

Supplementary materials

Design, synthesis, and anti-melanogenic effects of (2-substituted phenyl-1,3-dithiolan-4-yl)methanol (PDTM) derivatives

Do Hyun Kim¹, Su Jeong Kim¹, Sultan Ullah¹, Hwi Young Yun¹, Pusoon Chun^{2,*}, Hyung Ryong Moon^{1,*}

¹College of Pharmacy, Pusan National University, Busan 609-735, Republic of Korea

²College of Pharmacy, Inje University, 197 Inje-ro, Gimhae, Gyeongnam, 621-749, Republic

4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)phenol (PDTM1)

Diastereomeric mixture of 1:1.2; yellow solid (58%); ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.49 (s, 1H, OH), 9.45 (s, 1H, OH), 7.31 – 7.27 (m, 4H, Ar), 6.69 – 6.66 (m, 4H, Ar), 5.64 (s, 2H, 2-H), 5.16 (brs, 1H, OH), 5.10 (brs, 1H, OH), 4.00 (m, 1H, 4-H), 3.73 (m, 1H, 4-H), 3.67 (t, 1H, *J* = 9.5 Hz), 3.51 (t, 1H, *J* = 10.0 Hz), 3.46 – 3.40 (m, 4H), 3.28 – 3.25 (m, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 157.8, 157.5, 131.0, 129.8, 129.4, 128.1, 115.6, 115.5, 64.1, 63.5, 58.4, 57.4, 56.2, 54.6, 41.0, 40.7; LRMS (ESI-) *m/z* 227 (M-H)⁻; HRMS (ESI+) *m/z* C₁₀H₁₃O₂S₂ (M+H)⁺ calcd 229.0357, obsd 229.0350.

4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)benzene-1,2-diol (PDTM2)

Diastereomeric mixture of 1:1; redish sticky oil (86%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.02 (s, 1H, OH), 8.98 (s, 2H, OH), 8.95 (s, 1H, OH), 6.94 (d, 1H, *J* = 1.6 Hz, 2'-H), 6.91 (d, 1H, *J* = 2.0 Hz, 2'-H), 6.73 – 6.69 (m, 2H, 6'-H), 6.60 (d, 1H, *J* = 8.0 Hz, 5'-H), 6.59 (d, 1H, *J* = 8.4 Hz, 5'-H), 5.57 (s, 1H, 2-H), 5.56 (s, 1H, 2-H), 5.19 (t, 1H, *J* = 6.4 Hz, OH), 5.13 (t, 1H, *J* = 6.4 Hz, OH), 3.97 (m, 1H, 4-H), 3.73 – 3.63 (m, 2H), 3.53 – 3.39 (m, 5H), 3.26 – 3.21 (m, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 145.9, 145.6, 145.6, 145.5, 131.3, 128.6, 119.7, 119.2, 115.7, 115.5, 115.5, 115.4, 64.2, 63.5, 58.4, 57.2, 56.5, 54.9, 40.9, 40.7; LRMS (ESI+) *m/z* 299 (M+MeOH+Na)⁺; HRMS (ESI+) *m/z* C₁₀H₁₂NaO₃S₂ (M+Na)⁺ calcd 267.0126, obsd 267.0117.

4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)benzene-1,3-diol (PDTM3)

Diastereomeric mixture of 1:1.1; yellowish sticky oil (33%); ¹H NMR (400 MHz, CD₃OD) δ 7.45 (d, 1H, *J* = 8.8 Hz, 6'-H), 7.40 (d, 1H, *J* = 8.4 Hz, 6'-H), 6.26 (dd, 1H, *J* = 8.4, 2.4 Hz, 5'-H), 6.25 (dd, 1H, *J* = 8.4, 2.4 Hz, 5'-H), 6.22 (d, 2H, *J* = 2.4 Hz, 3'-H), 6.04 (s, 1H, 2-H), 5.95 (s, 1H, 2-H), 3.99 (m, 1H, 4-H), 3.83 (dd, 1H, *J* = 10.8, 9.6 Hz), 3.75 (m, 1H), 3.68 (dd, 1H, *J* = 11.2, 8.8 Hz), 3.59 – 3.54 (m, 2H), 3.44 – 3.36 (m, 2H), 3.31 – 3.26 (m, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆) δ 158.4, 158.2, 156.1, 155.6, 129.9, 129.5, 117.4, 114.4, 107.3, 107.0, 102.4, 102.4, 64.2, 63.6, 57.7, 56.9, 49.4, 48.2, 40.5, 40.3; LRMS (ESI+) *m/z* 267 (M+Na)⁺, 299 (M+MeOH+Na)⁺; HRMS (ESI-) *m/z* C₁₀H₁₁O₃S₂ (M-H)⁻ calcd 243.0155, obsd 243.0174.

4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)-2-methoxyphenol (PDTM4)

Diastereomeric mixture of 1:1; yellow solid (20%); ^1H NMR (500 MHz, $\text{CDCl}_3+\text{D}_2\text{O}$) δ 7.09 (d, 1H, $J = 2.0$ Hz, 2'-H), 7.08 (d, 1H, $J = 1.5$ Hz, 2'-H), 7.01 (dd, 1H, $J = 8.5, 2.0$ Hz, 6'-H), 6.99 (dd, 1H, $J = 8.0, 2.0$ Hz, 6'-H), 6.83 (d, 2H, $J = 8.0$ Hz, 5'-H), 5.65 (s, 1H, 2-H), 5.62 (s, 1H, 2-H), 4.17 (td, 1H, $J = 11.0, 6.0$ Hz, 4-H), 3.97 – 3.89 (m, 2H), 3.90 (s, 3H, OMe), 3.89 (s, 3H, OMe), 3.80 – 3.76 (m, 2H), 3.72 (dd, 1H, $J = 11.5, 6.0$ Hz), 3.53 (dd, 1H, $J = 12.5, 6.0$ Hz), 3.46 (dd, 1H, $J = 13.0, 2.5$ Hz), 3.37 (dd, 1H, $J = 12.5, 5.0$ Hz), 3.32 (dd, 1H, $J = 12.5, 5.0$ Hz); ^{13}C NMR (150 MHz, CDCl_3) δ 146.5, 146.5, 145.8, 145.7, 129.9, 127.5, 121.3, 121.1, 114.3, 114.1, 110.4, 110.2, 65.0, 63.6, 58.7, 57.4, 57.2, 56.1, 56.0, 55.9, 41.3, 40.7; LRMS (ESI+) m/z 279 (M+K- H_2O) $^+$, 297 (M+K) $^+$; HRMS (ESI+) m/z $\text{C}_{11}\text{H}_{14}\text{NaO}_3\text{S}_2$ (M+Na) $^+$ calcd 281.0282, obsd 281.0275.

