Carbohydrate Research 344 (2009) 734–738

Contents lists available at ScienceDirect

Carbohydrate Research

journal homepage: www.elsevier.com/locate/carres

Catechuic acid and ethyl 2,4,5-trihydroxybenzoate from D-glucose

Namdeo N. Bhujbal, Omprakash P. Bande, Dilip D. Dhavale *

Garware Research Centre, Department of Chemistry, University of Pune, Pune 411007, India

ARTICLE INFO

Article history:
Received 7 January 2009
Received in revised form 2 February 2009
Accepted 3 February 2009
Available online 8 February 2009

Keywords:
Aldol reaction
β-Ketoester
Carbocycles
Carbohydrates
Phenolic acids

ABSTRACT

Synthesis of catechuic acid (**1**) and ethyl 2,4,5-trihydroxybenzoate (**2**) from D-glucose-derived β-ketoester is described. The polyhydroxylated β-ketoester obtained from the hydrolysis of sugar β-ketoester **3** was subjected to an aldol-type condensation to get **4** that on enolization, dehydration, and hydrogenation afforded ethyl 2,4,5-trihydroxybenzoate (**2**). On the other hand, hydrogenation of aldol product **4** afforded polyhydroxylated keto-carbasugar **6**, which on mild acid treatment and ester hydrolysis in basic media led to catechuic acid **1**. Intermediate **4** is co-related to 3-dehydroshikimic acid, a biochemical intermediate from D-glucose in the synthesis of pro-catechuic acid.

1. Introduction

The phenolic acids and derivatives have significant importance in food chemistry, nutritional science, drug chemistry, and plant physiology.[1–6] For example, the spermidine derivatives of catechuic acid (**1**), namely agrobactin and parabactin (Fig. 1), are known to be iron chelators[7,8] and are used in the therapy of Cooley's anemia and as anticancer treatments.[9–11] Other phenolic compounds such as gallic acid, vanillic acid, ferulic acid, caffeic acid, chlorogenic acid, rosmarinic acid, and cichoric acid are known to be natural antioxidants[12,13] and antimutagenics,[14,15] while alkyl trihydroxybenzoates are antimicrobials and antagonists of shikimic acid.[16]

In general, synthesis of phenolic acids/esters involves both biochemical and chemical synthetic pathways. Frost and co-workers reported the biochemical conversion of D-glucose to pro-catechuic acid, gallic acid, vanillin, and mono-, di-, and trihydroxy benzenes via 3-dehydroshikimic acid.[17–24] Koppisch et al. biosynthesized 3,4-dihydroxybenzoate from erythrose-4-phosphate and phosphoenolpyruvate.[25] In addition, bio-transformations of aromatic compounds to the hydroxybenzoic acids using micro-organisms are known.[26–32] The chemical synthetic approaches to phenolic acids/esters involve (i) functionalization of phenols either by photolytic oxidation[33,34] or by the hydroxylation of salicylic acid and β-resorcylic acid,[35–37] (ii) carboxylation of procatechol followed by lithiation,[38] and (iii) TMSOTf-catalyzed [3+3] cyclization of 1,3-bis(silyl enol ether) with 1,1,3,3-tetramethoxypropane.[39] As an alternative, sugars are used as substrates in the chemical synthesis, wherein intramolecular ring closure of carbohydrates afforded polyhydroxylated carbocyclic or polyhydroxylated cyclohexenone derivatives that are converted to the phenolic compounds.[20,40–42] While working in the area of carbohydrate chemistry, we have synthesized sugar β-ketoesters and demonstrated their utility in the synthesis of griseolic acid and nojirimycin analogues.[43–49] We now demonstrate the transformation of sugar β-ketoesters **3a/b** to catechuic acid (**1**) and ethyl 2,4,5-trihydroxybenzoate (**2**) by emulating the biochemical cascade reactions (vide supra) of intramolecular aldol condensation and enolization that are known from poly-β-ketoesters to phenolic acids/esters.[50] Our results are reported herein.

2. Results and discussion

The required sugar β-ketoesters **3a** and **3b** were prepared on the 50-g scale from α-D-glucose as reported earlier by us in overall 35% and 28% yields, respectively.[43] As shown in Scheme 1, treatment of **3a** with 9:1 TFA–water at 0 °C for 2 h, followed by removal of solvent under reduced pressure[†] and column chromatography of the crude product afforded ethyl 4-*O*-benzyl-3,5-dihydroxy-6-oxocyclohex-1-ene carboxylate (**4a**) [Vasella et al.[51] reported the synthesis of analogous cyclohexenone, namely *tert*-butyl 3,4,5-tri-*O*-triethylsilyl-6-oxo-cyclohex-1-ene carboxylate, from methyl 6-deoxy-6-iodo-α-D-glucopyranoside in 50% yield. However, further conversion to catechuate derivative is not

---

[†] Our attempts to improve the yield of **4a/b** under variety of reaction conditions of acid catalyst (CSA/PTSA/H_2SO_4/HCl/$HClO_4$), solvent (CH_2Cl_2, benzene, EtOH, 1,4-dioxane), and temperatures (0 °C–reflux temperature) were unsuccessful.

