Supporting information

New Insights into the SAR and Binding Modes of Bis(hydroxyphenyl)-thiophenes and -benzenes: Influence of Additional Substituents on 17β-Hydroxysteroid Dehydrogenase Type 1 (17β-HSD1) Inhibitory Activity and Selectivity.

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a) spectroscopic data

2-(4-Fluorophenyl)-5-(3-methoxyphenyl)thiophene (3a). ^{1}H NMR (CD_3COCD_3): 7.72-7.71 (m, 2H), 7.45 (d, *J*= 3.6 Hz, 1H), 7.40 (d, *J*= 3.6 Hz, 1H), 7.31 (t, *J*= 7.9 Hz, 1H), 7.20 (d, *J*= 8.2 Hz, 1H), 7.20-7.18 (m, 3H), 6.88 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (CD_3COCD_3): 130.15, 127.30, 124.55, 117.80, 115.95, 115.80, 113.30, 110.80, 54.75 cm^{-1}.

3-[5-(4-Fluorophenyl)-2-thienyl]phenol (3). ^{1}H NMR (CD_3COCD_3): 8.48 (s, 1H), 7.73 (dd, *J*= 1.5 Hz and *J*= 8.2 Hz, 2H), 7.40-7.38 (m, 2H), 7.25-7.12 (m, 5H), 6.81 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 135.50, 133.15, 127.10, 126.50, 120.10, 117.45; IR: 3474, 2835, 1604, 1485, 1257, 802 cm^{-1}.

4-[5-(3-Methoxyphenyl)-2-thienyl]aniline (4a). ^{1}H NMR (CD_3COCD_3): 7.53 (dd, *J*= 1.2 Hz and *J*= 3.5 Hz, 1H), 7.50 (dd, *J*= 1.2 Hz and *J*= 5.3 Hz, 1H), 7.47-7.45 (m, 2H), 7.41-7.38 (m, 2H), 7.32-7.29 (m, 2H), 7.19 (dd, *J*= 1.2 Hz and *J*= 5.3 Hz, 1H), 6.97-6.95 (m, 1H), 3.92 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.20, 144.85, 138.40, 138.20, 136.60, 134.55, 131.00, 129.55, 129.00, 126.00, 124.45, 119.00, 113.90, 112.10, 55.65; IR: 3070, 2834, 1600, 1579, 1228, 1044, 692 cm^{-1}.

3-[5-(4-Aminophenyl)-2-thienyl]phenol (4). ^{1}H NMR (CD_3SOCD_3): 7.73 (d, *J*= 2.2 Hz, 2H), 7.49 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 2H), 7.30 (d, *J*= 2.2 Hz, 2H), 7.23 (t, *J*= 1.2 Hz, 1H), 7.11 (d, *J*= 1.0 Hz, 1H), 7.05 (s, 1H), 6.73 (d, *J*= 2.0 Hz, 1H); ^{13}C NMR (CD_3SOCD_3): 157.80, 142.90, 141.20, 134.55, 130.25, 126.35, 125.10, 124.80, 122.45, 116.10, 115.00, 111.85; IR: 3448, 2868, 1580, 1484, 1184, 804, 775 cm^{-1}.

4-[5-(3-Methoxyphenyl)-2-thienyl]benzenethiol (5a). ^{1}H NMR (CD_3COCD_3): 7.41 (d, *J*= 8.8 Hz, 2H), 7.38 (d, *J*= 3.8 Hz, 1H), 7.30 (t, *J*= 7.8 Hz, 1H), 7.23-7.21 (m, 1H), 7.19 (t, *J*= 2.2 Hz, 2H), 6.85-6.83 (m, 1H), 6.72 (d, *J*= 8.8 Hz, 2H), 3.85 (s, 3H); IR: 3080, 1491, 1243, 801 cm^{-1}.

3-[5-(4-Sulfanylphenyl)-2-thienyl]phenol (5). ^{1}H NMR (CD_3COCD_3): 8.52 (s, 1H), 7.41 (d, *J*= 3.8 Hz, 1H), 7.33-7.25 (m, 6H), 7.13-7.12 (m, 2H), 6.84 (d, *J*= 7.8 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 158.90, 150.70, 139.10, 138.80, 135.80, 131.15, 130.80, 130.15, 128.15, 127.35, 125.00, 117.85, 116.30, 113.30.

4-[5-(3-Methoxyphenyl)-2-thienyl]benzonitrile (6a). ^{1}H NMR (CD_3COCD_3): 7.90 (d, *J*= 8.8 Hz, 2H), 7.81 (d, *J*= 8.8 Hz, 2H), 7.67 (d, *J*= 3.8 Hz, 1H), 7.54 (d, *J*= 3.8 Hz, 1H), 7.35 (t, *J*= 8.0 Hz, 1H), 7.30 (d, *J*= 8.0 Hz, 1H), 7.25 (t, *J*= 2.0 Hz, 1H), 6.94-6.92 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.30, 146.45, 141.80, 139.20, 135.60, 133.70, 131.10, 127.70, 126.65, 126.05, 118.90, 114.65, 112.00, 111.40, 55.70; IR: 2925, 2223, 1601, 1575, 1112, 805 cm^{-1}.

4-[5-(3-Hydroxyphenyl)-2-thienyl]benzonitrile (6). ^{1}H NMR (CD_3COCD_3): 8.06 (s, 1H), 7.89 (d, *J*= 8.5 Hz, 2H), 7.80 (d, *J*= 8.5 Hz, 2H), 7.65 (d, *J*= 4.0 Hz, 1H), 7.47 (d, *J*= 4.0 Hz, 1H), 7.26 (t, *J*= 7.8 Hz, 1H), 7.20-7.18 (m, 2H), 6.87-6.85 (m, 1H); ^{13}C NMR (CD_3COCD_3): 158.95, 146.70, 141.60, 139.30, 135.85, 133.75, 131.15, 127.70, 126.65, 125.70, 117.80, 116.25, 113.30, 111.35; IR: 3379, 2239, 1582, 1321, 775 cm^{-1}.

2-(3-Fluorophenyl)-5-(3-methoxyphenyl)thiophene (8a). ^{1}H NMR (CD_3COCD_3): 7.53-7.50 (m, 2H), 7.48-7.44 (m, 3H), 7.33 (d, *J*= 8.2 Hz, 1H), 7.26 (d, *J*= 8.2 Hz, 1H), 7.23 (t, *J*= 2.0 Hz, 1H), 7.06 (t, *J*= 8.2 Hz, 1H), 6.90 (dd, *J*= 2.0 Hz and *J*= 8.2 Hz, 1H), 3.84 (s, 3H).

3-[5-(3-Fluorophenyl)-2-thienyl]phenol (8). ^{1}H NMR (CD_3COCD_3): 8.52 (s, 1H), 7.39-7.37 (m, 2H), 7.34-7.29 (m, 3H), 7.13 (t, *J*= 7.9 Hz, 1H), 7.06 (s, 1H), 7.05-7.03 (m, 1H), 6.95-6.92 (m, 1H), 6.71-6.68 (m, 1H); ^{13}C NMR (CD_3COCD_3): 163.15, 158.85, 145.15, 142.35, 137.40, 136.10, 131.90, 125.40, 122.20, 117.75, 115.00, 113.15, 112.60; IR: 3676, 2989, 1580, 1394, 1054, 775 cm^{-1}.

***N*-(3-[5-(3-Methoxyphenyl)-2-thienyl]phenyl)methanesulfonamide (9a).** ^{1}H NMR (CD_3COCD_3): 8.67 (s, 1H), 7.68 (t, *J*= 1.2 Hz, 1H), 7.50-7.48 (m, 2H), 7.45 (d, *J*= 3.5 Hz, 1H), 7.42 (t, *J*= 8.2 Hz, 1H), 7.36-7.34 (m, 2H), 7.30 (d, *J*= 7.80 Hz, 1H), 7.27 (t, *J*= 1.2 Hz, 1H), 6.90 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 3.87 (s, 3H), 3.05 (s, 3H); ^{13}C NMR (CD_3COCD_3): 160.30, 143.60, 142.65, 135.30, 130.15, 124.85, 124.75, 124.30, 121.25, 120.25, 119.15, 117.85, 116.85, 113.40, 54.80, 37.40; IR: 2934, 2838, 1648, 1244, 1166, 1039, 772 cm^{-1}.