2-Ethoxy-4-(4-(hydroxymethyl)-1,3-dithiolan-2-yl)phenol (PDTM5)

Diastereomeric mixture of 1:1.2; beige-colored solid (18%); ^1H NMR (500 MHz, CDCl_3) δ 7.07 (d, 1H, $J = 2.0$ Hz, 2'-H), 7.06 (d, 1H, $J = 2.0$ Hz, 2'-H), 6.99 (dd, 1H, $J = 8.0, 2.5$ Hz, 6'-H), 6.97 (dd, 1H, $J = 8.5, 2.0$ Hz, 6'-H), 6.83 (d, 2H, $J = 8.0$ Hz, 5'-H), 5.77 (brs, 2H, OH), 5.63 (s, 1H, 2-H), 5.60 (s, 1H, 2-H), 4.14 (m, 1H, 4-H), 4.12 (q, 4H, $J = 7.0$ Hz, CH_2CH_3), 3.95 (dd, 1H, $J = 10.0, 8.0$ Hz), 3.91 (m, 1H), 3.80 – 3.76 (m, 2H), 3.71 (dd, 1H, $J = 11.0, 6.0$ Hz), 3.52 (dd, 1H, $J = 11.5, 5.5$ Hz), 3.45 (dd, 1H, $J = 12.5, 3.0$ Hz), 3.36 (dd, 1H, $J = 13.0, 5.5$ Hz), 3.32 (dd, 1H, $J = 12.0, 5.5$ Hz), 2.06 (brs, 2H, OH), 1.44 (t, 6H, $J = 7.0$ Hz, CH_2CH_3); ^{13}C NMR (125 MHz, CDCl_3) δ 145.9, 145.8, 145.8, 145.8, 130.6, 129.1, 121.2, 120.9, 114.1, 114.0, 111.3, 111.1, 65.0, 64.5, 64.5, 63.6, 58.7, 57.4, 57.2, 55.9, 41.3, 40.7, 14.8, 14.8; LRMS (ESI+) m/z 311 (M+K) $^+$; HRMS (ESI+) m/z $\text{C}_{10}\text{H}_{17}\text{O}_3\text{S}_2$ (M+H) $^+$ calcd 273.0619, obsd 273.0611.

5-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)-2-methoxyphenol (PDTM6)

Obtained as a single diastereomer; white solid (24%); ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.04 (s, 1H, OH), 6.94 (d, 1H, $J = 2.0$ Hz, 2'-H), 6.83 (dd, 1H, $J = 8.0, 1.6$ Hz, 6'-H), 6.78 (d, 1H, $J = 8.4$ Hz, 5'-H), 5.60 (s, 1H, 2-H), 5.13 (brt, 1H, OH), 3.98 (m, 1H, 4-H), 3.71 (s, 3H, OMe), 3.51 (m, 1H, OCHH), 3.42 (m, 1H, OCHH), 3.41 (dd, 1H, $J = 12.0, 5.2$ Hz, 5-CHH), 3.26 (dd, 1H, $J = 12.0, 4.8$ Hz, 5-CHH); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$) δ 147.9 (C4'), 146.8 (C3'), 133.3 (C1'), 119.0 (C6'), 115.4 (C2'), 112.1 (C5'), 63.5 (C6), 58.4 (C4), 56.1 (OCH₃), 54.6 (C2), 40.7 (C5); LRMS (ESI+) m/z 297 (M+K) $^+$; HRMS (ESI+) m/z $\text{C}_{11}\text{H}_{15}\text{O}_3\text{S}_2$ (M+H) $^+$ calcd 259.0463, obsd 259.0454.

(2-(4-Methoxyphenyl)-1,3-dithiolan-4-yl)methanol (PDTM7)

Diastereomeric mixture of 1:1.2; beige-colored solid (85%); ^1H NMR (400 MHz, CDCl_3) δ 7.45 (d, 2H, $J = 8.8$ Hz, Ar), 7.44 (d, 2H, $J = 8.4$ Hz, Ar), 6.84 (d, 4H, $J = 8.8$ Hz, Ar), 5.66 (s, 1H, 2-H), 5.62 (s, 1H, 2-H), 4.16 (td, 1H, $J = 10.8, 6.0$ Hz, 4-H), 3.98 – 3.88 (m, 2H), 3.79 (s, 6H, OMe), 3.80 – 3.74 (m, 2H), 3.71 (dd, 1H, $J = 11.2, 6.0$ Hz), 3.52 (dd, 1H, $J = 12.0, 5.2$ Hz), 3.45 (dd, 1H, $J = 12.8, 2.0$ Hz), 3.36 (dd, 1H, $J = 12.8, 5.2$ Hz), 3.32 (dd, 1H, $J = 12.0, 4.4$ Hz), 2.13 (s, 2H, OH); ^{13}C NMR (125 MHz, CDCl_3) δ 159.6, 159.5, 131.3, 129.4, 129.4, 129.1, 114.0, 113.9, 65.0, 63.6, 58.7, 57.3, 56.9, 55.3, 55.3, 55.2, 41.3, 40.7; LRMS (ESI+) m/z 281 (M+K) $^+$; HRMS (ESI+) m/z $\text{C}_{11}\text{H}_{15}\text{O}_2\text{S}_2$ (M+H) $^+$ calcd 243.0513, obsd 243.0503.

(2-(3,4-Dimethoxyphenyl)-1,3-dithiolan-4-yl)methanol (PDTM8)

Diastereomeric mixture of 1:1; yellowish solid (64%); ^1H NMR (400 MHz, CDCl_3) δ 7.09 – 7.02 (m, 4H, Ar), 6.77 (d, 2H, $J = 8.0$ Hz, 5'-H), 5.65 (s, 1H, 2-H), 5.62 (s, 1H, 2-H),

4.17 (td, 1H, $J = 10.8, 6.0$ Hz, 4-H), 3.98 – 3.90 (m, 2H), 3.89 (s, 3H, OMe), 3.88 (s, 3H, OMe), 3.86 (s, 6H, OMe), 3.81 – 3.76 (m, 2H), 3.72 (dd, 1H, $J = 11.2, 6.4$ Hz), 3.52 (dd, 1H, $J = 12.0, 5.2$ Hz), 3.46 (dd, 1H, $J = 12.4, 2.4$ Hz), 3.37 (dd, 1H, $J = 12.4, 4.8$ Hz), 3.33 (dd, 1H, $J = 12.0, 4.8$ Hz), 2.02 (s, 2H, OH); ^{13}C NMR (125 MHz, CDCl_3) δ 149.1, 149.0, 149.0, 148.9, 131.6, 130.0, 120.5, 120.2, 111.1, 110.9, 110.8, 110.7, 64.9, 63.6, 58.6, 57.2, 57.2, 55.9, 55.9, 55.9, 55.7, 41.3, 40.7; LRMS (ESI+) m/z 295 (M+Na) $^+$, 311 (M+K) $^+$; HRMS (ESI+) m/z $\text{C}_{12}\text{H}_{17}\text{O}_3\text{S}_2$ (M+H) $^+$ calcd 273.0619, obsd 273.0607.

