

Structure-activity relationships of 3,3'-phenylmethylene-bis-4-hydroxycoumarins: selective and potent inhibitors of gram-positive bacteria

Kanokporn Petnapapun, Warinthorn Chavasiri and Pornthep Sompornpisut*

Supplementary information

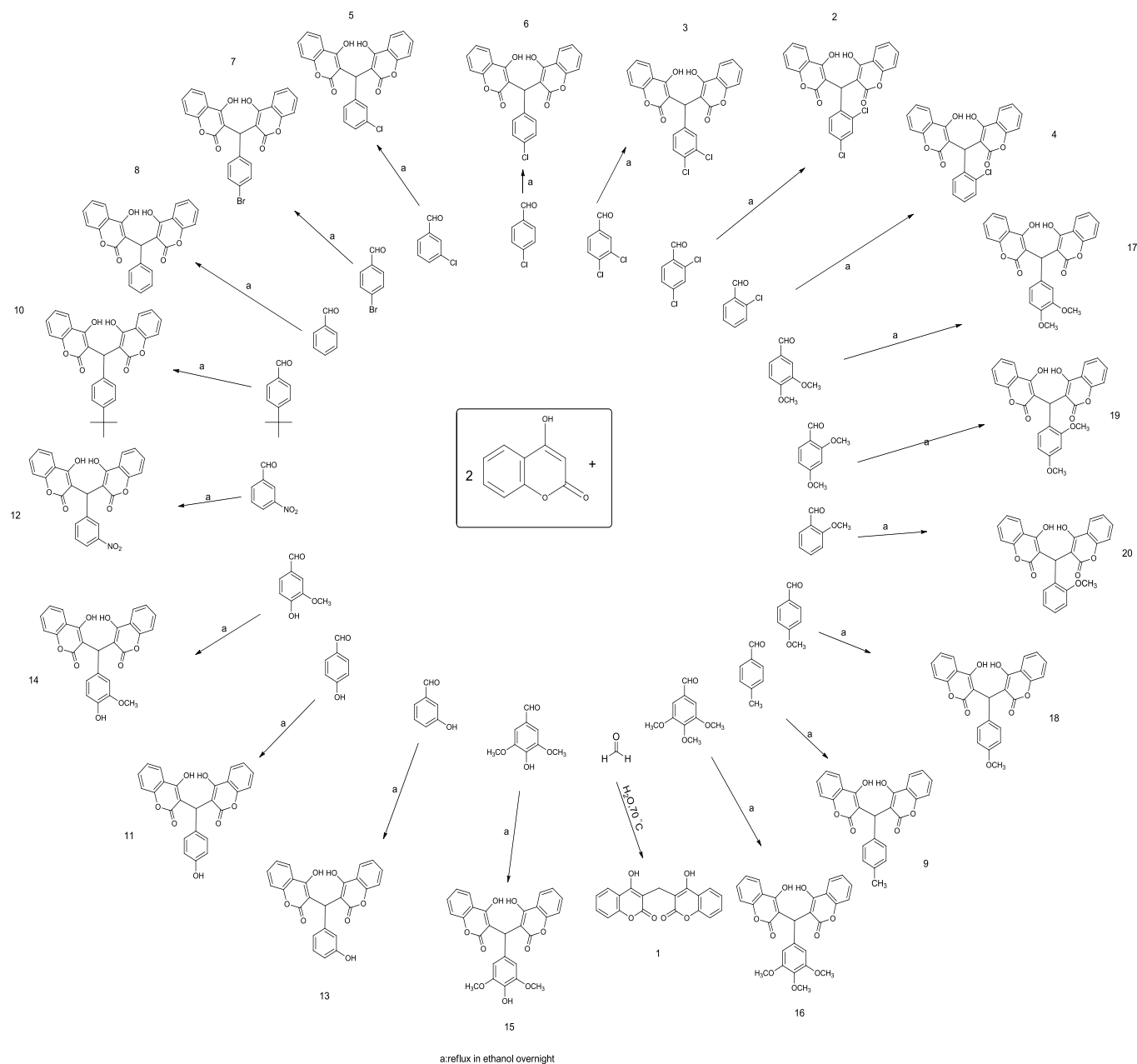
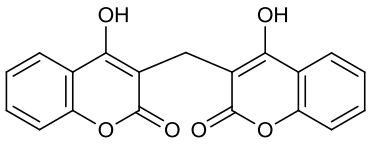
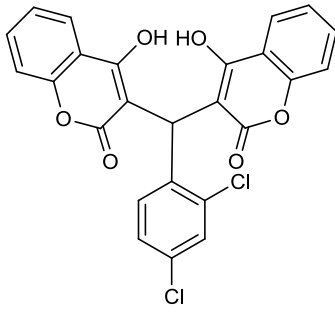


