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**PAPER**

# First diastereoselective synthesis of methyl caffeoyl- and feruloyl-*muco*-quinates†

**Rakesh Jaiswal, Michael H. Dickman and Nikolai Kuhnert***

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We report on a diastereoselective synthesis of six derivatives of caffeoyl- and feruloyl-*muco*-quinic acids. All the *muco*-quinic acid derivatives were obtained in excellent yield in five steps starting from quinic acid, caffeic acid and ferulic acid. Allyl ether protection of *trans*-hydroxy cinnamic acids was here introduced to chlorogenic acids synthesis. We show that *muco*-quinic acid derivatives, which are formally diastereoisomers of chlorogenic acids, can be readily distinguished by their tandem mass spectra.

## Introduction

Classically, chlorogenic acids are a large family of esters formed between quinic acid (**1**) and one to four residues of certain *trans* hydroxycinnamic acids, most commonly caffeic (**2**), *p*-coumaric and ferulic acids (**3**); sinapic, dimethoxycinnamic and trimethoxycinnamic acids also occur in some plant species, while various aliphatic acids may replace one or more of the *trans* cinnamic acid residues.[1] In the IUPAC system (−)-quinic acid **1** is defined as 1L-1(OH),3,4/5-tetrahydroxycyclohexane carboxylic acid and that nomenclature is used throughout this paper.[2] Chlorogenic acids form an important integral part of the human diet with an estimated intake of around 2 g of chlorogenic acids per human per day. Chlorogenic acids were reported to display a range of beneficial biological activities including sugar transport inhibition, opiate antagonism, anti-spasmodic activity, anti-HBV, HIV transcriptase inhibition and general anti-oxidative properties.[3] It is widely accepted that the known biosynthetic pathway produces esters of the 3*R*, 4*S*, 5*R* isomers of quinic acid,[4] which dominate most of the naturally occurring extracts. However, the occurrence of esters of other diastereoisomers of quinic acid has been reported including genuine natural products and products of food processing.

Firstly, some esters of diastereomers of quinic acid were reported as naturally occurring secondary plant metabolites such as 3,5-dicaffeoyl-*muco*-quinic acid, 1,3-dicaffeoyl-*epi*-quinic acid and 3,5-dicaffeoyl-*epi*-quinic acid.[5,6] Most commonly, esters of *epi*-quinic acid were reported in *Chrysanthemum morifolium* and *Ilex kudingcha*[6,7] but also esters of *muco*- and *scyllo*-quinic acid were reported in *Asimina triloba*, *Lactula indica* and *Aster scaber*.[3,8] Secondly, food processing results in epimerisation of the quinic acid core of chlorogenic acids. For example, around 80 different chlorogenic acid derivatives have been identified in the green coffee bean. Upon roasting, the number increases to at least 120 derivatives as judged by the occurrence of characteristic fragment ions at *m*/*z* 173 and 191 in tandem MS experiments. It can be assumed that several of these novel chlorogenic acid derivatives formed at elevated temperatures are diastereomers of naturally occurring chlorogenic acids. This assumption is supported by findings of Maier and Engelhardt[9,10] that roasted coffee beans contain all known stereoisomers of quinic acid. Whether these compounds have been formed after hydrolysis of the ester bond of diastereomers of chlorogenic acid or directly from quinic acid remains unclear.

Thirdly, Crozier recently reported on the human metabolism of chlorogenic acid derivatives. He could identify a series of so far unknown isomers of feruloyl quinic acid in the urine of coffee drinkers which were absent in the original beverage.[11] Here as well it can be assumed that several of these derivatives are diastereomers of naturally occurring chlorogenic acids, produced by human or gut microflora metabolism of chlorogenic acids.

Putting these pieces of evidence together, there is a strong need to obtain diastereomeric derivatives of chlorogenic acids. These should serve as authentic analytical standards when investigating extracts of plants, extracts of processed food and in metabolic studies. It should be noted that most chlorogenic acid derivatives are only produced in small amounts by the plants and due to the large number of structurally related compounds produced in a single plant, chromatographic resolution and preparative isolation has been found to be extremely difficult. However, due to the observation that regioisomers of chlorogenic acids can be readily distinguished by their fragmentation pattern in tandem MS experiments these authentic standards should as well allow us to extend the use of the mass spectrometrical method to the

*Jacobs University Bremen, Bremen, Germany.*
*E-mail: n.kuhnert@jacobs-university.de; Fax: +49-4212003229;*
*Tel: +49-4212003120*

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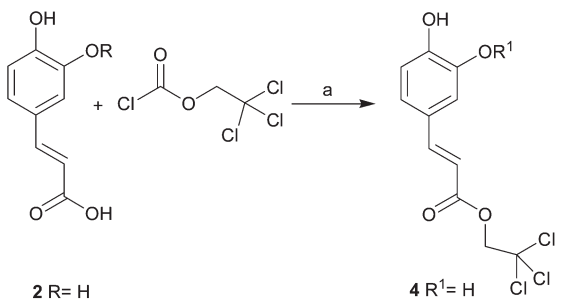
identification of novel chlorogenic acid derivatives even at trace levels in biological samples produced biosynthetically, through food processing such as cooking, roasting, steaming and so on or through metabolic pathways. Furthermore, with authentic samples in hand the questions as to whether diastereomeric compounds are biologically active and whether they can be readily distinguished by tandem mass spectrometry could be answered. This would add a highly useful structural chemistry dimension to the powerful method of tandem mass spectrometry.

In this paper we report on successful attempts to obtain selected diastereomeric chlorogenic acid derivatives by organic synthesis. Furthermore, we report on basic features of their tandem mass spectra and show that tandem mass spectrometry can be used as a reliable and predictive tool to assign relative stereochemistry in this class of compounds.

## Results and discussion

Several methods for the synthesis of chlorogenic acids have been reported, among which two are high yielding and efficient.[12–14] Most synthetic strategies rely on a condensation reaction between an acid chloride of an ester protected hydroxycinnamate and an appropriately protected derivative of quinic acid. Acetyl groups have been most commonly used for phenolic OH protection, however, this was found to be highly problematic and unreliable, since both acid or base induced deprotection[15] leads to incomplete or non-selective removal of the acetate groups with competing hydrolysis of the cinnamate quinic acid ester bonds.[16] The resulting product mixtures usually contained low amounts of products and were most frequently found to be inseparable by column chromatography or reversed phase preparative HPLC.[12,13] Other protecting groups such as Troc (trichloroethoxycarbonyl) and Boc (*tert*-butoxycarbonyl) also failed to protect efficiently the phenolic hydroxyl groups. Reaction of Troc-Cl with caffeic acid in the presence of organic bases like pyridine and triethylamine gave an emulsion during the aqueous acidic workup, from which ester **4** was isolated as the main product, surprisingly showing reaction of Troc-Cl with the carboxylic acid rather than the phenolic OHs. In our case, a single crystal structure study by X-ray diffraction of **4** established unambiguously the regiochemistry of this reaction product (Scheme 1, Fig. S3† and Table 1).




**Scheme 1** *Reagents and conditions*: (a) anhydrous $K_2CO_3$, acetone, NaOH, EtOH, reflux, 48 h.

In this work we employed *O*-allyl protection for the first time in chlorogenic acid chemistry and found the allyl group to be an efficient protecting group for the protection of the phenolic hydroxyl groups in the synthesis of chlorogenic acids.

For the allyl protection we used the Williamson ether synthesis reaction (Scheme 2, Fig. 2).[17] Acetone was found to be the solvent of choice, yielding allyl protected caffeic and ferulic acids **5** and **6** in excellent yields with no need for further purification after the aqueous workup.

In the next step allyl protected cinnamic acids were converted to their more reactive acid chlorides in quantitative yields using the Vilsmeier reagent oxalyl chloride and DMF.

For the quinic acid hydroxyl protection we used Ley's tetramethoxy butane protection (TMB), which gave protected methylester **9** in good yield (see Scheme 3).[18] The viscous colorless product was crystallised from a mixture of ethyl acetate and heptane (3 : 1); needle shaped white crystals of bis acetal protected quinic acid (**9**) (94%) were obtained. Single crystal X-ray analysis data and the structure for methyl TMB-protected quinate **9** are shown in Table 1 and Fig. S4,† respectively.

**Table 1** Crystal data and structure refinement for compounds **4**, **5**, **9** and **10**

| | Compound **4** | Compound **5** | Compound **9** | Compound **10** |
|---|---|---|---|---|
| Empirical formula | $C_{11}H_9Cl_3O_4$ | $C_{15}H_{16}O_4$ | $C_{14}H_{24}O_8$ | $C_{14}H_{24}O_8$ |
| MW | 311.53 | 260.28 | 320.33 | 320.33 |
| Crystal system | Triclinic | Triclinic | Monoclinic | Orthorhombic |
| Space group (no.) | $P\bar{1}$ (#2) | $P\bar{1}$ (#2) | $P2_1$ (#4) | $P2_12_12_1$ (#19) |
| *a*/Å | 5.6867(2) | 8.7884(5) | 9.0784(8) | 10.0094(11) |
| *b*/Å | 10.1514(4) | 9.8407(4) | 9.5830(7) | 12.1210(10) |
| *c*/Å | 22.3376(9) | 17.4343(10) | 9.3296(9) | 12.9524(12) |
| *α*/° | 85.717(2) | 79.265(3) | 90.000 | 90.000 |
| *β*/° | 83.067(2) | 85.517(4) | 104.683(4) | 90.000 |
| *γ*/° | 84.035(2) | 66.444(3) | 90.000 | 90.000 |
| *V*/Å$^3$ | 1270.62(8) | 1357.94(12) | 785.15(12) | 1571.4(3) |
| *Z* | 4 | 4 | 2 | 4 |
| *T*/°C | −100(2) | −100(2) | −100(2) | −100(2) |
| *λ*/Å | 0.71073 | 0.71073 | 0.71073 | 0.71073 |
| *D*/Mg m$^{-3}$ | 1.629 | 1.273 | 1.355 | 1.354 |
| *μ*/mm$^{-1}$ | 0.723 | 0.092 | 0.111 | 0.111 |
| $R[I > 2\sigma(I)]^a$ | 0.0436 | 0.0505 | 0.0393 | 0.0389 |
| $R_w$ (all data)$^b$ | 0.0728 | 0.1091 | 0.0512 | 0.0552 |

$^a$ $R = \sum||F_o| - |F_c||/\sum|F_o|$. $^b$ $R = (\sum[w(F_o^2 - F_c^2)^2]/\sum w(F_o^2)^2)^{1/2}$.

Several methods have been reported in the literature for the inversion of the secondary hydroxyl groups and were attempted in the synthesis of 3-inverted quinic acid. In the case of dicyclohexylcarbodiimide (DCC) esterification[19] of methyl TMB-protected quinate **9** with a variety of carboxylic acids (benzoic acid, acetic acid, *p*-nitrobenzoic acid, diacetyl-caffeic acid, diallyl-caffeic acid **5**, acetyl-ferulic acid, allyl-ferulic acid **6**, cinnamic acid and dimethoxycinnamic acid), and in direct kinetic resolution by Ru catalyst[20] in toluene at 70–80 °C for 48 h, only starting material was recovered. Similar results were obtained in the Vilsmeier reaction of protected quinic acid with DMF (*N*,*N*-dimethylformamide) salt.[21]

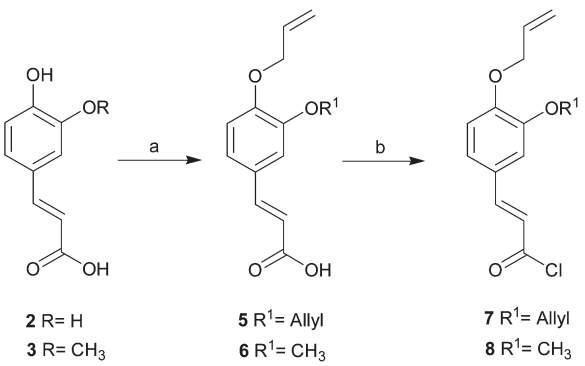
Mitsunobu conditions[22] using Cs salts of protected hydroxycinnamic acids **5** and **6** were attempted but failed to provide the inverted product **12**. However, using the more acidic *p*-nitrobenzoic acid Cs salt as a nucleophile provided inverted ester **11** in moderate yield, which could after hydrolysis and acylation be used as a starting material for the target chlorogenic acids (Scheme 4).