(2-(2,4-Dimethoxyphenyl)-1,3-dithiolan-4-yl)methanol (PDTM9)

Diastereomeric mixture of 1:1.5; yellow solid (15%); ^1H NMR (500 MHz, CDCl_3) δ 7.67 (d, 1H, $J = 8.0$ Hz, 6'-H), 7.64 (d, 1H, $J = 9.0$ Hz, 6'-H), 6.48 (dd, 1H, $J = 8.0, 2.5$ Hz, 5'-H), 6.48 (dd, 1H, $J = 8.5, 2.5$ Hz, 5'-H), 6.42 (d, 1H, $J = 2.5$ Hz, 3'-H), 6.41 (d, 1H, $J = 2.5$ Hz, 3'-H), 6.07 (s, 1H, 2-H), 5.98 (s, 1H, 2-H), 4.10 (m, 1H), 3.93 – 3.87 (m, 2H), 3.83 (s, 3H, OMe), 3.83 (s, 3H, OMe), 3.79 (s, 6H, OMe), 3.80 – 3.73 (m, 2H), 3.69 (dd, 1H, $J = 11.0, 6.0$ Hz), 3.41 – 3.33 (m, 3H), 3.30 (dd, 1H, $J = 12.0, 4.5$ Hz), 2.15 (s, 2H, OH); ^{13}C NMR (100 MHz, CDCl_3) δ 160.9, 160.7, 158.1, 157.6, 129.5, 129.1, 121.1, 118.9, 104.9, 104.6, 98.7, 98.4, 65.1, 64.1, 58.0, 57.2, 55.9, 55.9, 55.7, 55.7, 49.8, 48.6, 41.0, 39.9; LRMS (ESI+) m/z 271 (M+H-H $_2$) $^+$; HRMS (ESI+) m/z $\text{C}_{12}\text{H}_{17}\text{O}_3\text{S}_2$ (M+H) $^+$ calcd 273.0619, obsd 273.0609.

2-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)phenol (PDTM10)

Diastereomeric mixture of 1:1; red solid (79%); ^1H NMR (400 MHz, CD_3OD) δ 7.67 (d, 1H, $J = 8.0$ Hz, 6'-H), 7.66 (d, 1H, $J = 7.6$ Hz, 6'-H), 7.07 – 7.03 (m, 2H, 4'-H), 6.81 – 6.77 (m, 2H, 5'-H), 6.74 (d, 1H, $J = 8.0$ Hz, 3'-H), 6.74 (d, 1H, $J = 8.4$ Hz, 3'-H), 6.09 (s, 2H, 2-H), 4.01 (m, 1H, 4-H), 3.87 – 3.77 (m, 4H), 3.62 – 3.59 (m, 2H), 3.42 (dd, 1H, $J = 12.0, 3.2$ Hz), 3.33 – 3.28 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 155.2, 154.8, 130.3, 130.1, 130.1, 129.6, 122.2, 120.6, 120.5, 120.3, 117.3, 117.2, 65.1, 63.6, 58.4, 56.8, 54.8, 52.8, 41.3, 40.6; LRMS (ESI+) m/z 227 (M+H-H $_2$) $^+$; HRMS (ESI+) m/z $\text{C}_{10}\text{H}_{12}\text{NaO}_2\text{S}_2$ (M+Na) $^+$ calcd 251.0176, obsd 251.0163.

(2-(3,4,5-Trimethoxyphenyl)-1,3-dithiolan-4-yl)methanol (PDTM11)

Diastereomeric mixture of 1:1.3; yellowish sticky oil (62%); ^1H NMR (500 MHz, CDCl_3) δ 6.75 (s, 2H, 2'-H, 6'-H), 6.74 (s, 2H, 2'-H, 6'-H), 5.58 (s, 1H, 2-H), 5.56 (s, 1H, 2-H), 4.11 (m, 1H, 4-H), 3.94 – 3.84 (m, 2H), 3.83 (s, 6H, OMe), 3.82 (s, 6H, OMe), 3.79 (s, 6H, OMe), 3.76 – 3.72 (m, 2H), 3.68 (dd, 1H, $J = 11.0, 6.0$ Hz), 3.48 (dd, 1H, $J = 12.0, 5.0$ Hz), 3.44 (dd, 1H, $J = 13.0, 3.5$ Hz), 3.32 (dd, 1H, $J = 12.0, 5.5$ Hz), 3.31 (dd, 1H, $J = 12.0, 5.0$ Hz), 2.53 (s, 2H, OH); ^{13}C NMR (125 MHz, CDCl_3) δ 153.1, 153.1, 137.9, 137.7, 135.0, 133.5105.1, 104.9, 64.8, 63.6, 60.8, 60.8, 58.5, 57.4, 57.3, 56.1, 56.1, 56.0, 41.2, 40.7; LRMS (ESI+) m/z 325 (M+Na) $^+$, 341 (M+K) $^+$, 357 (M+MeOH+Na) $^+$; HRMS (ESI+) m/z $\text{C}_{13}\text{H}_{19}\text{O}_4\text{S}_2$ (M+H) $^+$ calcd 303.0725, obsd 303.0712.

