Supplementary information

Synthesis of New 4-(*tert*-Octyl)phenol Derivatives and Their Anticancer Activity against Human Prostate and Lung Cancer Cell Lines

Haiyan Che, Yuanying Fang, Santosh K. Gurung, Jun Luo, Deok Hyo Yoon,[†] Gi-Ho Sung,[‡] Tae Woong Kim,[†] and Haeil Park[*]

College of Pharmacy, [†]College of Natural Science (Biochemistry), Kangwon National University, Chunchon 200-701, Korea
[*]E-mail: haeilp@kangwon.ac.kr
[‡]Rural Development Administration, Suwon 441-707, Korea
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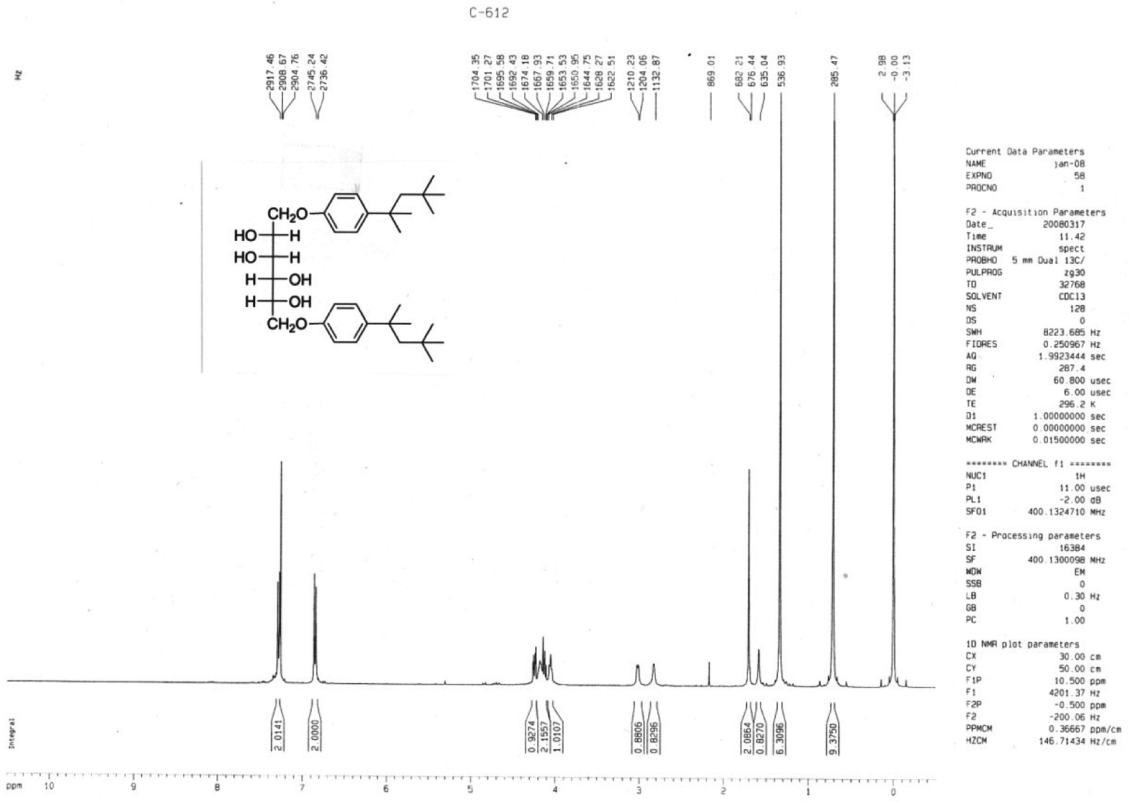
Materials and Methods for Active Compound 7

Analysis of Structure of 7. ^{1}H-NMR spectra were recorded on a Bruker Avance 300 (300 MHz) and Bruker DPX 400 (400 MHz). Chemical shifts are reported in ppm downfield relative to tetramethylsilane as an internal standard. ^{13}C-NMR spectra were recorded on a Bruker DPX 400 (100 MHz). Melting points were recorded on a Fisher-Johns microscopic scale melting point apparatus.

Preparation of Compound 7. Militarin analog MA-1 was prepared from D-mannitol following the procedure and conditions as described in the followings: Hydroxyl groups of D-mannitol were fully protected by benzyl groups. Selective debenzylation–acetylation of benzyl protecting groups on the primary alcohols using $ZnCl_2$–Ac_2O–HOAc, followed by deacetylation with K_2CO_3 in MeOH gave 2, 3, 4, 5-tetra-*O*-benzyl-D-mannitol. Tosylation of the intermediate with TsCl and DMAP in pyridine followed by reaction with 4-(*tert*-octyl)phenol, K_2CO_3 and KI in CH_3CN at reflux conditions and debenzylation with Pd/C-HCOOH gave militarin analog MA-1.