* Corresponding author. Tel.: +91 020 25691727; fax: +91 020 25691728.
E-mail address: ddd@chem.unipune.ernet.in (D.D. Dhavale).

0008-6215/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2009.02.002

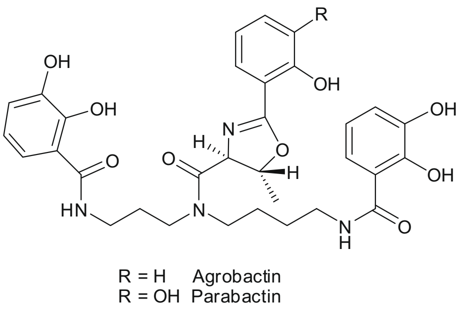
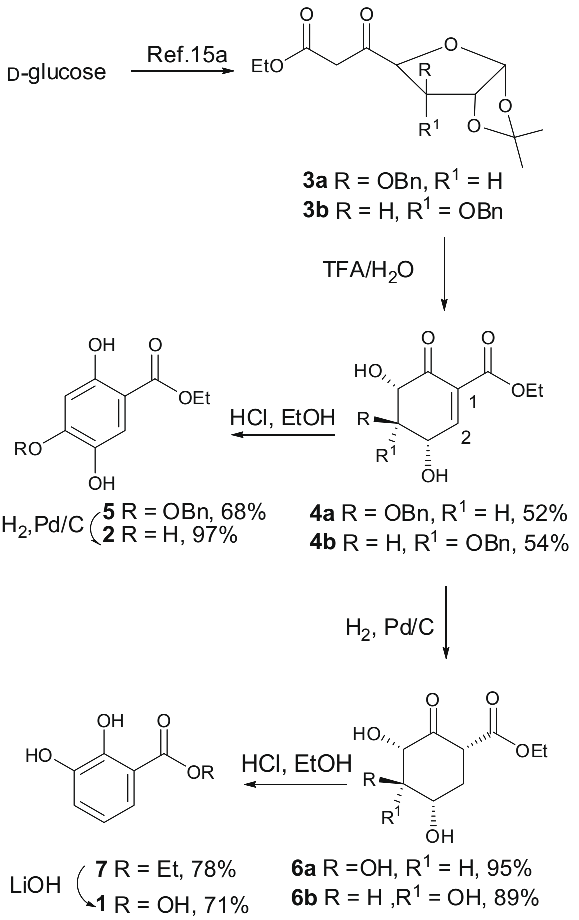


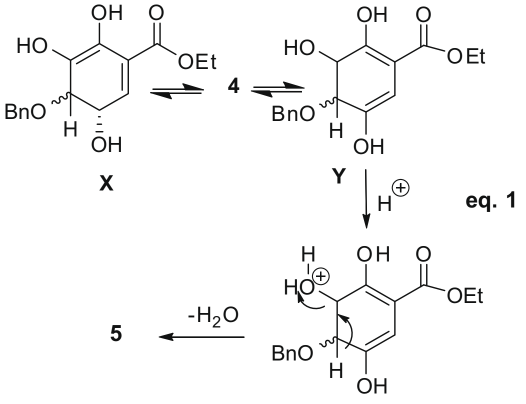
Figure 1.



Scheme 1. Synthesis of **1** and **2** from the β-ketoester.

reported.]. Reaction of **4a** with HCl (12 N, 1.0 equiv) in EtOH at reflux for 30 min afforded ethyl 4-*O*-benzyl 2,5-dihydroxybenzoate (**5**) as the only isolable product. The structure of **5** was confirmed by the ^{1}H–^{1}H COSY spectrum, wherein no cross-peaks were obtained in the aromatic region, suggesting that the aromatic protons at δ 6.52 and 7.34 are not mutually coupled and therefore are placed in the *para* position with respect to each other. In order to know the effect of orientation of the –OBn substituent, a similar reaction sequence was repeated with D-allose-derived β-ketoester **3b**. Thus, reaction of **3b** with TFA–water afforded **4b,** which on treatment with ethanolic HCl gave the identical product **5** as evident from the mixed mp and spectral data. In the final step, hydrogenolysis of **5** with 10% Pd/C in MeOH at 80 psi pressure afforded ethyl 2,4,5-trihydroxybenzoate (**2**) in overall 12% yield from D-glucose.

We believe that formation of **5** from cyclohexenone derivatives **4a**/**b** involves an enolization as the first step leading to formation of either **X** or **Y**, wherein loss of a water molecule from the protonated species **Y** afforded **5**, an immediate precursor to **2** (Eq. 1).[‡]



Targeting toward the synthesis of catechuic acid (**1**), hydrogenation of **4a** with 10% Pd/C in methanol under balloon pressure for 30 min afforded **6a**, wherein reduction of the double bond and removal of the –OBn protection took place simultaneously. Similarly, hydrogenation of **4b** at 80 psi pressure for 3 h afforded **6b**. In order to confirm the conformations of **6a** and **6b**, the assignment of proton signals in the ^{1}H NMR spectrum of **6a**/**6b** was made by decoupling experiments.[§] Thus, in the case of **6a**, appearance of H-3 at δ 4.34 as a doublet with *J* = 9.8 Hz and of H-4 at δ 3.45 as a triplet with *J* = 9.8 Hz indicates the axial orientation of H-3, H-4, and H-5. Furthermore, H-1 appeared at δ 3.90 as a doublet of doublets with *J* = 13.2 Hz and 5.0 Hz, indicating the axial orientation of H-1. This confirmed the conformation of **6a** with all the substituents in the equatorial orientation as shown in Figure 2.

