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PAPER

Laccase-catalysed α-arylation of cyclic β-dicarbonyl compounds†

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In this protocol we described an environmentally friendly synthesis of α-arylated cyclic β-dicarbonyl compounds employing various catechols as precursors through an oxidation/Michael addition sequence. The process proceeded under the catalysis of a commercially available laccase at room temperature with the use of aerial oxygen as the oxidant affording the products in moderate to excellent yields (36–96%). Furthermore, a highly functionalized cyclopentane bearing an all-carbon quaternary stereogenic centre was synthesized through the arylation in excellent diastereoselectivity (dr > 99 : 1, 95% ee).

Introduction

All-carbon quaternary stereogenic centres containing a 1,2-dihydroxylated aryl are present in a large number of biologically active compounds, such as verapamil,[1] mastigophorenes[2] and amaryllidaceae alkaloids.[3] Classically, this type of structural motif is constructed through Friedel–Crafts alkylation using catechol derivatives as nucleophiles.[4] Recently, a conceptionally distinct strategy, in which quinones are employed as Michael acceptors in 1,4-conjugated additions, has been applied to approach the compounds bearing arylated all-carbon quaternary stereogenic centres. Excellent results have been achieved in both metal- and organo-catalysed Michael addition reactions of carbonyl nucleophiles to *p*-quinones.[5] However, the scope of all these processes is limited to the use of *p*-quinononones as substrates, which are notoriously toxic. A breakthrough in this field was achieved by Dixon *et al*., who successfully utilized less toxic catechols as *o*-quinone precursors in an oxidation/Michael addition/rearomatisation sequence for the arylation of β-dicarbonyl compounds affording the products generally in high yields.[6a,b] Furthermore, this method was successfully applied by the same group for the total synthesis of (±)-poweline and (±)-buphanidrine.[6b,c] However, this well-developed organocatalytic oxidative coupling reaction still has several disadvantages from synthetic and environmental perspectives. For instance, the catalyst, polymer-supported BEMP (2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine; R-phrase: 34), is a corrosive base, while highly oxidizing and irritant polymer-supported periodate (R: 8-36/37/38) was employed as the oxidant. Furthermore, all the reactions were conducted at low temperature (−20 °C) and necessitate the use of irritant sodium hyposulphite (R: 7-22-31) (that also may cause fires) as the reducing agent for the rearomatisation of the products. Moreover, the spectrum of the catechols is restricted to the 3-substituted derivatives. No example using 4-substituted catechols as precursors has been reported in their protocol, while the use of non-substituted catechol results in a very low yield (18%). Therefore, development of a more environmentally benign method for the arylation of β-dicarbonyl compounds with broader reaction scope is of great interest.

Applications of enzymes as catalysts in organic synthesis have been investigated intensively, since high stereo- and regioselectivities are often obtained in many types of reactions under mild conditions employing non-toxic enzymes as promoters.[7] Laccases (EC 1.10.3.3), blue oxidoreductases of the multicopper oxidase family, find many applications not only in organic synthesis, but also in industry.[8,9] Especially interesting is the use of a laccase as a catalyst in oxidation reactions, because readily available aerial oxygen can be used as a stoichiometric oxidant for a wide spectrum of substrates, such as phenols, aminophenols, polyphenols and related compounds.[10]

Recently, we developed a laccase-catalysed arylation reaction between 3-substituted *N*-Boc-oxindoles and catechols affording the products in moderate to high yields and complete regioselectivities.[11] In continuation of our investigations in this field we envisaged a laccase-catalysed α-arylation of cyclic β-dicarbonyl compounds by catechols. The process is assumed to start with a laccase-catalysed oxidation of the catechol **A** to the corresponding *o*-quinone **C**, which subsequently gets involved in a Michael addition with the cyclic β-dicarbonyl compound **B** as a nucleophile (general base catalysis), forming the α-arylated compound **D** as a product with *para*/*meta* selectivity (Scheme 1).[12]

Results and discussion

The aromatic β-ketoester **1a** and the catechol (**2a**) were employed as standard substrates for optimization of the reaction conditions (Table 1).

In the first instance the reaction was performed in a mixture of acetonitrile and phosphate buffer under the catalysis of the

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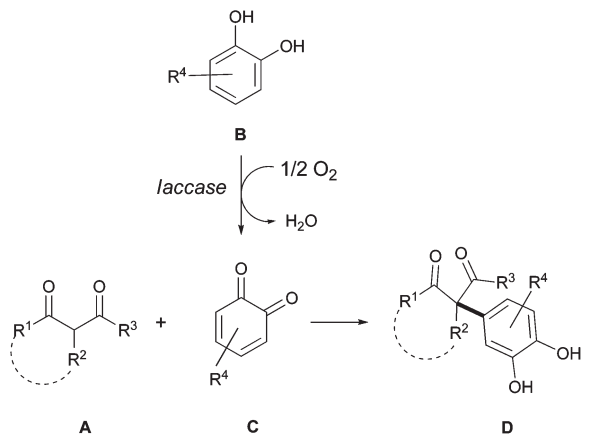
laccase from *Agaricus bisphorus* giving the product **3a** in moderately good yield (62%) (entry 1). Next, three additional laccases with the same catalyst load were tested for this arylation reaction. In the cases of the enzymes from *Trametes versicolor* and *Rhus vernicifera* only traces of the product **3a** were formed (entries 2–3). To our delight, when the laccase from *Pleurotus ostreatus* was utilized as the catalyst the reaction was completed within 21 h at room temperature affording the product **3a** in excellent yield (96%) (entry 4). Subsequently, a brief solvent screening was undertaken at room temperature using the laccase from *Pleurotus ostreatus* as the catalyst. When the reaction was carried out in the phosphate buffer without organic solvent, the reaction provided the product **3a** only in moderate yield (46%) (entry 5). In the cases of other mixtures of organic solvent and buffer, no better result concerning the yield was achieved (entries 6–8). Then we started to study the influence of the catalyst load on the outcome of this reaction. Lowering the catalyst load to 10 U, the reaction proceeded still smoothly and afforded the product **3a** after 21 h without decrease of yield (entry 9). When the catalyst amount was further lowered to 3 U, the yield of this reaction diminished also to 52% (entry 10).



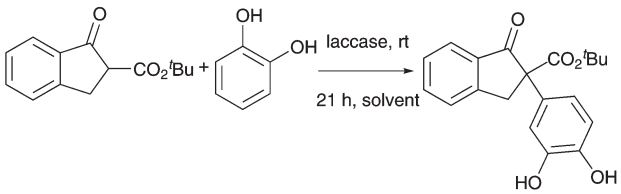
Scheme 1 Laccase-catalysed arylation of cyclic β-dicarbonyl compounds *via* an oxidation/Michael addition sequence.

After optimizing the reaction conditions we started to evaluate the scope of the reaction by varying the structure of both cyclic β-dicarbonyl compounds **1** and catechols **2**. At first the aromatic β-ketoester **1a** was reacted with various catechols **2a–d** (Table 2). In the case of 3-methyl catechol (**2b**) the reaction afforded the product **3b** in a moderately good yield (68%) and with complete regioselectivity (>99 : 1) (entry 2). In contrast, when 3-methoxy catechol (**2c**) was employed as the precursor the reaction gave only a complex mixture (entry 3). Using 3-bromo catechol (**2d**) as the starting material resulted in the formation of two regioisomers **3d** and **4d** as products with a ratio of 71 : 29 (entry 4).

