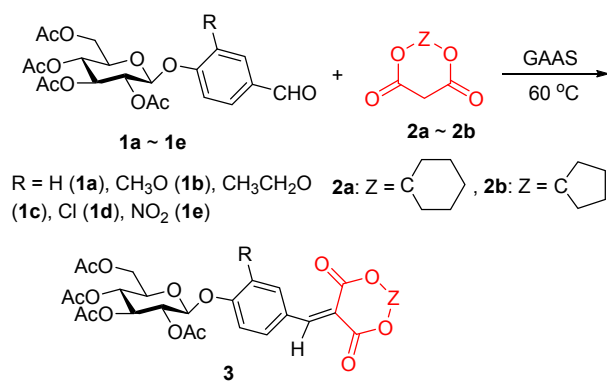
The research of a clean, safe and efficient synthetic methodology is one of the major focus areas of green chemistry. Organic reactions such as Friedel-Crafts alkylations, Michael addition, ring-opening reactions,[20] multicomponent reactions (MCR)[21,22] and tandem Knoevena-

gel-Michael addition[23] have been recently examined in percence of gluconic acid aqueous solution. In this paper, the synthesis of novel gastrodine intermediate derivatives via Knovenagel condensation of 4-formylphenyl-(2,3,4,6-tetra-*O*-acetyl)-*β-D*-glucopyranoside and 1,3-dioxane-4,6-dione in ethanol using gluconic acid aqueous solution (GAAS) as an effective biocatalyst was described (Scheme 1).

R = H (**1a**), CH₃O (**1b**), CH₃CH₂O (**1c**), Cl (**1d**), NO₂ (**1e**)

2a: Z = C（cyclohexylidene）, **2b**: Z = C（cyclopentylidene）

Scheme 1　Synthesis of **3**

2　Results and discussion

As depicted in Table 1, the investigations were initiated with 4-formylphenyl-(2,3,4,6-tetra-*O*-acetyl)-*β-D*-glucopyranoside (**1a**) and 2,2-pentylidene-1,3-dioxane-4,6-dione (**2a**) as the model system to find the optimal conditions. The neat experiment without any catalyst gave the desired product **3a** only in 18% yield (Table 1, Entry 1). Our next attempts were focused on the evaluation of the efficiency of various solvents under catalyst-free conditions. Only a trace amount of product was detected in hexane or water (Table 1, Entries 2, 3). A significant improvement was obtained in ethyl acetate, CH₃OH and acetonitrile, and the yield reached 76% with EtOH as the solvent (Table 1, Entries 4~7). Next, different catalysts were examined in the reaction, such as CH₃COOH, tartaric acid aqueous solution (TAAS), piperidine and GAAS, and the results showed that GAAS was superior (Table 1, Entries 8~11). When the amount of GAAS was decreased to 1 mL, the product yield was only 83%. While, with larger amount of GAAS was added, no further improvement of the product yields was observed (Table 1, Entries 12, 13). The optimum reaction time and reaction temperature were also investigated, respectively (Table 1, Entries 14, 15). Among the various reaction conditions, the condition in Table 1 Entry 11 was the most promising conditions.

With the optimized conditions established, we extended the process to different 1,3-dioxane-4,6-dione compounds and various 4-formylphenyl-(2,3,4,6-tetra-*O*-acetyl)-*β-D*-glucopyranoside derivatives. The results were summarized in Table 2. It was found that a series of aromatic aldehydes containing sugar moiety with electron donating or electron withdrawing substituent groups **1a**~**2e** were smoothly transformed to the corresponding target compounds **3a**~**3j** in good to excellent yields.

In order to investigate the recyclability and reusability of GAAS, the reaction mixture was filtered after completion of the reaction. The filtrate consisting GAAS and EtOH was recovered and then subjected to the next run in the model reaction. Interestingly, GAAS without lossing any appreciable catalytic activity in the fifth reused reactions, providing the corresponding product in almost unchanged yield (Table 3).