Oxidation of **9** with PCC followed by reduction with sodium triacetoxyborohydride yielded the protected *muco*-quinic acid **10** in improved yield (85% yield)[23] compared to the Mitsunobu reaction and Cs salt (50% yield).[21] After the oxidation–reduction sequence we obtained a 9 : 1 mixture of diastereomers, as judged by the integrals in the crude $^1$H-NMR spectrum (91% yield), which on recrystallisation gave 85% of the inverted *muco*-isomer **10**, whose structure could be confirmed by single crystal X-ray analysis (Table 1 and Fig. 1).[23] The diastereoselectivity of the reduction step can be rationalised by assuming interaction of the borohydride reagent with the free 1-OH alcohol followed by hydride delivery from the side of the 1-OH alcohol to produce an equatorially oriented 3-OH.

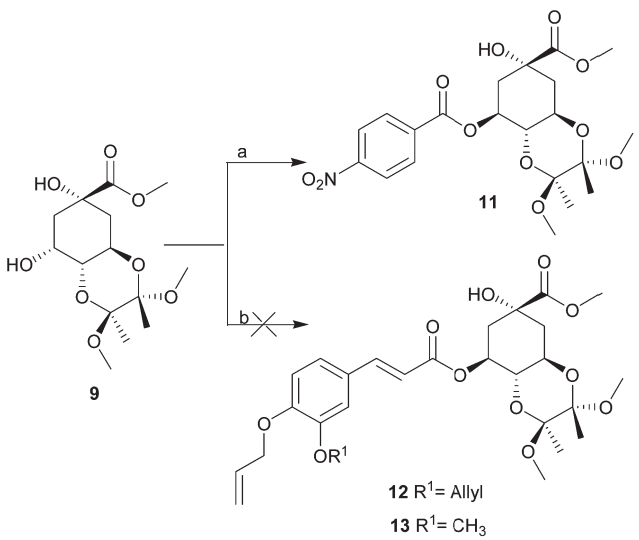
### Esterification

An esterification of methyl TMB-*muco*-quinate **10** and acid chloride **7** or **8** was performed in DCM at reflux temperature for 36 h in the presence of an organic base. For the monoacylation pyridine and 1.5 equivalents of acid chlorides **7** and **8** were used and for the hetero and homo diacylation triethylamine and 1.5 and 3 equivalents of acid chlorides (**7** and **8**) were used, respectively (Scheme 5).

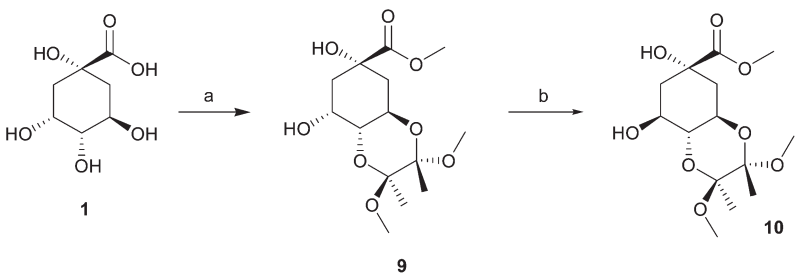
Deprotection of the allyl ether and the TMB group was achieved in one step in the presence of Pd/C catalyst, *p*-toluenesulfonic acid (*p*-TsOH), and aqueous methanol (90%) as a solvent.[24] When the temperature of the reaction was not higher than 60 °C we observed only deprotection of the allyl ether group, while at reflux temperature both groups were deprotected (Scheme 5). For compounds **12** and **13** we used a temperature of 60 °C followed by TFA treatment (Scheme 5) to yield compounds **20** and **21**.




**Scheme 2** *Reagents and conditions*: (a) anhydrous $K_2CO_3$, acetone, allylbromide, NaOH, EtOH, reflux 48 h (80–85%); (b) $(COCl)_2$, DMF, 0 °C, rt, 12 h.




**Scheme 4** *Reagents and conditions*: (a) DIAD, $PPh_3$, *p*-nitrobenzoic acid, toluene, 0 °C, rt, 5 h; (b) DIAD, $PPh_3$, cinnamic acids (**5** and **6**), toluene, 0 °C, rt, 5–48 h.




**Scheme 3** *Reagents and conditions*: (a) MeOH, 2,3-butanedione, trimethylorthoformate, reflux, 48 h; (b) PCC, DCM, rt, 15 h, charcoal, reflux, 2 h, $Na(OAc)_3BH$, $CH_3CN$, $CH_3COOH$, rt, 15 h.

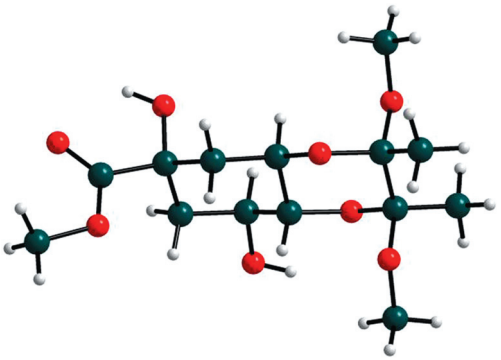


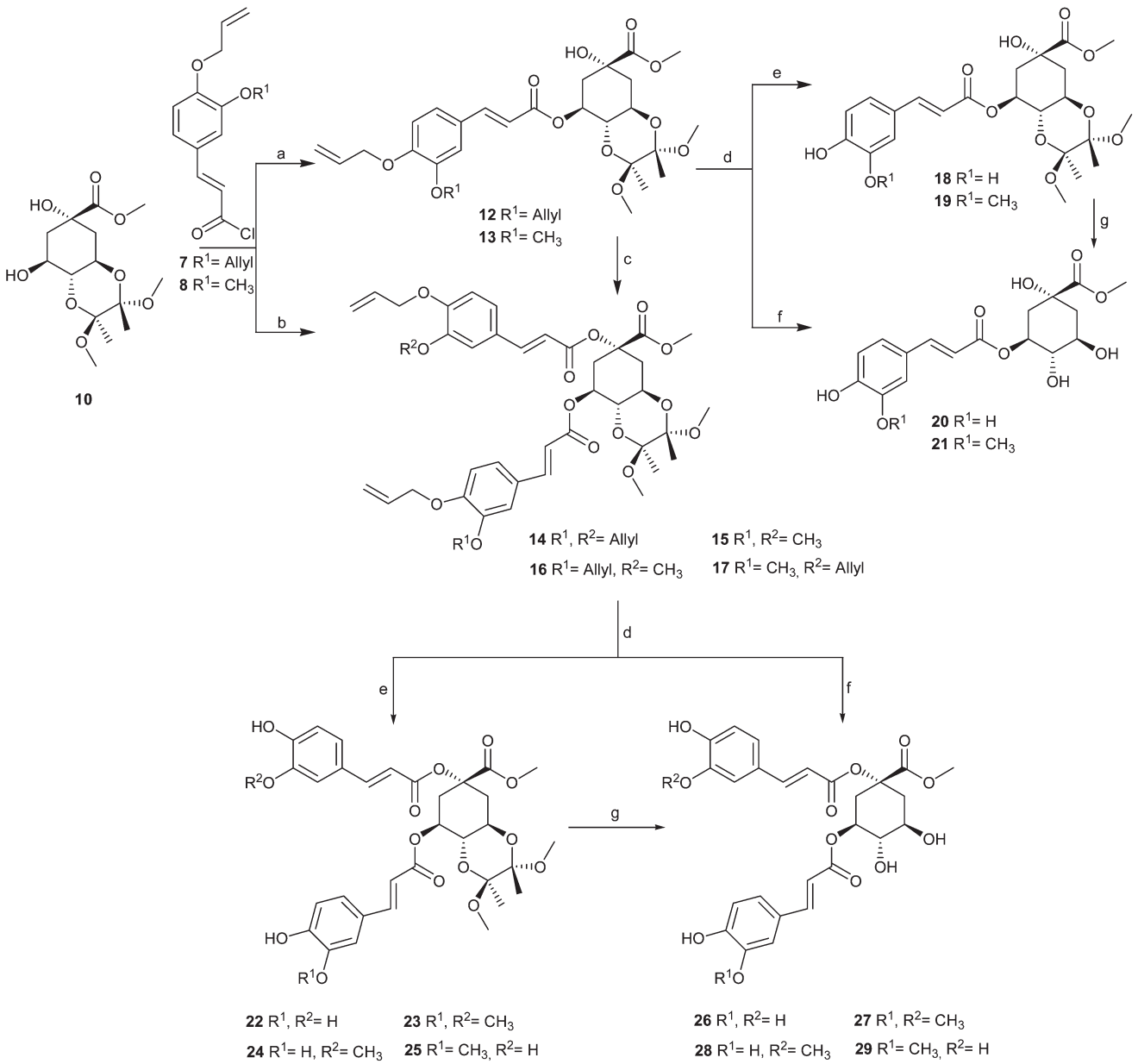
**Fig. 1** X-ray structure of methyl TMB-protected *muco*-quinate **10**.

Additionally we obtained a series of disubstituted *muco*-quinic acid derivatives. Using $NEt_3$ as a base, diacylation was observed to give, after deallylation, the two caffeoyl and feruloyl homoesters **26** and **27**. Using a sequential esterification reaction the two heterodiesters **28** and **29** could be obtained as well. All compounds show the expected spectroscopic data.

### Discriminating between methyl 1-caffeoyl-3-feruloyl-*muco*-quinate 29 and methyl 1-feruloyl-3-caffeoyl-*muco*-quinate 28 by tandem mass spectrometry

In our previous studies we have shown that regioisomers of chlorogenic acids show non-identical tandem mass spectra and their regiochemistry can thus be assigned using tandem MS data.






**Scheme 5** *Reagents and conditions*: (a) pyridine, DMAP, DCM, reflux, 48 h; (b); (c) triethylamine, DMAP, **7** or **8** DCM, reflux, 48 h; (d) Pd/C, methanol–$H_2O$ (9 : 1), *p*-TsOH; (e) 60 °C, 48 h; (f) reflux, 48 h; (g) TFA–water (9 : 1), 0 °C, rt, 2 h.

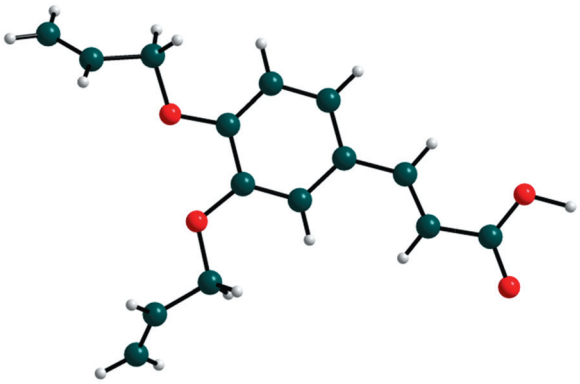


**Fig. 2** X-ray structure of 3,4-di-*O*-allyl caffeic acid **5**.

A similar behaviour was observed for caffeoyl and feruloyl *muco*-quinic acid derivatives. In this section a detailed mass spectrometric identification of methyl 1-caffeoyl-3-feruloyl-*muco*-quinate **29** and methyl 1-feruloyl-3-caffeoyl-*muco*-quinte **28** ($M_W$ 544) is discussed.