Then various cyclic β-dicarbonyl compounds **1b–e** bearing a cyclopentane or – as a singular example – a cycloheptane scaffold were reacted with different catechols **2a–c** (Table 3). Generally, these compounds **1b–e** were less reactive in comparison to indanone derivative **1a**. Notably, 3-methoxy catechol (**2c**) turned out to be more reactive than the other two catechols **2a** and **2b** (entry 3). In the case of non-substituted catechol **2a** and 3-methoxy catechol (**2c**) as substrates the corresponding products **3e**, **3g**, **3h** and **3k** were obtained in moderate to good yields (44–73%) and with complete regioselectivities (entries 1, 3, 4, 7). In contrast, using 3-methyl catechol (**2b**) as the precursor led to formation of a mixture of two regioisomers in all cases with moderate to excellent yields (36–92%) and high regioisomeric ratios (entries 2, 5, 6).

Furthermore, 4-substituted catechols **2e** and **2f** were also explored as precursors for the title reaction. In the case of

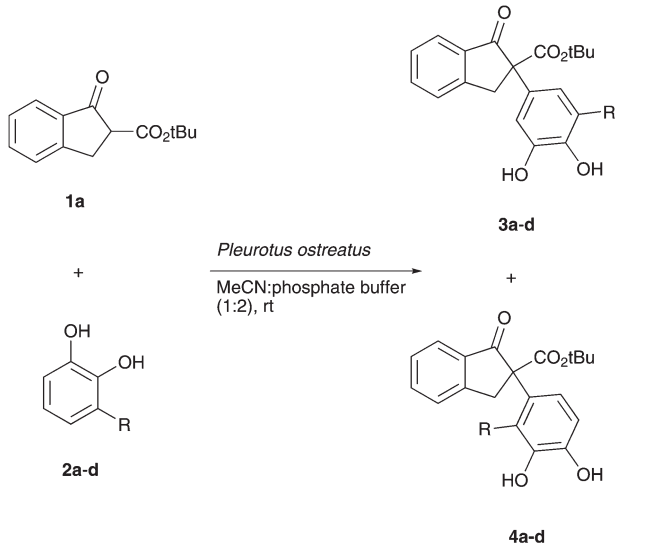
Table 1 Searches for laccase-catalysed arylation of cyclic β-dicarbonyl compounds[a]



Entry	Laccase	U^b (unit)	Solvent	Yield[c] (%)
1	*Agaricus bisphorus*	15	MeCN–phosphate buffer[d] (1 : 2)	62
2	*Rhus vernicifera*	15	MeCN–phosphate buffer[d] (1 : 2)	Traces
3	*Trametes versicolor*	15	MeCN–phosphate buffer[d] (1 : 2)	Traces
4	*Pleurotus ostreatus*	15	MeCN–phosphate buffer[d] (1 : 2)	96
5	*Pleurotus ostreatus*	15	Phosphate buffer[d]	46
6	*Pleurotus ostreatus*	15	EtOH–phosphate buffer[d] (1 : 2)	88
7	*Pleurotus ostreatus*	15	THF–phosphate buffer[d] (1 : 2)	86
8	*Pleurotus ostreatus*	15	MeCN–acetate buffer[e] (1 : 2)	78
9	***Pleurotus ostreatus***	**10**	**MeCN–phosphate buffer[d] (1 : 2)**	**96**
10	*Pleurotus ostreatus*	3	MeCN–phosphate buffer[d] (1 : 2)	52

[a] Reactions were performed on a scale of 0.25 mmol β-ketoester **1a**, 1.2 equiv. catechol (**2a**) in 3 mL solvent. [b] Activities of the laccases as given by the supplier. [c] Yields of the isolated product. [d] pH = 6.0, c = 0.2 M. [e] pH = 4.4, c = 0.2 M.

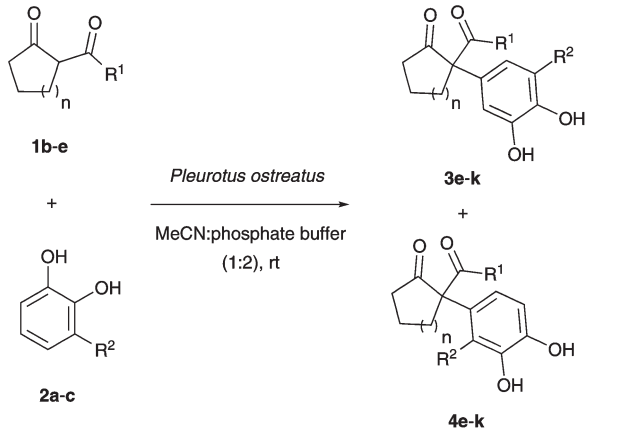
Table 2 Laccase-catalysed arylation of β-ketoester **1a** and catechols **2a–d**[a]



Entry	3	R	*t* (h)	Yield[b] (%)	3/4[c]
1	**a**	H (**2a**)	21	96	—
2	**b**	Me (**2b**)	21	68	>99 : 1
3	**c**	OMe (**2c**)	18	[d]	n.d.[e]
4	**d**	Br (**2d**)	18	52	71 : 29

[a] Reaction conditions: a mixture of 0.25 mmol β-ketoester **1a**, 1.2 equiv. catechol **2a–d** and 10 U of a laccase from *Pleurotus ostreatus* in 3 mL solvent was stirred at room temperature (pH = 6.0). [b] Combined yields of the isolated two regioisomers **3** and **4**. [c] Determined by ^{1}H-NMR-spectroscopy. [d] A complex mixture was obtained. [e] Not determined.

Table 3 Laccase-catalysed arylation of β-dicarbonyl compounds **1b–e** with catechols **2a–c**[a]



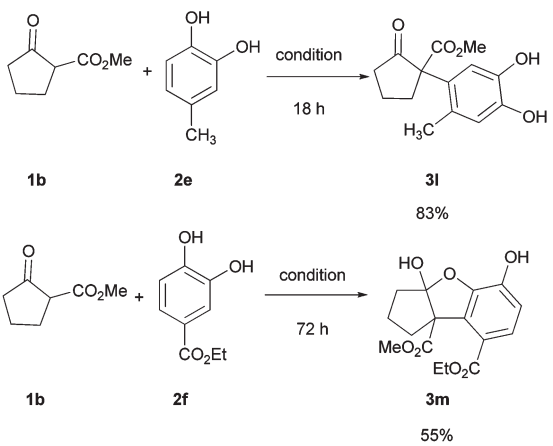
Entry	3	*N*	R^1	R^2	*t* (h)	Yield[b] (%)	3/4[c]
1	**e**	1	OMe (**1b**)	H (**2a**)	72	66	—
2	**f**	1	OMe (**1b**)	Me (**2b**)	72	92	93 : 7
3	**g**	1	OMe (**1b**)	OMe (**2c**)	18	73	>99 : 1
4	**h**	1	OEt (**1c**)	H (**2a**)	72	70	—
5	**i**	1	OEt (**1c**)	Me (**2b**)	72	86	96 : 4
6	**j**	3	OMe (**1d**)	Me (**2b**)	72	36	97 : 3
7	**k**	1	Me (**1e**)	H (**2a**)	72	44	—

[a] Reaction conditions: a mixture of 0.25 mmol β-dicarbonyl compounds **1b–e**, 1.2 equiv. catechol **2a–c** and 10 U of a laccase from *Pleurotus ostreatus* in 3 mL solvent was stirred at room temperature (pH = 6.0). [b] Combined yields of the isolated two regioisomers **3** and **4**. [c] Determined by ^{1}H-NMR-spectroscopy.