A plausible mechanism for the Knoevenagel reaction synthesis of 5-(4-(2,3,4,6-tetra-*O*-acetyl-*β-D*-glucopyranosyl))phenylmethylene-2,2-pentylidene-1,3-dioxane-4,6-dione (**3a**) is depicted in Scheme 2. GAAS as a biocatalyst

Table 1　Optimization of reaction conditions[a]

Entry	Solvent (mL)	Catalyst (mol%)	Time/h	Temperature/℃	Yield[b]/%
1	—	—	10	60	18
2	Hexane (10)	—	10	60	Trace
3	H₂O (10)	—	10	60	Trace
4	EtOAc (10)	—	10	60	34
5	CH₃CN (10)	—	8	60	63
6	CH₃OH (10)	—	8	60	71
7	CH₃CH₂OH (10)	—	8	60	76
8	CH₃CH₂OH (10)	AcOH (aq. 50%) (2)	6	60	70
9[c]	CH₃CH₂OH (10)	TAAS (aq. 10%) (2)	6	60	78
10	CH₃CH₂OH (10)	Piperidine (2)	6	60	81
11	**CH₃CH₂OH (10)**	**GAAS (aq. 50%) (2)**	**6**	**60**	**92**
12	CH₃CH₂OH (10)	GAAS (aq. 50%) (1)	8	60	83
13	CH₃CH₂OH (10)	GAAS (aq. 50%) (2)	6	60	92
14	CH₃CH₂OH (10)	GAAS (aq. 50%) (2)	6	50	81
15	CH₃CH₂OH (10)	GAAS (aq. 50%) (2)	6	70	86
16	CH₃CH₂OH (10)	GAAS (aq. 50%) (2)	5	60	88
17	CH₃CH₂OH (10)	GAAS (aq. 50%) (2)	8	60	90

[a] Reaction conditions: 4-formylphenyl-(2,3,4,6-tetra-*O*-acetyl)-*β-D*-glucopyranoside (1 mmol) and 2,2-pentylidene-1,3-dioxane-4,6-dione (1.2 mmol) were mixed in solvent (10 mL). [b] Isolated yields. [c] TAAS was tartaric acid aqueous solution (aq. 10%).
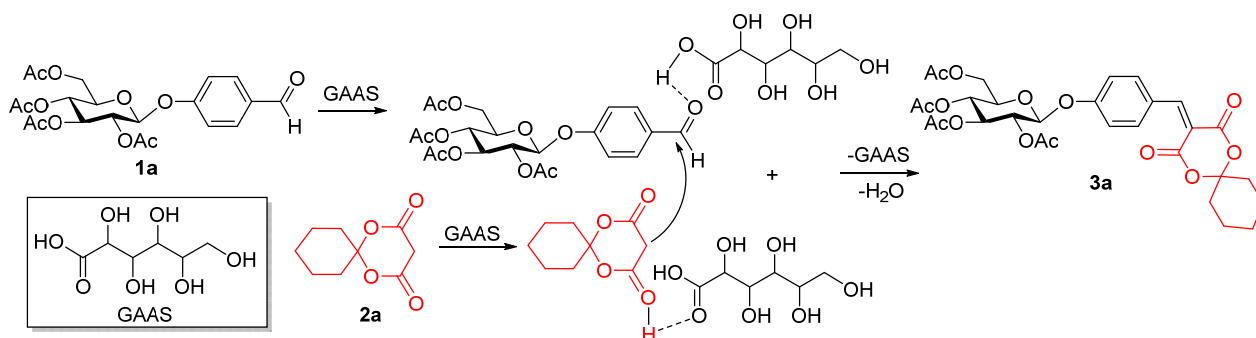
Scheme 2 Proposed mechanism for the imformation of **3a**

Table 2 Synthesis of compounds **3a**～**3j**[a]