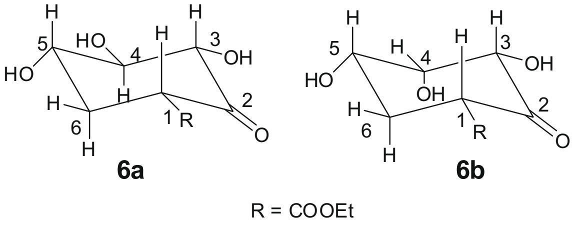


Figure 2. Conformations of **6a**/**6b**.

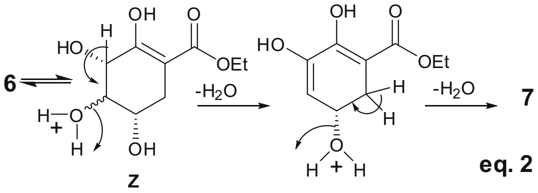
In case of **6b**, H-3 appeared at δ 4.35 as a doublet with *J* = 3.0 Hz, indicating an axial–equatorial orientation of H-3 and H-4, while H-1, H-4, and H-5 appeared as a multiplet in the range of δ 4.30–4.38, making it difficult to assign the conformation. However, we have tentatively assigned the conformation for **6b** (Fig. 2), based on the addition of the hydrogen from the β-face, making the –CO_2Et substituent equatorial as found in **6a**. In the next step, reaction of **6a** with a catalytic amount of HCl (12 N, 0.2 equiv) in ethanol at 60 °C for 30 min afforded ethyl catechuate (**7**). While performing an analogous reaction with **6b**, it was anticipated that the axial orientation of the C-4 hydroxy substituent (in **6a** C-4 hydroxy is equatorial) will lead to a different product. However, reaction of **6b** with ethanolic HCl at 60 °C for 1 h afforded an identical product **7** as evi-

---

[‡] Elimination of water molecule from protonated species **X** will lead to the formation of ethyl 4-*O*-benzyl-2,3-dihydroxybenzoate, and not to product **5** that was obtained.

[§] The ^{1}H and ^{13}C NMR spetra of **6a** and **6b** showed additional signals (<10%) due to the corresponding enol form.

dent from the spectral and analytical data. The formation of product **7** can be explained by assuming that the keto-compounds **6a**/**6b** under mild acidic reaction conditions remain in equilibrium with the enol form *Z*, wherein the quasi-axial orientation of the C4-OH group undergoes facile loss of two molecules of water to give ethyl catechuate (**7**) as the only product (Eq. 2).