4-methyl catechol (**2e**) the arylation reaction proceeded at position 5 of the phenyl ring selectively furnishing the product after 18 h in a high yield (83%) and complete regioselectivity (Scheme 2). In contrast, when 4-carboxylated catechol **2f** was used as an educt, the arylation reaction occurred at position 3 of the phenyl ring indicating that the electronic property of the substituent shows significant influence on the regioselectivity of this arylation reaction. Subsequently, the arylated product underwent an intramolecular ketalization forming the tricyclic compound **3m** as the final product in a moderately good yield (55%) (Scheme 2).

Moreover, the cyclic lactam **1f** was also investigated as a nucleophile for this laccase-catalysed arylation reaction by reacting with different catechols **2a–c** (Table 4). In all cases the reactions were completed within 21 h providing the products **3n–p** in high to excellent yields (83–91%) (entries 1–3). In the cases of catechol (**2a**) and 3-methoxy catechol (**2c**) only one regioisomer was obtained as a product (entries 1, 3), while the use of 3-methyl catechol (**2b**) as a substrate resulted in two regioisomers with a ratio of 90 : 10 (entry 2).

As shown in Scheme 3 the arylated product **3p** was successfully converted into its piperonylated derivative **5** by treatment with dibromomethane in the presence of caesium carbonate. In this process the crude **3p** could be used for the piperonylation directly furnishing the product **5** in a good yield (68%) over two steps, which can act as the precursor for the synthesis of



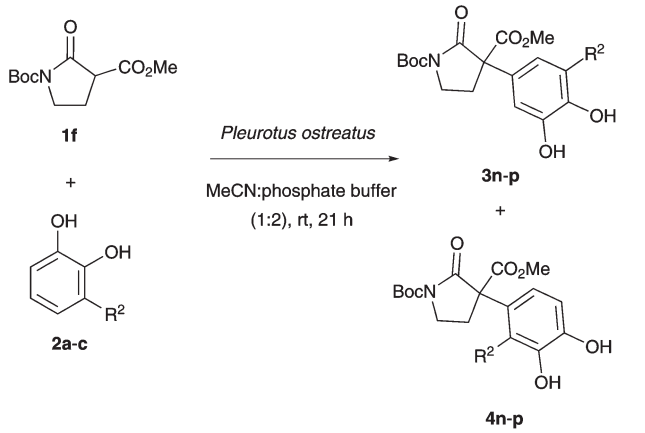
condition: *Pleurotus ostreatus*, MeCN:phosphate buffer (1:2), pH = 6.0, rt.

Scheme 2 Laccase-catalysed arylation of β-ketoester **1b** and 4-substituted catechols **2e** and **2f**.

(±)-poweline and (±)-buphanidrine according to the known literature.[6c]

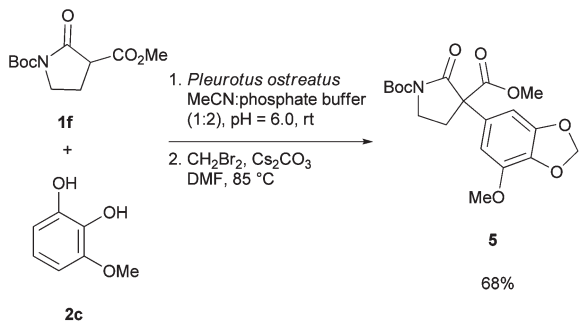
Furthermore, the enantioenriched β-ketoester **1g** (Scheme 4), which was synthesized through a quinine-catalysed asymmetric Michael addition,[13] was successfully employed as a nucleophile in the laccase-catalysed arylation reaction. Although the compound **1g** bears two nucleophilic centres, the α-position of the

Table 4 Laccase-catalysed arylation of β-ketoester **1f** and catechols **2a–c**[a]



Entry	3	R^2	Yield[b] (%)	3/4[c]
1	**n**	H (**2a**)	83	—
2	**o**	Me (**2b**)	91	90 : 10
3	**p**	OMe (**2c**)	88	>99 : 1

[a] Reaction conditions: a mixture of 0.25 mmol β-ketoester **1f**, 1.2 equiv. catechol **2a–c** and 10 U of a laccase from *Pleurotus ostreatus* in 3 mL solvent was stirred at room temperature (pH = 6.0). [b] Combined yields of the isolated two regioisomers **3** and **4**. [c] Determined by ^{1}H-NMR-spectroscopy.

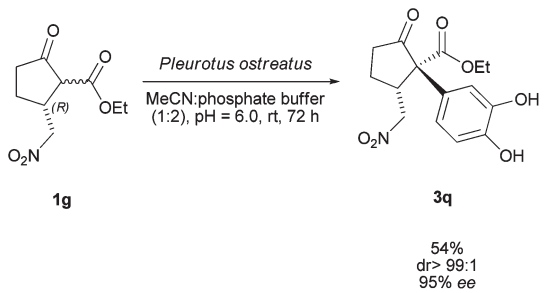


Scheme 3 Synthesis of piperonylated β-ketoester **5** over two steps.

ester group and the α-position of the nitro moiety, this process proceeded highly chemo-, regio- and diastereoselectively affording the highly functionalized cyclopentane **3q** containing an all-carbon quaternary stereogenic centre as the only product in a moderately good yield (54%) and an excellent enantiomeric excess (95% ee). The relative configuration of the compound **3q** was deduced by NOE measurements, also confirming the expected addition *anti* to the β-nitromethylene substituent. Based on this result and the reported fact that the stereogenic centres at C-2 of **1g** are *R*-configured, the newly formed stereogenic centre at C-1 of **3q** was assigned to be *S*.

Conclusions

In conclusion we have developed a laccase-catalysed α-arylation of cyclic β-dicarbonyl compounds by catechols. This process



Scheme 4 Diastereoselective arylation of the enantioenriched β-ketoester **1g**.

was efficiently promoted by a commercially available enzyme under mild reaction conditions employing aerial oxygen as the oxidizing agent without an additional reducing agent for the rearomatisation. Various catechols bearing substituents in different positions have been successfully employed as precursors for this arylation reaction furnishing the products in moderate to excellent yields (36–96%) and in most cases high regioselectivities. Furthermore, a highly functionalized cyclopentane bearing an all-carbon quaternary stereogenic centre has been synthesized through this arylation reaction in excellent diastereo- and enantioselectivity.

Experimental section

General methods

Preparative column chromatography was performed using silica gel 60, particle size 0.040–0.063 mm (230–240 mesh). Analytical TLC was carried out on pre-coated plastic sheets (Polygram® SIL G/UV254, Macherey-Nagel) with detection by ultraviolet irradiation (254 nm). ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Advance/DRX 600 at ambient temperature in $CDCl_3$ at 600 and 151 MHz. The chemical shifts are given in ppm relative to tetramethylsilane [^{1}H: $\delta(SiMe_4)$ = 0.00 ppm] as an internal standard or relative to the resonance of the solvent [^{13}C: $\delta(CDCl_3)$ = 77.0 ppm]. In spectra of higher order the δ and J values were not corrected. Coupling constants J were given in Hz. NMR signals were assigned by means of H-COSY, DEPT and HSQC.