Entry	R	Z	Time/h	Product	Yield[b]/%
1	H	C⬡ (cyclohexane)	6	**3a**	92
2	2-CH$_3$O	C⬡	8	**3b**	83
3	2-CH$_3$CH$_2$O	C⬡	8	**3c**	81
4	2-Cl	C⬡	6	**3d**	80
5	2-NO$_2$	C⬡	4	**3e**	78
6	H	C⬠ (cyclopentane)	6	**3f**	90
7	2-CH$_3$O	C⬠	4	**3g**	85
8	2-CH$_3$CH$_2$O	C⬠	5	**3h**	83
9	2-Cl	C⬠	7	**3i**	81
10	2-NO$_2$	C⬠	4	**3j**	80

[a] Reaction conditions: 4-formylphenyl-(2,3,4,6-tetra-*O*-acetyl)-*β*-*D*-glucopyranoside derivtives (1 mmol) and 1,3-dioxane-4,6-dione (1.2 mmol) were mixed in GAAS (2 mL) and EtOH (10 mL) at 60 ℃. [b] Isolated yields.

Table 3 Recycling experiments

Time	1st run	2nd run	3rd run	4th run	5th run
Yield/%	92	92	90	89	86

promoted the enolization of **2a** by forming hydrogen bonds with CO$_2$H and **2a**, thus it increases the nucleophilic character of the methylene carbon of **2a**. Meanwhile, it also increases the electrophilic character of the carbonyl of **1a** by forming hydrogen bonds with the carbonyl oxygen of **1a**. After the condensation reaction, the product **3a** is obtained.

3 Conclusions

In summary, GAAS was proved to be an effective bio-catalyst for the synthesis of novel gastrodine intermediate analogues under mild conditions. Different 1,3-dioxane-4,6-dione compounds and various aromatic aldehydes containing sugar moietes could be converted to the corresponding products with good to excellent yields (78%～92%). The operation and work-up procedures were very simple and no column chrommatography purification was needed. In addition, GAAS could be recycled and reused many times without lossing its effciency.

4 Experimental section

4.2 Chemical and instrument

All of the reagents purchased were of analytical reagent grade and used without further purification. Melting points were detected with a XT-4 digital micro melting point apparatus (Tianjin Tianpu Instrument Factory) without correction; ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV-400 instrument with CDCl$_3$ as solvent.

4.2 General procedure of the preparation of 5-(4-(2,3,4,6-tetra-*O*-acetyl-*β*-*D*-glucopyranosyl))phenyl-methylene-1,3-dioxane-4,6-dione derivatives

To a 50 mL tube equiped with a stirring bar were added 4-formylphenyl-(2,3,4,6-tetra-*O*-acetyl)-*β*-*D*-glucopyrano-side[8,24] (1 mmol), 1,3-dioxane-4,6-dione (1.2 mmol), GAAS (aqu. 50%) (2.0 mL) and EtOH (10 mL). The vessel was then sealed with a screw cap under 60 ℃ for the desired time. Upon completion of the reaction, as confirmed by thin-layer chromatography [*V*(petroleum ether)：*V*(EtOAc)＝4：1], the reaction mixture was cooled and filtered. The filtrate consisting GAAS and EtOH was recovered and then subjected to the next run in the model reaction. The crude solid residue was washed with water and purified by recrytallization from absolute EtOH to give the pure products.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-*D*-glucopyranosyl))phen-yl-methylene-2,2-pentylidene-1,3-dioxane-4,6-dione (**3a**): Light yellow solid, m.p. 157～159 ℃; ^{1}H NMR (400 MHz, CDCl$_3$) *δ*: 1.49～1.53 (m, 2H), 1.71～1.77 (m, 4H), 2.00～2.04 (m, 4H), 2.05 (s, 3H), 2.06 (s, 6H), 2.08 (s,