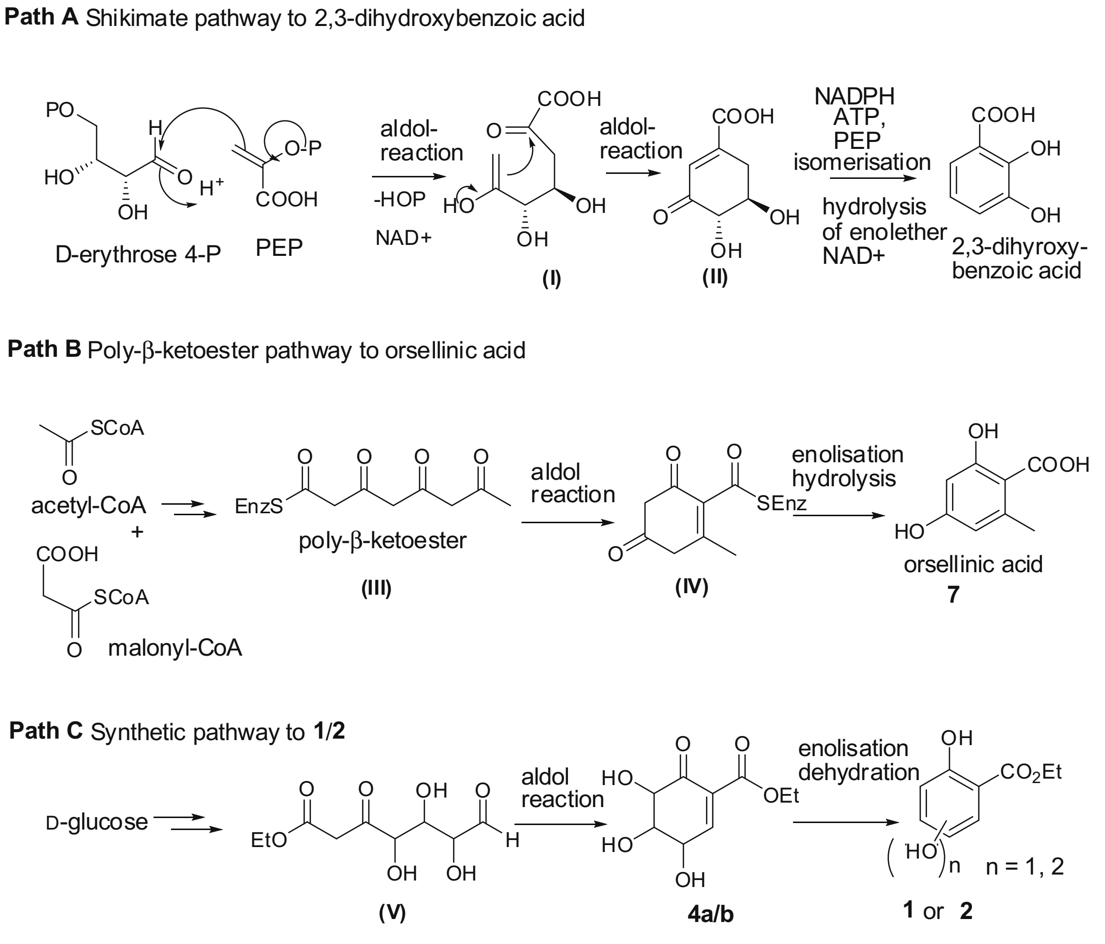
In the final step, treatment of **7** with LiOH in ethanol–water at room temperature afforded catechuic acid (**1**) in overall 11% yield from D-glucose. The physical constants and analytical data of **1** are found to be in accordance with those reported.[38] An interesting resemblance between the present chemical synthesis and biogenetic pathways to phenolic acids was noticed by us. The biogenesis of phenolic acids/esters mainly involves two different pathways: one involving shikimate and the other involving a poly-β-ketoester. In the shikimate pathway (Scheme 2, Path A), phosphoenolpyruvate and erythrose phosphate first form the α-ketoester **I** that is converted to the 3-dehydroshikimic acid (**II**) and then to isochorismic acid, leading to 2,3-dihydroxybenzoic acid. In the latter approach (Path B), one molecule of acetyl-CoA and three molecules of malonyl-CoA form the eight-carbon poly-β-ketoester **III** that undergoes an intramolecular aldol-type condensation and dehydration to give cyclohexenone derivative **IV**, which by enolization, dehydration, and hydrolysis cascade leads to the formation of orsellinic acid/6-methylsalicylic acid and related natural products.[50] In the present chemical synthesis of **1** and **2** from D-glucose, we have synthesized analogous hydroxylated seven-carbon β-ketoester **V** from D-glucose and converted it to catechuic acid (**1**) and ethyl 2,4,5-trihydroxybenzoate (**2**), mimicking the steps involved in the poly-β-ketoester biogenetic pathway (Path B).

In conclusion, catechuic acid (**1**) and ethyl 2,3,4-trihydroxybenzoate (**2**) were synthesized from D-glucose-derived β-ketoester **3**, which on opening of the 1,2-acetonide functionality follows an analogous path of aldol condensation, enolization and dehydration as known for the poly-β-ketoester biosynthetic pathway. A notable feature of our nonenzymatic approach is that all the carbon atoms of the D-glucose-derived β-ketoester are retained in the target molecules as in the biogenetic pathway, and the reaction sequence led to exclusive formation of the products (no other regioisomer).

3. Experimental

3.1. General

Melting points were recorded with a Thomas–Hoover capillary melting point apparatus, and are uncorrected. IR spectra were recorded with an FTIR instrument as a thin film or using KBr pellets, and are expressed in cm^{-1}. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR



Scheme 2. Biogenetic pathways.

spectra were recorded using $CDCl_3$ or D_2O as a solvent. Chemical shifts were reported in δ units (ppm) with reference to TMS as an internal standard, and J values are given in Hertz. Elemental analyses were carried out with a C, H-analyzer. Optical rotations were measured using a polarimeter at 25 °C. Thin-layer chromatography (TLC) was performed on pre-coated plates (0.25 mm, Silica Gel 60 F_{254}). Column chromatography was carried out with silica gel (100–200 mesh). The reactions were carried out in oven-dried glassware under dry N_2. MeOH and CH_2Cl_2 were purified and dried before use. Distilled *n*-hexane and EtOAc were used for column chromatography. Pd–C (10%) was purchased from σ–Aldrich and/or Fluka. After quenching the reaction with water, the workup involved washing of combined organic layers with water and brine, drying over anhydrous sodium sulfate, and evaporation of the solvent under reduced pressure.