Both isomers (**28** and **29**) showed a base peak at *m*/*z* 543 [methyl caffeoyl-feruloyl-*muco*-quinate–$H^+$]$^-$ and an $MS^2$ base peak at *m*/*z* 367 [methyl caffeoyl-*muco*-quinate–$H^+$]$^-$ by losing a feruloyl residue (Fig. 3). Isomer **29** produced an $MS^2$ secondary peak at *m*/*z* 349 [feruloyl-*muco*-quinic acid–$H_2O$–$H^+$]$^-$ with a lower intensity (20%) if compared to isomer **28** (70%) which suggested that the loss of the feruloyl residue for isomer **29** takes place easier than for isomer **28**. In the $MS^3$ spectra isomer **29** produced a secondary peak at *m*/*z* 215 which was completely absent (or its intensity was very low) for **28**. Isomer **29** produced the $MS^4$ base peak at *m*/*z* 161 [caffeic acid–$H_2O$–$H^+$]$^-$ while isomer **28** produced the $MS^4$ base peak at *m*/*z* 173 [*muco*-quinic acid–$H_2O$–$H^+$]$^-$. From the above arguments it is clear that these isomeric chlorogenic acids can be distinguished by their tandem mass spectra in the negative ion mode.

Furthermore, methyl 3-caffeoyl-*muco*-quinate **20**, methyl 3-feruloyl-*muco*-quinate **21**, methyl 1,3-dicaffeoyl-*muco*-quinate **26**, and methyl 1,3-diferuloyl-*muco*-quinate **27** show completely different tandem mass spectra (see ESI†) than the previously reported methyl quinates.[25]

Additionally we wanted to solve the question of whether two diastereoisomers of chlorogenic acids could be unambiguously distinguished based on their fragment spectra. For this purpose we obtained 3-caffeoyl and 3-feruloyl-*muco*-quinic acids **30** and **31** from intermediate **10** after base induced hydrolysis of the methyl ester functionality followed by chemoselective 3-OH acylation and deallylation (see ESI†). The final products **30** and **31** could not be obtained in analytically pure form (80% purity by $^1$H-NMR and LC-MS), however, the final products displayed only a single chromatographic peak at *m*/*z* 353 or 367 respectively in their extracted ion chromatograms.

A direct comparison between the tandem MS spectra of 3-caffeoyl quinic acid **32** and 3-caffeoyl-*muco*-quinic acid **30** (Fig. 4) shows that the two $MS^2$ spectra of the two diastereomeric compounds are indeed radically different and therefore allow distinction and assignment of diastereomeric quinic acid derivatives. In the $MS^2$ spectrum of the *muco* derivative a dehydrated quinic acid fragment ion at *m*/*z* 173 ($C_7H_7O_5$) is apparent, which is

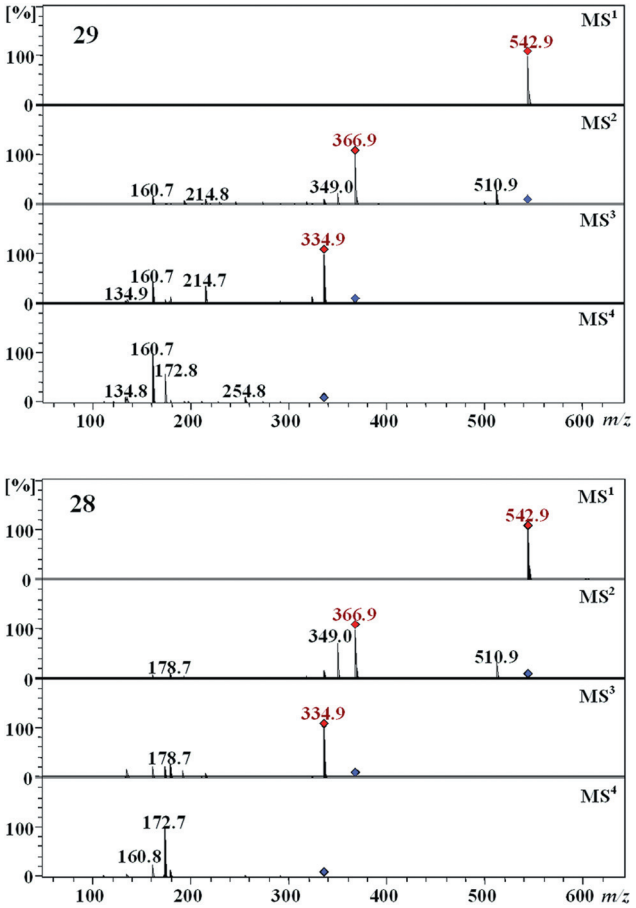



**Fig. 3** $MS^4$ spectra of methyl 1-caffeoyl-3-feruloyl-*muco*-quinate **29** and methyl 1-feruloyl-3-caffeoyl-*muco*-quinate **28** in negative ion mode (parent ion at *m*/*z* 543).

clearly absent from the quinic acid derivative. In earlier work we suggested that such dehydration occurs from a proton induced elimination of water from an inverted chair conformation of a quinic acid derivative.[1] The observation here suggests that in the 3-caffeoyl quinic acid derivative **32** a H-bond from 1-OH to the *syn* 3-acyl carbonyl stabilises the regular chair conformation in the gas phase ion, whereas for the *muco*-derivative this stabilisation is absent due to the 3-acyl equatorial position, hence allowing an inversion of the cyclohexane chair followed by dehydration in **31**. As observed previously the hydrogen bond arrays in the gas phase ions allow rationalisation of fragmentation patterns.

## Discussion of X-ray structures

In the literature single crystal structures of several quinic acid derivatives have been reported. The structures obtained here for diastereomeric compounds **9** and **10** reveal that the quinic acid adopts a perfect chair conformation with the ester substituent in an equatorial position. For compound **9** the 3-OH is clearly in an axial position, whereas for the 3-inverted epimer **10** the alcohol OH is in an equatorial position. Dihedral angles obtained from the structure analysis are in perfect agreement with $^3J_{HCCH}$ coupling constants according to the Karplus relationship.

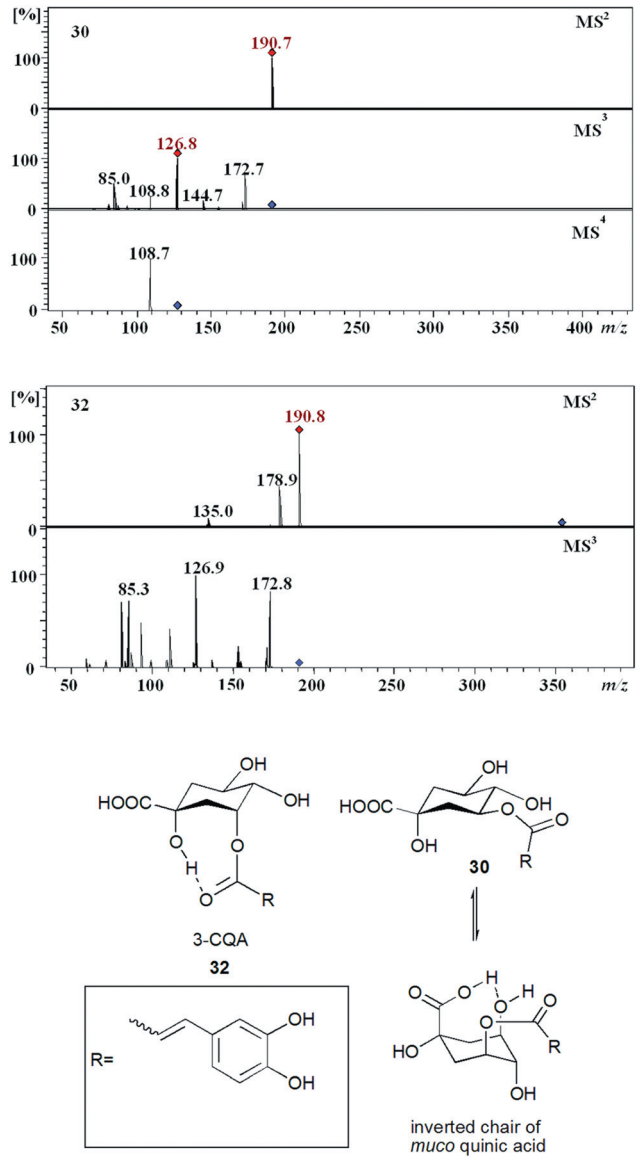



**Fig. 4** $MS^n$ spectra of 3-caffeoyl-*muco*-quinic acid **30** and 3-caffeoyl quinic acid **32** in negative ion mode (parent ion at *m*/*z* 353) with hydrogen bond arrays rationalising fragmentation mechanism.

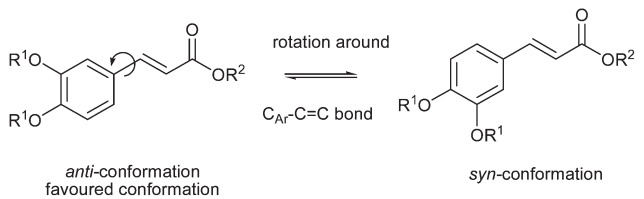



**Fig. 5** Two possible conformations of hydroxycinnamate derivatives.

More interesting are the two single crystal structures of hydroxycinnamate derivatives **4** and **5**, in particular since no structural information exists on hydroxycinnamate derivatives despite their ubiquitous presence in nature and in our diet. An interesting structural problem associated with such derivatives is the preferred conformation with respect to rotation around the $C_{Ar}$–C═C bond. Here two distinct conformations are possible with an *anti*-orientation of the aromatic 3-substituent with respect to the *trans* double bond or a *syn* orientation (Fig. 5). Both single crystal structures clearly show that the *anti*-conformation is preferred in the solid state, which is in line with molecular mechanics calculations at the MM-2 level.

## Conclusions

In conclusion, we have developed the first efficient diastereoselective synthesis of the *muco*-quinic acid derivatives. They are synthesized in good yield in 5 steps starting from quinic acid and cinnamic acids. This is the first time that allyl ether protection of phenolic hydroxyl group has been applied in chlorogenic acids synthesis. Removal of the protecting groups, allyl ether and acetal is achieved in one step. We show tandem MS data of all six derivatives of *muco*-quinic acid and clearly demonstrate that our hierarchical key for assignment of chlorogenic acid regiochemistry can be applied as well to diastereomeric derivatives. More importantly, we demonstrate that diastereoisomers of chlorogenic acids can be assigned on the sole basis of their fragment spectra. We provide the first X-ray crystal structure information of hydroxycinnamates. Finally, it is worth noting that in parallel to this work selected synthetic *muco*-quinic acid derivatives were recently tested for their anticancer activity and against DNA methyltransferase 3a (DNAMT3a) enzyme and found to be moderately active, highlighting the importance of these dietary compounds.[28]

## Experimental

All reagents for reactions were purchased from Sigma-Aldrich or Applichem and were used as obtained. Reactions were carried out using anhydrous solvents. Whenever possible the reactions were monitored by thin layer chromatography (TLC). TLC was performed on Macherey-Nagel aluminium-backed plates precoated with silica gel 60 ($UV_{254}$) and visualization of the spots was carried out using cerium ammonium molybdate staining under heating. Column chromatography was carried out on silica gel 60 (0.040–0.063 mm) under flash conditions. Melting points were determined in open capillaries using a Stuart SMP3 capillary melting point apparatus and are not corrected. FTIR spectra of solids were recorded on KBr plates using a Thermo Nicolet Avatar 360 FT-IR spectrometer; $\nu_{max}$ values expressed in $cm^{-1}$ are given for the main absorption bands. CD spectra were obtained using a Jasco J-810 spectrometer. $^1H$ NMR and $^{13}C$ NMR spectra were acquired on a JEOL ECX-400 spectrometer operating at 400 MHz for $^1H$ NMR and 100 MHz for $^{13}C$ NMR at room temperature in $CDCl_3$, DMSO-$d_6$, $D_2O$ or methanol-$d_4$ using a 5 mm probe. The chemical shifts ($\delta$) are reported in parts per million and were referenced to the residual solvent peak. The coupling constants ($J$) are quoted in hertz. The following abbreviations are used: s, singlet; d, doublet; t, triplet; m, multiplet; bs, broad signal; bd, broad doublet; dd, doublet of doublets, ddd, doublet of doublet of doublets. Mass spectra were recorded using a Bruker Daltonics HCT Ultra ion-trap spectrometer and high resolution mass spectra were recorded using a Bruker Daltonics micrOTOF spectrometer from methanolic or acetonitrile

solutions using the negative/positive electrospray ionization mode (ESI) and 1 M sodium formate solution as a calibrant.