3H), 3.92 (ddd, J＝7.6, 5.2, 2.4 Hz, 1H, H⁵), 4.18 (dd, J＝12.4, 2.4 Hz, 1H, H⁶ᵃ), 4.30 (dd, J＝12.4, 5.6 Hz, 1H, H⁶ᵇ), 5.18～5.23 (m, 2H), 5.31～5.33 (m, 2H), 7.05 (d, J＝8.8 Hz, 2H), 8.15 (d, J＝8.8 Hz, 2H), 8.34 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 20.58, 20.67, 22.19, 22.21, 24.15, 36.48, 36.52, 61.85, 68.11, 70.97, 72.37, 72.55, 97.95, 105.21, 113.38, 116.49, 116.79, 126.86, 131.80, 136.69, 156.66, 160.09, 160.71, 163.56, 169.21, 169.36, 170.16, 170.48. IR (KBr) ν_{max}: 2968, 2949, 2941, 1752, 1724, 1611, 1592, 1508, 1439, 1229, 1176, 1080 cm⁻¹; HRMS calcd for C₃₀H₃₄NaO₁₄ [M＋Na]⁺ 641.1846; found 641.1823.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-meoxyl)phenylmethylene-2,2-pentylidene-1,3-dioxane-4,6-dione (**3b**): Light yellow solid, m.p. 141～143 ℃; ¹H NMR (400 MHz, CDCl₃) δ: 1.49～1.53 (m, 2H), 1.71～1.77 (m, 4H), 2.00～2.03 (m, 4H), 2.05 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 2.08 (s, 3H), 3.86 (ddd, J＝7.6, 5.2, 2.4 Hz, 1H, H⁵), 3.89 (s, 3H), 4.18 (dd, J＝12.4, 2.4 Hz, 1H, H⁶ᵃ), 4.28 (dd, J＝12.4, 5.2 Hz, 1H, H⁶ᵇ), 5.13～5.20 (m, 2H), 5.31～5.33 (m, 2H), 7.13 (d, J＝8.4 Hz, 1H), 7.55 (dd, J＝8.4, 2.0 Hz, 1H), 8.18 (d, J＝2.0 Hz, 1H), 8.32 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 20.61, 20.69, 22.17, 22.22, 24.14, 36.44, 36.50, 56.14, 61.86, 68.21, 70.97, 72.32, 72.38, 99.48, 105.24, 113.29, 117.04, 117.45, 127.85, 130.29, 149.96, 150.78, 157.11, 160.25, 163.69, 169.27, 169.41, 170.24, 170.56; IR (KBr) ν_{max}: 2970, 2947, 2944, 1751, 1726, 1595, 1567, 1510, 1434, 1370, 1296, 1239, 1222, 1175, 1083, 1062, 1035 cm⁻¹; HRMS calcd for C₃₁H₃₆NaO₁₅ [M＋Na]⁺ 671.1952; found 671.1940.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-ethoxyl)phenylmethylene-2,2-pentylidene-1,3-dioxane-4,6-dione (**3c**): Light yellow solid, m.p. 153～156 ℃; ¹H NMR (400 MHz, CDCl₃) δ: 1.44 (t, J＝7.2 Hz, 3H), 1.49～1.53 (m, 2H), 1.71～1.77 (m, 4H), 2.00～2.03 (m, 4H), 2.04 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 3.87 (ddd, J＝7.6, 5.2, 2.4 Hz, 1H, H⁵), 4.11 (q, J＝7.2 Hz, 2H), 4.19 (dd, J＝12.4, 2.0 Hz, 1H, H⁶ᵃ), 4.28 (dd, J＝12.4, 5.2 Hz, 1H, H⁶ᵇ), 5.15～5.20 (m, 2H), 5.28～5.38 (m, 2H), 7.12 (d, J＝8.4 Hz, 1H), 7.53 (dd, J＝8.4, 2.0 Hz, 1H), 8.16 (d, J＝2.0 Hz, 1H), 8.31 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 14.64, 20.58, 20.61, 20.64, 20.67, 22.17, 22.22, 24.15, 36.44, 36.50, 61.88, 64.76, 68.27, 70.95, 72.28, 72.44, 99.31, 105.19, 113.14, 117.37, 118.26, 127.74, 130.29, 149.19, 151.01, 157.20, 160.26, 163.69, 169.08, 169.37, 170.20, 170.50; IR (KBr) ν_{max}: 2971, 2947, 2944, 1750, 1724, 1566, 1510, 1429, 1370, 1284, 1253, 1237, 1160, 1067, 1053, 1035 cm⁻¹; HRMS calcd for C₃₂H₃₈NaO₁₅ [M＋Na]⁺ 685.2108; found 685.2119.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-chloro)phenylmethylene-2,2-pentylidene-1,3-dioxane-4,6-dione (**3d**): light yellow solid, m.p. 126～128 ℃; ¹H NMR (400 MHz, CDCl₃) δ: 1.49～1.54 (m, 2H), 1.72～1.77 (m, 4H), 2.00～2.04 (m, 4H), 2.05 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 2.10 (s, 3H), 3.93 (ddd, J＝7.6, 5.2, 2.4 Hz, 1H, H⁵), 4.22 (dd, J＝12.4, 2.0 Hz, 1H, H⁶ᵃ), 4.30 (dd, J＝12.4, 5.2 Hz, 1H, H⁶ᵇ), 5.14～5.23 (m, 2H), 5.30～5.42 (m, 2H),