***N*-(3-[5-(3-Hydroxyphenyl)-2-thienyl]phenyl)methanesulfonamide (9).** ^{1}H NMR (CD_3COCD_3): 8.68 (s, 1H), 8.53 (s, 1H), 7.67 (s, 1H), 7.47 (d, *J*= 8.2 Hz, 1H), 7.43-7.40 (m, 3H), 7.30 (d, *J*= 8.8 Hz, 1H), 7.23 (t, *J*= 7.9 Hz, 1H), 7.18-7.16 (m, 2H), 6.83 (d, *J*= 8.2 Hz, 1H), 3.05 (s, 3H); ^{13}C NMR (CD_3COCD_3): 160.20, 143.60, 142.65, 135.30, 130.15, 129.30, 124.85, 124.75, 124.30, 121.20, 120.20, 119.15, 117.85, 116.85, 112.85, 110.80, 37.50; IR: 3499, 3279, 1587, 1470, 1308, 1142, 783 cm^{-1}.

***N*-(3-[5-(3-Methoxyphenyl)-2-thienyl]benzyl)methanesulfonamide (10a).** ^{1}H NMR (CD_3COCD_3): 7.77 (s, 1H), 7.65 (d, *J*= 7.5 Hz, 1H), 7.45-7.41 (m, 2H), 7.37-7.33 (m, 3H), 7.27 (d, *J*= 8.2 Hz, 1H), 7.24 (t, *J*= 1.8 Hz, 1H), 6.91 (dd, *J*= 2.5 Hz and *J*= 8.2 Hz, 1H), 4.40 (d, *J*= 6.4 Hz, 2H), 3.87 (s, 3H), 2.92 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 144.25,

144.00, 140.25, 136.35, 135.30, 131.05, 130.20, 128.75, 128.05, 125.70, 125.60, 125.50, 125.30, 118.70, 114.25, 111.70, 55.70, 47.45, 40.60.

***N*-(3-[5-(3-Hydroxyphenyl)-2-thienyl]benzyl)methanesulfonamide (10).** ^{1}H NMR (CD_3COCD_3): 8.44 (s, 1H), 7.73 (s, 1H), 7.60 (d, *J*= 7.8 Hz, 1H), 7.44 (d, *J*= 3.8 Hz, 1H), 7.41-7.39 (m, 2H), 7.34-7.32 (m, 1H), 7.22 (t, *J*= 7.8 Hz, 1H), 7.15-7.12 (m, 2H), 6.80-6.77 (m, 1H), 4.42 (d, *J*= 6.3 Hz, 2H), 3.02 (s, 3H); ^{13}C NMR (CD_3COCD_3): 165.20, 145.55, 139.15, 133.25, 129.05, 128.95, 128.75, 124.75, 125.60, 125.15, 119.20, 114.15, 110.80, 48.50, 41.80; IR: 3520, 2982, 1514, 1211, 785 cm^{-1}.

***N*-(3-[5-(3-Methoxyphenyl)-2-thienyl]phenyl)-4-methylbenzenesulfonamide (11a).** ^{1}H NMR (CD_3COCD_3): 7.62 (t, *J*= 1.5 Hz, 1H), 7.52 (d, *J*= 8.2 Hz, 2H), 7.38-7.30 (m, 5H), 7.28-7.22 (m, 5H), 6.74 (dd, *J*= 1.5 Hz and *J*= 8.2 Hz, 1H), 3.89 (s, 3H), 1.92 (s, 3H); IR: 2929, 1532, 1254, 1010, 896 cm^{-1}.

***N*-(3-[5-(3-Hydroxyphenyl)-2-thienyl]phenyl)-4-methylbenzenesulfonamide (11).** ^{1}H NMR (CD_3COCD_3): 7.78 (d, *J*= 8.2 Hz, 2H), 7.58 (t, *J*= 1.2 Hz, 1H), 7.36-7.34 (m, 2H), 7.32-7.27 (m, 3H), 7.24-7.22 (m, 2H), 7.20-7.16 (m, 3H), 6.86 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 1.97 (s, 3H); ^{13}C NMR (CD_3COCD_3): 171.10, 158.95, 144.75, 144.65, 143.25, 139.75, 137.95, 136.20, 136.00, 131.10, 130.80, 130.65, 128.15, 125.60, 125.30, 122.15, 120.35, 117.95, 117.65, 115.95, 113.20, 20.95; IR: 3621, 3001, 1515, 1236, 854 cm^{-1}.

3,5-Dibromo-2-(3-methoxyphenyl)thiophene (12c). ^{1}H NMR (CD_3COCD_3): 7.58 (t, *J*= 8.2 Hz, 1H), 7.25 (s, 1H), 7.18-7.14 (m, 2H), 7.02-7.00 (m, 1H), 3,86 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 134.70, 131.05, 115.10, 106.80, 55.80; IR: 2938, 1579, 1259, 1050, 822, 774 cm^{-1}.

3-Bromo-2-(3-methoxyphenyl)-5-(4-methoxyphenyl)thiophene (12b). ^{1}H NMR (CD_3COCD_3): 7.83 (d, *J*= 8.2 Hz, 1H), 7.64 (d, *J*= 7.8 Hz, 2H), 7.08 (s, 1H), 7.06 (t, *J*= 7.8 Hz, 1H), 6.95-6.92 (m, 1H), 6.91-6.90 (m, 1H), 6.74 (d, *J*= 7.8 Hz, 2H), 3.82 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (CD_3COCD_3): 163.10, 160.80, 141.95, 138.75, 132.05, 130.95, 128.00, 126.55, 122.70, 121.30, 115.90, 114.70, 110.60, 55.30, 54.95; IR: 3120, 2965, 1600, 1258, 852 cm^{-1}.

2,3-Bis(3-methoxyphenyl)-5-(4-methoxyphenyl)thiophene (12a). ^{1}H NMR (CD_3COCD_3): 7.80 (s, 1H), 7.68 (d, *J*= 8.2 Hz, 2H), 7.53 (m, 1H), 7.19 (t, *J*= 8.2 Hz, 1H), 7.06-7.03 (m, 2H), 6.86-6.84 (m, 2H), 6.65 (d, *J*= 8.2 Hz, 2H), 6.49-6.48 (m, 1H), 6.38-6.37 (m, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.75 (s, 3H); IR: 3021, 2928, 1536, 1258, 852 cm^{-1}.

3,3'-[5-(4-Hydroxyphenyl)thiene-2,3-diyl]diphenol (12). ^{1}H NMR (CD_3COCD_3); 8.56 (s, 1H), 8.52 (s, 1H), 8.47 (s, 1H), 7.51 (s, 1H), 7.39-7.28 (m, 8H), 6.86-6.82 (m, 4H); ^{13}C NMR (CD_3COCD_3): 160.65, 160.20, 141.65, 140.20, 139.20, 138.10, 132.85, 132.35, 131.60, 131.05, 129.75, 129.20, 122.95, 119.45, 118.50, 117.60, 117.30, 114.90; IR: 3425, 2970, 1609, 1196, 830, 791 cm^{-1}.

3,3'-(3-Methylthiene-2,5-diyl]diphenol (13). ^{1}H NMR (CD_3COCD_3): 8.20 (s, 2H), 7.35 (t, *J*= 7.8 Hz, 1H), 7.30-7.28 (m, 2H), 7.24 (t, *J*= 2.2 Hz, 1H), 7.21 (d, *J*= 8.2 Hz, 1H), 7.12 (t, *J*= 2.2 Hz, 1H), 7.07 (d, *J*= 8.2 Hz, 1H), 6.93 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 6.88 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (CD_3COCD_3): 158.85, 158.55, 142.30, 137.85, 136.70, 136.40, 135.00, 130.95, 130.65, 128.40, 120.70, 117.50, 116.30, 115.55, 115.40, 112.95, 35.85.