(2*R*,3*R*,4*R*,5*R*)-1,6-bis(4-(2,4,4-trimethylpentan-2-yl)-phenoxy)hexane-2,3,4,5-tetraol (7). Colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.27-7.29 (d, 4H, J = 8.8 Hz, Ph), 6.84-6.86 (d, 4H, J = 8.8 Hz, Ph), 4.23-4.26 (dd, 2H, J = 8.8 Hz, 3.1 Hz, H, H), 4.11-4.19 (m, 4H, J = 8.8 Hz, 6.2 Hz, H, H, H_2, H_5), 4.04-4.07 (t, 2H, J = 5.8 Hz, H_3, H_4), 3.01-3.02 (d, 2H, 2xOH), 2.83 (s, 2H, 2xOH), 1.71 (s, 4H, 2x-CH_2-), 1.34 (s, 12H, 4xMe), 0.71 (s, 18H, 6xMe); ^{13}C-NMR (100 MHz, $CDCl_3$) : δ 155.9 (C_1-Ph), 143.1 (C_4-Ph), 127.2 (C_3-Ph, C_5-Ph), 113.8 (C_2-Ph, C_6-Ph), 71.3 (C_3, C_4), 70.6 (C_2, C_5), 69.2 (C_1, C_6), 56.9 ($\underline{C}H_2$-octyl), 38.00 ($\underline{C}$-Me_2), 32.3 ($\underline{C}$-Me_3), 31.8 (Me_3), 31.7 (Me_2).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1667.93
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1132.87
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2.98
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Integral
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2.0000
0.9274
2.1957
1.0107
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0.8296
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0.8270
6.3096
9.3750
ppm
10
9
8
7
6
5
4
3
2
1
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H
HO
H
H
OH
H
OH
CH2O
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MCREST 0.00000000 sec
MCWRK 0.01500000 sec
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LB 0.30 Hz
GB 0
PC 1.00
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CY 50.00 cm
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F2P -0.500 ppm
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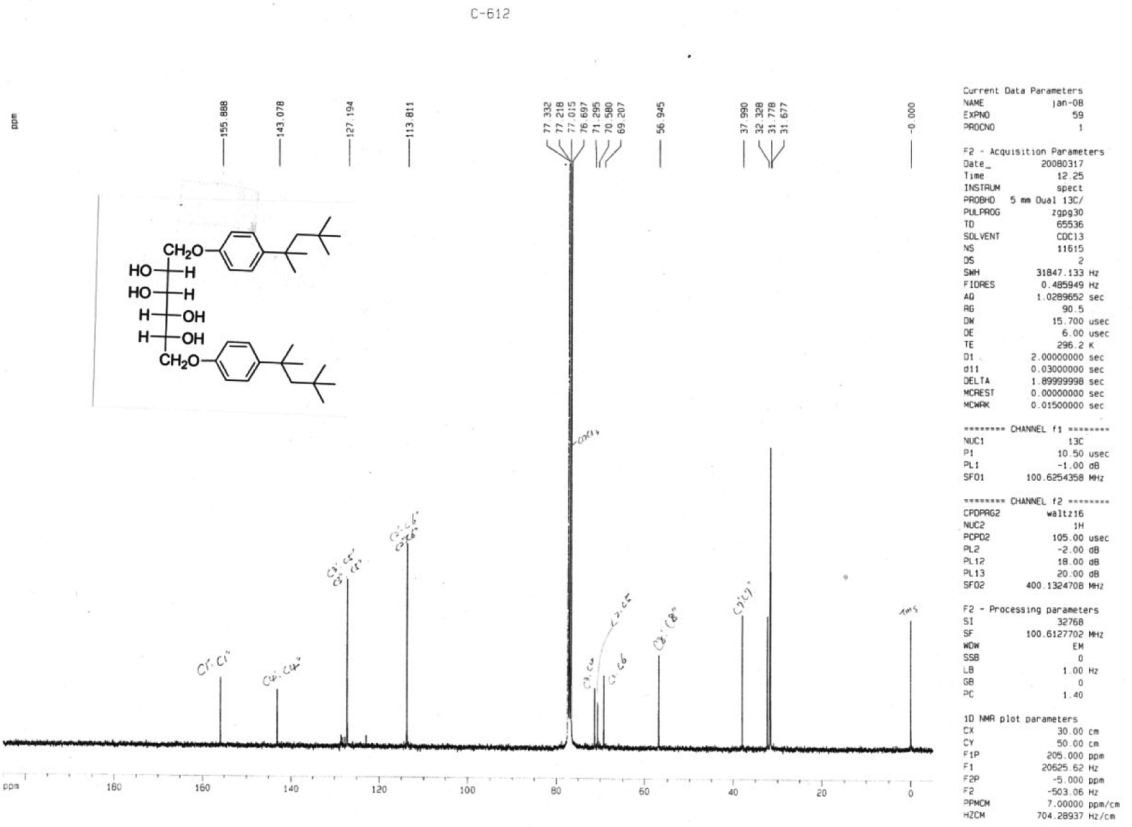
PPMCM 0.36667 ppm/cm
HZCM 146.71434 Hz/cm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CH2O
HO
H
HO
H
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OH
H
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DE 6.00 usec
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PL12 18.00 dB
PL13 20.00 dB
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