7.20 (d, J＝2.4 Hz, 1H), 8.01 (d, J＝2.4 Hz, 1H), 8.23 (s, 1H), 8.26 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 20.58, 20.59, 20.62, 20.68, 22.18, 24.10, 36.56, 36.59, 61.79, 68.08, 70.56, 72.26, 72.52, 99.26, 105.49, 114.93, 116.57, 124.51, 127.79, 134.39, 135.85, 155.07, 156.24, 159.76, 163.09, 169.10, 169.33, 170.16, 170.46; IR (KBr) ν_{max}: 2966, 2948, 2943, 1753, 1727, 1617, 1585, 1497, 1420, 1369, 1236, 1200, 1186, 1066, 1037 cm⁻¹; HRMS calcd for C₃₀H₃₃ClNaO₁₄ [M＋Na]⁺ 675.1457; found 675.1441.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-nitro)phenylmethylene-2,2-pentylidene-1,3-dioxane-4,6-dione (**3e**): Light yellow solid, m.p. 186～188 ℃; ¹H NMR (400 MHz, CDCl₃) δ: 1.49～1.55 (m, 2H), 1.72～1.78 (m, 4H), 2.00～2.04 (m, 4H), 2.05 (s, 3H), 2.07 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 3.96 (ddd, J＝7.6, 5.2, 2.8 Hz, 1H, H⁵), 4.23 (dd, J＝12.4, 2.4 Hz, 1H, H⁶ᵃ), 4.29 (dd, J＝12.4, 5.2 Hz, 1H, H⁶ᵇ), 5.18～5.29 (m, 2H), 5.32～5.37 (m, 2H), 7.39 (d, J＝8.8 Hz, 1H), 8.27 (d, J＝8.8 Hz, 1H), 8.31 (s, 1H), 8.61 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 20.50, 20.58, 20.68, 22.17, 24.03, 36.66, 36.70, 61.72, 67.91, 70.30, 72.09, 72.68, 99.41, 105.84, 116.54, 118.25, 127.06, 130.43, 138.85, 140.67, 152.31, 153.58, 159.49, 162.54, 169.12, 169.27, 170.14, 170.41; IR (KBr) ν_{max}: 2967, 2948, 2940, 1754, 1732, 1618, 1578, 1537, 1427, 1369, 1294, 1244, 1220, 1211, 1190, 1087, 1070, 1039 cm⁻¹; HRMS calcd for C₃₀H₃₃NNaO₁₆ [M＋Na]⁺ 686.1697; found 686.1672.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl))phenyl-methylene-2,2-butylidene-1,3-dioxane-4,6-dione (**3f**): Light yellow solid, m.p. 208～210 ℃; ¹H NMR (400 MHz, CDCl₃) δ: 1.87～1.92 (m, 4H), 2.05 (s, 3H), 2.06 (s, 6H), 2.08 (s, 3H), 2.19～2.23 (m, 4H), 3.93 (ddd, J＝7.6, 5.2, 2.4 Hz, 1H, H⁵), 4.18 (dd, J＝12.4, 2.4 Hz, 1H, H⁶ᵃ), 4.30 (dd, J＝12.4, 5.6 Hz, 1H, H⁶ᵇ), 5.16～5.24 (m, 2H), 5.31～5.33 (m, 2H), 7.06 (d, J＝8.8 Hz, 2H), 8.14 (d, J＝8.8 Hz, 2H), 8.32 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 20.59, 20.69, 23.25, 23.29, 38.47, 38.51, 61.83, 68.08, 70.95, 72.36, 72.54, 97.90, 113.59, 113.64, 116.53, 126.74, 131.82, 136.67, 136.68, 156.82, 160.80, 160.87, 164.21, 169.22, 169.37, 170.17, 170.50; IR (KBr) ν_{max}: 2966, 2955, 2944, 1754, 1727, 1613, 1595, 1511, 1437, 1223, 1183, 1082 cm⁻¹; HRMScalcd for C₂₉H₃₂NaO₁₄ [M＋Na]⁺ 627.1690; found 627.1674.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-meoxyl)phenylmethylene-2,2-butylidene-1,3-dioxane-4,6-dione (**3g**): light yellow solid, m.p. 156～158 ℃; ¹H NMR (400 MHz, CDCl₃) δ: 1.87～1.92 (m, 4H), 2.05 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 2.08 (s, 3H), 2.18～2.25 (m, 4H), 3.86 (ddd, J＝7.6, 5.2, 2.4 Hz, 1H, H⁵), 3.89 (s, 3H), 4.19 (dd, J＝12.4, 2.4 Hz, 1H, H⁶ᵃ), 4.28 (dd, J＝12.4, 5.2 Hz, 1H, H⁶ᵇ), 5.13～5.20 (m, 2H), 5.29～5.33 (m, 2H), 7.14 (d, J＝8.4 Hz, 1H), 7.54 (dd, J＝8.4, 2.0 Hz, 1H), 8.14 (d, J＝2.0 Hz, 1H), 8.30 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 20.60, 20.69, 23.23, 23.32, 38.44, 38.52, 56.12, 56.16, 61.88, 68.20, 70.96, 72.37, 99.65, 113.55, 113.65, 116.93, 117.46, 127.75, 130.28, 150.01, 150.90, 151.10, 157.19, 160.98, 164.31, 169.23, 169.38, 170.21, 170.51; IR (KBr)