Materials

All laccases used were purchased from Sigma Aldrich. Petroleum ether (40–60 °C) and ethyl acetate for column chromatography were distilled prior to use. All other chemicals and solvents were used as purchased from commercial suppliers without further purification.

General procedure for the α-arylation of the cyclic β-dicarbonyl compounds 3

To a mixture of β-dicarbonyl compounds **1** (0.25 mmol) and catechols **2** (0.30 mmol) in acetonitrile (1.0 mL) were added phosphate buffer (pH = 6.0, c = 0.2 M, 1.0 mL) and the solution of *Pleurotus ostreatus* (10 U) in phosphate buffer (pH = 6.0,

c = 0.2 M, 1.0 mL) successively. After stirring for 18 h (for **3d**, **3g** and **3l**), 21 h (for **3a**, **3b** and **3n–p**) or 72 h (for **3e**, **3f**, **3h–k**, **3m** and **3q**) at room temperature, the reaction mixture was treated with water and then extracted with ethyl acetate. The combined organic phase was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, filtered, and then the volatiles were removed under reduced pressure. The crude products were purified by flash column chromatography on silica gel affording the corresponding arylated cyclic β-dicarbonyl compounds **3** as products.

Procedure for the piperonylated β-ketoester 5 over two steps

To a mixture of the lactam **1f** (0.50 mmol) and catechol **2c** (0.60 mmol) in acetonitrile (2.0 mL) were added phosphate buffer (pH = 6.0, c = 0.2 M, 2.0 mL) and the solution of *Pleurotus ostreatus* (20 U) in phosphate buffer (pH = 6.0, c = 0.2 M, 2.0 mL) successively. After stirring for 21 h at room temperature, the reaction mixture was treated with water and then extracted with ethyl acetate. The combined organic phase was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, filtered, and then the volatiles were removed under reduced pressure. The crude product was dissolved in dry DMF (2.5 mL) and Cs_2CO_3 (0.75 mmol, 1.5 equiv.) as well as dibromomethane (0.75 mmol, 1.5 equiv.) were added successively at room temperature. After stirring for 3 h at 85 °C, the reaction was cooled to ambient temperature and then quenched with water. The mixture was extracted with ethyl acetate. The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$, filtered and then the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (petroleum ether–ethyl acetate = 3 : 1) affording the corresponding lactam **5** as a yellow syrup (134 mg, 68%).

Spectroscopic and analytical data

Characterisation of 3a. *tert*-Butyl 2-(3,4-dihydroxyphenyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**3a**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 7 : 3) as a colourless solid (82 mg, 96%). Mp. 139–141 °C; R_f = 0.13 (petroleum ether–ethyl acetate = 4 : 1); IR (film): 3398, 3003, 2971, 2946, 1742, 1688, 1606, 1591, 1530, 1435, 1366, 1290, 1262, 1229, 1217, 1151, 1122, 1080, 1034, 913, 880, 856, 834, 804, 784, 769, 743, 722, 703, 687 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.79 (d, J = 7.2 Hz, 1 H, H-7), 7.62 (dt, J = 7.8, 1.2 Hz, 1 H, H-5), 7.47 (d, J = 7.8 Hz, 1 H, H-4), 7.39 (t, J = 7.8 Hz, 1 H, H-6), 7.02 (d, J = 1.8 Hz, 1 H, H-2′), 6.73 (dd, J = 8.4, 2.4 Hz, H-6′), 6.71 (d, J = 8.4 Hz, 1 H, H-5′), 6.52 (brs, 1 H, OH), 5.54 (brs, 1 H, OH), 4.03 (d, J = 16.8 Hz, 1 H, H-3), 3.57 (d, J = 16.8 Hz, 1 H, H-3), 1.38 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 202.2 (C═O), 170.3 ($CO_2{}^tBu$), 152.6 (CCH_2), 143.9 (COH), 143.6 (COH), 135.7 (C-5), 135.0 (*C*CO), 130.5 (C-1′), 128.0 (C-6), 126.2 (C-4), 125.1 (C-7), 119.7 (C-6′), 115.2 (C-5′), 114.7 (C-2′), 83.0 ($CO_2C(CH_3)_3$), 65.6 (C-2), 40.7 (C-3), 27.8 (3 C, $CO_2C(CH_3)_3$) ppm; MS (ESI, positive ion): m/z (%): 363 $[M + Na]^+$ (62), 307 (100); anal. calcd for $C_{20}H_{20}O$: C, 70.58; H, 5.92; found: C, 70.33; H, 5.93.

Characterisation of 3b. *tert*-Butyl 2-(3,4-dihydroxy-5-methylphenyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**3b**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 4 : 1) as a pale yellow solid (60 mg, 68%). Mp. 169–170 °C; R_f = 0.19 (petroleum ether–ethyl acetate = 4 : 1); IR (film): 3501, 3312, 3001, 2971, 2945, 1742, 1688, 1608, 1591, 1528, 1422, 1366, 1287, 1229, 1217, 1205, 1151, 1093, 1077, 1054, 1008, 967, 929, 908, 870, 859, 842, 804, 778, 749, 732, 706 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.79 (d, J = 7.8 Hz, 1 H, H-7), 7.62 (t, J = 7.2 Hz, 1 H, H-5), 7.47 (d, J = 7.2 Hz, 1 H, H-4), 7.38 (t, J = 7.8 Hz, 1 H, H-6), 6.90 (d, J = 1.8 Hz, 1 H, H-2′), 6.71 (brs, 1 H, OH), 6.65 (d, J = 1.8 Hz, H-6′), 5.54 (brs, 1 H, OH), 4.03 (d, J = 17.4 Hz, 1 H, H-3), 3.57 (d, J = 17.4 Hz, 1 H, H-3), 2.19 (s, 3 H, CH_3), 1.37 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 202.2 (C═O), 170.2 ($CO_2{}^tBu$), 152.5 (CCH_2), 143.2 (COH), 142.1 (COH), 135.6 (C-5), 135.1 (*C*CO), 129.4 (C-1′), 127.9 (C-6), 126.2 (C-4), 125.1 (C-7), 124.4 (C-5′), 121.4 (C-2′), 112.4 (C-6′), 82.8 ($CO_2C(CH_3)_3$), 65.6 (C-2), 40.8 (C-3), 27.8 (3 C, $CO_2C(CH_3)_3$), 15.8 ($ArCH_3$) ppm; MS (ESI, positive ion): m/z (%): 377 $[M + Na]^+$ (45), 321 (100); anal. calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26; found: C, 71.07; H, 6.27.