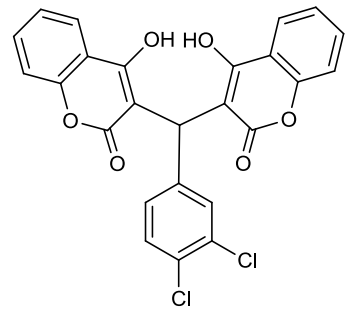
Figure S1 Synthesis of dicoumarol derivatives via condensation of 4-hydroxycoumarin with ortho-, meta- and para-substituted benzaldehydes



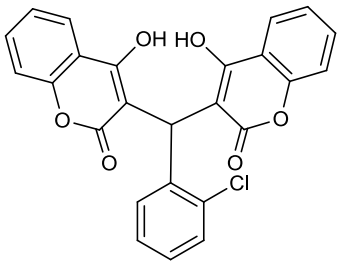
1



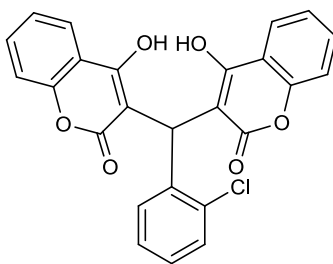
2



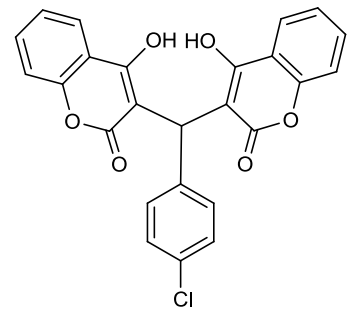
3



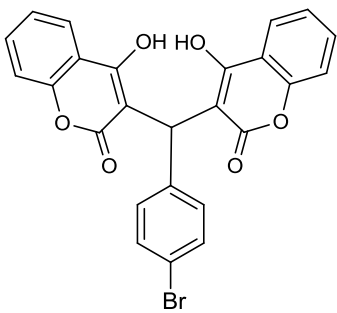
4



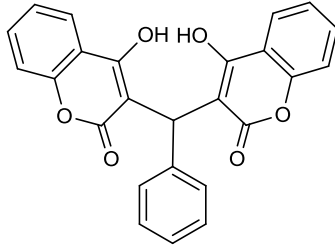
5



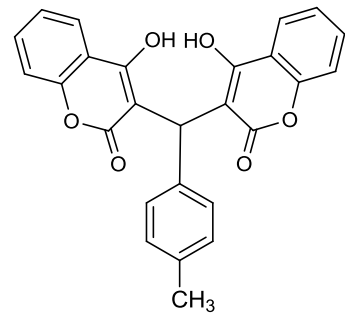
6



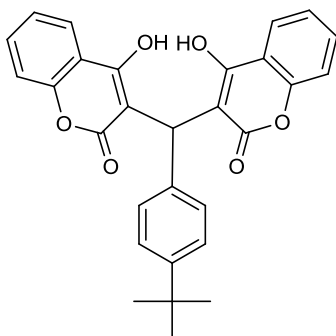
7



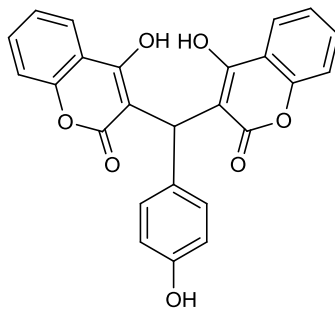
8



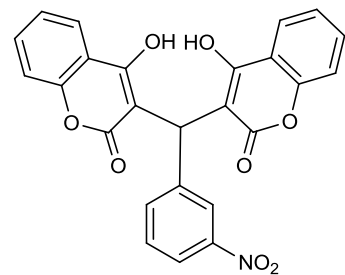
9



10



11



12

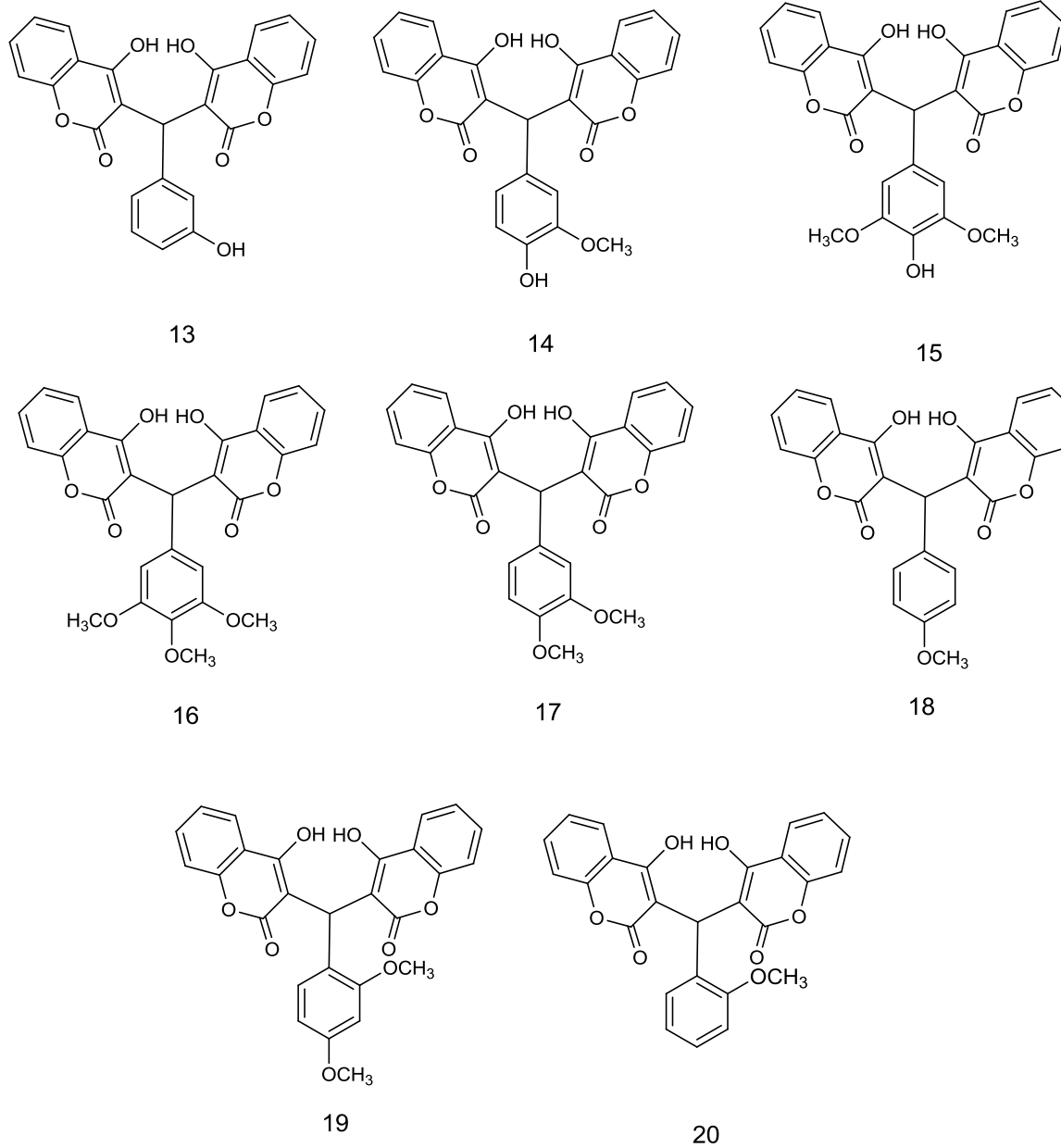


Figure S2 Schematic representation of the synthesis compounds 1-20.

Characteristic spectroscopic data

1. 3,3'-(methylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₁₉H₁₂O₆, Yield 85%; ¹H-NMR(CDCl₃) δ (ppm): 3.85(2H,s), 7.33-7.40(4H,m), 7.59(2H,t), 7.99(2H,d) and 11.30(2H,s)