v_{max}: 2970, 2947, 2941, 1751, 1723, 1605, 1585, 1506, 1429, 1374, 1246, 1225, 1163, 1069 cm^{-1}; HRMS calcd for C$_{30}$H$_{34}$NaO$_{15}$ [M＋Na]$^{+}$ 657.1795; found 657.1769.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-ethoxyl)Phenylmethylene-2,2-butylidene-1,3-dioxane-4,6-dione (**3h**): light yellow solid, m.p. 141～143 ℃; ^{1}H NMR (400 MHz, CDCl$_{3}$) *δ*: 1.45 (t, *J*＝6.8 Hz, 3H), 1.87～1.90 (m, 4H), 2.05 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 2.08 (s, 3H), 2.19～2.24 (m, 4H), 3.88 (ddd, *J*＝7.6, 5.2, 2.4 Hz, 1H, H^{5}), 4.11 (q, *J*＝6.8 Hz, 2H), 4.26～4.30 (m, 2H), 5.15～5.21 (m, 2H), 5.28～5.38 (m, 2H), 7.13 (d, *J*＝8.4 Hz, 1H), 7.53 (dd, *J*＝8.4, 2.0 Hz, 1H), 8.12 (s, 1H), 8.29 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_{3}$) *δ*: 14.64, 20.60, 20.62, 20.65, 20.69, 23.23, 23.33, 38.45, 38.53, 61.90, 64.79, 68.25, 70.94, 72.29, 72.42, 99.29, 113.39, 113.63, 117.37, 118.14, 127.62, 130.30, 149.23, 151.12, 157.32, 161.01, 163.34, 169.08, 169.37, 170.20, 170.51; IR (KBr) v_{max}: 2969, 2947, 2942, 1752, 1724, 1607, 1586, 1507, 1438, 1371, 1245, 1224, 1165, 1080 cm^{-1}; HRMS calcd for C$_{31}$H$_{36}$NaO$_{15}$ [M＋Na]$^{+}$ 671.1952; found 671.1969.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-chloro)phenylmethylene-2,2-butylidene-1,3-dioxane-4,6-dione (**3i**): White solid, m.p. 188～190 ℃; ^{1}H NMR (400 MHz, CDCl$_{3}$) *δ*: 1.88～1.91 (m, 4H), 2.05 (s, 3H), 2.07 (s, 3H), 2.09 (s, 3H), 2.10 (s, 3H), 2.18～2.24 (m, 4H), 3.93 (ddd, *J*＝7.6, 5.2, 2.4 Hz, 1H, H^{5}), 4.20～4.32 (m, 2H), 5.14～5.23 (m, 2H), 5.30～5.42 (m, 2H), 7.20 (d, *J*＝2.4 Hz, 1H), 8.00 (d, *J*＝4.4 Hz, 1H), 8.21 (s, 1H), 8.24 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_{3}$) *δ*: 20.60, 20.62, 20.69, 23.26, 23.29, 38.54, 38.58, 61.79, 68.07, 70.54, 72.25, 72.53, 99.24, 113.87, 115.20, 116.61, 124.58, 127.67, 134.38, 135.81, 155.19, 156.34, 160.51, 163.73, 169.10, 169.33, 170.16, 170.48; IR (KBr) v_{max}: 2966, 2948, 2944, 1757, 1730, 1616, 1591, 1497, 1430, 1375, 1239, 1221, 1192, 1082 cm^{-1}; HRMS calcd for C$_{29}$H$_{31}$ClNaO$_{14}$ [M＋Na]$^{+}$ 661.1300; found 661.1312.