Characterisation of 3d and 4d. *tert*-Butyl 2-(3-bromo-4,5-dihydroxyphenyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**3d**) and *tert*-butyl 2-(2-bromo-3,4-dihydroxyphenyl)-1-oxo-2,3-dihydro-1*H*-indene-2-carboxylate (**4d**) were isolated through flash column chromatography (petroleum ether–ethyl acetate = 4 : 1) as a colourless solid (54 mg, 52%). R_f = 0.30 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3487, 3285, 1742, 1686, 1607, 1590, 1523, 1466, 1418, 1368, 1328, 1283, 1250, 1210, 1128, 1151, 1075, 1052, 1018, 966, 943, 911, 882, 868, 855, 841, 801, 782, 756, 741, 725, 705, 684 cm^{-1}; ^1H NMR for **3c** (600 MHz, $CDCl_3$): δ = 7.81 (d, J = 7.8 Hz, 1 H, H-7), 7.64 (t, J = 7.8 Hz, 1 H, H-5), 7.48 (d, J = 7.2 Hz, 1 H, H-4), 7.45–7.40 (m, 1 H, H-6), 7.11 (d, J = 2.4 Hz, 1 H, H-6′), 6.99 (d, J = 1.8 Hz, H-2′), 5.90 (brs, 1 H, OH), 5.60 (brs, 1 H, OH), 4.04 (d, J = 17.4 Hz, 1 H, H-3), 3.53 (d, J = 17.4 Hz, 1 H, H-3), 1.39 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR for **3c** (151 MHz, $CDCl_3$): δ = 200.5 (C═O), 169.4 ($CO_2{}^tBu$), 152.0 (CCH_2), 144.4 (COH), 140.1 (COH), 135.6 (C-5), 135.0 (CCO), 132.1 (C-1′), 128.0 (C-6), 126.1 (C-4), 125.1 (C-7), 122.5 (C-2′), 114.6 (C-6′), 109.3 (C-3′), 83.0 ($CO_2C(CH_3)_3$), 65.0 (C-2), 40.5 (C-3), 27.8 (3 C, $CO_2C(CH_3)_3$) ppm; ^1H NMR for **4d** (600 MHz, $CDCl_3$): δ = 7.87 (d, J = 7.8 Hz, 1 H, H-7), 7.64 (t, J = 7.8 Hz, 1 H, H-5), 7.45–7.40 (m, 2 H, H-4, 6), 6.65 (d, J = 8.4 Hz, 1 H, H-5′), 6.63 (d, J = 8.4 Hz, H-6′), 6.00 (brs, 1 H, OH), 5.80 (brs, 1 H, OH), 4.45 (d, J = 17.4 Hz, 1 H, H-3), 3.31 (d, J = 17.4 Hz, 1 H, H-3), 1.41 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR for **4d** (151 MHz, $CDCl_3$): δ = 200.9 (C═O), 168.6 ($CO_2{}^tBu$), 153.2 (CCH_2), 143.6 (COH), 141.7 (COH), 135.9 (C-5), 135.0 (CCO), 131.9 (C-1′), 127.8 (C-6), 126.4 (C-4), 125.0 (C-7), 120.8 (C-6′), 113.8 (C-5′), 111.7 (C-2′), 83.0 ($CO_2C(CH_3)_3$), 65.0 (C-2), 40.5 (C-3), 27.8 (3 C, $CO_2C(CH_3)_3$) ppm; MS (ESI, positive ion): m/z (%): 441 $[M + Na]^+$ (29), 385 (100); HRMS (ESI): calcd for $C_{20}H_{19}O_5BrNa^+$: 441.0308; found: 441.0309.

Characterisation of 3e. Methyl 1-(3,4-dihydroxyphenyl)-2-oxocyclopentane-carboxylate (**3e**) was isolated through flash

column chromatography (petroleum ether–ethyl acetate = 2 : 1) as a colourless syrup (41 mg, 66%). R_f = 0.17 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3016, 2971, 1735, 1436, 1366, 1229, 1217, 750 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.93 (d, J = 2.4 Hz, 1 H, H-2′), 6.78 (d, J = 8.4 Hz, 1 H, H-5′), 6.74 (dd, J = 8.4, 2.4 Hz, 1 H, H-6′), 6.32 (brs, 2 H, OH), 3.71 (s, 3 H, CO_2CH_3), 2.80–2.75 (m, 1 H, H-5), 2.55–2.51 (m, 1 H, H-5), 2.48–2.43 (m, 1 H, H-3), 2.40–2.34 (m, 1 H, H-3), 2.00–1.87 (m, 2 H, H-4) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 213.7 (C═O), 172.1 (CO_2Me), 143.9 (2 C, C-3′ + C-4′), 127.5 (C-1′), 119.6 (C-6′), 115.4 (C-5′), 114.9 (C-2′), 64.5 (C-1), 53.2 (CO_2CH_3), 37.8 (C-3), 34.8 (C-5), 19.3 (C-4) ppm; MS (ESI, positive ion): m/z (%): 273 $[M + Na]^+$ (54), 255 (14), 245 (22), 228 (45), 195 (100); HRMS (ESI): calcd for $C_{13}H_{14}O_5Na^+$: 273.0733; found: 273.0732.

Characterisation of 3f. Methyl 1-(3,4-dihydroxy-5-methylphenyl)-2-oxocyclopentane-carboxylate (**3f**) and its regiomer **4f** were isolated through flash column chromatography (petroleum ether–ethyl acetate = 2 : 1) as a colourless solid (61 mg, 92%). Mp. 116–118 °C; R_f = 0.14 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3450, 3016, 2971, 2949, 1745, 1436, 1366, 1229, 1217, 1120, 982, 916, 848, 692 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.79 (s, 1 H, H-2′), 6.63 (s, 1 H, H-6′), 6.70 (brs, 1 H, OH), 5.67 (brs, 1 H, OH), 3.70 (s, 3 H, CO_2CH_3), 2.79–2.74 (m, 1 H, H-5), 2.55–2.51 (m, 1 H, H-5), 2.48–2.35 (m, 2 H, H-3), 2.20 (s, 3 H, CH_3), 1.99–1.87 (m, 2 H, H-4) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 214.0 (C═O), 172.1 (CO_2Me), 143.3 (COH), 142.5 (COH), 126.4, 124.7, 121.1 (C-6′), 112.4 (C-2′), 64.5 (C-1), 53.2 (CO_2CH_3), 37.8 (C-3), 34.9 (C-5), 19.2 (C-4), 15.8 ($ArCH_3$) ppm; MS (ESI, positive ion): m/z (%): 287 $[M + Na]^+$ (70), 242 (100); anal. calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10; found: C, 63.63; H, 6.10.

Characterisation of 3g. Methyl 1-(3,4-dihydroxy-5-methoxyphenyl)-2-oxocyclopentane-carboxylate (**3g**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 7 : 3) as a colourless solid (51 mg, 73%). Mp. 132–134 °C; R_f = 0.24 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3443, 2971, 1740, 1724, 1608, 1519, 1433, 1365, 1310, 1229, 1217, 1204, 1168, 1091, 1038, 1003, 946, 842, 808, 787, 734, 702 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.62 (d, J = 1.8 Hz, 1 H, H-2′), 6.57 (d, J = 1.8 Hz, 1 H, H-6′), 5.63 (brs, 2 H, OH), 3.85 (s, 3 H, OCH_3), 3.70 (s, 3 H, CO_2CH_3), 2.82–2.78 (m, 1 H, H-5), 2.53–2.48 (m, 1 H, H-5), 2.48–2.43 (m, 1 H, H-3), 2.39–2.33 (m, 1 H, H-3), 2.01–1.87 (m, 2 H, H-4) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 212.3 (C═O), 171.4 (CO_2Me), 147.0 (C-5′), 143.8 (C-3′), 132.3 (C-4′), 127.3 (C-1′), 108.1 (C-2′), 103.1 (C-6′), 64.4 (C-1), 56.3 ($ArOCH_3$), 53.0 (CO_2CH_3), 37.8 (C-3), 35.0 (C-5), 19.3 (C-4) ppm; MS (ESI, positive ion): m/z (%): 303 $[M + Na]^+$ (55), 287 (34), 273 (100), 252 (41); anal. calcd for $C_{14}H_{16}O_6$: C, 60.00; H, 5.75; found: C, 59.88; H, 5.76.