3.1.1. (3*S*,4*R*,5*S*) Ethyl 4-*O*-benzyl-3,5-dihydroxy-6-oxocyclohex-1-ene carboxylate (4a)

To an ice-cold solution of β-ketoester **3a** (1 g, 2.77 mmol) in CH_2Cl_2 (5 mL) was added 9:1 TFA–water (4 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h, and was brought to room temperature. The solvent was evaporated under reduced pressure to give a viscous oil. The oil was dissolved in CH_2Cl_2, adsorbed on silica gel, and loaded on a silica gel column. Purification by column chromatography (4:1 *n*-hexane–EtOAc) afforded **4a** as a white solid (0.452 g, 52%); mp 123–125 °C; R_f 0.593 (3:2 *n*-hexane–EtOAc); $[\alpha]_D$ −18.18 (*c* 0.110, CH_2Cl_2); IR (KBr): 3400–3200 (br), 1726, 1712, 1662 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (t, J = 7.2 Hz, 3H, CH_3), 1.42 (br s, exchanges with D_2O, 2H, OH), 3.68 (dd, J = 10.5, 8.7 Hz, 1H, 4-H), 4.31 (d, J = 10.5 Hz, 1H, H-5), 4.34 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 4.66 (dd, J = 8.7, 2.2 Hz, 1H, H-3), 4.76 (d, J = 11.4 Hz, 1H, OCH_2Ph), 5.17 (d, J = 11.4 Hz, 1H, OCH_2Ph), 7.32–7.49 (m, 5H, Ar-H), 7.69 (d, J = 2.2 Hz, 1H, H-2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 CH_3, 61.8 OCH_2CH_3, 70.0 C-3, 74.8 OCH_2Ph, 78.2 C-5, 85.4 C-4, 128.2, 128.3, 128.5 Ar-C, 129.2 C-1, 137.6 Ar-C, 156.2 C-2, 162.4 COOEt, 193.9 CO. Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.98; H, 6.02.

3.1.2. (3*S*,4*S*,5*S*) Ethyl 4-*O*-benzyl-3,5-dihydroxy-6-oxocyclohex-1-ene carboxylate (4b)

Reaction of sugar β-ketoester **3b** as reported for **4a** afforded **4b** as a white solid (0.47 g, 54%); mp 122–124 °C; R_f 0.56 (1:1 *n*-hexane–EtOAc); $[\alpha]_D$ +91.50 (*c* 0.113, CH_2Cl_2); IR (KBr): 3500–3000 (br), 1740, 1697, 1627 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, J = 7.2 Hz, 3H, CH_3), 2.6–4.05 (br s, exchanges with D_2O, 2H, 2 × OH), 4.27 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 4.38 (d, J = 2.4 Hz, 1H, H-5); 4.40–5.00 (m, 1H, H-4), 4.62 (d, J = 11.0 Hz, 1H, OCH_2Ph), 4.64 (br s, 1H, H-3), 4.98 (d, J = 11.0 Hz, 1H, OCH_2Ph), 7.22–7.46 (m, 5H, Ar-H), 7.47 (d, J = 2.1 Hz, 1H, H-2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 CH_3, 61.6 OCH_2CH_3, 67.2 OCH_2Ph, 75.6, 76.5, 82.5 C-3,4,5, 128.0, 128.1, 128.4, 128.6, 137.2 Ar-C, 155.8 C-2, 162.2 COOEt, 193.2 CO. Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.81; H, 5.86.

3.1.3. Ethyl 4-*O*-benzyl-2,5-dihydroxybenzoate (5)

A solution of **4a** (0.300 g, 1.04 mmol) and HCl (0.034 g, 1.04 mmol) in EtOH (5 mL) was refluxed for 1 h. The solution was cooled to room temperature, and the EtOH was removed under reduced pressure to give crude solid. Purification by column chromatography (9:1 *n*-hexane–EtOAc) afforded **5** as a white solid (0.192 g, 68%); mp 138 °C; R_f 0.90 (7.5:2.5 *n*-hexane–EtOAc); IR (KBr): 3500–3458 (br), 1728, 1664, 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.38 (t, J = 7.2 Hz, 3H, CH_3), 4.34 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 5.10 (s, 2H, OCH_2Ph), 5.25 (br s, exchanges with D_2O, 1H, OH), 6.52 (s, 1H, Ar-Ha), 7.34 (s, 1H, Ar-Hb), 7.38 (s, 5H, Ar-H), 10.27 (br s, exchanges with D_2O, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3 CH_3, 61.1 OCH_2CH_3, 71.1 OCH_2Ph, 100.4 C-3, 104.6 C-1, 113.4 C-6, 127.8, 128.6, 128.7, 135.0 Ar-C, 138.2 C-5, 151.8 C-2, 157.0 C-4, 169.85 COOEt. Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.42; H, 5.83. Reaction of **4b** (0.300 g, 1.04 mmol) with EtOH–HCl under identical conditions as described for **4a** afforded **5** as a white solid (0.186 g, 66%).