### X-ray crystallography

Crystals were mounted on a Hampton cryoloop in light oil for data collection at −100 °C. Indexing and data collection were performed on a Bruker D8 SMART APEX II CCD diffractometer with $\kappa$ geometry and Mo Kα radiation (graphite monochromator, $\lambda$ = 0.71073 Å). Data integration was performed using *SAINT*. Routine Lorentz and polarization corrections were applied. The SHELX[26] package was used for structure solution and refinement. Refinements were full-matrix least-squares against $F^2$ using all data. In the final refinement, all non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed in calculated positions. Crystallographic data are summarized in Table 1. The CCDC numbers of the compounds **4**, **5**, **9** and **10** are 821571, 821574, 821572 and 821573, respectively.

**Synthesis of methyl TMB-quinate 9.**[18] To a suspension of quinic acid (2 g, 10.40 mmol) in methanol (10 ml) were added 2,3-butanedione (1.86 mL, 21.20 mmol), trimethylorthoformate (5.56 mL, 50.80 mmol) and D-camphorsulfonic acid (121 mg, 0.52 mmol). The mixture was refluxed for 24 h, then cooled to room temperature and treated with sodium bicarbonate (80 mg, 0.80 mmol). The solvent was removed *in vacuo* to give a paste that was dissolved in ethyl acetate. Activated charcoal (4 g) was added and the mixture was refluxed for 4 h, then left to cool to room temperature. The mixture was filtered over a thick pad of silica gel which was further washed using ethyl acetate–methanol (9 : 1) and the resulting colorless filtrate was evaporated *in vacuo* to give a white solid. The crude residue was recrystallized from ethyl acetate to form white shiny needles of protected quinic acid **9** (2.96 g, 90%), mp 137–139 °C (Lit.[23] mp 139–140 °C); $\delta_H$ ($CDCl_3$): 1.26 (3H, s, $CH_3$), 1.31 (3H, s, $CH_3$), 1.89 (1H, d, *J* 12.4, 12.4, 6-*H*H), 2.03 (1H, dd, *J* 15.2, 2.3, 2-*H*H), 2.08 (1H, ddd, *J* 12.8, 3.21, 6-H*H*), 2.16 (1H, ddd, *J* 14.8, 2.75, 2-H*H*), 3.17 (1H, d, *J* 3.2, OH), 3.23 (3H, s, $COCH_3$), 3.25 (3H, s, $COCH_3$), 3.57 (1H, dd, *J* 9.1, 1.83, 4-H), 3.75 (3H, s, $COOCH_3$), 4.16 (1H, m, 3-H), 4.23 (1H, s, OH), 4.27 (1H, ddd, *J* 11, 9, 4, 5-H); $\delta_C$ ($CDCl_3$): 17.7 ($CH_3$), 17.8 ($CH_3$), 37.4 (C-2), 38.7 (C-6), 47.9 (CO*C*H$_3$), 48.0 (CO*C*H$_3$), 52.9 (COO*C*H$_3$), 62.7 (C-3), 69.2 (C-5), 72.86 (C-4), 75.8 (C-1), 99.8 (*C*OCH$_3$), 100.4 (*C*OCH$_3$), 174.3 (*C*OOCH$_3$); HRMS (ESI−): Exact mass calculated for $C_{14}H_{23}O_8$ [M − $H^+$]$^-$, 319.1398. Found 319.1403.

**Synthesis of methyl TMB-quinate ketone 33.**[23] To a stirred solution of protected quinic acid **9** (2 g, 6.25 mmol) in anhydrous dichloromethane (50 mL) was added PCC (7.72 g, 35.80 mmol) and the reaction mixture was stirred for 16 h at room temperature. The mixture was diluted with DCM (100 mL), filtered through a thick pad of silica gel and residue was washed with ethyl acetate. The brown filtrate was treated with activated charcoal and refluxed for 2 h. After cooling to room temperature, the mixture was filtered over a thick pad of silica gel which was washed with ethyl acetate–methanol (9 : 1, 200 mL). The filtrate was concentrated *in vacuo* and recrystallized from ethyl acetate to give the methyl TMB-quinate ketone **33** as a white solid (1.75 g, 88%), mp 216–217 °C (Lit.[23] mp 212–214 °C); $\delta_H$ ($CDCl_3$): 1.27 (3H, s, $CH_3$), 1.37 (3H, s, $CH_3$), 2.08 (1H, ddd, *J* 13.3, 3.7, 1.4, 6-*H*H), 2.33 (1H, dd, *J* 12.4, 12.4, 6-H*H*), 2.47 (1H, dd, *J* 14.2, 2.7, 2-*H*H), 2.87 (1H, d, *J* 14.2, 2-H*H*), 3.20 (3H, s, $COCH_3$), 3.23 (3H, s, $COCH_3$), 3.29 (1H, br s, OH), 3.81 (3H, s, $COOCH_3$), 4.23 (1H, m, 4-H), 4.39 (1H, d, *J* 10.1, 5-H); $\delta_C$ ($CDCl_3$): 17.5 ($CH_3$), 17.7 ($CH_3$), 37.9 (C-6), 48.0 (CO*C*H$_3$), 48.43 (CO*C*H$_3$), 49.1 (C-2), 53.7 (COO*C*H$_3$), 67.1 (C-5), 74.12 (C-1), 77.3 (C-4), 99.7 (*C*OCH$_3$), 100.6 (*C*OCH$_3$), 174.2 (*C*OOCH$_3$), 199.5 (C-3); HRMS (ESI−): Exact mass calculated for $C_{14}H_{21}O_8$ [M − $H^+$]$^-$, 317.1236. Found 317.1244.

**Synthesis of methyl TMB-*muco*-quinate 10.**[22] To a solution of acid ketone **33** (2 g, 6.29 mmol) in $CH_3CN$ (25 mL) and $CH_3COOH$ (25 mL) was added $Na(OAc)_3BH$ (5.3 g, 25 mmol). The mixture was stirred at room temperature for 15 h. Solvents were removed *in vacuo*, and the residue was dissolved in EtOAc and washed with $NaHCO_3$ solution (1 M, 50 mL). The aqueous layer was back extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$ and concentrated *in vacuo* to a white solid. Purification by flash column chromatography (ethyl acetate–petroleum ether, 1 : 1) gave a mixture of solid diols, which on recrystallisation gave inverted diol **10** (1.71 g, 85%) and starting diol **9** (4%), mp 168–169 °C (Lit.[22] mp 164–166 °C); $\delta_H$ ($CDCl_3$): 1.28 (3H, s, $CH_3$), 1.31 (3H, s, $CH_3$), 1.84 (1H, m), 1.98 (1H, m), 2.08 (1H, m), 2.16 (1H, m), 2.43 (1H, br s, OH), 3.24 (3H, s, $COCH_3$), 3.28 (3H, s, $COCH_3$), 3.46 (1H, dd, *J* 10, 10, 4-H), 3.79 (3H, s, $COOCH_3$), 3.94 (1H, m, 3-H), 4.01 (1H, m, 5-H); $\delta_C$ ($CDCl_3$): 17.7 ($CH_3$), 17.8 ($CH_3$), 37.9 (C-2), 40.6 (C-6), 47.9 (CO*C*H$_3$), 48.0 (CO*C*H$_3$), 53.3 (COO*C*H$_3$), 65.2 (C-3), 67.0 (C-5), 73.4 (C-1), 76.4 (C-4), 99.6 (*C*OCH$_3$), 99.6 (*C*OCH$_3$), 175.8 (*C*OOCH$_3$); HRMS (ESI−): Exact mass calculated for $C_{14}H_{23}O_8$ [M − $H^+$]$^-$, 319.1398. Found 319.1404.

**Synthesis of 3,4-di-*O*-allyl caffeic acid 5.** A mixture of caffeic acid (2 g, 11.10 mmol) and anhydrous potassium carbonate (15.03 g, 108.78 mmol) in acetone (100 mL) was stirred at room temperature for 0.5 h. To the mixture was added a solution of allyl bromide (4.7 g, 38.85 mmol) in acetone (10 mL) and the resulting mixture was refluxed for 48 h. The reaction was cooled to room temperature, filtered and the filtrate was dried *in vacuo*. The residue was suspended in ethanol (60 mL) and NaOH solution (2 M, 40 mL). The mixture was refluxed for 2 h. The solution was cooled to room temperature and poured into a beaker and acidified (pH = 2) with conc. HCl. The suspension was stirred at room temperature for 0.5 h and the solid was filtered off and washed successively with a 1 : 1 mixture of ethanol and water (200 mL). The solid was dried overnight in vacuum to yield a colorless powder (2.45 g, 85%) which on crystallization gave white needle-shaped crystals (Fig. 2 and Table 1), mp 158–159 °C (Lit.[27] mp 150–152 °C); $\delta_H$ ($CDCl_3$): 4.64 (4H, m, $C_{Ar}$–$OCH_2$), 5.29 (1H, d, *J* 9.62, CH*H*═CH), 5.31 (1H, d, *J* 9.60, CH*H*═CH), 5.45 (1H, d, *J* 16.94, *CH*H═CH), 5.45 (1H, d, *J* 16.94, *CH*H═CH), 6.07 (2H, m, $CH_2$═*CH*), 6.27 (1H, d, *J* 15.7, $C_{Ar}$–CH═*CH*), 6.87 (1H, d, *J* 8.6, $C_{Ar}$*H*), 7.09 (1H, d, *J* 1.7, $C_{Ar}$*H*), 7.11 (1H, dd, *J* 8.2, 1.9 $C_{Ar}$*H*), 7.69 (1H, d, *J* 15.7, $C_{Ar}$–*CH*); $\delta_C$ ($CDCl_3$): 69.5 ($C_{Ar}$–*O*$CH_2$), 70.1

($C_{Ar}$–O$CH_2$), 112.7 ($C_{Ar}$), 113.4 ($C_{Ar}$), 115.1 (*C*H–COO), 118.0 (*C*$H_2$=CH), 118.1 (*C*$H_2$=CH), 123.2 ($C_{Ar}$), 127.4 ($C_{Ar}$–CH), 132.7 ($CH_2$=*C*H), 133.1 ($CH_2$=*C*H), 146.8 ($C_{Ar}$–*C*H), 148.6 ($C_{Ar}$–$OCH_2$), 151.3 ($C_{Ar}$–$OCH_2$), 172.8 (COOH); HRMS (ESI−): Exact mass calculated for $C_{15}H_{15}O_4$ [M − $H^+$]$^-$, 259.0970. Found 259.0973.