3-Bromo-2,5-bis(3-methoxyphenyl)thiophene (14b). ^{1}H NMR (CD_3COCD_3): 7.81 (d, *J*= 8.2 Hz, 2H), 7.67 (d, *J*= 8.2 Hz, 2H), 7.28 (s, 1H), 7.06-7.03 (m, 2H), 6.95-6.93 (m, 1H), 6.66-6.64 (m, 1H), 3.85 (s, 6H); ^{13}C NMR (CD_3COCD_3): 163.25, 163.10, 142.90, 138.75, 131.10, 130.95, 125.20, 122.40, 121.40, 115.90, 114.95, 113.30, 112.20, 111.75, 55.25; IR: 3100, 2969, 1624, 1589, 1240, 695 cm^{-1}.

2,5-Bis(3-methoxyphenyl)-3-phenylthiophene (14a). ^{1}H NMR (CD_3COCD_3): 7.42 (s, 1H), 7.36-7.34 (m, 2H), 7.33-7.32 (m, 2H), 7.26-7.23 (m, 4H), 6.80-6.75 (m, 5H), 3.89 (s, 3H), 3.76 (s, 3H); IR: 3001, 2985, 1645, 1515, 852 cm^{-1}.

3,3'-(3-Phenylthiene-2,5-diyl)diphenol (14). ^{1}H NMR (CD_3COCD_3): 8.54 (s, 1H), 8.44 (s, 1H), 7.48 (s, 1H), 7.38-7.35 (m, 4H), 7.28-7.24 (m, 4H), 6.80-6.74 (m, 5H); ^{13}C NMR (CD_3COCD_3): 158.90, 158.45, 143.00, 139.90, 138.40, 137.40, 136.30, 136.10, 131.05, 131.00, 130.60, 129.80, 129.30, 128.00, 127.40, 121.20, 117.65, 116.70, 115.80, 115.30, 113.10, 113.05; IR: 3365, 3061, 2956, 1689, 1259, 764 cm^{-1}.

2,3,5-Tris(3-methoxyphenyl)thiophene (**15a**). ^{1}H NMR (CD_3COCD_3): 7.45 (s, 1H), 7.23 (t, *J*= 8.2 Hz, 1H), 7.20-7.18 (m, 2H), 7.13-7.11 (m, 2H), 6.80-6.78 (m, 4H), 6.75-6.73 (m, 3H), 3.87 (s, 3H), 3.71 (s, 3H), 3.68 (s, 3H); IR: 2989, 1689, 1212, 745 cm^{-1}.

3,3',3''-Thiene-2,3,5-triyltriphenol (15). ^{1}H NMR (CD_3COCD_3): 8.55 (s, 1H), 8.50 (s, 1H), 8.40 (s, 1H), 7.45 (s, 1H), 7.28-7.20 (m, 6H), 6.85-6.80 (m, 6H); ^{13}C NMR (CD_3COCD_3): 158.85, 158.45, 143.20, 139.85, 138.40, 137.42, 136.30, 136.10, 131.50, 130.55, 129.80, 129.25, 127.40, 121.15, 117.65, 116.70, 115.80, 113.10.

2-(3-Methoxyphenyl-5-methylphenyl)-5-(4-methoxyphenyl)thiophene (16a). ^{1}H NMR (CD_3COCD_3): 7.63 (d, *J*= 8.8 Hz, 2H), 7.41 (d, *J*= 3.8 Hz, 1H), 7.31 (d, *J*= 3.8 Hz, 1H), 7.09 (s, 1H), 7.02 (s, 1H), 7.00 (d, *J*= 8.8 Hz, 2H), 6.72 (s, 1H), 3.84 (s, 6H), 2.34 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 160.50, 143.15, 140.35, 136.25, 127.55, 125.35, 124.00, 119.40, 115.30, 114.70, 108.80, 55.70, 55.60, 21.50.

3-[5-(4-Hydroxyphenyl)-2-thienyl]-5-methylphenol (16). ^{1}H NMR (CD_3COCD_3): 8.57 (s, 1H), 8.36 (s, 1H), 7.51 (d, *J*= 8.5 Hz, 2H), 7.29 (d, *J*= 3.6 Hz, 1H), 7.21 (d, *J*= 3.6 Hz, 1H), 6.96 (s, 1H), 6.92 (s, 1H), 6.88 (d, *J*= 8.5 Hz, 2H), 6.60 (s, 1H), 2.26 (s, 3H); ^{13}C NMR (CD_3COCD_3): 157.85, 157.35, 143.45, 142.05, 139.95, 135.40, 126.85, 126.80, 125.95, 124.05, 122.65, 117.45, 115.85, 115.25, 109.30, 20.55; IR: 3308, 2948, 1593, 1220, 827 cm^{-1}.

2-(3-Fluoro-5-methoxyphenyl)-5-(4-methoxyphenyl)thiophene (17a). ^{1}H NMR (CD_3COCD_3): 7.64 (d, *J*= 8.8 Hz, 2H), 7.50 (d, *J*= 3.8 Hz, 1H), 7.34 (d, *J*= 3.8 Hz, 1H), 7.05-6.99 (m, 4H), 6.67 (dt, *J*= 2.2 Hz and *J*= 10.7 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (CD_3COCD_3): 165.00, 162.60, 160.70, 149.40, 145.20, 141.50, 137.75, 127.70, 126.50, 124.15, 115.35, 107.90, 104.95, 101.10, 56.20, 55.70; IR: 1581, 1462, 1255, 1178, 1139, 1059, 1034, 938, 803 cm^{-1}.

3-Fluoro-5-[5-(4-hydroxyphenyl)-2-thienyl]phenol (17). ^{1}H NMR (CD_3COCD_3): 7.54 (d, *J*= 8.8 Hz, 2H), 7.42 (d, *J*= 3.8 Hz, 1H), 7.28 (d, *J*= 3.8 Hz, 1H), 6.98 (t, *J*= 1.6 Hz, 1H), 6.94-6.89 (m, 3H), 6.53 (dt, *J*= 2.2 Hz and *J*= 10.4 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 165.00, 160.30, 158.50, 145.40, 141.30, 137.90, 127.80, 126.55, 126.10, 123.70, 116.80, 109.10, 104.05, 102.30; IR: 3400, 1265, 796 cm^{-1}.

5-[5-(4-Methoxyphenyl)-2-thienyl]-2-methylphenol (18a). ^{1}H NMR (CD_3COCD_3): 7.60 (d, *J*= 8.8 Hz, 2H), 7.30-7.28 (m, 2H), 7.15-7.08 (m, 3H), 6.98 (d, *J*= 8.8 Hz, 2H), 3.83 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (CD_3COCD_3): 143.55, 132.10, 127.90, 127.50, 124.85, 124.50, 123.95, 117.50, 115.30, 112.50; IR: 3400, 1249, 830, 795 cm^{-1}.

5-[5-(4-Hydroxyphenyl)-2-thienyl]-2-methylphenol (18). ^{1}H NMR (CD_3COCD_3): 7.52 (d, *J*= 8.8 Hz, 2H), 7.26 (d, *J*= 3.8 Hz, 1H), 7.23 (d, *J*= 3.8 Hz, 1H), 7.14-7.08 (m, 3H), 6.90 (d, *J*= 8.8 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR (CD_3COCD_3): 156.60, 132.15, 127.60, 124.50, 123.50, 117.50, 116.70, 112.40; IR: 3337, 1429, 1175, 1121, 855, 831, 796 cm^{-1}.

2-(4-Fluoro-3-methoxyphenyl)-5-(4-methoxyphenyl)thiophene (19a). ^{1}H NMR (CD_3COCD_3): 7.61 (d, *J*= 9.0 Hz, 2H), 7.41-7.39 (m, 2H), 7.31 (d, *J*= 3.8 Hz, 1H), 7.22-7.19 (m, 2H), 6.98 (d, *J*= 9.0 Hz, 2H), 3.98 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (CD_3COCD_3): 160.55, 152.70, 149.00, 144.40, 142.15, 132.20, 127.70, 127.60, 125.55, 124.10, 118.65, 117.10, 115.35, 111.70, 56.60, 55.70; IR: 1605, 1504, 1255, 1122, 1028, 833, 796 cm^{-1}.