Characterisation of 3h. Ethyl 1-(3,4-dihydroxyphenyl)-2-oxocyclopentane-carboxylate (**3h**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 2 : 1) as a colourless syrup (46 mg, 70%). R_f = 0.31 (petroleum ether–ethyl acetate = 3 : 2); IR (film): 2971, 1740, 1436, 1366, 1229, 1217, 750 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.94 (d, J = 1.8 Hz, 1 H, H-2′), 6.77 (d, J = 7.8 Hz, 1 H, H-5′), 6.74 (dd, J = 7.8, 1.8 Hz, 1 H, H-6′), 6.30 (brs, 2 H, OH), 4.18 (q, 2 H, J = 6.6 Hz, $CO_2CH_2CH_3$), 2.80–2.76 (m, 1 H, H-5), 2.54–2.50 (m, 1 H, H-5), 2.49–2.44 (m, 1 H, H-3), 2.39–2.34 (m, 1 H, H-3), 2.01–1.80 (m, 2 H, H-4), 1.22 (t, 3 H, J = 6.6 Hz, $CO_2CH_2CH_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 213.6 (C═O), 171.6 (CO_2Et), 143.8 (2 C, C-3′ + C-4′), 127.7 (C-1′), 119.6 (C-6′), 115.3 (C-5′), 114.9 (C-2′), 64.5 (C-1), 62.2 ($CO_2CH_2CH_3$), 37.7 (C-3), 34.8 (C-5), 19.3 (C-4), 14.0 ($CO_2CH_2CH_3$) ppm; MS (ESI, positive ion): m/z (%): 287 $[M + Na]^+$ (52), 259 (25), 242 (100), 214 (19); HRMS (ESI): calcd for $C_{14}H_{16}O_5Na^+$: 287.0890; found: 287.0888.

Characterisation of 3i. Ethyl 1-(3,4-dihydroxy-5-methylphenyl)-2-oxocyclopentanecarboxylate (**3i**) and its regiomer **4i** were isolated through flash column chromatography (petroleum ether–ethyl acetate = 3 : 1) as a colourless solid (60 mg, 86%). R_f = 0.18 (petroleum ether–ethyl acetate = 4 : 1); IR (film): 3539, 3237, 2971, 2953, 1737, 1600, 1527, 1448, 1420, 1366, 1354, 1304, 1290, 1257, 1228, 1217, 1667, 1116, 1057, 1018, 994, 967, 880, 857, 840, 830, 758, 736, 696, 678 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.78 (d, J = 1.8 Hz, 1 H, H-2′), 6.64 (s, 1 H, H-6′), 6.58 (brs, 1 H, OH), 5.60 (brs, 1 H, OH), 4.18 (q, 2 H, J = 7.2 Hz, $CO_2CH_2CH_3$), 2.79–2.74 (m, 1 H, H-5), 2.54–2.43 (m, 2 H, H-5, 3), 2.40–2.34 (m, 1 H, H-3), 2.20 (s, 3 H, CH_3), 1.99–1.89 (m, 2 H, H-4), 1.22 (t, 3 H, J = 7.2 Hz, $CO_2CH_2CH_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 213.9 (C═O), 171.6 (CO_2Et), 143.2 (COH), 142.4 (COH), 126.6, 124.5, 121.2 (C-6′), 112.5 (C-2′), 64.6 (C-1), 62.2 ($CO_2CH_2CH_3$), 37.8 (C-3), 34.9 (C-5), 19.3 (C-4), 15.8 ($ArCH_3$), 14.0 ($CO_2CH_2CH_3$) ppm; MS (ESI, positive ion): m/z (%): 301 $[M + Na]^+$ (45), 273 (100), 265 (28), 229 (94); anal. calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52; found: C, 64.47; H, 6.55.

Characterisation of 3j. Methyl 1-(3,4-dihydroxy-5-methylphenyl)-2-oxocycloheptane-carboxylate (**3j**) and its regiomer **4j** were isolated through flash column chromatography (petroleum ether–ethyl acetate = 3 : 1) as a pale yellow solid (27 mg, 36%). R_f = 0.38 (petroleum ether–ethyl acetate = 3 : 2); IR (film): 3430, 3309, 3016, 2970, 2947, 2864, 1727, 1684, 1621, 1605, 1530, 1449, 1429, 1366, 1309, 1310, 1263, 1229, 1217, 1149, 1140, 1102, 1092, 1069, 1047, 1002, 973, 960, 941, 912, 881, 868, 858, 842, 833, 804, 757, 738, 716, 658 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.56 (brs, 1 H, OH), 6.53 (d, J = 1.8 Hz, 1 H, H-2′), 6.51 (d, J = 1.8 Hz, 1 H, H-6′), 5.51 (brs, 1 H, OH), 3.68 (s, 3 H, CO_2CH_3), 3.73–3.69 (m, 1 H, H-7), 2.62–2.57 (m, 1 H, H-3), 2.53–2.49 (m, 1 H, H-3), 2.21 (s, 3 H, CH_3), 2.17–2.13 (m, 1 H, H-7), 1.98–1.92 (m, 1 H), 1.84–1.76 (m, 2 H), 1.70–1.56 (m, 2 H), 1.48–1.40 (m, 1 H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 210.9 (C═O), 173.3 (CO_2Me), 143.1 (COH), 142.3 (COH), 129.5, 124.5, 121.1 (C-2′), 112.6 (C-6′), 67.7 (C-1), 52.8 (CO_2CH_3), 41.8 (C-3), 33.6 (C-7), 30.5, 26.7, 25.6, 15.8 ($ArCH_3$) ppm; MS (ESI, positive ion): m/z (%): 291 $[M - H]^+$ (15), 263 (30), 259 (100), 231 (30), 203 (10), 194 (11), 149 (36); anal. calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90; found: C, 65.98; H, 6.93.