3.1.4. Ethyl 2,4,5-trihydroxybenzoate (2)

To a solution of **5** (0.100 g, 0.34 mmol) in MeOH (10 mL) was added 10% Pd/C (0.020 g) [Caution! Extreme fire hazard!]. The reaction mixture was hydrogenated at 80 psi pressure at room temperature for 3 h. The reaction mixture was filtered through Celite, and Celite was washed with MeOH. The solvent was evaporated under reduced pressure to give a solid. Purification by column chromatography (9:1 *n*-hexane–EtOAc) afforded **2** as a white solid (0.068 g, 97%); mp 165 °C; R_f 0.413 (7:3 *n*-hexane–EtOAc); IR (KBr): 3500–3333, 1751, 1641 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 1.28 (t, J = 7.2 Hz, 3H, CH_3), 4.22 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 6.27 (s, 1H, Ar-Ha), 7.10 (s, 1H, Ar-Hb), 7.70–9.50 (br s, exchanges with D_2O, 2H, 2 × OH), 10.40 (s, exchange with D_2O, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$, DMSO-d_6): δ 13.4 CH_3, 59.6 OCH_2CH_3, 102.1 C-1, 104.0 C-3, 113.4 C-6, 137.1 C-2, 152.2 C-4, 155.7 C-5, 168.7 COOEt. Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.50; H, 5.20.

3.1.5. Ethyl (3*S*,4*R*,5*S*)-trihydroxy-2-oxocyclohexane carboxylate (6a)

A solution of **4a** (0.400 g, 1.3 mmol) and 10% Pd/C (0.080 g) in MeOH (7 mL) [Caution! Extreme fire hazard!] was hydrogenated at 20 psi pressure at room temperature for 1 h. The reaction mixture was filtered through Celite, and Celite was washed with MeOH. The filtrate was then concentrated, and the residue was purified by column chromatography (2:3 *n*-hexane–EtOAc) to afford **6a** as a white solid (0.287 g, 95%); mp 148 °C; R_f 0.428 (EtOAc); $[\alpha]_D$ +4.66 (*c* 0.120, water); IR (KBr): 3427, 3337, 3246, 1743, 1718 cm^{-1}; ^1H NMR (300 MHz, D_2O): δ 1.26 (t, J = 7.2 Hz, 3H, CH_3); 1.93 (apparent quartet, J = 13.2 Hz, 5.0 Hz, 1H, H-6a); 2.38 (dt, J = 13.2, 5.0 Hz, 1H, H-6b), 3.45 (t, J = 9.8 Hz, 1H, H-4), 3. 90 (dd, J = 13.2, 5.0 Hz, 1H, H-1), 4.00 (ddd, J = 13.2, 9.8, 5.0 Hz, 1H, H-5), 4.22 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 4.34 (d, J = 9.8 Hz, 1H, H-3); ^{13}C NMR (75 MHz, D_2O): δ 13.6 CH_3, 30.9 C-6, 51.8 C-1, 62.9 OCH_2CH_3, 69.5 C-5, 77.9 C-4, 78.6 C-3, 173.7 COOEt, 204.6 CO. Anal. Calcd for $C_9H_{14}O_6$: C, 49.50; H, 6.47. Found: C, 49.77; H, 6.73.

3.1.6. Ethyl (3*S*,4*S*,5*S*)-trihydroxy-2-oxocyclohexane carboxylate (6b)

[Caution! Extreme fire hazard!] Hydrogenation of **4b** (0.300 g, 0.98 mmol) with 10% Pd/C (0.060 g) in MeOH (10 mL) at 80 psi pressure at room temperature for 3 h and workup as for **4a** gave a crude solid. Purification by column chromatography (3:7 *n*-hexane–EtOAc) afforded **6b** as a white solid (0.191g, 89%); mp 173–175 °C; R_f 0.346 (EtOAc); $[\alpha]_D$ −26.77 (*c* 0.200, water); IR (KBr): 3500–3400 (br), 3271, 1722 cm^{-1}; ^1H NMR (300 MHz, D_2O): δ 1.27 (t, J = 7.2 Hz, 3H, CH_3), 2.21–2.36 (m, 2H, H-6a,b), 4.23 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 4.29–4.36 (m, 3H, H-1,4,5), 4.35 (d, J = 3.0 Hz, 1H, H-3); ^{13}C NMR (75 MHz, D_2O): δ 11.4 CH_3, 27.8 C-6, 49.0 C-1, 60.6 OCH_2Ph, 65.0 C-5, 73.4 C-4, 74.3 C-3, 168.6 COOEt, 204.6 CO. Anal. Calcd for $C_9H_{14}O_6$: C, 49.50; H, 6.47. Found: C, 49.73; H, 6.66.

3.1.7. Ethyl catechuate (7)

A solution of **6a** (0.050 g, 0.229 mmol) and concd HCl (0.016 g, 0.0458 mmol) in EtOH (2 mL) was stirred at 60 °C for 30 min and was cooled to 0 °C. Neutralization by 10% $NaHCO_3$ (0.5 mL) and evaporation of the solvent under reduced pressure gave a crude solid. Purification by column chromatography (9.5:0.5 *n*-hexane–

EtOAc) afforded **7** as a white solid (0.033 g, 80%); mp 67 °C; R_f 0.80 (9:1 *n*-hexane–EtOAc); IR (KBr): 3500–3000 (br), 1734, 1674 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (t, *J* = 7.2 Hz, 3H, CH_3), 4.40 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 5.65 (s, exchange with D_2O, 1H, OH), 6.77 (t, *J* = 7.9 Hz, 1H, Ar-Hb), 7.08 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar-Hc), 7.36 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar-Ha), 10.97 (br s, exchanges with D_2O, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.2 CH_3, 61.6 OCH_2CH_3, 112.5 C-1, 119.0 C-5, 119.6 C-6, 120.4 C-4, 144.8 C-3, 148.7 C-2, 170.2 COOEt. Anal. Calcd for $C_9H_{10}O_4$: C, 59.54; H, 5.53. Found: C, 59.49; H, 5.61. The reaction of **6b** (0.050 g, 0.229 mmol) with EtOH–HCl as described for **6a** afforded **7** as a white solid (0.029 g, 78%).