5-(4-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-3-nitro)-phenylmethylene-2,2-butylidene-1,3-dioxane-4,6-dione (**3j**): White solid, m.p. 185～187 ℃; ^{1}H NMR (400 MHz, CDCl$_{3}$) *δ*: 1.88～1.94 (m, 4H), 2.06 (s, 3H), 2.07 (s, 3H), 2.10 (s, 3H), 2.12 (s, 3H), 2.19～2.24 (m, 4H), 3.96 (ddd, *J*＝7.6, 5.2, 2.8 Hz, 1H, H^{5}), 4.24 (dd, *J*＝12.4, 2.4 Hz, 1H, H^{6a}), 4.29 (dd, *J*＝12.4, 5.2 Hz, 1H, H^{6b}), 5.19～5.29 (m, 2H), 5.32～5.37 (m, 2H), 7.39 (d, *J*＝8.8 Hz, 1H), 8.26 (s, 1H), 8.29 (s, 1H), 8.60(s, 1H); ^{13}C NMR (100 MHz, CDCl$_{3}$) *δ*: 20.49, 20.56, 20.67, 23.25, 23.27, 38.61, 38.63, 61.69, 67.91, 70.29, 72.08, 72.68, 99.40, 114.16, 116.83, 118.30, 126.93, 130.41, 138.79, 140.71, 152.40, 153.68, 160.20, 163.16, 169.11, 169.27, 170.14, 170.41; IR (KBr) v_{max}: 3083, 2969, 2948, 2940, 1752, 1735, 1726, 1620, 1584, 1558, 1537, 1499, 1429, 1368, 1345, 1249, 1231, 1220, 1173, 1087 cm^{-1}; HRMS calcd for C$_{29}$H$_{31}$NaO$_{16}$ [M＋Na]$^{+}$ 672.1541; found 672.1555.

Supporting Information NMR spectra of **3a**～**3j** is available free of charge via the Internet at http://sioc-journal.cn/.

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