2-Fluoro-5-[5-(4-hydroxyphenyl)-2-thienyl]phenol (19). ^{1}H NMR (CD_3COCD_3): 7.54 (d, *J*= 8.8 Hz, 2H), 7.42 (d, *J*= 3.8 Hz, 1H), 7.28 (d, *J*= 3.8 Hz, 1H), 6.98 (t, *J*= 1.6 Hz, 1H), 6.94-6.89 (m, 3H), 6.53 (dt, *J*= 2.2 Hz and *J*= 10.4 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 165.00, 160.30, 158.50, 145.40, 141.30, 137.90, 127.80, 126.55, 126.10, 123.70, 116.80, 109.10, 104.05, 102.30; IR: 3400, 1265, 796 cm^{-1}.

2-(3,4-Dimethoxyphenyl)-5-(4-methoxyphenyl)thiophene (20a). ^{1}H NMR ($CDCl_3$): 7.56 (d, *J*= 8.2 Hz, 2H), 7.44 (d, *J*= 7.8 Hz, 1H), 7.20 (d, *J*= 3.9 Hz, 1H), 6.99 (d, *J*= 3.9 Hz, 1H), 6.70 (d, *J*= 8.2 Hz, 2H), 6.67 (d, *J*= 7.8 Hz, 1H), 6.43 (s, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.75 (s,

3H); ^{13}C NMR ($CDCl_3$): 160.80, 152.40, 149.70, 137.60, 135.60, 126.80, 126.70, 120.80, 117.85, 116.20, 114.10, 113.80, 111.90, 55.90, 55.50, 55.20; IR: 2963, 1536, 1212, 987 cm^{-1}.

4-[5-(4-Hydroxyphenyl)-2-thienyl]benzene-1,2-diol (20). ^1H NMR (CD_3OD): 7.54 (d, *J*= 8.2 Hz, 2H), 7.39 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H), 7.17 (d, *J*= 3.8 Hz, 1H), 6.95 (d, *J*= 3.8 Hz, 1H), 6.71 (d, *J*= 7.8 Hz, 2H), 6.62 (d, *J*= 7.8 Hz, 1H), 6.44 (s, 1H); ^{13}C NMR (CD_3OD): 159.30, 148.30, 147.80, 137.60, 136.60, 127.40, 126.60, 126.30, 119.70, 119.60, 118.70, 118.40, 117.80, 113.40.

2-(4-Methoxy-3-methylphenyl)-5-(3-methoxyphenyl)thiophene (21a). ^1H NMR (CD_3COCD_3): 7.36-7.34 (m, 2H), 7.30 (d, *J*= 3.7 Hz, 1H), 7.21-7.18 (m, 2H), 7.13 (d, *J*= 8.8 Hz, 1H), 7.08 (t, *J*= 1.8 Hz, 1H), 6.85 (d, *J*= 8.8 Hz, 1H), 6.76-6.74 (m, 1H), 3.74 (s, 3H), 3.73 (s, 3H), 2.10 (s, 3H); IR: 2999, 1569, 1256, 879, 736 cm^{-1}.

4-[5-(3-Hydroxyphenyl)-2-thienyl)-2-methyl]phenol (21). ^1H NMR (CD_3COCD_3): 8.25 (s, 1H), 8.23 (s, 1H), 7.44 (d, *J*= 1.5 Hz, 1H), 7.34-7.32 (m, 2H), 7.25-7.22 (m, 2H), 7.14-7.13 (m, 2H), 6.86 (d, *J*= 8.2 Hz, 1H), 6.78 (dd, *J*= 1.5 Hz and *J*= 8.2 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (CD_3COCD_3): 149.15, 140.90, 135.25, 131.05, 129.35, 129.30, 127.75, 121.75, 120.35, 119.65, 117.15, 20.50; IR: 3514, 2928, 2853, 1598, 798 cm^{-1}.

2-(3,4-Dimethoxyphenyl)-5-(3-methoxyphenyl)thiophene (22a). ^1H NMR (CD_3COCD_3): 7.44 (d, *J*= 3.8 Hz, 1H), 7.36 (d, *J*= 3.8 Hz, 1H), 7.33 (d, *J*= 7.8 Hz, 1H), 7.28-7.23 (m, 4H), 7.00 (d, *J*= 8.2 Hz, 1H), 6.89 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 144.65, 143.00, 136.50, 131.00, 128.10, 125.45, 124.30, 119.00, 113.90, 113.20, 111.55, 110.35, 56.25, 56.20, 55.65.

4-[5-(3-Hydroxyphenyl)-2-thienyl]benzene-1,2-diol (22). ^{1}H NMR (CD_3COCD_3): 7.33 (d, *J*= 3.8 Hz, 1H), 7.21-7.19 (m, 2H), 7.17 (d, *J*= 2.2 Hz, 1H), 7.14-7.12 (m, 2H), 7.06 (dd, *J*= 2.2 Hz and *J*= 8.2 Hz, 1H), 6.88 (d, *J*= 8.2 Hz, 1H), 6.79-6.78 (m, 1H); ^{13}C NMR (CD_3COCD_3): 146.40, 146.20, 144.75, 143.00, 130.95, 125.05, 123.65, 118.30, 117.50, 116.70, 115.35, 113.50, 112.90; IR: 3319, 2989 1581, 1221, 774 cm^{-1}.

2-(3-Fluoro-4-methoxyphenyl)-5-(3-methoxyphenyl)thiophene (23a). ^{1}H NMR (CD_3COCD_3): 7.49-7.44 (m, 3H), 7.38 (d, *J*= 3.9 Hz, 1H), 7.34 (t, *J*= 8.2 Hz, 1H), 7.25 (d, *J*= 7.8 Hz, 1H), 7.22-7.17 (m, 2H), 6.89 (dd, *J*= 1.5 Hz and *J*= 8.2 Hz, 1H), 3.92 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.20, 143.70, 136.30, 131.05, 125.65, 125.10, 122.55, 118.65, 115.10, 114.10, 113.85, 113.70, 111.65, 56.70, 55.70.

2-Fluoro-4-[5-(3-hydroxyphenyl)-2-thienyl]phenol (23). ^{1}H NMR (CD_3COCD_3): 8.86 (s, 1H), 8.51 (s, 1H), 7.44 (d, *J*= 12.2 Hz, 1H), 7.36-7.32 (m, 3H), 7.23 (t, *J*= 8.8 Hz, 1H), 7.15 (m, 2H), 7.07 (t, *J*= 8.8 Hz, 1H), 6.95 (d, *J*= 7.9 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 158.90, 153.50, 151.60, 145.60, 145.45, 143.60, 136.35, 131.00, 127.70, 125.20, 124.65, 122.80, 122.75, 119.25, 117.60, 115.60, 114.00, 113.80, 113.00; IR: 3332, 1582, 1550, 780 cm^{-1}.

2-(3-Methoxyphenyl)-5-[4-methoxy-3-(trifluoromethyl)phenyl]thiophene (24a). ^{1}H NMR (CD_3COCD_3): 7.87-7.85 (m, 2H), 7.45 (d, *J*= 3.9 Hz, 1H), 7.42 (d, *J*= 3.9 Hz, 1H), 7.32 (t, *J*= 7.9 Hz, 1H), 7.28-7.22 (m, 3H); 6.90 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 3.97 (s, 3H), 3.85 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 157.90, 144.00, 142.40, 136.20, 131.55, 127.55, 125.90, 125.70, 124.60, 124.55, 119.50, 118.70, 114.20, 111.65, 56.70, 55.65.

4-[5-(3-Hydroxyphenyl)-2-thienyl]-2-(trifluoromethyl)phenol (24). ^{1}H NMR (CD_3COCD_3): 7.71 (d, *J*= 2.3 Hz, 1H), 7.66 (dd, *J*= 2.3 Hz and *J*= 8.5 Hz, 1H), 7.29-7.27 (m,

2H), 7.14 (t, *J*= 7.9 Hz, 1H), 7.06-7.03 (m, 3H), 6.67-6.65 (m, 1H); ^{13}C NMR (CD_3COCD_3): 158.90, 143.90, 136.70, 131.40, 131.0, 125.30, 124.90, 118.70, 117.60, 115.70, 113.05; IR: 3491, 3387, 1583, 1490, 799 cm^{-1}.