2. 3,3'-(2,4-dichlorophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₄Cl₂O₆, Yield 72%; ¹H-NMR(CDCl₃) δ (ppm): 6.02(1H,s), 7.28(2H,d), 7.35-7.40(5H,m), 7.58(2H, t), 8.05(2H,dd), 10.95(1H,s) and 11.72(1H,s)

3. 3,3'-(3,4-dichlorophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₄Cl₂O₆, Yield 76%; ¹H-NMR(CDCl₃) δ (ppm): 6.01(1H,s), 7.06(1H,d), 7.27(2H,d), 7.36-7.46(4H,m), 7.65(2H, t), 8.04(2H,dd), 11.31(1H,s) and 11.58(1H,s)

4. 3,3'-(2-chlorophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₅ClO₆, Yield 78%; ¹H-NMR(CDCl₃) δ (ppm): 6.14(1H,s), 7.23(3H,m), 7.39(4H,m), 7.43(1H,d), 7.61(2H, t), 8.02(2H,d), 10.93(1H,s) 11.63(1H,s)

5. 3,3'-(3-chlorophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₅ClO₆, Yield 80%; ¹H-NMR(CDCl₃) δ (ppm): 6.03(1H,s), 7.24(4H,m), 7.37-7.41(4H,m), 7.62(2H,dt), 8.02(2H,s), 11.29(1H,s) and 11.60(1H,s)