4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)-2,6-dimethoxyphenol (PDTM12)

Obtained as a single diastereomer; beige-colored solid (34%); ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.42 (s, 1H, OH), 6.75 (s, 2H, 2'-H, 6'-H), 5.65 (s, 1H, 2-H), 5.13 (t, 1H, $J = 5.6$ Hz, OH), 4.02 (m, 1H, 4-H), 3.71 (s, 6H, OMe), 3.54 – 3.39 (m, 3H, OCH_2 , 5- CHH), 3.27 (dd, 1H, $J = 12.0, 4.8$ Hz, 5- CHH); ^{13}C NMR (125 MHz, $\text{DMSO}-d_6$) δ 148.0 (C3', C5'), 135.7 (C4'), 130.7 (C1'), 105.6 (C2', C6'), 63.5 (C6), 58.3 (C4), 56.2 (2* OCH_3), 55.3 (C2), 40.6 (C5); LRMS (ESI+) m/z 287 (M+H-H $_2$) $^+$, 309 (M+K-H $_2\text{O}$) $^+$; HRMS (ESI+) m/z $\text{C}_{12}\text{H}_{17}\text{O}_4\text{S}_2$ (M+H) $^+$ calcd 289.0568, obsd 289.0556.

2-Bromo-4-(4-(hydroxymethyl)-1,3-dithiolan-2-yl)phenol (PDTM13)

Obtained as a single diastereomer; yellow solid (39%); ^1H NMR (400 MHz, DMSO- d_6) δ 10.40 (brs, 1H, OH), 7.59 (d, 1H, $J = 2.4$ Hz, 2'-H), 7.31 (dd, 1H, $J = 8.4, 2.4$ Hz, 6'-H), 6.87 (d, 1H, $J = 8.4$ Hz, 5'-H), 5.64 (s, 1H, 2-H), 5.22 (brt, 1H, $J = 5.6$ Hz, OH), 3.75 (m, 1H, 4-H), 3.66 (m, 1H, OCHH), 3.44 (m, 1H, OCHH), 3.41 (dd, 1H, $J = 12.0, 3.6$ Hz, 5-CHH), 3.26 (dd, 1H, $J = 12.0, 5.2$ Hz, 5-CHH); ^{13}C NMR (125 MHz, DMSO- d_6) δ 154.4 (C4'), 132.7 (C2'), 130.8 (C1'), 129.0 (C6'), 116.6 (C5'), 109.3 (C3'), 64.0 (C6), 57.8 (C4), 55.0 (C2), 41.1 (C5); LRMS (ESI+) m/z 344 (M+K) $^+$, 346 (M+2+K) $^+$; HRMS (ESI-) m/z C₁₀H₁₀BrO₂S₂ (M-H) $^-$ calcd 304.9306, obsd 304.9311.

2,6-Dibromo-4-(4-(hydroxymethyl)-1,3-dithiolan-2-yl)phenol (PDTM14)

Diastereomeric mixture of 1:1.1; yellow solid (36%); ^1H NMR (400 MHz, DMSO- d_6) δ 10.09 (s, 1H, OH), 10.02 (s, 1H, OH), 7.65 (s, 2H, 2'-H, 6'-H), 7.62 (s, 2H, 2'-H, 6'-H), 5.66 (s, 1H, 2-H), 5.65 (s, 1H, 2-H), 5.20 (brs, 2H, OH), 4.03 (m, 1H, 4-H), 3.79 (m, 1H, 4-H), 3.66 (dd, 1H, $J = 10.4, 8.4$ Hz), 3.52 – 3.36 (m, 5H), 3.30 (dd, 1H, $J = 12.0, 4.4$ Hz), 3.27 (dd, 1H, $J = 12.0, 5.6$ Hz); ^{13}C NMR (125 MHz, DMSO- d_6) δ 151.0, 150.7, 136.1, 133.3, 132.1, 131.7, 111.8, 111.7, 64.0, 63.2, 58.4, 58.0, 57.5, 56.8, 41.1, 40.6; HRMS (ESI-) m/z C₁₀H₉Br₂O₂S₂ (M-H) $^-$ calcd 382.8411, obsd 382.8418.

4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)-2-methylphenol (PDTM15)

Obtained as a single diastereomer; yellow solid (39%); ^1H NMR (400 MHz, DMSO- d_6) δ 9.43 (brs, 1H, OH), 7.18 (d, 1H, $J = 2.0$ Hz, 2'-H), 7.12 (dd, 1H, $J = 8.4, 2.0$ Hz, 6'-H), 6.67 (d, 1H, $J = 8.4$ Hz, 5'-H), 5.59 (s, 1H, 2-H), 5.19 (brt, 1H, $J = 5.6$ Hz, OH), 3.74 – 3.63 (m, 2H, 4-H, OCHH), 3.43 – 3.33 (m, 2H, OCHH, 5-CHH), 3.23 (dd, 1H, $J = 12.4, 5.6$ Hz, 5-CHH), 2.06 (s, 3H, Me); ^{13}C NMR (125 MHz, DMSO- d_6) δ 155.9 (C4'), 130.8 (C1'), 127.8 (C2'), 127.0 (C6'), 124.3 (C3'), 114.8 (C5'), 64.1 (C6'), 57.3 (C4'), 56.3 (C2'), 41.0 (C5'), 16.4 (CH₃); LRMS (ESI+) m/z 241 (M+H-H₂) $^+$, 281 (M+K) $^+$; HRMS (ESI+) m/z C₁₁H₁₅O₂S₂ (M+H) $^+$ calcd 243.0513, obsd 243.0507.

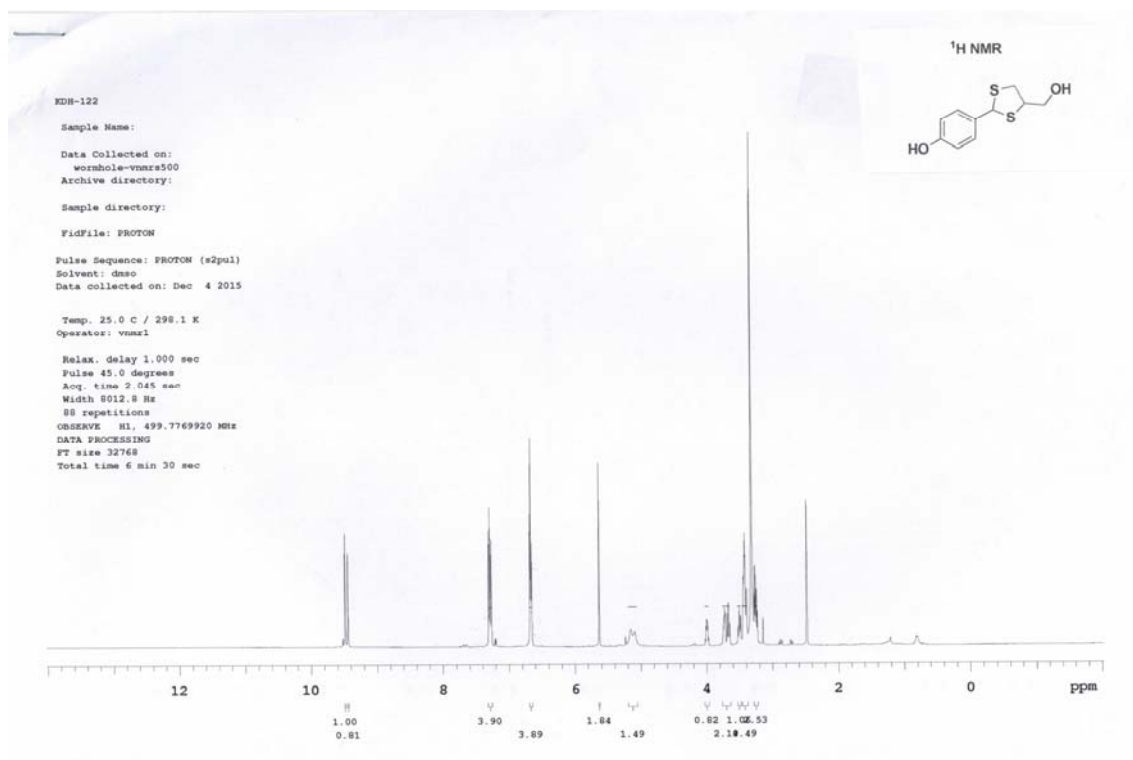
4-(4-(Hydroxymethyl)-1,3-dithiolan-2-yl)-2,6-dimethylphenol (PDTM16)