**Synthesis of 4-*O*-allyl ferulic acid 6.** A mixture of ferulic acid (2 g, 10.3 mmol) and anhydrous potassium carbonate (10.3 g, 74.5 mmol) in acetone (70 mL) was stirred at room temperature for 0.5 h. To the mixture was added a solution of allyl bromide (2.49 g, 20.60 mmol) in acetone (10 mL) and the resulting mixture was refluxed for 48 h. The reaction was cooled to room temperature, filtered and the filtrate was dried *in vacuo*. The residue was suspended in ethanol (60 mL) and NaOH solution (2 M, 40 mL). The mixture was refluxed for 2 h. The solution was cooled to room temperature and poured into a beaker and acidified (pH = 2) with conc. HCl. The suspension was stirred at room temperature for 0.5 h and the solid was filtered off and washed successively with a 1 : 1 mixture of ethanol and water (150 mL). The solid was dried overnight in vacuum to yield a colorless powder (2.03 g, 84%), mp 151–153 °C (Lit.[17] mp 150–152 °C); $\delta_H$ ($CDCl_3$): 3.90 (3H, s, $C_{Ar}$–$OCH_3$), 4.65 (2H, d, *J* 5.5, $C_{Ar}$–$OCH_2$), 5.30 (1H, d, *J* 10.2, CH*H*=CH), 5.45 (1H, d, *J* 16.4, C*H*H=CH), 6.08 (1H, m, $CH_2$=C*H*), 6.28 (1H, d, *J* 16, $C_{Ar}$–CH=C*H*), 6.87 (1H, d, *J* 8.8, $C_{Ar}$*H*), 7.08 (1H, d, *J* 1.8, $C_{Ar}$*H*), 7.14 (1H, dd, *J* 8.7, 1.8, $C_{Ar}$*H*), 7.73 (1H, d, *J* 16, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 55.9 ($C_{Ar}$–O*C*$H_3$), 69.8 ($C_{Ar}$–O*C*$H_2$), 110.3 ($C_{Ar}$), 112.9 ($C_{Ar}$), 114. 9 (*C*H–COO), 118.5 (*C*$H_2$=CH), 122.9 ($C_{Ar}$), 127.2 ($C_{Ar}$–CH), 132.7 ($CH_2$=*C*H), 147.0 ($C_{Ar}$–*C*H), 149.7 ($C_{Ar}$–$OCH_3$), 150.6 ($C_{Ar}$–$OCH_2$), 172.3 (COOH); HRMS (ESI+): Exact mass calculated for $C_{13}H_{13}O_4$ [M − $H^+$]$^-$, 233.0819. Found 233.0830.

**Synthesis of 3,4-di-*O*-allyl caffeic acid chloride 7.** 3,4-Di-*O*-allyl caffeic acid (2 g, 7.68 mmol) was suspended in toluene (40 mL) containing 5 drops of DMF, and oxalyl chloride (1.82 g, 14.36 mmol) was added at 0 °C. The suspension was stirred for 10 h at room temperature and a clear brown solution was formed. Toluene and unreacted oxalyl chloride were removed under reduced pressure. The yellow solid residue was washed with petroleum ether and dried *in vacuo* to give 3,4-di-*O*-allyl caffeic acid chloride **7** as a brown powder (2.05 g, 96%), mp 187–188 °C; $\delta_H$ ($CDCl_3$): 4.64 (4H, m, $C_{Ar}$–$OCH_2$), 5.30 (2H, d, *J* 10.5, CH*H*=CH), 5.43 (2H, d, *J* 16.49, C*H*H=CH), 6.07 (2H, m, $CH_2$=C*H*), 6.45 (1H, d, *J* 15.6, $C_{Ar}$–CH=C*H*), 6.88 (1H, d, *J* 8.7, $C_{Ar}$*H*), 7.08 (1H, d, *J* 1.6, $C_{Ar}$*H*), 7.15 (1H, dd, *J* 8.0, 1.8, $C_{Ar}$*H*), 7.74 (1H, d, *J* 15.6, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 69.6 ($C_{Ar}$–O*C*$H_2$), 70.1 ($C_{Ar}$–O*C*$H_2$), 113.2 ($C_{Ar}$), 113.3 ($C_{Ar}$), 118.2 (*C*H–COO), 118.3 (*C*$H_2$=CH), 119.8 (*C*$H_2$=CH), 124.7 ($C_{Ar}$), 126.2 ($C_{Ar}$–CH), 132.5 ($CH_2$=*C*H), 132.9 ($CH_2$=*C*H), 148.8 ($C_{Ar}$–*C*H), 150.9 ($C_{Ar}$–$OCH_2$), 152.3 ($C_{Ar}$–$OCH_2$), 166.1 (COCl).

**Synthesis of 4-*O*-allyl ferulic acid chloride 8.** 4-*O*-Allyl ferulic acid (1.80 g, 7.68 mmol) was suspended in toluene (40 mL) containing 5 drops of DMF and oxalyl chloride (1.82 g, 14.36 mmol) was added at 0 °C. The suspension was stirred for 10 h at room temperature and a clear yellow solution was formed. Toluene and unreacted oxalyl chloride were removed under reduced pressure. The yellow solid residue was washed with petroleum ether and dried *in vacuo* to give 4-*O*-allyl ferulic acid chloride **8** as a shiny yellow powder (1.71 g, 88%), mp 181–183 °C; $\delta_H$ ($CDCl_3$): 3.92 (3H, s, $C_{Ar}$–$OCH_3$), 4.66 (2H, d, *J* 5.4, $C_{Ar}$–$OCH_2$), 5.32 (1H, dd, *J* 10, CH*H*=CH), 5.41 (1H, d, *J* 15.6, C*H*H=CH), 6.07 (1H, m, $CH_2$=C*H*), 6.45 (1H, d, *J* 16, $C_{Ar}$–CH=C*H*), 6.88 (1H, d, *J* 8.2, $C_{Ar}$*H*), 7.06 (1H, d, *J* 1.8, $C_{Ar}$*H*), 7.13 (1H, dd, *J* 8.4, 2.0, $C_{Ar}$*H*), 7.76 (1H, d, *J* 16, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 56.1 ($C_{Ar}$–O*C*$H_3$), 69.8 ($C_{Ar}$–O*C*$H_2$), 110.7 ($C_{Ar}$), 112.9 ($C_{Ar}$), 118.7 (*C*H–COCl), 119.9 (*C*$H_2$=CH), 124.4 ($C_{Ar}$), 126.3 ($C_{Ar}$–CH), 132.5 ($CH_2$=*C*H), 149.9 ($C_{Ar}$–*C*H), 151.8 ($C_{Ar}$–$OCH_3$), 151.8 ($C_{Ar}$–$OCH_2$) 166.1 (COCl).

**Synthesis of methyl 3-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate 13.** To a solution of methyl TMB-*muco*-quinate **10** (1 g, 3.12 mmol) and 4-(dimethyl amino)-pyridine (DMAP) (77 mg, 0.63 mmol) in DCM (50 mL) were added pyridine (10 mL) and acid chloride **8** (1.18 g, 4.68 mmol) at room temperature. The reaction mixture was refluxed for 24 h and acidified with a 1 M HCl solution to pH = 3. The layers were separated and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 30–50%) to give methyl 3-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate **13** as a pale yellow powder (1.60 g, 96%), mp 101–103 °C; $\nu_{max}$/$cm^{-1}$ (KBr) 3423br, 3080w, 2992, 2951, 1749s, 1713s, 1631vs, 1597vs, 1264s, 1139; $\delta_H$ ($CDCl_3$): 1.24 (3H, s, $CH_3$), 1.26 (3H, s, $CH_3$), 1.86 (1H, dd, *J* 13.0, 11.4, 6-*H*H), 1.89 (1H, ddd, *J* 12.5, 5, 2.2, 2-*H*H), 1.97 (1H, t, *J* 12.5, 6-H*H*), 2.25 (1H, ddd, *J* 12.8, 5.0, 2.3, 2-H*H*), 3.20 (3H, S, $COCH_3$), 3.28 (3H, s, $COCH_3$), 3.75 (1H, t, *J* 10.1, 4-H), 3.75 (3H, s, $COOCH_3$), 3.87 (3H, s, $C_{Ar}$–$OCH_3$), 4.09 (1H, ddd, *J* 11.4, 5.0, 1.8, 3-H), 4.60 (2H, d, *J* 2.3, $C_{Ar}$–$OCH_2$), 5.27 (2H, m, CH*H*=CH), 5.38 (1H, ddd, *J* 12.8, 2.5, 1.4, C*H*H=CH), 6.1 (1H, m, $CH_2$=C*H*), 6.23 (1H, d, *J* 16.0, $C_{Ar}$–CH=C*H*), 6.82 (1H, d, *J* 8.7, $C_{Ar}$*H*), 7.04 (2H, m, $C_{Ar}$*H*), 7.57 (1H, d, *J* 16.0, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 17.7 ($CH_3$), 17.8 ($CH_3$), 37.5 (C-2), 38.9 (C-6), 47.8 ($COCH_3$), 48.0 ($COCH_3$), 53.2 ($COOCH_3$), 56.0 (Ar–O*C*$H_3$), 65.6 (C-3), 69.3 (C-5), 69.8 ($C_{Ar}$–O*C*$H_2$), 73.3 (C-4), 73.5 (C-1), 99.6 ($COCH_3$), 99.7 ($COCH_3$), 110.2 ($C_{Ar}$), 112.9 ($C_{Ar}$), 115.8 (*C*H–COO), 118.4 (*C*$H_2$=CH), 122.5 ($C_{Ar}$), 127.6 ($C_{Ar}$–CH), 132.8 ($CH_2$=*C*H), 144.9 ($C_{Ar}$–*C*H), 149.6 ($C_{Ar}$–$OCH_3$), 150.2 ($C_{Ar}$–$OCH_2$), 166.3 (CH–*C*OO), 175.2 (*C*$OOCH_3$); HRMS (ESI+): Exact mass calculated for $C_{27}H_{36}O_{11}Na$ [M + $Na^+$]$^+$, 559.2155. Found 559.2154.

**Synthesis of methyl 1,3-di-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate 15.** To a solution of methyl TMB-*muco*-quinate **10** (500 mg, 1.56 mmol) and DMAP (77 mg, 0.63 mmol) in DCM (50 mL) were added triethylamine (10 mL) and acid chloride **8** (1.34 g, 5.30 mmol) at room temperature. The reaction mixture was refluxed for 36 h and acidified with a 1 M HCl solution to pH = 3. The layers were separated and the aqueous phase was extracted with DCM (3 × 60 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 30–50%) to give methyl 1,3-di-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate **15**

as a pale yellow powder (856 mg, 73%), mp 134–136 °C; $\nu_{max}$/cm$^{-1}$ (KBr) 3544v, 2993, 2952, 2833, 1749, 1714, 1631, 1597, 1511, 1264, 1139, 1035; $\delta_H$ ($CDCl_3$): 3.92 (3H, s, $C_{Ar}$–$OCH_3$), 4.66 (2H, d, *J* 5.4, $C_{Ar}$–$OCH_2$), 5.32 (1H, dd, *J* 10, CH*H*═CH), 5.41 (1H, d, *J* 15.6, C*H*H═CH), 6.07 (1H, m, $CH_2$═C*H*), 6.45 (1H, d, *J* 16, $C_{Ar}$–CH═C*H*), 6.88 (1H, d, *J* 8.2, $C_{Ar}$*H*), 7.06 (1H, d, *J* 1.8, $C_{Ar}$*H*), 7.13 (1H, dd, *J* 8.4, 2.0, $C_{Ar}$*H*), 7.76 (1H, d, *J* 16, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 56.1 ($C_{Ar}$–O*C*H$_3$), 69.8 ($C_{Ar}$–O*C*H$_2$), 110.7 (*C*$_{Ar}$), 112.9 (*C*$_{Ar}$), 118.7 (*C*H–COCl), 119.9 (*C*H$_2$═CH), 124.4 (*C*$_{Ar}$), 126.3 (*C*$_{Ar}$–CH), 132.5 ($CH_2$═*C*H), 149.9 ($C_{Ar}$–*C*H), 151.8 (*C*$_{Ar}$–$OCH_3$), 151.8 (*C*$_{Ar}$–$OCH_2$) 166.1 (COCl).