6. 3,3'-(4-chlorophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₅ClO₆, Yield 78%; ¹H-NMR(CDCl₃) δ (ppm): 6.04(1H,s), 7.16(2H,d), 7.28(2H,d), 7.41(4H,m), 7.63(2H, t), 8.04(2H,dd), 11.33(1H,s) and 11.55(1H,s)

7. 3,3'-(4-bromophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₅BrO₆, Yield 75%; ¹H-NMR(CDCl₃) δ (ppm): 6.01(1H,s), 7.10(2H,d), 7.41(6H,m), 7.63(2H, t), 8.02(2H,dd), 11.33(1H,s) and 11.58(1H,s)

8. 3,3'-(phenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₆O₆, Yield 71%; ¹H-NMR(CDCl₃) δ (ppm): 6.13(1H,s), 7.20-7.45 (9H,m), 7.61 (2H,t), 8.1 (2H,d) 11.30(1H,s) and 11.60(1H,s)

9. 3,3'-(4-methylphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₆H₁₈O₆, Yield 82%; ¹H-NMR(CDCl₃) δ (ppm): 2.37(3H,s), 6.04(1H,s), 7.18(4H,t), 7.40(4H,t), 7.61(2H,t), 8.02(2H,dd), 11.28(1H,s) and 11.52(1H,s)

10. 3,3'-(4-tertbutylphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₉H₂₄O₆, Yield 85%; ¹H-NMR(CDCl₃) δ (ppm): 1.29(9H,s), 6.05(1H,s), 7.14(2H,d), 7.33(2H,d), 7.40(4H,d), 7.62(2H,dt), 8.02(2H,s), 11.28(1H,s) and 11.50(1H,s)