Diastereomeric mixture of 1:1.5; yellow solid (42%); ^1H NMR (400 MHz, DMSO- d_6) δ 8.34 (s, 1H, OH), 8.29 (s, 1H, OH), 7.03 (s, 2H, 2'-H, 6'-H), 7.01 (s, 2H, 2'-H, 6'-H), 5.56 (s, 2H, 2-H), 5.19 (t, 1H, $J = 5.6$ Hz, OH), 5.13 (t, 1H, $J = 5.6$ Hz, OH), 3.99 (m, 1H, 4-H), 3.74 – 3.62 (m, 3H), 3.53 – 3.89 (m, 4H), 3.25 (dd, 1H, $J = 11.6, 5.2$ Hz), 3.23 (dd, 1H, $J = 12.0, 5.6$ Hz), 2.10 (s, 12H, Me); ^{13}C NMR (125 MHz, DMSO- d_6) δ 153.6, 153.3, 130.8, 128.4, 128.1, 128.0, 124.5, 124.4, 64.1, 63.5, 58.4, 57.3, 56.4, 54.7, 41.0, 40.8, 17.0, 17.0; LRMS (ESI+) m/z 255 (M+H-H₂) $^+$, 295 (M+K) $^+$; HRMS (ESI+) m/z C₁₂H₁₇O₂S₂ (M+H) $^+$ calcd 257.0670, obsd 257.0663.

2,6-Di-*tert*-butyl-4-(4-(hydroxymethyl)-1,3-dithiolan-2-yl)phenol (PDTM17)

Diastereomeric mixture of 1:1.4; yellowish solid (59%); ^1H NMR (400 MHz, CDCl₃) δ 7.33 (s, 4H, 2'-H, 6'-H), 5.67 (s, 1H, 2-H), 5.64 (s, 1H, 2-H), 5.26 (brs, 2H, OH), 4.17 (m, 1H, 4-H), 3.98 (dd, 1H, $J = 10.4, 8.0$ Hz), 3.91 (m, 1H, 4-H), 3.81 – 3.76 (m, 2H), 3.72 (dd, 1H, $J = 10.8, 6.0$ Hz), 3.54 (dd, 1H, $J = 12.0, 5.6$ Hz), 3.46 (dd, 1H, $J = 12.4, 2.4$ Hz), 3.37 (dd, 1H, $J = 12.4, 5.2$ Hz), 3.32 (dd, 1H, $J = 12.0, 5.2$ Hz), 2.14 (brs, 2H, OH), 1.41 (s, 36H, *t*-Bu); ^{13}C NMR (125 MHz, CDCl₃) δ 153.9, 153.8, 135.9, 135.9, 129.0, 127.7, 125.0, 124.8, 65.0,

63.6, 58.6, 57.9, 57.1, 56.5, 41.3, 40.7, 34.4, 34.4, 30.2, 30.2; LRMS (ESI+) m/z 341 (M+H)⁺, 363 (M+Na)⁺, 379 (M+K)⁺, 395 (M+MeOH+Na)⁺; HRMS (ESI+) m/z C₁₈H₂₉O₂S₂ (M+H)⁺ calcd 341.1609, obsd 341.1600.



KDH-122

Sample Name:

Data Collected on:
wormhole-vnmr500

Archive directory:

Sample directory:

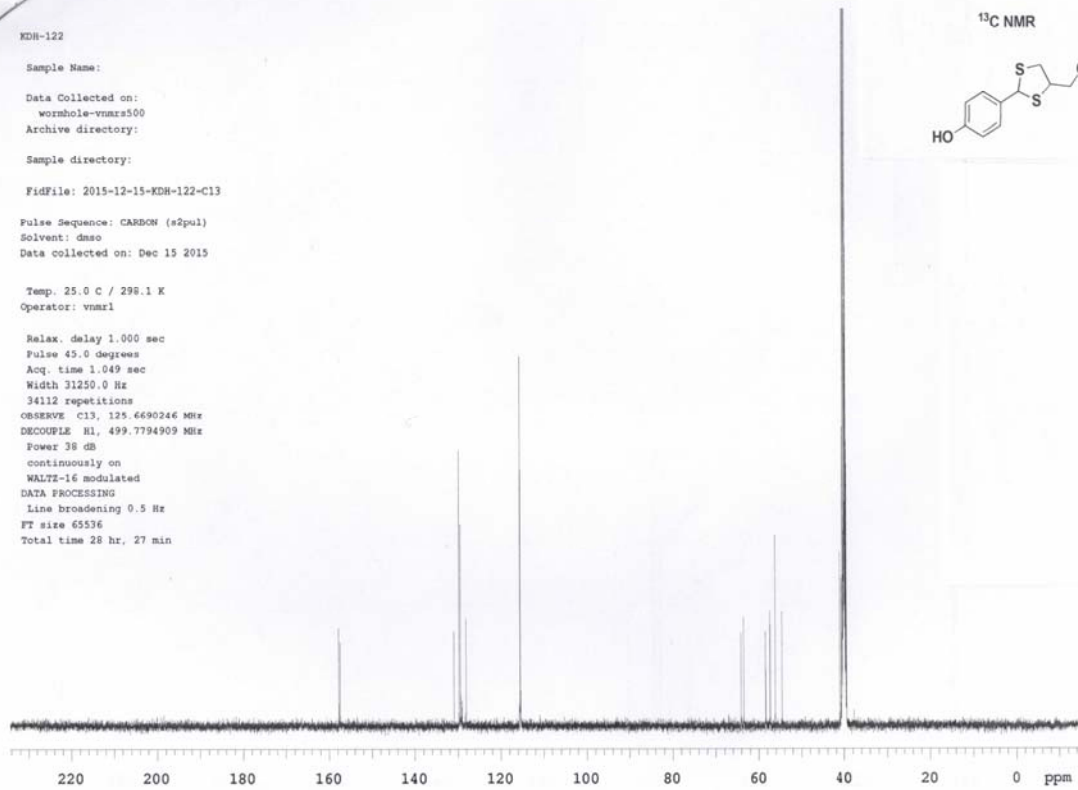
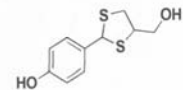
FidFile: 2015-12-15-KDH-122-C13