**Synthesis of methyl 3-*O*-(3,4-di-*O*-allyl)-caffeoyl-TMB-*muco*-quinate 12.** To a solution of methyl TMB-*muco*-quinate **10** (1 g, 3.12 mmol) and DMAP (77 mg, 0.63 mmol) in DCM (50 mL) were added pyridine (10 mL) and acid chloride **7** (1.30 g, 4.68 mmol) at room temperature. The reaction mixture was refluxed for 36 h and acidified with a 1 M HCl solution to pH = 3. The layers were separated and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 20–40%) to give methyl 3-*O*-(3,4-di-*O*-allyl)-caffeoyl-TMB-*muco*-quinate **12** as a pale yellow powder (1.66 g, 95%), mp 82–84 °C; $\nu_{max}$/cm$^{-1}$ (KBr) 3423, 2951, 2992, 3080, 1749, 1713, 1631, 1597, 1511, 1264, 1139, 1076; $\delta_H$ ($CDCl_3$): 1.28 (6H, s, $CH_3$), 1.85 (2H, m, 6-*H*H, 2-*H*H), 1.99 (1H, t, *J* 12.4, 6-H*H*), 2.23 (1H, m, 2-H*H*), 3.16 (1H, m, 2-H*H*), 3.24 (6H, s, $COCH_3$), 3.31 (3H, s, $COOCH_3$), 3.77 (1H, t, *J* 10, 4-H), 4.10 (1H, ddd, *J* 14.2, 12.3, 5, 3-H), 4.6 (4H, m, $C_{Ar}$–$OCH_2$), 5.29 (2H, d, *J* 9.62, CH*H*═CH), 5.43 (2H, d, *J* 16.9, C*H*H═CH), 6.06 (2H, m, $CH_2$═C*H*), 6.21 (1H, d, *J* 16, $C_{Ar}$–CH═C*H*), 6.85 (1H, d, *J* 8.7, $C_{Ar}$*H*), 7.04 (2H, m, $C_{Ar}$*H*), 7.56 (1H, d, *J* 16, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 17.7 ($CH_3$), 17.8 ($CH_3$), 37.5 (C-2), 38.7 (C-6), 47.7 (CO*C*H$_3$), 47.9 (CO*C*H$_3$), 53.2 (COO*C*H$_3$), 65.5 (C-3), 69.2 (C-5), 69.7 ($C_{Ar}$–O*C*H$_2$), 70.0($C_{Ar}$–O*C*H$_2$), 73.2 (C-4), 73.46 (C-1), 99.6 (*C*OCH$_3$), 99.9 (*C*OCH$_3$), 112.9 (*C*$_{Ar}$), 113.5 (*C*$_{Ar}$), 115.9 (*C*H–COO), 117.9 (*C*H$_2$═CH), 117.9 (*C*H$_2$═CH), 122.4 (*C*$_{Ar}$), 127.6 (*C*$_{Ar}$–CH), 132.9 ($CH_2$═*C*H), 133.2 ($CH_2$═*C*H), 144.8 ($C_{Ar}$–*C*H), 148.6 (*C*$_{Ar}$–$OCH_2$), 150.7 (*C*$_{Ar}$–$OCH_2$), 166.2 (CH–*C*OO), 175.3 (*C*OOCH$_3$); HRMS (ESI+): Exact mass calculated for $C_{29}H_{38}O_{11}Na$ [M + $Na^+$]$^+$, 585.2155. Found 559.2154.

**Synthesis of methyl 1,3-di-*O*-(3,4-di-*O*-allyl)-caffeoyl-methyl-TMB-*muco*-quinate 14.** To a solution of methyl TMB-*muco*-quinate **10** (500 mg, 1.56 mmol) and DMAP (77 mg, 0.63 mmol) in DCM (50 mL) were added triethylamine (15 mL) and acid chloride **7** (1.48 g, 5.30 mmol) at room temperature. The reaction mixture was refluxed for 36 h and acidified with a 1 M HCl solution to pH = 3. The layers were separated and the aqueous phase was extracted with DCM (3 × 60 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 20–40%) to give methyl 1,3-di-*O*-(3,4-di-*O*-allyl)-caffeoyl-TMB-*muco*-quinate **14** as a pale yellow powder (930 mg, 74%), mp 112–114 °C; $\nu_{max}$/cm$^{-1}$ (KBr) 3474, 2991, 2951, 1749, 1713, 1631, 1597, 1511, 1265, 1138, 1170, 1075; $\delta_H$ ($CDCl_3$): 1.28 (3H,s, $CH_3$), 1.29 (3H, s, $CH_3$), 2.05 (1H, t, *J* 13.2, 6-*H*H), 2.55 (1H, dd, *J* 13.2, 2-*H*H), 2.78 (1H, dd, *J* 13.7, 2.3, 6-H*H*), 3.78 (1H, t, *J* 10.1, 4-H), 3.99 (1H, ddd, *J* 12.8, 9.6, 5.8, 3-H), 4.62 (4H, m, $C_{Ar}$–$OCH_2$), 4.65 (4H, m, $C_{Ar}$–$OCH_2$), 5.29 (4H, m, CH*H*═CH), 5.43 (4H, m, C*H*H═CH), 6.07 (4H, m, $CH_2$═C*H*), 6.22 (1H, d, *J*, 16.1, $C_{Ar}$–CH═C*H*), 6.30 (1H, d, *J* 15.6, $C_{Ar}$–CH═C*H*), 6.85 (1H, d, *J* 8.7, $C_{Ar}$*H*), 6.87 (1H, d, *J* 7, $C_{Ar}$*H*), 7.06 (4H, m, $C_{Ar}$*H*), 7.57 (1H, *J* 16.1, $C_{Ar}$–C*H*), 7.62 (1H, *J* 15.6, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 17.7 ($CH_3$), 17.7 ($CH_3$), 34.7 (C-2), 36.4 (C-6), 47.8 (CO*C*H$_3$), 48.1 (CO*C*H$_3$), 52.8 (COO*C*H$_3$), 65.2 (C-3), 68.4 (C-5), 69.7 ($C_{Ar}$-O*C*H$_2$), 69.7 ($C_{Ar}$–O*C*H$_2$), 69.9 ($C_{Ar}$–O*C*H$_2$), 70.1 ($C_{Ar}$–O*C*H$_2$), 73.3 (C-4), 78.9 (C-1), 99.8 (*C*OCH$_3$), 99.8 (*C*OCH$_3$), 112.4 (*C*$_{Ar}$), 113.3 (*C*$_{Ar}$), 113.5 (*C*$_{Ar}$), 114.5 (*C*$_{Ar}$), 115.6 (*C*H–COO), 117.9 (*C*H–COO), 118.0 (*C*H$_2$═CH), 118.1 (*C*H$_2$═CH), 118.1 (*C*H$_2$═CH), 122.9 (*C*$_{Ar}$), 123.5 (*C*$_{Ar}$), 127.3 (*C*$_{Ar}$–CH), 127.5 (*C*$_{Ar}$–CH), 132.9 ($CH_2$═*C*H), 133.1 ($CH_2$═*C*H), 133.2 ($CH_2$═*C*H), 145.1 ($C_{Ar}$–*C*H), 146.6 ($C_{Ar}$–*C*H), 148.6 (*C*$_{Ar}$–$OCH_2$), 148.7 (*C*$_{Ar}$–$OCH_2$), 150.8 (*C*$_{Ar}$–$OCH_2$), 151.0 (*C*$_{Ar}$–$OCH_2$), 165.5 (CH–*C*OO), 166.1 (CH–*C*OO), 170.9 (*C*OOCH$_3$); HRMS (ESI+): Exact mass calculated for $C_{44}H_{52}O_{14}Na$ [M + $Na^+$]$^+$, 827.3255. Found 827.3256.

**Synthesis of methyl 1-*O*-(4-*O*-allyl)-feruloyl-3-*O*-(3,4-di-*O*-allyl)-caffeoyl-TMB-*muco*-quinate 16.** To a solution of methyl 3-*O*-(3,4-di-*O*-allyl)-caffeoyl-TMB-*muco*-quinate **12** (600 mg, 1.07 mmol) and DMAP (100 mg, 0.82 mmol) in DCM (50 mL) were added triethylamine (15 mL) and acid chloride **8** (541 mg, 2.14 mmol) at room temperature. The reaction mixture was refluxed for 36 h and acidified with a 1 M HCl solution to pH = 3. The layers were separated and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 20–40%) to give methyl 1-*O*-(4-*O*-allyl)-feruloyl-3-*O*-(3,4-di-*O*-allyl)-caffeoyl-TMB-*muco*-quinate **16** as a pale yellow powder (605 mg, 73%), mp 101–102 °C; $\nu_{max}$/cm$^{-1}$ (KBr) 3423, 1992, 2951, 3080, 1749, 1713, 1631, 1597, 1264, 1139; $\delta_H$ ($CDCl_3$): 1.27 (3H, s, $CH_3$), 1.28 (3H, s, $CH_3$), 1.90 (1H, dd, *J* 13.6, 11.5, 6-*H*H), 2.04 (1H, t, 12.8, 2-*H*H), 2.55 (1H, ddd, *J* 12.4, 6.9, 2-H*H*), 2.78 (1H, ddd, *J* 11.4, 6.8, 6-H*H*), 3.21 (3H, s, $CH_3$, $COCH_3$), 3.28 (3H, s, $CH_3$, $COCH_3$), 3.72 (3H,s, $CH_3$, $COOCH_3$), 3.8 (1H, t, *J* 10.1, 4-H), 3.9 (3H, s, $CH_3$, $C_{Ar}$–$OCH_3$), 3.97 (1H, ddd, *J* 14.1, 10, 4.5, 3-H), 4.64 (6H, m, $C_{Ar}$–$OCH_2$), 5.3 (3H, m, CH*H*═CH), 5.4 (1H, dd, *J* 8, 1.37, C*H*H═CH), 5.41 (1H, dd, *J* 11, 1.37, C*H*H═CH), 5.45 (1H, dd, *J*, 11.9, 1.8, C*H*H═CH), 6.06 (4H, m $CH_2$═C*H*), 6.25 (1H, d, *J* 16.0, $C_{Ar}$–CH═C*H*), 6.30 (1H, d, *J* 15.6, $C_{Ar}$–CH═C*H*), 6.83 (1H, d, *J* 8.7, $C_{Ar}$*H*), 6.86 (1H, d, *J* 8.2, $C_{Ar}$*H*), 7.02 (2H, s, $C_{Ar}$*H*), 7.05 (1H, dd, *J* 5.1, 2.3, $C_{Ar}$*H*), 7.08 (1H, dd, *J* 7.8, 1.8, $C_{Ar}$*H*), 7.59 (1H, d, *J* 16.0, $C_{Ar}$–C*H*), 7.62 (1H, d, *J* 16.0, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 17.7 ($CH_3$), 17.7 ($CH_3$), 34.7 (C-2), 36.4 (C-6), 47.8 (CO*C*H$_3$), 48.0 (CO*C*H$_3$), 52.8 (COO*C*H$_3$), 56.0 ($C_{Ar}$–O*C*H$_3$), 65.2 (C-3), 68.4 (C-5), 69.8 ($C_{Ar}$–O*C*H$_2$), 69.8 ($C_{Ar}$–O*C*H$_2$), 70.0 ($C_{Ar}$–O*C*H$_2$), 73.2 (C-4), 78.8 (C-1), 99.7 (*C*OCH$_3$), 99.8 (*C*OCH$_3$), 110.1 (*C*$_{Ar}$), 112.4 (*C*$_{Ar}$), 112.9 (*C*$_{Ar}$),

113.5 ($C_{Ar}$), 114.4 (*C*H–COO), 115.6 (*C*H–COO), 118.0 ($CH_2$═CH), 118.1 ($CH_2$═CH), 118.4 ($CH_2$═CH), 122.5 ($C_{Ar}$), 123.4 ($C_{Ar}$), 127.2 ($C_{Ar}$–CH), 127.5 ($C_{Ar}$–CH), 132.8 ($CH_2$═*C*H), 132.9 ($CH_2$═*C*H), 133.0 ($CH_2$═*C*H), 145.1 ($C_{Ar}$–*C*H), 146.6 ($C_{Ar}$–*C*H), 148.6 ($C_{Ar}$–$OCH_3$), 149.5 ($C_{Ar}$–$OCH_2$), 150.3 ($C_{Ar}$–$OCH_2$), 151.0 ($C_{Ar}$–$OCH_2$), 165.1 (CH–*C*OO), 166.1 (CH–*C*OO), 170.9 (*C*$OOCH_3$). HRMS (ESI+): Exact mass calculated for $C_{42}H_{50}O_{14}Na$ $[M + Na^+]^+$, 801.3098. Found 801.3098.