11. 3,3'-(4-hydroxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₆O₇, Yield 74%; ¹H-NMR(CDCl₃) δ (ppm): 5.48(1H,s,br), 6.12 (1H,s), 6.79 (2H,d), 7.08(2H,d),7.40 (4H,m), 7.62(2H,t), 8.02(2H,d), 11.31(1H,s) and 11.49(1H,s)

12. 3,3'-(3-nitrophenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₅NO₈, Yield 87%; ¹H-NMR(CDCl₃) δ (ppm): 6.13 (1H,s), 7.38-7.60(6H,m), 7.67(2H,t), 7.98-8.19(4H,m), 11.39(1H,s) and 11.58(1H,s)

13. 3,3'-(3-hydroxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₅H₁₆O₇, Yield 84%; ¹H-NMR(CDCl₃) δ (ppm): 6.10(1H,s), 6.70–6.85 (3H,m), 7.22 (1H,t), 7.41(4H,m),7.66 (2H,m) 8.05(2H,d), 11.28(1H,s) and 11.60(1H,s)

14. 3,3'-(4-hydroxy-3-methoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₆H₁₈O₈, Yield 83%; ¹H-NMR(CDCl₃) δ (ppm): 3.74(3H,s), 5.58(1H,s), 6.02(1H,s), 6.66(2H,t), 6.72(1H,d), 6.86(1H,d), 7.40(4H,d),7.61(2H,t), 8.03(1H,d), 11.25(1H,s) and 11.51(1H,s)

15. 3,3'-(4-hydroxy-3,5-dimethoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₇H₂₀O₉, Yield 87%; ¹H-NMR(CDCl₃) δ (ppm): 3.70(6H,s), 6.08(1H,s), 6.42(2H,s), 7.41(4H,d), 7.63(2H,t), 8.02(2H,d), 11.28(1H,s) and 11.53(1H,s)

16. 3,3'-(3,4,5-trimethoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₈H₂₂O₉, Yield 88%; ¹H-NMR(CDCl₃) δ (ppm): 3.70(6H,s), 3.83(3H,s), 6.06(1H,s), 6.40(2H,s), 7.35-7.42(4H,m), 7.62(2H,t), 8.03(2H,s), 11.28(1H,s) and 11.53(1H,s)

17. 3,3'-(3,4-dimethoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₇H₂₀O₈, Yield 83%; ¹H-NMR(CDCl₃) δ (ppm): 3.72(3H,s), 3.86(3H,s) 6.08(1H,s), 6.70(1H,s), 6.79(2H,dd), 7.40(4H,d), 7.61(2H,t), 8.03(2H,d) 11.29(1H,s) and 11.53(1H,s)

18. 3,3'-(4-methoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₆H₁₈O₇, Yield 81%; ¹H-NMR(CDCl₃) δ (ppm): 3.80(3H,s), 6.08(1H,s), 6.87(2H,d), 7.14(2H,d), 7.42(4H,d), 7.63(2H,t), 8.08(2H,d), 11.30(1H,s) and 11.51(1H,s)

19. 3,3'-(2-methoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₆H₁₈O₇, Yield 81%; ¹H-NMR(CDCl₃) δ (ppm): 3.58(3H,s), 6.08(1H,s), 6.86(1H,d), 6.95(1H, t), 7.24-7.41(6H,m), 7.59(2H,t), 8.01(2H,d), 11.18(1H,s) and 11.23(1H,s)

20. 3,3'-(2,4-dimethoxyphenylmethylene)bis-(4-hydroxy-2H-chromen-2-one)

Solid; Molecular formula: C₂₇H₂₀O₈, Yield 89%; ¹H-NMR(CDCl₃) δ (ppm): 3.55(3H,s), 3.80(3H,s) 6.01(1H,s), 6.43(2H,m), 7.17 (1H,d), 7.38 (4H,m), 7.59(2H,t), 8.02(2H,d), 11.15(1H,s) and 11.18(1H,s)