3.1.8. Preparation of catechuic acid (1)

A solution of **7** (0.050 g, 0.324 mmol) and LiOH (0.040 g, 0.972 mmol) in 4:1 water–EtOH (1 mL) was stirred at 25 °C for 2 h and was acidified by HCl. The solvent was evaporated under reduced pressure, and the residue was extracted with Et_2O (10 mL × 3). The combined extracts were dried over anhyd Na_2SO_4, and evaporation of the solvent afforded **1** as a white solid (0.030 g, 71%); mp 207 °C; reported mp 207–210 °C.[38] The spectral and analytical data were identical with those reported.[38]

Acknowledgments

We are grateful to Professor M.S. Wadia for helpful discussion. We are thankful to DST, New Delhi (Grant No. SR/S1/OC-21/2005), for the financial support. NNB is thankful to the UGC, New Delhi, for teacher fellowship.

Supplementary data

Copies of ^{1}H and ^{13}C NMR spectra of compounds **4a**, **4b**, **5**, **2**, **6a**, **6b**, **7** and of ^{1}H–^{1}H COSY spectrum of **5** are provided. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.02.002.

References

1. Bunzel, M.; Ralph, J.; Steinhart, H. *Czech J. Food Sci.* **2004**, *22*, 64–69.
2. Ralph, J.; Bunzel, M.; Marita, J. M.; Hatfield, R. D.; Lu, F.; Kim, H.; Schatz, P. F.; Grabber, J. H.; Steinhart, H. *Phytochem. Rev.* **2004**, *3*, 79–96.
3. Waldron, K. W.; Smith, A. C.; Parr, A. J.; Na, A.; Parker, M. L. *Trends Food Sci. Technol.* **1997**, *8*, 213–221.
4. Birosova, L.; Mikulasova, M.; Vaverkova, S. *J. Agric. Food Chem.* **2007**, *55*, 10183–10186.
5. Gomes, C. A.; Girao da Cruz, T.; Andrade, J. L.; Milhazes, N.; Borges, F.; Marques, M. P. M. *J. Med .Chem.* **2003**, *46*, 5395–5401.
6. Saulnier, L.; Crépeau, M.; Lahaye, M.; Thibault, J.; Garcia-Conesa, M. T.; Kroon, P. A.; Williamson, G. *Carbohydr. Res.* **1999**, *320*, 82–92.
7. Corey, E. J.; Battacharyya, S. *Tetrahedron Lett.* **1979**, 3919–3922.
8. Bluhm, M. E.; Kim, S. S.; Dertz, E. A.; Raymond, K. N. *J. Am. Chem. Soc.* **2002**, *124*, 2436–2437.
9. Jacobs, A. *Br. J. Haematol.* **1979**, *43*, 1.
10. Neilands, J. B. In *Development of Iron Chelators for Clinical Use*; Martell, A. E., Anderson, W. F., Badman, D. G., Eds.; Elsevier: Amsterdam, 1981.
11. Jacobs, A.; White, G. P.; Tait, G. H. *Biochem. Biophys. Res. Commun.* **1977**, *74*, 1626–1630.
12. Nakamura, Y.; Torikai, K.; Ohigashi, H. *J. Agric. Food Chem.* **2001**, *49*, 5674–5678.
13. Ueda, J.; Saito, N.; Shimazu, Y.; Ozawa, T. *Arch. Biochem. Biophys.* **1996**, *333*, 377–384.
14. Birosova, L.; Mikulasova, M.; Vaverkova, S. *Biomed. Pap. Med. Fac. Univ. Palacky Olomoc Czech Repub.* **2005**, *149*, 489–491.
15. Belicova, A.; Kriskova, L.; Nayg, M.; Krajcovic, J.; Ebringer, L. *Folia Microbiol.* **2001**, *47*, 511–514.
16. Carajal, G.; Penna, S.; Carbojal, E. J. *J. Revista Latiinoamericana. de. Microbiol.* **1962**, *5*, 45–53.
17. Draths, K. M.; Frost, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 2395–2400.
18. Li, K.; Frost, J. W. *J. Am. Chem. Soc.* **1998**, *120*, 10545–10546.
19. Hansen, C. A.; Dean, A. B.; Draths, K. M.; Frost, J. W. *J. Am. Chem. Soc.* **1999**, *121*, 3799–3800.
20. Kambourakis, S.; Frost, J. W. *J. Org. Chem.* **2000**, *65*, 6904–6909.
21. Gibson, J. M.; Thomas, P. S.; Thomas, J. D.; Barker, J. L.; Chandran, S. S.; Harrup, M. K.; Draths, K. M.; Frost, J. W. *Angew .Chem., Int. Ed.* **2001**, *40*, 1945–1946.
