

SUPPORTING INFORMATION

Synthesis of a 3,4,5-trimethoxy-benzoyl ester analog of epigallocatechin-3-gallate (EGCG): A potential route to the natural product green tea catechin, EGCG

Nurulain T. Zaveri*

Pharmaceutical Discovery Division, SRI International, 333 Ravenswood Ave, Menlo Park, CA 94025.

General. NMR spectra (^1H 300 MHz, ^{13}C 75 MHz) were recorded on a Varian Gemini 300 instrument. Chemical shifts are reported in ppm (δ) units, relative to CHCl_3 (7.26 ppm) or acetone- d_6 as standard. For ^1H NMR, the following abbreviations are used: br: broad; s: singlet; d: doublet; t: triplet; q: quartet; dd: doublet of doublets; m: multiplet; exch: proton exchanged on addition of D_2O . Mass spectra were obtained on a Ribermag Model R10-10C mass spectrometer using chemical ionization and desorption chemical ionization. High resolution mass spectra were performed by the University of Minnesota Department of Chemistry. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia.

2'-Hydroxy-4',6',3,4,5-pentabenzoyloxy-chalcone (5). ^1H NMR (300 MHz, CDCl_3): δ 4.87 (s, 4H, CH_2OPh), 5.12 (m, 6H, CH_2OPh), 6.18 (d, 1H, 3'-Ar-H), 6.25 (d, 1H, 5'-Ar-H), 6.70 (s, 2H, 2, 6-Ar-H), 7.19-7.45 (m, 25H, OBn-Ar-H), 7.66 (d, 1H, $\text{C}(\text{O})\text{-CH=CH-}$), 7.78 (d, 1H, $\text{C}(\text{O})\text{-CH=CH-}$), 14.21 (s, 1H, OH). ^{13}C NMR (75 MHz, CDCl_3): δ 70.39, 71.20, 75.26, 93.07, 95.22, 108.44, 127.10-128.83, 130.84, 135.80, 135.94, 136.89, 142.46, 152.92, 161.55, 165.24, 168.17, 192.63. Anal. Calcd. for $\text{C}_{50}\text{H}_{42}\text{O}_7$ (754.88): C 79.56, H 5.61; Found: C 79.47, H 5.64.

5,7,3',4',5'-Pentabenzoyloxyflav-3-ene (6). ^1H NMR (300 MHz, CDCl_3): δ 4.99, 5.03, 5.05, 5.09 (4s, 10 H, CH_2OPh), 5.53 (dd, $J=9.95$ and 3.29 Hz, 1H, 3-H), 5.72 (dd, $J=3.24$ and 1.95 Hz, 1H, 2-H), 6.13 and 6.20 (2d, $J=2.17$, 2H, 6, 8-Ar-H), 6.78 (s, 2H, 2', 6'-Ar-H), 6.86 (dd, $J=9.86$ and 1.57 Hz, 1H, 4-H), 7.25-7.41 (m, 25H, Ar-H).

2,3-trans-5,7,3',4',5'-Pentabenzoyloxyflavan-3-ol [(±) 5,7,3',4',5'-Pentabenzyl gallocatechin] (7). ¹H NMR (300 MHz, CDCl₃): δ 2.64 (dd, J= 16.45 and 8.88 Hz, 1H, 4-H axial), 3.10 (dd, J= 16.42 and 5.68 Hz, 1H, 4-H equatorial), 3.96 (m, 1H, 3-H), 4.61 (d, J= 8.12 Hz, 1H, 2-H), 5.05 (m, 10H, CH₂OPh), 6.20 and 6.28 (2s, 2H, 6,8-Ar-H), 6.73 (s, 2H, 2', 6'-Ar-H), 7.25-7.41 (m, 25H, Ar-H). MS (DCI-NH₃): 757 (M+H), 774 (M+NH₄).

5,7,3',4',5'-Pentabenzoyloxyflavan-3-one (8). ¹H NMR (300 MHz, CDCl₃): δ 3.41 (d, J= 21.3 Hz, 1H, 4-H), 3.39 (d, J= 21.3 Hz, 1H, 4-H), 5.03 (m, 10H, CH₂OPh), 5.24 (s, 1H, 2-H), 6.35 and 6.37 (2s, 2H, 6,8-Ar-H), 6.67 (s, 2H, 2', 6'-Ar-H), 7.25-7.41 (m, 25H, Ar-H).

2,3-cis 5,7,3',4',5'-Pentabenzoyloxyflavan-3-ol [(±) 5,7,3',4',5'-Pentabenzyl epigallocatechin] (9). ¹H NMR (300 MHz, CDCl₃): δ 1.61 (broad s, 1H, OH), 2.92 (dd, J= 17.13 and 4.40 Hz, 1H, 4-H), 3.02 (dd, J= 17.64 and 2.27 Hz, 1H, 4-H), 4.21 (m, 1H, 3-H), 4.90 (broad s, 1H, 2-H), 5.03 (s, 4H, CH₂OPh), 5.06 (s, 2H, CH₂OPh), 5.14 (s, 4H, CH₂OPh), 6.28 (s, 2H, 6,8-Ar-H), 6.81 (s, 2H, 2', 6'-Ar-H), 7.25-7.41 (m, 25H, Ar-H). MS (DCI-NH₃): 757 (M+H), 774 (M+NH₄).

2,3-trans- [(±) 3-O-(3,4,5-trimethoxybenzoyl) gallocatechin] (SR 13192). ¹H NMR (300 MHz, acetone-d₆): δ 2.79 (dd, J= 18.00 and 6.00 Hz, 1H, 4-H), 3.14 (dd, J= 17.70 and 6.40 Hz, 1H, 4-H), 3.81 (s, 3H, OCH₃), 3.87 (s, 6H, OCH₃), 5.06 (d, J= 7.5 Hz, 1H, 2-H), 5.31 (m, 1H, 3-H), 6.02 (d, J= 2.34 Hz, 1H, 8-H), 6.12 (d, J= 2.34 Hz, 1H, 6-H), 6.61 (s, 2H, 2'', 6''-Ar-H), 7.20 (s, 2H, 2', 6'-Ar-H). ¹³C NMR (75 MHz, acetone-d₆): δ 25.48, 56.51, 60.25, 71.72, 79.42, 95.54, 96.25, 106.77, 107.79, 146.25, 154.0, 158.75, 159.0. MS (DCI-NH₃): 501 (M+H). HRMS: Calcd. 501.4634, Found. 501.1376.

2,3-cis [(±) 3-O-(3,4,5-trimethoxybenzoyl) epigallocatechin] (SR 13193). ¹H NMR (300 MHz, acetone-d₆): δ 3.10 (m, 2H, 4-H), 3.79 (s, 3H, OCH₃), 3.86 (s, 6H, OCH₃), 5.20 (s, 1H, 2-H), 5.53 (m, 1H, 3-H), 6.08 (m, 2H, 6, 8-H), 6.71 (s, 2H, 2'', 6''-Ar-H), 7.20 (s, 2H, 2', 6'-Ar-H), 7.28 (s, 1H, OH, exch), 7.80 (s, 2H, two OH, exch), 8.09 (s, 1H, OH, exch), 8.29 (s, 1H, OH, exch). ¹³C NMR (75 MHz, acetone-d₆): δ 52.57, 83.07, 87.16, 97.39, 104.19, 121.89, 122.88, 124.96, 132.78, 134.27, 152.76, 157.30, 159.43, 169.83, 172.81, 180.44, 183.20, 183.91, 184.34, 192.67. MS (DCI-NH₃): 501 (M+H). HRMS: Calcd. 501.4634, Found. 501.1415.