**Synthesis of methyl 1-*O*-(3,4-di-*O*-allyl)-caffeoyl-3-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate 17.** To a solution methyl 3-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate **13** (700 mg, 1.30 mmol) and DMAP (100 mg, 0.82 mmol) in DCM (50 mL) were added triethylamine (15 mL) and acid chloride **7** (725 mg, 2.6 mmol) at room temperature. The reaction mixture was refluxed for 36 h and acidified with a 1 M HCl solution to pH ≈ 2. The layers were separated and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 20–40%) to give methyl 1-*O*-(3,4-di-*O*-allyl)-caffeoyl-3-*O*-(4-*O*-allyl)-feruloyl-TMB-*muco*-quinate **17** as a pale yellow powder (725 mg, 72%), mp 119–121 °C; $\nu_{max}/cm^{-1}$ (KBr) 3468, 3080, 2992, 2955, 1749, 1714, 1631, 1597, 1511, 1268, 1139, 1076; $\delta_H$ ($CDCl_3$): 1.25 (3H, s, $CH_3$), 1.25 (3H, s, $CH_3$), 1.86 (1H, d, *J* 13.7, 6-H*H*), 2.02 (1H, t, *J* 12.8, 2-H*H*), 2.53 (1H, d, *J* 12.82, 2-H*H*), 2.75 (1H, d, *J* 11.91, 6-H*H*), 3.18 (3H, s, $COCH_3$), 3.26 (3H, s, $COCH_3$), 3.69 (3H, s, $COOCH_3$), 3.76 (1H, t, *J* 10, 4-H), 3.90 (3H, s, $C_{Ar}$–$OCH_3$), 3.93 (1H, ddd, *J* 14.1, 10, 4.5, 3-H), 4.60 (6H, m, $C_{Ar}$–$OCH_2$), 5.25 (3H, m, CH*H*═CH), 5.38 (3H, m, C*H*H═CH), 6.02 (3H, m, $CH_2$═C*H*), 6.20 (1H, d, *J* 16, $C_{Ar}$–CH═C*H*), 6.32 (1H, d, *J* 16, $C_{Ar}$–CH═C*H*), 6.82 (1H, d, *J* 8.7, $C_{Ar}H$), 6.83 (1H, d, *J* 8.7, $C_{Ar}H$), 7.05 (4H, m, $C_{Ar}H$), 7.55 (1H, d, *J* 16.03, $C_{Ar}$–C*H*), 7.62 (1H, d, *J* 16.03, $C_{Ar}$–C*H*); $\delta_C$ ($CDCl_3$): 17.6 ($CH_3$), 17.6 ($CH_3$), 34.7 (C-2), 36.4 (C-6), 47.8 ($COCH_3$), 48.0 ($COCH_3$), 52.8 ($COOCH_3$), 56.0 ($C_{Ar}$–$OCH_3$), 653 (C-3), 68.4 (C-5), 69.7 ($C_{Ar}$–$OCH_2$), 70.1($C_{Ar}$–$OCH_2$), 73.3 (C-4), 78.9 (C-1), 99.8 (*C*$OCH_3$), 99.8 (*C*$OCH_3$), 109.9 ($C_{Ar}$), 112.8 ($C_{Ar}$), 112.9 ($C_{Ar}$), 113.5 ($C_{Ar}$), 114.5 (*C*H–COO), 115.6 (*C*H–COO), 117.9 ($CH_2$═CH), 118.0 ($CH_2$═CH), 118.4 ($CH_2$═CH), 122.9 ($C_{Ar}$), 123.2 ($C_{Ar}$), 127.3 ($C_{Ar}$–CH), 127.5 ($C_{Ar}$–CH), 132.8 ($CH_2$═*C*H), 132.9 ($CH_2$═*C*H), 133.2 ($CH_2$═*C*H), 145.1 ($C_{Ar}$–*C*H), 146.6 ($C_{Ar}$–*C*H), 148.6 ($C_{Ar}$–$OCH_3$), 149.7 ($C_{Ar}$–$OCH_2$), 150.6 ($C_{Ar}$–$OCH_2$), 150.8 ($C_{Ar}$–$OCH_2$), 165.5 (CH–*C*OO), 166.1 (CH–*C*OO), 170.8 (*C*$OOCH_3$); HRMS (ESI+): Exact mass calculated for $C_{42}H_{50}O_{14}Na$ $[M + Na^+]^+$, 801.3098. Found 801.3099.

**Synthesis of methyl 3-*O*-feruloyl-*muco*-quinate 21.** To a solution of ester **13** (537 mg, 1 mmol), and *p*-TsOH (20 mg, 0.105 mmol) in methanol–water (9 : 1, 30 mL) was added 10% Pd/C (195 mg) at room temperature. The reaction mixture was heated at 60 °C for 48 h, cooled to room temperature, filtered and methanol was removed *in vacuo*. Aqueous reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 60–80%) to give methyl 3-*O*-feruloyl-TMB-*muco*-quinate **19** pale yellow powder (471 mg, 95%). Methyl 3-*O*-feruloyl-TMB-*muco*-quinate **19** (471 mg, 0.95 mmol) was dissolved in TFA (90% aq. solution, 20 mL) at 0 °C and the solution was stirred for 2 h at room temperature. The solvents were removed *in vacuo* to afford the target pale yellow solid **21** in quantitative yield, mp 113–115 °C; $\nu_{max}/cm^{-1}$ (KBr) 3425, 2955, 2930, 1729, 1705, 1634, 1592, 1580, 1270, 1131, 1076; $\delta_H$ (MeOH-$d_4$): 1.56 (1H, t, *J* 12.0, 6-H*H*), 1.66 (1H, t, *J* 12.0, 2-H*H*), 1.93 (2H, m, 6-H*H* & 2-H*H*), 3.24 (1H, t, *J* 8.7, 4-H), 3.60 (3H, s, $COCH_3$), 3.78 (3H, s, $COOCH_3$), 4.84 (1H, br s, OH), 4.9 (1H, ddd, *J* 11.4, 5.0, 1.8, 5-H), 5.63 (1H, br s, OH), 6.39 (1H, d, *J* 15.6, $C_{Ar}$–CH═C*H*), 6.76 (1H, d, *J* 8.2, $C_{Ar}H$), 7.06 (1H, dd, *J* 8.2, 1.8, $C_{Ar}H$), 7.26 (1H, d, *J* 1.8, $C_{Ar}H$), 7.53 (1H, d, *J* 15.6, $C_{Ar}$–C*H*), 9.5 (1H, br s, $C_{Ar}$–O*H*); $\delta_c$ (MeOH-$d_4$): 38.0 (C-2), 40.6 (C-6), 52.3 ($COOCH_3$), 56.1 ($C_{Ar}$–$OCH_3$), 69.2 (C-3), 72.6 (C-5), 73.3 (C-4), 77.4 (C-1), 111.6 ($C_{Ar}$), 115.5 ($C_{Ar}$), 116.0 (*C*H–COO), 123.6 ($CH_2$═CH), 126.2 ($C_{Ar}$), 145.3 ($C_{Ar}$–CH), 148.4 ($C_{Ar}$–*C*H), 149.8 ($C_{Ar}$), 166.7 (CH–*C*OO), 175.2 (*C*$OOCH_3$); HRMS (ESI−): Exact mass calculated for $C_{18}H_{21}O_9$ $[M - H^+]^-$, 381.1192. Found 381.1191.

**Synthesis of methyl 1,3-di-*O*-feruloyl-*muco*-quinate 27.** To a solution of ester **15** (500 mg, 0.66 mmol), and *p*-TsOH (27 mg, 0.14 mmol) in methanol–water (9 : 1, 30 mL) was added 10% Pd/C (234 mg) at room temperature. The reaction mixture was refluxed for 48 h, cooled to room temperature, filtered and methanol was removed *in vacuo*. The aqueous reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 50–70%) to give methyl 1,3-di-*O*-feruloyl-*muco*-quinate **27** as a pale yellow powder (324 mg, 88%), mp 129–131 °C; $\nu_{max}/cm^{-1}$ (KBr) 3443, 2957, 1739, 1631, 1601, 1516, 1273, 1212, 1160; $\delta_H$ (acetone-$d_6$): 1.72 (1H, t, *J* 14.0, 6-H*H*), 1.85 (1H, t, *J* 15.1, 2-H*H*), 2.32 (1H, d, *J* 10.5, 6-H*H*), 2.45 (1H, d, *J* 11.5, 2-H*H*), 3.43 (1H, t, *J* 9.2, 4-H), 3.54 (3H, s, $C_{Ar}$–$OCH_3$), 3.65 (3H, s, $C_{Ar}$–$OCH_3$), 3.67 (3H, s, $COOCH_3$), 3.70 (1H, m, 3-H), 4.80 (1H, m, 5-H), 6.22 (1H, d, *J* 16, $C_{Ar}$–CH═C*H*), 6.28 (1H, d, *J* 16, $C_{Ar}$–CH═C*H*), 6.69 (1H, d, *J* 7.8, $C_{Ar}H$), 6.72 (1H, d, *J* 8.2, $C_{Ar}H$), 6.91 (1H, d, *J* 8.7, $C_{Ar}H$), 6.96 (1H, d, *J* 8.7, $C_{Ar}H$), 7.04 (1H, s, $C_{Ar}H$), 7.04 (1H, s, $C_{Ar}H$), 7.41 (1H, d, *J* 16, $C_{Ar}$–C*H*), 7.45 (1H, d, *J* 16, $C_{Ar}$–C*H*); $\delta_c$ (acetone-$d_6$): 37.3 (C-2), 38.8 (C-6), 53.2 ($COOCH_3$), 55.9 ($COCH_3$), 55.95 ($COCH_3$), 68.6 (C-3), 71.7 (C-5), 76.0 (C-4), 78.9 (C-1), 111.2 ($C_{Ar}$), 111.3 ($C_{Ar}$), 113.5 ($C_{Ar}$), 114.6 ($C_{Ar}$), 114.9 (*C*$OCH_3$), 115.8 (*C*$OCH_3$), 115.9 (*C*H–COO), 117.9 (*C*H–COO), 123.4 ($CH_2$═CH), 123.7 ($C_{Ar}$), 126.0 ($C_{Ar}$), 126.4 ($C_{Ar}$–CH), 146.2 ($C_{Ar}$–CH), 147.4 ($CH_2$═*C*H), 148.0 ($C_{Ar}$–*C*H), 148.1 ($C_{Ar}$–*C*H), 148.7 ($C_{Ar}$), 149.1 ($C_{Ar}$), 166.5 (CH–*C*OO), 167.6 (CH–*C*OO), 171.8 (*C*$OOCH_3$); HRMS (ESI−): Exact mass calculated for $C_{28}H_{29}O_{12}$ $[M - H^+]^-$, 557.1664. Found 557.1660.