Pulse Sequence: CARDCN (s2pul)
Solvent: dmsc
Data collected on: Dec 15 2015

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.049 sec
Width 31250.0 Hz
34112 repetitions
OBSERVE C13, 125.6690246 MHz
DECOUPLE H1, 499.7794909 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 28 hr, 27 min

¹³C NMR



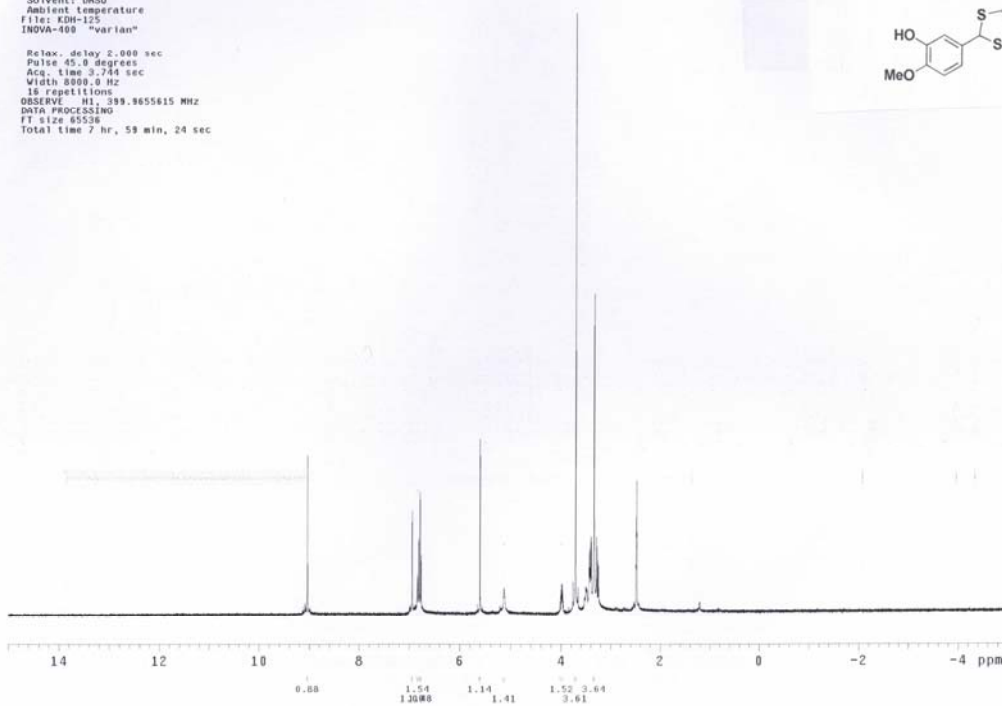
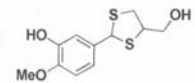
220 200 180 160 140 120 100 80 60 40 20 0 ppm

KDH-125

Pulse Sequence: s2pul
Solvent: DMSO
Ambient Temperature
File: KDH-125
INDVA-400 "varian"

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 3.748 sec
Width 8000.0 Hz
18 repetitions
OBSERVE H1, 399.9655615 MHz
DATA PROCESSING
FT size 65536
Total time 7 hr, 59 min, 24 sec

¹H NMR



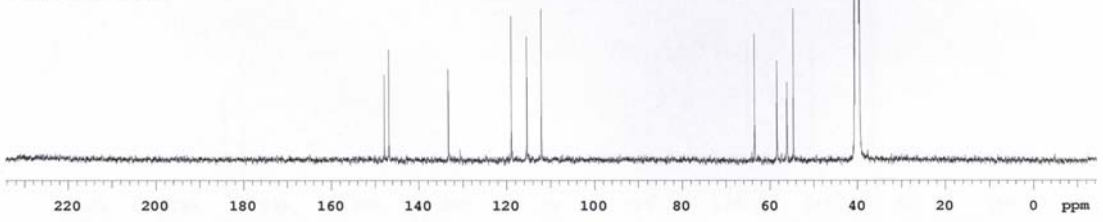
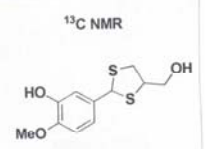
14 12 10 8 6 4 2 0 -2 -4 ppm