2-(6-Methoxybiphenyl-3-yl)-5-(3-methoxyphenyl)thiophene (25a). ^{1}H NMR (CD_3COCD_3): 7.67 (dd, *J*= 2.5 Hz and *J*= 8.5 Hz, 1H), 7.62 (d, *J*= 2.2 Hz, 1H), 7.58-7.56 (m, 2H), 7.40-7.45 (m, 5H), 7.31 (d, *J*= 8.5 Hz, 1H), 7.26-7.23 (m, 1H), 7.18 (t, *J*= 1.2 Hz, 1H), 7.16 (d, *J*= 8.5 Hz, 1H), 6.89 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 157.35, 144.30, 143.15, 136.50, 132.10, 131.00, 130.40, 128.85, 128.65, 128.00, 127.90, 126.70, 125.55, 124.40, 118.60, 114.00, 113.05, 111.55, 56.15, 55.65.

5-[5-(3-Hydroxyphenyl)-2-thienyl]biphenyl-2-ol (25). ^{1}H NMR (CD_3OD): 7.59 (d, *J*= 7.3 Hz, 2H), 7.51 (d, *J*= 2.1 Hz, 1H), 7.47 (dd, *J*= 2.1 Hz and *J*= 8.5 Hz, 1H), 7.42-7.39 (m, 3H), 7.30-7.20 (m, 6H), 6.94 (d, *J*= 8.3 Hz, 1H); ^{13}C NMR (CD_3OD): 154.10, 154.00, 141.60, 138.40, 134.85, 131.80, 129.15, 129.05, 127.70, 127.50, 126.55, 126.30, 125.40, 123.20, 122.50, 117.40, 116.10, 112.50; IR: 3498, 2963, 1512, 1020, 852 cm^{-1}.

[2-Methoxy-5-[5-(3-methoxyphenyl)-2-thienyl]phenyl]methanol (26c). ^{1}H NMR (CD_3COCD_3): 7.88 (d, *J*= 2.5 Hz, 1H), 7.62 (dd, *J*= 2.5 Hz and *J*= 8.5 Hz, 1H), 7.49 (d, *J*= 3.7 Hz, 1H), 7.39-7.37 (m, 2H), 7.32 (d, *J*= 7.5 Hz, 1H), 7.30 (d, *J*= 1.5 Hz, 1H), 7.07 (d, *J*= 8.5 Hz, 1H), 6.95 (dd, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 4.78 (s, 2H), 3.98 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (CD_3COCD_3): 170.95, 162.45, 161.25, 157.35, 144.85, 142.80, 136.50, 132.10, 131.15, 130.95, 127.45, 125.70, 125.00, 123.90, 118.70, 113.90, 111.55, 111.35, 59.70, 55.85, 55.65; IR: 3524, 1577, 1481, 1165, 776 cm^{-1}.

Ethyl (2*E*)-3-[2-Methoxy-5-[5-(3-methoxyphenyl)-2-thienyl]phenyl]acrylate (26a). ^{1}H NMR (CD_3COCD_3): 7.97-7.96 (m, 2H), 7.66 (dd, *J*= 2.0 Hz and *J*= 8.2 Hz, 1H), 7.42-7.40 (m, 2H), 7.32 (t, *J*= 8.2 Hz, 1H), 7.25-7.22 (m, 2H), 7.11 (d, *J*= 8.5 Hz, 1H), 6.89 (dd, *J*= 2.0 Hz and *J*= 8.2 Hz, 1H), 6.70 (d, *J*= 16.4 Hz, 1H), 3.95 (q, *J*= 7.2 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 1.30 (t, *J*= 7.2 Hz, 3H); ^{13}C NMR (CD_3COCD_3): 167.40, 161.20, 158.85, 139.75, 130.95, 129.50, 126.30, 125.50, 124.80, 120.30, 118.65, 114.00, 113.00, 111.65, 60.80, 56.30, 55.65, 14.70; IR: 3100, 2982, 1702, 1608, 1585, 1250, 1096, 895 cm^{-1}.

Ethyl (2*E*)-3-[2-hydroxy-5-[5-(3-hydroxyphenyl)-2-thienyl]phenyl]acrylate (26). ^{1}H NMR (CD_3COCD_3): 8.02 (d, *J*= 16.0 Hz, 1H), 7.94 (d, *J*= 2.2 Hz, 1H), 7.58 (dd, *J*= 1.8 Hz and *J*= 7.8 Hz, 1H), 7.41 (d, *J*= 3.8 Hz, 1H), 7.37 (d, *J*= 3.8 Hz, 1H), 7.25 (t, *J*= 7.8 Hz, 1H), 7.17-7.15 (m, 2H), 7.05 (d, *J*= 8.0 Hz, 1H), 6.78 (dt, *J*= 1.8 Hz and *J*= 7.8 Hz, 1H), 6.73 (d, *J*= 16.0 Hz, 1H), 4.21 (q, *J*= 6.9 Hz, 2H), 1.30 (t, *J*= 6.9 Hz, 3H); ^{13}C NMR (CD_3COCD_3): 167.55, 158.85, 157.20, 143.65, 143.30, 140.40, 130.95, 129.50, 127.40, 126.65, 125.15, 124.40, 122.90, 119.80, 117.75, 117.50, 115.50, 112.95, 60.70, 14.65; IR: 3349, 2958, 1730, 1565, 1254, 802, 756 cm^{-1}.

(2*E*)-3-[2-Methoxy-5-[5-(3-methoxyphenyl)-2-thienyl]phenyl]-*N*-phenylacrylamide (27a). ^{1}H NMR (CD_3COCD_3): 8.12 (s, 1H), 8.00 (d, *J*= 15.8 Hz, 1H), 7.89 (d, *J*= 2.2 Hz, 1H), 7.80 (d, *J*= 8.5 Hz, 1H), 7.71 (d, *J*= 1.2 Hz and *J*= 8.2 Hz, 1H), 7.47 (d, *J*= 4.0 Hz, 1H), 7.41 (d, *J*= 3.7 Hz, 1H), 7.35-7.32 (m, 3H), 7.31-7.26 (m, 1H), 7.22 (t, *J*= 1.8 Hz, 1H), 7.14 (d, *J*= 8.8 Hz, 1H), 7.09 (t, *J*= 7.8 Hz, 1H), 7.02 (d, *J*= 15.8 Hz, 1H), 6.90-6.88 (m, 1H), 3.95 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (CD_3COCD_3): 191.70, 161.25, 143.65, 136.40, 131.00, 129.60, 128.90, 126.15, 125.55, 124.60, 118.60, 114.00, 113.05, 111.65, 56.30, 55.70; IR: 3356, 2924, 2854, 1714, 1597, 1249, 690 cm^{-1}.

(2*E*)-3-[2-Hydroxy-5-[5-(3-hydroxyphenyl)-2-thienyl]phenyl]-*N*-phenylacrylamide (27). ^{1}H NMR (CD_3COCD_3): 8.01 (d, *J*= 15.7 Hz, 1H), 7.85 (d, *J*= 2.5 Hz, 1H), 7.83 (dd, *J*= 1.2 Hz and *J*= 8.8 Hz, 2H), 7.56 (dd, *J*= 2.5 Hz and *J*= 8.5 Hz, 1H), 7.36-7.30 (m, 5H), 7.24-7.22 (m, 1H), 7.16-7.14 (m, 1H), 7.09-7.06 (m, 4H); ^{13}C NMR (CD_3COCD_3): 191.65, 140.75, 136.95, 131.00, 129.55, 128.75, 125.15, 124.20, 124.10, 120.20, 119.30, 116.30, 113.05; IR: 3500, 2936, 1569, 1547, 896 cm^{-1}.

3-[2-Methoxy-5-[5-(3-methoxyphenyl)-2-thienyl]phenyl]-*N*-phenylpropanamide (28a). ^{1}H NMR (CD_3COCD_3): 7.69 (d, *J*= 7.8 Hz, 2H), 7.57 (d, *J*= 2.5 Hz, 1H), 7.50 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H), 7.39 (d, *J*= 3.8 Hz, 1H), 7.31 (t, *J*= 8.2 Hz, 1H), 7.28-7.20 (m, 5H), 7.01-6.97 (m, 3H), 6.88 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.06 (t, *J*= 8.2 Hz, 2H), 2.73 (t, *J*= 8.2 Hz, 2H); ^{13}C NMR (CD_3COCD_3): 171.40, 161.20, 158.35, 144.60, 142.80, 140.50, 136.55, 131.00, 130.95, 129.65, 129.45, 128.00, 127.55, 126.05, 125.50, 123.95, 121.00, 118.60, 113.85, 111.80, 111.50, 57.75, 55.95, 55.65, 37.60; IR: 3025, 2985, 1698, 1414, 784 cm^{-1}.