**Synthesis of methyl 3-*O*-caffeoyl-*muco*-quinate 20.** To a solution of ester **12** (562 mg, 1 mmol), and *p*-TsOH (40 mg, 0.21 mmol) in methanol–water (9 : 1, 30 mL) was added 10% Pd/C (390 mg) at room temperature. The reaction mixture was

heated at 60 °C for 48 h, cooled to room temperature, filtered and methanol was removed *in vacuo*. The aqueous reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 60–90%) to give methyl 3-*O*-caffeoyl-TMB-*muco*-quinate **18** as a pale yellow powder (461 mg, 93%). Methyl 3-*O*-caffeoyl-TMB-*muco*-quinate **18** (461 mg, 0.93 mmol) was dissolved in a TFA solution (90% aq. solution, 20 mL) at 0 °C and the solution was stirred for 2 h at room temperature. The solvents were removed *in vacuo* to afford the target pale yellow solid **20** in quantitative yield, mp 118–120 °C; $\nu_{max}/cm^{-1}$ (KBr) 3443, 3000, 2993, 2952, 2854, 1710, 1740, 1260, 1140, 1075; $\delta_H$ (MeOH-$d_4$): 1.57 (1H, m, 6-*H*H), 1.66 (1H, m, 2-*H*H), 1.86 (1H, m, 6-H*H*), 1.89 (1H, m, 2-H*H*), 3.24 (1H, t, *J* 8.7, 4-H), 3.56 (1H, m, 3-H), 3.59 (3H, s, $COOCH_3$), 4.9 (1H, ddd, *J* 10.5, 4.6, 5-H), 6.20 (1H, d, *J* 16.0, $C_{Ar}$–CH═C*H*), 6.72 (1H, d, *J* 8.2, $C_{Ar}H$), 6.95 (1H, d, *J* 8.2, $C_{Ar}H$), 7.01 (1H, s, $C_{Ar}H$), 7.43 (1H, d, *J* 16.0, $C_{Ar}$–C*H*); $\delta_c$ (MeOH-$d_4$): 37.5 (C-2), 40.3 (C-6), 51.7 ($COOCH_3$), 69.2 (C-3), 72.4 (C-5), 73.4 (C-4), 77.1 (C-1), 113.8 ($C_{Ar}$), 114.0 ($C_{Ar}$), 115.12 (*C*H–COO), 121.2 ($CH_2$═CH), 126.4 ($C_{Ar}$), 145.5 ($C_{Ar}$–CH), 145.7 9 ($C_{Ar}$–*C*H), 148.2 ($C_{Ar}$), 167.5 (CH–*C*OO), 175.0 (*C*OOCH$_3$); HRMS (ESI−): Exact mass calculated for $C_{17}H_{19}O_9$ [M − $H^+$]$^-$, 367.1035. Found 367.1025.

**Synthesis of methyl 1,3-di-*O*-caffeoyl-*muco*-quinate 22.** To a solution of ester **14** (600 mg, 0.75 mmol), and *p*-TsOH (60 mg, 0.315 mmol) in methanol–water (9 : 1, mmol) was added 10% Pd/C (585 mg) at room temperature. The reaction mixture was refluxed for 48 h, cooled to room temperature, filtered and methanol was removed *in vacuo*. The aqueous reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 50–70%) to give methyl 1,3-di-*O*-caffeoyl-*muco*-quinate **22** as a pale yellow powder (322 mg, 79%), mp 144–146 °C; $\nu_{max}/cm^{-1}$ (KBr) 3413, 1725, 1684, 1605, 1523, 1445, 1282, 1183, 1115, 1067; $\delta_H$ (MeOH-$d_4$): 1.90 (1H, m, 6-*H*H), 1.95 (1H, m, 2-*H*H), 2.53 (1H, m, 6-H*H*), 2.61 (1H, m, 2-H*H*), 3.53 (1H, t, 9.17, 4-H), 3.70 (1H, m, 3-H), 3.72 (3H, s, $COOCH_3$), 5.04 (1H, ddd, *J* 14.21, 4.58, 5-H), 6.27 (1H, d, *J* 16.1, $C_{Ar}$–C*H*), 6.29 (1H, d, *J* 16.1, $C_{Ar}$–CH═C*H*), 6.75 (1H, d, *J* 6.75, $C_{Ar}H$), 6.78 (1H, d, *J* 8.25, $C_{Ar}H$), 6.92 (1H, dd, *J* 7.79, 2.29, $C_{Ar}H$), 6.98 (1H, dd, *J* 8.25, 2.29, $C_{Ar}H$), 7.02 (1H, d, *J* 2.3, $C_{Ar}H$), 7.06 (1H, d, *J* 2.3, $C_{Ar}H$), 7.55 (1H, d, *J* 16.1, $C_{Ar}$–C*H*), 7.58 (1H, d, *J* 16.1, $C_{Ar}$–C*H*); $\delta_C$ (MeOH-$d_4$): 35.3 (C-2), 37.8 (C-6), 51.9 ($COOCH_3$), 68.9 (C-3), 71.6 (C-5), 76.7 (C-4), 78.7 (C-1), 112.7 ($C_{Ar}$), 113.7 ($C_{Ar}$), 113.9 ($C_{Ar}$), 113.9 ($C_{Ar}$), 115.2 (*C*H–COO), 115.3 (*C*H–COO), 121.7 ($CH_2$═CH), 122.1 ($C_{Ar}$), 126.1 ($C_{Ar}$), 126.4 ($C_{Ar}$–CH), 145.5 ($C_{Ar}$–CH), 145.5 ($CH_2$═*C*H), 146.0 ($C_{Ar}$–*C*H), 147.1 ($C_{Ar}$–*C*H), 148.3 ($C_{Ar}$), 148.7 ($C_{Ar}$), 166.1 (CH–*C*OO), 167.4 (CH–*C*OO), 171.4 (*C*OOCH$_3$); HRMS (ESI−): Exact mass calculated for $C_{26}H_{25}O_{12}$ [M − $H^+$]$^-$, 529.1351. Found 529.1351.

**Synthesis of methyl 1-*O*-feruloyl-3-*O*-caffeoyl-*muco*-quinate 28.** To a solution of ester **16** (500 mg, 0.64 mmol), and *p*-TsOH (40 mg, 0.21 mmol) in methanol–water (9 : 1) was added 10% Pd/C (375 mg) at room temperature. The reaction mixture was refluxed for 48 h, cooled to room temperature, filtered and methanol was removed *in vacuo*. Aqueous reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 50–70%) to give methyl 1-*O*-feruloyl-3-*O*-caffeoyl-*muco*-quinate **28** as a pale yellow powder (289 mg, 83%), mp 133–135 °C; $\nu_{max}/cm^{-1}$ (KBr) 3418, 2957, 1736, 1701, 1630, 1601, 1516, 1451, 1275, 1209, 1161; $\delta_H$ (acetone-$d_6$): 1.86 (1H, m, 6-*H*H), 1.93 (1H, m, 2-*H*H), 2.54 (1H, ddd, *J* 13.75, 4.6, 4.6, 6-H*H*), 2.65 (1H, ddd, *J* 13.5, 4.6, 4.6, 2-H*H*), 3.66 (3H, s, $C_{Ar}$–$OCH_3$), 3.73 (1H, m, 3-H), 3.87 (3H, s, $COOCH_3$), 5.06 (1H, ddd, *J* 11.7, 4.6, 4.6, 5-H), 6.35 (1H, d, *J* 16.3, $C_{Ar}$–CH═C*H*), 6.37 (1H, d, *J* 16.3, $C_{Ar}$–CH═C*H*), 6.83 (1H, d, *J* 8.3, $C_{Ar}H$), 6.86 (1H, d, *J* 8.3, $C_{Ar}H$), 7.08 (2H, m, $C_{Ar}H$), 7.19 (1H, d, *J* 2.1, $C_{Ar}H$), 7.28 (1H, d, 2.1, $C_{Ar}H$), 7.58 (1H, d, *J* 16.3, $C_{Ar}$–C*H*), 7.59 (1H, d, *J* 16.3, $C_{Ar}$–C*H*), 7.80 (3H, brs, Ar–O*H*); $\delta_c$ (acetone-$d_6$): 35.5 (C-2), 38.3 (C-6), 52.2 ($COOCH_3$), 55.5 ($COCH_3$), 69.2 (C-3), 71.1 (C-5), 77.3 (C-4), 78.8 (C-1), 110.2 ($C_{Ar}$), 113.6 ($C_{Ar}$), 114.7 ($C_{Ar}$), 114.9 ($C_{Ar}$), 115.3 (*C*OCH$_3$), 115.6 (*C*H–COO), 117.9 (*C*H–COO), 122.2 ($CH_2$═CH), 123.1 ($C_{Ar}$), 126.6 ($C_{Ar}$), 126.6 ($C_{Ar}$–CH), 145.2 ($C_{Ar}$–CH), 145.7 ($CH_2$═*C*H), 146.4 ($C_{Ar}$–*C*H), 147.7 ($C_{Ar}$–*C*H), 148.3 ($C_{Ar}$), 149.4 ($C_{Ar}$), 165.4 (CH–*C*OO), 166.2 (CH–*C*OO), 171.1 (*C*OOCH$_3$); HRMS (ESI−): Exact mass calculated for $C_{27}H_{27}O_{12}$ [M − $H^+$]$^-$, 557.1664. Found 557.1660.

**Synthesis of methyl 1-*O*-caffeoyl-3-*O*-feruloyl-*muco*-quinate 29.** To a solution of ester **17** (500 mg, 0.64 mmol), and *p*-TsOH (40 mg, 0.21 mmol) in methanol–water (9 : 1, mL) was added 10% Pd/C (375 mg) at room temperature. The reaction mixture was refluxed for 48 h, cooled to room temperature, filtered and methanol was removed *in vacuo*. Aqueous reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over $Na_2SO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel (ethyl acetate–petroleum ether, 50–70%) to give methyl 1-*O*-caffeoyl-3-*O*-feruloyl-*muco*-quinate **29** as a pale yellow powder (296 mg, 85%), mp 128–130 °C; $\nu_{max}/cm^{-1}$ (KBr) 3430, 3070, 2990, 2950, 1749, 1714, 1631, 1597, 1511, 1265, 1160, 1139, 1075; $\delta_H$ (acetone-$d_6$): 1.86 (1H, dd, *J* 13.5, 11.9, 6-*H*H), 1.92 (1H, dd, *J* 13.5, 11.7, 2-*H*H), 2.60 (1H, ddd, *J* 11.0, 4.6, 4.6, 6-H*H*), 2.64 (1H, ddd, *J* 11.0, 4.6, 4.6, 2-H*H*), 2.9 (2H, br s, OH), 3.55 (1H, t, *J* 9.2, 4-H), 3.67 (3H, s, $C_{Ar}$–$OCH_3$), 3.78 (1H, m, 3-H), 3.89 (3H, s, $COOCH_3$), 4.21 (1H, br s, OH), 4.48 (1H, br s, OH), 5.04 (1H, m, 5-H), 6.35 (1H, d, *J* 15.8, $C_{Ar}$–CH═C*H*), 6.38 (1H, d, *J* 15.8, $C_{Ar}$–CH═C*H*), 6.84 (1H, d, *J* 8.3, $C_{Ar}H$), 6.88 (1H, d, *J* 8.3, $C_{Ar}H$), 7.09 (1H, dd, *J* 3.1, 2.1, $C_{Ar}H$), 7.11 (1H, dd, *J* 3.1, 2.1, $C_{Ar}H$), 7.20 (1H, d, *J* 2.1, $C_{Ar}H$), 7.31 (1H, d, *J* 1.8, $C_{Ar}H$), 7.58 (1H, d, *J* 15.8, $C_{Ar}$–C*H*), 7.59 (1H, d, *J* 15.8, $C_{Ar}$–C*H*), 8.27 (3H, brs, $C_{Ar}$–O*H*); $\delta_c$ (acetone-$d_6$): 35.6 (C-2), 38.1 (C-6) 51.9 ($COOCH_3$), 55.5 ($COCH_3$), 69.2 (C-3), 71.5 (C-5), 77.1 (C-4), 78.7 (C-1), 110.4 ($C_{Ar}$), 113.8 ($C_{Ar}$), 114.6

($C_{Ar}$), 114.9 ($C_{Ar}$), 115.2 ($COCH_3$), 115.6 (*C*H–COO), 117.9 (*C*H–COO), 122.2 ($CH_2$═CH), 123.2 ($C_{Ar}$), 126.6 ($C_{Ar}$), 126.6 ($C_{Ar}$–CH), 145.3 ($C_{Ar}$–CH), 145.5 ($CH_2$═*C*H), 146.5 ($C_{Ar}$–*C*H), 147.9 ($C_{Ar}$–*C*H), 148.3 ($C_{Ar}$), 149.3 ($C_{Ar}$), 165.4 (CH–*C*OO), 166.3 (CH–*C*OO), 170.9 (*C*$OOCH_3$); HRMS (ESI−): Exact mass calculated for $C_{27}H_{27}O_{12}$ $[M - H^+]^-$, 557.1664. Found 557.1662.

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