Characterisation of 3k. 2-Acetyl-2-(3,4-dihydroxyphenyl)-cyclopentanone (**3k**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 3 : 1) as a colourless

syrup (25 mg, 42%). R_f = 0.18 (petroleum ether–ethyl acetate = 4 : 1); IR (film): 3385, 2971, 1735, 1697, 1605, 1520, 1435, 1355, 1262, 1228, 1217, 1204, 1122, 1006, 966, 865, 812, 786, 765, 735, 701 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.90 (d, J = 2.4 Hz, 1 H, H-2′), 6.87 (d, J = 8.4 Hz, 1 H, H-5′), 6.71 (dd, J = 8.4, 2.4 Hz, 1 H, H-6′), 2.84–2.70 (m, 1 H, H-3), 2.48–2.36 (m, 2 H, H-5), 2.34–2.29 (m, 1 H, H-3), 2.09 (s, 3 H, $COCH_3$), 191–1.86 (m, 2 H, H-4) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 215.4 (C═OMe), 205.9 (C-1), 144.1 (COH), 144.0 (COH), 129.4 (C-1′), 119.2 (C-6′), 115.7 (C-5′), 114.1 (C-2′), 71.8 (C-2), 39.1 (C-5), 34.0 (C-3), 26.8 (C-4), 19.0 (C═OCH_3) ppm; MS (ESI, positive ion): m/z (%): 257 $[M + Na]^+$ (39), 179 (100); HRMS (ESI): calcd for $C_{13}H_{14}O_4Na^+$: 257.0784; found: 257.0783.

Characterisation of 3l. Methyl 1-(4,5-dihydroxy-2-methylphenyl)-2-oxocyclopentane-carboxylate (**3l**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 7 : 3) as a colourless solid (56 mg, 83%). Mp. 153–155 °C; R_f = 0.38 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3473, 3004, 2971, 2954, 1742, 1723, 1602, 1519, 1437, 1397, 1366, 1322, 1296, 1278, 1226, 1218, 1164, 1140, 1094, 1061, 1011, 983, 937, 924, 914, 900, 859, 837, 828, 810, 760, 725, 705, 675 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.68 (s, 1 H, H-5′), 6.43 (s, 1 H, H-2′), 5.59 (brs, 2 H, OH), 3.75 (s, 3 H, CO_2CH_3), 3.01–2.96 (m, 1 H, H-5), 2.53–2.48 (m, 2 H, H-3), 2.30–2.26 (m, 1 H, H-5), 2.08–2.02 (m, 1 H, H-4), 2.06 (s, 3 H, CH_3), 1.87–1.79 (m, 1 H, H-4) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 215.3 (C═O), 171.8 (CO_2Me), 142.9 (COH), 140.9 (COH), 129.3, 129.0, 119.2 (C-5′), 114.7 (C-2′), 66.1 (C-1), 53.3 (CO_2CH_3), 39.1 (C-2), 35.8 (C-5), 19.6 (C-4), 19.3 ($ArCH_3$) ppm; MS (ESI, positive ion): m/z (%): 287 $[M + Na]^+$ (35), 242 (100); anal. calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10; found: C, 63.33; H, 6.10.

Characterisation of 3m. 8-Ethyl 8b-methyl 3a,5-di-hydroxy-2,3,3a,8b-tetrahydro-1*H*-cyclopenta[*b*]benzofuran-8,8b-dicarboxylate (**3m**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 7 : 3) as a colourless solid (45 mg, 55%). Mp. 154–155 °C; R_f = 0.19 (petroleum ether–ethyl acetate = 3 : 2); IR (film): 3416, 3134, 2982, 2951, 1698, 1633, 1596, 1508, 1480, 1437, 1381, 1328, 1305, 1290, 1264, 1233, 1212, 1192, 1172, 1108, 1088, 1039, 1003, 989, 962, 934, 897, 882, 832, 815, 774, 732, 676 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.4 Hz, 1 H, H-6), 6.82 (d, J = 8.4 Hz, H-7), 6.40 (brs, 1 H, OH), 4.34–4.21 (m, 2 H, $CO_2CH_2CH_3$), 3.68 (s, 3 H, CO_2CH_3), 3.09–3.01 (m, 1 H, H-1), 2.29–2.25 (m, 1 H, H-3), 2.12–2.05 (m, 1 H, H-3), 1.85–1.81 (m, 1 H, H-1), 1.55–1.46 (m, 2 H, H-2), 1.33 (t, J = 7.2 Hz, 3 H, $CO_2CH_2CH_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 172.1 (CO_2Me), 165.4 (CO_2Et), 146.3 (C-4a), 143.9 (C-5), 131.7, 125.5 (C-6), 121.9, 118.5, 115.6 (C-7), 67.1 (C-8b), 60.9 ($CO_2CH_2CH_3$), 52.7 (CO_2CH_3), 39.1 (C-3), 37.2 (C-1), 22.8 (C-2), 14.3 ($CO_2CH_2CH_3$) ppm; MS (ESI, positive ion): m/z (%): 345 $[M + Na]^+$ (23), 317 (23), 313 (62), 203 (10), 163 (100); anal. calcd for $C_{16}H_{18}O_7$: C, 59.44; H, 5.92; found: C, 59.40; H, 5.92.

Characterisation of 3n. 1-*tert*-Butyl 3-methyl 3-(3,4-dihydroxyphenyl)-2-oxopyrrolidine-1,3-dicarboxylate (**3n**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 3 : 2) as a colourless solid (73 mg, 83%). Mp. 153–151 °C; R_f = 0.11 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3456, 3016, 2971, 2946, 1737, 1522, 1438, 1366, 1318, 1279, 1266, 1230, 1217, 1205, 1153, 1124, 1093, 1060, 1045, 976, 915, 892, 882, 849, 789, 775, 753, 693, 682 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 7.11 (d, J = 2.4 Hz, 1 H, H-2′), 6.82 (d, J = 7.8 Hz, 1 H, H-5′), 6.79 (dd, J = 8.4, 2.4 Hz, 1 H, H-6′), 5.60 (brs, 2 H, OH), 3.79–3.74 (m, 1 H, H-5), 3.73 (s, 3 H, CO_2CH_3), 3.68–3.64 (m, 1 H, H-5), 2.92–2.89 (m, 1 H, H-4), 2.49–2.45 (m, 1 H, H-4), 1.53 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.5, 170.4, 150.1 ($NCO_2{}^tBu$), 144.1 (COH), 143.7 (COH), 127.9 (C-1′), 119.4 (C-6′), 115.3 (C-5′), 114.8 (C-2′), 83.8 ($CO_2C(CH_3)_3$), 61.2 (C-3), 53.5 (CO_2CH_3), 43.5 (C-5), 30.1 (C-4), 28.0 (3 C, $CO_2C(CH_3)_3$) ppm; MS (ESI, positive ion): m/z (%): 374 $[M + Na]^+$ (15), 274 (100); anal. calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99; found: C, 58.09; H, 6.02; N, 3.91.