3-[2-Hydroxy-5-[5-(3-hydroxyphenyl)-2-thienyl]phenyl]-*N*-phenylpropanamide (28). ^{1}H NMR (CD_3COCD_3): 9.29 (s, 1H), 8.48 (s, 1H), 8.47 (s, 1H), 7.67 (d, *J*= 7.5 Hz, 2H), 7.52 (s, 1H), 7.38-7.33 (m, 2H), 7.33-7.26 (m, 5H), 7.13-7.11 (m, 1H), 7.05-7.02 (m, 2H), 6.89 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H), 3.04 (t, *J*= 7.2 Hz, 2H), 2.78 (t, *J*= 7.2 Hz, 2H); ^{13}C NMR (CD_3COCD_3): 179.70, 129.50, 125.00, 124.20, 121.40, 120.30, 119.95, 119.60, 118.70, 117.10, 115.75, 114.60, 112.40, 112.30, 112.15, 111.00, 110.50, 35.50, 28.30; IR: 3525, 2985, 1695, 1524, 857 cm^{-1}.

2-Bromo-5-(3-fluoro-4-methoxyphenyl)thiophene (29b). ^{1}H NMR (CD_3COCD_3): 7.42 (dd, *J*= 2.5 Hz and *J*= 12.3 Hz, 1H), 7.36-7.35 (m, 1H), 7.21 (d, *J*= 3.9 Hz, 1H), 7.18 (t, *J*= 8.5 Hz,

1H), 7.15 (d, *J*= 3.9 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (CD_3COCD_3): 132.35, 124.55, 122.65, 115.15, 113.80, 111.05, 56.65; IR: 1515, 1446, 1309, 1274, 1128, 813, 796 cm^{-1}.

2-(3-Fluoro-4-methoxyphenyl)-5-(3-fluoro-5-methoxyphenyl)thiophene (29a). ^{1}H NMR (CD_3COCD_3): 7.57-7.55 (m, 2H), 7.53-7.50 (m, 1H), 7.46 (d, *J*= 4.1 Hz, 1H), 7.26 (t, *J*= 8.8 Hz, 1H), 7.13 (t, *J*= 2.2 Hz, 1H), 7.11-7.08 (m, 1H), 6.76 (dt, *J*= 2.2 Hz and *J*= 11.0 Hz, 1H), 4.00 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (CD_3COCD_3): 164.00, 162.65, 153.50, 148.50, 143.70, 142.25, 137.50, 126.50, 122.60, 115.05, 113.80, 108.00, 105.10, 101.25, 56.60, 56.20; IR: 2950, 1585, 1518, 1273, 1172, 1021, 965, 788 cm^{-1}.

2-Fluoro-4-[5-(3-fluoro-5-hydroxyphenyl)thien-2-yl]phenol (29). ^{1}H NMR (CD_3COCD_3): 9.00 (s, 2H), 7.55-7.53 (m, 2H), 7.44-7.40 (m, 2H), 7.14 (t, *J*= 8.5 Hz, 1H), 7.07 (d, *J*= 2.2 Hz, 1H), 7.04-7.01 (m, 1H), 6.64-6.60 (m, 1H); ^{13}C NMR (CD_3COCD_3): 164.90, 160.35, 152.50, 145.70, 143.85, 142.10, 137.65, 127.35, 126.20, 122.90, 114.00, 109.20, 104.10, 102.60; IR : 3327, 1597, 1495, 1433, 1244, 1183, 1130, 992, 786 cm^{-1}.

2-(3-Fluoro-4-methoxyphenyl)-5-(4-fluoro-3-methoxyphenyl)thiophene (30a). ^{1}H NMR (CD_3COCD_3): 7.47 (dd, *J*= 2.2 Hz and *J*= 12.6 Hz, 1H), 7.45-7.41 (m, 3H), 7.38 (d, *J*= 3.8 Hz, 1H), 7.26-7.21 (m, 1H), 7.20-7.15 (m, 2H), 3.98 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (CD_3COCD_3): 153.55, 151.85, 149.00, 148.30, 142.95, 131.95, 128.30, 125.65, 125.05, 122.45, 118.75, 117.20, 115.05, 113.85, 56.65, 54.95; IR: 2954, 1505, 1246, 1226, 1123, 793 cm^{-1}.

2-Fluoro-4-[5-(4-fluoro-3-hydroxyphenyl)thien-2-yl]phenol (30). ^{1}H NMR (CD_3COCD_3): 9.00 (s, 2H) 7.52 (dd, *J*= 2.5 Hz and *J*= 12.3 Hz, 1H), 7.43-7.37 (m, 4H), 7.24-7.22 (m, 2H),

7.13 (t, *J*= 8.8 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 152.00, 151.50, 146.20, 145.65, 143.15, 142.60, 127.55, 125.25, 124.70, 119.25, 117.90, 117.30, 115.65, 113.80; IR: 3256, 1691, 1597, 1549, 1504, 1431, 1259, 1114, 855, 792 cm^{-1}.

2-(3,5-Difluoro-4-methoxyphenyl)-5-(3-methoxyphenyl)thiophene (31a). ^{1}H NMR (CD_3COCD_3): 7.50 (d, *J*= 3.9 Hz, 1H), 7.47 (d, *J*= 3.9 Hz, 1H), 7.39-7.32 (m, 3H), 7.27-7.22 (m, 2H), 6.92-6.90 (m, 1H), 3.99 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 158.15, 155.70, 145.10, 141.30, 135.80, 131.10, 126.55, 125.75, 118.75, 114.40, 111.80, 110.25, 110.15, 110.05, 109.95, 62.40, 55.70; IR: 2967, 1612, 1456, 1212, 786 cm^{-1}.

2,6-Difluoro-4-[5-(3-hydroxyphenyl)-2-thienyl]phenol (31). ^{1}H NMR (CD_3COCD_3): 7.39 (d, *J*= 3.8 Hz, 1H), 7.37 (d, *J*= 3.8 Hz, 1H), 7.30 (d, *J*= 1.5 Hz, 1H), 7.28 (d, *J*= 1.5 Hz, 1H), 7.22 (t, *J*= 8.0 Hz, 1H), 7.15-7.12 (m, 2H), 6.80-6.78 (m, 1H); ^{13}C NMR (CD_3COCD_3): 158.00, 143.60, 135.25, 130.20, 124.80, 124.45, 120.05, 116.80, 114.90, 112.20, 108.85, 108.80, 108.75, 108.70; IR: 3436, 2962, 1607, 1016, 772 cm^{-1}.

2-(3,4-Difluorophenyl)-5-(3-methoxyphenyl)thiophene (32a). ^{1}H NMR (CD_3COCD_3): 7.61-7.57 (m, 1H), 7.47-7.42 (m, 3H), 7.35-7.29 (m, 2H), 7.22-7.18 (m, 2H), 6.87 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (CD_3COCD_3): 161.25, 151.90, 150.50, 141.60, 136.05, 132.70, 131.05, 126.35, 125.70, 122.95, 122.50, 118.95, 118.80, 115.20, 114.95, 114.30, 111.80, 55.65.

3-[5-(3,4-Difluorophenyl)-2-thienyl]phenol (32). ^{1}H NMR (CD_3COCD_3): 8.47 (s, 1H), 7.63-7.59 (m, 1H), 7.48-7.45 (m, 1H), 7.43 (d, *J*= 3.8 Hz, 1H), 7.38-7.31 (m, 2H), 7.22 (t, *J*= 7.5 Hz, 1H), 7.14-7.12 (m, 2H), 6.79 (dd, *J*= 1.8 Hz and *J*= 8.2 Hz, 1H); ^{13}C NMR (CD_3COCD_3): 158.85, 151.35, 150.80, 145.20, 141.40, 136.05, 132.80, 132.70, 131.10, 126.35, 125.40,

122.90, 122.80, 118.95, 117.75, 115.90, 115.15, 113.15; IR: 3498, 2963, 1612, 1515, 989 cm^{-1}.