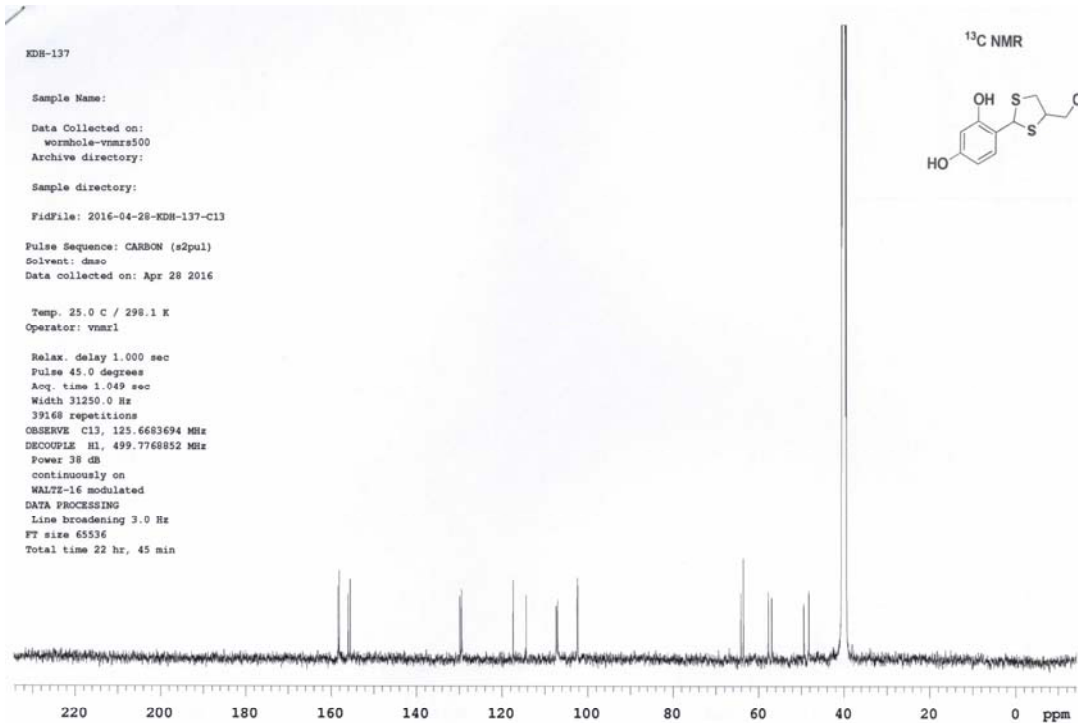
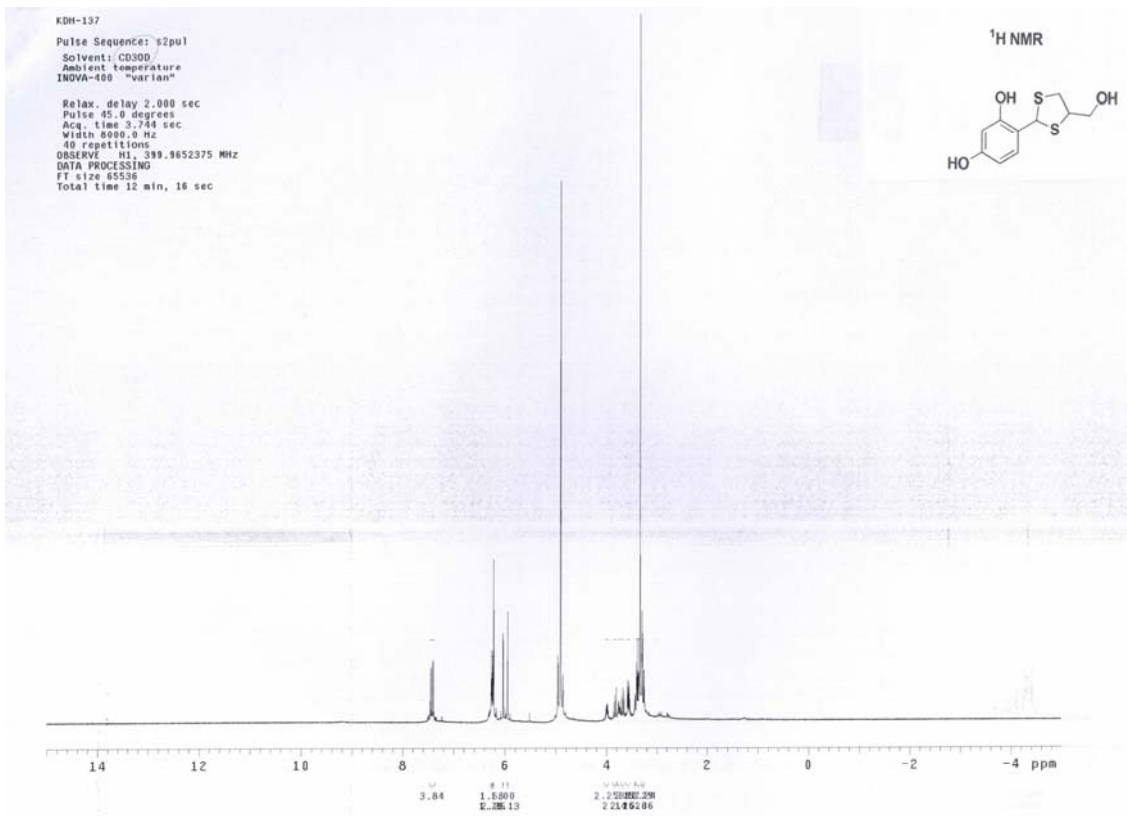
0.00 1.54 1.14 1.41 1.52 3.64

KDH-125
Sample Name:
Data Collected on:
wormhole-vnmr500
Archive directory:
Sample directory:
FidFile: 2016-04-26-KDH-125-C13
Pulse Sequence: CARBON (s2pul)
solvent: dmsd
Data collected on: Apr 26 2016

Temp. 25.0 C / 298.1 K
Operator: vnmr1

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.049 sec
Width 31250.0 Hz
32192 repetitions
OBSERVE C13, 125.6683694 MHz
DECOUPLE H1, 499.7768952 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 3.0 Hz
FT size 65536
Total time 22 hr, 45 min





KDH-122

Sample Name:

Data Collected on:
wormhole-vmrz500
Archive directory:

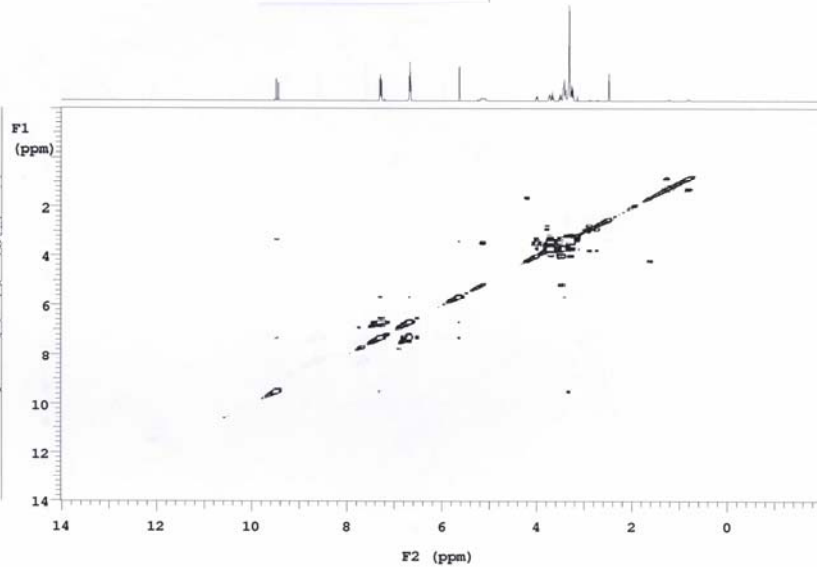
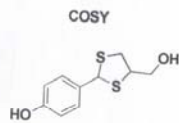
Sample directory:

FidFile: 2015-12-16-KDH-122-gCOSY

Pulse Sequence: gCOSY
Solvent: dmsc
Data collected on: Dec 16 2015

Temp. 25.0 C / 298.1 K
Operator: vmr1

Relax. delay 1.000 sec
Acq. time 0.150 sec
Width 8012.8 Hz
2D Width 8012.8 Hz
128 repetitions
128 increments
OBSERVE H1, 499.7769925 MHz
DATA PROCESSING
Sq. sine bell 0.075 sec
F1 DATA PROCESSING
Sq. sine bell 0.016 sec
FT size 4096 x 4096
Total time 5 hr, 24 min



KDH-122

Sample Name:

Data Collected on:
wormhole-vmrz500
Archive directory:

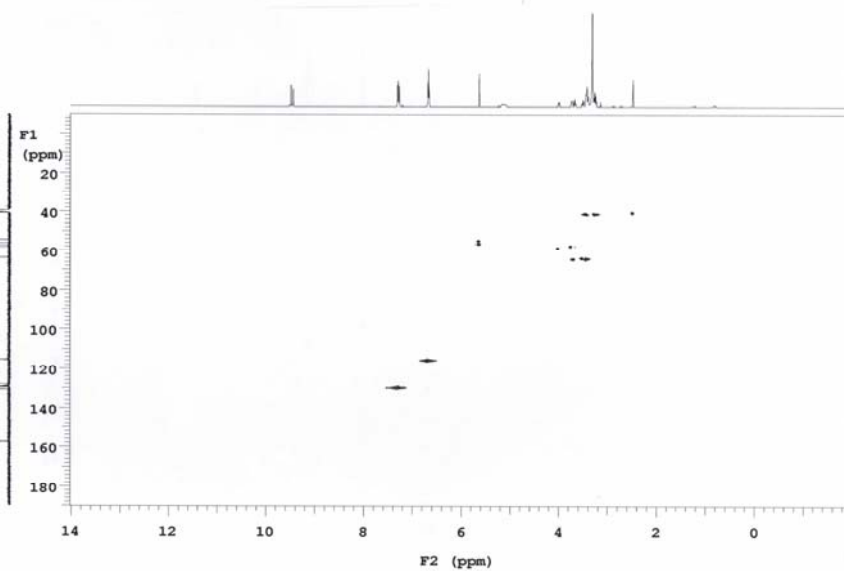
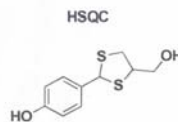
Sample directory:

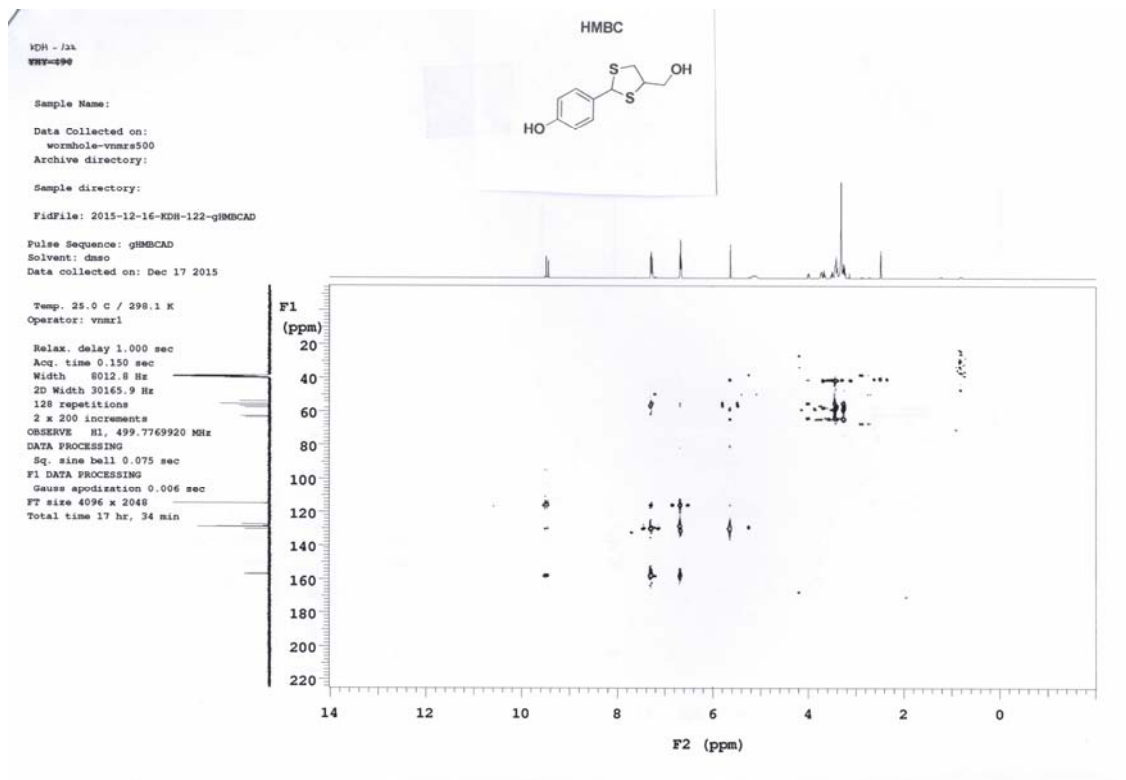
FidFile: 2015-12-16-KDH-122-gHSQCAD

Pulse Sequence: gHSQCAD
Solvent: dmsc
Data collected on: Dec 16 2015

Temp. 25.0 C / 298.1 K
Operator: vmr1

Relax. delay 1.000 sec
Acq. time 0.150 sec
Width 8012.8 Hz
2D Width 25133.5 Hz
128 repetitions
2 x 128 increments
OBSERVE H1, 499.7769920 MHz
DECOUPLE C13, 125.6803348 MHz
Power 46 dB
on during acquisition
off during delay
M40_id modulated
DATA PROCESSING
Gauss apodization 0.069 sec
F1 DATA PROCESSING
Line broadening 0.3 Hz
Gauss apodization 0.005 sec
FT size 4096 x 2048
Total time 10 hr, 54 min





Images of docking simulation of PDTMs