Characterisation of 3o. 1-*tert*-Butyl 3-methyl 3-(3,4-dihydroxy-5-methylphenyl)-2-oxo-pyrrolidine-1,3-dicarboxylate (**3o**) and its regiomer **4o** were isolated through flash column chromatography (petroleum ether–ethyl acetate = 3 : 2) as a pale yellow solid (83 mg, 91%). R_f = 0.12 (petroleum ether–ethyl acetate = 7 : 3); IR (film): 3430, 3336, 2955, 1780, 1714, 1618, 1605, 1523, 1425, 1370, 1310, 1295, 1249, 1212, 1144, 1111, 1089, 1065, 1023, 1001, 969, 948, 861, 848, 803, 776, 754, 740, 734, 706, 689 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.96 (d, J = 2.4 Hz, 1 H, H-2′), 6.66 (d, J = 2.4 Hz, 1 H, H-6′), 6.60 (brs, 1 H, OH), 5.65 (brs, 1 H, OH), 3.76–3.73 (m, 1 H, H-5), 3.72 (s, 3 H, CO_2CH_3), 3.67–3.63 (m, 1 H, H-5), 2.87–2.85 (m, 1 H, H-4), 2.50–2.46 (m, 1 H, H-4), 1.52 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.7 (2 C, CO_2Me, BocNC═O), 150.1 ($NCO_2{}^tBu$), 143.4 (COH), 142.8 (COH), 126.4 (C-1′), 124.5 (C-5′), 120.8 (C-6′), 112.4 (C-2′), 83.8 ($CO_2C(CH_3)_3$), 61.3 (C-3), 53.4 (CO_2CH_3), 43.6 (C-5), 30.2 (C-4), 28.0 (3 C, $CO_2C(CH_3)_3$), 15.8 ($ArCH_3$) ppm; MS (ESI, positive ion): m/z (%): 388 $[M + Na]^+$ (21), 288 (100); anal. calcd for $C_{18}H_{23}NO_7$: C, 59.17; H, 6.34; N, 3.84; found: C, 59.10; H, 6.52; N, 3.84.

Characterisation of 3p. 1-*tert*-Butyl 3-methyl 3-(3,4-dihydroxy-5-methoxyphenyl)-2-oxopyrrolidine-1,3-dicarboxylate (**3p**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 3 : 2) as a colourless solid (84 mg, 88%). Mp. 167–169 °C; R_f = 0.17 (petroleum ether–ethyl acetate = 3 : 2); IR (film): 3455, 3017, 2971, 2947, 1735, 1680, 1609, 1520, 1448, 1369, 1314, 1259, 1229, 1217, 1204, 1180, 1151, 1101, 1087, 972, 917, 844, 832, 776, 699 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.73 (d, J = 2.4 Hz, 1 H, H-2′), 6.63 (d, J = 2.4 Hz, 1 H, H-6′), 5.55 (brs, 2 H, OH), 3.82 (s, 3 H, OCH_3), 3.77–3.73 (m, 1 H, H-5), 3.75 (s, 3 H, CO_2CH_3), 3.68–3.64 (m, 1 H, H-5), 2.92–2.88 (m, 1 H, H-4), 2.46–2.42 (m, 1 H, H-4), 1.53 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.3, 169.8, 150.1 ($NCO_2{}^tBu$), 147.0 (C-5′), 143.8 (C-3′), 132.5 (C-4′), 127.3 (C-1′), 107.6 (C-6′), 102.9 (C-2′), 83.6 ($CO_2C(CH_3)_3$), 61.2 (C-3), 56.3 ($ArOCH_3$), 53.4 (CO_2CH_3), 43.4 (C-5), 30.2 (C-4), 28.0 (3 C, $CO_2C(CH_3)_3$) ppm; MS (ESI, positive ion): m/z (%): 404 $[M + Na]^+$ (17), 304 (100); HRMS (ESI): calcd for $C_{18}H_{23}NO_8Na^+$: 404.1316; found: 404.1314.

Characterisation of 3q. (1*S*,2*R*)-Ethyl 1-(3,4-dihydroxyphenyl)-2-(nitromethyl)-5-oxo-cyclopentane-carboxylate (**3q**) was isolated through flash column chromatography (petroleum ether–ethyl acetate = 4 : 1) as a yellow syrup (44 mg, 54%). R_f = 0.38 (petroleum ether–ethyl acetate = 3 : 2); the ee (95%) was determined by HPLC on a chiral stationary phase [Chiralpak IC, *n*-heptane–isopropanol = 8 : 2, 0.5 mL min^{-1}), t_R = 91 min (major), 152 min (minor)]; $[\alpha]_D^{20} = -28.4$ (c = 0.50, $CHCl_3$); IR (film): 3443, 2971, 1724, 1607, 1551, 1523, 1434, 1366, 1226, 1214, 1204, 1154, 1121, 1085, 1017, 871, 846, 809, 784, 737, 672, 662 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.84 (d, J = 8.4 Hz, 1 H, H-5′), 6.77 (d, J = 2.4 Hz, 1 H, H-2′), 6.67 (dd, J = 8.4, 2.4 Hz, 1 H, H-6′), 5.50 (brs, 2 H, OH), 4.80 (dd, J = 13.2, 3.0 Hz, 1 H, C*H*HNO_2), 4.66 (dd, J = 13.2, 10.2 Hz, 1 H, C*H*HNO_2), 4.28–4.23 (m, 2 H, $CO_2CH_2CH_3$), 3.37–3.34 (m, 1 H, C*H*CH_2NO_2), 2.76–2.71 (m, 1 H, H-4), 2.45–2.39 (m, 2 H, H-3, 4), 1.96–1.93 (m, 1 H, H-3), 1.28 (t, 3 H, J = 7.2 Hz, $CO_2CH_2CH_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 209.5 (C=O), 168.9 (CO_2Et), 143.9 (COH), 143.8 (COH), 127.2 (C-1′), 119.9 (C-6′), 115.7 (C-5′), 115.0 (C-2′), 76.6 (NO_2CH_2), 67.0 (C-1), 62.6 ($CO_2CH_2CH_3$), 44.5 (C-2), 36.7 (C-4), 24.4 (C-3), 14.1 ($CO_2CH_2CH_3$) ppm; MS (ESI, positive ion): m/z (%): 346 $[M + Na]^+$ (12), 299 (59), 277 (100), 249 (31); HRMS (ESI): calcd for $C_{15}H_{17}NO_7Na^+$: 346.0897; found: 346.0896.

Characterisation of 5. 1-*tert*-Butyl 3-methyl 3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)-2-oxopyrrolidine-1,3-dicarboxylate (**4**) R_f = 0.15 (petroleum ether–ethyl acetate = 4 : 1); IR (film): 3003, 2971, 2950, 1782, 1737, 1722, 1634, 1511, 1549, 1429, 1366, 1297, 1229, 1217, 1147, 1097, 1039, 969, 948, 926, 844, 803, 776, 732, 702 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 6.72 (s, 1 H, H-2′), 6.65 (s, 1 H, H-6′), 5.96 (s, 2 H, OCH_2O), 3.90 (s, 3 H, OCH_3), 3.77–3.73 (m, 1 H, H-5), 3.76 (s, 3 H, CO_2CH_3), 3.68–3.65 (m, 1 H, H-5), 2.95–2.91 (m, 1 H, H-4), 2.43–2.38 (m, 1 H, H-4), 1.54 (s, 9 H, $OC(CH_3)_3$) ppm; ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.1, 169.4, 150.0 ($NCO_2{}^tBu$), 149.1 (C-5′), 143.4 (C-3′), 135.2 (C-4′), 130.2 (C-1′), 107.5 (C-2′), 101.7 (2 C, C-6′ +OCH_2O), 83.6 ($CO_2C(CH_3)_3$), 61.4 (C-3), 56.9 ($ArOCH_3$), 53.5 (CO_2CH_3), 43.3 (C-5), 30.6 (C-4), 28.0 (3 C, $CO_2C(CH_3)_3$) ppm; MS (ESI, positive ion): m/z (%): 416 $[M + Na]^+$ (100), 316 (100); anal. calcd for $C_{19}H_{23}NO_8$: C, 58.01; H, 5.89; N, 3.56; found: C, 57.80; H, 5.92; N, 3.47.

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