4-(4-Methoxy-3-methylphenyl)-2-(3-methoxyphenyl)thiophene (34a). ^{1}H NMR ($CDCl_3$): 7.59 (d, *J*= 8.2 Hz, 1H), 7.48 (s, 1H), 7.14 (s, 1H), 6.99-6.97 (m, 2H), 6.92-6.90 (m, 2H), 6.41 (s, 1H), 6.39 (d, *J*= 7.2 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 2.22 (s, 3H); IR: 2987, 1526, 1253, 896 cm^{-1}.

4-[5-(3-Hydroxyphenyl)-3-thienyl]-2-methylphenol (34). ^{1}H NMR (CD_3COCD_3): 8.49 (s, 1H), 8.30 (s, 1H), 7.73 (s, 1H), 7.52 (s, 1H), 7.47-7.45 (m, 1H), 7.42 (d, *J*= 8.2 Hz, 1H), 7.24-7.19 (m, 3H), 6.87 (d, *J*= 8.2 Hz, 1H), 6.81-6.80 (m, 1H), 2.25 (s, 3H); ^{13}C NMR (CD_3COCD_3): 158.80, 155.85, 145.25, 144.15, 136.70, 130.95, 129.65, 128.30, 125.50, 125.40, 123.20, 118.40, 117.75, 115.85, 115.55, 113.25, 20.85.

4-(3-Fluoro-4-methoxyphenyl)-2-(3-methoxyphenyl)thiophene (35a). ^{1}H NMR (CD_3COCD_3): 7.95 (s, 1H), 7.72 (s, 1H), 7.66-7.60 (m, 2H), 7.42-7.39 (m, 3H), 7.26 (t, *J*= 8.8 Hz, 1H), 7.00-6.98 (m, 1H), 3.99 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (CD_3COCD_3): 162.10, 153.20, 148.80, 146.40, 143.40, 137.30, 131.80, 124.20, 123.90, 121.00, 119.70, 115.70, 115.50, 115.40, 115.10, 112.80, 57.50, 56.50.

2-Fluoro-4-[5-(3-hydroxyphenyl)-3-thienyl]phenol (35). ^{1}H NMR (CD_3COCD_3): 8.61 (s, 1H), 7.77 (d, *J*= 1.6 Hz, 1H), 7.56 (d, *J*= 1.6 Hz, 1H), 7.52 (dd, *J*= 2.2 Hz and *J*= 12.6 Hz, 1H), 7.44-7.42 (m, 1H), 7.26-7.21 (m, 3H), 7.05 (t, *J*= 8.6 Hz, 1H), 6.83-6.81 (m, 1H); ^{13}C NMR (CD_3COCD_3): 159.70, 154.40, 152.50, 146.50, 143.60, 137.30, 131.80, 130.00, 124.10, 123.90, 120.50, 119.80, 118.70, 116.60, 115.60, 114.20; IR: 3376, 3232, 1529, 1290, 1195, 774 cm^{-1}.

4-(4-Methoxy-3-methylphenyl)-2-(3-methoxyphenyl)-1,3-thiazole (37a). ^{1}H NMR ($CDCl_3$): 7.62 (d, *J*= 8.2 Hz, 2H), 7.55 (d, *J*= 7.8 Hz, 1H), 7.08 (t, *J*= 7.8 Hz, 1H), 6.96 (s, 1H), 6.90 (d, *J*= 7.8 Hz, 1H), 6.83-6.80 (m, 1H), 6.76 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$): 162.70, 162.10, 156.10, 139.70, 137.80, 133.60, 131.00, 125.80, 125.70, 124.85, 122.00, 121.55, 119.70, 119.40, 114.50, 55.50, 55.40, 16.50.

4-[2-(3-Hydroxyphenyl)-1,3-thiazol-5-yl]-2-methylphenol (37). ^{1}H NMR (CD_3COCD_3): 7.97 (s, 1H), 7.49 (t, *J*= 1.3 Hz, 1H), 7.45-7.43 (m, 2H), 7.32-7.30 (m, 1H), 7.29 (t, *J*= 7.8 Hz, 1H), 6.91-6.88 (m, 2H), 2.25 (s, 3H); ^{13}C NMR (CD_3COCD_3): 138.75, 137.50, 131.10, 130.00, 126.15, 118.25, 116.20, 18.70; IR: 3516, 2987, 1567, 1414, 817 cm^{-1}.

3,4''-Dimethoxy-4-methyl-1,1':4',1''-terphenyl (**39a**). ^{1}H NMR ($CDCl_3$): 7.29 (d, *J*= 2.2 Hz, 4H), 7.11-7.09 (m, 1H), 7.02 (t, *J*= 7.9 Hz, 2H), 6.88 (d, *J*= 7.6 Hz, 1H), 6.83 (t, *J*= 1.8 Hz, 1H), 6.57-6.55 (m, 2H), 3.53 (s, 6H), 1.97 (s, 3H); ^{13}C NMR ($CDCl_3$): 157.80, 142.70, 139.50, 133.00, 130.00, 129.60, 127.70, 127.30, 125.60, 119.80, 113.00, 112.90, 110.50, 55.70, 55.60, 16.70; IR: 2924, 1581, 1252, 778 cm^{-1}.

4-Methyl-1,1':4',1''-terphenyl-3,4''-diol (**39**)**.** ^{1}H NMR (CD_3COCD_3): 8.42 (s, 1H), 7.65 (d, *J*= 2.5 Hz, 4H), 7.46 (s, 1H), 7.37 (d, *J*= 8.2 Hz, 1H), 7.27 (t, *J*= 7.6 Hz, 1H), 7.16-7.14 (m, 2H), 6.92 (d, *J*= 8.2 Hz, 1H), 6.84 (d, *J*= 7.9 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (CD_3COCD_3): 158.80, 156.20, 143.00, 141.00, 139.80, 132.60, 130.80, 130.10, 128.00, 127.50, 126.00, 125.60, 118.80, 116.00, 115.20, 114.40, 16.40; IR: 3327, 1597, 1491, 1206, 819 cm^{-1}.

3-Fluoro-3'',4-dimethoxy-1,1':4',1''-terphenyl (40a). ^{1}H NMR (CD_3COCD_3): 7.72 (d, *J*= 2.6 Hz, 4H), 7.51-7.47 (m, 2H), 7.38 (t, *J*= 8.2 Hz, 1H), 7.27-7.20 (m, 3H), 6.95-6.93 (m,

1H), 3.93 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (CD_3COCD_3): 162.10, 155.30, 153.30, 149.10, 143.60, 141.50, 140.30, 135.20, 131.70, 129.20, 128.60, 124.40, 120.80, 115.90, 114.70, 114.10, 57.50, 56.50.

3''-Fluoro-1,1':4',1''-terphenyl-3,4''-diol (40). ^{1}H NMR (CD_3COCD_3): 8.76 (s, 1H), 8.46 (s, 1H), 7.70-7.66 (m, 4H), 7.47 (dd, *J*= 2.2 Hz and *J*= 8.2 Hz, 1H), 7.39-7.37 (m, 1H), 7.28 (t, *J*= 8.2 Hz, 1H), 7.18-7.15 (m, 2H), 7.10 (t, *J*= 8.5 Hz, 1H), 6.87-6.85 (m, 1H); ^{13}C NMR (CD_3COCD_3): 160.00, 154.80, 146.50, 143.90, 141.60, 140.70, 134.70, 132.00, 129.30, 128.80, 124.80, 120.30, 120.00, 116.50, 116.30, 116.10, 115.60; IR: 3365, 3184, 1491, 1165, 816, 783 cm^{-1}.

4-Fluoro-3,3''-dimethoxy-1,1':4',1''-terphenyl (**42a**). ^{1}H NMR ($CDCl_3$): 7.76 (d, *J*= 8.2 Hz, 2H), 7.70 (d, *J*= 8.6 Hz, 2H), 7.47 (t, *J*= 7.9 Hz, 1H), 7.33-7.28 (m, 3H), 7.24-7.22 (m, 2H), 7.03-7.01 (m, 1H), 4.04 (s, 3H), 3.96 (s, 3H); ^{13}C NMR ($CDCl_3$): 159.80, 152.90, 150.90, 147.50, 147.40, 141.70, 139.80, 139.20, 137.10, 129.60, 127.20, 119.20, 116.00, 115.90, 112.60, 112.10, 56.00, 54.90.