22. Ran, N.; Knop, D. R.; Draths, K. M.; Frost, J. W. *J. Am. Chem. Soc.* **2001**, *123*, 10927–10934.
23. Li, W.; Xie, D.; Frost, J. W. *J. Am. Chem. Soc.* **2005**, *127*, 2874–2882. and references cited therein.
24. Achkar, J.; Xian, M.; Zhao, H.; Frost, J. W. *J. Am. Chem. Soc.* **2005**, *127*, 5332–5333.
25. Koppisch, A. T.; Hotta, K.; Fox, D. T.; Ruggiero, C. E.; Kim, C.; Sanchez, T.; Iyer, S.; Browder, C. C.; Unkefer, P. J.; Unkefer, C. J. *J. Org. Chem.* **2008**, *73*, 5759–5765.
26. Sainsbury, M.; Dyke, S. F.; Moon, B. J. *J. Chem. Soc. C* **1970**, 1797–1800.
27. Groseclose, E. E.; Ribbons, D. W. *Biochem. Biophys. Res. Commun.* **1973**, *55*, 897–903.
28. Fetzner, S.; Muller, R.; Lingens, F. *Biol. Chem. Hoppe-Seyler* **1989**, *370*, 1173–1182.
29. Daumy, G. O.; Mccoll, A. S.; Andrews, G. C. *J. Chem. Soc., Chem. Commun.* **1979**, 1073a.
30. Shindo, K.; Nakamura, R.; Osawa, A.; Kagami, O.; Kanob, K.; Furukawa, K.; Misawa, N. *J. Mol. Catal. B: Enzym.* **2005**, *35*, 134–141.
31. Gramer, C. J.; Raymond, K. N. *Org. Lett.* **2001**, *3*, 2827–2830.
32. De Voss, J. J.; Rutter, K.; Schroeder, B. G.; Su, H.; Zhu, Y.; Barry, C. E., 3rd *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 1252–1257.
33. Nakanishi, I.; Nishizawa, C.; Ohkubo, K.; Takeshita, K.; Suzuki, K. T.; Ozawa, T.; Hecht, S. M.; Tanno, M.; Sueyoshi, S.; Miyata, N.; Okuda, H.; Fukuzumi, S.; Ikota, N.; Fukuhara, K. *Org. Biomol. Chem.* **2005**, *3*, 3263–3265.
34. Saito, S.; Kawabata, J. *Helv. Chim. Acta* **2006**, *89*, 1395–1406.
35. Forrest, J.; Petrow, V. *J. Chem. Soc.* **1950**, 2340–2342.
36. Rajgopalan, S.; Varadrajan, S. *Proc. Indian Acad. Sci. Sect. A* **1949**, *30*, 265–269.
37. Aghoramurthy, K.; Seshadri, T. R. *Proc. Indian Acad. Sci. Sect. A* **1952**, *35*, 327–331.
38. Huang, D.-S.; Ting, S.-H. *J. Chem. Res. (S)* **1994**, 500–501.
39. Sher, M.; Tam Dang, T. H.; Ahmed, Z.; Rashid, M. A.; Fischer, C.; Langer, P. *J. Org. Chem.* **2007**, *72*, 6284–6286.
40. Ferrier, R. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1455–1458.
41. Ferrier, R. J. *Chem. Rev.* **1993**, *93*, 2779. and references cited therein.
42. Chida, N.; Othuuka, M.; Ogura, K.; Ogawa, S. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2118–2121.
43. Dhavale, D. D.; Bhujbal, N. N.; Joshi, P.; Desai, S. G. *Carbohydr. Res.* **1994**, *263*, 303–307.
44. Vyavahare, V. P.; Chakraborty, C.; Maity, B.; Chattopadhyay, S.; Puranik, V. G.; Dhavale, D. D. *J. Med. Chem.* **2007**, *50*, 5519–5523.
45. Vyavahare, V. P.; Chattopadhyay, S.; Puranic, V. G.; Dhavale, D. D. *Synlett* **2007**, 559–562.
46. Dhavale, D. D.; Saha, N. N.; Desai, V. N. *J. Org. Chem.* **1997**, *62*, 7482–7484.
47. Saha, N. N.; Desai, V. N.; Dhavale, D. D. *J. Org. Chem.* **1994**, *64*, 1715–1719.
48. Karche, N. P.; Jachak, S. M.; Dhavale, D. D. *J. Org. Chem.* **2003**, *68*, 4531–4534.
49. Karche, N. P.; Jachak, S. M.; Dhavale, D. D. *J. Org. Chem.* **2001**, *66*, 6323–6332.
50. Paul, M. D. *Medicinal Natural Products, A Biosynthetic Approach*, 2nd ed.; John Wiley and Sons: New York, 2001. pp 61, 124.
51. Mirza, S.; Molleyres, L.; Vasella, A. *Helv. Chim. Acta* **1985**, *68*, 988–996.