4-Fluoro-1,1':4',1''-terphenyl-3,3''-diol (42). ^{1}H NMR (CD_3COCD_3): 8.72 (s, 1H), 8.41 (s, 1H), 7.68 (d, *J*= 3.8 Hz, 4H), 7.33 (dd, *J*= 2.2 Hz and *J*= 8.2 Hz, 1H), 7.29 (t, *J*= 8.2 Hz, 1H), 7.21-7.15 (m, 4H), 6.87-6.85 (m, 1H); ^{13}C NMR (CD_3COCD_3): 159.50, 146.60, 143.50, 140.70, 139.00, 131.50, 128.80, 128.70, 120.00, 119.90, 117.90, 117.80, 116.00, 115.20; IR: 3345, 1489, 1450, 1227, 809 cm^{-1}.

b) Table with elemental analysis of compounds 3 to 6, 8 to 32, 34 and 37.

compound	C, H, N calculated			C, H, N found		
	C	H	N	C	H	N
3	71.09	4.10	0.00	71.10	4.02	0.08
4	71.88	4.90	5.24	72.05	4.79	5.09
5	67.57	4.25	0.00	67.69	4.41	0.06
6	73.62	4.00	5.05	73.52	3.80	5.29
8	71.09	4.10	0.00	70.98	4.25	0.06
9	59.11	4.38	4.05	59.31	4.18	4.00
10	60.14	4.77	3.90	60.05	4.80	4.02
11	65.53	4.54	3.32	65.33	4.61	3.05
12	73.31	4.47	0.00	73.46	4.60	0.08
13	72.31	5.00	0.00	72.58	5.08	0.10
14	76.72	4.68	0.00	76.80	4.52	0.12
15	73.31	4.47	0.00	73.20	4.41	0.05
16	72.31	5.00	0.00	72.12	5.21	0.15
17	67.12	3.87	0.00	67.23	3.92	0.09
18	72.31	5.00	0.00	72.33	5.19	0.14
19	67.12	3.87	0.00	67.11	3.90	0.09
20	67.59	4.25	0.00	67.49	4.12	0.18
21	72.31	5.00	0.00	72.39	4.94	0.11
22	67.59	4.25	0.00	67.68	4.32	0.08
23	67.12	3.87	0.00	67.15	3.90	0.10
24	60.71	3.30	0.00	60.65	3.45	0.04
25	76.72	4.68	0.00	76.65	4.65	0.02
26	68.83	4.95	0.00	68.74	4.82	0.09
27	72.62	4.63	3.39	72.80	4.69	3.25
28	72.27	5.09	3.37	72.39	5.00	3.18
29				63.11	3.24	0.08
30	63.15	3.31	0.00	63.04	3.52	0.21
31				63.10	3.24	0.12
32	65.65	3.50	0.00	65.78	3.42	0.08
34	72.31	5.00	0.00	72.28	4.71	0.12
37	67.82	4.62	4.94	67.99	4.42	4.82

c) The purity of compounds **35, 39, 41** and **42** was determined using LC/MS as follows:

The Surveyor®-LC-system consisted of a pump, an autosampler, and a PDA detector. Mass spectrometry was performed on a TSQ® Quantum (ThermoFisher, Dreieich, Germany). The triple quadrupole mass spectrometer was equipped with an electrospray interface (ESI). The system was operated by the standard software Xcalibur®.

A RP C18 NUCLEODUR® 100-5 (3 mm) column (Macherey-Nagel GmbH, Duehren, Germany) was used as stationary phase. All solvents were HPLC grade.

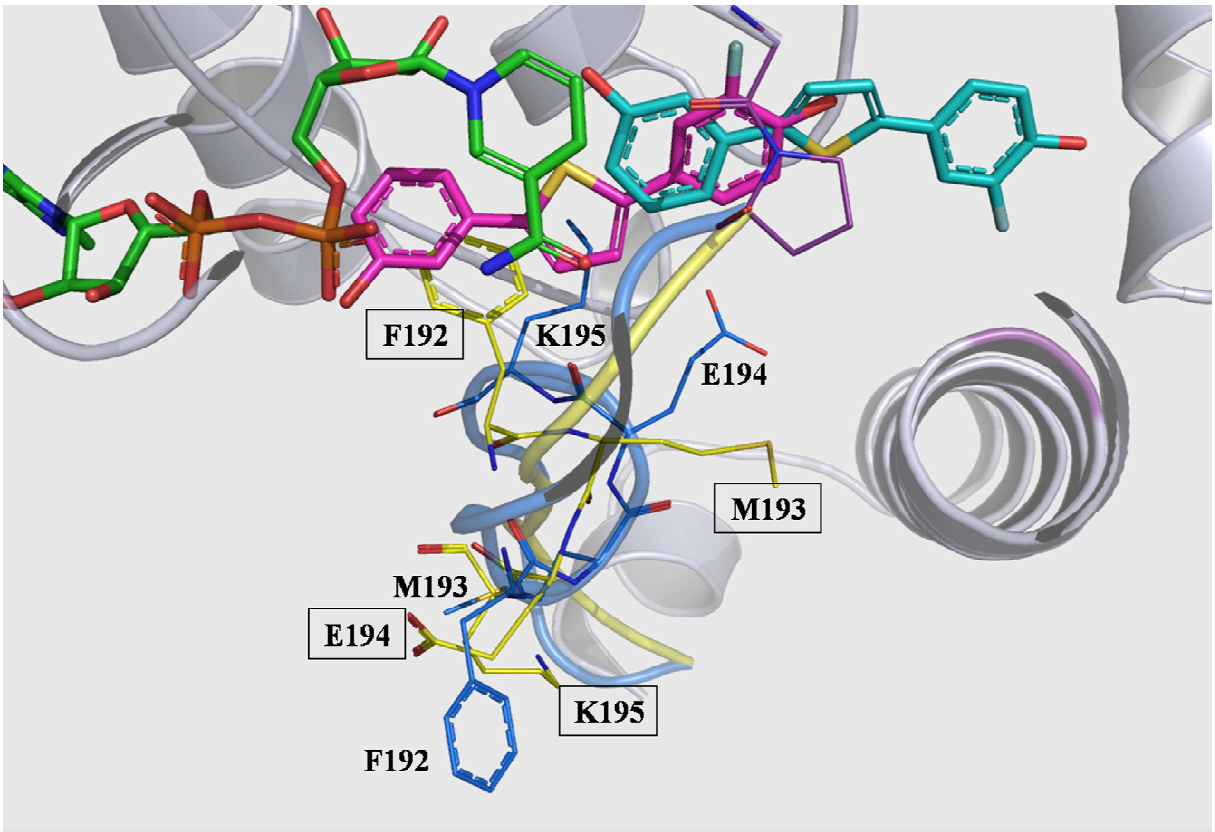
1st solvent system:

In an isocratic run a solvent system consisting of 0.1% formic acid and 0.1% formic acid in methanol (20:80) was chosen.

2nd solvent system:

In a gradient run the percentage of acetonitrile (containing 0.1% formic acid) in 0.1% formic acid in was increased from an initial concentration of 50% at 0 min to 100% at 3 min and kept at 100 % for 3.5 min.

In both cases the injection volume was 5 µl and flow rate was set to 350 µLmin. MS analysis was carried out at a spray voltage of 3800 V, a capillary temperature of 350 °C and a source CID of 10 V. Spectra were acquired in positive and negative ionization mode from 100 to 1000 m/z and full scan UV-mode.

Compound	**isocratic run**		**gradient run**		**MS (ESI) m/z**
	R_t (min)	HPLC purity (>%)	R_t (min)	HPLC purity (>%)	
35	8.50	99	10.54	99	287 $(M+H)^+$
39	13.56	98	10.90	99	277 $(M+H)^+$
40	8.13	98	10.54	98	280 $(M+H)^+$
42	10.98	99	10.66	99	280 $(M+H)^+$

d) Overlay of the binding poses of compound 23 obtained with 1FDT-A (represented in lila) and with 1FDT-B (marked in light blue). For the sake of clarity, the amino acids of the flexible loop are drawn in blue and yellow for 1FDT-A and 1FDT-B, respectively.